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, wählle ich fuer mich aus, und was ich an ihm nicht gut finde, das ändere ich.
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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 arylation reagents and therefore leads to more environmentally friendly and atom-economical\(^{1p}r\) processes (Scheme 1).

\[\text{Scheme 1 Traditional cross-coupling (a) vs. direct C–H arylation (b).}\]

A variety of transition metals such as palladium-\(^{1c,1j,1l,1m}\), ruthenium-\(^{1a,1d}\), rhodium-\(^{1g}\), cobalt-\(^{1b,1k}\)

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and nickel-catalyzed\textsuperscript{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 deficient late 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\textsuperscript{5a} and Eisenstein.\textsuperscript{5b}

\begin{equation}
\text{oxidative addition}
\begin{align*}
(i) & \quad \text{L}_n \text{M} + \text{H} \rightarrow \text{L}_n \text{M} \text{H} \rightarrow \left[ \text{L}_n \text{M} - \text{H} \right] \rightarrow \text{L}_n \text{M} \text{H} \\
(ii) & \quad \text{L}_n \text{M}^{\text{R}} + \text{H} \rightarrow \left[ \text{L}_n \text{M}^{\text{R}} - \text{H} \right] \rightarrow \text{L}_n \text{M}^{\text{R}} + \text{H} \\
(iii) & \quad \text{L}_n \text{M} \oplus \text{X} + \text{H} \rightarrow \left[ \text{L}_n \text{M} \oplus \text{X} - \text{H} \right] \rightarrow \text{L}_n \text{M} \oplus \text{X} \\
(iv) & \quad \text{L}_n \text{M}^{\text{X}} + \text{H} \rightarrow \left[ \text{L}_n \text{M}^{\text{X}} - \text{H} \right] \rightarrow \text{L}_n \text{M}^{\text{X}} \text{H} \\
(v) & \quad \text{L}_n \text{M}^{\text{O}} \text{O}^{\text{R}} + \text{H} \rightarrow \left[ \text{L}_n \text{M}^{\text{O}} \text{O}^{\text{R}} - \text{H} \right] \rightarrow \text{L}_n \text{M}^{\text{O}} \text{O}^{\text{R}} \text{H}
\end{align*}
\end{equation}

Scheme 2 Different Mechanisms for C–H Bond Metalation.

However, more recent computational mechanistic studies carried out by Ess and Periana\textsuperscript{6} showed that quantitative dissection of directional charge-transfer stabilization (orbital occupied to unoccupied stabilization) between the metal-ligand complex and the C(sp\textsuperscript{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


(heteroatom-substituted) secondary phosphine oxides\(^7\) or most prominently carboxylates (Scheme 2).\(^8\)

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 \(\text{Na}_2[\text{PdCl}_4]\) 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 \([\text{Cp*IrCl}_2]\) at ambient temperature. Detailed mechanistic studies through computational studies provided evidence for acetate-promoted process.

Based on these previous studies, Fagnou\(^10\) reported palladium-catalyzed direct arylation 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 \textit{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 \textit{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 \([\text{Ir(acac}^\dagger)\_2(X)] (X = \text{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

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

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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](image)

**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

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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). 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.

<table>
<thead>
<tr>
<th>additive</th>
<th>HIPrCl</th>
<th>PPh₃</th>
<th>Ad₂PO(H)</th>
<th>(PhO)₂PO(H)</th>
<th>NaOAc</th>
<th>AdCO₂H</th>
<th>tBuCO₂H</th>
<th>MesCO₂H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (%)</td>
<td>0</td>
<td>9</td>
<td>20</td>
<td>85</td>
<td>50</td>
<td>79</td>
<td>85</td>
<td>66</td>
</tr>
</tbody>
</table>

**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, a research area that so far had largely been dominated by the use of more expensive rhodium or palladium 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). Notably, optimization studies revealed less expensive [RuCl₂(p-cymene)]₂ to be

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optimal among a variety of ruthenium complexes, while Cu(OAc)$_2$·H$_2$O was found to be the terminal oxidant of choice. The annulation reaction occurred efficiently in polar protic solvent tAmOH, 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 annihilations with amides 10.](image)

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.](image)

Subsequently, Ackermann’s and Wang’s group developed two protocols for the synthesis of isoquinolones by ruthenium-catalyzed redox-neutral annihilations of alkynes with \( N \)-methoxy- and \( N \)-hydroxybenzamides 18, respectively (Scheme 8). 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 annihilations of alkynes.

![Scheme 8](image)

Scheme 8 Ruthenium-catalyzed alkyne annihilations 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\(^\text{25}\) developed a new approach to ruthenium-catalyzed oxidative annihilations employing simple aniline derivatives 20 (Scheme 9). Notable features of the new protocol include the unprecedented use of cationic ruthenium(II) complexes for oxidative annihilations 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](image)

Scheme 9 Pyrimidine-directed ruthenium-catalyzed alkyne annihilations.

Shortly after, the same group reported on the ruthenium-catalyzed oxidative annihilation of alkynes with ambient air as the ideal sacrificial oxidant.\(^\text{26}\) The aerobic annihilation reactions were accomplished with co-catalytic amounts of Cu(OAc)\(_2\)-H\(_2\)O employing differently substituted 2-arylindoles 22. Moreover, the remarkably broad scope of the ruthenium catalyst was exploited


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, 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 subsequently developed an alternative reaction procedure wherein the metal catalyst can be recycled 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 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](image.png)

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). 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.

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**Introduction**

![Scheme 1](image1.png)

**Scheme 1** 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 acetonilide, 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 2](image2.png)

**Scheme 2** 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

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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 alkyne with 2-aryl-1,3-dicarbonyl **33** compounds. These annulations of alkyne 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**.

Shortly thereafter, inspired by previous works on hydroxyl-directed transition-metal-catalyzed C–H bond functionalization, Wang\textsuperscript{41} developed a ruthenium-catalyzed vinilative dearomatization reaction of 1-aryl-2-naphthols 36 \textit{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.

\begin{scheme}
\begin{center}
\includegraphics[width=0.8\textwidth]{Scheme_15}
\end{center}
\caption{Ruthenium(II)-catalyzed alkyne annulations with 1-aryl-2-naphthols 36.}
\end{scheme}

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

\begin{scheme}
\begin{center}
\includegraphics[width=0.8\textwidth]{Scheme_16}
\end{center}
\caption{Ruthenium-catalyzed alkyne annulations with substituted amidines 38 and ketimines 40.}
\end{scheme}

\textsuperscript{43} J. Li, L. Ackermann, \textit{Tetrahedron} \textbf{2014}, \textit{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-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.](image)

### 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


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 organosilicones (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 preactivated starting materials (Scheme 18c). Therefore, different methods for the preparation of styrene derivatives by cross-dehydrogenative olefination reaction were reported in the past decades. 53

(a) Mizoroki-Heck reaction

(b) Alkenylation via transmetalation

(c) Twofold C–H bond functionalization

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.

Introduction

To overcome this disadvantage, a new method that utilized a directing group preinstalled in the substrate has been explored in recent years.\textsuperscript{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.\textsuperscript{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\textsuperscript{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\textsuperscript{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

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

\[
\text{Scheme 20 Ruthenium-catalyzed direct hydroalkylations of phenones 42.}
\]

Subsequently, Yi\textsuperscript{55} reported on chelation-assisted coupling reactions of arylamides 10 and unactivated alkenes 50 (Scheme 21). The cationic ruthenium hydride complex \([\eta^6-C_6H_6](PCy_3)(CO)RuH]^+\text{BF}_4^-\) 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.

\[
\text{Scheme 21 Ruthenium-catalyzed alkenylations of substituted benzamides 10.}
\]

Shortly thereafter, a great number of ruthenium-catalyzed alkenylation reactions appeared in the literature, and these transformations were rapidly expanded to a variety of directing groups (Scheme 22), including esters, anilines, amides, carboxylic acids, ketones, aldehydes, oxazolines, pyrazoles, triazoles and azoxybenzenes.\textsuperscript{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

the oxidative C–H bond alkenylations were also viable in an aerobic fashion, using cocatalytic amounts of Cu(OAc)$_2$·H$_2$O 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.\textsuperscript{60,54m}

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)$_2$·H$_2$O 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)\textsuperscript{61} and Ackermann


(Scheme 23b)\textsuperscript{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.

\[ \text{Scheme 23} \]

**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).\textsuperscript{54aa}

\[]

In 2008, Miura\textsuperscript{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-diallylbenzenes 72 which are important organic intermediates in material science (Scheme 25b).

In 2011, Zhang’s group\textsuperscript{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.

\begin{footnotesize}

\end{footnotesize}
Introduction

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

Subsequently, Huang and coworkers\(^\text{65}\) 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\(^\text{66}\) and subsequently Wang’s\(^\text{67}\) 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).

Scheme 28 Ruthenium-catalyzed C–H alkenylations of aryl carbamates 77.

Besides this, You’s group\(^\text{68}\) 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.

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A variety of differently substituted substrates 79 could be employed in this transformation, giving the ortho-alkenylation 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-alkenylation phenols 71 or ortho-alkylphenols (Scheme 29).

![Scheme 29 Palladium-catalyzed C–H alkenylations of aryl (2-pyridyl)methyl ethers 79.](image)

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).\(^\text{69a}\) 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).\(^\text{70b}\) 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).


Furthermore, Ge\textsuperscript{70} and Gevorgyan\textsuperscript{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).

Additionally, Song\textsuperscript{72} and Wang\textsuperscript{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\textsubscript{2} as the terminal oxidant allows performing this reaction in an economical fashion (Scheme 32).

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

Afterwards, rhodium-catalyzed C(sp^3)–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 rBuOH. 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.

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, Yu75a-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

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

\[ a) \]

![Scheme 3.4](image)

\[ b) \]

Scheme 3.4 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 through 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\(^3\))–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. 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 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

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six-membered ring formation.

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

Inspired by this study, in 2005, Daugulis\(^7^8\) 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^3^)–H or C(sp^3^)–H bond arylations, but also allowed for alkylations \(^7^9\), alkynylation \(^8^0\), acetoxylation \(^8^1\), aminations \(^8^2\), iodonations \(^8^3\) and selenations \(^8^4\). Importantly, ruthenium \(^8^5\), copper \(^8^6\), nickel \(^8^7\),

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\(^8^3\) H. Kodama, T. Katutira, T. Nishida, T. Hino, K. Tsubata, 2001, Patent WO 2001083421A

rhodium\textsuperscript{88c} and iron\textsuperscript{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.](image)

In 2014, Ackermann and coworkers\textsuperscript{89} found easily accessible 1,2,3-triazoles \textbf{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 compatible 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\textsuperscript{3})–H arylations of arenes, but also enabled more challenging C(sp\textsuperscript{3})–H functionalizations (Scheme 37).

\begin{flushleft}
\end{flushleft}
Although the iron-catalyzed C(sp^3)–H and C(sp^3)–H alkylations achieved in high yields with broad substrate scope, these transformations involve using of expensive diphosphine ligand, stoichiometric amounts of sacrificial oxidants which make this reaction not in an 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 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).

Very recently, Daugulis and coworkers reported on the cobalt(II)-catalyzed alkyne annihilations assisted by bidentate directing group in the presence of Mn(OAc)\(_2\) as the oxidant (Scheme 39). Electron-rich or electron-poor, amides were efficiently annulated, and a large variety of alkynes could be employed. Additionally, heteroarene-substituted amides were also suitable in this cobalt catalyzed system. It is noteworthy that terminal alkynes were reactive and gave the product in good yields with excellent chemo- and regioselectivity.
Shortly thereafter, the same research group extended the scope of this reaction to alkenylations using an analogous method.\(^\text{92}\) 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.](image)

### 1.5 Transition Metal-Catalyzed Benzophosphole Syntheses

Phosphorus-containing heterocycles represent important structural building blocks in organic synthesis, medicinal chemistry, and material science.\(^\text{93}\) They have been found widespread applications ranging from ligands in transition metal complexes\(^\text{94}\) to organic semiconductor devices in material science.\(^\text{95}\) 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 \(\text{di(benzo[}\text{b}]\text{phosphole oxide)benzene (DBPOB, 113)}\), electron-transporting material (ETM) \(\text{di(benzo[}\text{b}]\text{phosphole) sulfide(DBPSB, 114)}\)\(^\text{96}\) and highly luminescent \(\pi\)-conjugated materials 115.\(^\text{97}\) Therefore, there is a continued strong demand for chemo- and site-selective syntheses of this heteroaromatic scaffold.


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 41). However, these cyclization reactions were performed under strongly basic reaction conditions which reduced the functional group tolerance.

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 tetrayne \(^{120}\) (Scheme 42). These reactions proceeded in CH\(_2\)Cl\(_2\) 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.

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Shortly thereafter, Takai\textsuperscript{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 \textit{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 \textbf{122} were synthesized using this method.

Encouraged by Takai’s study, Nozaki\textsuperscript{105} reported on palladium-catalyzed intramolecular arylation reaction of phosphine triflate \textbf{123}. After the final oxidation with \text{H}_2\text{O}_2 at ambient temperature, the desired dibenzophosphole products were obtained in high yields (Scheme 45). It is noteworthy that the $\lambda^5$-phospha[7]helicenes \textbf{117} obtained by this method exhibited unique packing structure.
However, the instability of the hydrophosphine group in 123 limited the applicability of this method towards the synthesis of more complicated compound. Thus, this method needs considerable improvement. In this context, in 2013, Chatani\textsuperscript{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.

\textbf{Scheme 46} Palladium-catalyzed direct synthesis of phosphole derivatives from triarylphosphines 125.

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 stoichiometric 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).

\[
\begin{align*}
\text{Scheme 47 Ruthenium-catalyzed oxidative annulations with substituted pyrazoles 126.}
\end{align*}
\]

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


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

\begin{center}
\textbf{Scheme 48} Ruthenium-catalyzed oxidative alkenylations with substituted 2-aryl sulfonic acids \textbf{128}.
\end{center}

In the transition metal-catalyzed alkenylations, directing groups were usually introduced to achieve site-selective C–H functionalization.\textsuperscript{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-aryloxy pyridines \textbf{130}\textsuperscript{112a-c} as a preparative approach to the synthetically valuable alkenylated phenols \textbf{78}\textsuperscript{112d,e} in the third part of this work.

\begin{center}
\textbf{Scheme 49} Ruthenium-catalyzed oxidative alkenylations with substituted 2-aryloxy pyridines \textbf{130}.
\end{center}

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.\textsuperscript{1c, 113} Thus, we became attracted by cobalt-catalyzed C–H/N–H functionalization reactions of substituted benzamides \textbf{110} with activated alkenes \textbf{46} (Scheme \textbf{50}).


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 50 Cobalt-catalyzed oxidative functionalizations with benzamides 110.

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 1H-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. 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-arylpymrazole 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 AgSbF₆ as an additive, giving the desired product in 78% yield (entry 8). The carboxylate additives such as NaOAc, MesCO₂K 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)·H₂O in the presence of air (entry 9). Likewise, the desired oxidative annulation was not accomplished with CuBr₂ in lieu of Cu(OAc)₂·H₂O 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 tAmOH 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).

### 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 diphenylacetylene (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 methoxy 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-arylpiazoles 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

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**Table 1** Optimization of oxidative annulation with pyrazole 126

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>−</td>
<td>DCE</td>
<td>100</td>
<td>13</td>
</tr>
<tr>
<td>2</td>
<td>NaOAc</td>
<td>DCE</td>
<td>100</td>
<td>19</td>
</tr>
<tr>
<td>3</td>
<td>CsOAc</td>
<td>DCE</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>KO2CMes</td>
<td>DCE</td>
<td>100</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>KPF6</td>
<td>DCE</td>
<td>100</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>AgSO2CF3</td>
<td>DCE</td>
<td>100</td>
<td>38</td>
</tr>
<tr>
<td>7</td>
<td>AgBF4</td>
<td>DCE</td>
<td>100</td>
<td>46</td>
</tr>
<tr>
<td>8</td>
<td>AgSbF6</td>
<td>DCE</td>
<td>100</td>
<td>78</td>
</tr>
<tr>
<td>9</td>
<td>AgSbF6</td>
<td>DCE</td>
<td>100</td>
<td>77b</td>
</tr>
<tr>
<td>10</td>
<td>AgSbF6</td>
<td>DCE</td>
<td>100</td>
<td>0c</td>
</tr>
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<td>11</td>
<td>AgSbF6</td>
<td>DCE</td>
<td>100</td>
<td>0d</td>
</tr>
<tr>
<td>12</td>
<td>AgSbF6</td>
<td>NMP</td>
<td>120</td>
<td>0</td>
</tr>
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<td>120</td>
<td>41</td>
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<td>120</td>
<td>12</td>
</tr>
<tr>
<td>15</td>
<td>AgSbF6</td>
<td>1,4-dioxane</td>
<td>120</td>
<td>17</td>
</tr>
<tr>
<td>16</td>
<td>AgSbF6</td>
<td>DMF</td>
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<tr>
<td>17</td>
<td>AgSbF6</td>
<td>H2O</td>
<td>120</td>
<td>13</td>
</tr>
</tbody>
</table>

*Reaction conditions: 126a (0.5 mmol), 11a (1.0 mmol), Cu(OAc)2·H2O (1.0 mmol), [RuCl2(p-cymene)]2 (5.0 mol %), additive (20 mol %); isolated yields. *b* 1.0 equiv of oxidant. *c* CuBr2 as oxidant. *d* No catalyst.
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–l

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pyrazole 126</th>
<th>Product 127</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>126a</td>
<td>127aa</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>126b</td>
<td>127ba</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>126c</td>
<td>127ca</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>126d</td>
<td>127da</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>126e</td>
<td>127ea</td>
<td>76</td>
</tr>
</tbody>
</table>
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), diphenylacetylenes 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–11l 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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pyrazole 126</th>
<th>Alkyne 11</th>
<th>Product 127</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Pyrazole 126a" /></td>
<td><img src="image2" alt="Alkyne 11b" /></td>
<td><img src="image3" alt="Product 127ab" /></td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td><img src="image1" alt="Pyrazole 126a" /></td>
<td><img src="image4" alt="Alkyne 11c" /></td>
<td><img src="image5" alt="Product 127ac" /></td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td><img src="image1" alt="Pyrazole 126a" /></td>
<td><img src="image6" alt="Alkyne 11d" /></td>
<td><img src="image7" alt="Product 127ad" /></td>
<td>59</td>
</tr>
</tbody>
</table>

Ruthenium-Catalyzed Oxidative Alkyne Annulations
Ruthenium-Catalyzed Oxidative Alkyne Annulations

4. \[ R^2 = R^3 = \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126a
   \]
   \[
   11e
   \]
   \[
   127ae
   \]

5. \[ R^2 = R^3 = \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126a
   \]
   \[
   11f
   \]
   \[
   127af
   \]

