

Regioselective *N*-Methylation of 6-Chloroindolo[3,2-*c*]quinolines and Their Amination Reactivity at the C-6 Position

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The treatment of 6-chloroindolo[3,2-*c*]quinoline **6** with NaH–MeI led to methylation at N-11, forming **8**, while the reaction of **6** with MeI with heating gave the corresponding 5-methylated quinolinium salt whose S_NAr with water smoothly proceeded to form 5-methylindolo[3,2-*c*]quinolin-6-one **3b**. The amination reactivity at the C-6 was assigned in the order of **6** > 11-methylated **8**.

The roots of the climbing shrub *Cryptolepis sanguinolenta* growing naturally in Central and West Africa are used as a traditional herb medicine for the treatment of malaria and other health disorders.[1] Various indoloquinoline alkaloids, such as cryptolepine (5-methyl-5*H*-indolo[3,2-*b*]quinoline, **i**), neocryptolepine (5-methyl-5*H*-indolo[2,3-*b*]quinoline, **ii**), and isocryptolepine (5-methyl-5*H*-indolo[3,2-*c*]quinoline, **iii**) are found in the decoctions of the root of this plant (Figure 1).[2] These alkaloids are known for their potent antimalarial and anticancer activities. Besides having an aromatic tetracyclic arrangement with indole and quinoline units, another structural characteristic of these alkaloids is the *N*-Me group on the quinoline ring. Structure–activity relationship (SAR) studies using these indoloquinoline motifs indicated that their biological properties were significantly affected by the presence and the position of the *N*-Me group on the indoloquinoline core. For example, Kirby et al.[3] and Cimanga et al.[4] reported that cryptolepine (**i**) showed antiplasmodial activity, while quindoline, the N-5 demethylated derivative of **i**, was less active. Pieters et al. later reported that removal of the *N*-methyl group from the neocryptolepine (**ii**) core led to the complete loss of the antiplasmodial activity in the tested concentration range.[5] Furthermore, we found that the antiproliferative activities of the neocryptolepine derivatives were higher than the corresponding *N*-6 methyl congeners.[6] Accordingly, the regioselective introduction of a methyl group on the nitrogen atom is an important task in SAR study using these indoloquinoline families for better biological activities.

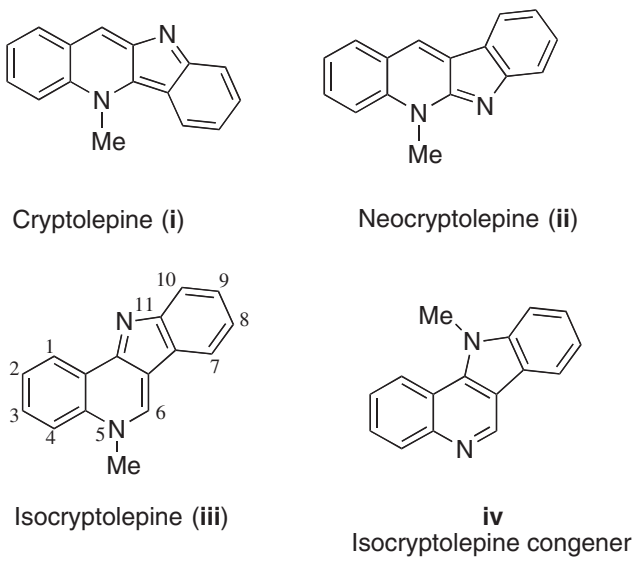

Figure 1. Some indoloquinolines **i**–**iii** from the African plant *Cryptolepis sanguinolenta* and isocryptolepine congener **iv**.

