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Annulation of internal alkynes through a hydroamination/aza-Heck reaction sequence for the regioselective synthesis of indoles

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Abstract

Highly regioselective annulation reactions of unsymmetrically substituted alkynes by primary 2-bromo or 2-chloroanilines are achieved with an efficient one-pot protocol, which relies on a regioselective $TiCl_4$-catalyzed intermolecular hydroamination and a subsequent palladium-catalyzed intramolecular aza-Heck reaction. The use of unsymmetrically substituted alkynes in this strategy enables the synthesis of diversely functionalized indoles, with a regioselectivity that is complementary to the one obtained when employing Larock's annulation reaction.

1. Introduction

Indole derivatives are likely to represent one of the most important structural classes in drug discovery.[1,2] Selected examples of indoles with activities relevance to biology include nonsteroidal anti-inflammatory drug indomethacin or 5HT-3 antagonist ondansetron.[1,2] Due to this prevalence of indoles in biologically active compounds, as well as natural products, a continued strong demand for the development of general, flexible, and regioselective methodologies for the synthesis of this structural motif exists.[3,4] Despite the development of a variety of effective strategies, the synthesis of indole derivatives featuring substituents at positions other than C5 remains challenging by classical protocols, such as the Fischer indole synthesis.[2] Consequently, metal-catalyzed reactions for the construction of the indole backbone were developed, largely relying on palladium-catalysis.[5] These approaches can be categorized into (a) the functionalization of existing indoles or (b) the de novo indole construction from benzenoid precursors through pyrrole ring assembly. Representative examples for the latter, inherently more modular, approach are depicted in Figure 1, with an emphasis on alkyne functionalization-based processes. The majority of these methodologies make use of entropically favorable cyclization reactions, Larock's elegant direct annulation of *ortho*-haloanilides with alkynes being a valuable exception (method **E**).[6]

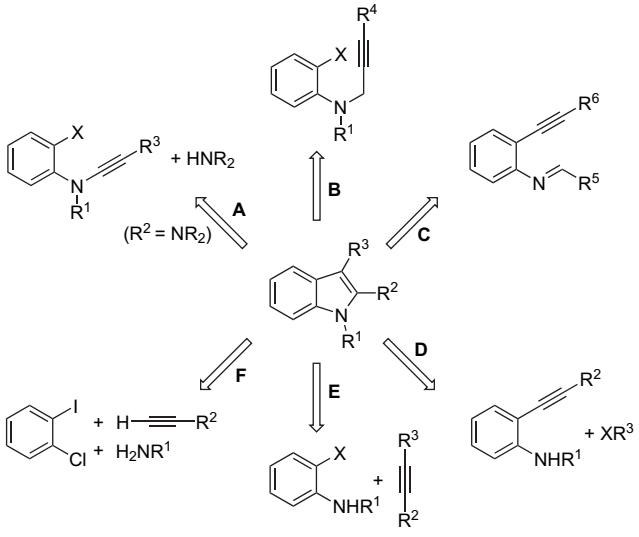

Figure 1. Retrosynthetic representation of selected alkyne functionalization-based palladium-catalyzed reactions for the assembly of the pyrrole ring.

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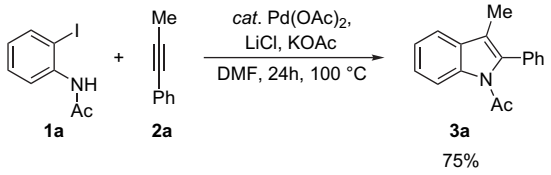
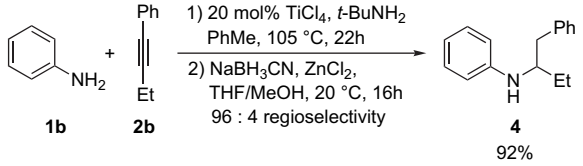
Examination of the literature revealed considerable room for the improvement of the existing procedures. For example, the *ortho*-haloaniline starting materials for the Larock annulation reaction, as well as for the initial Sonogashira reaction of method **D** proved, prior to our investigations,[7–9] not generally compatible with the use of chloroarenes,[10] displaying a wide variety of substituents.[6,11,12] Further, the Larock annulation reaction of unsymmetrically substituted alkynes by aniline derivatives yielded, with good to excellent selectivities, indole derivatives with the bulkiest group of the alkyne in the position 2 (for an example, see Scheme 1).[6,8,11] Consequently, the synthesis of indoles with the bulkiest substituent of the alkyne in position 3 required the use of 1-silyl-1-alkynes, and an additional subsequent functionalization of the resulting 2-silylindole.[6]



Scheme 1. Larock's direct annulation with unsymmetrical internal alkyne **2a**.

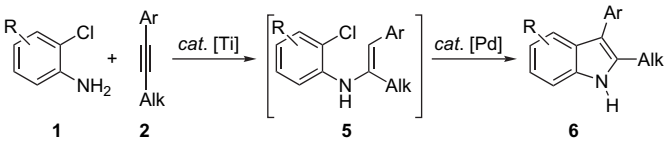
Thus, we became interested in the development of novel and flexible indole syntheses employing inexpensive and readily available aryl chlorides as electrophilic starting materials. While we reported previously on modular indole syntheses employing *ortho*-dihaloarenes (method **F** in Fig. 1),[13,14] we envisioned as well a one-pot indole synthesis starting from inexpensive 2-chloroanilines. Particularly, a protocol yielding indoles with the bulkiest substituent of the alkyne in position 3 was highly desirable, as it should prove complementary to the regioselectivity observed with Larock's annulation.

The hydroamination reaction, i.e., the direct addition of amines onto carbon–carbon multiple bonds, represents one of the most efficient and atom-economical approaches to substituted amines and imines from inexpensive feedstocks.[15–21] Titanium-based[16,22,23] hydroamination methodologies are especially attractive, inter alia due to low cost and low toxicity of the catalysts. During studies on user-friendly $TiCl_4$-catalyzed hydroamination reactions,[24–26] we realized that a variety of valuable aryl halides were tolerated by the catalytic system.[24] Furthermore, intermolecular $TiCl_4$-catalyzed hydroamination reactions of unsymmetrically substituted alkynes gave rise to the formal anti-Markovnikov addition products with good to excellent regioselectivities, as illustrated for the hydroamination of alkyne **2b** in Scheme 2.[24,27]



Scheme 2. $TiCl_4$-catalyzed intermolecular hydroamination of alkyne **2b** with formal anti-Markovnikov selectivity.

