The Synthesis of Fenical and Sims' Structure of Cycloeudesmol. Stereospecific Total Syntheses of (+)-7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[d]naphthalene, (+)-7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[d]naphthalene, (+)-7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[d]-naphthalene, and (±)-7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[d]naphthalene[1]

Masayoshi Ando,* Shinsei Sayama, and Kahei Takase

Department of Chemistry, Faculty of Science, Tohoku University, Aramaki-aza-Aoba, Sendai, 980 Japan

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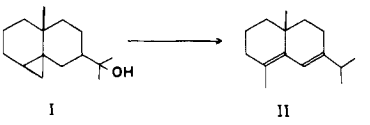
Stereospecific total syntheses of the four diastereoisomers of Fenical and Sims' structure of cycloeudesmol, (+)-7β-(1-hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[d]naphthalene (Ia), (+)-7α-(1-hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[d]naphthalene (Ib), (+)-7β-(1-hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[d]naphthalene (Ic), and (±)-7α-(1-hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[d]naphthalene (Id), were carried out with the object of establishing the structure of cycloeudesmol. The key step of these syntheses involves the Simmons–Smith reaction directed by the hydroxyl group at the allylic position or the homoallylic position.

Cycloeudesmol was isolated by Fenical and Sims from the marine alga *Chondria oppositiclada* Dawson[2] and was shown to be antibiotic toward *Staphylococcus aureus*, *Salmonella choleraesius*, *Mycobacterium smegmatis*, and *Candida albicans*.[3] The structure of this compound was proposed as shown in structure (I) on the basis of spectral data and its acid-catalyzed transformation to (+)-δ-selinene (II)[2] (Scheme I). Since the stereochemistries of the cyclopropyl and 1-ydroxy-1-methylethyl moieties in I are not clear, four stereoisomers (Ia, Ib, Ic, and Id) are possible for the proposed structure. Since it was considered that the stereoselective total syntheses of the four stereostructures Ia–d (Chart I) were a synthetic challenge, we decided to synthesize them with the object of establishing the structure of cycloeudesmol. This paper details the results of the total syntheses of the structures Ia–d.

Scheme I



I II

Chart I

Ia, $R^1 = C(CH_3)_2OH$; $R^2 = H$ Ic, $R^1 = C(CH_3)_2OH$; $R^2 = H$
Ib, $R^1 = H$, $R^2 = C(CH_3)_2OH$ Id, $R^1 = H$; $R^2 = C(CH_3)_2OH$

Chart II. The Numbering Employed in This Report

Results and Discussion

Since cycloeudesmol is a biologically active compound, we chose the easily available optically active compound, (−)-dihydrocarvone (1), as a common starting material for the purpose of getting the final products, Ia–d, as the optically active compounds. At the beginning of these syntheses we envisioned a general synthetic approach as summarized in Scheme II. The key step of this approach involved Simmons–Smith reaction of the appropriately functionalized allylic alcohols, A, B, C, and D. A highly stereoselective introduction of the cyclopropyl ring in these intermediates was expected because of the known directive effect of an allylic hydroxyl group.[4,5]

Synthesis of (+)-7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[d]naphthalene (Ia).[6] The starting material was the ketol (2),[7,8] which was prepared by condensation of (−)-dihydrocarvone (1) with 4-chloro-2-butanone in 38% yield[9] (Scheme III, Chart II). Ozonolysis of 2 gave diketo alcohol 3,[7,9] in 90% yield. Treatment of 3 with concentrated hydrochloric acid in acetic acid afforded diketone 4[7,9] in 87% yield by dehydration and spontaneous epimerization of acetyl group at C_7. The selective protection of the saturated carbonyl group in 4 was carried out in the following manner. Treatment of 4 with 1.2 molar equiv of ethylene glycol under the standard conditions gave a ca. 8:1:1 mixture of

(1) A portion of this work has appeared in preliminary form: Ando, M.; Sayama, S.; Takase, K. *Chem. Lett.* **1979**, 191, Ando, M.; Sayama S.; Takase, K. *Chem. Lett.* **1981**, 377.
(2) Fenical, W.; Sims, J. J. *Tetrahedron Lett.* **1974**, 1137.
(3) Sims, J. J.; Donnell, M. S.; Leary, J. V.; Lacy, G. H. *Antimicrob. Agents Chemother.* **1975**, *7*, 320.
(4) Simmons, H. E.; Cairns, T. L.; Valaduchick, S. A., Hoiness, C. M. *Org. React. (N.Y.)* **1973**, *20*, 1.
(5) Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468.
(6) After we have completed our synthesis of Ia, two reports of the synthesis of this compound have appeared: (a) Moss, R. A., Chen, E. Y.; Banger, J.; Matsuo, M. *Tetrahedron Lett.* **1978**, 4365. (b) Cain, D.; Chen, P. C.; Frobese, A. S.; Guton, J. T. III *J. Org. Chem.* **1979**, *44*, 4981.
(7) (a) Houghton, R. P.; Humber, D. C.; Pinder, A. R. *Tetrahedron Lett.* **1966**, 353. (b) Humber, D. C.; Pinder, A. R.; Williams, R. A. *J. Org. Chem.* **1967**, *32*, 2335.
(8) Marshall, J. A.; Fanta, W. I.; Roebke, H. *J. Org. Chem.* **1966**, *31*, 1016.
(9) The preparation of 2, 3, and 4 indicated in this paper are the modification of the Hortmann's syntheses of 5β-hydroxy-4,7β*H*-eudesm-11-en-3-one, 5β-hydroxy-4,7β*H*-noreudesmane-3,11-dione, and 7α*H*-12-noreudesm-4-ene-3,11-dione: Hortmann, A. G.; Martinelli, J. E.; Wang, Y.-S. *J. Org. Chem.* **1969**, *34*, 732.

0022-3263/85/1950-0251$01.50/0

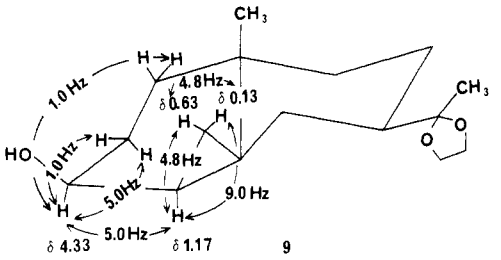


Figure 1.

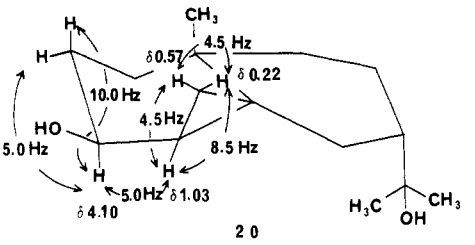
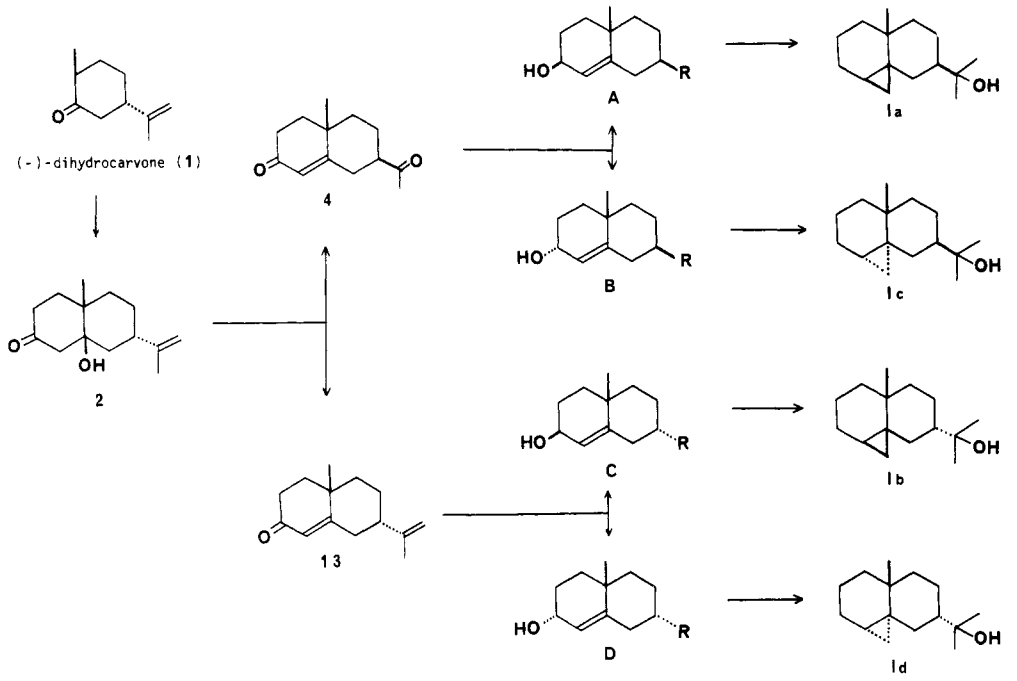


Figure 2.

Scheme II



the desired product **5**, the recovered diketone **4**, and diacetal **6**. Treatment of a 1:1 mixture of **4** and **6** with *p*-toluenesulfonic acid in refluxing benzene also gave the same equilibration mixture mentioned above. For practical purposes this mixture was reduced with lithium tri-*tert*-butoxyaluminum hydride to give the desired β-alcohol **7** accompanied by diacetal **6** and diol **8** in 57% yield after the chromatographic separation.

The Simmons–Smith reaction of **7** gave the β-cyclopropyl derivative **9** in 78% yield. The stereochemistry of **9** was determined on the basis of the reaction mechanism of the Simmons–Smith reaction of the cyclic allylic alcohols[4,5] as well as the analysis of the ^{1}H NMR spectrum (Figure 1).

Oxidation of **9** by the Collins procedure afforded keto acetal **10** in 86% yield. The Wolff–Kishner reduction of **10** and successive deacetalization gave ketone **12** in 57% overall yield. Treatment of **12** with methylmagnesium iodide afforded Ia in quantitative yield. The ^{1}H NMR spectral data of Ia shown in Table I are apparently different from those of natural cycloeudesmol reported in the literature by Fenical and Sims.[2]

Synthesis of (+)-7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (Ib).[10] The starting material of Ib is dienone **13**, which was prepared from **2** in 94% yield by dehydration with 10% aqueous potassium hydroxide[8] (Scheme IV). Epoxidation of **13** with 1.02 molar equiv of *m*-CPBA gave epoxy ketone **14** in 86% yield as a diastereomeric mixture of epoxide accompanied by over oxidized product **15**. The HPLC analysis showed that **14** was a 3:1 mixture of two diastereoisomers. Although we could separate **14** into two diastereoisomers by HPLC, we employed **14** without separation for practical purposes. Reduction of **14** with sodium borohydride gave β-alcohol **16** in 60% yield.

The Simmons–Smith reaction of **16** under the controlled conditions (at 10 °C, for 6 h) gave the desired β-cyclopropyl derivative **17** in 65% yield. It is noteworthy that the epoxide ring of **16** has no influence on the Simmons–Smith reagent under those reaction conditions. The stereochemical assignment is based on the reaction mechanism of the Simmons–Smith reaction of cyclic allylic alcohols[4,5] as well as the analysis of the ^{1}H NMR spectrum (Figure 2) of diol **20**, which was derived from **17** by the reduction with lithium aluminum hydride. Although the complete analysis of the ^{1}H NMR spectrum of **17** is impossible because **17** is a diastereomeric mixture of epoxide ring, the splitting pattern and chemical shift of C_2–H of **17** are very similar to those of **20** and completely different from those of **9**. Thus it is concluded that **17** has the same stereostructure as that of **20**.

Oxidation of **17** by the Collins procedure gave epoxy ketone **18** in 96% yield. The attempted Wolff–Kishner reduction of **18** gave no desired product **19**, probably because of the unstability of the epoxide ring of **18** under these reaction conditions. Collins oxidation of **20** gave hydroxy ketone **21** in quantitative yield. The Wolff–Kishner reduction of **21** gave Ib in 82% yield. The ^{1}H NMR spectral data of Ib shown in Table I are apparently different from those of natural cycloeudesmol reported in the literature by Fenical and Sims.[2]

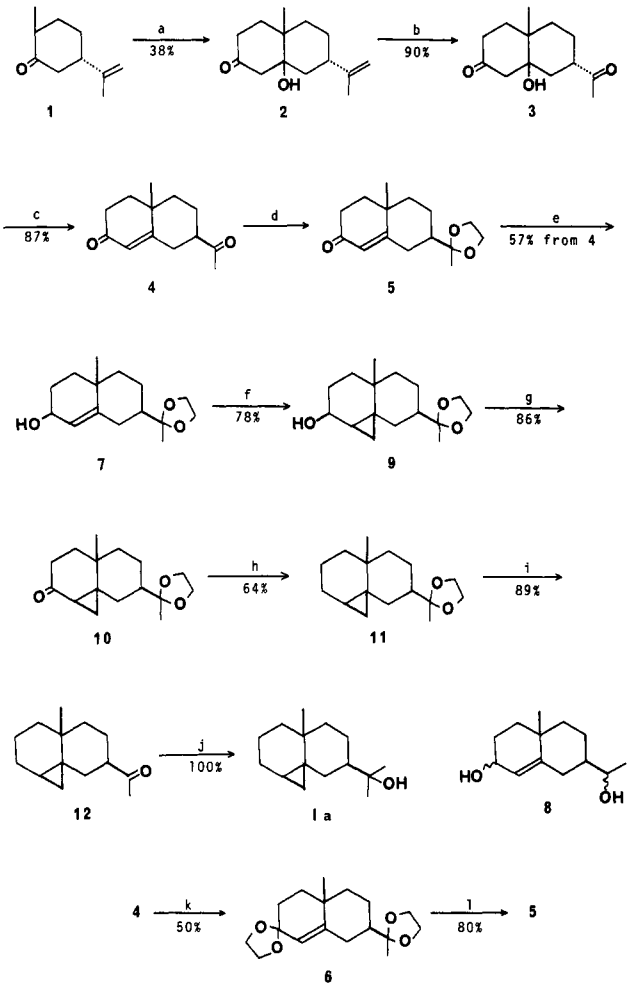
(10) After we had completed our synthesis of Ib, another synthesis of this compound appeared: Moss, R. A.; Chen, E. Y.; Banger, J.; Matsuo, M. *Tetrahedron Lett.* **1978**, 4365.

