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Selective C-3 and C-2 lithiation of 1-(2,2-diethylbutanoyl)indole

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Abstract—1-(2,2-Diethylbutanoyl)indole (**1**) can be lithiated regioselectively at C-3 by treatment with *sec*-BuLi–PMDTA in hexane at −78°C. In contrast, **1** is lithiated at C-2 with *sec*-BuLi–*tert*-BuOK in THF at −78°C. The generated C-3 and C-2 lithio species were trapped with a variety of electrophiles to give the corresponding substitution products.

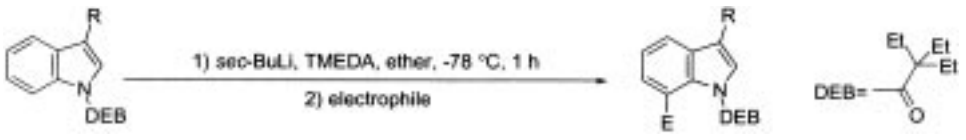
1. Introduction

It has been demonstrated that *N*-protected indoles can be lithiated at the C-2 position exclusively, and the resulting lithio species can be trapped with a variety of electrophiles to produce 2-substituted indoles.[1] The first example of this reaction was reported by Shirley and Roussell in 1953 in the lithiation of *N*-methyl indole.[2] Later in 1973, Sundberg and Russell investigated the utility of removable *N*-protecting groups for directed C-2 lithiation and found that the benzenesulfonyl group was especially useful.[3] After this report, a number of readily removable *N*-protecting groups, such as *tert*-butoxycarbonyl,[4] lithium carboxylate,[5] and *N*-*tert*-butylcarbamoyl groups[6] have been devised. However, the lithiation at other positions of the simple *N*-protected indoles has been scarcely studied.[7]

Recently, we have investigated the regioselective lithiation of indoles protected by conformationally restricted bulky acyl groups, and discovered that the 2,2-diethylbutanoyl (DEB) group can promote unprecedented C-7 lithiation under kinetically controlled conditions [*sec*-BuLi (1.5 eq), TMEDA (2.3 eq), ether, −78°C, 1 h] (Scheme 1).[8] This unusual lithiation has been demonstrated to be practically useful for the synthesis of 3,7-disubstituted indoles which are not readily available by conventional synthetic methods. During the course of this study, we observed that partial lithiation at the C-3 position of 1-(DEB)indole (**1**) occurred in some cases.[8] We thought this observation was also quite interesting because direct C-3 lithiation of *N*-protected indoles was very rare.[9] Therefore, we decided to carry out further experiments to establish the conditions to permit regioselective C-3 lithiation of the indole **1**.

2. Results and discussion

Following the procedure of a previous study,[8] regioselectivities of the lithiation of **1** were estimated by deuteration experiments. The results are summarized in Table 1. In the beginning, we speculated that the lithiation at the C-3 position might occur preferentially when coordinatively saturated lithiating agents were used, because a competitive C-7 lithiation, which must occur *via* initial coordination of DEB-carbonyl to a lithiating agent,[8] should be suppressed. Consequently, we first examined the effects of multidentate ligands on the regioselectivity. When **1** was treated with 1.5 eq of *sec*-BuLi in ether in the presence of 2.3 eq of a tridentate ligand, *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDTA), at −78°C for 1 h followed by quenching with MeOD, the substrate was recovered in 95% yield after chromatographic purification (entry 1). The ^{1}H NMR analysis of the recovered substrate indicated 56% deuterium incorporation at C-3 accompanied with 8% and 9% incorporation at C-7 and C-2, respectively. Thus, it was found that the regioselectivity of the lithiation of **1** changed dramatically from C-7 to C-3 only by using PMDTA in place of TMEDA.



Scheme 1.

Keywords: indoles; lithiation; regioselection; substitution.

