Synthetic study directed toward derivatives of biologically active indolo[2,3-a]carbazole

著者	Sato Masako, Suzuki Yoshiaki, Yamada Fumio, Somei Masanori
journal or publication title	Heterocycles
volume	80
number	2
page range	1027-1045
year	2010-01-01
URL	http://hdl.handle.net/2297/25289

doi: 10.3987/COM-09-S(S)79

SYNTHETIC STUDY DIRECTED TOWARD DERIVATIVES OF BIOLOGICALLY ACTIVE INDOLO[2,3-*a*]CARBAZOLE^{1#}

Masako Sato, Yoshiaki Suzuki, Fumio Yamada, and Masanori Somei*‡

Faculty of Pharmaceutical Sciences, Graduate School of Natural Science and
Technology, Kanazawa University, Kakuma-machi, Kanazawa, 920-1192, Japan
e-mail address: somei.home@topaz.plala.or.jp

Abstract – Various derivatives of (6*R**,6*aR**)-6-chloro-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (**8**) and 6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (**9**) are prepared. Preparations of (6*R**,6*aR**,11*aR**)-6-chloro-11*a*-cyano-6*a*-hydroxy- (**11**) and 12-substituted 6-(*Z*)-aminomethylidene-5,6,6*a*,11,11*a*,12-hexahydroindolo[2,3-*a*]carbazole-5-ones (**15**) are also reported.

We have proposed a new concept for evaluating originality and efficiency of synthetic method introducing three measures such as originality rate, intellectual property factor, and application potential factor and defined an ideal synthetic method.² In our continuing research, we have created a synthetic method,³ as one of the concrete example of the ideal synthesis, for 6-cyano-5-methoxy-12-methylindolo[2,3-*a*]carbazole (**1**, Scheme 1) isolated from blue-green alga *Nostoc sphaericum* (strain EX-5-1) by Moore and co-workers.⁴ The synthesis starts from indigo (**2**) and consists of six steps. Every compound involved in the synthesis has either a useful function or a biological activity. Thus, starting material is a widely used dye⁵ and the target **1** is a cytotoxic and antiviral alkaloid.⁴ The compound **3** exhibits potent biological activity against telomerase.⁶ In addition, we have discovered as intellectual properties that **4**, **6**, and **7** are potent inhibitors of blood platelet aggregation⁷ while **5** is a promising α_2 -blocker.⁸

It is natural, therefore, that we would expect to discover a compound becoming medicine in the future among derivatives of biologically active **5** and **7**. Now, we wish to report the synthesis of various deriva-

Dedicated to the 80th birthday of Prof. Emeritus, Akira Suzuki, Hokkaido University.

‡ Professor Emeritus of Kanazawa University. Present address: 56-7 Matsuhidai, Matsudo-shi, Chiba 270-2214, Japan.

tives of **5** and **7**. Interesting formations of (6*R**,6*aR**,11*aR**)-6-chloro-11*a*-cyano-6*a*-hydroxy-5,6,6*a*,11,11*a*,12-hexahydro- (**11**) and 12-substituted (*Z*)-6-aminomethylidene-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (**15**) are also reported.

Scheme 1

Scheme 2

First, the compound **5** was prepared according to our procedures³ from indigo in three steps in 73% overall yield. Subsequent treatment of **5** in *N,N*-dimethylformamide (DMF) in the presence of K₂CO₃ with *n*-butyl iodide, allyl bromide, propargyl bromide, benzyl bromide, phenethyl bromide, and (*E*)-cinnamyl bromide provided **8a**, **8b**, **8c**, **8d**, **8e**, and **8f** in the respective yields of 71, 96, 50, 78, 57, and 96% (Scheme 2). Similar treatment of **5** with reagents having a cyano or a carbonyl group such as

chloroacetonitrile, *N,N*-dimethyl-2-chloroacetamide, methyl bromoacetate, methyl acrylate, and phenacyl bromide afforded **8g**, **8h**, **8i**, **8j**, and **8k** in the respective yields of 62, 90, 72, 26, and 97%. Although the reaction of 1,3-dibromopropane with **5** similarly proceeded to give **8l** in 45% yield, ethyl 4-bromobutylate did not react with **5** at all. To overcome the problem, change of the base from K₂CO₃ to NaH in anhydrous DMF was successful to obtain the desired **8m** in 59% yield.

In the reaction of **5** with an *E,Z* mixture of 1,3-dichloropropene, NaH in anhydrous DMF was the reaction conditions of choice, providing 12-(*Z*)-**8n** and 12-(*E*)-(3-chloroallyl) derivatives **8o** in 42 and 24% yields, respectively. Under similar reaction conditions, **5** reacted with acetyl chloride to produce 12-acetyl compound **8p** in 41% yield.

With various 12-substituted (6*R**,6*aR**)-6-chloro-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one in hand, we next employed our reductive cyanation which realized transformation of **6** to **7**. Thus, the treatment of **8a** with NaCN in DMF-H₂O provided 12-*n*-butyl-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (**9a**) in 85% yield. A possible reaction mechanism is shown in Scheme 3. The initial step would be a nucleophilic substitution for 6β-chloride by cyanide from the back side to give **A**. After dehydration, the resultant **B** can form **C** by general acid promoted cyanide addition to the 6-position. Subsequent cyanide attack at one of the geminal cyano groups of **C** achieves the reductive cyanation with the liberation of dicyan and an enolate of **9a**. The other possible route is the enolization of 5-carbonyl of **A**, followed by the addition of cyanide at the imine carbon (C_{11a}) from the less sterically hindered α-side culminating in the formation of **D**. Subsequent cyanide attack at the 11α-cyano group and concomitant general acid promoted elimination of 6*a*β-hydroxy group liberates dicyan and **9a**.

Scheme 3. Possible Mechanism

On the basis of above results, the reductive cyanation was applied to **8b–h** and **8m** resulting in the formations of **9b**, **9c**, **9d**, **9e**, **9f**, **9g**, **9h**, and **9m** in the respective yields of 91, 72, 98, 85, 80, 54, 95, and 72%. In the case of **8i**, the reductive cyanation formed **9i** and **9q** in 17 and 43% yields, respectively. Similar reaction of **8k** removed the 12-phenacyl group to afford **10** in 27% yield together with 16% yield of starting material.

The structures of **9a–i** and **9m,q** were established unequivocally by pursuing X-ray single-crystal analysis of **9a** as a representative of them and the results are shown in Figure 1 and Table 1. It is interesting to note that this type of compounds **9** tends to involve a recrystallization solvent molecule in crystals. In fact, the ORTEP drawing of **9a** demonstrates EtOAc molecule.

Figure 1. ORTEP Drawing of **9a** ($R=0.049$)

Figure 2. ORTEP Drawing of **11** ($R=0.085$)

The reaction of **8l** with NaCN in DMF-H₂O provided **9l** and **9r** in 23 and 23% yields, respectively. The reaction of about 4:1 mixture of **8n** and **8o** produced **9n** and **9o** in 41 and 14% yields, respectively. It is interesting to note that the similar reaction of **8p** afforded **10** and the unexpected (6*R**,6*aR**,11*aR**)-6-chloro-11*a*-cyano-6*a*-hydroxy-5,6,6*a*,11,11*a*,12-hexahydroindolo[2,3-*a*]carbazole-5-one (**11**) in 22 and 74% yields, respectively, though formation of the desired **9p** was not observed at all.

Reduction of **11** with NaBH₄ proceeded slowly from the less hindered β-side to provide 5*α*-hydroxy compound **12a** in 47% yield. Further treatment of **12a** with acetic anhydride gave 5*α*-acetoxy compound **12b** in 30% yield. Comparing ¹H-NMR spectra of **12a** and **12b**, the coupling constant between H₅ and H₆ is shown to be 8.2 Hz, which proved their stereochemistries as shown in the Scheme 2.

It should be noted that the absorption bands of cyano group of **11**, **12a**, and **12b** were very weak or almost invisible in their infrared spectra. Therefore, X-ray single-crystal analysis of **11** was necessary for the determination of the structure. The results shown in Figure 2 and Table 2 demonstrate both the presence of the cyano group at the 11*a*-position and the stereochemistries of 6, 6*a*, and 11*a* positions being all *R**.

Methylation of **9d** with ethereal diazomethane smoothly proceeded to afford the corresponding methoxy compound **13** in 82% yield. All attempts to hydrolyze the 6-cyano group of **13** to 6-carboxy or 6-carbamoyl group with base were unsuccessful. Under severe conditions such as treatment of **13** with solid NaOH in refluxing ethylene glycol resulted in the methyl ether cleavage to afford **9d** in 62% yield.

Further attempt to obtain 6-formyl type compound **14** by the reaction of **9** with diisobutyl aluminum hydride (DIBAL) proceeded in an unexpected way. Thus the reduction of **9a** and **9d** with DIBAL afforded **15a** and **15b** in 73 and 47% yields, respectively. In the ¹H-NMR spectrum of **15a**, hydrogen bonded Ha was observed at lower δ 12.0 (1H, dd, *J*=13.8, 8.2 Hz), while Hb and Hc protons appeared at

δ 8.60 (1H, brt, $J=8.2$ Hz) and 8.84 (1H, dd, $J=13.8, 8.2$ Hz), respectively. On the addition of D₂O, both Ha and Hb protons disappeared and Hc collapsed to a singlet. Similar phenomena were observed in case of **15b**. Further treatment of **15a** with Ac₂O afforded *N*-acetyl compound **16** in 87% yield. These results prove the 6-aminomethylidene structures of **15a,b**.

A possible reaction mechanism for the transformation of **9** to **15** is shown in Scheme 4. The initial reaction of DIBAL with **9** forms aluminum complex **A**, followed by the intramolecular reduction of cyano group with hydride to afford **B**. Hydrolysis of **B** affords an enol form compound **C** which tautomerizes to a carbonyl form product **15** forming a stable enamide system.

In summary, we succeeded in preparing various derivatives of **8** and **9**, together with new classes of compound, **11** and **15**. Biological evaluations of new compounds in this report are in progress.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer and proton nuclear magnetic resonance (¹H-NMR) spectra with a JEOL GSX-500 spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a JEOL JMS-SX102A instruments. Column chromatography was performed on silica gel (SiO₂, 100—200 mesh, from Kanto Chemical Co., Inc.) throughout the present study.

