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Convenient synthesis of tryptophols and tryptophol homologues by hydroamination of alkynes

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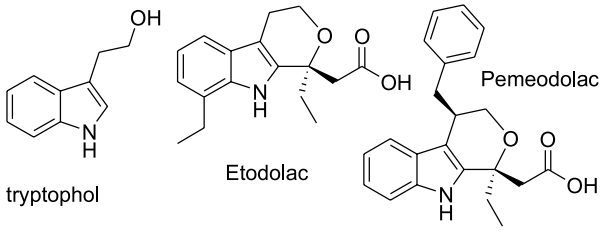
Abstract—A novel method is presented for the one-pot synthesis of substituted 3-(2-hydroxyethyl)- and 3-(3-hydroxypropyl)indoles (tryptophols and homotryptophols) from aryl hydrazines and silyl-protected ω-(hydroxyoalkyl)alkynes. Various tryptophol derivatives were prepared directly in good yield with excellent regioselectivity via a domino reaction sequence consisting of a titanium-catalyzed hydroamination of the alkyne, [3+3]-rearrangement of the resulting aryl hydrazone, and subsequent deprotection of the hydroxy group.

1. Introduction

There is a continuing interest in the development of new methods for the synthesis of indole derivatives due to their importance as building blocks for pharmaceuticals and natural products.[1] For some time, we have been involved in this area focusing on the application of catalytic methodologies such as hydrohydrazinomethylation of olefins,[2] carbonylations,[3] and hydroamination of alkynes[4] for the synthesis and refinement of indoles. Most notably, a new, one-pot method for the synthesis of functionalized tryptamines and tryptamine homologues starting from commercially available aryl hydrazines and chloroalkylalkynes has been developed by us.[5] Based on this work, we became interested in the preparation of tryptophol derivatives. Among the numerous naturally-occuring indoles, tryptophols[6] are characterized by a C-3 hydroxyethyl side chain that may or may not be α- and or β-substituted.

The production of tryptophol, by tryptophan metabolism, has been implicated as one of the pathophysiological mechanisms that provoke sleeping sickness upon infection by trypanosomes.[7] Therefore, it is not surprising that a number of derivatives are known to posses interesting biological activity, for example, esters of 5-methoxytryptophol show anti-cholinergic activity.[8] Of pharmaceutical importance is also 7-ethyltryptophol as this compound is used for the synthesis of Etodolac, a non-steroidal anti-inflammatory drug (NSAID).[9] In addition, 2-phenyl-2-(3-indolyl)-1-ethanol has been used to prepare Pemedolac, a compound that has been found to be one of the most potent analgesics known and that displays anti-inflammatory activity similar to that of Etodolac (Scheme 1).[10]



Scheme 1. Examples of biologically active tryptophols.

Although different creative approaches have been developed for the synthesis of tryptophols,[11] the Fischer indole reaction remains the most important method to create substituted indoles.[12] In this benchmark reaction, aldehydes or ketones react with aryl hydrazines to give the corresponding hydrazones, which subsequently undergo a [3,3]-sigmatropic rearrangement to yield the respective indole in the presence of a Brønstedt or Lewis acid. Despite its versatility, the Fischer indole reaction with aldehydes constitutes a two-step procedure, which sometimes proceeds in low yield. More specifically the synthesis of tryptophol-like compounds via Fischer indole synthesis can be troublesome due to side-reactions of the free or protected hydroxyaldehyde. An elegant solution to this problem has been described very recently by Campos et al., who used substituted enol ethers or enol lactones as a substitute for the hydroxyaldehyde.[13]

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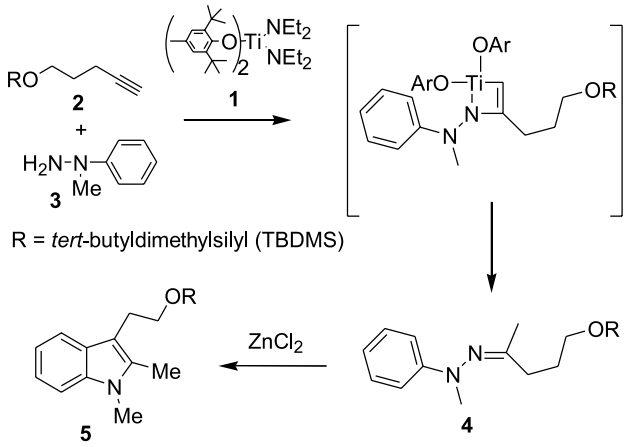
2. Results and discussion

Here, we describe for the first time a convenient synthesis of tryptophols from alkynes and aryl hydrazines. As shown in Scheme 2, our strategy involved as a key step, the titanium-catalyzed hydroamination of a suitably protected hydroxy-alkylalkyne to give the *N*-aryl-*N*-hydroxy-alkylhydrazone **4**. Then a [3,3]-sigmatropic rearrangement to the corresponding indole **5** should take place and finally deprotection will lead to the free tryptophol.



Scheme 2. Synthesis of tryptophols.

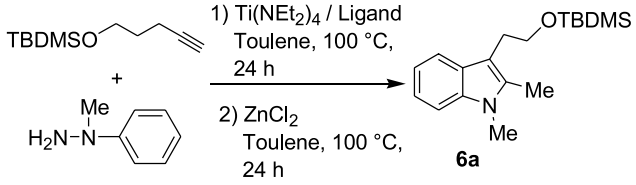
Indeed, when we reacted 1-*tert*-butyldimethylsilyloxy-4-pentyne **2** with *N*-methyl-*N*-phenylhydrazine **3** in the presence of 5 mol% bis(2,6-di-*tert*-butyl-4-methyl-phenoxo)-bis(diethylamido)titanium **1** (complex **1** is formed in situ from commercially available $Ti(NEt_2)_4$ and 2,6-di-*tert*-butyl-4-methylphenol)[14–16] the corresponding hydrazone **4** was the major product. Subsequent treatment of the reaction mixture with an excess of $ZnCl_2$ gave the corresponding silyl-protected tryptophol **6a** in 75% isolated yield!

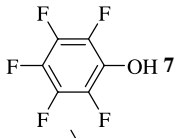
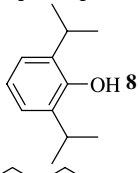
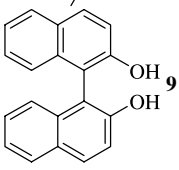
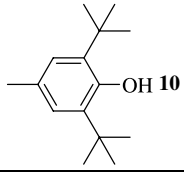
It is noteworthy that the initial hydrohydrazination reaction of the alkyne proceeds selectively to give exclusively the 2,3-disubstituted indole **6a** (Markovnikov isomer).[17] Selective formation of the 2-methyl-indole derivative **6a** instead of the corresponding homotryptophol is explained by the relative stability of the corresponding imidotitanium alkyne π-complexes,[4] which undergo a formal [2+2]-cycloaddition to give the titanaazacyclobutene derivative. Subsequent protonation by excess hydrazine and tautomerization leads to the hydrazone product **4** and the active catalyst is recovered.

The model reaction of 1-*tert*-butyldimethylsilyloxy-4-pentyne with *N*-methyl-*N*-phenylhydrazine proceeds in the presence of $Ti(NEt_2)_4$ and different aryloxo ligands. Subsequent addition of 3 equiv of $ZnCl_2$ allowed for the cyclization of the initially generated hydrazone into the corresponding indole.

The reactions using different aryloxo ligands were performed at 100 °C for 24 h in toluene in the presence of 5 mol% $Ti(NEt_2)_4$. As shown in Table 1, all tested ligands gave selectively the Markovnikov addition product. In general, the sterically hindered monodentate ligand **10** gave higher yield compared to the less sterically hindered monodentate ligands **7** and **8** (Table 1, entries 1, 2, and 6). By employing ligand **7** the catalytic activity decreased to give only <5% yield.