The recent increasing demand for the development of new anticancer agents stimulated molecular pharmacologists to apply these indoloquinolines as lead drugs of natural origin.[7] Among the three indoloquinolines, limited attention has been paid to the synthesis and biological evaluation of the derivatives of isocryptolepine (**iii**). Chen reported that the 6-anilino-11*H*-indolo[3,2-*c*]quinoline derivatives for in vitro antiproliferative evaluation against a 3-cell line panel consisting of MCF7 (Breast), NCI-H460 (Lung), and SF-268 (CNS), showed the mean GI_{50} value of 1.7–1.35 μM with the most active ones.[8] Tzeng reported the synthesis of 6-alkylamino-11*H*-indolo[3,2-*c*]quinolines and their twin derivatives for their antiproliferative activity against several cancer cells.[9]

In our ongoing program to find anticancer and antimalarial agents using derivatives of **ii**[10] and **iii** as a lead originating in plants, we attempted the regioselective *N*-methylation of the 6-substituted indolo[3,2-*c*]quinolines. In this paper, we report the synthetic access to the derivatives of 11-methylindolo-[3,2-*c*]quinoline, i.e., **iv**, and the introduction of an alkyl-

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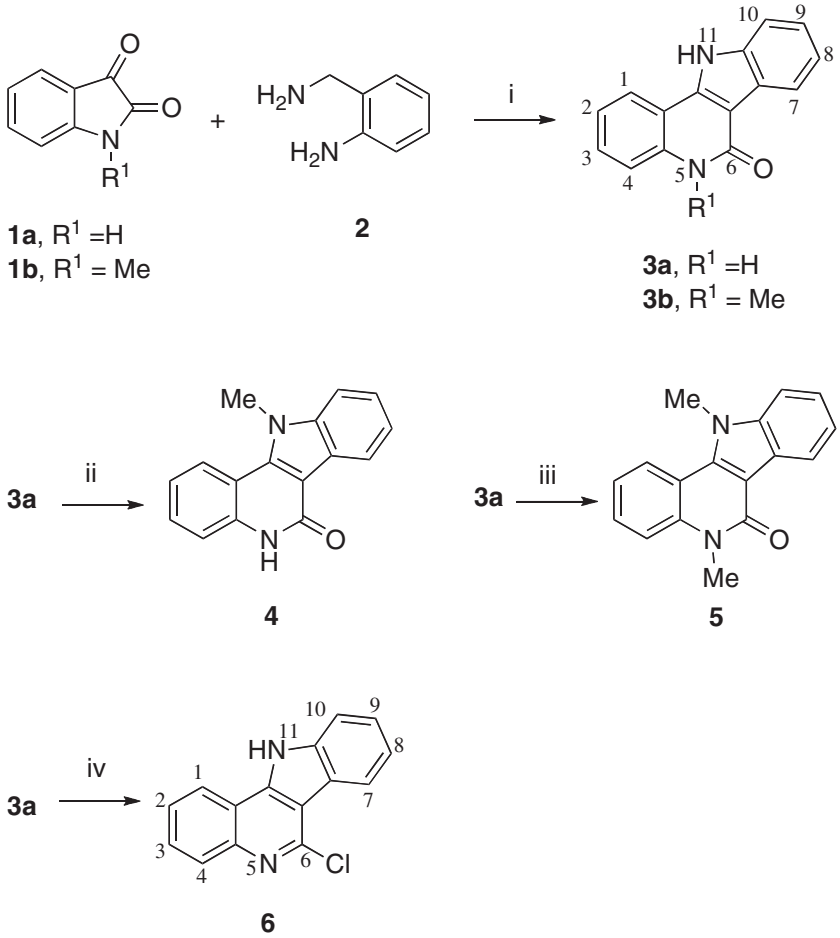


Scheme 1. Preparation of 5,6-dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-ones **3** and its 11-Me derivatives **4**, **5**, and 6-chloroindolo-[3,2-*c*]quinoline **6**. Reagents and conditions: (i) AcOH, heating; (ii) NaH (1.1 equiv)–MeI (1.3 equiv); (iii) NaH (3 equiv)–MeI (5 equiv); (iv) $POCl_3$, toluene, reflux, 6–12 h.

amino group at the C-6 position, affording the 6-alkylamino analogues.