6. \[ R^2 = R^3 = \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126a
   \]
   \[
   11g
   \]
   \[
   127ag
   \]

7. \[ nPr \equiv nPr \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126a
   \]
   \[
   11h
   \]
   \[
   127ah
   \]

8. \[ nPr \equiv nPr \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126i
   \]
   \[
   11h
   \]
   \[
   127ih
   \]

9. \[ nPr \equiv nPr \]
   \[
   \begin{array}{c}
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{H} \\
   \text{N} \\
   \text{O}_2\text{N} \\
   \end{array}
   \]
   \[
   126d
   \]
   \[
   11h
   \]
   \[
   127dh
   \]

10. \[ nPr \equiv nPr \]
    \[
    \begin{array}{c}
    \text{O}_2\text{N} \\
    \text{N} \\
    \text{H} \\
    \text{N} \\
    \text{H} \\
    \text{N} \\
    \text{O}_2\text{N} \\
    \text{N} \\
    \text{H} \\
    \text{N} \\
    \text{H} \\
    \text{N} \\
    \text{O}_2\text{N} \\
    \end{array}
    \]
    \[
    126b
    \]
    \[
    11h
    \]
    \[
    127bh
    \]
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 aryl pyrazoles 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.\textsuperscript{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).
Ruthenium-Catalyzed Oxidative Alkyne Annulations

(a)

\[
\begin{align*}
&\text{MeO} \quad \text{Ph} \quad \text{Ph} \\
&126f \quad (1.0 \text{ equiv}) + \\
&126a \quad (1.0 \text{ equiv}) \\
\end{align*}
\]

\[11a [\text{RuCl}_2(p\text{-cymene})_2] \quad (10 \text{ mol } \%)
\]

\[\text{AgSbF}_5 (40 \text{ mol } \%)
\]

\[\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O}
\]

\[\text{DCE}, \quad 100^\circ \text{C}, \quad 20 \text{ h}
\]

\[\text{under air}
\]

\[127fa: 19\%
\]

\[127aa: 27\%
\]

(b)

\[
\begin{align*}
&\text{Ph} \quad \text{Ph} \\
&\text{Ph} \quad n\text{Pr} \\
&11a \quad (3.0 \text{ equiv}) + \\
&11h \quad (3.0 \text{ equiv}) \\
\end{align*}
\]

\[126a [\text{RuCl}_2(p\text{-cymene})_2] \quad (5.0 \text{ mol } \%)
\]

\[\text{AgSbF}_5 (20 \text{ mol } \%)
\]

\[\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O}
\]

\[\text{DCE}, 100^\circ \text{C}, \quad 20 \text{ h}
\]

\[\text{under air}
\]

\[127ah: 11\%
\]

(c)

\[
\begin{align*}
&\text{OMe} \quad \text{F} \\
&\text{OMe} \quad \text{OMe} \\
&\text{OMe} \quad \text{OMe} \\
&11c \quad (3.0 \text{ equiv}) + \\
&11d \quad (3.0 \text{ equiv}) \\
\end{align*}
\]

\[126a [\text{RuCl}_2(p\text{-cymene})_2] \quad (5.0 \text{ mol } \%)
\]

\[\text{AgSbF}_5 (20 \text{ mol } \%)
\]

\[\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O}
\]

\[\text{DCE}, 100^\circ \text{C}, \quad 20 \text{ h}
\]

\[\text{under air}
\]

\[127ac: 32\%
\]

\[127ad: 14\%
\]

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$_2$O 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.

\[ \text{Scheme 53 Oxidative annulations with D$_2$O as the cosolvent.} \]

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($p$-cyrene)Cl]$_2$ can be replaced with SbF$_6$– and OAc– ones through interaction with AgSbF$_6$ assisted by of Cu(OAc)$_2$·H$_2$O 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 \textit{via} a reoxidation process.
Scheme S4 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. 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. 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)$_2$·H$_2$O (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$_2$CMe)$_2$(p-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

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Ruthenium-Catalyzed Oxidative Alkenylations of Arenes

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Additive</th>
<th>cat.[Ru]</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMA</td>
<td>---</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>43</td>
</tr>
<tr>
<td>2</td>
<td>DMA</td>
<td>MesCOOK</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>DMA</td>
<td>KPF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>DMA</td>
<td>NaOAc</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>56</td>
</tr>
<tr>
<td>5</td>
<td>DMA</td>
<td>AgSO$_2$CF$_3$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>52</td>
</tr>
<tr>
<td>6</td>
<td>DMA</td>
<td>AgPF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>58</td>
</tr>
<tr>
<td>7</td>
<td>DMA</td>
<td>AgBF$_4$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>56</td>
</tr>
<tr>
<td>8</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>91</td>
</tr>
<tr>
<td>9</td>
<td>DMF</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>70</td>
</tr>
<tr>
<td>10</td>
<td>DCE</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>11</td>
<td>tAmOH</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>12</td>
<td>1,4-dioxane</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>13</td>
<td>H$_2$O</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>14</td>
<td>PhMe</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>15</td>
<td>NMP</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>85</td>
</tr>
<tr>
<td>16</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>---</td>
<td>0$^b$</td>
</tr>
<tr>
<td>17</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>RuCl$_3$</td>
<td>0</td>
</tr>
<tr>
<td>18</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[Ru(O$_2$CMes)$_2$(p-cymene)]</td>
<td>trace</td>
</tr>
<tr>
<td>19</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(PPh$_3$)$_2$]</td>
<td>trace</td>
</tr>
<tr>
<td>20</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>0$^c$</td>
</tr>
<tr>
<td>21</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>85$^d$</td>
</tr>
<tr>
<td>22</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>59$^e$</td>
</tr>
<tr>
<td>23</td>
<td>DMA</td>
<td>AgSbF$_6$</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>48$^f$</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 128a (0.50 mmol), 46b (1.50 mmol), [RuCl$_2$(p-cymene)]$_2$ (5.0 mol %), additive (20 mol %), Cu(OAc)$_2$·H$_2$O (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) pre catalyst 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-diestereoselectivities. 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 129jb 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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sulfonic Acid 128</th>
<th>Product 129</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>128b</td>
<td>129bb</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>128c</td>
<td>129cb</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>128d</td>
<td>129db</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>128e</td>
<td>129eb</td>
<td>91</td>
</tr>
</tbody>
</table>
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-Vinyl-naphthalene (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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkene 46</th>
<th>Product 129</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{CO}_2\text{Et}$</td>
<td>R = Et (129lb)</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>$\text{CO}_2\text{Me}$</td>
<td>R = Me (129lc)</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>$\text{CO}_2\text{Bn}$</td>
<td>R = Bn (129ld)</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>$\text{CO}_2\text{Et}$</td>
<td>R = Et (129le)</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>$\text{CO}_2\text{Me}$</td>
<td>R = Me (129lf)</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>$\text{SO}_2\text{Ph}$</td>
<td>R = Ph (129lg)</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>$\text{CN}$</td>
<td>R = CN (129lh)</td>
<td>75</td>
</tr>
</tbody>
</table>

129lh (E:Z = 5:1)
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 bisalkenylation product 129jb2 was obtained as well, albeit in low yield (Scheme 55b).
4.1.3 Mechanistic studies

4.1.3.1 Intermolecular 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 128i and 128h which revealed electron-rich aromatic sulfonic acid 128i to be preferentially converted (Scheme 56).

4.1.3.2 Ruthenium-Catalyzed H/D Exchange Experiment

Further experimental support to provide the mechanistic rationale was obtained from oxidative alkenylations with D₂O 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$_2$O 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-cymene)]$_2$ species reacted with AgSbF$_6$ and Cu(OAc)$_2$·H$_2$O 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 Alkenylation of Arenes 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,\textsuperscript{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\textsubscript{6} (20 mol %) as an additive in tAmOH (entry 5). Importantly, this alkenylation product was also obtained in 73% yield with cocatalytic amounts of Cu(OAc)\textsubscript{2}·H\textsubscript{2}O 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)\textsubscript{2}·H\textsubscript{2}O or the ruthenium catalyst (entries 7 and 8).

![Table 7 Optimization of C–H bond alkenylation of substituted pyridine 130a](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Cu(OAc)\textsubscript{2}·H\textsubscript{2}O</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>KO\textsubscript{2}CMes</td>
<td>2.0</td>
<td>&lt;5</td>
</tr>
<tr>
<td>2</td>
<td>CsOAc</td>
<td>2.0</td>
<td>&lt;5</td>
</tr>
<tr>
<td>3</td>
<td>AgOAc</td>
<td>2.0</td>
<td>&lt;5</td>
</tr>
<tr>
<td>4</td>
<td>KPF\textsubscript{6}</td>
<td>2.0</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>AgSbF\textsubscript{6}</td>
<td>2.0</td>
<td><strong>83</strong></td>
</tr>
<tr>
<td>6</td>
<td>AgSbF\textsubscript{6}</td>
<td>0.3</td>
<td>73</td>
</tr>
<tr>
<td>7</td>
<td>AgSbF\textsubscript{6}</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>AgSbF\textsubscript{6}</td>
<td>2.0</td>
<td>0\textsuperscript{b}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: 130a (1.0 mmol), 46b (0.5 mmol), Cu(OAc)\textsubscript{2}·H\textsubscript{2}O (1.0 mmol), [RuCl\textsubscript{2}(p-cymene)]\textsubscript{2} (2.5 mol %), tAmOH (2.0 mL), AgSbF\textsubscript{6} (10 mol %); isolated yields.

\textsuperscript{b} Without [RuCl\textsubscript{2}(p-cymene)]\textsubscript{2}.

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 phenoxylypyridine 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-yl-oxy)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)\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phenol 130</th>
<th>Alkene 46</th>
<th>Product 131</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130a</td>
<td>46b</td>
<td>R\textsuperscript{2} = Et (131ab)</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>130a</td>
<td>46p</td>
<td>R\textsuperscript{2} = tBu (131ap)</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>130a</td>
<td>46d</td>
<td>R\textsuperscript{2} = Bn (131ad)</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>130b</td>
<td>46b</td>
<td>R\textsuperscript{2} = Et (131bb)</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>130b</td>
<td>46p</td>
<td>R\textsuperscript{2} = tBu (131bp)</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>130c</td>
<td>46b</td>
<td>R\textsuperscript{2} = Et (131cb)</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>130c</td>
<td>46p</td>
<td>R\textsuperscript{2} = tBu (131cp)</td>
<td>87</td>
</tr>
<tr>
<td>8</td>
<td>130d</td>
<td>46d</td>
<td>R\textsuperscript{2} = Bn (131cd)</td>
<td>92</td>
</tr>
</tbody>
</table>
Ruthenium-Catalyzed Oxidative Alkenylations of Arenes

9  
![Chemical Structure](130d.png)  
\[ R_2 = \text{Et} (131\text{db}) \]  
69

10  
![Chemical Structure](130e.png)  
\[ R_2 = \text{Et} (131\text{eb}) \]  
81

11  
![Chemical Structure](130f.png)  
\[ R_2 = \text{tBu} (131\text{ep}) \]  
79

12  
![Chemical Structure](130g.png)  
\[ R_2 = \text{Et} (131\text{fb}) \]  
82

13  
![Chemical Structure](131d.png)  
\[ R_2 = \text{tBu} (131\text{fp}) \]  
73

14  
![Chemical Structure](130h.png)  
\[ R_2 = \text{tBu} (131\text{gb}) \]  
76

15  
![Chemical Structure](130i.png)  
\[ R_2 = \text{tBu} (131\text{gp}) \]  
75

16  
![Chemical Structure](130j.png)  
\[ R_2 = \text{Bn} (131\text{gd}) \]  
82

17  
![Chemical Structure](130k.png)  
\[ R_2 = \text{Et} (131\text{hb}) \]  
76

18  
![Chemical Structure](130l.png)  
\[ R_2 = \text{tBu} (131\text{hp}) \]  
82

19  
![Chemical Structure](130m.png)  
\[ R_2 = \text{Bn} (131\text{hd}) \]  
88

20  
![Chemical Structure](130n.png)  
\[ R_2 = \text{Et} (131\text{ib}) \]  
78

21  
![Chemical Structure](130o.png)  
\[ R_2 = \text{tBu} (131\text{ip}) \]  
74

22  
![Chemical Structure](130p.png)  
\[ R_2 = \text{Et} (131\text{jb}) \]  
0

*Reaction conditions: 130 (1.0 mmol), 46 (0.5 mmol), Cu(OAc)$_2$·H$_2$O (1.0 mmol), [RuCl$_2$($\eta$-cymene)]$_2$ (2.5 mol %), tAmOH (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-alkenylation.
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*
Ruthenium-Catalyzed Oxidative Alkenylations of Arenes

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-ylxy directing group was less compatible in this reaction and hence gave an unsatisfactory yield (Scheme 59c).

\[ \text{Reaction conditions: } \text{130} (1.0 \text{ mmol}), \text{46} (0.5 \text{ mmol}), \text{Cu(OAc)}_2 \cdot \text{H}_2 \text{O} (1.0 \text{ mmol}), [\text{RuCl}_2(\text{p-cymene})]_2 (2.5–5 \text{ mol }%), \text{tAmOH} (2.0 \text{ mL}), \text{AgSbF}_6 (10–20 \text{ mol }%); \text{isolated yields.} \]
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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 130</th>
<th>Alkene 46</th>
<th>Product 131</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130w</td>
<td>46b</td>
<td>R² = Et (131wb)</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>130p</td>
<td>46p</td>
<td>R² = tBu (131wp)</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>130x</td>
<td>46b</td>
<td>R² = Et (131yb)</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>130y</td>
<td>46p</td>
<td>R² = tBu (131yp)</td>
<td>79</td>
</tr>
</tbody>
</table>

*Reaction conditions: 130 (1.0 mmol), 46 (0.5 mmol), Cu(OAc)₂·H₂O (1.0 mmol), [RuCl₂(p-cymene)]₂ (2.5 mol %), AgSbF₆ (10 mol %), tAmOH (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-enooate (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).
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-yl oxy cinnamate 131ab employing the previously published protocol, thereby yielding the desired free phenol 71a in high yield (Scheme 61).

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.
4.2.4.2 H/D Exchange Experiment

Mechanistic studies on the oxidative alkenylations in the presence of D$_2$O 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).
Ruthenium-Catalyzed Oxidative Alkenylations of Arenes

Scheme 63 Oxidative alkenylation with D$_2$O as the cosolvent.

4.2.5 Proposed Catalytic Cycle

Based on these studies and literature precedence, we propose 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-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)$_2$·H$_2$O 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, annihilations, aminations and hydroxylations. 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. In recent years, Yoshikai 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 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 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.

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 and ethyl acrylate. Unfortunately, no desired product was obtained (Table 11, entries 1–3). Further attempts showed that not the alkylated, but the cyclic product isoindolin-1-one could be obtained in 37% yield in the presence of 20 mol% Co(OAc)₂ and 2.0 equivalents of base using

---


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$_3$CH$_2$OH (4/1) proved to be optimal, affording the product 132ab in 60% yield. The oxidants such as AgOAc, AgCOF$_3$, AgNO$_3$, AgCO$_3$ and AgCO$_2$Ad 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$_3$CH$_2$OH = 4/1) at 100 °C under air (entry 34).

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>cat.[Co]</th>
<th>Solvent</th>
<th>Oxidant</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Cp*CoI$_2$]$_2$</td>
<td>CF$_3$CH$_2$OH</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>2</td>
<td>Co(acac)$_2$</td>
<td>CF$_3$CH$_2$OH</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>3</td>
<td>Co(OAc)$_2$</td>
<td>CF$_3$CH$_2$OH</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>4</td>
<td>Co(OAc)$_2$</td>
<td>PEG 400</td>
<td>Mn(OAc)$_2$</td>
<td>37</td>
</tr>
<tr>
<td>5</td>
<td>Co(OAc)$_2$</td>
<td>PEG 400</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^{b,c}$</td>
</tr>
<tr>
<td>6</td>
<td>Co(OAc)$_2$</td>
<td>Toluene</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>7</td>
<td>Co(OAc)$_2$</td>
<td>DMF</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>8</td>
<td>Co(OAc)$_2$</td>
<td>DMSO</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>Co(OAc)$_2$</td>
<td>1,4-dioxane</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>Co(OAc)$_2$</td>
<td>PhCl</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>Co(OAc)$_2$</td>
<td>PEG1000</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>12</td>
<td>Co(OAc)$_2$</td>
<td>DMPU</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>13</td>
<td>Co(OAc)$_2$</td>
<td>DCE</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>Co(OAc)$_2$</td>
<td>PEG 400/H$_2$O (4/1)</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>Co(OAc)$_2$</td>
<td>PEG 400/CF$_3$CH$_2$OH (4/1)</td>
<td>Mn(OAc)$_2$</td>
<td>60</td>
</tr>
<tr>
<td>16</td>
<td>Co(OAc)$_2$</td>
<td>glycerol</td>
<td>Mn(OAc)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>17</td>
<td>Co(OAc)$_2$</td>
<td>ethylene glycol</td>
<td>Mn(OAc)$_2$</td>
<td>&lt;5$^b$</td>
</tr>
<tr>
<td>18</td>
<td>---</td>
<td>PEG 400/CF$_3$CH$_2$OH (4/1)</td>
<td>Ag$_2$SO$_4$</td>
<td>39$^b$</td>
</tr>
<tr>
<td>19</td>
<td>Co(OAc)$_2$</td>
<td>PEG 400/CF$_3$CH$_2$OH (4/1)</td>
<td>Ag$_2$SO$_4$</td>
<td>39$^b$</td>
</tr>
</tbody>
</table>

---
Table 12 Scope of cobalt-catalyzed annulations with amides (110)$^a$
### Cobalt-Catalyzed Oxidative C–H Alkenylations

\[
\begin{align*}
\text{Amide} 110 & \quad + \quad \text{Alkene} 46 & \rightarrow & \text{Product} 132 \\
\text{Co(OAc)}_2 (20 \text{ mol %}) & \quad \text{AgOPiv} (2.0 \text{ equiv}) & \quad 100^\circ \text{C}, 18 \text{ h, air} & \quad \text{PEG 400/CF}_2\text{CH}_2\text{OH} (4/1)
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amide 110</th>
<th>Alkene 46</th>
<th>Product 132</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="110b" /></td>
<td><img src="image2" alt="46b" /></td>
<td><img src="image3" alt="132bb" /></td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td><img src="image4" alt="110b" /></td>
<td><img src="image5" alt="46d" /></td>
<td><img src="image6" alt="132bd" /></td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td><img src="image7" alt="110b" /></td>
<td><img src="image8" alt="46h" /></td>
<td><img src="image9" alt="132bh" /></td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td><img src="image10" alt="110b" /></td>
<td><img src="image11" alt="46f" /></td>
<td><img src="image12" alt="132bf" /></td>
<td>61</td>
</tr>
<tr>
<td>5</td>
<td><img src="image13" alt="110a" /></td>
<td><img src="image14" alt="46b" /></td>
<td><img src="image15" alt="132ab" /></td>
<td>73</td>
</tr>
<tr>
<td>6</td>
<td><img src="image16" alt="110a" /></td>
<td><img src="image17" alt="46f" /></td>
<td><img src="image18" alt="132af" /></td>
<td>63</td>
</tr>
<tr>
<td>7</td>
<td><img src="image19" alt="110c" /></td>
<td><img src="image20" alt="46b" /></td>
<td><img src="image21" alt="132cb" /></td>
<td>56</td>
</tr>
</tbody>
</table>
Cobalt-Catalyzed Oxidative C–H Alkenylations

8. **110d**

9. **110e**

10. **110f**

11. **110g**

12. **110h**

13. **110i**

14. **110j**

15. **110k**

---

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Cl</td>
<td><strong>110d</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>9</td>
<td>Br</td>
<td><strong>110e</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>10</td>
<td>I</td>
<td><strong>110f</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>11</td>
<td>NC</td>
<td><strong>110g</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>12</td>
<td>O$_2$N</td>
<td><strong>110h</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>13</td>
<td>F$_3$C</td>
<td><strong>110i</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td><strong>110j</strong></td>
<td>CO$_2$Et</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td><strong>110k</strong></td>
<td>CO$_2$Et</td>
</tr>
</tbody>
</table>
**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,\textsuperscript{78} Yu,\textsuperscript{121} Chatani\textsuperscript{122} and Shi,\textsuperscript{123} benzamides 147, 149–153 with bidentate auxiliaries did not afford the desired products. Reaction of benzamide 148 bearing a TAM directing group,\textsuperscript{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.](image)

### 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).

---


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.