Table 1. Reaction of 1-*tert*-butyldimethylsilyloxy-4-pentyne with *N*-methyl-*N*-phenylhydrazine[a]



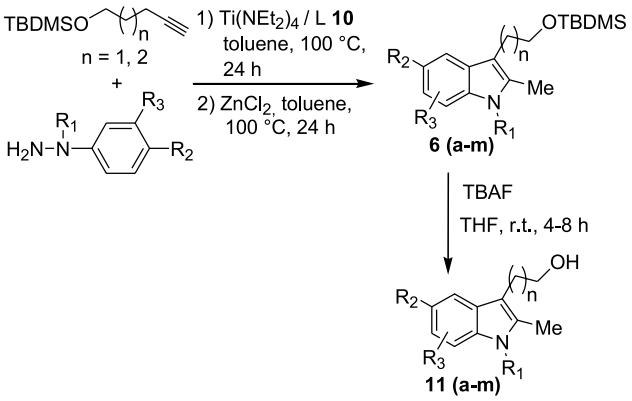
Entry	Ligand	$Ti(NEt_2)_4$ (mol%)	Ligand (mol%)	Yield[b] **6a** (%)
1	 **7**	5	10	<5
2	 **8**	5	10	70
3	 **9**	5	10	40
4	 **10**	1	2	58
5		2.5	5	62
6		5	10	75
7		10	20	90

[a] Reaction conditions: for hydroamination: 2.0 mmol 1-*tert*-butyldimethylsilyloxy-4-pentyne, 2.4 mmol *N*-methyl-*N*-phenylhydrazine, 4 ml toluene, 100 °C, 24 h. For Fischer indole cyclization: 6.0 mmol $ZnCl_2$, 100 °C, 24 h.
[b] Isolated yield based on 1-*tert*-butyldimethylsilyloxy-4-pentyne.

The reaction using bidentate ligand **9** gave 40% yield of the corresponding indole **6a** (Table 1, entry 3). Therefore, further optimization of reaction conditions was carried out by using ligand **10**. Next, we turned our interest to improve the yield of product **6a** by loading different concentration of catalyst.

As shown in Table 1, an excellent yield (90%) of indole was achieved applying 10 mol% $Ti(NEt_2)_4$ and 20 mol% of ligand **10** (Table 1, entry 7). Nevertheless, also at lower catalyst loading (1 mol% $Ti(NEt_2)_4$ and 2 mol% **10**) a good yield (58%) of the corresponding indole **6a** was obtained (Table 1, entry 4).

Next, we were interested to test the in situ catalyst system for the one-pot synthesis of various functionalized tryptophols (Scheme 3; Tables 2 and 3). For this purpose, we used two silyl-protected 2- and 3-hydroxyalkylalkynes and

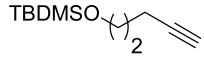
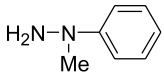
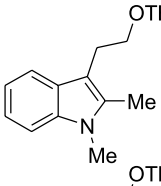
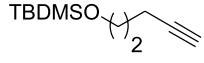
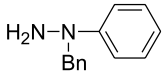
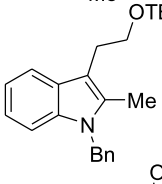
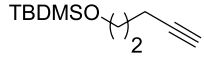
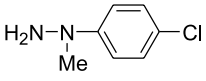
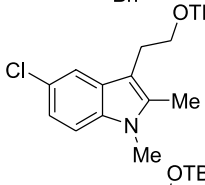
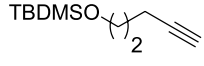
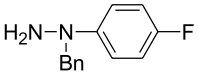
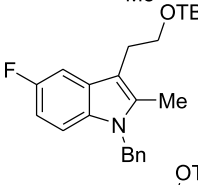
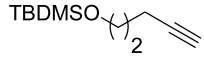
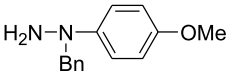
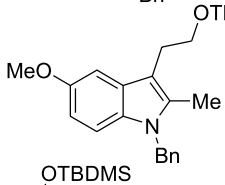
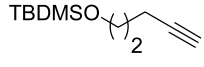
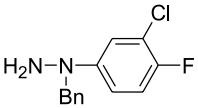
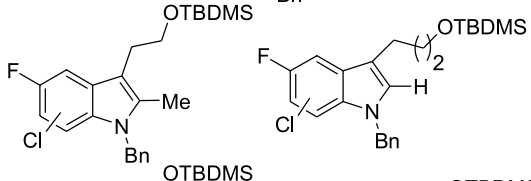
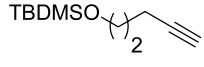
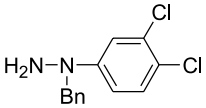
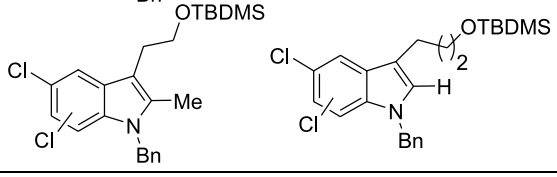


Scheme 3. Synthesis of different tryptophols.

various *N*,*N*-disubstituted aryl hydrazines. All formed indoles were deprotected by using *tetra*-*n*-butylammonium fluoride (TBAF) at room temperature for 4–8 h in THF.

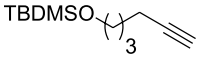
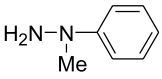
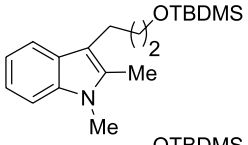
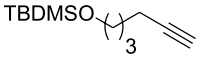
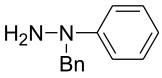
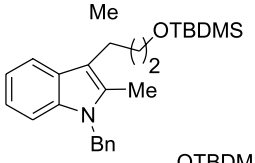
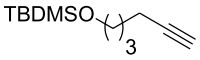
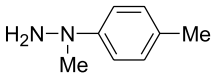
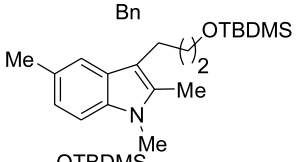
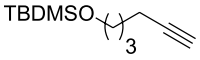
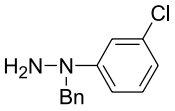
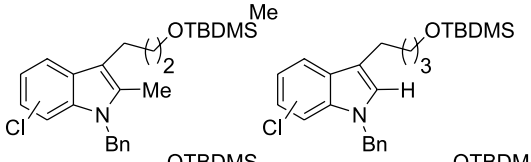
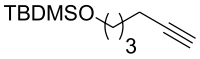
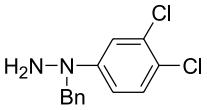
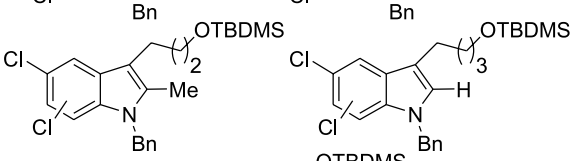
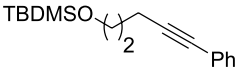
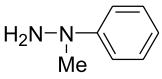
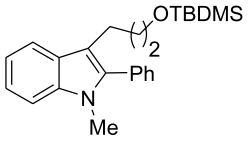
Regioselective hydroamination/cyclization to the corresponding indole products **6a**–**m** was possible for a range of aryl hydrazines with different substituents such as Me, Cl, F, MeO, and Bn (40–97% yield). Interestingly, it is not necessary to purify or isolate the silyl-protected tryptophol. Hence, the reaction of *N*-benzyl-4-fluoro-phenylhydrazine and *N*-methyl-4-methylphenylhydrazine with 1-*tert*-butyldimethylsilyloxy-4-pentyne, and 1-*tert*-butyldimethylsilyloxy-5-hexyne gave in a one-pot reaction the tryptophols **11d** and **11j** in good isolated yields (Table 2, entry 4 and Table 3, entry 3).

Table 2. Reaction of 1-*tert*-butyldimethylsilyloxy-4-pentyne with various substituted hydrazines[a]

Entry	Alkyne	Hydrazine	Product **6**		Yield[b] (%)	
					6	**11 (a–g)**
1				**6a**	90	81
2				**6b**	75	80
3				**6c**	84	90
4				**6d**	Not isolated	76
5				**6e**	80	85
6[c]				**6f**	95	83
7[d]				**6g**	84	89

[a] Reaction conditions: for hydroamination: 2–3 mmol 1-*tert*-butyldimethylsilyloxy-4-pentyne, 2.5–4.5 mmol arylhydrazine, 4 ml toluene, 100 °C, 24 h. For Fischer indole cyclization: 6.0 mmol $ZnCl_2$, 100 °C, 24 h. For deprotection of alcohol: 2 equiv TBAF, rt, 4–8 h, 10 ml THF.
[b] Isolated yield based on 1-*tert*-butyldimethylsilyloxy-4-pentyne.
[c] Markovnikov:*anti*-Markovnikov selectivity = 97:3; 4-Cl:6-Cl regioselectivity = ~2:1.
[d] Markovnikov:*anti*-Markovnikov selectivity = 84:16; 4-Cl:6-Cl regioselectivity = ~2:1.

