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$Sc(OTf)_3$-catalyzed efficient synthesis of β,β-bis(indolyl) ketones by the double indolylation of acetic acid 2-methylene-3-oxobutyl ester†

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In the presence of 5 mol% $Sc(OTf)_3$, double indolylation of acetic acid 2-methylene-3-oxo-butyl ester with differently substituted indoles readily afforded β,β-bis(indolyl) ketones. The reaction may proceed *via* a $Sc(OTf)_3$-catalyzed SN_2'-type substitution and subsequent conjugate addition.

Introduction

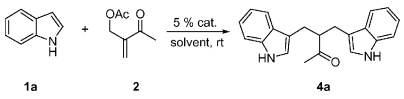
Indoles and their derivatives constitute an important class of biologically active natural products, which play a fundamental role in bioorganic chemistry.[1] Over the past few years, a large number of natural products containing a bis(indole) unit have been isolated from metabolites of terrestrial and marine organisms, which show interesting biological activity.[2] It has been reported that the reaction of indoles with aromatic or aliphatic aldehydes/ketones produced azafulvenium salts, which undergo further addition with the second molecule of indole to afford bis(indolyl) methanes in the presence of a Lewis acid.[3] Hao *et al.* reported a Pd(II)-catalyzed reaction for the synthesis of α-amino and α-hydroxy diindolylacetates.[4] Recently, Yadav *et al.* reported the gallium(III) halide-catalyzed double indolylation of phenylacetylene.[5] Thus, there is significant interest in the development of new efficient synthetic method to prepare compounds with two indole units.

Although protonic or Lewis acid-catalyzed reactions of indoles with α,β-enones have long been known,[6] so far there are no reports on analogous reactions involving α,β-enones with a leaving group at the β-position, which may lead to an efficient double indolylation reaction. In our previous work,[7] we have demonstrated a new functionalization of indoles *via* the palladium-catalyzed reaction of indoles with 2-acetoxymethyl substituted electron-deficient alkenes. This reaction usually needs long reaction time, high temperature and suffers from low yield and poor diversity for the starting indoles (for example, *N*-alkyl protected indoles are unreactive). Herein, we report the synthesis of bis(indolyl) ketones by the double indolylation of the carbon–carbon double bonds of acetic acid 2-methylene-3-oxobutyl ester **2** using 5% $Sc(OTf)_3$ as the catalyst.

Results and discussion

Preliminary studies have been carried out using indole **1a** and acetic acid 2-methylene-3-oxobutyl ester **2** under the catalysis of a series of potential metal salts catalysts (5 mol%) in CH_2Cl_2 (Table 1). Initial results indicated that $InCl_3$[8] (74%), $Cu(OTf)_2$ (76%), $In(OTf)_3$ (78%) and $Sc(OTf)_3$[9] (82%) all afforded good yields of bis(indolyl) ketone **4a** (entries 1–4, Table 1). However, $Sc(OTf)_3$ is the catalyst of choice based on its efficiency and tolerance to air. The reactions also proceeded well in other solvents, such as toluene, acetonitrile and THF (entries 5–7, Table 1).

Table 1 Optimization of reaction conditions for the reaction of indoles **1a** with acetic acid 2-methylene-3-oxobutyl ester **2**

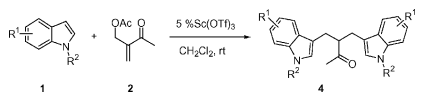


1a **2** **4a**

Entry	Solvent	Catalyst	Time/h	Yield of **4a** (%)
1	CH_2Cl_2	$InCl_3$	20	74
2	CH_2Cl_2	$In(OTf)_3$	20	78
3	CH_2Cl_2	$Cu(OTf)_2$	20	76
4	CH_2Cl_2	$Sc(OTf)_3$	20	82
5	CH_3CN	$Sc(OTf)_3$	23	80
6	Toluene	$Sc(OTf)_3$	25	79
7	THF	$Sc(OTf)_3$	23	76

A variety of differently substituted indoles **1** underwent smooth double functionalization with acetic acid 2-methylene-3-oxobutyl ester **2** to afford bis(indolyl) ketones **4** in moderate to good yields (Table 2). Two points should be noted: (1) the products derived from bromo-substituted indoles contained two carbon–bromo bonds, which may provide opportunities for further elaboration (Table 2, entries 5–7); (2) *N*-protected indoles, which are inert under our previous Pd-catalyzed protocol,[7] were also able to react with **2** to produce bis(indolyl) ketones **4** in reasonable yields (Table 2, entries 8–13).