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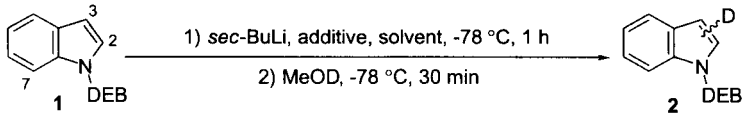
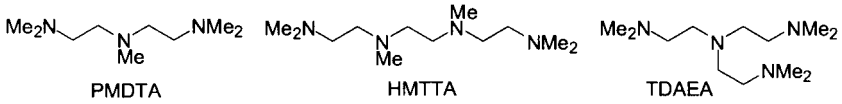
Table 1. Lithiation–deuteration of 1-(DEB)indole (**1**)



Entry	Base (eq)	Additive	Solvent	**2**+**1** (%)[a]	Deuterium content (%)[b]			
					C-7	C-2	C-3	total
1	1.5	PMDTA (2.3)	ether	95	8	9	56	73
2	1.5	HMTTA (2.3)	ether	93	21	15	22	58
3	1.5	TDAEA (2.3)	ether	95	0	0	10	10
4	3.0	TDAEA (4.5)	ether	95	2	4	20	26
5	1.5	PMDTA (2.3)	THF	90	4	8	54	66
6	1.5	PMDTA (2.3)	toluene	89	4	7	30	41
7	1.5	PMDTA (2.3)	hexane	92	2	2	41	45
8	2.0	PMDTA (3.0)	hexane	90	3	6	53	62
9	1.5	*tert*-BuOK (2.3)	THF	85	1	97	2	100

[a] Isolated yield.
[b] Deuterium content was estimated by ^{1}H NMR analysis.



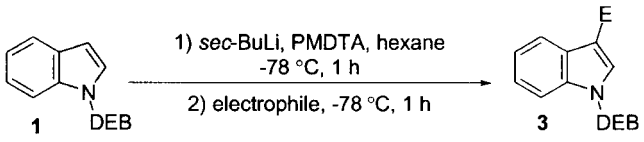
Next, the effects of tetradentate ligands such as 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTTA) and tris(*N,N*-dimethyl-2-aminoethyl)amine (TDAEA) were tested. In an experiment using HMTTA, the lithiation proceeded non-regioselectively at C-7, C-2, and C-3 positions (entry 2). On the other hand, TDAEA promoted regiospecific C-3 lithiation, although the level of deuterium content was very low (entry 3). Even if 3.0 eq of *sec*-BuLi was used, deuterium incorporation was only minimally improved (entry 4). Thus we judged PMDTA was the ligand of choice to effect regioselective C-3 lithiation at a reasonable reaction rate.

The solvent effect was also examined (entries 5–7). Within four kinds of solvents tested, hexane was found to be the best with respect to C-3 selectivity, although total deuterium incorporation was somewhat low (45%) (entry 7). When 2.0 eq of *sec*-BuLi was used, deuterium incorporation was improved to 62% without significant loss of the regioselectivity (entry 8). Thus, we decided to use these conditions [*sec*-BuLi (2.0 eq), PMDTA (3.0 eq), hexane, −78°C, 1 h] for further C-3 functionalization reactions.[10]

Finally, we tested a superbasic system, *sec*-BuLi–*tert*-BuOK, because it has been reported that *tert*-BuOK is an extremely powerful ligand showing similar effects to those of PMDTA in regioselective lithiations of some benzene derivatives.[11] In this case, however, the lithiation occurred regiospecifically at C-2 in excellent yield (entry 9). Although this was an unexpected result, the regiochemical control of the lithiation of the same substrate **1** by simply changing the reaction conditions was quite interesting and synthetically useful.

Having established the conditions for selective C-3 and C-2 lithiation of **1** *via* deuteration experiments, we next carried out functionalization at these positions. Thus **1** was lithiated with *sec*-BuLi (2.0 eq)– PMDTA (3.0 eq) in hexane at −78°C for 1 h, and the resulting lithio species was treated with an appropriate electrophile at the same temperature for 1 h. In general, pure 3-substituted 1-(DEB)indoles **3** were isolated after chromatography or simple crystallization in modest yields (Table 2). Unfortunately, however, in the reactions with hexachloroethane and 1,2-dibromo-1,1,2,2-tetrafluoroethane, the corresponding C-3 and C-2

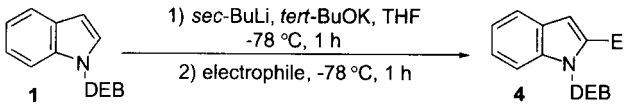
Table 2. Selective C-3 functionalization of 1-(DEB)indole (**1**)