Table 3. Reaction of different alkynes with various substituted hydrazines[a]

Entry	Alkyne	Hydrazine	Product **6**		Yield[b] (%)	
					6	**11 (h–m)**
1				**6h**	85	90
2				**6i**	97	84
3				**6j**	Not isolated	75
4[c]				**6k**	71	75
5[d]				**6l**	84	88
6				**6m**	40	84

[a] Reaction conditions: for hydroamination: 2–3 mmol silyl-protected alkyne, 2.5–4.5 mmol arylhydrazine, 4 ml toluene, 100 °C, 24 h. For Fischer indole cyclization: 6.0 mmol $ZnCl_2$, 100 °C, 24 h. For deprotection of alcohol: 2 equiv TBAF, room temperature, 4–8 h, 10 ml THF.
[b] Isolated yield based on alkyne.
[c] Markovnikov:*anti*-Markovnikov selectivity = 93:7; 4-Cl:6-Cl regioselectivity = ~2:1.
[d] Markovnikov:*anti*-Markovnikov selectivity = 83:17; 4-Cl:6-Cl regioselectivity = ~2:1.

Apart from terminal alkynes, an internal alkyne also reacted with *N*-methyl-*N*-phenylhydrazine to give the corresponding homotryptophol **6m** in 40% isolated yield (Table 3, entry 6).

In general, the hydrohydrazination step proceeds preferentially to the Markovnikov addition product. However, in case of disubstituted aryl hydrazines (Table 2, entries 6, 7 and Table 3, entries 4, 5) and *N*-benzyl-*N*-(3-chlorophenyl)hydrazine a small amount of the *anti*-Markovnikov addition product was also observed (M:*anti*-M = 84:16 to 97:3). In the second step subsequent cyclization of the hydrazones using an excess $ZnCl_2$ afforded the corresponding indoles in good yields (71–97%). The mixture of the Markovnikov and the *anti*-Markovnikov products (**11g** and **11l**) can be easily separated by column chromatography. However, it was not possible to separate the mixture of regioisomers (6-Cl:4-Cl) of the Markovnikov and the *anti*-Markovnikov products.

3. Conclusion

In conclusion, a new efficient method for the synthesis of functionalized tryptophols and tryptophol homologues has been developed. Starting from commercially available aryl hydrazines and alkynes, a variety of potentially active indoles are obtained selectively in the presence of a catalytic amount of $Ti(NEt_2)_4$ and 2,6-*tert*-butyl-4-methyl-phenol (**10**). The presented approach constitutes the most efficient access for the here shown substituted tryptophols and tryptophol homologues.

4. Experimental

4.1. General reagents

All reactions were carried out under an argon atmosphere. Starting materials were used as received from Aldrich, Fluka, Acros, and Strem and unless otherwise noted were used without further purification. Alkynes were degassed, flushed with argon and stored over molecular sieves (4 Å). Absolute solvents were purchased from Fluka®. The 2- and 3-hydroxyalkylalkynes were protected according to literature.[18]

Silica gel column chromatography was performed with 230–400 mesh ASTM silica gel from Merck,® which was used as received.

4.2. General spectroscopic methods

^{1}H and ^{13}C NMR data were recorded on a Bruker® ARX 400 with QNP probe head (^{1}H, 400.13 MHz), (^{13}C, 100.61, 125.75 MHz) at 25 °C. Resonances are reported in δ (ppm) relative to $CDCl_3$. Coupling constants J are reported in Hz. ^{1}H and ^{13}C NMR assignments, where given, were based on 2D experiments or comparison with related structures. The following abbreviations were used to specify multiplicity, shape, and other properties: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sept, septet; m, multiplet; br, broad.

MS data were obtained on AMD 402/3 of AMD Intectra®. Electron impact spectra (EI) were recorded at 70 eV, chemical ionization (CI) was with *iso*-butane.

Melting points (mp) of the solid compounds were recorded on a Leica Galen III on the glass slide and are uncorrected.

IR spectra of solid compounds were recorded as KBr pellets (nujol) on a Nicolet® Magna 550. Liquid compounds were analyzed capillarily. Absorption bands are given as wavenumbers $\tilde{\nu}$ in cm^{-1}.

4.3. General procedure for synthesis of tryptophols (GP)

Step 1 (*hydroamination/cyclization*). In an Ace-pressure tube under an argon atmosphere the ligand 2,6-*tert*-butyl-4-methylphenol (20 mol%) was dissolved in 4 ml toluene. To this solution hydrazine, alkyne, and $Ti(NEt_2)_4$ (10 mol%) were added. The reaction mixture was heated at 100 °C for 24 h, which resulted in the formation of the corresponding hydrazone. The pressure tube was opened under argon and 3 equiv $ZnCl_2$ was added. The reaction mixture was again heated at 100 °C for 24 h. After filtration and removal of the solvents in vacuo, the desired indole product was isolated by column chromatography in ethyl acetate/hexane.

Step 2 (*deprotection of alcohol*). The indole isolated after step 1 was dissolved in 10 ml THF and cooled to 0 °C. Then 2 equiv of TBAF was added slowly. The reaction mixture was stirred at room temperature for 4–8 h. After removal of the solvent in vacuo, the mixture was diluted with water and 5 ml of dichloromethane. The product was extracted with dichloromethane (3×25 ml). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography in ethyl acetate/hexane to yield the corresponding tryptophols.

4.3.1. 3-(2-{*tert*-Butyldimethylsilyloxy}ethyl)-1,2-dimethyl-1*H*-indole (6a). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.25 ml, 1.1 mmol) and *N*-methyl-*N*-phenylhydrazine (0.16 ml, 1.4 mmol) were employed. Isolated yield: 90%, light brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.50 (d, J=7.7 Hz, 1H), 7.22 (d, J=7.9 Hz, 1H), 7.13 (td, J=1.1, 7.5 Hz, 1H), 7.06 (td, J=1.0, 7.4 Hz, 1H), 3.75 (t, J=7.8 Hz, 2H), 3.62 (s, 3H), 2.96 (t, J=7.8 Hz, 2H), 2.35 (s, 3H), 0.89 (s, 9H), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.4, 133.6, 127.8, 120.4, 118.7, 117.8, 108.5, 107.4, 63.8, 29.4, 28.4, 25.9, 22.7, 10.2, −5.2. MS (EI, 70 eV) *m*/*z* (relative intensity): 303 (19) [M^+], 246 (30), 231 (2), 205 (3), 189 (1), 172 (16), 158 (100), 143 (6), 128 (3), 115 (6), 91 (2), 73 (8), 41 (4), 28 (3). HRMS Calcd for $C_{18}H_{29}NOSi$: 303.20184. Found: 303.20170.

4.3.2. *N*-Benzyl-3-(2-{*tert*-butyldimethylsilyloxy}ethyl)-2-methyl-1*H*-indole (6b). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.25 ml, 1.1 mmol) and *N*-benzyl-*N*-phenylhydrazine (0.19 ml, 1.4 mmol) were employed. Isolated yield: 75%, light brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.55–7.53 (m, 1H), 7.24–7.18 (m, 4H), 7.10–7.07 (m, 2H), 6.97–6.95 (dd, J=1.6, 8.3 Hz, 2H), 5.29 (s, 2H), 3.78 (t, J=7.5 Hz, 2H), 2.98 (t, J=7.6 Hz, 2H), 2.30 (s, 3H), 0.88 (s, 9H), 0.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=138.0, 136.4, 133.5, 128.6, 128.1, 127.1, 125.9, 120.7, 118.9, 117.9, 108.9, 108.3, 63.7, 46.5, 28.4, 25.9, 18.4, 10.3, −5.2. MS (EI, 70 eV) *m*/*z* (relative intensity): 379 (27) [M^+], 322 (24), 248 (10), 234 (88), 216 (5), 195 (11), 183 (13), 142 (7), 128 (1), 115 (3), 91 (100), 73 (10), 41 (4), 29 (3). HRMS Calcd for $C_{24}H_{33}NOSi$: 379.23315. Found: 379.23231.

4.3.3. 3-(2-{*tert*-Butyldimethylsilyloxy}ethyl)-5-chloro-1,2-dimethyl-1*H*-indole (6c). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.25 ml, 1.1 mmol) and *N*-(4-chlorophenyl)-*N*-methylhydrazine (0.22 ml, 1.65 mmol) were employed. Isolated yield: 84%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.49 (d, J=1.7 Hz, 1H), 7.14 (d, J=8.7 Hz, 1H), 7.09 (dd, J=1.7,8.5 Hz, 1H), 3.75 (t, J=7.4 Hz, 2H), 3.64 (s, 3H), 2.92 (t, J=7.4 Hz, 2H), 2.37 (s, 3H), 0.91 (s, 9H), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=135.1, 134.8, 128.9, 124.4, 120.4, 117.4, 109.3, 107.6, 63.7, 29.6, 28.2, 25.9, 18.3, 10.3, −5.3. MS (EI, 70 eV) *m*/*z* (relative intensity): 337 (18) [M^+], 322 (4), 280 (52), 265 (2), 245 (1), 206 (29), 192 (100), 171 (10), 154 (12), 140 (7), 128 (2), 115 (4), 105 (3), 91 (1), 88 (9), 73 (9), 57 (4), 41 (4), 28 (3). HRMS Calcd for $C_{18}H_{28}ClNOSi$: 337.16287. Found: 337.16330.

