# INTRAMOLECULAR *DIELS-ALDER* REACTION OF 3-FORMIMIDOYLINDOLES: SYNTHESIS OF FUSED PYRIDOINDOLE COMPOUNDS

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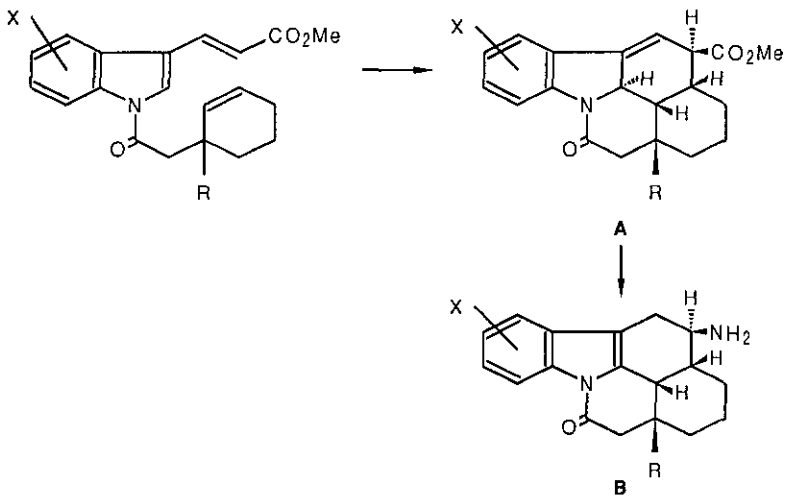
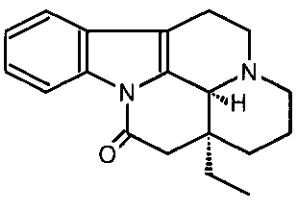
**Abstract** - Intramolecular Diels-Alder reaction of 3-formimidoylindoles having olefinic substituents at the 1-position of the indole ring gave stereoselectively fused pyridoindole compounds. Double bond migration from 2,3,3a,4,12,12a,-12b,12c-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-ones (**4**) to 2,3,3a,4,5,12,12a,12b-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (**5**) was performed using 10% Pd-C as a catalyst.

In the previous paper, we reported the facile synthesis of pentacyclic fused carbazole compounds (**A**)[1] and aminotetrahydrocarbazoles (**B**)[2] using stereoselective intramolecular Diels-Alder reaction of 3-(1*H*-indol-3-yl)-2-propenoates having cycloalkenyl substituents at the 1-position of the indole ring (**Scheme 1**). Among them,



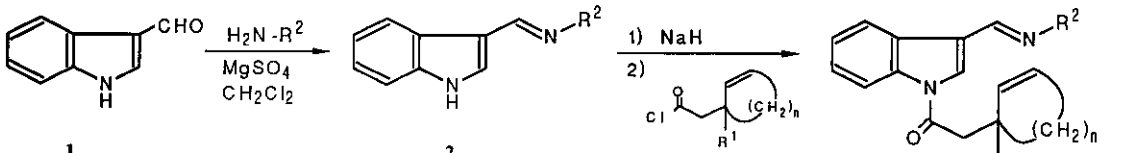

**Scheme 1**

the some 12-amino-2,3,3a,4,11,12,12a,12b-octahydroisoquino[2,1,8-*lma*]carbazoles showed potent antiarrhythmic activity.[3] Now, we wish to report the stereoselective synthesis of novel fused pyridoindole compounds (**4a-e**) by intramolecular Diels-Alder reaction of 3-formimidoylindoles (**3a-e**) having cycloalkenyl substituents at the 1-position of the indole ring, the reactivity of **4c-e** in the presence of palladium on carbon (Pd-C) to produce the indole derivatives (**5a,b and 6a,b**), and the catalytic hydrogenation of **4a,c-e** in the presence of platinum. Although there are many reports about Diels-Alder reaction of 1-azadienes for the synthesis of nitrogen-containing heterocycles,[4] Diels-Alder reaction of 3-formimidoylindoles has not yet been known so far.