Results and Discussion

Although various approaches to the 5,6-dihydro-11*H*-indolo-[3,2-*c*]quinolin-6(5*H*)-one (**3a**), the key starting point in this study, are known,[11] we prepared **3a** from isatin (**1a**) and 2-aminobenzylamine (**2**) according to the method by Bergman et al.[12] Similarly, the reaction of *N*-methylisatin (**1b**) and **2** smoothly afforded the corresponding 5-methylated **3b**. On the other hand, the successive treatment of **3a** with a slight excess of NaH and MeI (excess) afforded **4**, the 11-methylated isomer of **3b**. Exhausitive methylation using NaH (3 equivalents) followed with MeI (excess) led to the 5,11-dimethylated **5**. Furthermore, the 6-chloroindolo[3,2-*c*]quinoline **6** was prepared by dehydrative chlorination of the respective amide **3a** using $POCl_3$ under heating (Scheme 1).

We then tried the methylation of **6** using NaH as the base followed by treatment with MeI. The methylation of **6** proceeded at the N-11 to exclusively give **8** in 78% yield, which is in good accordance with the reported result in the indolo-[3,2-*c*]quinoline derivative.[13] A similar trend in the regioselectivity of the methylation at the N-11 was found in the case of 6-(4-methyl-1,4-diazepan-1-yl) **7**, prepared by amination of **6**, giving the corresponding **10**, accompanied by formation of tetraalkylammonium group at the trialkylamine of the side chain in 55% yield. This regioselective methylation at N-11 can be explained by the deprotonation of NH at N-11 due to its low pK_a value,[14] which was followed by *N*-alkylation without destroying the aromaticity of the pyridine ring.

On the other hand, the reaction of **6** with MeI while heating without a base at 100–110 °C in DMF–toluene led to the methylation at N-5 to form quinolinium salt **11**, which, without isolation, was transformed into **3b** in 82% yield from **6** by the reaction with water.[14] The regioselective methylation at N-5 is in good agreement with that reported for 11*H*-indolo[3,2-*c*]-quinoline.[15] This can be explained by the higher basicity of the nitrogen atom of the quinoline ring than that of the indole ring in the 11*H*-indolo[3,2-*c*]quinoline core.[16]

To avoid any ambiguity for confirmation of the *N*-methylated structures, the N-11 methylated **8** was subjected to X-ray crystallographic analyses, and the ORTEP is depicted in Figure 2.

In connection with our program to develop antimalarial and anticancer agents using indolo[3,2-*c*]quinoline motif as the lead compound, we examined nucleophilic substitution reactions with an appropriate amine at the C6 position of the 11-methyl derivative **8**, the congener of 6-chloroisocryptolepine. Amina-

