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# Synthetic Approach to Diterpene Alkaloids: Construction of the Bridged Azabicyclic Ring System of Kobusine

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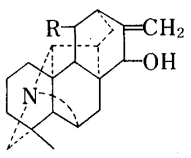
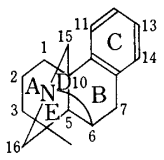
A synthetic study was carried out on the 1-azabicyclo[2.2.1]heptane partial structure (D/E ring system) of an aconite alkaloid, kobusine. A 1-azabicyclo[2.2.1]heptane system, (±)-6,15,16-iminopodocarpane-8,11,13-triene (**3**), was synthesized from the 4a-nitromethylhydrophenanthrone (**7**), which was obtained from the tetrahydrophenanthol (**4**) through an abnormal Reimer–Tiemann reaction. The bridged nitrogen structure was formed from the bicyclic chloramine (**23**) by means of the Hofmann–Löffler reaction. The structure of **3** was confirmed by X-ray diffraction analysis.

**Keywords**——(±)-6,15,16-iminopodocarpane-8,11,13-triene; 1,1-dimethyl-4a,10-methano-imino-1,2,3,4,4a,9,10,10a-octahydrophenanthrene; aziridine compound; reduction; N-halogenation; Hofmann–Löffler reaction; chloroformate; aconite alkaloid

Kobusine (**1**) is a constituent alkaloid of *Aconitum yesoense* NAKAI (Ranunclaceae), and its $C_{20}$ skeleton is heptacyclic. The structure was proposed on the basis of chemical studies by Okamoto *et al.*,[1] and later confirmed by an X-ray analysis of the methiodide.[2] The absolute configuration of **1** was deduced from the circular dichroism (CD) spectrum.[3] More recently, a simpler heptacyclic diterpene alkaloid, nominine (**2**), was isolated and its structure was elucidated by transformation from **1**.[3] These diterpene alkaloids—kobusine-type alkaloids—are characterized by the presence of a bridged azabicyclic structure (D/E rings) on the A/B rings.



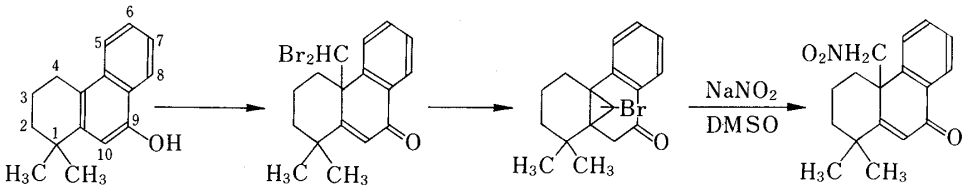

**1** : kobusine (R = −OH)
**2** : nominine (R = −H)




**3**

Chart 1

Our attention has been focused on the synthesis of the D/E ring system, *i.e.*, a 1-azabicyclo[2.2.1]heptane system, and we report here a synthesis of (±)-6,15,16-iminopodocarpane-8,11,13-triene (**3**), which corresponds to a partial structure of kobusine-type alkaloids. Our synthesis was designed on the basis of the idea that the nitromethylhydrophenanthrone (**7**) would be effective for construction of the azabicyclic ring since it bears a functionalized angular nitromethyl group. Compound **7** was obtained from tetrahydrophenanthol (**4**) by the method of Yamaguchi *et al.*[4] by means of an abnormal Reimer–Tiemann reaction[5] *via* the bromocyclopropane derivative (**6**) in *ca.* 8.0% overall yield.



