Cobalt- and Nickel-Catalyzed Functionalization of Unactivated C–Hal, C–O and C–H Bonds

Dissertation

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Abbreviation

acac	**acetyl acetonate**
Ad	**adamantyl**
Alk	**alkyl**
APT	**attached proton test**
aq.	**aqueous**
Ar	**aryl**
BDMAE	**bis (2-dimethylaminoethyl) ether**
Bn	**benzyl**
Bu	**butyl**
calc.	**calculated**
cat.	**catalytic**
Cy	**cyclohexyl**
CMD	**concerted metalation deprotonation**
cod	**1,5-cyclooctadiene**
Cp	**cyclopentadienyl**
DCM	**dichloromethane**
DMF	**dimethylformamide**
DG	**directing group**
Diglyme	**1-methoxy-2-(2-methoxyethoxy)ethane**
DME	**dimethoxyethane**
DMSO	**dimethyl sulfoxide**
DoM	**directed *ortho* metalation**
dcype	**1,2-bis(dicyclohexylphosphino)ethane**
dppe	**1,2-bis(diphenylphosphino)ethane**
dppf	**1,1'-bis(diphenylphosphino)-ferrocene**
dppp	**1,3-bis(diphenylphosphino) propane**
DPEphos	**bis[(2-diphenylphosphino)phenyl] ether**
DMPU	***N*,*N*'-dimethyl-*N*,*N*'-propylene urea**
EDG	**electron-donating group**
EI	**electron ionization**
equiv	**equivalent**
ESI	**electrospray ionization**
Et	**ethyl**
EWG	**electron-withdrawing group**
g	**gram**
GC	**gas chromatography**
Het	**hetero**
Hex	**hexyl**
HR	**high resolution**
Hz	**Hertz**
Hept	**heptyl**
(HA)SPO	**(heteroatom) substituted secondary**

(Het)Ar	**(hetero)arene**
I	**intensity**
i	***iso***
i.e.	***id est***
IPr	**1,3-bis(2,6-diisopropylphenyl)**
IR	**infrared spectroscopy**
J	**coupling constant**
KIE	**kinetic isotope effect**
L	**ligand**
LiHMDS	**Lithium bis(trimethylsilyl)amide**
mmol	**millimol**
MS	**mass spectrometry**
MS	**molecular sieves**
M	**metal**
M	**molar**
$[M]^+$	**molecular ion peak**
m	**multiplett**
M.p.	**melting point**
M.r.	**melting range**
m/z	**mass-to-charge ratio**
Me	**methyl**
Mes	**mesityl**
Mg	**milligram**
MHz	**megahertz**
mL	**milliliter**
m	***meta***
MTBE	**methyl *tert*-butyl ether**
N_2	**nitrogen**
NMP	***N*-methyl-2-pyrrolidone**
Ph	**phenyl**
Py	**2-pyridyl**
Pym	**2-pyrimidyl**
S-phos	**2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl**
tol	**tolyl**
Ts	***para*-toluenesulfonyl**
TEMPO	***(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl***
T	**temperature**
Tf	**trifluoromethanesulfonyl**
X	**(pseudo)halide**
X-phos	**2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl**
Xantphos	**4,5-bis(diphenylphosphino)-9,9-dimethylxanthene**

1. Introduction

1.1 Metal-Catalyzed C–H bonds Functionalization

During the past few decades, transition-metal catalysis has experienced an exponential growth in organic synthesis. It was shown great importance in many research areas and applied fileds, such as petroleum, chemical, energy, environmental and pharmaceutical sectors.[1] Especially the transition-metal-catalyzed C–C bond formation reactions have attracted significant attention around the world for almost half a century. The most famous transformation in this research area is arguably the transition-metal-catalyzed cross-coupling reaction.[2] Today, traditional cross-coupling chemistry is widely applied as a powerful synthetic tool in preparative organic chemistry. However, the formation of stoichiometric amounts of potentially harmful metal salts as by-products and the necessity of pre-functionalization of the substrates prove to be disadvantageous. To improve the atom- and setp-economy[3] of organic synthesis, more and more attentions are paid on direct functionalization of the otherwise inert C–H bonds (438.9 $kJ \cdot mol^{-1}$ for sp^3-hybridized bond in CH_4, 472.4 $kJ \cdot mol^{-1}$ for sp^2-hybridized bond in PhH)[4] in the past decade.[5]

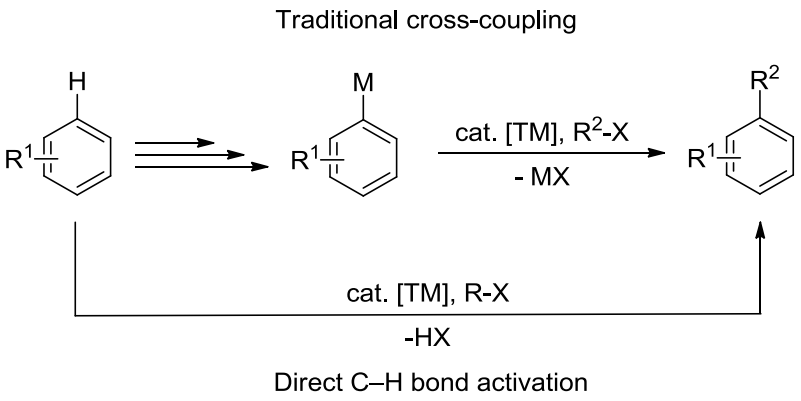
[1] a) *Modern Arylation Methods,* (Eds: L. Ackermann), Wiley-VCH, Weinheim, **2009**; b) *Transition Metals for Organic Synthesis* (Eds: M. Beller, C. Bolm, C.), *2nd ed.*, Wiley-VCH, Weinheim, **2004**.

[2] For selected reviews on C–C bond formation *via* traditional cross-coupling reactions, see: a) C. C. C. J. Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed*. **2012**, *51*, 5062–5085; b) H. Li, C. C. C. J. Seechurn T. J. Colacot, *ACS Catal*. **2012**, 2, 1147–1164; c) *Chem. Soc. Rev*. **2011**, *40*, 4877–5208, Special Issue 10 "Cross coupling reactions in organic synthesis"; d) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev*. **2011**, 111, 1346–1416; e) G. Cahiez and A. Moyeux, *Chem. Rev*. 2010, 110, 1435–1462; f) *Acc. Chem. Res*. **2008**, *41*, 1439–1564, Special Issue 11 "Cross Coupling"; g) A. Roglans, A. Pla-Quintana, M. Moreno-Mañas, *Chem. Rev*. **2006**, *106*, 4622–4643; h) J.-P. Corbet, G. Mignani, *Chem. Rev*. **2006**, *106*, 2651–2710, and references cited therein.

[3] For atom-economy conception, see: B. M. Trost, *Acc. Chem. Res*. **2002**, *35*, 695–705.

[4] a) S. J. Blanksby, G. B. Ellison, *Acc. Chem. Res*. **2003**, *36*, 255–263; b) F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463; c) D. F. McMillen, D. M. Golden, *Annu. Rev. Phys. Chem*. **1982**, *33*, 493–532; d) J. D. Cox, G. Pilcher, *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, London, **1970**.

[5] Selected reviews on C–H bond functionalizations: a) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236–10254; b) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960–9009; c) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.*, **2012**, *45*, 788–802; d) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885−1898; e) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315−1345; f) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624–655; g) P. Thansandote, M. Lautens, *Chem. Eur. J.* **2009**, *15*, 5874−5883, and references cited therein.



Scheme 1.1 Traditional cross-coupling reactions *versus* direct C–H bond cleavages.

In recent years, most attention has been paid to the development of late transition metals, mainly due to some advantages in terms of the diversity and tunability of the catalysts and their robustness. However, the relatively high price, low natural abundance and partly strong toxicity limited their application. Cobalt and nickel, comparing to their 4d and 5d analogues, are easily available in the earth's crust (Table 1.1).[6] In spite of showing great potential in the direct C–H bond functionalizations because of their low cost and unique reactivity profiles, these metals were comparatively underutilized.

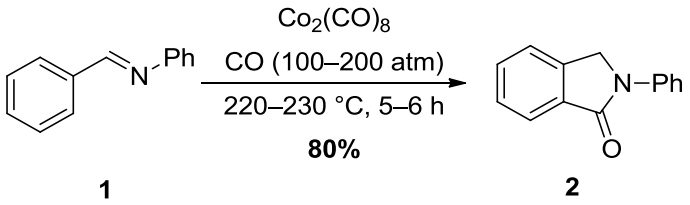
Transition-Metal	Nickel	Cobalt	Palladium	Platinum	Ruthenium	Rhodium
Abundance (g / ton)	**84**	**25**	**0.015**	**0.005**	**0.001**	**0.001**

Table 1.1 Abundance of selected transition metals in the earth's crust.

Cobalt-catalyzed traditional cross-coupling chemistry has been well studied since the middle of the last century.[7] However, the cobalt-catalyzed C–H bond functionalizations were still in its infancy. In 1955, the first example of directed C–H bond functionalization reactions was reported by Murahashi,[8] which set the stage for this research area. The treatment of a benzene solution of benzaldimine **1** with catalytic dicobalt octacarbonyl at high temperature and pressure led to the isolation of isoindoline **2** in good yield (Scheme 1.2). Therefore, seminal contributions were made by the Kisch, Brookhart and Klein group, which imply a

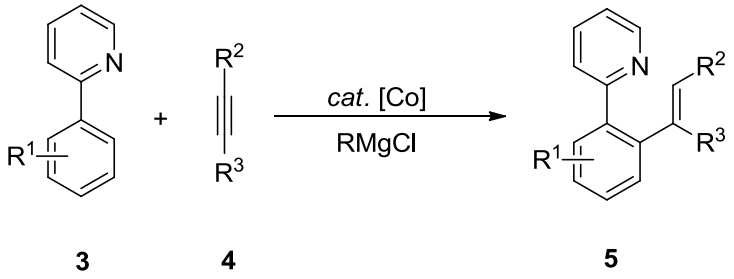
[6] P. Enghag, *Encyclopedia of the elements*; Wiley, Weinheim, **2004**.
[7] G. Cahiez, A. Moyeux, *Chem. Rev.* **2010**, *110*, 1435–1462, and references cited therein.
[8] S. Murahashi, *J. Am. Chem. Soc.* **1955**, *77*, 6403–6404.

high-potential catalytic activity of cobalt complexes towards C–H bond activation.[9] However, most of these studies were limited either by harsh reaction condition or by the need of stoichiometric cobalt species.[10]



Scheme 1.2 Cobalt-mediated synthesis of isoindoline **2**.

In 2010, Yoshikai and coworkers reported on the cobalt-catalyzed direct hydroarylation of alkynes through a chelation-assisted C–H bond activation (Scheme 1.3).[11] The catalytic system consisting of the cobalt salt and stoichiometric amounts of Grignard reagents showed high potential for further C–H bond functionalization. Based on this result, the alkynes **4** were efficiently converted with varies other substrates, such as imines, aldimines or indoles.[12]



Scheme 1.3 Cobalt-catalyzed hydroarylation of alkynes **4**.

In 2011, the Nakamura group disclosed the cobalt-catalyzed direct alkylation of benzamide with unreactivated primary alkyl chlorides,[13] which work was extended applying imines as

[9] Selected review: N. Yoshikai, *Synlett* **2011**, 1047–1051.

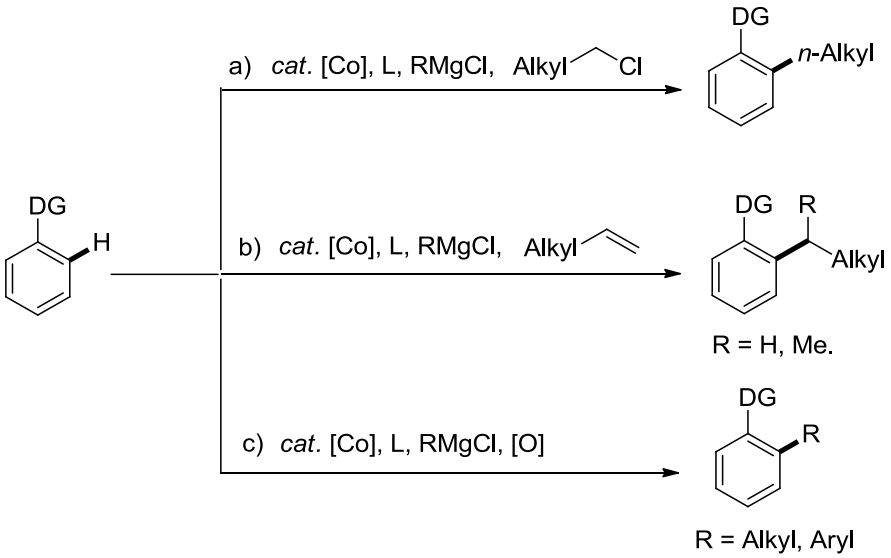
[10] A. A. Kuulkarni, O. Daugulis, *Syntheis* **2009**, 4087–4109, and references cited therein.

[11] K. Gao, P. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2010**, *132,* 12249–12251.

[12] a) T. Yamakawa, N. Yoshikai, *Tetrahedron* **2013**, *69*, 4459–4465; b) T. Yamakawa, N. Yoshikai, *Org. Lett.* **2013**, *15*, 196–199; c) B.-H. Tan, Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2012**, *51*, 9610–9614; d) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2012**, *51*, 4698–4701; e) P.-S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2011**, *133*, 17283–17295; f) Z. Ding, N. Yoshikai, *Synthesis* **2011**, 2561–2566; g). Z. Ding, N. Yoshikai, *Org. Lett.* **2010**, *12*, 4180–4183.

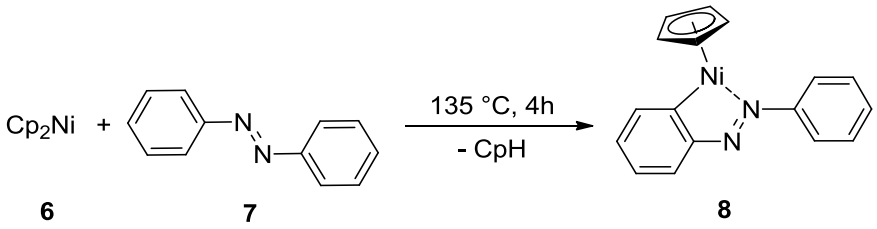
[13] Q. Chen, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2011**, *133,* 428–429

substrates by Yoshikai and coworkers in 2012 (Scheme 1.4a).[14] In the meantime, the alkylation was also achieved with alkenes using the corresponding arenes (Scheme 1.4b).[15] Moreover, the Grignard reagents could even be coupled directly into the *ortho*-position through cobalt-catalyzed chelation-assisted C–H bond activation, which was reported by the Shi and Nakamura groups (Scheme 1.4c).[16]



Scheme 1.4 Cobalt-catalyzed C–H bond functionalization.

Nickel-catalyzed C–H bond functionalization was reported by Kleiman and Dubeck in 1964 (Scheme 1.5).[17] The purple-blue organonickel species **8** was formed by heating a mixture of dicyclopentadienylnickel **6** with excess amount of azobenzene **7**.



Scheme 1.5 Nickel-mediated aromatic C–H bond activation.

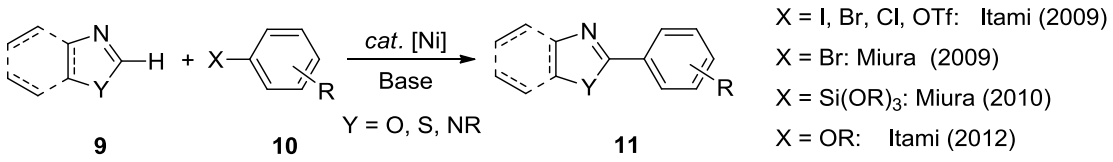
[14] K. Gao, P.-S. Lee, C. Long, N. Yoshikai, *Org. Lett.* **2012**, *14*, 4234–4237.

[15] a) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2013**, *52*, 8574–8578; b) K. Gao, N. Yoshikai, *Chem. Commun.* **2012**, *48*, 4305–4307; c) L. Ilies, Q. Chen, X. Zeng, E. Nakamura, *J. Am. Chem. Soc.* **2011***, 133,* 5221–5223; d) K. Gao, N. Yoshikai, *Angew. Chem. Int. Ed.* **2011**, *50*, 6888–6892; e) K. Gao, N. Yoshikai, *J. Am. Chem. Soc.* **2011***, 133,* 400–402.

[16] a) B. Li, Z. Wu, Y. Gu, C. Sun, B. Wang, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2011**, *50*, 1109–1113; b) Q. Chen, L. Ilies, N. Yoshikai, E. Nakamura, *Org. Lett.*, **2011**, *13*, 3232–3234.

[17] J. P. Kleiman, M. Dubeck, *J. Am. Chem. Soc.* **1963**, *85*, 1544–1545.

During the recent years, much effort has been dedicated towards the nickel-catalyzed direct arylations and even more challenging direct alkylations. In 2009, Itami and coworkers reported the nickel-catalyzed direct arylation of azoles **9**, where aryl halides and triflates were used as the electrophiles.[18] Similar results were also reported by Miura group applying aryl bromides.[19] One year later, Miura developed a nickel-catalyzed direct arylation of heteroarenes using organosilicon species as the aryl sources.[20] In 2012, Itami developed a direct arylation of heteroarenes with various phenol derivatives.[21] Aryl carbonates and triflates as well as less reactive sulfamates and tosylates were efficiently converted (Scheme 1.6).



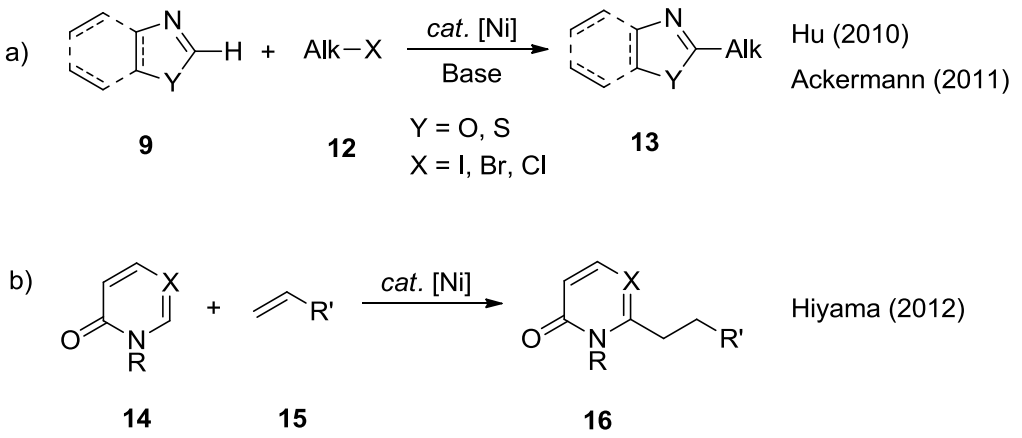
Scheme 1.6 Nickel-catalyzed C–H bond arylations.

In the meantime, the nickel-catalyzed direct alkylation of heterocycles **9** with alkyl halides **12** employing nickel pincer complexes and CuI was achieved by the Hu group in 2010.[22] Ackermann and coworkers reported the analogous direct alkylation employing the user-friendly nickel complex (Scheme 1.7a).[23] Moreover, the C–H bond alkylation with terminal alkenes **15** through nickel-catalyzed hydroarylation with pyridones **14** was developed by the Hiyama group in 2012 (Scheme 1.7b).[24]

Despite of these seminal contributions, the aforementioned transformations were still limited to the activation of more acidic C–H bonds. Thus, it is noteworthy that, in 2011, the Chatani group reported nickel-catalyzed chelation-assisted functionalization of inert C–H bonds in benzamides **17**. Thus, versatile approach to isoquinolone derivatives **18** was elaborated along

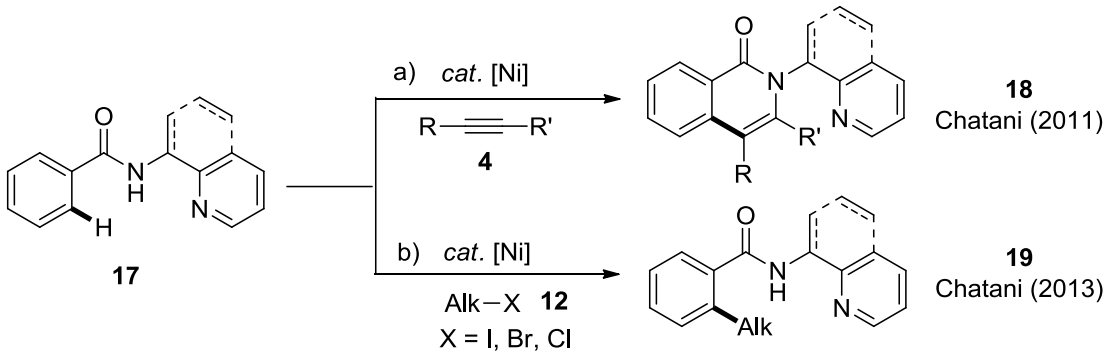
[18] J. Canivet, J. Yamaguchi, I. Ban, K. Itami, *Org. Lett.* **2009**, *11*, 1733–1736.
[19] H. Hachiya, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2009**, *11*, 1737–1740.
[20] H. Hachiya, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2010**, *49*, 2202–2205.
[21] a) K. Muto, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.* **2012**, *134*, 169–172; b) Also see: L. Ackermann, A. Althammer, S. Fenner, *Angew. Chem. Int. Ed.* **2009**, *48*, 201–204.
[22] O. Vechorkin, V. Proust, X. Hu, *Angew. Chem. Int. Ed.* **2010**, *49*, 3061–3064.
[23] L. Ackermann, B. Punji, W. Song, *Adv. Synth. Catal.* **2011**, *353*, 3325–3329.
[24] R. Tamura, Y. Yamada, Y. Nakao, T. Hiyama, *Angew. Chem. Int. Ed.* **2012**, *51*, 5679–5682.

the route of C–H/N–H bond activations (Scheme 1.8a).[25]



Scheme 1.7 Examples of nickel-catalyzed direct alkylation.

More recently, the nickel-catalyzed direct alkylation of benzamides **17** with alkyl halides **12** was also achieved through this chelation-assisted reaction manifold (Scheme 1.8b).[26]



Scheme 1.8 Nickel-catalyzed chelation-assisted C–H bonds functionalization.

1.2 Transition-Metal-Catalyzed Secondary Alkylation

The discovery of the ruthenium-catalyzed *ortho*-alkylation of aromatic ketones **20** with olefins **15** by Murai and coworkers[27] in 1993 opened a new paradigm in directed alkylations.[28] However, this strategy was limited to specific secondary alkylations, mainly because of the *anti*-Markovnikov selectivity of alkylations with terminal olefins, low

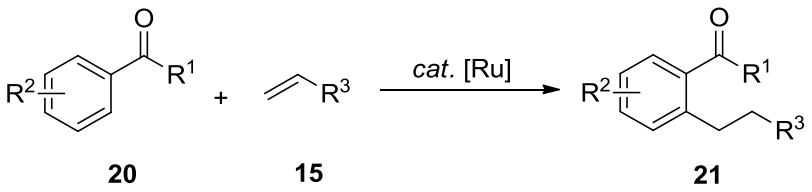
[25] H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 14952–14955.

[26] Y. Aihara, N. Chatani, *J. Am. Chem. Soc.*, **2013**, *135*, 5308–5311.

[27] S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, *366*, 529–531.

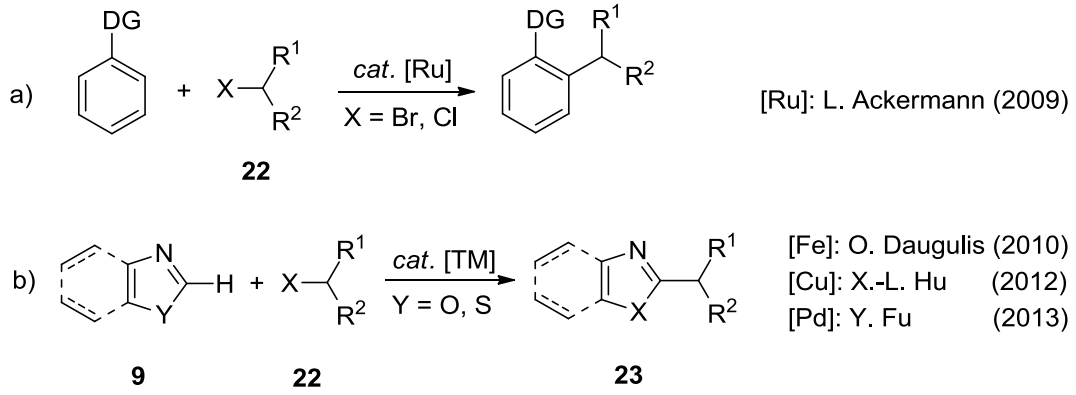
[28] Selected reviews: a) N. A. Foley, J. P. Lee, Z. Ke, T. B. Gunnoe, T. R. Cundari, *Acc. Chem. Res*. **2009**, *42*, 585–597; b) F. Kakiuchi, *Top. Organomet. Chem*. **2007**, *24*, 1–33; c) F. Kakiuchi, N. Chatani, *Adv. Synth. Catal*. **2003**, *345*, 1077–1101; Recent progress: d) M. Schinkel, I. Marek, L. Ackermann, *Angew. Chem. Int. Ed.* **2013**, *52*, 3977–3980.

reactivity of internal olefins and isomerization of internal acyclic olefins (Scheme 1.9).



Scheme 1.9 Ruthenium-catalyzed *ortho*-alkylation of ketones.

More recently, alkyl halides have emerged as important alternative reagents for the direct alkylation.[29] The alkylation of either reactive acidic C–H bonds in azoles or of inert ones in arenes with Lewis basic directing groups could be achieved through this strategy. Nevertheless, while successful for the primary alkylation, these electrophiles have been applied for only a handful of secondary alkylation (Scheme 1.10).[30]



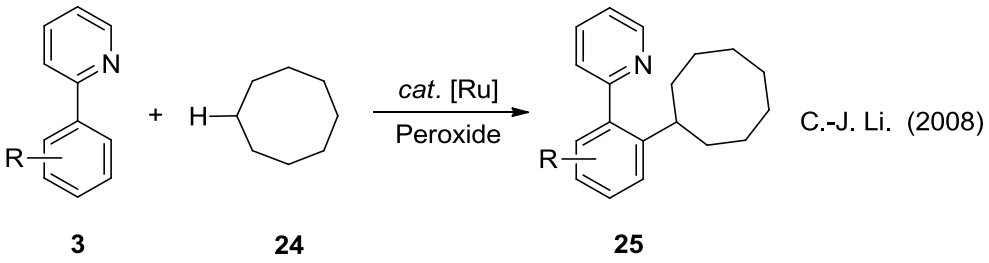
Scheme 1.10 Direct alkylations with secondary alkyl halides.

Besides alkyl halides **22**, other reagents were also utilized for secondary alkylations. In 2008, Li and coworkers reported the only example of ruthenium-catalyzed direct secondary alkylation through the cross dehydrogenative coupling (CDC) process (Scheme 1.11),[31] in which the unreactive cycloalkanes **24** were directly attached to the *ortho*-position of substituted 2-phenylpyridines **3** through activation of two C–H bonds.

[29] For review, see: L. Ackermann, *Chem. Commun.* **2010**, *46*, 4866–4877.

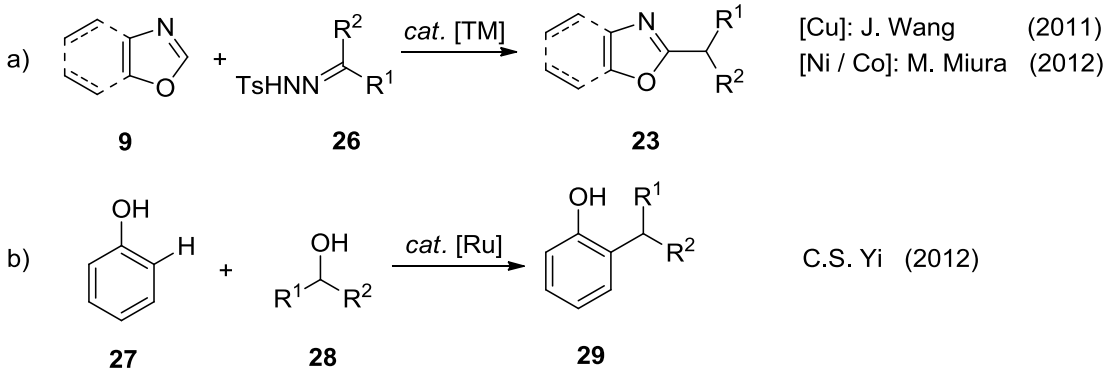
[30] Examples of transition-metal-catalyzed alkylation with secondary halides: a) L. Ackermann, P. Novak, R. Vicente, N. Hofmann, *Angew. Chem, Int. Ed.* **2009**, *48*, 6045–6048; b) N. Hofmann, L. Ackermann, *J. Am. Chem. Soc.* **2013**, *135*, 5877–5884; c) L. D. Tran, O. Daugulis, *Org. Lett.* **2010**, *12*, 4277–4279; d) P. Ren, Salihu, I.; Scopelliti, R., Hu, X. *Org. Lett.* **2012**, *14*, 1748–1751; e) B. Xiao, Z.-J. Liu, L. Liu, Y. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 616–619.

[31] G. Deng, L. Zhao, C.-J. Li, *Angew. Chem. Int. Ed.* **2008**, *47*, 6278–6282.



Scheme 1.11 Secondary alkylation through CDC process.

Three years later, the Wang group reported the first copper-catalyzed synthesis of the secondary alkyl-substituted heterocycles **9** through alkylation with *N*-tosylhydrazones **26**,[32] which was followed by Miura in 2012 with nickel and cobalt catalyst (Scheme 1.12a).[33] The diazo compound generated in situ from *N*-tosylhydrazones under the basic reation condition was used as the alkylation reagent. Additionally, the phenol-directed alkylation with the corresponding secondary alcohols **28** was developed by Yi and coworkers in 2012 (Scheme 1.12b).[34]



Scheme 1.12 Alkylations with other secondary electrophiles.

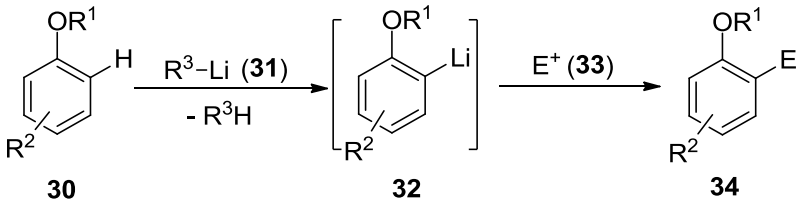
1.3 Phenol Derivatives in Cross-Couplings and C–H Bonds Functionalizations

Synthetic chemists are now able to provide a wide array of aryl, vinyl, allyl, and alkyl halides. However, such species are less available from natural sources and are not used as coupling partners in biosynthetic pathways. A key benefit of phenol- and ketone-based-electrophiles is

[32] X. Zhao, G. Wu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 3296–3299.
[33] T. Yao, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2012**, *51*, 775–779.
[34] D.-H. Lee, K.-H. Kwon, C. S. Yi, *J. Am. Chem. Soc.* **2012**, *134*, 7325–7328.

their ready accessibility. In the case of phenols, such compounds are naturally abundant or can readily be prepared from other easily available aromatic species.[35]

Additionally, oxygenation on the aromatic ring can facilitate the introduction of additional substituents *via* a number of pathways including, for example, electrophilic aromatic substitution. Depending on the nature of the phenol-derived substituent and the electrophile, it is often possible to control the predominant formation of *para*- or *ortho*-substituted products. The *ortho*-substitution of phenol derivatives **30** can also be achieved using directed *ortho*-metalation (DoM).[36] Through this methodology, numerous functional groups, such as phenols, ethers, carbamates, and sulfamates, can undergo the directed *ortho*-lithiation. Subsequent transformation of the resulting organolithium species **32** with electrophilic species E^+ **33** provides the *ortho*-substituted products **34** (Scheme 1.13).



Scheme 1.13 *Ortho*-functionalization through the DoM process.

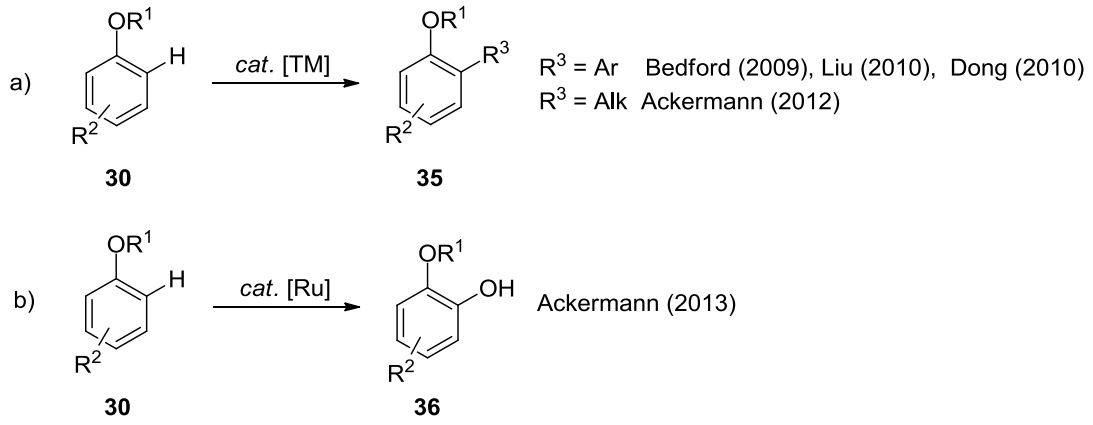
Furthermore, phenol derivatives could also be *ortho*-functionalized directly through transition-metal-catalyzed C–H bond functionalization (Scheme 1.14a).[37] Direct arylation and alkylation were both achieved with phenol esters, pivalates and carbamates as directing groups. Additionally, the *ortho*- and *para*-selective ruthenium-catalyzed oxygenation of the phenol derivatives **30** was recently developed by Ackermann and coworkers (Scheme 1.14b).[38]

[35] Z. Rappoport, *The Chemistry of Phenols*, John Wiley & Sons Ltd.: Chichester, U.K., **2003**.

[36] V. Snieckus, *Chem. Rev.* **1990**, *90*, 879–933.

[37] For examples of phenol-derived substituents as directing groups, see: a) B. Xiao, Y. Fu, J. Xu, T.-J. Gong, J.-J. Dai, J. Yi, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 468–469; b) R. B. Bedford, R. L. Webster, J. C. Mitchell, *Org. Biomol. Chem.* **2009**, *7*, 4853–4857; c) X. Zhao, C. S. Yeung, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 5837–5844; d) J. Li, C. Kornhaaß, L. Ackermann, *Chem. Commun.* **2012**, *48*, 11343–11345.

[38] W. Liu, L. Ackermann, *Org. Lett.* **2013**, *15*, 3484–3486.



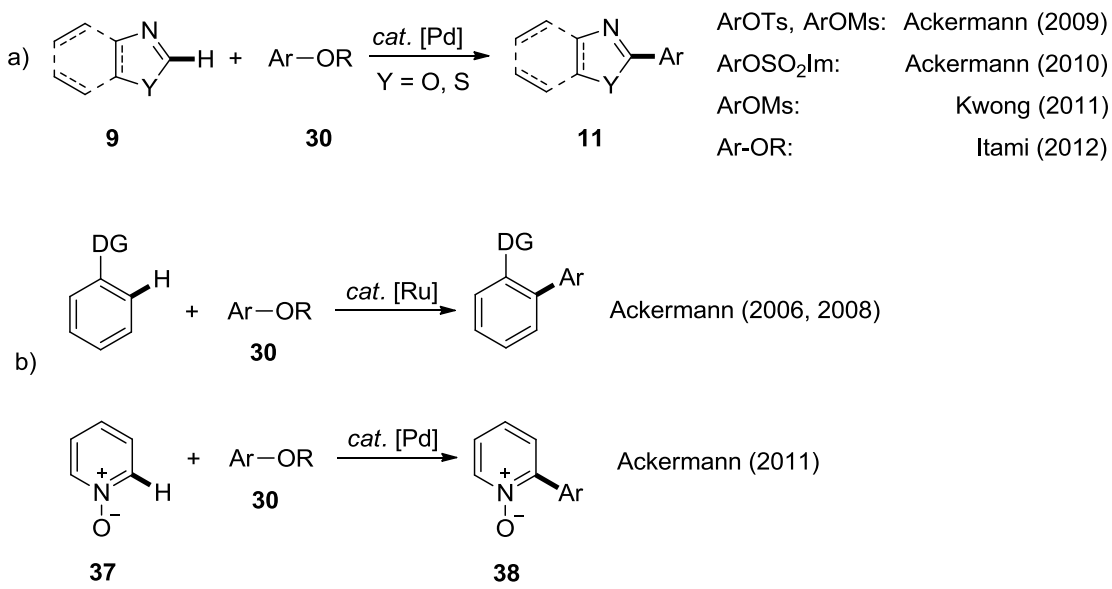
Scheme 1.14 Examples of hydroxyl-directed C–H activation.

Based on the aforementioned advantages, the phenol-derived electrophiles have been widely studied and utilized in the cross-coupling chemistry[39] and transition-metal-catalyzed C–N bond formations[40] through the C–O bonds activation during the past decades. However, the direct C–H bond arylations with phenol-based electrophiles was still limited because of the high activation energy of the C–O bonds. Recently, the Ackermann group reported the direct C–H bonds functionalization of heteroarenes with phenol derivatives using palladium complexes,[41] whereas nickel catalysts were utilized by Itami for the most recent direct arylations of C–H acidic azoles (Scheme 1.15a).[21]

[39] Selected reviews: a) S. I. Kozhushkov, H. K. Potukuchi, L. Ackermann, *Catal. Sci. Technol.* **2013**, *3*, 562–571; b) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346–1416; c) B.-J. Li, D.-G. Yu, C.-L. Sun, Z.-J. Shi, *Chem. Eur. J.* **2011**, *17*, 1728–1759; d) D.-G. Yu, B.-J. Li, Z.-J. Shi, *Acc. Chem. Res.* **2010**, *43*, 1486–1495; e) A. Littke, in *Modern Arylation Methods* (Ed.: L. Ackermann), Wiley-VCH, Weinheim, **2009**; pp 25–67, and references cited therein.

[40] For representative examples of C–N bond formation, see: a) T. Shimasaki, M. Tobisu, N. Chatani, *Angew. Chem. Int. Ed.* **2010**, *49*, 2929–2932; b) M. L. H. Mantel, A. T. Lindhardt, D. Lupp, T. Skrydstrup, *Chem.;Eur. J.* **2010**, *16*, 5437–5442; c) R. J. Lundgren, M. Stradiotto, *Angew. Chem. Int. Ed.* **2010**, *49*, 8686–8690; d) C. M. So, Z. Zhou, C. P. Lau, F. Y. Kwong, *Angew. Chem. Int. Ed.* **2008**, *47*, 6402–6406; e) H. N. Nguyen, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 11818–11819; f) A. H. Roy, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 8704–8705; g) X. Huang, K. W. Anderson, D. Zim, L. Jiang, A. Klapars, S. L.Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 6653–6655; h) C. Bolm, J. P. Hildebrand, J. Rudolph, *Synthesis* **2000**, 911–913; i) B. C. Hamann, J. F. Hartwig, *J. Am. Chem. Soc.* **1998**, *120*, 7369–7370

[41] a) L. Ackermann, A. Althammer, S. Fenner, *Angew. Chem. Int. Ed.* **2009**, *48*, 201–204; b) L. Ackermann, S. Barfüsser, J. Pospech, *Org. Lett.* **2010**, *12*, 724–726; c) C. M. So, C. P. Lau, F. Y. Kwong, *Chem. Eur. J.* **2011**, *17*, 761–765.



Scheme 1.15 Phenol-derived electrophiles for direct arylations.

Nevertheless, the direct arylation of unactivated arenes with phenol derivatives is, to date, unfortunately largely restricted to relatively expensive complexes of the rare transition metals, such as ruthenium and palladium (Scheme 1.15b).[42]

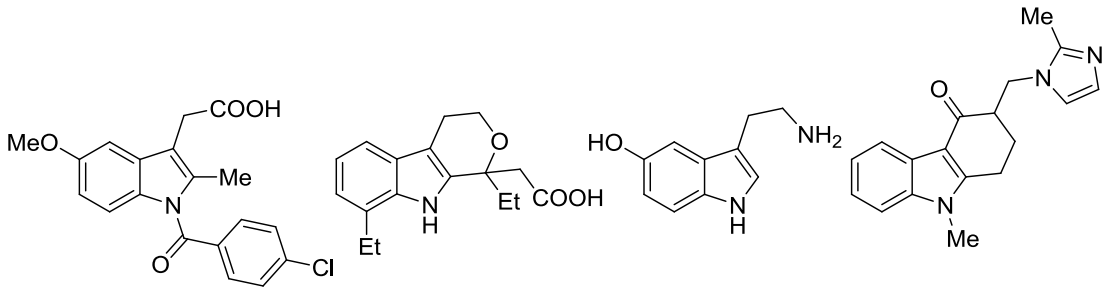
1.4 Transition-Metal-Catalyzed Indole Syntheses

Indole derivatives likely represent one of the most important structural building blocks in bioorganic chemistry, drug discovery and medicinal chemistry.[43] Representative examples of biologically active indoles include non-steroidal anti-inflammatory drugs indomethacin (**39**), and etodolac (**40**), neurotransmitter serotonin (**41**) and 5HT-3 antagonist ondansetron (**42**) (Scheme 1.16). Therefore, there is a continued strong demand for chemo- and site-selective syntheses of this heteroaromatic scaffold.[44]

[42] Examples of late transition-metal-catalyzed direct arylations of arenes with phenol-derivatives, [Pd]: a) L. Ackermann, S. Fenner, *Chem. Commun.* **2011**, *47*, 430–432; [Ru]: b) L. Ackermann, J. Pospech, H. K. Potukuchi, *Org. Lett.* **2012**, *14*, 2146–2149; c) L. Ackermann, M. Mulzer, *Org. Lett.* **2008**, *10*, 5043–5045; d) L. Ackermann, R. Vicente, A. Althammer, *Org. Lett.* **2008**, *10*, 2299–2302; e) L. Ackermann, A. Althammer, R. Born, *Angew. Chem. Int. Ed.* **2006**, *45*, 2619–2622.

[43] J. Alvarez-Builla, J. J. Vaquero, J. Barluenga, *Modern Heterocyclic Chemistry*, Wiley-VCH, Weinheim, **2011**.

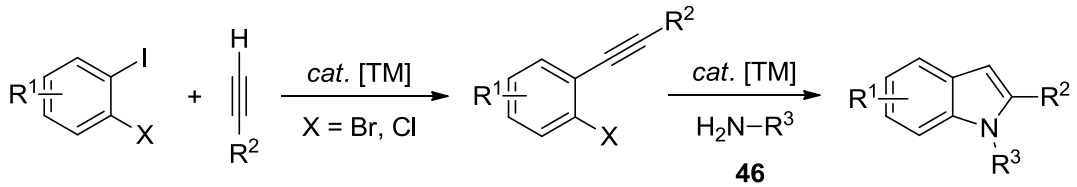
[44] Select reviews on the preparation of indoles: a) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. React.* **2012**, *76*, 281–534; b) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. Biomol. Chem.* **2011**, *9*, 641–652; c) K. Krüger, A. Tillack, M. Beller, *Adv. Synth. Catal.* **2008**, *350*, 2153–2167; d) L. Ackermann, *Synlett* **2007**, 507–526; e) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875–2911; f) D. A. Horton, G. T. Bourne, M. L. Smythe, *Chem. Rev.* **2003**, *103*, 893–930, and references cited therein.



39 **40** **41** **42**

Scheme 1.16 Selected biologically active indole derivatives.

In addition to the classical Fischer indole synthesis,[44e] the Larock indole synthesis[45] was widely studied during the last decade. Based on this methodology, significant progress has been accomplished with intramolecular addition reactions of *ortho*-alkynylanilines.[46] The easily accessible *ortho*-alkynylhaloarenes **45** were converted into the corresponding indole derivatives *via* a reaction cascade comprising intermolecular aminations of aryl halides and subsequent intramolecular hydroaminations of alkynes. Thereby, variously decorated indole derivatives **47** featuring substituents at different positions were synthesized with high efficacy (Scheme 1.17).



43 **44** **45** **47**

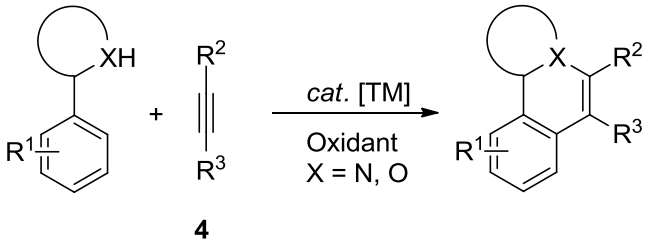
Scheme 1.17 Cascade reaction sequence for a modular synthesis of indoles.

Although the transition-metal-catalyzed C–C and C–N bond forming reactions have proved particularly valuable for indoles syntheses, these transformations largely utilized pre-functionalized starting materials. Recently, significantly more step-economical strategies

[45] a) For a review, see: R. C. *J. Organomet. Chem.* **1999**, *576*, 111–124; see also: b) C. Chen, D. R. Lieberman, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *J. Org. Chem.* **1997**, *62*, 2676–2677.

[46] Selected examples: a) L. Ackermann, S. Barfüßer, H. K. Potukuchi, *Adv. Synth. Catal.* **2009**, *351*, 1064–1072; b) L. Ackermann, R. Sandmann, M. V. Kondrashov, *Synlett* **2009**, 1219–1222; c) L. Ackermann, R. Sandmann, M. Schinkel, M. V. Kondrashov, *Tetrahderon* **2009**, *65*, 8930–8939; d) P.-Y. Yao, Y. Zhang, R. P. Hsung, K. Zhao, *Org. Lett.* **2008**, *10*, 4275–4278; e) R. Sanz, M. P. Castroviejo, V. Guilarte, A. Perez, F. J. Fananas, *J. Org. Chem.* **2007**, *72*, 5113–5118; f) Z.-Y. Tang, Q.-S. Hu, *Adv. Synth. Catal.* **2006**, *348*, 846–850; g) L. Ackermann, *Org. Lett.* **2005**, *7*, 439–442; h) L. T. Kaspar, L. Ackermann, *Tetrahedron* **2005**, *61*, 11311–11316.

were devised by methods that capitalize upon unactivated C–H bonds as latent functional groups.[47]



Scheme 1.18 Metal-catalyzed heterocycle syntheses through oxidative C–H activation.

In 2008, Glorius reported a rhodium-catalyzed indole synthesis through oxidative coupling of acetanilides and alkynes.[48] Since then, late transition metal catalysts, such as rhodium, palladium or ruthenium complexes have been widely utilized for the heterocycle syntheses by oxidative alkyne annulation through C–H/Het–H bond functionalizations (Scheme 1.18).[49] Remarkable, the use of copper (II) or silver (I) salts as the stoichiometric or cocatalytic oxidants proved to be crucial for the regeneration of the active species during the catalytic reactions.

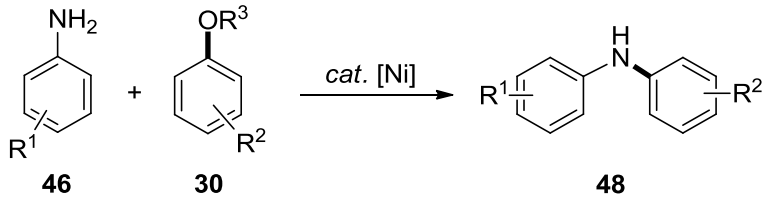
[47] For reviews, see: a) L. Ackermann, *Acc. Chem. Res.*, **2013**, *46*, DOI:10.1021/ar3002798; b) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.*, **2012**, *41*, 3651–3678; c) T. Satoh, M. Miura, *Chem. Eur. J.*, **2010**, *16*, 11212–11222.

[48] S. Würtz, S. Rakshit, J. J. Neumann, T. Droge, F. Glorius, *Angew. Chem. Int. Ed.*, **2008**, *47*, 7230–7233

[49] Selected examples, a) S. Park, B. Seo, S. Shin, J.-Y. Son, P. H. Lee, *Chem. Commun*. **2013**, *49*, 8671–8673; b) J. Du, B. Zhou, Y. Yang, Y. Li, *Chem. Asian J*. **2013**, *8*, 1386–1390; c) N. Quiñones, A. Seoane, R. García-Fandiño, J. L. Mascareñas, M. Gulías, *Chem. Sci*. **2013**, *4*, 2874–2879; d). Z. Shi, C. Tang, N. Jiao, *Adv. Synth. Cat*. **2012**, *354*, 2695–2700; e) M. V. Pham, B. Ye, N. Cramer, *Angew. Chem. Int. Ed*. **2012**, *51*, 10610–10614; f) H. Wang, C. Grohmann, C. Nimphius, F. Glorius, *J. Am. Chem. Soc.*, **2012**, *134*, 19592–19595; g) M. P. Huestis, L. N. Chan, D. R. Stuart, K. Fagnou, *Angew. Chem. Int. Ed.*, **2011**, *50*, 1338–1341; h) J. Chen, G. Song, C.-L. Pan, X. Li, *Org. Lett.*, **2010**, *12*, 5426–5429; i) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.*, **2008**, *130*, 16474–16475; j) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.*, **2010**, ***132***, 18326–18339; Activated alkynes: k) R. Bernini, G. Fabrizi, A. Sferrazza, S. Cacchi, *Angew. Chem. Int. Ed.* **2009**, *48*, 8078–8081; l) T. Piou, L. Neuville, J. Zhu, *Tetrahedron* **2013**, *69*, 4415–4420; m) L. Ren, Z. Shi, N. Jiao, *Tetrahedron* **2013**, *69*, 4408–4414; n) N. Zhang, B. Li, H. Zhong, J. Huang, *Org. Biomol. Chem*. **2012**, *10*, 9429–9439; o) Z. Shi, C. Zhang, S. Li, D. Pan, S. Ding, Y. Cui, N. Jiao, *Angew. Chem. Int. Ed.*, **2009**, *48*, 4572–4576; [Ru]: p) W. Ma, K. Graczyk, L. Ackermann, *Org. Lett*. **2012**, *14*, 6318–6321; q) M. Deponti, S. I. Kozhushkov, D. S. Yufit, L. Ackermann, *Org. Biomol. Chem*. **2013**, *11*, 142–148; r) C.-Z. Luo, P. Gandeepan, C.-H. Cheng, *Chem. Commun*. **2013**, *49*, 8528–8530; s) N. Kavitha, G. Sukumar, V. P. Kumar, P. S. Mainkar, S. Chandrasekhar, *Tetrahedron Lett*. **2013**, *54*, 4198–4201; t) P. Villuendas, E. P. Urriolabeitia, *J. Org. Chem*. **2013**, *78*, 5254–5263; u) B. Li, N. Wang, Ye Liang, S. Xu, B. Wang, *Org. Lett*. **2013**, *15*, 136–139; v) L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764–767, and references cited therein.