(6*R,6*aR**)-12-*n*-Butyl-6-chloro-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8a) from (6*R**,6*aR**)-6-Chloro-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (5)** —

General Procedure A: K₂CO₃ (72.1 mg, 0.52 mmol) and *n*-butyl iodide (0.34 mL, 2.90 mmol) were added to a solution of **5** (48.1 mg, 0.15 mmol) in DMF (3.0 mL), and the mixture was stirred for 20 min at rt. After addition of H₂O under ice cooling, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with EtOAc–hexane (1:5, v/v) to give **8a** (40.1 mg, 71%). **8a**: mp 187—189°C (decomp., orange prisms, recrystallized from CHCl₃). IR (KBr): 3421, 1653, 1479, 1346, 1086, 754 cm⁻¹. ¹H-NMR (CDCl₃) δ : 0.97 (3H, t, $J=7.4$ Hz), 1.39—1.50 (2H, m), 1.87—2.00 (2H, m),

3.11 (1H, s, disappeared on addition of D₂O), 4.63 (1H, ddd, $J=14.1, 8.2, 6.4$ Hz), 4.76 (1H, s), 4.87 (1H, ddd, $J=14.1, 8.2, 6.4$ Hz), 7.35 (1H, td, $J=7.7, 1.2$ Hz), 7.39 (1H, td, $J=7.7, 1.2$ Hz), 7.47 (1H, td, $J=7.7, 1.2$ Hz), 7.50 (1H, d, $J=7.7$ Hz), 7.50 (1H, td, $J=7.7, 1.2$ Hz), 7.72 (1H, d, $J=7.7$ Hz), 7.92 (1H, d, $J=7.7$ Hz), 8.39 (1H, d, $J=7.7$ Hz). MS m/z : 380 and 378 (M⁺). *Anal.* Calcd for C₂₂H₁₉N₂O₂Cl·1/8H₂O: C, 69.33; H, 5.09; N, 7.35. Found: C, 69.38; H, 5.11; N, 7.24.

(6R*,6aR*)-12-Allyl-6-chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8b)

from 5 — In the general procedure A, K₂CO₃ (754 mg, 5.44 mmol), allyl bromide (2.70 mL, 31.1 mmol), **5** (501 mg, 1.56 mmol), and DMF (10.0 mL) were used. The reaction time was 30 min. After column-chromatography, **8b** (540 mg, 96%) was obtained. **8b**: mp 202—203°C (decomp., yellow prisms, recrystallized from EtOAc). IR (KBr): 3400, 3110, 1665, 1562, 1457, 1333, 1140, 1087, 1017, 789, 747 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 5.16 (1H, dd, $J=17.1, 1.5$ Hz), 5.22 (1H, dd, $J=10.3, 1.5$ Hz), 5.35 (1H, s), 5.36 (1H, dd, $J=16.3, 5.4$ Hz), 5.53 (1H, dd, $J=16.3, 5.4$ Hz), 6.07—6.16 (1H, m), 6.84 (1H, s), 7.39 (1H, t, $J=8.1$ Hz), 7.40 (1H, t, $J=8.1$ Hz), 7.50 (1H, t, $J=7.5$ Hz), 7.55 (1H, t, $J=7.5$ Hz), 7.75 (1H, d, $J=8.1$ Hz), 7.77 (1H, d, $J=7.5$ Hz), 7.84 (1H, d, $J=7.5$ Hz), 8.19 (1H, d, $J=8.1$ Hz). MS m/z : 364 and 362 (M⁺). *Anal.* Calcd for C₂₁H₁₅N₂O₂Cl: C, 69.52; H, 4.17; N, 7.72. Found: C, 69.49; H, 4.17; N, 7.41.

(6R*,6aR*)-6-Chloro-6a-hydroxy-12-propargyl-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8c) from 5

— In the general procedure A, K₂CO₃ (44.2 mg, 0.32 mmol), propargyl bromide (0.14 mL, 1.83 mmol), **5** (29.5 mg, 0.09 mmol), and DMF (2.0 mL) were used. The reaction time was 1 h. After column-chromatography, **8c** (16.5 mg, 50%) was obtained. **8c**: mp 248°C (decomp., dark yellow powder, recrystallized from EtOAc–hexane). IR (KBr): 3359, 3286, 1653, 1475, 1086, 791, 746 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 3.48 (1H, t, $J=2.5$ Hz), 5.38 (1H, d, $J=1.5$ Hz, collapsed to s on addition of D₂O), 5.66 (1H, dd, $J=17.9, 2.5$ Hz), 5.78 (1H, dd, $J=17.9, 2.5$ Hz), 6.91 (1H, d, $J=1.5$ Hz, disappeared on addition of D₂O), 7.41 (1H, td, $J=7.7, 1.3$ Hz), 7.45 (1H, td, $J=7.7, 1.3$ Hz), 7.56 (1H, td, $J=7.7, 1.3$ Hz), 7.56 (1H, td, $J=7.7, 1.3$ Hz), 7.81 (1H, d, $J=7.7$ Hz), 7.84 (1H, d, $J=7.7$ Hz), 7.84 (1H, d, $J=7.7$ Hz), 8.19 (1H, d, $J=7.7$ Hz). MS m/z : 362 and 360 (M⁺). *Anal.* Calcd for C₂₁H₁₃N₂O₂Cl·1/2H₂O: C, 68.21; H, 3.82; N, 7.58. Found: C, 68.00; H, 3.73; N, 7.33.

(6R*,6aR*)-12-Benzyl-6-chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8d) from 5

— In the general procedure A, K₂CO₃ (619 mg, 4.48 mmol), benzyl bromide (3.10 mL, 25.6 mmol), **5** (413 mg, 1.28 mmol), and DMF (8.0 mL) were used. The reaction time was 75 min. After column-chromatography, **8d** (411 mg, 78%) was obtained. **8d**: mp 219.5—221.5 °C (yellow prisms, recrystallized from EtOAc–hexane). IR (KBr): 3356, 1685, 1577, 1473, 1142, 771 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 5.41 (1H, s), 5.99 (1H, d, $J=15.8$ Hz), 6.18 (1H, d, $J=15.8$ Hz), 6.91 (1H, br s, disappeared on addition of D₂O), 7.26 (1H, t, $J=7.2$ Hz), 7.30 (2H, t, $J=7.2$ Hz), 7.37 (2H, d, $J=7.2$ Hz), 7.40 (1H, td, $J=7.4, 1.2$ Hz), 7.42 (1H, td, $J=7.4, 1.2$ Hz), 7.42 (1H, td, $J=7.4, 1.2$ Hz), 7.54 (1H, td, $J=7.4, 1.2$ Hz),

7.64 (1H, d, $J=7.4$ Hz), 7.75 (1H, d, $J=7.4$ Hz), 7.86 (1H, d, $J=7.4$ Hz), 8.19 (1H, d, $J=7.4$ Hz). MS m/z : 414 and 412 (M^+). *Anal.* Calcd for $C_{25}H_{17}N_2O_2Cl \cdot 1/2H_2O$: C, 71.17; H, 4.30; N, 6.64. Found: C, 71.32; H, 4.25; N, 6.49.

(6*R,6*aR**)-6-Chloro-6*a*-hydroxy-12-phenethyl-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one**

(8e) from 5 — In the general procedure A, K_2CO_3 (45.0 mg, 0.33 mmol), phenethyl bromide (0.25 mL, 1.86 mmol), **5** (30.0 mg, 0.09 mmol), and DMF (2.0 mL) were used. The reaction time was 1 h. After column-chromatography, **8e** (22.6 mg, 57%) was obtained. **8e**: mp 183—184 °C (yellow needles, recrystallized from EtOAc–hexane). IR (KBr): 3361, 1655, 1477, 1146, 746 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 3.19 (2H, td, $J=13.8, 6.8$ Hz), 4.83 (1H, ddd, $J=13.8, 8.6, 6.8$ Hz), 5.04 (1H, ddd, $J=13.8, 8.6, 6.8$ Hz), 5.36 (1H, s), 6.84 (1H, br s, disappeared on addition of D_2O), 7.21 (1H, br t, $J=7.4$ Hz), 7.30 (2H, t, $J=7.4$ Hz), 7.35 (2H, d, $J=7.4$ Hz), 7.37 (1H, t, $J=7.5$ Hz), 7.41 (1H, t, $J=7.5$ Hz), 7.43 (1H, t, $J=7.5$ Hz), 7.58 (1H, t, $J=7.5$ Hz), 7.73 (1H, d, $J=7.5$ Hz), 7.84 (1H, d, $J=7.5$ Hz), 7.86 (1H, d, $J=7.5$ Hz), 8.15 (1H, d, $J=7.5$ Hz). MS m/z : 428 and 426 (M^+). *Anal.* Calcd for $C_{26}H_{19}N_2O_2Cl \cdot 1/2H_2O$: C, 71.64; H, 4.62; N, 6.43. Found: C, 71.86; H, 4.43; N, 6.40.

(6*R,6*aR**)-6-Chloro-12-(*E*)-cinnamyl-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one**

(8f) from 5 — In the general procedure A, K_2CO_3 (157 mg, 1.14 mmol), cinnamyl bromide (0.79 mL, 6.49 mmol), **5** (105 mg, 0.32 mmol), and DMF (6.0 mL) were used. The reaction time was 1 h. After column-chromatography, **8f** (137 mg, 96%) was obtained. **8f**: mp 205—208 °C (brown plates, recrystallized from EtOAc–hexane). IR (KBr): 3390, 1648, 1579, 1473, 1145, 757 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 5.36 (1H, d, $J=1.5$ Hz, collapsed to s on addition of D_2O), 5.51 (1H, ddd, $J=16.5, 5.9, 1.2$ Hz), 5.71 (1H, ddd, $J=16.5, 5.9, 1.2$ Hz), 6.53 (1H, dt, $J=16.5, 5.9$ Hz), 6.69 (1H, d, $J=16.5$ Hz), 6.85 (1H, d, $J=1.5$ Hz, disappeared on addition of D_2O), 7.22 (1H, t, $J=7.4$ Hz), 7.28 (2H, t, $J=7.4$ Hz), 7.37 (2H, d, $J=7.4$ Hz), 7.40 (1H, td, $J=7.6, 1.2$ Hz), 7.41 (1H, td, $J=7.6, 1.2$ Hz), 7.50 (1H, td, $J=7.6, 1.2$ Hz), 7.55 (1H, td, $J=7.6, 1.2$ Hz), 7.80 (1H, d, $J=7.6$ Hz), 7.85 (1H, d, $J=7.6$ Hz), 7.85 (1H, d, $J=7.6$ Hz), 8.20 (1H, d, $J=7.6$ Hz). MS m/z : 440 and 438 (M^+). *Anal.* Calcd for $C_{27}H_{19}N_2O_2Cl \cdot 1/2EtOAc$: C, 72.12; H, 4.80; N, 5.80. Found: C, 71.84; H, 4.68; N, 5.83.

(6*R,6*aR**)-6-Chloro-12-cyanomethyl-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one**

(8g) from 5 — In the general procedure A, K_2CO_3 (159 mg, 1.15 mmol), chloroacetonitrile (0.42 mL, 6.56 mmol), **5** (106 mg, 0.33 mmol), and DMF (3.0 mL) were used. The reaction time was 15 min. After column-chromatography, **8g** (72.6 mg, 62%) was obtained. **8g**: mp 249.5—251.5 °C (decomp., yellow prisms, recrystallized from EtOAc). IR (KBr): 3350, 1648, 1615, 1574, 1472, 1345, 1083, 797, 780, 747 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 5.41 (1H, d, $J=1.5$ Hz, collapsed on addition of D_2O), 5.99 (1H, d, $J=18.1$ Hz), 6.10 (1H, d, $J=18.1$ Hz), 6.95 (1H, d, $J=1.5$ Hz, disappeared on addition of D_2O), 7.42 (1H, td, $J=7.6, 1.1$ Hz), 7.49 (1H, td, $J=7.6, 1.1$ Hz), 7.57 (1H, td, $J=7.6, 1.1$ Hz), 7.62 (1H, td, $J=7.6, 1.1$ Hz),

7.82 (1H, d, $J=7.6$ Hz), 7.85 (1H, d, $J=7.6$ Hz), 7.95 (1H, d, $J=7.6$ Hz), 8.21 (1H, d, $J=7.6$ Hz). *Anal.* Calcd for $C_{20}H_{12}N_3O_2Cl$: C, 66.40; H, 3.34; N, 11.61. Found: C, 66.70; H, 3.33; N, 11.37.