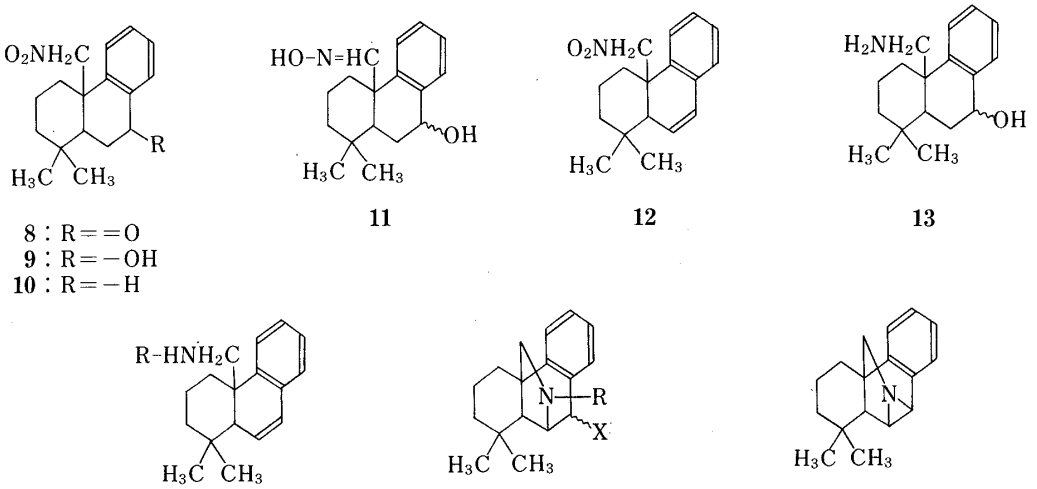
4 5 6 7

Chart 2

Reduction of **7** with zinc in an acidic medium gave only **4**, resulting from denitroalkylation of the 4a-nitromethyl group. Catalytic hydrogenation of **7** with 10% Pd–C in EtOH at room temperature gave a dihydro compound (**8**) in 73% yield, and treatment of **8** with $NaBH_4$ gave a saturated alcohol (**9**) in 60% yield, accompanied with a deoxygenated compound (**10**), the oxime alcohol (**11**) and **4** in yields of 0.5%, 3.0% and 2.7%, respectively.

The A/B ring junction of **8** and **9** thus obtained was deduced to be *trans* on the basis of the following transformations. Compound **9** was treated with saturated HCl–EtOH to give **12**, which on hydrogenation with 10% Pd–C in EtOH at room temperature provided **10** in 49% yield. Oxidation of **10** by the method of Wenkert and Jackson[6] led to the monoketone **8**, expected as the product from an A/B *trans* isomer,[6] in 82% yield. The latter product was identical with that obtained from **7**. In the nuclear magnetic resonance (NMR) spectrum of **12**, olefinic protons at $C_{10}$ and $C_9$ were observed at $\delta$: 6.12 (dd, $J=3.3$ and 9.5 Hz) and $\delta$: 6.73 (dd, $J=3.3$ and 9.5 Hz), respectively, and the double-doublet absorption of the proton at $C_9$ was attributed to allylic coupling between $C_{10a}$ and $C_9$. This is consistent with *trans* structures of **8** and **9** at the A/B ring.

Reduction of **9** with Raney Ni in EtOH at room temperature yielded a methylamine (**13**) in 63% yeild, and dehydration of **13** with saturated HCl–EtOH gave an olefinic amine (**14**) in quantitative yield. This compound has two functional groups, the methylamino and the ethylene groups, which are available for the formation of the bridged aziridine by oxidation.



8 : R=O
9 : R=−OH
10 : R=−H

11 12 13

14 : R=−H
15 : R=−COCH$_3$
19 : R=−CO$_2$CH$_2$C$_6$H$_5$

17 : R=−CO$_2$C$_2$H$_5$, X=−Cl
18 : R=−CO$_2$CH$_2$C$_6$H$_5$, X=−Cl
20 : R=−CO$_2$C$_2$H$_5$, X=−H
21 : R=−CO$_2$CH$_2$C$_6$H$_5$, X=−H

16

Chart 3

Treatment of **14** with $Pb(OAc)_4$ in cold $CH_2Cl_2$ according to the method of Nagata[7] afforded the aziridine (**16**) which, without purification because of its instability, was reacted with ethyl or benzyl chloroformate in an ice bath to give the chlorocarbamate (**17** or **18** in 45%

or 63% yield, respectively). The ring opening of the aziridine ring was regiospecific. The bridged pyrrolidine structure constitutes the D ring of the aconite alkaloids. In the reaction of **16** with the benzyl ester, the benzyl carbamate (**19**) of **14** was obtained as a by-product after chromatography.

In the NMR spectra of **17** and **18**, the $C_9$ benzal protons appeared at lower field ($\delta$: 5.24 and 5.26) than in the case of **9** ($\delta$: 4.86) and **13** ($\delta$: 4.74). This is due to the effect of the chloro function which was introduced at $C_9$ by regioselective opening of the N–$C_9$ bond.

Reduction of **18** with Raney Ni in EtOH at room temperature afforded the amine (**22**) as an oil in 56% yield, but reduction with $PtO_2$ gave only the dechloro product (**21**).

By application of the Hofmann–Löffler reaction,[8] the product **22** was converted into the N-halo compound by treatment with *N*-halosuccinimide in $CH_2Cl_2$ under cooling. Compound **22** reacted with the N-chloro reagent to give the desired *N*-chloramine (**23**) in 85% yield, while the reaction with the N-bromo reagent gave an azomethine (**24**), with liberation of hydrogen bromide, in 57.5% yield. The structure of **23** was fully characterized by NMR, mass spectrum (MS), and elemental analysis. The structure of **24** was supported by NMR and other spectral data.