Eburnamonine

Compounds (**5a,b**) are considered to be the analogue of vinca alkaloids, such as eburnamonine which shows vasodilation activity.[5]



| | $R^2$ | Yield (%) |
|---|---|---|
| 2a | Me | 100.0 |
| 2b | Bn | 89.5 |

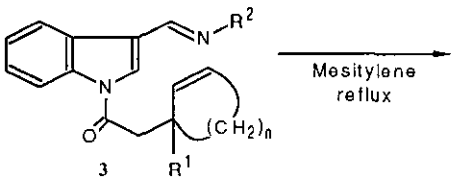
Bn = $CH_2Ph$

| | $R^1$ | $R^2$ | n | Yield (%) |
|---|---|---|---|---|
| 3a | H | Me | 2 | 62.3 |
| 3b | H | Me | 3 | 84.6 |
| 3c | Me | Me | 3 | 69.6 |
| 3d | Et | Me | 3 | 83.6 |
| 3e | Et | Bn | 3 | 79.0 |

**Scheme 2**

The starting materials (**3a-e**) of the intramolecular Diels-Alder reaction were prepared *via* two steps from indole-3-carboxaldehyde (**1**) as shown in Scheme 2. Treatment of indole-3-carboxaldehyde with the amines in the presence of $MgSO_4$ in dichloromethane, followed by acylation with acyl chlorides in THF gave **3a-e.** Intramolecular Diels-Alder reaction of the compounds (**3a-e**) was carried out under reflux in mesitylene to give the pentacyclic compounds (**4a-e**) in 14-58% yields (Scheme 3). Yields of these reactions depended on the presence of the angular alkyl substituents ($R^1$), the ring size (**n**), and the stability of the products (**4**) and the starting materials (**3**). Generally, the indoline compounds (**4**) were relatively unstable in comparison with the

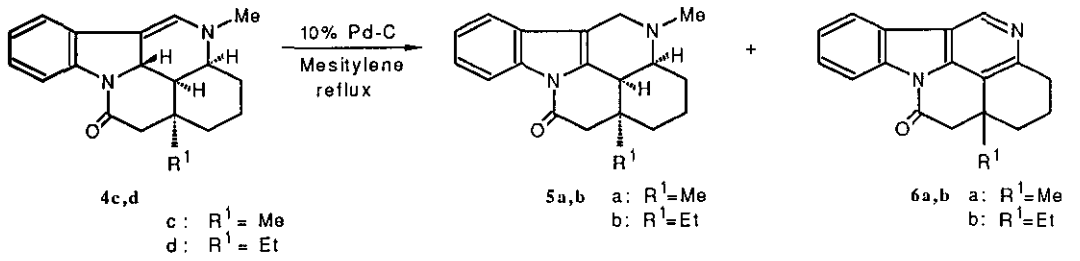
corresponding indole compounds (**5**) and dehydrogenated compounds (**6**). Structural elucidation of the compounds (**4a-e**) was accomplished on the basis of spectral data ($^1$H-nmr, ir and ms) and X-ray analysis[6] of **7b**, the hydrogenation product of **4c**, which will be mentioned later. The ir spectra of **4a-e** showed absorption at 1651-1658 cm$^{-1}$ for an amide carbonyl group. The $^1$H-nmr spectrum ($CDCl_3$) of **4a** was characterized by a doublet at δ 6.42 (*J*=2.6 Hz) assigned to the proton at the 4 position and a double doublet at δ 4.09 (J=9.9,

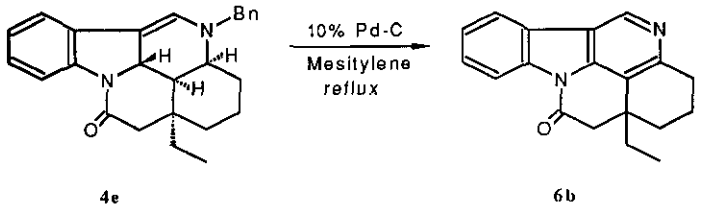



| | $R^1$ | $R^2$ | n | Yield (%) |
|---|---|---|---|---|
| 4a | H | Me | 2 | 43.8 |
| 4b | H | Me | 3 | 14.4 |
| 4c | Me | Me | 3 | 30.5 |
| 4d | Et | Me | 3 | 54.8 |
| 4e | Et | Bn | 3 | 58.0 |

Scheme 3

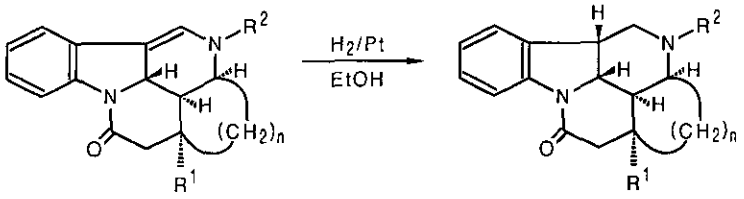
2.6 Hz) assigned to the proton at the 11c position.[7] Also, the $^1$H-nmr spectra ($CDCl_3$) of **4b-e** were characterized by a doublet at δ 6.25-6.43 (J=2.6 Hz) assigned to the proton at the 5 position and a double doublet at δ 4.77-4.93 (J=10.6, 2.6 Hz) assigned to the proton at the 12c position.[7] The mass spectrum of **4a** showed a molecular ion peak at m/z=266.