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]$_3$-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.
Cobalt-Catalyzed Oxidative C–H Alkenylations

5.3.3 Kinetic Isotope Effect Studies

Furthermore, cobalt-catalyzed C–H alkenylations with isotopically labeled substrate \([\text{D}_4]-110b\) revealed an intermolecular kinetic isotope effect (KIE) of \(k_H/k_D \approx 1.4\) (Scheme 69a), and the intramolecular KIE determined with substrate \([\text{D}]_1-110b\) 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)
5.4 Proposed Catalytic Cycle

Based on the mechanistic studies discussed above and taking into account previous report, 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. 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[\textit{b}]phospholes. 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 \textit{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. 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, we became attracted by silver-mediated C−H/P−H functionalization of substituted phosphate oxides with alkynes for the convenient benzo[\textit{b}]phosphole oxides synthesis.

6.1. Optimization Studies

Our initial efforts focused on the annulation of diphenylacetylene (\textit{11a}) with ethyl phenylphosphinate (\textit{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$_2$CO$_3$, Ag$_2$O or AgOTs led to inferior results (entries 10−12), whereas only traces of the product were obtained when using AgO$_2$CCF$_3$ or AgO$_3$SCF$_3$ (entries 13 and 14). Switching the oxidant from silver salts

Silver-Mediated Alkyne Annulations by C–H/P–H Functionalizations

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

![Diagram](https://example.com/diagram.png)

<table>
<thead>
<tr>
<th>Entry</th>
<th>cat.</th>
<th>Solvent</th>
<th>Oxidant</th>
<th>T ($^\circ$C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[RuCl$_2$(p-cymene)]$_2$</td>
<td>DCE</td>
<td>AgOAc</td>
<td>80</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>---</td>
<td>DCE</td>
<td>AgOAc</td>
<td>80</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>---</td>
<td>DCE</td>
<td>AgOAc</td>
<td>120</td>
<td>46</td>
</tr>
<tr>
<td>4</td>
<td>---</td>
<td>o-xylene</td>
<td>AgOAc</td>
<td>120</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>---</td>
<td>tAmOH</td>
<td>AgOAc</td>
<td>120</td>
<td>51</td>
</tr>
<tr>
<td>6</td>
<td>---</td>
<td>DMF</td>
<td>AgOAc</td>
<td>120</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>---</td>
<td>DMSO</td>
<td>AgOAc</td>
<td>120</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>---</td>
<td>NMP</td>
<td>AgOAc</td>
<td>120</td>
<td>52</td>
</tr>
<tr>
<td>9</td>
<td>---</td>
<td>DMA</td>
<td>AgOAc</td>
<td>120</td>
<td>51</td>
</tr>
<tr>
<td>10</td>
<td>---</td>
<td>DMSO</td>
<td>Ag$_2$CO$_3$</td>
<td>120</td>
<td>31</td>
</tr>
<tr>
<td>11</td>
<td>---</td>
<td>DMSO</td>
<td>Ag$_2$O</td>
<td>120</td>
<td>25</td>
</tr>
<tr>
<td>12</td>
<td>---</td>
<td>DMSO</td>
<td>AgOT$_3$</td>
<td>120</td>
<td>17</td>
</tr>
<tr>
<td>13</td>
<td>---</td>
<td>DMSO</td>
<td>AgO$_2$SCF$_3$</td>
<td>120</td>
<td>trace</td>
</tr>
<tr>
<td>14</td>
<td>---</td>
<td>DMSO</td>
<td>AgO$_2$CCF$_3$</td>
<td>120</td>
<td>trace</td>
</tr>
<tr>
<td>15</td>
<td>---</td>
<td>DMSO</td>
<td>Zn(OAc)$_2$</td>
<td>120</td>
<td>trace</td>
</tr>
<tr>
<td>16</td>
<td>---</td>
<td>DMSO</td>
<td>MnO$_2$</td>
<td>120</td>
<td>trace</td>
</tr>
<tr>
<td>17</td>
<td>---</td>
<td>DMSO</td>
<td>AgOAc</td>
<td>120</td>
<td>trace$^b$</td>
</tr>
</tbody>
</table>

$^a$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

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

Table 14 Oxidative annulations of substrates 121 with diphenylacetylene (11a)\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phosphine Oxide 121</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Product 117</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>121a</td>
<td>120</td>
<td>12</td>
<td>117aa</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>121b</td>
<td>120</td>
<td>12</td>
<td>117ba</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>121c</td>
<td>120</td>
<td>12</td>
<td>117ca</td>
<td>49</td>
</tr>
<tr>
<td>4</td>
<td>121d</td>
<td>100</td>
<td>2</td>
<td>117da</td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td>121e</td>
<td>120</td>
<td>2</td>
<td>117ea</td>
<td>46</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: 121 (0.50 mmol), 11a (1.00 mmol), AgOAc (2.0 equiv), DMSO (2.0 mL), under N\textsubscript{2}; isolated yield.

Scheme 71 Silver-mediated oxidative annulation 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.\(^\text{126}\)

**Table 15** Scope of oxidative annulation for phosphine oxide**121** with alkynes **11a**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phosphine Oxide 121</th>
<th>Alkyne 11</th>
<th>Product 117</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Phosphine Oxide" /></td>
<td><img src="image" alt="Alkyne" /></td>
<td><img src="image" alt="Product" /></td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Phosphine Oxide" /></td>
<td><img src="image" alt="Alkyne" /></td>
<td><img src="image" alt="Product" /></td>
<td>64</td>
</tr>
</tbody>
</table>

Silver-Mediated Alkyne Annulations by C–H/P–H Functionalizations

3. $\text{121a}$  

4. $\text{121a}$  

5. $\text{121g}$  

6. $\text{121g}$  

7. $\text{121g}$  

8. $\text{121g}$  

9. $\text{121g}$
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.](image)

### 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)

![Scheme 73 Intermolecular competition experiments.](image)
An intermolecular competition experiment between \textit{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\textsuperscript{127} and Miura\textsuperscript{128}, we proposed a plausible mechanism for this silver-mediated reaction (Scheme 75). First, a phosphoryl radical 158 was generated from di-\textit{o}-tolylphosphine oxide (121h) through a P–H bond cleavage \textit{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 \textit{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

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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 1H-pyrazoles 126 by C–H/N–H bond functionalizations under air. In this project, the desired oxidative annulation was not accomplished with CuBr₂ in lieu of Cu(OAc)₂·H₂O 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 alkenes 11 such as dialkylalkynes and tolanes were also suitable substrates under the optimized reaction conditions. Furthermore, oxidative annulations with unsymmetrically substituted alkenes 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.
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.

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

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.
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 annihilations 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)$_2$·H$_2$O 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 annihilations 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 N₂ atmosphere using pre-dried glassware 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-Amyl alcohol (tAmOH) was used as supplied by Merck or stirred over sodium chips for 5 h at 120 °C and distilled under ambient pressure; water (H₂O) 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 CaH₂ 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 CaH₂ 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 from BARLOWO-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 KMnO₄ 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, 0.2 μm) prior to separation.

**Nuclear Magnetic Resonance Spectroscopy (NMR)**
Nuclear magnetic resonance (NMR) spectroscopy was performed at 300 400 or 600 MHz (*¹H NMR*), 75, 100 or 125 MHz (*¹³C NMR, APT*), 283 MHz (*¹⁹F NMR*) and 122 MHz (*³¹P 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 (ṽ) 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 microTOF from 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
- Pyrazoles 126a–126l, 141, 130
- Arylsulfonic acids 128d, 128f, 128g, 128h
- 1,2-Phenoxyypyridines 130a–130y, 141, 132
- Pyrimidines 142 and 143, 134
- Amides 110a–110r, 147, 149, 150, 152, 153
- Isotopically labeled substrates [D]5-110b, 136
- Phenylphosphinates 121a, 121f
- SPOs 121b–121e, 121g–121h

The following compound was obtained by the generous courtesy of the person named below:

Karsten Rauch: [RuCl2(p-cymene)]2.

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8.3 General Procedures

General Procedure A: Ruthenium-Catalyzed Oxidative Alkyne Annulation with Substituted 1H-Pyrazoles (126)
A suspension of 5-(4-nitrophenyl)-1H-pyrazole (126a) (95.0 mg, 0.50 mmol), diphenylacetylene (11a) (178.0 mg, 1.00 mmol), [RuCl₂(p-cymene)]₂ (15.3 mg, 5.0 mol %), AgSbF₆ (34.3 mg, 20 mol %) and Cu(OAc)₂·H₂O (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. NH₄Cl/NH₃ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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), [RuCl₂(p-cymene)]₂ (15.3 mg, 5.0 mol %), AgSbF₆ (34.4 mg, 20 mol %) and Cu(OAc)₂·H₂O (200 mg, 1.00 mmol) in DMA (2.0 mL) was stirred at ambient temperature under N₂ 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 (CH₂Cl₂/MeOH: 15/1→10/1) to yield 129ab (131.0 mg, 91%) as an off-white solid.

General Procedure C: 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), [RuCl₂(p-cymene)]₂ (15.3 mg, 5.0 mol %), AgSbF₆ (35.0 mg, 0.10 mmol, 20 mol %) and Cu(OAc)₂·H₂O (200.0 mg, 1.00 mmol) in DMF (2.0 mL) was stirred at ambient temperature under N₂ 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 (CH₂Cl₂/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-tolyl)pyridine (130a) (185.4 mg, 1.00 mmol), ethyl acrylate (46b) (52.0
mg, 0.52 mmol), [RuCl₂(p-cymene)]₂ (7.6 mg, 2.5 mol %), AgSbF₆ (18.5 mg, 10 mol %) and Cu(OAc)₂·H₂O (200 mg, 1.00 mmol) in tAmOH (2.0 mL) was stirred at ambient temperature under N₂ 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. NH₄Cl/NH₃ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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 CF₃CH₂OH (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 H₂O and extracted with tBuOMe (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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 N₂ 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 Na₂SO₄. 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 1H-Pyrazoles by C–H/N–H Bond Functionalizations

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

The general procedure A was followed using 5-(4-nitrophenyl)-1H-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.

1H NMR (300 MHz, d6-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).

13C NMR (75 MHz, d6-DMSO): δ = 145.7 (Cq), 140.9 (CH), 137.3 (Cq), 136.1 (Cq), 134.0 (Cq), 131.7 (Cq), 130.8 (CH), 130.1 (CH), 128.9 (Cq), 127.9 (CH), 127.7 (CH), 127.3 (CH), 127.1 (CH), 127.0 (Cq), 125.1 (CH), 122.5 (Cq), 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 calcld for C23H15N2+[M]+ 365.1159, found 365.1154.

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

The general procedure A was followed using 5-{4-(trifluoromethyl)phenyl}-1H-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.

1H NMR (300 MHz, CDCl3): 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).

13C NMR (75 MHz, CDCl3): δ = 141.4 (CH), 137.7 (Cq), 137.7 (Cq), 135.1 (Cq), 132.6 (Cq), 131.4 (CH), 130.7 (CH), 129.7 (Cq), 129.5 (J_C-F = 33 Hz, Cq), 128.6 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 126.2 (Cq), 125.8 (Cq), 124.3 (CH), 124.0 (J_C-F = 273 Hz, Cq), 123.9 (J_C-F = 4 Hz, CH), 123.9 (J_C-F = 4 Hz, CH), 98.8 (CH).

19F NMR (CDCl3, 283 MHz): δ = −62.3 (s).

IR (neat): 3065, 1355, 1309, 1123, 1078, 787, 754, 694 cm⁻¹.
MS (El) 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_{23}H_{16}F_{3}N_{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)-1H-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$_3$): $\delta$ = 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$_3$): $\delta$ = 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 (El) 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-(1H-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$_3$): $\delta$ = 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$_3$): $\delta$ = 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)-1H-pyrazole (126e) (98.0 mg, 0.50 mmol) 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.

1H 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).

13C 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)-1H-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.

1H NMR (300 MHz, CDCl₃): 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).

13C NMR (75 MHz, CDCl₃): δ = 159.1 (C_q), 141.1 (CH), 138.6 (C_q), 136.7 (C_q), 136.2 (C_q), 133.2 (C_q), 131.5 (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 (CH₃).
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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 C₃₂H₁₉N₂O⁺ [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-α]isoquinoline (127ga)

The general procedure A was followed using 5-(4-methylphenyl)-1H-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.

¹H NMR (300 MHz, CDCl₃): δ = 8.11 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 2.1 Hz, 1H), 7.42–7.16 (m, 11H), 7.07 (d, J = 2.2 Hz, 1H), 2.40 (s, 3H).

¹³C NMR (75 MHz, CDCl₃): δ = 141.0 (CH), 138.6 (C₉), 137.7 (C₉), 136.4 (C₉), 136.2 (C₉), 133.2 (C₉), 131.6 (CH), 130.8 (CH), 130.0 (C₉), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.1 (CH), 126.3 (CH), 123.8 (C₉), 123.5 (CH), 121.8 (C₉), 97.0 (CH), 21.8 (CH₃).

IR (neat): 3051, 3023, 1622, 1481, 1412, 1347, 813, 762 cm⁻¹.


HR-MS (EI) m/z calcd for C₂₄H₁₉N₂O⁺ [M+H]+ 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-α]isoquinolin (127ha):

The general procedure A was followed using N,N-dimethyl-4-(1H-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.

¹H NMR (300 MHz, CDCl₃): 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).

¹³C NMR (75 MHz, CDCl₃): δ = 149.6 (C₉), 141.0 (CH), 138.9 (C₉), 136.5 (C₉), 136.4 (C₉), 133.5 (C₉), 131.5 (CH), 131.4 (C₉), 130.8 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.0 (CH), 124.7
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(CH), 123.6 (Cq), 115.2 (Cq), 114.4 (CH), 107.7 (CH), 95.5 (CH), 40.5 (CH3).

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–NMe2]⁺, 290 (7), 180 (40), 159 (25), 131 (10).

HR-MS (ESI) m/z calcd for C25H22N3⁺ [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)-1H-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.

1H NMR (300 MHz, d6-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).

13C NMR (75 MHz, CDCl3): δ = 140.8 (CH), 138.3 (Cq), 136.3 (Cq), 136.1 (Cq), 133.1 (Cq), 132.5 (Cq), 132.1 (Cq), 131.6 (CH), 130.9 (CH), 128.5 (Cq), 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 (Cq), 122.5 (Cq), 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 C27H19N2⁺ [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)-1H-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.

1H NMR (300 MHz, CDCl3): 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).
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\(^{13}\text{C NMR}\) (75 MHz, CDCl\(_3\)): \(\delta = 146.0\) (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** (EI) \(m/z\) calcd for C\(_{23}\)H\(_{15}\)N\(_3\)O\(_2\)\(^+\) [M\(^+\)] 365.1159, found 365.1160.

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

The general procedure \(A\) was followed using 1-methyl-3-(1H-pyrazol-5-yl)-1\text{-H}-indole (126l) (97.0 mg, 0.49 mmol), and diphenylacetylene (11a) (182.0 mg, 1.02 mmol) and Cu(OAc)\(_2\)\cdot H\(_2\)O (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.

**\(^{1}\text{H NMR}\)** (300 MHz, CDCl\(_3\)): \(\delta = 8.19\) (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).

**\(^{13}\text{C NMR}\)** (75 MHz, CDCl\(_3\)): \(\delta = 142.2\) (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\(_3\)O\(_2\)\(^+\) [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\text{-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.

**\(^{1}\text{H NMR}\)** (300 MHz, CDCl\(_3\)): \(\delta = 8.48–8.23\) (m, 3H), 8.04 (d, \(J = 2.3\) Hz, 1H), 7.34–6.98 (m, 9H), 2.37 (s, 3H), 2.33 (s, 3H).
**Experimental Section**

\[ ^{13}C \text{ NMR} (75 \text{ MHz, CDCl}_3): \delta = 146.7 (C_q), 141.5 (CH), 138.6 (C_q), 138.5 (C_q), 137.5 (C_q), 137.2 (C_q), 131.6 (C_q), 131.1 (CH), 130.4 (CH), 129.3 (C_q), 129.2 (CH), 128.8 (CH), 127.8 (C_q), 124.7 (CH), 123.6 (C_q), 122.6 (CH), 121.3 (CH), 99.8 (CH), 21.4 (CH), 21.3 (CH). \]

**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) \(m/z\) calcld for C\(_{25}\)H\(_{19}\)N\(_3\)O\(_2\) \([M]\)^+ 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.

**\(^1H \text{ NMR}\) (300 MHz, CDCl\(_3\)): \(\delta = 8.38–8.28\) (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).**

**\(^{13}C \text{ NMR}\) (75 MHz, CDCl\(_3\)): \(\delta = 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) \(m/z\) calcld for C\(_{25}\)H\(_{20}\)N\(_3\)O\(_4\) \([M+H]^+\) 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.

