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LITHIATION OF 1-ALKOXYINDOLE DERIVATIVES[1,#]

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Abstract – Lithiation of 1-alkoxyindoles, 3-dimethylaminomethyl- and 3-dimethylaminoethyl-1-methoxyindole occurred regioselectively at the 2-position. The introduction of a sterically bulky group into the 2-position of 3-dimethylaminomethyl-1-methoxyindoles directed the lithiation to the 4-position.

INTRODUCTION

We have opened the door to the chemistry of 1-hydroxyindoles and succeeded in the large-scale preparation of 1-methoxyindole[3] (**2a**) from 2,3-dihydroindole (**1**), a cheap and industrial raw material. We have also disclosed that 1-methoxy group function as a directing group for the regioselective lithiation at the 2-position,[4,5] and various 2-substituted indoles became readily accessible.[6,7]

For the lithiation at the 2-position of indole, *t*-BuLi has often been employed but because of its intrinsic pyrophoric and unstable nature its handling requires low temperature (–80 °C, dry ice-acetone) and well

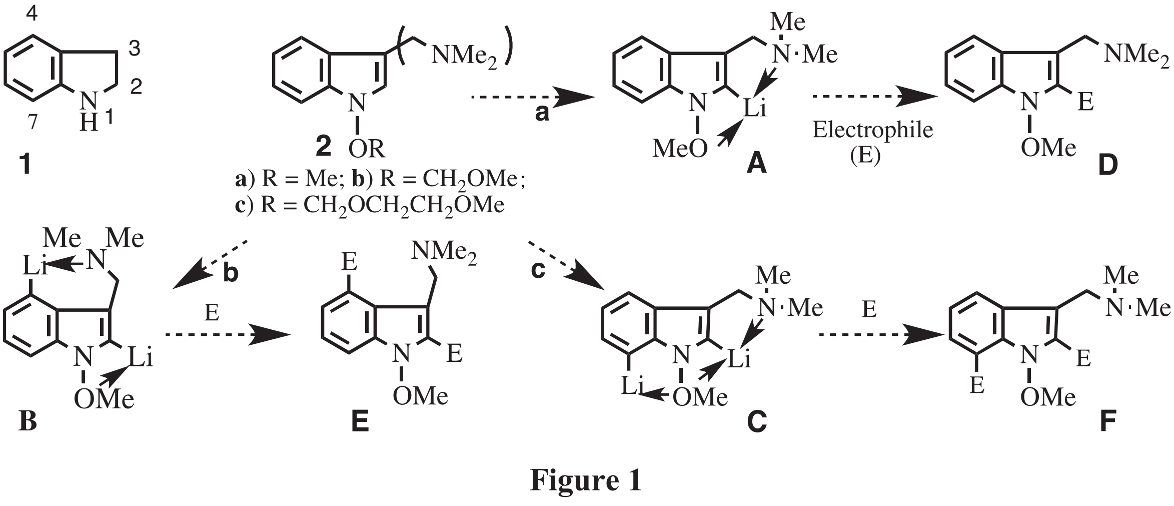


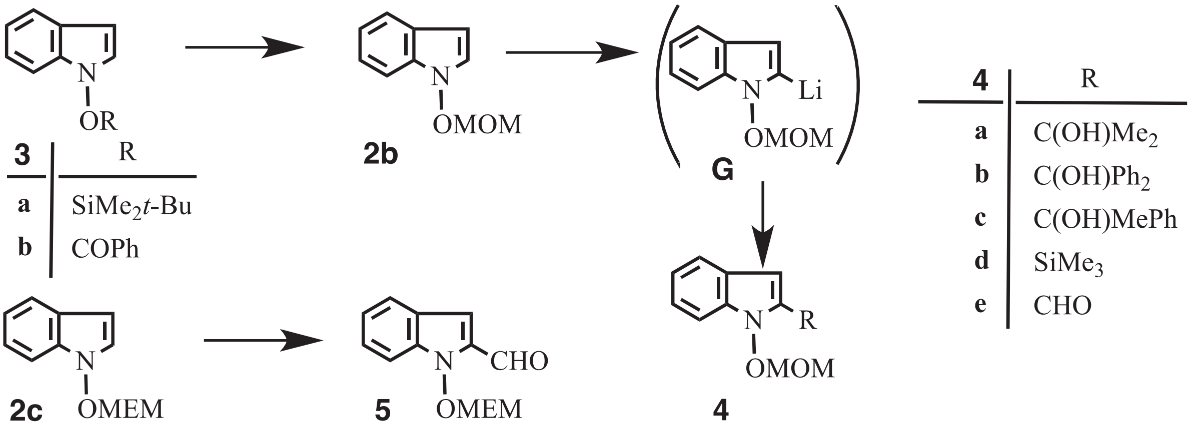
Figure 1

Dedicated to the 70th birthday of Professor Dr. Kiyoshi Tomioka

trained technique. If the milder and safer lithium reagent, such as *n*-BuLi, was applicable at the temperature as close to rt as possible, the lithiation method would be more desirable and useful for the large-scale preparation of variety of substituted indoles. To achieve the idea, one possibility is to change the 1-methoxy group to 1-methoxymethoxy (MOM, **2b**, Figure 1) or 1-(2-methoxy)ethoxymethoxy (MEM, **2c**) group which could stabilize the generated 2-lithio species by coordination. The other possibility to realize both the use of *n*-BuLi and raising the reaction temperature to rt would be an introduction of additional directing group, reaction path **a** in Figure 1 (for example, dimethylaminomethyl group), to the 3-position to make 2-lithio species (**A**) more stable and reactive to the subsequent reaction with electrophiles to give 2-substituted indoles (**D**). The dimethylaminomethyl group at the 3-position would have another possibility to realize double lithiation at either the 2- and 4-positions (**B**) or 2- and 7-positions (**C**) following the respective reaction path **b** and **c**. Subsequent treatment with electrophiles would provide 2,4-disubstituted (**E**) or 2,7-disubstituted indoles (**F**). According to the above expectations, we have examined lithiation of 1-alkoxyindoles. This report is a full report of previous communications[6,7] with many new results.

I. Preparation of 1-MOM- and 1-MEM-indole and their lithiation

We have already reported a direct synthetic method for 1-(*t*-butyldimethylsilyloxy)indole (**3a**) and 1-benzoyloxyindole (**3b**) from **1** (Scheme 1). From these compounds, **3a** and **3b**, we have now found a convenient synthetic method for 1-methoxymethoxy- (1-MOM-indole, **2b**) and 1-(2-methoxy)-ethoxymethoxyindole (1-MEM-indole, **2c**) in high yields.



4	R
a	$C(OH)Me_2$
b	$C(OH)Ph_2$
c	C(OH)MePh
d	$SiMe_3$
e	CHO

Scheme 1

Thus, treatment of **3a** with fluoride followed by reaction with methoxymethyl (MOM) chloride and 2-(methoxy)ethoxymethyl (MEM) chloride afforded **2b** and **2c** in 98 and 98% yields, respectively. On the other hand, treatments of **3b** with KO*t*Bu in THF and subsequent reaction with MOM-chloride and MEM-chloride gave **2b** and **2c** in 97% and 100% yields, respectively.

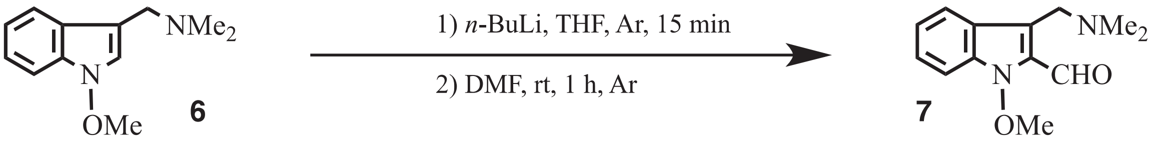
With **2b** and **2c** in hand, we examined their lithiation and found as expected that the presence of MOM group at the 1-position make it possible to raise the lithiation temperature to 0 °C with *n*-BuLi. The resulted lithium species reacted with such electrophiles as acetone, benzophenone, acetophenone, trimethylsilyl chloride, and DMF at rt to provide **4a**, **4b**, **4c**, **4d**, and **4e** in 89, 99, 88, 91, and 96% yields, respectively. In the case of **2c** lithiation with *n*-BuLi were successfully carried out at rt (12 °C). Subsequent reaction with DMF afforded a single spot on tlc, but the product was found to be very unstable and decomposed during column-chromatography on SiO_2, nevertheless 1-[(2-methoxyethoxy)methoxy]indole-2-carbaldehyde (**5**) was isolated in 17% yield.

II. Lithiation of 3-dimethylaminomethyl-1-methoxyindole and its reaction with electrophiles

The results of typical lithiation of 3-dimethylaminomethyl-1-methoxyindole (**6**) and its reaction with electrophiles are summarized in Table 1. Lithiation with both *t*-BuLi and *n*-BuLi and subsequent trap of the lithiated species (**A**, Figure 1) with DMF afforded almost the same yield of **7** (more than 87%) as shown in Entries 1–4, respectively. However, the respective reaction temperatures needed for *t*-BuLi and *n*-BuLi were different: –80 °C (dry ice-acetone) *vs* –18 °C (ice-NaCl). Using *n*-BuLi even at –18 °C, the yield of **7** achieved 96% (Entry 3).

Although various reaction conditions were carried out aiming at double lithiation as imagined in **B** and **C** (Figure 1), expected products were not observed at all.

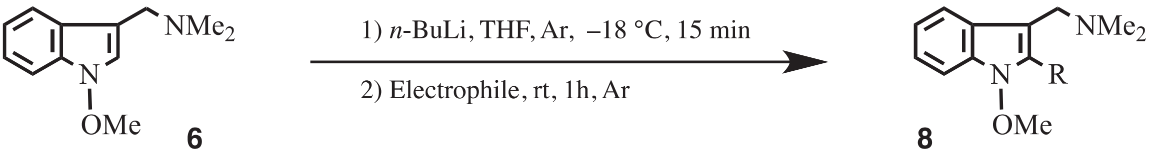
Table 1. Regioselective lithiation at the 2-position of 1-methoxygramine (**6**)



		Reaction	Conditions		Yield	(%) of
Entry	Alkyl Lithium	(mol eq.)	Temp. (°C)	Time (min)	**7**	Recovery
1	*t*-BuLi	(2.2)	–80	15	92	4
2	〃	〃	–18 (ice-NaCl)	15	92	5
3	*n*-BuLi	(2.2)	–18	15	96	2
4	〃	(1.1)	–18	15	87	8
5	〃	〃	0	15	36	39
6	〃	〃	0	2	24	53

Next, we attempted to establish convenient synthetic method for 2-substituted 1-methoxygramines (**8**, Table 2). Employing *n*-BuLi as a lithiation reagent at –18 °C (ice-NaCl), such electrophiles as trimethylsilyl chloride, diphenyl disulfide, dimethyl disulfide, di-*sec*-butyl disulfide, and trimethylstannyl chloride trapped the lithiated species (**A**, Figure 1) to afford **8a**, **8b**, **8c**, **8d**, and **8e** in 97, 99, 95, 97, and 88% yields, respectively and the results are shown in Table 2.

Table 2. Introduction of electrophile to the 2-position of 1-methoxygramine (**6**)



Entry	Electrophile	Product	R	Yield (%)
1	TMSCl	**8a**	TMS	97
2	Ph_2S_2	**8b**	SPh	99
3	Me_2S_2	**8c**	SMe	95
4	*sec* -Bu_2S_2	**8d**	S*sec*-Bu	97
5	Me_3SnCl	**8e**	$SnMe_3$	88

Thus, 2-substituted gramines are now readily accessible. Palladium catalyzed Stille type reaction of **8e** with iodobenzene did not produce coupling product at all.

III. Regio selective lithiation at the 4-position of 8a-d

Having sterically hindered group at the 2-position, we expected the lithiation of 1-methoxygramines (**8a-d**) would occur at the 4-position. First, using 1-methoxy-2-trimethylsilylgramine (**8a**) as a starting material, lithiation was carried out with *t*-BuLi in THF at –78 °C (dry ice-acetone), followed by the reaction with DMF. Changing reaction conditions, the reaction was extensively studied, and found that 4-lithiation did not occur as long as THF was used (Table 3, Entry 1).

The Results of nOe of **9**

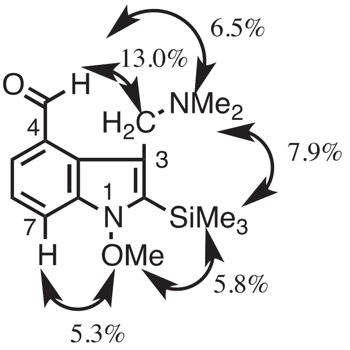
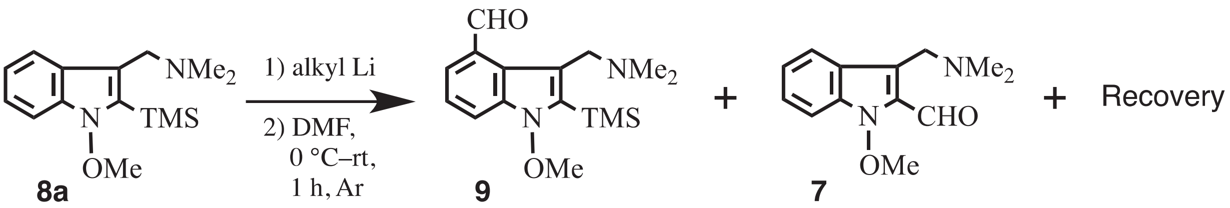


Figure 2

It is interesting to note that when the solvent was changed to ether instead of THF, the desired 4-formylindole product (**9**) generated in 23% yield (Entry 2). Raising the lithiation temperature from –78 °C to rt, the yield of **9** gradually improved (Entries 2–5), and under ether reflux conditions, the yield of **9** reached to the maximum (70%, Entry 6) together with 14% yield of **7**.

