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

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**Abstract** – Various derivatives of (6*R**,6a*R**)-6-chloro-6a-hydroxy-5,6,6a,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**,6a*R**,11a*R**)-6-chloro-11a-cyano-6a-hydroxy- (**11**) and 12-substituted 6-(*Z*)-aminomethylidene-5,6,6a,11,11a,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 dye[5] 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 aggregation[7] while **5** is a promising $a_2$-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 derivatives of **5** and **7**. Interesting formations of (6*R**,6a*R**,11a*R**)-6-chloro-11a-cyano-6a-hydroxy-

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

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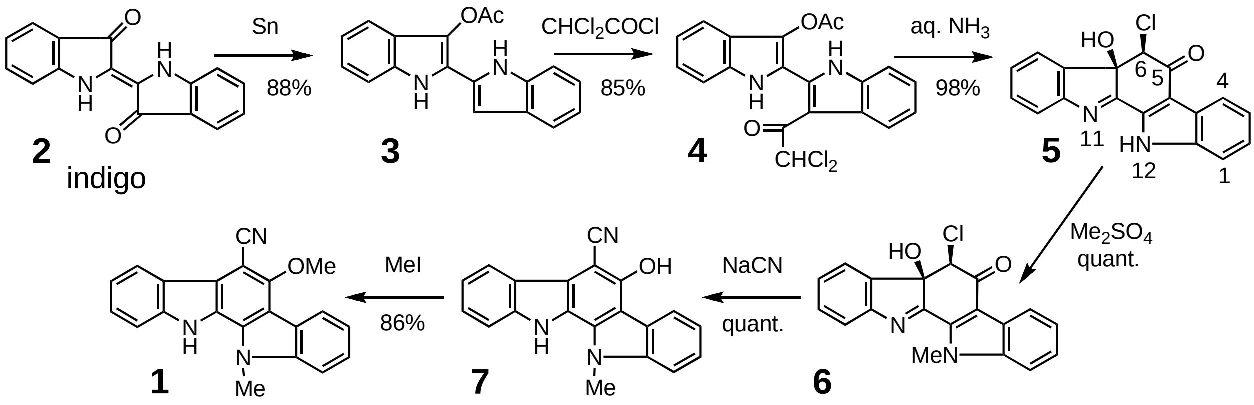
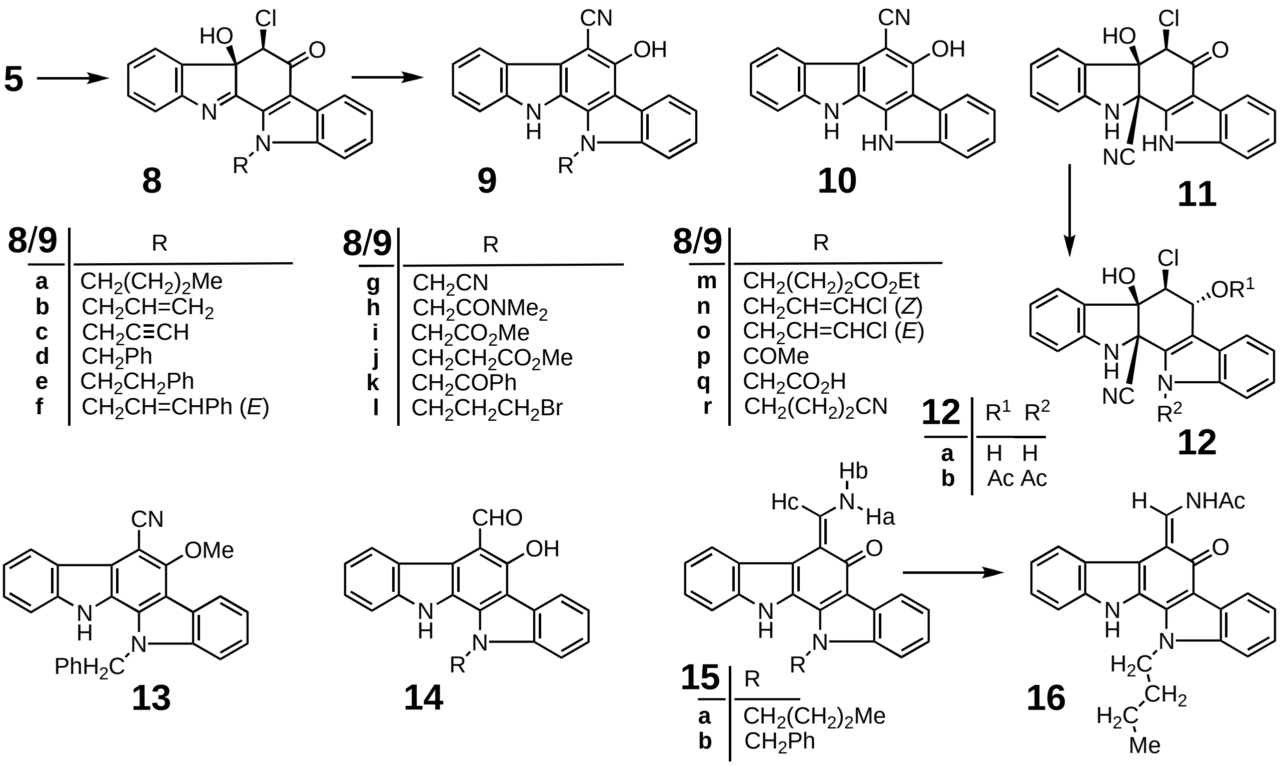
5,6,6a,11,11a,12-hexahydro- (**11**) and 12-substituted (*Z*)-6-aminomethylidene-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (**15**) are also reported.

