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REDUCTIVE CYCLIZATION OF 3-CYANOMETHYLOXINDOLES TO HEXAHYDRO-2-OXOPYRROLO[2,3-*b*]INDOLES WITH LITHIUM ALUMINUM HYDRIDE

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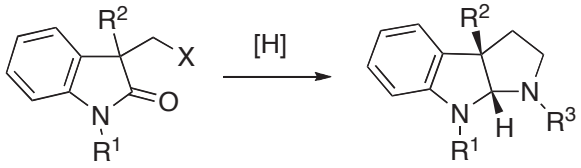
Abstract – Reduction of 3-cyanomethyloxindoles with lithium aluminum hydride at low temperature proceeded smoothly with cyclization to afford hexahydro-2-oxopyrrolo[2,3-*b*]indoles.

INTRODUCTION

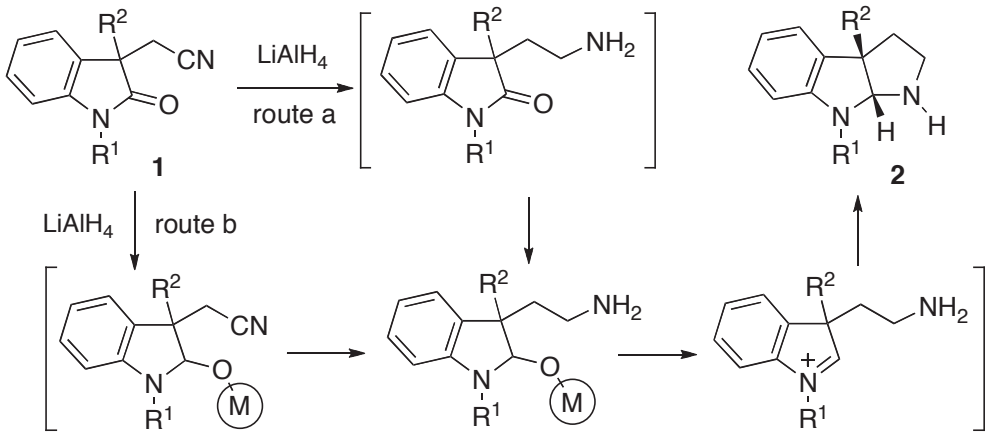
The hexahydropyrrolo[2,3-*b*]indole alkaloids constitute a large family of natural products.[1] The reductive cyclization of oxindoles possessing a C_2N unit such as 2-aminoethyl,[2,3] 2-azidoethyl,[4] 2-hydrazonoethyl,[5] carbamoylmethyl,[6-7] and cyanomethyl groups[8-10] at the C3 position are useful for constructing the pyrroloindole framework (Scheme 1). Among them, the reduction of 3-cyanomethyloxindoles **1** with $LiAlH_4$ under heating conditions is a convenient and efficient route to hexahydropyrroloindoles **2**.[10] This reaction could conceivably proceed through any of the following route: a) an initial reduction of the cyano group to an amino group followed by a second reduction of the lactam moiety to aminal, and cyclization to pyrroloindole, or b) the contrary reductive way (Scheme 2). In our synthetic studies of pyrroloindole alkaloids,[11] we have also utilized this methodology. To date, we have found that the $LiAlH_4$ reduction of 3-cyanomethyloxindoles **1** at low temperature proceeds



X = CH_2NHR^3, CH_2N_3, $CH{=}NNR_2$, $CONHR^3$, CN

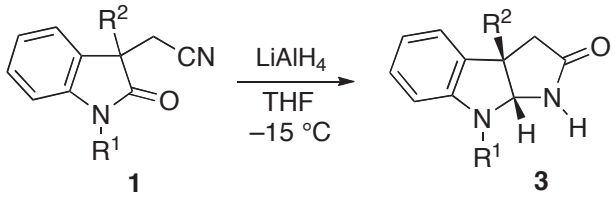
Scheme 1. Reductive cyclization of oxindoles possessing a C_2N unit

This paper is dedicated to Dr. Albert Eschenmoser on the occasion of his 85th birthday.