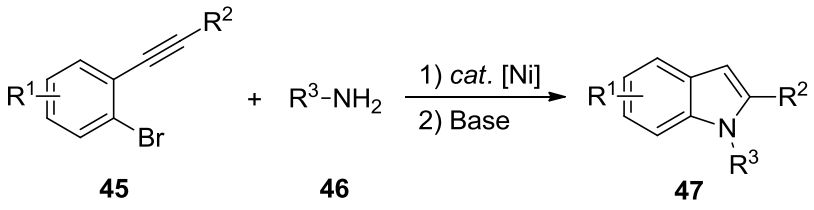
2. Objectives

Transition-metal-catalyzed arylation of amines with aryl halides are among the most important methods for the selective formation of C–N bonds. Particularly, the use of phenol-derived electrophiles in catalyzed arylations is highly attractive. However, the strategy was limited to the use of the expensive late transition metals. Consequently, nickel-catalyzed aminaitions would be a useful protocol for organic synthesis and constituted our first project (Scheme 2.1).



Scheme 2.1 Nickel-catalyzed direct arylation of amines **46**.

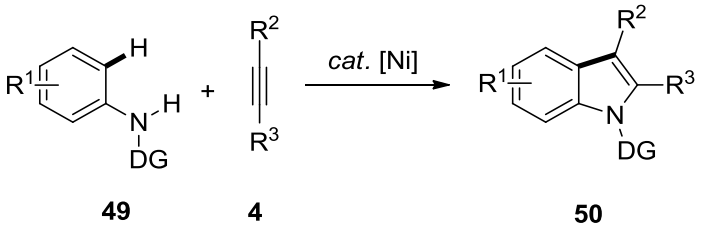
As was mentioned above, the preparation of substituted indoles is of key importance in practical synthetic chemistry. Among other methods, the reaction cascade comprising intermolecular aminations of aryl halides and subsequent intramolecular hydroaminations of alkynes was widely studied in the past few years. Comparing to the application of the late transition metals like palladium and rhodium as the catalysts, the nickel-catalyzed indole synthesis from appropriate *ortho*-substituted aryl halides was the second research project (Scheme 2.2).



Scheme 2.2 Nickel-catalyzed base-mediated indole synthesis.

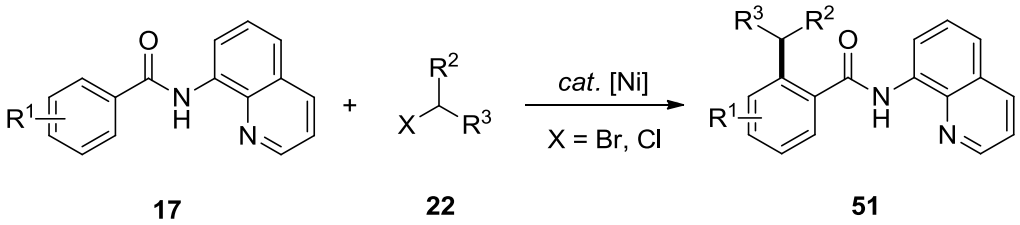
Alternatively, we became interested in the indole synthesis by oxidative alkyne annulation through C–H/N–H bond functionalization. The previously reported reactions mainly relied on

the use of late transition metals and stoichiometric amount of metal oxidant, which limited their application. To overcome these limitations, we set out to develop an unprecedented nickel-catalyzed alkyne annulation with electron-rich anilines **49** devoid of copper (II) or silver (I) salts as the sacrificial oxidants in the third project (Scheme 2.3).



Scheme 2.3 Nickel-catalyzed indole synthesis through C–H/N–H activation.

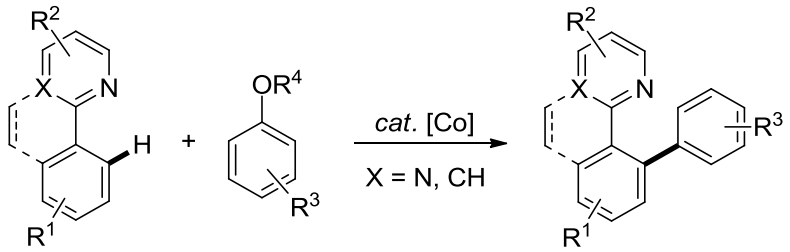
Transition-metal-catalyzed direct alkylations, especially of relatively unreactive arenes, with secondary alkylating reagents remain to be a challenging research topic. During recent years, chelation-assistance has offered a useful tool for C–H bond functionalizations. However, the application of bidentate directing groups towards alkylation with secondary alkylating reagents is still not available. It would be of high interest to explore a nickel-catalyzed secondary alkylation of the inert arenes, which is the goal of our forth project (Scheme 2.4).



Scheme 2.4 Nickel-catalyzed chelation-assisted secondary alkylation.

Efficient methods for the selective preparation of biaryls are of key importance, as these structural motifs are crucial building blocks for natural products, liquid crystals, and functional materials. Although the cobalt-catalyzed C–H bond functionalization was well studied during the past years, the direct arylation with aryl halides have proven elusive. Moreover, the direct arylation of unactivated arenes with phenol derivatives is, to date, restricted to the relatively expensive late transition metals, such as ruthenium and palladium. Therefore, the cobalt-catalyzed direct arylation with unreactive phenol derivatives was the

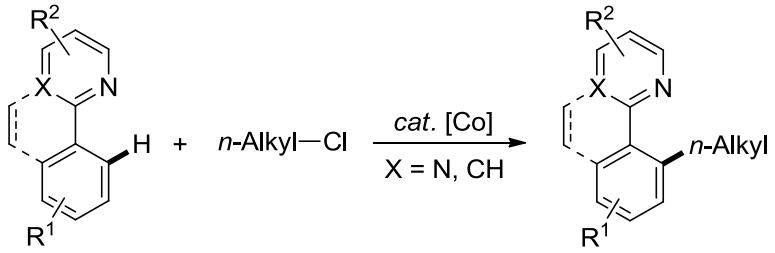
prime focus of the fifth project (Scheme 2.5).



3 **30** **52**

Scheme 2.5 Cobalt-catalyzed direct arylation by C–H/C–O cleavages.

Cobalt-catalyzed direct alkylations of benzamides and imines have been established by the Nakamura and Yoshikai groups. However, the moderate yields and poor selectivities of the reported procedures prompted us to search for novel direct alkylations with unactivated alkyl chlorides **12a**, and this task is the main purpose of the last project (Scheme 2.6).



3 **12a** **53**

Scheme 2.6 Cobalt-catalyzed direct alkylations with alkyl chlorides **12a**.

Results and Discussion

3. Nickel-Catalyzed Aminations of Aryl Sulfamates

Transition-metal-catalyzed arylations of amines with aryl halides are among the most important methods for the selective formation of C–N bonds. Particularly, the use of phenol-derived electrophiles in catalyzed arylations is highly attractive, since they are readily accessible and can be easily implemented as directing groups in site-selective arene functionalization strategies. While these user-friendly electrophiles were recently employed for efficient C–C bond formations, their use in transition-metal-catalyzed aminations has unfortunately thus far proven elusive. Ackermann and coworkers previously reported on the development of efficient amination reactions for modular heteroarene syntheses.[50] However, these protocols mainly used palladium, copper and titanium catalysts and were limited to the use of aryl halides. In 2010, Chatani developed an efficient nickel-catalyzed arylation of secondary amines with aryl pivalates.[51] However, the protocol was limited to the application of activated phenol derivatives. The aminations performed with the less reactive aryl tosylates, mesylates and sulfamates were unknown. Continuing these investigations, we examined the ability of nickel complexes to catalyze aminations with aryl sulfamates, and these results are summarized in this chapter.[52]

3.1 Optimization Studies of Nickel-Catalyzed Aminations

At the outset of our studies, we tested various ligands and bases in the nickel-catalyzed amination of aryl sulfamate **30aa** (Table 3.1). While representative monodentate phosphine ligands provided only unsatisfactory results (entries 2–7), nickel complexes derived from N-heterocyclic carbene (NHC) precursors (entries 8–9) or bidentate phosphine ligands

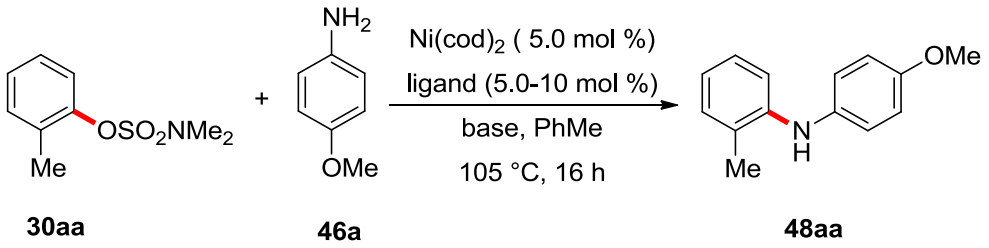
[50] For representative examples, see: a) L. Ackermann, S. Barfüsser, H. K. Potukuchi, *Adv. Synth. Catal.* **2009**, *351*, 1064–1072; b) L. Ackermann, R. Sandmann, L. T. Kaspar, *Org. Lett.* **2009**, *11*, 2031–2034; c) L. Ackermann, R. Sandmann, M. V. Kondrashov, *Synlett* **2009**, 1219–1222; d) L. Ackermann, R. Sandmann, A. Villar, L. T. Kaspar, *Tetrahedron* **2008**, *64*, 769–777; e) L. Ackermann, J. H. Spatz, C. J. Gschrei, R. Born, A. Althammer, *Angew. Chem. Int. Ed.* **2006**, *45*, 7627–7630; f) L. Ackermann, R. Born, *Angew. Chem. Int. Ed.* **2005**, *44*, 2444–2447 and references cited therein.

[51] T. Shimasaki, M. Tobisu, N. Chatani, *Angew. Chem. Int. Ed.* **2010**, *49*, 2929–2932.

[52] L. Ackermann, R. Sandmann, W. Song, *Org. Lett.* **2011**, *13,* 1784–1786.

(entries 12–14) displayed improved catalytic activities. Notably, the best results were

Table 3.1 Optimization of nickel-catalyzed amination with sulfamate **30aa**.[a]



30aa **46a** **48aa**

Entry	Ligand (mol %)	Base	Yield (%)[b]
1	--	NaO*t*-Bu	--
2	$(1\text{-Ad})_2$P(O)H (10) (**54**)	NaO*t*-Bu	--
3	HASPO (*i*-Pr) (10) (**55**)	NaO*t*-Bu	--
4	PPh_3 (10) (**56**)	NaO*t*-Bu	--
5	PCy_3 (10) (**57**)	NaO*t*-Bu	--
6	S-Phos (10) (**58**)	NaO*t*-Bu	--
7	X-Phos (10) (**59**)	NaO*t*-Bu	--
8	HIPrCl (10) (**60**)	NaO*t*-Bu	85
9	sHIPrCl (10) (**61**)	NaO*t*-Bu	82
10	phenathroline (5) (**62**)	NaO*t*-Bu	8
11	dppp (5) (**63**)	NaO*t*-Bu	--
12	dppe (5) (**64**)	NaO*t*-Bu	52
13	*rac*-BINAP (5) (**65**)	NaO*t*-Bu	54
14	**dppf (5) (66)**	**NaO*t*-Bu**	**95**
15	dppf (5)	NaO*t*-Bu	65
16	dppf (5)	NaO*t*-Bu	--
17 [c]	dppf (5)	NaO*t*-Bu	--

[a] Reaction conditions: **30aa** (0.50 mmol), **46a** (0.75 mmol), $Ni(cod)_2$ (5.0 mol %), L (5.0–10 mol %), base (0.75 mmol), PhMe (2.0 mL), 105 ℃ , 16 h. [b] Yields of isolated products. [c] $Co_2(CO)_8$ (5.0 mol %).

accomplished with dppf as the ligand, along with NaO*t*-Bu as the optimal choice of base. Interestingly, the cobalt complex which was efficient for the C–C bond formations did not

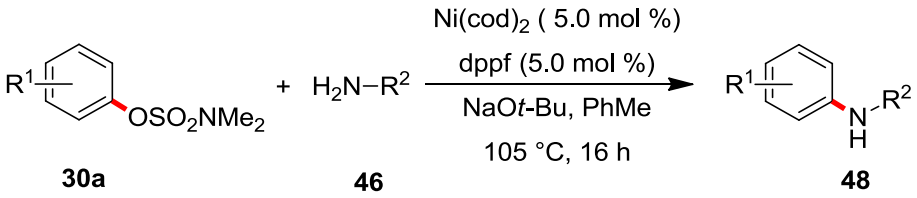
deliver the desired product here (entry 17).

3.2 Scope of Nickel-Catalyzed Amination of Aryl Sulfamates

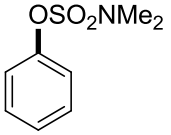
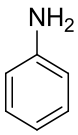
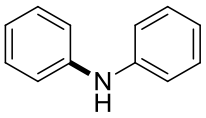
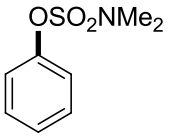
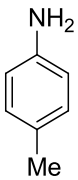
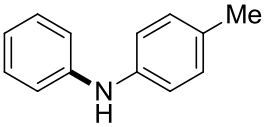
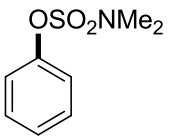
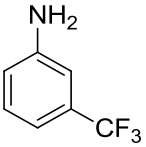
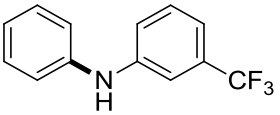
3.2.1 Nickel-Catalyzed Direct Arylations of Primary Amines

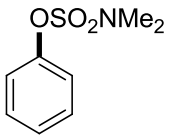
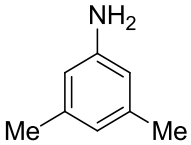
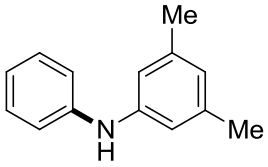
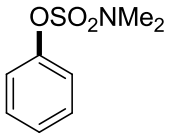
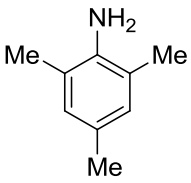
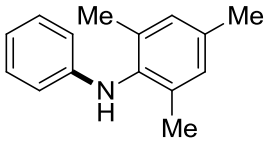
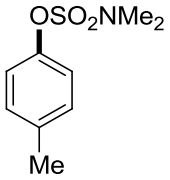
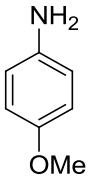
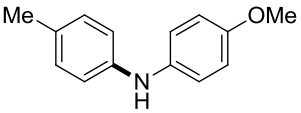
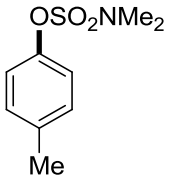
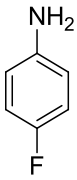
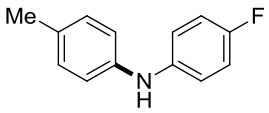
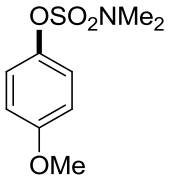
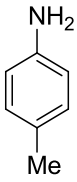
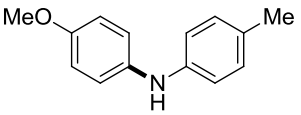
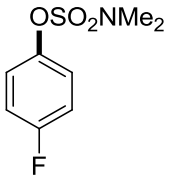
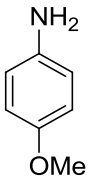
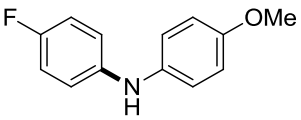
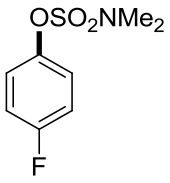
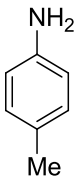
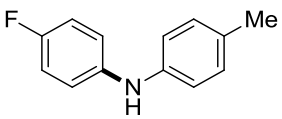
With the optimized catalytic system in hands, we explored its scope in the nickel-catalyzed amination of differently substituted sulfamates **30a** (Table 3.2). Either electron-poor or less reactive electron-rich sulfamates delivered the desired products in excellent yields (entries 8–10). Moreover, aniline derivatives **46** bearing electron-withdrawing as well as electron-donating substituents efficiently delivered the products **48**, even when being sterically hindered. Importantly, challenging *n*-alkyl amines were converted with comparable catalytic efficacy (entries 13–14).

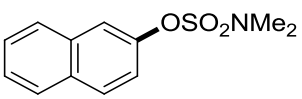
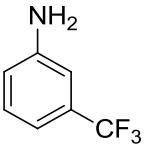
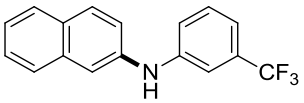
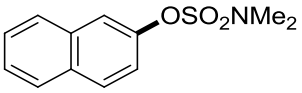
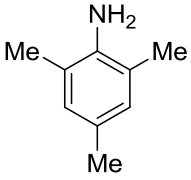
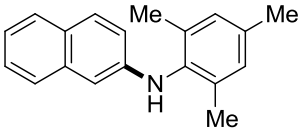
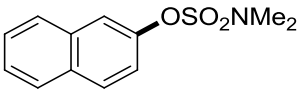
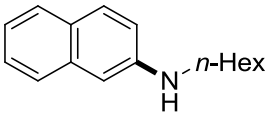
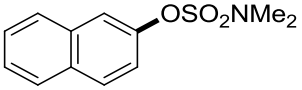
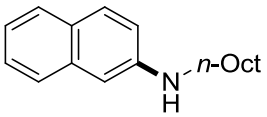
Table 3.2 Nickel-catalyzed direct arylation with aryl sulfamates[a]



30a **46** **48**

Entry	Sulfamate	Amine	Product	Yield (%)[b]
1	 **30ab**	 **46b**	 **48bb**	94
2	 **30ab**	 **46c**	 **48bc**	95
3	 **30ab**	 **46d**	 **48bd**	83

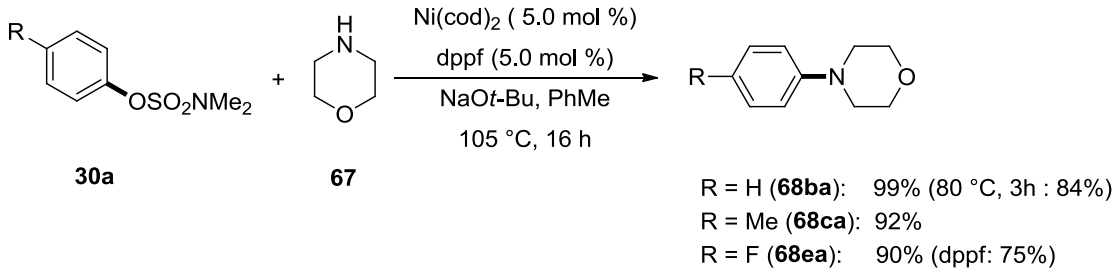
4				96
	30ab	**46e**	**48be**	
5				96
	30ab	**46f**	**48bf**	
6				84
	30ac	**46a**	**48ca**	
7				82%
	30ac	**46g**	**48cg**	
8				80
	30ad	**46c**	**48dc**	
9				88
	30ae	**46a**	**48ea**	
10				87
	30ae	**46c**	**48ec**	

11				98
	30af	**46d**	**48fd**	
12				85
	30af	**46f**	**48ff**	
13		*n*-Hex–NH_2		75
	30af	**46h**	**48fh**	
14		*n*-Oct–NH_2		73
	30af	**46i**	**48fi**	

[a] Reaction conditions: **30a** (0.50 mmol), **46** (0.75 mmol), $Ni(cod)_2$ (5.0 mol %), dppf (5.0 mol %), NaO*t*-Bu (1.0 mmol), PhMe (1.0 mL), 105 °C, 16 h; [b] Yield of isolated product.

3.2.2 Nickel-Catalyzed Direct Arylations of Secondary Amines

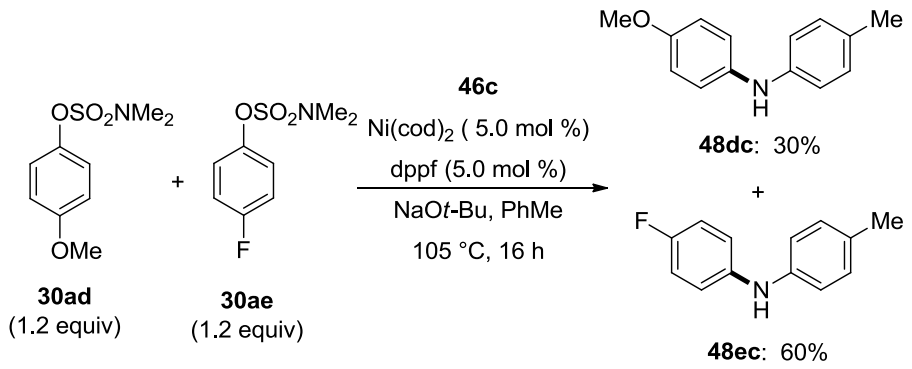
Compared to the arylations of primary amines the direct arylations of alkyl-substituted secondary amines **67** only gave moderate conversion with dppf as the ligand. However, a nickel catalyst generated in situ from an NHC precursor provided significant better results. The amination proceeded with high efficacy even at a lower reaction temperature (Scheme 3.1).



Scheme 3.1 Nickel-catalyzed arylation of morpholine **68**.

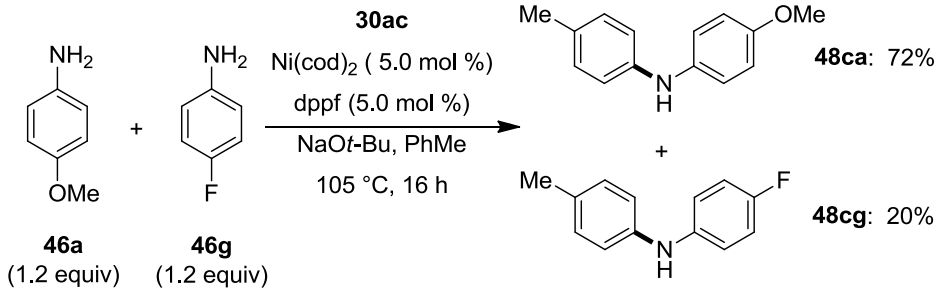
3.3 Intermolecular Competition Reactions

Intermolecular competition experiments were carried out to investigate the relative reaction rates. The reaction between electron-rich and electron-poor aryl sulfamates **30ad** and **30ae** revealed the latter to display a significantly higher inherent reactivity (Scheme 3.2).



Scheme 3.2 Competition experiments with different sulfamates **30a**.

Additionally, the electron-rich aniline **46a** gave much higher conversion than its electron-deficient analogue **46g** (Scheme 3.3).



Scheme 3.3 Competition experiments with different anilines **46**.

3.4 Conclusion

In summary, we have elaborated the unprecedented general nickel-catalyzed arylations of primary **46** and secondary amines **67** through challenging C–O bond activations in sulfamates **30a**. Hence, nickel catalyst derived from ligand dppf allowed for arylations with aryl sulfamates as electrophiles, whereas the direct arylations of secondary amines worked more efficiently with *N*-heterocyclic carbene (NHC) precursor as the ligand.

4. Nickel-Catalyzed Amination/Hydroamination for Indole Synthesis

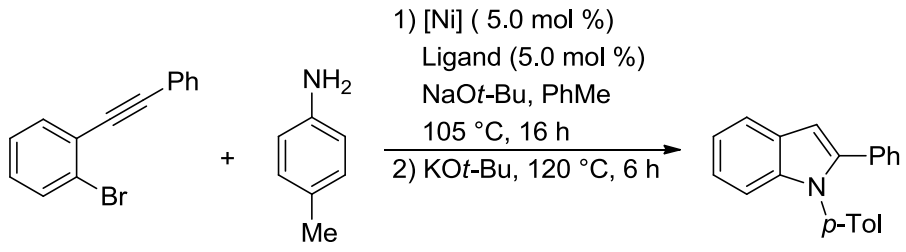
In the previous research of the Ackermann group, palladium and copper complexes were found to enable the formation of indoles bearing *inter alia* aryl-, alkyl- or alkoxycarbonyl-substituents on nitrogen. In continuation of these studies, we became interested in exploring the unprecedented use of inexpensive nickel catalysts for a modular indole synthesis starting from *ortho*-alkynylhaloarenes through a reaction cascade comprising intermolecular aminations of aryl halides and subsequent intramolecular hydroaminations of alkynes, the results of which are disclosed in this chapter.[53]

4.1 Optimization Studies of Nickel-Catalyzed Indole Synthesis

At the outset of these studies, we probed representative ligands and nickel compounds for the envisioned amination/hydroamination sequential synthesis of indole (Table 4.1). Notably, no conversion of starting material **45aa** to the desired product **47ac** occurred in the absence of a stabilizing ligand, irrespective of the oxidation state of the nickel precursors (entries 1–2). While monodentate phosphine ligands provided only unsatisfactory catalysis, improved isolated yields were obtained with precursors of NHCs. However, nickel complexes derived from bidentate ligands proved to be superior, with dppf being optimal (entries 3–14). Generally, the use of additional base KO*t*-Bu proved beneficial to ensure quantitative cyclization of the intermediate to the desired indole. Importantly, decreased loading of KO*t*-Bu could even improve the isolated yields, which means a base-mediated intramolecular hydroamination occured after the amination (entry 15).

[53] L. Ackermann, W. Song, R. Sandmann, *J. Organomet. Chem.* **2011***, 696,* 195–201.

Table 4.1: Optimization study of nickel-catalyzed indole synthesis[a]



45aa **46c** **47ac**

Entry	[Ni]	Ligand (mol %)	Yield (%)
1	$NiCl_2$	--	--
2	$Ni(cod)_2$	--	--
3	$Ni(cod)_2$	PPh_3 (10) (**56**)	--
4	$Ni(cod)_2$	PCy_3 (10) (**57**)	--
5	$Ni(cod)_2$	$(1\text{-}Ad)_2P(O)H$ (10) (**54**)	10
6	$Ni(cod)_2$	X-Phos (10) (**59**)	--
7	$Ni(cod)_2$	IMesHCl (10) (**69**)	12
8	$Ni(cod)_2$	IPrHCl (10) (**60**)	51
9	$Ni(cod)_2$	sHIPrCl (10) (**61**)	47
10	$Ni(cod)_2$	phenathroline (**62**)	49
11	$Ni(cod)_2$	*rac*-BINAP (**65**)	31
12	$Ni(cod)_2$	dppp (**63**)	46
13	$Ni(cod)_2$	dppe (**64**)	71
14	**$Ni(cod)_2$**	**dppf (66)**	**88**
15[b]	**$Ni(cod)_2$**	**dppf**	**92**

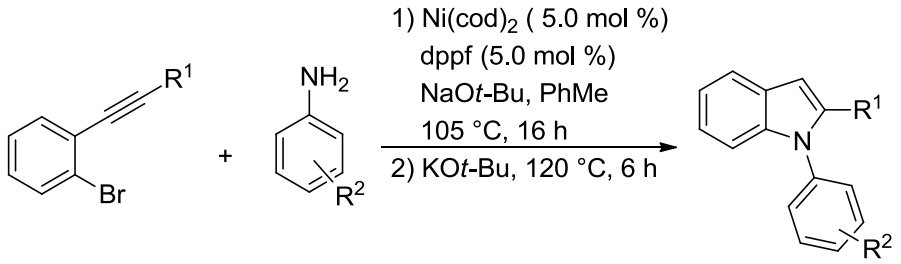
[a] Reaction conditions: **45aa** (1.0 equiv), **46c** (1.5 equiv), [Ni] (5.0 mol %), ligand (5.0 mol %), NaO*t*-Bu (1.5 equiv), PhMe (2.0 mL), 105 °C, 16 h; KO*t*-Bu (3.0 equiv), 120 °C, 6 h; isolated yields. [b] KO*t*-Bu (0.6 equiv).

4.2 Scope of Nickel-Catalyzed Indole Synthesis

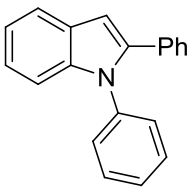
4.2.1 Nickel-Catalyzed Indole Synthesis with Aniline Derivatives

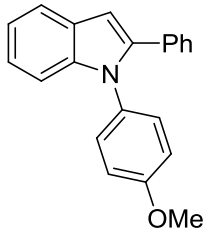
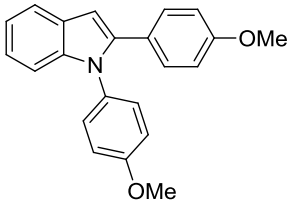
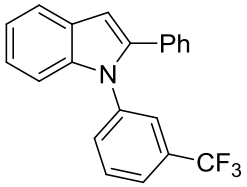
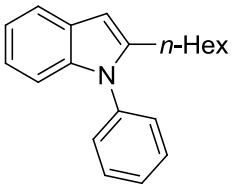
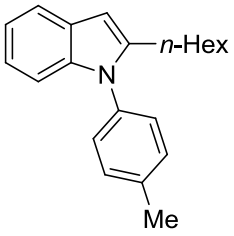
With an optimized catalytic system in hands, we probed its scope in the amination/hydroamination reaction sequence employing aniline derivatives **46** (Table 4.2). Notably, differently substituted aromatic amines could be employed, bearing either electron-donating or electron-withdrawing substituents (entries 1–4). Furthermore, the nickel catalyst was not restricted to the use of tolane derivatives. Indeed, substrates displaying alkyl-substituted alkynes were converted with an efficacy being comparable to the one observed when using the corresponding aryl-substituted analogues (entries 5–7). Moreover, sterically hindered aniline derivatives **46f** and **46j** provided the desired indoles in high yields, as did a nucleophile bearing a further Lewis-basic pyridyl moiety **46k** (entries 8–10).

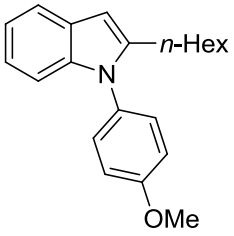
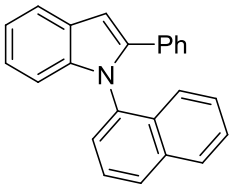
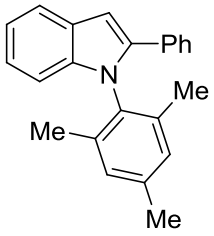
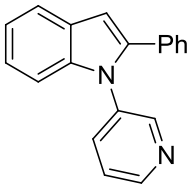
Table 4.2 Nickel-catalyzed amination/hydroamination-based indole synthesis with aniline derivatives **46**.[a]



45a **46** **47**

Entry	**45**	**46**	**47**	Yield (%)[b]
1	Ph	H		86
	45aa	**46b**	**47ab**	

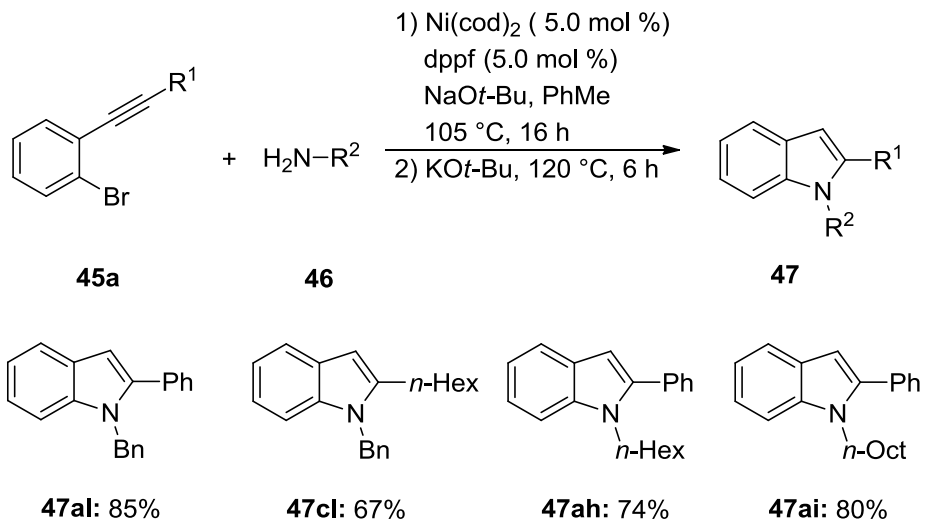
2	Ph	4-OMe		98
	45aa	**46a**	**47aa**	
3	4-$MeOC_6H_4$	4-MeO		89
	45ab	**46a**	**47ba**	
4	Ph	3-CF_3		72
	45aa	**46d**	**47ad**	
5	*n*-Hex	H		78
	45ac	**46b**	**47cb**	
6	*n*-Hex	4-Me		81
	45ac	**46c**	**47cc**	

7	*n*-Hex	4-MeO		75
	45ac	**46a**	**47ca**	
8	Ph	1-Naphthyl		78
	45aa	**46j**	**47aj**	
9	Ph	Mes		81
	45aa	**46f**	**47af**	
10	Ph	3-py		74
	45aa	**46k**	**47ak**	

[a] Reaction conditions: **45a** (0.5 mmol), **46** (0.75 mmol), [Ni(cod)$_2$] (5.0 mol %), dppf (5.0 mol %), NaO*t*-Bu (1.5 equiv), PhMe (2.0 mL), 105 °C, 16h; KO*t*-Bu (3.0 equiv), 120 °C, 6h. [b] Yield of isolated product.

4.2.2 Nickel-Catalyzed Indole Synthesis with Benzyl and Alkyl Amines

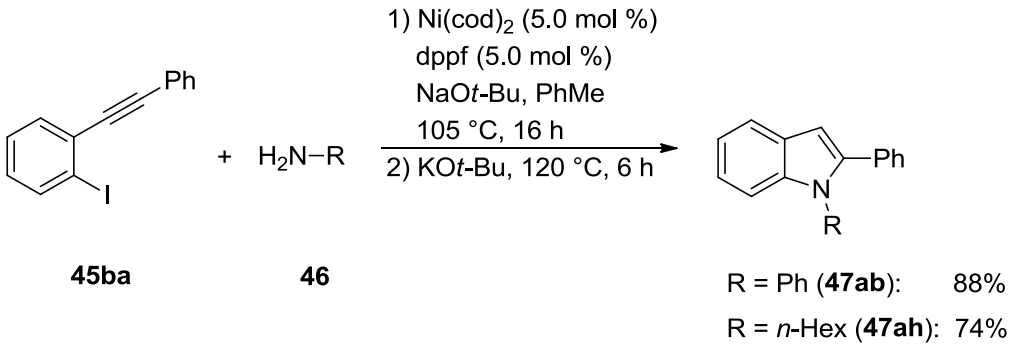
To our delight the nickel catalyst derived from dppf also enabled the preparation of indoles when using benzyl or even more challenging *n*-alkyl amines (Scheme 4.1).



Scheme 4.1 Nickel-catalyzed indole synthesis with benzyl and alkyl amines.

4.2.3 Nickel-Catalyzed Indole Synthesis with Aryl Iodides as Electrophiles

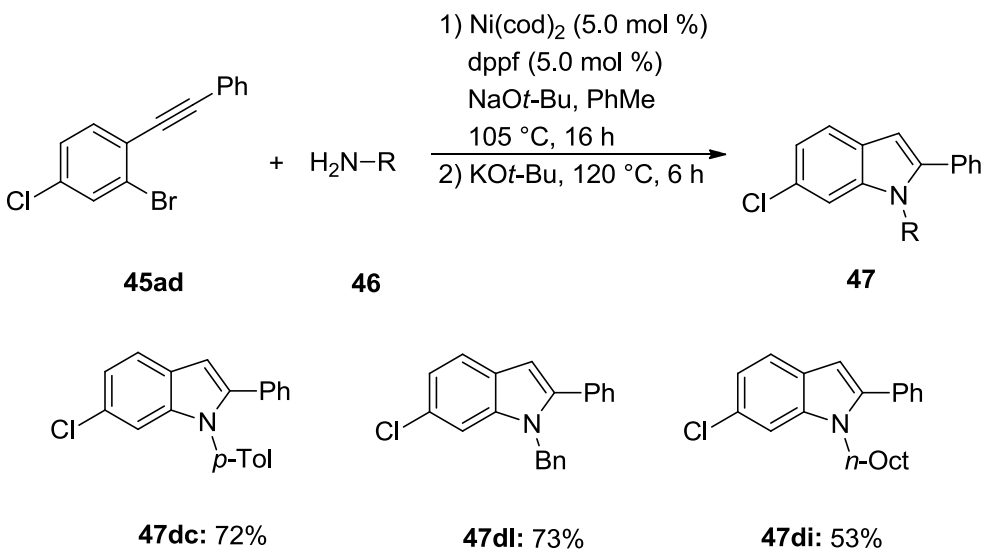
Notably, the catalytic system was further not limited to aryl bromides **45a** as electrophiles, but also proved amenable to an efficient amination/hydroamination sequence with aryl iodides **45b** as starting material. As was observed for the corresponding bromoarenes, the intermolecular amination as well as the intramolecular hydroamination occurred readily with both aniline derivatives and alkyl amines, thereby yielding the corresponding indoles **47**, respectively (Scheme 4.2).



Scheme 4.2 Nickel-catalyzed indole synthesis from iodide **45ba**.

4.2.4 Nickel-Catalyzed Chloro-Substituted Indole Synthesis

Finally, we exploited the excellent chemoselectivity of the dppf derived catalyst for the synthesis of indoles highlighting 6-chloro-substituents **45ad**, a valuable asset for further catalyzed functionalizations (Scheme 4.3).



Scheme 4.3 Nickel-catalyzed sequential synthesis of chloro-substituted indoles.

4.3 Conclusion

In summary, we have devised a versatile nickel catalyst for a sequential indole synthesis consisting of intermolecular aminations of aryl halides and subsequent intramolecular hydroaminations. Thus, an in situ generated complex derived from the ligand dppf (**66**) allowed for efficient transformations of *ortho*-alkynylhaloarenes with aryl as well as alkyl-substituted amines, and enabled the chemoselective synthesis of chloro-substituted indoles.

5. Nickel-Catalyzed Indole Synthesis *via* Oxidative Alkyne Annulation by Anilines

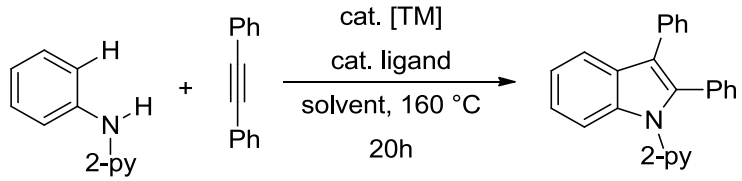
While nickel-catalyzed C–C and C–N bond forming reactions have particularly proven to be valuable for the preparation of indoles, these transformations largely relied on prefunctionalized starting materials. Moreover, the previous indole synthesis based on the direct C–H bonds activation normally called for the use of expensive late transition metals and the addition of stoichiometric amounts of oxidants, which limited their further application. Recently, Chatani reported a nickel-catalyzed isoquinolone synthesis through an annulation process without the extra use of oxidant, which overcame the disadvantages of the traditional annulation chemistry. In consideration of the practical importance of modular indole syntheses, we hence became interested in developing unprecedented nickel-catalyzed alkyne annulations by electron-rich anilines, which are discussed in this chapter.[54]

5.1 Optimization Studies of Nickel-Catalyzed Indole Synthesis *via* Oxidative Annulation by Anilines

We commenced our studies by identifying the reaction conditions for the nickel-catalyzed indole synthesis with *N*-(pyridine-2-yl)aniline **49aa** (Table 5.1). Comparing to other ligands, bidentate phosphine ligand dppf, in combination with $Ni(cod)_2$, proved to be optimal (entries 1–10). We were pleased to find that stoichiometric amounts of copper(II) or silver(I) salts were not required as sacrificial oxidants—a notable advantage over previously developed protocols. Interestingly, the formation of indole occurred most efficiently in the absence of solvents, thereby further improving the environmentally benign nature of our approach (entry 14). Control experiments verified that the formation of indole was neither achieved in the absence of $Ni(cod)_2$ nor without the dppf ligand (entries 15–16). Moreover, our studies revealed that representative palladium or cobalt complexes *in lieu* of the nickel(0) catalyst were ineffective (entries 17–18).

[54] W. Song, L. Ackermann, *Chem. Commun.* **2013**, *49*, 6638–6640.

Table 5.1 Optimization study of nickel-catalyzed indole synthesis *via* alkyne annulation by anilines[a]



49aa **4a** **50aa'**

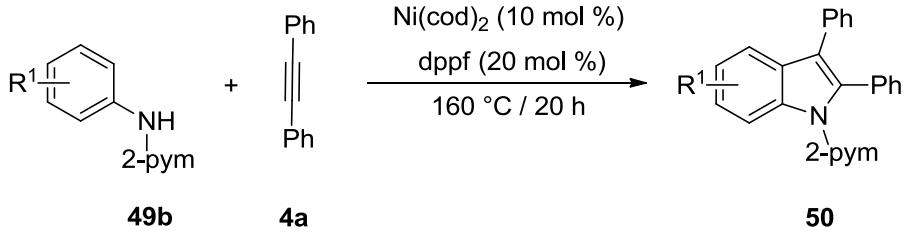
Entry	TM	Ligand	Solvent	Yield (%)
1	$Ni(cod)_2$	TMEDA (**70**)	PhMe	--
2	$Ni(cod)_2$	terpyridine (**71**)	PhMe	--
3	$Ni(cod)_2$	PPh_3[b] (**56**)	PhMe	40
4	$Ni(cod)_2$	dcype (**72**)	PhMe	--
5	$Ni(cod)_2$	*rac*-BINAP (**65**)	PhMe	21
6	$Ni(cod)_2$	dppp (**63**)	PhMe	30
7	$Ni(cod)_2$	DPEphos (**73**)	PhMe	30
8	$Ni(cod)_2$	Xantphos (**74**)	PhMe	43
9	$Ni(cod)_2$	dppf (**66**)	PhMe	48
10[c]	$Ni(cod)_2$	dppf	PhMe	63
11[c]	$Ni(cod)_2$	dppf	*m*-xylene	45
12[c]	$Ni(cod)_2$	dppf	*o*-xylene	35
13[c]	$Ni(cod)_2$	PPh_3[b]	--	65
14[c]	**$Ni(cod)_2$**	**dppf**	**--**	**82**
15[c]	--	dppf	--	--
16[c]	$Ni(cod)_2$	--	PhMe	--
17[c]	$Pd_2(dba)_3$	dppf	PhMe	--
18[c]	$Co_2(CO)_8$	dppf	PhMe	--

[a] Reaction conditions: **49aa** (0. 50 mmol), **4a** (1.50 mmol), [TM] (10 mol %), ligand (20 mol %), 160 °C, 20 h, isolated yields. [b] PPh_3 (40 mol %). [c] **4a** (2.50 mmol).

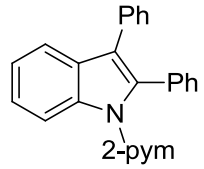
5.2 Scope of Nickel-Catalyzed Oxidative Annulation with Anilines

5.2.1 Nickel-Catalyzed Oxidative Annulation with Differently Functionalized Anlines

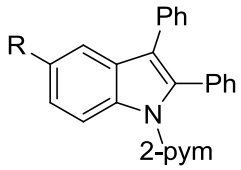
With an optimized catalytic system in hand, we explored its versatility in the oxidative annulation of diphenylacetylene **4a** (Scheme 5.1). Given that the *N*-2-pyrimidyl group is easily removed from the indole nucleus, we focused our studies on the use of *N*-pyrimidyl-substituted anilines **49b** for enlarging the scope. We were delighted to find that



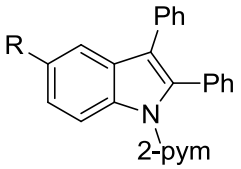
49b **4a** **50**



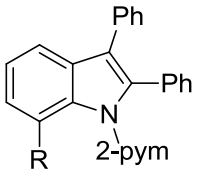
50aa: 81%
66%[a]
50%[b]



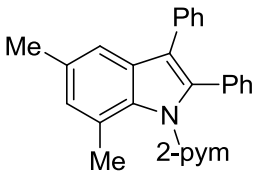
R = Ph (**50ba**): 68%
R = OMe (**50ca**): 67%
R = F (**50da**): 82%



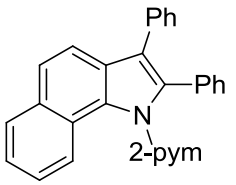
R = Cl (**50ea**): 55%
R = Ac (**50fa**): 68%
R = CN (**50ga**): 70%



R = F (**50ha**): 72%
R = OMe (**50ia**): 66%
R = Me (**50ja**): 65%



50ka: 49%



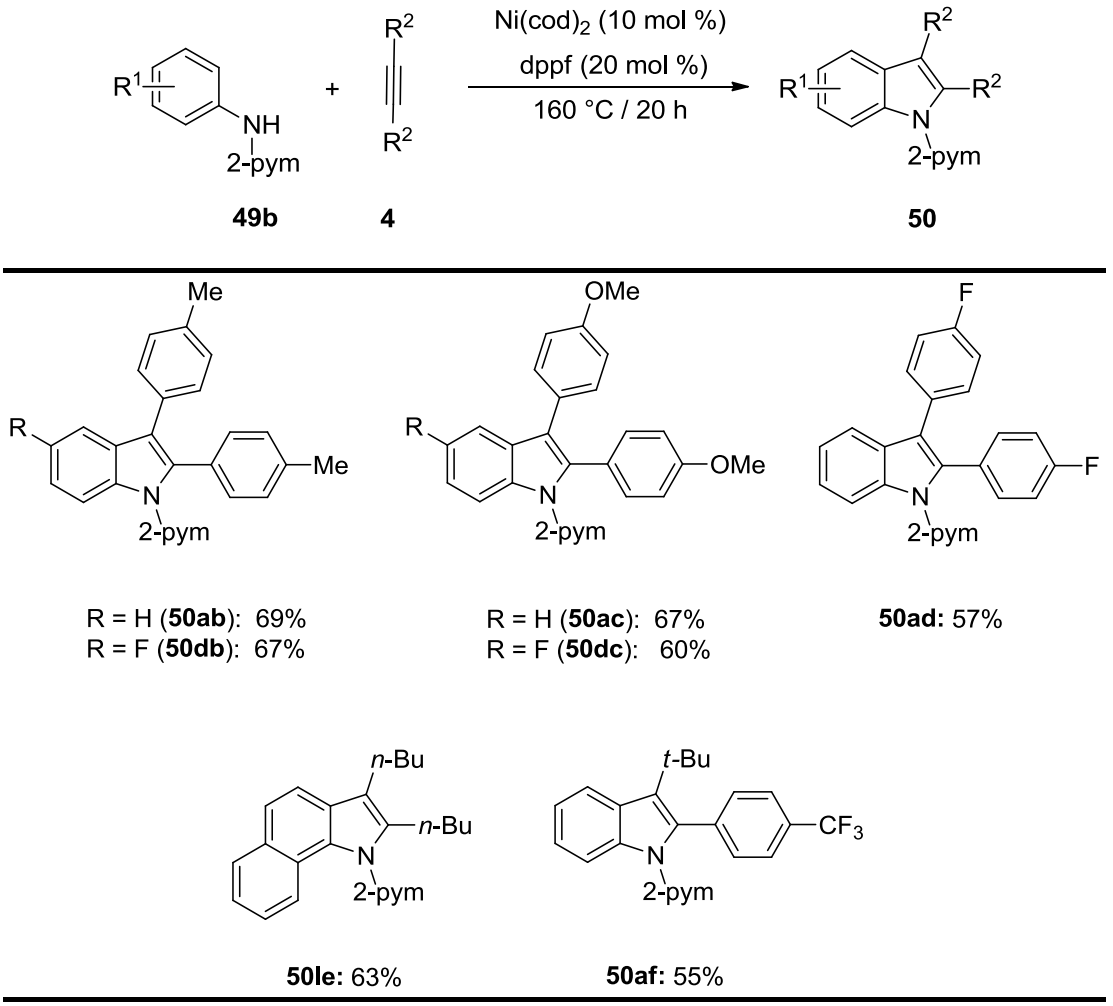
50la: 90%

Reaction conditions: **49b** (0. 50 mmol), **4a** (2.50 mmol), $Ni(cod)_2$ (10 mol %), dppf (20 mol %), 160 °C, 20 h; isolated yields. [a] $Ni(cod)_2$ (5.0 mol %), dppf (10 mol %). [b] **4a** (1.5 mmol).

Scheme 5.1 Scope of oxidative annulation with functionalized anlines **49b**.

the challenging pyrimidyl-substituted substrate was converted with a comparably high efficacy compared to reactions with the more electron-rich aniline. Additionally, half amount

of the catalyst also delivered the product in good yield. However, the decreased amount of diphenylacetylene caused a dramatic drop of the isolated yield. The optimized nickel(0) catalyst proved to be widely applicable, and allowed for the use of functionalized as well as sterically hindered *ortho*-substituted anilines, thereby furnishing the desired indoles **50**. It is particularly notable that reactive electrophilic functional groups, such as the chloro, acetyl or cyano substituents, were well tolerated, which should prove instrumental for further derivatization of the thus obtained products.



Scheme 5.2. Scope of nickel-catalyzed oxidative annulation with different alkynes **4**.

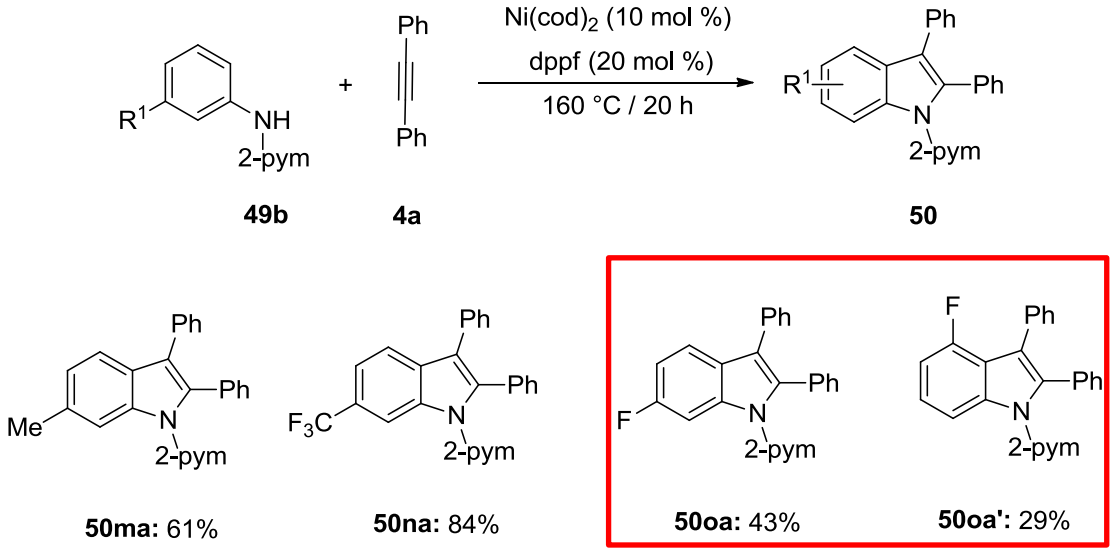
5.2.2 Nickel-Catalyzed Oxidative Annulation with Different Alkynes

Subsequently, we tested the scope of the nickel catalyst with a representative set of substituted alkynes (Scheme 5.2). We observed that tolane derivatives featuring either electron-donating or electron-withdrawing groups were efficiently converted under the optimized reaction

conditions. Noteworthy, the catalytic system was not restricted to tolanes. Indeed, dialkylalkyne **4e** provided the desired product as well. Importantly, the C–H/N–H bond functionalization with the unsymmetrical alkyne **4f** yielded the corresponding indole **50af** with excellent regioselectivity.

