to substrate. Reaction volumes were 5 mL organic, 1 mL aqueous.

Samples of 0.1 mL were withdrawn at appropriate time intervals and added to 0.1 mL of dilute HCl and 0.5 mL of toluene. The upper phase was injected onto a capillary GC column. Each reaction profile was constructed from 5–8 samples. Conversions were derived from the ratio of starting material to *o*-dichlorobenzene as internal standard. Results were reproducible to ±5%. Phenethyl alcohol formation was negligible.

Kinetics. This reaction deviates from first order at high conversion due to catalyst decomposition.[12] We have chosen to fit first-order curves up to the point of significant deviation. For reactions at high catalyst concentration this is up to about 80% while for others it may be as low as 30%. Evaluation by initial rate procedures yields essentially the same results and conclusions.

The phase diagram was constructed by equilibrating about 90 compositions for 5 days at 44 °C (±0.2) in a thermostated water bath. Each composition was placed in a tube identical to those used for reactions, sealed additionally with Parafilm, checked against loss in weight, and the number of phases recorded.

Photomicrographs were obtained on a Nikkon microscope system equipped with crossed polars at 100 or 400× magnification.

Registry No. NaOH, 1310-73-2; phenethyl bromide, 103-63-9; tetrapropylammonium bromide, 1941-30-6; tetrabutylammonium bromide, 1643-19-2; tetrapentylammonium bromide, 866-97-7; hexylammonium bromide, 4328-13-6; styrene, 100-42-5.

Synthesis of All Stereoisomers of Eudesm-11-en-4-ol. 1. Stereospecific Synthesis of the Trans- and Cis-Fused Octahydro-8-hydroxy-4a,8-dimethyl-2(1*H*)-naphthalenones. Conformational Analysis of the Cis-Fused Compounds

Ronald P. W. Kesselmans, Joannes B. P. A. Wijnberg,* and Aede de Groot*

Laboratory of Organic Chemistry, Agricultural University, Dreyenplein 8, 6703 HB Wageningen, The Netherlands

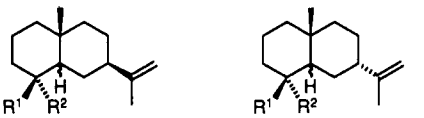
Nanne K. de Vries

DSM Research, P.O. Box 18, 6160 MD Geleen, The Netherlands

Received May 29, 1991

An efficient method has been developed for the synthesis of the octahydro-8-hydroxy-4a,8-dimethyl-2-(1*H*)-naphthalenones **9a–d**, which are suitable intermediates in the total synthesis of trans- and cis-fused 1-hydroxyeudesmane sesquiterpenes. Starting from the trans-fused dione **7** the corresponding hydroxy ketones **9a** and **b** could be easily prepared. The cis-fused hydroxy ketones **9c** and **d** were synthesized starting from the dione **8**. Protection of the C(7) carbonyl function of **8** as its dimethyl acetal followed by treatment with CH_3Li gave the hydroxy ketone **9c**. On the other hand, protection of the C(7) carbonyl function of **8** as its ethylene acetal and subsequent treatment with CH_3MgI afforded the hydroxy ketone **9d** as the main product. NMR studies revealed that **9c** exists predominantly in the steroid conformation and that **9d** exists exclusively in the nonsteroid conformation.

Examinations of the defensive secretion of termite soldiers of a number of genera have revealed the presence of several eudesmane alcohols. The cis-fused amiteol (**1**) is the major compound of the secretion of *Amitermes excellens*.[1] The trans-fused eudesmane sesquiterpenes, intermedeol (**2**) and neointermedeol (**3**), have been isolated from the secretion of *Velocitermes velox*[2] and *Subulitermes bailey*,[3] respectively. The latter compounds have also been found in several plant species,[4] just as another trans-fused stereoisomer, selin-11-en-4α-ol (**4**).[5] The existing confusion around the structure elucidation of these eudesmanes,[6-11] the poor availability of physical and spectral data, and their interesting biological activities[1,2,4b] have initiated a synthetic program at our laboratory leading to all possible stereoisomers of these eudesmane alcohols (Figure 1).



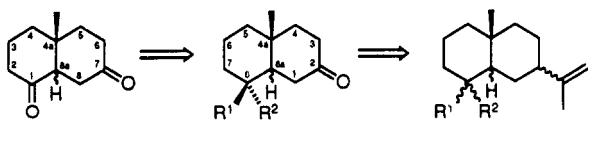
1 : β H; $R^1 = CH_3$; R^2 = OH **2** : α H; $R^1 = CH_3$; R^2 = OH
3 : α H; R^1 = OH; $R^2 = CH_3$ **5** : α H; R^1 = OH; $R^2 = CH_3$
4 : α H; $R^1 = CH_3$; R^2 = OH **6** : β H; R^1 = OH; $R^2 = CH_3$

Figure 1.

