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SYNTHESIS OF MACROCYCLIC TERPENOIDS BY INTRAMOLECULAR CYCLIZATION XIII.[1] STEREOSELECTIVE SYNTHESIS OF (±)-CUBITENE, A COMPONENT OF DEFENSE SECRETION OF TERMITES

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Abstract -- Stereoselective synthesis of cubitene (1), a novel diterpene isolated from defense secretion of termites, has been accomplished using an intramolecular reaction of α-sulfenyl carbanion with epoxide. Hydride reduction of the ketone 11 obtained by Claisen rearrangement occurred in unexpectedly high stereoselectivity yielding the chlorohydrin 12 with the desired stereochemistry.

Frontal gland secretions of termite soldiers are known to play an important role in the defense against potential predators.[2] The secretions are also interesting because they are a rich source of terpenoids with novel carbon skeletons such as cembrane, trinervitane, and kempane.[3] Cubitene (1), one of the major components of the defense secretion of East African termite, Cubitermes umbratus,[4] is a diterpene having a hitherto unknown carbon skeleton, i.e. an irregular isoprenoid arrangement with cis-oriented isopropenyl groups on a twelve-membered ring.[5] The novel structure 1 has been established by spectroscopic analyses, chemical degradation, and X-ray crystallographic analysis except the absolute configuration.

In 1975, we reported an efficient method of synthesizing medium- and macrocyclic terpenoids, i.e. an anion-induced intramolecular cyclization, and have synthesized a series of ten- and fourteen-membered ring terpenes based on this methodology.[6] This paper describes the stereoselective synthesis of (±)-cubitene (1) as an extension of our anion-induced cyclization methodology.[7] Meanwhile a non-stereoselective synthesis of 1 has been reported by Vig et al.[8]

The retrosynthetic analysis was outlined in Scheme I. By applying our anion-induced cyclization method, the twelve-membered ring should be constructed from the epoxide 2. The immediate precursor 2 would be derived via the chloroketone 3 from the acetal 4 by Claisen rearrangement. The acetal would be synthesized from the allylic alcohol 5 and the acetal 6. The crucial step in this scheme is the stereoselective reduction of the ketone 3 since the configuration of resulting hydroxyl group determines the relative stereochemistry of two isopropenyl groups in 1.

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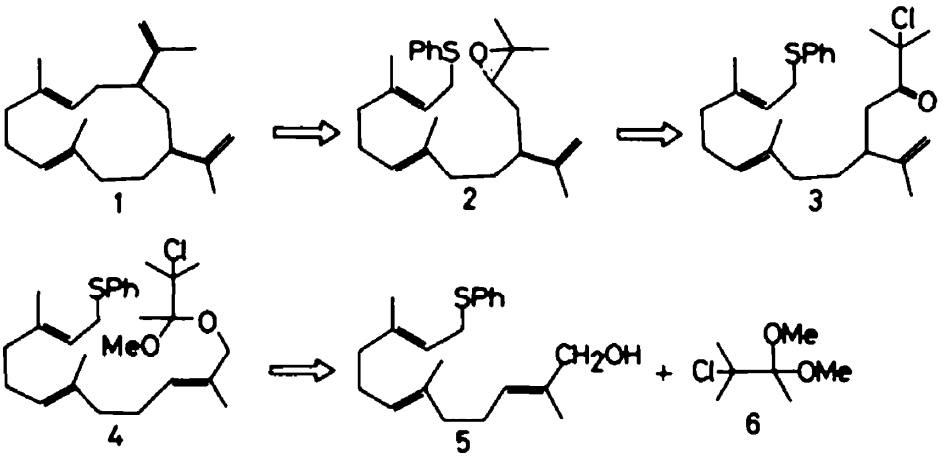


Scheme I

In order to prepare the allylic alcohol 5, the epoxide 7[6b] was first treated with acid to yield the diol 8, which was cleaved with sodium periodate. The resulting aldehyde 9 was allowed to react with (ethoxycarbonylethylidene)triphenylphosphorane to afford the unsaturated ester 10 selectively in 97% yield, which was reduced with lithium aluminum hydride to furnish the desired allylic alcohol 5 in 85% yield. The next steps, acetal exchange, elimination of methanol and Claisen rearrangement were performed in one pot. The allylic alcohol 5 and chloroacetal 6[9] were gradually heated in toluene with catalytic amount of 2,4-dinitrophenol and refluxed for 6 hours with distillation of volatile materials to afford the chloroketone 11 in 61% yield.

