# SYNTHESIS OF FUSED AMINOTETRAHYDROCARBAZOLE COMPOUNDS

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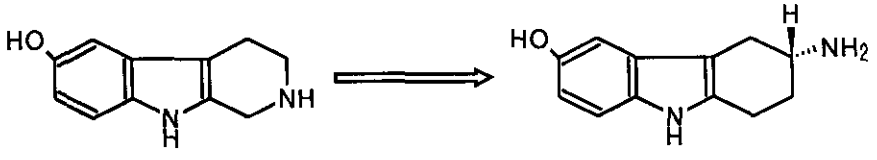
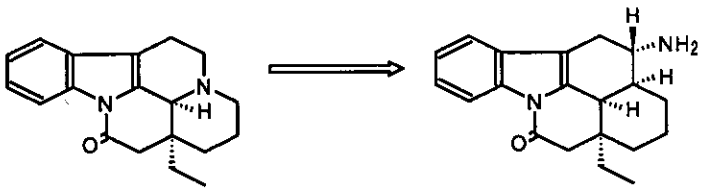
**Abstract** - Intramolecular Diels-Alder reaction of 3-(1*H*-indol-3-yl)-2-propenoates having olefinic substituents at the 1-position of the indole ring gave stereoselectively pentacyclic fused indole compounds in good yield. Aminotetrahydrocarbazoles derivatives (**8**, **21**, **22**) were obtained by Curtius rearrangment *via* carboxylic acid derivatives. Some of these compounds showed interesting pharmacological activity such as antiarrhythmic activity.

There are many naturally occurring fused indole compounds such as vinca alkaloids and some of them shows important pharmacological activities. For example, eburnamonine[1] and vincamine are known as vasodilators.[2] Friedman[3] reported that both of the two conformationally restricted analogues of serotonin, 6-hydroxytetrahydro-β-carboline and 6-hydroxy-3-aminotetrahydrocarbazole, are potent competitive inhibitors of serotonin uptake into hypothamic synaptosomes. Therefore, it is presumed that the nitrogen atom in vinca alkaloids must not necessarily be located at the bridgehead position in the pentacyclic fused indole skeleton in order to show biological activities. Therefore, aminotetrahydrocarbazole derivative (**8**) was expected to exhibit biological activities. The effects of the presence of an amino nitrogen and ring size in aminotetrahydrocarbazole derivatives on biological activities were also our interest. However, there has been no report about the synthesis of aminotetrahydrocarbazole derivatives. In the previous paper, we reported the synthesis of pentacyclic fused indole compounds by stereoselective intramolecular Diels-Alder reaction of (**E**)- and (**Z**)-3-(1*H*-indol-3-yl)-2-propenoates that have olefinic substituents at the 1-position of the indole ring.[4]