Entry	Electrophile	Product	E	Yield (%)[a]
1	DMF	**3a**	CHO	49
2	CO_2	**3b**	CO_2H	51
3	$ClCO_2Et$	**3c**	CO_2Et	34
4	Cl_3CCCl_3	**3d**	Cl	47[b]
5	BrF_2CCBrF_2	**3e**	Br	59[c]
6	TMSCl	**3f**	TMS	58

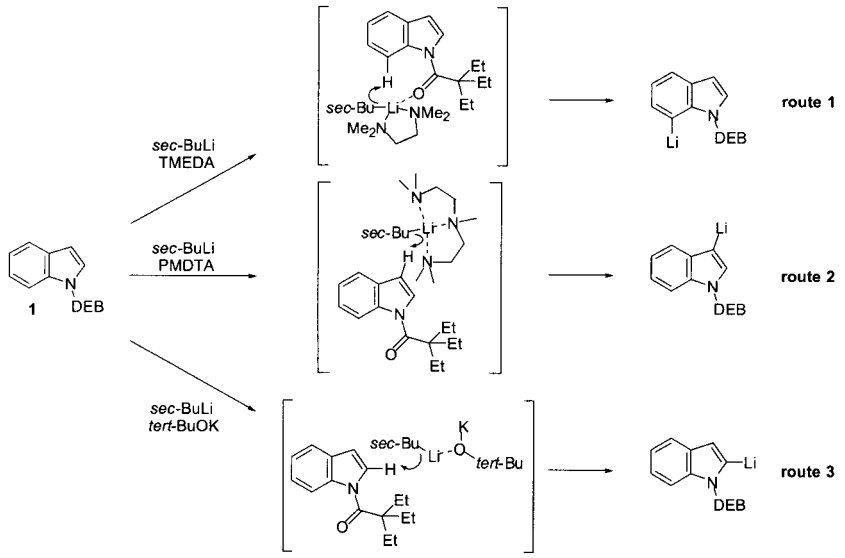
[a] Isolated yield.
[b] A 96:4 mixture of C-3 and C-2 products.
[c] An 88:12 mixture of C-3 and C-2 products.

Table 3. Selective C-2 functionalization of 1-(DEB)indole (**1**)



Entry	Electrophile	Product	E	Yield (%)[a]
1	MeI	**4a**	Me	93
2	CO_2	**4b**	CO_2H	56
3	$ClCO_2Et$	**4c**	CO_2Et	90
4	Cl_3CCCl_3	**4d**	Cl	82
5	BrF_2CCBrF_2	**4e**	Br	59
6	TMSCl	**4f**	TMS	89
7	PhSSPh	**4g**	SPh	96

[a] Isolated yield.



Scheme 2.

halogenated products were isolated as inseparable mixtures (entries 4 and 5).

Next, C-2 functionalization was carried out by the metalation of **1** with *sec*-BuLi (1.5 eq)– *tert*-BuOK (2.3 eq) in THF at −78°C for 1 h, followed by the reactions with electrophiles. As shown in Table 3, the expected products **4a–g** were obtained in good to excellent yields.

Finally, we would like to propose a plausible mechanistic explanation for the regioselectivities of the lithiation of 1-(DEB)indole (**1**) (Scheme 2). As we have shown in a previous paper,[8] a coordinatively unsaturated *sec*-BuLi–TMEDA complex binds to the conformationally fixed DEB-carbonyl and then deprotonates the nearest C-7 proton (route 1). This is an example of the kinetically controlled regioselective lithiation *via* complex-induced proximity effect (CIPE).[12] In the reaction with coordinatively saturated *sec*-BuLi–PMDTA complex,[13] CIPE is no longer significant and the lithiation occurs, in general, at the thermodynamically most acidic position selectively.[11] In the case of 1-(DEB)indole, however, the most acidic C-2 proton is shielded by a bulky alkyl substituent of the 1-DEB group. Therefore, a bulky *sec*-BuLi–PMDTA complex may not be able to access the C-2 proton and be obliged to react with the next acidic C-3 proton (route 2). On the other hand, a relatively small super base (*sec*-BuLi–*tert*-BuOK)[14] can reach the C-2 proton to generate the C-2 lithio species (route 3).