Table I. ^{1}H NMR Spectral Data Comparison between Cycloeudesmol and Compounds Ia, Ib, Ic, and Id

condn	chemical shift, δ				
	C_1–H (exo)	C_1–H (endo)	C_{1a}	C_{4a}–CH_3	$C(OH)(CH_3)_2$
		Cycloeudesmol[a]			
220 MHz, in CCl_4	0.35 (d, J = 5.0)	0.47 (d, J = 5.0)		1.00	1.25, 1.33
		Ia			
90 MHz, in CCl_4	0.07~0.26 (m)		0.60 (m)	1.00	1.13, 1.13
200 MHz, in $CDCl_3$	0.13 (dd, J = 4.5, 9.0 Hz)	0.20 (dd, J = 4.5, 4.5 Hz)	0.68 (m)	0.98	1.14, 1.16
		Ib			
90 MHz, in CCl_4	0.10 (dd, J = 4.5, 9.0 Hz)	0.25 (dd, J = 4.5, 4.5 Hz)	0.70 (m)	0.95	1.13, 1.13
200 MHz, in $CDCl_3$	0.10 (1 H, dd, J = 4.5, 9.0 Hz)	0.27 (dd, J = 4.5, 4.5 Hz)	0.75 (m)	0.94	1.16, 1.17
		Ic			
90 MHz, in CCl_4	0.05 (dd, J = 4.5, 9.0 Hz)	0.40 (ddd, J = 1.5, 4.5, 4.5 Hz)	0.73 (m)	1.10	1.13, 1.13
200 MHz, in $CDCl_3$	0.02 (dd, J = 4.5, 9.0 Hz)	0.39 (ddd, J = 2.0, 4.5, 4.5 Hz)	0.73 (m)	1.07	1.14, 1.15
		Id			
90 MHz, in CCl_4	0.20 (dd, J = 4.5, 9.0 Hz)	0.46 (ddd, J = 2.0, 4.5, 4.5 Hz)	0.67 (m)	1.18	1.16, 1.16
200 MHz, in $CDCl_3$	0.21 (dd, J = 4.5, 9.0 Hz)	0.48 (ddd, J = 1.8, 4.5, 4.5 Hz)	0.70 (m)	1.17	1.18, 1.18

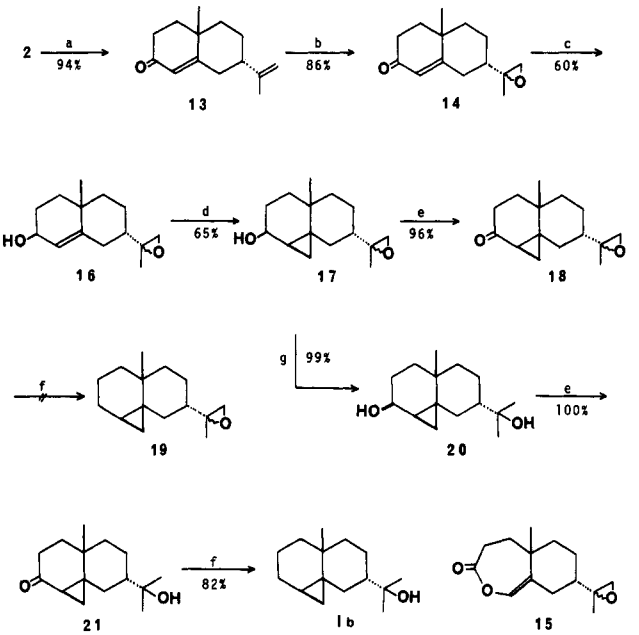
[a] The value reported in reference 2.

Scheme III[a]



[a] (a) NaH, EtOH, THF, $Cl(CH_2)_2C(=O)CH_3$; (b) O_3, CH_2Cl_2, MeOH, then NaI, MeOH, AcOH; (c) HCl, AcOH; (d) 1.2 mol equiv of ethylene glycol, p-TsOH, benzene, reflux; (e) LiAl(t-BuO)$_3$H, THF; (f) Zn(Cu)-CH_2I_2, ether; (g) CrO_3·2Py, CH_2Cl_2; (h) 85% NH_2NH_2·H_2O, KOH, diethylene glycol, 110–120 °C (1 h), 180 °C (3 h); (i) 20% aqueous AcOH, EtOH, reflux; (j) MeMgI, ether; (k) excess ethylene glycol, p-TsOH, benzene, reflux; (l) 1 mol equiv of 4, p-TsOH, benzenene reflux.

Scheme IV[a]



[a] (a) 10% KOH aqueous solution, reflux; (b) m-CPBA, CH_2Cl_2; (c) $NaBH_4$, MeOH; (d) Zn(Cu)-CH_2I_2, ether, DME; (e) CrO_3·2Py, CH_2Cl_2; (f) 85% NH_2NH_2·H_2O, KOH, diethylene glycol; (g) $LiAlH_4$, ether.

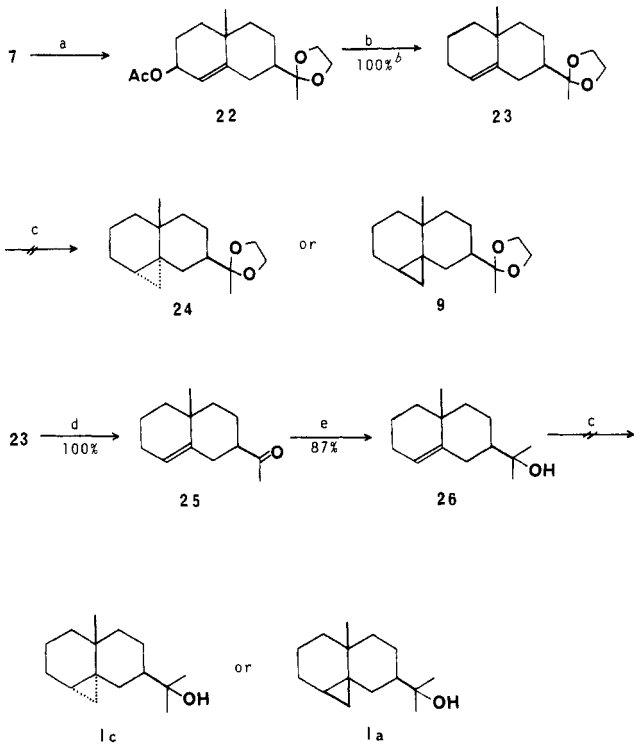
Synthesis of (+)-7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Ic).[11] At the beginning of the synthesis of Ic we envisioned an approach which consisted of the Simmons–Smith reaction of trisubstituted olefins such as acetal **23** and alcohol **26** shown in Scheme V, since we expected that the reagent approached from the less hindered α-side of **23** or **26**. The olefins **23** and **26** were prepared in the following manner.

Acetylation of **7** and successive reduction of the resulting acetate **22** with lithium in liquid ammonia gave the desired trisubstituted olefin **23** in quantitative yield. Deacetalization of **23** afforded ketone **25** in quantitative yield. Treatment of **25** with methylmagnesium iodide gave the desired tertiary alcohol **26** in 87% yield.

The Simmons–Smith reaction of **23** and **26** under the analogous reaction conditions to the allylic alcohols **7** and **16** gave recovered starting material. Under more drastic conditions the Simmons–Smith reaction of **23** and **26** gave

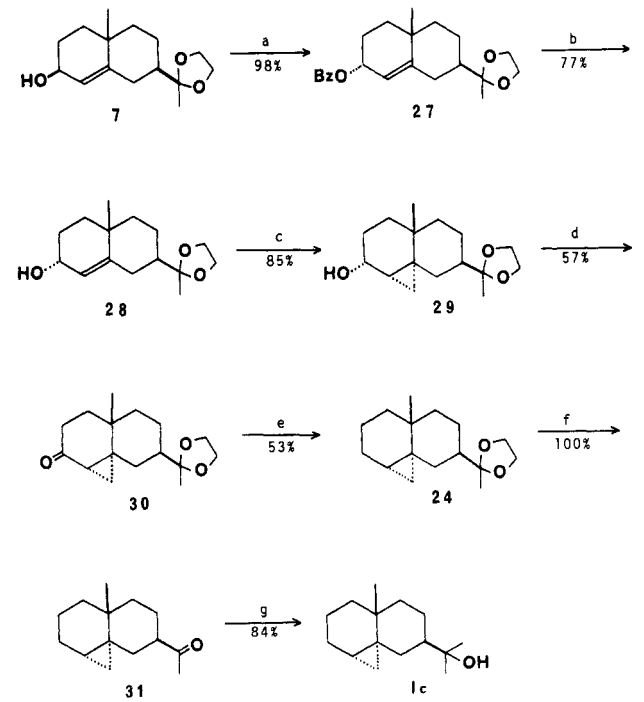
(11) After we had completed our synthesis of Ic, another synthesis of this compound appeared: Moss, R. A.; Chen, E. Y. *J. Org. Chem.* **1981**, *46*, 1466.

Scheme V[a]



[a] (a) Ac_2O, Pyr; (b) Li, liquid NH_3; (c) Zn(Cu)-CH_2I_2, ether, DME; (d) 10% aqueous AcOH, EtOH; (e) MeMgI, ether. [b] Overall yield from 7 based on recovered 7.

Scheme VI[a]

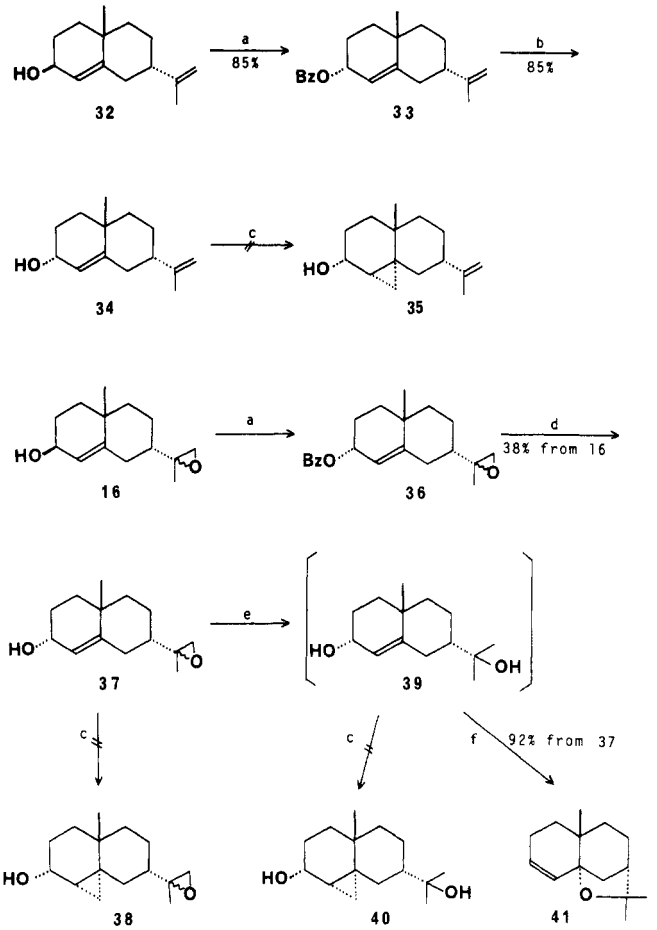


[a] (a) $(C_6H_5)_3P$, $C_6H_5CO_2H$, EtOC(=O)N=NC(=O)OEt, THF; (b) 2 M aqueous KOH, MeOH; (c) Zn(Cu)-CH_2I_2, ether, DME; (d) $CrO_3 \cdot 2Pyr$, CH_2Cl_2; (e) 85% $NH_2NH_2 \cdot H_2O$, KOH, diethylene glycol; (f) 20% aqueous AcOH, EtOH; (g) MeMgI, ether. Bz = benzoyl.

a complex mixture probably because of the instability of acetal and tertiary hydroxyl groups under these reaction conditions.

Since we failed in the introduction of α-cyclopropyl ring by the Simmons–Smith reaction of the simple trisubstituted olefins, **23** and **26**, our attention was focused on the

Scheme VII[a]



[a] (a) $(C_6H_5)_3P$, $C_6H_5CO_2H$, EtOC(=O)N=NC(=O)OEt, THF; (b) 2 M aqueous KOH, MeOH; (c) Zn(Cu)-CH_2I_2, ether, DME; (d) 2 M aqueous K_2CO_3, MeOH; (e) $LiAlH_4$; (f) silica gel. Bz = benzoyl.

Simmons–Smith reaction of a 2α-allylic alcohol such as **28**. 2α-Allylic alcohol **28** was prepared from 2β-allylic alcohol **7** by the Mitsunobu's procedure[12] as shown in Scheme VI. Thus treatment of **7** with benzoic acid in the presence of triphenylphosphine and diethyl azodicarboxylate gave benzoate **27** in 98% yield. Hydrolysis of **27** with 2 M potassium hydroxide gave **28** in 77% yield.

The Simmons–Smith reaction of **28** under mild conditions (17 °C, 17 h) gave the desired product **29** in 85% yield. The stereochemical assignment is based on the reaction mechanism of the Simmons–Smith reaction of cyclic allylic alcohols[4,5] as well as the following conversion. The Collins oxidation of **29** afforded keto acetal **30** in 57% yield. The Wolff–Kishner reduction of **30** and successive deacetalization of the resulting acetal **24** gave ketone **31** in 53% yield. The intermediates **30**, **24**, and **31** are completely different compounds from the corresponding β-cyclopropyl derivatives **10**, **11**, and **12** on the basis of the ^1H NMR spectra. Treatment of **31** with methylmagnesium iodide afforded Ic in 84% yield. The ^1H NMR spectral data of Ic shown in Table I are apparently different from those of natural cycloeudesmol reported in the literature by Fenical and Sims.[2]

Attempted Synthesis of 7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Id) in the Optically Active Form. To establish the synthesis of Id in the optically active form

(12) Mitsunobu, O.; Eguchi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427.

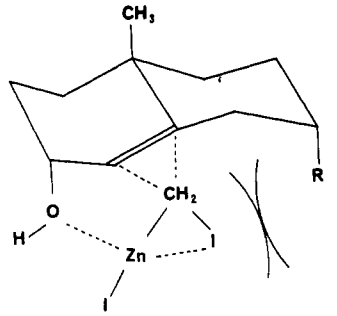


Figure 3.

by the similar methodology employed in the syntheses of Ia, Ib, and Ic, we decided to attempt the Simmons–Smith reaction of 2α-allylic alcohols bearing an α-axial side chain at C_7 such as **34**, **37**, and **39** (Scheme VII). Treatment of **32** with benzoic acid in the presence of triphenylphosphine and diethyl azodicarboxylate in THF[12] gave 2α-benzoyloxy derivative **33** in 85% yield. Hydrolysis of **33** with a 2 M aqueous solution of potassium hydroxide gave the desired 2α-allylic alcohol **34** in 85% yield. Simmons–Smith reaction to **34** in a mixture of ether and dimethoxyethane at room temperature or refluxing temperature gave a complex mixture. Inoue and Sawada's modification of the Simmons–Smith reaction[13] to **34** also gave a complex mixture.

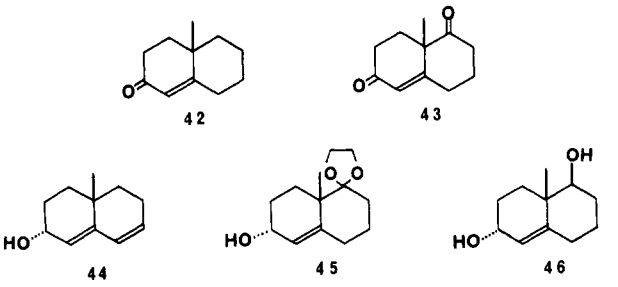
Then we prepared α-allylic alcohols **37** and **39** in the following manner. Treatment of **16** with benzoic acid in the presence of triphenylphosphine and diethyl azodicarboxylate in THF[12] and successive hydrolysis of the resulting 2α-benzoate (**36**) gave **37**. Reduction of **37** with lithium aluminum hydride gave **39** as an unstable compound. The attempted purification of **39** on silica gel column chromatography gave tetrahydrofuran derivative **41** in 92% yield. The attempt of the Simmons–Smith reaction of **37** and **39** gave a complex mixture in which the desired cyclopropyl derivatives **38** and **40** were not detected.

