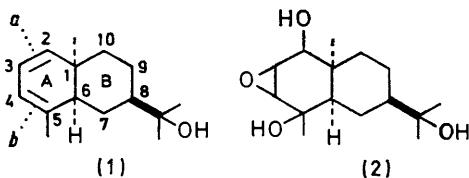


The Oxidation of (+)-Occidentalol with *t*-Butyl Chromate

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The oxidation of (+)-occidentalol (1) with *t*-butyl chromate affords 8-(1-hydroxy-1-methylethyl)-1,5-dimethylbicyclo[4.4.0]dec-4-ene-2,3-dione (3), (+)-2-hydroxy-9-(1-hydroxy-1-methylethyl)-2,6-dimethylbicyclo[4.4.0]dec-4-en-3-one (4), (+)-3-[2-carboxy-5-(1-hydroxy-1-methylethyl)-2-methylcyclohexyl]but-2-enoic acid (6), and (+)-3-(1-hydroxy-1-methylethyl)-6,9-dimethyl-8-oxabicyclo[4.3.0]non-9-en-7-one (8). Mechanistic implications of the oxidation, based on the various products identified, are discussed.

A STUDY of the oxidation by *t*-butyl chromate of monocyclic terpenes containing an endocyclic ethylenic bond has shown that an active allylic methylene group is oxidised preferentially to an $\alpha\beta$ -unsaturated ketone group.¹ Of conjugated diene compounds, only *p*-mentha-1,3-diene² and 3-benzoyl-1,2,3,4,7,8-hexahydro-4,4,8-trimethylnaphthalene³ have been subjected to this oxidation. In the former case, hydroxylation of either of the two conjugated carbon-carbon double bonds and subsequent oxidation of the resulting diols to the hydroxy-ketones occurred in addition to aromatisation.



In contrast, this oxidant oxidised only one of conjugated ethylenic linkages of the latter compound to yield the mono-unsaturated α -diketone. The oxidation of the

conjugated diene, (+)-occidentalol (1), the configuration of which was recently determined^{4,5} as that shown, with permanganate-periodate has been shown to give the unexpected oxide (2).⁶ We have examined the corresponding oxidation with *t*-butyl chromate.

The oxidation was carried out at room temperature for 24 h in benzene containing glacial acetic acid and acetic anhydride. The bicyclic dione (3) (23% yield), the enone (4) (10%), the dioic acid (6) (19%), and the lactone (8) (7%) were isolated by column chromatography. These compounds were identified on the basis of the following considerations. The dione (3) exhibited a molecular ion at m/e 250 in its mass spectrum, bands in the i.r. at 1725 and 1670 cm^{-1} , and a u.v. absorption at 435 nm (ϵ 24) in ethanol. This absorption indicated⁷ an α -diketone chromophore in which the dihedral angle (θ) between the carbonyl groups is greater than that in 9 β -benzoyloxy-6,10,10-trimethylbicyclo[4.4.0]dec-1-ene-3,4-dione.³ The presence of an ethylenic linkage conjugated with the α -diketone group was deduced from the n.m.r. signals for a single olefinic proton (δ 6.22 p.p.m.) and a 3-proton doublet due to a vinylic methyl group (2.14), as well as by the i.r. band at 1620 cm^{-1} .

¹ T. Suga, *Bull. Chem. Soc. Japan*, 1958, **31**, 569.

² T. Matsuura and T. Suga, *J. Org. Chem.*, 1965, **30**, 518.

³ N. B. Haynes, D. Redmore, and C. J. Timmons, *J. Chem. Soc.*, 1963, 2420.

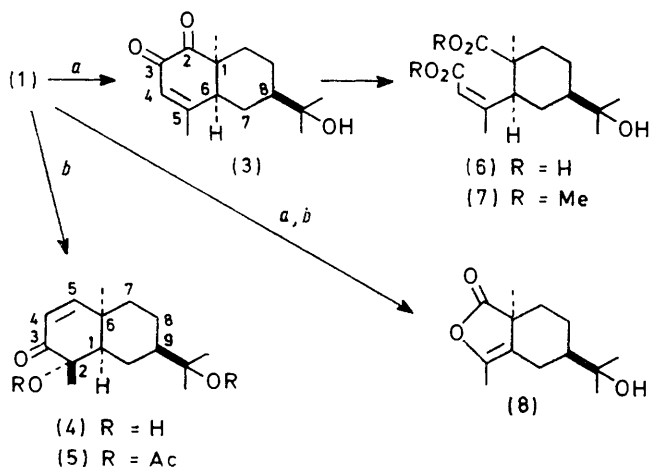
⁴ A. G. Hortmann and J. B. De Roos, *J. Org. Chem.*, 1969, **34**, 736.

⁵ M. Ando, K. Nanaumi, T. Nakagawa, T. Asao, and K. Takase, *Tetrahedron Letters*, 1970, 3891.

⁶ E. von Rudloff, *Tetrahedron Letters*, 1966, 993.

⁷ H. Birnbraum, R. C. Cookson, and N. Lewin, *J. Chem. Soc.*, 1961, 1224.

