Cationic Ir(I)-Catalyzed sp^3 C–H Bond Alkenylation of Ureas with Alkynes for the Synthesis of 2,3-Disubstituted Indoles

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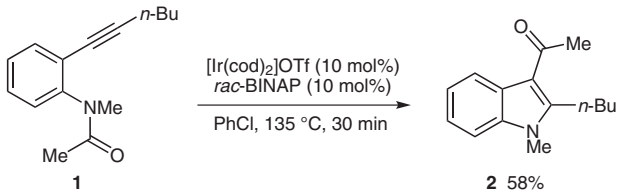
Abstract: Secondary sp^3 C–H bond activation of ureas was achieved by a cationic Ir(I)–JOSIPHOS catalyst. Regioselective C–H bond cleavage adjacent to the nitrogen atom in *N*-benzylureas and an *N*-allyl urea possessing a 2-alkynylphenyl group, and subsequent intramolecular reaction with an alkyne along with double-bond isomerization provided 2,3-disubstituted indoles.

Key words: C–H bond activation, directing group, indoles, iridium, ureas

The direct functionalization of C–H bonds is an ideal transformation in organic synthesis, because C–H bonds are ubiquitous in organic molecules, and the introduction of activating groups, such as halogens and metals, is unnecessary. However, C–H bonds are generally more stable than carbon–heteroatom bonds, therefore, some ingenious tricks are required for the regioselective cleavage of C–H bonds. The directed C–H bond activation by transition-metal catalysts has led to the drastic development of this area, where the Murai's carbonyl-directed C–H activation by a Ru catalyst is a monumental work.[1] In last decade, various directing groups have been reported for the initiation of C–H bond cleavage, and many synthetically useful transformations have been disclosed.[2] Among them, sp^2 C–H bond activation such as aromatic and vinylic C–H bonds has been a main research topic, and the examples of sp^3 C–H bond activation are relatively few,[3] in particular, those of secondary sp^3 C–H bond activation are scarce and limited to benzylic and allylic positions.[4] We herein disclose that a cationic Ir–diphosphine complex promotes benzylic and allylic secondary sp^3 C–H bond cleavage using urea as a directing group, and that the following intramolecular reaction with alkynes results in the formation of substituted indoles.[5]

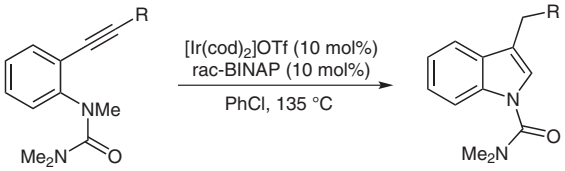
We have focused on the development of cationic iridium(I)-catalyzed C–H bond activation and reported on the carbonyl-directed sp^2 C–H bond cleavage for the reaction with alkynes, alkenes, and ketones.[6] We recently achieved an amide-directed sp^3 C–H bond alkenylation by the intermolecular reaction with alkynes.[3h] We next examined an intramolecular reaction of (2-alkynylphenyl)amide **1** under the previously reported conditions, but *N*-methyl indole **2** was obtained via acetyl rearrangement, which was already reported using Pt catalysts,[7] and C–H bond cleavage at the methyl group did not proceed at all (Scheme 1).



1 **2** 58%

Scheme 1 Ir(I)-catalyzed indole synthesis from amide **1** via acetyl rearrangement

We changed the directing group from amide to urea and subjected 1-[2-(hex-1-ynyl)phenyl]-1,3,3-trimethylurea (**3a**) to the same reaction conditions (Scheme 2). To our delight, 3-pentylindole **4a** was obtained in good yield initiated by primary sp^3 C–H bond activation of the methyl group. Phenyl and trimethylsilyl groups were also available as substituents at the alkyne terminus, and the corresponding 3-substituted indoles **4b** and **4c** were obtained.



