Transition Metal-Catalyzed C–H Functionalization for Sustainable Syntheses of Alkenes and Heterocycles

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子曰：三人行，必有我师焉。择其善者而从之，其不善者而改之。

Confucius said: In a group of three people, there is always something I can learn from. Choose to follow the strengths of others, use the shortcomings to reflect upon ourselves.

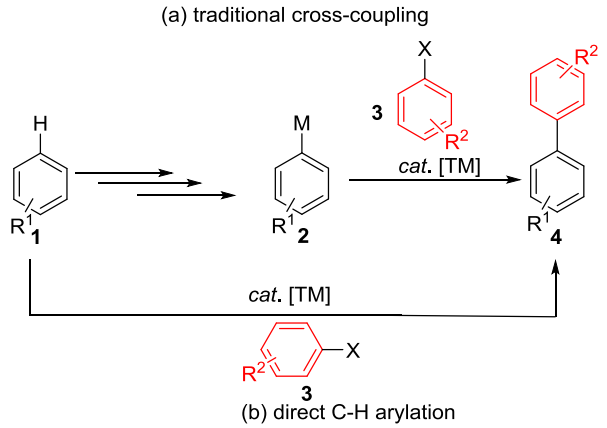
Konfuzius sprach: Wenn ich mit drei Menschen zusammen wandere, kann immer einer von ihnen mein Lehrer sein: Denn was ich Gutes an ihm erkenne, waehle ich fuer mich aus, und was ich an ihm nicht gut finde, das aendere ich.

Contents

1. Introduction

1.1 Transition Metal-Catalyzed Direct C–H Functionalizations

In the past decade, transition metal-catalyzed direct C−H functionalizations[1] emerged as a new stage for innovations owing to their widespread applications to the rapid assembly of diversified complex molecular structures, particularly in the fields of material science,[2] medicinal chemistry[3] and natural product synthesis.[4] The direct catalytic method bypasses the need of preactivated reaction partners and has advantages over classical cross-coupling reactions based on organometallics arylating reagents and therefore leads to more environmentally friendly and atom-economical[1p–r] processes (Scheme 1).



Scheme 1 Traditional cross-coupling (a) *vs.* direct C–H arylation (b).

A variety of transition metals such as palladium-,[1c,1j,1l,1m] ruthenium-,[1a,1d] rhodium-,[1g] cobalt-[1b,1k]

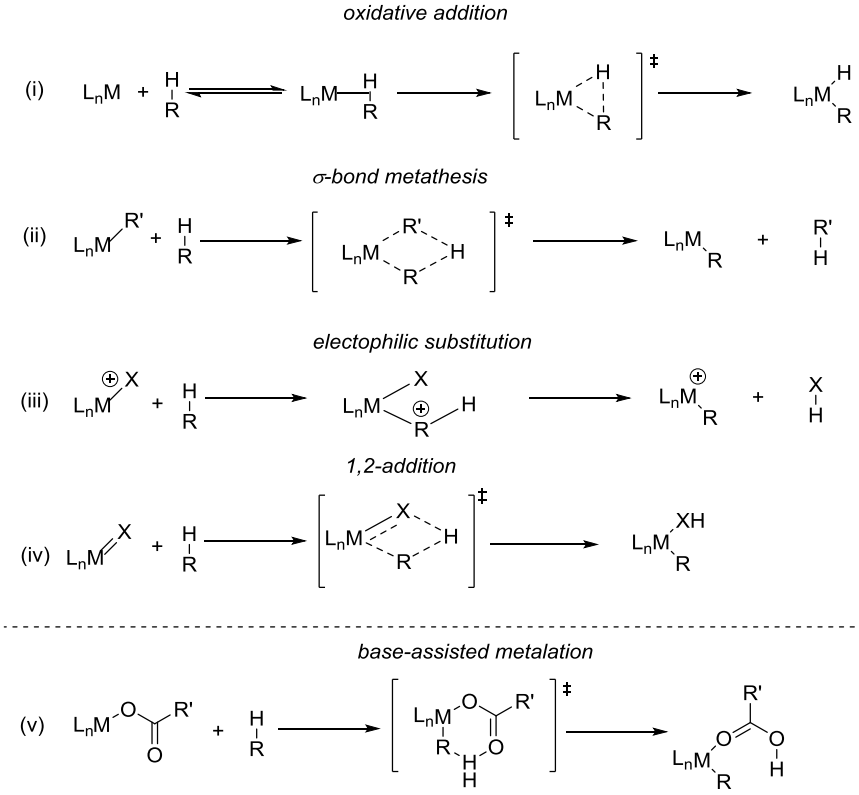
[1] For recent reviews on C–H bond functionalizations, see (a) S. De Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, *Adv. Synth. Catal*. **2014**, *356*, 1461–1479; (b) K. Gao, N. Yoshikai, *Acc. Chem. Res*. **2014**, *47*, 1208−1219; (c) X.-F. Wu, H. Neumann, M. Beller, *Chem. Rev*. **2013**, *113*, 1−35; (d) B. Li, P. H. Dixneuf, *Chem. Soc. Rev.*, **2013**, *42*, 5744–5767; (e) T. A. Ramirez, B. G. Zhao, Y. Shi, *Chem.Soc. Rev*. **2012**, *41*, 931–942; (f) Z.-Z. Shi, C. Zhang, C.-H. Tang, N. Jiao, *Chem. Soc. Rev*. **2012**, *41*, 3381–3430; (g) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814–825; (h) J. L. Bras, J. Muzart, *Chem. Rev*. **2011**, *111*, 1170–1214; (i) L. Ackermann, *Chem. Commun.* **2010**,*46*, 4866-4877; (j) T.W. Lyons, M. S. Sanford, *Chem. Rev*. **2010**, *110*, 1147–1169; (k) A. A. Kulkarni, O. Daugulis, *Synthesis* **2009**, 4087–4109; (l) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel, J.-Q. Yu, *Chem. Soc. Rev*. **2009**, *38*, 3242–3272; (m) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu. *Angew. Chem. Int. Ed*. **2009**, *48*, 5094–5115; (n) L. Ackermann, R. Vicente, A. Kapdi, *Angew. Chem. Int. Ed*. **2009**, *48*, 9792–9826. For the *principles* of atom- and step-economy, see: (o) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695–705. (p) B. M. Trost, *Science* **1991**, *254*, 1471–1477; (q) P. A. Wender, V. A. Verma, T. J. Paxton, T, H. Pillow, *Acc. Chem. Res*. **2008**, *41*, 40–49.

[2] Y. Segawa, T. Maekawa, K. Itami, *Angew. Chem. Int. Ed*. **2014**, *53*, 2–18.

[3] And following the recent reviews on C–H functionalizations in medicinal chemistry, see (a). P. M. Wright, I. B. Seiple, A. G. Myers, *Angew. Chem. Int. Ed*. **2014**, *53*, 8840–8869; (b) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed*. **2012**, *51*, 8960–9009; (c) J. Magano, J. R. Dunetz, *Chem. Rev*. **2011**, *111*, 2177–2250.

[4] For recent reviews on C–H bond functionalizations in the synthesis of natural products, see: (a) D. Wang, S. Gao, *Org. Chem. Front.* **2014**, *1*, 556–566; (b) Y.-K. Chen, S. W. Youn, *Chem. Eur. J.* **2012**, *18*, 9452–9474; (c) W. R. Gutekunst, P. S. Baran, *Chem. Soc. Rev*. **2011**, *40*, 1976–1991.

and nickel-catalyzed[1k] direct site-, chemo- and enantioselective C–H activations have been explored. Based on this research, detailed mechanistic studies were also carried out. Traditionally, four different modes of action were primarily considered, that is (**i**) oxidative addition with electron-rich late transition metals, (**ii**) σ-bond metathesis with early transition metals, (**iii**) electrophilic activation with electron deficientlate transition metals, and (**iv**) 1,2-addition of early to middle transition metals with imido, alkylidene, and oxo complexes (Scheme 2). These results of computational studies of these mechanisms on different theoretical levels were summarized by Ackermann[5a] and Eisenstein.[5b]



Scheme 2 Different Mechanisms for C–H Bond Metalation.

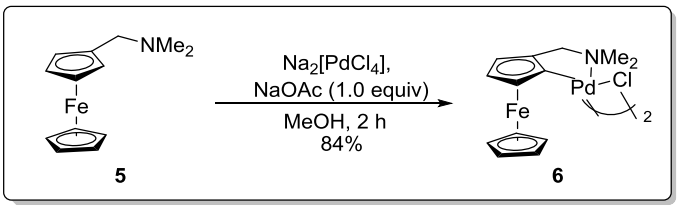
However, more recent computational mechanistic studies carried out by Ess and Periana[6] showed that quantitative dissection of directional charge-transfer stabilization (orbital occupied to unoccupied stabilization) between the metal-ligand complex and the C(sp^3)–H bond energies that revealed a continuum of electrophilic, ambiphilic, and nucleophilic interactions. Detailed experimental analysis provided strong evidence for novel C–H metalation mechanisms relying on the assistance of a bifunctional ligand bearing an additional Lewis-basic heteroatom, such as

[5] (a) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315–1345; (b) D. Balcells, E. Clot, O. Eisenstein, *Chem. Rev.* **2010**, *110*, 749–823.

[6] D. H. Ess, W. A. Goddard, R. A. Periana, *Organometallics* **2010**, *29*, 6459–6472.

(heteroatom-substituted) secondary phosphine oxides[7] or most prominently carboxylates (Scheme 2).5[a]

As early as 1972, Shaw[8] and coworkers found that the additive NaOAc accelerated cyclometalation reactions with iridium, platinum, or palladium complexes. A representative example was the cyclometalation of *N*,*N*-dimethylaminomethyl ferrocene (5) with $Na_2[PdCl_4]$ in the presence of stoichiometric amounts of this base. Control experiments showed that the NaOAc was essential for the transformation. Subsequently, Davies[9] and coworkers carried out similar cyclometalation reactions of *N*,*N*-dimethylbenzylamines with $[Cp^*IrCl_2]_2$ at ambient temperature. Detailed mechanistic studies through computational studies provided evidence for acetate-promoted process.



Scheme 3 NaOAc Assisted Cyclopalladation of Amine **5.**

Based on these previous studies, Fagnou[10] reported palladium-catalyzed direct arylations of perfluorobenzenes in the presence of potassium carbonate. However, electron-deficient arenes were favored in this reaction indicating a pathway different from the electrophilic aromatic substitution. Furthermore, computational studies showed that the reaction proceeds *via* a concerted arene metalation and that the C–H bond cleaving process depends directly on the acidity of the C–H bond being cleaved. They proposed the transformation *via* a 6-membered transition state (Scheme 4). Fagnou used the term concerted metalation deprotonation (CMD),[11] which also emphasized the dual role of the metal and the (intramolecular) base. Subsequently, Ess and coworkers carried out a transition state energy decomposition study of C–H activation of benzene and methane by $[Ir(acac')_2(X)]$ (X = OAc and OH).[12] Hydroxide can only act as an intramolecular base with a 4-membered transition state (Scheme 4), but acetate can through a 4-membered or

[7] (a) L. Ackermann, *Isr. J. Chem*. **2010**, *50*, 652–663; (b) L. Ackermann, *Synlett* **2007**, 507–526; (c) L. Ackermann, *Synthesis* **2006**, 1557–1571; (d) N. V. Dubrovina, A. Börner, *Angew. Chem. Int. Ed.* **2004**, *43*, 5883–5886.

[8] (a) J. C. Gaunt, B. L. Shaw, *J. Organomet. Chem*. **1975**, *102*, 511–516; (b) J. M. Duff, B. E. Mann, B. L. Shaw, B. Turtle, *J. Chem. Soc. Dalton Trans*. **1974**, 139–145; (c) J. M. Duff, B. L. Shaw, *J. Chem. Soc*., *Dalton Trans*. **1972**, 2219–2225.

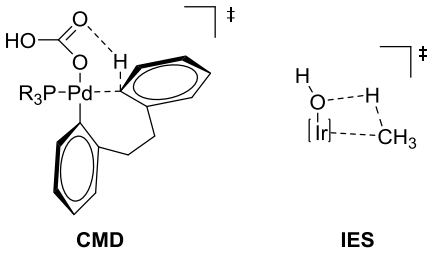
[9] D. L. Davies, O. Al-Duaij, J. Fawcett, M. Giardiello, S. T. Hilton, D. R. Russell, *Dalton. Trans.* **2003**, 4132–4138.

[10] M. Lafrance, C. N. Rowley, T. K. Woo, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 8754–8756.

[11] D. Lapointe, K. Fagnou, *Chem. Lett*. **2010**, *39*, 1118–1126.

[12] D. H. Ess, S. M. Bischof, J. Oxgaard, R. A. Periana, W. A. Goddard, *Organometallics* **2008**, *27*, 6440–6445.

6-membered transition state, whereas the later is favored due to its lower energy state. The term internal electrophilic substitution (IES) was suggested for the C–H metalation of benzene with an Ir–OH bond. However, Davies[13] suggested that this did not show the importance of the heteroatom lone pair in the activation of the C–H bond, and this concerted dual activation made these processes different from a conventional electrophilic process and their selectivity different to conventional electrophilic aromatic substitution. Hence, to differentiate these intramolecular metalations mechanistically, this process was considered as an ambiphilic metal ligand activation (AMLA).[14]



Scheme 4 Different types of transition states.

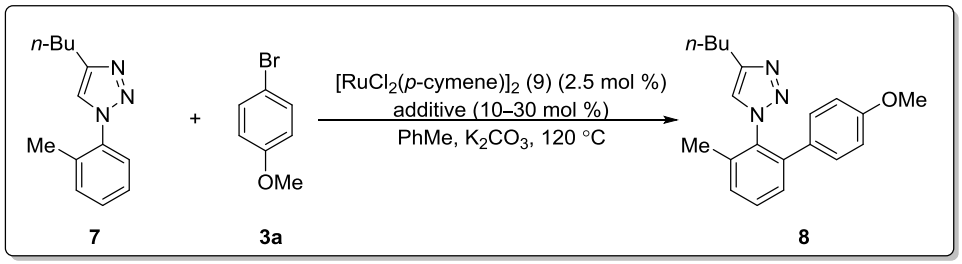
1.2 Ruthenium-Catalyzed Direct C–H Functionalizations

In recent years, transition metal-catalyzed C–H bond functionalizations as an efficient tool to construct C–C and C–X (X = halide, N, O, S) bonds with great progress have been achieved. However, these transition metal catalysts were typically based on platinum, rhodium, iridium and palladium. Inexpensive ruthenium complexes (prices of platinum, rhodium, iridium, palladium, and ruthenium = $1238, $1180, $570, $787 and $ 56 US per troy ounce, respectively) have not been explored widely for this C–H bond transformation. Notably, pioneering studies[15] highlighted the potential of efficient ruthenium-catalyzed C–H bond activation with the development of effective catalysts for site-selective addition reactions of C–H bonds onto C–C multiple bonds.

Encouraged by these previous studies, Ackermann's group focused attention on the application of ruthenium complexes for chelation-assisted C–H bond functionalizations. A variety of cocatalytic additives[16] such as NHCs, phosphines and SPOs were tested in the ruthenium-catalyzed arylation reaction with triazole substrates **7**.[17] Finally, they found hindered carboxylates emerged to be the

[13] Y. Boutadla, D. L. Davies, S. A. Macgregor, A. I. Poblador-Bahamonde, *Dalton Trans.* **2009**, 5820–5831.
[14] Y. Boutadla, D. L. Davies, S. A. Macgregor, A. I. Poblador-Bahamonde, *Dalton Trans.* **2009**, 5887–5893.
[15] (a) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, *366*, 529–531; (b) L. N. Lewis, J. F. Smith, *J. Am. Chem. Soc.* **1986**, *108*, 2728–2735.
[16] (a) L. Ackermann, M. Mulzer, *Org. Lett.* **2008**, *10*, 5043–5045; (b) L. Ackermann, R. Born, R. Vicente, *ChemSusChem*, **2009**, 546–549.
[17] L. Ackermann, R. Vicente, A. Althammer, *Org. Lett.* **2008**, *10*, 2299–2302.

most effective catalyst and exerted an optimal rate acceleration in direct C–H bond arylations, whereas carbonate-assisted formation of cyclometalated ruthenium(III)–NHC complexes as not of any relevance (Scheme 5).[18] It is noteworthy that the carboxylate-assisted ruthenium(II) catalytic system can be broadly applied in direct arylations with various organic electrophiles, including aryl halides, pseudohalides and phenols. The mechanism was studied in great detail as well.



additive	---	HIPrCl	PPh_3	$Ad_2PO(H)$	$(PhO)_2PO(H)$	NaOAc	$AdCO_2H$	tBuCO$_2$H	$MesCO_2H$
Yield (%)	0	9	20	85	50	79	85	66	93

Scheme 5 Efficacy of different additives in ruthenium(II)-catalyzed arylations.

1.2.1 Carboxylate-Assisted Ruthenium-Catalyzed Oxidative Alkyne Annulation

Based on the previous studies on ruthenium-catalyzed direct arylations, Ackermann's group tested carboxylates as cocatalytic additives for ruthenium(II)-catalyzed oxidative C−H bond functionalizations,[19] a research area that so far had largely been dominated by the use of more expensive rhodium[20] or palladium[21] complexes.

Considering the importance of step-economical syntheses of bioactive heterocycles, we particularly became attracted by oxidative annulations through C−H/Het−H bond cleavages. As a proof of concept, our group set out to devise ruthenium-catalyzed oxidative annulations of alkynes through C−H and N−H bond cleavages for the synthesis of potential bioactive isoquinolones (Scheme 6).[22] Notably, optimization studies revealed less expensive $[RuCl_2(p\text{-cymene})]_2$ to be

[18] (a) L. Ackermann, N. Hofmann, R. Vicente, *Org. Lett.* **2011**, *13*, 1875–1877; (b) L. Ackermann, R. Vicente, H. K. Potukuchi, V. Pirovano, *Org. Lett.* **2010**, *12*, 5032–5035.

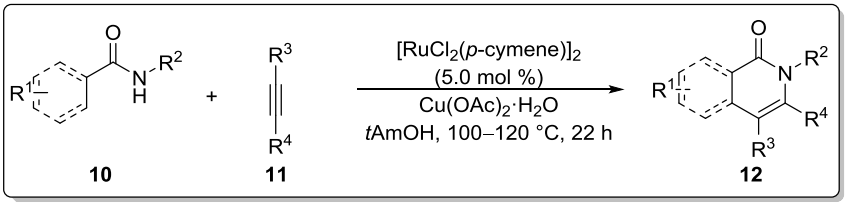
[19] Selected reviews: (a) L. Ackermann, *Org. Process Res. Dev.* **2015**, *18*, 260–269; (b) L. Ackermann, *Acc. Chem. Res.* **2014**, *47*, 281–295; (c) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879–5918.

[20] (a) G, Song, F. Wang, X. Li, *Chem. Soc. Rev*. **2012**, *41*, 3651–3678; (b) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212−11222.

[21] (a). C. Zhu, R. Wang, J. R. Falck. *Chem. Asian J*. **2012**, *7*, 1502–1514; (b) K. M. Engle, T. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res*. **2012**, *45*, 788–802.

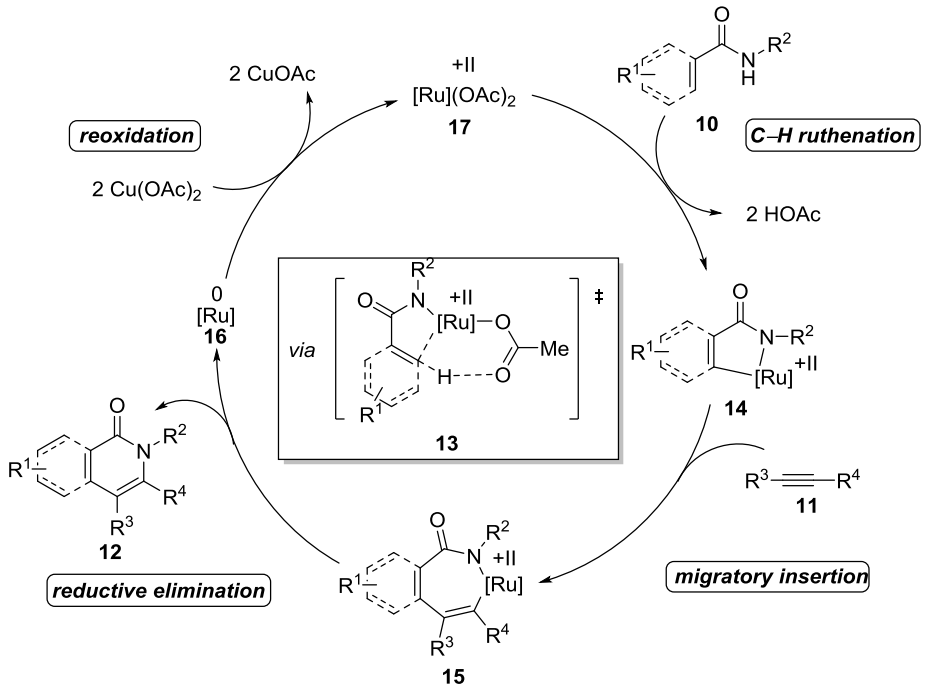
[22] L. Ackermann, A. V. Lygin, N. Hofmann, *Angew. Chem. Int. Ed.* **2011**, *50*, 6379–6382.

optimal among a variety of ruthenium complexes, while $Cu(OAc)_2 \cdot H_2O$ was found to be the terminal oxidant of choice. The annulation reaction occurred efficiently in polar protic solvent *t*AmOH, whereas the corresponding hydroarylation product was also formed in apolar solvents. The optimized ruthenium(II) catalyst proved to be tolerant of valuable electrophilic functional groups, and was found to be applicable to benzamides **10** with different substituents on nitrogen. Furthermore, the ruthenium(II) catalyst also enabled the C–H/N–H functionalizations with alkenyl-substituted amides[23] **10**, giving the desired isoquinolone in good yield and with high selectivity. Importantly, the annulation process proceeded with excellent regioselectivity when using unsymmetrical aryl/alkyl or alkenyl/alkyl alkynes **11**.



Scheme 6 Ruthenium (II)-catalyzed alkyne annulations with amides **10**.

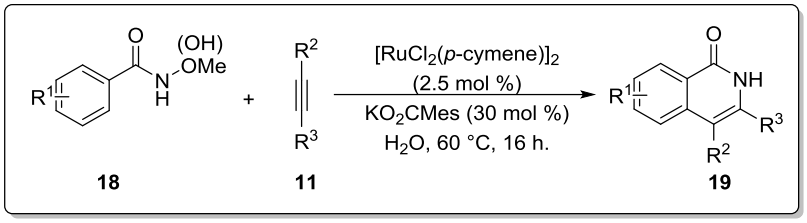
Detailed mechanistic studies revealed that the ruthenium-catalyzed oxidative annulation proceeded through an initial intermolecular carboruthenation *via* initial rate-limiting acetate-assisted C–H bond ruthenation, followed by a migratory insertion of alkyne **11**, and subsequent intramolecular C–N bond formation by reductive elimination (Scheme 7).



Scheme 7 Proposed mechanism of carboxylate-assisted oxidative annulation reactions.

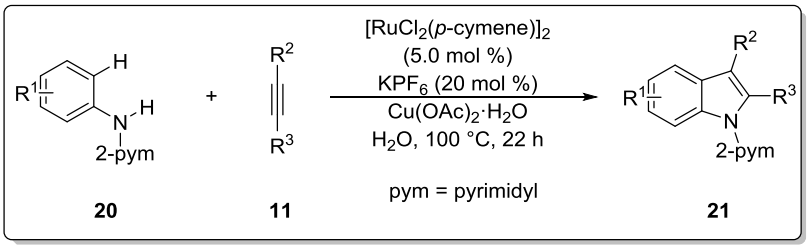
[23] L. Ackermann, A. V. Lygin, N. Hofmann. *Org. Lett.* **2011**, *13*, 3278–3281.

Subsequently, Ackermann's and Wang's group developed two protocols for the synthesis of isoquinolones by ruthenium-catalyzed redox-neutral annulations of alkynes with *N*-methoxy- and *N*-hydroxybenzamides **18**, respectively (Scheme 8).[24] These reactions were performed under mild reaction conditions with a wide range of substrates. Importantly, this redox-neutral strategy bypassed the need of wasteful metal oxidant and led to a more economic synthesis. Additionally, the extraordinary robustness and chemoselectivity of the ruthenium(II) carboxylate catalyst allowed for the direct use of free hydroxamic acids in annulations of alkynes.



Scheme 8 Ruthenium-catalyzed alkyne annulations by C–H/N–O bond cleavages.

Indoles are ubiquitous structural motifs in biologically active compounds and natural products. Therefore, their modular syntheses continued to be of strongly interest. In this context, Ackermann's group[25] developed a new approach to ruthenium-catalyzed oxidative annulations employing simple aniline derivatives **20** (Scheme 9). Notable features of the new protocol include the unprecedented use of cationic ruthenium(II) complexes for oxidative annulations of alkynes along with a removable directing group, and an excellent chemoselectivity that enabled C–H bond transformations in water as a green reaction medium.



Scheme 9 Pyrimidine-directed ruthenium-catalyzed alkyne annulations.

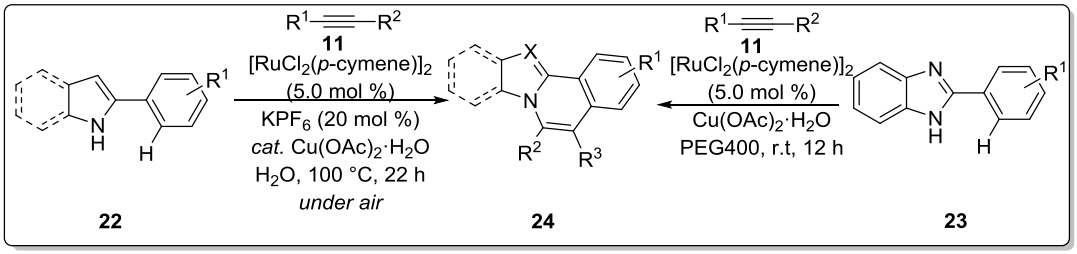
Shortly after, the same group reported on the ruthenium-catalyzed oxidative annulation of alkynes with ambient air as the ideal sacrificial oxidant.[26] The aerobic annulation reactions were accomplished with co-catalytic amounts of $Cu(OAc)_2 \cdot H_2O$ employing differently substituted 2-arylindoles **22**. Moreover, the remarkably broad scope of the ruthenium catalyst was exploited

[24] (a) L. Ackermann, S. Fenner, *Org. Lett.* **2011**, *13*, 6548–6551; (b) B. Li, H. Feng, S. Xu, B. Wang, *Chem. Eur. J.* **2011**, *17*, 12573–12577; (c) F. Yang, L. Ackermann, *J. Org. Chem.* **2014**, *79*, 12070–12082.

[25] L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764–767.

[26] L. Ackermann, L. Wang, A. V. Lygin, *Chem. Sci.* **2012**, *3*, 177–180.

for oxidative annulations with 2-arylpyrroles to deliver pyrrolo[2,1-*a*]isoquinolines **24**, structural analogues of bioactive marine alkaloids (Scheme 10). Compared to previously reported rhodium-catalyzed transformations,[27] the highly selective conversion of *n*-alkyl-substituted alkynes is a beneficial feature which can be achieved in ruthenium-catalyzed annulation processes. Experimental mechanistic studies provided strong evidence for a concerted deprotonative metalation through acetate assistance. Additionally, Chandrasekhar's group[28] subsequently developed an alternative reaction procedure wherein the metal catalyst can be recycled[29] for preparing various benzimidazoisoquinolines. Interestingly, all reactions when carried out in PEG 400 as a solvent medium delivered the desired products in similar yields even at ambient temperature. Moreover, employment of PEG 400[29] resulted in the enhanced cyclability of the catalyst, thus providing its successful use for a few times with minimal loss of activity (Table 1).



Scheme 10 Ruthenium-catalyzed alkyne annulations with indoles, pyrroles and pyrazoles.

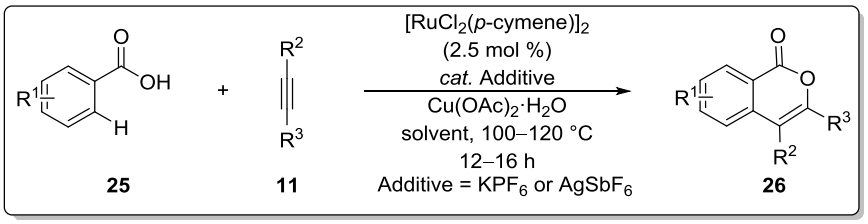
In 2012, Ackermann's and Jeganmohan's groups independently developed an atom- and step economical method for the synthesis of isocoumarins **26** through oxidative annulations of alkynes with carboxylic acids **25** using an inexpensive ruthenium catalyst (Scheme 11).[30] A wide range of substrates with differently substituted functional groups such as halogen, ester and hydroxyl group were well tolerated and afforded the corresponding products in high yields and excellent regioselectivity. Unsymmetrical alkynes **11** reacted with benzoic acid regioselectively as well to afford the decorated isocoumarins in good yield. This catalytic reaction was also compatible with heteroaromatic and alkenyl acids as substrates.

[27] K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 2068–2071.

[28] N. Kavitha, G. Sukumar, V. P. Kumar, P. S. Mainkar, S. Chandrasekhar, *Tetrahedron Lett*. **2013**, *54*, 4198–4201.

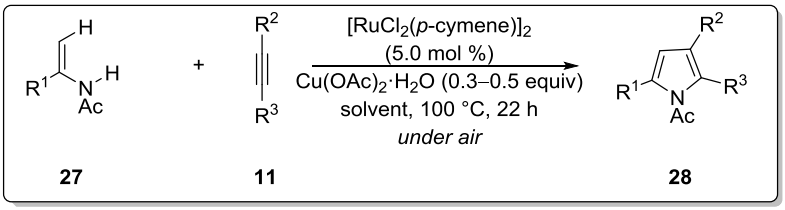
[29] L. Ackermann, R. Vicente, *Org. Lett.* **2009**, *11*, 4922–4925.

[30] (a) S. Warratz, C. Kornhaaß, A. Cajaraville, B. Niepötter, D. Stalke, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, DOI: 10.1002/anie.201500600; (b) R. K. Chinnagolla, M. Jeganmohan, *Chem. Commun*. **2012**, *48*, 2030–2032; (c) L. Ackermann, J. Pospech, K. Graczyk, K. Rauch, *Org. Lett.* **2012**, *14*, 930–933.



Scheme 11 Ruthenium-catalyzed oxidative alkyne annulations with substituted benzoic acids **25**.

Encouraged by the previous work on Rh(III)-catalyzed oxidative alkyne annulations with enamides [31] and acetanilide, [32] Ackermann, [33] Wang [34] and Liu [35] achieved annulations of enamides in the presence of a ruthenium(II) catalyst (Scheme 12). These protocols could be applied to the annulations of a variety of different substrates **27** bearing electron-deficient groups. Moreover, dialkylsubstituted substrates and unsymmetrical alkynes **11** were also converted smoothly in this catalytic system and delivered the desired products **28** in high yields.

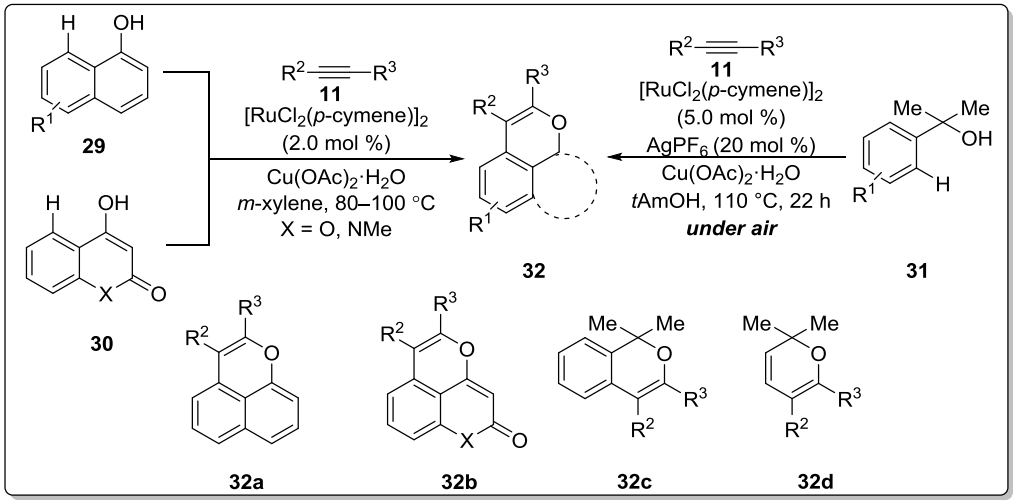


Scheme 12 Ruthenium-catalyzed oxidative alkyne annulations with enamides **27**.

The hydroxyl group was firstly employed as weakly-chelation directing group by Miura in 1997.[36] In the following decades, significant advances in direct C–H bond functionalizations were represented by the development of palladium, rhodium and iridium catalysts that proved applicable to hydroxyl group as a versatile Lewis basic directing group.[37] Based on these reports, Ackermann's group developed ruthenium-catalyzed alkyne annulations with naphthols **29**[38] and benzylic alcohols **31** (Scheme 13).[39] These transformations could be extended to compounds

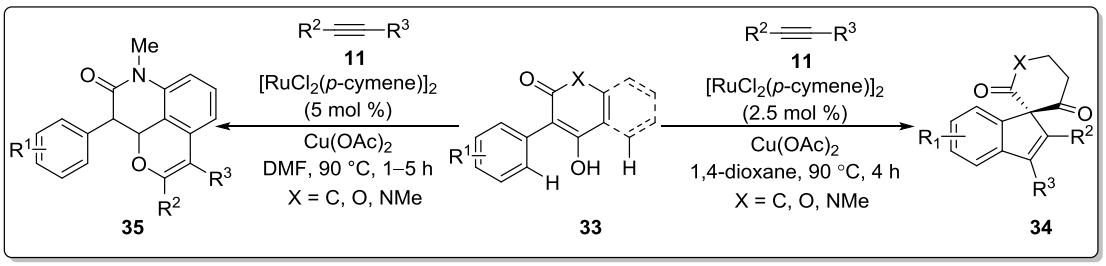
[31] S. Rakshit, F. W. Patureau, F. Glorius, *J. Am. Chem. Soc*. **2010**, *132*, 9585–9587.
[32] D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326–18339.
[33] L. Wang, L. Ackermann, *Org. Lett.* **2013**, *15*, 176–179.
[34] B. Li, N. Wang, Y. Liang, S. Xu, B. Wang, *Org. Lett*. **2013**, *15*, 136–139.
[35] K. Murugan, S. Liu, *Tetrahedron Lett*. **2013**, *54*, 2608–2611.
[36] T. Satoh, Y. Kawamura, M. Miura, M. Nomura, *Angew Chem Int. Ed. Engl.* **1997**, *36*, 1740–1742.
[37] (a) E. M.Simmons, J. F. Hartwig, *Nature* **2012**, *483*, 70–73; (b) Y. Lu, D. Leow, X. Wang, K. M. Engle, J.-Q. Yu, *Chem. Sci*. **2011**, *2*, 967–971; (c) B. Xiao, T.-J. Gong, Z.-J. Liu, J.-H. Liu, D.-F. Luo, J. Xu, L. Liu, *J. Am. Chem. Soc*. **2011**, *133*, 9250–9253; (d) X. Wang, Y. Lu, H.-X. Dai, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 12203–12205; (e) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 9548–9551; (f) J. C. Lewis, J. Wu, R. G. Bergman, J. A. Ellman, *Organometallics* **2005**, *24*, 5737–5746; (g) R. B. Bedford, S. J. Coles, M. B. Hursthouse, M. E. Limmert, *Angew. Chem. Int. Ed*. **2003**, *42*, 112–114; (h) Y. Kawamura, T. Satoh, M. Miura, M. Nomura, *Chem. Lett.* **1999**, 961–962; (i) T. Satoh, Y. Kawamura, M. Miura, M. Nomura, *Angew. Chem. Int. Ed.* **1997**, *36*, 1740–1742.
[38] V. S. Thirunavukkarasu, M. Donati, L. Ackermann, *Org. Lett.* **2012**, *14*, 3416–3419.
[39] S. Nakanowatari, L. Ackermann, *Chem. Eur. J.* **2014**, *20*, 5409–5413.

containing a variety of different functional groups including both electron-donating and electron-withdrawing ones. Remarkably, the resulting annulated pyrans **32** possess fluorescence properties which can potentially be used in material science. Mechanistic studies provided evidence for a carboxylate-assisted C–H bond ruthenation.



Scheme 13 Ruthenium(II)-catalyzed alkyne annulations with naphthols **29** and benzylic alcohols **31**.

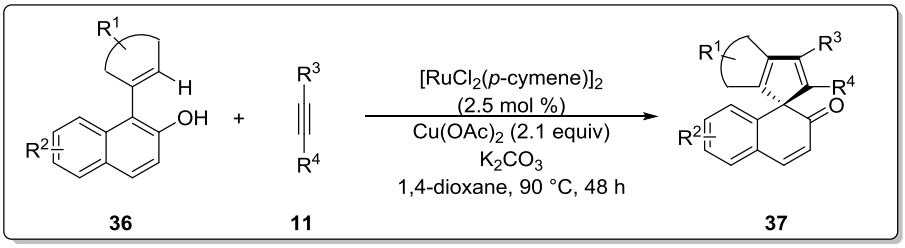
In 2012, Lam's group [40] reported on the synthesis of spiroindenes by enolate-directed ruthenium-catalyzed oxidative annulation of alkynes with 2-aryl-1,3-dicarbonyl **33** compounds. These annulations of alkynes involved functionalization of C(sp^3)–H and C(sp^2)–H bonds, thus resulting in products containing all-carbon quaternary centers **34**. A wide range of spiroindenes were obtained with high levels of regioselectivity under this catalytic condition. Thereafter, when using 3-aryl-4-hydroxyquinolin-2-ones **33** as substrates for the ruthenium-catalyzed oxidative annulation reactions, the benzopyran derivatives **35** were obtained as the main products in high isolated yields (Scheme 14), whereas only minor amounts of the spiroindenes **34** were formed. On the other hand, employing a palladium catalyst, the spiroindene compounds **34** can be obtained predominantly in high yields with high regioselectivity.



Scheme 14 Ruthenium-catalyzed alkyne annulations with 2-aryl-1,3-dicarbonyl compounds **33**.

[40] (a) S. R. Chidipudi, I. Khan, H. W. Lam, *Angew. Chem. Int. Ed*. **2012**, *51*, 12115–12119; (b) J. D. Dooley, S. R. Chidipudi, H. W. Lam, *J. Am. Chem. Soc.* **2013**, *135*, 10829−10836.

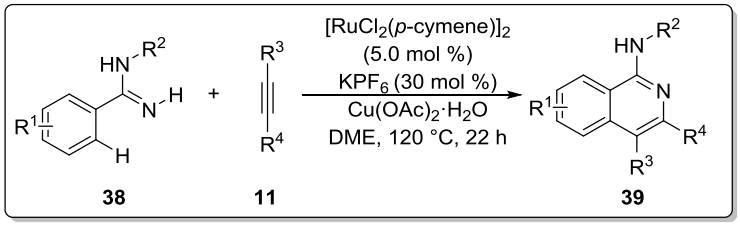
Shortly thereafter, inspired by previous works on hydroxyl-directed transition-metal-catalyzed C–H bond functionalization, Wang[41] developed a ruthenium-catalyzed vinylative dearomatization reaction of 1-aryl-2-naphthols **36** *via* C–H activation strategy (Scheme 15). At the beginning of this study, rhodium and palladium catalyst were also evaluated under the optimized reaction conditions, but only resulted in unsatisfactory yields. The effective ruthenium catalyst can enable this transformation successfully to deliver the desired spirocyclic products in high yields. Importantly, unsymmetrical alkynes were also applicable as the coupling partners and afforded the corresponding products **37** with excellent regioselectivity. This transformation provides a facile route to access a class of highly functionalized spirocyclic compounds.



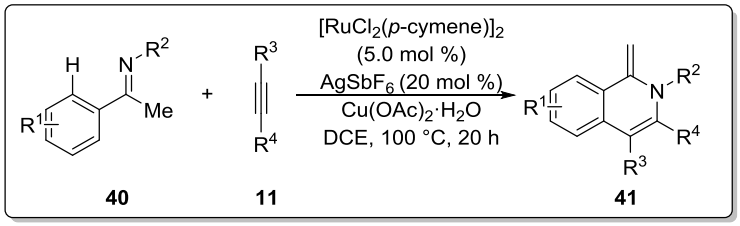
Scheme 15 Ruthenium(II)-catalyzed alkyne annulations with 1-aryl-2-naphthols **36**.

Very recently, Ackermann's group developed ruthenium(II)-catalyzed oxidative alkyne annulations with amidines **38** (Scheme 16a).[42] This ruthenium catalytic system was also applicable to the ketimine substrates **40** (Scheme 16b)[43] for the preparation of isoquinolines **41** which are key structural motifs of various heterocyclic compounds.

a)



b)



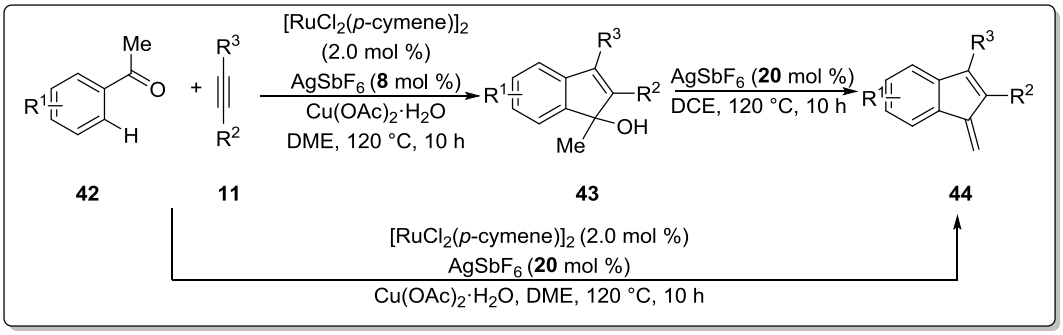
Scheme 16 Ruthenium-catalyzed alkyne annulations with substituted amidines **38** and ketimines **40**.

[41] J. Nan, Z. Zuo, L. Luo, L. Bai, H. Zheng, Y. Yuan, J. Liu, X. Luan, Y. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 17306−17309.

[42] J. Li, M. John, L. Ackermann, *Chem. Eur. J.* **2014**, *20*, 5403–5408.

[43] J. Li, L. Ackermann, *Tetrahedron* **2014**, *70*, 3342–3348.

Lately, Jeganmohan and coworkers[44] successfully developed a highly regioselective cyclization of phenones **42** with alkynes which provided an efficient route to the preparation of indenols **43** and benzofulvenes **44**. Interestingly, the amount of silver salt plays an important role in the reaction. When the amount of silver salt exceeded 8 mol % in the presence of 2 mol % of $[RuCl_2(p\text{-cymene})]_2$, a different type of dehydration product, namely a benzofulvene derivative **44**, started to appear. Therefore, two different products were obtained by controlling the amount of $AgSbF_6$ under otherwise identical reaction conditions (Scheme 17).



Scheme 17 Ruthenium(II)-catalyzed alkyne annulations with phenones **42**.

1.3 Transition-Metal-Catalyzed Direct Alkenylation of Arenes

Styrene derivatives are useful intermediates in synthetic organic chemistry and represent key structural motifs in natural products,[45] medicinal chemistry[46] and material sciences.[47] Among others, several catalytic methods for the preparation of styrene derivatives have been developed. For example, the palladium-catalyzed Mizoroki-Heck reaction is one of the most popular and powerful tools for the formation of C–C bonds that offer a straightforward approach for the construction of olefinated products (Scheme 18a).[48] Under these reaction conditions, aryl halides

[44] R. K. Chinnagolla, M. Jeganmohan, *Eur. J. Org. Chem.* **2012**, 417–423.

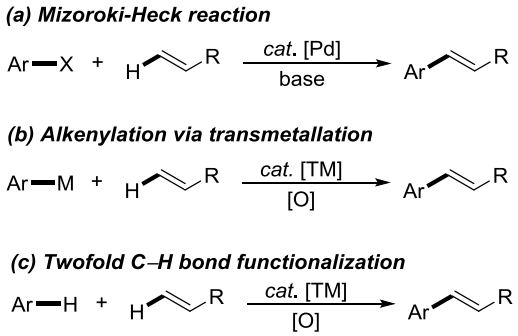
[45] (a) P. Nguyen, J. Yang, M. N. Uddin, S. Park, S. Lim, D. Jung, D. R. Williams, W. Oh, *J. Nat. Prod*. **2013**, *76*, 2080−2087; (b) S. W. Chae, A. Han, J. H. Park, J. Y. Rhie, H. Lim, E. Seo, H. J. Lee, *J. Nat. Prod.* **2013**, *76*, 2277−2281; (c) B. H. Park,Y. R. Lee,W. S. Lyoob, *Synthesis* **2009**, *13*, 2146–2154; (d) B. S. Siddiqui, H. Aslan, S. Begus, S. T. Ali, *Nat. Prod. Res*. **2007**, *21*, 736–741; (e) J. Cheel, C.Theoduloz, J. Rodriguez, G. Saud, P. D. S. Caligari, G. Schmeda-Hirschmann, *J. Agric. Food Chem*.**2005**, *53*, 8512–8518.

[46] (a) R. S. P. Singh, D. Michel, U. Das, J. R. Dimmock, J. Alcorn, *Bioorg. Med. Chem. Lett*. **2014**, *24*, 5199–5202; (b) T. Chuprajob, C. Changtam, R. Chokchaisiri, W. Chunglok, N. Sornkaew, A. Suksamrarn, *Bioorg. Med. Chem. Lett.* **2014**, *24*,2839–2844; (c) N. Sharma, D. Mohanakrishnan, A. Shard, A. Sharma, A. K. Sinha, D. Sahal, *J. Med. Chem.* **2012**, *55*, 297−311; (d) Q.-Y. Wei, H. Jiang, J.-X. Zhang, C. Zhang, P.-F. Guo, *Asian J. Chem.* **2012**, *24*, 2383–2388; (e) K. Patel, C. Karthikeyan, N. S. H. N. Moorthy, G. S. Deora, V. R. Solomon, H. Lee, P. Trivedi, *Med. Chem. Res*. **2012**, *21*, 1780–1784.

[47] (a) J. Wencel-Delord, F. Glorius, *Nat. Chem*. **2013**, *5*, 369–375; (b) Q. Jiang, Z. Lei, *Biotechnol. Bioprocess Eng*. **2011**, *16*,1187–1195; (b) M. M. da Silva Paula, C. V. Franco, M. C. Baldin, L. Rodrigues, T. Barichello, G. D. Savi, L. F. Bellato, M. A. Fiori, L. da Silva, *Mater. Sci. Eng.* C, **2009**, *29*, 647–650; (c) J. C. Garay-Jimenez, D. Gergeres, A. Young, D. V. Limand, E. Turos, *Nanomed.Nanotechnol. Biol. Med*. **2009**, *5*, 443–451.

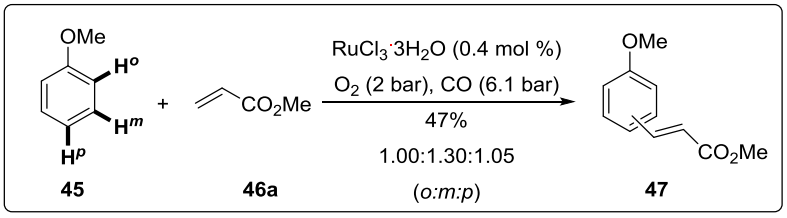
[48] S. Bräse, A. de Meijere, *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, New York, **2004**, Chapter 5.

and pseudohalides can be used as the coupling partners. However, the stoichiometric amounts of halide salts as side products generated by this transformation can cause extensive environmental pollution. Another method is the transition-metal-catalyzed alkenylation of organometallic nucleophilic reagents such as organomercuric acetates, [49] organoboronic acids [50] and organofluorosilicates (Scheme 18b).[51] However, most of these starting materials were prepared in several steps from the corresponding aryl halides. Some side products generated from these transformations were also not environmentally friendly. In contrast, the cross-dehydrogenative alkenylations developed by Fujiwara and Moritani[52] between unactivated arenes and olefins by twofold C–H bond activation is one of the most ideal strategies to achieve olefination of arenes because it bypasses the need of preactived starting materials (Scheme 18c). Therefore, different methods for the preparation of styrene derivatives by cross-dehydrogenative olefination reaction were reported in the past decades.



Scheme 18 Strategies for the metal-catalyzed preparation of styrenes.

However, as several C–H bonds of similar reactivity are usually available in a molecule, in the most cases these transformations could be achieved with only poor site-selectivity (Scheme 19).[53]



Scheme 19 Ruthenium(III)-catalyzed oxidative alkenylations with anisole **45**.

[49] R. F. Heck, *J. Am. Chem. Soc.* **1969**, *91*, 6707–6714.

[50] H. A. Dieck, R. F. Heck, *J. Org. Chem.* **1975**, *40*, 1083–1090.

[51] J. Yoshida, K.Tamao, H. Yamamoto, T. Kakui, T. Uchida, M. Kumada, *Organometallics* **1982**, *1*, 542–549.

[52] (a) I. Moritani, Y. Fujiwara, *Tetrahedron Lett.* **1967**, *8*, 1119–1122; (b) Y. Fujiwara, I. Moritani, M. Matsuda, *Tetrahedron* **1968**, *24*, 4819–4824. (c) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, *34*, 633–639; (d) E. M. Ferreira, H. Zhang, B. M. Stolz, *Oxidative Heck-Type Reactions (Fujiwara-Moritani Reactions)*, in *The Mizoroki-Heck Reaction* (Ed.: M. Oestreich), Wiley, Chichester, **2009**, pp. 345–382; (e) T. Satoh, M, Miura, in *Metal-Catalyzed Cross-Coupling Reactions and More*; (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**, vol. 3, pp. 1389–1426.

[53] (a) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed*. **2012**, *51*, 10236–10254; (b) H. Weissman, X. Song, D. Milstein, *J. Am. Chem. Soc.* **2001**, *123*, 337–338.

To overcome this disadvantage, a new method that utilized a directing group preinstalled in the substrate has been explored in recent years.[54] In most cases, directing groups always contain a heteroatom which can coordinate to the transition metal catalyst to achieve C–H functionalization in good yield and high regioselectivity. In this context, a great number of transition-metal-catalyzed alkenylations of arene bearing different directing group have been reported in the last decade.

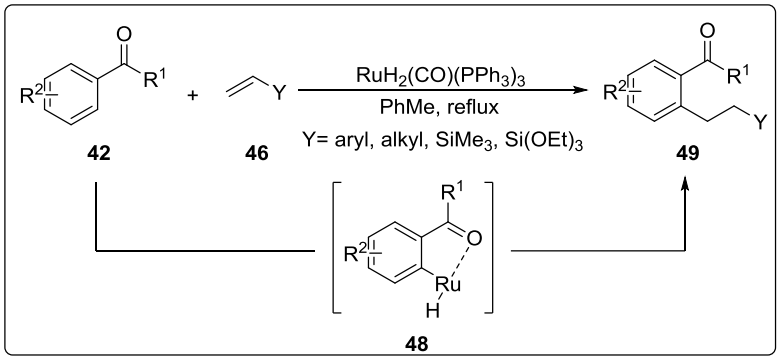
1.3.1 Ruthenium-Catalyzed Direct Alkenylation of Arenes

Transition metal-catalyzed alkenylations have been achieved with great progress since 1967, when Fujiwara and Moritani reported the first example of the palladium-catalyzed direct oxidative coupling reactions.[52a] However, almost all of these reactions were performed in the presence of expensive rhodium and palladium catalysts. In contrast, significantly less expensive ruthenium complexes have been only recently exploited as catalysts for oxidative C–H bond alkenylations of arenes.

As early as 1986, Lewis and Smith[15b] reported that ruthenium complexes containing *ortho*-metalated triphenyl phosphite linkages reacted with ethylene to give ortho alkylation on the triphenyl phosphite ligands. The ruthenium complex together with phenoxide catalyzed the selective *ortho* alkylation of phenol. Inspired by this study, in 1993, Murai[15a] reported ruthenium-catalyzed couplings of alkenes with arenes **42** bearing ketone as an *ortho*-directing group (Scheme 20). In this reaction, the low valent ruthenium(0) species is coordinated by the aromatic carbonyl group and subsequently activates the neighboring aromatic C–H bond. However, the double bond was not preserved in this coupling reaction. Therefore, this reaction is

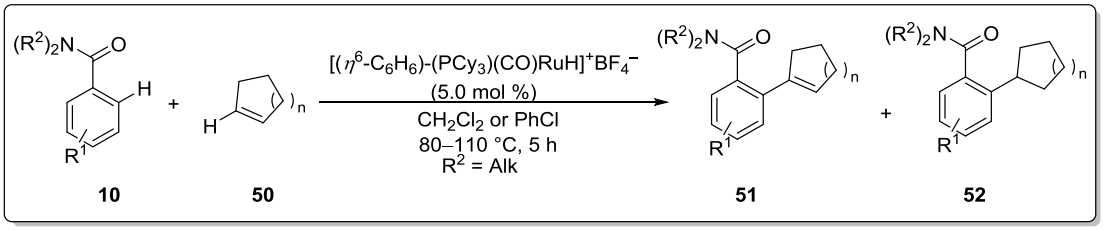
[54] (a) C. Zhang, J. Ji, P. Sun. *J. Org. Chem*. **2014**, *79*, 3200−3205; (b) C. Zhang, M. Wang, Z. Fan, L. Sun, A. Zhang, *J. Org. Chem*. **2014**, *79*, 7626−7632; (c) K. Parthasarathy, C. Bolm, *Chem. Eur. J*. **2014**, *20*, 4896–4900; (d) J. Karthikeyan, N. Yoshikai, *Org. Lett*. **2014**, *16*, 4224−4227; (e) X. Huang, J. Huang, C. Du, X. Zhang, F. Song, J. You, *Angew. Chem. Int. Ed*. **2013**, *52*, 12970–12974; (f) S. Hu, D. Wang, J. Liu, X. Li, *Org. Biomol. Chem.* **2013**, *11*, 2761–2765; (g) B. C. Chary, S. Kim. *Org. Biomol. Chem*.**2013**, *11*, 2761–2765; (h) L. Jiao, M. Oestreich, *Org.Lett*. **2013**, *15*, 5374–5377; (i) X. Zhang, Q. Zhu, Y. Zhang, Y. Li, Z. Shi. *Chem. Eur. J.* **2013**, *19*, 11898–11903; (j) H. Wang, R. Hu, H. Zhang, A. Zhou, S. Yang. *Org. Lett*. **2013**, *15*, 5302–5305; (k) J. Mo, S. Lim, S. Park, T. Ryu, S. Kim, P. Lee, *RSC Adv*. **2013**, *3*, 18296–18299; (l) N. Schroeder, T. Besset, F. Glorius, *Adv. Synth. Catal*. **2012**, *354*, 579–583; (m) L. Ackermann, L. Wang, R. Wolfram, A. V. Lygin, *Org. Lett.* **2012**, *14*, 728–731; (n) K. Graczyk, W. Ma, L. Ackermann, *Org. Lett.* **2012**, *14*, 4110–4113; (o) P. Zhao, R. Niu, F. Wang, K. Han, X. Li. *Org. Lett*. **2012**, *14*, 4166–4169; (p) X. Wei, F. Wang, G. Song, Z. Du. X. Li, *Org. Biomol. Chem*. **2012**, *10*, 5521–5524; (q) J. Zhang, T. P. Loh, *Chem. Commun*. **2012**, *48*, 11232–11234; (r) P. Kishor, S. Pimparkar, P. Madasamy, M. Jeganmohan, *Chem.Commun.* **2012**, *48*, 7140–7142; (s) P. Kishor, M. Jeganmohan, *Org. Lett.* **2012**, *14*, 1134–1137; (t) Y. Hashimoto, T. Ortloff, K. Hirano, T. Satoh, C. Bolm, M. Miura, *Chem. Lett.* **2012**, *41*, 151–153; (u) L. Ackermann, J. Pospech, *Org. Lett.* **2011**, *13*, 4153–4155; (v) F. W. Patureau, T. Besset, F. Glorius, *Angew. Chem. Int. Ed*. **2011**, *50*, 1064–1067; (w) K. Padala, M. Jeganmohan, *Org. Lett*. **2011**, *13*, 6144–6147; (x) K. M. Engle, D. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed*. **2010**, *49*, 6169–6173. For recent reviews, see: (y) S. I. Kozhushkov, L. Ackermann, *Chem. Sci.* **2013**, *4*, 886–896; (z) F. Zhang, D. R. Spring, *Chem. Soc. Rev*. **2014**, *43*, 6894–6905; (aa) C. Wang, Y. Huang, *Synlett* **2013**, *24*, 145–149.

not an alkenylation reaction, but rather a hydroarylation of an alkene **46**.



Scheme 20 Ruthenium-catalyzed direct hydroalkylations of phenones **42**.

Subsequently, Yi[55] reported on chelation-assisted coupling reactions of arylamides **10** and unactivated alkenes **50** (Scheme 21). The cationic ruthenium hydride complex $[(\eta^6\text{-}C_6H_6)(PCy_3)(CO)RuH]^+BF_4^-$ enabled these alkenylation reactions efficiently to give the *ortho*-alkenylamides **51** in good yields (up to 84%). Interestingly, an excess of the alkene **50** as well as of the newly formed alkenylated benzamide **51** served as the hydrogen scavenger which enabled this transformation without any external oxidant.

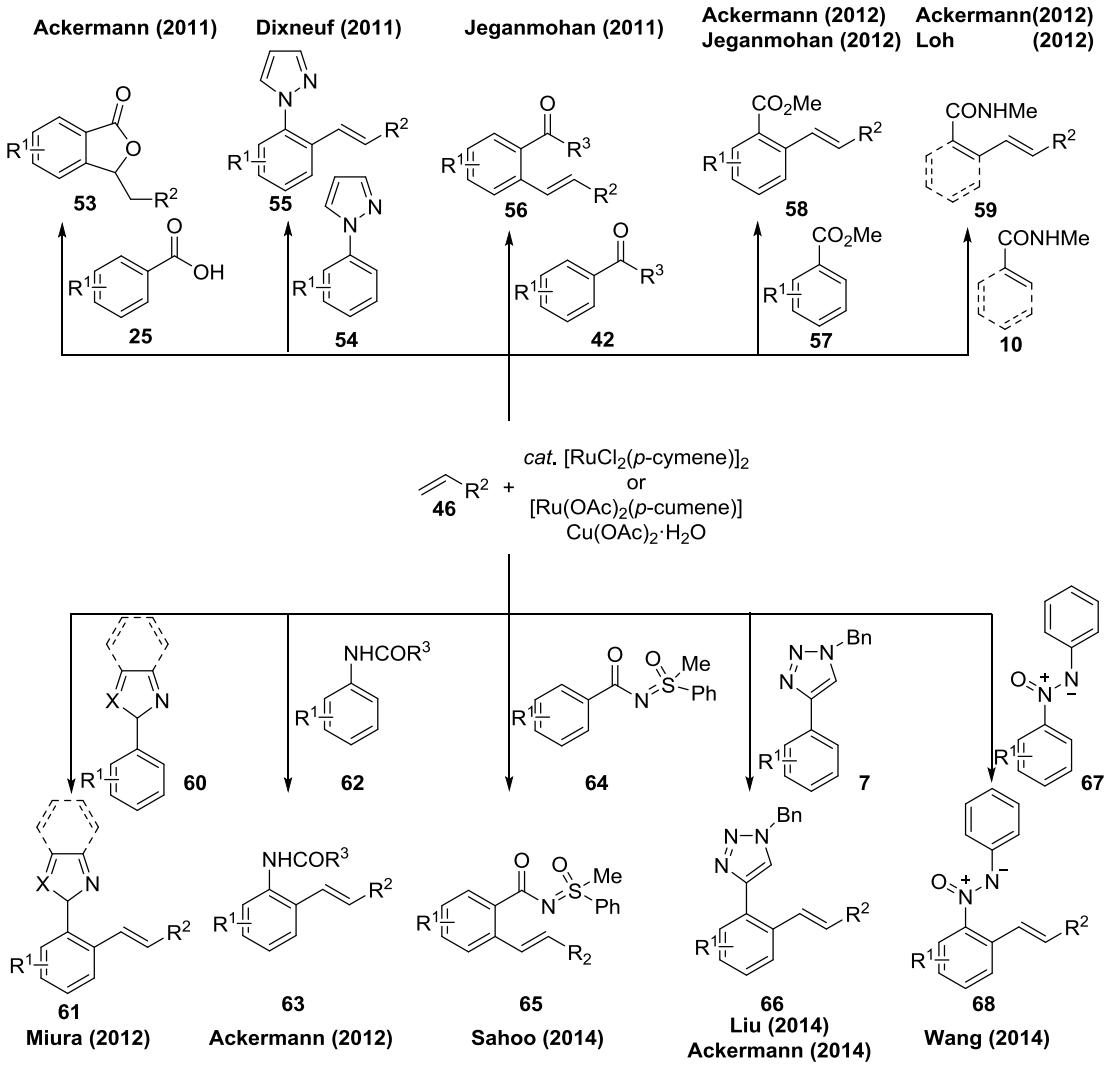


Scheme 21 Ruthenium-catalyzed alkenylations of substituted benzamides **10**.

Shortly thereafter, a great number of ruthenium-catalyzed alkenylation reactions appeared in the literature, and these transformation were rapidly expanded to a variety of directing groups (Scheme 22), including esters,[54n,54r] anilines, amides,[54m,54q,54t] carboxylic acids,[54u] ketones,[54w] aldehdyes,[54s] oxazolines,[56] pyrazoles[57], triazoles[58] and azoxybenzenes.[59] These transformations proceeded smoothly in the presence of cationic ruthenium(II) complexes and copper oxidants to give the desired products in good yield with high regio- and site-selectively. Importantly, some of

[55] K. Kwon, D. W. Lee, C. S. Yi, *Organometallics* **2010**, *29*, 5748–5750.
[56] B. Li, K. Devaraj, C. Darcel, P. Dixneuf, *Green Chem.* **2012**, *14*, 2706–2709.
[57] (a) P. B. Arockiam, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *Green Chem.* **2011**, *13*, 3075–3078; (b) Y. Hashimoto, T. Ueyama, T. Fukutani, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2011**, *40*, 1165–1166.
[58] (a) X. Li, K. Liu, G. Zou, P. Liu, *Eur. J. Org. Chem.* **2014**, 7878–7888; (b) C. Tirler, L. Ackermann, *Tetrahedron* **2015**, doi:10.1016/j.tet.2015.02.033
[59] H. Li, X. Xie, L. Wang, *Chem. Commun.* **2014**, *50*, 4218–4221.

the oxidative C–H bond alkenylations were also viable in an aerobic fashion, using cocatalytic amounts of $Cu(OAc)_2 \cdot H_2O$ under an atmosphere of ambient air. It is noteworthy that heterocyclic substrates such as indole and thiophene derivatives were also compatible in the ruthenium catalyzed reactions.[60,54m]



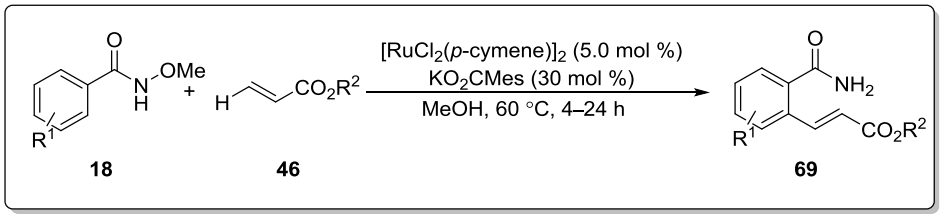
Scheme 22 Recent ruthenium-catalyzed alkenylations of arenes with various directing groups.

It is important to mention that all these transformations relied on copper(II) acetate as the reoxidant or oxidant. Thus, in most case, the $Cu(OAc)_2 \cdot H_2O$ proved to be essential for these transformations, since it not only acted as the (co)oxidant but also served as the source of acetate for the carboxylate-assisted C−H bond activation step. However, the using of stoichiometric or cocatalytic amount of metal oxidant in these reactions led to the generation of stoichiometric amounts of undesired waste. Based on this context, Wang (Scheme 23a)[61] and Ackermann

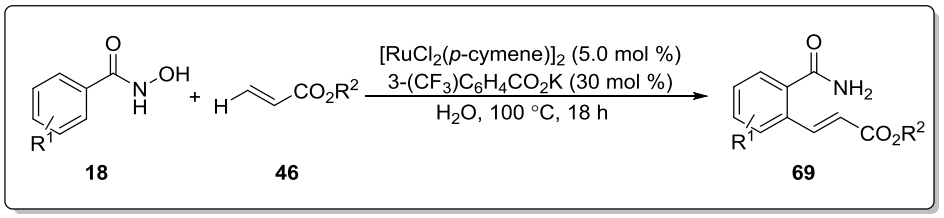
[60] V. Lanke, K. R. Prabhu, *Org. Lett.* **2013**, *15*, 6262–6265.
[61] B. Li, J. Ma, N. Wang, H. Feng, S. Xu, B. Wang, *Org. Lett.* **2012**, *14*, 736−739.

(Scheme 23b)[62] reported ruthenium-catalyzed oxidative alkenylations under notably mild reaction conditions of *N*-methoxy- and *N*-hydroxybenzamides **18** bearing the C(O)NH(OMe) and C(O)NHOH groups, respectively, as oxidizing directing group. Remarkably, cocatalytic amounts of carboxylates were found to be indispensable for achieving efficient C−H bond functionalizations, with optimal results being accomplished with KO_2CMes or NaOAc as the co-catalysts, respectively.

a)



b)

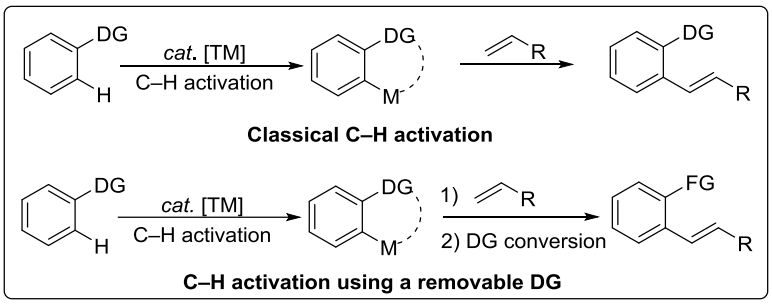


Scheme 23 Ruthenium-catalyzed C–H alkenylations by using internal oxidizing directing groups.

1.3.2 Transition Metal-Catalyzed Direct Alkenylation of Arenes with Removable Directing Groups

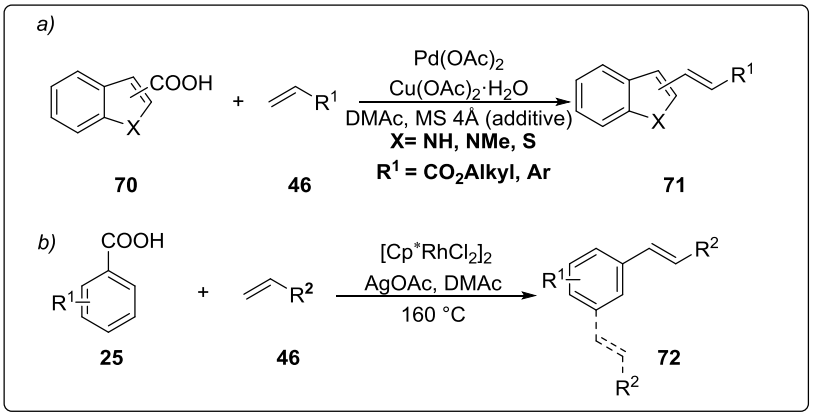
In recent years, directing group-assisted transition metal-catalyzed oxidative alkenylations have been achieved with great progress, and a large variety of decorated styrenes were prepared from this protocol. However, the directing groups are always difficult to be removed or transformed to other functional groups under mild conditions. This restriction has greatly limited the structural diversity of the products and subsequent application in the synthesis of complex molecules. Therefore, the necessity of novel, readily accessible substrates containing easily attachable and removable directing groups is obvious (Scheme 24).[54aa]

[62] F. Yang, L. Ackermann. *J. Org. Chem*. **2014**, *79*, 12070−12082.



Scheme 24 Comparison of two strategies for C–H bond alkenylations.