Scheme 2. Ambiguous routes of $LiAlH_4$-reductive cyclization: M = Li or Al

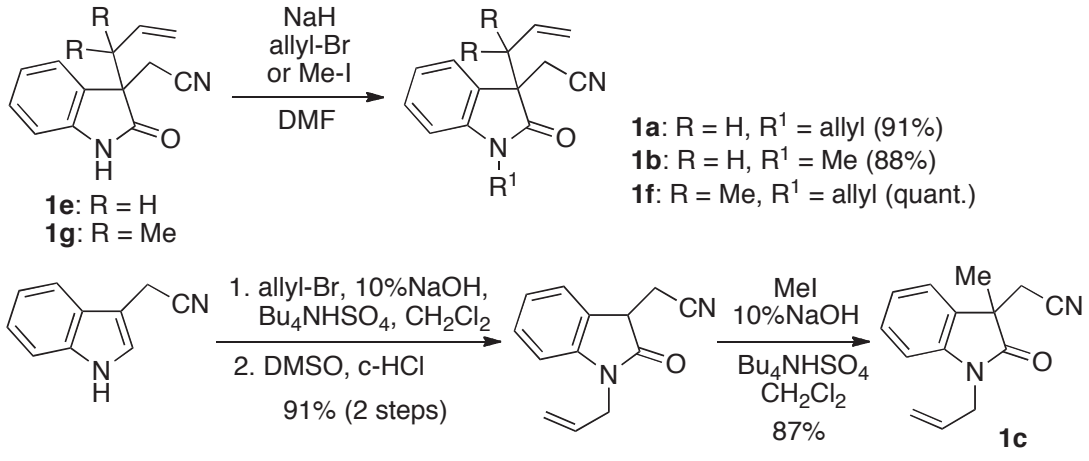
smoothly to provide hexahydro-2-oxopyrroloindoles **3** (Scheme 3) and that, contrary to the above considerations, the reductive cyclization of **1** to **2** includes the reduction process of **3**. In this paper, we describe a new $LiAlH_4$-reductive cyclization of oxindoles **1** to 2-oxopyrroloindoles **3**.



Scheme 3. $LiAlH_4$-Reductive cyclization at low temperature

RESULTS AND DISCUSSION

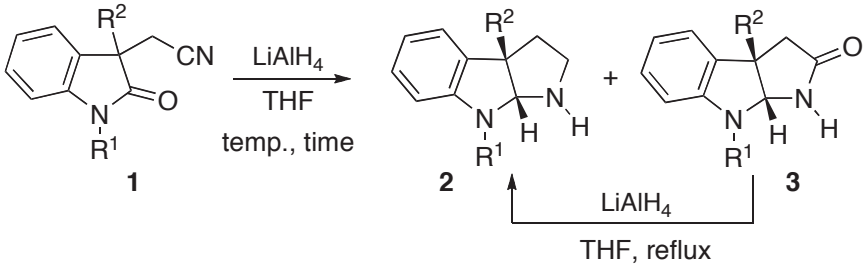
3-Cyanomethyloxindoles **1a**, **1b**, and **1f** were obtained by *N*-alkylation of **1e** and **1g**, which were prepared according to our synthetic methods, respectively (Scheme 4).[11d] Oxindole **1c** was prepared from



Scheme 4. Preparation of oxindoles **1a-c**, **1f**

commercially available 3-cyanomethylindole by allylation, oxidation, and methylation, and **1d** was obtained according to the reported method.[9]

Next we attempted the reduction of compounds **1a-g** with $LiAlH_4$ in THF under several conditions (Scheme 5, Table 1). We initially performed the ordinary reduction of **1a** with $LiAlH_4$ in THF under reflux conditions for 10 min to obtain the corresponding pyrroloindole **2a** in 60% yield (entry 1). When $LiAlH_4$-reduction of **1a** was carried out at room temperature, 2-oxopyrroloindole **3a** was formed in 11% yield together with **2a** (68%) (entry 2). On treatment at the lower temperature (–15 °C) for 10 min, the starting compound was remained, but the formation of **3a** was increased (entry 3). Furthermore, a prolonged reaction (1.5 h) under the same temperature provided **3a** (64%) in preference to **2a** (5%) (entry 4). Reduction of **3a** with $LiAlH_4$ under reflux conditions gave **2a** (89%).[12] These results indicate that **3a** is an intermediate in the $LiAlH_4$-reductive cyclization of **1a** to **2a**.