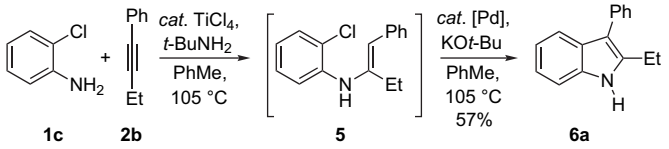
Consequently, we probed the use of enamines **5** derived from 2-chloroanilines **1** and unsymmetrically substituted alkynes **2** in intramolecular palladium-catalyzed aza-Heck reactions (Scheme 3). Importantly, this strategy should prove complementary to Larock's annulation reaction with respect to its regioselectivity. Herein, we wish to present a full account[28] on this one-pot indole synthesis, consisting of an intermolecular titanium-catalyzed hydroamination and a palladium-catalyzed intramolecular aza-Heck reaction.



Scheme 3. Regioselective annulation of internal alkynes **2**.

2. Results and discussion

At the outset of our studies, we explored the planned regioselective one-pot synthesis of indoles employing 2-chloroaniline (**1c**) (Scheme 4). Since the $TiCl_4$-catalyzed intermolecular hydroamination of 2-haloanilines **1** was well elaborated previously in our laboratories,[24] we focused on the development of effective reaction conditions for the subsequent palladium-catalyzed intramolecular aza-Heck reaction of the resulting 2-chlorophenyl-substituted enamine **5** within a one-pot procedure.



Scheme 4. One-pot synthesis of indole **6a** used for the optimization of palladium catalysts.

2.1. Annulation with palladium complexes derived from imidazolium salts

Initially, we explored palladium complexes derived from in situ generated *N*-heterocyclic carbenes (NHC)[29–31] for the regioselective one-pot strategy. Most effective catalysis was accomplished with commercially available imidazolium salt HIPrCl **7** (Fig. 2) as precursor for a sterically hindered carbene.[28]

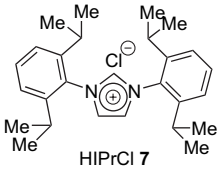
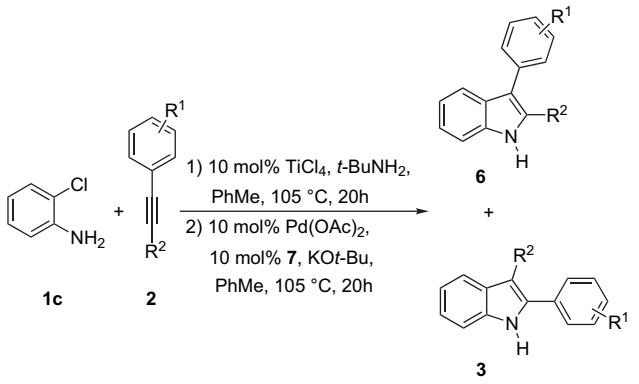


Figure 2. Imidazolium salt **7**.

Consequently, its scope was probed in the hydroamination/aza-Heck sequence for the annulation of various internal alkynes by 2-chloroaniline (**1c**) (Table 1). Generally, the desired 3-aryl-substituted indoles **6** were obtained with good to

Table 1
Scope of indole synthesis with 2-chloroaniline (**1c**)[a]



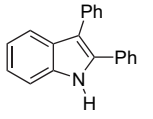
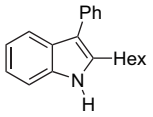
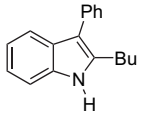
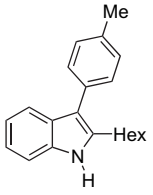
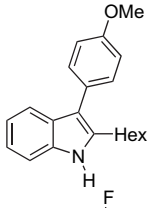
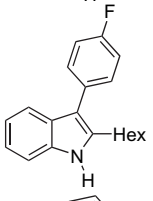
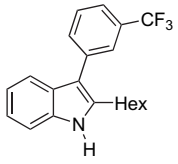
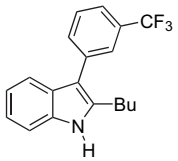
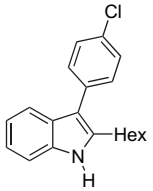
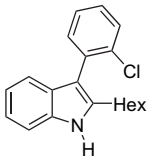
Entry	R^1	R^2	Product		Yield (%)	**6/3**[b]
1	H	Ph		**6b**	76	—
2	H	Hex		**6c**	81[c]	92:8
3	H	Bu		**6d**	81[c]	92:8
4	4-Me	Hex		**6e**	81[c]	92:8
5	4-MeO	Hex		**6f**	66	>99:<1
6	4-F	Hex		**6g**	74[d]	>99:<1
7	3-F_3C	Hex		**6h**	82[d]	97:3
8	3-CF_3	Bu		**6i**	84[d]	97:3

Table 1 (*continued*)

Entry	R^1	R^2	Product		Yield (%)	**6/3**[b]
9	4-Cl	Hex		**6j**	67[e]	>99:<1
10	2-Cl	Hex		**6k**	46[e]	>99:<1

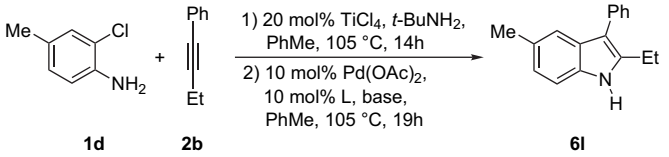
[a] Isolated yields.
[b] GC-analysis.
[c] Isolated with up to 8% of a regioisomer.
[d] Isolated with up to 5% of a regioisomer.
[e] Using 2-bromoaniline.

excellent regioselectivities.[32] Functional groups, such as F- (entry 6), F_3C- (entries 7 and 8), or Cl-substituents (entries 9 and 10) were tolerated by the catalytic system. While *para*- and *meta*-substituted aryl alkynes were efficiently converted, the preparation of the corresponding *ortho*-substituted analog **6k** occurred with significantly reduced isolated yield (entry 10). Unfortunately, the application to the synthesis of aza-indoles using the corresponding pyridine derivatives proved thus far less successful.