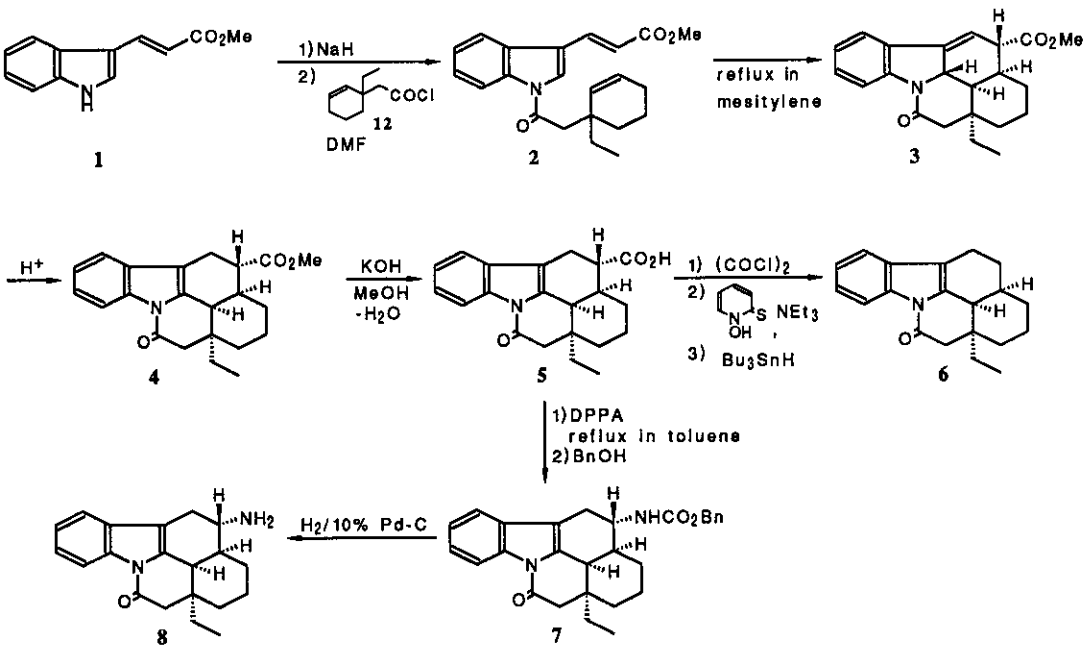



6-hydroxytetrahydro-β-carboline 6-hydroxy-3-aminotetrahydrocarbazole



**Eburnamonine** **8**

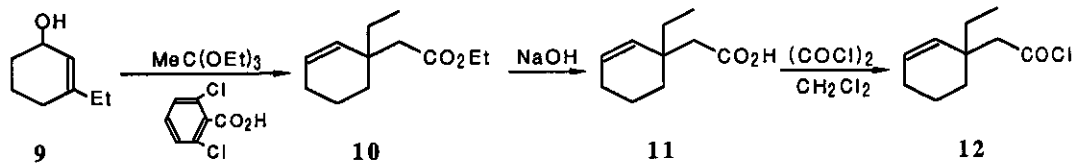
Now we wish to report the facile syntheses of several aminotetrahydrocarbazole derivatives *via* stereoselective intramolecular Diels-Alder reaction.




**Scheme 1**

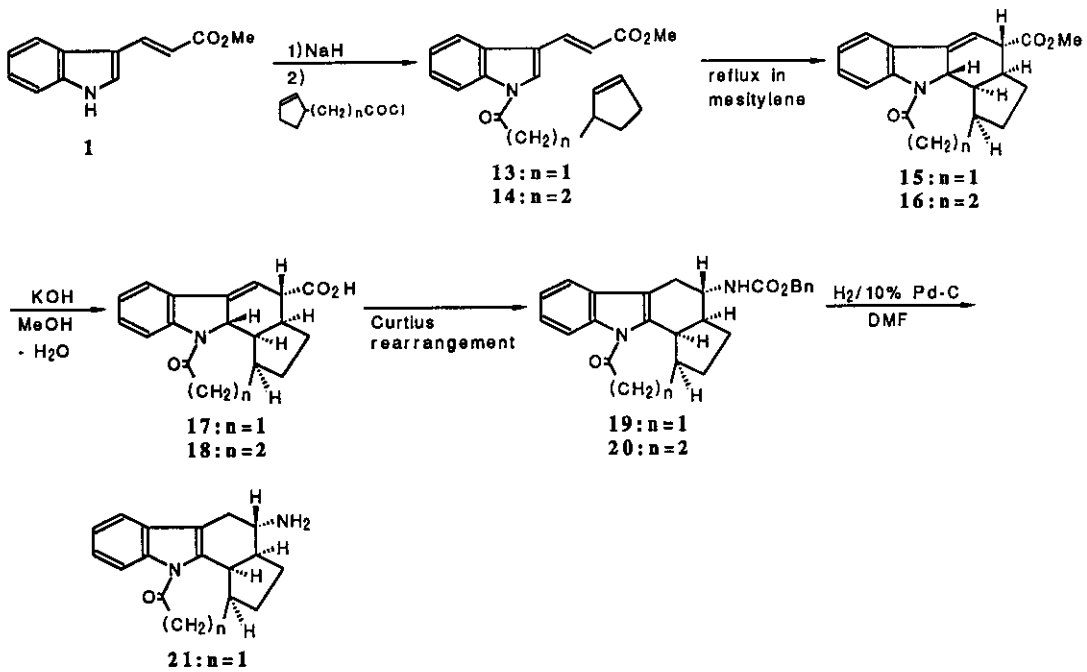
The synthetic route to the isoquino[2,1,8-*lma*]carbazol-5(1*H*)-one derivatives is shown in **Scheme 1**. Amide (**2**) was prepared by acylation of the indolepropenoate (**1**)[5] with the acid chloride (**12**). Intramolecular Diels-Alder reaction of **2** was carried out under reflux in mesitylene to give the indoline compound (**3**) in 74.5% yield. The transformation from **3** to indole compound (**4**) was performed by refluxing in dioxane in the presence of HCl as a catalyst. The stereochemistry of **4** was determined by X-ray analysis.[4] The carboxylic acid (**5**), a synthetic key compound, was obtained by alkaline hydrolysis of **4**. Decarboxylation of **5** using Barton's method[6] gave (3aα,12α,12aα,12bα)-3aα-ethyl-2,3,3a,4,11,12,12a,12b-octahydroisoquino[2,1,8-*lma*]carbazol-5(1*H*)-one (**6**). Treatment of **5** with diphenylphosphoryl azide (**DPPA**) in toluene, followed by Curtius rearrangement and alcoholysis with benzyl alcohol, gave the carbamate (**7**) in 46.4% yield. Catalytic hydrogenation of **7** over 10% palladium on carbon afforded the (3aα,12α,12aα,12bα)-12-amino-3aα-ethyl-