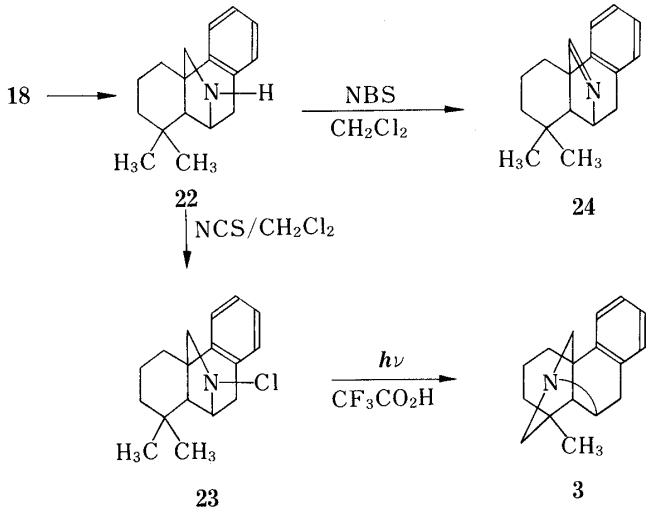



Chart 4

In order to construct the bond between the $CH_3$ at $C_1$ and the nitrogen atom, **23** was irradiated with a 400W high-pressure mercury lamp in trifluoroacetic acid under a nitrogen atmosphere at room temperature for 5 h. The major product was an oily material isolated in 38.7% yield. The methiodide was a crystalline material, mp 269—270 °C. The structure was assigned as **3** on the basis of the NMR spectral data. In the NMR spectrum of this compound, a methyl signal was observed at $\delta$: 1.04 instead of the two methyl signals at $\delta$: 0.99 and 1.10 of

TABLE I. $^{13}$C-NMR Data for **3**[a]

| | | | | | |
|---|---|---|---|---|---|
| C(1) | 26.62 | C(7) | 30.68 | C(13) | 125.00 |
| C(2) | 18.42 | C(8) | 135.38 | C(14) | 128.15 |
| C(3) | 37.17 | C(9) | 148.94 | C(15) | 64.69 |
| C(4) | 37.50 | C(10) | 41.88 | C(16) | 62.99 |
| C(5) | 54.62 | C(11) | 121.01 | C(17) | 29.14 |
| C(6) | 65.17 | C(12) | 128.15 | | |

*a*) In ppm downfield from TMS; solvent, $CDCl_3$.

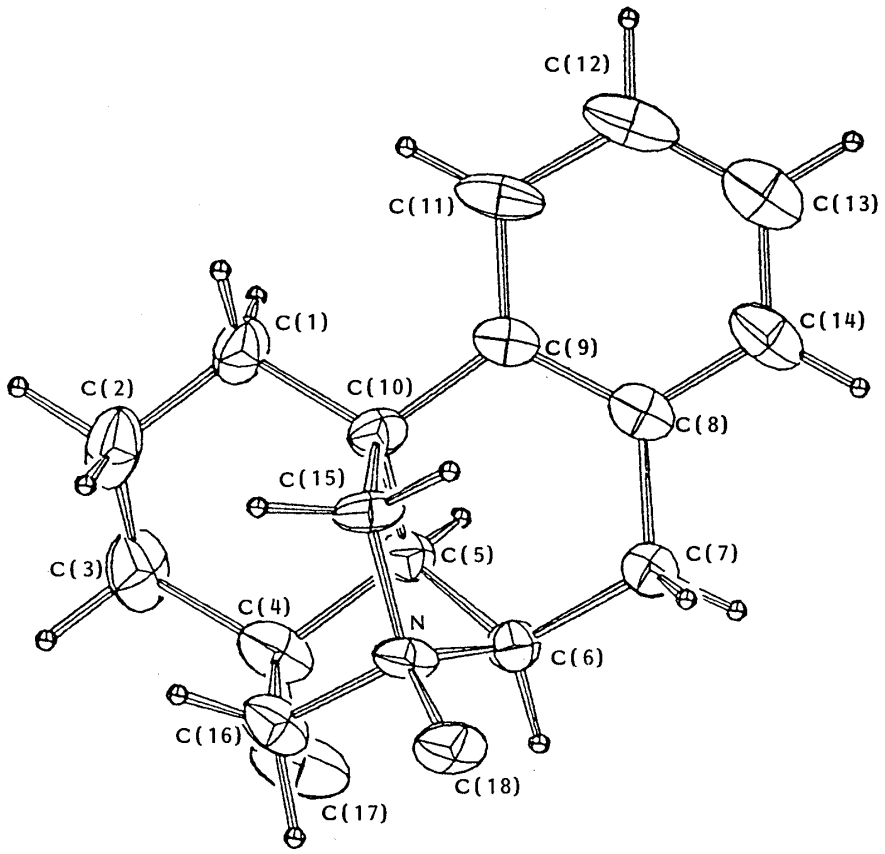



Chart 5. Perspective View of **3**

TABLE II. The Bond Lengths of **3**

| Atom 1 | Atom 2 | Length (S.D.) (Å) | Atom 1 | Atom 2 | Length (S.D.) (Å) |
|---|---|---|---|---|---|
| C9 | –C8 | 1.430 (32) | C4 | –C3 | 1.537(38) |
| C9 | –C10 | 1.510 (31) | C4 | –C16 | 1.597 (29) |
| C9 | –C11 | 1.388 (28) | C4 | –C17 | 1.539 (35) |
| C8 | –C7 | 1.520 (30) | C3 | –C2 | 1.506 (42) |
| C8 | –C14 | 1.407 (35) | C2 | –C1 | 1.523 (40) |
| C7 | –C6 | 1.520 (32) | C15 | –N | 1.490 (25) |
| C6 | –C5 | 1.560 (28) | C16 | –N | 1.549 (28) |
| C6 | –N | 1.523 (27) | C18 | –N | 1.529 (25) |
| C5 | –C10 | 1.540 (29) | C11 | –C12 | 1.435 (37) |
| C5 | –C4 | 1.554 (33) | C12 | –C13 | 1.407 (40) |
| C10 | –C1 | 1.538 (33) | C13 | –C14 | 1.356 (36) |
| C10 | –C15 | 1.594 (27) | | | |

S.D.: standard deviation.