(1) Naya, Y.; Prestwich, G. D.; Spanton, S. G. *Tetrahedron Lett.* **1982**, *23*, 3047.
(2) Valterova, I.; Krecek, J.; Vrkoc, J. *Acta Entomol. Bohemoslov.* **1988**, *85*, 241.
(3) Prestwich, G. D.; Collins, M. S. *Biochem. System. Ecol.* **1981**, *9*, 83.
(4) For example, see: (a) Zalkow, V. B.; Shaligram, A. M.; Zalkow, L H. *Chem. Ind.* **1964**, 194. (b) Pinder, A. R.; Kerr, S. K. *Phytochemistry* **1980**, *19*, 1871.
(5) For example, see: (a) Corbett, R. E.; Smith, R. A. J. *Tetrahedron Lett.* **1967**, 1009. (b) Matsuo, A.; Ishii, O.; Suzuki, M.; Nakayama, M.; Hayashi, S. *Z. Naturforsch., B* **1982**, *37b*, 1636.
(6) Zalkow, L. H.; Zalkow, V. B.; Brannon, D. R. *Chem. Ind.* **1963**, 38.
(7) Chetty, G. L.; Zalkow, V. B.; Zalkow, L. H. *Tetrahedron Lett.* **1968**, 3223.
(8) Thappa, R. K.; Dhar, K. L.; Atal, C. K. *Phytochemistry* **1979**, *18*, 671.
(9) Huffman, J. W.; Pinder, A. R. *Ibid.* **1980**, *19*, 2468.
(10) Sulser, H.; Scherer, J. R.; Stevens, K. L. *J. Org. Chem.* **1971**, *36*, 2422.
(11) (a) Huffman, J. W.; Zalkow, L. H. *Tetrahedron Lett.* **1973**, 751. (b) Huffman, J. W.; Miller, C. A.; Pinder, A. R. *J. Org. Chem.* **1976**, *41*, 3705.

0022-3263/91/1956-7232$02.50/0

Scheme I

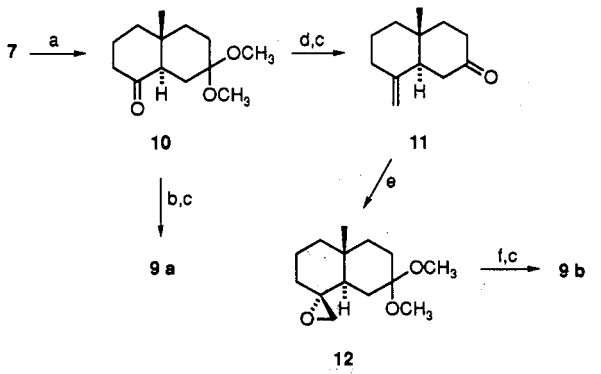


7 : α H
8 : β H

9 a : α H; R¹ = OH; R² = CH₃
9 b : α H; R¹ = CH₃; R² = OH
9 c : β H; R¹ = OH; R² = CH₃
9 d : β H; R¹ = CH₃; R² = OH

R¹, R² = CH₃, OH

Scheme II[a]



[a] Key: (a) $(CH_3O)_3CH$, *p*-TsOH, CH_2Cl_2; (b) CH_3MgI, ether; (c) HCl, acetone, H_2O; (d) $Ph_3P{=}CH_2$, DMSO; (e) $(CH_3O)_3CH$, *p*-TsOH, CH_3OH, then MMPP; (f) $LiAlH_4$, THF.

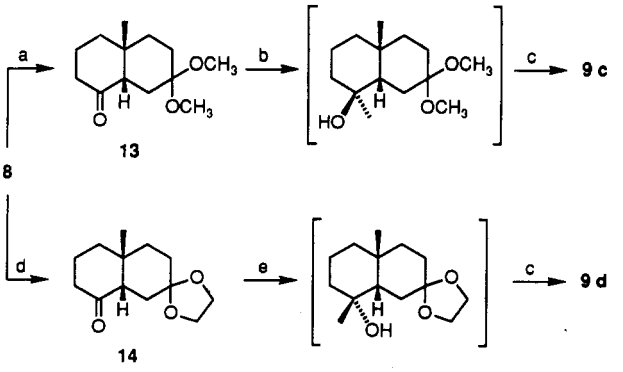
Until now the syntheses of **2**,[11b,12] **3**,[13] the unnatural paradisiol (**5**),[11b] and the cis-fused stereoisomer **6**[14] have been reported. Since a general and effective method for the selective synthesis of the trans- and cis-fused diones (**7** and **8**, respectively) had been developed by us,[15,16] it was obvious and challenging to use these diones as key intermediates in our synthetic approach to these stereoisomeric sesquiterpene alcohols (Scheme I).

In this paper, we describe the conversion of the diones **7** and **8** into the corresponding hydroxy ketones **9a,b** and **9c,d**, respectively. The stereochemistry and conformational analysis of the cis-fused hydroxy ketones **9c** and **9d** were determined by high-field NMR spectroscopy in combination with molecular mechanics calculations.

