Ruthenium(II)-Catalyzed C–H Arylations of Arenes

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vorgelegt von

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aus

Bremen

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Erklärung

Ich versichere, dass ich die vorliegende Dissertation in der Zeit
von November 2012 bis September 2016 am

Institut für Organische und Biomolekulare Chemie
der Georg-August-Universität Göttingen

auf Anregung und unter Anleitung von

Herrn Prof. Dr. Lutz Ackermann

selbständig durchgeführt und keine anderen als die angegebenen
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Göttingen, den 19.08.2016

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Contents

Abbreviations

Ac	acetyl
Ad	adamantyl
Alk	alkyl
Ar	aryl
ARB	Angiotension Receptor Blocker
ASTM	American Society for Testing and Materials
BHT	butylated hydroxytoluene
Bn	benzyl
n-Bu	*n*-butyl
t-Bu	*tert*-butyl
calcd.	calculated
cat.	catalytic
CMD	concerted metalation-deprotonation
COSY	correlated spectroscopy
d	doublet
δ	chemical shift
DFT	density function theory
DG	directing group
Ed.	editor
EI	electron ionization
equiv	equivalents
ESI	electronspray ionization
Et	ethyl
ET	electron transfer
eV	electron volt
FT	Fourier transform
g	gram
GC	gas chromatography
h	hour
HASPO	heteroatom substituted secondary phosphine oxide
HMBC	heteronuclear multiple bond correlation
HRMS	high resolution mass spectrometry

HSQC	heteronuclear single quantum coherence
Hz	Hertz
IR	infrared spectroscopy
J	coupling constant
KIE	kinetic isotope effect
$[M^+]$	molecular ion peak
m	meta
m	multiplet
Me	methyl
Mes	mesityl
min	minute
mL	milliliter
mmol	millimol
m. p.	melting point
MPV	membrane pump vacuum
MS	mass spectrometry
m/*z*	mass/charge
NMP	*N*-Methyl-2-pyrrolidone
NMR	nuclear magnetic resonance spectroscopy
NOESY	nuclear Overhauser enhancement spectroscopy
o	*ortho*
OPV	oil pump vacuum
p	*para*
Ph	phenyl
Piv	pivaloyl
ppm	parts per million
i-Pr	*iso*-propyl
R	rest
s	singulet
SET	single-electron-transfer
SPO	secondary phosphine oxide
SPS	solvent purification system
t	time
t	triplet

TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
Tf	triflyl
TLC	thin layer chromatography
TM	transition metal
UV	ultraviolet

1 Introduction

1.1 Transition metal-catalyzed C–H activation/C–C formation

One of the fundamental demands in academic and industrial chemical research areas is to devise competitive solutions for expedient access to important compounds in material and life sciences.[1-4] In this context, the design of novel strategies to construct C–C bonds for the ideal synthesis of bi(hetero)aryls, which are a key molecular framework found in relevant bioactive compounds, has received considerable attention from the organic synthesis community.[5-14] A representative set of economically valuable agrochemicals and pharmaceuticals containing bi(hetero)aryl units as core structures are illustrated in Figures 1 and 2.[6,15-19]

Classical methods for constructing bi(hetero)aryls involve reactions such as the Ullmann-type coupling,[20,21] the Scholl reaction[22] and the Gomberg-Bachmann reaction[23] typically use harsh conditions, which are often not broadly applicable and can produce unsatisfactory yields.

For this reason, more efficient and selective transition metal-catalyzed cross-coupling reactions were developed. Palladium catalysis in particular has emerged as an indispensable tool for the synthesis of bi(hetero)aryl structures, becoming the method of choice for academic and industrial applications.[14] The huge contribution of palladium-catalyzed cross-coupling reactions was highlighted by the award of the Nobel Prize in Chemistry in 2010 for Akira Suzuki, Ei-ichi Negishi and Richard F. Heck.[24]

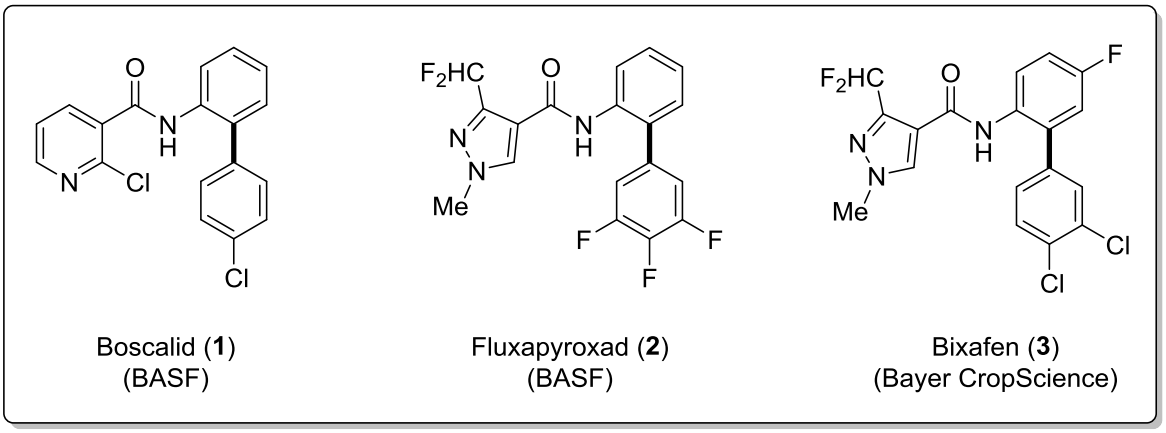


Figure 1: Selected bioactive bi(hetero)aryls present in top-selling agrochemicals.

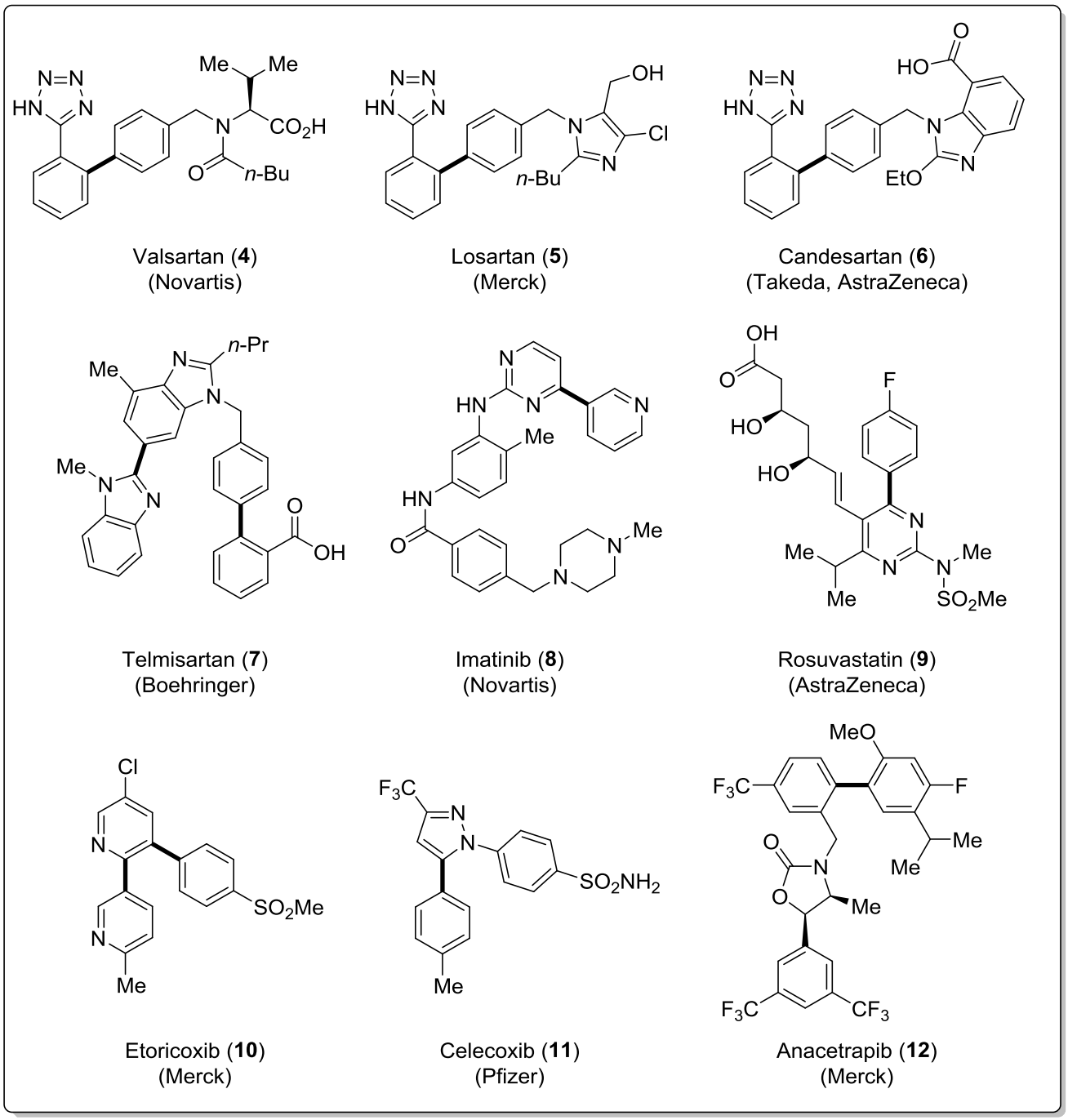
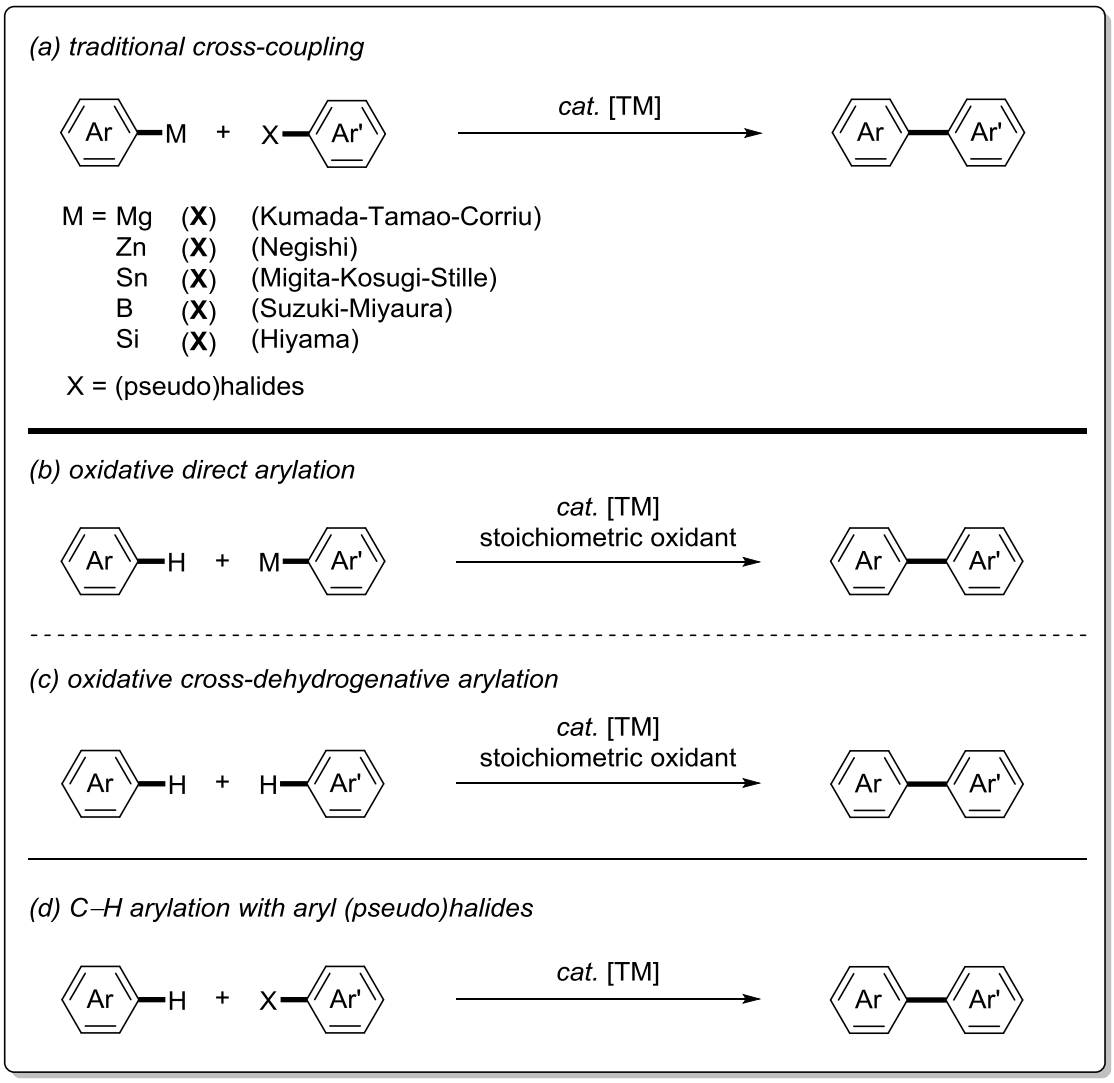


Figure 2: Selected bioactive bi(hetero)aryls present in top-selling pharmaceuticals.

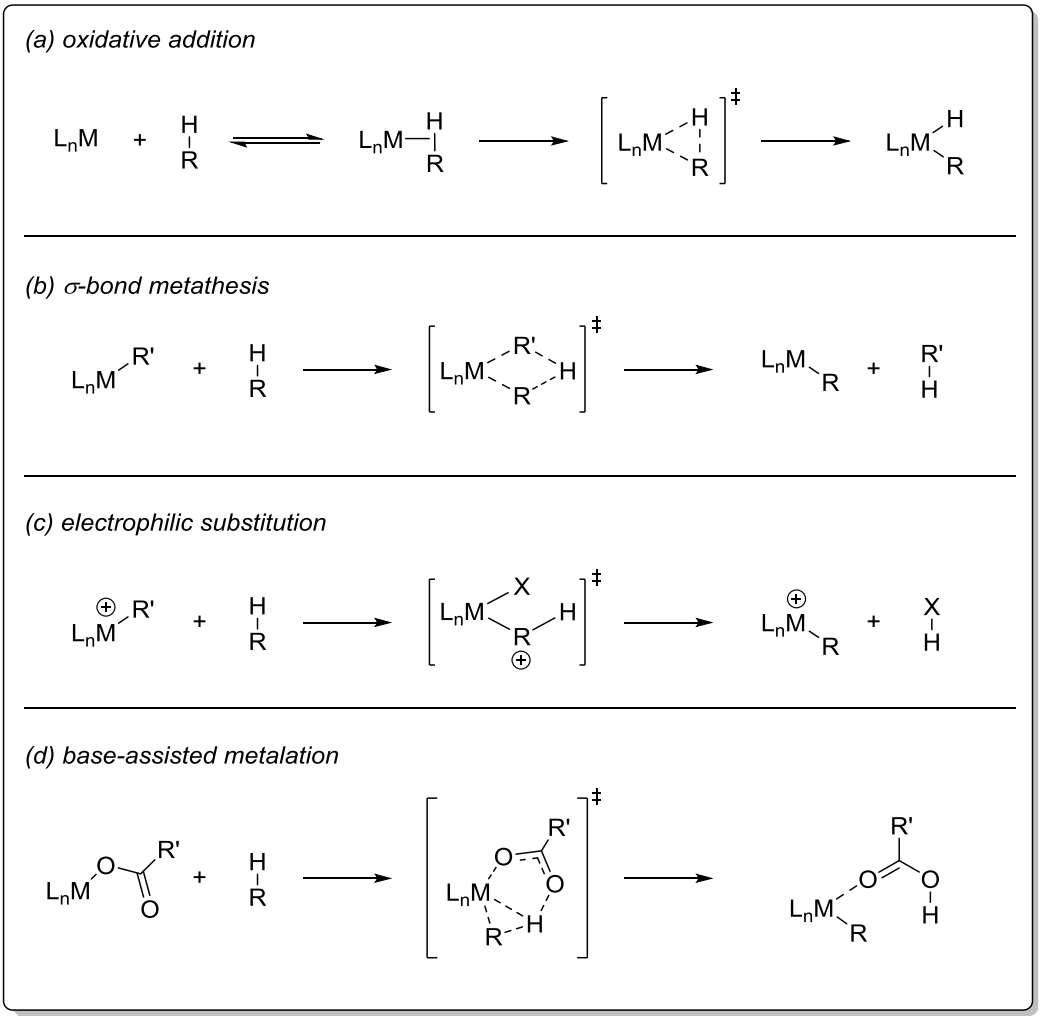
Despite these advances, cross-coupling processes show a fundamental drawback as both coupling partners have to be prefunctionalized, typically from the corresponding simple arene.[6] Generally, one partner is an unavailable or expensive organometallic compound as the aryl nucleophile, the other is an organic (pseudo)halide as the aryl electrophile (C–M/C–X coupling, M = metal), which are found in the Kumada-Tamao-Corriu, Negishi, Migita-Kosugi-Stille, Suzuki-Miyaura and Hiyama cross-coupling reactions (Scheme 1a).[9,14] One solution to this problem is to directly modify C–H bonds, the simplest and most common

structural motifs in organic compounds.[6,15] In this respect, a more attractive strategy uses an otherwise inert C–H bond as a latent functional group to avoid substrate prefunctionalization, thus enhancing the step-economy and reducing the waste formation of a process, resulting in an advanced economical and environmentally friendly alternative.[6,15,16] An improvement to decrease the number of preactivated starting materials was realized *via* oxidative direct arylations with organometallic reagents (Scheme 1b).[6,25-28] Oxidative cross-dehydrogenative coupling (CDC) of two non-prefuntionalized arenes is the most attractive method (Scheme 1c), unfortunately, at this stage it remains difficult to control the chemo- and regioselectivity.[6,29-33] In addition, stoichiometric terminal oxidants are usually required in addition to metal salts and an overstoichiometric quantity of the arene is necessary.[6,7,15] Therefore, a more synthetically useful approach is represented by direct C–H bond transformation with aryl (pseudo)halides as coupling partner (Scheme 1d).[5-13,15-17,34]



Scheme 1: Strategies for transition metal-catalyzed C(sp^2)–C(sp^2) bond formation: (a) traditional cross-coupling and (b-d) C–H functionalization.

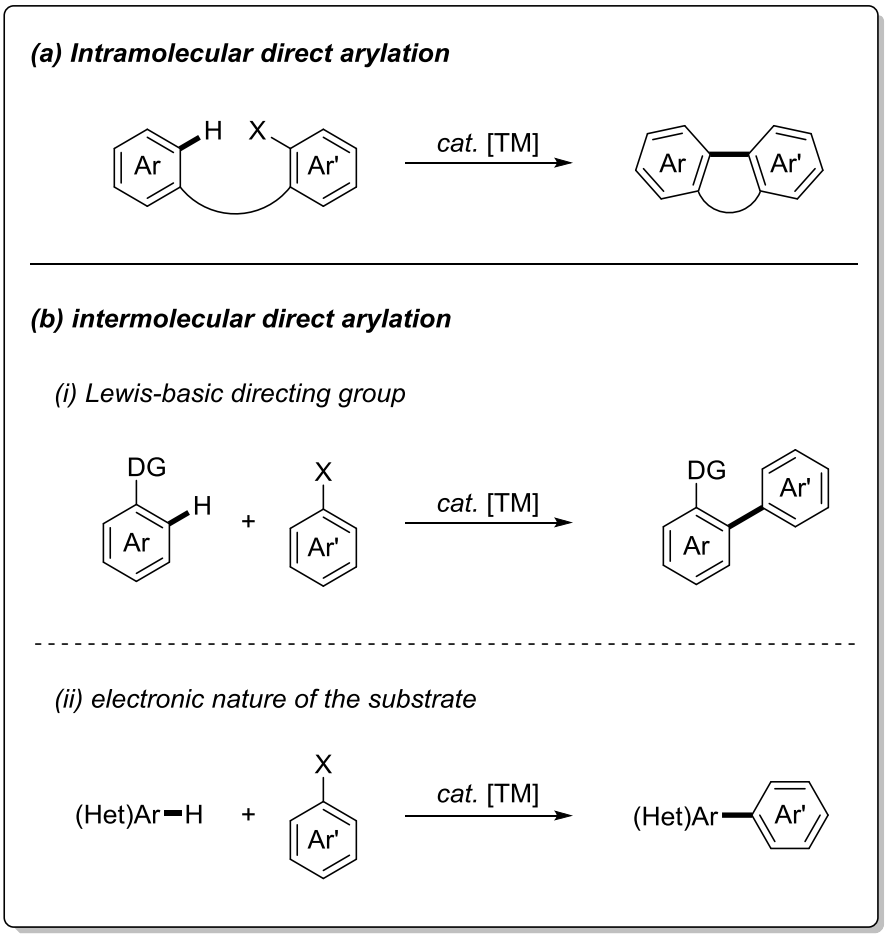
Different modes of the mechanisms for the key C–H metalation are summarized in Scheme 2: (a) Oxidative addition with electron-rich late transition metals, (b) σ-bond metathesis with early transition metals, (c) electrophilic substitution with electron-deficient late transition metals and (d) base-assisted metalation with, for instance, secondary phosphine oxides (SPOs) or carboxylates acting as an internal base.[7,13,35,36] It should be mentioned that the exact mechanism for any given example depends on the nature of the transition metal and ligand, as well as the base and solvent.[13,35]



Scheme 2: Different mechanisms for C–H metalation.

A key challenge in C–H bond activation relates to achieving regioselective intra- or intermolecular direct arylation, due to the prevalence of C–H bonds in organic molecules possessing comparable dissociation energies.[9,13,15] Several strategies currently exist to control the site-selective functionalization of specific C–H bonds (Scheme 3).[6,37,38] Intramolecular direct arylations apply tethered reacting groups to decrease the number of potent C–H bonds in a system to improve the site-selectivity (Scheme 3a).[6,13]

Another strategy for intermolecular direct arylations (Scheme 3b) based on compounds containing Lewis-basic directing groups, which coordinate to the transition metal to ensure the approximation to a specific C–H bond, providing the cyclometalated species (Scheme 3i).[6,13,37,38] Additionally, the steric properties of the substrate affect the C–H functionalization, often causing the reaction to occur at the less-hindered C–H bond. From a synthetic point of view, it is highly important to remove or convert the directing group after the desired transformation into other functionalities for further postsynthetic goals.[39-41] An alternative concept for intermolecular direct arylations (Scheme 3b) is the influence of the electronic nature of the arene, wherein the differently electronically activated C–H bonds rely on the inherent reactivity of the heteroarene (Scheme 3ii).[6,37,38]

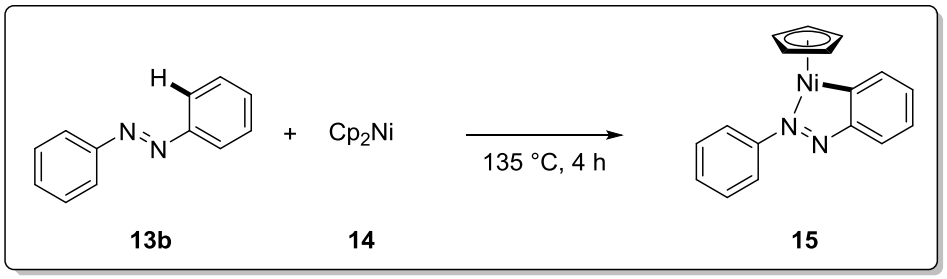


Scheme 3: Concepts to control the positional selectivity of the C–H functionalization.

In the following sections relevant contributions for C–H bond activation chemistry are represented, with the main focus on transition metal-catalyzed direct C–H arylations, including significant mechanistic insights.

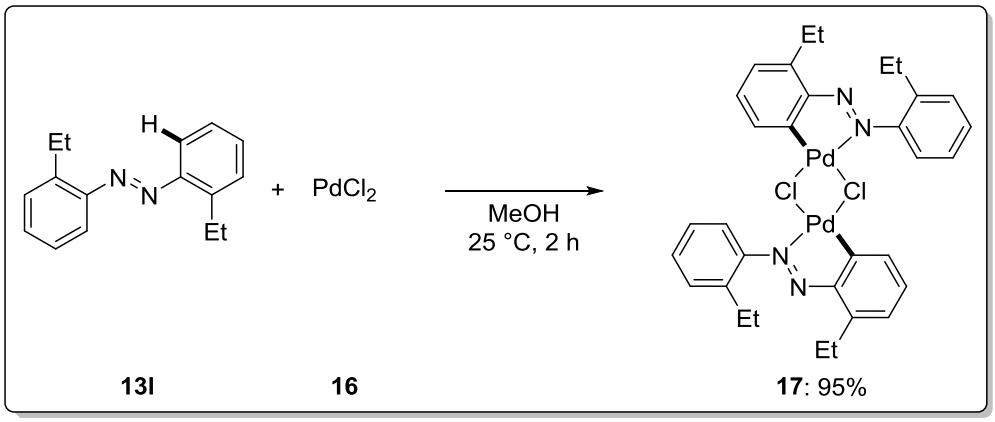
1.2 Stoichiometric metalation reactions

Coordination chemistry is of primary mechanistic significance for insights into potential reactivities and selectivities, in order to explore novel chemical transformations.[6] A pioneering study for the stoichiometric metalation of specific C–H bonds using a directing group to control the site-selectivity was revealed by Kleiman and Dubeck in 1963. The *ortho*-C–H bond cleavage in azobenzene **13b** by dicyclopentadienylnickel **14** led to the cyclometalated complex **15** (Scheme 4).[42,43]



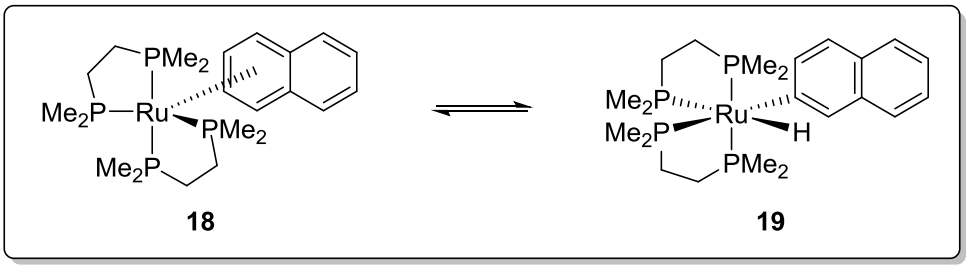
Scheme 4: Preparation of cyclonickelated complex **15** reported by Kleiman and Dubeck in 1963.

Subsequently, Cope disclosed the chelation-assisted direct palladation of azobenzene **13l** at 25 °C (Scheme 5).[44,45] Additional examples of cyclometalation reactions by transition metal complexes were reported by Stone and Bruce.[46-48]



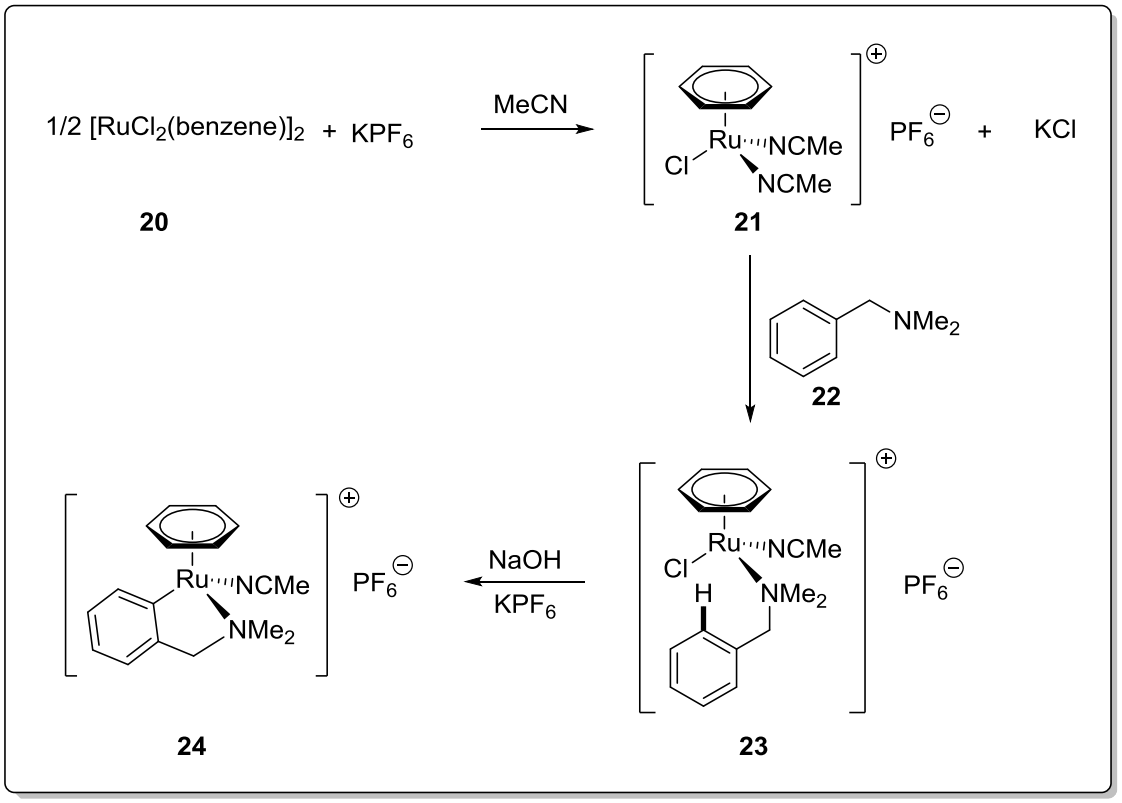
Scheme 5: Synthesis of cyclometalated complex **17** *via* C–H bond activation.

In 1965, Chatt and Davidson illustrated an oxidative addition of a C(sp^2)–H bond from a π-coordinated naphthalene ruthenium complex **18** (Scheme 6). The ruthenium(0) complex is also active in a C(sp^3)–H bond functionalization of a methyl group in the dmpe [1,2-bis(dimethylphosphino)ethane] ligand.[43,49,50]



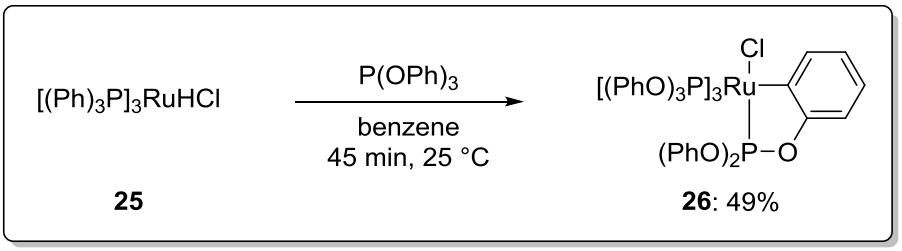
Scheme 6: Oxidative addition of a C–H bond to yield Ru(H)(2-naphthyl)(dmpe)$_2$ (**19**).

A noteworthy preparation of a cationic cycloruthenated complex **24** by direct intramolecular C–H activation was reported by Pfeffer in 1999 (Scheme 7).[6,51,52]



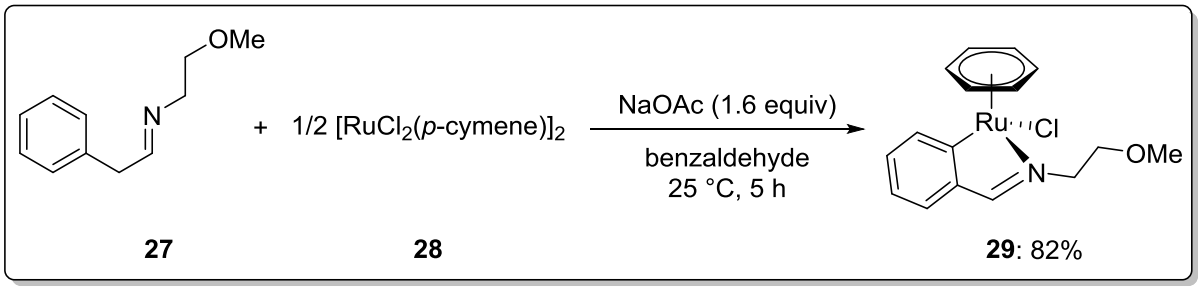
Scheme 7: Synthesis of cationic ruthena(II)cycle **24** by direct intramolecular C–H metalation.

Knoth and Schunn[53,54] as well as Robinson[55,56] independently revealed that ruthenium hydrido complex **25** in conjunction with triphenyl phosphite as ligand provided the cycloruthenated complex **26** (Scheme 8).[6]



Scheme 8: Synthesis of five-membered ruthena(II)cycle **26**.

Notable base-assisted cyclometalations were reported for iridium, rhodium and ruthenium species. One representative example for direct *ortho*-C–H activation of *N*-alkyl aldimine **27** by $[RuCl_2(p\text{-cymene})]_2$ (**29**) is illustrated in Scheme 9.[7,57]

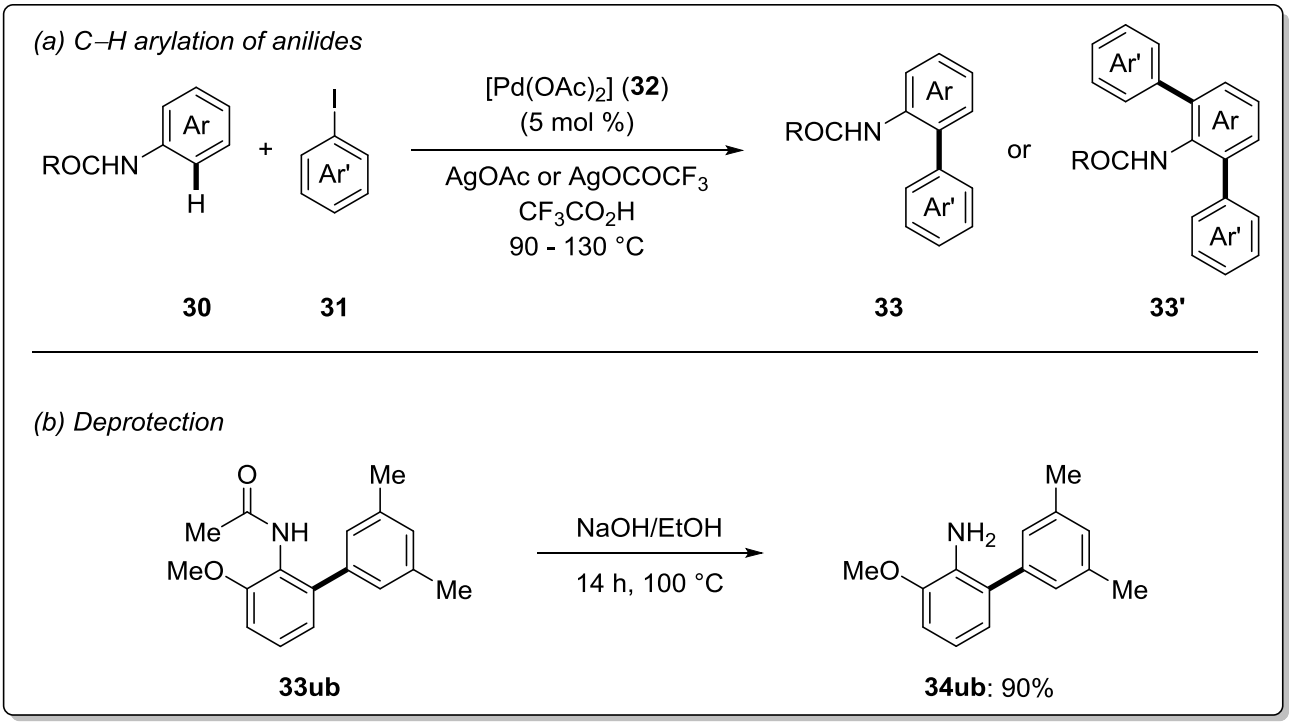


Scheme 9: Based-assisted formation of organometallic ruthenium(II) complex **29**.

1.3 Transition metal-catalyzed C–H functionalizations

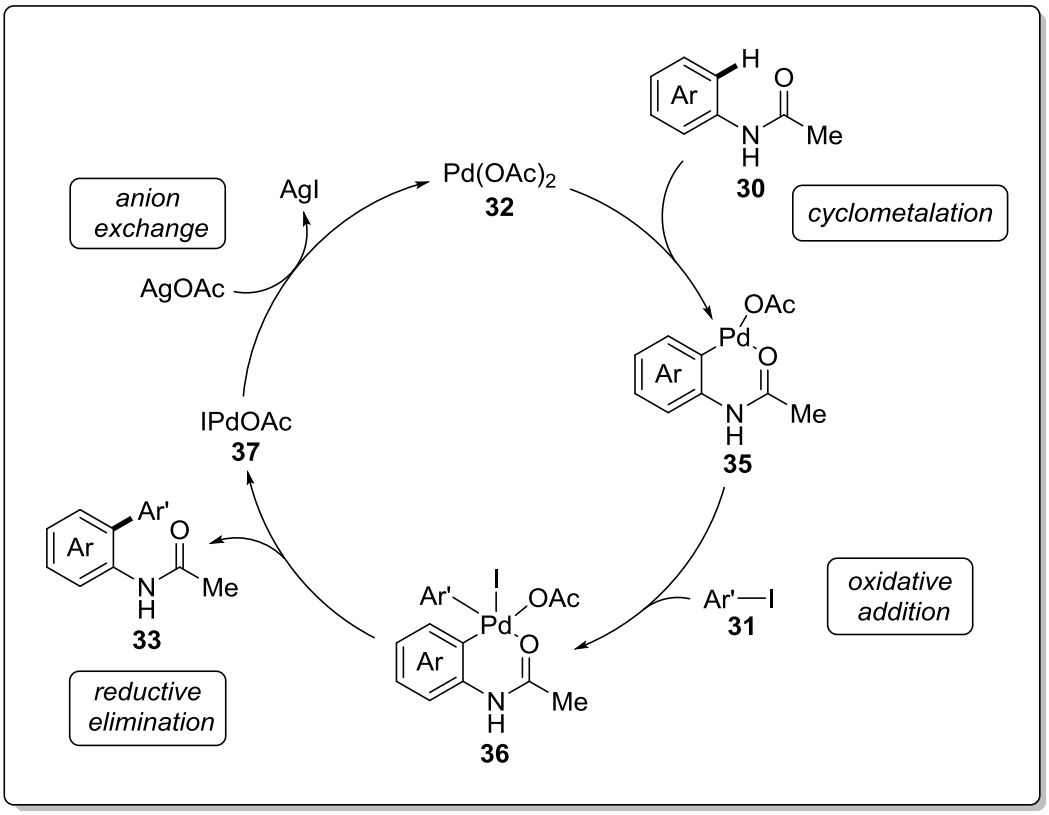
The stoichiometric metalation reactions previously highlighted brought substantial progress for direct functionalization approaches of otherwise inert C–H bonds.

In 1984, Tremont presented a palladium-promoted *ortho*-C–H alkylation of acetanilides **30a** employing alkyl iodides as the coupling partner.[58,59] Inspired by this contribution, Daugulis published in 2005 a broadly applicable and efficient palladium-catalyzed C–H arylation of anilides **30** using aryl iodides **31** as arylating reagents, and stoichiometric amounts of silver(I) salts. These additives were required for iodide removal from the palladium coordination sphere (Scheme 10a).[12,60,61] Subsequently, the products **33** can be deprotected under basic hydrolysis conditions to generate valuable *ortho*-arylated anilines (Scheme 10b).[6] Moreover, the use of iodonium salts as coupling partners was successfully applied to this transformation.[62] Li demonstrated another palladium-catalyzed C–H arylation of aniline carbamate derivatives with diaryliodonium salts in good yields, including a straightforward removal of the carbamate directing group to provide the valuable 2-aminobiaryls.[41] Unfortunately, the iodonium salts are either not commercially available or rather expensive and in this regard provide a less attractive option for a cost-effective synthesis.[60]



Scheme 10: Access to *ortho*-arylated anilines by palladium catalysis.

A proposed catalytic cycle is initiated by cyclopalladation of the anilide **30** followed by oxidative addition of the organic electrophile **31** to provide the highly active palladium(IV) species **36**. Afterwards, reductive elimination liberates product **33** and finally anion exchange regenerates the catalytically active palladium(II) complex **34** to complete the cycle (Scheme 11).[6,12]



Scheme 11: Proposed catalytic cycle for palladium-catalyzed C–H arylation.

Several accounts have appeared on palladium-catalyzed *ortho*-C–H arylations of anilide derivatives.[6,12,27,28,62-64] Shi described methods to construct C–C bonds *via* C–H activation. First, a Hiyama-type coupling between acetanilides **30** and trialkoxyarylsilanes.[27] Second, a Suzuki-Miyaura Type coupling of *N*-alkyl acetanilides **30** with aromatic boronic acids, another class of transmetalating reagents that can be employed for such direct arylation reactions.[28] Nevertheless, in either instance silver(I) and copper(II) salts are used as terminal oxidants. Third, an oxidative cross-dehydrogenative arylation (CDA) was devised without the requirement for prefunctionalized acetanilides or the corresponding arenes, which are commercially readily available.[29] Additionally, Buchwald developed an oxidative arylation of anilides by twofold C–H activation to manufacture biaryls in the presence of oxygen as the terminal oxidant.[30] Further recent reports of palladium-catalyzed CDAs among anilides and

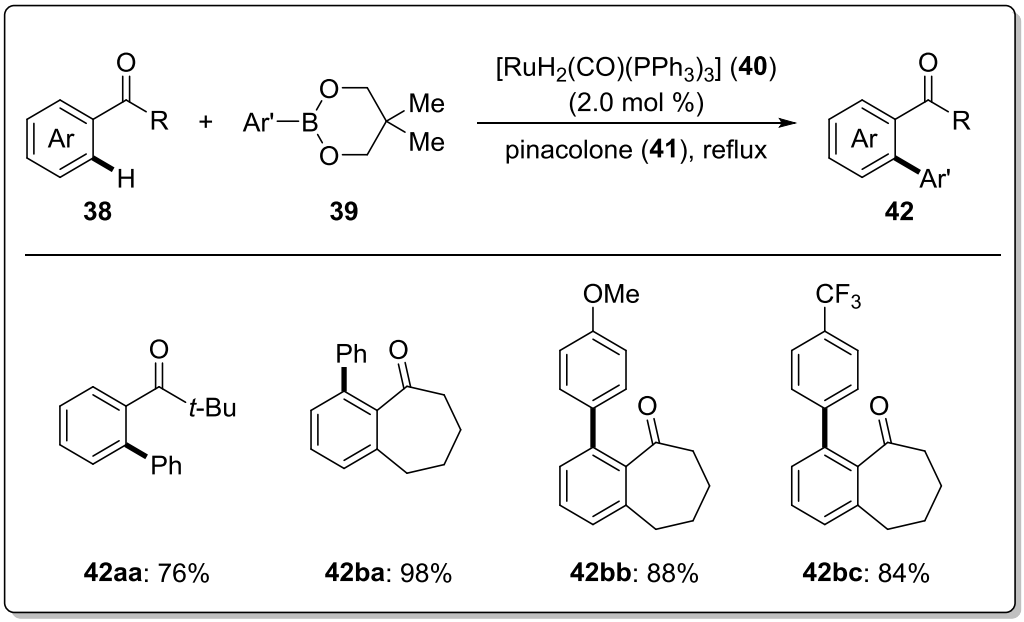
arenes were reported by Dong,[31] Glorius[32] and You.[33] However, regioisomeric mixtures were often obtained, with the arenes as arylating reagents being used in overstoichiometric amounts.

Lipshutz described sophisticated C–H arylations of urea derivatives with aryl iodides or arylboronic acids as coupling partners at 25 °C, affording an alternative route to synthetically valuable *ortho*-arylated anilines, after deprotection of the dimethylurea moiety under basic reaction conditions.[63,64]

Recent accounts for transition metal-catalyzed *ortho*-arylations of anilides were published by Wang[65] and Cheng.[66]

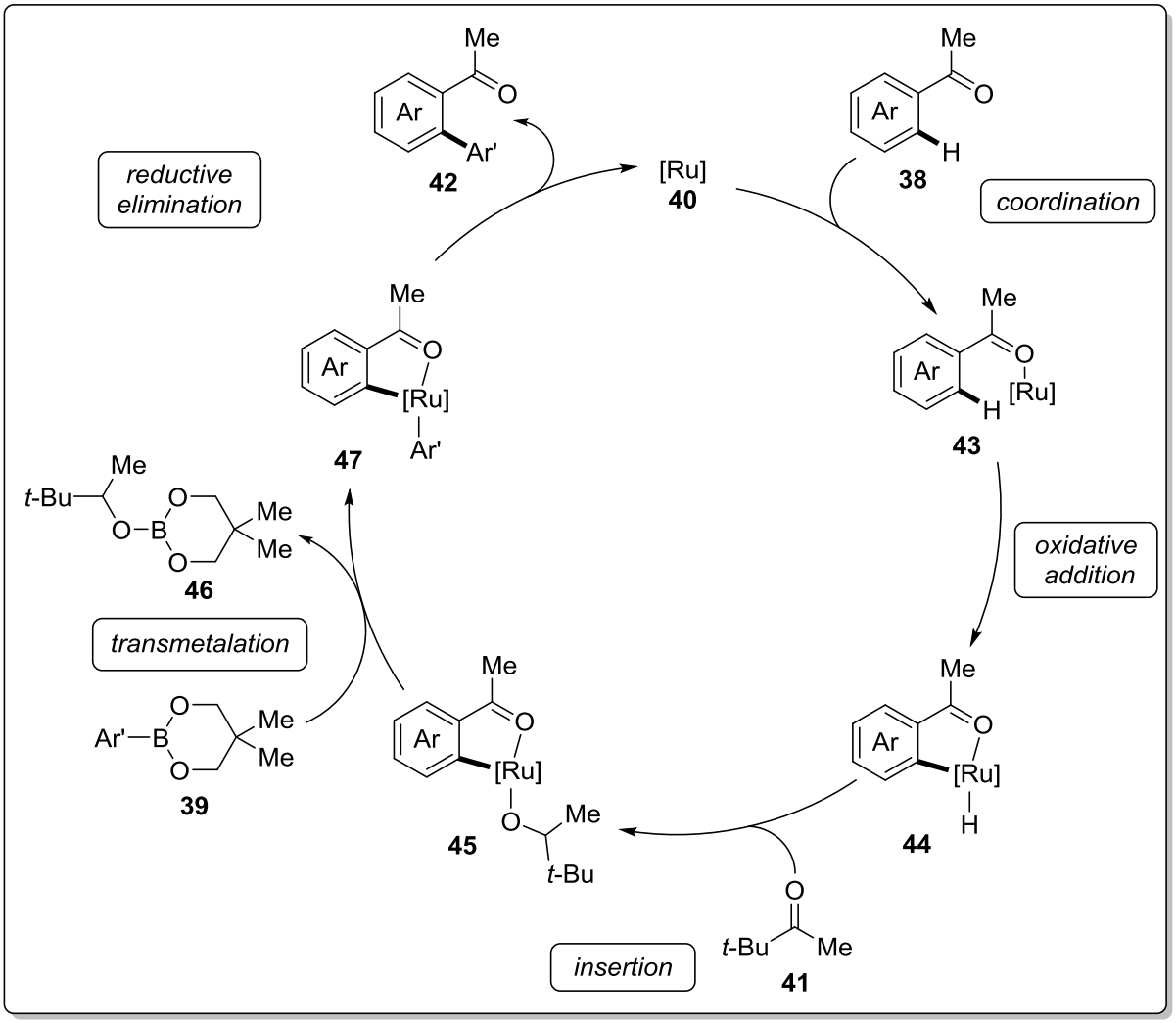
To date, palladium has been the most investigated transition metal in coupling chemistry, but from an economical point of view interest in utilizing the less expensive transition metal ruthenium are gaining importance as a feasible alternative.[15,44a] In this regard, the recently published ruthenium-catalyzed C–H arylation by Lakshman demonstrated a superior performance against the palladium counterpart for 6-phenylpurine derivatives, which are of great importance in medicinal chemistry.[67,68]

In 1986, Lewis presented the first ruthenium(0)-catalyzed C–C bond formation by chelation assistance.[69] Kakiuchi, Chatani and Murai rendered crucial contributions for ruthenium(0)-catalyzed transformations concerning hydroalkylation and hydroalkenylation,[70-72] silylation,[73,74] and arylation.[6,75,76] An interesting work is the efficient ruthenium(0)-catalyzed C–H arylation of aryl ketones **38** using boronates **39** as arylating reagents with an ample scope and relevant mechanistic insights (Scheme 12).



Scheme 12: Ruthenium(0)-catalyzed C–H arylation of aryl ketones **38** with boronates **39** in pinacolone.

