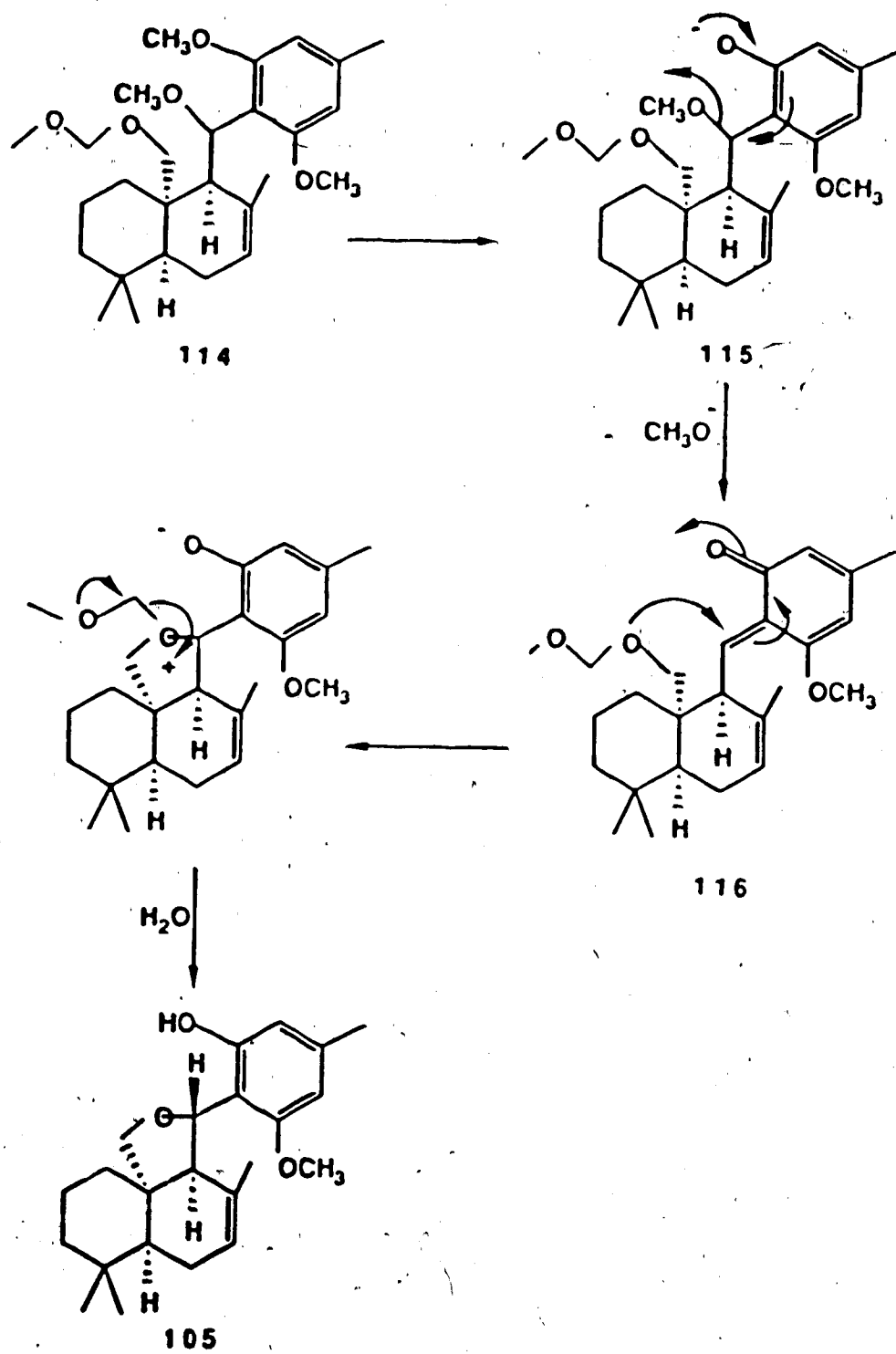


data are in agreement with the assigned structure. The compound showed no absorption due to hydroxyl group in its ir spectrum. In the  $^1\text{H}$  nmr spectrum, the aromatic protons were observed at  $\delta$  6.38 as a singlet. The benzylic proton appeared at  $\delta$  4.90 as a doublet with a coupling constant of 10 Hz. The methylene protons between two oxygen atoms appeared as a singlet at  $\delta$  4.80, and the anisole methyl protons appeared at  $\delta$  3.80 as a singlet. Although the molecular ion peak corresponding to the expected molecular formula was not observed in the mass spectrum of the compound, a fragment resulting from the loss of a methanol unit was observed at  $m/z$  370.3508.

With the hydroxyl group of compound 103 properly protected, the demethylation was attempted. Accordingly, ether 114 was treated with potassium ethanethiolate in *N,N*-dimethylformamide at 125°C for 8 hours. The reaction proceeded cleanly and a product was formed in good yield (60%). Surprisingly, this compound showed the absence of methoxymethyl group and the benzylic methoxy group in the  $^1\text{H}$  nmr spectrum. A comparison of its spectral data with those previously obtained for phenol 105 revealed that it is identical with phenol 105. A mechanistic rationale for the formation of this compound is outlined in Scheme 11. After the initial demethylation, the resulting phenoxide 115 could, in principle, eliminate the benzylic methoxy group to give the intermediate 116. Michael addition followed by



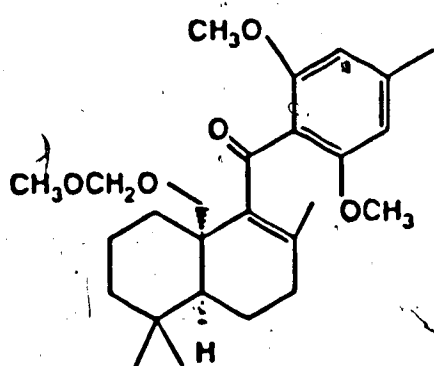
Scheme 11

the elimination of a methoxymethyl unit could then lead to the formation of the observed product 105.

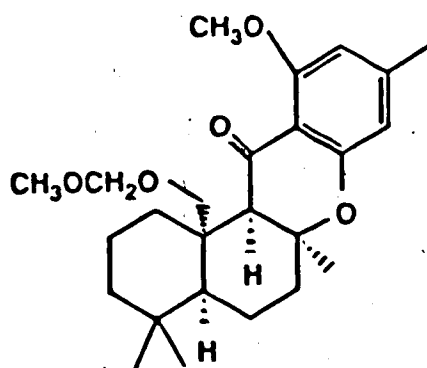
An alternative process for the formation of ring C is to oxidise the benzylic hydroxyl group to a ketone, with concomitant migration of the carbon-carbon double bond into conjugation with the ketone thus formed (103 → 117).

Demethylation followed by Micheal addition could, in principle, give ketone 118. Towards this end, alcohol 103 was subjected to oxidation with pyridinium chlorochromate, buffered with sodium acetate, in dichloromethane at room temperature for 3 hours. Apparently, these oxidation conditions were too severe. Neither the starting material nor the desired product was isolated. Instead, a complex mixture containing a number of unidentifiable compounds was formed. Consequently, alcohol 103 was subjected to Swern oxidation by treatment with a mixture of oxalyl chloride and dimethyl sulfoxide at  $-60^{\circ}\text{C}$ , followed by gradual warm-up to  $-10^{\circ}\text{C}$  and addition of triethylamine. Under these conditions, a major product was formed in 52% yield. To our disappointment, this compound was identified as ether 104 by comparison of the spectral data. Presumably, due to the ease of cyclisation to form ring E, the substrate took this course of reaction; the expected intermediate 119 underwent a substitution reaction with the neighbouring ether oxygen instead of the desired oxidation as shown Scheme 12.

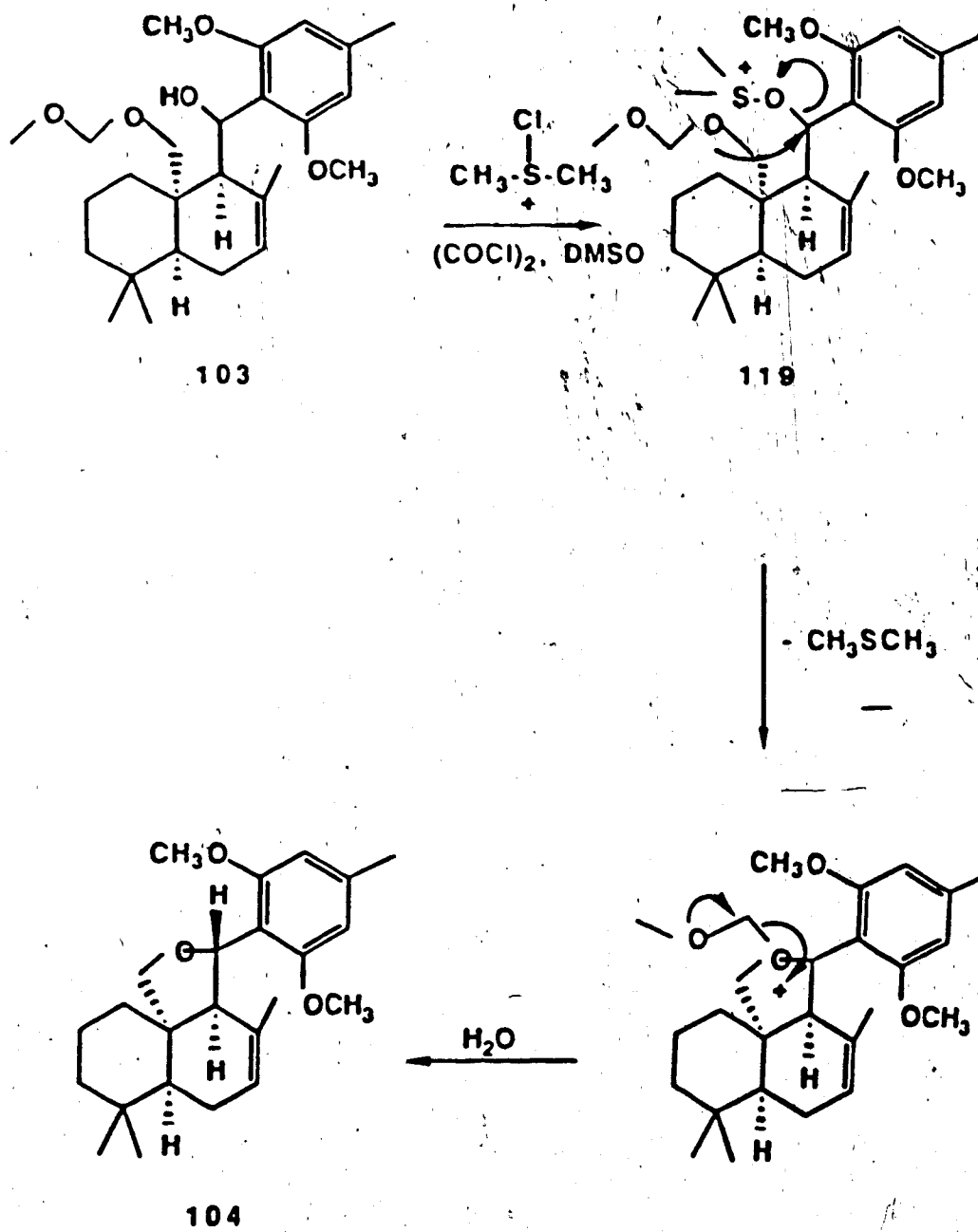
To inhibit the undesired E ring formation, an excellent possibility exists, which involves the formation



117



118

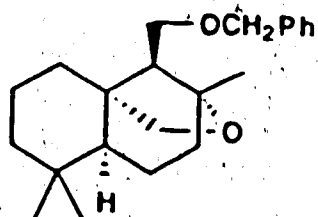


Scheme 12

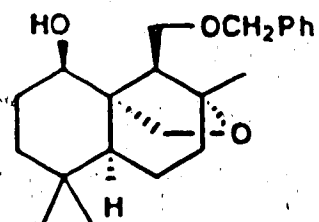
of a bridged system as shown in compound 120. The bridged ether would serve for two purposes. The E ring formation is now sterically forbidden. In addition, it serves also to protect the hydroxyl group.

The most direct route leading to compound 120 would involve cyclisation of diol 74 to give 121 followed by the removal of the secondary hydroxyl group. Treatment of diol 74 with aqueous hydrochloric acid in refluxing tetrahydrofuran gave, in 60% yield a hydroxy ether which showed a hydroxyl absorption band at  $3510\text{ cm}^{-1}$  in the ir spectrum. In the mass spectrum, a molecular ion peak at 344.2353 was in accord with the expected molecular formula  $\text{C}_{22}\text{H}_{32}\text{O}_3$ . These spectral data were in agreement with the desired reaction product 121. However, in the  $^1\text{H}$  nmr spectrum, a doublet of doublets at  $\delta$  3.32 ( $J = 8, J' = 6\text{ Hz}$ ) could be readily attributed to a hydroxyl proton, since it disappeared on addition of deuterium oxide. The coupling pattern of this signal suggested the presence of an hydroxymethylene unit. Based on this evidence, the structure 122 was assigned to the compound.

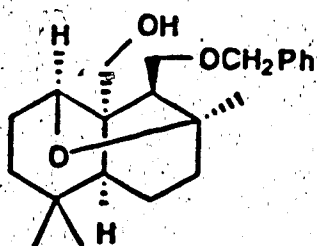
In further confirmation of the structure, compound 122 was converted to the corresponding xanthate 123 by treatment with excess sodium hydride, carbon disulfide and methyl iodide in 1,2-dimethoxyethane for 5 hours. The xanthate thus obtained in 58% yield showed a thiocarbonyl absorption at  $1240\text{ cm}^{-1}$  in the ir spectrum. A molecular ion peak at 434.1947 was displayed in the mass spectrum in accord



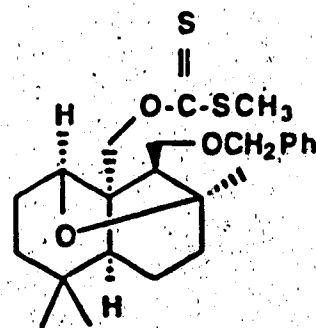
120



121



122



123

with the expected molecular formula  $C_{24}H_{34}S_2O_3$ . The  $^1H$  nmr spectrum clearly indicated that the xanthate moiety was linked to a methylene carbon. Two mutually coupled doublets ( $J = 12$  Hz) characteristic of a methylene group attached to a xanthate moiety appeared at  $\delta$  4.82 and 4.56.

As a consequence of the above observations an alternative route leading to the cyclic ether 120 was investigated. Diether 91 was selectively hydrolysed and cyclised with aqueous hydrochloric acid in refluxing tetrahydrofuran to give the desired cyclic ether 120 in 53% yield. The ir spectrum of the compound showed absorption at  $1073\text{ cm}^{-1}$  for the five-membered cyclic ether. A molecular ion peak at 328.2399 in the mass spectrum suggested a molecular formula of  $C_{22}H_{32}O_2$ . In the  $^1H$  nmr spectrum, the aromatic protons were observed as a multiplet at  $\delta$  7.40, while the benzylic protons appeared as two doublets at  $\delta$  4.78 and 4.72, each with a coupling constant of 12 Hz. The methylene protons adjacent to the oxygen atom appeared as a singlet at  $\delta$  3.54. The three singlets at  $\delta$  1.34, 0.96 and 0.84 were assigned to the methyl groups.

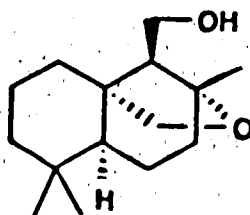
The cleavage of the benzyl ether linkage present in compound 120 was effected by dissolving metal reduction. On treatment with excess of lithium metal in liquid ammonia for 2 hours, the compound was converted to the corresponding alcohol 124 in 83% yield. The compound showed a characteristic hydroxyl absorption in the ir spectrum at  $3400\text{ cm}^{-1}$ . The  $^1H$  nmr spectrum displayed a complex multiplet



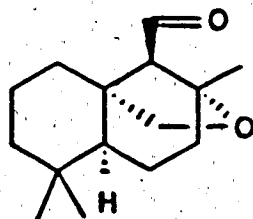
between  $\delta$  3.70 and 3.40 for the four methylene protons adjacent to the oxygen atoms. Furthermore, signals due to aromatic protons were not observed. The mass spectrum of the compound confirmed the molecular formula to be  $C_{15}H_{26}O_2$  with a molecular ion peak at 238.1938.

Oxidation of the alcohol **124** with pyridinium chlorochromate in dichloromethane at room temperature for 2 hours resulted in the formation of the desired aldehyde **125** in 81% yield. A molecular ion peak at 236.1782 in the mass spectrum confirmed the required molecular formula  $C_{15}H_{24}O_2$ . In the  $^1H$  nmr spectrum, a doublet with a coupling constant of 4 Hz at  $\delta$  10.78 was assigned to the aldehydic proton. The methylene protons adjacent to the oxygen atom were observed as a singlet at  $\delta$  3.74. Three more singlets were observed at  $\delta$  1.30, 0.96 and 0.74 for the methyl groups.