The carbonyl function at C(7) of the trans-fused dione **7** could be selectively protected with trimethyl orthoformate in the presence of *p*-TsOH at room temperature in CH_2Cl_2 as a solvent to give the trans-fused dimethyl acetal **10**.[16,17] Treatment of **10** with CH_3MgI and subsequent hydrolysis of the acetal function afforded the β-hydroxy ketone **9a** in 80% yield as the sole product (Scheme II). It is obvious that steric hindrance of the angular methyl group at C(4a) prevents a β-attack of the Grignard reagent.

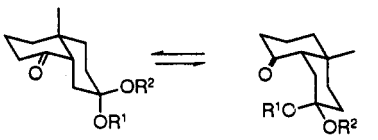
For the synthesis of the α-hydroxy ketone **9b** the trans-fused dimethyl acetal **10** was treated with $Ph_3P{=}CH_2$ in DMSO. Isolation of a pure product was only possible after hydrolysis of the acetal function and in this way the olefinic ketone **11** was obtained.[18] A solution of **11** in CH_3OH was treated with MMPP in the presence of trimethyl orthoformate and a catalytic amount of acid to prevent a Baeyer–Villiger oxidation. The so-obtained crude epoxy acetal **12** was reduced with $LiAlH_4$, and after hydrolysis of the acetal function **9b** was isolated in an overall yield of 69%.

Scheme III[a]



[a] Key: (a) $(CH_3O)_3CH$, *p*-TsOH, CH_2Cl_2; (b) CH_3Li, THF, −78 °C; (c) HCl, acetone, H_2O; (d) MED, *p*-TsOH, CH_2Cl_2; (e) CH_3MgI, ether.

Chart I



A (steroid) B (nonsteroid)

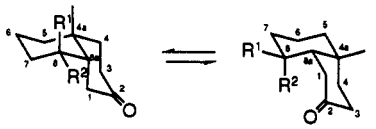
13 : $R^1 = R^2 = CH_3$
14 : $R^1 + R^2 = CH_2 - CH_2$

The cis-fused dione **8** could be selectively protected with trimethyl orthoformate or 2-butanone dioxolane (MED) to afford **13** or **14**, respectively. When the *dimethyl* acetal **13** was treated with CH_3MgI in ether as a solvent at room temperature, no addition products could be detected. Only partial epimerization at C(8a) was observed. Probably, the carbonyl group in **13** was converted into its enolate which upon hydrolysis gave the original ketone **13** together with its 8a-epimer **10**. On the other hand, treatment of **13** with CH_3Li in THF as a solvent at −78 °C, under which conditions enolization is much less important,[19] followed by hydrolysis of the acetal function afforded exclusively the cis-fused β-hydroxy ketone **9c** in 81% yield (Scheme III). Treatment of the *ethylene* acetal **14** with CH_3Li in ether at room temperature gave a 3:1 mixture of **9c** and **9d**, respectively. An almost complete reversal of the stereochemistry at C(8) was observed when **14** was treated with CH_3MgI in ether at room temperature. Hydrolysis of the ethylene acetal function gave the cis-fused α-hydroxy ketone **9d** in 78% yield together with a small quantity (10%) of **9c**.

In order to explain these results, we assume that the conformational equilibrium **A** (steroid) ⇌ **B** (nonsteroid), as depicted in Chart I, plays an important role in the selectivity of the addition reaction to **13** and **14**. The more bulky dimethyl acetal group in **13** forces this compound into its steroid conformation **13A**. The ethylene acetal

(12) Zalkow, L. H.; Smith, M.; Chetty, G. L.; Shaligram, A. W.; Ingwalson, P. *Ibid.* **1976**, *41*, 3710.
(13) (a) Mackenzie, B. D.; Angelo, M. M.; Wolinsky, J. *Ibid.* **1979**, *44*, 4042. (b) Kawamata, T.; Harimaya, K.; Inayama, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3770.
(14) Baker, R.; Organ, A. J.; Walmsley, S. A.; Webster, M.; Galas, A. M. R. *J. Chem. Res., Miniprint* **1984**, 1401.
(15) (a) Wijnberg, J. B. P. A.; Vader, J.; de Groot, Ae. *J. Org. Chem.* **1983**, *48*, 4380. (b) Wijnberg, J. B. P. A.; Jongedijk, G.; de Groot, Ae. *Ibid.* **1985**, *50*, 2650.
(16) Wijnberg, J. B. P. A.; Kesselmans, R. P. W.; de Groot, Ae. *Tetrahedron Lett.* **1986**, *27*, 2415.
(17) The trans-fused dimethyl acetal **10** could also be prepared in high yield from a mixture of **7** and **8**.[15a]
(18) The olefinic ketone **11** could also be prepared in good yield from a mixture of **10** and **13**.[15a]
(19) Buhler, J. D. *J. Org. Chem.* **1973**, *38*, 904.