**Scheme 1**




**Scheme 2**

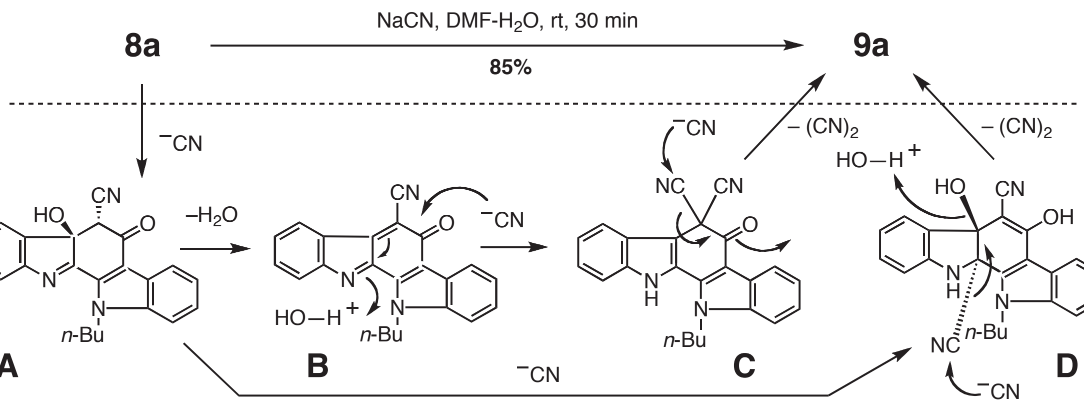



First, the compound **5** was prepared according to our procedures[3] from indigo in three steps in 73% overall yield. Subsequent treatment of **5** in *N*,*N*-dimethylformamide (DMF) in the presence of $K_2CO_3$ with *n*-butyl iodide, allyl bromide, propargyl bromide, benzyl bromide, phenethyl bromide, 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 $K_2CO_3$ 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**,6a*R**)-6-chloro-6a-hydroxy-5,6,6a,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-$H_2O$ 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 6b-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 a-side culminating in the formation of **D**. Subsequent cyanide attack at the 11a-cyano group and concomitant general acid promoted elimination of 6ab-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)

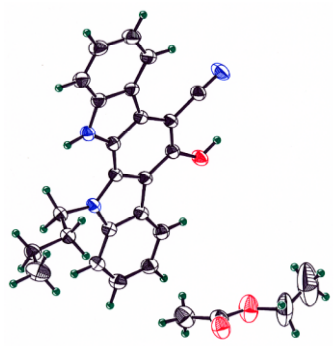
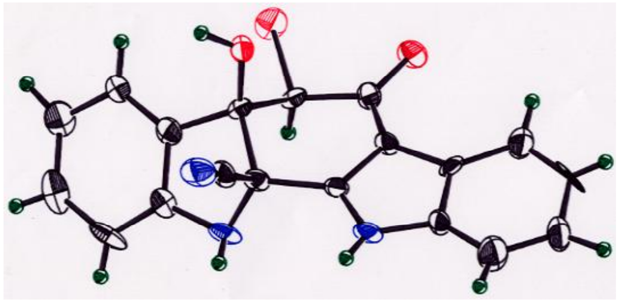