**\(^1H \text{ NMR}\) (300 MHz, CDCl\(_3\)): \(\delta = 8.40 (dd, J = 8.8, 2.2\) 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).**

**\(^{13}C \text{ NMR}\) (75 MHz, CDCl\(_3\)): \(\delta = 162.7 (J_{C,F} = 250\) Hz, C\(_q\)), 162.3 (J\(_{C,F} = 250\) Hz, C\(_q\)), 146.9...**
(C\textsubscript{q}), 141.9 (CH), 137.7 (C\textsubscript{q}), 137.3 (C\textsubscript{q}), 133.1 (\textsuperscript{3}J\textsubscript{C-F} = 8 Hz, CH), 132.6 (\textsuperscript{3}J\textsubscript{C-F} = 8 Hz, CH), 130.4 (\textsuperscript{4}J\textsubscript{C-F} = 3 Hz, C\textsubscript{q}), 130.0 (C\textsubscript{q}), 128.0 (\textsuperscript{4}J\textsubscript{C-F} = 3 Hz, C\textsubscript{q}), 127.9 (C\textsubscript{q}), 124.9 (CH), 123.0 (C\textsubscript{q}), 122.3 (CH), 121.8 (CH), 115.9 (\textsuperscript{2}J\textsubscript{C-F} = 22 Hz, CH), 115.4 (\textsuperscript{2}J\textsubscript{C-F} = 22 Hz, CH), 100.2 (CH).

$^{19}$F NMR (283 MHz, CDCl\textsubscript{3}): $\delta = -111.23$ (s), $-112.84$ (s).

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

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

HR-MS (ESI) m/z calcd for C\textsubscript{23}H\textsubscript{14}F\textsubscript{2}N\textsubscript{3}O\textsubscript{2}+ [M+H]\textsuperscript{+} 402.1049, found 402.1034.

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

![Chemical structure](image)

The general procedure A was followed using 5-(4-nitrophenyl)-1H-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\textsubscript{3}): $\delta = 8.37$ (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\textsubscript{3}): $\delta = 146.9$ (C\textsubscript{q}), 141.9 (CH), 137.4 (C\textsubscript{q}), 137.3 (C\textsubscript{q}), 135.3 (C\textsubscript{q}), 134.4 (C\textsubscript{q}), 132.8 (C\textsubscript{q}), 132.6 (CH), 132.0 (CH), 130.3 (C\textsubscript{q}), 129.7 (C\textsubscript{q}), 129.1 (CH), 128.7 (CH), 128.0 (C\textsubscript{q}), 125.0 (CH), 122.8 (C\textsubscript{q}), 122.2 (CH), 121.9 (CH), 100.3 (CH).

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

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

HR-MS (ESI) m/z calcd for C\textsubscript{23}H\textsubscript{14}F\textsubscript{2}N\textsubscript{3}O\textsubscript{2}+ [M+H]\textsuperscript{+} 434.0458, found 434.0441.

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

![Chemical structure](image)

The general procedure A was followed using 5-(4-nitrophenyl)-1H-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\textsubscript{3}): $\delta = 8.39$ (dd, $J = 8.8$, 2.2 Hz, 1H), 8.31 (d, $J = 8.8$ Hz, 1H), 8.26 (d,
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$J = 2.1$ 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$_3$): $\delta = 146.9$ (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$_q$), 122.2 (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$_{14}$Br$_2$N$_3$O$_2$ $^+$ [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)-1H-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$_3$): $\delta = 8.41$ (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), 7.94–7.99 (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$_3$): $\delta = 165.8$ (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$_3$O$_6$ $^+$ [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)-1H-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.
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M. p. = 123–124 °C.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 8.73$ (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, $J = 7.3$Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 146.7$ (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$_3$), 21.2 (CH$_3$), 14.4 (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) $m/z$ calcld for C$_{17}$H$_{20}$N$_3$O$_2$ $[M+H]^+$ 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)-1H-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$_3$): $\delta = 8.58$ (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, $J = 8.0$Hz, 2H), 3.04 (t, $J = 8.0$Hz, 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$_3$): $\delta = 139.6$ (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) $m/z$ calcld for C$_{21}$H$_{23}$N$_3$O$_2$ $[M+H]^+$ 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-(1H-pyrazol-5-y)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.

**1H NMR** (300 MHz, CDCl₃): δ = 8.16 (d, J = 8.2 Hz, 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 = 7.3 Hz, 3H).

**13C NMR** (75 MHz, CDCl₃): δ = 140.4 (CH), 138.8 (C₀), 136.5 (C₀), 129.0 (CH), 128.9 (C₀), 128.1 (CH), 126.4 (C₀), 124.8 (CH), 119.2 (C₀), 118.2 (C₀), 110.9 (C₀), 99.0 (CH), 30.1 (CH₂), 29.5 (CH₂), 23.8 (CH₂), 21.2 (CH₂), 14.4 (CH₃), 14.3 (CH₃).

**IR** (neat): 2962, 2933, 2874, 1355, 1339, 1310, 1117, 1079 cm⁻¹.

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

**HR-MS** (ESI) m/z calcd for C₁₆H₁₃N₃O⁺ [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}-1H-pyrazole (**126b**) (106.0 mg, 0.50 mmol) and oct-4-yn-1-yl (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.

**1H NMR** (300 MHz, CDCl₃): 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, 1.2 Hz, 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).

**13C NMR** (75 MHz, CDCl₃): δ = 140.2 (CH), 138.2 (C₀), 136.8 (C₀), 129.3 (³JC=32 Hz, C₀), 128.7 (C₀), 125.9 (³JC=1 Hz, C₀), 124.6 (CH), 124.3 (³JC=272 Hz, C₀), 122.4 (³JC=3 Hz, CH), 121.2 (³JC=4 Hz, CH), 118.8 (C₀), 98.4 (CH), 30.1 (CH₂), 29.5 (CH₂), 23.8 (CH₂), 21.2 (CH₂), 14.4 (CH₃), 14.4 (CH₃).

**19F NMR** (283 MHz, CDCl₃): 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+H]⁺, 305 (60), 291 (100), 264 (50), 249 (20), 223 (10), 202 (10).

**HR-MS** (ESI) m/z calcd for C₁₃H₁₃F₃N₃O⁺ [M+H]⁺ 321.1573, found: 321.1573.

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

The general procedure **A** was followed using 5-(4-nitrophenyl)-1H-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:...
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15/1) yielded 127ai (76.0 mg, 50%) as a yellow solid.

**M. p.** = 178–180°C.

**1H NMR** (300 MHz, CDCl3): 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).

**13C NMR** (75 MHz, CDCl3): δ = 146.7 (Cq), 141.1 (CH), 137.9 (Cq), 136.7 (Cq), 132.8 (Cq), 130.1 (CH), 130.0 (Cq), 129.4 (CH), 128.8 (CH), 128.2 (Cq), 124.9 (CH), 121.4 (CH), 120.5 (CH), 116.2 (Cq), 99.8 (CH), 15.1 (CH3).

**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 C18H13N3O2+ [M]+ 303.1002, found: 303.1010.

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

The general procedure A was followed using 5-(4-nitrophenoxy)-1H-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.

**1H NMR** (300 MHz, CDCl3): 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), 7.12 (d, J = 7.3 Hz, 3H).

**13C NMR** (75 MHz, CDCl3): δ = 160.1 (Cq), 146.7 (Cq), 141.1 (CH), 137.9 (Cq), 136.7 (Cq), 132.8 (Cq), 130.1 (CH), 129.1 (Cq), 128.5 (Cq), 125.1 (CH), 124.9 (Cq), 121.4 (Cq), 121.1 (CH), 120.6 (CH), 114.3 (CH), 99.6 (CH), 55.3 (CH3), 32.9 (CH2), 28.0 (CH2), 22.7 (CH2), 13.7 (CH3).

**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 C22H22N3O3+ [M+H]+ 376.1656, found 376.1654.

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

The general procedure A was followed using 5-(4-nitrophenoxy)-1H-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 brown solid.

**M. p. = 98–100 °C.**

**1H NMR** (300 MHz, CDCl₃): 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).

**13C NMR** (75 MHz, CDCl₃): 160.2 (C₉), 146.8 (C₉), 141.2 (CH), 137.9 (C₉), 136.7 (C₉), 131.1 (CH), 129.2 (C₉), 128.6 (C₉), 125.2 (CH), 125.0 (C₉), 121.5 (C₉), 121.2 (CH), 120.6 (CH), 114.4 (CH), 99.6 (CH), 55.3 (CH₃), 31.3 (CH₂), 30.7 (CH₂), 29.3 (CH₂), 28.3 (CH₂), 22.5 (CH₂), 14.0 (CH₃).

**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).


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

The general procedure A was followed using 4-(1H-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.**

**1H NMR** (300 MHz, CDCl₃): 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).

**13C NMR** (75 MHz, CDCl₃): 160.1 (C₉), 141.1 (CH), 137.7 (C₉), 136.8 (C₉), 131.1 (CH), 129.6 (CH), 129.0 (C₉), 128.8 (CH), 127.1 (C₉), 125.0 (C₉), 124.9 (CH), 120.6 (C₉), 119.1 (C₉), 114.4 (CH), 111.0 (C₉), 99.1 (CH), 55.3 (CH₃), 32.9 (CH₂), 28.0 (CH₂), 22.8 (CH₂), 13.7 (CH₃).

**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: C₂₃H₂₂N₃O⁺ [M+H⁺] 356.1757, found 356.1749.

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Intermolecular Competition Experiment between Substrates 126f and 126a

A mixture of 5-(4-methoxyphenyl)-1H-pyrazole (126f) (87.5 mg, 0.50 mmol), 5-(4-nitrophenyl)-1H-pyrazole (126a) (95.7 mg, 0.50 mmol), diphenylacetylene (11a) (89.4 mg, 0.50 mmol), [RuCl$_2$(p-cymene)]$_2$ (30.7 mg, 10 mol %), AgSbF$_6$ (69 mg, 40 mol %) and Cu(OAc)$_2$·H$_2$O (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$_4$Cl/NH$_3$ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na$_2$SO$_4$. 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)-1H-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-cymene)]$_2$ (15.4 mg, 5.0 mol %), AgSbF$_6$ (36.2 mg, 20 mol %) and Cu(OAc)$_2$·H$_2$O (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.
NH₄Cl/NH₃ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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.

**Intemolecular Competition Experiment between Alkynes 11c and 11d**

A mixture of 5-(4-nitrophenyl)-1H-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), [RuCl₂(p-cymene)]₂ (15.7 mg, 5.0 mol %), AgSbF₆ (36.2 mg, 20 mol %) and Cu(OAc)₂·H₂O (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. NH₄Cl/NH₃ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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 (29.0 mg, 14%) as yellow solids. Their spectral data were identical to those reported above.
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Ruthenium(II)-Catalyzed H/D Exchange with Arylpyrazole 126a Employing D₂O as the Cosolvent

The general procedure A was followed using 5-(4-nitrophenyl)-1H-pyrazole (126a) (95.0 mg, 0.50 mmol), diphenylacetylene (11a) (179 mg, 1.00 mmol), [RuCl₂(p-cymene)]₂ (15.4 mg, 5.0 mol %), AgSbF₆ (35.1 mg, 20 mol %) and Cu(OAc)₂ (91.7 mg, 0.50 mmol) in a solvent mixture of DCE and D₂O (1.8/0.2 mL). Purification by column chromatography (n-hexane/EtOAc: 10/1→2/1) yielded reisolated partially deuterated starting material [Dₙ]-126a (27 mg, 28%) and product [Dₙ]-127aa (44 mg, 24%) as yellow solids. The deuterium incorporations in [Dₙ]-127aa and [Dₙ]-126a were estimated by ¹H NMR 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 (CH₂Cl₂/MeOH: 10/1) yielded 129ab (131.0 mg, 91%) as an off-white solid.

M. p. = 222–224 °C.

¹H NMR (300 MHz, d₆-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).

¹³C NMR (100 MHz, d₆-DMSO): δ = 166.0 (C₉), 147.6 (CH), 145.3 (C₉), 133.9 (C₉), 132.9 (C₉), 132.3 (C₉), 130.9 (CH), 130.0 (CH), 119.7 (CH), 59.5 (CH₂), 21.7 (CH₃), 21.2 (CH₃), 14.2 (CH₃).

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 C₁₃H₁₅O₅S⁺ [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, 1.50 mmol). Purification by column chromatography (CH₂Cl₂/MeOH: 15/1→10/1) yielded 129bb (126.0 mg, 92%) as an off-white solid.

M. p. = 285–287°C.

¹H NMR (300 MHz, d₆-DMSO): \( \delta = 8.85 \) (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).

¹³C NMR (125 MHz, d₆-DMSO): \( \delta = 166.1 \) (Cₛ), 147.7 (CH), 145.4 (Cₜ), 136.4 (Cₜ), 133.0 (Cₜ), 132.8 (CH), 127.8 (CH), 125.6 (CH), 117.0 (CH), 59.5 (CH₂), 22.3 (CH₃), 14.2 (CH₃).

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 C₁₂H₁₃O₅S [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 (CH₂Cl₂/MeOH: 15/1→10/1) yielded 129cb (126.0 mg, 92%) as an off-white solid.

M. p. = 217–219°C.

¹H NMR (300 MHz, d₆-DMSO): \( \delta = 8.78 \) (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).

¹³C NMR (125 MHz, d₆-DMSO): \( \delta = 165.8 \) (C₄), 158.5 (d, \( 1J_{C,F} = 249.4 \) Hz, C₄), 144.6 (d, \( 4J_{C,F} = 3.6 \) Hz, CH), 134.7 (d, \( 3J_{C,F} = 2.6 \) Hz, C₄), 134.3 (d, \( 2J_{C,F} = 14.5 \) Hz, C₄), 129.7 (d, \( 3J_{C,F} = 9.6 \) Hz, CH), 123.2 (d, \( 4J_{C,F} = 3.2 \) Hz, CH), 118.9 (CH), 117.6 (d, \( 2J_{C,F} = 25.3 \) Hz, CH), 59.8 (CH₂), 14.2 (CH₃).

¹⁹F NMR (283 MHz, d₆-DMSO): \( \delta = –108.6 \) (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 C₁₁H₁₀FO₅S [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$_2$Cl$_2$/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): $\delta$ = 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): $\delta$ = 166.1 (C$_q$), 160.5 (d, $^1$J$_{C-F} = 244.6$ Hz, C$_q$), 146.3 (d, $^4$J$_{C-F} = 2.1$ Hz, CH), 142.4 (d, $^4$J$_{C-F} = 3.0$ Hz, C$_q$), 140.0 (d, $^3$J$_{C-F} = 7.9$ Hz, C$_q$), 135.6 (d, $^3$J$_{C-F} = 8.0$ Hz, C$_q$), 118.9 (d, $^2$J$_{C-F} = 20.6$ Hz, CH), 118.4(CH), 111.8 (d, $^2$J$_{C-F} = 21.7$ Hz, CH), 59.7 (CH$_2$), 22.2 (d, $^4$J$_{C-F} = 1.5$ Hz, CH$_3$), 14.2 (CH$_3$).

$^{19}$F NMR (283 MHz, $d_6$-DMSO): $\delta$ = –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$_5$S [M–H]$^+$ 287.0396, 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$_2$Cl$_2$/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): $\delta$ = 9.28–9.25 (m, 1H), 9.18 (d, $J$ = 16.1 Hz, 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): $\delta$ = 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$_5$S [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 (CH₂Cl₂/MeOH: 15/1→10/1) yielded 129fb (114.0 mg, 72%) as an off-white solid.

M. p. = 212–214 °C.

(E-isomer): ¹H NMR (300 MHz, d₆-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).¹³C NMR (100 MHz, d₆-DMSO): δ = 166.7 (C₂), 151.6 (C₃), 151.2 (C₄), 142.0 (CH), 137.3 (C₅), 122.7 (C₆), 120.6 (CH), 116.3 (CH), 113.2 (CH), 59.4 (CH₂), 57.7 (CH₃), 56.3 (CH₃), 14.2 (CH₃).

(Z-isomer): ¹H NMR (300 MHz, d₆-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).¹³C NMR (100 MHz, d₆-DMSO): δ = 165.4 (C₂), 151.0 (C₃), 149.7 (C₄), 140.4 (CH), 136.7 (C₅), 124.4 (C₆), 118.4 (CH), 113.5 (CH), 112.0 (CH), 58.6 (CH₂), 57.1 (CH₃), 55.9 (CH₃), 13.8 (CH₃).

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 C₁₃H₁₅O₇S [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 (CH₂Cl₂/MeOH: 20/1→10/1) yielded 129hb (110.0 mg, 75%) as an off-white solid.

M. p. = 292–294 °C.

¹H NMR (300 MHz, d₆-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).

¹³C NMR (125 MHz, d₆-DMSO): δ = 165.9 (C₂), 161.2 (dd, J = 247.0, 14.0 Hz, C₃), 159.3 (dd, J = 252.0, 13.0 Hz, C₄), 143.3 (m, CH), 136.4 (dd, J = 9.3, 3.9 Hz, C₅), 131.6 (dd, J = 15.0, 4.0 Hz, C₆), 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 (CH₂), 14.1 (CH₃).

¹⁹F NMR (283 MHz, d₆-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 C₁₁H₆F₂O₃S [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$_2$Cl$_2$/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): $\delta$ = 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): $\delta$ = 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$_5$S–[M–H]$^+$ 255.0333, found 255.0334.

(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$_2$Cl$_2$/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): $\delta$ = 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): $\delta$ = 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$_5$S [M–H]$^+$ 269.0489, found 269.0501.

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

The general procedure B was followed using 3-methylbenzenesulfonic
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acid (128k) (80.0 mg, 0.45 mmol) and ethyl acrylate (46b) (150.0 mg, 1.50 mmol). Purification by column chromatography (CH$_2$Cl$_2$/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$_2$O): $\delta$ = 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): $\delta$ = 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$_5$S [M–H]$^+$ 269.0489, found 269.0500.

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

(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$_2$Cl$_2$/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): $\delta$ = 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): $\delta$ = 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$_5$S [M–H]$^+$ 283.0646, found 283.0645.

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

(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$_2$Cl$_2$/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): $\delta = 8.86$ (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), 1.64–1.37 (m, 2H), 1.42–1.33 (m, 2H), 0.91 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (125 MHz, $d_6$-DMSO): $\delta = 166.2$ (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 calcld for C$_{15}$H$_{19}$O$_5$S [M–H]$^+$ 311.0959, found 311.0960.

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

(E)-2-[3-(Benzyloxy)-3-oxoprop-1-en-1-yl]-4,6-dimethylbenzenesulfonic Acid (129ld):

$^1$H NMR (400 MHz, $d_6$-DMSO): $\delta = 8.94$ (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): $\delta = 166.0$ (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 calcld for C$_{18}$H$_{17}$O$_5$S [M–H]$^+$ 345.0802, found 345.0804.