2,3,3a,4,11,12,12a,12b-octahydroisoquno[2,1,8-*lma*]carbazol-5(1*H*)-one (**8**).




**Scheme 2**

The starting material, (1-ethyl-2-cyclohexen-1-yl)acetyl chloride (**12**) was prepared *via* three steps from 3-ethyl-2-cyclohexen-1-ol (**9**) as shown in **Scheme 2**. Claisen rearrangement[7] of **9** under reflux in triethyl orthoacetate in the presence of 2,6-dichlorobenzoic acid gave the ethyl (1-ethyl-2-cyclohexen-1-yl)acetate (**10**). Alkaline hydrolysis of **10** followed by chlorination with oxalyl chloride afforded **12**.




**Scheme 3**

Amino fused indole compounds containing a five or a seven membered ring (**21** and **22**), were also synthesized as illustrated in **Scheme 3**. Intramolecular Diels-Alder reaction of the amides (**13** and **14**), which were prepared from indolylpropenoate (**1**), followed by alkaline hydrolysis gave the carboxylic acids (**17** and **18**), respectively. The stereochemistry of **15** was determined by X-ray analysis.[4] Curtius rearrangement of **17** and **18**, followed by alcoholysis gave the carbamate (**19** and **20**), which were accompanied with double bond migration. Removal of protecting group was carried out by catalytic hydrogenolysis to give the amines (**21** and **22**) in good yields, respectively.

Some of these aminotetrahydrocarbozole derivatives showed interesting pharmacological activity such as antiarrhythmic activity. Structure and activity relationship of these compouds will be shown elsewhere in future.

## EXPERIMENTAL

All melting points are uncorrected. Ir spectra were measured on a JASCO A-102 spectrophotometer. $^1$H-Nmr spectra were recorded with a Varian T-60A(60 MHz), EM-390(90 MHz) or JEOL JNM-EX270(270 MHz) spectrometer, and the chemical shifts are expressed in ppm from tetramethylsilane as an internal standard: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Ms were obtained with a JEOL JMS-01SG, JMS-G300 or JMS-505W mass spectrometer. Merck silica gel (kieselgel 60 Art. 7734) was employed for column chromatography.

**Methyl (E)-3-[1-[2-(1-ethyl-2-cyclohexen-1-yl)acetyl]-1*H*-indol-3-yl]-2-propenoate (2)** To a solution of methyl (E)-3-(1*H*-indol-3-yl)-2-propenoate (**1**) (4.02 g, 20 mmol) in DMF (20 ml) was added 55% NaH (0.92 g, 21.1 mmol) and the mixture was stirred at room temperature for 30 min. After cooling the mixture in an ice-bath, 2-(1-ethyl-2-cyclohexen-1-yl)acetyl chloride (3.90 g, 20.9 mmol) was added and the mixture was stirred for 0.5 h. The reaction mixture was poured into ice-water and extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with AcOEt-hexane (3:7) to give **2** (2.05 g, 63%) as pale yellow needles. mp 71-75°C. Recrystallization from hexane gave colorless needles. mp 74-76°C. *Anal.* Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.26; H, 7.16; N, 3.99. Ir (KBr) cm$^{-1}$: 1715, 1640. $^1$H-Nmr ($CDCl_3$) δ: 0.90 (3H, t, J=8 Hz), 1.35-2.20 (8H, m), 2.78, 2.98 (each 1H, d, J=15 Hz), 3.83 (3H, s), 5.30-5.90 (2H, m), 6.58 (1H, d, J=16 Hz), 7.20-7.55 (2H, m), 7.77 (1H, s), 7.65-8.00 (2H, m), 8.40-8.70 (1H, m). Ms m/z: 351 ($M^+$).