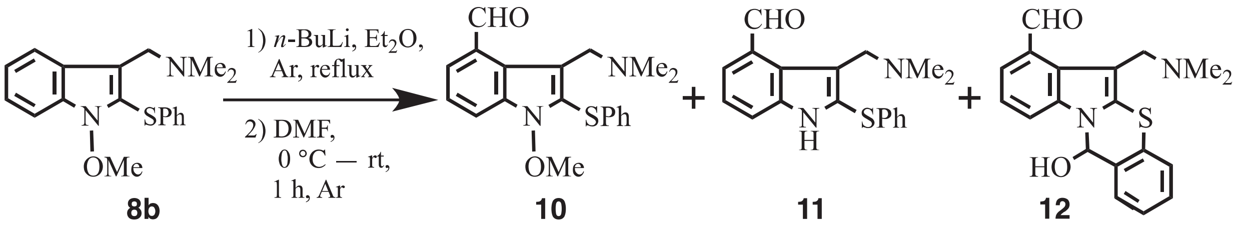
The structure of **9** was proved by observing nOe. Among the four adjacent substituents, formyl proton, *N,N*-dimethylamino, trimethylsilyl, and methoxy groups, significant nOe was observed and the results are shown in Figure 2.

Table 3. Regioselective lithiation at the 4-position of 2-trimethylsilylindole (**8a**)

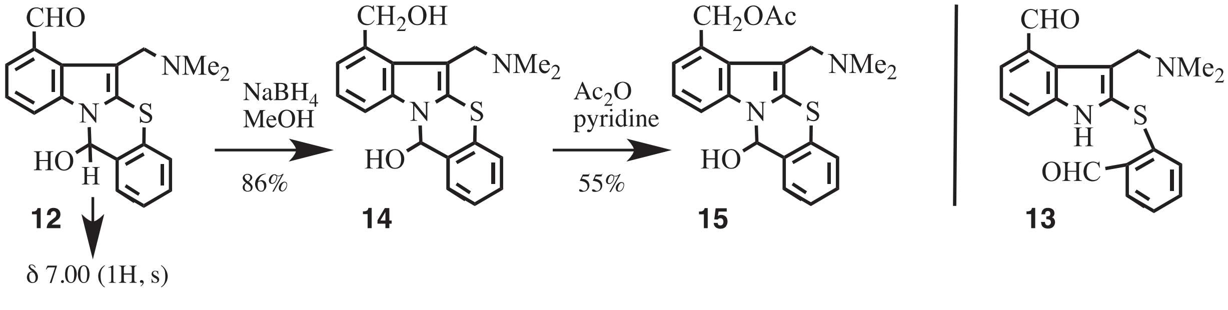


Entry	Alkyl Lithium (mol eq.)	Solvent	Reaction Conditions Temp. (°C)	Time (min)	Yield (%) of 9	7	Recovery
1	*t*-BuLi (1.1)	THF	–78	15	0	0	99
2	" (3.1)	Et_2O	–80 then 0	15 then 60	23	0	11
3	*n*-BuLi (3.1)	"	–18 then 0	15 then 60	11	0	79
4	"	"	rt	75	34	8	33
5	"	"	reflux	60	60	14	5
6	"	"	reflux	90	70	14	7

Table 4. Lithiation of 1-methoxygramine (**8b**) having 2-phenylthio group



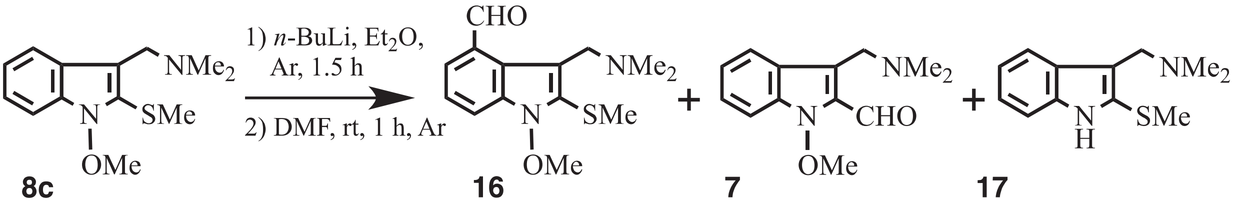
Entry	Reaction Conditions *n*-BuLi (mol eq.)	Time (h)	Yield (%) of 10	11	12	Recovery
1	5.0	3.5	17	7	33	0
2	5.0	2.5	25	15	30	0
3	3.1	1.5	34	15	24	10
4	2.0	1.5	45	10	0	6
5	1.7	1.5	67	6	0	7
6	1.0	1.5	41	0	0	19



Scheme 2

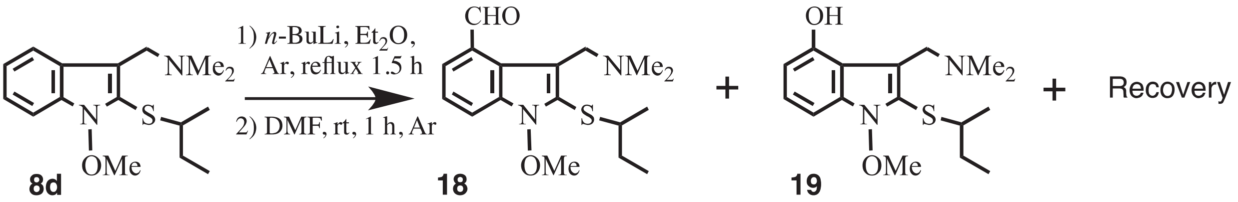
Secondly, using 1-methoxy-2-phenylthiogramine (**8b**), lithiation was carried out with *n*-BuLi in refluxing ether, followed by the reaction with DMF, and the results are summarized in Table 4. Under every reaction conditions, 4-formylindoles (**10, 11,** and **12**) were obtained in varied yields (Entries 1–6) together with small amount of 6-(dimethylaminomethyl)-7-formyl-12-hydroxy-12*H*-indolo[2,1-*b*][1,3]benzothiazine (**12**).

Table 5. Regioselective lithiation at the 4-position of 2-methylthioindole (**8c**)



Entry	Reaction *n*-BuLi (mol eq.)	Conditions Temp. (°C)	Yield (%) of **16**	 **7**	 **17**	Recovery
1	1.7	reflux	11	15	trace	20
2	3.0	reflux	27	17	0	0
3	3.0	20	43	13	0	8
4	3.0	0	38	7	0	29

Table 6. Regioselective lithiation at the 4-position of 2-(*sec*-butylthio)indole (**8d**)



Entry	*n*-BuLi (mol eq.)	Reaction Time with DMF (min)	Yield (%) of **18**	 **19**	Recovery
1	1.7	60	45	7	13
2	3.0	60	59	5	3
3	3.0	30	66	trace	0
4	3.0	15	67	10	5

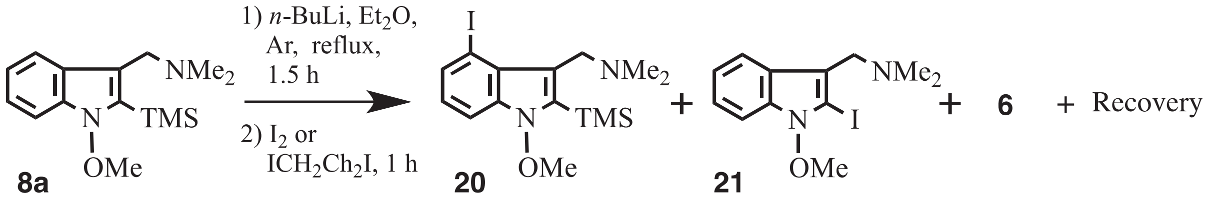
The aminal structure of **12** was determined by the presence of aminal proton at δ 7.00 as a singlet in its ^{1}H-NMR spectrum. The formation of **12** can be explained as follows. The lithiation of *ortho*-position of phenylthio substituent of **11**, followed by the reaction with DMF, afford an unstable intermediate **13** Subsequent cyclization between indole NH and formyl group results in the formation of **12** (Scheme 2).

The structure was further confirmed by leading it to **14** in 86% yield and **15** in 55% yield by the reduction with $NaBH_4$ and subsequent acetylation with Ac_2O, respectively.

Thirdly, using 1-methoxy-2-methylthiogramine (**8c**), lithiation was carried out with *n*-BuLi in ether, followed by the reaction with DMF, and the results are summarized in Table 5. In this case, 4-formylindole (**16**), 2-formylindole (**7**), and 2-methylthiogramine (**17**) were obtained in varied yield as shown in Table 5 (Entries 1–4). The maximum yield of **16** was realized when the lithiation was performed at 20 °C (Entry 3). Replacement of 2-methylthio group by lithium was observed resulting in the formation of **7**.

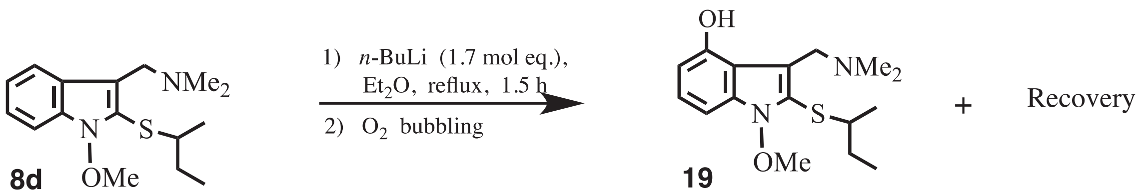
Finally, using 1-methoxy-2-*sec*-butylthiogramine (**8d**), lithiation was carried out with *n*-BuLi in refluxing ether, followed by the reaction with DMF. In this case, 4-formylindole (**18**) was obtained in good yields under examined reaction conditions as shown in Table 6 (Entries 1–4). Although in small amounts, formation of 4-hydroxy product (**19**) was observed.

Table 7. Introduction of iodine to the 4-position of indole (**8a**)



Entry	Reaction Conditions		Yield (%) of			
	Reagent (mol eq.)	Temp. (°C)	**20**	**21**	**6**	Recovery
1	I_2 (0.8)	rt	0	0	26	46
2	I_2 (6.0)	0	37	11	8	16
3	ICH_2CH_2I (3.0)	rt	35	9	0	7

Table 8. Introduction of hydroxy group to the 4-position of indole (**8d**)



Entry	Reaction Conditions with O_2		Yield (%) of	
	Time (h)	Temp. (°C)	**19**	Recovery
1*	0.5	r.t.	20	27
2*	3.0	–78	19	56
3	3.0	–78	31	30
4	3.0	–18	27	38

* O_2 atmosphere using O_2 gas balloon

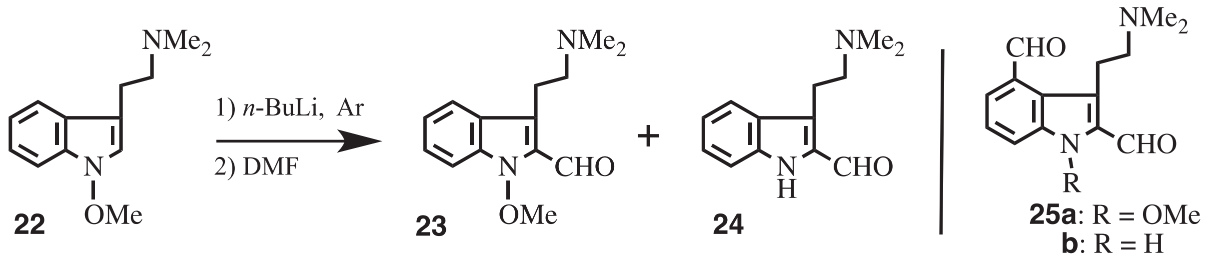
We next tried introduction of iodine into 4-position. Utilizing 1-methoxy-2-trimethylsilylgramine (**8a**) as a substrate, lithiation was carried out as usual. Iodine and 1,2-diiodoethane were used as electrophiles and the results are summarized in Table 7. Products were 4-iodo- (**20**) and 2-iodoindoles (**21**) together with 1-methoxygramine (**6**). Although the yield is still not satisfactory, this method enabled us to get 4-iodoindole derivative as a versatile building block.

In the lithiation of **8d** we isolated 4-hydroxyindole (**19**) as a by-product. We decided to obtain this compound positively (Table 8). Oxygen gas was bubbled into the ether solution of lithiated **8d** or lithiation was carried out under oxygen atmosphere and the results are shown in Table 8. Reaction temperatures were changed from rt to –78 °C but the yield of 4-hydroxyindole (**19**) was around 20–30% yield. For improving the yield further examination of the reaction conditions are necessary.