Scheme 4

The indoles (**5a,b**) were prepared by double bond migration of **4c,d** with 10% Pd-C under refluxing in mesitylene in 38.9 and 58.1% yields, respectively (Scheme 4). The dehydrogenation products (**6a,b**) were simultaneously obtained in 29.5 and 15.0% yields, respectively, in these reactions. The ir spectra of **5a** and **6a** showed absorption at 1710 and 1700 $cm^{-1}$ for an amide carbonyl group, respectively. The $^1$H-nmr spectrum ($CDCl_3$) of **5a** was characterized by a double doublet at δ 3.55 (J=15.8, 3.4 Hz) and 3.87 (J=15.8, 2.2 Hz) assigned to the methylene protons at the 5 position. The $^1$H-nmr spectrum ($CDCl_3$) of **6a** was characterized by a singlet at δ 8.99 assigned to the proton at the 5 position. The mass spectra of **5a** and **6a** showed molecular ion peaks at m/z=294 and 276, respectively. On the other hand, treatment of the *N*-benzyl compound (**4e**) with 10% Pd-C in mesitylene gave only aromatized compound (**6b**).




4 7

| | $R^1$ | $R^2$ | n | Yield (%) |
|---|---|---|---|---|
| 7a | H | Me | 2 | 78.3 |
| 7b | Me | Me | 3 | 83.3 |
| 7c | Et | Me | 3 | 95.8 |
| 7d | Et | Bn | 3 | 31.9 |

Scheme 5

Catalytic hydrogenation of **4a,c-e** over platinum afforded the **7a-d** as a single stereoisomer in high yields. (Scheme 5) The stereochemistry of **7b** was determined by X-ray analysis.[6]

These pyridoindole derivatives (**4, 5, 6** and **7**) did not have pharmacological activity, such as antiarrhythmic activity or antihypertensive activity.

In summary, we have developed a new method for stereoselective synthesis of novel fused pyridoindole compounds using intramolecular Diels-Alder reaction of 3-formimidoylindoles. The double bond migration from **4** to **5** was performed by heating in the presence of 10% Pd-C.

## EXPERIMENTAL

All melting points are uncorrected. Ir spectra were measured on a JASCO FT-IR8300 spectrophotometer. $^1$H-Nmr spectra were recorded with a 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 or a JEOL JMS-AX505H mass spectrometer.

Merck silica gel (kieselgel 60 Art. 9385) was employed for column chromatography.

**3-(*N*-Methylformimidoyl)-1*H*-indole (2a)**[8] A mixture of indole-3-carboxaldehyde (**1**) (14.52 g, 0.1 mol), methylamine (40% in MeOH) (10 ml, 0.245 mol) and $MgSO_4$ (50 g) in $CH_2Cl_2$ (200 ml) was refluxed with stirring for 5 h. Then more, methylamine (40% in MeOH) (10 ml, 0.245 mol) was added, and the reaction mixture was refluxed for an additional 2 h. The $MgSO_4$ was filtered off and the filtrate was concentrated *in vacuo*. The residue was washed with isopropyl ether - hexane to give **2a** (16.00 g, 100%) as orange crystals. Recrystallization from $CH_2Cl_2$-hexane gave pale brown crystals. mp 105-106 °C. *Anal.* Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 76.03; H, 6.66; N, 17.56. Ir (KBr) $cm^{-1}$: 1641 (C=N). $^1$H-Nmr ($CDCl_3$) δ: 3.52 (3H, s), 7.17-7.42 (3H, m), 7.49 (1H, s), 8.20-8.30 (1H, m), 8.50 (1H, s), 14.00 (1H, b). Ms m/z: 158 ($M^+$).

**3-(*N*-Benzylforminidoyl)-1*H*-indole (2b)** A mixture of indole-3-carboxaldehyde (**1**) (20 g, 0.138 mol), benzylamine (17.75 g, 0.166 mol) and $MgSO_4$ (50 g) in $CH_2Cl_2$ (300 ml) was refluxed with stirring for 10 h. The $MgSO_4$ was filtered off and the filtrate was concentrated *in vacuo*. The residue was washed with isopropyl ether to give **2b** (28.92 g, 89.5%) as pale yellow prisms. Recrystallization from isopropyl ether gave colorless prisms. mp 126-128 °C. *Anal.* Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.25; H, 6.18; N, 11.90. Ir (KBr) $cm^{-1}$: 1626 (C=N). $^1$H-Nmr ($CDCl_3$) δ: 4.83 (2H, s), 7.17-7.45 (9H, m), 8.31-8.43 (1H, m), 8.58 (1H, s), 15.00 (1H, b). Ms m/z: 234 ($M^+$).

