Palladium-Catalyzed C–O and C–C Coupling Reactions of Electron-Rich Indoles

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Abstract: A novel palladium-catalyzed formation of indole aryl ethers is described. In general, the corresponding indole ethers are obtained in the presence of $Pd(OAc)_2$ combined with *N*-phenyl-2-(di-1-adamantylphosphino)pyrrole in high yields.

Key words: indoles, diaryl ethers, palladium, cross-coupling

Diaryl ethers form an important class of organic compounds throughout the life science and polymer industries.[1] Aryl ethers, including oxygen heterocycles, have been reported to possess significant biological activity; for example, natural products of the isodityrosin family, vancomycin,[2] angiotensin-converting enzyme inhibitor K-13,[3] (+)-piperazinomycin,[4] and antitumor compounds such as bouvardin and bastadin.[5] Until recently, the most general synthesis for the preparation of diaryl ethers was the classic Ullmann ether synthesis, but it is often limited by harsh reaction conditions, use of stoichiometric amounts of copper and the necessity of a large excess of the phenolic substrate.[6] In the last decade a number of interesting and improved methods for diaryl ether formation have been reported.[7] For instance, the palladium-catalyzed coupling of phenols and aryl halides is an important extension of other reported carbon–heteroatom bond-forming reactions.[8] In this regard intermolecular palladium-catalyzed C–O bond formation in the presence of electron-rich bulky aryldialkylphosphines by Buchwald and co-workers is also noteworthy.[9]

Based on our continuing interest in the synthesis and derivatization of indoles[10] as well as in Pd-catalyzed coupling reactions,[11] very recently we developed a convenient protocol for electron-rich 3-siloxy- and 3-alkoxyindoles.[10d] In the present paper we describe for the first time the Pd-catalyzed aryl ether synthesis of different 5-bromoindoles.

In exploratory experiments, we investigated the influence of different electron-rich sterically demanding ligands on the coupling of 5-bromo-3-(*tert*-butyldimethylsiloxy)-1,2-dimethyl-1*H*-indole (**13**) with *o*-cresol, which served as our model reaction. As shown in Table 1, most of the ligands gave only traces of the desired product. The best yield of the corresponding indole **16** (34%) was achieved with the in-house-developed ligand *N*-phenyl-2-(di-1-adamantylphosphino)pyrrole (**7**) (Table 1, entry 7).[12]

Apparently, a subtle balance of steric and electronic factors of the ligand is important to activate the Pd center. Hence, the replacement of the dicyclohexyl substituents of ligand **10** by di-*tert*-butyl and, more importantly, by di-1-adamantyl substituents (ligand **11** and **7**, respectively) led to a significant increase of the product yield. Further variation of different bulky ligands showed no appreciable improvements. Apart from **7** only the Buchwald ligand **12** (Table 1, entry 12) gave the corresponding indole in noticeable yield (15%). Apparently, our model reaction was challenging and further modification of the reaction parameters was necessary.

Therefore, we examined the influence of different bases, metal precursors, temperatures (100–160 °C), and the catalyst concentration (0.5–6 mol% Pd). The results of this optimization study are shown in Table 2. Neither the change of base nor the variation of the palladium source raised the product yield. However, applying 2 mol% $Pd(OAc)_2$ at 120 °C enhanced the yield of **16** from 34% (Table 2, entry 2) to 83% (Table 2, entry 5). Doubling the catalyst concentration gave a similar yield at 100 °C (Table 2, entry 13). Also ligand **12** gave an improved yield, however, somewhat lower compared to **7** (Table 2, entry 4 vs entry 3). As expected the reaction did not work without any ligand, base, or catalyst.

Next, we were interested in the scope and limitation of the catalyst system for different phenols and indoles. All reactions in Table 3 were performed at 120 °C for 24 hours in toluene in the presence of 2 mol% $Pd(OAc)_2$, 4 mol% *N*-phenyl-2-(di-1-adamantylphosphino)pyrrole (**7**) and 2 equivalents of K_3PO_4.

As shown in Table 3, the corresponding indole products **16–23** were obtained in moderate to good yields (52–85%). The Pd catalyst system works well with various alkylated phenols and different N-protected indole derivatives. There is no significant difference in reactivity between 2-, 3-, and 4-methylphenol and 2,6-dimethylphenol (Table 3, entries 1,4,5,6). The *N*-benzyl- and *N*-Boc-protected indoles gave an improved yield of the coupling product (Table 3, entries 2,3). Unfortunately, under the same reaction conditions 5-bromoindole and 6-bromoindole with a free NH-group gave either no ether products or only traces (<2%). In none of these reactions we have observed reductive dehalogenation of the bromoindoles. Noteworthy, the C–O coupling reaction of the simple *N*-Boc-indole proceeded smoothly in 85% yield (Table 3, entry 8).