In 2008, Miura[63] succeeded in preparing a series of *meta*-substituted stilbenes and 2- or 3-vinylindole derivatives **71** from readily available carboxylic acids and alkenes through precisely ordered *ortho*-olefination/decarboxylation under palladium and rhodium catalysis (Scheme 25). For the unsubstituted benzoic acid **25**, double olefination took place at the 2- and 6-positions to form selective 1,3-dialkenylbenzenes **72** which are important organic intermediates in material science (Scheme 25b).

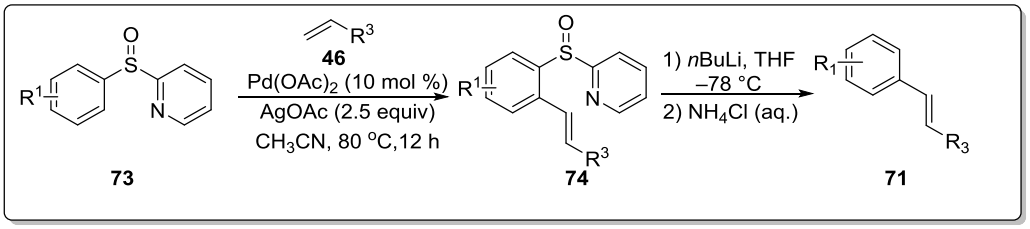


Scheme 25 Palladium- and rhodium-catalyzed oxidative alkenylations of carboxylic acids.

In 2011, Zhang's group[64] disclosed an efficient method for the palladium(II)-catalyzed alkenylation and arylation of arenes **73** by using 2-pyridyl sulfoxide as the directing group (Scheme 26). The directing group can easily be removed or converted to another synthetically useful moiety.

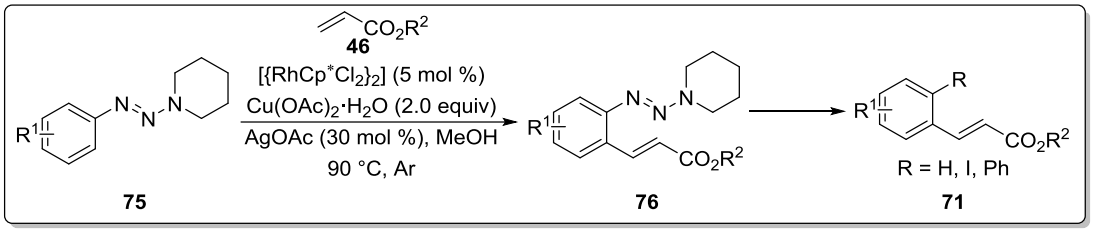
[63] (a) A. Maehara, H. Tsurugi, T. Satoh, M. Miura, *Org. Lett.* **2008**, *10*, 1159–1162; (b) S. Mochida, K. Hirano, T. Satoh, M. Miura, *Org. Lett*. **2010**, *12*, 5776–5779.

[64] M. Yu, Z. Liang, Y. Wang, Y. Zhang, *J. Org. Chem*. **2011**, *76*, 4987–4994.



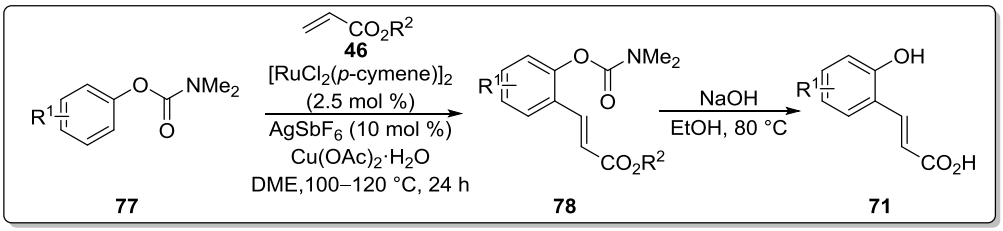
Scheme 26 Palladium-catalyzed alkenylations of substituted 2-pyridyl sulfoxides **73**.

Subsequently, Huang and coworkers[65] developed the triazene-directed aromatic C–H bond activation followed by oxidative coupling to synthesize olefinated arenes **71** (Scheme 27). This versatile directing group can participate in various transformations such as facile removal, halogen exchange, and direct C–H cross-coupling.



Scheme 27 Rhodium-catalyzed oxidative alkenylations of triazene **75**.

Ackermann's[66] and subsequently Wang's[67] group reported ruthenium(II)-catalyzed oxidative C–H alkenylations using carbamates as the directing groups. Substrates **77** decorated with different functional groups, such as halides, were tolerated very well and afforded the corresponding products **78** in good yields with high regio- and stereo-selectivities. Importantly, the carbamate directing group was easily removed under basic reaction conditions to deliver the desired phenol derivatives **71** (Scheme 28).

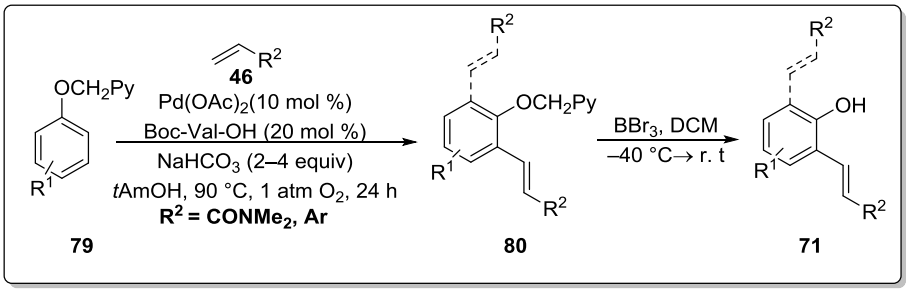


Scheme28 Ruthenium-catalyzed C–H alkenylations of aryl carbamates **77**.

Besides this, You's group[68] found that (2-pyridyl)methylether can serve as an efficient directing group for amino acid ligand-accelerated *ortho*-C–H olefination of aryl (2-pyridyl)methyl ethers **79**.

[65] C. Wang, H. Chen, Z. Wang, J. Chen, Y. Huang, *Angew. Chem. Int. Ed*. **2012**, *51*, 7242–7245.
[66] J. Li, C. Kornhaaß, L. Ackermann, *Chem. Commun.* **2012**, *48*, 11343–11345.
[67] B. Li, J. Ma, Y. Liang, N. Wang, S. Xu, H. Song, B. Wang, *Eur. J. Org. Chem.* **2013**, 1950–1962.
[68] X. Cong, J. You, G. Gao, J. Lan, *Chem. Commun.* **2013**, *49*, 662–664.

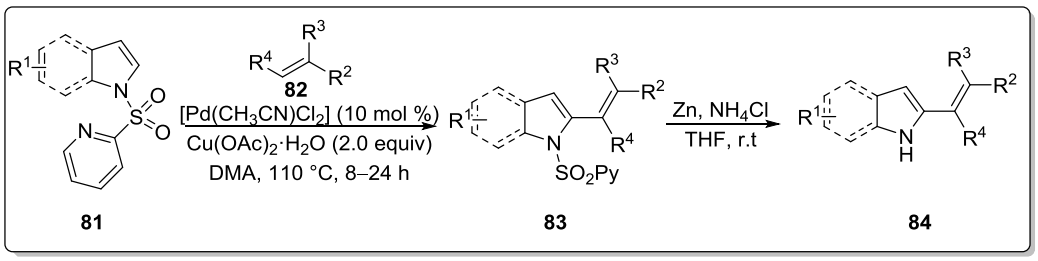
A variety of differently substituted substrates **79** could be employed in this transformation, giving the *ortho*-alkenylated products **80** in good to excellent yields with high regioselectivity. Especially, non-activated alkenes can also serve as coupling partners. Additionally, the scope of this methodology can be expanded to the diolefination of substrate **79**. At last, the 2-pyridylmethyl group can easily be removed through several different methods giving the *ortho*-alkenyl phenols **71** or *ortho*-alkylphenols (Scheme 29).



Scheme 29 Palladium-catalyzed C–H alkenylations of aryl (2-pyridyl)methyl ethers **79**.

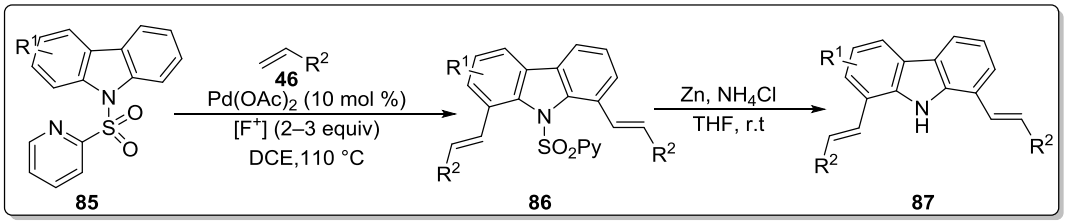
The 2-pyridylsulfonyl directing group was found to be efficient for the palladium-catalyzed alkenylation of pyrroles and indoles **81**, as was reported by Carretero and coworkers (Scheme 30a).[69a] Both electron-withdrawing and electron-donating substituents on the aryl ring of the indole **81** did not significantly affect the transformation. It is noteworthy that substituted alkenes **82,** such as methylmethacrylate, α-ethylacrolein, and methyl styrene also reacted smoothly under this reaction condition. Subsequently, it was found that this directing group was also suitable for carbazole substrates **85** when changing the oxidant to *N*-fluoro-2,4,6-trimethylpyridinium triflate ([F^+] in Scheme 30b).[70b] Importantly, the 2-pyridylsulfonyl group can easily be removed under reductive conditions to generate the potential bioactive NH-free pyrrole, indole and carbazole derivatives **84** and **87** (Scheme 30).

a)



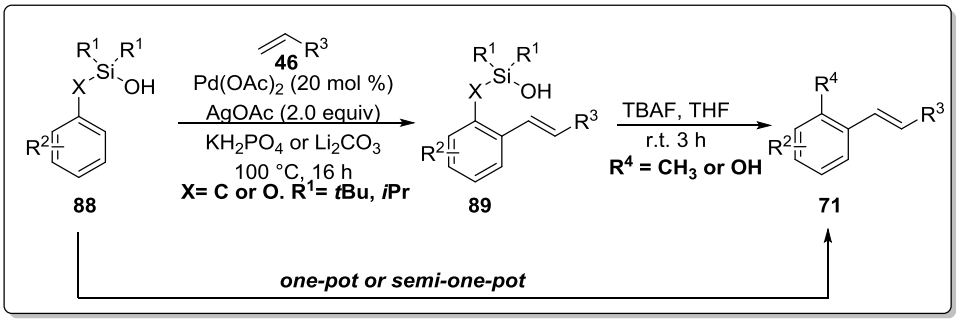
[69] (a) A. Garca-Rubia, R. G. Arras, J. C. Carretero, *Angew. Chem. Int. Ed.* **2009**, *48*, 6511–6515; (b) B. Urones, R. G. Arrayás, J. C. Carretero, *Org. Lett.* **2013**, *15*, 1120–1123.

b)



Scheme 30 Palladium-catalyzed C–H alkenylations of substituted indoles, pyrroles and carbazoles.

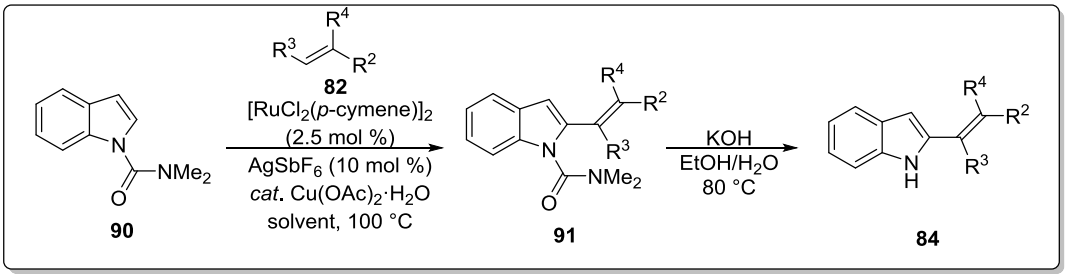
Furthermore, Ge[70] and Gevorgyan[71] introduced silanol as an effective directing group for the direct olefination of arenes through palladium-catalyzed C–H activation. Substrates **88** decorated with both electron-donating and electron-withdrawing groups were successfully transformed under this reaction conditions to afford the desired products **89** in high yields. Some important functional groups, such as chloride and ester, were well tolerated in this catalytic system. In addition, the silanol group can be removed in the presence of TBAF at ambient temperature. Importantly, the C–H activation/desilylation transformation of benzyldiisopropylsilanol and phenol-derived silanols **88** can be achieved in an one-pot or a semi-one-pot fashion which provided a novel and attractive approach for the synthesis of *ortho*-alkenyl-substituted styrene derivatives **71** (Scheme 31).



Scheme 31 Palladium-catalyzed direct alkenylations of arenes **88** with silanol as a removable directing group.

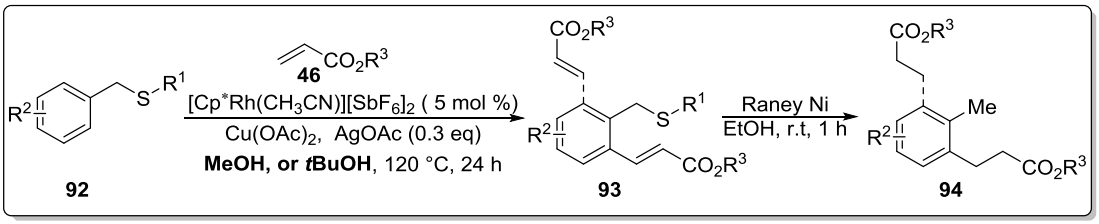
Additionally, Song[72] and Wang[73] reported highly efficient and selective ruthenium-catalyzed C2-olefination of indoles **90** by using the *N*,*N*-dimethylcarbamoyl as a removable directing group. In this olefination reaction, the non-activated styrene derivatives **82** successfully participated as well. Other related *N*-heteroarenes such as pyrroles and carbazoles could also be used and yielded the corresponding products in good yields with high site-selectivity. The employment of O_2 as the terminal oxidant allows performing this reaction in an economical fashion (Scheme 32).

[70] C. Wang, H. Ge, *Chem. Eur. J.* **2011**, *17*, 14371–14374.
[71] C. Huang, B. Chattopadhyay, V. Gevorgyan, *J. Am. Chem. Soc.* **2011**, *133*, 12406–12409.
[72] L. Zhang, S. Yang, X. Huang, J. You, F. Song, *Chem. Commun.* **2013**, *49*, 8830–8832.
[73] B. Li, J. Ma, W. Xie, H. Song, S. Xu, B. Wang, *J. Org. Chem.* **2013**, *78*, 9345−9353.



Scheme 32 Ruthenium-catalyzed C–H alkenylations of indoles **90**.

Afterwards, rhodium-catalyzed C(sp^2)–H bond alkenylation by using the thioether directing group has been achieved by Shi's group.[74] Interestingly, monoalkenylated products **93** could be obtained selectively by using MeOH as the solvent, whereas only dialkenylation can be achieved in *t*BuOH. The directing group can easily be removed at ambient temperature in the presence of Raney nickel (Scheme 33). Notably, the double C–H bond functionalization of alkenes could not be preserved under these conditions, thus providing *o*-tolylpropanoates **94**, which are also important substrates in organic synthesis.



Scheme 33 Controllable (di)alkenylations of benzyl thioether **92** through rhodium-catalyzed C–H activation.

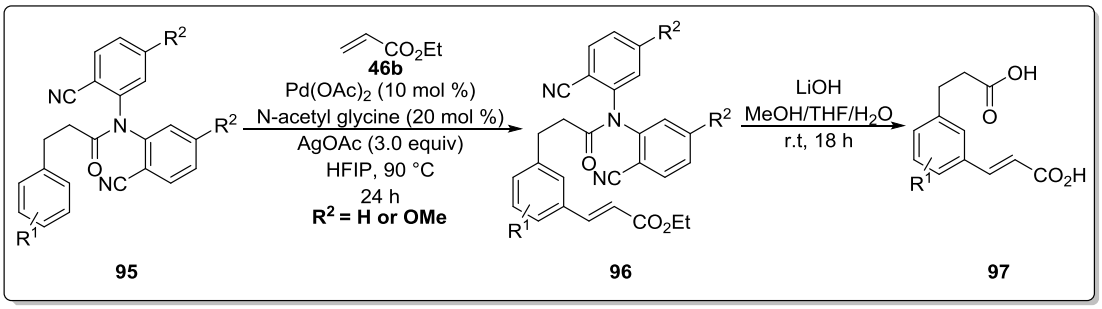
So far, great progress has been achieved in transition metal-catalyzed oxidative alkenylations with different removable directing groups. These protocols usually use the *σ*-chelating directing groups, which lead to *ortho*-selectivity through the formation of conformationally rigid five- to seven-membered cyclic intermediates. Despite the broad utility of this approach, proximity-driven reactivity prevents the activation of remote C–H bonds. Subsequently, Yu[75a–d] developed a template approach to activate remote *meta* C–H bonds of several different classes of substrates (Scheme 34). The detailed strategy was the installation of a linear "end-on" coordinative nitrile group which can be accommodated in a macrocyclic cyclophane-like pre-transitionstate, thus overcoming the inherent limitations of traditional directed *ortho* C–H activation. After the removal of the directing group, a series of 7-vinylquinoline derivates **100** and diacids **97**, which

[74] X. Zhang, Q. Zhu,Y. Zhang, Y. Li, Z.-J. Shi, *Chem. Eur. J.* **2013**, *19*, 11898–11903.

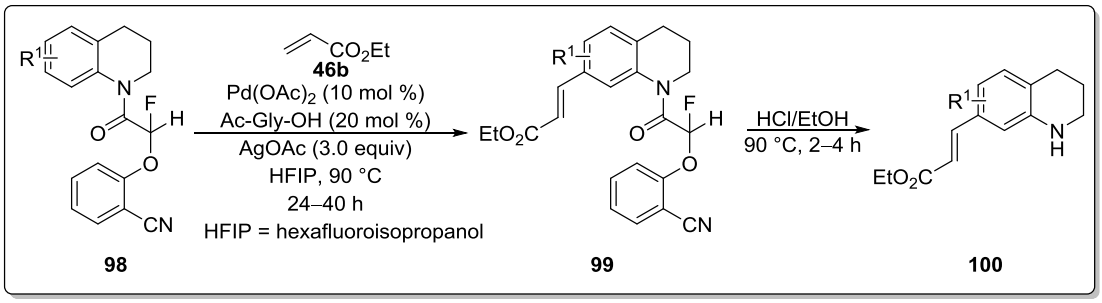
[75] (a) D. Leow, G. Li, T.-S. Mei, J.-Q. Yu, *Nature* **2012**,*486*, 518–522; (b) Y.-F. Yang, G.-J. Cheng, P. Liu, D. Leow, T.-Y. Sun, P. Chen, X. Zhang, J.-Q. Yu, Y.-D. Wu, K. N. Houk, *J. Am. Chem. Soc.* **2014**, *136*, 344–355;(c) R. Tang, G. Li, J.-Q. Yu, *Nature* **2014**, 215–220; (d) Y. Deng, J.-Q. Yu, *Angew. Chem. Int. Ed*. **2015**, *54*, 888–891; (e) For the review on this topic, see: (f) J. Yang, *Org. Biomol. Chem*.**2015**, *13*, 1930–1941.

are commonly used as building blocks in drug discovery, were obtained.

a)



b)



Scheme 34 Activation of remote *meta* C–H bonds assisted by an "end-on" template.

1.4 Transition Metal-Catalyzed C–H Functionalizations Assisted by Bidentate Directing Groups

As discussed above, chelation-assisted transition metal-catalyzed direct C–H functionalizations were considered to be an effective protocol for the formation of C–X (X = C, O, S, N, halides) bonds though a C–H cleavage. So far, a variety of heteroatom-containing directing groups such as pyridine, pyrimidine, oxazoline, amide, ester and ketone, were employed in these transformations. In this context, a number of catalytic systems aimed at C(sp^2)–H bonds functionalizations of arenes and heteroarenes have been developed. Additionally, in several cases the benzylic C(sp^3)–H bonds were also viable in these reactions.[76] However, the number of more challenging functionalizations of unactivated C(sp^3)–H bonds under these catalytic conditions still remains greatly limited.

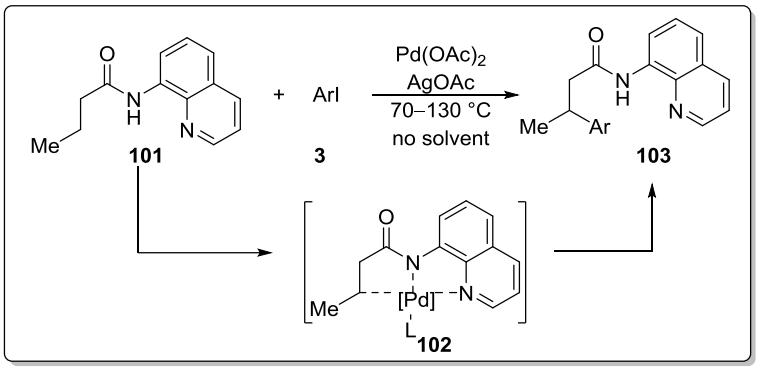
In 1993, van Koten[77] and coworkers found that bidentate coordination limits the degree of freedom of the ligand around the coordination sphere of the metal thus allowing one to govern the cyclo-palladation selectively toward C(sp^2)–H or C(sp^3)–H bond activation *via* five- or

[76] D. Shabashov, O. Daugulis, *Org. Lett*. **2005**, *7*, 3657–3659.

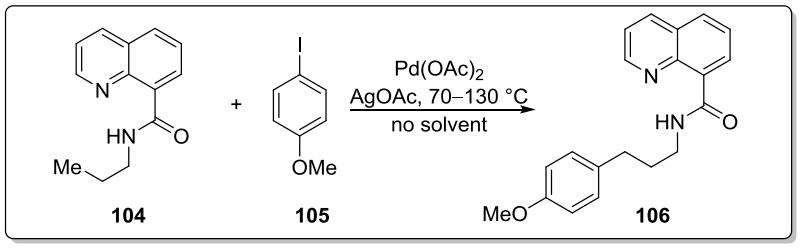
[77] P. L. Alsters, P. F. Engel, M. P. Hogerheide, M. Copijn, A. L. Spek, G. van Koten, *Organometallics* **1993**, *12*,1831–1844.

six-membered ring formation.

a)



b)



Scheme 35 Palladium-catalyzed direct C(sp^3)–H bonds arylation.

Inspired by this study, in 2005, Daugulis[78] realized and reported palladium-catalyzed direct C(sp^3)–H bond arylations assisted by 8-aminoquinoline-derived bidentate directing group, which surmounts the limitations of monodentates. This new process based on C(sp^3)–H activation allows for the β-arylation of carboxamides **101** (Scheme 35a) and *γ*-arylation of amine derivatives **104** (Scheme 35b) to afford the corresponding products **103** and **106**, respectively, in good yields. Remarkably, this palladium catalytic system was not only restricted to the C(sp^2)–H or C(sp^3)–H bond arylations, but also allowed for alkylations[79] alkynylations,[80] acetoxylations,[81] aminations,[82] iodinations[83] and selenations.[84] Importantly, ruthenium,[85] copper,[86] nickel,[87a,b]

[78] V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc*. **2005**, *127*, 13154–13155.

[79] (a) S. Zhang, Q. Li, G. He, W. A. Nack, G. Chen, *J. Am. Chem. Soc.* **2015**, *137*, 531–539; (b) S. Zhang, G. He, W. A. Nack, Y. Zhao, Q. Li, G. Chen, *J. Am. Chem. Soc*. **2013**, *135*, 2124−2127; (c) Y. Zhao, G. Chen, *Org. Lett*. **2011**, *13*, 4850–4853.

[80] (a) Y. Zhao, G. He, W. A. Nack, G. Chen, *Org. Lett.* **2012**, *14*, 2948−2951; (b) Y. Ano, M. Tobisu, N. Chatani, *Org. Lett.* **2012**, *14*, 354–357; (c) Y. Ano, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 12984–12986.

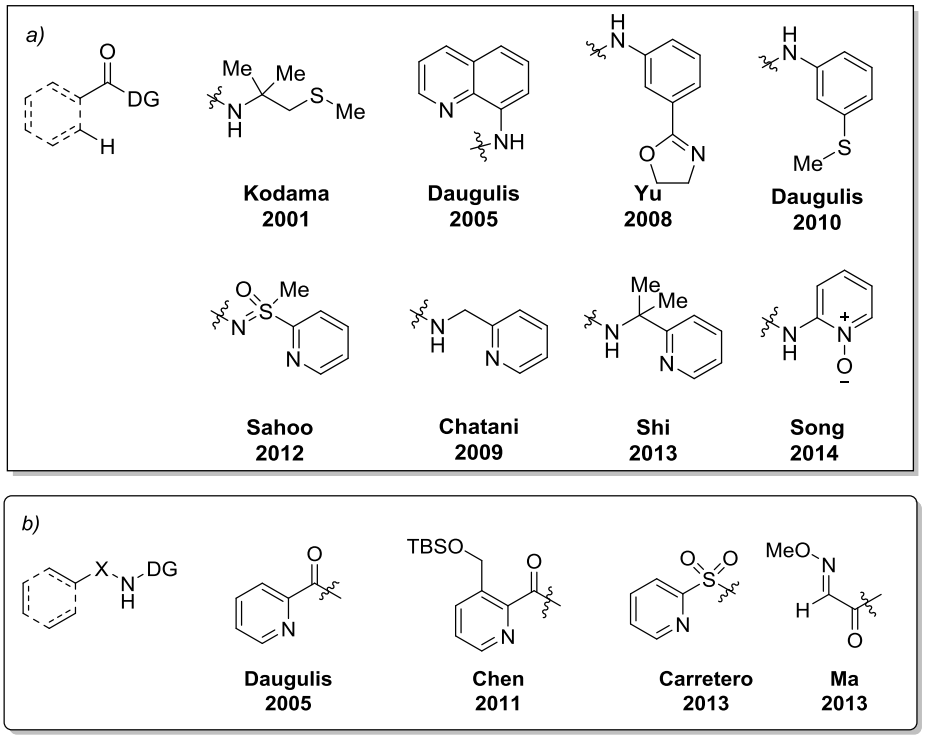
[81] (a) S. Zhang, G. He, Y. Zhao, K. Wright, W. A. Nack, G. Chen, *J. Am. Chem. Soc.* **2012**, *134*, 7313–7316; (b) R. K. Rit, M. R. Yadav, A. K. Sahoo, *Org. Lett.* **2012**, *14*, 3724–3727; (c) L. D. Tran, O. Daugulis, *Angew. Chem. Int. Ed*. **2012**, *51*, 5188–5191; (d) B. V. S. Reddy, L. R. Reddy, E. J. Corey, *Org. Lett.* **2006**, *8*, 3391–3394; (e) F. Gou, X. Wang, P. Huo, H. Bi, Z. Guan, Y. Liang, *Org. Lett.* **2009**, *11*, 5726–5729.

[82] (a) Y. He, C. Zhang, M. Fan, Z. Wu, D. Ma, *Org. Lett.* **2015**, *17*, 496–499; (b) G. He, Y. Zhao, S. Zhang, C. Lu, G. Chen. *J. Am. Chem. Soc*. **2012**, *134*, 3−6; (c) E. T. Nadres, O. Daugulis, *J. Am. Chem.Soc.* **2012**, *134*, 7−10.

[83] H. Kodama, T. Katutira, T. Nishida, T. Hino, K. Tsubata, **2001**, Patent WO 2001083421A

[84] M. Iwasaki, Y. Tsuchiya, K. Nakajima, Y. Nishihara, *Org. Lett*. **2014**, *16*, 4920−4923.

rhodium[88c] and iron[88] catalysts were also found to be applicable in this bidentate-assisted catalytic system, meanwhile, variety of bidentate directing groups were introduced for this C–H functionalization (Scheme 36).



Scheme 36 Representative bidentate directing groups developed in recent years.

In 2014, Ackermann and coworkers[89] found easily accessible 1,2,3-triazoles **107** which are available in a modular fashion can also serve as the bidentate directing group for the iron-catalyzed arylation reactions. With this catalytic system, benzamides substrates bearing differently substituted groups direct transformed efficiently under a considerably mild reaction conditions. Importantly, alkenylic substrate was also compatiable and delivering the thermodynamically less-stable Z-olefin as the sole product. It is noteworthy that the user-friendly iron catalyst was not limited to C(sp^2)–H arylations of arenes, but also enabled more challenging C(sp^3)–H functionalizations (Scheme 37).

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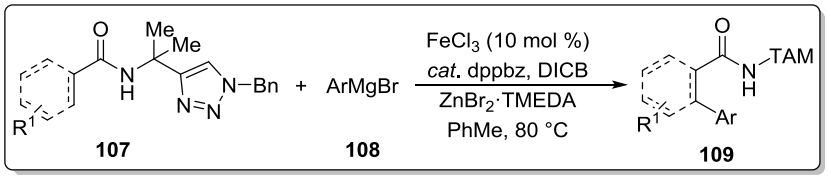
[85] (a) G. Rouquet, N. Chatani, *Chem. Sci*. **2013**, *4*, 2201–2208; (b) S. Inoue, H. Shiota, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc*. **2009**, *131*, 6898–6899.

[86] (a) Y. Liu, Y. Liu, X. Yin, W. Gu, B. Shi, *Chem. Eur. J*. **2015**, *21*, 205–209; (b) Z. Wang, J. Ni, Y. Kuninobu, M. Kanai, *Angew. Chem. Int. Ed.* **2014**, *53*, 3496–3499; (c) W. Zhu, D. Zhang, N. Yang, H. Liu, *Chem. Commun*. **2014**, *50*, 10634−10636; (d) J. Dong, F. Wang, J. You, *Org. Lett*. **2014**, *16*, 2884−2887.

[87] (a) X. Wu, Y. Zhao, H. Ge, *Chem. Eur. J*. **2014**, *20*, 9530–9533; (b) H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc*. **2011**, *133*, 14952–14955; (c) K. Shibata, N. Chatani, *Org. Lett*. **2014**, *16*, 5148–5151.

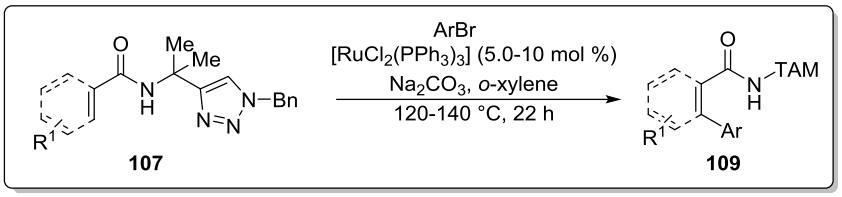
[88] (a) L. Ilies, T. Matsubara, S. Ichikawa, S. Asako, E. Nakamura, *J. Am. Chem. Soc*. **2014**, *136*, 13126−13129; (b) E. R. Fruchey, B. M. Monks, S. P. Cook, *J. Am. Chem. Soc*. **2014**, *136*, 13130−13133.

[89] Q. Gu, H. H. Al Mamari, K. Graczyk, E. Diers, L. Ackermann, *Angew. Chem. Int. Ed*. **2014**, *53*, 3868–3871.



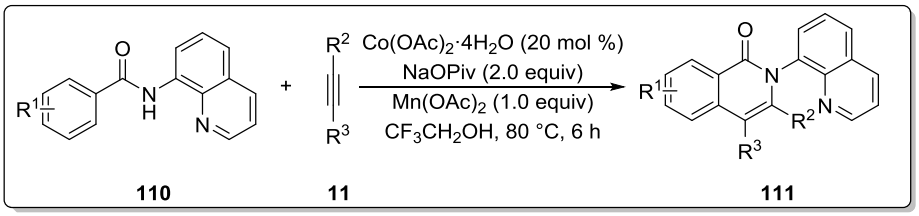
Scheme 37 Iron-catalyzed C–H arylations directed by TAM.

Although the iron-catalyzed C(sp^2)–H and C(sp^3)–H alkylations achieved in high yields with broad substrate scope, these transformations inolve using of expensive diphosphine ligand, stoichiometric amounts of sacrificial oxidants which make this reaction not in a economically fashion. What's more, the using of highly reactive Grignard reagents as the arylating reagent led a lower functional group tolerance. Therefore, Ackermann's group [90] developed ruthenium-catalyzed alkylations with the TAM (triazolyldimethylmethyl) directing groups. The ruthenium(II) catalyzed C–H functionalization protocol was applicable to user-friendly aryl bromides as the arylating reagents under mild reaction conditions which allowed chemoselective C–H arylations of TAM amides bearing variety of functional groups (Scheme 38).



Scheme 38 Ruthenium-catalyzed arylations directed by TAM.

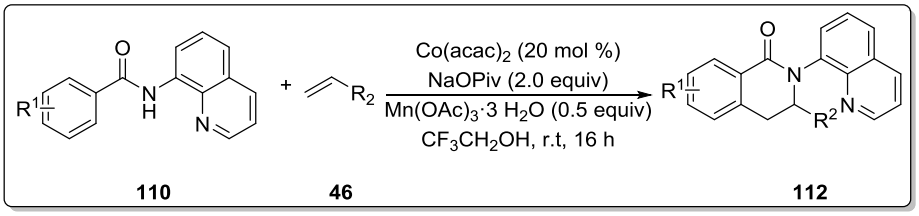
Very recently, Daugulis and coworkers reported on the cobalt(II)-catalyzed alkyne annulations assisted by bidentate directing group in the presence of $Mn(OAc)_2$ as the oxidant (Scheme 39).[91] Electron-rich or electron-poor, amides **110** were efficiently annulated, and a large variety of alkynes could be employed. Additionally, heteroarene-substituted amides **11** were also suitable in this cobalt catalyzed system. It is noteworthy that terminal alkynes **11** were reactive and gave the product in good yields with excellent chemo- and regioselectivity.



Scheme 39 Cobalt-catalyzed oxidative alkyne annulations of amides **110**.

[90] H. H. Al Mamari, E. Diers, L. Ackermann, *Chem. Eur. J.* **2014**, *20*, 9739–9743;
[91] L. Grigorjeva, O. Daugulis, *Angew. Chem. Int. Ed.* **2014**, *53*, 10209–10212.

Shortly thereafter, the same research group extended the scope of this reaction to alkenylations using an analogous method.[92] These transformations proceeded efficiently at ambient temperature with good functional groups tolerance. Importantly, unactivated alkenes such as ethylene and cyclopentene were also reactive in this reaction (Scheme 40).



Scheme 40 Cobalt-catalyzed oxidative alkenylations of amides **110**.

1.5 Transition Metal-Catalyzed Benzophosphole Syntheses

Phosphorus-containing heterocycles represent important structural building blocks in organic synthesis, medicinal chemistry, and material science.[93] They have been found widespread applications ranging from ligands in transition metal complexes[94] to organic semiconductor devices in material science.[95] Particularly, benzophosphole derivatives have been extensively studied because of their unique optical and electronic properties. Representative examples of useful benzophospholes include *n*-type molecular material di(benzo[*b*]phosphole oxide)benzene (DBPOB, **113**), electron-transporting material (ETM) di(benzo[*b*]phosphole) sulfide(DBPSB, **114**)[96] and highly luminescent π-conjugated materials **115**.[97] Therefore, there is a continued strong demand for chemo-and site-selective syntheses of this heteroaromatic scaffold.

[92] L. Grigorjeva, O. Daugulis, *Org. Lett*. **2014**, *16*, 4684−4687.

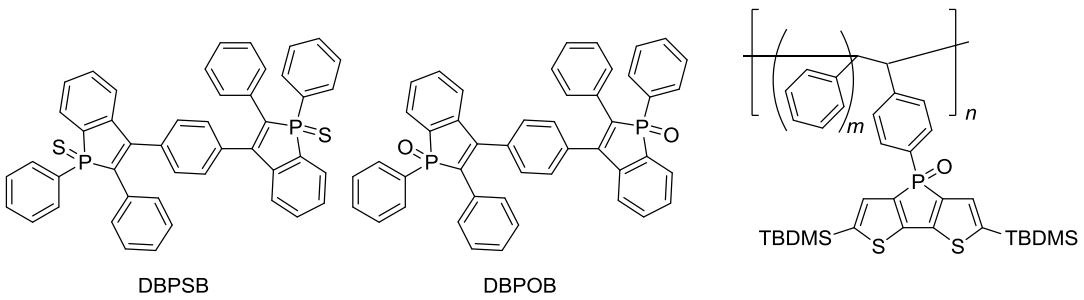
[93] For a recent review, see: (a) T. Baumgartner, *Acc. Chem. Res.* **2014**, *47*, 1613−1622; (b). M. Stolar, T. Baumgartner, *Chem. Asian J*. **2014**, *9*, 1212–1215; (c) T. Baumgartner, R. Réau, *Chem. Rev.* **2006**, *106*, 4681−4727; (d) F. Mathey, *Angew. Chem. Int. Ed*. **2003**, *42*, 1578–1604. For selected examples, see: (e) X. He, A. Y. Y. Woo, J. Borau-Garcia, T. Baumgartner, *Chem. Eur. J*. **2013**, *19*, 7620–7630; (f) Y. Ren, T. Baumgartner, *J. Am. Chem. Soc*. **2011**, *133*, 1328–1340; (g) Y. Matano, A. Saito, T. Fukushima, Y. Tokudome, F. Suzuki, D. Sakamaki, H. Kaji, A. Ito, K. Tanaka, H. Imahori, *Angew. Chem. Int. Ed*. **2011**, *50*, 8016–8020; (h) Y. Ren, W. H. Kan, M. A. Henderson, P. G. Bomben, C. P. Berlinguette, V. Thangadurai, T. Baumgartner, *J. Am. Chem. Soc*. **2011**, *133*, 17014–17026; (i) T.Sanji, K. Shiraishi, M. Tanaka, *Org. Lett.* **2007**, *9*, 3611–3614.

[94] (a) L. Weber, *Angew. Chem., Int. Ed*. **2002**, *41*, 563–572; (b) L. Ackermann, A. R. Kapdi, C. Schulzke, *Org. Lett.* **2010**, *12*, 2298–2301; (c) L. Ackermann, R. Vicente, N. Hofmann, *Org. Lett.* **2009**,*11*, 4274–4276.

[95] J. Casado, R. Reau, J. T. L. Navarrete, *Chem.Eur. J.* **2006**, *12*, 3759–3767.

[96] H. Tsuji, K. Sato, Y. Sato, E. Nakamura, *J. Mater. Chem.* **2009**, *19*, 3364–3366.

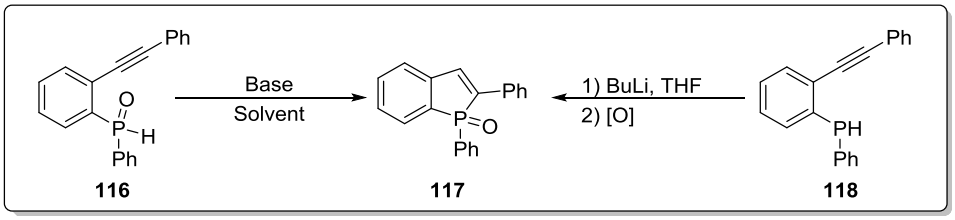
[97] T. Baumgartner, T. Neumann, B. Wirges, *Angew. Chem. Int. Ed.* **2004**, *43*, 6197–6201.



113 **114** **115**

Scheme 41 Selected functional material structures of benzophosphole derivatives.

In 1971, Mislow and coworkers[98] reported the first route for the synthesis of benzophospholes **117**. However, this multistep method not only involved metalation of a P–X bond with a stoichiometric amount of organolithium or organomagnesium species, but also delivered the desired product in low yield. Subsequently, Winter,[99] Berr,[100] Nakamura[101] and Tanaka[102] developed several similar protocols for the synthesis of decorated benzophospholes **117** consisting of the cyclization of diphenylphosphinoxides **116** or diphenylphosphines **118** with alkynyl groups preinstalled in the *ortho* position (Scheme 42). However, these cyclization reactions were performed under strongly basic reaction conditions which reduced the functional group tolerance.

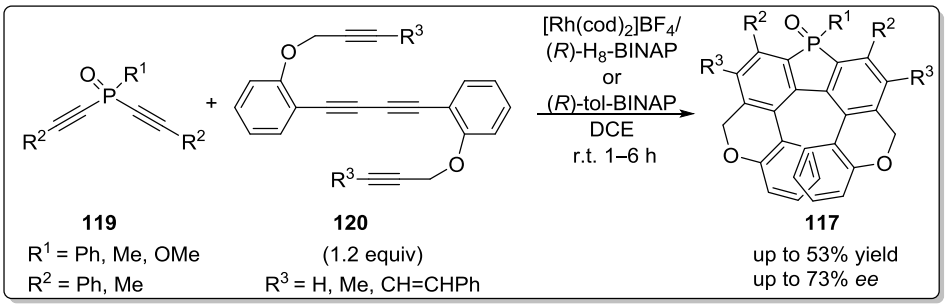


116 **117** **118**

Scheme 42 Preparation of benzophospholes **117** under strong basic conditions.

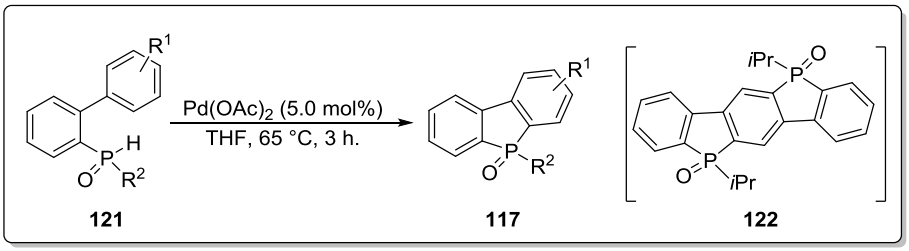
In order to address these drawbacks, Tanaka's group[103] developed a rhodium-catalyzed asymmetric synthesis of benzopyrano- or naphthopyrano-fused helical phosphafluorenes *via* double [2+2+2] cycloaddition of dialkynyl phosphorus compounds **119** with phenol- or naphthol-linked tetraynes **120** (Scheme 43). These reactions proceeded in CH_2Cl_2 at ambient temperature to give the product in acceptable yield with good enantioselectivities. Importantly, the phosphafluorene compounds possess special photophysical properties which can be potentially applied to organic semiconducting material.

[98] W. Egan, R. Tang, G. Zon, K. Mislow, *J. Am. Chem. Soc.* **1971**, *94*, 6205–6216.
[99] W. Winter, *Tetrahedron Lett.* **1975**, *45*, 3913–3914.
[100] G. Märkl, G. Y. Jim, K.-P. Berr, *Tetrahedron Lett*. **1993**, *34*, 3103–3106.
[101] H. Tsuji, K. Sato, L. Ilies, Y. Itoh, Y. Sato, E. Nakamura, *Org. Lett*. **2008**, *10*, 2263–2265.
[102] T. Sanji, K. Shiraishi, T. Kashiwabara, M. Tanaka, *Org. Lett*. **2008**, *10*, 2689–2692.
[103] N. Fukawa, T. Osaka, K. Noguchi, K. Tanaka, *Org. Lett*. **2010**, *12*, 1324–1327.



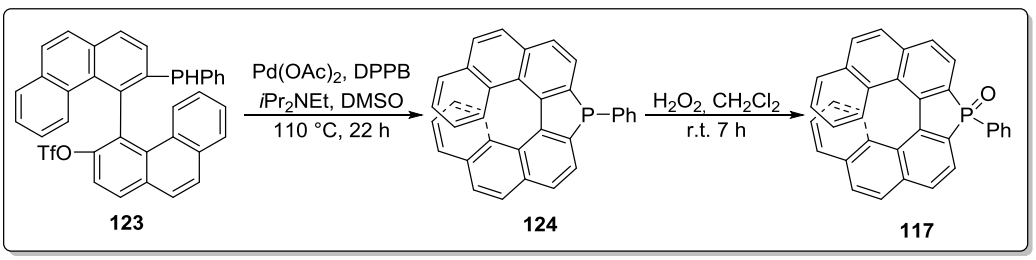
Scheme 43 Rhodium-catalyzed enantioselective synthesis of fused helical phosphafluorenes **117**.

Shortly thereafter, Takai[104] developed a new protocol for the synthesis of dibenzophosphole oxides catalyzed by palladium (Scheme 44). This reaction successfully transformed P–H and C–H bond *via* intramolecular dehydrogenative cyclization under mild reaction conditions, which tolerated a wide range of functional groups. Especially, the chloride- and thiophene-substituted substrates were also compatible under this catalytic system and afforded the desired products in high yields. Additionally, more complicated molecules such as ladder-type dibenzophosphole oxides **122** were synthesized using this method.



Scheme 44 Palladium-catalyzed intramolecular dehydrogenative cyclization reactions.

Encouraged by Takai's study, Nozaki[105] reported on palladium-catalyzed intramolecular arylation reaction of phosphine triflate **123**. After the final oxidation with H_2O_2 at ambient temperature, the desired dibenzophosphole products were obtained in high yields (Scheme 45). It is noteworthy that the λ^5-phospha[7]helicenes **117** obtained by this method exhibited unique packing structure.

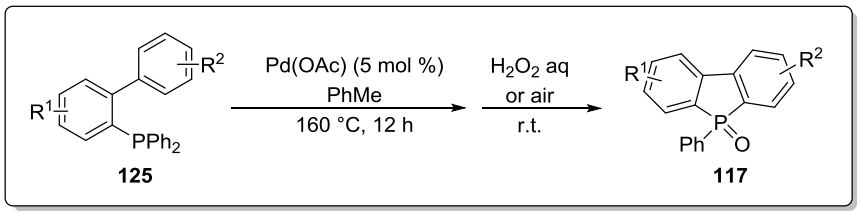


Scheme 45 Synthesis of λ^5-phospha[7]helicenes **117**.

[104] (a) Y. Kuninobu, T. Yoshida, K. Takai, *J. Org. Chem*. **2011**, *76*, 7370–7376; (b) Y. Kuninobu, K. Origuchi, K. Takai, *Heterocycles*. **2012**, *85*, 3029–3034.

[105] K. Nakano, H. Oyama, Y. Nishimura, S. Nakasako, K. Nozaki, *Angew. Chem. Int. Ed*. **2012**, *51*, 695–699.

However, the instability of the hydrophosphine group in **123** limited the applicability of this method towards the synthesis of more complicateds compound. Thus, this method needs considerable improvement. In this context, in 2013, Chatani[106] reported the palladium-catalyzed direct synthesis of phosphole derivatives from stable triarylphosphines **125** through cleavage of C–H and C–P bonds (Scheme 46). A wide range of substrates bearing ether, amine, ketone, ester, nitrile, and fluoride substituents worked very well in this reaction. Particularly, the chlorides and bromides were also well tolerated, thus can serve as handles for further structural modification of the useful phosphole skeleton **117**.



Scheme 46 Palladium-catalyzed direct synthesis of phosphole derivatives from triarylphosphines **125**.

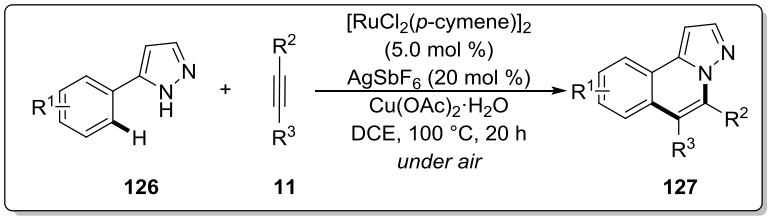
.

[106] K. Baba, M. Tobisu, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11892–11895.

2. Objectives

During recent years, remarkable progress was achieved in transition metal-catalyzed C−H bond functionalization. Among such methods, oxidative C−H bond functionalizations are particularly attractive because they bypass the need for preactivated reaction partners. For example, oxidative annulations that involve sequential C−H and Het−H bond cleavages allow for the modular assembly of regioselectively decorated heterocycles. These structures are key motifs of natural products, functional materials and pharmaceutical drugs.[107] Whereas other researchers have devised relatively expensive palladium or rhodium[54v, 108] complexes for oxidative alkyne annulations, this project focused on the application of significantly less expensive, yet robust ruthenium complexes.

Rhodium-catalyzed oxidative alkyne annulation with pyrazoles has been reported in 2011.[109] Undesired heavy metal salt as by-product resulted from stoichimetric amounts of copper(II) salt as the sacrificial oxidant, which made this catalytic system to work not in an atom economical fashion. Importantly, that attempts to activate heteroaryl C−H bonds by rhodium(III) catalyst only resulted in low yields. Therefore, we became interested in ruthenium-catalyzed oxidative alkyne annulations with substituted 1*H*-pyrazoles **126** (Scheme 47).



Scheme 47 Ruthenium-catalyzed oxidative annulations with substituted pyrazoles **126**.

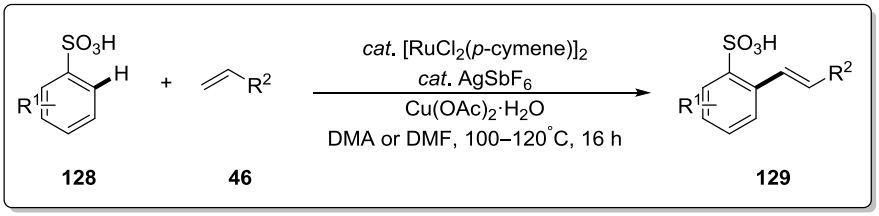
As mentioned above, transition metal-catalyzed alkenylations of arenes became an attractive tool for the preparation of styrene derivatives. Prompted by the results on rhodium-catalyzed oxidative

[107] Selected reviews: (a) Y. L. Janin, *Chem. Rev*. **2012**, *112*, 3924–3958; (b) J. Elguero, A. M. S. Silva, A. C. Tomé, in *Modern Heterocyclich Chemistry* (Eds.: J.Alvarez-Builla, J. J.Vaquero, J. Barluenga), Wiley-VCH, Weinheim, **2011**, Vol. 2, pp 635–725; (c) S. Fustero, M. Sanchez-Rosello, P.Barrio, A. Simon-Fuentes, *Chem. Rev.* **2011**, *111*, 6984–7034.

[108] Reviews: (a) G. Song, F. Wang, X. Li, *Chem. Soc. Rev*. **2012**, *41*, 3651–3678; (b) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta*, **2012**, *45*, 31–41; (c) J. Wencel-Delord, T. Droege, F. Liu, F. Glorius, *Chem. Soc. Rev*. **2011**, *40*, 4740–4761; (d) T. Satoh, M. Miura, *Chem., Eur. J*. **2010**, *16*, 11212–11222, and references cited therein. Selected examples: (e) N. Umeda, K. Hirano, T. Satoh, N. Shibata, H. Sato, M. Miura, *J. Org. Chem*. **2011**, *76*, 13–24; (f) D. R.Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc*. **2008**, *130*, 16474–16475; (g) K. Ueura, T. Satoh, M. Miura, *J. Org. Chem*. **2007**, *72*, 5362–5367.

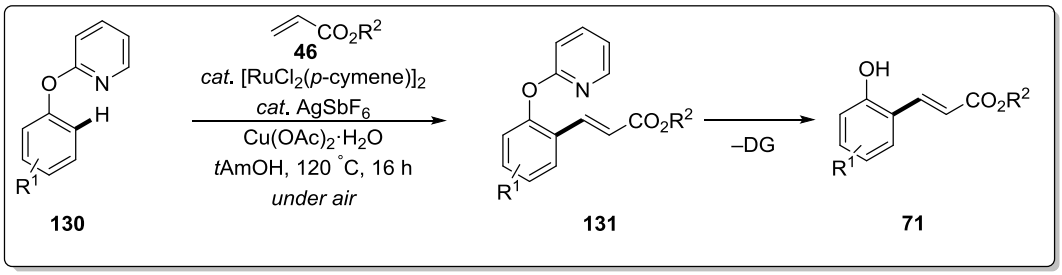
[109] X. Li, M. Zhao, *J. Org. Chem*. **2011**, *76*, 8530–8536.

alkenylations of arenes assisted by sulfonic acid directing group,[110] we explored the alternative ruthenium-catalyzed alkenylations with arylsulfonic acids **128**, which also expanded the synthetic utility of ruthenium catalytic systems.[111] These reactions were carried out by using $Cu(OAc)_2 \cdot H_2O$ as oxidant in DMA or DMF as a solvent (Scheme 48).



Scheme 48 Ruthenium-catalyzed oxidative alkenylations with substituted 2-arylsulfonic acids **128**.

In the transition metal-catalyzed alkenylations, directing groups were usually introduced to achieve site-selective C–H functionalization.[54] However, the commonly applied directing groups are usually difficult to remove or modify under mild conditions. Herein, we devised ruthenium-catalyzed oxidative alkenylations with 2-aryloxypyridines **130**[112a–c] as a preparative approach to the synthetically valuable alkenylated phenols **78**[112d,e] in the third part of this work.



Scheme 49 Ruthenium-catalyzed oxidative alkenylations with substituted 2-aryloxypyridines **130**.

The last few decades have witnessed significant progress in the area of transition metal-catalyzed C−H bond functionalization. However, most of the catalytic processes employ scarce second-row transition metal catalysts. The development of catalysts based on earth-abundant first-row transition metals that allow mild C−H functionalization are still in challenge.[1c, 113] Thus, we became attracted by cobalt-catalyzed C–H/N–H functionalization reactions of substituted benzamides **110** with activated alkenes **46** (Scheme 50).

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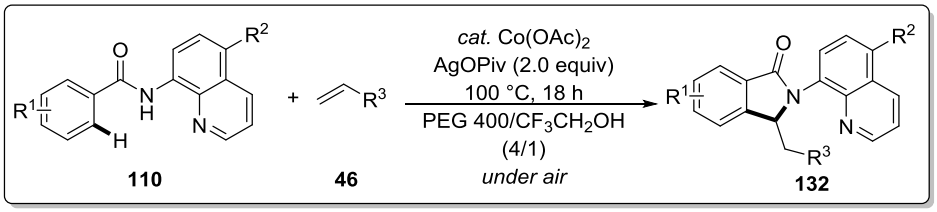
[110] Y. Dong, G. Liu, *Chem. Commun.* **2013**, *49*, 8066–8068.

[111] W. Ma, R. Mei, G. Tenti, L. Ackermann, *Chem. Eur. J.* **2014**, *20*, 15248–15251.

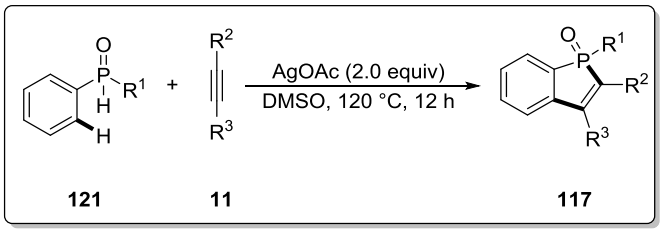
[112] (a) W. Ma, L. Ackermann, *Chem. Eur. J.* **2013**, *19*, 13925–13928. For the further synthetic development of this strategy and analogous palladium-catalyzed alkenylations, see: (b) H. Kinuta, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2015**, *137*, 1593–1600; (c) B. Liu, H.-Z. Jiang, B.-F. Shi, *J. Org. Chem.* **2014**, *79*, 1521–1526. Representative transformations of **71**: (d) D. A. Barancelli, A. G. Salles, Jr. J. G. Taylor, C. R. D. Correia, *Org. Lett.* **2012**, *14*, 6036–6039; (e) C. E. Henry, O. Kwon, *Org. Lett.* **2007**, *9*, 3069–3072.

[113] Recent reviews more: (a) B. Su, Z.-C. Cao, Z.-J. Shi, *Acc. Chem. Res.* **2015**, *48*, 886–896; (b) L. Ackermann, *J. Org. Chem.* **2014**, *79*, 8948–8954.



Scheme 50 Cobalt-catalyzed oxidative functionalizations with benzamides **110**.

The preparation of benzophosphole derivatives **117** mainly relied on the cyclization of phenylphosphoric compounds with alkynyl groups being preinstalled in the *ortho* position. However, these precursors are usually synthesized through complicated multistep preparations. Therefore, the silver-mediated C–H/P–H bonds functionalization reactions of substituted phosphine oxides **121** with alkynes **11** could be the most ideal strategy for the convenient benzo[*b*]phosphole oxide synthesis (Scheme 51).



Scheme 51 Silver-mediated alkyne annulation with substituted phosphinates and aryl-substituted SPOs.

Result and Discussion

3 Ruthenium (II)-Catalyzed Alkyne Annulation with Aryl-substituted 1*H*-Pyrazoles by C–H/N–H Functionalizations

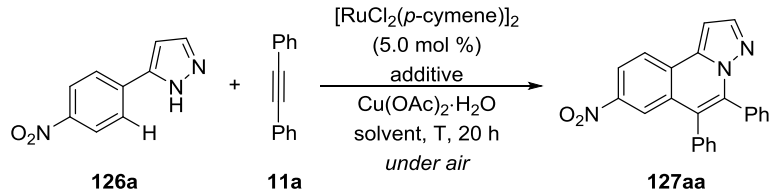
Pyrazole derivatives are an important class of compounds, because of their wide applications in organic synthesis, pharmaceutical chemistry and material science. Especially they play an important role in organometallic chemistry and in catalysis as they have been employed as precursors for *N*-heterocyclic carbenes.[114] Several synthetic methodologies for the construction of these pyrazole derivatives have been developed in the past decades, particularly, reactions that involve the sequential functionalization of C–H and N–H bonds. Unfortunately, as of yet these transformations have mostly relied on the use of rhodium complexes. Conversely, significantly less expensive ruthenium(II) complexes were only very recently identified as catalysts for alkenylations and annulations *via* oxidative C–H bond functionalizations.

3.1. Optimization Studies

Initially, we chose 5-arylpyrazole **126a** and diphenylacetylene (**11a**) as model substrates to optimize the reaction conditions (Table 1). The results summarized in entries 1–8 showed that the reaction was most efficient with $AgSbF_6$ as an additive, giving the desired product in 78% yield (entry 8). The carboxylate additives such as NaOAc, $MesCO_2K$ CsOAc were not effective, and only gave the product in low yield. We were pleased to find that nearly the same yield can be obtained by using 1.0 equivalence of $Cu(OAc)\cdot H_2O$ in the presence of air (entry 9). Likewise, the desired oxidative annulation was not accomplished with $CuBr_2$ in lieu of $Cu(OAc)_2\cdot H_2O$ as the terminal oxidant, thereby indicating the importance of carboxylate assistance (entry 10). Upon further screening of a variety of protic and aprotic solvents, DCE was identified as being the optimal reaction medium, whereas *t*AmOH only afforded the desired product in a moderate yield (entries 12–17). Control experiments showed that the catalytic reaction was completely inactive in the absence of the catalyst (entry 11).

[114] (a) R. Jothibasu, H. V. Huynh, *Chem. Commun*. **2010**, *46*, 2986–2988; (b) W. A. Herrmann, J. Schuetz, G. D. Frey, E. Herdtweck, *Organometallics* **2006**, *25*, 2437–2448. For a recent review, see: (c) O. Schuster, L. R. Yang, H. G. Raubenheimer, M. Albrecht, *Chem. Rev*. **2009**, *109*, 3445–3478.

Table 1 Optimization of oxidative annulation with pyrazole **126a**[a]



Entry	Additive	Solvent	T (°C)	Yield (%)
1	–	DCE	100	13
2	NaOAc	DCE	100	19
3	CsOAc	DCE	100	6
4	KO_2CMes	DCE	100	16
5	KPF_6	DCE	100	30
6	$AgSO_3CF_3$	DCE	100	38
7	$AgBF_4$	DCE	100	46
8	**$AgSbF_6$**	**DCE**	**100**	**78**
9	**$AgSbF_6$**	**DCE**	**100**	**77[b]**
10	$AgSbF_6$	DCE	100	0[c]
11	$AgSbF_6$	DCE	100	0[d]
12	$AgSbF_6$	NMP	120	0
13	$AgSbF_6$	*t*-AmOH	120	41
14	$AgSbF_6$	*o*-xylene	120	12
15	$AgSbF_6$	1,4-dioxane	120	17
16	$AgSbF_6$	DMF	120	0
17	$AgSbF_6$	H_2O	120	13

[a] Reaction conditions: **126a** (0.5 mmol), **11a** (1.0 mmol), $Cu(OAc)_2·H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), solvent (2.0 mL), additive (20 mol %); isolated yields. [b] 1.0 equiv of oxidant. [c] $CuBr_2$ as oxidant. [d] No catalyst.

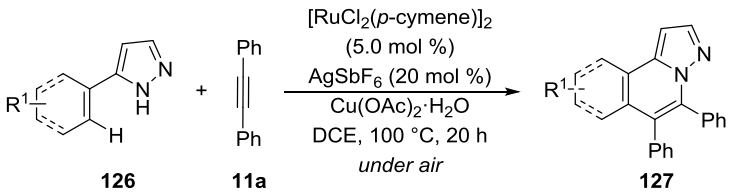
3.2 Scope of the Ruthenium-Catalyzed Oxidative Alkyne Annulations

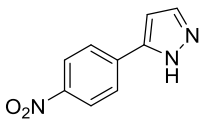
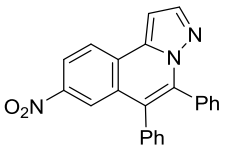
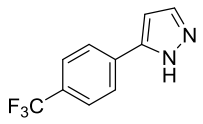
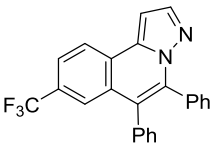
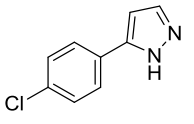
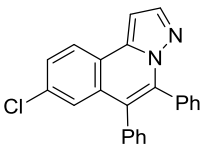
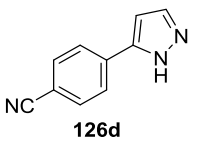
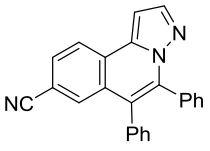
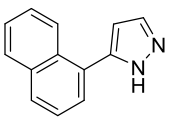
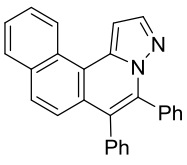
3.2.1 Ruthenium-Catalyzed Annulations with Arylsubstituted Pyrazoles

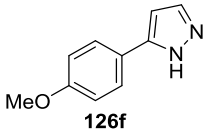
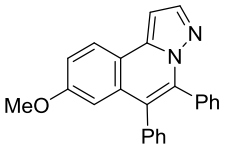
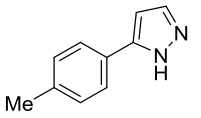
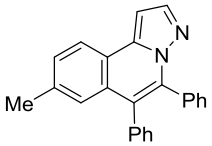
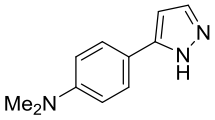
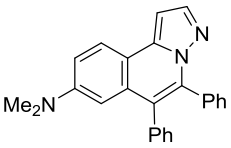
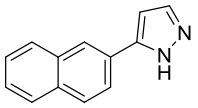
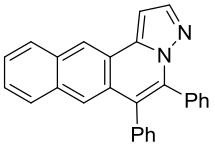
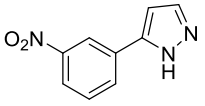
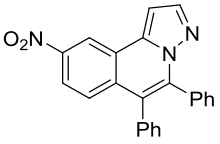
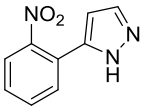
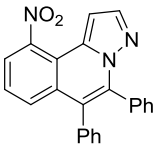
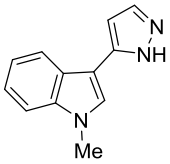
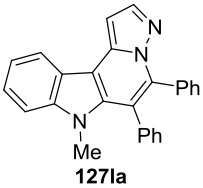
With the optimized catalytic system in hand, the reaction scope with respect to arylpyrazole **126** was investigated by using diphenylactylene (**11a**) as the standard coupling partner. To our delight, the catalyst was widely applicable, and thus, proved to be tolerant of various important functional groups (Table 2). Regardless of the electron-rich groups such as metoxy and amino (entries 6 and 8) or the electron-withdrawing groups, such as nitro-, trifluoro-**,** chloro- or cyano-substituted substrates (entries 1–4), in the *para* position of the 5-arylpyrazoles **126**, all of the annulations gave the anticipated results with good to excellent yields. On the other hand, arenes bearing electron-withdrawing substituents were found to be significantly more reactive. The oxidative

functionalizations of *meta*-substituted arenes **126i** and **126j** proceeded with excellent site selectivities at the less sterically encumbered C−H bond (entries 9 and 10). However, *ortho*-substituted substrates, such as compound **126k,** were not compatible in this reaction (entry 11). The cationic ruthenium(II) catalyst was not restricted to the use of aryl-substituted pyrazole derivatives, but efficiently converted heteroaromatic pyrazole (**126l**) as well (entry 12). Importantly, employment of rather expensive rhodium(III) catalyst in these annulations only resulted in unsatisfactory low yields.

Table 2 Oxidative annulation of diphenylacetylene **11a** with pyrazoles **126a**[a]



Entry	Pyrazole 126	Product 127	Yield (%)
1	 **126a**	 **127aa**	77
2	 **126b**	 **127ba**	70
3	 **126c**	 **127ca**	69
4	 **126d**	 **127da**	66
5	 **126e**	 **127ea**	76

6	 **126f**	 **127fa**	57
7	 **126g**	 **127ga**	42
8	 **126h**	 **127ha**	60
9	 **126i**	 **127ia**	70
10	 **126j**	 **127ja**	43
11	 **126k**	 **127ka**	0
12	 **126l**	 **127la**	58

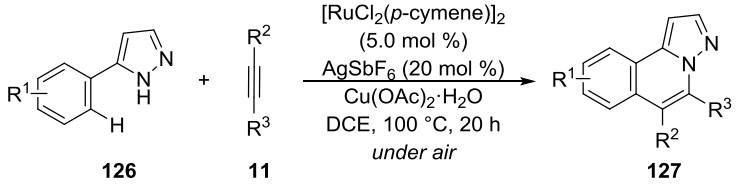
[a] Reaction conditions: **126** (0.50 mmol), **11a** (1.00 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), DCE (2.0 mL), and $AgSbF_6$ (20 mol %); isolated yields.