3. Conclusion

We have demonstrated that direct C-7, C-3, and C-2 lithiation of the indole ring can be achieved selectively by using 1-(DEB)indole (**1**) as a common substrate. These results are especially interesting, because the regioselectivities are controlled essentially only by the effects of the ligands employed in the lithiation reactions.

4. Experimental

Melting points were determined with a Yanagimoto micro melting points apparatus and are uncorrected. IR spectra were obtained with a Perkin–Elmer System 2000 instrument. ^{1}H NMR spectra were recorded at 200 MHz on a Varian Gemini-200 instrument or at 400 MHz on a JEOL JMS GX-400 instrument. All signals were expressed as ppm down field from tetramethylsilane used as an internal standard (δ-value in $CDCl_3$). High resolution mass spectra were recorded on a JEOL JMS-DX303 instrument. Elemental analysis was performed at the microanalytical laboratory in Nagasaki University. Column chromatography was conducted on Silica Gel 60, 70–230 mesh ASTM (E. Merck). Flash chromatography was conducted on Silica Gel 60, 230–400 mesh ASTM (E. Merck). Solvents were dried (Na-benzophenone ketyl for ether and THF, CaH_2 for toluene and hexane) and distilled shortly before use. Reactions were carried out under an atmosphere of argon if necessary. *sec*-BuLi was purchased from Kanto Chemical Co., Inc and used after titration with 2,5-dimethoxybenzyl alcohol. 1-(DEB)indole (**1**) was synthesized according to the literature procedure.[8]

4.1. Lithiation–deuteration of 1-(DEB)indole (1)

1-(DEB)indole (**1**) (97 mg, 0.40 mmol) and an appropriate additive were added to a solvent (5 mL) and the solution was cooled to −78°C. *sec*-BuLi was added dropwise to the solution over 5 min at the same temperature. After being stirred for 1 h, MeOD (72 μL, 1.8 mmol) was added to the mixture and stirred for an additional 30 min. The mixture was quenched with saturated aqueous NH_4Cl at −78°C and the whole was warmed to room temperature. The mixture was extracted with ether and the extract was washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, hexane–ethyl acetate=50:1 to 10:1) to give the mixture of deuterated products **2** and unreacted substrate **1**. The deuterium content was determined by

integration of the signals H-7, H-2, and H-3 protons of the ^{1}H NMR spectra (200 MHz). The signals at δ 8.51, δ 7.78, and δ 6.61 were assigned to be H-7, H-2, and H-3 protons, respectively.

4.2. Selective C-3 functionalization of 1-(DEB)indole (1). General procedure

To a solution of **1** (97 mg, 0.40 mmol) in ether (5 mL) was added PMDTA (250 μL, 1.2 mmol) and the mixture was cooled to −78°C. *sec*-BuLi (800 μL, 1.0 M in hexane–cyclohexane, 0.80 mmol) was added dropwise to the solution over 5 min at the same temperature. After being stirred for 1 h, an appropriate electrophile (1.6 mmol) was added as a neat liquid or as a hexane solution, and the mixture was stirred for an additional 1 h. The mixture was quenched with saturated aqueous NH_4Cl and the whole was warmed to room temperature. The mixture was extracted with ether and the extract was washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography over SiO_2, (hexane–ethyl acetate=50:1 to 10:1, unless otherwise mentioned) to give the corresponding 3-substituted product **3**.