The stereocontrol of the reduction of 11 is crucial for the diastereoselective synthesis of 1. Metal hydride reduction of the ketones bearing a heteroatom at the β-position has now been established to proceed with high stereoselectivity (1,3-asymmetric induction) because of their coordination to the reducing agents.[10] However, so far as we are aware, the same reduction of the ketones lacking any coordinating groups is almost non-stereoselective.[11] Considering this, we studied the reduction of 11 under various conditions. The results are summarized in Table I. Two epimeric alcohols (12 and 13) were formed in almost quantitative yield in various ratios changing from 2:1 to 10:1, the most desirable result being achieved by DIBAH in hexane at -78°C. Thus, the reduction took place in remarkably high stereoselectivity even in the absence of coordinating groups.[12] Although the stereochemistry of 12 and 13 could not be determined at this stage, the major product 12 was found to have the desired stereochemistry by its subsequent conversion to natural cubitene (1) (vide infra). The chlorohydrins 12 and 13 could be separated by flash column chromatography. The ^{1}H NMR spectra of these epimers are very similar to each other; the chemical shift of one of the vinyl methyl signals (1.58 ppm in 12 versus 1.52 ppm in 13) is the only distinguishing feature. Each epimeric chlorohydrins were then treated with anhydrous potassium carbonate to yield the epoxides 2 and 14, respectively, in 99% yields.