(6*R,6*aR**)-6-Chloro-12-*N,N*-dimethylcarbamoylmethyl-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8h) from 5** — In the general procedure A, K_2CO_3 (89.2 mg, 0.65 mmol), *N,N*-dimethyl-2-chloroacetamide (0.66 mL, 6.46 mmol), **5** (104 mg, 0.32 mmol), and DMF (6.0 mL) were used. The reaction time was 1.5 h. After column-chromatography, **8h** (118 mg, 90%) was obtained. **8h**: mp 257—258°C (decomp., dark brown prisms, recrystallized from MeOH). IR (KBr): 3410, 1670, 1647, 1583, 1481, 775, 756 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 2.90 (3H, s), 3.24 (3H, s), 5.31 (1H, s), 5.64 (1H, d, $J=16.8$ Hz), 5.81 (1H, d, $J=16.8$ Hz), 6.83 (1H, s, disappeared on addition of D_2O), 7.37 (1H, td, $J=7.5, 1.2$ Hz), 7.39 (1H, td, $J=7.5, 1.2$ Hz), 7.47 (1H, td, $J=7.5, 1.2$ Hz), 7.52 (1H, td, $J=7.5, 1.2$ Hz), 7.66 (1H, d, $J=7.5$ Hz), 7.72 (1H, d, $J=7.5$ Hz), 7.82 (1H, d, $J=7.5$ Hz), 8.17 (1H, d, $J=7.5$ Hz). MS m/z : 409 and 407 (M^+). *Anal.* Calcd for $C_{22}H_{18}N_3O_3Cl \cdot 1/4H_2O$: C, 64.08; H, 4.52; N, 10.19. Found: C, 64.21; H, 4.52; N, 10.00.

(6*R,6*aR**)-6-Chloro-6*a*-hydroxy-12-methoxycarbonylmethyl-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8i) from 5** — In the general procedure A, K_2CO_3 (68.2 mg, 0.48 mmol), methyl bromoacetate (0.16 mL, 1.61 mmol), **5** (51.8 mg, 0.16 mmol), and DMF (2.0 mL) were used. The reaction time was 30 min. After column-chromatography, **8i** (45.8 mg, 72%) was obtained. **8i**: mp 223—224.5°C (decomp., brown prisms, recrystallized from EtOAc). IR (KBr): 3415, 1749, 1655, 1479, 1342, 1086, 1012, 800, 777, 756 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 3.74 (3H, s), 5.36 (1H, s), 5.58 (1H, d, $J=18.0$ Hz), 5.81 (1H, d, $J=18.0$ Hz), 6.84 (1H, s, disappeared on addition of D_2O), 7.39 (1H, t, $J=7.8$ Hz), 7.42 (1H, t, $J=7.8$ Hz), 7.48—7.56 (2H, m), 7.73 (1H, d, $J=7.8$ Hz), 7.79 (1H, d, $J=7.8$ Hz), 7.82 (1H, d, $J=7.8$ Hz), 8.18 (1H, d, $J=7.8$ Hz). *Anal.* Calcd for $C_{21}H_{15}N_2O_4Cl$: C, 63.89; H, 3.83; N, 7.10. Found: C, 63.65; H, 3.84; N, 6.89.

(6*R,6*aR**)-6-Chloro-6*a*-hydroxy-12-[2-(methoxycarbonyl)ethyl]-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8j) from 5** — In the general procedure A, K_2CO_3 (68.7 mg, 0.47 mmol), methyl acrylate (0.29 mL, 3.16 mmol), **5** (50.8 mg, 0.16 mmol), and DMF (3.0 mL) were used. The reaction time was 30 min. After column-chromatography, **8j** (17.0 mg, 26%) and the unreacted **5** (18.5 mg, 36%) were obtained in the order of elution. **8j**: mp 216.5—218°C (decomp., yellow powder, recrystallized from EtOAc). IR (KBr): 3431, 1714, 1680, 1583, 1479, 1439, 1215, 1146, 773, 754 cm^{-1} . 1H -NMR (DMSO- d_6) δ : 3.02 (2H, t, $J=7.2$ Hz), 3.58 (3H, s), 4.86 (1H, dt, $J=14.2, 7.2$ Hz), 5.14 (1H, dt, $J=14.2, 7.2$ Hz), 5.33 (1H, d, $J=1.5$, collapsed on addition of D_2O), 6.79 (1H, d, $J=1.5$, disappeared on addition of D_2O), 7.39 (1H, td, $J=7.7, 1.2$ Hz), 7.40 (1H, td, $J=7.7, 1.2$ Hz), 7.51 (1H, td, $J=7.7, 1.2$ Hz), 7.55 (1H, td, $J=7.7, 1.2$ Hz), 7.77 (1H, d, $J=7.7$ Hz), 7.83 (1H, d, $J=7.7$ Hz), 7.87 (1H, d, $J=7.7$ Hz), 8.17 (1H, d, $J=7.7$ Hz). *Anal.* Calcd for $C_{22}H_{17}N_2O_4Cl$: C, 64.59; H, 4.19; N, 6.66. Found: C, 64.63; H, 4.19; N, 6.85.

(6*R,6*aR**)-6-Chloro-6*a*-hydroxy-12-phenacyl-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-5-one**

(8k) from 5 — In the general procedure A, K₂CO₃ (172 mg, 1.25 mmol), phenacyl bromide (1.42 g, 7.10 mmol), **5** (115 mg, 0.33 mmol), and DMF (6.0 mL) were used. The reaction time was 1.5 h. After column-chromatography, **8k** (152 mg, 97%) was obtained. **8k**: mp 217—219°C (yellow plates, recrystallized from EtOAc—hexane). IR (KBr): 3372, 1697, 1579, 1475, 1230, 752 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ: 5.36 (1H, d, *J*=1.4 Hz, collapsed to s on addition of D₂O), 6.38 (1H, d, *J*=18.3 Hz), 6.52 (1H, d, *J*=18.3 Hz), 6.84 (1H, d, *J*=1.4 Hz, disappeared on addition of D₂O), 7.34 (1H, td, *J*=7.6, 1.3 Hz), 7.42 (1H, td, *J*=7.6, 1.3 Hz), 7.45 (1H, td, *J*=7.6, 1.3 Hz), 7.47 (1H, td, *J*=7.6, 1.3 Hz), 7.51 (1H, d, *J*=8.3 Hz), 7.67 (2H, t, *J*=8.3 Hz), 7.76 (1H, d, *J*=7.6 Hz), 7.77 (1H, t, *J*=8.3 Hz), 7.80 (1H, d, *J*=7.6 Hz), 8.17 (1H, d, *J*=7.6 Hz), 8.18 (1H, d, *J*=7.6 Hz), 8.21 (1H, d, *J*=7.6 Hz). MS *m/z*: 442 and 440 (M⁺). *Anal.* Calcd for C₂₆H₁₇N₂O₃Cl: C, 70.83; H, 3.89; N, 6.35. Found: C, 70.67; H, 3.91; N, 6.24.

(6*R,6*aR**)-12-(3-Bromopropyl)-6-chloro-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-*a*]carbazole-**

5-one (8l) from 5 — In the general procedure A, K₂CO₃ (45.7 mg, 0.33 mmol), 1,3-dibromopropane (0.19 mL, 1.89 mmol), **5** (30.5 mg, 0.09 mmol), and DMF (2.0 mL) were used. The reaction time was 50 min. After column-chromatography, **8l** (18.9 mg, 45%) was obtained. **8l**: mp 148—150°C (orange plates, recrystallized from CHCl₃). IR (KBr): 3400, 1651, 1581, 1479, 1080, 758 cm⁻¹. ¹H-NMR (CDCl₃) δ: 2.51—2.63 (2H, m), 3.12 (1H, br s, disappeared on addition of D₂O), 3.46 (1H, ddd, *J*=10.4, 6.9, 5.7 Hz), 3.52 (1H, ddd, *J*=10.4, 6.9, 5.7 Hz), 4.76 (1H, s), 4.80 (1H, ddd, *J*=14.2, 7.6, 6.5 Hz), 5.02 (1H, dt, *J*=14.4, 7.1 Hz), 7.36 (1H, td, *J*=7.8, 1.1 Hz), 7.41 (1H, td, *J*=7.8, 1.1 Hz), 7.50 (1H, td, *J*=7.8, 1.1 Hz), 7.52 (1H, td, *J*=7.8, 1.1 Hz), 7.62 (1H, d, *J*=7.8 Hz), 7.73 (1H, d, *J*=7.8 Hz), 7.92 (1H, d, *J*=7.8 Hz), 8.39 (1H, d, *J*=7.8 Hz). HR-MS (FAB⁺): Calcd for C₂₁H₁₆N₂O₂⁸¹Br³⁷Cl: 447.0112. Found: 447.0084. C₂₁H₁₆N₂O₂⁷⁹Br³⁷Cl: 445.0132. Found: 445.0109. C₂₁H₁₆N₂O₂⁸¹Br³⁵Cl: 445.0141. Found: 445.0109. C₂₁H₁₆N₂O₂⁷⁹Br³⁵Cl: 443.0162. Found: 443.0132. *Anal.* Calcd for C₂₁H₁₆N₂O₂BrCl·1/4H₂O: C, 56.27; H, 3.71; N, 6.25. Found: C, 56.33; H, 3.65; N, 5.95.