4.3.4. *N*-Benzyl-3-(2-{*tert*-butyldimethylsilyloxy}ethyl)-5-methoxy-2-methyl-1*H*-indole (6e). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.47 ml, 2.0 mmol) and *N*-(4-methoxyphenyl)-*N*-methylhydrazine (228 mg, 2.4 mmol) were employed. Isolated yield: 80%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.22–7.17 (m, 3H), 7.12 (d, J=8.4 Hz, 1H), 7.08–6.99 (m, 2H), 6.80–6.69 (m, 2H), 5.26 (s, 2H), 3.82 (s, 3H), 3.69 (t, J=6.5 Hz, 2H), 2.70 (t, J=6.5 Hz, 2H), 2.01 (s, 3H), 0.87 (s, 9H), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=154.9, 141.5, 137.9, 132.3, 128.6, 128.5, 127.1, 125.8, 110.5, 109.9, 107.9, 100.2, 62.1, 55.8, 46.4, 28.5, 25.9, 18.2, 10.3, −5.3. MS (EI, 70 eV) *m*/*z* (relative intensity): 409 (32) [M^+], 352 (16), 303 (12), 278 (3), 264 (46), 251 (100), 212 (12), 186 (4), 160 (22), 144 (3), 129 (1), 115 (2), 91 (74), 73 (9), 59 (5), 41 (5), 28 (19). HRMS Calcd for $C_{25}H_{35}NO_2Si$: 409.24371. Found: 409.24235.

4.3.5. *N*-Benzyl-3-(2-{*tert*-butyldimethylsilyloxy}ethyl)-4-chloro-5-fluoro-2-methyl-1*H*-indole/*N*-benzyl-3-(2-{*tert*-butyldimethylsilyloxy}ethyl)-6-chloro-5-fluoro-2-methyl-1*H*-indole (2:1) (6f). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.47 ml, 2.0 mmol) and *N*-(3-chloro-4-fluorophenyl)-*N*-benzylhydrazine (413 mg, 1.65 mmol) were employed. Isolated yield: 95%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.32–7.17 (m, 3H), 7.00 (dd, $J_{H,H}$=3.9 Hz, $J_{F,H}$=8.7 Hz, 1H), 6.95–6.91 (m, 2H), 6.85 (t, $J_{H,H}$=$J_{F,H}$=8.9 Hz, 1H), 5.25 (s, 2H), 3.87 (t, J=7.1 Hz, 2H), 3.22 (t, J=7.1 Hz, 2H), 2.34 (s, 3H), 0.89 (s, 9H), 0.03 (s, 6H)/7.36 (d, $J_{F,H}$=9.0 Hz, 1H), 7.34–7.17 (m, 3H), 7.18 (d, $J_{F,H}$=6.1 Hz, 1H), 6.95–6.91 (m, 2H), 5.23 (s, 2H), 3.78 (t, J=7.0 Hz, 2H), 2.92 (t, J=7.0 Hz, 2H), 2.31 (s, 3H), 0.88 (s, 9H), 0.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=154.1, 137.2, 137.1, 133.6, 128.6, 127.4, 125.7, 125.0, 109.9, 109.2, 109.1, 107.7, 64.8, 46.7, 28.5, 25.9, 18.3, 10.5, −5.3/153.9, 137.0, 135.9, 133.7, 128.6, 127.4, 127.0, 125.7, 114.3, 109.2, 108.9, 104.2, 64.4, 46.7, 28.2, 25.9, 18.3, 10.4, −5.2. MS (EI, 70 eV) *m/z* (relative intensity): 432 (10) [M^+], 397 (15), 340 (7), 316 (19), 286 (42), 262 (2), 235 (32), 205 (5), 195 (4), 185 (2), 159 (6), 142 (4), 129 (6), 115 (8), 99 (3), 91 (100), 77 (7), 65 (19), 57 (7), 49 (21), 41 (7), 28 (5). HRMS Calcd for $C_{24}H_{31}{}^{35}ClFNOSi$: 431.18475. Found: 431.18489.

4.3.6. *N*-Benzyl-3-(2-{*tert*-butyldimethylsilyloxy}ethyl)-4,5-dichloro-2-methyl-1*H*-indole/*N*-benzyl-3-(2-(*tert*-butyldimethylsilyloxy(ethyl)-5,6-dichloro-2-methyl-1*H*-indole (2:1) (6g). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-4-pentyne (0.47 ml, 2.0 mmol) and *N*-(3,4-dichlorophenyl)-*N*-benzylhydrazine (440 mg, 1.65 mmol) were employed. Isolated yield: 84%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.29–7.24 (m, 3H), 7.14 (d, J=8.7 Hz, 1H), 7.01 (d, J=8.7 Hz, 1H), 6.93–6.91 (m, 2H), 5.29 (s, 2H), 3.85 (t, J=6.4 Hz, 2H), 3.79 (t, J=6.4 Hz, 2H), 2.31 (s, 3H), 0.90 (s, 9H), 0.03 (s, 6H)/7.63 (s, 1H), 7.29–7.24 (m, 3H), 7.25 (s, 1H), 6.93–6.91 (m, 2H), 5.25 (s, 2H), 3.70 (t, J=6.5 Hz, 2H), 3.94 (t, J=6.5 Hz, 2H), 2.28 (s, 3H), 0.89 (s, 9H), 0.02 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.8, 136.5, 136.2, 128.1, 127.5, 125.4, 125.7, 123.5, 122.1, 120.6, 110.4, 108.4, 63.5, 46.7, 28.1, 25.9, 18.2, 10.4, −5.3/136.9, 135.8, 135.2, 128.1, 128.0, 127.5, 125.7, 124.3, 121.9, 119.2, 112.5, 108.7, 64.8, 46.7, 28.5, 25.9, 18.3, 10.4, −5.3. MS (EI, 70 eV) *m/z* (relative intensity): 447 (5) [M^+ −H], 390 (15), 356 (1), 316 (5), 302 (14), 291 (5), 265 (49), 251 (3), 215 (2), 181 (1), 145 (1), 115 (1), 91 (100), 75 (4), 65 (6), 57 (4), 41 (3), 28 (2). HRMS Calcd for $C_{24}H_{31}{}^{35}Cl_2NOSi$: 447.15521. Found: 447.15576.

4.3.7. 3-(3-{*tert*-Butyldimethyl)silyloxy}propyl)-1,2-dimethyl-1*H*-indole (6h). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-5-hexyne (0.49 ml, 2.0 mmol) and *N*-methyl-*N*-phenylhydrazine (0.28 ml, 2.4 mmol) were employed. Isolated yield: 85%, light brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.51 (d, J=7.9 Hz, 1H), 7.22 (d, J=7.9 Hz, 1H), 7.12 (t, J=1.0, 7.5 Hz, 1H), 7.04 (td, J=0.8, 7.4 Hz, 1H), 3.64 (t, J=6.1 Hz, 2H), 3.62 (s, 3H), 2.77 (t, J=6.1 Hz, 2H), 2.34 (s, 3H), 1.80 (quint, J=6.8 Hz, 2H), 0.92 (s, 9H), 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.5, 132.7, 127.7, 120.3, 118.4, 118.0, 110.9, 108.3, 62.4, 34.0, 29.4, 25.9, 20.4, 18.2, 10.1, −5.2. MS (EI, 70 eV) *m/z* (relative intensity): 317 (44) [M^+], 302 (4), 260 (70), 245 (6), 232 (5), 202 (4), 184 (13), 170 (7), 158 (100), 144 (8), 130 (4), 115 (3), 89 (11), 75 (6), 59 (8), 41 (1), 29 (1). HRMS Calcd for $C_{19}H_{31}NOSi$: 317.21750. Found: 317.21704.