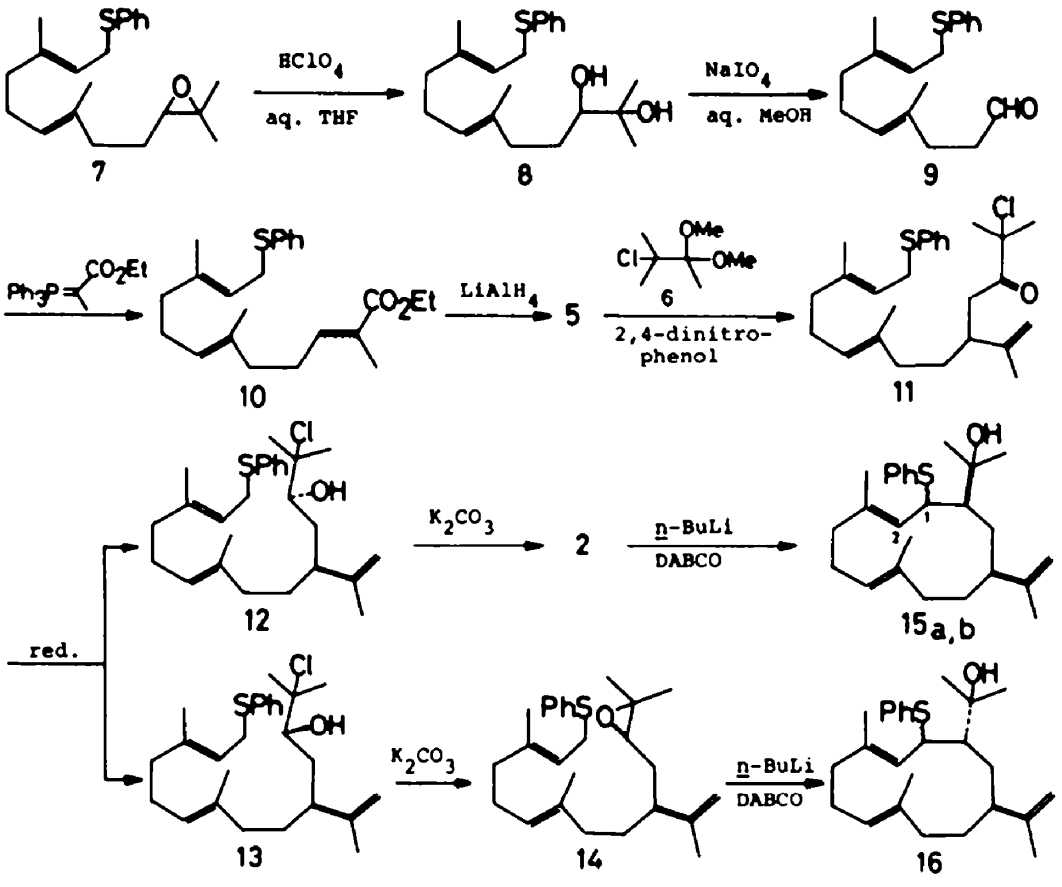


Table I. Reduction of the ketone 11[a]

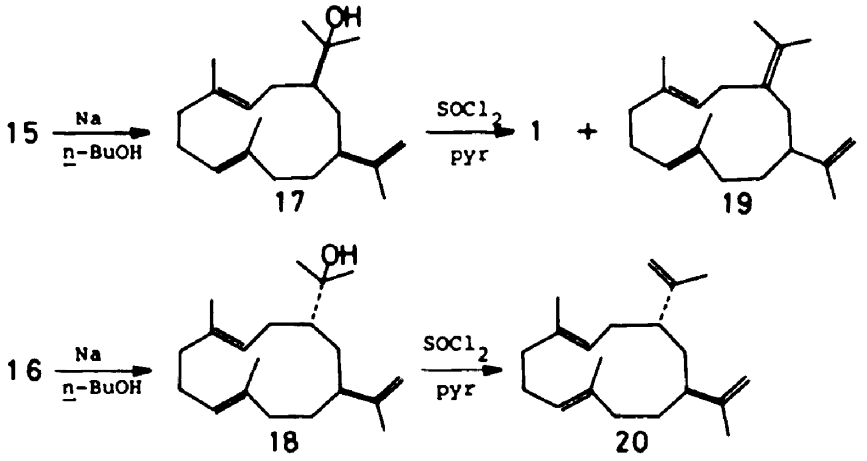
Reagents	Conditions	Ratio (12:13)[b]
$NaBH_4$	MeOH, 0°C	2 : 1
	-50°C	5 : 1
	-78°C	5 : 1
$NaBH_4$-Alox	ether, r.t.	3 : 1
DIBAH	hexane, -78°C	10 : 1

[a] Yields were almost quantitative.

[b] The ratios of products were determined by HPLC (Micropack SI-5; hexane-ether, 97:3; detecting the UV intensity at 260 nm).

When the epoxide 2 in dry THF was treated with n-butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) initialy at -78°C and then at 0°C[13] under high dilution conditions (usually 100 mg/100 mL of THF), two products (15a and 15b) were formed in a ratio of 2:3 in 73% yield. Although the ^1H NMR spectrum of the mixture was rather complicated, it showed two sets of double doublets signals assigned to H-1 [15a: 3.93 ppm (J=11.3, 6.0 Hz, 15b: 4.04 ppm

(J=10.5, 4.5 Hz)] and a pair of doublets due to H-2 [15a: 5.19 ppm (J=11.3 Hz, 15b: 5.35 ppm (J=10.5 Hz)] indicating both to be cyclized products. Without separation, the mixture was subjected to desulfurization using sodium and n-butanol,[14] thereby yielding a single alcohol 17. This result demonstrated that 15a and 15b are epimers of each other at C-1 and not geometrical isomers at the C-2 double bond. The fact that the ^{13}C NMR spectrum of 17 showed methyl signals at higher field (14.69 and 15.01 ppm) revealed that both double bonds in the ring retain E-configuration and therefore no isomerization of double bonds occurred during the cyclization and desulfurization steps.[15] In contrast, the cyclization of 14 under the same conditions resulted in the formation of essentially single product 16. Desulfurization of 16 by the same procedure as described above afforded the alcohol 18, which showed ^1H NMR signals of H-1 and H-2 at 4.31 ppm (br.d, J=9.5 Hz) and 5.47 ppm (br.d, J=9.5 Hz), respectively. Finally 17 was dehydrated with thionyl chloride to give a tetraene 1 (61%) and its isomer 19 (9%). The synthetic 1 was shown to be identical with natural cubitene by the comparison of ^1H and ^{13}C NMR spectra. The structure of 19 was readily derived by the observation of five methyl signals in the ^1H NMR spectrum. Similar dehydration of 18 afforded an diastereoisomeric tetraene 20, trans-cubitene, in 66% yield. Thus, the anion-induced intramolecular cyclization methodology provided an excellent tool for the synthesis of twelve-membered ring terpenoids.