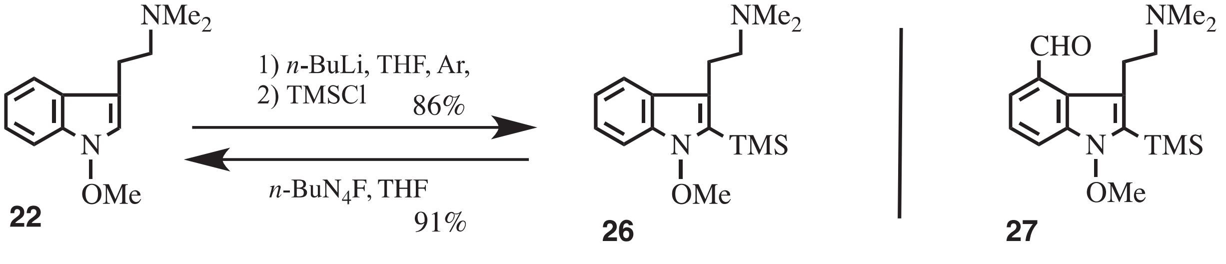
IV. Lithiation of 3-dimethylaminoethyl-1-methoxyindole (22, lespedamine)[8]

We could prove that dimethylaminomethyl group at the 3-position of indole nucleus can act as a ligand for the lithium at the 4-position. If the carbon number of the side chain is elongated by one carbon, namely changing dimethylaminomethyl to dimethylaminoethyl group, what will happen in the lithiation. Does the yield of 4-substituted indoles improve? To answer this question, we tried lithiation of lespedamine (**22**).[8]

Table 9. Lithiation of lespedamine



Entry	n-BuLi	Reaction	Conditions		Yield (%) of		
	(mol eq.)	Solvent	Temp (°C)	Time (min)	**23**	**24**	**25a** or **25b**
1	2.2	Et_2O	reflux	90	55	19	0
2	1.5	THF	–18	15	91	0	0

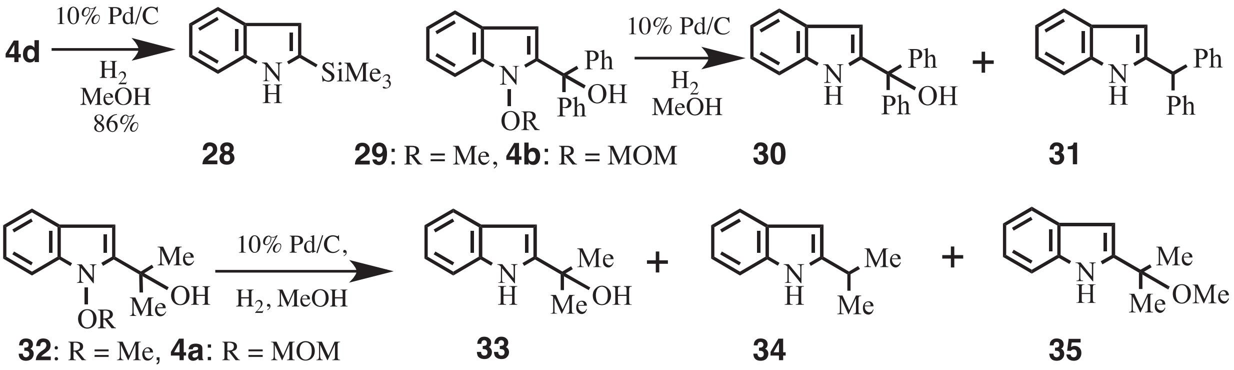


Scheme 3

Lithiation was carried out as usual in refluxing Et_2O or THF with *n*-BuLi, followed by the reaction with DMF, and the results are summarized in Table 9. In this case, production of only 2-formylindoles, **23** and **24** were observed. Even a trace amount of formation of **25a** and **25b** was not observed at all. Trapping of the lithium species with TMS-Cl afforded 2-trimethylsilylated lespedamine (**26**) in 86% yield (Scheme 3). Since **26** has a sterically bulky trimethylsilyl group at the 2-position, further attempt to get 4-formyllespedamine (**27**) by lithiation was performed under various reaction conditions *in vain*. These results suggest that 3-dimethylaminoethyl group cannot function as a ligand to enable lithiation at the 4-position, while it facilitates 2-lithiation effectively. Treatment of **26** with fluoride in THF afforded **22** in 91% yield.

V. Reductive removal of 1-alkoxygroup

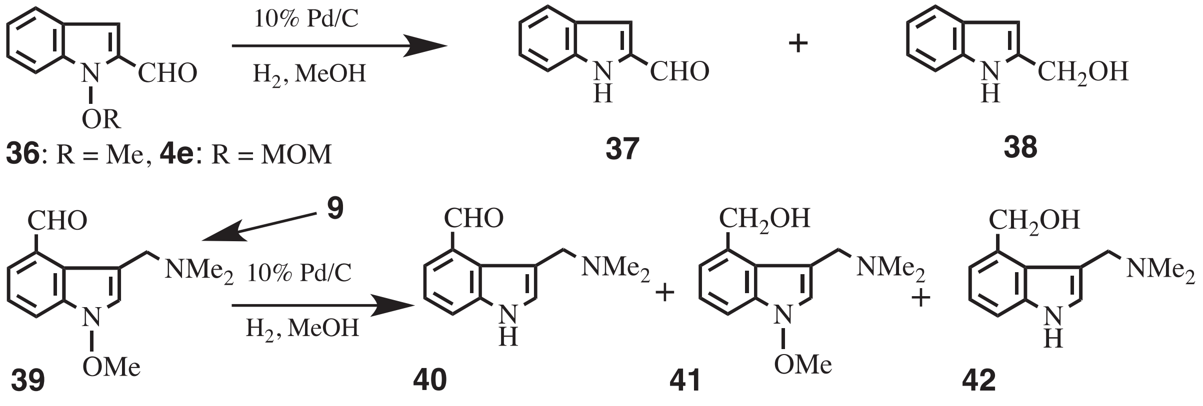
Removal of 1-methoxy- and 1-methoxymethoxy group was attained easily by catalytic hydrogenolysis over 10% Pd/C under hydrogen at rt and atmospheric pressure. Thus, compound **4d** produced 2-trimethylsilylindole (**28**) in 86% yield (Scheme 4). Whereas **29** afforded **30** and **31** in 74 and 9% yields, respectively. Compound **4b** also provided **30** and **31** in the respective yields of 90 and 6%. In the reduction of **32**, **33**, **34**, and **35** were formed in 85, 4, and 7% yields, respectively. Similarly, compound **4a** gave **33**, **34**, and **35** in the respective yields of 87, 3, and 8%.



Scheme 4

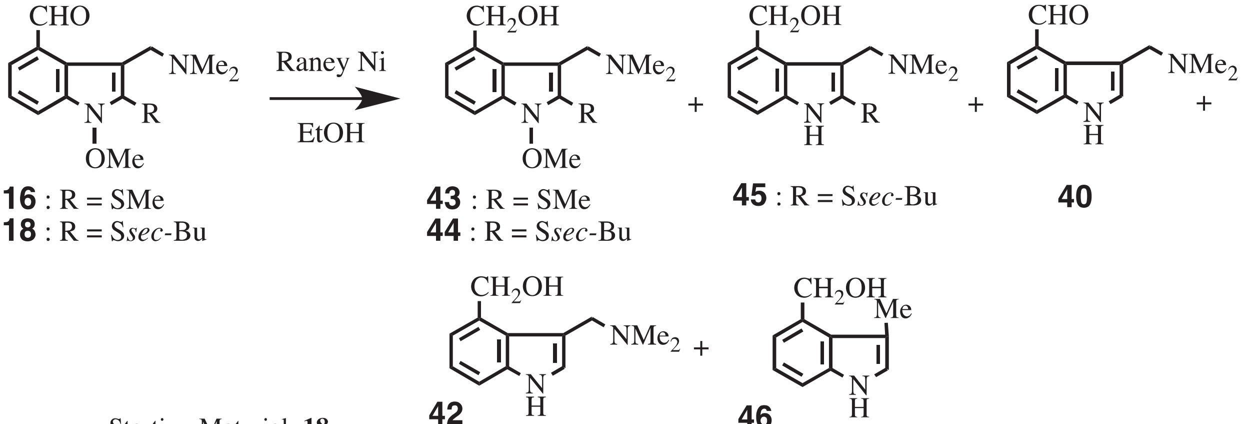
In the reduction of **36**, over reduction occurred partly to afford **37** and **38** in the respective yields of 62 and 22% (Scheme 5). Reduction of **4e** produced **37** and **38** in the respective yields of 67 and 26%. Reduction of 4-formyl-1-methoxygramine (**39**), prepared from **9,** afforded 4-formylgramine (**40**), indole-4-methanols, (**41** and **42**) in 8, 15, and 37% yields, respectively.

Attempts to remove 1-methoxy and 2-alkylthio group at the same time were examined by the reduction of **16** and **18** with Raney Ni. Contrary to our expectation, in fact complex mixture of products was obtained and the results are summarized in Table 10.



Scheme 5

Table 10. Removal of 1-methoxy group by Raney Ni reduction



Starting Material: **18**

Entry	Raney Ni*	Reaction Temp. (°C)	Conditions Time (min)	**44**	**45**	Yield (%) of **40**	**42**	**46**	Recovery
1	20	7 — 18	30	4	9	3	24	14	7
2	10	10 —15	30	14	-	5	9	-	47
3	10	12 —21	60	10	-	-	12	-	49

* Ratio of Raney Ni to starting material by weight.

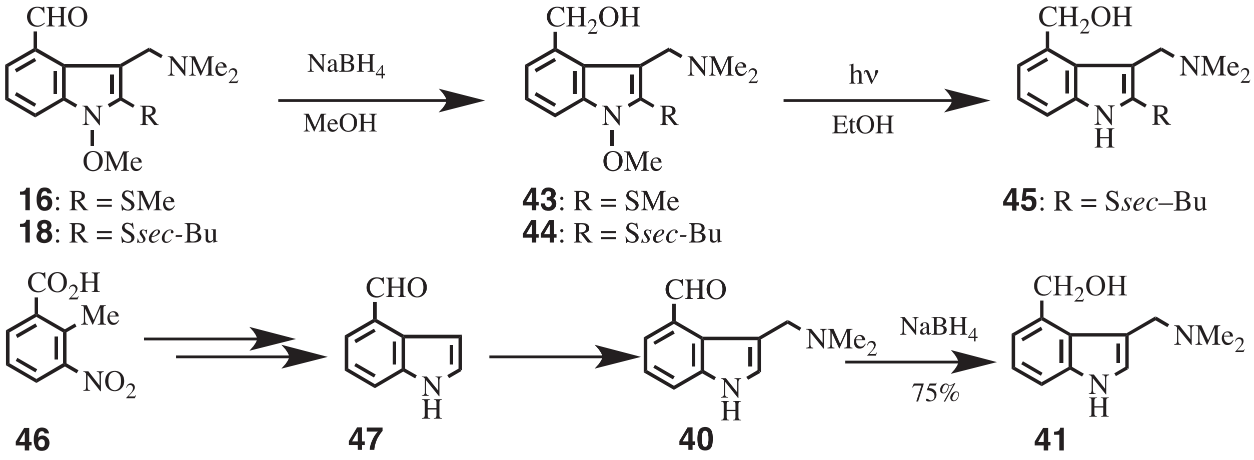
Starting Material: **16**

Entry	Raney Ni*	Reaction Temp. (°C)	Conditions Time (min)	**43**	Yield (%) of **40**	**42**	**46**	Recovery
1	40	0 — 7	45	-	trace	20	24	-
2	20	3 —14	30	-	20	28	16	19
3	10	18 — 28	90	trace	11	10	-	62

Under the reaction conditions in Entry 1, **18** formed **44**, **45, 40**, **42**, and **46** in 4, 9, 3, 24, and 14% yields, respectively. Similarly, **16** afforded **40**, **42**, and **46** in 20, 28, and 16% yields, respectively. In both compounds, reaction conditions were not found to obtain a single product.

Photo-reduction is another possible method to remove 1-methoxygroup. So, we applied it to **43** and **44**, which are prepared from the respective starting materials, **16** and **18**, by the reduction with $NaBH_4$. Irradiation of ethanol solution of **44** with 100W mercury lamp provided 20% yield of demethoxylated product (**45**, Scheme 6).

The structure of **40**, having a formyl group at the 4-position, was unequivocally determined by comparing it with the authentic sample **40** derived from the Mannich reaction of indole-4-carbaldehyde (**47**), which was prepared from 2-methyl-3-nitrobenzoic acid (**46**) through Leimgruber-Batcho method in long synthetic steps. $NaBH_4$ reduction of **40** confirmed the structure of **41**.



Scheme 6

In conclusion, our 1-hydroxyindole chemistry gave high added value to 2,3-dihydroindole (**1**), which is inexpensive and supplied in large quantities as a by-product of the coal industry. It is no longer necessary to discard it as an industrial waste, but it is reborn into useful building block for the synthesis of biologically active substances such as phytoalexins,[11] fungicides,[11] plant root growth promotor,[12] blood platelet aggregation inhibitor,[13] new promising substance for treating osteoporosis,[14] hair tonic,[15] cosmetic materials,[15] α_2 inhibitor for erectile dysfunction,[16] intermediate for ergot alkaloid,[17] and so on. 2,3-Dihydroindole (**1**) would play important and useful role for the social and the earth contribution[18] in varied ways in the near future, employing 1-hydroxyindole chemistry.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL JNM-GSX 500 or FX100S spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 or JEOL SX-102A spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60) (SiO_2) or Merck Aluminum Oxide GF_{254} (Type 60/E) (Al_2O_3). Column chromatography was performed on silica gel (SiO_2, 100–200 mesh, from Kanto Chemical Co. Inc.) or activated alumina (Al_2O_3, 300 meshes, from Wako Pure Chemical Industries, Ltd.) throughout the present study.

1-Methoxymethoxyindole (2b) from 1-(*t*-butyldimethylsilyloxy)indole (3a) — A suspension of KO*t*Bu (91.2 mg, 0.81 mmol, 2.4 mol eq.) and $(n\text{-}Bu)_4NF\cdot 3H_2O$ (111.1 mg, 0.35 mmol, 1.0 mol eq.) in anhydrous THF (1.0 mL) was added to a solution of **3a** (85.4 mg, 0.34 mmol) and methoxymethyl chloride (56.2 mg, 0.69 mmol, 2.0 mol eq.) in anhydrous THF (2.0 mL) and stirred at rt for 1 h. Water was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:7, v/v) as an eluent to give **2b** (59.7 mg, 98%).

1-Methoxymethoxyindole (2b) from 1-benzoyloxyindole (3b) [Method A] — 8% aq. NaOH (1.0 mL) was added to a solution of **3b** (46.0 mg, 0.19 mmol) and stirred at rt for 10 min. The reaction mixture was poured into sat. aq. brine (20 mL) and the whole was made acidic (pH 4) by adding 8% aq. HCl. The whole was extracted with benzene. The benzene solution, containing 1-hydroxyindole, was rapidly dried over Na_2SO_4. To the benzene solution, K_2CO_3 (487.2 mg, 3.53 mmol, 18 mol eq.), $(n\text{-}Bu)_4NHSO_4$ (8.2 mg, 0.02 mmol, 0.1 mol eq.), and methoxymethyl chloride (46.2 mg, 0.57 mmol, 3 mol eq.) in benzene (1.0 mL) were added and stirred at rt for 3 h. Water was added, and the benzene layer was separated, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:7, v/v) as an eluent to give **2b** (25.6 mg, 74%). **2b**: mp 27—27.5 °C (colorless prisms, recrystallized from hexane). IR (KBr): 2970, 1445, 1330, 1230, 1182, 1100, 1089, 1030, 920, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 3.66 (3H, s), 5.17 (2H, s), 6.37 (1H, d, *J*=3.5 Hz), 7.11 (1H, t, *J*=7.4 Hz), 7.20—7.26 (2H, m), 7.42 (1H, d, *J*=8.1 Hz), 7.58 (1H, d, *J*=7.9 Hz). MS *m/z*: 177 (M^+). *Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.64; H, 6.33; N, 7.86.

