Cobalt-Catalyzed Chelation-Assisted Alkylation of Arenes with Primary and Secondary Alkyl Halides

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Abstract: Cobalt–N-heterocyclic carbene catalytic systems have been developed for chelation-assisted *ortho*-alkylation of aromatic compounds with alkyl halides. Aryl imines can be selectively monoalkylated at room temperature by various primary or secondary alkyl chlorides or bromides. The catalytic system can also be applied to 2-arylpyridine derivatives, which in the absence of steric hindrance are amenable to dialkylation by an excess of the alkyl halide. Mechanistic experiments, including reactions of stereochemical probes and radical clocks, indicate that the reaction involves single-electron transfer from the cobalt center to the alkyl halide to form the corresponding alkyl radical, which has a finite lifetime before it undergoes C–C bond formation.

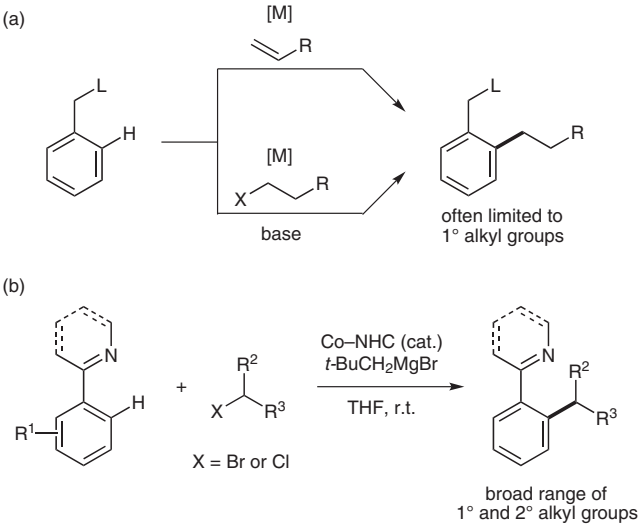
Key words: functionalization, catalysis, cobalt, alkylations, alkyl halides, radical reaction

1 Introduction

The alkylation of aromatic compounds is among the most important C–C bond-forming transformations in organic synthesis. Since the discovery by Murai et al.[1] of the ruthenium-catalyzed *ortho*-alkylation of aromatic ketones with olefins, the chelation-assisted hydroarylation of alkenes in the presence of transition-metal catalysts has evolved into a versatile approach that complements the classical Friedel–Crafts alkylation.[2,3] However, unlike Friedel–Crafts chemistry, this approach has met with limited success in the introduction of secondary alkyl groups. There are several reasons for this, including the anti-Markovnikov selectivity of terminal alkenes,[4,5] the low reactivity of internal alkenes, and the isomerization of alkenes bearing allylic hydrogens. In addition, some alkenes, such as cyclobutene, are not readily available from commercial sources, despite their potential utility.

Recently, *ortho*-alkylation with alkyl halides as alkylating agents has attracted significant attention as an alternative to the hydroarylation approach.[6,7] Nevertheless, this approach has also met with limited success in the introduction of secondary alkyl groups, with a few exceptions.[7h] Only a handful of examples of alkylation with secondary alkyl halides have been reported in the literature,[8–10] presumably because of their low reactivity toward transition-metal catalysts and the propensity of secondary alkyl–metal complexes to undergo β-hydride elimination (Scheme 1, a).

We have recently been interested in cobalt catalysis for C–H bond-functionalization reactions, including those involving chelation-assisted C–H activation.[11] In the course of our research program, we recently found that a cobalt–N-heterocyclic carbene (NHC) catalyst, in combination with a neopentyl Grignard reagent, efficiently promotes *ortho*-alkylation of aromatic ketimines by alkyl chlorides or bromides (Scheme 1, b).[12] The reaction permits the introduction of a variety of primary or secondary alkyl groups under mild conditions. In this article, we report the full details of this reaction, along with the results of an expanded investigation of the substrate scope and the reaction mechanism.



Scheme 1 Cobalt-catalyzed *ortho*-alkylation of arenes with alkyl halides

2 *Ortho*-Alkylation of Aryl Imines

We previously developed cobalt–NHC catalytic systems for *ortho* C–H functionalization with an aryl aldimine or an aryl chloride as the electrophile. Cobalt catalysts generated from a cobalt salt, an imidazolium salt, and neopentylmagnesium bromide promote the addition of 2-arylpyridines to aryl aldimines,[13] as well as the *ortho*-arylation of aryl ketimines with aryl chlorides.[14] Ackermann and co-workers had also developed cobalt–NHC systems

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for *ortho*-arylation of 2-arylpyridines or *N*-pyridylindoles with aryl sulfamates or carbamates;[15] the scope of this reaction was later extended to include *ortho*-arylations and *ortho*-alkylations of the same substrates with the corresponding chlorides.[16] We therefore surmised that a similar catalytic system might also permit *ortho* C–H alkylation with an alkyl halide as the electrophile.

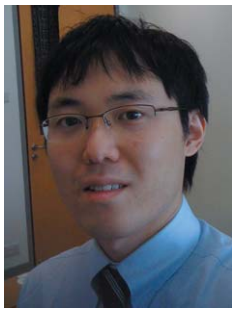
To test this hypothesis, we chose the acetophenone imine **1a** and 1-chlorooctane (**2a**) as model reactants for screening the reaction conditions (Table 1). A catalytic system consisting of cobalt(II) bromide (10 mol%), 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (IMes·HCl; 10 mol%), and neopentylmagnesium bromide (2 equiv), which is effective for *ortho*-arylation, promoted the reaction to afford the alkylation product **3aa** in a moderate yield of 38% (Table 1, entry 1). Other typical NHC preligands such as 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride hydrochloride (IPr·HCl) and 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride (SIMes·HCl) were less effective (entries 2 and 3). Further screening showed that 1,3-diisopropyl-2,5-dihydro-1*H*-imidazol-3-ium tetrafluoroborate (**L1**) gave rise to a higher catalytic activity, improving the yield to 64% (entry 4). Whereas the unsaturated analogue **L2** and the *tert*-butyl analogue **L3** gave poorer results (entries 5 and 6, respectively), the benzo-fused analogue **L4** further improved the yield to 82% (entry 7). As we observed in our previous studies,[13,14] neopentylmagnesium bromide was the Grignard reagent of choice among other primary and secondary Grignard reagents, as it caused *ortho*-neopentylation to only a small extent (< 2% in most cases).

With **L1** and **L4** as preligands, we next examined the effects of the leaving group. Whereas the reaction of 1-bromooctane (**2a′**) proceeded smoothly using both **L1** and **L4** (entries 8 and 9), 1-iodooctane (**2a″**) gave only low yields of product **3aa** (entries 10 and 11) because of an undesirable dehydrohalogenation side reaction. Octyl tosylate (**2a***) took part in the reaction at an elevated temperature of 60 °C, giving **3aa** in moderate yields (entries 12 and 13). However, we found that by simply mixing **2a*** and neopentylmagnesium bromide, substantial displacement of the tosyloxy group with the bromide anion occurred, even at room temperature. This observation suggests that the alkylation with **2a*** involves prior conversion of **2a*** into **2a′**.

Biographical Sketches

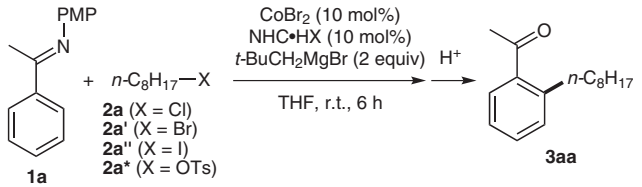
Ke Gao received his B.Sc. (2006) and M.Sc. (2009) degrees from Fudan University under the supervision of Professor Jie Wu. He subsequently moved to Professor Naohiko Yoshikai's group at Nanyang Technological University where he recently completed his Ph.D. studies, which focused on the development of cobalt-catalyzed C–H bond functionalizations. He is currently pursuing his postdoctoral studies in Professor Atsuhiro Osuka and Professor Hideki Yorimitsu's group at Kyoto University.

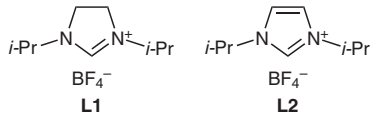
Takeshi Yamakawa received his B.Sc. (2008; supervised by Professor Eiichi Nakamura) and M.Sc. (2010; supervised by Professor Shu Kobayashi) degrees from The University of Tokyo. In 2010, he joined Professor Naohiko Yoshikai's group at Nanyang Technological University to pursue his Ph.D. studies. His current research is focused on the development of C–H functionalization reactions catalyzed by cobalt and other transition metals.

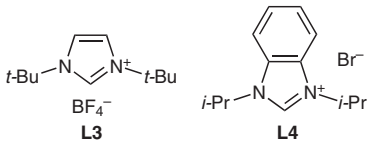


Naohiko Yoshikai received his B.Sc. (2000), M.Sc. (2002), and Ph.D. (2005) degrees from the University of Tokyo under the guidance of Professor Eiichi Nakamura, and then served as an Assistant Professor at the same institution (2005–2009). In 2009, he moved to Singapore to join the faculty of Nanyang Technological University as a Nanyang Assistant Professor and a Research Fellow of the Singapore National Research Foundation. He has been awarded the Thieme Chemistry Journal Award (2011) and the Chemical Society of Japan Award for Young Chemists (2014). His research interests focus on the development and mechanistic study of new transition metal-catalyzed reactions and on the synthetic applications of such reactions.

Table 1 Screening of NHC Preligands and Leaving Groups[a]







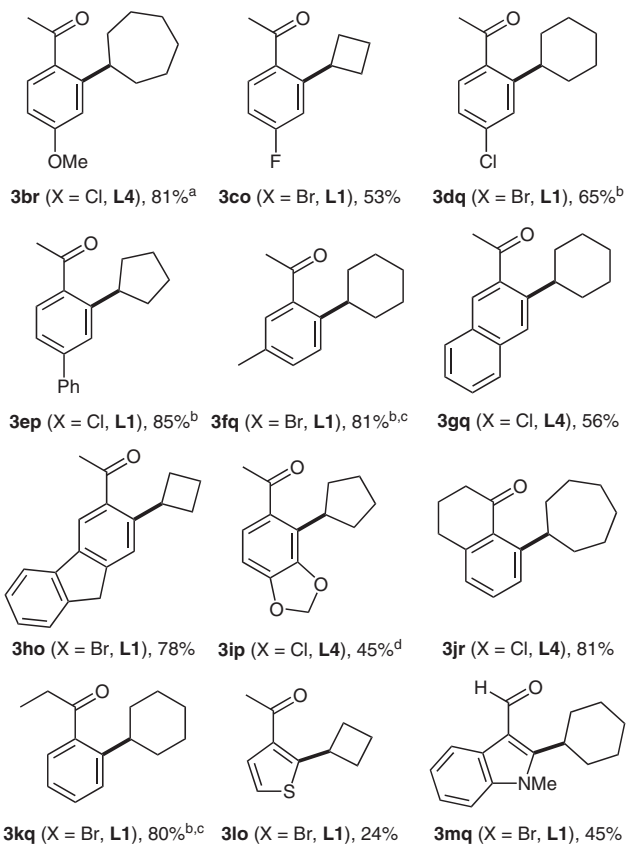
Entry	X	NHC·HX	Yield[b] (%)
1	Cl	IMes·HCl	38
2	Cl	IPr·HCl	13
3	Cl	SIMes·HCl	20
4	Cl	**L1**	64
5	Cl	**L2**	38
6	Cl	**L3**	14
7	Cl	**L4**	82[c]
8	Br	**L1**	79[c]
9	Br	**L4**	57
10	I	**L1**	14
11	I	**L4**	6
12	OTs	**L1**	64[c]
13	OTs	**L4**	49[c]

[a] 0.3 mmol scale; $Me(CH_2)_7X$ (1.2–1.5 equiv).
[b] Determined by GC with tridecane as an internal standard.
[c] Isolated yield.
[d] The reaction was performed at 60 °C.