Synthesis of (±)-7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Id). Since the attempted Simmons–Smith reaction of 2α-allylic alcohols **34**, **37**, and **39** was unsuccessful because of the severe steric hindrance between the incoming Simmons–Smith reagent and the axial side chain at C_7 (Figure 3), we envisioned different approaches to (±)-Id which consisted of the introductions of the cyclopropyl moiety at $C_{1(8a)}$ and the side chain at C_7 in this order to the appropriately functionalized decalin derivatives. Although the compounds in this section are racemic, the nomenclature and the indication of the stereochemistry of these compounds are based on one of enantiomers for the convenience of expression.

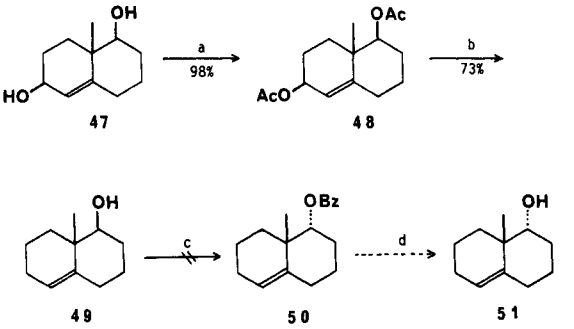
We envisioned the approach employing 2α-allylic alcohols such as **44**, **45**, and **46** which were conveniently functionalized for the introduction of a cyclopropyl moiety to the double bond at the $C_{1(8a)}$ position by the Simmons–Smith reagent directed by the α-hydroxyl group[4,5] at C_2 and the successive introduction of the α(axial)-side-chain at C_7 utilizing the functional groups in the B ring. The compounds **44**, **45**, and **46** were prepared from an α,β-unsaturated ketone (**42**)[14,15] and the Wieland–Misher ketone (**43**)[16] by the standard methodology (Chart III). Unfortunately the Simmons–Smith reaction[4,5] of **44**, **45**, and **46** were unsuccessful.

Since the various attempts of the introduction of the α-cyclopropyl moiety to the $C_{1(8a)}$ position by the Simmons–Smith reaction directed by the 2α-hydroxyl group were unsuccessful mainly because of their instability in the reaction conditions, our attention was focused on the 5α-homoallylic alcohol (**51**) which was expected to be more stable than the 2α-allylic alcohols such as **44**, **45**, and **46** in the reaction conditions.[17] The 5α-homoallylic alcohol

Chart III

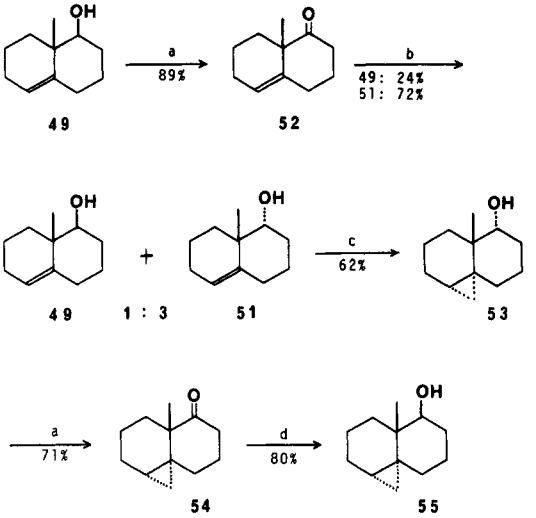


Scheme VIII[a]



[a] (a) Ac_2O, Pyr; (b) Li, liquid NH_3; (c) $(C_6H_5)_3P$, $C_6H_5CO_2H$, EtOC(=O)N=NC(=O)Et; (d) $LiAlH_4$, ethyl ether. Bz = benzoyl.

Scheme IX[a]



[a] (a) PCC, CH_2Cl_2; (b) lithium tri-*sec*-butylborohydride, THF, -78 °C; (c) Zn(Cu)-CH_2I_2, ether, DME; (d) $NaBH_4$, MeOH, 0 °C.

(13) Sawada, S.; Inoue, Y. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2669.
(14) Marshall, J. A.; Fanta, W. I. *J. Org. Chem.* **1964**, *29*, 2501 and references cited therein.
(15) **42** are prepared by the modifications of our syntheses of 7α-isopropenyl-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**13**).
(16) Ramachandran, S.; Newman, M. S. *Org. Synth.* **1961**, *41*, 38.
(17) The Simmons–Smith reaction to the homoallylic alcohols have been reported in the following: (a) Reference 4 and the literature cited there. (b) Ireland, R. E.; Dauson, M. I.; Kowalski, C. J.; Lipinski, C. A.; Marshall, D. R.; Tilley, J. W.; Bordner, J.; Trus, B. L. *J. Org. Chem.* **1975**, *40*, 973. (c) Grieco, P. A.; Oguri, T.; Wang, C. J.; Williams, E. *J. Org. Chem.* **1977**, *42*, 4113.

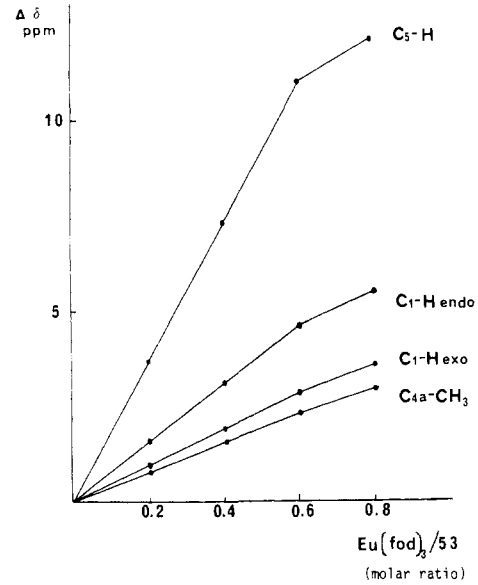


Figure 4. Change in chemical shift in the ^1H NMR spectrum of **53** in carbon tetrachloride.

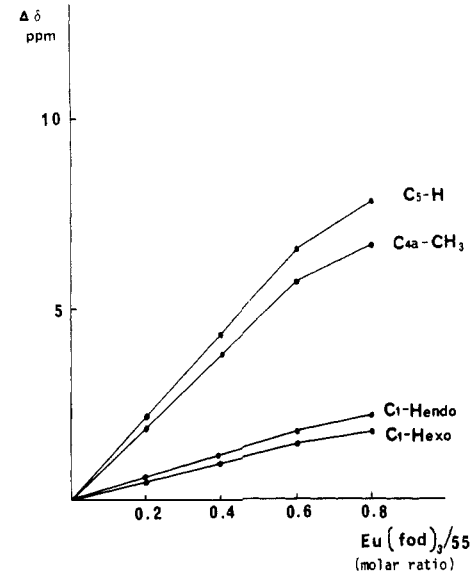


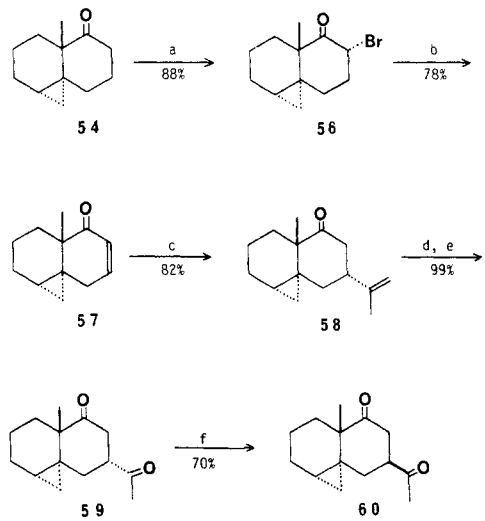
Figure 5. Change in chemical shift in the ^1H NMR spectrum of **55** in carbon tetrachloride.

(**51**) was prepared as shown in Scheme VIII and Scheme IX. Acetylation of **47**[18] gave a diacetate (**48**) in 98% yield. Reduction of **48** with lithium and liquid ammonia in a small amount of ether gave a 5β-alcohol (**49**) in 73% yield accompanied by a 15% yield of **47**. An attempt at the direct conversion of **49** to **51** by Mitsunobu's procedure[12] was unsuccessful probably because of the severe steric hindrance at the C_5-position by the angular methyl group. Then our attention was focused on the reduction of a ketone (**52**) by the appropriate reducing agent. Oxidation of **49** with pyridinium chlorochromate[19] gave **52** in 89% yield. Reduction of **52** with lithium tri-*sec*-butylborohydride[20] gave a 3:1 mixture of the desired 5α-alcohol (**51**) and the 5β-alcohol (**49**) in a quantitative yield. The mixture was separated easily by the column chromatography of silica gel to give a 72% yield of **51** and a 24% yield of **49**. The undesired **49** was converted to **51** by repeated oxidation and reduction procedures.

The Simmons–Smith reaction of **51** gave an α-cyclopropyl derivative (**53**) in 62% yield. The introduction of cyclopropyl moiety at the $C_{1(8a)}$ double bond of **51** was fully supported by the analysis of the ^1H NMR spectrum of **53** shown in the Experimental Section. The stereochemical assignment of the newly introduced cyclopropyl moiety of **53** is based on the reaction mechanism of the Simmons–Smith reaction of the cyclic homoallylic alcohols[17] as well as the comparison of the paramagnetic shift in the ^1H NMR spectra[21] of **53** and its epimeric β-alcohol **55** induced by the lanthanide shift reagent, $Eu(fod)_3$, in carbon tetrachloride. The $\Delta\delta$ values of C_1-protones of **53** are larger than those of **55** as shown in Figure 4 and Figure 5. This result is well explained by the fact that the product of Simmons–Smith reaction of the 5α-alcohol (**51**) posses an α-cyclopropyl moiety.

Oxidation of **53** with pyridinium chlorochromate gave a ketone **54** in 71% yield. Bromination of **54** with phenyltrimethylammonium perbromide[22] and successive

Scheme X[a]



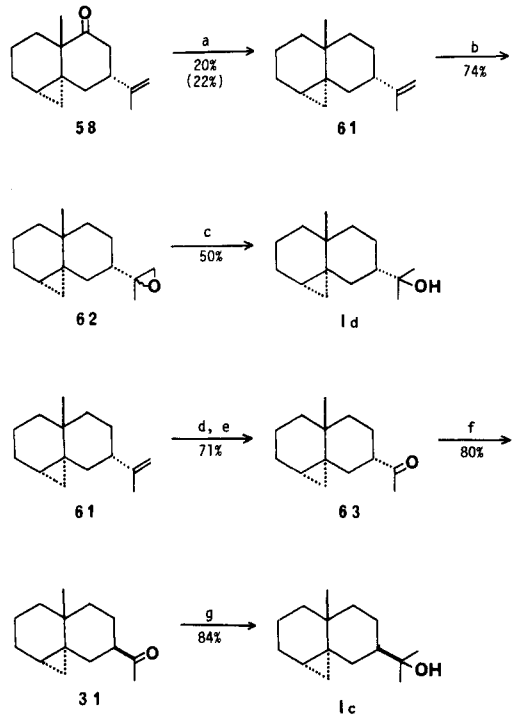
[a] (a) PTAB, THF; (b) LiBr, Li_2CO_3, DMF, 110–120 °C, 4 h; (c) $[CH_2=C(CH_3)]_2CuLi$, THF, DME; (d) O_3, CH_2Cl_2, MeOH, −70 °C; (e) NaI; (f) 2 M aqueous KOH, MeOH.

dehydrobromination of the resulting α-bromo ketone (**56**) gave an α,β-unsaturated ketone (**57**) in 69% overall yield. Conjugate addition of lithium diisopropenylcuprate[23] to **57** gave an addition product (**58**) in 82% yield as a single stereoisomer (Scheme X). The stereochemical evidence of **58** was obtained by the following transformation. Ozonolysis of **58** gave the corresponding α(*axial*)-acetyl derivative (**59**), which gave a 1:3 mixture of **59** and a thermodynamically more stable β(*equatorial*)-acetyl derivative (**60**) by treatment with 2 M KOH in methanol at room temperature. The highly stereochemical control of conjugate addition in **57** is well explained as the result of the reaction being controlled by stereoelectronic factors.[24]

The Wolff–Kishner reduction of **58** gave the corresponding hydrocarbon (**61**) in 22% yield (Scheme XI). The low yield in this step is based on the severe steric hindrance of the C_5-carbonyl group of **58** by the angular

(18) Boyce, C. B. C.; Whitehurst, J. S. *J. Chem. Soc.* **1960**, 2680.
(19) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(20) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.
(21) Kime, K. A.; Sievers, R. E. *Aldrichimica Acta* **1977**, *10*, 54 and the references cited there.
(22) Fiser, L. F.; Fiser, M. "Reagent for Organic Synthesis"; John Wiley and Sons, Inc.: New York, 1967; Vol. 1, p 855.
(23) (a) Seebach, D.; Neumann, H. *Chem. Ber.* **1974**, *107*, 847. (b) Vig, O. P.; Kapur, J. C.; Sharma, S. D. *J. Indian Chem. Soc.* **1968**, *45*, 1026.
(24) (a) Marshall, J. A.; Cohen, G. M. *J. Org. Chem.* **1971**, *36*, 877. (b) Marshall, J. A.; Andersen, N. H. *J. Org. Chem.* **1966**, *31*, 667.

Scheme XI[a]



[a] (a) 85% $NH_2NH_2 \cdot H_2O$, KOH, diethylene glycol, 80–110 °C (30 min), 200 °C (3 h); (b) *m*-CPBA, CH_2Cl_2; (c) $LiAlH_4$, ether; (d) O_3, CH_2Cl_2, MeOH; (e) NaI; (f) 2 M aqueous KOH, MeOH; (g) MeMgI, ether. (The yield in parentheses is based on the recovered **58**.)

methyl group, the α(*axial*)-isopropenyl group, and the cyclopropyl moiety, and the volatile nature of the product **61**. The structure of **61** was unambiguously established by the following transformation. Ozonolysis of **61** and successive treatment of the resulting α(*axial*)-acetyl derivative (**63**) with 2 M KOH in methanol gave a thermodynamically more stable β(*equatorial*)-acetyl derivative (**31**) in 57% yield, which was identical with the authentic **31** in their ^{1}H NMR spectra. **31** has already been converted to Ic.

Epoxidation of **61** and successive reduction of the resulting epoxide (**62**) with lithium aluminum hydride afforded (±)-Id as an oil. Although the structure of (±)-Id was fully supported by its unambiguous synthesis above mentiond as well as the analyses of its spectral data, its ^{1}H NMR spectral data in carbon tetrachloride were found to differ from those of cycloeudesmol reported by Fenical and Sims as shown in Table I.