1-Methoxymethoxyindole (2b) from 1-benzoyloxyindole (3b) [Method B] — A suspension of KO*t*Bu (53.2 mg, 0.47 mmol, 2.9 mol eq.) in anhydrous THF (4.0 mL) was added to a mixture of a solution of **3b** (38.6 mg, 0.16 mmol) and methoxymethyl chloride (52.0 mg, 0.64 mmol, 4.0 mol eq.) in anhydrous THF (2.0 mL) and the whole was stirred at rt for 1 h. Water and sat. aq. $NaHCO_3$ was added to make the reaction mixture alkaline, and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified as described in Method A. Yield of **2b** was 27.8 mg (97%).

1-(2-Methoxy)ethoxymethoxyindole (2c) from 1-(*t*-butyldimethylsilyloxy)indole (3a) — A suspension of KO*t*Bu (97.2 mg, 0.87 mmol, 2.3 mol eq.) and (n-Bu)$_4$NF·3H$_2$O (125.8 mg, 0.39 mmol, 1.0 mol eq.) in anhydrous THF (1.0 mL) was added to a solution of **3a** (94.9 mg, 0.38 mmol) and 2-methoxyethoxymethyl chloride (98.8 mg, 0.79 mmol, 2.1 mol eq.) in anhydrous THF (2.0 mL) and stirred at rt for 1 h. Water was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:3, v/v) as an eluent to give **2c** (83.3 mg, 98%). **2c**: colorless oil. IR (film): 2920, 2890, 1450, 1320, 1220, 1105, 1030, 920, 875, 845, 760, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.41 (3H, s), 3.59—3.65 (2H, m), 3.93—3.99 (2H, m), 5.27 (2H, s), 6.36 (1H, dd, *J*=3.5, 1.0 Hz), 7.10 (1H, ddd, *J*=7.9, 6.9, 1.0 Hz), 7.22 (1H, ddd, *J*=8.3, 6.9, 1.0 Hz), 7.33 (1H, d, *J*=3.5 Hz), 7.42 (1H, dd, *J*=8.3, 1.0 Hz), 7.58 (1H, ddd, *J*=7.9, 1.0, 1.0 Hz). High resolution MS (HR-MS) *m/z*: Calcd for $C_{12}H_{15}NO_3$: 221.1050. Found: 221.1049.

1-(2-Methoxyethoxy)methoxyindole (2c) from 1-benzoyloxyindole (3b) — A suspension of KO*t*Bu (77.4 mg, 0.69 mmol, 3.0 mol eq.) in anhydrous THF (3.0 mL) was added to a mixture of a solution of **3b** (54.5 mg, 0.23 mmol) and 2-methoxyethoxymethyl chloride (81.4 mg, 0.65 mmol, 2.8 mol eq.) in anhydrous THF (2.0 mL) and the whole was stirred at rt for 1 h. Water and sat. aq. $NaHCO_3$ were added to make the reaction mixture alkaline, and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by column-chromatography on SiO_2 with CH_2Cl_2 as an eluent to give **2c** (50.8 mg, 100%).

Synthesis of α,α-dimethyl-1-(methoxymethoxy)indole-2-methanol (4a) from 2b [Scheme 1] General Procedure — Under Ar atmosphere, n-BuLi (1.6 M hexane solution, 0.26 mL, 0.42 mmol, 1.0 mol eq.) was slowly added to a solution of **2b** (72.0 mg, 0.41 mmol) in anhydrous THF (2.0 mL) at 0 °C and stirred for 15 min. To the reaction mixture was added acetone (0.14 mL, 1.09 mmol, 4.7 mol eq.) and stirred at rt for 30 min. Water was added to the reaction mixture under ice cooling and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:9, v/v) as an eluent to give **2b** (7.0 mg, recovery, 10%) and **4a** (85.3 mg, 89%). **4a**: colorless oil). IR (film): 3420, 2990, 2940, 1450, 1160, 1060, 910, 750 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.71 (6H, s), 3.67 (3H, s), 5.35 (2H, s), 6.25 (1H, d, *J*=1.0 Hz), 7.01 (1H, ddd, *J*=8.5, 6.8, 1.0 Hz), 7.14 (1H, ddd, *J*=8.5, 6.8, 1.0 Hz), 7.43 (1H, dd, *J*=6.8, 1.0 Hz), 7.46 (1H, dd, *J*=6.8, 1.0 Hz). HR-MS *m/z*: Calcd for $C_{13}H_{17}NO_3$: 235.1208. Found: 235.1218.

Synthesis of α,α-diphenyl-1-(methoxymethoxy)indole-2-methanol (4b) from 2b — In the general procedure described in **4a** from **2b**, n-BuLi (1.6 M hexane solution, 0.32 mL, 0.51 mmol, 1.0 mol eq.), **2b** (88.8 mg, 0.50 mmol), benzophenone (460.0 mg, 2.52 mmol, 5.0 mol eq.) in anhydrous THF (2.0 mL) were used. The same work-up and purification by column-chromatography on SiO_2 with EtOAc–hexane

(1:15, v/v) as an eluent gave **4b** (162.0 mg, 99%). **4b**: mp 138—139 °C (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3490, 3400, 1445, 970, 740, 700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.40 (3H, s), 4.76 (2H, s), 4.80 (1H, s), 5.76 (1H, s), 7.10 (1H, t, *J*=7.6 Hz), 7.23 (1H, t, *J*=7.6 Hz), 7.28—7.46 (12H, m). MS *m/z*: 359 (M^+). *Anal*. Calcd for $C_{23}H_{21}NO_3$: C, 76.88; H, 5.89; N, 3.90. Found: C, 77.12; H, 5.95; N, 3.88.

Synthesis of α-methyl-α-phenyl-1-(methoxymethoxy)indole-2-methanol (4c) from 2b — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.30 mL, 0.48 mmol, 1.0 mol eq.), **2b** (84.8 mg, 0.48 mmol), and acetophenone (0.28 mL, 2.40 mmol, 5.0 mol eq.) were used. The same work-up and purification as Entry 1 by column-chromatography on SiO_2 with EtOAc–hexane (1:9, v/v) as an eluent gave **4c** (125.3 mg, 88%) and **2b** (9.4 mg, recovery, 11%). **4c**: mp 72—73.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3430, 2980, 2940, 1445, 1225, 1145, 1075, 1050, 950, 940, 910, 800, 770, 740, 705, 670, 580 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.94 (3H, s), 3.64 (3H, s), 4.52 (1H, d, *J*=6.6 Hz), 4.83 (1H, d, *J*=6.6 Hz), 6.46 (1H, d, *J*=1.0 Hz), 7.03 (1H, ddd, *J*=8.0, 7.0, 1.0 Hz), 7.14 (1H, ddd, *J*=8.4, 7.0, 1.0 Hz), 7.22 (1H, br t, *J*=7.5 Hz), 7.30 (2H, br t, *J*=7.5 Hz), 7.37 (1H, dd, *J*=8.4, 1.0 Hz), 7.40 (2H, br d, *J*=7.5 Hz), 7.50 (1H, dd, *J*=8.0, 7.0 Hz). MS *m/z*: 297 (M^+). *Anal*. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.46; H, 6.47; N, 4.67.

Synthesis of 1-(methoxymethoxy)-2-(trimethylsilyl)indole (4d) from 2b — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.30 mL, 0.48 mmol, 1.0 mol eq.), **2b** (85.4 mg, 0.48 mmol), and trimethylsilyl chloride (0.32 mL, 2.52 mmol, 5.2 mol eq.) were used. The same work-up and purification as Entry 1 by column-chromatography on SiO_2 with EtOAc–hexane (1:15, v/v) as an eluent gave **4d** (109.6 mg, 91%). **4d**: colorless oil. IR (film): 2950, 1465, 1250, 1165, 1095, 1065, 923, 905, 845, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.37 (9H, s), 3.66 (3H, s), 5.21 (2H, s), 6.49 (1H, br s), 7.06 (1H, d, *J*=7.3, 7.3 Hz), 7.21 (1H, dd, *J*=8.3, 7.3 Hz), 7.48 (1H, d, *J*=8.3 Hz), 7.53 (1H, d, *J*=7.3 Hz). HR-MS *m/z*: Calcd for $C_{13}H_{19}NO_2Si$: 249.1184. Found: 249.1194.

Synthesis of 1-(methoxymethoxy)indole-2-carbaldehyde (4e) from 2b — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.56 mL, 0.89 mmol, 1.1 mol eq.), **2b** (145.6 mg, 0.82 mmol), and anhydrous DMF (0.64 mL, 8.22 mmol, 10 mol eq.) were used. The same work-up and purification by column-chromatography on SiO_2 with CH_2Cl_2–hexane (2:1, v/v) as an eluent gave **4e** (162.0 mg, 96%). **4e**: pale brown oil. IR (film): 2950, 2820, 1675, 1670, 1665, 1610, 1520, 1400, 1160, 1130, 1080, 950, 925, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.68 (3H, s), 5.33 (2H, s), 7,17 (1H, d, *J*=1.0 Hz), 7.19 (1H, ddd, *J*=8.3, 6.9, 1.0 Hz), 7.44 (1H, ddd, *J*=7.7, 6.9, 1.0 Hz), 7.54 (1H, dd, *J*=7.7, 1.0 Hz), 7.59 (1H, ddd, *J*=8.3, 1.0, 1.0 Hz), 9.91 (1H, s). HR-MS *m/z*: Calcd for $C_{11}H_{11}NO_3$: 205.0738. Found: 205.0743.

1-[(2-Methoxyethoxy)methoxy]indole-2-carbaldehyde (5) from 2c — Under Ar atmosphere, *n*-BuLi

(1.6 M hexane solution, 0.12 mL, 0.19 mmol, 1.1 mol eq.) was slowly added to a solution of **2c** (37.7 mg, 0.17 mmol) in anhydrous THF (2.0 mL) at rt (12 °C) and stirred for 15 min. To the reaction mixture was added anhydrous DMF (0.12 mL, 1.55 mmol, 9.1 mol eq.) and stirred at rt for 30 min. Water was added to the reaction mixture under ice cooling and the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column-chromatography on SiO_2 with EtOAc–hexane (1:2, v/v) as an eluent to give **5** (7.4 mg, 17%). **5**: pale yellow oil. IR (film): 2920, 2890, 2810, 1675, 1520, 1130, 1110, 950, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.33 (3H, s), 3.51—3.57 (2H, m), 3.90—3.96 (2H, m), 5.40 (2H, s), 7.19 (1H, ddd, *J*=8.0, 7.2, 1.0 Hz), 7.27 (1H, s), 7.44 (1H, ddd, *J*=8.4, 7.2, 1.0 Hz), 7.60 (1H, dd, *J*=8.4, 1.0 Hz), 7.71 (1H, dd, *J*=8.0, 1.0 Hz), 9.90 (1H, s). HR-MS *m/z*: Calcd for $C_{13}H_{15}NO_4$: 249.0999. Found: 249.0985.

3-(Dimethylaminomethyl)-1-methoxyindole-2-carbaldehyde (7) from 3-(dimethylaminomethyl)-1-methoxyindole (6) [Table 1, Entry 1] General Procedure — Under Ar atmosphere, *t*-BuLi (1.7 M pentane solution, 0.46 mL, 0.51 mmol, 2.2 mol eq.) was slowly added to a solution of **6** (46.0 mg, 0.23 mmol) in anhydrous THF (1.0 mL) at –80 °C (dry ice-acetone) with stirring. After stirring was continued for 15 min, anhydrous DMF (0.5 mL, excess) was added. The temperature of the whole was raised to rt and stirred for 1 h. After adding water to the reaction mixture under ice cooling, the whole was extracted with EtOAc–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by p-TLC on Al_2O_3 with Et_2O–hexane (5:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.73—0.29 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **7** (48.3 mg, 92%). Extraction of the band having an *Rf* value of 0.29—0.15 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **6** (1.7 mg, recovery, 4%). **7**: colorless oil. IR (film): 2950, 2811, 2774, 1669, 1618, 1537, 1418, 1338, 1174, 1012, 938, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.30 (6H, s), 3.89 (2H, s), 4.17 (3H, s), 7.18 (1H, ddd, *J*=8.4, 8.1, 1.1 Hz), 7.43 (1H, ddd, *J*=8.4, 8.1, 1.1 Hz), 7.48 (1H, dt, *J*=8.4, 1.1 Hz), 7.85 (1H, dt, *J*=8.1, 1.1 Hz), 10.27 (1H, s). HR-MS *m/z*: Calcd for $C_{13}H_{16}N_2O_2$: 232.1211. Found: 232.1214.

[Entry 2] In the general procedure, lithiation was carried out at –18 °C (ice–NaCl) using *t*-BuLi (1.7 M pentane solution, 0.46 mL, 0.57 mmol, 2.2 mol eq.), **6** (53.8 mg, 0.26 mmol), and anhydrous THF (1.0 mL). After the reaction with anhydrous DMF (0.5 mL, excess), the same work-up as Entry 1 afforded **7** (56.3 mg, 92%) and **6** (2.7 mg, recovery, 5%).

[Entry 3] In the general procedure, lithiation was carried out at –18 °C (ice–NaCl) using *n*-BuLi (1.6 M pentane solution, 0.46 mL, 0.57 mmol, 2.2 mol eq.), **6** (68.6 mg, 0.34 mmol), and anhydrous THF (1.0 mL). After the reaction with anhydrous DMF (0.5 mL, excess), the same work-up as Entry 1 afforded **7** (74.6 mg, 96%) and **6** (1.0 mg, recovery, 2%).

[Entry 4] In the general procedure, lithiation was carried out at –18 °C (ice–NaCl) using *n*-BuLi (1.6 M pentane solution, 0.21 mL, 0.34 mmol, 1.1 mol eq.), **6** (62.8 mg, 0.31 mmol), and anhydrous THF (1.0 mL). After the reaction with anhydrous DMF (0.5 mL, excess), the same work-up as Entry 1 afforded **7** (52.3 mg, 87%) and **6** (5.4 mg, recovery, 8%).