4.3.8. *N*-Benzyl-3-(3-{*tert*-butyldimethylsilyloxy}propyl)-2-dimethyl-1*H*-indole (6i). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-5-hexyne (0.49 ml, 2.0 mmol) and *N*-benzyl-*N*-phenylhydrazine (0.43 ml, 3.0 mmol) were employed. Isolated yield: 97%, light brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.57–7.55 (m, 1H), 7.24–7.17 (m, 4H, H-21), 7.10–7.05 (m, 2H), 6.94 (d, J=6.9 Hz, 2H), 5.28 (s, 2H), 3.63 (t, J=7.4 Hz, 2H), 2.81 (t, J=7.4 Hz, 2H), 2.28 (s, 3H), 1.84 (quint, J=7.3 Hz, 2H), 0.91 (s, 9H), 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=138.2, 136.4, 132.6, 128.9, 128.6, 127.1, 125.9, 120.6, 118.7, 118.1, 111.6, 108.8, 62.4, 46.4, 33.8, 25.9, 20.4, 18.2, 10.1, −5.2. MS (EI, 70 eV) *m/z* (relative intensity): 393 (51) [M^+], 378 (2), 336 (32), 308 (1), 286 (11), 245 (8), 234 (23), 195 (12), 167 (2), 143 (6), 115 (2), 91 (100), 76 (6), 57 (8), 41 (3). HRMS Calcd for $C_{25}H_{36}NOSi$: [M^+ +H]: 394.25662. Found: 394.25622.

4.3.9. *N*-Benzyl-3-(3-{*tert*-butyldimethylsilyloxy}propyl)-3-chloro-2-methyl-1*H*-indole/*N*-benzyl-3-(3-{tert-butyldimethylsilyloxy}propyl)-3-dichloro-2-methyl-1*H*-indole (2:1) (6k). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-5-hexyne (0.49 ml, 2.0 mmol) and *N*-(3-chlorophenyl)-*N*-benzylhydrazine (696 mg, 3.0 mmol) were employed. Isolated yield: 71%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.34–7.30 (m, 3H), 7.26–7.24 (m, 2H), 7.04 (t, J=8.2 Hz, 1H), 6.59–6.56 (m, 2H), 4.61 (s, 2H), 3.62 (t, J=6.0 Hz, 2H), 2.21 (t, J=6.0 Hz, 2H), 1.93 (s, 3H), 1.64–1.58 (m, 2H), 0.88 (s, 9H), 0.03 (s, 6H)/7.34–7.30 (m, 3H), 7.21–7.19 (m, 3H), 6.59–6.56 (m, 2H), 4.61 (s, 2H), 3.62 (t, J=6.8 Hz, 2H), 2.21 (t, J=6.8 Hz, 2H), 1.93 (s, 3H), 1.64–1.58 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=137.7, 135.5, 130.1, 128.7, 127.0, 126.5, 125.7, 123.4, 116.6, 112.1, 110.5, 62.5, 54.0, 31.7, 25.9, 24.9, 18.1, 10.2, −5.3/137.7, 135.5, 130.1, 128.7, 127.0, 126.5, 125.7, 123.4, 116.6, 112.1, 110.5, 62.5, 54.0, 31.7, 25.9, 24.9, 18.1, 10.2, −5.3. MS (EI, 70 eV) *m/z* (relative intensity): 427 (39) [M^+ −H], 412 (2), 370 (45), 342 (6), 320 (1), 295 (3), 279 (14), 268 (17), 234 (10), 204 (2), 177 (2), 143 (2), 115 (2), 101 (2), 91 (100), 73 (6), 65 (5), 58 (4), 41 (3), 29 (1). HRMS Calcd for $C_{25}H_{34}{}^{35}ClNOSi$: 427.20981. Found: 427.20884.

4.3.10. *N*-Benzyl-3-(3-{*tert*-butyldimethylsilyloxy}propyl)-4,5-dichloro-2-methyl-1*H*-indole/*N*-benzyl-3-(3-(*tert*-butyldimethylsilyloxy(propyl)-5,6-dichloro-2-methyl-1*H*-indole (2:1) (6l). According to GP (step 1), 1-*tert*-butyldimethylsilyloxy-5-hexyne (0.49 ml, 2.0 mmol) and *N*-(3,4-dichlorophenyl)-*N*-benzylhydrazine (801 mg, 3.0 mmol) were employed. Isolated yield: 84%, brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.28–7.20 (m, 3H), 7.10 (d, J=8.7 Hz, 1H), 7.00 (d, J=8.7 Hz, 1H), 6.90–6.87 (m, 2H), 5.28 (s, 2H), 3.66 (t, J=6.4 Hz, 2H), 3.00 (t, J=6.4 Hz, 2H), 2.28 (s, 3H), 1.64–1.60 (m, 2H), 0.91 (s, 9H, H), 0.05 (s, 6H)/7.65 (s, 1H), 7.28–7.20 (m, 3H), 7.25 (s, 1H), 6.90–6.87 (m, 2H), 5.26 (s, 2H), 3.60 (t, J=6.2 Hz, 2H), 2.75 (t, J=6.2 Hz, 2H), 2.27 (s, 3H), 1.58–1.50 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 137.1, 135.6, 130.5, 128.8, 128.4, 127.8, 127.5, 127.1, 125.7, 121.9, 110.3, 108.3, 62.5, 46.6, 35.6, 25.9, 22.9, 18.4, 10.4, −5.3/137.0, 130.5, 130.2, 128.7, 128.3, 127.8, 125.5, 123.5, 122.1, 119.1, 114.9, 108.7, 61.9, 46.7, 33.6, 25.9, 21.6, 18.3, 10.4, −5.3. MS (EI, 70 eV) *m/z* (relative intensity): 462 (75) [M^+], 448 (8), 406 (100), 387 (18), 313 (28), 268 (25), 235 (6), 211 (7), 171 (8), 115 (8), 92 (20), 77 (15), 65 (4), 57 (11), 41 (9), 28 (5). HRMS Calcd for $C_{23}H_{33}{}^{35}Cl_2NOSi$: 461.17084. Found: 461.17087.

4.3.11. 2-(1,2-Dimethyl-1*H*-indole-3-yl)ethanol (11a).[19] According to GP (step 2), product **6a** (300 mg, 1.0 mmol) and TBAF-trihydrate (630 mg, 2.0 mmol) were employed. Isolated yield: 81%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.52 (d, J=7.9 Hz, 1H), 7.25 (d, J=7.8 Hz, 1H), 7.16 (td, J=1.1, 8.1 Hz, 1H), 7.07 (td, J=1.0, 7.9 Hz, 1H), 3.81 (t, J=6.4 Hz, 2H), 3.65 (s, 3H), 2.98 (t, J=6.4 Hz, 2H), 2.37 (s, 3H), 1.52 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.6, 134.2, 127.7, 120.7, 118.9, 117.8, 108.6, 106.6, 62.9, 29.5, 27.9, 10.2. MS (EI, 70 eV) *m/z* (relative intensity): 189 (49) [M^+], 170 (1), 158 (100), 143 (18), 128 (7), 115 (15), 102 (6), 91 (4), 84 (69), 77 (5), 57 (4), 47 (20), 41 (5), 29 (7). FT IR (neat, cm^{-1}): 3366, 3052, 2934, 1614, 1566, 1473, 1432, 1411, 1370, 1331, 1245, 1193, 1149, 1129, 1041, 1021, 909, 886, 738, 647, 609, 560, 433. HRMS Calcd for $C_{12}H_{15}NO$: 189.11537. Found: 189.11525.

4.3.12. 2-(*N*-Benzyl-2-methyl-1*H*-indole-3-yl)ethanol (11b).[19] According to GP (step 2), product **6b** (296 mg, 0.78 mmol) and TBAF-trihydrate (492 mg, 1.6 mmol) were employed. Isolated yield: 80%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.57 (d, J=8.3 Hz, 1H), 7.27–7.19 (m, 4H), 7.14–7.07 (m, 2H), 6.96 (dd, J=1.6, 6.5 Hz, 2H), 5.30 (s, 2H), 3.84 (t, J=6.5 Hz, 2H), 3.02 (t, J=6.5 Hz, 2H), 2.31 (s, 3H), 1.49 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=137.8, 136.5, 134.0, 128.7, 127.9, 127.2, 125.9, 121.0, 119.2, 117.9, 109.0, 107.4, 62.9, 46.5, 28.0, 10.3. MS (EI, 70 eV) *m/z* (relative intensity): 265 (100) [M^+], 234 (66), 218 (49), 189 (2), 143 (24), 128 (6), 115 (13), 102 (14), 91 (89), 77 (14), 65 (33), 51 (10), 39 (11), 31 (22). FT IR (neat, cm^{-1}): 3311, 3054, 2923, 2863, 1614, 1604, 1567, 1494, 1471, 1452, 1435, 1369, 1339, 1297, 1262, 1219, 1191, 1176, 1125, 1083, 1035, 1014, 922, 903, 873, 817, 749, 724, 694, 652, 554, 454, 432. HRMS Calcd for $C_{18}H_{19}NO$: 265.14667. Found: 265.14531.