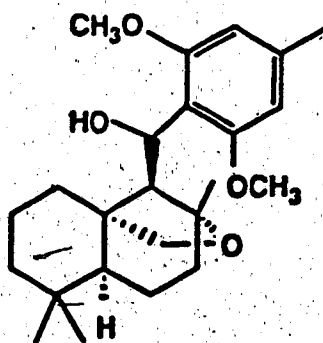
Addition of aldehyde **125** to a solution of the lithium reagent **99** in ether at room temperature resulted in the formation of the adduct **126**. The compound obtained in 90% yield showed, in the ir spectrum, an absorption due to a hydroxyl group at  $3400\text{ cm}^{-1}$  and no carbonyl absorptions. In the  $^1H$  nmr spectrum, the presence of singlets at  $\delta$  6.46 (2H), 3.76 (6H) and 2.30 (3H) indicated the incorporation of the orcinol moiety into the compound. Although the molecular ion corresponding to the expected molecular formula was not observed in the mass spectrum, a fragment resulting from the loss of a water molecule was observed at  $m/z$  370.2506. The presence of only one set of signals in the  $^1H$  nmr



124



125



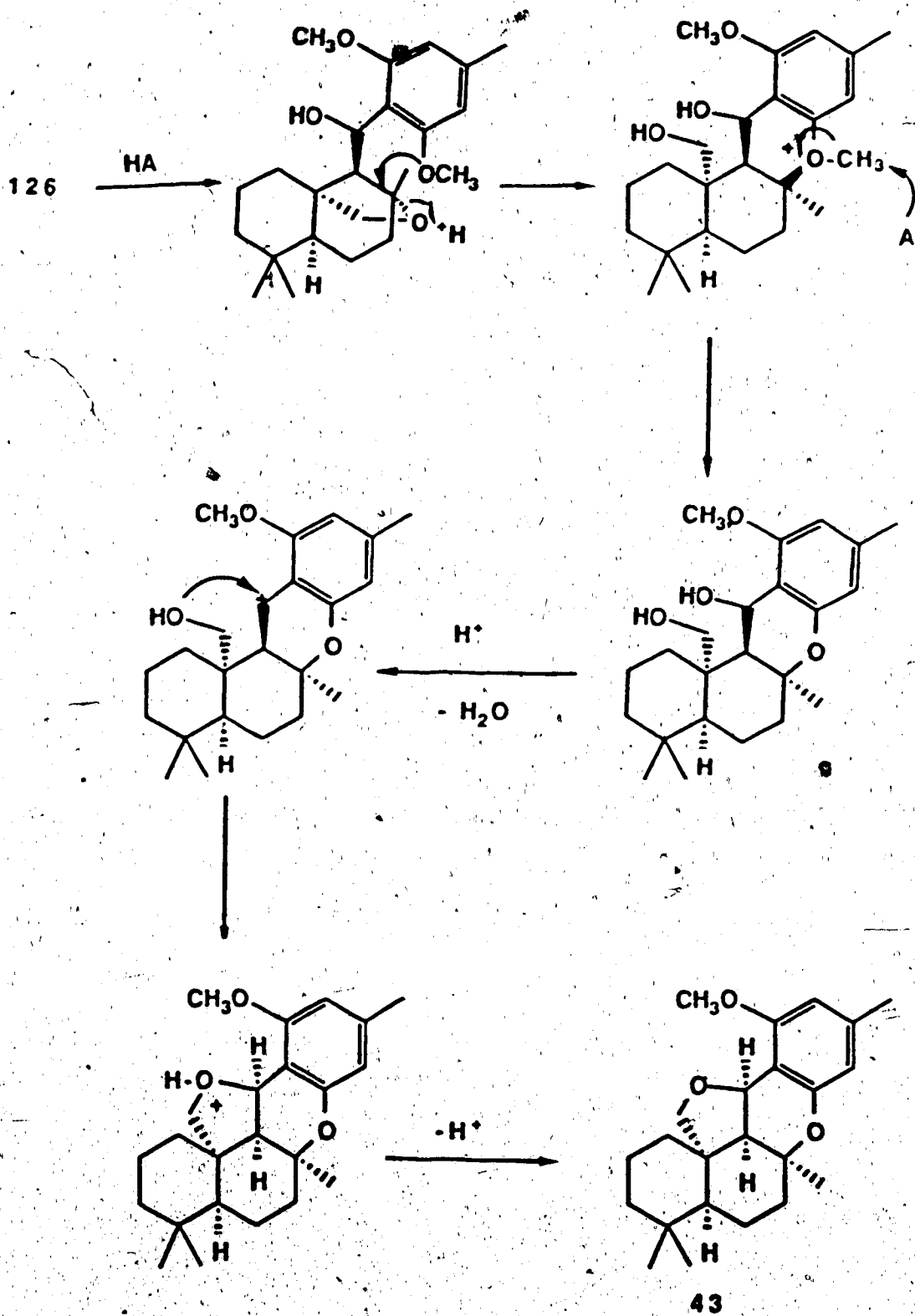
126

spectrum suggested that the coupling product was formed as a single stereoisomer. Its stereochemistry at the newly generated chiral centre remains, however, to be determined.

As shown in Scheme 13, alcohol 126 could, in principle, undergo consecutive cyclisations to provide siccanin methyl ether (43) under acid catalysis. However, the compound was found to be stable to 1 N aqueous hydrochloric acid in refluxing tetrahydrofuran and to boron tribromide in dichloromethane at room temperature.<sup>89</sup> In both cases, the starting material was recovered intact. At the present time, we are studying the demethylation of compound 126 in order to enhance its reactivity towards the formation of ether rings C and E.

Studies are also currently being undertaken on an approach, which is also designed to induce the C ring formation prior to the formation of ring E. This approach employs, as the starting material, acetal 84 which was readily available as a by-product from the reaction of diol 74 with chloromethyl methyl ether and sodium hydride (*vide supra*).

Debenzylation of the acetal 84 with lithium metal in liquid ammonia gave alcohol 127 in 58% yield. The compound showed, in the ir spectrum, an absorption band at  $3400\text{ cm}^{-1}$  due to hydroxy group. In the  $^1\text{H}$  nmr spectrum, no signals were observed for the aromatic protons. A broad singlet at  $\delta$  5.40 was attributed to the vinylic proton. Two doublets, each with a coupling constant of 8 Hz, appeared at  $\delta$  5.20 and 4.84



Scheme 13

due to the methylene protons adjacent to two oxygen atoms. In addition, three singlets for the methyl groups were observed at  $\delta$  1.80, 0.94 and 0.82. Although in the mass spectrum, a molecular ion peak due to the expected molecular formula was not observed, a fragment resulting from the loss of a water molecule appeared at  $m/z$  248.1788.

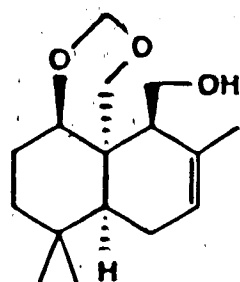
Oxidation of the alcohol 127 with pyridinium chlorochromate in dichloromethane for 3 hours gave the corresponding aldehyde 128 in 80% yield. The mass spectrum of the compound suggested the molecular formula  $C_{16}H_{24}O_3$  with a molecular ion at 264.1720. In the ir spectrum, the compound showed the absence of any hydroxyl absorptions. An intense band at  $1711\text{ cm}^{-1}$  suggested the presence of a carbonyl group. In the  $^1\text{H}$  nmr spectrum of the compound, a doublet with a coupling constant of 2 Hz was observed at  $\delta$  10.16. This signal was readily attributed to the aldehydic proton. The vinylic proton was observed as a broad singlet at  $\delta$  5.50, whereas the methylene protons adjacent to two oxygen atoms appeared as a pair of doublets, each with a coupling constant of 6 Hz, at  $\delta$  5.24 and 4.92.

When aldehyde 128 was subjected to treatment with the magnesium reagent 102 derived from orcinol dimethyl ether 98, a mixture of two epimeric alcohols 129 was formed. The major alcohol, which was obtained in 59% yield, showed a hydroxyl absorption at  $3320\text{ cm}^{-1}$  in the ir spectrum. In the  $^1\text{H}$  nmr spectrum, the singlets at  $\delta$  6.28 (2H), 3.76 (3H) and 2.30 (3H) were attributed to the orcinol moiety. The vinylic

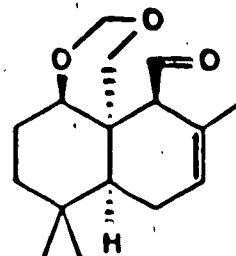
proton appeared at  $\delta$  5.50 as a broad singlet and the methylene protons adjacent to two oxygen atoms were displayed as doublets at  $\delta$  5.12 and 4.80, each with a coupling constant of 7 Hz.

The minor product obtained in 23% yield displayed, in the ir spectrum, a strong absorption at  $3520\text{ cm}^{-1}$  characteristic of hydroxy group. The  $^1\text{H}$  nmr spectrum showed singlets at  $\delta$  6.14 (2H), 3.80 (6H) and 2.30 (3H) due to the orcinol moiety. A broad singlet at  $\delta$  5.66 was due to the vinylic proton and two doublets ( $J = 7\text{ Hz}$  each) observed at  $\delta$  5.18 and 4.92 were attributed to the methylene protons adjacent to two oxygen atoms. Although the molecular ion corresponding to the expected molecular formula was not observed in the mass spectrum, a fragment resulting from the loss of a water molecule was displayed at  $m/z$  398.2467.

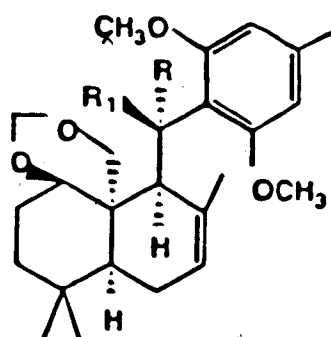
The conversion of the minor alcohol 129 to the corresponding phenol 130 was easily carried out with potassium ethanethiolate in *N,N*-dimethylformamide at  $125^\circ\text{C}$ . The phenol 130 obtained in 80% yield showed the following spectral properties in accord with the assigned structure. A strong absorption at  $3440\text{ cm}^{-1}$  in the ir spectrum suggested the presence of a hydroxyl group. The mass spectrum displayed a fragment at  $m/z$  401.2316 resulting from loss of a proton. In the  $^1\text{H}$  nmr spectrum, singlets were observed at  $\delta$  6.48 (1H), 6.22 (1H), 3.74 (3H) and 2.30 (3H) due to the orcinol portion of the molecule. The methylene protons adjacent to two



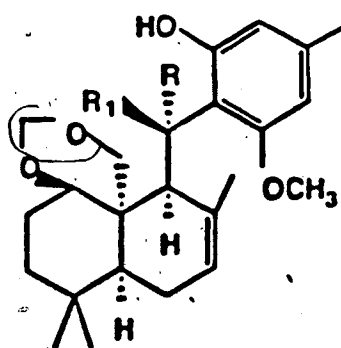
127



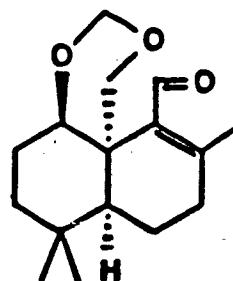
128

R, R<sub>1</sub> = H, OH

129

R, R<sub>1</sub> = H, OH

130



131

oxygen atoms were displayed at  $\delta$  5.20 and 4.82 as doublets each with a coupling constant of 6 Hz.

While the conversion of the minor alcohol 129 to the corresponding phenol 130 was rather straightforward, the attempted demethylation of the major alcohol 129 gave rise to rather unexpected results. Its treatment with potassium ethanethiolate resulted in the formation of two products, one of which was readily identified as orcinol monomethyl ether (107). The other was found to be aldehyde 131 which showed a strong absorption at  $1667\text{ cm}^{-1}$  in the ir spectrum indicating the presence of a conjugated carbonyl group. In the  $^1\text{H}$  nmr spectrum, the signals due to the orcinol moiety and the vinylic proton were absent, whereas an aldehydic proton appeared at  $\delta$  10.34 as a singlet. Furthermore, a methyl singlet was found in the unusually lowfield at  $\delta$  2.18 indicating the migration of the carbon-carbon double bond into conjugation with the carbonyl group. The molecular formula  $\text{C}_{16}\text{H}_{24}\text{O}_3$  was confirmed by the mass spectrum showing a molecular ion peak at 264.1724. The formation of compounds 107 and 131 could be rationalised by invoking a mechanistic pathway similar to that outlined in Scheme 8 for the degradation of 105 to give 106 and 107.

In conclusion, the Diels-Alder approach described in this thesis can be applied rather effectively to the construction of the carbon skeleton of siccanin (1) as demonstrated in the synthesis of isosiccanin methyl ether (109). The application of this approach to the synthesis of



the naturally occurring compound requires effective control of the two inter-related asymmetric centres present in C ring. In order to achieve this, two modifications are under current investigation. One involves the use of alcohol 126 as a potential synthetic intermediate and the other proceeds via the alcohols 129.

## EXPERIMENTAL

### General

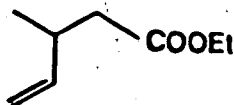
Melting points were recorded on a Kofler hot stage apparatus and are uncorrected. Elemental analyses were performed by the microanalytical laboratory of this department. Infrared (ir) spectra were recorded on a Perkin-Elmer model 457 or Nicolet 7-199 FT-IR spectrophotometer. Proton nuclear magnetic resonance ( $^1\text{H}$  nmr) spectra were recorded on a Bruker WP-80, Bruker WH-200 or Bruker WH-400 spectrometer and were obtained on solutions in deuteriochloroform with tetramethylsilane as internal standard. Carbon-13 nuclear magnetic resonance spectra ( $^{13}\text{C}$  nmr) were recorded on a Bruker WH-200 or Bruker WH-400 spectrometer and were recorded on solutions in deuteriochloroform. The following abbreviations are used: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra (ms) were recorded using an A.E.I. model MS-9, MS-12 or MS-50 mass spectrometer.

### Materials

Flash chromatography developed by Still<sup>45</sup> was used routinely for the purification and separation of the product mixtures. Nitrogen and argon were passed through a purification train of Fieser's solution,<sup>90</sup> concentrated sulfuric acid, and pellets of potassium hydroxide. Solvents

used for reactions were purified as follows: tetrahydrofuran and 1,2-dimethoxyethane by distillation from a blue or purple solution of sodium benzophenone ketyl under an argon atmosphere; dimethyl sulfoxide and *N,N*-dimethylformamide by distillation over calcium hydride at reduced pressure; benzene, diethyl ether and toluene by distillation over lithium aluminium hydride; methylene chloride by distillation over phosphorus pentoxide. Hexane and ethyl acetate for chromatography were distilled prior to use.

*Ethyl 3-methyl-4-pentenoate (57)*

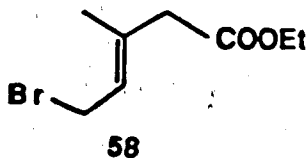


57

A solution of crotyl alcohol (53.3 mL, 0.73 mol), triethyl orthoacetate (600 mL, 3.697 mol) and propionic acid (3.5 g, 0.047 mol) was heated at 138°C for 3 h, with a Dean-Stark apparatus to collect ethyl alcohol produced. The mixture was allowed to cool to room temperature and 750 mL of 1 M aqueous oxalic acid solution was slowly added. After being stirred at room temperature for 4 h, the mixture was extracted with ether. The ethereal extracts were washed with aqueous saturated sodium bicarbonate solution and saturated sodium chloride solution, dried over anhydrous magnesium

sulfate, filtered and concentrated. Distillation of the residue at room temperature at 3 mm pressure gave ester 57 (75.6 g, 72 %) as a yellow oil; ir (neat): 1730 (C=O) and 1640  $\text{cm}^{-1}$  (C=C);  $^1\text{H}$  nmr  $\delta$ : 5.81 (ddd, 1H,  $J = 18$ ,  $J' = 10$ ,  $J'' = 7$  Hz, -CH=), 5.02 (dm, 1H,  $J = 18$  Hz, -CH=CHH), 4.98 (dm, 1H,  $J = 10$  Hz, -CH=CHH), 4.12 (q, 2H,  $J = 7$  Hz, -COOCH<sub>2</sub>-), 2.68 (m, 1H, -CH(CH<sub>3</sub>)-), 2.27 (m, 2H, -CH<sub>2</sub>-), 1.24 (t, 3H,  $J = 7$  Hz, -COOCH<sub>2</sub>CH<sub>3</sub>) and 1.05 (d, 3H,  $J = 7$  Hz, -CH<sub>3</sub>); hrms  $M^+$ : 142.0988 (calcd. for C<sub>8</sub>H<sub>14</sub>O<sub>2</sub>: 142.0992).

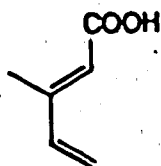
*Ethyl 5-bromo-3-methyl-3-pentenoate (58)*



A solution of pentenoate 57 (66.31 g, 0.46 mol), N-bromosuccinimide (88.08 g, 0.46 mol) and azobisisobutyronitrile (1.6 g, 1 mmol) in carbon tetrachloride (1.5 L) was heated under reflux for 2 h under an argon atmosphere. The resulting mixture was cooled to 0°C. After being stirred at 0°C for 4 h, it was filtered. The residue was washed thoroughly with ice-cold carbon tetrachloride. The filtrate was washed with 1 M sodium thiosulfate solution and water. Drying, filtration and concentration gave the crude product which was distilled at

72°C and 1 mm pressure to give bromo-ester **58** (76.2 g, 75 % yield) as a 4:3 mixture of two geometric isomers; ir (neat): 1735 (C=O) and 1665  $\text{cm}^{-1}$  (C=C);  $^1\text{H}$  nmr  $\delta$ : 5.62 (m, 1H, =CH), 4.11 (q, 2H,  $J = 7$  Hz,  $-\text{COOCH}_2-$ ), 3.96 (d, 2H,  $J = 8$  Hz,  $\text{CH}_2\text{Br}$ ), 3.09, 3.02 (both s, total 2H,  $-\text{CH}_2-\text{COO}-$ ), 1.84, 1.78 (both d, total 3H,  $J = 1$  Hz,  $-\text{CH}_3$ ) and 1.24 (t, 3H,  $J = 7$  Hz,  $-\text{COOCH}_2\text{CH}_3$ ); hrms  $m/z$ : 141.0912 [base peak; calcd. for  $\text{C}_8\text{H}_{13}\text{O}_2$  ( $\text{M}^+-\text{Br}$ ): 141.0914].