Next, we explored the scope of the Co–**L1** and Co–**L4** catalytic systems for the alkylation of imine **1a** with a variety of primary alkyl chlorides or bromides (Table 2). The reaction of 1-bromohexane on a 10 mmol scale gave ketone **3ab** in 77% yield (Table 2, entry 1). 5-Bromopent-1-ene gave the expected alkylation product **3ad** as the major product, accompanied by a small amount of the isomer **3ad′** arising from olefin isomerization (entry 4). Chemoselective C–Br bond cleavage/alkylation was achieved for 1-bromo-4-fluorobutane and 1-bromo-4-chlorobutane (entries 5 and 6). On the other hand, 6-bromohexyl tosylate gave the expected product **3ag**, along with a minor product **3ag′** bearing a 6-bromohexyl group (entry 7). The latter product appears to have formed through tosylate–bromide exchange between the major product **3ag** and neopentylmagnesium bromide (see above). Dihalogenated substrates containing both alkyl–Cl and aryl–X (X = F or Cl) moieties underwent chemoselective activation of the former, affording the ketones **3ah** and **3ai** in good yields (entries 8 and 9). Alkyl halides hindered at the β-position, such as 1-bromo-2,2-dimethylpropane, (chloromethyl)(trimethyl)silane, or (bromomethyl)cyclopentane, participated smoothly in the reaction (entries 10–12). The presence of acetal or secondary amide groups in the alkyl bromide was tolerated (entries 13 and 14). An alkyl chloride containing a pyridine ring reacted rather sluggishly, presumably as a result of coordination of the pyridine nitrogen atom to the catalyst (entry 15).

The present catalytic system also allowed alkylation of imine **1a** with a broad range of secondary alkyl chlorides or bromides, as summarized in Table 3. Four-membered to twelve-membered cycloalkyl halides participated in the reaction to afford the corresponding products **3ap**–**at** in moderate to good yields (Table 3, entries 1–7). *tert*-Butoxycarbonyl-protected 4-bromopiperidine also gave the corresponding product **3au**, albeit in moderate yield (entry 8). With the Co–**L1** catalyst, acyclic secondary alkyl halides such as 1-chloro- or 1-bromopropane or 2-bromobutane gave the alkylation products **3av** and **3aw** in moderate yields and with high ratios of the secondary to primary isomers ($i/n \leq 99{:}1$; entries 9–11). In these cases, the Co–**L4** catalyst improved the product yields by about 10–20%, but caused a deterioration in the secondary-to-primary ratios (i/n = 8:2 to 7:3). With 3-bromopentane as the substrate, the 3-pentylation product **3ax** was formed exclusively (entry 12). Secondary alkyl chlorides containing aromatic moieties, including one bearing a *para*-chlorophenyl group, were also amenable to the reaction (entries 13–15). The reaction of *exo*-2-chloronorbornane resulted in predominant formation of the *exo*-arylation product (entry 16).

Next, we explored the scope of the aromatic imines by using randomly chosen cycloalkyl halides as the reaction partners (Figure 1). Imines derived from *para*-substituted (methoxy, fluoro, chloro, or phenyl) acetophenones gave the corresponding products **3br**, **3co**, **3dq**, and **3eq** in moderate to good yields, whereas *p*-bromoacetophenone imine gave a complex mixture of products arising from *ortho*-alkylation and cross-coupling on the C–Br bond. Alkylation of *m*-tolyl, 2-naphthyl, or 3-fluorenyl groups occurred at the less-hindered position with exclusive regioselectivity to give the products **3fq**, **3gq**, and **3ho**, respectively. On the other hand, a methylenedioxy group exhibited a directing effect so that alkylation took place at the proximate carbon atom, giving the product **3ip** and its regioisomer in a ratio of 84:16. Tetralone- and propiophenone-derived imines also participated smoothly in the reaction to give products **3jr** and **3kq**, respectively. The C2 positions of thiophene and indole were also amenable to the alkylation, giving the corresponding cyclohexylated products **3lo** and **3mq** in modest yields.



3br (X = Cl, **L4**), 81%[a] **3co** (X = Br, **L1**), 53% **3dq** (X = Br, **L1**), 65%[b]

3ep (X = Cl, **L1**), 85%[b] **3fq** (X = Br, **L1**), 81%[b,c] **3gq** (X = Cl, **L4**), 56%

3ho (X = Br, **L1**), 78% **3ip** (X = Cl, **L4**), 45%[d] **3jr** (X = Cl, **L4**), 81%

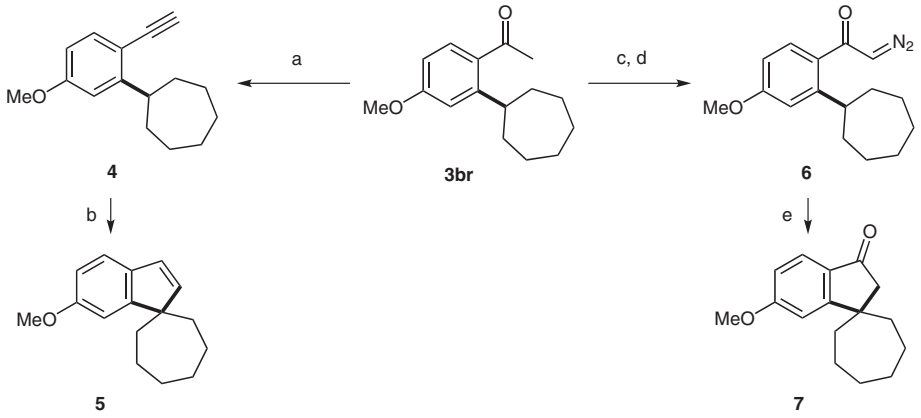
3kq (X = Br, **L1**), 80%[b,c] **3lo** (X = Br, **L1**), 24% **3mq** (X = Br, **L1**), 45%

Figure 1 Products of cycloalkylation of various aryl imines (0.3 mmol scale; reaction time = 24 h). [a] Reaction time 6 h. [b] Additional *t*-$BuCH_2MgBr$ (1 equiv) was added after 2, 4, or 5 h. [c] Two equivalents of the alkyl halide were used. [d] Obtained as a mixture with its regioisomer in a ratio of 84:16.

The present cycloalkylation products can be transformed into unique benzo-fused spirocycles through manipulation of the acetyl and cycloalkyl groups (Scheme 2). Conversion of the acetyl group of **3br** into an ethynyl group was followed by platinum-catalyzed carbocyclization[17] to afford indene **5** in a moderate yield. Alternatively, diazo transfer to the acetyl group of **3br** and subsequent rhodium-catalyzed intramolecular C–H insertion gave indenone **7** in 27% overall yield (unoptimized).

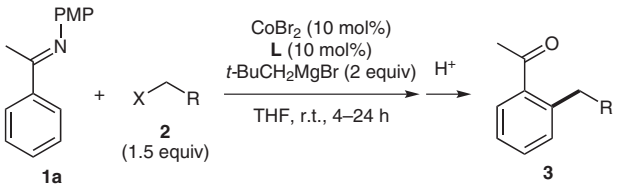
3 *Ortho*-Alkylation of 2-Arylpyridines

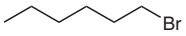
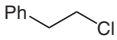
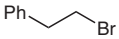
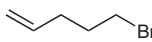
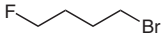
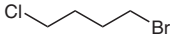
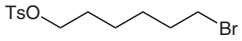
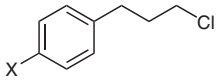
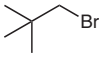
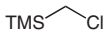
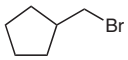
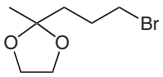
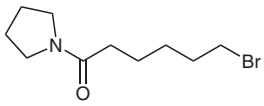
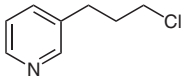
The present catalytic system can also be used in the *ortho*-alkylation of 2-arylpyridine derivatives with primary and secondary alkyl chlorides or bromides (Scheme 3). The reaction of 2-phenylpyridine (**8a**) with 1-chlorooctane (**2a**; 1.5 equiv) in the presence of the Co–**L1** catalytic system gave the monoalkylation product **9aa** in 71% yield, accompanied by the dialkylation product **10aa** in 16% yield. A similar result was obtained in the reaction of **8a** with neopentyl bromide (see **9aj**). The formation of dialkylation product **10aa** was noteworthy because the reaction of aryl imines does not produce any dialkylation products (see above), and also because the Ackermann catalytic system [$Co(acac)_3$, IMes·HCl, CyMgBr, in 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one (DMPU)] did not cause dialkylation of the same substrate.[16] When the reaction was performed with increased amounts of 1-chlorooctane (**2a**; 2.5 equiv) and *t*-$BuCH_2MgBr$ (3 equiv), **10aa** was obtained as the dominant product in 76% yield. *ortho*-Dialkylation was also possible with secondary alkyl halides as the alkylating agents. Thus, *para*-substituted 2-arylpyridine derivatives reacted with 2.5 equivalents of 2-chloropropane, cyclobutyl bromide, or cyclohexyl chloride to afford the dialkylation products **10bv**, **10cp**, and **10dr**, respectively, in moderate to good yields, accompanied by a small amount of the corresponding monoalkylation products. Exclusive monoalkylation was achieved by using 2-arylpyridine derivatives bearing a *meta*-substituent on the aryl moiety or a 3-substituent on the pyridine ring (see **10ep**, **10fr**, and **10gp**). Of note was the substrate bearing a *meta*-chlorophenyl group, which underwent cyclohexylation at the more hindered *ortho*-position (**10fr**), presumably because of secondary directing effect of the lone pair of the chlorine atom.[18] Similar secondary directing effects have also been observed in



Scheme 2 Transformations of cycloalkylation product **3br** into benzo-fused spirocycles. Reaction conditions: (a) LDA, $ClP(O)(OEt)_2$, THF, –78 °C to r.t., then LDA, –78 °C to r.t., 56%; (b) $PtCl_2$, CuBr, toluene, 100 °C, 77%; (c) LiHMDS, THF, –78 °C, then $F_3CCO_2CH_2CF_3$, –78 °C to r.t.; (d) 4-$AcNHC_6H_4SO_2N_3$, H_2O, Et_3N, MeCN, r.t., 75% (two steps); (e) $Rh_2(OAc)_4$, CH_2Cl_2, r.t., 36%.

Table 2 Alkylation of Imine **1a** with Primary Alkyl Halides[a]



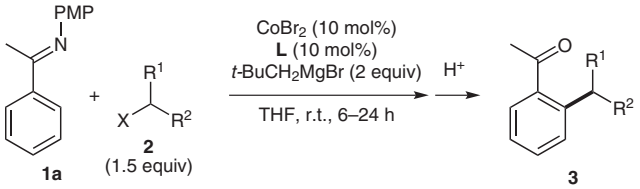
Entry		Substrate	Ligand	Time (h)	Product(s)	Yield[b] (%)
1[c]	**2b′**		**L1**	6	**3ab**	77
2	**2c**		**L4**	24	**3ac**	73
3	**2c′**		**L1**	24	**3ac**	82
4	**2d′**		**L1**	6	**3ad** [R = $(CH_2)_3CH{=}CH_2$] **3ad′** [R = $(CH_2)_2CH{=}CHMe$]	66[d] 6[d]
5	**2e′**		**L1**	24	**3ae** [R = $(CH_2)_4F$]	73
6	**2f′**		**L1**	24	**3af** [R = $(CH_2)_4Cl$]	80
7	**2g′**		**L1**	4	**3ag** [R = $(CH_2)_6OTs$] **3ag′** [R = $(CH_2)_6Br$]	71 18
8	**2h**	 (X = F)	**L4**	24	**3ah**	77
9	**2i**	(X = Cl)	**L4**	24	**3ai**	61
10	**2j′**		**L1**	13	**3aj**	86
11	**2k**		**L1**	24	**3ak**	65
12	**2l′**		**L1**	14	**3al**	87
13	**2m′**		**L4**	24	**3am** [R = $(CH_2)_3COMe$]	69
14[e]	**2n′**		**L1**	24	**3an**	41[f]
15	**2o**		**L1**	24	**3ao**	19[g]

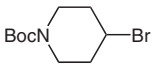
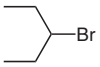
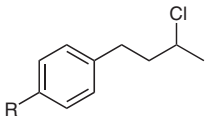
[a] Unless otherwise noted, the reaction was performed on a 0.3 mmol scale.
[b] Isolated yield.
[c] 10 mmol scale.
[d] Obtained as a mixture. The ratio was determined by ^{1}H NMR.
[e] Two equivalents of **2n′** were used, and an additional one equivalent of *t*-$BuCH_2MgBr$ was added after 2 h.
[f] Obtained as a mixture with **2n′** and its β-elimination product.
[g] Obtained as a mixture with 4-$MeO(C_6H_4)NH_2$.