3a R = *n*-Bu
3b R = Ph
3c R = TMS

4a 79%, 1.5 h
4b 49%, 24 h
4c 40%, 24 h

Scheme 2 Ir(I)-catalyzed indole synthesis from urea **3** initiated by primary sp^3 C–H bond cleavage

We further tried secondary sp^3 C–H bond activation of a benzylic position under the same reaction conditions and obtained 2-phenyl-3-pentylindole **6a**, albeit in low yield due to the low conversion of urea **5a** (Table 1, entry 1). To improve the yield, we screened various diphosphine ligands for cationic Ir(I) complex. When DPPF was used, the yield significantly increased (Table 1, entry 4). After screening several ferrocenyl ligands, we determined JOSIPHOS to be the best ligand, but urea **5a** was not completely consumed even after 48 hours (Table 1, entry 5).

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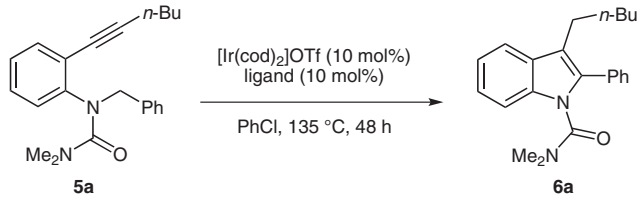
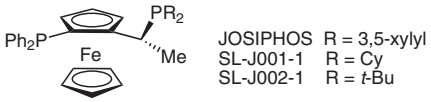
Table 1 Screening of Various Diphosphine Ligands in the Ir(I)-Catalyzed Secondary sp^3 C–H Bond Activation



5a **6a**

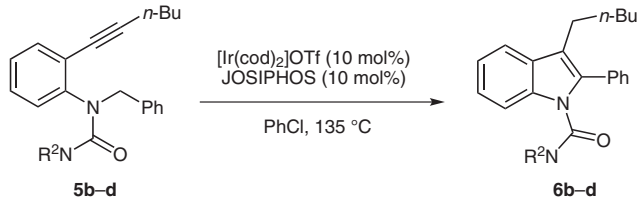
Entry	Ligand[a]	Yield of **6a** (%)
1	*rac*-BINAP	26
2	(*S*)-SEGPHOS	32
3	(*R*,*R*)-MeDUPHOS	24
4	DPPF	40
5	JOSIPHOS	53
6	SL-JOO1-1	trace
7	SL-JOO2-1	trace

[a] SEGPHOS: 5,5′-bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole, MeDUPHOS: 1,2-bis(2,5-dimethylphospholano)benzene, DPPF: 1,1′-bis(diphenylphosphino)ferrocene.



We next examined substituents on the nitrogen atom, which can electronically and/or sterically affect the directing ability of the urea group (Table 2). When a pyrrolidinyl group was used as the NR_2 moiety, desired indole **6b** was not obtained at all, and a rearranged product was mainly produced (58% yield, Table 2, entry 1). In contrast, a piperidinyl group was installed, desired indole **6c** was obtained, but urea **5c** partly remained unconsumed (Table 2, entry 2). Finally, when a diethylamino group was used, complete consumption of the substrate was observed, and indole **6d** was obtained in the highest yield of 75% (Table 2, entry 3).

Table 2 Screening of Various Ureas in the Ir(I)-Catalyzed Secondary sp^3 C–H Bond Activation

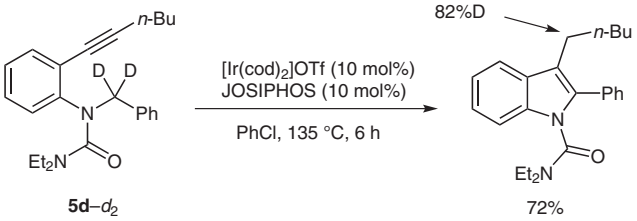


5b–d **6b–d**

Entry	NR_2	Urea	Time (h)	Yield of **6** (%)
1		**5b**	3	n.d.
2		**5c**	24	**6c** 45
3	NEt_2	**5d**	6	**6d** 75