Table 2 $Sc(OTf)_3$-catalyzed synthesis of β,β-bis(indolyl) ketones by the reaction of indoles **1** with acetic acid 2-methylene-3-oxobutyl ester **2**



1 **2** **4**

	Indole			
Entry	R^1	R^2	Time/h	Yield of **4** (%)
1	5-MeO	H (**1b**)	16	74 (**4b**)
2	5-Me	H (**1c**)	16	70 (**4c**)
3	4-Bn	H (**1d**)	24	71 (**4d**)
4	5-Bn	H (**1e**)	24	81 (**4e**)
5	5-Br	H (**1f**)	22	75 (**4f**)
6	4-Br	H (**1g**)	26	74 (**4g**)
7	6-Br	H (**1h**)	16	88 (**4h**)
8	H	CH_3 (**1i**)	18	80 (**4i**)
9	H	*n*-Bu (**1j**)	20	71 (**4j**)
10	H	Allyl (**1k**)	20	77 (**4k**)
11	H	Bn (**1l**)	19	78 (**4l**)
12	5-Bn	CH_3 (**1m**)	24	79 (**4m**)
13	6-Bn	CH_3 (**1n**)	17	61 (**4n**)

† Electronic supplementary information (ESI) available: ^1H NMR and ^{13}C NMR spectra of compounds **4**. See http://www.rsc.org/suppdata/ob/b5/b503378k/

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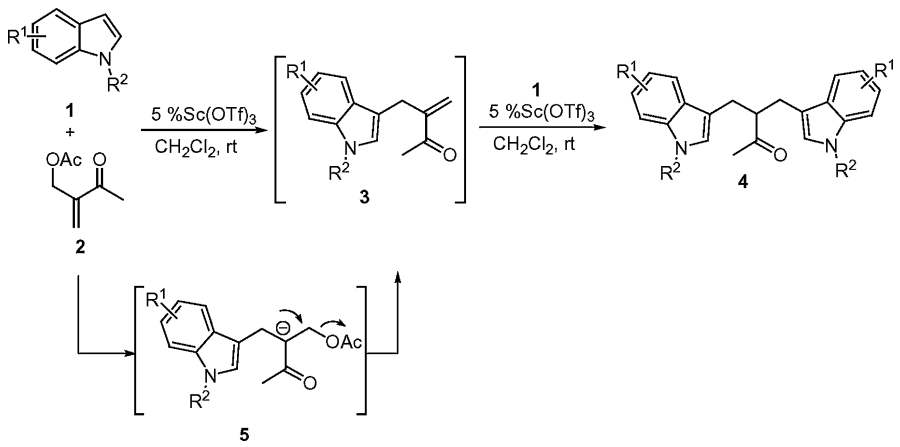

Scheme 1

The reaction may proceed in the following sequence: first, indole **1** reacted with acetic acid 2-methylene-3-oxobutyl ester **2** to produce intermediate **3** *via* the carbonyl group directed SN_2'-type substitution, which has been isolated by varying the ratio of the starting materials. Then, the intermediate **3** acted as a Michael-acceptor to react with another molecule of indole **1** to afford the final β,β-bis(indolyl) ketone product **4** (Scheme 1).

Conclusions

In summary, we have developed a simple and efficient procedure for the double indolylation of indoles with acetic acid 2-methylene-3-oxobutyl ester **2** in the presence of 5% $Sc(OTf)_3$ as catalyst. The presence of two indole units and carbonyl group may be further elaborated to afford otherwise unattainable indole derivatives with potential biological reactivity and diversity of structure. Further studies in this area are being conducted in our laboratory.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Mercury 300 spectrometer using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were obtained using HP 5989A spectrometers. IR spectra were measured on Avatar 360 spectrophotometer. High-resolution mass spectra were carried out with Concept 1H spectrometer. TLC was performed on precoated plates (0.25 mm, silica gel 60 F254).

