Terpenoids. XI.[1] Mayurone Oxide

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Synopsis. Epoxidation of mayurone **7** gave mayurone oxide **21** in good yield. Grignard methylation of **21** gave epoxy alcohols, **17** and **22**. Thujopsadiene monoepoxide **23** was synthesized from **21** by Wittig reaction. Oxide **21** and **23** were found in the autoxidation product of **1**. Oxide **21** was found in the autoxidation product of **2**, **3**, and **6**.

Oxidation of thujopsene **1** under various conditions[1-3] generally gave a complicated mixture including mayurone **7**.[4] Our current concern is the full characterization of the complicated mixture in order to determine the reaction mechanism and to control the reaction specific to a chiral thujopsane derivative bearing versatile functionalities. During the time consuming separation and isolation of the minor products from permanganate oxidation of **1**, some epoxy ring containing products are indicated as well as **5**[3] and **17**[1] isolated earlier.

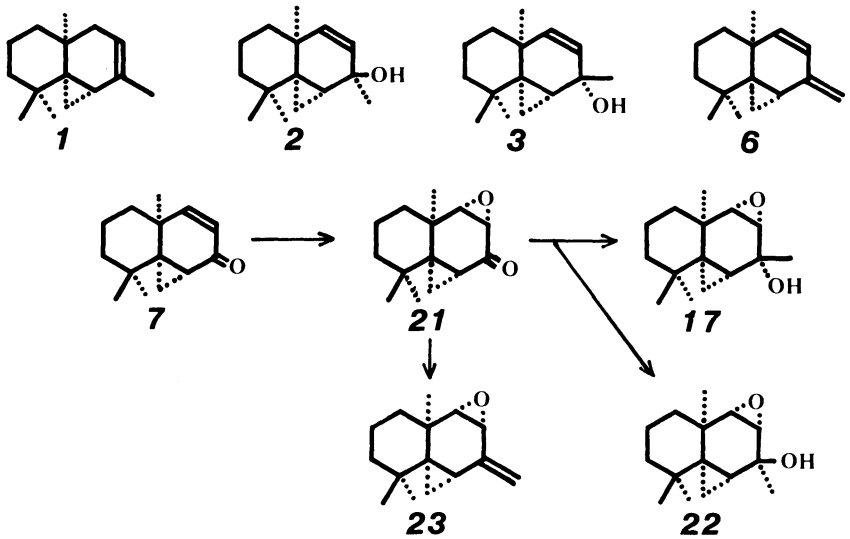
Direct epoxidation of **1** failed under various conditions,[5] but an epoxidation of mayurone **7** gave a new oxide **21** in high yield. The compound **21** was a useful intermediate to synthesize some standard samples of epoxy-ring-containing thujopsanes for the characterization of minor products in the oxidation products of **1**.

Results and Discussion

Mayurone **7** gave only an epoxide in high yield upon treatment with alkaline hydrogen peroxide in aqueous methanol. The epoxidation is highly diastereoselective, i.e., no epimeric epoxide was found in the products by GLC and ^{1}H NMR analyses. The ^{1}H NMR of the epoxide showed two vicinal protons on an epoxy ring, one of which showed a long-range coupling constant of 1.6 Hz. The configuration of the epoxy ring was further established as the structure **21** by correlation to a known epoxide **17**[1] as described below. A Grignard methylation of **21** at low temperature occurred at the carbonyl group, giving a mixture of two epoxy alcohols. They were separated by silica-gel chromatography to about an 8:1 product ratio. Since the minor product was identical with **17**,[1] α-configuration of the epoxy ring in **21** was established. The major epoxy alcohol mp 80 °C was assigned as structure **22**. Interestingly, the stereoselectivity in the methylation is reversed on going from mayurone[3] **7** to its epoxide **21**, due to a subtle difference in steric hindrance around the carbonyl groups.

Reaction of **21** with triphenylphosphonium methylide gave a new thujopsane derivative **23**, assigned by IR and ^{1}H NMR spectra.

Since our major interest was the full characterization of the complicated mixture from **1** by permanganate oxidation in anhydrous acetone,[3] reanalysis by GLC of the mixture was attempted briefly. The result suggested the presence of the new compounds **21** and **23**, but their direct formation by permanganate oxidation is unlikely. Rather they were considered to have arisen from secondary autoxidation of the major components in the product, i.e., **1** (unreacted), **2**, **3**, and **6**,[3] during the time consuming separations. Therefore the autoxidation was examined on these components separately. Mayurone oxide **21** and thujopsadiene 8α,9-epoxide **23** were found in the products of the autoxidation of **1**. Mayurone oxide **21** was also found in the autoxidation products of thujopsadiene **6** and 9-thujopsen-8-ols **2** and **3** besides **7**. These results show that the complex mixture from permanganate oxidation of **1** is partly due to the autoxidation of the primary products.