With the optimal conditions in hand, we next examined the substrate scope (Table 3). We first introduced electron-withdrawing groups on the benzene ring (Table 3, entries 1–3). As a result, the corresponding 2-arylindoles **6e**–**g** were obtained, and especially in the case of trifluoromethyl group, urea **5g** was completely consumed within 3 hours, and the highest yield of 80% was achieved (Table 3, entry 3). An electron-donating group could be installed at the meta position (Table 3, entry 4).[8] In addition to the benzylic position, a secondary sp^3 C–H bond of the allylic position of urea **5i** was also activated, and 2-vinylindole **6i** was obtained, part of which was hydrogenated at the vinyl group to afford 2-ethylindole (Table 3, entry 5).[9] As for the substituent on the alkyne terminus, phenyl group was also used, and 2-phenyl-3-benzylindole **6j** was afforded in moderate yield (Table 3, entry 6). This reaction provides a synthetic protocol of 2,3-disubstituted indoles.[10]

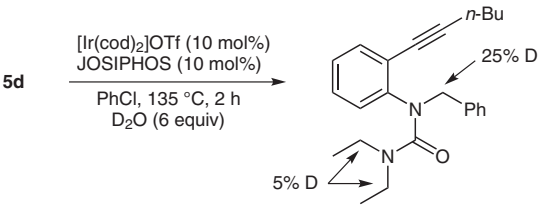
As a mechanistic study, we first subjected deuterated substrate **5d**-d_2 to the same reaction conditions (Scheme 3). As a result, high rate of deuterium incorporation was ascertained in the obtained indole.



5d-d_2 72%

Scheme 3 Reaction using deuterated substrate **5d**-d_2

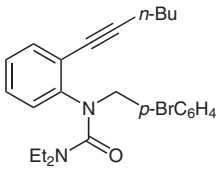
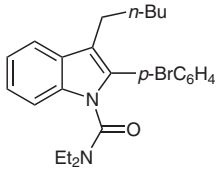
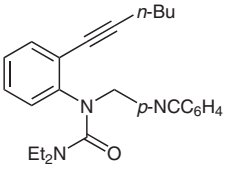
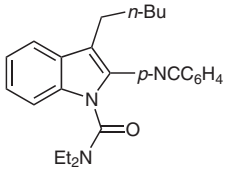
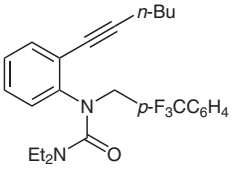
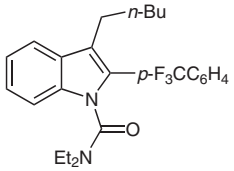
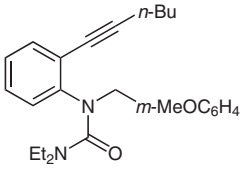
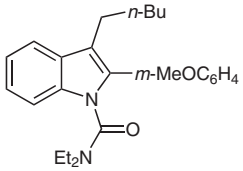
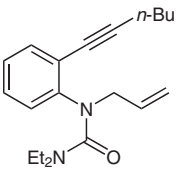
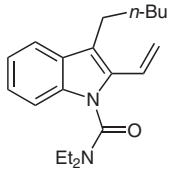
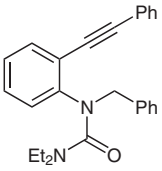
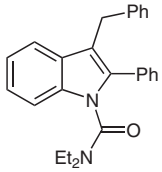
We next examined the reaction of urea **5d** in the presence of excess amounts of D_2O, quenched it after 2 hours and recovered unreacted urea **5d** (Scheme 4). Deuterium incorporation (25%) was observed at the expected benzylic position along with slight deuterium incorporation at the methylene moiety.



Scheme 4 Reaction in the presence of D_2O

Based on the above results, we now assume the present reaction is likely initiated by secondary sp^3 C–H bond cleavage. Subsequent intramolecular carboiridation to alkynes, reductive elimination, and isomerization of an *exo* double bond would provide 2-substituted indoles (Scheme 5).