5.2.3 Nickel-Catalyzed Oxidative Annulation with *meta*-Substituted Anlines

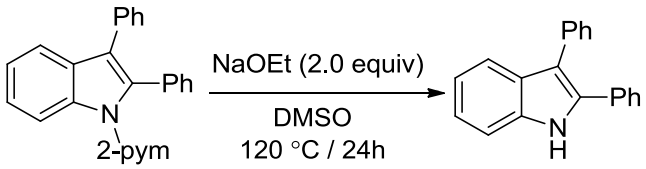
Considering the remarkable reactivity of the nickel(0) catalyst, we became interested in rationalizing its mode of action. To this end, we conducted intramolecular competition experiments with *meta*-substituted anilines. The site-selectivity of the C–H bond functionalization was largely governed by steric interactions, while a less steric hindered fluoro-substituent **49bo** led to significant amounts of products through C–H bond functionalization at the C-2 position as compared to the methyl- and trifluoromethyl-substituted substrates **49bm** and **49bn** (Scheme 5.3).



Scheme 5.3 Nickel-catalyzed oxidative annulation with *meta*-substituted anilines.

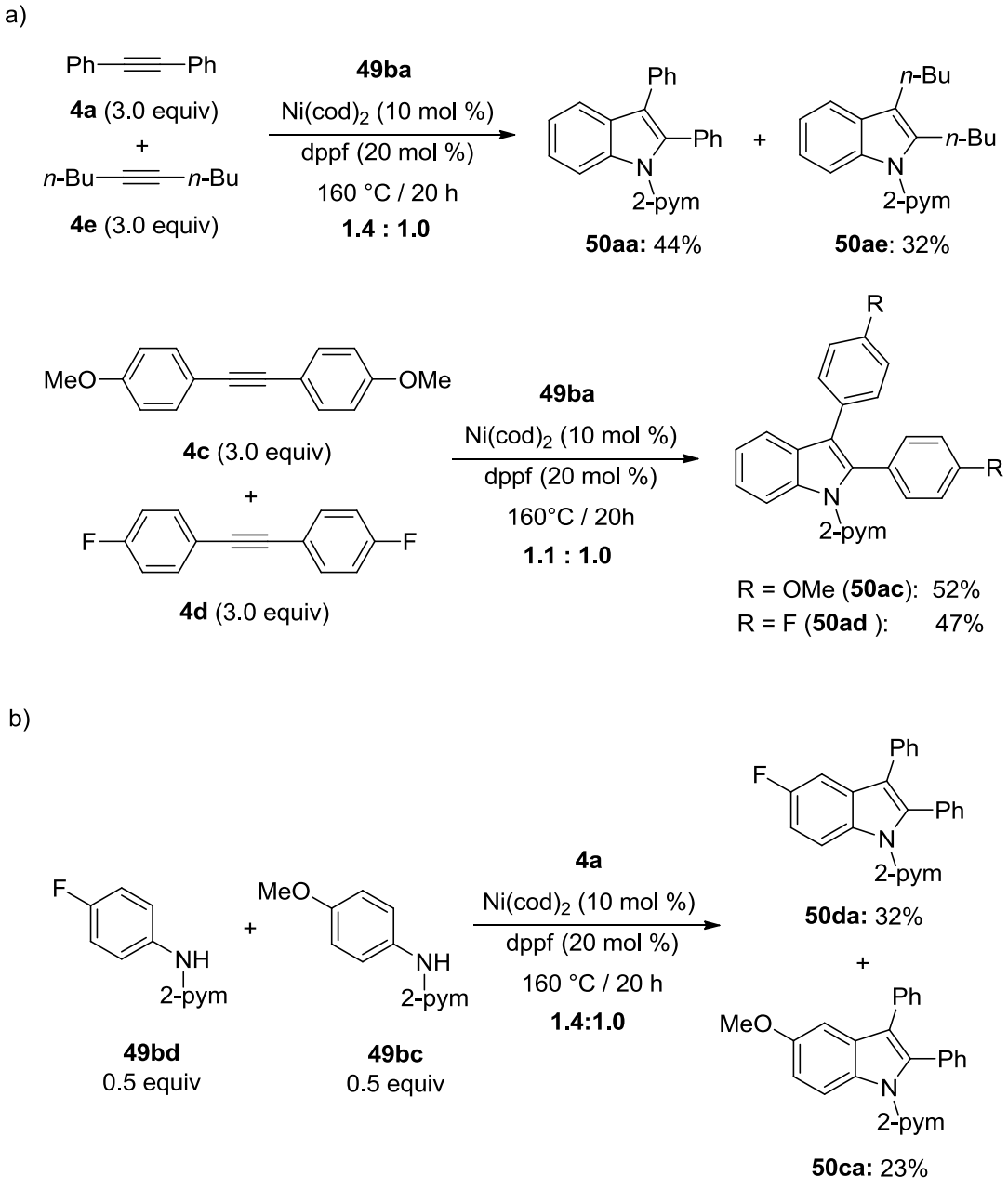
5.3 Removal of the Directing Group

For future practical applications it is important to note that the 2-pyrimidyl group was easily removed from indole to deliver the corresponding NH-free indole **75**. To our delight, after reacted with NaOEt in DMSO for 24 hours, the NH-free indole was obtained in an excellent yield (Scheme 5.4).



50aa **75:** 92%

Scheme 5.4 Removal of the directing group in the indole derivative **50aa**.



Scheme 5.5 Intermolecular competition experiments.

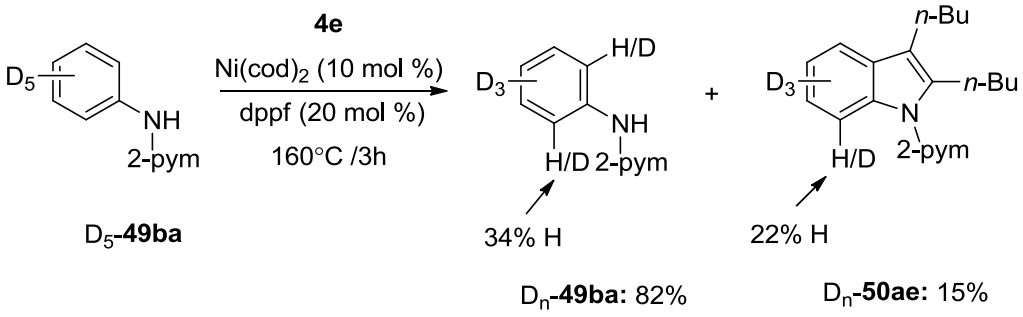
5.4 Mechanistic Studies

5.4.1 Intermolecular Competition Experiments

A series of competition reactions was carried out to understand the reaction mechanism. The intermolecular competition experiments with differently substituted alkynes **4** highlighted aryl acetylenes to be preferentially converted, and the electron-donating group on the alkynes also enhanced the reactivity (Scheme 5.5a), while electron-deficient arenes were found to be slightly more reactive (Scheme 5.5b). These experimental findings can be rationalized in terms of a rate-determining migratory alkyne insertion.

5.4.2 Experiments with Deuterium-Labeled Arenes

Additionally, we performed oxidative annulations with isotopically labeled substrate $[D]_5$-**49ba** (Scheme 5.6), revealing a considerable H/D exchange. Notably, the scrambling with the free N–H functionality exclusively occurred in the *ortho*-positions of the arene. These results, thus, provide strong support for an intrinsically reversible C–H bond metalation event to be operative.



Scheme 5.6 Intermolecular competition experiments.

Based on the mechanistic studies we consequently proposed the catalytic cycle to involve an initial reversible C–H bond metalation of aniline. Subsequent rate-determining migratory insertion and reductive elimination furnished the desired indole and regenerated the catalytically active nickel complex.

5.5 Conclusion

In summary, we have reported on an unprecedented nickel-catalyzed oxidative alkyne annulation by electron-rich anilines with removable directing groups. The C–H/N–H bond functionalization proceeded with excellent chemo-, regio- and site-selectivities in the absence of metal salts as oxidants, thereby furnishing substituted indoles **50** with broad scope. Experimental mechanistic studies provided strong support for a reversible C–H bond activation, and are suggestive of a rate-limiting migratory alkyne insertion.

6. Nickel-Catalyzed Chelation-Assisted Secondary Alkylation

Later, we get interested in the nickel-catalyzed C–C bond formations. In 2011, we published a nickel-catalyzed primary alkylation of the azoles with alkyl halides.[23] However, the secondary alkylation was proved unsuccessful under the elaborated reaction condition. Until now, there is no example for the nickel-catalyzed secondary alkylation of inert arenes.

Bidentate directing groups have attracted much attention during recent years due to their remarkable potential to activate the *ortho* C–H bonds in arenes. Since the pioneering direct arylation study by Daugulis,[55] a variety of reactions utilizing an *N*,*N*-bidentate assisted transformation of C–H bonds have been developed.[56] Thus, we developed the first nickel-catalyzed secondary alkylation through C–H bond functionalizations of arenes.

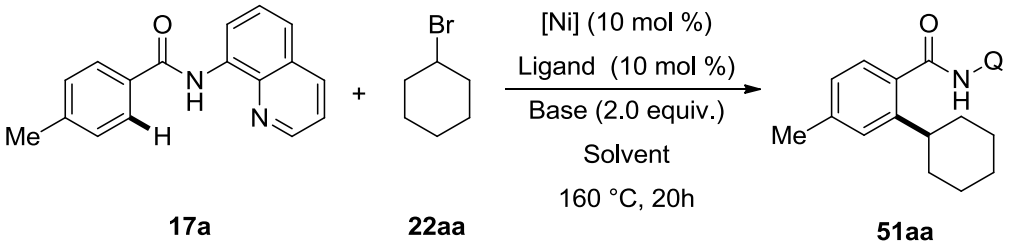
6.1 Optimization Studies of Nickel-Catalyzed Secondary Alkylation

We initiated our studies by exploring the reaction conditions for the desired direct secondary alkylation of *N*-quinolin-8-yl benzamide **17a** with bromocyclohexane **22aa** as the electrophile (Table 6.1). At the outset, we tested a diverse array of commercially available nickel precursors. Among other nickel sources, (DME)$NiCl_2$ was found to be most suitable, and showed an even better activity as compared to the commonly used $Ni(cod)_2$ (entries 1–5).

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

[56] [Pd]: a) B. V. S. Reddy, L. R. Reddy, E. Corey, J. *Org. Lett.* **2006**, *8*, 3391–3394; b) R. Giri, N. Maugel, B. M. Foxman, J.-Q. Yu, *Organometallics* **2008**, *27*, 1667–1670; c) F.-R. Gou, X.-C. Wang, P.-F. Huo, H.-P. Bi, Z.-H. Guan, Y.-M. Liang, *Org. Lett.* **2009**, *11*, 5726–5729; d) D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2010**, *132*, 3965–3972; e) G. He, G. Chen, *Angew. Chem. Int. Ed.* **2011**, *50*, 5192–5196; f) Y. Zhao, G. Chen, *Org. Lett.* **2011**, *13*, 4850–4853; g) B. V. S. Reddy, G. Revathi, A. S. Reddy, J. S. Yadav, *Tetrahedron Lett.* **2011**, *52*, 5926–5929; h) Y. Ano, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 12984–12986; i) G. He, Y. Zhao, S. Zhang, C. Lu, G. Chen, *J. Am. Chem. Soc.* **2012**, *134*, 3–6; j) E. T. Nadres, O. Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 7–10; k) Y. Ano, M. Tobisu, N. Chatani, *Org. Lett.* **2012**, *14*, 354–357; l) Y. Xie, Y. Yang, L. Huang, X. Zhang, Y. Zhang, *Org. Lett.* **2012**, *14*, 1238–1241; m) L. D. Tran, O. Daugulis, *Angew. Chem. Int. Ed.* **2012**, *51,* 5188–5191; n) S.-Y. Zhang, G. He, Y. Zhao, K. Wright, W. A. Nack, G. Chen, *J. Am. Chem. Soc.* **2012**, *134*, 7313–7316; o) N. Rodríguez, J. A. Romero-Revilla, M. Á. Fernández-Ibáñez, J. C. Carretero, *Chem. Sci.* **2013**, *4*, 175–179; p) S.-Y. Zhang, G. He, W. A. Nack, Y. Zhao, Q. Li, G. Chen, *J. Am. Chem. Soc.* **2013**, *135*, 2124–2127; [Cu]: q) L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 18237–18240; r) M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2013**, *52*, 4457–4461; [Ru]: s) S. Inoue, H. Shiota, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2009**, *131*, 6898–6899; t) N. Hasegawa, V. Charra, S. Inoue, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 8070–8073; u) K. Shibata, N. Hasegawa, Y. Fukumoto, N. Chatani, *ChemCatChem* **2012**, *4*, 1733–1736; v) N. Hasegawa, K. Shibata, V. Charra, S. Inoue, Y. Fukumoto, N. Chatani, *Tetrahedron* **2013**, *69*, 4466–4472; w) Y. Aihara, N. Chatani, *Chem. Sci.* **2013**, *4*, 664–670; [Ni]: x) H. Shiota, Y. Ano, Y. Ahihara, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 14952–14955; [Fe]: y) R. Shang, L. Ilies, A. Matsumoto, E. Nakamura, *J. Am. Chem. Soc.* **2013**, *135*, 6030–6032.

Table 6.1: Optimization of the nickel-catalyzed secondary alkylation.[a]

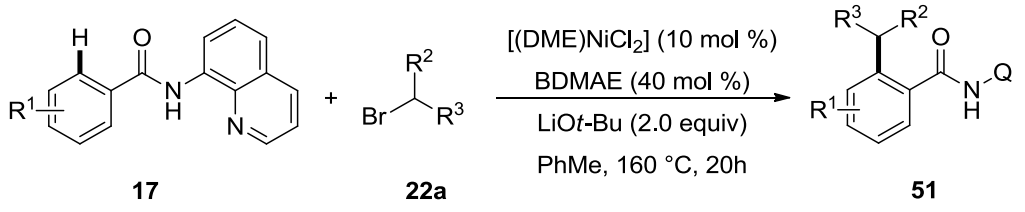


17a **22aa** **51aa**

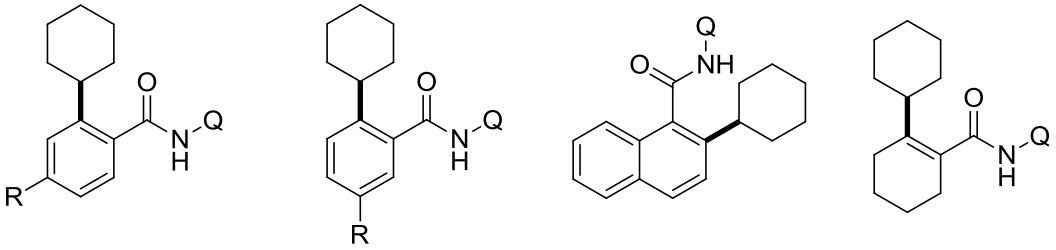
Entry	[Ni]	Ligand	Base	Solvent	Yield (%)[b]
1	$Ni(acac)_2$	--	LiO*t*-Bu	*o*-xylene	10
2	$Ni(cod)_2$	--	LiO*t*-Bu	*o*-xylene	52
3	$Ni(OTf)_2$	--	LiO*t*-Bu	*o*-xylene	33
4	$NiCl_2$	--	LiO*t*-Bu	*o*-xylene	--
5	$(DME)NiCl_2$	--	LiO*t*-Bu	*o*-xylene	55
6	$(DME)NiCl_2$	PPh_3 (**56**)	LiO*t*-Bu	*o*-xylene	30
7	$(DME)NiCl_2$	IPrHCl (**60**)	LiO*t*-Bu	*o*-xylene	--
8	$(DME)NiCl_2$	X-phos (**59**)	LiO*t*-Bu	*o*-xylene	20
9	$(DME)NiCl_2$	DME (**76**)	LiO*t*-Bu	*o*-xylene	60
10	$(DME)NiCl_2$	BDMAE (**77**)	LiO*t*-Bu	*o*-xylene	70
11	$(DME)NiCl_2$	phenanthroline (**62**)	LiO*t*-Bu	*o*-xylene	--
12	$(DME)NiCl_2$	*L*-proline (**78**)	LiO*t*-Bu	*o*-xylene	22
13	$(DME)NiCl_2$	TMEDA (**70**)	LiO*t*-Bu	*o*-xylene	45
14	$(DME)NiCl_2$	BDMAE	Na_2CO_3	*o*-xylene	--
15	$(DME)NiCl_2$	BDMAE	Cs_2CO_3	*o*-xylene	--
16	$(DME)NiCl_2$	BDMAE	NaOAc	*o*-xylene	--
17	$(DME)NiCl_2$	BDMAE	LiO*t*-Bu	Dioxane	71
18	$(DME)NiCl_2$	BDMAE	LiO*t*-Bu	PhMe	76
19[c]	**$(DME)NiCl_2$**	**BDMAE**	**LiO*t*-Bu**	**PhMe**	**86**

[a] Reaction conditions: **17a** (0.50 mmol), **22aa** (1.0 mmol), [Ni] (10 mol %), ligand (20 mol %), base (2.0 equiv), solvent (1.0 mL), 160 °C, 20 h. [b] Yield of isolated product. [c] BDMAE (40 mol %).

Thereafter, we explored a set of representative ligands with the (DME)$NiCl_2$ as the nickel source. Comparing to other ligands, the BDMAE (Bis (2-dimethylaminoethyl) ether) and DME (Dimethoxyethane) were found to provide higher conversion to the desired product, and the BDMAE was proved to be the optimal choice (entries 6–13). Subsequently, we probed a variety of bases and solvents for the secondary alkylation of the substrate. The most effective transformation was accomplished with LiO*t*-Bu as the base. On the contrary, the alkylation occurred with significantly reduced efficacy when other bases were employed (entries 14–16). Moreover, a higher efficacy was found when toluene was used as the solvent instead of *o*-xylene (entries 17–19).



17 **22a** **51**

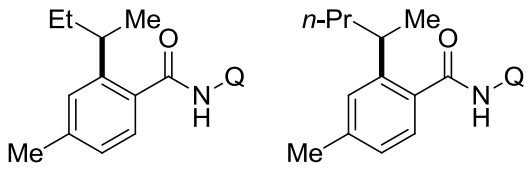


R = H (**51ba**): 80%
R = F (**51ca**): 83%
R = CF_3 (**51da**): 73%
R = OMe (**51ea**): 52%
R = Ph (**51fa**): 86%
R = Cl (**51ga**): 64%

R = Me (**51ha**): 54%
R = CF_3 (**51ia**): 64%

51ja: 61%

51ka: 58%



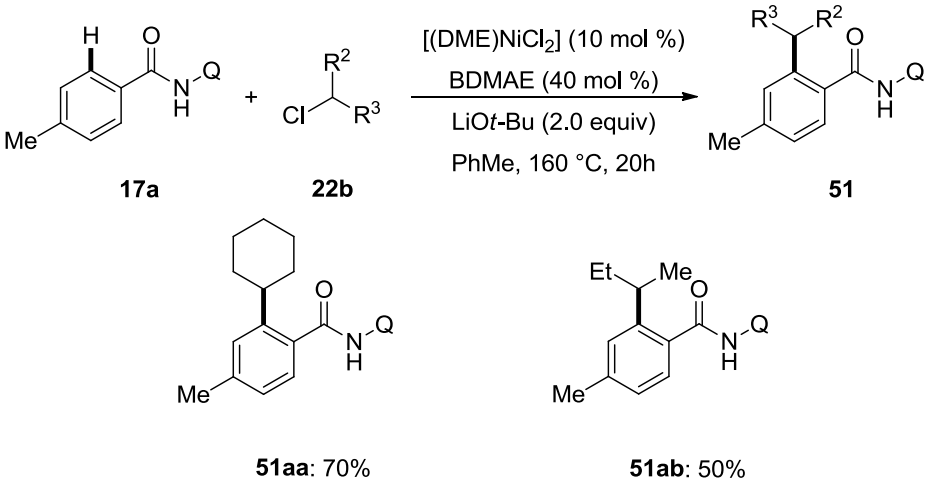
51ab: 52% **51ac**: 75%

Scheme 6.1. Nickel-catalyzed alkyaltions with secondary alkyl bromides **22a**.

6.2 Scope of Nickel-Catalyzed Secondary Alkylation

6.2.1 Nickel-Catalyzed Alkylation with Secondary Alkyl Bromides

With the optimized catalytic system in hands, we probed its scope in the C–H bonds functionalization of diversely substituted arenes **17** with secondary alkyl bromides **20a**. To our delight, good selectivity was achieved even without substitution on the *ortho*-position. Thus, only mono-substituted product **51** was obtained in high efficacy. Generally, the electron-withdrawing groups tended to deliver the alkylation product in higher yields as compared to the electron-donating derivatives. Moreover, a variety of functional groups were tolerated in this reaction. The reaction with *meta*-substituted substrates resulted in the selective alkylation at the less hindered C–H bonds. Most probably, the regioselectivity was rather controlled by the steric nature of the substituent. Additionally, the *a,β*-unsaturated amide **17k** could also be applied for the secondary alkylation reaction. Consequently, a variety of alkyl bromides **22a** were proved to be applicable to the alkylation reaction. To our delight, acyclic secondary alkyl bromides were also amendable to the reaction conditions, without formation of isomerizations by-products.



Scheme 6.2. Nickel-catalyzed secondary alkylation with alkyl chlorides **22b**.

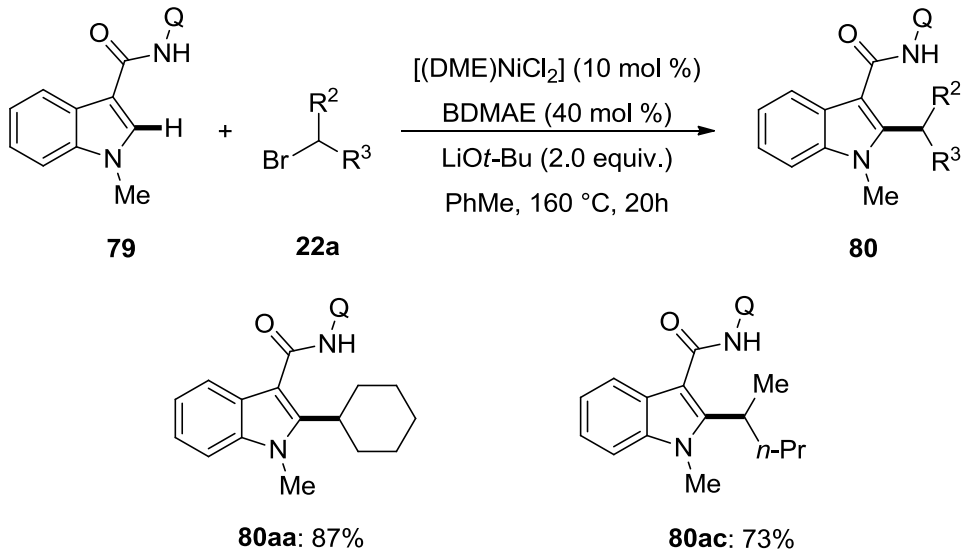
6.2.2 Nickel-Catalyzed Alkylations with Secondary Alkyl Chlorides

We were pleased to observe that the less reactive secondary alkyl chlorides **22b** turned out to be viable electrophiles as well, even without addition of NaI. However, somewhat lower

yields of the desired products **51** were obatained as compared to the analogous reactions with bromides **22a**.

6.2.3 Nickel-Catalyzed Alkylations of Indoles with Secondary Electrophiles

Likewise, indoles **79** served as valuable substrates for the nickel-catalyzed secondary alkylation. Secondary alkylation with either cyclic or acyclic alkyl bromides delivered the desired products in high efficacy.



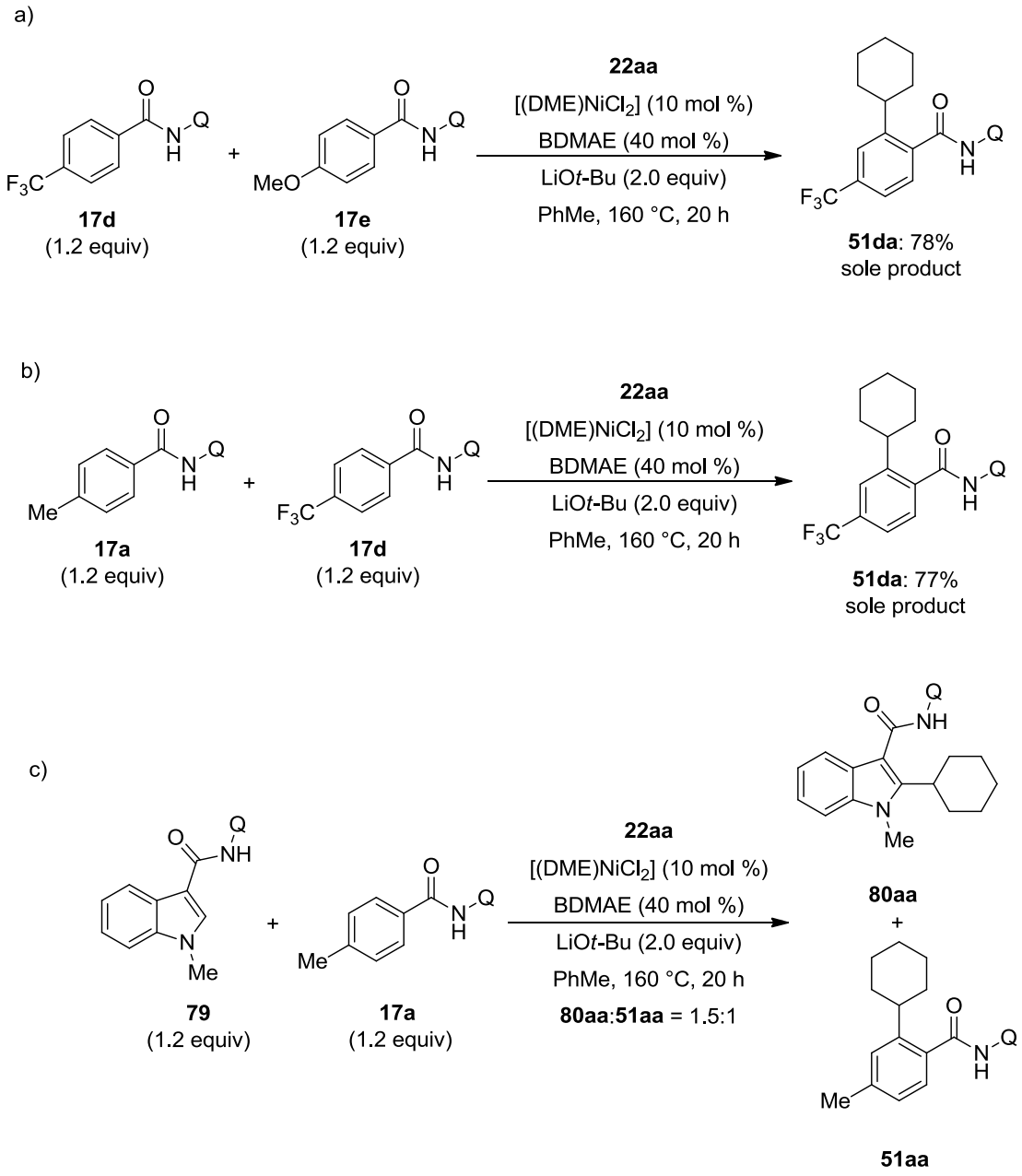
Scheme 6.3. Nickel-catalyzed secondary alkylation of indole **79**.

6.3 Mechanistic Studies

6.3.1 Intermolecular Competition Reactions

Continuing our investigations of these chelation-assisted reactions, we performed several intermolecular competition experiments on direct alkylations of variously substituted arenes **17a**, **17d** and **17e** as well as of indole **79** with the goal to elucidate the mode of action of this unique active nickel catalyst. These experiments revealed the substrate **17d** with an electron-withdrawing group to react faster than its electron-enriched (**17e**, Scheme 6.4a) and electron-neutral (**17a**, Scheme 6.4b) analogues. On the other hand, arene **17a** displayed comparable reactivity in its competition experiment with indole **79** with the slightly enhanced reactivity of the latter (Scheme 6.4c). Both results indicated the significance of the kinetic C–

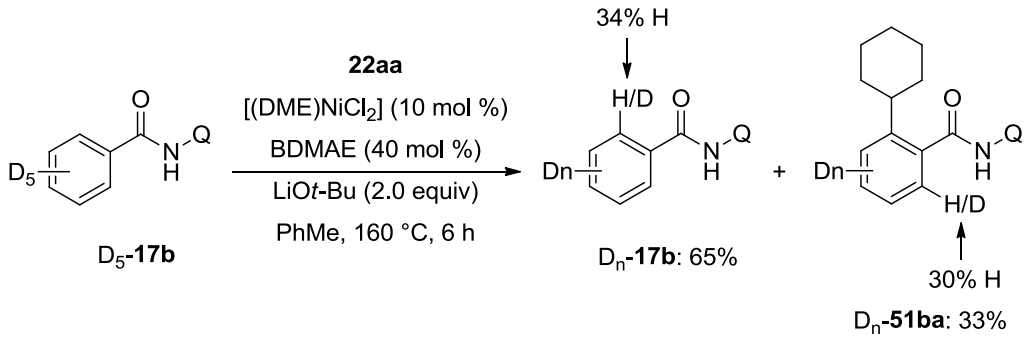
H bond acidity for the success of the nickel-catalyzed alkylations.



Scheme 6.4 Intermolecular competition experiments with different (hetero)arenes**.**

6.3.2 Reaction with Deuterium-labeled Substrate

Additionally, we performed the secondary alkylation with isotopically labeled substrate $[D]_5$-**17b**, revealing a considerable H/D exchange exclusively occurring in the *ortho*-positions of the arene. This result, thus, provided strong support for a reversible C–H bond metalation event to be operative and indicate that cleavage of the C−H bond likely is not the rate-determining step (Scheme 6.5).



Scheme 6.5. Reaction with deuterium-labeled substrate D_5-**17b**.

6.4 Conclusion

A nickel-catalyzed direct secondary alkylation of unreactive arenes through chelation-assisted C−H bonds activation was developed. A series of substituted arenes was efficiently converted and good chemo- and site-selectivities were achieved. Different kinds of electrophiles were used to deliver the desired products in high efficacy, even with unreactive secondary alkyl chlorides.

7. Cobalt-Catalyzed Direct Arylations *via* C–O bond Cleavages

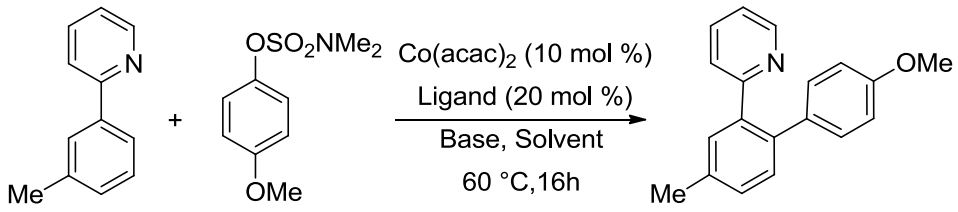
Biaryl derivatives are important building blocks in organic synthesis, especially with applications to natural products synthesis, medicinal chemistry, and materials science.[1a] The most commonly used methods for aryl-aryl bond formations involve traditional transition-metal-catalyzed cross couplings of aryl halides with metal reagents. However, these methods are limited by the preparation of the prerequisite organometallic reagents and the formation of stoichiometric amount of by-products. The direct introduction of the aryl electrophiles through C–H bond cleavages[57] has been widely studied during the past decades as an alternative strategy for biaryl bond formations. The reactivity of arylating electrophiles toward transition metals typically follows the trend ArI > ArBr ≈ ArOTf >> ArCl > ArOTs. However, their prices and accessibility follows almost the same trend. While aryl halides are still widely applied as electrophiles for direct arylations, recent focus has been shifted towards the use of phenol derivatives, which are inexpensive, readily accessible, and can easily be implemented as directing groups in versatile arene functionalization strategies. In recent years, cobalt-catalyzed C–H bond activation was well studied. However, cobalt-catalyzed direct arylation of inert arenes with phenol electrophiles are not available. In this chapter, we will focus on this area and describe the first cobalt-catalyzed direct arylation *via* the direct C–H/C–O bond cleavages.[58]

7.1 Optimization Studies of Cobalt-Catalyzed Direct Arylations

We initiated our studies by exploring the reaction conditions for the direct arylation with electronically deactivated sulfamate **30ad** employing $Co(acac)_2$ as the pre-catalyst in DMPU as the solvent (Table 7.1). While unsatisfactory results were obtained in the absence of ligands (entry 1) as well as with the mono- or bidentate phosphine ligands or phenanthroline (entries 2–4), the *N*-heterocyclic carbene (NHC) precursors showed higher efficacies for catalytic C–

[57] L. Ackermann, R. Vicente, *Metal-Catalyzed Direct Arylations*, in *Modern Arylation Methods* (Ed.: L. Ackermann), Wiley-VCH, Weinheim, **2009**, pp. 311–333.
[58] W. Song, L. Ackermann, *Angew. Chem. Int. Ed.* **2012**, *51*, 8251–8254.

Table 7.1 Optimization of the direct arylation reaction with sulfamate **30ad**.[a]



3a **30ad** **52ad**

Entry	Ligand	Base	Solvent	Yield (%)[b]
1	--	CyMgCl	DMPU	15
2 [c]	dppe (**64**)	CyMgCl	DMPU	--
3	PCy_3 (**57**)	CyMgCl	DMPU	21
4 [c]	phenanthroline (**62**)	CyMgCl	DMPU	11
5	sIPrHCl (**61**)	CyMgCl	DMPU	42
6	sIMesHCl (**81**)	CyMgCl	DMPU	40
7	IPrHCl (**60**)	CyMgCl	DMPU	47
8	**IMesHCl** (**69**)	**CyMgCl**	**DMPU**	**82**
9	IMesHCl	KO*t*-Bu	DMPU	--
10	IMesHCl	LiHMDS	DMPU	--
11	IMesHCl	MeMgCl	DMPU	59
12	IMesHCl	*t*-BuMgCl	DMPU	40
13	IMesHCl	CyMgCl	NMP	--
14	IMesHCl	CyMgCl	toluene	--
15[d]	IMesHCl	CyMgCl	DMPU	38
16[e]	IMesHCl	CyMgCl	DMPU	--
17[f]	IMesHCl	CyMgCl	DMPU	80

[a] Reaction conditions: **3a** (0.75 mmol), **30ad** (0.50 mmol), $Co(acac)_2$ (10 mol %), ligand (20 mol %), base (2.0 equiv), solvent (1.0 mL), 60 °C, 16 h. [b] Yield of isolated product. [c] 10 mol % of ligand was used. [d] Reaction runs at 23 °C. [e] Without $Co(acac)_2$. [f] $Co(acac)_3$ (10 mol %).

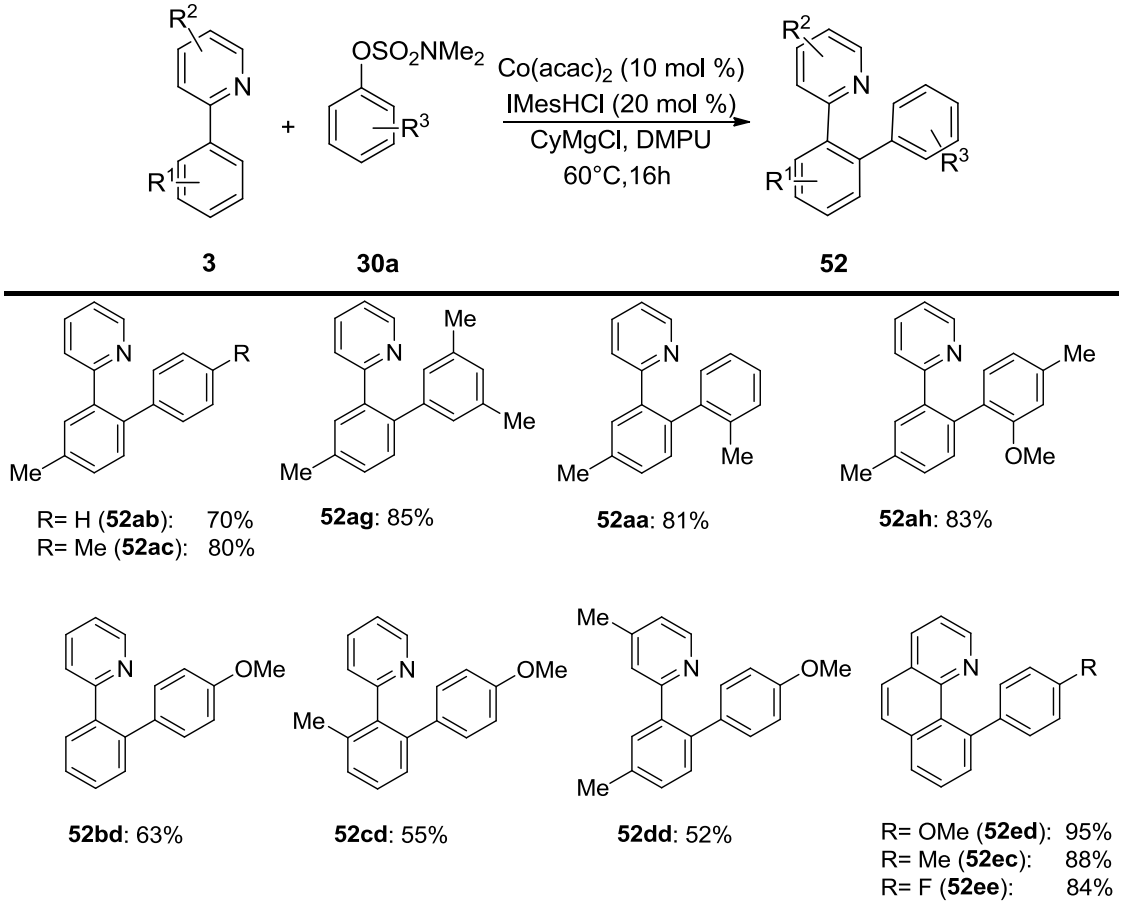
H bond transformations (entries 5–7) with IMesHCl (**69**) delivering the optimal yield (entry 8). Notably, LiHMDS or KO*t*Bu as bases failed to affect the desired direct arylation with aryl sulfamates (entries 9, 10), while CyMgCl was found to be the base of choice. Among the

solvents tested, polar aprotic DMPU proved beneficial for the direct arylation. Notably, comparable catalytic efficacies were obtained using both cobalt(II) and cobalt(III) complexes (entries 8, 17).

7.2 Scope of Cobalt-Catalyzed Direct Arylations

7.2.1 Cobalt-Catalyzed Direct Arylations with Aryl Sulfamates

With the optimized reaction condition in hands, we explored the scope of the cobalt-catalyzed C–H bond arylation with differently substituted aryl sulfamates **30a**. Notably, electron-rich-and thus deactivated for an oxidative addition-aryl sulfamates were effectively converted, even when bearing sterically hindered *ortho*-substituents. Moreover, various pyridyl-substituted arenes **3** chemoselectively provided the desired monoarylated products **52**. Besides, benzo[*h*]quinolones (**3e**) could also be arylated, furnishing the desired compounds in high efficiency (Scheme 7.1).



Scheme 7.1 Cobalt-catalyzed direct arylations with aryl sulfamates **30a**.

7.2.2 Cobalt-Catalyzed Direct Arylations with Aryl Carbamates

The cobalt catalyst was not restricted to the use of sulfamates **30a** as the electrophiles, but also allowed for the first C–H bond arylations of arenes with widely accessible aryl carbamates **30b**. Both electron-rich and functionalized, electron-deficient aryl carbamates were converted with remarkably high catalytic efficacy. Furthermore, both electron-rich and electron-poor arenes **3** could deliver the desired products **52** in high yield. Considering the reaction mechanism, an intramolecular competition experiment with *meta*-fluoro-substituted arene **3g** site-selectively furnished biaryl through functionalization of the kinetically more acidic C–H bond. Most probably, this selectivity resulted from the concerted action of the chelating effect of 2-pyridyl moiety and the well-documented *ortho*-orienting influence of the fluorine substituents.[59] Moreover, aryl carbamates **30bi**/**30bj** which are functionalized with sterically hindered substituents in the *ortho*-position, delivered the desired products, thereby illustrating the power of aryl carbamates for strategies that merge directed ortho metalation (DoM) and C–H bond functionalization. Additionally, differently substituted pyridyl-directing groups could be employed to give the desired products **52dd/52hd** with high site-selectivity, as could a less electron-donating 2-pyrimidyl-substituent **52id** (Scheme 7.2).

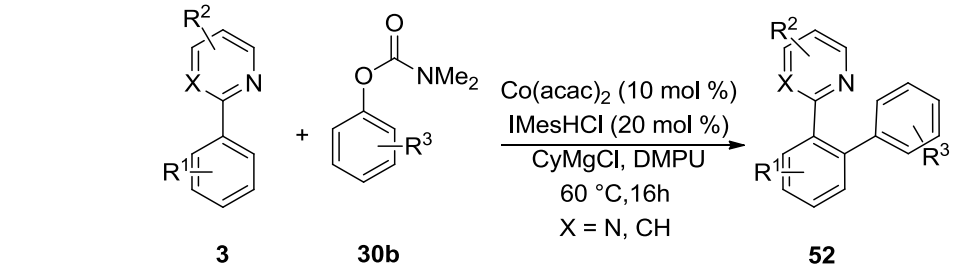
7.2.3 Direct Arylation at Ambient Temperature

Interestingly, the direct arylation with carbamate **30b** worked efficiently even at ambient temperature. While, the direct arylation with other phenol-derived electrophiles at room temperature afforded product **52ad** only in lower yields (Scheme 7.3).

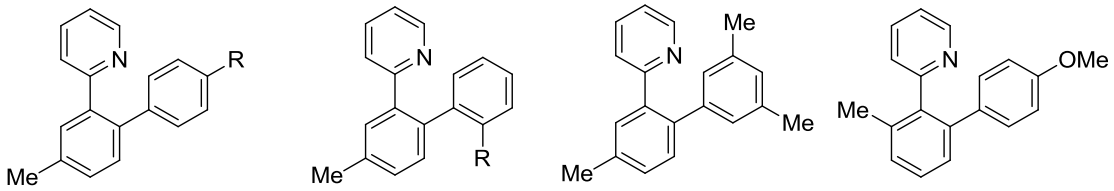
7.2.4 Cobalt-Catalyzed Direct Arylation of Heteroarenes

Likewise, heteroarenes could also serve as valuable substrates for the cobalt-catalyzed direct arylation with aryl sulfamates **30a** and carbamates **30b**. Indeed, *N*-substituted indoles **82** were selectively arylated at the C-2 position, which allowed for the synthesis of, among other products, sterically encumbered heterobiaryl (Scheme 7.4), a feature that should prove instrumental for future applications to asymmetric C–H bond arylations.

[59] For reviews, see: a) E. Clot, O. Eisenstein, N. Jasim, S. A. Macgregor, J. E. McGrady, R. N. Perutz, *Acc. Chem. Res*. **2011**, *44*, 333–348; b) M. E. Evans, C. L. Burke, S Yaibuathes, E. Clot, O. Eisenstein, W. D. Jones, *J. Am. Chem. Soc*. **2009**, *131*, 13464–13473; c) E. Clot, C. Mégret, O. Eisenstei, R. N. Perutz, *J. Am. Chem. Soc*. **2009**, *131*, 7817–7827.



3 **30b** **52**

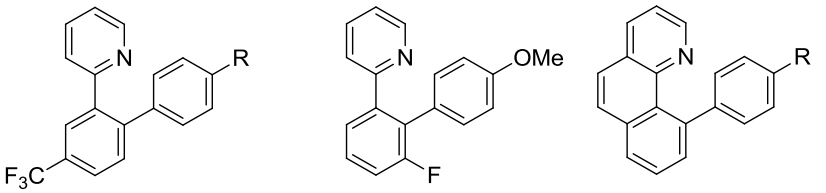


R= H (**52ab**): 71%
R= Me (**52ac**): 81%
R= OMe (**52ad**): 90%

R = Me (**52aa**): 77%
R = Ph (**52ai**): 72%
R = TMS (**52aj**): 76%

52ag: 86%

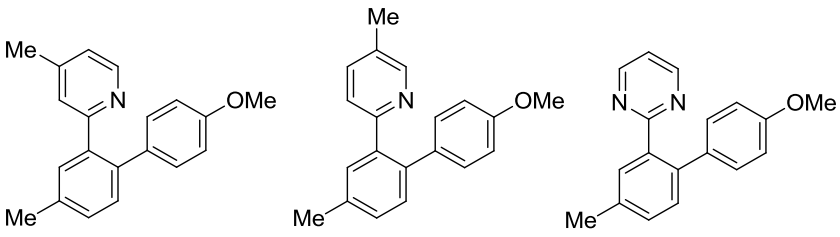
52cd: 63%



R= Me (**52fc**): 87%
R= OMe (**52fd**): 93%

52gd: 90%

R= Me (**52ec**): 86%
R= OMe(**52ed**): 96%
R= F (**52ee**): 82%

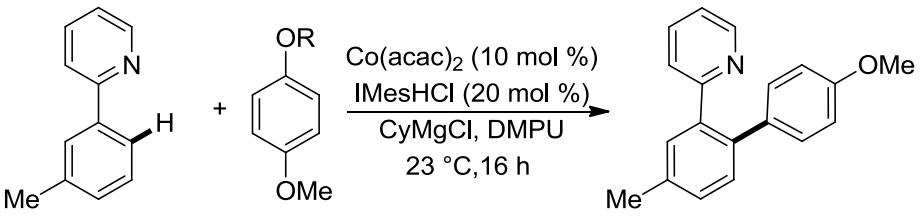


52dd: 84%

52hd: 82%

52id: 95%

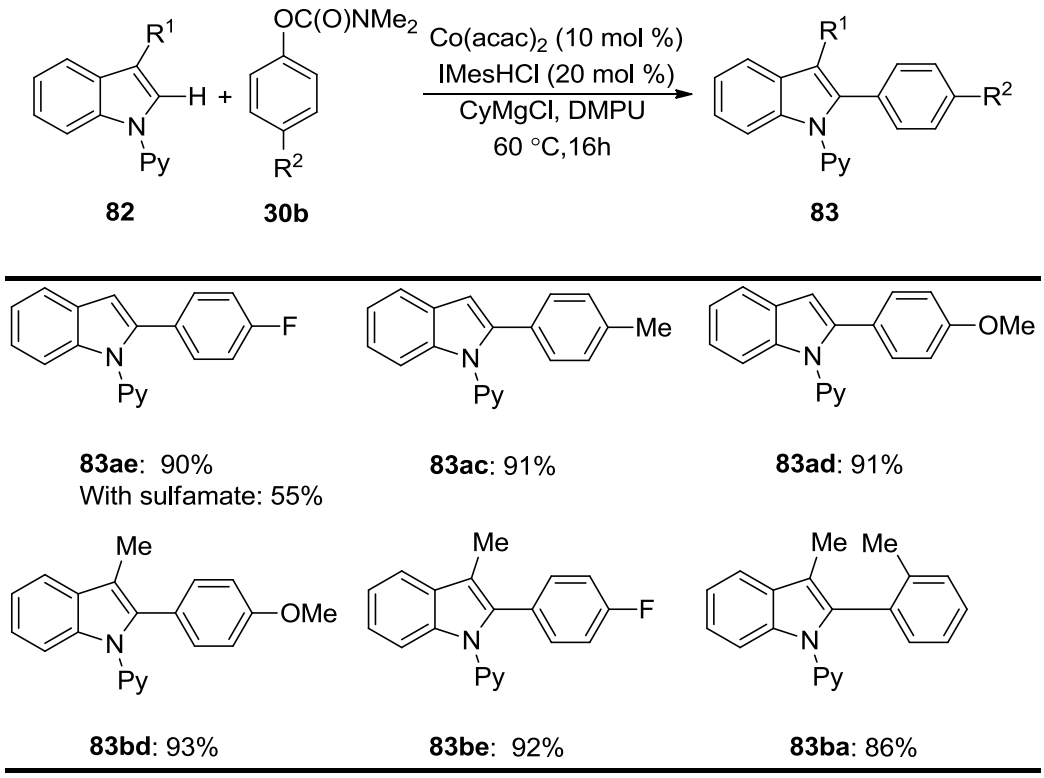
Scheme 7.2 Cobalt-catalyzed direct arylations with aryl carbamates **30b**.



3a **52ad**

30ad: R = SO_2NMe_2 38%
30bd: R = $C(O)NMe_2$ 74%
30cd: R = $P(O)(OEt)_2$ 32%
30dd: R = Tf , 15%

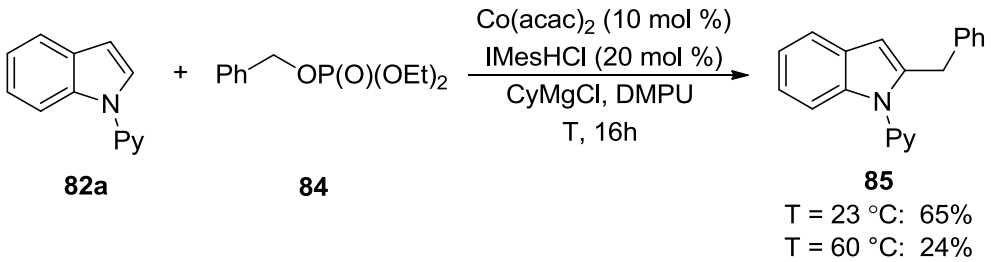
Scheme 7.3 Cobalt-catalyzed direct arylations with aryl electrophiles **30ad-30dd**.