(6*R,6*aR**)-6-Chloro-12-[3-(ethoxycarbonyl)propyl]-6*a*-hydroxy-5,6,6*a*,12-tetrahydroindolo[2,3-**

***a*]carbazole-5-one (8m) from 5** — **General Procedure B**: A solution of **5** (28.9 mg, 0.09 mmol) in anhydrous DMF (2.0 mL) was added to 60% NaH (3.7 mg, 0.09 mmol) at 0°C with stirring under argon atmosphere. After additional stirring at rt, ethyl 4-bromobutylate (0.26 mL, 1.79 mmol) was added and the mixture was stirred for 1 h at rt. After addition of EtOAc, the whole was washed successively with H₂O, brine, and dried over Na₂SO₄, then evaporated under reduced pressure to leave an oil, which was column-chromatographed repeatedly on SiO₂ with EtOAc—hexane (1:2, v/v) to give **8m** (23.2 mg, 59%) and unreacted **5** (2.80 mg, 10%) in the order of elution. **8m**: (brown viscous oil). IR (film): 3367, 1707, 1672, 1579, 1481, 1200, 750 cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.15 (3H, t, *J*=7.1 Hz), 2.17 (2H, q, *J*=7.1 Hz), 2.38—2.43 (2H, m), 4.04 (2H, q, *J*=7.1 Hz), 4.70 (1H, dt, *J*=14.2, 7.1 Hz), 4.91 (1H, dt, *J*=14.2, 7.1 Hz),

5.32 (1H, d, $J=1.3$ Hz, collapsed to s on addition of D₂O), 6.82 (1H, d, $J=1.3$ Hz, disappeared on addition of D₂O), 7.39 (1H, t, $J=7.8$ Hz), 7.41 (1H, t, $J=7.8$ Hz), 7.52 (1H, td, $J=7.8, 1.2$ Hz), 7.55 (1H, td, $J=7.8, 1.2$ Hz), 7.76 (1H, d, $J=7.8$ Hz), 7.84 (1H, d, $J=7.8$ Hz), 7.84 (1H, d, $J=7.8$ Hz), 8.19 (1H, d, $J=7.8$ Hz). HR-MS m/z : Calcd for C₂₄H₂₁N₂O₄³⁷Cl: 438.1160. Found: 438.1140. C₂₄H₂₁N₂O₄³⁵Cl: 436.1189. Found: 436.1184.

(6R*,6aR*)-6-Chloro-12-[(Z)-3-chloroallyl]- (8n) and -12-[(E)-3-chloroallyl]-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8o) from 5 — In the general procedure B, **5** (63.5 mg, 0.20 mmol), anhydrous DMF (4.0 mL), 60% NaH (7.90 mg, 0.20 mmol), and (*E,Z*) mixture of 1,3-dichloropropene (0.36 mL, 3.94 mmol) were used. After repeated column-chromatography, **8n** (32.9 mg, 42%), **8o** (18.4 mg, 24%), and unreacted **5** (9.10 mg, 14%) were obtained in the order of elution. **8n**: mp 207—209°C (decomp., yellow powder, recrystallized from EtOAc). IR (KBr): 3381, 1649, 1616, 1581, 1475, 802, 754, 739 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 5.34 (1H, s), 5.48 (1H, ddd, $J=16.1, 6.5, 2.3$ Hz), 5.73 (1H, ddd, $J=16.1, 6.5, 2.3$ Hz), 6.17 (1H, q, $J=6.5$ Hz), 6.63 (1H, dt, $J=6.5, 2.3$ Hz), 6.84 (1H, br s, disappeared on addition of D₂O), 7.40 (1H, td, $J=7.6, 1.1$ Hz), 7.43 (1H, td, $J=7.6, 1.1$ Hz), 7.53 (1H, td, $J=7.6, 1.1$ Hz), 7.55 (1H, td, $J=7.6, 1.1$ Hz), 7.68 (1H, d, $J=7.6$ Hz), 7.78 (1H, d, $J=7.6$ Hz), 7.84 (1H, d, $J=7.6$ Hz), 8.19 (1H, d, $J=7.6$ Hz). MS m/z : 400, 398, and 396 (M⁺). *Anal.* Calcd for C₂₁H₁₄N₂O₂Cl₂·1/4H₂O: C, 62.78; H, 3.64; N, 6.97. Found: C, 63.00; H, 3.58; N, 6.95. **8o**: brown oil. IR (film): 3417, 1653, 1577, 1471, 1146, 748 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 5.34 (1H, d, $J=1.5$ Hz, collapsed to s on addition of D₂O), 5.36 (1H, ddd, $J=13.4, 6.8, 1.7$ Hz), 5.53 (1H, ddd, $J=13.4, 6.8, 1.7$ Hz), 6.30 (1H, dt, $J=13.4, 6.8$ Hz), 6.74 (1H, d, $J=13.4$ Hz), 6.81 (1H, d, $J=1.5$ Hz, disappeared on addition of D₂O), 7.40 (1H, td, $J=7.6, 1.1$ Hz), 7.42 (1H, t, $J=7.6$ Hz), 7.52 (1H, td, $J=7.6, 1.1$ Hz), 7.55 (1H, td, $J=7.6, 1.1$ Hz), 7.80 (1H, d, $J=7.6$ Hz), 7.84 (1H, d, $J=7.6$ Hz), 7.87 (1H, d, $J=7.6$ Hz), 8.18 (1H, d, $J=7.6$ Hz). HR-MS m/z : Calcd for C₂₁H₁₄N₂O₂³⁷Cl₂: 400.0374. Found: 400.0339. C₂₁H₁₄N₂O₂³⁷Cl³⁵Cl: 398.0403. Found: 398.0406. C₂₁H₁₄N₂O₂³⁵Cl₂: 396.0433. Found: 396.0449.

(6R*,6aR*)-12-Acetyl-6-chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8p) from 5 — In the general procedure B, **5** (47.4 mg, 0.15 mmol), anhydrous DMF (2.0 mL), 60% NaH (5.80 mg, 0.15 mmol), and acetyl chloride (0.21 mL, 2.94 mmol) were used. After repeated column-chromatography, **8p** (22.2 mg, 41%) and unreacted **5** (10.9 mg, 23%) were obtained in the order of elution. **8p**: mp 209—211°C (decomp., yellow fine needles, recrystallized from EtOAc). IR (KBr): 3332, 1695, 1685, 1571, 1284, 1263, 760 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 2.92 (3H, s), 5.31 (1H, s), 7.08 (1H, br s, disappeared on addition of D₂O), 7.44 (1H, td, $J=7.9, 1.3$ Hz), 7.52 (1H, t, $J=7.9$ Hz), 7.58 (1H, td, $J=7.9, 1.3$ Hz), 7.61 (1H, td, $J=7.9$ Hz), 7.80 (1H, d, $J=7.9$ Hz), 7.83 (1H, d, $J=7.9$ Hz), 8.22 (2H, d, $J=7.9$ Hz). MS m/z : 366 and 364 (M⁺). *Anal.* Calcd for C₂₀H₁₃N₂O₃Cl·EtOAc: C, 63.65; H, 4.67; N, 6.19. Found: C, 63.42; H, 4.53; N, 6.37.

12-*n*-Butyl-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (9a) from 8a — General Procedure C: NaCN (239 mg, 5.72 mmol) was added to a solution of **8a** (61.5 mg, 0.16 mmol) in DMF (4.0 mL) and H₂O (2.0 mL), and the mixture was stirred for 0.5 h at rt. After addition of H₂O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with EtOAc–hexane (1:3, v/v) to give **9a** (48.9 mg, 85%). **9a**: mp 251–253°C (pale gray powder, recrystallized from EtOAc). IR (KBr): 3311, 2206, 1705, 1630, 1576, 1414, 737 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ: 0.81 (3H, t, *J*=7.4 Hz), 1.28 (2H, sex, *J*=7.4 Hz), 1.82 (2H, quin, *J*=7.4 Hz), 4.86 (2H, t, *J*=7.4 Hz), 7.27 (1H, t, *J*=7.7 Hz), 7.31 (1H, t, *J*=7.7 Hz), 7.48 (1H, t, *J*=7.7 Hz), 7.50 (1H, t, *J*=7.7 Hz), 7.72 (1H, d, *J*=7.7 Hz), 7.74 (1H, d, *J*=7.7 Hz), 8.39 (1H, d, *J*=7.7 Hz), 8.45 (1H, d, *J*=7.7 Hz), 10.7 (1H, s, disappeared on addition of D₂O), 11.5 (1H, s, disappeared on addition of D₂O). MS *m/z*: 353 (M⁺). *Anal.* Calcd for C₂₃H₁₉N₃O: C, 78.16; H, 5.42; N, 11.89. Found: C, 77.95; H, 5.47; N, 11.69.

12-Allyl-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (9b) from 8b — In the general procedure C, NaCN (1.50 g, 28.9 mmol), **8b** (349 mg, 0.96 mmol), DMF (18.0 mL), and H₂O (9.0 mL) were used. After column-chromatography, **9b** (294 mg, 91%) was obtained. **9b**: mp 236.5–238°C (decomp., pale gray cotton fibers, recrystallized from Et₂O–hexane). IR (KBr): 3440, 2110, 1625, 1458, 1416, 1354, 1168, 916, 736 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ: 4.75 (1H, d, *J*=17.4 Hz), 5.06 (1H, d, *J*=10.5 Hz), 5.49–5.53 (2H, m), 6.10–6.20 (1H, m), 7.26 (1H, t, *J*=7.6 Hz), 7.33 (1H, t, *J*=7.6 Hz), 7.47 (1H, t, *J*=7.6 Hz), 7.49 (1H, t, *J*=7.6 Hz), 7.69 (2H, d, *J*=7.6 Hz), 8.39 (1H, d, *J*=7.6 Hz), 8.44 (1H, d, *J*=7.6 Hz), 10.73 (1H, br s, disappeared on addition of D₂O), 11.53 (1H, s, disappeared on addition of D₂O). MS *m/z*: 337 (M⁺). *Anal.* Calcd for C₂₂H₁₅N₃O: C, 78.32; H, 4.48; N, 12.46. Found: C, 78.08; H, 4.47; N, 12.29.

6-Cyano-5-hydroxy-12-propargylindolo[2,3-*a*]carbazole (9c) from 8c — In the general procedure C, NaCN (112 mg, 2.29 mmol), **8c** (27.5 mg, 0.08 mmol), DMF (2.0 mL), and H₂O (1.0 mL) were used. After column-chromatography, **9c** (18.5 mg, 72%) was obtained. **9c**: mp 268–270°C (decomp., pale brown powder, recrystallized from CHCl₃). IR (KBr): 3454, 3263, 2206, 1633, 1460, 1242, 742 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ: 3.30–3.31 [1H, m, clearly appeared at 3.23 (1H, t, *J*=2.2 Hz) on addition of D₂O], 5.75 (2H, d, *J*=2.2 Hz), 7.28 (1H, t, *J*=7.8 Hz), 7.36 (1H, t, *J*=7.8 Hz), 7.49 (1H, t, *J*=7.8 Hz), 7.54 (1H, t, *J*=7.8 Hz), 7.72 (1H, d, *J*=7.8 Hz), 7.81 (1H, d, *J*=7.8 Hz), 8.39 (1H, d, *J*=7.8 Hz), 8.46 (1H, d, *J*=7.8 Hz), 10.8 (1H, s, disappeared on addition of D₂O), 11.7 (1H, s, disappeared on addition of D₂O). MS *m/z*: 335 (M⁺). *Anal.* Calcd for C₂₂H₁₃N₃O·1/2H₂O: C, 76.73; H, 4.10; N, 12.20. Found: C, 76.86; H, 3.91; N, 11.96.