[Entry 5] In the general procedure, lithiation was carried out at 0 °C using *n*-BuLi (1.6 M pentane solution, 0.19 mL, 0.30 mmol, 1.1 mol eq.), **6** (55.6 mg, 0.27 mmol), and anhydrous THF (1.0 mL). After the reaction with anhydrous DMF (0.5 mL, excess) at 0 °C for 15 min, the same work-up as Entry 1 afforded **7** (23.0 mg, 36%) and **6** (21.8 mg, recovery, 39%).

[Entry 6] In the general procedure, lithiation was carried out at 0 °C using *n*-BuLi (1.6 M pentane solution, 0.19 mL, 0.30 mmol, 1.1 mol eq.), **6** (59.6 mg, 0.29 mmol), and anhydrous THF (1.0 mL). After the reaction with anhydrous DMF (0.5 mL, excess) at 0 °C for 2 min, the same work-up as Entry 1 afforded **7** (16.5 mg, 24%) and **6** (31.4 mg, recovery, 53%).

Synthesis of 3-(dimethylaminomethyl)-l-methoxy-2-(phenylthio)indole (8b) from 6 [Table 2, Entry 2] General Procedure — Under Ar atmosphere, *n*-BuLi (1.6 M hexane solution, 1.00 mL, 1.58 mmol, 1.5 mol eq.) was slowly added to a solution of **6** (215.0 mg, 1.05 mmol) in anhydrous THF (2.5 mL) at –18 °C (ice–NaCl) and stirred for 15 min. To the reaction mixture was added a solution of Ph_2S_2 (357.1 mg, 1.64 mmol) in anhydrous THF (1.5 mL) and stirred at rt for 1 h. Water was added to the reaction mixture under ice cooling and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) as an eluent to give **8b** (328.3 mg, 99%). **8b**: colorless oil. IR (film): 3070, 2998, 2951, 2827, 2776, 1583, 1479, 1452, 1441, 1338, 1022, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.25 (6H, s), 3.73 (2H, s), 4.00 (3H, s), 7.10—7.24 (6H, m), 7.30 (1H, ddd, *J*=8.3, 8.1, 1.1 Hz), 7.42 (1H, d, *J*=8.3 Hz), 7.82 (1H, d, *J*=8.1 Hz). HR-MS *m/z*: Calcd for $C_{18}H_{20}N_2OS$: 312.1295. Found: 312.1307.

3-(Dimethylaminomethyl)-1-methoxy-2-(methylthio)indole (8c) from 6 [Table 2, Entry 3] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.85 mL, 1.36 mmol, 1.5 mol eq.), **6** (126.3 mg, 0.62 mmol) in anhydrous THF (2.0 mL), and Me_2S_2 (0.34 mL, 3.72 mmol) in anhydrous THF (1.5 mL) were used. After the same work-up as Entry 2 and purification by column-chromatography on Al_2O_3 with Et_2O–hexane (1:4, v/v) **8c** (147.9 mg, 95%) was obtained. **8c**: colorless oil. IR (film): 3060, 2987, 2946, 2816, 2771, 1456, 1443, 1367, 1336, 1312, 1260, 1225, 1181, 1150, 1131, 1043, 1011, 994, 953, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.27 (6H, s), 2.42 (3H, s), 3.70 (2H, s), 4.13 (3H, s), 7.12 (1H, dd, *J*=8.1, 7.0, 0.9 Hz), 7.25 (1H, ddd, *J*=8.1, 7.0, 0.9 Hz), 7.39 (1H, dt, *J*=8.1, 0.9 Hz), 7.70 (1H, dt, *J*=8.1, 0.9 Hz). HR-MS *m/z*: Calcd for $C_{13}H_{18}N_2OS$: 250.1138. Found: 250.1121.

2-(*sec*-Butylthio)-3-(dimethylaminomethyl)-1-methoxyindole (8d) from 6 [Table 2, Entry 4] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.97 mL, 2.06 mmol, 1.7 mol eq.), **6** (211.6 mg, 1.37 mmol) in anhydrous THF (3.0 mL), and *sec*-Bu_2S_2 (0.54 mL, 4.11 mmol) in anhydrous THF (1.5 mL) were used. After the same work-up and purification by column chromatography on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) as an eluent, **8d** (293.9 mg, 97%) and **6** (3.1 mg, recovery, 2%) were obtained. **8d**: pale yellow oil. IR (film): 2963, 2934, 2815, 2776, 1454, 1439, 1364, 1335, 1223, 1179, 1151, 1129, 1044, 1013, 994, 954, 850, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.01 (3H, t, *J*=7.3 Hz), 1.20 (3H, d, *J*=6.6 Hz), 1.51 (1H, sept, *J*=7.3 Hz), 1.63 (1H, ddq, *J*=14.0, 7.3, 6.6 Hz), 2.27 (6H, s), 3.26 (1H, sext, *J*=6.6 Hz), 3.69 (2H, s), 4.10 (3H, s), 7.10 (1H, ddd, *J*=8.2, 7.1, 1.1 Hz), 7.25 (1H, ddd, *J*=8.2, 7.1, 1.1 Hz), 7.38 (1H, br d, *J*=8.2 Hz), 7.41 (1H, br d, *J*=8.2 Hz). HR-MS *m/z*: Calcd for $C_{16}H_{24}N_2OS$: 292.1608. Found: 292.1615.

3-(Dimethylaminomethyl)-1-methoxy-2-(trimethylstannyl)indole (8e) from 6 [Table 2, Entry 5] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.92 mL, 1.47 mmol, 2.2 mol eq.), **6** (136.1 mg, 0.67 mmol) in anhydrous THF (3.0 mL), and Me_3SnCl (613.1 mg, 3.08 mmol, 4.6 mol eq. in anhydrous THF (1.5 mL) were used. After the same work-up and purification by column chromatography on Al_2O_3 with Et_2O–hexane (1:2, v/v) as an eluent, **8e** (215.0 mg, 88%) and **6** (16.0 mg, recovery, 12%) were obtained. **8e**: colorless oil. IR (film): 2983, 2948, 2856, 2819, 2767, 1572, 1499, 1458, 1441, 1367, 1329, 1283, 1225, 1179, 1150, 1116, 1308, 1013, 956, 850, 771, 735, 525 cm^{-1}. ^1H-NMR (CD_3OD) δ: 0.44 (9H, s), 2.24 (6H, s), 3.58 (2H, br s), 4.02 (3H, s), 7.02 (1H, ddd, *J*=7.9, 7.1, 0.9 Hz), 7.14 (1H, ddd, *J*=8.3, 7.1, 0.9 Hz), 7.36 (1H, dt, *J*=8.3, 0.9 Hz), 7.57 (1H, dt, *J*=7.9, 0.9 Hz). MS *m/z*: 372 [^{124}Sn], 370 [^{122}Sn], 368 [^{120}Sn], 367 [^{119}Sn], 366 [^{118}Sn], 365 [^{117}Sn], 364 [^{116}Sn] and 363 [^{115}Sn] (M^+). *Anal.* Calcd for $C_{15}H_{24}N_2OSn$: C, 49.08; H, 6.59; N, 7.63. Found: C, 49.14; H, 6.62; N, 7.43.

3-(Dimethylaminomethyl)-1-methoxy-2-(trimethylsilyl)indole (8a) from 6 [Table 2, Entry 1] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 1.14 mL, 1.83 mmol, 2.2 mol eq.), **6** (170.0 mg, 0.83 mmol) in anhydrous THF (3.0 mL), and TMSCl (0.70 mL, 4.98 mmol) in anhydrous THF (1.5 mL) were used. The reaction mixture was made pH 8 by adding sat. aq. $NaHCO_3$. After the same work-up and purification as Entry 2, **8a** (209.8 mg, 97%) and **6** (9.8 mg, recovery, 6%) were obtained. **8a**: colorless oil. IR (film): 2940, 2810, 2761, 1496, 1457, 1440, 1329, 1240, 1146, 1128, 1012, 863, 848, 739 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.44 (9H, s), 2.22 (6H, s), 3.57 (2H, br s), 4.02 (3H, s), 7.07 (1H, ddd, *J*=8.1, 7.0, 1.1 Hz), 7.20 (1H, ddd, *J*=8.1, 7.0, 1.1 Hz), 7.36 (1H, dt, *J*=8.1, 1.1 Hz), 7.71 (1H, dt, *J*=8.1, 1.1 Hz). HR-MS *m/z*: Calcd for $C_{15}H_{24}N_2OSi$: 276.1657. Found: 276.1671.

Lithiation of 3-(dimethylaminomethyl)-1-methoxy-2-(trimethylsilyl)indole 8a [Table 3, Entry 1] General Procedure — Under Ar atmosphere, *t*-BuLi (1.7 M pentane solution, 0.10 mL, 0.17 mmol, 1.1 mol eq.) was slowly added to a solution of **8a** (40.7 mg, 0.15 mmol) in anhydrous THF (1.0 mL) at –78 °C (dry ice-acetone) with stirring. After stirring was continued for 15 min, anhydrous DMF (0.5 mL, excess) was added. The temperature of the whole was raised to rt and stirred for 1 h. After adding water to the reaction mixture under ice cooling, the whole was extracted with EtOAc–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give **8a** (40.2 mg, recovery, 99%).

[Table 3, Entry 2] — In the general procedure described in Entry 1, *t*-BuLi (1.7 M pentane solution, 0.27 mL, 0.47 mmol, 3.1 mol eq.), **8a** (40.4 mg, 0.15 mmol) in anhydrous Et_2O (1.0 mL), anhydrous DMF (0.2 mL, excess) were used. After the same work-up as Entry 1, purification was carried out with p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:1:0.1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.52—0.36 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **8a** (4.3 mg, recovery, 11%). Extraction of the band having an *Rf* value of 0.27—0.12 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded 3-(dimethylaminomethyl)-1-methoxy-2-(trimethylsilyl)indole-4-carbaldehyde (**9**) (10.4 mg, 23%). **9**: mp 86.5—87.5 °C (colorless prisms, recrystallized from Et_2O–hexane). IR (KBr): 2949, 2820, 2766, 1670, 1603, 1394, 1344, 1244, 1129, 1019, 846, 749 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.48 (9H, s), 2.17 (6H, s), 3.69 (2H, br s), 4.03 (3H, s), 7.29 (1H, t, *J*=7.7 Hz), 7.58 (1H, dd, *J*=7.7, 1.0 Hz), 7.68 (1H, dd, *J*=7.7, 1.0 Hz), 10.53 (1H, s). MS *m/z*: 304 (M^+). *Anal.* Calcd for $C_{16}H_{24}N_2O_2Si$: C, 63.12; H, 7.95; N, 9.20. Found: C, 63.12; H, 7.91; N, 9.11.

[Table 3, Entry 3] — In the general procedure described in Entry 1, *n*-BuLi (1.6 M pentane solution, 0.24 mL, 0.37 mmol, 3.1 mol eq.), **8a** (33.5 mg, 0.12 mmol) in anhydrous Et_2O (1.0 mL) were used at –18 °C (ice-NaCl). The reaction with anhydrous DMF (0.3 mL, excess) was carried out at rt for 1 h. After the same work-up and purification as Entry 2, **8a** (26.5 mg, recovery, 79%) and **9** (4.2 mg, 11%) were obtained.

[Table 3, Entry 4] — In the general procedure described in Entry 1, *n*-BuLi (1.6 M pentane solution, 0.30 mL, 0.48 mmol, 3.1 mol eq.), **8a** (43.0 mg, 0.16 mmol) in anhydrous Et_2O (1.3 mL) were used at rt. The reaction with anhydrous DMF (0.3 mL, excess) was carried out at rt for 1 h. The same work-up and purification as Entry 2 were performed. Extraction of the band having an *Rf* value of 0.88—0.75 gave **8a** (14.1 mg, recovery, 33%). Bands of *Rf* value of 0.75—0.69 and 0.69—0.38 afforded **7** (3.0 mg, 8%), and **9** (16.2 mg, 34%), respectively.

[Table 3, Entry 6] — In the general procedure in Entry 1, *n*-BuLi (1.6 M pentane solution, 0.20 mL, 0.31 mmol, 3.1 mol eq.), **8a** (28.2 mg, 0.10 mmol) in anhydrous Et_2O (1.0 mL) were used and refluxed for 1.5 h. The reaction with anhydrous DMF (0.3 mL, excess) was carried out at rt for 1 h. The same work-up and purification as Entry 2, **8a** (1.9 mg, recovery, 7%), **7** (3.3 mg, 14%) and **9** (21.8 mg, 70%), respectively.