Ackermann's cobalt-catalyzed *ortho*-arylation of 2-arylpyridines with *meta*-alkoxy and -fluoro substituents.[15,16] Arylpyridine derivatives having only one reactive site also participated in the reaction with secondary alkyl halides (see **10hv**, **10iq**, and **10jq**).

The high catalytic activity of the present system allowed the sequential introduction of different alkyl groups onto 2-phenylpyridine in a one-pot operation (Scheme 4). Thus, the reaction of **8a** and 2-phenylethyl bromide (1.5 equiv) was performed under the standard monoalkylation conditions, followed by addition of excess amounts of 1-chlorooctane (**2a**; 3.0 equiv) and *t*-$BuCH_2MgBr$ (3.5

Table 3 Alkylation of **1a** with Secondary Alkyl Halides[a]



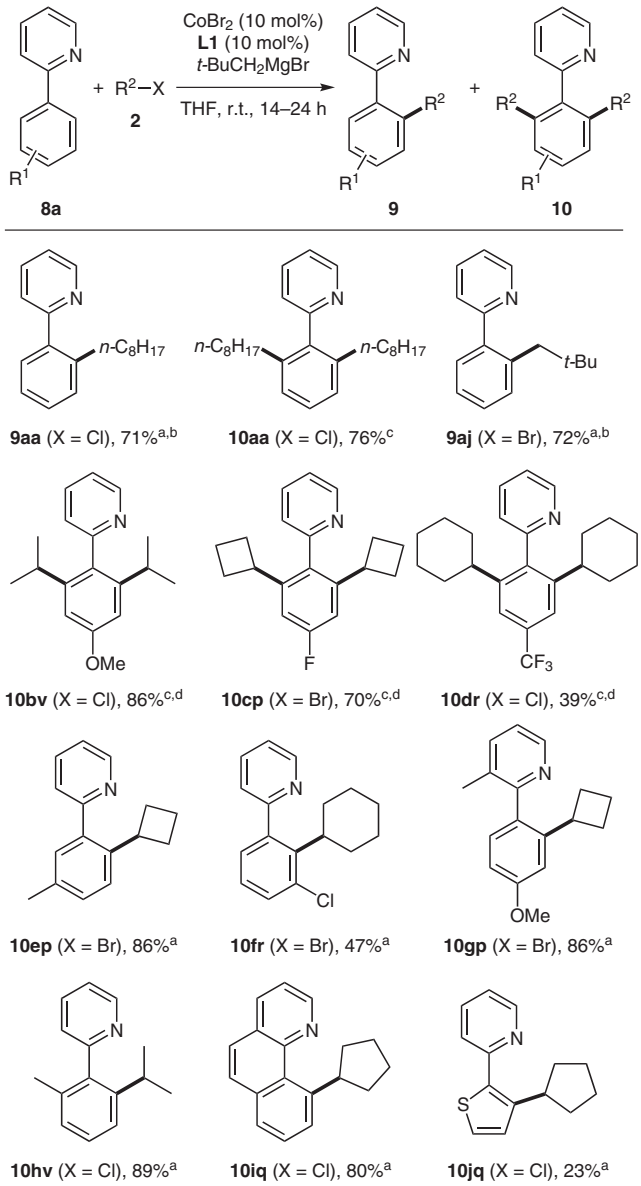
Entry	Alkyl halide		L	Time (h)	Product	Yield (%)[b]
1	**2p**	*c*-C_4H_7Cl	**L4**	24	**3ap**	51
2	**2p′**	*c*-C_4H_7Br	**L1**	24	**3ap**	75
3[c]	**2q**	*c*-C_5H_9Cl	**L1**	24	**3aq**	78
4	**2r**	*c*-$C_6H_{11}Cl$	**L4**	12	**3ar**	73
5	**2r′**	*c*-$C_6H_{11}Br$	**L1**	6	**3ar**	90
6	**2s**	*c*-$C_7H_{13}Cl$	**L4**	24	**3as**	84
7[c,d]	**2t**	*c*-$C_{12}H_{23}Cl$	**L1**	24	**3at**	65
8[c,d]	**2u**		**L1**	24	**3au**	42
9	**2v**	*i*-C_3H_7Cl	**L1**	6	**3av** (*i*/*n* = 99:1)[e]	65
10	**2v′**	*i*-C_3H_7Br	**L1**	6	**3av** (*i*/*n* = 93:7)[e]	68
11	**2w′**	*s*-C_4H_9Br	**L1**	6	**3aw** (*i*/*n* = 94:6)[e]	56
12	**2x′**		**L1**	24	**3ax**	63
13	**2y** (R = H)		**L1**	24	**3ay** (*i*/*n* = 94:6)[e]	76
14	**2z** (R = OMe)		**L1**	24	**3az** (*i*/*n* = 94:6)[e]	61
15	**2aa** (R = Cl)		**L1**	12	**3aaa** (*i*/*n* = 86:14)[e]	75
16	**2ab**		**L1**	24	**3aab** (*exo*/*endo* = 90:10)	82

[a] The reaction was performed on a 0.3 mmol scale.
[b] Isolated yield.
[c] An additional one equivalent of *t*-$BuCH_2MgBr$ was added after 2 or 5 h.
[d] Two equivalents of the alkyl halide were used.
[e] The ratio of the secondary and primary alkylation products.

equiv) to afford the unsymmetrically substituted dialkylation products **11** in 50% isolated yield, along with the symmetric dialkylation products derived from 1-chlorooctane and 2-phenylethyl bromide as byproducts (19% and 4% GC yields, respectively).[19]

4 Mechanistic Investigations

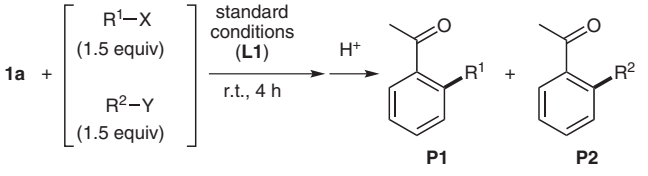
Having established the synthetic scope of the *ortho*-alkylation reaction, we turned our attention to its mechanism. The reaction appears to have some relevance to the cobalt-catalyzed cross-coupling reactions of alkyl halides and aryl Grignard reagents developed by Yorimitsu and Oshima and their co-workers,[20] and by Cahiez and co-workers.[21] However, the scopes of the alkyl halides for these reactions do not completely overlap with those for the present reaction. The cross-coupling reaction can be applied to primary and secondary alkyl iodides and bromides, but not to chlorides. We therefore became particularly interested in the carbon–halogen bond-activation step of the present reaction. Below, we describe a series of experiments that we performed to gain insight into this step.



Scheme 3 *ortho*-Alkylation of 2-arylpyridines with alkyl halides. [a] 1.5 equivalents of alkyl halide and two equivalents of *t*-$BuCH_2MgBr$ were used. [b] Dialkylation products were obtained as byproducts (<20% yield). [c] 2.5 equivalents of alkyl halide and three equivalents of *t*-$BuCH_2MgBr$ were used. [d] Monoalkylation products were obtained as byproducts (<10% yield).

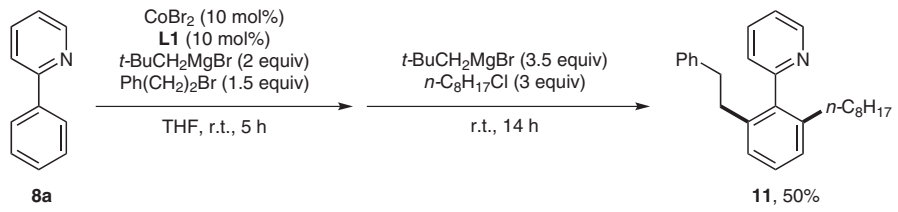
The chemoselective activation of the alkyl bromide moiety over the alkyl chloride moiety in the reaction of 1-bromo-4-chlorobutane prompted us to investigate the chemoselectivity of the reaction systematically by means of intermolecular competition experiments (Table 4). Not unexpectedly, competition between 1-bromodecane and 1-chlorooctane in the reaction with imine **1a** resulted in predominant formation of the alkylation product of the former (Table 4, entry 1). In a similar manner, the reaction using a mixture of 2-bromopropane-d_7 and 2-chloropropane resulted in predominant incorporation of the deuterated isopropyl group (entry 2). Interestingly, a primary and a secondary alkyl bromide (1-bromodecane and bromocyclohexane, respectively) exhibited a similar reactivity, and produced the corresponding products in ~1:1 ratio (entry 3). We also examined the effect of the ring size of the cycloalkyl halide on its relative reactivity. Chlorocyclohexane reacted in preference to chlorocyclobutane (entry 4), whereas it was less reactive than chlorocyclopentane or chlorocycloheptane (entries 5 and 6, respectively).

Table 4 Intermolecular Competition of Two Alkyl Halides[a]



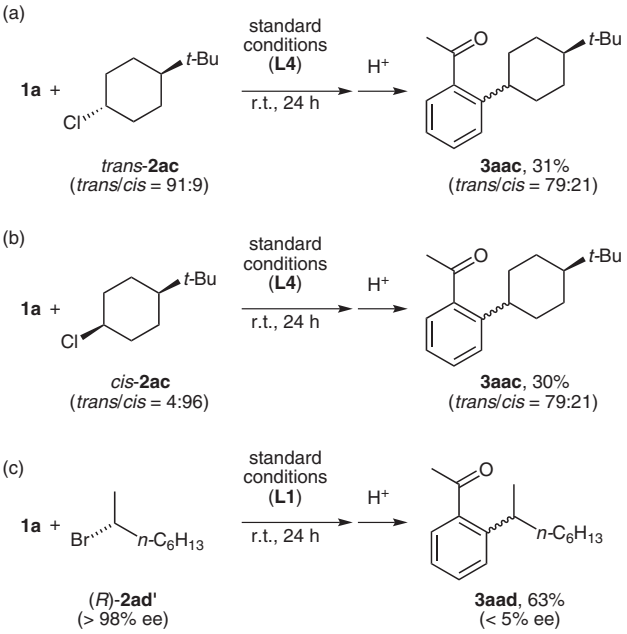
Entry	R^1X	R^2Y	Yield[b] (%)	
			P1	**P2**
1	*n*-$C_{10}H_{21}Br$	*n*-$C_8H_{17}Cl$	64	2
2	*i*-C_3D_7Br	*i*-C_3H_7Cl	74	6
3	*n*-$C_{10}H_{21}Br$	*c*-$C_6H_{11}Br$	36	33
4	*c*-$C_6H_{11}Cl$	*c*-C_4H_7Cl	35	12
5	*c*-$C_6H_{11}Cl$	*c*-$C_5H_{11}Cl$	10	58
6	*c*-$C_6H_{11}Cl$	*c*-$C_7H_{13}Cl$	11	64

[a] The reaction was performed on a 0.3 mmol scale.
[b] Estimated by GC using tridecane as an internal standard.