General procedure

A mixture of indole (1.25 mmol), acetic acid 2-methylene-3-oxo-butyl ester (0.5 mmol) and 5 mol% of $Sc(OTf)_3$ in CH_2Cl_2 (2 mL) was stirred at room temperature for the time specified in Table 2. Upon completion of the reaction as indicated by TLC, the reaction mixture was concentrated under vacuum and the resulting crude product was purified by column chromatography on silica gel (eluent: ethyl acetate–petroleum ether, 1 : 5) to afford the pure β,β-bis(indole) ketone.

4-(1*H*-Indol-3-yl)-3-(1*H*-indol-3-ylmethyl)butan-2-one (4a). The reaction of indole **1a** (74 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (31 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 65 mg (82%) of **4a**: solid; mp: 44–45 °C (ethyl acetate–petroleum ether); IR(neat) 3415, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.01 (brs, 2 H), 7.51 (d, J = 8.1 Hz, 2 H), 7.32 (d, J = 8.1 Hz, 2 H), 7.17 (t, J = 8.1 Hz, 2 H), 7.08 (t, J = 8.1 Hz, 2 H), 6.92 (s, 2 H), 3.51–3.39 (m, 1 H), 3.15 (d, J = 8.4 Hz, 1 H), 3.11 (d, J = 8.4 Hz, 1 H), 2.99 (d, J = 6.0 Hz, 1 H), 2.94 (d, J = 6.0 Hz, 1 H), 1.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.2, 136.1, 127.1, 122.3, 121.8, 119.2, 118.5, 113.1, 111.2, 53.9, 30.5, 27.6; MS *m/z* (%) 84 (100), 316 (M^+, 5.77); HRMS *m/z* (MALDI) calcd for $C_{21}H_{20}N_2ONa^+$(M^+ + Na) 339.1468. Found 339.1462.

4-(5-Methoxy-1*H*-indol-3-yl)-3-(5-methoxy-1*H*-indol-3-ylmethyl)butan-2-one (4b). The reaction of indole **1b** (180 mg, 1.25 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (71 mg, 0.5 mmol) and 5 mol% of $Sc(OTf)_3$ (12 mg) in 2 mL of CH_2Cl_2 afforded 139.3 mg (74%) of **4b**: solid; mp: 63–64 °C (ethyl acetate–hexane); IR(neat) 3410, 1702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.98 (brs, 2 H), 7.25–7.19 (m, 2 H), 6.95 (s, 2 H), 6.89–6.80 (m, 4 H), 3.77 (s, 6 H), 3.47–3.39 (m, 1 H), 3.14 (d, J = 8.4 Hz, 1 H), 3.09 (d, J = 8.4 Hz, 1 H), 2.94 (d, J = 6.0 Hz, 1 H), 2.90 (d, J = 6.0 Hz, 1 H), 1.91 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.6, 153.9, 131.4, 127.5, 123.1, 113.3, 112.0, 111.9, 100.4, 55.7, 53.6, 30.8, 27.5; MS *m/z* (%) 160 (100), 376 (M^+, 21.75); HRMS *m/z* (MALDI) calcd for $C_{23}H_{25}N_2O_3^+$(M^+ + H) 377.1860. Found 377.1850; anal. calcd for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.43; N, 7.44%; found: C, 73.28; H, 6.41; N, 7.33%.

4-(5-Methyl-1*H*-indol-3-yl)-3-(5-methyl-1*H*-indol-3-ylmethyl)-butan-2-one (4c). The reaction of indole **1c** (168 mg, 1.25 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (70 mg, 0.5 mmol) and 5 mol% of $Sc(OTf)_3$ (12 mg) in 2 mL of CH_2Cl_2 afforded 120.9 mg (70%) of **4c**: solid; mp: 145–146 °C (ethyl acetate–hexane); IR(neat) 3410, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.92 (brs, 2 H), 7.25 (s, 4 H), 7.03 (d, J = 8.1 Hz, 2 H), 6.92 (s, 2 H), 3.54–3.41 (m, 1 H), 3.15 (d, J = 8.4 Hz, 1 H), 3.10 (d, J = 8.4 Hz, 1 H), 2.97 (d, J = 5.7 Hz, 1 H), 2.92 (d, J = 5.7 Hz, 1 H), 2.43 (s, 6 H), 1.88 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.8, 134.6, 128.5, 127.4, 123.6, 122.4, 118.4, 113.1, 110.8, 53.7, 30.8, 27.6, 21.5; MS *m/z* (%) 144 (100), 344 (M^+, 16.01); HRMS *m/z* (MALDI) calcd for $C_{23}H_{25}N_2O^+$(M^+ + H) 345.1961. Found 345.1957; anal. calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13%; found: C, 80.20; H, 7.06; N, 8.09%.