*3-Methyl-2,4-pentadienoic acid (60)*

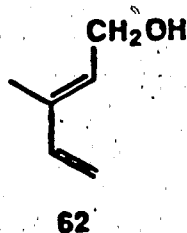


**60**

Bromo-ester **58** (24.8 g, 11.2 mmol) was added to a methanolic (285 mL) solution of sodium hydroxide (14.07 g, 0.35 mol) under an argon atmosphere. The resulting solution was heated under reflux for 24 h, poured into ice-cold water and extracted with ether. The ether extracts were discarded. The aqueous solution was carefully acidified with 1 N hydrochloric acid to pH 1. The solution was then extracted with methylene chloride. The organic extracts were washed with saturated aqueous sodium chloride solution, dried with anhydrous magnesium sulfate, filtered and concentrated to

yield a yellow residue. Column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in hexane, gave pure acid **58** (10 g, 80% yield) as a yellow oil; ir (neat): 1700 (C=O) and 1600  $\text{cm}^{-1}$  (C=C); hrms  $M^+$ : 112.0523 (calcd. for  $\text{C}_6\text{H}_8\text{O}_2$  : 112.0523). The  $^1\text{H}$  nmr spectrum showed two sets of signals integrated to a ratio of 3:1; the major set (*trans*-isomer)  $\delta$ : 6.42 (dd, 1H,  $J = 18$ ,  $J' = 10$  Hz,  $-\text{CH}=\text{CH}_2$ ), 5.78 (bs, 1H,  $=\text{CH}-\text{COOH}$ ), 5.60 (d, 1H,  $J = 18$  Hz,  $=\text{CHH}$ ), 5.40 (d, 1H,  $J = 10$  Hz,  $=\text{CHH}$ ) and 2.26 (d, 3H,  $J = 1$  Hz,  $-\text{CH}_3$ ); the minor set (*cis*-isomer)  $\delta$ : 7.80 (dd, 1H,  $J = 16$ ,  $J' = 10$  Hz,  $-\text{CH}=\text{CH}_2$ ), 5.64 (bs, 1H,  $=\text{CH}-\text{COOH}$ ), 5.48 (d, 1H,  $J = 16$  Hz,  $-\text{CHH}$ ), 5.38 (d, 1H,  $J = 10$  Hz,  $=\text{CHH}$ ), and 2.00 (d, 3H,  $J = 1$  Hz,  $-\text{CH}_3$ ).

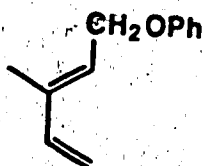
3-Methyl-2,4-pentadien-1-ol (**62**)



At  $0^\circ\text{C}$ , to a suspension of lithium aluminium hydride (2.37 g, 0.06 mol) in anhydrous ether (25 mL), was added dropwise a solution of acid **60** (9.36 g, 0.08 mol) in 15 mL of ether. After the addition (ca. 30 min), the reaction mixture was allowed to warm up to room temperature and was stirred for 8 h under an argon atmosphere. The mixture was

then cooled to 0°C and treated successively with water (2.3 mL), 15% aqueous sodium hydroxide solution (2.3 mL) and water (6.9 mL) again. After being stirred for 15 min, the inorganic salts were removed by filtration and washed with ether. Concentration of the filtrate, followed by column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in hexane, gave the alcohol **62** (4.8 g, 58% yield) as a yellow oil; ir (CHCl<sub>3</sub> cast): 3470 (OH) and 1600 cm<sup>-1</sup> (C=C). The <sup>1</sup>H nmr spectrum showed two sets of signals integrated to a ratio of 3:1; the major set (*trans*-isomer) δ: 6.76 (dd, 1H, J = 12, J' = 6 Hz, -CH=CH<sub>2</sub>), 5.63 (d, 2H, J = 6 Hz, =CHH), 5.48 (d, 1H, J = 12 Hz, =CHH), 4.25 (d, 2H, J = 7 Hz, -CH<sub>2</sub>OH) and 1.75 (d, 3H, J = 1 Hz, -CH<sub>3</sub>); the minor set δ: 6.76 (dd, 1H, J = 10, J' = 6 Hz, -CH=CH<sub>2</sub>) 5.63 (d, 1H, J = 10 Hz, =CHH), 5.48 (d, 1H, J = 6 Hz, =CHH), 4.25 (d, 2H, J = 7 Hz, -CH<sub>2</sub>OH) and 1.80 (d, 3H, J = 1 Hz, =C-CH<sub>3</sub>)

*5-Benzzyloxy-3-methyl-1,3-pentadiene (56)*



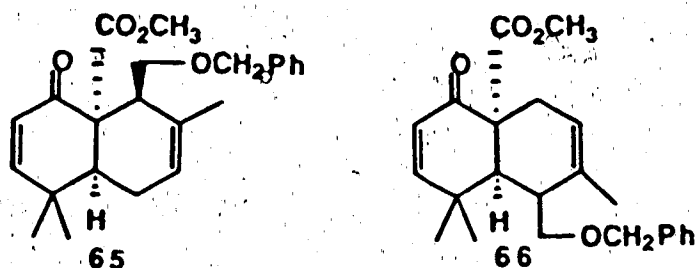
**56**

Sodium hydride (50% dispersion in oil, 1.35 g, 28 mmol) was washed three times with freshly distilled tetrahydrofuran (THF). It was then suspended in 10 mL of

distilled THF and cooled to 0°C under an argon atmosphere. Alcohol 62 (2.3 g, 23 mmol) in 10 mL of THF was slowly added (ca. 10 min) with stirring. After 5 min, benzyl bromide (4.81 g, 23 mmol) was slowly added. The reaction mixture was allowed to warm up to room temperature and stirred at this temperature for 12 h. The mixture was then cooled to 0°C and ice-cold water was added dropwise until the excess of sodium hydride was destroyed. The resulting mixture was extracted with ether. The extracts were washed with 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. The residual oil was subjected to column chromatography on silica gel. Elution with 5% ethyl acetate in hexane gave pure 56 (3.6 g, 83 %) as a yellow liquid; ir (neat): 1600 (C=C) and 1110  $\text{cm}^{-1}$  (C-O-C); hrms m/z: 189.1279 ( $M^+ + 1$ , calcd. for  $\text{C}_{13}\text{H}_{17}\text{O}$ : 189.1279), 91.0549 (base peak, calcd. for  $\text{C}_7\text{H}_7$ : 91.0549). The  $^1\text{H}$  nmr spectrum showed two sets of signals, integrating to a ratio of 3:1; the major set (corresponding to the *trans*-isomer)  $\delta$ : 7.30 (m, 5H, aromatic), 6.40 (dd, 1H,  $J = 10$ ,  $J' = 8$  Hz,  $-\text{CH}=\text{CH}_2$ ), 5.68 (t, 1H,  $J = 8$  Hz,  $-\text{CH}-\text{CH}_2\text{O}-$ ), and 1.74 (bs, 3H,  $-\text{CH}_3$ ); the minor set (corresponding to the *cis*-isomer)  $\delta$ : 7.30 (m, 5H, aromatic), 6.72 (dd, 1H,  $J = 10$ ,  $J' = 8$  Hz,  $-\text{CH}=\text{CH}_2\text{O}-$ ) and 1.86 (bs, 3H,  $-\text{CH}_3$ ).



(1*R*\*, 6*S*\*, 10*S*\*)-10-Benzylloxymethyl-1-carbomethoxy-5,5,9-trimethylbicyclo[4.4.0]deca-3,8-dien-2-one (**65**) and (1*R*\*, 6*S*\*)-7-Benzylloxymethyl-1-carbomethoxy-5,5,8-trimethylbicyclo[4.4.0]deca-3,8-dien-2-one (**66**)



A. Using ether as a solvent:

Enone ester **45** (180 mg, 1 mmol) in 5 mL of dry ether was cooled to  $-20^{\circ}\text{C}$  under an argon atmosphere. To this solution, was added anhydrous ferric chloride<sup>a</sup> (165 mg, 1 mmol) and the resulting mixture was stirred with a mechanical stirrer. Diene **56** (380 mg, 2 mmol) in 10 mL of dry ether was slowly added to the reaction mixture over a period of 10 min. Stirring at  $-20^{\circ}\text{C}$  was continued for 48 h, and the reaction mixture was warmed to room temperature and extracted with ether. The ether extracts were washed with water, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave diene **56** (96 mg, 52% recovered) enriched now with the *cis*-isomer. Further elution

with 10% ethyl acetate in hexane gave the Diels-Alder adduct **65** (199 mg, 84% yield, based on the consumed starting material) as a white solid; m.p. 80-82°C (hexane); ir (CHCl<sub>3</sub> cast): 1728 (ester C=O) and 1688 cm<sup>-1</sup> (enone C=O); hrms M<sup>+</sup>: 368.1962 (calcd. for C<sub>23</sub>H<sub>28</sub>O<sub>4</sub>: 368.1988). <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 6.28 (dd, 1H, J = 11, J' = 2 Hz, -CH=CH-CO-), 5.88 (d, 1H, J = 11 Hz, -CH=CH-CO-), 5.25 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.48 (d, 1H, J = 12 Hz, -O-CHH-Ph), 4.42 (d, 1H, J = 12 Hz, -O-CHH-Ph), 4.16 (dd, 1H, J = 11, J' = 7 Hz, -CHH-OCH<sub>2</sub>Ph), 3.54 (s, 3H, -OCH<sub>3</sub>), 3.52 (dd, 1H, J = 11, J' = 4 Hz, -CHH-OCH<sub>2</sub>Ph), 1.84 (bs, 3H, =C-CH<sub>3</sub>), 1.14 and 1.10 (both s, 3H each, gem-dimethyl); <sup>13</sup>C nmr δ: 196.09, 174.53, 152.61, 138.45, 132.97, 128.10, 127.65, 127.26, 126.74, 119.57, 72.43, 70.26, 60.10, 51.93, 46.65, 37.57, 27.82, 27.64, 27.16 and 20.76. Anal calcd. for C<sub>23</sub>H<sub>28</sub>O<sub>4</sub>: C, 74.95; H, 7.66. Found: C, 74.79; H, 7.46.

Further elution with 10% ethyl acetate in hexane gave the adduct **66** (20 mg, 8% yield, based on the consumed starting material) as a viscous oil; ir (neat): 1745 (ester C=O) and 1679 cm<sup>-1</sup> (enone C=O); hrms M<sup>+</sup>: 368.1987 (calcd. for C<sub>23</sub>H<sub>28</sub>O<sub>4</sub>: 368.1988); <sup>1</sup>H nmr δ: 7.30 (m, 5H, aromatic), 6.59 (d, 1H, J = 9 Hz, -CH=CH-CO-), 5.92 (dd, 1H, J = 9, J' = 2 Hz, -CH=CH-CO-), 5.46 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.50 (s, 2H, -O-CH<sub>2</sub>Ph), 3.70 (s, 3H, -OCH<sub>3</sub>), 3.68 (m, 2H, -CH<sub>2</sub>-OCH<sub>2</sub>Ph), 1.18 and 1.02 (both s, 3H each, gem-dimethyl); <sup>13</sup>C nmr δ: 197.44, 172.85, 157.96, 138.41, 132.27, 128.25, 128.22, 127.57,

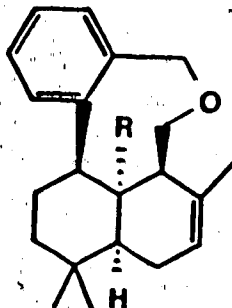
127.46, 123.90, 120.81, 119.79, 72.81, 68.55, 57.39, 52.40, 40.36, 37.56, 35.96, 31.69, 30.42, 24.24 and 23.51.

Final elution with 25% ethyl acetate in hexane gave (62 mg, 34% recovered) of the starting enone ester 45

*B. Using dichloromethane as a solvent.*

Keto ester 45 (860 mg, 4.8 mmol) in 10 mL of dry dichloromethane was cooled to  $-20^{\circ}\text{C}$  under an argon atmosphere. To this solution, was added anhydrous ferric chloride (0.77 g, 4.8 mmol) and the resulting solution was stirred with a mechanical stirrer. Diene 56 (1.80 g, 9.6 mmol) in 15 mL of dichloromethane was slowly added over a period of 5 min and stirring was continued for 24 h. The solution was warmed to room temperature. Water was added to the reaction mixture and the resulting solution was extracted with dichloromethane. The organic solution was washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 5% solution of ethyl acetate in hexane gave diene 56 (0.35 g, 20% recovered). Further elution with 10% ethyl acetate in hexane gave the keto ester 65 (0.97 g, 55% yield) as a white solid. Further elution with 10% ethyl acetate in hexane gave keto ester 66 (0.69 g, 39% yield). Compounds 65 and 66 thus obtained were found to be identical to those obtained as above.

(1*R*\*, 2*S*\*, 6*S*\*, 10*S*\*)-2, 3-(*o*-Benzeno)-8, 12, 12-trimethyl-5-oxatricyclo[9.3.1.0<sup>6,12</sup>]pentadeca-8-ene (68)

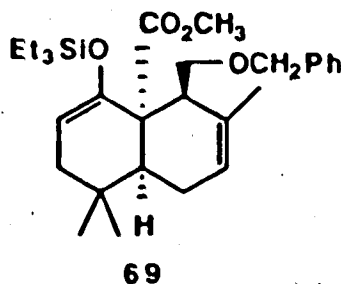


68

Keto ester 65 (100 mg, 0.26 mmol) was dissolved in 3 mL of freshly distilled dichloromethane under an argon atmosphere at 0°C. To this solution, triethylsilane (ca. 1 mL) was added and the resulting solution was stirred for 5 min. Gaseous boron trifluoride was bubbled through the reaction mixture for 5 min. The reaction mixture was stirred for an additional period of 5 min and water was added. The resulting solution was extracted with dichloromethane and the extracts were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, elution with 5% ethyl acetate in hexane, gave pure ether 68 (0.037 g, 39% yield); ir (CHCl<sub>3</sub> cast): 1725 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 354.2200 (calcd. for C<sub>23</sub>H<sub>30</sub>O<sub>3</sub>: 354.2215); <sup>1</sup>H nmr δ: 7.00 (m, 4H, aromatic), 5.70 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.68 (s, 2H, -

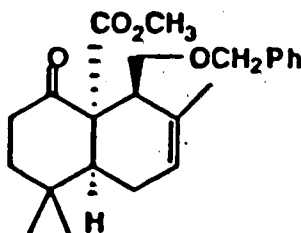
OCH<sub>2</sub>Ph), 3.66 (s, 3H, -OCH<sub>3</sub>), 1.80 (bs, 3H, -C-CH<sub>3</sub>), 1.00 and 0.92 (each s, 3H each, gem-dimethyl).

(1R\*, 6S\*, 10S\*)-10-Benzyloxymethyl-1-carbomethoxy-5,5,9-trimethyl-2-triethylsilyloxybicyclo[4.4.0]deca-2,8-diene (**69**)



Finely divided keto-ester **65** (4.61 g, 12 mmol) was dissolved in 15 mL of freshly distilled benzene under an argon atmosphere. To this solution, triethylsilane (7.28 g, 0.06 mol) and tris-(triphenylphosphine)rhodium(I) chloride (0.15 g, 0.6 mmol) were added. The mixture was stirred at room temperature for 24 h. At the end of the reaction period, the mixture was diluted with hexane and concentrated to give crude silyl enol ether **69**. Column chromatography on silica gel, eluting with a solution of 1% ethyl acetate in hexane, gave pure **69** (6.05 g, 100% yield) as a colourless oil; ir (neat): 1720 (C=O) and 1660 cm<sup>-1</sup> (C=C); hrms M<sup>+</sup>: 484.3013 (calcd. for C<sub>29</sub>H<sub>44</sub>O<sub>4</sub>Si: 484.3009). <sup>1</sup>H nmr δ: 7.30 (m, 5H, aromatic), 5.24 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.50 (m, 1H, -O-C=CH-) and 3.72 (s, 3H, -OCH<sub>3</sub>).

(1*R*\*, 6*S*\*, 10*S*\*)-10-Benzoyloxymethyl-1-carbomethoxy-5,5,9-trimethylbicyclo[4.4.0]deca-8-en-2-one (70)

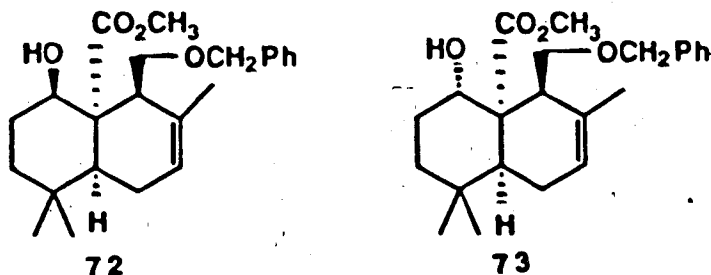


70

Pure silyl-enol ether **69** (6.05 g, 12 mmol) was dissolved in 20 mL of distilled tetrahydrofuran, and tetra-*n*-butylammonium fluoride (2.61 g, 12 mmol) was added dropwise to the resulting solution. The reaction mixture was stirred at room temperature for 4 h, after which period it was diluted with hexane and then concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure keto-ester **70** (4.6 g, 100% yield) as a white solid; m.p. 40-42°C (hexane); ir (CHCl<sub>3</sub> cast): 1720 (ester C=O) and 1715 cm<sup>-1</sup> (ketone C=O); hrms M<sup>+</sup>: 370.2144 (calcd. for C<sub>23</sub>H<sub>30</sub>O<sub>4</sub>: 370.2144); <sup>1</sup>H nmr δ: 7.30 (m, 5H, aromatic), 5.30 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.46 (d, 1H, J = 13 Hz, -O-CHHPh), 4.40 (d, 1H, J = 13 Hz, -OCHHPh), 4.00 (dd, 1H, J = 11, J' = 7 Hz, -CHH-OCH<sub>2</sub>Ph), 3.60 (s, 3H, -OCH<sub>3</sub>), 3.44 (dd, 1H, J = 11, J' = 7 Hz, -CHH-OCH<sub>2</sub>Ph), 2.94 (m, 1H, -CHH-CO-), 2.70 (bs, 1H, -CHH-CO-), 1.80 (bs, 3H, =C-CH<sub>3</sub>), 1.14 and 0.90 (each s, 3H each, gem-dimethyl); <sup>13</sup>C nmr δ: 207.85, 174.69, 138.33, 133.49, 128.03, 127.50, 127.19,

119.44, 72.30, 69.59, 63.13, 51.83, 49.07, 46.53, 37.08, 35.82, 34.01, 27.97, 27.74, 25.14 and 20.63. Anal. Calcd. for  $C_{23}H_{30}O_4$ : C, 74.55%; H, 8.17. Found C, 74.46%; H, 8.23.