Table 3 Substrate Scope of the Ir(I)-Catalyzed Secondary sp^3 C–H Bond Activation for the Synthesis of Indoles[a]

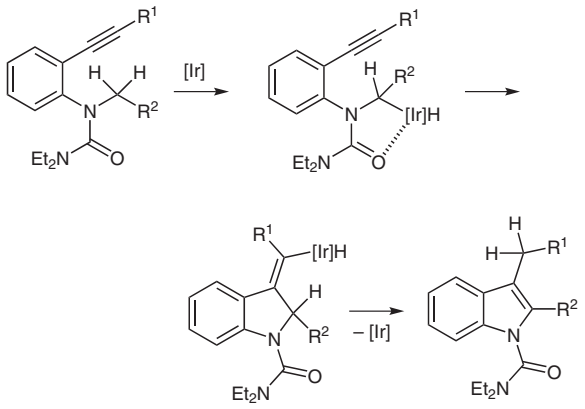
Entry	Substrate	Product	Time (h)	Yield of **6** (%)
1	 **5e**	 **6e**	24	54
2	 **5f**	 **6f**	48	64
3	 **5g**	 **6g**	**3**	80
4	 **5h**	 **6h**	24	75
5[b]	 **5i**	 **6i**	24	61
6	 **5j**	 **6j**	24	48

[a] $[Ir(cod)_2]OTf$ (10 mol%) and JOSIPHOS (10 mol%) in chlorobenzene at 135 °C.
[b] Hydrogenated product of the vinyl group was included (ca. 1/3).

In conclusion, we achieved a cationic Ir(I)-catalyzed indole synthesis initiated by secondary sp^3 C–H bond activation. Selective C–H bond cleavage at benzylic and allylic positions proceeded with the aid of an urea moiety as a directing group, and 2-aryl- and 2-vinyl-3-substituted indoles were obtained. The use of urea as a directing group and the choice of substituent on the urea were a key to success. Preliminary mechanistic studies by labeling experiments elucidated that secondary sp^3 C–H bond cleavage and intramolecular alkyne insertion seemed to be involved in a catalytic cycle. The application of our iridium-catalyzed sp^3 C–H bond activation for other types of transformations are under way in our laboratory.

Synthesis of Compounds 6d–j

$[Ir(cod)_2]OTf$ (5.6 mg, 10 μmol), JOSIPHOS (6.4 mg, 10 μmol), and ureas **5d–j** (0.10 mmol) were placed in a Schlenk tube, which was then evacuated and backfilled with argon (3×). Chlorobenzene (0.2 mL) was added into the reaction vessel. The reaction mixture



Scheme 5 A possible mechanism of Ir(I)-catalyzed indole synthesis initiated by secondary sp^3 C–H bond cleavage

was then stirred at 135 °C for appropriate hours listed in Tables 2 and 3, then the solvent was evaporated under reduced pressure. The resultant crude products were purified by TLC to give indoles **6d–j**.

1-Benzyl-3,3-diethyl-1-[2-(hex-1-ynyl)phenyl]urea (5d)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 7.4 Hz, 6 H), 0.92 (t, *J* = 7.4 Hz, 3 H), 1.39–1.55 (m, 4 H), 2.37 (t, *J* = 7.4 Hz, 2 H), 3.12 (q, *J* = 7.4 Hz, 4 H), 4.76 (s, 2 H), 6.82 (dd, *J* = 7.4, 1.7 Hz, 1 H), 7.07 (ddd, *J* = 7.4, 7.4, 1.7 Hz, 1 H), 7.09 (ddd, *J* = 7.4, 7.4, 1.7 Hz, 1 H), 7.14–7.22 (m, 3 H), 7.32 (d, *J* = 7.4 Hz, 2 H), 7.41 (dd, *J* = 7.4, 1.7 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.7, 13.7, 19.5, 22.1, 30.7, 41.9, 54.3, 77.8, 96.8, 122.0, 125.7, 126.8, 127.9, 128.0, 128.2, 128.8, 133.6, 139.0, 146.9, 161.8. IR (neat): 3062, 2960, 2933, 2871, 1650, 1486, 1413, 1270, 1072, 759, 700 cm^{-1}. HRMS (FAB$^+$): *m/z* calcd for $C_{24}H_{31}N_2O$: 363.2436; found: 363.2430 [M + H].