Experimental

General. Nuclear magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded on Varian EM-390 or XL-200, or JEOL FX-90Q spectrometers in CCl_4 or $CDCl_3$ solution with $(CH_3)_4Si$ as an internal standard. Infrared spectra (IR) were taken on a JASCO IRA-2 spectrometer as a thin film (neat) or KBr disk. Mass spectra (MS) were measured on a Hitachi M-52 spectrometer. B.p. in parenthesis denotes base peak. High-resolution mass spectra (HRMS) were obtained on a Shimadzu LKB-9000 spectrometer. Melting points were determined on a Fischer micro melting point apparatus and uncorrected.

Anhydrous solvents. Tetrahydrofuran (THF) and ether were distilled from $LiAlH_4$ prior to use. Hexane, toluene, and n-butanol were dried by refluxing with sodium.

2,6,10-Trimethyl-12-(phenylthio)-6E,10E-dodecadiene-2,3-diol (8). A solution of the epoxide 7[6b] (610 mg, 1.8 mmol) and a catalytic amount of $HClO_4$ in THF-H_2O (3:1, 60 mL) was stirred at room temperature for 4 h. The reaction mixture was poured into dil. $NaHCO_3$ solution and extracted with $CHCl_3$ three times. The combined extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent in vacuo followed by chromatography on silica gel ($CHCl_3$) gave the diol 8 (570 mg, 89%) as a colorless oil: IR (neat) 3450, 1586, 740, 690 cm^{-1}; ^1H NMR δ (CCl_4) 1.10(s, 3H), 1.12(s, 3H), 1.59(br.s, 3H), 3.20(dd, J=8.8,3.0 Hz, 1H), 3.46(d, J=7.5 Hz, 2H), 4.95-5.23(m, 1H), 5.26(br.t, J=7.5 Hz, 1H), 7.0-7.6(m, 5H); MS m/z 348(M^+), 221, 153, 143 (b.p.); HRMS, calcd for $C_{21}H_{32}O_2S$ m/z 348.2121, found m/z 348.2126.

4,8-Dimethyl-10-(phenylthio)-4E,8E-decadienal (9). To a solution of the diol 8 (3.00 g, 8.62 mmol) in THF-H_2O (3:1, 80 mL) was added $NaIO_4$ (2.03 g, 9.48 mmol) in small portions at room temperature. After being stirred for 6 h, the mixture was poured into water and extracted with ether three times. The ether layers were washed with water and brine, and then dried on $MgSO_4$. Evaporation of the solvent followed by chromatography on silica gel (benzene) yielded 9 (2.40 g, 97%) as a colorless oil: IR (neat) 1710 cm^{-1}; ^1H NMR δ (CCl_4) 1.57(br.s, 6H), 3.46(d, J=7.5 Hz, 2H), 5.03(m, 1H), 5.23(br.t, J=7.5 Hz, 1H), 7.0-7.3(m, 5H), 9.58(m, 1H); MS m/z 288(M^+), 161, 93(b.p.) 81; HRMS, calcd for $C_{18}H_{24}OS$ m/z 288.1547, found m/z 288.1547.