4.2.1. 1-(2,2-Diethylbutanoyl)indole-3-carboxaldehyde (3a). This compound was obtained as colorless oil (53 mg, 49%). The spectroscopic data of this product were completely identical with those of an authentic sample.[8]

4.2.2. 1-(2,2-Diethylbutanoyl)indole-3-carboxylic acid (3b). This compound was prepared by the reaction with an excess amount of dry ice and was purified successively by column chromatography over SiO_2 [hexane–ethyl acetate =10:1 to ethyl acetate–*n*–propanol–water=4:1:2 (upper phase)] and recrystallization (ether–hexane) to give **3b** (59 mg, 51%) as colorless prisms, mp 146.0–148.5°C; IR (KBr) 2969, 1714, 1677, 1553, 1453, 1300, 1267, 1222, 1194, 1148, 1131, 1019, 822, 759 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.87 (t, J=7.3 Hz, 9H), 1.94 (q, J=7.3 Hz, 6H), 7.38–7.45 (m, 2H), 8.20–8.24 (m, 1H), 8.42–8.46 (m, 1H), 8.56 (s, 1H); MS *m/z* 287 (M^+); HRMS calcd for $C_{17}H_{21}NO_3$ 287.1521, found 287.1513.

4.2.3. Ethyl 1-(2,2-Diethylbutanoyl)indole-3-carboxylate (3c). This compound was obtained as colorless solid after column chromatography (43 mg, 34%); mp 76.0–78.5°C; IR (KBr) 2967, 1702, 1545, 1453, 1384, 1349, 1310, 1249, 1195, 1131, 1102, 1044, 1007, 821, 760, 705 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.85 (t, J=7.3 Hz, 9H), 1.46 (t, J=7.3 Hz, 3H), 1.92 (q, J=7.3 Hz, 6H), 4.44 (q, J=7.3 Hz, 2H), 7.34–7.42 (m, 2H), 8.13–8.18 (m, 1H), 8.42–8.45 (m, 1H), 8.44 (s, 1H); MS *m/z* 315 (M^+); HRMS calcd for $C_{19}H_{25}NO_3$ 315.1834, found 315.1821.

4.2.4. 3-Choloro-1-(2,2-diethylbutanoyl)indole (3d). This compound was isolated as a 96:4 mixture of **3d** and **4d** as colorless oil (53 mg, 47%); IR (neat) 3185, 2971, 2881, 1700, 1446, 1384, 1342, 1288, 1204, 1150, 1019, 993, 824, 749, 712 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.84 (t, J=7.3 Hz, 9H), 1.88 (q, J=7.3 Hz, 6H), 7.35 (dt, J=1.1 and 7.3 Hz, 1H), 7.41 (ddd, J=1.5, 7.3 and 8.4 Hz, 1H), 7.59 (dd, J=1.5 and 7.3 Hz, 1H), 7.78 (s, 1H), 8.51 (d, J=8.4 Hz, 1H); MS *m/z* 277 (M^+); HRMS calcd for $C_{16}H_{20}ClNO$ 277.1233, found 277.1228.

4.2.5. 3-Bromo-1-(2,2-diethylbutanoyl)indole (3e). This compound was isolated as an 88:12 mixture of **3e** and **4e** (75 mg, 59%); IR (neat) 3182, 3052, 2970, 2881, 1698, 1544, 1470, 1445, 1384, 1356, 1342, 1285, 1204, 1150, 1105, 1019, 972, 824, 749 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.84 (t, J=7.3 Hz, 9H), 1.89 (q, J=7.3 Hz, 6H), 7.35 (dt, J=1.1 and 7.3 Hz, 1H), 7.40 (ddd, J=1.5, 7.3 and 8.1 Hz, 1H), 7.54 (dd, J=1.5 and 7.3 Hz, 1H), 7.83 (s, 1H), 8.49 (d, J=8.1 Hz, 1H); MS *m/z* 321 (M^+); HRMS calcd for $C_{16}H_{20}BrNO$ 321.0728, found 321.0733.

4.2.6. 1-(2,2-Diethylbutanoyl)-3-trimethylsilylindole (3f). This compound was obtained as colorless solid after column chromatography (74 mg, 58%), mp 50.0–56.0°C; IR (KBr): 2968, 1697, 1601, 1520, 1470, 1449, 1346, 1305, 1251, 1207, 1151, 987, 927, 840, 768, 749 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.38 (s, 9H), 0.84 (t, J=7.3 Hz, 9H), 1.89 (q, J=7.3 Hz, 6H), 7.26 (dt, J=1.1 and 7.3 Hz, 1H), 7.33 (ddd, J=1.5, 7.3 and 8.1 Hz, 1H), 7.61 (dd, J=1.1 and 7.3 Hz, 1H), 7.70 (s, 1H), 8.49 (d, J=8.1 Hz, 1H); MS *m/z* 315 (M^+); HRMS calcd for $C_{19}H_{29}NOSi$ 315.2018, found 315.2016.