1-(4-Bromobenzyl)-3,3-diethyl-1-[2-(hex-1-ynyl)phenyl]urea (5e)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 7.1 Hz, 6 H), 0.93 (t, *J* = 7.3 Hz, 3 H), 1.39–1.57 (m, 4 H), 2.38 (t, *J* = 7.1 Hz, 2 H), 3.12 (q, *J* = 7.1 Hz, 4 H), 4.69 (s, 2 H), 6.81 (dd, *J* = 7.4, 1.7 Hz, 1 H), 7.13 (ddd, *J* = 7.2, 7.2, 2.1 Hz, 1 H), 7.09 (ddd, *J* = 7.4, 7.4, 1.7 Hz, 1 H), 7.22 (d, *J* = 8.3 Hz, 2 H), 7.33 (d, *J* = 8.3 Hz, 2 H), 7.43 (dd, *J* = 7.2, 2.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.5, 13.6, 19.4, 22.0, 30.6, 41.8, 53.7, 77.7, 96.8, 120.6, 121.8, 125.8, 127.8, 128.3, 130.6, 130.9, 133.7, 137.9, 146.5, 161.6. IR (neat): 2960, 2933, 2871, 1646, 1486, 1417, 1274, 1178, 796, 759 cm^{-1}. HRMS (FAB$^+$): *m/z* calcd for $C_{24}H_{30}BrN_2O$: 441.1541; found: 441.1560 [M + H].

1-(4-Cyanobenzyl)-3,3-diethyl-1-[2-(hex-1-ynyl)phenyl]urea (5f)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.1 Hz, 6 H), 0.92 (t, *J* = 7.3 Hz, 3 H), 1.37–1.54 (m, 4 H), 2.34 (t, *J* = 7.1 Hz, 2 H), 3.13 (q, *J* = 7.1 Hz, 4 H), 4.77 (s, 2 H), 6.85 (dd, *J* = 7.6, 1.7 Hz, 1 H), 7.11 (ddd, *J* = 7.3, 7.3, 2.2 Hz, 1 H), 7.15 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1 H), 7.44 (dd, *J* = 7.3, 2.2 Hz, 1 H), 7.47 (d, *J* = 8.3 Hz, 2 H), 7.52 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.5, 13.6, 19.3, 22.0, 30.5, 41.8, 54.2, 77.5, 97.0, 110.5, 119.1, 121.7, 125.9, 127.4, 128.5, 129.2, 131.7, 133.8, 144.6, 146.5, 161.3. IR (neat): 2962, 2933, 2873, 2227, 1610, 1654, 1486, 1378, 1272, 761, 752 cm^{-1}. HRMS (FAB$^+$): *m/z* calcd for $C_{25}H_{30}N_3O$: 388.2389; found: 388.2379 [M + H].