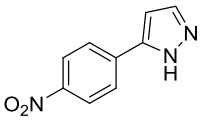
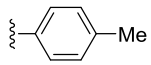
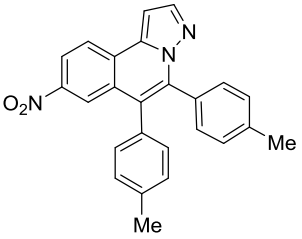
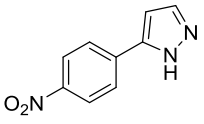
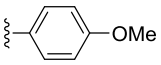
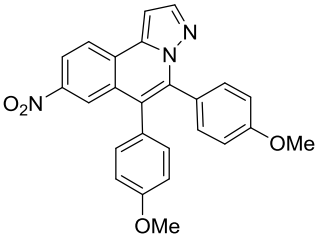
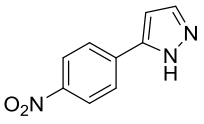
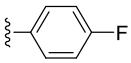
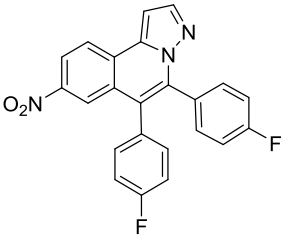
3.2.2 Scope of the Annulation with Different Alkynes

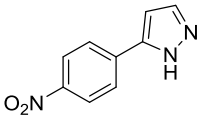
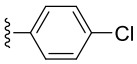
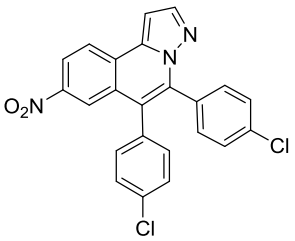
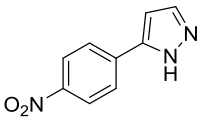
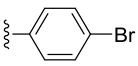
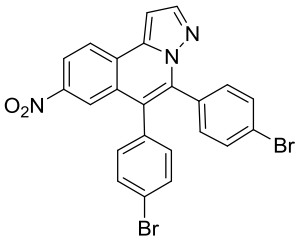
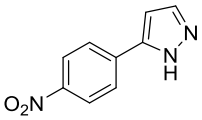
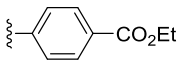
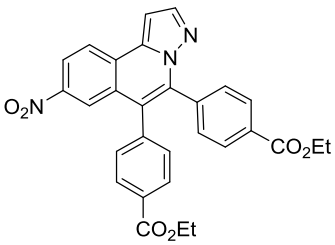
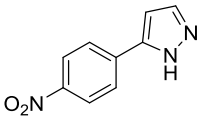
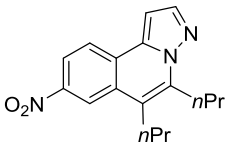
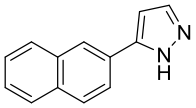
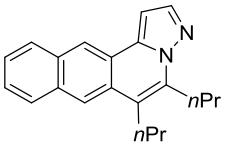
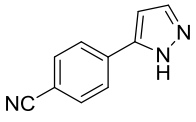
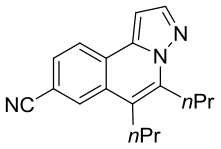
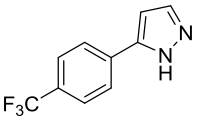
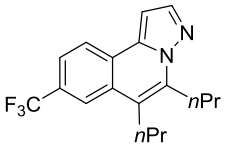
Thereafter, we probed different tolane derivatives **11** in the oxidative annulation reactions. Thus,

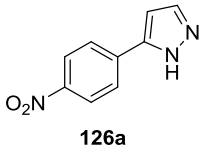
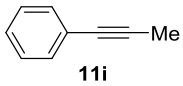
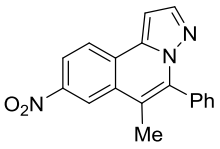
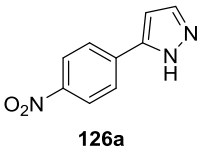
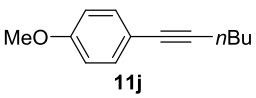
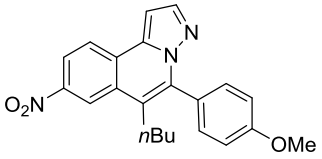
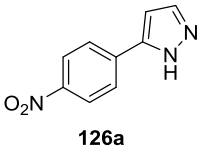
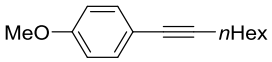
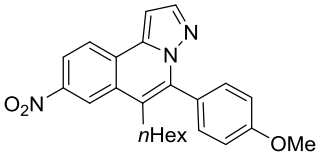
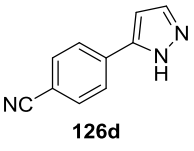
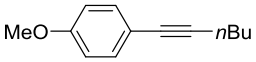
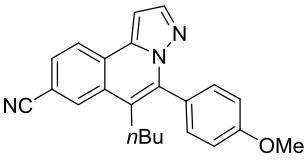
electron-rich groups such as methoxyl (**11c**) and electron-deficient ones such as fluoro (**11d**), chloro (**11e**), and ester (**11g**), diphenylacetylences reacted with pyrazole **126a** smoothly to afford the corresponding product **127ac, 127ad, 127ae** and **127ag**, respectively, in good yields (entries 2–4, 6). However, methyl- and bromo-decorated tolanes **11b** and **11f** were less efficiently converted and gave only moderate yields (entries 1 and 5). Additionally, the ruthenium catalyst was not limited to the use of tolane derivatives but was also found to be applicable to aliphatic alkynes, such as oct-4-yne (**11h**). Treatment of these aliphatic alkynes with differently decorated pyrazoles afforded the annulation products in 46–65% yield (entries 7–10). Unsymmetrically substituted alkynes **11i**–**11k** displayed good regioselectivities, thereby furnishing the products **127ai**–**127ak** and **127dj** in high isolated yields (entries 11–14).

Table 3 Scope of oxidative annulations of alkynes **11** with pyrazoles **126**



Entry	Pyrazole 126	Alkyne 11	Product 127	Yield(%)
1	 **126a**	$R^2 = R^3 =$  **11b**	 **127ab**	41
2	 **126a**	$R^2 = R^3 =$  **11c**	 **127ac**	76
3	 **126a**	$R^2 = R^3 =$  **11d**	 **127ad**	59

4	 **126a**	$R^2 = R^3 =$  **11e**	 **127ae**	54
5	 **126a**	$R^2 = R^3 =$  **11f**	 **127af**	42
6	 **126a**	$R^2 = R^3 =$  **11g**	 **127ag**	59
7	 **126a**	**11h**	 **127ah**	46
8	 **126i**	**11h**	 **127ih**	61
9	 **126d**	**11h**	 **127dh**	52
10	 **126b**	**11h**	 **127bh**	65

11	 **126a**	 **11i**	 **127ai**	50
12	 **126a**	 **11j**	 **127aj**	72
13	 **126a**	 **11k**	 **127ak**	63
14	 **126d**	 **11j**	 **127dj**	68

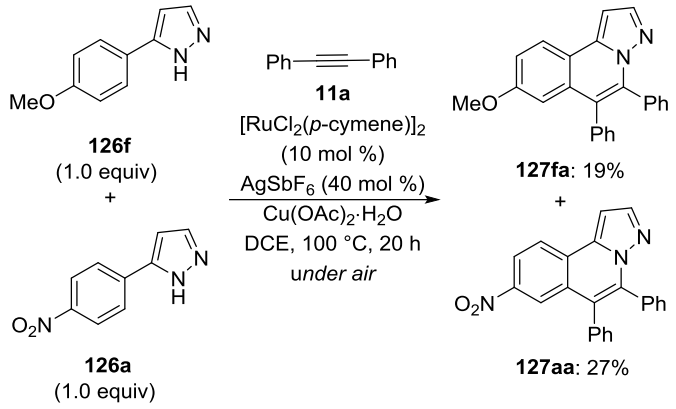
[a] Reaction conditions: **126** (0.5 mmol), **11** (1.0 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), DCE (2.0 mL) and $AgSbF_6$ (20 mol %); isolated yields.

3.3 Mechanistic Studies

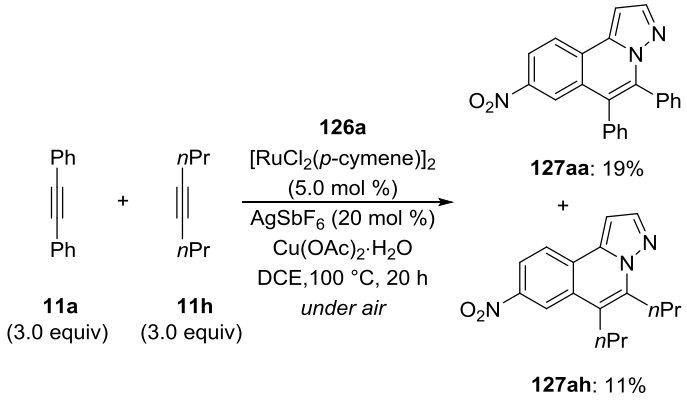
3.3.1 Intermolecular Competition Experiments

Given the remarkable catalytic activity of the ruthenium(II) catalyst, its mode of action was also studied in detail. To this end, intermolecular competition experiments between two different substituted arylpyrazoles showed that the electron-deficient substrate **126a** was more reactive than the electron-rich one **126f** (Scheme 52a), in contrast to the recently reported rhodium-catalyzed annulation process.[109] Competition experiments between differently decorated alkynes highlighted alkyl alkyne **11h** to be less reactive than aryl alkyne **11a** (Scheme 52b), particularly when the latter possesses electron-donating substituents as in alkyne **11c** (Scheme 52c).

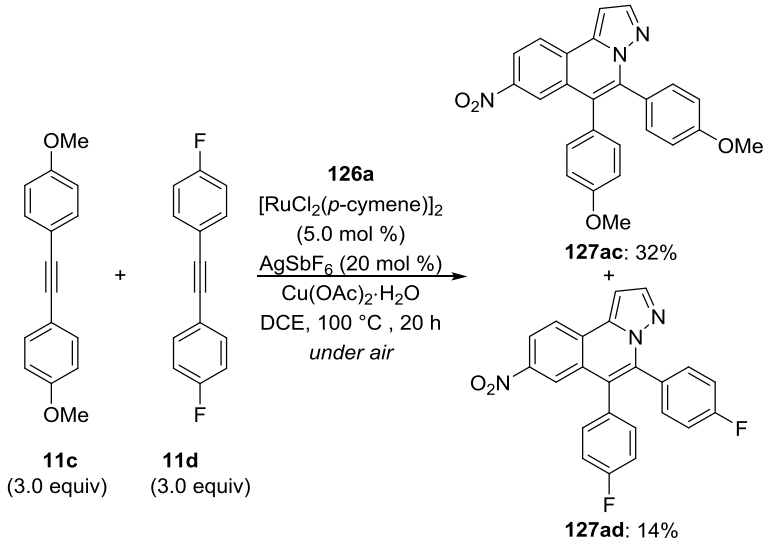
(a)



(b)



(c)

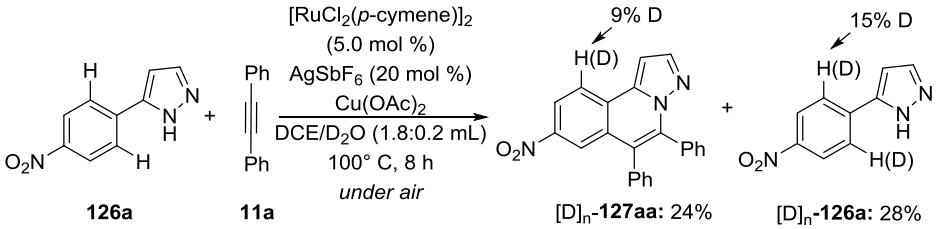


Scheme 52 Intermolecular competition experiments

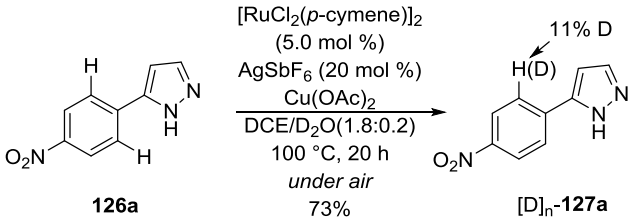
3.3.2. Ruthenium-Catalyzed H/D Exchange Experiments

For the better understanding of the mechanism, two deuteration experiments conducted with D_2O as the cosolvent were carried out. The results of H/D scrambling in the annulation product $[D]_n$-**127aa** (Scheme 53a) and pyrazole substrate $[D]_n$-**127a** (Scheme 53b) indicated that the C–H bond activation step is reversible under the optimized reaction conditions.

a)



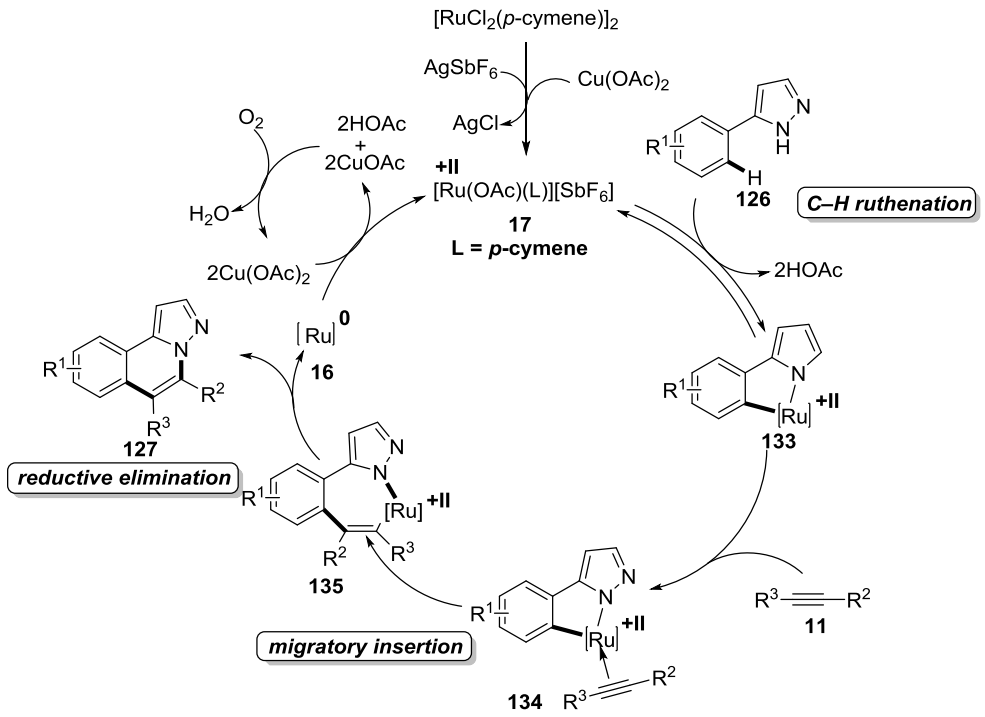
b)



Scheme 53 Oxidative annulations with D_2O as the cosolvent.

3.4 Proposed Catalytic Cycle

Based on our mechanistic studies, the following catalytic cycle for the ruthenium(II)-catalyzed aerobic annulations is proposed (Scheme 54). Initially, the chloride ligands in the complex $[Ru(p\text{-cymene})Cl_2]_2$ can be replaced with SbF_6^- and OAc^- ones through interaction with $AgSbF_6$ assisted by of $Cu(OAc)_2{\cdot}H_2O$ to generate the cationic ruthenium(II) complex **17**. The unique activity of **17** allowed it to react with arylpyrazole **126** to form five-membered intermediate **133** through a reversible metalation process. Thereafter, alkyne coordination and a subsequent migratory insertion furnished a seven-membered ruthenacycle **135** through the intermediate **134**. The formed complex **135** would then undergo reductive elimination to deliver the desired product **127** and a ruthenium(0) species **16**. Finally, the active ruthenium complex can be regenerated *via* a reoxidation process.



Scheme 54 Proposed catalytic cycle.

4. Ruthenium(II)-Catalyzed C–H Bond Alkenylation of Arenes

4.1 Ruthenium(II)-Catalyzed Oxidative C–H Alkenylation with Substituted Benzenesulfonic Acids

Aromatic sulfonic acid derivatives represent an important class of structural constituents in biologically active compounds, such as pharmaceuticals and agrochemicals, and also serve as building blocks for natural products and pharmaceutical synthesis.[115] Furthermore, due to the hydrophilicity of sulfonic acid and sulfone group, they were widely used in the modification of drug basic skeleton. Therefore, the preparation of compound containing benzenesulfonic acid moieties is of continued strong interest. Particularly, transition metal-catalyzed direct C–H bond transformations are highly attractive because of their ideal step economy.[1r] Previous reported studies on alkenylations with sulfonic acids as directing groups employed rhodium complexes. However, the use of less expensive ruthenium catalysts for sulfonic acid group directed C–H bond activation has, thus far, proven to be elusive.

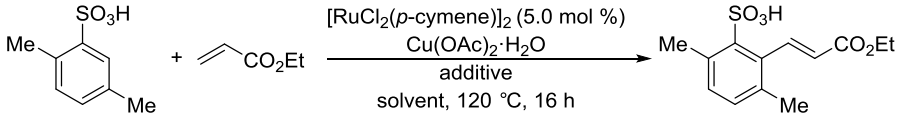
4.1.1 Optimization Studies

We commenced our studies by exploring the effect of representative co-catalytic additives, solvents and ruthenium precursors for the proposed twofold C–H bond functionalizations. The alkenylation of substituted benzenesulfonic acid **128a** was carried out at 120 °C in the presence of $Cu(OAc)_2 \cdot H_2O$ (2.0 equiv) in DMA under N_2 and gave the desired product **129ab** in 43% yield (Table 4, entry 1). A set of representative additives was subsequently probed, and $AgSbF_6$ was identified as being optimal (entries 2−8). Among various solvents, the desired C−H bond functionalization occurred most efficiently in polar aprotic solvents such as DMF and NMP, affording product **129ab** in 70% and 85% yield, respectively (entries 9 and 15). Upon employing $RuCl_3$, $[RuCl_2(PPh_3)_3]$ and $[Ru(O_2CMes)_2(p\text{-cymene})]$ as catalysts (entries 17−19) as well as without ruthenium complex (entry 16), no product or only trace amounts were obtained. Notably, the use of $CuBr_2$ as the oxidant did not deliver the desired product (entry 20), thereby indicating carboxylate assistance to be of key relevance. It is noteworthy that the yield decreased when the

[115] (a) J. Wrobel, D. Green, J. Jetter, W. Kao, J. Rogers, M. C. Pe′rez, J. Hardenburg, D. C. Deecher, F. J. Lo′pez, B. J. Arey and E. S. Shen, *Bioorg. Med. Chem*., **2002**, *10*, 639–656; (b) L. Zhuang, J. S. Wai, M. W. Embrey, T. E. Fisher, M. S. Egbertson, L. S. Payne, J. P. Guare Jr., J. P. Vacca, D. J. Hazuda, P. J. Felock, A. L. Wolfe, K. A. Stillmock, M. V. Witmer, G. Moyer, W. A. Schleif, L. J. Gabryelski, Y. M. Leonard, J. J. Lynch Jr., S. R. Michelson, S. D. Young, *J. Med. Chem*., **2003**, *46*, 447–453.

reaction was performed at lower temperature (entry 21) or under air (entry 22).

Table 4 Optimization of oxidative alkenylation of **128a** with sulfonic acid **46b**[a]



128a **46b** **129ab**

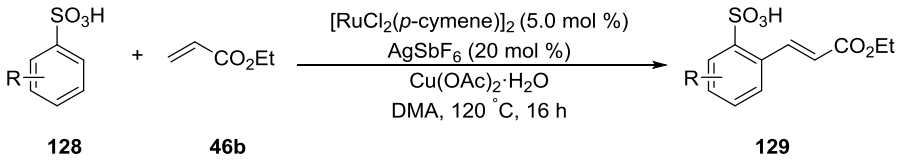
Entry	Solvent	Additive	*cat.*[Ru]	Yield (%)
1	DMA	---	$[RuCl_2(p\text{-cymene})]_2$	43
2	DMA	MesCOOK	$[RuCl_2(p\text{-cymene})]_2$	56
3	DMA	KPF_6	$[RuCl_2(p\text{-cymene})]_2$	60
4	DMA	NaOAc	$[RuCl_2(p\text{-cymene})]_2$	56
5	DMA	$AgSO_3CF_3$	$[RuCl_2(p\text{-cymene})]_2$	52
6	DMA	$AgPF_6$	$[RuCl_2(p\text{-cymene})]_2$	58
7	DMA	$AgBF_4$	$[RuCl_2(p\text{-cymene})]_2$	56
8	**DMA**	**$AgSbF_6$**	$[RuCl_2(p\text{-cymene})]_2$	**91**
9	DMF	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	70
10	DCE	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	trace
11	*t*AmOH	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	trace
12	1,4-dioxane	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	trace
13	H_2O	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	trace
14	PhMe	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	trace
15	NMP	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	85
16	DMA	$AgSbF_6$	---	0[b]
17	DMA	$AgSbF_6$	$RuCl_3$	0
18	DMA	$AgSbF_6$	$[Ru(O_2CMes)_2(p\text{-cymene})]$	trace
19	DMA	$AgSbF_6$	$[RuCl_2(PPh_3)_2]$	trace
20	DMA	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	0[c]
21	DMA	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	85[d]
22	DMA	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	59[e]
23	DMA	$AgSbF_6$	$[RuCl_2(p\text{-cymene})]_2$	48[f]

[a] Reaction conditions: **128a** (0.50 mmol), **46b** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), additive (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.0 mmol), solvent (2.0 mL), 120 °C, 16 h, under N_2; isolated yield. [b] Without catalyst. [c] $CuBr_2$ as oxidant. [d] 100 °C. [e] Under air. [f] 2.5 mol % catalyst.

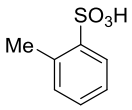
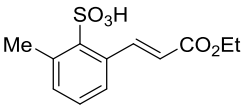
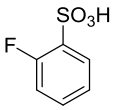
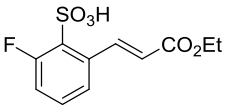
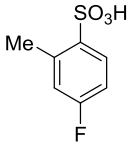
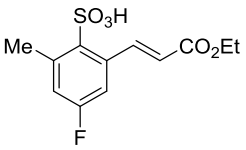
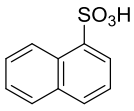
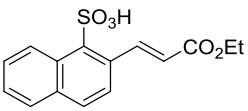
4.1.2. Scope and Limitations

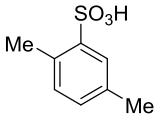
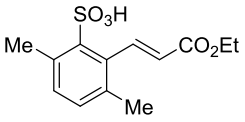
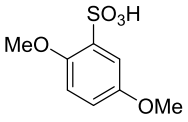
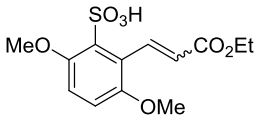
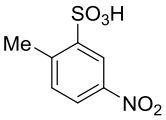
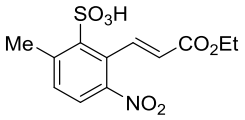
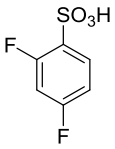
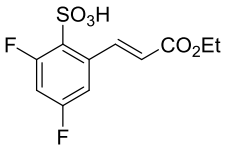
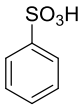
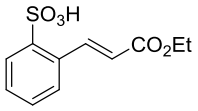
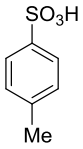
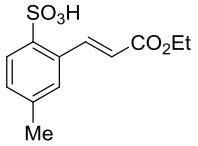
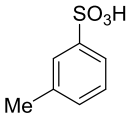
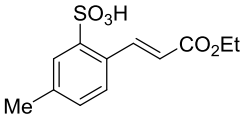
With the optimized conditions in hand, we explored the scope of alkenylations with differently substituted benzenesulfonic acids **128** (Table 5). The cationic ruthenium(II) precatalyst proved to be broadly applicable, as both electron-deficient (entries 2, 3 and 8) as well as electron-rich benzenesulfonic acids (entry 5) were found to be suitable substrates and delivered the corresponding alkenylated products **129** in high yields with excellent *E*-diastereoselectivities. Notably, when we employed 2,5-dimethoxybenzenesulfonic acid (**128f**) as the substrate (entry 6), the reaction successfully provided the product **129fb** in 72% yield as a mixture of two diastereomers (*E:Z* = 2.3:1). If the substrate altered to *p*-toluenesulfonic acid (**128j**), only monoalkenylated product 1**29jb** was obtained (entry 10). To examine the regioselectivity, *meta*-substituted substrate **128k** was tested, and the sole product **128kb** was obtained in high yield (entry 11). This indicated the selectivity of this conversion to be strongly influenced by steric interactions.

Table 5 Scope of oxidative alkenylations of substituted benzenesulfonic acids **128**[a]



128 **46b** **129**

Entry	Sulfonic Acid 128	Product 129	Yield(%)
1	 **128b**	 **129bb**	92
2	 **128c**	 **129cb**	92
3	 **128d**	 **129db**	94
4	 **128e**	 **129eb**	91

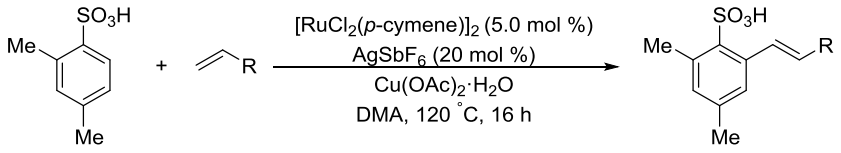
5	 **128a**	 **129ab**	91
6	 **128f**	 **129fb** (E:Z = 2.3:1)	72
7	 **128g**	 **129gb**	0
8	 **128h**	 **129hb**	75
9	 **128i**	 **129ib**	54[b]
10	 **128j**	 **129jb**	87[b]
11	 **128k**	 **129kb**	83

[a] Reaction conditions: **128** (0.50 mmol), **46b** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), solvent (2.0 mL), 120°C, 16 h, under N_2; isolated yield. [b] **128**:**46b** = 2:1.

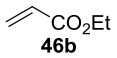
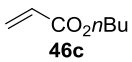
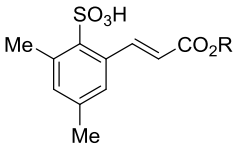
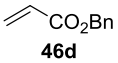
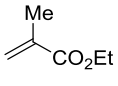
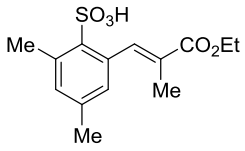
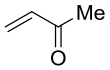
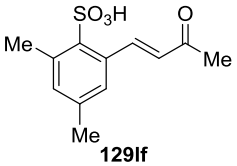
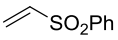
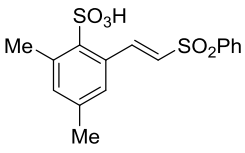
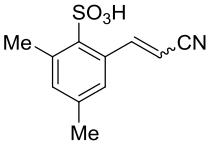
We then investigated the scope of alkenes **46** that can be used for the ruthenium-catalyzed *ortho*-alkenylation reaction (Table 6). A variety of alkenes appeared to be suitable substrates for this C–H bond activation. When *n*-butyl acrylate (**46c**) (entry 2), benzyl acrylate (**46d**) (entry 3), methyl vinyl ketone (**46f**) (entry 5), (vinylsulfonyl)benzene (**46g**) (entry 6), acrylonitrile (**46h**) (entry 7) and diethyl vinylphosphonate (**46i**) (entry 8) were used in this reaction, and the corresponding products were obtained in excellent isolated yields. However, the ethyl methacrylate (**46e**) (entry 4) as well as 2-vinylpyridine (**46o**) (entry 14) were not compatible in this reaction. To our delight, electron-poor styrenes such as 1,2,3,4,5-pentafluoro-6-vinylbenzene (**46l**) (entry 11),

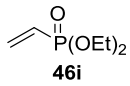
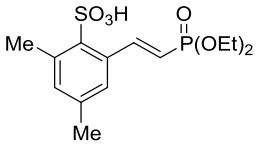
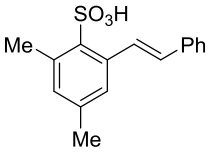
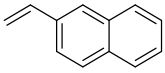
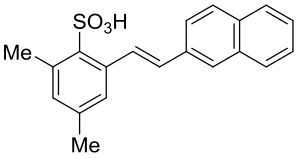
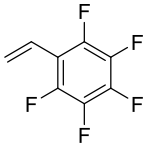
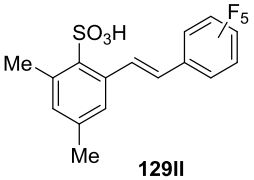
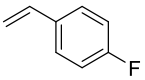
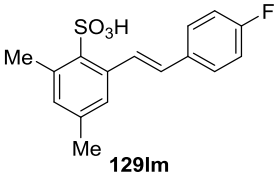
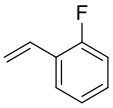
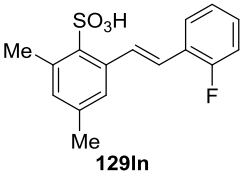
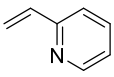
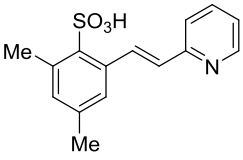
1-fluoro-4-vinylbenzene (**46m**) (entry 12) or 1-fluoro-2-vinylbenzene (**46n**) (entry 13) reacted with 2,4-dimethylbenzenesulfonic acid (**128l)** to afford the corresponding olefinated sulfonic acid derivatives **129ll**–**129ln** in good to excellent yields. 2-Vinylnaphthalene (**46k**) was also found to be a good olefin substrate under the tested reaction conditions (entry 10), whereas the reactivity of styrene (**46j**) (entry 9) was lower.

Table 6 Scope of oxidative alkenylations with different alkenes **46**[a]



128l **46** **129**

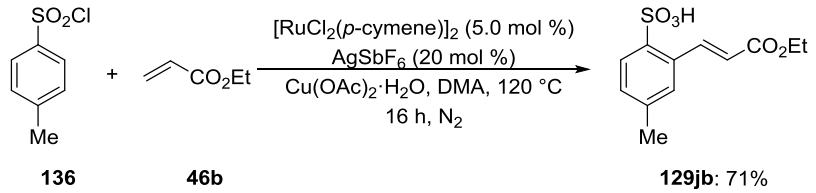
Entry	Alkene 46	Product 129	Yield(%)
1	 **46b**	R = Et (**129lb**)	85
2	 **46c**	 R = *n*Bu (**129lc**)	78
3	 **46d**	R = Bn (**129ld**)	84
4	 **46e**	 **129le**	0
5	 **46f**	 **129lf**	95
6	 **46g**	 **129lg**	92
7	 **46h**	 **129lh** (E:Z = 5:1)	75

8	 **46i**	 **129li**	94
9	 **46j**	 **129lj**	15[b]
10	 **46k**	 **129lk**	51[b,c]
11	 **46l**	 **129ll**	53[b,c]
12	 **46m**	 **129lm**	60[b]
13	 **46n**	 **129ln**	69[b,c]
14	 **46o**	 **129lo**	0

[a] Reaction conditions: **126l** (0.50 mmol), **46** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), DMA (2.0 mL), 120 °C, 16 h, under N_2; isolated yield. [b] 100 °C, DMF. [c] $AgSbF_6$. (40 mol %)

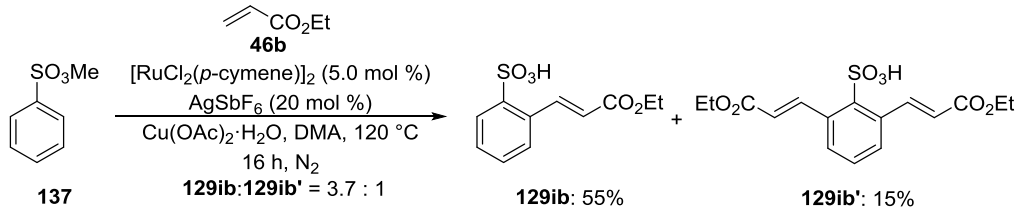
Notably, 4-methylbenzenesulfonyl chloride (**136**) and methyl benzenesulfonate (**137**) also performed in this oxidative alkenylations very well and afforded the olefinated sulfonic acids **129jb** and **129ib** in good yields (Scheme 55a). In the latter case, the bisalkenylated product **129jb'** was obtained as well, albeit in low yield (Scheme 55b).

a)



136 **46b** **129jb**: 71%

b)



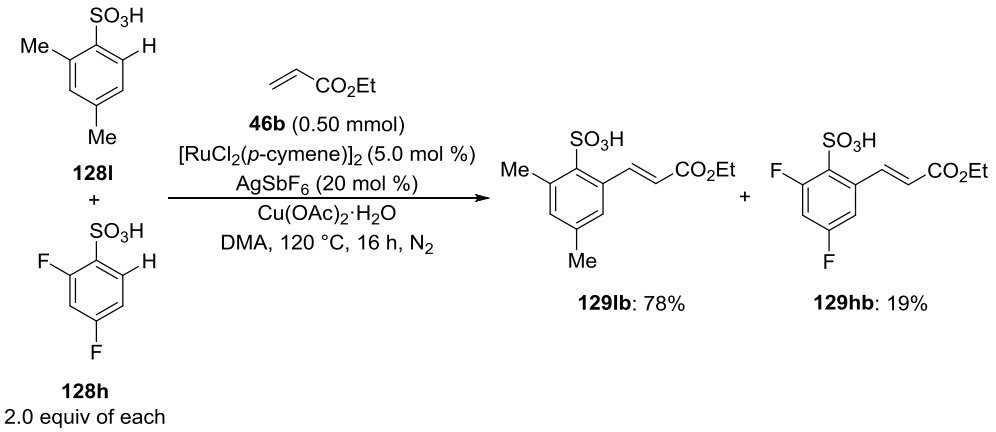
137 **129ib**: 55% **129ib'**: 15%

Scheme 55 Ruthenium-catalyzed oxidative alkenylations with substrates **136** and **137**.

4.1.3 Mechanistic studies

4.1.3.1 Intermocular Competition Experiment

Given the remarkable catalytic activity of the cationic ruthenium(II) complex, we initiated mechanistic studies to unravel its mode of action. To this end, we performed intermolecular competition experiment between differently substituted arenes **128l** and **128h** which revealed electron-rich aromatic sulfonic acid **128l** to be preferentially converted (Scheme 56).



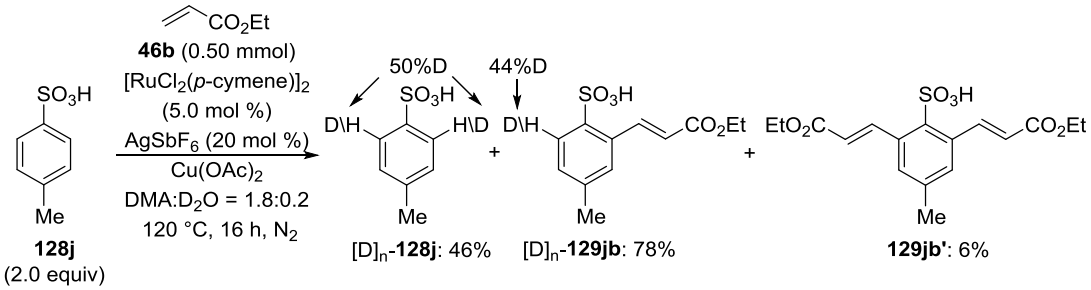
129lb: 78% **129hb**: 19%

Scheme 56 Competition experiment between arene sulfonic acids **128l** and **128h**.

4.1.3.2 Ruthenium-Catalyzed H/D Exchange Experiment

Further experimental support to provide the mechanistic rationale was obtained from oxidative alkenylations with D_2O as a cosolvent. The results indicated a significant H/D scrambling in the

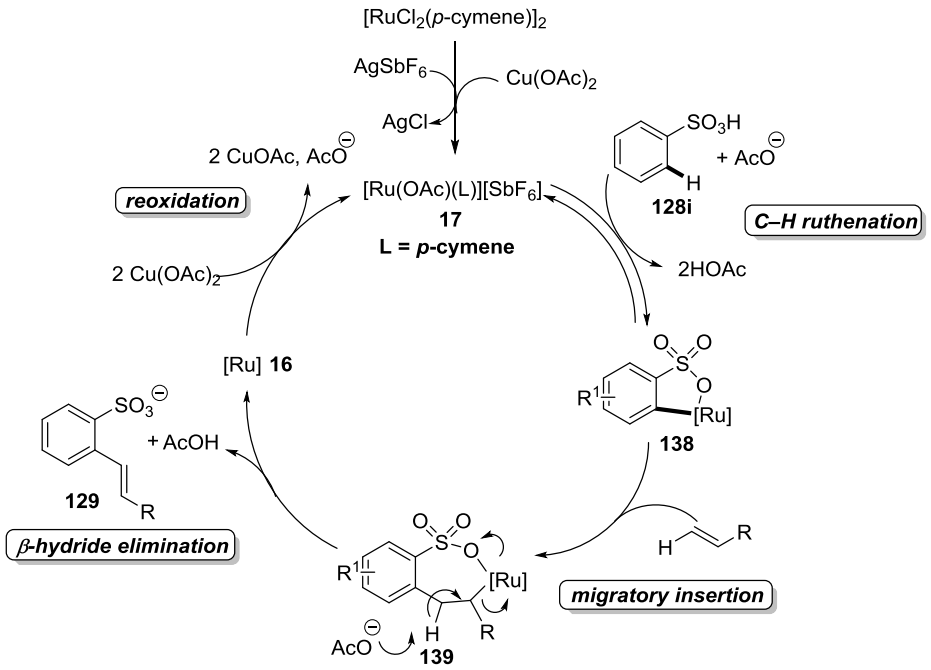
ortho positions of the reisolated substrate [D]$_n$-**128j** and in the product [D]$_n$-**129jb**.



Scheme 57 Oxidative alkenylations with D_2O as the cosolvent.

4.1.4 Proposed Catalytic Cycle

Based on these mechanistic experiments and on the results of previously reported studies, we proposed a plausible catalytic cycle (Scheme 58). Initially, the $[RuCl_2(p\text{-cymene})]_2$ species reacted with $AgSbF_6$ and $Cu(OAc)_2{\cdot}H_2O$ to form a cationic ruthenium(II) complex **17**. After coordination, reversible cyclometalation through a base-assisted internal electrophilic substitution (BIES) gave five-membered ruthenium intermediate **138**. Thereafter, coordination and insertion of the alkene **46** into the Ru–C bond of the complex **138** provided the seven-membered species **139**. Finally, acetate-initiated β-hydride elimination and released the desired product **129** and regenerated the catalytically active ruthenium(II) complex **17** for the next catalytic cycle.



Scheme 58 Proposed mechanism for the alkenylation reaction.

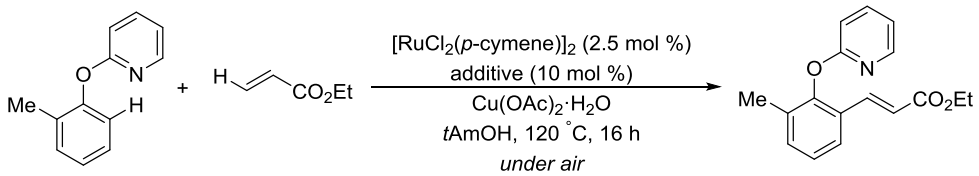
4.2 Ruthenium(II)-Catalyzed C–H Bond Alkenylationof Arene Bearing Removable Directing Group

In recent years, a number of directing groups for the C−H alkenylation reaction catalyzed by ruthenium complex have been developed. However, the transformation of these directing groups in a number of cases remains a major problem, whereas the methods that exploited removable directing groups are scarce. Therefore, we developed ruthenium-catalyzed twofold C−H functionalization with arenes and heteroarenes using easily cleavable pyridin-2-yloxy directing groups.

4.2.1 Optimization Studies

Initially, we selected 2-(*o*-tolyloxy)pyridine (**130a**) and ethyl acrylate (**46b**) as model substrates to screen the reaction conditions (Table 7). While carboxylate additives were found to be mandatory for ruthenium-catalyzed direct arylations with aryl halides,[116] they proved to be ineffective for the desired oxidative C–H bond alkenylation of **130a** (entries 1–3). To our delight, the coupled product **131ab** was isolated in 83% yield when using $AgSbF_6$ (20 mol %) as an additive in *t*AmOH (entry 5). Importantly, this alkenylation product was also obtained in 73% yield with cocatalytic amounts of $Cu(OAc)_2{\cdot}H_2O$ under an atmosphere of ambient air as the sacrificial oxidant (entry 6). Furthermore, control experiments verified that no desired product was observed in the absence of $Cu(OAc)_2{\cdot}H_2O$ or the ruthenium catalyst (entries 7 and 8).

Table 7 Optimization of C−H bond alkenylation of substituted pyridine **130a**[a]



130a **46b** **131ab**

Entry	Additive	$Cu(OAc)_2.H_2O$	Yield (%)
1	KO_2CMes	2.0	<5
2	CsOAc	2.0	<5
3	AgOAc	2.0	<5
4	KPF_6	2.0	25
5	**$AgSbF_6$**	**2.0**	**83**
6	$AgSbF_6$	0.3	73
7	$AgSbF_6$	--	0
8	$AgSbF_6$	2.0	0[b]

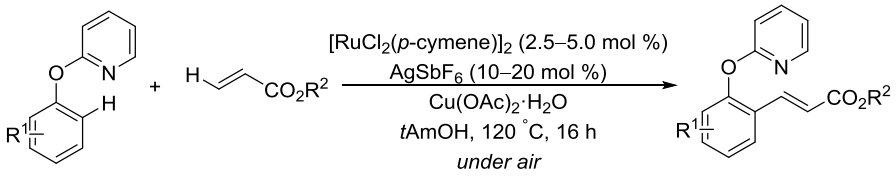
[a] Reaction conditions: **130a** (1.0 mmol), **46b** (0.5 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), *t*AmOH (2.0 mL), $AgSbF_6$ (10 mol %); isolated yields.
[b] Without $[RuCl_2(p\text{-cymene})]_2$.

[116] L. Ackermann, E. Diers, A. Manvar, *Org. Lett.* **2012**, *14*, 1154–1157.

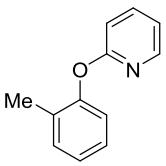
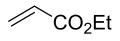
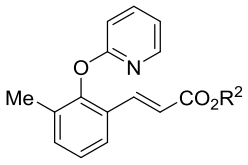
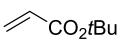
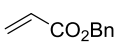
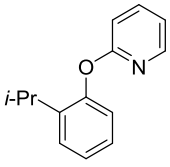
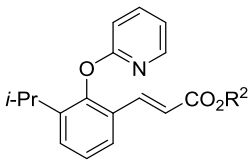
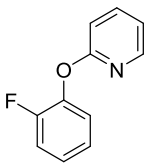
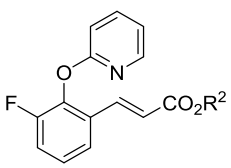
4.2.2 Scope and Limitations of the Ruthenium-Catalyzed Oxidative Alkenylations

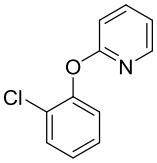
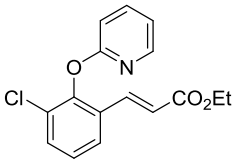
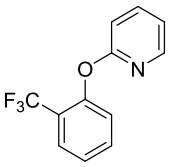
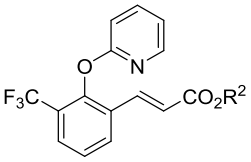
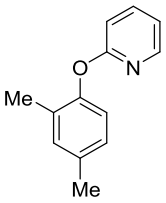
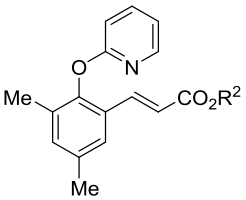
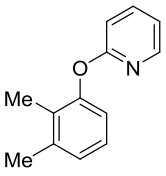
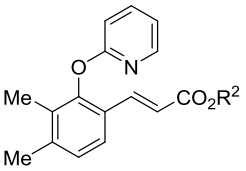
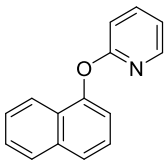
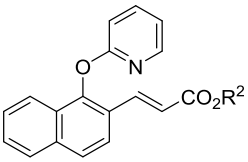
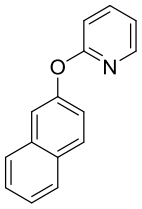
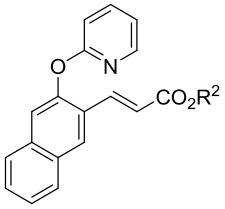
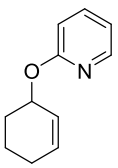
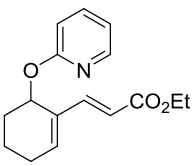
With the optimized conditions in hand, we explored the versatility of this monoalkenylation reaction (Table 8). Gratifyingly, substrates with both electron-donating (entries 1–5, 12–16) and electron-withdrawing substituents (entries 6–11) at the *ortho* position of the phenyl ring were viable and furnished the desired products **131** in high isolated yields, thus indicating the general applicability of phenoxylpyridine substrates **130**. Notably, halogen substituents at the *ortho* position of the phenyl ring in substrates **130c** and **130d** were also tolerated under this catalytic system (entry 9). This could provide a versatile synthetic handle for further functionalization of the products **130db**. Furthermore, oxidative alkenylations with α- and β-naphthol derivatives **130h** and **130i**, respectively, delivered the desired alkenylated products with excellent site selectivities (entries 17–21). In contrast, 2-(cyclohex-1-en-1-yloxy)pyridine (**130j**) decomposed under this reaction condition, thus led no desired product. Importantly, the catalytic C−H bond functionalizations occurred with excellent diastereoselectivities, delivering the *E* diastereomers as the sole products in all cases.

Table 8 Scope of oxidative alkenylation with arenes (**130**)[a]



130 **46** **131**

Entry	Phenol 130	Alkene 46	Product 131	Yield(%)
1	 **130a**	 **46b**	 R^2 = Et (**131ab**)	83
2		 **46p**	R^2 = *t*Bu (**131ap**)	81
3		 **46d**	R^2 = Bn (**131ad**)	75
4	 **130b**	**46b**	 R^2 = Et (**131bb**)	87
5		**46p**	R^2 = *t*Bu (**131bp**)	93
6	 **130c**	**46b**	 R^2 = Et (**131cb**)	81
7		**46p**	R^2 = *t*Bu (**131cp**)	87
8		**46d**	R^2 = Bn (**131cd**)	92

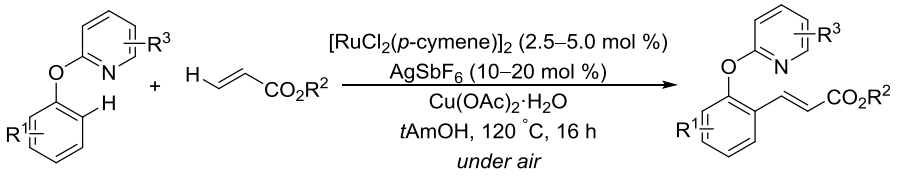
9	 **130d**	**46b**	 **131db**		69
10	 **130e**	**46b**		R^2 = Et (**131eb**)	81
11		**46p**		R^2 = *t*Bu (**131ep**)	79
12	 **130f**	**46b**		R^2 = Et (**131fb**)	82
13		**46p**		R^2 = *t*Bu (**131fp**)	73
14	 **130g**	**46b**		R^2 = Et (**131gb**)	76
15		**46p**		R^2 = *t*Bu (**131gp**)	75
16		**46d**		R^2 = Bn (**131gd**)	82
17	 **130h**	**46b**		R^2 = Et (**131hb**)	76
18		**46p**		R^2 = *t*Bu (**131hp**)	82
19		**46d**		R^2 = Bn (**131hd**)	88
20	 **130i**	**46b**		R^2 = Et (**131ib**)	78
21		**46p**		R^2 = *t*Bu (**131ip**)	74
22	 **130j**	**46b**	 **131jb**		0

[a]Reaction conditions: **130** (1.0 mmol), **46** (0.5 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), *t*AmOH (2.0 mL), $AgSbF_6$ (10 mol %); isolated yields.

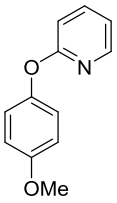
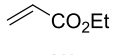
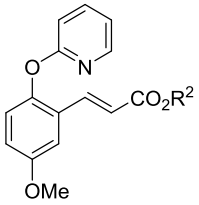
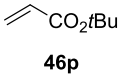
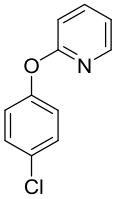
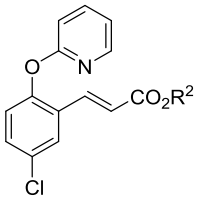
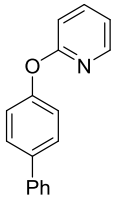
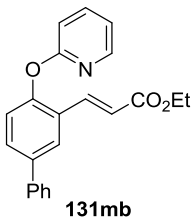
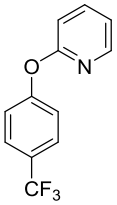
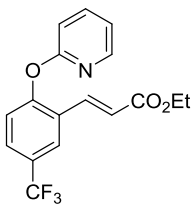
Moreover, this catalytic system could not only be applied in substrates bearing *ortho* substituents, but also various of phenol derivatives with *para* substitution provided the mono-alkenylated

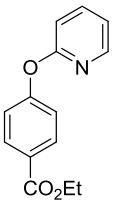
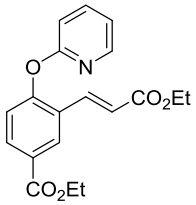
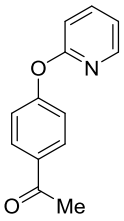
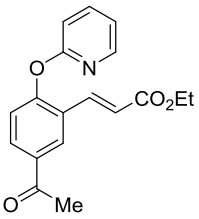
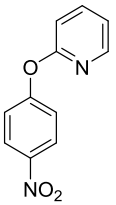
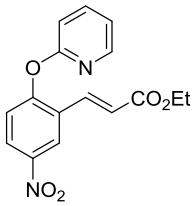
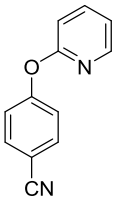
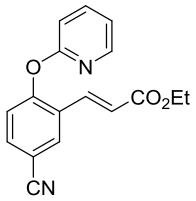
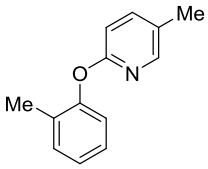
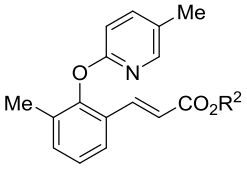
products **131** in good yields with good chemo- and site- selectivities as well (Table 9). Notably, starting materials with both electron-donating and -withdrawing groups, including methoxy (**130k**) (entry 1) and important electrophilic functional groups, such as chloro (**130l**), ester (**130o**), ketone (**130p**), or nitro (**130q**) substituents (entries 3, 7–9), were well tolerated under this catalytic conditions. However, cyano group (**130r**) was not compatible in this reaction, probably as a result of the competitive coordination of the cyano group to the metal center, thus inhibiting the C–H activation. In addition, this C–H bond alkenylation was also readily feasible in compound **130s** with substituted pyridine ring (entries 11 and 12).

Table 9 Scope of oxidative alkenylations with substituted substrates **130**[a]



130 **46** **131**

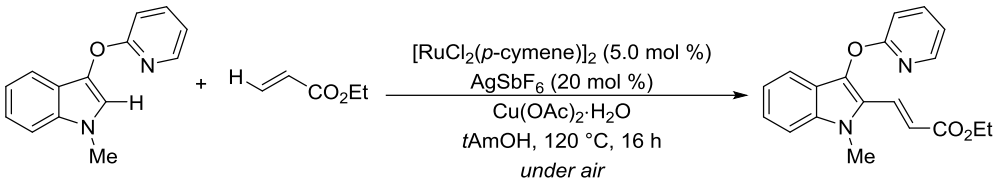
Entry	Phenol 130	Alkyne 46	Product 131	Yield(%)
1	 **130k**	 **46b**	 R^2 = Et (**131kb**)	68
2		 **46p**	R^2 = *t*Bu (**131kp**)	65
3	 **130l**	**46b**	 R^2 = Et (**131lb**)	68
4		**46p**	R^2 = *t*Bu (**131lp**)	76
5	 **130m**	**46b**	 **131mb**	64
6	 **130n**	**46b**	 **131nb**	79

7	 **130o**	**46b**	 **131ob**		67
8	 **130p**	**46b**	 **131pb**		70
9	 **130q**	**46b**	 **131qb**		65
10	 **130r**	**46b**	 **131rb**		0
11	 **130s**	**46b**		R^2 = Et (**131sb**)	77
12		**46p**		R^2 = *t*Bu (**131sp**)	76

[a] Reaction conditions: **130** (1.0 mmol), **46** (0.5 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5–5 mol %), *t*AmOH (2.0 mL), $AgSbF_6$ (10–20 mol %); isolated yields.

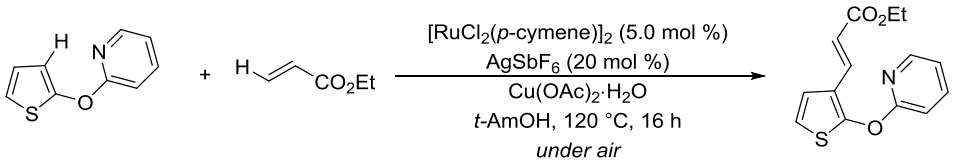
Furthermore, it was delighted to observe that heteroarenes proved to be suitable substrates as well, delivering the synthetically useful indole **131tb** (Scheme 59a) and thiophene **131ub** (Scheme 59b). However, the benzo[*b*]thiophene **130v** with a pyridin-2-yloxy directing group was less compatible in this reaction and hence gave an unsatisfactory yield (Scheme 59c).

a



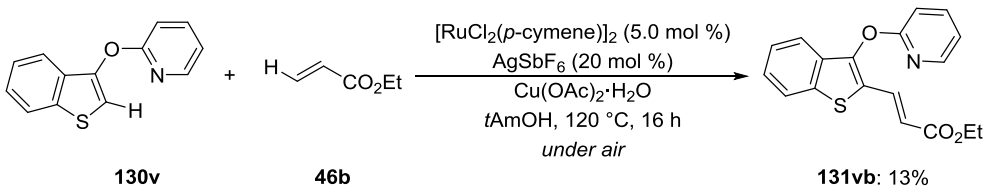
130t **46b** **131tb**: 83%

b



130u **46b** **131ub**: 70%

c

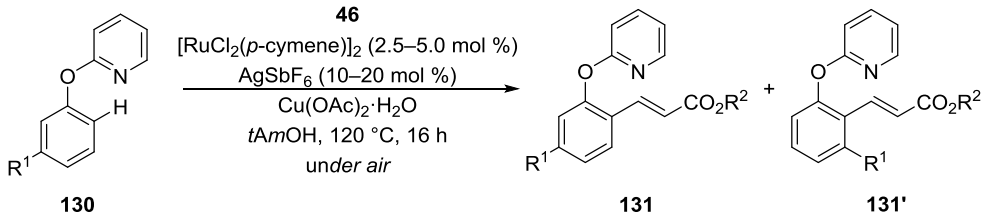


130v **46b** **131vb**: 13%

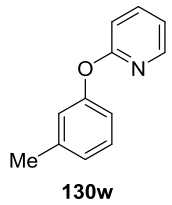
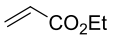
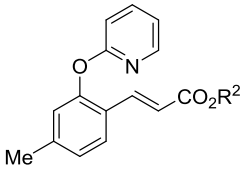
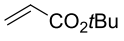
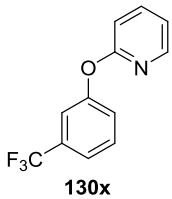
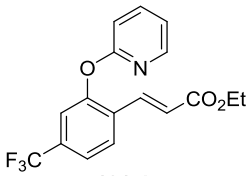
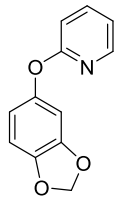
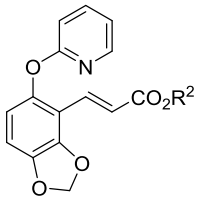
Scheme 59 Scope of oxidative alkenylation with heterocyclic substrates.

The site-selectivity of the oxidative C–H bond functionalization with *meta*-substituted phenol derivatives **130w** and **130x** was largely controlled by steric interactions, thus delivering the alkenylated products **131wb**, **131wp** and **131xb** in good yields (Table 10, entries 1–3). In contrast, the substrate **130y** reacted with alkenes **46b** and **46p** affording the alkenylated products **131yb** and **131yp** on the more sterically hindered position, most probably as a result of a notable secondary chelation effect exerted by the acetal moiety (entries 4 and 5).

Table 10 Oxidative alkenylations with *meta*-substituted substrates[a]

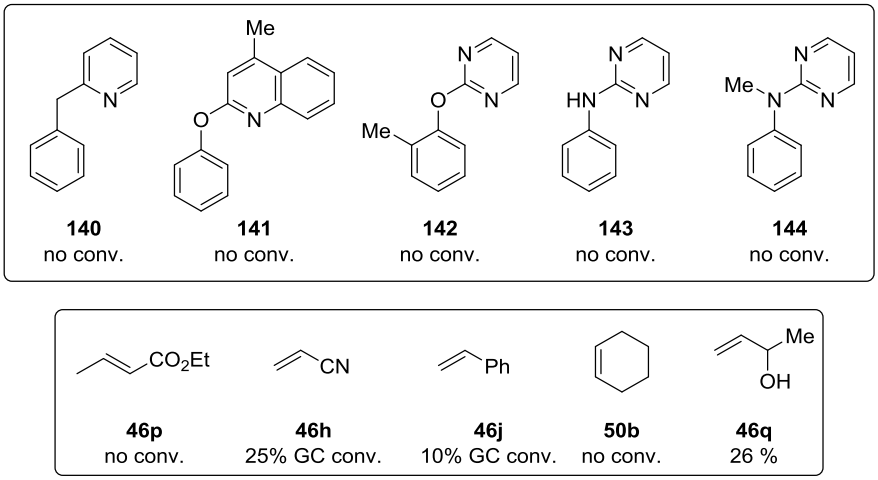


130 131 131'

Entry	Substrate 130	Alkene 46	Product 131		Yield(%)
1				R^2 = Et (**131wb**)	85
2	130w	46b  46p		R^2 = *t*Bu (**131wp**)	70
3	 130x	46b	 131xb		87
4		46b		R^2 = Et (**131yb**)	76
5	130y	46p		R^2 = *t*Bu (**131yp**)	79

[a] Reaction conditions: **130** (1.0 mmol), **46** (0.5 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $AgSbF_6$ (10 mol %), *t*AmOH (2.0 mL); isolated yields.

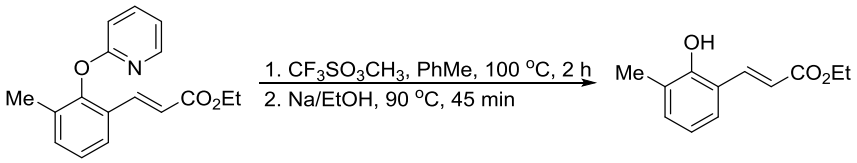
Replacement of the oxygen between the pyridine and the aryl rings in substrate **130** with methylene (as in benzylpyridine **140**) or amino moieties (as in compounds **143** and **144**) completely inhibited the C–H functionalizations (Scheme 60). The same effect was observed upon changing the pyridine directing group with a pyrimidine (substrate **142**) or quinoline (compound **141**) ones. Besides, unactivated simple alkenes such as cyclohexene (**50b**) and styrene (**46j**) were not compatible in this reaction. Acrylonitrile (**46h**), ethyl (*E*)-but-2-enoate (**46p**) and but-3-en-2-ol (**46q**) were also not efficient coupling partners, as they delivered the corresponding products with low conversions (Scheme 60).



Scheme 60 Substrates with limited activity towards the alkenylation process.

4.2.3 Removal of the directing group

Furthermore, we were delighted to find that the directing group could easily be removed from pyridin-2-yloxycinnamate **131ab** employing the previously published protocol,[116] thereby yielding the desired free phenol **71a** in high yield (Scheme 61).



131ab **71a:** 75%

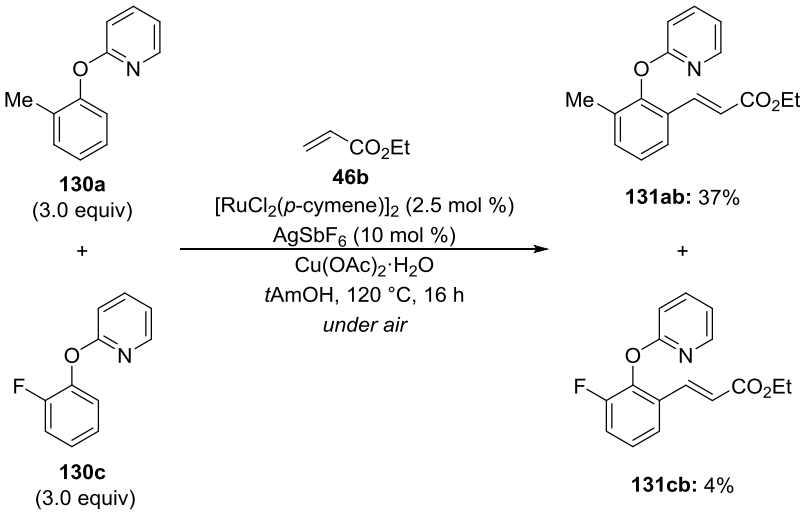
Scheme 61 Removal of the directing group

4.2.4 Mechanistic Studies

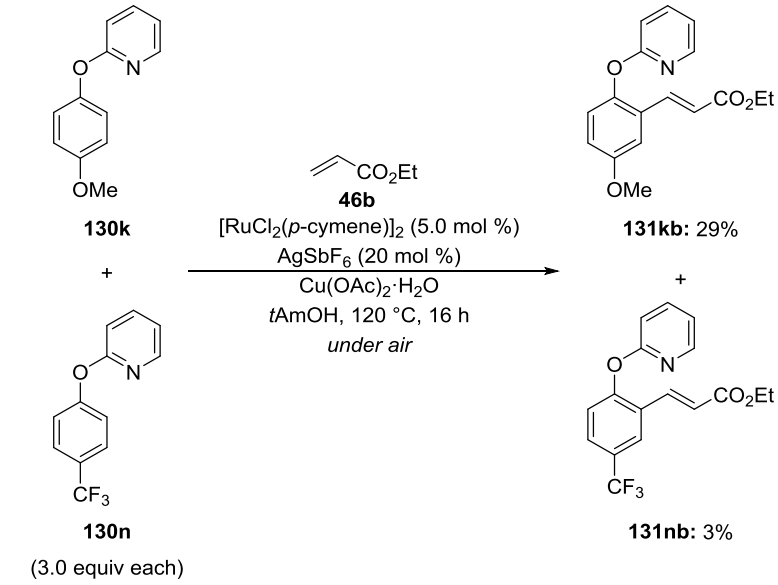
4.2.4.1. Intermolecular Competition Experiments

Given the remarkable catalytic activity of the cationic ruthenium(II) complex, we initiated mechanistic studies to elucidate its mode of action. To this end, we performed intermolecular competition experiments between electron-rich (**130a** and **130k**) and electron-deficient (**130c** and **130n**) substrates. The results of this study revealed the electron-rich substrates **130a** *versus* **130c** (Scheme 62a) and **130k** *versus* **130n** (Scheme 62b) to be preferentially converted in both cases.

a)



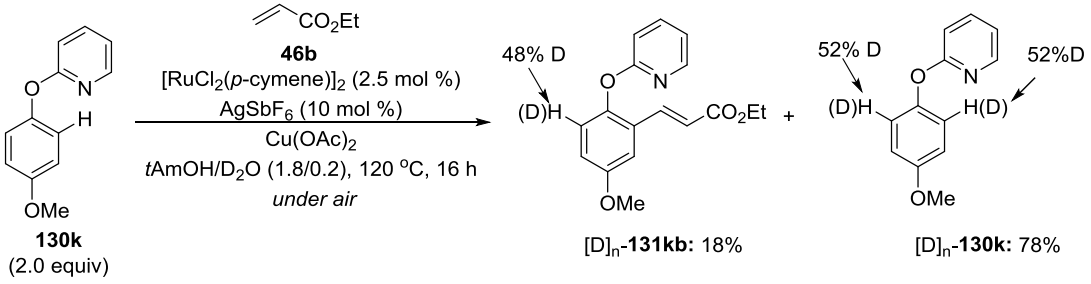
b)



Scheme 62 Intermolecular competition experiments

4.2.4.2 H/D Exchange Experiment

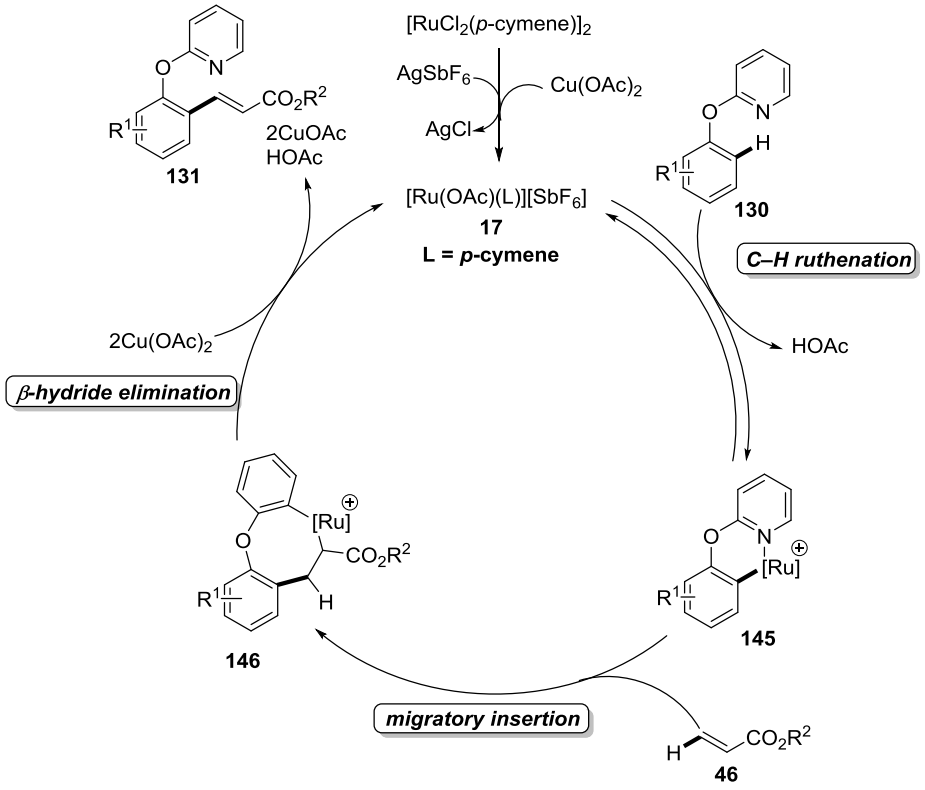
Mechanistic studies on the oxidative alkenylations in the presence of D_2O as a cosolvent showed a significant H/D scrambling in the *ortho* positions of the reisolated substrate [D_n]-**130k** as well as of the product [D]$_n$-**131kb**, thus indicating the reversible nature of a C–H ruthenation step (Scheme 63).



Scheme 63 Oxidative alkenylation with D_2O as the cosolvent.

4.2.5 Proposed Catalytic Cycle

Based on these studies and literature precedence, we proposed the C–H bond activation to occur by a reversible electrophilic-type metalation event (Scheme 64). The catalytic cycle is likely initiated by the removal of chloride from $[RuCl_2(p\text{-cymene})]_2$, followed by a reversible C–H bond insertion directed by the nitrogen atom of the pyridine moiety. The formed six-membered cycloruthenated complex **145** subsequently underwent a migratory insertion with the alkene **46** to furnish the intermediate **146**. Finally, β-hydride elimination yielded the desired product **131**, whereas reductive elimination and oxidation by $Cu(OAc)_2 \cdot H_2O$ regenerated the catalytically active ruthenium(II) complex **17**.



Scheme 64 Proposed mechanism for the ruthenium(II)-catalyzed C–H alkenylations.

5. Cobalt(II)-Catalyzed Oxidative Annulation through C–H Alkenylations: Regio- and Site-Selective Access to Isoindolin-1-one

Over the last decades, a vast majority of complexes of transition metals such as palladium, rhodium or ruthenium, have been developed and employed for catalyzed alkenylations, annulations, aminations and hydroxylations.[54y, 117] However, high cost of these catalysts greatly limited their application in industry. Thus, the developments of catalysts based on earth-abundant first-row transition metals are valuable.

Cobalt was the first metal used in so-called chelation-assisted C−H bond functionalization.[118] In recent years, Yoshikai[119] reported on cobalt-catalyzed intermolecular hydroarylation of alkynes. Pyridine, pyrimidine, ketimine and aldimine were employed as the directing group for these reactions at ambient temperature, and gave the styrene derivatives in good yields and high stereoselectivities. Ackermann's group[120] reported cobalt-catalyzed C–H arylation with organic electrophiles. However, employment of Grignard reagents was essential for these transformations which caused low functional groups tolerance. Daugulis[91] reported cobalt-catalyzed alkyne annulation using 8-aminoquinoline-derived bidentate directing groups (Scheme 38). These reactions were performed under mild reaction conditions without using the Grignard reagent, thus enabling a wide range of substrates to be applied. Encouraged by this work, we became attracted to develop cobalt-catalyzed oxidative alkenylations with easily accessible *N*-(quinolin-8-yl)benzamides **110**.

5.1 Optimization Studies

Initially, we examined the reaction conditions previously established by Daugulis for the cobalt-catalyzed oxidative alkenylations of 4-methyl-*N*-(quinolin-8-yl)benzamide (**110a**) and ethyl acrylate (**46b**). Unfortunately, no desired product was obtained (Table 11, entries 1–3). Further attempts showed that not the alkenylated, but the cyclic product isoindolin-1-one **132ab** could be obtained in 37% yield in the presence of 20 mol% $Co(OAc)_2$ and 2.0 equivalents of base using

[117] V. S. Thirunavukkarasu, S. I. Kozhushkov, L. Ackermann, *Chem. Commun.* **2014**, *50*, 29−39, and references cited therein.

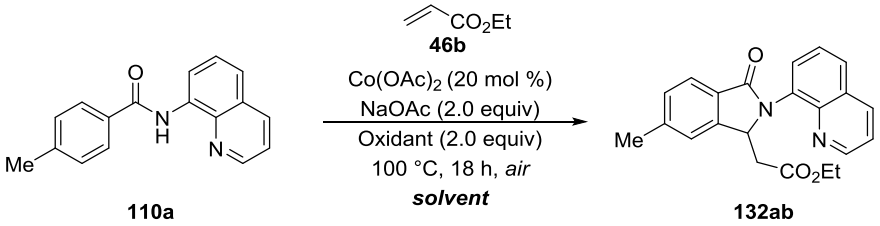
[118] (a) S. Murahashi, *J. Am. Chem. Soc*. **1955**, *77*, 6403−6404; (b) A. C. Cope, R. W. Siekman, *J. Am. Chem. Soc*. **1965**, *87*, 3272−3273.