Experimental

Mayurone oxide 21 from Mayurone 7: Mayurone 74 mg was added to a mixture of 30% H_2O_2 (0.15 ml), 6 M-NaOH (0.024 ml; 1 M=1 mol dm^{-3}) and methanol (1.0 ml) and the mixture was stirred for 1 h at room temperature. After the addition of water (50 ml) and sat. NaCl (20 ml), the mixture was extracted with ether–hexane (2:1). Evaporation of the solvent gave **21** 79 mg as the sole product. **21**: mp 93.5—94.5 °C (from methanol). IR (KBr) 3020, 2950, 1680, 1488, 1465, 1446, 1390, 1380, 1366, 1290, 1247, 1172, 1040, 1018, 980, 965, 945, 912, 868, 840, 828, 780, 770, 650, and 446 cm^{-1}. ^1H NMR ($CDCl_3$) δ=0.57 (3H, s), 1.10 (3H, s), 1.53 (3H, s), 3.04 (1H, d, J=4.0 Hz), 3.25 (1H, dd, J=4.0 and 1.6 Hz), and 0.64—2.18 (9H, m).

Grignard Methylation of 21: Mayurone oxide **21** (0.50 g) in dry THF (10 ml) was cooled to −70 °C. Methylmagnesium iodide (1.37 M, 1.66 ml) was added under an argon atmosphere and stirred for 1 h at −70 °C. The reaction mixture was hydrolyzed with aqueous ammonium acetate solution at −50 °C, extracted with ether–hexane (1:1), and dried over sodium sulfate. The solvent was evaporated and the residue was chromatographed on a silica-gel column. Hexane–CH_2Cl_2 (8:2 to 7:3) eluted unchanged **21** (0.25 g). Hexane–CH_2Cl_2 (1:1) and CH_2Cl_2 eluted **22** (228 mg) and ether–CH_2Cl_2 (1:19) eluted **17** (27.5 mg) mp 106 °C, identified by IR and ^1H NMR.[1] **22**: mp 78—80 °C. IR (KBr) 3470, 3380 (OH), 3100, 2950, 2930, 1480, 1370, 1128, 1090, 1050, 965, 938, 908, 858, 822, 812, 801, 742, 606, and 503 cm^{-1}. ^1H NMR ($CDCl_3$) δ=0.26 (1H, dd, J=10.1 and 4.3 Hz), 0.55 (3H, s), 0.89 (1H, dd, J=5.6 and 4.3 Hz), 1.02 (3H, s), 1.33 (3H, s), 1.46 (3H, s), 2.66 (1H, d, J=3.8 Hz), and 2.93 (1H, dd, J=3.8 and 2.0 Hz).

Thujopsadiene Monoepoxide 23 from Mayurone Oxide 21: To a suspension of methyltriphenylphosphonium bromide, 200 mg (0.56 mmol) in 5 ml of tetrahydrofuran, 0.28 ml of 1.55 M butyl lithium in hexane was added at −40 °C. After stirring the mixture for 30 min, 100 mg of mayurone oxide **21**, 0.46 mmol was added at room temperature and the mixture was refluxed for 4 h. Four ml of aqueous sodium chloride solution was added and the organic layer was separated. GLC analysis of the layer showed **23**, 39%, **21**, 11%, triphenylphosphine oxide 39% and unidentifiable products 11%. The products were chromatographed on silica gel. Hexane–CH_2Cl_2 eluted 47 mg of **23**. Oil, IR (neat) 3080, 3050, 3000, 2850, 1633 (CH_2=C), 1460, 1385, 1370, 1253, 1170, 1043, 945, 903, 878, 863, 832, 805, 762, and 682 cm^{-1}. ^1H NMR ($CDCl_3$) δ=0.58 (3H, s), 1.04 (3H, s), 1.38 (3H, s), 2.77 (1H, d, J=4 Hz), 3.41 (1H, dd, J=4 and 1.5 Hz), and 5.16 (2H, broad s).

Compounds 21 and 23 in Autoxidation Products of 1: In the autoxidation products of thujopsene (23.8 g) reported previously,[1] a fraction (265 mg, 1.1%, 90% pure by GC) just after the elution of dimeric peroxide **16** was found to be **23** by comparison of the IR. The crude mayurone fraction was combined and rechromatographed on SiO_2 gel affording **21** (28 mg, 0.1%) preceeding the mayurone fraction, identified by IR.

Compound 21 from Allylic Alcohol 2: A sample of alcohol **2** (93% pure) was autoxidized on standing for 6 months. Gas chromatography showed **6**, 6%, **2**, 21%, **7**, 33%, and **21**, 14%.

Compound 21 from Allylic Alcohol 3: Alcohol **3** 0.50 g was autoxidized on standing for more than 6 months. Gas chromatography showed **6**, 52%, **3**, 2%, **7**, 23%, and **21**, 10%. Alumina and silica gel chromatography gave 0.02 g of **21**, identified by IR.

Compound 21 from Thujopsadiene 6: Thujopsadiene **6** was synthesized from mayurone and methylmagnesium iodide. The diene **6**, 2.88 g was autoxidized on standing for more than 6 months. Gas chromatography showed **6**, 53%, **7**, 32%, and **21**, 6%. Silica-gel chromatography gave 0.05 g of **21**, identified by IR.

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