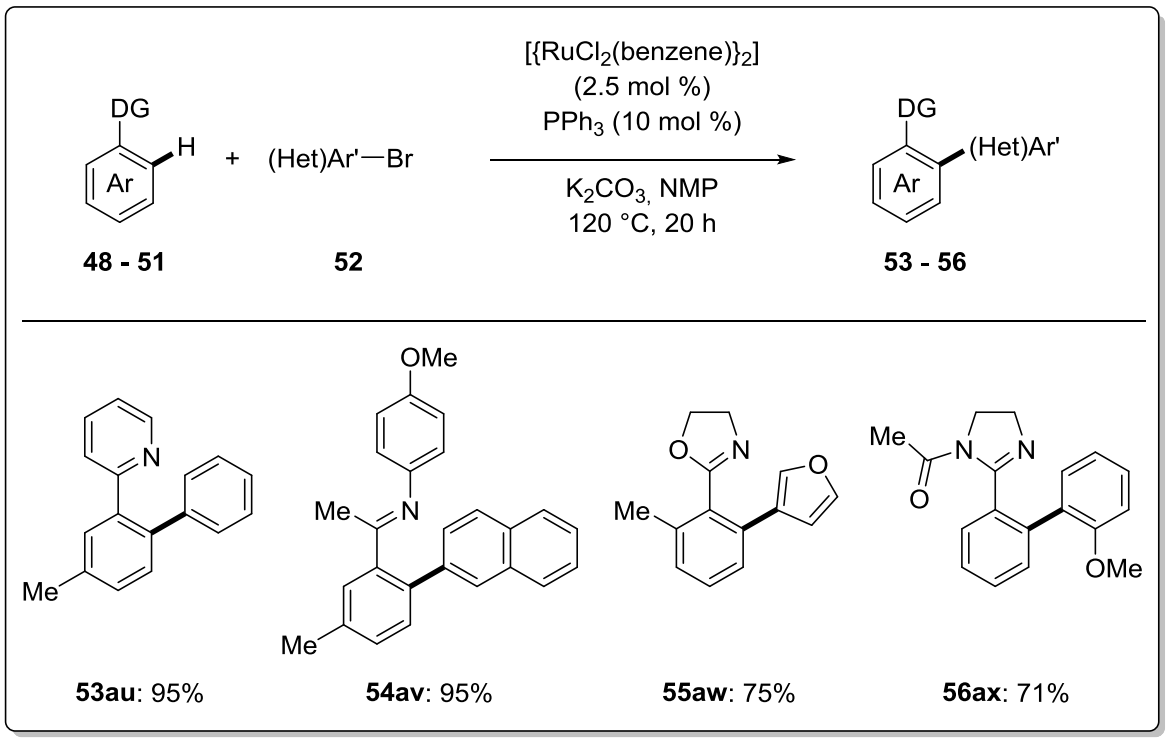
The aliphatic ketone pinacolone **41** has an essential function as acceptor for the hydrogen of the *ortho*-C–H bond of aryl ketone **38** and the $B(OR)_2$ moiety of the aryl boronate **39**. The use of pinacolone **41** suppressed the reduction of the aryl ketone **38** to achieve high yields. The kinetic isotope effects for the inter- and intramolecular competition experiments indicated that the oxygen of the ketone carbonyl group coordinates to the ruthenium-complex prior to C–H bond cleavage. A proposed catalytic cycle is illustrated in Scheme 13. Initially the carbonyl oxygen of the ketone **38** coordinates to the ruthenium species **40**. Thereafter, oxidative addition to provide the five-membered ruthenacycle **44** followed by insertion of pinacolone **41** into the [Ru]–H bond to deliver the alkoxy ruthenium complex **45**. Transmetalation and subsequent reductive elimination leads to the desired product **42** and regenerates the active catalyst **40**.[6,75,76]



Scheme 13: Proposed catalytic cycle for ruthenium(0)-catalyzed C–H arylation.

Recent reports for ruthenium-catalyzed C–H arylations using boron-based arylating reagents were published by Szostak,[77] Ramana,[78] Jeganmohan,[25] and Wan.[26]

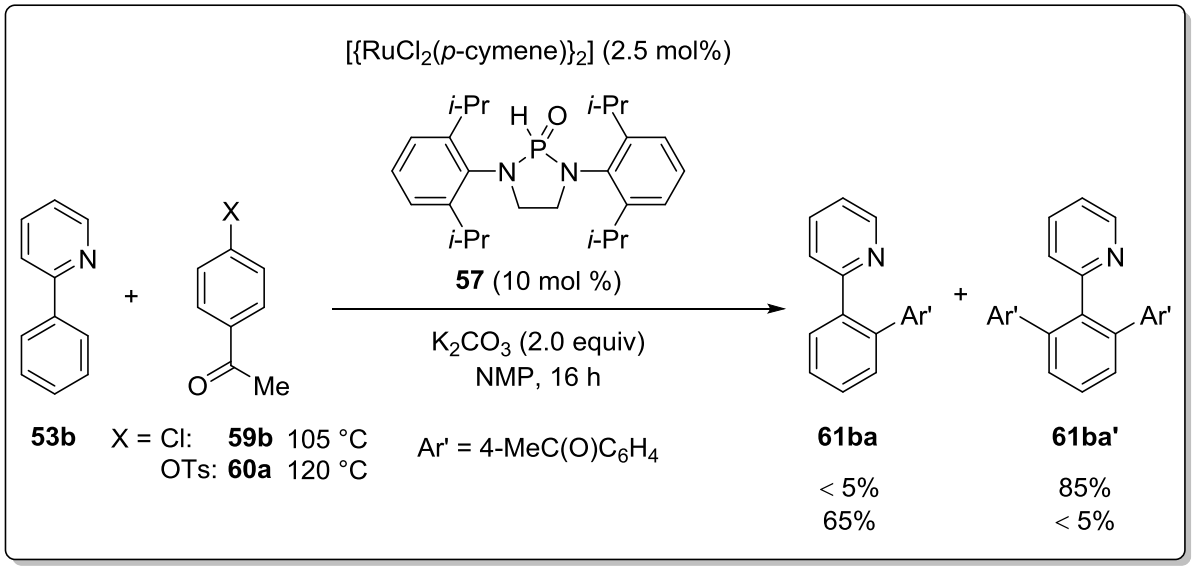
In 2008, Miura published the first transition metal-catalyzed direct arylation of azobenzene with arylboronic acids as coupling partners and a rhodium complex as catalyst, achieving unsatisfactory yields.[79] Thereafter, Zeng reported a palladium-catalyzed *ortho*-arylation of azoarenes with aryl acylperoxides.[80] Further progress was represented by rhodium- and palladium-catalyzed direct functionalizations of azoarenes.[81-98] Despite these advances, at that time there existed no report for the transition metal-catalyzed C–H arylation, using aryl halides as coupling partners for expedient access to *ortho*-arylated anilines, after a simple reduction of the azo group. In 2001, Oi and Inoue presented an overall isohypsic ruthenium-catalyzed direct arylation with readily available and ecologically benign aryl bromides **52** as coupling partner by chelation assistance of the pyridyl-substituted arenes **48**.[99] Thereafter, this catalytic system proved to be applicable to aryl imines **49**, oxazolines **50** and imidazolines **51**, which can be subsequently converted into other functionalities for further chemical transformations (Scheme 14).[6,100,101]



Scheme 14: Ruthenium(II)-catalyzed C–H arylation with (hetero)aryl bromides **52**.

From the economical point of view the use of the inexpensive $[RuCl_3(H_2O)_n]$ catalyst is desirable. In this context, Ackermann presented a $[RuCl_3(H_2O)_n]$-catalyzed C–H arylation of pyridine, oxazoline and pyrazole as pronucleophiles using aryl bromides, even the more challenging sterically hindered *ortho*-substituted, in the absence of an additional co-catalyst.[102] The challenging but inexpensive and readily accessible chlorides as arylating reagents arouse interest in academia and beyond. Ackermann presented a highly efficient

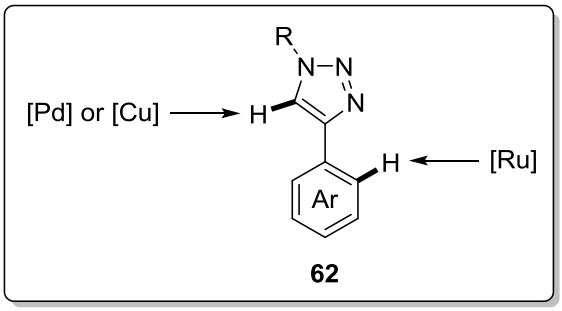
ruthenium(II) catalytic system based on the secondary phosphine oxide (SPO) $(1\text{-Ad})_2P(O)H$ as pre-ligand for C–H functionalization of pyridines and imines with aryl chlorides.[103] The exchange of the pre-ligand $(1\text{-Ad})_2P(O)H$ through heteroatom substituted secondary phosphine oxide (HASPO) **57** enhanced the catalyst performance, realizing a direct arylation of pyridine **53**, oxazoline **55** and pyrazole **58** derivatives with aryl chlorides **59** and even tosylates **60**.[104] Of note is the general trend for the mono- or diarylation, which is controlled by the selection of the appropriate electrophile. Thus, aryl chloride **59b** provided mainly the diarylated product **61ba'**, while the analogous aryl tosylate **60a** furnished to monoarylated product **61ba** (Scheme 15).[6,104]



Scheme 15: Selective ruthenium(II)-catalyzed C–H arylation controlled by the choice of the electrophile.

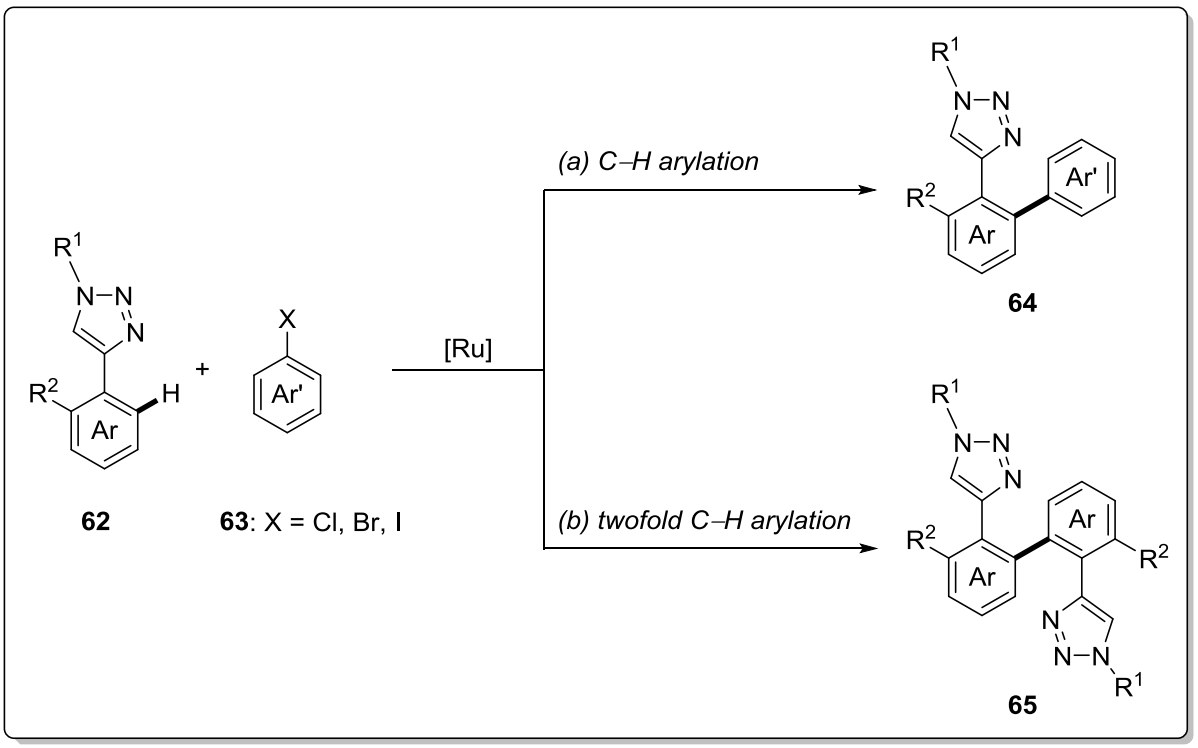
The use of aryl pseudo-halides as surrogates for aryl halides is an attractive option, since they can be manufactured from cost-effective and easily accessible phenols.[105] Referring to this, ruthenium(II)-catalyzed C–H arylation of oxazolinyl-, pyrazolyl- and pyridyl- substituted arenes with phenols *via* C–H and C–OH bond functionalizations represented a further advance, regarding the step economy of such processes.[106,107]

The impact of the regio- and chemoselectivity by transition metal-catalyzed C–H arylations was also demonstrated on 1,2,3-triazoles **62**. The palladium- or copper-catalyzed direct functionalizations occurred selectively at the triazol moiety, whereas the ruthenium(II) catalysis was selectively achieved at the arene moiety (Scheme 16).[108-110]



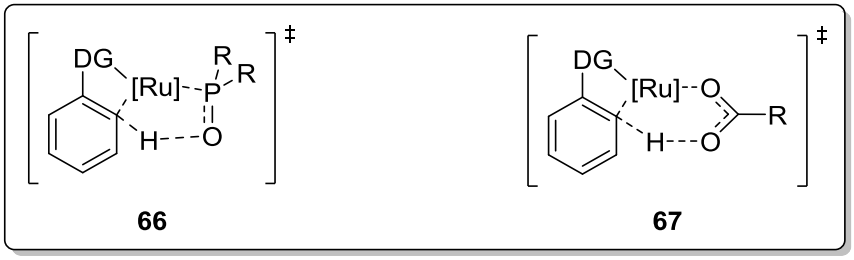
Scheme 16: Complementary regioselectivities in transition metal-catalyzed C–H functionalizations of 1,2,3-triazoles **62**.

The chemoselectivity for the carboxylate-assisted ruthenium(II)-catalyzed C–H arylation of 1,2,3-triazol-4-yl-substituted arenes **62** with aryl halides **63** was discovered to depend on the substitution pattern of both substrates. The catalytic system exhibited a wide substrate scope for the direct arylation (Scheme 17a), but the use of electron-rich *ortho*-alkylated arenes **62** in conjunction with *ortho*-substituted aryl halides **63** preferentially led to the oxidative dehydrogenative homo-coupling product **65** (Scheme 17b).[108]



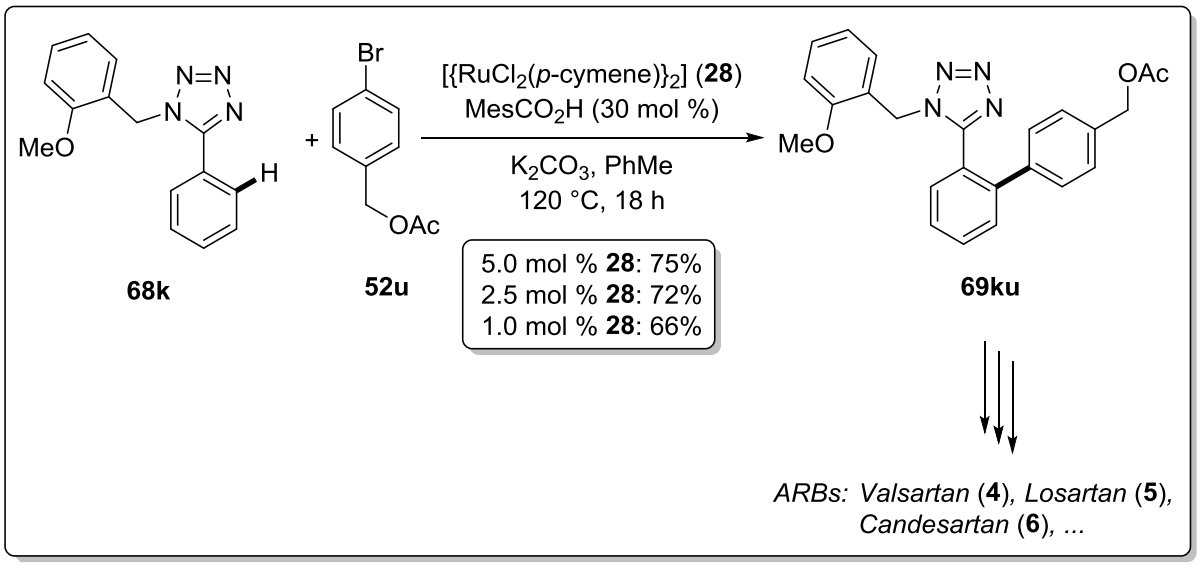
Scheme 17: Chemoselectivity of ruthenium(II)-catalyzed C–H functionalization: (a) direct arylation versus (b) oxidative dehydrogenative homo-coupling.

Fundamental mechanistic studies on palladium-catalyzed C–H bond activation[111] and subsequent functionalization led to the assumption that the C–H bond cleavage is assisted by basic pre-ligands such as carboxylates or carbonates in a concerted metalation-deprotonation (CMD) process.[6,7,112-116] A concerted metalation-deprotonation (CMD)[110] mechanism in the ruthenium-catalyzed C–H arylations using the beneficial effect of pre-ligands to facilitate the elementary step of the C–H ruthenation, proceeding *via* five- or six-membered transition state **66** or **67**, respectively (Scheme 18).[7]



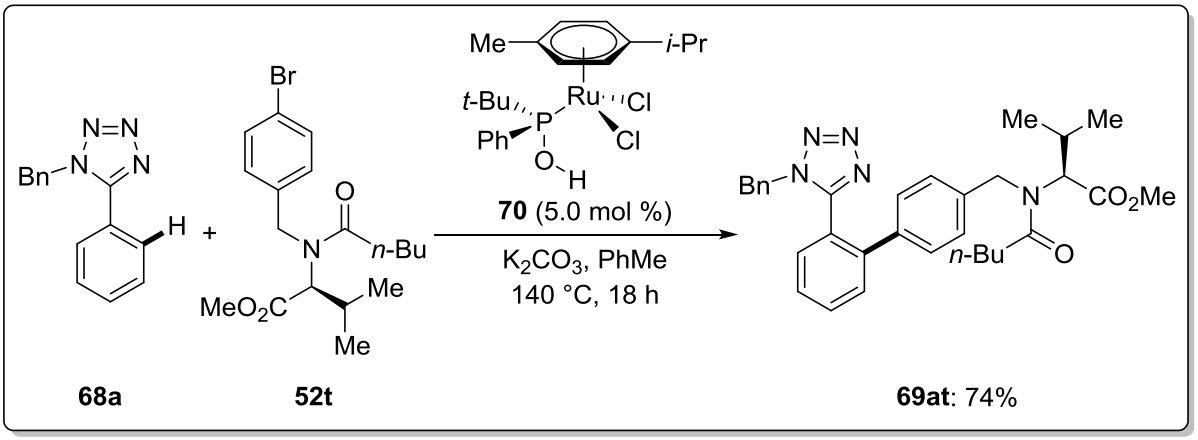
Scheme 18: Proposed transition states **66** and **67** for base-assisted intramolecular cycloruthenation.

The efficient and selective carboxylate-assisted ruthenium-catalyzed C–H functionalizations proved to be robust and broadly applicable.[7,15,117] The catalytic system represented an ecologically benign and economically attractive tool for the synthesis of important bioactive compounds. Concerning this matter, the practical importance of the ruthenium-catalyzed C–H arylation strategy was demonstrated by the synthesis of 5-biaryl-1*H*-tetrazoles **69ku**, key structural motifs in a variety of nonpeptidic angiotensin II receptor blockers (ARBs) (Scheme 19).[15,17,118-122] Previously, the biaryl tetrazoles were synthesized through palladium-catalyzed cross-coupling reactions with the fundamental drawback on the synthesis and use of prefuntionalized starting materials, which is cost-ineffective and harmful to the environment.[123-125]



Scheme 19: Application of ruthenium(II)-catalyzed C–H arylation for the synthesis of **69ku**, key intermediate of ARBs.

Recently, Ackermann reported a step-economical direct synthesis of protected Valsartan[126-130] **69at** *via* C–H activation and set the stage for an atom-economical approach to blockbuster antihypertension drugs, which should prove instrumental for industrial applications (Scheme 20).[131] Unfortunately, the ruthenium(II)-catalyzed C–H arylations of 5-aryl-1*H*-tetrazoles were not compatible to the readily available and economically more attractive aryl chlorides at this stage.



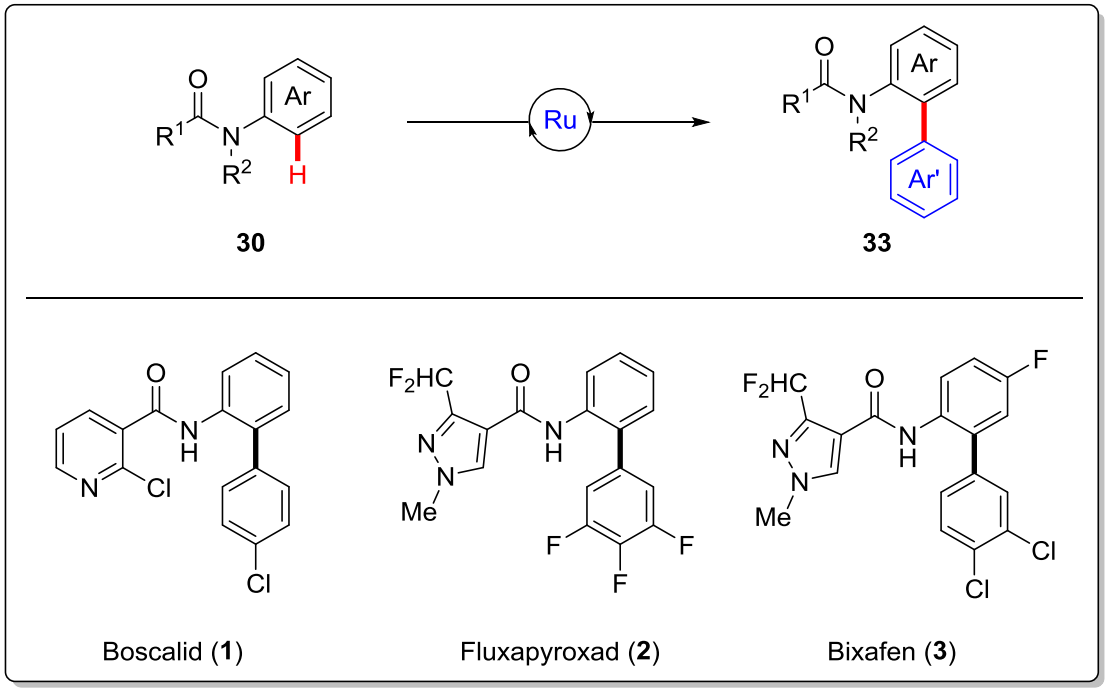
Scheme 20: Step-economical access to protected Valsartan **69at** by ruthenium-catalyzed C–H arylation.

The development of innovative environmentally benign and economically attractive catalytic processes for C–H arylation and its application to practical and scalable syntheses of valuable bi(hetero)aryls as key molecular frameworks in various bioactive compounds is an ongoing key interest in academia and industry.

2 Objectives

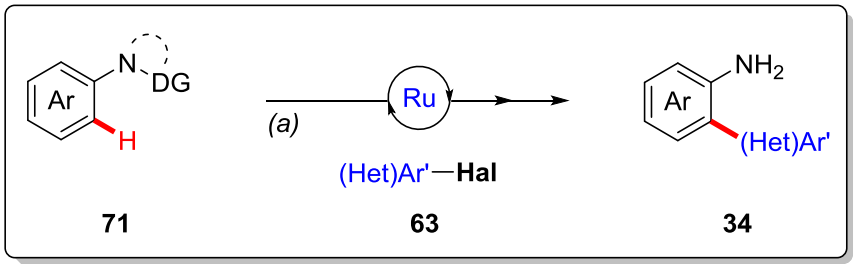
The goal of this work was to devise environmentally friendly and cost-effective novel concepts for the efficient synthesis of biaryl units as core structure in biologically active compounds, which are of great importance to the agrochemical and pharmaceutical industries.[6,9,15,17] To address this challenge, the direct C–H bond arylation processes are in high demand.[5-13,15-17] Particularly, robust and versatile ruthenium(II) complexes have emerged as powerful catalysts for selective C–H transformations by chelation assistance.[10,15,17,117,132,133] Moreover, kinetic investigations should be carried out for the clarification of the reaction mechanism.

The mono-selective C–H arylation of anilides received considerable attention, as 2-aminobiaryls are key structural frameworks in drug and crop protection agents.[6,12,27,28,60-64] Recently, palladium-catalyzed *ortho*-C–H functionalizations of anilides had been developed by several research groups, contrary to ruthenium-catalyzed systems, which are rarely explored.[6,29-31,33,132,134-136] In this context, it should take advantage of the less expensive ruthenium for the demanding direct arylation of anilides **30** in a broadly applicable and highly selective fashion (Scheme 21).



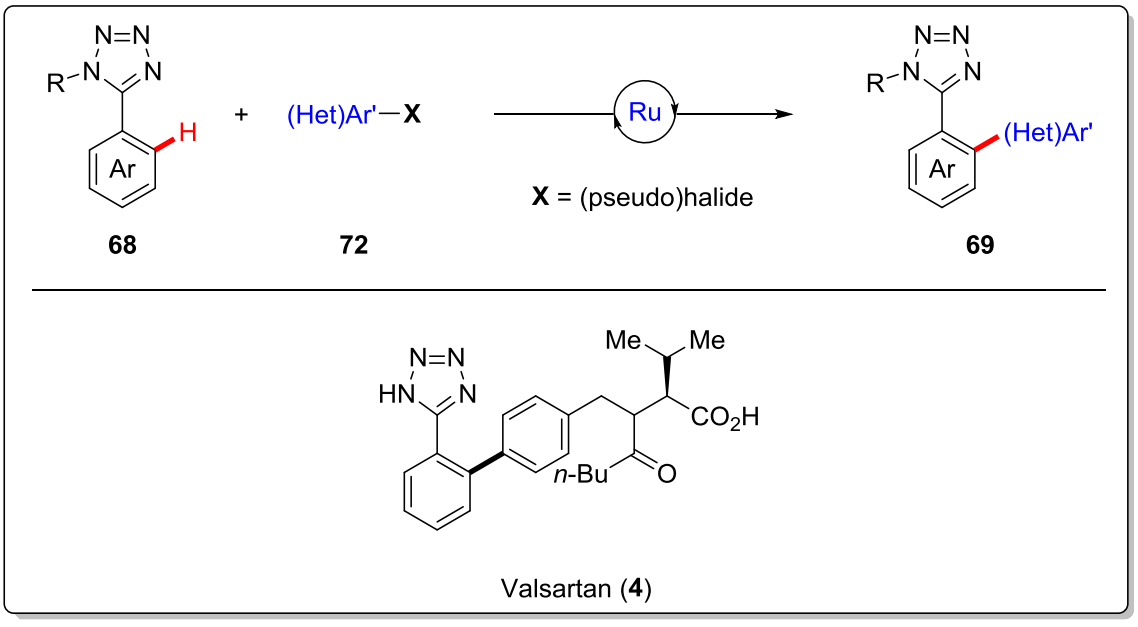
Scheme 21: Ruthenium(II)-catalyzed C–H arylation for syntheses of key intermediates **33** of relevance to fungicides.

After a successful solution for the previously described issue *via* an oxidative ruthenium(II)-catalyzed C–H arylation of anilides **30** with boron-based arylating reagents, additional investigations were required for an overall redox-neutral variant to avoid stoichiometric metal salts as terminal oxidants using aryl halides **63** as coupling partners[7] along with direct access to synthetically useful *ortho*-arylated anilines (Scheme 22).



Scheme 22: A general concept for expedient access to *ortho*-arylated anilines **34** *via* C–H activation strategy.

The outstanding performance of the ruthenium(II) complexes by chelation assistance was among others highlighted by prior findings and should be exploited in the drug development.[15,17,117] In this respect, Ackermann recently reported the most step-economical access to the nonpeptidic angiotensin II receptor blocker (ARB) Valsartan (**4**).[131] Further improvement should be done by employing challenging aryl chlorides concerning the cost efficiency, which would be a promising achievement for future industrial applications (Scheme 23).



Scheme 23: Step-economical approach for blockbuster antihypertension drug Valsartan (**4**) by C–H arylation.

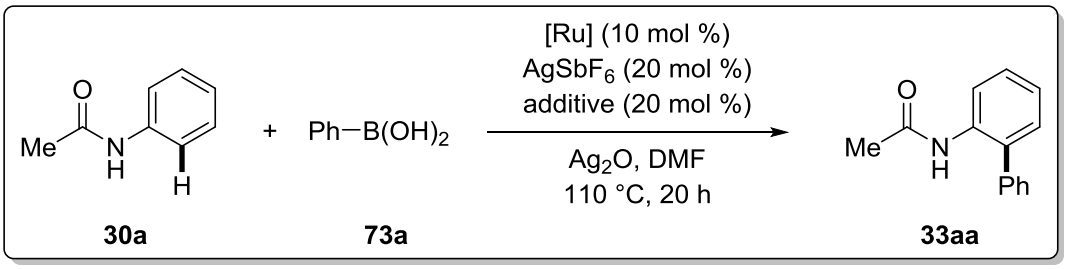
3 Results and Discussion

3.1 Ruthenium(II)-catalyzed C–H arylation of anilides with boronic acids, borinic acids and potassium trifluoroborates

3.1.1 Optimization of C–H arylation of acetanilide with phenylboronic acids

During the comprehensive and systematic optimization studies, different additives, ruthenium catalysts, solvents and oxidants were tested to deliver the desired product **33aa** (Tables 1–3). Initial reactions revealed that in the absence of the catalyst no product was formed (Table 1, entry 1). The combination of [{$RuCl_2$(*p*-cymene)}$_2$] and $Cu(OTf)_2$ provided the best result, whereas $AgSbF_6$ accomplished an effective cationic ruthenium(II) species. Utilization of the less expensive $CuSO_4$ and CuO additives was successful as well (entries 5–6). Other ruthenium catalysts or additives gave less satisfactory results. Afterwards, a catalyst loading of 5.0 mol % was shown to be essential to obtain good yields of the *ortho*-arylated product **33aa** (entry 15). Reducing the catalyst loading resulted in unsatisfactory yields of biaryl product **33aa** (entry 16).

Table 1: Effect of additives and ruthenium catalysts.[a]



30a **73a** **33aa**

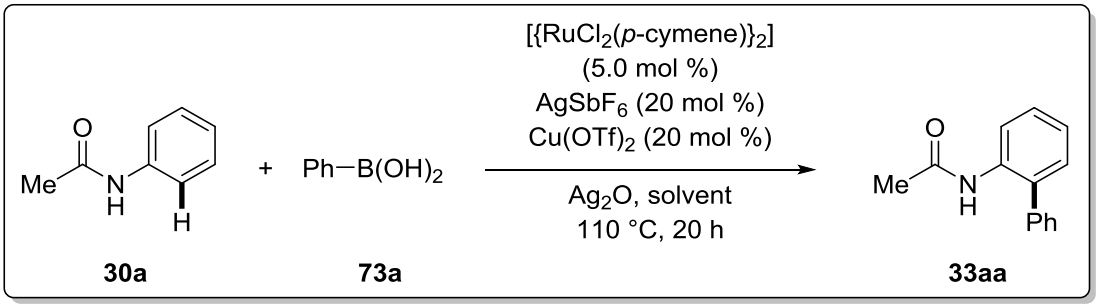
entry	[Ru]	additive	yield / %[b]
1	---	$Cu(OTf)_2$	---
2	[{$RuCl_2$(*p*-cymene)}$_2$]	---	34[c]
3	[{$RuCl_2$(*p*-cymene)}$_2$]	$Cu(TFA)_2{\cdot}(H_2O)_n$	27
4	[{$RuCl_2$(*p*-cymene)}$_2$]	$CuBr_2$	35
5	[{$RuCl_2$(*p*-cymene)}$_2$]	$CuSO_4$	58
6	[{$RuCl_2$(*p*-cymene)}$_2$]	CuO	69
7	[{$RuCl_2$(*p*-cymene)}$_2$]	$Zn(OTf)_2$	74

8	[{$RuCl_2$(*p*-cymene)}$_2$]	NaOTf	65
9	[{$RuCl_2$(*p*-cymene)}$_2$]	AgOTf	59
10	[{$RuCl_2$(*p*-cymene)}$_2$]	AgOTf	49[d]
11	[{$RuCl_2$(*p*-cymene)}$_2$]	TfOH	50
12	[$RuCl_3(H_2O)_n$]	$Cu(OTf)_2$	---
13	[$Cp^*Ru(PPh_3)_2Cl$]	$Cu(OTf)_2$	21
14	[{$RuCl_2$(benzene)}$_2$]	$Cu(OTf)_2$	22
15	[{$RuCl_2$(*p*-cymene)}$_2$]	$Cu(OTf)_2$	77[c]
16	[{$RuCl_2$(*p*-cymene)}$_2$]	$Cu(OTf)_2$	48[b,e]

[a] General reaction conditions: **30a** (1.0 mmol), **73a** (1.5 mmol), [Ru] (10 mol %), $AgSbF_6$ (20 mol %), additive (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h. [b] By ^{1}H-NMR using CH_2Br_2 as internal standard. [c] Isolated yields. [d] In the absence of $AgSbF_6$. [e] [{$RuCl_2$(*p*-cymene)}$_2$] (2.5 mol %), $AgSbF_6$ (10 mol %).

An extensive screening confirmed DMF as the solvent of choice, while other solvent systems gave inferior results under otherwise identical reaction conditions (Table 2).

Table 2: Effect of solvents.[a]



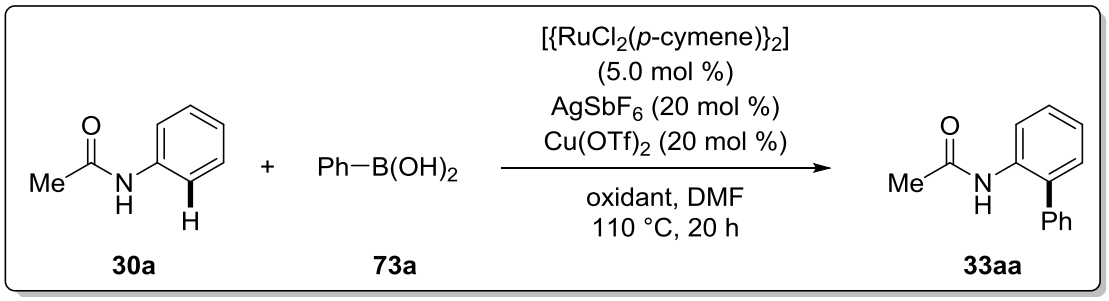
entry	solvent	yield / %[b]
1	*t*-BuOH	30
2	*t*-AmOH	44
3	MeOH	70
4	EtOAc	55
5	DME	50
6	DCE	57
7	THF	55[c]
8	DMF	77[c]

9	DMF/MeOH	42[d]
10	DMF/THF	65[d]

[a] General reaction conditions: **30a** (1.0 mmol), **73a** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), solvent (3.0 mL), 110 °C, 20 h. [b] By ^{1}H-NMR using CH_2Br_2 as internal standard. [c] Isolated yields. [d] Solvent mixture (3.0 mL, 1:1).

Extended testing of the terminal oxidants displayed Ag_2O as most effective compared to other oxidants, which resulted in unsatisfactory yields of **33aa** (Table 3).

Table 3: Effect of oxidants.[a]



entry	oxidant	yield / %[b]
1	*p*-benzoquinone	---
2	$PhI(OAc)_2$	---
3	$NaIO_4$	---
4	$K_2S_2O_8$	---
5	$(NH_4)_2S_2O_8$	---
6	AgF	44
7	$AgBF_4$	50
8	Ag_2O	77[c]

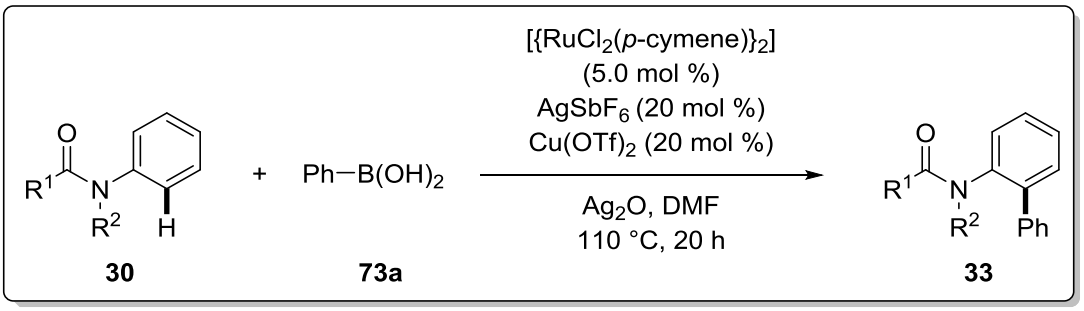
[a] General reaction conditions: **30a** (1.0 mmol), **73a** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), oxidant (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h. [b] By ^{1}H-NMR using CH_2Br_2 as internal standard. [c] Isolated yields.

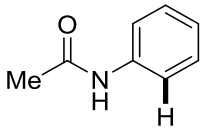
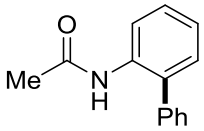
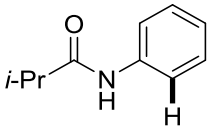
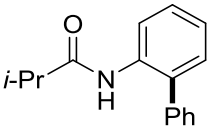
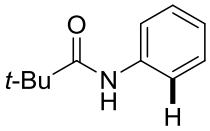
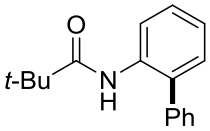
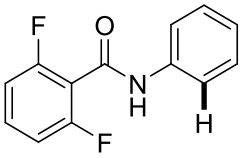
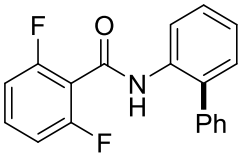
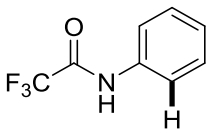
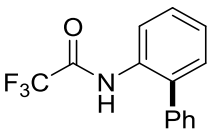
The most efficient mono-selective C–H arylation on *N*-phenylacetamide (**30a**) with phenylboronic acid (**73a**) as arylating reagent was achieved with [{$RuCl_2$(*p*-cymene)}$_2$] as catalyst and $AgSbF_6$, which generated *in situ* an active cationic ruthenium(II) precursor, $Cu(OTf)_2$ as additive and Ag_2O as terminal oxidant in DMF as solvent to afford the desired product **33aa** in an excellent yield (Table 1, entry 15).

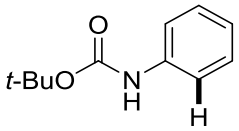
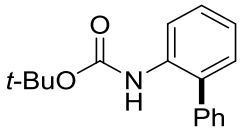
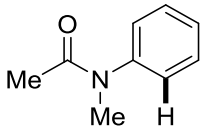
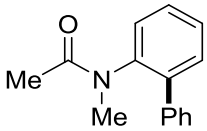
3.1.2 Influence of *N*-substituents on anilides

Afterwards, the influence of different *N*-substituents on anilides **30** on the C–H arylation was investigated (Table 4). The results showed that the acetyl group provided an unsurpassed result (entry 1). The sterically demanding *N*-substituted anilides **30b** and **30c** as well as the aryl substituted anilide **30d** resulted in inferior outcomes (entries 2–4). Additionally, more electron-deficient anilides **30e** and **30f** were unsuccessfully subjected to the reaction conditions (entries 5 and 6). Furthermore, the tertiary anilide **30g** was not effective, proving the necessity of the acidic N–H moiety for the *ortho*-C–H arylation (entry 7).

Table 4: Influence of *N*-substituents on anilides **30**.[a]



entry	**30**		**33**		yield / %
1		**30a**		**33aa**	77
2		**30b**		**33ba**	55
3		**30c**		**33ca**	45
4		**30d**		**33da**	30
5		**30e**		**33ea**	---

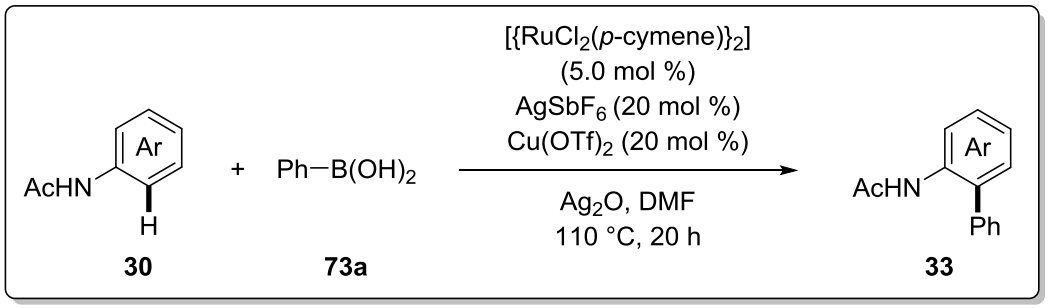
6		**30f**		**33fa**	---
7		**30g**		**33ga**	---

[a] General reaction conditions: **30** (1.0 mmol), **73a** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h; isolated yields.

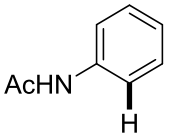
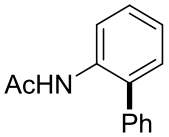
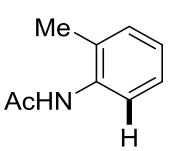
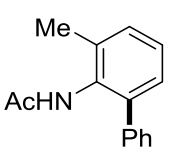
3.1.3 Scope of C–H arylation of acetanilides with boron-based arylating reagents

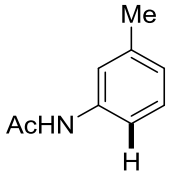
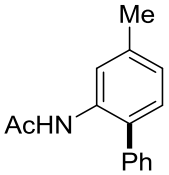
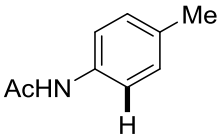
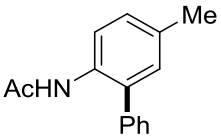
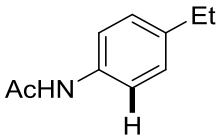
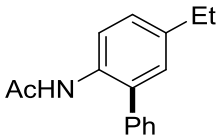
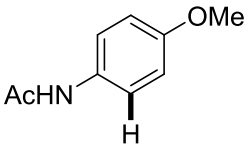
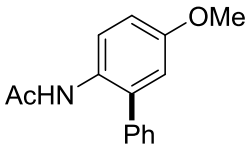
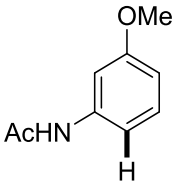
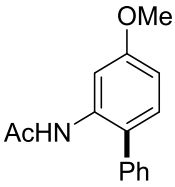
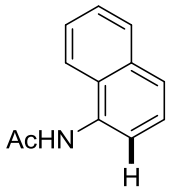
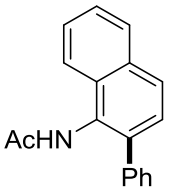
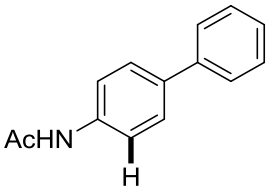
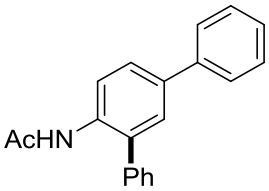
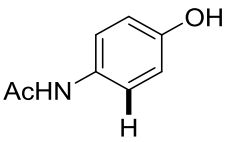
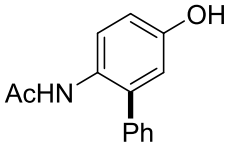
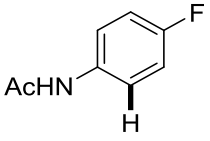
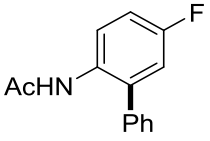
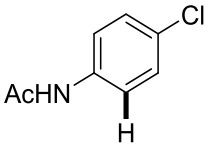
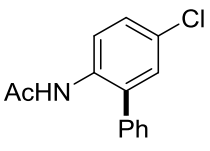
With the optimized catalytic system in hand, the substrate scope of the site-selective C–H arylation was successfully studied with the parent acetanilide **30a** as well as the *ortho*-, *meta*- and *para*-substituted anilides **30** bearing electron-donating or electron-withdrawing groups, respectively (Table 5). Thus, the electronic character of anilides **30** had no significant impact on the performance of the catalytic system. The desired products **33** were obtained in good yields with an excellent selective mono-arylation, even for *para*-substituted anilides **30**. Intramolecular competition experiments with *meta*-substituted anilides **30i** and **30m** revealed a superb regioselectivity at the less sterically demanding C-6 position of the arene (entries 3 and 7).

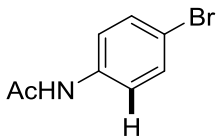
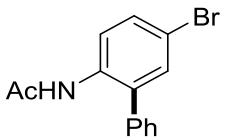
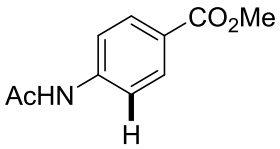
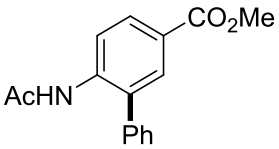
Table 5: Scope of C–H arylation of acetanilides **30** with phenylboronic acid (**73a**).[a]



30 **73a** **33**

entry	**30**		**33**		yield / %
1		**30a**		**33aa**	77
2		**30h**		**33ha**	34

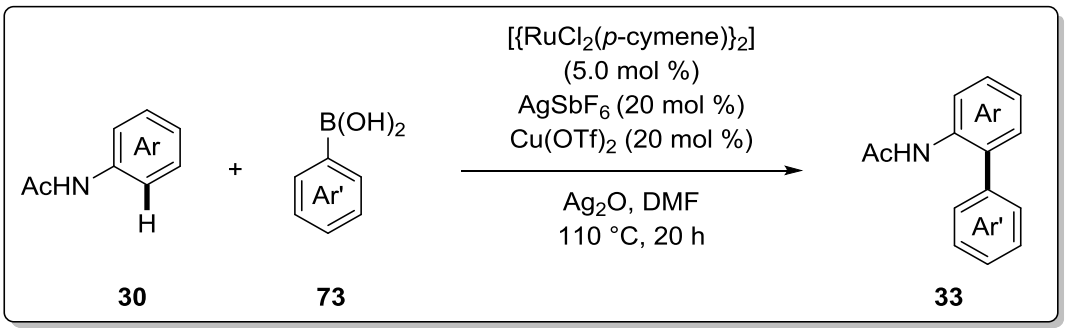
3		**30i**		**33ia**	78
4		**30j**		**33ja**	79
5		**30k**		**33ka**	63
6		**30l**		**33la**	76
7		**30m**		**33ma**	72
8		**30n**		**33na**	29
9		**30o**		**33oa**	54
10		**30p**		**33pa**	69
11		**30q**		**33qa**	71
12		**30r**		**33ra**	67

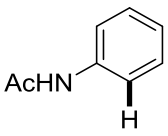
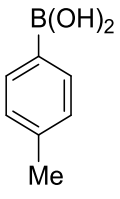
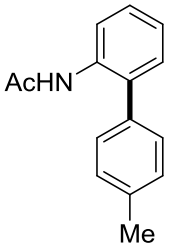
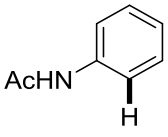
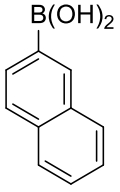
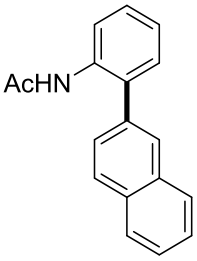
13		**30s**		**33sa**	63
14		**30t**		**33ta**	58

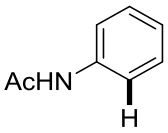
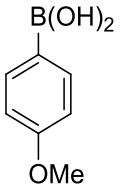
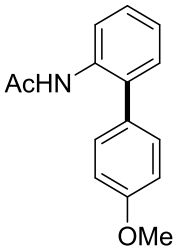
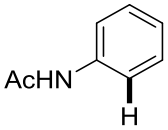
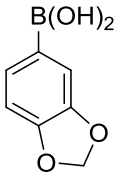
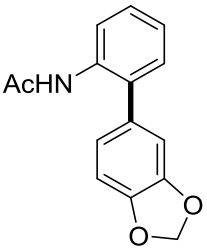
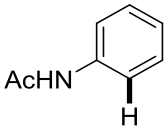
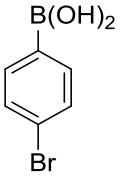
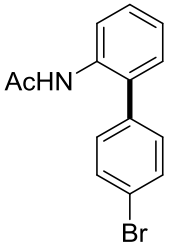
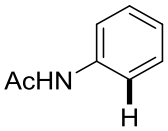
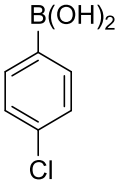
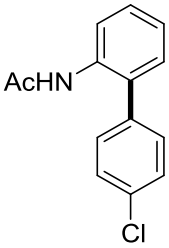
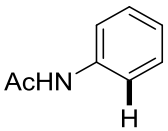
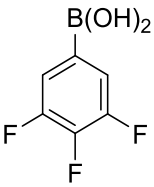
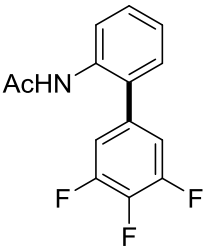
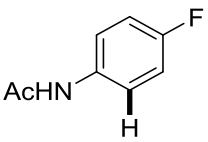
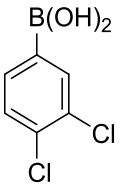
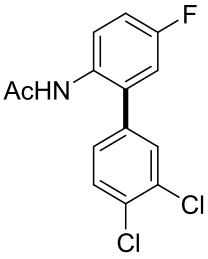
[a] General reaction conditions: **30** (1.0 mmol), **73a** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h; isolated yields.

The ample scope demonstrated the high chemoselectivity by fully tolerating valuable electrophilic functional groups, including fluoro, chloro, bromo, hydroxyl, ether or ester substituents, indicating great potential for further postsynthetic transformations. The electronic nature of the arylboronic acids **73** did not play a crucial role (Table 6). Both electron-rich and electron-poor boronic acids **73** provided the desired products **33** in a site-selective manner in high yields.