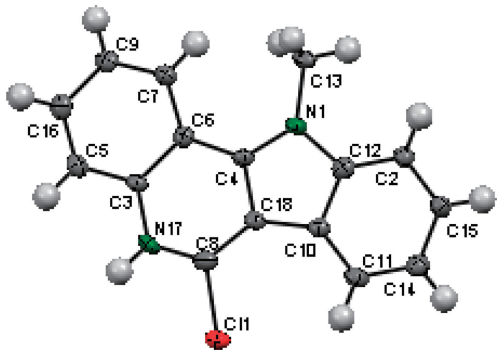
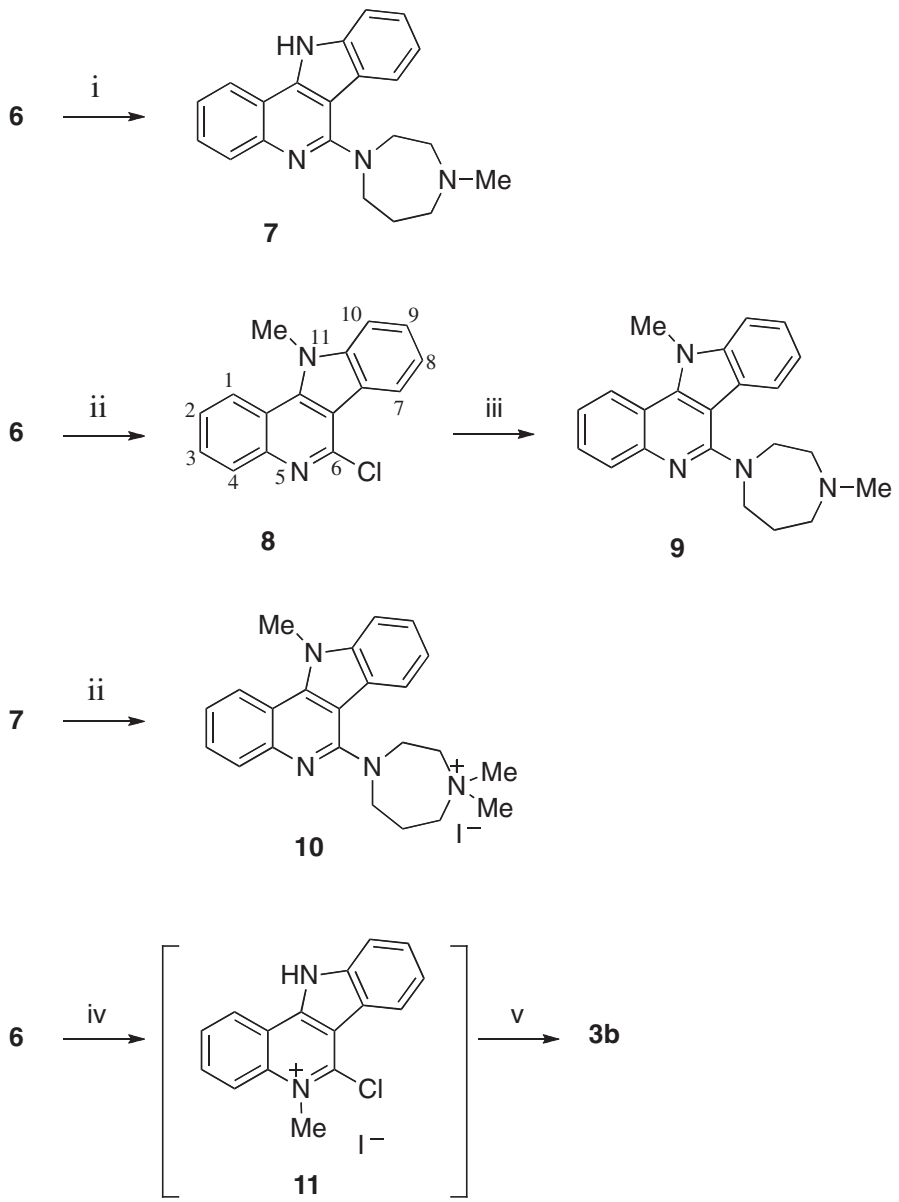


Figure 2. ORTEP drawing of crystal **8**.

tion of **6** with 1-methyl-1,4-diazepane proceeded at 100 °C within 20 min, giving **7** in 52% yield, while the same amination reaction of **8** occurred by heating at 120 °C for 10 h, giving the corresponding 6-aminated **9** in 48% yield. The inconvenience of a long reaction time and low yield was avoided by applying MW irradiation at the same temperature, giving **9** in 55% yield for 3 h. Namely, the N-11-methylated **8** is less reactive for nucleophilic substitition than **6** (Scheme 2).