Since the total syntheses of the four stereoisomers of I have been completed and they are found to differ from natural cycloeudesmol, it is concluded that the structure proposed by Fenical and Sims is wrong. The ^{1}H NMR spectra of four stereoisomers, Ia–d, showed three cyclopropyl protons, respectively, as shown in Table I. Without exception the coupling patterns of the three protons of compounds, Ia–d, are those of the typical 1,1,2-trisubstituted cyclopropane derivatives (J^{gem} = 4.5 Hz, J^{vic}_{cis} = 9.0 Hz, J^{vic}_{trans} = 4.5 Hz). On the contrary the ^{1}H NMR spectrum of natural cycloeudesmol reported by Fenical in the literature[2] showed typical AB type two protons [δ 0.35 (1 H, J = 5.0 Hz), 0.47 (1 H, J = 5.0 Hz)]. The coupling constant (J = 5.0 Hz) is in good accordance with the geminal coupling constant of cyclopropane derivatives. No vicinal coupling of these protons was recorded in the literature. To explain the above mentioned ^{1}H NMR spectrum, cycloeudesmol should have a 1,1,2,2-tetrasubstituted cyclopropane ring rather than a 1,1,2-trisubstituted one.

Chart IV

III IV

Since it is clear that cycloeudesmol has the eudesmane skeleton by its transformation to (+)-δ-selinene,[2] the possible structure of cycloeudesmol is 1,1,2,2-tetrasubstituted cyclopropane derivative III, which is identical with the structure proposed by Kurosawa for isocycloeudesmol.[25] Actually the reported ^{1}H NMR spectrum of cycloeudesmol is in good accordance with that of isocycloeudesmol reported by Kurosawa[25] except the signal of a secondary methyl group. Although there was no description of the secondary methyl group in the literature reported by Fenical,[2] the chart of the ^{1}H NMR spectrum (220 MHz, in CCl_4) kindly provided by him showed the signal of a secondary methyl group at δ 1.02 partially obscured by the tertiary methyl signal at δ 1.00. From above mentioned observations we concluded that Fenical's "cycloeudesmol" and Kurosawa's "isocycloeudesmol" were the same compounds.[26] Kurosawa also noticed that they were the same compound by the comparisons of their spectral data, and finally he determined the stereochemistry of cycloeudesmol by X-ray crystallographic analysis as shown in structure IV (Chart IV).[27,28]

Experimental Section

All melting points were uncorrected. Mass spectra were recorded at 25 eV unless otherwise stated.

8aβ-Hydroxy-7α-isopropenyl-4aβ-methyl-1,4,4a,5,6,7,8,8a-octahydro-2(3*H*)-naphthalenone (2). To NaH (50% oil dispersion, 11.15 g, 0.232 mol) in freshly distilled anhydrous THF (194 mL) containing absolute ethanol (0.65 mL) was added (–)-dihydrocarvone (**1**, 36.64 g, 0.227 mmol). After refluxing under N_2 atmosphere for 6 h the mixture was cooled to –7 °C (ice–salt bath) and 4-chloro-2-butanone (25.94 g, 0.243 mol) was added dropwise with stirring during ca. 3 h. The temperature was maintained at 0 °C during the addition and for 1.5 h afterward. Aqueous acetic acid (20%, 3.3 mL) and water (33 mL) were added successively into the reaction mixture. The THF layer was separated from the resulting aqueous layer which was then extracted with ether. The combined organic layers were washed with a saturated NaCl aqueous solution (3 × 100 mL), dried (Na_2SO_4), and concentrated to give an oil, which was distilled under reduced pressure. The first fraction (bp 39 °C (0.1 torr)) gave recovered (–)-dihydrocarvone (11.85 g, 32%). The second fraction (bp 104–142 °C (0.07 torr)) gave a crystalline material (25.26 g), which was recrystallized from a mixture of ether (40 mL) and cyclohexane (30 mL) to give **2** (13.66 g, 38% based on unrecovered **1**): mp 105 °C (lit.[7] mp 105–106 °C); IR (KBr) 3540, 3060, 1700, 1640, 1272, 1200, 1150, 1122, 1058, 1025, 1002, 888, 875 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.20 (3 H, s), 1.70 (3 H, s), and 4.70 (2 H, m); $[\alpha]^{20}_D$ –43.0° (*c* 1.47, $CHCl_3$). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.57; H, 10.13.

7α-Acetyl-8aβ-hydroxy-4aβ-methyl-1,4,4a,5,6,7,8,8a-octahydro-2(3*H*)-naphthalenone (3). Ozone was bubbled into a solution of **2** (8.892 g, 40.0 mmol) in a mixture of methylene chloride (32 mL) and methanol (15 mL) at –70 °C until the solution became blue. The reaction mixture was poured into a

(25) Suzuki, T.; Kikuchi, H.; Kurosawa, E. *Chem. Lett.* **1980**, 1267.
(26) (a) The private communication to Kurosawa, E. dated Dec 12, 1980. (b) The private communications to Fenical, W. and Sims, J. J. dated Jan 8, 1981, and Jan 22, 1981.
(27) Suzuki, T.; Furusaki, A.; Kikuchi, H.; Kurosawa, E.; Katayama, C. *Tetrahedron Lett.* **1981**, *22*, 3423.
(28) Recently the total synthesis of (±)-IV has been reported: Chen, E. Y. *Tetrahedron Lett.* **1982**, *23*, 4769. We have also completed the total synthesis of (±)-IV by completely different procedures. The results will be reported in the near future.

mixture of NaI (15.2 g, 101 mmol), methanol (28 mL), and acetic acid (20 mL) at 0 °C (ice bath) and stirred for 15 min at this temperature and for 1.5 h at room temperature. The resulting dark brown solution was poured into the stirring 0.2 M $Na_2S_2O_3$ aqueous solution (320 mL) and extracted with ethyl acetate (3 × 40 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give spectroscopically pure **3** (8.063 g, 90%) as a crystalline material, which was recrystallized from a mixture of ethyl acetate and petroleum ether to give colorless needles: mp 145 °C (lit.[7] mp 142–143 °C); IR (KBr) 3400, 1710, 1680, 1288, 1222, 1148, 1124, 1055, 1042, 1002 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.21 (3 H, s), 2.14 (3 H, s); $[\alpha]^{20}_D$ −41.1° (*c* 1.60, $CHCl_3$). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.39; H, 8.68.

7β-Acetyl-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (4). A mixture of **3** (5.607 g, 25 mmol) and concentrated hydrochloric acid (9.65 mL) in acetic acid (200 mL) was allowed to stand at room temperature (16–19 °C) for 26 h under N_2, poured into a saturated NaCl aqueous solution (750 mL), and extracted with ether (5 × 150 mL). The combined extracts were washed succesively with a saturated $NaHCO_3$ aqueous solution (3 × 150 mL) and a saturated NaCl aqueous solution (3 × 150 mL), dried (Na_2SO_4), and concentrated to give spectroscopically pure **4** (4.475 g, 87%) as a crystalline material, which was recrystallized from ether to give colorless needles: mp 108–108.5 °C (lit.[7] mp 106–107 °C); IR (KBr) 3000, 1703, 1670, 1615, 1272, 1243, 1200, 1162 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.27 (3 H, s), 2.13 (3 H, s), and 5.67 (1 H, m); $[\alpha]^{20}_D$ +88.5° (*c* 1.80, $CHCl_3$). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.59; H, 8.76.

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (5). A solution of **4** (413 mg, 2.00 mmol), *p*-toluenesulfonic acid monohydrate (41 mg), and ethylene glycol (134 μL, 2.40 mmol) in anhydrous benzene (40 mL) was refluxed in the flask equipped with a Dean–Stark column packed with 4 Å molecular sieves for 4.5 h under N_2, cooled, and poured into a saturated NaCl aqueous solution (40 mL). The benzene layer was separated and the aqueous layer was further extracted with benzene (2 × 10 mL). The combined benzene layer was washed with a saturated NaCl aqueous solution (20 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (525 mg), which was ca. 8:1:1 mixture of the desired monoacetal (**5**), the starting material (**4**), and the undesired diacetal (**6**) from the analysis of the NMR spectrum. This crude material was employed in the following experiment for practical purposes.

This crude material was then chromatographed over silica gel (Merck, 70–230 mesh, 25 g) and eluted with chloroform to give spectroscopically pure **5** (395 mg, 79%) as an oil: IR ($CHCl_3$) 3040, 1660, 1615, 1085, 1070, 1038 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.25 (3 H, s), 1.30 (3 H, s), 3.98 (4 H, s), 5.83 (1 H, s).

7β-[1,1-(Ethylenedioxy)ethyl]-2β-hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (7). A solution of the crude acetal **5** (80% purity, 525 mg) in a mixture of anhydrous benzene (8 mL) and anhydrous THF (33 mL) was added dropwise to the mixture of $LiAl(t\text{-}BuO)_3H$ (0.94 g, 3.7 mmol) and anhydrous THF (13 mL). After completion of addition the mixture was refluxed for 4 h, cooled (0 °C), poured into the stirring aqueous solution of 2 M KOH (5 mL, 10 mmol) at 0 °C, and kept at this temperature for 1 h. The mixture was poured into a saturated NaCl aqueous solution (50 mL) and extracted with ether (3 × 30 mL). The combined extracts were washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oil (530 mg), which was chromatographed over silica gel (Merck, 70–230 mesh) and eluted with chloroform to give spectroscopically pure **7** (287 mg, 57% from **4**), which was recrystallized from petroleum ether to give needles: mp 93 °C; IR (KBr) 3460, 1655, 1135, 1126, 1095, 1070, 1040, 1028, 1008, 842, 812 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.11 (3 H, s), 1.26 (3 H, s), 3.92 (4 H, m), 4.15 (1 H, broad d, J = 9.0 Hz), 5.35 (1 H, m, $W_{h/2}$ = 5.0 Hz, $J_{1,2}$ = 2.0 Hz from decoupling experiment); $[\alpha]^{20}_D$ +29.0° (*c* 1.09, $CHCl_3$). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H 9.59. Found: C, 71.36; H, 9.56.

7β-[1,1-(Ethylenedioxy)ethyl]-2,2-(ethylenedioxy)-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (6). A solution of **4** (413 mg, 2.00 mmol), *p*-toluenesulfonic acid monohydrate (41 mg), and ethylene glycol (4 mL, 72 mmol) in anhydrous benzene (40 mL) was refluxed in the flask equipped with a Dean–Stark column packed with 4 Å molecular sieves for 8 h, cooled, and poured into a saturated NaCl aqueous solution (40 mL). The benzene layer was separated and the aqueous layer was further extracted with benzene (2 × 10 mL). The combined benzene layer was washed with a saturated NaCl aqueous solution (20 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (593 mg) as a crystalline material, which was recrystallized from ether to give **6** (295 mg, 50%) as prisms: mp 86 °C; IR (KBr) 2990, 1655, 1140, 1090, 1070, 1042, 1008, 858 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.12 (3 H, s), 1.27 (3 H, s), 4.02 (8 H, s), 5.48 (1 H, s); $[\alpha]^{20}_D$ +1.1° (*c* 1.65, $CHCl_3$). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.43; H, 9.04.

The Equilibrium Reaction of Diketone (4) and Diacetal (6). A mixture of **4** (206 mg, 1.00 mmol), **6** (294 mg, 1.00 mmol), and *p*-toluenesulfonic acid monohydrate (20 mg) in anhydrous benzene (40 mL) was refluxed in the flask equipped with a Dean-Stark column packed with 4 Å molecular sieves for 8 h under N_2 and treated in the same manner as the monoacetalization of **4** to give an oily material, which was ca. 8:1:1 mixture of **5**, **4**, and **6** from the analysis of the NMR spectrum.

7β-[1,1-(Ethylenedioxy)ethyl]-2β-hydroxy-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (9). Into a stirring mixture of zinc–copper couple (10.24 g, 157 mmol), I_2 (10 mg), and anhydrous ether (40 mL) was added a few drops of CH_2I_2 under N_2. The mixture was refluxed for a few minutes to initiate the reaction and then the oil bath was removed. Remaining CH_2I_2 (total volume 4.48 mL, 56 mmol) was added dropwise into the reaction mixture at room temperature (ca. 20 °C) in 30 min. The solution was kept refluxing gently during the addition of CH_2I_2. After completion of the addition of CH_2I_2, the mixture was kept at 30–35 °C (bath temperature) under stirring and refluxed gently for 1 h and cooled. **7** (252 mg, 1.00 mmol) in anhydrous DME (15 mL) was added into the mixture at room temperature (ca. 20 °C) and stirring was continued for 17 h at this temperature. The reaction mixture was filtered through Celite under reduced pressure and the residue was washed with ether (30 mL). The combined filtrates was washed successively with a saturated NH_4Cl aqueous solution (2 × 30 mL), a saturated $NaHCO_3$ solution (2 × 30 mL), and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 11 g) and eluted successively with a mixture of $CHCl_3$ and CCl_4 (1:1, 400 mL), $CHCl_3$ (300 mL), and ethyl acetate (80 mL). The fraction eluted with $CHCl_3$ gave **9** (207 mg, 78%) as a colorless oil: IR (neat) 3450, 3180, 1148, 1090, 1080, 1040 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.13 (1 H, dd, J = 4.8, 9.0 Hz), 0.63 (1 H, dd, J = 4.8, 4.8 Hz), 1.00 (3 H, s), 1.17 (C_{1a}–H from decoupling experiment), 1.21 (3 H, s), 3.89 (4 H, m), 4.33 (1 H, tt, J = 1.0, 5.0 Hz); $[\alpha]^{20}_D$ −31.5° (*c* 0.26, $CHCl_3$); MS, *m/e* (relative intensity) 266 (0.4, M^+), 251 (1.6), 248 (0.8), 233 (095), 204 (0.9), 171 (0.9), 147 (1.6), 134 (2.4), 132 (2.3), 107 (2.1), 89 (1.9), 88 (7.5), 87 (100, $CH_3\overset{\frown}{C{=}O^+CH_2CH_2O}$), 43 (5.8), 18 (2.3).

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-1,1aα,4,4a,5,6,7,8-octahydro-2(3*H*)-cyclopropa[*d*]naphthalenone (10). Chromic anhydride (299 mg, 2.99 mmol) was added to a mixture of anhydrous methylene chloride (25 mL) and anhydrous pyridine (537 μL, 6.65 mmol) at 0 °C and the mixture was stirred for 15 min. Then **9** (40 mg, 0.15 mmol) dissolved in anhydrous methylene chloride (15 mL) was added and the mixture was stirred at 0 °C for 6 h and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution (3 × 50 mL) and a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 4 g) and eluted successively with a mixture of $CHCl_3$ and CCl_4 (1:1) and $CHCl_3$. The fraction eluted with $CHCl_3$ gave **10** (34 mg, 86%) as a colorless oil: IR (CCl_4) 3190, 1685, 1235, 1145, 1085, 1040 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.65–1.04 (2 H, m) [0.81, 0.84 (1 H each, C_1–H) from decoupling experiment], 1.09 (3 H, s), 1.21 (3 H, s), 1.55 (C_{1a}–H, from decoupling experiment), 2.1–2.45 (2 H, m), 3.88 (4 H, m).