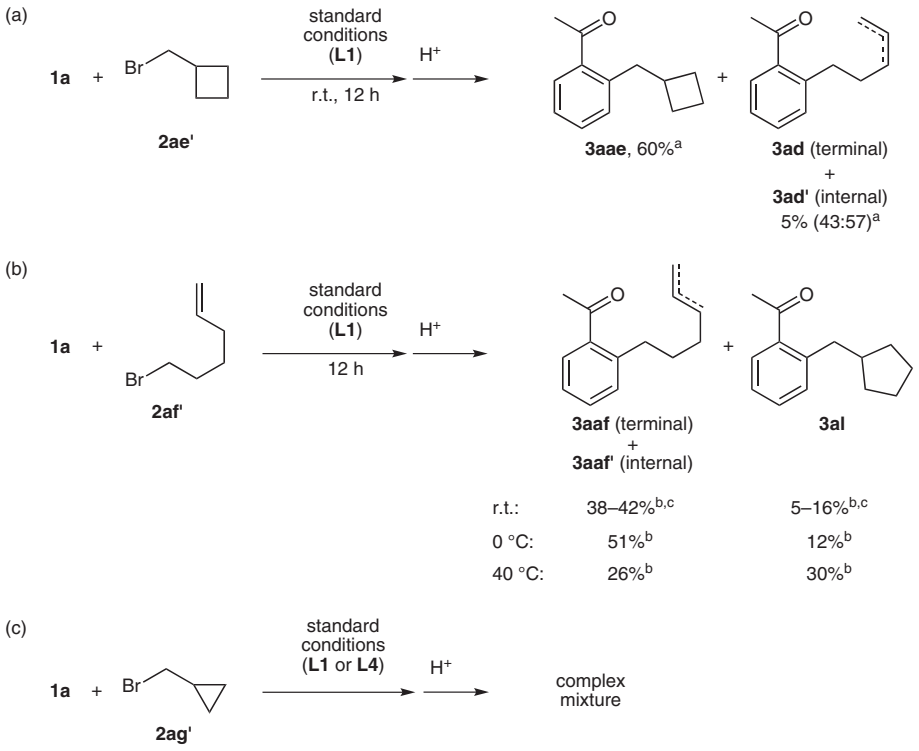
Scheme 4 Sequential *ortho*-alkylation with different alkyl halides

The *exo*/*endo* selectivity of 90:10 in the reaction of *exo*-2-chloronorbornane (Table 3, entry 16) shows that the reaction is not stereospecific. Given this result, we examined the stereochemical course of the reaction by using several probes (Scheme 5). Reactions of imine **1a** with the *trans*- and *cis*-isomers of 1-chloro-4-*tert*-butylcyclohexane (**2ac**) resulted in the formation of the corresponding alkylation product **3aac** with the same *trans*/*cis* ratio of ~8:2 (Scheme 5, a and b). Therefore, the diastereochemical information present in the starting materials was completely lost during the reaction. Furthermore, the reaction of imine **1a** with (2*R*)-2-bromooctane **2ad** (> 98% ee) gave the product **3aad** as a virtually racemic mixture, clearly showing involvement of a stereochemical mutation process (Scheme 5, c).



Scheme 5 Reactions with stereochemistry probes

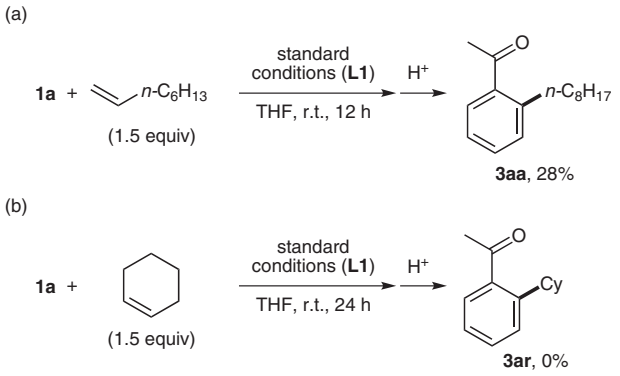
The results described above are indicative of a radical process in the reaction. To probe this possibility further, we performed radical clock experiments (Scheme 6). The reaction of imine **1a** with (bromomethyl)cyclobutane (**2ae′**) under the standard conditions afforded a direct alkylation product **3aae** in 60% yield along with the ring-opening alkylation byproducts **3ad** and **3ad′** (Scheme 6, a). The identity of the byproducts was confirmed by comparison with authentic samples (Table 2, entry 4). The formation of **3ad** and **3ad′** suggests that the reaction involves a cyclobutylmethyl radical, which can undergo ring-opening to give a 4-pentenyl radical at a rate of 5×10^3 s^{-1}.[22] Another probe substrate, 6-bromohex-1-ene (**2af′**), showed somewhat puzzling behavior (Scheme 6, b). In three runs performed under the standard conditions at room temperature, the direct alkylation products **3aaf**/**3aaf′** were obtained in a modest overall yield of ~40%, accompanied by a various amounts (5–16%) of the ring-closing alkylation product **3al**. The identity of **3al** was confirmed by comparison with an authentic sample (Table 2, entry 12).[23] We observed a certain correlation between the reaction temperature and the fate of **2af′**. Thus, whereas formation of the direct alkylation products was favored at a low temperature (0 °C), ring-closing alkylation overrode direct al-



Scheme 6 Radical clock experiments. [a] Isolated yield. [b] Determined by GC using tridecane as an internal standard. [c] Results from three runs.

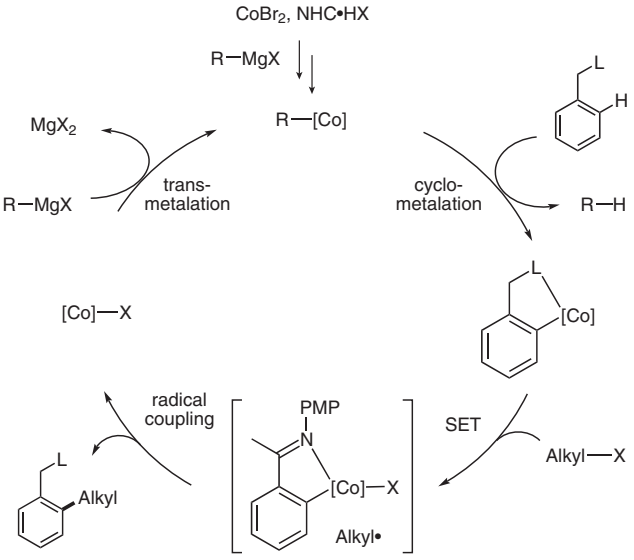
kylation at a higher temperature (40 °C). Although we have not identified the factors that are responsible for the irreproducibility and the varying yield, our observations support the formation of a 5-hexenyl radical and its cyclization to form a cyclopentylmethyl radical (rate constant = 2.3×10^5 s^{-1})[22] in the cobalt-catalyzed reaction. Note that, for unknown reasons, the reaction using (bromomethyl)cyclopropane (**2ag′**) gave a complex mixture, in which we could detect neither a direct alkylation product nor a ring-opening alkylation product (Scheme 6, c).

Finally, we performed control experiments using alkenes instead of alkyl halides (Scheme 7). The reaction of imine **1a** with oct-1-ene gave the *ortho*-octylation product **3aa** in 28% yield (Scheme 7, a), which was significantly lower than that obtained using 1-bromooctane (Table 1, entry 8). Furthermore, cyclohexene failed to give the corresponding cyclohexylated product **3ar** (Scheme 7, b). These observations indicate that the major pathway of the present reaction does not involve the formation of an alkene through dehydrohalogenation of alkyl halide.



Scheme 7 Control experiments using olefins as reaction partners

Although further experiments are necessary to completely characterize the reaction mechanism of the C–X cleavage step and the C–H activation step, we propose the catalytic cycle outlined in Scheme 8. The first step is assumed to be cyclometalation of the aryl imine or 2-arylpyridine with an organocobalt species.[24] The resulting cobaltacycle intermediate undergoes single-electron transfer to the alkyl halide,[25] resulting in the formation of the corresponding alkyl radical and one-electron oxidation of the cobalt center. The alkyl radical then undergoes radical coupling with the aryl group on the cobalt center to afford the *ortho*-alkylation product. Transmetalation between the resulting cobalt halide and the Grignard reagent regenerates the alkylcobalt species. The radical clock experiments suggest that the radical coupling process should occur at a relatively fast rate.



Scheme 8 Proposed catalytic cycle

5 Conclusions

We have developed cobalt-based catalytic systems for imine- and pyridine-directed *ortho*-alkylation of aromatic compounds with alkyl chlorides or bromides. The reaction features mild reaction temperatures, a broad scope of primary and secondary alkyl halides, and useful chemoselectivity. Mechanistic experiments indicate that the reaction involves a unique combination of cobalt-mediated cyclometalation and single-electron transfer processes. Exploration of other electrophilic reaction partners for cobalt-catalyzed o*rtho* C–H functionalization is currently ongoing.

All reactions involving air- or moisture-sensitive compounds were performed by standard Schlenk techniques in oven-dried reaction vessels under N_2. Analytical TLC was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed on 40–63 μm silica gel (Si 60, Merck). ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) spectrometers. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from TMS (0 ppm) or $CHCl_3$ (77.0 ppm), respectively, as internal standards. GC analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and an Agilent J&W DB-5 capillary column (0.25 mm i.d. × 30 m, 0.25 μm film thickness). HPLC analysis was performed by using a Shimadzu LC-20 AD system equipped with Shimadzu SPD-20A UV–vis detector and a Daicel Chiralpak IC column. High-resolution mass spectra were obtained with a Waters Q-Tof Premier LC HR mass spectrometer. Unless otherwise noted, reagents were purchased from Aldrich, Alfa Aesar, or other commercial suppliers, and were used as received. THF was distilled over Na/benzophenone. 1,3-Diisopropyl-1*H*-benzimidazol-3-ium bromide (**L4**) was synthesized according to the procedure described in the literature.[26] Neopentylmagnesium bromide was prepared from neopentyl bromide and Mg turnings in anhyd THF, and titrated before use. Aryl imines and 2-arylpyridines were synthesized according to the literature procedures.[27,28] Alkyl halides **2h**,[12] **2i**,[12] **2n′**,[12] **2o**,[12] **2t**,[29] **2y**,[30] **2z**,[30] **2aa**,[30] *trans*/*cis*-**2ac**,[31] and (*R*)-**2ad′**[32] were synthesized according to the procedures described in the literature. Characterization data for halides **2z** and **2aa** are given in the Supporting Information.

1-(2-Octylphenyl)ethanone (3aa): Typical Procedure

A 10 mL Schlenk tube was charged with $CoBr_2$ (6.6 mg, 0.03 mmol), 1,3-diisopropyl-1*H*-benzimidazol-3-ium bromide (**L4**; 8.5 mg, 0.03 mmol), 4-methoxy-*N*-[(1*E*)-1-phenylethylidene]aniline (**1a**, 67.6 mg, 0.30 mmol), 1-chlorooctane (**2a**, 76.5 μL, 0.45

mmol), and THF (0.69 mL). A 1.92 M solution of *t*-$BuCH_2MgBr$ in THF (0.31 mL, 0.60 mmol) was added dropwise at 0 °C, and the mixture was stirred at r.t. for 6 h. The reaction was quenched by the addition of 3 M aq HCl (1.0 mL), and the mixture was stirred at r.t. for 1 h, then extracted with EtOAc (3 × 10 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane–EtOAc (40:1)] to give a light-yellow oil: yield; 57.3 mg (82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.2 Hz, 3 H), 1.26–1.35 (m, 10 H), 1.53–1.59 (m, 2 H), 2.57 (s, 3 H), 2.83 (t, *J* = 8.0 Hz, 2 H), 7.22–7.26 (m, 2 H), 7.36–7.40 (m, 1 H), 7.60–7.62 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 29.3, 29.4, 29.7, 29.9, 31.9 (two signals overlapping), 34.0, 125.5, 128.9, 131.1, 131.2, 138.0, 142.9, 202.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{25}O$: 233.1905; found: 233.1903.

1-(2-Hexylphenyl)ethanone (3ab)
The reaction was performed on a 10-mmol scale in a 100-mL two-necked flask to give a light-yellow oil; yield: 1.58 g (77%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, 3 H), 1.28–1.38 (m, 6 H), 1.54–1.58 (m, 2 H), 2.57 (s, 3 H), 2.83 (t, *J* = 8.0 Hz, 2 H), 7.22–7.26 (m, 2 H), 7.35–7.39 (m, 1 H), 7.60–7.62 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.6, 29.4, 29.9, 31.7, 31.8, 34.0, 125.5, 128.9, 131.1, 131.2, 138.1, 142.8, 202.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{21}O$: 205.1592; found: 205.1594.

1-[2-(2-Phenylethyl)phenyl]ethanone (3ac)[33]
Light-yellow oil; yield: 48.9 mg (73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3 H), 2.96 (t, *J* = 8.0 Hz, 2 H), 3.22 (t, *J* = 8.0 Hz, 2 H), 7.24–7.35 (m, 7 H), 7.44 (td, *J* = 7.5 Hz, 1.3 Hz, 1 H), 7.72 (dd, *J* = 7.7 Hz, 1.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.6, 36.3, 38.2, 125.8, 125.9 (two signals overlapping), 128.2, 128.6, 129.2, 131.42, 131.45, 137.8, 141.9, 201.9.