Chart II



A (steroid) B (nonsteroid)

9c : $R^1 = OH$, $R^2 = CH_3$
9d : $R^1 = CH_3$, $R^2 = OH$

Table I. ^1H NMR Data (400 MHz) for Compounds 9c and 9d[a]

proton on carbon no.[b]	9c[c]	9d[c]	9d[d]
1	2.45, dd	2.51, m	2.67, dd (J = 1.8, 15.8 Hz)
	2.36, dd		2.36, dd (J = 6.6, 15.8 Hz)
3	2.36, m	2.42, m	2.62, m (J = 1.9, 5.7, 15.5 Hz)
		2.30, m	2.39, m (J = 7.3, 13.0, 15.5 Hz)
4	1.90, m, H_{ax}	2.65, m, H_{ax}	2.94, m, H_{ax}
	1.45, m, H_{eq}	1.25, m, H_{eq}	1.16, m, H_{eq}
5[e]	1.6, m	1.57, m	1.52, m
	1.2, m	1.35, m	1.20, m
6	1.65, m, H_{ax}	1.80, m, H_{ax}	2.03, m, H_{ax}
	1.45, m, H_{eq}	1.35, m, H_{eq}	1.39, m, H_{eq}
7[e]	1.60, m	1.57, m	1.52, m
	1.35, m	1.35, m	1.20, m
8a	1.72, dd	1.53, dd	1.26, dd (J = 1.8, 6.6 Hz)
CH_3(4a)	1.10, s	1.17, s	1.05, s[e]
CH_3(8)	1.25, s	1.22 s	1.06, s[e]
OH	*f*	0.87, br s	0.76, br s

[a] Chemical shifts in ppm relative to the $CDCl_3$ singlet (δ 7.23) or C_6D_6 singlet (δ 7.40). [b] See Chart II. [c] Recorded in $CDCl_3$. [d] Recorded in C_6D_6. [e] Assignments for these protons are interchangeable. [f] Obscured by other resonances.

group in **14** exerts a lesser destabilizing effect on the nonsteroid conformation **14B**, as a result of which **14** can exist as the equilibrium mixture **14A** ⇌ **14B** at room temperature.[20] The selective formation of **9c**, starting from **13**, must arise from an α attack of CH_3Li on the steroid conformer **13A**. This result indicates that the methyl group at C(4a) controls the approach to the carbonyl group. Similar arguments can be used for the predominant formation of **9c** starting from **14**. Treatment of **13** with CH_3MgI in ether at room temperature does not give any addition products, which leads to the conclusion that the carbonyl function in **13A** is too sterically hindered for reaction with the lesser nucleophilic and more bulky CH_3MgI. The observation that the cis-fused ethylene acetal **14** upon treatment with CH_3MgI under the same circumstances gives preferably the formation of **9d** indicates that the addition of CH_3MgI must proceed from the β face of the nonsteroid conformer **14B**.[21]

For the structure elucidation of the cis-fused hydroxy ketones **9c** and **9d** two issues were important. Firstly, the configuration of the methyl and hydroxy group around C(8) had to be established. Secondly, since most *cis*-decalins are conformationally mobile,[23] the conformation of **9c** and **9d** had to be determined (**A** (steroid) or **B** (nonsteroid), see Chart II). In order to solve these problems, the relevant ^1H and ^{13}C resonances of **9c** and **9d** were assigned using 1-D and 2-D NMR methods. Thus, ^1H assignments were established via ^1H–^1H COSY measurements. The results are listed in Table I.

Table II. ^{13}C NMR Data (100 MHz) for Compounds 9c and 9d in $CDCl_3$[a]

carbon no.[b]	9c[c]	9d[c]	9c (major)[d]	9c (minor)[d]
1	39.3	38.0		
2	212.9	213.0		
3	37.1	37.4		
4	36.1	32.1		
4a	33.3	32.5		
5[e]	35.4	39.8		
6	18.8	17.3	19.2	17.9
7[e]	38.8	40.8		
8	73.0	71.9		
8a	52.5	51.8	52.5	51.4
CH_3(4a)	29.3	29.0		
CH_3(8)	26.9	30.4	23.6	30.5

[a] Chemical shifts in ppm relative to the $CDCl_3$ triplet at δ 77.0. [b] See Chart II. [c] At 298 K. [d] At 221 K. [e] Assignments are interchangeable.

In principle, the conformation of **9c** and **9d** can be determined from the coupling constants $J_{H(1ax)H(8a)}$ and $J_{H(1eq)H(8a)}$, that is, if these compounds have one rigid conformation. As can be seen in Table I, even at 400 MHz no coupling constant could be determined due to chemical shift equivalency of H(1) and H(3), except for **9d** in C_6D_6. From these coupling constants, it can be estimated that **9d** must possess the nonsteroid conformation **B** since the steroid conformation **A** requires a 180° angle between H(8a) and H(1ax). This would result in a coupling constant of at least 9 Hz, whereas the largest coupling constant measured is 6.6 Hz.

The nonsteroid conformation **B** for **9d** is supported by three other facts: (i) Low-temperature ^{13}C measurements show that this compound exists essentially in one conformation (vide infra), which is a prerequisite for conformational analysis by coupling constants. (ii) A NOE-effect between H(4ax) and H(6ax) was observed, which is only possible in the nonsteroid conformation. (iii) Molecular mechanics calculations of the conformational equilibrium [**A** ⇌ **B**], using the consistent valence force field,[24] showed a free energy difference of 4.3 kcal/mol for **9d** (**9d(B)** being the more stable conformer), and 0.9 kcal/mol for **9c** in favor of **9c(A)** as the stable conformer. In terms of conformational equilibria this means that the population of **9d(B)** is reduced to less than 0.1%, rendering it essentially unobservable by ^{13}C NMR. The population of **9c(A)** is approximately 80–90% depending upon the accuracy of the calculations.