**Figure 2.** ORTEP Drawing of **11** (R=0.085)



The reaction of **8l** with NaCN in DMF-$H_2O$ 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**,6a*R**,11a*R**)-6-chloro-11a-cyano-6a-hydroxy-5,6,6a,11,11a,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 $NaBH_4$ proceeded slowly from the less hindered β-side to provide 5α-hydroxy compound **12a** in 47% yield. Further treatment of **12a** with acetic anhydride gave 5α-acetoxy compound **12b** in 30% yield. Comparing $^1$H-NMR spectra of **12a** and **12b**, the coupling constant between $H_5$ and $H_6$ 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 11a-position and the stereochemistries of 6, 6a, and 11a positions being all *R**.

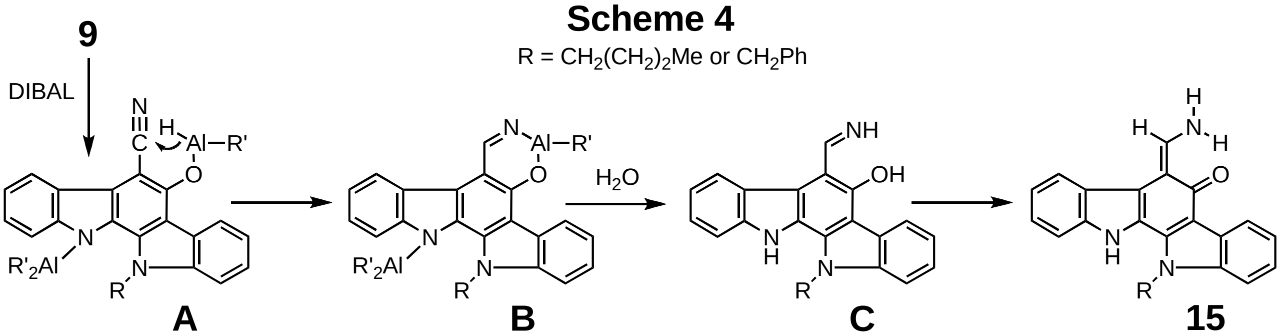
Methylation of **9d** with ethereal diazomethane smoothly proceeded to afford the corresponding methoxy compound **13** in 82% yield. All attempts to hydrolyze the 6-cyano group of **13** to 6-carboxy or 6-carbamoyl group with base were unsuccessful. Under severe conditions such as treatment of **13** 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 $^1$H-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 $D_2O$, 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 $Ac_2O$ 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.

**Scheme 4**




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 ($^1$H-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 ($SiO_2$, 100—200 mesh, from Kanto Chemical Co., Inc.) throughout the present study.

**(6*R**,6a*R**)-12-*n*-Butyl-6-chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8a) from (6*R**,6a*R**)-6-Chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (5) — General Procedure A:** $K_2CO_3$ (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 $H_2O$ under ice cooling, the whole was extracted with EtOAc. The extract was washed with 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 (1:5, v/v) to give **8a** (40.1 mg, 71%). **8a**: mp 187—189˚C (decomp., orange prisms, recrystallized from $CHCl_3$). IR (KBr): 3421, 1653, 1479, 1346, 1086, 754 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) 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 $D_2O$), 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 $C_{22}H_{19}N_2O_2Cl\cdot 1/8H_2O$: C, 69.33; H, 5.09; N, 7.35. Found: C, 69.38; H, 5.11; N, 7.24.

**(6*R**,6a*R**)-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, $K_2CO_3$ (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 $cm^{-1}$. $^1$H-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 $C_{21}H_{15}N_2O_2Cl$: C, 69.52; H, 4.17; N, 7.72. Found: C, 69.49; H, 4.17; N, 7.41.

**(6*R**,6a*R**)-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, $K_2CO_3$ (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 $cm^{-1}$. $^1$H-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 $D_2O$), 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 $D_2O$), 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 $C_{21}H_{13}N_2O_2Cl\cdot 1/2H_2O$: C, 68.21; H, 3.82; N, 7.58. Found: C, 68.00; H, 3.73; N, 7.33.

**(6*R**,6a*R**)-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, $K_2CO_3$ (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 $cm^{-1}$. $^1$H-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 $D_2O$), 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**,6a*R**)-6-Chloro-6a-hydroxy-12-phenethyl-5,6,6a,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 $C_{26}H_{19}N_2O_2Cl\cdot1/2H_2O$: C, 71.64; H, 4.62; N, 6.43. Found: C, 71.86; H, 4.43; N, 6.40.