3,3-Diethyl-1-[4-(trifluoromethyl)benzyl]-1-[2-(hex-1-ynyl)phenyl]urea (5g)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ= 0.83 (t, *J* = 7.1 Hz, 6 H), 0.91 (t, *J* = 7.1 Hz, 3 H), 1.36–1.54 (m, 4 H), 2.34 (t, *J* = 7.1 Hz, 2 H), 3.14 (q, *J* = 7.1 Hz, 4 H), 4.78 (s, 2 H), 6.87 (dd, *J* = 7.6, 1.8 Hz, 1 H), 7.11 (ddd, *J* = 7.3, 7.3, 1.8 Hz, 1 H), 7.15 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1 H), 7.44 (dd, *J* = 7.3, 1.8 Hz, 1 H), 7.45–7.50 (br, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.6, 13.6, 19.4, 22.1, 30.7, 41.9, 54.2, 77.7, 97.1, 121.9, 124.8, 124.9, 125.9, 127.6, 128.5, 128.8, 129.1, 133.8, 143.2, 146.8, 161.6. IR (neat): 2962, 2935, 2873, 1660, 1644, 1488, 1427, 1322, 1160, 1068, 761, 754 cm^{-1}. HRMS (FAB$^+$): *m/z* calcd for $C_{25}H_{30}F_3N_2O$: 431.2310; found: 431.2299 [M + H].

3,3-Diethyl-1-(3-methoxybenzyl)-1-[2-(hex-1-ynyl)phenyl]urea (5h)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.1 Hz, 6 H), 0.91 (t, *J* = 7.1 Hz, 3 H), 1.38–1.57 (m, 4 H), 2.37 (t, *J* = 7.1 Hz, 2 H), 3.13 (q, *J* = 7.1 Hz, 4 H), 3.73 (s, 3 H), 4.74 (s, 2 H), 6.72 (dd, *J* = 8.0, 1.7 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.90 (s, 1 H), 6.92 (d, *J* = 8.0 Hz, 1 H), 7.06–7.15 (m, 3 H), 7.42 (dd, *J* = 7.1, 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.6, 13.6, 19.4, 22.0, 30.6, 41.8, 54.2, 55.1, 77.7, 96.8, 112.4,113.9, 120.9, 121.9, 125.6, 127.8, 128.2, 128.8, 133.5, 140.7, 146.9, 159.3, 161.7. IR (neat): 3060, 2932, 2872, 1645, 1595, 1487, 1378, 762, 698 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{25}H_{32}N_2NaO_2$: 415.2361; found: 415.2366 [M + Na].

1-Allyl-3,3-diethyl-1-[2-(hex-1-ynyl)phenyl]urea (5i)
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 6.8 Hz, 6 H), 0.93 (t, *J* = 7.4 Hz, 3 H), 1.46–1.59 (m, 4 H), 2.43 (t, *J* = 7.3 Hz, 2 H), 3.08 (q, *J* = 6.8 Hz, 4 H), 4.14 (d, *J* = 5.7 Hz, 2 H), 4.99–5.04 (m, 2 H), 6.05 (ddt, J_d = 17.0, 10.2 Hz, J_t = 5.7 Hz, 1 H), 6.97 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.09 (ddd, *J* = 7.4, 7.4, 1.4 Hz, 1 H), 7.19 (ddd, *J* = 7.7, 7.7, 1.4 Hz, 1 H), 7.41 (dd, *J* = 7.4, 1.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.7, 13.7, 19.4, 22.1, 30.8, 41.9, 53.8, 77.7, 96.6, 116.8, 122.1, 125.7, 127.9, 128.3, 133.5, 135.4, 146.9, 161.7. IR (neat): 2960, 2933, 2871, 1650, 1646, 1486, 1407, 1378, 1270, 1000, 921, 796, 761 cm^{-1}. HRMS (FAB$^+$): *m/z* calcd for $C_{20}H_{29}N_2O$: 313.2280; found: 313.2270 [M + H].

1-Benzyl-3,3-diethyl-1-[2-(2-phenylethynyl)phenyl]urea (5j)
White solid; mp 65–70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.1 Hz, 6 H), 3.15 (q, *J* = 7.1 Hz, 4 H), 4.86 (s, 2 H), 6.94 (dd, *J* = 7.6, 1.0 Hz, 1 H), 7.13–7.23 (m, 5 H), 7.29–7.38 (m, 5 H), 7.48–7.49 (m, 2 H), 7.55 (dd, *J* = 7.3, 1.7 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.7, 42.0, 54.8, 86.7, 95.1, 121.4, 123.2, 125.8, 126.9, 128.0, 128.4, 128.5, 128.9, 129.1, 131.7, 133.6, 138.8, 147.0, 161.8 (a pair of aromatic peaks is overlapped). IR (KBr disk): 3060, 2975, 2933, 2873, 1646, 1494, 1477, 1442, 1413, 1268, 1070, 757, 694 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{26}H_{26}N_2NaO$: 405.1943; found: 405.1946 [M + Na].