**23**. The $^{13}$C-NMR signals of this compound were assigned as shown in Table I, and the MS showed a base peak at *m/e* 239.1674, corresponding to $C_{17}H_{21}N$ (Calcd. 239.1674 $M^+$). A single-crystal X-ray diffraction analysis of the methiodide was performed in order to confirm the proposed structure. Crystal data: formula, $C_{18}H_{24}IN$; space group, $P2_1/c$ (monoclinic); cell dimensions, $a=11.707$, $b=13.809$, $c=10.616$ Å, $z=4$; independent reflections, 1778; final *R* value, 0.10 including H atoms. A perspective drawing of **3** is shown in Chart 5.

Thus, we succeeded in constructing the nitrogen-bridged partial structure of kobusine-type alkaloids.

TABLE III. The Bond Angles of **3**

| Atom 1 | Atom 2 | Atom 3 | Angles (S.D.) (°) | Atom 1 | Atom 2 | Atom 3 | Angles (S.D.) (°) |
|---|---|---|---|---|---|---|---|
| C8 | –C9 | –C10 | 116.1 (18) | C3 | –C4 | –C16 | 112.4 (20) |
| C8 | –C9 | –C11 | 119.5 (19) | C3 | –C4 | –C17 | 110.4 (21) |
| C10 | –C9 | –C11 | 124.4 (19) | C5 | –C4 | –C16 | 101.1 (17) |
| C7 | –C8 | –C9 | 120.2 (18) | C5 | –C4 | –C17 | 111.5 (19) |
| C7 | –C8 | –C14 | 119.8 (19) | C16 | –C4 | –C17 | 108.8 (19) |
| C9 | –C8 | –C14 | 119.9 (20) | C2 | –C3 | –C4 | 113.8 (23) |
| C6 | –C7 | –C8 | 115.5 (18) | C1 | –C2 | –C3 | 113.9 (23) |
| C5 | –C6 | –C7 | 113.0 (17) | N | –C15 | –C10 | 101.9 (16) |
| C5 | –C6 | –N | 91.5 (14) | N | –C16 | –C4 | 101.6 (17) |
| C7 | –C6 | –N | 116.8 (17) | C12 | –C11 | –C9 | 118.7 (21) |
| C10 | –C5 | –C6 | 100.7 (16) | C13 | –C12 | –C11 | 120.8 (23) |
| C10 | –C5 | –C4 | 112.1 (17) | C14 | –C13 | –C12 | 119.9 (24) |
| C6 | –C5 | –C4 | 103.0 (17) | C8 | –C14 | –C13 | 121.0 (23) |
| C1 | –C10 | –C9 | 112.2 (18) | C6 | –N | –C15 | 105.2 (15) |
| C1 | –C10 | –C5 | 112.5 (17) | C6 | –N | –C16 | 103.8 (15) |
| C1 | –C10 | –C15 | 113.4 (17) | C6 | –N | –C18 | 116.4 (15) |
| C9 | –C10 | –C5 | 109.5 (17) | C15 | –N | –C16 | 109.1 (15) |
| C9 | –C10 | –C15 | 107.3 (16) | C15 | –N | –C18 | 113.1 (16) |
| C5 | –C10 | –C15 | 101.4 (16) | C16 | –N | –C18 | 108.7 (15) |
| C3 | –C4 | –C5 | 112.2 (20) | C10 | –C1 | –C2 | 111.0 (20) |

S.D.: standard deviation.

## Experimental

All melting points were measured under a microscope (Yanaco MP-S2) and are uncorrected. Infrared (IR) spectra were recorded on a JASCO IRA-1 spectrophotometer. NMR spectra were taken with a JEOL PS-100 machine using tetramethylsilane (TMS) as an internal standard. MS were determined with a JEOL-01SG-2 instrument.

The abbreviations used are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

**1,1-Dimethyl-4a-nitromethyl-9-oxo-1,2,3,4,4a,9-hexahydrophenanthrene (7)**——According to the method of Yamaguchi, **7** was obtained as colorless crystals, mp 174—175 °C, from the tetrahydrophenanthol (**4**) by means of an abnormal Reimer–Tiemann reaction *via* the bromocyclopropane (**6**) in *ca.* 8.0% overall yield from **4**.