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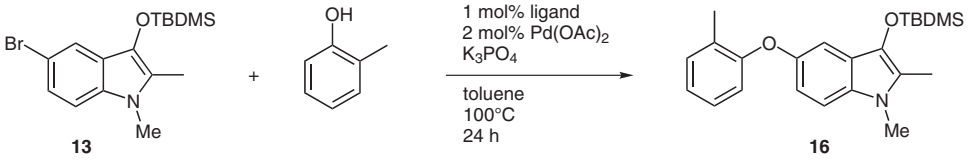
Table 1 Model Reaction of Indole **13** with *o*-Cresol[a]



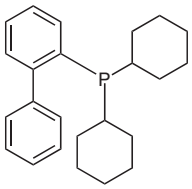
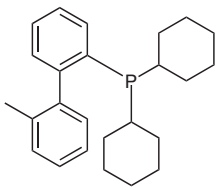
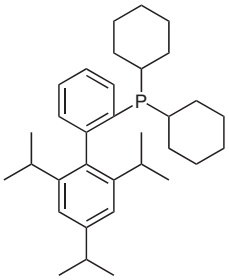
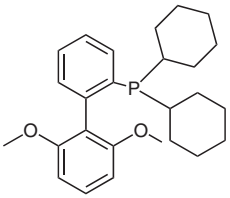
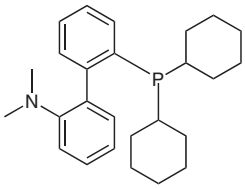
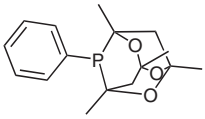
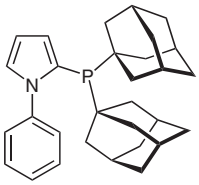
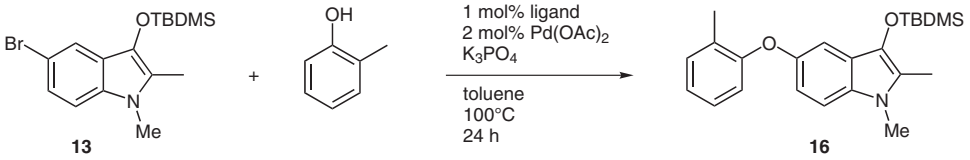
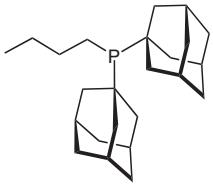
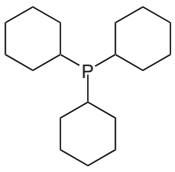
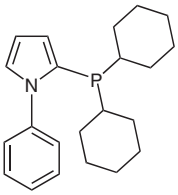
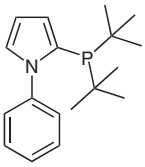
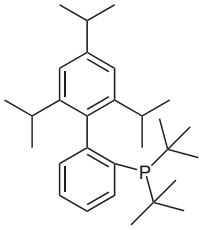
Entry	Ligand		Yield (%)[b]
1		**1**	<1
2		**2**	<1
3		**3**	1
4		**4**	<1
5		**5**	<1
6		**6**	<1
7		**7**	34

Table 1 Model Reaction of Indole **13** with *o*-Cresol[a] (continued)



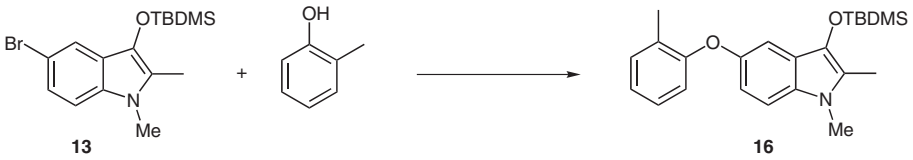
Entry	Ligand		Yield (%)[b]
8		**8**	<1
9		**9**	<1
10		**10**	<1
11		**11**	2
12		**12**	15

[a] Reaction conditions: indole **13** (0.14 mmol), *o*-cresol (0.17 mmol), $Pd(OAc)_2$ (1 mol%), ligand (2 mol%), K_3PO_4 (0.28 mmol), solvent: toluene (3 mL), 24 h, 100 °C.
[b] GC yield based on **13** with hexadecane as internal standard.

Interestingly, in the case of the coupling reaction with α-naphthol we could not isolate the desired ether compounds. To our surprise instead of the indole ethers, we obtained 5-(4-hydroxynaphthyl)indoles by selective C–C coupling reaction (Table 4). It should be noted that the resulting 5-arylindole motif is reported to be present in potent agonists of the CNS neurotransmitter serotonin.[13] For example Yang reported the first preparation of this class of compounds via the Suzuki cross-coupling of indolylboronic acids with aryl bromides.[14] Although probably not generally applicable, our reaction presented here allows for a much easier access of such compounds.