**(6*R**,6a*R**)-6-Chloro-12-(*E*)-cinnamyl-6a-hydroxy-5,6,6a,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 $C_{27}H_{19}N_2O_2Cl\cdot1/2EtOAc$: C, 72.12; H, 4.80; N, 5.80. Found: C, 71.84; H, 4.68; N, 5.83.

**(6*R**,6a*R**)-6-Chloro-12-cyanomethyl-6a-hydroxy-5,6,6a,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**,6a*R**)-6-Chloro-12-*N*,*N*-dimethylcarbamoylmethyl-6a-hydroxy-5,6,6a,12-tetrahydroin-dolo-[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 $cm^{-1}$. $^1$H-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**,6a*R**)-6-Chloro-6a-hydroxy-12-methoxycarbonylmethyl-5,6,6a,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 $cm^{-1}$. $^1$H-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**,6a*R**)-6-Chloro-6a-hydroxy-12-[2-(methoxycarbonyl)ethyl]-5,6,6a,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 $cm^{-1}$. $^1$H-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**,6a*R**)-6-Chloro-6a-hydroxy-12-phenacyl-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8k) from 5** — In the general procedure A, $K_2CO_3$ (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 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) δ: 5.36 (1H, d, *J*=1.4 Hz, collapsed to s on addition of $D_2O$), 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 $D_2O$), 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 $C_{26}H_{17}N_2O_3Cl$: C, 70.83; H, 3.89; N, 6.35. Found: C, 70.67; H, 3.91; N, 6.24.

**(6*R**,6a*R**)-12-(3-Bromopropyl)-6-chloro-6a-hydroxy-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (8l) from 5** — In the general procedure A, $K_2CO_3$ (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 $CHCl_3$). IR (KBr): 3400, 1651, 1581, 1479, 1080, 758 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) δ: 2.51—2.63 (2H, m), 3.12 (1H, br s, disappeared on addition of $D_2O$), 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 $C_{21}H_{16}N_2O_2{}^{81}Br^{37}Cl$: 447.0112. Found: 447.0084. $C_{21}H_{16}N_2O_2{}^{79}Br^{37}Cl$: 445.0132. Found: 445.0109. $C_{21}H_{16}N_2O_2{}^{81}Br^{35}Cl$: 445.0141. Found: 445.0109. $C_{21}H_{16}N_2O_2{}^{79}Br^{35}Cl$: 443.0162. Found: 443.0132. *Anal*. Calcd for $C_{21}H_{16}N_2O_2BrCl\cdot 1/4H_2O$: C, 56.27; H, 3.71; N, 6.25. Found: C, 56.33; H, 3.65; N, 5.95.

**(6*R**,6a*R**)-6-Chloro-12-[3-(ethoxycarbonyl)propyl]-6a-hydroxy-5,6,6a,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 fot 1 h at rt. After addition of EtOAc, the whole was washed successively with $H_2O$, brine, and dried over $Na_2SO_4$, then evaporated under reduced pressure to leave an oil, which was column-chromatographed repeatedly on $SiO_2$ 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 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) 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 $D_2O$), 6.82 (1H, d, *J*=1.3 Hz, disappeared on addition of $D_2O$), 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 $C_{24}H_{21}N_2O_4{}^{37}Cl$: 438.1160. Found: 438.1140. $C_{24}H_{21}N_2O_4{}^{35}Cl$: 436.1189. Found: 436.1184.

**(6*R**,6a*R**)-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 $D_2O$), 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 $C_{21}H_{14}N_2O_2Cl_2\cdot 1/4H_2O$: 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 $D_2O$), 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 $D_2O$), 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 $C_{21}H_{14}N_2O_2{}^{37}Cl_2$: 400.0374. Found: 400.0339. $C_{21}H_{14}N_2O_2{}^{37}Cl^{35}Cl$: 398.0403. Found: 398.0406. $C_{21}H_{14}N_2O_2{}^{35}Cl_2$: 396.0433. Found: 396.0449.