Table 6: Scope of C–H arylation of acetanilides **30** with arylboronic acids **73**.[a]

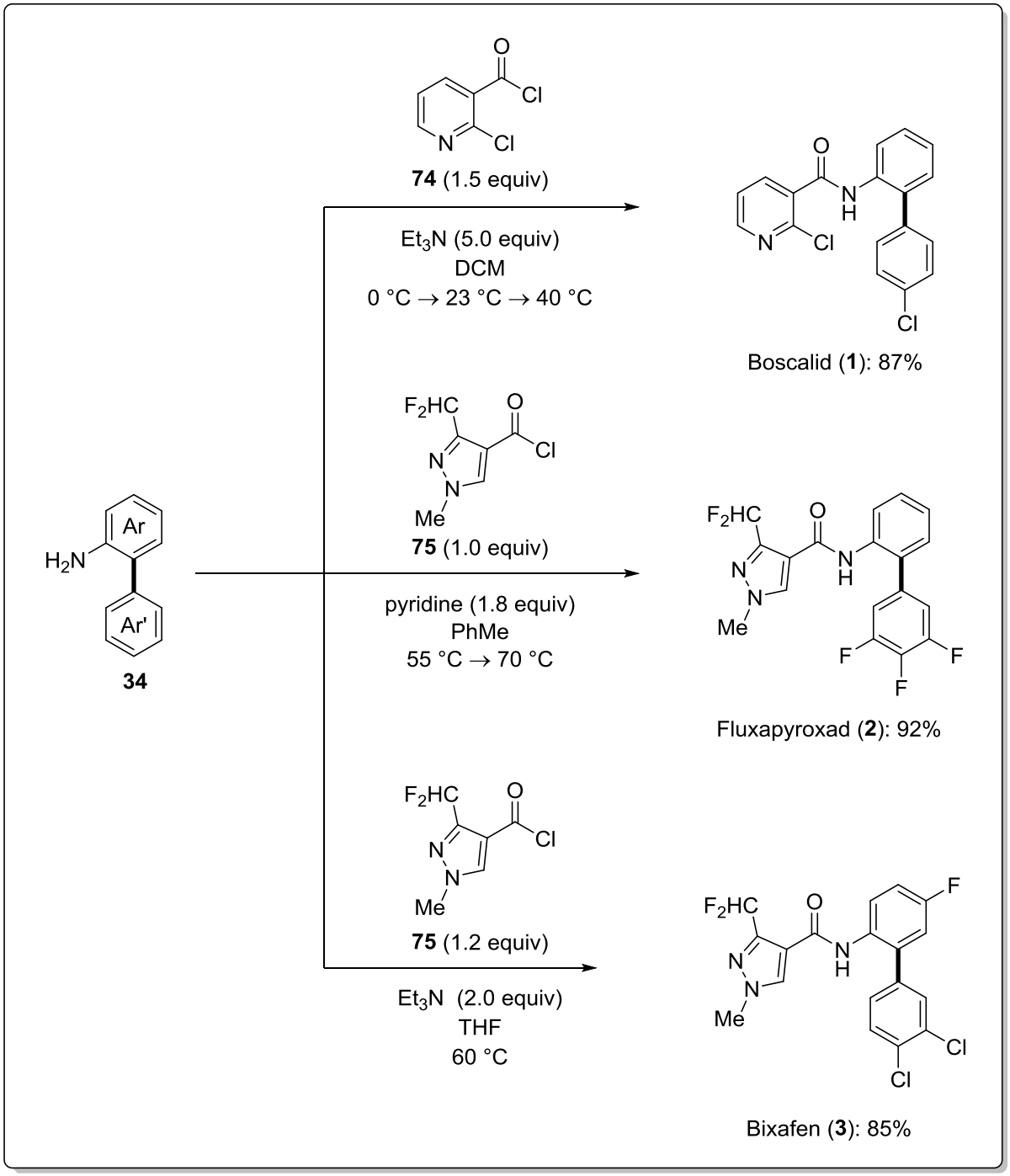


entry	**30**	**73**	**33**	yield / %
1	 **30a**	 **73b**	 **33ab**	82
2	 **30a**	 **73c**	 **33ac**	64

3		**30a**		**73d**		**33ad**	83
4		**30a**		**73e**		**33ae**	68
5		**30a**		**73f**		**33af**	63
6		**30a**		**73g**		**33ag**	70
7		**30a**		**73h**		**33ah**	68, 54[b]
8		**30q**		**73i**		**33qi**	63

[a] General reaction conditions: **30** (1.0 mmol), **73** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h; isolated yields. [b] **30a** (8.0 mmol), **73h** (12 mmol).

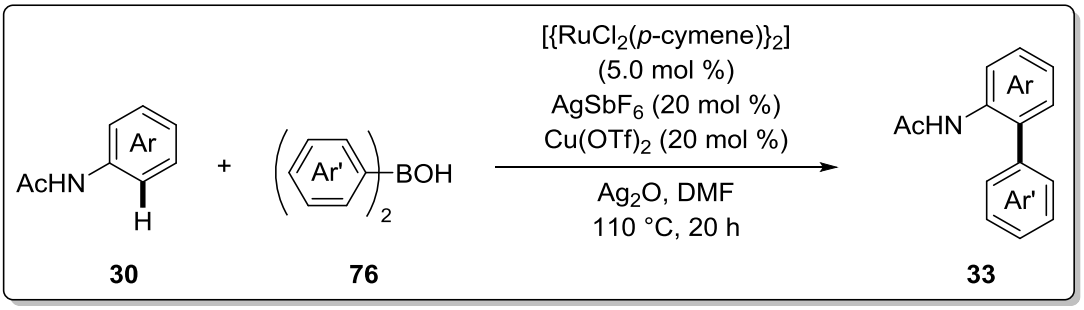
Of particular note are the key intermediates **33ag**, **33ah** and **33qi** (entries 6–8), used in the manufacture of Boscalid (**1**), Fluxapyroxad (**2**) and Bixafen (**3**) after removal of the acyl group (Scheme 24).[137-139] In addition, a gram-scale synthesis was realised with this practical method for the valuable building block **33ah** in a comparable yield (entry 7).



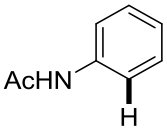
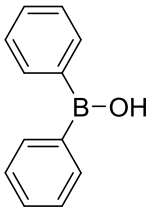
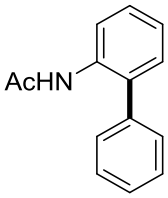
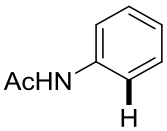
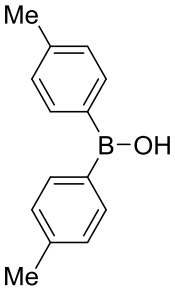
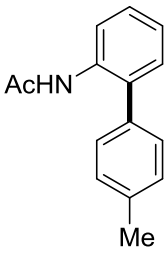
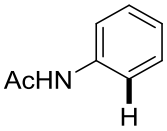
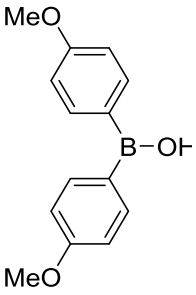
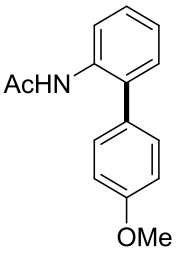
Scheme 24: Syntheses of important antifungal agrochemicals.

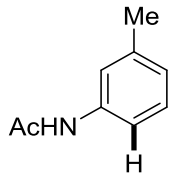
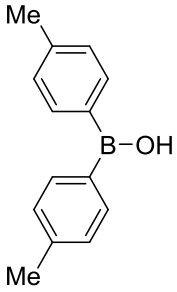
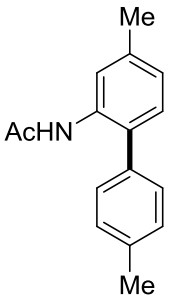
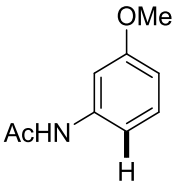
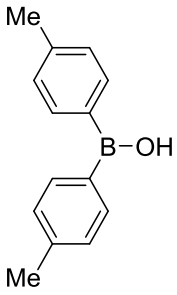
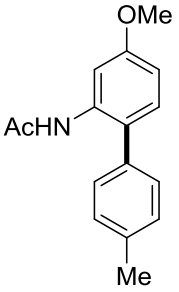
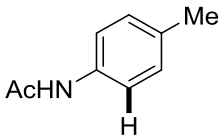
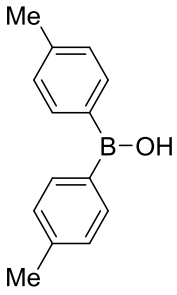
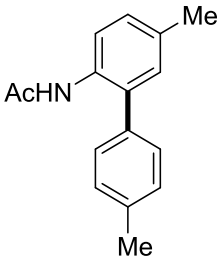
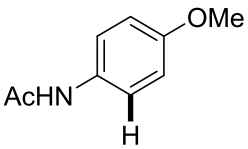
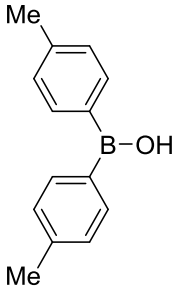
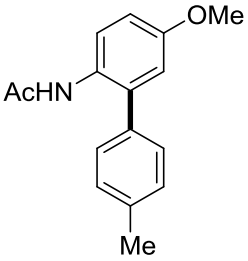
The substrate scope was successfully completed with borinic acids **76** and potassium trifluoroborates **77** as arylating reagents. At this stage, conventional boron-based arylating reagents are limited to boronic acids **73** and boronates for ruthenium-catalyzed C–H functionalization.[25,26,75,76,140,141] For that reason, the use of borinic acids **76** reinforced the utility of this catalytic system (Table 7).

Table 7: Scope of C–H arylation of acetanilides **30** with arylborinic acids **76**.[a]



30 **76** **33**

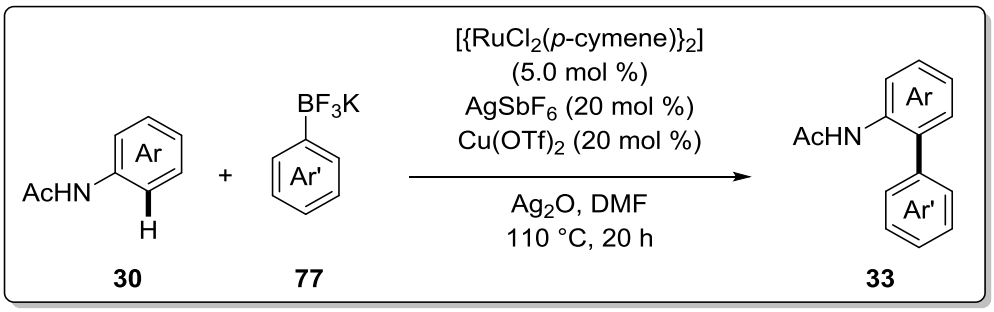
entry	**30**		**76**		**33**		yield / %
1		**30a**		**76a**		**33aa**	65
2		**30a**		**76b**		**33ab**	59
3		**30a**		**76d**		**33ad**	62

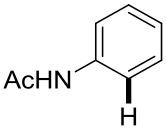
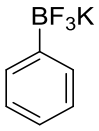
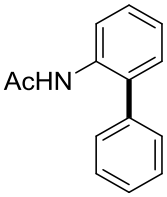
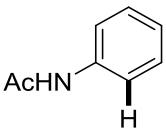
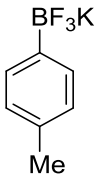
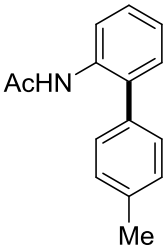
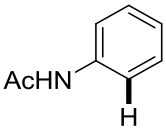
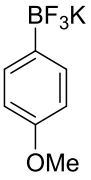
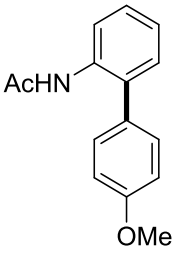
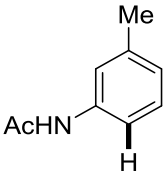
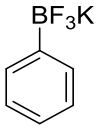
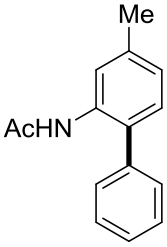
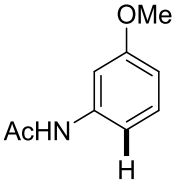
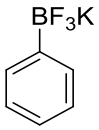
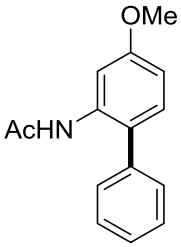
4		**30i**		**76b**		**33ib**	61
5		**30m**		**76b**		**33mb**	64
6		**30h**		**76b**		**33hb**	63
7		**30l**		**76b**		**33lb**	61

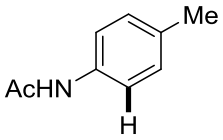
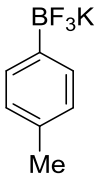
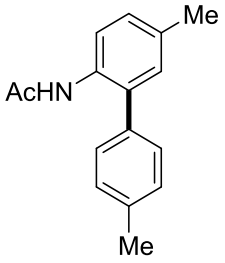
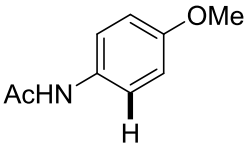
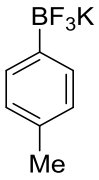
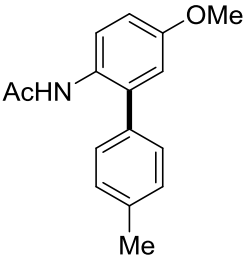
[a] General reaction conditions: **30** (1.0 mmol), **76** (3.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h; isolated yields.

Potassium trifluoroborates **77** are effective surrogates to boronic acids **73** in metal-catalyzed cross-coupling reactions,[142-144] which were also successfully subjected to this reaction conditions (Table 8).

Table 8: Scope of C–H arylation of acetanilides **30** with potassium aryltrifluoroborates **77**.[a]



entry	**30**		**77**		**33**		yield / %
1		**30a**		**77a**		**33aa**	52
2		**30a**		**77b**		**33ab**	63
3		**30a**		**77d**		**33ad**	53
4		**30i**		**77a**		**33ia**	54
5		**30m**		**77a**		**33ma**	53

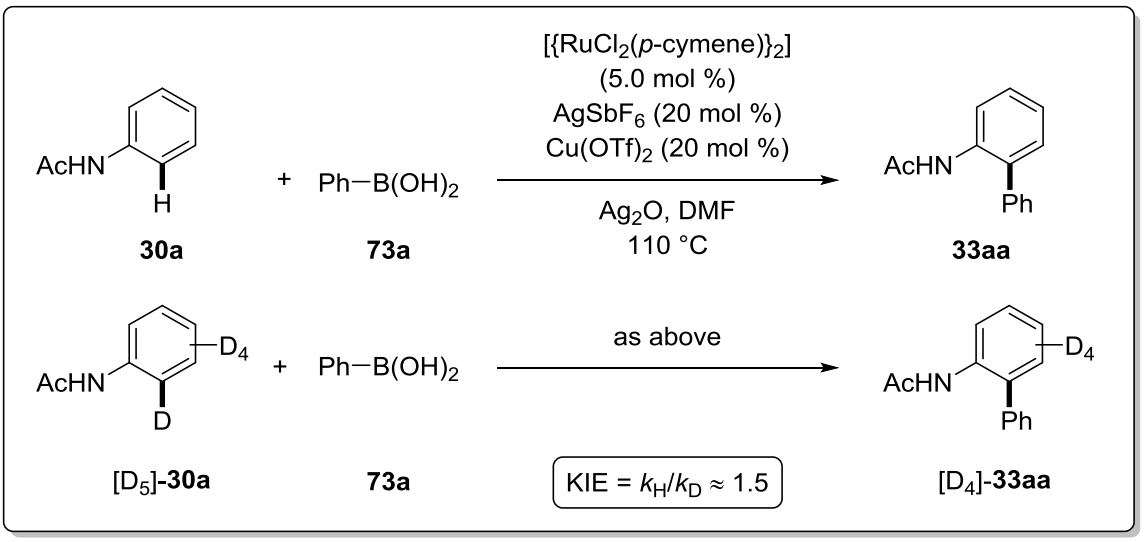
6		**30h**		**77b**		**33hb**	55
7		**30l**		**77b**		**33lb**	56

[a] General reaction conditions: **30** (1.0 mmol), **77** (3.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C, 20 h; isolated yields.

3.1.4 Mechanistic studies

3.1.4.1 Kinetic isotope effect (KIE)

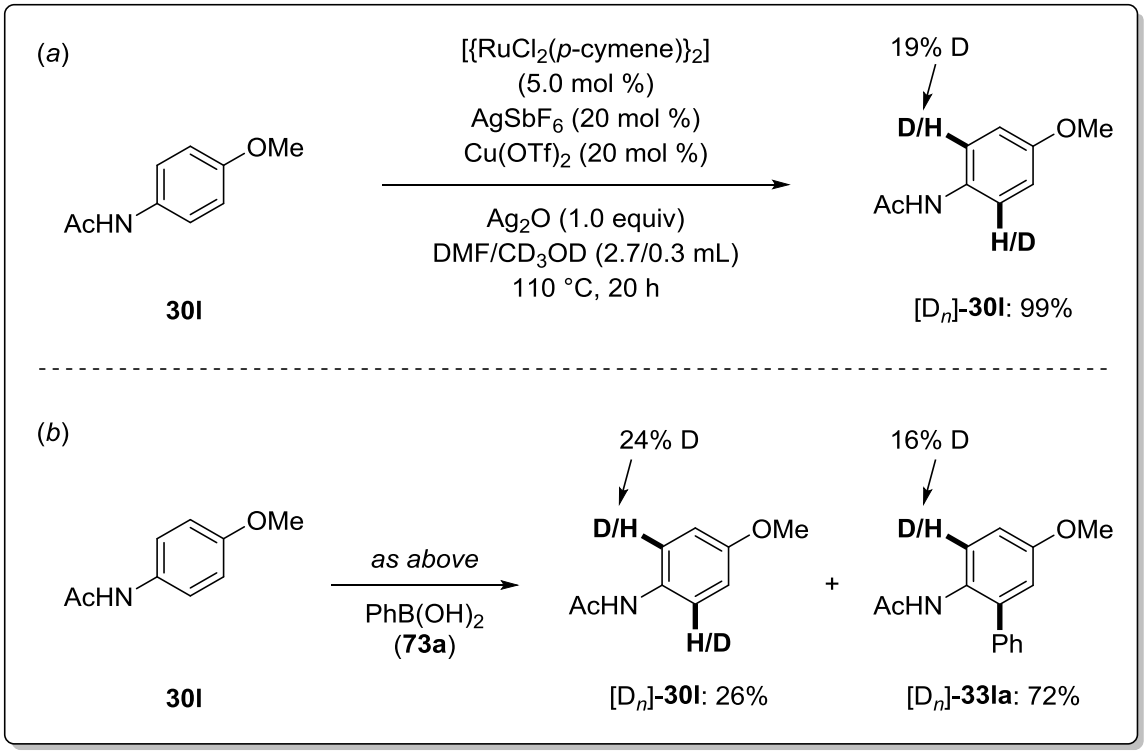
Two independent ruthenium-catalyzed C–H arylations with unlabelled substrate **30a** and isotopically labelled substrate [D_5]-**30a** were conducted respectively to determine an intermolecular kinetic isotope effect (KIE) of $k_H/k_D \approx 1.5$ by means of the initial rates, which indicates that the C–H activation is not involved in the rate-determining step (Scheme 25).



Scheme 25: Intermolecular kinetic isotope effect study by two independent reactions.

3.1.4.2 H/D Exchange experiments

The reversible nature of the C–H ruthenation step in this direct arylation was confirmed through two H/D exchange experiments in the presence of methanol-d_4 as co-solvent. The first experiment was conducted in the absence of a boron-based arylating reagent and revealed a significant H/D scrambling, exclusively in the *ortho*-position of the reisolated acetanilide [D_n]-**30l** (Scheme 26a). The second reaction was performed under the standard conditions. Once again, a notable amount of deuterium incorporation in the *ortho*-position of the recovered starting material [D_n]-**30l** and the product [D_n]-**33la** was recognized (Scheme 26b).

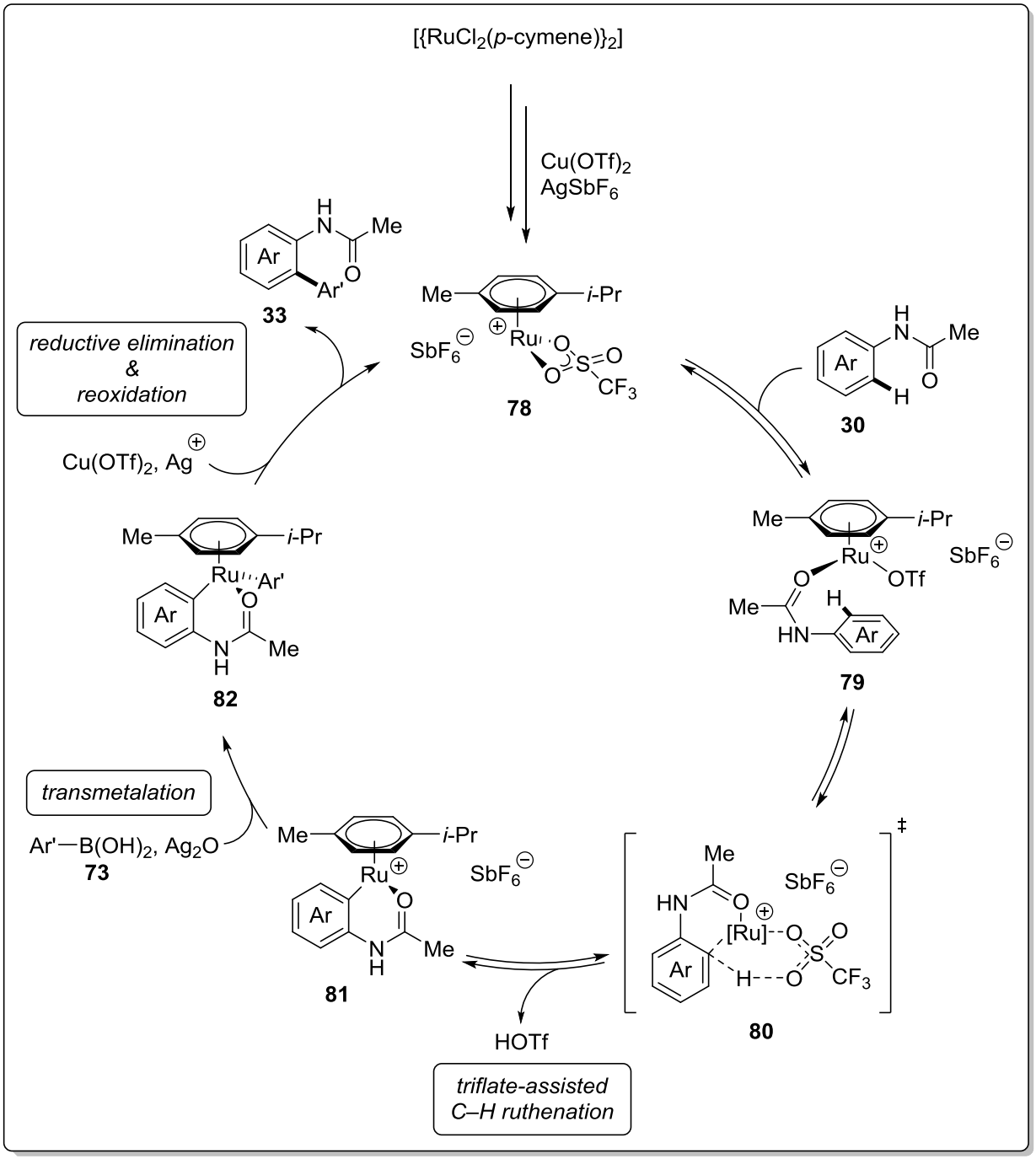


Scheme 26: H/D Exchange experiments with methanol-d_4 as co-solvent.

3.1.4.3 Proposed catalytic cycle

A postulated catalytic cycle for the ruthenium(II)-catalyzed C–H arylation of anilides **30** is outlined in Scheme 27. The first step is the *in situ* formation of the active cationic ruthenium(II) precursor **78**. The carbonyl oxygen of the anilide **30** coordinates to the cationic ruthenium(II) species **78** to provide ruthenium complex **79**. The reversible triflate-assisted *ortho*-C–H bond ruthenation is facilitated *via* a six-membered inner-sphere concerted ruthenation-deprotonation transition state **80**, delivering the six-membered ruthena(II)cycle **81**

as a key intermediate.[7] Subsequently, an irreversible transmetalation by the boron-based arylating reagent accelerated through Ag_2O acting as base supplies ruthenium intermediate **82**. The final step affords the desired *ortho* monoarylated product **33** by reductive elimination, while reoxidation of the ruthenium(0) intermediate in the presence of $Cu(OTf)_2$ and Ag^+ regenerates the active ruthenium(II) catalyst **78** to fulfill the catalytic cycle.[25]



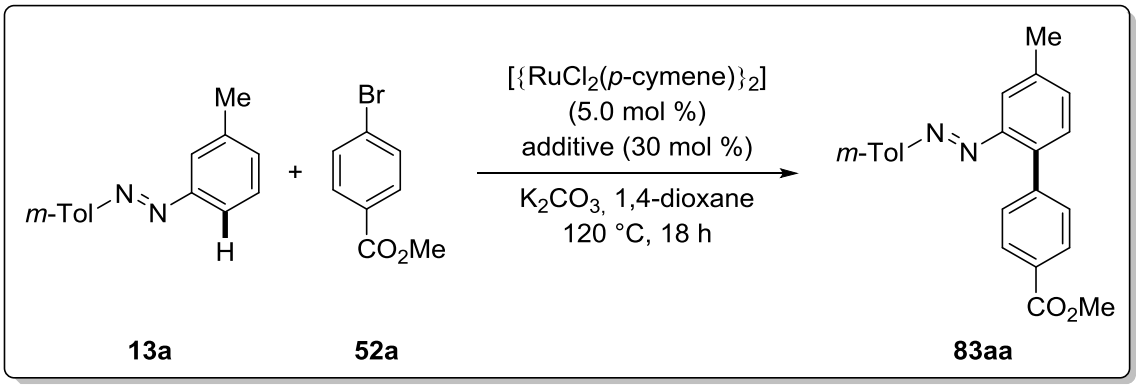
Scheme 27: Postulated catalytic cycle for ruthenium(II)-catalyzed C–H arylation of anilides **30**.

3.2 Ruthenium(II)-catalyzed C–H arylation of azoarenes by carboxylate assistance

3.2.1 Optimization of C–H arylation of azoarene 13a with aryl bromide 52a

The development of the catalytic reaction commenced with a thorough investigation of several reaction conditions on the azoarene **13a** providing the desired C–H arylated product **83aa** (Tables 9–11). Initial studies revealed [{$RuCl_2$(*p*-cymene)}$_2$] as the superior catalyst, whereas the C–H functionalization did not proceed in the absence of a ruthenium source (Table 9, entry 1). The testing of various pre-ligands disclosed $MesCO_2H$[7,15] as the most suitable co-catalytic additive (entries 2–11). Performing the reaction with other carboxylic acids or different co-catalysts, such as phosphines,[7,120-122] secondary phosphine oxides (SPOs)[7,103,104] or phosphoric acid diester $(PhO)_2P(O)OH$[7,110] provided inferior yields. The optimal loading of $MesCO_2H$ was found to be 30 mol % but could also be reduced without a substantial decrease in reactivity (entries 11–12).

Table 9: Effect of additives.[a]



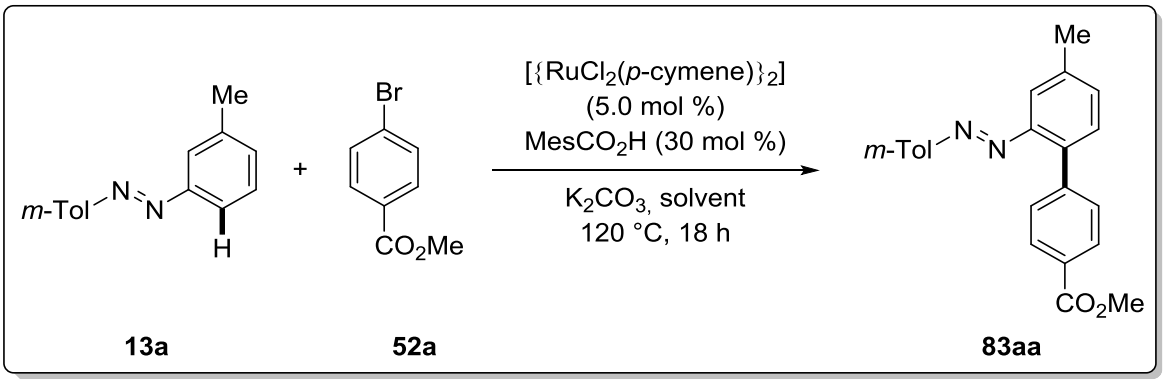
entry	additive	yield / %
1	$MesCO_2H$	---[b]
2	PPh_3	44
3	*t*-BuPhP(O)H	43
4	$(PhO)_2P(O)OH$	74
5	KPF_6	75
6	acetamide	64
7	KOAc	79

8	AcOH	37
9	*t*-$BuCO_2H$	76
10	1-$AdCO_2H$	45
11	$MesCO_2H$	87
12	$MesCO_2H$	83[c]

[a] General reaction conditions: **13a** (1.0 mmol), **52a** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), additive (30 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 120 °C, 18 h; isolated yields. [b] In the absence of [{$RuCl_2$(*p*-cymene)}$_2$]. [c] $MesCO_2H$ (15 mol %).

Among the solvents 1,4-dioxane emerged as the most effective, while the use of THF, MTBE, DME, *t*-AmOH, DCE, toluene or *o*-xylene delivered lower yields (Table 10).

Table 10: Effect of solvents.[a]

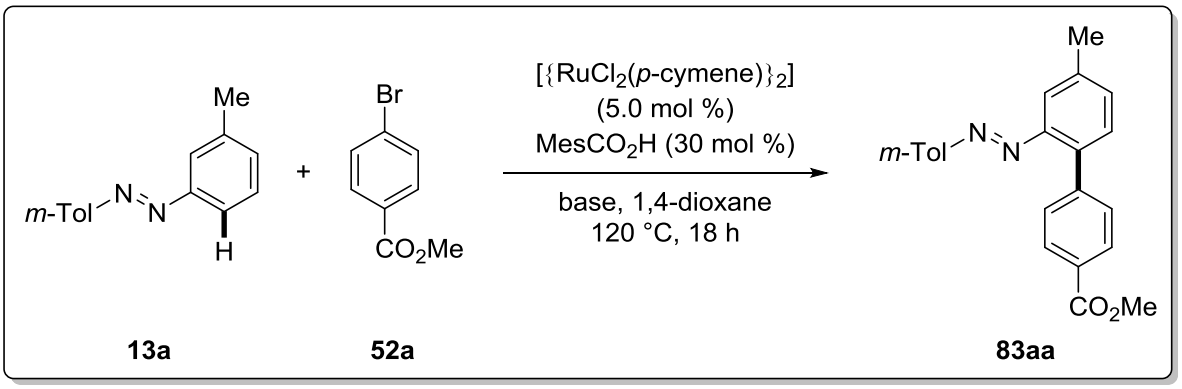


entry	solvent	yield / %
1	1,4-dioxane	87
2	THF	42
3	MTBE	32
4	DME	39
5	*t*-AmOH	75
6	DCE	43
7	PhMe	83
8	*o*-xylene	84

[a] General reaction conditions: **13a** (1.0 mmol), **52a** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), K_2CO_3 (1.0 mmol), solvent (2.0 mL), 120 °C, 18 h; isolated yields.

Several bases were probed and K_2CO_3 accomplished the best result (Table 11). The utilization of Ag_2CO_3, Cs_2CO_3 or $(NH_4)_2CO_3$ as bases failed to deliver the desired product **83aa** under otherwise identical reaction conditions (entries 3–5). Furthermore, the application of KOAc and K_3PO_4 was not successfully implemented (entries 6 and 7), which revealed that the combination of the carbonate moiety and the potassium cation plays a crucial role for this C–H transformation.[154]

Table 11: Effect of bases.[a]



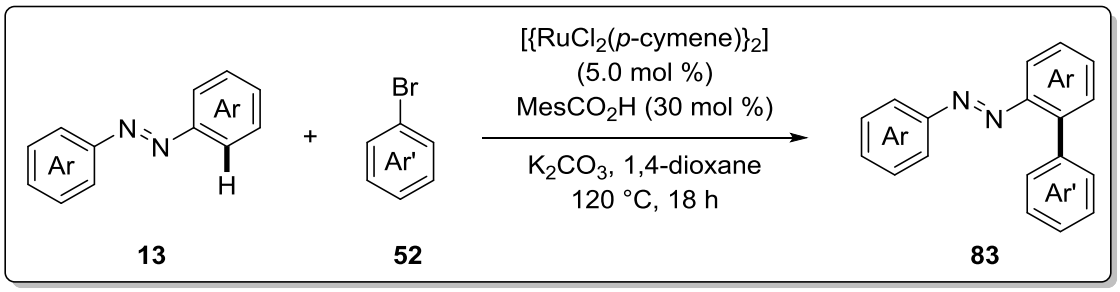
entry	base	yield / %
1	K_2CO_3	87
2	Na_2CO_3	75
3	Ag_2CO_3	0
4	Cs_2CO_3	0
5	$(NH_4)_2CO_3$	0
6	KOAc	23
7	K_3PO_4	0
8	CsOPiv	0

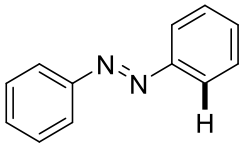
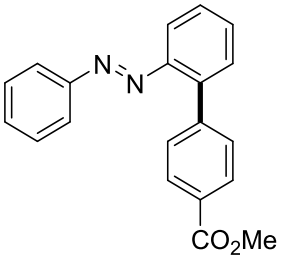
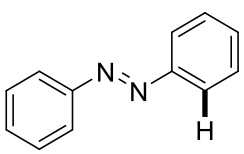
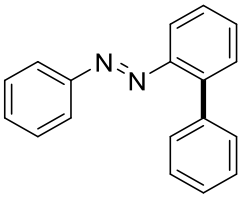
[a] General reaction conditions: **13a** (1.0 mmol), **52a** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (3 mol %), base (1.0 mmol), 1,4-dioxane (2.0 mL), 120 °C, 18 h; isolated yields.

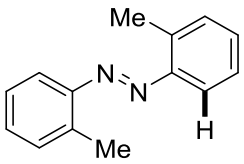
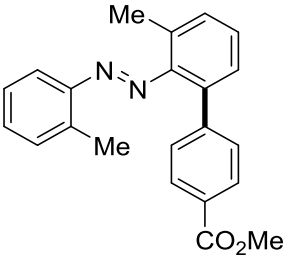
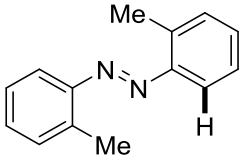
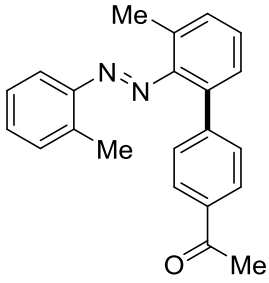
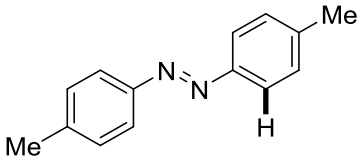
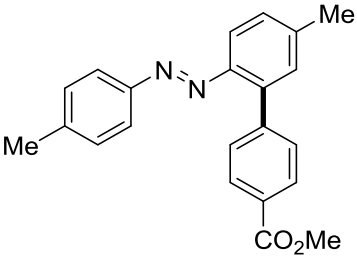
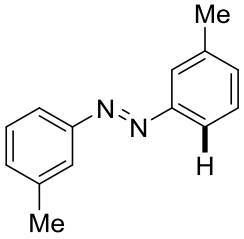
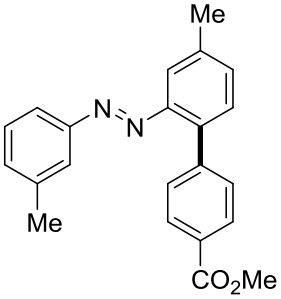
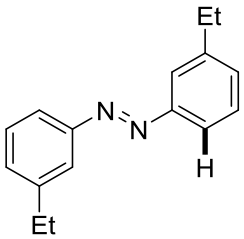
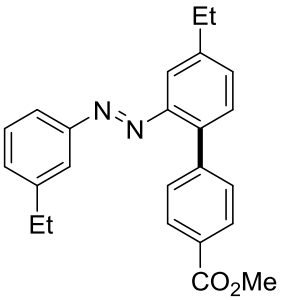
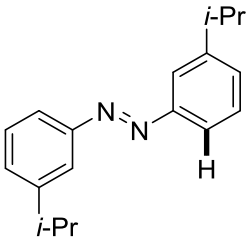
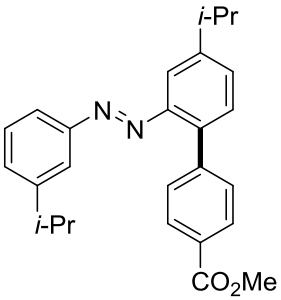
3.2.2 Scope of C–H arylation of azoarenes with (hetero)aryl halides

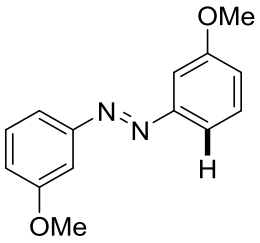
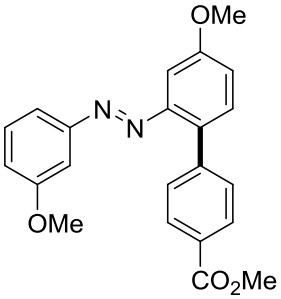
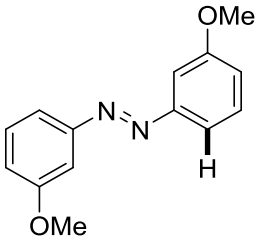
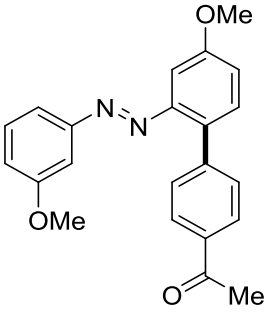
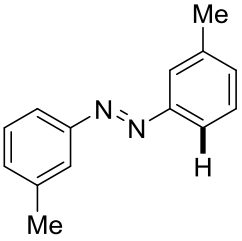
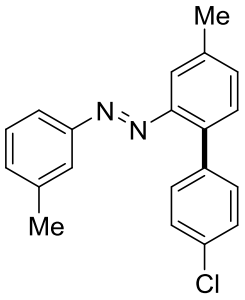
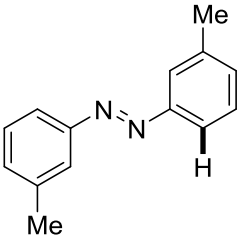
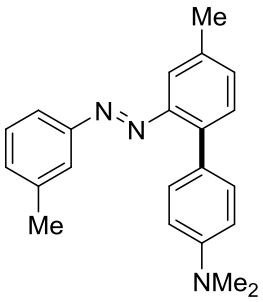
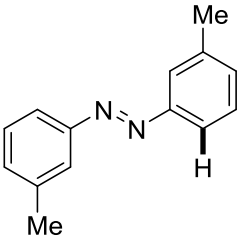
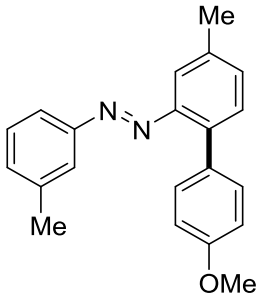
Under the optimal reaction conditions, a representative range of symmetrical azoarenes **13** exhibited a high reactivity in this chemo- and site-selective C–H functionalization with (hetero)aryl halides **63** providing the appropriate biaryl products **83** in moderate to excellent yields (Table 12). The ruthenium(II) catalytic system demonstrated in intramolecular competition experiments with *meta*-substituted azoarenes **13a** and **13e - 13g** an expedient site-selectivity at the less hindered C-6 position of the arene (entries 6–21). Several aryl electrophiles **52** were used and featured only a minor impact concerning the electronic nature of the aromatic moiety. Interestingly, aryl iodide **31a** proved to be compatible with the system in an outstanding yield (entry 6). The C–H transformation was chemoselective for valuable electrophilic functional groups, such as chloride, amine, ether, aldehyde, enolizable ketone, ester, cyano or nitro substituents, providing opportunities for further late-stage derivatization. Performing this C–H activation with electron-deficient azoarenes **13** resulted in no conversion (entries 22–26), illustrating that the electronic character of differently substituted azoarenes **13** is a dominant factor in this process.

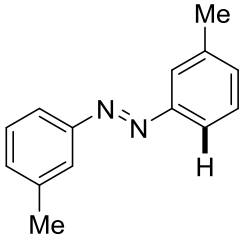
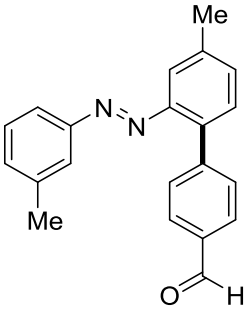
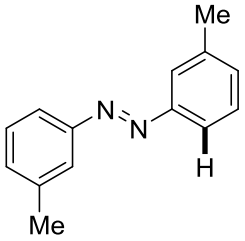
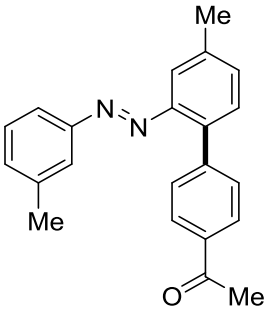
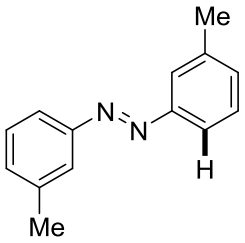
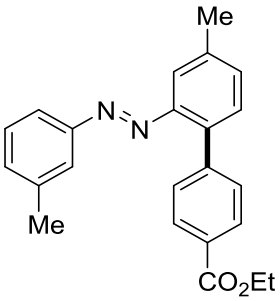
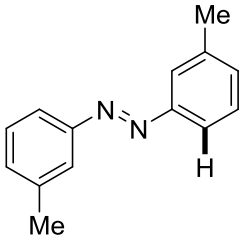
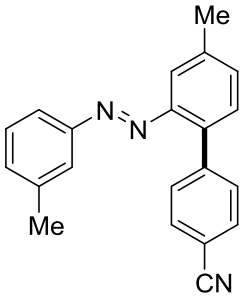
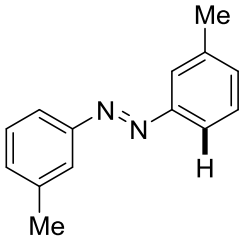
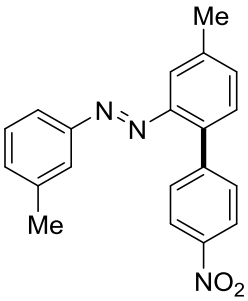
Table 12: Scope of C–H arylation of azoarenes **13** with aryl bromides **52**.[a]

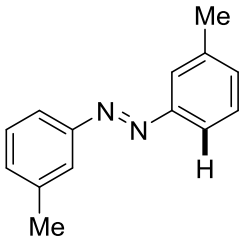
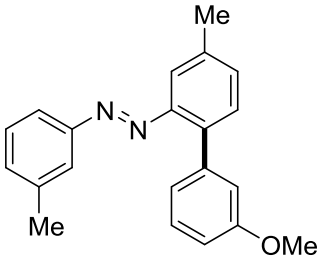
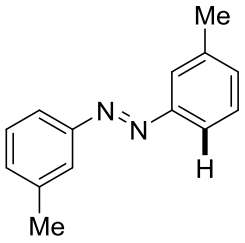
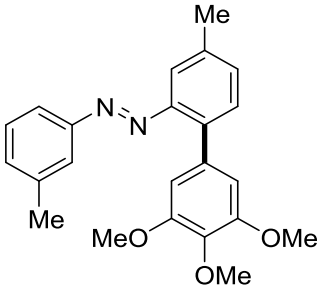
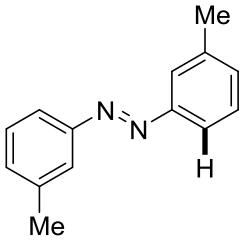
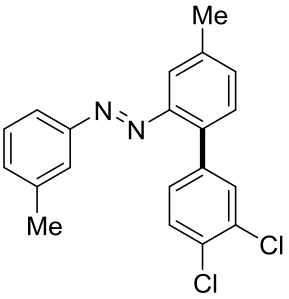
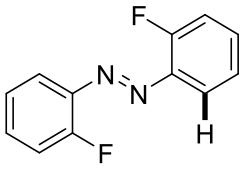
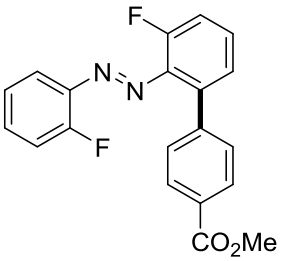
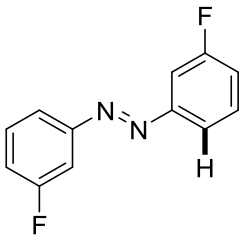
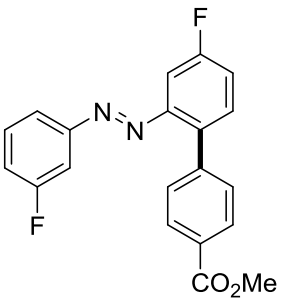
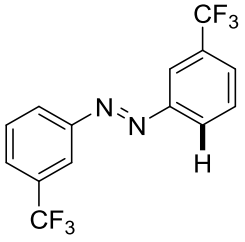
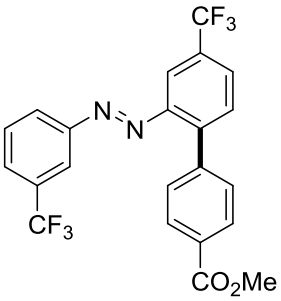


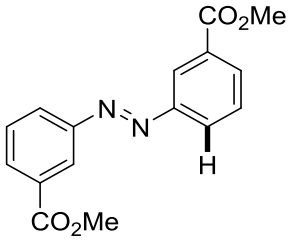
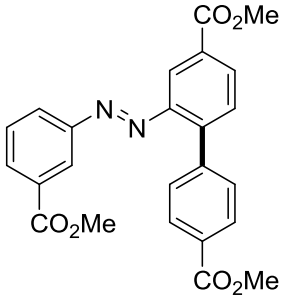
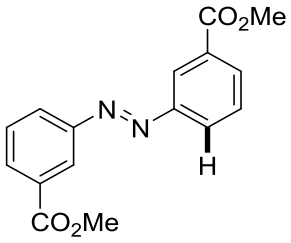
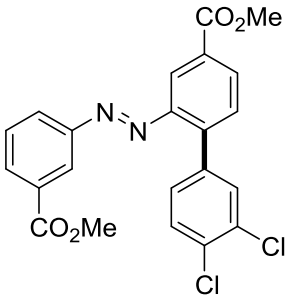
entry	**13**		**83**		yield / %
1		**13b**		**83ba**	59
2		**13b**		**83bb**	53

3		**13c**		**83ca**	60
4		**13c**		**83cc**	53
5		**13d**		**83da**	65
6		**13a**		**83aa**	87, 83[b] with Ar'I: 89
7		**13e**		**83ea**	83, 79[b]
8		**13f**		**83fa**	80, 75[b]

9		**13g**		**83ga**	74
10		**13g**		**83gc**	53
11		**13a**		**83ad**	58
12		**13a**		**83ae**	56
13		**13a**		**83af**	67

14		**13a**		**83ag**	51
15		**13a**		**83ac**	65
16		**13a**		**83ah**	63
17		**13a**		**83ai**	64
18		**13a**		**83aj**	54

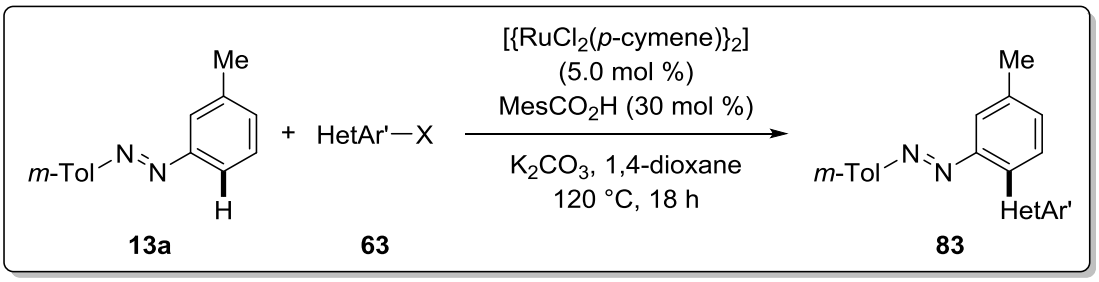
19		**13a**		**83ak**	56
20		**13a**		**83al**	86
21		**13a**		**83am**	63
22		**13h**		**83ha**	---
23		**13i**		**83ia**	---
24		**13j**		**83ja**	---

25		**13k**		**83ka**	---
26		**13k**		**83km**	---

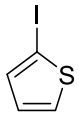
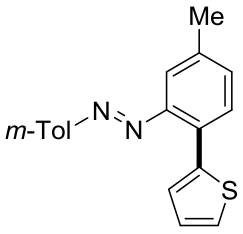
[a] General reaction conditions: **13** (1.0 mmol), **52** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), base (1.0 mmol), 1,4-dioxane (2.0 mL), 120 °C, 18 h; isolated yields. [b] KOAc (30 mol %).

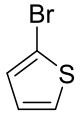
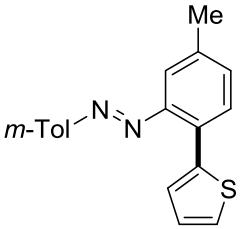
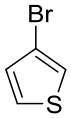
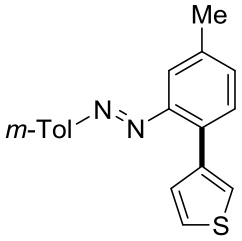
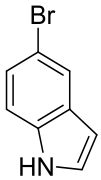
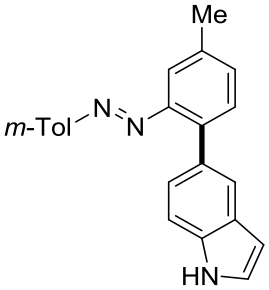
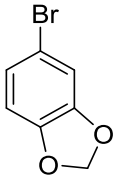
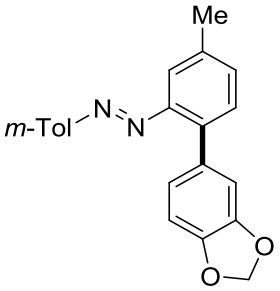
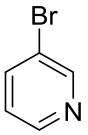
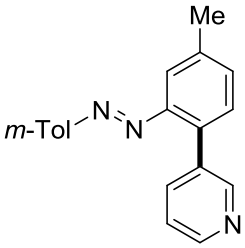
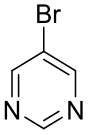
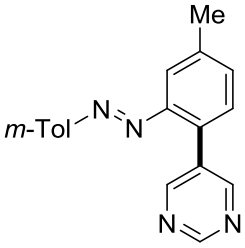
In an atom- and step-economical manner, various heteroaryl electrophiles **31n** and **52n - 52s** delivered the desired C–H arylated products **83** in moderate to high yields (Table 13). Based on the relevance of heteroarenes as valuable building blocks in numerous bioactive compounds, these findings highlight the synthetic utility of the method. The direct arylation with the electron-deficient pyridinyl **52r** and pyrimidinyl **52s** bromide was less effective (entries 5 and 6).