**1-[2-(2-Cyclopenten-1-yl)acetyl]-3-(*N*-methylformimidoyl)-1*H*-indole (3a)** To a solution of **2a** (1.00 g, 6.32 mmol) in THF (20 ml) was added portionwise 55% NaH (290 mg, 6.65 mmol) with stirring at ice cooling under a nitrogen atmosphere. After 15 min, 2-(2-cyclopenten-1-yl)acetyl chloride (0.92 g, 6.36 mmol) was added dropwise to the mixture, and the whole mixture was stirred for 30 min with ice cooling. The reaction mixture was diluted with AcOEt, washed with water and saturated NaCl, dried over $MgSO_4$, and concentrated *in vacuo*. The resulting crystalline product was washed with hexane to give **3a** (1.048 g, 62.3%) as pale yellow needles. Recrystallization from $CH_2Cl_2$-isopropyl ether gave colorless needles. mp 116-117 °C. *Anal.* Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.62; H, 7.02; N, 10.49. Ir (KBr) $cm^{-1}$: 1720 (C=O), 1648. $^1$H-Nmr ($CDCl_3$) δ: 1.49-1.55 (1H, m), 2.20-2.50 (3H, m), 2.87-3.08 (2H, m), 3.27-3.43 (1H, m), 3.55 (3H, s), 5.73-5.88 (2H, m), 7.32-7.46 (2H, m), 7.74 (1H, s), 8.23-8.28 (1H, m), 8.46 (1H, s), 8.44-8.52 (1H, m). Ms m/z: 266 ($M^+$).

**1-[2-(2-Cyclohexen-1-yl)acetyl]-3-(*N*-methylformimidoyl)-1*H*-indole (3b)** The compound (**2a**) (2.00 g, 12.6 mmol) was treated with 2-(2-cyclohexen-1-yl)acetyl chloride (2.10 g, 13.2 mmol) in the same manner as the

preparation of **3a** to give **3b** (2.99 g, 84.6%), mp 103-104 °C (isopropyl ether). *Anal.* Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.40; H, 7.29; N, 9.97. Ir (KBr) $cm^{-1}$: 1719 (C=O), 1647. $^1$H-Nmr ($CDCl_3$) δ: 1.32-2.10 (6H, m), 2.80-3.00 (3H, m), 3.56 (3H, s), 5.58-5.70 (1H, m), 5.73-5.86 (1H, m), 7.30-7.48 (2H, m), 7.74 (1H, s), 8.23-8.29 (1H, m), 8.46 (1H, s), 8.42-8.51 (1H, m). Ms m/z: 280 ($M^+$).

**1-[2-(1-Methyl-2-cyclohexen-1-yl)acetyl]-3-(*N*-methylformimidoyl)-1*H*-indole (3c)** The compound (**2a**) (5.00 g, 31.6 mmol) was treated with 2-(1-methyl-2-cyclohexen-1-yl)acetyl chloride (5.73 g, 33.2 mmol) in the same manner as the preparation of **3a** to give **3c** (6.47 g, 69.6%), mp 70-72 °C (hexane). *Anal.* Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.56; H, 7.82; N, 9.42. Ir (KBr) $cm^{-1}$: 1728, 1655. $^1$H-Nmr ($CDCl_3$) δ: 1.24 (3H, s), 1.55-1.88 (4H, m), 1.90-2.12 (2H, m), 2.83, 2.98 (each 1H, d, J=14.8 Hz), 3.56 (3H, d, J=2.0 Hz), 5.62 (1H, d, J=10.0 Hz), 5.69 (1H, dt, J=10.0, 3.3 Hz), 7.28-7.46 (2H, m), 7.74 (1H, s), 8.26 (1H, d, J=6.6 Hz), 8.47 (1H, q, J=2.0 Hz), 8.51 (1H, d, J=7.3 Hz). Ms m/z: 294 ($M^+$).