(1*R*\*, 2*R*\*, 6*S*\*, 10*S*\*)-10-Benzyloxymethyl-1-carbomethoxy-5,5,9-trimethylbicyclo[4.4.0]deca-8-en-2-ol (**72**) and (1*R*\*, 2*S*\*, 6*S*\*, 10*S*\*)-10-Benzyloxymethyl-1-carbomethoxy-5,5,9-trimethylbicyclo[4.4.0]deca-8-en-2-ol (**73**)

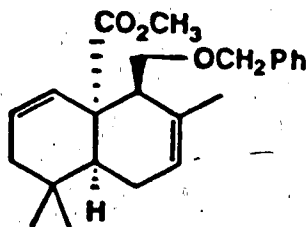


Keto ester **70** (160 mg, 4.4 mmol) was dissolved in 5 mL of distilled ether and the solution was cooled to 0°C under an argon atmosphere. To this ice-cold solution, diisobutylaluminium hydride (180 mg, 13.2 mmol) was slowly added. The reaction mixture was stirred at 0°C for 12 h and then ice-cold water was slowly added until evolution of hydrogen ceased. The resulting solution was extracted with ether. The extracts were washed with 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave alcohol **72** (57 mg, 35% yield)

as a colourless oil; ir (CHCl<sub>3</sub> cast): 3520 (OH) and 1717 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 372.2293 (calcd. for C<sub>23</sub>H<sub>32</sub>O<sub>4</sub>: 372.2300); <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 5.32 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.46 (d, 1H, J = 12 Hz, -O-CHHPh), 4.40 (d, 1H, J = 12 Hz, -O-CHHPh), 4.03 (dd, 1H, J = 8, J' = 5 Hz, -CHH-OCH<sub>2</sub>Ph), 3.78 (m, 1H, -CHOH), 3.62 (s, 3H, -OCH<sub>3</sub>), 3.46 (dd, 1H, J = 8, J' = 5 Hz, -CHH-OCH<sub>2</sub>Ph), 1.86 (s, 3H, =C-CH<sub>3</sub>), 1.18 and 0.96 (each s, 3H each, gem-dimethyl). Further elution with 7% ethyl acetate in hexane gave alcohol 73 (47 mg, 28% yield) as a colourless oil; ir (CHCl<sub>3</sub> cast): 3560 (O-H) and 1705 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 372.2292 (calcd. for C<sub>23</sub>H<sub>32</sub>O<sub>4</sub>: 372.2201); <sup>1</sup>H nmr δ: 7.28 (m, 5H, aromatic), 5.40 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.46 (d, 1H, J = 11 Hz, -O-CHHPh), 4.40 (d, 1H, J = 11 Hz, -O-CHHPh), 3.84 (dd, 1H, J = 9, J' = 3 Hz, -CHH-OCH<sub>2</sub>Ph), 3.60 (m, 1H, -CHOH), 3.58 (s, 3H, -OCH<sub>3</sub>), 3.52 (dd, 1H, J = 9, J' = 5 Hz, -CHH-OCH<sub>2</sub>Ph), 1.84 (s, 3H, =C-CH<sub>3</sub>), 0.92 and 0.84 (each s, 3H each, gem-dimethyl).



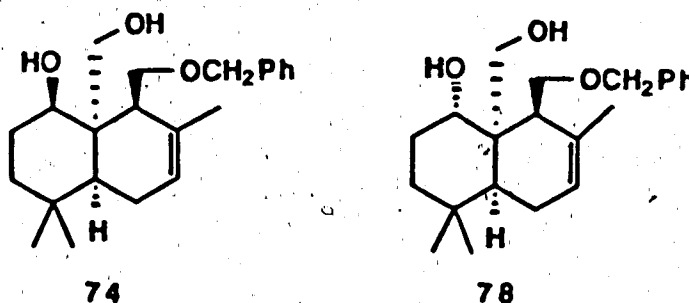
(1*R*\*, 6*S*\*, 10*S*\*)-10-Benzylloxymethyl-1-carbomethoxy-5,5,9-trimethylbicyclo[4.4.0]deca-2,8-diene (77)



77

Alcohol 73 (80 mg, 0.22 mmol) was dissolved in 5 mL of distilled pyridine under an argon atmosphere. To this solution, phosphorous oxychloride (0.03 mL, 0.33 mmol) was added. The resulting solution was stirred at 80°C. After 8 h at this temperature, the reaction mixture was cooled to room temperature and diluted with water. The resulting solution was extracted with ether, and the ethereal extracts were washed with 1 N hydrochloric acid and a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a solution of 5% ethyl acetate in hexane, gave pure diene 77 (50 mg, 69% yield); ir (CHCl<sub>3</sub> cast): 1725 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 354.2210 (calcd. for C<sub>23</sub>H<sub>30</sub>O<sub>3</sub>: 354.2195); <sup>1</sup>H nmr δ: 7.22 (m, 5H, aromatic), 5.78 (bd, 1H, J = 6 Hz, -CH<sub>2</sub>CH=CH-), 5.68 (m, 1H, -CH<sub>2</sub>CH=CH-), 5.40 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.38 (s, 2H, -OCH<sub>2</sub>Ph), 3.60 (s, 3H, -OCH<sub>3</sub>), 1.64 (bs, 3H, =C-CH<sub>3</sub>), 0.94 and 0.88 (each s, 3H each, gem-dimethyl).

(1R\*,2R\*,6S\*,10S\*)-10-Benzyloxymethyl-1-hydroxymethyl-5,5,9-trimethylbicyclo[4.4.0]deca-8-ene-2-ol (74) and (1R\*,2R\*,6S\*,10S\*)-10-Benzyloxymethyl-1-hydroxymethyl-5,5,9-trimethyl bicyclo[4.4.0]deca-8-ene-2-ol (78)



A. Using Sodium Bis(methoxyethoxy)aluminium Hydride (Red-Al) as the Reducing Reagent

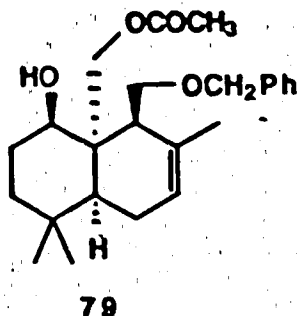
Keto ester 70 (5.90 g, 15.9 mmol) was dissolved in 25 mL of dry ether under an argon atmosphere. The solution was cooled to 0°C and Red-Al (15.9 g, 79 mmol) in 25 mL of dry ether was added slowly (ca. 5 min). After being stirred at room temperature for 7 h, the reaction mixture was cooled to 0°C and ice-cold water was added cautiously until all the excess of Red-AL was destroyed. The resulting mixture was extracted with ether. The ether solution was washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered, and concentrated. Column chromatography of the residue on

silica gel, eluting with 20% ethyl acetate in hexane, gave pure diol **78** (530 mg, 9.7% yield); ir (CHCl<sub>3</sub> cast): 3424 (O-H) and 1363 cm<sup>-1</sup> (CH<sub>3</sub>); hrms m/z: 344.2397 (M<sup>+</sup>, calcd. for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>: 344.2351) and 326.2256 (M<sup>+</sup>-18, calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>: 326.2251); <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 5.80 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.80 (d, 1H, J = 12 Hz, -O-CHHPh), 4.62 (d, 1H, J = 12 Hz, -O-CHHPh), 3.82 (d, 1H, J = 10 Hz, -CHHOH), 3.72 (d, 1H, J = 10 Hz, -CHHOH), 3.32 (dd, 1H, J = 11, J' = 3 Hz, -CHH-OCH<sub>2</sub>Ph), 3.17 (dd, 1H, J = 11, J' = 3 Hz, -CHH-OCH<sub>2</sub>Ph), 3.00 (bt, 1H, J = 9 Hz, -CHOH), 1.80 (t, 3H, J = 0.5 Hz, -C-CH<sub>3</sub>), 0.84 and 0.76 (each s, 3H each, gem-dimethyl). Further elution with 20% ethyl acetate in hexane, gave pure diol **74** as a white solid (3.90 g, 71% yield); m.p. 90-92°C (hexane); ir (CHCl<sub>3</sub> cast): 3400 (O-H) and 1385 cm<sup>-1</sup> (CH<sub>3</sub>); hrms M<sup>+</sup>: 344.2364 (calcd. for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>: 344.2356); <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 5.44 (bs, 1H, CH<sub>3</sub>-C=CH), 4.59 (d, 1H, J = 12 Hz, -O-CHHPh), 4.57 (d, 1H, J = 12 Hz, -O-CHHPh), 4.10 (t, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>Ph), 3.78 (dd, 1H, J = 10, J' = 3 Hz, -CHH-OCH<sub>2</sub>Ph), 3.68 (d, 1H, J = 12 Hz, -CHHOH), 3.60 (m, 1H, -CHOH), 3.36 (d, 1H, J = 12 Hz, -CHHOH), 1.76 (bs, 3H, -C-CH<sub>3</sub>), 0.94 and 0.78 (each s, 3H each, gem-dimethyl); <sup>13</sup>C nmr δ: 136.49, 130.10, 128.39, 128.04, 123.39, 77.81, 76.37, 73.11, 69.28, 65.64, 45.05, 41.49, 41.12, 38.32, 33.31, 32.99, 29.54, 28.59, 24.61, 24.13, 22.96 and 15.12. Anal Calcd. for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>: C, 76.69; H, 9.37; Found: C, 76.71; H, 9.40.

*B. Using Diisobutylaluminium Hydride (Dibal-H) as the Reducing Reagent*

Keto ester **70** (200 mg, 0.54 mmol) was dissolved in 5 mL of freshly distilled ether, and cooled to 0°C. To this solution, Dibal-H (380 mg, 2.7 mmol) in 10 mL of ether was added dropwise and the solution was gradually warmed up to room temperature. After stirring at room temperature for 10 h under an argon atmosphere, the solution was cooled again to 0°C. Water was slowly added to destroy the unreacted reducing reagent, and the resulting solution was extracted with ether. Ether extracts were washed with an aqueous solution of 1 N hydrochloric acid solution and a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 25% solution of ethyl acetate in hexane, gave pure diol **74** (137 mg, 74% yield), which was shown to be identical in all respects to that obtained previously.

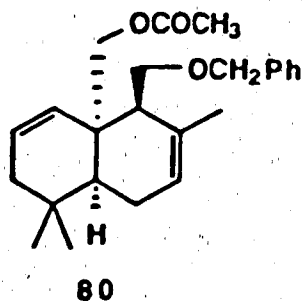
(1*R*\*,2*R*\*,6*S*\*,10*S*\*)-1-Acetoxymethyl-10-benzyloxymethyl-5,5,9-trimethylbicyclo[4.4.0]deca-8-en-2-ol (79)



Diol 74 (140 mg, 3.9 mmol) was dissolved in 2 mL of distilled pyridine at room temperature. 4-(*N,N*-Dimethylamino)pyridine (10 mg) and acetic anhydride (0.048 g, 4.7 mmol) were added to the solution. The reaction mixture was stirred at 80°C under an argon atmosphere for 12 h. It was then cooled to 0°C and an aqueous solution of 1 N hydrochloric acid was added. The resulting solution was extracted with ether, washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 15% ethyl acetate in hexane, gave pure acetate 79 (180 mg, 77% yield) as a white solid; m.p. 80-82°C (hexane); ir (CHCl<sub>3</sub> cast): 3420 (O-H) and 1741 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 386.2456 (calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>: 386.2457); <sup>1</sup>H nmr δ: 7.36 (m, 5H, aromatic), 5.55 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.58 (d, 1H, J= 11hz, -O-CHHPh), 4.54 (d, 1H, J= 11 Hz, -O-CHHPh), 4.18 (d, 1H, J = 11 Hz, -CHH-OCOCH<sub>3</sub>), 3.92 (d, 1H, J = 11 Hz, -CHH-OCOCH<sub>3</sub>), 3.60 (bs, 1H, -CHOH), 2.12

(s, 3H, -CO-CH<sub>3</sub>), 1.72 (s, 3H, -C-CH<sub>3</sub>), 1.06 and 0.94 (each s, 3H each, gem-dimethyl).

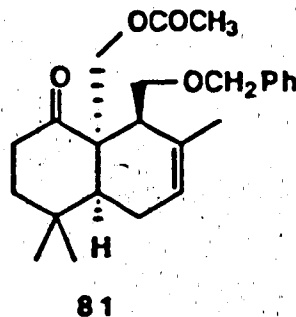
(1*R*\*, 6*S*\*, 10*S*\*)-1-Acetoxymethyl-10-benzoyloxymethyl-5,5,9-trimethylbicyclo[4.4.0]deca-2,8-diene (**80**)



Acetate **79** (30 mg, 0.083 mmol) was dissolved in 1 mL of pyridine under an argon atmosphere. Phosphorus oxychloride (25 mg, 0.17 mmol) was added. The reaction mixture was heated at 80°C for 6 h. Water was added to the reaction mixture after it was cooled to room temperature. The resulting solution was extracted with ether and the extracts were washed with an aqueous solution of 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave diene **80** (16 mg, 53% yield) as a yellow oil; ir (CHCl<sub>3</sub> cast): 1741 (C=O), and 1235 cm<sup>-1</sup> (-C-O-); hrms m/z: 308.2149 (M<sup>+</sup>- 60, calcd. for C<sub>22</sub>H<sub>28</sub>O: 308.2140); cims m/z: 386 (M + NH<sub>4</sub><sup>+</sup>); <sup>1</sup>H nmr δ: 7.36 (m, 5H,

aromatic), 5.82 (m, 1H,  $-\text{CH}_2-\text{CH}=\text{C}-$ ), 5.68 (d, 1H,  $J = 12$  Hz,  $\text{CH}_2-\text{CH}=\text{CH}-$ ), 5.58 (bs, 1H,  $\text{CH}_3-\text{C}=\text{CH}-$ ), 4.50 (d, 1H,  $J = 11$  Hz,  $-\text{OCH}_2\text{Ph}$ ), 4.44 (d, 1H,  $J = 11$  Hz,  $-\text{OCH}_2\text{Ph}$ ), 3.60 (dd, 1H,  $J = 10, J' = 3$  Hz,  $-\text{CHH}-\text{OCH}_2\text{Ph}$ ), 3.38 (t, 1H,  $J = 10$  Hz,  $-\text{CHH}-\text{OCH}_2\text{Ph}$ ), 2.08 (s, 3H,  $-\text{CO}-\text{CH}_3$ ), 1.86 (s, 3H,  $-\text{C}-\text{CH}_3$ ), 1.00 and 0.84 (each s, 3H each, gem-dimethyl).

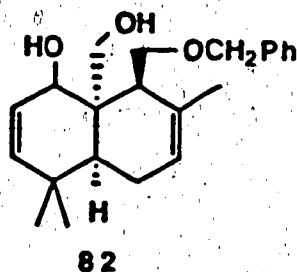
(1*R*\*, 6*S*\*, 10*S*\*)-1-Acetoxymethyl-10-benzyloxymethyl-5,5,9-trimethylbicyclo[4.4.0]deca-8-en-2-one (**81**)



To a slurry of pyridinium chlorochromate (300 mg, 14 mmol) in 15 mL of dichloromethane, was added a solution of acetate **79** (118 mg, 4.5 mmol) in 5 mL of dichloromethane at room temperature. The mixture was stirred at room temperature for 4 h. It was then diluted with ether, filtered over magnesium sulfate and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave ketone **81** (90 mg, 79% yield) as a viscous oil; ir ( $\text{CHCl}_3$  cast): 1745 (ester  $\text{C}=\text{O}$ ) and 1690  $\text{cm}^{-1}$  (ketone  $\text{C}=\text{O}$ ); hrms  $M^+$ : 384.2296 (calcd. for  $\text{C}_{24}\text{H}_{32}\text{O}_4$ : 384.2301);  $^1\text{H}$  nmr  $\delta$ :

7.30 (m, 5H, aromatic), 5.56 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.46 (d, 1H, J = 12 Hz, -O-CHHPH), 4.38 (d, 1H, J = 12 Hz, -O-CHHPH), 4.16 (d, 1H, J = 10 Hz, -CHH-OCOCH<sub>3</sub>), 3.88 (d, 1H, J = 10 Hz, -CHH-OCOCH<sub>3</sub>), 3.50 (dd, 1H, J = 8, J' = 4 Hz, -CHH-OCH<sub>2</sub>Ph), 3.32 (t, 1H, J = 8 Hz, -CHH-OCH<sub>2</sub>Ph), 2.02 (s, 3H, -COCH<sub>3</sub>), 1.82 (s, 3H, =C-CH<sub>3</sub>), 1.00 and 0.82 (each s, 3H each, gem-dimethyl).