In conclusion, we have presented a general palladium-catalyzed diaryl ether formation of electron-rich indoles to 3,5-dioxyindole derivatives, which constitute a novel class of electron-rich indoles. Different alkylated phenols reacted in the presence of $Pd(OAc)_2$ and *N*-phenyl-2-(di-1-adamantylphosphino)pyrrole (**7**) to give potentially bioactive indole derivatives.

Table 2 Optimization of the Model Reaction of Indole **13** with *o*-Cresol[a]

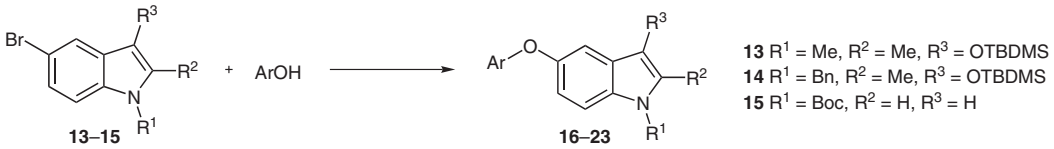


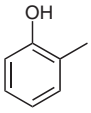
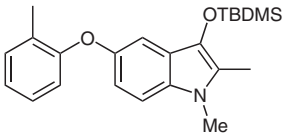
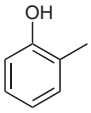
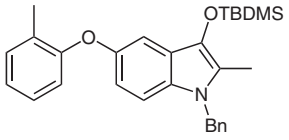
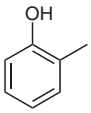
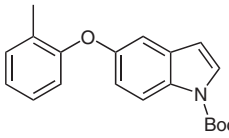
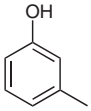
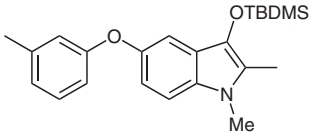
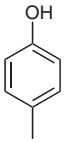
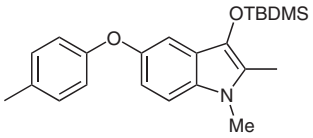
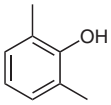
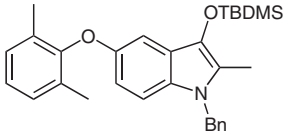
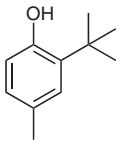
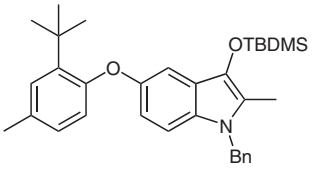
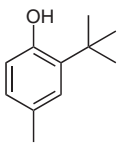
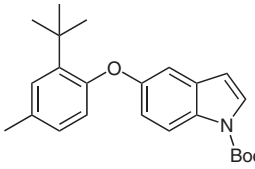
Entry	Pd source	Catalyst (mol%)	Ligand **7** (mol%)	Solvent	Base	Temperature (°C)	Yield (%)[b]
1	$Pd(OAc)_2$	0.5	1	toluene	K_3PO_4	100	25
2	$Pd(OAc)_2$	1	2	toluene	K_3PO_4	100	34
3	$Pd(OAc)_2$	2	4	toluene	K_3PO_4	100	75
4	$Pd(OAc)_2$	2	4[c]	toluene	K_3PO_4	100	60
5	$Pd(OAc)_2$	2	4	toluene	K_3PO_4	120	83
6	$Pd(OAc)_2$	2	4	toluene	K_3PO_4	140	75
7	$Pd(OAc)_2$	2	4	toluene	K_3PO_4	160	71
8	Pd_2dba_3	2	4	toluene	K_3PO_4	100	44
9	Pd_2dba_3	2	4	toluene	K_3PO_4	120	38
10	$PdCl_2$	2	4	toluene	K_3PO_4	100	<1
11	$PdCl_2$	2	4	toluene	K_3PO_4	120	1
12	$Pd(OAc)_2$	3	6	toluene	K_3PO_4	100	76
13	$Pd(OAc)_2$	4	8	toluene	K_3PO_4	100	77
14	$Pd(OAc)_2$	4	8	THF	K_3PO_4	100	25
15	$Pd(OAc)_2$	4	8	toluene	LiHMDS	100	1
16	$Pd(OAc)_2$	4	8	THF	LiHMDS	100	<1
17	$Pd(OAc)_2$	4	8	toluene	*t*-BuONa	100	2
18	$Pd(OAc)_2$	4	8	THF	*t*-BuONa	100	<1
19	$Pd(OAc)_2$	4	8	toluene	Cs_2CO_3	100	15
20	$Pd(OAc)_2$	4	8	THF	Cs_2CO_3	100	3
21	$Pd(OAc)_2$	4	8	toluene	*t*-BuOK	100	10
22	$Pd(OAc)_2$	4	8	THF	*t*-BuOK	100	<1
23	$Pd(OAc)_2$	4	8	toluene	–	100	<1
24	$Pd(OAc)_2$	6	12	toluene	K_3PO_4	100	70