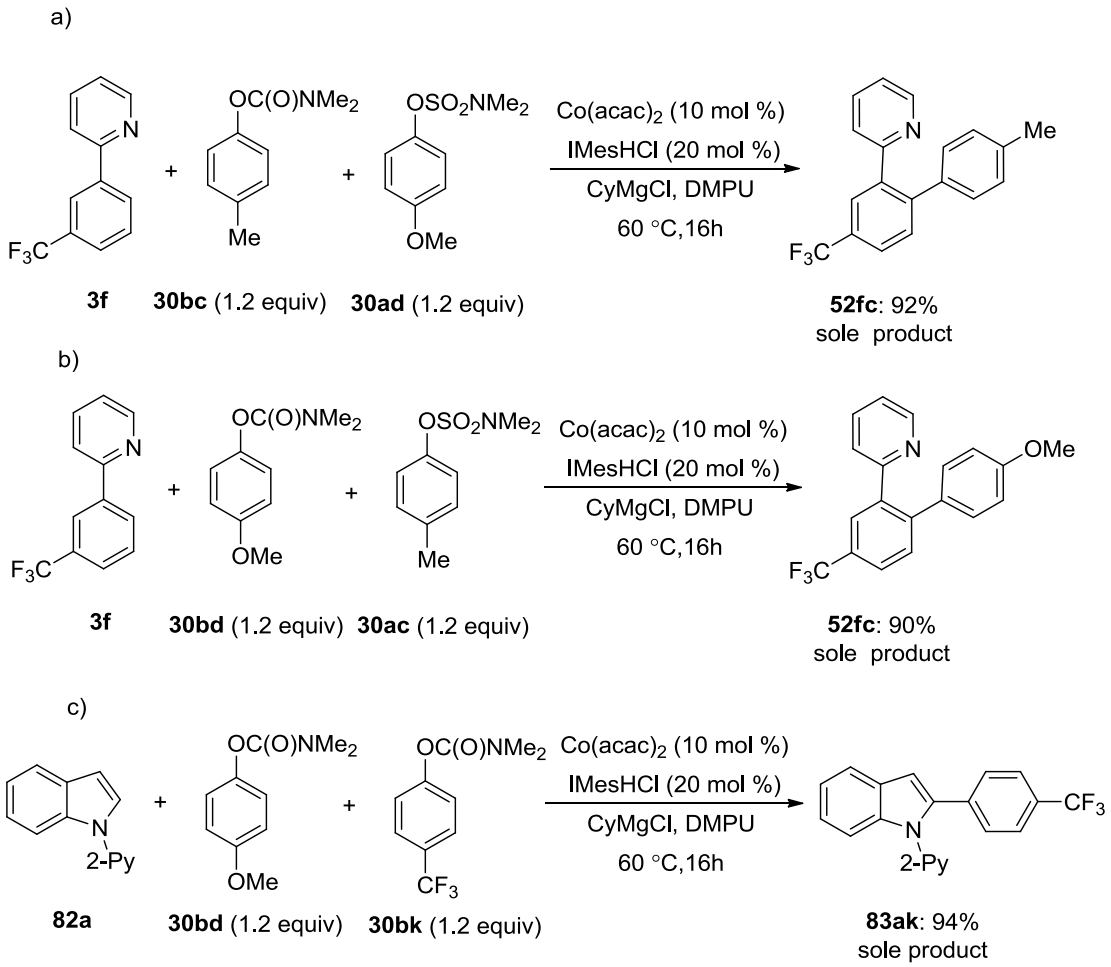
Scheme 7.4 Cobalt-catalyzed direct arylation of indoles **82**.

7.3 Cobalt-Catalyzed Direct Benzylation with Phosphate

Intriguingly, the inexpensive cobalt catalyst also enabled direct benzylation reactions on indoles. The $C(sp^2)$–$C(sp^3)$ bond formation was realized with benzyl phosphate **84** under remarkably mild reaction conditions. On the contrary, lower yield was observed when the temperature was increased. Additionaly, only trace amounts of product could be detected when 2-phenyl pyridine **3** was used as substrate (Scheme 7.5).



Scheme 7.5 Cobalt-catalyzed direct benzylation of indole **82a** with phosphate **84**.

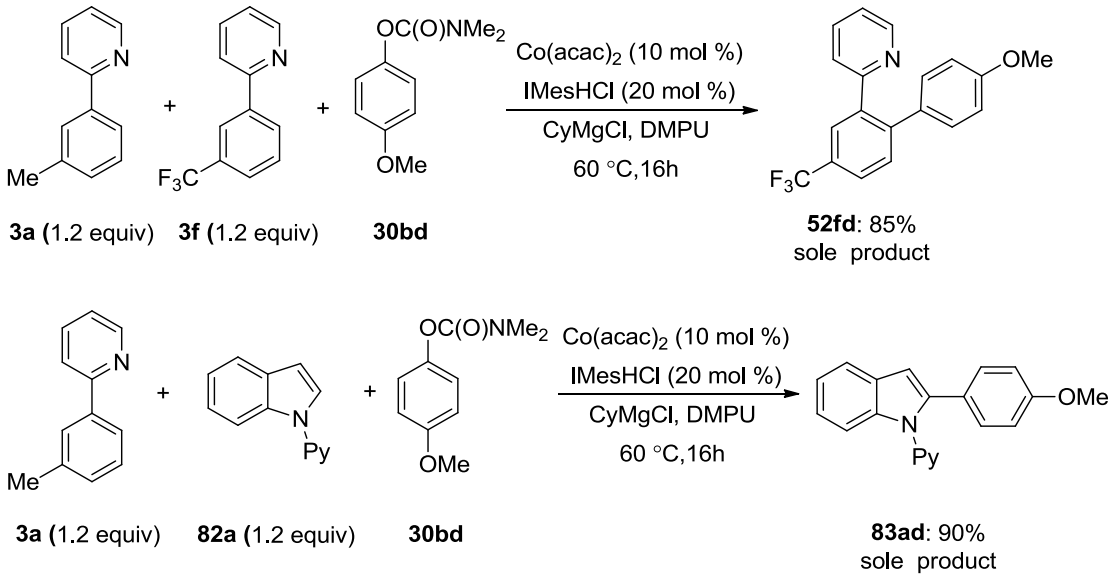


Scheme 7.6 Competition experiments with different electrophiles.

7.4 Mechanistic Studies

7.4.1 Intermolecular Competition Reactions

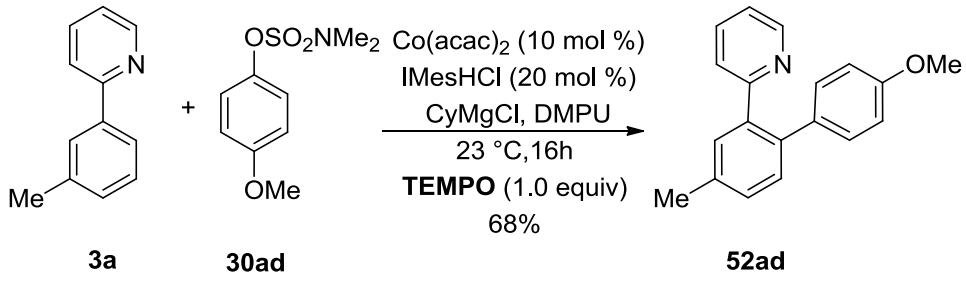
Considering the unique reactivity of the cobalt catalyst, we became interested in probing its mode of action. To this end, intermolecular competition experiments between aryl sulfamates **30a** and carbamates **30b** revealed the latter to display a significantly higher inherent reactivity and electron-deficient carbamates were preferentially converted (Scheme 7.6). Moreover, intermolecular competition experiments with differently substituted arenes **3** and heteroarenes **82** provided strong support for a non-SEAr-type reaction manifold. Instead, the reactivity of the arene is likely governed by the kinetic C–H bond acidity, as is indicated by the selective conversion of indole **82a**, as compared to arene **3a** (Scheme 7.7).



Scheme 7.7 Competition experiments with different (hetero)arenes.

7.4.2 Reaction in the Presence of Radical Scavenger

The direct arylation with aryl sulfamate **30ad** in the presence of one equivalent of 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO) led to the formation of the desired product **52ad** in 68% yield. The result is comparable to that obtained in the absence of the radical scavenger (82%). This finding suggests that a radical reaction mechanism in the direct C–H/C–O arylation is unlikely (Scheme 7.8).



Scheme 7.8 Cobalt-catalyzed direct arylation in presence of TEMPO.

7.5 Conclusion

In summary, we have reported on the first use of inexpensive cobalt catalysts for direct C–H bond arylation and benzylation with phenol-derived organic electrophiles through challenging C–H/C–O bond cleavage. The high catalytic efficacy of the versatile cobalt catalyst set the stage for unprecedented transition-metal-catalyzed direct arylations and benzylations of

arenes with easily accessible fluorine-free aryl sulfamates, carbamates, and phosphates, which even proved to be viable at ambient temperature. Importantly, mechanistic studies provided strong evidence for a non-radical reaction manifold.

8. Cobalt-Catalyzed Direct Primary and Secondary Alkylation with Unreactive Alkyl Chlorides

Having identified a highly effective cobalt catalyst for direct arylations with aryl sulfamates **30a** and carbamates **30b**, we were subsequently interested in exploring challenging C–H bond alkylations with *β*-hydrogen-containing alkyl chlorides under non-acidic reaction conditions. In contrast to the widely utilized $C(sp^2)$−$C(sp^2)$ bond forming processes, the corresponding transformations of unactivated alkyl halides are less developed, most probably because of the difficult oxidatative addition and due to the strong tendency of the intermediate metalated alkyls to undergo *β*-hydride elimination reactions, overall leading to undesired β-eliminations of the organic electrophiles. Particularly, secondary alkyl halides have proven to be extremely challenging substrates, as these alkyl halides are more sterically demanding and electron-rich, thereby rendering the elementary step of oxidative addition rather difficult. Yet, remarkable advances are constituted by *ortho*-selective palladium-, nickel-, copper-, and ruthenium-catalyzed direct alkylations. On the contrary, studies on cobalt-catalyzed direct alkyaltions are scarce. To overcome these limitations, in this chapter, we devised reaction conditions for versatile high effective and site-selective cobalt-catalyzed direct alkylations of arenes with primary and secondary alky chlorides.[60]

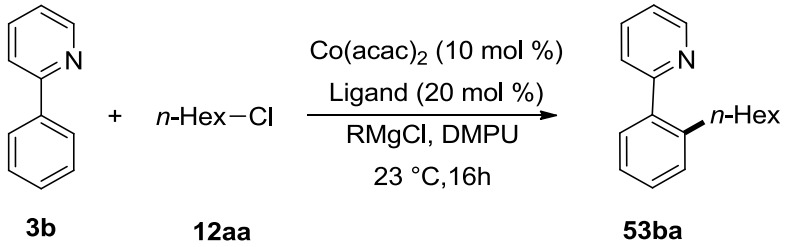
8.1 Optimization Studies of Cobalt-Catalyzed Direct Alkylations

Based on our previous studies on cobalt-catalyzed direct arylations of arenes **3**, we initiated the optimization studies by using cobalt(II) complexes together with Grignard reagents as the base. However, only unsatisfactorily low conversions of 2-phenylpyridine (**3b**) were observed in the absence of an additional ligand (Table 8.1, entries 1–3). A set of representative ligands was therefore subsequently probed, and improved results were accomplished by using NHC-coordinated cobalt catalysts, with IPrHCl (**60**) delivering optimal yields (entries 4–9). Moreover, an appropriate amount of the base was essential for increasing both the yields and the site-selectivity (entries 9–11). Notably, a nickel(II) complex did not give the desired

[60] B. Punji, W. Song, G. A. Shevchenko, L. Ackermann, *Chem. Eur. J.* **2013**, *19*, 10605–10610.

product **53ba** under otherwise identical reaction conditions (entry 12), thus highlighting the power of cobalt-catalyzed C−H bond functionalizations.

Table 8.1 Optimization of cobalt-catalyzed direct alkylations.[a]



3b **12aa** **53ba**

Entry	Ligand	RMgCl	Yield (%)[b]
1	--	*t*-BuMgCl (3.0)	5
2	--	MeMgCl (3.0)	15
3	--	CyMgCl (3.0)	27
4	dppe (**64**)	MeMgCl (3.0)	6
5	PCy_3 (**57**)	MeMgCl (3.0)	10
6[c]	Phenanthroline (**62**)	MeMgCl (3.0)	27
7	IMesHCl (**69**)	MeMgCl (3.0)	30
8	IPrHCl (**60**)	MeMgCl (3.0)	34
9	IPrHCl	CyMgCl (3.0)	67
10	IPrHCl	CyMgCl (1.6)	78
11	**IPrHCl**	**CyMgCl (2.0)**	**90**
12[d]	IPrHCl	CyMgCl (2.0)	--

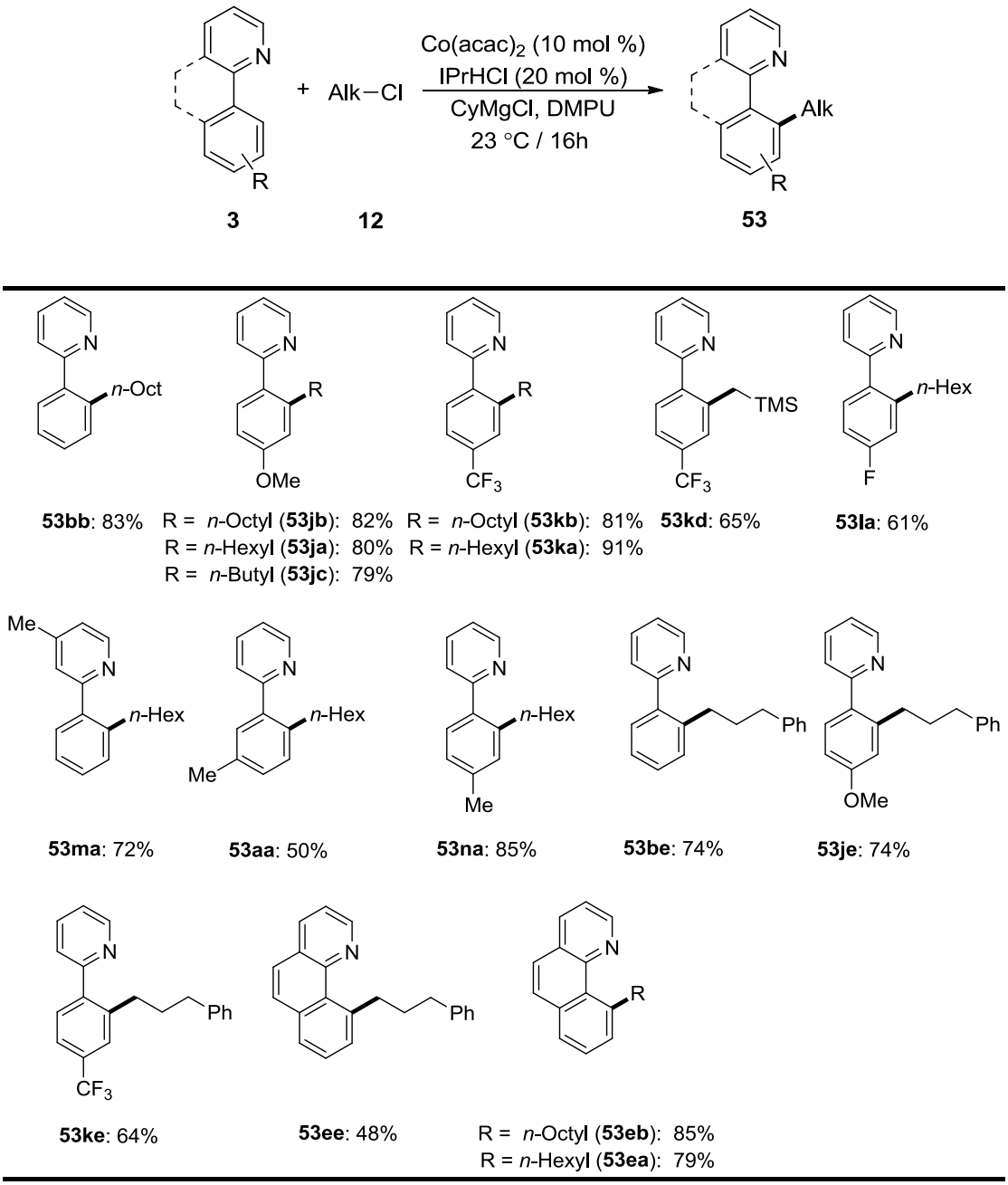
[a] Reaction conditions: **3b** (0.50 mmol), **12aa** (0.75 mmol), $Co(acac)_2$ (10 mol %), ligand (20 mol %), RMgCl, DMPU (1.0 mL), 23 °C, 16 h. [b] Yield of isolated product. [c] phenanthroline (10 mol %). [d] $Ni(acac)_2$ (10 mol %) was used.

8.2 Scope of Cobalt-Catalyzed Direct Alkylations

8.2.1 Cobalt-Catalyzed Alkylations of Arenes with Primary Alkyl Chlorides

The scope of the optimized catalytic system was, thereafter, explored for the direct alkylation of arenes **3** with unactivated, *β*-hydrogen-containing primary alkyl chlorides **12a** (Scheme

8.1). Differently decorated arenes thereby delivered the desired products **53** with excellent chemo- and site-selectivities using a variety of primary alkyl chlorides.

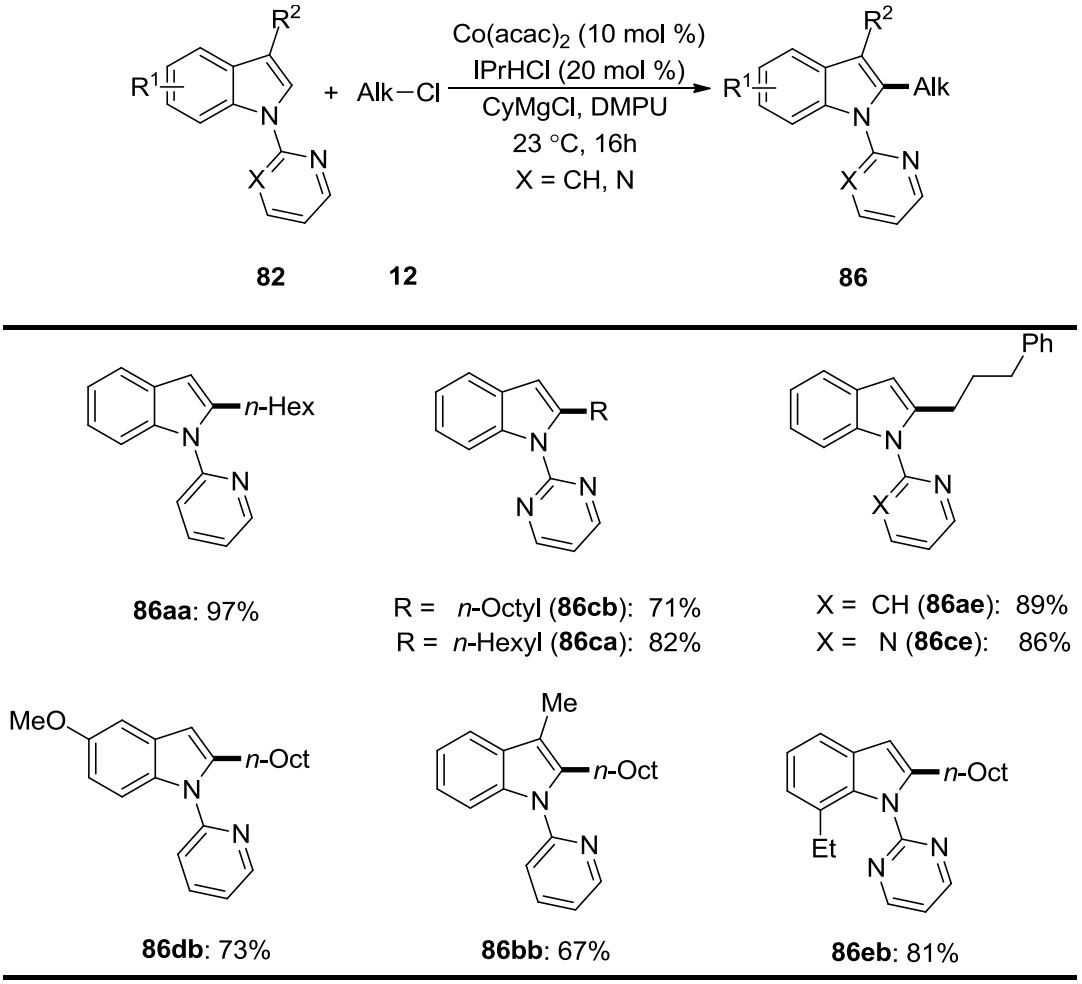


Scheme 8.1 Scope of cobalt-catalyzed direct alkylations with alkyl chlorides **12a**.

8.2.2 Cobalt-Catalyzed Primary Alkylations of Indoles

Consequently, we became attracted by applying the optimized cobalt catalysts in the direct functionalization of *N*-heteroaryl indoles **82** (Scheme 8.2). Notably, both *N*-pyridyl- as well as *N*-pyrimidyl-substituted heteroarenes were efficiently converted, the latter of which being

particularly attractive because of their removable directing group. The catalytic system displayed a notably wide substrate scope, as was among others illustrated by the successful use of various *n*-alkyl chlorides **12a**. Furthermore, substituted indoles **82a**–**82e** proved to be viable substrates, even when being sterically congested through substituents in the position C-3 or C-7 of the indole nucleus.

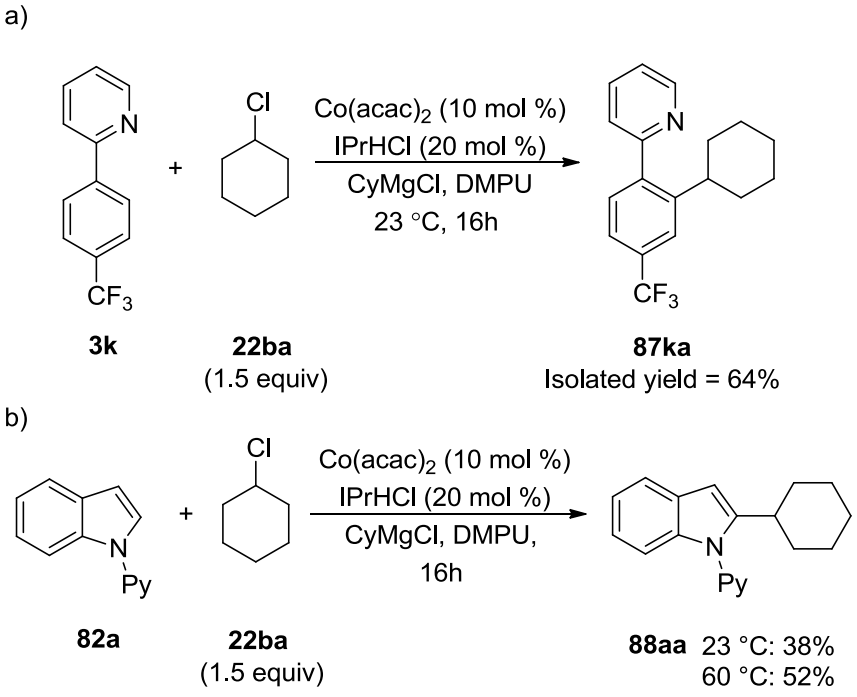


Scheme 8.2 Scope of cobalt-catalyzed direct alkylations of indoles **82**.

8.2.3 Cobalt-Catalyzed Secondary Alkylations with Alkyl Chlorides

Finally, we were particularly pleased to observe that the optimized cobalt catalytic system even allowed for direct alkylations with challenging secondary alkyl halides **22b**. Notably, these C−H bond functionalizations occurred with excellent *ortho*-selectivity through chelation assistance and proved amenable to direct arene as well as heteroarene functionalizations (Scheme 8.3). Notably, in contrast to alkylations of arenes **3** (Scheme 8.1) and to benzylation

of indoles **82** (Scheme 7.5), the alkylation of the indole **82a** with cyclohexyl chloride **22ba** proceeded more efficiently at slightly elevated reaction temperature (Scheme 8.3b).

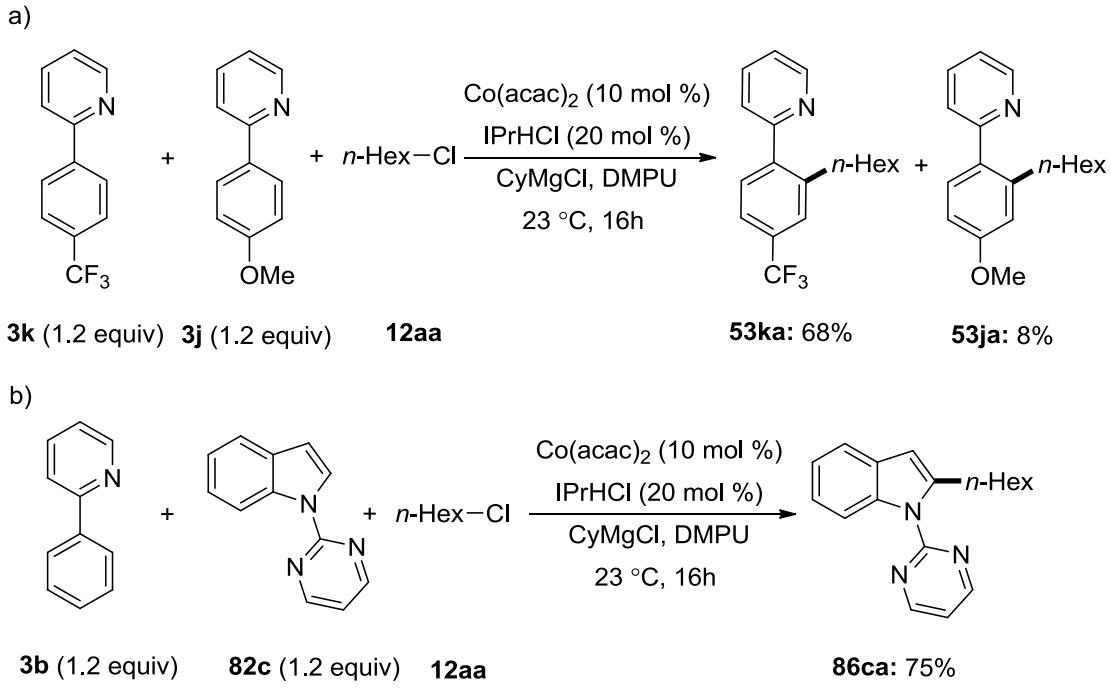


Scheme 8.3 Cobalt-catalyzed direct secondary alkylations.

8.3 Mechanistic Studies

8.3.1 Intermolecular Competition Reactions

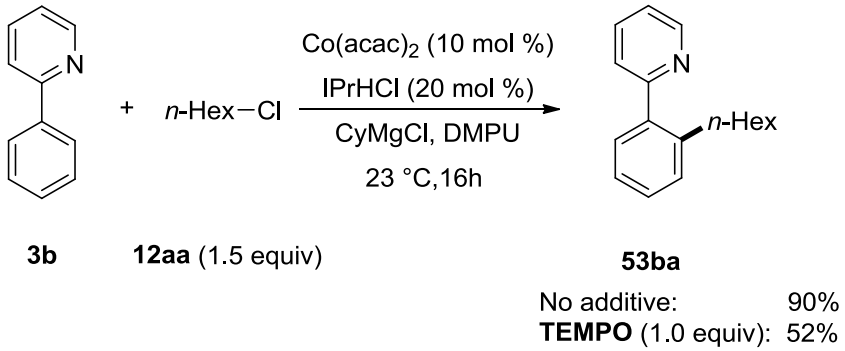
Given the high catalytic activity and selectivity of the cobalt catalysts under mild reaction conditions, we became intrigued in gaining insight into its mode of action. To this end, we performed a series of competition experiments, which revealed that electron-deficient arene **3k** reacted preferentially in the cobalt-catalyzed direct alkylations (Scheme 8.4a), thus rendering a simple electrophilic C−H bond activation manifold less likely to be operative. Moreover, the analogous functionalization of the electron-rich heteroaromatic indole **82c** occurred preferentially (Scheme 8.4b), which can be rationalized in terms of its increased kinetic C−H bond acidity due to the inductive effect exerted by the heteroatom.



Scheme 8.4 Intermolecular competition experiments: C−H bond alkylation.

8.3.2 Reaction in Presence of Radical Scavenger

Furthermore, we performed cobalt-catalyzed direct alkylations in the presence of stoichiometric amounts of the radical scavenger TEMPO (Scheme 8.5). A somewhat reduced yield was obtained after the reaction, which can be explained with SET-type elementary steps.



Scheme 8.5 Cobalt-catalyzed direct alkylation in presence of radical scavenger.

8.4 Conclusion

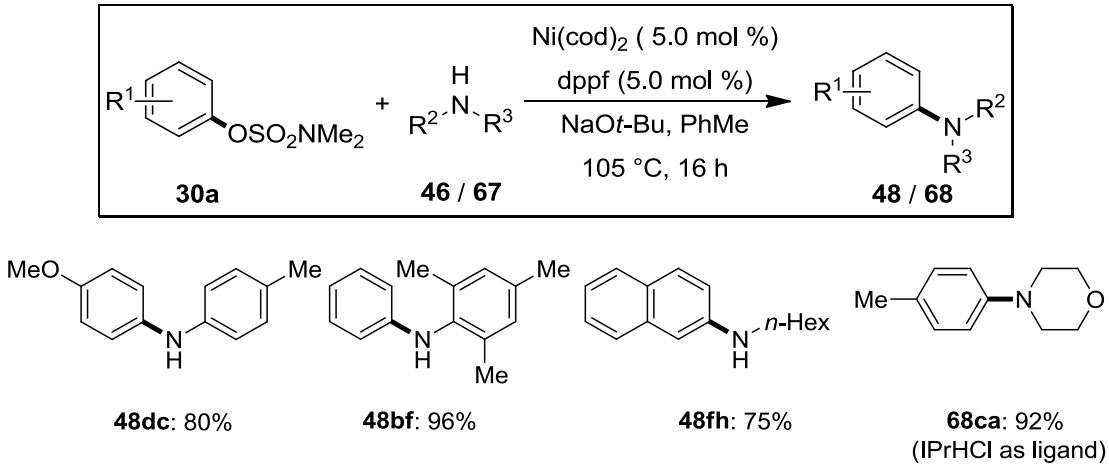
In summary, we have reported on the development of cobalt catalysts for direct C−H bond alkylations of heteroaryl-substituted arenes and heteroarenes with cost-effective chlorides as the electrophiles. Particularly, catalytic complexes derived from inexpensive $Co(acac)_2$ and

N-heterocyclic carbene (NHC) precursors proved to be highly effective at ambient reaction temperature. The C−H bond functionalizations proceeded with excellent chemo- and site-selectivities as well as ample scope. Notably, this cobalt-NHC catalyst allowed for difficult direct alkylations with various *β*-hydrogen-containing pimary alkyl chlorides. Moreover, challenging secondary alkyl chlorides proved to be for the first time suitable substrates for *ortho*-selective C−H bond alkylations as well.

9. Summary

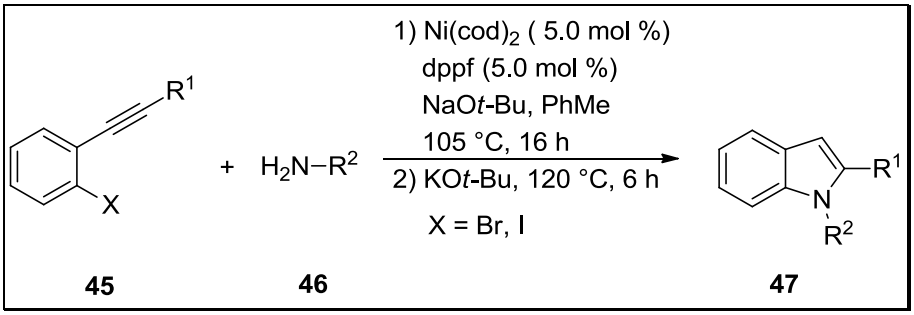
This thesis focused on development of first row transition-metal-catalyzed C–C/C–N bond formations. The inexpensive nickel and cobalt complexes were introduced to facilitate different kinds of novel chemical transformations.

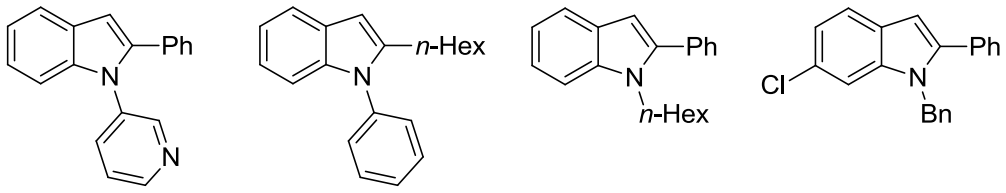
In the first project, the nickel complexes catalyzed C–N bond formations through challenging C–O bond cleavages. Direct arylations of primary and secondary amines were achieved using $Ni(cod)_2$ combined with dppf **66** or IPrHCl **60** as the (pre)ligands (Scheme 9.1).



Scheme 9.1 Nickel-catalyzed direct arylation of amines.

Consequently, the nickel catalyst in situ derived from the complex $Ni(cod)_2$ and dppf ligand was applied for amination/hydroamination sequential synthesis of indole. Differently substituted indoles **47** were synthesized from the *ortho*-alkynylhaloarenes **45** with aryl- as well as alkyl-substituted amines **46** (Scheme 9.2).

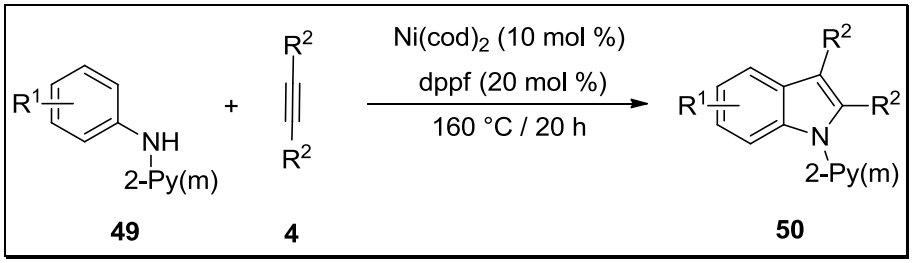


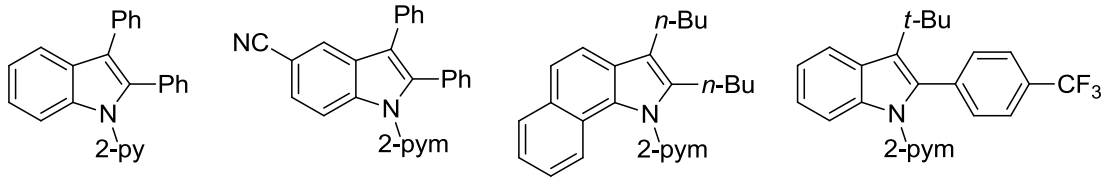


47ak: 74% **47cb:** 78% **47ah:** 74% **47dl:** 73%

Scheme 9.2 Nickel-catalyzed base-mediated synthesis of indole **47**.

Later, the indole synthesis through an unprecedented nickel-catalyzed oxidative alkyne annulation by electron-rich anilines **49** was reported. The C–H/N–H bond functionalization proceeded with excellent chemo-, regio- and site-selectivities in the absence of metal salts as the terminal oxidants, thereby furnishing substituted indoles **50** with broad scope (Scheme 9.3).

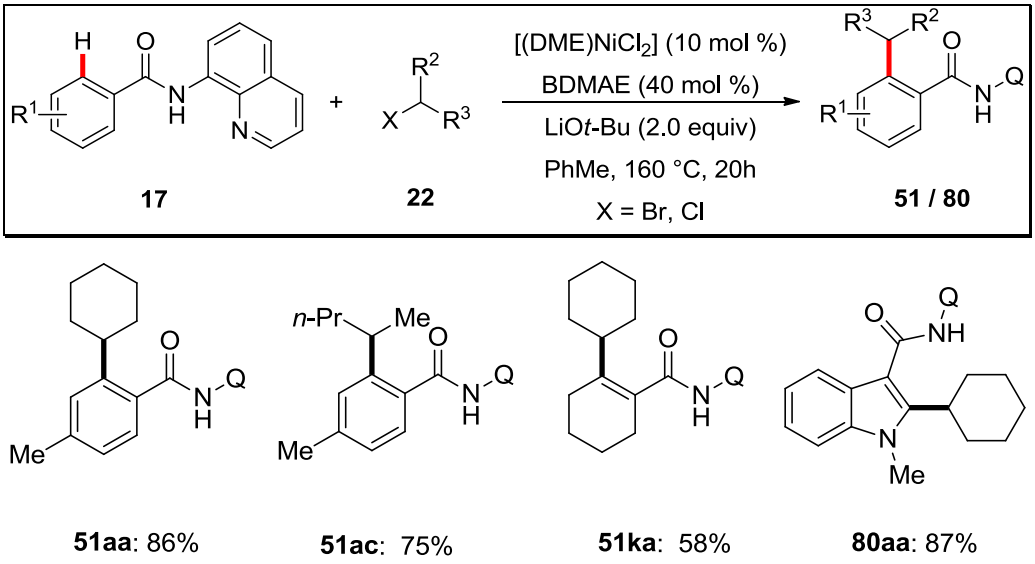




50aa': 82% **50ga**: 70% **50le**: 63% **50af**: 55%

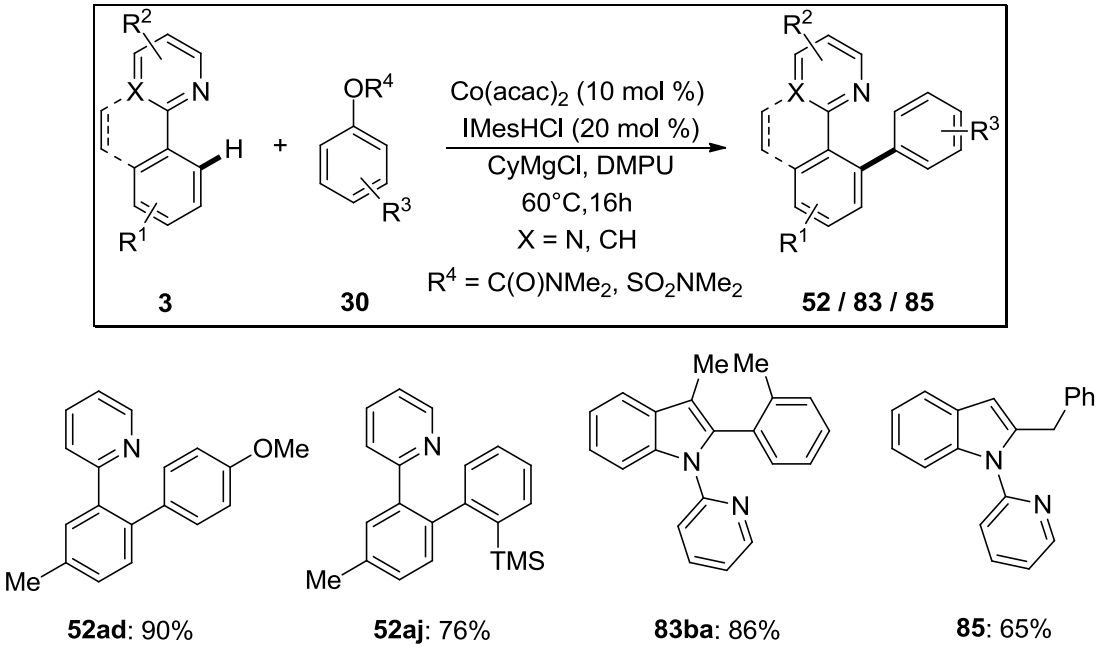
Scheme 9.3 Nickel-catalyzed indole synthesis through C–H/N–H bond activations.

Besides the nickel-catalyzed C–N bond formations, nickel-catalyzed chelation-assisted secondary alkylation was subsequently developed. A series of secondary alkylation products **51/80** were obtained by using the complexes derived from (DME)$NiCl_2$ and the user-friendly ligand BDMAE (Scheme 9.4).



Scheme 9.4 Nickel-catalyzed chelation-assisted secondary alkylation.

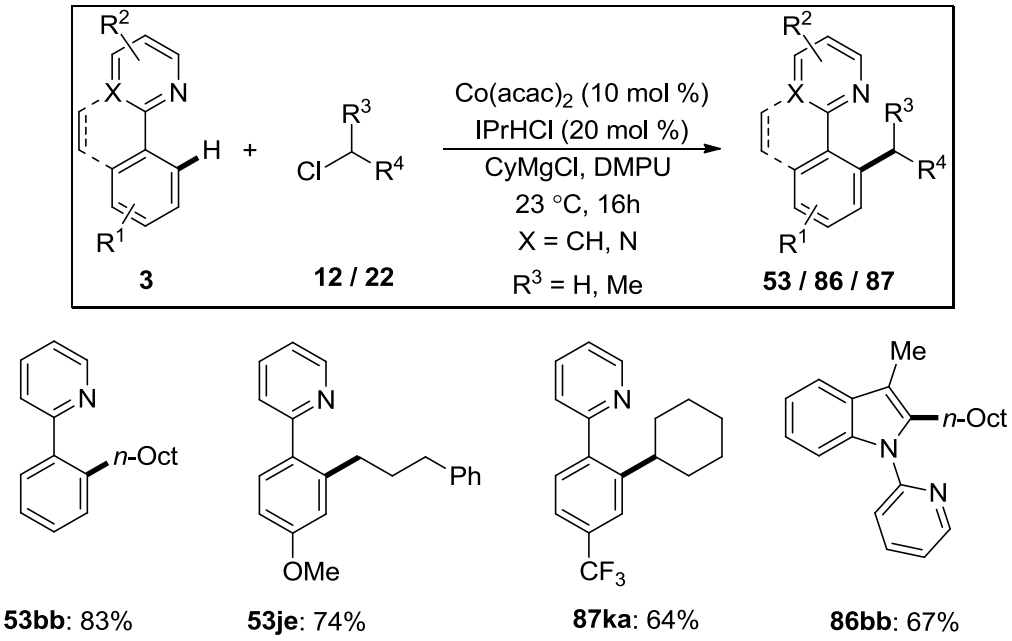
In the fifth project, cobalt-catalyzed direct C–H bond functionalization was developed. The cobalt complexes derived from N-heterocyclic carbene (NHC) precursors enabled the direct arylation and benzylation with phenol-derived organic electrophiles through challenging C–H/C–O bond cleavage (Scheme 9.5).



Scheme 9.5 Cobalt-catalyzed direct arylation/benzylation by C–H/C–O cleavages.

Finally, the cobalt complexes also facilitated the challenging direct primary and secondary alkylation of inert arenes. Both high efficacy and good selectivities were achieved with

unreactive alkyl chloride as the electrophiles even at ambient reaction temperature (Scheme 9.6).



Scheme 9.6 Cobalt-catalyzed direct alkylation by C–H bonds cleavages.

10. Experimental

10.1 General Remarks

All reactions involving moisture- or air-sensitive reagents or products were performed under a N_2 atmosphere using pre-dried glassware and standard Schlenk techniques. Syringes for handling of dry solvents were flushed with dry nitrogen threefold prior to use.

Solvents

All solvents for reactions involving moisture-sensitive reagents were dried, distilled and stored under inert atmosphere (argon or nitrogen) according to the following standard procedures.

solvent	**drying method**
Dichloromethan	Purified using an solvent purification system (SPS) from MBRAUN.
N,N-Dimethylformamide	Dried over CaH2 for 8 h, degassed and distilled under reduced pressure.
N-Methyl-2-pyrrolidone	Stirred for 4 h at 150 °C over CaH2 and subsequently distilled under reduced pressure.
Tetrahydrofuran	Purified using an SPS solvent purification system from MBRAUN.
Toluene	Either predried over KH followed by distillation from sodium benzophenone ketyl or purified using a solvent purification system from MBRAUN.
1,4-Dioxane	Dried by distillation from sodium benzophenone ketyl.
o-Xylene	Either predried over KH followed by distillation from sodium benzophenone ketyl or purified using a solvent
1,3-Dimethyl-tetrahydro-pyrimidinone	Dried over CaH2 for 8 h, degassed and distilled under reduced pressure.

Vacuum

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

Melting Points

Melting points were measured using a *Stuart® Melting Point Apparatus SMP3* from BARLOWORLD SCIENTIFIC. Reported values are uncorrected and are given as a range (M.r.), if the melting occurred not at a specific melting point (M.p.).

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates (MACHEREY-NAGEL) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light and developed by treatment with a KMnO4 solution followed by careful applying a heat gun. Chromatographic purification of products was accomplished by flash column chromatography on MERCK silica gel, grade 60 (0.040–0.063 mm and 0.063–0.200 mm, 70–230 mesh astimated).

High Performance Liquid Chromatography

Preparative and analytical separations were performed on an HPLC-System from KNAUER (*Smartline Pump 100*, Dynamic Mixing Chamber, Injection- and Control-Valve, *Smartline UV Detector 2500*). Separation column *ChiralPak IC* (250×20 mm or 4.6×250 mm) from DAICEL CHEM. IND. (LTD) was used. Organic solvents of HPLC grade were employed. All samples were filtered through Polytetrafluorethylen Filter from ROTH (Ø 25 mm, 0.2 µm) or VWR (Ø 13 mm, 0.2 µm) prior to separation.

Gas Chromatograpgy

The conversion of the reactions was monitored applying coupled gas chromatography/mass spectrometry using *G1800C GCDplus* with mass detector *HP 5971*, *5890 Series II* with mass detector *HP 5972* from HEWLETT-PACKARD and *7890A GC-System* with mass detector *5975C (Triplex-Axis-Detector)* from AGILENT TECHNOLOGIES equipped with *HP-5MS* columns (30 m×0.25 mm×0.25 µm) were used.

Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy was performed at 300 or 600 MHz (^{1}H-NMR), 75.5 or 125 MHz (^{13}C-NMR, APT) and 282 MHz (^{19}F-NMR) on BRUKER *AM 250*, VARIAN *Unity-300* and *Inova 500* instruments. Chemical shifts are reported as δ-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively, or the standard trimethylsilyl (TMS) peak.

	^{1}H-NMR	^{13}C-NMR
$CDCl_3$:	7.26 ppm	77.0 ppm
DMSO-D_6 :	2.49 ppm	49.5 ppm

For characterization of the observed resonance multiplicities the following abbrevations were applied: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *m* (multiplet), *dd* (doublet of doublet), *dt* (doublet of triplet), or analogue representations. The coupling constants *J* are reported in Hertz (Hz).

Infrared Spectroscopy

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

Mass Spectrometry

EI- and EI-HR-MS 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-HR-MS spectra were recorded on a BRUKER *APEX IV* or a BRUKER *DALTONIC* (7T, Transform Ion Cyclotron Resonance (FTICR)) mass spectrometer. The ratios of mass to charge are indicated, intensities relative to the base peak (I = 100) are written in parentheses.

10.2 Starting Materials

The following starting materials were prepared according to modified literature procedures: Aryl sulfamates **30a**, [61] *ortho*-alkynylbromoarenes **45**, [62] *N*-phenylpyridine **49a**, [63] *N*-arylpyrimidines **49b**, [64] *N*-(pentadeuteriophenyl)-pyrimidin-2-amine $[D]_5$-**49ba**, [65] diarylalkynes **4**,[66] *N*-quinolin-8-yl benzamides **17**,[67] phenylpyridines **3**,[68] aryl carbamates **30b**,[69] *N*-pyridylindoles **82**,[70] benzyl phosphate **84**.[71] Other chemicals were obtained from commercial sources and were used without further purification.

10.3 Representative Procedure

Representative Procedure A: Nickel-catalyzed amination of sulfamates 30a.

To a solution of $[Ni(cod)_2]$ (6.9 mg, 0.025 mmol, 5.0 mol %), dppf (**66**) (13.9 mg, 0.025 mmol, 5.0 mol %) and NaO*t*-Bu (96 mg, 0.75 mmol) in PhMe (1.0 mL) were added sulfamate **30aa** (108 mg, 0.50 mmol) and aniline **46a** (92 mg, 0.75 mmol) at ambient temperature. The resulting mixture was stirred for 16h at 105 ℃ . Sat. aq. $NaHCO_3$ (60 mL) was added at ambient temperature, and the reaction mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The remaining residue was purified by column chromatography on silica (*n*-hexane/ EtOAc 50/1) to yield **48aa** (101 mg, 95%) as a white solid.

Representative Procedure B: Nickel-catalyzed indole synthesis with aryl bromides 45.

To a solution of $[Ni(cod)_2]$ (6.9 mg, 0.025 mmol, 5.0 mol %), dppf (**66**) (13.9 mg, 0.025 mmol, 5.0 mol %) and NaO*t*-Bu (96 mg, 0.750 mmol) in PhMe (2 mL) were added alkynyl bromide

[61] J. F. King, T. M. Lee, *Can. J. Chem.* **1981**, *59*, 356–361.
[62] L. Ackermann, *Org. Lett.* **2005**, *7*, 439–442.
[63] J. Chen, G. Song, C.-L. Pan, X. Li, *Org. Lett.* **2010**, *12*, 5426–5429.
[64] L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764–767.
[65] Y. Liu, Y. Bai, J. Zhang, Y. Li, J. Jiao, X. Qi, *Eur. J. Org. Chem.* **2007**, 6084–6088.
[66] J. Matthew, C. Lucas, B. Julia, L. Tendai, L. Kami, G. Ronald, J. Christopher, A. Paul, *Org. Lett.* **2002**, *4*, 3199–3202.
[67] Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2013**, *135*, 5308–5311.
[68] V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, W. A. Herrmann, *Angew. Chem. Int. Ed.* **2000**, *39*, 1602–1604.
[69] F. Garcia, M. MacPartlin, J. V. Morey, D. Nobuto, Y. Kondo, H. Naka, M. Uchiyama, A. E. H. Wheatley, *Eur. J. Org. Chem.* **2008**, 644–647.
[70] L. Ackermann, A. V. Lygin, *Org. Lett*. **2011**, *13*, 3332–3335.
[71] M. McLaughlin, *Org. Lett.* **2005**, *7*, 4875–4878.

45aa (129 mg, 0.500 mmol) and aniline **46c** (80 mg, 0.75 mmol) at ambient temperature. The resulting mixture was stirred for 16h at 105 ℃. At ambient temperature, KO*t*-Bu (168 mg, 1.50 mmol) was added under N_2 and the resulting mixture was stirred for 6h at 120 ℃. EtOAc (5 mL) and H_2O (5 mL) were added to the cooled suspension. The separated aqueous layer was extracted with EtOAc (3 x 10 mL) and combined organic layers were washed with H_2O (10 mL) and brine (10 mL). Drying with Na_2SO_4 and purification by column chromatography (*n*-hexane/ EtOAc 500/1) yielded **47ac** (125 mg, 88%) as a white solid

Representative Procedure C: Nickel-catalyzed Alkyne Annulation by Anilines 49.