**Methyl (3aα,12α,12aα,12bα,12cβ)-1,2,3,3a,4,5,12,12a,12b,12c-decahydro-3aα-ethyl-5-oxoisoquino[2,1,8-*lma*]carbazole-12-carboxylate (3)** A solution of **2** (4.92 g, 14 mmol) in mesitylene (50 ml) was refluxed for 20 h and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with AcOEt-hexane (3:7) to give **3** (3.67 g, 74.6%) as colorless crystals. mp 119-121°C. Recrystallization from isopropyl ether gave colorless needles. mp 120-122°C. *Anal.* Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.13: H, 7.17; N, 3.99. Ir (KBr) cm$^{-1}$: 1730, 1655. $^1$H-Nmr ($CDCl_3$) δ: 0.92 (3H, t, J=7 Hz), 1.20-2.90 (12H, m), 3.05 (1H, t, J=4 Hz), 3.71 (3H, s), 4.78 (1H, dt, J=3, 12 Hz), 5.88 (1H, t, J=3 Hz), 6.95-7.55 (3H, m), 8.15 (1H, d, J=8 Hz). Ms m/z: 351 ($M^+$).

**Methyl (3aα,12α,12aα,12bα)-1,2,3,3a,4,5,11,12,12a,12b-decahydro-3aα-ethyl-5-oxoisoquino[2,1,8-*lma*]-carbazole-12-carboxylate (4)** A mixture of **3** (3.50 g, 9.96 mmol) and 15% HCl/EtOH (0.2 ml) in dioxane

(50 ml) was refluxed with stirring for 0.5 h, and concentrated *in vacuo*. The residue was crystallized from hexane to give **4** (3.42 g, 97.7%) as colorless crystals. mp 135-138 °C. Recrystallization from isopropyl ether gave colorless needles. mp 140-141 °C. *Anal.* Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 74.99; H, 7.16; N, 3.99. Ir (KBr) $cm^{-1}$: 1725, 1695. $^1$H-Nmr ($CDCl_3$) δ: 0.90 (3H, t, J=7 Hz), 0.73-1.93 (9H, m), 2.38-3.38 (6H, m), 3.70 (3H, s), 7.10-7.55 (3H, m), 8.28-8.54 (3H, m). Ms m/z: 351 ($M^+$).

**(3aα,12α,12aα,12bα)-1,2,3,3a,4,5,11,12,12a,12b-Decahydro-3aα-ethyl-5-oxoisoquino[2,1,8-*lma*]carbazole-12-carboxylic acid (5)** A mixture of **4** (3.00 g, 8.54 mmol) and KOH (1.00 g, 17.8 mmol) in water (4 ml) and MeOH (64 ml) was refluxed with stirring for 0.5 h. The reaction mixture was poured into ice-water and acidified with conc. HCl. The resulting crystalline solid was collected by filtration and washed with water to give **5** (2.58 g, 89.6%) as colorless crystals. mp 222-227 °C. Recrystallization form dioxane-isopropyl ether gave colorless crystals. mp 228-230 °C. *Anal.* Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C,74.65; H, 6.77; N, 4.08. Ir (KBr) $cm^{-1}$: 1710, 1630. $^1$H-Nmr (DMSO-$d_6$) δ: 0.88 (3H, t, J=7 Hz), 0.70-1.87 (9H, m), 2.25-3.25 (6H, m), 7.15-7.60 (3H, m), 8.15-8.30 (1H, m). Ms m/z: 337 ($M^+$).

**(3aα,12α,12aα,12bα)-3aα-Ethyl-2,3,3a,4,11,12,12a,12b-octahydroisoquino[2,1,8-*lma*]carbazol-5(1*H*)-one (6)** A mixture of **5** (3.54 g, 10.5 mmol) and oxalyl chloride (1.4 ml, 16 mmol) in $CH_2Cl_2$ (20 ml) was stirred under reflux for 2 h and concentrated *in vacuo*. The residue was dissolved in $CH_2Cl_2$ (20 ml), and the solution was added dropwise to a *N*-hydroxy-2-pyridinethione (1.47 g, 11.6 mmol) and triethylamine (1.8 ml, 12.9 mmol) in $CH_2Cl_2$ (20 ml) with stirring and ice-water cooling. The mixture was stirred for 1 h at the same temperature. The reaction mixture was washed with water, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in toluene (50 ml), and tributyltin hydride (4.2 ml, 11.5 mmol) was added to this solution. The mixture was stirred for 2 h at 80-90 °C under nitrogen, and then washed with 1N HCl, saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with AcOEt-hexane (3:17) to give **6** (1.30 g, 42.2%) as colorless crystals. mp 185-187 °C. Recrystallization from AcOEt gave colorless prisms. mp 187-189°C. *Anal.* Calcd for $C_{20}H_{23}NO$: C, 81.87; H,7.90; N, 4.77. Found: C, 81.43; H, 7.85; N, 4.69. Ir (KBr) $cm^{-1}$: 1695, 1622. $^1$H-Nmr ($CDCl_3$) δ: 0.90 (3H, t, J=7 Hz), 0.73-1.93 (9H, m), 2.38-3.38 (6H, m), 3.70 (3H, s), 7.10-7.55 (3H, m), 8.28-8.54 (3H, m). Ms m/z: 293 ($M^+$).