**1-[2-(1-Ethyl-2-cyclohexen-1-yl)acetyl]-3-(*N*-methylformimidoyl)-1*H*-indole (3d)** The compound (**2a**) (2.00 g, 12.6 mmol) was treated with 2-(1-ethyl-2-cyclohexen-1-yl)acetyl chloride (2.46 g, 13.2 mmol) in the same manner as the preparation of **3a** to give **3d** (2.90 g, 74.6%), mp 102-103 °C (isopropyl ether-hexane). *Anal.* Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 78.18; H, 8.07; N, 9.04. Ir (KBr) $cm^{-1}$: 1717 (C=O), 1646. $^1$H-Nmr ($CDCl_3$) δ: 0.90 (3H, t, J=7.3 Hz), 1.54-1.80 (6H, m), 1.94-2.07 (2H, m), 2.85, 2.98 (each 1H, d, J=15.2 Hz), 3.56 (3H, d, J=2.0 Hz), 5.58 (1H, d, J=9.9 Hz), 5.74 (1H, ddd, J=9.9, 4.0, 3.3 Hz), 7.31-7.44 (2H, m), 7.75 (1H, s), 8.23-8.30 (1H, m), 8.45-8.49 (1H, m), 8.49-8.55 (1H, m). Ms m/z: 308 ($M^+$).

**3-(*N*-Benzylformimidoyl)-1-[2-(1-ethyl-2-cyclohexen-1-yl)acetyl]-1*H*-indole (3e)** The compound (**2b**) (2.00 g, 8.54 mmol) was treated with 2-(1-ethyl-2-cyclohexen-1-yl)acetyl chloride (1.67 g, 8.98 mmol) in the same manner as the preparation of **3a** to give **3e** (2.54 g, 77.4%), mp 79-80 °C (hexane). *Anal.* Calcd for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29. Found: C, 81.38; H, 7.43; N, 7.36. Ir (KBr) $cm^{-1}$: 1686 (C=O), 1645. $^1$H-Nmr ($CDCl_3$) δ: 0.90 (3H, t, J=7.3 Hz), 1.43-1.78 (6H, m), 1.85-2.06 (2H, m), 2.85, 2.98 (each 1H, d, J=14.5 Hz), 4.86 (2H, s), 5.58 (1H, d, J=9.9 Hz), 5.74 (1H, ddd, J=9.9, 4.0, 3.3 Hz), 7.23-7.50 (7H, m), 7.79 (1H, s), 8.35-8.42 (1H, m), 8.47-8.55 (1H, m), 8.56 (1H, s). Ms m/z: 384 ($M^+$).

**3-Methyl-1,2,2a,3,11,11a,11b,11c-octahydro-10*H*-cyclopent[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-10-one (4a)** A solution of **3a** (1.00 g, 3.75 mmol) in mesitylene (10 ml) was refluxed with stirring for 48 h under nitrogen atmosphere and then cooled. The reaction mixture was purified by silica gel column chromatography (50% AcOEt/hexane and then 5% MeOH/$CH_2Cl_2$) to give **4a** (438 mg, 43.8%) as pale brown prisms. Recrystallization from $CH_2Cl_2$-isopropyl ether gave pale brown prisms. mp 179-184 °C (decomp.). *Anal.*

Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.43; H, 6.83; N, 10.44. Ir (KBr) $cm^{-1}$: 1657(C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.53-1.86 (3H, m), 2.02-2.28 (2H, m), 2.33 (1H, dd, J=15.8, 7.3 Hz), 2.56-2.73 (1H, m), 2.87 (1H, dd, J=15.8, 8.6 Hz), 3.00 (3H, s), 3.12-3.24 (1H, m), 4.09 (1H, dd, J=9.9, 2.6 Hz), 6.42 (1H, d, J=2.6 Hz). 6.91-7.50 (2H, m), 7.12-7.18 (1H, m), 7.86-7.93 (1H, m). Ms m/z: 266 ($M^+$).

**4-Methyl-2,3,3a,4,12,12a,12b,12c-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one** (4b) The compound (**3b**) (2.00 g, 7.13 mmol) was heated in the same way as **4a**, and the reaction mixture was purified by silica gel column chromatography (20% AcOEt/hexane and then 30% AcOEt/hexane) to give **4b** (412 mg, 20.6%). Recrystallization from AcOEt-hexane gave pale brown prisms. mp 155-165 °C (decomp.). *Anal.* Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.32; H, 7.23; N, 9.96. Ir (KBr) $cm^{-1}$: 1651(C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.18-2.14 (7H, m), 2.26-2.40 (1H, m), 2.32 (1H, dd, J=18.5, 1.2 Hz), 2.86 (1H, dd, J=18.5, 8.8 Hz), 2.97 (3H, s), 3.07-3.20 (1H, m), 4.77 (1H, dd, J=10.6, 2.6 Hz), 6.26 (1H, d, J=2.6 Hz), 6.90-7.00 (2H, m), 7.03-7.12 (1H, m), 7.88-7.98 (1H, m). Ms m/z: 280 ($M^+$).