**1,1-Dimethyl-4a-nitromethyl-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (8)**——(1) Reduction of **7**: A solution of **7** (504 mg, 1.77 mmol) in EtOH (50 ml) was hydrogenated over 10% Pd–C (223 mg) at atmospheric pressure at room temperature. After removal of the catalyst, the solvent was evaporated off *in vacuo* to give a pale brown oil, which was chromatographed on silica gel (300 g) with $CH_2Cl_2$–*n*-$C_6H_{12}$ (3 : 1). The starting material (**4**, 9.5 mg, 2.4%), the dihydro compound (**8**, 372 mg, 73.4%), and the saturated alcohol (**9**, 73.3 mg, 14.3%) were eluted successively.

**8**: mp 119—121 °C (colorless prisms, recrystallized from $CH_2Cl_2$–*n*-$C_6H_{12}$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1680, 1545, 1384. NMR $\delta$: 0.95 (6H, s), 4.68 (2H, q, $J$ = 10 Hz). MS *m/e*: 287 ($M^+$). *Anal.* Calcd for $C_{17}H_{21}NO_3$: C, 71.05; H, 7.37; N, 4.87. Found: C, 71.30; H, 7.44; N, 5.01.

(2) Oxidation of **10**: A 10% chromic acid solution (1 ml) in 80% AcOH was added to a solution of **10** (23.2 mg, 0.085 mmol) in AcOH (3 ml) and the mixture was stirred at room temperature under nitrogen for 40 h. The resulting mixture was diluted with saturated NaCl (40 ml) and extracted with $CH_2Cl_2$ (20 ml). The extract was washed with 5% $Na_2CO_3$ (20 ml) and $H_2O$ (20 ml), then dried over $Na_2SO_4$. Evaporation of the solvent left a crude product, which was chromatographed on preparative thin-layer chromatography (p-TLC: silica-gel plates) with $CH_2Cl_2$–*n*-$C_6H_{12}$ (7 : 3), and recrystallized from *n*-$C_6H_{12}$ to give 20.1 mg (82.3%) of the ketone. The ketone was identical with **8** (IR, NMR, and mixed mp).

**1,1-Dimethyl-4a-nitromethyl-9-hydroxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (9)**——(1) Reduction of **8**: A mixture of **8** (780 mg, 2.72 mmol) and $NaBH_4$ (150 mg) in EtOH (40 ml) was stirred for 2.5 h at room temperature and then 5% AcOH (50 ml) was added to the reaction mixture. The resulting mixture was extracted with $CH_2Cl_2$ (50 ml), and the extract was washed with 5% $K_2CO_3$ (50 ml) and $H_2O$ (50 ml), then dried over $Na_2SO_4$. The solvent was evaporated off *in vacuo* to give 464 mg (59.1%) of **9** as white crystals after recrystallization from $CH_2Cl_2$–*n*-$C_6H_{12}$. mp 121—123 °C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3485, 1543, 1384. NMR $\delta$: 0.92 (3H, s), 0.96 (3H, s), 4.86 (2H, s), 4.86 (1H). MS *m/e*: 289 ($M^+$). *Anal.* Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.78; H, 8.08; N, 4.90.

(2) Direct Conversion of **7**: The alcoholic solution, obtained by hydrogenation of **7** (1.52 g, 5.34 mmol) as described above was filtered to remove the catalyst, then reacted with $NaBH_4$ (1.234 g) at room temperature for 3 h, and worked up as above to give **9** (930 mg, 60.3%) after recrystallization from $CH_2Cl_2$–*n*-$C_6H_{12}$. Silica-gel (100 g) chromatography of the mother liquor with $CH_2Cl_2$ afforded a deoxygenated product (**10**, 6.6 mg, 0.45%), the starting material (**4**, 33.2 mg, 2.75%), **9** (265.5 mg, 17.2%), and an oxime-alcohol (**11**, 45.6 mg, 3.1%).

**11**: mp 147—149 °C (white crystals, recrystallized from $CH_2Cl_2$–*n*-$C_6H_{12}$), IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300. NMR $\delta$: 0.85 (3H, s), 0.98 (3H, s), 4.76 (1H, m), 7.66 (1H, s), 7.94 (1H, s). MS *m/e*: 273 ($M^+$). *Anal.* Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.39; H, 8.48; N, 5.07.

**1,1-Dimethyl-4a-nitromethyl-1,2,3,4,4a,10a-hexahydrophenanthrene (12)**——A solution of **9** (101.9 mg, 0.35 mmol) in saturated HCl–EtOH (10 ml) was refluxed for 2 h. After removal of the solvent *in vacuo*, the residue was treated with $CH_2Cl_2$ (30 ml) and $H_2O$ (20 ml). The $CH_2Cl_2$ layer was washed with 5% $Na_2CO_3$ (20 ml) and $H_2O$ (20 ml), then dried over $Na_2SO_4$. The solvent was evaporated off *in vacuo* to give 69.0 mg (63.4%) of **12**, mp 93—97 °C (colorless prisms, recrystallized from *n*-$C_5H_{10}$).IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1540, 1382. NMR $\delta$: 0.98 (6H, d, $J$=2.7 Hz), 2.40 (1H, t, $J$=3.3 Hz), 4.77 (2H, q, $J$=10 Hz), 6.12 (1H, dd, $J$=3.3 and 9.5 Hz), 6.73 (1H, dd, $J$=3.3 and 9.5 Hz). MS *m/e*: 271 ($M^+$). *Anal.* Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.29; H, 7.90; N, 5.07.