Conclusion

In summary, we described the regioselective methylation at the N-11 of 6-chloro-11*H*-indolo[3,2-*c*]quinoline (**6**), giving **8**, whose amination at the C6 position by S_NAr led to the corresponding 11-methyl-6-alkylamino derivative **9**, the congener of the isocryptolepine derivative. On the other hand, the methyl-



Scheme 2. Regioselective methylations of 6-chloroindolo[3,2-*c*]quinolines and aminations at the C6 by S_NAr. Reagents and conditions: (i) 1-methyl-1,4-diazepane, heating; (ii) NaH (1.3–1.7 equiv)–MeI (1.3–1.7 equiv); (iii) 1-methyl-1,4-diazepane, MW heating; (iv) MeI (10 equiv), heating; (v) H_2O.

ation of **6** while heating followed by hydration of the resulting 5-methylquinolinium salt **11** provided 5-methyl-5,6-dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-one (**3b**). Further study of the resulting 6-alkylaminoindolo[3,2-*c*]quinoline derivatives for their antimalarial and anticancer activities is currently underway in our laboratory.

Experimental

Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254) and flash chromatography was performed on silica gel (230–400 mesh) using a gradient solvent system. The ^{1}H NMR and ^{13}C NMR spectra were measured on a Varian INOVA-600 spectrometer (600 MHz) with DMSO-d_6 as the solvent. Chemical shifts (δ) were determined using tetramethylsilane (TMS) as an internal standard and the coupling constants (J) are given in hertz. Melting points were determined on a J-Science RFS-10 hot stage microscope. MW reaction was performed with μReactor EX, Shikoku Instrumentation Co., Ltd., operated at 2.46 GHz. 1-Methylisatin (**1b**) was prepared by *N*-methylation of isatin (**1a**).[17]

Synthesis of 5,6-Dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-one (3a). A mixture of isatin (**1a**, 2.94 g, 20 mmol) and 2-aminobenzylamine (**2**, 4.88 g, 40 mmol) was heated at reflux in AcOH (50 mL) for 10 h, whereupon the reaction mixture was poured into water. The solids formed were collected by filtration. The crude product was purified by flash chromatography (SiO_2, hexane–AcOEt = 2:1 v/v) to give **3a** as beige solids. Yield: 4.14 g (88%). $R_f = 0.43$ (hexane–AcOEt = 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.53 (s, 1H), 11.40 (s, 1H), 8.17 (d, $J = 7.8$ Hz, 2H), 7.59 (d, $J = 8.1$ Hz, 1H), 7.47–7.43 (m, 2H), 7.33 (t, $J = 7.6$ Hz, 1H), 7.27–7.22 (dt, $J = 15.3$, 7.5 Hz, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 160.3, 141.1, 138.4, 138.1, 129.6, 124.8, 124.4, 122.5, 121.9, 121.5, 121.2, 116.5, 112.4, 112.2, 106.9.

The same reaction of **1b** and **2** in AcOH afforded 5-methyl-5,6-dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-one (**3b**) in 60% yield; $R_f = 0.5$ (hexane–AcOEt = 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.55 (s, 1H), 8.28–8.23 (dd, $J = 22.4$, 7.8 Hz, 2H), 7.61–7.60 (m, 3H), 7.39–7.35 (m, 2H), 7.26 (t, $J = 7.5$ Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 159.5, 140.1, 139.2, 138.3, 130.1, 125.1, 124.6, 123.1, 122.2, 121.6, 121.3, 116.2, 113.4, 112.2, 106.4, 29.0.