[a] Reaction conditions: indole **13** (0.14 mmol), *o*-cresol (0.17 mmol), Pd complex (0.5–6 mol%) and ligand **7** (1–12 mol%), base (0.28 mmol), solvent: (3 mL), 24 h.
[b] GC yield based on **13** with hexadecane as internal standard.
[c] Reaction with ligand **12** (Table 1, entry 12).

All reactions were carried out under an argon atmosphere. Chemicals were purchased from Aldrich, Fluka, Acros, and Strem, and unless otherwise noted were used without further purification. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, MS, HRMS, and IR spectroscopy. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 300, AV 400, and AV 500 spectrometer. The ^{1}H and ^{13}C NMR chemical shifts are reported relative to the center of solvent resonance [$CDCl_3$: 7.25 ppm(^{1}H), 77.0 ppm (^{13}C)]. Mass spectra were recorded on a MAT 95XP spectrometer (Thermo Electron Corporation). IR spectra were recorded on a FTIR Nicolet 6700 (Thermo Electron Corporation). GC was performed on a Hewlett Packard HP 6890 chromatograph with a 30 m HP5 column. All yields reported in Tables 1 and 2 refer to GC yields using hexadecane as an internal standard. The spectral data of compounds **13** and **14** prepared by literature procedure[10d] are reported below.

Table 3 Reaction of Indole Derivatives with Different Phenols[a]



Entry	ArOH	Product		Yield (%)[b]
1			**16**	60
2			**17**	80
3			**18**	75
4			**19**	52
5			**20**	50
6			**21**	50
7			**22**	80
8			**23**	85

[a] Reaction conditions: indole derivative (0.35 mmol), substituted phenol (0.42 mmol), $Pd(OAc)_2$ (2 mol%), **7** (4 mol%), K_3PO_4 (0.7 mmol), solvent: toluene (3 mL), 24 h, 120 °C.
[b] Isolated yield based on the starting indole.

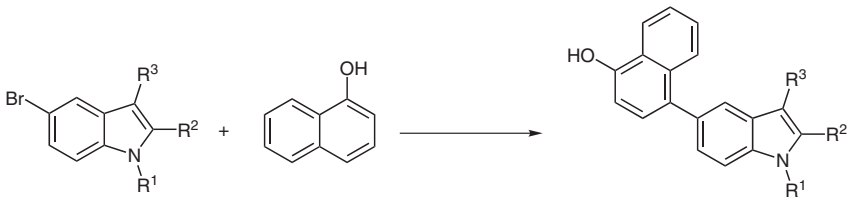
5-Bromo-3-(*tert*-butyldimethylsiloxy)-1,2-dimethyl-1*H*-indole (13)[10d]

FTIR (KBr): 3072, 2955, 2933, 2896, 2858, 1479, 1377, 1286, 1245, 891, 839, 806, 780 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 1.9 Hz, 1 H), 7.15 (dd, *J* = 1.9, 8.5 Hz, 1 H), 7.03 (d, *J* = 8.5 Hz, 1 H), 3.56 (s, 3 H), 2.27 (s, 3 H), 1.07 (s, 9 H), 0.14 (s, 6 H).

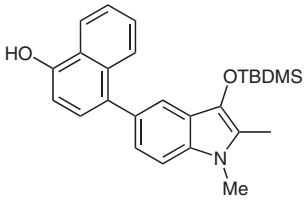
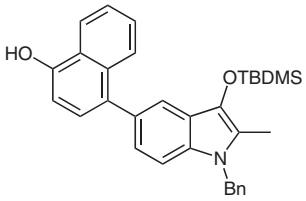
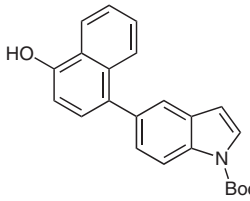
^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 132.5 (q), 129.9 (q), 124.2 (q), 123.4, 123.3 (q), 119.7, 111.8 (q), 110.1, 29.8, 26.1, 18.3 (q), 9.5, –3.8.

Table 4 Reaction of Indole Derivatives with α-Naphthol[a]



13–15

24 R^1 = Me, R^2 = Me, R^3 = OTBDMS
25 R^1 = Bn, R^2 = Me, R^3 = OTBDMS
26 R^1 = Boc, R^2 = H, R^3 = H

Entry	Product		Yield (%)[b]
1		**24**	60
2		**25**	65
3		**26**	85

[a] Reaction conditions: indole derivative (0.35 mmol), α-naphthol (0.42 mmol), $Pd(OAc)_2$ (2 mol%), **7** (4 mol%), K_3PO_4 (0.7 mol), solvent: toluene (3 mL), 24 h, 120 °C.
[b] Isolated yield based on the starting indole.