Table 13: Scope with respect to heteroaromatic halides **63**.[a]



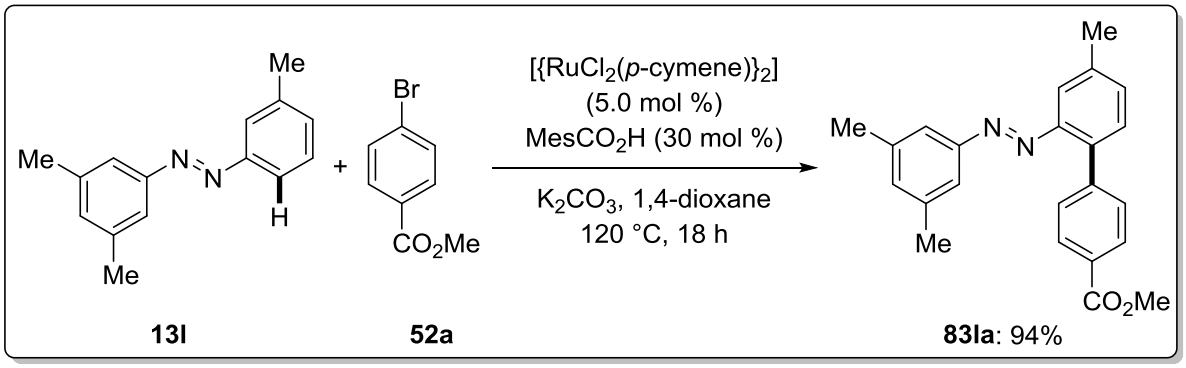
13a **63** **83**

entry	HetAr'–X	**83**	yield / %
1		**31n** 	**83an** 64

2		**52n**		**83an**	62
3		**52o**		**83ao**	51
4		**52p**		**83ap**	54
5		**52q**		**83aq**	74
6		**52r**		**83ar**	31
7		**52s**		**83as**	28

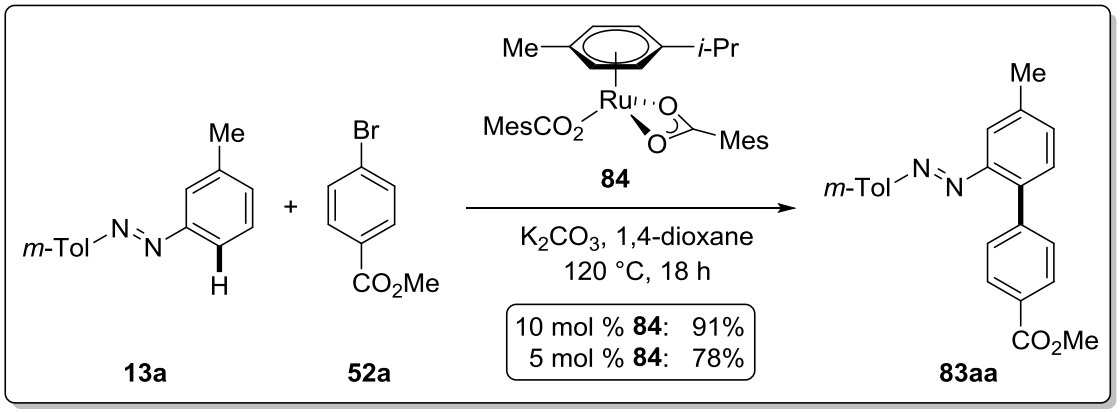
[a] General reaction conditions: **13a** (1.0 mmol), **63** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), base (1.0 mmol), 1,4-dioxane (2.0 mL), 120 °C, 18 h; isolated yields.

In addition, the unsymmetrical azoarene **13l** reacted smoothly under otherwise identical reaction conditions, providing **83la** in an excellent regioselectivity and yield (Scheme 28).



Scheme 28: C–H Functionalization of unsymmetrical azoarene **13l**.

The working mode of the well-defined robust ruthenium(II) biscarboxylate catalyst **84**[146] was also tested and supplied improved results compared to the *in situ* formed system (Scheme 29).

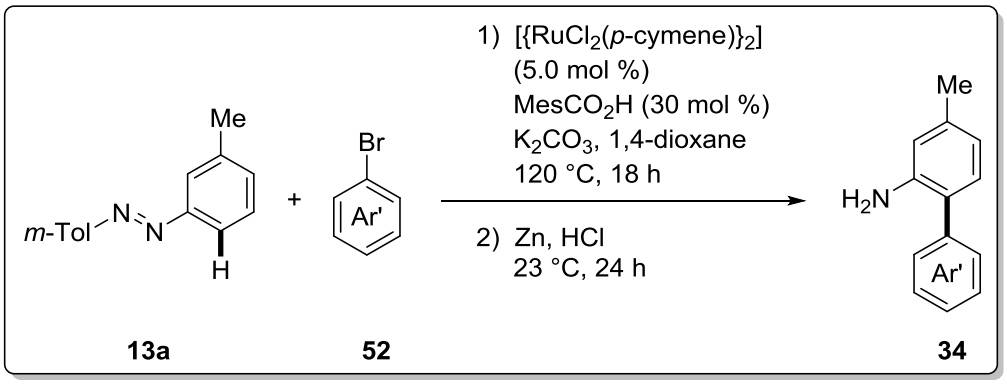


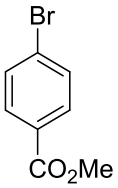
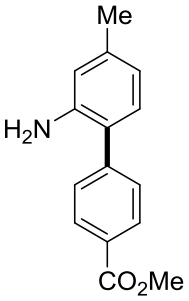
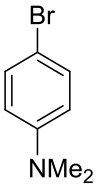
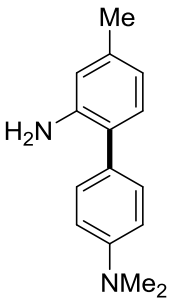
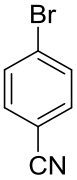
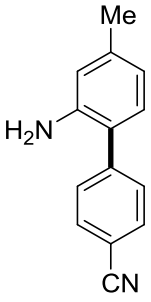
Scheme 29: Ruthenium(II) biscarboxylate catalyst **84** for the C–H arylation.

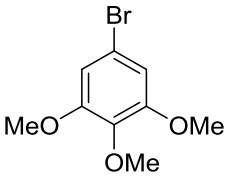
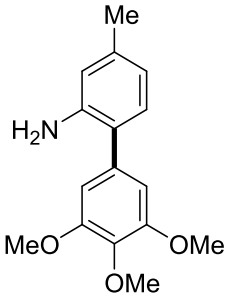
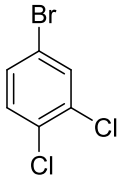
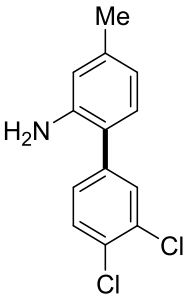
3.2.3 One-pot synthesis for expedient access to *ortho*-arylated anilines

A straightforward method to obtain *ortho*-arylated anilines **34** was achieved in a sustainable and efficient one pot synthesis *via* C–H funtionalization as the key step (Tabel 14). A practical strategy starting from azoarenes **13** by applying C–H arylation and following reduction of the azo group[147-151] provided the corresponding products **34**.

Table 14: Practical one-pot synthesis to *ortho*-arylated anilines **34**.[a]



entry	**52**		**34**		yield / %
1		**52a**		**34aa**	84
2		**52e**		**34ae**	52
3		**52i**		**34ai**	61

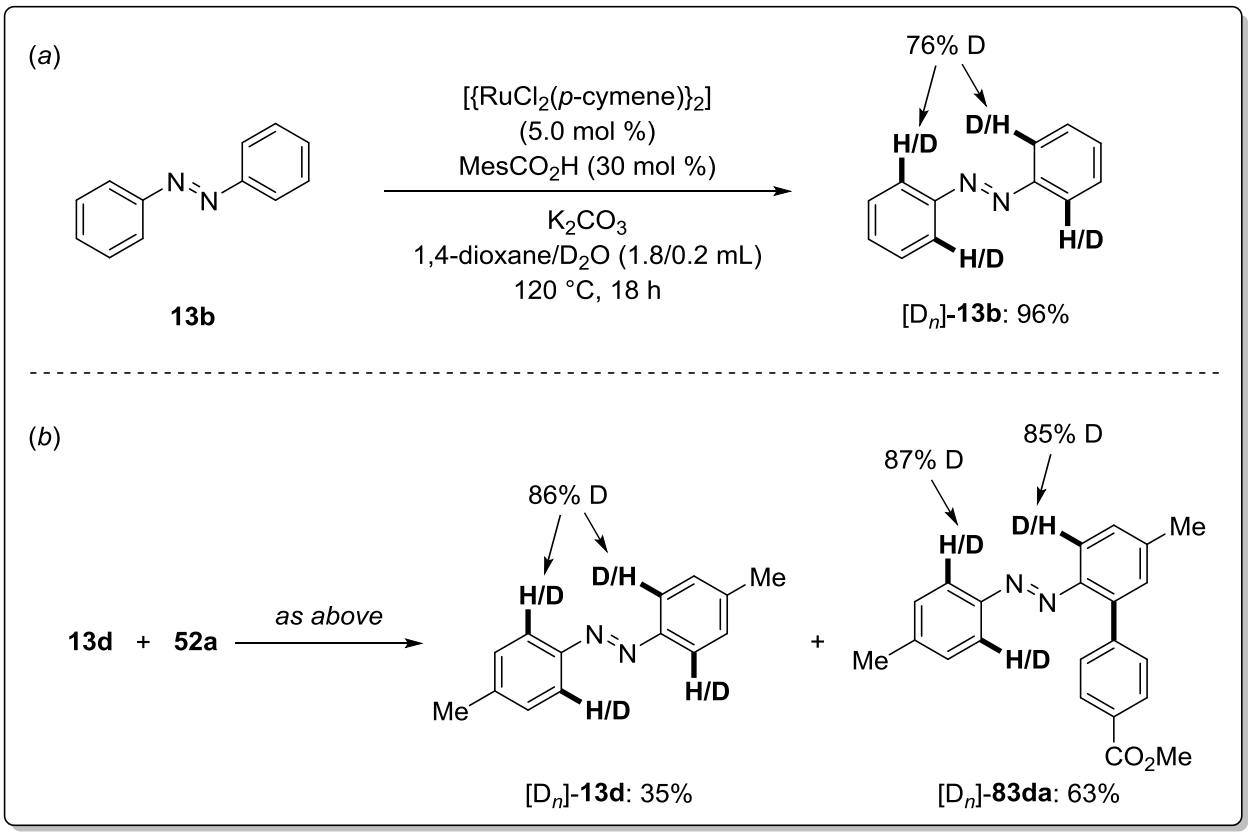
4		**52l**		**34al**	84
5		**52m**		**34am**	60

[a] General reaction conditions: 1) **13a** (1.0 mmol), **52** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), base (1.0 mmol), 1,4-dioxane (2.0 mL), 120 °C, 18 h; 2) Zn (2.5 mol %), HCl (0.4 mL), 23 °C, 24 h; isolated yields.

3.2.4 Mechanistic studies

3.2.4.1 H/D Exchange experiments

To obtain insights into the mechanism of the ruthenium(II)-catalyzed C–H activation of azoarenes, H/D exchange experiments with D_2O as the co-solvent were conducted. In the absence of the aryl bromide, a significant H/D scrambling solely in the *ortho*-position of the recovered azoarene [D_n]-**13b** was observed (Scheme 30a). For the standard reaction conditions, a considerable amount of deuterium incorporation in the *ortho*-position of the reisolated starting material [D_n]-**13d** and the product [D_n]-**83da** was detected (Scheme 30b). These results revealed the reversible nature of the C–H ruthenation step. Furthermore, it demonstrated the potential of the ruthenium catalyst towards the remarkably selective cleavage of C–H bonds.[146]

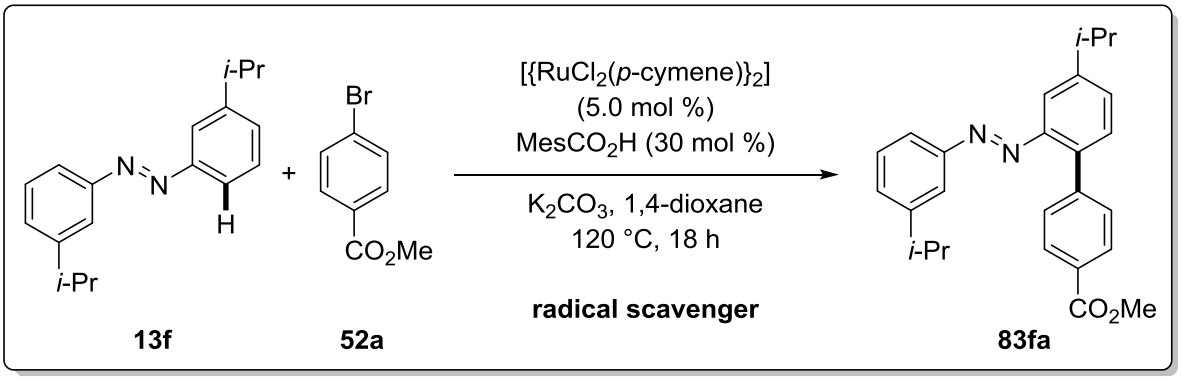


Scheme 30: H/D Scrambling studies in the presence of D_2O.

3.2.4.2 Experiments with radical scavengers

The catalytic performance of the ruthenium(II)-carboxylate complex was considerably inhibited in the presence of typical radical scavengers, suggesting that a SET-type C–X cleavage process may be operative here (Table 15).[131]

Table 15: Influence of radical scavengers in the C–H arylation process.[a]



13f **52a** **83fa**

entry	radical scavenger	yield / %
1	---	80
2	TEMPO	---
3	$Ph_2C{=}CH_2$	32
4	BHT	33

[a] General reaction conditions: **13f** (1.0 mmol), **52a** (0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), radical scavenger (1.0 equiv), 120 °C, 18 h; isolated yields. TEMPO = 2,2,6,6-tetramethylpiperidine 1-oxyl, BHT = butylated hydroxytoluene.

3.2.4.3 Hammett plot analysis

The investigation of the initial rate for the ruthenium(II)-catalyzed carboxylate-assisted C–H arylations with diversely *para*-substituted aryl bromides **52** displayed a rate acceleration preferably influenced through electron-donating groups (Figure 3).

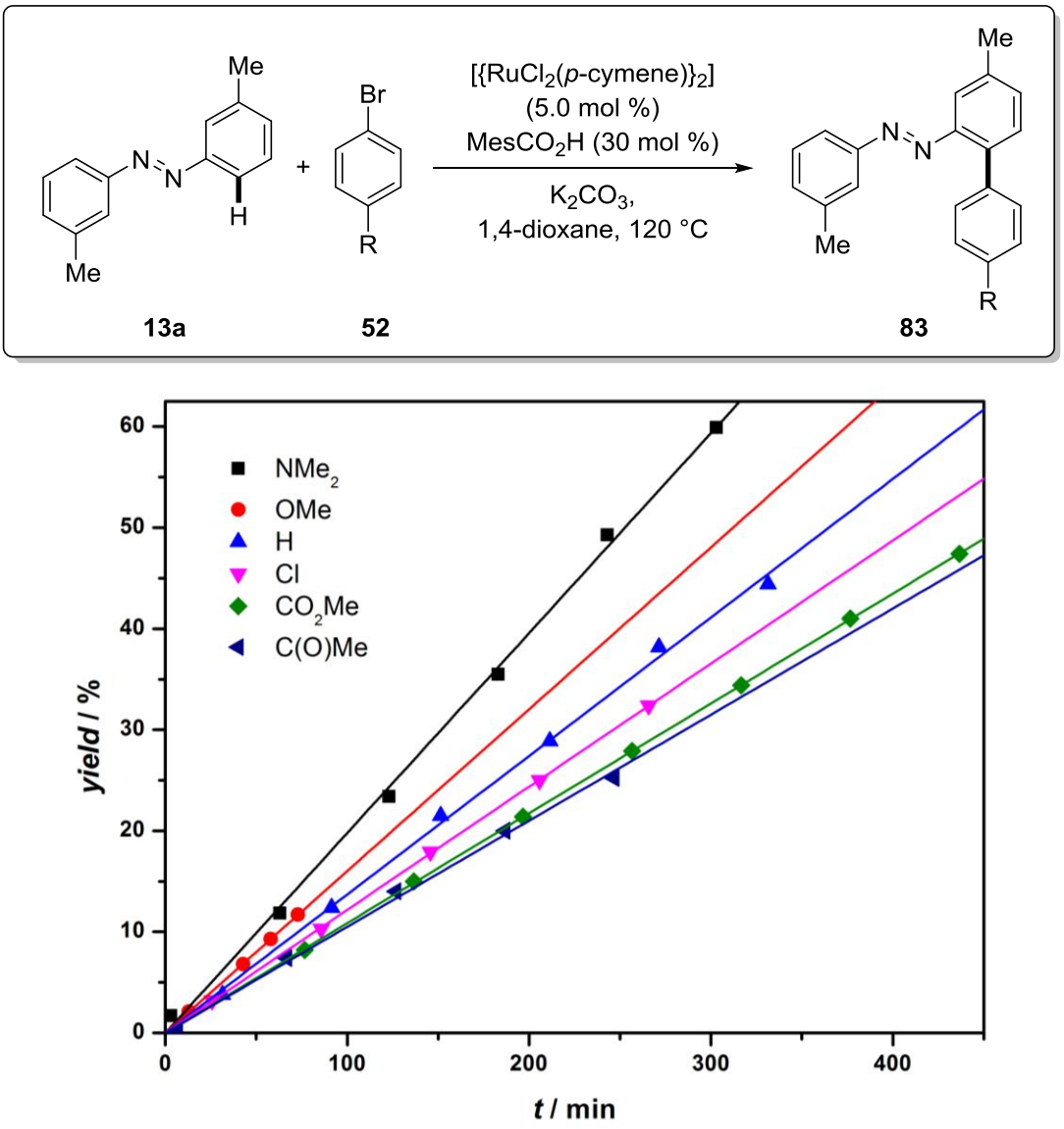


Figure 3: Comparison of the initial rates exerted by the different aryl bromides **52**.

Afterwards, a Hammett plot was constructed from the correlation between the initial rate and the corresponding σ_p value (Figure 4). The plot resulted in a linear fit with a negative slope of $\rho = -0.21 \pm 0.01$, suggesting the C–H activation promoted by electron-donating substituents. In contrast to the previous findings, this result implies a C–X cleavage as rate-determining

step is less likely for the direct arylations. Additionally, the value of $\rho = -0.21 \pm 0.01$ is rather small, and values of this magnitude are more difficult to accurately interpret.[152-156]

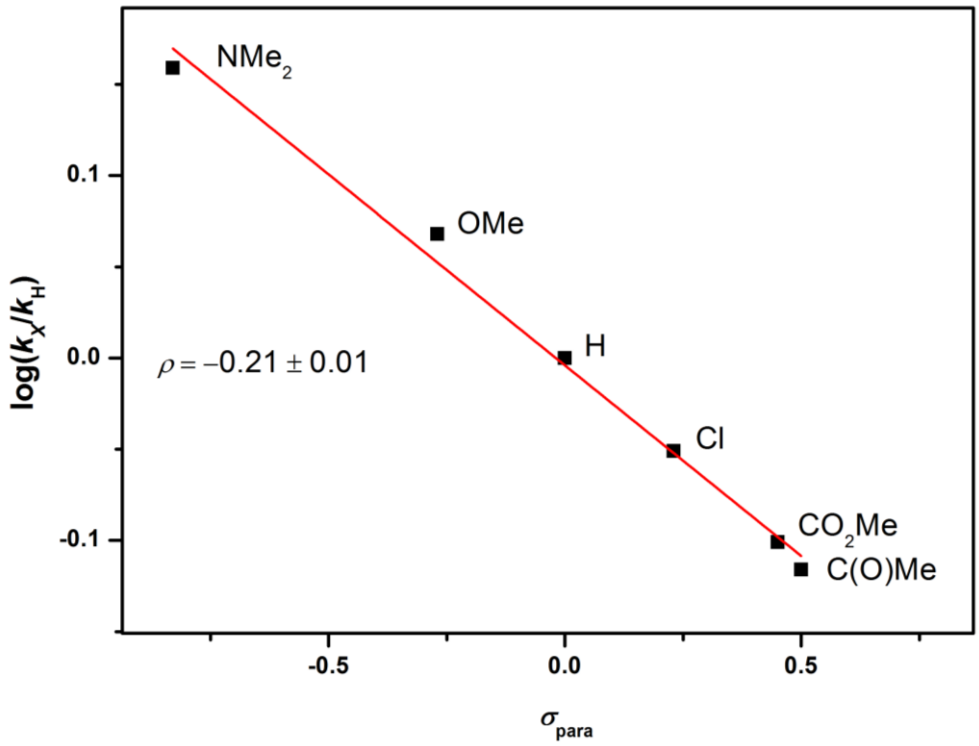
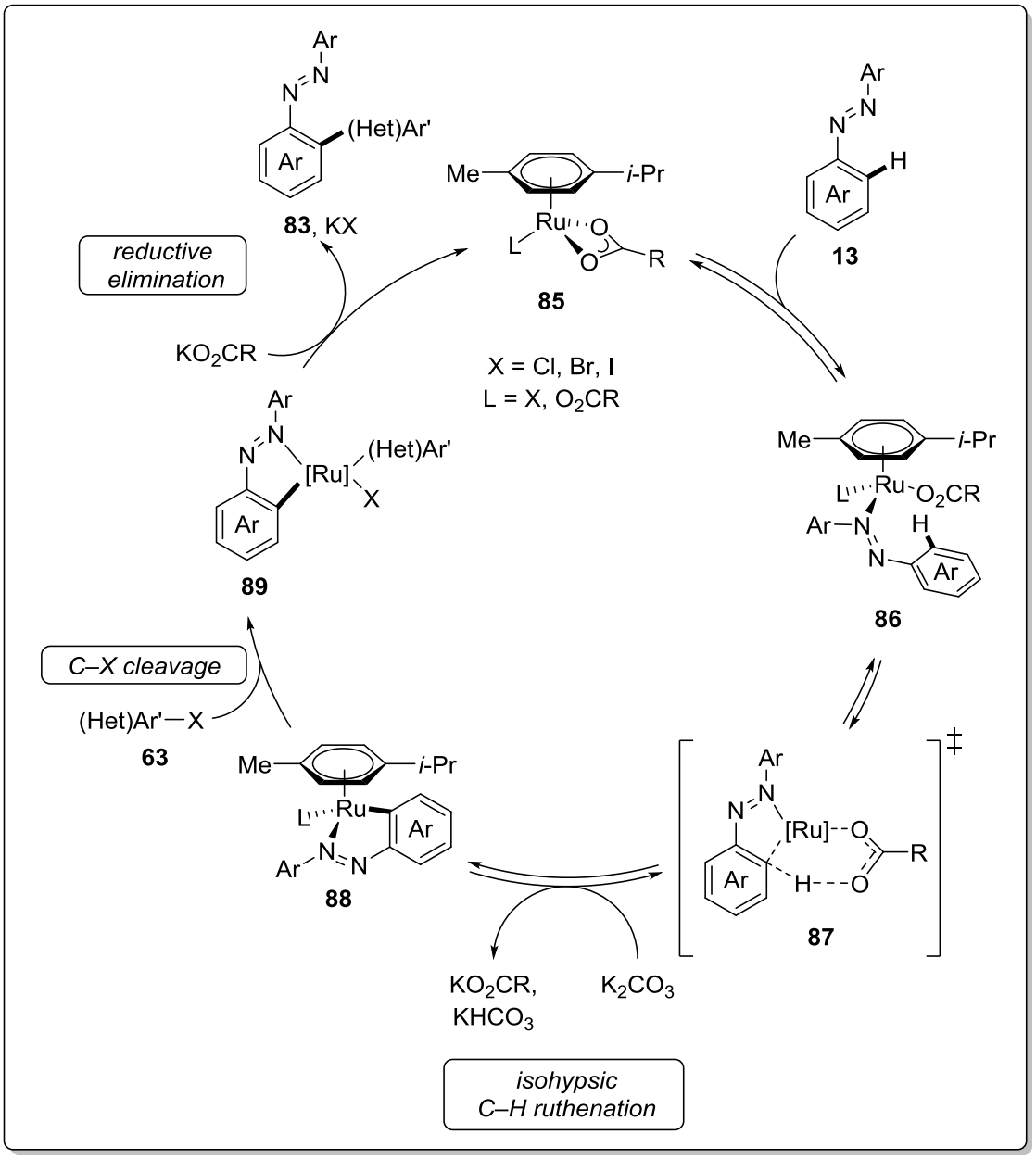


Figure 4: Hammett plot correlation of azoarene **13a** with *para*-substituted aryl bromides **52**.

3.2.4.4 Proposed catalytic cycle

Based on the experimental studies, a detailed catalytic cycle for the ruthenium(II)-catalyzed *ortho*-C–H arylation by carboxylate assistance is delineated in Scheme 31. In the initial stage, the active ruthenium(II)-carboxylate complex **85** is formed *in situ*, followed by coordination of the azoarene **13** to deliver complex **86**. Afterwards, a reversible isohypsic *ortho*-C–H bond ruthenation is promoted *via* a six-membered inner-sphere concerted ruthenation-deprotonation transition state **87**, providing the five-membered ruthena(II)cycle **88** as a key intermediate.[7,107,146] Here, it is proposed that the carboxylic acid facilitates the C–H bond cleavage, which serves as a catalytic proton shuttle from the transition state of the CMD process to the insoluble carbonate base.[146] Thereafter, formal oxidative addition of the aryl electrophile **63** by a SET-type *via* homolytic C–X bond cleavage affords the reactive ruthenium(IV) species **90**. Finally, reductive elimination releases the desired biaryl product **83** and regenerates the active ruthenium(II) catalyst **85** required for another turnover of the catalytic cycle.[15,117]



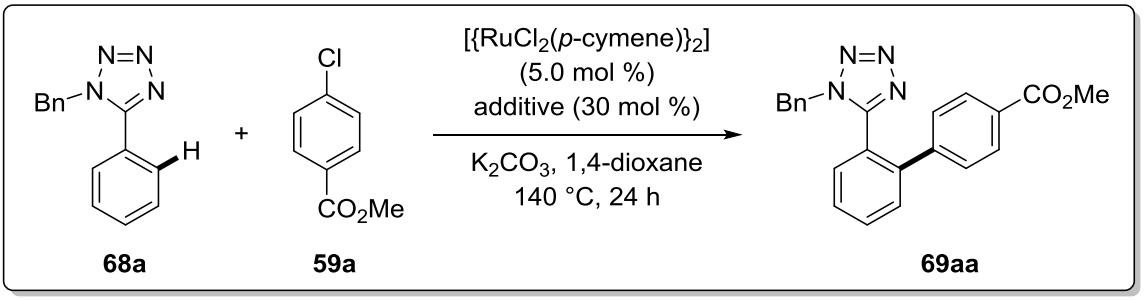
Scheme 31: Proposed catalytic cycle for the ruthenium(II)-catalyzed C–H arylation.

3.3 Ruthenium(II)-catalyzed C–H arylation of 5-aryl-1*H*-tetrazoles

3.3.1 Optimization of C–H arylation of 1*H*-tetrazole 68a with aryl chloride 59a

At the outset, various reaction conditions were evaluated for the ruthenium-catalyzed C–H arylation of 1-benzyl-5-phenyl-1*H*-tetrazole (**68a**) using inexpensive aryl chloride **59a** in a high chemo- and positional-selectivity (Tables 16–20). Preliminary studies of the co-catalyst identified mono-*N*-protected amino acids (MPAAs)[157-159] and carboxylic acids[7,15] as key pre-ligands in this respect (Table 16). The tetrazole-directed arylation was less effective in the absence of additives (entry 1). It is noteworthy that further co-cataltytic additives, such as secondary phosphine oxides (SPOs),[7,103,104] the phosphoric acid diester $(PhO)_2P(O)OH$[7,117] or KOAc[40,118] provided the C–H arylated product **69aa** in lower yields (entries 2–5). In light of these findings, an extensive screening of several carboxylic acids and MPAAs was conducted (entries 6–28). The use of adamantyl carboxylic acid and pivalic acid gave inferior results compared to mesityl carboxylic acid (entries 6–8). A set of representative MPAAs was tested and Piv-Val-OH emerged as the most effective co-catalyst, whereas dipeptides furnished the desired product **69aa** in unsatisfactory yields (entries 23–25). The optimal pre-ligand loading of Piv-Val-OH was 30 mol % (entries 11 and 26–28).

Table 16: Effect of co-catalyst.[a]



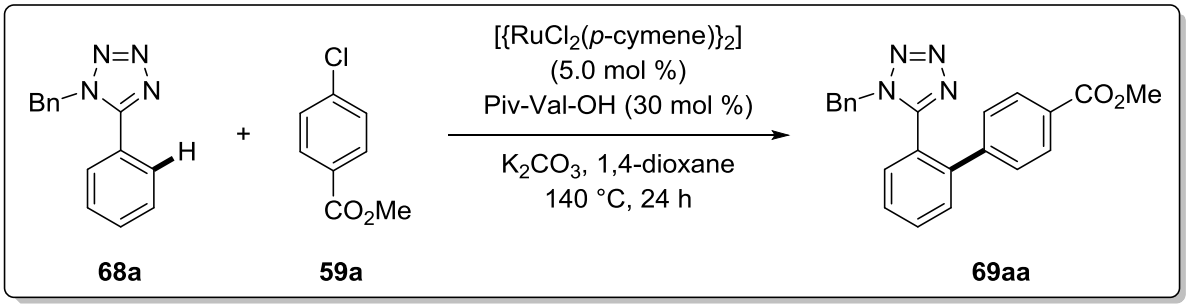
entry	additive	yield / %
1	---	22
2	*t*-BuPhP(O)H	36
3	$(n\text{-Bu})_2P(O)H$	32
4	$(PhO)_2P(O)OH$	38
5	KOAc	36
6	$(1\text{-Ad})CO_2H$	36

7	*t*-$BuCO_2H$	39
8	$MesCO_2H$	47
9	Piv-Ala-OH	39
10	Phth-Ala-OH	35
11	Piv-Val-OH	58
12	Piv-Leu-OH	42
13	Ac-Ile-OH	46
14	Piv-Ile-OH	51
15	Ada-Ile-OH	48
16	MeO_2C-Ile-OH	37
17	Boc-Ile-OH	41
18	Piv-Phe-OH	44
19	Phth-Phe-OH	41
20	Piv-Met-OH	16
21	Piv-Asp-OH	50
22	Piv-Asn-OH	17
23	Phth-Ala-Trp-OH	29
24	Boc-Val-Gly-OH	45
25	Boc-Ile-Phe-OH	32
26	Piv-Val-OH	44[b]
27	Piv-Val-OH	52[c]
28	Piv-Val-OH	54[d]

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), additive (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (2.0 mL), 140 °C, 24 h; isolated yields. [b] Piv-Val-OH (10 mol %). [c] Piv-Val-OH (20 mol %). [d] Piv-Val-OH (40 mol %).

The ruthenium(II)-catalyzed chelation-assisted C–H activation revealed a significant temperature- and concentration-dependence under otherwise identical reaction conditions (Table 17).

Table 17: Effect of concentration.[a]



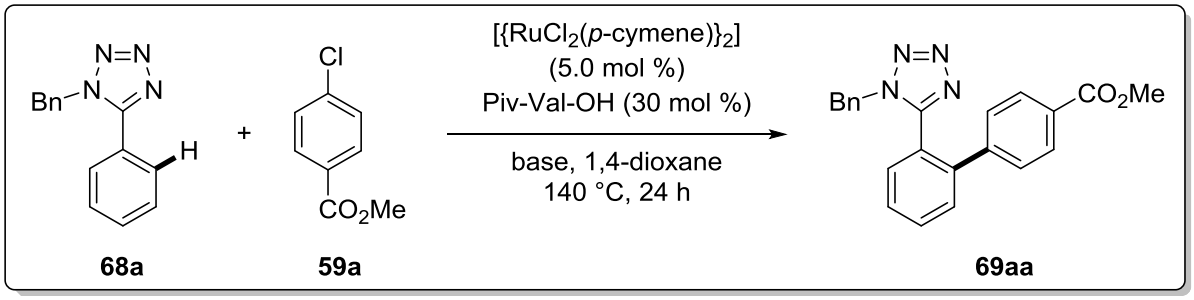
68a **59a** **69aa**

entry	c / mol L^{-1}	yield / %
1	neat	61
2	1.00	77[b]
3	0.300	64
4	0.150	58
5	0.150	17[c]
6	0.100	40
7	0.075	34

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), Piv-Val-OH (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (mol L^{-1}), 140 °C, 24 h; isolated yields. [b] 10% of diarylated product **69aa'** was isolated. [c] 120 °C.

Further optimization studies under otherwise identical reaction conditions disclosed K_2CO_3 as stoichiometric and insoluble base of choice, which improved the activity of the ruthenium(II) catalyst in conjunction with the soluble pre-ligand Piv-Val-OH (Table 18). In this context, it is worth mentioning that Fagnou revealed a considerable influence of the catalytic efficiency exerted by the solubility of bases in palladium catalysis.[160] This observation was confirmed through the previously discussed ruthenium(II)-catalyzed C–H arylation of azoarenes (Table 11).

Table 18: Effect of bases.[a]



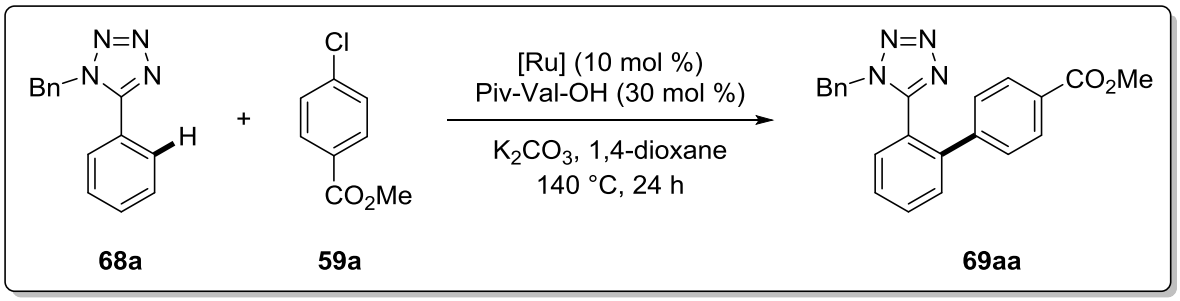
68a **59a** **69aa**

entry	base	yield / %
1	K_2CO_3	77[b]
2	K_2CO_3	69[c,d]
3	K_2CO_3	18[e]
4	Na_2CO_3	74[d]
5	$(NH_4)_2CO_3$	---
6	K_3PO_4	21

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), Piv-Val-OH (30 mol %), base (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C, 24 h; isolated yields. [b] 10% of diarylated product **69aa'** was isolated. [c] (0.60 mmol). [d] 5% of diarylated product **69aa'** was isolated. [e] K_2CO_3 (0.30 mmol).

The direct C–H functionalization did not proceed in the absence of the ruthenium catalyst or with the inexpensive [$RuCl_3(H_2O)_n$] (Table 19, entries 1–2). A range of well-defined robust ruthenium(II) complexes[131,146,157] were tested and delivered a comparable catalytic efficiency towards the *in situ* generated counterparts (entries 3–7).

Table 19: Effect of ruthenium sources.[a]



68a **59a** **69aa**

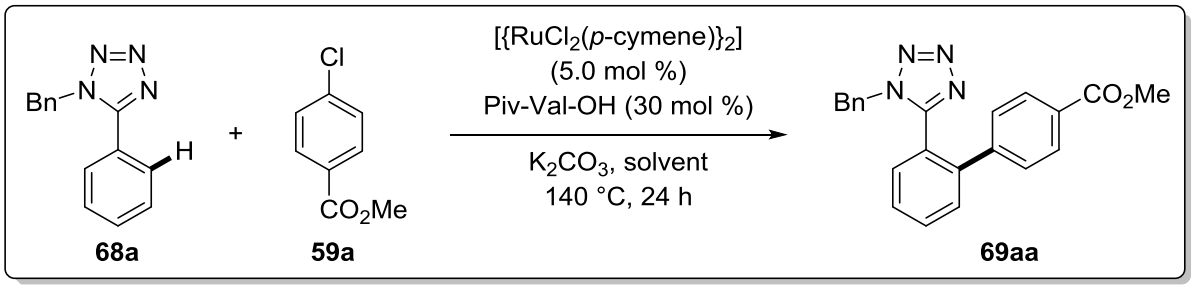
entry	[Ru]	yield / %
1	---	---
2	[$RuCl_3(H_2O)_n$]	---[c]

3	[{$RuCl_2$(*p*-cymene)}$_2$]	77[b]
4	[Ru(O_2CMes)$_2$(*p*-cymene)]	68[d,e]
5	[$RuCl_2$(*p*-cymene)(*t*-BuPhPHO)]	58[d]
6	[$RuCl_2$(*p*-cymene)(*n*-Bu_2PHO)]	46[d]
7	[RuCl(O-Val-Piv)(*p*-cymene)]	79[b,d]

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [Ru] (10 mol %), Piv-Val-OH (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C, 24 h; isolated yields. [b] 10% of diarylated product **69aa'** was isolated. [c] [Ru] (5.0 mol %). [d] In the absence of additive. [e] 7% of diarylated product **69aa'** was isolated.

Among different solvents 1,4-dioxane proved to be the most suitable one (Table 20). Unfortunately, more sustainable solvents, such as H_2O[161] and γ-valerolactone,[162] were unsuccessfully employed (entries 2–3). Other solvents, including toluene, NMP, DMA, DMF or *t*-AmOH, also resulted in inferior yields (entries 4–8).

Table 20: Effect of solvents.[a]



68a **59a** **69aa**

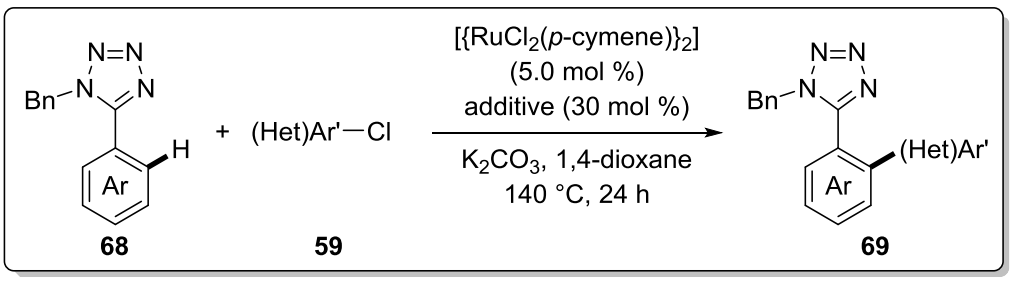
entry	solvent	yield / %
1	1,4-dioxane	77[b]
2	H_2O	---
3	γ-valerolactone	24
4	PhMe	28
5	NMP	54[c]
6	DMA	52[d]
7	DMF	16
8	*t*-AmOH	15

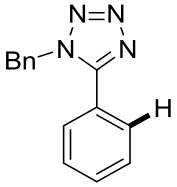
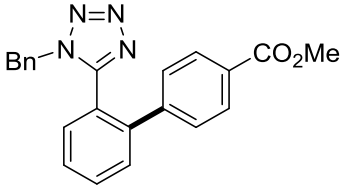
[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), Piv-Val-OH (30 mol %), K_2CO_3 (0.90 mmol), solvent (0.3 mL), 140 °C, 24 h; isolated yields. [b] 10% of diarylated product **69aa'** was isolated. [c] 32% of diarylated product **69aa'** was isolated. [d] 31% of diarylated product **69aa'** was isolated.

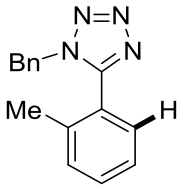
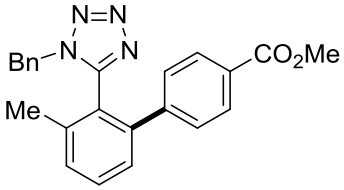
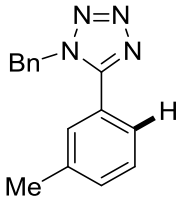
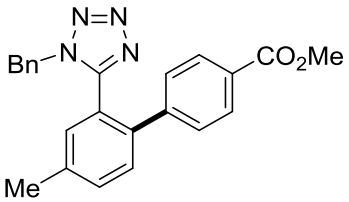
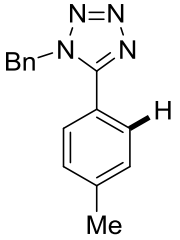
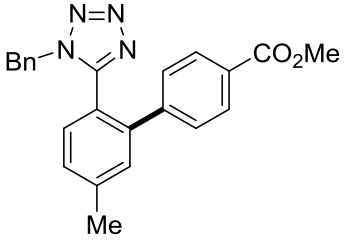
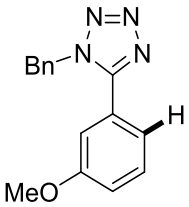
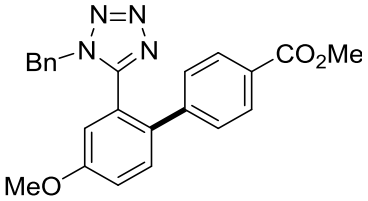
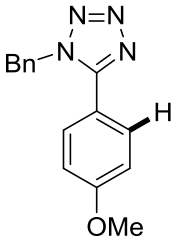
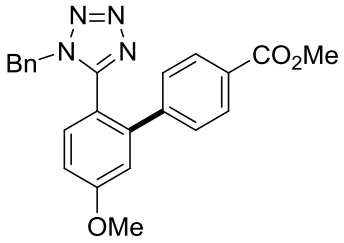
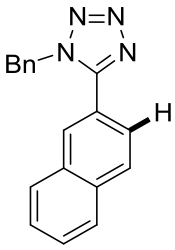
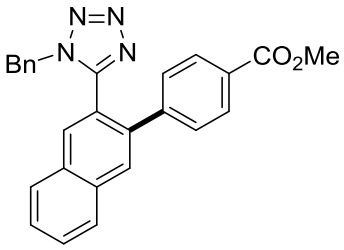
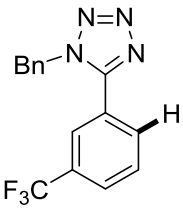
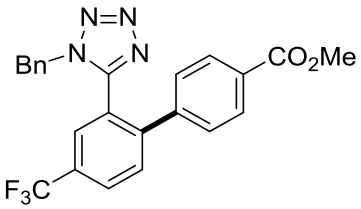
3.3.2 Scope of C–H arylation of 5-aryl-1*H*-tetrazole with (hetero)aryl electrophiles

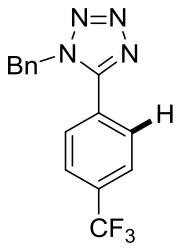
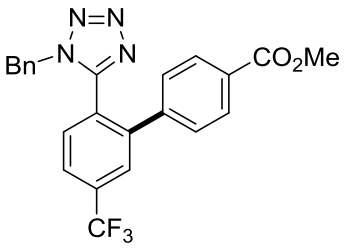
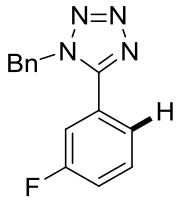
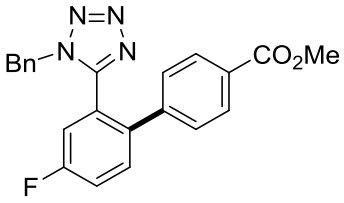
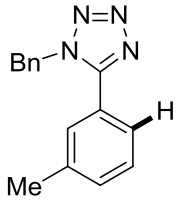
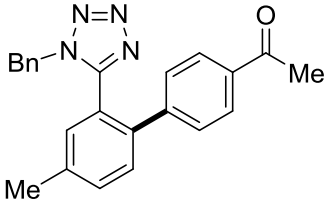
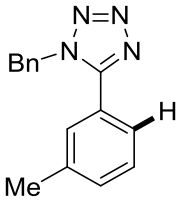
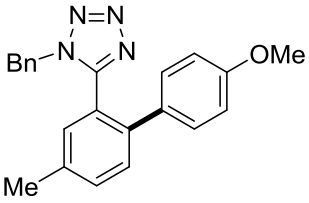
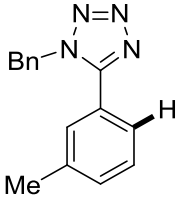
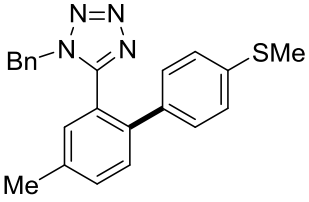
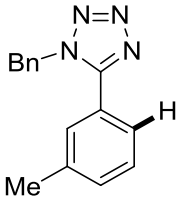
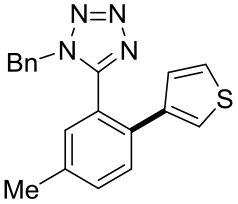
Initially, the scope of 5-aryl-1*H*-tetrazoles **68** with cost-effective aryl chloride **59a** as electrophilic coupling partner was explored for the novel optimized reaction (Table 21, entries 1–10). Thereby, it was observed that unsubstituted tetrazole **68a** was successfully employed contrarily to *ortho*-substituted **68b**, which failed (entries 1–2). Intramolecular competition studies exemplified a synthetically useful site-selectivity at the less congested C-6 position of 5-aryl-1*H*-tetrazoles with a *meta* substitution pattern in substrates **68c**, **68e** and **68g** (entries 3, 5 and 7). Moreover, the *para*-substituted tetrazole **68d** was productively converted but minor effective towards *meta*-substituted substrate **68c** in the appropriate *ortho*-arylated product **69da** (entry 4). Unfortunately, tetrazolyl-substituted arenes **68** with decreased electron density induced by electron-withdrawing groups displayed no reactivity (entries 8–10), which indicates that a formal oxidative addition of the aryl chloride to the ruthenium complex is the rate-determining step. Subsequently, the C–H transformation with respect to (hetero)aryl chlorides **59** was investigated. Fortunately, the electronic nature of the aryl electrophiles **59** had little impact on this process and both electron-poor as well as more challenging electron-rich substrates were readily applied to the direct functionalization. Furthermore, heteroaryl chloride **59e** furnished the C–H arylated product **69ce** in a reasonable yield (entry 14). The user-friendly ruthenium(II) catalyst presented an excellent chemoselectivity in relation to expedient electrophilic functional groups, such as enolizable ketone, ester, ether or thioether substituents, offering a great possibility to late-stage diversification.

Table 21: Scope of C–H arylation of 5-aryl-1*H*-tetrazole **68** with aryl chlorides **59**.[a]



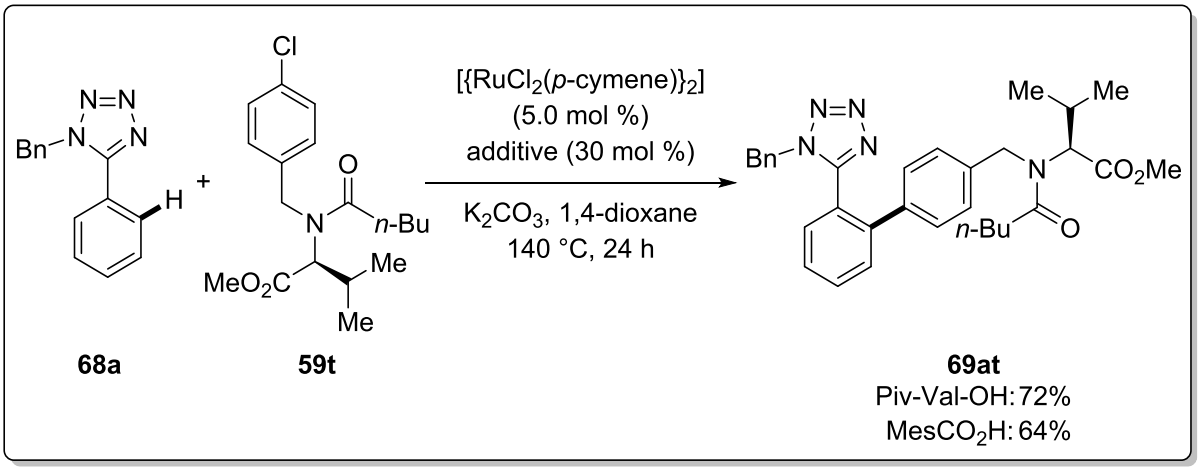
entry	**68**	**69**	yield / %[a]	yield / %[b]
1	 **68a**	 **69aa**	77	68

2		**68b**		**69ba**	---	---
3		**68c**		**69ca**	89	81
4		**68d**		**69da**	62	53
5		**68e**		**69ea**	59	51
6		**68f**		**69fa**	70	61
7		**68g**		**69ga**	57	49
8		**68h**		**69ha**	---	---

9		**68i**		**69ia**	---	---
10		**68j**		**69ja**	---	---
11		**68c**		**69cb**	83	77
12		**68c**		**69cc**	84	75
13		**68c**		**69cd**	64	56
14		**68c**		**69ce**	67	59

[a] General reaction conditions: **68** (0.30 mmol), **59** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), Piv-Val-OH (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C, 24 h; isolated yields. [b] **68** (0.30 mmol), **59** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C, 24 h; isolated yields.

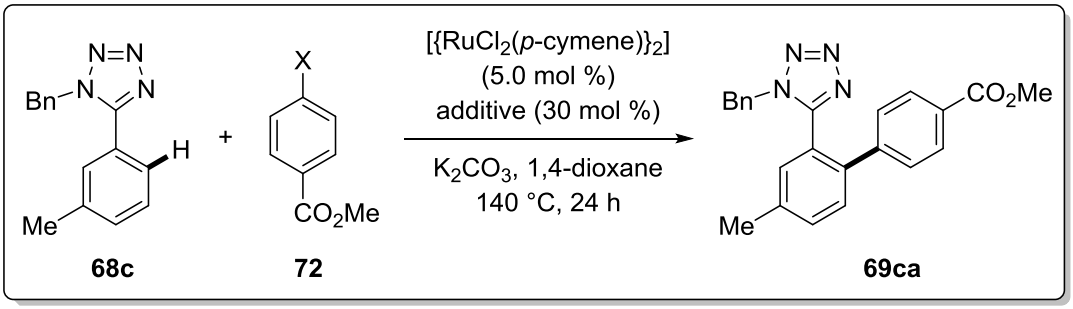
The outstanding potential of the developed catalytic system for C–H arylation was emphasized by the promising direct synthesis of the protected blockbuster drug Valsartan **69at** with aryl chloride **59t** as the electrophilic arylating reagent (Scheme 32).