**4,12a-Dimethyl-2,3,3a,4,12,12a,12b,12c-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one(4c)** The compound (**3c**) (6.00 g, 20.4 mmol) was heated for 72 h in the same way as **4a**, and the reaction mixture was purified by silica gel column chromatography (20% AcOEt/hexane and then 50% AcOEt/hexane) to give **4c** (1.83 g, 30.5%). Recrystallization from $CH_2Cl_2$-isopropyl ether gave a pale brown powder. mp 120-137 °C (decomp.). *Anal.* Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.65; H, 7.65; N, 9.43. Ir (KBr) $cm^{-1}$: 1653(C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.21 (3H, s), 1.24-1.87 (6H, m), 1.80 (1H, dd, J=10.6, 5.3 Hz), 2.48 (2H, s), 2.96 (3H, s), 3.26 (1H, m), 4.83 (1H, dd, J=10.6, 2.6 Hz), 6.25 (1H, d, J=2.6 Hz), 6.89-7.02 (2H, m), 7.02-7.09 (1H, m), 7.88-7.95 (1H, m). Ms m/z: 294 ($M^+$).

**12a-Ethyl-4-methyl-2,3,3a,4,12,12a,12b,12c-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (4d)** In the same way as **4b**, **4d** was prepared from **3d** in 54.8% yield, mp 135-140 °C (decomp.) (AcOEt). *Anal.* Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.78; H, 7.79, N, 9.16. Ir (KBr) $cm^{-1}$: 1652(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.89 (3H, t, J=7.3 Hz), 1.20-1.77 (7H, m), 1.85 (1H, dd, J=10.6, 4.6 Hz), 1.92-2.06 (1H, m), 2.29, 2.54 (each 1H, d, J=18.5 Hz), 2.95 (3H, s), 3.21 (1H, m), 4.86 (1H, dd, J=10.6, 2.6 Hz), 6.25 (1H, d, J=2.6 Hz), 6.90-6.98 (2H, m), 7.03-7.11 (1H, m), 7.88-7.96 (1H, m). Ms m/z: 308 ($M^+$).

**4-Benzyl-12a-ethyl-2,3,3a,4,12,12a,12b,12c-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (4e)** In the same way as **4b**, **4e** was prepared from **3e** in 58.0% yield, as an amorphous solid. Ir (KBr) $cm^{-1}$: 1658(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.77 (3H, t, J=7.3 Hz), 1.32-1.97 (9H, m), 2.28, 2.52 (each 1H, d, J=18.5 Hz), 3.25-3.38 (1H, m), 4.32, 4.38 (each 1H, d, J=15.8 Hz), 4.93 (1H, dd, J=10.6, 2.6 Hz), 6.43 (1H,

d, J=2.6 Hz), 6.91-7.03 (2H, m), 7.05-7.13 (1H, m), 7.20-7.46 (5H, m), 7.92-7.98 (1H, m). Ms m/z: 384 ($M^+$). Hrms m/z: 384.2203 ($M^+$) (Calcd for $C_{26}H_{28}N_2O$: 384.2203).

**4,12a-Dimethyl-2,3,3a,4,5,12,12a,12b-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (5a) and 12a-methyl-2,3,12,12a-tetrahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (6a)** A mixture of **4c** (1.50 g, 5.10 mmol) and 10% Pd-C (0.75 g) in mesitylene (30 ml) was refluxed with stirring for 10 h under nitrogen atmosphere. The catalyst was filtered off and the filtrate was concentrated *in vacuo*. The residue was separated by silica gel column chromatography (30% AcOEt/hexane and then 5% EtOH/AcOEt) to give the less polar product **6a** (415 mg, 29.5%) and the more polar product **5a** (584 mg, 38.9%). **5a**: Recrystallization from AcOEt-hexane gave colorless needles. mp 148-153 °C. *Anal.* Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.63; H, 7.61; N,9.42. Ir (KBr) $cm^{-1}$: 1710(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.98-1.78 (6H, m), 1.22 (3H, s), 2.54, 2.75 (each 1H, d, J=16.8 Hz), 2.65 (3H, s), 3.04-3.12 (1H, m), 3.17-3.28 (1H, m), 3.55 (1H, dd, J=15.8, 3.4 Hz), 3.87 (1H, dd, J=15.8, 2.2 Hz), 7.22-7.40 (3H, m), 8.36-8.43 (1H, m). Ms m/z: 294 ($M^+$). **6a**: Recrystallization from AcOEt gave pale brown prisms. mp 203-208 °C. *Anal.* Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.32; H, 5.93; N, 10.08. Ir (KBr) $cm^{-1}$: 1700(C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.40 (3H, s), 1.70-1.86 (1H, m), 1.93-2.03 (1H, m), 2.10-2.33 (2H, m), 2.82, 2.92 (each 1H, d, J=15.8 Hz), 2.87-3.03 (1H, m), 3.12-3.27 (1H, m), 7.40-7.58 (2H, m), 8.00 (1H, d, J=7.3 Hz), 8.43 (1H, d, J=7.9 Hz), 8.99 (1H, s). Ms m/z: 276 ($M^+$).