MS (EI, 70 eV): *m*/*z* (%) = 353 (69), 299 (12), 239 (13), 225 (21), 217 (100), 202 (18), 158 (42), 143 (14), 131 (13), 115 (11), 75 (19), 57 (22).

HRMS: *m*/*z* calcd for $C_{16}H_{24}BrNOSi$: 353.0805; found: 353.0807.

1-Benzyl-5-bromo-3-(*tert*-butyldimethylsiloxy)-2-methyl-1*H*-indole (14)[10d]

FTIR (KBr): 3065, 2950, 2925, 2856, 1578, 1471, 1454, 1372, 1289, 1253, 1182, 1087, 896, 873, 839, 824, 807, 790, 782, 732, 699 cm^{-1}.

^1H NMR (300.13 Hz, $CDCl_3$): δ = 7.39 (d, *J* = 1.8 Hz, 1 H), 7.04 (m, 3 H), 6.93 (dd, *J* = 1.8, 8.6 Hz, 1 H), 6.81 (d, *J* = 8.6 Hz, 1 H), 6.68 (m, 2 H), 5.02 (s, 2 H), 2.02 (s, 3 H), 0.87 (s, 9 H), –0.03 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 137.9 (q), 132.5 (q), 130.4 (q), 129.0, 127.5, 125.9, 124.0 (q), 123.8, 123.7 (q), 119.9, 112.1 (q), 110.6, 46.7, 26.1, 18.3 (q), 9.5, –3.9.

MS (EI, 70 eV): *m*/*z* (%) = 431 (100), 429 (95), 293 (30), 234 (4), 202 (31), 115 (10), 91 (63), 73 (98), 59 (11), 57 (3).

HRMS: *m*/*z* calcd for $C_{22}H_{28}BrNOSi$: 429.11181; found: 429.111561.

5-Aryloxyindole Derivatives 16–26; General Procedure

In an Ace pressure tube under argon, N-protected 5-bromoindole derivative (0.35 mmol), phenol derivative (0.42 mmol), $Pd(OAc)_2$ (2 mol%), *N*-phenyl-2-(di-1-adamantylphosphino)pyrrole (**7**; 4 mol%), and K_3PO_4 (0.7 mmol) were dissolved in toluene (3 mL). The pressure tube was fitted with a Teflon cap and heated at 120 °C for 24 h. After removal of the solvent in vacuo, the corresponding indole product is isolated by column chromatography in hexane–EtOAc.

3-(*tert*-Butyldimethylsiloxy)-1,2-dimethyl-5-(2-methylphenoxy)-1*H*-indole (16)

FTIR (KBr): 3052, 2941, 1481, 1437, 1375, 1282, 1244, 1223, 1211, 1186, 1141, 1130, 1069, 932, 892, 872, 843, 828, 782, 756 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.22 (m, 1 H), 7.13 (d, *J* = 8.7 Hz, 1 H), 7.06 (m, 1 H), 6.97 (m, 2 H), 6.80 (dd, *J* = 2.4, 8.7 Hz, 1 H), 6.75 (dd, *J* = 1.1, 8.0 Hz, 1 H), 3.59 (s, 3 H), 2.33 (s, 3 H), 2.28 (s, 3 H), 1.01 (s, 9 H), 0.09 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 157.1 (q), 150.2 (q), 131.3, 130.7 (q), 130.5 (q), 128.8 (q), 127.0, 124.0 (q), 122.5, 122.0 (q), 177.7, 113.4, 109.4, 106.7, 29.8, 26.1, 18.3 (q), 16.5, 9.5, –4.0.

MS (EI, 70 eV): *m*/*z* (%) = 381 (41), 276 (19), 275 (100), 218 (59), 177 (14), 163 (7), 144 (26), 112 (7), 75 (6), 57 (7).

HRMS: *m*/*z* calcd for $C_{23}H_{31}NO_2Si$: 381.21186; found: 381.211376.