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (11). A mixture of **10** (56

mg, 0.21 mmol), 85% $NH_2NH_2 \cdot H_2O$ (133 μL, 2.26 mmol), KOH (167 mg, 3.00 mmol), and diethylene glycol (2 mL) was refluxed at 110–120 °C (bath temperature) for 1 h and at 180 °C (bath temperature) for 3 h under N_2, cooled, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ether (5 × 10 mL). The combined extracts were washed with a saturated NaCl aqueous solution (3 × 20 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (53 mg), which was chromatographed over silica gel (Merck, 70–230 mesh, 4 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give **11** (34 mg, 64%) as a colorless oil: IR (neat) 3050, 1250, 1140, 1085, 1035, 1005 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.08–0.28 (2 H, m), 0.55–0.95 (1 H, m), 0.99 (3 H, s), 1.22 (3 H, s), 3.90 (4 H, m); $[\alpha]^{20}_D$ +18.2° (*c* 0.14, $CHCl_3$); MS, *m/e* (relative intensity) 250 (0.5, M^+), 235 (1.0), 159 (1.2), 147 (1.1), 137 (4.6), 133 (1.6), 121 (1.0), 95 (1.5), 91 (1.1), 89 (1.9), 88 (7.5), 87 (100, $CH_3\overline{C{=}O^+CH_2CH_2O}$), 58 (1.4), 45 (1.6), 43 (12), 28 (6.2), 18 (1.7).

7β-Acetyl-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (12). A solution of **11** (34 mg, 0.14 mmol) in a mixture of ethanol (3 mL) and 20% aqueous acetic acid (3 mL) was refluxed for 2 h, cooled, poured into a saturated NaCl aqueous solution (40 mL), and extracted with ether (3 × 15 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (2 × 20 mL) and a saturated NaCl aqueous solution (2 × 20 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Kanto-Gel, 100 mesh) and eluted with a mixture of CCl_4 and $CHCl_3$ (1:1) to give **12** (25 mg, 89%) as a colorless oil: IR (CCl_4) 3050, 1710, 1252 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 0.08–0.95 (3 H, m), 1.02 (3 H, s), 2.10 (3 H, s); MS, *m/e* (relative intensity) 206 (49, M^+), 191 (28), 163 (98), 148 (24), 137 (20), 122 (27), 121 (43), 109 (38), 107 (70), 95 (53), 93 (54), 81 (100), 79 (21), 67 (42), 43 (61), 28 (83), 18 (41).

7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (Ia). Into an ether solution of methylmagnesium iodide [prepared from Mg powder (32 mg, 1.32 mmol) and methyl iodide (75 μL, 1.20 mmol) in anhydrous ether (5 mL)] was added **12** (25 mg, 0.12 mmol) in anhydrous ether (5 mL). The solution was stirred at room temperature for 2 h under N_2, poured into a saturated NH_4Cl aqueous solution (30 mL), and extracted with ether (3 × 15 mL). The combined extracts were washed successively with a 0.2 M $Na_2S_2O_3$ aqueous solution (25 mL), a saturated $NaHCO_3$ solution (25 mL), and a saturated NaCl aqueous solution (25 mL × 2), dried (Na_2SO_4), and concentrated to give a semisolidal crude product, which was chromatographed over silica gel (Wako C-200) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give spectroscopically pure Ia (27 mg, 100%). The product solidified on standing and was recrystallized from hexane to give colorless needles: mp 79 °C (lit.[6] mp 72.5–73.0 °C, 75 °C); IR ($CHCl_3$) 3600, 3050, 2930, 2860, 1470, 1440, 1385, 1375, 1320, 1260, 1150, 1080, 1005, 920, 905, 875 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.13 (1 H, dd, *J* = 4.5, 9.0 Hz), 0.20 (1 H, dd, *J* = 4.5, 4.5 Hz), 0.68 (1 H, m), 0.98 (3 H, s), 1.14 (3 H, s), 1.16 (3 H, s); NMR (CCl_4, 90 MHz) δ 0.07–0.26 (2 H, m), 0.60 (1 H, m), 1.00 (3 H, s), 1.13 (6 H, s); $[\alpha]^{20}_D$ +11.4° (*c* 0.43, $CHCl_3$); MS, *m/e* (relative intensity) 222 (4, M^+), 204 (28), 189 (19), 164 (34), 161 (38), 149 (56), 135 (20), 123 (25), 122 (26), 109 (22), 107 (22), 105 (42), 95 (22), 93 (24), 82 (18), 81 (24), 67 (17), 59 (100).

7α-Isopropenyl-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (13). A solution of **2** (1.556 g, 7.00 mmol) in a 10% KOH aqueous solution (35 mL) was heated (bath temperature 90–105 °C) for 7 h under N_2, cooled, poured into a saturated NaCl aqueous solution (40 mL), and extracted with ethyl acetate (3 × 40 mL). The combined extracts were washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Kanto-Gel, 100 mesh, 50 g) and eluted with chloroform to give **13** (1.341 g, 94%) as a crystalline material, which was recrystallized from pentane to give needles, mp 38 °C: IR (CCl_4) 3090, 1670, 1615, 1252, 1235, 892 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.27 (3 H, s), 1.73 (3 H, broad s), 2.55 (3 H, m), 4.78 (1 H, broad s), 4.85 (1 H, broad s), 5.67 (1 H, broad s); $[\alpha]^{20}_D$ +181.1° (*c* 0.99, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.11; H, 9.86.

7α-(1,2-Epoxy-1-methylethyl)-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (14). A solution of *m*-chloroperoxybenzoic acid (purity 85%, 1.360 g, 6.70 mmol) and **13** (1.341 g, 6.56 mmol) in anhydrous CH_2Cl_2 (30 mL) was allowed to stand at room temperature for 5 h. The mixture was poured into an aqueous KI solution and extracted with $CHCl_3$ (3 × 15 mL). The combined extracts were washed successively with a 0.2 M $Na_2S_2O_3$ aqueous solution, a saturated $NaHCO_3$ aqueous solution, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Kanto-Gel, 100 mesh, 50 g) and eluted with $CHCl_3$ to give **14** (1.250 g, 86%) as a mixture of stereoisomers of the epoxide ring. This was employed in the next step as a starting material.

In another experiment was obtained 480 mg of an oily crude product starting from 469 mg (2.30 mmol) of **13** by the analogous procedure mentioned above. This was subsequently separated by HPLC [10 μm silica gel (Kyowa gel MIC-SI-10), 30 cm × 10 mm i.d. column EtOAc–hexane (3:7), flow rate 3 mL/min].

The first peak gave an enol lactone **15** (48 mg, 9%) as a colorless oil: IR (neat) 3050, 1760, 1655 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.17 (3 H, s), 1.26 (3 H, s), 2.33 (1 H, d, *J* = 5.0 Hz), 2.63 (1 H, d, *J* = 5.0 Hz), 6.02 (1 H, m); $[\alpha]^{20}_D$ −58.0° (*c* 0.77, $CHCl_3$); MS (10 eV), *m/e* (relative intensity) 236 (M^+, 92), 218 (84), 208 (69), 207 (50), 205 (88), 191 (100), 178 (66), 162 (82), 107 (94).

The second peak gave the major stereoisomer of epoxide **14a** (198 mg, 39%), which was recrystallized from pentane to give plates: mp 58 °C; IR (KBr) 3080, 3060, 3040, 1676, 1622 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.23 (3 H, s), 1.24 (3 H, s), 2.62 (1 H, d, *J* = 4.0 Hz), 5.58 (1 H, m); $[\alpha]^{20}_D$ +118.2° (*c* 1.20, $CHCl_3$); MS (10 eV), *m/e* (relative intensity) 220 (47, M^+), 202 (98), 190 (76), 189 (71), 164 (55), 163 (100). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.21.

The third peak gave the minor stereoisomer of epoxide **14b** (64 mg, 13%), which was recrystallized from pentane to give plates: mp 70 °C; IR (KBr) 3060, 1675, 1630 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.23 (6 H, s), 2.56 (1 H, d, *J* = 4.4 Hz), 5.53 (1 H, m); $[\alpha]^{20}_D$ +106.1° (*c* 1.68, $CHCl_3$); MS (10 eV), *m/e* (relative intensity) 220 (17, M^+), 202 (44), 192 (35), 189 (27), 164 (41), 163 (100), 162 (61). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 75.82; H, 9.15.

7α-(1,2-Epoxy-1-methylethyl)-2β-hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (16). Into a solution of **14** (3:1 mixture of two stereoisomer, 1.25 g, 5.67 mmol) in methanol (15 mL) was added $NaBH_4$ (215 mg, 5.67 mmol) by portions. The mixture was allowed to stand at 0 °C for 5 h, poured into a saturated NaCl aqueous solution (100 mL), and extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed with a saturated NaCl aqueous solution, dried, and concentrated to give oily crude product, which was chromatographed over silica gel (Kanto-Gel, 100 mesh, 50 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give **16** (763 mg, 60%) as a colorless oil: IR (CCl_4) 3620, 3420, 3040 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.13 (3 H, s), 1.30 (3 H, s), 2.46 (1 H, d, *J* = 5.0 Hz), 2.70 (0.3 H, d, *J* = 5.0 Hz), 2.91 (0.7 H, d, *J* = 5.0 Hz), 4.19 (1 H, m, $J_{1,2}$ = 2.0 Hz from decoupling experiment), 5.33 (1 H, m).

In another experiment the major epoxide **14a** (50 mg) gave an oily crude product (53 mg) by the analogous procedure mentioned above. This was subsequently purified by the combination of TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9, R_f 0.19) and the pipe-to-pipe distillation to give **16a** (26 mg, 52%) as a colorless oil, bp 120 °C (0.05 mmHg). This was identical with the major component of the mixture of epoxide **16** above mentioned: $[\alpha]^{20}_D$ +38.7° (*c* 0.61, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 222 (1.0, M^+), 204 (12), 163 (30), 124 (100), 107 (10). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.00; H, 9.93.

7α-(1,2-Epoxy-1-methylethyl)-2β-hydroxy-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (17). Into a stirring mixture of zinc–copper couple (5.12 g, 78 mmol), I_2 (10 mg), anhydrous ether (25 mL), and anhydrous DME (4 mL) was added CH_2I_2 (1.12 mL, 14 mmol) under N_2. The mixture was refluxed for a few minutes to initiate the reaction. CH_2I_2 (1.12 mL, 14 mmol) was further added dropwise into the reaction mixture at room temperature (ca. 20 °C) in 30 min. The solution was kept refluxing gently during the addition of CH_2I_2. After completion

of the addition of CH_2I_2, the mixture was kept at 30–35 °C (bath temperature) under stirring and refluxed gently for 1 h and cooled. **16** (116 mg, 0.52 mmol) in anhydrous DME (4 mL) was added into the mixture at 10 °C (bath temperature) and continued stirring for 6 h at this temperature. The reaction mixture was filtered through Celite under reduced pressure and the residue was washed with ether (20 mL). The combined filtrates were washed successively with a saturated NH_4Cl aqueous solution (2 × 20 mL), a saturated $NaHCO_3$ solution (2 × 20 mL), and a saturated NaCl aqueous solution, dried (Na_2SO_4) and concentrated to give an oily crude product (140 mg), which was chromatographed over silica gel (Merck, 70–230 mesh, 7 g) and eluted successively with CCl_4 (150 mL) and $CHCl_3$ (200 mL). The fraction eluted with $CHCl_3$ gave **17** (80 mg, 65%) as needles: mp 69–70 °C; IR ($CHCl_3$) 3600, 3440, 3050 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.16 (1 H, dd, J = 5.0, 9.0 Hz), 0.56 (1 H, dd, J = 5.0, 5.0 Hz), 0.94 (3 H, s), *ca.* 1.1 (C_{1a}–H from decoupling experiment), 1.28 (3 H, s), 2.47 (0.7 H, d, J = 4.5 Hz), 2.52 (0.3 H, d, J = 4.5 Hz), 2.67 (1 H, broad d, J = 4.5 Hz), 4.16 (1 H, m) $[\alpha]^{20}_D$ +8.8° (*c* 0.13, $CHCl_3$); MS, *m/e* (relative intensity) 236 (0.4, M^+), 218 (23, $M^+ - H_2O$), 200 (20), 187 (23), 177 (24), 160 (55), 146 (45), 131 (40), 121 (31), 119 (38), 107 (48), 106 (36), 105 (73), 95 (31), 93 (50), 81 (100), 67 (31), 28 (34).

7α-(1,2-Epoxy-1-methylethyl)-4aβ-methyl-1,1aα,4,4a,5,6,7,8-octahydro-2(3*H*)-cyclopropa[*d*]naphthalenone (18). Chromic anhydride (197 mg, 1.97 mmol) was added into a mixture of anhydrous methylene chloride (20 mL) and anhydrous pyridine (354 μL, 4.39 mmol) at 0 °C and the mixture was stirred for 20 min. Then **17** (20 mg, 0.085 mmol) in anhydrous methylene chloride (10 mL) was added and the mixture was stirred stirred at 0 °C for 12 h and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution (3 × 30 mL) and a saturated NaCl aqueous solution (3 × 30 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 2 g) and eluted with chloroform to give **18** (19 mg, 96%) as a colorless oil: IR (CCl_4) 3040, 1690, 1252, 920, 892, 860, 838 cm^{-1}; NMR (CCl_4, 60 MHz) δ 0.5–1.0 (2 H, m), 1.12 (3 H, s), 1.27 (3 H, s), 2.33 (1 H, d, J = 5.0 Hz), 2.68 (1 H, d, J = 5.0 Hz).

7α-(1-Hydroxy-1-methylethyl)-2β-hydroxy-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (20). A solution of **17** (25 mg, 0.106 mmol) in anhydrous ether (1 mL) was added to the mixture of $LiAlH_4$ (30 mg, 0.79 mmol) and anhydrous ether (2 mL). The mixture was stirred for 7 h at 16 °C under N_2, poured into the mixture of a saturated NaCl aqueous solution (10 mL) and a 2 M NaOH aqueous solution (2 mL). The mixture was stirred for a few minutes and the ether layer was separated. The aqueous layer was further extracted with ethyl acetate (10 mL). The combined organic layer was washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give a crystalline crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 1.5 g) and eluted with chloroform to give spectroscopically pure **20** (25 mg, 99%) as a crystalline material. This was recrystallized from a mixture of ethyl acetate and hexane to give needles: mp 152 °C; IR (KBr) 3300, 3090, 3020, 1255, 1154, 1102, 1070, 1038, 1022, 1015, 1010, 932, 922, 890, 868, 800 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.22 (1 H, dd, J = 4.5, 8.5 Hz), 0.57 (1 H, dd, J = 4.5, 4.5 Hz), 0.94 (3 H, s), 1.03 (C_{1a}–H from decoupling experiment), 1.13 (3 H, s), 1.15 (3 H, s), 4.10 (1 H, ddd, J = 5.0, 5.0, 10.0 Hz); $[\alpha]^{20}_D$ +10.3° (*c* 0.73, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 220 (13, $M^+ - H_2O$), 205 (17), 202 (15), 187 (46), 177 (40), 162 (49), 159 (31), 150 (100), 149 (20), 146 (23), 138 (92), 124 (50).