The results of the calculations are supported by ^{13}C NMR measurements. The assignments were established by 2-D NMR ^1H–^{13}C chemical shift correlation measurements, and the results are listed in Table II. Comparison of the data in Table II with those for two similar compounds (which only lack the hydroxy group at C(8)) shows a good overall agreement.[25] As expected, the measurements at lower temperatures (298 K down to 221 K) showed that the spectrum of **9d** was essentially temperature independent, whereas for **9c** exchange phenomena were observed. At 221 K, a major and minor form were seen (approximately 4:1). Comparison of the chemical

(20) (a) According to molecular mechanics calculation **13A** is 1.0 kcal more stable then **13B**, while **14A** is only 0.1 kcal more stable then **14B**.[20b] (b) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127.

(21) Treatment of **14** with CH_3Li and MgI_2 in ether at room temperature afforded a 1:3 mixture of **9c** and **9d**, respectively. This result indicates that either the reaction of **14** with in situ generated CH_3MgI has taken place[22a] or that MgI_2 coordinates **14** to the nonsteroid conformation (**14B**).[22b]

(22) (a) Wakefield, B. J. *Organolithium Methods*; Academic Press Limited: London, 1988, 159. (b) Tamura, Y.; Annoura, H.; Fujioka, H. *Tetrahedron Lett.* **1987**, *28*, 5681.

(23) Browne, L. M.; Klinck, R. E.; Stothers, J. B. *Org. Magn. Reson.* **1979**, *12*, 561.

(24) Lifson, S.; Hagler, A. T.; Dauber, P. *J. Am. Chem. Soc.* **1979**, *101*, 5111.

(25) Caine, D.; Smith, T. L. *J. Org. Chem.* **1978**, *43*, 755.

shifts of the minor form with those for **9d** shows that it has the nonsteroid conformation. Thus, **9c** preferentially adopts the steroid conformation **A**, in accordance with the calculations.

This left only the configuration around C(8) to be established. This was accomplished by NOE-difference measurements with multiple irradiation.[26] Since **9c** is in conformational equilibrium at room temperature, NOE data for this compound are hard to interpret because it would remain uncertain from which form the NOE effect originated.[27] Therefore, NOE difference measurements were only performed for **9d**. Once the configuration around C(8) for this compound is known, it is assumed that, because of the chemical history of **9c** and **9d**, the other configuration can be assigned to **9c**. Irradiation of the C(1) protons of **9d** at δ 2.51 gives NOEs with both methyl groups at C(4a) and C(8), as well as with H(8a). Irradiation of H(4ax) at δ 2.65 gives NOEs with H(4eq), H(3eq), the hydroxyl proton, and with H(6ax). These data confirm that **9d** exists in the nonsteroid conformation **B** and are consistent with the assignment $R^1 = CH_3$, R^2 = OH for **9d**. This leaves R^1 = OH, $R^2 = CH_3$ for compound **9c**.

In this paper we have shown that stereocontrol on the C(8) stereoisomeric center in the trans- and cis-fused hydroxy ketones can be achieved. The conversion of the hydroxy ketones into the corresponding eudesm-11-en-4-ols will be described in the next paper.

Experimental Section

Melting points were determined on an Olympus HSA melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Philips PU 9706 infrared spectrophotometer, and peak positions are expressed in cm^{-1}. NMR spectra were recorded on a Varian EM-390 at 90 MHz (^1H), a Bruker 200 E at 200 MHz (^1H) and at 50 MHz (^{13}C), and a Bruker AM-400 at 400 MHz (^1H) and at 100 MHz (^{13}C). Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0). NMR multiplicities are recorded by use of the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet; br, broad; *J*, coupling constant; Hz, hertz. COSY, ^1H–^{13}C correlation, and NOE experiments were carried out on a Bruker AM-400. Typical parameters for the COSY-45 experiments are as follows: 90° pulse = 6 μs (5 mm selective probe), a spectral width of 900 Hz in t_1 and t_2 was used, and 128 experiments with 8 transients each were done. Before fourier transformation, zero filling was used once and no window functions were applied. For the ^1H–^{13}C heteronuclear shift correlation spectra: 90° carbon pulse = 6 μs, 90° proton pulse = 11 μs (5-mm dual probe). Spectral width in t_1 = 800 Hz, in t_2 = 3787.9 Hz with a size of 256·1 K. A total of 128 experiments with 128 transients each were done. Delays used in the pulse sequence were 3.3 and 2.2 ms. Sine-bell window functions without phase shift were used for the fourier transformation. Mass spectral data were determined on either an AEI MS 902 spectrometer or a VG Micromass 7070 F spectrometer at 70 eV. Elemental analyses were determined on a Carlo Erba elemental analyzer 1106. Gas–liquid chromatography (GC) analyses were carried out on a Varian Vista 6000 gas chromatograph with a flame ionization detector and a DB-17 fused silica capillary column, 30 m × 0.25 i.d., film thickness 0.25 μm. Peak areas were integrated electronically with a Spectra-Physics integrator SP 4290. Column chromatography was performed using ICN alumina B-Super I or ICN alumina N-super I. Flash chromatography was performed using Merck silica gel 60 (230–400 mesh).