Scheme 32: Step-economical access of protected Valsartan **69at** *via* C–H arylation.

In addition, different aryl-(pseudo)halides **72** were screened as electrophiles. The reaction conditions were not convenient for the aryl mesylate and tosylate (entries 1–4). However, aryl chloride, bromide and iodide as well as phenol-derived aryl triflate were found to be compatible in this protocol supplying moderate to excellent yields (Table 22, entries 5–12).[105]

Table 22: Scope of aryl-(pseudo)halides **72** as electrophiles.[a]

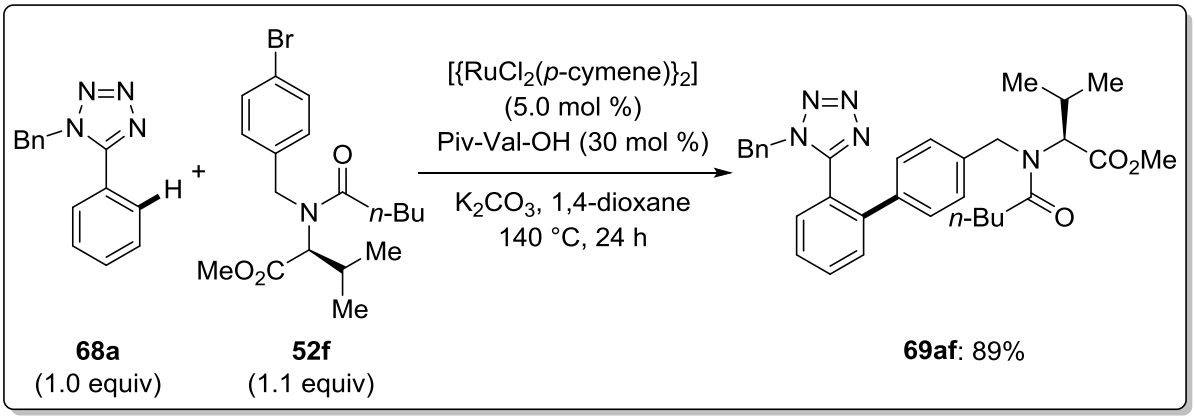


entry	X	additive	yield / %
1	OMs	Piv-Val-OH	---
2	OMs	$MesCO_2H$	---
3	OTs	Piv-Val-OH	---
4	OTs	$MesCO_2H$	---
5	OTf	Piv-Val-OH	64

6	OTf	$MesCO_2H$	51
7	Cl	Piv-Val-OH	89
8	Cl	$MesCO_2H$	81
9	Br	Piv-Val-OH	97
10	Br	$MesCO_2H$	95
11	I	Piv-Val-OH	96
12	I	$MesCO_2H$	95

[a] General reaction conditions: **68c** (0.30 mmol), **72** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), additive (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C, 24 h; isolated yields.

The importance of the C–H activation approach is among others reflected by the expedient access to molecular frameworks of blockbuster drugs. Based on this powerful strategy, the protected antihypertension drug Valsartan **69at** was prepared in excellent yield utilizing 4-bromo aryl amino acid derivative **52f** as coupling partner (Scheme 33). This environmentally friendly and sustainable C–C bond formation illustrated a great opportunity for commercial industrial applications in a sustainable mode.



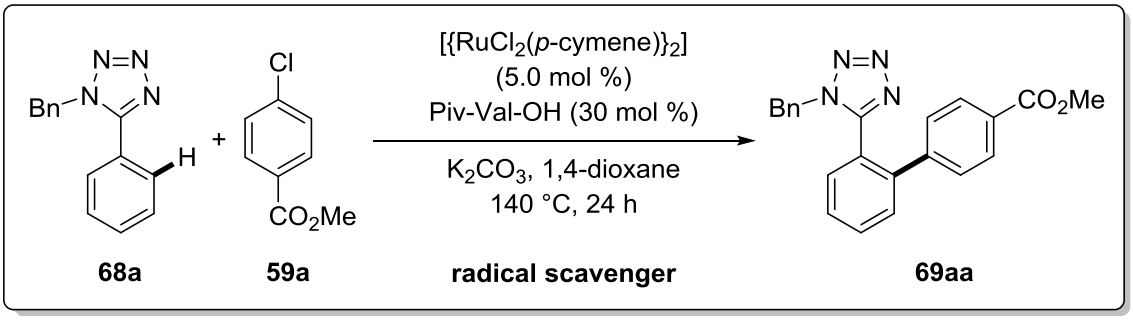
Scheme 33: Practical synthesis of protected Valsartan **69at** *via* C–H arylation.

3.3.3 Mechanistic studies

3.3.3.1 Experiments with radical scavengers

In the presence of stoichiometric amounts of radical scavengers under otherwise identical reaction conditions the C–H transformation completely failed to provide the desired C–H arylated product **69aa** (Table 23). Therefore, a SET-type C–X activation *via* homolytic bond cleavage is suggested to be operating in this system.[131]

Table 23: Influence of radical scavengers in the C–H arylation process.[a]



entry	radical scavenger	yield / %
1	---	80[b]
2	TEMPO	---
3	$Ph_2C{=}CH_2$	---
4	BHT	---

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), Piv-Val-OH (30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), radical scavenger (1.0 equiv), 140 °C, 24 h; isolated yields. [b] 10% of diarylated product **69aa'** was also isolated. TEMPO = 2,2,6,6-tetramethylpiperidine 1-oxyl, BHT = butylated hydroxytoluene.

3.3.3.2 Initial rate comparison

The mechanistic observation depicted a substantial initial rate acceleration affected by the pre-ligands for the formation of **69aa** (Figure 5). Piv-Val-OH and $MesCO_2H$ exhibited a high initial rate, when compared to an experiment performed in the absence of the co-catalytic additive.

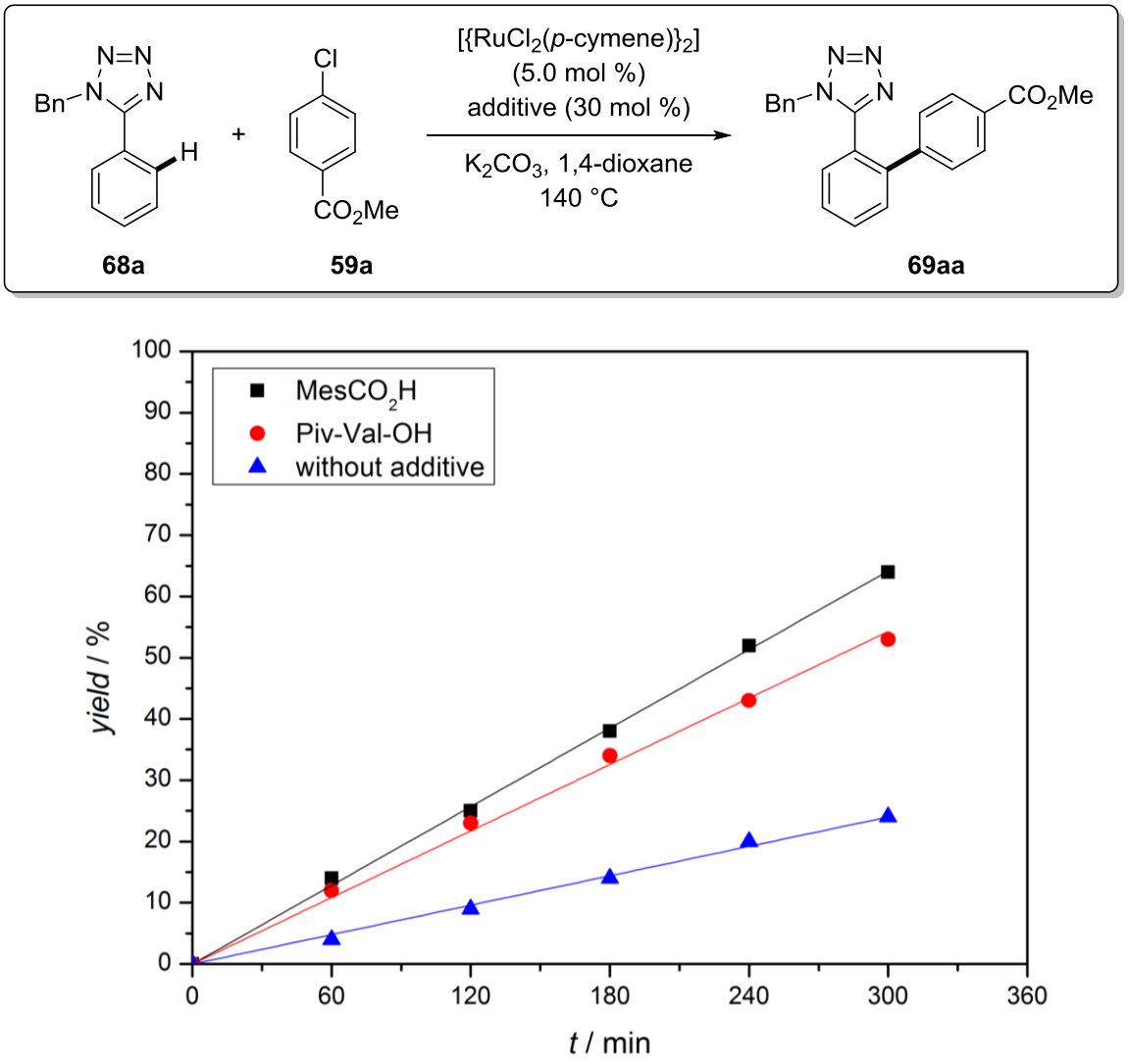


Figure 5: Initial rate comparison with and without additives.

3.3.3.3 Comparison of the kinetic reaction profile

In the initial stage of the reaction, the *in situ* formed ruthenium(II)-carboxylate complex has a faster rate versus the ruthenium(II)-MPAA complex (Figures 5 and 6). After a reaction time of approximately 5 h, deactivation-type behaviour was recognized for the carboxylate catalyst, resulting in superior yields being achieved after 24 h with the ruthenium(II)-MPAA catalyst, reflecting its long-term catalyst stability (Figure 6).

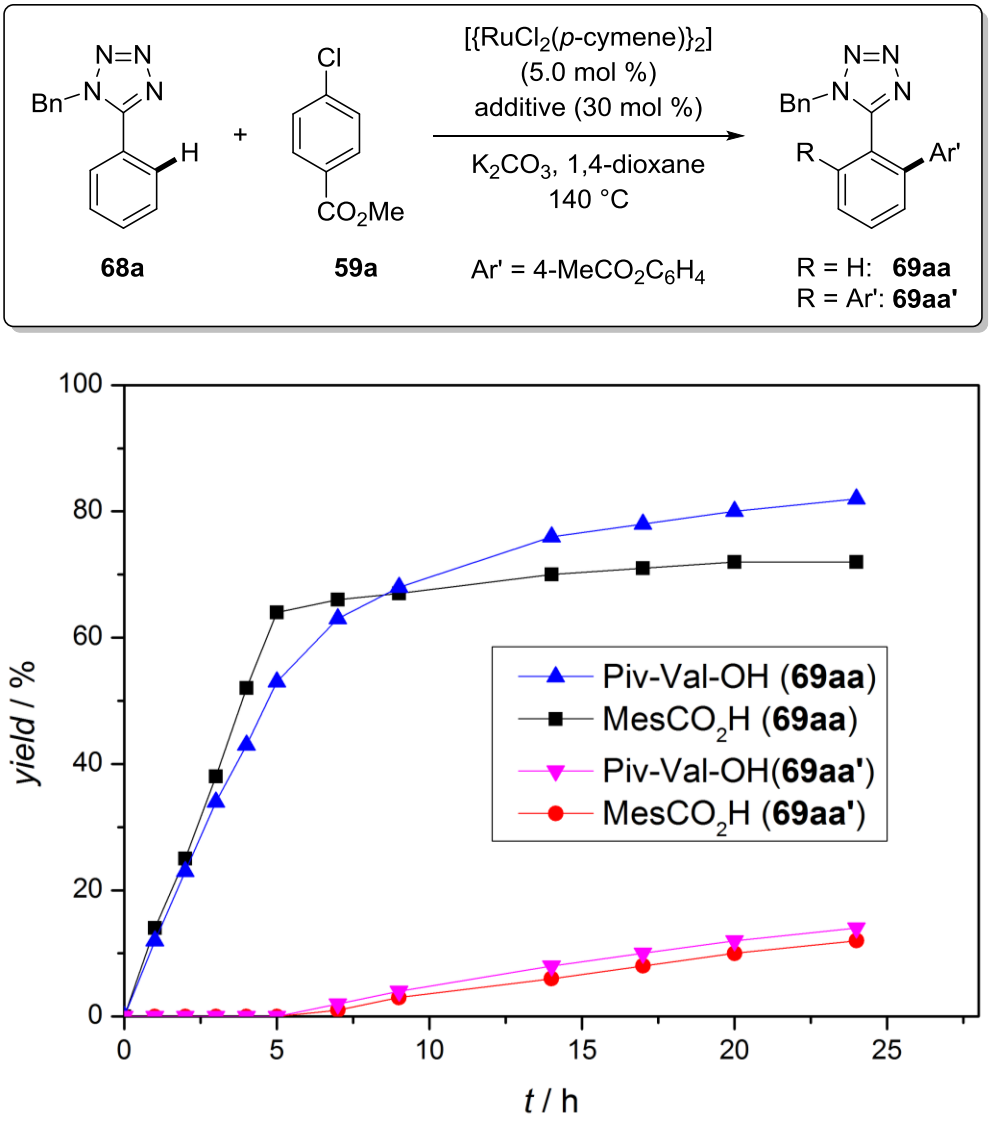
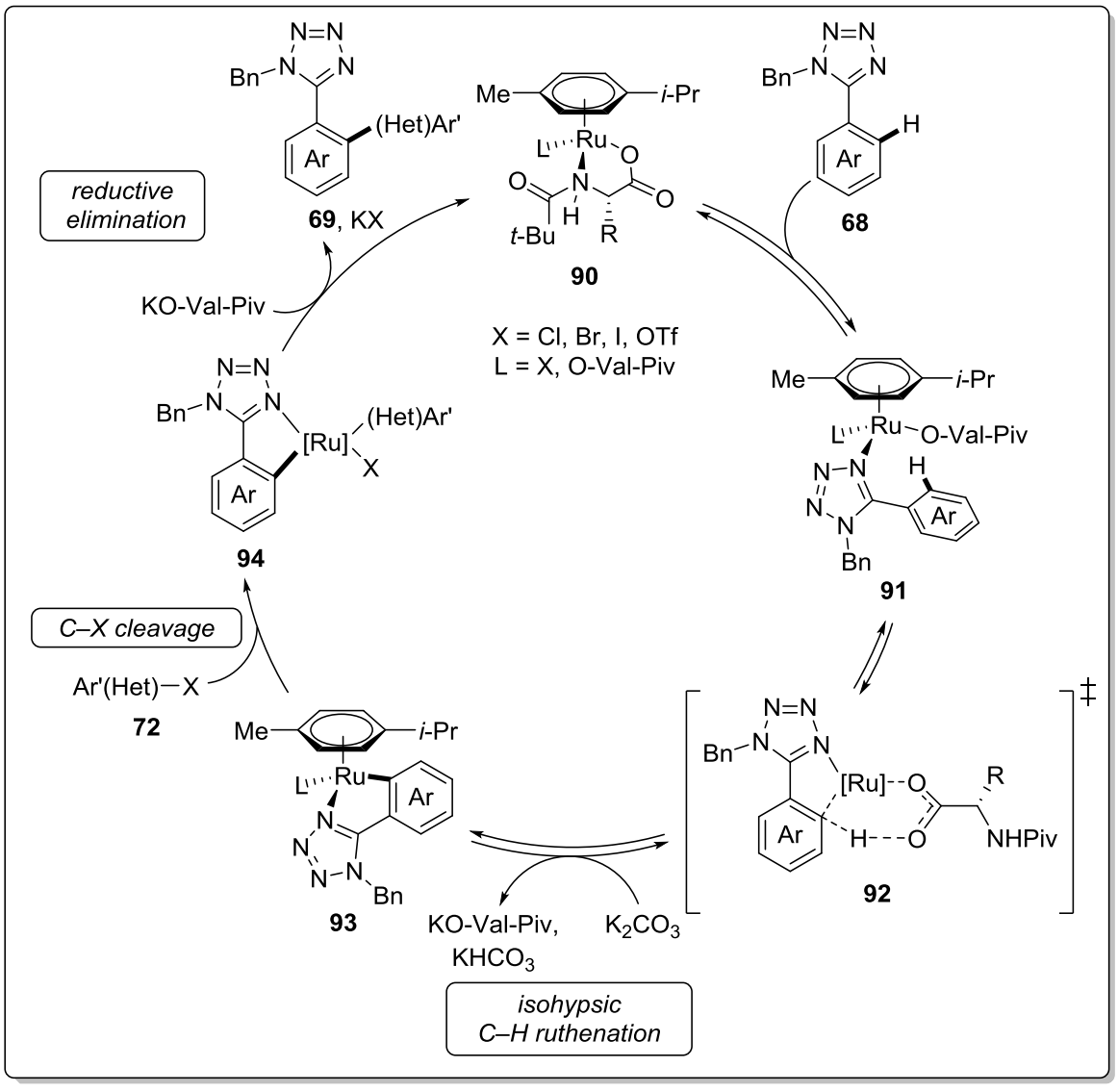


Figure 6: Comparison of the kinetic reaction profile between $MesCO_2H$ and Piv-Val-OH as pre-ligands.

3.3.3.4 Proposed catalytic cycle

In relation to the previous findings on ruthenium(II)-catalyzed direct C–H arylations through chelation assistance, the catalytic cycle commences by *in situ* formation of the ruthenium(II)-MPAA complex **90** (Scheme 34). The active catalyst complex **90** generates in a reversible redox-neutral *ortho*-C–H ruthenation the cycloruthenated complex **93** through a six-membered inner-sphere concerted ruthenation-deprotonation transition state **92**.[7,107,146] Here, it is proposed that the amino acid facilitates the C–H bond cleavage serving as a catalytic proton shuttle from the transition state of the CMD process to the insoluble carbonate base.[107,146,157] Subsequently, formal oxidative addition of the aryl electrophile **72** by a SET-type C–X activation provides the ruthenium(IV) species **94**. Finally, reductive elimination liberates the desired C–H functionalized product **69** and regenerates the active catalyst **90**.

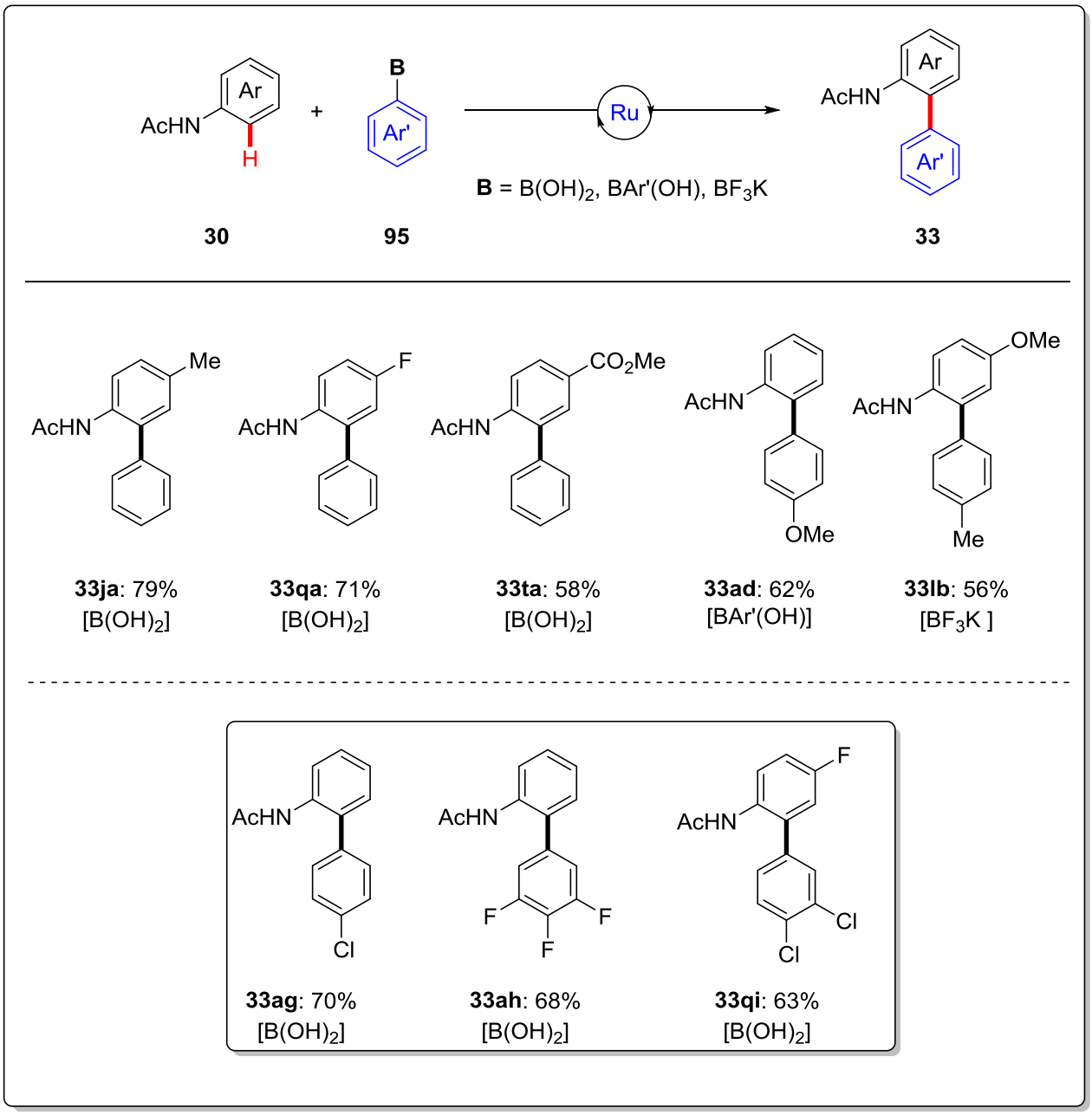


Scheme 34: Proposed catalytic cycle for the C–H arylation.

4 Summary and Outlook

Biaryls are key structural motifs of numerous bioactive compounds of relevance to agrochemicals and drugs, among others. Transition metal-catalyzed direct functionalization processes of otherwise inert C–H bonds emerged as a more sustainable alternative to the classically used cross-coupling reactions for the synthesis of biaryls. For this reason, the research was focused on the development of novel methods for efficient and selective direct C–H transformations to construct biaryl scaffolds in an atom- and step-economical manner.

The first part of this thesis described an efficient and generally applicable method for the ruthenium(II)-catalyzed oxidative C–H arylation of anilides **30** accomplished with boron-based arylating reagents **95** (Scheme 35). The high activity of the catalytic system was not restricted to boronic acids **73** as coupling partners, but enabled the first ruthenium(II)-catalyzed direct arylations using borinic acids **76** or potassium trifluoroborates **77**. An *in situ* generated cationic ruthenium(II) catalyst promoted the highly chemo- and mono-selective C–H funtionalization in excellent yields with a broad substrate scope. Here, electron-donating and -withdrawing groups on the arene of both anilides and aromatic boron-based reagents were compatible with this transformation to set the stage after removal of the acyl group for valuable 2-aminobiaryls, which are key structural frameworks in drugs and crop protection agents.[163]

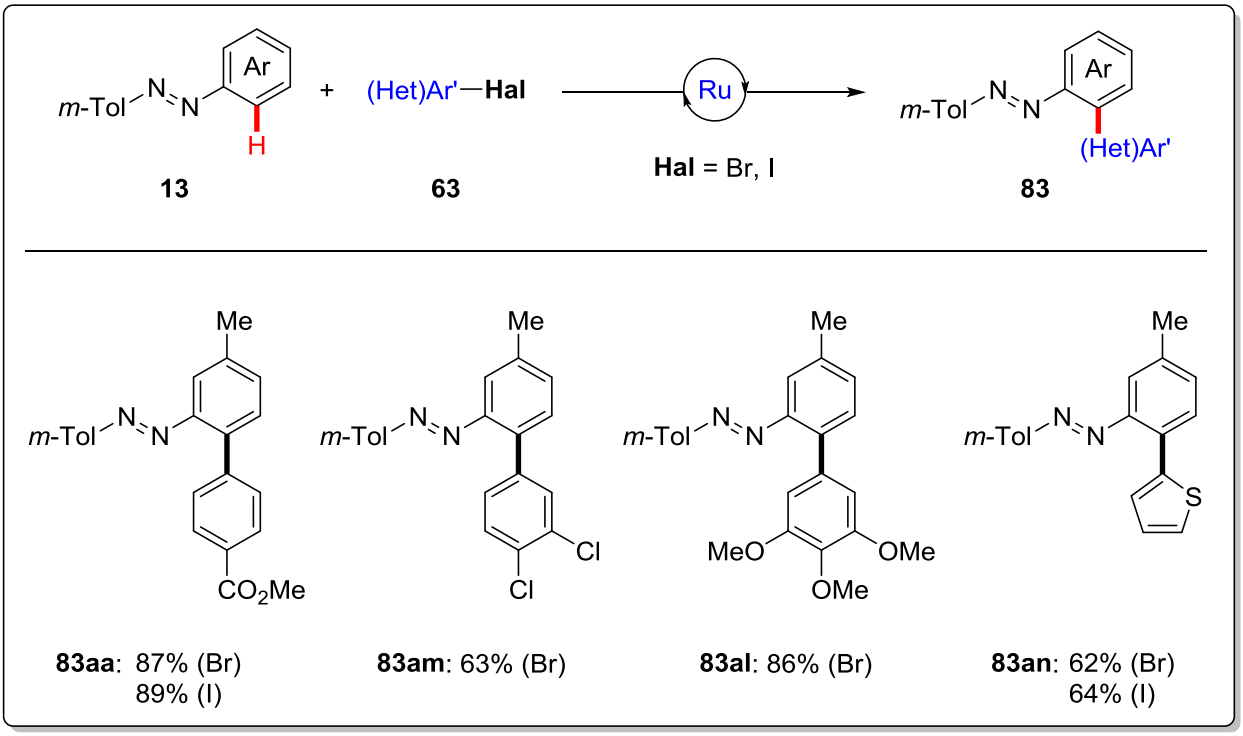


Scheme 35: Ruthenium(II)-catalyzed *ortho*-C–H arylation of anilides **30** with boron-based arylating reagents **95**.

From a synthetic point of view, a considerable application for 2-aminobiaryls is reflected by the manufacture of fungicides.[137-139]

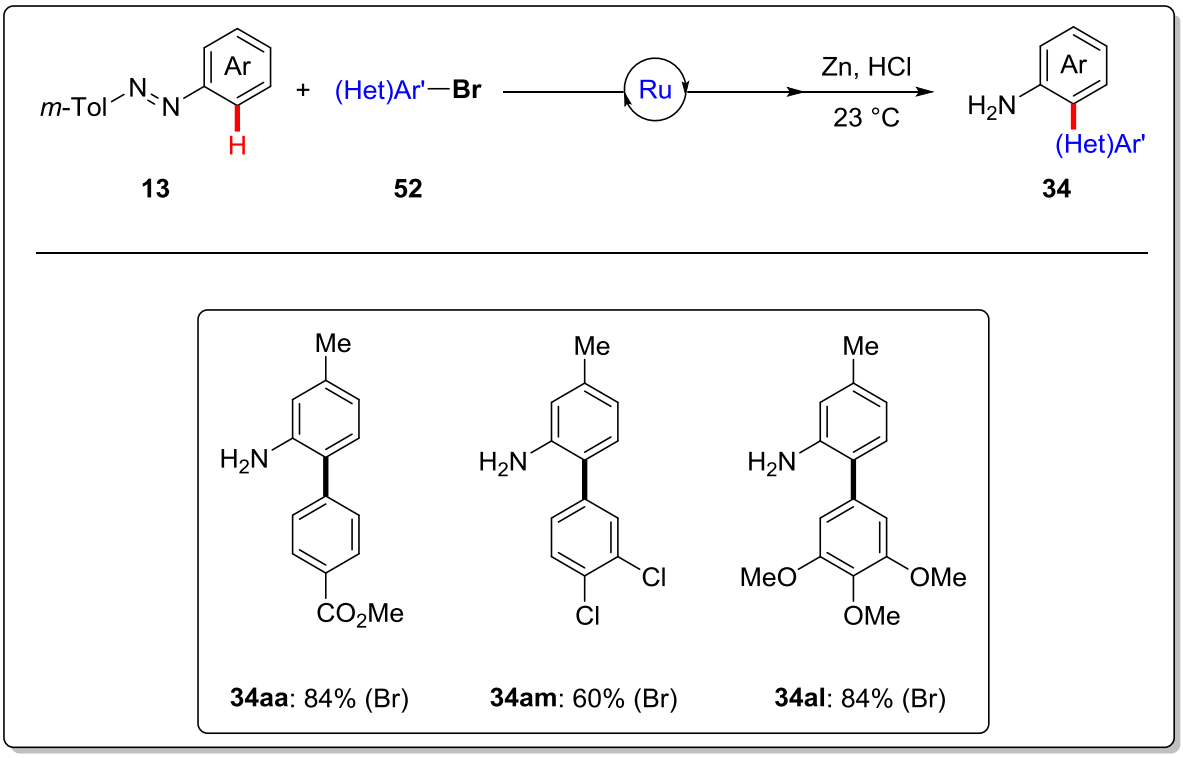
Prospective investigations could be addressed to isohypsic catalytic systems for C–H arylations of anilides employing aryl halides as electrophilic coupling partners. The overall redox-neutral C–H functionalizations proceed in the absence of stoichiometric metal salts as terminal oxidant in contrast to the oxidative processes, which is desirable for sustainable chemistry.

The second project represented the first isohypsic C–H arylation of azoarenes **13** by carboxylate assistance (Scheme 36). The direct arylation was consistent with electron-deficient as well as electron-rich (hetero)aryl halides **63** as electrophilic coupling partners delivering the desired *ortho*-arylated azoarenes **83**. Notably, the catalytic system showed high levels of chemo- and site-selectivity with an ample substrate scope. The broad functional group tolerance demonstrates to be convenient for further late-stage diversifications.



Scheme 36: Ruthenium(II)-catalyzed C–H arylation of azoarenes **13** with (hetero)aryl halides **72**.

A straightforward one-pot synthesis starting from azoarene **13** by applying C–H arylation as the key reaction and subsequent reduction of the azo group provides the corresponding synthetically useful 2-aminobiaryl **34** in a highly economical manner (Scheme 37).[164]

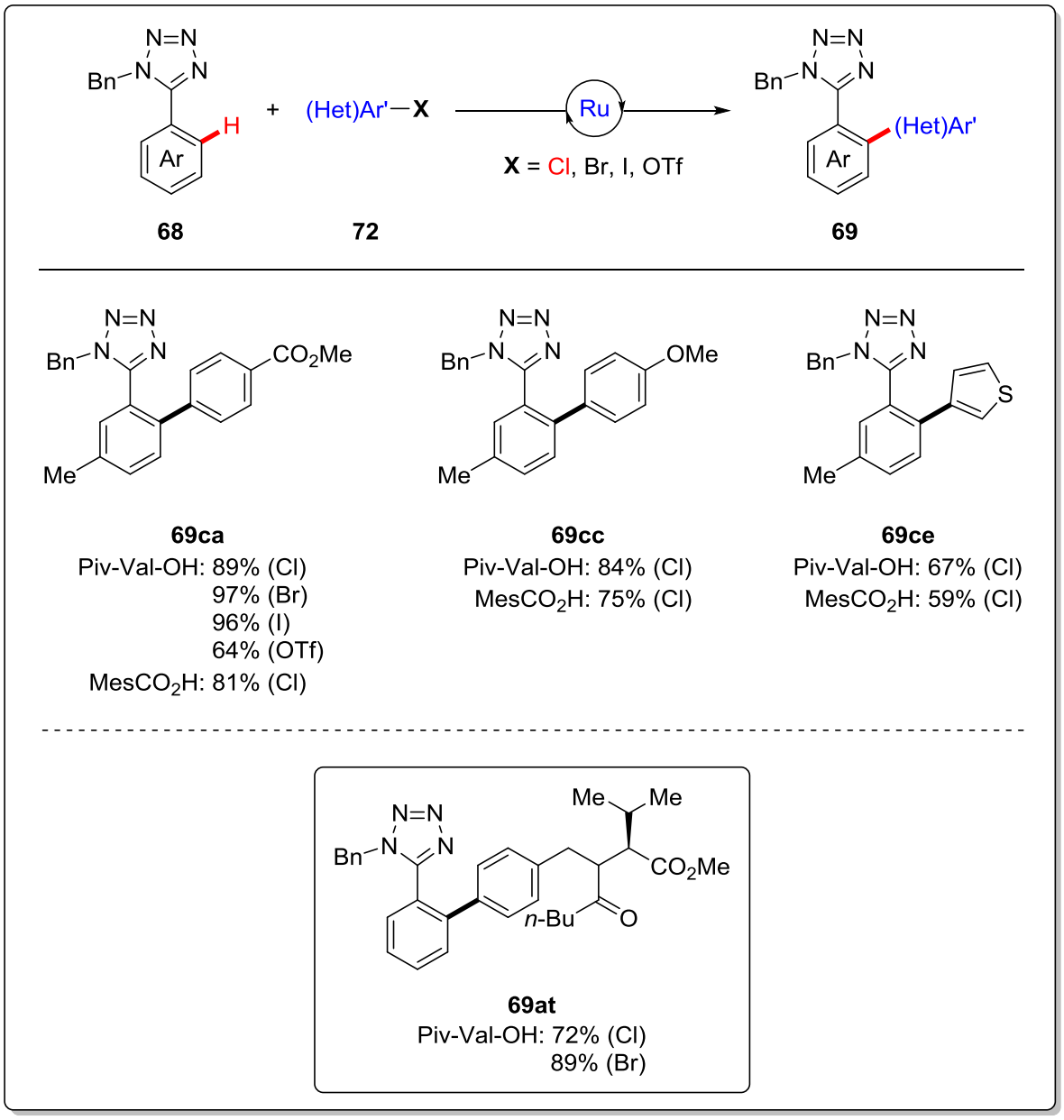


Scheme 37: Straightforward method to achieve access to *ortho*-arylated anilines **34**.

The development of direct 2,2'-C–H diarylation of azoarenes and subsequent reduction of the azo group in an one-pot process to afford twice the desired *ortho*-arylated anilines is of particular interest in relation to the atom- and step-economy.

The research was further focused on the improvement of redox-neutral ruthenium(II)-catalyzed C–H arylation systems. Here, an unprecedented highly efficient C–H functionalization of 5-aryl-1*H*-tetrazoles **68** deploying readily available and cost-effective aryl chlorides **59** is illustrated in Scheme 38. Optimal outcomes were achieved for a range of tetrazoles **68** with Piv-Val-OH as the pre-ligand of choice to facilitate the C–H activation. The outstanding performance of the *in situ* generated ruthenium(II) amino acid catalyst resulted from the increased long-term stability, which was revealed in a comparative kinetic study. The novel catalytic system was characterized by a broad substrate scope including various aryl electrophiles **72** with an excellent chemo- and site-selectivity affording the desired biaryl tetrazoles **69**, which are contained as essential framework of blockbuster antihypertension drugs.

The practical importance of the C–H activation strategy was reflected by the direct synthesis of the protected angiotensin II receptor blocker Valsartan **69at** in a highly step-economical fashion, which should prove beneficial in the industrial sector.[165]



Scheme 38: Expedient access to antihypertension drugs *via* ruthenium(II)-catalyzed C–H arylation of tetrazoles.

These findings highlight the great significance of pre-ligands to improve the robustness, reactivity and selectivity of ruthenium(II) catalysts for C–H activation, which was realised using mono-*N*-protected α-amino acids. The next challenging level is to take advantage of the chiral amino acid ligands for asymmetric C–H transformations based on ruthenium catalysis.

5 Experimental Section

5.1 General Remarks

All reactions involving moisture- or air-sensitive reagents or products were conducted under an atmosphere of nitrogen, using standard Schlenk techniques and pre-dried glassware. Syringes for handling of dry solvents or liquid reagents were evacuated and purged with nitrogen threefold prior to use. Analytical data of substances that are known in the literature were compared with those described in the literature.

5.1.1 Solvents

All solvents for reactions were purified using a MBRAUN Solvent Purification System 800 (MB SPS 800) or were dried, degassed, distilled and stored under an inert atmosphere (argon or nitrogen) according to following standard procedures.

***t*-Amyl alcohol** (*t*-AmOH) was dried over Na for 5 h and distilled under ambient pressure.

***t*-Butyl alcohol** (*t*-BuOH) was dried over Na and distilled under ambient pressure and stored over molecular sieves (4 Å).

1,2-Dichloroethane (DCE) was dried over CaH_2 for 8 h and distilled under ambient pressure.

1,2-Dimethoxyethane (DME) was dried over Na for 12 h and distilled over Na/benzophenone under ambient pressure.

***N*,*N*-Dimethylacetamide** (DMA) was dried over CaH_2 and distilled under reduced pressure.

***N*,*N*-Dimethylformamide** (DMF) was dried over CaH_2 for 8 h and distilled under reduced pressure.

1,4-Dioxane was dried over Na for 12 h and distilled over Na/benzophenone under ambient pressure.

Methanol (MeOH) was dried over $Mg(OEt)_2$ for 3 h and distilled under ambient pressure.

***N*-Methyl-2-pyrrolidone** (NMP) was stirred for 6 h in CaH_2 and subsequently distilled under reduced pressure.

Tetrahydrofuran (THF) was purified using a MB SPS 800 and distilled under ambient pressure.

Toluene (PhMe) was dried over Na and distilled over Na/benzophenone under ambient pressure.

Water (H_2O) was degassed for 2 h and ultrasonicated.

***o*-Xylene** was distilled over Na/benzophenone under reduced pressure.

5.1.2 Vacuum

Following pressures were measured on the used vacuum pumps and are not corrected: membrane pump vacuum (MPV): 5.0 mbar, oil pump vacuum (OPV): 0.1 mbar.

5.1.3 Melting Point

Melting points were measured using a Stuart® *Melting Point Apparatus SMP3* (Barloworld Scientific).

5.1.4 Chromatography

Analytical TLC was performed on 0.25 mm silica gel 60F plates (Macherey-Nagel) with 254 nm fluorescent indicator from Merck. Plates were visualized under ultraviolet light. 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, 70–230 mesh ASTM).

5.1.5 Gas Chromatography

Monitoring of the reaction progress *via* coupled gas chromatography-mass spectrometry was performed using Hewlett-Packard *G1800C GCDplus* with mass detector *HP 5971*, *5890 Series II* with mass detector *HP 5972* and Agilent Technologies *7890A GC-System* with mass detector *5975C (Triplex-Axis-Detector). HP-5MS* columns (30 m × 0.25 mm, film 0.25 μm) were used.

5.1.6 Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectra were recorded at 300, 400, 500, 600 MHz (^{1}H-NMR), at 75, 126 MHz (^{13}C-NMR, APT) and at 282 MHz (^{19}F-NMR) respectively, on Bruker *Avance III HD* 400 and 500, or Varian *Mercury* 300, *Inova* 500 and 600 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.[166]

	^{1}H-NMR	^{13}C-NMR
$CDCl_3$	7.26 ppm	77.16 ± 0.06 ppm
DMSO-d_6	2.50 ppm	39.52 ± 0.06 ppm

For the characterization of the observed signal multiplicities, the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet). Coupling constants *J* are reported in Hertz (Hz).

5.1.7 Infrared Spectroscopy

Infrared spectra were recorded using a Bruker *Alpha-P ATR FT-IR* spectrometer. Liquid samples were measured as a film, and solid samples were measured neat. The analysis of the spectra was carried out using the software from Bruker *OPUS 6*. The absorption is given in wave numbers (cm^{-1}) and the spectra were recorded in the range of 4000–400 cm^{-1}.

5.1.8 Mass Spectrometry

EI- and EI-HRMS spectra were measured on a *Time-of-Flight* mass spectrometer *AccuTOF* 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-HRMS spectra were recorded on a Bruker *APEX IV* or a Bruker *Daltonic* (7T, Fourier-Transform Ion Cyclotron Resonance (FTICR)) mass spectrometer. The ratio of mass to charge are indicated, intensities relative to the base peak (I = 100) are given in parentheses.

5.1.9 Reagents

Chemicals obtained from commercial sources (purity > 95%) were used without further purification.

The following compounds were synthesized according to known literature procedures:
[{$RuCl_2$(*p*-cymene)}$_2$] and [Ru(O_2CMes)$_2$(*p*-cymene)] by the courtesy of *Karsten Rauch*.
[RuCl(O-Val-Piv)(*p*-cymene)] by the courtesy of *M. Sc. Svenja Warratz*.
Potassium phenyltrifluoroborate (**77a**), potassium *p*-tolyltrifluoroborate (**77b**) and potassium *p*-methoxyphenyltrifluoroborate (**77d**) by the courtesy of *B. Sc. Valentin Müller*.

Anilides **30** were synthesized according to a previously described procedure.[167]

Azoarenes **13** were synthesized according to previously described procedures.[168,169]
(*E*)-1,2-Di-*o*-tolyldiazene (**13c**), (*E*)-1,2-di-*p*-tolyldiazene (**13d**), (*E*)-1,2-bis(3-ethylphenyl)diazene (**13e**), (*E*)-1,2-bis(3-*iso*propylphenyl)diazene (**13f**) and dimethyl 3,3'-(diazene-1,2-diyl)(*E*)-dibenzoate (**13k**) by the courtesy of *B. Sc. Valentin Müller*.

5-Aryl-1*H*-tetrazoles **68** were synthesized according to a previously described procedure.[122]
1-Benzyl-5-(naphthalen-2-yl)-1*H*-tetrazole (**68g**) by the courtesy of *Dr. Emelyne Diers*.

5.2 General Procedures

5.2.1 General Procedure A: Ruthenium(II)-catalyzed C–H-arylation of anilides 30 with boronic acids 73

In a 20 mL pre-dried screw-capped sealed tube, a suspension of anilide **30** (1.0 mmol, 1.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (30.6 mg, 5.0 mol %), $AgSbF_6$ (68.7 mg, 20 mol %), Ag_2O (232 mg, 1.0 equiv), $Cu(OTf)_2$ (72.3 mg, 20 mol %) and boronic acid **73** (1.5 mmol, 1.5 equiv) in dry DMF (3.0 mL) was stirred at 110 °C for 20 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc), concentrated and dried *in vacuo*.

5.2.2 General Procedure B: Ruthenium(II)-catalyzed C–H-arylation of acetanilides 30 with borinic acids 76

In a 20 mL pre-dried screw-capped sealed tube, a suspension of acetanilide **30** (1.0 mmol, 1.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (30.6 mg, 5.0 mol %), $AgSbF_6$ (68.7 mg, 20 mol %), Ag_2O (232 mg, 1.0 equiv), $Cu(OTf)_2$ (72.3 mg, 20 mol %) and borinic acid **76** (1.5 mmol, 3.0 equiv) in dry DMF (3.0 mL) was stirred at 110 °C for 20 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc), concentrated and dried *in vacuo*.

5.2.3 General Procedure C: Ruthenium(II)-catalyzed C–H-arylation of acetanilides 30 with potassium trifluoroborates 77

In a 20 mL pre-dried screw-capped sealed tube, a suspension of acetanilide **30** (0.50 mmol, 1.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), Ag_2O (116 mg, 1.0 equiv), $Cu(OTf)_2$ (36.2 mg, 20 mol %) and potassium trifluoroborate **77** (1.5 mmol, 3.0 equiv) in dry DMF (3.0 mL) was stirred at 110 °C for 20 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The

crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc), concentrated and dried *in vacuo*.

5.2.4 General Procedure D: Ruthenium(II)-catalyzed C–H-arylation of azoarenes 13

In a 20 mL pre-dried screw-capped sealed tube, a suspension of azoarene **13** (1.0 mmol, 2.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %), K_2CO_3 (138 mg, 1.0 mmol) and (hetero)aryl halide **63** (0.50 mmol, 1.0 equiv) in 1,4-dioxane (2.0 mL) was stirred at 120 °C for 18 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica (*n*-hexane/CH_2Cl_2) or (*n*-hexane/EtOAc/NEt_3), concentrated and dried *in vacuo*.

5.2.5 General Procedure E: One-pot synthesis of o*rtho*-arylated anilines 34

In a 20 mL pre-dried screw-capped sealed tube, a suspension of azoarene (**13a**) (1.0 mmol, 2.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %), K_2CO_3 (138 mg, 1.0 mmol) and aryl bromide **52** (0.50 mmol, 1.0 equiv) in 1,4-dioxane (2.0 mL) was stirred at 120 °C for 18 h under a N_2 atmosphere. To the reaction mixture Zn (164 mg, 2.5 mmol) and HCl (0.4 mL) were added at 23 °C and stirred for 24 h at 23 °C under a N_2 atmosphere. The suspension was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc), concentrated and dried *in vacuo*.

5.2.6 General Procedure F: Ruthenium(II)-catalyzed C–H arylation of 5-aryl-1*H*-tetrazoles 68

In a 20 mL pre-dried screw-capped sealed tube, a suspension of 5-aryl-1*H*-tetrazole **68** (0.30 mmol, 1.0 equiv), [{$RuCl_2$(*p*-cymene)}$_2$] (9.2 mg, 5.0 mol %), Piv-Val-OH (18.1 mg, 30 mol %), K_2CO_3 (138 mg, 0.90 mmol) and (hetero)aryl electrophile **72** (0.90 mmol, 3.0 equiv) in 1,4-dioxane (0.3 mL) was stirred at 140 °C for 24 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a

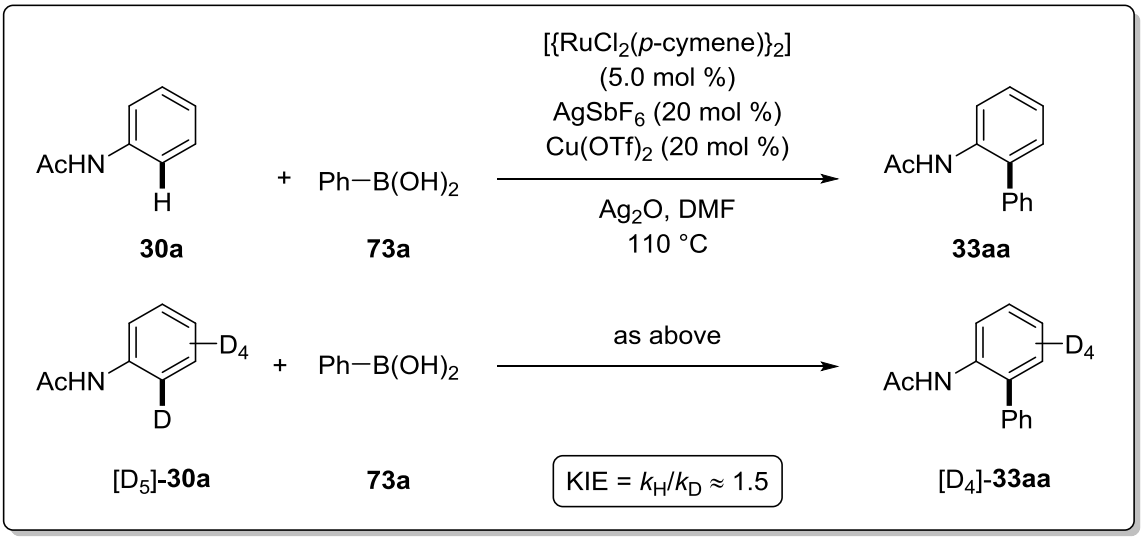
pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc) or (CH_2Cl_2/EtOAc), concentrated and dried *in vacuo*.

5.3 Procedures

5.3.1 Procedure G: Kinetic isotope effect (KIE) study of acetanilide (30a) and isotopically labeled acetanilide [D_5]-30a

Two independent reactions were conducted to determine the intermolecular kinetic isotope effect (KIE) value by comparison of the initial rates. In a 10 mL schlenk flask, a suspension of acetanilide (**30a**) (135 mg, 1.0 mmol) or [D_5]-**30a** (140 mg, 1.0 mmol) respectively, [{$RuCl_2$(*p*-cymene)}$_2$] (30.6 mg, 5.0 mol %), $AgSbF_6$ (68.7 mg, 20 mol %), Ag_2O (232 mg, 1.0 equiv), $Cu(OTf)_2$ (72.3 mg, 20 mol %) and phenylboronic acid (**73a**) (183 mg, 1.5 equiv) in dry DMF (3.0 mL) was stirred at 110 °C under a N_2 atmosphere. For 60 min, an aliquot (0.1 mL) was removed by a syringe every 10 min and directly analyzed by ^{1}H-NMR to provide the following conversions (Table 24, Figure 7).

Table 24: Intermolecular kinetic isotope effect study by two independent reactions.[a]



entry	*t* / min	**30a** / %	**33a** / %	[D_5]-**30a** / %	[D_4]-**33aa** / %
1	0	100	0	100	0
2	10	91	9	92	8
3	20	79	21	84	16

4	30	70	30	77	23
5	40	58	42	69	31
6	50	47	53	63	37
7	60	38	62	58	42

[a] General reaction conditions: **30a** (1.0 mmol) or [D_5]-**30a** (1.0 mmol), **73a** (1.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OTf)_2$ (20 mol %), Ag_2O (1.0 equiv), DMF (3.0 mL), 110 °C for the corresponding time; ^{1}H-NMR conversions.

The data from two independent reactions are collected in the Table 24 and the intermolecular kinetic isotope effect (KIE) of $k_H/k_D \approx 1.5$ was determined by means of the initial rates exemplified in Figure 7.