***N*,*N*-Diethyl-3-pentyl-2-phenyl-1*H*-indole-1-carboxamide (6d)**
Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.8 Hz, 3 H), 0.86–0.99 (br, 6 H), 1.22–1.33 (m, 4 H), 1.66 (tt, *J* = 7.7, 7.7 Hz, 2 H), 2.76 (m, 2 H), 2.87–3.78 (br, 4 H), 7.18 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.26 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.35–7.48 (m, 6 H), 7.62 (d, *J* = 8.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 13.9, 22.4, 24.3, 30.5, 31.8, 41.5, 111.1, 116.9, 119.4, 120.7, 123.2, 127.9, 128.3, 128.6, 129.5, 131.9, 134.8, 135.9, 153.7. IR (neat): 2928, 1682, 1455, 1422, 1321, 1277, 741 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{24}H_{30}N_2NaO$: 385.2256; found: 385.2251 [M + Na].

2-(4-Bromophenyl)-*N*,*N*-diethyl-3-pentyl-1*H*-indole-1-carboxamide (6e)

White oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.7 Hz, 3 H), 0.89–1.05 (br, 6 H), 1.25–1.30 (m, 4 H), 1.64 (tt, *J* = 7.5, 7.5 Hz, 2 H), 2.71–2.75 (m, 2 H), 2.81–3.69 (br, 4 H), 7.19 (dd, *J* = 7.4, 7.4 Hz, 1 H), 7.26 (dd, *J* = 8.0 Hz, 7.4 Hz, 1 H), 7.34 (d, *J* = 8.3 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 1 H), 7.56 (d, *J* = 8.3 Hz, 2 H), 7.62 (d, *J* = 7.3 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.1, 13.9, 22.4, 24.3, 30.4, 31.8, 41.6, 111.1, 117.6, 119.5, 120.9, 122.1, 123.5, 128.5, 130.9, 131.0, 131.5, 133.6, 136.0, 153.5. IR (neat): 2928, 1681, 1216, 825, 743 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{24}H_{29}BrN_2NaO$: 463.1361; found: 463.1354 [M + Na].

2-(4-Cyanophenyl)-*N*,*N*-diethyl-3-pentyl-1*H*-indole-1-carboxamide (6f)

White solid; mp 99–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3 H), 0.94–1.05 (br, 6 H), 1.25–1.30 (m, 4 H), 1.66 (tt, *J* = 7.6, 7.6 Hz, 2 H), 2.73–2.77 (m, 2 H), 2.87–3.55 (br, 4 H), 7.22 (dd, *J* = 7.8, 7.8 Hz, 1 H) 7.31 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.40 (d, *J* = 7.8 Hz, 1 H), 7.58 (d, *J* = 8.3 Hz, 2 H), 7.64 (d, *J* = 7.8 Hz, 1 H), 7.73 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.3, 13.9, 22.3, 24.3, 30.4, 31.8, 41.8, 111.2, 111.3, 118.7, 119.2, 119.9, 121.2, 124.2, 128.5, 129.9, 132.1, 132.8, 136.3, 136.8, 153.3. IR (KBr disk): 1716, 1683, 1068, 750 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{25}H_{29}N_3NaO$: 410.2208; found: 410.2189 [M + Na].