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

$^1$H NMR (400 MHz, $d_6$-DMSO): $\delta = 8.94$ (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): $\delta = 166.0$ (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 calcld for C$_{18}$H$_{17}$O$_5$S [M–H]$^+$ 345.0802, found 345.0804.
15/1→10/1) yielded **129lf** (120.0 mg, 95%) as a pale solid.

**M. p.** = 260–262 °C.

**1H NMR** (400 MHz, $d_6$-DMSO): $\delta$ = 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).

**13C NMR** (125 MHz, $d_6$-DMSO): $\delta$ = 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$_4$S [M–H$^+$] 253.0540, found 253.0542.

**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$_2$Cl$_2$/MeOH: 15/1→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): $\delta$ = 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): $\delta$ = 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): $\delta$ = 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): $\delta$ = 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$_3$S [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$_2$Cl$_2$/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): $\delta$ = 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): $\delta$ = 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): $\delta$ = 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$_6$PS [M–H]$^+$ 347.0724, found 347.0726.

The spectral data were in accordance with those reported in the literature.$^{110}$
The general procedure C was followed using 2,4-dimethylbenzenesulfonic acid (128l) (91.5 mg, 0.49 mmol) and 2-vinyl-naphthalene (46k) (230.0 mg, 1.49 mmol), AgSbF$_6$ (69.0 mg, 0.20 mmol, 41 mol%). Purification by column chromatography (CH$_2$Cl$_2$/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): $\delta = 8.57$ (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): $\delta = 142.1$ (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$_3$S [M]$^+$ 338.0971, found 338.0978.

(E)-2,4-Dimethyl-6-[2-(naphthalen-2-yl)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$_2$Cl$_2$/MeOH: 15/1–10/1) yielded 129ll (101.0 mg, 53%) as an off-white solid.

$^1$H NMR (500 MHz, $d_6$-DMSO): $\delta = 8.68$ (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): $\delta = 143.8$ (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): $\delta = -(143.9–144.0)$ (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), 113
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(HR-MS (ESI) m/z calcd for C_{16}H_{10}F_2O_5S [M–H^{-}] 377.0276, found 377.0270.

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

The general procedure C was followed using 2,4-dimethylbenzenesulfonic acid (128i) (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/Methanol: 10/1) yielded 129Im (92.0 mg, 60%) as an off-white solid.

M. p. = 237–239 °C.

1H 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).

13C NMR (125 MHz, d_6-DMSO): δ = 161.0 (d, 1J_{CF} = 243 Hz, C_q), 141.9 (d, 4J_{CF} = 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_{CF} = 7.9 Hz, CH), 125.5 (CH), 124.9 (CH), 115.2 (d, 2J_{CF} = 21.4 Hz, CH), 22.5 (CH_3), 20.4 (CH_3).

19F 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 (129In):

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

M. p. = 289–291 °C.

1H 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).

13C NMR (125 MHz, d_6-DMSO): δ = 159.2 (d, 1J_{CF} = 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_{CF} = 3.5 Hz, CH), 131.9 (CH), 128.4 (d, 3J_{CF} = 8.2 Hz, CH), 126.9 (d, 3J_{CF} = 3.9 Hz, CH), 125.6 (d, 2J_{CF} = 12.2 Hz, C_q), 125.1 (CH), 124.3 (CH), 118.2 (CH), 115.4 (d, 2J_{CF} = 21.8 Hz, CH), 22.4 (CH_3), 20.4 (CH_3).
**Experimental Section**

$^{19}$F NMR (283 MHz, $d_6$-DMSO): $\delta = -(119.2-119.3)$ (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$_3$S [M–H]$^+$ 305.0653, found 305.0652.

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

![Reaction Scheme](image)

The general procedure B was followed using 4-methylbenzenesulfonyl chloride 136 (96.0 mg, 0.50 mmol), ethyl acrylate (46b) (157.0 mg, 1.57 mmol), [RuCl$_2$(p-cymene)]$_2$ (15.5 mg, 5.0 mol%), AgSbF$_6$ (36.0 mg, 20 mol%) and Cu(OAc)$_2$H$_2$O (200.0 mg, 1.00 mmol) in DMA. Purification by column chromatography (CH$_2$Cl$_2$/MeOH: 20/1→15/1) yielded product 129jb (96.2 mg, 71%) as a pale yellow solid. Its spectral data were identical to those reported above.

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

![Reaction Scheme](image)

The general procedure B was followed using methyl benzenesulfonate (137) (86.0 mg, 0.50 mmol), ethyl acrylate (46b) (157.0 mg, 1.57 mmol), [RuCl$_2$(p-cymene)]$_2$ (15.5 mg, 5.0 mol%), AgSbF$_6$ (36.0 mg, 20 mol%) and Cu(OAc)$_2$H$_2$O (200.0 mg, 1.00 mmol) in DMA. Purification by column chromatography (CH$_2$Cl$_2$/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): $\delta = 8.83$ (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): $\delta = 166.0$ (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$_3$), 14.2 (CH$_3$).
IR (neat): 3497, 2982, 1697, 1632, 1309, 1162, 1026, 670, 595 cm\(^{-1}\).

HR-MS: (ESI) \(m/z\) calcld for C\(_{16}\)H\(_{17}\)O\(_7\)S [M–H\(^+\)] 353.0700, found 353.0700.

**Intemolecular Competition Experiment between Substrates 128l 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, 0.51 mmol), [RuCl\(_2\)(p-cymene)]\(_2\) (15.3 mg, 5.0 mol %), AgSbF\(_6\) (35.0 mg, 20 mol %) and Cu(OAc)\(_2\)-H\(_2\)O (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\(_2\)Cl\(_2\)/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 \(^1\)H NMR spectroscopy applying their spectral data reported above.

**Ruthenium(II)-Catalyzed H/D Exchange in Alkenylation of Substrate 128j Employing D\(_2\)O 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-cymene)]\(_2\) (15.5 mg, 5.0 mol %), AgSbF\(_6\) (36.0 mg, 20 mol %) and Cu(OAc)\(_2\) (183.0 mg, 1.00 mmol) in a solvent mixture of DMA and D\(_2\)O (1.8/0.2 mL). Purification by column chromatography (CH\(_2\)Cl\(_2\)/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 1H 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-yl)oxyphenyl]acrylate (131ab):

\[
\begin{align*}
&\text{The general procedure D was followed using } 2-(o-tolyloxy)pyridine(130a)
\text{ (185.4 mg, 1.00 mmol), ethyl acrylate } (46b) \text{ (52.0 mg, 0.52 mmol), }
\text{[RuCl}_2(p\text{-cymene})_2 \text{ (7.6 mg, 2.5 mol %), AgSbF}_6 \text{ (18.5 mg, 10 mol %) and }
\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O (207.6 mg, 1.04 mmol). Purification by column chromatography } (n\text{-hexane/EtOAc: 12/1} \rightarrow 10/1) \text{ yielded } 131ab \text{ (122.0 mg, 83%) as a colorless solid.}
\end{align*}
\]

M. p. = 114–116°C

1H NMR (300 MHz, CDCl₃): 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 = 7.1 Hz, 2H), 2.08 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H).

13C NMR (75 MHz, CDCl₃): 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 (CH₂), 16.6 (CH₃), 14.2 (CH₃).

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}NO₃ [M]^+ 283.1208, found 283.1211.

(E)-tert-Butyl 3-[3-methyl-2-(pyridin-2-yl)oxyphenyl]acrylate (131ap):

\[
\begin{align*}
&\text{The general procedure D was followed using } 2-(o-tolyloxy)pyridine(130a) \text{ (185.1 mg, 1.00 mmol), tert-butyl acrylate (46p) (62.2 mg, 0.49 mmol), [RuCl}_2(p\text{-cymene})_2 \text{ (7.7 mg, 2.5 mol %), and AgSbF}_6 \text{ (17.9 mg, 11 mol %). Purification by column chromatography } (n\text{-hexane/EtOAc: 15/1) yielded } 131ap \text{ (123.0 mg, 81%) as a colorless solid.}
\end{align*}
\]

M. p. = 98–100°C.

1H NMR (300 MHz, CDCl₃): 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).
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\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 166.1\) (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) \([\text{M}^+]\), 254 (20), 238 (45), 318 (40), 194 (15), 180 (20), 167 (22), 78 (27).

HR-MS (EI) \(m/z\) calcd for C\(_{19}\)H\(_{22}\)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-tolylpyridine)(130a) (186.2 mg, 1.00 mmol), benzyl acrylate (46d) (79.2 mg, 0.49 mmol), [RuCl\(_2\)(p-cymene)]\(_2\) (7.7 mg, 12.5 \(\mu\)mol, 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\(_3\)): \(\delta = 8.16–8.13\) (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\(_3\)): \(\delta = 166.6\) (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) \([\text{M}^+]\), 254 (22), 238 (15), 210 (100), 194 (45), 182 (50), 167 (30), 91 (70).

HR-MS (EI) \(m/z\) calcd for C\(_{22}\)H\(_{20}\)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-isopropylbenzoyl)pyridine (130b) (215.0 mg, 1.00 mmol), ethyl acrylate (46b) (49.3 mg, 0.49 mmol), [RuCl\(_2\)(p-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\(_3\)): \(\delta = 8.10\) (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).
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$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 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$_{21}$N$_3$O$_3$ [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-isoproplyphenoxy)-pyridine (1b) (212.0 mg, 0.99 mmol), tert-butyl acrylate (46p) (62.7 mg, 0.49 mmol), [RuCl$_2$(p-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$_3$): $\delta$ = 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, $J$ = 7.7, 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$_3$): $\delta$ = 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-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$_3$): $\delta$ = 8.09 (ddd, $J$ = 5.0, 2.0, 0.8 Hz, 1H), 7.82 (d, $J$ = 16.2 Hz, 1H),
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7.73 (dd, 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$_3$): $\delta$ = 166.6 (C$_q$), 162.6 (C$_q$), 155.5 ($^1$J$_{C,F}$ = 251 Hz, C$_q$), 147.4 (CH), 140.0 ($^2$J$_{C,F}$ = 13 Hz, C$_q$), 139.6 (CH), 137.8 ($^2$J$_{C,F}$ = 4 Hz, CH), 130.3 ($^3$J$_{C,F}$ = 2 Hz, C$_q$), 125.8 ($^3$J$_{C,F}$ = 8 Hz, CH), 122.9 ($^3$J$_{C,F}$ = 4 Hz, CH), 121.0 (CH), 118.9 (CH), 117.8 ($^2$J$_{C,F}$ = 19 Hz, CH), 110.7 (CH), 60.6 (CH$_2$), 14.2 (CH$_3$).

$^{19}$F NMR (283 MHz, CDCl$_3$): $\delta$ = –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 calcld for C$_{16}$H$_{14}$FNO$_3^+$ [M]$^+$ 287.0952, found 287.0953.

(E)-$\textit{tert}$-Butyl 3-[3-fluoro-2-(pyridin-2-yl oxy)phenyl]acrylate (131cp):

\[
\begin{align*}
\text{The general procedure D was followed using 2-} & \text{-} \text{(2-fluorophenoxy) pyridine (131c) (188.0 mg, 0.99 mmol), \textit{tert}-butyl acrylate (46p) (63.3 mg, 0.49 mmol), [RuCl$_2$(p-cymene)$_2$ (7.9 mg, 2.6 mol %), and AgSbF$_6$ (18.6 mg, 11 mol %). Purification by column chromatography (n-hexane/EtOAc:} \\
\text{15/1} & \text{-} \text{12/1) yielded 131cp (136.0 mg, 87%) as a colorless solid.}
\end{align*}
\]

M. p. = 108–110°C.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.09 (dd, 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$_3$): $\delta$ = 165.9 (C$_q$), 162.6 (C$_q$), 156.4 ($^1$J$_{C,F}$ = 249 Hz, C$_q$), 147.4 (CH), 139.9 ($^2$J$_{C,F}$ = 13 Hz, C$_q$), 139.6 (CH), 136.7 ($^2$J$_{C,F}$ = 3 Hz, CH), 130.5 ($^3$J$_{C,F}$ = 2 Hz, C$_q$), 125.8 ($^3$J$_{C,F}$ = 8 Hz, CH), 122.8 (CH), 122.7 ($^3$J$_{C,F}$ = 3 Hz, CH), 118.8 (CH), 117.6 ($^2$J$_{C,F}$ = 19 Hz, CH), 110.7 (CH), 80.7 (C$_q$), 28.1 (CH$_3$).

$^{19}$F NMR (283 MHz, CDCl$_3$): $\delta$ = –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 calcld for C$_{18}$H$_{14}$FNO$_3$ [M]$^+$ 315.1265, found 315.1286.

(E)-$\textit{Benzy l}$ 3-[3-Fluoro-2-(pyridin-2-yl oxy)phenyl]acrylate (131cd):

\[
\begin{align*}
\text{The general procedure D was followed using 2-} & \text{-} \text{(2-fluorophenoxy) pyridine}
\end{align*}
\]

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(131c) (188.0 mg, 0.99 mmol), benzyl acrylate (46d) (69.3 mg, 0.43 mmol), [RuCl₂(p-cymene)]₂ (7.8 mg, 2.5 mol %), and AgSbF₆ (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.

**¹H NMR** (300 MHz, CDCl₃): δ = 8.10 (dd, 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).

**¹³C NMR** (75 MHz, CDCl₃): δ = 166.3 (Cₗ), 162.5 (Cₗ), 155.4 (JC₂F = 249 Hz, Cₗ), 147.3 (CH), 140.0 (JC₂F = 13 Hz, Cₗ), 139.6 (CH), 138.3 (JC₂F = 3 Hz, CH), 135.8 (Cₗ), 147.3 (CH), 139.6 (CH), 138.3 (JC₂F = 3 Hz, CH), 128.1 (CH), 128.1 (CH), 125.8 (JC₂F = 8 Hz, CH), 122.8 (JC₂F = 3 Hz, CH), 120.5 (CH), 118.8 (CH), 117.9 (JC₂F = 19 Hz, CH), 110.6 (CH), 66.3 (CH₂).

**¹⁹F NMR** (283 MHz, CDCl₃): 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 calcld for C₂₁H₁₄FNO₃⁺ [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), [RuCl₂(p-cymene)]₂ (7.8 mg, 2.5 mol %), and AgSbF₆ (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.

**¹H NMR** (300 MHz, CDCl₃): 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).

**¹³C NMR** (75 MHz, CDCl₃): δ = 166.5 (Cₗ), 162.6 (Cₗ), 148.5 (Cₗ), 147.4 (CH), 139.7 (CH), 138.2 (CH), 131.8 (CH), 130.6 (Cₗ), 129.1 (Cₗ), 126.2 (CH), 126.0 (CH), 121.0 (CH), 118.7 (CH), 110.8 (CH), 60.5 (CH₂), 14.2 (CH₃).

**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 calcld for C₁₆H₁₄ClNO₃⁺ [M⁺] 303.0657, found 303.0666.
**(E)-Ethyl 3-[2-(Pyridin-2-ylxy)-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), [RuCl2(η-cymene)]2 (7.8 mg, 2.5 mol %), and AgSbF6 (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.

1H NMR (300 MHz, CDCl3): \(\delta = 8.01\) (dd, \(J = 5.0, 2.0, 0.8, 1H\), 7.84 (dd, \(J = 7.9, 1.6\) Hz, 1H), 7.71 (m, 1H), 7.70 (dd, \(J = 8.3, 7.2, 2.0\) Hz, 1H), 7.61 (d, \(J = 16.1\) Hz, 1H), 7.44–7.30 (m, 1H), 7.05 (dt, \(J = 8.3, 0.9\) Hz, 1H), 6.95 (dd, \(J = 7.2, 5.0, 0.9\) 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).

13C NMR (75 MHz, CDCl3): \(\delta = 166.2\) (Cq), 163.5 (Cq), 149.8 (\(^3 J_{CF} = 2.0\) Hz, Cq), 147.3 (CH), 139.7 (CH), 137.5 (CH), 131.1 (CH), 130.9 (Cq), 128.6 (\(^3 J_{CF} = 5.0\) Hz, CH), 125.6 (CH), 125.0 (\(^3 J_{CF} = 32\) Hz, Cq), 124.9 (\(^1 J_{CF} = 272\) Hz, Cq), 121.2 (CH), 118.7 (CH), 110.7 (CH), 60.5 (CH2), 14.1 (CH3).

19F NMR (283 MHz, CDCl3): \(\delta = -61.7\) (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 calcld for C17H13F3NO3+: [M]+ 337.0920, found 337.0919.

**(E)-tert-Butyl 3-[2-(pyridin-2-ylxy)-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), [RuCl2(η-cymene)]2 (7.7 mg, 2.5 mol %), and AgSbF6 (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.

1H NMR (300 MHz, CDCl3): \(\delta = 8.05–8.02\) (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, \(J = 8.3\) Hz, 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).

13C NMR (75 MHz, CDCl3): \(\delta = 165.4\) (Cq), 163.5 (Cq), 149.7 (Cq), 147.3 (CH), 139.7 (CH), 136.4 (CH), 131 (Cq), 130.9 (CH), 128.4 (\(^3 J_{CF} = 5.0\) Hz, CH), 125.6 (CH), 125.4 (\(^3 J_{CF} = 33\) Hz, Cq), 123.1 (CH), 123.0 (\(^1 J_{CF} = 272\) Hz, Cq), 118.6 (CH), 110.7 (CH), 80.6 (Cq), 28.0 (CH3).
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$^{19}$F NMR (283 MHz, CDCl$_3$): $\delta = -61.7$.

IR (neat): 2970, 1699, 1427, 1334, 1261, 1235, 1129, 783 cm$^{-1}$.

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 calcld for C$_{19}$H$_{18}$F$_3$NO$_3$ [M]$^+$ 365.1329, found 365.1246.

**(E)-Ethyl 3-[(3,5-dimethyl-2-(pyridin-2-xyloxy)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$_2$($p$-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$_3$): $\delta = 8.10$ (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$_3$): $\delta = 166.9$ (C$q$), 163.3 (C$q$), 148.5 (C$q$), 147.7 (CH), 139.3 (CH), 145.0 (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 calcld for C$_{18}$H$_{19}$NO$_3$ [M]$^+$ 297.1365, found 297.1369.

**(E)-tert-Butyl 3-[(3,5-dimethyl-2-(pyridin-2-xyloxy)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$_2$($p$-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.
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$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 8.10$ (s, $J = 4.7$, 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$_3$): $\delta = 166.2$ (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-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$_3$): $\delta = 8.12–8.09$ (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$_3$): $\delta = 167.0$ (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$_{16}$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-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$_3$): $\delta$ = 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), 1.45 (s, 9H).