1-Benzyl-3-(*tert*-butyldimethylsiloxy)-2-methyl-5-(2-methylphenoxy)-1*H*-indole (17)

FTIR (KBr): 3064, 3031, 2958, 2929, 2852, 1586, 1570, 1477, 1373, 1358, 1298, 1256, 1235, 1212, 1185, 1143, 935, 867, 838, 781, 728 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.23 (m, 4 H), 7.07 (m, 2 H), 7.00 (d, *J* = 2.3 Hz, 1 H), 6.97 (dd, *J* = 1.4, 7.4 Hz, 1 H), 6.92 (m, 2 H), 6.77 (m, 2 H), 5.23 (s, 2 H), 2.32 (s, 3 H), 2.22 (s, 3 H), 1.01 (s, 9 H), 0.11 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 156.9 (q), 150.5 (q), 138.4 (q), 131.3, 131.0 (q), 130.5 (q), 129.0 (q), 129.1, 127.4, 127.0, 126.0, 123.8 (q), 122.6, 122.4 (q), 117.9, 113.6, 109.9, 106.6, 46.8, 26.1, 18.3 (q), 9.5, –4.0.

MS (CI, isobutane): *m*/*z* (%) = 458 (34), 457 (63), 351 (100), 295 (6), 91 (12), 73 (30).

HRMS: *m*/*z* calcd for $C_{29}H_{35}NO_2Si$: 457.24316; found: 457.242447.

***tert*-Butyl 5-(2-Methylphenoxy)indole-1-carboxylate (18)**

FTIR (KBr): 3151, 3120, 3058, 2974, 2921, 1733, 1490, 1462, 1372, 1350, 1278, 1258, 1231, 1213, 1186, 1160, 1118, 1082, 1024 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.8 Hz, 1 H), 7.59 (d, *J* = 3.7 Hz, 1 H), 7.25 (m, 1 H), 7.13 (m, 1 H), 7.04 (m, 2 H), 6.99 (dd, *J* = 1.3, 7.9 Hz,1 H), 6.46 (dd, *J* = 0.6, 3.7 Hz, 1 H), 2.29 (s, 3 H), 1.67 (s, 9 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.8 (q), 153.6 (q), 149.9 (q), 131.7 (q), 131.6, 131.4 (q), 129.7 (q), 127.2, 127.1, 123.5, 119.0, 116.2, 115.8, 109.4, 107.3, 83.9 (q), 28.5, 16.6.

MS (EI, 70 eV): *m*/*z* (%) = 323 (45), 268 (32), 267 (100), 223 (73), 222 (19), 207 (11), 161 (17), 117 (86), 104 (8), 91 (12), 85 (5), 69 (11), 57 (66).

HRMS: *m*/*z* calcd for $C_{20}H_{21}NO_3$: 323.15160; found: 323.150899.

3-(*tert*-Butyldimethylsiloxy)-1,2-dimethyl-5-(3-methylphenoxy)-1*H*-indole (19)

FTIR (KBr): 3054, 3036, 2950, 2929, 2860, 1481, 1376, 1283, 1254, 1212, 1157, 837, 778 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.09 (m, 2 H), 7.05 (d, *J* = 2.1 Hz, 1 H), 6.76 (m, 2 H), 6.67 (m, 2 H), 3.54 (s, 3 H), 2.22 (s, 3 H), 2.21 (s, 3 H), 0.96 (s, 9 H), 0.05 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 159.8 (q), 149.0 (q), 139.7 (q), 131.1 (q), 130.5 (q), 129.3, 124.1 (q), 122.7, 122.0 (q), 117.8, 144.4, 114.3, 109.4, 108.4, 29.8, 26.0, 21.6, 18.3 (q), 9.5, –4.0.

MS (EI, 70 eV): *m*/*z* (%) = 381 (100), 324 (9), 267 (4), 251 (9), 218 (4), 217 (22), 73 (12), 56 (2).

HRMS: *m*/*z* calcd for $C_{23}H_{31}NO_2Si$: 381.21186; found: 381.211345.

3-(*tert*-Butyldimethylsiloxy)-1,2-dimethyl-5-(4-methylphenoxy)-1*H*-indole (20)

FTIR (KBr): 3027, 2954, 2925, 2852, 1579, 1507, 1483, 1463, 1377, 1289, 1243, 1228, 1205, 1133, 932, 892, 871, 858, 837, 800, 785 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.8 Hz, 1 H), 7.13 (d, *J* = 2.1 Hz, 1 H), 7.09 (m, 2 H), 6.85 (m, 3 H), 3.62 (s, 3 H), 2.32 (s, 3 H), 2.31 (s, 3 H), 1.05 (s, 9 H), 0.14 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 157.5 (q), 149.4 (q), 131.3 (q), 131.0 (q), 130.5 (q), 130.1, 124.1 (q), 122.1 (q), 117.3, 114.1, 109.4, 108.1, 29.8, 26.1, 20.8, 18.4 (q), 9.6, –4.0.

MS (EI, 70 eV): *m*/*z* (%) = 381 (100), 325 (7), 266 (9), 251 (8), 217 (26), 73 (12), 56 (2).

HRMS: *m*/*z* calcd for $C_{23}H_{31}NO_2Si$: 381.21186; found: 381.211563.