**Benzyl *N*-[(3aα,12α,12aα,12bα)-1,2,3,3a,4,5,11,12,12a,12b-decahydro-3aα-ethyl-5-oxoisoquino[2,1,8-*lma*]-carbazol-12-yl]carbamate (7)** A mixture of **5** (2.30 g, 6.82 mmol), diphenylphosphoryl azide (**DPPA**) (2.25 g, 8.18 mmol) and triethylamine (1.5 ml, 10.8 mmol) in toluene (20 ml) was refluxed with stirring for 1 h. After adding benzyl alcohol (5 ml), the reaction mixture was refluxed for 2 h . The reaction mixture was washed with 10% HCl, and saturated NaCl, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was

purified by silica gel column chromatography with AcOEt-hexane (1:4), to give **7** (1.40 g, 46.4%) as colorless crystals. mp 173-175 °C. Recrystallization from AcOEt-hexane gave colorless needles. mp 178-179 °C. *Anal.* Calcd for $C_{28}H_{30}N_2O_3$: C, 75.99; H, 6.83; N, 6.33. Found: C, 75.84; H, 6.81; N, 6.36. Ir (KBr) $cm^{-1}$: 3340, 1722, 1685. $^1$H-Nmr ($CDCl_3$) δ: 0.73 (3H, t, J=7 Hz), 0.60-3.15 (13H, m), 4.20 (1H, br), 5.18 (2H, dd, J=12.0, 15.0 Hz), 5.66 (1H, d, J=8 Hz), 7.05-7.55 (8H, m), 8.30-8.50 (1H, m). Ms m/z: 442 ($M^+$)

**(3aα,12α,12aα,12bα)-12-Amino-3aα-ethyl-2,3,3a,4,11,12,-12a,12b-octahydroisoquino[2,1,8-*lma*]carbazol-5(1*H*)-one (8)** A mixture of **7** (1.30 g, 2.94 mmol) and 10% Pd-C (0.5 g) in DMF (20 ml) was stirred at room temperature under atmospheric pressure of hydrogen until the absorption of hydrogen ceased. The catalyst was filtered off and the filtrate was condensed under reduced pressure. Maleic acid was added to this solution, and the resulting crystals were collected by filtration. Recrystallization from EtOH-AcOEt gave the maleate of **8** (0.958 g, 76.8%) as colorless needles. mp 216-216.5 °C (decomp.). *Anal.* Calcd for $C_{24}H_{28}N_2O_5$: C, 67.91; H, 6.65; N, 6.60. Found: C, 67.80; H, 6.62; N, 6.60. Ir (KBr) $cm^{-1}$: 1720, 1630. $^1$H-Nmr (DMSO-$d_6$) δ: 0.90 (3H, t, J=4 Hz) 1.25-2.00(6H, m), 2.35-3.25 (7H, m), 3.75 (1H, br), 6.08 (2H, s), 7.20-7.67 (3H, m), 8.20-8.45 (1H, m). Ms m/z: 308 ($M^+$).

**Ethyl (1-ethyl-2-cyclohexen-1-yl)acetate (10)** A mixture of 3-ethyl-2-cyclohexen-1-ol (**9**) (41.2 g, 0.326 mol) and 2,6-dichlorobenzoic acid (3.11 g, 16.3 mmol) in triethyl orthoacetate (600 ml) was refluxed with stirring for 16 h and concentrated *in vacuo*. The residue was distilled under reduced pressure to give **10** (34.34 g, 53.7%) as a colorless oil, bp 94-96 °C/2.5 mmHg. $^1$H-Nmr ($CDCl_3$) δ: 0.83 (3H, t, J=7 Hz), 1.22 (3H, t, J=7 Hz), 1.10-2.10 (8H, m), 2.28 (2H, s), 4.06 (2H, q, J=7 Hz), 5.32-5.85 (2H, m). Hrms m/z: 196.1464 ($M^+$) (Calcd for $C_{12}H_{20}O_2$: 196.1463).