Scheme 5. $LiAlH_4$-Reductive cyclization

Table 1. Reduction of 3-cyanomethyloxindoles **1a-g** with $LiAlH_4$ in THF

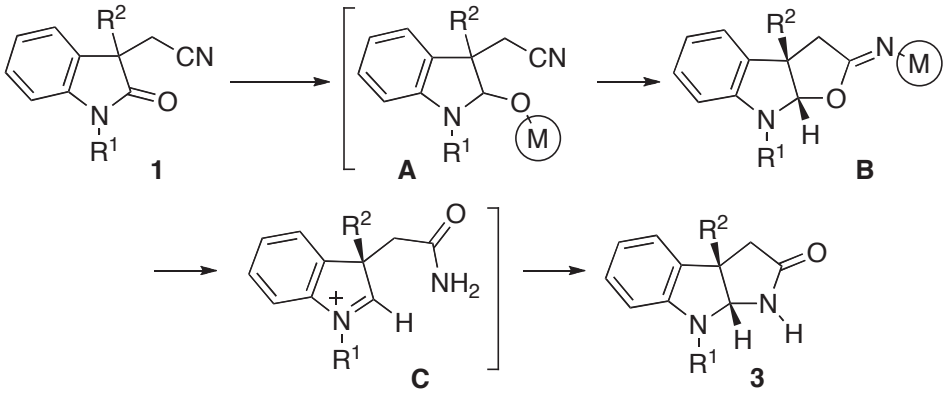
				reaction		yield (%)	
entry	**1**	R^1	R^2	temp. (°C)	time (min)	**2**	**3**
1	**1a**	allyl	allyl	reflux	10	60	-
2	**1a**	allyl	allyl	r.t.	10	68	11
3	**1a**	allyl	allyl	–15	10	2	53[a]
4	**1a**	allyl	allyl	–15	1.5 h	5	64
5	**1b**	Me	allyl	–15	5	-	64[a]
6	**1c**	allyl	Me	–15	5	-	80
7	**1d**	Me	Me	–15	5	-	79[a]
8	**1e**	H	allyl	–15	1.5 h	-	-[b]
9	**1e**	H	allyl	reflux	3.5 h	54	-
10	**1f**	allyl	*t*-pentenyl	reflux	5 h	28	-
11	**1g**	H	*t*-pentenyl	reflux	20 h	46	-

a) Recovered starting oxindole: **1a** (27%), **1b** (10%), **1d** (24%). b) No reaction.

To the best of our knowledge, this is the first example of the formation of 2-oxopyrroloindole **3** in $LiAlH_4$-reduction, thus we attempted the reduction of **1b-d** at –15 °C for 5 min to give the same results in the formation of **3b-d** in good yields, respectively (entries 5-7). In the case of R^1 = H, the desired

reduction of **1e** at −15 °C did not occurred at all, but the high-temperature reaction afforded **2e** in 54% yield (entries 8, 9). The reduction of **1f** and **1g** both possessing a bulky substituent at the C3 site required prolonged heating to give the corresponding **2f** and **2g** [13] (entries 10, 11). The low-temperature reductive cyclization of **1** to **3** is affected by the bulkiness of the C3-substituent and the presence of NH of the lactam moiety.

The formation of **3** is explained by the initial reduction of the lactam moiety of **1** to the aminal intermediate **A**. Once the aminal **A** cyclizes to form the furan ring **B**, the ring opening generates the iminium species **C** followed by cyclization of the amide moiety to **3** (Scheme 6).



Scheme 6. Possible route of $LiAlH_4$-reductive cyclization of **1** to **3**: M = Li or Al

In summary, we developed a method for the preparation of 2-oxopyrroloindole **3** by $LiAlH_4$-reductive cyclization of oxindoles **1** at low temperature, and demonstrated that **3** is an intermediate in the high-temperature reduction to pyrroloindole **2**.