1-(2-Pent-4-en-1-ylphenyl)ethanone (3ad)
Obtained as a mixture with 1-{2-[(3*E*)-pent-3-en-1-yl]phenyl}ethanone (**3ad′**) as a light-yellow oil; yield: 40.9 mg (72%; **3ad**/**3ad′** = 92:8).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64–1.71 (m, 2 H), 2.10–2.15 (m, 2 H), 2.57 (s, 3 H), 2.86 (t, *J* = 6.0 Hz, 2 H), 4.97 (ddt, *J* = 10.2 Hz, 2.0 Hz, 1.1 Hz, 1 H), 5.02 (ddt, *J* = 17.1 Hz, 1.7 Hz, 1.6 Hz, 1 H), 5.85 (ddt, *J* = 17.0 Hz, 10.3 Hz, 6.6 Hz, 1 H), 7.24–7.28 (m, 2 H), 7.39 (td, *J* = 7.4 Hz, 1.2 Hz, 1 H), 7.64 (dd, *J* = 8.4 Hz, 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.9, 30.9, 33.5, 33.7, 114.6, 125.7, 129.1, 131.2, 131.3, 137.9, 138.6, 142.5, 202.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}O$: 189.1279; found: 189.1280.

1-[2-(4-Fluorobutyl)phenyl]ethanone (3ae)
Light-yellow oil; yield: 42.5 mg (73%)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67–1.82 (m, 4 H), 2.58 (s, 3 H), 2.89 (t, *J* = 7.6 Hz, 2 H), 4.46 (dt, $^1J_{C–F}$ = 47.2 Hz, *J* = 5.6 Hz, 2 H), 7.25–7.29 (m, 2 H), 7.40 (td, *J* = 7.4 Hz, *J* = 1.2 Hz, 1 H), 7.66 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.3 (d, $^3J_{C–F}$ = 5.2 Hz), 29.8, 30.3 (d, $^2J_{C–F}$ = 19.2 Hz), 33.5, 84.0 (d, $^1J_{C–F}$ = 163 Hz), 125.9, 129.3, 131.2, 131.4, 137.7, 142.3, 201.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}FO$: 195.1185; found: 195.1185.

1-[2-(4-Chlorobutyl)phenyl]ethanone (3af)
Light-yellow oil; yield: 50.4 mg (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70–1.75 (m, 2 H), 1.81–1.86 (m, 2 H), 2.58 (s, 3 H), 2.87 (t, *J* = 7.6 Hz, 2 H), 3.55 (t, *J* = 6.8 Hz, 2 H), 7.25–7.29 (m, 2 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.9, 29.8, 32.5, 33.2, 44.8, 125.9, 129.3, 131.2, 131.5, 137.6, 142.1, 201.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}ClO$: 211.0890; found: 211.0887.

6-(2-Acetylphenyl)hexyl 4-Methylbenzenesulfonate (3ag)
Brown oil; yield: 80.4 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31–1.40 (m, 4 H), 1.50–1.53 (m, 2 H), 1.62–1.66 (m, 2 H), 2.44 (s, 3 H), 2.57 (s, 3 H), 2.79 (t, *J* = 7.6 Hz, 2 H), 4.01 (t, *J* = 6.4 Hz, 2 H), 7.21–7.27 (m, 2 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 7.37 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1 H), 7.64 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 1 H), 7.79 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 25.1, 28.7, 28.9, 29.9, 31.5, 33.8, 70.6, 125.7, 127.8, 129.1, 129.8, 131.1, 131.4, 133.2, 137.7, 142.6, 144.6, 202.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{27}O_4S$: 375.1630; found: 375.1632.

1-[2-(6-Bromohexyl)phenyl]ethanone (3ag′)
Light-yellow oil; yield: 15.0 mg (18%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41–1.49 (m, 4 H), 1.54–1.63 (m, 2 H), 1.83–1.90 (m, 2 H), 2.84 (s, 3 H), 2.84 (t, *J* = 7.6 Hz, 2 H), 3.40 (t, *J* = 6.8 Hz, 2 H), 7.24–7.27 (m, 2 H), 7.39 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H), 7.64 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 28.8, 29.9, 31.5, 32.7, 33.89, 33.93, 125.7, 129.1, 131.1, 131.3, 137.8, 142.7, 202.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}BrO$: 283.0698; found: 283.0697.

1-{2-[3-(4-Fluorophenyl)propyl]phenyl}ethanone (3ah)
Light-yellow oil; yield: 59.2 mg (77%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85–1.93 (m, 2 H), 2.57 (s, 3 H), 2.67 (t, *J* = 7.6 Hz, 2 H), 2.89 (t, *J* = 7.6 Hz, 2 H), 6.96 (t, *J* = 8.4 Hz, 2 H), 7.13–7.17 (m, 2 H), 7.23–7.29 (m, 2 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.66 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.8, 33.4, 33.7, 35.0, 118.9 (d, $^2J_{C–F}$ = 21 Hz), 125.8, 129.2, 129.6 (d, $^3J_{C–F}$ = 8 Hz), 131.1, 131.4, 137.7, 137.9 (d, $^4J_{C–F}$ = 4 Hz), 142.3, 161.1 (d, $^1J_{C–F}$ = 241 Hz), 202.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}FO$: 257.1338; found: 257.1342.

1-{2-[3-(4-Chlorophenyl)propyl]phenyl}ethanone (3ai)
Light-yellow oil; yield: 49.9 mg (61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82–1.93 (m, 2 H), 2.57 (s, 3 H), 2.66 (t, *J* = 7.6 Hz, 2 H), 2.88 (t, *J* = 7.6 Hz, 2 H), 7.13 (d, *J* = 8.4 Hz, 2 H), 7.22–7.29 (m, 4 H), 7.39 (td, *J* = 7.6 Hz, 1.2 Hz, 1 H), 7.66 (dd, *J* = 7.6 Hz, 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.8, 33.2, 33.7, 35.2, 125.9, 128.3, 129.3, 129.8, 131.2, 131.4, 131.5, 137.7, 140.8, 142.3, 202.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}ClO$: 273.1045; found: 273.1046.

1-[2-(2,2-Dimethylpropyl)phenyl]ethanone (3aj)
Light-yellow oil; yield: 49.3 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (s, 9 H), 2.56 (s, 3 H), 2.94 (s, 2 H), 7.19 (d, *J* = 7.6 Hz, 1 H), 7.23–7.27 (m, 1 H), 7.35 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H), 7.54 (dd, *J* = 7.6 Hz, *J* = 0.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4, 30.2, 32.6, 44.4, 125.7, 127.9, 130.0, 133.3, 138.5, 140.4, 203.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{19}O$: 191.1436; found: 191.1431.

1-{2-[(Trimethylsilyl)methyl]phenyl}ethanone (3ak)
Light-yellow oil; yield: 40.4 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.05 (s, 9 H), 2.56 (s, 3 H), 2.62 (s, 2 H), 7.06 (d, *J* = 7.6 Hz, 1 H), 7.14 (t, *J* = 6.8 Hz, 1 H), 7.30 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1 H), 7.69 (dd, *J* = 7.6 Hz, *J* = 0.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.6, 25.2, 29.5, 123.7, 130.0, 131.0, 131.3, 135.5, 142.3, 201.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{19}OSi$: 207.1205; found: 207.1201.

1-[2-(Cyclopentylmethyl)phenyl]ethanone (3al)
Yellow oil; yield: 52.7 mg (87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13–1.21 (m, 2 H), 1.47–1.54 (m, 2 H), 1.57–1.69 (m, 4 H), 2.00–2.08 (m, 1 H), 2.57 (s, 3 H), 2.89 (d, *J* = 7.3 Hz, 2 H), 7.22–7.26 (m, 2 H), 7.37 (t, *J* = 7.8 Hz, 1 H), 7.60 (d, *J* = 7.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.0, 30.3, 32.7, 39.5, 42.1, 125.8, 129.0, 131.2, 131.7, 138.5, 142.3, 202.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{19}O$: 203.1436; found: 203.1436.

5-(2-Acetylphenyl)pentan-2-one (3am)
Orange oil; yield: 42.1 mg (69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83–1.89 (m, 2 H), 2.12 (s, 3 H), 2.47 (t, *J* = 7.6 Hz, 2 H), 2.56 (s, 3 H), 2.82 (t, *J* = 7.6 Hz, 2 H), 7.24–7.28 (m, 2 H), 7.37 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.6, 29.7, 29.8, 33.1, 43.3, 125.9, 129.3, 131.2, 131.5, 137.6, 141.9, 201.9, 208.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{17}O_2$: 205.1229; found: 205.1224.

1-[2-(6-Oxo-6-pyrrolidin-1-ylhexyl)phenyl]ethanone (3an)
Obtained as a mixture with 1-(6-bromohexanoyl)pyrrolidine and 1-[(4*E*)-hex-4-enoyl]pyrrolidine; yield: 41% (by weight and ^{1}H NMR analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38–1.45 (m, 2 H), 1.55–1.70 (m, 4 H), 1.82–1.87 (m, 2 H), 1.90–1.95 (m, 2 H), 2.26 (t, *J* = 8.0 Hz, 2 H), 2.56 (s, 3 H), 2.83 (t, *J* = 8.0 Hz, 2 H), 3.40 (t, *J* = 6.8 Hz, 2 H), 3.45 (t, *J* = 6.8 Hz, 2 H), 7.23–7.25 (m, 2 H), 7.38 (t, *J* = 7.6 Hz, 1 H), 7.61 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.4, 24.8, 26.1, 29.5, 29.9, 31.5, 33.9, 34.7, 45.6, 46.6, 125.6, 129.0, 131.2, 131.3, 137.9, 142.6, 171.9, 202.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{26}NO_2$: 288.1964; found: 288.1965.

1-[2-(3-Pyridin-3-ylpropyl)phenyl]ethanone (3ao)
Obtained as a mixture with 4-methoxyaniline; yield: 19% (by weight and ^{1}H NMR analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.89–1.95 (m, 2 H), 2.57 (s, 3 H), 2.69 (t, *J* = 8.0 Hz, 2 H), 2.90 (t, *J* = 8.0 Hz, 2 H), 7.18–7.30 (m, 3 H), 7.40 (td, *J* = 7.6 Hz, 1.2 Hz, 1 H), 7.51 (dd, *J* = 7.6 Hz, 1.0 Hz, 1 H), 7.68 (dd, *J* = 7.6 Hz, 1.2 Hz, 1 H), 8.43 (d, *J* = 4.0 Hz, 1 H), 8.45 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 33.0 (two signals overlapping), 33.8, 123.2, 126.0, 129.4, 131.2, 131.5, 135.8, 137.5, 139.9, 147.2, 149.9, 152.8, 201.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{18}NO$: 240.1388; found: 240.1386.

1-(2-Cyclobutylphenyl)ethanone (3ap)
Light-yellow oil; yield: 26.5 mg (51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69–1.82 (m, 1 H), 1.96–2.17 (m, 3 H), 2.32–2.38 (m, 2 H), 2.54 (s, 3 H), 4.02 (m, 1 H), 7.21–7.25 (m, 1 H), 7.40–7.46 (m, 2 H), 7.51 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 29.4, 30.0, 38.1, 125.4, 127.2, 127.8, 131.0, 138.2, 144.9, 203.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{15}O$: 175.1123; found: 175.1125.

1-(2-Cyclopentylphenyl)ethanone (3aq)[34]
Light-yellow oil; yield: 35.7 mg (63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54–1.62 (m, 2 H), 1.66–1.71 (m, 2 H), 1.78–1.83 (m, 2 H), 2.03–2.09 (m, 2 H), 2.57 (s, 3 H), 3.43–3.48 (m, 1 H), 7.19–7.23 (m, 1 H), 7.39–7.41 (m, 2 H), 7.45 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 30.7, 35.1, 41.5, 125.2, 127.1, 127.3, 130.9, 139.9, 145.2, 204.0.

1-(2-Cyclohexylphenyl)ethanone (3ar)[34]
Light-yellow oil; yield: 44.2 mg (73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.21 (m, 1 H), 1.39–1.44 (m, 4 H), 1.73–1.85 (m, 5 H), 2.57 (s, 3 H), 3.00–3.07 (m, 1 H), 7.20–7.24 (m, 1 H), 7.37–7.40 (m, 2 H), 7.47 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.2, 26.9, 30.8, 34.5, 40.0, 125.3, 127.1, 127.6, 130.9, 139.1, 146.6, 203.8.