2.2. Optimization of the one-pot annulation

The most commonly used ligands for palladium-catalyzed Heck reactions are phosphorus-based.[33–35] Therefore, we explored a variety of phosphine (pre)ligands for the palladium-catalyzed intramolecular aza-Heck reaction within our one-pot annulation of internal alkynes. Additionally, we wished to expand our approach to the regioselective preparation of indoles with substituents on the benzenoid backbone. Thus, we chose as a test reaction the one-pot annulation of alkyne **2b** with aniline **1d** (Table 2). Not surprisingly, PPh_3 (**8**) as ligand did not enable an efficient palladium-catalyzed aza-Heck reaction of the 2-chlorophenyl-substituted enamine derived from aniline **1d** at a reaction temperature of 105 °C (entry 1). Monophosphine biaryl ligands **9**–**12** (Fig. 3) were probed (entries 2–5), and provided an isolated yield comparable to the one obtained with the previously used imidazolium salt HIPrCl **7** (entry 6). Interestingly, with air- and moisture-stable secondary phosphine oxide[36] $(1\text{-Ad})_2P(O)H$ **13**[37] an efficient intramolecular aza-Heck-reaction with an aryl chloride was accomplished (entry 7). However, a complex derived from PCy_3 (**14**) proved superior to all other catalytic systems studied in the annulation of alkyne **2b** (entry 8). Among a variety of bases KO-*t*-Bu was found superior (entries 8–11).

Table 2
Optimization of the palladium catalyst[a]



1d 2b 6l

Entry	Ligand (L)	Base	Isolated yield (%)
1	PPh_3 (**8**)	KO-*t*-Bu	2[b]
2	R^1=*i*-Pr, R^2=H, R^3=H, R^4=H (**9**)	KO-*t*-Bu	10[b]
3	R^1=Cy, R^2=NMe_2, R^3, R^4=H (**10**)	KO-*t*-Bu	40
4	R^1=Cy, R^2, R^3, R^4=*i*-Pr (**11**)	KO-*t*-Bu	50
5	R^1=Cy, R^2, R^3=OMe, R^4=H (**12**)	KO-*t*-Bu	55
6	HIPrCl **7**	KO-*t*-Bu	52
7	$(1\text{-Ad})_2P(O)H$ (**13**)	KO-*t*-Bu	55
8	PCy_3 (**14**)	KO-*t*-Bu	71
9	PCy_3 (**14**)	K_2CO_3	—
10	PCy_3 (**14**)	K_3PO_4	—
11	PCy_3 (**14**)	Cs_2CO_3	—

[a] Isolated yield of analytically pure product.
[b] GC-conversion.

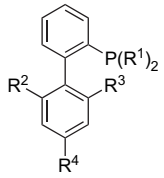
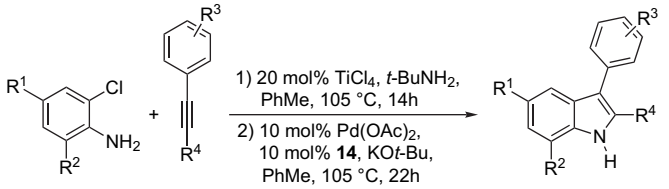


Figure 3. General structure of monophosphine biaryl ligands.

2.3. Scope of the annulation protocol

With an optimized catalyst in hand, we probed its scope in the annulation of various aryl-substituted alkynes **2** by substituted primary 2-chloroanilines **1** (Table 3). Both symmetrically as well as unsymmetrically substituted aryl alkynes could be employed providing comparable isolated yields

Table 3
Regioselective synthesis of indoles **6**[a]



1 2 6

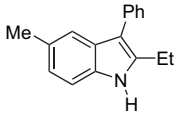
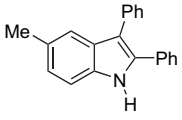
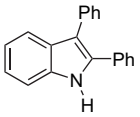
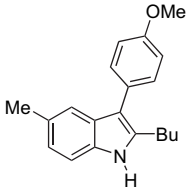
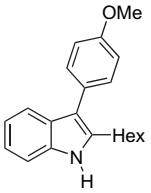
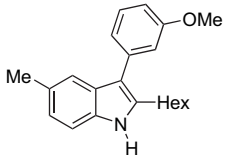
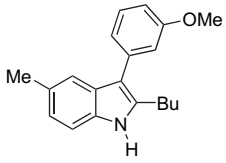
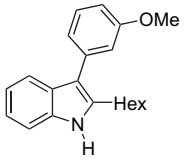
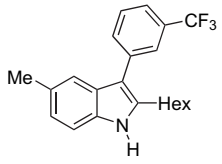
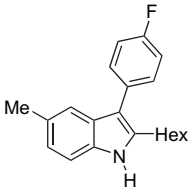
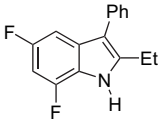
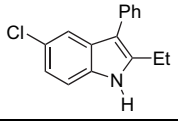
Entry	R^1	R^2	R^3	R^4	Product		Isolated yield (%)
1	Me	H	H	Et		**6l**	71
2	Me	H	H	Ph		**6m**	71

Table 3 (*continued*)

Entry	R^1	R^2	R^3	R^4	Product		Isolated yield (%)
3	H	H	H	Ph		**6b**	74
4	Me	H	4-MeO	Bu		**6n**	58[c]
5	H	H	4-MeO	Hex		**6f**	68
6	Me	H	3-MeO	Hex		**6o**	51[c]
7	Me	H	3-MeO	Bu		**6p**	55[c]
8	H	H	3-MeO	Hex		**6q**	71
9	Me	H	3-F_3C	Hex		**6r**	71[c]
10	Me	H	4-F	Hex		**6s**	54[c]
11[b]	F	F	H	Et		**6t**	52
12[b]	Cl	H	H	Et		**6u**	53

[a] Isolated yield of analytically pure product.
[b] Starting from the corresponding 2-bromoaniline.
[c] Isolated with up to 4% of a regioisomer.