EXPERIMENTAL

General. ^{1}H-NMR spectra were obtained using a JEOL JNM-EX-300, or JNM-EX-400 spectrometer with tetramethylsilane as an internal standard. *J*-Values are given in Hz. Mass spectra were obtained using a JEOL JMS-DX302 or JMS-700 instrument with a direct inlet system operating at 70 eV. IR spectra were recorded with a Shimadzu FTIR-8100 spectrophotometer. All mp values are uncorrected, and were measured on a Yanagimoto micromelting point apparatus. Elemental analyses were obtained using a Yanaco CHN Corder MT-6 elemental analyzer. Column chromatography was carried out on silica gel (Kanto Chemical Co. Inc., Silica Gel 60N, 100-200 mesh and Merck, Silica Gel 60, 230-400 mesh).

General Alkylation Procedure

To a suspension of NaH (60%) (16.5 mmol) in dry DMF (30 mL) was added a solution of the corresponding oxindole **1e** or **1g** (15 mmol) in dry DMF (20 mL) at 0 °C, and then the stirring mixture

was warmed up to room temperature to keep at the same temperature for 1 h. After cooling to 0 °C, alkyl halide (16.5 mmol) was added to the resulted mixture. After 15 min., the reaction mixture was quenched with water (300 mL), and the mixture was extracted with diethyl ether. The extract was washed with brain, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography with EtOAc-hexane (1 : 1 – 5) to afford the alkylated product **1a** (91%),[14] **1b** (88%)[11d] or **1f** (quant. yield), respectively.

1-Allyl-3-cyanomethyl-3-*t*-pentenyloxindole (1f)

Prepared from **1g** as colorless crystals; mp 99-100 °C (AcOEt); IR ($CHCl_3$) ν 2252, 1707, 1612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (3H, s), 1.15 (3H, s), 2.86 (1H, d, *J* = 16.4 Hz), 3.01 (1H, d, *J* = 16.4 Hz), 4.29 (1H, tdd, *J* = 16.4, 5.4, 1.2 Hz), 4.47 (1H, tdd, *J* = 16.4, 5.4, 1.2 Hz), 5.09 (1H, d, *J* = 17.6 Hz), 5.20 (1H, d, *J* = 10.7 Hz), 5.23 (1H, qd, *J* = 10.3, 1.2 Hz), 5.29 (1H, qd, *J* = 17.1, 1.2 Hz), 5.82 (1H, tdd, *J* = 17.1, 10.3, 5.4 Hz), 6.06 (1H, dd, *J* = 17.6, 10.7 Hz), 6.88 (1H, d, *J* = 7.8 Hz), 7.09 (1H, td, *J* = 7.8, 1.0 Hz), 7.32 (1H, d, *J* = 7.8 Hz), 7.34 (1H, td, *J* = 7.8, 1.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.1, 22.1, 41.8, 42.6, 54.8, 109.2, 115.0, 116.6, 117.8, 122.1, 125.3, 127.5, 129.0, 130.8, 141.9, 143.4, 175.7; MS (EI) *m*/*z* (%) 280 (M^+, 6), 212 (100), 185 (45), 69 (33), 41 (15). Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.04; H, 7.45; N, 10.02.

Preparation of 1-Allyl-3-cyanomethyl-3-methyloxindole (1c)

A mixture of 3-cyanomethylindole (3.0 g, 19.2 mmol), allyl bromide (2.49 mL, d = 1.398, 28.8 mmol), 10% NaOH (20 mL), and tetrabutylammoniun hydrosulfate (1.3 g, 3.84 mmol) in CH_2Cl_2 (60 mL) was stirred at room temperature. After consumption of the starting indole, the resulted mixture was extracted with CH_2Cl_2, and the extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with EtOAc-hexane (1 : 4) to give 1-allyl-3-cyanomethylindole (3.43 g, 91%) as a pale yellow oil; IR ($CHCl_3$) ν 2251, 1645, 1616 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (2H, s), 4.68 (2H, d, *J* = 5.3 Hz), 5.09 (1H, dd, *J* = 17.0, 1.1 Hz), 5.21 (1H, dd, *J* = 10.2, 1.1 Hz), 5.96 (1H, ddt, *J* = 17.0, 10.2, 5.3 Hz), 7.07 (1H, s), 7.16 (1H, t, *J* = 7.8 Hz), 7.25 (1H, t, *J* = 7.8 Hz), 7.31 (1H, d, *J* = 7.8 Hz), 7.56 (1H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 48.8, 103.4, 110.0, 117.7, 118.18, 118.22, 119.8, 122.4, 126.3, 126.6, 133.0, 136.5. HRMS (EI) *m*/*z* 196.1004 (M^+, $C_{13}H_{12}N_2$ requires 196.1000).