4-(4-Benzyloxy-1*H*-indol-3-yl)-3-(4-benzyloxy-1*H*-indol-3-ylmethyl)butan-2-one (4d). The reaction of indole **1d** (111.5 mg, 0.5 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (28 mg, 0.2 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 76.2 mg (71%) of **4d**: solid; mp: 157–158 °C (ethyl acetate–hexane); IR(neat) 3409, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (brs, 2 H), 7.40–7.20 (m, 10 H), 6.96 (t, J = 7.8 Hz, 2 H), 6.87 (d, J = 7.8 Hz, 2 H), 6.71 (s, 2 H), 6.37 (d, J = 7.8 Hz, 2 H), 4.86 (s, 4 H), 3.60–3.49 (m, 1 H), 3.22 (d, J = 8.4 Hz, 1 H), 3.17 (d, J = 8.4 Hz, 1 H), 3.04 (d, J = 6.3 Hz, 1 H), 2.99 (d, J = 6.3 Hz, 1 H), 1.57 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.0, 153.6, 138.0, 137.7, 128.3, 127.5, 127.2, 122.5, 121.3, 117.3, 114.2, 104.5, 100.6, 69.3, 54.6, 30.0, 28.9; MS *m/z* (MALDI) 91 (100), 528 (M^+, 100); HRMS *m/z* (MALDI) calcd for $C_{35}H_{32}N_2O_3Na^+$(M^+ + Na) 551.2305.

Found 551.2305; anal. calcd for $C_{35}H_{32}N_2O_3$: C, 79.52; H, 6.10; N, 5.30%; found: C, 79.43; H, 6.17; N, 5.15%.

4-(5-Benzyloxy-1*H*-indol-3-yl)-3-(5-benzyloxy-1*H*-indol-3-ylmethyl)butan-2-one (4e). The reaction of indole **1e** (111.5 mg, 0.5 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (28 mg, 0.2 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 85.7 mg (81%) of **4e**: solid; mp: 56–57 °C (ethyl acetate–hexane); IR(neat) 3416, 1702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.92 (brs, 2 H), 7.43–7.23 (m, 10 H), 7.19 (d, $J = 5.1$ Hz, 2 H), 6.98–6.84 (m, 6 H), 4.93 (s, 4 H), 3.40–3.29 (m, 1 H), 3.11 (d, $J = 8.4$ Hz, 1 H), 3.06 (d, $J = 8.4$ Hz, 1 H), 2.91 (d, $J = 6.0$ Hz, 1 H), 2.86 (d, $J = 6.0$ Hz, 1 H), 1.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.5, 153.0, 137.5, 131.5, 128.4, 127.7, 127.5, 123.2, 113.3, 112.8, 111.9, 102.0, 70.7, 53.7, 30.8, 29.7, 27.4; MS *m/z* (MALDI) 528 (M^+, 100); HRMS *m/z* (MALDI) calcd for $C_{35}H_{32}N_2O_3Na^+$(M^+ + Na) 551.2305. Found 551.2300; anal. calcd for $C_{35}H_{32}N_2O_3$: C, 79.52; H, 6.10; N, 5.30%; found: C, 79.47; H, 6.12; N, 5.15%.