**(6*R**,6a*R**)-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 $D_2O$), 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 $C_{20}H_{13}N_2O_3Cl\cdot EtOAc$: 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 $H_2O$ (2.0

mL), and the mixture was stirred for 0.5 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 an oil, which was column-chromatographed on $SiO_2$ 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 $cm^{-1}$. $^1$H-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 $D_2O$), 11.5 (1H, s, disappeared on addition of $D_2O$). MS *m/z*: 353 ($M^+$). *Anal*. Calcd for $C_{23}H_{19}N_3O$: 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 $H_2O$ (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 $Et_2O$–hexane). IR (KBr): 3440, 2110, 1625, 1458, 1416, 1354, 1168, 916, 736 $cm^{-1}$. $^1$H-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 $D_2O$), 11.53 (1H, s, disappeared on addition of $D_2O$). MS *m/z*: 337 ($M^+$). *Anal*. Calcd for $C_{22}H_{15}N_3O$: 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 $H_2O$ (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 $CHCl_3$). IR (KBr): 3454, 3263, 2206, 1633, 1460, 1242, 742 $cm^{-1}$. $^1$H-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 $D_2O$], 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 $D_2O$), 11.7 (1H, s, disappeared on addition of $D_2O$). MS *m/z*: 335 ($M^+$). *Anal*. Calcd for $C_{22}H_{13}N_3O\cdot 1/2H_2O$: 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 $H_2O$ (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 $cm^{-1}$. $^1$H-NMR (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 $C_{26}H_{17}N_3O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{27}H_{19}N_3O·H_2O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{28}H_{19}N_3O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{21}H_{12}N_4O\cdot 1/8H_2O$: 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˚C (gray powder, recrystallized from MeOH). IR (KBr): 3311, 2216, 1651, 1635, 1412, 742 $cm^{-1}$. $^1H$-NMR (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 $C_{23}H_{18}N_4O_2$: 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 ˚C (pale gray powder, recrystallized from EtOAc–hexane). IR (KBr): 3410, 2220, 1720, 1630, 1458, 1417, 1240, 1177, 737 $cm^{-1}$. $^1H$-NMR (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 $C_{22}H_{15}N_3O_3$: 369.1114. Found: 369.1114. **9q**: mp 198—200˚C (decomp., gray powder, recrystallized from MeOH–$H_2O$). IR (KBr): 3367, 2208, 1724, 1631, 1462, 1412, 1323, 1173, 741, 428 $cm^{-1}$. $^1H$-NMR (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 $C_{21}H_{13}N_3O_3\cdot 1/2H_2O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{22}H_{16}N_3O^{81}Br$: 419.0456. Found: 419.0491. $C_{22}H_{16}N_3O^{79}Br$: 417.0477. Found: 417.0451. **9r**: (brown viscous oil). IR (film): 3342, 2262, 2210, 1633, 1452, 1400, 756 $cm^{-1}$. $^1$H-NMR (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 $C_{23}H_{16}N_4O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{25}H_{21}N_3O_3·1/2H_2O$: 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 $cm^{-1}$. $^1$H-NMR (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 $C_{22}H_{15}N_3O^{37}Cl$: 374.0874. Found: 374.0908. $C_{22}H_{15}N_3O^{35}Cl$: 372.0903. Found: 372.0892. **9o**: (pale pink viscous oil). IR (film): 3448, 2218, 1630, 1464, 1417, 742 $cm^{-1}$. $^1$H-NMR (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**,6a*R**,11a*R**)-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˚C (pale gray powder, recrystallized from $CHCl_3$). IR (KBr): 3373, 2208, 1646, 1569, 1389, 1351, 1324, 1236, 743 $cm^{-1}$. $^1$H-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˚C (yellow prisms, recrystallized from $CHCl_3$). IR (KBr): 3465, 2219 (very weak), 1673, 1468, 773 $cm^{-1}$. $^1$H-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.

**(5R*,6*S**,6a*R**,11a*R**)-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 $cm^{-1}$. $^1$H-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 $D_2O$), 7.15 (1H, s, disappeared on addition of $D_2O$), 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 $D_2O$). HR-MS ($FAB^+$) *m/z:* Calcd for $C_{19}H_{15}N_3O_2{}^{37}Cl$: 354.0824. Found: 354.0871. $C_{19}H_{15}N_3O_2{}^{35}Cl$: 352.0853. Found: 352.0846.

**(5R*,6*S**,6a*R**,11a*R**)-6-Chloro-11a-cyano-5,12-diacetyl-6a-hydroxy-5,6,6a,11,11a,12-hexahydro-indolo[2,3-*a*]carbazole (12b) from 12a** — $Ac_2O$ (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 $SiO_2$ 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% $D_2O$, 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 $C_{23}H_{19}N_3O_4{}^{37}Cl$: 438.1035. Found: 438.1040. $C_{23}H_{19}N_3O_4{}^{35}Cl$: 436.1004. Found: 436.1051.