Solvents were dried and distilled fresh by common practice. For all dry reactions, flasks were dried at 150 °C and flushed with dry nitrogen just before use, and reactions were carried out under an atmosphere of dry nitrogen. Product solutions were dried over anhydrous sodium sulfate, unless otherwise noted, prior to evaporation of the solvent under reduced pressure by using a rotary evaporator. 2-Butanone dioxolane (MED) was prepared from 2-butanone as reported.[28]

Starting Material. A ca. 2:1 mixture of the diones **7** and **8**, respectively, was prepared from (±)-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone[29] (92.0 g, 0.5 mol) in 60% overall yield as described.[15] In this synthesis Oxone (potassium hydrogen persulfate) was used in place of *m*-CPBA.[30] The compounds **10** and **11** were prepared from the mixture of the diones **7** and **8** as described.[15] Treatment of a solution of **10** in aqueous acetone with PPTS afforded pure **7** in almost quantitative yield.[16]

(4aα,8aα)-(±)-Hexahydro-4a-methyl-1(2*H*),7(8*H*)-naphthalenedione (8). To a stirred solution of 6.21 g (34.5 mmol) of trans-fused dione **7** in 30 mL of CH_3OH and 8 mL of trimethyl orthoformate, cooled to 0 °C, was added dropwise a solution of 0.15 mL (2.7 mmol) of concd H_2SO_4 in 10 mL of CH_3OH. After the solution was stirred at room temperature for 6 days, 0.58 mL (7.2 mmol) of pyridine was added. The reaction mixture was allowed to stir for 30 min, concentrated under reduced pressure, and then diluted with 200 mL of water. The aqueous solution was extracted with three 250-mL portions of CH_2Cl_2. The combined organic layers were dried over K_2CO_3 and evaporated. The remaining residue was chromatographed on basic alumina (activity IV) (10:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 6.85 g of the corresponding cis-fused tetramethyl diacetal[16] (^1H NMR ($CDCl_3$, 90 MHz) δ 0.73–2.67 (m, 13 H), 1.08 (s, 3 H), 3.14 (s, 3 H), 3.18 (s, 6 H), 3.22 (s, 3 H)). The so-obtained diacetal was taken up in 200 mL of acetone, and 20 mL of water and 0.500 g (2.0 mmol) of PPTS were added. The reaction mixture was stirred at room temperature for 20 h and then diluted with 200 mL of saturated aqueous $NaHCO_3$. After evaporation of the acetone under reduced pressure, the remaining aqueous solution was extracted with three 250-mL portions of CH_2Cl_2. The organic layers were washed with brine and dried over a 1:1 mixture of Na_2SO_4 and K_2CO_3. Evaporation afforded 4.32 g (70%) of the cis-fused dione **8**,[15a] which was used without further purification for the next reactions.

(4aα,8aα,8aβ)-(±)-Octahydro-8-hydroxy-4a,8-dimethyl-2-(1*H*)-naphthalenone (9a). To 200 mL of 0.6 M CH_3MgI in ether was added dropwise a solution of 7.51 g (33.2 mmol) of dimethyl acetal **10** in 100 mL of dry ether. The reaction mixture was allowed to stir at room temperature for 1 h. The excess of CH_3MgI was then quenched by the careful addition of saturated aqueous NH_4Cl. After addition of 150 mL of water, the two-phase mixture was separated and the aqueous layer was extracted with three 100-mL portions of ether. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was taken up in a mixture of 100 mL of acetone, and 4 mL of 5% aqueous HCl was added. The reaction mixture was stirred at room temperature for 45 min and diluted with 100 mL of saturated aqueous $NaHCO_3$. After evaporation of the acetone under reduced pressure, the remaining aqueous solution was extracted with three 100-mL portions of CH_2Cl_2. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was flash chromatographed (3:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 5.90 g (80%) of **9a**: mp 130–131 °C (from diisopropyl ether); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.90–2.00 (m, 10 H), 1.06 (s, 3 H), 1.15 (s, 3 H), 2.10–2.60 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.75 (q), 17.75 (t), 29.69 (q), 33.29 (s), 37.90 (t), 38.01 (t), 40.38 (t), 40.66 (t), 42.12 (t), 50.49 (d), 71.25 (s), 213.03 (s); mass spectrum *m/e* (relative intensity) 196 (M^+, 84), 181 (30), 178 (16), 167 (37), 164 (21), 153 (49), 148 (100), 138 (47), 111 (81), 109 (74); calcd for $C_{12}H_{20}O_2$ (M^+) *m/e* 196.1463, found 196.1460. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.27. Found: C, 73.69; H, 10.27.