4-(5-Bromo-1*H*-indol-3-yl)-3-(5-bromo-1*H*-indol-3-ylmethyl)-butan-2-one (4f). The reaction of indole **1f** (245 mg, 1.25 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (71 mg, 0.5 mmol) and 5 mol% of $Sc(OTf)_3$ (12 mg) in 2 mL of CH_2Cl_2 afforded 178.5 mg (75%) of **4f**: solid; mp: 152–153 °C (ethyl acetate–petroleum ether); IR(neat) 3429, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.15 (brs, 2 H), 7.62 (s, 2 H), 7.29–7.18 (m, 4 H), 7.01 (s, 2 H), 3.41–3.28 (m, 1 H), 3.15 (d, $J = 8.4$ Hz, 1 H), 3.10 (d, $J = 8.4$ Hz, 1 H), 2.95 (d, $J = 6.0$ Hz, 1 H), 2.90 (d, $J = 6.0$ Hz, 1 H), 1.95 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.9, 134.8, 129.0, 125.0, 123.5, 121.2, 113.1, 112.8, 112.7, 53.8, 30.6, 27.2; MS *m/z* (%) 210 (100), 472 (M^+(^{79}Br), 6.62), 474 (M^+(^{79}Br^{81}Br), 12.88), 476 (M^+(^{81}Br), 6.46); HRMS *m/z* (MALDI) calcd for $C_{21}H_{19}N_2O^{79}Br_2^+$($M^+$ + H) 472.9859. Found 472.9855.

4-(4-Bromo-1*H*-indol-3-yl)-3-(4-bromo-1*H*-indol-3-ylmethyl)-butan-2-one (4g). The reaction of indole **1g** (111 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (38.5 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 94.6 mg (74%) of **4g**: solid; mp: 177–178 °C (ethyl acetate–hexane); IR(neat) 3414, 1697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 (brs, 2 H), 7.31–7.16 (m, 4 H), 7.05–6.92 (m, 4 H), 3.83–3.69 (m, 1 H), 3.32–3.12 (m, 4 H), 1.88 (s, 3 H); ^{13}C NMR (75 MHz, DMSO): δ 212.2, 137.7, 125.9, 124.7, 122.6, 121.9, 112.9, 112.1, 111.1, 55.3, 30.1, 27.5; MS *m/z* (%) 208 (100), 472 (M^+(^{79}Br), 16.21), 474 (M^+(^{79}Br^{81}Br), 29.14), 476 (M^+(^{81}Br), 14.59); HRMS *m/z* (MALDI) calcd for $C_{21}H_{18}N_2O_{79}Br_2Na^+$($M^+$ + Na) 494.9678. Found 494.9692; anal. calcd for $C_{21}H_{18}N_2OBr_2$: C, 53.19; H, 3.88; N, 5.91%; found: C, 53.22; H, 3.93; N, 5.64%.

4-(6-Bromo-1*H*-indol-3-yl)-3-(6-bromo-1*H*-indol-3-ylmethyl)-butan-2-one (4h). The reaction of indole **1h** (120 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (35.4 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 103.8 mg (88%) of **4h**: solid; mp: 44–45 °C (ethyl acetate–hexane); IR(neat) 3425, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (brs, 2 H), 7.49 (d, $J = 1.2$ Hz, 2 H), 7.23 (d, $J = 8.1$ Hz, 2 H), 7.19 (dd, $J_1 = 8.1$ Hz, $J_2 = 1.2$ Hz, 2 H), 6.92 (s, 2 H), 3.41–3.29 (m, 1 H), 3.12 (d, $J = 8.7$ Hz, 1 H), 3.07 (d, $J = 8.7$ Hz, 1 H), 2.93 (d, $J = 6.0$ Hz, 1 H), 2.88 (d, $J = 6.0$ Hz, 1 H), 1.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.2, 136.9, 126.1, 122.9, 122.7, 119.9, 115.6, 114.1, 113.6, 53.9, 30.8, 27.5; MS *m/z* (%) 210 (100), 472 (M^+(^{79}Br), 13.19), 474 (M^+(^{79}Br^{81}Br), 24.06), 476 (M^+(^{81}Br), 11.97); HRMS *m/z* (MALDI) calcd for $C_{21}H_{18}N_2O^{79}Br_2Na^+$($M^+$ + Na) 494.9678. Found 494.9703; anal. calcd for $C_{21}H_{18}N_2OBr_2$: C, 53.19; H, 3.88; N, 5.91%; found: C, 53.38; H, 4.20; N, 5.50%.