**12a-Ethyl-4-methyl-2,3,3a,4,5,12,12a,12b-octahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (5b) and 12a-ethyl-2,3,12,12a-tetrahydrobenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (6b)** A mixture of **4d** (2.00 g, 6.48 mmol) and 10% Pd-C (1.00 g) in mesitylene (40 ml) was refluxed for 6 h under nitrogen atmosphere. The catalyst was filtered off and the filtrate was concentrated *in vacuo*. The residue was separated by silica gel column chromatography (30% AcOEt/hexane and then 5% EtOH/AcOEt) to give the less polar product **6b** (282 mg, 15.0%) and the more polar product **5b** (1.162 g, 58.1%). **5b**: Recrystallization from isopropyl ether gave colorless needles. mp 137-139 °C. *Anal.* Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.76; H, 7.85; N, 9.08. Ir (KBr) $cm^{-1}$: 1699(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.93 (3H, t, J=7.6 Hz), 0.98-1.87 (8H, m), 2.57, 2.69 (each 1H, d, J=16.6 Hz), 2.65 (3H, s), 3.10-3.17 (1H, m), 3.19-3.29 (1H, m), 3.56 (1H, dd, J=15.6, 3.4 Hz), 3.88 (1H, dd, J=15.6, 2.4 Hz), 7.22-7.38 (3H, m), 8.36-8.41 (1H, m). Ms m/z: 308 ($M^+$). **Hydrochloride of 6b**: The residue was converted to the hydrochloride of **6b** with 4N-HCl/dioxane. The crystals were recrystallized from EtOH-AcOEt to give the hydrochloride of **6b** as pale yellow prisms. mp 220-250 °C (decomp.). *Anal.* Calcd for $C_{19}H_{18}N_2O$·HCl: C, 69.83; H, 5.86; N, 8.57; Cl, 10.85. Found: C, 70.07; H, 6.03; N, 8.59; Cl, 10.77. Ir (KBr) $cm^{-1}$: 1728 (C=O). $^1$H-Nmr (DMSO-$d_6$) δ: 0.87 (3H, t, J=7.3 Hz), 1.52-2.17 (6H, m), 2.99-3.41 (2H, m), 3.12 (2H, s), 7.59-7.81 (2H, m), 8.38 (1H,

d, J=8.3 Hz), 8.45 (1H, d, J=7.6 Hz), 9.64 (1H, s). Ms m/z: 290 ($M^+$).

**1,2,2a,3,4,4a,11,11a,11b,11c-Decahydro-3-methyl-10*H*-cyclopent[*de*]indolo[3,2,1-*ij*]naphthyridin-10-one (7a)** A mixture of **4a** (2.00 g, 7.51 mmol) and $PtO_2$ (0.5 g) in EtOH (40 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 purified by silica gel column chromatography (AcOEt and then 10% EtOH/AcOEt) to give **7a** (1.578 g, 78.3%) as colorless crystals. Recrystallization from isopropyl ether gave colorless prisms. mp 167-170 °C. *Anal.* Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.22; H, 7.56; N, 10.35. Ir (KBr) $cm^{-1}$: 1664 (C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.55-2.15 (5H, m), 2.28-2.77 (5H, m), 2.39 (3H, s), 3.13 (1H, dd, J=11.2, 8.6 Hz), 3.92-4.14 (2H, m), 7.00-7.27 (3H, m), 8.01 (1H, d, J=8.6 Hz). Ms m/z: 268 ($M^+$).