4.3. Selective C-2 functionalization of 1-(DEB)indole (1). General procedure

To a solution of **1** (97 mg, 0.40 mmol) in THF (5 mL) was added a solution of *tert*-BuOK (890 μL, 1.0 M in THF, 0.89 mmol) and the mixture was cooled to −78°C. *sec*-BuLi (760 μL, 0.80 M in hexane–cyclohexane, 0.60 mmol) was added dropwise to the solution over 5 min at the same temperature. After being stirred for 1 h, an appropriate electrophile (1.6 mmol) was added as a neat liquid or as a THF solution, and the mixture was stirred for an additional 1 h. The mixture was quenched with saturated aqueous NH_4Cl and the whole was warmed to room temperature. The mixture was extracted with ether and the extract was washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography over SiO_2, (hexane–ethyl acetate=50:1, unless otherwise mentioned) to give corresponding product **4**.

4.3.1. 1-(2,2-Diethylbutanoyl)-2-methylindole (4a). This compound was obtained as colorless oil (97 mg, 93%); IR (neat) 3053, 2972, 2882, 1698, 1564, 1454, 1384, 1286, 1198, 1158, 1138, 1107, 1020, 1008, 960, 840, 787, 741 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.86 (t, J=7.3 Hz, 9H), 1.83 (q, J=7.3 Hz, 6H), 2.41 (d, J=0.7 Hz, 3H), 6.31 (t, J=0.7 Hz, 1H), 7.09–7.16 (m, 2H), 7.36–7.40 (m, 1H), 7.45–7.49 (m, 1H). MS *m/z* 257 (M^+); HRMS calcd for $C_{17}H_{23}NO$ 257.1780, found 257.1767.

4.3.2. 1-(2,2-Diethylbutanoyl)indole-2-carboxylic acid (4b). This compound was prepared by the reaction with an excess amount of dry ice and was purified successively by column chromatography (SiO_2, CH_2Cl_2) and recrystallization (CH_2Cl_2–hexane) to give **4b** (64 mg, 56%) as colorless needles, mp 118.5–120.0°C; IR (KBr) 3391, 3046, 2970, 2946, 2880, 1782, 1716, 1621, 1530, 1460, 1342, 1312,

1226, 1168, 1144, 1061, 1031, 950, 820, 747, 735 cm^{-1}; ^1H NMR (400 MHz) δ 0.94 (t, J=7.7 Hz, 9H), 1.76 (q, J=7.7 Hz, 6H), 7.18 (ddd, J=1.1, 7.0 and 8.1 Hz, 1H), 7.24 (dd, J=1.1 and 2.2 Hz, 1H), 7.38 (ddd, J=1.1, 7.0 and 8.1 Hz, 1H), 7.45 (dq, J=1.1 and 8.1 Hz, 1H), 7.71 (dd, J=1.1 and 8.1 Hz, 1H), 9.00 (br s, 1H). Anal. calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 71.21; H, 7.32; N, 4.84.

4.3.3. Ethyl 1-(2,2-diethylbutanoyl)indole-2-carboxylate (4c). This compound was obtained as colorless oil (113 mg, 90%); IR (neat) 3053, 2977, 2942, 2884, 1713, 1612, 1531, 1444, 1382, 1296, 1245, 1208, 1154, 1102, 1024, 970, 831, 766, 745 cm^{-1}; ^1H NMR (400 MHz) δ 0.82 (t, J=7.3 Hz, 9H), 1.39 (t, J=7.3 Hz, 3H), 1.70 (q, J=7.3 Hz, 6H), 4.37 (q, J=7.3 Hz, 2H), 7.18 (ddd, J=1.1, 7.0 and 8.1 Hz, 1H), 7.27 (d, J=0.7 Hz, 1H), 7.33 (ddd, J=1.1, 7.0 and 8.4 Hz, 1H), 7.39 (dq, J=1.1 and 8.4 Hz, 1H), 7.65 (dt, J=1.1 and 8.1 Hz, 1H); MS *m/z* 315 (M^+); HRMS calcd for $C_{19}H_{25}NO_3$ 315.1834, found 315.1842.