Ethyl 2,6,10-trimethyl-12-(phenylthio)-2E,6E,10E-dodecatrienoate (10). To a solution of the aldehyde 9 (273 mg, 0.95 mmol) in 10 mL of benzene was added (ethoxycarbonylethylidene)triphenylphosphorane (412 mg, 1.14 mmol) and the mixture was stirred at room temperature overnight. Benzene was evaporated in vacuo. The residue was chromatographed on silica gel (benzene) to afford 10 (341 mg, 97%) as a colorless oil: IR (neat) 1705 cm^{-1}; ^1H NMR δ (CCl_4) 1.26(t, J=7.2 Hz, 3H), 1.59(br.s, 6H), 1.80(br.s, 3H), 3.46(d, J=7.5 Hz, 2H), 4.11(q, J=7.2 Hz, 2H), 4.94- 5.21(m, 1H), 5.26(br.t, J=7.5 Hz, 1H), 6.59(br.t, J=6.7 Hz, 1H), 7.0-7.3(m, 5H); MS m/z 372 (M^+), 218(b.p.), 178. Anal. calcd for $C_{23}H_{32}O_2S$: C, 74.19; H, 8.60. found: C, 74.03; H, 8.42.

2,6,10-Trimethyl-12-(phenylthio)-2E,6E,10E-dodecatriene-1-ol (5). To an ice-cooled suspension of $LiAlH_4$ (20 mg, 0.76 mmol) in 20 mL of dry ether was added the ester 10 (341 mg, 0.92 mmol) in 10 mL of dry ether over 30 min with stirring. After stirring for an additional 12 h at 0 °C, the reaction was quenched with water and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by passing through a short column of silica gel (CH_2Cl_2) to give 5 (258 mg, 85%) as a colorless oil: IR (neat) 3330, 1660, 1585, 735, 685 cm^{-1}; ^1H NMR δ (CCl_4) 1.60 (br.s, 6H), 1.64(br.s, 3H), 3.45(d, J=7.5 Hz, 2H), 3.87(br.s, 2H), 4.90-5.16(m, 1H), 5.26(br.t, J=7.5 Hz, 2H), 6.95-7.32 (m, 5H); MS m/z 330(M^+), 222, 95(b.p.), 93; HRMS, calcd for $C_{21}H_{30}OS$ m/z 330.2016, found m/z 330.2049.

2-Chloro-5-isopropenyl-2,8,12-trimethyl-14-(phenylthio)-8E,12E-tetradecadien-3-one (11). A solution of 5 (534 mg, 1.6 mmol), chloroacetal 6[9] (1.34 g, 8.1 mmol), and 2,4-dinitrophenol (29 mg) in 10 mL of dry toluene was placed in a dry flask equipped with a short-pass distillation head and a drying tube. The mixture was heated gradually up to 140°C over 3 h. During the time small amount of methanol was distilled off. The temperature was maintained at 140°C for 6 h. After cooling, the mixture was chromatographed on a short column of silica gel (benzene) to remove polar materials. Re-chromatography of the benzene eluants on silica gel (benzene) afforded 11 (438 mg, 61%) as a colorless oil: IR (neat) 1718, 892 cm^{-1}; ^1H NMR δ (CCl_4) 1.59(br.s, 6H), 1.62(br.s, 6H), 1.68(br.s, 3H), 3.46(d, J=7.5 Hz, 2H), 4.70(br.s, 2H), 5.02 (m, 1H), 5.27(br.t, J=7.5 Hz, 1H), 7.0-7.3(m, 5H); Ms m/z 434 and 432(M^+), 135(b.p.), 81; HRMS, calcd for $C_{26}H_{37}OClS$ m/z 432.2252, found m/z 432.2295.

Reduction of 11. (1) With $NaBH_4$. To an ice-cooled solution of 11 (20 mg, 0.046 mmol) in 10 mL of methanol was added $NaBH_4$ (0.9 mg, 0.023 mmol) with stirring. After 30 min, the mixture was diluted with water and extracted with $CHCl_3$. The organic layer was washed with water and brine and dried ($MgSO_4$).

Evaporation of the solvent afforded a colorless oil (20 mg). The ratio of 12 and 13 obtained by HPLC analysis (hexane-ether, 95:5) was 2:1. 11 (46 mg) was similarly reduced with $NaBH_4$ at -50°C to give the same mixture (45 mg). The ratio of 12 and 13 was 5:1.