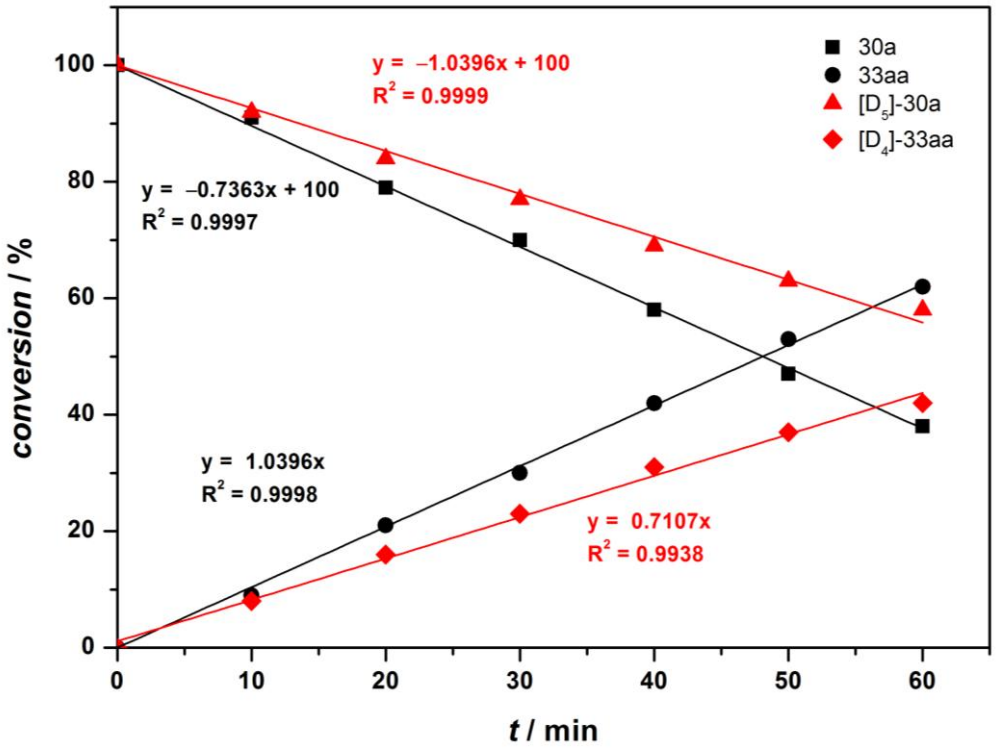


Figure 7: Initial rate data for C–H arylation of **30a** and [D_5]-**30a**.

5.3.2 Procedure H: H/D-Exchange experiments of acetanilide 30l

In a 20 mL pre-dried screw-capped sealed tube, a suspension of acetanilide **30l** (165 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (30.6 mg, 5.0 mol %), $AgSbF_6$ (68.7 mg, 20 mol %), Ag_2O (232 mg, 1.0 equiv) and $Cu(OTf)_2$ (72.3 mg, 20 mol %) in dry DMF/CD_3OD (2.7 mL/0.3 mL) was stirred at 110 °C for 20 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) to yield [D_n]-**30l** (164 mg, 99%) as a colorless solid. The deuterium incorporation in [D_n]-**30l** was determined by ^{1}H-NMR spectroscopy (Scheme 26a).

In a 20 mL pre-dried screw-capped sealed tube, a suspension of acetanilide **30l** (165 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (30.6 mg, 5.0 mol %), $AgSbF_6$ (68.7 mg, 20 mol %), Ag_2O (232 mg, 1.0 equiv), $Cu(OTf)_2$ (72.3 mg, 20 mol %) and phenylboronic acid (**73a**) (183 mg, 1.5 equiv) in dry DMF/CD_3OD (2.7 mL/0.3 mL) was stirred at 110 °C for 20 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) to yield [D_n]-**30l** (43 mg, 26%) and [D_n]-**33la** (174 mg, 72%) as colorless solids. The deuterium incorporation in [D_n]-**30l** and [D_n]-**33la** were determined by ^{1}H-NMR spectroscopy (Scheme 26b).

5.3.3 Procedure I: H/D-Exchange experiments of azoarene 13

In a 20 mL pre-dried screw-capped sealed tube, a suspension of (*E*)-1,2-diphenyldiazene (**13b**) (182 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %) and K_2CO_3 (138 mg, 1.0 mmol) in 1,4-dioxane/D_2O (1.8/0.2 mL) was stirred at 120 °C for 18 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2: 7/3) to yield [D_n]-**13b** (178 mg, 96%) as an orange solid. The deuterium incorporation in [D_n]-**13b** was determined by ^{1}H-NMR spectroscopy (Scheme 30a).

In a 20 mL pre-dried screw-capped sealed tube, a suspension of (*E*)-1,2-di-*p*-tolyldiazene (**13d**) (210 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %), K_2CO_3 (138 mg, 1.0 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.5 mmol) in 1,4-dioxane/D_2O (1.8/0.2 mL) was stirred at 120 °C for 18 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2: 7/3) to yield [D_n]-**13d** (75 mg, 35%) and [D_n]-**83da** (109 mg, 63%) as orange solids. The deuterium incorporation in [D_n]-**13d** and [D_n]-**83da** were determined by ^{1}H-NMR spectroscopy (Scheme 30b).

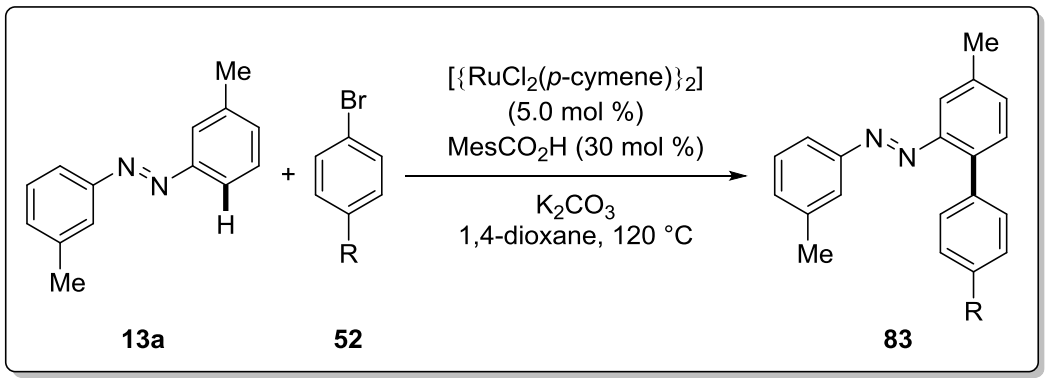
5.3.4 Procedure J: Experiments with radical scavengers for azoarene 13f

In a 20 mL pre-dried screw-capped sealed tube, a suspension of azoarene **13f** (266 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %), K_2CO_3 (138 mg, 1.0 mmol), methyl 4-bromobenzoate (**52a**) (108 mg, 0.5 mmol) and a radical scavenger (1.0 equiv) in 1,4-dioxane (2.0 mL) was stirred at 120 °C for 18 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica (*n*-hexane/CH_2Cl_2: 7/3) providing the following yields of **83fa** as an orange solid (Table 15).

5.3.5 Procedure K: Hammett plot analysis

In a 20 mL pre-dried screw-capped sealed tube, a suspension of (*E*)-1,2-di-*m*-tolyldiazene (**13a**) (210 mg, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $MesCO_2H$ (24.6 mg, 30 mol %), K_2CO_3 (138 mg, 1.0 mmol) and *para*-substituted aryl bromide **52** (0.5 mmol) in 1,4-dioxane (3.0 mL) was stirred at 120 °C under a N_2 atmosphere. For the indicated interval, an aliquot (0.1 mL) was removed by a syringe and directly analyzed by GC of the desired product **37** using *n*-dodecane as internal standard (Table 25, Figures 3 and 4).

Table 25: Hammett plot study of azoarene **13a** with *para*-substituded aryl bromides **52**.[a]



entry	R	σ_p	initial rate	$\log(k_X/k_H)$
1	$N(Me)_2$	-0.83	0.19785	0.159
2	OMe	-0.27	0.16019	0.068
3	H	0	0.13705	0
4	Cl	0.23	0.12183	-0.051
5	CO_2Me	0.45	0.10869	-0.101
6	C(O)Me	0.50	0.105	-0.116

[a] General reaction conditions: **13a** (1.0 mmol), **52** (0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (30 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (3.0 mL), 120 °C, 18 h; GC yields.

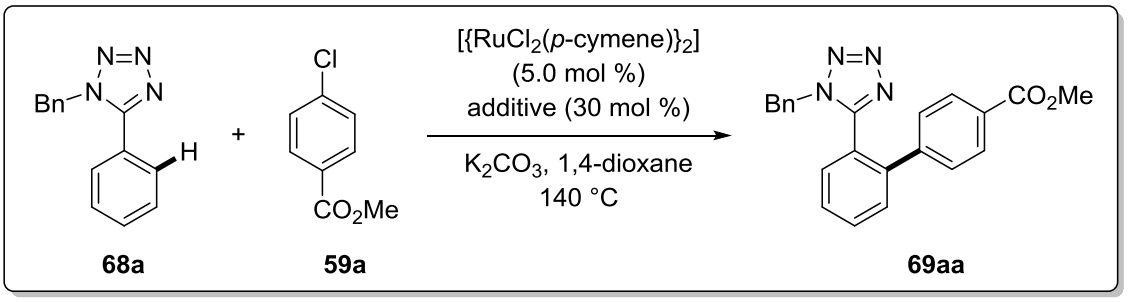
5.3.6 Procedure L: Experiments with radical scavengers for tetrazole 68a

In a 20 mL pre-dried screw-capped sealed tube, a suspension of 1-benzyl-5-phenyl-1*H*-tetrazole (**68a**) (70.9 mg, 0.30 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (9.2 mg, 5.0 mol %), Piv-Val-OH (18.1 mg, 30 mol %), K_2CO_3 (124 mg, 0.90 mmol), methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol) and a radical scavenger (1.0 equiv) in 1,4-dioxane (0.3 mL) was stirred at 140 °C for 24 h under a N_2 atmosphere. At ambient temperature, the reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography on silica (*n*-hexane/EtOAc: 4/1) yielded **69aa** (86 mg, 77%) as colorless solid (Table 23).

5.3.7 Procedure M: Initial rate acceleration of formation of tetrazole 69aa enabled by pre-ligand

Three different reaction conditions were investigated: [a] with $MesCO_2H$, [b] with Piv-Val-OH and [c] without additive. Five seperate reactions were conducted simultaneously for each reaction condition. In a 20 mL pre-dried screw-capped sealed tube, a suspension of 1-benzyl-5-phenyl-1*H*-tetrazole (**68a**) (70.9 mg, 0.30 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (9.2 mg, 5.0 mol %), $MesCO_2H$ (14.8 mg, 30 mol %), K_2CO_3 (124 mg, 0.90 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol) in 1,4-dioxane (0.3 mL) was stirred at 140 °C for the corresponding time. Upon completion, the sealed tube was quickly cooled down in an ice bath. The reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. Subsequently, CH_2Br_2 (21 µL, 0.30 mmol) was added as internal standard in $CDCl_3$ and directly analyzed by ^{1}H-NMR to provide the following yields (Table 26, Figure 5).

Table 26: Initial rate comparison for the C–H arylation with and without additives.[a]



68a **59a** **69aa**

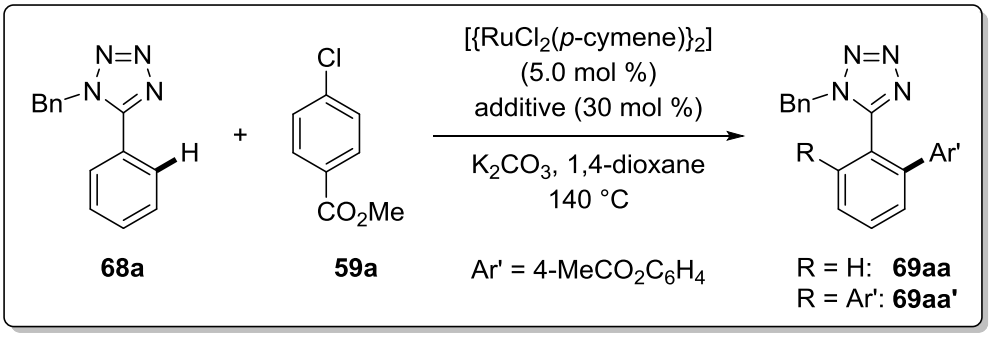
entry	*t* / min	**69aa**[a] / %	**69aa**[b] / %	**69aa**[c] / %
1	0	0	0	0
2	60	14	12	4
3	120	25	23	9
4	180	38	34	14
5	240	52	43	20
6	300	64	53	24

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (14.8 mg, 30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C for the corresponding time; yields were determined by ^{1}H-NMR using CH_2Br_2 (21 µL, 0.30 mmol) as internal standard. [b] Piv-Val-OH (18.1 mg, 30 mol %). [c] without additive.

5.3.8 Procedure N: Kinetic reaction profile of formation of tetrazole 69aa

Two different reaction conditions were investigated: [a] with $MesCO_2H$ and [b] with Piv-Val-OH. Eleven seperate reactions were conducted simultaneously for each reaction condition. In a 20 mL pre-dried screw-capped sealed tube, a suspension of 1-benzyl-5-phenyl-1*H*-tetrazole (**68a**) (70.9 mg, 0.30 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (9.2 mg, 5.0 mol %), $MesCO_2H$ (14.8 mg, 30 mol %), K_2CO_3 (124 mg, 0.90 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol) in 1,4-dioxane (0.3 mL) was stirred at 140 °C for the corresponding time. Upon completion, the sealed tube was quickly cooled down in an ice bath. The reaction mixture was diluted with EtOAc (75 mL), filtered through a pad of Celite and silica gel, and the solvents were removed *in vacuo*. Subsequently, CH_2Br_2 (21 µL, 0.30 mmol) was added as internal standard in $CDCl_3$ and directly analyzed by ^{1}H-NMR to provide the following yields (Table 27, Figure 6).

Table 27: Kinetic reaction profile for the C–H arylation of tetrazole **68a** exerted by additives.[a]



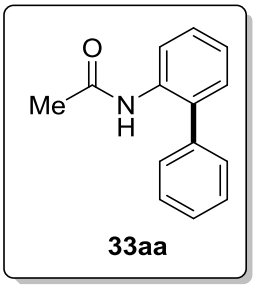
entry	*t* / h	**69aa**[a] / %	**69aa'**[a] / %	**69aa**[b] / %	**69aa'**[b] / %
1	0	0	0	0	0
2	1	14	0	12	0
3	2	25	0	23	0
4	3	38	0	34	0
5	4	52	0	43	0
6	5	64	0	53	0
7	7	66	1	63	2
8	9	67	3	68	4
9	14	70	6	76	8
10	17	71	8	78	10

11	20	72	10	80	12
12	24	72	12	82	14

[a] General reaction conditions: **68a** (0.30 mmol), **59a** (0.90 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5.0 mol %), $MesCO_2H$ (14.8 mg, 30 mol %), K_2CO_3 (0.90 mmol), 1,4-dioxane (0.3 mL), 140 °C for the corresponding time; yields were determined by ^{1}H-NMR using CH_2Br_2 (21 µL, 0.30 mmol) as internal standard. [b] Piv-Val-OH (18.1 mg, 30 mol %).

6 Analytical Data

Synthesis of *N*-([1,1'-Biphenyl]-2-yl)acetamide (33aa)



33aa

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33aa** (162 mg, 77%) as a colorless solid.

The general procedure **B** was followed using **30a** (135 mg, 1.00 mmol) and hydroxydiphenylborane (**76a**) (273 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33aa** (137 mg, 65%) as a colorless solid.

The general procedure **C** was followed using **30a** (67.6 mg, 0.50 mmol) and potassium phenyltrifluoroborate (**77a**) (276 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33aa** (55 mg, 52%) as a colorless solid.

M. p.: 113–115 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.2 Hz, 1H), 7.51–7.30 (m, 6H), 7.24–7.13 (m, 3H), 1.98 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.2 (C_q), 138.1 (C_q), 134.6 (C_q), 132.2 (C_q), 130.0 (CH), 129.1 (CH), 129.0 (CH), 128.2 (CH), 127.9 (CH), 124.3 (CH), 121.7 (CH), 24.4 (CH_3).

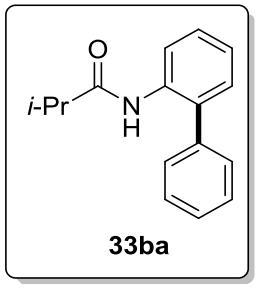
IR (ATR): 3284, 3230, 3054, 3027, 1658, 1531, 1433, 1301, 755, 662 cm^{-1}.

MS (EI) *m/z* (relative intensity): 211 ([M^+] 34), 169 (100), 139 (7), 115 (5), 43 (15).

HR-MS (EI) *m/z* for $C_{14}H_{13}NO$ [M^+] calcd.: 211.0997.
found: 211.0996.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of *N*-([1,1'-Biphenyl]-2-yl)isobutyramide (33ba)



33ba

The general procedure **A** was followed using **30b** (163 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ba** (132 mg, 55%) as a colorless solid.

M. p.: 126–128 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.2 Hz, 1H), 7.54–7.33 (m, 6H), 7.28–7.13 (m, 3H), 2.4 (hept, *J* = 6.8 Hz, 1H), 1.2 (d, *J* = 6.8 Hz, 6H).

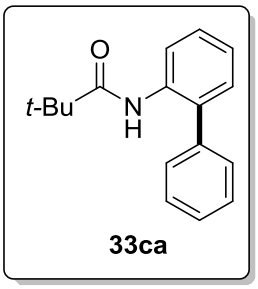
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 174.8 (C_q), 138.1 (C_q), 134.9 (C_q), 132.1 (C_q), 129.9 (CH), 129.3 (CH), 129.0 (CH), 128.4 (CH), 128.0 (CH), 124.0 (CH), 121.3 (CH), 36.7 (CH), 19.3 (CH_3).

IR (ATR): 3218, 2964, 1649, 1520, 1480, 1239, 1203, 1099, 776, 542 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 ([M^+] 29), 169 (100), 71 (6), 43 (30).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO$ [M^+] calcd.: 239.1310.
found: 239.1314.

Synthesis of *N*-([1,1'-Biphenyl]-2-yl)pivalamide (33ca)



33ca

The general procedure **A** was followed using **30c** (177 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ca** (114 mg, 45%) as a colorless solid.

M. p.: 68–69 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.37 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.54–7.33 (m, 7H), 7.24 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.17 (dd, *J* = 7.4, 1.7 Hz, 1H), 1.09 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 176.1 (C_q), 138.0 (C_q), 135.0 (C_q), 132.0 (C_q), 129.6 (CH), 129.2 (CH), 128.9 (CH), 128.4 (CH), 127.9 (CH), 123.8 (CH), 120.8 (CH), 39.8 (C_q), 27.4 (CH_3).

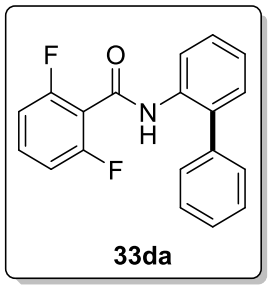
IR (ATR): 3259, 3056, 2970, 2904, 2868, 1646, 1503, 1477, 771, 647 cm^{-1}.

MS (EI) *m/z* (relative intensity): 253 ([M^+] 53), 169 (60), 57 (100), 41 (17).

HR-MS (EI) *m/z* for $C_{17}H_{19}NO$ [M^+] calcd.: 253.1467.
found: 253.1472.

The analytical data are in accordance with those reported in the literature.[170]

Synthesis of *N*-([1,1'-Biphenyl]-2-yl)-2,6-difluorobenzamide (33da)



33da

The general procedure **A** was followed using **30d** (233 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33da** (93 mg, 30%) as a colorless solid.

M. p.: 127–128 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.48 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.50–7.17 (m, 9H), 6.90 (t, J = 8.2 Hz, 2H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 159.8 (C_q, $J_{C–F}$ = 246.4, 6.7 Hz), 158.2 (C_q), 137.5 (C_q), 134.2 (C_q), 132.5 (C_q), 131.8 (CH, $J_{C–F}$ = 10.3 Hz), 130.1 (CH), 129.3 (CH), 128.9 (CH), 128.4 (CH), 128.0 (CH), 124.9 (CH), 121.7 (CH), 114.4 (C_q, $J_{C–F}$ = 19.6 Hz), 112.0 (CH, $J_{C–F}$ = 20.5, 4.4 Hz).

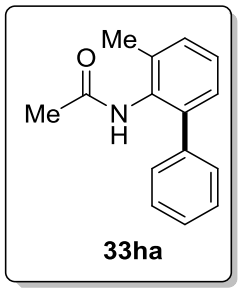
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -(111.85–112.02) (m).

IR (ATR): 3218, 3058, 3031, 1653, 1623, 1516, 1462, 1303, 1005, 741 cm^{-1}.

MS (EI) *m/z* (relative intensity): 309 ([M^+] 57), 167 (14), 141 (100), 113 (21), 63 (7).

HR-MS (EI) *m/z* for $C_{19}H_{13}F_2NO$ [M^+] calcd.: 309.0965.
found: 309.0960.

Synthesis of *N*-(3-Methyl-[1,1'-biphenyl]-2-yl)acetamide (33ha)



33ha

The general procedure **A** was followed using **30h** (149 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ha** (76 mg, 34%) as a colorless solid.

M. p.: 125–127 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.43–7.30 (m, 5H), 7.29–7.24 (m, 2H), 7.21–7.14 (m, 1H), 6.64 (s, 1H), 2.31 (s, 3H), 2.00 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 169.4 (C_q), 139.7 (C_q), 139.6 (C_q), 136.9 (C_q), 132.6 (C_q), 130.2 (CH), 128.9 (CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 127.4 (CH), 23.0 (CH_3), 18.5 (CH_3).

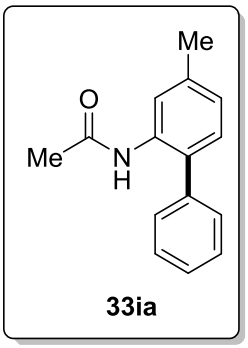
IR (ATR): 3269, 3024, 2956, 2922, 1646, 1516, 1463, 1365, 1289, 790 cm^{-1}.

MS (EI) *m/z* (relative intensity): 225 ([M^+] 36), 183 (100), 167 (31), 43 (26).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO$ [M^+] calcd.: 225.1154.
found: 225.1146.

The analytical data are in accordance with those reported in the literature.[29]

Synthesis of *N*-(4-Methyl-[1,1'-biphenyl]-2-yl)acetamide (33ia)



The general procedure **A** was followed using **30i** (149 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ia** (175 mg, 78%) as a colorless solid.

The general procedure **C** was followed using **30i** (74.6 mg, 0.50 mmol) and potassium phenyltrifluoroborate (**77a**) (276 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ia** (61 mg, 54%) as a colorless solid.

M. p.: 139–141 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.04 (s, 1H), 7.50–7.28 (m, 5H), 7.21–7.08 (m, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 2.38 (s, 3H), 1.98 (s, 3H).

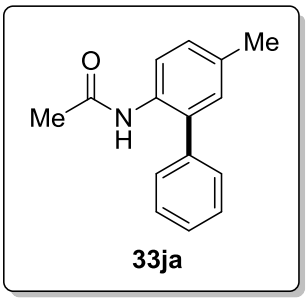
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 138.3 (C_q), 138.1 (C_q), 134.3 (C_q), 129.7 (CH), 129.4 (C_q), 129.2 (CH), 128.9 (CH), 127.6 (CH), 125.1 (CH), 122.2 (CH), 24.6 (CH_3), 21.5 (CH_3).

IR (ATR): 3224, 3029, 2916, 1652, 1539, 1476, 1412, 1297, 820, 763 cm^{-1}.

MS (EI) *m/z* (relative intensity): 225 ([M^+] 54), 183 (100), 167 (30), 43 (20).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO$ [M^+] calcd.: 225.1154.
found: 225.1159.

Synthesis of *N*-(5-Methyl-[1,1'-biphenyl]-2-yl)acetamide (33ja)



33ja

The general procedure **A** was followed using **30j** (149 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ja** (178 mg, 79%) as a colorless solid.

M. p.: 107–109 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.3 Hz, 1H), 7.50–7.31 (m, 5H), 7.16 (dd, J = 8.3, 2.2 Hz, 1H), 7.04 (m, 2H), 2.33 (s, 3H), 1.99 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 138.3 (C_q), 134.0 (C_q), 132.3 (C_q), 132.0 (C_q), 131.0 (CH), 129.1 (CH), 128.9 (CH), 128.8 (CH), 127.7 (CH), 121.9 (CH), 24.5 (CH_3), 20.9 (CH_3).

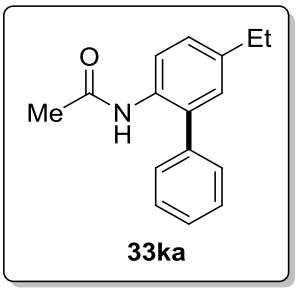
IR (ATR): 3235, 3057, 3029, 2922, 1655, 1524, 1505, 1488, 1366, 761 cm^{-1}.

MS (EI) *m/z* (relative intensity): 225 ([M^+] 54), 183 (100), 167 (18), 43 (22).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO$ [M^+] calcd.: 225.1154.
found: 225.1154.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of *N*-(5-Ethyl-[1,1'-biphenyl]-2-yl)acetamide (33ka)



33ka

The general procedure **A** was followed using **30k** (163 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ka** (151 mg, 63%) as a colorless solid.

M. p.: 64–65 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.3 Hz, 1H), 7.54–7.31 (m, 5H), 7.20 (dd, J = 8.3, 2.3 Hz, 1H), 7.13 (s, 1H), 7.09 (d, J = 2.3 Hz, 1H), 2.65 (q, J = 7.6 Hz, 2H), 2.00 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H).

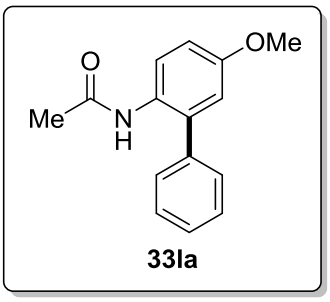
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 140.3 (C_q), 138.3 (C_q), 132.5 (C_q), 132.1 (C_q), 129.3 (CH), 129.0 (CH), 128.8 (CH), 127.6 (CH), 127.5 (CH), 122.2 (CH), 28.3 (CH_2), 24.4 (CH_3), 15.6 (CH_3).

IR (ATR): 3267, 3027, 2964, 2930, 2871, 1659, 1513, 1487, 1297, 767 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 ([M^+] 58), 197 (58), 182 (100), 180 (19), 167 (16), 43 (37).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO$ [M^+] calcd.: 239.1310.
found: 239.1306.

Synthesis of *N*-(5-Methoxy-[1,1'-biphenyl]-2-yl)acetamide (33la)



33la

The general procedure **A** was followed using **30l** (165 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 1/1) yielded **33la** (183 mg, 76%) as a colorless solid.

M. p.: 112–114 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.9 Hz, 1H), 7.50–7.28 (m, 5H), 6.98 (s, 1H), 6.88 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.78 (d, *J* = 3.0 Hz, 1H), 3.78 (s, 3H), 1.97 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.2 (C_q), 156.3 (C_q), 138.1 (C_q), 134.7 (C_q), 128.9 (CH), 128.8 (CH), 127.8 (CH), 127.6 (C_q), 124.3 (CH), 115.3 (CH), 113.3 (CH), 55.5 (CH_3), 24.2 (CH_3).

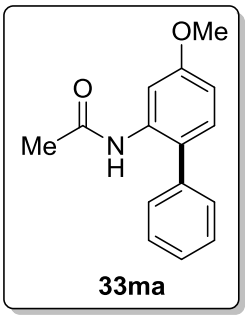
IR (ATR): 3263, 3058, 2969, 2939, 2838, 1664, 1480, 1270, 1178, 701 cm^{-1}.

MS (EI) *m/z* (relative intensity): 241 ([M^+] 71), 199 (76), 184 (100), 154 (21), 128 (11), 43 (34).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO_2$ [M^+] calcd.: 241.1103.
found: 241.1106.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of *N*-(4-Methoxy-[1,1'-biphenyl]-2-yl)acetamide (33ma)



33ma

The general procedure **A** was followed using **30m** (165 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ma** (174 mg, 72%) as a colorless solid.

The general procedure **C** was followed using **30m** (82.6 mg, 0.50 mmol) and potassium phenyltrifluoroborate (**77a**) (276 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ma** (64 mg, 53%) as a colorless solid.

M. p.: 91–93 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 2.6 Hz, 1H), 7.49–7.42 (m, 2H), 7.40–7.36 (m, 1H), 7.35–7.29 (m, 2H), 7.17 (s, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.84 (s, 3H), 2.00 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 159.4 (C_q), 137.9 (C_q), 135.6 (C_q), 130.6 (CH), 129.3 (CH), 129.0 (CH), 127.6 (CH), 124.2 (C_q), 110.5 (CH), 106.2 (CH), 55.5 (CH_3), 24.8 (CH_3).

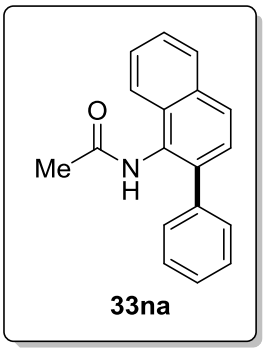
IR (ATR): 3241, 3033, 2953, 2831, 1652, 1309, 1233, 762, 724, 698 cm^{-1}.

MS (EI) *m/z* (relative intensity): 241 ([M^+] 74), 199 (100), 170 (16), 156 (19), 84 (9), 43 (34).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO_2$ [M^+] calcd.: 241.1103.
found: 241.1107.

The analytical data are in accordance with those reported in the literature.[27]

Synthesis of *N*-(2-Phenylnaphthalen-1-yl)acetamide (33na)



33na

The general procedure **A** was followed using **30n** (185 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33na** (76 mg, 29%) as a colorless solid.

M. p.: 135–136 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.01–7.90 (m, 2H), 7.70–7.28 (m, 10H), 2.13 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 173.7 (C_q), 139.0 (C_q), 138.3 (C_q), 133.9 (C_q), 132.8 (C_q), 130.6 (C_q), 129.7 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 126.7 (CH), 122.1 (CH), 26.2 (CH_3).

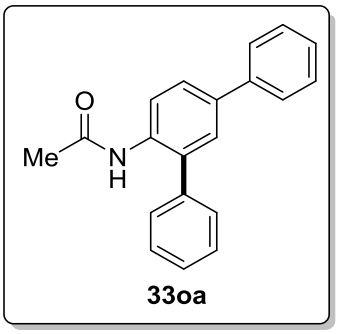
IR (ATR): 3059, 2955, 2923, 2853, 1700, 1364, 1223, 994, 826, 760 cm^{-1}.

MS (EI) *m/z* (relative intensity): 261 ([M^+] 61), 219 (100), 43 (19).

HR-MS (EI) *m/z* for $C_{18}H_{15}NO$ [M^+] calcd.: 261.1154.
found: 261.1153.

The analytical data are in accordance with those reported in the literature.[171]

Synthesis of *N*-([1,1':3',1''-Terphenyl]-4'-yl)acetamide (33oa)



33oa

The general procedure **A** was followed using **30o** (211 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33oa** (155 mg, 54%) as a colorless solid.

M. p.: 114–115 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, J = 8.5 Hz, 1H), 7.63–7.55 (m, 3H), 7.54–7.36 (m, 8H), 7.33 (d, J = 7.2 Hz, 1H), 7.17 (s, 1H), 2.03 (s, 3H).

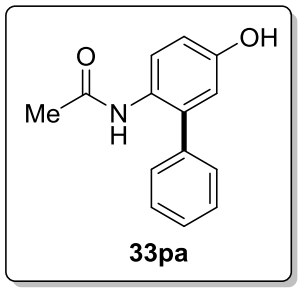
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.3 (C_q), 140.4 (C_q), 138.2 (C_q), 137.2 (C_q), 134.1 (C_q), 132.6 (C_q), 129.3 (CH), 129.2 (CH), 128.8 (CH), 128.7 (CH), 128.2 (CH), 127.3 (CH), 127.0 (CH), 126.9 (CH), 121.9 (CH), 24.5 (CH_3).

IR (ATR): 3289, 3029, 2925, 1651, 1503, 1478, 760, 694, 649, 598 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287 ([M^+] 46), 245 (100), 43 (19).

HR-MS (EI) *m/z* for $C_{20}H_{17}NO$ [M^+] calcd.: 287.1310.
found: 287.1316.

Synthesis of *N*-(5-Hydroxy-[1,1'-biphenyl]-2-yl)acetamide (33pa)



33pa

The general procedure **A** was followed using **30p** (151 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 3/7) yielded **33pa** (157 mg, 69%) as a pale yellow viscous oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, J = 9.5 Hz, 1H), 7.53 (s, 1H), 7.43–7.32 (m, 3H), 7.30–7.24 (m, 2H), 7.05 (s, 1H), 6.73–6.67 (m, 2H), 1.99 (s, 3H).

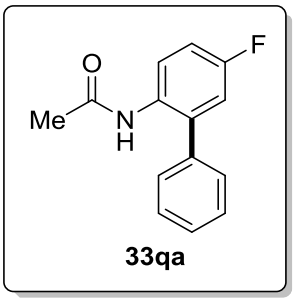
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 169.7 (C_q), 154.1 (C_q), 138.1 (C_q), 136.1 (C_q), 128.8 (CH), 128.6 (CH), 127.6 (CH), 126.0 (C_q), 125.7 (CH), 117.1 (CH), 115.3 (CH), 23.9 (CH_3).

IR (ATR): 3268, 3057, 2959, 2795, 1524, 1488, 1433, 1299, 1199, 726 cm^{-1}.

MS (EI) *m/z* (relative intensity): 227 ([M^+] 44), 185 (100), 154 (11), 43 (14).

HR-MS (EI) *m/z* for $C_{14}H_{13}NO_2$ [M^+] calcd.: 227.0946.
found: 227.0945.

Synthesis of *N*-(5-Fluoro-[1,1'-biphenyl]-2-yl)acetamide (33qa)



33qa

The general procedure **A** was followed using **30q** (153 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33qa** (163 mg, 71%) as a colorless solid.

M. p.: 131–133 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.20–8.05 (m, 1H), 7.59–7.28 (m, 5H), 7.17–6.88 (m, 3H), 2.00 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 159.1 (C_q, $J_{C–F}$ = 244.1 Hz), 137.0 (C_q, $J_{C–F}$ = 1.5 Hz), 134.4 (C_q, $J_{C–F}$ = 7.7 Hz), 130.6 (C_q, $J_{C–F}$ = 2.9 Hz), 129.0 (CH), 128.9 (CH), 128.3 (CH), 123.9 (CH, $J_{C–F}$ = 8.1 Hz), 116.5 (CH, $J_{C–F}$ = 22.9 Hz), 114.8 (CH, $J_{C–F}$ = 21.8 Hz), 24.4 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -(117.76–118.03) (m).

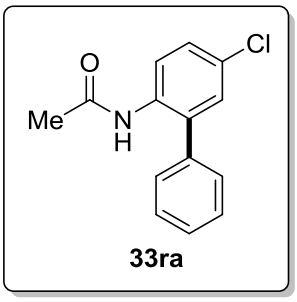
IR (ATR): 3274, 3238, 3031, 1659, 1533, 1483, 1410, 1180, 871, 771 cm^{-1}.

MS (EI) *m/z* (relative intensity): 229 ([M^+] 34), 187 (100), 104 (14), 84 (14), 43 (21).

HR-MS (EI) *m/z* for $C_{14}H_{12}FNO$ [M^+] calcd.: 229.0903.
found: 229.0904.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of *N*-(5-Chloro-[1,1'-biphenyl]-2-yl)acetamide (33ra)



33ra

The general procedure **A** was followed using **30r** (169 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ra** (165 mg, 67%) as a colorless solid.

M. p.: 126–127 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.8 Hz, 1H), 7.50–7.39 (m, 3H), 7.34–7.27 (m, 3H), 7.20 (d, J = 2.5 Hz, 1H), 7.10 (s, 1H), 1.98 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 136.7 (C_q), 133.6 (C_q), 133.2 (C_q), 129.6 (CH), 129.3 (C_q), 129.1 (CH), 128.9 (CH), 128.3 (CH), 128.1 (CH), 122.8 (CH), 24.5 (CH_3).

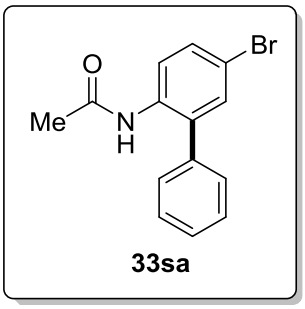
IR (ATR): 3257, 3188, 3029, 1647, 1520, 1390, 1367, 820, 767, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity): 245 ([M^+] 36), 203 (100), 167 (44), 139 (12), 43 (34).

HR-MS (EI) *m/z* for $C_{14}H_{12}ClNO$ [M^+] calcd.: 245.0607.
found: 245.0604.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of *N*-(5-Bromo-[1,1'-biphenyl]-2-yl)acetamide (33sa)



33sa

The general procedure **A** was followed using **30s** (214 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33sa** (182 mg, 63%) as a colorless solid.

M. p.: 127–128 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.7 Hz, 1H), 7.55–7.43 (m, 4H), 7.41–7.30 (m, 3H), 7.08 (s, 1H), 2.01 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.2 (C_q), 136.8 (C_q), 134.0 (C_q), 133.9 (C_q), 132.7 (CH), 131.3 (CH), 129.4 (CH), 129.1 (CH), 128.6 (CH), 123.0 (CH), 116.9 (C_q), 24.5 (CH_3).

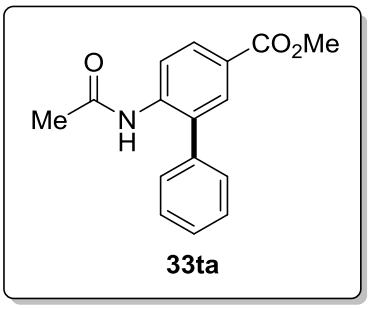
IR (ATR): 3278, 3055, 3025, 1651, 1515, 1386, 1369, 768, 700, 672 cm^{-1}.

MS (EI) *m/z* (relative intensity): 289 ([M^+] 31), 247 (100), 167 (71), 139, (23), 84 (20), 43 (32).

HR-MS (EI) *m/z* for $C_{14}H_{12}BrNO$ [M^+] calcd.: 289.0102.
found: 289.0103.

The analytical data are in accordance with those reported in the literature.[163b]

Synthesis of Methyl 6-acetamido-[1,1'-biphenyl]-3-carboxylate (33ta)



33ta

The general procedure **A** was followed using **30t** (193 mg, 1.00 mmol) and phenylboronic acid (**73a**) (183 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ta** (156 mg, 58%) as a colorless solid.

M. p.: 136–137 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.46 (d, J = 8.7 Hz, 1H), 8.01 (dd, J = 8.7, 2.1 Hz, 1H), 7.90 (d, J = 2.1 Hz, 1H), 7.54–7.40 (m, 3H), 7.38–7.34 (m, 2H), 7.31 (s, 1H), 3.87 (s, 3H), 2.02 (s, 3H).

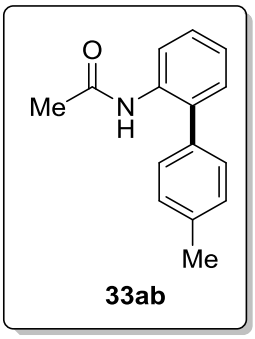
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 166.4 (C_q), 138.8 (C_q), 136.9 (C_q), 131.4 (CH), 131.0 (C_q), 130.0 (CH), 129.3 (CH), 129.1 (CH), 128.4 (CH), 125.3 (C_q), 120.0 (CH), 52.1 (CH_3), 24.9 (CH_3).

IR (ATR): 3358, 3030, 2949, 1711, 1679, 1585, 1511, 1296, 1106, 770 cm^{-1}.

MS (EI) *m/z* (relative intensity): 269 ([M^+] 49), 227 (100), 196 (92), 167 (29), 43 (21).

HR-MS (EI) *m/z* for $C_{16}H_{15}NO_3$ [M^+] calcd.: 269.1052.
found: 269.1056.

Synthesis of *N*-(4'-Methyl-[1,1'-biphenyl]-2-yl)acetamide (33ab)



33ab

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and *p*-tolylboronic acid (**73b**) (204 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ab** (185 mg, 82%) as a colorless solid.

The general procedure **B** was followed using **30a** (135 mg, 1.00 mmol) and hydroxydi-*p*-tolylborane (**76b**) (315 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ab** (133 mg, 59%) as a colorless solid.

The general procedure **C** was followed using **30a** (67.6 mg, 0.50 mmol) and potassium *p*-tolyltrifluoroborate (**77b**) (297 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ab** (71 mg, 63%) as a colorless solid.

M. p.: 106–108 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, J = 8.2 Hz, 1H), 7.44–7.06 (m, 8H), 2.41 (s, 3H), 2.01 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 137.6 (C_q), 135.0 (C_q), 134.6 (C_q), 132.0 (C_q), 130.0 (CH), 129.7 (CH), 128.9 (CH), 128.1 (CH), 124.1 (CH), 121.4 (CH), 24.6 (CH_3), 21.2 (CH_3).

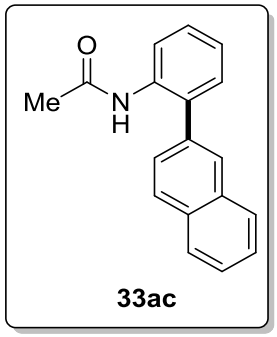
IR (ATR): 3340, 2956, 2921, 2853, 1515, 1442, 1282, 817, 756, 680 cm^{-1}.

MS (EI) *m/z* (relative intensity): 225 ([M^+] 55), 183 (100), 167 (37), 43 (26).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO$ [M^+] calcd.: 225.1154.
found: 225.1149.

The analytical data are in accordance with those reported in the literature.[27]

Synthesis of *N*-{2-(Naphthalen-2-yl)phenyl}acetamide (33ac)



33ac

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and naphthalen-2-ylboronic acid (**73c**) (258 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ac** (167 mg, 64%) as a colorless solid.

M. p.: 131–132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.30 (d, J = 8.2 Hz, 1H), 8.00–7.82 (m, 4H), 7.61–7.53 (m, 2H), 7.49 (dd, J = 8.4, 1.7 Hz, 1H), 7.41 (td, J = 7.8, 1.7 Hz, 1H), 7.35 (d, J = 6.8 Hz, 1H), 7.28–7.12 (m, 2H), 1.99 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.3 (C_q), 135.5 (C_q), 134.9 (C_q), 133.5 (C_q), 132.6 (C_q), 132.1 (C_q), 130.2 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.0 (CH), 126.7 (CH), 126.6 (CH), 124.4 (CH), 121.8 (CH), 24.6 (CH_3).

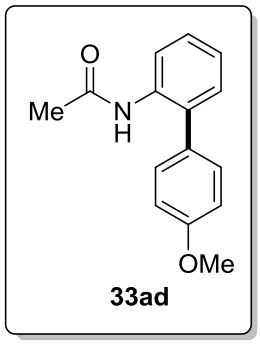
IR (ATR): 3261, 3053, 3025, 1643, 1522, 1443, 1368, 1275, 856, 817 cm^{-1}.

MS (EI) *m/z* (relative intensity): 261 ([M^+] 47), 219 (100), 189 (14), 43 (17).

HR-MS (EI) *m/z* for $C_{18}H_{15}NO$ [M^+] calcd.: 261.1154.
found: 261.1153.

The analytical data are in accordance with those reported in the literature.[172]

Synthesis of *N*-(4'-Methoxy-[1,1'-biphenyl]-2-yl)acetamide (33ad)



33ad

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and *p*-methoxyphenylboronic acid (**73d**) (228 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ad** (200 mg, 83%) as a colorless solid.

The general procedure **B** was followed using **30a** (135 mg, 1.00 mmol) and hydroxybis(4-methoxyphenyl)borane (**76d**) (363 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ad** (150 mg, 62%) as a colorless solid.

The general procedure **C** was followed using **30a** (67.6 mg, 0.50 mmol) and potassium *p*-methoxyphenyltrifluoroborate (**77d**) (321 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ad** (64 mg, 53%) as a colorless solid.

M. p.: 135–137 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.2 Hz, 1H), 7.34–7.24 (m, 3H), 7.23–7.09 (m, 3H), 6.98 (d, J = 8.6 Hz, 2H), 3.84 (s, 3H), 2.00 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.3 (C_q), 159.3 (C_q), 134.8 (C_q), 132.0 (C_q), 130.3 (CH), 130.2 (C_q), 130.1 (CH), 128.0 (CH), 124.3 (CH), 121.6 (CH), 114.4 (CH), 55.2 (CH_3), 24.4 (CH_3).

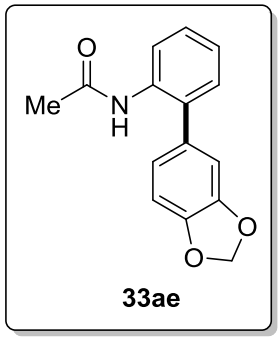
IR (ATR): 3351, 3012, 2921, 2842, 1690, 1439, 1239, 1175, 832, 770 cm^{-1}.

MS (EI) *m/z* (relative intensity): 241 ([M^+] 54), 199 (100), 184 (37), 154 (24), 128 (12), 43 (30).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO_2$ [M^+] calcd.: 241.1103.
found: 241.1110.

The analytical data are in accordance with those reported in the literature.[27]

Synthesis of *N*-{2-(Benzo[*d*][1,3]dioxol-5-yl)phenyl}acetamide (33ae)



33ae

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and benzo[*d*][1,3]dioxol-5-ylboronic acid (**73e**) (249 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ae** (174 mg, 68%) as a colorless solid.

M. p.: 111–112 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.2 Hz, 1H), 7.37–7.30 (m, 1H), 7.24–7.08 (m, 3H), 6.91 (dd, J = 7.6, 0.8 Hz, 1H), 6.85–6.77 (m, 2H), 6.03 (s, 2H), 2.04 (s, 3H).

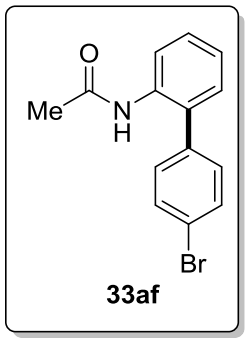
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.3 (C_q), 148.3 (C_q), 147.5 (C_q), 134.9 (C_q), 131.8 (C_q), 131.7 (C_q), 130.1 (CH), 128.3 (CH), 124.2 (CH), 122.6 (CH), 121.5 (CH), 109.7 (CH), 108.8 (CH), 101.3 (CH_2), 24.6 (CH_3).

IR (ATR): 3320, 2890, 1668, 1522, 1445, 1224, 1032, 927, 807, 756 cm^{-1}.

MS (EI) *m/z* (relative intensity): 255 ([M^+] 65), 213 (100), 182 (13), 154 (34), 127 (12), 43 (30).

HR-MS (EI) *m/z* for $C_{15}H_{13}NO_3$ [M^+] calcd.: 255.0895.
found: 255.0901.

Synthesis of *N*-(4'-Bromo-[1,1'-biphenyl]-2-yl)acetamide (33af)



33af

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and *p*-bromophenylboronic acid (**73f**) (301 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33af** (183 mg, 63%) as a colorless solid.

M. p.: 138–139 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, J = 8.2 Hz, 1H), 7.57–7.53 (m, 2H), 7.32 (ddd, J = 8.5, 6.5, 2.5 Hz, 1H), 7.23–7.11 (m, 5H), 1.97 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.4 (C_q), 137.2 (C_q), 134.4 (C_q), 132.1 (CH), 131.8 (C_q), 130.8 (CH), 129.9 (CH), 128.6 (CH), 124.8 (CH), 122.7 (CH), 122.1 (C_q), 24.1 (CH_3).

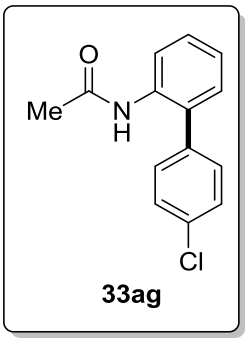
IR (ATR): 3262, 3056, 3028, 1651, 1524, 1445, 1283, 1070, 826, 758 cm^{-1}.

MS (EI) *m/z* (relative intensity): 289 ([M^+] 29), 247 (100), 167 (65), 139 (18), 43 (29).

HR-MS (EI) *m/z* for $C_{14}H_{12}BrNO$ [M^+] calcd.: 289.0102.
found: 289.0104.

The analytical data are in accordance with those reported in the literature.[173]

Synthesis of *N*-(4'-Chloro-[1,1'-biphenyl]-2-yl)acetamide (33ag)



33ag

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and *p*-chlorophenylboronic acid (**73g**) (235 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ag** (172 mg, 70%) as a colorless solid.

M. p.: 114–116 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.16 (d, J = 8.2 Hz, 1H), 7.46–7.40 (m, 2H), 7.39–7.32 (m, 1H), 7.31–7.26 (m, 2H), 7.20–7.17 (m, 2H), 7.01 (s, 1H), 2.01 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 136.5 (C_q), 134.4 (C_q), 134.0 (C_q), 131.3 (C_q), 130.5 (CH), 129.9 (CH), 129.1 (CH), 128.6 (CH), 124.6 (CH), 122.2 (CH), 24.6 (CH_3).

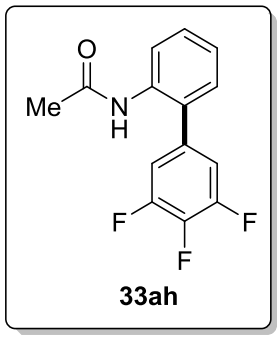
IR (ATR): 3247, 3031, 2924, 2854, 1635, 1527, 1369, 1283, 1086, 828 cm^{-1}.

MS (EI) *m/z* (relative intensity): 245 ([M^+] 35), 203 (100), 167 (43), 139 (12), 84 (17), 43 (36).

HR-MS (EI) *m/z* for $C_{14}H_{12}ClNO$ [M^+] calcd.: 245.0607.
found: 245.0599.

The analytical data are in accordance with those reported in the literature.[172]

Synthesis of *N*-(3',4',5'-Trifluoro-[1,1'-biphenyl]-2-yl)acetamide (33ah)



33ah

The general procedure **A** was followed using **30a** (135 mg, 1.00 mmol) and (3,4,5-trifluorophenyl)boronic acid (**73h**) (264 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ah** (180 mg, 68%) as a colorless solid.