1-(2-Cycloheptylphenyl)ethanone (3as)
Light-yellow oil; yield: 54.6 mg (84%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53–1.71 (m, 8 H), 1.76–1.80 (m, 2 H), 1.87–1.92 (m, 2 H), 2.57 (s, 3 H), 3.15–3.20 (m, 1 H), 7.17–7.22 (m, 1 H), 7.35–7.41 (m, 2 H), 7.45 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.4, 27.7, 30.7, 36.9, 41.6, 125.0, 127.37, 127.42, 131.0, 138.2, 148.7, 203.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{21}O$: 217.1592; found: 217.1593.

1-(2-Cyclododecylphenyl)ethanone (3at)
Light-yellow oil; yield: 55.9 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36–1.75 (m, 20 H), 1.75–1.82 (m, 2 H), 2.56 (s, 3 H), 3.39–3.42 (m, 1 H), 7.18–7.22 (m, 1 H), 7.38–7.43 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 23.0, 23.2, 24.0 (two signals overlapping), 30.8, 31.8, 34.1, 125.1, 126.9, 128.0, 130.6, 140.3, 146.1, 204.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{31}O$: 287.2375; found: 287.2377.

***tert*-Butyl 4-(2-Acetylphenyl)piperidine-1-carboxylate (3au)**
Brown oil; yield: 38.4 mg (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 9 H), 1.58–1.63 (m, 2 H), 1.77–1.80 (m, 2 H), 2.57 (s, 3 H), 2.73–2.84 (m, 2 H), 3.29 (tt, *J* = 12.0 Hz, 3.3 Hz, 1 H), 4.18–4.23 (br s, 2 H), 7.26 (t, *J* = 7.4 Hz, 1 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 7.2 Hz, 1 H), 7.57 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5, 30.4, 33.2, 38.0, 44.5, 79.4, 125.8, 127.2, 128.4, 131.4, 138.4, 145.0, 154.9, 203.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{26}NO_3$: 304.1913; found: 304.1916.

1-(2-Isopropylphenyl)ethanone (3av)[35]
Light-yellow oil; yield: 31.5 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 6.8 Hz, 6 H), 2.57 (s, 3 H), 3.47 (septet, *J* = 6.8 Hz, 1 H), 7.22–7.25 (m, 1 H), 7.41–7.43 (m, 2 H), 7.48 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.1, 29.2, 30.7, 125.3, 126.5, 127.6, 131.0, 138.9, 147.6, 203.7.

1-(2-(*sec*-Butyl)phenyl)ethanone (3aw)
Light-yellow oil; yield: 29.6 mg (56%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.6 Hz, 3 H), 1.23 (d, *J* = 6.8 Hz, 3 H), 1.53–1.67 (m, 2 H), 2.56 (s, 3 H), 3.17 (app. sextet, *J* = 7.0 Hz, 1 H), 7.22 (td, *J* = 7.6 Hz, *J* = 1.6 Hz, 1 H), 7.35 (d, *J* = 7.6 Hz, 1 H), 7.39–7.46 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.2, 22.0, 30.8, 31.1, 36.2, 125.3, 126.8, 127.3, 130.8, 139.8, 146.4, 203.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{17}O$: 177.1279; found: 177.1274.

1-[2-(1-Ethylpropyl)phenyl]ethanone (3ax)
Light-yellow oil; yield: 36.1 mg (63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77 (t, *J* = 7.4 Hz, 6 H), 1.52–1.61 (m, 2 H), 1.63–1.72 (m, 2 H), 2.54 (s, 3 H), 2.94–3.02 (m, 1 H), 7.22 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H), 7.31 (d, *J* = 7.6 Hz, 1 H), 7.38–7.44 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.0, 29.3, 31.1, 43.2, 125.2, 126.9, 127.0, 130.6, 141.2, 144.4, 204.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}O$: 191.1436; found: 191.1438.

1-[2-(1-Methyl-3-phenylpropyl)phenyl]ethanone (3ay)
Light-yellow oil; yield: 57.8 mg (76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 6.8 Hz, 3 H), 1.86–2.02 (m, 2 H), 2.46–2.52 (m, 1 H), 2.53 (s, 3 H), 2.57–2.62 (m, 1 H), 3.33–3.89 (m, 1 H), 7.12–7.14 (m, 2 H), 7.17 (d, *J* = 7.6 Hz, 1 H), 7.24–7.28 (m, 3 H), 7.42–7.45 (m, 2 H), 7.50 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5, 30.6, 34.0, 34.3, 40.0, 125.5, 125.6, 126.8, 127.5, 128.2 (two signals overlapping), 131.0, 139.6, 142.4, 146.1, 203.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}O$: 253.1592; found: 253.1594.

1-{2-[3-(4-Methoxyphenyl)-1-methylpropyl]phenyl}ethanone (3az)
Light-yellow oil; yield: 51.4 mg (61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.8 Hz, 3 H), 1.87–1.95 (m, 2 H), 2.37–2.45 (m, 1 H), 2.48–2.56 (m, 4 H), 3.30–3.36 (m, 1 H), 3.78 (s, 3 H), 6.80 (d, *J* = 8.4 Hz, 2 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 7.25–7.27 (m, 1 H), 7.42–7.44 (m, 2 H), 7.49 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 30.7, 33.2, 34.4, 40.3, 55.3, 113.7, 125.5, 126.9, 127.6, 129.2, 131.1, 134.6, 139.7, 146.2, 157.7, 203.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}O$: 283.1698; found: 283.1703.

1-{2-[3-(4-Chlorophenyl)-1-methylpropyl]phenyl}ethanone (3aaa)
Light-yellow oil; yield: 64.5 mg (75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.8 Hz, 3 H), 1.83–1.95 (m, 2 H), 2.39–2.47 (m, 1 H), 2.51–2.59 (m, 4 H), 3.33–3.38 (m, 1 H), 7.04 (d, *J* = 8.4 Hz, 2 H), 7.10 (d, *J* = 8.4 Hz, 2 H), 7.23–7.27 (m, 1 H), 7.39–7.47 (m, 2 H), 7.50 (dd, *J* = 1.2 Hz, 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5, 30.6, 33.4, 34.2, 39.9, 125.5, 126.7, 127.7, 128.3, 129.6, 131.1, 131.3, 139.4, 140.9, 146.0, 203.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{20}ClO$: 287.1203; found: 287.1203.

1-[2-(*exo*-Bicyclo[2.2.1]heptan-2-yl)phenyl]ethanone (3aab)[3c]
Light-yellow oil; yield: 52.6 mg (82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21–1.32 (m, 2 H), 1.37–1.43 (m, 1 H), 1.47–1.51 (m, 1 H), 1.53–1.61 (m, 3 H), 1.68–1.86 (m, 1 H), 2.35 (d, *J* = 18.4 Hz, 2 H), 2.56 (s, 3 H), 3.19 (dd, *J* = 8.9 Hz, 6.0 Hz, 1 H), 7.20 (td, *J* = 8.0 Hz, *J* = 1.6 Hz, 1 H), 7.36–7.42 (m, 2 H), 7.49 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.7, 30.4, 30.6, 36.6, 37.0, 40.2, 42.6, 43.4, 125.0, 126.4, 128.0, 130.7, 139.3, 146.2, 203.7.

1-(2-Cycloheptyl-4-methoxyphenyl)ethanone (3br)
The reaction was performed on a 10 mmol scale to give a light-yellow oil; yield: 2.10 g (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56–1.63 (m, 6 H), 1.69–1.78 (m, 4 H), 1.87–1.92 (m, 2 H), 2.54 (s, 3 H), 3.45–3.50 (m, 1 H), 3.83 (s, 3 H), 6.70 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1 H), 6.88 (d, *J* = 2.8 Hz, 1 H), 7.59 (d, *J* = 8.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.5, 27.7, 30.0, 36.9, 41.1, 55.2, 109.6, 113.3, 129.9, 131.2, 153.0, 161.9, 201.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{23}O_2$: 247.1698; found: 247.1693.

1-(2-Cyclobutyl-4-fluorophenyl)ethanone (3co)
Light-yellow oil; yield: 30.4 mg (53%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77–1.80 (m, 1 H), 1.80–1.81 (m, 3 H), 1.98–2.39 (m, 2 H), 2.53 (s, 3 H), 4.04–4.08 (m, 1 H), 6.90 (td, *J* = 8.0 Hz, *J* = 2.4 Hz, 1 H), 7.09 (dd, *J* = 10.8 Hz, *J* = 2.4 Hz, 1 H), 7.57 (dd, *J* = 8.8 Hz, *J* = 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 29.3, 29.8, 38.1, 112.1 (d, $^2J_{C–F}$ = 21 Hz), 114.6 (d, $^2J_{C–F}$ = 21 Hz), 130.9 (d, $^3J_{C–F}$ = 9 Hz), 134.0, 149.2 (d, $^3J_{C–F}$ = 8 Hz), 164.4 (d, $^1J_{C–F}$ = 250 Hz), 200.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}FO$: 193.1029; found: 193.1032.

1-(4-Chloro-2-cyclohexylphenyl)ethanone (3dq)
Orange oil; yield: 45.9 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23–1.29 (m, 1 H), 1.36–1.43 (m, 4 H), 1.73–1.83 (m, 5 H), 2.55 (s, 3 H), 3.08–3.11 (m, 1 H), 7.20 (dd, *J* = 8.4 Hz, 2.0 Hz, 1 H), 7.35 (d, *J* = 2.0 Hz, 1 H), 7.44 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 26.7, 30.6, 34.4, 39.8, 125.5, 127.6, 129.3, 137.0, 137.1, 149.1, 202.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}ClO$: 237.1046; found: 237.1041.

1-(3-Cyclopentylbiphenyl-4-yl)ethanone (3ep)
Yellow solid; yield: 67.6 mg (85%); mp 78.5–79.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65–1.75 (m, 4 H), 1.84–1.87 (m, 2 H), 2.13–2.15 (m, 2 H), 2.62 (s, 3 H), 3.07–3.63 (m, 1 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.44–7.49 (m, 3 H), 7.58–7.65 (m, 3 H), 7.60 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 30.5, 35.1, 41.5, 124.0, 126.0, 127.2, 127.8, 128.3, 128.8, 138.3, 140.5, 143.8, 146.2, 203.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{21}O$: 265.1592; found: 265.1591.

1-(2-Cyclohexyl-5-methylphenyl)ethanone (3fq)
Light-yellow oil; yield: 38.1 mg (53%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22–1.29 (m, 1 H), 1.34–1.45 (m, 4 H), 1.73–1.83 (m, 5 H), 2.34 (s, 3 H), 2.55 (s, 3 H), 2.97–3.01 (m, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.26 (s, 1 H), 7.27 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 26.2, 26.9, 30.7, 34.6, 39.6, 127.0, 128.1, 131.6, 134.8, 139.1, 143.5, 203.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{21}O$: 217.1592; found: 217.1593.

1-(3-Cyclohexylnaphthalen-2-yl)ethanone (3gq)
Yellow oil; yield: 42.6 mg (56%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.35 (m, 1 H), 1.42–1.55 (m, 4 H), 1.78–1.98 (m, 5 H), 2.70 (s, 3 H), 3.21–3.27 (m, 1 H), 7.46 (td, *J* = 8.0 Hz, *J* = 1.2 Hz, 1 H), 7.53 (td, *J* = 8.0 Hz, *J* = 1.2 Hz, 1 H), 7.78 (s, 1 H), 7.83 (t, *J* = 8.0 Hz, 2 H), 8.03 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3, 27.0, 30.6, 34.9, 39.6, 125.7, 125.9, 127.4, 127.6, 128.2, 128.6, 130.6, 134.5, 137.9, 143.7, 203.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}O$: 253.1592; found: 253.1591.