**1,1-Dimethyl-4a-nitromethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (10)**——**10** (23.2 mg, 77.3%) was obtained by the catalytic reduction of **12** (29.8 mg, 0.11 mmol) over 10% Pd–C (52.6 mg) in EtOH (10 ml). It was identical with **10** separated by chromatography from the mother liquor of **9** (IR and NMR). mp 91—92 °C (colorless plates, recrystallized from $CH_2Cl_2$–*n*-$C_6H_{12}$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1540, 1375. NMR $\delta$: 0.90 (3H, s), 0.97 (3H, s), 4.73 (2H, q, $J$=9.6 Hz). MS *m/e*: 273 ($M^+$). *Anal.* Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.84; H, 8.47; N, 4.92.

**1,1-Dimethyl-4a-aminomethyl-9-hydroxy-1,2,3,4,4a,-9,10,10a-octahydrophenanthrene (13)**——A solution of **9** (433.5 mg, 1.5 mmol) in EtOH (100 ml) was hydrogenated over Raney Ni at room temperature to give 247.2 mg (63.6%) of **13** as white crystals after recrystallization from benzene. mp 165—167 °C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3330, 3260. NMR $\delta$: 0.90 (6H, s), 2.82 (2H, q, $J$=12 Hz), 4.74 (1H, t, $J$=9 Hz). MS *m/e*: 212 ($M^+ - CH_2NH_2 + H_2O + 1$). *Anal.* Calcd for $C_{17}H_{25}NO$: C, 78.71; H, 9.72; N, 5.40. Found: C, 78.86; H, 9.88; N, 5.39.

**1,1-Dimethyl-4a-aminomethyl-1,2,3,4,4a,10a-hexahydrophenanthrene (14)**——**14** (280 mg, 98.7%) was obtained as an oil by the reaction of **13** (304.8 mg, 1.18 mmol) with saturated HCl–EtOH (20 ml) in the same manner as described for **12**. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3360. NMR $\delta$: 0.95 (3H, s), 1.30 (3H, s), 6.00 (1H, dd, $J$=3 and 10 Hz), 6.55 (1H, dd, $J$=3 and 10 Hz). MS *m/e* 241 ($M^+$).

The acetate (**15**) was prepared from **14** by treatment with acetic anhydride in pyridine for elemental analysis. mp 156—157 °C (white needles, recrystallized from *n*-$C_6H_{12}$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3320, 1640. NMR $\delta$: 0.98 (3H, s), 1.10 (3H, s), 1.88 (3H, s), 4.04 (2H, q, $J$=9.3 Hz), 6.02 (1H, dd, $J$=2.7 and 9.3 Hz), 6.55 (1H, dd, $J$=2.7 and 9.3 Hz). MS *m/e*: 283 ($M^+$). *Anal.* Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.59; H, 9.02; N, 4.83.

**1,1-Dimethyl-4a,10-(*N*-ethoxycarbonyl-methanoimino)-9-chloro-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (17)**——A mixture of **14** (302 mg, 1.25 mmol), $Pb(OAc)_4$ (556 mg), and anhydrous $K_2CO_3$ (173 mg) in $CH_2Cl_2$ (60 ml) was stirred for 2 h in an ice bath under nitrogen. The mixture was filtered, and the $CH_2Cl_2$ layer was washed with 5% $K_2CO_3$ (30 ml) and $H_2O$ (50 ml), then dried over $Na_2SO_4$, and evaporated *in vacuo* at room temperature to give an oil (327.6 mg). A solution of the oil in $ClCH_2CH_2Cl$ (30 ml) was immediately treated with ethyl chloroformate (1.42 g) under nitrogen in an ice bath for 2 h. The solvent was evaporated off *in vacuo* at room temperature. The residue was chromatographed on $Al_2O_3$ (100 g) with $CH_2Cl_2$–*n*-$C_6H_{12}$ (1 : 2) to give 198.7 mg (45.6%) of **17** as white crystals after recrystallization from *n*-$C_6H_{12}$. mp 128—130 °C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1710, 704. NMR $\delta$: 0.95 (3H, s), 1.06 (3H, s), 1.26 (3H, tt, $J$=7.0 Hz), 2.96 (1H, dd, $J$=4.5 and 10 Hz), 3.60 (1H, dd, $J$=4.0 and 10 Hz), 4.10 (2H, q, $J$=3.0 and 7.0 Hz), 4.38 (1H, dd, $J$=3.0 and 10 Hz), 5.24 (1H, dd, $J$=3.0 and 10 Hz). MS *m/e*: 349 ($M^+ + 2$), 347 ($M^+$). *Anal.* Calcd for $C_{20}H_{26}ClNO_2$: C, 69.05; H, 7.53; N, 4.03. Found: C, 69.15; H, 7.59; N, 4.28.