Aniline **49aa** (85.5 mg, 0.50 mmol), tolane (**4a)** (446 mg, 2.50 mmol), $Ni(cod)_2$ (13.8 mg, 10.0 mol %), and dppf (**66**) (55.4 mg, 20.0 mol %) were stirred at 160 ℃ for 20 h in a sealed tube. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1→5:1) to yield **50aa'** as a white solid (142 mg, 82%).

Representative Procedure D: Nickel-catalyzed secondary alkylation with alkyl bromides 22a.

To a mixture of benzamide **17a** (131 mg, 0.50 mmol), bromocyclohexane (**22aa)** (163 mg, 1.00 mmol), $(DME)NiCl_2$ (11 mg, 10.0 mol %), BDMAE (**77**) (32 mg, 40.0 mol %) and LiO*t*-Bu (80 mg, 1.00 mmol) was added PhMe (1.0 mL). Thereafter, the resulted mixture was stirred under N_2 at 160 ℃ for 20 h. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 20:1) to yield **51aa** as a white solid (148 mg, 86%).

Representative Procedure E: Cobalt-catalyzed direct arylation with aryl sulfamate 30a.

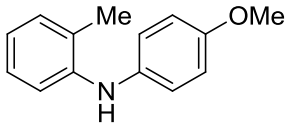
To a mixture of arene **3a** (127 mg, 0.75 mmol), sulfamate **30ad** (116 mg, 0.50 mmol), $Co(acac)_2$ (12.8 mg, 10.0 mol %), and IMesHCl (**69**) (34.0 mg, 20.0 mol %) in DMPU (1.0 mL) was added CyMgCl (0.50 mL, 1.00 mmol) slowly. Thereafter, the reaction mixture was stirred under N_2 at 60 ℃ for 16 h. At ambient temperature, aq NH_4Cl (2.0 mL) and H_2O (2.0 mL) were added, and the reaction mixture was extracted with MTBE (3 × 30 mL). The combined

organic phase was washed with brine (50 mL) and dried over Na_2SO_4. After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1→5:1) to yield **52ad** as a white solid (112 mg, 82%).

Representative Procedure F: Cobalt-catalyzed direct alkylation with alkyl chlorides 12a. To a mixture of arene **3b** (78 mg, 0.50 mmol), 1-chlorohexane **(12aa)** (90 mg, 0.75 mmol), $Co(acac)_2$ (12.8 mg, 10.0 mol %) and IPrHCl (**60**) (42.5 mg, 20.0 mol %) in DMPU (1.0 mL) was slowly added CyMgCl (0.50 mL, 1.00 mmol). Thereafter, the reaction mixture was stirred under N_2 at 23 ℃ for 16 h. At ambient temperature, aq. sat. NH_4Cl (2.0 mL) and H_2O (2.0 mL) were added, and the reaction mixture was extracted with MTBE (3 × 30 mL). The combined organic phase was washed with brine (50 mL) and dried over Na_2SO_4. After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 20:1) to yield **53ba** as colorless oil (106 mg, 90%).

10.4 Analytical Data

4-Methoxy-*N*-*o*-tolylbenzenamine (48aa)



The general procedure **A** was followed using **30aa** (108 mg, 0.50 mmol) and **46a** (92 mg, 0.75 mmol). After purification by column chromatography **48aa** (101 mg, 95%) was obtained as a white solid. (m.p. 84°C).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.14 (d, J = 7.5 Hz, 1H), 7.11-6.75 (m, 4H), 6.93-6.73 (m, 3H), 5.18 (s, 1H), 3.79 (s, 3H), 2.25 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.1 (C_q), 143.3 (C_q), 136.3 (C_q), 130.7 (CH), 126.8 (CH), 125.3 (C_q), 122.1 (CH), 119.9 (CH), 115.2 (CH), 114.7 (CH), 55.6 (CH_3), 17.8 (CH_3).

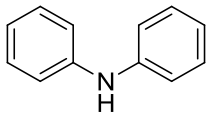
IR (KBr): 3403, 3061, 2854, 2339, 1683, 1594, 1112, 1035, 747, 668 cm^{-1}.

MS (EI) *m/z* (relative intensity): 213 (84) [M+], 198 (100), 180 (10), 154 (8), 91 (6), 77 (3).

HR-MS (ESI) m/z calcd for $C_{14}H_{15}NO$ 213.1154, found 213.1156.

The spectral data were in accordance with those reported in the literature.[72]

Diphenylamine (48bb)



The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **46b** (70 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48bb** (80 mg, 94%) was obtained as a white solid (m.p. 53℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.31-7.23 (m, 4H), 7.05 (d, J = 7.5 Hz, 4H), 6.92 (t, J = 7.2 Hz, 4H), 5.68 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.1 (C_q), 129.3 (CH), 121.0 (CH), 117.8 (CH).

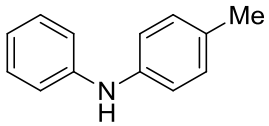
IR (KBr): 3395, 3043, 2338, 1716, 1592, 1418, 1311, 1172, 746, 691 cm^{-1}.

MS (EI) m/z (relative intensity) 169 (100) [M^+], 141 (4), 115 (4), 77 (10), 51 (14).

HR-MS (EI) m/z calcd for [$C_{12}H_{11}N$] 169.0891, found 169.0890.

The spectral data were in accordance with those reported in the literature.[73]

4-Methyl-*N*-phenylbenzenamine (48bc)



The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **46c** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48bc** (87 mg, 95%) was obtained as a white solid (m.p. 90℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.25 (t, J = 7.2 Hz, 2H), 7.18-6.95 (m, 6H), 6.95-6.80 (m, 1H), 5.61 (s, 1H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.9 (C_q), 140.3 (C_q), 130.9 (C_q), 129.8 (CH), 129.3 (CH), 120.3 (CH), 118.9 (CH), 116.8 (CH), 20.7 (CH_3).

[72] Chen, L.; Yu, G.; Li, F.; Zhu, X.; Zhang, B.; Guo, R.; Li, X.; Yang, Q.; Jin, S.; Liu, C.; Liu, S. *J. Organomet. Chem.* **2010**, *695*, 1768–1775.

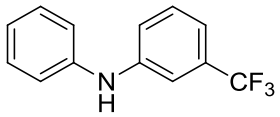
[73] Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029–3036.

IR (KBr): 3393, 3018, 2362, 1595, 1395, 1110, 877, 745, 693 cm^{-1}.

MS (EI) m/z (relative intensity) 183 (100) [M^+], 167 (18), 154 (2), 77 (11), 51 (6).

HR-MS (EI) m/z calcd for [$C_{13}H_{13}N$] 183.1084, found 183.1050.

***N*-Phenyl-3-(triflouromethyl)aniline (48bd)**



The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **46d** (121 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48bd** (98 mg, 83%) was obtained as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.37-7.27 (m, 4H), 7.21-7.02 (m, 5H), 5.81 (s, 1H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ = 143.9 (C_q), 141.7 (C_q), 131.6 (C_q, $^2J_{C\text{-}F}$ = 33 Hz), 129.7 (CH), 129.5 (CH), 124.0 (C_q, $^1J_{C\text{-}F}$ = 271 Hz), 122.2 (CH), 119.6 (CH, $^4J_{C\text{-}F}$ = 1 Hz), 118.9 (CH), 116.8 (CH, $^3J_{C\text{-}F}$ = 4 Hz), 113.1 (CH, $^3J_{C\text{-}F}$ = 4 Hz).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.8 (s).

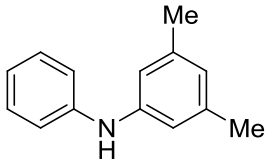
IR (film): 3401, 3039, 2539, 1940, 1594, 1497, 1337, 1217, 997, 923, 874, 746, 658 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (100) [M^+], 216 (10), 167 (50), 139 (10), 114 (20), 84 (70), 65 (40).

HR-MS (EI) m/z calcd for [$C_{13}H_{10}F_3N$] 237.0765, found 237.0766.

The spectral data were in accordance with those reported in the literature.[74]

3,5-Dimethyl-*N*-phenylbenzenamine (48be)



The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **46e** (91 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48be** (95 mg, 96%) was obtained as a pale yellow solid (m.p. 52 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.32-7.22 (m, 2H), 7.11-7.04 (m, 2H), 6.96-6.89 (m, 1H), 6.72 (s, 2H), 6.60 (s, 1H), 5.62 (s, 1H), 2.28 (s, 6H).

[74] Carroll, M. A.; Wood R. A., *Tetrahedron* **2007**, *63*, 11349–11354.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.2 (C_q), 142.9 (C_q), 138.9 (C_q), 129.2 (CH), 122.8 (CH), 120.73 (CH), 117.8 (CH), 115.5 (CH), 21.5 (CH_3).

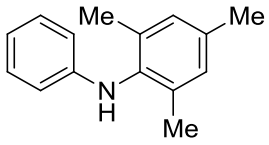
IR (KBr): 3393, 3026, 2917, 2856, 1591, 1376, 1376, 1331, 1033, 750, 690 cm^{-1}.

MS (EI) m/z (relative intensity) 197 (100) [M^+], 181 (24), 167 (10), 77 (10), 51 (5).

HR-MS (EI) m/z calcd for [$C_{14}H_{15}N$] 197.1204, found 197.1206.

The spectral data were in accordance with those reported in the literature.[75]

2,4,6-Trimethyl-*N*-phenylbenzenamine (48bf)



The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **46f** (101 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48bf** (101 mg, 96%) was obtained as a pale yellow solid (m.p. 57 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.14 (t, J = 7.6 Hz, 2H), 6.94 (s, 2H), 6.80-6.65 (m, 1H), 6.49 (d, J = 7.3 Hz, 2H), 5.09 (s, 1H), 2.30 (s, 3H), 2.17 (s, 6H).

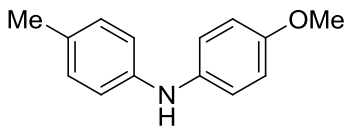
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.5 (C_q), 135.8 (C_q), 135.4 (C_q), 135.3 (C_q), 129.1 (CH), 129.1 (CH), 117.8 (CH), 113.2 (CH), 21.0 (CH_3), 18.3 (CH_3).

IR (KBr): 3390, 3014, s2917, 2856, 1600, 1375, 1312, 1027, 746, 693, 625 cm^{-1}.

MS (EI) m/z (relative intensity) 211 (100) [M^+], 196 (34), 181 (15), 134 (12), 77 (12), 51 (7).

HR-MS (EI) m/z calcd for [$C_{15}H_{17}N$] 211.1361, found 211.1367.

4-Methoxy-*N*-*p*-tolylbenzenamine (48ca) (48dc)



The general procedure **A** was followed using **30ac** (108 mg, 0.50 mmol) and **46a** (92 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48ca** (89 mg, 84%) was obtained as a white solid (m.p. 82 ℃).

The general procedure **A** was followed using **30ad** (116 mg, 0.50 mmol) and **46c** (80 mg,

[75] C. C. Tzschucke, J. M. Murphy, J. F. Hartwig, *Org. Lett.* **2007**, *9*, 761–764.

0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48dc** (85 mg, 80%) was obtained as a white solid (m.p. 82 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.11-6.93 (m, 4H), 6.92-6.76 (m, 4H), 5.39 (s, 1H), 3.78 (s, 3H), 2.27 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8 (C_q), 142.4 (C_q), 136.6 (C_q), 129.8 (CH), 129.3 (C_q), 121.1 (CH), 116.6 (CH), 114.7 (CH), 55.6 (CH_3), 20.5 (CH_3).

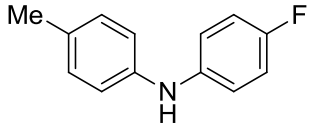
IR (KBr): 3415, 2951, 2835, 1613, 1516, 1316, 1179, 1106, 739, 703 cm^{-1}.

MS (EI) m/z (relative intensity) 213 (68) [M^+], 198 (100), 154 (11), 77 (3), 43 (16).

HR-MS (EI) m/z calcd for [$C_{14}H_{15}NO$] 213.1154, found 213.1146.

The spectral data were in accordance with those reported in the literature.[76]

4-Methoxy-*N*-*p*-tolylbenzenamine (48cg) (48ec)



The general procedure **A** was followed using **30ac** (108 mg, 0.50 mmol) and **46g** (83 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48cg** (81 mg, 82%) was obtained as a colorless oil.

The general procedure **A** was followed using **30ae** (110 mg, 0.50 mmol) and **46c** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48ec** (88 mg, 87%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.42-7.45 (d, J = 8.2 Hz, 2H), 7.15-7.13 (d, J = 8.2 Hz, 2H), 7.04-7.07 (d, J = 8.5 Hz, 2H), 6.95-6.97 (d, J = 8.5 Hz, 2H), 5.82 (s, 1H), 2.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.2 (C_q), 138.3 (C_q), 133.0 (C_q), 130.0 (CH), 129.8 (CH), 121.2 (C_q), 120.9 (CH), 114.8 (CH), 21.0 (CH_3)..

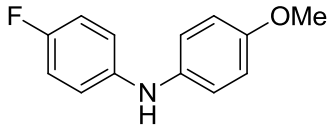
IR (KBr): 3415, 2951, 2835, 1612, 1515, 1316, 1179, 1106, 729, 704 cm^{-1}.

MS (EI) m/z (relative intensity) 201 (68) [M^+], 188 (100), 152 (11), 77 (3), 43 (16).

HR-MS (ESI) m/z calcd for [$C_{13}H_{13}FNO+H]^+$ 202.1032. Found: 202.1040

[76] B. H. Lipshutz, D. W. Chung, B. Rich, *Adv. Synth. Catal.s* **2009**, *351*, 1717–1721.

4-Methoxy-*N*-*p*-tolylbenzenamine (48ea)



The general procedure **A** was followed using **30ae** (110 mg, 0.50 mmol) and **46a** (82 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48ea** (96 mg, 88%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.02–6.98 (m, 2H), 6.94–6.83 (m, 6H), 5.37 (s, 1H), 3.79 (s, 3H).

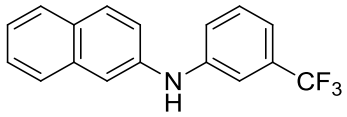
^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.2 (C_q), 155.0 (C_q), 141.1 (C_q), 136.5 (CH), 121.2 (C_q), 117.7 (CH), 115.7 (CH), 114.7 (CH), 55.6 (CH_3).

IR (KBr): 3414, 2952, 2839, 1612, 1515, 1316, 1179, 1100, 729, 702 cm^{-1}.

MS (EI) m/z (relative intensity) 217 (61) [M^+], 195 (100), 145 (11), 78 (15), 43 (20).

HR-MS (ESI) m/z calcd for $[C_{13}H_{13}FNO]^+$ 217.0903. Found: 217.0905

***N*-(3-(Trifluoromethyl)phenyl)naphthalen-2-amine (48fd)**



The general procedure **A** was followed using **30af** (126 mg, 0.50 mmol) and **46d** (121 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48fd** (146 mg, 98%) was obtained as a pale pink solid (m.p. 70 ℃).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84-7.74 (m, 2H), 7.69 (d, J = 7.0 Hz, 1H), 7.537-7.40 (m, 2H), 7.40-7.29 (m, 3H), 7.29-7.22 (m, 2H), 7.18 (d, J = 6.9 Hz, 1H), 5.99 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 143.8 (C_q), 139.3 (C_q), 134.3(C_q), 131.8 (C_q, $^{2}J_{C\text{-}F}$ = 33 Hz), 129.8 (CH), 129.7 (CH), 129.4 (CH), 127.6 (CH), 126.6 (CH), 126.5 (CH), 124.1 (CH), 124.0 (C_q, $^{1}J_{C\text{-}F}$ = 272 Hz), 120.4 (CH), 120.1 (CH), 117.3 (CH, $^{4}J_{C\text{-}F}$ = 3.7 Hz), 116.8 (CH, $^{3}J_{C\text{-}F}$ = 4 Hz), 113.1 (CH, $^{3}J_{C\text{-}F}$ = 4 Hz).

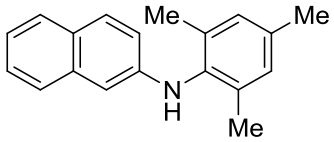
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.8 (s). IR (film): 3398, 3058, 2362, 1596, 1336, 1171, 1069, 851, 753, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287 (100) [M^+], 266 (7), 217 (21), 115 (12), 75 (2).

HR-MS (EI) m/z calcd for [$C_{17}H_{12}F_3N$] 287.0922, found 287.0915.

The spectral data were in accordance with those reported in the literature.[77]

***N*-Mesitylnaphthalen-2-amine (48ff)**



The general procedure **A** was followed using **30af** (126 mg, 0.50 mmol) and **46f** (101 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48ff** (111 mg, 85%) was obtained as a pale brown solid (m.p. 82℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.66 (dd, J = 4.8, 4.6 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.36-7.28 (m, 1H), 7.23-7.13 (m, 1H), 6.99 (s, 2H), 6.95 (dd, J = 2.2, 2.7 Hz, 1H), 6.54 (d, J = 2.7 Hz, 1H), 5.27 (s, 1H), 2.34 (s, 3H), 2.20 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.3 (C_q), 136.0 (C_q), 135.6 (C_q), 135.3 (C_q), 135.0 (C_q), 129.3 (CH), 129.1 (CH), 127.8 (CH), 127.6 (CH), 126.2 (CH), 125.9 (CH), 122.1 (CH), 117.4 (CH), 105.7 (CH), 21.0 (CH_3), 18.2 (CH_3).

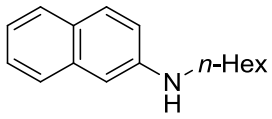
IR (KBr): 3391, 2915, 1632, 1601, 1516, 1310, 1249, 1181, 808, 745 cm^{-1}.

MS (EI) m/z (relative intensity) 261 (100) [M^+], 245 (25), 231 (20), 115 (15), 77 (6), 43 (16).

HR-MS (EI) m/z calcd for [$C_{19}H_{19}N$] 261.1517, found 261.1517.

The spectral data were in accordance with those reported in the literature.[78]

***N*-Hexylnaphthalen-2-amine (48fh)**



The general procedure **A** was followed using **30af** (126 mg, 0.50 mmol) and **46h** (76 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48fh** (85 mg, 75%) was obtained as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.68 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.41-7.32 (m, 1H), 7.25-7.15 (m, 1H), 6.87 (dd, J = 2.2, 2.2 Hz, 1H), 6.80 (d, J = 2.1 Hz, 1H), 3.76 (s,

[77] N. L. Smith, **1951**, US 2572066 19511023.

[78] S. B. Cortright, J. C. Huffman, R. A. Yoder, J. N. Coalter, J. N. Johnston, *Organometallics* **2004**, *23*, 2238–2250.

1H), 3.21 (t, J = 7.2 Hz, 2H), 1.76-1.58 (m, 2H), 1.55-1.25 (m, 6H), 1.01-0.87 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ= 146.1 (C_q), 135.3 (C_q), 128.8 (CH), 127.6 (CH), 127.4 (C_q), 126.2 (CH), 125.8 (CH), 121.7 (CH), 117.9 (CH), 105.1 (CH), 44.0 (CH_2), 31.6 (CH_2), 29.4 (CH_2), 26.9 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

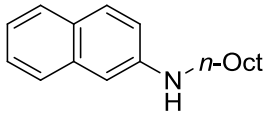
IR (KBr): 3409, 3050, 2954, 2927, 2856, 1604, 1516, 1358, 1145, 745 cm^{-1}.

MS (EI) m/z (relative intensity) 227 (28) [M^+], 156 (100), 127 (14), 115 (9), 77 (2), 43 (15).

HR-MS (EI) m/z calcd for [$C_{16}H_{21}N$] 227.1674, found 227.1670.

The spectral data were in accordance with those reported in the literature.[79]

_N_-Octylnaphthalen-2-amine (48fi)



The general procedure **A** was followed using **30af** (126 mg, 0.50 mmol) and **46i** (97 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 50:1) **48fi** (93 mg, 73%) was obtained as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.72-7.55 (m, 3H), 7.40-7.29 (m, 1H), 7.24-7.12 (m, 1H), 6.87 (dd, J = 2.6, 2.5 Hz, 1H), 6.80 (d, J = 2.3 Hz, 1H), 3.81 (s, 1H), 3.20 (t, J = 7.2 Hz, 2H), 1.77-1.61 (m, 2H), 1.52-1.16 (m, 10H), 0.98-0.76 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ= 146.0 (C_q), 135.3 (C_q), 128.8 (CH), 127.6 (CH), 127.4 (C_q), 126.3 (CH), 125.9 (CH), 121.8 (CH), 118.0 (CH), 104.3 (CH), 44.1 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 27.2 (CH_2), 22.7 (CH_2), 14.1 (CH_3).

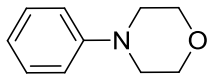
IR (KBr): 3412, 3050, 2926, 2854, 1604, 1517, 1359, 1249, 1145, 746 cm^{-1}.

MS (EI) m/z (relative intensity) 255 (62) [M^+], 156 (100), 127 (20), 115 (11), 77 (2), 43 (5).

HR-MS (EI) m/z calcd for [$C_{18}H_{25}N$] 255.1987, found 255.1982.

The spectral data were in accordance with those reported in the literature.[80]

4-Phenylmorpholine (68ba)



[79] N. Montazeri, M. Tavana, S. Yousefian, F. T. Firooz, *Asian. J. Chem.* **2012**, *24*, 840–842.
[80] E. Bergmann, L. Haskelberg, *J. Chem. Soc.* **1939**, 1–5.

The general procedure **A** was followed using **30ab** (101 mg, 0.50 mmol) and **67** (65 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **68ba** (80 mg, 99%) was obtained as a white solid (m.p. 55℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.33-7.21 (m, 2H), 6.95-6.83 (m, 2H), 3.85 (t, J = 4.8 Hz, 4H), 3.14 (t, J = 5.0 Hz, 4H).

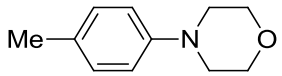
^{13}C NMR (75 MHz, $CDCl_3$): δ= 151.3 (C_q), 129.2 (CH), 120.0 (CH), 115.7 (CH), 66.9 (CH_2), 49.4 (CH_2).

IR (KBr): 3406, 3059, 3024, 1597, 1498, 1375, 1298, 1175, 1119, 732, 697 cm^{-1}.

MS (EI) m/z (relative intensity) 163 (48) [M^+], 105 (100), 77 (35), 55 (30), 43 (70).

HR-MS (EI) m/z calcd for [$C_{10}H_{13}NO$] 163.0997, found 163.0994.

4-*p*-Tolylmorpholine (68ca)



The general procedure **A** was followed using **30ac** (108 mg, 0.50 mmol) and **67** (65 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **68ca** (81 mg, 92%) was obtained as a pale yellow solid (m.p. 47 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.08 (d, J = 8.2 Hz, 2H), 6.86-6.79 (m, 2H), 3.84 (t, J = 4.8 Hz, 4H), 3.09 (t, J = 4.6 Hz, 4H), 2.26 (s, 3H).

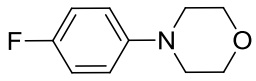
^{13}C NMR (75 MHz, $CDCl_3$): δ= 149.2 (C_q), 129.7 (CH), 129.6 (C_q), 116.3 (CH), 66.9 (CH_2), 49.9 (CH_2), 20.4 (CH_3).

IR (KBr): 3398, 2958, 2852, 1699, 1558, 1513, 1259, 1117, 745, 695 cm^{-1}.

MS (EI) m/z (relative intensity) 177 (28) [M^+], 119 (50), 91 (11), 58 (18), 43 (100).

HR-MS (EI) m/z calcd for [$C_{11}H_{15}NO$] 177.1154, found 177.1154.

4-(4-Fluorophenyl)morpholine (68ea)



The general procedure **A** was followed using **30ae** (110 mg, 0.50 mmol) and **67** (65 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **68ea** (81 mg, 90%) was obtained as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.02-6.91 (m, 2H), 6.90-6.79 (m, 2H), 3.84 (t, J = 4.8 Hz, 4H), 3.06 (t, J = 4.5 Hz, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.3 (C_q, $^1J_{C\text{-}F}$ = 240 Hz), 147.9 (C_q, $^4J_{C\text{-}F}$ = 4 Hz), 117.4.0 (CH, $^3J_{C\text{-}F}$ = 7 Hz), 124.0 (CH, $^2J_{C\text{-}F}$ = 22 Hz), 66.9 (CH_2), 50.3 (CH_2).

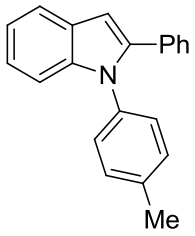
IR (KBr): 3395, 3056, 2285, 2824, 1726, 1511, 1375, 1239, 1120, 711 cm^{-1}.

MS (EI) m/z (relative intensity) 181 (52) [M^+], 123 (100), 95 (25), 75 (12), 57 (5).

HR-MS (EI) m/z calcd for [$C_{10}H_{12}FNO$] 181.0903, found 181.0907.

The spectral data were in accordance with those reported in the literature.[81]

2-Phenyl-1-(*p*-tolyl)-1*H*-indole (47ac)



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46c** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ac** (125 mg, 88%) as a white solid (m.p. 97-98 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (dd, J = 5.7, 3.3Hz, 1H), 7.44-7.03 (m, 12H), 6.81 (s, 1H), 2.41 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 140.8, 139.1, 137.0, 135.9, 132.6, 129.9, 128.9, 128.2, 128.1, 127.8, 127.2, 122.2, 120.5, 120.4, 110.7, 103.4, 21.1.

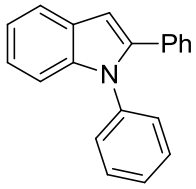
IR (KBr): 3054, 3033, 2920, 1514, 1451, 1356, 1322, 1208, 1108, 1022, 741, 696 cm^{-1}.

MS (EI) m/z (relative intensity) 283 (100) [M^+], 267 (14), 165 (13), 133 (9).

HR-MS (EI) m/z calcd for $C_{21}H_{17}N$ 283.1361, found 283.1359.

1,2-Diphenyl-1*H*-indole (47ab)

[81] Li, X.; Yang, D.; Jiang, Y.; Fu, H. *Green Chem.* **2010**, *12*, 1097–1105.



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46b** (70 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ab** (115 mg, 86%) was obtained as a white solid (m.p. 83-84 ℃).

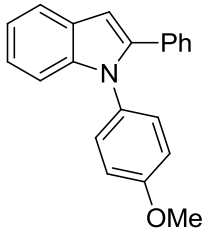
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (m, 1H), 7.48-7.14 (m, 13H), 6.85 (d, J = 0.8 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7, 139.0, 138.5, 132.5, 129.2, 129.0, 128.3, 128.1, 128.0, 127.3, 127.2, 122.3, 120.7, 120.5, 110.6, 103.7.

IR (KBr): 3056, 1597, 1495, 1451, 1377, 1352, 1321, 795, 755, 697 cm^{-1}. MS (EI) m/z (relative intensity) 269 (100) [M^+], 268 (35), 165 (26), 133 (27), 127 (12).

HR-MS (ESI) m/z calcd for $[C_{20}H_{15}N+H]^+$ 270.1277, found 270.1275.

1-(*p*-Anisyl)-2-phenyl-1*H*-indole (47aa)



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46a** (92 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47aa** (146 mg, 98%) was obtained as a white solid (m.p. 143-144 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (m, 1H), 7.42-7.12 (m, 10H), 6.97 (d, J = 8.9 Hz, 2H), 6.85 (s, 1H), 3.86 (s, 3H).

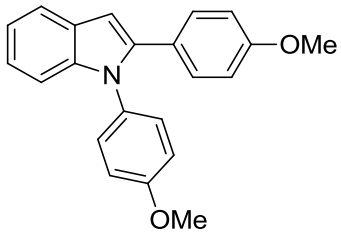
^{13}C NMR (75 MHz, $CDCl_3$): δ 158.5, 140.8, 139.3, 132.6, 131.3, 129.1, 128.8, 128.1, 128.1, 127.2, 122.1, 120.5, 120.4, 114.4, 110.6, 103.1, 55.4.

IR (KBr): 3054, 2956, 2835, 1612, 1512, 1460, 1294, 1175, 1031, 842, 754, 694 cm^{-1}.

MS (EI) m/z (relative intensity) 299 (100) [M^+], 284 (26), 256 (10), 254 (16).

HR-MS (EI) m/z calcd for $C_{21}H_{17}NO$ 299.1310, found 299.1313.

1,2-Di-*p*-anisyl-1*H*-indole (**47ba**).



The general procedure **B** was followed using **45ab** (144 mg, 0.50 mmol) and **46a** (92 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc, 100/1) indole **47ba** (147 mg, 89%) was obtained as a yellow solid (m.p. 136-137 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (m, 1H), 7.23-7.13 (m, 7H), 6.93 (dt, J = 9.8, 3.4 Hz, 2H), 6.80 (dt, J = 9.8, 3.1 Hz, 2H), 6.73 (d, J = 0.7 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H).

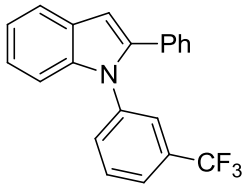
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.9, 158.5, 140.8, 139.2, 131.4, 130.1, 129.2, 128.2, 125.1, 121.8, 120.4, 120.2, 114.4, 113.6, 110.5, 102.2, 55.4, 55.2.

IR (KBr): 3000, 2933, 2838, 1608, 1541, 1513, 1456, 1361, 1249, 1116, 1031, 834, 740, 646 cm^{-1}.

MS (EI) *m/z* (relative intensity) 329 (100) [M^+], 314 (36), 298 (2), 283 (5), 271 (5), 254 (15), 242 (16), 215 (3), 190 (2).

HR-MS (ESI) *m/z* calcd for $[C_{22}H_{19}NO_2+H]^+$ 330.1489, found 330.1489.

2-Phenyl-1-{*m*(-trifluoromethyl)phenyl}-1*H*-indole (47ad).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46d** (121 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ad** (115 mg, 72%) was obtained as a white solid (m.p. 91-92℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (m, 1H), 7.67-7.47 (m, 3H), 7.39 (d, J = 7.9 Hz, 1H), 7.34-7.16 (m, 8H), 6.83 (s, 1H).

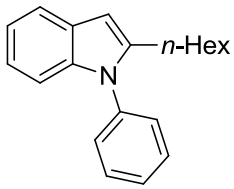
^{13}C NMR (75 MHz, $CDCl_3$): δ 140.6, 139.1, 138.6, 132.0, 131.8 ($^2J_{C,F}$ = 34 Hz), 131.2, 129.8, 129.0, 128.5, 128.3, 127.6, 124.7 ($^3J_{C,F}$ = 4 Hz), 123.7 ($^3J_{C,F}$ = 4 Hz), 122.8, 121.5 ($^1J_{C,F}$ = 251 Hz), 121.2, 120.8, 110.2, 104.6.

IR (KBr): 3059, 1597, 1496, 1456, 1375, 1326, 1129, 799, 752, 698 cm^{-1}.

MS (EI) m/z (relative intensity) 337 (100) [M^+], 336 (19), 267 (14), 165 (26), 133 (23).

HR-MS (ESI) m/z calcd for $[C_{21}H_{14}NF_3+H]^+$ 338.1151, found 338.1152.

2-*n*-Hexyl-1-phenyl-1*H*-indole (47cb).



The general procedure **B** was followed using **45ac** (133 mg, 0.50 mmol) and **46b** (70 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47cb** (108 mg, 78%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71-7.47 (m, 4H), 7.42 (t, J = 4.2 Hz, 2H), 7.23-7.11 (m, 3H), 6.50 (s, 1H), 2.76-2.58 (t, J = 7.6 Hz, 2H), 1.71-1.58 (m, 2H), 1.40-1.20 (m, 6H), 0.93 (t, J = 6.8 Hz, 3H).

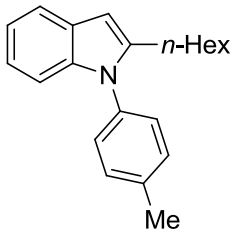
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.0, 138.3, 138.1, 129.4, 128.3, 128.1, 127.8, 121.0, 119.9, 119.6, 109.9, 100.1, 31.5, 28.9, 28.6, 27.1, 22.5, 14.0.

IR (KBr): 3056, 2927, 2857, 1596, 1498, 1459, 1392, 1211, 1016, 778, 762, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (44) [M^+], 220 (46), 207 (100), 191 (6), 178 (7), 165 (3), 152 (2), 128 (6).

HR-MS (EI) m/z calcd for $C_{20}H_{23}N$ 277.1830, found 277.1831.

2-*n*-Hexyl-1-*p*-tolyl-1*H*-indole (47cc).



The general procedure **B** was followed using **45ac** (133 mg, 0.50 mmol) and **46c** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47cc** (117 mg, 81%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66 (m, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.29 (m, 2H), 7.20-7.10 (m, 3H), 6.48 (s, 1H), 2.70 (t, J = 7.8 Hz, 2H), 2.52 (s, 3H), 1.71-1.60 (m, 2H), 1.32 (m, 6H), 0.94 (t, J = 6.8 Hz, 3H).

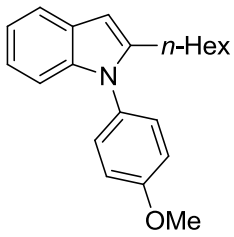
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.1, 138.4, 137.6, 135.4, 130.0, 128.1, 128.0, 120.8, 119.8, 119.5, 110.0, 99.8, 31.5, 28.9, 28.6, 27.0, 22.5, 21.2, 14.0.

IR (KBr): 3054, 2954, 2926, 2858, 1608, 1514, 1459, 1394, 1211, 1017, 817, 741 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (46) [M^+], 221 (100), 220 (66), 205 (34), 204 (44).

HR-MS (EI) m/z calcd for $C_{21}H_{25}N$ 291.1987, found 291.1978.

1-(*p*-Anisyl)-2-*n*-hexyl-1*H*-indole (47ca).



The general procedure **B** was followed using **45ac** (133 mg, 0.50 mmol) and **46a** (92 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ca** (113 mg, 75%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (m, 1H), 7.33-7.23 (m, 2H), 7.19-6.99 (m, 5H), 6.43 (s, 1H), 3.91 (s, 3H), 2.62 (t, J = 7.4 Hz, 2H), 1.69-1.55 (m, 2H), 1.28 (s, 6H), 0.90 (t, J = 5.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 142.3, 138.6, 130.7, 129.4, 128.0, 120.8, 119.7, 119.5, 114.5, 109.9, 99.6, 55.5, 31.5, 28.9, 28.6, 27.0, 22.5, 14.1.

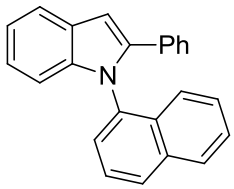
IR (KBr): 3050, 2928, 2857, 1580, 1547, 1460, 1294, 1211, 1036, 831, 778, 742 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (51) [M^+], 237 (100), 205 (29), 192 (11), 43 (15).

HR-MS (EI) m/z calcd for $C_{21}H_{25}NO$ 307.1936, found 307.1936.

The spectral data are in accordance with those reported in literature. [82]

1-Naphthyl-2-phenyl-1*H*-indole (47aj).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46j** (107 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47aj** (124 mg, 78%) was obtained as a yellow solid (m.p. 73-74 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (t, J = 7.4 Hz, 2H), 7.75 (m, 1H), 7.55-7.42 (m, 3H), 7.42-7.30 (m, 2H), 7.26-7.04 (m, 7H), 6.94 (d, J = 0.8 Hz, 1H), 6.82 (dd, J = 8.2, 0.9 Hz , 1H).

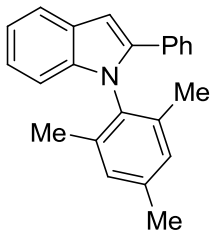
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.1, 140.2, 135.3, 134.3, 132.5, 131.3, 128.6, 128.3, 128.2, 128.2, 128.1, 127.3, 127.2, 127.1, 126.5, 125.5, 123.6, 122.2, 120.6, 120.5, 111.2, 103.2.

IR (KBr): 3053, 1599, 1509, 1460, 1403, 1317, 1215, 1017, 796, 747, 695 cm^{-1}.

MS (EI) m/z (relative intensity) 319 (100) [M^+], 302 (4), 289 (3), 241 (8), 215 (5), 190 (2).

HR-MS (EI) m/z calcd for $C_{24}H_{17}N$ 319.1361, found 319.1364.

1-Mesityl-2-phenyl-1*H*-indole (47af).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46f** (101 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47af** (124 mg, 81%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (dd, J = 6.2, 2.8 Hz, 1H), 7.43-7.18 (m, 7H), 7.03 (s, 2H), 7.00-6.90 (m, 2H), 2.42 (s, 3H), 1.93 (s, 6H).

[82] L. Ackermann, S. Barfüer, H. K. Potukuchi, *Adv. Synth. Catal*. **2009**, *351*, 1064–1072.

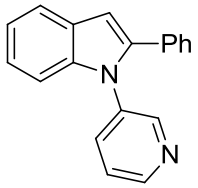
^{13}C NMR (75 MHz, $CDCl_3$): δ 140.5, 138.0, 137.9, 136.9, 133.9, 132.8, 129.2, 128.2, 128.2, 127.4, 127.2, 122.1, 120.4, 120.2, 110.5, 102.0, 21.1, 17.7.

IR (KBr): 3054, 3027, 2919, 1604, 1486, 1371, 1209, 1030, 854, 793, 741, 696 cm^{-1}.

MS (EI) m/z (relative intensity) 311 (100) [M^+], 310 (17), 296 (20), 237 (13).

HR-MS (ESI) m/z calcd for $[C_{23}H_{21}N+H]^+$ 312.1747, found 312.1741.

2-Phenyl-1-(3-pyridyl)-1*H*-indole (47ak).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46k** (71 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ak** (98 mg, 74%) was obtained as a white oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70-8.55 (m, 2H), 7.74 (m, 1H), 7.55 (m, 1H), 7.41-7.18 (m, 9H), 6.87 (s, 1H).

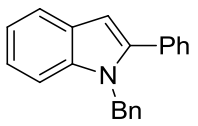
^{13}C NMR (75 MHz, $CDCl_3$): δ 148.9, 148.0, 140.6, 138.7, 135.2, 135.1, 131.8, 129.0, 128.5, 128.4, 127.6, 123.7, 122.8, 121.2, 120.7, 110.0, 104.7.

IR (KBr): 3053, 1482, 1426, 1326, 1208, 1024, 798, 749, 703 cm^{-1}.

MS (EI) m/z (relative intensity) 270 (100) [M^+], 241 (8), 216 (3), 190 (4), 165 (12), 134 (11).

HR-MS (EI) m/z calcd for $C_{19}H_{14}N_2$ 270.1157, found 270.1161.

1-Benzyl-2-phenyl-1*H*-indole (47al).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46l** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47al** (120 mg, 85%) was obtained as a white solid (m.p. 95-96 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (dd, J = 5.9, 0.8 Hz, 1H), 7.36-7.14 (m, 11H), 7.07-7.02 (m, 2H), 6.66 (s, 1H), 5.37 (s, 2H).

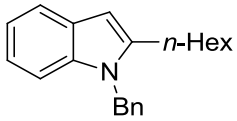
^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 138.2, 138.0, 132.7, 129.2, 128.7, 128.5, 128.3, 128.0, 127.1, 126.0, 121.9, 120.5, 120.1, 110.5, 102.3, 47.7.

IR (KBr): 3056, 3029, 2917, 1603, 1488, 1454, 1348, 1312, 1163, 730, 698, 670 cm^{-1}.

MS (EI) m/z (relative intensity) 283 (50) [M^+], 165 (12), 91 (100), 65 (9).

HR-MS (ESI) m/z calcd for $[C_{21}H_{17}N+H]^+$ 284.1434, found 284.1434.

1-Benzyl-2-*n*-hexyl-1*H*-indole (47cl).



The general procedure **B** was followed using **45ac** (133 mg, 0.50 mmol) and **46l** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47cl** (95 mg, 67%) was obtained as a white solid (m.p. 68-69 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (m, 1H), 7.36-7.06 (m, 6H), 6.98 (d, J = 8.1 Hz, 2H), 6.38 (s, 1H), 5.34 (s, 2H), 2.69 (t, J = 7.8 Hz, 2H), 1.82-1.61 (m, 2H), 1.48-1.19 (m, 6H), 0.90 (dd, J = 5.76, 6.11 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 141.4, 138.0, 137.1, 128.7, 128.2, 127.2, 125.9, 120.7, 120.0, 119.4, 109.3, 99.3, 46.3, 31.6, 29.0, 28.4, 26.7, 22.5, 14.1.

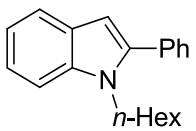
IR (KBr): 3031, 2953, 2921, 2851, 1650, 1541, 1453, 1352, 1309, 1250, 773, 733, 697 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (70) [M^+], 234 (32), 221 (94), 130 (23), 91 (100), 65 (14).

HR-MS (EI) m/z calcd for $C_{21}H_{25}N$ 291.1987, found 291.1978.

The spectral data are in accordance with those reported in literature.[83]

1-*n*-Hexyl-2-phenyl-1*H*-indole (47ah).



[83] Z. Y. Tang, Q. S. Hu, *Adv. Synth. Catal*. **2006**, *348*, 846–850.

The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46h** (76 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ah** (102 mg, 74%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J = 7.6 Hz, 1H), 7.62-7.43 (m, 6H), 7.32 (m, 1H), 7.23 (m, 1H), 6.62 (s, 1H), 4.22 (t, J = 7.6 Hz, 2H), 1.86-1.70 (m, 2H), 1.40-1.10 (m, 6H), 0.91 (t, J = 6.8 Hz, 3H).

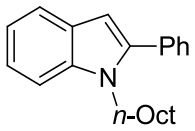
^{13}C NMR (75 MHz, $CDCl_3$): δ 141.3, 137.3, 133.3, 129.4, 128.4, 128.2, 127.8, 121.4, 120.5, 119.7, 110.0, 102.0, 43.9, 31.2, 29.9, 26.4, 22.4, 13.9.

IR (KBr): 3056, 2954, 2859, 1646, 1462, 1350, 1313, 1166, 744, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (44) [M^+], 221 (11), 206 (100), 204 (15), 178 (12), 165 (19).

HR-MS (ESI) m/z calcd for $[C_{20}H_{23}N+H]^+$ 278.1903, found 278.1900.

1-*n*-Octyl-2-phenyl-1*H*-indole (47ai).



The general procedure **B** was followed using **45aa** (129 mg, 0.50 mmol) and **46i** (97 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47ai** (120 mg, 80%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, J = 7.8 Hz, 1H), 7.59-7.36 (m, 6H), 7.26 (m, 1H), 7.15 (m, 1H), 6.55 (s, 1H), 4.16 (t, J = 7.7 Hz, 2H), 1.77-1.65 (m, 2H), 1.34-1.09 (m, 10H), 0.89 (t, J = 6.9 Hz, 3H).

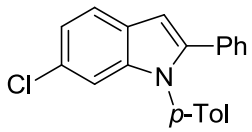
^{13}C NMR (75 MHz, $CDCl_3$): δ 141.3, 137.3, 133.3, 129.4, 128.4, 128.2, 127.9, 121.4, 120.5, 119.7, 110.0, 102.0, 43.9, 31.7, 29.9, 29.1, 29.0, 26.7, 22.6, 14.1.

IR (KBr): 3030, 2926, 2855, 1606, 1462, 1350, 1163, 1016, 786, 743, 700 cm^{-1}.

MS (EI) m/z (relative intensity) 305 (43) [M^+], 207 (16), 206 (100), 193 (13), 165 (9).

HR-MS (ESI) m/z calcd for $[C_{22}H_{27}N+H]^+$ 306.2216, found 306.2218.

6-Chloro-2-phenyl-1-*p*-tolyl-1*H*-indole (47dc).



The general procedure **B** was followed using **45ad** (145 mg, 0.50 mmol) and **46c** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47dc** (113 mg, 72%) was obtained as a white solid (m.p. 112-113℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, J = 8.4 Hz, 1H), 7.30-7.19 (m, 8H), 7.16-7.05 (m, 3H), 6.75 (s, 1H), 2.41 (s, 3H).

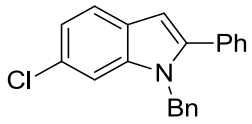
^{13}C NMR (75 MHz, $CDCl_3$): δ 141.5, 139.5, 137.5, 135.3, 132.1, 130.1, 128.8, 128.2, 128.0, 127.6, 127.5, 126.7, 121.2, 121.2, 110.7, 103.2, 21.2.

IR (KBr): 3057, 3034, 1604, 1514, 1457, 1378, 1071, 927, 759, 732, 695 cm^{-1}.

MS (EI) m/z (relative intensity) 317 (100) [M^+], 281 (23), 267 (14), 239 (3), 179 (6), 165 (8).

HR-MS (EI) m/z calcd for $C_{21}H_{16}ClN$ 317.0971, found 317.0968.

1-Benzyl-6-chloro-2-phenyl-1*H*-indole (47dl).



The general procedure **B** was followed using **45ad** (145 mg, 0.50 mmol) and **46l** (80 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47dl** (115 mg, 73%) was obtained as a white solid (m.p. 130-131℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, J = 8.4 Hz, 1H), 7.47-7.06 (m, 10H), 6.99 (d, J = 6.3 Hz, 2H) 6.61 (s, 1H), 5.31 (s, 2H).

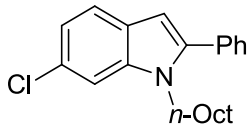
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.6, 138.4, 137.6, 132.2, 129.2, 128.9, 128.6, 128.3, 127.7, 127.3, 126.9, 125.9, 121.4, 120.9, 110.5, 102.4, 47.8.

IR (KBr): 3060, 3030, 1605, 1460, 1384, 1073, 916, 760, 732, 698 cm^{-1}.

MS (EI) m/z (relative intensity) 317 (80) [M^+], 226 (8), 199 (12), 91 (100), 65 (15), 43 (13).

HR-MS (EI) m/z calcd for $C_{21}H_{16}ClN$ 317.0971, found 317.0971.

6-Chloro-1-*n*-octyl-2-phenyl-1*H*-indole (47di).



The general procedure **B** was followed using **45ad** (145 mg, 0.50 mmol) and **46i** (97 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 500:1) indole **47di** (91 mg, 53%) was obtained as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60-7.34 (m, 7H), 7.10 (d, J = 8.4 Hz, 1H), 6.48 (s, 1H), 4.09 (t, J = 7.5 Hz, 2H), 1.75-1.55 (m, 2H), 1.32-1.10 (m, 10H), 0.87 (t, J = 6.9 Hz, 3H).

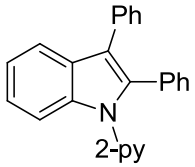
^{13}C NMR (75 MHz, $CDCl_3$): δ 142.1, 137.8, 132.8, 129.4, 128.5, 128.1, 127.3, 126.7, 121.3, 120.3, 110.0, 102.1, 44.1, 31.7, 29.8, 29.0, 28.9, 26.6, 22.6, 14.1.

IR (KBr): 3062, 2926, 2856, 1607, 1463, 1341, 1302, 1068, 919, 810, 759, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 339 (81) [M^+], 242 (38), 240 (100), 227 (23), 205 (88).

HR-MS (ESI) m/z calcd for $[C_{22}H_{26}ClN+H]^+$ 340.1827, found 340.1814.

2,3-Diphenyl-1-(pyridin-2-yl)-1*H*-indole (50aa')



The general procedure **C** was followed using **49aa** (85.5 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50aa'** (142 mg, 82%) was obtained as a white solid (m.p. 159–160 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (ddd, J = 4.8, 2.0, 0.9 Hz, 1H), 7.78–7.65 (m, 2H), 7.59–7.52 (m, 1H), 7.42–7.06 (m, 13H), 6.82 (dt, J = 8.0, 0.9 Hz, 1H).

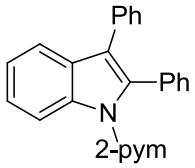
^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8 (C_q), 149.1 (CH), 137.6 (CH), 137.4 (C_q), 135.9 (C_q), 134.6 (C_q), 131.7 (C_q), 130.9 (CH), 130.3 (CH), 128.3 (C_q), 128.2 (CH), 128.1 (CH), 127.4 (CH), 126.1 (CH), 123.4 (CH), 122.2 (CH), 121.6 (CH), 121.5 (CH), 119.6 (CH), 118.2 (C_q), 111.5 (CH).

IR (neat): 3050, 1582, 1464, 1388, 1028, 696 cm^{-1}.

MS (EI) m/z (relative intensity) 346 (100) [M^+], 267 (25), 165 (11), 78 (15), 51 (11).

HR-MS (EI) m/z calcd for $[C_{25}H_{18}N_2]^+$ 346.1470, found 346.1478.

2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50aa)



The general procedure **C** was followed using **49ba** (86 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50aa** (141 mg, 81%) was obtained as a white solid (m.p. 148–149 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.28–8.20 (m, 1H), 7.83–7.76 (m, 1H), 7.47–7.29 (m, 7H), 7.24 (m, 5H), 7.01 (t, J = 4.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9 (CH), 157.8 (C_q), 136.9 (C_q), 136.0 (C_q), 134.1 (C_q), 132.7 (C_q), 130.2 (CH), 130.1 (CH), 129.1 (C_q), 128.1 (CH), 127.7 (CH), 126.9 (CH), 126.3 (CH), 123.8 (CH), 122.1 (CH), 120.1 (C_q), 119.6 (CH), 117.4 (CH), 112.6 (CH).

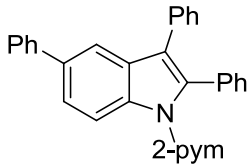
IR (neat): 3054, 1556, 1416, 1257, 1027, 847 cm^{-1}.

MS (EI) m/z (relative intensity) 347 (100) [M^+], 267 (16), 165 (5), 77 (3), 53 (3).

HR-MS (EI) m/z calcd for $[C_{24}H_{17}N_3]^+$ 347.1422, found 347.1417.

The spectral data were in accordance with those reported in the literature.[84]

2,3,5-Triphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ba)



The general procedure **C** was followed using **49bb** (124 mg, 0.50 mmol) and 4**a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ba** (144 mg, 68%) was obtained as a white solid (m.p. 207–208 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.9 Hz, 2H), 8.27 (dd, J = 8.6, 0.6 Hz, 1H), 7.94 (dd, J = 1.9, 0.6 Hz, 1H), 7.74–7.67 (m, 2H), 7.64 (dd, J = 8.6, 1.9 Hz, 1H), 7.51–7.31 (m, 8H), 7.27–7.16 (m, 5H), 7.06 (t, J = 4.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (CH), 157.9 (C_q), 142.0 (C_q), 136.7 (C_q), 136.4 (C_q),

[84] J. Chen, Q. Pang, Y. Sun, X. Li, *J. Org. Chem.* **2011**, *76*, 3523–3526.