1-(2-Cyclobutyl-9*H*-fluoren-3-yl)ethanone (3ho)
Light-yellow oil; yield: 59.2 mg (75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85–1.90 (m, 1 H), 2.02–2.19 (m, 1 H), 2.14–2.19 (m, 2 H), 2.41–2.48 (m, 2 H), 2.61 (s, 3 H), 3.88 (s, 2 H), 4.13–4.18 (m, 1 H), 7.35 (t, *J* = 6.8 Hz, 1 H), 7.42 (t, *J* = 7.2 Hz, 1 H), 7.56 (d, *J* = 7.6 Hz, 1 H), 7.71 (s, 1 H), 7.80 (s, 1 H), 7.86 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 29.6, 29.9, 36.5, 38.4, 118.4, 120.4, 124.8, 125.1, 126.8, 127.5, 136.5, 139.9, 140.8, 144.30, 144.33, 144.4, 202.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{19}O$: 263.1436; found: 263.1435.

1-(4-Cyclopentyl-1,3-benzodioxol-5-yl)ethanone (3ip)
Pale-yellow solid; obtained partially in a pure form [yield: 17.2 mg (25%)] and partially as a mixture with its regioisomer [yield: 13.9 mg (20%), ratio = 64:36]; mp 65.8–66.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.60–1.64 (m, 2 H), 1.80–1.93 (m, 6 H), 2.53 (s, 3 H), 3.45–3.54 (m, 1 H), 5.98 (s, 2 H), 6.68 (d, *J* = 8.0 Hz, 1 H), 7.12 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4, 30.4, 31.9, 38.6, 101.0, 105.3, 123.5, 128.4, 134.6, 146.4, 149.7, 201.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}O_3$: 233.1178; found: 233.1178.

8-Cycloheptyl-3,4-dihydronaphthalen-1(2*H*)-one (3jr)
Orange oil; yield: 59.4 mg (81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55–1.65 (m, 6 H), 1.70–1.82 (m, 4 H), 1.88–1.91 (m, 2 H), 2.03–2.10 (m, 2 H), 2.66 (t, *J* = 6.8 Hz, 2 H), 2.92 (t, *J* = 6.0 Hz, 2 H), 3.84–3.89 (m, 1 H), 7.04 (d, *J* = 7.6 Hz, 1 H), 7.27 (d, *J* = 6.4 Hz, 1 H), 7.34 (t, *J* = 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 27.7, 27.8, 31.2, 37.0, 40.8, 41.3, 125.8, 125.9, 130.3, 132.2, 145.1, 153.2, 200.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{23}O$: 243.1749; found: 243.1750.

1-(2-Cyclohexylphenyl)propan-1-one (3kq)
Light-yellow oil; yield: 51.8 mg (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.2 Hz, 3 H), 1.22–1.30 (m, 1 H), 1.37–1.44 (m, 4 H), 1.73–1.84 (m, 5 H), 2.86 (q, *J* = 7.2 Hz, 2 H), 2.83–2.89 (m, 1 H), 7.19–7.23 (m, 1 H), 7.37–7.39 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.4, 26.2, 26.8, 34.6, 36.3, 40.2, 125.3, 126.7, 127.0, 130.4, 139.6, 146.0, 207.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{21}O$: 217.1592; found: 217.1595.

1-(2-Cyclobutyl-3-thienyl)ethanone (3lo)
Light-yellow oil; yield: 15.1 mg (24%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84–1.90 (m, 1 H), 1.98–2.12 (m, 3 H), 2.48 (s, 3 H), 2.49–2.53 (m, 2 H), 4.34–4.40 (m, 1 H), 7.06 (d, *J* = 5.6 Hz, 1 H), 7.35 (d, *J* = 5.6 Hz, 1 H)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 29.8, 31.2, 36.0, 121.1, 129.4, 134.6, 160.3, 193.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{13}OS$: 181.0687; found: 181.0692.

2-Cyclohexyl-1-methyl-1*H*-indole-3-carbaldehyde (3mq)
Brown oil; yield: 32.4 mg (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.47 (m, 3 H), 1.84–2.05 (m, 7 H), 3.20–3.26 (m, 1 H), 3.80 (s, 3 H), 7.28–7.29 (m, 3 H), 8.36–8.38 (m, 1 H), 10.4 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 27.0, 30.9, 32.9, 37.4, 109.3, 114.0, 121.7, 122.9, 123.2, 126.1, 136.9, 155.2, 184.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO$: 242.1545; found: 242.1545.

(2-Ethynyl-5-methoxyphenyl)cycloheptane (4)
A solution of LDA in THF (10 mL) was prepared from *i*-$PrNH_2$ (148.7 mg, 1.47 mmol) and a 1.6 M solution of BuLi hexane (1.30 mL, 1.47 mmol) at 0 °C. A solution of ketone **3br** (350 mg, 1.4 mmol) in THF (5 mL) was added dropwise to the LDA solution at –78 °C, and the resulting mixture was stirred for 1 h. $ClP(O)(OEt)_2$ (265.7 mg, 1.54 mmol) was added, and the mixture was gradually warmed to r.t. and then added dropwise to a solution of LDA (3.15 mmol) in THF (prepared as above) at –78 °C. The resulting mixture was warmed to r.t. over 3 h and the reaction was quenched with H_2O. The mixture was extracted with hexane (3 × 10 mL) and the extracts were washed successively with 1 M HCl (10 mL), H_2O (10 mL), and aq $NaHCO_3$ (10 mL). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane–EtOAc (10:1)] to give a yellow oil; yield: 181.7 mg (56%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.60–1.66 (m, 6 H), 1.70–1.74 (m, 2 H), 1.78–1.84 (m, 2 H), 1.91–1.96 (m, 2 H), 3.18 (s, 1 H), 3.20–3.25 (m, 1 H), 3.80 (s, 3 H), 6.66 (dd, *J* = 8.4 Hz, 2.4 Hz, 1 H), 6.77 (d, *J* = 2.4 Hz, 1 H), 7.40 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.5, 27.8, 35.8, 43.8, 55.2, 79.2, 82.6, 110.4, 111.9, 112.8, 134.2, 154.1, 160.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{21}O$: 229.1592; found: 229.1593.

6′-Methoxyspiro[cycloheptane-1,1′-indene] (5)
A mixture of alkyne **4** (68.5 mg, 0.30 mmol), CuBr (86.1 mg, 0.60 mmol), and $PtCl_2$ (8.0 mg, 0.03 mmol) in toluene (3 mL) was stirred at 100 °C for 24 h. When the reaction was complete, the dark solid was removed from the mixture by filtration through a pad of Celite, which was then washed with Et_2O (3 × 5 mL). The combined filtrate was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane–EtOAc (10:1 to 5:1)] to give a yellow oil; yield: 53.0 mg (77%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55–1.60 (m, 2 H), 1.67–1.79 (m, 6 H), 1.81–1.85 (m, 4 H), 3.83 (s, 3 H), 6.51 (d, *J* = 5.6 Hz, 1 H), 6.59 (d, *J* = 5.6 Hz, 1 H), 6.75 (dd, *J* = 8.0 Hz, 2.4 Hz, 1 H), 6.96 (d, *J* = 2.0 Hz, 1 H), 7.16 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.5, 29.9, 36.9, 55.5, 56.8, 108.8, 110.9, 121.3, 127.6, 135.4, 143.8, 156.9, 158.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{21}O$: 229.1592; found: 229.1592.

1-(2-Cycloheptyl-4-methoxyphenyl)-2-diazoethanone (6)
A solution of ketone **3br** (289 mg, 1.2 mmol) in THF (5 mL) was added over 1 min to a 1.0 M solution of LiHMDS (1.30 mL) in THF (10 mL) at –78 °C. The mixture was stirred for 30 min and then $F_3CCO_2CH_2CF_3$ (282.3 mg, 1.44 mmol) was added over 2–3 min. The mixture was stirred for a further 3 h, allowed to warm to r.t., and poured into a separatory funnel together with Et_2O (10 mL) and 5% aq HCl (20 mL). The separated aqueous layer was extracted with Et_2O (30 mL), and the organic layers were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give a yellow oil. This oil was placed in a dry, 50 mL, three-necked, round bottomed flask under N_2 and dissolved in MeCN (10 mL). H_2O (0.02 mL) and Et_3N (0.25 mL) were added, followed by dropwise addition of a solution of 4-$AcNHC_6H_4SO_2N_3$ (432.4 mg, 1.8 mmol) in MeCN (10 mL). The resulting solution was stirred at r.t. for 8 h, then poured into a separatory funnel with Et_2O (20 mL). The organic layer was washed successively with 5% aq NaOH (3 × 20 mL), H_2O (3 × 20 mL), and brine, then dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane–EtOAc (30:1 to 5:1)] to give a yellow oil; yield: 240.9 mg (75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53–1.61 (m, 6 H), 1.63–1.70 (m, 2 H), 1.72–1.77 (m, 2 H), 1.87–2.00 (m, 2 H), 3.24–3.37 (m, 1 H), 3.77 (s, 3 H), 5.52 (s, 1 H), 6.64 (dd, *J* = 2.4 Hz, 8.4 Hz, 1 H), 6.84 (d, *J* = 2.4 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2, 27.6, 36.7, 41.3, 55.0, 56.1, 109.8, 113.0, 128.8, 129.1, 151.2, 161.4, 189.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{21}N_2O_2$: 273.1602; found: 273.1603.

6′-Methoxyspiro[cycloheptane-1,1′-inden]-3′(2′*H*)-one (7)
A solution of diazo compound **6** (81.7 mg, 0.30 mmol) in CH_2Cl_2 (22.5 mL) was added dropwise to a suspension of $Rh_2(OAc)_4$ (2.7 mg, 6 μmol) in CH_2Cl_2 (7.5 mL) at r.t. over 6 h by using a syringe pump. The resulting mixture was stirred for an additional 3 h and then concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane–EtOAc (10:1)] to give a yellow oil; yield: 26.2 mg (36%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56–1.62 (m, 2 H), 1.65–1.72 (m, 6 H), 1.75–1.79 (m, 2 H), 1.90 (t, *J* = 12.0 Hz, 2 H), 2.60 (s, 2 H), 3.89 (s, 3 H), 6.87 (dd, *J* = 8.0 Hz, 2.4 Hz, 1 H), 6.93 (d, *J* = 2.4 Hz, 1 H), 7.62 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.6, 28.5, 41.9, 45.8, 50.3, 55.6, 107.6, 114.7, 125.1, 128.2, 165.4, 168.2, 204.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{21}O_2$: 245.1542; found: 245.1544.

2-(2-Octylphenyl)pyridine (9aa)[2d]
Yellow oil; yield: 57.3 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 3 H), 1.17–1.26 (m, 10 H), 1.43–1.47 (m, 2 H), 2.70 (t, *J* = 8.0 Hz, 2 H), 7.23–7.39 (m, 6 H), 7.71–7.76 (m, 1 H), 8.69 (d, *J* = 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 29.1, 29.2, 29.4, 31.2, 31.8, 32.9, 121.5, 124.1, 125.7, 128.2, 129.66, 129.68, 136.0, 140.3, 140.8, 149.1, 160.3.

2-(2,6-Dioctylphenyl)pyridine (10aa)
Obtained as a mixture with 2-[2-(2,2-dimethylpropyl)-6-(2-phenylethyl)phenyl]pyridine; yield: 76% (by weight and ^{1}H NMR analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.3 Hz, 6 H), 1.11–1.16 (m, 16 H), 1.21–1.25 (m, 4 H), 1.37–1.42 (m, 4 H), 2.29 (t, *J* = 7.8 Hz, 4 H), 7.11 (d, *J* = 7.8 Hz, 2 H), 7.22–7.26 (m, 3 H), 7.72 (td, *J* = 7.8, 1.8 Hz, 1 H), 8.69–8.71 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.8, 29.3, 29.4, 29.7, 31.3, 32.0, 33.8, 121.7, 125.2, 126.7, 128.1, 135.9, 140.0, 140.1, 149.5, 159.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{42}N$: 380.3317; found: 380.3316.

2-[2-(2,2-Dimethylpropyl)phenyl]pyridine (9aj)[7a]
Colorless oil; yield: 48.4 mg (72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.64 (s, 9 H), 2.88 (s, 2 H), 7.19–7.39 (m, 6 H), 7.71 (td, *J* = 7.8 Hz, 1.8 Hz, 1 H), 8.66–8.68 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 33.0, 45.1, 121.6, 125.0, 126.2, 127.6, 130.3, 132.6, 136.2, 137.7, 141.7, 149.1, 161.5.