$^13$C NMR (75 MHz, CDCl$_3$): $\delta$ = 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), 20.4 (CH$_2$), 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 calc for C$_{23}$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-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$_3$): $\delta$ = 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$_3$): $\delta$ = 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, 1378, 1195, 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 calc for C$_{23}$H$_{23}$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-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.
Experimental Section

M. p. = 156–158 °C

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 8.06$ (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$_3$): $\delta = 166.8$ (C$_q$), 164.2 (C$_q$), 148.8 (C$_q$), 147.9 (CH), 138.6 (CH), 135.6 (C$_q$), 128.0 (CH), 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) $m/z$ calcld for C$_{20}$H$_{17}$NO$_3$ [M]+ 319.1208, found 319.1217.

(E)-tert-Butyl 3-[1-(Pyridin-2-xyloxy)naphthalen-2-yl]acrylate (131hp):

The general procedure D was followed using 2-(naphthalen-1-xyloxy)-pyridine (130h) (222.0 mg, 1.00 mmol), tert-butyl acrylate (46p) (65.2 mg, 0.51 mmol), [RuCl$_2$(p-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$_3$): $\delta = 8.06$ (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$_3$): $\delta = 166.1$ (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, 1712, 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) $m/z$ calcld C$_{22}$H$_{21}$NO$_3$ [M]$^+$ 347.1516, found 347.1520.

(E)-Benzyl 3-[1-(pyridin-2-xyloxy)naphthalen-2-yl]acrylate (131hd):

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The general procedure D was followed using 2-(naphthalen-1-ylxylo)-pyridine (130h) (222.0 mg, 1.00 mmol), benzyl acrylate (46d) (82.2 mg, 0.51 mmol), [RuCl₂(p-cymene)]₂ (7.8 mg, 2.5 mol %), AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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, 1.3 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).

¹³C NMR (75 MHz, CDCl₃): δ = 166.6 (C₉), 164.2 (C₉), 148.9(Cq), 147.9 (CH), 139.2 (CH), 136.1 (Cq), 135.7 (Cq), 128.5 (CH), 128.1 (CH), 128.1 (CH), 128.0 (CH), 128.0 (Cq), 127.5 (CH), 126.9 (CH), 126.0 (CH), 124.0 (Cq), 123.2 (CH), 119.3 (CH), 118.5 (CH), 110.2(CH), 66.2 (CH₂).

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 C₂₅H₁₉NO₃ [M⁺] 381.1359, found 381.1367.

(E)-Ethyl 3-[3-(Pyridin-2-ylxylo)naphthalen-2-yl]acrylate (131ib):

The general procedure D was followed using 2-(naphthalen-2-ylxylo)pyridine (130i) (221.0 mg, 1.00 mmol), ethyl acrylate (46b) (50.6 mg, 0.51 mmol), [RuCl₂(p-cymene)]₂ (15.5 mg, 5.0 mol %), and AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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).

¹³C NMR (75 MHz, CDCl₃): δ = 166.9 (C₉), 163.6 (C₉), 150.4 (Cq), 147.9 (CH), 139.7 (CH), 139.5 (CH), 134.7 (Cq), 130.8 (Cq), 129.0 (CH), 128.3 (CH), 127.4 (CH), 127.3(Cq), 127.2 (CH), 125.8 (CH), 120.4 (CH), 118.9 (CH), 118.8(CH), 111.7 (CH), 60.4 (CH₂), 14.3 (CH₃).

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 calc'd for C_{20}H_{17}NO_{3}^+ [M]^+ 319.1203, found 319.1217.

(E)-tert-Butyl 3-[3-(pyridin-2-yl)oxy]naphthalen-2-yl]acrylate (131ip):

The general procedure D was followed using 2-(naphthalen-2-yl)oxy)pyridine (130i) (220.0 mg, 0.99 mmol), tert-butyl acrylate (46p) (66.0 mg, 0.52 mmol), [RuCl_2(p-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.

^1H 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).

^13C 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 calc'd for C_{22}H_{23}NO_3 [M]^+ 347.1516, found 347.1510.

(E)-Ethyl 3-[5-methoxy-(pyridin-2-yl)oxy]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-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.

^1H 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).

^13C 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 calc'd for C_{17}H_{17}NO_3 [M]^+ 299.1152, found 299.1154.
Experimental Section

(E)-tert-Butyl 3-{5-methoxy-2-(pyridin-2-ylxy)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-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$_3$): $\delta = 8.14$ (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$_3$): $\delta = 166.1$ (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, 1235, 1172, 1109, 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]$^+$ 327.1456, found 327.1472.

(E)-Ethyl 3-{5-chloro-2-(pyridin-2-ylxy)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-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$_3$): $\delta = 8.14$–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, $J = 8.7$Hz, 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$_3$): $\delta = 166.5$ (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$_3$), 14.2 (CH$_3$).

IR (neat): 2981, 1708, 1463, 1426, 1235, 1172, 1109, 776 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.
Experimental Section

(E)-tert-Butyl 3-(5-chloro-2-(pyridin-2-yl)oxy)phenyl]acrylate (131lp):

\[ \text{The general procedure D was followed using 2-(4-chlorophenoxy)pyridine} \]

\[ \text{(131l) (208.0 mg, 1.01 mmol), tert-butyl acrylate (46p) (62.5 mg, 0.49 mmol),} \]

\[ [\text{RuCl}_2(p\text{-cymene})]_2 (7.8 mg, 2.5 mol %), \text{and AgSbF}_6 (17.9 mg, 11 mol %).} \]

Purification by column chromatography (n-hexane/EtOAc: 15/1) yielded 131lp (123.0 mg, 76%) as a colorless solid.

M. p. = 102–104 °C.

\[ ^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta = 8.14 \text{ (dd, } J = 4.9, 2.0, 0.9 \text{ Hz, 1H}), 7.72 \text{ (dd, } J = 8.3, 7.2, 2.0 \text{ Hz, 1H}), 7.70 \text{ (d, } J = 16.1 \text{ Hz, 1H}), 7.63 \text{ (d, } J = 2.6 \text{ Hz, 1H}), 7.33 \text{ (dd, } J = 8.7, 2.6 \text{ Hz, 1H}), 7.06 \text{ (d, } J = 8.7 \text{ Hz, 1H}), 7.03–6.98 \text{ (m, 2H), 6.38 (d, } J = 16.1 \text{ Hz, 1H), 1.48 (s, 9H).} \]

\[ ^{13}\text{C NMR (75 MHz, CDCl}_3\text{): } \delta = 165.8 \text{ (C}_q\text{), 163.1 (C}_q\text{), 151.0 (C}_q\text{), 147.6 (CH), 139.7 (CH), 136.4 (CH), 130.7 (CH), 130.4 (C}_q\text{), 129.1 (C}_q\text{), 127.4 (CH), 123.9 (CH), 122.7 (CH), 118.9 (CH), 111.7 (CH), 80.7 (C}_q\text{), 28.1 (CH}_3\text{).} \]

IR (neat): 2978, 1699, 1425, 1295, 1238, 1190, 974 cm\textsuperscript{-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 calc for C\textsubscript{18}H\textsubscript{16}ClNO\textsubscript{3}+: [M]+ 331.0970, found 331.0978.

(E)-Ethyl 3-[4-(pyridin-2-yl)oxy]-[1,1'-biphenyl]-3-yl]acrylate (131mb):

\[ \text{The general procedure D was followed using ethyl 2-([1,1'-biphenyl]-4-yl)oxy)-} \]

\[ \text{pyridine (130mb) (253.0 mg, 1.02 mmol), ethyl acrylate (46b) (48.3 mg, 0.48} \]

\[ \text{mmol), [RuCl}_2(p\text{-cymene})]_2 (15.3 mg, 5.0 mol %), AgSbF}_6 (36.2 mg, 22 mol} \]

\[ \%). Purification by column chromatography (n-hexane/EtOAc: 30:1→20/1) yielded} 131mb \text{ (106.0 mg, 64%) as a colorless oil.} \]

\[ ^1\text{H NMR (300 MHz, CDCl}_3\text{): } \delta = 8.20 \text{ (dd, } J = 4.9, 2.0, 0.8 \text{ Hz, 1H}), 7.95 \text{ (d, } J = 16.2 \text{ Hz, 1H), 7.88} \]

\[ \text{ (d, } J = 2.3 \text{ Hz, 1H), 7.74 \text{ (dd, } J = 8.3, 7.2, 2.0 \text{ Hz, 1H), 7.61–7.58 (m, 3H), 7.49–7.42 (m, 2H),} \]

\[ 7.40–7.34 (m, 1H), 7.19 \text{ (d, } J = 8.5 \text{ Hz, 1H), 7.06–7.01 (m, 2H), 6.57 \text{ (d, } J = 16.2 \text{ Hz, 1H), 4.23 (q, } J = 7.1 \text{ Hz, 2H), 1.30 (t, } J = 7.1 \text{ Hz, 3H).} \]

\[ ^{13}\text{C NMR (75 MHz, CDCl}_3\text{): } \delta = 166.8 \text{ (C}_q\text{), 163.3 (C}_q\text{), 152.2 (C}_q\text{), 147.7 (CH), 140.0 (C}_q\text{), 139.7} \]

\[ \text{ (CH), 138.8 (CH), 138.2 (C}_q\text{), 129.9 (CH), 128.8 (CH), 127.5 (C}_q\text{), 127.4 (CH), 127.0 (CH), 126.6} \]

\[ \text{ (CH), 122.7 (CH), 120.0 (CH), 118.8 (CH), 111.8 (CH), 60.4 (CH}_2\text{), 14.2 (CH}_3\text{).} \]

IR (neat): 2980, 1706, 1464, 1426, 1235, 1165, 757, 695 cm\textsuperscript{-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 calc for C\textsubscript{22}H\textsubscript{16}NO\textsubscript{3}+: [M]+ 345.1359, found 345.1371. 
(E)-Ethyl 3-[(2-(Pyridin-2-yl)oxy)-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), [RuCl3(p-cymene)]2 (15.6 mg, 5.1 mol %), and AgSbF6 (36.7
mg, 22 mol %). Purification by column chromatography (n-hexane/EtOAc:
15/1) yielded 131nb (128.0 mg, 79%) as a colorless oil.

1H NMR (300 MHz, CDCl3): 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). 13C
NMR (75 MHz, CDCl3): δ = 166.4 (Cq), 162.6 (Cq), 155.3 (Cq), 147.7 (CH), 140.0 (CH), 137.4
(CH), 127.7 (Cq), 127.6 (1JC,F = 4 Hz, CH), 127.1 (1JC,F = 33 Hz, Cq), 125.3 (1JC,F = 4 Hz, CH), 123.7
(1JC,F = 272 Hz, Cq), 122.5 (CH), 121.4 (CH), 119.6 (CH), 112.3 (CH), 60.7 (CH2), 14.2 (CH3).

19F NMR (283 MHz, CDCl3): 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 C17H14F3NO5⁺ [M]+ 337.0920, found 337.0917.

(131ob):

The general procedure D was followed using ethyl 4-(pyridin-2-yl)benzoate
(130a) (241.0 mg, 0.99 mmol), ethyl acrylate (46b) (48.0 mg, 0.48 mmol),
[RuCl3(p-cymene)]2 (15.8 mg, 5.4 mol %), and AgSbF6 (36.5 mg, 22 mol %).
Purification by column chromatography (n-hexane/EtOAc: 10/1) yielded 131ob
(110 mg, 67%) as a colorless oil.

1H NMR (300 MHz, CDCl3): 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).

13C NMR (75 MHz, CDCl3): δ = 166.6 (Cq), 165.5 (Cq), 162.7 (Cq), 156.4 (Cq), 147.8 (CH), 139.9
(CH), 137.9 (CH), 132.1 (CH), 129.7 (CH), 127.0 (Cq), 126.9 (Cq), 121.6 (CH), 120.8 (CH), 119.5
(CH), 112.3 (CH), 61.1(CH2), 60.5 (CH3), 14.3 (CH3), 14.2 (CH3).

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 C₁₉H₁₉NO₅⁺ [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), [RuCl₂(p-cymene)]₂ (15.7 mg, 4.8 mol %), and AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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 (dd, 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).

¹³C NMR (75 MHz, CDCl₃): δ = 196.4 (C₉), 166.6 (C₉), 162.6 (C₉), 156.63 (C₉), 147.8 (CH), 140.0 (CH), 138.0 (CH), 133.6 (C₉), 130.9 (CH), 128.6 (CH), 127.2 (C₉), 121.8 (CH), 121.0 (CH), 119.6 (CH), 112.4 (CH), 60.6 (CH₂), 26.5 (CH₃), 14.2 (CH₃).

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 C₁₉H₁₈NO₄⁺ [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-(nitrophenoxyl)pyridine (130q) (215.3 mg, 1.00 mmol), ethyl acrylate (46b) (49.0 mg, 0.49 mmol), [RuCl₂(p-cymene)]₂ (15.6 mg, 5.2 mol %), and AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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 (dd, 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).

¹³C NMR (75 MHz, CDCl₃): δ = 166.2 (C₉), 162.1 (C₉), 157.6 (C₉), 147.8 (CH), 144.2 (C₉), 140.3 (CH), 136.6(CH), 127.9 (C₉), 125.7 (CH), 123.5 (CH), 122.4 (CH), 122.1 (CH), 120.2 (CH), 112.7 (CH), 60.8 (CH₂), 14.2 (CH₃).
Experimental Section

(E)-Ethyl 3-[3-methyl-2-[(5-methylpyridin-2-yl)oxy]phenyl]acrylate (131sb):

The general procedure D was followed using 5-methyl-2-(α-tolyl)oxy)-pyridine (130s) (197.7 mg, 0.99 mmol), ethyl acrylate (46b) (49.7 mg, 0.50 mmol), [RuCl₂(p-cymene)]₂ (7.8 mg, 2.5 mol %), AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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 (d, 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), 1.46 (s, 9H). Purification by column chromatography (n-hexane/EtOAc: 15/1) yielded 131sb (120.0 mg, 75%) as a colorless oil.

(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-(α-tolyl)oxy)-pyridine (130s) (198.7 mg, 1.00 mmol), tert-butyl acrylate (46p) (62.5 mg, 0.49 mmol), [RuCl₂(p-cymene)]₂ (7.9 mg, 2.6 mol %), AgSbF₆ (17.8 mg, 11 mol %). Purification by column chromatography (n-hexane/EtOAc: 15/1) yielded 131sp (18.3 mg, 75%) as a colorless oil.

¹H NMR (300 MHz, CDCl₃): 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 (d, 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).

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 calc for C₁₆H₁₉N₂O₃⁺ [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-(α-tolyl)oxy)-pyridine (130s) (197.7 mg, 0.99 mmol), ethyl acrylate (46b) (49.7 mg, 0.50 mmol), [RuCl₂(p-cymene)]₂ (7.8 mg, 2.5 mol %), AgSbF₆ (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.

¹H NMR (300 MHz, CDCl₃): 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 (d, 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), 1.46 (s, 9H). Purification by column chromatography (n-hexane/EtOAc: 15/1) yielded 131sb (120.0 mg, 75%) as a colorless oil.

¹H NMR (300 MHz, CDCl₃): 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 (d, 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).

IR (neat): 2987, 1704, 1426, 1341, 1230, 1193, 770, 740 cm⁻¹.
Experimental Section

**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)-1H-indol-2-yl]acrylate (131tb):*

The general procedure D was followed using ethyl 1-methyl-3-(pyridin-2-yloxy)-1H-indole (130t) (228.0 mg, 1.02 mmol), ethyl acrylate (46b) (51.7 mg, 0.52 mmol), [RuCl$_2$(*p*-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$_3$): $\delta$ = 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$_3$): $\delta$ = 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$_2$O$_3$ [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*-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$_3$): $\delta$ = 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).
13C NMR (75 MHz, CDCl₃): δ = 166.6 (C₉), 162.3 (C₉), 141.2 (C₉), 140.5 (CH), 138.8 (CH), 133.6 (CH), 132.7 (C₆), 125.0 (CH), 124.0 (CH), 122.1 (CH), 120.5 (CH), 106.4 (CH), 60.6 (CH₂), 14.2 (CH₃).

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 C₁₄H₁₃NO₃⁺ [M⁺] 275.061, found 275.0616.

(E)-Ethyl 3-[4-Methyl-2-(pyridin-2-yloxy)phenyl]acrylate (131wb):

The general procedure D was followed using 2-(m-tolyl)pyridine (130w) (185.4 mg, 1.00 mmol), ethyl acrylate (46b) (50.7 mg, 0.51 mmol), [RuCl₂(p-cymene)]₂ (7.7 mg, 2.5 mol %), and AgSbF₆ (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

¹H NMR (300 MHz, CDCl₃): 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).

¹³C NMR (75 MHz, CDCl₃): δ = 167.0 (C₉), 163.4 (C₉), 152.8 (C₉), 147.8 (CH), 142.0 (C₉), 139.5 (CH), 138.8 (CH), 127.8 (CH), 126.2 (CH), 124.5 (C₉), 122.8 (CH), 118.6 (CH), 118.6 (CH), 111.6 (CH), 60.3 (CH₂), 21.4 (CH₃), 14.2 (CH₃).

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 C₁₇H₁₇NO₃⁺ [M⁺] 283.120, 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-tolyl)pyridine (130w) (186.0 mg, 1.00 mmol), tert-butyl acrylate (46p) (67.0 mg, 0.52 mmol), [RuCl₂(p-cymene)]₂ (7.9 mg, 2.5 mol %), AgSbF₆ (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.
Experimental Section

\( ^1 \text{H NMR} \) (300 MHz, CDCl\(_3\)): \( \delta = 8.15 \) (dd, \( J = 5.0, 2.0, 0.8 \) 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).

\( ^{13} \text{C NMR} \) (75 MHz, CDCl\(_3\)): \( \delta = 166.4 \) (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) \( m/2 \) (relative intensity): 311 (7) [M]\(^+\), 254 (7), 238 (16), 210 (100), 194 (12), 167 (15), 115 (5), 78 (15).

HR-MS (EI) \( m/2 \) calcd for C\(_{19}\)H\(_{23}\)NO\(_3\)^+ [M]\(^+\) 311.1516, found 311.1522.

\( \text{(E)-Ethyl 3-\{2-(pyridin-2-yl)oxy\}phenyl} \)acrylate (131xb):

\[
\text{The general procedure D was followed using 2-\{3-(trifluoromethyl)phenoxy\}pyridine (130x) (241.0 mg, 1.00 mmol), ethyl acrylate (46b) (50.1 mg, 0.50 mmol), [RuCl}_2(p\text{-cymene})_2 (7.6 mg, 2.5 mol %), AgSbF}_6 (17.9 mg, 10 mol %). Purification by column chromatography (n-hexane/EtOAc: 30/1→20/1) yielded 131xb (146.0 mg, 87%) as a colorless oil.}
\]

\( ^1 \text{H NMR} \) (300 MHz, CDCl\(_3\)): \( \delta = 8.15 \) (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, \( J = 8.3 \) Hz, 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).