4.3.4. 2-Choloro-1-(2,2-diethylbutanoyl)indole (4d). This compound was obtained as colorless oil (90 mg, 82%); IR (neat) 3127, 3065, 2974, 2943, 2883, 1731, 1714, 1522, 1445, 1384, 1268, 1194, 1154, 1098, 1073, 1017, 956, 844, 819, 784, 743 cm^{-1}; ^1H NMR (400 MHz) δ 0.88 (t, J=7.3 Hz, 9H), 1.84 (q, J=7.3 Hz, 6H), 6.51 (d, J=0.7 Hz, 1H), 7.15 (dt, J=1.1 and 7.3 Hz, 1H), 7.20 (ddd, J=1.1, 7.3 and 8.4 Hz, 1H), 7.32 (dd, J=1.1 and 8.4 Hz, 1H), 7.49 (dq, J=0.7 and 7.3 Hz, 1H); MS *m/z* 277 (M^+); HRMS calcd for $C_{16}H_{20}ClNO$ 277.1233, found 277.1248.

4.3.5. 2-Bromo-1-(2,2-diethylbutanoyl)indole (4e). This compound was obtained as colorless oil (75.3 mg, 59%); IR (neat) 3125, 3066, 2974, 2942, 2882, 1730, 1512, 1443, 1384, 1268, 1196, 1154, 1142, 1094, 1067, 1016, 948, 840, 785, 742 cm^{-1}; ^1H NMR (400 MHz): δ 0.89 (t, J=7.3 Hz, 9H), 1.84 (q, J=7.3 Hz, 6H), 6.65 (d, J=0.7 Hz, 1H), 7.14 (dt, J=1.1 and 7.3 Hz, 1H), 7.18 (ddd, J=1.1, 7.3 and 8.4 Hz, 1H), 7.31 (d, J=8.4 Hz, 1H), 7.50 (dq, J=0.7 and 7.3 Hz, 1H); MS *m/z* 321 (M^+); HRMS calcd for $C_{16}H_{20}BrNO$ 321.0728, found 321.0714.

4.3.6. 1-(2,2-Diethylbutanoyl)-2-trimethylsilylindole (4f). This compound was obtained as colorless solid after column chromatography (112 mg, 89%), mp 65.0–66.0°C; IR (KBr) 3068, 2971, 2881, 1681, 1512, 1469, 1441, 1381, 1351, 1295, 1272, 1244, 1200, 1155, 1112, 1097, 964, 908, 843, 763, 739 cm^{-1}; ^1H NMR (400 MHz) δ 0.31 (s, 9H), 0.80 (t, J=7.3 Hz, 9H), 2.00 (q, J=7.3 Hz, 6H), 6.89 (s, 1H), 7.17 (t, J=7.3 Hz, 1H), 7.25 (ddd, J=1.5, 7.0 and 8.4 Hz, 1H), 7.55 (d, J=7.0 Hz, 1H), 7.79 (d, J=8.4 Hz, 1H); MS *m/z* 315 (M^+); HRMS calcd for $C_{19}H_{29}NOSi$ 315.2018, found 315.2025.

4.3.7. 1-(2,2-Diethylbutanoyl)-2-(phenylthio)indole (4g). This compound was obtained as colorless oil (133 mg, 96%); IR (neat) 3062, 2974, 2941, 2882, 1729, 1713, 1583, 1476, 1437, 1384, 1272, 1197, 1155, 1104, 1023, 958, 844, 816, 739 cm^{-1}; ^1H NMR (400 MHz) δ 0.81 (t, J=7.3 Hz, 9H), 1.84 (q, J=7.3 Hz, 6H), 6.84 (d, J=0.7 Hz, 1H), 7.07–7.28 (m, 7H), 7.37 (dd, J=0.7 and 8.4 Hz, 1H), 7.56 (d, J=8.1 Hz, 1H). MS *m/z* 351 (M^+); HRMS calcd for $C_{22}H_{25}NOS$ 351.1657, found 351.1650.

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