(1α,4aβ,8aα)-(±)-Octahydro-7,7-dimethoxy-4a-methylspiro[naphthalen-1(2*H*),2′-oxirane] (12). To a stirred solution of 6.41 g (36.0 mmol) of methylene ketone **11** in 200 mL of CH_3OH were added 20 mL of trimethyl orthoformate and 0.222 g (1.13 mmol) of *p*-TsOH. The solution was allowed to stir at room

(26) Kinns, M.; Sanders, J. K. M. *J. Magn. Reson.* **1984**, *56*, 518.
(27) Sanders, J. K. M.; Hunter, B. K. *Modern NMR Spectroscopy*; Oxford University Press: Oxford, 1987, 204.
(28) Bauduin, G.; Pietrasanta, Y. *Tetrahedron* **1973**, *29*, 4225.
(29) Heathcock, C. H.; Ellis, J. E. *Tetrahedron Lett.* **1971**, 4995.
(30) Suryawanshi, S. N.; Fuchs, P. L. *Ibid.* **1981**, *22*, 4201.

temperature for 30 min, and then 20.2 g (40.8 mmol) of MMPP was added. The reaction mixture was stirred at room temperature for an additional 17 h, after which time 350 mL of 10% aqueous $Na_2S_2O_3$ and 200 mL of saturated aqueous $NaHCO_3$ were added. The aqueous solution was extracted with five 200-mL portions of CH_2Cl_2. The combined organic layers were washed with brine, dried over a 1:1 mixture of Na_2SO_4 and K_2CO_3, and evaporated. The crude epoxide **12** (8.00 g) (^1H NMR ($CDCl_3$, 90 MHz) δ 0.70–2.10 (m, 13 H), 0.87 (s, 3 H), 2.57 (m, 2 H), 3.10 (s, 3 H), 3.16 (s, 3 H)) was used without further purification for the next reaction.

(4aα,8β,8aβ)-(±)-Octahydro-8-hydroxy-4a,8-dimethyl-2-(1*H*)-naphthalenone (9b). To a stirred suspension of 2.94 g (77.0 mmol) of $LiAlH_4$ in 150 mL of dry THF, cooled to 0 °C, was added dropwise a solution of 8.00 g of crude epoxide **12** in 100 mL of dry THF. The reaction mixture was allowed to stir at room temperature for 24 h and then heated at reflux for 11 h. The excess $LiAlH_4$ was quenched at 0 °C by the careful addition of saturated aqueous Na_2SO_4. After addition of 300 mL of water, the two-phase mixture was separated, and the aqueous layer was extracted with four 150-mL portions of EtOAc. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue (8.91 g) was hydrolyzed as described for the synthesis of **9a**. The workup and flash chromatography (4:1–2:1 petroleum ether (bp 40–60 °C)/EtOAc) gave 4.80 g (69% overall from **11**) of **9b**: mp 55–56.5 °C (lit.[31] mp 57–58.5 °C); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.00–1.90 (m, 10 H), 1.06 (s, 3 H), 1.11 (s, 3 H), 2.05–2.65 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.72 (q), 20.03 (t), 21.83 (q), 34.28 (s), 37.74 (t), 38.04 (t), 39.93 (t), 42.66 (t), 43.32 (t), 53.76 (d), 71.61 (s), 212.03 (s); mass spectrum *m/e* (relative intensity) 196 (M^+, 100), 181 (21), 178 (23), 167 (38), 163 (19), 153 (53), 138 (56), 111 (98), 109 (96); calcd for $C_{12}H_{20}O_2$ (M^+) *m/e* 196.1463, found 196.1465.

(4aα,8aα)-(±)-Octahydro-7,7-dimethoxy-4a-methyl-1-(2*H*)-naphthalenone (13). To a stirred solution of 6.23 g (34,6 mmol) of cis-fused dione **8** in 100 mL of CH_2Cl_2 were added 10 mL of trimethyl orthoformate and 0.340 g (1.78 mmol) of *p*-TsOH. The reaction mixture was stirred at room temperature for 45 min, after which time 0.160 g (2.35 mmol) of imidazole was added. The reaction mixture was allowed to stir for an additional 10 min and then concentrated under reduced pressure. The remaining residue was chromatographed on neutral alumina (activity II) (10:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 7.47 g (96%) of **13**: ^1H NMR ($CDCl_3$, 90 MHz) δ 0.77–2.67 (m, 13 H), 0.97 (s, 3 H), 3.17 (s, 3 H), 3.22 (s, 3 H). This material was sensitive to atmospheric moisture, and satisfactory analytical values could not be obtained.