\( ^{13} \text{C NMR} \) (75 MHz, CDCl\(_3\)): \( \delta = 166.4 \) (C\(_q\)), 162.7 (C\(_q\)), 152.7 (C\(_q\)), 147.7 (CH), 139.9 (CH), 137.4 (CH), 132.6 (\( ^2 \text{J}_{\text{CF}} = 33 \) Hz, C\(_q\)), 130.8 (C\(_q\)), 128.4 (CH), 123.3 (\( ^1 \text{J}_{\text{CF}} = 273 \) Hz, C\(_q\)), 121.9 (CH), 121.6 (\( ^3 \text{J}_{\text{CF}} = 4 \) Hz, CH), 119.60 (\( ^1 \text{J}_{\text{CF}} = 4 \) Hz, CH), 119.4 (CH), 111.9 (CH), 60.7 (CH\(_2\)), 14.2 (CH\(_3\)).

\( ^{19} \text{F NMR} \) (283 MHz, CDCl\(_3\)): \( \delta = -62.9 \) (s).

IR (neat): 2983, 1713, 1415, 1325, 1236, 1165, 1109, 777 cm\(^{-1}\).

MS (EI) \( m/2 \) (relative intensity): 337 (15) [M]\(^+\), 308 (15), 292 (20), 264 (100), 248 (7), 236 (16), 215 (12), 167(15).

HR-MS (EI) \( m/2 \) calcd for C\(_{17}\)H\(_{19}\)F\(_2\)NO\(_3\)^+ [M]\(^+\) 337.0920, found 337.0927.

\( \text{(E)-Ethyl 3-\{5-(pyridin-2-yl)oxy\}benzo[d][1,3]dioxol-4-yl} \)acrylate (131yb):

\[
\text{The general procedure D was followed using 2-\{benzo[d][1,3]dioxol-5-yl\}oxy} \)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.
**Experimental Section**

M. p. = 90–92 °C.

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.15\) (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\(_3\)): \(\delta = 167.2\) (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) \(m/z\) calcld for C\(_{17}\)H\(_{15}\)NO\(_5\) \([M]^+\) 313.0945, found 313.0955.

**Removal of the directing group**

To a solution of (E)-ethyl 3-{5-(pyridin-2-yloxy)phenyl}acrylate (131yp) (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\textsubscript{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\textsubscript{2}O (75 mL) was added, and the resulting mixture was extracted with EtOAc (3 \times 50 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{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):

\[
M. \text{ p.} = 119−121^\circ \text{C}.
\]

\text{^1H NMR (300 MHz, CDCl}_3\text{): } \delta = 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).

\text{^13C NMR (75 MHz, CDCl}_3\text{): } \delta = 168.1 (\text{C}_q), 153.6 (\text{C}_q), 140.6 (\text{CH}), 132.7 (\text{CH}), 126.2 (\text{CH}), 124.1 (\text{C}_q), 121.6 (\text{C}_q), 120.4 (\text{CH}), 118.1 (\text{CH}), 108.2 (\text{CH}_2), 15.9 (\text{CH}_3), 14.3 (\text{CH}_3).

\text{IR (neat): } 3318, 2982, 1681, 1316, 1220, 1183, 1029, 778 \text{ cm}^{-1}.

\text{MS (EI) m/z (relative intensity): } 206 (15) [\text{M}]^+, 160 (85), 132 (100), 115 (7), 105 (35), 91 (10), 77 (25), 43 (30).

\text{HR-MS (EI) m/z calcld for C}_{12}H_{14}O_{3}^+ [\text{M}]^+ 206.0937, \text{ found 206.0948}.

The spectral data were in accordance with those reported in the literature.\textsuperscript{140}

Intermolecular Competition Experiment between Substrates 130a and 130c

\[\text{Me} \quad \text{CO}_2\text{Et} \quad \text{RuCl}_2(p\text{-cyrene})_2 \quad \text{AgSbF}_6 \quad \text{Cu(OAc)}_2 \cdot \text{H}_2\text{O} \quad \text{tAmOH, 120 °C, 16 h under air} \]

\[\begin{align*}
\text{130a} & \quad \text{(3.0 equiv)} \quad \text{46b} \quad \text{131ab: 37\%} \\
\text{130c} & \quad \text{(3.0 equiv)} \quad + \\
\text{131cb: 4\%}
\end{align*}\]

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), [RuCl₂(p-cymene)]₂ (7.9 mg, 2.6 mol %), AgSbF₆ (18.5 mg, 11 mol %) and Cu(OAc)₂·H₂O (200 mg, 1.00 mmol) in tAmOH (2.0 mL) was stirred at ambient temperature for 5 min under N₂ 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. NH₄Cl/NH₃ (1:1, 10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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.

Intemolecular 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), [RuCl₂(p-cymene)]₂ (15.5 mg, 5.0 mol %), AgSbF₆ (35.1 mg, 20 mol %) and Cu(OAc)₂·H₂O (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 Substrate 130k with D₂O 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), [RuCl₂(p-cymene)]₂ (7.8 mg, 5.0 mol %), AgSbF₆ (18.5 mg, 10 mol %) and Cu(OAc)₂ (186.0 mg, 1.02 mmol) in a solvent mixture of tAmOH and D₂O (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 ¹H 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.

¹H NMR (400 MHz, CDCl₃): 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).

¹³C NMR (100 MHz, CDCl₃): δ = 170.0 (Cₐ), 168.2 (Cₐ), 150.2 (CH), 145.4 (Cₐ), 144.7 (Cₐ), 136.3 (CH), 133.4(Cₐ), 132.1 (Cₐ), 131.9 (CH), 130.4 (CH), 129.3 (Cₐ), 128.4 (CH), 128.0 (CH), 126.3 (CH), 124.3 (CH), 122.5 (CH), 121.5 (CH), 60.5 (CH₂), 59.5 (CH), 38.0 (CH₃), 13.8 (CH₃).

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).
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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$_3$): $\delta = 8.84$ (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), 7.39–7.27 (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$_3$): $\delta = 169.9$ (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$_3$): $\delta = 8.84$ (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$_3$): $\delta = 167.8$ (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 (El) 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 C₁₀H₁₃N₂O⁺ [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.

1H NMR (300 MHz, CDCl₃): 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).

13C NMR (75 MHz, CDCl₃): δ = 205.6 (C₉), 168.2 (C₉), 150.4 (CH), 146.2 (C₉), 144.6 (C₉), 136.3 (CH), 133.6 (C₉), 132.0 (CH), 131.9 (C₉), 130.1 (CH), 129.4 (C₉), 128.3 (CH), 128.2 (CH), 126.3 (CH), 124.3 (CH), 122.8 (CH), 121.6 (CH), 50.9 (CH), 46.7 (CH₂), 30.5 (CH₃).

IR (neat): 3042, 2922, 1688, 1499, 1470, 1394, 1362, 1150 cm⁻¹.

MS (El) 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 C₂₀H₁₆N₂O₂⁺ [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.

1H NMR (300 MHz, CDCl₃): 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).

13C NMR (125 MHz, CDCl₃): δ = 170.0 (C₉), 168.3 (C₉), 150.1 (CH), 145.8 (C₉), 144.6 (C₉), 142.5 (C₉), 136.2 (CH), 133.5 (C₉), 130.4 (CH), 129.5 (C₉), 129.3 (CH), 129.3 (C₉), 127.9 (CH), 124.5 (C₉), 122.8 (CH), 121.6 (CH), 50.9 (CH), 46.7 (CH₂), 30.5 (CH₃).
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126.3 (CH), 124.0 (CH), 122.9 (CH), 121.4 (CH), 60.5 (CH₂), 59.4 (CH), 38.2 (CH₂), 22.1 (CH₃), 13.9 (CH₃).

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 C₂₂H₂₁N₂O₃⁺ [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.

¹H NMR (500 MHz, CDCl₃): 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).

¹³C NMR (125 MHz, CDCl₃): δ = 205.8 (Cₗ), 168.2 (Cₗ), 150.3 (CH), 146.6 (Cₗ), 144.7 (Cₗ), 142.7 (Cₗ), 136.3 (CH), 133.8 (Cₗ), 130.1 (CH), 129.4 (Cₗ), 129.3 (CH), 128.0 (CH), 126.3 (CH), 124.1 (CH), 123.3 (CH), 121.5 (CH), 58.8 (CH), 46.8 (CH₂), 30.5 (CH₃), 22.0 (CH₃).

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 C₂₁H₁₈N₂O₃⁺ [M+H]⁺ 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.

¹H NMR (500 MHz, CDCl₃): δ = 8.84 (dd, J = 4.2, 1.8 Hz, 1H), 8.17 (dd, J = 8.3, 1.8 Hz, 1H),
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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).

1H NMR (125 MHz, CDCl3): δ = 170.0 (Cq), 167.9 (Cq), 163.0 (Cq), 150.0 (CH), 147.7 (Cq), 144.6 (Cq), 136.1 (CH), 133.5 (Cq), 130.3 (CH), 129.2 (Cq), 127.8 (CH), 126.2 (CH), 125.5 (CH), 124.6 (Cq), 121.4 (CH), 114.9 (CH), 107.4 (CH), 60.5 (CH2), 59.2 (CH), 55.6 (CH3), 38.2 (CH2), 13.9 (CH3).

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 C22H20N2O4⁺ [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, 0.5 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.

1H NMR (500 MHz, CDCl3): 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 (dddd, 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 = 7.2 Hz, 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).

13C NMR (125 MHz, CDCl3): δ = 169.6 (Cq), 167.1 (Cq), 150.2 (CH), 147.0 (Cq), 144.4 (Cq), 138.2 (Cq), 136.2 (CH), 133.0 (Cq), 130.6 (Cq), 130.2 (CH), 129.3 (Cq), 128.9 (CH), 128.2 (CH), 126.2 (CH), 125.4 (CH), 123.1 (CH), 121.5 (CH), 60.7 (CH2), 59.1 (CH), 37.7 (CH2), 13.9 (CH3).

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 C21H17ClN3O4⁺ [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-
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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.

\[ ^1H \text{NMR} (500 MHz, CDCl}_3]: \delta = 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, 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 = 7.1 Hz, 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).

\[ ^13C \text{NMR} (125 MHz, CDCl}_3]: \delta = 169.8 (C_\text{q}), 167.4 (C_\text{q}), 150.3 (CH), 147.3 (C_\text{q}), 144.5 (C_\text{q}), 136.4 (CH), 133.0 (C_\text{q}), 131.9 (CH), 131.1 (C_\text{q}), 130.4 (CH), 129.4 (C_\text{q}), 128.3 (CH), 126.7 (C_\text{q}), 126.4 (CH), 126.2 (CH), 125.7 (CH), 121.6 (CH), 60.7 (CH\text{z}), 59.1 (CH), 37.7 (CH\text{z}), 13.9 (CH_3).

IR (neat): 2988, 2924, 1727, 1692, 1396, 1374, 1192, 830, 687 cm\(^{-1}\).

\[ \text{MS (EI)} m/z \text{ (relative intensity)}: 424 (15) [M]^+ , 379 (5), 351 (100), 272 (10), 242 (10), 229 (10), 128 (10).

\[ \text{HR-MS (ESI)} m/z \text{ calcd for C}_{21}H_{17}BrN_{2}O_{3}^+ [M]^+ 424.0417, \text{ 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.

\[ ^1H \text{NMR} (400 MHz, CDCl}_3]: \delta = 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).

\[ ^13C \text{NMR} (100 MHz, CDCl}_3]: \delta = 170.0 (C_\text{q}), 167.6 (C_\text{q}), 150.3 (CH), 147.3 (C_\text{q}), 144.5 (C_\text{q}), 137.7 (CH), 136.3 (CH), 133.0 (C_\text{q}), 132.1 (CH), 131.7 (C_\text{q}), 130.4 (CH), 129.4 (C_\text{q}), 128.3 (CH), 126.3 (CH), 125.7 (CH), 121.6 (CH), 98.9 (C_\text{q}), 60.7 (CH\text{z}), 59.0 (CH), 37.7 (CH\text{z}), 13.9 (CH_3).

IR (neat): 2981, 2914, 1729, 1683, 1400, 1191, 826, 687 cm\(^{-1}\).

\[ \text{MS (EI)} m/z \text{ (relative intensity)}: 472 (35) [M]^+ , 427 (5), 399 (100), 385 (10), 272 (25), 243 (10), 229 (10), 102 (10).

\[ \text{HR-MS (ESI)} m/z \text{ calcd for C}_{21}H_{17}IN_{2}O_{3}^+ [M]^+ 472.0278, \text{ found 472.0291.}

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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$_3$): $\delta$ = 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, $J = 8.0$, 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$_3$): $\delta$ = 169.6 (C$_q$), 166.4 (C$_q$), 150.5 (CH), 145.9 (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$_3$O$_3$ $^+$ [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$_3$): $\delta$ = 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$_3$): $\delta$ = 169.4 (C$_q$), 166.1 (C$_q$), 150.5 (CH), 150.4 (C$_q$), 146.4 (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$_3$).
144.2 (C_q), 137.6 (C_q), 136.5 (CH), 132.6 (C_q), 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\(_3\)O\(_5\) [M\(^+\)] 391.1163, found 391.1174.

**Ethyl 2-[3-oxo-2-(quinolin-8-yl)-6-(trifluoromethyl)isoindolin-1-yl]acetate (132ib):**

![Ethyl 2-[3-oxo-2-(quinolin-8-yl)-6-(trifluoromethyl)isoindolin-1-yl]acetate](image)

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\(_3\)):** \(\delta = 8.85 \text{ (dd, } J = 4.2, 1.8 \text{ Hz, } 1H), 8.21 \text{ (dd, } J = 8.3, 1.8 \text{ Hz, } 1H), 8.08 \text{ (dt, } J = 7.9, 0.8 \text{ Hz, } 1H), 7.90–7.83 \text{ (m, } 3H), 7.82–7.78 \text{ (m, } 1H), 7.63 \text{ (t, } J = 7.8 \text{ Hz, } 1H), 7.43 \text{ (dd, } J = 8.3, 4.2 \text{ Hz, } 1H), 6.36 \text{ (dd, } J = 7.3, 5.1 \text{ Hz, } 1H) 3.86 \text{ (q, } J = 7.1 \text{ Hz, } 2H), 2.79 \text{ (dd, } J = 16.1, 5.1 \text{ Hz, } 1H), 2.61 \text{ (dd, } J = 16.1, 7.3 \text{ Hz, } 1H), 0.99 \text{ (t, } J = 7.1 \text{ Hz, } 3H).\)

**\(^{13}\)C NMR (125 MHz, CDCl\(_3\)):** \(\delta = 170.0 \text{ (C_q), 166.9 (C_q), 150.4 (CH), 145.8 (C_q), 144.4 (C_q), 136.4 (CH), 135.4 (q, } J = 1.4 \text{ Hz, } C_q), 133.8 \text{ (q, } J_{C-F} = 3.2 \text{ Hz, } C_q) 132.8 \text{ (C_q), 130.4 (CH), 129.4 (C_q), 128.4 (CH), 126.4 (CH), 125.7 (q, } J_{C-F} = 3.7 \text{ Hz, } CH), 124.9 (CH), 123.8 \text{ (q, } J_{C-F} = 272.6 \text{ Hz, } C_q) 121.7 (CH), 120.1 \text{ (q, } J_{C-F} = 3.9 \text{ Hz, } CH), 60.8 \text{ (CH_2), 59.5 (CH), 37.5 (CH_2), 13.8 (CH_3).}\)

**\(^{19}\)F NMR (282 MHz, CDCl\(_3\)):** \(\delta = -62.4.\)

**IR (neat):** 3346, 1667, 1532, 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\(_3\)N\(_2\)O\(_3\) [M\(^+\)] 414.1186, found 414.1183.

**Ethyl 2-[4-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl]acetate (132jb):**

![Ethyl 2-[4-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl]acetate](image)

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\(_3\)):** \(\delta = 8.86 \text{ (dd, } J = 4.2, 1.7 \text{ Hz, } 1H), 8.20 \text{ (dd, } J = 8.3, 1.7 \text{ Hz, } 1H), 7.85–7.82 \text{ (m, } 2H), 7.61 \text{ (dd, } J = 8.3, 7.3 \text{ Hz, } 1H) 7.58–7.54 \text{ (m, } 1H), 7.42 \text{ (dd, } J = 8.3, 4.2 \text{ 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$_3$): $\delta$ = 169.8 (C$_q$), 165.1 (d, $^3$J$_{C,F}$ = 2.5 Hz, C$_q$), 159.3 (d, $^1$J$_{C,F}$ = 261.0 Hz, C$_q$), 150.2 (CH), 148.2 (d, $^3$J$_{C,F}$ = 2.8 Hz, C$_q$), 144.4 (C$_q$), 136.6 (CH), 133.9 (d, $^3$J$_{C,F}$ = 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, $^3$J$_{C,F}$ = 12.9 Hz, C$_q$), 118.5 (d, $^4$J$_{C,F}$ = 4.2 Hz, CH), 115.7 (d, $^3$J$_{C,F}$ = 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$_3$): $\delta$ = −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$_2$O$_3$+ [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$_3$): $\delta$ = 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$_3$): $\delta$ = 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$_2$O$_3$+ [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.**

$^1$H NMR (500 MHz, CDCl$_3$): $\delta = 8.85$ (dd, $J = 4.2$, 1.7 Hz, 1H), 8.18 (ddd, $J = 8.3$, 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$_3$): $\delta = 170.3$ (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 ($CH_3$).

IR (neat): 2980, 2926, 1717, 1683, 1398, 1181, 794 cm$^{-1}$.

MS (EI) $m/z$ (relative intensity): 374 (25) [M]$^+$, 329 (5), 301 (100), 287 (10), 257 (10), 129 (10).

HR-MS (ESI) $m/z$ calcd for C$_{23}$H$_{22}$N$_2$O$_3$+ [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$_3$): $\delta = 8.85$ (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$_3$): $\delta = 169.5$ (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$_2$O$_3$+ [M]$^+$ 374.1625, found 374.1623.
### Experimental Section

**Ethyl 2-{2-(5-methoxyquinolin-8-yl)-6-methyl-3-oxoisooindolin-1-yl}acetate (132nb):**

![Chemical Structure](image)

The general procedure E was followed using \(N\)-(5-methoxyquinolin8-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\(\rightarrow\)1/1) yielded 132nb (61.0 mg, 63%) as a colorless solid.

**M. p.** = 137–139 °C.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 8.81\) (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\(_3\)): \(\delta = 170.1\) (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\(_2\)O\(_4\)\(^+\) [M]\(^+\) 390.1574, found 390.1570.

**2-{2-(5-Methoxyquinolin-8-yl)-6-methyl-3-oxoisooindolin-1-yl}acetonitrile (132nh):**

The general procedure E was followed using \(N\)-(5-methoxyquinolin8-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\(\rightarrow\)1/1) yielded 132nh (55.0 mg, 64%) as a colorless solid.