**(1-Ethyl-2-cyclohexen-1-yl)acetic acid (11)** A mixture of **10** (69.70 g, 0.355 mol) and KOH (39.80 g, 0.709 mol) in MeOH (400 ml) and water (100 ml) was refluxed with stirring for 2 h and concentrated *in vacuo*. The residue was dissolved in water, washed with ether, acidified with conc. HCl, and extracred with $CH_2Cl_2$. The extract was dried over $MgSO_4$, and concentrated *in vacuo* to give **11** (56.36 g, 94.4%) as a pale brown viscous oil. $^1$H-Nmr ($CDCl_3$) δ: 0.83 (3H, t, J=7 Hz), 1.30-2.10 (8H, m), 2.30 (2H, s), 5.10-5.82 (2H, m), 11.69 (1H, s). Hrms m/z: 168.1143 ($M^+$) (Calcd for $C_{10}H_{16}O_2$: 168.1150).

**(1-Ethyl-2-cyclohexen-1-yl)acetyl chloride (12)** A mixture of **11** (24.83 g, 0.148 mol) and oxalyl chloride (26 ml, 0.297 mol) in $CH_2Cl_2$ (100 ml) was refluxed with stirring for 2 h and concentrated *in vacuo*. The residue was distilled to give **12** ( 24.47 g, 88.6%) as a colorless oil, bp 82-83 °C/2 mmHg. $^1$H-Nmr ($CDCl_3$) δ: 0.84 (3H, t, J=7 Hz), 1.30-2.15 (8H, m), 2.91 (2H, s), 5.05-5.88 (2H, m). Hrms m/z: 186.0816 ($M^+$) (Calcd for $C_{10}H_{15}{}^{35}ClO$: 186.0811).

**Methyl (E)-3-[1-(2-cyclopenten-1-yl)acetyl-1*H*-indol-3-yl]-2-propenoate (13)** To a solution of **1** (4.02 g, 20 mmol) in DMF (40 ml) was added 55% NaH (0.96 g, 22 mmol) and the mixture was stirred at room temperature for 1 h. After cooling the mixture in an ice-bath, (2-cyclopenten-1-yl)acetyl chloride prepared from (2-cyclopenten-1-yl)acetic acid (3.78 g, 30 mmol) was added and the mixture was stirred for 2 h. The reaction mixture was poured into ice-water and extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with AcOEt-hexane(1:1), and recrystallized from hexane to afford **13** (5.05 g, 82%) as pale yellow needles. mp 105-106.5 °C. *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.78; H, 6.10; N, 4.53. Ir (KBr) $cm^{-1}$: 1710, 1630. $^1$H-Nmr ($CDCl_3$) δ: 1.20-1.85 (1H, m), 2.05-2.55 (3H, m), 2.85-3.05 (2H, m), 3.15-3.50 (1H, m), 3.83 (3H, s), 5.70-5.95 (2H, m), 6.55 (1H, d, J=16 Hz), 7.22-7.56 (2H, m), 7.60-7.98 (3H, m), 8.40-8.65 (1H, m). Ms m/z: 309 ($M^+$).

**Methyl (E)-3-[1-[3-(2-cyclopenten-1-yl)propionyl]-1*H*-indol-3-yl]-2-propenoate (14)** The compound (**1**) was treated with 3-(2-cyclopenten-1-yl)propionyl chloride in the same way as **13** to give **14** in 76.0% yield, mp 86-87 °C (isopropyl ether). *Anal.* Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.25; H, 6.21; N, 4.56. Ir (KBr) $cm^{-1}$: 1730, 1700, 1625. $^1$H-Nmr ($CDCl_3$) δ: 1.30-3.05 (9H, m), 3.84 (3H, s), 5.62-5.91 (2H, m), 6.56 (1H, d, J=17 Hz), 7.25-7.56 (2H, m), 7.68-7.98 (3H, m), 8.40-8.60 (1H, m). Ms m/z: 323 ($M^+$).