[119] (a) K. Gao, P.-S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc*. **2010**, *132*, 12249−12251; (b) P. -S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2011**, *133*, 17283−17295; (c) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed*. **2012**, *51*, 4698–4701.

[120] (a) W. Song, L. Ackermann, *Angew. Chem. Int. Ed.* **2012**, *51*, 8251−8254; (b) B. Punji, W. Song, G. A. Shevchenko, L. Ackermann, *Chem. Eur. J.* **2013**, *19*, 10605−10610.

$Mn(OAc)_2$ as the oxidant in PEG 400 as the solvent at 100 °C for 18 h under air (entry 4). To our delight, among the tested solvents (entries 5–18) the mixture of PEG 400 and CF_3CH_2OH (4/1) proved to be optimal, affording the product **132ab** in 60% yield. The oxidants such as AgOAc, $AgCOCF_3$, $AgNO_3$, $AgCO_3$ and $AgCO_2Ad$ were not effective for this transformation furnishing only moderate yields of isoindolin-1-one**132ab** (entries 21–24, 26). AgOPiv turned out to be the most efficient oxidant and resulted in complete consumption of substrate **110a**, yielding compound **132ab** in 65% yield. Decreasing the temperature to 60 °C led to a lower yield (entry 31). Interestingly, the absence of any base resulted in a higher yield (entry 33). Furthermore, additional experiments verified that the transformation did not proceed without oxidant or catalyst (entries 18 and 34). Therefore, the optimized conditions were ultimately identified as 20 mol % $Co(OAc)_2$, 2.0 equivalents AgOPiv in a solvent mixture (PEG 400/CF_3CH_2OH = 4/1) at 100 °C under air (entry 34).

Table 11 Optimization of C–H bond alkenylation of amide **110a**[a]



Entry	*cat.*[Co]	Solvent	Oxidant	Yield (%)
1	$[Cp^*CoI_2]_2$	CF_3CH_2OH	$Mn(OAc)_2$	<5[b]
2	$Co(acac)_2$	CF_3CH_2OH	$Mn(OAc)_2$	<5[b]
3	$Co(OAc)_2$	CF_3CH_2OH	$Mn(OAc)_2$	<5[b]
4	$Co(OAc)_2$	PEG 400	$Mn(OAc)_2$	37
5	$Co(OAc)_2$	PEG 400	$Mn(OAc)_2$	<5[b,c]
6	$Co(OAc)_2$	Toluene	$Mn(OAc)_2$	<5[b]
7	$Co(OAc)_2$	DMF	$Mn(OAc)_2$	<5[b]
8	$Co(OAc)_2$	DMSO	$Mn(OAc)_2$	0
9	$Co(OAc)_2$	1,4-dioxane	$Mn(OAc)_2$	0
10	$Co(OAc)_2$	PhCl	$Mn(OAc)_2$	0
11	$Co(OAc)_2$	PEG1000	$Mn(OAc)_2$	<5[b]
12	$Co(OAc)_2$	DMPU	$Mn(OAc)_2$	<5[b]
13	$Co(OAc)_2$	DCE	$Mn(OAc)_2$	0
14	$Co(OAc)_2$	PEG 400/H_2O (4/1)	$Mn(OAc)_2$	0
15	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	$Mn(OAc)_2$	60
16	$Co(OAc)_2$	glycerol	$Mn(OAc)_2$	0
17	$Co(OAc)_2$	ethylene glycol	$Mn(OAc)_2$	<5[b]
18	---	PEG 400/CF_3CH_2OH (4/1)	$Mn(OAc)_2$	0
19	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	Ag_2SO_4	39[b]

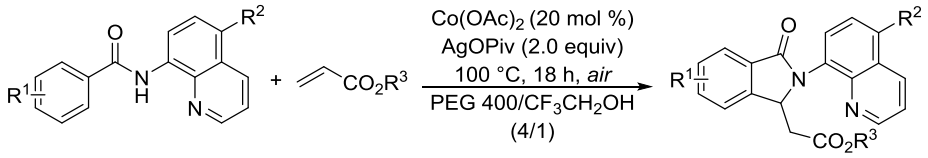
20	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	Ag_2O	22
21	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	$AgNO_3$	61
22	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	Ag_2CO_3	47
23	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOAc	48
24	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	$AgCOCF_3$	51
25	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOPiv	65
26	$Co(OAc)_2$	PEG400/CF_3CH_2OH (4/1)	$AgCO_2Ad$	59
27	$Co(OAc)_2$	PEG400/CF_3CH_2OH (4/1)	$Cu(OAc)_2{\cdot}H_2O$	0
28	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	$Zn(OAc)_2$	0
29	$Co(OAc)_2$	PEG400/CF_3CH_2OH (4/1)	$PhI(OAc)_2$	<5[b]
30	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOPiv	<5[b]
31	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOPiv	49[d]
32	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOPiv	12[b]
33	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	AgOPiv	**73**[e]
34	$Co(OAc)_2$	PEG 400/CF_3CH_2OH (4/1)	--	<5[b,e]

[a] Reaction conditions: **110a** (0.25 mmol), ethyl acrylate **46b** (0.50 mmol), $Co(OAc)_2$ (20 mol %), NaOAc (2.0 equiv), solvent (2.5 mL), 100 °C, 18 h; isolated yields. [b] GCMS conversion. [c] Under N_2. [d] 60 °C. [e] Without NaOAc.

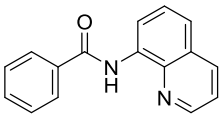
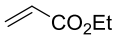
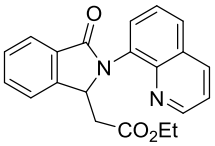
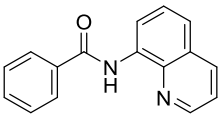
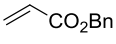
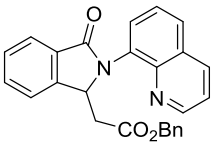
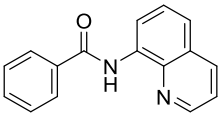
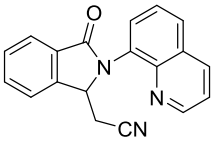
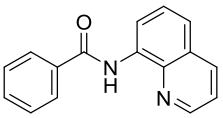
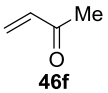
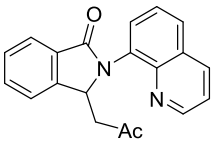
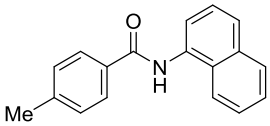
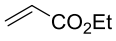
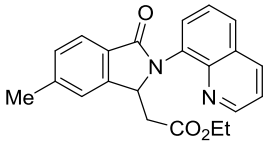
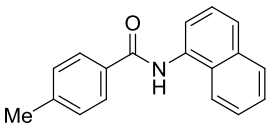
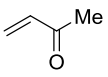
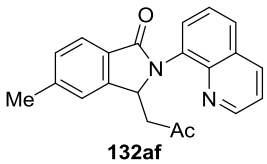
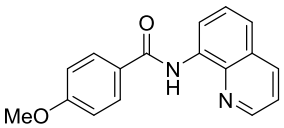
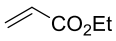
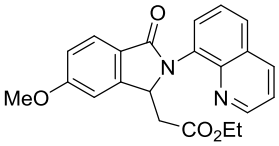
5.2 Scope and Limitations

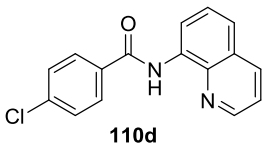
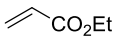
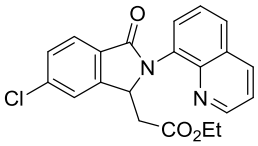
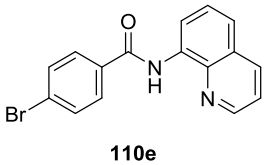
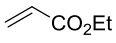
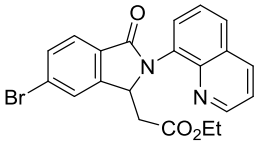
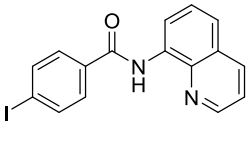
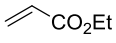
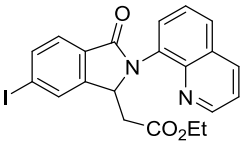
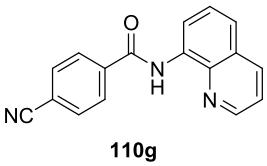
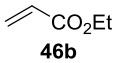
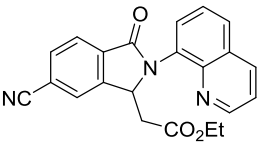
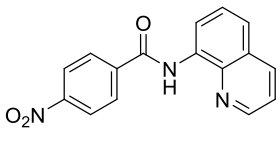
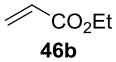
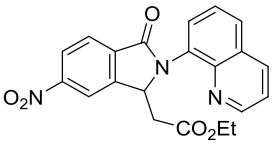
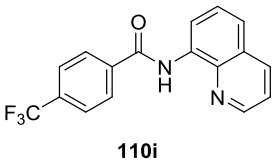
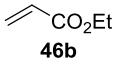
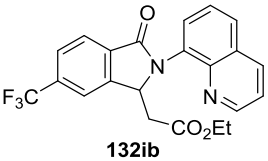
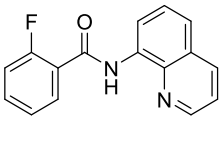
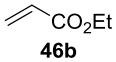
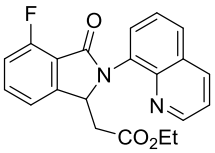
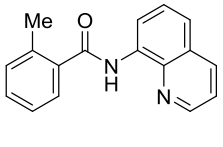
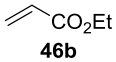
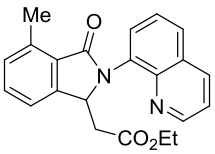
With the optimized reaction conditions in hand, we expanded the scope of the alkenylations (Table 12). Various alkenes, such as benzyl acrylate (**46d**) and methyl vinyl ketone (**46f**), were successfully employed under this condition, affording the corresponding product **132bd** and **132bf** in good yields (entries 2 and 4). Despite its high tendency to polymerize, acrylonitrile (**46h**) was also compatible in this reaction, furnishing compounds **132bn** and **132nh** in 75% and 64% isolated yields, respectively (entries 3 and 19). Good to excellent yields were obtained when a series of *para*-substituted *N*-(quinolin-8-yl)benzamides **110** was used as substrates with electron-deficient (entries 13 and 14) or electron-rich substituents (entries 7, 13 and 16). More importantly, various functional groups, such as halides (Cl, Br, I) (**110d**–**110f**), nitril (**110g**), nitro (**110h**) or trifluoro (**110i**) were well tolerated by this catalytic system (entries 8–13). The *ortho*-substituted substrates, such as **110j** and **110k,** also reacted efficiently, however, giving the desired product **132jb** and **132kb** in moderate yield (entries 14 and 15). Unfortunately, heteroarenes **110o** and **110p** (entries 20 and 21) as well as ferrocene (**110q**) or acrylamide derivative (**110r**) (entries 22 and 23) were not compatible in this reaction.

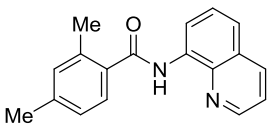
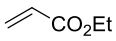
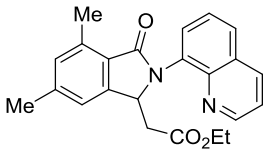
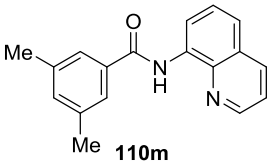
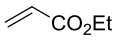
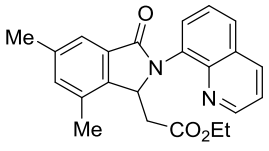
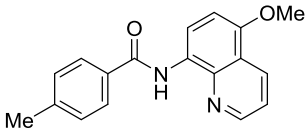
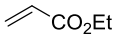
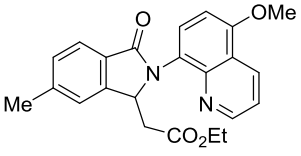
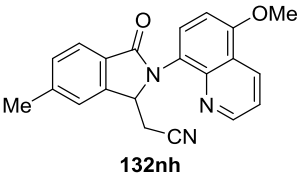
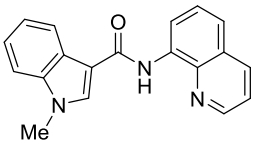
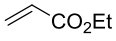
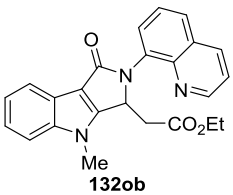
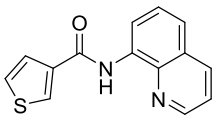
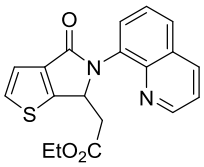
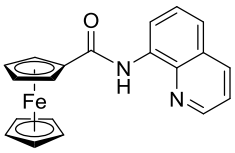
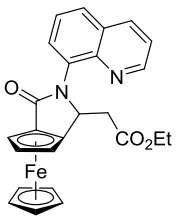
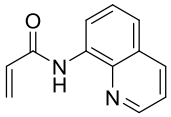
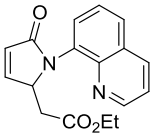
Table 12 Scope of cobalt-catalyzed annulations with amides (**110**)[a]



110 **46** **132**

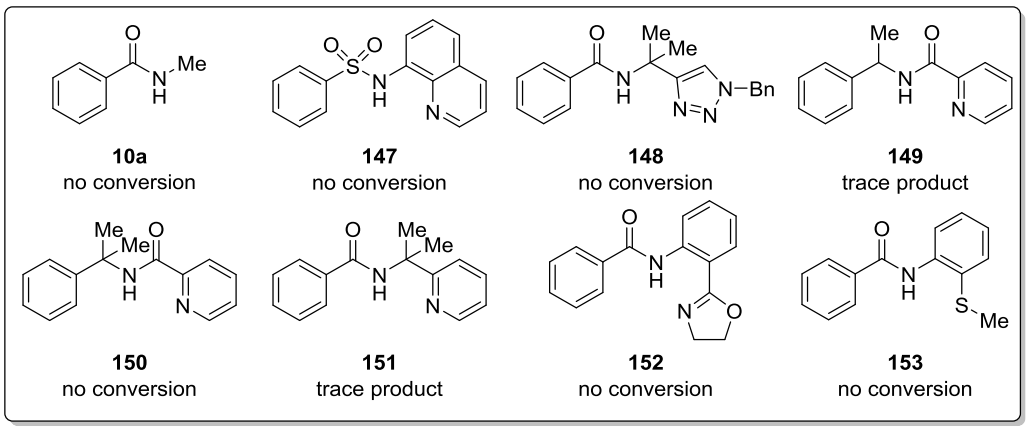
Entry	Amide 110	Alkene 46	Product 132	Yield (%)
1	 **110b**	 **46b**	 **132bb**	85
2	 **110b**	 **46d**	 **132bd**	77
3	 **110b**	 **46h**	 **132bh**	75
4	 **110b**	 **46f**	 **132bf**	61
5	 **110a**	 **46b**	 **132ab**	73
6	 **110a**	 **46f**	 **132af**	63
7	 **110c**	 **46b**	 **132cb**	56

8	 **110d**	 **46b**	 **132db**	77
9	 **110e**	 **46b**	 **132eb**	84
10	 **110f**	 **46b**	 **132fb**	80
11	 **110g**	 **46b**	 **132gb**	58
12	 **110h**	 **46b**	 **132hb**	50
13	 **110i**	 **46b**	 **132ib**	80
14	 **110j**	 **46b**	 **132jb**	54
15	 **110k**	 **46b**	 **132kb**	51

16	 **110l**	 **46b**	 **132lb**	61
17	 **110m**	 **46b**	 **132mb**	70
18	 **110n**	 **46b**	 **132nb**	63
19	**110n**	 **46h**	 **132nh**	64
20	 **110o**	 **46b**	 **132ob**	0
21	 **110p**	**46b**	 **132pb**	0
22	 **110q**	**46b**	 **132qb**	0
23	 **110r**	**46b**	 **132rb**	0

[a] Reaction conditions: **110** (0.25 mmol), alkene **46** (0.50 mmol), $Co(OAc)_2$ (20 mol %), solvent (2.5 mL), 100 °C, 18 h, isolated yields**.**

Thereafter, an investigation of cobalt(II)-catalyzed alkenylations with ethyl acrylate **46b** using different directing groups was carried out (Scheme 65). Not surprisingly, no reaction occurred when the quinolyl substituent in substrate **110** was replaced by methyl as in *N*-methylbenzamide (**10a**). On the other hand, whereas arenes with bidentate DGs commonly demonstrated high reactivity in the C–H functionalization of inactive C–H bonds, as demonstrated by the work of the groups of Daugulis,[78] Yu,[121] Chatani[122] and Shi,[123] benzamides **147**, **149**–**153** with bidentate auxiliaries did not afford the desired products. Reaction of benzamide **148** bearing a TAM directing group,[89,90] which has been demonstrated to be a powerful auxiliary in various ruthenium- and iron-catalyzed C–H functionalization reactions of aromatic and aliphatic acids also failed in this case.



Scheme 65 Substrates displaying limited activity in the cobalt-catalyzed alkenylations.

5.3 Mechanistic Studies

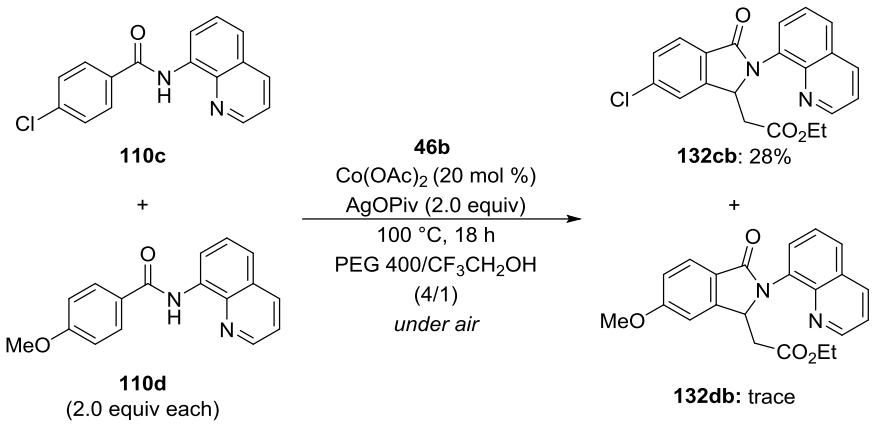
5.3.1 Inter- and Intramolecular Competition Experiments

Given the high catalytic activity of the optimized cobalt(II) catalyst, we became interested in delineating its mode of action. For this purpose, intermolecular competition experiments with amides **110c** and **110d** were performed. The reaction selectively yielded chloro-substituted isoindolin-1-one **132cb** as the sole product (Scheme 66).

[121] R. Giri, N. Maugel, B. M. Foxman, J.-Q. Yu, *Organometallics* **2008**, *27*, 1667–1670; (b). M. Shang, H. Wang, S. Sun, H. Dai, J.-Q. Yu. *J. Am. Chem. Soc.***2014**, *136*, 3354–3357.

[122] N. Hasegawa, V. Charra, S. Inoue, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.***2011**, *133*, 8070–8073.

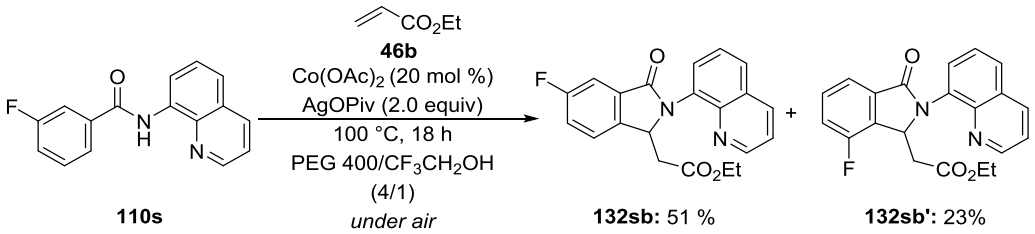
[123] F.-J. Chen, S. Zhao, F. Hu, Chen, K. Zhang, Q. Zhang, B.-F. Shi, *Chem. Sci.* **2013**, *4*, 4187–4192.



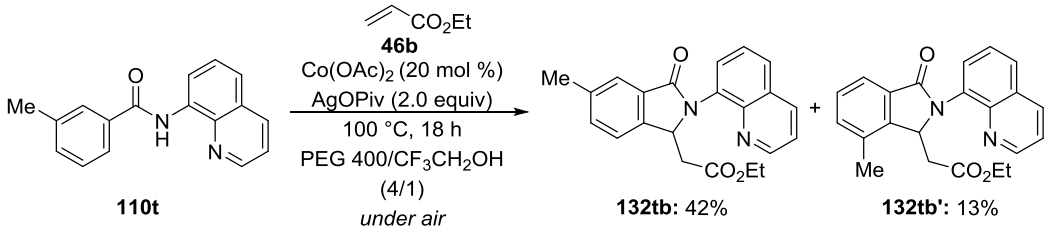
Scheme 66 Intermolecular competition reaction between different amides.

Additionally, intramolecular competition experiments with *meta*-fluoro- (**110s**) (Scheme 67a) and *meta*-methyl-substituted amide (**110t**) (Scheme 67b) were carried out and gave essentially the same result: in both cases sterically less hindered isomers **132sb** and **132tb** were obtained as the major products in 50% and 42% yield, respectively, whereas the yields of compounds **132sb'** and **132tb'** were 23% and 13%, respectively.

a)



b)

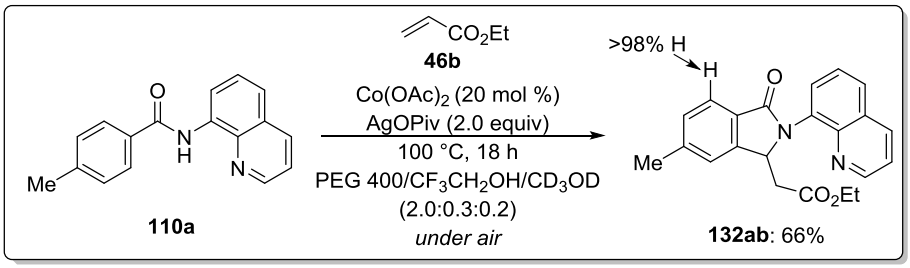


Scheme 67 Intramolecular competition reactions of amides **110s** and **110t**.

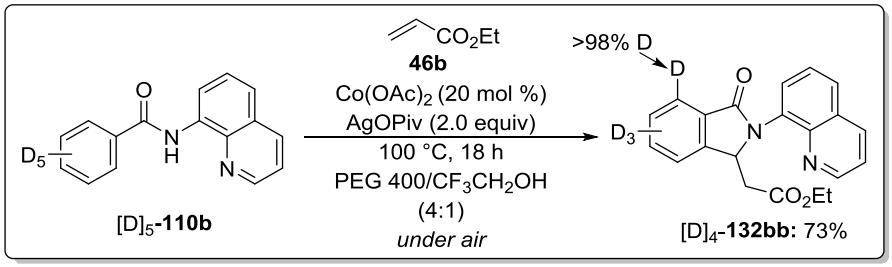
5.3.2 Cobalt-Catalyzed Attempted H/D Exchange Experiments

Mechanistic studies with either deuterated solvent $[D]_4$-MeOH (Scheme 68a) or isotopically labeled substrate $[D]_5$-**110b** (Scheme 68b) showed no H/D scrambling. These observations allow one to postulate an irreversible C−H metalation step accomplished by a bidentate- coordinated cobalt complex **154**.

a)



b)

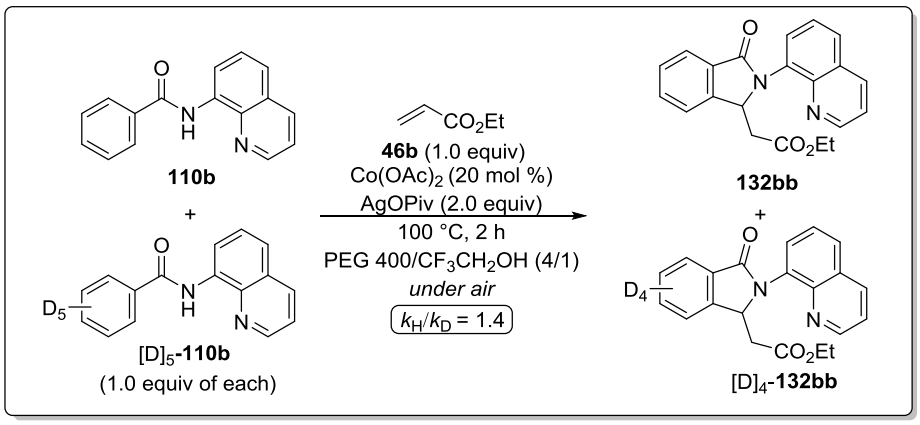


Scheme 68 Oxidative alkenylation with cosolvent $[D]_4$-MeOH or with isotopically labeled substrate $[D]_5$-**110b**.

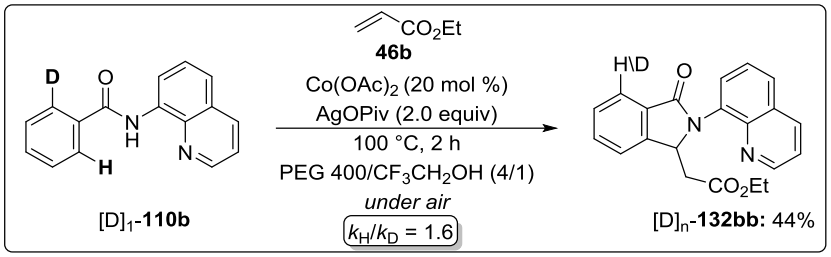
5.3.3 Kinetic Isotope Effect Studies

Furthermore, cobalt-catalyzed C–H alkenylations with isotopically labeled substrate $[D_4]$-**110b** revealed an intermolecular kinetic isotope effect (KIE) of $k_H/k_D \approx 1.4$ (Scheme 69a), and the intramolecular KIE determined with substrate $[D]_1$-**110b** was $k_H/k_D \approx 1.6$ (Scheme 69b). This is in line with a suggestion of the C–H bond metalation step being not rate-determining.

a)



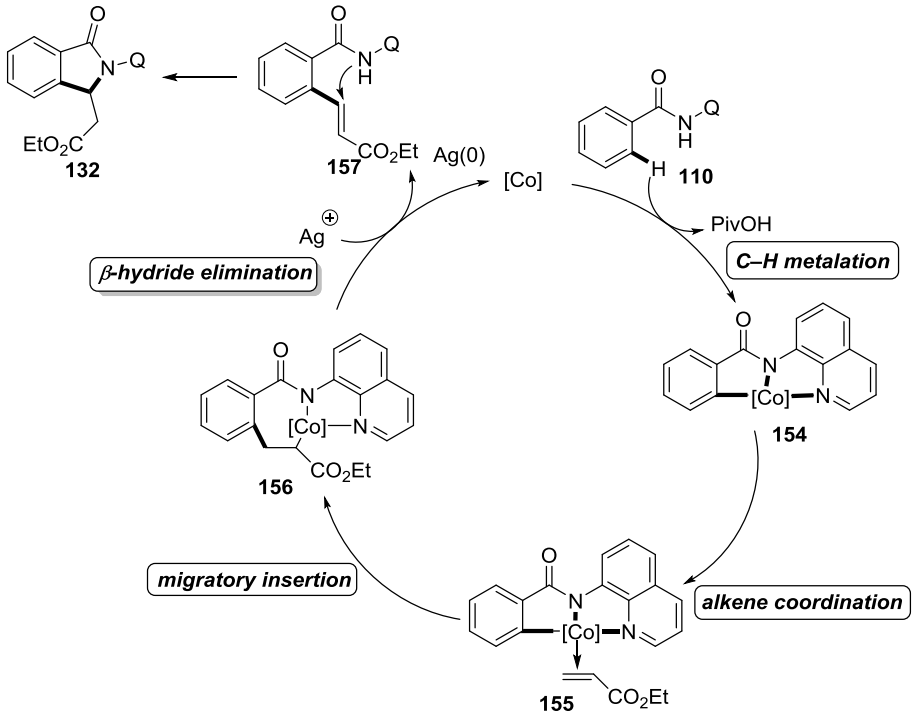
b)



Scheme 69 Studies on the kinetic isotope effect.

5.4 Proposed Catalytic Cycle

Based on the mechanistic studies discussed above and taking into account previous report,[91] a plausible catalytic cycle was proposed (Scheme 70). Initially, the cobalt species chelated with the amide and the quinoline moieties in **110** undergoes *ortho*-C–H bond activation to give the corresponding Co–Ar intermediate **154**. Subsequent coordination of the alkene coupling partner and 1,2-migratory insertion provided a seven-membered cobalt intermediate **156**. The latter underwent *β*-hydride elimination assisted by HOAc to provide the uncyclized alkenylation product **157**. At last, compound **157** entered the intramolecular aza-Michel addition to give the isoindolin-1-one-**132**.



Scheme 70 Proposed catalytic cycle.

6 Silver-Mediated Alkyne Annulations by C−H/P−H Functionalizations: Step-Economical Access to Benzophospholes

Phosphorus-containing heterocycles play an integral role in organic synthesis, medicinal chemistry and material science.[93] Particularly the phosphorous analogues of indole benzophospholes **117**, have emerged as an indispensable structural motif for the construction of conjugated heteroarenes with potential applications in advanced electronic devices. Therefore, their site-selective preparation is of increasing interest. Several methods have been devised for the synthesis of benzo[*b*]phospholes.[99–103] However, most of these approaches relied on the cyclization with pre-functionalized arenes bearing phosphorus- or halide-substituted moieties. In recent years, transition metal-catalyzed derivatizations have emerged as a valuable tool for organic synthesis. Thereby, various *N*-heterocyclic compounds were prepared mostly employing ruthenium, rhodium, palladium, or nickel catalysts in combination with a stoichiometric oxidant. In contrast, the synthesis of phosphorus-containing heterocycles through C−H functionalizations continues to be scarce.[104–106] Given our interest in ruthenium-catalyzed C−H bond activation as well as in the use of secondary phosphine oxides (SPO) as preligands in metal catalysis,[124] we became attracted by silver-mediated C−H/P−H functionalization of substituted phosphine oxides with alkynes for the convenient benzo[*b*]phosphole oxides synthesis.

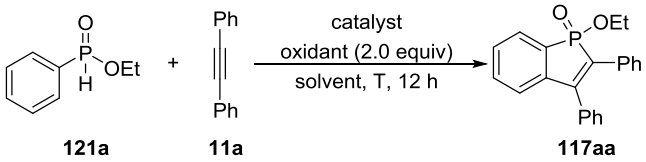
6.1. Optimization Studies

Our initial efforts focused on the annulation of diphenylacetylene (**11a**) with ethyl phenylphosphinate (**121a**) (Table 13). The use of catalytic amounts of ruthenium complex along with AgOAc as the oxidant in DCE provided the desired product 1-ethoxy-2,3-diphenylphosphindole 1-oxide (**117aa**) in unsatisfactory yield (entry 1). Control experiments verified that the reaction proceeded even in the absence of a metal catalyst, and the product was obtained in 17% yield (entry 2). Among various solvents, DMF and DMSO were found to be optimal (entries 3−9). It is notable that a change of the silver salt to Ag_2CO_3, Ag_2O or AgOTs led to inferior results (entries 10−12), whereas only traces of the product were obtained when using AgO_2CCF_3 or AgO_3SCF_3 (entries 13 and 14). Switching the oxidant from silver salts

[124] (a) L. Ackermann, S. Barfüsser, C. Kornhaass, A. R. Kapdi, *Org. Lett*. **2011**, *13*, 3082–3085; (b) L. Ackermann, A. R. Kapdi, S. Fenner, C. Kornhaaß, C. Schulzke, *Chem. Eur. J.* **2011**, *17*, 2965–2971; (c) L. Ackermann, R. Born, J. H. Spatz, D. Meyer, *Angew. Chem. Int. Ed*. **2005**, *44*, 7216–7219; (d) L. Ackermann, *Org. Lett.* **2005**, *7*, 3123–3125; (e) L. Ackermann, R. Born, *Angew. Chem. Int. Ed*. **2005**, *44*, 2444–2447; Reviews: (f) L. Ackermann, *Isr. J. Chem*. **2010**, *50*, 652–663; (g) L. Ackermann, *Synthesis* **2006**, 1557–1571.

to $Zn(OAc)_2$ or MnO_2 furnished the desired product only in trace quantities as well (entries 15 and 16). Furthermore, it is noteworthy that the addition of 2.0 equivalents of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) as radical scavenger completely suppressed the reaction (entry 17), thus indicating the reaction to proceed by SET processes.[125]

Table 13 Silver-mediated oxidative cyclization of ethylphenylphosphinate **121a** with diphenylacetylene **11a**[a]



121a **11a** **117aa**

Entry	*cat.*	Solvent	Oxidant	T (°C)	Yield (%)
1	$[RuCl_2(p\text{-cymene})]_2$	DCE	AgOAc	80	21
2	---	DCE	AgOAc	80	17
3	---	DCE	AgOAc	120	46
4	---	*o*-xylene	AgOAc	120	51
5	---	*t*AmOH	AgOAc	120	51
6	---	**DMF**	**AgOAc**	**120**	**60**
7	---	**DMSO**	**AgOAc**	**120**	**60**
8	---	NMP	AgOAc	120	52
9	---	DMA	AgOAc	120	51
10	---	DMSO	Ag_2CO_3	120	31
11	---	DMSO	Ag_2O	120	25
12	---	DMSO	AgOTs	120	17
13	---	DMSO	AgO_3SCF_3	120	trace
14	---	DMSO	AgO_2CCF_3	120	trace
15	---	DMSO	$Zn(OAc)_2$	120	trace
16	---	DMSO	MnO_2	120	trace
17	---	DMSO	AgOAc	120	trace[b]

[a] Reaction conditions: **121a** (0.50 mmol), **11a** (1.00 mmol), catalyst (5.0 mol %), oxidant (2.0 equiv), solvent (2.0 mL), under N_2; isolated yield. [b] TEMPO (2.0 equiv).

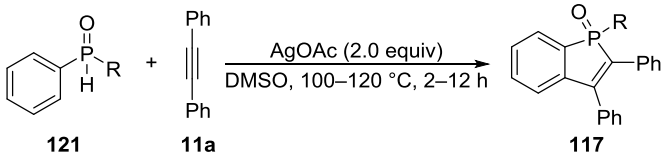
6.2 Scope of the Silver-Mediated Alkyne Annulations

Having identified the optimal reaction conditions (Table 13, Entry 7), we explored the scope of the silver-mediated alkyne annulation by varying the substitution pattern of substrate **121** (Table 14). A wide range of phosphinates and aryl- or alkyl-substituted SPO bearing groups, such as methyl, *tert*-butyl, cyclohexyl, and ethoxy, were converted efficiently, thus affording the corresponding products **117aa**–**117ea** in good yield (entries 1–5). Notably, phosphinate-substituted thiophene

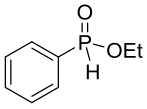
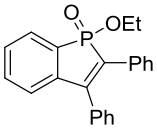
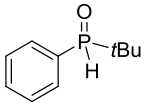
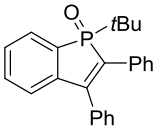
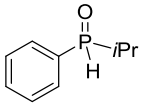
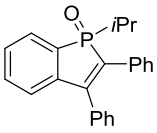
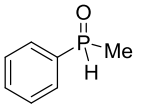
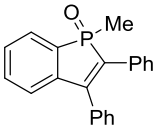
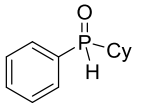
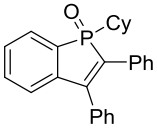
[125] E. C. Ashby, *Acc. Chem. Res.* **1988**, *21*, 414–421.

121f proved to be a suitable substrate as well (Scheme 71).

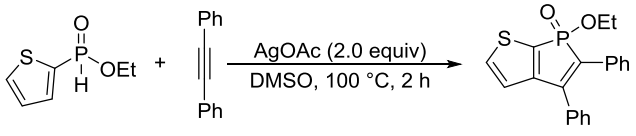
Table 14 Oxidative annulations of substrates **121** with diphenylacetylene (**11a**)[a]



121 **11a** **117**

Entry	Phosphine Oxide 121	T (°C)	*t* (h)	Product 117	Yield(%)
1	 **121a**	120	12	 **117aa**	60
2	 **121b**	120	12	 **117ba**	55
3	 **121c**	120	12	 **117ca**	49
4	 **121d**	100	2	 **117da**	54
5	 **121e**	120	2	 **117ea**	46

[a] Reaction conditions: **121** (0.50 mmol), **11a** (1.00 mmol), AgOAc (2.0 equiv), DMSO (2.0 mL), under N_2; isolated yield.

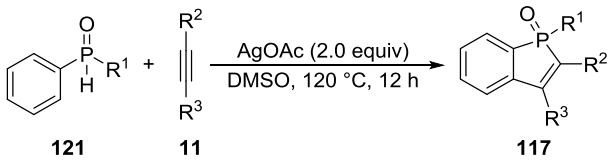


121f **11a** **117fa:** 41%

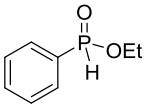
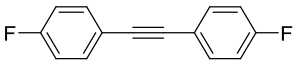
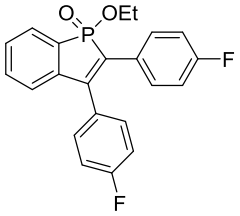
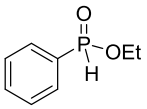
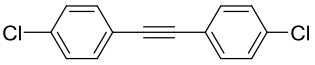
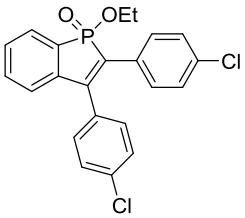
Scheme 71 Silver-mediated oxidativeannulation with heterocycle substrate **121f**.

Thereafter, differently decorated tolane derivatives were tested in the silver-mediated annulation process (Table 15). The C–H/P–H bonds functionalizations with tolanes **11** occurred with high catalytic efficacy, affording products **117ad, 117ae, 117am, 117ha, 117hc** and **117ge** in good yields (entries 1–7). Symmetrical dialkylalkynes, such as oct-4-yne (**11h**) reacted with diphenylphosphine oxide (**121g**) to furnish the desired product **117gh** in moderate yield (entry 8). Unsymmetrically substituted alkynes **11i**, **11n**, **11o** likewise delivered the desired products **117gi**, **117gn** and **117go** (entries 9−11). Notably, the cyclizations with alkyl-substituted phenylacetylenes proceed with excellent regioselectivities, and only the 3-phenylsubstituted regioisomers bearing the alkyl substituent neighboring to the phosphorus atom was obtained. Such regioselectivity was only rarely observed in ruthenium(II)-catalyzed annulations of alkynes through C–H/X–H bonds activation.[126]

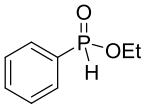
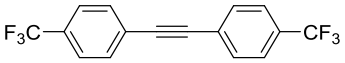
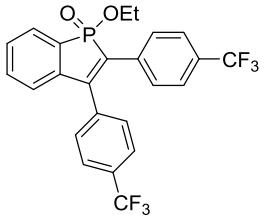
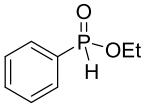
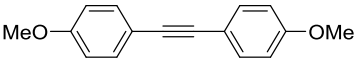
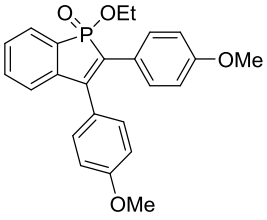
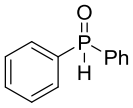
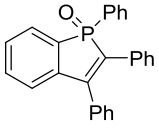
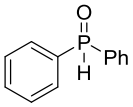
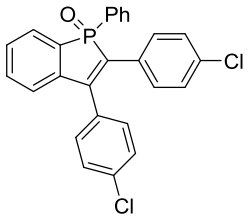
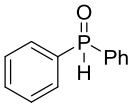
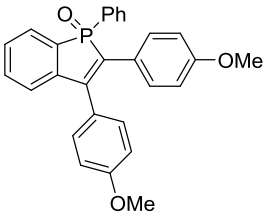
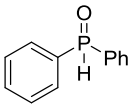
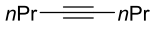
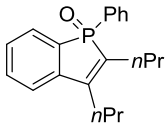
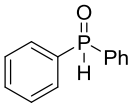
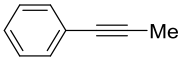
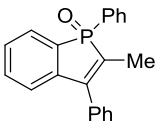
Table 15 Scope of oxidative annulation forphosphine oxide**121** with alkynes **11**[a]

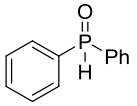
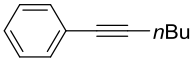
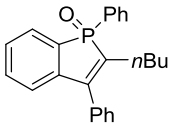
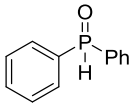
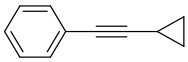
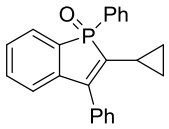


121 **11** **117**

Entry	Phosphine Oxide 121	Alkyne 11	Product 117	Yield(%)
1	 **121a**	 **11d**	 **117ad**	50
2	 **121a**	 **11e**	 **117ae**	64

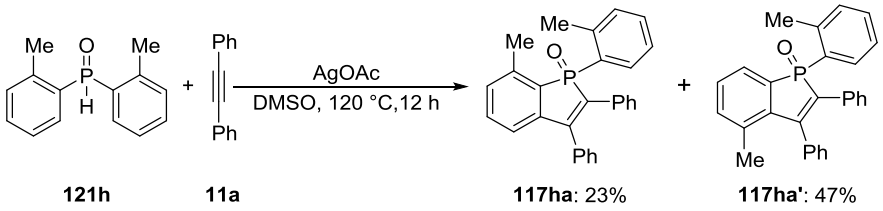
[126] M. Deponti, S. I. Kozhushkov, D. S. Yufit, L. Ackermann, *Org. Biomol. Chem.* **2013**, *11*, 142–148, and references cited therein.

3	 **121a**	 **11m**	 **117am**	53
4	 **121a**	 **11c**	 **117ac**	27
5	 **121g**	**11a**	 **117ga**	66
6	 **121g**	**11e**	 **117ge**	64
7	 **121g**	**11c**	 **117gc**	32
8	 **121g**	 **11h**	 **117gh**	55
9	 **121g**	 **11i**	 **117gi**	53

10	 **121g**	 **11n**	 **117gn**	59
11	 **121g**	 **11o**	 **117go**	42

[a] Reaction conditions: **121** (0.50 mmol), **11** (1.00 mmol), AgOAc (2.0 equiv), DMSO (2.0 mL), under N_2; isolated yield.

During further studies on the reactivity of various substrates **121**, we were surprised to find that the promoted annulation by AgOAc with di(*o*-tolyl)phosphine oxide (**121h**) afforded the phosphindole derivative **117ha** as a 1:2 mixture with the unexpected regioisomer **117ha'** as a major product (Scheme 72). This result can be explained as a consequence of a [1,2] migration of the phosphor-containing moiety in the aryl fragment in one of the intermediates. Most probably, this unexpected C−P bond cleavage proceeded through a radical mechanism.



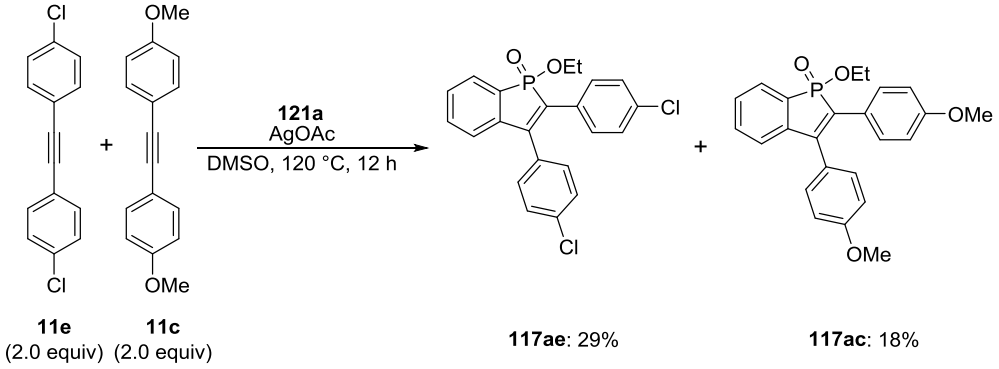
Scheme 72 Silver-mediated oxidative annulations with SPO **121h**.

6.3 Mechanistic Studies

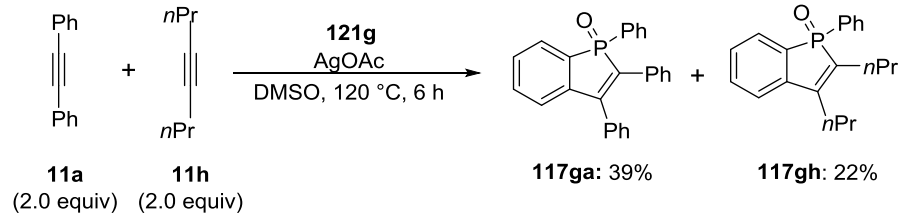
6.3.1 Intermolecular Competition Experiments

Intermolecular competition experiments with an excess of alkynes **11c** and **11e** indicated electron-deficient alkynes to be more reactive (Scheme 73a). Furthermore, intermolecular competition experiments between diaryl- and dialkylalkynes **11a** and **11h** revealed tolane (**11a**) to be preferentially converted (Scheme 73b)

a)

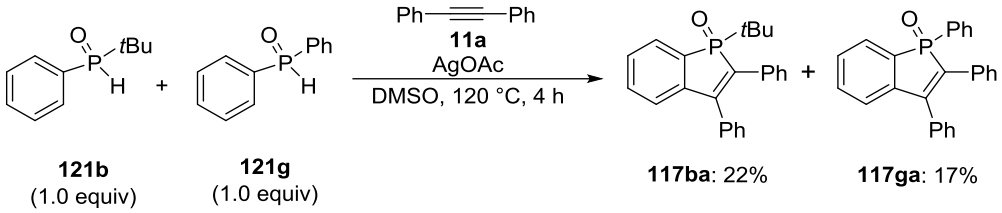


b)



Scheme 73 Competition experiments between alkynes **121**.

An intermolecular competition experiment between *tert*-butylphenylphosphine oxide (**121b**) and diphenylphosphine oxide (**121g**) disclosed the reaction to be less dependent on the substitution at the phosphorus atom (Scheme 74).



Scheme 74 Competition experiments between phosphine oxides **121b** and **121g**.

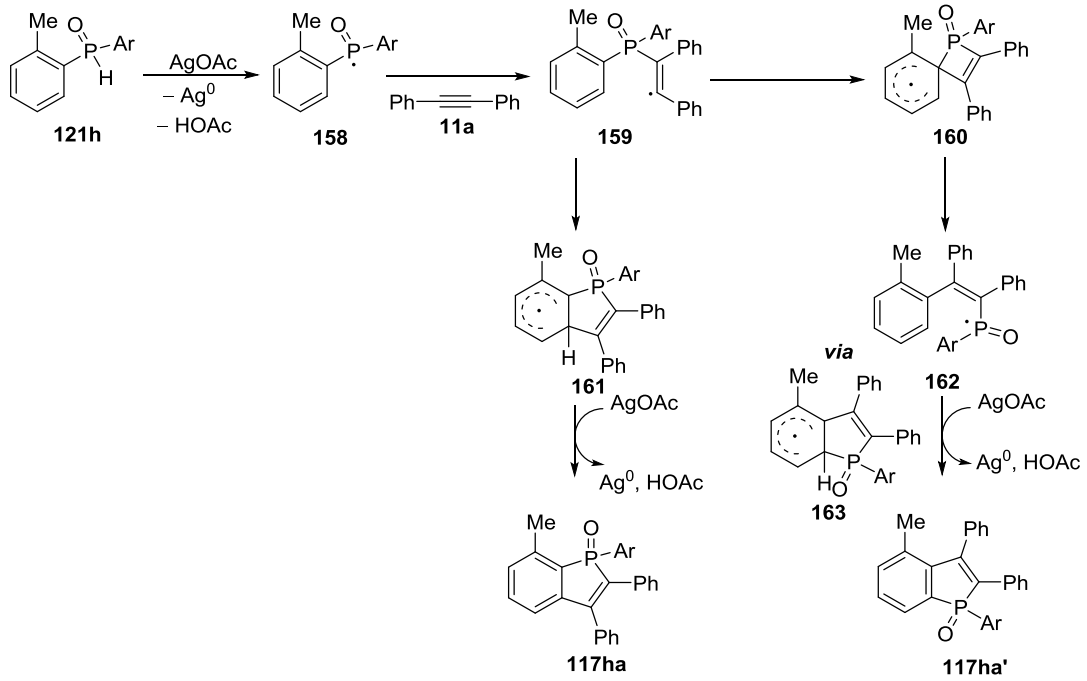
6.4 Proposed Mechanism

Based on the observations mentioned above and the results of previous reports by Duan[127] and Miura,[128] we proposed a plausible mechanism for this silver-mediated reaction (Scheme 75). First, a phosphoryl radical **158** was generated from di-*o*-tolylphosphine oxide (**121h**) through a P–H bond cleavage *via* oxidation with silver acetate, followed by the radical addition to the alkyne **11a** to afford alkenyl radical species **159**. Subsequently, the intramolecular attack of the alkenyl radical **159** onto the *ortho* position of an aryl ring furnished bicyclic radical intermediate **161**. After oxidation with a second equivalent of AgOAc to remove a hydrogen atom, the phosphorus-containing heterocyclic product **117ha** was obtained. However, formation of an unexpected isomer **117ha'** in this reaction (Scheme 72) indicated that this annulation reaction could involve an [1,2] migration step as an unanticipated pathway. The detailed process was supposed to start with an attack of the alkenyl radical **159** onto the phosphorus-substituted carbon atom to form a spiro[3.5]nonatrienyl radical **160** containing a four-membered intermediate. Subsequent C−P bond cleavage furnished the phosphoryl radical **162**, which attacked the neighboring carbon atom of the aryl ring and then underwent oxidation with AgOAc to afford the

[127] Y.-R. Chen, W.-L. Duan, *J. Am. Chem. Soc*. **2013**, *135*, 16754–16757.

[128] Y. Unoh, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed*. **2013**, *52*, 12975–12979.

phosphorus heterocycle **117ha'**.

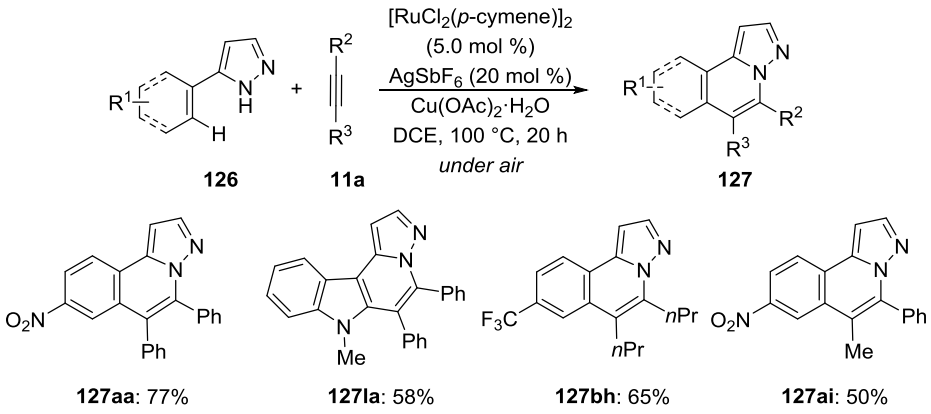


Scheme 75 Proposed mechanism of silver-mediated oxidative annulations.

7 Summary and Outlook

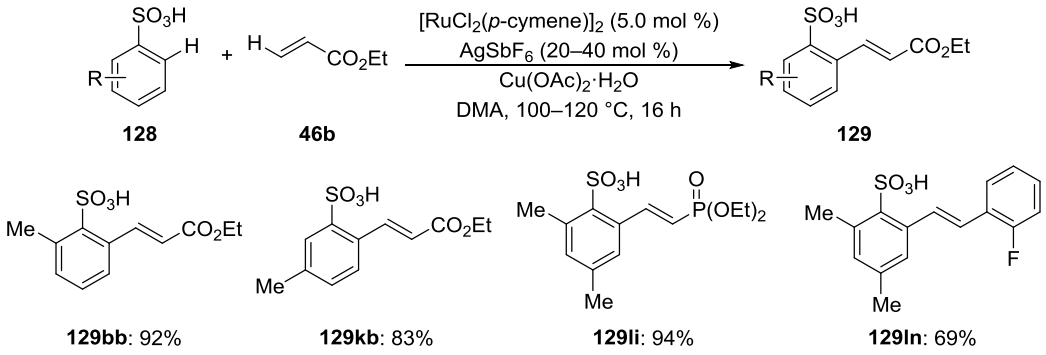
Transition metal-catalyzed direct C–H functionalizations have emerged as an attractive strategy in the development of sustainable green chemistry. By using this approach, the C–H transformations, such as alkenylation and annulation reactions, can be successfully achieved under mild reaction conditions.

In the first part of this work, we devised ruthenium(II)-catalyzed oxidative alkyne annulations with substituted 1*H*-pyrazoles **126** by C–H/N–H bond functionalizations under air. In this project, the desired oxidative annulation was not accomplished with $CuBr_2$ in lieu of $Cu(OAc)_2 \cdot H_2O$ as the terminal oxidant, thereby indicating the importance of carboxylate assistance. For the substrate scope, we were pleased to find that these reactions are tolerant of different substituent on the aryl ring. A wide range of alkynes **11** such as dialkylalkynes and tolanes were also suitable substrates under the optimized reaction conditions. Furthermore, oxidative annulations with unsymmetrically substituted alkynes occurred with excellent regioselectivities. (Scheme 76).



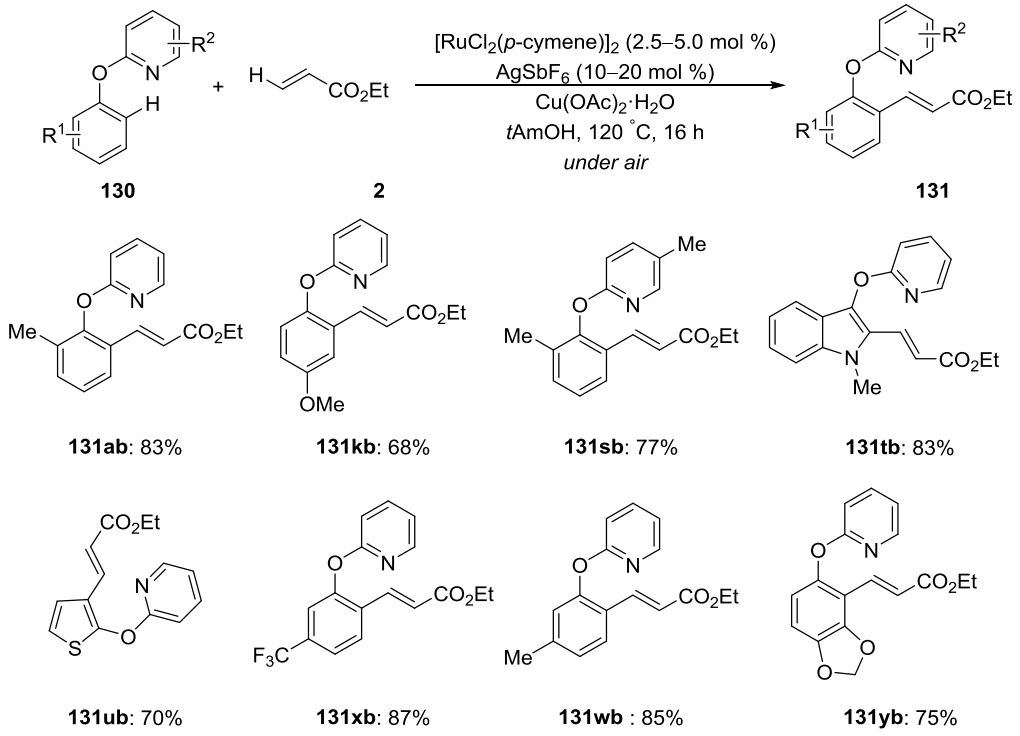
Scheme 76 Ruthenium(II)-catalyzed alkyne annulations with pyrazoles **126** by C–H/N–H functionalization.

A ruthenium(II) catalyst could also be applied to the oxidative alkenylations with benzenesulfonic acids **128** *via* twofold C–H bond cleavages (Scheme 77). Not only differently substituted aromatic sulfonic acids, but also benzenesulfonyl chloride (**136**) and methyl benzenesulfonates **137** can efficiently be transformed to afford the corresponding products **129** in high yields. Importantly, unactivated styrenes as alkenylating agents were also compatible for this reaction.



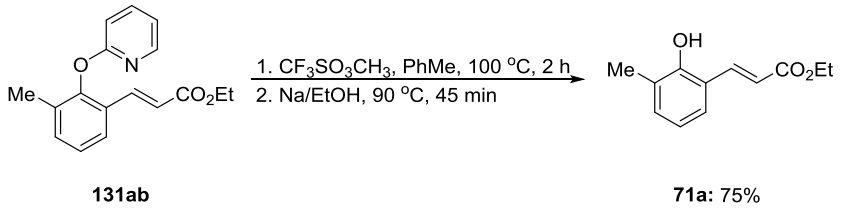
Scheme 77 Ruthenium-catalyzed oxidative alkenylations with substituted sulfonic acid.

In the third project, the ruthenium(II)-catalyzed direct alkenylation of arenes **130** bearing a removable directing group was achieved. The established catalytic system proved to be broadly applicable and, hence, furnished the desired products **131** in high yields. Especially, heteroarenes as substrates such as substituted indole **130t** and thiophene **130u** were efficiently converted.



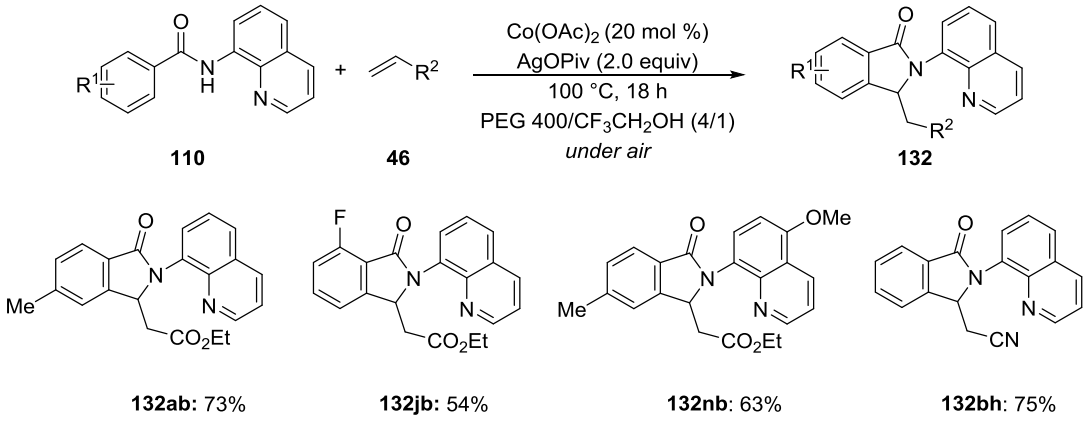
Scheme 78 Ruthenium(II)-catalyzed oxidative alkenylations of substituted phenyloxylpyridines **130**.

Importantly, the directing group could be removed easily yielding the *ortho*-vinyl phenol **71a** which is an important intermediate in organic synthesis (Scheme 79).



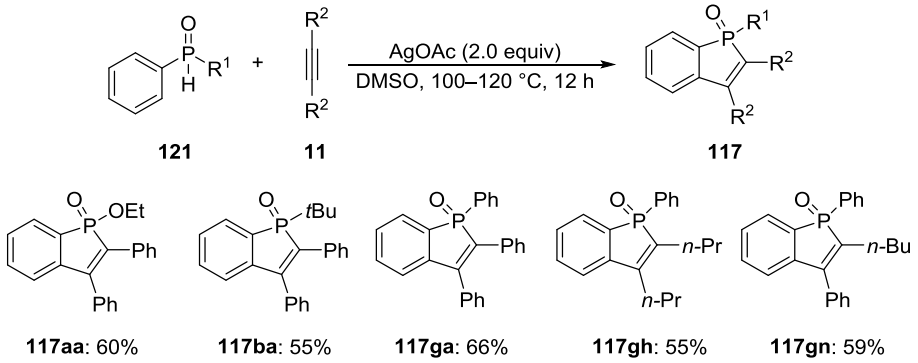
Scheme 79 Removal of the directing group.

In the fourth project, cobalt acetate was found to be an efficient catalyst for the C–H functionalization in benzamides **110** by using a bidentate directing group (Scheme 80). This earth-abundant first-row transition metal catalyst can enable the transformation smoothly with a widely range functional groups tolerance, to furnish the isoindolin-1-ones **132** in high yields. In contrast, ruthenium- and rhodium-catalyzed reactions of the substrates **110** with acrylates **46** resulted in the hydroarylation of the latter.[86a,88c]



Scheme 80 Cobalt-catalyzed oxidative C–H alkenylations with bidentate directing group.

In the fifth project, the silver-mediated alkyne annulation *via* C–H/P–H bonds was developed. This transformation proceeded with excellent chemo- and site-selectivities in the presence of silver acetate as the terminal oxidant, thereby furnishing substituted phosphindole **117** with broad scope. The radical mechanism of the C–H/C–P functionalization was unraveled though detailed mechanistic studies.



Scheme 81 Silver mediated alkyne annulations *via* C−H/P−H functionalization.

In summary, the rapid progress of C–H functionalization chemistry over the last decade has provided numerous efficient protocols for forming new chemical bonds. Especially, the ruthenium(II)-catalyzed direct C–H alkenylations and annulations have been proven viable with a broad substrates scope and excellent chemo-, regio-, and site-selectivity. These carboxylate-assisted ruthenium(II)-catalyzed C–H functionalizations were even allowed in an aerobic fashion with $Cu(OAc)_2 \cdot H_2O$ under an atmosphere of ambient air. Yet, less expensive first-row transition metal complexes such as cobalt salts were also identified as versatile catalysts for step-economical chelation-assisted direct C−H alkenylations in user-friendly solvent. Finally, we developed silver-mediated alkyne annulations by C–H/P–H functionalizations.

Although the development of new reactions and catalysts continues to evolve at a rapid pace, successful applications of these methods to the synthesis of complex natural products, bioactive compounds and functional materials are still rare. Therefore, the development of new transition metal-catalyzed direct C–H functionalizations that can be used in the synthesis of complex molecules are still in great demand.

8 Experimental Section

8.1 General Remarks

Unless otherwise noted, all reactions were performed under a N_2 atmosphere using pre-driedglassware and standard Schlenk techniques.

Solvents

All solvents for reactions involving moisture-sensitive reagents were dried, distilled and stored under inert atmosphere (argon or nitrogen) according to the following standard procedures. *tert*-Amylalcohol (*t*AmOH) was used as supplied by Merck or stirred over sodium chips for 5 h at 120 °C and distilled under ambient pressure; water (H_2O) was degassed before its use applying repeated Freeze-Pump-Thaw degassing procedure; 1,2-dichloroethane (DCE), *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), acetonitrile (MeCN) and dimethylacetamide (DMA) were dried over CaH_2 for 8 h, degassed and distilled under reduced pressure; dichloromethane and tetrahydrofuran (THF) were purified using a solvent purification system (SPS) from MBRAUN; *N*-methyl-2-pyrrolidone (NMP) was stirred over CaH_2 for 4 h at 150 °C and subsequently distilled under reduced pressure; ethanol (EtOH) was distilled from magnesium ethanolate; toluene (PhMe) was pre-dried over KH followed by distillation from sodium benzophenone ketyl; 1,4-dioxane was dried by distillation from sodium benzophenone ketyl.

Vacuum

The following pressures were measured on the used vacuum pumps and were not corrected: membrane pump vacuum (MPV): 0.5 mbar, oil pump vacuum (OPV): 0.1 mbar.

Melting Points (M. p.)

Melting points were measured using a *Stuart® Melting Point Apparatus SMP3* fromBARLOWO-RLD SCIENTIFIC. Reported values are uncorrected.

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates (MACHEREY-NAGEL) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light or developed by treatment with a $KMnO_4$ solution followed by careful applying a heat gun. Chromatographic purification of products was accomplished by flash column

chromatography on MERCK silica gel, grade 60 (0.040–0.063 mm and 0.063–0.200 mm).

Gas Chromatography (GC)

The conversion of the reactions was monitored applying coupled gas chromatography/mass spectrometry using *G1760C GCD plus* with mass detector *HP 5971, 5890 Series II* with mass detector *HP 5972* from HEWLETT-PACKARD and *7890A GC-System* with mass detector *5975C (Triplex-Axis-Detector)* from AGILENT TECHNOLOGIES equipped with *HP-5MS* columns (30 m × 0.25 mm × 0.25 m) instruments.

High Performance Liquid Chromatography (HPLC)

Preparative and analytical separations were performed on an HPLC-System from KNAUER (*Smartline Pump 100*, Dynamic Mixing Chamber, Injection- and Control-Valve, *Smartline UV Detector 2500*). Separation normal phase column (250 × 10 mm) from MACHEREY-NAGEL (MN) was used. Organic solvents of HPLC grade were employed. All samples were filtered through Polytetrafluoroethylene Filter from ROTH (Ø 25 mm, 0.2 µm) or VWR (Ø 13 mm, 0.2µm) prior to separation.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (NMR) spectroscopy was performed at 300 400 or 600 MHz (^{1}H NMR), 75, 100 or 125 MHz (^{13}C NMR, APT), 283 MHz (^{19}F NMR) and 122 MHz (^{31}P NMR) on BRUKER *AM 250*, VARIAN *Unity-300* and *Inova 500* instruments. Chemical shifts are reported as δ-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively, or the standard trimethylsilyl (TMS) peak. For characterization of the observed resonance multiplicities the following abbreviations were applied: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *m* (multiplet), *dd* (doublet of doublet), *dt* (doublet of triplet), or analogue representations. The coupling constants *J* are reported in Hertz (Hz).

Infrared Spectroscopy (IR)

Infrared spectra were recorded on a BRUKER *Alpha-P* ATR-spectrometer. Liquid probes have been measured as films and solid probes neat. Analysis of the spectral data has been done by using the *OPUS 3.1* software from BRUKER, respectively *OPUS 6*. Absorption ($\tilde{\nu}$) is given in wave numbers (cm^{-1}). Spectra were recorded in the range of 4000 to 400 cm^{-1}.

Mass Spectrometry (MS)

MS (EI) and HR-MS (EI) were measured on a Time-of-Flight mass spectrometer Accu TOF from JOEL. ESI-mass spectra were recorded on an Ion-Trap mass spectrometer LCQ from FINNIGAN or on a Time-of-Flight mass spectrometer microTOFfrom BRUKER. ESI-HR-MS spectra were recorded on a BRUKER APEX IV or a BRUKER DALTONIC {7T, Fourier Transform Ion Cyclotron Resonance (FTICR)} mass spectrometer. The ratios of mass to charge (m/z) are indicated, intensities relative to the base peak (I = 100) are given in parentheses.

Reagents

Chemicals obtained from commercial sources with purity above 95% were used without further purification. Anhydrous arylsulfonic acid (**128**) was prepared by heating the monohydrate to 160 °C under vacuum for 1 h.

8.2 Synthesis of Starting Materials

The following starting materials were synthesized according to previously described methods: Alkynes **11b–11g, 11j–11l**,[129] pyrazoles **126a–126l, 141**,[130] arylsulfonic acids **128d**, **128f**, **128g**, **128h**,[131]2-phenoxypyridines **130a–130y, 141**,[132] pyrimidines **142**[133] and **143,**[134] amides **110a–110r, 147, 149, 150, 152, 153**,[92] **148b**,[88a] **151**,[135] isotopically labeled substrates $[D]_5$-**110b**,[136] $[D]_1$-**110b**, [137] phenylphosphinates **121a**, **121f**,[138] SPOs **121b–121e**, **121g–121h**.[139]
The following compound was obtained by the generous courtesy of the person named below:
Karsten Rauch: $[RuCl_2(p\text{-cymene})]_2$.