Synthesis of 11-Methyl-5,6-dihydroindolo[3,2-*c*]quinolin-6(5*H*)-one (4). 5,6-Dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-one (**3a**, 117 mg, 0.5 mmol) was dried over P_2O_5 under vacuum and dissolved in DMF (2 mL). To this solution was added NaH (13.2 mg, 0.55 mmol) with cooling on an ice-bath and stirred for 1 h, and then MeI (0.04 mL, 0.65 mmol) and the resulting mixture was stirred at room temperature for 3 h. The mixture was filtered and the solids were washed with brine and dried over P_2O_5 under vacuum. The crude product was purified by column chromatography (SiO_2, hexane–AcOEt 20:1 to 5:1 v/v) to afford yellow **4** as solids. Yield: 59 mg (48%). $R_f = 0.30$ (hexane–AcOEt 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.54 (s, 1H), 8.46 (d, $J = 8.2$ Hz, 1H), 8.29 (d, $J = 7.7$ Hz, 1H), 7.78 (d, $J = 8.4$ Hz, 1H), 7.52 (dt, $J = 7.7$, 3.7 Hz, 2H), 7.42 (ddd, $J = 8.3$, 7.1, 1.2 Hz, 1H), 7.29 (ddd, $J = 8.3$, 4.7, 1.6 Hz, 2H), 4.31 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 159.9, 140.4, 139.8, 138.9, 129.4, 124.5, 123.9, 123.7, 122.0 (2C), 121.8, 121.3, 117.0, 113.1, 110.7, 107.4, 33.9.

5,11-Dimethyl-5,6-dihydroindolo[3,2-*c*]quinolin-6(5*H*)-one (**5**) was prepared by the reaction of **3** (117 mg, 0.5 mmol) and NaH (36 mg, 1.5 mmol) followed with MeI (0.16 mL, 2.5 mmol) in DMF (2 mL) at room temperature for 3 h. Usual workup followed by purification by column chromatography (SiO_2, hexane–AcOEt 20:1 to 5:1 v/v) afforded **5** as white solids. Yield: 57 mg (67%). $R_f = 0.57$ (hexane–AcOEt 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.52 (m, 1H), 8.33 (m, 1H), 7.77 (d, $J = 8.4$ Hz, 1H), 7.66 (m, 2H), 7.43 (dddd, $J = 14.6$, 8.2, 6.8, 1.5 Hz, 2H), 7.38 (td, $J = 7.5$, 0.8 Hz, 1H), 4.29 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 159.2, 140.0, 139.5, 139.2, 129.8, 124.7, 124.1 (2C), 122.1, 121.9, 121.4, 116.4, 114.1, 110.7, 106.9, 34.0, 29.2.

Synthesis of 6-Chloro-11*H*-indolo[3,2-*c*]quinolone (6). A mixture of 5,6-dihydro-11*H*-indolo[3,2-*c*]quinolin-6(5*H*)-one (**3a**, 234 mg, 1.0 mmol) and $POCl_3$ (2 mL) was heated at reflux for 12 h. After cooling to room temperature, the mixture was poured into cold aqueous $NaHCO_3$. The solids precipitated were collected by filtration. The crude product was purified by flash chromatography (SiO_2, hexane–AcOEt 20:1 to 10:1 v/v) to give **6** as yellow solids. Yield: 209 mg (83%). $R_f = 0.79$ (hexane–AcOEt = 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 13.09 (s, 1H), 8.54 (dd, $J = 8.0$, 0.9 Hz, 1H), 8.39 (d, $J = 8.0$ Hz, 1H), 8.04 (d, $J = 8.3$ Hz, 1H), 7.77 (m, 2H), 7.71 (m, 1H), 7.58–7.52 (m, 1H), 7.39 (t, $J = 7.5$ Hz, 1H), 3.99 (d, $J = 7.1$ Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 144.9, 144.8, 142.4, 139.2, 129.6, 128.8, 126.7, 126.5, 122.7, 121.7 (2C), 121.2, 117.0, 113.0, 111.8.