12-Benzyl-6-Cyano-5-hydroxyindolo[2,3-*a*]carbazole (9d) from 8d — In the general procedure C, NaCN (123 mg, 3.06 mmol), **8d** (32.9 mg, 0.08 mmol), DMF (2.0 mL), and H₂O (1.0 mL) were used. After column-chromatography, **9d** (30.1 mg, 98%) was obtained. **9d**: mp 243–244°C (decomp., gray

needles, recrystallized from EtOAc). IR (KBr): 3282, 2200, 1635, 1576, 1169, 739 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 6.13 (2H, s), 7.14—7.25 (5H, m), 7.27 (1H, td, $J=7.7$, 1.7 Hz), 7.32 (1H, td, $J=7.7$, 1.7 Hz), 7.43 (1H, td, $J=7.7$, 1.7 Hz), 7.46 (1H, td, $J=7.7$, 1.7 Hz), 7.64 (1H, d, $J=7.7$ Hz), 7.65 (1H, d, $J=7.7$ Hz), 8.40 (1H, d, $J=7.7$ Hz), 8.46 (1H, d, $J=7.7$ Hz), 10.8 (1H, br s, disappeared on addition of D_2O), 11.7 (1H, s, disappeared on addition of D_2O). MS m/z : 387 (M^+). *Anal.* Calcd for $\text{C}_{26}\text{H}_{17}\text{N}_3\text{O}$: C, 80.60; H, 4.42; N, 10.85. Found: C, 80.46; H, 4.47; N, 10.78.

12-Benzyl-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (9d) from 13 — Crushed NaOH powder (675 mg, 16.9 mmol) was added to a solution of **13** (9.6 mg, 0.02 mmol) in ethylene glycol (3.0 mL), and the mixture was refluxed for 2 h with stirring. After addition of H_2O , the whole was extracted with EtOAc. The extract was washed with H_2O and brine, dried over Na_2SO_4 , and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:3, v/v) to give **9d** (5.7 mg, 62%).

6-Cyano-5-hydroxy-12-phenethylindolo[2,3-*a*]carbazole (9e) from 8e — In the general procedure C, NaCN (117 mg, 2.27 mmol), **8e** (32.3 mg, 0.08 mmol), DMF (2.0 mL), and H_2O (1.0 mL) were used. After column-chromatography, **9e** (25.8 mg, 85%) was obtained. **9e**: mp 255—257°C (decomp., pale brown powder, recrystallized from acetone). IR (KBr): 3282, 2212, 1628, 1410, 1238, 742, 700 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 3.10 (2H, t, $J=7.2$ Hz), 5.12 (2H, t, $J=7.2$ Hz), 7.04—7.08 (1H, m), 7.11 (4H, d, $J=4.4$ Hz), 7.26 (1H, t, $J=7.9$ Hz), 7.27 (1H, t, $J=7.9$ Hz), 7.38 (1H, td, $J=7.9$, 0.98 Hz), 7.48 (1H, td, $J=7.9$, 0.98 Hz), 7.54 (1H, d, $J=7.9$ Hz), 7.72 (1H, d, $J=7.9$ Hz), 8.34 (1H, d, $J=7.9$ Hz), 8.45 (1H, d, $J=7.9$ Hz), 10.7 (1H, br s, disappeared on addition of D_2O), 11.6 (1H, s, disappeared on addition of D_2O). MS m/z : 401 (M^+). *Anal.* Calcd for $\text{C}_{27}\text{H}_{19}\text{N}_3\text{O}\cdot\text{H}_2\text{O}$: C, 77.31; H, 5.05; N, 10.02. Found: C, 77.37; H, 4.85; N, 9.81.

12-(*E*)-Cinnamyl-6-Cyano-5-hydroxyindolo[2,3-*a*]carbazole (9f) from 8f — In the general procedure C, NaCN (159 mg, 3.23 mmol), **8f** (47.3 mg, 0.10 mmol), DMF (3.0 mL), and H_2O (1.5 mL) were used. After column-chromatography, **9f** (35.8 mg, 80%) was obtained. **9f**: yellow viscous oil. IR (film): 3467, 2216, 1631, 1414, 1173, 741 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 5.66 (2H, d, $J=5.1$ Hz), 6.44 (1H, d, $J=15.9$ Hz), 6.56 (1H, dt, $J=15.9$, 5.1 Hz), 7.17 (1H, t, $J=7.4$ Hz), 7.22 (2H, t, $J=7.4$ Hz), 7.26 (2H, d, $J=7.4$ Hz), 7.28 (1H, t, $J=7.7$ Hz), 7.34 (1H, t, $J=7.7$ Hz), 7.47 (1H, td, $J=7.7$, 0.88 Hz), 7.50 (1H, td, $J=7.7$, 0.88 Hz), 7.71 (1H, d, $J=7.7$ Hz), 7.77 (1H, d, $J=7.7$ Hz), 8.41 (1H, d, $J=7.7$ Hz), 8.45 (1H, d, $J=7.7$ Hz), 10.8 (1H, br s, disappeared on addition of D_2O), 11.6 (1H, s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $\text{C}_{28}\text{H}_{19}\text{N}_3\text{O}$: 413.1528. Found: 413.1529.

6-Cyano-12-cyanomethyl-5-hydroxyindolo[2,3-*a*]carbazole (9g) from 8g — In the general procedure C, NaCN (1.45 g, 27.8 mmol), **8g** (333 mg, 0.93 mmol), DMF (24.0 mL), and H_2O (12.0 mL) were used. After column-chromatography, **9g** (168 mg, 54%) was obtained. **9g**: mp 272.5—275°C (decomp., pale

gray powder, recrystallized from EtOAc–hexane). IR (KBr): 3300, 2230, 1630, 1580, 1414, 1320, 1178, 902, 745 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 6.17 (2H, s), 7.31 (1H, t, $J=8.0$ Hz), 7.42 (1H, t, $J=8.0$ Hz), 7.53 (1H, t, $J=8.0$ Hz), 7.56 (1H, t, $J=8.0$ Hz), 7.73 (1H, d, $J=8.0$ Hz), 7.88 (1H, d, $J=8.0$ Hz), 8.41 (1H, d, $J=8.0$ Hz), 8.47 (1H, d, $J=8.0$ Hz), 10.93 (1H, s, disappeared on addition of D_2O), 11.90 (1H, s, disappeared on addition of D_2O). MS m/z : 336 (M^+). *Anal.* Calcd for $\text{C}_{21}\text{H}_{12}\text{N}_4\text{O}\cdot 1/8\text{H}_2\text{O}$: C, 74.49; H, 3.65; N, 16.55. Found: C, 74.70; H, 3.62; N, 16.25.

6-Cyano-12-*N,N*-dimethylcarbamoylmethyl-5-hydroxyindolo[2,3-*a*]carbazole (9h) from 8h — In the general procedure C, NaCN (119 mg, 2.43 mmol), **8h** (33.1 mg, 0.81 mmol), DMF (2.0 mL), and H_2O (1.0 mL) were used. After column-chromatography, **9h** (29.6 mg, 95%) was obtained. **9h**: mp $>300^\circ\text{C}$ (gray powder, recrystallized from MeOH). IR (KBr): 3311, 2216, 1651, 1635, 1412, 742 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 2.86 (3H, s), 3.33 (3H, s), 5.75 (2H, s), 7.27 (1H, t, $J=7.8$ Hz), 7.31 (1H, t, $J=7.8$ Hz), 7.45 (1H, t, $J=7.8$ Hz), 7.47 (1H, t, $J=7.8$ Hz), 7.59 (1H, d, $J=7.8$ Hz), 7.67 (1H, d, $J=7.8$ Hz), 8.38 (1H, d, $J=7.8$ Hz), 8.45 (1H, d, $J=7.8$ Hz), 10.7 (1H, br s, disappeared on addition of D_2O), 11.5 (1H, s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $\text{C}_{23}\text{H}_{18}\text{N}_4\text{O}_2$: 382.1430. Found: 382.1421.

6-Cyano-5-hydroxy-12-methoxycarbonylmethyl- (9i) and 12-Carboxymethyl-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (9q) from 8i — In the general procedure C, NaCN (395 mg, 7.64 mmol), **8i** (100 mg, 0.25 mmol), DMF (4.0 mL), and H_2O (2.0 mL) were used. After column-chromatography, **9i** (15.5 mg, 17%) was obtained. The aqueous layer was made acidic by adding aq. 8% HCl and extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4 , and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 with CHCl_3 –MeOH–AcOH (46:5:0.5, v/v) to give **9q** (38.6 mg, 43%). **9i**: mp $>300^\circ\text{C}$ (pale gray powder, recrystallized from EtOAc–hexane). IR (KBr): 3410, 2220, 1720, 1630, 1458, 1417, 1240, 1177, 737 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 3.69 (3H, s), 5.80 (2H, s), 7.28 (1H, t, $J=7.3$ Hz), 7.35 (1H, t, $J=7.3$ Hz), 7.45–7.52 (2H, m), 7.65 (1H, d, $J=7.3$ Hz), 7.66 (1H, d, $J=7.3$ Hz), 8.39 (1H, d, $J=7.7$ Hz), 8.44 (1H, d, $J=7.7$ Hz), 10.79 (1H, s, disappeared on addition of D_2O), 11.65 (1H, s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $\text{C}_{22}\text{H}_{15}\text{N}_3\text{O}_3$: 369.1114. Found: 369.1114. **9q**: mp 198–200 $^\circ\text{C}$ (decomp., gray powder, recrystallized from MeOH– H_2O). IR (KBr): 3367, 2208, 1724, 1631, 1462, 1412, 1323, 1173, 741, 428 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 5.64 (2H, s), 7.26 (1H, t, $J=7.8$ Hz), 7.33 (1H, t, $J=7.8$ Hz), 7.41–7.51 (2H, m), 7.63 (1H, d, $J=8.3$ Hz), 7.65 (1H, d, $J=8.3$ Hz), 8.38 (1H, d, $J=7.8$ Hz), 8.43 (1H, d, $J=7.8$ Hz), 10.74 (1H, br s, disappeared on addition of D_2O), 11.70 (1H, s, disappeared on addition of D_2O). MS m/z : 355 (M^+). *Anal.* Calcd for $\text{C}_{21}\text{H}_{13}\text{N}_3\text{O}_3\cdot 1/2\text{H}_2\text{O}$: C, 69.22; H, 3.87; N, 11.53. Found: C, 69.20; H, 3.92; N, 11.27.