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8.3 General Procedures

General Procedure A: Ruthenium-Catalyzed Oxidative Alkyne Annulation with Substituted 1*H*-Pyrazoles (126)

A suspension of 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.0 mg, 0.50 mmol), diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.3 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (100 mg, 0.50 mmol) in DCE (2.0 mL) was stirred at ambient temperature for 5 min and then at 100 °C for 20 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq. NH_4Cl/NH_3 (1:1, 10mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→8/1) to yield **127aa** (139.0 mg, 77%) as a yellow solid.

General Procedure B: Ruthenium(II)-Catalyzed Oxidative C–H Alkenylations of Sulfonic Acids, Chlorides and Methyl Benzenesulfonate.

A suspension of 2,5-dimethylphenylsulfonic acid (**128a**) (94.0 mg, 0.50 mmol), ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.00 mmol) in DMA (2.0 mL) was stirred at ambient temperature under N_2 for 5 min and then at 120 °C for 16 h. At ambient temperature, the solvent was removed *in vacuo*, and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH: 15/1→10/1) to yield **129ab** (131.0 mg, 91%) as an off-white solid.

General ProcedureC: Ruthenium(II)-Catalyzed Oxidative C–H Alkenylations of Sulfonic Acids

A suspension of 2,4-dimethylphenylsulfonic acid (**128l**) (92.3 mg, 0.50 mmol), 4-fluorostyrene (**46m**) (183.0 mg, 1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (35.0 mg, 0.10 mmol, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (200.0 mg, 1.00 mmol) in DMF (2.0 mL) was stirred at ambient temperature under N_2 for 5 min and then at 100 °C for 16 h. At ambient temperature, the solvent was removed *in vacuo*, and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH: 15/1→10/1) to yield **129lm** (92.0 mg, 60%) as an off-white solid.

General Procedure D: Ruthenium(II)-Catalyzed C–H Alkenylations of Phenols with Removable Directing Groups

A suspension of 2-(*o*-tolyloxy)pyridine (**130a**) (185.4 mg, 1.00 mmol), ethyl acrylate (**46b**) (52.0

mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.6 mg, 2.5 mol %), $AgSbF_6$ (18.5 mg, 10 mol %) and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.00 mmol) in *t*AmOH (2.0 mL) was stirred at ambient temperature under N_2 for 5 min and then at 120 °C for 16 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq. NH_4Cl/NH_3 (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents in *vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→10/1) to yield **131ab** (122.0 mg, 83%) as a colorless solid.

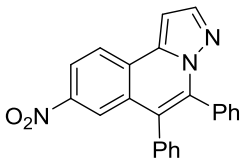
General procedure E: Cobalt-Catalyzed Oxidative C–H Bond Alkenylations with Bidentate Directing Group: A suspension of 4-methyl-*N*-(quinolin-8-yl)benzamide (**110a**) (65.6 mg, 0.25 mmol), ethyl acrylate (**46b**) (50 mg, 0.50 mmol), $Co(OAc)_2$ (9.0 mg, 20 mol %) and AgOPiv (105.0 mg, 2.0 equiv) in a PEG 400 (2.0 mL) and CF_3CH_2OH (0.5 mL) mixture solvent was stirred at 100 °C for 18 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with H_2O and extracted with *t*BuOMe (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1→1/1) to yield **132ab** (66.0 mg, 73%) as a white solid.

General procedure F: Silver-Mediated Alkyne Annulations by C−H/P−H Functionalizations: A suspension of ethyl phenylphosphinate (**121a**) (85.0 mg, 0.50 mmol), diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol) and AgOAc (166.0 mg, 1.00 mmol) in DMSO (2.0 mL) was stirred under N_2 atmosphere at ambient temperature and then at 120 °C for 12 h. At ambient temperature, the reaction mixture was diluted with water and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents in *vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→2/1) to yield **121aa** (104.0 mg, 60%) as an off-white oil.

8.4 Analytical Data

8.4.1 Analytical Data for the Products of the Ruthenium-Catalyzed Alkyne Annulation with Substituted 1*H*-Pyrazoles by C–H/N–H Bond Functionalizations

6-Nitro-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127aa):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.6 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 8/1) yielded **127aa** (139.0 mg, 77%) as a yellow solid.

M. p. = 182–184 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.66 (d, J = 8.8 Hz, 1H), 8.41 (dd, J = 8.8, 2.2 Hz, 1H), 8.13–8.06 (m, 1H), 8.02 (d, J = 2.2 Hz, 1H), 7.67 (d, J = 1.6 Hz, 1H), 7.38–7.27 (m, 10H).

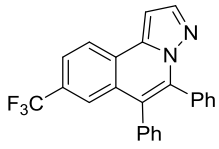
^{13}C NMR (75 MHz, d_6-DMSO): δ = 145.7 (C_q), 140.9 (CH), 137.3 (C_q), 136.1 (C_q), 134.0 (C_q), 131.7 (C_q), 130.8 (CH), 130.1 (CH), 128.9 (C_q), 127.9 (CH), 127.7 (CH), 127.3 (CH), 127.1 (CH), 127.0 (C_q), 125.1 (CH), 122.5 (C_q), 121.0 (CH), 120.7 (CH), 100.4 (CH).

IR (neat): 3055, 1535, 1487, 1424, 1391, 751, 689, 649 cm^{-1}.

MS (EI) *m/z* (relative intensity): 365 (90) $[M]^+$, 364 (100)$[M–H]^+$, 334 (20), 318 (40), 290 (20), 214 (10), 158 (15), 105 (15), 77 (10).

HR-MS(EI) *m/z* calcd for $C_{23}H_{15}N_2^+$ $[M]^+$ 365.1159, found 365.1154.

6-(Trifluoromethyl)-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127ba):



The general procedure **A** was followed using 5-{4-(trifluoro-methyl)phenyl}-1*H*-pyrazole (**126b**) (107.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127ba** (137.0 mg, 70%) as an off-white solid.

M. p. = 137–139 °C.

^{1}H NMR(300 MHz, $CDCl_3$): δ = 8.32 (d, J = 8.3 Hz, 1H), 8.04–8.03 (m, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.71 (s, 1H), 7.34–7.30 (m, 8H), 7.23–7.18 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.4 (CH), 137.7 (C_q), 137.7 (C_q), 135.1 (C_q), 132.6 (C_q), 131.4 (CH), 130.7 (CH), 129.7 (C_q), 129.5 ($^2J_{C\text{-}F}$ = 33 Hz, C_q), 128.6 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 126.2 (C_q), 125.8 (C_q), 124.3 (CH), 124.0 ($^1J_{C\text{-}F}$ = 273 Hz, C_q), 123.9 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 123.9 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 98.8 (CH).

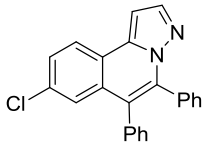
^{19}F NMR ($CDCl_3$, 283 MHz): δ = −62.3 (s).

IR (neat): 3065, 1355, 1309, 1123, 1078, 787, 754, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 388 (50) $[M]^+$, 387 (100) $[M–H]^+$, 360 (5), 340 (7), 333 (7), 290 (5), 174 (4), 77 (3).

HR-MS (ESI) *m/z* calcd for $C_{24}H_{16}F_3N_2^+$ $[M+H]^+$ 389.1260, found 389.1255.

6-Chloro-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127ca):



The general procedure **A** was followed using 5-(4-chlorophenyl)-1*H*-pyrazole (**126c**) (90.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (179.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127ca** (124.0 mg, 69%) as an off-white solid.

M. p. = 83–85 °C.

^{1}H NMR(300 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.6 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.54 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.37–7.27 (m, 8H), 7.20–7.17 (m, 2H), 7.10 (d, *J* = 2.2 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.3 (CH), 138.0 (C_q), 137.4 (C_q), 135.4 (C_q), 133.7 (C_q), 132.7 (C_q), 131.4 (CH), 131.3 (C_q), 130.7 (CH), 128.5 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 127.5 (CH), 126.0 (CH), 125.1 (CH), 123.1 (C_q), 122.4 (C_q), 97.8 (CH).

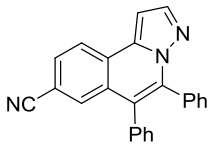
IR (neat): 3058, 1443, 1411, 780, 760, 713, 693, 650 cm^{-1}.

MS (EI) *m/z* (relative intensity): 355 $[M+H]^+$, 354 (80) $[M]^+$, 353 (100) $[M–H]^+$, 318 (10), 290 (30), 214 (10), 159 (70), 144 (30), 130 (20).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{16}ClN_2^+$ $[M+H]^+$ 355.0997, found 355.0993.

The spectral data are in accordance with those reported in the literature.[109]

6-Cyano-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127ca):



The general procedure **A** was followed using 4-(1*H*-pyrazol-5-yl)benzonitrile (**126d**) (84.9 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127da** (114.0 mg, 66%) as a light yellow solid.

M. p. = 207–209°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.80–7.75 (m, 2H), 7.36–7.30 (m, 8H), 7.23 (d, *J* = 2.2 Hz, 1H), 7.20–7.16 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.6 (CH), 138.1 (C_q), 137.4 (C_q), 134.7 (C_q), 132.2 (C_q), 131.6 (CH), 131.3 (CH), 130.6 (CH), 130.0 (C_q), 129.1 (CH), 128.8 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 126.5 (C_q), 124.4 (CH), 123.1 (C_q), 118.8 (C_q), 111.0 (C_q), 99.5 (CH).

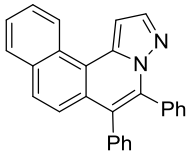
IR (neat): 3058, 2225, 1410, 1342, 830, 755, 721, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity)**:** 345 (73) $[M]^+$, 344 (100) $[M–H]^+$, 317 (12), 290 (12), 214 (3), 171 (5), 158 (5), 144 (5).

HR-MS (ESI) *m/z* calcd for $C_{24}H_{16}N_3^+$ $[M+H]^+$ 346.1339, found 346.1334.

The spectral data are in accordance with those reported in the literature.[109]

3,4-Diphenylbenzo[*h*]pyrazolo[5,1-*a*]isoquinoline (127ea):



The general procedure **A** was followed using 5-(naphthalen-1-yl)-1*H*-pyrazole (**126e**) (98.0mg, 0.50mmol) and diphenylacetylene (**11a**) (179.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127ea** (142.0 mg, 76%) as an off-white solid.

M. p. = 192–194°C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 9.15 (d, *J* = 8.6 Hz, 1H), 8.17 (d, *J* = 2.3 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.91–7.86 (m, 2H), 7.77–7.72 (m, 1H), 7.34–7.24 (m, 11H).

^{13}C NMR (75 MHz, d_6-DMSO): δ = 141.6 (CH), 137.0 (C_q), 136.2 (C_q), 136.1 (C_q), 133.4 (C_q), 132.0 (C_q), 131.4 (CH), 130.7 (CH), 128.9 (CH), 128.6 (C_q), 128.6 (CH), 128.0 (C_q),128.0 (CH), 128.0 (CH), 127.9 (CH), 127.5 (CH), 127.2 (CH), 126.7 (CH), 125.1 (CH), 123.9 (C_q), 123.7 (CH), 119.6 (C_q), 101.3 (CH).

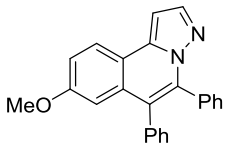
IR (neat): 3045, 1437, 1375, 822, 744, 730, 681, 659 cm^{-1}.

MS (EI) *m/z* (relative intensity)**:** 370 (90) $[M]^+$, 369 (100)$[M–H]^+$, 342 (10), 313 (5), 265 (10), 237 (5), 184 (5), 170 (5).

HR-MS (ESI) *m/z* calcd for $C_{27}H_{18}N_2^+$ $[M]^+$ 370.1465, found 370.1468.

The spectral data are in accordance with those reported in the literature.[109]

6-Methoxy-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127fa):



The general procedure **A** was followed using 5-(4-methoxyphenyl)-1*H*-pyrazole (**126f**) (84.0 mg, 0.48 mmol) and diphenylacetylene (**11a**) (180.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127fa** (97.0 mg, 57%) as a light yellow solid.

M. p. = 237–239 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 2.3 Hz, 1H), 7.37–7.19 (m, 11H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.84 (d, *J* = 2.3 Hz, 1H), 3.73 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1 (C_q), 141.1 (CH), 138.6 (C_q), 136.7 (C_q), 136.2 (C_q), 133.2 (C_q), 131.6 (C_q), 131.5 (CH), 130.8 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 127.2 (CH), 125.2 (CH), 123.6 (C_q), 118.3 (C_q), 116.4 (CH), 108.6 (CH), 96.4 (CH), 55.2 (CH_3).

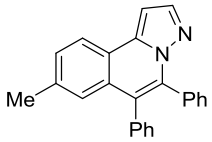
IR (neat): 3028, 2966, 1610, 1481, 1418, 1217, 1025, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 350 (90) $[M]^+$, 349 (100)$[M–H]^+$, 306 (20), 278 (10), 175 (10), 159 (15), 139 (15), 77 (5).

HR-MS (ESI) *m/z* calcd for $C_{24}H_{19}N_2O^+$ $[M+H]^+$ 351.1492 found 351.1482.

The spectral data are in accordance with those reported in the literature.[109]

6-Methyl-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127ga)



The general procedure **A** was followed using 5-(4-methylphenyl)-1*H*-pyrazole (**126g**) (79.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **127ga** (70.0 mg, 42%) as a yellow solid.

M. p. = 112–114 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 2.1 Hz, 1H), 7.42 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.36–7.16 (m, 11H), 7.07 (d, *J* = 2.2 Hz, 1H), 2.40 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.0 (CH), 138.6 (C_q), 137.7 (C_q), 136.4 (C_q), 136.2 (C_q), 133.2 (C_q), 131.6 (CH), 130.8 (CH), 130.0 (C_q), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.9 (CH), 127.1 (CH), 126.3 (CH), 123.8 (C_q), 123.5 (CH), 121.8 (C_q), 97.0 (CH), 21.8 (CH_3).

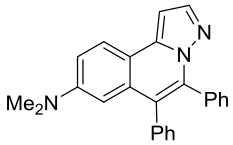
IR(neat): 3051, 3023, 1622, 1481, 1412, 1347, 813, 762 cm^{-1}.

MS (EI) *m/z* (relative intensity): 333 (100) $[M-H]^+$, 306 (5), 290 (5), 279 (10), 245 (5), 202 (5), 158 (5).

HR-MS (EI) *m/z* calcd for $C_{24}H_{18}N_2^+$ $[M]^+$ 334.1465, found 334.1456.

The spectral data are in accordance with those reported in the literature.[109]

6-(*N*,*N*-dimethyl)-3,4-diphenylpyrazolo[5,1-*a*]isoquinolin (127ha):



The general procedure **A** was followed using *N*,*N*-dimethyl-4-(1*H*-pyrazol-5-yl)aniline (**126h**) (93.4 mg, 0.50 mmol) and diphenylacetylene (**11a**) (179.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127ha** (109.0 mg, 60%) as a light yellow solid.

M. p. = 228−230 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.9 Hz, 1H), 7.92 (d, *J* = 2.1 Hz, 1H), 7.35–7.21 (m, 10H), 7.08 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.92 (d, *J* = 2.1 Hz, 1H), 6.55 (d, *J* = 2.6 Hz, 1H), 2.90 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6 (C_q), 141.0 (CH), 138.9 (C_q), 136.5 (C_q), 136.4 (C_q), 133.5 (C_q), 131.5 (CH), 131.4 (C_q), 130.8 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.0 (CH), 124.7

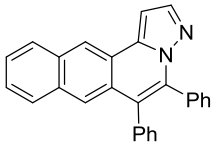
(CH), 123.6 (C_q), 115.2 (C_q), 114.4 (CH), 107.7 (CH), 95.5 (CH), 40.5 (CH_3).

IR (neat): 3109, 2920, 1604, 1485, 1442, 1413, 724, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 363 (100) $[M]^+$, 362 (75) $[M–H]^+$, 346 (20), 319 (5)$[M–NMe_2]^+$, 290 (7), 180 (40), 159 (25), 131 (10).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{22}N_3^+$ $[M+H]^+$ 364.1808, found 364.1809.

3,4-Diphenylbenzo[*g*]pyrazolo[5,1-*a*]isoquinoline (127ia):



The general procedure **A** was followed using 5-(naphthalen-2-yl)-1*H*-pyrazole (**126i**) (97.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (179.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **127ia** (129.0 mg, 70%) as an off-white solid.

M. p. = 272−274 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.97 (s, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 2.0 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.72 (s, 1H), 7.61–7.56 (m, 1H), 7.53–7.47 (m, 1H), 7.51 (d, *J* = 2.0 Hz, 1H), 7.34–7.23 (m, 10H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.8 (CH), 138.3 (C_q), 136.3 (C_q), 136.1 (C_q), 133.1 (C_q), 132.5 (C_q), 132.1 (C_q), 131.6 (CH), 130.9 (CH), 128.5 (C_q), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 127.2 (CH), 126.5 (CH), 126.2 (CH), 125.9 (CH), 123.8 (C_q), 122.5 (C_q), 122.2 (CH), 99.1 (CH).

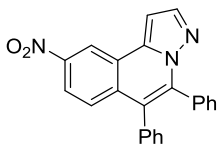
IR (neat): 3053, 1488, 1442, 1390, 889, 748, 723, 693 cm^{-1}.

MS (EI) *m/z* (relative intensity): 370 (95) $[M]^+$, 369 (100)$[M–H]^+$, 264 (5), 207 (10), 184 (50), 177 (25), 170 (20), 156 (10).

HR-MS (ESI) *m/z* calcd for $C_{27}H_{19}N_2^+$ $[M+H]^+$ 371.1543, found 371.1535.

The spectral data are in accordance with those reported in the literature.[109]

7-Nitro-3,4-diphenylpyrazolo[5,1-*a*]isoquinoline (127ja):



The general procedure **A** was followed using 5-(3-nitrophenyl)-1*H*-pyrazole (**126j**) (94.3 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127ja** (78.0 mg, 43%) as a yellow solid.

M. p. = 180−182 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.04 (d, *J* = 2.4 Hz, 1H), 8.19 (dd, *J* = 9.1, 2.4 Hz, 1H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.36–7.25 (m, 8H), 7.27 (d, *J* = 2.2 Hz, 1H), 7.19–7.16 (m, 2H).

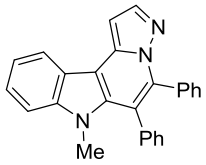
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.0(C_q), 142.0 (CH), 139.7 (C_q), 137.9 (C_q), 135.0 (C_q), 134.3 (C_q), 132.2 (C_q), 131.4 (CH), 130.5 (CH), 128.9 (CH), 128.4 (CH), 128.1 (CH), 128.1 (CH), 127.8 (CH), 123.9 (C_q), 123.2 (C_q), 121.6 (CH), 119.4 (CH), 99.3 (CH).

IR (neat): 3059, 1511, 1490, 1330, 758, 736, 714, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 365 (85) $[M]^+$, 364 (100)$[M–H]^+$, 318 (40), 290 (10), 158 (10), 144 (5), 77 (3).

HR-MS (ESI)*m/z* calcd for $C_{23}H_{15}N_3O_2^+$ $[M]^+$ 365.1159, found 365.1160.

1-Methyl-5,6-diphenyl-7*H*-pyrazolo[1',5':1,2]pyrido[4,3-*b*]indole (127la):



The general procedure **A** was followed using 1-methyl-3-(1*H*-pyrazol-5-yl)-1*H*-indole (**126l**) (97.0 mg, 0.49 mmol), and diphenylacetylene (**11a**) (182.0 mg, 1.02 mmol) and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127la** (107.0 mg, 58%) as a light yellow solid.

M. p. = 221–223 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.7 Hz, 1H), 8.08 (d, *J* = 2.2 Hz, 1H), 7.50–7.38 (m, 3H), 7.32–7.29 (m, 10H), 7.00 (d, *J* = 2.2 Hz, 1H), 3.27 (s, 3H).

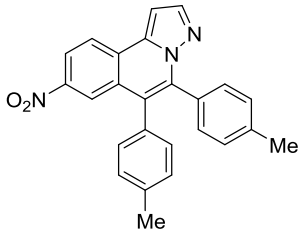
^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.2 (CH), 140.5 (C_q), 137.3 (C_q), 136.1 (C_q), 135.3 (C_q), 134.6 (C_q), 133.1 (C_q), 131.8 (CH), 130.8 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 124.6 (CH), 121.6 (C_q), 120.6 (CH), 120.5 (CH), 115.0 (C_q), 109.4 (CH), 107.7 (C_q), 93.9 (CH), 32.1 (CH_3).

IR (neat): 3047, 1632, 1462, 1371, 1261, 884, 714, 692 cm^{-1}.

MS (EI) *m/z* (relative intensity): 373 (100) $[M]^+$, 357 (15), 329 (10), 179 (60), 165 (15), 151 (10), 138 (5), 77 (5).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{20}N_3^+$ $[M+H]^+$ 374.1652, found 374.1647.

6-Nitro-5,6-di-*p*-tolylpyrazolo[5,1-*a*]isoquinoline(**127ab**):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.4 mg, 0.50 mmol) and 1,2-di-*p*-tolylethyne (**11b**) (206.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **127ab** (81.0 mg, 41 %) as a yellow solid.

M. p. = 240–242 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48–8.23 (m, 3H), 8.04 (d, *J* = 2.3 Hz, 1H), 7.34–6.98 (m, 9H), 2.37 (s, 3H), 2.33 (s, 3H).

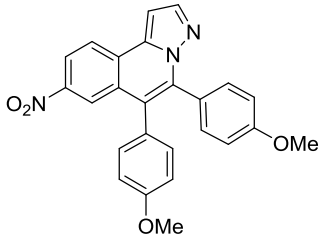
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.7 (C_q), 141.5 (CH), 138.6 (C_q), 138.5 (C_q), 137.5 (C_q), 137.2 (C_q), 131.6 (C_q), 131.1 (CH), 130.4 (CH), 129.3 (C_q), 129.2 (CH), 128.8 (CH), 127.8 (C_q), 124.7 (CH), 123.6 (C_q), 122.6 (CH), 121.3 (CH), 99.8 (CH), 21.4 (CH_3), 21.3 (CH_3).

IR (neat): 3024, 1607, 1520, 1503, 1417, 1354, 1337, 1310 cm^{-1}.

MS (EI) *m/z* (relative intensity): 392 (100) $[M–H]^+$, 346 (25), 331 (5), 304 (5), 291 (5), 165 (10), 119 (5).

HR-MS (EI) *m/z* calcd for $C_{25}H_{19}N_3O_2^+$ $[M]^+$ 393.1472, found 393.1468.

3,4-Bis(4-methoxyphenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (127ac):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.8 mg, 0.50 mmol) and 1,2-bis(4-methoxyphenyl)acetylene(**11c**) (239.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127ac** (161.0 mg, 76%) as a yellow solid.

M. p. = 207–209 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38–8.28 (m, 3H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.29–7.23 (m, 3H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.90–6.84 (m, 4H), 3.84 (s, 3H), 3.80 (s, 3H).

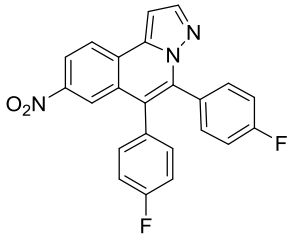
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5 (C_q), 159.0 (C_q), 146.7 (C_q), 141.5 (CH), 138.4 (C_q), 137.2 (C_q), 132.5 (CH), 132.0 (CH), 130.5 (C_q), 127.8 (C_q), 126.9 (C_q), 124.7 (CH), 124.5 (C_q), 123.4 (C_q), 122.6 (CH), 121.3 (CH), 114.0 (CH), 113.6 (CH), 99.9 (CH), 55.2 (CH_3), 55.1 (CH_3).

IR (neat): 2833, 1517, 1504, 1338, 1246, 1178, 1028, 783 cm^{-1}.

MS (EI) *m/z* (relative intensity): 425 (100) $[M]^+$, 424 (90), 394 (35), 378 (20), 335 (5), 292 (5), 91 (10).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{20}N_3O_4^+$ $[M+H]^+$ 426.1448, found 426.1444.

3,4-Bis(4-fluorophenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (127ad):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.1 mg, 0.50 mmol) and 1,2-bis(4-fluorophenyl)acetylene (**11d**) (215.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **127ad** (119.0 mg, 59%) as a yellow solid.

M. p. = 184–186°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.40 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.34 (d, *J* = 8.8 Hz, 1H), 8.30 (d, *J* = 2.2 Hz, 1H), 8.07 (d, *J* = 2.2 Hz, 1H), 7.35–7.28 (m, 3H), 7.20–7.16 (m, 2H), 7.10–7.01 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.7 ($^1J_{C\text{-}F}$ = 250 Hz, C_q), 162.3 ($^1J_{C\text{-}F}$ = 250 Hz, C_q), 146.9

(C_q), 141.9 (CH), 137.7 (C_q), 137.3 (C_q), 133.1 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 132.6 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 130.4 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 130.0 (C_q), 128.0 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 127.9 (C_q), 124.9 (CH), 123.0 (C_q), 122.3 (CH), 121.8 (CH), 115.9 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 115.4 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 100.2 (CH).

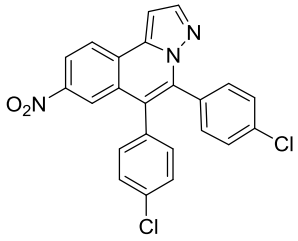
^{19}F NMR (283 MHz, $CDCl_3$): δ = –111.23 (s), –112.84 (s).

IR (neat): 1599, 1500, 1334, 1222, 1156, 840, 820, 784 cm^{-1}.

MS (EI) *m/z* (relative intensity): 401 (100) $[M]^+$, 400 (85) $[M–H]^+$, 354 (30), 326 (12), 301 (6), 232 (6), 176 (10), 98 (5).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{14}F_2N_3O_2^+$ $[M+H]^+$ 402.1049, found 402.1034.

3,4-Bis(4-chlorophenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (127ae):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.0 mg, 0.50 mmol) and 1,2-bis(4-chlorophenyl)acetylene (**11e**) (247.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127ae** (117.0 mg, 54%) as a yellow solid.

M. p. = 212–214 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 2.2 Hz, 1H), 8.02 (d, *J* = 2.2 Hz, 1H), 7.34–7.27 (m, 4H), 7.25–7.22 (m, 3H), 7.13–7.08 (m, 2H).

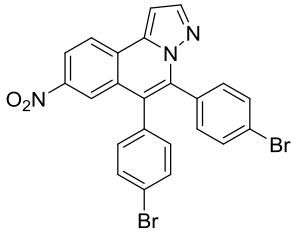
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9 (C_q), 141.9 (CH), 137.4 (C_q), 137.3 (C_q), 135.3 (C_q), 134.4 (C_q), 132.8 (C_q), 132.6 (CH), 132.0 (CH), 130.3 (C_q), 129.7 (C_q), 129.1 (CH), 128.7 (CH), 128.0 (C_q), 125.0 (CH), 122.8 (C_q), 122.2 (CH), 121.9 (CH), 100.3 (CH).

IR (neat): 1514, 1487, 1333, 1090, 848, 835, 787, 741 cm^{-1}.

MS (EI) *m/z* (relative intensity): 433 (100) $[M]^+$, 432 (80) $[M–H]^+$, 386 (25), 351 (15), 324 (10), 288 (10), 158 (10), 146 (10).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{14}{}^{35}Cl_2N_3O_2^+$ $[M+H]^+$ 434.0458, found 434.0441.

3,4-Bis(4-bromophenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (**127af**):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.3 mg, 0.50 mmol) and 1,2-bis(4-bromophenyl)ethyne (**11f**) (335.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **127af** (113.0 mg, 42%) as a yellow solid.

M. p. = 234–236 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.26 (d,

J = 2.1 Hz, 1H), 8.04 (d, *J* = 2.1 Hz, 1H), 7.52–7.45 (m, 4H), 7.26 (d, *J* = 2.2 Hz, 1H), 7.26–7.17 (m, 2H), 7.09–7.04 (m, 2H).

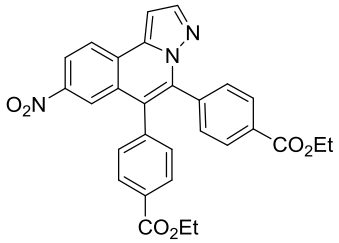
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9 (C_q), 141.9 (CH), 137.4 (C_q), 137.3 (C_q), 133.3 (C_q), 132.9 (CH), 132.2 (CH), 132.1 (CH), 131.6 (CH), 130.8 (C_q), 129.6 (C_q), 128.0 (C_q), 125.0 (CH), 123.7 (C_q), 122.7 (C_q), 122.7 (C_q), 122.2 (CH), 121.9 (CH), 100.3 (CH).

IR(neat): 3085, 1586, 1512, 1332, 1065, 1010, 905, 847 cm^{-1}.

MS (EI) *m/z* (relative intensity):521 (100) $[M+H]^+$, 493 (10), 475 (15), 443 (20), 397 (15), 316 (20), 288 (20), 158 (20).

HR-MS (ESI) *m/z*calcd for $C_{23}H_{14}{}^{79}Br_2N_3O_2^+$ $[M+H]^+$ 521.9447, found 521.9441.

Diethyl 4,4'-(6-Nitropyrazolo[5,1-*a*]isoquinoline-3,4-diyl)dibenzoate (127ag):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.6 mg, 0.50 mmol) and diethyl 4,4'-(ethyne-1,2-diyl)dibenzoate (**11g**) (324.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 6/1) yielded **127ag** (150.0 mg, 59%) as a yellow solid.

M. p. = 199–200 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.41 (dd, *J* = 8.8, 2.1 Hz, 1H), 8.35 (d, *J* = 8.8 Hz, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 8.05 (d, *J* = 2.3 Hz, 1H), 8.04–7.99 (m, 4H), 7.44–7.40 (m, 2H), 7.32–7.29 (m, 3H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

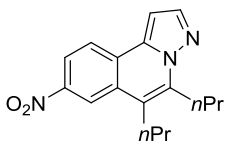
^{13}CNMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 165.7 (C_q), 146.8 (C_q), 141.9 (CH), 138.9 (C_q), 137.3 (C_q), 137.2 (C_q), 136.1 (C_q), 131.3 (CH), 130.8 (C_q), 130.6 (CH), 130.3 (C_q), 129.8 (CH), 129.3 (CH), 129.3 (C_q), 127.9 (C_q), 124.9 (CH), 123.0 (C_q), 122.1 (CH), 121.9 (CH), 100.3 (CH), 61.2 (CH_2), 61.1 (CH_2), 14.4 (CH_3), 14.3 (CH_3).

IR (neat): 2982, 1715, 1523, 1420, 1343, 1272, 1103, 1021 cm^{-1}.

MS (EI) *m/z* (relative intensity): 509 (5) $[M]^+$, 479 (3), 267 (10), 239 (8), 134 (10), 98 (25), 59 (27), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{29}H_{24}N_3O_6^+$ $[M+H]^+$ 510.1660, found 510.1643.

6-Nitro-3,4-di-*n*-propylpyrazolo[5,1-*a*]isoquinoline (**127ah**):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.3 mg, 0.50 mmol) and oct-4-yne (**11h**) (110.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **127ah** (68.0 mg, 46%) as a yellow solid.

M. p. = 123−124 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 2.2 Hz, 1H), 8.29 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 8.02 (d, *J* = 2.3 Hz, 1H), 7.11 (d, *J* = 2.3 Hz, 1H), 3.29 (t, *J* = 8.0 Hz, 2H), 2.99 (t, *J* = 8.0 Hz, 2H), 1.89–1.78 (m, 2H), 1.77–1.68 (m, 2H), 1.14 (t, *J* = 7.3 Hz, 3H), 1.13 (t, *J* = 7.3Hz, 3H).

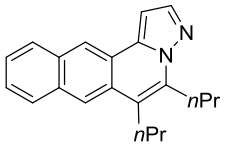
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.7 (C_q), 140.6 (CH), 139.0 (C_q), 136.3 (C_q), 129.0 (C_q), 127.7 (C_q), 125.0 (CH), 120.4 (CH), 120.0 (CH), 119.0 (C_q), 99.5 (CH), 30.2 (CH_2), 29.6 (CH_2), 23.9 (CH_2), 21.2 (CH_2), 14.4 (CH_3), 14.3 (CH_3).

IR (neat): 2956, 2927, 2870, 1520, 1338, 1319, 901, 782 cm^{-1}.

MS (EI) *m/z* (relative intensity): 297 (80) $[M]^+$, 268 (95), 252 (55), 222 (100), 194 (30), 178 (25), 152 (25), 127 (15).

HR-MS (ESI) *m/z*calcd for $C_{17}H_{20}N_3O_2^+$ $[M+H]^+$ 298.1550, found 298.1551.

3,4-Di-*n*-propylbenzo[*g*]pyrazolo[5,1-*a*]isoquinoline (127ih):



The general procedure **A** was followed using 5-(naphthalen-2-yl)-1*H*-pyrazole (**126i**) (97.1 mg, 0.50 mmol) and oct-4-yne (**11h**) (115.0 mg, 1.04 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 50/1) yielded **127ih** (92.0 mg, 61%) as an off-white solid.

M. p. = 130–132 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.58 (s, 1H), 8.27 (s, 1H), 8.03–7.98 (m, 2H), 7.96 (d, *J* = 2.1 Hz, 1H) , 7.56–7.51 (m, 2H), 7.14 (d, *J* = 2.1 Hz, 1H), 3.29 (t, *J* = 8.0Hz, 2H), 3.04 (t, *J* = 8.0Hz, 2H), 1.94–1.73 (m, 4H), 1.18 (t, *J* = 7.3 Hz, 3H), 1.15 (t, *J* = 7.3 Hz, 3H).

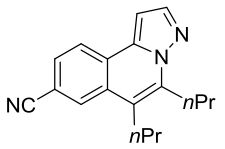
^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6 (CH), 137.5 (C_q), 136.4 (C_q), 132.6 (C_q), 131.5 (C_q), 128.3 (CH), 127.6 (CH), 127.4 (C_q), 126.1 (CH), 126.0 (CH), 122.6 (C_q), 122.6 (CH), 122.4 (CH), 118.6 (C_q), 98.7 (CH), 30.1 (CH_2), 29.9 (CH_2), 23.6 (CH_2), 21.7 (CH_2), 14.6 (CH_3), 14.4 (CH_3).

IR (neat): 2955, 2930, 2870, 1396, 1088, 922, 879, 787 cm^{-1}.

MS (EI) *m/z* (relative intensity): 302 (97) $[M]^+$, 273 (100), 259 (35), 245 (35), 231 (28), 203 (28), 189 (15), 151 (20).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{23}N_2^+$ $[M+H]^+$ 303.1856, found 303.1854.

3,4-Di-*n*-propylpyrazolo[5,1-*a*]isoquinoline-6-carbonitrile (127dh):



The general procedure **A** was followed using 4-(1*H*-pyrazol-5-yl)benzonitrile (**126d**) (84.5 mg, 0.50 mmol) and oct-4-yne (**2h**) (110.0 mg, 1.00 mmol). Purification by column chromatography

(*n*-hexane/EtOAc: 30/1) yielded **127dh** (71.0 mg, 52%) as a light yellow solid.

M. p. = 122–124 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.2Hz, 1H), 8.14 (s, 1H), 8.01 (d, *J* = 2.2 Hz, 1H), 7.70 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.08 (d, *J* = 2.2 Hz, 1H), 3.28 (t,*J* = 8.1 Hz, 2H), 2.93 (t,*J* = 8.1 Hz, 2H), 1.89–1.76 (m, 2H), 1.75–1.62 (m, 2H), 1.13 (t, *J* = 7.3 Hz, 3H), 1.12 (t, *J* = 7.3Hz, 3H).

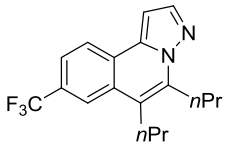
^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.4 (CH), 138.8 (C_q), 136.5 (C_q), 129.0 (CH), 128.9 (C_q), 128.1 (CH), 126.4 (C_q), 124.8 (CH), 119.2 (C_q), 118.2 (C_q), 110.9 (C_q), 99.0 (CH), 30.1 (CH_2), 29.5 (CH_2), 23.8 (CH_2), 21.2 (CH_2), 14.4 (CH_3), 14.3 (CH_3).

IR (neat): 2962, 1258, 1088, 1050, 1017, 777, 741, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 277 (55) $[M]^+$, 262 (50), 248 (100), 234 (30), 221 (40), 206 (30), 192 (10), 152 (20).

HR-MS (ESI) *m/z* calcd for $C_{18}H_{20}N_3^+$ $[M+H]^+$ 278.1652, found 278.1653.

3,4-Di-*n*-propyl-6-(trifluoromethyl)pyrazolo[5,1-*a*]isoquinoline (127bh):



The general procedure **A** was followed using 5-{4-(trifluoromethyl)-phenyl}-1*H*-pyrazole (**126b**) (106.0 mg, 0.50 mmol)and oct-4-yne(**1h**) (113.0 mg, 1.03 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 50/1) yielded **127bh** (104.0 mg, 65%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 1.8 Hz, 1H), 8.00 (d, *J* = 2.2 Hz, 1H), 7.71 (dd, *J* = 8.4, 1.2Hz, 1H), 7.07 (d, *J* = 2.2 Hz, 1H), 3.30 (t, *J* = 8.0 Hz 2H), 2.98 (t, *J* = 8.0 Hz 2H), 1.90–1.77 (m, 2H), 1.75–1.65 (m, 2H), 1.10 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.2 (CH), 138.2 (C_q), 136.8 (C_q), 129.3 ($^2J_{C\text{-}F}$ = 32 Hz, C_q), 128.7 (C_q), 125.9 ($^4J_{C\text{-}F}$ = 1 Hz, C_q), 124.6 (CH), 124,3 ($^1J_{C\text{-}F}$ = 272Hz, C_q), 122.4 ($^3J_{C\text{-}F}$ = 3 Hz, CH), 121.2 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 118.8 (C_q), 98.4 (CH), 30.1 (CH_2), 29.5 (CH_2), 23.8 (CH_2), 21.2 (CH_2), 14.4 (CH_3), 14.4 (CH_3).

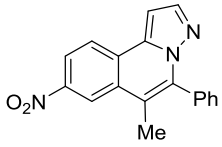
^{19}F NMR (283 MHz, $CDCl_3$): δ = –62.2 (s).

IR(neat): 2961, 2933, 2874, 1355, 1339, 1310, 1117, 1079 cm^{-1}.

MS (EI) *m/z* (relative intensity): 320 (90) $[M]^+$, 305 (60), 291 (100), 264 (50), 249 (20), 223 (10), 202 (10).

HR-MS (ESI) *m/z* calcd for $C_{18}H_{20}F_3N_2^+$ $[M+H]^+$ 321.1573, found: 321.1573.

4-Methyl-6-nitro-3-phenylpyrazolo[5,1-*a*]isoquinoline (127ai):



The general procedure was **A** followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.5 mg, 0.50 mmol) and (prop-1-yn-1-yl)benzene (**11i**) (120.0 mg, 1.03 mmol). Purification by column chromatography (*n*-hexane/EtOAc:

15/1) yielded **127ai** (76.0 mg, 50%) as a yellow solid.

M. p. = 178–180°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 2.2 Hz, 1H), 8.41 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.28 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 2.2 Hz, 1H), 7.66–7.54 (m, 3H), 7.50–7.47 (m, 2H), 7.19 (d, *J* = 2.2 Hz, 1H), 2.44 (s, 3H).

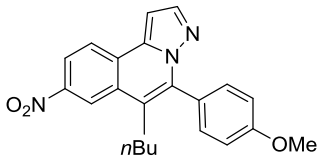
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.7(C_q), 141.1 (CH), 137.9 (C_q), 136.7 (C_q), 132.8 (C_q), 130.1 (CH), 130.0 (C_q), 129.4 (CH), 128.8 (CH), 128.2 (C_q), 124.9 (CH), 121.4 (CH), 120.5 (CH), 116.2 (C_q), 99.8 (CH), 15.1 (CH_3).

IR (neat): 3090, 3055, 1520, 1333, 798, 761, 737, 706 cm^{-1}.

MS (EI) *m/z*(relative intensity): 303 (90) $[M]^+$, 302 (100), 256 (50), 244 (10), 229 (10), 202 (10), 128 (15), 115 (10).

HR-MS (EI) *m/z* calcd for $C_{18}H_{13}N_3O_2^+$ $[M]^+$ 303.1002, found:303.1010.

4-(*n*-Butyl)-3-(4-methoxyphenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (127aj):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.7 mg, 0.50 mmol) and 1-(hex-1-yn-1-yl)-4-methoxybenzene (**11j**) (193.0 mg, 1.03 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127aj** (135.0 mg, 72%) as a yellow solid.

M. p. = 107–108 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 2.2 Hz, 1H), 8.38 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 2.2 Hz, 1H), 7.38(d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 2.2 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 3.91 (s, 3H), 2.85–2.80 (m, 2H), 1.66–1.56 (m, 2H), 1.40–1.32 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).

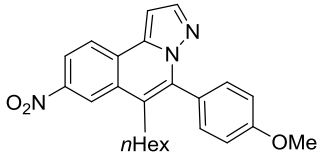
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 146.7 (C_q), 141.1 (CH), 137.9 (C_q), 136.7 (C_q), 131.1 (CH), 129.1 (C_q), 128.5 (C_q), 125.1 (CH), 124.9 (C_q), 121.4 (C_q), 121.1 (CH), 120.6 (CH), 114.3(CH), 99.6 (CH), 55.3 (CH_3), 32.9 (CH_2), 28.0 (CH_2), 22.7 (CH_2), 13.7 (CH_3).

IR (neat): 2957, 2930, 2871, 1518, 1507, 1336, 1288, 1246 cm^{-1}.

MS (EI) *m/z* (relative intensity) 375 (25) $[M]^+$, 333 (100), 286 (18), 242 (15), 214 (12), 143 (10), 101 (5), 77 (5).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{22}N_3O_3^+$ $[M+H]^+$ 376.1656, found 376.1654.

3-(*n*-Hexyl)-4-(4-methoxyphenyl)-6-nitropyrazolo[5,1-*a*]isoquinoline (127ak):



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (94.7 mg, 0.50 mmol) and

1-methoxy-4-(oct-1-yn-1-yl)benzene (**11k**) (218.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **127ak** (127.0 mg, 63%) as a brownsolid.

M. p. = 98–100 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 2.2 Hz, 1H), 8.39 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.28 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 2.2 Hz, 1H), 7.53–7.30 (m, 2H), 7.17 (d, *J* = 2.2 Hz, 1H), 7.15–7.06 (m, 2H), 3.91 (s, 3H), 2.84–2.79 (m, 2H), 1.67–1.56 (m, 2H),1.38–1.21 (m, 6H), 0.86 (t, *J* = 6.6 Hz, 3H).

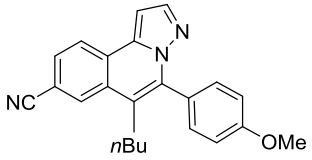
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (C_q), 146.8 (C_q), 141.2 (CH), 137.9 (C_q), 136.7 (C_q), 131.1 (CH), 129.2 (C_q), 128.6 (C_q), 125.2 (CH), 125.0 (C_q), 121.5 (C_q), 121.2 (CH), 120.6 (CH), 114.4 (CH), 99.6 (CH), 55.3 (CH_3), 31.3 (CH_2), 30.7 (CH_2), 29.3 (CH_2), 28.3 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (neat): 2954, 2927, 2855, 1712, 1520, 1508, 1338, 1292 cm^{-1}.

MS (EI) *m/z* (relative intensity): 403 (60) $[M]^+$, 332 (100), 286 (45), 271 (10), 259 (10), 242 (20), 216 (10), 189 (3).

HR-MS (ESI) *m/z* calcd for: $C_{24}H_{26}N_3O_3^+$ $[M+H]^+$ 404.1969, found 404.1978.

4-(*n*-Butyl)-6-cycno-3-(4-methoxyphenyl)pyrazolo[5,1-a]isoquinoline (127dj)



The general procedure **A** was followed using 4-(1*H*-pyrazol-5-yl)benzonitrile (**126d**) (85.1 mg, 0.50 mmol) and 1-(hex-1-yn-1-yl)-4-methoxybenzene (**11j**) (192.0 mg, 1.02 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→10/1) yielded **127dj** (121.0 mg, 68%) as a light yellow solid.

M. p. = 174–175 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 1.5 Hz 1H), 7.94 (d, *J* = 2.2 Hz, 1H), 7.78 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 2.2 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 3H), 2.78–2.71 (m, 2H), 1.62–1.52 (m, 2H), 1.40–1.24 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H).

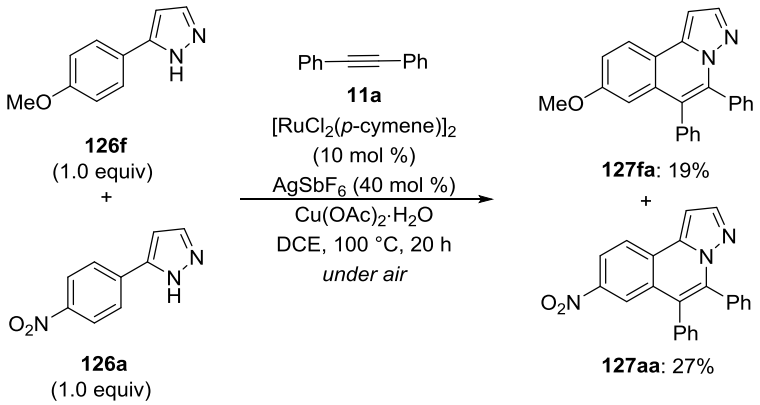
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 141.1 (CH), 137.7 (C_q), 136.8 (C_q), 131.1 (CH), 129.6 (CH), 129.0 (C_q), 128.8 (CH), 127.1 (C_q), 125.0 (C_q), 124.9 (CH), 120.6 (C_q), 119.1 (C_q), 114.4 (CH), 111.0 (C_q), 99.1 (CH), 55.3 (CH_3), 32.9 (CH_2), 28.0 (CH_2), 22.8 (CH_2), 13.7 (CH_3).

IR (neat): 2955, 2932, 2224, 1507, 1462, 1417, 1242, 1178 cm^{-1}.

MS (EI) *m/z* (relative intensity): 355 (50) $[M]^+$, 326 (10), 312 (100), 285 (15), 268 (20), 242 (20), 214 (10), 177 (5).

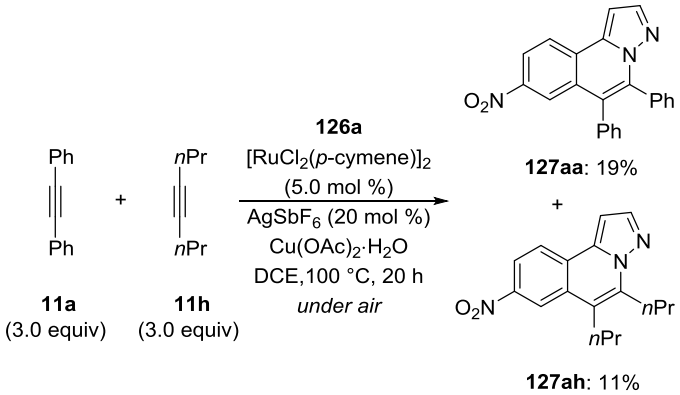
HR-MS (ESI) *m/z* calcd for: $C_{23}H_{22}N_3O^+$ $[M+H]^+$ 356.1757, found 356.1749.

Intermolecular Competition Experiment between Substrates 126f and 126a



A mixture of 5-(4-methoxyphenyl)-1*H*-pyrazole (**126f**) (87.5 mg, 0.50 mmol), 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.7 mg, 0.50 mmol), diphenylacetylene (**11a**) (89.4 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (30.7 mg, 10 mol %), $AgSbF_6$ (69 mg, 40 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (200 mg, 1.00 mmol) in DCE (2.0 mL) was stirred at ambient temperature for 5 min and then at 100 °C for 20 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq. NH_4Cl/NH_3 (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude products were purified by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→8/1) to yield **127fa** (34.0 mg, 19%) and **127aa** (49.0 mg, 27%).Their spectral data were identical to those reported above.

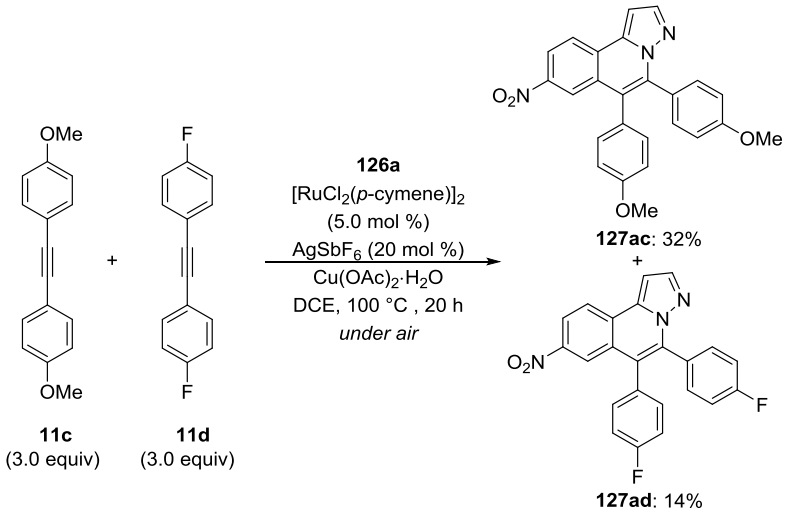
Intermolecular Competition Experiment between Alkynes 11a and 11h



A mixture of 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.0 mg, 0.50 mmol), diphenylacetylene (**11a**) (271.0 mg, 1.52 mmol), oct-4-yne(**11h**) (175.0 mg, 1.59 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 5.0 mol %), $AgSbF_6$ (36.2 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (102.0 mg, 0.51 mmol) in DCE (2.0 mL) was stirred at ambient temperature for 5 min and then at 100 °C for 20 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq.

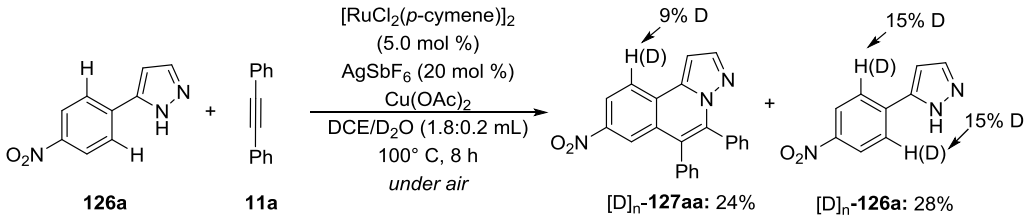
NH_4Cl/NH_3 (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→8/1) to yield **127aa** (35.0 mg, 19%) and **127ah** (17.0 mg, 11%) as yellow solids. Their spectral data were identical to those reported above.

Intermolecular Competition Experiment between Alkynes 11c and 11d



A mixture of 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.3 mg, 0.50 mmol), 1,2-bis(4-methoxyphenyl)acetylene (**11c**) (356.0 mg, 1.50 mmol), 1,2-bis(4-fluorophenyl)acetylene(**11d**) (320 mg, 1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.7 mg, 5.0 mol %), $AgSbF_6$ (36.2 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (102 mg, 0.50 mmol) in DCE (2.0 mL) was stirred at ambient temperature for 5 min, and then at 100 °C for 20 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq. NH_4Cl/NH_3 (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude products were purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→10/1) to yield **127ac** (69.0 mg, 32%) and **127ad** (29.0mg, 14%) as yellow solids. Their spectral data were identical to those reported above.

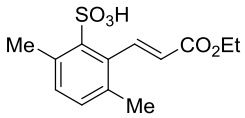
Ruthenium(II)-Catalyzed H/D Exchange with Arylpyrazole 126a Employing D_2O as the Cosolvent



The general procedure **A** was followed using 5-(4-nitrophenyl)-1*H*-pyrazole (**126a**) (95.0 mg, 0.50 mmol), diphenylacetylene (**11a**) (179 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 5.0 mol %), $AgSbF_6$ (35.1 mg, 20 mol %) and $Cu(OAc)_2$ (91.7 mg, 0.50 mmol) in a solvent mixture of DCE and D_2O (1.8/0.2 mL). Purification by column chromatography (*n*-hexane/EtOAc: 10/1→2/1) yielded reisolated partially deuterated starting material $[D]_n$-**126a** (27 mg, 28%) and product $[D]_n$-**127aa** (44 mg, 24%) as yellow solids. The deuterium incorporations in $[D]_n$-**127aa** and $[D]_n$-**126a** were estimated by ^{1}HNMR spectroscopy.

8.4.2 Analytical Data for the Products of the Ruthenium(II)-Catalyzed Oxidative C–H Alkenylations of Sulfonic Acids, Chloride and Benzenesulfonate.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-3,6-dimethylbenzenesulfonic Acid (129ab):



The general procedure **B** was followed using 2,5-dimethylbenzenesulfonic acid (**128a**) (94.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129ab** (131.0 mg, 91%) as an off-white solid.

M. p. = 222−224 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.15 (d, J = 16.4 Hz, 1H), 7.09 (d, J = 7.8 Hz, 1H), 7.01 (d, J= 7.8 Hz, 1H), 5.63 (d, J = 16.4 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 2.52 (s, 3H), 2.16 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H).

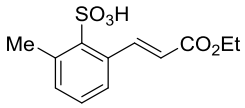
^{13}C NMR (100 MHz, d_6-DMSO): δ = 166.0 (C_q), 147.6 (CH), 145.3 (C_q), 133.9 (C_q), 132.9 (C_q), 132.3 (C_q), 130.9 (CH), 130.0 (CH), 119.7 (CH), 59.5 (CH_2), 21.7 (CH_3), 21.2 (CH_3), 14.2 (CH_3).

IR (neat): 3446 (br), 2982, 1699, 1640, 1310, 1179, 1059, 654 cm^{-1}.

MS (EI) *m/z* (relative intensity): 267 (5) $[M–OH]^+$, 237 (5), 203 (65), 175 (100), 157 (25), 129 (30), 115 (30), 91 (20).

HR-MS (ESI) *m/z* calcd for $C_{13}H_{15}O_5S^-$ $[M–H^+]$ 283.0646, found 283.0649.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-6-methylbenzenesulfonic Acid (129bb):



The general procedure **B** was followed using 2-methylbenzenesulfonic acid (**128b**) (87.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129bb** (126.0 mg, 92%) as an off-white solid.

M. p. = 285−287°C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.85 (d, J = 15.9 Hz, 1H), 7.50–7.31 (m, 1H), 7.20 (m, 2H), 6.10 (d, J = 15.9 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H).

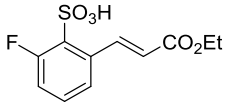
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.1 (C_q), 147.7 (CH), 145.4 (C_q), 136.4 (C_q), 133.0 (C_q), 132.8 (CH), 127.8 (CH), 125.6 (CH), 117.0 (CH), 59.5 (CH_2), 22.3 (CH_3), 14.2 (CH_3).

IR (neat): 3504 (br), 1698, 1632, 1364, 1308, 1186, 1167, 664 cm^{-1}.

MS (EI) *m/z* (relative intensity): 253 (5) $[M–OH]^+$, 230 (15), 223 (10), 196 (15), 189 (50), 161 (100), 143 (10), 115 (40).

HR-MS (ESI) *m/z*calcd for $C_{12}H_{13}O_5S$ $[M–H^+]$ 269.0489, found 269.0490.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-6-fluorobenzenesulfonic Acid (129cb):



The general procedure **B** was followed using 2-fluorobenzenesulfonic acid (**128c**) (88.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129cb** (126.0 mg, 92%) as an off-white solid.

M. p. = 217−219 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.78 (d, J = 16.0 Hz, 1H), 7.45–7.42 (m, 1H), 7.36–7.29 (m, 1H), 7.19–7.12 (m, 1H), 6.27 (d, J = 16.0 Hz, 1H), 4.16 (dq, J = 7.1, 1.1 Hz, 2H), 1.23 (dt, J = 7.1, 1.1 Hz, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 165.8 (C_q), 158.5 (d, $^1J_{C\text{-}F}$ = 249.4 Hz, C_q), 144.6 (d, $^4J_{C\text{-}F}$ = 3.6 Hz, CH), 134.7 (d, $^3J_{C\text{-}F}$ = 2.6 Hz, C_q), 134.3 (d, $^2J_{C\text{-}F}$ = 14.5 Hz, C_q), 129.7 (d, $^3J_{C\text{-}F}$ = 9.6 Hz, CH), 123.2 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, CH), 118.9 (CH) , 117.6 (d, $^2J_{C\text{-}F}$ = 25.3 Hz, CH), 59.8 (CH_2), 14.2 (CH_3).

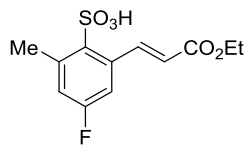
^{19}F NMR (283 MHz, d_6-DMSO): δ = –108.6 (ddd, J = 10.7, 5.2, 1.4 Hz).

IR (neat): 3470 (br), 2984, 1698, 1634, 1462, 1231, 1189, 655 cm^{-1}.

MS (EI) *m/z* (relative intensity): 257 (5) $[M–OH]^+$, 229 (5), 193 (35), 165 (100), 120 (15), 109 (15), 83 (10), 43 (15).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{10}FO_5S$ $[M–H^+]$ 273.0238, found 273.0329.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-4-fluoro-6-methylbenzenesulfonic Acid (129db):



The general procedure **B** was followed using 4-fluoro-2-

methylbenzenesulfonic acid (**128d**) (95.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129db** (136.0 mg, 94%) as a white solid.

M. p. = 261−263 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.79 (d, J = 16.0 Hz, 1H), 7.23–7.19 (m, 1H), 7.07–7.02 (m, 1H), 6.19 (d, J = 16.0 Hz, 1H), 4.15 (q, J = 7.4. Hz, 2H), 2.56 (s, 3H), 1.22 (t, J = 7.4 Hz, 3H).

^{13}C NMR (75 MHz, d_6-DMSO): δ = 166.1 (C_q), 160.5 (d, $^1J_{C\text{-}F}$ = 244.6 Hz, C_q), 146.3 (d, $^4J_{C\text{-}F}$ = 2.1 Hz, CH), 142.4 (d, $^4J_{C\text{-}F}$ = 3.0 Hz, C_q), 140.0 (d, $^3J_{C\text{-}F}$ = 7.9 Hz, C_q), 135.6 (d, $^3J_{C\text{-}F}$ = 8.0 Hz, C_q), 118.9 (d, $^2J_{C\text{-}F}$ = 20.6 Hz, CH), 118.4(CH), 111.8 (d, $^2J_{C\text{-}F}$ = 21.7 Hz, CH), 59.7 (CH_2), 22.2 (d, $^4J_{C\text{-}F}$ = 1.5 Hz, CH_3), 14.2 (CH_3).

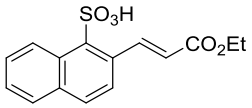
^{19}F NMR (283 MHz, d_6-DMSO): δ = –115.0.

IR (neat): 3489 (br), 2984, 1694, 1588, 1322, 1214, 1184, 1095 cm^{-1}.

MS (EI) *m/z* (relative intensity): 271 (5) $[M–OH]^+$, 207 (50), 179 (100), 133 (25), 123 (15), 109 (10), 83 (10), 43 (15).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{12}FO_5S$ $[M–H^+]$ 287.0395, found 287.0396.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)naphthalene-1-sulfonic Acid (129eb):



The general procedure **B** was followed using naphthalene-1-sulfonic acid (**129e**) (105.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **3ea** (141.0 mg, 91%) as a white solid.

M. p. = 281−283 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 9.28–9.25 (m, 1H), 9.18 (d, J = 16.1Hz, 1H), 7.87–7.82 (m, 2H), 7.65–7.61 (m, 1H), 7.50–7.45 (m, 2H), 6.28 (d, J = 16.1 Hz, 1H), 4.22–4.14 (m, 2H), 1.29–1.23 (m, 3H).

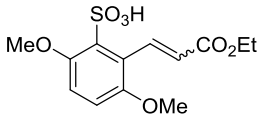
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.1 (C_q), 147.0 (CH), 143.6 (C_q), 133.9 (C_q), 129.9 (C_q), 129.5 (C_q), 129.1 (CH), 128.9 (CH), 127.3 (CH), 126.0 (CH), 125.6 (CH), 124.8 (CH), 118.3 (CH), 59.7 (CH_2), 14.3 (CH_3).

IR (neat): 3481 (br), 2984, 1695, 1628, 1267, 1183, 1053, 612 cm^{-1}.

MS (EI) *m/z*(relative intensity): 304 (15) $[M–2H]^+$, 267 (5), 225 (55), 197 (100), 161 (50), 139 (50), 115 (40), 43 (95).

HR-MS (ESI) *m/z* calcd for $C_{15}H_{13}O_5S$ $[M–H^+]$ 305.0489, found 305.0500.

2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-3,6-dimethoxybenzenesulfonic Acid (129fb): (*E:Z* = 2.3:1).



The general procedure **B** was followed using 2,5-dimethoxy-

benzenesulfonic acid (**128f**) (109.5 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129fb** (114.0 mg, 72%) as an off-white solid.

M. p. = 212−214 °C.

(*E*-isomer): ^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.30 (d, J = 16.2 Hz, 1H), 7.00 (s, 2H), 6.09 (d, J = 16.2 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 1.23(t, J = 7.1 Hz, 3H).**^{13}C NMR** (100 MHz, d_6-DMSO): δ = 166.7 (C_q), 151.6 (C_q), 151.2 (C_q), 142.0 (CH), 137.3 (C_q), 122.7 (C_q), 120.6 (CH), 116.3 (CH), 113.2 (CH), 59.4 (CH_2), 57.7 (CH_3), 56.3 (CH_3), 14.2 (CH_3).

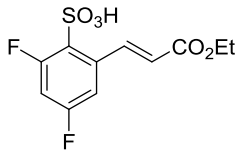
(*Z*-isomer): ^{1}H NMR (300 MHz, d_6-DMSO): δ = 7.19 (d, J = 12.2 Hz, 1H), 6.88 (s, 1H), 6.87 (s, 1H), 5.74 (d, J = 12.2 Hz, 1H), 3.89 (q, J = 7.1 Hz, 2H), 3.68 (s, 3H), 3.55 (s, 3H), 1.01 (t, J = 7.1 Hz, 3H).**^{13}CNMR** (100 MHz, d_6-DMSO): δ = 165.4 (C_q), 151.0 (C_q), 149.7 (C_q), 140.4 (CH), 136.7 (C_q), 124.4 (C_q), 118.4 (CH), 113.5 (CH), 112.0 (CH), 58.6 (CH_2), 57.1 (CH_3), 55.9 (CH_3), 13.8 (CH_3).

IR (neat): 3457 (br), 2979, 2838, 1697, 1636, 1466, 1248, 1173 cm^{-1}.

MS (EI) *m/z* (relative intensity): 315 (5) $[M–H]^+$, 235 (55), 207 (100), 192 (20), 177 (20), 165 (15), 43 (18).

HR-MS (ESI) *m/z*calcd for $C_{13}H_{15}O_7S$ $[M–H^+]$ 315.0544, found 315.0548.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-4,6-difluorobenzenesulfonic Acid (129hb)



The general procedure **B** was followed using 2,4-difluorobenzenesulfonic acid (**128h**) (98.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 20/1→10/1) yielded **129hb** (110.0 mg, 75%) as an off-white solid.

M. p. = 292−294 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.77 (d, J = 16.0 Hz, 1H), 7.42–7.37 (m, 1H), 7.25–7.16 (m, 1H), 6.41 (d, J = 16.0 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 1.25 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 165.9 (C_q), 161.2 (dd, J = 247.0, 14.0 Hz, C_q), 159.3 (dd, J = 252.0, 13.0 Hz, C_q), 143.3 (m, CH), 136.4 (dd, J = 9.3, 3.9 Hz, C_q), 131.6 (dd, J = 15.0, 4.0 Hz, C_q), 120.3 (CH), 110.0 (dd, J = 22.2, 3.6 Hz, CH), 105.5 (dd, J = 29.8, 25.1 Hz, CH), 59.9 (CH_2), 14.1 (CH_3).

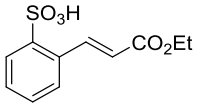
^{19}F NMR (283 MHz, d_6-DMSO): δ = –103.9 (t), –110.4 (q).

IR (neat): 3463 (br), 2982, 1702, 1603, 1584, 1309, 1186, 1098 cm^{-1}.

MS (EI) *m/z* (relative intensity): 275 (5) $[M–OH]^+$, 247 (5), 211 (35), 183 (100), 167 (20), 138 (15), 101 (10), 43 (28).

HR-MS (ESI) *m/z* calcd for $C_{11}H_9F_2O_5S$ $[M–H^+]$ 291.0144, found 291.0144.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)benzenesulfonic Acid (129ib)



The general procedure **B** was followed using benzenesulfonic acid (**128i**) (163.0 mg, 1.03 mmol) and ethyl acrylate (**46b**) (51.0 mg, 0.51 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 12/1→10/1) yielded **129ib** (71.0 mg, 54%) as a white solid.

M. p. = 259−261 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.70 (d, J = 16.2 Hz, 1H), 7.82–7.72 (m, 2H), 7.35–7.32 (m, 2H), 6.42 (d, J = 16.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 1.23 (t, J = 7.1 Hz, 3H).

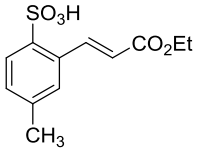
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.0 (C_q), 147.0 (C_q), 144.0 (CH), 131.3 (C_q), 128.9 (CH), 128.8 (CH), 126.8 (CH), 126.5 (CH), 118.0 (CH), 59.7 (CH_2), 14.2 (CH_3).

IR (neat): 3455 (br), 1692, 1633, 1316, 1183, 1024, 611 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 (5) $[M–OH]^+$, 211 (5), 175 (50), 147 (100), 137 (5), 103 (10), 91 (10), 43 (10).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{11}O_5S^-$ $[M–H^+]$ 255.0333, found 255.0334.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-4-methylbenzenesulfonic Acid (129jb):



The general procedure **B** was followed using 4-methylbenzenesulfonic acid (**129j**) (172.3 mg, 1.00 mmol) and ethyl acrylate (**46b**) (51.1 mg, 0.51 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 20/1→15/1) yielded **129jb** (120.0 mg, 87%) as a pale white solid.

M. p. = 289−291 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.67 (d, J = 16.2 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.58 (s, 1H), 7.15 (d, J = 7.8 Hz, 1H), 6.42 (d, J = 16.2 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 2.29 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H).

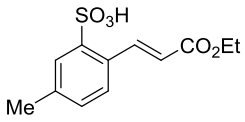
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.0 (C_q), 144.4 (C_q), 144.0 (CH), 138.3 (C_q), 131.1 (C_q), 129.4 (CH), 127.0 (CH), 126.9 (CH), 117.9 (CH), 59.7 (CH_2), 20.5 (CH_3), 14.2 (CH_3).

IR (neat): 3448 (br), 2979, 1696, 1634, 1318, 1182, 1023, 680 cm^{-1}.

MS (EI) *m/z* (relative intensity): 253 (5) $[M–OH]^+$, 243 (10), 189 (35), 161 (80), 115 (30), 83 (20), 55 (45), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{13}O_5S$ $[M–H^+]$ 269.0489, found 269.0501.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-5-methylbenzenesulfonic Acid (129kb):



The general procedure **B** was followed using 3-methylbenzenesulfonic

acid (**128k**) (80.0 mg, 0.45 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129kb** (105.0 mg, 83%) as a white solid.

M. p. = 123−125 °C.

^{1}H NMR (300 MHz, D_2O): δ = 8.28 (d, J = 15.9 Hz, 1H), 7.57 (s, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.17 (d, J = 7.9 Hz, 1H), 6.22 (d, J = 15.9 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 2.20 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H).

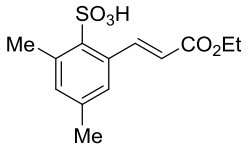
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.1 (C_q), 146.9 (C_q), 144.0 (CH), 138.8 (C_q), 129.3 (CH), 128.5 (C_q), 127.4 (CH), 126.5 (CH), 117.0 (CH), 59.6 (CH_2), 20.9 (CH_3), 14.2 (CH_3).

IR (neat): 3452 (br), 2935, 1706, 1636, 1319, 1189, 1027, 623 cm^{-1}.

MS (EI) *m/z* (relative intensity): 253 (10) [M–OH]$^+$, 225 (5), 213 (15), 189 (70), 161 (100), 113 (15), 115 (35), 64 (20).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{13}O_5S$ [M–H$^+$] 269.0489, found 269.0500.