(entries 1–3). When using unsymmetrically substituted alkynes the corresponding 3-aryl indoles **6** could be isolated with good regioselectivities. Additionally, functionalities, such as ethers (entries 4–8), alkyl fluorides (entry 9), as well as aryl fluorides (entries 10, and 11) and chlorides (entry 12) were tolerated by the two catalytic systems.

3. Conclusions

In summary, we described the development of a one-pot annulation strategy of internal alkynes with primary 2-bromo- or 2-chloroanilines, yielding regioselectively various indole derivatives. The reaction sequence commences with a user-friendly $TiCl_4$-catalyzed intramolecular hydroamination. This sets the stage for an intramolecular palladium-catalyzed aza-Heck reaction, which was most effectively accomplished with PCy_3 as ligand. For unsymmetrically substituted aryl alkynes our one-pot annulation approach yields selectively 3-aryl-substituted indoles. With respect to its regioselectivity, our approach to substituted indoles proved to be complementary to Larock's frequently employed direct annulation.

4. Experimental

4.1. General

All catalytic reactions were carried out on a 1.00–4.76 mmol scale under N_2 using pre-dried glassware. Chemicals were obtained from commercial sources, and were used without further purification. PhMe was distilled from sodium-benzophenone under nitrogen and stored over molecular sieves (4 Å). Yields refer to isolated compounds, estimated to be >95% pure as determined by ^1H NMR and GC, unless otherwise stated. Flash chromatography: Merck silica gel 60 (230–400 mesh). NMR: ^1H was recorded on a Varian Unity 300, Bruker AC 300, or AMX 600, ^{13}C was recorded on a Varian Mercury 300, Unity 300, Bruker AC 300, AMX 600, or Inova 500, ^{19}F was recorded on a Mercury 300 in the solvent indicated; chemical shifts (δ) are given in parts per million, coupling constants (J) in hertz.

4.2. Representative procedure for annulation of alkynes with imidazolium salt **7** as preligand

4.2.1. 2,3-Diphenylindole (**6b**)[38]

2-Chloroaniline (**1c**) (610 mg, 4.76 mmol) and tolan (1.02 g, 5.70 mmol) were added to a solution of $TiCl_4$ (0.05 mL, 0.47 mmol) and *t*-$BuNH_2$ (0.30 mL, 2.86 mmol) in PhMe (5 mL) and the resulting mixture was stirred for 20 h at 105 °C. The solvent was partially removed and KO-*t*-Bu (1.60 g, 14.0 mmol), HIPrCl (**7**) (202 mg, 0.48 mmol), and $Pd(OAc)_2$ (106 mg, 0.48 mmol) were added. The mixture was stirred at 105 °C for 24 h. CH_2Cl_2 (75 mL) and aq HCl (2 M, 50 mL) were added to the cold suspension. The separated aqueous phase was washed with CH_2Cl_2 (2×75 mL). The combined organic phases were washed with satd aq $NaHCO_3$ (50 mL) and brine (50 mL). Drying with $MgSO_4$ and purification by column chromatography (SiO_2, *n*-pentane/Et_2O 20:1→10:1→4:1) yielded 2,3-diphenylindole (**6b**) (974 mg, 76%) as an off-white solid. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.22 (br s, 1H), 7.67 (d, J=7.8 Hz, 1H), 7.45–7.12 (m, 13H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.9, 135.1, 134.1, 132.7, 130.2, 128.8, 128.7, 128.5, 128.2, 127.7, 126.2, 122.7, 120.4, 119.7, 115.2, 110.9. MS (EI) *m/z* (relative intensity) 269 (100) [M^+], 254 (4), 239 (5), 165 (11), 134 (6), 127 (4). HRMS (EI) *m/z* calcd for $C_{20}H_{15}N$ 269.1204, found 269.1198.

4.2.2. 2-Ethyl-3-phenylindole (**6a**)[39]

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-phenyl-1-butyne (**2b**) (195 mg, 2.00 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6a** (192 mg, 57%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→20:1→10:1) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.87 (br s, 1H), 7.61 (d, J=7.5 Hz, 1H), 7.47–7.37 (m, 4H), 7.27–7.23 (m, 2H), 7.15–7.06 (m, 2H), 2.81 (q, J=7.6 Hz, 2H), 1.24 (t, J=7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.2, 135.5, 135.1, 129.6, 128.5, 127.9, 125.9, 121.6, 119.9, 118.9, 113.9, 110.4, 19.7, 14.3. IR (KBr): 3404, 3055, 2970, 2931, 1601, 1459, 1460, 772, 752, 703 cm^{-1}. MS *m/z* (relative intensity) 221 (100) [M^+], 206 (98), 179 (15), 102 (5). HRMS (EI) *m/z* calcd for $C_{16}H_{15}N$ 221.1204, found 221.1182.

4.2.3. 2-n-Hexyl-3-phenylindole (**6c**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-phenyl-1-octyne (244 mg, 1.31 mmol), HIPrCl (**7**) (57 mg, 0.13 mmol), and $Pd(OAc)_2$ (29 mg, 0.13 mmol), **6c** (295 mg, 81%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→20:1) as a yellow oil. Ratio of regioisomers: 7:86:7 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.92 (br s, 1H), 7.66–7.63 (m, 1H), 7.51–7.43 (m, 4H), 7.33–7.28 (m, 2H), 7.21–7.08 (m, 2H), 2.83 (t, J=7.8 Hz, 2H), 1.67 (tt, J=7.8, 7.8 Hz, 2H), 1.36–1.23 (m, 6H), 0.86 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.1, 135.5, 135.2, 129.6, 128.4, 127.9, 125.8, 121.5, 119.8, 118.9, 114.4, 110.3, 31.5, 29.5, 29.1, 26.3, 22.5, 14.0. IR (KBr): 3409, 3057, 2955, 2927, 2856, 1496, 1460, 772, 744, 702 cm^{-1}. MS (EI) *m/z* (relative intensity) 277 (48) [M^+], 206 (100), 179 (9). HRMS (EI) *m/z* calcd for $C_{20}H_{23}N$ 277.1830, found 277.1839.