To a solution of 1-allyl-3-cyanomethylindole (3.0 g, 15.3 mmol) in DMSO (5.25 mL) was gradually added concentrated HCl (35 mL) at 0 °C. After stirring at room temperature for 4 h, the reaction mixture was diluted with water (10 mL), neutralized with K_2CO_3 (powder), and extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with EtOAc-hexane (1 : 1) to give 1-allyl-3-cyanomethyloxindole (3.24 g, quant. yield) as a pale yellow oil; IR ($CHCl_3$) ν 2253, 1714,

1647, 1614 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (1H, dd, *J* = 16.9, 8.8 Hz), 3.13 (1H, dd, *J* = 16.9, 4.7 Hz), 3.71 (1H, dd, *J* = 8.8, 4.7 Hz), 4.36 (2H, d, *J* = 5.3 Hz), 5.23 (1H, d, *J* = 10.5 Hz), 5.25 (1H, d, *J* = 15.5 Hz), 5.85 (1H, ddt, *J* = 15.5, 10.5, 5.3 Hz), 6.88 (1H, d, *J* = 7.8 Hz), 7.13 (1H, t, *J* = 7.8 Hz), 7.33 (1H, t, *J* = 7.8 Hz), 7.51 (1H, d, *J* = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 41.3, 42.5, 109.5, 117.0, 117.9, 123.0, 124.2, 125.5, 129.2, 130.7, 143.3, 173.9. HRMS (EI) *m*/*z* 212.0948 (M^+, $C_{13}H_{12}N_2O_2$ requires 212.0950).

A mixture of 1-allyl-3-cyanomethyloxindole (3.0 g, 14.1 mmol), methyl iodide (1.30 mL, d = 2.317, 21.2 mmol), 10% NaOH (20 mL), and tetrabutylammoniun hydrosulfate (0.96 g, 2.83 mmol) in CH_2Cl_2 (60 mL) was stirred at room temperature. After consumption of the starting oxindole, the resulted mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with EtOAc-hexane (2 : 3) to give **1c** (3.20 g, 87%) as a pale yellow oil; IR ($CHCl_3$) ν 2251, 1715, 1647, 1614 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (3H, s), 2.60 (1H, d, *J* = 16.5 Hz), 2.86 (1H, d, *J* = 16.5 Hz), 4.32 (1H, ddt, *J* = 14.7, 5.2, 1.8 Hz), 4.39 (1H, ddt, *J* = 14.7, 5.2, 1.8 Hz), 5.22 (1H, dt, *J* = 17.4, 1.8 Hz), 5.23 (1H, dt, *J* = 10.8, 1.8 Hz), 5.86 (1H, ddt, *J* = 17.4, 10.8, 5.2 Hz), 6.90 (1H, d, *J* = 7.5 Hz), 7.13 (1H, t, *J* = 7.5 Hz), 7.34 (1H, t, *J* = 7.5 Hz), 7.47 (1H. d, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 26.3, 42.4, 44.8, 109.5, 116.5, 117.7, 123.06, 123.13, 129.0, 130.8, 130.9, 141.8, 177.2. MS (EI) *m*/*z* (%) 226 (M^+, 64), 186 (100). 158 (10), 143 (8), 130 (14). HRMS (EI) *m*/*z* 226.1111 (M^+, $C_{14}H_{14}N_2O$ requires 226.1106).