2-(2,6-Diisopropyl-4-methoxyphenyl)pyridine (10bv)
Light-yellow solid; yield: 69.3 mg (86%); mp 81.6–82.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (d, *J* = 6.8 Hz, 6 H), 1.11 (d, *J* = 6.8 Hz, 6 H), 2.47–2.54 (m, 2 H), 3.85 (s, 3 H), 6.75 (s, 2 H), 7.24 (t, *J* = 7.6 Hz, 2 H), 7.68–7.73 (m, 1 H), 8.69–8.71 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.7, 24.0, 55.1, 108.1, 121.4, 125.4, 131.7, 135.6, 148.1, 149.3, 159.6, 159.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{24}NO$: 270.1858; found: 270.1859.

2-(2,6-Dicyclobutyl-4-fluorophenyl)pyridine (10cp)
Yellow solid; yield: 59.2 mg (70%); mp 62.3–63.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63–1.69 (m, 3 H), 1.71–1.82 (m, 5 H), 1.91 (t, *J* = 9.2 Hz, 2 H), 1.97–2.06 (m, 2 H), 3.26–3.33 (m, 2 H), 6.93 (d, J_{H-F} = 10.0 Hz, 2 H), 7.15 (d, *J* = 7.6 Hz, 1 H), 7.23–7.26 (m, 1 H), 7.68–7.72 (m, 1 H), 8.68 (d, *J* = 5.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 29.2, 29.8, 38.4 (d, $^4J_{C-F}$ = 1 Hz), 110.3 (d, $^2J_{C-F}$ = 21 Hz), 121.7, 125.3, 134.1, 135.7, 146.1 (d, $^3J_{C-F}$ = 8 Hz), 149.3, 158.8, 163.0 (d, $^1J_{C-F}$ = 243 Hz).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{21}FN$: 282.1658; found: 282.1657.

2-[2,6-Dicyclohexyl-4-(trifluoromethyl)phenyl]pyridine (10dr)
White solid; yield: 45.4 mg (39%); mp 140.8–142.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94–1.06 (m, 4 H), 1.12–1.23 (m, 2 H), 1.31–1.43 (m, 4 H), 1.58–1.70 (m, 8 H), 1.82 (d, *J* = 12.4 Hz, 2 H), 2.08 (tt, *J* = 3.0 Hz, 11.6 Hz, 2 H), 7.20 (d, *J* = 8.0 Hz, 1 H), 7.29–7.32 (m, 1 H), 7.38–7.46 (m, 2 H), 7.72–7.78 (m, 1 H), 8.71 (d, *J* = 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9, 26.6, 26.7, 33.8, 34.3, 41.2, 120.3 (q, $^3J_{C-F}$ = 4 Hz), 122.0, 124.4, 127.0 (q, $^1J_{C-F}$ = 248 Hz), 130.3 (q, $^2J_{C-F}$ = 31 Hz), 135.8, 142.3, 146.6, 149.4, 158.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{29}F_3N$: 388.2252; found: 388.2255.

2-(2-Cyclobutyl-5-methylphenyl)pyridine (10ep)
Yellow oil; yield: 57.9 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.71–1.73 (m, 1 H), 1.82–1.87 (m, 1 H), 1.98–2.06 (m, 4 H), 2.37 (s, 3 H), 3.76–3.81 (m, 1 H), 7.17 (s, 1 H), 7.19–7.25 (m, 2 H), 7.32–7.35 (m, 2 H), 7.68–7.73 (m, 1 H), 8.67–8.69 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.2, 20.9, 30.0, 37.7, 121.5, 124.1, 126.5, 129.0, 130.1, 135.1, 135.8, 139.6, 140.7, 149.2, 160.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{18}N$: 224.1439; found: 224.1441.

2-(3-Chloro-2-cyclohexylphenyl)pyridine (10fr)
Light-yellow oil; yield: 38.3 mg (47%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13–1.23 (m, 3 H), 1.35–1.44 (m, 2 H), 1.65–1.80 (m, 5 H), 2.70 (tt, *J* = 2.8 Hz, 11.6 Hz, 1 H), 7.26–

7.29 (m, 1 H), 7.30–7.34 (m, 4 H), 7.73–7.77 (m, 1 H), 8.69–8.70 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 26.7, 34.3, 39.5, 122.0, 124.1, 127.9, 128.4, 129.6, 131.1, 136.1, 141.5, 144.1, 149.4, 158.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{19}ClN$: 272.1206; found: 272.1205.

2-(2-Cyclobutyl-4-methoxyphenyl)-3-methylpyridine (10gp)
Light-yellow oil; yield: 57.9 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65–1.78 (m, 3 H), 1.82–2.09 (m, 3 H), 2.09 (s, 3 H), 3.38–3.47 (m, 1 H), 3.85 (s, 3 H), 6.77 (dd, *J* = 2.4 Hz, 8.4 Hz, 1 H), 6.94 (d, *J* = 2.4 Hz, 1 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 7.15 (dd, *J* = 4.8 Hz, 7.6 Hz, 1 H), 7.53 (d, *J* = 6.8 Hz, 1 H), 8.46–8.48 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0, 19.3, 29.3, 38.1, 55.2, 110.3, 112.3, 121.9, 129.6, 131.8, 131.9, 137.4, 145.2, 146.4, 159.3, 159.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{20}NO$: 254.1545; found: 254.1541.

2-(2-Isopropyl-6-methylphenyl)pyridine (10hv)
Obtained as a mixture with 2-(4-tolyl)pyridine (**8h**); yield: 89% (by weight and ^{1}H NMR analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 4.8 Hz, 3 H), 1.13 (d, *J* = 4.8 Hz, 3 H), 2.00 (s, 3 H), 2.57–2.64 (m, 1 H), 7.10 (d, *J* = 7.2 Hz, 1 H), 7.11–7.31 (m, 4 H), 7.72–7.77 (m, 1 H), 8.72–8.73 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 23.91, 23.94, 30.1, 121.5, 122.7, 124.5, 127.2, 128.2, 135.6, 136.0, 139.5, 146.4, 149.5, 159.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{18}N$: 212.1439; found: 212.1440.

10-Cyclopentylbenzo[*h*]quinoline (10iq)
Light-yellow oil; yield: 59.5 mg (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74–1.81 (m, 2 H), 1.86–1.96 (m, 4 H), 2.37–2.43 (m, 2 H), 5.71–5.75 (m, 1 H), 7.47 (dd, *J* = 4.4 Hz, 8.0 Hz, 1 H), 7.62–7.67 (m, 2 H), 7.79 (t, *J* = 8.4 Hz, 2 H), 7.85 (d, *J* = 7.6 Hz, 1 H), 8.14 (dd, *J* = 2.0 Hz, 8.0 Hz, 1 H), 9.02–9.03 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.7, 34.7, 43.5, 120.5, 125.3, 126.0, 126.5, 127.4, 127.6, 129.1, 129.4, 135.3, 135.4, 146.9, 147.2, 148.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{18}N$: 248.1439; found: 248.1437.

2-(3-Cyclopentyl-2-thienyl)pyridine (10jq)
Brown oil; yield: 15.7 mg (23%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63–1.70 (m, 4 H), 1.82–1.83 (m, 2 H), 2.03–2.09 (m, 2 H), 3.49–3.53 (m, 1 H), 7.06 (d, *J* = 5.6 Hz, 1 H), 7.16–7.19 (m, 1 H), 7.32 (d, *J* = 5.6 Hz, 1 H), 7.50 (d, *J* = 8.0 Hz, 1 H), 7.69–7.23 (m, 1 H), 8.64–8.65 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.7, 34.9, 39.3, 121.4, 122.6, 126.0, 127.6, 136.3, 137.6, 144.8, 149.7, 153.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{16}NS$: 230.1003; found: 230.1004.

2-[2-Octyl-6-(2-phenylethyl)phenyl]pyridine (11)
Colorless oil; yield: 55.6 mg (50%)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 3 H), 1.13–1.16 (m, 8 H), 1.20–1.25 (m, 2 H), 1.40–1.41 (m, 2 H), 2.28–2.34 (m, 2 H), 2.57–2.76 (m, 4 H), 6.91 (d, *J* = 7.0 Hz, 2 H), 7.09–7.19 (m, 6 H), 7.27 (t, *J* = 7.5 Hz, 2 H), 7.71 (td, *J* = 7.7 H, 1.8 Hz, 1 H), 8.73 (d, *J* = 4.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 29.3, 29.4, 29.7, 31.3, 32.0, 33.7, 36.3, 38.0, 121.9, 125.2, 125.9, 126.8, 127.1, 128.3, 128.38, 128.44, 136.0, 139.8, 140.2, 141.1, 142.3, 149.6, 159.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{34}N$: 372.2691; found: 372.2689.

1-[2-(4-*tert*-Butylcyclohexyl)phenyl]ethanone (3aac)
Light-yellow oil; yield: 23.8 mg (31%; *trans*/*cis* = 79:21).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*) = 0.88 (s, 9 H), 1.08–1.22 (m, 3 H), 1.35–1.48 (m, 2 H), 1.79–1.93 (m, 4 H), 2.57 (s, 3 H), 2.98 (tt, *J* = 12.0 Hz, 3.2 Hz, 1 H), 7.20–7.24 (m, 1 H), 7.37–7.40 (m, 2 H), 7.47–7.48 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*trans*) = 27.6, 27.7, 30.8, 32.5, 34.8, 40.0, 47.9, 125.3, 127.0, 127.7, 130.9, 139.3, 146.4, 203.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{27}O$: 259.2062; found: 259.2057.

1-[2-(1-Methylheptyl)phenyl]ethanone (3aad)
Obtained as a mixture with the linear isomer **3aa** and the *ortho*-neopentylation product **3aj**; yield: 63% (by weight and ^{1}H NMR analysis). See the Supporting Information for the determination of the enantiomeric excess.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.85 (m, 3 H), 1.09–1.26 (m, 11 H), 1.46–1.66 (m, 2 H), 2.52 (s, 3 H), 3.23 (sextet, *J* = 7.3 Hz, 1 H), 7.18–7.23 (m, 1 H), 7.34–7.45 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.7, 22.8, 27.9, 29.6, 31.0, 32.0, 34.7, 38.6, 125.5, 127.1, 127.5, 131.1, 139.9, 146.9, 204.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{25}O$: 233.1905; found: 233.1908.

1-[2-(Cyclobutylmethyl)phenyl]ethanone (3aae)
Obtained as a mixture with the ring-opening alkylation products **3ad** and **3ad′**; yield: 60% (by weight and ^{1}H NMR analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67–1.74 (m, 2 H), 1.77–1.85 (m, 2 H), 1.95–2.02 (m, 2 H), 2.52–2.60 (m, 4 H), 2.97 (d, *J* = 7.6 Hz, 2 H), 7.21 (d, *J* = 7.6 Hz, 1 H), 7.25 (d, *J* = 7.6 Hz, 1 H), 7.34–7.38 (m, 1 H), 7.60 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3, 28.3, 30.0, 37.1, 40.3, 125.6, 128.8, 130.9, 131.0, 138.2, 140.8, 202.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{17}O$: 189.1279; found: 189.1274.

1-(2-Hex-5-en-1-ylphenyl)ethanone (3aaf)
Obtained as an 88:12 mixture with 1-{2-[(4*E*)-hex-4-en-1-yl]phenyl}ethanone (**3aaf′**) as a yellow oil; yield: 58.6 mg (97%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44–1.50 (m, 2 H), 1.55–1.61 (m, 2 H), 2.06–2.11 (m, 2 H), 2.58 (s, 3 H), 2.85 (t, *J* = 7.6 Hz, 2 H), 4.94 (ddt, *J* = 10.2 Hz, 2.0 Hz, 1.1 Hz, 1 H), 5.00 (ddt, *J* = 17.1 Hz, 1.9 Hz, 1.6 Hz, 1 H), 5.81 (ddt, *J* = 17.0 Hz, 10.2 Hz, 6.7 Hz, 1 H), 7.24–7.27 (m, 2 H), 7.39 (td, *J* = 7.6 Hz, 1.2 Hz, 1 H), 7.63 (dd, *J* = 7.6 Hz, 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.9, 29.9, 31.3, 33.6, 33.8, 114.3, 125.6, 129.0, 131.1, 131.2, 137.9, 138.9, 142.7, 202.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{19}O$: 203.1436; found: 203.1437.

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