(4aα,8α,8aα)-(±)-Octahydro-8-hydroxy-4a,8-dimethyl-2-(1*H*)-naphthalenone (9c). To a stirred solution of 40 mL (64.0 mmol) of CH_3Li (1.6 M in ether), cooled to −78 °C, was added dropwise over a period of 30 min a solution of 2.25 g (10.0 mmol) of crude **13** in 100 mL of dry THF. When the addition was complete, the reaction mixture was allowed to stir at −78 °C for an additional 30 min. The excess CH_3Li was then quenched by careful addition of saturated aqueous NH_4Cl. After addition of 100 mL of water, the two-phase mixture was separated, and the aqueous layer was extracted with three 100-mL portions of EtOAc. The combined organic layers were washed with brine, dried, and evaporated. The crude product (^1H NMR ($CDCl_3$, 90 MHz) δ 0.65–2.10 (m, 14 H), 1.16 (s, 3 H), 1.20 (s, 3 H), 3.15 (s, 3 H), 3.20 (s, 3 H)) was hydrolyzed as described for the synthesis of **9a**. The workup and flash chromatography (3:1 petroleum ether (bp 40–60 °C)/EtOAc) gave 1.59 g (81%) of **9c**: ^1H NMR, see Table I; ^{13}C NMR, see Table II; mass spectrum *m/e* (relative intensity) 196 (M^+, 81), 181 (26), 178 (22), 167 (28), 161 (14), 154 (53), 138 (48), 111 (100), 109 (94); calcd for $C_{12}H_{20}O_2$ (M^+) *m/e* 196.1463, found 196.1464. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.27. Found: C, 73.61; H, 10.08.

(4'aα,8'aα)-(±)-Octahydro-4'a-methylspiro[1,3-dioxolane-2,2'(8'*H*)-naphthalen-8'-one] (14). To a stirred solution of 5.57 g (30.9 mmol) of cis-fused dione **8** in 100 mL of CH_2Cl_2 were added 20 mL of MED, a catalytic amount of ethylene glycol, and 0.160 g (0.84 mmol) of *p*-TsOH. The reaction mixture was stirred at room temperature for 45 min, after which time 0.078 g (1.15 mmol) of imidazole was added. The reaction mixture was allowed to stir for an additional 10 min and then concentrated under reduced pressure. The remaining residue was flash chromatographed (5:1–2:1) petroleum ether (bp 40–60 °C)/EtOAc) to give, in order of elution, 4.79 g (69%) of **14** and 0.58 g (10%) of the starting material **8**. The compound **14** had spectral characteristics identical with those reported in the literature.[32]

(4aα,8β,8aα)-(±)-Octahydro-8-hydroxy-4a,8-dimethyl-2-(1*H*)-naphthalenone (9d). The ethylene acetal **14** (4.79 g, 21.4 mmol) was treated with CH_3MgI for 3 h as described for the synthesis of **9a**. After the workup, the crude reaction product (^1H NMR ($CDCl_3$, 90 MHz) δ 0.80–2.70 (m, 14 H), 0.98 (s, 3 H), 1.17 (s, 3 H), 3.95 (m, 4 H)) was hydrolyzed for 18 h as described for the synthesis of **9a**. The workup and flash chromatography (5:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 3.25 g (78%) of **9d** along with 0.42 g (10%) of **9c**.

9d: mp 117–119 °C (from diisopropyl ether); IR (CCl_4)[33] 3620, 3600, 1710 cm^{-1}; ^1H NMR, see Table I; ^{13}C NMR, see Table II; mass spectrum *m/e* (relative intensity) 196 (M^+, 100), 181 (17), 178 (22), 167 (24), 163 (12), 154 (52), 138 (46), 111 (98), 109 (89); calcd for $C_{12}H_{20}O_2$ (M^+) *m/e* 196.1463, found 196.1463. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.27. Found: C, 73.25; H, 10.43.

Acknowledgment. We would like to thank Dr. R. J. Meier for doing the molecular mechanics calculations, H. A. J. Linssen for recording the NOE-difference spectra, A. van Veldhuizen for recording ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra, and C. J. Teunis and H. Jongejan for mass spectral data and elemental analyses.

Abbreviations: MMPP, magnesium monoperoxyphthalate; Oxone, a mixture of $KHSO_5$, $KHSO_4$, and K_2SO_4 in the ratio of 2:1:1, respectively.

Registry No. (±)-**7**, 87332-36-3; (±)-**8**, 87332-37-4; (±)-**8** bis(dimethyl acetal), 136391-43-0; (±)-**9a**, 136391-44-1; (±)-**9b**, 58844-48-7; (±)-**9c**, 136391-47-4; (±)-**9c** dimethyl acetal, 136391-46-3; (±)-**9d**, 136391-49-6; (±)-**9d** ethylene acetal, 136391-48-5; (±)-**10**, 87262-04-2; (±)-**11**, 87332-41-0; (±)-**12**, 136391-45-2; (±)-**13**, 87262-35-9; (±)-**14**, 96412-14-5.

(31) Brown, E. D.; Sam, T. W.; Sutherland, J. K.; Torre, A. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2326.

(32) Marshall, J. A.; Pike, M. T.; Carroll, R. D. *J. Org. Chem.* **1966**, *31*, 2933.

(33) Dilution of the hydroxy ketone caused a decrease in intensity of the absorption band for bonded OH stretching and a concominant increase in the intensity of the free hydroxyl absorption, which leads to the conclusion that **9d** has no intramolecular hydrogen bonds.