1-Benzyl-3-(*tert*-butyldimethylsiloxy)-5-(2,6-dimethylphenoxy)-2-methyl-1*H*-indole (21)

FTIR (KBr): 3027, 2954, 2925, 2856, 1588, 1571, 1495, 1472, 1374, 1359, 1299, 1266, 12221, 1191, 1143, 1082, 935, 858, 837, 781 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.24 (m, 3 H), 7.06 (m, 4 H), 6.92 (m, 2 H), 6.74 (dd, *J* = 2.3, 8.6 Hz, 1 H), 6.59 (d, *J* = 2.3 Hz, 1 H), 5.20 (s, 2 H), 2.19 (s, 3 H), 2.15 (s, 3 H), 0.96 (s, 9 H), 0.03 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 152.2 (q), 151.9 (q), 138.5 (q), 132.0 (q), 130.8 (q), 129.5 (q), 129.0, 128.9, 127.4, 126.1, 124.8, 123.6 (q), 122.2 (q), 110.6, 109.8, 101.0, 46.8, 25.9, 18.3 (q), 16.6, 9.4, –4.2.

MS (EI, 70 eV): *m*/*z* (%) = 472 (37), 471 (100), 297 (3), 202 (5), 91 (21), 73 (43).

HRMS: *m*/*z* calcd for $C_{30}H_{37}NO_2Si$: 471.25881; found: 471.258729.

1-Benzyl-3-(*tert*-butyldimethylsiloxy)-5-(2-*tert*-butyl-4-methylphenoxy)-2-methyl-1*H*-indole (22)

FTIR (KBr): 3060, 3027, 2925, 2856, 1588, 1570, 1456, 1373, 1360, 1300, 1254, 1228, 1145, 1089, 936, 839, 815, 780 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.25 (m, 3 H), 7.16 (d, *J* = 2.0 Hz, 1 H), 7.07 (m, 2 H), 6.93 (m, 2 H), 6.86 (m, 1 H), 6.76 (dd, *J* = 2.5, 8.7 Hz, 1 H), 6.66 (d, *J* = 8.3 Hz, 1 H), 5.23 (s, 2 H), 2.30 (s, 3 H), 2.22 (s, 3 H), 1.45 (s, 9 H), 1.02 (s, 9 H), 0.12 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.7 (q), 150.7 (q), 139.7 (q), 138.4 (q), 131.2 (q), 130.9 (q), 130.5 (q), 128.9, 127.7, 127.5, 127.4, 126.1, 123.8 (q), 122.5 (q), 119.0, 114.2, 109.8, 107.3, 46.8, 34.9 (q), 30.9, 26.1, 21.2, 18.4 (q), 9.5, –4.0.

MS (EI, 70 eV): *m*/*z* (%) = 514 (62), 513 (100), 293 (4), 223 (3), 202 (5), 149 (4), 117 (4), 91 (18), 73 (43), 57 (11).

HRMS: *m*/*z* calcd for $C_{33}H_{43}NO_2Si$: 513.30576; found: 513.305329.

***tert*-Butyl 5-(2-*tert*-Butyl-4-methylphenoxy)indole-1-carboxylate (23)**

FTIR (KBr): 3452, 3153, 2954, 2864, 1731, 1494, 1463, 1372, 1350, 1332, 1258, 1210, 1161, 1116, 1082, 1024, 955, 844, 826, 811, 763, 722 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.8 Hz, 1 H), 7.58 (d, *J* = 3.6 Hz, 1 H), 7.19 (d, *J* = 2.1 Hz, 1 H), 7.10 (d, *J* = 2.4 Hz, 1 H), 6.98 (dd, *J* = 2.4, 9.0 Hz, 1 H), 6.92 (ddd, *J* = 0.6, 2.2, 8.2 Hz, 1 H), 6.70 (d, *J* = 8.2 Hz, 1 H), 6.47 (dd, *J* = 0.5, 3.8 Hz, 1 H), 2.33 (s, 3 H), 1.66 (s, 9 H), 1.43 (s, 9 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.4 (q), 153.8 (q), 149.7 (q), 140.4 (q), 132.1 (q), 131.6 (q), 131.1 (q), 127.8, 127.5, 126.8, 119.8, 116.2, 116.0, 109.9, 107.2, 83.7 (q), 34.7 (q), 30.2, 28.2, 21.1.

MS (EI, 70 eV): *m*/*z* (%) = 379 (37), 323 (100), 308 (85), 279 (65), 264 (65), 248 (16), 147 (28), 117 (15), 57 (73), 41 (26).

HRMS: *m*/*z* calcd for $C_{24}H_{29}NO_3$: 379.21420; found: 379.214105.