12-(3-Bromopropyl)-6-cyano- (9l) and 6-Cyano-12-(3-cyanopropyl)-5-hydroxyindolo[2,3-*a*]carbazole (9r) from 8l — In the general procedure C, NaCN (107 mg, 2.18 mmol), **8l** (32.2 mg, 0.07 mmol), DMF (2.0 mL), and H_2O (1.0 mL) were used. After column-chromatography, **9l** (6.9 mg, 23%)

and **9r** (6.1 mg, 23%) were obtained in the order of elution. **9l**: (brown viscous oil). IR (film): 3423, 2210, 1633, 1454, 1246, 746 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 2.40 (2H, q, $J=6.9$ Hz), 3.56 (2H, t, $J=6.9$ Hz), 4.95 (2H, t, $J=6.9$ Hz), 7.28 (1H, t, $J=7.7$ Hz), 7.34 (1H, t, $J=7.7$ Hz), 7.49 (1H, td, $J=7.7$, 1.2 Hz), 7.53 (1H, td, $J=7.7$, 1.2 Hz), 7.73 (1H, d, $J=7.7$ Hz), 7.78 (1H, d, $J=7.7$ Hz), 8.40 (1H, d, $J=7.7$ Hz), 8.46 (1H, d, $J=7.7$ Hz), 10.8 (1H, br s, disappeared on addition of D_2O), 11.6 (1H, s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{O}^{81}\text{Br}$: 419.0456. Found: 419.0491. $\text{C}_{22}\text{H}_{16}\text{N}_3\text{O}^{79}\text{Br}$: 417.0477. Found: 417.0451. **9r**: (brown viscous oil). IR (film): 3342, 2262, 2210, 1633, 1452, 1400, 756 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 2.19 (2H, q, $J=7.3$ Hz), 2.61 (2H, t, $J=7.3$ Hz), 4.89 (2H, t, $J=7.3$ Hz), 7.28 (1H, t, $J=8.0$ Hz), 7.34 (1H, t, $J=7.7$ Hz), 7.49 (1H, t, $J=8.0$ Hz), 7.53 (1H, t, $J=8.0$ Hz), 7.72 (1H, d, $J=8.0$ Hz), 7.77 (1H, d, $J=8.0$ Hz), 8.40 (1H, d, $J=8.0$ Hz), 8.46 (1H, d, $J=8.0$ Hz), 10.8 (1H, s, disappeared on addition of D_2O), 11.6 (1H, s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $\text{C}_{23}\text{H}_{16}\text{N}_4\text{O}$: 364.1324. Found: 364.1324.

6-Cyano-12-[3-(ethoxycarbonyl)propyl]-5-hydroxyindolo[2,3-*a*]carbazole (9m) from 8m — In the general procedure C, NaCN (301 mg, 5.83 mmol), **8m** (84.8 mg, 0.19 mmol), DMF (4.0 mL), and H_2O (2.0 mL) were used. After column-chromatography, **9m** (53.3 mg, 72%) was obtained. **9m**: mp 258—260°C (pale brown powder, recrystallized from CHCl_3). IR (KBr): 3292, 2210, 1711, 1633, 1242, 1169, 741 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 1.07 (3H, t, $J=7.1$ Hz), 2.13 (2H, quin, $J=7.2$ Hz), 2.41 (2H, t, $J=7.2$ Hz), 3.95 (2H, q, $J=7.1$ Hz), 4.86 (2H, t, $J=7.2$ Hz), 7.28 (1H, t, $J=7.8$ Hz), 7.33 (1H, t, $J=7.8$ Hz), 7.49 (1H, td, $J=7.8$, 1.7 Hz), 7.51 (1H, td, $J=7.8$, 1.7 Hz), 7.72 (1H, d, $J=7.8$ Hz), 7.76 (1H, d, $J=7.8$ Hz), 8.39 (1H, d, $J=7.8$ Hz), 8.46 (1H, d, $J=7.8$ Hz), 10.7 (1H, br s, disappeared on addition of D_2O), 11.6 (1H, s, disappeared on addition of D_2O). MS m/z : 411 (M^+). Anal. Calcd for $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_3 \cdot 1/2\text{H}_2\text{O}$: C, 71.41; H, 5.27; N, 9.99. Found: C, 71.58; H, 5.28; N, 9.78.

12-(Z)-3-Chloroallyl- (9n) and 12-(E)-3-Chloroallyl)-6-cyano-5-hydroxyindolo[2,3-*a*]carbazole (9o) from 8n and 8o — In the general procedure C, NaCN (208 mg, 4.25 mmol), about 2:1 mixture of **8n** and **8o** (56.2 mg, 0.14 mmol), DMF (3.0 mL), and H_2O (1.5 mL) were used. After repeated column-chromatography, **9n** (21.5 mg, 41%) and **9o** (7.3 mg, 14%) were obtained in the order of elution. **9n**: >300 °C (gray powder, recrystallized from EtOAc). IR (KBr): 3454, 2208, 1628, 1412, 742 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 5.64 (2H, d, $J=6.6$ Hz), 6.12 (1H, q, $J=6.6$ Hz), 6.58 (1H, d, $J=6.6$ Hz), 7.28 (1H, t, $J=7.9$ Hz), 7.35 (1H, t, $J=7.9$ Hz), 7.48 (1H, t, $J=7.9$ Hz), 7.52 (1H, t, $J=7.9$ Hz), 7.59 (1H, d, $J=7.9$ Hz), 7.70 (1H, d, $J=7.9$ Hz), 8.40 (1H, d, $J=7.9$ Hz), 8.46 (1H, d, $J=7.9$ Hz), 10.8 (1H, br s, disappeared on addition of D_2O), 11.7 (1H, s, disappeared on addition of D_2O). HR-MS (FAB^+) m/z : Calcd for $\text{C}_{22}\text{H}_{15}\text{N}_3\text{O}^{37}\text{Cl}$: 374.0874. Found: 374.0908. $\text{C}_{22}\text{H}_{15}\text{N}_3\text{O}^{35}\text{Cl}$: 372.0903. Found: 372.0892. **9o**: (pale pink viscous oil). IR (film): 3448, 2218, 1630, 1464, 1417, 742 cm^{-1} . $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 5.53 (2H, br d, $J=6.3$ Hz), 6.25 (1H, dt, $J=12.9$, 6.3 Hz), 6.51 (1H, d, $J=12.9$ Hz), 7.28 (1H, t, $J=7.8$ Hz), 7.34 (1H, t,

$J=7.8$ Hz), 7.48 (1H, td, $J=7.8$, 1.7 Hz), 7.51 (1H, td, $J=7.8$, 1.7 Hz), 7.71 (1H, d, $J=7.8$ Hz), 7.77 (1H, d, $J=7.8$ Hz), 8.40 (1H, d, $J=7.8$ Hz), 8.45 (1H, d, $J=7.8$ Hz), 10.8 (1H, br s, disappeared on addition of D_2O), 11.6 (1H, br s, disappeared on addition of D_2O). HR-MS m/z : Calcd for $C_{22}H_{14}N_3O^{37}Cl$: 373.0796. Found: 373.0790. $C_{22}H_{14}N_3O^{35}Cl$: 371.0825. Found: 371.0819.

6-Cyano-5-hydroxyindolo[2,3-*a*]carbazole (10) and (6*R,6*aR**,11*aR**)-6-chloro-11a-cyano-6a-hydroxy-5,6,6a,11,11a,12-hexahydroindolo[2,3-*a*]carbazole-5-one (11) from 8p** — In the general procedure C, NaCN (109 mg, 2.23 mmol), **8p** (27.1 mg, 0.74 mmol), DMF (2.0 mL), and H_2O (1.0 mL) were used. After repeated column-chromatography with EtOAc–hexane (1:2, v/v) and $CHCl_3$ –MeOH (99:1, v/v), **10** (19.2 mg, 74%) and **11** (5.6 mg, 22%) were obtained in the order of elution. **10**: mp $>300^\circ C$ (pale gray powder, recrystallized from $CHCl_3$). IR (KBr): 3373, 2208, 1646, 1569, 1389, 1351, 1324, 1236, 743 cm^{-1} . 1H -NMR ($DMSO-d_6$) δ : 7.25 (1H, td, $J=0.9$, 7.8 Hz), 7.28 (1H, d, $J=7.8$ Hz), 7.42–7.47 (2H, m), 7.73 (2H, ddd, $J=0.9$, 5.9, 6.7 Hz), 8.33 (1H, d, $J=7.8$ Hz), 8.39 (1H, d, $J=7.8$ Hz), 10.62 (1H, br s, disappeared on addition of D_2O), 11.62 (1H, br s, disappeared on addition of D_2O), 11.59 (1H, s, disappeared on addition of D_2O). Anal. Calcd for $C_{19}H_{11}N_3O$: C, 76.76; H, 3.73; N, 14.13. Found: C, 76.81; H, 3.63; N, 14.12. **11**: mp 231–233 $^\circ C$ (yellow prisms, recrystallized from $CHCl_3$). IR (KBr): 3465, 2219 (very weak), 1673, 1468, 773 cm^{-1} . 1H -NMR ($DMSO-d_6$) δ : 5.17 (1H, br s, disappeared on addition of D_2O), 6.79 (1H, d, $J=7.7$ Hz), 6.85 (1H, td, $J=7.7$, 1.2 Hz), 7.20 (1H, td, $J=7.7$, 1.2 Hz), 7.27 (1H, td, $J=7.7$, 1.2 Hz), 7.35 (1H, td, $J=7.7$, 1.2 Hz), 7.37 (1H, s, disappeared on addition of D_2O), 7.42 (1H, s, disappeared on addition of D_2O), 7.47 (1H, d, $J=7.7$ Hz), 7.63 (1H, d, $J=7.7$ Hz), 7.95 (1H, d, $J=7.7$ Hz), 12.6 (1H, br s, disappeared on addition of D_2O). HR-MS (FAB^+) m/z : Calcd for $C_{13}H_{12}N_3O_2^{37}Cl$: 352.0667. Found: 352.0701. $C_{13}H_{12}N_3O_2^{35}Cl$: 350.697. Found: 350.0703. Anal. Calcd for $C_{13}H_{12}N_3O_2Cl \cdot 1/2CHCl_3$: C, 57.20; H, 3.08; N, 10.26. Found: C, 56.94; H, 3.12; N, 9.99.

6-Cyano-5-hydroxyindolo[2,3-*a*]carbazole (10) from 8k — In the general procedure C, NaCN (11.2 mg, 3.23 mmol), **8k** (47.3 mg, 0.10 mmol), DMF (2.0 mL), and H_2O (0.1 mL) were used. After column-chromatography, unreacted **8k** (5.5 mg, 16%) and **10** (6.1 mg, 27%) were obtained in the order of elution. **(5*R**,6*S**,6*aR**,11*aR**)-6-Chloro-11a-cyano-5,6a-dihydroxy-5,6,6a,11,11a,12-hexahydroindolo[2,3-*a*]carbazole (12a) from 11** — $NaBH_4$ (4.5 mg, 0.12 mmol) was added to a solution of **11** (14.1 mg, 0.04 mmol) in MeOH (2.0 mL), and the mixture was stirred for 1.5 h at rt. After addition of H_2O , the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4 , and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:3, v/v) to give **12a** (6.6 mg, 47%) and unreacted **11** (7.5 mg, 53 %) in the order of elution. **12a**: yellow viscous oil. IR (film): 3342, 2235 (almost invisible), 1655, 1585, 748 cm^{-1} . 1H -NMR ($DMSO-d_6$) δ : 3.93 (1H, d, $J=8.5$ Hz), 5.06 (1H, t, $J=8.5$ Hz, collapsed to d on addition of D_2O), 5.72 (1H, t, $J=8.5$ Hz, disappeared on addition of D_2O), 6.83 (1H, d, $J=7.5$ Hz), 6.87 (1H, td, $J=7.5$, 1.3 Hz), 7.06 (1H, t, $J=7.5$

Hz), 7.13 (1H, s, disappeared on addition of D₂O), 7.15 (1H, s, disappeared on addition of D₂O), 7.19 (1H, td, $J=7.5$, 1.3 Hz), 7.21 (1H, td, $J=7.5$, 1.3 Hz), 7.48 (1H, d, $J=7.5$ Hz), 7.51 (1H, d, $J=7.5$ Hz), 7.81 (1H, d, $J=7.5$ Hz), 11.3 (1H, s, disappeared on addition of D₂O). HR-MS (FAB⁺) m/z : Calcd for C₁₉H₁₅N₃O₂³⁷Cl: 354.0824. Found: 354.0871. C₁₉H₁₅N₃O₂³⁵Cl: 352.0853. Found: 352.0846.