M. p.: 140–141 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.1 Hz, 1H), 7.40 (ddd, J = 8.5, 5.9, 3.1 Hz, 1H), 7.24–7.17 (m, 2H), 7.06–6.97 (m, 2H), 6.93 (s, 1H), 2.07 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 151.4 (C_q, $J_{C\text{-}F}$ = 251.6, 10.0, 4.2 Hz), 139.5 (C_q, $J_{C\text{-}F}$ = 253.1, 15.0 Hz), 134.6 (C_q), 134.5 (C_q), 130.5 (C_q), 129.8 (CH), 129.5 (CH), 125.1 (CH), 123.3 (CH), 113.5 (CH, $J_{C\text{-}F}$ = 16.1, 5.4 Hz), 24.3 (CH_3).

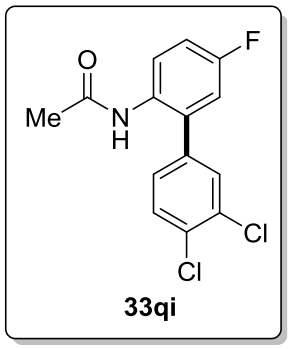
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -(132.8–133.0) (m), -161.0 (tt, $J_{C\text{-}F}$ = 20.6, 6.5 Hz).

IR (ATR): 3263, 3040, 2934, 2864, 1660, 1526, 1483, 1359, 872, 762 cm^{-1}.

MS (EI) *m/z* (relative intensity): 265 ([M^+] 29), 223 (100), 203 (16), 175 (5), 169 (5), 84 (6), 43 (41).

HR-MS (EI) *m/z* for $C_{14}H_{10}F_3NO$ [M^+] calcd.: 265.0714.
found: 265.0718.

Synthesis of *N*-(3',4'-Dichloro-5-fluoro-[1,1'-biphenyl]-2-yl)acetamide (33qi)



33qi

The general procedure **A** was followed using **30q** (153 mg, 1.00 mmol) and (3,4-dichlorophenyl)boronic acid (**73i**) (286 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 6/4) yielded **33qi** (188 mg, 63%) as a colorless solid.

M. p.: 146–148 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.02–7.94 (m, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 7.18 (dd, J = 8.2, 2.1 Hz, 1H), 7.12–7.01 (m, 1H), 6.96–6.93 (m, 2H), 2.02 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 168.5 (C_q), 159.5 (C_q, $J_{C\text{-}F}$ = 246.4 Hz), 137.2 (C_q, $J_{C\text{-}F}$ = 1.6 Hz), 133.3 (C_q), 133.0 (C_q, $J_{C\text{-}F}$ = 7.6 Hz), 132.8 (C_q), 131.0 (CH), 130.9 (CH), 130.4 (C_q, $J_{C\text{-}F}$ = 2.7 Hz), 128.2 (CH), 125.4 (CH, $J_{C\text{-}F}$ = 8.0 Hz), 116.5 (CH, $J_{C\text{-}F}$ = 23.2 Hz), 115.7 (CH, $J_{C\text{-}F}$ = 21.9 Hz), 24.2 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -116.6 (s).

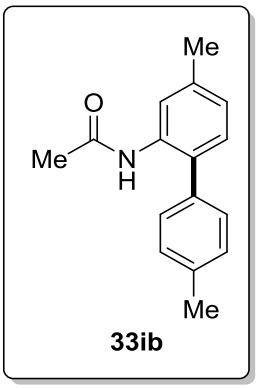
IR (ATR): 3242, 3190, 1652, 1529, 1472, 1371, 1183, 863, 702, 685 cm^{-1}.

MS (EI) *m/z* (relative intensity): 297 ([M^+] 48), 255 (100), 219 (40), 185 (52), 157 (17), 43 (60).

HR-MS (EI) *m/z* for $C_{14}H_{10}Cl_2FNO$ [M^+] calcd.: 297.0123.
found: 297.0128.

The analytical data are in accordance with those reported in the literature.[32]

Synthesis of *N*-(4,4'-Dimethyl-[1,1'-biphenyl]-2-yl)acetamide (33ib)



33ib

The general procedure **B** was followed using **30i** (149 mg, 1.00 mmol) and hydroxydi-*p*-tolylborane (**76b**) (315 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33ib** (146 mg, 61%) as a colorless solid.

M. p.: 120–121 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.28–7.20 (m, 4H), 7.15 (s, 1H), 7.10 (d, J = 7.7 Hz, 1H), 6.96 (d, J = 7.7 Hz, 1H), 2.40 (s, 3H), 2.38 (s, 3H), 1.99 (s, 3H).

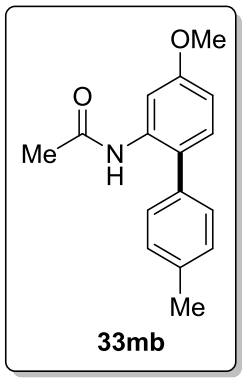
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 138.1 (C_q), 137.4 (C_q), 135.1 (C_q), 134.4 (C_q), 129.8 (CH), 129.6 (CH), 129.3 (C_q), 129.1 (CH), 125.1 (CH), 122.1 (CH), 24.5 (CH_3), 21.4 (CH_3), 21.1 (CH_3).

IR (ATR): 3621, 3304, 3274, 1663, 1538, 1479, 1291, 812, 608, 530 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 ([M^+] 76), 197 (100), 181 (29), 43 (31).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO$ [M^+] calcd.: 239.1310.
found: 239.1311.

Synthesis of *N*-(4-Methoxy-4'-methyl-[1,1'-biphenyl]-2-yl)acetamide (33mb)



The general procedure **B** was followed using **30m** (165 mg, 1.00 mmol) and hydroxydi-*p*-tolylborane (**76b**) (315 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33mb** (163 mg, 64%) as a colorless solid.

M. p.: 82–83 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.97 (s, 1H), 7.28–7.18 (m, 5H), 7.10 (d, J = 8.4 Hz, 1H), 6.69 (dd, J = 8.6, 2.7 Hz, 1H), 3.82 (s, 3H), 2.39 (s, 3H), 2.00 (s, 3H).

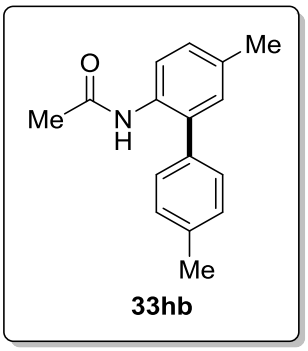
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 159.4 (C_q), 137.4 (C_q), 135.7 (C_q), 134.9 (C_q), 130.6 (CH), 129.7 (CH), 129.2 (CH), 124.2 (C_q), 110.4 (CH), 106.2 (CH), 55.4 (CH_3), 24.7 (CH_3), 21.1 (CH_3).

IR (ATR): 3330, 2965, 1668, 1581, 1475, 1419, 1305, 1235, 1041, 803 cm^{-1}.

MS (EI) *m/z* (relative intensity): 255 ([M^+] 77), 213 (100), 170 (32), 43 (29).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO_2$ [M^+] calcd.: 255.1259.
found: 255.1257.

Synthesis of *N*-(4',5-Dimethyl-[1,1'-biphenyl]-2-yl)acetamide (33hb)



33hb

The general procedure **B** was followed using **30h** (149 mg, 1.00 mmol) and hydroxydi-*p*-tolylborane (**76b**) (315 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33hb** (151 mg, 63%) as a colorless solid.

The general procedure **C** was followed using **30h** (74.6 mg, 0.50 mmol) and potassium *p*-tolyltrifluoroborate (**77b**) (297 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33hb** (66 mg, 55%) as a colorless solid.

M. p.: 97–98 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.4 Hz, 1H), 7.27–7.21 (m, 4H), 7.13 (dd, J = 8.4, 2.1 Hz, 1H), 7.09 (s, 1H), 7.03 (s, 1H), 2.40 (s, 3H), 2.32 (s, 3H), 1.99 (s, 3H).

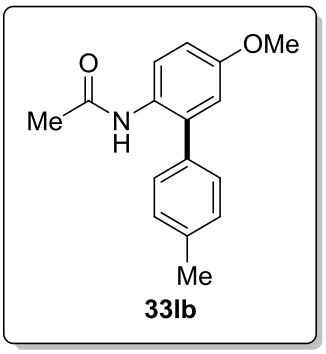
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 137.6 (C_q), 135.3 (C_q), 133.9 (C_q), 132.3 (C_q), 132.1 (C_q), 130.6 (CH), 129.6 (CH), 129.0 (CH), 128.7 (CH), 121.8 (CH), 24.4 (CH_3), 21.1 (CH_3), 20.8 (CH_3).

IR (ATR): 3365, 3025, 2922, 2865, 1673, 1509, 1290, 815, 731, 667 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 ([M^+] 63), 197 (100), 180 (39), 43 (29).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO$ [M^+] calcd.: 239.1310.
found: 239.1312.

Synthesis of *N*-(5-Methoxy-4'-methyl-[1,1'-biphenyl]-2-yl)acetamide (33lb)



33lb

The general procedure **B** was followed using **30l** (165 mg, 1.00 mmol) and hydroxydi-*p*-tolylborane (**76b**) (315 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33lb** (156 mg, 61%) as a colorless solid.

The general procedure **C** was followed using **30l** (82.6 mg, 0.50 mmol) and potassium *p*-tolyltrifluoroborate (**77b**) (297 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **33lb** (72 mg, 56%) as a colorless solid.

M. p.: 109–110 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.9 Hz, 1H), 7.27–7.20 (m, 4H), 7.00 (s, 1H), 6.86 (dd, J = 8.9, 3.0 Hz, 1H), 6.77 (d, J = 3.0 Hz, 1H), 3.77 (s, 3H), 2.39 (s, 3H), 1.97 (s, 3H).

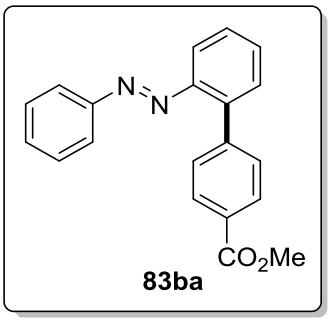
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 168.3 (C_q), 156.3 (C_q), 137.7 (C_q), 135.2 (C_q), 134.6 (C_q), 129.6 (CH), 128.8 (CH), 127.8 (C_q), 124.1 (CH), 115.4 (CH), 113.1 (CH), 55.4 (CH_3), 24.1 (CH_3), 21.1 (CH_3).

IR (ATR): 3269, 3022, 2971, 2921, 1660, 1520, 1267, 1176, 1031, 801 cm^{-1}.

MS (EI) *m/z* (relative intensity): 255 ([M^+] 86), 213 (89), 198 (100), 43 (19).

HR-MS (EI) *m/z* for $C_{16}H_{17}NO_2$ [M^+] calcd.: 255.1259.
found: 255.1263.

Synthesis of Methyl (*E*)-2'-(phenyldiazenyl)-[1,1'-biphenyl]-4-carboxylate (83ba)



83ba

The general procedure **D** was followed using **13b** (182 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ba** (93 mg, 59%) as an orange solid.

M. p.: 128–129 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.09 (d, J = 8.6 Hz, 2H), 7.80–7.72 (m, 3H), 7.57–7.52 (m, 4H), 7.51–7.42 (m, 4H), 3.94 (s, 3H).

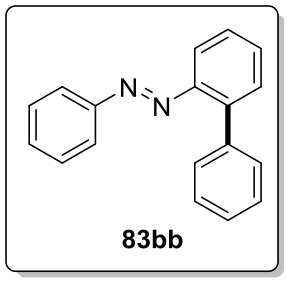
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.2 (C_q), 152.7 (C_q), 149.6 (C_q), 143.7 (C_q), 140.2 (C_q), 131.1 (CH), 130.9 (CH), 130.9 (CH), 130.7 (CH), 129.1 (CH), 128.9 (CH), 128.8 (C_q), 128.7 (CH), 123.3 (CH), 116.0 (CH), 52.1 (CH_3).

IR (ATR): 3071, 2947, 2920, 2848, 1721, 1437, 1273, 1103, 774, 736, 686, 541 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 ([M^+] 58), 301 (100), 257 (40), 211 (44), 152 (91), 77 (94).

HR-MS (EI) *m/z* for $C_{20}H_{16}N_2O_2$ [M^+] calcd.: 316.1212.
found: 316.1205.

Synthesis of (*E*)-1-([1,1'-Biphenyl]-2-yl)-2-phenyldiazene (83bb)



The general procedure **D** was followed using **13b** (182 mg, 1.00 mmol) and bromobenzene (**52b**) (79 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc/NEt_3: 88/6/6) yielded **83bb** (68 mg, 53%) as an orange viscous oil.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.81–7.75 (m, 2H), 7.62–7.35 (m, 12H).

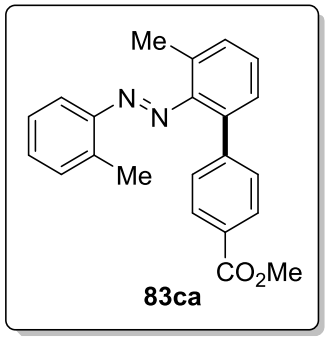
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.9 (C_q), 149.8 (C_q), 141.2 (C_q), 138.9 (C_q), 131.1 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 129.1 (CH), 128.1 (CH), 127.7 (CH), 127.3 (CH), 123.3 (CH), 116.0 (CH).

IR (ATR): 3058, 3030, 1470, 1149, 1008, 770, 730, 685, 535, 497 cm^{-1}.

MS (EI) *m/z* (relative intensity): 258 ([M^+] 42), 152 (82), 84 (100), 77 (70).

HR-MS (EI) *m/z* for $C_{18}H_{14}N_2$ [M^+] calcd.: 258.1157.
found: 258.1152.

Synthesis of Methyl (*E*)-3'-methyl-2'-(*o*-tolyldiazenyl)-[1,1'-biphenyl]-4-carboxylate (83ca)



83ca

The general procedure **D** was followed using **13c** (210 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ca** (103 mg, 60%) as an orange solid.

M. p.: 123–124 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.97 (d, J = 8.1 Hz, 2H), 7.38–7.26 (m, 9H), 3.92 (s, 3H), 2.47 (s, 3H), 2.28 (s, 3H).

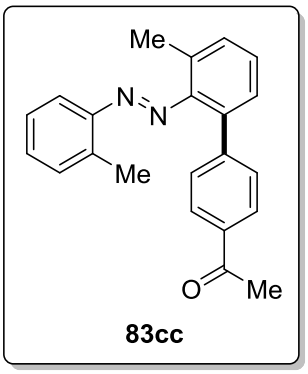
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.1 (C_q), 150.9 (C_q), 150.7 (C_q), 145.4 (C_q), 138.5 (C_q), 134.7 (C_q), 131.3 (CH), 131.2 (CH), 131.1 (CH), 130.8 (C_q), 130.1 (CH), 129.1 (CH), 128.9 (CH), 128.1 (CH), 128.0 (C_q), 126.3 (CH), 115.0 (CH), 52.0 (CH_3), 19.2 (CH_3), 17.1 (CH_3).

IR (ATR): 3059, 2951, 2923, 2844, 1719, 1608, 1398, 1272, 1179, 1101, 856, 766, 739, 712 cm^{-1}.

MS (EI) *m/z* (relative intensity): 344 ([M^+] 60), 329 (93), 285 (30), 225 (50), 165 (99), 91 (100), 65 (34).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_2O_2$ [M^+] calcd.: 344.1525.
found: 344.1526.

Synthesis of (*E*)-1-{3'-Methyl-2'-(*o*-tolyldiazenyl)-[1,1'-biphenyl]-4-yl}ethan-1-one (83cc)



83cc

The general procedure **D** was followed using **13c** (210 mg, 1.00 mmol) and 1-(4-bromophenyl)ethan-1-one (**52c**) (100 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83cc** (87 mg, 53%) as an orange solid.

M. p.: 125–126 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.89 (d, J = 8.6 Hz, 2H), 7.37–7.29 (m, 6H), 7.26 (d, J = 0.8 Hz, 2H), 7.24–7.15 (m, 1H), 2.59 (s, 3H), 2.46 (s, 3H), 2.27 (s, 3H).

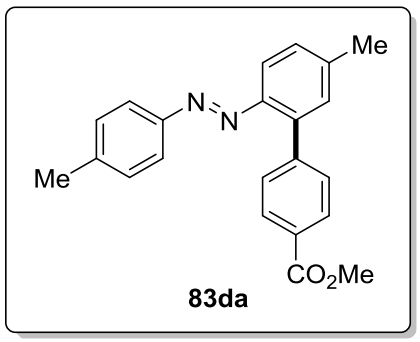
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 198.0 (C_q), 151.0 (C_q), 150.8 (C_q), 145.7 (C_q), 138.5 (C_q), 135.2 (C_q), 134.7 (C_q), 131.5 (CH), 131.4 (CH), 131.3 (CH), 130.9 (C_q), 130.4 (CH), 128.9 (CH), 128.2 (CH), 128.0 (CH), 126.4 (CH), 115.0 (CH), 26.5 (CH_3), 19.1 (CH_3), 17.0 (CH_3).

IR (ATR): 3054, 2961, 2923, 1679, 1603, 1356, 1264, 955, 766, 600 cm^{-1}.

MS (EI) *m/z* (relative intensity): 328 ([M^+] 100), 285 (32), 209 (25), 165 (45), 91 (98), 65 (27), 43 (90).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_2O$ [M^+] calcd.: 328.1576.
found: 328.1569.

Synthesis of Methyl (*E*)-5'-methyl-2'-(*p*-tolyldiazenyl)-[1,1'-biphenyl]-4-carboxylate (83da)



83da

The general procedure **D** was followed using **13d** (210 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83da** (112 mg, 65%) as an orange solid.

M. p.: 138–139 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.08 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.37–7.35 (m, 1H), 7.27 (ddq, J = 8.2, 2.0, 0.6 Hz, 1H), 7.25–7.21 (m, 2H), 3.94 (s, 3H), 2.46 (s, 3H), 2.39 (s, 3H).

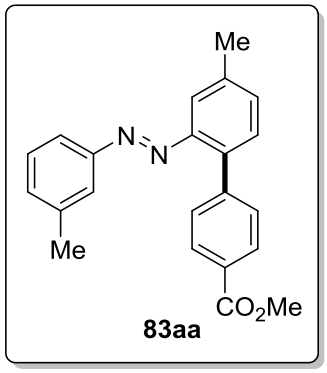
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.2 (C_q), 151.0 (C_q), 147.6 (C_q), 143.9 (C_q), 141.4 (C_q), 141.1 (C_q), 140.0 (C_q), 131.1 (CH), 130.8 (CH), 129.7 (CH), 129.5 (CH), 128.7 (CH), 128.6 (C_q), 123.1 (CH), 115.8 (CH), 52.1 (CH_3), 21.5 (CH_3), 21.5 (CH_3).

IR (ATR): 3029, 2948, 2921, 2844, 1721, 1599, 1437, 1274, 1149, 1112, 824, 702, 565, 385 cm^{-1}.

MS (EI) *m/z* (relative intensity): 344 ([M^+] 66), 329 (73), 285 (29), 225 (47), 165 (86), 91 (100), 65 (25).

HR-MS (ESI) *m/z* for $C_{22}H_{21}N_2O_2$ [M+H^+] calcd.: 345.1603.
found: 345.1599.

Synthesis of Methyl (*E*)-4'-methyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-carboxylate (83aa)



83aa

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83aa** (150 mg, 87%) as an orange solid.

M. p.: 136–137 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.10 (d, J = 8.0 Hz, 2H), 7.64 (s, 1H), 7.60–7.53 (m, 4H), 7.49 (d, J = 7.8 Hz, 1H), 7.40–7.32 (m, 2H), 7.30–7.24 (m, 1H), 3.96 (s, 3H), 2.48 (s, 3H), 2.42 (s, 3H).

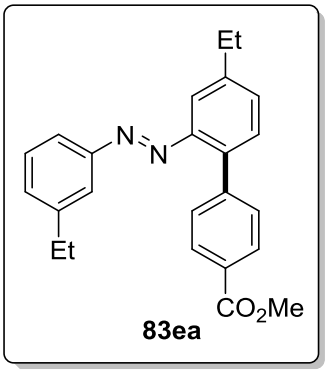
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.0 (C_q), 152.7 (C_q), 149.3 (C_q), 143.6 (C_q), 138.8 (C_q), 138.7 (C_q), 137.1 (C_q), 131.7 (CH), 131.5 (CH), 130.7 (CH), 130.4 (CH), 128.8 (CH), 128.7 (CH), 128.5 (C_q), 124.2 (CH), 119.8 (CH), 116.1 (CH), 52.1 (CH_3), 21.4 (CH_3), 21.3 (CH_3).

IR (ATR): 3030, 2951, 2914, 2850, 1721, 1606, 1438, 1279, 1106, 829, 790 cm^{-1}.

MS (EI) *m/z* (relative intensity): 344 ([M^+] 60), 329 (80), 285 (38), 225 (43), 165 (87), 91 (100), 65 (25), 43 (22).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_2O_2$ [M^+] calcd.: 344.1525.
found: 344.1511.

Synthesis of Methyl (*E*)-4'-ethyl-2'-{(3-ethylphenyl)diazenyl}-[1,1'-biphenyl]-4-carboxylate (83ea)



83ea

The general procedure **D** was followed using **13e** (238 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ea** (155 mg, 83%) as an orange solid.

M. p.: 81–82 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.07 (d, *J* = 8.6 Hz, 2H), 7.68–7.65 (m, 1H), 7.61–7.59 (m, 1H), 7.57–7.52 (m, 3H), 7.50 (dd, *J* = 7.9, 0.5 Hz, 1H), 7.39 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.29–7.26 (m, 1H), 3.94 (s, 3H), 2.77 (q, *J* = 7.6 Hz, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.32 (t, *J* = 7.6 Hz, 3H), 1.26 (t, *J* = 7.6 Hz, 3H).

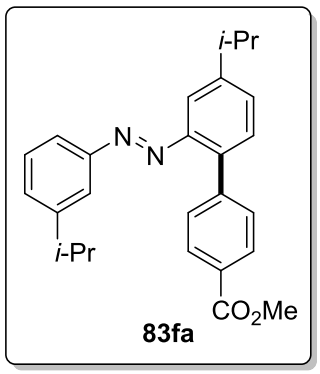
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.2 (C_q), 153.0 (C_q), 149.6 (C_q), 145.3 (C_q), 145.2 (C_q), 143.8 (C_q), 137.5 (C_q), 130.9 (CH), 130.7 (CH), 130.6 (CH), 130.5 (CH), 129.0 (CH), 128.8 (CH), 128.6 (C_q), 123.4 (CH), 119.8 (CH), 115.0 (CH), 52.1 (CH_3), 28.7 (CH_2), 28.7 (CH_2), 15.4 (CH_3), 15.3 (CH_3).

IR (ATR): 2962, 2930, 2871, 1717, 1606, 1439, 1273, 1181, 1102, 691 cm^{-1}.

MS (EI) *m/z* (relative intensity): 372 ([M^+] 89), 357 (100), 313 (45), 239 (61), 180 (35), 165 (75), 105 (91), 77 (32).

HR-MS (ESI) *m/z* for $C_{24}H_{25}N_2O_2$ [M+H^+] calcd.: 373.1916.
found: 373.1915.

Synthesis of Methyl (*E*)-4'-*iso*propyl-2'-{(3-*iso*propylphenyl)diazenyl}-[1,1'-biphenyl]-4-carboxylate (83fa)



83fa

The general procedure **D** was followed using **13f** (266 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83fa** (160 mg, 80%) as an orange solid.

M. p.: 92–93 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.07 (d, J = 8.5 Hz, 2H), 7.71 (t, J = 1.8 Hz, 1H), 7.63 (d, J = 1.9 Hz, 1H), 7.56–7.50 (m, 4H), 7.43 (dd, J = 8.0, 1.9 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.32–7.29 (m, 1H), 3.93 (s, 3H), 3.04 (sept, J = 6.9 Hz, 1H), 2.97 (sep, J = 6.9 Hz, 1H), 1.33 (d, J = 6.9 Hz, 6H), 1.27 (d, J = 6.9 Hz, 6H).

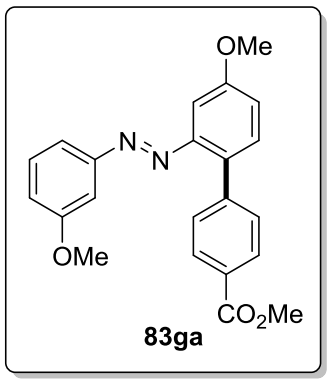
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.2 (C_q), 153.1 (C_q), 150.0 (C_q), 149.9 (C_q), 149.5 (C_q), 143.8 (C_q), 137.7 (C_q), 130.9 (CH), 130.6 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.6 (C_q), 122.4 (CH), 119.6 (CH), 113.7 (CH), 52.1 (CH_3), 34.1 (CH), 34.0 (CH), 23.9 (CH_3), 23.8 (CH_3).

IR (ATR): 2959, 2889, 2868, 1718, 1607, 1439, 1273, 1113, 858, 835, 797, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity): 400 ([M^+] 96), 385 (100), 341 (41), 253 (45), 211 (47), 179 (43), 119 (78), 91 (42).

HR-MS (EI) *m/z* for $C_{26}H_{28}N_2O_2$ [M^+] calcd.: 400.2151.
found: 400.2138.

Synthesis of Methyl (*E*)-4'-methoxy-2'-{(3-methoxyphenyl)diazenyl}-[1,1'-biphenyl]-4-carboxylate (83ga)



83ga

The general procedure **D** was followed using **13g** (242 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ga** (139 mg, 74%) as an orange solid.

M. p.: 145–146 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.06 (d, J = 8.6 Hz, 2H), 7.53–7.48 (m, 3H), 7.44 (ddd, J = 7.8, 1.7, 1.0 Hz, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.35–7.33 (m, 1H), 7.27 (dd, J = 2.6, 1.7 Hz, 1H), 7.13 (dd, J = 8.5, 2.7 Hz, 1H), 7.02–6.98 (m, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.78 (s, 3H).

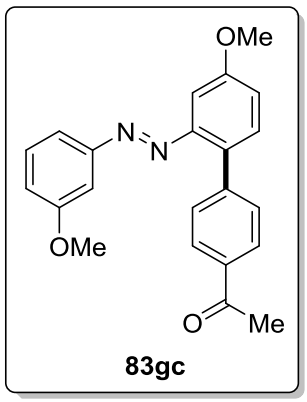
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.1 (C_q), 160.3 (C_q), 160.0 (C_q), 153.9 (C_q), 150.0 (C_q), 143.5 (C_q), 133.5 (C_q), 131.6 (CH), 130.9 (CH), 129.8 (CH), 128.7 (CH), 128.4 (C_q), 118.4 (CH), 118.0 (CH), 117.4 (CH), 106.2 (CH), 99.3 (CH), 55.6 (CH_3), 55.3 (CH_3), 52.1 (CH_3).

IR (ATR): 2950, 2902, 2834, 1719, 1597, 1519, 1481, 1433, 1270, 1132, 1103, 1039, 887, 782, 683 cm^{-1}.

MS (EI) *m/z* (relative intensity): 376 ([M^+] 64), 361 (100), 317 (53), 241 (38), 182 (35), 139 (54), 107 (65), 77 (38).

HR-MS (ESI) *m/z* for $C_{22}H_{21}N_2O_4$ [M+H^+] calcd.: 377.1501.
found: 377.1491.

Synthesis of (*E*)-1-{4'-Methoxy-2'-[(3-methoxyphenyl)diazenyl]-[1,1'-biphenyl]-4-yl}ethan-1-one (83gc)



83gc

The general procedure **D** was followed using **13g** (242 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52c**) (100 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83gc** (96 mg, 53%) as an orange solid.

M. p.: 155–156 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.98 (d, J = 8.5 Hz, 2H), 7.56–7.47 (m, 3H), 7.44 (ddd, J = 7.8, 1.4, 1.3 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 2.8 Hz, 1H), 7.29–7.23 (m, 1H), 7.13 (dd, J = 8.6, 2.7 Hz, 1H), 7.00 (ddd, J = 8.0, 2.7, 1.2 Hz, 1H), 3.91 (s, 3H), 3.78 (s, 3H), 2.63 (s, 3H).

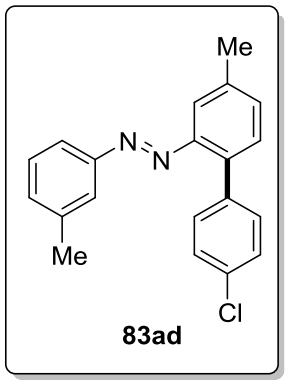
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 198.1 (C_q), 160.4 (C_q), 160.2 (C_q), 154.0 (C_q), 150.2 (C_q), 143.8 (C_q), 135.4 (C_q), 133.4 (C_q), 131.6 (CH), 131.1 (CH), 129.9 (CH), 127.6 (CH), 118.5 (CH), 118.0 (CH), 117.4 (CH), 106.4 (CH), 99.4 (CH), 55.6 (CH_3), 55.3 (CH_3), 26.6 (CH_3).

IR (ATR): 3068, 3005, 2961, 2940, 2915, 2834, 1673, 1604, 1513, 1269, 1132, 1040, 887, 819, 782, 634 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 ([M^+] 100), 317 (57), 139 (38), 107 (53), 92 (24), 77 (30), 43 (54).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_2O_3$ [M^+] calcd.: 360.1474.
found: 360.1466.

Synthesis of (*E*)-1-(4'-Chloro-4-methyl-[1,1'-biphenyl]-2-yl)-2-(*m*-tolyl)diazene (83ad)



83ad

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 1-bromo-4-chlorobenzene (**52d**) (96 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc/NEt_3: 88/6/6) yielded **83ad** (93 mg, 58%) as an orange solid.

M. p.: 120–121 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.73–7.69 (m, 1H), 7.60 (s, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.53 (s, 1H), 7.42 (d, J = 7.9 Hz, 1H), 7.38–7.36 (m, 3H), 7.36–7.32 (m, 2H), 7.29–7.25 (m, 1H), 2.45 (s, 3H), 2.41 (s, 3H).

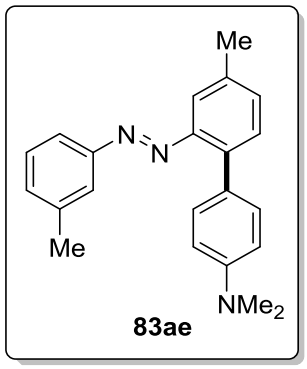
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.9 (C_q), 149.5 (C_q), 139.0 (C_q), 138.5 (C_q), 137.3 (C_q), 137.1 (C_q), 133.2 (C_q), 132.1 (CH), 131.8 (CH), 131.7 (CH), 130.4 (CH), 128.9 (CH), 127.7 (CH), 124.2 (CH), 120.0 (CH), 116.2 (CH), 21.4 (CH_3), 21.2 (CH_3).

IR (ATR): 3049, 3028, 2949, 2920, 2859, 1596, 1479, 1092, 1005, 811, 788, 747, 687 cm^{-1}.

MS (EI) *m/z* (relative intensity): 320 ([M^+] 67), 201 (54), 166 (93), 91 (100), 65 (35).

HR-MS (ESI) *m/z* for $C_{20}H_{18}ClN_2$ [M+H^+] calcd.: 321.1159.
found: 321.1141.

Synthesis of (*E*)-*N*,*N*,4'-Trimethyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-amine (83ae)



83ae

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 4-bromo-*N*,*N*-dimethylaniline (**52e**) (100 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ae** (92 mg, 56%) as an orange solid.

M. p.: 124–125 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.68 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.38–7.34 (m, 3H), 7.33–7.31 (m, 1H), 7.25 (d, *J* = 6.8 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.00 (s, 6H), 2.44 (s, 3H), 2.42 (s, 3H).

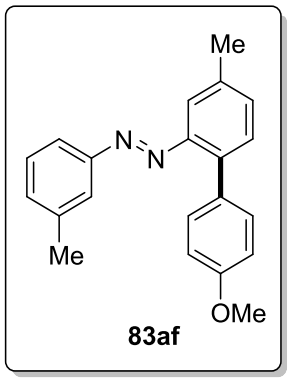
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 153.1 (C_q), 149.7 (C_q), 149.6 (C_q), 138.8 (C_q), 138.2 (C_q), 136.7 (C_q), 131.8 (CH), 131.5 (CH), 131.3 (CH), 130.3 (CH), 128.8 (CH), 126.7 (C_q), 124.0 (CH), 120.2 (CH), 116.2 (CH), 111.8 (CH), 40.6 (CH_3), 21.4 (CH_3), 21.1 (CH_3).

IR (ATR): 2915, 2858, 2803, 1611, 1528, 1494, 1444, 1353, 1196, 806, 686, 532 cm^{-1}.

MS (EI) *m/z* (relative intensity): 329 ([M^+] 100), 285 (12), 210 (29), 167 (19), 91 (19), 65 (8).

HR-MS (EI) *m/z* for $C_{22}H_{23}N_3$ [M^+] calcd.: 329.1892.
found: 329.1874.

Synthesis of (*E*)-1-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-2-(*m*-tolyl)diazene (83af)



The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 1-bromo-4-methoxybenzene (**52f**) (94 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83af** (106 mg, 67%) as an orange solid.

M. p.: 121–122 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.66 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.53 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.43–7.38 (m, 2H), 7.37–7.31 (m, 2H), 7.29–7.23 (m, 1H), 6.97 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.46 (s, 3H), 2.43 (s, 3H).

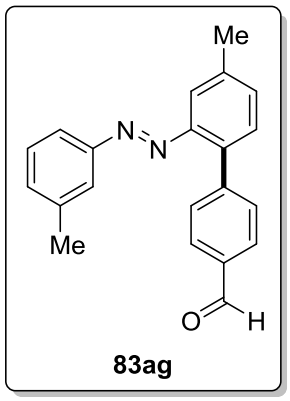
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 158.8 (C_q), 152.9 (C_q), 149.4 (C_q), 138.8 (C_q), 137.7 (C_q), 137.3 (C_q), 131.9 (CH), 131.5 (CH), 131.4 (CH), 131.1 (C_q), 130.4 (CH), 128.7 (CH), 124.0 (CH), 120.0 (CH), 116.0 (CH), 113.0 (CH), 55.3 (CH_3), 21.4 (CH_3), 21.2 (CH_3).

IR (ATR): 2962, 2914, 2856, 1606, 1518, 1249, 1177, 1016, 816, 791, 689, 538 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 ([M^+] 100), 301 (40), 197 (67), 182 (65), 153 (42), 91 (78), 65 (30).

HR-MS (EI) *m/z* for $C_{21}H_{20}N_2O$ [M^+] calcd.: 316.1576.
found: 316.1577.

Synthesis of (*E*)-4'-Methyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-carbaldehyde (83ag)



83ag

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 4-bromobenzaldehyde (**52g**) (93 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ag** (80 mg, 51%) as an orange solid.

M. p.: 101–102 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 10.07 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.1 Hz, 2H), 7.59 (s, 1H), 7.57 (s, 1H), 7.54 (d, J = 7.3 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.38 (ddd, J = 7.8, 1.8, 0.8 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.25 (d, J = 9.7 Hz, 1H), 2.47 (s, 3H), 2.40 (s, 3H).

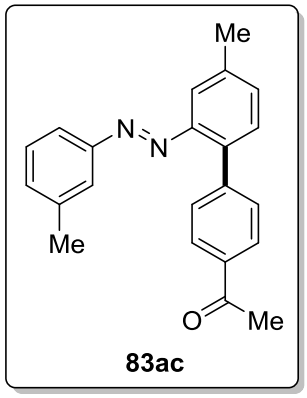
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 192.2 (C_q), 152.8 (C_q), 149.5 (C_q), 145.4 (C_q), 139.3 (C_q), 139.0 (C_q), 137.0 (C_q), 134.9 (C_q), 131.9 (CH), 131.7 (CH), 131.5 (CH), 130.5 (CH), 128.9 (CH), 128.9 (CH), 124.3 (CH), 119.9 (CH), 116.3 (CH), 21.4 (CH_3), 21.3 (CH_3).

IR (ATR): 2915, 2816, 2727, 1694, 1603, 1210, 818, 792, 686, 537 cm^{-1}.

MS (EI) *m/z* (relative intensity): 314 ([M^+] 79), 195 (32), 165 (60), 152 (47), 91 (100), 65 (31), 43 (33).

HR-MS (EI) *m/z* for $C_{21}H_{18}N_2O$ [M^+] calcd.: 314.1419.
found: 314.1430.

Synthesis of (*E*)-1-{4'-Methyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-yl}ethan-1-one (83ac)



83ac

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 1-(4-bromophenyl)ethan-1-one (**52c**) (100 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ac** (106 mg, 65%) as an orange solid.

M. p.: 123–124 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.00 (d, J = 8.6 Hz, 2H), 7.61 (s, 1H), 7.59–7.51 (m, 4H), 7.46 (d, J = 7.8 Hz, 1H), 7.39–7.29 (m, 2H), 7.28–7.21 (m, 1H), 2.64 (s, 3H), 2.47 (s, 3H), 2.40 (s, 3H).

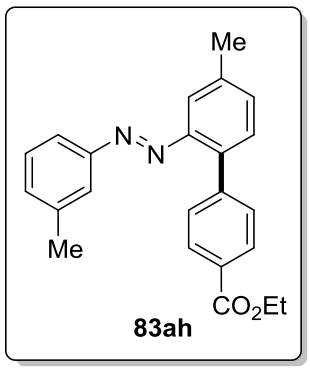
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 198.1 (C_q), 152.9 (C_q), 149.6 (C_q), 144.0 (C_q), 139.0 (C_q), 138.9 (C_q), 137.2 (C_q), 135.6 (C_q), 131.9 (CH), 131.7 (CH), 131.0 (CH), 130.5 (CH), 129.0 (CH), 127.6 (CH), 124.4 (CH), 119.9 (CH), 116.3 (CH), 26.5 (CH_3), 21.2 (CH_3), 21.1 (CH_3).

IR (ATR): 2914, 2856, 2723, 1679, 1600, 1266, 819, 797, 688, 599 cm^{-1}.

MS (EI) *m/z* (relative intensity): 328 ([M^+] 100), 285 (44), 209 (25), 165 (41), 91 (83), 65 (19), 65 (20), 43 (76).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_2O$ [M^+] calcd.: 328.1576.
found: 328.1572.

Synthesis of Ethyl (*E*)-4'-methyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-carboxylate (83ah)



83ah

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and ethyl 4-bromobenzoate (**52h**) (115 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ah** (113 mg, 63%) as an orange solid.

M. p.: 94–95 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.09 (d, J = 8.5 Hz, 2H), 7.63–7.60 (m, 1H), 7.58–7.50 (m, 4H), 7.47 (d, J = 7.9 Hz, 1H), 7.39–7.30 (m, 2H), 7.28–7.22 (m, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.47 (s, 3H), 2.41 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H).

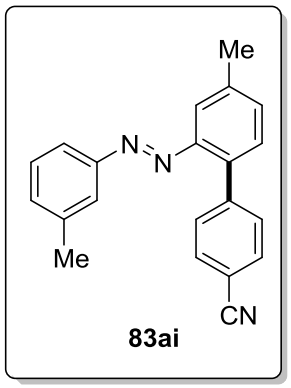
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.8 (C_q), 153.0 (C_q), 149.6 (C_q), 143.7 (C_q), 139.0 (C_q), 138.9 (C_q), 137.4 (C_q), 131.9 (CH), 131.7 (CH), 130.8 (CH), 130.6 (CH), 129.0 (C_q), 128.9 (CH), 128.8 (CH), 124.4 (CH), 119.9 (CH), 116.3 (CH), 60.9 (CH_2), 21.3 (CH_3), 21.1 (CH_3), 14.3 (CH_3).

IR (ATR): 2979, 2921, 2867, 1713, 1607, 1268, 1180, 1100, 775, 688 cm^{-1}.

MS (EI) *m/z* (relative intensity): 358 ([M^+] 47), 329 (100), 285 (37), 239 (19), 211 (17), 165 (60), 91 (80), 65 (14).

HR-MS (EI) *m/z* for $C_{23}H_{22}N_2O_2$ [M^+] calcd.: 358.1681.
found: 358.1669.

Synthesis of (*E*)-4'-Methyl-2'-(*m*-tolyldiazenyl)-[1,1'-biphenyl]-4-carbonitrile (83ai)



83ai

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 4-bromobenzonitrile (**52i**) (91 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ai** (100 mg, 64%) as an orange solid.

M. p.: 121–122 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.58 (d, J = 8.6 Hz, 2H), 7.59–7.56 (m, 2H), 7.55 (d, J = 8.6 Hz, 2H), 7.53–7.51 (m, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.39–7.33 (m, 2H), 7.27 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H), 2.41 (s, 3H).

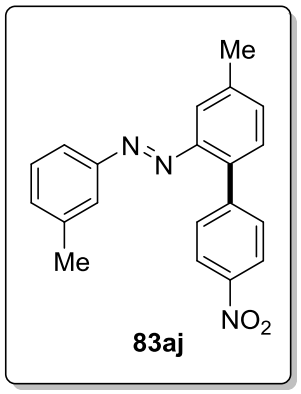
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.8 (C_q), 149.3 (C_q), 143.8 (C_q), 139.5 (C_q), 139.1 (C_q), 136.5 (C_q), 132.0 (CH), 131.8 (CH), 131.4 (CH), 131.2 (CH), 130.3 (CH), 129.0 (CH), 124.1 (CH), 120.0 (CH), 119.1 (C_q), 116.3 (CH), 110.7 (C_q), 21.3 (CH_3), 21.3 (CH_3).

IR (ATR): 2968, 2919, 2857, 2225, 1603, 1484, 812, 787, 682, 589, 544 cm^{-1}.

MS (EI) *m/z* (relative intensity): 311 ([M^+] 58), 192 (56), 165 (32), 119 (18), 91 (100), 65 (27).

HR-MS (EI) *m/z* for $C_{21}H_{17}N_3$ [M^+] calcd.: 311.1422.
found: 311.1419.

Synthesis of (*E*)-1-(4-Methyl-4'-nitro-[1,1'-biphenyl]-2-yl)-2-(*m*-tolyl)diazene (83aj)



83aj

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 1-bromo-4-nitrobenzene (**52j**) (101 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83aj** (89 mg, 54%) as an orange solid.

M. p.: 134–135 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.25 (d, J = 8.9 Hz, 2H), 7.63–7.57 (m, 4H), 7.53 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.38 (ddd, J = 7.9, 1.8, 0.6 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.27 (d, J = 7.5 Hz, 1H), 2.48 (s, 3H), 2.41 (s, 3H).

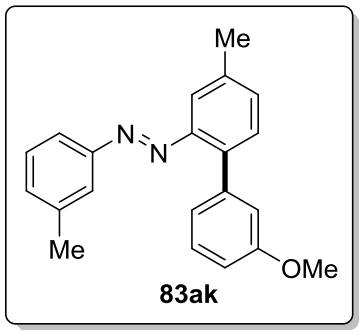
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.8 (C_q), 149.3 (C_q), 146.9 (C_q), 145.9 (C_q), 139.8 (C_q), 139.1 (C_q), 136.1 (C_q), 132.1 (CH), 131.8 (CH), 131.5 (CH), 130.4 (CH), 129.0 (CH), 124.3 (CH), 122.7 (CH), 119.9 (CH), 116.4 (CH), 21.4 (CH_3), 21.3 (CH_3).

IR (ATR): 2915, 2856, 1596, 1506, 1345, 853, 810, 786, 733, 695, 685 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 ([M^+] 39), 212 (32), 165 (56), 119 (22), 91 (100), 65 (24).

HR-MS (EI) *m/z* for $C_{20}H_{17}N_3O_2$ [M^+] calcd.: 331.1321.
found: 331.1319.

Synthesis of (*E*)-1-(3'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-2-(*m*-tolyl)diazene (83ak)



83ak

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 1-bromo-3-methoxybenzene (**52k**) (94 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ak** (89 mg, 56%) a viscous orange liquid.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.65 (m, 2H), 7.57–7.54 (m, 1H), 7.51 (ddd, J = 7.8, 4.0, 1.4 Hz, 1H), 7.40–7.31 (m, 3H), 7.26 (d, J = 7.4 Hz, 1H), 7.09–7.03 (m, 2H), 6.97–6.92 (m, 1H), 3.81 (s, 3H), 2.48 (s, 3H), 2.42 (s, 3H).

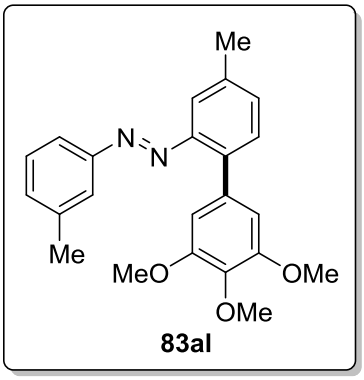
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 158.9 (C_q), 153.0 (C_q), 149.6 (C_q), 140.2 (C_q), 138.9 (C_q), 138.1 (C_q), 138.0 (C_q), 131.6 (CH), 131.5 (CH), 130.6 (CH), 128.8 (CH), 128.4 (CH), 123.8 (CH), 123.5 (CH), 120.3 (CH), 116.3 (CH), 116.1 (CH), 113.0 (CH), 55.2 (CH_3), 21.3 (CH_3), 21.2 (CH_3).

IR (ATR): 3024, 2918, 2832, 1599, 1477, 1283, 1208, 1023, 821, 786, 746, 688 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 ([M^+] 100), 285 (52), 197 (55), 182 (69), 153 (40), 91 (86), 65 (34).

HR-MS (EI) *m/z* for $C_{21}H_{20}N_2O$ [M^+] calcd.: 316.1576.
found: 316.1571.

Synthesis of (*E*)-1-(*m*-Tolyl)-2-(3',4',5'-trimethoxy-4-methyl-[1,1'-biphenyl]-2-yl)diazene (83al)



83al

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 5-bromo-1,2,3-trimethoxybenzene (**52l**) (124 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83al** (161 mg, 86%) as an orange solid.

M. p.: 138–139 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.64 (m, 2H), 7.54–7.48 (m, 2H), 7.38–7.32 (m, 2H), 7.25 (d, J = 7.7 Hz, 1H), 6.68 (s, 2H) 3.91 (s, 3H), 3.81 (s, 6H), 2.45 (s, 3H), 2.39 (s, 3H).

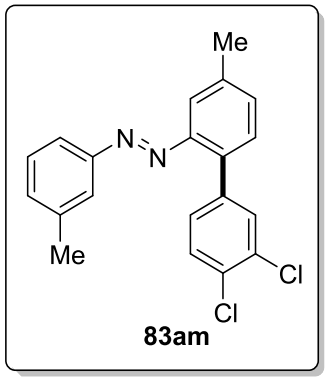
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.9 (C_q), 152.4 (C_q), 149.7 (C_q), 138.9 (C_q), 138.1 (C_q), 137.8 (C_q), 137.3 (C_q), 134.3 (C_q), 131.7 (CH), 131.5 (CH), 130.3 (CH), 128.9 (CH), 123.5 (CH), 120.5 (CH), 116.3 (CH), 108.3 (CH), 60.9 (CH_3), 56.0 (CH_3), 21.3 (CH_3), 21.1 (CH_3).

IR (ATR): 2948, 2921, 2825, 1584, 1449, 1412, 1235, 1120, 1011, 817, 790, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity): 376 ([M^+] 45), 345 (100), 226 (33), 211 (30), 91 (37).

HR-MS (EI) *m/z* for $C_{23}H_{24}N_2O_3$ [M^+] calcd.: 376.1787.
found: 376.1787.

Synthesis of (*E*)-1-(3',4'-Dichloro-4-methyl-[1,1'-biphenyl]-2-yl)-2-(*m*-tolyl)diazene (83am)



The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 4-bromo-1,2-dichlorobenzene (**52m**) (113 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83am** (112 mg, 63%) as an orange solid.

M. p.: 127–128 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.62–7.56 (m, 4H), 7.46 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.38–7.33 (m, 2H), 7.29–7.25 (m, 2H), 2.46 (s, 3H), 2.42 (s, 3H).

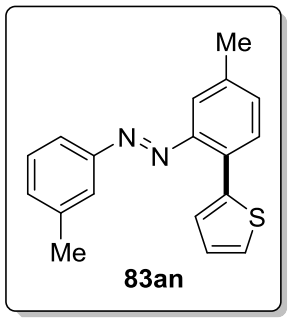
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.9 (C_q), 149.1 (C_q), 139.1 (C_q), 139.0 (C_q), 138.8 (C_q), 136.0 (C_q), 132.6 (CH), 131.9 (CH), 131.8 (CH), 131.7 (C_q), 131.3 (C_q), 130.2 (CH), 130.1 (CH), 129.4 (CH), 129.0 (CH), 123.7 (CH), 120.5 (CH), 116.2 (CH), 21.4 (CH_3), 21.2 (CH_3).

IR (ATR): 3026, 2918, 2858, 1601, 1463, 1371, 1133, 1027, 882, 826, 808, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity): 354 ([M^+] 55), 235 (43), 200 (62), 165 (61), 91 (100), 65 (36).

HR-MS (EI) *m/z* for $C_{20}H_{16}Cl_2N_2$ [M^+] calcd.: 354.0691.
found: 354.0686.

Synthesis of (*E*)-1-{5-Methyl-2-(thiophen-2-yl)phenyl}-2-(*m*-tolyl)diazene (83an)



83an

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 2-bromothiophene (**52n**) (82 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83an** (91 mg, 62%) as a viscous orange liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.83 (d, J = 8.7 Hz, 1H), 7.74 (m, 2H), 7.55–7.29 (m, 6H), 7.14 (dd, J = 5.2, 3.8 Hz, 1H), 2.48 (s, 3H), 2.45 (s, 3H).

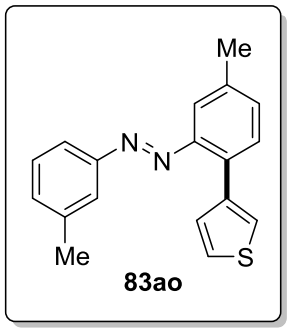
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.8 (C_q), 148.3 (C_q), 139.8 (C_q), 138.9 (C_q), 137.9 (C_q), 131.8 (CH), 131.6 (CH), 130.9 (C_q), 128.8 (CH), 128.3 (CH), 126.8 (CH), 124.7 (CH), 122.8 (CH), 120.6 (CH), 120.4 (CH), 116.2 (CH), 21.3 (CH_3), 21.1 (CH_3).