General Reductive Cyclization Procedure

To a solution of 3-cyanomethyloxindole **1** (1.86 mmol) in dry THF (1.6 mL) was added $LiAlH_4$ (powder 95%, 18.6 mmol). The mixture was stirred at the corresponding reaction temperature for the desired period (Table 1), quenched with THF-H_2O (1 : 1), and filtrated through Cerite. The filtrate was washed with sat. aq. Na_2CO_3, and the aqueous layer was extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with EtOAc-hexane (1 : 1) to give the corresponding **2** and/or **3**. The products **2e**, **2g**, and **3d** were confirmed by direct comparison to these spectral data with that of the authentic samples.[11d, 14b]

3a,8-Diallyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (2a)

A colorless oil; IR ($CHCl_3$) ν 1639, 1605 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91 (1H, ddd, *J* = 11.1, 10.8, 6.8 Hz), 1.99 (1H, ddd, *J* = 11.1, 5.7, 1.8 Hz), 2.22 (1H, br), 2.43 (1H, dd, *J* = 13.9, 8.2 Hz), 2.60 (1H, ddt, *J* = 13.9, 8.2, 1.3 Hz), 2.73 (1H, td, *J* = 10.8, 5.7 Hz), 3.00 (1H, ddd, *J* = 10.8, 6.8, 1.8 Hz), 3.78-3.91 (2H, m), 4.74 (1H, s), 5.00-5.09 (2H, m), 5.13 (1H, dq, *J* = 10.2, 1.6 Hz), 5.22 (1H, dq, *J* = 17.0, 1.6 Hz), 5.68 (1H, dddd, *J* = 16.5, 10.1, 8.1, 6.2 Hz), 5.85 (1H, ddt, *J* = 17.0, 10.2, 5.3 Hz), 6.30 (1H, d, *J*

= 7.5 Hz), 6.61 (1H, t, *J* = 7.5 Hz), 6.99-7.05 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.3, 43.8, 45.4, 47.8, 56.0, 87.2, 105.1, 116.2, 116.6, 117.6, 123.2, 127.7, 133.6, 134.4, 134.9, 150.7. MS (EI) *m*/*z* (%) 240 (M^+, 100), 199 (76), 182 (38), 170 (31), 158 (35), 130 (14). HRMS (EI) *m*/*z* 240.1629 (M^+, $C_{16}H_{20}N_2$ requires 240.1626).

3a,8-Diallyl-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-2(1*H*)-one (3a)

White powder; mp 121-124 °C (AcOEt/hexane); IR ($CHCl_3$) ν 3426, 3204, 1694, 1641, 1607 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.47 (1H, dd, *J* = 14.1, 7.8 Hz), 2.54 (1H, dd, *J* = 14.1, 7.8 Hz), 2.65 (2H, s), 3.78-3.90 (2H, m), 5.00 (1H, s), 5.02-5.11 (2H, m), 5.23 (1H, dq, *J* = 10.2, 1.5 Hz), 5.34 (1H, dq, *J* = 17.4, 1.5 Hz), 5.66 (1H, m), 5.95 (1H, ddt, *J* = 17.4, 10.2, 5.7 Hz), 6.06 (1H, br), 6.47 (1H, d, *J* = 7.5 Hz), 6.75 (1H, t, *J* = 7.5 Hz), 7.06 (1H, d, *J* = 7.5 Hz), 7.13 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.0, 42.8, 48.5, 51.4, 81.3, 107.3, 117.8, 118.4, 119.1, 123.4, 128.7, 132.9, 133.5, 133.7, 148.6, 176.9. MS (EI) *m*/*z* (%) 254 (M^+, 99), 213 (100), 170 (29). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.57; H, 7.30; N, 10.97.

3a-Allyl-8-methyl-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-2(1*H*)-one (3b)

Colorless crystals; mp 124-126 °C (AcOEt/hexane). IR ($CHCl_3$) ν 3428, 3202, 1693, 1639, 1607 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49 (1H, dd, *J* = 14.1, 8.1 Hz), 2.53 (1H, dd, *J* = 14.1, 7.5 Hz), 2.65 (2H, s), 2.85 (3H, s), 4.95 (1H, s), 5.08-5.16 (2H, m), 5.69 (1H, dddd, *J* = 17.0, 10.0, 8.1, 7.5 Hz), 6.42 (1H, d, *J* = 7.5 Hz), 6.73 (1H, t, *J* = 7.5 Hz), 7.04 (1H, d, *J* = 7.5 Hz), 7.17 (1H, t, *J* = 7.5 Hz), 7.18 (1H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.8, 42.0, 42.4, 51.6, 82.9, 107.1, 118.4, 119.2, 123.3, 128.9, 133.0, 133.5, 149.4, 176.9. MS (EI) *m*/*z* 228 (M^+, 100), 187 (95), 160 (20), 144 (36). HRMS (EI) *m*/*z* 228.1260 (M^+, $C_{14}H_{16}N_2O$ requires 228.1263). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.50; H, 7.06; N, 12.18.