4-[3-(*tert*-Butyldimethylsiloxy)-1,2-dimethyl-1*H*-indol-5-yl]naphthalen-1-ol (24)

FTIR (KBr): 3058, 3044, 2953, 2925, 2852, 1588, 1472, 1375, 1345, 1272, 1252, 870, 840, 825, 803, 781, 762 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1 H), 7.83 (d, *J* = 8.4 Hz, 1 H), 7.38 (d, *J* = 1.3 Hz, 1 H), 7.35 (m, 1 H), 7.26 (m, 1 H), 7.11 (m, 3 H), 6.73 (d, *J* = 7.7 Hz, 1 H), 5.14 (s, 1 H, OH), 3.53 (s, 3 H), 2.20 (s, 3 H), 0.89 (s, 9 H), 0.03 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 150.5 (q), 135.0 (q), 133.5 (q), 133.2 (q), 131.0 (q), 130.6 (q), 127.2, 126.9, 126.3, 125.5 (q), 125.2, 124.6 (q), 123.5, 123.4 (q), 121.8, 118.9, 108.5, 108.2, 29.8, 26.1, 18.4 (q), 9.5, –4.0.

MS (EI, 70 eV): *m*/*z* (%) = 417 (100), 360 (11), 287 (5), 167 (4), 149 (13), 97 (9), 83 (11), 73 (7), 57 (18), 43 (17).

HRMS: *m*/*z* calcd for $C_{26}H_{31}NO_2Si$: 417.21186; found: 417.211468.

4-[1-Benzyl-3-(*tert*-butyldimethylsiloxy)-2-methyl-1*H*-indol-5-yl]naphthalen-1-ol (25)

FTIR (KBr): 3023, 2929, 2864, 1471, 1452, 1376, 1347, 1278, 1253, 1231, 1212, 1048, 862, 842, 822, 803, 783, 764, 732 cm^{-1}.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.3 Hz, 1 H), 7.99 (d, *J* = 8.3 Hz, 1 H), 7.57 (d, *J* = 1.1 Hz, 1 H), 7.48 (m, 1 H), 7.41 (m, 1 H), 7.27 (m, 5 H), 7.16 (dd, *J* = 1.1, 6.3 Hz, 1 H), 7.00 (m, 2 H), 6.87 (d, *J* = 7.7 Hz, 1 H), 5.31 (s, 2 H), 5.28 (s, 1 H, OH), 2.27 (s, 3 H), 1.04 (s, 9 H), 0.18 (s, 6 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 150.4 (q), 138.3 (q), 134.8 (q), 133.3 (q), 133.0 (q), 131.2 (q), 131.0 (q), 128.8, 127.3, 127.0, 126.8, 126.2, 126.0, 125.0, 124.4 (q), 123.7, 123.0 (q), 122.0 (q), 121.6, 118.8, 108.4, 108.3, 46.8, 26.2, 18.1 (q), 9.4, –4.1.

MS (EI, 70 eV): *m*/*z* (%) = 493 (100), 402 (4), 345 (2), 319 (3), 261 (2), 218 (3), 153 (2), 112 (16), 91 (12), 73 (33), 57 (12), 44 (15).

HRMS: *m*/*z* calcd for $C_{32}H_{35}NO_2Si$: 493.24316; found: 493.242367.

***tert*-Butyl 5-(4-Hydroxynaphthalen-1-yl)indole-1-carboxylate (26)**

FTIR (ATR): 3358, 3150, 3110, 3044, 2981, 2932, 1368, 1334, 1239, 1155, 1133, 1078, 1044, 1022, 812, 763, 726 cm^{-1}.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 8.28 (m, 1 H), 8.21 (d, *J* = 8.5 Hz, 1 H), 7.89 (m, 1 H), 7.67 (d, *J* = 3.7 Hz, 1 H), 7.63 (d, *J* = 1.6 Hz, 1 H), 7.50 (m, 1 H), 7.42 (m, 2 H), 7.27 (d, *J* = 7.6 Hz, 1 H), 6.89 (d, *J* = 7.6 Hz, 1 H), 6.62 (d, *J* = 3.7 Hz, 1 H), 5.82 (s, 1 H, OH), 1.71 (s, 9 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 151.0 (q), 149.9 (q), 135.4 (q), 134.1 (q), 133.4 (q), 133.0 (q), 130.7 (q), 127.1, 126.8, 126.4 (two signals, detected by CORE), 126.2, 125.0, 124.5 (q), 122.4, 121.9, 114.7, 108.1, 107.5, 83.8 (q), 28.2.

MS (EI, 70 eV): *m*/*z* (%) = 359 (40), 304 (31), 303 (96), 260 (52), 259 (100), 258 (83), 242 (21), 231 (17), 230 (39), 229 (11), 228 (27), 202 (19), 101 (10), 57 (30).

HRMS: *m*/*z* calcd for $C_{23}H_{21}NO_3$: 359.15160; found: 359.151449.

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