4.2.4. 2-n-Butyl-3-phenylindole (**6d**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-phenyl-1-hexyne (237 mg, 1.5 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6d** (303 mg, 81%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→20:1→10:1) as a yellow oil. Ratio of regioisomers: 8:85:7 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.95 (br s, 1H), 7.73–7.69 (m, 1H), 7.59–7.49 (m, 4H), 7.39–7.35 (m, 2H), 7.26–7.15 (m, 2H), 2.89 (t, J=7.8 Hz, 2H), 1.71 (tt, J=7.8, 7.8 Hz, 2H), 1.49–1.36 (m, 2H), 0.96 (t, J=7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.0, 135.5, 135.2, 129.6,

128.4, 127.9, 125.8, 121.5, 119.8, 118.9, 114.4, 110.3, 32.0, 26.1, 22.5, 13.8. IR (KBr): 3409, 3057, 2957, 2928, 1496, 1460, 771, 744, 702 cm^{-1}. MS (EI) *m/z* (relative intensity) 249 (43) [M^+], 206 (100), 23 (10). HRMS (EI) *m/z* calcd for $C_{18}H_{19}N$ 249.1517, found 249.1525.

4.2.5. 2-n-Hexyl-3-(4-methylphenyl)indole (**6e**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-(4-methylphenyl)-1-octyne (300 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6e** (354 mg, 81%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1) as a yellow oil. Ratio of regioisomers: 9:81:10 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.95 (br s, 1H), 7.65–7.62 (m, 1H), 7.42–7.09 (m, 7H), 2.85 (t, J=7.8 Hz, 2H), 2.44 (s, 3H), 1.70 (tt, J=7.8, 7.8 Hz, 2H), 1.39–1.41 (m, 6H), 0.88 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.9, 135.4, 135.2, 132.4, 129.5, 129.2, 128.1, 121.4, 119.8, 118.9, 114.3, 110.3, 31.6, 29.9, 29.1, 26.4, 22.6, 21.2, 14.0. IR (KBr): 3408, 3052, 2926, 2955, 2857, 1511, 1460, 1330, 819, 744 cm^{-1}. MS (EI) *m/z* (relative intensity) 291 (55) [M^+], 234 (11), 220 (100), 205 (36), 178 (7). HRMS (EI) *m/z* calcd for $C_{21}H_{25}N$ 291.1987, found 291.1975.

4.2.6. 2-n-Hexyl-3-(4-methoxyphenyl)indole (**6f**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-(4-methoxyphenyl)-1-octyne (324 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6f** (306 mg, 66%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→20:1→10:1) as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.97 (br s, 1H), 7.63 (d, J=7.6 Hz, 1H), 7.45–7.42 (m, 2H), 7.36–7.33 (m, 1H), 7.22–7.10 (m, 2H), 7.07–7.02 (m, 2H), 3.90 (s, 3H), 2.84 (t, J=7.8 Hz, 2H), 1.70 (tt, J=7.8, 7.8 Hz, 2H), 1.39–1.26 (m, 6H), 0.90 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.9, 135.8, 135.8, 135.1, 130.7, 128.2, 127.8, 121.4, 119.7, 118.8, 113.9, 110.3, 55.3, 31.5, 29.9, 29.1, 26.3, 22.5, 14.0. IR (KBr): 3406, 3056, 2955, 2928, 2856, 1510, 1460, 1243, 1175, 831, 745 cm^{-1}. MS (EI) *m/z* (relative intensity) 307 (90) [M^+], 250 (5), 236 (100), 220 (9), 205 (25), 192 (12). HRMS (EI) *m/z* calcd for $C_{21}H_{25}NO$ 307.1936, found 307.1939.

4.2.7. 3-(4-Fluorophenyl)-2-n-hexylindole (**6g**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-(4-fluorophenyl)-1-octyne (306 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6g** (329 mg, 74%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→20:1→10:1) as a yellow oil. Ratio of regioisomers: 5:95:0 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.98 (br s, 1H), 7.60–7.57 (m, 1H), 7.47–7.42 (m, 2H), 7.37–7.34 (m, 1H), 7.22–7.10 (m, 4H), 2.83 (t, J=7.7 Hz, 2H), 1.69 (tt, J=7.7, 7.7 Hz, 2H), 1.41–1.24 (m, 6H), 0.88 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.4 (d, J=244 Hz), 136.1, 135.1, 131.4 (d, J=3 Hz), 131.1 (d, J=8 Hz), 128.0, 121.6, 120.0, 118.6, 115.3 (d, J=21 Hz), 113.5, 110.4, 31.5, 29.8, 29.0, 26.3, 22.5, 14.0. ^{19}F NMR ($CDCl_3$, 375 MHz): δ −115.9 (tt, J=9.2, 5.7 Hz). IR (KBr): 3956, 3404, 3056, 3956, 2928, 2857, 1507, 1460, 1222, 1156, 835, 745 cm^{-1}. MS (EI) *m/z* (relative intensity) 295 (50) [M^+], 238 (9), 224 (100), 197 (11), 177 (2). HRMS (EI) *m/z* calcd for $C_{20}H_{22}FN$ 295.1736, found 295.1732.

4.2.8. 3-(3-Trifluoromethylphenyl)-2-n-hexylindole (**6h**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-(3-trifluoromethylphenyl)-1-octyne (382 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6h** (422 mg, 82%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→20:1→10:1) as a yellow oil. Ratio of regioisomers: 4:93:3 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.04 (br s, 1H), 7.78–7.77 (m, 1H), 7.71–7.67 (m, 1H), 7.63–7.57 (m, 3H), 7.39–7.36 (m, 1H), 7.22 (ddd, J=7.4, 7.4, 1.3 Hz, 1H), 7.16 (ddd, J=7.4, 7.4, 1.3 Hz, 1H), 2.86 (t, J=7.8 Hz, 2H), 1.72 (tt, J=7.8, 7.8 Hz, 2H), 1.39–1.24 (m, 6H), 0.88 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.6, 136.4, 135.2, 132.7, 130.4 (q, J=32 Hz), 128.9, 127.6, 126.2 (q, J=4 Hz), 124.3 (q, J=272 Hz), 122.5 (q, J=4 Hz), 121.9, 120.3, 118.5, 113.2, 110.5, 31.5, 29.8, 29.0, 26.3, 22.5, 14.0. ^{19}F NMR ($CDCl_3$, 375 MHz): δ −61.4. IR (KBr): 3405, 3060, 2958, 2929, 2858, 1461, 1323, 1306, 1166, 1127, 1073, 804 cm^{-1}. MS (EI) *m/z* (relative intensity) 345 (50) [M^+], 288 (15), 274 (100), 254 (6), 204 (17). HRMS (EI) *m/z* calcd for $C_{21}H_{22}F_3N$ 345.1704, found 345.1695.