**Methyl (2aα,11α,11aα,11bα,11cβ)-2,2a,3,4,11,11a,11b,11c-octahydro-4-oxo-1*H*-cyclopent[*de*]indolo[3,2,1-*ij*]quinoline-11-carboxylate (15)** A solution of **13** (619 mg, 2 mmol) in mesitylene (20 ml) was refluxed for 4 h and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with AcOEt-hexane (1:1) to give **15** (585 mg, 95.0%) as colorless crystals. mp 152-153 °C. Recrystallization from $CH_2Cl_2$-hexane gave colorless plates. mp 154-155 °C. *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.64; H, 6.16; N, 4.53. Ir (KBr) $cm^{-1}$: 1730, 1665. $^1$H-Nmr ($CDCl_3$) δ: 1.54-1.87 (4H, m), 2.10-2.59 (5H, m), 2.81-2.90 (1H, m), 2.95-2.99 (1H, m), 3.81 (3H, s), 3.99 (1H, dt, J=2.9 11.0 Hz), 6.18 (1H, t, J=2.9 Hz), 7.06-7.12 (1H, m), 7.26-7.33 (1H, m), 7.47 (1H, d, J=7.7 Hz), 8.04 (1H, d, J=8.1 Hz). Ms m/z: 309 ($M^+$).

**Methyl (2aα,12α,12aα,12bα,12cβ)-1,2,2a,3,4,5,12,12a,12b,12c-decahydro-5-oxocyclopent[*de*]indolo[3,2,1-*jk*]benzazepine-12-carboxylate (16)** In the same way as **15**, **16** was prepared from **14** in 57.0% yield, mp 158.5-160.5 °C (AcOEt-isopropyl ether). *Anal.* Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.06; H, 6.45; N, 4.25. Ir (KBr) $cm^{-1}$: 1740, 1670. $^1$H-Nmr ($CDCl_3$) δ: 1.48-2.97 (12H, m), 3.80 (3H, s), 4.30 (1H, dt, J=3, 11 Hz), 6.15 (1H, t, J=3 Hz), 6.90-7.48 (3H, m), 8.32 (1H, d, J=8 Hz). Ms m/z: 323 ($M^+$).

**(2aα,11α,11aα,11bα,11cβ)-2,2a3,4,11,11a,11b,11c-Octahydro-4-oxo-1*H*-cyclopent[*de*]indolo[3,2,1-*ij*]-quinoline-11-carboxylic acid (17)** A mixture of **15** (6.19 g, 20 mmol) and KOH (1.68 g, 29.9 mmol) in water (20 ml) and MeOH (80 ml) was refluxed with stirring for 10 min. The reaction mixture was poured into ice-water and acidified with conc. HCl. The resulting crystalline solid was collected by filtration and washed with water to give **17** (5.91 g, 100%) as colorless crystals. mp 204-208 °C (decomp.). Recrystallization from 70% EtOH gave colorless crystals, mp 214-216 °C (decomp.). *Anal.* Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.13; H, 5.76; N, 4.84. Ir (KBr) $cm^{-1}$: 1700, 1665. $^1$H-Nmr (DMSO-$d_6$) δ: 1.20-3.05 (m), 4.15 (1H, dt, J=3, 15 Hz), 6.23, (1H, t, J=3 Hz), 6.95-7.50 (2H, m), 7.60(1H, d, J=7 Hz), 7.90 (1H, d, J=8 Hz). Ms m/z: 295 ($M^+$).

**(2aα,12α,12aα,12bα,12cβ)-1,2,2a,3,4,5,12,12a,12b,12c-Decahydro-5-oxocyclopent[*de*]indolo[3,2,1-*jk*]-benzazepine-12-carboxylic acid (18)** In the same way as **17**, **18** was prepared from **16** in 94.7% yield, mp 235-236°C (decomp.) (EtOH). *Anal.* Calcd for $C_{19}H_{19}NO_3$ : C, 73.77; H, 6.19; N, 4.53 Found: C, 73.56; H, 6.17; N, 4.51. Ir (KBr) $cm^{-1}$: 1715, 1625. $^1$H-Nmr (DMSO-$d_6$) δ: 1.10-4.80 (13H, m), 6.27 (1H, t, J=3 Hz), 6.90-7.42 (2H, m), 7.58 (1H, d, J=8 Hz), 8.20 (1H, d, J=8 Hz). Ms m/z: 309 ($M^+$).