(5R*,6S*,6aR*,11aR*)-6-Chloro-11a-cyano-5,12-diacetyl-6a-hydroxy-5,6,6a,11,11a,12-

hexahydroindolo[2,3-*a*]carbazole (12b) from 12a — Ac₂O (1.0 mL) was added to a solution of **12a** (10.0 mg, 0.03 mmol) in pyridine (2.0 mL), and the mixture was stirred for 14 h at rt. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO₂ with EtOAc–hexane (1:3, v/v) to give **12b** (3.7 mg, 30%) and unreacted **12a** (5.7 mg, 57 %) were obtained in the order of elution. **12b**: pale yellow oil. IR (film): 3390, 1749, 1705, 1610, 1373, 744 cm⁻¹. ¹H-NMR (DMSO-*d*₆ + 5% D₂O, 90°C) δ : 2.13 (3H, s), 2.96 (3H, s), 4.41 (1H, d, $J=8.3$ Hz), 6.56 (1H, d, $J=8.3$ Hz), 6.90 (1H, td, $J=7.5$, 1.7 Hz), 6.97 (1H, d, $J=7.5$ Hz), 7.24 (1H, td, $J=7.5$, 1.7 Hz), 7.37–7.42 (2H, m), 7.48 (1H, d, $J=7.5$ Hz), 7.52 (1H, td, $J=7.5$, 1.7 Hz), 7.94 (1H, d, $J=7.5$ Hz). HR-MS (FAB⁺) m/z : Calcd for C₂₃H₁₉N₃O₄³⁷Cl: 438.1035. Found: 438.1040. C₂₃H₁₉N₃O₄³⁵Cl: 436.1004. Found: 436.1051.

12-Benzyl-6-cyano-5-methoxyindolo[2,3-*a*]carbazole (13) from 9d — Excess amount of ethereal CH₂N₂ was added to a solution of **9d** (88.0 mg, 0.22 mmol) in MeOH (6.0 mL) and the mixture was stirred for 1.5 h at rt. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with CHCl₃–MeOH–28% aq. NH₃ (46:0.5:0.05, v/v) to give **13** (75.1 mg, 82%). **13**: mp 228.0–228.5°C (colorless needles, recrystallized from EtOAc). IR (KBr): 3338, 2208, 1628, 1560, 1390, 741 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 4.26 (3H, s), 6.16 (2H, s), 7.19 (2H, t, $J=7.7$ Hz), 7.20 (1H, t, $J=7.7$ Hz), 7.24 (1H, d, $J=7.7$ Hz), 7.26 (1H, d, $J=7.7$ Hz), 7.33 (1H, t, $J=7.4$ Hz), 7.38 (1H, t, $J=7.4$ Hz), 7.50 (1H, td, $J=7.4$, 1.9 Hz), 7.51 (1H, td, $J=7.4$, 1.9 Hz), 7.69 (1H, d, $J=7.4$ Hz), 7.71 (1H, d, $J=7.4$ Hz), 8.29 (1H, d, $J=7.4$ Hz), 8.48 (1H, d, $J=7.4$ Hz), 11.9 (1H, s, disappeared on addition of D₂O). MS m/z : 401 (M⁺). *Anal.* Calcd for C₂₇H₁₉N₃O·1/2H₂O: C, 79.00; H, 4.91; N, 10.24. Found: C, 79.09; H, 4.90; N, 9.99.

6-(Z)-Aminomethylidene-12-*n*-butyl-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (15a) from 9a — **General Procedure D**: A 1.0 M solution of DIBAL in toluene (2.7 mL, 2.67 mmol) was added to a solution of **9a** (31.4 mg, 0.09 mmol) in anhydrous THF (2.0 mL) under ice cooling and the mixture was stirred under N₂ atmosphere at rt for 3 h. After addition of MeOH and aq. Rochelle salt, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO₂ with CHCl₃–MeOH (99:1, v/v) to give **15a** (23.0 mg, 73%). **15a**: mp 170–172°C (decomp., dark yellow prisms, recrystallized from EtOAc). IR (KBr): 3400, 1628, 1610, 1577, 1560, 1421, 737 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 0.82 (3H, t, $J=7.4$ Hz), 1.29 (2H, sex, $J=7.4$ Hz), 1.81 (2H, quin, $J=7.4$ Hz), 4.77 (2H, t, $J=7.4$ Hz), 7.14 (1H, td,

$J=7.8$, 1.2 Hz), 7.22 (1H, t, $J=7.8$ Hz), 7.29 (1H, t, $J=7.8$ Hz), 7.31 (1H, td, $J=7.8$, 1.2 Hz), 7.62 (1H, d, $J=7.8$ Hz), 7.63 (1H, d, $J=7.8$ Hz), 8.02 (1H, d, $J=7.8$ Hz), 8.47 (1H, d, $J=7.8$ Hz), 8.60 (1H, br t, $J=8.2$ Hz, disappeared on addition of D_2O), 8.84 (1H, dd, $J=13.8$, 8.2 Hz, collapsed to s on addition of D_2O), 11.1 (1H, s, disappeared on addition of D_2O), 12.0 (1H, dd, $J=13.8$, 8.2 Hz, disappeared on addition of D_2O). HR-MS m/z : Calcd for $C_{23}H_{21}N_3O$: 355.1685. Found: 355.1693.

6-(Z)-Aminomethylidene-12-*n*-benzyl-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (15b) from 9d — In the general procedure D, DIBAL (1.4 mL, 1.45 mmol), **9d** (18.7 mg, 0.05 mmol), THF (2.0 mL) were used. The reaction time was 19 h. After column-chromatography, **15b** (6.9 mg, 47%) was obtained. **15b**: mp $207\text{--}209^\circ\text{C}$ (decomp., yellow powder, recrystallized from EtOAc). IR (KBr): 3450, 1628, 1610, 1577, 1560, 1410, 742 cm^{-1} . $^1\text{H-NMR}$ ($DMSO-d_6$) δ : 6.04 (2H, s), 7.12—7.28 (9H, m), 7.53 (1H, d, $J=7.5$ Hz), 7.54 (1H, d, $J=7.5$ Hz), 8.04 (1H, d, $J=7.5$ Hz), 8.49 (1H, dd, $J=7.5$, 1.7 Hz), 8.68 (1H, br t, $J=8.4$ Hz, disappeared on addition of D_2O), 8.88 (1H, dd, $J=13.6$, 8.4 Hz, collapsed to s on addition of D_2O), 11.2 (1H, s, disappeared on addition of D_2O), 12.1 (1H, dd, $J=13.6$, 8.4 Hz, disappeared on addition of D_2O). HR-MS (FAB^+) m/z : Calcd for $C_{26}H_{20}N_3O$: 390.1606. Found: 390.1631.

6-Acetoaminomethylidene-12-*n*-butyl-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (16) from 15a — Ac_2O (0.75 mL) was added to a solution of **15a** (16.1 mg, 0.05 mmol) in pyridine (1.5 mL), and the mixture was stirred for 1.5 h at rt. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 successively with EtOAc–hexane (1:3, v/v) and $CHCl_3$ –MeOH–28% aq. NH_3 (46:0.5:0.05, v/v) to give **16** (15.7 mg, 87%). **16**: red viscous oil. IR (film): 3354, 1685, 1620, 1610, 1552, 1415, 1273, 752, 739 cm^{-1} . $^1\text{H-NMR}$ ($CDCl_3$) δ : 0.92 (3H, t, $J=7.5$ Hz), 1.37 (2H, sex, $J=7.5$ Hz), 1.81 (2H, quin, $J=7.5$ Hz), 2.28 (3H, s), 4.02 (2H, t, $J=7.5$ Hz), 7.17 (1H, dd, $J=7.3$, 1.6 Hz), 7.25 (1H, td, $J=7.3$, 1.6 Hz), 7.30 (1H, td, $J=7.3$, 1.6 Hz), 7.32 (1H, td, $J=7.3$, 1.6 Hz), 7.34 (1H, td, $J=7.3$, 1.6 Hz), 7.42 (1H, d, $J=7.3$ Hz), 7.91 (1H, d, $J=7.3$ Hz), 8.24 (1H, s, disappeared on addition of D_2O), 8.44 (1H, dd, $J=7.3$, 1.6 Hz), 8.59 (1H, d, $J=10.4$ Hz, collapsed to s on addition of D_2O), 13.4 (1H, d, $J=10.4$ Hz, disappeared on addition of D_2O). HR-MS m/z : Calcd for $C_{25}H_{23}N_3O_2$: 397.1791. Found: 397.1790.

X-Ray Crystallographic Analysis of 9a and 11— All measurements were made on a Rigaku AFC5R diffract meter with graphite monochromated $Cu-K\alpha$ radiation ($\lambda=1.54178\text{ \AA}$). The structure was solved by direct methods using MITHRIL.⁹ Non-hydrogen atoms were refined anisotropically.

9a: a single crystal ($0.20\times0.20\times0.30\text{ mm}$) was obtained by recrystallization from EtOAc. Crystal data: $C_{23}H_{19}N_3O\cdot C_4H_8O_2$, $M=441.53$, triclinic, space group PT (#2), $a=10.626(1)\text{ \AA}$, $b=12.276(1)\text{ \AA}$, $c=9.912(1)\text{ \AA}$, $\alpha=104.474(8)^\circ$, $\beta=110.402(9)^\circ$, $\gamma=81.84(1)^\circ$, $V=1431.8(2)\text{ \AA}^3$, $Z=2$, $D_{\text{calc}}=1.252\text{ g/cm}^3$, $F(000)=468$, and $\mu(CuK\alpha)=6.26\text{ cm}^{-1}$. The final cycle of full-matrix least-squares refinement was based on 2807 observed reflections ($I > 3.00\sigma(I)$, $2\theta < 120.2^\circ$) and 386 variable parameters. The final

refinement converged with $R=0.049$ and $R_w=0.059$.

11: a single crystal (0.20x0.10x0.20 mm) was obtained by recrystallization from CHCl_3 . Crystal data: $\text{C}_{19}\text{H}_{12}\text{N}_3\text{O}_2$, $M=349.78$, monoclinic, space group $P2_1/a$ (#14), $a=14.408$ (5) Å, $b=14.096$ (3) Å, $c=17.928$ (4) Å, $\beta=93.60$ (2)°, $V=3634$ (2) Å³, $Z=8$, $D_{\text{calc}}=1.278$ g/cm³, $F(000)=1440$, and $\mu(\text{CuK}\alpha)=20.08$ cm⁻¹.