4.3.13. 2-(5-Chloro-2-methyl-1*H*-indole-3-yl)ethanol (11c). According to GP (step 2), product **6c** (539 mg, 1.6 mmol) and TBAF (1 M in THF, 3.14 ml, 3.14 mmol) were employed. Isolated yield: 90%, white solid, mp: 64–67 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.46 (d, J=2.0 Hz, 1H), 7.13 (d, J=8.7 Hz, 1H), 7.09 (dd, J=2.0, 8.7 Hz, 1H), 3.78 (t, J=6.5 Hz, 2H), 3.62 (s, 3H), 2.93 (t, J=6.5 Hz, 2H), 2.36 (s, 3H), 1.49 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=135.7, 135.0, 128.7, 124.6, 120.8, 117.3, 109.5, 106.6, 62.8, 29.6, 27.8, 10.3. MS (EI, 70 eV) *m/z* (relative intensity): 223 (34) [M^+], 192 (100), 177 (9), 157 (16), 142 (6), 128 (4), 115 (10), 101 (3), 87 (1), 75 (3), 63 (1), 56 (1), 42 (2), 31 (5). FT IR (nujol, cm^{-1}): 3288, 2930, 2870, 1611, 1569, 1477, 1433, 1409, 1371, 1331, 1283, 1261, 1245, 1200, 1174, 1134, 1072, 1048, 985, 935, 897, 862, 809, 787, 747, 636, 585, 533, 476, 428. HRMS Calcd for $C_{12}H_{14}{}^{35}ClNO$: 223.07639. Found: 223.07672.

4.3.14. 2-(*N*-Benzyl-5-fluoro-2-methyl-1*H*-indole-3-yl) ethanol (11d). According to GP (step 2), crude product **6d** (964 mg, 3.0 mmol) and TBAF (1 M in THF, 6.0 ml, 6.0 mmol) were employed. Isolated yield: 76%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.28–7.24 (m, 3H), 7.19 (dd, $J_{H,H}$=2.3 Hz, $J_{F,H}$=9.5 Hz, 1H), 7.19 (dd, $J_{F,H}$= 4.0 Hz, $J_{H,H}$=8.5 Hz, 1H), 6.93 (d, J=6.5 Hz, 2H), 6.83 (td, $J_{H,H}$=2.3 Hz, $J_{H,H}$=$J_{F,H}$=9.1 Hz, 1H), 5.27 (s, 2H), 3.82 (t, J=6.5 Hz, 2H), 2.97 (t, J=6.5 Hz, 2H), 2.31 (s, 3H), 1.57 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=159.0, 137.5, 135.8, 133.0, 128.8, 127.3, 125.8, 124.9, 109.6, 190.5, 109.1, 107.6, 62.8, 46.7, 28.0, 10.4. MS (EI, 70 eV) *m/z* (relative intensity): 283 (5) [M^+], 266 (6), 252 (33), 239 (4), 213 (17), 199 (7), 162 (2), 122 (7), 115 (1), 91 (100), 75 (5), 65 (13), 39 (3), 28 (2). FT IR (neat, cm^{-1}): 3357, 3063, 3030, 2935, 2877, 1706, 1622, 1604, 1583, 1506, 1482, 1453, 1419, 1359, 1300, 1250, 1204, 1139, 1140, 969, 851, 791, 728, 694, 629, 589, 433. HRMS Calcd for $C_{18}H_{18}FNO$: 283.13724. Found: 283.13764.

4.3.15. 2-(*N*-Benzyl-5-methoxy-2-methyl-1*H*-indole-3-yl) ethanol (11e). According to GP (step 2), product **6e** (328 mg, 0.8 mmol) and TBAF (1 M in THF, 1.6 ml, 1.6 mmol) were employed. Isolated yield: 85%, light green solid, mp: 78–80 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.26–7.20 (m, 3H), 7.12 (m, 1H), 7.10–7.02 (m, 2H), 6.75 (dd, J=2.1 Hz, J= 8.6 Hz, 2H), 5.28 (s, 2H), 3.80 (s, 3H), 3.68 (t, J=7.5 Hz, 2H), 2.75 (t, J=7.5 Hz, 2H), 2.04 (s, 3H), 1.47 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=154.0, 141.0, 137.9, 135.6, 134.7, 132.4, 128.7, 125.8, 110.7, 109.9, 101.9, 99.1, 62.0, 55.8, 46.4, 28.1, 10.4. MS (EI, 70 eV) *m/z* (relative intensity): 295 (66) [M^+], 264 (31), 251 (75), 236 (6), 218 (2), 174 (7), 160 (57), 147 (4), 130 (5), 116 (4), 91 (100), 77 (3), 65 (10), 39 (2), 29 (1). FT IR (nujol, cm^{-1}): 3368, 3052, 2931, 2852, 1610, 1596, 1460, 1445, 1372, 1321, 1249, 1186, 1128, 1085, 969, 877, 739, 692, 540, 432. HRMS Calcd for $C_{19}H_{21}NO_2$: 295.15723. Found: 295.15768.

4.3.16. 2-(*N*-Benzyl-4-chloro-5-fluoro-2-methyl-1*H*-indole-3-yl)ethanol/2-(*N*-benzyl-6-chloro-5-fluoro-2-methyl-1*H*-indole-3-yl)ethanol (2:1) (11f). According to GP (step 2), product **6f** (518 mg, 1.2 mmol) and TBAF (1 M in THF, 2.4 ml, 2.4 mmol) were employed. Isolated yield: 83%, white solid, mp: 74–77 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.27–7.18 (m, 3H), 6.99 (dd, $J_{H,H}$=3.9 Hz, $J_{F,H}$=8.9 Hz, 1H), 6.92–6.88 (m, 3H), 5.26 (m, 2H), 3.88 (t, J=6.8 Hz, 2H), 3.24 (t, J=6.8 Hz, 2H), 2.32 (s, 3H), 1.56 (br, 1H, OH)/7.29 (d, $J_{F,H}$=9.9 Hz, 1H), 7.27–7.18 (m, 3H), 7.16 (d, $J_{F,H}$=6.0 Hz, 1H), 6.92–6.88 (m, 2H), 5.23 (s, 2H), 3.80 (t, J=6.6 Hz, 2H), 2.94 (t, J=6.6 Hz, 2H), 2.30 (s, 3H), 1.56 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=152.4, 136.9, 137.1, 133.7, 128.8, 127.5, 125.7, 124.8, 110.1, 109.5, 109.3, 107.8, 64.1, 46.8, 28.2, 10.5/152.2, 137.3, 136.3, 132.8, 128.8, 127.5, 126.7, 125.6, 114.0, 109.5, 107.9, 104.1, 62.7, 46.7, 27.9, 10.4. MS (EI, 70 eV) *m/z* (relative intensity): 317 (13) [M^+], 286 (64), 262 (2), 235 (42), 205 (5), 195 (5), 185 (1), 159 (6), 145 (4), 129 (6), 117 (3), 109 (4), 99 (2), 91 (100), 77 (4), 65 (14), 57 (5), 49 (20), 41 (4), 28 (7). FT IR (nujol, cm^{-1}): 3355, 3029, 2929, 2856, 1604, 1568, 1486, 1467, 1445, 1414, 1371, 1356, 1299, 1263, 1242, 1217, 1177, 1147, 1062, 1025, 986, 935, 856, 796, 766, 691, 605, 532, 465, 432. HRMS Calcd for $C_{18}H_{17}{}^{35}ClFNO$: 317.12207. Found: 317.12568.

4.3.17. 2-(*N*-Benzyl-4,5-dichloro-2-methyl-1*H*-indole-3-yl)ethanol/2-(*N*-Benzyl-5,6-dichloro-2-methyl-1*H*-indole-3-yl)ethanol (2:1) (11g, M). According to GP (step 2), product **6g** (897 mg, 2.0 mmol) and TBAF (1 M in THF, 4.0 ml, 4.0 mmol) were employed. Isolated yield: 60%, off white solid, mp: 95–97 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.27–7.22 (m, 3H), 7.12 (d, J=8.5 Hz, 1H), 7.02 (d, J=8.7 Hz, 1H), 6.92–6.88 (dd, J=1.0, 7.0 Hz, 2H), 5.27 (s, 2H), 3.88 (t, J=6.7 Hz, 2H), 3.25 (t, J=6.7 Hz, 2H), 2.33 (s, 3H,), 1.55 (br, 1H, OH)/7.64 (s, 1H), 7.27–7.22 (m, 3H), 7.25 (s, 1H), 6.92–6.88 (dd, J=1.0, J=7.0 Hz, 2H), 5.23 (s, 2H), 3.81 (t, J=6.5 Hz, 2H), 2.95 (t, J=6.5 Hz, 2H), 2.30 (s, 3H), 1.55 (br, 1H, OH) . ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.8, 136.2, 136.0, 128.2, 127.5, 125.8, 125.7, 123.8, 122.2, 119.0, 110.5, 108.5, 64.1, 46.8, 28.4, 10.5/136.9, 135.4, 135.2, 128.2, 128.0, 127.5, 125.8, 124.7, 123.0, 119.2, 108.2, 107.6, 62.8, 46.8, 27.8, 10.4. MS (EI, 70 eV) *m/z* (relative intensity): 333 (16) [M^+ −H], 302 (23), 289 (13), 254 (2), 215 (2), 198 (2), 175 (3), 142 (4), 111 (1), 99 (2), 91 (100), 85 (26), 77 (2), 65 (10), 57 (2), 43 (11), 29 (4). FT IR (nujol, cm^{-1}): 3356, 3029, 2928, 2856, 1678, 1603, 1537, 1499, 1457, 1426, 1411, 1370, 1345, 1290, 1243, 1222, 1207, 1176, 1147, 1062, 1027, 996, 933, 865, 776, 716, 696, 613, 525, 435, 439. HRMS Calcd for $C_{18}H_{17}{}^{35}Cl_2NO$: 333.06873. Found: 333.06876.