(1R\*, 6S\*, 10S\*)-10-Benzyloxymethyl-1-hydroxymethyl-5,5,9-trimethylbicyclo[4.4.0]deca-3,8-dien-2-ol (82)

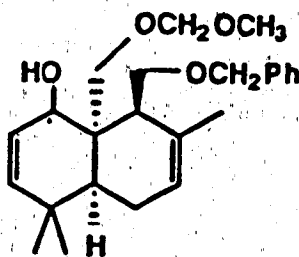


To a solution of the Diels-Alder adduct **65** (1.47 g, 4 mmol) in 15 mL of dry ether at 0°C, was added Red-Al (4.05 g, 0.02 mol) in 10 mL of ether. The reaction mixture was warmed up to 27°C. After being stirred at this temperature for 5 h, the reaction mixture was cooled again to 0°C. Ice-cold water was added slowly to destroy excess Red-Al and the resulting solution was extracted with ether. Ethereal extracts were washed with an aqueous solution of 1 N hydrochloric acid and a saturated aqueous solution of sodium



chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 20% ethyl acetate in hexane, gave pure diol **82** (1.02 g, 74% yield) as a white solid; ir (CHCl<sub>3</sub> cast): 3400 cm<sup>-1</sup> (O-H); cims m/z: 343 (M<sup>+</sup>+1); <sup>1</sup>H nmr δ: 7.28 (m, 5H, aromatic), 5.56 (dd, 1H, J = 8, J' = 2 Hz, -CH=CH-CHOH-), 5.40 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.26 (dd, 1H, J = 8, J' = 1 Hz, -CH=CH-CHOH-), 4.48 (d, 1H, J = 12 Hz, -O-CHHPh), 4.38 (d, 1H, J = 12 Hz, -O-CHHPh), 4.26 (m, 1H, -CHOH), 4.13 (d, 1H, J = 10 Hz, -CHHOH), 3.70 (t, J = 10 Hz, -CHH-OCH<sub>2</sub>Ph), 3.50 (dd, 1H, J = 10, J' = 4 Hz, -CHH-OCH<sub>2</sub>Ph), 3.38 (d, 1H, J = 10 Hz, -CHHOH), 1.72 (bs, 3H, =C-CH<sub>3</sub>), 0.98 and 0.82 (each s, 3H each, gem-dimethyl). Anal Calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>3</sub>: C, 77.14; H, 8.83; Found: C, 76.74; H, 8.93.

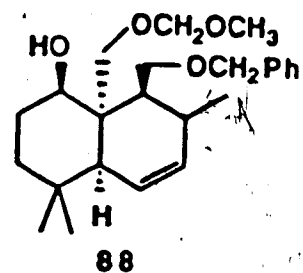
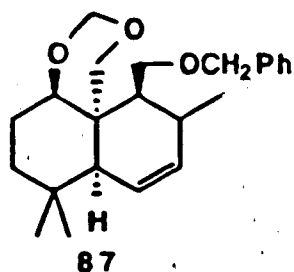
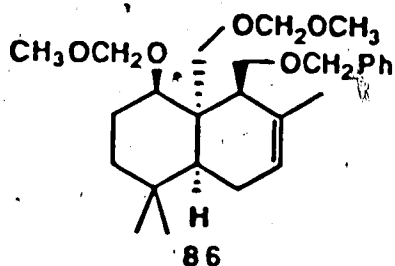
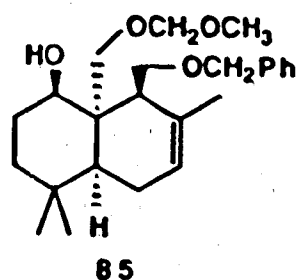
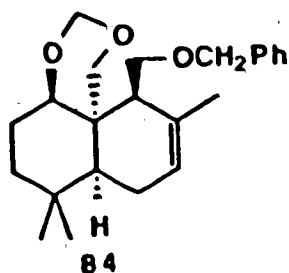
(1R\*,6S\*,10S\*)-10-Benzyloxymethyl-1-methoxymethoxymethyl-5,5,9-trimethylbicyclo[4.4.0]dec-3,8-dien-2-ol (**83**)

**83**

Sodium hydride (50% dispersion in oil, 118 mg, 2.4 mmol) was washed three times with freshly distilled 1,2-

dimethoxyethane and was then suspended in 10 mL of dry 1,2-dimethoxyethane under an argon atmosphere. Diol **82** (170 mg, 0.5 mmol) in 5 mL of 1,2-dimethoxyethane was slowly added to the suspension. The resulting mixture was stirred at 0°C for 5 min. Chloromethyl methyl ether (0.05 mL, 0.6 mmol) was added and the reaction mixture was gradually warmed up to room temperature. The resulting solution was stirred for 1 h, and cooled again to 0°C. Water was added to destroy unreacted sodium hydride. The resulting solution was extracted with ether, washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 10% solution of ethyl acetate in hexane, gave pure ether **83** (120 mg, 61% yield); ir (CHCl<sub>3</sub> cast): 3420 cm<sup>-1</sup> (OH); hrms M<sup>+</sup>: 386.2451 (calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>: 386.2457); <sup>1</sup>H nmr δ: 7.32 (s, 5H, aromatic), 5.70 (dm, 1H, J = 10 Hz, -CH=CH-CHOH), 5.48 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.30 (dd, 1H, J = 10, J' = 2 Hz, -CH=CH-CHOH), 4.62 (s, 2H, -OCH<sub>2</sub>Ph), 3.16 (s, 3H, -OCH<sub>3</sub>), 1.72 (bs, 3H, =C-CH<sub>3</sub>), 1.04 and 0.86 (each s, 3H each, gem-dimethyl).

(1*R*\*,2*R*\*,6*S*\*,10*S*\*)-10-Benzyloxymethyl-1-methoxymethoxy  
methyl-5,5,9-trimethyl bicyclo[4.4.0]dec-8-en-2-ol (85)



#### A. Using Sodium Hydride as a Base

Sodium hydride (50% dispersion in oil, 550 mg; 0.01 mol) was washed twice with freshly distilled 1,2-dimethoxyethane under an argon atmosphere, suspended in 10 mL of dry 1,2-dimethoxyethane and cooled to  $-10^{\circ}\text{C}$ . Diol 74 (1.20 g, 3.5 mmol) in 5 mL of 1,2-dimethoxyethane was then slowly added and the resulting mixture was stirred for 10 min. Chloromethyl methyl ether (0.32 mL, 4.2 mmol) was slowly added. After 30 min, water was slowly added to the reaction mixture and the temperature was slowly raised to room

temperature. The resulting solution was extracted with ether. The extracts were washed with a saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave acetal **84** (490 mg, 59% yield); ir (CHCl<sub>3</sub> cast): 1106 cm<sup>-1</sup> (C-O-C); hrms M<sup>+</sup>: 356.2355 (calcd. for C<sub>23</sub>H<sub>32</sub>O<sub>3</sub>: 356.2352); <sup>1</sup>H nmr δ: 7.34 (m, 5H, aromatic), 5.34 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.14 (d, 1H, J = 6 Hz, -O-CHH-O-), 4.80 (d, 1H, J = 6 Hz, -OCHHO-), 4.56 (d, 1H, J = 12 Hz, -OCHHPh), 4.50 (d, 1H, J = 12 Hz, -OCHHPh), 4.25 (dd, 1H, J = 10, J' = 4 Hz, -CHH-OCH<sub>2</sub>Ph), 3.92 (dd, 1H, J = 10, J' = 6 Hz, -CHH-OCH<sub>2</sub>Ph), 3.78 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.36 (dd, 1H, J = 13, J' = 2 Hz, -OCH<sub>2</sub>-OCH-), 3.13 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O), 1.81 (bs, 3H, =C-CH<sub>3</sub>), 0.86 and 0.78 (each s, 3H each, gem-dimethyl). Further elution with 7% ethyl acetate gave ether **86** (0.14 g, 9% yield); ir (CHCl<sub>3</sub> cast): 1147 and 1109 cm<sup>-1</sup> (C-O-C); cims m/z: 450 (M + NH<sub>4</sub><sup>+</sup>); hrms m/z: 326.2242 (M<sup>+</sup> - 106, calcd. for C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>: 326.2246); <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 5.32 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.70 (d, 1H, J = 12 Hz, -O-CHH-Ph), 4.64 (d, 1H, J = 12 Hz, -O-CHH-Ph), 4.62, 4.52 (each s, 2H each, 2 x -O-CH<sub>2</sub>-O-), 4.40 (dd, 1H, J = 9, J' = 2 Hz, -CHH-OCH<sub>2</sub>Ph), 3.78 (dd, 1H, J = 11, J' = 6 Hz, -CH-OCH<sub>2</sub>O-), 3.58 (t, 1H, J = 9 Hz, -CHH-OCH<sub>2</sub>Ph), 3.48 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.36, 3.34 (each s, 3H each, 2 x -OCH<sub>3</sub>), 3.29 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 1.79 (s, 3H, =C-CH<sub>3</sub>), 0.92 and 0.72 (each s, 3H each, gem-dimethyl). Further

elution with 10% ethyl acetate in hexane gave hydroxy ether **85** (351 mg, 26% yield) as a white solid; m.p. 55-56°C (hexane);  $^1\text{H}$  nmr  $\delta$ : 7.32 (m, 5H, aromatic), 5.49 (bs, 1H,  $\text{CH}_3\text{-C=CH-}$ ), 4.60 (d, 1H,  $J = 9$  Hz,  $\text{-O-CHH-Ph}$ ), 4.58 (d, 1H,  $J = 9$  Hz,  $\text{-O-CHH-Ph}$ ), 4.54 (d, 1H,  $J = 7$  Hz,  $\text{-O-CHH-O-}$ ), 4.50 (d, 1H,  $J = 7$  Hz,  $\text{-O-CHH-O-}$ ), 4.03 (dd, 1H,  $J = 10$ ,  $J' = 7$  Hz,  $\text{-CHH-OCH}_2\text{Ph}$ ), 3.74 (dd, 1H,  $J = 10$ ,  $J' = 2$  Hz,  $\text{-CHH-OCH}_2\text{Ph}$ ), 3.64 (d, 1H,  $J = 10$  Hz,  $\text{-CHH-OCH}_2\text{O-}$ ), 3.32 (s, 3H,  $\text{-OCH}_3$ ), 3.24 (d, 1H,  $J = 10$  Hz,  $\text{-CHH-OCH}_2\text{-O-}$ ), 1.70 (bs, 3H,  $\text{-C-CH}_3$ ), 1.00 and 0.82 (each s, 3H each, *gem*-dimethyl); ir ( $\text{CHCl}_3$  cast): 3460 (OH), 1096 and 1041  $\text{cm}^{-1}$  (C-O-C); hrms  $M^+$ : 388.2614 (calcd. for  $\text{C}_{24}\text{H}_{36}\text{O}_4$ : 388.2614);  $^{13}\text{C}$  nmr  $\delta$ : 137.05, 131.02, 128.43, 128.01, 127.90, 124.23, 96.86, 73.35, 72.81, 71.42, 68.78, 55.41, 44.94, 44.12, 39.57, 35.03, 33.33, 32.09, 27.89, 27.20, 25.45 and 22.59. Anal Calcd. for  $\text{C}_{24}\text{H}_{36}\text{O}_4$ : C, 74.17; H, 9.34; Found: C, 73.86; H, 9.21. On increasing the polarity of the eluent to 20% ethyl acetate in hexane gave acetal **87** (80 mg, 7% yield) was obtained; ir (neat): 1110  $\text{cm}^{-1}$  (C-O-C); hrms  $M^+$ : 356.2344 (calcd. for  $\text{C}_{23}\text{H}_{32}\text{O}_3$ : 356.2351);  $^1\text{H}$  nmr  $\delta$ : 7.28 (m, 5H, aromatic), 5.52 (m, 1H,  $\text{CH}_3\text{CH-CH=CH-}$ ), 5.42 (bd, 1H,  $J = 9$  Hz,  $\text{CH}_3\text{CH-CH=CH-}$ ), 5.15 (d, 1H,  $J = 6$  Hz,  $\text{-OCHHO-}$ ), 4.84 (d, 1H,  $J = 6$  Hz,  $\text{-OCHHO-}$ ), 4.50 (d, 1H,  $J = 11$  Hz,  $\text{-OCHHPh}$ ), 4.46 (d, 1H,  $J = 11$  Hz,  $\text{-OCHHPh}$ ), 1.19 (d, 3H,  $J = 7$  Hz,  $\text{-CH-CH}_3$ ), 0.99 and 0.74 (each s, 3H each, *gem*-dimethyl). On further elution hydroxy ether **88** (70 mg, 5% yield) was isolated; ir (neat): 3500  $\text{cm}^{-1}$  (OH); hrms  $M^+$ : 388.2606 (calcd. for  $\text{C}_{24}\text{H}_{36}\text{O}_4$ :

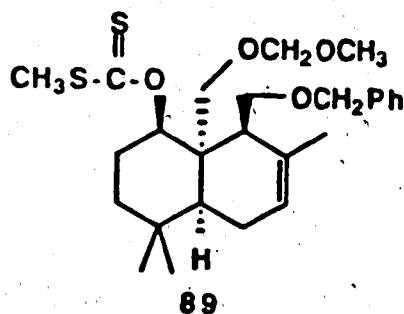
388.2614);  $^1\text{H}$  nmr  $\delta$ : 7.26 (m, 5H, aromatic), 5.56 (m, 1H,  $\text{CH}_3\text{CH}=\text{CH}-$ ), 5.38 (bd, 1H,  $J = 8$  Hz  $\text{CH}_3\text{CH}=\text{CH}-$ ), 4.60 (d, 1H,  $J = 11$  Hz,  $-\text{OCHHPH}$ ), 4.56 (d, 1H,  $J = 11$  Hz,  $-\text{OCHHPH}$ ), 4.46 (d, 1H,  $J = 7$  Hz,  $-\text{OCHHO}-$ ), 4.44 (d, 1H,  $J = 7$  Hz,  $-\text{OCHHO}-$ ), 3.83 (m, 2H,  $-\text{CH}_2-\text{OCH}_2\text{Ph}$ ), 3.64 (d, 1H,  $J = 8$  Hz,  $-\text{CHH}-\text{OCH}_2\text{O}-$ ), 3.35 (s, 3H,  $-\text{OCH}_3$ ), 3.23 (d, 1H,  $J = 4$  Hz,  $-\text{CHOH}$ ), 3.09 (d, 1H,  $J = 8$  Hz,  $-\text{CHH}-\text{OCH}_2\text{O}-$ ), 1.13 (d, 3H,  $J = 7$  Hz,  $-\text{CH}-\text{CH}_3$ ), 1.00 and 0.76 (each s, 3H each, *gem*-dimethyl).

*B. Using Potassium Hydride as a Base.*

Potassium hydride (35% dispersion in oil, 405 mg, 0.01 mol) was washed twice with freshly distilled 1,2-dimethoxyethane under an argon atmosphere. It was then suspended in 10 mL of 1,2-dimethoxyethane and cooled to  $-10^\circ\text{C}$ . Diol 74 (694 mg, 0.002 mol) in 2 mL of 1,2-dimethoxyethane was then slowly added and the mixture was stirred for 10 min. Chloromethyl methyl ether (195 mg, 2.4 mmol) was added. After 15 min, water was slowly added to the reaction mixture and the temperature was gradually raised to room temperature. The resulting solution was extracted with ether and the extracts were washed with an aqueous solution of saturated sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane gave ether 86 (178 mg, 21% yield) as a colourless

paste, identical in all respects to the one described above. Further elution with 10% ethyl acetate in hexane gave hydroxy ether 85 (540 mg, 70% yield) as a white solid. The compound thus obtained was shown to possess the same physical properties as the one described previously.

(1*R*\*,2*S*\*,6*S*\*,10*R*\*)-2-Benzylloxymethyl-10-methylmercapto thionocarbonyloxy-1-methoxymethoxymethyl-3,7,7-trimethyl bicyclo[4.4.0]dec-3-ene (89)



#### A. 1,2-Dimethoxyethane as Solvent

Sodium hydride (50% dispersion in oil, .470 mg, 0.01 mol) was washed 3 times with freshly distilled 1,2-dimethoxyethane. It was then suspended in 10 mL of 1,2-dimethoxyethane under an argon atmosphere and cooled to 0°C. A solution of alcohol 85 (763 mg, 2.0 mmol) in 10 mL of 1,2-dimethoxyethane was slowly added to the suspension. After stirring for 10 min carbon disulfide (1.49 g, 20 mmol) and

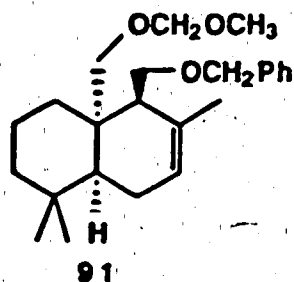
methyl iodide (2.71 g, 20 mmol) were added. The reaction mixture was stirred at room temperature for 6 h, and again cooled to 0°C. Water was added slowly to the reaction mixture and the resulting solution was extracted with dichloromethane. Organic layer was washed respectively with aqueous 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **89** (0.876 g, 94% yield) as a pale yellow oil;  $^1\text{H}$  nmr  $\delta$ : 7.30 (m, 5H, aromatic), 5.82 (dd, 1H,  $J = 10$ ,  $J' = 5$  Hz,  $-\text{CH}-\text{OCS}-$ ), 5.35 (bs, 1H,  $\text{CH}_3-\text{C}=\text{CH}-$ ), 4.60 (d, 1H,  $J = 8$  Hz,  $-\text{O}-\text{CHPh}$ ), 4.52 (d, 1H,  $J = 8$  Hz,  $-\text{O}-\text{CHPh}$ ), 4.50 (d, 1H,  $J = 8$  Hz,  $-\text{O}-\text{CHH}-\text{O}-$ ), 4.48 (d, 1H,  $J = 8$  Hz,  $-\text{O}-\text{CHH}-\text{O}-$ ), 4.16 (dd, 1H,  $J = 9$ ,  $J' = 2$  Hz,  $-\text{CHH}-\text{OCH}_2\text{Ph}$ ), 3.58 (dd, 1H,  $J = 9$ ,  $J' = 7$  Hz,  $-\text{CHH}-\text{OCH}_2\text{Ph}$ ), 3.37 (d, 1H,  $J = 12$  Hz,  $-\text{CHH}-\text{OCH}_2\text{O}-$ ), 3.30 (s, 3H,  $-\text{OCH}_3$ ), 3.29 (d, 1H,  $J = 12$  Hz,  $-\text{CHH}-\text{OCH}_2\text{O}-$ ), 2.50 (s, 3H,  $-\text{SCH}_3$ ), 1.76 (s, 3H,  $-\text{C}-\text{CH}_3$ ), 1.00 and 0.80 (each s, 3H each, *gem*-dimethyl);  $^{13}\text{C}$  nmr  $\delta$ : 133.97, 128.21, 127.59, 120.96, 97.06, 84.24, 77.63, 76.37, 72.97, 72.34, 72.29, 55.47, 44.34, 43.97, 39.14, 36.45, 32.92, 32.09, 24.66, 23.88, 23.46 and 18.54; ir ( $\text{CHCl}_3$  cast): 1223 (C=S) and 1048  $\text{cm}^{-1}$  (C-O-C); cims  $m/z$ : 496 ( $\text{M} + \text{NH}_4^+$ ); hrms  $m/z$ : 431.2247 ( $\text{M}^+-47$ , calcd. for  $\text{C}_{25}\text{H}_{35}\text{O}_5\text{S}$ : 431.2256), 371.2571 ( $\text{M}^+-108$ , calcd. for  $\text{C}_{24}\text{H}_{35}\text{O}_3$ : 371.2586).