4.2.9. 2-n-Butyl-3-(3-trifluoromethylphenyl)indole (**6i**)

Following the general procedure using 2-chloroaniline (**1c**) (191 mg, 1.50 mmol), 1-(3-trifluoromethylphenyl)-1-hexyne (339 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6i** (398 mg, 84%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→15:1) as a yellow solid. Ratio of regioisomers: 3:96:3 (GC). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.03 (br s, 1H), 7.79 (m, 1H), 7.72–7.69 (m, 1H), 7.65–7.58 (m, 3H), 7.38 (d, J=6.3 Hz, 1H), 7.26–7.15 (m, 2H), 2.86 (t, J=7.6 Hz, 2H), 1.71 (tt, J=7.6, 7.6 Hz, 2H), 1.41 (tq, J=7.6, 7.6 Hz, 2H), 0.93 (t, J=7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.6, 136.4, 135.2, 132.7, 130.4 (q, J=32 Hz), 128.9, 127.6, 126.1 (q, J=4 Hz), 124.3 (q, J=272 Hz), 122.5 (q, J=4 Hz), 121.9, 120.3, 118.4, 113.2, 110.5, 31.9, 26.0, 22.4, 13.7. ^{19}F NMR ($CDCl_3$, 375 MHz): δ −61.4. IR (KBr): 3411, 3366, 3060, 2955, 2928, 2863, 1460, 1326, 1308, 1163, 1124, 1073, 802, 747, 702 cm^{-1}. MS (EI) *m/z* (relative intensity) 317 (46) [M^+], 274 (100), 254 (6), 204 (22), 178 (6). HRMS (EI) *m/z* calcd for $C_{19}H_{18}F_3N$ 317.1391, found 317.1411.

4.2.10. 3-(4-Chlorophenyl)-2-n-hexylindole (**6j**)

Following the general procedure using 2-bromoaniline (258 mg, 1.50 mmol), 1-(4-chlorophenyl)-1-octyne (331 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$

(34 mg, 0.15 mmol), **6j** (312 mg, 67%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→30:1→15:1) as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.00 (br s, 1H), 7.60–7.57 (m, 1H), 7.43 (m, 4H), 7.37–7.34 (m, 1H), 7.22–7.10 (m, 2H), 2.83 (t, J=7.8 Hz, 2H), 1.69 (tt, J=7.8, 7.8 Hz, 2H), 1.40–1.23 (m, 6H), 0.88 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.6, 135.6, 134.4, 132.0, 131.2, 129.0, 128.1, 122.1, 120.5, 119.0, 113.7, 110.8, 31.9, 30.2, 29.4, 26.7, 22.9, 14.4. IR (KBr): 3403, 3055, 2955, 2927, 2856, 1493, 1460, 1090, 1014, 820, 744 cm^{-1}. MS (EI) *m/z* (relative intensity) 311 (61) [M^+], 254 (10), 240 (48), 205 (100), 130 (4). HRMS (EI) *m/z* calcd for $C_{20}H_{22}NCl$ 311.1441, found 311.1417.

*4.2.11. 3-(2-Chlorophenyl)-2-n-hexylindole (**6k**)*

Following the general procedure using 2-bromoaniline (258 mg, 1.50 mmol), 1-(2-chlorophenyl)-1-octyne (331 mg, 1.50 mmol), HIPrCl (**7**) (64 mg, 0.15 mmol), and $Pd(OAc)_2$ (34 mg, 0.15 mmol), **6h** (214 mg, 46%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1→20:1→10:1) as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.01 (br s, 1H), 7.57–7.54 (m, 1H), 7.44–7.41 (m, 1H), 7.38–7.32 (m, 4H), 7.20 (ddd, J=7.5, 7.5, 1.3 Hz, 1H), 7.12 (ddd, J=7.5, 7.5, 1.0 Hz, 1H), 2.76–2.66 (m, 2H), 1.71–1.59 (m, 2H), 1.33–1.21 (m, 6H), 0.87 (t, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.0, 135.0, 135.0, 134.2, 133.1, 129.7, 128.2, 128.1, 126.4, 121.4, 119.7, 119.2, 112.1, 110.4, 31.5, 29.2, 28.8, 26.7, 22.5, 14.0. IR (KBr): 3409, 3058, 2928, 2857, 1479, 1462, 1434, 1332, 1066, 1036, 820, 741 cm^{-1}. MS (EI) *m/z* (relative intensity) 311 (52) [M^+], 254 (12), 240 (49), 217 (14), 205 (100), 130 (4). HRMS (EI) *m/z* calcd for $C_{20}H_{22}NCl$ 311.1441, found 311.1444.

*4.3. Representative procedure for annulation with PCy_3 (**14**) as ligand*

*4.3.1. 2-Ethyl-5-methyl-3-phenylindole (**6l**)*

To a well-stirred solution of *t*-$BuNH_2$ (88 mg, 1.2 mmol) in PhMe (2 mL) was added dropwise $TiCl_4$ (38 mg, 0.2 mmol). After stirring for 10 min 2-chloro-4-methylaniline (142 mg, 1.00 mmol) and alkyne **2b** (130 mg, 1.00 mmol) were added. The reaction mixture was stirred at 105 °C for 20 h and was thereafter allowed to cool to ambient temperature. $Pd(OAc)_2$ (22 mg, 0.10 mmol), PCy_3 (**14**) (28 mg, 0.10 mmol), KO-*t*-Bu (337 mg, 3.00 mmol), and PhMe (2 mL) were added and the reaction was heated at 105 °C for 21 h. CH_2Cl_2 (10 mL) and aq HCl (2 M, 5 mL) were added to the cold suspension. The separated aqueous layer was extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL). Drying with $MgSO_4$ and purification by column chromatography (*n*-hexane/EtOAc, 20:1→15:1) yielded **6l** as a yellow oil (166 mg, 71%). ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (br s, 1H), 7.43–7.34 (m, 5H), 7.26–7.16 (m, 2H), 6.92 (d, J=8.5 Hz, 1H), 2.81 (q, J=7.6 Hz, 2H), 2.35 (s, 3H), 1.24 (t, J=7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.3, 135.6, 133.4, 129.6, 129.2, 128.4, 128.1, 125.8, 123.0, 118.6, 113.4, 110.0, 21.5, 19.7, 14.3. IR (film): 3401, 3051, 2970, 2931, 2872, 2361, 2339, 1603, 1312, 1265, 1012, 876 cm^{-1}. MS (EI) *m/z* (relative intensity) 235 (100) [M^+], 220 (56), 204 (23), 178 (6), 103 (6). HRMS (ESI) *m/z* calcd for $C_{17}H_{18}N$ 236.1434, found 236.1434.