4.3.18. 3-(*N*-Benzyl-4,5-dichloro-1*H*-indole-3-yl)propanol/3-(*N*-Benzyl-5,6-dichloro-1*H*-indole-3-yl)propanol (2:1) (11g, *anti*-M). According to GP (step 2), product **6g** (1155.0 mg, 2.5 mmol) and TBAF (1 M in THF, 5.0 ml, 5.0 mmol) were employed. Isolated yield: 29%, off white solid, mp: 97–99 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.38–7.25 (m, 3H), 7.13 (d, J=8.7 Hz, 1H), 7.03 (d, J=8.7 Hz, 1H), 6.91–6.89 (dd, J=1.0, 6.3 Hz, 2H), 6.5 (s, 1H), 5.31 (s, 2H), 3.73–3.68 (m, 2H), 2.79 (t, J=6.5 Hz, 2H), 2.02–1.91 (m, 2H), 1.57 (br, 1H, OH)/7.62 (s, 1H), 7.38–7.25 (m, 3H), 7.24 (s, 1H), 6.91–6.89 (dd, J=1.0, 6.3 Hz, 2H), 6.3 (s, 1H), 5.27 (s, 2H), 3.73–3.68 (m, 2H), 2.76 (t, J=6.5 Hz, 2H), 2.02–1.91 (m, 2H), 1.57 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.8, 136.1, 130.8, 128.9, 127.5, 125.8, 125.6, 123.8, 122.3, 119.1, 110.8, 108.8, 61.8, 46.7, 31.0, 22.9/136.9, 135.4, 130.2, 128.5, 128.0, 127.5, 125.6, 124.7, 123.0, 119.2, 108.5, 107.5, 61.8, 46.5, 31.0, 22.9. MS (EI, 70 eV) *m/z* (relative intensity): 333 (16) [M^+ −H], 302 (100), 289 (34), 254 (5), 215 (4), 199 (2), 176 (7), 141 (5), 115 (3), 101 (2), 91 (85), 85 (21), 77 (4), 65 (8), 57 (2), 43 (13), 29 (5). FT IR (nujol, cm^{-1}): 3357, 3028, 2928, 2856, 1602, 1587, 1498, 1479, 1445, 1419, 1392, 1350, 1291, 1266, 1245, 1227, 1186, 1137, 1088, 1047, 996, 942, 875, 756, 716, 699, 623, 582, 475, 432. HRMS Calcd for $C_{18}H_{17}{}^{35}Cl_2NO$: 333.06873. Found: 333.06876.

4.3.19. 3-(1,2-Dimethyl-1*H*-indole-3-yl)propanol (11h). According to GP (step 2), product **6h** (507 mg, 1.6 mmol) and TBAF (1 M in THF, 3.2 ml, 3.2 mmol) were employed. Isolated yield: 90%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.51 (d, J=7.7 Hz, 1H), 7.23 (d, J=8.1 Hz, 1H), 7.14 (td, J=1.3, 8.2 Hz, 1H), 7.06 (td, J=1.2, 8.0 Hz, 1H), 3.67 (t, J=6.5 Hz, 2H), 3.64 (s, 3H, H), 2.81 (t, J=6.5 Hz, 2H), 2.35 (s, 3H), 1.87 (quint, J=6.5 Hz, 2H), 1.32 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.5, 132.8, 127.6, 120.4, 118.6, 117.8, 110.4, 108.5, 62.5, 33.6, 29.4, 20.4, 10.1. MS (EI, 70 eV) *m/z* (relative intensity): 203 (13) [M^+], 172 (1), 158 (87), 143 (7), 128 (6), 115 (100), 102 (1), 91 (1), 75 (1), 65 (1), 55 (1), 42 (2), 28 (1). FT IR (neat, cm^{-1}): 3355, 3051, 2935, 2855, 1613, 1566, 1472, 1440, 1410, 1370, 1331, 1247, 1191, 1148, 1128, 1060, 1013, 983, 919, 856, 738, 654, 559, 433. HRMS Calcd for $C_{13}H_{17}NO$: 203.13101. Found: 203.13123.

4.3.20. 3-(*N*-Benzyl-2-methyl-1*H*-indole-3-yl)propanol (11i).[20] According to GP (step 2), product **6i** (707 mg, 1.8 mmol) and TBAF (1 M in THF, 3.6 ml, 3.6 mmol) were employed. Isolated yield: 84%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.57–7.54 (m, 1H), 7.25–7.16 (m, 4H), 7.07–7.05 (m, 2H), 6.93 (d, J=6.5 Hz, 2H), 5.27 (s, 2H), 3.64 (t, J=6.3 Hz), 2.83 (t, J=6.3 Hz, 2H), 2.27 (s, 3H), 1.89 (quint, J=6.3 Hz, 2H), 1.49 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=138.0, 136.4, 132.6, 128.6, 127.8, 127.1, 125.8, 120.7, 118.9, 118.9, 111.1, 108.9, 62.4, 46.4, 33.4, 20.4, 10.1. MS (EI, 70 eV) *m/z* (relative intensity): 279 (31) [M^+], 234 (68), 218 (41), 189 (4), 142 (23), 129 (8), 115 (18), 102 (11), 91 (100), 77 (14), 65 (23), 51 (13), 39 (11), 31 (17). FT IR (neat, cm^{-1}): 3361, 3053, 3029, 2933, 2858, 1605, 1584, 1567, 1495, 1468, 1453, 1415, 1367, 1336, 1300, 1260, 1180, 1147, 1062, 1028, 974, 919, 850, 738, 696, 634, 558, 455, 434. HRMS Calcd for $C_{19}H_{20}NO$: 279.16231. Found: 279.16249.

4.3.21. 3-(1,2,3-Trimethyl-1*H*-indole-3-yl)propanol (11j). According to GP (step 2), crude product **6j** and TBAF (1 M in THF, 6.0 ml, 6.0 mmol) were employed. Isolated yield: 75%, white solid, mp: 49–51 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.28 (s, 1H), 7.11 (d, J=8.1 Hz, 1H), 6.95 (dd, J=1.6, 8.3 Hz, 1H), 3.65 (t, J=6.4 Hz, 2H), 3.60 (s, 3H), 2.77 (t, J=6.4 Hz, 2H, H), 2.44 (s, 3H), 2.32 (s, 3H), 1.87 (quint, J=6.4 Hz, 2H), 1.45 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=135.6, 134.9, 132.8,

127.7, 121.9, 117.6, 109.8, 108.1, 62.6, 33.6, 29.4, 21.4, 20.4, 10.1. MS (EI, 70 eV) *m/z* (relative intensity): 217 (27) [M^+], 198 (1), 186 (2), 172 (100), 157 (5), 142 (2), 128 (2), 115 (4), 91 (2), 77 (1), 57 (2), 39 (1), 28 (1). FT IR (nujol, cm^{-1}): 3295, 3014, 2917, 2850, 1619, 1581, 1565, 1489, 1443, 1410, 1370, 1321, 1299, 1246, 1208, 1181, 1156, 1135, 1072, 1028, 912, 896, 862, 781, 751, 694, 661, 586, 505, 430. HRMS Calcd for $C_{14}H_{19}NO$: 217.14667. Found: 217.14671.