8-Allyl-3a-methyl-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-2(1*H*)-one (3c)

White powder; mp 147-148 °C (AcOEt/hexane); IR ($CHCl_3$) ν 3428, 1695, 1643, 1607 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (3H, s), 2.52 (1H, d, *J* = 17.0 Hz), 2.73 (1H, d, *J* = 17.0 Hz), 3.81 (1H, ddt, *J* = 15.8, 6.2, 1.2 Hz), 3.89 (1H, ddt, *J* = 15.8, 6.2, 1.2 Hz), 4.90 (1H, s), 5.21 (1H, dq, *J* = 10.1, 1.2 Hz), 5.33 (1H, dq, *J* = 17.0, 1.2 Hz), 5.92 (1H, ddt, *J* = 17.0, 10.1, 6.2 Hz), 6.45 (1H, d, *J* = 7.5 Hz), 6.74 (1H, t, *J* = 7.5 Hz), 7.05 (1H, d, *J* = 7.5 Hz), 7.10 (1H, t, *J* = 7.5 Hz), 7.15 (1H, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 44.0, 48.1, 48.7, 84.0, 107.3, 117.9, 118.6, 122.7, 128.6, 133.8, 135.1, 148.1, 177.0. MS (EI) *m*/*z* 228 (M^+, 100), 201 (14), 184 (39), 170 (21), 144 (10). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.85; H, 7.23; N, 12.31.

8-Allyl-1,2,3,3a,8,8a-hexahydro-3a-(2-methylbut-3-en-2-yl)pyrrolo[2,3-*b*]indole (2f)

A colorless oil; IR ($CHCl_3$) ν 1635, 1601 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (3H, s), 1.11 (3H, s), 1.87 (1H, ddd, *J* = 11.7, 5.1, 0.7 Hz,), 1.97 (1H, br), 2.08 (1H, ddd, *J* = 11.7, 11.4, 7.0 Hz), 2.55 (1H, ddd,

J = 11.4, 11.0, 5.1 Hz), 2.97 (1H, ddd, *J* = 11.0, 7.0, 0.7 Hz), 3.82 (1H, tdd, *J* = 16.5, 4.9, 1.7 Hz), 3.90 (1H, tdd, *J* = 16.5, 5.6, 1.4 Hz), 4.77 (1H, s), 5.02 (1H, dd, *J* = 17.4, 1.2 Hz), 5.08 (1H, dd, *J* = 10.7, 1.2 Hz), 5.14 (1H, qd, *J* = 10.3, 1.4 Hz), 5.25 (1H, qd, *J* = 17.1, 1.7 Hz), 5,87 (1H, dddd, *J* = 17.1, 10.3, 5.6, 4.8 Hz), 6.01 (1H, dd, *J* = 17.4, 10.7 Hz), 6.28 (1H, d, *J* = 7.5 Hz), 6.57 (1H, td, *J* = 7.5, 1.0 Hz), 7.04 (1H, td, *J* = 7.5, 1.0 Hz), 7.11 (1H, 1d, *J* = 7.5, 1.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 23.6, 37.6, 41.3, 46.2, 47.6, 63.5, 84.9, 104.5, 113.0, 115.9, 116.0, 124.8, 127.7, 131.8, 134.5, 144.9, 151.3. MS (EI) *m*/*z* 268 (M^+, 22), 199 (100), 158 (26). HRMS (EI) *m*/*z* 268.1941 (M^+, $C_{18}H_{24}N_2$ requires 268.1939).

Reduction of 3a with $LiAlH_4$ to 2a

A suspension of 2-oxopyrroloindole **3a** (10.4 mg, 0.041 mmol) and $LiAlH_4$ (powder 92%, 16.9 mg, 0.41 mmol) in dry THF (410 μmL) was heated under reflux for 1.5 h. The reaction mixture was allowed to treat in the same manner as the reductive protocol described above to give pyrroloindole **2a** (8.7 mg, 89%).

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