Lithiation of 3-(dimethylaminomethyl)-1-methoxy-2-(phenylthiol)indole (8b) [Table 4, Entry 1] General Procedure — Under Ar atmosphere, *n*-BuLi (1.6 M pentane solution, 1.0 mL, 1.60 mmol, 5.0

mol eq.) was slowly added to a solution of **8b** (98.4 mg, 0.32 mmol) in anhydrous Et_2O (1.5 mL) with stirring. After stirring was continued at reflux for 3.5 h, anhydrous DMF (1.0 mL, excess) was added. The whole was stirred at rt for 1 h. After adding water to the reaction mixture under ice cooling, the whole was extracted with EtOAc–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give residue, which was subjected to column-chromatography on SiO_2 with EtOAc–MeOH (95:5, v/v) as an eluent to give 3-(dimethylaminomethyl)-1-methoxy-2-(phenylthio)indole-4-carbaldehyde (**10**) (17.8 mg, 17%), 3-(dimethylaminomethyl)-2-(phenylthio)indole-4-carbaldehyde (**11**) (6.8 mg, 7%), and 6-(dimethylaminomethyl)-7-formyl-12-hydroxy-12*H*-indolo[2,1-*b*][1,3]benzothiazine (**12**, 35.4 mg, 33%) in the order of elution. **10**: mp 117—118 °C (colorless prisms, recrystallized from Et_2O). IR (KBr): 2978, 2951, 2903, 2814, 2773, 1671, 1600, 1480, 1444, 1340, 1132, 1018, 738 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.19 (6H, br s), 3.82 (2H, br s), 4.04 (3H, s), 7.15 (2H, dd, *J*=7.9, 1.3 Hz), 7.17 (1H, tt, *J*=7.3, 1.3 Hz), 7.24 (2H, ddt, *J*=7.9, 7.3, 1.3 Hz), 7.41 (1H, t, *J*=7.8 Hz), 7.66 (1H, dd, *J*=7.8, 1.1 Hz), 7.81 (1H, dd, *J*=7.8, 1.1 Hz), 10.70 (1H, br s). MS *m/z*: 340 (M^+). *Anal.* Calcd for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23. Found: C, 67.16; H, 5.95; N, 8.09. **11**: pale brown oil. IR (film): 3302, 2952, 2862, 2811, 2771, 1669, 1607, 1476, 1440, 1344, 1013, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.28 (6H, br s), 3.94 (2H, br s), 7.14—7.18 (2H, m), 7.20 (1H, tt, *J*=7.1, 1.4 Hz), 7.26 (2H, tt, *J*=7.1, 1.4 Hz), 7.31 (1H, dd, *J*=7.8, 7.3 Hz), 7.56 (1H, br d, *J*=7.8 Hz), 7.78 (1H, br d, *J*=7.3 Hz), 10.64 (1H, br s). HR-MS *m/z*: Calcd for $C_{18}H_{18}N_2OS$: 310.1138. Found: 310.1140. **12**: mp 171.5—172.5 °C (yellow powder, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3392, 2948, 2823, 2775, 1647, 1602, 1524, 1433, 1396, 1365, 1330, 1025, 759 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.26 (6H, s), 3.63 (1H, br d, *J*=13.4 Hz), 3.78 (1H, br d, *J*=13.4 Hz), 7.00 (1H, s), 7.32 (1H, t, *J*=7.8 Hz), 7.36 (1H, ddd, *J*=7.8, 7.6, 1.1 Hz), 7.41 (1H, ddd, *J*=7.8, 7.6, 1.1 Hz), 7.46 (1H, dd, *J*=7.8, 1.1 Hz), 7.60 (1H, dd, *J*=7.6, 1.1 Hz), 7.82 (1H, d, *J*=7.8 Hz), 7.84 (1H, d, *J*=7.8 Hz), 10.63 (1H, s). MS *m/z*: 338 (M^+). *Anal.* Calcd for $C_{19}H_{18}N_2O_2S \cdot H_2O$: C, 64.02; H, 5.37; N, 7.86. Found: C, 64.33; H, 5.07; N, 7.77.

[Table 4, Entry 5] — In the General Procedure, *n*-BuLi (1.6 M pentane solution, 0.19 mL, 0.31 mmol, 1.7 mol eq.), **8b** (54.5 mg, 0.18 mmol) in anhydrous Et_2O (2.0 mL) were used. After stirring was continued at reflux for 1.5 h, anhydrous DMF (0.4 mL, excess) was added. After the same work-up and column-chromatography as Entry 1, **10** (39.6 mg, 67%), **11** (3.3 mg, 6%), and **8b** (4.0 mg, recovery, 7%) were obtained.

6-(Dimethylaminomethyl)-12-hydroxy-7-hydroxymethyl-12*H*-indolo[2,1-*b*][1,3]benzothiazine (14) from 12 — $NaBH_4$ (9.5 mg, 0.26 mmol, 3.8 mol eq.) was added to a solution of **12** (22.6 mg, 0.07 mmol) in MeOH (3.0 mL) with stirring for 10 min under ice cooling. After adding water, the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Recrystallization of the solid residue with CH_2Cl_2–MeOH (97:3, v/v) afforded **14** (20.0 mg). The mother liquor was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.59—0.47 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded extra **14** (4.9 mg). Total yield of **14** was 24.9 mg (86%). **14**: mp 289—291 °C (decomp, colorless amorphous solid from CH_2Cl_2–MeOH). IR (KBr): 3096, 2952, 2823, 2770, 2658, 1597, 1576, 1534, 1477, 1432, 1367, 1340, 1285, 1263, 1168, 1077, 1005, 844, 763, 744 cm^{-1}. ^1H-NMR (5% CD_3OD in $CDCl_3$) δ: 2.34 (6H, s), 3.74 (1H, br d, *J*=13.6 Hz), 3.97 (1H, d, *J*=13.6 Hz), 4.78 (1H, d, *J*=12.6 Hz), 4.91 (1H, d, *J*=12.6 Hz), 6.96 (1H, s), 7.05 (1H, d, *J*=7.3 Hz), 7.18 (1H, dd, *J*=8.0, 7.3 Hz), 7.34 (1H, dt, *J*=7.3, 1.7 Hz), 7.38 (1H, dt, *J*=7.3, 1.7 Hz), 7.44 (1H, dd, *J*=7.3, 1.7 Hz), 7.57 (1H, dd, *J*=7.3, 1.7 Hz), 7.58 (1H, d, *J*=8.0 Hz). HR-MS *m/z*: Calcd for $C_{19}H_{20}N_2O_2S$: 340.1244. Found: 340.1248.

7-(Acetoxymethyl)-6-(dimethylaminomethyl)-12-hydroxy-12*H*-indolo[2,1-*b*][1,3]benzothiazine (15) from 14 — Ac_2O (0.5 mL) was added to a solution of **14** (9.8 mg, 0.03 mmol) in pyridine (1.0 ml) and stirred at rt for 7 h. Water and sat. aq. $NaHCO_3$ were added and the alkaline solution was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.77—0.62 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **15** (6.1 mg, 55%). **15**: pale yellow oil. ^1H-NMR ($CDCl_3$) δ: 2.07 (3H, s), 2.77 (6H, br s), 3.50 (1H, br d, *J*=13.3 Hz), 3.63 (1H, br d, *J*=13.3 Hz), 5.62 (1H, d, *J*=12.0 Hz), 5.66 (1H, d, *J*=12.0 Hz), 6.96 (1H, s), 7.21—7.25 (2H, m), 7.33 (1H, dt, *J*=7.6, 1.3 Hz), 7.38 (1H, dt, *J*=7.6, 1.3 Hz), 7.44 (1H, dd, *J*=7.6, 1.3 Hz), 7.56 (1H, dd, *J*=7.6, 1.3 Hz), 7.58—7.62 (1H, m). HR-MS *m/z*: Calcd for $C_{21}H_{22}N_2O_3S$: 382.1349. Found: 382.1349.

Lithiation of 3-(dimethylaminomethyl)-1-methoxy-2-(methylthio)indole (8c) [Table 5, Entry 1] General Procedure — Under Ar atmosphere, *n*-BuLi (1.6 M pentane solution, 0.22 mL, 0.34 mmol, 1.7 mol eq.) was slowly added to a solution of **8c** (50.6 mg, 0.20 mmol) in anhydrous Et_2O (1.5 mL) with stirring. After stirring was continued at reflux for 1.5 h, anhydrous DMF (0.4 mL, excess) was added. The whole was stirred at rt for 1 h. After adding water to the reaction mixture under ice cooling, the whole was extracted with EtOAc–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give residue, which was subjected to p-TLC on Al_2O_3 with Et_2O–hexane (2:1, v/v) as a developing solvent. Extractions of the bands having an *Rf* value of 0.82—0.71 and 0.62—0.53 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **8c** (10.2 mg, recovery, 20%) and **7** (7.0 mg, 15%), respectively. From the band of *Rf* 0.53—0.41, the mixture of 3-(dimethyaminomethyl)-1-methoxy-2-(methylthio)indole-4-carbaldehyde (**16**) and 3-(dimethylaminomethyl)-2-(methylthio)indole (**17**) were obtained. The mixture was purified by p-TLC on SiO_2 with

$CHCl_3$–MeOH–30% aq. NH_3–hexane (184:20:2:1, v/v) as a developing solvent to give **16** (5.9 mg, 11%, *Rf* 0.62—0.41) and **17** (0.8 mg, *Rf* 0.29—0.18). **16**: mp 68.5—69.0 °C (colorless prisms, recrystallized from Et_2O–hexane). IR (KBr): 2942, 2802, 2751, 1678, 1603, 1513, 1428, 1398, 1336, 1235, 1123, 1013, 963, 849, 803, 787, 756 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.21 (6H, br s), 2.46 (3H, s), 3.76 (2H, br s), 4.16 (3H, s), 7.35 (1H, dd, *J*=8.1, 7.6 Hz), 7.63 (1H, dd, *J*=8.1, 1.0 Hz), 7.78 (1H, dd, *J*=7.6, 1.0 Hz), 10.67 (1H, s). MS *m/z*: 279 (M^+). *Anal.* Calcd for $C_{14}H_{18}N_2O_2S$: C, 60.41; H, 6.52; N, 10.06. Found: C, 60.53; H, 6.54; N, 9.94. **17**: ^{1}H-NMR ($CDCl_3$) δ: 2.43 (9H, br s), 3.95 (2H, br s), 7.15 (1H, br t, *J*=7.9 Hz), 7.22 (1H, br t, *J*=7.9 Hz), 7.34 (1H, br d, *J*=7.9 Hz), 7.69 (1H, br d, *J*=7.9 Hz). HR-MS *m/z*: Calcd for $C_{12}H_{16}N_2S$: 220.1032. Found: 220.1031.

[Table 5, Entry 3] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.31 mL, 0.51 mmol, 3.0 mol eq.), **8c** (41.2 mg, 0.17 mmol) in anhydrous Et_2O (1.0 mL), anhydrous DMF (0.3 mL, excess) were used. After the same work-up and purification as Entry 1, **8c** (3.3 mg, recovery, 8%), **7** (5.1 mg, 13%), and **16** (19.7 mg, 43%) were obtained.

Lithiation of 2-(*sec*-butylthio)-3-(dimethylaminomethyl)-1-methoxyindole (8d) [Table 6, Entry 1] General Procedure — Under Ar atmosphere, *n*-BuLi (1.6 M pentane solution, 0.09 mL, 0.15 mmol, 1.7 mol eq.) was slowly added to a solution of **8d** (24.7 mg, 0.09 mmol) in anhydrous Et_2O (1.0 mL) with stirring. After stirring was continued at reflux for 1.5 h, anhydrous DMF (0.3 mL, excess) was added. The whole was stirred at rt for 1 h. After adding water to the reaction mixture under ice cooling, the whole was extracted with EtOAc–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give residue, which was subjected to p-TLC on Al_2O_3 with Et_2O–hexane (2:1, v/v) as a developing solvent. Extractions of the bands having an *Rf* value of 0.65—0.53, 0.53—0.35, and 0.26—0.14 with CH_2Cl_2–MeOH (95:5, v/v) afforded **8d** (3.3 mg, recovery, 13%), 2-(*sec*-butylthio)-3-(dimethylaminomethyl)-1-methoxyindol-4-ol (**19**) (1.8 mg, 7%), and 2-(*sec*-butylthio)-3-(dimethylaminomethyl)-1-methoxyindole-4-carbaldehyde (**18**) (12.1 mg, 45%), respectively. **18**: yellow oil. IR (film): 2969, 2927, 2867, 2813, 2763, 1676, 1604, 1458, 1395, 1336, 1240, 1130, 1016, 793 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.03 (3H, t, *J*=7.5Hz), 1.23 (3H, d, *J*=6.6 Hz), 1.50—1.60 (1H, m), 1.65 (1H, ddq, *J*=14.5, 7.5, 6.6 Hz), 2.20 (6H, s), 3.34 (1H, sext, *J*=6.6 Hz), 3.76 (2H, s), 4.13 (3H, s), 7.35 (1H, dd, *J*=8.4, 7.5 Hz), 7.62 (1H, d, *J*=8.4 Hz), 7.77 (1H, dd, *J*=7.5, 1.0 Hz), 10.68 (1H, s). HR-MS *m/z*: Calcd for $C_{17}H_{24}N_2O_2S$: 320.1557. Found: 320.1570. **19**: red brown oil. IR (film): 2964, 2933, 2867, 2559, 1624, 1581, 1487, 1461, 1374, 1263, 1004, 985, 774, 733 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.01 (3H, t, *J*=7.5 Hz), 1.20 (3H, d, *J*=6.8 Hz), 1.50 (1H, sept, *J*=7.5 Hz), 1.63 (1H, ddq, *J*=14.1, 7.5, 6.8 Hz), 2.41 (6H, s), 3.17 (1H, sext, *J*=6.8 Hz), 3.79 (2H, s), 4.08 (3H, s), 6.51 (1H, d, *J*=7.8 Hz), 6.84 (1H, d, *J*=8.1 Hz), 7.14 (1H, dd, *J*=8.1, 7.8 Hz), 13.40 (1H, br s, D_2O exchange). HR-MS *m/z*: Calcd for $C_{16}H_{24}N_2O_2S$:

308.1557. Found: 308.1557.

[Table 6, Entry 3] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.20 mL, 0.33 mmol, 3.0 mol eq.), **8d** (30.7 mg, 0.11 mmol) in anhydrous Et_2O (1.0 mL), anhydrous DMF (0.3 mL, excess) were used. The reaction time with DMF was 0.5 h. After the same work-up and purification as Entry 1, **19** (trace) and **20** (22.2 mg, 66%) were obtained.