(2) With DIBAH. To a solution of 11 (20 mg, 0.046 mmol) in 10 mL of dry hexane under argon was added a 15% solution of DIBAH in hexane (0.026 mL, 1.2 eq) at -78°C. After stirring for 1 h, the reaction was quenched with water and the product was extracted with hexane. The hexane layer was washed with brine and dried ($MgSO_4$). Evaporation of the solvent afforded the same mixture (19 mg) as described above. The ratio of 12 and 13 was 10:1.

(3) With $NaBH_4$-Alox. To a stirred mixture of $NaBH_4$-Alox (46 mg) in 1.5 mL of ether was added 11 (116 mg) in 1.5 mL of ether. The mixture was stirred at room temperature overnight. The precipitates were filtered off and washed with ether. The combined filtrates were washed with brine and dried ($MgSO_4$). Evaporation of the solvent yielded the same mixture (116 mg). The ratio of 12 and 13 was 3:1.

The mixture was separated by flash column chromatography (400 mesh SiO_2) using hexane-ether (15:1) as eluent. 12: colorless oil, IR (neat) 3350, 890 cm^{-1}; ^1H NMR δ (CCl_4) 1.51(s, 3H), 1.58(br.s, 6H), 1.68(br.s, 3H), 3.35-3.55(m, 1H), 3.46(d, J=7.5 Hz, 2H), 4.73(br.s, 2H), 5.02 (m, 1H), 5.25(br.t, J=7.5 Hz, 1H), 7.0-7.3(m, 5H); MS m/z 436 and 434(M^+), 135(b.p.), 107; HRMS, calcd for $C_{26}H_{39}OClS$ m/z 434.2405, found m/z 434.2422. 13: colorless oil, IR (neat) 3470, 890 cm^{-1}; ^1H NMR δ (CCl_4) 1.51(br.s, 3H), 1.52(br.s, 3H), 1.58(br.s, 9H), 3.35(dd, J =10.0, 2.5 Hz, 1H), 4.66-4.83(m, 2H), 5.02(m,1H), 5.26(br.t, J=7.5 Hz, 1H), 7.0-7.3(m, 5H); MS m/z 436 and 434(M^+), 121, 95(b.p.). Anal. calcd for $C_{26}H_{39}OClS$: C, 71.94; H, 8.82. found: C, 71.60; H, 9.08.

(3S*)-[2(S*),3-Epoxy-3-methylbutyl]-2,6,10-trimethyl-12-(phenylthio)-1,6E,10E-dodecatriene (2). A mixture of 12 (360 mg, 0.83 mmol) and anhyd K_2CO_3 (460 mg, 4 eq) in 20 mL of methanol was stirred vigorously at room temperature. After 30 min, methanol was evaporated. The residue was dissolved in ether and the ether solution was washed with brine, dried ($MgSO_4$), and concentrated to give 2 (328 mg, 99%) as a colorless oil: IR (neat) 1641, 890 cm^{-1}; ^1H NMR δ (CCl_4) 1.20(s, 3H), 1.22(s, 3H), 1.58(br.s, 6H), 1.66(br.s, 3H), 2.49(t, J=6.0 Hz, 1H), 3.45(d, J=7.5 Hz, 2H), 4.69(br.s, 2H), 5.00(m, 1H), 5.24(br.t, J=7.5 Hz, 1H), 7.0-7.3(m, 5H); MS m/z 398(M^+), 176, 135(b.p.), 71; HRMS, calcd for $C_{26}H_{38}OS$ m/z 398.2638, found m/z 398.2662.

(3S*)-[2(R*),3-Epoxy-3-methylbutyl]-2,6,10-trimethyl-12-(phenylthio)-1,6E,10E-dodecatriene (14). The chlorohydrin 13 (94 mg) in 5 mL of methanol was similarly treated with 4 eq of anhyd K_2CO_3. After the same work-up, 88 mg (99%) of 14 was obtained as a colorless oil: IR (neat) 1640, 890 cm^{-1}; ^1H NMR δ (CCl_4) 1.18 (s, 3H), 1.22(s, 3H), 1.59(br.s, 6H), 1.64(br.s, 3H), 2.46(dd, J=7.5,4.5 Hz, 1H), 3.47(d, J=7.5 Hz, 2H), 4.74(br.s, 2H), 5.02(m, 1H), 5.25(br.t, J=7.5 Hz, 1H), 7.0-7.3 (m, 5H); MS m/z 398(M^+), 176, 135,71(b.p.); HRMS, calcd for $C_{26}H_{38}OS$ m/z 398.2638, found m/z 398.2623.