**Benzyl *N*-[(2aα,11α,11aα,11bα)-2,2a,3,4,10,11,11a,11b-octahydoro-4-oxo-1*H*-cyclopent[*de*]indolo[3,2,1-*ij*]-quinolin-11-yl]carbamate (19)** A mixture of **17** (41.35 g, 0.14 mol) and oxalyl chloride (18 ml, 0.205 mol) in $CH_2Cl_2$ (500 ml) was refluxed for 2 h and concentrated *in vacuo*. To a solution of the residue in acetone (200 ml) was added a solution of sodium azide (13.65 g, 0.21 mol) in water (50 ml) at 0 °C. After stirring for 30 min, the reaction mixture was poured into ice water and extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. A solution of the residue in toluene (200 ml) was refluxed with stirring for 30 min. After adding benzyl alcohol (50 ml), the reaction mixture was refluxed for 1 h and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with $CH_2Cl_2$ to give **19** (34.09 g, 61%) as pale yellow crystals. mp 170-172 °C. Recrystallization from AcOEt-hexane gave pale yellow needles. mp 172-173 °C. *Anal.* Calcd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00. Found: C, 75.04; H, 5.84; N, 6.85. Ir (KBr) $cm^{-1}$: 3220, 1705, 1690. $^1$H-Nmr ($CDCl_3$) δ: 0.70-1.48 (2H, m), 1.55-2.05 (2H, m), 2.20-3.18 (7H, m), 4.23 (1H, b), 5.10 (1H, s), 5.00-5.40 (1H, br), 7.13-7.50 (8H, m), 8.20-8.45 (1H, m). Ms m/z: 400 ($M^+$).

**Benzyl *N*-[(2aα,12α,12aα,12bα,12cβ)-1,2,2a,3,4,5,11,12,12a,12b-decahydro-5-oxocyclopent[*de*]indolo[3,2,1-*jk*]benzazepin-12-yl]carbamate (20)** In the same way as **19**, **20** was prepared from **18** in 51.9% yield, mp 167-168°C (AcOEt-isopropyl ether). *Anal.* Calcd for $C_{26}H_{26}N_2O_3$ : C, 75.34; H, 6.32; N, 6.76. Found: C, 75.21; H, 6.32; N, 6.74. Ir (KBr) $cm^{-1}$: 3380, 1710, 1685. $^1$H-Nmr ($CDCl_3$) δ: 0.90-3.15 (12H, m), 3.43 (1H, t, J=4 Hz), 4.22 (1H, m), 5.07 (2H, s), 5.30 (1H, d, J=7 Hz), 7.13-7.50 (8H, m), 8.30-8.55 (1H, m). Ms m/z:

414 ($M^+$).

**(2aα,11α,11aα,11bα)-11-Amino-1,2,2a,3,10,11,11a,11b-octahydro-4*H*-cyclopent[*de*]indolo[3,2,1-*ij*]quinolin-4-one (21)** A mixture of **19** (10 g, 25 mmol) and 10% Pd-C (5 g) in DMF (150 ml) was stirred at room temperature under atmospheric pressure of hydrogen until the absorption of hydrogen ceased. The catalyst was filtered off and the filtrate was concentrated *in vacuo*. The residue was dissolved in EtOH. Maleic acid (3 g) was added to this solution, and the resulting crystals were collected by filtration. The crystals were recrystallized from EtOH-AcOEt to give the maleate of **21** (7.22 g, 76.0%) as colorless scaly crystals. mp 197-198 °C (decomp.). *Anal.* Calcd for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.79; H, 5.72; N, 7.12. Ir (KBr) $cm^{-1}$: 3430, 1700. $^1$H-Nmr (DMSO-$d_6$) δ: 0.80-2.10 (4H, m), 2.45-3.45 (7H, m), 3.80 (1H, br), 6.08 (2H, s), 7.15-7.45 (2H, m), 7.45-7.68 (1H, m), 8.15-8.40 (1H, m). Ms m/z: 266 ($M^+$).

**(2aα,12α,12aα,12bα,12cβ)-12-Amino-1,2,2a,3,4,5,11,12,12a,12b-decahydrocyclopent[*de*]indolo[3,2,1-*jk*]-benzazepin-5(1*H*)-one (22)** In the same way as **21**, the maleate of **22** was prepared from **20** in 47.4% yield, mp 205°C (decomp.) (AcOEt-EtOH). *Anal.* Calcd for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07. Found: C, 66.63; H, 6.04; N, 6.83. Ir (KBr) $cm^{-1}$: 3150, 1685. $^1$H-Nmr (DMSO-$d_6$) δ: 0.90-3.30 (12H, m), 3.50-3.88 (2H, m), 6.08 (2H, s), 6.70-8.80 (2H, br), 7.17-7.65 (3H, m), 8.22-8.48 (1H, m). Ms m/z: 280 ($M^+$).

## ACKNOWLEDGEMENTS

The authors thank Dr. Toshihiko Hashimoto (Sankyo Research Laboratories) for his helpful discussions.

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Received, 16th August, 1991