**12-Benzyl-6-cyano-5-methoxyindolo[2,3-*a*]carbazole (13) from 9d** — Excess amount of ethereal $CH_2N_2$ 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 $SiO_2$ with $CHCl_3$–MeOH–28% aq. $NH_3$ (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 $D_2O$). MS *m/z*: 401 ($M^+$). *Anal*. Calcd for $C_{27}H_{19}N_3O\cdot 1/2H_2O$: 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 $N_2$ 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 $Na_2SO_4$, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on $SiO_2$ with $CHCl_3$–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.

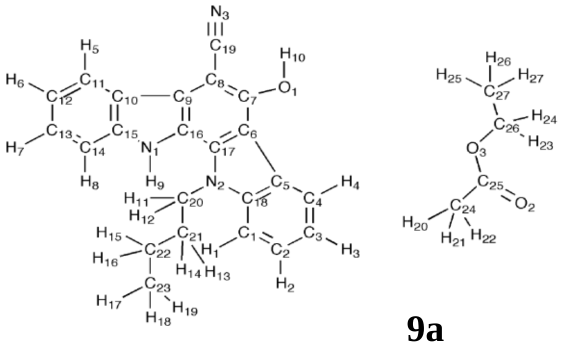
**6-(*Z*)-Aminomethylidene-12-*n*-benzyl-5,6,11,12-tetrahydroindolo[2,3-*a*]carbazole-5-one (15b) from 9d** — In the general procedure D, DIBAL (1.4 mL, 1.45 mmol), **9d** (18.7 mg, 0.05 mmol), THF (2.0 mL) were used. The reaction time was 19 h. After column-chromatography, **15b** (6.9 mg, 47%) was obtained. **15b**: mp 207—209˚C (decomp., yellow powder, recrystallized from EtOAc). IR (KBr): 3450, 1628, 1610, 1577, 1560, 1410, 742 $cm^{-1}$. $^1$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 $cm^{-1}$. $^1$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.

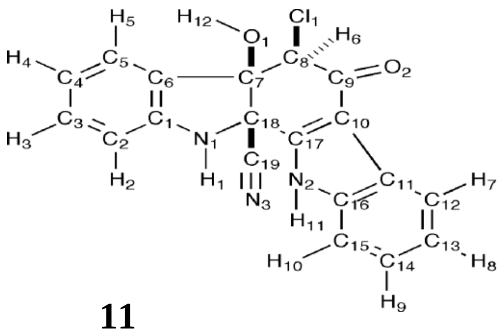
**X-Ray Crystallographic Analysis of 9a and 11**— All measurements were made on a Rigaku AFC5R diffract meter with graphite monochromated Cu-$K\alpha$ radiation ($\lambda$=1.54178 Å). The structure was solved by direct methods using MITHRIL.[9] Non-hydrogen atoms were refined anisotropically.

**9a**: a single crystal (0.20x0.20x0.30 mm) was obtained by recrystallization from EtOAc. Crystal data: $C_{23}H_{19}N_3O·C_4H_8O_2$, *M*=441.53, triclinic, space group $P\bar{1}$ (#2), *a*=10.626 (1)Å, *b*=12.276 (1)Å, *c*=9.912 (1)Å, $\alpha$=104.474 (8)°, $\beta$=110.402 (9)°, $\gamma$=81.84 (1)°, *V*=1431.8 (2)$Å^3$, *Z*=2, $D_{calc}$=1.252 g/$cm^3$, *F*(000)=468, and $\mu$(Cu$K\alpha$)=6.26 $cm^{-1}$. The final cycle of full-matrix least-squares refinement was based on 2807 observed reflections ($I$ >3.00$\sigma$ ($I$), 2$\theta$ < 120.2°) 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: $C_{19}H_{12}N_3O_2$, *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)Å$^3$, *Z*=8, $D_{calc}$=1.278 g/cm$^3$, *F*(000)=1440, and $\mu$(Cu*K*$\alpha$)=20.08 cm$^{-1}$. The final cycle of full-matrix least-squares refinement was based on 2139 observed reflections ($I > 3.00\sigma(I)$, $2\theta < 120.4°$) and 583 variable parameters. The final refinement converged with *R*=0.085 and *R*w=0.091.



**9a**



**11**

**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 | *B (eq)* | atom | x | y | z | *B* (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) | | | | | |

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