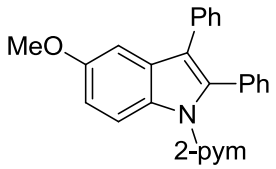
135.7 (C_q), 134.0 (C_q), 132.7 (C_q), 130.4 (CH), 130.2 (CH), 129.7 (C_q), 128.6 (CH), 128.3 (CH), 127.8 (CH), 127.3 (CH), 127.1 (CH), 126.6 (CH), 126.5 (CH), 123.5 (CH), 120.5 (C_q), 118.1 (CH), 117.6 (CH), 112.9 (CH).

IR (neat): 3041, 1560, 1417, 1228, 915, 722 cm^{-1}.

MS (EI) m/z (relative intensity) 423 (100) [M^+], 346 (10), 264 (3), 77 (3), 43 (2).

HR-MS (EI) m/z calcd for $[C_{30}H_{21}N_3]^+$ 423.1735, found 423.1743.

5-Methoxy-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ca)



The general procedure **C** was followed using **49bc** (101 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **50ca** (127 mg, 67%) was obtained as a white solid (m.p. 186–187 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.59 (d, J = 4.9 Hz, 2H), 8.10 (dd, J = 9.0, 0.6 Hz, 1H), 7.36–7.23 (m, 5H), 7.21–7.11 (m, 6H), 7.03 (t, J = 4.9 Hz, 1H), 6.98 (dd, J = 9.0, 2.6 Hz, 1H), 3.83 (s, 3H).

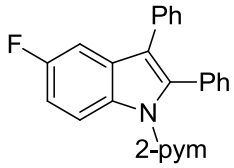
^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9 (CH), 155.8 (C_q), 136.7 (C_q), 134.3 (C_q), 134.3 (C_q), 132.9 (C_q), 131.9 (C_q), 130.3 (CH), 130.2 (CH), 129.9 (C_q), 128.2 (CH), 127.7 (CH), 126.9 (CH), 126.4 (CH), 120.3 (C_q), 117.3 (CH), 113.7 (CH), 113.2 (CH), 101.6 (CH), 55.8 (CH_3).

IR (neat): 3052, 2988, 1572, 1420, 1161, 730 cm^{-1}.

MS (EI) m/z (relative intensity) 377 (100) [M^+], 334 (35), 254 (10), 79 (4), 53 (3).

HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3O]^+$ 377.1528, found 377.1522.

5-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50da)



The general procedure **C** was followed using **49bd** (95 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50da** (149

mg, 82%) was obtained as a white solid (m.p. 176–177 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (d, J = 4.9 Hz, 2H), 8.12 (dd, J = 9.0, 4.6 Hz, 1H), 7.40–7.09 (m, 11H), 7.09–7.02 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2 (C_q, $^1J_{C\text{-}F}$ = 237.8 Hz), 158.0 (CH), 157.8 (C_q), 137.6 (C_q), 133.7 (C_q), 133.3 (C_q), 132.5 (C_q), 130.2 (CH), 130.1 (CH), 129.9 (C_q, $^3J_{C\text{-}F}$ = 10.0 Hz), 128.3 (CH), 127.8 (CH), 127.2 (CH), 126.6 (CH), 120.0 (C_q, $^4J_{C\text{-}F}$ = 4.6 Hz), 117.7 (CH), 113.8 (CH, $^3J_{C\text{-}F}$ = 9.4 Hz), 111.7 (CH, $^2J_{C\text{-}F}$ = 25.8 Hz), 104.8 (CH, $^2J_{C\text{-}F}$ = 24.4 Hz).

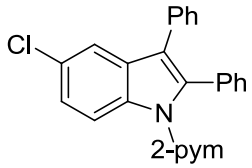
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.4–121.6) (m).

IR (neat): 3051, 1561, 1418, 1178, 913, 731 cm^{-1}.

MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (14), 181 (4), 79 (2), 53 (3).

HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1315.

5-Chloro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ea)



The general procedure **C** was followed using **49be** (103 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ea** (104 mg, 55%) was obtained as a white solid (m.p. 169–170 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, J = 4.9 Hz, 2H), 8.07 (d, J = 8.9 Hz, 1H), 7.64 (d, J = 2.0 Hz, 1H), 7.40–7.10 (m, 11H), 7.08 (t, J = 4.9 Hz, 1H).

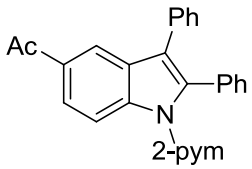
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1 (CH), 157.7 (C_q), 137.3 (C_q), 135.3 (C_q), 133.5 (C_q), 132.4 (C_q), 130.4 (C_q), 130.2 (CH), 130.2 (CH), 128.3 (CH), 127.8 (CH), 127.7 (C_q), 127.3 (CH), 126.8 (CH), 123.9 (CH), 119.7 (C_q), 119.1 (CH), 117.8 (CH), 113.9 (CH).

IR (neat): 3051, 1603, 1415, 1069, 956 cm^{-1}.

MS (EI) m/z (relative intensity) 381 (100) [M^+], 345 (25), 172 (15), 79 (2), 53 (3).

HR-MS (EI) m/z calcd for $[C_{24}H_{16}ClN_3]^+$ 381.1033, found 381.1035.

1-(2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indol-5-yl) ethanone (50fa)



The general procedure **C** was followed using **49bf** (107 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50fa** (132 mg, 68%) was obtained as a white solid (m.p. 171–172 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.31 (d, J = 1.2 Hz, 1H), 8.11 (d, J = 8.8 Hz, 1H), 7.98 (dd, J = 8.9, 1.6 Hz, 1H), 7.45–7.02 (m, 11H), 2.64 (s, 3H).

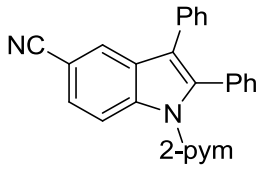
^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.0 (C_q), 158.2 (CH), 157.4 (C_q), 139.4 (C_q), 137.5 (C_q), 133.3 (C_q), 132.0 (C_q), 131.8 (C_q), 130.2 (CH), 130.1 (CH), 128.7 (C_q), 128.4 (CH), 127.8 (CH), 127.3 (CH), 126.7 (CH), 123.9 (CH), 121.2 (CH), 120.7 (C_q), 118.2 (CH), 112.4 (CH), 26.7 (CH_3).

IR (neat): 3053, 1672, 1467, 1180, 948 cm^{-1}.

MS (EI) m/z (relative intensity) 389 (100) [M^+], 346 (36), 172 (5), 79 (4), 43 (12).

HR-MS (EI) m/z calcd for $[C_{26}H_{19}N_3O]^+$ 389.1528, found 389.1531.

2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indole-5-carbonitrile (50ga)



The general procedure **C** was followed using **49bg** (98 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **50ga** (130 mg, 70%) was obtained as a white solid (m.p. 193–194 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (d, J = 4.9 Hz, 2H), 8.13 (dd, J = 8.6, 0.8 Hz, 1H), 8.02 (dd, J = 1.7, 0.7 Hz, 1H), 7.54 (dd, J = 8.6, 1.6 Hz, 1H), 7.40–7.06 (m, 11H).

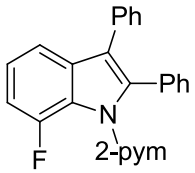
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (CH), 157.2 (C_q), 138.4 (C_q), 138.2 (C_q), 132.7 (C_q), 131.5 (C_q), 130.1 (CH), 130.0 (CH), 128.9 (C_q), 128.4 (CH), 127.9 (CH), 127.7 (CH), 127.0 (CH), 126.5 (CH), 124.9 (CH), 120.2 (C_q), 119.7 (C_q), 118.5 (CH), 113.5 (CH), 105.1 (C_q).

IR (neat): 3051, 2221, 1561, 1204, 971 cm^{-1}.

MS (EI) m/z (relative intensity) 372 (100) [M^+], 292 (12), 186 (7), 79 (2), 53 (3).

HR-MS (EI) m/z calcd for $[C_{25}H_{16}N_4]^+$ 372.1375, found 372.1364.

7-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ha)



The general procedure **C** was followed using **49bh** (95 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ha** (131 mg, 72%) was obtained as a white solid (m.p. 201–202 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (d, J = 4.9 Hz, 2H), 7.50 (dd, J = 8.0, 0.8 Hz, 1H), 7.38–7.06 (m, 12H), 6.96 (ddd, J = 12.1, 8.0, 0.8 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (C_q), 158.2 (CH), 149.7 (C_q, $^1J_{C\text{-}F}$ = 245.6 Hz), 137.9 (C_q), 134.0 (C_q), 132.0 (C_q, $^3J_{C\text{-}F}$ = 4.3 Hz), 131.2 (C_q), 130.8 (CH), 130.2 (CH), 128.3 (CH), 127.9 (CH), 127.7 (CH), 126.4 (CH), 124.9 (C_q, $^2J_{C\text{-}F}$ = 9.8 Hz), 121.6 (CH, $^3J_{C\text{-}F}$ = 7.0 Hz), 119.4 (CH), 118.7 (C_q, $^4J_{C\text{-}F}$ = 2.3 Hz), 115.6 (CH, $^4J_{C\text{-}F}$ = 3.3 Hz), 109.3 (CH, $^2J_{C\text{-}F}$ = 18.1 Hz).

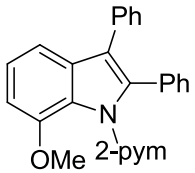
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -127.9 (dd, J = 12.2, 4.7 Hz).

IR (neat): 3033, 1559, 1432, 1224, 979, 727 cm^{-1}.

MS (EI) m/z (relative intensity) 365 (100) [M^+], 288 (20), 181 (4), 79 (5), 43 (18).

HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1318.

7-Methoxy-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ia)



The general procedure **C** was followed using **49bi** (101 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **50ia** (125 mg, 66%) was obtained as a white solid (m.p. 190–191 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.68 (d, J = 4.9 Hz, 2H), 7.39–7.25 (m, 5H), 7.23–7.06 (m, 8H), 6.71 (d, J = 7.9 Hz, 1H), 3.62 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 157.6 (CH), 146.9 (C_q), 137.6 (C_q), 134.7 (C_q),

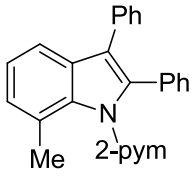
131.5 (C_q), 131.0 (CH), 130.2 (CH), 130.0 (C_q), 128.2 (CH), 127.8 (CH), 127.6 (C_q), 127.4 (CH), 126.0 (CH), 121.7 (CH), 119.3 (CH), 117.9 (C_q), 112.8 (CH), 105.0 (CH), 55.9 (CH_3).

IR (neat): 3046, 1561, 1433, 1242, 924, 702 cm^{-1}.

MS (EI) m/z (relative intensity) 377 (100) [M^+], 334 (32), 256 (25), 79 (6), 53 (6).

HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3O]^+$ 377.1528, found 377.1523.

7-Methyl-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ja)



The general procedure **C** was followed using **49bj** (93 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ja** (117 mg, 65%) was obtained as a white solid (m.p. 151–152 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.70 (d, J = 4.9 Hz, 2H), 7.63 (dt, J = 7.9, 0.6 Hz, 1H), 7.40–7.09 (m, 12H), 7.03 (d, J = 7.2 Hz, 1H), 1.96 (s, 3H).

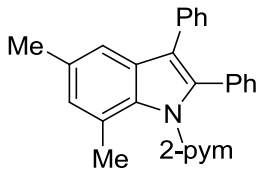
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 157.9 (CH), 137.8 (C_q), 136.6 (C_q), 134.6 (C_q), 131.7 (C_q), 131.0 (CH), 130.3 (CH), 128.7 (C_q), 128.1 (CH), 127.7 (CH), 127.4 (CH), 126.1 (CH), 125.9 (CH), 121.5 (C_q), 121.4 (CH), 119.7 (CH), 118.0 (C_q), 117.9 (CH), 19.4 (CH_3).

IR (neat): 3024, 1560, 1442, 1231, 920, 786 cm^{-1}.

MS (EI) m/z (relative intensity) 361 (100) [M^+], 284 (20), 178 (3), 77 (2), 53 (4).

HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3]^+$ 361.1579, found 361.1566.

5, 7-Dimethyl-2, 3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ka)



The general procedure **C** was followed using **49bk** (100 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1–5:1) **50ka** (93 mg, 49%) was obtained as a white solid (m.p. 182–183 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.68 (d, J = 4.9 Hz, 2H), 7.40–7.06 (m, 12H), 6.86 (s, 1H),

2.40 (s, 3H), 1.92 (s, 3H).

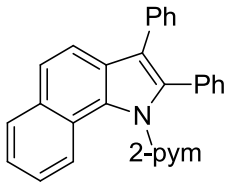
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8 (C_q), 158.0 (CH), 138.0 (C_q), 135.1 (C_q), 134.8 (C_q), 131.8 (C_q), 131.0 (CH), 130.8 (C_q), 130.3 (CH), 129.1 (C_q), 128.1 (CH), 127.7 (CH), 127.6 (CH), 127.3 (CH), 126.0 (CH), 121.2 (C_q), 119.5 (CH), 117.9 (C_q), 117.4 (CH), 21.3 (CH_3), 19.3 (CH_3).

IR (neat): 3050, 1557, 1462, 1230, 919, 728 cm^{-1}.

MS (EI) m/z (relative intensity) 375 (100) [M^+], 298 (23), 179 (3), 79 (2), 43 (5).

HR-MS (EI) m/z calcd for $[C_{26}H_{21}N_3]^+$ 375.1735, found 375.1748.

2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-benzo[g]indole (50la)



The general procedure **C** was followed using **49bl** (110 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50la** (178 mg, 90%) was obtained as a white solid (m.p. 180–181 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.76 (d, J = 4.9 Hz, 2H), 7.99 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.56–7.47 (m, 2H), 7.46–7.35 (m, 3H), 7.35–7.15 (m, 8H), 6.92 (d, J = 8.7 Hz, 1H).

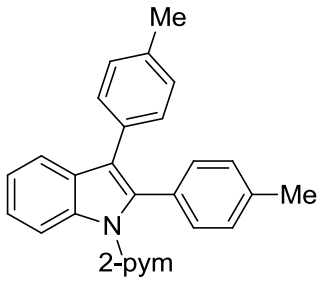
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C_q), 158.8 (CH), 137.0 (C_q), 134.3 (C_q), 131.9 (C_q), 131.4 (C_q), 131.3 (C_q), 131.1 (CH), 130.3 (CH), 129.1 (CH), 128.2 (CH), 127.7 (CH), 127.3 (CH), 126.1 (CH), 125.1 (CH), 124.8 (C_q), 123.6 (CH), 122.8 (CH), 122.0 (C_q), 120.6 (CH), 120.3 (CH), 119.3 (CH), 118.9 (C_q).

IR (neat): 3047, 2948, 1560, 1267, 911, 736 cm^{-1}.

MS (EI) m/z (relative intensity) 397 (100) [M^+], 317 (10), 213 (4), 98 (6), 43 (8).

HR-MS (EI) m/z calcd for $[C_{28}H_{19}N_3]^+$ 397.1579, found 397.1574.

1-(Pyrimidin-2-yl)-2,3-di-*p*-tolyl-1*H*-indole (50ab)



The general procedure **C** was followed using **49ba** (86 mg, 0.50 mmol) and **4b** (515 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ab** (129 mg, 69%) was obtained as a white solid (m.p. 161–162 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.20–8.12 (m, 1H), 7.80–7.67 (m, 1H), 7.41–7.25 (m, 4H), 7.23–6.99 (m, 7H), 2.41 (s, 3H), 2.33 (s, 3H).

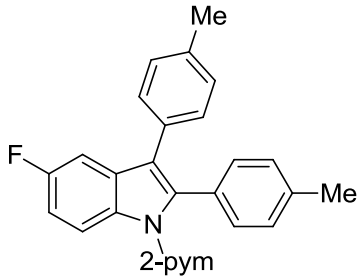
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (C_q), 157.9 (CH), 136.9 (C_q), 136.5 (C_q), 135.9 (C_q), 135.8 (C_q), 131.2 (C_q), 130.1 (CH), 130.0 (CH), 129.8 (C_q), 129.3 (C_q), 128.9 (CH), 128.5 (CH), 123.6 (CH), 122.0 (CH), 119.7 (C_q), 119.6 (CH), 117.4 (CH), 112.4 (CH), 21.2 (CH_3), 21.2 (CH_3).

IR (neat): 3017, 2196, 1519, 1318, 980, 760 cm^{-1}.

MS (EI) m/z (relative intensity) 375 (100) [M^+], 286 (10), 172 (3), 79 (2), 43 (3).

HR-MS (EI) m/z calcd for $[C_{26}H_{21}N_3]^+$ 375.1735, found 375.1731.

5-Fluoro-1-(pyrimidin-2-yl)-2,3-di-*p*-tolyl-1*H*-indole (50db)



The general procedure **C** was followed using **49bd** (90 mg, 0.50 mmol) and **4b** (515 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50db** (132 mg, 67%) was obtained as a white solid (m.p. 141–142 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.04 (q, J = 4.5 Hz, 1H), 7.30 (dd, J = 9.4, 2.6 Hz, 1H), 7.22–6.95 (m, 10H), 2.36 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2 (C_q, $^{1}J_{C\text{-}F}$ = 236.3 Hz), 158.1 (CH), 157.9 (C_q), 137.5 (C_q), 136.9 (C_q), 136.1 (C_q), 133.3 (C_q), 130.8 (C_q), 131.1 (C_q, $^{3}J_{C\text{-}F}$ = 9.9 Hz), 130.0 (CH),

129.9 (CH), 129.6 (C_q), 129.1 (CH), 128.6 (CH), 119.7 (C_q, $^4J_{C\text{-}F}$ = 4.8 Hz), 117.6 (CH), 113.5 (CH, $^3J_{C\text{-}F}$ = 9.9 Hz), 111.4 (CH, $^2J_{C\text{-}F}$ = 25.8 Hz), 104.8 (CH, $^2J_{C\text{-}F}$ = 24.9 Hz), 21.3 (CH_3), 21.2 (CH_3).

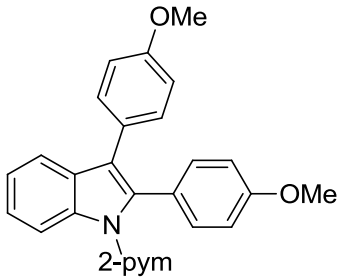
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.8–122.2) (m).

IR (neat): 2921, 1614, 1520, 1419, 1153, 976 cm^{-1}.

MS (EI) m/z (relative intensity) 393 (100) [M^+], 302 (8), 181 (3), 79 (3), 43 (7).

HR-MS (EI) m/z calcd for $[C_{26}H_{20}FN_3]^+$ 393.1641, found 393.1643.

2,3-Bis(4-methoxyphenyl)-1-(pyrimidin-2-yl)-1*H*-indole (50ac)



The general procedure **C** was followed using **49ba** (86 mg, 0.50 mmol) and **4c** (595 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **50ac** (136 mg, 67%) was obtained as a white solid (m.p. 166–167 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.14–8.04 (m, 1H), 7.71–7.60 (m, 1H), 7.36–7.18 (m, 4H), 7.12–7.00 (m, 3H), 6.94–6.83 (m, 2H), 6.80–6.66 (m, 2H), 3.81 (s, 3H), 3.76 (s, 3H).

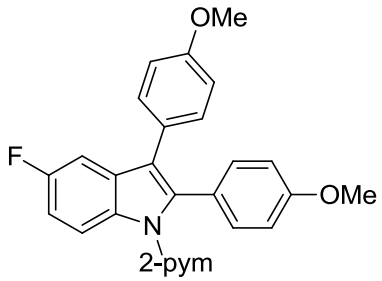
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5 (C_q), 158.1 (C_q), 158.1 (C_q), 158.0 (CH), 136.8 (C_q), 135.6 (C_q), 131.4 (CH), 131.3 (CH), 129.4 (C_q), 126.6 (C_q), 125.2 (C_q), 123.5 (CH), 122.0 (CH), 119.5 (CH), 119.3 (C_q), 117.4 (CH), 113.7 (CH), 113.3 (CH), 112.4 (CH), 55.1 (CH_3), 55.0 (CH_3).

IR (neat): 2930, 1558, 1416, 1241, 1029, 727 cm^{-1}.

MS (EI) m/z (relative intensity) 407 (100) [M^+], 392 (20), 241 (9), 79 (2), 43 (5).

HR-MS (EI) m/z calcd for $[C_{26}H_{21}N_3O_2]^+$ 407.1634, found 407.1631.

5-Fluoro-2,3-bis(4-methoxyphenyl)-1-(pyrimidin-2-yl)-1*H*-indole (50dc)



The general procedure **C** was followed using **49bd** (90 mg, 0.50 mmol) and **4c** (595 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **50dc** (127 mg, 60%) was obtained as a white solid (m.p. 159–160 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.02 (ddd, J = 9.0, 4.6, 0.4 Hz, 1H), 7.27 (ddd, J = 9.4, 2.6, 0.4 Hz, 1H), 7.24–7.17 (m, 2H), 7.08 (t, J = 4.9 Hz, 1H), 7.05–6.96 (m, 3H), 6.91–6.83 (m, 2H), 6.75–6.68 (m, 2H), 3.81 (s, 3H), 3.76 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q, $^{1}J_{C\text{-}F}$ = 237.2 Hz), 158.7 (C_q), 158.3 (C_q), 158.1 (CH), 158.0 (C_q), 137.2 (C_q), 133.2 (C_q), 131.4 (CH), 131.2 (CH), 130.2 (C_q, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 126.2 (C_q), 125.0 (C_q), 119.2 (C_q, $^{4}J_{C\text{-}F}$ = 4.8 Hz), 117.6 (CH), 113.9 (CH), 113.5 (CH, $^{3}J_{C\text{-}F}$ = 8.9 Hz), 113.4 (CH), 111.4 (CH, $^{2}J_{C\text{-}F}$ = 25.1 Hz), 104.7 (CH, $^{2}J_{C\text{-}F}$ = 25.1 Hz), 55.2 (CH_3), 55.1 (CH_3).

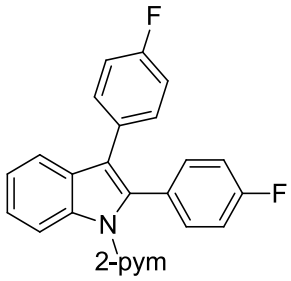
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.7–122.2) (m).

IR (neat): 2931, 1609, 1560, 1134, 975, 759 cm^{-1}.

MS (EI) m/z (relative intensity) 425 (100) [M^+], 350 (8), 259 (9), 79 (2), 43 (5).

HR-MS (EI) m/z calcd for $[C_{26}H_{20}FN_3O_2]^+$ 425.1540, found 425.1544.

2,3-Bis(4-fluorophenyl)-1-(pyrimidin-2-yl)-1*H*-indole (50ad)



The general procedure **C** was followed using **49ba** (86 mg, 0.50 mmol) and **4d** (536 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ad** (109 mg, 57%) was obtained as a white solid (m.p. 199–200 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.16 (dt, J = 8.1, 0.9 Hz, 1H), 7.62

(ddd, J = 7.9, 1.3, 0.7 Hz, 1H), 7.38–7.31 (m, 1H), 7.30–7.23 (m, 3H), 7.15–6.98 (m, 5H), 6.94-6.84 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (C_q, $^1J_{C\text{-}F}$ = 247.7 Hz), 161.6 (C_q, $^1J_{C\text{-}F}$ = 245.8 Hz), 158.1 (CH), 157.8 (C_q), 136.8 (C_q), 135.1 (C_q), 131.9 (CH, $^3J_{C\text{-}F}$ = 8.2 Hz), 131.8 (CH, $^3J_{C\text{-}F}$ = 8.2 Hz), 129.9 (C_q, $^4J_{C\text{-}F}$ = 3.6 Hz), 129.0 (C_q), 128.8 (C_q, $^4J_{C\text{-}F}$ = 4.2 Hz), 124.1 (CH), 122.4 (CH), 129.5 (C_q), 119.4 (CH), 117.6 (CH), 115.3 (CH, $^2J_{C\text{-}F}$ = 21.2 Hz), 115.0 (CH, $^2J_{C\text{-}F}$ = 21.2 Hz), 112.8 (CH).

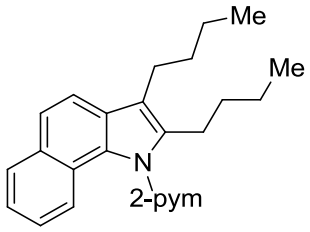
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(113.8–114.8) (m), -(115.3–116.3) (m).

IR (neat): 3052, 1561, 1419, 1221, 946, 746 cm^{-1}.

MS (EI) m/z (relative intensity) 383 (100) [M$^+$], 303 (14), 181 (8), 79 (3), 43 (5).

HR-MS (EI) m/z calcd for $[C_{24}H_{15}F_2N_3]^+$ 383.1234, found 383.1231.

2,3-Di-*n*-butyl-1-(pyrimidin-2-yl)-1*H*-benzo[g]indole (50le)



The general procedure **C** was followed using **49bl** (110 mg, 0.50 mmol) and **4e** (345 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1→10:1) **50le** (112 mg, 63%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.90 (d, J = 4.9 Hz, 2H), 7.89 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 7.37–7.22 (m, 2H), 7.20–7.10 (m, 1H), 6.78 (d, J = 8.5 Hz, 1H), 2.91–2.72 (m, 4H), 1.80–1.61 (m, 2H), 1.58–1.40 (m, 2H), 1.40–1.17 (m, 4H), 0.99 (t, J = 7.3 Hz, 3H), 0.81 (t, J = 7.3 Hz, 3H).

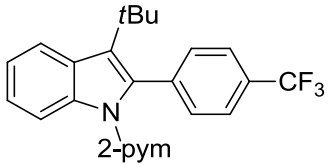
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (C_q), 159.1 (CH), 137.4 (C_q), 131.3 (C_q), 130.5 (C_q), 129.1 (CH), 126.4 (C_q), 124.5 (CH), 122.8 (CH), 122.0 (C_q), 121.9 (CH), 120.9 (CH), 119.8 (CH), 118.6 (CH), 116.2 (C_q), 33.3 (CH_2), 32.4 (CH_2), 24.6 (CH_2), 24.1 (CH_2), 22.8 (CH_2), 22.4 (CH_2), 14.1 (CH_3), 13.7 (CH_3).

IR (neat): 2954, 1558, 1417, 1274, 926, 740 cm^{-1}.

MS (EI) m/z (relative intensity) 357 (65) [M$^+$], 314 (100), 272 (78), 165 (6), 43 (7).

HR-MS (EI) m/z calcd for $[C_{24}H_{27}N_3]^+$ 357.2205, found 357.2200.

3-(*tert*-Butyl)-2-{4-(trifluoromethyl)phenyl}-1-(pyrimidin-2-yl)-1*H*-indole (50af)



The general procedure **C** was followed using **49ba** (86 mg, 0.50 mmol) and **4f** (565 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50af** (108 mg, 55%) was obtained as a white solid (m.p. 178–179 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.47 (dd, J = 4.9, 0.9 Hz, 2H), 8.02–7.87 (m, 2H), 7.78 (s, 4H), 7.37–7.16 (m, 2H), 6.95 (td, J = 4.9, 0.9 Hz, 1H), 1.34 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.8 (CH), 157.3 (C_q), 139.7 (C_q), 136.9 (C_q), 132.8 (CH), 132.8 (C_q), 129.6 (C_q, $^2J_{C\text{-}F}$ = 32.6 Hz), 128.1 (C_q), 126.6 (C_q), 126.0 (C_q, $^1J_{C\text{-}F}$ = 271.3 Hz), 123.4 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.2 (CH), 122.5 (CH), 121.0 (CH), 117.5 (CH), 112.4 (CH), 33.5 (C_q), 32.3 (CH_3).

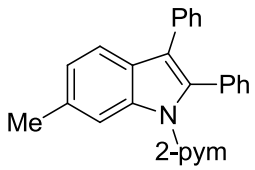
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -62.8 (s).

IR (neat): 2955, 1619, 1421, 1106, 955 cm^{-1}.

MS (EI) m/z (relative intensity) 395 (43) [M^+], 380 (100), 286 (14), 183 (20), 79 (3).

HR-MS (EI) m/z calcd for $[C_{23}H_{20}F_3N_3]^+$ 395.1609, found 395.1619.

6-Methyl-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50ma)



The general procedure **C** was followed using **49bm** (93 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50ma** (110 mg, 61%) was obtained as a white solid (m.p. 154–155 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (d, J = 4.9 Hz, 2H), 7.99 (s, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.39–7.11 (m, 11H), 7.06 (t, J = 4.9 Hz, 1H), 2.55 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (C_q), 158.0 (CH), 137.3 (C_q), 135.4 (C_q), 134.3 (C_q),

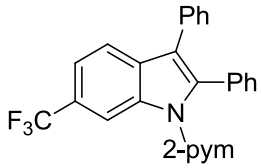
133.8 (C_q), 132.9 (C_q), 130.3 (CH), 130.2 (CH), 128.1 (CH), 127.7 (CH), 127.0 (C_q), 126.8 (CH), 126.3 (CH), 123.7 (CH), 120.1 (C_q), 119.3 (CH), 117.4 (CH), 112.4 (CH), 21.9 (CH_3).

IR (neat): 3025, 2916, 1556, 1418, 1196, 920 cm^{-1}.

MS (EI) m/z (relative intensity) 361 (100) [M^+], 284 (9), 172 (6), 79 (5), 53 (5).

HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3]^+$ 361.1579, found 361.1576.

2,3-Diphenyl-1-(pyrimidin-2-yl)-6-(trifluoromethyl)-1*H*-indole (50na)



The general procedure **C** was followed using **49bn** (120 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50na** (175 mg, 84%) was obtained as a white solid (m.p. 175–176 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66 (dd, J = 4.9, 0.6 Hz, 2H), 8.44 (s, 1H), 7.76 (dd, J = 8.3, 0.6 Hz, 1H), 7.50 (ddd, J = 8.3, 1.0, 0.6 Hz, 1H), 7.39–7.03 (m, 11H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (CH), 157.5 (C_q), 138.7 (C_q), 135.9 (C_q), 133.4 (C_q), 132.1 (C_q), 131.5 (C_q), 130.2 (CH), 130.2 (CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 126.9 (C_q, $^1J_{C\text{-}F}$ = 272.0 Hz), 126.8 (CH), 125.6 (C_q, $^2J_{C\text{-}F}$ = 32.1 Hz), 120.1 (CH), 120.0 (C_q), 118.8 (CH, $^3J_{C\text{-}F}$ = 3.6 Hz), 118.1 (CH), 110.4 (CH, $^3J_{C\text{-}F}$ = 4.3 Hz).

^{19}F-NMR (283 MHz, $CDCl_3$): δ = -60.6 (s).

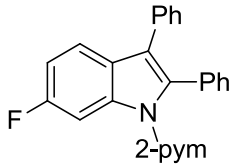
IR (neat): 3064, 2920, 1564, 1420, 1157, 917 cm^{-1}.

MS (EI) m/z (relative intensity) 415 (100) [M^+], 338 (11), 239 (4), 79 (7), 53 (8).

HR-MS (EI) m/z calcd for $[C_{25}H_{16}F_3N_3]^+$ 415.1296, found 415.1284.

6-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50oa) and 4-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50oa')

The general procedure **C** was followed using **49bo** (95 mg, 0.50 mmol) and **4a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **50oa** (78 mg, 43%) was obtained as a white solid (m.p. 160–161 ℃) and **50oa'** (52 mg, 29%) was obtained as a white solid (m.p. 124–125 ℃).



6-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50oa):

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, J = 4.9 Hz, 2H), 7.91 (dd, J = 10.4, 2.3 Hz, 1H), 7.59 (dd, J = 8.7, 5.7 Hz, 1H), 7.38–7.10 (m, 10H), 7.07 (t, J = 4.9 Hz, 1H), 7.01 (td, J = 9.0, 2.3 Hz, 1H).

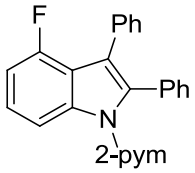
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.7 (C_q, $^{1}J_{C\text{-}F}$ = 237.2 Hz), 158.1 (CH), 157.8 (C_q), 137.0 (C_q, $^{3}J_{C\text{-}F}$ = 12.5 Hz), 136.3 (C_q, $^{4}J_{C\text{-}F}$ = 4.2 Hz), 133.8 (C_q), 132.6 (C_q), 130.2 (CH), 130.1 (CH), 128.3 (CH), 127.8 (CH), 127.1 (CH), 126.6 (CH), 125.7 (C_q), 120.4 (CH, $^{3}J_{C\text{-}F}$ = 10.4 Hz), 120.1 (C_q), 117.7 (CH), 110.5 (CH, $^{2}J_{C\text{-}F}$ = 24.4 Hz), 99.8 (CH, $^{2}J_{C\text{-}F}$ = 28.2 Hz).

^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(118.1–118.4) (m).

IR (neat): 3056, 1979, 1562, 1416, 1122, 974 cm^{-1}.

MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (14), 172 (3), 79 (2), 53 (3).

HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1327.



4-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (50oa'):

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 7.86 (dd, J = 8.3, 0.7 Hz, 1H), 7.37–7.05 (m, 12H), 6.90 (ddd, J = 11.0, 7.9, 0.7 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2 (CH), 157.8 (C_q), 156.7 (C_q, $^{1}J_{C\text{-}F}$ = 246.7 Hz), 139.0 (C_q, $^{3}J_{C\text{-}F}$ = 9.6 Hz), 136.6 (C_q, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 134.1 (C_q, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 132.1 (C_q), 131.0 (CH, $J_{C\text{-}F}$ = 2.1 Hz), 130.3 (CH), 127.7 (CH), 127.5 (CH), 127.2 (CH), 126.5 (CH), 124.0 (CH, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 118.1 (CH), 117.9 (C_q, $^{3}J_{C\text{-}F}$ = 3.1 Hz), 117.5 (C_q, $^{2}J_{C\text{-}F}$ = 17.8 Hz), 108.4 (CH, $^{4}J_{C\text{-}F}$ = 3.9 Hz), 107.7 (CH, $^{2}J_{C\text{-}F}$ = 19.5 Hz).

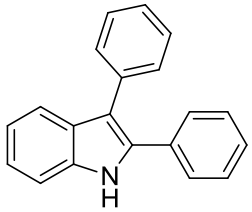
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(118.5–119.5) (m).

IR (neat): 3036, 1562, 1433, 1264, 973, 761 cm^{-1}.

MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (15), 182 (2), 79 (3), 53 (4).

HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1314.

2,3-Diphenyl-1*H*-indole (75)



A mixture of **50aa** (174 mg, 0.50 mmol), NaOEt (102 mg, 1.50 mmol) and DMSO (2.0 mL) was stirred at 120 °C under a nitrogen atmosphere for 24 h. After cooling to ambient temperature, the reaction mixture was diluted with EtOAc (75 mL) and washed with brine (30 mL). The aqueous phase was extracted with EtOAc (2×30 mL), and the combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents in vacuum, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) to yield **75** (124 mg, 92%) as a white solid (m.p. 120–121 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (s_{br}, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.50–7.22 (m, 12H), 7.21–7.12 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9 (C_q), 135.0 (C_q), 134.1 (C_q), 132.7 (C_q), 130.1 (CH), 128.8 (C_q), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.7 (CH), 126.2 (CH), 122.7 (CH), 120.4 (CH), 119.7 (CH), 115.1 (C_q), 110.9 (CH).

IR (neat): 3055, 1504, 1250, 1147, 956, 737 cm^{-1}.

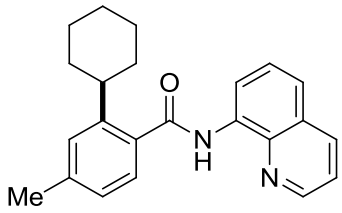
MS (EI) m/z (relative intensity) 269 (100) [M^+], 165 (18), 105 (19), 77 (14), 51 (4).

HR-MS (EI) m/z calcd for $[C_{20}H_{15}N]^+$ 269.1204, found 269.1199.

The spectral data were in accordance with those reported in the literature.[85]

2-Cyclohexyl-4-methyl-*N*-(quinolin-8-yl)benzamide (51aa)

[85] A. Arcadi, S. Cacchi, G. Fabrizi, A. Goggiamani, A. Iazzetti, F. Marinelli, *Org. Biomol. Chem.* **2013**, *11*, 545–548.



The general procedure **D** was followed using **17a** (131 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51aa** (148 mg, 86%) was obtained as a white solid (m.p. 177–178 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.12 (s, 1H), 8.94 (dd, J = 7.3, 1.1 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.15 (dd, J = 8.3, 1.7 Hz, 1H), 7.63–7.47 (m, 3H), 7.42 (dd, J = 8.3, 4.3 Hz, 1H), 7.23 (s, 1H), 7.09 (dd, J = 7.8, 1.1 Hz, 1H), 3.14 (tt, J = 11.7, 3.3 Hz, 1H), 2.40 (s, 3H), 1.99 (d, J = 12.8 Hz, 2H), 1.83–1.70 (m, 2H), 1.67–1.15 (m, 6H).

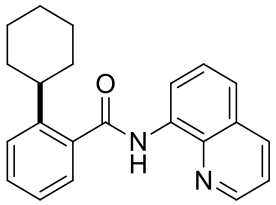
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8 (C_q), 148.1 (CH), 146.1 (C_q), 140.2 (C_q), 138.5 (C_q), 136.3 (CH), 134.9 (C_q), 133.7 (C_q), 128.0 (C_q), 127.7 (CH), 127.4 (CH), 127.3 (CH), 126.5 (CH), 121.6 (CH), 121.6 (CH), 116.4 (CH), 40.3 (CH), 34.7 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 21.6 (CH_3).

IR (ATR): 3339, 2935, 2849, 1665, 1609, 1264, 828, 691 cm^{-1}.

MS (EI) m/z (relative intensity) 344 (43) [M^+], 200 (100), 144 (79), 105 (35), 43 (20).

HR-MS (EI) m/z calcd for $[C_{23}H_{24}N_2O]^+$ 344.1889, found 344.1888.

2-Cyclohexyl-*N*-(quinolin-8-yl)benzamide (51ba)



The general procedure **D** was followed using **17b** (124 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ba** (132 mg, 80%) was obtained as a white solid (m.p. 140–141 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.14 (s, 1H), 8.98 (dd, J = 7.3, 1.4 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.14 (dd, J = 8.3, 1.7 Hz, 1H), 7.63–7.56 (m, 2H), 7.53 (dd, J = 8.3, 1.6 Hz, 1H), 7.46–7.38 (m, 3H), 7.32–7.25 (m, 1H), 3.15 (tt, J = 11.7, 3.3 Hz, 1H), 2.02 (d, J = 12.8 Hz, 2H), 1.85–1.63 (m, 3H), 1.57–1.20 (m, 5H).

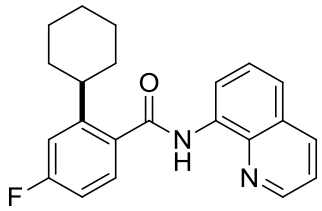
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.6 (C_q), 148.1 (CH), 145.9 (C_q), 138.5 (C_q), 136.5 (C_q), 136.2 (CH), 134.7 (C_q), 130.2 (CH), 127.9 (C_q), 127.3 (CH), 127.2 (CH), 127.0 (CH), 125.8 (CH), 121.7 (CH), 121.6 (CH), 116.5 (CH), 40.3 (CH), 34.6 (CH_2), 26.7 (CH_2), 26.0 (CH_2).

IR (ATR): 3335, 2924, 2852, 1667, 1424, 1263, 996, 797 cm^{-1}.

MS (EI) m/z (relative intensity) 330 (48) [M^+], 186 (70), 144 (100), 91 (42), 41 (17).

HR-MS (EI) m/z calcd for $[C_{22}H_{22}N_2O]^+$ 330.1732, found 330.1744.

2-Cyclohexyl-4-fluoro-*N*-(quinolin-8-yl)benzamide (51ca)



The general procedure **D** was followed using **17c** (133 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ca** (145 mg, 83%) was obtained as a white solid (m.p. 123–124 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 8.93 (dd, J = 7.3, 1.4 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.13 (dd, J = 8.3, 1.7 Hz, 1H), 7.60 (dd, J = 6.0, 2.6 Hz, 1H), 7.56 (t, J = 3.6 Hz, 1H), 7.52 (dd, J = 8.3, 1.6 Hz, 1H), 7.41 (dd, J = 8.3, 4.3 Hz, 1H), 7.10 (dd, J = 10.7, 2.6 Hz, 1H), 6.95 (td, J = 8.3, 2.6 Hz, 1H), 3.18 (tt, J = 11.7, 3.3 Hz, 1H), 2.01 (d, J = 12.2 Hz, 2H), 1.83–1.61 (m, 3H), 1.51–1.18 (m, 5H).

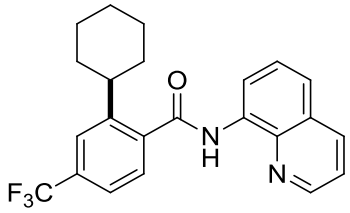
^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5 (C_q), 163.7 (C_q, $^1J_{C\text{-}F}$ = 248.8 Hz), 149.3 (C_q, $^1J_{C\text{-}F}$ = 7.4 Hz), 148.1 (CH), 138.3 (C_q), 136.2 (CH), 134.5 (C_q), 132.4 (C_q, $^4J_{C\text{-}F}$ = 3.0 Hz), 129.2 (CH, $^3J_{C\text{-}F}$ = 8.9 Hz), 127.8 (C_q), 127.2 (CH), 121.7 (CH), 121.5 (CH), 116.4 (CH), 113.9 (CH, $^2J_{C\text{-}F}$ = 21.7 Hz), 112.6 (CH, $^2J_{C\text{-}F}$ = 21.9 Hz), 40.4 (CH, $^4J_{C\text{-}F}$ = 1.2 Hz), 34.5 (CH_2), 26.6 (CH_2), 26.0 (CH_2).

IR (ATR): 3327, 2936, 2853, 1663, 1480, 1262, 954, 794 cm^{-1}.

MS (EI) m/z (relative intensity) 348 (41) [M^+], 204 (68), 144 (100), 130 (40), 109 (34).

HR-MS (EI) m/z calcd for $[C_{22}H_{21}FN_2O]^+$ 348.1638, found 348.1643.

2-Cyclohexyl-*N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide (51da)



The general procedure **D** was followed using **17d** (158 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51da** (146 mg, 73%) was obtained as a white solid (m.p. 136–137 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.14 (s, 1H), 8.94 (dd, J = 7.0, 2.1 Hz, 1H), 8.74 (dd, J = 4.3, 1.7 Hz, 1H), 8.16 (dd, J = 8.3, 1.7 Hz, 1H), 7.72–7.66 (m, 2H), 7.64–7.52 (m, 2H), 7.43 (dd, J = 8.3, 4.3 Hz, 1H), 3.16 (tt, J = 11.7, 3.3 Hz, 1H), 2.08–1.93 (m, 2H), 1.89–1.62 (m, 3H), 1.60–1.15 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1 (C_q), 148.2 (CH), 146.8 (C_q), 139.6 (C_q, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 138.3 (C_q), 136.2 (CH), 134.2 (C_q), 132.0 (C_q, $^{2}J_{C\text{-}F}$ = 32.2 Hz), 127.9 (C_q), 127.6 (CH), 127.2 (CH), 124.9 (C_q, $^{1}J_{C\text{-}F}$ = 271.2 Hz), 123.9 (CH, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 122.7 (CH, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 122.1 (CH), 121.7 (CH), 116.7 (CH), 40.6 (CH), 34.5 (CH_2), 26.6 (CH_2), 25.9 (CH_2).

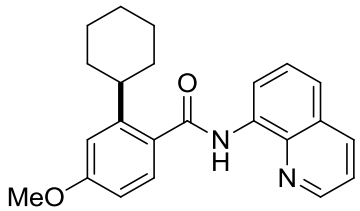
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.7 (s).

IR (ATR): 3338, 2926, 2854, 1672, 1427, 1228, 788 cm^{-1}.

MS (EI) m/z (relative intensity) 398 (23) [M^+], 236 (47), 144 (100), 129 (14), 43 (14).

HR-MS (EI) m/z calcd for $[C_{23}H_{21}F_3N_2O]^+$ 398.1606, found 398.1618.

2-Cyclohexyl-4-methoxy-*N*-(quinolin-8-yl)benzamide (51ea)



The general procedure **D** was followed using **17e** (139 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **51ea** (94 mg, 52%) was obtained as a white solid (m.p. 109–110 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.12 (s, 1H), 8.93 (dd, J = 7.3, 1.1 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.14 (dd, J = 8.3, 1.7 Hz, 1H), 7.63–7.54 (m, 2H), 7.51 (dd, J = 8.3, 1.5 Hz,

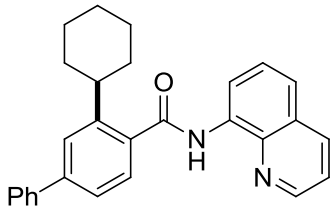
1H), 7.41 (dd, *J* = 8.3, 4.3 Hz, 1H), 6.95 (d, *J* = 2.6 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.6 Hz, 1H), 3.85 (s, 3H), 3.22 (tt, *J* = 11.7, 3.3 Hz, 1H), 2.01 (d, *J* = 12.8 Hz, 2H), 1.81–1.63 (m, 3H), 1.54–1.18 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3 (C_q), 161.1 (C_q), 148.7 (C_q), 148.1 (CH), 138.5 (C_q), 136.2 (CH), 134.9 (C_q), 129.1 (CH), 129.0 (C_q), 127.9 (C_q), 127.4 (CH), 121.6 (CH), 121.5 (CH), 116.3 (CH), 113.1 (CH), 110.4 (CH), 55.2 (CH_3), 40.3 (CH), 34.6 (CH_2), 26.7 (CH_2), 26.1 (CH_2).

IR (ATR): 3337, 2921, 2850, 1664, 1446, 1262, 984, 794 cm^{-1}.

MS (EI) m/z (relative intensity) 360 (25) [M^+], 217 (100), 199 (54), 144 (38), 43 (15). **HR-MS** (EI) m/z calcd for $[C_{23}H_{24}N_2O_2]^+$ 360.1838, found 360.1830.

3-Cyclohexyl-*N*-(quinolin-8-yl)-[1, 1'-biphenyl]-4-carboxamide (51fa)



The general procedure **D** was followed using **17f** (162 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51fa** (175 mg, 86%) was obtained as a white solid (m.p. 154–155 ℃).

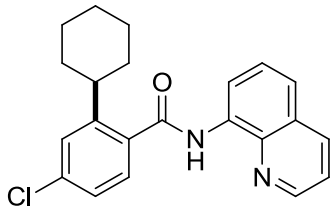
^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.18 (s, 1H), 8.97 (dd, *J* = 7.3, 1.4 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.66–7.58 (m, 4H), 7.55 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.53–7.42 (m, 4H), 7.38 (tt, *J* = 7.3, 1.3 Hz, 1H), 3.21 (tt, *J* = 11.7, 3.3 Hz, 1H), 2.06 (d, *J* = 12.4 Hz, 2H), 1.88–1.61 (m, 3H), 1.59–1.21 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5 (C_q), 148.2 (CH), 146.7 (C_q), 143.1 (C_q), 140.1 (C_q), 138.6 (C_q), 136.3 (CH), 135.4 (C_q), 134.8 (C_q), 128.8 (CH), 128.0 (C_q), 127.9 (CH), 127.7 (CH), 127.5 (CH), 127.3 (CH), 126.0 (CH), 124.7 (CH), 121.8 (CH), 121.7 (CH), 116.6 (CH), 40.6 (CH), 34.8 (CH_2), 26.8 (CH_2), 26.1 (CH_2).

IR (ATR): 3329, 2920, 2849, 1672, 1424, 1257, 912, 791 cm^{-1}.

MS (EI) m/z (relative intensity) 406 (35) [M^+], 262 (100), 221 (40), 144 (53), 43 (22). **HR-MS** (EI) m/z calcd for $[C_{28}H_{26}N_2O]^+$ 406.2045, found 406.2040.

4-Chloro-2-cyclohexyl-*N*-(quinolin-8-yl)benzamide (51ga)



The general procedure **D** was followed using **17g** (141 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ga** (116 mg, 64%) was obtained as a white solid (m.p. 156–157 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 8.92 (dd, J = 7.1, 1.7 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.14 (dd, J = 8.3, 1.7 Hz, 1H), 7.62–7.55 (m, 1H), 7.55–7.50 (m, 2H), 7.43 (t, J = 4.1 Hz, 1H), 7.40 (d, J = 1.7 Hz, 1H), 7.24 (dd, J = 8.3, 2.1 Hz, 1H), 3.13 (tt, J = 11.7, 3.3 Hz, 1H), 1.99 (d, J = 12.6 Hz, 2H), 1.84–1.60 (m, 3H), 1.53–1.17 (m, 5H).

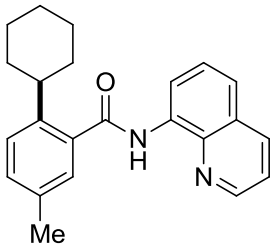
^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5 (C_q), 148.2 (CH), 148.1 (C_q), 138.4 (C_q), 136.3 (CH), 136.3 (C_q), 134.8 (C_q), 134.5 (C_q), 128.6 (CH), 127.9 (C_q), 127.4 (CH), 127.3 (CH), 126.0 (CH), 121.9 (CH), 121.6 (CH), 116.5 (CH), 40.4 (CH), 34.4 (CH_2), 26.5 (CH_2), 25.9 (CH_2).

IR (ATR): 3325, 2936, 2852, 1664, 1424, 1225, 986, 792 cm^{-1}.

MS (EI) m/z (relative intensity) 364 (28) [M^+], 220 (38), 144 (100), 115 (26), 41 (16).

HR-MS (EI) m/z calcd for $[C_{22}H_{21}ClN_2O]^+$ 364.1342, found 364.1348.

2-Cyclohexyl-5-methyl-*N*-(quinolin-8-yl)benzamide (51ha)



The general procedure **D** was followed using **17h** (131 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ha** (92 mg, 54%) was obtained as a sticky oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 8.96 (dd, J = 7.3, 1.4 Hz, 1H), 8.74 (dd, J = 4.3, 1.7 Hz, 1H), 8.15 (dd, J = 8.3, 1.7 Hz, 1H), 7.63–7.56 (m, 1H), 7.53 (dd, J = 8.3, 1.6 Hz, 1H), 7.45–7.37 (m, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.29–7.22 (m, 1H), 3.07 (tt, J = 11.8, 3.3 Hz, 1H), 2.37 (s, 3H), 1.99 (d, J = 12.8 Hz, 2H), 1.84–1.60 (m, 3H), 1.57–1.44 (m, 2H), 1.40–1.18

(m, 3H).