*4.3.2. 5-Methyl-2,3-diphenylindole (**6m**)*[8]

Following the general procedure, indole **6m** (208 mg, 71%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 30:1→25:1→15:1→5:1) as an off-white solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8,14 (br s, 1H), 7.45–7.26 (m, 12H), 7.09 (d, J=8.1 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.2, 134.2, 134.2, 132.8, 130.2, 129.7, 129.0, 128.6, 128.5, 128.1, 127.6, 126.1, 124.3, 119.2, 114.7, 110.5, 21.5. IR (KBr): 3369, 3058, 2361, 2338, 1617, 1506, 1316, 1306, 1295, 1255, 1030, 914 cm^{-1}. MS (EI) *m/z* (relative intensity) 283 (100) [M^+], 267 (12), 133 (7). HRMS (ESI) *m/z* calcd for $C_{21}H_{18}N$ 284.1434, found 284.1434.

*4.3.3. 2-n-Butyl-3-(4-methoxyphenyl)-5-methylindole (**6n**)*

Following the general procedure, indole **6n** (168 mg, 58%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 30:1→25:1→15:1) as a yellow oil. Ratio of regioisomers: 97:3 (GC). ^1H NMR (300 MHz, $CDCl_3$): δ 7.88 (br s, 1H), 7.43–7.37 (m, 3H), 7.22 (d, J=8.2 Hz, 1H), 7.04–6.97 (m, 3H), 3.88 (s, 3H), 2.81 (t, J=7.7 Hz, 2H), 2.43 (s, 3H), 1.71–1.60 (m, 2H), 1.44–1.31 (m, 2H), 0.90 (t, J=7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 135.9, 133.4, 130.7, 129.0, 128.4, 128.0, 122.8, 118.5, 113.9, 113.6, 109.9, 55.3, 32.0, 26.1, 22.5, 21.5, 13.8. IR (film, CH_2Cl_2): 3399, 2956, 2930, 2859, 2361, 2338, 1510, 1464, 1243, 1174, 1036, 833 cm^{-1}. MS (EI) *m/z* (relative intensity) 293 (18) [M^+], 250 (8), 206 (18), 150 (35), 135 (71), 121 (100). HRMS (ESI) *m/z* calcd for $C_{20}H_{24}NO$ 294.1852, found 294.1852.

*4.3.4. 2-n-Hexyl-3-(3-methoxyphenyl)-5-methylindole (**6o**)*

Following the general procedure, indole **6o** (164 mg, 51%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 30:1→25:1) as a yellow oil. Ratio of regioisomers: 96:4 (GC). ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (br s, 1H), 7.43–7.35 (m, 2H), 7.24 (d, J=8.1 Hz, 1H), 7.09–6.98 (m, 3H), 6.89–6.86 (m, 1H), 3.86 (s, 3H), 2.84 (t, J=6.0 Hz, 2H), 2.42 (s, 3H), 1.73–1.63 (m, 2H), 1.39–1.19 (m, 6H), 0.86 (t, J=6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 137.1, 136.3, 133.4, 129.3, 129.2, 128.1, 123.0, 122.2, 118.6, 115.2, 113.9, 111.3, 110.0, 55.2, 31.6, 29.8, 29.1, 26.4, 22.5, 21.5, 14.0. IR (film): 3402, 2956, 2929, 2589, 2361, 1844, 1608, 1486, 1464, 1281, 1265, 1048, 871 cm^{-1}. MS (EI) *m/z* (relative intensity) 321 (100) [M^+], 250 (54), 234 (6). HRMS (ESI) *m/z* calcd for $C_{22}H_{28}NO$ 322.2165, found 322.2167.

*4.3.5. 2-n-Butyl-3-(3-methoxyphenyl)-5-methylindole (**6p**)*

Following the general procedure, indole **6p** (163 mg, 55%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 30:1→25:1→20:1) as a yellow oil. Ratio of regioisomers: 97:3 (GC). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (br s, 1H), 7.43–7.35 (m, 2H), 7.24 (d, J=8.2 Hz, 1H), 7.09–6.98 (m, 3H), 6.89–6.86 (m, 1H), 3.87 (s, 3H), 2.85 (t, J=7.4 Hz, 2H), 2.43 (s, 3H), 1.72–1.63 (m, 2H), 1.44–1.34 (m, 2H), 0.90 (t, J=7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 137.0, 136.2, 133.4, 129.3, 129.2, 128.1, 123.0, 122.2, 118.6, 115.2, 113.9, 111.3, 110.0, 55.2, 32.0, 26.2, 22.5, 21.5, 13.8. IR (film): 3456, 3053, 2959, 2361, 1601, 1490, 1458, 1265, 1048, 1023, 896 cm^{-1}. MS (EI) *m/z* (relative intensity) 293 (100) [M$^+$], 250 (79), 235 (9). HRMS (ESI) *m/z* calcd for $C_{20}H_{24}NO$ 294.1852, found 294.1853.