Cyclization. (1) From 2. In a well-dried 500 mL three-necked flask equipped with gas inlet tube and a two-way stopcock with drying tube was placed the epoxide 2 (320 mg, 0.80 mmol) and the flask was evacuated with stirring for 1.5 h. Freshly sublimed DABCO (90 mg, 0.80 mmol) was added under argon and evacuation was continued for an additional 30 min. Dry THF (300 mL) was added under argon and the flask was cooled with dry-ice methanol bath. After 20 min, 15% hexane solution of n-BuLi (0.96 mL, 1.2 eq) was added dropwise. Usually the solution turned to yellow after addition of the first drop of n-BuLi. After stirring for 70 min at -70°C, the cooling bath was replaced with an ice-water bath and stirring was continued overnight. Most of the THF was evaporated *in vacuo* and the residue was dissolved in ether. The ether solution was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue (336 mg) was passed through a short column of silica gel (hexane-ether, 5:1) to give 15 (232 mg, 73%, ca. 2:3 mixture of diastereomers) as a colorless oil: IR (neat) 3450, 1640, 885,685 cm^{-1}; ^1H NMR δ (CCl_4) 1.16, 1.22, 1.25, and 1.28(each s, total 6H), 1.50, 1.60, 1.61, and 1.68(each br.s, total 9H), 3.93(dd, J=11.3,6.0 Hz)

and 4.04(dd, J=10.5,4.5 Hz)(2H), 4.70-5.07(m, 1H), 5.20(d, J=11.3 Hz) and 5.35 (d, J=10.5 Hz)(1H), 7.0-7.3(m, 5H); MS m/z 398(M^+), 232, 231(b.p.), 110; HRMS, calcd for $C_{26}H_{38}OS$ m/z 398.2638, found m/z 398.2627.

(2) From 14. The epoxide 14 (234 mg, 0.59 mmol) was cyclized similarly to give 16 (172 mg, 73%) as colorless needles (dil. methanol), mp 89-91°C : IR (KBr) 3490, 1640, 895 cm^{-1}; ^1H NMR δ (CCl_4) 1.21(s, 3H), 1.33(s, 3H), 1.54(br.s, 3H), 1.57(br.s, 3H), 1.76(br.s, 3H), 4.31(br.d, J=9.5 Hz, 1H), 4.71(m, 2H), 4.8-5.0 (m, 1H), 5.47(br.d, J=9.5 Hz, 1H), 7.0-7.3(m, 5H); MS m/z 398(M^+), 231(b.p.), 135, 110. Anal. calcd for $C_{26}H_{38}OS$: C, 78.39; H, 9.55. found: C, 78.01; H, 9.61.

2-[(1R*)-4,8-Dimethyl-11(S*)-isopropenyl-3E,7E-cyclododecadienyl]-2-propanol (17). To a stirred solution of 15 (62 mg, 0.16 mmol) in absolute n-butanol (15 mL) under nitrogen was added sodium in small pieces at 80°C. Addition of sodium was continued until the starting material disappeared on TLC (total ca. 500 mg). The reaction mixture was poured into water and was extracted with ether. The combined extracts were washed with water and brine, dried ($MgSO_4$), and then concentrated. The residue was chromatographed on silica gel (hexane-ether, 20:1) to afford 17 (42 mg, 93%) as a colorless oil: IR (neat) 3380, 1639, 885 cm^{-1}; ^1H NMR δ (CCl_4) 1.14(s, 3H), 1.18(s, 3H), 1.54(br.s, 3H), 1.62(br.s, 3H), 4.63 (br. s, 1H), 4.69(br.s, 1H), 4.86(m, 1H), 5.08(br.t, J=7.5 Hz, 1H); ^{13}C NMR δ ($CDCl_3$) 14.69(q), 15.01(q), 17.89(q), 25.07 (t), 27.55(q), 28.00(t), 28.13(t), 31.27(t), 31.46(t), 36.62(t), 40.21(t), 41.45(d), 45.43(d), 73.63(s), 112.15(t), 125.46(d), 127.09(d), 132.77(s), 133.69(s), 148.63(s); MS m/z 290 (M^+), 272 (b.p.), 257, 135; HRMS, calcd for $C_{20}H_{34}O$ m/z 290.2608, found m/z 290.260.