3-(Dimethylaminomethyl)-4-iodo-1-methoxy-2-(trimethylsilyl)indole (22) from 3-(dimethylaminomethyl)-1-methoxy-2-(trimethylsilyl)indole (8a) [Table 7, Entry 2] — Under Ar atmosphere, *n*-BuLi (1.6 M hexane solution, 0.30 mL, 0.47 mmol, 3.1 mol eq.) was slowly added to a solution of **8a** (42.2 mg, 0.15 mmol) in anhydrous Et_2O (3.0 mL) and refluxed for 1.5 h. A solution of I_2 (112.0 mg, 0.44 mmol, 2.9 mol eq.) in anhydrous Et_2O (1.5 mL) was added at rt and stirred for 1 h. After addition of 10% aq. $Na_2S_2O_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as a developing solvent. Extractions of bands having an *Rf* value of 0.41—0.27, 0.26—0.21, and 0.21—0.09 with $CHCl_3$–MeOH–30% aq. NH_3 (46:4:0.4, v/v) afforded a mixture of 3-(dimethylaminomethyl)-4-iodo-1-methoxy-2-(trimethylsilyl)indole (**20**) and **8a** (30.3 mg), 3-(dimethylaminomethyl)-2-iodo-1-methoxyindole (**21**) (5.3 mg, 11%), and **6** (2.0 mg, 8%), respectively. A mixture of **20** and **8a** was separated by p-TLC on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v). Band of *Rf* 0.56—0.32 gave **20** (22.6 mg, 37%). Band of *Rf* 0.32—0.12 gave **8a** (6.8 mg, recovery, 16%). **20**: colorless oil. IR (film): 2959, 2818, 2780, 1597, 1547, 1459, 1336, 1247, 1148, 1137, 1121, 1033, 1008, 954, 862, 839, 761, 738 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.38 (9H, s), 2.20 (6H, br s), 3.81 (2H, br s), 3.93 (3H, s), 6.78 (1H, br t, *J*=7.7 Hz), 7.29 (1H, d, *J*=7.7 Hz), 7.53 (1H, d, *J*=7.7 Hz). HR-MS *m/z*: Calcd for $C_{15}H_{23}N_2OSiI$: 402.0623. Found: 402.0621. **21**: colorless oil. IR (film): 3074, 2949, 2827, 2784, 1438, 1363, 1339, 1300, 1248, 1179, 1108, 1096, 1040, 1025, 987, 948, 841, 735 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.35 (6H, s), 3.68 (2H, br s), 4.07 (3H, s), 7.09 (1H, ddd, *J*=8.1, 7.1, 0.9 Hz), 7.19 (1H, ddd, *J*=8.1, 7.1, 0.9 Hz), 7.44 (1H, br d, *J*=8.1 Hz), 7.64 (1H, br d, *J*=8.1 Hz). HR-MS *m/z*: Calcd for $C_{12}H_{15}N_2OI$: 330.0229. Found: 330.0215.

[Table 7, Entry 3] — Under Ar atmosphere, *n*-BuLi (1.6 M hexane solution, 0.30 mL, 0.47 mmol, 3.1 mol eq.) was slowly added to a solution of **8a** (42.2 mg, 0.15 mmol) in anhydrous Et_2O (2.5 mL) and refluxed for 1.5 h. A solution of ICH_2CH_2I (133.5 mg, 0.47 mmol, 3.0 mol eq.) in anhydrous Et_2O (2.0 mL) was added at rt and stirred for 1 h. After addition of 10% aq. $Na_2S_2O_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:1:0.1, v/v) as a developing solvent. Extractions of bands having an *Rf* value of 0.53—0.38, 0.38—0.31, and 0.31—0.22 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **20** (22.2 mg, 35%), **8a** (3.2 mg, recovery, 7%), **21** (4.6 mg, 9%), respectively.

[Table 8, Entry 3] — In the general procedure, *n*-BuLi (1.6 M hexane solution, 0.15 mL, 0.24 mmol, 1.7 mol eq.), **8d** (40.0 mg, 0.14 mmol) in anhydrous Et_2O (2.0 mL) were used. After refluxing for 1.5 h, the whole was cooled to –78 °C, and oxygen gas was bubbled into the reaction mixture for 3 h with stirring. After the same work-up and purification as Entry 1, **19** (12.9 mg, 31%) and **8d** (13.1 mg, recovery, 30%) were obtained.

Lithiation of 3-(dimethylaminoethyl)-1-methoxyindole (22) [Table 9, Entry 1] General Procedure — Under Ar atmosphere, *n*-BuLi (1.6 M hexane solution, 0.25 ml, 0.40 mmol, 2.2 mol eq.) was slowly added to a solution of **22** (38.9 mg, 0.18 mmol) in anhydrous Et_2O (2.0 mL) and refluxed for 1.5 h. After addition of anhydrous DMF (0.3 ml, excess) the mixture was stirred at rt for 30 min. Water was added, then the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extractions of bands having an *Rf* value of 0.63—0.47 and 0.47—0.31 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **23** (18.7 mg, 55%) and **24** (7.3 mg, 19%), respectively. **23**: pale yellow oil. IR (film): 2954, 2828, 2733, 1673, 1536, 1532, 1462, 1443, 1381, 1343, 1245, 1180, 1040, 938, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.37 (6H, s), 2.63 (2H, t, *J*=8.1 Hz), 3.26 (2H, t, *J*=8.1 Hz), 4.16 (3H, s), 7.18 (1H, ddd, *J*=8.1, 6.6, 1.3 Hz), 7.44 (1H, ddd, *J*=8.3, 6.6, 1.0 Hz), 7.47 (1H, d, *J*=8.3 Hz), 7.72 (1H, d, *J*=8.1 Hz), 10.15 (1H, s). HR-MS *m/z*: Calcd for $C_{14}H_{18}N_2O_2$: 246.1367. Found: 246.1374. **24**: pale yellow oil. IR (film): 3308, 2957, 2827, 1660, 1573, 1536, 1462, 1330, 1230, 1040, 881, 741 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.42 (6H, s), 2.72 (2H, br t, *J*=8.1 Hz), 3.32 (2H, br t, *J*=8.1 Hz), 7.17 (1H, ddd, *J*=8.2, 4.6, 3.2 Hz), 7.38—7.40 (2H, m), 7.75 (1H, d, *J*=8.2 Hz), 8.57 (1H, br s, D_2O exchange), 10.03 (1H, s). HR-MS *m/z*: Calcd for $C_{13}H_{16}N_2O$: 216.1262. Found: 216.1270.

[Table 9, Entry 2] — In the general procedure for Entry 1, *n*-BuLi (1.6 M hexane solution, 0.16 mL, 0.26 mmol, 1.5 mol eq.), **22** (36.2 mg, 0.17 mmol) in anhydrous THF (1.0 mL), reaction temperature and time, 18 °C and 15 min, and anhydrous DMF (0.1 mL, excess) were employed. After the same work-up and purification as Entry 1, **23** (37.3 mg, 91%) was obtained.

Lithiation of 22 [Scheme 3] — Under Ar atmosphere, *n*-BuLi (1.6 M hexane solution, 0.17 mL, 0.27 mmol, 1.5 mol eq.) was slowly added to a solution of **22** (39.0 mg, 0.18 mmol) in anhydrous THF (1.0 mL) and stirred at –18 °C for 15 min. After addition of TMSCl (0.1 mL, excess), stirring was continued at rt for 1 h. Sat. aq. $NaHCO_3$ was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of band having an *Rf* value of 0.71—0.41 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded 3-(dimethylaminoethyl)-1-methoxy-2-(trimethylsilyl)indole (**26**) (44.5 mg, 86%). **26**: pale yellow brown oil. IR (film): 2962, 2823, 2781, 1503, 1461, 1440, 1334, 1251, 1159, 1128, 1057, 1042, 1012, 840, 756, 737 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 0.44 (9H, s), 2.39 (6H, s), 2.55—2.58 (2H, m), 2.99—3.04 (2H, m), 4.00 (3H, s), 7.08 (1H, dd, *J*=7.8, 7.1 Hz), 7.22 (1H, dd, *J*=8.1, 7.1 Hz), 7.37 (1H, d, *J*=8.1 Hz), 7.59 (1H, d, *J*=7.8 Hz). HR-MS *m/z*: Calcd for $C_{16}H_{26}N_2OSi$: 290.1812. Found: 290.1809.

22 from 26 — *n*-Bu$_4$NF·3H$_2$O (100.0 mg, 0.32 mmol, 1.3 mol eq.) was added to a solution of **26** (68.8 mg, 0.24 mmol) in THF (12.0 mL) and the whole was stirred at rt for 40 min. Water and sat. aq. NaHCO$_3$ were added. The alkaline mixture was extracted with CH$_2$Cl$_2$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na$_2$SO$_4$, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO$_2$ with CHCl$_3$–MeOH–30% aq. NH$_3$ (46:3:0.3, v/v) as a developing solvent. Extractions of the bands having an *Rf* value of 0.65—0.59 and 0.53—0.27 with CHCl$_3$–MeOH–30% aq. NH$_3$ (46:5:0.5, v/v) afforded **26** (3.0 mg, recovery, 4%) and **22** (46.9 mg, 91%), respectively.

2-Trimethylsilylindole (28) from 4d [General Procedure] — A suspended solution of 10% Pd/C (40.8 mg) in MeOH (5.0 mL) was added to a solution of **4d** (39.2 mg, 0.16 mmol) in MeOH (5.0 mL). The whole was stirred under hydrogen at rt and atmospheric pressure for 1 h. After removal of catalyst by filtration, solvent was evaporated. Resultant residue was purified by column-chromatography on Al$_2$O$_3$ with hexane–benzene (3:1, v/v) as an eluent to give **28** (25.7 mg, 86%). **28**: colorless oil. IR (film): 3410. 2950, 1245, 1105, 840, 750 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 0.37 (9H, s), 6.73 (1H, br s), 7.08 (1H, dd, *J*=7.8. 7.0 Hz), 7.17 (1H, dd, *J*=8.2, 7.0 Hz), 7.39 (1H, d, *J*=8.2 Hz), 7.62 (1H, d, *J*=7.8 Hz), 9.90 (1H, s). HR-MS *m/z*: Calcd for $C_{11}H_{15}NSi$: 189.0973. Found: 189.0974.

α,α-Diphenylindole-2-methanol (30) and 2-(diphenylmethyl)indole (31) from 4b; Catalytic hydrogenation of 4b — In the general procedure for catalytic hydrogenation of **4d**, 10% Pd/C (66.2 mg) in MeOH (5.0 mL) and **4b** (187.0 mg, 0.52 mmol) were used. The whole was hydrogenated at rt for 45 min. After the same work-up and purification using CH$_2$Cl$_2$ hexane (1:1) as an eluent, **31** (8.9 mg, 6%) and **30** (150.3 mg, 90%) were obtained. **30**: mp 128—129 °C (colorless needles, recrystallized from Et$_2$O–hexane). IR (KBr): 3480, 3395, 3310, 1489, 1444, 1286, 1168, 1153, 1138, 985, 793, 749, 693 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 2.90 (1H, br s, D$_2$O exchange), 6.11 (1H, dd, *J*=2.2, 0.7 Hz), 6.90—7.29 (13H, m), 7.29—7.58 (1H, m), 8.24 (1H, br s, D$_2$O exchange). MS *m/z*: 299 (M$^+$). *Anal.* Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.19; H, 5.51; N, 4.76. **33**: colorless oil. IR (film): 3400, 3069, 3025, 1602, 1497, 1412, 1139, 1091, 790, 774, 746, 700 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 5.55 (1H, s), 6.05 (1H, s), 6.86—7.36 (13H, m), 7.36—7.52 (1H, m), 7.70 (1H, br s). HR-MS *m/z*: Calcd for $C_{21}H_{17}N$: 283.1360. Found: 283.1362.

Reduction of 29 — In the general procedure for catalytic hydrogenation of **4d**, **29** (86.6 mg, 0.26 mmol), 10% Pd/C (30.0 mg), and MeOH (9.0 mL) were used and reduction was carried out at rt for 3 h. After the same work-up and purification, **30** (57.9 mg, 74%) and **31** (14.0 mg, 19%) were obtained.

2-(Indol-2-yl)propan-2-ol (33), 2-isopropylindole (34), 2-(1-methoxy-1-methylethyl)indole (35) from 4a; Catalytic hydrogenation of 4a — In the general procedure for catalytic hydrogenation of **4d**, 10% Pd/C (22.4 mg) in MeOH (5.0 mL) and **4a** (64.7 mg, 0.27 mmol) were used. The whole was hydrogenated at rt for 15 min. After the same work-up and purification, **34** (1.5 mg, 3%), **35** (4.0 mg, 8%), and **33** (41.7 mg, 87%) were obtained in the order of elution. **33**: mp 105—106 °C (pale brown needles, recrystallized from CH_2Cl_2−hexane). IR (KBr): 3515, 3280, 1459, 1322, 1294, 1163, 1138, 937, 846, 788, 751, 723 cm^{-1}. ^1H-NMR (CD_3OD) δ: 1.63 (6H, s), 6.24 (1H, d, *J*=0.7 Hz), 6.90 (1H, dd, *J*=7.1, 7.1 Hz), 7.00 (1H, dd, *J*=7.1, 7.1 Hz), 7.29 (1H, d, *J*=7.1 Hz), 7.41 (1H, d, *J*=7.1 Hz). MS *m/z*: 175 (M^+). *Anal.* Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.11; H, 7.55; N, 7.71. **35**: mp 119.5—120.5 °C (colorless prisms, recrystallized from CH_2Cl_2−hexane). IR (KBr): 3280, 1456, 1292, 1251, 1233, 1150, 1060, 809, 786, 751, 730 cm^{-1}. ^1H-NMR (CD_3OD) δ: 1.60 (6H, s), 3.06 (3H, s), 6.30 (1H, d, *J*=7.0 Hz), 6.90 (1H, dd, *J*=7.0, 7.0 Hz), 7.03 (1H, dd, *J*=7.0, 7.0 Hz), 7.30 (1H, d, *J*=7.0 Hz), 7.43 (1H, d, *J*=7.0 Hz). MS *m/z*: 189 (M^+). *Anal.* Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.93; H, 8.01; N, 7.99. **34**: mp 74—75 °C (lit.,[9] mp 72—73 °C, colorless plates, recrystallized from CH_2Cl_2−hexane). IR (KBr): 3395, 2965, 1546, 1462, 1410, 1302, 780, 750, 684 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.36 (6H, d, *J*=6.8 Hz), 3.07 (1H, hept, *J*=6.8 Hz), 6.24 (1H, s), 7.06 (1H, dd, *J*=7.7, 7.7 Hz), 7.11 (1H, dd, *J*=7.7, 7.7 Hz), 7.30 (1H, d, *J*=7.7 Hz), 7.53 (1H, d, *J*=7.7 Hz), 7.89 (1H, br s, D_2O exchange). MS *m/z*: 159 (M^+). *Anal.* Calcd for $C_{11}H_{13}N$: C, 82.97; H, 8.23; N, 8.80. Found: C, 82.73; H, 8.26; N, 8.70.