(*E*)-2-(3-Ethoxy-3-oxoprop-1-en-1-yl)-4,6-dimethylbenzenesulfonic Acid (129lb):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.0 mg, 0.50 mmol) and ethyl acrylate (**46b**) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129lb** (120.0 mg, 85%) as a white solid.

M. p. = 189−191 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.86 (d, J = 15.9 Hz, 1H), 7.18 (d, J = 2.0 Hz, 1H), 7.01 (d, J = 2.0 Hz, 1H), 6.09 (d, J = 15.9 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 2.55 (s, 3H), 2.25 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.1 (C_q), 147.7 (CH), 142.9 (C_q), 136.9 (C_q), 136.3 (C_q), 133.4 (CH), 132.8 (C_q), 126.0 (CH), 116.8 (CH), 59.5 (CH_2), 22.0 (CH_3), 20.2 (CH_3), 14.2 (CH_3).

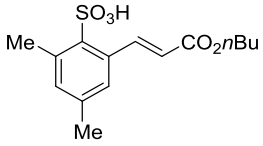
IR (neat): 3387 (br), 2978, 1697, 1633, 1176, 1093, 1025, 680 cm^{-1}.

MS (EI) *m/z* (relative intensity): 267 (5) [M–OH]$^+$, 239 (5), 161 (5), 134 (15), 112 (10), 98 (20), 57 (30), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{13}H_{15}O_5S$ [M–H$^+$] 283.0646, found 283.0645.

The spectral data were in accordance with those reported in the literature. [110]

(*E*)-2-(3-*n*-Butoxy-3-oxoprop-1-en-1-yl)-4,6-dimethylbenzenesulfonic Acid (129lc):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.5 mg, 0.50 mmol) and butyl acrylate (**46c**) (192.0 mg, 1.50 mmol). Purification by column

chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129lc** (123.0 mg, 78%) as a white solid.

M. p. = 208−210 °C.

^{1}H NMR (400 MHz, d_6-DMSO)): δ = 8.86 (d, J = 15.9 Hz, 1H), 7.17 (s, 1H), 7.00 (s, 1H), 6.08 (d, J = 15.9 Hz, 1H), 4.11 (t, J = 6.6 Hz, 2H), 2.54 (s, 3H), 2.24 (s, 3H), 1.64–1.57 (m, 2H), 1.42–1.33 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.2 (C_q), 147.7 (CH), 142.9 (C_q), 136.9 (C_q), 136.3 (C_q), 133.4 (CH), 132.8 (C_q), 126.0 (CH), 116.7 CH), 63.2 (CH_2), 30.3 (CH_2), 22.0 (CH_3), 20.2 (CH_3), 18.6 (CH_2), 13.5 (CH_3).

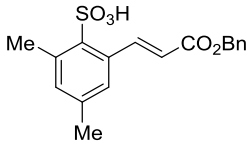
IR (neat): 3417 (br), 2959, 2932, 2874, 1695, 1633, 1172, 1091, 1020 cm^{-1}**.**

MS (EI) *m/z* (relative intensity): 310 (1) $[M–2H]^+$, 234 (5), 202 (5), 146 (20), 134 (24), 118 (25), 89 (10), 64 (20), 44 (100).

HR-MS (ESI) *m/z* calcd for $C_{15}H_{19}O_5S$ $[M–H^+]$ 311.0959, found 311.0960.

The spectral data were in accordance with those reported in the literature.[110]

(*E*)-2-{3-(Benzyloxy)-3-oxoprop-1-en-1-yl}-4,6-dimethylbenzenesulfonic Acid (129ld):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.0 mg, 0.50 mmol) and benzyl acrylate (**46d**) (237.0 mg, 1.46 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129ld** (145.0 mg, 84%) as an off-white solid.

M. p. = 241−243 °C.

^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.94 (d, J = 15.9 Hz, 1H), 7.41–7.31 (m, 5H), 7.19 (s, 1H), 7.00 (s, 1H), 6.16 (d, J = 15.9 Hz, 1H), 5.20 (s, 2H), 2.54 (s, 3H), 2.24 (s, 3H).

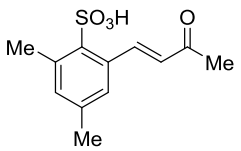
^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.0 (C_q), 148.3 (CH), 143.0 (C_q), 137.0 (C_q), 136.3 (C_q), 136.2 (C_q), 133.6 (CH), 132.7 (C_q), 128.2 (CH), 127.7 (CH), 127.6 (CH), 126.0 (CH), 116.4 (CH), 65.0 (CH_2), 22.0 (CH_3), 20.2 (CH_3).

IR (neat): 3425 (br), 1695, 1631, 1167, 1090, 1020, 680, 656 cm^{-1}.

MS (EI) *m/z* (relative intensity): 345 (5) $[M–H]^+$, 299 (3), 265 (5), 219 (5), 206 (10), 197 (20), 180 (5), 91 (100).

HR-MS (ESI) *m/z*calcd for $C_{18}H_{17}O_5S$ $[M–H^+]$ 345.0802, found 345.0804.

(*E*)-2,4-Dimethyl-6-(3-oxobut-1-en-1-yl)benzenesulfonic Acid (129lf):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (92.5 mg, 0.50 mmol)and methyl vinylketone (**46f**) (110.0 mg, 1.57 mmol). Purification by column chromatography (CH_2Cl_2/MeOH:

15/1→10/1) yielded **129lf** (120.0 mg, 95%) as a pale solid.

M. p. = 260−262 °C.

^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.88 (d, J = 16.3 Hz, 1H), 7.18 (s, 1H), 7.02 (s, 1H), 6.28 (d, J = 16.3 Hz, 1H), 2.56 (s, 3H), 2.27 (s, 3H), 2.26 (s, 3H).

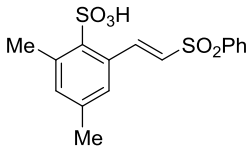
^{13}C NMR (125 MHz, d_6-DMSO): δ = 198.1 (C_q), 147.0 (CH), 143.1 (C_q), 137.0 (C_q), 136.5 (C_q), 133.6 (CH), 132.9 (C_q), 126.6 (CH), 125.7 (CH), 26.6 (CH_3), 22.0 (CH_3), 20.2 (CH_3).

IR (neat): 3492 (br), 1669, 1594, 1387, 1178, 1088, 1019, 690 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 (3) $[M–CH_3]^+$, 134 (5), 112 (5), 101 (10), 84 (10), 66 (10), 58 (40), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{13}O_4S$ $[M–H^+]$ 253.0540, found 253.0542.

(*E*)-2,4-Dimethyl-6-{2-(phenylsulfonyl)vinyl}benzenesulfonic Acid (129lg):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.3 mg, 0.50 mmol) and (vinylsulfonyl)benzene (**46g**) (254.0 mg, 1.51 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129lg** (163.0 mg, 92%) as a pale yellow solid.

M. p. = 214−216 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.90 (d, J = 15.3 Hz, 1H), 7.95–7.92 (m, 2H), 7.72–7.59 (m, 3H), 7.15 (s, 1H), 7.04 (s, 1H), 6.95 (d, J = 15.3 Hz, 1H), 2.55 (s, 3H), 2.23 (s, 3H).

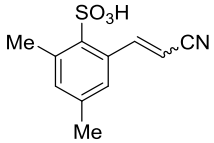
^{13}C NMR (125 MHz, d_6-DMSO): δ = 146.1 (CH), 143.3 (C_q), 141.2 (C_q), 137.2 (C_q), 136.6 (C_q), 134.2 (CH), 133.1 (CH), 130.9 (C_q), 129.2 (CH), 126.9 (CH), 126.4 (CH), 125.9 (CH), 21.8 (CH_3), 20.1 (CH_3).

IR (neat): 3417 (br), 1614, 1596, 1303, 1142, 1083, 684, 651 cm^{-1}.

MS (EI) *m/z* (relative intensity): 299 (3), 284 (5), 271 (10), 239 (40), 211 (100), 183 (20), 165 (30), 119 (25).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{15}O_5S_2$ $[M–H^+]$ 351.0366, found 351.0368.

2-(2-Cyanovinyl)-4,6-dimethylbenzenesulfonic Acid (*E:Z* = 5:1) (129lh):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (92.7 mg, 0.50 mmol) and acrylonitrile (**46h**) (84.0 mg, 1.58 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129lh** (88.0 mg, 75%) as a pale yellow solid.The ratio of the two isomers was 5:1, as estimated by ^{1}H NMR spectroscopy.

M. p. = 293−295°C

(***E*-isomer**):**^{1}H NMR** (300 MHz, d_6-DMSO): δ = 8.67 (d, J = 16.7 Hz, 1H), 7.18 (s, 1H), 7.04 (s, 1H), 5.98 (d, J = 16.7 Hz, 1H), 2.51 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 153.1 (CH), 142.6 (C_q), 137.1 (C_q), 136.4 (C_q), 134.2 (CH), 131.9 (C_q), 125.3 (CH), 119.1 (C_q), 95.2 (CH), 21.9 (CH_3), 20.2 (CH_3).

(***Z*-isomer**):**^{1}H NMR** (300 MHz, d_6-DMSO): δ = 8.14 (d, J = 11.7 Hz, 1H), 7.21 (s, 1H), 7.06 (s, 1H), 5.62 (d, J = 11.7 Hz, 1H), 2.53 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 153.8 (CH), 142.3 (C_q), 137.0 (C_q), 136.6 (C_q), 133.5 (CH), 131.9 (C_q), 125.1 (CH), 117.7 (C_q), 94.0 (CH), 21.5 (CH_3), 20.3 (CH_3).

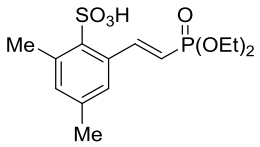
IR (neat): 3459 (br), 2228, 1616, 1595, 1181, 696, 570, 526 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (5) $[M]^+$, 197 (25), 170 (20), 157 (20), 142 (15), 129 (15), 97 (55), 83 (100).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{10}NO_3S$ $[M–H^+]$ 236.0387, found 236.0392.

The spectral data were in accordance with those reported in the literature.[110]

(*E*)-2-{2-(Diethoxyphosphoryl)vinyl}-4,6-dimethylbenzenesulfonic Acid (129li):



The general procedure **B** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.8 mg, 0.50 mmol) and diethyl vinylphosphonate (**46i**) (259.0 mg, 1.58 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129li** (165.0 mg, 94%) as an off-white solid.

M. p. = 137−139 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.57 (dd, J = 22.7, 17.5 Hz, 1H), 7.15 (s, 1H), 7.00 (s, 1H), 5.95 (dd, J = 20.5, 17.5 Hz, 1H), 4.07–3.98 (m, 4H), 2.55 (s, 3H), 2.25 (s, 3H), 1.26 (t, J = 7.0 Hz, 6H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 150.7 (d, J = 8.7 Hz, CH), 142.7 (d, J = 1.7 Hz, C_q), 137.1 (C_q), 136.4 (d, J = 1.4 Hz, C_q), 134.0 (d, J = 24.1 Hz, C_q), 133.4 (CH), 125.9(d, J = 1.9 Hz, CH), 112.9 (d, J = 186.5 Hz, CH), 61.1 (d, J = 5.4 Hz, CH_2), 22.0 (CH_3), 20.2 (CH_3), 16.2 (d, J = 6.2 Hz, CH_3).

^{31}P NMR (122 MHz, d_6-DMSO): δ = 19.4.

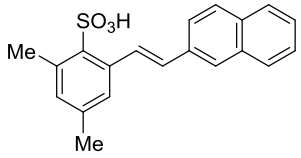
IR (neat): 3394 (br), 2979, 1615, 1597, 1194, 1014, 969, 684 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 (3) $[M–OH]^+$, 284 (3), 267 (70), 239 (30), 211 (100), 193 (15), 177 (5), 115 (10).

HR-MS (ESI) *m/z* calcd for$C_{14}H_{20}O_6PS$ $[M–H^+]$ 347.0724, found 347.0726.

The spectral data were in accordance with those reported in the literature.[110]

(*E*)-2,4-Dimethyl-6-{2-(naphthalen-2-yl)vinyl}benzenesulfonicAcid (129lk):



The general procedure **C** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (91.5 mg, 0.49 mmol) and 2-vinylnaphthalene (**46k**) (230.0 mg, 1.49 mmol), $AgSbF_6$ (69.0 mg, 0.20 mmol, 41 mol %). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129lk** (86.0 mg, 51%) as a pale yellow solid.

M. p. = 223−225 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.57 (d, J = 16.3 Hz, 1H), 7.90–7.85 (m, 4H), 7.72 (d, J = 8.0 Hz,1H), 7.51–7.41 (m, 2H), 7.32 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 16.3 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 2.54 (s, 3H), 2.26 (s, 3H).

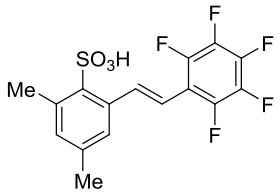
^{13}C NMR (100 MHz, d_6-DMSO): δ = 142.1 (C_q), 136.7 (C_q), 136.3 (C_q), 135.9 (C_q), 135.5 (C_q), 133.3 (C_q), 132.2 (C_q), 131.9 (CH), 131.7 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 126.9 CH), 126.2 (CH), 125.6 (CH), 125.6 (CH), 125.1 (CH), 123.9 (CH), 22.5 (CH_3), 20.4 (CH_3).

IR (neat): 3413 (br), 1594, 1177, 1093, 1024, 961, 719, 687 cm^{-1}.

MS (EI) *m/z* (relative intensity): 338 (15) $[M]^+$, 323 (10), 288 (45), 259 (45), 239 (15), 155 (75), 127 (70), 43 (100).

HR-MS (EI) *m/z* calcd for $C_{20}H_{18}O_3S$ $[M]^+$ 338.0971, found 338.0978.

(*E*)-2,4-Dimethyl-6-{2-(2,3,4,5,6-pentafluorophenyl)vinyl}benzenesulfonic Acid (129ll):



The general procedure **C** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.0 mg, 0.50 mmol) and 1,2,3,4,5-pentafluoro-6-vinylbenzene (**46l**) (291.0 mg, 1.65 mmol, but with twofold amount of $AgSbF_6$ (69.0 mg, 0.20 mmol, 40 mol%). Purification by column chromatography (CH_2Cl_2/MeOH: 15/1→10/1) yielded **129ll** (101.0 mg, 53%) as an off-white solid.

^{1}H NMR (500 MHz, d_6-DMSO): δ = 8.68 (d, J = 16.6 Hz, 1H), 7.22 (d, J = 2.2 Hz, 1H), 6.98 (d, J = 2.2 Hz, 1H), 6.55 (d, J = 16.6 Hz, 1H), 2.57 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 143.8 (m, C_q), 142.3 (C_q), 140.8 (t, J = 7.5 Hz, CH), 138.5 (m, C_q), 137.1 (m, C_q), 137.0 (C_q), 136.3 (C_q), 134.8 (C_q), 132.6 (CH), 125.3 (CH), 113.0 (m, C_q), 110.5 (CH), 22.2 (CH_3), 20.3 (CH_3).

^{19}F NMR (283 MHz, d_6-DMSO): δ = –(143.9−144.0) (m), –158.28 (t, J = 22.0 Hz), –(163.8−164.0) (m).

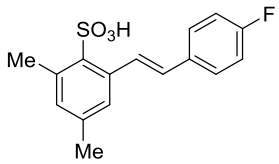
IR (neat): 3422(br), 1518, 1497, 1179, 1087, 956, 577 cm^{-1}.

MS (EI) *m/z* (relative intensity): 378 (5) $[M]^+$, 298 (100), 283 (60), 233 (20), 197 (40), 181 (20),

64 (30).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{10}F_5O_3S$ [M–H$^+$] 377.0276, found 377.0270.

(*E*)-2-(4-Fluorostyryl)-4,6-dimethylbenzenesulfonic Acid (129lm):



The general procedure **C** was followed using 2,4-dimethyl-benzenesulfonic acid (**128l**) (92.3 mg, 0.50 mmol) and 1-fluoro-4-vinylbenzene (**46m**) (183.0 mg, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH: 10/1) yielded **129lm** (92.0 mg, 60%) as an off-white solid.

M. p. = 237−239 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.36 (d, J = 16.2 Hz, 1H), 7.53–7.47 (m,2H), 7.24–7.18 (m, 3H), 6.88 (s, 1H), 6.78 (d, J = 16.3 Hz, 1H), 2.53 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 161.0 (d, $^1J_{C\text{-}F}$ = 243 Hz, C_q), 141.9 (d, $^4J_{C\text{-}F}$ = 3.0 Hz, C_q), 136.5 (C_q), 136.1 (C_q), 135.3 (C_q), 134.7 (d, J = 3.1 Hz, C_q), 131.5 (CH), 131.2 (CH), 127.8 (d, $^3J_{C\text{-}F}$ = 7.9 Hz, CH), 125.5 (CH), 124.9 (CH), 115.2 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, CH), 22.5 (CH_3), 20.4 (CH_3).

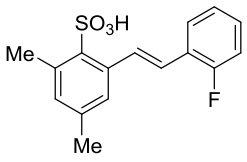
^{19}F NMR (283 MHz, d_6-DMSO): δ = –110.6 (s).

IR (neat): 3395 (br), 2924, 1597, 1507, 1219, 1172, 1091, 1022 cm^{-1}.

MS (EI) *m/z* (relative intensity): 299 (5), 285 (10), 267 (30), 239 (25), 154 (10), 134 (35), 98 (75).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{14}FO_3S$ [M–H$^+$] 305.0653, found 305.0652.

(*E*)-2-(2-Fluorostyryl)-4,6-dimethylbenzenesulfonic Acid (129ln):



The general procedure **C** was followed using 2,4-dimethylbenzenesulfonic acid (**128l**) (93.0. mg, 0.5 mmol), 1-fluoro-2-vinylbenzene (**11n**) (183.0 mg, 1.50 mmol), and $AgSbF_6$ (69.0 mg, 40 mol%). Purification by column chromatography (CH_2Cl_2 /MeOH: 15:1→10:1) yielded **129ln** (105.6 mg, 69%) as an off-white solid.

M. p. = 289–291 °C.

^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.48 (d, J = 16.4 Hz, 1H), 7.70–7.59 (m, 1H), 7.35–7.15 (m, 4H), 6.93 (s, 1H), 6.84 (d, J = 16.4 Hz, 1H), 2.56 (s, 3H), 2.27 (s, 3H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 159.2 (d, $^1J_{C\text{-}F}$ = 246.2 Hz, C_q), 142.0 (C_q), 136.8 (C_q), 136.2 (C_q), 135.3 (C_q), 134.0 (d, $^3J_{C\text{-}F}$ = 3.5 Hz, CH), 131.9 (CH), 128.4 (d, $^3J_{C\text{-}F}$ = 8.2 Hz, CH), 126.9 (d, $^3J_{C\text{-}F}$ = 3.9 Hz, CH), 125.6 (d, $^2J_{C\text{-}F}$ = 12.2 Hz, C_q), 125.1 (CH), 124.3 (CH), 118.2 (CH), 115.4 (d, $^2J_{C\text{-}F}$ = 21.8 Hz, CH), 22.4 (CH_3), 20.4 (CH_3).

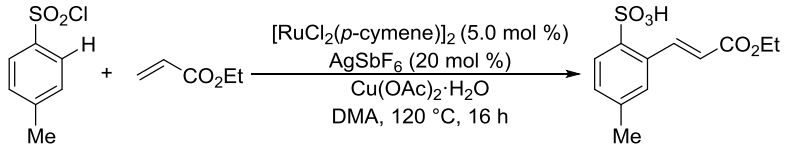
^{19}F NMR (283 MHz, d_6-DMSO): δ = –(119.2−119.3) (m).

IR (neat): 3438 (br), 2957, 2920, 1605, 1486, 1455, 1194, 1091, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity): 304 (12) $[M–2H]^+$, 291 (4), 226 (80), 211 (20), 197 (48), 180 (12), 158 (13), 64 (100).

HR-MS: (ESI) *m/z* calcd for $C_{16}H_{14}FO_3S$ $[M–H^+]$ 305.0653, found 305.0652.

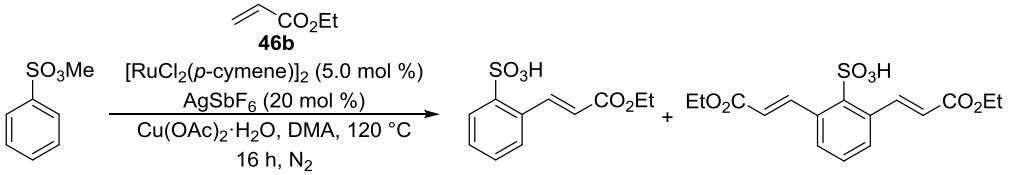
Ruthenium(II)-Catalyzed Oxidative Alkenylation of 4-Methylbenzenesulfonyl Chloride 136.



136 **46b** **129jb**: 71%

The general procedure **B** was followed using 4-methylbenzenesulfonyl chloride **136** (96.0 mg, 0.50mmol), ethyl acrylate (**46b)** (157.0 mg, 1.57 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.5 mg, 5.0 mol %), $AgSbF_6$ (36.0 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (200.0 mg, 1.00 mmol) in DMA. Purification by column chromatography (CH_2Cl_2/MeOH: 20/1→15/1) yielded product **129jb** (96.2 mg, 71%) as a paleyellow solid. Its spectral data were identical to those reported above.

Ruthenium(II)-Catalyzed Oxidative Alkenylation of Methyl Benzenesulfonate (137)



137 129ib:129ib' = 3.7 : 1 **129ib**: 55% **129ib'**: 15%

The general procedure **B** was followed using methyl benzenesulfonate (**137**) (86.0 mg, 0.50mmol), ethyl acrylate (**46b)** (157.0 mg, 1.57 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.5 mg, 5.0 mol %), $AgSbF_6$ (36.0 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (200.0 mg, 1.00 mmol) in DMA. Purification by column chromatography (CH_2Cl_2/MeOH: 20/1→15/1) yielded monoalkenylated benzenesulfonic acid **129ib** (70 mg, 55%) and dialkenylated product **129ib'** (27 mg, 15%) as pale yellow solids. The spectral data of **129ib** were identical to those reported above.

2,6-Bis{(E)-3-ethoxy-3-oxoprop-1-en-1-yl}benzenesulfonic Acid (**129ib'**):

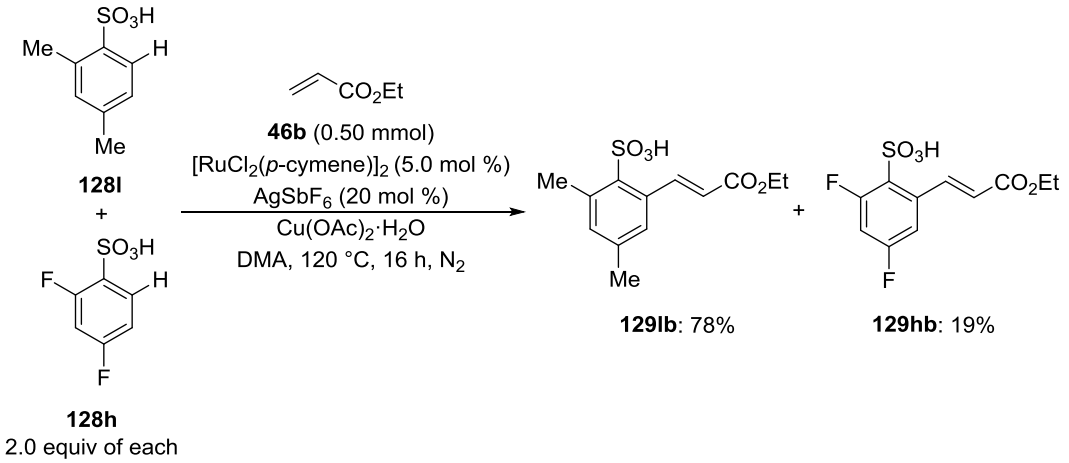
^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.83 (d, J = 15.9 Hz, 2H), 7.62 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.7 Hz, 1H), 6.20 (d, J = 15.9 Hz, 2H), 4.18 (q, J = 7.1 Hz, 4H), 1.26 (t, J = 7.1 Hz, 6H).

^{13}C NMR (125 MHz, d_6-DMSO): δ = 166.0 (C_q), 146.2 (CH), 145.7 (C_q), 133.3 (C_q), 129.2 (CH), 128.5 (CH), 118.0 (CH), 59.7 (CH_2), 14.2 (CH_3).

IR (neat): 3497, 2982, 1697, 1632, 1309, 1162, 1026, 670, 595 cm^{-1}.

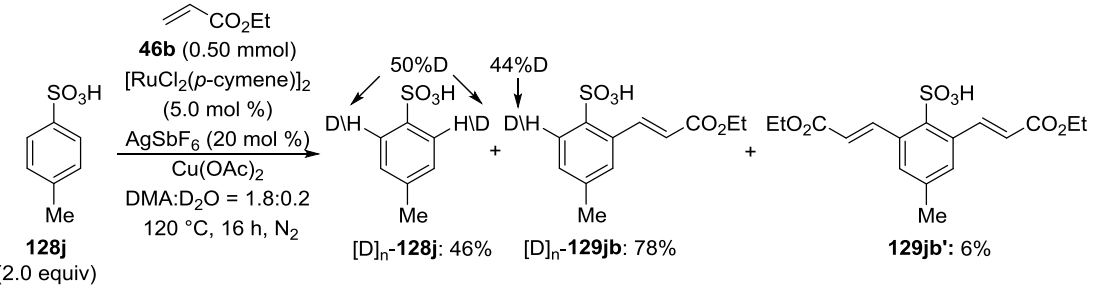
HR-MS: (ESI) *m/z* calcd for $C_{16}H_{17}O_7S$ [M–H^+] 353.0700, found 353.0700.

Intermolecular Competition Experiment between Substrates128l and 128h



A suspension of 2,4-dimethylphenylsulfonic acid **128l** (187.0 mg, 1.00 mmol), 2,4-difluorobenzenesulfonic acid **128h** (194.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (51.5 mg, 0.51mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (35.0 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (200 mg, 1.00 mmol) in DMA (2.0 mL) was stirred at ambient temperature under N_2 for 5 min and then at 120 °C for 16 h under N_2. At ambient temperature, the solvent was removed *in vacuo*, and the crude products were purified by column chromatography on silica gel (CH_2Cl_2/MeOH: 10/1) to yield 142 mg of the acids **129lb** (78%) and **129hb** (19%) as an inseparable mixture. The ratio of product **129lb**/**129hb** was estimated by ^1H NMR spectroscopy applying their spectral data reported above.

Ruthenium(II)-Catalyzed H/D Exchange in Alkenylation of Substrate 128j Employing D_2O as the Cosolvent

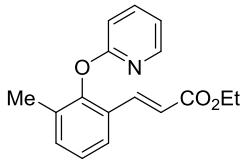


The general procedure **B** was followed using 4-methylbenzenesulfonic acid **128j** (174.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (50.2 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.5 mg, 5.0 mol %), $AgSbF_6$ (36.0 mg, 20mol %) and $Cu(OAc)_2$ (183.0 mg, 1.00 mmol) in a solvent mixture of DMA and D_2O (1.8/0.2 mL). Purification by column chromatography (CH_2Cl_2/MeOH: 20/1→15/1)

yielded [D]$_n$-**129jb** (105.0 mg, 78%) as an off-white solid and reisolated starting material [D]$_n$-**128j** (80.0 mg, 46%). The deuterium incorporation in [D]$_n$-**129jb** and [D]$_n$-**128j** were estimated by ^{1}H NMR spectroscopy.

8.4.3 Ruthenium(II)-Catalyzed C–H Bond Alkenylation of Arenes Bearing Removable Directing Groups.

(*E*)-Ethyl 3-{3-Methyl-2-(pyridin-2-yloxy)phenyl}acrylate (131ab):



The general procedure **D** was followed using 2-(*o*-tolyloxy)pyridine(**130a**) (185.4 mg, 1.00 mmol), ethyl acrylate (**46b**) (52.0 mg, 0.52 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (7.6 mg, 2.5 mol %), $AgSbF_6$ (18.5 mg, 10 mol %) and $Cu(OAc)_2 \cdot H_2O$ (207.6 mg, 1.04 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 12/1→10/1) yielded **131ab** (122.0 mg, 83%) as a colorless solid.

M. p. = 114−116 ^{o}C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.76 (d, *J* = 16.1 Hz, 1H), 7.70−7.63 (m, 1H), 7.52−7.49 (m, 1H), 7.29–7.24 (m, 1H), 7.16 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.95–6.90 (m, 2H), 6.40 (d, *J* = 16.1 Hz, 1H), 4.16 (q, *J* = 7.1Hz, 2H), 2.08 (s, 3H), 1.24 (t, *J* = 7.1Hz, 3H).

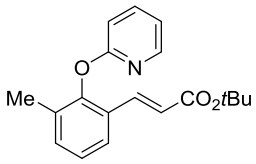
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 163.2 (C_q), 150.7 (C_q), 147.8 (CH), 139.6 CH), 139.2 (CH), 133.1(CH), 132.3 (C_q), 128.3 (C_q), 125.6 (CH), 125.3 (CH), 119.7 (CH), 118.1 (CH), 110.3 (CH), 60.3 (CH_2), 16.6 (CH_3), 14.2 (CH_3).

IR (neat): 2974, 2928, 1699, 1629, 1422, 1242, 1165, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 283 (15) $[M]^+$, 254 (10), 238 (15), 210 (100), 180 (10), 167 (15), 131 (10), 78 (20).

HR-MS (EI) *m/z* calcd for $C_{17}H_{17}NO_3$ $[M]^+$ 283.1208, found 283.1211.

(*E*)-*tert*-Butyl 3-{3-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (131ap):



The general procedure **D** was followed using 2-(*o*-tolyloxy)pyridine(**130a**) (185.1 mg, 1.00 mmol), *tert*-butyl acrylate (**46p**) (62.2 mg, 0.49 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (7.7 mg, 2.5 mol %), and $AgSbF_6$ (17.9 mg, 11 mol %) Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131ap** (123.0 mg, 81%) as a colorless solid.

M. p. = 98−100^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09–8.06 (m,1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.68–7.62 (m, 1H), 7.51 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.34–7.21 (m, 1H), 7.15 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.99–6.83 (m, 2H), 6.33 (d, *J* =16.1 Hz, 1H), 2.08 (s, 3H), 1.44 (s, 9H).

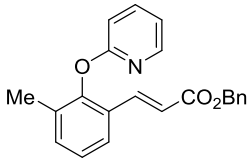
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 163.2 (C_q), 150.6 (C_q), 147.7 (CH), 139.5 (CH), 138.0 (CH), 132.8 (CH), 132.2 (C_q), 128.3 (C_q), 125.5 (CH), 125.0 (CH), 121.4 (CH), 118.0 (CH), 110.2 (CH), 80.2 (C_q), 28.1 (CH_3), 16.6 (CH_3).

IR (neat): 2986, 1695, 1421, 1325, 1265, 1238, 1161, 779 cm^{-1}.

MS (EI) *m/z* (relative intensity): 311 (30) $[M]^+$, 254 (20), 238 (45), 318 (40), 194 (15), 180 (20), 167 (22), 78 (27).

HR-MS (EI) *m/z* calcd for $C_{19}H_{21}NO_3^+$ $[M]^+$ 311.1516, found 311.1529.

(*E*)-Benzyl 3-{3-Methyl-2-(pyridin-2-yloxy)phenyl}acrylate (131ad):



The general procedure **D** was followed using 2-(*o*-tolyloxy)pyridine(**130a**) (186.2 mg, 1.00 mmol), benzyl acrylate (**46d**) (79.2 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 12.5 μmol, 2.5 mol %), and $AgSbF_6$ (18.2 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131ad** (127.0 mg, 75%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.16−8.13 (m, 1H), 7.91 (d, *J* = 16.1 Hz, 1H), 7.67 (td, *J* = 7.8, 2.0 Hz, 1H), 7.47 (d, *J* = 2.2 Hz, 1H), 7.36−7.32 (m, 5H), 7.21 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.02−6.94 (m, 3H), 6.52 (d, *J* = 16.1 Hz, 1H), 5.19 (s, 2H), 2.36 (s, 3H).

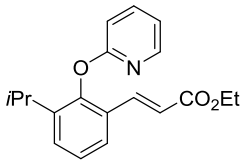
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 163.5 (C_q), 150.6 (C_q), 147.60 (CH), 139.5 (CH), 139.4 (CH), 136.0 (C_q), 134.7 (C_q), 132.1 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 128.0 (CH), 126.9 (C_q), 122.4 (CH), 118.9 (CH), 118.5 (CH), 111.4 (CH), 66.1 (CH_2), 20.8 (CH_3).

IR (neat): 3031, 2948, 1709, 1464, 1426, 1239, 1161, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 345 (30) $[M]^+$, 254 (22), 238 (15), 210 (100), 194 (45), 182 (50), 167 (30), 91 (70).

HR-MS (EI) *m/z* calcd for $C_{22}H_{19}NO_3^+$ $[M]^+$ 345.1359, found 345.1362.

(*E*)-Ethyl-3-{3-isopropyl-2-(pyridin-2-yloxy)phenyl}acrylate (131bb):



The general procedure **D** was followed using 2-(2-isopropylphenoxy)pyridine (**130b**) (215.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (49.3 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), $AgSbF_6$ (19.1 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→12/1) yielded **131bb** (134.0 mg, 87%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (ddd, *J* = 5.0, 2.0, 0.6 Hz, 1H), 7.74 (d, *J* = 16.1 Hz, 1H), 7.65 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.51 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.25 (dd, *J* = 7.7, 7.8 Hz, 1H), 7.01–6.83 (m, 2H), 6.39 (d, *J* = 16.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.02 (hept, *J* = 6.9 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 6H).

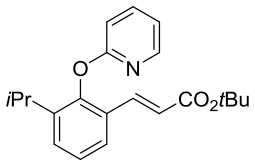
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_q), 163.7 (C_q), 149.4 (C_q), 147.7 (CH), 142.4 (C_q), 139.5 (CH), 139.4 (CH), 128.8 (C_q), 128.3 (CH), 126.0 (CH), 125.1 (CH), 119.6 (CH), 118.1 (CH), 110.1 (CH), 60.2 (CH_2), 27.0 (CH), 22.9 (CH_3), 14.1 (CH_3).

IR (neat): 2963, 1709, 1424, 1260, 1237, 1168, 1135, 774 cm^{-1}.

MS (EI) *m/z* (relative intensity): 311 (30) $[M]^+$, 294 (10), 268 (70), 238 (100), 222 (20), 196 (20), 120 (30), 78 (35).

HR-MS (EI) *m/z* calcd for $C_{19}H_{21}NO_3^+$ $[M]^+$ 311.1516, found 311.1524.

(*E*)-*tert*-Butyl 3-{3-isopropyl-2-(pyridin-2-yloxy)phenyl}acrylate (131bp)



The general procedure **D** was followed using 2-(2-isopropylphenoxy)-pyridine (**1b**) (212.0 mg, 0.99 mmol), *tert*-butyl acrylate (**46p**) (62.7 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (18.1 mg, 11 mol%). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131bp** (155.0 mg, 93%) as a colorless solid.

M. p. = 104−106 °C.

^{1}H NMR (300 MHz, $CDCl_3$):δ = 8.11 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.70–7.65 (m, 1H), 7.65 (d, *J* = 16.0 Hz, 1H), 7.52 (dd, *J* =7.7, 1.6 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.25 (dd, *J* = 7.8, 7.7 Hz, 1H), 6.96–6.91 (m, 2H), 6.31 (d, *J* = 16.0 Hz, 1H), 3.03 (hept, *J* = 6.9 Hz, 1H), 1.44 (s, 9H), 1.14 (d, *J* = 6.9 Hz, 6H).

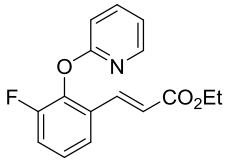
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 163.8 (C_q), 149.3 (C_q), 147.8 (CH), 142.4 (C_q), 139.5 (CH), 138.4 (CH), 128.6 (CH), 128.5 (C_q), 126.0 (CH), 124.9 (CH), 121.5 (CH), 118.0 (CH), 110.1 (CH), 80.2 (C_q), 28.1 (CH_3), 27.1 (CH), 23.0 (CH_3).

IR (neat): 2969, 1698, 1421, 1325, 1262, 1233, 1157, 779 cm^{-1}.

MS (EI) *m/z* (relative intensity): 339 (20) $[M]^+$, 296 (10), 266 (33), 238 (100), 222 (20), 196 (22), 120 (10), 78 (12).

HR-MS (EI) *m/z* calcd for $C_{21}H_{25}NO_3$ $[M]^+$ 339.1829, found 339.1840.

(*E*)-Ethyl 3-{3-fluoro-2-(pyridin-2-yloxy)phenyl}acrylate (131cb):



The general procedure **D** was followed using 2-(2-fluorophenoxy)pyridine (**130c**) (189.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (54.9 mg, 0.55 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.5 mol %), and $AgSbF_6$ (18.7 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 12/1→10/1) yielded **131cb**(128 mg, 81%) as a yellow solid.

M. p. = 74–76 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (ddd, *J* =5.0, 2.0, 0.8 Hz, 1H), 7.82 (d, *J* = 16.2 Hz, 1H),

7.73 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.26–7.15 (m, 2H), 7.08 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.01 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.49 (d, *J* = 16.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 162.6 (C_q), 155.5 ($^1J_{C\text{-}F}$ = 251 Hz, C_q), 147.4 (CH), 140.0 ($^2J_{C\text{-}F}$ = 13 Hz, C_q), 139.6 (CH), 137.8 ($^4J_{C\text{-}F}$ = 4 Hz, CH), 130.3 ($^3J_{C\text{-}F}$ = 2 Hz, C_q), 125.8 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 122.9 ($^4J_{C\text{-}F}$ = 4 Hz, CH), 121.0 (CH), 118.9 (CH), 117.8 ($^2J_{C\text{-}F}$ = 19 Hz, CH), 110.7 (CH), 60.6 (CH_2), 14.2 (CH_3).

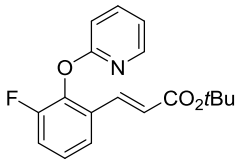
^{19}F NMR (283 MHz, $CDCl_3$): δ = –126.21 (s).

IR (neat): 2987, 1710, 1426, 1265, 1226, 1170, 981, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287(10) $[M]^+$, 258 (15), 242 (15), 214 (100), 185 (20), 136 (10), 107 (15), 78 (55).

HR-MS (EI) *m/z* calcd for $C_{16}H_{14}FNO_3^+$ $[M]^+$ 287.0952, found 287.0953.

(*E*)-*tert*-Butyl 3-{3-fluoro-2-(pyridin-2-yloxy)phenyl}acrylate (131cp):



The general procedure **D** was followed using 2-(2-fluorophenoxy) pyridine (**131c**) (188.0 mg, 0.99 mmol), *tert*-butyl acrylate (**46p**) (63.3 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (18.6 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→12/1) yielded **131cp** (136.0 mg, 87%) as a colorless solid.

M. p. = 108–110 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.74 (d, *J* = 16.1 Hz, 1H), 7.72 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.23–7.14 (m, 2H), 7.07 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.00 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.42 (d, *J* = 16.1 Hz, 1H), 1.48 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9 (C_q), 162.6 (C_q), 156.4 ($^1J_{C\text{-}F}$ = 249 Hz, C_q), 147.4 (CH), 139.9 ($^2J_{C\text{-}F}$ = 13 Hz, C_q), 139.6 (CH), 136.7 ($^4J_{C\text{-}F}$ = 3 Hz, CH), 130.5 ($^3J_{C\text{-}F}$ = 2.0 Hz, C_q), 125.8 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 122.8 (CH), 122.7 ($^4J_{C\text{-}F}$ = 3 Hz, CH), 118.8 (CH), 117.6 ($^2J_{C\text{-}F}$ = 19 Hz, CH), 110.7 (CH), 80.7 (C_q), 28.1 (CH_3).

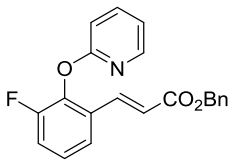
^{19}F NMR (283 MHz, $CDCl_3$): δ = –126.36.

IR (neat): 2980, 1702, 1463, 1424, 1268, 1228, 1134, 773 cm^{-1}.

MS (EI) *m/z* (relative intensity): 315 (5) $[M]^+$, 259 (10), 242 (25), 214 (100), 198 (10), 185 (15), 136 (7), 78 (18).

HR-MS (EI) *m/z* calcd for $C_{18}H_{18}FNO_3$ $[M]^+$ 315.1265, found 315.1286.

(*E*)-Benzyl 3-{3-Fluoro-2-(pyridin-2-yloxy)phenyl}acrylate (**131cd**):



The general procedure **D** was followed using 2-(2-fluorophenoxy) pyridine

(**131c**) (188.0 mg, 0.99 mmol), benzyl acrylate (**46d**) (69.3 mg, 0.43 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), and $AgSbF_6$ (18.1 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131cd** (137.0 mg, 92%) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.91 (d, *J* = 16.1 Hz, 1H), 7.73 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.48–7.44 (m, 1H), 7.40–7.33 (m, 5H), 7.27–7.14 (m, 2H), 7.09 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.01 (ddd, *J* = 7.2, 5.0, 0.9, 1H), 6.57 (d, *J* = 16.1, 1H), 5.23 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3 (C_q), 162.5 (C_q), 155.4 ($^1J_{C\text{-}F}$ = 249 Hz, C_q), 147.3 (CH), 140.0 ($^2J_{C\text{-}F}$ = 13 Hz, C_q), 139.6 (CH), 138.3 ($^4J_{C\text{-}F}$ = 3 Hz, CH), 135.8 (C_q), 130.1 ($^3J_{C\text{-}F}$ = 2.0 Hz, C_q), 128.5 (CH), 128.1 (CH), 128.1 (CH), 125.8 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 122.8 ($^4J_{C\text{-}F}$ = 3 Hz, CH), 120.5 (CH), 118.8 (CH), 117.9 ($^2J_{C\text{-}F}$ = 19 Hz, CH), 110.6 (CH), 66.3 (CH_2).

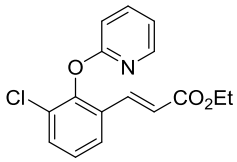
^{19}F NMR (283 MHz, $CDCl_3$): δ = –126.13 (s).

IR (neat): 3064, 2952, 1712, 1460, 1427, 1266, 1232, 773 cm^{-1}.

MS (EI) *m/z* (relative intensity): 349(40) $[M]^+$, 330 (10), 258 (15), 242 (13), 214 (100), 198 (40), 186 (40), 91 (65).

HR-MS (EI) *m/z* calcd for $C_{21}H_{16}FNO_3^+$ $[M]^+$ 349.1109, found 349.1111.

(*E*)-Ethyl 3-{3-Chloro-2-(pyridin-2-yloxy)phenyl}acrylate (131db):



The general procedure **D** was followed using 2-(2-chlorophenoxy)pyridine (**130d**) (205.5 mg, 1.00 mmol), ethyl acrylate (**46b**) (52.8 mg, 0.53 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), and $AgSbF_6$ (18.1 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131db** (111.0 mg, 69%) as a colorless solid.

M. p. = 103−105 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (ddd, *J* = 5.0, 1.9, 0.8 Hz, 1H), 7.77 (d, *J* = 16.2 Hz, 1H), 7.76−7.70 (m, 1H), 7.64–7.54 (m, 1H), 7.48 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.22 (dd, *J* = 7.9, 8.0 Hz, 1H), 7.06 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.99 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.46 (d, *J* = 16.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

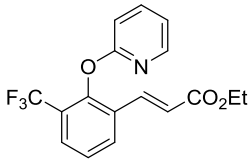
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 162.6 (C_q), 148.5 (C_q), 147.4 (CH), 139.7 (CH), 138.2 (CH), 131.8 (CH), 130.6 (C_q), 129.1 (C_q), 126.2 (CH), 126.0 (CH), 121.0 (CH), 118.7 (CH), 110.8 (CH), 60.5 (CH_2), 14.2 (CH_3).

IR (neat): 2975, 1699, 1423, 1322, 1262, 1239, 1190, 770 cm^{-1}.

MS (EI) *m/z* (relative intensity): 303 (20) $[M]^+$, 268 (65), 258 (25), 240 (60), 230 (100), 209 (13), 196 (20), 167 (25).

HR-MS (EI) *m/z*calcd for $C_{16}H_{14}ClNO_3^+$ $[M]^+$ 303.0657, found 303.0666.

(*E*)-Ethyl 3-{2-(Pyridin-2-yloxy)-3-(trifluoromethyl)phenyl}acrylate (131eb):



The general procedure **D** was followed using 2-{2-(trifluoromethyl)phenoxy}pyridine (**130e**) (236.0 mg, 0.99 mmol), ethyl acrylate (**46b**) (50.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), and $AgSbF_6$ (18.3 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 12/1→10/1) yielded **131eb** (136.0 mg, 81%) as a colorless solid.

M. p. = 44−46 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (ddd, *J* = 5.0, 2.0, 0.8, 1H), 7.84 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.71 (m, 1H), 7.70 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.61 (d, *J* = 16.1 Hz, 1H), 7.44–7.30 (m, 1H), 7.05 (dt, *J* = 8.3, 0.9Hz, 1H), 6.95 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.40 (d, *J* = 16.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2 (C_q), 163.5 (C_q), 149.8 ($^3J_{C\text{-}F}$ = 2.0 Hz, C_q), 147.3 (CH), 139.7 (CH), 137.5 (CH), 131.1 (CH), 130.9 (C_q), 128.6 ($^3J_{C\text{-}F}$ = 5.0 Hz, CH), 125.6 (CH), 125.0 ($^2J_{C\text{-}F}$ = 32 Hz, C_q), 124.9 ($^1J_{C\text{-}F}$ = 272 Hz, C_q), 121.2 (CH), 118.7 (CH), 110.7 (CH), 60.5 (CH_2), 14.1 (CH_3).

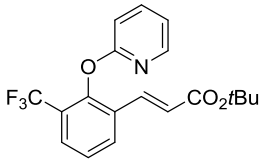
^{19}F NMR (283 MHz, $CDCl_3$): δ = –61.7 (s).

IR (neat): 2987, 1708, 1425, 1328, 1231, 1136, 1104, 777 cm^{-1}.

MS (EI) *m/z* (relative intensity):337 (20) $[M]^+$, 292 (20), 264 (100), 244 (25), 196 (15), 167 (10), 51 (15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{14}F_3NO_3^+$ $[M]^+$ 337.0920, found 337.0919.

(*E*)-*tert*-Butyl 3-{2-(pyridin-2-yloxy)-3-(trifluoromethyl)phenyl}acrylate (131ep):



The general procedure **D** was followed using 2-{2-(trifluoromethyl)-phenoxy}pyridine (**131e**) (233.0 mg, 0.97 mmol), *tert*-butyl acrylate (**46p**) (63.8 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), and $AgSbF_6$ (18.7 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131ep** (144.0 mg, 79%) as an off-white solid.

M. p. = 78−80 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–8.02 (m, 1H), 7.87–7.83 (m, 1H), 7.73–7.71 (m, 2H), 7.52 (d, *J* = 16.0 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.8 Hz, 1H), 7.06 (d, *J* = 8.3, 1H), 6.97 (ddd, *J* = 7.2, 5.0, 1.0 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 1.43 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4 (C_q), 163.5 (C_q), 149.7 (C_q), 147.3 (CH), 139.7 (CH), 136.4 (CH), 131 (C_q), 130.9 (CH), 128.4 ($^3J_{C\text{-}F}$ = 5.0 Hz, CH), 125.6 (CH), 125.4 ($^2J_{C\text{-}F}$ = 33 Hz, C_q), 123.1 (CH), 123.0 ($^1J_{C\text{-}F}$ = 272 Hz, C_q), 118.6 (CH), 110.7 (CH), 80.6 (C_q), 28.0 (CH_3).

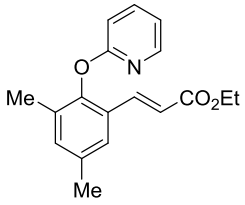
^{19}F NMR (283 MHz, $CDCl_3$): δ = –61.7.

IR (neat): 2970, 1699, 1427, 1334, 1261, 1235, 1129, 783cm^{-1}.

MS (EI) *m/z* (relative intensity): 365 (5) $[M]^+$, 309 (6), 292 (17), 264 (100), 244 (17), 196 (10), 167 (7), 78 (20).

HR-MS (EI) *m/z* calcd for $C_{19}H_{18}F_3NO_3$ $[M]^+$ 365.1239, found 365.1246.

(*E*)-Ethyl 3-{3,5-dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (131fb):



The general procedure **D** was followed using 2-(2,4-dimethylphenoxy)-pyridine (**130f**) (195.0 mg, 0.98 mmol), ethyl acrylate(**46b**) (53.4 mg, 0.53 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.5 mol %), and $AgSbF_6$ (18.7 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→12/1) yielded **131fb** (130.0 mg, 82%) as a colorless solid.

M. p. = 73−75 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (ddd, *J* = 4.9, 2.0, 1.0 Hz, 1H), 7.75 (d, *J* = 16.1 Hz, 1H), 7.67 (ddd, *J* = 8.2, 7.2, 2.0 Hz, 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 6.96–6.91 (m, 2H), 6.41 (d, *J* = 16.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 2.06 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

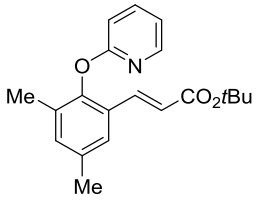
^{13}C NMR (75 MHz, $CDCl_3$):δ = 166.9 (C_q), 163.3 (C_q), 148.5 (C_q), 147.7 (CH), 139.5 (CH), 139.3 (CH), 135.0 (C_q), 134.0 (CH), 131.8 (C_q), 127.7 (C_q), 125.7 (CH), 119.5 (CH), 118.0 (CH), 110.3 (CH), 60.2 (CH_2), 20.9 (CH_3), 16.5 (CH_3), 14.2 (CH_3).

IR (neat): 2982, 1698, 1428, 1281, 1234, 1202, 1040, 774 cm^{-1}.

MS (EI) *m/z* (relative intensity): 297 (30) $[M]^+$, 280 (10), 268 (15), 252 (25), 224 (100), 203 (30), 175 (25), 78(40).

HR-MS (EI) *m/z* calcd for $C_{18}H_{19}NO_3$ $[M]^+$ 297.1365, found 297.1369.

(*E*)-*tert*-Butyl 3-{3,5-Dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (131fp):



The general procedure **D** was followed using 2-(2,4-dimethylphenoxy)-pyridine (**130f**) (199.0 mg, 1.00 mmol), *tert*-butyl acrylate (**46p**) (65.2 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), and $AgSbF_6$ (17.9 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131fp** (120.0 mg, 73%) as a colorless solid.

M. p. = 146−148 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (ddd, *J* = 4.7, 2.0, 1.0, 1H), 7.67 (ddd, *J* =8.2, 7.3, 2.0 Hz, 1H) 7.66 (d, *J* = 16.0 Hz, 1H), 7.38–7.29 (m,1H), 7.10–7.09 (m, 1H), 6.95–6.91 (m, 2H), 6.33 (d, *J*=16.0 Hz, 1H), 2.34 (s, 3H), 2.07 (s, 3H), 1.46 (s, 9H).

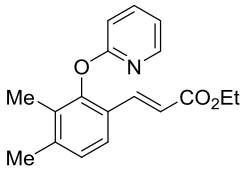
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2 (C_q), 163.4 (C_q), 148.5 (C_q), 147.8 (CH), 139.5 (CH), 138.2 (CH), 134.9 (C_q), 133.8 (CH), 131.8 (C_q), 127.9 (C_q), 125.5 (CH), 121.2 (CH), 117.9 (CH), 110.3 (CH), 80.2 (C_q), 28.1 (CH_3), 20.9 (CH_3), 16.6 (CH_3).

IR (neat): 2971, 1694, 1425, 1239, 1153, 1131, 870, 781 cm^{-1}.

MS (EI) *m/z* (relative intensity): 325 (10) $[M]^+$, 268 (10), 252 (32), 224 (100), 206 (13), 194 (7), 175 (20), 78 (10).

HR-MS (EI) *m/z* calcd for $C_{20}H_{23}NO_3$ $[M]^+$ 325.1672, found 325.1683.

(*E*)-Ethyl 3-{3,4-Dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (131gb):



The general procedure **D** was followed using 2-(2,3-dimethylphenoxy)pyridine (**130g**) (200.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (47.7 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.6 mol %), and $AgSbF_6$ (18.2 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→10/1) yielded **131gb** (108.0 mg, 76%) as a colorless solid.

M. p. = 128−130 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.12–8.09 (m, 1H), 7.74 (d, *J* = 16.1 Hz, 1H), 7.68 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.96–6.92 (m, 2H), 6.38 (d, *J* = 16.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.33 (s, 3H), 2.02 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

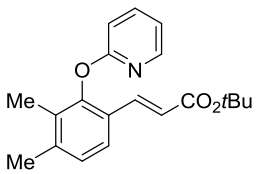
^{13}C NMR (75MHz, $CDCl_3$): δ = 167.0 (C_q), 163.4 (C_q), 150.5 (C_q), 147.8 (CH), 141.1 (C_q), 139.6 (CH), 139.5 (CH), 130.8 (C_q), 127.4 (CH), 125.8 (C_q), 124.5 (CH), 118.6 (CH), 118.0 (CH), 110.3 (CH), 60.2 (CH_2) 20.4 (CH_3), 14.2 (CH_3), 12.9 (CH_3).

IR (neat): 2982, 1711, 1254, 1236, 1200, 1168, 1141, 782 cm^{-1}.

MS (EI) *m/z* (relative intensity): 297 (30) $[M]^+$, 268 (15), 252 (20), 224 (100), 203 (15), 181 (15), 115 (10), 78 (20).

HR-MS (EI) *m/z* calcd for $C_{18}H_{19}NO_3^+$ $[M]^+$ 297.1359, found 297.1360.

(*E*)-*tert*-Butyl 3-{3,4-Dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (131gp):



The general procedure **D** was followed using 2-(2,3-dimethylphenoxy)-pyridine (**130g**) (200.8 mg, 1.01 mmol), *tert*-butyl acrylate (**46p**) (64.5 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (18.2 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131gp** (122.0 mg, 75%) as a colorless solid.

M. p. = 115−117 °C.

^{1}H NMR (300 MHz, $CDCl_3$):δ = 8.12–8.08 (m, 1H), 7.65 (d, *J* = 16.0 Hz, 1H), 7.71–7.65 (m, 1H), 7.44 (d, *J*=8.1 Hz, 1H), 7.07(d, *J*= 8.1 Hz, 1H), 6.99–6.85 (m, 2H), 6.31 (d, *J*=16.0 Hz, 1H), 2.02 (s, 3H), 2.02 (s, 3H), 1.45 (s, 9H).

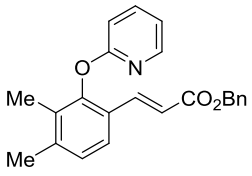
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3(C_q), 163.5 (C_q) 150.4 (C_q), 147.8 (CH), 140.8 (C_q), 139.5 (CH), 138.4 (CH), 130.7 (C_q), 127.3 (CH), 125.9 (C_q), 124.3 (CH), 120.4 (CH), 117.9 (CH), 110.3 (CH), 80.1 (C_q), 28.1 (CH_3), 20.4 (CH_3), 12.9 (CH_3).

IR (neat): 2974, 1698, 1256, 1234, 1150, 987, 824, 782 cm^{-1}.

MS (EI) *m/z*(relative intensity): 325 (10) $[M]^+$, 268 (10), 252 (20), 224 (100), 208 (10), 194 (5), 175, (15), 115 (7).

HR-MS (EI) *m/z* calcd for $C_{20}H_{23}NO_3^+$ $[M]^+$ 325.1672, found 325.1685.

(*E*)-Benzyl 3-{3,4-Dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (131gd):



The general procedure **D** was followed using 2-(2,3-dimethylphenoxy)-pyridine (**130g**) (199.0 mg, 1.00 mmol), benzyl acrylate (**2d**) (84.9 mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (17.6 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131gd** (153.0 mg, 82%) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15–8.11 (m, 1H), 7.85 (d, *J* = 16.1 Hz, 1H), 7.72–7.66 (m, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.37–7.35 (m, 5H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.96 (m, 2H), 6.47 (d, *J* = 16.1 Hz, 1H), 5.19 (s, 2H), 2.34 (s, 3H), 2.05 (s, 3H).

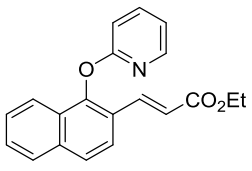
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_q) 163.3 (C_q), 150.5 (C_q), 147.7 (CH), 141.2 (C_q), 140.0 (CH), 139.5 (CH), 136.0 (C_q), 130.7 (C_q), 128.4 (CH), 128.0 (CH), 127.9 (CH), 127.3 (CH), 125.6 (C_q), 124.4 (CH), 118.0 (CH), 117.9 (CH), 110.2 (CH), 65.9 (CH_2), 20.3 (CH_3), 12.8 (CH_3).

IR (neat): 3032, 2946, 1708, 1427, 1237, 1195, 1152, 777 cm^{-1}.

MS (EI) *m/z* (relative intensity): 359 (40) $[M]^+$, 344 (10), 268 (25), 252 (15), 224 (100), 208 (30), 181 (25), 91 (70).

HR-MS (EI) *m/z* calcd for $C_{23}H_{21}NO_3^+$ $[M]^+$ 359.1516, found 359.1535.

(*E*)-Ethyl 3-{1-(pyridin-2-yloxy)naphthalen-2-yl}acrylate (131hb):



The general procedure **D** was followed using 2-(naphthalen-1-yloxy)-pyridine (**130h**) (221.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (50.3 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (18.6 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→12/1) yielded **131hb** (121.0 mg, 76%) as a colorless solid.

M. p. = 156−158 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 8.00 (d, *J* = 16.1 Hz, 1H), 7.91–7.79 (m, 2H), 7.75 (s, 2H), 7.71 (ddd, *J* =8.3, 7.2, 2.0 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.03 (dt, *J* = 8.3, 0.8 Hz, 1H), 6.96 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.54 (d, *J* = 16.1 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

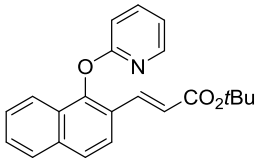
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8(C_q), 164.2 (C_q), 148.8 (C_q), 147.9 (CH), 139.7 (CH), 138.6 (CH), 135.6 (C_q), 128.0 (CH), 128.0 (C_q), 127.4 (CH), 126.8 (CH), 126.0 (CH), 124.2 (C_q), 123.3 (CH), 123.2 (CH), 119.8 (CH), 118.4 (CH), 110.2 (CH), 60.4 (CH_2), 14.2 (CH_3).

IR (neat): 2987, 1712, 1292, 1256, 1234, 1174, 1138, 783 cm^{-1}.

MS (EI) *m/z* (relative intensity): 319 (10) [M], 290 (25), 274 (15), 246 (65), 225 (100), 197 (80), 168 (20), 139 (30).

HR-MS (EI) *m/z* calcd for $C_{20}H_{17}NO_3$ $[M]^+$ 319.1208, found 319.1217.

(*E*)-*tert*-Butyl 3-{1-(Pyridin-2-yloxy)naphthalen-2-yl}acrylate (131hp):



The general procedure **D** was followed using 2-(naphthalen-1-yloxy)-pyridine (**130h**) (222.0 mg, 1.00 mmol), *tert*-butyl acrylate (**46p**) (65.2 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), and $AgSbF_6$ (18.3 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131hp** (145.0 mg, 82%) as an off-white solid.

M. p. = 126−128 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.92 (d, *J* = 16.2 Hz, 1H), 7.85 (m, 2H), 7.78–7.75 (m, 2H), 7.71 (ddd, *J* = 8.4, 7.2, 2.0 Hz, 1H), 7.50 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.41 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.09–7.00 (m, 1H), 6.96 (ddd, *J* = 7.2, 5.0, 1.0 Hz, 1H), 6.48 (d, *J* = 16.2 Hz, 1H), 1.49 (s, 9H).

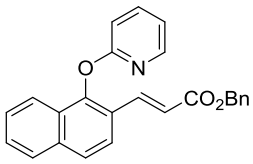
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 164.3(C_q), 148.6 (C_q), 147.9 (CH), 139.7 (CH), 137.5 (CH), 135.5 (C_q), 128.1(C_q), 128.0 (CH), 127.3 (CH), 126.8 (CH), 125.9(CH), 124.2(C_q), 123.2(CH), 123.1(CH), 121.5(CH), 118.4 (CH), 110.2 (CH), 80.4 (C_q), 28.1 (CH_3).

IR (neat): 2974, 1698, 1257, 1232, 1160, 1072, 985, 779 cm^{-1}.

MS (EI) *m/z* (relative intensity): 347 (15) $[M]^+$, 290 (15), 274 (30), 246 (90), 217 (50), 196 (100), 168 (42), 139 (28).

HR-MS (EI) *m/z* calcd $C_{22}H_{21}NO_3$ $[M]^+$ 347.1516, found 347.1520.

(*E*)-Benzyl 3-{1-(pyridin-2-yloxy)naphthalen-2-yl}acrylate (131hd):



The general procedure **D** was followed using 2-(naphthalen-1-yloxy)-pyridine (**130h**) (222.0 mg, 1.00 mmol), benzyl acrylate(**46d**) (82.2 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), $AgSbF_6$ (18.6 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131hd** (169.0 mg, 88%) as an off-white solid.

M. p. = 128−130 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 16.1 Hz, 1H), 8.06 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.87–7.84 (m, 2H), 7.75 (m, 2H), 7.72 (ddd, *J* = 8.4, 7.2, 2.0 Hz, 1H), 7.51 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.43 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.38–7.34 (m, 5H), 7.04 (ddd, *J* = 8.3, 0.9, 0.8 Hz, 1H), 6.97 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.60 (d, *J* = 16.1 Hz, 1H), 5.21 (s, 2H).

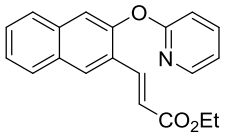
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 164.2 (C_q), 148.9(C_q), 147.9 (CH), 139.7 (CH), 139.2 (CH), 136.1 (C_q), 135.7 (C_q), 128.5 (CH), 128.1 (CH), 128.1 (CH), 128.0 (CH), 128.0 (C_q), 127.5 (CH), 126.9 (CH), 126.0 (CH), 124.0 (C_q), 123.2 (CH), 123.2 (CH), 119.3 (CH), 118.5 (CH), 110.2(CH), 66.2 (CH_2).

IR (neat): 2960, 1708, 1427, 1256, 1230, 1163, 1136, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 381 (5) $[M]^+$, 287 (20), 246 (50), 217 (35), 196 (10), 139 (15), 91 (100).

HR-MS (EI) *m/z* calcd $C_{25}H_{19}NO_3$ $[M]^+$ 381.1359, found 381.1367.

(*E*)-Ethyl 3-{3-(Pyridin-2-yloxy)naphthalen-2-yl}acrylate (131ib):



The general procedure **D** was followed using 2-(naphthalen-2-yloxy)pyridine (**130i**) (221.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (50.6 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.5 mg, 5.0 mol %), and $AgSbF_6$ (35.7 mg, 20 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131ib** (126.0 mg, 78%) as a colorless solid.

M. p. = 124−126 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19−8.16 (m, 1H), 8.16 (s, 1H), 7.96 (d, *J* = 16.1 Hz, 1H), 7.87–7.84 (m, 1H), 7.80–7.66 (m, 2H), 7.52 (s, 1H), 7.54–7.38 (m, 2H), 7.05–7.00 (m, 2H), 6.64 (d, *J* = 16.1 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

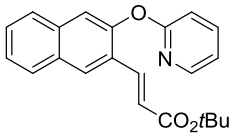
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9 (C_q), 163.6 (C_q), 150.4 (C_q), 147.9 (CH), 139.7 (CH), 139.5 (CH), 134.7 (C_q), 130.8 (C_q), 129.0 (CH), 128.3 (CH), 127.4 (CH), 127.3(C_q), 127.2 (CH), 125.8 (CH), 120.4 (CH), 118.9 (CH), 118.8(CH), 111.7 (CH), 60.4 (CH_2), 14.3 (CH_3).

IR (neat): 2986, 1702, 1426, 1313, 1264, 1246, 1176, 781 cm^{-1}.

MS (EI) *m/z* (relative intensity): 319 (15) $[M]^+$, 290 (50), 274 (15), 246 (100), 217 (45), 197 (20), 139 (25), 78 (20).

HR-MS (EI) *m/z* calcd for $C_{20}H_{17}NO_3^+$ $[M]^+$ 319.1203, found 319.1217.

(*E*)-*tert*-Butyl 3-{3-(pyridin-2-yloxy)naphthalen-2-yl}acrylate (131ip):



The general procedure **D** was followed using 2-(naphthalen-2-yloxy)-pyridine (**130i**) (220.0 mg, 0.99 mmol), *tert*-butyl acrylate (**46p**) (66.0 mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.7 mg, 5.1 mol %), $AgSbF_6$ (35.7 mg, 20 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131ip** (133.0 mg, 74%) as a colorless solid.

M. p. = 138−140°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25–8.10 (m, 2H), 7.87 (d, *J* = 16.0 Hz, 1H), 7.86–7.83 (m, 1H), 7.76–7.70 (m, 2H), 7.52–7.43 (m, 3H), 7.04–7.00 (m, 2H), 6.56 (d, *J* = 16.0 Hz, 1H), 1.50 (s, 9H).

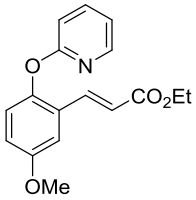
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 163.7 (C_q), 150.3 (C_q), 147.8 (CH), 139.6 (CH), 138.3 (CH), 134.6 (C_q), 130.9 (C_q), 128.5 (CH), 128.3 (CH), 127.5 (C_q), 127.3 (CH), 127.2 (CH), 125.8 (CH), 122.2 (CH), 118.8 (CH), 118.8 (CH), 111.7 (CH), 80.4(C_q), 28.1 (CH_3).

IR (neat): 2972, 1701, 1423, 1231, 1134, 1091, 863, 780 cm^{-1}.

MS (EI) *m/z* (relative intensity): 347 (30) $[M]^+$, 290 (30), 274 (40), 246 (100), 230 (35), 217 (40), 196 (33), 139 (20).

HR-MS (EI) *m/z* calcd for $C_{22}H_{21}NO_3$ $[M]^+$ 347.1516, found 347.1510.

(*E*)-Ethyl 3-{5-methoxy-2-(pyridin-2-yloxy)phenyl}acrylate (131kb):



The general procedure **D** was followed using 2-(4-methoxyphenoxy)pyridine (**131k**) (201.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (49.0 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.6 mol %), and $AgSbF_6$ (17.8 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→10/1) yielded **131kb** (99.0 mg, 68%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (ddd, *J* = 4.9, 2.0, 0.8, 1H), 7.81 (d, *J* = 16.1 Hz, 1H), 7.67 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.14 (d, *J* = 3.0 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 1H), 6.98–6.92 (m, 3H), 6.44 (d, *J* = 16.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

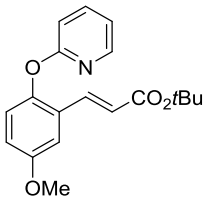
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_q), 163.8 (C_q), 156.5 (C_q), 147.6 (CH), 146.3 (C_q), 139.4 (CH), 138.7 (CH), 128.1 (C_q), 123.8 (CH), 119.8 (CH), 118.4 (CH), 117.5 (CH), 111.5 (CH), 111.1 (CH), 60.4 (CH_2), 55.5 (CH_3), 14.2 (CH_3).

IR (neat): 2980, 1706, 1464, 1425, 1232, 1173, 1031, 775 cm^{-1}.

MS (EI) *m/z* (relative intensity): 299 (20) $[M]^+$, 270 (45), 254 (20), 226 (100), 205 (45), 177 (43), 154 (30), 133 (20).

HR-MS (EI) *m/z* calcd for $C_{17}H_{17}NO_4$ $[M]^+$ 299.1152, found 299.1154.