#### B. Using Tetrahydrofuran as Solvent



Sodium hydride (50% dispersion in oil, 130 mg, 2.6 mmol) was washed 3 times with freshly distilled tetrahydrofuran. It was then suspended in 10 mL of tetrahydrofuran under an argon atmosphere and a solution of alcohol **85** (340 mg, 0.9 mmol) in 10 mL of tetrahydrofuran was slowly added. After stirring 10 min, carbon disulfide (0.2 mL, 3.5 mmol) and methyl iodide (0.5 g, 3.6 mmol) were added. The reaction mixture was stirred at room temperature for 24 h, and cooled to 0°C. Water was added slowly to the reaction mixture and the resulting solution was extracted with dichloromethane. The organic layer was washed with an aqueous solution of 1 N hydrochloric acid and a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **89** (70 mg, 31% yield, based on consumed starting material) as a pale yellow oil. The compound thus obtained was found to be identical in all respects to the one isolated before. Further elution with 15% ethyl acetate in hexane gave pure hydroxy ether **85** (150 mg, 44% recovery).

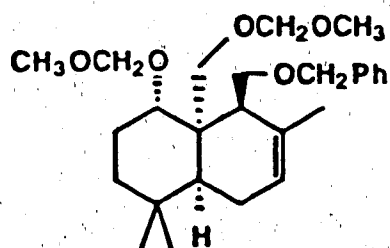
*(1S\*,2S\*,6S\*)-2-Benzylloxymethyl-1-methoxymethoxymethyl-3,7,7,-trimethylbicyclo[4.4.0]deca-3-ene (91) From Xanthate*



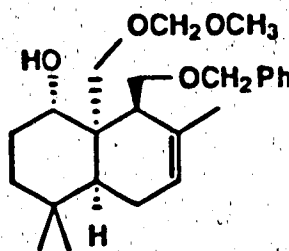
The xanthate **89** (980 mg, 2 mmol), tri-*n*-butyltin hydride (1.75 g, 6 mmol) and azobisisobutyronitrile (100 mg) were dissolved in freshly distilled toluene (20 mL). The solution was degassed by bubbling argon through it for 20 min. The resulting solution was then refluxed for 3 h at 120°C. The reaction mixture was cooled to room temperature and concentrated. The residue on column chromatography over silica gel, eluting with 2% ethyl acetate in hexane, gave pure **91** as a colourless viscous oil (740 mg, 97% yield); ir (CHCl<sub>3</sub> cast): 1100 and 1050 cm<sup>-1</sup> (-C-O-C); cims *m/z*: 390 (M + NH<sub>4</sub><sup>+</sup>); hrms M<sup>+</sup>: 372.2678 (calcd. for C<sub>24</sub>H<sub>36</sub>O<sub>3</sub>: 372.2669); <sup>1</sup>H nmr δ: 7.24 (m, 5H, aromatic), 5.38 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.53 (d, 1H, J = 6 Hz, -O-CHHPh), 4.48 (d, 1H, J = 6 Hz, -O-CHHPh), 4.40 (d, 1H, J = 12 Hz, -O-CHH-O-), 4.36 (d, 1H, J = 12 Hz, -O-CHH-O-), 3.62 (dd, 1H, J = 10, J' = 5 Hz, -CHH-OCH<sub>2</sub>Ph), 3.45 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.40 (dd, 1H, J = 10, J' = 5 Hz, -CHH-OCH<sub>2</sub>Ph), 3.28 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.26 (s, 3H, -OCH<sub>3</sub>), 1.66 (bs, 3H, =C-CH<sub>3</sub>), 0.94 and 0.74 (each s, 3H each, gem-dimethyl); <sup>13</sup>C nmr δ: 138.93, 134.34, 128.23, 127.61, 122.08, 96.90, 74.24, 72.94, 70.03, 55.41, 45.64, 42.31, 40.20, 36.05, 33.33, 31.45, 27.95,

25.93, 24.43, 22.87, and 18.77. Anal Calcd. for  $C_{24}H_{36}O_3$ : C, 77.36; H, 9.74; Found C, 76.97; H, 9.57.

(1*R*\*, 2*S*\*, 6*S*\*, 10*S*\*)-10-Benzyloxymethyl-1-methoxymethoxymethyl-5,5,9-trimethylbicyclo[4.4.0]dec-8-ene-2-ol (93)



92

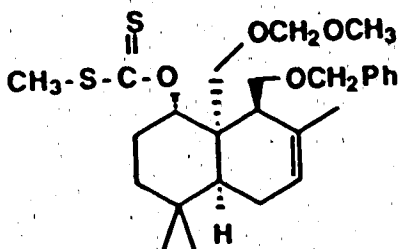


93

Potassium hydride (35% dispersion in oil, 390 mg, 7.5 mmol) was washed twice with freshly distilled 1,2-dimethoxyethane under an argon atmosphere. It was then suspended in 10 mL of 1,2-dimethoxyethane and cooled to  $-10^{\circ}\text{C}$ . Diol 78 (530 mg, 1.5 mmol) in 2 mL of 1,2-dimethoxyethane was then slowly added and the mixture was stirred for 10 min. Chloromethyl methyl ether (160 mg, 2.3 mmol) was slowly added. After 15 min water was slowly added to the reaction mixture and the temperature was gradually raised to room temperature. The resulting solution was extracted with ether. The extracts were washed with aqueous saturated sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated.

Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave ether **92** (440 mg, 68% yield); ir (CHCl<sub>3</sub>): 1109 and 1051 cm<sup>-1</sup> (C-O-C); hrms M<sup>+</sup>: 432.2872 (calcd. for C<sub>26</sub>H<sub>40</sub>O<sub>5</sub>: 432.2876); <sup>1</sup>H nmr δ: 7.32 (m, 5H, aromatic), 5.32 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.70 (d, 1H, J = 7 Hz, -OCHHPh), 4.62 (d, 1H, J = 7 Hz, -OCHHPh), 4.60 and 4.50 (each s, 2H each, 2 x -O-CH<sub>2</sub>-O-), 4.41 (d, 1H, J = 9 Hz, -CHH-OCH<sub>2</sub>O-), 3.78 (dd, 1H, J = 12, J' = 6 Hz, -CHH-OCH<sub>2</sub>Ph), 3.56 (dd, 1H, J = 7, J' = 6 Hz, -CHH-OCH<sub>2</sub>Ph), 3.42 (d, 1H, J = 9 Hz, -CHH-OCH<sub>2</sub>O-), 3.34 and 3.32 (each s, 3H each, 2 x -OCH<sub>3</sub>), 1.80 (bs, 3H, =C-CH<sub>3</sub>), 0.90 and 0.72 (each s, 3H each, gem-dimethyl). Further elution with 10% ethyl acetate in hexane, gave pure hydroxy ether **93** (145 mg, 26% yield); ir (CHCl<sub>3</sub> cast): 3450 (OH), 1109 cm<sup>-1</sup> (C-O-C); hrms m/z: 356.2350 (M<sup>+</sup>-32, calcd. for C<sub>23</sub>H<sub>32</sub>O<sub>3</sub>: 356.2350); <sup>1</sup>H nmr δ: 7.32 (s, 5H, aromatic), 5.52 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.58 (s, 2H, -OCH<sub>2</sub>Ph), 4.52 (s, 2H, -OCH<sub>2</sub>O-), 3.38 (s, 3H, -OCH<sub>3</sub>), 1.80 (bs, 3H, =C-CH<sub>3</sub>), 1.06 and 0.88 (each s, 3H each, gem-dimethyl).

(1R\*,2S\*,6S\*,10S\*)-2-Benzoyloxymethyl-10-methylmercaptiothionocarbonyloxy-1-methoxymethoxymethyl-3,7,7-trimethylbicyclo[4.4.0]dec-3-ene (**94**).



94

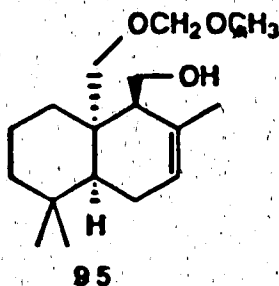
Sodium hydride (50% dispersion in oil, 90 mg, 1.86 mmol) was washed 3 times with freshly distilled 1,2-dimethoxyethane. It was then suspended in 10 mL of 1,2-dimethoxyethane under an argon atmosphere and cooled to 0°C. A solution of alcohol **93** (140 mg, 0.37 mmol) in 5 mL of 1,2-dimethoxyethane was added to the suspension. The resulting solution was stirred for 10 min and then carbon disulfide (0.2 mL, 3.7 mmol) and methyl iodide (0.25 mL, 3.7 mmol) were added. The reaction mixture was stirred at room temperature for 6 h, and then cooled to 0°C. Water was added slowly to the reaction mixture and the resulting solution was extracted with dichloromethane. The organic layer was washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **94** (0.15 g, 83% yield) as a pale yellow oil; ir (CHCl<sub>3</sub> cast): 1223 cm<sup>-1</sup> (C=S); <sup>1</sup>H nmr δ: 7.30 (m, 5H, aromatic), 6.08 (dd, 1H, J = 7, J' = 5 Hz, -CH-OC=S), 5.50 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.58 (s, 2H, -OCH<sub>2</sub>Ph), 4.50 (d, 1H, J = 12 Hz, -OCHHO-),

4.44 (d, 1H,  $J = 12$  Hz, -OCHHO-), 3.76 (dd, 1H,  $J = 10$ ,  $J' = 5$  Hz, -CHH-OCH<sub>2</sub>Ph), 3.65 (d, 1H,  $J = 9$  Hz, -CHH-OCH<sub>2</sub>O-), 3.54 (dd, 1H,  $J = 10$ ,  $J' = 7$  Hz, -CHE-OCH<sub>2</sub>Ph), 3.52 (d, 1H,  $J = 9$  Hz, -CHE-OCH<sub>2</sub>O-), 3.34 (s, 3H, -OCH<sub>3</sub>), 2.52 (s, 3H, -SCH<sub>3</sub>), 1.76 (bs, 3H, -C-CH<sub>3</sub>), 1.00 and 0.86 (each s, 3H each, gem-dimethyl).

*(1S\*,2S\*,6S\*)-2-Benzylloxymethyl-1-methoxymethoxymethyl-3,7,7-trimethylbicyclo[4.4.0]dec-3-ene (91) from Xanthate 94*

The xanthate **94** (150 mg, 0.31 mmol), tri-*n*-butyltin hydride (140 mg, 0.46 mmol) and azobisisobutyronitrile (15 mg) were dissolved in freshly distilled toluene (10 mL). The solution was degassed by bubbling argon gas through it for 20 min. The resulting solution was then refluxed for 3 h at 120°C. The reaction mixture was cooled to room temperature and concentrated. The residue, on column chromatography on silica gel, eluting with 2% ethyl acetate in hexane, gave pure **91** as a colourless viscous oil (114 mg, 98% yield). The compound thus obtained was found to be identical with the one obtained before.

(1*S*\*,2*S*\*,6*S*\*)-2-Hydroxymethyl-1-methoxymethoxymethyl-3,7,7-trimethylbicyclo[4.4.0]dec-3-ene (95)



#### A. Using Liquid Ammonia

At  $-78^{\circ}\text{C}$ , a solution of benzyl ether 91 (640 mg, 1.7 mmol) in 5 mL of dry ether and *t*-butyl alcohol (ca. 5 drops) was added, over a period of 5 min, to freshly distilled ammonia (20 mL) under an argon atmosphere. Lithium metal (200 mg, 0.028 g-atom) was added in small portions over a period of 5 min. The resulting blue solution was stirred for 5 h, during which period the blue colour was discharged. Methanol was added dropwise and the excess of ammonia was allowed to evaporate at room temperature. Water was added and the resulting mixture was extracted with ether. The ethereal extracts were washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in hexane gave pure alcohol 55 (400 mg, 82% yield) as a

colourless paste; ir ( $\text{CHCl}_3$  cast): 3450 (O-H), 1107  $\text{cm}^{-1}$  (C-O-C); cims m/z: 300 ( $\text{M} + \text{NH}_4^+$ ); hrms m/z: 219.1747 ( $\text{M}^+ - 63$ , calcd. for  $\text{C}_{15}\text{H}_{23}\text{O}$ : 219.1749), and 201.1646 ( $\text{M}^+ - 81$ , calcd. for  $\text{C}_{15}\text{H}_{21}$ : 201.1643);  $^1\text{H}$  nmr  $\delta$ : 5.64 (bs, 1H,  $\text{CH}_3\text{-C=CH-}$ ), 4.64 (s, 2H,  $-\text{O-CH}_2\text{-O-}$ ), 3.82 (m, 2H,  $-\text{CH}_2\text{OH}$ ), 3.56 (d, 1H,  $J = 11$  Hz,  $-\text{CHH-OCH}_2\text{O-}$ ), 3.42 (d, 1H,  $J = 11$  Hz,  $-\text{CHH-OCH}_2\text{O-}$ ), 3.38 (s, 3H,  $-\text{OCH}_3$ ), 1.80 (d, 3H,  $J = 1$  Hz,  $=\text{C-CH}_3$ ), 1.06 and 0.90 (each s, 3H each, gem-dimethyl);  $^{13}\text{C}$  nmr  $\delta$ : 133.63, 124.08, 96.82, 74.25, 61.27, 55.42, 48.61, 43.33, 40.63, 35.52, 33.28, 31.30, 28.69, 24.42, 23.09 and 22.86. Anal Calcd. for  $\text{C}_{17}\text{H}_{30}\text{O}_3$ : C, 72.28; H, 10.71; Found: C, 71.97; H, 10.38.

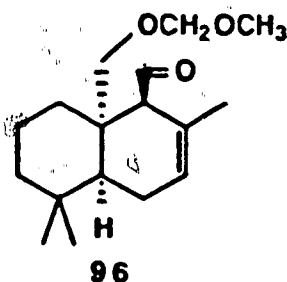
#### B. Using Diethylamine

At  $-10^\circ\text{C}$ , a solution of benzyl ether **91** (500 mg, 1.3 mmol) in 5 mL of dry ether and t-butyl alcohol (ca. 5 drops) was added, over a period of 5 min, to freshly distilled diethylamine (20 mL) under an argon atmosphere. Lithium metal (200 mg, 0.028 g-atom) was added in small portions over a period of 5 min. The resulting blue solution was stirred for 5 h, during which period the blue colour was discharged. Methanol was added dropwise and the excess of amine was allowed to evaporate at room temperature. Water was added and the resulting solution was extracted with ether. The ethereal extracts were washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium-



sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in hexane, gave pure alcohol 55 (400 mg, 82% yield) as a colourless paste. The compound thus obtained was readily identified with the compound obtained previously.

(1*S*\*, 2*S*\*, 6*S*\*)-2-Formyl-1-methoxymethoxymethyl-3,7,7-trimethylbicyclo[4.4.0]dec-3-ene (96)



#### A. Using Swern's Oxidation Procedure

A solution of dimethyl sulfoxide (0.26 mL, 3.7 mmol) in dichloromethane (2 mL) was added dropwise to a solution of oxalyl chloride (0.23 mL, 2.7 mmol) in 2 mL dichloromethane at  $-78^{\circ}\text{C}$  under an argon atmosphere. The mixture was stirred for 15 min, and a dichloromethane solution of the alcohol 95 (0.15 g, 0.5 mmol) was added dropwise at  $-60^{\circ}\text{C}$ . The mixture was allowed to warm up to  $0^{\circ}\text{C}$ .

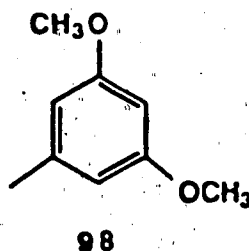
Triethylamine (2 mL) in dichloromethane (2 mL) was added dropwise and the reaction was warmed up to room temperature. It was then poured into 20 mL of ice-cold water and the organic layer separated, washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure aldehyde **96** (130 mg, 89% yield) as a colourless paste; ir (CHCl<sub>3</sub> cast): 1672 (C=O), 1147 and 1108 cm<sup>-1</sup> (C-O-C); cims m/z: 298 (M + NH<sub>4</sub><sup>+</sup>); hrms M<sup>+</sup>: 280.2038 (calcd. for C<sub>17</sub>H<sub>28</sub>O<sub>3</sub>: 280.2038); <sup>1</sup>H nmr δ: 9.80 (d, 1H, J = 3 Hz, -CHO), 5.62 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.63 (d, 1H, J = 12 Hz, -O-CHH-O-), 4.60 (d, 1H, J = 12 Hz, -O-CHH-O-), 3.41 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.37 (s, 3H, -OCH<sub>3</sub>), 3.25 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 2.84 (bs, 1H, CH-CHO), 1.98 (bs, 3H, =C-CH<sub>3</sub>), 0.98 and 0.75 (each s, 3H each, gem-dimethyl). <sup>13</sup>C nmr δ: 203.03, 126.42, 123.33, 95.67, 75.34, 57.66, 54.30, 40.55, 40.37, 38.09, 32.27, 31.50, 28.84, 23.22, 22.86, 21.73 and 18.52.