7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1,1aα,4,4a,5,6,7,8-octahydro-2(3*H*)-cyclopropa[*d*]naphthalenone (21). Chromic anhydride (158 mg, 1.58 mmol) was added to a mixture of anhydrous methylene chloride (10 mL) and anhydrous pyridine (255 μL, 3.16 mmol) at 0 °C and the mixture was stirred for 15 min. Then **20** (13 mg, 0.055 mmol) dissolved in anhydrous methylene chloride (3 mL) was added and the mixture was stirred for 14 h at 0 °C and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution (3 × 15 mL) and a saturated NaCl aqueous solution (3 × 15 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 1 g) and eluted successively with a mixture of $CHCl_3$ and CCl_4 (1:1) and $CHCl_3$. The fraction eluted with $CHCl_3$ gave **21** (13 mg, 100%) as a colorless oil: IR (neat) 3450, 3190, 1680 cm^{-1}; NMR (CCl_4, 60 MHz) δ 0.57–0.92 (2 H, m), 1.12 (9 H, s).

7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aα-decahydrocyclopropa[*d*]naphthalene (Ib). A mixture **21** (13 mg, 0.055 mmol), 85% $NH_2NH_2 \cdot H_2O$ (38 μl, 0.65 mmol), KOH (38 mg, 0.68 mmol), and diethylene glycol (1 mL) was refluxed at 110–120 °C (bath temperature) for 1 h and at 180 °C (bath temperature) for 3 h under N_2, cooled, poured into a saturated NaCl aqueous solution (20 mL), and extracted with ethyl acetate (2 × 10 mL). The combined extracts were washed with a saturated aqueous solution (2 × 10 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 1 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give Ib (10 mg, 82%) as a colorless oil: IR (neat) 3400, 3070, 2980, 2940, 2860, 1468, 1368, 1260, 1140, 1105, 1030, 1010, 930, 920, 890, 860, 820, 790 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.10 (1 H, dd, J = 4.5, 9.0 Hz), 0.27 (1 H, dd, J = 4.5, 4.5 Hz), 0.75 (1 H, m), 0.94 (3 H, s), 1.16 (3 H, s), 1.17 (3 H, s); NMR (CCl_4, 90 MHz) δ 0.10 (1 H, dd, J = 4.5, 9.0 Hz), 0.25 (1 H, dd, J = 4.5, 4.5 Hz), 0.70 (1 H, m), 0.95 (3 H, s), 1.13 (6 H, s); $[\alpha]^{20}_D$ +35.6° (*c* 0.20, $CHCl_3$); MS, *m/e* (relative intensity) 222 (1, M^+), 205 (16), 204 (73), 189 (43), 162 (22), 161 (100), 150 (17), 149 (29), 147 (19), 135 (22), 133 (22), 123 (18), 122 (23), 121 (22), 120 (22), 119 (17), 109 (13), 108 (13), 107 (31), 106 (9), 105 (53), 95 (20), 93 (31), 91 (16), 81 (28), 79 (21), 67 (17), 59 (63).

7β-[1,1-(Ethylenedioxy)ethyl]-2β-acetoxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (22). A mixture of **7** (126 mg, 0.5 mmol), acetic anhydride (142 μL, 1.5 mmol), and anhydrous pyridine (526 μL, 6.5 mmol) was allowed to stand at room temperature for 23 h, poured into a saturated NaCl aqueous solution, and extracted with ethyl acetate (2 × 20 mL). The combined extracts were washed successively with 1 M HCl (2 × 25 mL), a saturated $NaHCO_3$ aqueous solution (2 × 25 mL), and a saturated NaCl aqueous solution (2 × 25 mL), dried (Na_2SO_4), and concentrated to give spectroscopically pure **22** (150 mg, 100%), which was recrystallized from hexane to give scales: mp 76 °C; IR (KBr) 1728, 1665, 1232, 1142, 1042, 1010, 852 cm^{-1}; NMR (CCl_4, 60 MHz), δ 1.12 (3 H, s), 1.18 (3 H, s), 1.96 (3 H, s), 3.86 (4 H, s), 5.14 (1 H, broad d, J = 6.0 Hz), 5.28 (1 H, m); $[\alpha]^{20}_D$ −34.7° (*c* 0.87, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 294 (0.05, M^+), 279 (1.7), 234 (4.7), 232 (1.7), 190 (3.8), 172 (1.4), 87 (100, $CH_3\overline{C{=}O^+CH_2CH_2O}$). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.47; H, 8.94.

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (23). Lithium (11 mg, 1.59 mmol) was added to dry liquid ammonia (25 mL) at −78 °C and stirred for 10 min at this temperature and then the solution of **22** (60 mg, 0.20 mmol) in ether (5 mL) was added to the mixture. The deep blue solution was efficiently stirred at −78 °C for 1.5 h. Ammonium chloride (100 mg) was cautiously added to discharge the color. Ammonia was evaporated at room temperature and the residue was dissolved in a mixture of ether (15 mL) and water (15 mL). The organic layer was separated and the aqueous layer was extracted with ether (2 × 15 mL). The combined organic layer was washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product (62 mg), which was chromatographed over silica gel (Kanto-Gel, 100 mesh, 3 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1). The first fraction gave **23** (27 mg, 56%) as a crystalline material: IR (KBr) 1230, 1185, 1140, 1125, 1089, 1055, 860, 800 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.03 (3 H, s), 1.18 (3 H, s), 3.83 (4 H, s), 5.30 (1 H, m).

The second band gave **7** (23 mg, 44%).

7β-Acetyl-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (25). A solution of **23** (20 mg, 0.085 mmol) in a mixture of ethanol (3 mL) and 10% aqueous acetic acid (3 mL) was refluxed for 1.5 h, cooled, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give spectroscopically pure **25** (16.3 mg, 100%) as a colorless oil: IR (neat) 1710, 800 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.00 (3 H, s), 2.00 (3 H, s), 5.28 (1 H, m).

7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (26). Into an ether solution of methylmagnesium iodide [prepared from Mg powder (32 mg, 1.32 mmol) and methyl iodide (75 μL, 1.20 mmol) in anhydrous ether (3 mL)] was added **25** (18 mg, 0.094 mmol) in anhydrous ether (3 mL). The solution was stirred at room temperature for 2 h under N_2, poured into a saturated NH_4Cl aqueous solution (30 mL), and extracted with ethyl acetate (2 × 15 mL). The combined extracts were washed successively with 0.2 M $Na_2S_2O_3$ aqueous solution (25 mL), a saturated $NaHCO_3$ solution (25 mL), and a saturated NaCl aqueous solution (2 × 25 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Wako, C-200) and eluted with CCl_4 and a mixture of CCl_4 and $CHCl_3$ (1:1). The fraction eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) gave **26** (17 mg, 87%) as a colorless oil: IR (neat 3400, 1660, 1250, 1135, 1118, 1095, 1075, 1005, 800 cm^{-1}; NMR (CCl_4, 60 MHz) δ 0.97 (3 H, s), 1.06 (6 H, s), 5.21 (1 H, m).

2α-(Benzoyloxy)-7β-[1,1-(ethylenedioxy)ethyl]-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (27). Into a mixture of **7** (106 mg, 0.42 mmol), triphenylphosphine (220 mg, 0.84 mmol), and benzoic acid (102 mg, 0.84 mmol) in anhydrous THF (15 mL) was added 95% diethyl azodicarboxylate (139 μL, 0.84 mmol) in THF (5 mL) at room temperature. The mixture was stirred for 17 h at room temperature, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (15 mL) and a saturated NaCl aqueous solution (15 mL), dried (Na_2SO_4), and concentrated to give crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 5 g) and eluted with CCl_4 to give **27** (146 mg, 98%) as a pale yellow oil: IR (eat) 3080, 1715, 1605, 1589, 1265, 1215, 1105, 1065, 1040, 1020, 952, 870, 802, 780, 710 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.08 (3 H, s), 1.28 (3 H, s), 3.93 (4 H, s), 5.30–5.70 (2 H, m), 7.4–7.7 (3 H, m), 8.0–8.2 (2 H, m); $[\alpha]^{20}_D$ +122.1° (*c* 0.27, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 356 (0.1, M^+), 294 (0.9), 234 (2.5), 122 (100), 87 (12.9). Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13, H, 7.92. Found: C, 73.77; H, 7.77.

7β-[1,1-(Ethylenedioxy)ethyl]-2α-hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (28). A mixture of **27** (431 mg, 1.21 mmol), methanol (15 mL), and a 2 M KOH aqueous solution (15 mL) was stirred at 40 °C for 30 h under N_2, poured into a saturated NaCl aqueous solution (50 mL), and extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed with a saturated NaCl aqueous solution (30 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 20 g) and eluted with chloroform to give **28** (235 mg, 77%). This was recrystallized from hexane to give needles: mp 111 °C; IR (KBr) 3350, 3050, 1655, 1212, 1185, 1160, 1145, 1118, 1102, 1090, 1065, 1032, 998, 985, 860 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.03 (3 H, s), 1.27 (3 H, s), 3.93 (4 H, s), 4.13 (1 H, m), 5.53 (1 H, d, *J* = 4.0 Hz); $[\alpha]^{20}_D$ +81.0° (*c* 0.38, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 252 (0.01, M^+), 237 (1.1), 234 (1.3), 190 (1.6), 124 (3.0), 87 (100, $CH_3\overset{\frown}{C{=}C^+CH_2CH_2O}$). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39, H, 9.59. Found: C, 71.69; H, 9.63.

7β-[1,1-(Ethylenedioxy)ethyl]-2α-hydroxy-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (29). Into a stirring mixture of zinc–copper couple (2.56 g, 39 mmol), I_2 (5 mg), anhydrous ether (20 mL), and anhydrous DME (3 mL) was added CH_2I_2 (0.56 mL, 7 mmol) under H_2. The mixture was refluxed for a few minutes to initiate the reaction. CH_2I_2 (0.56 mL, 7.0 mmol) was further added dropwise into the reaction mixture at room temperature (17 °C) in 15 min. The solution was kept refluxing gently during the addition of CH_2I_2. After completion of the addition of CH_2I_2, the mixture was kept at 35–38 °C (bath temperature) under stirring, refluxed gently for 30 min, and cooled. **28** (66 mg, 0.26 mmol) in anhydrous DME (3 mL) was added into the mixture at room temperature and continued stirring for 17 h at room temperature. The reaction mixture was filtered through Celite under reduced pressure and the residue was washed with ether (10 mL). The combined filtrates were washed successively with a saturated NH_4Cl aqueous solution (2 × 10 mL), a saturated $NaHCO_3$ solution (2 × 10 mL), and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 3.5 g) and eluted succesively with CCl_4 and $CHCl_3$. The fraction eluted with $CHCl_3$ gave **29** (59 mg, 85%) as a colorless oil: IR (neat) 3400, 3060, 1112, 1034 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 0.17 (1 H, dd, *J* = 5.0, 9.0 Hz), 0.77 (2 H, m), 1.06 (3 H, s), 1.28 (3 H, s), 3.93 (4 H, s), 4.37 (1 H, m, $W_{h/2}$ = 10 Hz); MS, *m/e* 266 (M^+).

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-1,1aβ,4,4a,5,6,7,8-octahydro-2(3*H*)-cyclopropa[*d*]naphthalenone (30). Chromic anhydride (897 mg, 8.97 mmol) was added to a mixture of anhydrous methylene chloride (20 mL) and anhydrous pyridine (1.45 mL, 17.96 mmol) at 0 °C and the mixture was stirred for 15 min. Then **29** (110 mg, 0.41 mmol) dissolved in anhydrous methylene chloride (3 mL) was added and the mixture was stirred at 0 °C for 6 h and filtered through Celite under reduced pressure. The filtrate was washed succesively with a saturated $NaHCO_3$ aqueous solution (3 × 30 mL), 2 M HCl (2 × 30 mL), and a saturated NaCl aqueous solution (3 × 30 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 6 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give **30** (62 mg, 57%) as a colorless oil: IR (neat) 3090, 1680, 1230, 1145, 1090, 1040 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 0.63–1.00 (2 H, m), 1.07 (3 H, s), 1.24 (3 H, s), 3.90 (4 H, s); MS, *m/e* 264 (M^+).

7β-[1,1-(Ethylenedioxy)ethyl]-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (24). A mixture of **30** (30 mg, 0.113 mmol), 85% $NH_2NH_2{\cdot}H_2O$ (133 μl, 2.26 mmol), KOH (167 mg, 3.00 mmol), and diethylene glycol (2 mL) was refluxed at 110–120 °C (bath temperature) for 1 h and at 180 °C (bath temperature) for 3 h under N_2, cooled, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed with a saturated NaCl aqueous solution (3 × 20 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 2 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:1) to give **24** (15 mg, 53%) as a colorless oil: IR (neat) 3080, 1245, 1220, 1150, 1100, 1045 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 0–1.0 (3 H, m), 1.13 (3 H, s), 1.27 (3 H, s), 3.94 (4 H, s).

7β-Acetyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (31). A solution of **24** (15 mg, 0.06 mmol) in a mixture of ethanol (3 mL) and 20% aqueous acetic acid (3 mL) was refluxed for 2 h, cooled, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (2 × 20 mL) and a saturated NaCl aqueous solution (2 × 20 mL), dried (Na_2SO_4), and concentrated to give **31** (12.4 mg, 100%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 0–1.00 (3 H, m), 1.14 (3 H, s), 2.15 (3 H, s); $[\alpha]^{20}_D$ 0.0° (*c* 0.03, $CHCl_3$); MS (13.5 eV), *m/e* (relative intensity) 206 (59, M^+), 191 (100), 163 (75).

7β-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Ic). Into an ether solution of methylmagnesium iodide [prepared from Mg powder (32 mg, 1.32 mmol) and methyl iodide (75 μL, 1.20 mmol) in anhydrous ether (5 mL)] was added **31** (10 mg, 0.05 mmol) in anhydrous ether (5 mL). The solution was stirred at room temperature for 2 h under N_2, poured into a saturated NH_4Cl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed successively with 0.2 M $Na_2S_2O_3$ aqueous solution (25 mL), a saturated $NaHCO_3$ solution (25 mL), and a saturated NaCl aqueous solution (2 × 25 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh) and eluted with CCl_4 and a mixture of CCl_4 and $CHCl_3$ (1:1). The latter fraction gave Ic (9 mg, 84%) as a crystalline material (mp 39–41 °C), which was recrystallized from pentane to give needles: mp 52 °C; IR (neat) 3400, 3070, 2980, 2930, 2860, 1465, 1452, 1435, 1395, 1368, 1352, 1275, 1250, 1190, 1160, 1132, 1108, 1098, 1090, 1078, 1040, 1018, 1008, 932, 898, 870, 852, 812, 795, 765, 755, 700 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.02 (1 H, dd, *J* = 4.5, 9.0 Hz), 0.39 (1 H, ddd, *J* = 2.0, 4.5, 4.5 Hz), 0.73 (1 H, m), 1.07 (3 H, s), 1.14 (3 H, s), 1.15 (3 H, s); NMR (CCl_4, 90 MHz) δ 0.05 (1 H, dd, *J* = 4.5, 9.0 Hz), 0.40 (1 H, ddd, *J* = 1.5, 4.5, 4.5 Hz), 0.73 (1 H, m), 1.10 (3 H, s), 1.13 (6 H, s); $[\alpha]^{20}_D$ +49.9° (*c* 0.57, $CHCl_3$); MS,

m/e (relative intensity) 222 (4, M^+), 204 (38), 189 (20), 164 (22), 161 (47), 149 (47), 135 (18), 133 (13), 123 (25), 122 (29), 121 (14), 119 (12), 109 (43), 105 (32), 95 (20), 93 (20), 81 (26), 82 (26), 67 (19), 59 (100).