*4.3.6. 2-n-Hexyl-3-(3-methoxyphenyl)indole (**6q**)*

Following the general procedure, indole **6q** (224 mg, 71%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 50:1→30:1→20:1→10:1) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (br s, 1H), 7.69–7.66 (m, 1H), 7.41–7.33 (m, 2H), 7.21–7.07 (m, 4H), 6.90–6.87 (m, 1H), 3.87 (s, 3H), 2.87 (t, J=8.7 Hz, 2H), 1.75–1.65 (m, 2H), 1.41–1.25 (m, 6H), 0.87 (t, J=6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 136.8, 136.2, 135.1, 129.4, 127.8, 122.1, 121.5, 119.9, 118.9, 115.0, 114.2, 111.5, 110.3, 55.2, 31.6, 29.9, 29.1, 26.4, 22.5, 14.0. IR (KBr): 3465, 2956, 2928, 2856, 2361, 2336, 2252, 1601, 1457, 1329, 1163, 1049 cm^{-1}. MS (EI) *m/z* (relative intensity) 307 (28) [M$^+$], 236 (24), 204 (5), 113 (75), 85 (29), 43 (100). HRMS (ESI) *m/z* calcd for $C_{21}H_{26}NO$ 308.2009, found 308.2010.

*4.3.7. 3-(3-Trifluoromethylphenyl)-2-n-hexyl-5-methylindole (**6r**)*

Following the general procedure, indole **6r** (256 mg, 71%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 50:1→30:1→25:1) as a yellow oil. Ratio of regioisomers: 99:1 (GC). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (br s, 1H), 7.47–7.38 (m, 3H), 7.26–7.15 (m, 3H), 7.05–7.02 (m, 1H), 2.81 (t, J=7.6 Hz, 2H), 2.46 (s, 3H), 1.73–1.63 (m, 2H), 1.39–1.25 (m, 6H), 0.89 (t, J=6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.8, 136.6, 133.5, 132.8, 130.4 (q, J=31.4 Hz), 129.6, 128.9, 127.8, 126.2 (q, J=3.7 Hz), 124.3 (q, J=272.8 Hz), 123.4, 122.5 (q, J=3.7 Hz), 118.1, 112.8, 110.2, 31.5, 29.8, 29.0, 26.3, 22.5, 21.5, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.5 (s). IR (film): 3460, 3401, 3049, 2927, 2857, 2361, 1507, 1265, 1221, 1156, 1093, 874 cm^{-1}. MS (EI) *m/z* (relative intensity) 359 (26) [M$^+$], 288 (21), 253 (4), 159 (25). HRMS (ESI) *m/z* calcd for $C_{22}H_{25}NF_3$ 360.1934, found 360.1933.

*4.3.8. 3-(4-Fluorophenyl)-2-n-hexyl-5-methylindole (**6s**)*

Following the general procedure, indole **6s** (168 mg, 54%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 50:1→30:1) as a yellow oil. Ratio of regioisomers: 98:2 (GC). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (br s, 1H), 7.75–7.25 (m, 6H), 7.06–7.03 (m, 1H), 2.38 (t, J=6.6 Hz, 2H), 2.45 (s, 3H), 1.75–1.65 (m, 2H), 1.37–1.24 (m, 6H), 0.87 (t, J=6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4 (d, J=244 Hz), 136.3, 133.5, 131.6, 131.6, 131.2 (d, J=8 Hz), 129.3, 128.3, 123.2, 118.4, 115.4 (d, J=20 Hz), 110.2, 31.6, 29.9, 29.1, 26.4, 22.6, 21.6, 14.1. ^{19}F NMR (282 MHz, $CDCl_3$): −117.3 (tt, J=9.0, 5.0 Hz). IR (KBr): 3400, 2957, 2929, 2859, 2361, 2339, 2247, 1331, 1166, 1128, 1073, 908 cm^{-1}. MS (EI) *m/z* (relative intensity) 309 (4) [M$^+$], 238 (9), 113 (98), 43 (100). HRMS (ESI) *m/z* calcd for $C_{21}H_{25}NF$ 310.1966, found 310.1969.

*4.3.9. 2-Ethyl-5,7-difluoro-3-phenylindole (**6t**)*

Following the general procedure, indole **6t** (134 mg, 52%) was obtained after purification by column chromatography (SiO_2, *n*-pentane/Et_2O 30:1) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (br s, 1H), 7.50–7.42 (m, 4H), 7.37–7.32 (m, 1H), 7.11–7.07 (dd, J=9.5, 2.2 Hz, 1H), 6.76–6.68 (ddd, J=11.7, 9.5, 2.2 Hz, 1H), 2.90 (q, J=7.7 Hz, 2H), 1.35 (t, J=7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.2 (dd, J=237, 10 Hz), 148.1 (dd, J=237, 14 Hz), 139.5 (d, J=1 Hz), 134.4 (d, J=1 Hz), 130.5 (dd, J=11, 7 Hz), 129.3, 128.6, 126.4, 119.8, 115.1 (dd, J=5, 3 Hz), 100.0 (dd, J=24, 4 Hz), 96.6 (dd, J=30, 21 Hz), 19.8, 14.0. IR (ATR): 3462, 2972, 1653, 1587, 1494, 1438, 1294, 1113, 978, 701 cm^{-1}. MS (EI) *m/z* (relative intensity) 257 (100) [M$^+$], 242 (67), 240 (17), 222 (17), 214 (8), 200 (4). HRMS (EI) *m/z* calcd for $C_{16}H_{13}F_2N$ 257.1016, found 257.0994.

*4.3.10. 5-Chloro-2-ethyl-3-phenylindole (**6u**)*

Following the general procedure, indole **6u** (136 mg, 53%) was obtained after purification by column chromatography (SiO_2, *n*-hexane/EtOAc, 30:1→20:1→5:1) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (br s, 1H), 7.60 (d, J=1.7 Hz, 1H), 7.51–7.44 (m, 4H), 7.36–7.30 (m, 1H), 7.27–7.24 (m, 1H), 7.12 (dd, J=2.0, 8.6 Hz, 1H), 2.89 (q, J=7.6 Hz, 2H), 1.32 (t, J=7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6, 134.7, 133.5, 129.5, 129.1, 128.6, 126.2, 125.7, 121.7, 118.4, 113.8, 111.3, 19.7, 14.2. IR (KBr): 3417, 3055, 2971, 2931, 2873, 2361, 2338, 1496, 1466, 1311, 1065, 870 cm^{-1}. MS (EI) *m/z* (relative intensity) 255 (89) [M$^+$], 240 (32), 205 (48), 84 (39), 56 (65), 43 (100). HRMS (ESI) *m/z* calcd for $C_{16}H_{15}ClN$ 256.0888, found 256.0888.

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