#### B. Using Pyridinium Chlorochromate

To a stirred slurry of pyridinium chlorochromate (70 mg; 0.3 mmol) in 5 mL of dichloromethane was added in one portion a solution of alcohol **95** (60 mg, 0.2 mmol) in 2 mL of dichloromethane at room temperature. The resulting dark brown solution was stirred at room temperature for 3 h and diluted with ether. The ethereal solution was filtered over magnesium

sulfate. The filtrate was concentrated and the residue, on column chromatography, eluting with 5% ethylacetate, in hexane gave **96** (47 mg, 80% yield). The compound thus obtained was in all respects identical with the one obtained by Swern's oxidation procedure described above

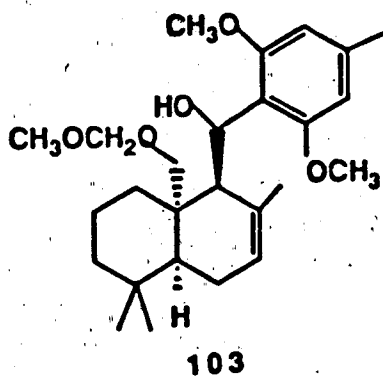
*Orcinol Dimethyl Ether (98)*



7  
To a solution of orcinol (15.0 g, 0.12 mol) in 90 mL of methanol, sodium metal (6.0 g, 0.25 g-atom) was slowly added. The mixture was refluxed for 30 min. Dimethyl sulfate (ca. 50 mL) was slowly added until a light red solution was obtained. A 30% aqueous solution of sodium hydroxide was gradually added until a pale yellow solution was obtained. The addition of dimethyl sulfate and sodium hydroxide were alternated for three times. To the final alkaline solution, water was added and the resulting solution was extracted with ether. The ethereal extracts were washed with 30% aqueous sodium hydroxide, 10% acetic acid and water, dried over anhydrous magnesium sulfate, filtered and concentrated. The

residue was distilled at 110°C and 117 mm pressure to give pure orcinol dimethyl ether **98** (16.5 g, 90% yield) as a colourless oil; ir (neat): 1607 and 1597  $\text{cm}^{-1}$  (Ar-O-C); hrms  $M^+$ : 152.0841 (calcd. for  $\text{C}_9\text{H}_{12}\text{O}_2$ : 152.0837);  $^1\text{H}$  nmr:  $\delta$ 6.36 (s, 3H, aromatic), 3.76 (s, 6H,  $-\text{OCH}_3$ ) and 2.20 (s, 3H, Ar- $\text{CH}_3$ ).

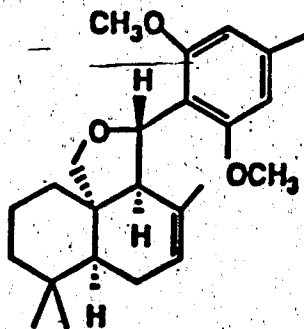
(1*S*\*, 2*S*\*, 6*S*\*)-10-(2,6-Dimethoxy-4-methyl-hydroxybenzyl)-1-methoxymethoxymethyl-3,7,7-trimethylbicyclo[4.4.0]dec-3-ene  
(**103**)



To a solution of orcinol dimethyl ether **98** (140 mg, 1 mmol) in 5 mL of ether under an argon atmosphere was added *n*-butyllithium (36 mg, 0.5 mmol). The resulting solution was stirred at room temperature for 2 h and then cooled to -78°C. Magnesium bromide etherate (146 mg, 0.5 mmol) was added in one portion and the resulting mixture stirred for 10 min. Aldehyde **96** (53 mg, 0.2 mmol) in 1 mL of ether was added slowly. The mixture was allowed to warm up to room temperature. After 2 h water was added. The organic layer was separated and washed with 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium

sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure alcohol **103** (60 mg, 70% yield) as a white solid; ir (CHCl<sub>3</sub> cast): 3540 cm<sup>-1</sup> (O-H); hrms m/z: 370.2506 (M<sup>+</sup> - 62, calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>3</sub>: 370.2507), and 181.0865 (base peak, calcd. for C<sub>10</sub>H<sub>13</sub>O<sub>3</sub>: 181.0865); <sup>13</sup>C nmr δ: 157.64, 137.86, 137.34, 126.29, 124.25, 118.32, 106.41, 104.33, 98.93, 96.79, 94.65, 68.97, 67.66, 67.01, 65.86, 63.96, 58.37, 56.46, 54.55, 52.44, 24.73, 16.09 and 14.42; <sup>1</sup>H nmr δ: 6.36 (s, 2H, aromatic), 5.86 (m, 1H, CH<sub>3</sub>-C=CH-), 5.44 (dd, 1H, J = 10, J' = 4 Hz, -CH-OH), 4.62 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.38 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.00 (d, 1H, J = 10 Hz, -CH-CHOH), 3.80 (s, 6H, 2 x Ar-OCH<sub>3</sub>), 3.32 (s, 3H, -OCH<sub>3</sub>), 3.22 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 2.98 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 2.24 (s, 3H, Ar-CH<sub>3</sub>), 1.44 (s, 3H, -C-CH<sub>3</sub>), 1.10 and 0.92 (each s, 3H each, gem-dimethyl).

(1S\*, 4S\*, 5S\*, 9S\*)-4-(2,6-Dimethoxy-4-methylphenyl)-3-oxa-6,10,10-trimethyltricyclo[7.4.0.0<sup>1,5</sup>]tridec-6-ene (**104**)



104

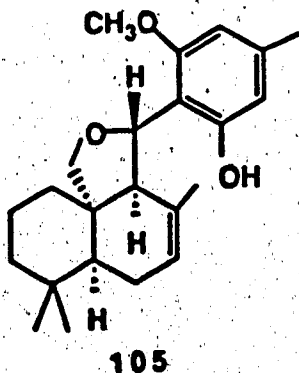
### A. Using Pyridine Hydrochloride

A solution of alcohol **103** (110 mg, 2.5 mmol) and pyridine hydrochloride (58 mg, 5 mmol) in dichloromethane (10 mL) was refluxed under an argon atmosphere for 3 h. Water was added to the reaction mixture and the organic layer separated, washed with aqueous saturated sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **104** (94 mg, 100% yield) as a white solid; m.p. 179-181°C (hexane), ir (CHCl<sub>3</sub> cast): 1608, 1560 (Ar-O-C), and 1125 cm<sup>-1</sup> (C-O-C); hrms M<sup>+</sup>: 370.2510 (Calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>3</sub>: 370.2508); <sup>13</sup>C nmr δ: 140.44, 131.59, 121.09, 76.59, 75.89, 70.48, 55.80, 51.64, 47.26, 46.73, 33.94, 33.16, 29.71, 29.38, 27.96, 27.88, 22.04, 21.99, 19.81, 18.98 and 15.28; <sup>1</sup>H nmr δ: 6.30 (s, 2H, aromatic), 5.34 (d, 1H, J = 12 Hz, Ar-CH-O-), 5.18 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.22 (d, 1H, J = 8 Hz, -CHH-O-CHAr), 3.78 (s, 6H, 2 x Ar-OCH<sub>3</sub>), 3.66 (dd, 1H, J = 8, J' = 2 Hz, -CHH-O-CHAr), 2.34 (s, 3H, Ar-CH<sub>3</sub>), 1.58 (t, 3H, J = 1 Hz, =C-CH<sub>3</sub>), 0.96 and 0.84 (s each, 3H each, gem-dimethyl). Anal Calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>3</sub>: C, 78.78; H, 9.25; Found C, 78.75; H, 8.97.

### B. Using Swern's Oxidation Procedure.

To a solution of oxalyl chloride (20 mg, 0.16 mmol) and dimethyl sulfoxide (30 mg, 0.32 mmol) in 5 mL of dichloromethane at  $-60^{\circ}\text{C}$ , was added alcohol **103** (35 mg, 0.08 mmol) in 2 mL of dry dichloromethane. The resulting solution was stirred under an argon atmosphere and gradually warmed to  $-10^{\circ}\text{C}$ . Triethylamine (40 mg, 0.4 mmol) was added and the solution was warmed to room temperature. Ice-cold water was added and the resulting solution was extracted with dichloromethane. The extracts were washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 5% solution of ethyl acetate in hexane, gave pure **104** (15 mg, 51% yield).

(1*S*\*, 4*S*\*, 5*S*\*, 9*S*\*)-4-(2-Hydroxy-6-methoxy-4-methyl phenyl)-6,10,10-trimethyl-3-oxatricyclo[7.4.0.0<sup>1,5</sup>]tridec-6-ene (**105**)

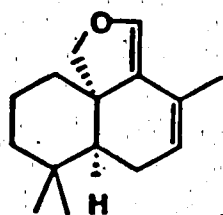


To a solution of potassium hydride (35% dispersion in oil, 25 mg, 2.2 mmol), in 2 mL of *N,N*-dimethylformamide, was added ethanethiol (14 mg, 2.2 mmol). The mixture was

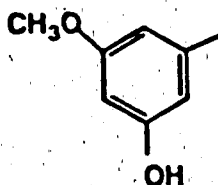
stirred at room temperature under an argon for 5 min. A solution of cyclic ether **104** (17 g, 0.45 mmol) in 1 mL of *N,N*-dimethylformamide was added to it. After being heated for 12 h at 130°C, the reaction mixture was cooled to room temperature and a 6 N aqueous solution of hydrochloric acid was added dropwise until pH 1. The reaction mixture was then extracted with ether. The extracts were washed with aqueous saturated sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 10% solution of ethyl acetate in hexane, gave pure **105** (11 mg, 67% yield); m.p. 149-151°C (hexane); ir (CHCl<sub>3</sub> cast): 3360 (O-H), 1585 (Ar-O-C) and 1101 cm<sup>-1</sup> (C-O-C); h<sub>ms</sub> m/z: 355.2236 (M<sup>+</sup>-1, calcd. for C<sub>23</sub>H<sub>31</sub>O<sub>3</sub>: 355.2273); <sup>1</sup>H nmr δ: 7.80 (s, 1H, -OH), 6.38 and 6.22 (each s, 1H each, aromatic), 5.40 (d, 1H, J = 10 Hz, Ar-CH-O-), 5.28 (bs, 3H, CH<sub>3</sub>-C=CH-), 4.26 (d, 1H, J = 11 Hz, -CHH-O-), 3.74 (s, 3H, Ar-OCH<sub>3</sub>), 3.68 (d, 1H, J = 11 Hz, -CHH-O-), 2.38 (s, 3H, Ar-CH<sub>3</sub>), 1.56 (s, 3H, =C-CH<sub>3</sub>), 0.92 and 0.84 (s each, 3H each, gem-dimethyl).



(1R\*,9S\*)-6,10,10-Trimethyl-3-oxatricyclo[7.3.0.0<sup>1,5</sup>]tridec-4,6-diene (106) and Orcinol Monomethyl Ether (107)



106

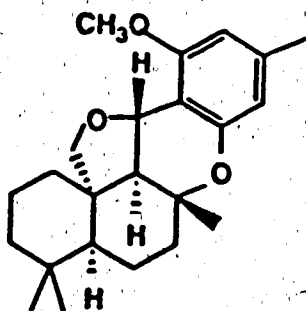


107

To a solution of phenol 105 (10 mg, 0.03 mmol) in 2 mL of dichloromethane at 0°C, was added boron trifluoride etherate (ca. 2 drops). The resulting pink solution was stirred under an argon atmosphere and was gradually warmed to room temperature. During this period, the colour of the solution was discharged. After 30 min water was added and the resulting mixture extracted with dichloromethane. The organic extracts were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 10% solution of ethyl acetate in hexane, gave diene ether 106 (4 mg, 61% yield); ir (CHCl<sub>3</sub> cast): 1260 cm<sup>-1</sup> (=C-O-C); hrms M<sup>+</sup>: 218.1688 (Calcd. for C<sub>15</sub>H<sub>22</sub>O<sub>2</sub>: 218.1671); <sup>1</sup>H nmr δ: 6.26 (bs, 1H, -O-CH=C); 5.26 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.56 (d, 1H, J = 7 Hz, -CHH-O-), 3.80 (d, 1H, J = 7 Hz, -CHH-O-), 1.76 (s, 3H, =C-CH<sub>3</sub>), 0.86 and 0.82 (each s, 3H each, gem-dimethyl). Further elution with 15% ethyl acetate in hexane,

gave orcinol monomethyl ether **107** (3 mg, 72% yield); ir (CHCl<sub>3</sub> cast): 3400 (OH), 1597 cm<sup>-1</sup> (Ar-O-C); hrms M<sup>+</sup>: 138.0680 (Calcd. for C<sub>8</sub>H<sub>10</sub>O<sub>2</sub>: 138.0680); <sup>1</sup>H nmr δ: 6.30, 6.24 and 6.20 (each s, 1H each, aromatic), 3.74 (s, 3H, -OCH<sub>3</sub>) and 2.24 (s, 3H, Ar-CH<sub>3</sub>).

*Isosiccanin Methyl Ether (109)*



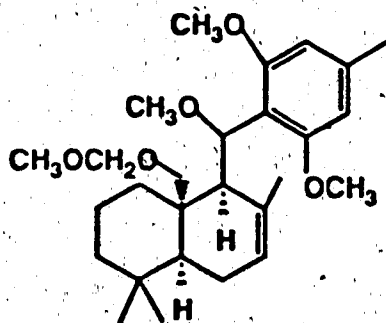
**109**

Phenol **105** (25 mg, 0.07 mmol) was dissolved in 2 mL of methanol. To this solution, mercuric acetate (110 g, 0.35 mmol) was added and the resulting solution was stirred under an argon atmosphere at room temperature for 8 h. Sodium borohydride (5 mg, 0.1 mmol) was added and the mixture was stirred for 30 min. The resulting solution was concentrated and the residue was extracted with ether. The ethereal extracts were washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 5% solution of ethyl acetate in hexane, gave pure isosiccanin methyl ether (**109**)

(18 mg, 72% yield) as a white solid; m.p. 208-209°C (hexane); ir (CHCl<sub>3</sub> cast): 1616 (Ar-O-C) and 1114, cm<sup>-1</sup> (C-O-C); hrms m/z: 271.1332 (M<sup>+</sup> - 85, calcd. for C<sub>17</sub>H<sub>19</sub>O<sub>3</sub>: 271.1334); <sup>1</sup>H nmr δ: 6.32 and 6.24 (each s, 1H each, aromatic), 5.56 (bs, 1H, Ar-CH-O-), 4.16 (d, 1H, J = 8 Hz, -CHH-O-), 3.80 (s, 3H, -OCH<sub>3</sub>), 3.56 (dd, 1H, J = 8, J' = 1 Hz, -CHH-O-), 2.28 (s, 3H, Ar-CH<sub>3</sub>), 1.50 (s, 3H, -OC-CH<sub>3</sub>), 0.84 and 0.82 (each s, 3H each, gem-dimethyl).

(1S\*,2S\*,6S\*)-2-(2,6-Dimethoxy-4-methyl-methoxybenzyl)-1-methoxymethoxymethyl-3,7,7-trimethyl bicyclo[4.4.0]dec-3-ene.

(114)



114

Potassium hydride (35% dispersion in oil, 30 mg, 0.2 mmol) was washed three times with freshly distilled 1,2-dimethoxyethane. It was then suspended in 5 mL of 1,2-dimethoxyethane and stirred at 0°C under an argon atmosphere. Alcohol 103 (20 mg, 0.48 mmol) in 2 mL of 1,2-dimethoxyethane was added dropwise to the suspension. After 5 min, methyl iodide (20 mg, 1.4 mmol) was added. The mixture was stirred

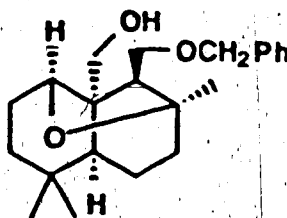
for 3 h at room temperature, water was added and the mixture extracted with ether. The ethereal extracts were washed with 1 N aqueous hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **110** (18 mg, 83% yield); ir (CHCl<sub>3</sub> cast): 1608 (Ar-O-C), 1110 and 1097 cm<sup>-1</sup> (C-O-C); hrms m/z: 370.2506. (M<sup>+</sup>-76, calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>3</sub> = 370.3508) and 195.0993 (base peak, calcd. for C<sub>11</sub>H<sub>15</sub>O<sub>3</sub> = 195.1111); <sup>1</sup>H nmr δ: 6.36 (bs, 2H, aromatic), 5.72 (bs, 1H, CH<sub>3</sub>-C=CH-), 4.92 (d, 1H, J = 10 Hz, -O-CH-Ar), 4.64 (s, 2H, -O-CH<sub>2</sub>-O-), 4.80 (s, 6H, 2 x Ar-OCH<sub>3</sub>), 3.46 (d, 1H, J = 11 Hz, -CHH-OCH<sub>2</sub>O-), 3.36 (s, 3H, Ar-C-OCH<sub>3</sub>), 3.10 (s, 3H, -CH<sub>2</sub>-O-CH<sub>3</sub>), 3.08 (d, 1H, J = 11 Hz, -CHH-OCH<sub>2</sub>O-), 2.32 (s, 3H, Ar-CH<sub>3</sub>), 1.84 (t, 3H, J = 1 Hz, =C-CH<sub>3</sub>), 1.04 and 0.88 (s each, 3H each, gem-dimethyl).

**Compound 105 from Ether 114.**

Ether **114** (20 mg, 0.04 mmol) in 1 mL of *N,N*-dimethylformamide was added to a mixture of potassium hydride (35% dispersion in oil, 8 mg, 0.2 mmol) and ethanethiol (12 mg, 0.2 mmol) in 5 mL of *N,N*-dimethylformamide. The resulting solution was heated under an argon atmosphere at 125°C for 8 h and then cooled to room temperature. The solution was acidified (pH 1) with 6 N hydrochloric acid and extracted

with ether. The extracts were washed with a saturated solution of aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a solution of 15% ethyl acetate in hexane, gave pure phenol 105 (9 mg, 60% yield).