4.3.22. 3-(*N*-Benzyl-4-chloro-1*H*-indole-3-yl)propanol/ 3-(*N*-Benzyl-6-chloro-1*H*-indole-3-yl) propanol (2:1) (11k). According to GP (step 2), product **6k** (728 mg, 1.7 mmol) and TBAF (1 M in THF, 3.4 ml, 3.4 mmol) were employed. Isolated yield: 75%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.45 (d, J=8.3 Hz, 1H), 7.30–7.21 (m, 4H), 6.92 (t, J=8.2 Hz, 1H), 6.91–6.89 (m, 2H), 5.27 (s, 2H), 3.70 (t, J=6.3 Hz, 2H), 3.05 (t, J=6.3 Hz, 2H), 2.29 (s, 3H), 1.91–1.80 (m, 2H), 1.40, (br, 1H, OH)/7.30–7.21 (m, 3H), 7.17 (d, J=1.8 Hz, 1H), 6.98–6.94 (m, 2H), 6.91–6.89 (m, 2H), 5.23 (s, 2H), 3.64 (t, J=6.2 Hz, 2H), 2.81 (t, J=6.2 Hz, 2H), 2.27 (s, 3H), 1.91–1.80 (m, 2H), 1.40, (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 137.4, 136.8, 135.6, 128.7, 127.3, 126.5, 125.3, 124.3, 120.6, 119.5, 108.9, 107.7, 62.4, 46.6, 33.4, 21.5, 10.2/ 137.9, 134.3, 133.5, 128.7, 127.3, 126.6, 125.7, 125.3, 118.8, 111.6, 107.9, 62.2, 46.6, 32.2, 21.0, 10.1. MS (EI, 70 eV) *m/z* (relative intensity): 313 (70) [M^+], 268 (94), 254 (17), 246 (3), 204 (3), 178 (4), 164 (3), 142 (6), 115 (5), 100 (2), 91 (100), 77 (4), 65 (17), 55 (5), 43 (12), 29 (7). FT IR (neat, cm^{-1}): 3354, 3028, 2928, 2855, 1605, 1598, 1567, 1496, 1477, 1445, 1419, 1373, 1356, 1298, 1263, 1243, 1219, 1176, 1137, 1068, 1027, 996, 932, 835, 766, 726, 696, 609, 532, 445, 433. HRMS Calcd for $C_{19}H_{20}{}^{35}ClNO$: 313.12335. Found: 313.12378.

4.3.23. 3-(*N*-Benzyl-4,5-dichloro-2-methyl-1*H*-indole-3-yl)propanol/3-(*N*-Benzyl-5,6-dichloro-2-methyl-1*H*-indole-3-yl)propanol (2:1) (11l, M). According to GP (step 2), product **6l** (1155.0 mg, 2.5 mmol) and TBAF (1 M in THF, 5.0 ml, 5.0 mmol) were employed. Isolated yield: 62%, white solid, mp: 70–73 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.25–7.21 (m, 3H), 7.10 (d, J=8.5 Hz, 1H), 6.99 (d, J=8.5 Hz, 1H), 6.89–6.87 (m, 2H), 5.25 (s, 2H), 3.69 (t, J=6.4 Hz, 2H), 3.04 (t, J=6.4 Hz, 2H), 2.29 (s, 3H), 1.95–1.82 (m, 2H), 1.54 (br, 1H, OH)/7.60 (s, 1H), 7.25–7.21 (m, 3H), 7.24 (s, 1H), 6.89–6.87 (m, 2H), 5.21 (s, 2H), 3.64 (t, J=6.3 Hz, 2H), 2.77 (t, J=6.3 Hz, 2H), 2.27 (s, 3H), 1.95–1.82 (m, 2H), 1.54 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=137.0, 135.9, 135.0, 128.8, 127.4, 127.1, 125.7, 125.6, 124.4, 122.0, 111.1, 108.4, 62.2, 46.6, 35.3, 21.0, 10.2/137.0, 135.5, 130.1, 128.8, 127.6, 127.4, 125.7, 123.6, 122.1, 119.0, 112.1, 110.4, 61.9, 46.6, 33.3, 20.20, 10.1. MS (EI, 70 eV) *m/z* (relative intensity): 347 (14) [M^+ −H], 302 (100), 286 (54), 267 (7), 238 (11), 205 (6), 185 (3), 158 (4), 149 (7), 128 (3), 115 (4), 99 (5), 91 (90), 77 (8), 65 (27), 57 (4), 41 (2), 31 (6). FT IR (nujol, cm^{-1}): 3425, 3064, 3030, 2936, 2864, 1604, 1591, 1496, 1473, 1448, 1411, 1355, 1299, 1219, 1162, 1133, 1102, 1060, 1028, 889, 867, 837, 787, 732, 698, 632, 595, 456, 429. HRMS Calcd for $C_{19}H_{19}{}^{35}Cl_2NOSi$: 347.08438. Found: 347.08328.

4.3.24. 3-(*N*-Benzyl-4,5-dichloro-1*H*-indole-3-yl)butanol/ 3-(*N*-Benzyl-5,6-dichloro-1*H*-indole-3-yl) butanol (2:1) (11l, *anti*-M). According to GP (step 2), product **6l** (1155.0 mg, 2.5 mmol) and TBAF (1 M in THF, 5.0 ml, 5.0 mmol) were employed. Isolated yield: 26%, white solid, mp: 71–74 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.27–7.21 (m, 3H), 7.09 (d, J=8.7 Hz, 1H), 6.96 (d, J=8.5 Hz, 1H), 6.87 (dd, J=1.8, 7.3 Hz, 2H), 5.25 (s, 2H), 3.62–3.58 (m, 2H), 2.69–2.62 (m, 2H), 1.80–1.72 (m, 2H), 1.70–1.60 (m, 2H), 1.47 (br, 1H, OH)/7.61 (s, 1H), 7.27–7.21 (m, 3H), 7.25 (s, 1H), 6.87 (dd, J=1.8, 7.3 Hz, 2H), 5.21 (s, 2H), 3.62–3.58 (m, 2H), 2.69–2.62 (m, 2H), 1.80–1.72 (m, 2H), 1.70–1.60 (m, 2H), 1.47 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.0, 136.61, 135.8, 128.9, 127.6, 127.5, 125.7, 125.6, 124.3, 122.1, 110.6, 108.7, 62.3, 46.6, 32.1, 26.4, 24.3/136.9, 135.5, 130.2, 128.9, 128.8, 127.6, 125.7, 122.9, 122.1, 120.6, 112.1, 110.4, 62.3, 46.4, 32.1, 26.3, 24.2. MS (EI, 70 eV) *m/z* (relative intensity): 347 (45) [M^+], 302 (21), 289 (58), 276 (7), 253 (8), 238 (3), 214 (5), 198 (4), 175 (9), 149 (6), 149 (5), 127 (4), 111 (6), 99 (32), 91 (100), 71 (14), 65 (38), 57 (15), 43 (25), 31 (23). FT IR (nujol, cm^{-1}): 3351, 3087, 3064, 3030, 2936, 2867, 1604, 1588, 1563, 1539, 1496, 1452, 1406, 1355, 1330, 1259, 1209, 1155, 1141, 1121, 1101, 1069, 1029, 983, 946, 906, 868, 837, 776, 732, 698, 654, 575, 468, 456. HRMS Calcd for $C_{19}H_{19}{}^{35}Cl_2NO$: 347.08438. Found: 347.08555.

4.3.25. 3-(1-Methyl-2-phenyl-1*H*-indole-3-yl)propanol (11m). According to GP (step 2), crude product **6m** and TBAF (1 M in THF, 0.6 ml, 0.6 mmol) were employed. Isolated yield: 84%, colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.59 (d, J=7.9 Hz, 1H), 7.48–7.41 (m, 4H), 7.31–7.27 (m, 2H), 7.21 (td, J=1.2, 7.6 Hz, 1H), 7.09 (td, J=1.0, 6.9 Hz, 1H), 3.73 (s, 3H), 3.52 (t, J=6.6 Hz, 2H), 2.94 (t, J=6.6 Hz, 2H), 1.80 (quint, J=6.6 Hz, 2H), 1.52 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=136.7, 136.6, 135.5, 129.7, 128.5, 127.0, 125.9, 121.3, 119.6, 114.4, 108.8, 61.6, 32.6, 29.4, 20.7. MS (EI, 70 eV) *m/z* (relative intensity): 265 (67) [M^+], 247 (1), 232 (4), 220 (100), 204 (25), 179 (10), 165 (4), 152 (2), 144 (14), 115 (10), 102 (4), 91 (2), 77 (4), 57 (5), 42 (10), 28 (3). FT IR (neat, cm^{-1}): 3373, 3053, 2933, 2871, 1601, 1553, 1493, 1440, 1402, 1371, 1328, 1255, 1209, 1177, 1152, 1131, 1091, 1058, 940, 924, 844, 771, 743, 703, 675, 639, 610, 565, 501. HRMS Calcd for $C_{18}H_{19}NO$: 265.14667. Found: 265.14601.

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