The final cycle of full-matrix least-squares refinement was based on 2139 observed reflections ($I > 3.00\sigma$ (I), $2\theta < 120.4^\circ$) and 583 variable parameters. The final refinement converged with $R=0.085$ and $R_w=0.091$.

Table 1. Positional parameters and B (eq) for **9a**

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.1896 (2)	0.0654 (1)	0.2830 (2)	5.17 (7)	C (25)	0.8209 (3)	0.1822 (2)	0.4815 (3)	5.7 (1)
O (2)	0.8726 (2)	0.2458 (2)	0.4463 (2)	6.8 (1)	C (26)	0.8428 (5)	0.0413 (4)	0.2759 (6)	13.3 (3)
O (3)	0.7980 (3)	0.0789 (2)	0.4049 (3)	9.5 (1)	C (27)	0.7667 (9)	-0.0363 (6)	0.1729 (8)	21.5 (5)
N (1)	0.0708 (2)	0.5274 (2)	0.3777 (2)	4.45 (7)	H (1)	0.509 (2)	0.389 (2)	0.869 (3)	5.95 (2)
N (2)	0.2986 (2)	0.4020 (1)	0.6128 (2)	4.22 (7)	H (2)	0.623 (3)	0.213 (2)	0.915 (3)	6.40 (2)
N (3)	-0.0727 (2)	0.1111 (2)	-0.0436 (2)	6.4 (1)	H (3)	0.557 (3)	0.044 (2)	0.740 (3)	6.28 (2)
C (1)	0.4849 (2)	0.3141 (2)	0.7977 (3)	4.9 (1)	H (4)	0.384 (2)	0.038 (2)	0.528 (3)	5.15 (1)
C (2)	0.5501 (3)	0.2129 (2)	0.8240 (3)	5.4 (1)	H (5)	-0.157 (2)	0.342 (2)	-0.052 (3)	5.09 (1)
C (3)	0.5126 (3)	0.1118 (2)	0.7237 (3)	5.2 (1)	H (6)	-0.274 (3)	0.505 (2)	-0.126 (3)	6.00 (1)
C (4)	0.4083 (2)	0.1100 (2)	0.5931 (3)	4.6 (1)	H (7)	-0.242 (3)	0.687 (2)	0.028 (3)	6.98 (2)
C (5)	0.3407 (2)	0.2114 (2)	0.5630 (2)	3.99 (8)	H (8)	-0.081 (2)	0.706 (2)	0.267 (3)	5.72 (1)
C (6)	0.2318 (2)	0.2423 (2)	0.4405 (2)	3.86 (8)	H (9)	0.100 (3)	0.590 (2)	0.449 (3)	5.73 (2)
C (7)	0.1590 (2)	0.1778 (2)	0.3048 (2)	4.01 (8)	H (10)	0.141 (3)	0.023 (2)	0.199 (3)	6.84 (2)
C (8)	0.0627 (2)	0.2318 (2)	0.2019 (2)	3.86 (3)	H (11)	0.342 (2)	0.516 (2)	0.805 (3)	5.66 (1)
C (9)	0.0400 (2)	0.3508 (2)	0.2369 (2)	3.77 (8)	H (12)	0.221 (2)	0.560 (2)	0.670 (2)	5.14 (1)
C (10)	-0.0494 (2)	0.4286 (2)	0.1542 (2)	3.92 (8)	H (13)	0.387 (3)	0.586 (2)	0.563 (3)	5.93 (2)
C (11)	-0.1435 (2)	0.4178 (2)	0.0126 (3)	4.6 (1)	H (14)	0.500 (2)	0.522 (2)	0.674 (2)	4.98 (1)
C (12)	-0.2120 (3)	0.5135 (2)	-0.0309 (3)	5.4 (1)	H (15)	0.493 (3)	0.667 (2)	0.881 (3)	7.68 (2)
C (13)	-0.1906 (3)	0.6193 (2)	0.0626 (3)	5.5 (1)	H (16)	0.377 (3)	0.729 (2)	0.779 (3)	6.35 (2)
C (14)	-0.0988 (2)	0.6326 (2)	0.2020 (3)	5.1 (1)	H (17)	0.578 (4)	0.822 (3)	0.837 (4)	10.11 (3)
C (15)	-0.0274 (2)	0.5367 (2)	0.2456 (3)	4.11 (8)	H (18)	0.506 (3)	0.769 (3)	0.657 (4)	8.47 (2)
C (16)	0.1126 (2)	0.4148 (2)	0.3728 (2)	3.90 (8)	H (19)	0.636 (3)	0.706 (3)	0.750 (4)	8.73 (2)
C (17)	0.2103 (2)	0.3601 (2)	0.4755 (2)	3.85 (8)	H (20)	0.784 (4)	0.294 (3)	0.661 (4)	12.09 (4)
C (18)	0.3802 (2)	0.3122 (2)	0.6663 (2)	4.11 (8)	H (21)	0.818 (5)	0.169 (3)	0.677 (4)	12.49 (4)
C (19)	-0.0130 (2)	0.1663 (2)	0.0641 (3)	4.53 (9)	H (22)	0.690 (4)	0.194 (3)	0.585 (4)	9.56 (3)
C (20)	0.3138 (2)	0.5187 (2)	0.6928 (3)	4.3 (1)	H (23)	0.8414	0.1026	0.2341	15.7
C (21)	0.4179 (2)	0.5752 (2)	0.6672 (3)	4.5 (1)	H (24)	0.9349	0.0096	0.3072	15.7
C (22)	0.4549 (3)	0.6848 (2)	0.7781 (3)	5.3 (1)	H (25)	0.6867	-0.0365	0.1940	24.4
C (23)	0.5509 (4)	0.7498 (3)	0.7514 (5)	7.9 (2)	H (26)	0.7501	-0.0229	0.0803	24.4
C (24)	0.7723 (5)	0.2105 (4)	0.6095 (4)	7.6 (2)	H (27)	0.8146	-0.1098	0.1789	24.4

Table 2. Positional parameters and *B* (eq) for **11**

atom	x	y	z	<i>B</i> (eq)	atom	x	y	z	<i>B</i> (eq)
O (1)	0.7922 (7)	0.2474 (7)	0.6700 (7)	3.4 (6)	C (14)	0.451 (1)	0.322 (1)	0.369 (1)	6 (1)
O (2)	0.7431 (8)	0.0971 (7)	0.4962 (6)	4.4 (6)	C (15)	0.503 (1)	0.304 (2)	0.408 (1)	6 (1)
N (1)	0.870 (1)	0.426 (1)	0.5746 (1)	3.8 (8)	C (16)	0.581 (1)	0.359 (1)	0.449 (1)	3.9 (9)
N (2)	0.648 (1)	0.406 (1)	0.4915 (8)	3.6 (8)	C (17)	0.713 (1)	0.349 (1)	0.5217 (8)	2.7 (8)
N (3)	0.721 (1)	0.479 (1)	0.6840 (9)	5.0 (9)	C (18)	0.794 (1)	0.378 (1)	0.5773 (9)	2.8 (8)
Cl (1)	0.9116 (3)	0.1120 (3)	0.5924 (3)	5.2 (3)	C (19)	0.752 (1)	0.434 (1)	0.639 (1)	3.4 (9)
C (1)	0.948 (1)	0.409 (1)	0.595 (1)	3.1 (8)	H (1)	0.864 (7)	0.469 (6)	0.539 (6)	−2 (3)
C (2)	1.032 (2)	0.455 (1)	0.599 (1)	5 (1)	H (2)	0.991 (7)	0.247 (7)	0.714 (6)	0 (2)
C (3)	1.104 (1)	0.418 (2)	0.649 (1)	5 (1)	H (3)	1.14 (1)	0.30 (1)	0.725 (8)	5 (4)
C (4)	1.091 (1)	0.339 (1)	0.692 (1)	5 (1)	H (4)	1.147 (8)	0.450 (8)	0.665 (6)	0 (3)
C (5)	1.005 (1)	0.295 (1)	0.685 (1)	3.3 (9)	H (5)	1.044 (6)	0.501 (6)	0.579 (5)	−2 (2)
C (6)	0.938 (1)	0.329 (1)	0.635 (1)	3.5 (9)	H (6)	0.889 (7)	0.230 (8)	0.522 (6)	1 (3)
C (7)	0.841 (1)	0.206 (1)	0.6145 (8)	2.5 (7)	H (7)	0.56 (1)	0.13 (1)	0.420 (9)	5 (5)
C (8)	0.847 (1)	0.212 (1)	0.5558 (8)	2.7 (8)	H (8)	0.444 (6)	0.194 (6)	0.360 (5)	−1 (2)
C (9)	0.759 (1)	0.102 (1)	0.5139 (9)	4 (1)	H (9)	0.382 (7)	0.333 (7)	0.342 (6)	1 (2)
C (10)	0.691 (1)	0.258 (1)	0.4996 (9)	2.8 (7)	H (10)	0.49 (1)	0.442 (9)	0.410 (8)	2 (4)
C (11)	0.612 (1)	0.263 (1)	0.4514 (8)	3.6 (8)	H (11)	0.658 (7)	0.453 (6)	0.497 (6)	−2 (2)
C (12)	0.555 (1)	0.196 (1)	0.413 (1)	6 (1)	H (12)	0.804 (6)	0.267 (6)	0.719 (5)	−1 (2)
C (13)	0.483 (1)	0.225 (1)	0.372 (2)	7 (1)					

REFERENCES AND NOTES

1. This report is Part 136 of a series entitled “The Chemistry of Indoles.” Part 135: K. Yamada, Y. Tanaka, and M. Somei, *Heterocycles*, 2009, **79**, 635.
2. Review: M. Somei, *Heterocycles*, 2008, **75**, 1021 and references cited therein.
3. M. Somei, F. Yamada, Y. Suzuki, S. Ohmoto, and H. Hayashi, *Heterocycles*, 2004, **64**, 483. H. Hayashi, Y. Suzuki, and M. Somei, *Heterocycles*, 1999, **51**, 1233. H. Hayashi, S. Ohmoto, and M. Somei, *Heterocycles*, 1997, **45**, 1647.
4. G. Knübel, L. K. Larsen, R. E. Moore, I. A. Levine, and G. M. L. Patterson, *J. Antibiotics*, 1990, **43**, 1236.
5. Review of indigo dye: P. E. McGovern and R. H. Michel, *Acc. Chem. Res.*, 1990, **23**, 152 and references cited therein.
6. Potent biological activity of **3** and its derivatives was reported: T. Ebara, T. Takahashi, and M. Maeda, Abstract of Papers, No. 2, 120th Annual Meeting of Pharmaceutical Society of Japan, Gifu, March, 2000, p. 136.
7. M. Somei, J. Kimura, and S. Takano, JP Patent 4248814 (2009).
8. The invention is now under application for a patent.
9. C. J. Gilmore, *J. Appl. Cryst.*, 1984, **17**, 42.