2α-(Benzoyloxy)-7α-isopropenyl-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (33). Into a mixture of **32** (92 mg, 0.44 mmol), triphenylphosphine (236 mg, 0.90 mmol), and benzoic acid (110 mg, 0.90 mmol) in anhydrous THF (15 mL) was added 95% diethyl azodicarboxylate (149 μL, 0.90 mmol) in anhydrous THF (5 mL) at room temperature. The mixture was stirred for 19 h at room temperature, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (15 mL) and a saturated NaCl aqueous solution (15 mL), dried (Na_2SO_4), and concentrated to give crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 5 g) and eluted with CCl_4 to give **33** (117 mg, 85%) as a pale yellow oil: IR (neat) 3090, 1715, 1605, 1589, 1260, 1105, 1088, 1062, 1020, 888, 705 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.11 (3 H, s), 1.70 (3 H, s), 4.82 (1 H, broad s), 4.90 (1 H, broad s), 5.43 (1 H, m), 5.58 (1 H, d, *J* = 5.0 Hz), 7.37–7.60 (3 H, m), 7.9–8.2 (2 H, m).

2α-Hydroxy-7α-isopropenyl-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (34). A mixture of **33** (149 mg, 0.48 mmol), methanol (5 mL), and a 2 M KOH aqueous solution (5 mL) was stirred at 40 °C for 30 h under N_2, poured into a saturated NaCl aqueous solution (20 mL), and extracted with ethyl acetate (3 × 10 mL). The combined extracts were washed with a saturated NaCl aqueous solution (15 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 8 g) and eluted with $CHCl_3$ to give **34** (84 mg, 85%) as a colorless oil: IR (neat) 3350, 3100, 1035, 1022, 985, 888, 868, 848; NMR ($CDCl_3$, 60 MHz) δ 1.07 (3 H, s), 1.72 (3 H, s), 4.09 (1 H, m, $W_{h/2}$ = 14 Hz), 4.89 (2 H, s), 5.53 (1 H, d, *J* = 4.0 Hz).

7α-(1,2-Epoxy-1-methylethyl)-2α-hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (37). Into a mixture of **16** (407 mg, 1.83 mmol), triphenylphosphine (960 mg, 3.66 mmol), benzoic acid (447 mg, 3.66 mmol), and anhydrous THF (40 mL) was added 95% diethyl azodicarboxylate (607 μL, 3.66 mmol) in anhydrous THF (8 mL) at room temperature. The mixture was stirred for 19 h at room temperature and then treated in the usual manner to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 30 g) and eluted with CCl_4 to give **36** (538 mg, 90%) as pale yellow oil.

A mixture of **36** (538 mg, 1.65 mmol), methanol (20 mL), and a 2 M K_2CO_3 aqueous solution (20 mL) was stirred at 70 °C for 1.5 h under N_2, poured into a saturated NaCl aqueous solution (20 mL), and extracted with ethyl acetate (4 × 30 mL). The combined extracts were treated as usual to give an oily crude product, which was chromatographed over silica gel (Merck, finer than 230 mesh, 30 g) and eluted with $CHCl_3$ to give **37** (156 mg, 38% from **16**) as a colorless oil: IR (neat) 3425, 1250, 1055, 1030, 984, 900, 882, 860, 840, 770 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.05 (3 H, s), 1.33 (3 H, s), 2.47 (1 H, d, *J* = 4.5 Hz), 2.94 (1 H, d, *J* = 4.5 Hz), 4.07 (1 H, m, $W_{h/2}$ = 10 Hz), 4.67 (1 H, d, *J* = 4.0 Hz); MS, *m/e* (relative intensity) 222 (3, M^+), 204 (50, $M^+ - H_2O$), 163 (60), 147 (100), 146 (37), 131 (47), 124 (43), 108 (34), 107 (34), 105 (59), 93 (37), 91 (79), 81 (43), 79 (44), 67 (37), 55 (30), 43 (34), 41 (31).

Ether Derivative 41 from 37. A mixture of **37** (47 mg, 0.21 mmol) and $LiAlH_4$ (100 mg, 2.64 mmol) in anhydrous ether (5 mL) was stirred at 0 °C for 4 h and then treated as usual to give the crude diol **39**, which was chromatographed over silica gel (Merck, finer than 230 mesh, 2 g) and eluted with $CHCl_3$ to give **41** (40 mg, 92%) as an oily material.

All the compounds shown in the following experimental details are racemic. The nomenclature and the indication of the stereochemistry of these compounds are based on one of enantiomers for the convenience of expression.

2β,5β-Diacetoxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (48). A mixture of **47** (900 mg, 4.94 mmol), acetic anhydride (1.42 mL, 15.0 mmol), and pyridine (5.26 mL, 65.0 mmol) was allowed to stand at room temperature for 12 h and then worked up as usual to give spectroscopically pure **48** (1.292 g, 98%) as a colorless crystalline material, which was recrystallized from a mixture of ether and hexane (1:1) to give colorless prisms: mp 75 °C; IR (KBr) 3025, 1736, 1670, 1235, 1025, 855 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.17 (3 H, s), 2.04 (6 H, s), 4.53 (1 H, dd, *J* = 4.5, 10.5 Hz), 5.22 (1 H, m), 5.38 (1 H, m). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.71; H, 8.49.

5β-Hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (49). Lithium (1.00 g, 144 mmol) was added to a mixture of **48** (3.154 g, 11.84 mmol), anhydrous ether (8 mL), and dry liquid ammonia (60 mL) in the flask equipped with a dry ice condenser at −70 °C while stirring. The deep blue solution was efficiently stirred at −78 °C for 1.5 h. Ammonium chloride (3.0 g) was cautiously added to discharge the color. Ammonia was evaporated at room temperature and the residue was dissolved in a mixture of ethyl acetate (50 mL) and a saturated NaCl aqueous solution (50 mL). The organic layer was separated and the aqueous layer was furthe extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed successively with a saturated NH_4Cl aqueous solution (2 × 30 mL) and a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 150 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:2) to give **49** (1.436 g, 73%) as a colorless oil: IR ($CHCl_3$) 3610, 3425, 1660, 1028, 988, 930, 863 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.02 (3 H, s), 3.34 (1 H, dd, *J* = 4.5, 10.5 Hz), 5.44 (1 H, broad t, *J* = 3.0 Hz); MS, *m/e* (relative intensity) 166 (M^+, 25), 148 ($M^+ - H_2O$, 90), 133 (39), 122 (48), 109 (50), 107 (27), 95 (25), 93 (27), 91 (30), 81 (25), 79 (23), 67 (27), 28 (66), 18 (100), 17 (41).

The fractions eluted with ethyl acetate gave **47** (324 mg, 15%). The yield of **49** based on recovered **47** is 86%.

4aβ-Methyl-2,3,4,4a,7,8-hexahydro-5(6*H*)-naphthalenone (52). A mixture of **49** (1.276 g, 7.68 mmol) and pyridinium chlorochromate (2.484 g, 11.50 mmol) in anhydrous CH_2Cl_2 (70 mL) was stirred at 0 °C for 12 h and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution (2 × 50 mL), a 1 M HCl aqueous solution (2 × 50 mL), a saturated $NaHCO_3$ aqueous solution (2 × 50 mL), and a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was chromatographed over silica gel (Merck, 70–230 mesh, 60 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:3) to give **52** (1.121 g, 89%) as a colorless oil: IR ($CHCl_3$) 1702, 1660, 860 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.30 (3 H, s), 5.48 (1 H, ddd, *J* = 1.5, 4.2, 4.2 Hz); MS, *m/e* (relative intensity) 164 (M^+, 85), 149 (39), 121 (56), 108 (25), 93 (67), 79 (38), 28 (100), 18 (58).

5α-Hydroxy-4aβ-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene (51). To a 1 M THF solution of lithium tri-*sec*-butylborohydride (4.50 mL, 4.50 mmol) was added **52** (364 mg, 2.22 mmol) in anhydrous THF (5 mL) at −78 °C. After the mixture was stirred at −78 °C for 2 h, a 2 M KOH aqueous solution (5 mL) and 30% H_2O_2 (5 mL) were successively added into the mixture dropwise at −74 to −65 °C under stirring. The mixture was stirred at this temperature for 30 min, then warmed to room temperature, poured into a mixture of a saturated NaCl aqueous solution (40 mL) and a 20% K_2CO_3 aqueous solution (30 mL), and extracted with ethyl acetate (5 × 50 mL). The combined extracts were washed with a saturated NaCl aqueous solution (4 × 50 mL), dried (Na_2SO_4), and concentrated to give a 1:3 mixture of **49** and **51** (360 mg) as a crystalline material, which was subsequently chromatographed over silica gel (Merck, 70–23 mesh, 20 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:5) to give spectroscopically pure **51** (265 mg, 72%) as a crystalline material. This was recrystallized from a mixture of ether and hexane (1:1) to give colorless needles: mp 59 °C; IR (KBr) 3380, 1660, 1062, 1050, 1000, 989, 965, 883, 873, 862, 808, 715 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.11 (3 H, s), 3.45 (1 H, m, $W_{h/2}$ = 13.0 Hz), 5.57 (1 H, m). Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.19; H, 10.75.

The fractions eluted with a mixture of $CHCl_3$ and CCl_4 (1:2–1:3) gave **49** (89 mg, 24%).

The yield of **51** based on recovered **49** is 97%.

5α-Hydroxy-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]-naphthalene (53). To a stirred mixture of zinc–copper couple (7.264 g, 111.0 mmol), I_2 (15 mg), anhydrous ether (60 mL), and anhydrous DME (2.27 mL) was added CH_2I_2 (4.15 mL, 51.5 mmol). The mixture was refluxed for a few minutes to initiate

the reaction. CH_2I_2 (4.15 mL, 51.5 mmol) was further added dropwise into the reaction mixture at room temperature in 30 min. The solution was kept refluxing gently during the addition of CH_2I_2. After completion of the addition of CH_2I_2, the mixture was kept at 30–35 °C (bath temperature) with stirring and refluxing gently for 1 h and cooled. **51** (664 mg, 3.99 mmol) in anhydrous DME (11.3 mL) was added into the mixture at 10 °C (bath temperature) and continued stirring for 1 h at this temperature. The reaction mixture was filtered through Celite under reduced pressure and the residue was washed with ether (30 mL). The combined filtrates were washed successively with a saturated NH_4Cl aqueous solution (2 × 50 mL), a saturated $NaHCO_3$ aqueous solution (2 × 50 mL), a 1 M $Na_2S_2O_3$ aqueous solution (2 × 50 mL), and a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give oily crude product, which was chromatographed over silica gel (Merck, 200 mesh, 40 g) and eluted with a mixture of $CHCl_3$ and CCl_4 (1:9) to give **53** (450 mg, 62%) as a colorless oil: NMR ($CDCl_3$, 200 MHz) δ 0.27 (1 H, dd, J = 5.0, 10.5 Hz), 0.60 (2 H, m), 1.14 (3 H, s), 3.38 (1 H, m, $W_{h/2}$ = 6.0 Hz); MS, m/e (relative intensity) 180 (M^+, 3), 162 (100), 147 (48), 133 (29), 119 (28), 111 (50), 109 (21), 107 (25), 106 (23), 105 (25), 95 (39), 94 (22), 93 (34), 91 (22), 82 (50), 81 (58), 67 (50), 55 (24).

4aβ-Methyl-1aβ-octahydro-5(6*H*)-cyclopropa[*d*]naphthalenone (54). A mixture of **53** (360 mg, 2.00 mmol) and pyridinium chlorochromate (885 mg, 4.11 mmol) in anhydrous CH_2Cl_2 (40 mL) was stirred at 0 °C for 1 h and at room temperature for 6 h. The mixture was filtered through Celite under reduced pressure and the residue was washed with $CHCl_3$ (40 mL). The combined filtrates were worked up as usual to give oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.61 gave spectroscopically pure **54** (252 mg, 71%): IR ($CHCl_3$) 1680 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.16 (1 H, dd, J = 4.5, 9.0 Hz), 0.37 (1 H, ddd, J = 2.0, 4.5, 4.5 Hz), 0.92 (1 H, m), 1.40 (3 H, s); MS, m/e (relative intensity) 178 (M^+, 30), 137 (100), 135 (40), 107 (54), 97 (48), 95 (65), 94 (43), 93 (81), 91 (35), 82 (43), 81 (54), 79 (70), 77 (30), 67 (76), 55 (30), 41 (32), 28 (56), 18 (73).

5β-Hydroxy-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (55). To a stirred solution of **54** (20 mg, 0.112 mmol) in methanol (10 mL) was added $NaBH_4$ (40 mg, 1.06 mmol) by portions. The mixture was stirred at 0 °C for 4 h and then worked up as usual to give oily crude **55**, which does not contain **53** judging from the analysis of NMR spectrum. The crude **55** was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$) to give spectroscopically pure **55** (16 mg, 80%) as a colorless oil: NMR (CCl_4, 90 MHz) δ 0.07 (1 H, dd, J = 4.5, 9.0 Hz), 0.44 (1 H, ddd, J = 2.0, 4.5, 4.5 Hz), 0.74 (1 H, m), 1.09 (3 H, s), 3.37 (1 H, dd, J = 5.3, 10.0 Hz).

6α-Bromo-4aβ-methyl-1aβ-octahydro-5(6*H*)-cyclopropa[*d*]naphthalenone (56). To a stirred solution of **54** (205 mg, 1.15 mmol) in anhydrous THF (5 mL) was added phenyltrimethylammonium perbromide (PTAB) (432 mg, 1.15 mmol) at 0 °C. The mixture was stirred at 0–10 °C for 30 min, poured into a mixture of a saturated $NaHCO_3$ aqueous solution (20 mL), 1 M $Na_2S_2O_3$ aqueous solution (20 mL), and a saturated NaCl aqueous solution (20 mL), and extracted with ethyl acetate (5 × 20 mL). The combined extracts were washed successively with a saturated NaCl aqueous solution (3 × 30 mL), dried (Na_2SO_4), and concentrated to give a crude oily product (320 mg), which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.63 gave **56** (261 mg, 88%) as a pale yellow oil: IR ($CHCl_3$) 1715 cm^{-1}; NMR (CCl_4, 60 MHz) δ 0.18 (1 H, dd, J = 4.5, 9.0 Hz), 0.45 (1 H, dd, J = 2.0, 4.5, 4.5 Hz), 0.95 (1 H, m), 1.36 (3 H, s), 5.05 (1 H, dd, J = 6.0, 12.0 Hz).