4-(1-Methyl-1*H*-indol-3-yl)-3-(1-methyl-1*H*-indol-3-ylmethyl)-butan-2-one (4i). The reaction of indole **1i** (82 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (35.5 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 68.9 mg (80%) of **4i**: oil; IR(neat) 1708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, $J = 8.1$ Hz, 2 H), 7.38–7.22 (m, 4 H), 7.19–7.11 (m, 2 H), 6.87 (s, 2 H), 3.74 (s, 6 H), 3.56–3.43 (m, 1 H), 3.22 (d, $J = 8.4$ Hz, 1 H), 3.17 (d, $J = 8.4$ Hz, 1 H), 3.05 (d, $J = 6.0$ Hz, 1 H), 3.00 (d, $J = 6.0$ Hz, 1 H), 1.91 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.5, 136.9, 127.6, 127.0, 121.4, 118.73, 118.68, 111.9, 109.1, 54.2, 32.5, 30.7, 27.6; MS *m/z* (%) 144 (100), 344 (M^+, 21.61); HRMS *m/z* (MALDI) calcd for $C_{23}H_{24}N_2ONa^+$(M^+ + Na) 367.1781. Found 367.1791.

4-(1-Butyl-1*H*-indol-3-yl)-3-(1-butyl-1*H*-indol-3-ylmethyl)-butan-2-one (4j). The reaction of indole **1j** (102.8 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (37.6 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 81.1 mg (71%) of **4j**: oil; IR(neat) 1709 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, $J = 8.1$ Hz, 2 H), 7.29 (d, $J = 8.1$ Hz, 2 H), 7.18 (t, $J = 7.5$ Hz, 2 H), 7.06 (t, $J = 7.5$ Hz, 2 H), 6.86 (s, 2 H), 4.03 (t, $J = 6.9$ Hz, 4 H), 3.23–3.37 (m, 1 H), 3.13 (d, $J = 8.4$ Hz, 1 H), 3.09 (d, $J = 8.4$ Hz, 1 H), 2.98 (d, $J = 6.0$ Hz, 1 H), 2.93 (d, $J = 6.0$ Hz, 1 H), 1.83 (s, 3 H), 1.80–1.70 (m, 4 H), 1.37–1.21 (m, 4 H), 0.90 (t, $J = 7.5$ Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.7, 136.2, 127.7, 126.0, 121.3, 118.8, 118.6, 112.0, 109.3, 54.3, 45.8, 32.3, 31.0, 27.6, 20.1, 13.6; MS *m/z* (%) 186 (100), 428 (M^+, 11.69); HRMS *m/z* (MALDI) calcd for $C_{29}H_{36}N_2ONa^+$(M^+ + Na) 451.2720. Found 451.2735.

4-(1-Allyl-1*H*-indol-3-yl)-3-(1-allyl-1*H*-indol-3-ylmethyl)butan-2-one (4k). The reaction of indole **1k** (100 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (35.7 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 76.1 mg (77%) of **4k**: oil; IR(neat) 1709 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, $J = 8.1$ Hz, 2 H), 7.27 (d, $J = 8.1$ Hz, 2 H), 7.19 (t, $J = 7.5$ Hz, 2 H), 7.08 (t, $J = 7.5$ Hz, 2 H), 6.87 (s, 2 H), 6.01–5.83 (m, 2 H), 5.15 (d, $J = 10.5$ Hz, 2 H), 5.02 (d, $J = 17.1$ Hz, 2 H), 4.64 (d, $J = 5.4$ Hz, 4 H), 3.49–3.38 (m, 1 H), 3.15 (d, $J = 8.7$ Hz, 1 H), 3.10 (d, $J = 8.7$ Hz, 1 H), 2.98 (d, $J = 5.7$ Hz, 1 H), 2.94 (d, $J = 5.7$ Hz, 1 H), 1.84 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.5, 136.3, 133.4, 127.8, 126.0, 121.5, 118.9, 118.8, 116.9, 112.5, 109.5, 54.2, 48.5, 30.9, 27.6; MS *m/z* (%) 170 (100), 396 (M^+, 13.88); HRMS *m/z* (MALDI) calcd for $C_{27}H_{28}N_2ONa^+$(M^+ + Na) 419.2094. Found 419.2111.