(*E*)-*tert*-Butyl 3-{5-methoxy-2-(pyridin-2-yloxy)phenyl}acrylate (131kp):



The general procedure **D** was followed using 2-(4-methoxyphenoxy)pyridine (**130k**) (202.0 mg, 1.00 mmol), *tert*-butyl acrylate (**46p**) (64.0 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), and $AgSbF_6$ (18.5 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 10/1→7/1) yielded **131kp** (107.0 mg, 65%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.72 (d, *J* = 16.1 Hz, 1H), 7.67 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.14 (d, *J* = 3.0 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 1H), 6.99–6.92 (m, 3H), 6.36 (d, *J* = 16.1 Hz, 1H), 3.83 (s, 3H), 1.47 (s, 9H).

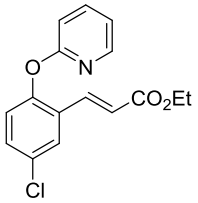
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 163.9 (C_q), 156.6 (C_q), 147.6 (CH), 146.2 (C_q), 139.5 (CH), 137.7 (CH), 128.3 (C_q), 123.8 (CH), 121.6 (CH), 118.3 (CH), 117.4 (CH), 111.3 (CH), 111.2 (CH), 80.4 (C_q), 55.6 (CH_3), 28.1 (CH_3).

IR (neat): 2976, 1703, 1464, 1425, 1233, 1198, 1142, 776 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (20) $[M]^+$, 270 (30), 254 (40), 226 (100), 198 (20), 176 (65), 154 (15), 78 (27).

HR-MS (EI) *m/z* calcd for $C_{19}H_{21}NO_4$ $[M]^+$ 327.1465, found 327.1472.

(*E*)-Ethyl 3-{5-chloro-2-(pyridin-2-yloxy)phenyl}acrylate (131lb):



The general procedure **D** was followed using 2-(4-chlorophenoxy)pyridine (**130l**) (204.0 mg, 0.99 mmol), ethyl acrylate (**46b**) (47.0 mg, 0.47 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), $AgSbF_6$ (18.1 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131lb** (96.0 mg, 68%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14–8.12 (m, 1H), 7.79 (d, *J* = 16.1 Hz, 1H), 7.72 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.62 (d, *J* = 2.6 Hz, 1H), 7.34 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.05 (d, *J* = 8.7Hz, 1H), 7.04–6.99 (m, 2H), 6.45 (d, *J* = 16.1 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

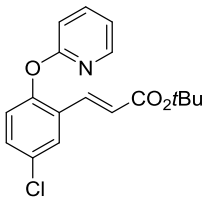
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 163.1 (C_q), 151.2 (C_q), 147.6(CH), 139.8 (CH), 137.5 (CH), 130.9 (CH), 130.4 (C_q), 128.9 (C_q), 127.5 (CH), 123.9 (CH), 120.9 (CH), 119.0 (CH), 111.7 (CH), 60.6 (CH_2), 14.2 (CH_3).

IR (neat): 2981, 1708, 1463, 1426, 1235, 1172, 1109, 773 cm^{-1}.

MS (EI) *m/z* (relative intensity): 303 (30) $[M]^+$, 274 (35), 258 (33), 230 (100), 209 (30), 202 (25), 167 (40), 78 (50).

HR-MS (EI) *m/z* calcd for $C_{16}H_{14}ClNO_3^+$ $[M]^+$ 303.0657, found 303.0656.

(*E*)-*tert*-Butyl 3-{5-chloro-2-(pyridin-2-yloxy)phenyl}acrylate (131lp):



The general procedure **D** was followed using 2-(4-chlorophenoxy)pyridine (**131l**) (208.0 mg, 1.01 mmol), *tert*-butyl acrylate (**46p**) (62.5 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), and $AgSbF_6$ (17.9 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131lp** (123.0 mg, 76%) as a colorless solid.

M. p. = 102−104 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.72 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.70 (d, *J* = 16.1Hz, 1H), 7.63 (d, *J* = 2.6 Hz, 1H), 7.33 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 1H), 7.03–6.98 (m, 2H), 6.38 (d, *J* = 16.1 Hz, 1H), 1.48 (s, 9H).

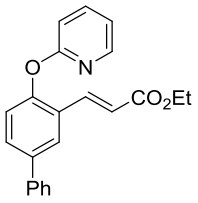
^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 163.1 (C_q), 151.0 (C_q), 147.6 (CH), 139.7 (CH), 136.4 (CH), 130.7 (CH), 130.4 (C_q), 129.1 (C_q), 127.4 (CH), 123.9 (CH), 122.7 (CH), 118.9 (CH), 111.7 (CH), 80.7 (C_q), 28.1 (CH_3).

IR (neat): 2978, 1699, 1425, 1295, 1238, 1156, 1140, 974 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 (10) $[M]^+$, 274 (10), 258 (30), 230 (100), 214 (15), 201(15), 167 (20), 78 (40).

HR-MS (EI) *m/z* calcd for $C_{18}H_{18}ClNO_3^+$ $[M]^+$ 331.0970, found 331.0978.

(*E*)-Ethyl 3-{4-(pyridin-2-yloxy)-[1,1'-biphenyl]-3-yl}acrylate (131mb):



The general procedure **D** was followed using ethyl 2-([1,1'-biphenyl]-4-yloxy)-pyridine (**130m**) (253.0 mg, 1.02 mmol), ethyl acrylate (**46b**) (48.3 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (36.2 mg, 22 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 30/1→20/1) yielded **131mb** (106.0 mg, 64%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.95 (d, *J* = 16.2 Hz, 1H), 7.88 (d, *J* = 2.3 Hz, 1H), 7.74 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.61–7.58 (m, 3H), 7.49–7.42 (m, 2H), 7.40–7.34 (m, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 7.06–7.01 (m, 2H), 6.57 (d, *J* = 16.2 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

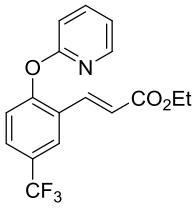
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 163.3 (C_q), 152.2 (C_q), 147.7 (CH), 140.0 (C_q), 139.7 (CH), 138.8 (CH), 138.2 (C_q), 129.9 (CH), 128.8 (CH), 127.5 (C_q), 127.4 (CH), 127.0 (CH), 126.6 (CH), 122.7 (CH), 120.0 (CH), 118.8 (CH), 111.8 (CH), 60.4 (CH_2), 14.2 (CH_3).

IR (neat): 2980, 1706, 1464, 1426, 1235, 1165, 757, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity): 345 (35) $[M]^+$, 316 (60), 300 (25), 272 (100), 251 (50), 244 (35), 223 (40), 165 (25).

HR-MS (EI) *m/z* calcd for $C_{22}H_{19}NO_3^+$ $[M]^+$ 345.1359, found 345.1371.

(*E*)-Ethyl 3-{2-(Pyridin-2-yloxy)-5-(trifluoromethyl)phenyl}acrylate (131nb):



The general procedure **D** was followed using ethyl 2-{4-(trifluoromethyl)-phenoxy}pyridine (**130n**) (236.0 mg, 0.99 mmol), ethyl acrylate (**46b**) (48.0 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.6 mg, 5.1 mol %), and $AgSbF_6$ (36.7 mg, 22 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131nb** (128.0 mg, 79%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18–8.16 (m, 1H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.90 (d, *J* = 16.1 Hz, 1H), 7.77 (ddd, *J* = 8.2, 7.3, 2.0 Hz, 1H), 7.62 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.14–6.94 (m, 2H), 6.55 (d, *J* = 16.1 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 166.4 (C_q), 162.6 (C_q), 155.3 (C_q), 147.7 (CH), 140.0 (CH), 137.4 (CH), 127.7 (C_q), 127.6 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 127.1 ($^2J_{C\text{-}F}$ =33 Hz, C_q), 125.3 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 123.7 ($^1J_{C\text{-}F}$ = 272 Hz, C_q), 122.5 (CH), 121.4 (CH), 119.6 (CH), 112.3 (CH), 60.7 (CH_2), 14.2 (CH_3).

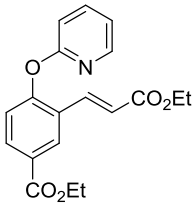
^{19}F NMR (283 MHz, $CDCl_3$): δ = –62.35 (s).

IR (neat): 2983, 1716, 1641, 1267, 1162, 1123, 1073, 773 cm^{-1}.

MS (EI) *m/z* (relative intensity): 337 (10) $[M]^+$, 308 (15), 292 (17), 264 (100), 248 (7), 236 (15), 215 (10), 167 (13).

HR-MS (EI) *m/z* calcd for $C_{17}H_{14}F_3NO_3^+$ $[M]^+$ 337.0920, found 337.0917.

(*E*)-Ethyl 3-{(3-ethoxy-3-oxoprop-1-en-1-yl)}-4-(pyridin-2-yloxy)benzoate (131ob):



The general procedure **D** was followed using ethyl 4-(pyridin-2-yloxy)benzoate (**130o**) (241.0 mg, 0.99 mmol), ethyl acrylate (**46b**) (48.0 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.8 mg, 5.4 mol %), and $AgSbF_6$ (36.5 mg, 22 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **131ob** (110 mg, 67%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 2.1 Hz, 1H), 8.17 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 8.04 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.91 (d, *J* = 16.1 Hz, 1H), 7.75 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.05 (m, 2H), 6.58 (d, *J* = 16.1 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).

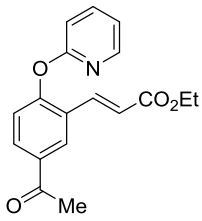
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 165.5 (C_q), 162.7 (C_q), 156.4 (C_q), 147.8 (CH), 139.9 (CH), 137.9 (CH), 132.1 (CH), 129.7 (CH), 127.0 (C_q), 126.9 (C_q), 121.6 (CH), 120.8 (CH), 119.5 (CH), 112.3 (CH), 61.1(CH_2), 60.5 (CH_2), 14.3 (CH_3), 14.2 (CH_3).

IR (neat): 2980, 1708, 1591, 1427, 1232, 1172, 1108, 763 cm^{-1}.

MS (EI) *m/z* (relative intensity): 341 (15) $[M]^+$, 312 (15), 296 (20), 268 (100), 247 (10), 240 (50), 219 (12), 167 (15).

HR-MS (EI) *m/z* calcd for $C_{19}H_{19}NO_5^+$ $[M]^+$ 341.1258, found 341.1256.

(*E*)-Ethyl 3-{5-acetyl-2-(pyridin-2-yloxy)phenyl}acrylate (131pb):



The general procedure **D** was followed using 1-{4-(pyridin-2-yloxy)phenyl}-ethanone (**130p**) (213.2 mg, 1.00 mmol), ethyl acrylate (**46b**) (53.0 mg, 0.53 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.7 mg, 4.8 mol %), and $AgSbF_6$ (35.9 mg, 20 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 6/1) yielded **131pb** (115.0 mg, 70%) as a colorless solid.

M. p. = 99−101 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 2.2 Hz, 1H), 8.19–8.17 (m, 1H), 7.97 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.92 (d, *J* = 16.2 Hz, 1H), 7.78 (ddd,*J* = 8.3, 7.2, 2.0 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 1H), 7.11–7.04 (m, 2H), 6.59 (d, *J* = 16.2 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.62 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

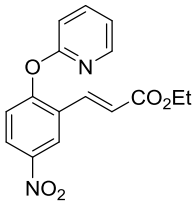
^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.4 (C_q), 166.6 (C_q), 162.6 (C_q), 156.63 (C_q), 147.8 (CH), 140.0 (CH), 138.0 (CH), 133.6 (C_q), 130.9 (CH), 128.6 (CH), 127.2 (C_q), 121.8 (CH), 121.0 (CH), 119.6 (CH), 112.4 (CH), 60.6 (CH_2), 26.5 (CH_3), 14.2 (CH_3).

IR (neat): 2985, 1713, 1677, 1594, 1241, 1173, 975, 855 cm^{-1}.

MS (EI) *m/z* (relative intensity): 311 (25) $[M]^+$, 282 (30), 266 (30), 238 (100), 222 (15), 196 (25), 167 (17), 78 (35).

HR-MS (EI) *m/z* calcd for $C_{18}H_{17}NO_4^+$ $[M]^+$ 311.1152, found 311.1159.

(*E*)-Ethyl 3-{5-nitro-2-(pyridin-2-yloxy)phenyl}acrylate (131qb):



The general procedure **D** was followed using 2-(4-nitrophenoxy)pyridine (**130q**) (215.3 mg, 1.00 mmol), ethyl acrylate (**46b**) (49.0 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.6 mg, 5.2 mol %), and $AgSbF_6$ (35.1 mg, 21 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131qb** (100.0 mg, 65%) as an off-white solid.

M. p. = 72−74 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 2.8 Hz, 1H), 8.22 (dd, *J* = 9.0, 2.8 Hz, 1H), 8.18 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.89 (d, *J* = 16.2 Hz, 1H), 7.82 (ddd, *J* = 8.2, 7.2, 2.0 Hz, 1H), 7.22 (d, *J* = 9.0 Hz, 1H), 7.15–7.10 (m, 2H), 6.59 (d, *J* = 16.2 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

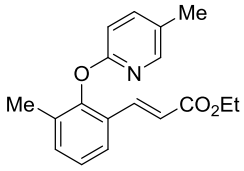
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2 (C_q), 162.1 (C_q), 157.6 (C_q), 147.8 (CH), 144.2 (C_q), 140.3 (CH), 136.6(CH), 127.9 (C_q), 125.7 (CH), 123.5 (CH), 122.4 (CH), 122.1 (CH), 120.2 (CH), 112.7 (CH), 60.8 (CH_2), 14.2 (CH_3).

IR (neat): 2987, 1704, 1426, 1341, 1230, 1193, 770, 740 cm^{-1}.

MS (EI) *m/z* (relative intensity): 314 (20) $[M]^+$, 285 (20), 269 (25), 241(100), 213 (22), 195 (55), 167 (20), 78 (45).

HR-MS (EI) *m/z* calcd for $C_{16}H_{14}N_2O_5^+$ $[M]^+$ 314.0897, found 314.0911.

(*E*)-Ethyl 3-{3-methyl-2-[(5-methylpyridin-2-yl)oxy]phenyl}acrylate (131sb):



The general procedure **D** was followed using 5-methyl-2-(*o*-tolyloxy)-pyridine (**130s**) (197.7 mg, 0.99 mmol), ethyl acrylate (**46b**) (49.7 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.5 mol %), $AgSbF_6$ (18.3 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **130sb** (114.0 mg, 77%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 1.3 Hz, 1H), 7.79 (d, *J* = 16.1 Hz, 1H), 7.54–7.47 (m, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.17 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.42 (d, *J* = 16.1 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.24 (s, 3H), 2.10 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

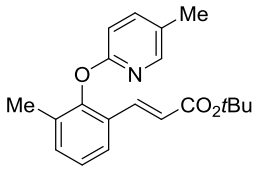
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 161.5 (C_q), 150.9 (C_q), 147.3 (CH), 140.4 (CH), 139.3 (CH), 133.0 (CH), 132.4 (C_q), 128.3 (C_q), 127.2 (C_q), 125.5 (CH), 125.3 (CH), 119.6 (CH), 109.5 (CH), 60.3 (CH_3), 17.4 (CH_3), 16.6 (CH_3), 14.2 (CH_3).

IR (neat): 2980, 2926, 1708, 1479, 1459, 1265, 1237, 1161 cm^{-1}.

MS (EI) *m/z* (relative intensity): 297 (40) [M], 268 (15), 252 (35), 224 (100), 208 (18), 194 (17), 181 (27), 161 (17).

HR-MS (EI) *m/z* calcd for $C_{18}H_{19}NO_3^+$ $[M]^+$ 297.1359, found 297.1358.

(*E*)-*tert*-Butyl 3-{3-methyl-2-[(5-methylpyridin-2-yl)oxy]phenyl}acrylate (131sp):



The general procedure **D** was followed using 5-methyl-2-(*o*-tolyloxy)-pyridine (**130s**) (198.7 mg, 1.00 mmol), *tert*-butyl acrylate (**46p**) (62.5 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), $AgSbF_6$ (17.8 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131sp** (120.0 mg, 75%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91–7.89 (m, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.53–7.46 (m, 2H), 7.29–7.25 (m, 1H), 7.15 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.34 (d, *J* = 16.1 Hz, 1H), 2.24 (s, 3H), 2.10 (s, 3H), 1.46 (s, 9H).

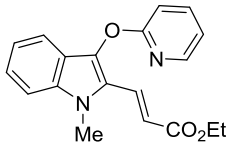
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1 (C_q), 161.5 (C_q), 150.8 (C_q), 147.2 (CH), 140.4 (CH), 138.1 (CH), 132.7 (CH), 132.3 (C_q), 128.4 (C_q), 127.1 (C_q), 125.4 (CH), 125.0 (CH), 121.3 (CH), 109.5 (CH), 80.2 (C_q), 28.1 (CH_3), 17.3 (CH_3), 16.6 (CH_3).

IR (neat): 3007, 2976, 1704, 1479, 1238, 1145, 775, 730 cm^{-1}.

MS (EI) *m/z* (relative intensity): 325 (40) $[M]^+$, 268 (15), 252 (45), 224 (100), 208 (18), 194 (13), 181 (20), 161 (10).

HR-MS (EI) *m/z* calcd for $C_{20}H_{23}NO_3^+$ $[M]^+$ 325.1672, found 325.1681.

(*E*)-Ethyl 3-{1-Methyl-3-(pyridin-2-yloxy)-1*H*-indol-2-yl}acrylate (131tb):



The general procedure **D** was followed using ethyl 1-methyl-3-(pyridin-2-yloxy)-1*H*-indole (**130t**) (228.0 mg, 1.02 mmol), ethyl acrylate (**46b**) (51.7 mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 4.8 mol %), and $AgSbF_6$ (36.1 mg, 21 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 1/1) yielded **131tb** (137.0 mg, 83%) as an off-white solid.

M. p. = 218−220 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.66 (d, *J* = 16.2 Hz, 1H), 7.47 (ddd, *J* = 9.4, 6.5, 2.1 Hz, 1H), 7.40–7.26 (m, 3H), 7.26–7.22 (m, 1H), 7.13 (ddd, *J* = 8.0, 6.7, 1.3 Hz, 1H), 6.76–6.73 (m, 1H), 6.28 (dt, *J* = 6.7, 1.3 Hz, 1H), 6.02 (d, *J* = 16.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

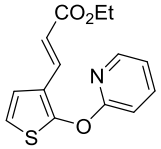
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 162.6 (C_q), 140.3 (CH), 139.3 (CH), 136.9 (C_q), 129.7 (CH), 129.0 (C_q), 124.7 (CH), 123.7 (C_q), 122.1 (CH), 121.4 (CH), 120.8 (CH), 118.8 (C_q), 118.3 (CH), 110.0 (CH), 106.6 (CH), 60.7 (CH_2), 30.7 (CH_3), 14.2 (CH_3).

IR (neat): 2981, 2941, 1724, 1665, 1594, 1529, 1177, 750 cm^{-1}.

MS (EI) *m/z* (relative intensity): 322 (100) $[M]^+$, 293(15), 249 (90), 228 (80), 221 (25), 205 (30), 200 (60), 170 (15).

HR-MS (EI) *m/z* calcd for $C_{19}H_{18}N_2O_3^+$ $[M]^+$ 322.1312, found 322.1311.

(*E*)-Ethyl 3-{2-(pyridin-2-yloxy)thiophen-3-yl}acrylate (131ub):



The general procedure **D** was followed using ethyl 2-(thiophen-2-yloxy)pyridine (**130u**) (177.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (48.0 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.5 mg, 5.3 mol %), $AgSbF_6$ (36.1 mg, 22 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 1/1) yielded **131ub** (92.0 mg, 70%) as an off-white solid.

M. p. = 110−112°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42 (ddd, *J* = 9.0, 6.5, 2.1 Hz, 1H), 7.33 (d, *J* = 5.8 Hz, 1H), 7.27 (d, *J* = 16.1 Hz, 1H), 7.26−7.22 (m, 2H), 6.66 (d, *J* = 9.4 Hz, 1H), 6.27 (d, *J* = 16.1 Hz, 1H), 6.26.(dt, *J* = 6.8, 1.3 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

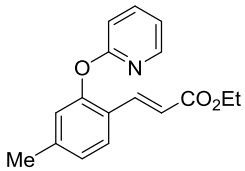
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 162.3 (C_q), 141.2 (C_q), 140.5 (CH), 138.8 (CH), 133.6 (CH), 132.7 (C_q), 125.0 (CH), 124.0 (CH), 122.1 (CH), 120.5 (CH), 106.4 (CH), 60.6 (CH_2), 14.2 (CH_3).

IR (neat): 3069, 2977, 1701, 1665, 1592, 1306, 1280, 1172 cm^{-1}.

MS (EI) *m/z* (relative intensity): 275 (55) $[M]^+$, 246 (50), 230 (10), 202 (100), 186 (13), 181 (45), 173 (50), 153 (25).

HR-MS (EI) *m/z* calcd for $C_{14}H_{13}NO_3S^+$ $[M]^+$ 275.0611, found 275.0616.

(*E*)-Ethyl 3-{4-Methyl-2-(pyridin-2-yloxy)phenyl}acrylate (131wb):



The general procedure **D** was followed using 2-(*m*-tolyloxy)pyridine (**130w**) (185.4 mg, 1.00 mmol), ethyl acrylate (**46b**) (50.7 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), and $AgSbF_6$ (18.3 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→12/1) yielded **131wb** (121.0 mg, 83%) as a colorless solid.

M. p. = 45−47°C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.85 (d, *J* = 16.1 Hz, 1H), 7.70 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.05−6.89 (m, 4H), 6.43 (d, *J* = 16.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

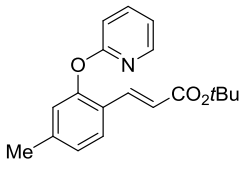
^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0 (C_q), 163.4 (C_q), 152.8 (C_q), 147.8 (CH), 142.0 (C_q), 139.5 (CH), 138.8 (CH), 127.8 (CH), 126.2 (CH), 124.5 (C_q), 122.8 (CH), 118.6 (CH), 118.6 (CH), 111.6 (CH), 60.3 (CH_2), 21.4 (CH_3), 14.2 (CH_3).

IR (neat): 2980, 1709, 1316, 1234, 1172, 1103, 1029, 781 cm^{-1}.

MS (EI) *m/z* (relative intensity): 283 (40) $[M]^+$, 254 (45), 238 (35), 210 (100), 194 (20), 182 (25), 167 (35), 78 (35).

HR-MS (EI) *m/z* calcd for $C_{17}H_{17}NO_3^+$ $[M]^+$ 283.1203, found 283.1214.

(*E*)-*tert*-Butyl 3-{4-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (131wp):



The general procedure **D** was followed using 2-(*m*-tolyloxy)pyridine (**130w**) (186.0 mg, 1.0 mmol), *tert*-butyl acrylate (**46p**) (67.0 mg, 0.52 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.5 mol %), $AgSbF_6$ (17.9 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131wp** (113.0 mg, 70%) as a colorless solid.

M. p. = 137−139 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.73 (d, *J* = 16.1 Hz, 1H), 7.67 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.02−6.92 (m, 3H), 6.88 (d, *J* = 1.7 Hz, 1H), 6.33 (d, *J* = 16.1 Hz, 1H), 2.33 (s, 3H), 1.46 (s, 9H).

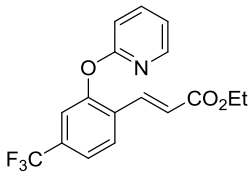
^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (C_q), 163.5 (C_q), 152.6 (C_q), 147.8 (CH), 141.8 (C_q), 139.5 (CH), 137.7 (CH), 127.6 (CH), 126.2 (CH), 124.7 (C_q), 122.8 (CH), 120.4 (CH), 118.6 (CH), 111.6 (CH), 80.2 (C_q), 28.1 (CH_2), 21.5 (CH_3).

IR (neat): 2977, 1702, 1266, 1235, 1140, 1098, 984, 782 cm^{-1}.

MS (EI) *m/z* (relative intensity): 311 (7) $[M]^+$, 254 (7), 238 (16), 210 (100), 194 (12), 167 (15), 115 (5), 78 (15).

HR-MS (EI) *m/z* calcd for $C_{19}H_{21}NO_3^+$ $[M]^+$ 311.1516, found 311.1522.

(*E*)-Ethyl 3-{2-(pyridin-2-yloxy)-4-(trifluoromethyl)phenyl}acrylate (131xb):



The general procedure **D** was followed using 2-{3-(trifluoromethyl)phenoxy}pyridine (**130x**) (241.0 mg, 1.00 mmol), ethyl acrylate(**46b**) (50.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.6 mg, 2.5 mol %), $AgSbF_6$ (17.9 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 30/1→20/1) yielded **131xb** (146.0 mg, 87%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (dd, *J* = 5.2, 1.9 Hz, 1H), 7.87 (d, *J* = 16.2 Hz, 1H), 7.78–7.72 (m, 1H), 7.76 (d, *J* = 8.3Hz, 1H), 7.46 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.37 (d, *J* = 1.8 Hz, 1H), 7.07–7.03 (m, 2H), 6.54 (d, *J* = 16.2 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (C_q), 162.7 (C_q), 152.7 (C_q), 147.7 (CH), 139.9 (CH), 137.4 (CH), 132.6 ($^2J_{C\text{-}F}$ = 33 Hz, C_q), 130.8(C_q), 128.4 (CH), 123.3 ($^1J_{C\text{-}F}$ = 273 Hz, C_q), 121.9 (CH), 121.6($^3J_{C\text{-}F}$ = 4 Hz, CH), 119.60 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 119.4 (CH), 111.9 (CH), 60.7 (CH_2), 14.2 (CH_3).

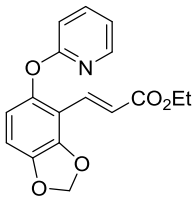
^{19}F NMR (283 MHz, $CDCl_3$): δ = –62.9 (s).

IR (neat): 2983, 1713, 1415, 1325, 1236, 1165, 1109, 777 cm^{-1}.

MS (EI) *m/z* (relative intensity): 337 (15) $[M]^+$, 308 (15), 292 (20), 264 (100), 248 (7), 236 (16), 215 (12), 167(15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{14}F_3NO_3^+$ $[M]^+$ 337.0920, found 337.0927.

(*E*)-Ethyl 3-{5-(pyridin-2-yloxy)benzo[*d*][1,3]dioxol-4-yl}acrylate (131yb):



The general procedure **D** was followed using 2-(benzo[*d*][1,3]dioxol-5-yloxy)-pyridine (**130y**) (217.0 mg, 1.00 mmol), ethyl acrylate (**46b**) (48.2 mg, 0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.7 mol %), and $AgSbF_6$ (19.3 mg, 12 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1→8/1) yielded **131yb** (114.0 mg, 76%) as a colorless solid.

M. p. = 90−92 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (ddd, *J* = 5.0, 2.0, 1.0 Hz, 1H), 7.69 (ddd, *J* = 8.2, 7.2, 2.0 Hz, 1H) 7.67 (d, *J* = 16.2 Hz, 1H), 7.04–6.91 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 16.2 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 6.10 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H).

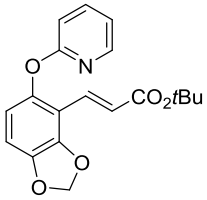
^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.2 (C_q), 164.0 (C_q), 147.7 (CH), 147.4 (C_q), 146.9 (C_q), 144.8 (C_q), 139.6 (CH), 133.9 (CH), 122.7 (CH), 118.5 (CH), 114.7 (CH), 112.7 (C_q), 111.2 (CH), 109.3 (CH), 102.2 (CH_2), 60.4 (CH_2), 14.2 (CH_3).

IR (neat): 2976, 2900, 1695, 1455, 1425, 1304, 1234, 1185 cm^{-1}.

MS (EI) *m/z* (relative intensity): 313 (22) $[M]^+$, 284 (70), 268 (25), 240 (100), 219 (45), 190 (40), 182 (22), 154 (33).

HR-MS (EI) *m/z* calcd for $C_{17}H_{15}NO_5^+$ $[M]^+$ 313.0945, found 313.0955.

(*E*)-*tert*-Butyl 3-{5-(pyridin-2-yloxy)benzo[*d*][1,3]dioxol-4-yl}acrylate (131yp):



The general procedure **D** was followed using 2-(benzo[*d*][1,3]dioxol-5-yloxy)pyridine (**130y**) (220.0 mg, 1.02 mmol), *tert*-butyl acrylate (**46p**) (63.4 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 2.6 mol %), and $AgSbF_6$ (18.2 mg, 11 mol %). Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **131yp** (135.0 mg, 79%) as a colorless solid.

M. p. = 111−113°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (ddd, *J* = 4.9, 2.0, 1.0 Hz, 1H), 7.68 (m, 1H), 7.58 (d, *J* = 16.2 Hz, 1H), 6.99–6.94 (m, 2H), 6.81 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 16.2 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.10 (s, 2H), 1.46 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 164.0 (C_q), 147.6(CH), 147.2 (C_q), 146.8 (C_q), 144.8 (C_q), 139.5 (CH), 132.9 (CH), 124.5 (CH), 118.4 (CH), 114.7 (CH), 112.8 (C_q), 111.2 (CH), 109.1 (CH), 102.1 (CH_2), 80.3 (C_q), 28.1 (CH_3).

IR (neat): 2984, 2916, 1698, 1451, 1420, 1232, 1065, 857 cm^{-1}.

MS (EI) *m/z* (relative intensity): 341 (25) $[M]^+$, 284 (40), 268 (50), 240 (100), 224 (20), 212 (27), 190 (65), 154 (25).

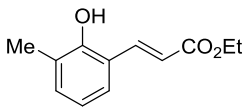
HR-MS (EI) *m/z* calcd for $C_{19}H_{19}NO_5^+$ $[M]^+$ 341.1258, found 341.1263.

Removal of the directing group

To a solution of (*E*)-ethyl 3-{3-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (**131ab**) (142.0 mg, 0.50 mmol) in PhMe (20 mL) under N_2 was added MeOTf (144.4 mg, 96μL, 0.88 mmol). The reaction mixture was stirred under N_2 at 100 °C for 2 h and then allowed to cool down to ambient temperature. Evaporation of the solvent *in vacuo* yielded a solid which was used without further

purification. Under N_2, the solution of this solid in anhydrous EtOH (5.0 mL) was carefully added to a solution of sodium ethanolate prepared from Na (300 mg, 13.0 mmol) in anhydrous ethanol (15 mL). The reaction mixture was stirred at 90 °C for 45 min, then allowed to cool down to ambient temperature, and the solvent was evaporated *in vacuo*. H_2O (75 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvent *in vacuo*, the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1) to yield **78a** (78.0 mg, 75%) as a colorless solid.

(*E*)-Ethyl 3-(2-hydroxy-3-methylphenyl)acrylate (71a):



M. p. = 119−121°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 16.1 Hz, 1H), 7.36 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.16−7.13 (m, 1H), 6.84 (t, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 16.1 Hz, 1H), 6.22 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1 (C_q), 153.6 (C_q), 140.6 (CH), 132.7 (CH), 126.2 (CH), 124.1 (C_q), 121.6 (C_q), 120.4 (CH), 118.1 (CH), 60.5 (CH_2), 15.9 (CH_3), 14.3 (CH_3).

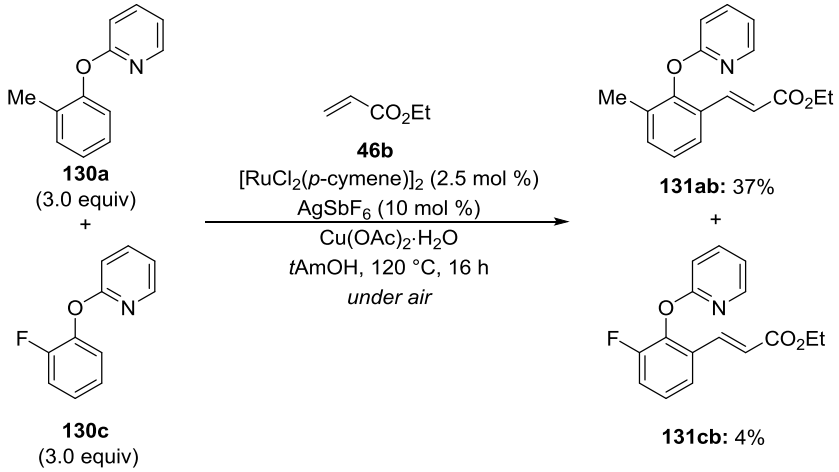
IR (neat): 3318, 2982, 1681, 1316, 1220, 1183, 1029, 778 cm^{-1}.

MS (EI) *m*/z (relative intensity): 206 (15) $[M]^+$, 160 (85), 132 (100), 115 (7), 105 (35), 91 (10), 77 (25), 43 (30).

HR-MS (EI) *m/z* calcd for $C_{12}H_{14}O_3^+$ $[M]^+$ 206.0937, found 206.0948.

The spectral data were in accordance with those reported in the literature.[140]

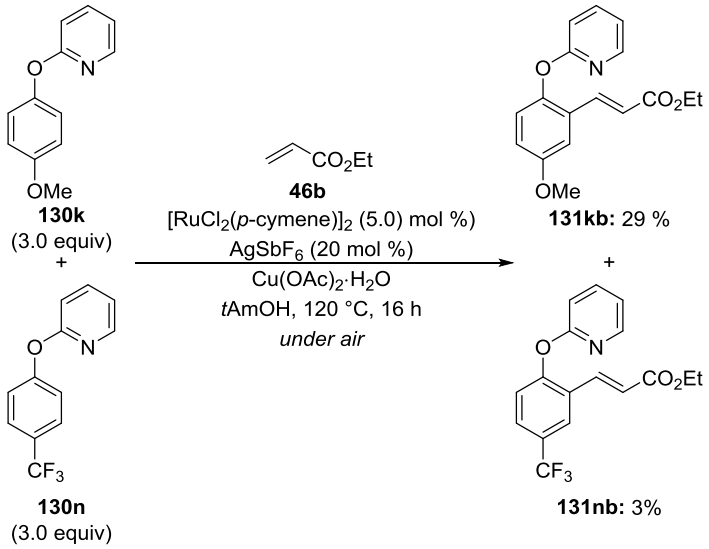
Intermolecular Competition Experiment between Substrates 130a and 130c



[140] R. A. Bunce, J. D. Moore, *Org. Prep. Proceed. Int.* **1997**, *29*, 293–299.

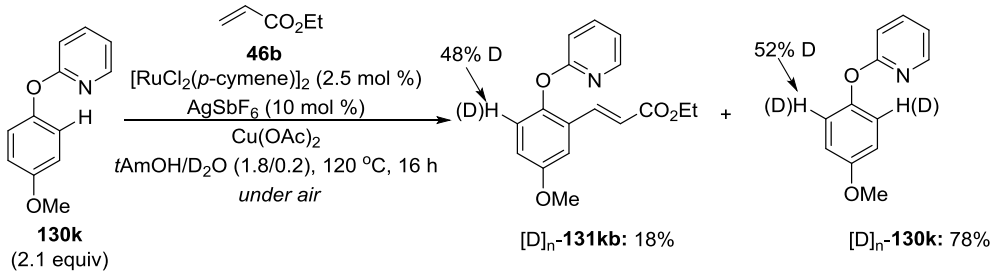
A mixture of 2-(*o*-tolyloxy)pyridine (**130a**) (274.0 mg, 1.48 mmol), 2-(2-fluorophenoxy)pyridine(**130c**) (279.0 mg, 1.47 mmol), ethyl acrylate (**46b**) (49.2 mg, 0.49 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.9 mg, 2.6 mol %), $AgSbF_6$ (18.5 mg, 11 mol %) and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.00 mmol) in *t*AmOH (2.0 mL) was stirred at ambient temperature for 5 min under N_2 and then stirred at 120 °C for 16 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was diluted with sat. aq. NH_4Cl/NH_3 (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvent in *vacuo*, the crude products were purified by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→10/1) to yield **131ab** (51.0 mg, 37%) and **131cb** (6.0 mg, 4%). The spectral data of compounds **131ab** and **131cb**were identical to those reported above.

Intermolecular Competition Experiment between Substrates 130k and 130n



The general procedure **D** was followed using 2-(4-methoxyphenoxy)pyridine (**130k**) (299.0 mg, 1.49 mmol), 2-{4-(trifluoromethyl)phenoxy}pyridine (**130n**) (358.0 mg, 1.50 mmol), ethyl acrylate (**46b**) (50.5 mg, 0.51 mmol), $[RuCl_2(p\text{-cymene})]_2$(15.5 mg, 5.0 mol %), $AgSbF_6$ (35.1 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 20/1→15/1) yielded **131kb** (44.0 mg, 29%) and **131nb** (6.0 mg, 3%).Their spectral data were identical to those reported above.

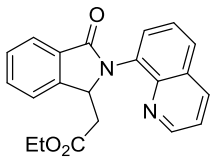
Ruthenium-Catalyzed H/D Exchange in Substrate130k with D_2O as the Cosolvent



The general procedure **D** was followed using 2-(4-methoxyphenoxy)pyridine (**130k**) (213.0 mg, 1.06 mmol), ethyl acrylate (**46b**) (49.6 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 5.0 mol %), $AgSbF_6$ (18.5 mg, 10 mol %) and $Cu(OAc)_2$ (186.0 mg, 1.02 mmol) in a solvent mixture of *t*AmOH and D_2O (1.8/0.2 mL). Purification by column chromatography (*n*-hexane /EtOAc: 15/1→8/1) yielded $[D]_n$-**131kb** (27.0 mg, 18%) as a colorless oil and reisolated partially deuterated starting material $[D]_n$-**130k** (167.0 mg, 78%). The deuterium incorporation in $[D]_n$-**131kb** and $[D]_n$-**130k** were estimated by ^{1}H NMR spectroscopy.

8.4.4 Cobalt(II)-Catalyzed Oxidative Annulation through C–H Bond Alkenylations: Regio- and Site- Selective Access to Isoindolin-1-one

Ethyl 2-{3-Oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (**132bb**):



The general procedure **E** was followed using *N*-(quinolin-8-yl)benzamide (**110b**) (62.0 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132bb** (74.0 mg, 85 %) as a colorless solid.

M. p. = 145−147 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (ddd, *J* = 8.3, 1.8, 0.4 Hz, 1H), 7.98–7.96 (m, 1H), 7.86 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.83 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.63–7.58 (m, 2H), 7.56–7.49 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.30 (t, *J* = 6.3 Hz, 1H), 3.79 (q, *J* = 7.2 Hz, 2H), 2.72 (dd, *J* = 15.9, 5.6 Hz, 1H), 2.60 (dd, *J* = 15.9, 6.9 Hz, 1H), 0.96 (t, *J* = 7.2 Hz, 3H).

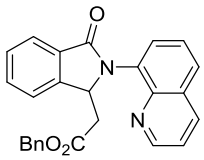
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0 (C_q), 168.2 (C_q), 150.2 (CH), 145.4 (C_q), 144.7 (C_q), 136.3 (CH), 133.4(C_q), 132.1 (C_q), 131.9 (CH), 130.4 (CH), 129.3 (C_q), 128.4 (CH), 128.0 (CH), 126.3 (CH), 124.3 (CH), 122.5 (CH), 121.5 (CH), 60.5 (CH_2), 59.5 (CH), 38.0 (CH_2), 13.8 (CH_3).

IR (neat): 3062, 2968, 2928, 1695, 1248, 1154, 764, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity): 346 (25) $[M]^+$, 301 (10), 273 (100), 259 (10), 231 (10), 204 (10), 129 (10), 43 (10).

HR-MS (EI) *m/z* calcd for $C_{21}H_{18}N_2O_3^+$ $[M]^+$ 346.1312, found 346.1314.

Benzyl 2-{3-Oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (**132bd**):



The general procedure **E** was followed using *N*-(quinolin-8-yl)benzamide (**110b**) (62.0 mg, 0.25 mmol) and benzyl acrylate (**46d**) (82.0 mg, 0.51 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132bd** (79.0 mg, 77%) as a colorless solid.

M. p. = 67−69 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.97–7.96 (m, 1H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.55 (dt, *J* = 1.3, 7.4 Hz, 1H), 7.52–7.46 (m, 2H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29–7.27 (m, 3H), 7.12–7.10 (m, 2H), 6.32 (dd, *J* = 7.2, 5.3 Hz, 1H), 4.97–4.60 (m, 2H), 2.80 (dd, *J* = 16.0, 5.3 Hz, 1H), 2.65 (dd, *J* = 16.0, 7.2 Hz, 1H).

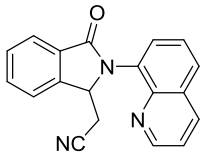
^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.9 (C_q), 168.2 (C_q), 150.1 (CH), 145.3 (C_q), 144.5 (C_q), 136.4 (CH), 135.1 (C_q), 133.3 (C_q), 132.0 (C_q), 131.9 (CH), 130.4 (CH), 129.3 (C_q), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.2 (CH), 128.0 (CH), 126.3 (CH), 124.3 (CH), 122.5 (CH), 121.5 (CH), 66.4 (CH_2), 59.5 (CH), 37.9 (CH_2).

IR (neat): 3038, 2950, 1731, 1692, 1395, 1145, 730, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 408 (20) $[M]^+$, 273 (100), 230 (10), 181 (40), 169 (10), 131 (15), 91 (20).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{20}N_2O_3^+$ $[M]^+$ 408.1468, found 408.1456.

2-{3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetonitrile (**132bh**):



The general procedure **E** was followed using *N*-(quinolin-8-yl)benzamide (**110b**) (62.5 mg, 0.25 mmol) and acrylonitrile (**46h**) (50.0 mg, 0.94 mmol).Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132bh** (56.0 mg, 75%) as a colorless solid.

M. p. = 196−198 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.23 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.98 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.87 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.70–7.65 (m, 3H), 7.61–7.58 (m, 1H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.35 (dd, *J* = 6.9, 4.0 Hz, 1H), 2.82 (dd, *J* = 16.9, 4.0 Hz, 1H), 2.60 (dd, *J* = 16.9, 6.9 Hz, 1H).

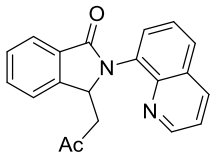
^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8 (C_q), 150.2 (CH), 144.2 (C_q), 143.2 (C_q), 136.7 (CH), 132.6 (CH), 132.2 (C_q), 132.1 (C_q), 130.4 (CH), 129.4 (C_q), 129.3 (CH), 128.3 (CH), 126.7 (CH), 124.7 (CH), 122.3 (CH), 121.7 (CH), 115.7 (C_q), 58.0 (CH), 22.1 (CH_2).

IR (neat): 1692, 1498, 13971204, 790, 727, 693, 619 cm^{-1}.

MS (EI) *m/z* (relative intensity): 299 (100) $[M]^+$, 270 (40), 259 (40), 231 (40), 130 (60), 101 (25), 43 (25).

HR-MS (ESI) *m/z* calcd for $C_{19}H_{13}N_3O^+$ $[M]^+$299.1053, found 299.1060.

3-(2-oxopropyl)-2-(quinolin-8-yl)isoindolin-1-one (**132bf**):



The general procedure **E** was followed using *N*-(quinolin-8-yl)benzamide (**110b**) (62.0 mg, 0.25 mmol) and methyl vinyl ketone (**46f**) (36.0 mg, 0.51 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132bf** (48.0 mg, 61%) as a colorless solid.

M. p. = 136−138 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.97–7.94 (m, 1H), 7.83 (td, *J* = 7.6, 1.5 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.60–7.47 (m, 3H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.33 (dd, *J* = 8.2, 4.7 Hz, 1H), 2.85 (dd, *J* = 17.4, 4.7 Hz, 1H), 2.68 (dd, *J* = 17.4, 8.2 Hz, 1H), 1.87 (s, 3H).

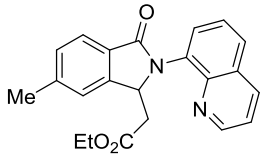
^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.6 (C_q), 168.2 (C_q), 150.4 (CH), 146.2 (C_q), 144.6 (C_q), 136.3 (CH), 133.6 (C_q), 132.0 (CH), 131.9 (C_q), 130.1 (CH), 129.4 (C_q), 128.3 (CH), 128.2 (CH), 126.3 (CH), 124.3 (CH), 122.8 (CH), 121.6 (CH), 59.0 (CH), 46.7 (CH_2), 30.5 (CH_3).

IR (neat): 3042, 2922, 1688, 1499, 1470, 1394, 1362, 1150 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 (5) $[M]^+$, 274 (30), 273 (100)$[M–Ac]^+$, 229 (10), 129 (10), 101 (10), 43 (20).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{16}N_2O_2^+$ $[M]^+$ 316.1206, found 316.1215.

Ethyl 2-{6-methyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132ab):



The general procedure **E** was followed using 4-methyl-*N*-(quinolin-8-yl)benzamide (**110a**) (65.5 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.5 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132ab** (66.0 mg, 73%) as a colorless solid.

M. p. = 132−134 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.86−7.81 (m, 3H), 7.61 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.34–7.30 (m, 2H), 6.24 (t, *J* = 6.3 Hz, 1H), 3.79 (qd, *J* = 7.1, 2.3 Hz, 2H). 2.70 (dd, *J* = 15.9, 5.7 Hz, 1H), 2.58 (dd, *J* = 15.9, 6.9 Hz, 1H), 2.48 (s, 3H), 0.97 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0 (C_q), 168.3 (C_q), 150.1 (CH), 145.8 (C_q), 144.6 (C_q), 142.5 (C_q), 136.2 (CH), 133.5 (C_q), 130.4 (CH), 129.5 (C_q), 129.3 (CH), 129.3 (C_q), 127.9 (CH),

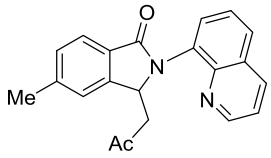
126.3 (CH), 124.0 (CH), 122.9 (CH), 121.4 (CH), 60.5 (CH_2), 59.4 (CH), 38.2 (CH_2), 22.1 (CH_3), 13.9 (CH_3).

IR (neat): 2975, 2944, 2902, 1696, 1587, 1475, 1404, 1243, 1209 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 (25) $[M]^+$, 287 (100), 273 (10), 207 (10), 143 (10); 115 (5), 44 (5).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{21}N_2O_3^+$ $[M+H]^+$ 361.1547, found 361.1548.

5-Methyl-3-(2-oxopropyl)-2-(quinolin-8-yl)isoindolin-1-one (132af):



The general procedure **E** was followed using 4-methyl-*N*-(quinolin-8-yl)benzamide (**110a**) (65.2 mg, 0.25 mmol) and methyl vinyl ketone (**46f**) (35.0 mg, 0.5 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132af** (52.0 mg, 63%) as a colorless solid.

M. p. = 166−167 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.84–7.80 (m, 3H), 7.60 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.32–7.29 (m, 2H), 6.29 (dd, *J* = 8.3, 4.6 Hz, 1H), 2.83 (dd, *J* = 17.5, 4.6 Hz, 1H), 2.67 (dd, *J* = 17.5, 8.3 Hz, 1H), 2.46 (s, 3H), 1.88 (s, 3H).

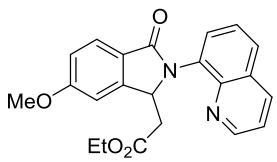
^{13}CNMR (125 MHz, $CDCl_3$): δ = 205.8 (C_q), 168.2 (C_q), 150.3 (CH), 146.6 (C_q), 144.7 (C_q), 142.7 (C_q), 136.3 (CH), 133.8 (C_q), 130.1 (CH), 129.4 (C_q, 2C), 129.3 (CH), 128.0 (CH), 126.3 (CH), 124.1 (CH), 123.3 (CH), 121.5 (CH), 58.8 (CH), 46.8 (CH_2), 30.5 (CH_3), 22.0 (CH_3).

IR (neat): 3041, 2957, 2905, 1688, 1616, 1393, 1144, 795, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 330 (5) $[M]^+$, 288 (30), 287 (100), 272 (5), 143 (10), 115 (10), 43 (5).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{18}N_2O_2^+$ $[M]^+$ 330.1363; found 330.1369.

Ethyl 2-{6-Methoxy-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132cb):



The general procedure **E** was followed using 4-methoxy-*N*-(quinolin-8-yl)benzamide (**110c**) (69.5 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.5 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132cb** (53.0 mg, 56%) as a colorless solid.

M. p. = 131−133 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.8 Hz, 1H),

7.87 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.84 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.81 (dd, *J* = 8.3, 1.4 Hz, 1H). 7.60 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.09–6.96 (m, 2H), 6.37–6.17 (m, 1H), 3.87 (s, 3H), 3.80 (q, *J* = 7.1 Hz, 2H), 2.70 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.57 (dd, *J* = 16.0, 7.1 Hz, 1H), 0.97 (t, *J* = 7.1 Hz, 3H).

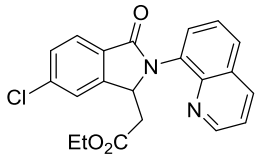
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0 (C_q), 167.9 (C_q), 163.0 (C_q), 150.0 (CH), 147.7 (C_q), 144.6 (C_q), 136.1 (CH), 133.5 (C_q), 130.3 (CH), 129.2 (C_q), 127.8 (CH), 126.2 (CH), 125.5 (CH), 124.6 (C_q), 121.4 (CH), 114.9 (CH), 107.4 (CH), 60.5 (CH_2), 59.2 (CH), 55.6 (CH_3), 38.2 (CH_2), 13.9 (CH_3).

IR (neat): 2968, 2937, 1683, 1605, 1250, 788, 693 cm^{-1}.

MS (EI) *m/z* (relative intensity): 376 (30) $[M]^+$, 331 (5), 304 (30), 303 (100), 289 (10), 231 (5), 129 (5).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{20}N_2O_4^+$ $[M]^+$ 376.1418, found 376.1429.

Ethyl 2-{6-chloro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132db):



The general procedure **E** was followed using 4-chloro-N-(quinolin-8-yl)benzamide (**110d**) (70.0 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132db** (73.0 mg, 77 %) as a colorless solid.

M. p. = 121−123 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.89 (dd, *J* = 8.1, 0.5 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.61 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.58–7.57 (m, 1H), 7.49 (ddd, *J* = 8.1, 1.8, 0.6 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.29–6.27 (m, 1H), 3.85 (q, *J* = 7.2Hz, 2H), 2.73 (dd, *J* = 16.2, 5.2 Hz, 1H), 2.57 (dd, *J* = 16.2, 7.3 Hz, 1H), 1.00 (t, *J* = 7.2 Hz, 3H).

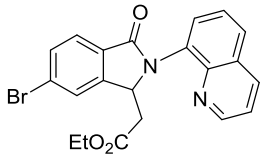
^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.6 (C_q), 167.1 (C_q), 150.2 (CH), 147.0 (C_q), 144.4 (C_q), 138.2 (C_q), 136.2 (CH), 133.0 (C_q), 130.6 (C_q), 130.2 (CH), 129.3 (C_q), 128.9 (CH), 128.2 (CH), 126.2 (CH), 125.4 (CH), 123.1 (CH), 121.5 (CH), 60.7 (CH_2), 59.1 (CH), 37.7 (CH_2), 13.9 (CH_3).

IR (neat):2975, 2952, 1730, 1692, 1398, 1228, 1148, 788 cm^{-1}.

MS (EI) *m/z* (relative intensity): 380 (20) $[M]^+$, 335 (5), 307 (100), 293 (10), 229 (10), 163 (10), 43 (15).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}ClN_2O_3^+$ $[M]^+$ 380.0922; found 380.0931.

Ethyl 2-{6-bromo-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132eb):



The general procedure **E** was followed using 4-bromo-*N*-(quinolin-

8-yl)benzamide (**110e**) (81.6 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132eb** (89.0 mg, 84%) as a colorless solid.

M. p. = 155−156 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.86–7.82 (m, 3H), 7.75–7.74 (m, 1H), 7.66 (ddd, *J* = 8.1, 1.7, 0.6 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.28 (dd, *J* = 7.3, 5.2 Hz, 1H), 3.85 (q, *J* = 7.1Hz, 2H), 2.73 (dd, *J* = 16.2, 5.2 Hz, 1H), 2.58 (dd, *J* = 16.2, 7.3 Hz, 1H), 1.00 (t, *J* = 7.1 Hz, 3H).

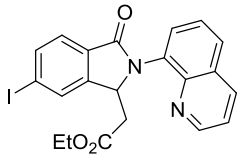
^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8 (C_q), 167.4 (C_q), 150.3 (CH), 147.3 (C_q), 144.5 (C_q), 136.4 (CH), 133.0 (C_q), 131.9 (CH), 131.1 (C_q), 130.4 (CH), 129.4 (C_q), 128.3 (CH), 126.7 (C_q), 126.4 (CH), 126.2 (CH), 125.7 (CH), 121.6 (CH), 60.7 (CH_2), 59.1 (CH), 37.7 (CH_2), 13.9 (CH_3).

IR (neat): 2988, 2924, 1727, 1692, 1396, 1374, 1192, 830, 687 cm^{-1}.

MS (EI) *m/z* (relative intensity): 424 (15) $[M]^+$, 379 (5), 351 (100), 272 (10), 242 (10), 229 (10), 128 (10).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}{}^{79}BrN_2O_3{}^+$ $[M]^+$ 424.0417, found 424.0424.

Ethyl 2-{6-iodo-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132fb):



The general procedure **E** was followed using 4-iodo-*N*-(quinolin-8-yl)benzamide (**110f**) (94.0 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132fb** (94.0 mg, 80%) as a colorless solid.

M. p. = 176−178 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (ddd, *J* = 8.3, 1.8, 0.4 Hz, 1H), 7.96 (dt, *J* = 1.4, 0.7 Hz, 1H), 7.89–7.83 (m, 3H), 7.70 (ddd, *J* = 8.0, 0,6, 0.3 Hz, 1H), 7.65–7.59 (m, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.42–6.12 (m, 1H), 3.84 (q, *J* = 7.1 Hz, 2H), 2.72 (dd, *J* = 16.1, 5.3 Hz, 1H), 2.57 (dd, *J* = 16.1, 7.2 Hz, 1H), 1.00 (t, *J* = 7.1 Hz, 3H).

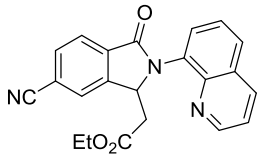
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0 (C_q), 167.6 (C_q), 150.3 (CH), 147.3 (C_q), 144.5 (C_q), 137.7 (CH), 136.3 (CH), 133.0 (C_q), 132.1 (CH), 131.7 (C_q), 130.4 (CH), 129.4 (C_q), 128.3 (CH) , 126.3 (CH), 125.7 (CH), 121.6 (CH), 98.9 (C_q), 60.7 (CH_2), 59.0 (CH), 37.7 (CH_2), 13.9 (CH_3).

IR (neat): 2981, 2914, 1729, 1683, 1400, 1191, 826, 687 cm^{-1}.

MS (EI) *m/z* (relative intensity): 472 (35) $[M]^+$, 427 (5), 399 (100), 385 (10), 272 (25), 243 (10), 229 (10), 102 (10).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}IN_2O_3{}^+$ $[M]^+$ 472.0278, found 472.0291

Ethyl 2-{6-cyano-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132gb):



The general procedure **E** was followed using 4-cyano-*N*-(quinolin-8-yl)benzamide (**110g**) (68.3 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132gb** (54.0 mg, 58%) as a colorless solid.

M. p. = 179−181 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.12–8.03 (m, 1H), 7.92 (s, 1H), 7.87 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.85 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.36 (dd, *J* = 7.7, 4.8 Hz, 1H), 3.89 (q, *J* = 7.1 Hz, 2H), 2.77 (dd, *J* = 16.5, 4.8 Hz, 1H), 2.57 (dd, *J* = 16.5, 7.7 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H).

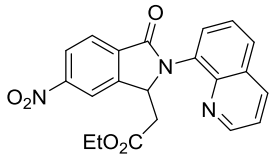
^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.6 (C_q), 166.4 (C_q), 150.5 (CH), 145.9 (C_q), 144.3 (C_q), 136.4 (CH), 136.1 (C_q), 132.5 (C_q), 132.3 (CH), 130.2 (CH), 129.4 (C_q), 128.6 (CH), 127.0 (CH), 126.3 (CH), 125.1 (CH), 121.7 (CH), 118.3 (C_q), 115.4 (C_q), 60.9 (CH_2), 59.3 (CH), 37.2 (CH_2), 13.9 (CH_3).

IR (neat):3077, 2978, 2938, 2227, 1689, 1259, 787, 681 cm^{-1}.

MS (EI) *m/z* (relative intensity): 371 (20) $[M]^+$, 326 (5), 298 (100), 268 (5), 256 (5), 229 (10), 128 (10), 43 (25).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{17}N_3O_3^+$ $[M]^+$ 371.1264, found 371.1266.

Ethyl 2-{6-nitro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate(132hb):



The general procedure **E** was followed using 4-nitro-*N*-(quinolin-8-yl)benzamide (**110h**) (73.2 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132hb** (49.0 mg, 50%) as a colorless solid.

M. p. = 178−180 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.47 (dt, *J* = 1.8, 0.7 Hz, 1H), 8.42–8.40 (m, 1H), 8.23 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.13–8.11 (m, 1H), 7.88 (ddd, *J* = 14.0, 7.8, 1.4 Hz, 2H), 7.65 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.42 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.90 (q, *J* = 7.1 Hz, 2H), 2.82 (dd, *J* = 16.4, 4.9 Hz, 1H), 2.63 (dd, *J* = 16.4, 7.4 Hz, 1H), 1.03 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.4 (C_q), 166.1 (C_q), 150.5 (CH), 150.4 (C_q), 146.4 (C_q),

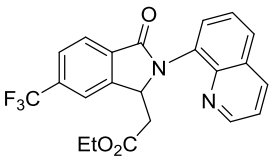
144.2 (C_q), 137.6 (C_q), 136.5 (CH), 132.6 (C_q), 130.2 (CH), 129.4 (C_q), 128.7 (CH), 126.4 (CH), 125.3 (CH), 124.1 (CH), 121.8 (CH), 118.6 (CH), 61.0 (CH_2), 59.5 (CH), 37.2 (CH_2), 13.9 (CH_3).

IR (neat): 3081, 2980, 2927, 1725, 1687, 1527, 1341, 788, 737 cm^{-1}.

MS (EI) *m/z* (relative intensity): 391 (20) $[M]^+$, 346 (5), 318 (100), 304 (5), 272 (30), 243 (10), 229 (10), 43 (10).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}N_3O_5^+$ $[M]^+$ 391.1163, found 391.1174.

Ethyl 2-{3-oxo-2-(quinolin-8-yl)-6-(trifluoromethyl)isoindolin-1-yl}acetate(132ib):



The general procedure **E** was followed using *N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide (**110i**) (79.2 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132ib** (83.0 mg, 80%) as a colorless solid.

M. p. = 103−105 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.08 (dt, *J* = 7.9, 0.8 Hz, 1H), 7.90–7.83 (m, 3H), 7.82– 7.78 (m, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.36 (dd, *J* = 7.3, 5.1 Hz, 1H), 3.86 (q, *J* = 7.1 Hz, 2H), 2.79 (dd, *J* = 16.1, 5.1 Hz, 1H), 2.61 (dd, *J* = 16.1, 7.3 Hz, 1H), 0.99 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0 (C_q), 166.9 (C_q), 150.4 (CH), 145.8 (C_q), 144.4 (C_q) , 136.4 (CH), 135.4 (q, *J* = 1.4 Hz, C_q), 133.8 (q, $^2J_{C\text{-}F}$ = 32.7 Hz, C_q) 132.8 (C_q), 130.4 (CH), 129.4 (C_q), 128.4 (CH), 126.4 (CH), 125.7 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, CH), 124.9 (CH), 123.8 (q, $^1J_{C\text{-}F}$ = 272.6 Hz, C_q) 121.7 (CH), 120.1 (q, $^3J_{C\text{-}F}$ = 3.9 Hz, CH), 60.8 (CH_2), 59.5 (CH), 37.5 (CH_2), 13.8 (CH_3).

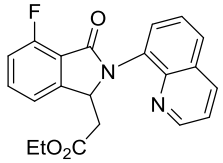
^{19}F NMR (282 MHz, $CDCl_3$) δ =–62.4.

IR (neat): 3346, 1667, 1532, 1323, 1114, 828, 794, 765 cm^{-1}.

MS (EI) *m/z* (relative intensity): 414 (20) $[M]^+$, 369 (5), 341 (100), 327 (10), 229 (5), 197 (5), 101 (5).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{17}F_3N_2O_3^+$ $[M]^+$ 414.1186, found 414.1183.

Ethyl 2-{4-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate(132jb):



The general procedure **E** was followed using 2-fluoro-*N*-(quinolin-8-yl)benzamide (**110j**) (66.7 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132jb** (49.0 mg, 54%) as a colorless solid.

M. p. = 63−65 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.85–7.82 (m, 2H), 7.61 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.58–7.54 (m, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.33

(dd, *J* = 7.5, 0.8 Hz, 1H), 7.16–7.12 (m, 1H), 6.30 (t, *J* = 6.1 Hz, 1H), 3.81 (q, *J* = 7.2 Hz, 2H), 2.72 (dd, *J* = 16.1, 5.4 Hz, 1H), 2.60 (dd, *J* = 16.1, 6.9 Hz, 1H), 0.97 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8 (C_q), 165.1 (d, $^3J_{C\text{-}F}$ = 2.5 Hz, C_q), 159.3 (d, $^1J_{C\text{-}F}$ = 261.0 Hz, C_q), 150.2 (CH), 148.2 (d, $^3J_{C\text{-}F}$ = 2.8 Hz, C_q), 144.4 (C_q), 136.6 (CH), 133.9 (d, $^3J_{C\text{-}F}$ = 7.7 Hz, CH), 132.9 (C_q), 130.6 (CH), 129.4 (C_q), 128.2 (CH), 126.4 (CH), 121.6 (CH), 119.5 (d, $^2J_{C\text{-}F}$ = 12.9 Hz, C_q), 118.5 (d, $^4J_{C\text{-}F}$ = 4.2 Hz, CH), 115.7 (d, $^2J_{C\text{-}F}$ = 19.3 Hz, CH), 60.6 (CH_2), 59.2 (CH), 37.9 (CH_2), 13.8 (CH_3).

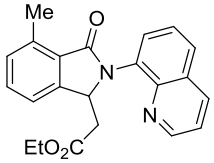
^{19}F NMR (282 MHz, $CDCl_3$): δ = –117.8.

IR (neat): 3046, 2981, 1696, 1626, 1477, 1394, 1028, 830 cm^{-1}.

MS (EI) *m/z* (relative intensity): 364 (25) $[M]^+$, 319 (5), 291 (100), 277 (10), 249 (10), 84 (20), 43 (35).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}FN_2O_3^+$ $[M]^+$ 364.1218, found 364.1227.

Ethyl 2-{4-methyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate(132kb):



The general procedure **E** was followed using 2-methyl-*N*-(quinolin-8-yl)benzamide (**110k**) (67.5 mg, 0.26 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132kb** (48.0 mg, 51%) as a colorless solid.

M. p. = 99−101 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.85–7.82 (m, 2H), 7.61 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.46–7.43 (m, 1H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35–7.33 (m, 1H), 7.25–7.24 (m, 1H), 6.21 (t, *J* = 6.3 Hz, 1H), 3.80–3.73 (m, 2H), 2.76 (s, 3H), 2.71 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.61 (dd, *J* = 15.8, 6.6 Hz, 1H), 0.94 (t, *J* = 7.2 Hz, 3H).

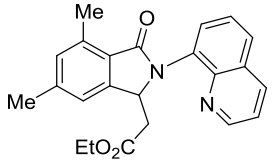
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2 (C_q), 169.1 (C_q), 150.2 (CH), 146.0 (C_q), 144.9 (C_q), 138.3 (C_q), 136.3 (CH), 133.6 (C_q), 131.5 (CH), 130.6 (CH), 130.4 (CH), 129.3 (C_q), 129.0 (C_q), 128.0 (CH), 126.3 (CH), 121.4 (CH), 119.9 (CH), 60.6 (CH_2), 58.8 (CH), 38.4 (CH_2), 17.4 (CH_3), 13.8 (CH_3).

IR (neat): 2978, 2925, 1729, 1688, 1473, 1394, 789, 624 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 (20) $[M]^+$, 315 (5), 288 (20), 287 (100), 273 (10), 243 (5), 143 (10), 115 (10).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{20}N_2O_3^+$ $[M]^+$ 360.1468, found 360.1468.

Ethyl 2-{4,6-dimethyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate(132lb):



The general procedure **E** was followed using 2,4-dimethyl-*N*-(quinolin-8-yl)benzamide (**110l**) (69.0 mg, 0.25 mmol) and ethyl acrylate (**46b**)

(50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132lb** (57.0 mg, 61%) as a colorless solid.

M. p. = 100−102 °C.

^{1}HNMR (500 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.84–7.80 (m, 2H), 7.60 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.14 (d, *J* = 1.5 Hz, 1H), 7.06 (d, *J* = 1.5 Hz, 1H), 6.17 (t, *J* = 6.2 Hz, 1H), 3.80–3.73 (m, 2H), 2.71 (s, 3H), 2.68 (dd, *J* = 15.8, 5.9 Hz, 1H), 2.60 (dd, *J* = 15.8, 6.6 Hz, 1H), 2.42 (s, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

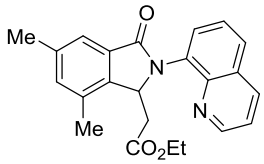
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3 (C_q), 169.1 (C_q), 150.2 (CH), 146.5 (C_q), 144.9 (C_q), 142.0 (C_q), 138.0 (C_q), 136.2 (CH), 133.8 (C_q), 131.4 (CH), 130.6 (CH), 129.3 (C_q), 127.8 (CH), 126.6 (C_q), 126.2 (CH), 121.4 (CH), 120.4 (CH), 60.4 (CH_2), 58.7 (CH), 38.5 (CH_2), 21.8 (CH_3), 17.3 (CH_3), 13.8 (CH_3).

IR (neat): 2980, 2926, 1717, 1683, 1395, 1158, 1139, 796, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 374 (25) $[M]^+$, 329 (5), 301 (100), 287 (10), 257 (10), 128(10), 43 (10).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{22}N_2O_3^+$ $[M]^+$ 374.1625, found 374.1627.

Ethyl 2-{5,7-dimethyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132mb):



The general procedure **E** was followed using 3,5-dimethyl-*N*-(quinolin-8-yl)benzamide (**110m**) (68.0 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132mb** (65.0 mg, 70%) as a colorless solid.

M. p. = 151−152 °C**.**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (ddd, *J* = 8.3, 1.8, 0.4 Hz, 1H), 7.96 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.82 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.63 (dd, *J* = 8.3, 7.4 Hz, 1H), 7.61 (s, 1H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.20–7.19 (m, 1H), 6.30 (t, *J* = 4.8 Hz, 1H), 3.63–3.53 (m, 2H), 2.73–2.72 (m, 2H), 2.44 (s, 3H), 2.42 (s, 3H), 0.82 (t, *J* = 7.1 Hz, 3H).

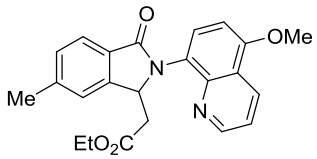
^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.5 (C_q), 168.6 (C_q), 150.0 (CH), 144.8 (C_q), 140.2 (C_q), 138.5 (C_q), 136.3 (CH), 134.5 (CH), 133.4 (C_q), 132.7 (C_q), 132.2 (C_q), 130.8 (CH), 129.3 (C_q), 127.7 (CH), 126.4 (CH), 122.0 (CH), 121.3 (CH), 60.3 (CH_2), 59.3 (CH), 36.3 (CH_2), 21.2 (CH_3), 18.3 (CH_3), 13.6 (CH_3).

IR (neat):2980, 2925, 2897, 1732, 1691, 1398, 1181, 794 cm^{-1}.

MS (EI) *m/z* (relative intensity): 374 (25) $[M]^+$, 329 (5), 301 (100), 287 (10), 257 (5), 157 (5), 129 (10).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{22}N_2O_3^+$ $[M]^+$ 374.1625, found 374.1623.

Ethyl 2-{2-(5-methoxyquinolin-8-yl)-6-methyl-3-oxoisoindolin-1-yl}acetate (132nb):



The general procedure **E** was followed using *N*-(5-methoxy-quinolin8-yl)-4-methylbenzamide (**110n**) (72.5 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol) Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132nb** (61.0 mg, 63%) as a colorless solid.

M. p. = 137−139 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.81 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.57 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.36 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.32 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.31–7.29 (m, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.05 (t, *J* = 6.3 Hz, 1H), 4.00 (s, 3H), 3.85–3.76 (m, 2H), 2.72 (dd, *J* = 15.9, 5.6 Hz, 1H), 2.60 (dd, *J* = 15.9, 6.9 Hz, 1H), 2.46 (s, 3H), 0.96 (t, *J* = 7.1 Hz, 3H).