**M. p.** = 227–228 °C.

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.83–8.81\) (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\(_3\)): \(\delta = 168.2\) (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
Experimental Section

(C\textsubscript{q}), 120.7 (CH), 116.0 (C\textsubscript{q}), 104.1 (CH), 57.8 (CH), 56.0 (CH\textsubscript{3}), 22.1 (CH\textsubscript{3}), 22.0 (CH\textsubscript{2}).

IR (neat): 2964, 2930, 2912, 1686, 1587, 1407, 1274, 1080 cm\textsuperscript{-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\textsubscript{21}H\textsubscript{17}N\textsubscript{3}O\textsubscript{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, 0.5 mmol). Purification by column chromatography (n-hexane/EtOAc: 2/1→1/1) yielded 132s (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):

\[ \text{M. p. = 168–170 °C.} \]

\[ \text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): } \delta = 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 (dd, J = 9.1, 8.4, 2.5 Hz, 1H), 6.26 (dd, J = 7.2, 5.3 Hz, 1H), 3.83 (q, J = 7.2 Hz, 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).

\[ \text{\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): } \delta = 169.9 (C\textsubscript{q}), 167.2 (d, \textsuperscript{4}J_{CF} = 3.5 Hz, C\textsubscript{q}), 163.0 (d, \textsuperscript{4}J_{CF} = 247.5 Hz, C\textsubscript{q}), 150.3 (CH), 144.5 (C\textsubscript{q}), 140.9 (d, \textsuperscript{4}J_{CF} = 2.4 Hz, C\textsubscript{q}), 136.3 (CH), 134.3 (d, \textsuperscript{3}J_{CF} = 8.8 Hz, C\textsubscript{q}), 133.1 (C\textsubscript{q}), 130.3 (CH), 129.4 (C\textsubscript{q}), 128.3 (CH), 126.3 (CH), 124.3 (d, \textsuperscript{3}J_{CF} = 8.3 Hz, CH), 121.6 (CH), 119.4 (d, \textsuperscript{2}J_{CF} = 23.6 Hz, CH), 110.9 (d, \textsuperscript{2}J_{CF} = 23.4 Hz, CH), 60.6 (CH\textsubscript{2}), 59.2 (CH), 37.9 (CH\textsubscript{2}), 13.8 (CH\textsubscript{3}).

\[ \text{\textsuperscript{19}F NMR (282 MHz, CDCl\textsubscript{3}): } \delta = -(112.9–113.0) (m).

IR (neat): 3047, 1733, 1697, 1619, 1502, 1424, 1376, 1226 cm\textsuperscript{-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\textsubscript{21}H\textsubscript{17}FN\textsubscript{2}O\textsubscript{3}+ [M]+ 364.1218, found 364.1231.

Ethyl 2-{(7-fluoro-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl)acetate (132sb'):

\[ \text{M. p. = 144–146 °C.} \]

\[ \text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): } \delta = 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,
Experimental Section

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).

13C NMR (125 MHz, CDCl3): δ = 169.2 (Cq), 167.3 (d, JCF = 2.3 Hz, Cq), 157.6 (d, JCF = 250.2 Hz, Cq), 150.3 (CH), 144.6 (Cq), 136.4 (CH), 135.5 (d, JCF = 4.3 Hz, Cq), 132.9 (Cq), 130.8 (d, JCF = 16.7 Hz, Cq), 130.7 (CH), 130.5 (d, JCF = 6.6 Hz, CH), 129.3 (Cq), 128.2 (CH), 126.4 (CH), 121.6 (CH), 120.3 (d, JCF = 3.7 Hz, CH), 118.7 (d, JCF = 20.0 Hz, CH), 60.5 (CH2), 57.7 (d, JCF = 2.1 Hz, CH), 36.4 (d, JCF = 1.1 Hz, CH2), 13.7 (CH3).

19F NMR (283 MHz, CDCl3): 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 C21H17FN2O3+[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.

1H NMR (300 MHz, CDCl3): 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).

13C NMR (125 MHz, CDCl3): δ = 170.2 (Cq), 168.4 (Cq), 150.2 (CH), 144.7 (Cq), 142.7 (Cq), 138.4 (Cq), 136.3 (CH), 133.6 (Cq), 132.9 (CH), 132.2 (Cq), 130.4 (CH), 129.4 (Cq), 128.0 (CH), 126.3 (CH), 124.5 (CH), 122.3 (CH), 121.5 (CH), 60.5 (CH2), 59.4 (CH), 38.2 (CH2), 21.3 (CH3), 13.8 (CH3).

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 C22H20N3O3+[M]+ 360.1468, found 360.1471.

Ethyl 2-{7-Methyl-3-oxo-2-(quinolin-8-yl)isoindolin-1-yl}acetate (132tb'):
Experimental Section

M. p. = 139–141 °C.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 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$_3$): $\delta$ = 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, 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$_2$O$_3$ $^+$ [M$^+$] 360.1468, found 360.1469.

Intermolecular Competition Experiments between Amides 110c and 110d

The general procedure $\text{E}$ 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$_3$OD 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$_3$CH$_2$OH/CD$_3$OD (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$_3$CH$_2$OH (2.0/0.5 mL) was stirred at 100 °C for 18 h under ambient atmosphere of air. The reaction mixture was diluted with H$_2$O (20 mL) and extracted with tBuOMe (3 x 25 mL). The combined organic layers were washed with brine (50 mL) and dried over Na$_2$SO$_4$. 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$_3$): $\delta$ = 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).
**Experimental Section**

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 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$_4$N$_2$O$_3$+$[M]^+$350.1563, found 350.1575.

**Studies on the Kinetic Isotope Effect.**

![Chemical structure diagram]

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.

![Chemical structure diagram]

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$_{18}$]-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**
Experimental Section

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, $J$ = 5.8 Hz, 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$_2$P$^+$ [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-1H-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-1H-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\(_3\)): \(\delta = 7.91–7.67\) (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\(_3\)): \(\delta = 148.4\) (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\(_3\)): \(\delta = 56.7\).

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-1H-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 (87.0 mg, 54%) as a colorless solid.

M.p. = 162–164 °C.

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.90–7.70\) (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\(_3\)): \(\delta = 147.0\) (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\(_3\)).
Experimental Section

$^{31}$P NMR (122 MHz, CDCl$_3$): $\delta$ = 45.2.

IR (neat): 3056, 3029, 1715, 1290, 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 calc 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$_3$): $\delta$ = 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$_3$): $\delta$ = 148.4 (d, $J = 19.4$ Hz, C$_q$), 142.6 (d, $J = 24.8$ Hz, C$_q$), 133.1 (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$_3$): $\delta$ = 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 calc 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)ethylene (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$_3$): $\delta$ = 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$_3$): $\delta$ = 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
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(CH), 127.9 (d, J = 1.3 Hz, CH), 125.3 (d, J = 14.8 Hz, CH), 62.4 (d, J = 6.4 Hz, CH₂), 16.4 (d, J = 6.2 Hz, CH₃).

³¹P NMR (122 MHz, CDCl₃): 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 C₂₀H₁₈O₂P₂⁺ [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, 0.5 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.

¹H NMR (300 MHz, CDCl₃): 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).

¹³C NMR (75 MHz, CDCl₃): δ = 162.7 (d, ¹J_{CF} = 249.5 Hz, C₀), 162.3 (d, ¹J_{CF} = 249.5 Hz, C₀), 147.4 (dd, J = 28.0, 1.4 Hz, C₀), 141.5 (d, J = 34.0 Hz, C₀), 133.1 (d, J = 2.2 Hz, CH), 130.9 (d, J = 8.2 Hz, CH), 130.7 (dd, ³J_{CF} = 8.0, 5.8 Hz, CH), 129.5 (d, J = 125.8 Hz, C₀), 129.4 (dd, J = 18.3, 3.5 Hz, C₀), 129.1 (d, J = 11.3 Hz, CH), 128.3 (dd, J = 9.2, 3.5 Hz, C₀), 127.7 (d, J = 8.9 Hz, CH), 127.0 (d, J = 134.4 Hz, C₀), 123.7 (d, J = 13.4 Hz, CH), 116.2 (d, ²J_{CF}= 21.6 Hz, CH), 115.5 (d, ²J_{CF}= 21.9 Hz, CH), 62.1 (d, J = 6.6 Hz, CH₂), 16.4 (d, J = 5.9 Hz, CH₃).

¹⁹F NMR (282 MHz, CDCl₃): δ = -111.7–117.8 (m), –(112.4–112.5) (m), 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 C₂₂H₁₈F₂O₂P⁺ [M+H]⁺ 383.1007, found 383.1000.

2,3-Bis(4-chlorophenyl)-1-ethoxy-1H-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)
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(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.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_{3} \]: } \delta = 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).

\[ ^{13}C \text{ NMR (75 MHz, CDCl}_{3} \]: } \delta = 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}).

\[ ^{31}P \text{ NMR (122 MHz, CDCl}_{3} \]: } \delta = 46.0.

IR (neat): 2982, 1484, 1226, 1089, 1013, 769, 737, 501 cm\textsuperscript{–}1.

MS (EI) m/z (relative intensity): 414 (100) [M]\textsuperscript{+}, 385 (90), 367 (60), 322 (20), 286 (20), 250 (35), 139 (20).

HR-MS (ESI) m/z calcd for C\textsubscript{22}H\textsubscript{18}Cl\textsubscript{2}O\textsubscript{2}P [M+H]\textsuperscript{+} 415.0416, found 415.0409.

1-Ethoxy-2,3-bis{4-(trifluoromethyl)phenyl}-1H-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.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_{3} \]: } \delta = 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).

\[ ^{13}C \text{ NMR (125 MHz, CDCl}_{3} \]: } \delta = 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}).

\[ ^{19}F \text{ NMR (282 MHz, CDCl}_{3} \]: } \delta = –(62.6–63.0) (m).

\[ ^{31}P \text{ NMR (122 MHz, CDCl}_{3} \]: } \delta = 44.4.

IR (neat): 2984, 1736, 1616, 1320, 1163, 1109, 1065, 1016 cm\textsuperscript{–}1.

MS (EI) m/z (relative intensity): 482 (85) [M]\textsuperscript{+}, 453 (100), 435 (60), 388 (20), 320 (15), 141 (20).
HR-MS (EI) m/z calcd for C_{24}H_{17}F_{6}O_{2}P^{+} [M]^{+} 482.0865, found 482.0850.

1-Ethoxy-2,3-bis(4-methoxyphenyl)-1H-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-methoxyphenyl)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.

{\textit{^1}H} NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 7.73–7.67 \text{ (m, 1H)}, 7.42–7.30 \text{ (m, 4H)}, 7.17 \text{ (d, } J = 8.3 \text{ Hz, 2H}), 7.13–7.09 \text{ (m, 1H)}, 6.92 \text{ (dd, } J = 7.4, 1.6 \text{ Hz, 2H})\), 6.74–6.71 (2H), 4.11–3.96 (2H), 3.82 (s, 3H), 3.74 (s, 3H), 1.21 (t, \( J = 7.0 \text{ Hz, 3H})\).

{\textit{^{13}C} NMR} (75 MHz, CDCl\textsubscript{3}): \(\delta = 159.6 \text{ (C\textsubscript{q})}, 159.1 \text{ (C\textsubscript{q})}, 146.6 \text{ (d, } J = 28.1 \text{ Hz, C\textsubscript{q})}, 142.4 \text{ (d, } J = 34.6 \text{ Hz, C\textsubscript{q})}, 132.9 \text{ (d, } J = 2.2 \text{ Hz, CH})\), 130.4 (CH), 130.3 (d, \( J = 6.3 \text{ Hz, CH})\), 128.8 (d, \( J = 125.3 \text{ Hz, C\textsubscript{q})}, 128.5 \text{ (d, } J = 11.2 \text{ Hz, CH})\), 127.5 (d, \( J = 8.7 \text{ Hz, CH})\), 127.1 (d, \( J = 125.5 \text{ Hz, C\textsubscript{q})}, 126.1 \text{ (d, } J = 11.2 \text{ Hz, C\textsubscript{q})}, 125.0 \text{ (d, } J = 9.3 \text{ Hz, C\textsubscript{q})}, 123.5 \text{ (d, } J = 13.5 \text{ Hz, CH})\), 114.4 (CH), 113.8 (CH), 61.9 (d, \( J = 6.3 \text{ Hz, CH})\), 55.2 (CH), 55.1 (CH), 16.4 (d, \( J = 6.2 \text{ Hz, CH})\).

{\textit{^{31}P} NMR} (122 MHz, CDCl\textsubscript{3}): \(\delta = 47.5\).

IR (neat): 2988, 2933, 2836, 1243, 1218, 1174, 1022, 508 cm\textsuperscript{-1}.

MS (EI) m/z (relative intensity): 406 (100) \([\text{M}]^{+}\), 377 (40), 359 (30), 345 (10), 226 (10), 135 (10), 43 (10).

HR-MS (EI) m/z calcd for C_{24}H_{24}O_{4}P^{+} [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

{\textit{^1}H} NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 7.81–7.68 \text{ (m, 3H)}, 7.48–7.31 \text{ (m, 10H)}, 7.25–7.22 \text{ (m, 3H)}, 7.11–7.07 \text{ (m, 3H})\).

{\textit{^{13}C} NMR} (75 MHz, CDCl\textsubscript{3}): \(\delta = 150.0 \text{ (d, } J = 21.8 \text{ Hz, C\textsubscript{q})}, 143.7 \text{ (d, } J = 27.2 \text{ Hz, C\textsubscript{q})}, 134.2 \text{ (d, } J = 95.7 \text{ Hz, C\textsubscript{q})}, 134.2 \text{ (d, } J = 15.2 \text{ Hz, C\textsubscript{q})}, 132.9 \text{ (d, } J = 2.0 \text{ Hz, CH})\), 132.6 \text{ (d, } J = 10.0 \text{ Hz, C\textsubscript{q})}, 132.12 \text{ (d, } J = 2.9 \text{ Hz, CH})\), 132.0 (d, \( J = 105.7 \text{ Hz, C\textsubscript{q})}, 130.91 \text{ (d, } J = 10.6 \text{ Hz, CH})\), 129.9 (d, \( J = 99.6 \text{ Hz, C\textsubscript{q})}, 129.1 \text{ (d, } J = 2.9 \text{ Hz, CH})\), 129.1 (d, \( J = 12.7 \text{ Hz, CH})\), 129.0 (br, CH), 128.9 (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\(_3\)): \(\delta = 40.2\).

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-1H-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.

\(^1H\) NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.67–7.60\) (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\(_3\)): \(\delta = 149.0\) (d, \(J = 21.5\) Hz, C\(_q\)), 143.1 (d, \(J = 26.5\) Hz, C\(_q\)), 134.9 (C\(_q\)), 134.0 (C\(_q\)), 134.2 (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, \(J = 12.4\) Hz, CH), 128.7 (CH), 123.9 (d, \(J = 10.9\) Hz, CH).

\(^{31}P\) NMR (122 MHz, CDCl\(_3\)): \(\delta = 39.9\).

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\(_2\)OP^+ [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-methoxyphenyl)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.
**Experimental Section**

M. p. = 85–87 °C

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.79–7.62$ (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).

$^1$C NMR (125 MHz, CDCl$_3$): $\delta = 159.5$ (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$_3$): $\delta = 39.5$.

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$_3$P$^+$ [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$_3$): $\delta = 7.61–7.54$ (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$_3$): $\delta = 150.2$ (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$_3$): $\delta = 40.0$.

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.\textsuperscript{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-yl)benzene (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.

\( ^1H \) NMR (300 MHz, CDCl\(_3\)): \( \delta = 7.71–7.64 \) (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\(_3\)): \( \delta = 150.0 \) (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), 128.5 (d, \( J = 10.6 \) Hz, CH), 128.3 (d, \( J = 11.1 \) Hz, CH), 10.7 (d, \( J = 10.7 \) Hz, CH\(_3\)).

\( ^{31}P \) NMR (122 MHz, CDCl\(_3\)): \( \delta = 41.5 \).

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.\textsuperscript{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 (11i) (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.

\( ^1H \) NMR (300 MHz, CDCl\(_3\)): \( \delta = 7.71–7.64 \) (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\(_3\)): \( \delta = 150.2 \) (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$_3$): $\delta = 39.9$.

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$_{23}$O$_2$P$^+$ [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 2 h. 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$_3$): $\delta = 7.73–7.66$ (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$_3$): $\delta = 149.9$ (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$_3$): $\delta = 38.6$.

IR (neat): 3057, 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 12 h. Purification by column chromatography (n-hexane/EtOAc: 2/1) yielded 117ha (47.0 mg, 23%) and 117ha' (95.0 mg, 47%) as colorless solids.

7-Methyl-2,3-diphenyl-1-(o-tolyl)phosphindole 1-Oxide (117ha):
Experimental Section

**M. p.** = 163–165 °C

\[^1^H\text{NMR}\] (300 MHz, CDCl\(_3\)): \(\delta = 8.32\) (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).

\[^{13}^C\text{NMR}\] (125 MHz, CDCl\(_3\)): \(\delta = 150.0\) (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), 128.4 (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).

\[^{31}^P\text{NMR}\] (122 MHz, CDCl\(_3\)): \(\delta = 37.4\).

\text{IR} (neat): 3057, 1560, 1444, 1186, 793, 753, 714, 686 cm\(^{-1}\).

\text{MS (EI) } \text{m/z (relative intensity): } 406\ (100) [M]^+ , 391 (10), 329 (15), 313 (10), 265 (10), 228 (40), 181 (10).

\text{HR-MS (EI) } \text{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’):

\text{M. p.} = 69–71 °C

\[^1^H\text{NMR}\] (300 MHz, CDCl\(_3\)): \(\delta = 8.16\) (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).

\[^{13}^C\text{NMR}\] (75 MHz, CDCl\(_3\)): \(\delta = 152.3\) (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\(_3\)).

\[^{31}^P\text{NMR}\] (122 MHz, CDCl\(_3\)): \(\delta = 38.2\).

\text{IR} (neat): 3056, 2928, 1591, 1442, 1194, 1173, 812, 714 cm\(^{-1}\).

\text{MS (EI) } \text{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\(_2\)O and extracted with EtOAc (3 \( \times \) 25 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\). 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 \( \rightarrow \) 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\(_2\)O and extracted with EtOAc (3 \( \times \) 25 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\). 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 \( \rightarrow \) 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**

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, 1.00 mmol) in DMSO (2.0 mL) was stirred at 120 °C for 4h under N₂. At ambient temperature, the reaction mixture was diluted with water and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na₂SO₄. 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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
<th>Abbreviation</th>
<th>Definition</th>
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<td>Å</td>
<td>Ångström</td>
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