**1,1-Dimethyl-4a,10-(*N*-benzoxycarbonyl-methanoimino)-9-chloro-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (18)**——As described in the case of **17**, a mixture of **14** (259 mg, 1.04 mmol), $Pb(OAc)_4$ (479 mg), and anhydrous $K_2CO_3$ (296 mg) in $CH_2Cl_2$ (50 ml) was stirred for 4 h, followed by treatment with benzyl chloroformate (50%, 2 ml) and then chromatography on $Al_2O_3$ (100 g) with $CH_2Cl_2$–*n*-$C_6H_{12}$ (1 : 3) to give 267.7 mg (63.0%) of **18** as an oil and 30.4 mg (7.8%) of the benzyl carbamate of **14** (**19**) as white crystals after recrystallization from *n*-$C_6H_{12}$. **18**: IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1705, 700. NMR $\delta$: 0.90 (3H, d, $J$=2 Hz), 1.02 (3H, d, $J$=2 Hz), 2.98 and 3.62 (each 1H, dd, $J$=3.0 and 10.5 Hz), 4.42 (1H, dd, $J$=2.8 and 8.4 Hz), 5.06 (1H, q, $J$=11.5 Hz), 5.18 (1H, s), 5.26 (1H, dd, $J$=3.3 and 11.5 Hz). MS *m/e*: 411 ($M^+ + 2$), 409 ($M^+$). *Anal.* Calcd for $C_{25}H_{28}ClNO_2$: C, 73.24; H, 6.88; N, 3.42. Found: C, 73.38; H, 7.18; N, 3.17.

**19**: mp 151 °C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3310, 1686. NMR $\delta$: 1.06 (6H, d, $J$=12 Hz), 5.03 (2H, q, $J$=12 Hz), 6.03 (1H, dd, $J$=3.2 and 9.7 Hz), 6.53 (1H, dd, $J$=3.2 and 9.7 Hz). MS *m/e*: 375 ($M^+$). *Anal.* Calcd for $C_{25}H_{29}NO_2$: C, 79.96; H, 7.79; N, 3.73. Found: C, 79.75; H, 7.93; N, 3.90.

**1,1-Dimethyl-4a,10-(*N*-ethoxycarbonyl-methanoimino)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (20)**——A solution of **17** (118.5 mg, 0.34 mmol) in EtOH (20 ml) was reduced over $PtO_2$ (80 mg) at room temperature. The mixture was filtered, the filtrate was evaporated, and the residue was extracted with $CH_2Cl_2$ (20 ml). The extract was washed with 5% $K_2CO_3$ (15 ml) and $H_2O$ (10 ml), then dried over $Na_2SO_4$. Purification by p-TLC with $CH_2Cl_2$–*n*-$C_6H_{12}$ (1 : 1)

gave 83 mg (77.7%) of **20** as an oil. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1705. NMR $\delta$: 0.95 (3H, s), 1.00 (3H, s), 1.26 (3H, tt, $J$=7 Hz), 4.12 (2H, qq, $J$=2.0 and 7.0 Hz), 4.36 (1H, d, $J$=10.0 Hz). MS $m/e$: 313 ($M^+$).

**1,1-Dimethyl-4a,10-(*N*-benzoxycarbonyl-methanoimino)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (21)**——In the same manner as described for **20**, a solution of **18** (154.8 mg, 0.38 mmol) in EtOH (30 ml) was treated with $PtO_2$ (59.3 mg) and anhydrous $K_2CO_3$ (38.2 mg), followed by chromatography on $Al_2O_3$ (70 g) with $CH_2Cl_2$–$n$-$C_6H_{12}$ (1 : 1) to give 58.4 mg (41.2%) of **21** as an oil. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1690, 1670. NMR $\delta$: 0.92 (3H, s), 0.98 (3H, d, $J$=3.0 Hz), 2.9—3.44 (2H, m), 3.21 (1H, dd, $J$=3.0 and 10.0 Hz), 3.65 (1H, dd, $J$=3.0 and 10.0 Hz), 4.37 (1H, tt, $J$=3.0 and 8.0 Hz), 5.05 (1H, q, $J$=8.0 and 12.0 Hz), 5.14 (1H, s). MS $m/e$: 375 ($M^+$). *Anal.* Calcd for $C_{25}H_{29}NO_2$: C, 79.96; H, 7.79; N, 3.73. Found: C, 79.92; H, 8.02; N, 3.60.

**1,1-Dimethyl-4a,10-methanoimino-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (22)**——A solution of **18** (315.2 mg, 0.77 mmol) in EtOH (30 ml) was reduced catalytically over Raney Ni at room temperature. After removal of the solvent, the residue was treated with a mixture of $CH_2Cl_2$ (30 ml) and 5% $K_2CO_3$ (30 ml). The $CH_2Cl_2$ layer was washed with $H_2O$ (30 ml), dried over $Na_2SO_4$, and evaporated *in vacuo* to give a brown oil, followed by chromatography on $Al_2O_3$ (70 g) with EtOAc–EtOH (5%) to give 104.8 mg (56.6%) of **22** as an oil. MS $m/e$: 241 ($M^+$). NMR $\delta$: 0.94 (3H, s), 1.05 (3H, s), 2.97 (1H, dd, $J$=3.0 and 16.0 Hz), 3.04 (2H, q, $J$=10.0 Hz), 3.60 (1H, t, $J$=3.0 Hz).