Reduction of 32 — In the general procedure for catalytic hydrogenation of **4d**, **32** (123.0 mg, 0.60 mmol), 10% Pd/C (41.0 mg), and MeOH (10.0 mL) were used and reduction was carried out at rt for 4 h. After the same work-up and purification, **33** (3.4 mg, 4%), **34** (89.2 mg, 85%), and **35** (8.2 mg, 7%) were obtained.

37 and 38 from 4e; Catalytic hydrogenation of 4e — In the general procedure for catalytic hydrogenation of **4d**, 10% Pd/C (17.2 mg) in MeOH (5.0 mL) and **4e** (42.3 mg, 0.21 mmol) were used. After the same work-up and purification, **37** (20.3 mg, 67%) and **38** (8.0 mg, 26%) were obtained in the order of elution. In the similar reaction when hydrogenation time was prolonged to 10 min, **38** was obtained in 96% yield as a sole product. **37**: mp 145—146 °C (lit.,[10] 140—146 °C, colorless plates, recrystallized from MeOH−H_2O). IR (KBr): 3160, 1673, 1526, 1343, 1132, 821, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 7.01—7.31 (2H, m), 7.31—7.52 (2H, m), 7.72 (1H, d, *J*=7.8 Hz), 9.16 (1H, br s), 9.83 (1H, s). MS *m/z*: 145 (M^+). *Anal.* Calcd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.34; H, 4.67; N, 9.50. **38**: mp 72.5—73.5 °C (lit.[9] 75—77 °C, colorless plates, recrystallized from MeOH−H_2O). IR (KBr):

3365, 3230, 1449, 1418, 1293, 1285, 1140, 1059, 1017, 1005, 890, 873, 848, 630, 619, 502 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.77 (2H, s), 6.36 (1H, s), 6.90—7.37 (3H, m), 7.37—7.62 (1H, m), 8.27 (1H, br s). MS *m/z*: 147 (M^+). *Anal.* Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.41; H, 6.15; N, 9.38.

Reduction of 36 — In the general procedure for catalytic hydrogenation of **4d**, **36** (69.9 mg, 0.40 mmol), 10% Pd/C (25.0 mg), and MeOH (7.0 mL) were used and reduction was carried out at rt for 1 h. After the same work-up and purification, **37** (36.1 mg, 62%) and **38** (13.0 mg, 22%) were obtained.

3-(Dimethylaminomethyl)-1-methoxyindole-4-carbaldehyde (39) from 3-(dimethylaminomethyl)-1-methoxy-2-(trimethylsilyl)indole-4-carbaldehyde (9) — *n*-$Bu_4NF·3H_2O$ (31.7 mg, 0.10 mmol, 1.3 mol eq) was added to a solution of **9** (22.8 mg, 0.08 mmol) in THF (5.0 mL) and the whole was stirred at rt for 30 min. Water and sat. aq. $NaHCO_3$ were added. The alkaline mixture was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.47—0.18 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **39** (16.9 mg, 97%). **39**: mp 94—95 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3441, 3120, 2949, 2826, 2773, 1680, 1607, 1562, 1542, 1459, 1438, 1398, 1334, 1302, 1240, 1109, 1018, 961, 906, 856, 790, 761, 746, 678 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.24 (6H, s), 3.64 (2H, br s), 4.11 (3H, s), 7.34 (1H, dd, *J*=8.1, 7.6 Hz), 7.37 (1H, br s), 7.66 (1H, dd, *J*=8.1, 1.0 Hz), 7.78 (1H, dd, *J*=7.6, 1.0 Hz), 10.63 (1H, s). MS *m/z*: 232 (M^+). *Anal.* Calcd for $C_{13}H_{16}N_2O_2·1/8H_2O$: C, 66.56; H, 6.98; N, 11.94. Found: C, 66.80; H, 6.98; N, 11.82.

40 from 39 — A solution of **39** (36.4 mg, 0.16 mmol) in EtOH (50.0 mL) was irradiated under Ar atmosphere with 100W mercury lamp at rt for 40 min with stirring. EtOH was evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.41—0.27 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **40** (9.2 mg, 29%).

Catalytic hydrogenation of 39 — 10% Pd/C (9.3 mg) was added to a solution of **39** (16.8 mg, 0.07 mmol) in MeOH (2.0 mL) and reduction was carried out under H_2 atmosphere with stirring for 4 h. After removal of the catalyst by filtration through Al_2O_3 layer, the filtrate was evaporated. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v). Extractions of the bands having an *Rf* value of 0.80—0.67, 0.53—0.30, and 0.10—0.03 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded 3-(dimethylaminomethyl)-1-methoxyindole-4-methanol (**41**) (2.5 mg, 15%), **42** (5.4 mg, 37%), and **40** (1.2 mg, 8%), respectively. **41**: mp 90—91 °C (colorless prisms, recrystallized from hexane). IR (KBr): 3107, 2945, 2827, 1473, 1361, 1338, 1305, 1248, 1209, 1173, 1113, 1011, 985, 844, 785, 746 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.27 (6H, s), 3.80 (2H, s), 4.07 (3H, s), 4.82 (2H, s), 6.94 (1H, dd, *J*=7.1, 0.9 Hz), 7.15 (1H, dd, *J*=8.3, 7.1 Hz), 7.39 (1H, dd, *J*=8.3, 0.9 Hz), 7.40 (1H, s). MS *m/z*: 234 (M$^+$). *Anal*. Calcd for $C_{13}H_{18}N_2O_2\cdot 1/8H_2O$: C, 66.01; H, 7.78; N, 11.84. Found: C, 66.17; H, 7.62; N, 11.75.

Reduction of 3-(dimethylaminomethyl)-1-methoxy-2-(methylthio)indole-4-carbaldehyde (16) with Raney Nickel [Table 10 Entry 1, From 16]: General Procedure — Raney Ni (2.145 g) was added to a solution of 25.5% aq. NaOH (30.0 mL) and stirred for 30 min. Supernatant solution was removed by decantation and precipitates were washed twice with water and then EtOH. A solution of **16** (53.1 mg, 0.19 mmol) in EtOH (3.0 mL) was added, and the whole was stirred with ultrasonic wave at 0–7 °C for 45 min. The whole was filtered through Al_2O_3 layer to remove Raney Nickel. Evaporation of the filtrate under reduced pressure leave a residue, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) as a developing solvent. Extractions of bands having an *Rf* value of 0.44—0.32, 0.27—0.12, and 0.06—0.01 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **46** (7.4 mg, 24%), **42** (7.9 mg, 20%), and **40** (0.9 mg, trace).

[Table 10 Entry 3, From 16] — In the general procedure with Raney Nickel, 25.5% aq. NaOH (30.0 mL), Raney Ni (516.8 mg), EtOH (4.0 mL), **16** (50.8 mg, 0.18 mmol) in EtOH (3.0 mL). After ultrasonic wave treatment for 1 h at 18–28 °C and the same work-up and purification, 3-(dimethylaminomethyl)-1-methoxy-2-(methylthio)indole-4-methanol (**43**) (trace), **16** (31.6 mg, recovery, 62%), **42** (3.7 mg, 10%), and **40** (4.0 mg, 11%) were obtained. **43**: mp 66—67 °C (colorless prisms, recrystallized from Et_2O–hexane). IR (KBr): 2954, 2860, 2824, 2799, 1470, 1457, 1442, 1424, 1370, 1342, 1304, 1289, 1213, 1179, 1133, 1100, 1032, 1002, 983, 823, 781, 748 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.33 (6H, s), 2.41 (3H, s), 4.00 (2H, br s), 4.12 (3H, s), 4.83 (2H, br s), 7.01 (1H, d, *J*=7.1 Hz), 7.20 (1H, dd, *J*=8.4, 7.1 Hz), 7.36 (1H, d, *J*=8.4 Hz). MS *m/z*: 280 (M$^+$). *Anal*. Calcd for $C_{14}H_{20}N_2O_2S\cdot 1/4H_2O$: C, 59.02; H, 7.25; N, 9.83. Found: C, 59.35; H, 7.08; N, 9.76.

Reduction of 2-(*sec*-butylthio)-3-(dimethylaminomethyl)-1-methoxyindole-4-carbaldehyde (18) with Raney Nickel [Table 10, Entry 1, From 18] — In the general procedure from **16** with Raney Nickel, 25.5% aq. NaOH (30.0 mL), Raney Ni (1.0473 g), EtOH (4.0 mL) and **18** (52.0 mg, 0.16 mmol) in EtOH (2.5 mL) were used. After ultrasonic wave treatment for 30 min at 7–18 °C and the same work-up, the resultant residue was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extractions of bands in the order of having large *Rf* value, 2-(*sec*-butylthio)-3-(dimethylaminomethyl)-1-methoxyindole-4-methanol (**44**, 2 mg, 4 %), 2-(*sec*-butylthio)-3-(dimethylaminomethyl)indole-4-methanol (**45**, 4.1 mg, 9%), **18** (3.8 mg, recovery, 7%), **46** (3.7 mg, 14%), **42** (8.0 mg, 24%), and **40** (1.0 mg, 3%) were obtained. **44**: pale yellow oil. IR (film): 3154, 2965, 2948, 2864, 2823, 2778, 1462, 1368, 1341, 1216, 1181, 1137, 1103, 1029, 1003, 961, 843, 784, 751 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.02 (3H, t, *J*=7.4 Hz), 1.21 (3H, d, *J*=6.8 Hz), 1.52 (1H, sept, *J*=6.8 Hz), 1.63 (1H, ddq, *J*=13.9, 7.4, 6.8 Hz), 2.34 (6H, s), 3.26 (1H, sext, *J*=6.8 Hz), 4.02 (1H, br d, *J*=13.5 Hz), 4.06 (1H, br d, *J*=13.5 Hz), 4.10 (3H, s), 4.83 (1H, br d, *J*=11.5 Hz), 4.88 (1H, br d, *J*=11.5 Hz), 7.01 (1H, d, *J*=7.3 Hz), 7.22 (1H, dd, *J*=8.1, 7.3 Hz), 7.36 (1H, d, *J*=8.1 Hz), 8.70 (1H, br s, D_2O exchange). HR-MS *m/z*: Calcd for $C_{17}H_{26}N_2O_2S$: 322.1713. Found: 322.1713. **45**: mp 177—178 ℃(colorless prisms, recrystallized from MeOH). IR (KBr): 3158, 2981, 2933, 2876, 2852, 2831, 2786, 1439, 1368, 1339, 1279, 1248, 1210, 1179, 1049, 1001, 840, 793, 751 cm^{-1}. ^1H-NMR (CD_3OD) δ: 1.03 (3H, t, *J*=7.4 Hz), 1.22 (3H, d, *J*=6.7 Hz), 1.52 (1H, ddq, *J*=13.3, 7.4, 6.7 Hz), 1.63 (1H, ddq, *J*=13.3, 7.4, 6.7 Hz), 2.32 (6H, s), 3.14 (1H, sext, *J*=6.7 Hz), 4.10 (2H, br s), 4.85 (2H, s), 6.90 (1H, dd, *J*=7.1, 0.9 Hz), 7.07 (1H, dd, *J*=8.2, 7.1 Hz), 7.30 (1H, dd, *J*=8.2, 0.9 Hz). MS *m/z*: 292 (M^+). *Anal.* Calcd for $C_{16}H_{24}N_2OS\cdot 1/6H_2O$: C, 65.05; H, 8.30; N, 9.48. Found: C, 65.09; H, 8.42; N, 9.13.

3-(Dimethylaminomethyl)-1-methoxy-2-(methylthio)indole-4-methanol (43) from 16 — $NaBH_4$ (20.0 mg, 0.54 mmol, 4.5 mol eq.) was added to a solution of **16** (34.1 mg, 0.12 mmol) in MeOH (2.0 mL) and stirred at rt for 30 min. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.59—0.29 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) afforded **43** (27.4 mg, 80%).

2-(*sec*-Butylthio)-3-(dimethylaminomethyl)-1-methoxyindole-4-methanol (44) from 18 — $NaBH_4$ (35.0 mg, 0.93 mmol, 3.6 mol eq.) was added to a solution of **18** (82.7 mg, 0.26 mmol) in MeOH (2.0 mL) and stirred at rt for 1 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.77–0.44 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) afforded **44** (69.8 mg, 84%).

2-(*sec*-Butylthio)-3-(dimethylaminomethyl)indole-4-methanol (45) from 44 — A solution of **44** (22.7 mg, 0.07 mmol) in EtOH (50.0 mL) was irradiated under Ar atmosphere with 100W mercury lamp at rt for 10 min with stirring. EtOH was evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46:3:0.3, v/v) as a developing solvent. Extractions of the bands having an *Rf* value of 0.88–0.77 and 0.68–0.65 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **44** (2.3 mg, recovery, 10%) and **45** (4.1 mg, 20%), respectively.

40 from indole-4-carbaldehyde (47) — 37% aq. HCHO (38.0 mg, 0.44 mmol, 1.2 mol eq) was added to a solution of 50% aq. $NHMe_2$ (49.8 mg, 0.55 mmol, 1.5 mol eq) in AcOH (1.0 mL) and then a solution of

47 (50.7 mg, 0.35 mmol) in AcOH (2.0 mL) was added with stirring at rt. After making the reaction mixture alkaline by adding 8% NaOH solution, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on Al_2O_3 with CH_2Cl_2–MeOH (95:5, v/v). Extraction of the band having an *Rf* value of 0.40–0.03 with $CHCl_3$–MeOH–30% aq. NH_3 (46:5:0.5, v/v) afforded **56** (52.3 mg, 72%).

3-(Dimethylaminomethyl)indole-4-methanol (41) from 40 — $NaBH_4$ (39.2 mg, 1.00 mmol, 4.9 mol eq) was added to a solution of **40** (41.8 mg, 0.21 mmol) in MeOH (2.0 mL) and stirred at rt for 20 min. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The resultant residue was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–30% aq. NH_3 (46: 5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.77—0.44 with $CHCl_3$–MeOH–30% aq. NH_3 (46: 5:0.5, v/v) afforded **41** (31.5 mg, 75%).

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