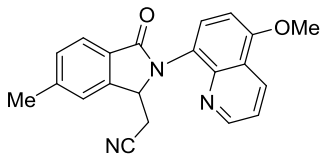
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1 (C_q), 168.4 (C_q), 154.9 (C_q), 150.4 (CH), 145.7 (C_q), 145.2 (C_q), 142.3 (C_q), 130.9 (CH), 130.6 (CH), 129.6 (C_q), 129.2 (CH), 125.8 (C_q), 123.9 (CH), 122.9 (CH), 121.5 (C_q), 120.4 (CH), 103.8 (CH), 60.5 (CH_2), 59.3 (CH), 55.9 (CH_3), 38.1(CH_2), 22.0 (CH_3), 13.9 (CH_3).

IR (neat): 3049, 2980, 2941, 1695, 1404, 1271, 1242, 1150 cm^{-1}.

MS (EI) *m/z* (relative intensity): 390 (25) $[M]^+$, 345 (5), 317 (100), 302 (10), 287 (5), 245 (5), 159 (5), 115 (5).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{22}N_2O_4^+$ $[M]^+$ 390.1574, found 390.1570.

2-{2-(5-Methoxyquinolin-8-yl)-6-methyl-3-oxoisoindolin-1-yl}acetonitrile (132nh):



The general procedure **E** was followed using *N*-(5-methoxy-quinolin8-yl)-4-methylbenzamide (**110n**) (72.5 mg, 0.25 mmol) and acrylonitrile (**46h**) (29.0 mg, 0.55 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132nh** (55.0 mg, 64%) as a colorless solid.

M. p. = 227−228 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.83–8.81 (m, 1H), 8.65–8.61 (m, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.84 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.49–7.48 (m, 1H), 7.44–7.38 (m, 2H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.08 (dd, *J* = 6.9, 3.9 Hz, 1H), 4.05 (s, 3H), 2.84 (dd, *J* = 16.8, 3.9 Hz, 1H), 2.62 (dd, *J* = 16.7, 6.9 Hz, 1H), 2.53 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2 (C_q), 155.2 (C_q), 150.5 (CH), 145.0 (C_q), 143.6 (C_q), 143.2 (C_q), 131.4 (CH), 130.8 (CH), 130.2 (CH), 129.7 (C_q), 124.6 (C_q), 124.4 (CH) 122.7 (CH), 121.7

(C_q), 120.7 (CH), 116.0 (C_q), 104.1 (CH), 57.8 (CH), 56.0 (CH_3), 22.1 (CH_3), 22.0 (CH_2).

IR (neat): 2964, 2930, 2912, 1686, 1587, 1407, 1274, 1080 cm^{-1}.

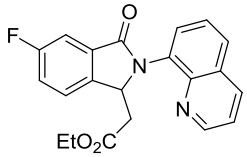
MS (EI) *m/z* (relative intensity): 343 (100) $[M]^+$, 328 (10), 303 (65), 260 (25), 232 (15), 160(75),115 (20).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}N_3O_2^+$ $[M]^+$ 343.1315, found 343.1318.

Reaction with 3-fluoro-*N*-(quinolin-8-yl)benzamide (**110s**):

The general procedure **E** was followed using 3-fluoro-*N*-(quinolin-8-yl)benzamide (**110s**) (65.6 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132sb** (46.0 mg, 51%) and **132sb'** (21.0 mg, 23%) as colorless solids.

Ethyl 2-{5-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132sb):



M. p. = 168−170 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 2H), 7.64–7.59 (m, 2H), 7.53 (ddt, *J* = 8.3, 4.4, 0.6 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (ddd, *J* = 9.1, 8.4, 2.5 Hz, 1H), 6.26 (dd, *J* = 7.2, 5.3 Hz, 1H), 3.83 (q, *J* = 7.2Hz, 2H), 2.72 (dd, *J* = 16.0, 5.3 Hz, 1H), 2.56 (dd, *J* = 16.0, 7.2 Hz, 1H), 0.99 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.9 (C_q), 167.2 (d, $^4J_{C\text{-}F}$ = 3.5 Hz, C_q), 163.0 (d, $^1J_{C\text{-}F}$ = 247.5 Hz, C_q), 150.3 (CH), 144.5 (C_q), 140.9 (d, $^4J_{C\text{-}F}$ = 2.4 Hz, C_q), 136.3 (CH), 134.3 (d, $^3J_{C\text{-}F}$ = 8.8 Hz, C_q), 133.1 (C_q), 130.3 (CH), 129.4 (C_q), 128.3 (CH), 126.3 (CH), 124.3 (d, $^3J_{C\text{-}F}$ = 8.3 Hz, CH), 121.6 (CH), 119.4 (d, $^2J_{C\text{-}F}$ = 23.6 Hz, CH), 110.9 (d, $^2J_{C\text{-}F}$ = 23.4 Hz, CH), 60.6 (CH_2), 59.2 (CH), 37.9 (CH_2), 13.8 (CH_3).

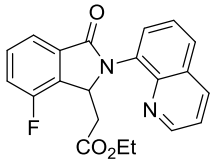
^{19}F NMR (282 MHz, $CDCl_3$): δ = –(112.9–113.0) (m).

IR (neat): 3047, 1733, 1697, 1619, 1502, 1424, 1376, 1226 cm^{-1}.

MS (EI) *m/z* (relative intensity): 364 (20) $[M]^+$, 319 (5), 291 (100), 277 (10), 248 (10), 101 (10), 43 (20).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}FN_2O_3^+$ $[M]^+$ 364.1218, found 364.1231.

Ethyl 2-{7-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132sb'):



M. p. = 144−146 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.21 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.90–7.84 (m, 2H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.63 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.55–7.48 (m, 1H), 7.43 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.32–7.25 (m,

1H), 6.44 (t, *J* = 5.2 Hz, 1H), 4.26–3.36 (m, 2H), 2.85 (dd, *J* = 15.5, 5.8 Hz, 1H), 2.77 (dd, *J* = 15.5, 4.6 Hz, 1H), 0.88–0.83 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.2 (C_q), 167.3 (d, $^4J_{C\text{-}F}$ = 2.3 Hz, C_q), 157.6 (d, $^1J_{C\text{-}F}$ = 250.2 Hz, C_q), 150.3 (CH), 144.6 (C_q), 136.4 (CH), 135.5 (d, $^3J_{C\text{-}F}$ = 4.3 Hz, C_q), 132.9 (C_q), 130.8 (d, $^2J_{C\text{-}F}$ = 16.7 Hz, C_q), 130.7 (CH), 130.5 (d, $^3J_{C\text{-}F}$ = 6.6 Hz, CH), 129.3 (C_q), 128.2 (CH), 126.4 (CH) , 121.6 (CH), 120.3 (d, $^4J_{C\text{-}F}$ = 3.7 Hz, CH), 118.7 (d, $^2J_{C\text{-}F}$ = 20.0 Hz, CH), 60.5 (CH_2), 57.7 (d, $^3J_{C\text{-}F}$ = 2.1 Hz, CH), 36.4 (d, $^4J_{C\text{-}F}$ = 1.1 Hz, CH_2), 13.7 (CH_3).

^{19}F NMR (283 MHz, $CDCl_3$): δ = –119.95 (dd, *J* = 9.2, 4.6 Hz).

IR (neat): 2920, 1731, 1695, 1615, 1501, 1393, 1247, 1144, 749 cm^{-1}.

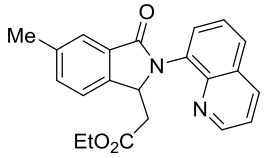
MS (EI) *m/z* (relative intensity): 364 (20) $[M]^+$, 319 (5), 291 (100), 277 (10), 248 (10), 101(10), 43 (20).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{17}FN_2O_3^+$ $[M]^+$ 364.1218, found 364.1231.

Reaction with 3-methyl-*N*-(quinolin-8-yl)benzamide (**110t**):

The general procedure **E** was followed using 3-methyl-*N*-(quinolin-8-yl)benzamide (**110t**) (65.3 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132tb** (38.0 mg, 42%) and **132tb'** (12.0 mg, 13%) as colorless solids.

Ethyl 2-{5-methyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132tb):



M. p. = 171−172 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.86–7.81 (m, 2H), 7.78−7.77 (m, 1H), 7.61 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.43–7.38 (m, 3H), 6.24 (t, *J* = 6.3 Hz, 1H), 3.79 (q, *J* = 7.2 Hz, 2H), 2.70 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.57 (dd, *J* = 15.8, 6.9 Hz, 1H), 2.46 (s, 3H), 0.99–0.94 (m, 3H).

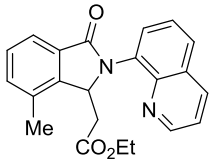
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2 (C_q), 168.4 (C_q), 150.2 (CH), 144.7 (C_q), 142.7 (C_q), 138.4 (C_q), 136.3 (CH), 133.6 (C_q), 132.9 (CH), 132.2 (C_q), 130.4 (CH), 129.4 (C_q), 128.0 (CH), 126.3 (CH), 124.5 (CH), 122.3 (CH), 121.5 (CH), 60.5 (CH_2), 59.4 (CH), 38.2 (CH_2), 21.3 (CH_3), 13.8 (CH_3).

IR (neat): 2981, 2928, 1731, 1692, 1494, 1227, 1188, 1161, 1139 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 (25) $[M]^+$, 315 (5), 287 (100), 273 (10), 243 (5), 143 (10), 115 (20).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{20}N_2O_3^+$ $[M]^+$ 360.1468, found 360.1471.

Ethyl 2-{7-Methyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132tb'):



M. p. = 139−141 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.98 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.85–7.79 (m, 2H), 7.71–7.56 (m, 1H), 7.44–7.36 (m, 3H), 6.36 (t, *J* = 4.7 Hz, 1H), 3.69–3.38 (m, 2H), 2.75 (d, *J* = 4.7 Hz, 2H), 2.48 (s, 3H), 0.80 (t, *J* = 7.1 Hz, 3H).

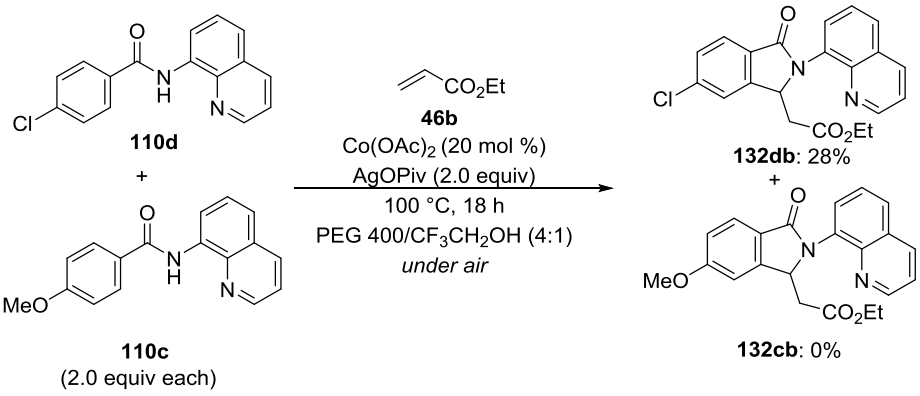
^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.4 (C_q), 168.4 (C_q), 150.1 (CH), 144.8 (C_q), 142.9 (C_q), 136.3 (CH), 133.5 (CH), 133.2 (C_q), 132.6 (C_q), 132.5 (C_q), 130.8 (CH), 129.3 (C_q), 128.5 (CH), 127.8 (CH), 126.4 (CH), 121.8 (CH), 121.4 (CH), 60.3 (CH_2), 59.5 (CH), 36.1 (CH_2), 18.4 (CH_3), 13.6 (CH_3).

IR (neat): 2974, 2922, 1725, 1686, 1503, 1395, 1285, 1141 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 (25) $[M]^+$, 315 (5), 287 (100), 273 (10), 245 (5), 143 (10), 43 (20).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{20}N_2O_3^+$ $[M]^+$ 360.1468, found 360.1469.

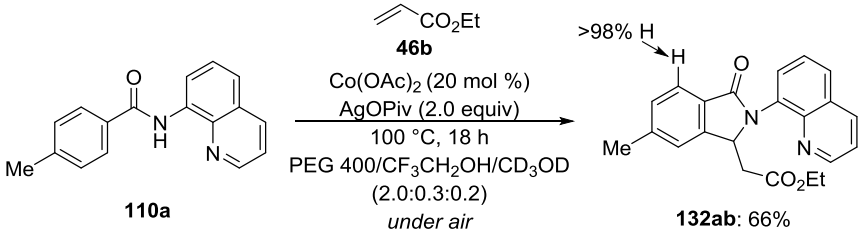
Intermolecular Competition Experimentsbetween Amides 110c and 110d



The general procedure **E** was followed using 4-chloro-*N*-(quinolin-8-yl)benzamide (**110d**) (140.0 mg, 0.50 mmol), 4-methoxy-*N*-(quinolin-8-yl)benzamide (**110c**) (139.0 mg, 0.50 mmol), ethyl acrylate (**46b**) (25.0 mg, 0.25 mmol), $Co(OAc)_2$ (9.0 mg, 20 mol %) and AgOPiv (105.0 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1→1/1) yielded **132db** (27.0 mg, 28%).

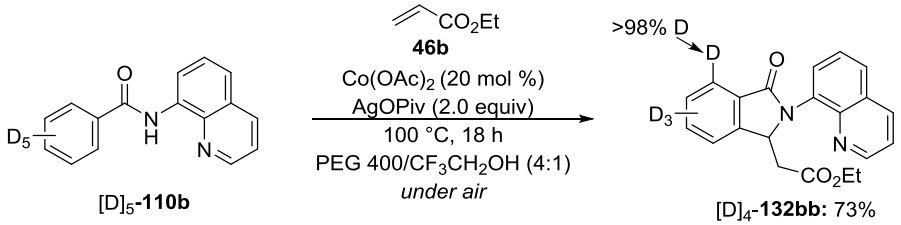
Analytic data of the compound **132bd** were identical to those reported above.

Oxidative Alkenylation with CD_3OD as Isotopically Labeled Cosolvent:



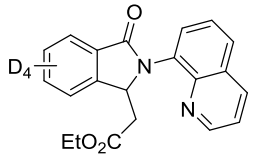
The general procedure **E** was followed using 4-methyl-*N*-(quinolin-8-yl)benzamide (**110a**) (65.5 mg, 0.25 mmol), ethyl acrylate (**46b**) (51.0 mg, 0.51 mmol), $Co(OAc)_2$ (9.0 mg, 20 mol %) and AgOPiv (105.0 mg, 2.0 equiv) in a solvent mixture of PEG 400/CF_3CH_2OH/CD_3OD (2.0/0.3/0.2 mL). Purification by column chromatography (*n*-hexane /EtOAc: 2/1→1/1) yielded **132ab** (60.0 mg, 66%) as a colorless solid. Its spectral data were identical to those reported above. The negligible deuterium incorporation in **132ab** was confirmed by ^{1}H NMR spectroscopy.

Studies on Cobalt-Catalyzed H/D Exchange with Substrate [D]$_5$-110b



A mixture of *N*-(quinolin-8-yl)benzamide-2,3,4,5,6-d_5 ([D]$_5$-**110b**) (62.5 mg, 0.25 mmol), ethyl acrylate (**46b**) (50.0 mg, 0.50 mmol), $Co(OAc)_2$ (9.0 mg, 20 mol %) and AgOPiv (105.0 mg, 2.0 equiv) in PEG 400/CF_3CH_2OH (2.0/0.5 mL) was stirred at 100 °C for 18 h under an ambient atmosphere of air. The reaction mixture was diluted with H_2O (20 mL) and extracted with *t*BuOMe (3 × 25 mL). The combined organic layers were washed with brine (50 mL) and dried over Na_2SO_4. After filtration and evaporation of the solvents in *vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) to yield [D]$_4$-**132bb** (64.0 mg, 73%) as a colorless solid. The negligible hydrogen incorporation in [D]$_4$-**132bb** was confirmed by ^{1}H NMR spectroscopy.

Ethyl 2-{3-Oxo-2-(quinolin-8-yl)isoindolin-1-yl-4,5,6,7-d$_4$}acetate ([D]$_4$-132bb):



M. p. = 149−151 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.86 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.84 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.62 (dd, *J* = 8.3, 7.4 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.31 (dd, *J* = 7.0, 5.5 Hz, 1H), 3.80 (q, *J* = 7.1 Hz, 2H), 2.72 (dd, *J* = 15.9, 5.5 Hz, 1H), 2.60 (dd, *J* = 15.9, 7.0 Hz, 1H), 0.96 (t, *J* = 7.1 Hz, 3H).

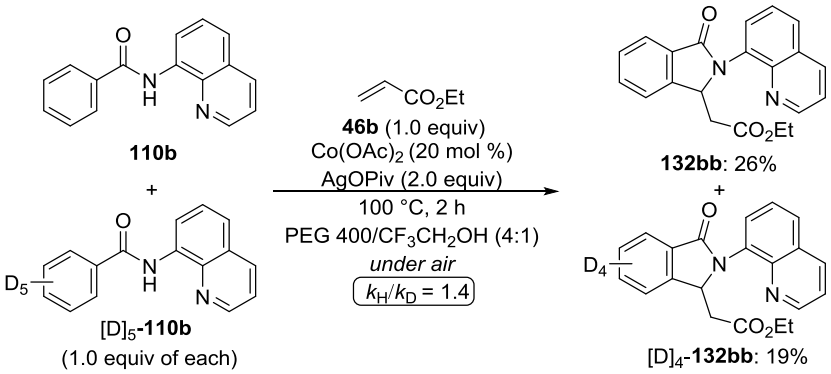
^{13}CNMR (125 MHz, $CDCl_3$): δ = 170.1 (C_q), 168.3 (C_q), 150.2 (CH), 145.4 (C_q), 144.7 (C_q), 136.3 (CH), 133.5 (C_q), 132.0 (C_q), 131.4 (CD), 130.4 (CH), 129.3(C_q), 128.0 (CH), 127.9 (CD), 126.4 (CH), 123.9 (CD), 122.2 (CD), 121.5 (CH), 60.5 (CH_2), 59.5 (CH), 38.1 (CH_2), 13.8 (CH_3).

IR (neat): 3061, 2968, 2927, 1727, 1694, 1405, 1159, 1028 cm^{-1}.

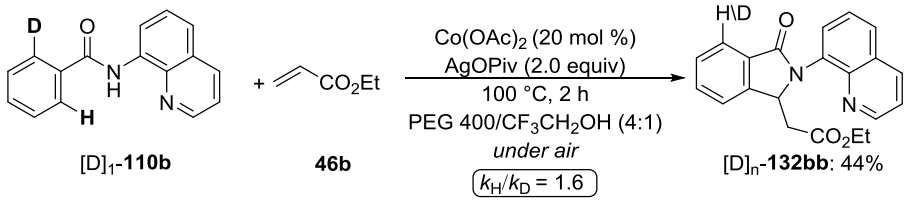
MS (EI) *m/z* (relative intensity): 350 (20) $[M]^+$, 305 (5), 277 (100), 263 (10), 235 (5), 133(5), 43 (10).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{14}D_4N_2O_3^+[M]^+$350.1563, found 350.1575.

Studies on the Kinetic Isotope Effect.



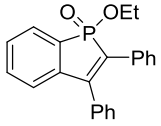
The representative procedure **E** was followed using *N*-(quinolin-8-yl)benzamide (**110b**) (37.0 mg, 0.15 mmol), *N*-(quinolin-8-yl)benzamide-2,3,4,5,6-d_5 ([D_5]-**110b**) (38.0 mg, 0.15 mmol) and ethyl acrylate (**46b**) (14 mg, 0.14 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded a mixture of [D]$_4$-**132bb** and [H]$_4$-**132bb**. The kinetic isotope effect of this reaction was estimated to be 1.4, as determined by ^{1}HNMR spectroscopy.



The representative procedure **E**was followed using [D]$_1$-**110b** (62.0 mg, 0.25 mmol) and ethyl acrylate (**46b**) (50.0 mg, 0.25 mmol). Purification by column chromatography (n-hexane/EtOAc: 2/1) yielded [D]$_n$-**132bb** (37.0 mg, 43%) as a colorless solid. The intramolecular KIE was estimated to be 1.6, as determined by ^{1}H NMR spectroscopy.

8.4.5 Analytical Data for the Products of Silver-Mediated Alkyne Annulations by C−H/P−H Bonds Functionalizations

1-Ethoxy-2,3-diphenylphosphindole 1-Oxide (117aa):



The general procedure **F** was followed using ethyl phenylphosphinate (**121a**) (82.1 mg, 0.48 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117aa** (99.0 mg, 60%) as an off-white oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.64 (m, 1H), 7.48–7.32 (m, 7H), 7.32–7.14 (m, 5H), 7.13–7.18 (m, 1H), 4.41–3.86 (m, 2H), 1.23 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.5 (d, *J* = 27.6 Hz, C_q), 141.8 (d, *J* = 34.0 Hz, C_q), 133.8 (d, *J* = 18.1 Hz, C_q), 132.9 (d, *J* = 2.1 Hz, CH), 132.4 (d, *J* = 9.3 Hz, C_q), 131.4 (d, *J* = 125.0 Hz, C_q), 128.9 (d, *J* = 10.8 Hz, CH), 128.9 (d, *J* = 5.8Hz, CH), 128.8 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (d, *J* = 8.8 Hz, CH), 127.1 (d, *J* = 134.0 Hz, C_q), 126.2 (CH), 123.8 (d, *J* = 13.4 Hz, CH), 62.0 (d, *J* = 6.4 Hz, CH_2), 16.4 (d, *J* = 6.2 Hz, CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 45.9.

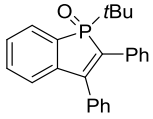
IR (film): 3058, 2979, 1440, 1221, 1026, 939, 697, 524 cm^{-1}.

MS (EI) *m/z* (relative intensity): 346 (100) $[M]^+$, 317 (90), 299 (80), 252 (50), 77 (10).

HR-MS (EI) *m/z* calcd for $C_{22}H_{20}O_2P^+$ $[M+H]^+$ 347.1195, found 347.1220.

The spectral data were in accordance with those reported in the literature.[127]

1-(*tert*-Butyl)-2,3-diphenyl-1*H*-phosphindole 1-Oxide (117ba):



The general procedure **F** was followed using *tert*-butyl(phenyl)phosphine oxide (**121b**) (91.3 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) afforded **117ba** (98.0 mg, 55%) as a colorless solid.

M. p. = 215–217 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81–7.75 (m, 1 H), 7.44–7.28 (m, 7 H), 7.20–7.07 (m, 6 H), 1.05 (d, *J* = 15.2 Hz, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2 (d, *J* = 19.0 Hz, C_q), 144.0 (d, *J* = 24.0 Hz, C_q), 134.5 (d, *J* = 9.4 Hz, C_q), 134.1 (d, *J* = 13.9 Hz, C_q), 132.4 (d, *J* = 2.0 Hz, CH), 132.1 (d, *J* = 84.7 Hz, C_q), 129.6 (d, *J* = 8.5 Hz, CH), 129.5 (d, *J* = 94.4 Hz, C_q), 129.1 (d, *J* = 4.9 Hz, CH), 129.0 (CH), 128.7 (CH), 128.4 (CH), 128.2 (d, *J* = 8.7 Hz, CH), 127.7 (CH), 123.8 (d, *J* = 9.8 Hz, CH), 32.8 (d, *J* = 68.1 Hz, C_q), 24.2 (CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 60.3.

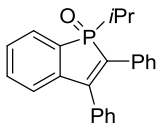
IR (neat): 3055, 2963, 1863, 1439, 1259, 1174, 1065, 1021 cm^{-1}.

MS (EI): *m/z* (relative intensity): 358 (25) $[M]^+$, 302 (100), 283 (15), 252 (20), 196 (5), 57 (10).

HR-MS (EI): *m/z* calcd for $C_{24}H_{24}OP^+$ $[M+H]^+$ 359.1559, found 359.1554.

The spectral data were in accordance with those reported in the literature.[127]

1-Isopropyl-2,3-diphenyl-1*H*-phosphindole 1-Oxide (117ca):



The general procedure **F** was followed using isopropyl(phenyl)phosphine oxide (**121c**) (84.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ca** (85.0 mg, 49%) as colorless solid.

M.p. = 153–155 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91–7.67 (m, 1H), 7.49–7.31 (m, 7H), 7.29–6.97 (m, 6H), 2.32–2.14 (m, 1H), 1.25 (dd, *J* = 16.4, 7.2 Hz, 3H), 0.90 (dd, *J* = 18.0, 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.4 (d, *J* = 19.1 Hz, C_q), 142.7(d, *J* = 24.4 Hz, C_q), 133.1 (d, *J* = 13.9 Hz, C_q), 132.4 (d, *J* = 9.7 Hz, C_q), 131.4 (d, *J* = 1.9 Hz, CH), 130.8 (d, *J* = 87.8 Hz, CH), 128.0 (d, *J* = 96.5 Hz, C_q), 128.0 (d, *J* = 8.8 Hz, CH), 127.8 (CH), 127.8 (d, *J* = 5.4 Hz, CH), 127.7 (CH) , 127.4 (d, *J* = 9.8 Hz, CH), 127.2 (d, *J* = 14.3 Hz, CH), 127.2 (CH), 126.7 (CH) , 122.7 (d, *J* = 10.0 Hz, CH), 26.5 (d, *J* = 68.2 Hz, CH), 14.5 (CH_3), 14.1 (d, *J* = 2.3 Hz, CH_3).

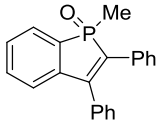
^{31}P NMR (122 MHz, $CDCl_3$): δ = 56.7.

IR (neat): 3056, 2961, 2928, 1444, 1256, 1181, 1068, 1028, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 344 (25) $[M]^+$, 302 (100), 283 (15), 252 (20), 196 (5), 57 (10).

HR-MS (EI) *m/z* calcd for $C_{23}H_{21}OP^+$ $[M]^+$ 344.1325, found 344.1331.

1-Methyl-2,3-diphenyl-1*H*-phosphindole 1-Oxide (117da):



The general procedure **F** was followed using methyl(phenyl)phosphine oxide (**121d**) (71.9 mg, 0.51 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117da** (87.0mg, 54%) as a colorless solid.

M.p. = 162–164 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.70 (m, 1H), 7.45–7.27 (m, 7H), 7.25–7.02 (m, 6H), 1.68 (d, *J* = 13.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.0 (d, *J* = 21.0 Hz, C_q), 141.7 (d, *J* = 26.6 Hz, C_q), 133.1 (d, *J* = 14.7 Hz, C_q), 133.0 (d, *J* = 93.9 Hz, C_q), 131.8 (d, *J* = 10.3 Hz, C_q), 131.7 (d, *J* = 2.4 Hz, CH), 130.6 (d, *J* = 103.0 Hz, C_q), 128.0 (CH), 127.9 (CH), 127.9 (d, *J* = 5.6 Hz, CH), 127.7 (CH), 127.5 (d, *J* = 9.5 Hz, CH), 127.4 (CH), 127.2 (d, *J* = 9.6 Hz, CH), 127.0 (CH), 122.9 (d, *J* = 10.6 Hz, CH), 13.8 (d, *J* = 69.2 Hz, CH_3).

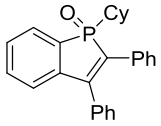
^{31}P NMR (122 MHz, $CDCl_3$): δ = 45.2.

IR (neat): 3056, 3029, 1715, 1290, 1179, 759, 744, 729, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 315 (100) $[M]^+$, 301 (5), 252 (20), 157 (5), 43 (25).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}OP^+$ $[M]^+$ 316.1012, found 316.1005.

1-Cyclohexyl-2,3-diphenylphosphindole 1-Oxide (117ea):



The general procedure **F** was followed using cyclohexyl(phenyl)phosphine oxide (**121e**) (104.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ea** (88.0 mg, 46%) as a yellow gum.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.79–7.67 (m, 1H), 7.42–7.24 (m, 7H), 7.24–7.07 (m, 5H), 7.12–7.00 (m, 1H), 2.10–1.84 (m, 2H), 1.81–1.63 (m, 2H), 1.61–1.44 (m, 2H), 1.42–1.27 (m, 1H), 1.22–0.89 (m, 4H), 0.88–0.69 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ= 148.4 (d, J = 19.4 Hz, C_q), 142.6 (d, J = 24.8 Hz, C_q), 133.1 (d, J = 14.0 Hz, C_q), 132.5 (d, J = 9.7 Hz, C_q), 131.3 (d, J = 2.0 Hz, CH), 131.0 (d, J = 87.8 Hz, C_q), 128.4 (d, J = 96.5 Hz, C_q), 128.0 (d, J = 8.6 Hz, CH), 127.8 (CH), 127.8 (d, J = 5.3 Hz, CH), 127.6 (br, CH), 127.3 (d, J = 9.7 Hz, CH), 127.2 (d, J = 11.8 Hz, CH), 127.1 (CH), 126.7 (CH) , 122.6 (d, J = 10.0 Hz, CH), 36.4 (d, J = 68.4 Hz, CH), 25.3 (d, J = 13.5 Hz, CH_2), 25.1 (d, J = 14.4 Hz, CH_2), 24.8 (d, J = 1.7 Hz, CH_2), 24.2 (d, J = 3.4 Hz, CH_2), 24.1 (CH_2).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 53.8.

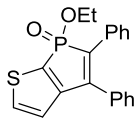
IR (neat): 3055, 2927, 2852, 1735, 1445, 1174, 761, 735, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 384 (100) $[M]^+$, 329 (20), 302 (80), 283 (20), 252 (35).

HR-MS (EI) *m/z*calcd for $C_{26}H_{25}OP^+$ $[M]^+$ 384.1638, found 384.1559.

The spectral data were in accordance with those reported in the literature.[127]

6-Ethoxy-4,5-diphenylphospholo[2,3-*b*]thiophene 6-Oxide (117fa):



The general procedure **F** was followed using ethyl thiophen-2-ylphosphinate (**121f**) (86.8 mg, 0.49 mmol) and 1,2-bis(4-chlorophenyl)ethyne (**11a**) (178.0 mg, 1.00 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117fa** (71.0 mg, 41%) as a yellow gum**.**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 8H), 7.26–7.24 (m, 1H), 7.22–7.19 (m, 3H), 4.09–3.94 (m, 2H), 1.23 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.6 (d, J = 47.0 Hz, C_q), 141.1 (d, J = 22.1 Hz, C_q), 134.0 (d, J = 17.1 Hz, C_q), 132.5 (d, J = 8.7 Hz, C_q), 129.9 (d, J = 136.6 Hz, C_q), 129.7 (d, J = 130.4 Hz, C_q), 129.6 (d, J = 14.8 Hz, CH), 129.3 (CH), 128.8 (CH), 128.8 (d, J = 6.3 Hz, CH), 128.4 (CH), 128.3

(CH), 127.9 (d, J = 1.3 Hz, CH), 125.3 (d, J = 14.8 Hz, CH), 62.4 (d, J = 6.4 Hz, CH_2), 16.4 (d, J = 6.2 Hz, CH_3).

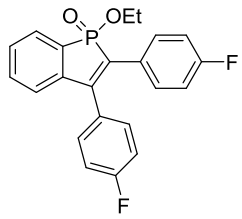
^{31}P NMR (122 MHz, $CDCl_3$): δ = 36.7.

IR (neat): 3062, 2981, 2926, 1710, 1224, 1019, 951, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity): 352 (100) $[M]^+$, 323(70), 305 (75), 276 (15), 258 (25), 213 (20), 105 (40).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{18}O_2PS^+$ $[M+H]^+$ 353.0760, found 353.0760.

1-Ethoxy-2,3-bis(4-fluorophenyl)phosphindole 1-Oxide (117ad):



The general procedure **F** was followed using ethyl phenylphosphinate (**121a**) (87.4 mg, 0.51 mmol) and 1,2-bis(4-fluorophenyl)ethyne (**11d**) (217.0 mg, 1.01 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ad** (96.0 mg, 50%) as a yellow solid.

M. p. = 99–101 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77–7.70 (m, 1H), 7.47–7.30 (m, 4H), 7.24–7.20 (m, 2H), 7.13–7.06 (m, 3H), 6.94–6.87 (m, 2H), 4.16–4.02 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.7 (d, $^1J_{C\text{-}F}$ = 249.5 Hz, C_q), 162.3 (d, $^1J_{C\text{-}F}$ = 249.5 Hz, C_q), 147.4 (dd, J = 28.0, 1.4 Hz, C_q), 141.5 (d, J = 34.0 Hz, C_q), 133.1 (d, J = 2.2 Hz, CH), 130.9 (d, J = 8.2 Hz, CH), 130.7 (dd, $^3J_{C\text{-}F}$ = 8.0, 5.8 Hz, CH), 129.5 (d, J = 125.8 Hz, C_q), 129.4 (dd, J = 18.3, 3.5 Hz, C_q), 129.1 (d, J = 11.3 Hz, CH), 128.3 (dd, J = 9.2, 3.5 Hz, C_q), 127.7 (d, J = 8.9 Hz, CH), 127.0 (d, J = 134.4 Hz, C_q), 123.7 (d, J = 13.4 Hz, CH), 116.2 (d, $^2J_{C\text{-}F}$= 21.6 Hz, CH), 115.5 (d, $^2J_{C\text{-}F}$= 21.9 Hz, CH), 62.1 (d, J = 6.6 Hz, CH_2), 16.4 (d, J = 5.9 Hz, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –(111.7–117.8) (m), –(112.4–112.5) (m),

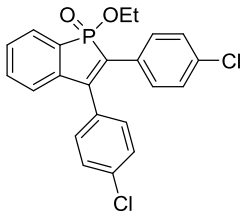
^{31}P NMR (122 MHz, $CDCl_3$): δ = 45.19, 45.18.

IR (neat): 3057, 2985, 1498, 1217, 1031, 955, 774, 526 cm^{-1}.

MS (EI) *m/z* (relative intensity): 382 $[M]^+$ (100), 353 (100), 335 (80), 288 (50), 123 (20), 95 (10).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{18}F_2O_2P^+$ $[M+H]^+$ 383.1007, found 383.1000.

2,3-Bis(4-chlorophenyl)-1-ethoxy-1*H*-phosphindole 1-Oxide (117ae):



The general procedure **F** was followed using ethyl phenylphosphinate (**121a**) (85.9 mg, 0.50 mmol) and 1,2-bis(4-chlorophenyl)ethyne (**11e**)

(250.0 mg, 1.01 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ae** (132.0 mg, 64%) as a yellow gum.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78–7.71 (m, 1H), 7.49–7.35 (m, 4H), 7.32–7.29 (m, 2H), 7.21–7.16 (m, 4H), 7.10–7.06 (m, 1H), 4.16–4.02 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7 (d, *J* = 28.0 Hz, C_q), 141.1 (d, *J* = 34.0 Hz, C_q), 134.9 (C_q), 134.1(C_q), 133.1 (d, *J* = 2.2 Hz, CH), 131.9 (d, *J* = 18.1 Hz, C_q), 130.7 (d, *J* = 8.8 Hz, C_q), 130.3 (CH), 130.1 (d, *J* = 5.9 Hz, CH), 130 (d, *J* = 125.1 Hz, C_q), 129.4 (CH), 129.3 (d, *J* = 11.6 Hz, CH), 128.8 (CH), 127.8 (d, *J* = 8.9 Hz, CH), 127.1 (d, *J* = 134.4 Hz, C_q), 123.7 (d, *J* = 13.5 Hz, CH), 62.2 (d, *J* = 6.4 Hz, CH_2), 16.5 (d, *J* = 6.0 Hz, CH_3).

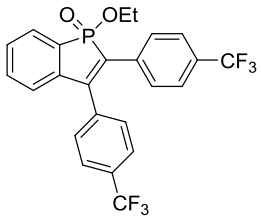
^{31}P NMR (122 MHz, $CDCl_3$): δ = 46.0.

IR (neat): 2982, 1484, 1226, 1089, 1013, 769, 737, 501 cm^{-1}.

MS (EI) *m/z* (relative intensity): 414 (100) $[M]^+$, 385 (90), 367 (60), 322 (20), 286 (20), 250 (35), 139 (20).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{18}Cl_2O_2P$ $[M+H]^+$415.0416, found 415.0409.

1-Ethoxy-2,3-bis{4-(trifluoromethyl)phenyl}-1*H*-phosphindole 1-Oxide (117am):



The general procedure **F** was followed using ethyl phenylphosphinate (**121a**) (84.9 mg, 0.50 mmol) and 1,2-bis{4-(trifluoromethyl)phenyl}-ethyne (**11m**) (318.0 mg, 1.01 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117am** (127.0 mg, 53%) as a colorless gum.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85–7.75 (m, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.62–7.42 (m, 6H), 7.45–7.34 (m, 2H), 7.14–7.01 (m, 1H), 4.19–4.09 (m, 2H), 1.27 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.5 (d, *J* = 27.7 Hz, C_q), 140.6 (q, *J* = 33.8 Hz, C_q), 137.1 (d, *J* = 17.8 Hz, C_q), 135.7 (d, *J* = 9.0 Hz, C_q), 133.2 (d, *J* = 2.3 Hz, CH), 132.4 (d, *J* = 2.9 Hz, CH), 132.0 (d, *J* = 9.8 Hz, CH), 131.0 (q, *J* = 33.3 Hz, C_q), 130.2 (d, *J* = 97.1 Hz, C_q), 129.7 (d, *J* = 11.2 Hz, CH), 129.3 (CH) , 129.0 (d, *J* = 5.7 Hz, CH), 128.5 (d, *J* = 13.1 Hz, CH), 128.1 (d, *J* = 8.9 Hz, CH), 127.1 (d, *J* = 133.6 Hz, C_q), 125.7–125.5 (m, CH), 125.4 (q, *J* = 4.0 Hz, CH), 123.9 (d, *J* = 13.4 Hz, CH), 123.7 (q, *J* = 272 Hz, C_q), 123.6 (q, *J* = 272 Hz, C_q), 62.4 (d, *J* = 6.4 Hz, CH_2), 16.6 (d, *J* = 6.0 Hz, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –(62.6–63.0) (m).

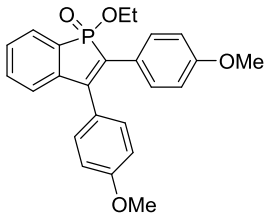
^{31}P NMR (122 MHz, $CDCl_3$): δ = 44.4.

IR (neat): 2984, 1736, 1616, 1320, 1163, 1109, 1065, 1016 cm^{-1}.

MS (EI) *m/z* (relative intensity): 482 (85) $[M]^+$, 453 (100), 435 (60), 388 (20), 320 (15), 141 (20).

HR-MS (EI) *m/z* calcd for $C_{24}H_{17}F_6O_2P^+$ $[M]^+$ 482.0865, found 482.0850.

1-Ethoxy-2,3-bis(4-methoxyphenyl)-1*H*-phosphindole 1-Oxide(117ac):



The general procedure **F** was followed using ethyl phenylphosphinate (**121a**) (84.9 mg, 0.50 mmol) and 1,2-bis(4-methoxylphenyl)ethyne (**11c**) (238.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ac** (55.0 mg, 27%) as a yellow solid.

M. p. = 111–113 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.67 (m, 1H), 7.42–7.30 (m, 4H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.13–7.09 (m, 1H), 6.92 (dd, *J* = 7.4, 1.6 Hz, 2H), 6.74–6.71 (m, 2H), 4.11–3.96 (m, 2H), 3.82 (s, 3H), 3.74 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6 (C_q), 159.1 (C_q), 146.6 (d, *J* = 28.1 Hz, C_q), 142.4 (d, *J* = 34.6 Hz, C_q), 132.9 (d, *J* = 2.2 Hz, CH), 130.4 (CH), 130.3 (d, *J* = 6.3 Hz, CH), 128.8 (d, *J* = 125.3 Hz, C_q), 128.5 (d, *J* = 11.2 Hz, CH), 127.5 (d, *J* = 8.7 Hz, CH), 127.1 (d, *J* = 125.5 Hz, C_q), 126.1 (d, *J* = 11.2 Hz, C_q), 125.0 (d, *J* = 9.3 Hz, C_q), 123.5 (d, *J* = 13.5 Hz, CH), 114.4 (CH), 113.8 (CH) , 61.9 (d, *J* = 6.3 Hz, CH_2), 55.2 (CH_3), 55.1 (CH_3), 16.4 (d, *J* = 6.2 Hz, CH_3).

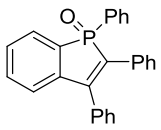
^{31}P NMR (122 MHz, $CDCl_3$): δ = 47.5.

IR (neat): 2988, 2933, 2836, 1243, 1218, 1174, 1022, 508 cm^{-1}.

MS (EI) *m/z* (relative intensity): 406 (100) $[M]^+$, 377 (40), 359 (30), 345 (10), 226 (10), 135 (10), 43 (30).

HR-MS (EI) *m/z* calcd for $C_{24}H_{24}O_4P^+$ $[M+H]^+$ 407.1407, found 407.1404.

1,2,3-Triphenylphosphindole 1-Oxide (117ga):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (99.1 mg, 0.49 mmol) and diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ga** (123.0 mg, 66%) as an off-white solid.

M. p. = 177–179 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81−7.68 (m, 3H), 7.48−7.31 (m, 10H), 7.25−7.22 (m, 3H), 7.11−7.07 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0 (d, *J* = 21.8 Hz, C_q), 143.7 (d, *J* = 27.2 Hz, C_q), 134.2 (d, *J* = 95.7 Hz, C_q), 134.2 (d, *J* = 15.2 Hz, C_q), 132.9 (d, *J* = 2.0 Hz, CH), 132.6 (d, *J* = 10.0 Hz, C_q), 132.12 (d, *J* = 2.9 Hz, CH), 132.0 (d, *J* = 105.7 Hz, C_q), 130.91 (d, *J* = 10.6 Hz, CH), 129.9 (d, *J* = 99.6 Hz, C_q),129.1 (d, *J* = 2.9 Hz, CH), 129.1 (d, *J* = 12.7 Hz, CH), 129.0 (br, CH), 128.9 (CH),

128.8 (d, *J* = 12.7 Hz, CH), 128.6 (CH), 128.2 (CH), 127.8 (CH), 124.0 (d, *J* = 10.8 Hz, CH).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 40.2.

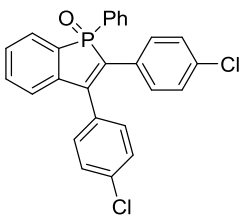
IR (neat): 3067, 3043, 1436, 1194, 766, 723, 691, 519 cm^{-1}.

MS (EI) *m/z* (relative intensity): 378 (60) $[M]^+$, 377 (100), 299 (25), 252 (20), 77 (5).

HR-MS (EI) *m/z* calcd for $C_{26}H_{19}OP^+$ $[M]^+$ 378.1168, found 378.1184.

The spectral data were in accordance with those reported in the literature.[127]

2,3-Bis(4-chlorophenyl)-1-phenyl-1*H*-phosphindole 1-Oxide (117ge):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (101.0 mg, 0.50 mmol) and 1,2-bis(4-chlorophenyl)ethyne (**11e**) (246.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ge** (143.0 mg, 64%) as a yellow gum.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67–7.60 (m, 3H), 7.42–7.28 (m, 7H), 7.19–7.07 (m, 5H), 7.02–6.99 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.0 (d, *J* = 21.5 Hz, C_q), 143.1 (d, *J* = 26.5 Hz, C_q), 134.9 (C_q), 134.0 (C_q), 133.8 (d, *J* = 95.6 Hz, C_q), 133.05 (d, *J* = 2.0 Hz, CH), 132.38 (d, *J* = 2.6 Hz, CH), 132.2 (d, *J* = 15.4 Hz, C_q), 131.7 (d, *J* = 106.2 Hz, C_q), 130.9 (d, *J* = 10.2 Hz, C_q), 130.8 (d, *J* = 10.7 Hz, CH), 130.4 (CH), 130.1 (d, *J* = 5.5 Hz, CH), 129.5 (d, *J* = 10.6 Hz, CH), 129.4 (CH), 129.3 (d, *J* = 9.8 Hz, CH), 129.2 (d, *J* = 100.0 Hz, C_q), 128.9 (d, *J* = 12.4, CH), 128.7 (CH), 123.9 (d, *J* = 10.9 Hz, CH).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 39.9.

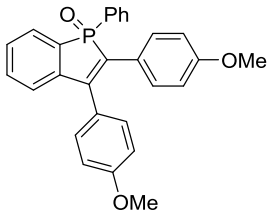
IR (neat): 3056, 2961, 1733, 1585, 1195, 1088, 1014, 844, 725 cm^{-1}.

MS (EI) *m/z* (relative intensity): 445 (100) $[M–H]^+$, 411 (10) $[M–Cl]^+$, 367 (15), 322 (10), 252 (15).

HR-MS (EI) *m/z* calcd for $C_{26}H_{17}Cl_2OP^+$ $[M]^+$ 446.0389, found 446.0386.

The spectral data were in accordance with those reported in the literature.[128]

2,3-Bis(4-methoxyphenyl)-1-phenylphosphindole 1-Oxide (117gc):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (101.0 mg, 0.50 mmol) and 1,2-bis(4-methoxylphenyl)ethyne (**11c**) (238.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117gc** (70.0 mg, 32 %) as a yellow solid.

M. p. = 85−87 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79–7.62 (m, 3H), 7.48–7.31 (m, 5H), 7.28–7.18 (m, 5H), 6.96 (dd, *J* = 8.8, 1.1 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 3.67 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ= 159.5 (C_q), 158.8 (C_q), 148.1 (d, *J* = 21.9 Hz, C_q), 144.0 (d, *J* = 27.2 Hz, C_q), 132.7 (d, *J* = 2.0 Hz), 132.6 (d, *J* = 97.0 Hz, C_q), 131.6 (d, *J* = 106 Hz, C_q), 130.8 (d, *J* = 10.6 Hz, CH), 130.3, 130.2 (d, *J* = 6.0 Hz, CH), 129.9 (d, *J* = 99 Hz, C_q), 128.8 (d, *J* = 9.4 Hz, CH), 128.7 (d, *J* = 12.2 Hz, CH), 128.5 (d, *J* = 10.6 Hz, CH), 128.4 (d, *J* = 12.2 Hz, CH), 126.3 (d, *J* = 15.5 Hz, CH), 125.1(d, *J* = 10.2 Hz, C_q), 123.6 (d, *J* = 10.9 Hz, C_q), 114.3 (CH), 113.6 (CH), 55.2 (CH_3), 55,0 (CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 39.5.

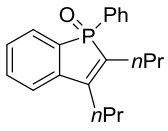
IR (neat): 3004, 2960, 2836, 1604, 1500, 1437, 1245, 1174 cm^{-1}.

MS (EI) *m/z* (relative intensity)**:** 438 (100) $[M]^+$, 423(10), 394 (10), 351 (5), 277 (15), 226 (5), 77 (5).

HR-MS (EI) *m/z* calcd for $C_{28}H_{23}O_3P^+$ $[M]^+$ 438.1379, found 438.1364.

The spectral data were in accordance with those reported in the literature.[128]

1-Phenyl-2,3-di-*n*-propyl-1*H*-phosphindole 1-Oxide (117gh):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (103.0 mg, 0.51 mmol) and oct-4-yne (**11h**) (115.0 mg, 1.04 mmol), heating at 100 °C for 4h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117gh** (87.0 mg, 55%) as a colorless solid.

M. p. = 78–80 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61–7.54 (m, 2H), 7.50–7.38 (m, 3H), 7.35–7.27 (m, 3H), 7.23–7.17 (m, 1H), 2.55–2.50 (m, 2H), 2.44–2.11 (m, 2H), 1.60–1.54 (m, 2H), 1.40–1.29 (m, 2H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.78 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.2 (d, *J* = 19.9 Hz, C_q), 143.5 (d, *J* = 29.2 Hz, C_q), 134.6 (d, *J* = 95.8 Hz, C_q), 132.6 (d, *J* = 2.0 Hz, CH), 132.2 (d, *J* = 105.3 Hz, C_q), 131.7 (d, *J* = 2.7 Hz, CH), 130.8 (d, *J* = 10.6 Hz, CH), 130.2 (d, *J* = 96.9 Hz, C_q), 128.6 (d, *J* = 11.8 Hz, CH), 128.5 (CH), 128.1 (d, *J* = 10.5 Hz, CH), 121.3 (d, *J* = 11.3 Hz, CH), 28.6 (d, *J* = 13.2 Hz, CH_2), 28.3 (d, *J* = 10.8 Hz, CH_2), 22.4 (d, *J* = 1.9 Hz, CH_2), 21.9(d, *J* = 1.9 Hz, CH_2), 14.5 (CH_3), 14.4 (CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 40.0.

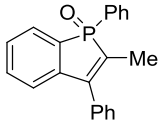
IR (neat): 3060, 2959, 2935, 2871, 1434, 1195, 1104, 690 cm^{-1}.

MS (EI) *m/z* (relative intensity): 310 (50) $[M]^+$, 295 (30), 281 (100), 265 (10), 253 (30).

HR-MS (EI) *m/z* calcd for $C_{20}H_{23}OP^+$ $[M]^+$ 310.1481, found 310.1483.

The spectral data were in accordance with those reported in the literature.[127]

2-Methyl-1,3-diphenylphosphindole 1-Oxide (117gi):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (120.0 mg, 0.59 mmol) and (prop-1-yn-1-ylbenzene) (**11i**) (120.0 mg, 1.03 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117gi** (99.0 mg, 53%) as a colorless solid.

M. p. = 87–89 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.64 (m, 2H), 7.61–7.55 (m, 1H), 7.47–7.32 (m, 7H), 7.29–7.19 (m, 3H), 7.04 (dd, *J* = 7.6, 3.0 Hz, 1H), 1.83 (d, *J* = 12.4 Hz, 3H).

^{13}C NMR (75 MHz $CDCl_3$): δ = 150.0 (d, *J* = 21.9 Hz, C_q), 144.2 (d, *J* = 28.1 Hz, C_q), 133.5 (d, *J* = 15.7 Hz, C_q), 132.8 (d, *J* = 2.0 Hz, CH), 132.2 (d, *J* = 2.9 Hz, CH), 132.0 (d, *J* = 96.7 Hz, C_q), 131.5 (d, *J* = 105.6 Hz, C_q), 130.9 (d, *J* = 10.6 Hz, CH), 129.2 (d, *J* = 98.2 Hz, C_q), 129.0(d, *J* = 9.5 Hz, C_q), 128.9 (d, *J* = 12.3 Hz, CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.3 (d, *J* = 10.6 Hz, CH), 123.1 (d, *J* = 11.1 Hz, CH), 10.7 (d, *J* = 10.7 Hz, CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 41.5.

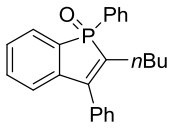
IR (neat): 3055, 1734, 1588, 1436, 1198, 1153, 1129, 722 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 (100) $[M]^+$, 315 (80)$[M–H]^+$, 301 (5), 237 (15), 191 (15), 165 (15), 77 (15).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}OP^+$ $[M]^+$ 316.1012, found 316.0997.

The spectral data were in accordance with those reported in the literature.[127]

2-*n*-Butyl-1,3-diphenylphosphindole 1-Oxide (117gn):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (122.0 mg, 0.60 mmol) and (hex-1-yn-1-yl)benzene (**11n**) (179.0 mg, 1.13 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117gn** (127.0 mg, 59%) as a colorless gum.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.64 (m, 2H), 7.55–7.49 (m, 1H), 7.47–7.36 (m, 5H), 7.29 (dt, *J* = 7.6, 1.5 Hz, 2H), 7.23–7.16 (m, 3H), 6.93 (ddt, *J* = 7.6, 3.0, 0.9 Hz, 1H), 2.43–2.28 (m, 1H), 2.19–2.04 (m, 1H), 1.35–1.17 (m, 2H), 1.12–0.93 (m, 2H), 0.56 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2 (d, *J* = 22.2 Hz, C_q), 144.2 (d, *J* = 28.0 Hz, C_q), 136.7 (d, *J* = 93.5 Hz, C_q), 133.8 (d, *J* = 16.2 Hz, C_q), 132.7 (d, *J* = 2.1 Hz, CH), 132.0 (d, *J* = 2.9 Hz, CH), 131.7 (d, *J* = 105.1 Hz, C_q), 130.8 (d, *J* = 10.6 Hz, CH), 130.0 (d, *J* = 97.2 Hz, C_q),128.7 (d, *J* = 10.1 Hz, CH), 128.7 (CH),128.6 (CH), 128.6 (CH), 128.4 (d, *J* = 10.6 Hz, CH), 128.4 (CH),

123.09 (d, J = 10.9 Hz, CH), 30.7 (d, J = 1.9 Hz, CH_2), 26.3 (d, J = 10.1 Hz, CH_2), 22.5 (CH_2), 13.4 (CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 39.9.

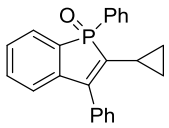
IR (neat): 3057, 2956, 2930, 2870, 1588, 1437, 1194, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity): 358 (20) $[M]^+$, 329 (40), 316 (100), 237 (15), 189 (10), 165 (10).

HR-MS (EI) *m/z* calcd for $C_{24}H_{23}OP^+$ $[M]^+$ 358.1481, found 358.1473.

The spectral data were in accordance with those reported in the literature.[128]

2-Cyclopropyl-1,3-diphenylphosphindole 1-Oxide (117go):



The general procedure **F** was followed using diphenylphosphine oxide (**121g**) (104.0 mg, 0.51 mmol) and (cyclopropylethynyl)benzene (**11o**) (142.0 mg, 1.00 mmol), heating at 100 °C for 2h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117go** (73.0 mg, 42%) as a colorless solid.

M. p. = 141–143 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.66 (m, 2H), 7.47–7.33 (m, 9H), 7.28 (td, J = 7.6, 1.5 Hz, 1H), 7.19–7.12 (m, 1H), 6.96 (dd, J = 7.6, 3.0 Hz, 1H), 1.64–1.50 (m, 1H), 1.22–1,14 (m, 1H), 0.73–0.64 (m, 1H), 0.47 (dd, J = 7.4, 7.4 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9 (d, J = 21.8 Hz, C_q), 143.5 (d, J = 26.6 Hz, C_q), 137.2 (d, J = 96.6 Hz, C_q), 134.0 (d, J = 15.3 Hz, C_q), 132.7 (d, J = 2.1 Hz, CH), 132.0 (d, J = 2.9 Hz, CH), 131.7 (d, J = 106.4 Hz, C_q), 130.7 (d, J = 10.7 Hz, CH), 130.4 (d, J = 97.6 Hz, C_q),128.9 (CH), 128.8 (d, J = 12.3 Hz, CH) 128.6 (CH), 128.5 (d, J = 10.1 Hz, CH), 128.4 (CH), 128.1 (d, J = 10.7 Hz, CH), 122.4 (d, J = 10.8 Hz, CH), 10.9 (d, J = 9.3 Hz, CH), 7.3 (d, J = 3.0 Hz, CH_2), 6.9 (d, J = 2.3 Hz, CH_2).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 38.6.

IR (neat): 3056, 1585, 1438, 1191, 1173, 778, 753, 719 cm^{-1}.

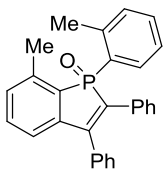
MS (EI) *m/z* (relative intensity): 342 (100) $[M]^+$, 327 (10), 263 (20), 215 (20), 43 (20).

HR-MS (EI) *m/z* calcd for $C_{23}H_{19}OP^+$ $[M]^+$ 342.1168, found 342.1169.

Annulation with di-*o*-tolylphosphine oxide (**121h**):

The general procedure **F** was followed using di-*o*-tolylphosphine oxide (**121h**) (115.0 mg, 0.50 mmol) and diphenylacetylene (**11a**) (179.0 mg, 1.00 mmol), heating at 120 °C for 12h. Purification by column chromatography (*n*-hexane/EtOAc: 2/1) yielded **117ha** (47.0 mg, 23%) and**117ha'**(95.0 mg, 47%) ascolorless solids.

7-Methyl-2,3-diphenyl-1-(*o*-tolyl)phosphindole 1-Oxide (117ha):



M. p. = 163–165 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32 (ddd, *J* = 13.5, 7.3, 1.9 Hz, 1H), 7.41–7.28 (m, 6H), 7.16–7.08 (m, 2H), 7.16–7.08 (m, 4H), 7.06–6.98 (m, 4H), 2.29 (s, 3H), 2.16 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.0 (d, *J* = 21.6 Hz, C_q), 144.5 (d, *J* = 27.1 Hz, C_q), 141.0 (d, *J* = 9.2 Hz, C_q), 140.4 (d, *J* = 11.3 Hz, C_q), 134.7 (d, *J* = 8.9 Hz, CH), 134.5 (d, *J* = 14.9 Hz, C_q), 133.6 (d, *J* = 95.2 Hz, C_q),132.9 (C_q), 132.8 (d, *J* = 1.1 Hz, CH), 132.0 (d, *J* = 2.8 Hz, CH), 131.3 (d, *J* = 11.2 Hz, CH), 130.6 (d, *J* = 9.3 Hz, CH), 129.4 (d, *J* = 104.3 Hz, C_q), 128.8 (CH), 128.7 (CH), 128.7 (CH), 128.4 (CH), 128.0 (CH), 127.4 (d, *J* = 94.9 Hz, C_q), 127.5 (d, *J* = 1.2 Hz, CH), 126.1 (d, *J* = 11.5 Hz, CH), 121.8 (d, *J* = 10.7 Hz, CH), 20.0 (d, *J* = 4.2 Hz, CH), 19.3 (d, *J* = 4.6 Hz, CH).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 37.4.

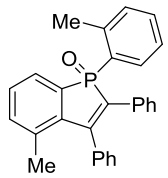
IR (neat): 3057, 1560, 1444, 1186, 793, 753, 714, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity): 406 (100) $[M]^+$, 391 (10), 329 (15), 313 (10), 265 (10), 228 (40), 181 (10).

HR-MS (EI) *m/z* calcd for $C_{28}H_{23}OP^+$ $[M]^+$ 406.1481, found 406.1497.

The spectral data were in accordance with those reported in the literature.[128]

4-Methyl-2,3-diphenyl-1-(*o*-tolyl)phosphindole 1-Oxide (117ha'):



M. p. = 69–71 °C

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.16 (ddd, *J* = 13.6, 7.6, 1.5 Hz, 1H), 7.48 (ddd, *J* = 10.4, 6.8, 1.5 Hz, 1H), 7.39–7.27 (m, 5H), 7.26–7.18 (m, 4H), 7.16–7.05 (m, 3H), 7.04−6.99 (m, 3H), 2.25 (s, 3H), 1.74 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3 (d, *J* = 21.3 Hz, C_q), 141.1 (d, *J* = 10.8 Hz, C_q), 140.8 (d, *J* = 26.3 Hz, C_q), 137.6 (d, *J* = 15.1 Hz, C_q), 137.3 (d, *J* = 2.1 Hz, CH), 135.6 (d, *J* = 10.7 Hz, C_q), 135.3 (d, *J* = 91.5 Hz, C_q), 134.2 (d, *J* = 9.5 Hz, CH), 132.9 (d, *J* = 9.5 Hz, C_q), 132.6 (d, *J* = 104 Hz, C_q), 132.2 (d, *J* = 2.9 Hz, CH), 131.4 (d, *J* = 11.3 Hz, CH), 129.1 (d, *J* = 11.2 Hz, CH), 128.8 (d, *J* = 5.4 Hz, CH), 128.5 (d, *J* = 3.8 Hz, CH), 128.1 (d, *J* = 12.9 Hz, CH), 128.1 (d, *J* = 1.3 Hz, CH), 128.0 (CH), 127.6 (d, *J* = 96.5 Hz, C_q), 127.5 (CH), 127.0 (d, *J* = 10.3 Hz, CH), 126.0 (d, *J* = 11.8 Hz, CH), 21.4 (CH_3), 20.2 (d, *J* = 4.1 Hz, CH_3).

^{31}P NMR (122 MHz, $CDCl_3$): δ = 38.2.

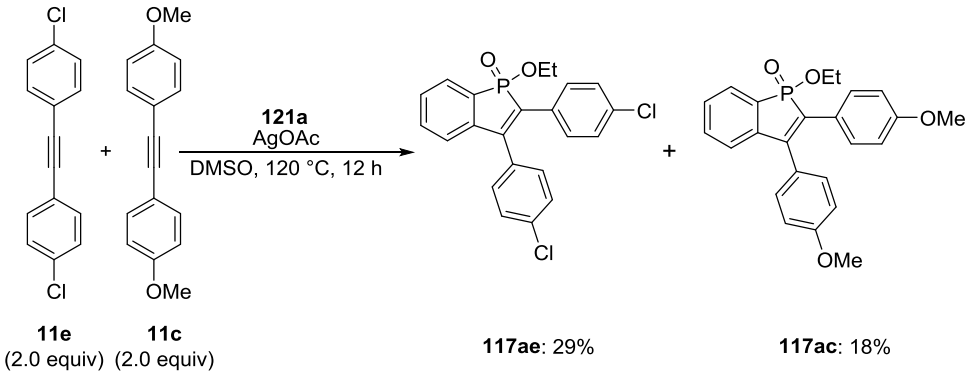
IR (neat): 3056, 2928, 1591, 1442, 1194, 1173, 812, 714 cm^{-1}.

MS (EI) *m/z* (relative intensity): 406 (100) $[M]^+$, 391 (5), 329 (15), 313 (5), 265 (15), 228 (80), 210 (20), 181 (15).

HR-MS (EI) *m/z* calcd for $C_{28}H_{23}OP^+$ $[M]^+$ 406.1481, found 406.1485.

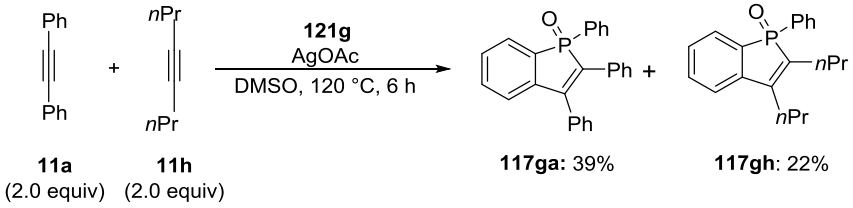
The spectral data were in accordance with those reported in the literature.[128]

Intermolecular Competition Experiment between Alkynes 11e and 11c:



A mixture of ethyl phenylphosphinate (**121a**) (85.0 mg, 0.50 mmol), 1,2-bis(4-chlorophenyl)ethyne (**11e**) (248.0 mg, 1.00 mmol), 1,2-bis(4-methoxyphenyl)ethyne (**11c**) (238.0 mg, 1.00 mmol) and AgOAc (166.0 mg, 1.0 mmol) in DMSO (2.0 mL) was stirred at 120 °C for 12h under N_2. At ambient temperature, the reaction mixture was diluted with H_2O and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude products were purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→ 2/1) to yield **117ae** (60 mg, 29%) and **117ac** (37.0 mg, 18%) as light yellow solids. The spectral data of compounds **117ae** and **117ac** were identical to those reported above.

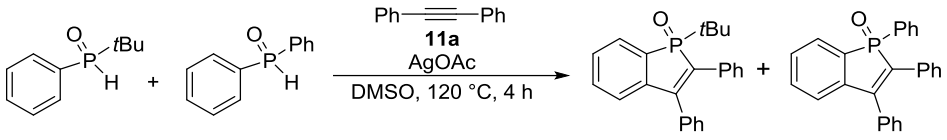
Intermolecular Competition Experiment between Alkynes 11a and 11h



A mixture of diphenylphosphine oxide (**121g**) (100.4 mg, 0.50 mmol), diphenylacetylene (**11a**) (178.0 mg, 1.00 mmol), oct-4-yne (**11h**) (110.0 mg, 1.00 mmol) and AgOAc (332.0 mg, 2.00 mmol) in DMSO (2.0 mL) was stirred at 120 °C for 6h under N_2. At ambient temperature, the reaction mixture was diluted with H_2O and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude products were purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→ 2/1) to yield **117ga** (74.0 mg, 38%) and **117gh** (34.0 mg, 22%) as light yellow solids. The spectral

data of compounds **117ga** and **117gh** were identical to those reported above.

Intermolecular Competition Experiment between Phosphine Oxides 121b and 121g



121b (1.0 equiv) **121g** (1.0 equiv) **117ba**: 22% **117ga**: 17%

A mixture of diphenylacetylene (**11a**) (89.0 mg, 0.50 mmol), *tert*-butyl(phenyl)phosphine oxide (**121b**) (91.3 mg, 0.50 mmol), diphenylphosphine oxide (**121g**) (101.0 mg, 0.50 mmol), AgOAc (168 mg, 1.00mmol) in DMSO (2.0 mL) was stirred at 120 °C for 4h under N_2. At ambient temperature, the reaction mixture was diluted with water and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→ 2/1) to yield **117ba** (40.0 mg, 22%) and **117ga** (32.0 mg, 17%) as light yellow solids. The spectral data of compounds **117ba** and **117ga** were identical to those reported above.

9 List of Abbreviations

Å	Ångström	ESI	electronspray ionization
Ac	acetyl	Et	ethyl
Ad	adamantly	FG	functional group
Alk	alkyl	g	gram
AMLA	ambiphilic metal-ligand activation	GC	gas chromatography
aq.	aqueous	h	hour
Ar	aryl	Het	hetero(aryl)
APT	attached proton test	Hept	heptyl
atm	*atmospheric pressure*	HPLC	high performance liquid chromatography
ATR	attenuated total reflectance	HR-MS	high resolution mass spectrometry
BIES	Base-assisted internal electrophilic substitution	Hz	Hertz
		i	*iso*
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl	IES	internal electrophilic substitution
Bn	benzyl	IR	infrared spectroscopy
Boc	*tert*-butyloxycarbonyl	*J*	coupling constant
Bu	butyl	KIE	kinetic isotope effect
Bz	benzoyl	L	ligand
calc.	calculated	Leu	leucine
cat.	catalytic	*m*	meta
CMD	concerted-metalation-deprotonation	m	multiplet
cod	1,5-cyclooctadien	M	molar
conv.	conversion	$[M^+]$	molecular ion peak
Cp	cyclopentadienyl	Me	methyl
Cy	cyclohexyl	Mes	mesityl
δ	chemical shift	mg	milligram
d	doublet	MHz	megahertz
DCM	dichloromethane	min	minute
dd	doublet of doublet	mL	milliliter
DFT	density functional theory	mmol	millimol
DG	directing group	M. p.	melting point
DMA	*N*,*N*-dimethylacetamide	MPV	membrane pump vacuum
DME	dimethoxyethane	MS	mass spectrometry
DMF	*N*,*N*-dimethylformamide	*m/z*	mass-to-charge ratio
DMSO	dimethyl sulfoxide	*n*	*normal*
DPPB	1,4-Bis(diphenylphosphino)butane	NBS	*N*-bromosuccinimide
DPPH	2,2-diphenyl-1-picrylhydrazyl	NHC	*N*-heterocyclic carbene
dt	doublet of triplet	NIS	*N*-iodosuccinimide
Ed.	editor	NMP	*N*-methylpyrrolidinone
EI	electron ionization	NMR	nuclear magnetic resonance
equiv	equivalent	NXS	*N*-halosuccinimides

o	ortho	SPS	solvent purification system
OPV	oil pump vacuum	*t*	*tert*
p	para	t	triplet
Ph	phenyl	*T*	temperature
Piv	pivaloyl	TEMPO	2,2,6,6-tetramethylpiperidin-1-yloxy
ppm	parts per million	Tf	trifluoromethanesulfonate
Pr	propyl	TFA	trifluoroacetic acid
PTSA	*p*-toluenesulfonic acid	TFAA	trifluoroacetic anhydride
Py	pyridyl	THF	tetrahydrofuran
PyDipSi	pyridyldiisopropylsilyl	TLC	thin layer chromatography
pym	pyrimidyl	TM	transition metal
q	quartet	TMS	trimethylsilyl
R	rest	Ts	*para*-toluenesulfonyl
rac	racemic	TS	transition state
ref.	reference	$\tilde{\nu}$	absorption
s	singlet	wt%	weight by volume
sat.	saturated	X	(pseudo)halide
sec	*secondary*	PyDipSi	pyridyldiisopropylsilyl
S_E^{Ar}	electrophilic aromatic substitution	XPhos	2-dicyclohexylphosphino-2′,4′,6′-tri-isopropylbiphenyl
SET	single electron transfer		
SPO	secondary phosphine oxides		

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