The picrate and HCl salt were prepared from **22** for elemental analysis. Picrate: mp 253—255 °C (dec.). *Anal.* Calcd for $C_{23}H_{26}N_4O_7$: C, 58.71; H, 5.57; N, 11.91. Found: C, 58.63; H, 5.50; N, 11.69. HCl salt: mp 230—235 °C (subl.). *Anal.* Calcd for $C_{17}H_{24}ClN$: C, 73.47; H, 8.71; N, 5.04. Found: C, 73.28; H, 8.74; N, 5.04.

**1,1-Dimethyl-4a,10-(*N*-chloro-methanoimino)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (23)**——A mixture of **22** (125.0 mg, 0.52 mmol) and *N*-chlorosuccinimide (143.9 mg) in $CH_2Cl_2$ (30 ml) was stirred for 3 h under nitrogen in an ice bath. The mixture was washed with 5% $Na_2CO_3$ (30 ml) and $H_2O$ (30 ml), then dried over $Na_2SO_4$, and evaporated *in vacuo* at room temperature. The residue was chromatographed on silica-gel (30 g) with $CH_2Cl_2$–$n$-$C_6H_{12}$ (1 : 2) to give 122.5 mg (85.6%) of **23** as an oil. NMR $\delta$: 0.99 (3H, s), 1.10 (3H, s), 2.94 (1H, dd, $J$=4.0 and 17 Hz), 3.07 (1H, d, $J$=11.0 Hz), 3.71 (2H, d, $J$=11.0 Hz), 3.76 (1H, m). MS $m/e$: 277 ($M^+$+2), 275 ($M^+$), (Found: $M^+$+2 277.1412 and $M^+$ 275.1441. $C_{17}H_{22}ClN$ required $M^+$+2 277.1411 and $M^+$ 275.1441). *Anal.* Calcd for $C_{17}H_{22}ClN$: C, 74.03; H, 8.04; N, 5.08. Found: C, 74.31; H, 8.15; N, 4.91.

**1,1-Dimethyl-4a,10-methenoimino-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (24)**——In the same manner as described for **23**, crude **24** was prepared from 35.4 mg (0.15 mmol) of **22** and *N*-bromosuccinimide (47.8 mg) in $CH_2Cl_2$ (30 ml), and chromatographed on $Al_2O_3$ (100 g) with $CHCl_3$–$n$-$C_6H_{12}$ (1 : 1) to give 20.2 mg (57.5%) of **24** as an oil. NMR $\delta$: 0.80 (3H, s), 0.98 (3H, s), 4.44 (1H, m), 7.44 (1H, s). MS $m/e$: 239 ($M^+$) (Found: $M^+$ 239.1672. $C_{17}H_{21}N$ requires $M^+$ 239.1674).

**(±)-6,15,16-Iminopodocarpane-8,11,13-triene (3)**——A solution of **23** (141.3 mg, 0.51 mmol) in $CF_3COOH$ (2 ml) was irradiated with a 400W high-pressure mercry lamp under nitrogen at room temperature for 5 h. Trifluoroacetic anhydride (2 ml) was added to the resulting solution and stirring was continued at room temperature for 2 h. After removal of the solvent *in vacuo*, the residue was refluxed with 5% KOH–EtOH (20 ml) for 2 h, then $H_2O$ (20 ml) was added to the resulting solution. The solution was concentrated *in vacuo* and extracted with $CH_2Cl_2$ (20 ml × 4). The $CH_2Cl_2$ layer was extracted with 5% $H_2SO_4$ (20 ml × 5) and the aqueous extract was basified with anhydrous $K_2CO_3$ and reextracted with $CH_2Cl_2$ (20 ml). The extract was dried over $Na_2SO_4$ and evaporated *in vacuo* to give a brown oil, which was chromatographed on $Al_2O_3$ (200 g) with $CHCl_3$ to give 47.5 mg (38.7%) of **3** as an oil. NMR $\delta$: 1.04 (3H, s), 2.53 (2H, q, $J$=12.7 Hz), 3.07 (2H, q, $J$=18.0 Hz), 3.46 (1H, d, $J$=6.0 Hz). MS $m/e$: 239 ($M^+$) (Found: $M^+$ 239.1674. $C_{17}H_{21}N$ required $M^+$ 239.1674).

The methiodide was prepared for elemental analysis and X-ray analysis. mp 269—270 °C. MS $m/e$: 239 ($M^+ - CH_3I$). *Anal.* Calcd for $C_{18}H_{24}IN$: C, 56.70; H, 6.34; N, 3.67. Found: C, 56.49; H, 6.45; N, 3.67.

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