2-[(1S*)-4,8-Dimethyl-11(S*)-isopropenyl-3E,7E-cyclododecadienyl]-2-propanol (18). The sulfide 16 (90 mg, 0.23 mmol) was similarly treated with sodium and n-butanol to give 18 (60 mg, 92%) as a colorless oil; IR (neat) 3400, 1640, 880 cm^{-1}; ^1H NMR δ (CCl_4) 1.22(s, 6H),1.58(br.s, 6H), 1.67(br.s, 3H), 4.66(br.s, 2H), 4.83(br.dd, J=6.7,7.5 Hz, 1H), 5.22(br.t, J=7.5 Hz, 1H); ^{13}C NMR δ ($CDCl_3$) 15.14(q), 17.04(q), 19.13(q), 25.60(t), 26.63(q), 27.02(q), 27.55(t), 30.81(t), 36.16(t), 37.99(t), 39.30(t), 40.28(t), 48.76(d), 73.57(s), 110.25(t), 125.85(d) 127.61(d), 133.23(s), 134.53(s), 149.81(s); MS m/z 290(M^+), 272(b.p.), 257, 122. Anal. calcd for $C_{20}H_{34}O$: C, 82.76; H, 11.72. found: C, 82.49; H, 11.96.

Dehydration of 17. To an ice-cooled solution of 17 (95 mg, 0.33 mmol) in 2 mL of dry pyridine was added 0.03 mL (1.2 eq) of $SOCl_2$ via syringe with stirring. After 30 min, the mixture was poured into water and extracted with hexane. The hexane layer was washed well with water, dried ($MgSO_4$), and concentrated in vacuo. The residue was passed through a short column of alumina (hexane) to give a colorless oil (84 mg). Separation by preparative TLC on SiO_2-10% $AgNO_3$ (hexane) yielded 1 (57 mg, 61%) as a colorless oil (lit.[6] mp 33.5-40 °C)[16] and 19 (8 mg, 9%) as a colorless oil. The ^1H and ^{13}C NMR spectra of 1 were identical with those of natural cubitene. 19: IR (neat) 2925, 1639, 1445, 1375, 881 cm^{-1}; ^1H NMR δ ($CDCl_3$) 1.56(br.s, 3H), 1.61(br.s, 3H), 1.71(br.s, 9H), 4.68 (br.s, 2H), 4.92-5.25(m, 2H); MS m/z 272(M^+, b.p.), 256, 81; HRMS, calcd for $C_{20}H_{32}$ m/z 272.2502, found m/z 272.2495.

Dehydration of 18. The isomeric alcohol 18 (37 mg) was dehydrated similarly to give 20 (25 mg, 72%) as a colorless oil: IR (neat) 2910, 1640, 880 cm^{-1}; ^1H NMR δ ($CDCl_3$) 1.61(br.s, 9H), 1.70(br.s, 3H), 4.61(br.s, 2H), 4.66(br.s, 2H), 4.90(br.dd, J=6.0,7.5 Hz, 1H), 5.27(br.t, J=7.5 Hz, 1H); ^{13}C NMR δ ($CDCl_3$) 15.14(q), 16.58(q), 19.00(q), 20.50(q), 25.72(t), 28.26(t), 34.53(t), 36.49(t), 39.49(t), 40.60(t,d), 44.98(d), 108.03(t), 110.19(t), 126.12(d), 127.03(d), 133.75(s), 134.40(s), 149.75(s), 151.90(s); MS m/z 272(M^+, b.p.), 244, 148; HRMS, calcd for $C_{20}H_{32}$ m/z 272.2502, found m/z 272.2512.

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