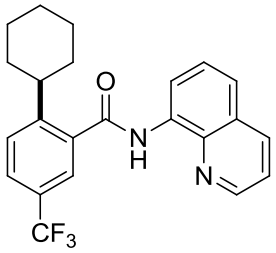
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8 (C_q), 148.1 (CH), 142.9 (C_q), 138.5 (C_q), 136.5 (C_q), 136.2 (CH), 135.4 (C_q), 134.8 (C_q), 130.9 (CH), 128.0 (C_q), 127.7 (CH), 127.4 (CH), 126.9 (CH), 121.7 (CH), 121.6 (CH), 116.5 (CH), 40.2 (CH), 34.7 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 20.8 (CH_3).

IR (ATR): 3335, 2923, 2851, 1663, 1424, 1262, 936, 794 cm^{-1}.

MS (EI) m/z (relative intensity) 344 (52) [M^+], 200 (100), 144 (98), 91 (38), 41 (20).

HR-MS (EI) m/z calcd for $[C_{23}H_{24}N_2O]^+$ 344.1889, found 344.1887.

2-Cyclohexyl- 5-(trifluoromethyl)-*N*-(quinolin-8-yl)-benzamide (51ia)



The general procedure **D** was followed using **17i** (158 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ia** (128 mg, 64%) was obtained as a white solid (m.p. 110–111 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.13 (s, 1H), 8.93 (dd, J = 7.0, 2.1 Hz, 1H), 8.75 (dd, J = 4.3, 1.7 Hz, 1H), 8.17 (dd, J = 8.3, 1.7 Hz, 1H), 7.84 (s, 1H), 7.69 (dd, J = 8.3, 1.7 Hz, 1H), 7.64–7.52 (m, 3H), 7.44 (dd, J = 8.3, 4.3 Hz, 1H), 3.14 (tt, J = 11.7, 3.3 Hz, 1H), 2.01 (d, J = 12.3 Hz, 2H), 1.87–1.62 (m, 3H), 1.59–1.14 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1 (C_q), 149.8 (C_q, $^4J_{C\text{-}F}$ = 1.1 Hz), 148.3 (CH), 138.5 (C_q), 137.1 (C_q), 136.3 (CH), 134.3 (C_q), 128.2 (C_q, $^2J_{C\text{-}F}$ = 32.2 Hz), 127.9 (C_q), 127.7 (CH), 127.3 (CH), 126.8 (CH, $^3J_{C\text{-}F}$ = 3.7 Hz), 125.7 (C_q, $^1J_{C\text{-}F}$ = 271.2 Hz), 124.2 (CH, $^3J_{C\text{-}F}$ = 3.7 Hz), 122.2 (CH), 121.7 (CH), 116.8 (CH), 40.7 (CH), 34.4 (CH_2), 26.5 (CH_2), 25.9 (CH_2).

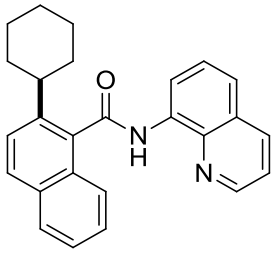
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.4 (s).

IR (ATR): 3347, 2927, 2853, 1669, 1422, 1250, 997, 780 cm^{-1}.

MS (EI) m/z (relative intensity) 398 (30) [M^+], 236 (43), 144 (100), 130 (25), 41 (13).

HR-MS (EI) m/z calcd for $[C_{23}H_{21}F_3N_2O]^+$ 398.1606, found 398.1609.

2-Cyclohexyl-*N*-(quinolin-8-yl)-1-naphthamide (51ja)



The general procedure **D** was followed using **17j** (149 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ja** (115 mg, 61%) was obtained as a white solid (m.p. 193–194 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 9.11 (dd, J = 7.4, 1.4 Hz, 1H), 8.64 (dd, J = 4.2, 1.7 Hz, 1H), 8.17 (dd, J = 8.3, 1.7 Hz, 1H), 8.02–7.93 (m, 1H), 7.90 (d, J = 8.7 Hz, 1H), 7.86–7.81 (m, 1H), 7.70–7.62 (m, 1H), 7.59 (dd, J = 8.3, 1.4 Hz, 1H), 7.54 (d, J = 8.7 Hz, 1H), 7.48–7.37 (m, 3H), 2.96 (tt, J = 11.7, 3.3 Hz, 1H), 2.00 (m, 2H), 1.84–1.50 (m, 5H), 1.43–1.08 (m, 3H).

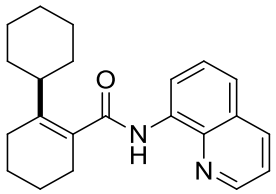
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5 (C_q), 148.3 (CH), 141.8 (C_q), 138.5 (C_q), 136.2 (CH), 134.5 (C_q), 133.2 (C_q), 131.9 (C_q), 130.2 (C_q), 129.4 (CH), 128.0 (C_q), 127.9 (CH), 127.4 (CH), 126.9 (CH), 125.6 (CH), 125.1 (CH), 124.5 (CH), 122.0 (CH), 121.6 (CH), 116.9 (CH), 42.1 (CH), 34.2 (CH_2, split by atropisomeric effect), 26.6 (CH_2), 26.0 (CH_2).

IR (ATR): 3336, 2922, 2848, 1670, 1446, 1214, 997, 796 cm^{-1}.

MS (EI) m/z (relative intensity) 380 (31) [M^+], 237 (100), 195 (40), 144 (42), 55 (4).

HR-MS (EI) m/z calcd for $[C_{26}H_{24}N_2O]^+$ 380.1889, found 380.1895.

***N*-(quinolin-8-yl)-[1, 1'-bi(cyclohexan)]-1-ene-2-carboxamide (51ka)**



The general procedure **D** was followed using **17k** (126 mg, 0.50 mmol) and **20aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ka** (97 mg, 58%) was obtained as a white solid (m.p. 146–147 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.80 (s, 1H), 8.84 (dd, J = 7.3, 1.4 Hz, 1H), 8.75 (dd, J = 4.3, 1.7 Hz, 1H), 8.13 (dd, J = 8.3, 1.7 Hz, 1H), 7.57–7.45 (m, 2H), 7.41 (dd, J = 8.3, 4.3 Hz,

1H), 2.59 (tt, J = 11.7, 3.3 Hz, 1H), 2.47–2.33 (m, 2H), 2.14–2.00 (m, 2H), 1.77–1.57 (m, 8H), 1.55–1.28 (m, 3H), 1.27–0.97 (m, 3H).

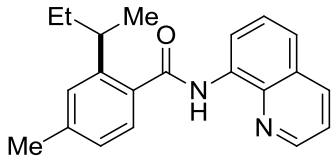
^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8 (C_q), 148.0 (CH), 143.0 (C_q), 138.5 (C_q), 136.2 (CH), 134.7 (C_q), 129.3 (C_q), 127.9 (C_q), 127.4 (CH), 121.5 (CH), 121.3 (CH), 116.4 (CH), 43.1 (CH), 31.2 (CH_2), 27.3 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 24.1 (CH_2), 22.4 (CH_2), 22.4 (CH_2).

IR (ATR): 3340, 2921, 2834, 1662, 1423, 1231, 997, 769 cm^{-1}.

MS (EI) m/z (relative intensity) 334 (28) [M^+], 190 (100), 144 (56), 91 (18), 41 (21).

HR-MS (EI) m/z calcd for $[C_{22}H_{26}N_2O]^+$ 334.2045, found 334.2061.

2-(*sec*-Butyl)-4-methyl-*N*-(quinolin-8-yl)benzamide (51ab)



The general procedure **D** was followed using **17a** (131 mg, 0.50 mmol) and **22ab** (137 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ab** (85 mg, 52%) was obtained as colorless oil.

The general procedure **D** was followed using **17a** (131 mg, 0.50 mmol) and **22bb** (92 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ab** (83 mg, 50%) was obtained as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 8.94 (dd, J = 7.3, 1.4 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.15 (dd, J = 8.3, 1.7 Hz, 1H), 7.61–7.51 (m, 2H), 7.49 (d, J = 7.9 Hz, 1H), 7.42 (dd, J = 8.3, 4.3 Hz, 1H), 7.19 (s, 1H), 7.10 (ddd, J = 7.9, 1.7, 0.7 Hz, 1H), 3.24 (dt, J = 7.0, 7.0 Hz, 1H), 2.40 (s, 3H), 1.77–1.55 (m, 2H), 1.29 (d, J = 6.7 Hz, 3H), 0.83 (t, J = 7.0 Hz, 3H).

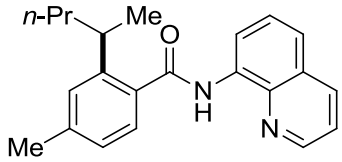
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 (C_q), 148.2 (CH), 146.0 (C_q), 140.2 (C_q), 138.5 (C_q), 136.3 (CH), 134.9 (C_q), 134.4 (C_q), 127.9 (C_q), 127.4 (CH), 127.2 (CH), 127.0 (CH), 126.5 (CH), 121.6 (CH), 121.5 (CH), 116.4 (CH), 36.8 (CH), 31.1 (CH_2), 22.3 (CH_3), 21.6 (CH_3), 12.3 (CH_3).

IR (ATR): 3350, 2960, 2871, 1671, 1422, 1260, 919, 789 cm^{-1}.

MS (EI) m/z (relative intensity) 318 (55) [M^+], 159 (100), 142 (46), 91 (27), 43 (8).

HR-MS (EI) m/z calcd for $[C_{21}H_{22}N_2O]^+$ 318.1732, found 318.1730.

4-Methyl-2-(pentan-2-yl)-*N*-(quinolin-8-yl)benzamide (51ac)



The general procedure **D** was followed using **17a** (131 mg, 0.50 mmol) and **22ac** (151 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **51ac** (125 mg, 75%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.12 (s, 1H), 8.96 (dd, J = 7.3, 1.1 Hz, 1H), 8.73 (dd, J = 4.3, 1.7 Hz, 1H), 8.13 (dd, J = 8.3, 1.7 Hz, 1H), 7.62–7.54 (m, 1H), 7.54–7.47 (m, 2H), 7.40 (dd, J = 8.3, 4.3 Hz, 1H), 7.22 (s, 1H), 7.09 (ddd, J = 7.8, 1.7, 0.7 Hz, 1H), 3.36 (dt, J = 6.9, 6.9 Hz, 1H), 2.41 (s, 3H), 1.77–1.47 (m, 2H), 1.31 (d, J = 6.9 Hz, 3H), 1.40–1.12 (m, 2H), 0.82 (t, J = 7.3 Hz, 3H).

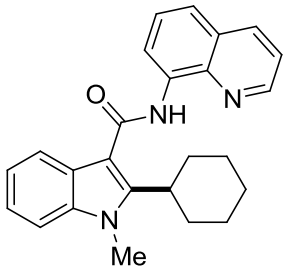
^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8 (C_q), 148.1 (CH), 146.2 (C_q), 140.2 (C_q), 138.5 (C_q), 136.2 (CH), 134.8 (C_q), 134.3 (C_q), 127.9 (C_q), 127.3 (CH), 127.2 (CH), 126.9 (CH), 126.5 (CH), 121.6 (CH), 121.5 (CH), 116.4 (CH), 40.6 (CH_2), 34.9 (CH), 22.7 (CH_3), 21.5 (CH_3), 20.9 (CH_2), 14.1 (CH_3).

IR (ATR): 3350, 2956, 2869, 1672, 1422, 1258, 789 cm^{-1}.

MS (EI) m/z (relative intensity) 332 (18) [M^+], 159 (100), 145 (29), 91 (15), 41 (6).

HR-MS (EI) m/z calcd for $[C_{22}H_{24}N_2O]^+$ 332.1889, found 332.1891.

2-Cyclohexyl-1-methyl-*N*-(quinolin-8-yl)-1H-indole-3-carboxamide (80aa)



The general procedure **D** was followed using **79** (150.5 mg, 0.50 mmol) and **22aa** (163 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **80aa** (167 mg, 87%) was obtained as a white solid (m.p. 159–160 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.48 (s, 1H), 9.02 (dd, J = 7.7, 1.2 Hz, 1H), 8.77 (dd, J =

4.2, 1.7 Hz, 1H), 8.18–8.10 (m, 2H) 7.65–7.55 (m, 1H), 7.49 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.38–7.32 (m, 1H), 7.32–7.22 (m, 2H), 3.87 (s, 3H), 3.74 (tt, *J* = 12.4, 3.1 Hz, 1H), 2.21–2.03 (m, 2H), 2.01–1.74 (m, 5H), 1.59–1.26 (m, 3H).

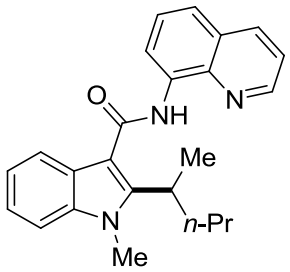
^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7 (C_q), 148.8 (C_q), 148.0 (CH), 138.7 (C_q), 136.6 (C_q), 136.2 (CH), 135.5 (C_q), 128.0 (C_q), 127.5 (CH), 125.7 (C_q), 121.8 (CH), 121.4 (CH), 121.1 (CH), 120.8 (CH), 119.4 (CH), 116.0 (CH), 109.3 (CH), 109.0 (C_q), 36.7 (CH), 31.3 (CH_3), 30.6 (CH_2), 26.9 (CH_2), 25.9 (CH_2).

IR (ATR): 3354, 2925, 2851, 1651, 1421, 1236, 988, 790 cm^{-1}.

MS (EI) m/z (relative intensity) 383 (10) [M^+], 240 (100), 171 (8), 144 (14), 43 (5).

HR-MS (EI) m/z calcd for $[C_{25}H_{25}N_3O]^+$ 383.1998, found 383.2001.

1-Methyl-2-(pentan-2-yl)-*N*-(quinolin-8-yl)-1*H*-indole-3-carboxamide (80ac)



The general procedure **D** was followed using **79** (150.5 mg, 0.50 mmol) and **22ac** (151 mg, 1.00 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **80ac** (135 mg, 73%) was obtained as a white solid (m.p. 159–160 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.53 (s, 1H), 9.00 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.22–8.17 (m, 1H) 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.39–7.33 (m, 1H), 7.32–7.26 (m, 2H), 4.16 (dt, *J* = 7.6, 7.6 Hz, 1H), 3.85 (s, 3H), 2.08–1.73 (m, 2H), 1.53 (d, *J* = 7.1 Hz, 3H), 1.48–1.22 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

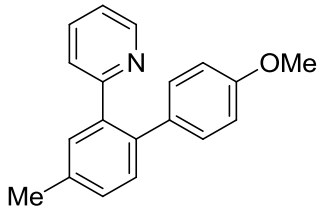
^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.6 (C_q), 149.5 (C_q), 148.1 (CH), 138.8 (C_q), 136.8 (C_q), 136.2 (CH), 135.6 (C_q), 128.0 (C_q), 127.5 (CH), 125.5 (C_q), 121.8 (CH), 121.4 (CH), 121.3 (CH), 120.7 (CH), 119.5 (CH), 116.1 (CH), 109.3 (CH), 109.2 (C_q), 37.5 (CH_2), 31.4 (CH_3), 30.8 (CH), 21.4 (CH_2), 19.2 (CH_3), 14.1 (CH_3).

IR (ATR): 3350, 2952, 2868, 1651, 1420, 1238, 937, 793 cm^{-1}.

MS (EI) m/z (relative intensity) 371 (11) [M^+], 228 (100), 198 (16), 144 (7), 41 (2).

HR-MS (EI) m/z calcd for $[C_{24}H_{25}N_3O]^+$ 371.1998, found 383.2003.

2-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)pyridine (52ad)



With aryl sulfamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ad** (116 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52ad** (112 mg, 82%) was obtained as a white solid (m.p. 89-90 ℃).

With aryl carbamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52ad** (123mg, 90%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.51-7.46 (m, 1H), 7.34 (td, J = 7.7, 1.8 Hz, 1H), 7.31-7.21 (m, 2H), 7.11-7.00 (m, 3H), 6.85 (td, J = 8.9, 1.0 Hz, 1H), 6.79-6.72 (m, 2H), 3.76 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6 (C_q), 158.4 (C_q), 149.4 (CH), 139.1 (C_q), 137.4 (C_q), 137.0 (C_q), 135.2 (CH), 133.7 (C_q), 131.0 (CH), 130.7 (CH), 130.4 (CH), 129.3 (CH), 125.5 (CH), 121.2 (CH), 113.5 (CH), 55.2 (CH_3), 21.0 (CH_3).

IR (ATR): 2962, 2836, 1583, 1486, 1293, 1108, 1033, 891, 748, 568 cm^{-1}.

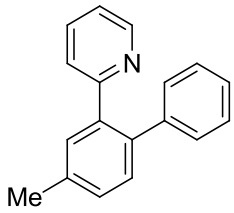
MS (EI) m/z (relative intensity) 275 (45) [M^+], 274 (100), 231 (35), 152 (3), 78 (3).

HR-MS (EI) m/z calcd for $[C_{19}H_{17}NO]^+$ 275.1310, found 275.1300.

The spectral data were in accordance with those reported in the literature.[86]

2-(4-Methyl-[1,1'-biphenyl]-2-yl)pyridine (52ab)

[86] L. Ackermann, R. Vicente, H. K. Potukuchi, V. Pirovano, *Org. Lett.* **2010**, *12*, 5032–5035.



With aryl sulfamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ab** (101 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ab** (85 mg, 70%) was obtained as a colorless oil.

With aryl carbamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30bb** (83 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ab** (87mg, 71%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.60-7.50 (m, 1H), 7.40-7.06 (m, 9H), 6.86 (dt, J = 7.9, 1.1 Hz, 1H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q), 149.4 (CH), 141.3 (C_q), 139.2 (C_q), 137.8 (C_q), 137.4 (C_q), 135.1 (CH), 131.1 (CH), 130.4 (CH), 129.7 (CH), 129.3 (CH), 128.0 (CH), 126.5 (CH), 125.5 (CH), 121.3 (CH), 21.1 (CH_3).

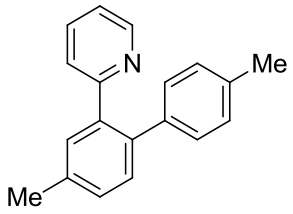
IR (ATR): 3023, 2918, 1585, 1442, 1283, 1149, 1094, 1008, 792, 573 cm^{-1}.

MS (EI) m/z (relative intensity) 245 (28) [M^+], 244 (100), 202 (6), 121 (5), 77 (4).

HR-MS (ESI) m/z calcd for $[C_{18}H_{15}N+H]^+$ 246.1277, found 246.1277.

The spectral data were in accordance with those reported in the literature.[87]

2-(4,4'-Dimethyl-[1,1'-biphenyl]-2-yl)pyridine (52ac)



With aryl sulfamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ac** (108 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ac** (103 mg, 80%) was obtained as a white solid (m.p. 75-76 ℃).

With aryl carbamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol)

[87] B. Li, Z. Wu, Y. Gu, C. Sun, B. Wang, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2011**, *50*, 1109–1113.

and **30bc** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ac** (104 mg, 81%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.52-7.48 (m, 1H), 7.36 (td, J = 7.7, 1.9 Hz, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.26-7.22 (m, 1H), 7.08 (ddd, J = 7.3, 4.8, 1.1 Hz, 1H), 7.01 (m, 4H), 6.86 (dt, J = 7.9, 1.0 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H).

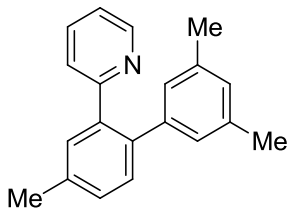
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5 (C_q), 149.4 (CH), 139.2 (C_q), 138.3 (C_q), 137.7 (C_q), 137.2 (C_q), 136.1 (C_q), 135.1 (CH), 131.1 (CH), 130.5 (CH), 129.6 (CH), 129.3 (CH), 128.8 (CH), 125.5 (CH), 121.2 (CH), 20.4 (2×CH_3).

IR (ATR): 3019, 2917, 1584, 1488, 1233, 1110, 1065, 1005, 785, 616 cm^{-1}.

MS (EI) m/z (relative intensity) 259 (30) [M^+], 258 (100), 202 (3), 121 (4), 78 (2).

HR-MS (ESI) m/z calcd for $[C_{19}H_{17}N+Na]^+$ 282.1253, found 282.1260.

2-(3',4,5'-Trimethyl-[1,1'-biphenyl]-2-yl)pyridine (52ag)



With aryl sulfamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ag** (115 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ag** (115 mg, 85%) was obtained as a colorless oil.

With aryl carbamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30bg** (97 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ag** (117 mg, 86%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.58-7.44 (m, 1H), 7.36 (td, J = 7.8, 1.8 Hz, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.26-7.21 (m, 1H), 7.07 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 6.87 (dt, J = 7.9, 1.1 Hz, 1H), 6.84-6.80 (m, 1H), 6.78-6.68 (m, 2H), 2.42 (s, 3H), 2.17 (s, 6H).

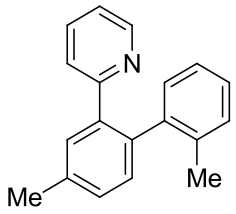
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 149.3 (CH), 141.2 (C_q), 139.3 (C_q), 138.1 (C_q), 137.4 (C_q), 137.1 (C_q), 134.9 (CH), 131.0 (CH), 130.4 (CH), 129.2 (CH), 128.1 (CH), 127.7 (CH), 125.4 (CH), 121.1 (CH), 21.2 (CH_3), 21.0 (CH_3).

IR (ATR): 3017, 2917, 1585, 1432, 1207, 1149, 1039, 851, 745, 583 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (40) [M^+], 272 (100), 258 (16), 121 (2), 69 (9).

HR-MS (ESI) m/z calcd for $[C_{20}H_{19}N+H]^+$ 274.1590, found 274.1590.

2-(2',4-Dimethyl-[1,1'-biphenyl]-2-yl)pyridine (52aa)



With aryl sulfamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30aa** (108 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52aa** (105 mg, 81%) was obtained as a white solid (m.p. 100-101 ℃).

With aryl carbamate: The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ba** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52aa** (100 mg, 77%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (ddd, J = 5.0, 1.9, 1.0 Hz, 1H), 7.63 (s, 1H), 7.33-7.24 (m, 2H), 7.23-7.11 (m, 4H), 7.11-7.01 (m, 2H), 6.77 (dt, J = 8.0, 1.1 Hz, 1H), 2.47 (s, 3H), 1.88 (s, 3H).

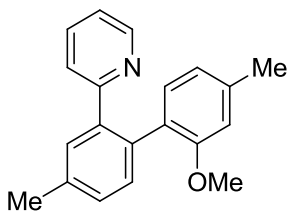
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8 (C_q), 149.4 (CH), 141.1 (C_q), 139.5 (C_q), 137.4 (C_q), 137.3 (C_q), 136.1 (C_q), 135.0 (CH), 130.1 (3×CH), 129.9 (CH), 129.0 (CH), 127.1 (CH), 125.5 (CH), 124.5 (CH), 121.2 (CH), 21.1 (CH_3), 20.0 (CH_3).

IR (ATR): 2917, 2835, 1583, 1480, 1433, 1260, 1152, 1065, 791, 617 cm^{-1}.

MS (EI) m/z (relative intensity) 259 (8) [M^+], 244 (100), 165 (6), 122 (3), 79 (4).

HR-MS (EI) m/z calcd for $[C_{19}H_{17}N]^+$ 259.1361, found 259.1353.

2-(2'-Methoxy-4,4'-dimethyl-[1,1'-biphenyl]-2-yl)pyridine (52ah)



The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30ah** (123 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ah** (120 mg, 83%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (dt, J = 4.9, 0.9 Hz, 1H), 7.55 (s, 1H), 7.32 (td, J = 7.7, 1.8 Hz, 1H), 7.26-7.24 (m, 2H), 7.10-6.98 (m, 2H), 6.88 (d, J = 7.9 Hz, 1H), 6.72 (dt, J = 7.6, 0.7 Hz, 1H), 6.51 (s, 1H), 3.31 (s, 3H), 2.42 (s, 3H), 2.32 (s, 3H).

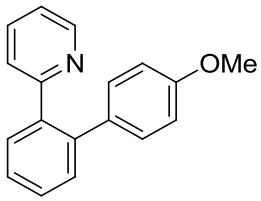
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8 (C_q), 156.0 (C_q), 149.1 (CH), 140.1 (C_q), 138.5 (C_q), 137.2 (C_q), 134.9 (CH), 134.1 (C_q), 131.2 (CH), 131.1 (CH), 130.3 (CH), 129.0 (CH), 127.5 (C_q), 123.6 (CH), 121.3 (CH), 120.9 (CH), 111.6 (CH), 54.8 (CH_3), 21.6 (CH_3)，21.1 (CH_3).

IR (ATR): 2919, 2835, 1584, 1489, 1433, 1277, 1163, 1004, 791, 618 cm^{-1}.

MS (EI) m/z (relative intensity) 289 (1) [M^+], 258 (100), 242 (7), 129 (4), 78 (2).

HR-MS (EI) m/z calcd for $[C_{20}H_{19}NO]^+$ 289.1467, found 289.1472.

2-(4'-Methoxy-[1,1'-biphenyl]-2-yl)pyridine (52bd)



The general procedure **E** was followed using **3b** (116 mg, 0.75 mmol) and **30ad** (116 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52bd** (82 mg, 63%) was obtained as a white solid (m.p. 72-73 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.71-7.61 (m, 1H), 7.46-7.34 (m, 4H), 7.12-7.01 (m, 3H), 6.88 (dt, J = 8.0, 1.0 Hz, 1H), 6.80-6.71 (m, 2H), 3.77 (s, 3H).

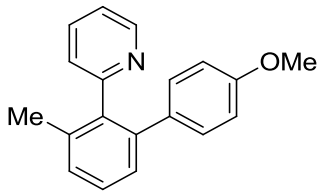
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 158.7 (C_q), 149.5 (CH), 140.3 (C_q), 139.6 (C_q), 135.1 (CH), 133.9 (C_q), 130.8 (CH), 130.5 (CH), 130.4 (CH), 128.5 (CH), 127.3 (CH), 125.4 (CH), 121.2 (CH), 113.7 (CH), 55.2 (CH_3).

IR (ATR): 3067, 2969, 2839, 1607, 1582, 1440, 1148, 1037, 830, 561 cm^{-1}.

MS (EI) m/z (relative intensity) 261 (42) [M^+], 260 (100), 217 (50), 191 (10), 78 (2).

HR-MS (EI) m/z calcd for $[C_{18}H_{15}NO]^+$ 261.1154, found 261.1142.

2-(4'-Methoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (52cd)



With aryl sulfamate: The general procedure **E** was followed using **3c** (127 mg, 0.75 mmol) and **30ad** (116 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52cd** (74 mg, 55%) was obtained as a colorless oil.

With aryl carbamate: The general procedure **E** was followed using **3c** (127 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52cd** (86 mg, 63%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.45 (td, J = 7.8, 1.9 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.26-7.21 (m, 2H), 7.07 (ddd, J = 7.3, 4.9, 1.2 Hz, 1H), 7.00-6.94 (m, 2H), 6.86 (dt, J = 7.9, 1.1 Hz, 1H), 6.68-6.62 (m, 2H), 3.71 (s, 3H), 2.15 (s, 3H).

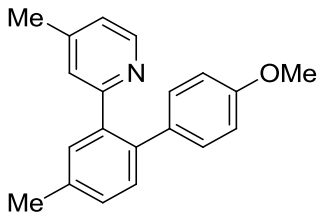
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0 (C_q), 158.2 (C_q), 148.9 (CH), 140.9 (C_q), 139.5 (C_q), 136.7 (C_q), 135.6 (CH), 134.3 (C_q), 130.7 (CH), 129.1 (CH), 128.0 (CH), 127.6 (CH), 125.6 (CH), 121.2 (CH), 113.2 (CH), 55.1 (CH_3), 20.4 (CH_3).

IR (ATR): 2955, 2835, 1608, 1584, 1510, 1423, 1244, 1177, 1028, 674 cm^{-1}.

MS (EI) m/z (relative intensity) 275 (42) [M^+], 274 (100), 231 (18), 152 (4), 78 (2).

HR-MS (EI) m/z calcd for $[C_{19}H_{17}NO]^+$ 275.1310, found 275.1301.

2-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-4-methylpyridine (52dd)



With aryl sulfamate: The general procedure **E** was followed using **3d** (137 mg, 0.75 mmol) and **30ad** (116 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52dd** (75 mg, 52%) was obtained as a colorless oil.

With aryl carbamate: The general procedure **E** was followed using **3d** (137 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52dd** (122 mg, 84%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48 (d, J = 4.9, 1H), 7.47 (s, 1H), 7.33-7.21 (m, 2H), 7.12-7.00 (m, 2H), 6.91 (dd, J = 5.0, 1.0 Hz, 1H), 6.80-6.71 (m, 3H), 3.78 (s, 3H), 2.42 (s, 3H), 2.11 (s, 3H).

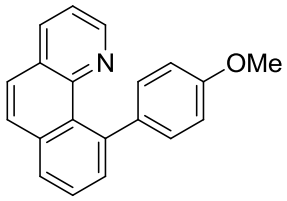
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q), 158.3 (C_q), 149.0 (CH), 146.2 (C_q), 139.1 (C_q), 137.7 (C_q), 136.9 (C_q), 133.8 (C_q), 131.0 (CH), 130.7 (CH), 130.3 (CH), 129.1 (CH), 126.3 (CH), 122.3 (CH), 113.4 (CH), 55.2 (CH_3), 21.0 (CH_3)，20.9 (CH_3).

IR (ATR): 2920, 2835, 1599, 1559, 1463, 1242, 1176, 1036, 887, 578 cm^{-1}.

MS (EI) m/z (relative intensity) 289 (11) [M^+], 288 (100), 245 (25), 137 (3), 63 (2).

HR-MS (ESI) m/z calcd for $[C_{20}H_{19}NO+H]^+$ 290.1539, found 290.1539.

10-(4-Methoxyphenyl)benzo[*h*]quinoline (52ed)



With aryl sulfamate: The general procedure **E** was followed using **3e** (134 mg, 0.75 mmol) and **30ad** (116 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ed** (132 mg, 95%) was obtained as a light yellow solid (m.p. 123-124 ℃).

With aryl carbamate: The general procedure **E** was followed using **3e** (134 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ed** (134 mg, 96%) was obtained as a light yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (dd, J = 4.3, 1.9 Hz, 1H), 8.06 (dd, J = 7.8, 1.9 Hz, 1H), 7.88 (dd, J = 7.8, 1.4 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.69-7.62 (m, 2H), 7.53 (dd, J = 7.2, 1.4 Hz, 1H), 7.34-7.32 (m, 3H), 6.98-6.90 (m, 2H), 3.89 (s, 3H).

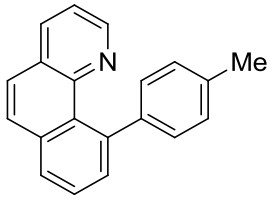
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (C_q), 147.0 (C_q), 146.9 (CH), 141.4 (C_q), 138.9 (C_q), 135.2 (CH), 135.1 (C_q), 131.7 (CH), 129.8 (CH), 129.1 (C_q), 128.3 (CH), 127.7 (CH), 127.2 (C_q), 127.0 (CH), 125.9 (CH), 121.0 (CH), 112.8 (CH), 55.3 (CH_3).

IR (ATR): 3030, 2967, 1879, 1568, 1435, 1234, 1171, 1044, 848, 579 cm^{-1}.

MS (EI) m/z (relative intensity) 285 (20) [M^+], 284 (100), 241 (38), 120 (7), 43 (6).

HR-MS (ESI) m/z calcd for $[C_{20}H_{15}NO+H]^+$ 286.1226, found 286.1225.

10-(*p*-Tolyl)benzo[*h*]quinoline (52ec)



With aryl sulfamate: The general procedure **E** was followed using **3e** (134 mg, 0.75 mmol) and **30ac** (108 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ec** (119 mg, 88%) was obtained as a colorless oil.

With aryl carbamate: The general procedure **E** was followed using **3e** (134 mg, 0.75 mmol) and **30bc** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ec** (115 mg, 86%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.44 (dd, J = 4.3, 1.9 Hz, 1H), 8.07 (dd, J = 7.9, 1.8 Hz, 1H), 7.89 (dd, J = 7.9, 1.0 Hz, 1H), 7.83 (d, J = 8.7 Hz, 1H), 7.71-7.61 (m, 2H), 7.52 (dd, J = 7.3, 1.3 Hz, 1H), 7.30 (dd, J = 7.9, 4.3 Hz, 1H), 7.26-7.16 (m, 4H), 2.45 (s, 3H).

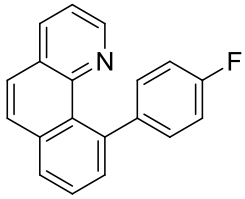
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9 (C_q), 146.8 (CH), 143.4 (C_q), 141.7 (C_q), 135.2 (CH), 135.1 (C_q), 135.0 (C_q), 131.6 (CH), 129.1 (C_q), 128.6 (CH), 128.3 (CH), 128.1 (CH), 127.8 (CH), 127.2 (C_q), 127.0 (CH), 125.9 (CH), 121.0 (CH), 21.3 (CH_3).

IR (ATR): 3044, 2917, 1620, 1588, 1418, 1210, 1131, 1040, 973, 556 cm^{-1}.

MS (EI) m/z (relative intensity) 269 (25) [M^+], 268 (100), 133 (5), 91 (2), 43 (4).

HR-MS (EI) m/z calcd for $[C_{20}H_{15}N]^+$ 269.1204, found 269.1194.

10-(4-Fluorophenyl)benzo[*h*]quinoline (52ee)



With aryl sulfamate: The general procedure was **E** followed using **3e** (134 mg, 0.75 mmol) and **30ae** (110 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ee** (115 mg, 84%) was obtained as a yellow solid (m.p. 115-116 ℃).

With aryl carbamate: The general procedure was **E** followed using **3e** (134 mg, 0.75 mmol) and **30be** (92 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52ee** (112 mg, 82%) was obtained as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.45 (dd, J = 4.3, 1.9 Hz, 1H), 8.10 (dd, J = 8.0, 2.0 Hz, 1H), 7.93 (dd, J = 8.0, 1.4 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.74-7.64 (m, 2H), 7.53 (dd, J = 7.3, 1.5 Hz, 1H), 7.38-7.25 (m, 3H), 7.15-7.04 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5 (C_q, $^{1}J_{C\text{-}F}$ = 243.7 Hz), 146.8 (CH), 146.7 (C_q), 142.2 (C_q, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 140.6 (C_q), 135.2 (CH), 135.0 (C_q), 131.5 (CH), 130.5 (CH, $^{3}J_{C\text{-}F}$ = 8.4 Hz), 129.0 (C_q), 128.3 (CH), 128.1 (CH), 127.2 (C_q), 127.0 (CH), 126.0 (CH), 121.1 (CH), 114.1 (CH, $^{2}J_{C\text{-}F}$ = 21.1 Hz).

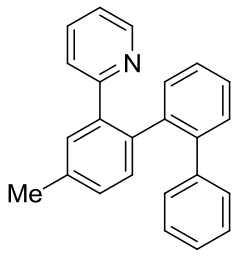
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -118.1 — -118.3 (m).

IR (ATR): 3046, 2925, 1603, 1567, 1420, 1214, 1156, 1015, 828, 570 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (28) [M^+], 272 (100), 252 (8), 136 (9), 44 (7).

HR-MS (EI) m/z calcd for $[C_{19}H_{12}FN]^+$ 273.0954, found 273.0943.

2-(4-methyl-[1,1':2',1''-terphenyl]-2-yl)pyridine (52ai)



The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30bi** (120 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52ai**

(116 mg, 72%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.34 (ddd, J = 4.8, 1.6, 0.9 Hz, 1H), 7.46-7.17 (m, 8H), 7.16-6.94 (m, 4H), 6.74-6.62 (m, 3H), 2.40 (s, 3H).

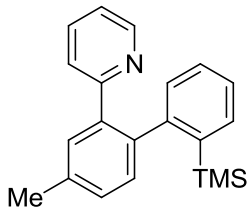
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2 (C_q), 148.9 (CH), 140.9 (C_q), 140.5 (C_q), 139.7 (C_q), 139.3 (C_q), 137.1 (C_q), 137.0 (C_q), 134.8 (CH), 131.5 (CH), 130.5 (CH), 129.9 (CH), 129.1 (CH), 129.0 (CH), 127.4 (2×CH), 127.3 (CH), 127.3 (CH), 126.2 (CH), 124.1 (CH), 120.6 (CH), 21.0 (CH_3).

IR (ATR): 3054, 3018, 1713, 1585, 1472, 1150, 1007, 824, 767, 616 cm^{-1}.

MS (EI) m/z (relative intensity) 321 (40) [M^+], 244 (100), 152 (6), 79 (10), 43 (7).

HR-MS (EI) m/z calcd for $[C_{24}H_{19}N]^+$ 321.1517, found 321.1519.

2-(4-methyl-2'-(trimethylsilyl)-[1,1'-biphenyl]-2-yl)pyridine (52aj)



The general procedure **E** was followed using **3a** (127 mg, 0.75 mmol) and **30bj** (119 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 25:1) **52aj** (118 mg, 76%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 7.71-7.67 (m, 1H), 7.57 (dd, J = 7.3, 1.5 Hz, 1H), 7.31-7.13 (m, 5H), 7.02 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.99-6.95 (m, 1H), 6.76 (dd, J = 8.1, 1.0 Hz, 1H), 2.47 (s, 3H), -0.04 (s, 9H).

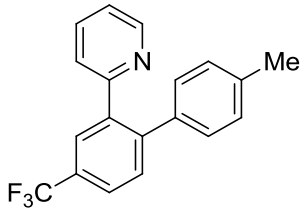
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1 (C_q), 149.1 (CH), 147.6 (C_q), 139.5 (C_q), 138.9 (C_q), 138.6 (C_q), 137.4 (C_q), 134.8 (2×CH), 131.1 (CH), 130.6 (CH), 130.6 (CH), 128.3 (CH), 128.0 (CH), 125.9 (CH), 124.7 (CH), 121.0 (CH), 21.0 (CH_3), 0.36 (CH_3).

IR (ATR): 3049, 2952, 1586, 1426, 1248, 1121, 1085, 837, 687, 621 cm^{-1}.

MS (EI) m/z (relative intensity) 317 (2) [M^+], 244 (100), 202 (2), 73 (3), 43 (4).

HR-MS (ESI) m/z calcd for $[C_{21}H_{23}NSi+H]^+$ 318.1673, found 318.1673.

2-(4'-Methyl-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)pyridine (52fc)



The general procedure **E** was followed using **3f** (167 mg, 0.75 mmol) and **30bc** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **52fc** (136 mg, 87%) was obtained as a white solid (m.p. 77-78 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.95 (dd, J = 1.2, 0.6 Hz, 1H), 7.67 (ddd, J = 8.0, 2.0, 0.6 Hz, 1H), 7.51 (d, J = 8.0, 1H), 7.40 (td, J = 7.8, 1.8 Hz, 1H), 7.13 (ddd, J = 7.8, 4.8, 1.2 Hz, 1H), 7.08-7.00 (m, 4H), 6.88 (td, J = 7.9, 1.1 Hz, 1H), 2.31 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1 (C_q), 149.7 (CH), 144.1 (C_q), 140.1 (C_q), 137.7 (C_q), 137.2 (C_q), 135.4 (CH), 131.0 (CH), 129.8 (C_q, $^{2}J_{C\text{-}F}$ = 31.9 Hz), 129.4 (CH), 129.0 (CH), 127.6 (CH , $^{3}J_{C\text{-}F}$ = 3.8 Hz), 125.3 (CH), 125.1 (CH, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 124.3 (C_q, $^{1}J_{C\text{-}F}$ = 271.5 Hz), 121.8 (CH), 21.1 (CH_3).

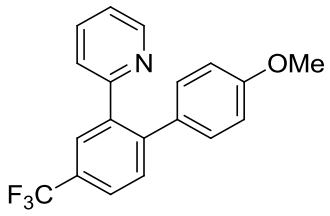
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.4 (s).

IR (ATR): 2925, 1612, 1587, 1439, 1254, 1164, 1078, 1059, 748, 585 cm^{-1}.

MS (EI) m/z (relative intensity) 313 (35) [M^+], 312 (100), 242 (4), 155 (2), 78 (2).

HR-MS (ESI) m/z calcd for $[C_{19}H_{14}F_3N+H]^+$ 314.1158, found 314.1151.

2-(4'-Methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)pyridine (52fd)



The general procedure **E** was followed using **3f** (167 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52fd** (148 mg, 93%) was obtained as a white solid (m.p. 77-78 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.94 (dd, J = 1.2, 0.7 Hz, 1H), 7.68 (ddd, J = 8.0, 2.1, 0.7 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.42 (td, J = 7.8,

1.8 Hz, 1H), 7.13 (ddd, J = 7.8, 4.9, 1.2 Hz, 1H), 7.09-7.03 (m, 2H), 6.88 (td, J = 7.9, 1.1 Hz, 1H), 6.81-6.75 (m, 2H), 3.23 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1 (C_q), 158.1 (C_q), 149.7 (CH), 143.6 (C_q), 139.8 (C_q), 135.5 (CH), 132.3 (C_q), 130.7 (CH), 129.5 (C_q, $^2J_{C\text{-}F}$ = 32.8 Hz), 127.7 (CH), 127.6 (CH , $^3J_{C\text{-}F}$ = 3.7 Hz), 125.3 (CH), 124.1 (C_q, $^1J_{C\text{-}F}$ = 271.5 Hz), 125.1 (CH, $^3J_{C\text{-}F}$ = 3.7 Hz), 121.9 (CH), 113.8 (CH), 55.2 (CH_3).

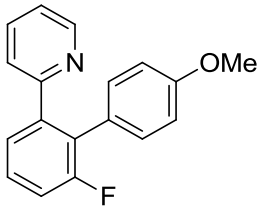
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.4 (s).

IR (ATR): 2938, 1610, 1587, 1401, 1276, 1123, 1083, 1061, 828, 553 cm^{-1}.

MS (EI) m/z (relative intensity) 329 (26) [M$^+$], 328 (100), 285 (32), 142 (2), 78 (2).

HR-MS (EI) m/z calcd for $[C_{19}H_{14}F_3NO]^+$ 329.1027, found 329.1025.

2-(6-Fluoro-4'-methoxy-[1,1'-biphenyl]-2-yl)pyridine (52gd)



The general procedure **E** was followed using **3g** (130 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52gd** (126 mg, 90%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.48 (ddd, J = 7.8, 1.4, 0.4 Hz, 1H), 7.41-7.32 (m, 2H), 7.22-7.13 (m, 1H), 7.11-7.04 (m, 3H), 6.86-6.75 (m, 3H), 3.76 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0 (C_q, $^1J_{C\text{-}F}$ = 245.1 Hz), 158.8 (C_q), 158.1 (C_q, $^3J_{C\text{-}F}$ = 3.3 Hz), 149.4 (CH), 142.1 (C_q, $^3J_{C\text{-}F}$ = 3.1 Hz), 135.2 (CH), 131.8 (CH, $^4J_{C\text{-}F}$ = 1.7 Hz), 128.6 (CH, $^3J_{C\text{-}F}$ = 9.0 Hz), 127.8 (C_q, $^2J_{C\text{-}F}$ = 17.1 Hz), 126.1 (C_q), 125.9 (CH, $^4J_{C\text{-}F}$ = 3.3 Hz), 125.3 (CH), 121.5 (CH), 115.5 (CH, $^2J_{C\text{-}F}$ = 23.4 Hz), 113.5 (CH), 55.2 (CH_3).

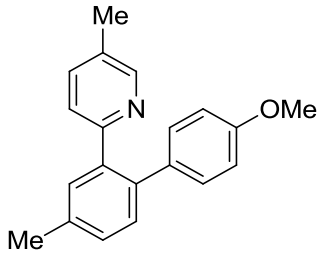
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -115.8 (dd, J = 9.6, 5.4 Hz).

IR (ATR): 3003, 2835, 1606, 1586, 1425, 1177, 1036, 832, 748, 584 cm^{-1}.

MS (EI) m/z (relative intensity) 279 (45) [M$^+$], 278 (100), 235 (50), 117 (7), 78 (2).

HR-MS (ESI) m/z calcd for $[C_{18}H_{14}FNO+H]^+$ 280.1131, found 280.1132.

2-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-5-methylpyridine (52hd)



The general procedure **E** was followed using **3h** (137 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **52hd** (118 mg, 82%) was obtained as a white solid (m.p. 114-115 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.54-8.41 (m, 1H), 7.55-7.45 (m, 1H), 7.35-7.13 (m, 3H), 7.12-7.01 (m, 2H), 6.84-6.69 (m, 3H), 3.78 (s, 3H), 2.42 (s, 3H), 2.29 (s, 3H).

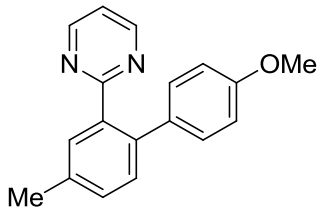
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (C_q), 156.6 (C_q), 149.7 (CH), 139.0 (C_q), 137.3 (C_q), 136.9 (C_q), 135.8 (CH), 133.8 (C_q), 131.0 (CH), 130.7 (CH), 130.5 (C_q), 130.3 (CH), 129.0 (CH), 124.9 (CH), 113.4 (CH), 55.1 (CH_3), 21.0 (CH_3)，18.1 (CH_3).

IR (ATR): 2919, 1607, 1560, 1471, 1241, 1134, 1032, 878, 725, 589 cm^{-1}.

MS (EI) m/z (relative intensity) 289 (41) [M^+], 288 (100), 245 (25), 137 (4), 58 (6).

HR-MS (EI) m/z calcd for $[C_{20}H_{19}NO]^+$ 289.1467, found 289.1454.

2-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)pyrimidine (52id)



The general procedure **E** was followed using **3i** (128 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **52id** (131 mg, 95%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 5.1 Hz, 2H), 7.55 (s, 1H), 7.35-7.25 (m, 2H), 7.10-6.97 (m, 3H), 6.78-6.69 (m, 2H), 3.76 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5 (C_q), 158.2 (C_q), 156.8 (CH), 138.1 (C_q), 137.9 (C_q),

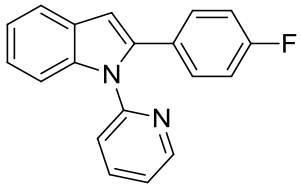
136.8 (C_q), 133.9 (C_q), 131.0 (CH), 130.5 (CH), 130.1 (2× CH), 118.3 (CH), 113.4 (CH), 55.2 (CH_3), 21.0 (CH_3).

IR (ATR): 3029, 2921, 2852, 1606, 1552, 1436, 1240, 1108, 1031, 583 cm^{-1}.

MS (EI) m/z (relative intensity) 276 (52) [M^+], 275 (100), 232 (32), 152 (8), 43 (10).

HR-MS (EI) m/z calcd for $[C_{18}H_{16}N_2O]^+$ 276.1263, found 276.1255.

2-(4-Fluorophenyl)-1-(pyridin-2-yl)-1*H*-indole (83ae)



With aryl sulfamate: The general procedure **E** was followed using **82a** (146 mg, 0.75 mmol) and **30ae** (110 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **83ae** (83 mg, 55%) was obtained as a white solid (m.p. 147-148 ℃).

With aryl carbamate: The general procedure **E** was followed using **82a** (146 mg, 0.75 mmol) and **30be** (92 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **83ae** (130 mg, 90%) was obtained as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.68-8.55 (m, 1H), 7.74-7.56 (m, 3H), 7.26-7.17 (m, 5H), 7.00-6.92 (m, 2H), 6.90 (dd, J = 8.0, 0.8 Hz, 1H), 6.75 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.1 (C_q, $^1J_{C\text{-}F}$ = 247.4 Hz), 151.9 (C_q), 149.3 (CH), 138.9 (C_q), 138.4 (C_q), 137.9 (CH), 130.4 (CH, $^3J_{C\text{-}F}$ = 8.2 Hz), 128.8 (C_q, $^4J_{C\text{-}F}$ = 3.4 Hz), 128.6 (C_q), 123.1 (CH), 121.9 (CH), 121.7 (CH), 121.4 (CH), 120.5 (CH), 115.4 (CH, $^2J_{C\text{-}F}$ = 21.5 Hz), 111.4 (CH), 105.5 (CH).

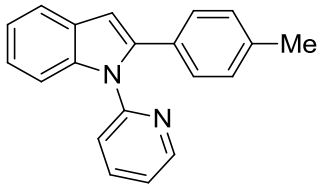
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -114.1 — -114.3 (m).

IR (ATR): 3052, 2840, 1584, 1436, 1261, 1179, 1154, 1045, 838, 586 cm^{-1}.

MS (EI) m/z (relative intensity) 288 (68) [M^+], 287 (100), 183 (10), 143 (11), 78 (9).

HR-MS (EI) m/z calcd for $[C_{19}H_{13}FN_2]^+$ 288.1063, found 288.1062.

1-(Pyridin-2-yl)-2-(*p*-tolyl)-1*H*-indole (83ac)



The general procedure **E** was followed using **82a** (146 mg, 0.75 mmol) and **30bc** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **83ac** (134 mg, 91%) was obtained as a light yellow solid (m.p. 82-83 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.73-7.58 (m, 3H), 7.27-7.15 (m, 5H), 7.09 (d, J = 8.5 Hz, 2H), 6.90 (dd, J = 8.0, 0.7 Hz, 1H), 6.78 (s, 1H), 2.34 (s, 3H).

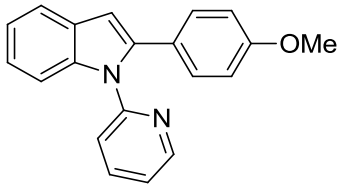
^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.2 (C_q), 149.1 (CH), 140.0 (C_q), 138.4 (C_q), 137.7 (CH), 137.3 (C_q), 129.8 (C_q), 129.0 (CH), 128.8 (C_q), 128.6 (CH), 122.8 (CH), 122.1 (CH), 121.5 (CH), 121.3 (CH), 120.4 (CH), 111.5 (CH), 105.1 (CH), 21.2 (CH_3).

IR (ATR): 3027, 2922, 1578, 1469, 1434, 1261, 1148, 1043, 850, 588 cm^{-1}.