4aβ-Methyl-1,1aβ,2,3,4,4a-hexahydro-5(8*H*)-cyclopropa[*d*]naphthalenone (57). A mixture of **56** (230 mg, 0.89 mmol), Li_2CO_3 (888 mg, 12.0 mmol), and LiBr (992 mg, 11.5 mmol) in anhydrous DMF (5 mL) was stirred at 110–120 °C (bath temperature) for 4 h, cooled, and poured into a mixture of a saturated NaCl aqueous solution (30 mL), a saturated $NaHCO_3$ aqueous solution (30 mL), and a 1 M $Na_2S_2O_3$ aqueous solution (10 mL) and extracted with ethyl acetate (5 × 30 mL). The combined extracts were washed successively with a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.55 gave spectroscopically pure **57** (123 mg, 78%): IR ($CHCl_3$) 1670 cm^{-1}; NMR (CCl_4, 90 MHz) δ 0.23 (1 H, dd, J = 5.0, 9.0 Hz), 0.43 (1 H, ddd, J = 1.5, 5.0, 5.0 Hz), 0.92 (1 H, m), 1.29 (3 H, s), 2.86 (1 H, broad d, J = 19.0 Hz, $C_{8\beta}$–H), 5.85 (1 H, ddd, J = 1.5, 3.0, 10.0 Hz), 6.72 (1 H, ddd J = 2.0, 5.5, 10.0 Hz), (from decoupling experiment, $J_{8\alpha H,8\beta H}$ = 19.0 Hz, $J_{8\beta H,6H}$ = 3.0 Hz, $J_{8\beta H,7H}$ = 2.0 Hz, $J_{8\beta H,1H_{endo}}$ = 1.5 Hz, $J_{8\alpha H,6H}$ = 1.5 Hz, $J_{8\alpha H,7H}$ = 5.5 Hz); MS, m/e (relative intensity) 176 (M^+, 20), 135 (100), 133 (34), 105 (34), 95 (84), 91 (80), 79 (67), 55 (52), 28 (74).

7α-Isopropenyl-4aβ-methyl-1aβ-octahydro-5(6*H*)-cyclopropa[*d*]naphthalenone (58). To a stirred mixture of anhydrous DME (2 mL) and a 2.10 M pentane solution of t-BuLi (5.20 mL, 10.92 mmol) at −78 °C was added 2-bromopropene (692 mg, 5.72 mmol) in anhydrous THF (2 mL). Subsequently CuI (494 mg, 2.59 mmol) was added at −70 °C and the mixture was stirred at −70 °C for 30 min. The color of the solution was turned dark brown. **57** (89 mg, 0.505 mmol) in anhydrous DME (5 mL) was added into the mixture and stirred for 4 h. During this period the reaction temperature was gradually raised from −70 to 0 °C. The mixture was poured into a saturated NH_4Cl aqueous solution (50 mL) and extracted with ethyl acetate (5 × 30 mL). The combined extracts were washed successively with a saturated NH_4Cl aqueous solution (2 × 50 mL), a saturated $NaHCO_3$ aqueous solution (2 × 50 mL), and a saturated NaCl aqueous solution (3 × 50 mL), dried (Na_2SO_4), and concentrated to give a pale yellow oil, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.60 gave **58** (90 mg, 82%): IR ($CHCl_3$) 1705 cm^{-1}; NMR (CCl_4, 90 MHz) δ 0.27 (1 H, dd, J = 5.0, 90 Hz), 0.41 (1 H, ddd, J = 1.5, 5.0, 5.0 Hz), 0.80 (1 H, m), 1.30 (3 H, s), 1.69 (3 H, s), 4.69 (2 H, broad s); MS, m/e (relative intensity) 218 (M^+, 45), 203 (15), 190 (20), 177 (100), 176 (53), 161 (30), 147 (30), 137 (50), 133 (33), 122 (38), 121 (37), 109 (55), 108 (32), 107 (80), 105 (34), 95 (60), 94 (38), 93 (98), 91 (50), 82 (53), 81 (55), 79 (73), 67 (61), 55 (30).

7α-Acetyl-4aβ-methyl-1aβ-octahydro-5(6*H*)-cyclopropa[*d*]naphthalenone (59). Ozone was bubbled into a solution of **58** (40 mg, 0.183 mmol) in a mixture of CH_2Cl_2 (15 mL) and methanol (6 mL) at −70 °C untill the solution became blue. Subsequently dry oxygen was bubbled into the solution to release excess ozone from the reaction mixture. The reaction mixture was poured into a mixture of NaI (1 g) in methanol (20 mL) and stirred at 0 °C for 2 h. The resulting dark brown solution was poured into the stirred 0.2 M $Na_2S_2O_3$ aqueous solution (25 mL) and extracted with ether (5 × 20 mL). The combined extracts were washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give spectroscopically pure **59** (40 mg, 99%) as a colorless oil: IR ($CHCl_3$) 1705 cm^{-1}; NMR (CCl_4, 60 MHz) δ 0.20–0.58 (2 H, m), ca. 1.0 (1 H, m), 1.28 (3 H, s), 2.11 (3 H, s); MS, m/e (relative intensity) 220 (M^+, 34), 205 (30), 179 (34), 177 (60), 161 (40), 160 (62), 159 (71), 145 (31), 122 (39), 107 (85), 105 (35), 95 (38), 93 (94), 91 (33), 67 (59), 55 (35), 43 (83).

7β-Acetyl-4aβ-methyl-1aβ-octahydro-5(6*H*)-cyclopropa[*d*]naphthalenone (60). A mixture of **59** (20 mg, 0.09 mmol), a 2 M KOH aqueous solution (10 mL), and methanol (10 mL) was stirred at room temperature (0–20 °C) for 15 h and worked up as usual to give an oily material, which was separated by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$–EtOAc, 9:1). The first band (R_f 0.51) gave **60** (14 mg, 70%) as a colorless oil: IR ($CHCl_3$) 1700 cm^{-1}; NMR (CCl_4, 90 MHz) δ 0.22 (1 H, dd, J = 5.0, 9.0 Hz), 0.46 (1 H, ddd, J = 2.0, 5.0, 5.0 Hz), 0.90 (1 H, m), 1.39 (3 H, s), 2.10 (3 H, s); MS, m/e (relative intensity) 220 (M^+, 46), 205 (19), 179 (58), 177 (44), 139 (42), 137 (25), 123 (24), 122 (35), 121 (21), 119 (26), 107 (59), 105 (27), 95 (41), 94 (29), 93 (61), 82 (53), 81 (100), 79 (41), 67 (49), 55 (22), 43 (83), 41 (22).

The second band (R_f 0.43) gave **59** (5 mg, 25%).

7α-Isopropenyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (61). A mixture of **58** (59 mg, 0.27 mmol), 85% $NH_2NH_2·H_2O$ (190 μL, 3.23 mmol), KOH (238 mg, 4.24 mmol), and diethylene glycol (3 mL) was heated at 80–110 °C (bath temperature) for 30 min, then refluxed for 3 h at 200 °C (bath temperature), cooled, poured into a saturated NaCl aqueous solution (50 mL), and extracted with ethyl acetate (4 × 15 mL). The combined extracts were washed with a saturated NaCl aqueous solution (3 × 40 mL), dried (Na_2SO_4), and concentrated to give an oily crude product, which was separated by TLC (Merck,

silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The first band (R_f 0.68) gave **61** (11 mg, 20%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 0.0–0.85 (3 H, m), 1.13 (3 H, s), 1.73 (3 H, broad s), 4.76 (1 H, m), 4.83 (1 H, m).

The second band (R_f 0.409) gave **58** (5 mg, 8%).

7α-(1,2-Epoxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (62). A solution of **61** (15 mg, 0.073 mmol) and *m*-chloroperoxybenzoic acid (purity 85%, 20 mg, 0.099 mmol) in anhydrous CH_2Cl_2 (8 mL) was allowed to stand at room temperature for 3 h. The mixture was poured into a 1 M KI aqueous solution (50 mL) and extracted with $CHCl_3$ (4 × 15 mL). The combined extracts were washed successively with a 0.2 M $Na_2S_2O_3$ aqueous solution (30 mL), a saturated $NaHCO_3$ aqueous solution (2 × 30 mL), and a saturated NaCl aqueous solution (3 × 30 mL), dried (Na_2SO_4), and concentrated to give **62** (12 mg, 74%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 1.06 (3 H, s), 1.19 (3 H, s), 2.37 (1 H, d, J = 5.0 Hz), 2.72 (1 H, d, J = 5.0 Hz).

7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Id). To a stirred solution of **62** (12 mg, 0.05 mmol) in anhydrous ether at 0 °C was added $LiAlH_4$ (50 mg, 1.32 mmol). The mixture was stirred at 0 °C for 1.5 h, poured into a mixture of a saturated NaCl aqueous solution (50 mL) and ice, and extracted with ethyl acetate (4 × 20 mL). The combined extracts were washed with a saturated NaCl aqueous solution (4 × 50 mL), dried (Na_2SO_4), and concentrated to give oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.26 gave Id (6 mg, 50%) as a colorless oil: IR ($CHCl_3$) 3580, 3420 cm^{-1}; NMR (CCl_4, 90 MHz) δ 0.20 (1 H, dd, J = 4.5, 9.0 Hz), 0.46 (1 H, ddd, J = 2.0, 4.5, 4.5 Hz), 0.67 (1 H, m), 1.16 (6 H, s), 1.18 (3 H, s); NMR ($CDCl_3$, 200 MHz) δ 0.208 (1 H, dd, J = 4.5, 9.0 Hz), 0.475 (1 H, J = 1.8 4.5, 4.5 Hz), *ca.* 0.70 (1 H, m), 1.172 (3 H, s), 1.182 (6 H, s); MS, *m/e* (relative intensity) 222 (M^+, 0.5), 204 (54), 189 (27), 162 (23), 161 (100), 149 (45), 135 (25), 133 (18), 123 (28), 122 (34), 121 (21), 119 (16), 109 (45), 108 (18), 107 (38), 105 (45), 95 (23), 93 (39), 91 (14), 82 (37), 81 (43), 79 (21), 67 (32), 59 (95).

7α-Acetyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (63). Ozone was bubbled into a solution of **61** (7 mg, 0.03 mmol) in a mixture of CH_2Cl_2 (15 mL) and methanol (10 mL) at −70 °C untill the solution became blue. The reaction mixture was worked up as usual and purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$) to give **63** (5 mg, 71%) as a colorless oil: NMR (CCl_4, 60 MHz) δ 0–0.67 (3 H, m), 1.12 (3 H, s), 2.08 (3 H, s).

7β-Acetyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (31). A mixture of **63** (5 mg, 0.024 mmol), a 2 M KOH aqueous solution (10 mL), and methanol (10 mL) was stirred for 24 h at room temperature and worked up as usual to give oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$) to give **31** (4 mg, 80%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 0–1.0 (3 H, m), 1.14 (3 H, s), 2.15 (3 H, s); MS (13.5 eV), *m/e* (relative intensity) 206 (M^+, 59), 191 (100), 163 (75).

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Registry No. 1, 619-02-3; 2, 4895-25-4; 3, 4895-26-5; 4, 4895-27-6; 5, 93860-75-4; 6, 93782-42-4; 7, 93860-76-5; 8, 93782-43-5; 9, 93860-77-6; 10, 93860-78-7; 11, 93782-44-6; 12, 93860-79-8; 13, 93860-80-1; 14 (isomer 1), 93860-81-2; 14 (isomer 2), 93860-82-3; 15 (isomer 1), 93782-45-7; 15 (isomer 2), 93860-83-4; 16 (isomer 1), 70037-13-7; 16 (isomer 2), 70052-22-1; 17 (isomer 1), 93860-84-5; 17 (isomer 2), 93860-85-6; 18 (isomer 1), 93782-46-8; 18 (isomer 2), 93860-86-7; 20, 93860-87-8; 21, 93782-47-9; 22, 93782-48-0; 23, 93782-49-1; 24, 93860-88-9; 25, 93782-50-4; 26, 4895-29-8; 27, 93860-89-0; 28, 93860-90-3; 29, 93860-91-4; 30, 93860-92-5; 31, 76548-22-6; 32, 93860-93-6; 33, 93782-51-5; 34, 93860-94-7; 36 (isomer 1), 93782-52-6; 36 (isomer 2), 93860-95-8; 37 (isomer 1), 93860-96-9; 37 (isomer 2), 93860-97-0; 41, 93860-98-1; 47, 65083-11-6; 48, 93860-99-2; 49, 93861-00-8; 51, 93861-01-9; 52, 93861-02-0; 53, 93861-03-1; 54, 93861-04-2; 55, 93861-05-3; 56, 93861-06-4; 57, 93861-07-5; 58, 93861-08-6; 59, 93782-53-7; 60, 93861-09-7; 61, 93861-10-0; 62 (isomer 1), 93782-54-8; 62 (isomer 2), 93861-11-1; 63, 93861-12-2; Ia, 71962-31-7; Ib, 93860-74-3; Ic, 76548-19-1; (±)-Id, 78781-34-7; III, 75744-72-8; IV, 53823-06-6; 4-chloro-2-butanone, 6322-49-2; $(CH_2{=}C(CH_3))_2CuLi$, 21329-14-6.

Notes

Kinetic Investigation of the Staphylococcal Protease Catalyzed Hydrolysis of Glutamyl Analogues: γ-Methyleneglutamic and γ-Carboxyglutamic Acid

Randal A. Hoke, Jude Holmes, Jr.,[1] and Richard G. Hiskey*

The W. R. Kenan, Jr. Laboratories of Chemistry, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27514

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As characterized by Drapeau,[2] the extracellular serine protease isolated from *Staphylococcus aureus* strain V8 was shown to cleave specifically on the carboxyl side of either aspartyl or glutamyl linkages. Ensnouf and Prowse[3] found that the *S. aureus* protease did not cleave γ-carboxyglutamyl (Gla) bonds at an appreciable rate. This finding was later confirmed by Marsh,[4] who was able to isolate the Gla containing region (1–39) of the coagulation protein prothrombin by cleavage with *S. aureus* protease.

Recently, we described a procedure for the chemical modification of Gla residues in peptides[5] and proteins.[6] This conversion of Gla to γ-methyleneglutamyl (γ-mGlu) has been performed on the fragment-1 region (1–156) of prothrombin. Between two and eight out of a possible ten Gla residues have been shown to modify under various reaction conditions. Since γ-methyleneglutamic acid is

(1) Undergraduate research student.
(2) Drapeau, G. R.; Boily, Y.; Houmard, J. *J. Biol. Chem.* **1972**, *247*, 6720–6726.
(3) Esnouf, M. P.; Prowse, C. V. *Biochim. Biophys. Acta* **1977**, *490*, 471–476.
(4) Marsh, H. C.; Sarasua, M. M.; Mader, D. A.; Hiskey, R. G.; Koehler, K. A. *J. Biol. Chem.* **1981**, *256*, 7863–7870.
(5) Boggs, N. T., III; Bruton, H. D.; Craig, D. H.; Helpern, J. A.; Marsh, H. C.; Pegram, M. D.; Vandenbergh, D. J.; Koehler, K. A.; Hiskey, R. G. *J. Org. Chem.* **1982**, *47*, 1812–1816.
(6) Wright, S. F.; Bourne, C. D.; Hoke, R. A.; Koehler, K. A.; Hiskey, R. G. *Anal. Biochem.* **1984**, *139*, 82–90.

0022-3263/85/1950-0264$01.50/0