4-(1-Benzyl-1*H*-indol-3-yl)-3-(1-benzyl-1*H*-indol-3-ylmethyl)-butan-2-one (4l). The reaction of indole **1l** (129.4 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (35.5 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 96.2 mg (78%) of **4l**: oil; IR(neat) 1708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, $J = 7.8$ Hz, 2 H), 7.27–6.96 (m, 16 H), 6.88 (s, 2 H), 5.19 (s, 4 H), 3.47–3.38 (m, 1 H), 3.15 (d, $J = 8.7$ Hz, 1 H), 3.14 (d, $J = 8.7$ Hz, 1 H), 2.98 (d, $J = 6.0$ Hz, 1 H), 2.93 (d, $J = 6.0$ Hz, 1 H), 1.80 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.4, 137.6, 136.5, 128.6, 127.9, 127.4, 126.6, 126.4, 121.7, 119.0, 118.9, 112.8, 109.7, 54.2, 49.7, 31.1, 27.6; MS *m/z* (%) 91 (100), 496 (M^+, 12.05); HRMS *m/z* (MALDI) calcd for $C_{35}H_{32}N_2ONa^+$(M^+ + Na) 519.2407. Found 519.2430.

4-(5-Benzyloxy-1-methyl-1*H*-indol-3-yl)-3-(5-benzyloxy-1-methyl-1*H*-indol-3-ylmethyl)butan-2-one (4m). The reaction of indole **1g** (148 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (37.7 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 116.8 mg (79%) of **4g**: solid; mp: 112–113 °C (ethyl acetate–hexane); IR(neat) 1708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.42–7.21 (m, 10 H), 7.20 (d, $J = 9.0$ Hz, 2 H), 7.03 (s, 2 H), 6.98 (t, $J = 9.0$ Hz, 2 H), 6.86 (s, 2 H), 5.00 (s, 4 H), 3.77 (s, 6 H), 3.37–3.23 (m, 1 H), 3.16 (d, $J = 8.4$ Hz, 1 H), 3.11 (d, $J = 8.4$ Hz, 1 H), 2.96 (d, $J = 6.0$ Hz, 1 H), 2.92 (d, $J = 6.0$ Hz, 1 H), 1.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.3, 152.7, 137.5, 132.5, 128.3, 127.8,

127.7, 127.6, 112.3, 111.5, 109.9, 102.2, 70.7, 54.0, 32.6, 30.7, 27.3; MS *m/z* (MALDI) 250 (100), 556 (M^+, 52.98); HRMS *m/z* (MALDI) calcd for $C_{37}H_{36}N_2O_3Na^+$(M^+ + Na) 579.2618. Found 579.2622; anal. calcd for $C_{37}H_{36}N_2O_3$: C, 79.83; H, 6.52; N, 5.03%; found: C, 79.72; H, 6.52; N, 4.97%.

4-(6-Benzyloxy-1-methyl-1*H*-indol-3-yl)-3-(6-benzyloxy-1-methyl-1*H*-indol-3-ylmethyl)butan-2-one (4n). The reaction of indole **1n** (144 mg, 0.625 mmol), acetic acid 2-methylene-3-oxo-butyl ester **2** (34.6 mg, 0.25 mmol) and 5 mol% of $Sc(OTf)_3$ (4.8 mg) in 2 mL of CH_2Cl_2 afforded 83.2 mg (61%) of **4n**: solid; mp: 147–148 °C (ethyl acetate–hexane); IR(neat) 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, J = 8.1 Hz, 4 H), 7.42–7.27 (m, 8 H), 6.86 (d, J = 1.8 Hz, 1 H), 6.83 (s, 3 H), 6.72 (s, 2 H), 5.13 (s, 4 H), 3.65 (s, 6 H), 3.43–3.31 (m, 1 H), 3.10 (d, J = 8.4 Hz, 1 H), 3.05 (d, J = 8.4 Hz, 1 H), 2.93 (d, J = 5.7 Hz, 1 H), 2.88 (d, J = 5.7 Hz, 1 H), 1.87 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.5, 155.4, 137.6, 137.4, 128.5, 127.8, 127.5, 126.0, 122.4, 119.5, 112.1, 109.2, 94.3, 70.6, 54.3, 32.6, 30.8, 27.7; MS *m/z* (MALDI) 251 (100), 556 (M^+, 17.45); HRMS *m/z* (MALDI) calcd for $C_{37}H_{36}N_2O_3Na^+$(M^+ + Na) 579.2618. Found 579.2636; anal. calcd for $C_{37}H_{36}N_2O_3$: C, 79.83; H, 6.52; N, 5.03%; found: C, 79.69; H, 6.53; N, 4.90%.

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