***N*,*N*-Diethyl-3-pentyl-2-[4-(trifluoromethyl)phenyl]-1*H*-indole-1-carboxamide (6g)**

White solid; mp 57–59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.9 Hz, 3 H), 0.88–1.02 (br, 6 H), 1.23–1.33 (m, 4 H), 1.66 (tt, *J* = 7.6, 7.6 Hz, 2 H), 2.73–2.77 (m, 2 H), 2.92–3.46 (br, 4 H), 7.29 (dd, *J* = 7.7, 7.7 Hz, 1 H), 7.29 (dd, *J* = 7.7, 7.7 Hz, 1 H), 7.41 (d, *J* = 7.7 Hz, 1 H), 7.59 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 7.7 Hz, 1 H), 7.67 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 13.9, 22.4, 24.3, 30.5, 31.8, 41.8, 111.1, 118.5, 119.7, 121.0, 123.8, 125.2, 125.3, 128.5, 129.7, 133.3, 135.7, 136.2, 153.4. IR (KBr disk): 2931, 1682, 1324, 1216, 1018, 843, 744 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{25}H_{29}F_3N_2NaO$: 453.2130; found: 453.2124 [M + Na].

***N*,*N*-Diethyl-2-(3-methoxyphenyl)-3-pentyl-1*H*-indole-1-carboxamide (6h)**

Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 7.0 Hz, 3 H), 0.87–0.98 (br, 6 H), 1.24–1.34 (m, 4 H), 1.67 (tt, *J* = 7.9, 7.9 Hz, 2 H), 2.76–2.79 (m, 2 H), 2.96–3.52 (br, 4 H), 3.83 (s, 3 H), 6.91 (d, *J* = 8.0 Hz, 1 H), 7.02 (s, 1 H), 7.06 (d, *J* = 8.0 Hz, 1 H), 7.18 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.25 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.33 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.42 (d, *J* = 7.8 Hz, 1 H), 7.61 (d, *J* = 7.6 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.9, 14.1, 22.5, 24.5, 30.6, 31.9, 41.9, 55.4, 111.1, 113.9, 114.9, 117.1, 119.5, 120.8, 122.1, 123.3, 128.7, 129.4, 133.2, 134.8, 136.1, 153.8, 159.5. IR (neat): 2930, 1680, 1456, 1321, 1221, 743 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{25}H_{29}N_2NaO_2$: 415.2361; found: 415.2343 [M + Na].

***N*,*N*-Diethyl-3-pentyl-2-vinyl-1*H*-indole-1-carboxamide (6i)**

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.6 Hz, 3 H), 1.19–1.27 (m, 8 H), 1.49–1.59 (m, 4 H), 2.23–2.29 (m, 2 H), 2.77–2.98 (br, 2 H), 3.30–3.48 (br, 2 H), 6.17–6.25 (m, 1 H), 6.50 (d, *J* = 15.6 Hz, 1 H), 7.05–7.24 (m, 4 H), 7.79–7.81 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 13.9, 22.4, 24.3, 30.5, 31.8, 41.3, 111.1, 116.9, 119.4, 120.4, 120.6, 123.2, 127.9, 128.3, 128.6, 129.5, 131.9, 135.9, 153.7. IR (neat): 2931, 1682, 1423, 1278, 743 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{20}H_{28}N_2NaO$: 335.2099; found: 335.2093 [M + Na].

3-Benzyl-*N*,*N*-diethyl-2-phenyl-1*H*-indole-1-carboxamide (6j)

Pale red solid; mp 107–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–1.02 (m, 6 H), 2.58–3.75 (br, 4 H), 4.09–4.21 (br, 2 H), 7.08–7.47 (m, 14 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 30.4, 41.8, 111.1, 114.1, 119.8, 119.8, 120.9, 123.4, 125.8, 128.1, 128.3, 128.4, 128.6, 129.4, 131.4, 136.0, 136.1, 141.0, 153.5. IR (KBr disk): 2933, 1681, 1216, 744, 700 cm^{-1}. HRMS (ESI$^+$): *m/z* calcd for $C_{26}H_{26}N_2NaO$: 405.1943; found: 405.1926 [M + Na].

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