Synthesis of 6-Chloro-11-methyl-11*H*-indolo[3,2-*c*]quinoline (8). 6-Chloro-11*H*-indolo[3,2-*c*]quinoline (**6**, 500 mg, 2.0 mmol) was dried over P_2O_5 under vacuum and dissolved in THF (5 mL). To this solution was added NaH (62.4 mg, 2.6 mmol) with cooling on an ice-bath. After being stirred for 1 h, MeI (0.15 mL, 2.6 mmol) was added and the mixture was stirred at room temperature for 3 h. The solids precipitated were collected by filtration and washed with brine and water. The crude products were purified by column chromatography (SiO_2, hexane–AcOEt 10:1 v/v) to afford **8** as yellow solids; mp 198–200 °C. Yield: 415 mg (78%). $R_f = 0.81$ (hexane–AcOEt = 1:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.81 (d, $J = 8.3$ Hz, 1H), 8.50 (d, $J = 7.9$ Hz, 1H), 8.08 (d, $J = 8.2$ Hz, 1H), 7.94 (d, $J = 8.3$ Hz, 1H), 7.80 (t, $J = 7.5$ Hz, 1H), 7.72 (t, $J = 7.5$ Hz, 1H), 7.62 (t, $J = 7.6$ Hz, 1H), 7.44 (t, $J = 7.5$ Hz, 1H), 4.43 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 145.7, 145.0, 141.7, 140.8, 129.3, 129.3, 126.62 (C), 123.6, 122.1, 121.8, 120.2, 117.7, 111.8, 111.2, 34.1. HRMS (ESI) calcd for $C_{16}H_{12}ClN_2$ $[M + H]^+$ Exact Mass: 267.0689, found 267.0697.

1,1-Dimethyl-4-(11-methyl-11*H*-indolo[3,2-*c*]quinolin-6-yl)-1,4-diazepanium Iodide (10). 6-(4-Methyl-1,4-diazepan-1-yl)-11*H*-indolo[3,2-*c*]quinoline (**7**, 500 mg, 1.5 mmol) was dried over P_2O_5 under vacuum and dissolved in THF (5 mL). To this solution was added NaH (62.4 mg, 2.6 mmol) with cooling on an ice-bath. After being stirred for 1 h, MeI (0.15 mL, 2.6 mmol) was added and the mixture was stirred at room temperature for 3 h. The solids precipitated were collected by filtration and washed with water and CH_2Cl_2. White solids, mp

224–226 °C. Yield: 55%. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.70 (d, $J = 8.2$ Hz, 1H), 8.10 (d, $J = 7.9$ Hz, 1H), 7.90–7.88 (m, 2H), 7.68 (m, 1H), 7.56–7.50 (m, 2H), 7.41 (t, $J = 7.4$ Hz, 1H), 4.40 (s, 3H), 4.07 (s, 2H), 3.92–3.90 (m, 2H), 3.77–3.75 (m, 2H), 3.71–3.69 (m, 2H), 3.24 (s, 6H), 2.29 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 157.0, 145.6, 142.1, 140.3, 128.6, 128.6, 125.2, 124.0, 123.0, 122.2, 121.4, 120.5, 116.6, 110.7, 106.5, 65.6, 65.3, 54.0, 53.2, 44.4, 34.1, 23.2. HRMS (ESI) calcd for $C_{23}H_{27}N_4$ $[M - I]^+$ Exact Mass: 359.2230, found 359.2466.

Synthesis of 6-(4-Methyl-1,4-diazepan-1-yl)-11*H*-indolo-[3,2-*c*]quinoline (7). A mixture of **6** (1.2 g, 4.8 mmol) and excess of 1-methyl-1,4-diazepane (1.5 g, 13 mmol) in DMF (5 mL) was heated together at 100 °C for 20 min. The progress was monitored by TLC. Then the reaction mixture was extracted with CH_2Cl_2 and the extracts were washed with water, dried over $MgSO_4$, and concentrated. The resulting brown mixture was purified by column chromatography (SiO_2, AcOEt/2 M ammonia in MeOH 90:10 v/v) to give **7** as white solids; mp 77–79 °C. Yield: 820 mg (52%). $R_f = 0.55$ (AcOEt/2 M ammonia in MeOH 8:2 v/v). ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.59 (s, 1H), 8.34 (d, $J = 8.0$ Hz, 1H), 8.00 (d, $J = 8.0$ Hz, 1H), 7.77 (d, $J = 8.3$ Hz, 1H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.56 (dd, $J = 8.3$, 7.0 Hz, 1H), 7.41 (ddd, $J = 11.2$, 10.6, 7.5 Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 1H), 3.96–3.88 (m, 2H), 3.88–3.81 (m, 2H), 2.72–2.67 (m, 2H), 2.67–2.60 (m, 2H), 2.29 (s, 3H), 1.97 (dd, $J = 8.4$, 3.0 Hz, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 157.4, 145.3, 142.9, 139.0, 128.8, 127.8, 124.8, 123.1, 122.6, 122.2, 122.2, 120.9, 115.6, 112.1, 106.1, 58.8, 57.1, 52.0, 51.0, 47.1, 27.7. HRMS (ESI) calcd for $C_{21}H_{23}N_4$ $[M + H]^+$ Exact Mass: 331.1923, found 331.1921.