(1*R*\*, 3*R*\*, 6*S*\*, 10*S*\*)-10-Hydroxymethyl-3, 3, 7-trimethyl-2-oxatricyclo[4.3.1.1.<sup>3,10</sup>]undecane (**122**)

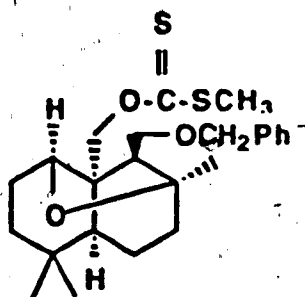


122

A solution of diol **74** (330 mg, 0.9 mmol) and aqueous solution of 1 N hydrochloric acid (2 mL) in tetrahydrofuran (10 ml) was heated to reflux for 3 h under an argon atmosphere. The resulting solution was cooled to room temperature and extracted with ether. The ethereal extracts were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 15% solution of ethyl acetate in hexane, gave pure hydroxy ether **122** (200 mg, 59% yield); ir (CH<sub>2</sub>Cl<sub>2</sub> cast): 3510 (OH)

and  $1107\text{ cm}^{-1}$  (C-O-C); hrms  $M^+$ : 344.2353 (Calcd. for  $C_{22}H_{32}O_3$ : 344.2351);  $^1\text{H}$  nmr  $\delta$ : 7.42 (m, 5H, aromatic), 4.62 (s, 2H, -OCH<sub>2</sub>Ph), 3.25 (dd, 1H,  $J = 8$ ,  $J' = 4$  Hz, -OH), 1.25 (s, 3H, -OC-CH<sub>3</sub>), 1.16 and 1.08 (each s, 3H each, gem-dimethyl).

(1*R*\*, 3*R*\*, 6*S*\*, 10*S*\*)-10-Methylmercaptothionocarbonyloxy-3,3,7-trimethyl-2-oxa-tricyclo[4.3.1.1.<sup>3,10</sup>]undecane (123)

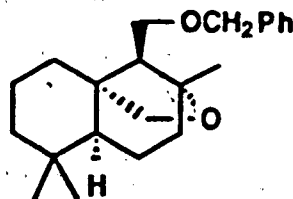


123

Sodium hydride (50% dispersion in oil, 70 mg, 2.8 mmol) was washed 3 times with freshly distilled 1,2-dimethoxyethane. It was then suspended in 10 mL of 1,2-dimethoxyethane under an argon atmosphere and cooled to 0°C. A solution of alcohol 122 (200 mg, 0.55 mmol) in 5 mL of 1,2-dimethoxyethane was slowly added to the suspension. After stirring for 10 min, carbon disulfide (1 mL) and methyl iodide (1 mL) were added. The reaction mixture was stirred at room temperature for 6 h, and then cooled to 0°C. Water was added slowly to the reaction mixture and the resulting solution was extracted with dichloromethane. The organic layer was washed with aqueous 1 N hydrochloric acid and

saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure **123** (140 mg, 58% yield) as a pale yellow oil; ir (CHCl<sub>3</sub> cast): 1240 cm<sup>-1</sup> (C=S); hrms M<sup>+</sup>: 434.1947 (calcd. for C<sub>24</sub>H<sub>34</sub>S<sub>2</sub>O: 434.1950); <sup>1</sup>H nmr δ: 7.30 (s, 5H, aromatic), 4.83 (d, 1H, J = 12 Hz, -CHH-OCS), 4.56 (d, 1H, J = 12 Hz, -CHH-OCS), 3.90 (bs, 1H, -CHHOCH<sub>2</sub>Ph), 3.58 (dd, J = 6, J' = 2 Hz, -CHHOCH<sub>2</sub>Ph), 2.52 (s, 3H, -SCH<sub>3</sub>), 1.30 (s, 3H, -OC-CH<sub>3</sub>), 1.02 and 0.98 (each s, 3H each, gem-dimethyl).

(1R\*,4R\*,7S\*,12S\*)-12-Benzyloxymethyl-4,8,8-trimethyl-3-oxatricyclo[4.3.1.1<sup>1,4</sup>]dodecane (**120**)

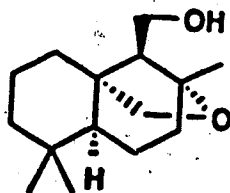


**120**

A solution of alcohol **91** (340 mg, 1.2 mmol) and aqueous solution of 1 N hydrochloric acid (2 mL) in tetrahydrofuran (10 mL) was heated to reflux for 3 h under an argon atmosphere. The resulting solution was cooled to room temperature and extracted with ether. The ethereal

extracts were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 5% solution of ethyl acetate in hexane, gave pure hydroxy ether **120** (150 mg, 53% yield); ir (neat):  $1073\text{ cm}^{-1}$  (C-O-C); hrms  $M^+$ : 328.2399 (calcd. for  $C_{22}H_{32}O_2$ : 328.2402);  $^1\text{H}$  nmr  $\delta$ : 7.40 (s, 5H aromatic), 4.64 (d, 1H,  $J = 12\text{ Hz}$ , -OCHHPh), 4.52 (d, 1H,  $J = 12\text{ Hz}$ , -OCHHPh), 3.96 (dd, 1H,  $J = 8, J' = 5\text{ Hz}$ , -CHH-OCH<sub>2</sub>Ph), 3.62 (t, 1H,  $J = 8\text{ Hz}$ , -CHH-OCH<sub>2</sub>Ph), 1.52 (s, 3H, -OC-CH<sub>3</sub>), 0.96 and 0.84 (each s, 3H each, *gem*-dimethyl).

(1*R*\*, 4*R*\*, 7*S*\*, 12*S*\*)-12-hydroxymethyl-4,8,8-trimethyl-3-oxatricyclo[4.3.1.1.<sup>1,4</sup>]dodecane (**124**)



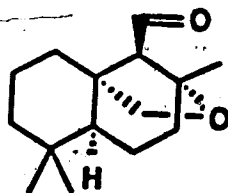
**124**

At  $-78^\circ\text{C}$ , a solution of benzyl ether **120** (450 mg, 1.4 mmol) in 10 mL of ether and *t*-butyl alcohol (ca. 5 drops) was added, over a period of 5 min, to freshly distilled ammonia (15 mL) under an argon atmosphere. Lithium metal (100



mg, 0.014 g-atom) was added in small portions. The resulting blue coloured solution was stirred for 3 h, during which period the blue colour was discharged. Methanol was added dropwise and the excess of ammonia was allowed to evaporate at room temperature overnight. Water was added and the resulting solution was extracted with ether. The ethereal extracts were washed with 1N aqueous hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in Hexane, gave pure alcohol **124** (270 mg, 83% yield); ir (CHCl<sub>3</sub> cast): 3420 cm<sup>-1</sup> (OH); hrms M<sup>+</sup>: 238.1938 (calcd. for C<sub>15</sub>H<sub>26</sub>O<sub>2</sub>: 238.1933); <sup>1</sup>H nmr δ: 3.70- 3.40 (m, 4H, -CH<sub>2</sub>O- and -CH<sub>2</sub>OH), 1.30 (s, 3H, -OC-CH<sub>3</sub>), 0.90 and 0.80 (each s, 3H each, *gem*-dimethyl).

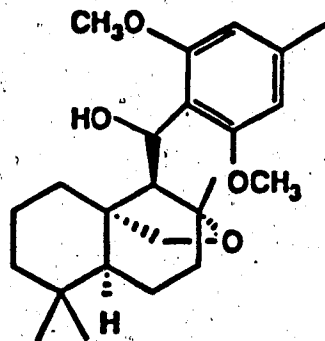
(1R\*,4R\*,7S\*,12S\*)-12-Formyl-4,8,8-trimethyl-3-oxatricyclo[4.3.1.1<sup>1,4</sup>]dodecane (**125**)



125

To a slurry of pyridinium chlorochromate (110 mg, 0.5 mmol) in 10 mL of dichloromethane, was added a solution of alcohol 119 (40 mg, 0.17 mmol) at room temperature. The mixture was stirred under an argon atmosphere for 4 h. It was then diluted with ether, filtered through magnesium sulfate and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure aldehyde 125 (22 mg, 81% yield); ir (CHCl<sub>3</sub> cast): 1740 cm<sup>-1</sup> (C=O); hrms M<sup>+</sup>: 236.1782 (calcd. for C<sub>15</sub>H<sub>24</sub>O<sub>2</sub>: 236.1788); <sup>1</sup>H nmr δ: 10.6 (d, 1H, J = 2 Hz, -CHO), 3.70 (s, 2H, -OCH<sub>2</sub>-), 1.58 (s, 3H, -OC-CH<sub>3</sub>), 0.92 and 0.80 (each s, 3H each, gem-dimethyl):

(1R\*,4R\*,7S\*,12S\*)-12-(2,6-Dimethoxy-4-methyl-hydroxybenzyl)-4,8,8-trimethyl-3-oxa-tricyclo[4.3.1.1.1,4]dodecane (126)

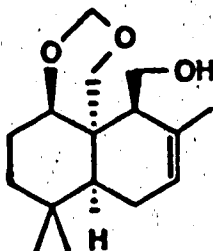


126

At 0°C, to a solution of orcinol dimethyl ether (130 mg, 0.85 mmol) in 5 mL of ether under an argon was added n-butyl lithium (33 mg, 0.51 mmol) in hexane. After stirring for 2 h aldehyde 125 (40 mg, 0.17 mmol) in 2 mL of ether was

slowly added. The mixture was allowed to warm up to room temperature. After 2 h, water was added. The mixture was extracted with ether. The extracts were washed with aqueous 1 N hydrochloric acid and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with a 15% solution of ethyl acetate in hexane, gave orcinol dimethyl ether (0.03 g). Further elution gave alcohol 126 (60 mg, 91% yield); ir (CHCl<sub>3</sub> cast): 3400 (OH) and 1120 cm<sup>-1</sup> (C-O-C); hrms m/z: 370.2506 (M<sup>+</sup> - 18, calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>3</sub>: 370.2510); <sup>1</sup>H nmr δ: 6.46 (s, 2H, aromatic), 5.62 (dd, 1H, J = 8, J' = 2 Hz, -CHOH), 3.82 (s, 6H, -OCH<sub>3</sub>), 3.50 (d, 1H, J = 11 Hz, -CHH-O-), 3.24 (d, 1H, J = 11 Hz, -CHH-O-), 2.32 (s, 3H, Ar-CH<sub>3</sub>), 1.70 (s, 3H, -OC-CH<sub>3</sub>), 1.16 and 0.92 (each s, 3H each, gem-dimethyl).

(1R\*,6R\*,10S\*,14S\*)-14-Hydroxymethyl-3,5-dioxa-9,9,13-trimethyltricyclo[8.4.0.0<sup>1,6</sup>]tetradec-12-ene. (127)



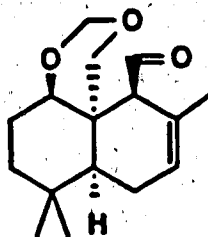
127

At  $-78^{\circ}\text{C}$ , a solution of benzyl ether 83 (1.50 g, 4.0 mmol) in ether (10 mL) and *t*-butylalcohol (ca. 1ml) was added over a period of 5 min to freshly distilled ammonia (25 mL) under argon atmosphere. Lithium metal (400 g, 0.056 g-atom) was added in small portions over a period of 5 min. The resulting blue coloured solution was stirred for 5 h, during which period the blue colour was discharged. Methanol was added dropwise and the excess of ammonia was allowed to evaporate at room temperature overnight. Water was added and the resulting solution was extracted with ether. The ethereal extracts were washed with aqueous 1 N hydrochloric acid solution and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered and concentrated.

Column chromatography of the residue on silica gel, eluting with 25% ethyl acetate in hexane, gave pure 127 (618 mg, 55% yield); ir ( $\text{CHCl}_3$  cast): 3540 (O-H), 1174 and 1106  $\text{cm}^{-1}$  (C-O-C); hrms  $m/z$ : 248.1788 ( $\text{M}^+-18$ , calcd. for  $\text{C}_{16}\text{H}_{24}\text{O}_2$ : 248.1786);  $^1\text{H}$  nmr  $\delta$ : 5.40 (bs, 1H,  $\text{CH}_3\text{-C=CH-}$ ), 5.21 (d, 1H,  $J = 8$  Hz, -O-

CHH-O-), 4.86 (d, 1H,  $J = 8$  Hz, -O-CHH-O-), 3.98 (m, 1H, -OCH<sub>2</sub>O-CH-), 3.80 (d, 1H,  $J = 11$  Hz, -CHH-OCH<sub>2</sub>O-), 3.18 (d, 1H,  $J = 11$  Hz, -CHH-OCH<sub>2</sub>O-), 1.80 (s, 3H, -C-CH<sub>3</sub>), 0.96 and 0.82 (each s, 3H each, gem-di-methyl).

(1R\*, 6R\*, 10S\*, 14S\*)-14-Formyl-3,5-dioxa-9,9,13-trimethyl tricyclo[8.4.0.0<sup>1,6</sup>]tetradec-12-ene (128)

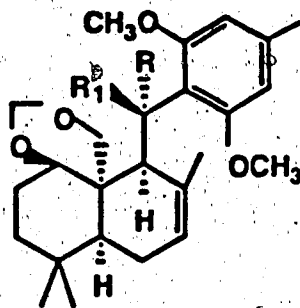


128

To a slurry of pyridinium chlorochromate (300 mg, 1.4 mmol) in 10 mL of dichloromethane, was added a solution of alcohol 127 (250 mg, 0.9 mmol) in 2 mL of dichloromethane at room temperature. The mixture was stirred under an argon atmosphere for 4 h. It was then diluted with ether, filtered through magnesium sulfate and concentrated. Column chromatography of the residue on silica gel, eluting with 5% ethyl acetate in hexane, gave pure aldehyde 128 (198 mg, 80% yield) as a viscous oil; ir (CHCl<sub>3</sub> cast): 2858 (CHO), 1711 (C=O), 1175 and 1105 cm<sup>-1</sup> (C-O-C); hrms M<sup>+</sup>: 264.1720 (Calcd. for C<sub>16</sub>H<sub>24</sub>O<sub>3</sub>: 264.1726); <sup>1</sup>H nmr  $\delta$ : 10.16 (d, 1H,  $J = 2$  Hz, -CHO), 5.70 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.26 (d, 1H,  $J = 9$  Hz, -O-

CHH-O-), 4.82 (d, 1H,  $J = 9$  Hz, -O-CHH-O-), 3.82 (d, 1H,  $J = 10$  Hz, -CHH-OCH<sub>2</sub>O-), 3.50 (m, 1H, -CH-OCH<sub>2</sub>O-), 3.32 (d, 1H,  $J = 10$  Hz, -CHH-OCH<sub>2</sub>O-), 1.72 (bs, 3H, =C-CH<sub>3</sub>), 0.90 and 0.68 (each s, 3H each, gem-dimethyl).

(1R\*,6R\*,10S\*,14S\*)-14-(2,6-Dimethoxy-4-methylhydroxybenzyl)-9,9,13-trimethyl-3,5-dioxatricyclo[8.4.0.0<sup>1,6</sup>]tetradec-12-ene (129)



R, R<sub>1</sub> = H, OH

129

To a solution of orcinol dimethyl ether (408 mg, 2.6 mmol) in 5 mL of ether under an argon atmosphere was added *n*-butyllithium (0.10 g, 1.5 mmol) in hexane. The resulting mixture was stirred at room temperature for 2 h and then cooled to -78°C. Magnesium bromide etherate (380 mg, 1.5 mmol) was added in one portion and the resulting mixture was stirred for 30 min. Aldehyde 128 (140 mg, 0.5 mmol) in 2 mL of ether was slowly added. The mixture was allowed to warm up to room temperature. After 2 h water was added. The resulting solution was extracted with ether. The extracts were washed with aqueous 1 N hydrochloric acid, saturated aqueous sodium

chloride, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography of the residue on silica gel, eluting with 10% ethyl acetate in hexane, gave the major epimer of **129** (121 mg, 58% yield); ir (CHCl<sub>3</sub> cast): 3540 (O-H), 1607, 1597 (Ar-O-C), 1172 and 1150 cm<sup>-1</sup> (C-O-C); hrms m/z: 264.1730 (M<sup>+</sup>-152, calcd. for C<sub>16</sub>H<sub>24</sub>O<sub>3</sub>: 264.1725); <sup>1</sup>H nmr δ: 6.30 (s, 2H, aromatic), 5.50 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.32 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.82 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.58 (bs, 1H, -CHOH), 3.78 (s, 6H, 2 x Ar-OCH<sub>3</sub>), 3.68 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.44 (dd, 1H, J = 10, J' = 4 Hz, -CHH-OCH<sub>2</sub>O-), 3.18 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 2.30 (s, 3H, Ar-CH<sub>3</sub>), 1.80 (s, 3H, =C-CH<sub>3</sub>), 0.98 and 0.92 (each s, 3H each, gem-di-methyl). Further elution with 15% ethyl acetate in hexane gave 35 mg (28% yield) of the minor epimer of **129**; ir (CHCl<sub>3</sub> cast): 3500 (O-H), 1610, 1582 (Ar-O-C), 1146 and 1124 cm<sup>-1</sup> (C-O-C); hrms m/z: 398.2467 (M<sup>+</sup>-18, calcd. for C<sub>25</sub>H<sub>34</sub>O<sub>4</sub>: 398.2456); <sup>1</sup>H nmr δ: 6.34 (s, 2H, aromatic), 5.82 (dd, 1H, J = 10, J' = 2 Hz, -CHOH), 5.64 (bs, 1H, CH<sub>3</sub>-C=CH-), 5.18 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.92 (d, 1H, J = 7 Hz, -O-CHH-O-), 4.30 (dd, 1H, J = 10, J' = 4 Hz, -CH-OCH<sub>2</sub>O-), 3.76 (s, 6H, 2 x Ar-OCH<sub>3</sub>), 3.52 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 3.10 (d, 1H, J = 10 Hz, -CHH-OCH<sub>2</sub>O-), 2.30 (s, 3H, Ar-CH<sub>3</sub>), 1.30 (bs, 3H, =C-CH<sub>3</sub>), 1.18 and 0.92 (each s, 3H each, gem-dimethyl).

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