**2,3,3a,4,5,5a,12,12a,12b,12c-Decahydro-4,12a-dimethylbenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (7b)** In the same manner as the preparation of **7a**, **7b** was prepared from **4c** in 83.3% yield, mp 166-176 °C (isopropyl ether). *Anal.* Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.97; H, 8.07; N, 9.48. Ir (KBr) $cm^{-1}$: 1664 (C=O). $^1$H-Nmr ($CDCl_3$) δ: 1.06-1.99 (7H, m), 1.15 (3H, s), 2.40 (2H, s), 2.46 (3H, s), 2.51-2.92 (3H, m), 3.72-3.85 (1H, m), 4.26 (1H, dd, J=11.9, 10.6 Hz), 6.98-7.27 (3H, m), 8.06 (1H, d, J=8.6 Hz). Ms m/z: 296 ($M^+$).

**2,3,3a,4,5,5a,12,12a,12b,12c-Decahydro-12a-ethyl-4-methylbenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (7c)** In the same manner as the preparation of **7a**, **7c** was prepared from **4d** in 95.8% yield, mp 151-153 °C (isopropyl ether). *Anal.* Calcd for $C_{20}H_{26}N_2O$: C, 77.38; H, 8.44; N, 9.02. Found: C, 77.46; H, 8.90; N, 8.92. Ir (KBr) $cm^{-1}$: 1655(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.85 (3H, t, J=7.6 Hz), 1.10-2.00 (9H, m), 2.18, 2.52 (each 1H, d, 16.2 Hz), 2.46 (3H, s), 2.50-2.93 (3H, m), 3.72-3.87 (1H, m), 4.29 (1H, dd, J=11.5, 10.2 Hz), 6.99-7.28 (3H, m), 8.06 (1H, d, J=7.9 Hz). Ms m/z; 310 ($M^+$).

**4-Benzyl-2,3,3a,4,5,5a,12,12a,12b,12c-decahydro-12a-ethylbenz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one (7d)** In the same manner as the preparation of **7a**, **7d** was prepared from **4e** in 31.9% yield, mp 130-132 °C (isopropyl ether). *Anal.* Calcd for $C_{26}H_{30}N_2O$: C, 80.79; H, 7.82; N, 7.25. Found: C, 80.99; H, 8.03; N, 7.20. Ir (KBr) $cm^{-1}$: 1667(C=O). $^1$H-Nmr ($CDCl_3$) δ: 0.85 (3H, t, J=7.6 Hz), 1.20-1.78 (8H, m), 1.90 (1H, dd, J=11.2, 6.3 Hz), 2.18, 2.52 (each 1H, d, J=16.5 Hz), 2.64-2.94 (3H, m), 3.57, 3.84 (each 1H, d, J=13.9 Hz), 3.58-3.75 (1H, m), 4.32 (1H, dd, J=11.6, 10.6 Hz), 6.93-7.37 (8H, m), 8.05 (1H, d, J=7.9 Hz). Ms m/z: 386 ($M^+$).

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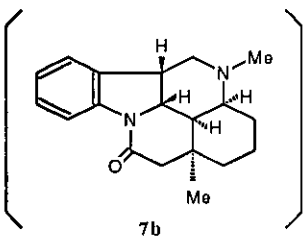
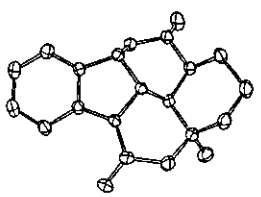
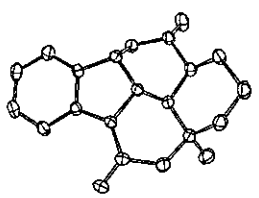
6. Crystal data of **7b**: $C_{19}H_{24}N_2O$=296.4, monoclinic, $P2_1/C$, a=9.227(4)Å, b=12.132(2)Å, c=14.181(8)Å, β=102.04(4)°, V=1552.5(11)Å$^3$, Z=4, Dc=1.27 g/cm$^3$, μ=(Cu-Kα)=6,2 cm$^{-1}$, R=0.0513.

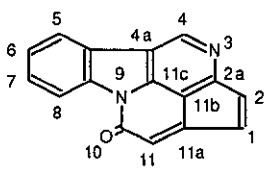


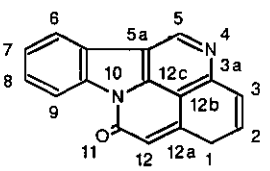

7b





7. Numberings of the atoms of the pentacyclic fused pyridoindole compounds are shown below.




10*H*-cyclopent[*de*]indolo[3,2,1-*ij*]naphthyridin-10-one benz[*de*]indolo[3,2,1-*ij*][1,6]naphthyridin-11(1*H*)-one

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