IR (ATR): 3050, 2917, 2858, 1599, 1482, 1240, 1083, 814, 790, 695, 515, 446 cm^{-1}.

MS (EI) *m/z* (relative intensity): 292 ([M^+] 40), 259 (33), 173 (47), 129 (35), 91 (100), 65 (31).

HR-MS (EI) *m/z* for $C_{18}H_{16}N_2S$ [M^+] calcd.: 292.1034.
found: 292.1023.

Synthesis of (*E*)-1-{5-Methyl-2-(thiophen-3-yl)phenyl}-2-(*m*-tolyl)diazene (83ao)



83ao

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 3-bromothiophene (**52o**) (82 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ao** (75 mg, 51%) as a viscous orange liquid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.67 (m, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.51–7.46 (m, 1H), 7.39 (d, J = 7.7 Hz, 1H), 7.36–7.33 (m, 3H), 7.31 (ddd, J = 7.9, 1.9, 0.7 Hz, 1H), 7.27 (d, J = 7.5 Hz, 1H), 2.45 (s, 3H), 2.43 (s, 3H).

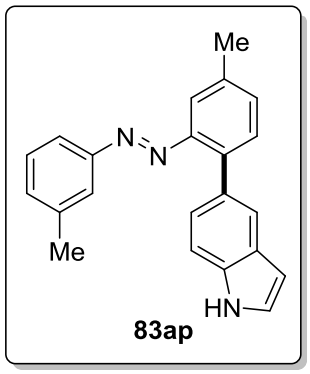
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 153.0 (C_q), 149.6 (C_q), 139.0 (C_q), 139.0 (C_q), 137.8 (C_q), 132.6 (C_q), 131.7 (CH), 131.7 (CH), 129.9 (CH), 129.9 (CH), 128.9 (CH), 124.8 (CH), 124.3 (CH), 124.1 (CH), 120.3 (CH), 116.3 (CH), 21.4 (CH_3), 21.2 (CH_3).

IR (ATR): 3089, 3025, 2913, 2855, 1607, 1494, 1190, 1082, 861, 824, 783, 741 cm^{-1}.

MS (EI) *m/z* (relative intensity): 292 ([M^+] 100), 173 (68), 129 (40), 91 (79), 65 (23).

HR-MS (EI) *m/z* for $C_{18}H_{16}N_2S$ [M^+] calcd.: 292.1034.
found: 292.1024.

Synthesis of (*E*)-5-{4-Methyl-2-(*m*-tolyldiazenyl)phenyl}-1*H*-indole (83ap)



83ap

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 5-bromo-1*H*-indole (**52p**) (98 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83ap** (88 mg, 54%) as a yellow solid.

M. p.: 72–73 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.17 (bs, 1H), 7.77–7.70 (m, 1H), 7.64–7.51 (m, 3H), 7.40 (ddd, J = 8.4, 0.8, 0.8 Hz, 1H), 7.35 (ddd, J = 7.8, 1.8, 0.6 Hz, 1H), 7.32–7.28 (m, 2H), 7.26–7.18 (m, 4H), 2.46 (s, 3H), 2.36 (s, 3H).

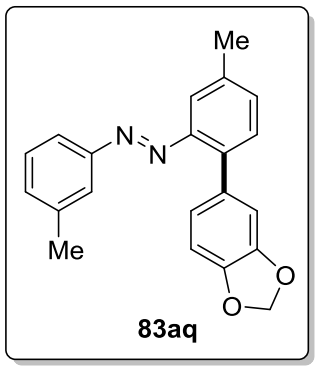
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 153.1 (C_q), 149.8 (C_q), 139.3 (C_q), 138.8 (C_q), 137.1 (C_q), 135.1 (C_q), 131.5 (CH), 131.3 (CH), 131.1 (CH), 130.5 (C_q), 128.8 (CH), 127.7 (C_q), 125.8 (CH), 124.5 (CH), 123.9 (CH), 123.1 (CH), 120.3 (CH), 116.1 (CH), 109.9 (CH), 103.1 (CH), 21.3 (CH_3), 21.1 (CH_3).

IR (ATR): 3089, 3025, 2913, 2855, 1607, 1494, 1480, 1190, 1082, 861, 824, 783, 741, 684 cm^{-1}.

MS (EI) *m/z* (relative intensity): 325 ([M^+] 100), 219 (25), 204 (21), 191 (27), 179 (48), 91 (21).

HR-MS (EI) *m/z* for $C_{22}H_{19}N_3$ [M^+] calcd.: 325.1579.
found: 325.1580.

Synthesis of (*E*)-1-{2-(Benzo[*d*][1,3]dioxol-5-yl)-5-methylphenyl}-2-(*m*-tolyl)diazene (83aq)



The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 5-bromobenzo[*d*][1,3]dioxole (**52q**) (101 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83aq** (122 mg, 74%) as an orange solid.

M. p.: 131–132 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.63 (d, *J* = 0.7 Hz, 1H), 7.61 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.50 (d, *J* = 0.7 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.36 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.32 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 1H), 7.25 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 1H), 6.99 (dd, *J* = 1.6, 0.7 Hz, 1H), 6.87 (d, *J* = 1.6 Hz, 1H), 6.86 (d, *J* = 0.7 Hz, 1H), 6.00 (s, 2H), 2.44 (s, 3H), 2.41 (s, 3H).

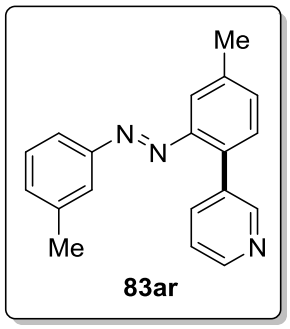
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 153.1 (C_q), 149.7 (C_q), 147.3 (C_q), 147.0 (C_q), 139.0 (C_q), 137.9 (C_q), 137.8 (C_q), 132.8 (C_q), 131.6 (CH), 131.5 (CH), 130.6 (CH), 128.9 (CH), 124.8 (CH), 124.0 (CH), 120.3 (CH), 116.3 (CH), 111.3 (CH), 107.6 (CH), 101.1 (CH_2), 21.3 (CH_3), 21.0 (CH_3).

IR (ATR): 2914, 1475, 1338, 1217, 1035, 935, 801, 686, 637, 530 cm^{-1}.

MS (EI) *m/z* (relative intensity): 330 ([M^+] 60), 329 (100), 224 (29), 181 (29), 153 (53), 91 (44), 65 (16), 43 (15).

HR-MS (EI) *m/z* for $C_{21}H_{18}N_2O_2$ [M^+] calcd.: 330.1368.
found: 330.1360.

Synthesis of (*E*)-3-{4-Methyl-2-(*m*-tolyldiazenyl)phenyl}pyridine (83ar)



The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 3-bromopyridine (**52r**) (79 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc/NEt_3: 88/6/6) yielded **83ar** (45 mg, 31%) as an orange solid.

M. p.: 107–108 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.73 (dd, *J* = 2.4, 0.7 Hz, 1H), 8.58 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.75 (ddd, *J* = 7.9, 2.4, 1.7 Hz, 1H), 7.61–7.57 (m, 2H), 7.56 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.38 (ddd, *J* = 7.8, 1.8, 0.7 Hz, 1H), 7.35–7.31 (m, 2H), 7.25 (ddd, *J* = 7.8, 1.8, 0.7 Hz, 1H), 2.47 (s, 3H), 2.39 (s, 3H).

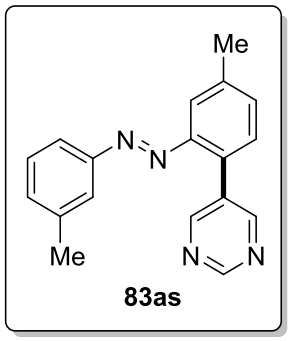
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 152.8 (C_q), 151.0 (CH), 149.4 (C_q), 148.1 (CH), 139.1 (C_q), 139.0 (C_q), 137.9 (CH), 135.1 (C_q), 134.6 (C_q), 132.0 (CH), 131.9 (CH), 130.5 (CH), 128.9 (CH), 124.1 (CH), 122.5 (CH), 120.1 (CH), 116.3 (CH), 21.3 (CH_3), 21.2 (CH_3).

IR (ATR): 3023, 2917, 1412, 997, 829, 799, 709, 689, 626, 487 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287 ([M^+] 63), 286 (81), 168 (76), 91 (100), 65 (35), 43 (58).

HR-MS (EI) *m/z* for $C_{19}H_{17}N_3$ [M^+] calcd.: 287.1422.
found: 287.1409.

Synthesis of (*E*)-5-{4-Methyl-2-(*m*-tolyldiazenyl)phenyl}pyrimidine (83as)



83as

The general procedure **D** was followed using **13a** (210 mg, 1.00 mmol) and 5-bromopyrimidine (**52s**) (79 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc/NEt_3: 88/6/6) yielded **83as** (40 mg, 28%) as an orange solid.

M. p.: 126–127 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 9.18 (s, 1H), 8.85 (s, 2H), 7.67 (d, J = 0.7 Hz, 1H), 7.59 (d, J = 0.7 Hz, 1H), 7.56 (ddd, J = 7.7, 1.9, 0.7 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.42 (dd, J = 7.8, 0.7 Hz, 1H), 7.34 (dd, J = 7.7, 7.7 Hz, 1H), 7.26 (ddd, J = 7.7, 1.9, 0.7 Hz, 1H), 2.48 (s, 3H), 2.40 (s, 3H).

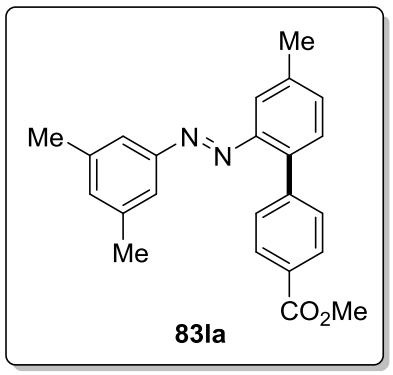
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 157.5 (CH), 157.0 (CH), 152.7 (C_q), 149.2 (C_q), 140.2 (C_q), 139.1 (C_q), 132.6 (C_q), 132.4 (CH), 132.3 (CH), 131.7 (C_q), 130.1 (CH), 129.1 (CH), 124.2 (CH), 120.1 (CH), 116.5 (CH), 21.4 (CH_3), 21.3 (CH_3).

IR (ATR): 3052, 2918, 1547, 1410, 999, 825, 786, 722, 686, 532 cm^{-1}.

MS (EI) *m/z* (relative intensity): 288 ([M^+] 29), 261 (35), 142 (29), 115 (32), 91 (100), 65 (35), 43 (86).

HR-MS (EI) *m/z* for $C_{18}H_{16}N_4$ [M^+] calcd.: 288.1375.
found: 288.1371.

Synthesis of Methyl (*E*)-2'-{(3,5-dimethylphenyl)diazenyl}-4'-methyl-[1,1'-biphenyl]-4-carboxylate (83la)



83la

The general procedure **D** was followed using **13l** (224 mg, 1.00 mmol) and methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2: 7/3) yielded **83la** (168 mg, 94%) as an orange solid.

M. p.: 159–160 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.08 (d, J = 8.5 Hz, 2H), 7.54–7.51 (m, 3H), 7.46 (d, J = 7.8 Hz, 1H), 7.39 (s, 2H), 7.35 (dd, J = 7.8, 1.2 Hz, 1H), 7.10–7.07 (m, 1H), 3.94 (s, 3H), 2.46 (s, 3H), 2.35 (s, 6H).

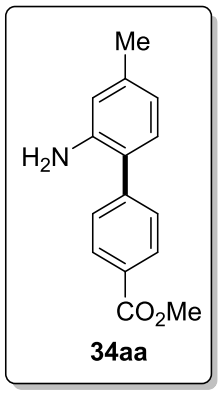
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 167.2 (C_q), 153.0 (C_q), 149.6 (C_q), 143.7 (C_q), 138.9 (C_q), 138.7 (C_q), 137.0 (C_q), 132.7 (CH), 131.5 (CH), 130.8 (CH), 130.5 (CH), 128.8 (CH), 128.6 (C_q), 121.0 (CH), 116.3 (CH), 52.1 (CH_3), 21.3 (CH_3), 21.2 (CH_3).

IR (ATR): 2951, 2915, 2854, 1720, 1606, 1438, 1278, 1105, 859, 829, 775, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity): 358 ([M^+] 61), 343 (59), 299 (27), 225 (36), 165 (72), 105 (100), 77 (25).

HR-MS (ESI) *m/z* for $C_{23}H_{22}N_2O_2$ [$M+H^+$] calcd.: 359.1754.
found: 359.1754.

Synthesis of Methyl 2'-amino-4'-methyl-[1,1'-biphenyl]-4-carboxylate (34aa)



The general procedure **E** was followed using **13a** (210 mg, 1.00 mmol), methyl 4-bromobenzoate (**52a**) (108 mg, 0.50 mmol), Zn (164 mg, 2.50 mmol) and HCl (0.40 mL). Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **34aa** (101 mg, 84%) as a colorless solid.

M. p.: 136–137 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.08 (d, J = 8.6 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 7.7 Hz, 1H), 6.65 (ddd, J = 7.7, 1.6, 0.7 Hz, 1H), 6.59 (s, 1H), 3.92 (s, 3H), 3.71 (s, 2H), 2.30 (s, 3H).

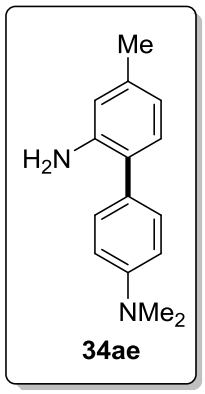
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.9 (C_q), 144.5 (C_q), 143.2 (C_q), 139.2 (C_q), 130.2 (CH), 130.0 (CH), 129.0 (CH), 128.6 (C_q), 123.7 (C_q), 119.8 (CH), 116.5 (CH), 52.1 (CH_3), 21.2 (CH_3).

IR (ATR): 3442, 3360, 2947, 2915, 2164, 1703, 1604, 1435, 1280, 1178, 1103, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 241 ([M^+] 100), 210 (31), 167 (35), 84 (24), 49 (38).

HR-MS (EI) *m/z* for $C_{15}H_{15}NO_2$ [M^+] calcd.: 241.1103.
found: 241.1109.

Synthesis of *N*4',*N*4',4-Trimethyl-[1,1'-biphenyl]-2,4'-diamine (34ae)



34ae

The general procedure **E** was followed using **13a** (210 mg, 1.00 mmol), 4-bromo-*N*,*N*-dimethylaniline (**52e**) (100 mg, 0.50 mmol), Zn (164 mg, 2.50 mmol) and HCl (0.40 mL). Purification by column chromatography (*n*-hexane/EtOAc: 1/1) yielded **34ae** (59 mg, 52%) as a colorless solid.

M. p.: 122–123 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.31 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 7.6 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 6.62 (ddd, J = 7.6, 1.5, 0.6 Hz, 1H), 6.58 (s, 1H), 3.65 (s, 2H), 2.97 (s, 6H), 2.28 (s, 3H).

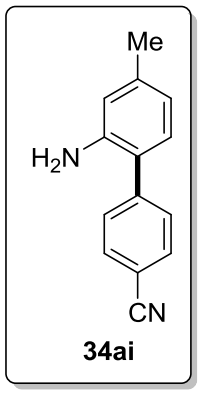
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 149.4 (C_q), 143.5 (C_q), 137.6 (C_q), 130.3 (CH), 129.8 (CH), 127.6 (C_q), 125.2 (C_q), 119.5 (CH), 116.2 (CH), 112.9 (CH), 40.7 (CH_3), 21.2 (CH_3).

IR (ATR): 3443, 3360, 2917, 1605, 1527, 1499, 1219, 1060, 944, 802 cm^{-1}.

MS (EI) *m/z* (relative intensity): 226 ([M^+] 100), 211 (14), 182 (12), 113 (10).

HR-MS (EI) *m/z* for $C_{15}H_{18}N_2$ [M^+] calcd.: 226.1470.
found: 226.1465.

Synthesis of 2'-Amino-4'-methyl-[1,1'-biphenyl]-4-carbonitrile (34ai)



34ai

The general procedure **E** was followed using **13a** (210 mg, 1.00 mmol), 4-bromobenzonitrile (**52i**) (91 mg, 0.50 mmol), Zn (164 mg, 2.50 mmol) and HCl (0.40 mL). Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **34ai** (64 mg, 61%) as a colorless solid.

M. p.: 121–122 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.69 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 7.7 Hz, 1H), 6.66 (ddd, J = 7.7, 1.6, 0.7 Hz, 1H), 6.60 (s, 1H), 3.75 (s, 2H), 2.30 (s, 3H).

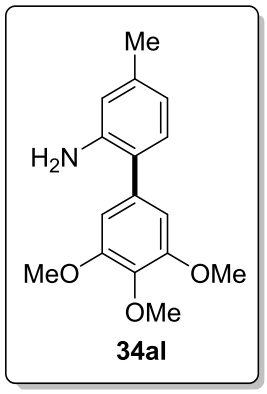
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 144.6 (C_q), 143.0 (C_q), 139.7 (C_q), 132.5 (CH), 130.1 (CH), 129.8 (CH), 122.8 (C_q), 120.1 (CH), 118.9 (C_q), 116.7 (CH), 110.5 (C_q), 21.2 (CH_3).

IR (ATR): 3441, 3363, 2297, 2228, 1618, 1512, 1490, 1399, 1170, 1003, 843 cm^{-1}.

MS (EI) *m/z* (relative intensity): 208 ([M^+] 100), 192 (19), 43 (10).

HR-MS (EI) *m/z* for $C_{14}H_{12}N_2$ [M^+] calcd.: 208.1000.
found: 208.0999.

Synthesis of 3',4',5'-Trimethoxy-4-methyl-[1,1'-biphenyl]-2-amine (34al)



34al

The general procedure **E** was followed using **13a** (210 mg, 1.00 mmol), 5-bromo-1,2,3-trimethoxybenzene (**52l**) (124 mg, 0.50 mmol), Zn (164 mg, 2.50 mmol) and HCl (0.40 mL). Purification by column chromatography (*n*-hexane/EtOAc: 1/1) yielded **34al** (115 mg, 84%) as a colorless solid.

M. p.: 136–137 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.02 (d, J = 7.6 Hz, 1H), 6.64 (s, 2H), 6.63 (dd, J = 7.7, 0.6 Hz, 1H), 6.59 (s, 1H), 3.88 (s, 3H), 3.85 (s, 6H), 3.73 (s, 2H), 2.29 (s, 3H).

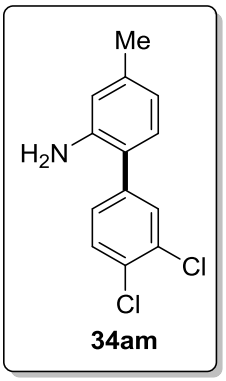
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 153.3 (C_q), 143.2 (C_q), 138.4 (C_q), 136.9 (C_q), 135.0 (C_q), 130.0 (CH), 124.9 (C_q), 119.4 (CH), 116.2 (CH), 106.1 (CH), 60.8 (CH_3), 56.1 (CH_3), 21.1 (CH_3).

IR (ATR): 3421, 3350, 2960, 2834, 1583, 1449, 1237, 1117, 1025, 834 cm^{-1}.

MS (EI) *m/z* (relative intensity): 273 ([M^+] 100), 258 (71), 198 (14), 144 (16), 43 (12).

HR-MS (EI) *m/z* for $C_{16}H_{19}NO_3$ [M^+] calcd.: 273.1365.
found: 273.1372.

Synthesis of 3',4'-Dichloro-4-methyl-[1,1'-biphenyl]-2-amine (34am)



34am

The general procedure **E** was followed using **13a** (210 mg, 1.00 mmol), 4-bromo-1,2-dichlorobenzene (**52m**) (113 mg, 0.50 mmol), Zn (164 mg, 2.50 mmol) and HCl (0.40 mL). Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **34am** (76 mg, 60%) as a colorless solid.

M. p.: 125–126 °C.

^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 7.64 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.37 (dd, J = 8.3, 2.1 Hz, 1H), 6.88 (d, J = 7.8 Hz, 1H), 6.58 (s, 1H), 6.46 (ddd, J = 7.8, 1.3, 0.6 Hz, 1H), 4.82 (s, 2H), 2.19 (s, 3H).

^{13}C-NMR (DMSO-d_6, 126 MHz): δ = 144.9 (C_q), 140.5 (C_q), 138.1 (C_q), 131.1 (C_q), 130.6 (CH), 130.4 (CH), 129.8 (CH), 129.0 (CH), 128.9 (C_q), 120.5 (C_q), 117.8 (CH), 116.0 (CH), 20.8 (CH_3).

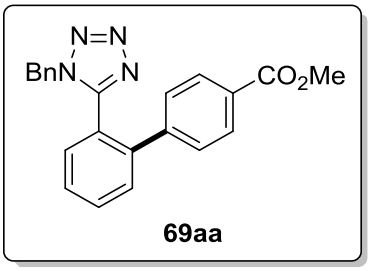
IR (ATR): 3462, 3376, 2922, 2853, 1616, 1465, 1373, 1132, 1029, 827 cm^{-1}.

MS (EI) *m/z* (relative intensity): 251 ([M^+] 100), 215 (24), 181 (35), 84 (27), 58 (18).

HR-MS (EI) *m/z* for $C_{13}H_{11}Cl_2N$ [M^+] calcd.: 251.0269.
found: 251.0264.

Synthesis of Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-[1,1'-biphenyl]-4-carboxylate (69aa) and Dimethyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (69aa')

The general procedure **F** was followed using **68a** (70.9 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **69aa** (86 mg, 77%) and **69aa'** (15 mg, 10%) as colorless solids.



69aa

M. p.: 109–110 °C.

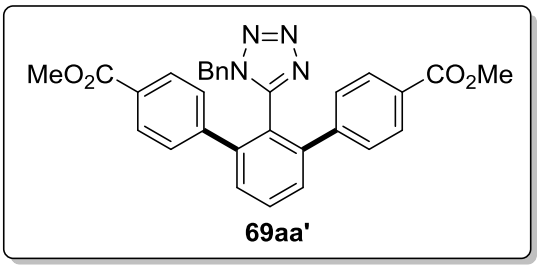
^{1}H-NMR ($CDCl_3$, 500 MHz): 7.90 (d, *J* = 8.4 Hz, 2H), 7.64 (ddd, *J* = 7.6, 7.6, 1.4 Hz, 1H), 7.56 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.46 (ddd, *J* = 7.6, 7.6, 1.4 Hz, 1H), 7.35 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.19 (tt, *J* = 7.4, 1.8 Hz, 1H), 7.15–7.10 (m, 4H), 6.75 (d, *J* = 8.4 Hz, 2H), 4.83 (s, 2H), 3.90 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.4 (C_q), 154.2 (C_q), 143.2 (C_q), 140.7 (C_q), 132.9 (C_q), 131.6 (CH), 131.2 (CH), 130.2 (CH), 130.0 (CH), 129.6 (C_q), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 122.7 (C_q), 52.3 (CH_3), 50.9 (CH_2).

IR (ATR): 2951, 1717, 1435, 1403, 1278, 1103, 1007, 911, 753, 723 cm^{-1}.

MS (EI) *m/z* (relative intensity): 370 ([M^+] 19), 369 (58), 341 (14), 164 (17), 91 (100), 65 (14).

HR-MS (ESI) *m/z* for $C_{22}H_{19}N_4O_2$ [$M+H^+$] calcd.: 371.1503.
found: 371.1503.



69aa'

M. p.: 180–181 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): 7.82 (d, *J* = 8.6 Hz, 4H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.24 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.13 (dd, *J* = 7.8, 7.8 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 4H), 6.68 (dd, *J* = 7.8, 1.2 Hz, 2H), 4.69 (s, 2H), 3.88 (s, 6H).

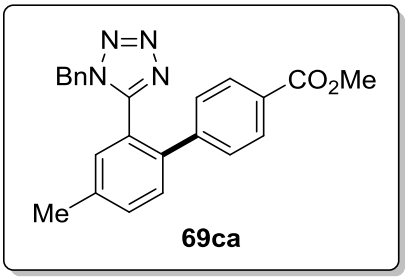
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.5 (C_q), 152.3 (C_q), 143.1 (C_q), 142.7 (C_q), 132.3 (C_q), 131.5 (CH), 130.0 (CH), 129.6 (CH), 129.5 (C_q), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.1 (CH), 121.3 (C_q), 52.2 (CH_3), 50.8 (CH_2).

IR (ATR): 2951, 1719, 1433, 1271, 1100, 1017, 864, 769, 721, 704 cm^{-1}.

MS (EI) *m/z* (relative intensity): 504 ([M^+] 44), 503 (51), 325 (23), 239 (27), 91 (100), 58 (33).

HR-MS (ESI) *m/z* for $C_{30}H_{25}N_4O_4$ [M+H^+] calcd.: 505.1870.
found: 505.1868.

Synthesis of Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-4'-methyl-[1,1'-biphenyl]-4-carboxylate (69ca)



69ca

The general procedure **F** was followed using **68c** (75.1 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (CH_2Cl_2/EtOAc: 24/1) yielded **69ca** (103 mg, 89%) as a colorless solid.

M. p.: 111–112 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.87 (d, J = 8.4 Hz, 2H), 7.46–7.39 (m, 2H), 7.21–7.05 (m, 6H), 6.73 (d, J = 8.4 Hz, 2H), 4.79 (s, 2H), 3.87 (s, 3H), 2.35 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.3 (C_q), 154.3 (C_q), 143.2 (C_q), 138.6 (C_q), 137.8 (C_q), 132.9 (C_q), 132.3 (CH), 131.7 (CH), 130.1 (CH), 129.9 (CH), 129.4 (C_q), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.6 (CH), 122.5 (C_q), 52.2 (CH_3), 50.9 (CH_2), 20.9 (CH_3).

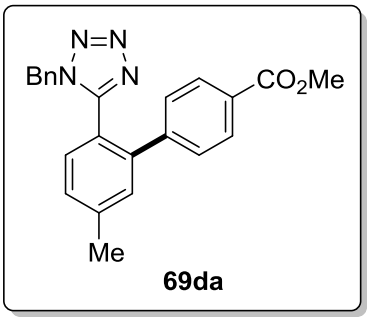
IR (ATR): 2951, 1712, 1606, 1434, 1275, 1185, 866, 823, 776, 727 cm^{-1}.

MS (EI) *m/z* (relative intensity): 384 ([M^+] 27), 383 (71), 355 (19), 178 (15), 91 (100), 65 (14).

HR-MS (EI) *m/z* for $C_{23}H_{20}N_4O_2$ [M^+] calcd.: 384.1586.
found: 384.1574.

Synthesis of Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-5'-methyl-[1,1'-biphenyl]-4-carboxylate (69da) and Dimethyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-5'-methyl-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (69da')

The general procedure **F** was followed using **68d** (75.1 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (CH_2Cl_2/EtOAc: 24/1) yielded **69da** (72 mg, 62%) and **69da'** (24 mg, 15%) as colorless solids.



69da

M. p.: 125–126 °C.

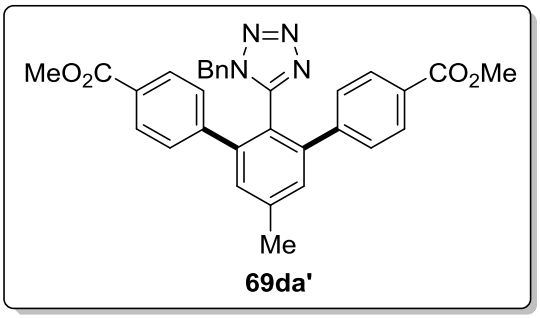
^{1}H-NMR ($CDCl_3$, 300 MHz): 7.88 (d, *J* = 8.4 Hz, 2H), 7.36 (s, 1H), 7.30–7.08 (m, 7H), 7.16 (d, *J* = 8.4 Hz, 2H), 4.81 (s, 2H), 3.89 (s, 3H), 2.47 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.3 (C_q), 154.2 (C_q), 143.3 (C_q), 141.9 (C_q), 140.5 (C_q), 132.9 (C_q), 131.0 (CH), 130.9 (CH), 129.9 (CH), 129.5 (C_q), 129.1 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.6 (CH), 119.7 (C_q), 52.2 (CH_2), 50.8 (CH_3), 21.5 (CH_3).

IR (ATR): 2951, 1718, 1435, 1277, 1182, 1102, 859, 823, 721, 705 cm^{-1}.

MS (EI) *m/z* (relative intensity): 384 ([M^+] 31), 383 (76), 355 (23), 178 (19), 91 (100), 65 (14), 43 (19).

HR-MS (ESI) *m/z* for $C_{23}H_{21}N_4O_2$ [$M+H^+$] calcd.: 385.1659.
found: 385.1663.



69da'

M. p.: 194–195 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): 7.80 (d, *J* = 8.6 Hz, 4H), 7.33 (s, 2H), 7.22 (tt, *J* = 7.4, 1.4 Hz, 1H), 7.12 (dd, *J* = 7.6, 7.6 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 4H), 6.68 (dd, *J* = 7.8, 1.2 Hz, 2H), 4.67 (s, 2H), 3.87 (s, 6H), 2.53 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.3 (C_q), 152.3 (C_q), 143.2 (C_q), 142.4 (C_q), 141.7 (C_q), 132.4 (C_q), 130.6 (CH), 129.4 (CH), 129.3 (C_q), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.9 (CH), 118.3 (C_q), 52.2 (CH_3), 50.7 (CH_2), 21.5 (CH_3).

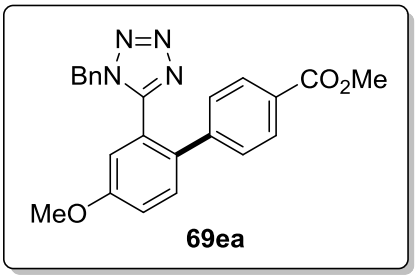
IR (ATR): 2949, 1711, 1610, 1435, 1269, 1183, 1110, 1017, 856, 723 cm^{-1}.

MS (EI) *m/z* (relative intensity): 518 ([M^+] 67), 517 (84), 339 (23), 253 (27), 91 (100), 43 (51).

HR-MS (ESI) *m/z* for $C_{31}H_{27}N_4O_4$ [$M+H^+$] calcd.: 519.2027.
found: 519.2015.

Synthesis of Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (69ea) and Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-6'-methoxy-[1,1'-biphenyl]-4-carboxylate (69ea'')

The general procedure **F** was followed using **68e** (79.9 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **69ea** (71 mg, 59%) and **69ea''** (11 mg, 9%) as colorless solids.



69ea

M. p.: 128–129 °C.

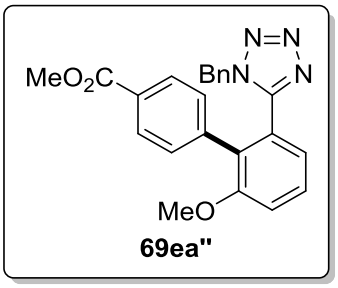
^{1}H-NMR ($CDCl_3$, 300 MHz): 7.89 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.20–7.08 (m, 6H), 6.80 (d, *J* = 2.7 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 4.80 (s, 2H), 3.88 (s, 3H), 3.75 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.5 (C_q), 159.4 (C_q), 154.2 (C_q), 143.0 (C_q), 132.9 (C_q), 132.8 (C_q), 131.5 (CH), 130.0 (CH), 129.1 (C_q), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 123.7 (C_q), 118.0 (CH), 115.7 (CH), 55.6 (CH_3), 52.2 (CH_3), 50.9 (CH_2).

IR (ATR): 2951, 1716, 1607, 1435, 1274, 1224, 1103, 1023, 826, 719 cm^{-1}.

MS (EI) *m/z* (relative intensity): 400 ([M^+] 17), 399 (42), 371 (12), 91 (100), 65 (13).

HR-MS (ESI) *m/z* for $C_{23}H_{21}N_4O_3$ [$M+H^+$] calcd.: 401.1608.
found: 401.1610.



69ea"

M. p.: 121–122 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): 7.86 (d, *J* = 8.4 Hz, 2H), 7.43 (dd, *J* = 8.4, 7.7 Hz, 1H), 7.22 (tt, *J* = 7.4, 1.4 Hz, 1H), 7.20–7.15 (m, 3H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.93 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.83 (dd, *J* = 8.4, 1.4 Hz, 2H), 4.91 (s, 2H), 3.88 (s, 3H), 3.80 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.6 (C_q), 156.8 (C_q), 153.8 (C_q), 139.1 (C_q), 133.1 (C_q), 130.3 (CH), 130.0 (C_q), 129.7 (CH), 129.3 (C_q), 129.2 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 124.8 (C_q), 122.8 (CH), 113.8 (CH), 56.0 (CH_3), 52.2 (CH_3), 50.9 (CH_2).

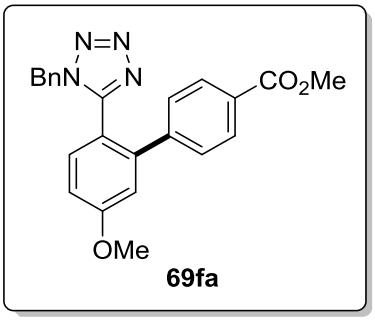
IR (ATR): 2952, 1713, 1609, 1460, 1263, 1101, 1027, 801, 774, 754 cm^{-1}.

MS (EI) *m/z* (relative intensity): 400 ([M^+] 40), 399 (83), 371 (17), 91 (100), 65 (12).

HR-MS (ESI) *m/z* for $C_{23}H_{21}N_4O_3$ [$M+H^+$] calcd.: 401.1608.
found: 401.1600.

Synthesis of Methyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-5'-methoxy-[1,1'-biphenyl]-4-carboxylate (69fa) and Dimethyl 2'-(1-benzyl-1*H*-tetrazol-5-yl)-5'-methoxy-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (69fa')

The general procedure **F** was followed using **68f** (79.9 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (CH_2Cl_2/EtOAc: 24/1) yielded **69fa** (84 mg, 70%) and **69fa'** (19 mg, 12%) as colorless solids.



69fa

M. p.: 143–144 °C.

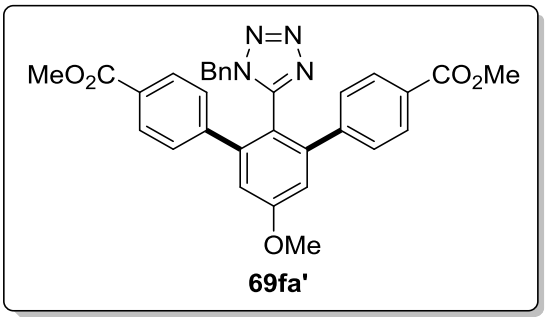
^{1}H-NMR ($CDCl_3$, 300 MHz): 7.88 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 1H), 7.18 (tt, *J* = 7.4, 1.4 Hz, 1H), 7.15–7.20 (m, 4H), 7.04 (d, *J* = 2.6 Hz, 1H), 6.97 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 2H), 4.81 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.4 (C_q), 161.8 (C_q), 154.1 (C_q), 143.2 (C_q), 142.3 (C_q), 133.0 (C_q), 132.6 (CH), 130.0 (CH), 129.6 (C_q), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.6 (CH), 115.8 (CH), 114.5 (C_q), 113.8 (CH), 55.6 (CH_3), 52.2 (CH_3), 50.7 (CH_2).

IR (ATR): 2947, 1720, 1607, 1436, 1288, 1213, 1107, 1012, 855, 725 cm^{-1}.

MS (EI) *m/z* (relative intensity): 400 ([M^+] 22), 399 (62), 371 (23), 91 (100), 65 (14).

HR-MS (ESI) *m/z* for $C_{23}H_{21}N_4O_3$ [$M+H^+$] calcd.: 401.1608.
found: 401.1610.



69fa'

M. p.: 179–180 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): 7.81 (d, J = 8.6 Hz, 4H), 7.18–7.10 (m, 3H), 7.02 (s, 2H), 7.00–6.97 (m, 4H), 6.70 (dd, J = 7.8, 1.2 Hz, 2H), 4.67 (s, 2H), 3.94 (s, 3H), 3.88 (s, 6H).

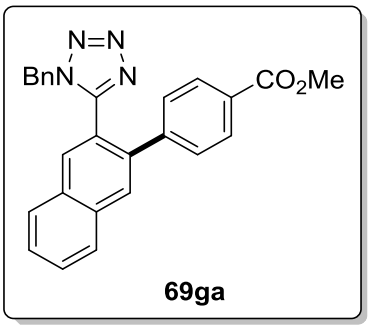
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.3 (C_q), 161.2 (C_q), 152.3 (C_q), 144.2 (C_q), 143.1 (C_q), 132.5 (C_q), 129.5 (C_q), 129.4 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.0 (CH), 115.4 (CH), 113.3 (C_q), 55.8 (CH_3), 52.2 (CH_3), 50.7 (CH_2).

IR (ATR): 2949, 1717, 1594, 1434, 1272, 1178, 1100, 1016, 854, 723 cm^{-1}.

MS (EI) *m/z* (relative intensity): 534 ([M^+] 51), 533 (73), 339 (13), 91 (100), 58 (55).

HR-MS (ESI) *m/z* for $C_{31}H_{27}N_4O_5$ [M+H^+] calcd.: 535.1976.
found: 535.1975.

Synthesis of Methyl 4-{3-(1-benzyl-1*H*-tetrazol-5-yl)naphthalen-2-yl}benzoate (69ga)



69ga

The general procedure **F** was followed using **68g** (85.9 mg, 0.30 mmol) and methyl 4-chlorobenzoate (**59a**) (154 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 7/3) yielded **69ga** (72 mg, 57%) as a colorless solid.

M. p.: 162–163 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.03 (s, 1H), 7.96 (dd, J = 8.3, 1.2 Hz, 1H), 7.93 (d, J = 8.3 Hz, 2H), 7.91 (s, 1H), 7.84 (dd, J = 8.3, 1.2 Hz, 1H), 7.65 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.60 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.24 (d, J = 8.3 Hz, 2H), 7.15 (tt, J = 7.4, 1.3 Hz, 1H), 7.08 (dd, J = 7.3, 7.2 Hz, 2H), 6.75 (dd, J = 8.1, 1.3 Hz, 2H), 4.89 (s, 2H), 3.91 (s, 3H).

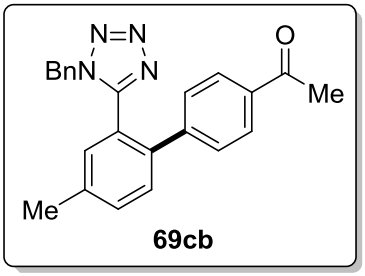
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 166.5 (C_q), 154.4 (C_q), 143.4 (C_q), 137.0 (C_q), 134.2 (C_q), 132.9 (C_q), 132.1 (CH), 132.0 (C_q), 130.1 (CH), 129.8 (CH), 129.5 (C_q), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 128.1 (CH), 127.7 (CH), 127.6 (CH), 120.5 (C_q), 52.3 (CH_3), 51.0 (CH_2).

IR (ATR): 2951, 1708, 1606, 1430, 1277, 1100, 900, 777, 732, 477 cm^{-1}.

MS (EI) *m/z* (relative intensity): 420 ([M^+] 20), 419 (40), 207 (38), 91 (100), 73 (25), 65 (12).

HR-MS (ESI) *m/z* for $C_{26}H_{21}N_4O_2$ [M+H^+] calcd.: 421.1659.
found: 421.1655.

Synthesis of 1-{2'-(1-Benzyl-1*H*-tetrazol-5-yl)-4'-methyl-[1,1'-biphenyl]-4-yl}ethan-1-one (69cb)



69cb

The general procedure **F** was followed using **68c** (75.1 mg, 0.30 mmol) and 1-(4-chlorophenyl)ethan-1-one (**59b**) (139 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **69cb** (92 mg, 83%) as a colorless solid.

M. p.: 128–129 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.79 (d, J = 8.5 Hz, 2H), 7.44 (s, 1H), 7.44 (s, 1H), 7.18 (tt, J = 7.3, 1.3 Hz, 1H), 7.16–7.10 (m, 5H), 6.74 (dd, J = 8.1, 1.3 Hz, 2H), 4.83 (s, 2H), 2.54 (s, 3H), 2.36 (s, 3H).

^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 197.3 (C_q), 154.3 (C_q), 143.4 (C_q), 138.7 (C_q), 137.7 (C_q), 136.0 (C_q), 132.9 (C_q), 132.4 (CH), 131.7 (CH), 130.1 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 122.4 (C_q), 50.9 (CH_2), 26.6 (CH_3), 20.9 (CH_3).

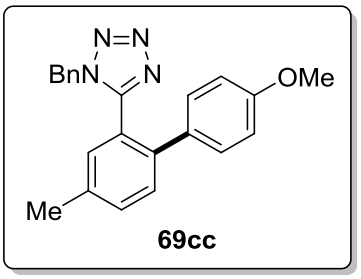
IR (ATR): 2921, 1679, 1605, 1403, 1357, 1265, 1101, 957, 821, 719 cm^{-1}.

MS (EI) *m/z* (relative intensity): 368 ([M^+] 35), 367 (87), 339 (22), 178 (17), 91 (100), 65 (12), 43 (19).

HR-MS (ESI) *m/z* for $C_{23}H_{21}N_4O$ [$M+H^+$] calcd.: 369.1710.
found: 369.1707.

The analytical data are in accordance with those reported in the literature.[118]

Synthesis of 1-Benzyl-5-(4'-methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-1*H*-tetrazole (69cc)



69cc

The general procedure **F** was followed using **68c** (75.1 mg, 0.30 mmol) and 1-chloro-4-methoxybenzene (**59c**) (128 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **69cc** (90 mg, 84%) as a colorless solid.

M. p.: 121–122 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.40 (d, J = 7.9 Hz, 1H), 7.37 (dd, J = 8.1, 1.3 Hz, 1H), 7.16 (tt, J = 7.3, 1.3 Hz, 1H), 7.12 (d, J = 7.6 Hz, 2H), 7.10 (s, 1H), 7.02 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 6.73 (dd, J = 8.1, 1.3 Hz, 2H), 4.74 (s, 2H), 3.75 (s, 3H), 2.32 (s, 3H).

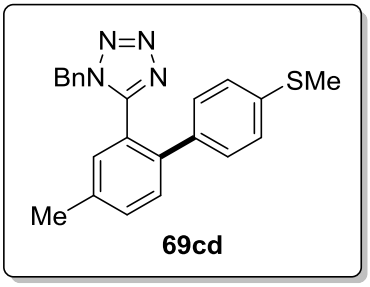
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 159.2 (C_q), 154.9 (C_q), 138.3 (C_q), 137.3 (C_q), 133.1 (C_q), 132.2 (CH), 131.6 (CH), 131.0 (C_q), 129.9 (CH), 129.6 (CH), 128.5 (CH), 128.3 (CH), 127.8 (CH), 122.1 (C_q), 114.3 (CH), 55.2 (CH_3), 50.7 (CH_2), 20.7 (CH_3).

IR (ATR): 2941, 1610, 1484, 1450, 1249, 1180, 1099, 1033, 852, 721 cm^{-1}.

MS (EI) *m/z* (relative intensity): 356 ([M^+] 37), 355 (71), 327 (28), 165 (16), 91 (100), 65 (12).

HR-MS (ESI) *m/z* for $C_{22}H_{21}N_4O$ [$M+H^+$] calcd.: 357.1710.
found: 357.1707.

Synthesis of 1-Benzyl-5-{4-methyl-4'-(methylthio)-[1,1'-biphenyl]-2-yl}-1*H*-tetrazole (69cd)



69cd

The general procedure **F** was followed using **68c** (75.1 mg, 0.30 mmol) and (4-chlorophenyl)(methyl)sulfane (**59d**) (143 mg, 0.90 mmol). Purification by column chromatography (CH_2Cl_2/EtOAc: 24/1) yielded **69cd** (71 mg, 64%) as a pale yellow solid.

M. p.: 116–117 °C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.41 (d, J = 0.7 Hz, 1H), 7.40 (dd, J = 1.7, 0.6 Hz, 1H), 7.18 (tt, J = 7.3, 1.3 Hz, 1H), 7.14 (dd, J = 7.4, 5.6 Hz, 2H), 7.13–7.11 (m, 1H), 7.10 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 8.7 Hz, 2H), 6.73 (dd, J = 8.1, 1.3 Hz, 2H), 4.78 (s, 2H), 2.44 (s, 3H), 2.34 (s, 3H).

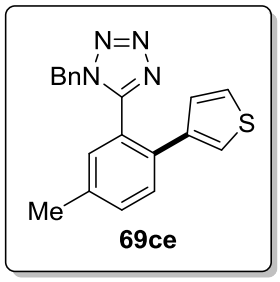
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 154.7 (C_q), 138.8 (C_q), 138.1 (C_q), 137.8 (C_q), 135.1 (C_q), 133.0 (C_q), 132.3 (CH), 131.7 (CH), 129.9 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 127.8 (CH), 126.3 (CH), 122.2 (C_q), 50.8 (CH_2), 20.8 (CH_3), 15.2 (CH_3).

IR (ATR): 2921, 1477, 1439, 1241, 1092, 812, 722, 694, 548, 527 cm^{-1}.

MS (EI) *m/z* (relative intensity): 372 ([M^+] 61), 371 (42), 343 (20), 206 (14), 91 (100), 65 (11), 43 (11).

HR-MS (EI) *m/z* for $C_{22}H_{20}N_4S$ [M^+] calcd.: 372.1409.
found: 372.1414.

Synthesis of 1-Benzyl-5-{5-methyl-2-(thiophen-3-yl)phenyl}-1*H*-tetrazole (69ce)



69ce

The general procedure **F** was followed using **68c** (75.1 mg, 0.30 mmol) and 3-chlorothiophene (**59e**) (107 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 6/1) yielded **69ce** (67 mg, 67%) as a pale yellow solid.

M. p.: 96–97 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.48 (d, J = 7.9 Hz, 1H), 7.37 (dq, J = 7.9, 0.8 Hz, 1H), 7.24 (q, J = 3.0 Hz, 1H), 7.18 (tt, J = 7.3, 1.3 Hz, 1H), 7.16–7.12 (m, 2H), 7.09–7.07 (m, 1H), 6.95 (dd, J = 3.0, 1.4 Hz, 1H), 6.79–6.75 (m, 3H), 4.81 (s, 2H), 2.33 (s, 3H).

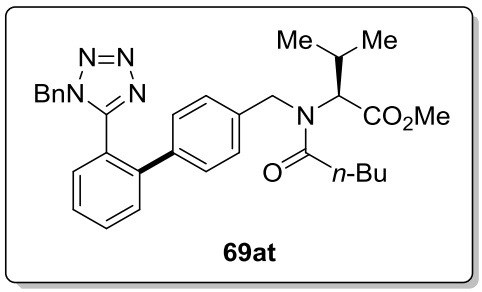
^{13}C-NMR ($CDCl_3$, 126 MHz): δ = 154.7 (C_q), 139.4 (C_q), 137.8 (C_q), 133.5 (C_q), 133.0 (C_q), 132.3 (CH), 131.6 (CH), 129.6 (CH), 128.6 (CH), 128.5 (CH), 127.9 (CH), 127.4 (CH), 126.7 (CH), 123.2 (CH), 122.1 (C_q), 50.8 (CH_2), 20.8 (CH_3).

IR (ATR): 2954, 1482, 1409, 1243, 1103, 853, 802, 728, 695, 647 cm^{-1}.

MS (EI) *m/z* (relative intensity): 332 ([M^+] 26), 213 (24), 198 (20), 185 (42), 91 (100), 65 (25), 43 (18).

HR-MS (EI) *m/z* for $C_{19}H_{16}N_4S$ [M^+] calcd.: 332.1096.
found: 332.1097.

Synthesis of Methyl *N*-{[2'-(1-benzyl-1*H*-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl]methyl}-*N*-pentanoyl-L-valinate (69at)



69at

The general procedure **F** was followed using **68a** (70.9 mg, 0.30 mmol) and aryl chloride **59t** (306 mg, 0.90 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **69at** (117 mg, 72%) as a colorless solid.

Alternatively the general procedure **F** was followed with **68a** (70.9 mg, 0.30 mmol) and aryl bromide **52t** (127 mg, 0.33 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **60at** (144 mg, 89%) as a colorless solid.

M. p.: 74–75 °C.

^{1}H-NMR (DMSO-d_6, 120 °C, 300 MHz): δ = 7.70 (ddd, J = 7.8, 7.6, 1.5 Hz, 1H), 7.58 (dd, J = 7.8, 1.3 Hz, 1H), 7.52 (dd, J = 7.4, 1.3 Hz, 1H), 7.45 (dd, J = 7.6, 1.3 Hz, 1H), 7.31–7.18 (m, 3H), 7.11 (d, J = 8.2 Hz, 2H), 7.01 (d, J = 8.2 Hz, 2H), 6.93–6.85 (m, 2H), 5.08 (s, 2H), 4.69 (d, J = 16.9 Hz, 1H), 4.50 (d, J = 16.9 Hz, 1H), 4.47–4.38 (m, 1H), 3.40 (s, 3H), 2.45–2.20 (m, 3H), 1.63–1.48 (m, 2H), 1.38–1.23 (m, 2H), 0.96 (d, J = 6.5 Hz, 3H), 0.90–0.80 (m, 6H).

^{13}C-NMR (DMSO-d_6, 120 °C, 75 MHz): δ = 172.8 (C_q), 169.7 (C_q), 153.5 (C_q), 140.9 (C_q), 137.3 (C_q), 136.7 (C_q), 133.0 (C_q), 130.7 (CH), 130.1 (CH), 129.6 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.1 (CH), 127.0 (CH), 126.1 (CH), 122.0 (C_q), 50.5 (CH_3), 49.9 (CH_2), 47.0 (CH_2), 31.8 (CH_2), 26.9 (CH), 26.3 (CH_2), 21.0 (CH_2), 18.9 (CH_3), 17.9 (CH_3), 12.8 (CH).

IR (ATR): 2958, 1736, 1648, 1468, 1405, 1202, 1057, 1007, 820, 720 cm^{-1}.

MS (EI) *m/z* (relative intensity): 539 ([M^+] 5), 454 (83), 396 (22), 340 (69), 325 (38), 192 (25), 91 (100), 57 (29).

HR-MS (EI) *m/z* for $C_{32}H_{37}N_5O_3$ [M^+] calcd.: 539.2896.
found: 539.2894.

The analytical data are in accordance with those reported in the literature.[131]

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Publikationen

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