Synthesis of 11-Methyl-6-(4-methyl-1,4-diazepan-1-yl)-11*H*-indolo[3,2-*c*]quinoline (9). Method A. A mixture of **8** (53 mg, 0.2 mmol) and excess of 1-methyl-1,4-diazepane (68 mg, 0.6 mmol) in DMF (1 mL) was heated together at 120 °C for 10 h. The progress of the reaction was monitored by TLC. Then the reaction mixture was extracted with CH_2Cl_2 and the extracts were washed with water, dried over $MgSO_4$, and concentrated. The resulting brown mixture was purified by column chromatography (SiO_2, AcOEt/2 M ammonia in MeOH 90:10 v/v) to give **9** as yellow oil. Yield: 33 mg (48%). $R_f = 0.63$ (AcOEt/2 M ammonia in MeOH 8:4 v/v).

Method B. A mixture of **8** (53 mg, 0.2 mmol) and excess of 1-methyl-1,4-diazepane (68 mg, 0.6 mmol) in DMF was heated together at 120 °C by MW irradiation at 150 W for 3 h. The mixture was worked up as before. Yield: 38 mg (55%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.61 (d, $J = 8.3$ Hz, 1H), 8.06 (d, $J = 7.9$ Hz, 1H), 7.83–7.80 (dd, $J = 19.8$, 8.3 Hz, 2H), 7.59 (dd, $J = 8.2$, 7.0 Hz, 1H), 7.48 (dd, $J = 8.1$, 7.2 Hz, 1H), 7.41 (dd, $J = 8.1$, 7.1 Hz, 1H), 7.35 (t, $J = 7.5$ Hz, 1H), 4.34 (s, 3H), 3.86–3.84 (m, 2H), 3.80–3.78 (m, 2H), 2.67–2.63 (m, 4H), 2.27 (s, 3H), 1.95–1.91 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 157.5, 146.0, 142.0, 140.2, 128.4, 128.3, 124.8, 123.0, 122.8, 122.3, 121.0, 120.8, 116.3, 110.4, 106.5, 58.6, 56.9, 52.2, 51.1, 47.0, 33.9, 27.5. HRMS (ESI) calcd for $C_{22}H_{25}N_4$ $[M + H]^+$ Exact Mass: 345.2079, found 345.2078.

Preparation of 3b from 6. A mixture of **6** (1.0 g, 4.0 mmol) and MeI (2.5 mL, 40 mmol) in DMF (10 mL) was heating at 120 °C for 8 h. After cooling to ambient temperature, water (excess) was added to the reaction mixture. The solids precipitated were collected by filtration, and recrystallized from MeOH/Et_2O to afford **3b** as white solids. Yield: 0.81 g (82%).

Crystallographic data have been deposited with The Cambridge Crystallographic Data Centre: Deposition number CCDC-931679 for compound **8**. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; e-mail: data_request@ccdc.cam.ac.uk).

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Supporting Information

Experimental procedure and spectral data including ^{1}H NMR and ^{13}C NMR spectra of **3a**, **3b**, **4**, **5**, **6**, **7**, **8**, **9**, and **10** are provided. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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