MS (EI) m/z (relative intensity) 284 (95) [M^+], 283 (100), 268 (18), 134 (6), 78 (10).

HR-MS (EI) m/z calcd for $[C_{20}H_{16}N_2]^+$ 284.1313, found 284.1301.

2-(4-Methoxyphenyl)-1-(pyridin-2-yl)-1*H*-indole (83ad)



The general procedure **E** was followed using **82a** (146 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **83ad** (137 mg, 91%) was obtained as a white solid (m.p. 122-123 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.72-7.53 (m, 3H), 7.27-7.13 (m, 5H), 6.94-6.67 (m, 4H), 3.78 (s, 3H).

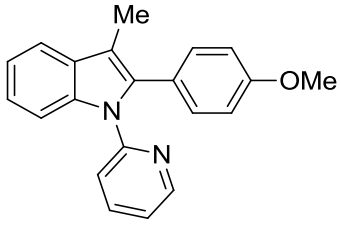
^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q), 152.4 (C_q), 149.2 (CH), 140.0 (C_q), 138.5 (C_q), 137.7 (CH), 130.1 (CH), 128.9 (C_q), 125.4 (C_q), 122.7 (CH), 122.1 (CH), 121.5 (CH), 121.3 (CH), 120.3 (CH), 113.9 (CH), 111.5 (CH), 104.8 (CH), 55.3 (CH_3).

IR (ATR): 2972, 1567, 1496, 1447, 1235, 1146, 1024, 966, 842, 589 cm^{-1}.

MS (EI) m/z (relative intensity) 300 (100) [M^+], 285 (18), 256 (33), 128 (9), 78 (14).

HR-MS (EI) m/z calcd for $[C_{20}H_{16}N_2O]^+$ 300.1263, found 300.1265.

2-(4-Methoxyphenyl)-3-methyl-1-(pyridin-2-yl)-1*H*-indole (83bd)



The general procedure **E** was followed using **82b** (156 mg, 0.75 mmol) and **30bd** (98 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **83bd** (146 mg, 93%) was obtained as a white solid (m.p. 136-137 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64-8.54 (m, 1H), 7.79-7.69 (m, 1H), 7.67-7.58 (m, 1H), 7.53 (dd, *J* = 7.7, 2.1 Hz, 1H), 7.25-7.10 (m, 5H), 6.91-6.81 (m, 2H), 6.74 (dt, *J* = 8.0, 0.9 Hz, 1H), 3.81 (s, 3H), 2.38 (s, 3H).

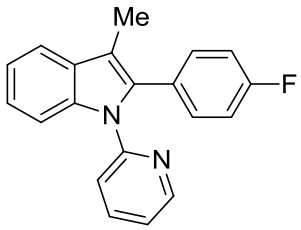
^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8 (C_q), 152.4 (C_q), 148.9 (CH), 137.4 (CH), 137.1 (C_q), 135.5 (C_q), 131.5 (CH), 129.7 (C_q), 124.8 (C_q), 122.9 (CH), 121.5 (CH), 120.8 (CH), 120.7 (CH), 118.7 (CH), 113.7 (CH), 112.0 (C_q), 111.5 (CH), 55.2 (CH_3), 9.5 (CH_3).

IR (ATR): 2928, 2840, 1505, 1435, 1288, 1149, 1070, 1040, 836, 578 cm^{-1}.

MS (EI) m/z (relative intensity) 314 (100) [M^+], 299 (14), 236 (12), 128 (3), 78 (9).

HR-MS (EI) m/z calcd for $[C_{21}H_{18}N_2O]^+$ 314.1419, found 314.1421.

2-(4-Fluorophenyl)-3-methyl-1-(pyridin-2-yl)-1*H*-indole (83be)



The general procedure **E** was followed using **82b** (156 mg, 0.75 mmol) and **30be** (92 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **83be** (147 mg, 92%) was obtained as a white solid (m.p. 151-152 ℃).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.57 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.78-7.49 (m, 3H),

7.29-7.12 (m, 5H), 7.06-6.96 (m, 2H), 6.78 (dd, J = 8.0, 0.8 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.8 (C_q, $^1J_{C\text{-}F}$ = 247.1 Hz), 152.0 (C_q), 149.0 (CH), 137.5 (CH), 137.1 (C_q), 134.6 (C_q), 131.9 (CH, $^3J_{C\text{-}F}$ = 8.7 Hz), 129.5 (C_q), 128.4 (C_q, $^4J_{C\text{-}F}$ = 3.4 Hz), 123.3 (CH), 121.4 (CH), 121.0 (CH), 120.9 (CH), 118.9 (CH), 115.4 (CH, $^2J_{C\text{-}F}$ = 21.5 Hz), 112.6 (C_q), 111.4 (CH), 9.44 (CH_3).

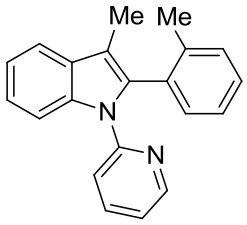
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -114.2 — -114.4 (m).

IR (ATR): 2919, 2839, 1672, 1580, 1432, 1213, 1145, 1071, 846, 576 cm^{-1}.

MS (EI) m/z (relative intensity) 302 (100) [M^+], 287 (18), 224 (20), 143 (14), 78 (26).

HR-MS (EI) m/z calcd for $[C_{20}H_{15}FN_2]^+$ 302.1219, found 302.1225.

3-Methyl-1-(pyridin-2-yl)-2-(*o*-tolyl)-1*H*-indole (83ba)



The general procedure **E** was followed using **82b** (156 mg, 0.75 mmol) and **30ba** (90 mg, 0.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1) **83ba** (128 mg, 86%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.55 (ddd, J = 4.9, 2.0, 0.9 Hz, 1H), 7.93-7.86 (m, 1H), 7.71-7.63 (m, 1H), 7.50-7.41 (m, 1H), 7.31-7.17 (m, 6H), 7.07 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H), 6.69 (dt, J = 8.0, 0.9 Hz, 1H), 2.24 (s, 3H), 2.03 (s, 3H).

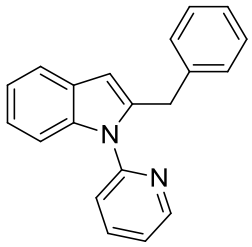
^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.0 (C_q), 148.7 (CH), 138.3 (C_q), 137.3 (CH), 136.6 (C_q), 135.2 (C_q), 132.1 (C_q), 131.6 (CH), 130.0 (CH), 129.4 (C_q), 128.3 (CH), 125.5 (CH), 122.9 (CH), 120.7 (CH), 120.5 (CH), 119.9 (CH), 118.6 (CH), 112.5 (C_q), 111.9 (CH), 19.8 (CH_3), 9.3 (CH_3).

IR (ATR): 2916, 2840, 1587, 1435, 1254, 1148, 1072, 1013, 845, 575 cm^{-1}.

MS (EI) m/z (relative intensity) 298 (100) [M^+], 220 (28), 167 (7), 128 (4), 78 (10).

HR-MS (EI) m/z calcd for $[C_{21}H_{18}N_2]^+$ 298.1470, found 298.1468.

2-Benzyl-1-(pyridin-2-yl)-1*H*-indole (85)



The general procedure **E** was followed using **82a** (146 mg, 0.75 mmol) and **84** (122 mg, 0.50mmol) at ambient temperature. After purification by column chromatography (*n*-hexane/ EtOAc 20:1) **85** (92 mg, 65%) was obtained as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69-8.60 (m, 1H), 7.78 (td, J = 7.7, 2.1 Hz, 1H), 7.56 (dd, J = 5.7, 3.4 Hz, 1H), 7.34-7.23 (m, 3H), 7.22-7.00 (m, 7H), 6.40-6.34 (m, 1H), 4.25 (s, 2H).

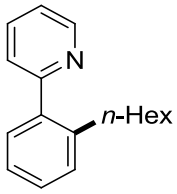
^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.3 (C_q), 149.5 (CH), 140.1 (C_q), 138.7 (C_q), 138.1 (CH), 137.4 (C_q), 128.8 (CH), 128.4 (C_q), 128.1 (CH), 126.1 (CH), 122.0 (CH), 121.9 (CH), 121.2 (CH), 120.6 (CH), 120.1 (CH), 110.0 (CH), 104.1 (CH), 34.0 (CH_2).

IR (ATR): 2971, 1565, 1494, 1441, 1230, 1145, 1024, 966, 842, 575 cm^{-1}.

MS (EI) m/z (relative intensity) 284 (100) [M^+], 206 (95), 178 (20), 128 (9), 78 (40).

HR-MS (EI) m/z calcd for $[C_{20}H_{16}N_2]^+$ 284.1313, found 284.1312.

2-(2-*n*-Hexylphenyl)pyridine (53ba)



The general procedure **F** was followed using **3b** (78 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ba** (106 mg, 90%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.74 (td, J = 7.8, 1.8 Hz, 1H), 7.38 (dt, J = 7.8, 1.1 Hz, 1H), 7.35−7.21 (m, 5H), 2.69 (t, J = 7.8 Hz, 2H), 1.53−1.35 (m, 2H), 1.26−1.10 (m, 6H), 0.81 (t, J = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.4 (C_q), 149.1 (CH), 140.8 (C_q), 140.3 (C_q), 136.0 (CH), 129.7 (CH), 129.7 (CH), 128.2 (CH), 125.7 (CH), 124.1 (CH), 121.6 (CH), 32.9 (CH_2), 31.5 (CH_2), 31.2 (CH_2), 29.1 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

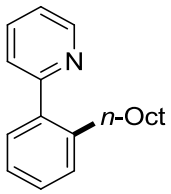
IR (neat): 2954, 2924, 2855, 1585, 1466, 1377, 1023, 746 cm^{-1}.

MS (EI) m/z (relative intensity) 239 (15) [M^+], 182 (100), 167 (65), 115 (3), 43 (33).

HR-MS (EI) m/z calcd for $[C_{17}H_{21}N]^+$ 239.1674, found 239.1666.

The analytical data were in accordance with those reported in the literature.[88]

2-(2-*n*-Octylphenyl)pyridine (53bb)



The general procedure **F** was followed using **3b** (78 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53bb** (110 mg, 83%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.74 (td, J = 7.8, 1.9 Hz, 1H), 7.38 (dt, J = 7.8, 1.0 Hz, 1H), 7.36−7.22 (m, 5H), 2.69 (t, J = 7.9 Hz, 2H), 1.52−1.35 (m, 2H), 1.32−1.09 (m, 10H), 0.86 (t, J = 6.7 Hz, 3H).

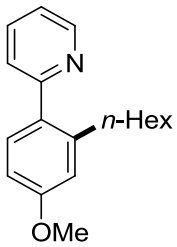
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.4 (C_q), 149.1 (CH), 140.8 (C_q), 140.3 (C_q), 136.0 (CH), 129.7 (CH), 129.7 (CH), 128.2 (CH), 125.7 (CH), 124.1 (CH), 121.5 (CH), 32.9 (CH_2), 31.8 (CH_2), 31.2 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

IR (neat): 2922, 2853, 1585, 1424, 1148, 1023, 989, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 267 (11) [M^+], 182 (100), 167 (55), 78 (3), 41 (8).

HR-MS (EI) m/z calcd for $[C_{19}H_{25}N]^+$ 267.1987, found 267.1988.

2-(2-*n*-Hexyl-4-methoxyphenyl)pyridine (53ja)



The general procedure **F** was followed using **3j** (93 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ja** (107 mg,

[88] L. Ackermann, P. Novák, R. Vicente, N. Hofmann, *Angew. Chem. Int. Ed.* **2009**, *48*, 6045–6048.

80%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.64 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.69 (td, J = 7.8, 1.9 Hz, 1H), 7.32 (dt, J = 7.8, 1.1 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 7.19 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.84−6.75 (m, 2H), 3.82 (s, 3H), 2.68 (t, J = 7.7 Hz, 2H), 1.50−1.35 (m, 2H), 1.27−1.06 (m, 6H), 0.80 (t, J = 6.9 Hz, 3H).

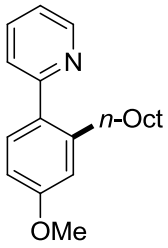
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 159.5 (C_q), 149.1 (CH), 142.5 (C_q), 136.0 (CH), 133.2 (C_q), 131.0 (CH), 124.1 (CH), 121.2 (CH), 115.2 (CH), 110.9 (CH), 55.2 (CH_3), 33.2 (CH_2), 31.5 (CH_2), 31.1 (CH_2), 29.1 (CH_2), 22.4 (CH_2), 14.0 (CH_3).

IR (neat): 2954, 2925, 2855, 1586, 1463, 1377, 1091, 785 cm^{-1}.

MS (EI) m/z (relative intensity) 269 (38) [M^+], 212 (100), 197 (46), 154 (28), 41 (8).

HR-MS (EI) m/z calcd for $[C_{18}H_{23}NO]^+$ 269.1780, found 269.1774.

2-(4-Methoxy-2-*n*-octylphenyl)pyridine (53jb)



The general procedure **F** was followed using **3j** (93 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53jb** (122 mg, 82%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.64 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.69 (td, J = 7.8, 1.9 Hz, 1H), 7.32 (dt, J = 7.8, 1.1 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 7.19 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.84−6.76 (m, 2H), 3.82 (s, 3H), 2.68 (t, J = 7.7 Hz, 2H), 1.52−1.33 (m, 2H), 1.31−1.04 (m, 10H), 0.84 (t, J = 6.9 Hz, 3H).

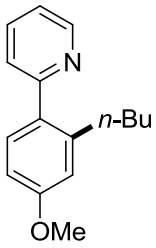
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 159.5 (C_q), 149.1 (CH), 142.5 (C_q), 136.0 (CH), 133.2 (C_q), 131.0 (CH), 124.1 (CH), 121.2 (CH), 115.2 (CH), 110.9 (CH), 55.2 (CH_3), 33.2 (CH_2), 31.8 (CH_2), 31.2 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

IR (neat): 2923, 2853, 1586, 1463, 1277, 1128, 1059, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 297 (14) [M^+], 212 (100), 197 (32), 154 (24), 43 (15).

HR-MS (EI) m/z calcd for $[C_{20}H_{27}NO]^+$ 297.2093, found 297.2091.

2-(2-*n*-Butyl-4-methoxyphenyl)pyridine (53jc)



The general procedure **F** was followed using **3j** (93 mg, 0.50 mmol) and **12ac** (52 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53jc** (95 mg, 79%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.64 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.69 (td, J = 7.8, 1.9 Hz, 1H), 7.33 (dt, J = 7.8, 1.1 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 7.19 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.85−6.74 (m, 2H), 3.82 (s, 3H), 2.69 (t, J = 7.7 Hz, 2H), 1.50−1.36 (m, 2H), 1.29−1.11 (m, 2H), 0.77 (t, J = 7.2 Hz, 3H).

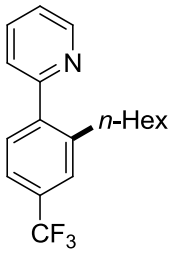
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 159.5 (C_q), 149.1 (CH), 142.4 (C_q), 136.0 (CH), 133.2 (C_q), 131.0 (CH), 124.1 (CH), 121.2 (CH), 115.2 (CH), 110.9 (CH), 55.2 (CH_3), 33.4 (CH_2), 32.8 (CH_2), 22.5 (CH_2), 13.8 (CH_3).

IR (neat): 2954, 2929, 1586, 1462, 1378, 1128, 1017, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 241 (24) [M^+], 212 (100), 197 (25), 154 (17), 41 (3).

HR-MS (EI) m/z calcd for $[C_{16}H_{19}NO]^+$ 241.1467, found 241.1463.

2-{2-*n*-Hexyl-4-(trifluoromethyl)phenyl}pyridine (53ka)



The general procedure **F** was followed using **3k** (112 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ka** (140 mg, 91%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.76 (td, J = 7.8, 1.9 Hz, 1H), 7.56−7.46 (m, 2H), 7.42 (d, J = 7.6 Hz, 1H), 7.76 (dt, J = 7.8, 1.0 Hz, 1H), 7.28 (ddd,

J = 7.6, 4.9, 1.2 Hz, 1H), 2.71 (t, *J* = 7.9 Hz, 2H), 1.54−1.35 (m, 2H), 1.33−1.02 (m, 6H), 0.80 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.0 (C_q), 149.4 (CH), 143.6 (C_q), 141.8 (C_q), 136.3 (CH), 130.3 (C_q, $^2J_{C\text{-}F}$ = 32.5 Hz), 130.1 (CH), 126.4 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.6 (C_q, $^1J_{C\text{-}F}$ = 271.3 Hz), 124.0 (CH), 122.5 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 122.2 (CH), 32.9 (CH_2), 31.4 (CH_2), 30.9 (CH_2), 29.0 (CH_2), 22.4 (CH_2), 14.0 (CH_3).

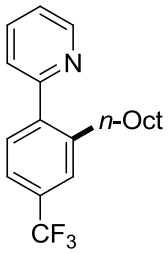
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −62.56 (s).

IR (neat): 2927, 2857, 1587, 1467, 1267, 1091, 990, 748 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (12) [M^+], 250 (100), 235 (72), 167 (10), 43 (12).

HR-MS (EI) m/z calcd for $[C_{18}H_{20}F_3N]^+$ 307.1548, found 307.1544.

2-(2-*n*-Octyl-4-(trifluoromethyl)phenyl)pyridine (53kb)



The general procedure **F** was followed using **3k** (112 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53kb** (135 mg, 81%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.68 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.76 (td, *J* = 7.8, 1.9 Hz, 1H), 7.58−7.39 (m, 3H), 7.36 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.28 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 2.71 (t, *J* = 7.9 Hz, 2H), 1.52−1.36 (m, 2H), 1.32−1.07 (m, 10H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.0 (C_q), 149.4 (CH), 143.6 (C_q), 141.8 (C_q), 136.3 (CH), 130.3 (C_q, $^2J_{C\text{-}F}$ = 32.1 Hz), 130.1 (CH), 126.4 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.5 (C_q, $^1J_{C\text{-}F}$ = 271.3 Hz), 124.0 (CH), 122.5 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 122.2 (CH), 32.9 (CH_2), 31.8 (CH_2), 31.0 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

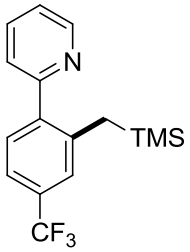
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −62.55 (s).

IR (neat): 2923, 2853, 1586, 1463, 1277, 1128, 1059, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 335 (12) [M^+], 250 (100), 235 (50), 69 (8), 43 (23).

HR-MS (EI) m/z calcd for $[C_{20}H_{24}F_3N]^+$ 335.1861, found 335.1851.

2-{4-(Trifluoromethyl)-2-((trimethylsilyl)methyl)phenyl}pyridine (53kd)



The general procedure **F** was followed using **3k** (112 mg, 0.50 mmol) and **12ad** (92 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53kd** (101 mg, 65%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.68 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.75 (td, J = 7.8, 1.9 Hz, 1H), 7.46−7.31 (m, 4H), 7.25 (ddd, J = 7.8, 1.9, 1.1 Hz, 1H), 2.48 (s, 2H), −0.22 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.5 (C_q), 149.2 (CH), 142.0 (C_q), 140.2 (C_q), 136.4 (CH), 130.5 (CH), 130.1 (C_q, $^{2}J_{C\text{-}F}$ = 33.4 Hz), 126.5 (CH, $^{3}J_{C\text{-}F}$ = 4.3 Hz), 124.4 (CH), 124.2 (C_q, $^{1}J_{C\text{-}F}$ = 271.3 Hz), 122.1 (CH), 120.9 (CH, $^{3}J_{C\text{-}F}$ = 4.3 Hz), 23.8 (CH_2), −1.6 (CH_3).

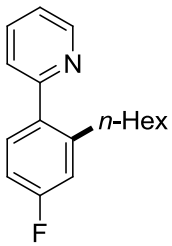
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −62.73 (s).

IR (neat): 2955, 2856, 1587, 1406, 1248, 1120, 991, 746 cm^{-1}.

MS (EI) m/z (relative intensity) 309 (3) [M^+], 294 (100), 216 (18), 167 (15), 73 (37).

HR-MS (ESI) m/z calcd for $[C_{16}H_{18}F_3NSi+H]^+$ 310.1233, found 310.1240.

2-(4-Fluoro-2-*n*-hexylphenyl)pyridine (53la)



The general procedure **F** was followed using **3l** (87 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53la** (78 mg, 61%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.67 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.74 (td, J = 7.6, 1.9 Hz, 1H), 7.37−7.22 (m, 3H), 7.05−6.89 (m, 2H), 2.68 (t, J = 7.9 Hz, 2H), 1.53−1.36 (m, 2H), 1.31−1.07 (m, 6H), 0.82 (t, J = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.6 (C_q, $^1J_{C\text{-}F}$ = 243.7 Hz), 159.4 (C_q), 149.2 (CH), 143.5 (C_q, $^3J_{C\text{-}F}$ = 7.7 Hz), 136.4 (C_q, $^4J_{C\text{-}F}$ = 2.9 Hz), 136.2 (CH), 131.4 (CH, $^3J_{C\text{-}F}$ = 8.5 Hz), 124.1 (CH), 121.7 (CH), 116.1 (CH, $^2J_{C\text{-}F}$ = 21.3 Hz), 112.5 (CH, $^2J_{C\text{-}F}$ = 21.3 Hz), 32.9 (CH_2, $^4J_{C\text{-}F}$ = 1.3 Hz), 31.4 (CH_2), 30.8 (CH_2), 29.0 (CH_2), 22.4 (CH_2), 14.0 (CH_3).

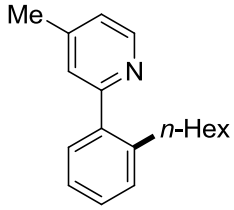
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −(114.6−114.4) (m).

IR (neat): 2955, 2856, 1608, 1564, 1427, 1150, 953, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 257 (17) [M$^+$], 200 (100), 185 (62), 133 (4), 41 (8).

HR-MS (EI) m/z calcd for $[C_{17}H_{20}FN]^+$ 257.1580, found 257.1579.

2-(2-*n*-Hexylphenyl)-4-methylpyridine (53ma)



The general procedure **F** was followed using **3m** (85 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ma** (92 mg, 72%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.51 (dd, J = 5.0, 0.5 Hz, 1H), 7.36−7.15 (m, 5H), 7.05 (ddd, J = 5.0, 1.6, 0.7 Hz, 1H), 2.66 (t, J = 7.9 Hz, 2H), 2.38 (s, 3H), 1.51−1.35 (m, 2H), 1.26−1.06 (m, 6H), 0.80 (t, J = 7.0 Hz, 3H).

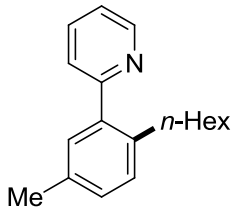
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.2 (C_q), 148.8 (CH), 147.0 (C_q), 140.8 (C_q), 140.4 (C_q), 129.6 (CH), 129.6 (CH), 128.1 (CH), 125.6 (CH), 125.0 (CH), 122.6 (CH), 32.9 (CH_2), 31.5 (CH_2), 31.2 (CH_2), 29.1 (CH_2), 22.5 (CH_2), 21.1 (CH_3), 14.0 (CH_3).

IR (neat): 2954, 2923, 2854, 1599, 1467, 1291, 1040, 749 cm^{-1}.

MS (EI) m/z (relative intensity) 253 (14) [M$^+$], 196 (100), 181 (43), 91 (2), 43 (8).

HR-MS (EI) m/z calcd for $[C_{18}H_{23}N]^+$ 253.1830, found 253.1835.

2-(2-*n*-Hexyl-5-methylphenyl)pyridine (53aa)



The general procedure **F** was followed using **3a** (85 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53aa** (63 mg, 50%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.73 (td, J = 7.8, 1.9 Hz, 1H), 7.37 (dt, J = 7.8, 1.0 Hz, 1H), 7.28−7.10 (m, 4H), 2.66 (t, J = 7.8 Hz, 2H), 2.35 (s, 3H), 1.51−1.34 (m, 2H), 1.30−1.06 (m, 6H), 0.82 (t, J = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.4 (C_q), 149.1 (CH), 140.2 (C_q), 137.6 (C_q), 135.9 (CH), 135.1 (C_q), 130.4 (CH), 129.6 (CH), 129.0 (CH), 124.1 (CH), 121.5 (CH), 32.5 (CH_2), 31.5 (CH_2), 31.3 (CH_2), 29.1 (CH_2), 22.5 (CH_2), 20.9 (CH_3), 14.0 (CH_3).

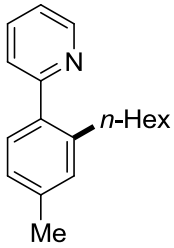
IR (neat): 2954, 2923, 2855, 1587, 1425, 1287, 1109, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 253 (16) [M^+], 196 (100), 181 (44), 167 (2), 41 (10).

HR-MS (EI) m/z calcd for $[C_{18}H_{23}N]^+$ 253.1830, found 253.1834.

The analytical data were in accordance with those reported in the literature.[89]

2-(2-*n*-Hexyl-4-methylphenyl)pyridine (53na)



The general procedure **F** was followed using **3n** (85 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53na** (107 mg, 85%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.69 (td, J = 7.8, 1.9 Hz, 1H), 7.34 (dt, J = 7.8, 1.0 Hz, 1H), 7.27−7.16 (m, 2H), 7.13−7.00 (m, 2H), 2.65 (t, J = 7.9 Hz, 2H), 2.36 (s, 3H), 1.50−1.33 (m, 2H), 1.28−1.04 (m, 6H), 0.80 (t, J = 6.9 Hz, 3H).

[89] Z.-Q. Lei, H. Li, Y. Li, X.-S. Zhang, K. Chen, X. Wang, J. Sun; Z.-J. Shi, *Angew. Chem. Int. Ed.* **2012**, *51,* 2690–2694.

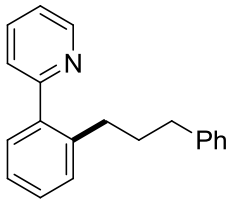
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.4 (C_q), 149.1 (CH), 140.6 (C_q), 137.9 (C_q), 137.5 (C_q), 136.0 (CH), 130.4 (CH), 129.7 (CH), 126.4 (CH), 124.1 (CH), 121.3 (CH), 32.9 (CH_2), 31.5 (CH_2), 31.3 (CH_2), 29.1 (CH_2), 22.5 (CH_2), 21.2 (CH_3), 14.0 (CH_3).

IR (neat): 2954, 2923, 2856, 1613, 1561, 1296, 1091, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 253 (23) [M^+], 196 (100), 181 (48), 167 (14), 41 (9).

HR-MS (EI) m/z calcd for $[C_{18}H_{23}N]^+$ 253.1830, found 253.1834.

2-{2-(3-Phenyl-*n*-propyl)phenyl}pyridine (53be)



The general procedure **F** was followed using **3b** (78 mg, 0.50 mmol) and **12ae** (116 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53be** (101 mg, 74%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.69 (td, J = 7.7, 1.9 Hz, 1H), 7.41−6.97 (m, 11H), 2.73 (t, J = 7.8 Hz, 2H), 2.50 (t, J = 7.6 Hz, 2H), 1.77 (tt, J = 7.8, 7.6 Hz, 2H).

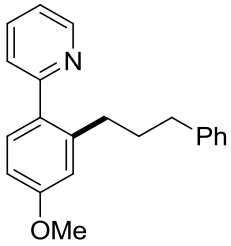
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.9 (C_q), 148.8 (CH), 142.2 (C_q), 140.2 (C_q), 140.0 (C_q), 136.4 (CH), 129.8 (CH), 129.8 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 125.9 (CH), 125.6 (CH), 124.1 (CH), 121.7 (CH), 35.6 (CH_2), 32.7 (CH_2), 32.5 (CH_2).

IR (neat): 3024, 2929, 2858, 1585, 1495, 1264, 1090, 745 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (3) [M^+], 182 (100), 167 (57), 91 (6), 43 (5).

HR-MS (ESI) m/z calcd for $[C_{20}H_{19}N+H]^+$ 274.1590, found 274.1594.

2-{4-Methoxy-2-(3-phenyl-*n*-propyl)phenyl}pyridine (53je)



The general procedure **F** was followed using **3j** (93 mg, 0.50 mmol) and **12ae** (116 mg, 0.75

mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53je** (112 mg, 74%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.61 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.64 (td, J = 7.7, 1.9 Hz, 1H), 7.36−6.99 (m, 8H), 6.86−6.75 (m, 2H), 3.82 (s, 3H), 2.75 (t, J = 7.9 Hz, 2H), 2.51 (t, J = 7.6 Hz, 2H), 1.79 (tt, J = 7.9, 7.6 Hz, 2H).

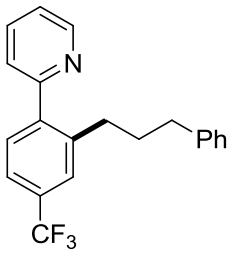
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.9 (C_q), 159.5 (C_q), 149.1 (CH), 142.2 (C_q), 141.9 (C_q), 136.0 (CH), 133.2 (C_q), 131.1 (CH), 128.3 (CH), 128.2 (CH), 125.6 (CH), 124.0 (CH), 121.2 (CH), 115.3 (CH), 111.1 (CH), 55.2 (CH_3), 35.6 (CH_2), 32.8 (CH_2), 32.6 (CH_2).

IR (neat): 3025, 2932, 2857, 1604, 1495, 1234, 988, 745 cm^{-1}.

MS (EI) m/z (relative intensity) 303 (3) [M^+], 212 (100), 197 (30), 91 (21), 51 (3).

HR-MS (EI) m/z calcd for $[C_{21}H_{21}NO]^+$ 303.1623, found 303.1623.

2-{2-(3-Phenyl-*n*-propyl)-4-(trifluoromethyl)phenyl}pyridine (53ke)



The general procedure **F** was followed using **3k** (112 mg, 0.50 mmol) and **12ae** (116 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ke** (109 mg, 64%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.70 (td, J = 7.8, 1.9 Hz, 1H), 7.57−7.46 (m, 2H), 7.43 (d, J = 7.8 Hz, 1H), 7.36−7.08 (m, 5H), 7.08−6.97 (m, 2H), 2.77 (t, J = 7.8 Hz, 2H), 2.51 (t, J = 7.6 Hz, 2H), 1.79 (tt, J = 7.8, 7.6 Hz, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.8 (C_q), 149.4 (CH), 143.7 (C_q), 141.8 (C_q), 141.3 (C_q), 136.4 (CH), 130.3 (C_q, $^{2}J_{C\text{-}F}$ = 32.5 Hz), 130.2 (CH), 128.3 (CH), 128.2 (CH), 126.5 (CH, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 125.7 (CH), 124.2 (C_q, $^{1}J_{C\text{-}F}$ = 271.3 Hz), 123.9 (CH), 122.7 (CH, $^{3}J_{C\text{-}F}$ = 4.2 Hz), 122.2 (CH), 35.6 (CH_2), 32.5 (CH_2), 32.4 (CH_2).

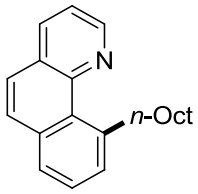
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −62.55 (s).

IR (neat): 2954, 2931, 1587, 1467, 1327, 1163, 996, 746 cm^{-1}.

MS (EI) m/z (relative intensity) 341 (3) [M^+], 250 (100), 235 (92), 91 (21), 51 (7).

HR-MS (EI) m/z calcd for $[C_{21}H_{18}F_3N]^+$ 341.1391, found 341.1394.

10-*n*-Octylbenzo[*h*]quinoline (53eb)



The general procedure **F** was followed using **3e** (90 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53eb** (124 mg, 85%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (dd, J = 4.3, 1.9 Hz, 1H), 8.13 (dd, J = 8.0, 1.9 Hz, 1H), 7.82−7.71 (m, 2H), 7.66−7.50 (m, 3H), 7.46 (dd, J = 8.0, 4.3 Hz, 1H), 3.85 (t, J = 7.6 Hz, 2H), 1.85−1.65 (m, 2H), 1.60−1.15 (m, 10H), 0.87 (t, J = 6.9 Hz, 3H).

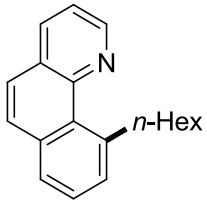
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 148.4 (C_q), 147.2 (CH), 143.8 (C_q), 135.5 (C_q), 135.4 (CH), 130.9 (CH), 129.3 (C_q), 129.0 (CH), 127.4 (CH), 127.3 (C_q), 126.8 (CH), 125.3 (CH), 120.6 (CH), 38.4 (CH_2), 32.0 (CH_2), 31.8 (CH_2), 30.2 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3).

IR (neat): 3047, 2921, 2850, 1621, 1567, 1319, 1058, 757 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (21) [M^+], 206 (100), 191 (43), 98 (3), 43 (17).

HR-MS (EI) m/z calcd for $[C_{21}H_{25}N]^+$ 291.1987, found 291.1989.

10-*n*-Hexylbenzo[*h*]quinoline (53ea)



The general procedure **F** was followed using **3e** (90 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **53ea** (104 mg, 79%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (dd, J = 4.3, 1.9 Hz, 1H), 8.12 (dd, J = 8.0, 1.9 Hz, 1H), 7.82−7.72 (m, 2H), 7.67−7.50 (m, 3H), 7.45 (dd, J = 8.0, 4.3 Hz, 1H), 3.85 (t, J = 7.7 Hz,

2H), 1.86−1.67 (m, 2H), 1.64−1.28 (m, 6H), 0.91 (t, J = 7.0 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 148.4 (C_q), 147.2 (CH), 143.8 (C_q), 135.5 (C_q), 135.3 (CH), 130.9 (CH), 129.3 (C_q), 129.0 (CH), 127.4 (CH), 127.3 (C_q), 126.8 (CH), 125.3 (CH), 120.6 (CH), 38.4 (CH_2), 31.9 (CH_2), 31.7 (CH_2), 29.9 (CH_2), 22.8 (CH_2), 14.2 (CH_3).

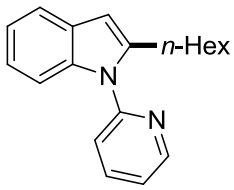
IR (neat): 3024, 2919, 2850, 1591, 1421, 1319, 1029, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 263 (12) [M$^+$], 206 (100), 191 (52), 131 (4), 41 (8).

HR-MS (EI) m/z calcd for $[C_{19}H_{21}N]^+$ 263.1674, found 263.1669.

The analytical data were in accordance with those reported in the literature.[90]

2-*n*-Hexyl-1-(pyridin-2-yl)-1*H*-indole (86aa)



The general procedure **F** was followed using **82a** (97 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86aa** (134 mg, 97%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.88 (td, J = 7.9, 2.0 Hz, 1H), 7.61−7.50 (m, 1H), 7.41 (dt, J = 7.9, 0.9 Hz, 1H), 7.35−7.26 (m, 2H), 7.18−7.02 (m, 2H), 6.43 (s, 1H), 2.82 (t, J = 7.7 Hz, 2H), 1.65−1.45 (m, 2H), 1.39−1.10 (m, 6H), 0.83 (t, J = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.5 (C_q), 150.0 (CH), 141.8 (C_q), 138.3 (CH), 137.3 (C_q), 128.7 (C_q), 122.0 (CH), 121.5 (CH), 121.2 (CH), 120.6 (CH), 119.8 (CH), 110.0 (CH), 102.1 (CH), 31.5 (CH_2), 29.0 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

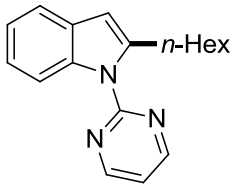
IR (neat): 3053, 2926, 2856, 1584, 1468, 1315, 1095, 737 cm^{-1}.

MS (EI) m/z (relative intensity) 278 (22) [M$^+$], 221 (20), 207 (100), 130 (10), 78 (7).

HR-MS (EI) m/z calcd for $[C_{19}H_{22}N_2]^+$ 278.1783, found 278.1782.

2-*n*-Hexyl-1-(pyrimidin-2-yl)-1*H*-indole (86ca)

[90] B. Li, Z.-H. Wu, Y.-F. Gu, C.-L. Sun, B.-Q. Wang, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2011**, *50*, 1109–1113.



The general procedure **F** was followed using **82c** (98 mg, 0.50 mmol) and **12aa** (90 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86ca** (115 mg, 82%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (d, J = 4.9 Hz, 2H), 8.24−8.13 (m, 1H), 7.57−7.45 (m, 1H), 7.22−7.09 (m, 3H), 6.45 (s, 1H), 3.13 (t, J = 7.8 Hz, 2H), 1.70−1.51 (m, 2H), 1.45−1.17 (m, 6H), 0.86 (t, J = 6.9 Hz, 3H).

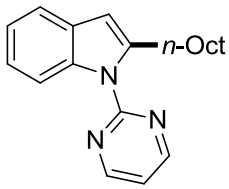
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.3 (C_q), 158.1 (CH), 142.4 (C_q), 136.9 (C_q), 129.4 (C_q), 122.3 (CH), 121.7 (CH), 119.6 (CH), 117.0 (CH), 113.5 (CH), 105.4 (CH), 31.7 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

IR (neat): 2925, 2855, 1558, 1454, 1348, 1152, 929, 739 cm^{-1}.

MS (EI) m/z (relative intensity) 279 (38) [M^+], 221 (24), 208 (100), 130 (12), 43 (4).

HR-MS (EI) m/z calcd for $[C_{18}H_{21}N_3]^+$ 279.1735, found 279.1730.

2-*n*-Octyl-1-(pyrimidin-2-yl)-1*H*-indole (86cb)



The general procedure **F** was followed using **82c** (98 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86cb** (109 mg, 71%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (d, J = 4.9 Hz, 2H), 8.25−8.10 (m, 1H), 7.57−7.45 (m, 1H), 7.22−7.09 (m, 3H), 6.45 (s, 1H), 3.13 (t, J = 7.8 Hz, 2H), 1.68−1.50 (m, 2H), 1.44−1.14 (m, 10H), 0.85 (t, J = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.3 (C_q), 158.1 (CH), 142.4 (C_q), 136.9 (C_q), 129.4 (C_q), 122.3 (CH), 121.7 (CH), 119.6 (CH), 117.0 (CH), 113.5 (CH), 105.4 (CH), 31.9 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 22.7 (CH_2), 14.1 (CH_3).

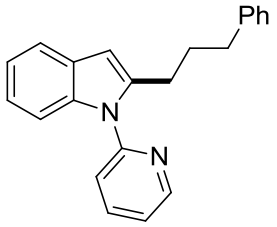
IR (neat): 2923, 2852, 1558, 1454, 1347, 1082, 985, 739 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (38) [M^+], 221 (27), 209 (100), 130 (9), 43 (11).

HR-MS (EI) m/z calcd for $[C_{20}H_{25}N_3]^+$ 307.2048, found 307.2055.

The analytical data were in accordance with those reported in the literature.[91]

2-(3-Phenyl-*n*-propyl)-1-(pyridin-2-yl)-1*H*-indole (86ae)



The general procedure **F** was followed using **82a** (97 mg, 0.50 mmol) and **12ae** (116 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86ae** (138 mg, 89%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.64 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.93−7.80 (m, 1H), 7.65−7.52 (m, 1H), 7.46−7.03 (m, 10H), 6.48 (s, 1H), 2.90 (t, J = 7.7 Hz, 2H), 2.63 (t, J = 7.9 Hz, 2H), 1.90 (tt, J = 7.9, 7.7 Hz, 2H).

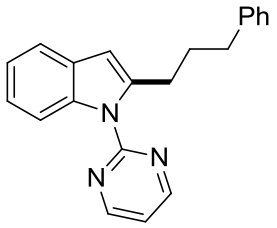
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.5 (C_q), 149.6 (CH), 142.0 (C_q), 141.1 (C_q), 138.2 (CH), 137.3 (C_q), 128.6 (C_q), 128.4 (CH), 128.3 (CH), 125.7 (CH), 122.0 (CH), 121.6 (CH), 121.0 (CH), 120.6 (CH), 119.9 (CH), 110.1 (CH), 102.4 (CH), 35.4 (CH_2), 30.3 (CH_2), 28.0 (CH_2).

IR (neat): 3024, 2933, 2859, 1584, 1468, 1346, 1051, 735 cm^{-1}.

MS (EI) m/z (relative intensity) 312 (23) [M^+], 221 (35), 208 (100), 130 (8), 44 (8).

HR-MS (EI) m/z calcd for $[C_{22}H_{20}N_2]^+$ 312.1626, found 312.1621.

2-(3-Phenyl-*n*-propyl)-1-(pyrimidin-2-yl)-1*H*-indole (86ce)



The general procedure **F** was followed using **82c** (98 mg, 0.50 mmol) and **12ae** (116 mg, 0.75

[91] Z. Ding, N. Yoshikai, *Beilstein J. Org. Chem.* **2012**, *8*, 1536–1542.

mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86ce** (135 mg, 86%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.71 (d, J = 4.9 Hz, 2H), 8.30−8.14 (m, 1H), 7.58−7.43 (m, 1H), 7.30−7.07 (m, 8H), 6.47 (s, 1H), 3.20 (t, J = 7.1 Hz, 2H), 2.68 (t, J = 7.7 Hz, 2H), 1.95 (tt, J = 7.7, 7.1 Hz, 2H).

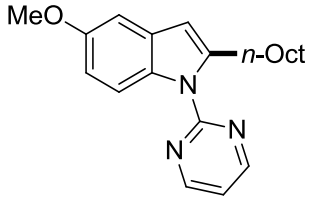
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.2 (C_q), 158.1 (CH), 142.2 (C_q), 141.8 (C_q), 136.9 (C_q), 129.3 (C_q), 128.5 (CH), 128.3 (CH), 125.7 (CH), 122.5 (CH), 121.7 (CH), 119.6 (CH), 117.0 (CH), 113.7 (CH), 105.8 (CH), 35.6 (CH_2), 30.9 (CH_2), 28.9 (CH_2).

IR (neat): 3024, 2931, 1558, 1495, 1348, 1206, 1152, 738 cm^{-1}.

MS (EI) m/z (relative intensity) 313 (32) [M^+], 222 (18), 208 (100), 130 (16), 91 (11).

HR-MS (ESI) m/z calcd for $[C_{21}H_{19}N_3+H]^+$ 314.1652, found 314.1649.

5-Methoxy-2-*n*-octyl-1-(pyrimidin-2-yl)-1*H*-indole (86db)



The general procedure **F** was followed using **82d** (113 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86db** (123 mg, 73%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.74 (d, J = 4.9 Hz, 2H), 8.16 (d, J = 9.0 Hz, 1H), 7.09 (t, J = 4.9 Hz, 1H), 6.99 (d, J = 2.8 Hz, 1H), 6.81 (dd, J = 9.0, 2.8 Hz, 1H), 6.37 (s, 1H), 3.84 (s, 3H), 3.13 (t, J = 7.3 Hz, 2H), 1.69−1.51 (m, 2H), 1.44−1.14 (m, 10H), 0.86 (t, J = 6.8 Hz, 3H).

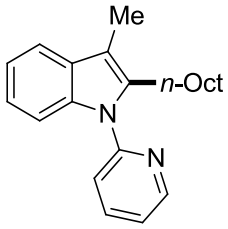
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.4 (C_q), 158.0 (CH), 155.4 (C_q), 143.2 (C_q), 131.9 (C_q), 130.2 (C_q), 116.7 (CH), 114.8 (CH), 111.2 (CH), 105.5 (CH), 102.2 (CH), 55.7 (CH_3), 31.9 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 22.7 (CH_2), 14.1 (CH_3).

IR (neat): 2923, 2853, 1614, 1557, 1292, 1139, 985, 736 cm^{-1}.

MS (EI) m/z (relative intensity) 337 (28) [M^+], 252 (20), 238 (100), 195 (22), 41 (8).

HR-MS (EI) m/z calcd for $[C_{21}H_{27}N_3O]^+$ 337.2154, found 337.2151.

3-Methyl-2-*n*-octyl-1-(pyridin-2-yl)-1*H*-indole (86bb)



The general procedure **F** was followed using **82b** (104 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86bb** (121 mg, 67%) was obtained as a colorless oil.

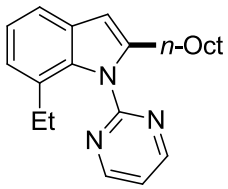
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.86 (td, J = 7.9, 1.9 Hz, 1H), 7.56−7.46 (m, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.33−7.25 (m, 2H), 7.18−7.04 (m, 2H), 2.87 (t, J = 7.7 Hz, 2H), 2.29 (s, 3H), 1.40−1.02 (m, 12H), 0.83 (t, J = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.9 (C_q), 149.5 (CH), 138.2 (CH), 137.3 (C_q), 136.5 (C_q), 129.5 (C_q), 121.7 (CH), 121.6 (CH), 121.1 (CH), 120.1 (CH), 118.1 (CH), 109.8 (C_q), 109.7 (CH), 31.8 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 24.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3), 8.8 (CH_3).

IR (neat): 2922, 2853, 1585, 1458, 1361, 1222, 1014, 736 cm^{-1}.

MS (EI) m/z (relative intensity) 320 (38) [M^+], 221 (100), 207 (30), 144 (17), 43 (24). **HR-MS** (EI) m/z calcd for $[C_{22}H_{28}N_2]^+$ 320.2252, found 320.2257.

7-Ethyl-2-*n*-octyl-1-(pyrimidin-2-yl)-1*H*-indole (86eb)



The general procedure **F** was followed using **82e** (112 mg, 0.50 mmol) and **12ab** (111 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1) **86eb** (135 mg, 81%) was obtained as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.85 (d, J = 4.9 Hz, 2H), 7.40 (d, J = 6.9 Hz, 1H), 7.32 (d, J = 4.9 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.40 (s, 1H), 2.62 (t, J = 7.5 Hz, 2H), 2.24 (q, J = 7.5 Hz, 2H), 1.59−1.43 (m, 2H), 1.36−1.11 (m, 10H), 0.94 (t, J = 7.5 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.6 (C_q), 158.4 (CH), 142.6 (C_q), 135.9 (C_q), 129.9 (C_q),

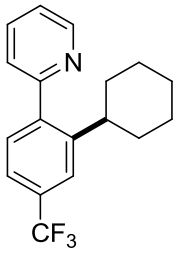
127.8 (C_q), 122.4 (CH), 121.2 (CH), 119.2 (CH), 117.8 (CH), 102.9 (CH), 31.8 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.4 (CH_2), 27.5 (CH_2), 25.6 (CH_2), 22.6 (CH_2), 14.1 (CH_3), 13.9 (CH_3).

IR (neat): 2924, 2853, 1559, 1415, 1347, 1218, 1095, 741 cm^{-1}.

MS (EI) m/z (relative intensity) 335 (47) [M^+], 236 (100), 222 (72), 156 (7), 41 (11).

HR-MS (EI) m/z calcd for $[C_{22}H_{29}N_3]^+$ 335. 4858, found 335.4861.

2-{2-Cyclohexyl-4-(trifluoromethyl)phenyl}pyridine (87ka)



The general procedure **F** was followed using **3k** (112 mg, 0.50 mmol) and **22ba** (89 mg, 0.75 mmol). After purification by column chromatography (*n*-hexane/DCM 2:1) **87ka** (98 mg, 64%) was obtained as a white solid (m.p. 75−76 °C).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 7.75 (td, J = 7.9, 1.9 Hz, 1H), 7.61(s, 1H), 7.52−7.44 (m, 1H), 7.42 (dt, J = 7.9, 0.7 Hz, 1H), 7.32 (dt, J = 7.9, 1.0 Hz, 1H), 7.28 (ddd, J = 7.9, 4.9, 1.2 Hz, 1H), 2.78 (tt, J = 11.9, 3.2 Hz, 1H), 1.86−1.58 (m, 5H), 1.53−1.32 (m, 2H), 1.30−1.04 (m, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.0 (C_q), 149.4 (CH), 146.5 (C_q), 143.3 (C_q, $^4J_{C\text{-}F}$ = 1.6 Hz), 136.2 (CH), 130.4 (C_q, $^2J_{C\text{-}F}$ = 32.5 Hz), 130.2 (CH), 124.3 (C_q, $^1J_{C\text{-}F}$ = 271.3 Hz), 124.0 (CH), 123.3 (CH, $^3J_{C\text{-}F}$ = 3.9 Hz), 122.3 (CH, $^3J_{C\text{-}F}$ = 3.9 Hz), 122.2 (CH), 39.9 (CH), 34.2 (CH_2), 26.6 (CH_2), 26.0 (CH_2).

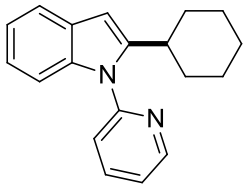
^{19}F-NMR (283 MHz, $CDCl_3$): δ = −62.5 (s).

IR (neat): 2926, 2852, 1587, 1429, 1272, 989 cm^{-1}.

MS (EI) m/z (relative intensity) 305 (50) [M^+], 304 (100), 248 (35), 235 (18), 161 (7).

HR-MS (EI) m/z calcd for $[C_{18}H_{18}F_3N]^+$ 305.1391, found 305.1391.

2-Cyclohexyl-1-(pyridin-2-yl)-1*H*-indole (88aa)



The general procedure **F** was followed using **82a** (97 mg, 0.50 mmol) and **22ba** (89 mg, 0.75 mmol). The mixture was stirred at 60 ℃ for 16 h. After purification by column chromatography (*n*-hexane/EtOAc 20:1) **88aa** (72 mg, 52%) was obtained as a white solid (m.p. 89−90 °C).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.66 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.88 (td, *J* = 7.9, 2.0 Hz, 1H), 7.63−7.53 (m, 1H), 7.42 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.32 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H), 7.29−7.21 (m, 1H), 7.17−7.04 (m, 2H), 6.45 (t, *J* = 0.8 Hz, 1H), 2.82 (tt, *J* = 11.5, 3.3 Hz, 1H), 2.00−1.83 (m, 2H), 1.81−1.61 (m, 3H), 1.50−1.32 (m, 2H), 1.31−1.11 (m, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.7 (C_q), 149.6 (CH), 147.2 (C_q), 138.3 (CH), 137.3 (C_q), 128.5 (C_q), 122.1 (CH), 121.5 (CH), 121.4 (CH), 120.4 (CH), 119.9 (CH), 109.9 (CH), 99.8 (CH), 35.6 (CH), 33.2 (CH_2), 26.4 (CH_2), 26.2 (CH_2).

IR (neat): 2925, 2852, 1585, 1436, 1264, 997 cm^{-1}.

MS (EI) m/z (relative intensity) 276 (100) [M^+], 219 (78), 130 (16), 78 (18).

HR-MS (EI) m/z calcd for $[C_{19}H_{20}N_2]^+$ 276.1626, found 276.1618.

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