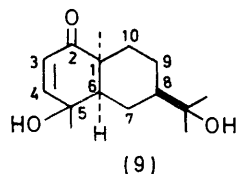
The hydroxy-enone (4) showed m/e 252 (M^+) in its mass spectrum, ν_{\max} 1670 cm^{-1} , and λ_{\max} 234 and 342 nm (ϵ 8520 and 63), thus demonstrating the presence of an



SCHEME

The oxidation of (+)-occidentol (1) with *t*-butyl chromate

$\alpha\beta$ -unsaturated ketone group. A *cis*-disubstituted ethylene linkage in this group was deduced from signals for two olefinic protons in the n.m.r. spectrum. The i.r. spectrum and the formation of the diacetate (5) on treatment with acetic anhydride in the presence of toluene-*p*-sulphonic acid confirmed the presence of two hydroxy-groups. Four 3-proton n.m.r. signals (singlet) due to tertiary methyl groups indicated that the hydroxy-groups are tertiary. Consequently the additional hydroxy-group must be at C-2 [in (4)] or C-5 [in (9)]. However, these spectral data only suggest the possibility of structure (4) or (9). Structure (4) is favoured by the



u.v. spectrum, since the γ -hydroxy- $\alpha\beta$ -unsaturated ketone function of structure (9) would exhibit a hypsochromic shift to give a maximum at 215–220 nm.⁸⁻¹⁰

The stereochemistry at C-2 in (4) was deduced as follows. The long-range coupling¹¹ (J 2.0 Hz) of the M or W type between the vinyl proton at C-5 and the proton at C-1 suggested that the B-ring of the compound is in the most stable chair conformation, with *eq*-methyl and *eq*-hydroxyisopropyl groups. The i.r. spectrum in the hydroxy-stretching region showed four bands, at 3635 (ϵ 34), 3622 (66), 3592 (80), and 3490 cm^{-1} (6)

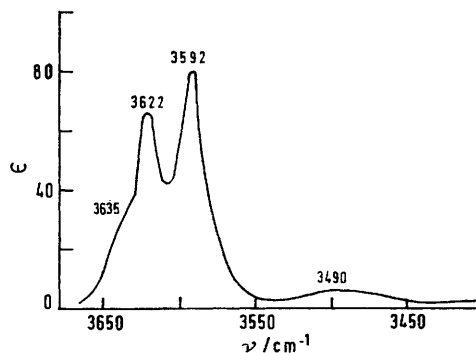
⁸ T. G. Halsall, W. J. Rodewald, and D. Willis, *J. Chem. Soc.*, 1959, 2798.

⁹ T. A. Geissman and G. A. Ellestad, *J. Org. Chem.*, 1962, **27**, 1855.

¹⁰ R. J. Conca and W. Bergmann, *J. Org. Chem.*, 1953, **18**, 1104.

[dilute solution in carbon tetrachloride (see Figure)]. The two high-frequency bands can be attributed to free hydroxy-stretching, due to the hydroxyisopropyl group and the 2-hydroxy-group. The third band was assigned to the intramolecular OH \cdots π system and the fourth to the OH \cdots O system adjacent to the ketone group.¹²⁻¹⁴ Since the A-ring has been postulated to exist in the most stable half-chair conformation,¹⁵ the 2-hydroxy-group should be in the axial orientation (α -configuration), and will easily form an OH \cdots π hydrogen bond as shown in (4a).

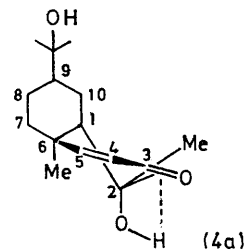
The dicarboxylic acid (6) showed a molecular ion at m/e 284 in its mass spectrum, ν_{\max} 3300, 2550, 1690, and 1630 cm^{-1} , and λ_{\max} 224 nm (ϵ 4580), which suggested the presence of an $\alpha\beta$ -unsaturated carboxylic acid group, together with a saturated carboxy-group. This was



FIGURE

confirmed by the formation of the dimethyl ester (7) and by the n.m.r. spectrum, which showed signals for one olefinic proton at δ 5.75 and one vinylic methyl at 1.86 p.p.m. The spectral data also establish the position of the ethylenic linkage and structure (6) may, therefore, be assigned to this dicarboxylic acid.

Elemental analysis and the mass spectrum of the enolic lactone (8) indicated $\text{C}_{13}\text{H}_{20}\text{O}_3$ for its molecular



formula. The presence of a γ -enolic lactone or γ -lactol group was demonstrated by ν_{\max} at 1770 cm^{-1} , and λ_{\max} at 227 nm (ϵ 40), which suffered a bathochromic

¹¹ T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, 1966, 3663.

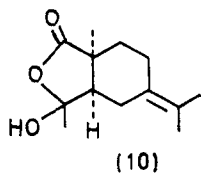
¹² M. Tichy, *Adv. Org. Chem.*, 1965, **5**, 115.

¹³ L. Joris and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1968, **90**, 4599.

¹⁴ T. Suga, T. Shishibori, and T. Matsuura, *Bull. Chem. Soc. Japan*, 1968, **41**, 944.

¹⁵ E. Toromanoff, *Topics Stereochem.*, 1967, **2**, 160.

shift to 282 nm (ϵ 30) in alkaline solution. The presence of an ethylene group was established from the i.r. ν_{\max} at 1674 cm^{-1} , but the n.m.r. spectrum did not show any signal for an olefinic proton. These spectral data implied the γ -enolic lactone (8), and not the γ -lactol (10) structure. This interpretation was supported by the results of ozonolysis, which did not afford acetone,



together with the n.m.r. spectrum, which exhibited three 3-proton singlets due to tertiary methyl groups (δ 1.29 and 1.32 p.p.m.) and one 3-proton singlet due to a vinylic methyl group (1.62). Thus, the enolic lactone was unambiguously assigned structure (8).

From the variety of products isolated, it is clear that the oxidation of occidentalol (1) with *t*-butyl chromate has involved attack at either of the two conjugated carbon-carbon double bonds, to produce the α -hydroxy-enone (4) and the dione (3), and further oxidation of the dione (3) to the dicarboxylic acid (6). For the formation of the α -hydroxy-enone (4), the fact that the 2-hydroxy-group has the α -configuration supports the supposition that the oxidant molecules attack the sterically less hindered α -face of occidentalol. Presumably this is also the case for the formation of the dione (3). As explained previously,³ the attack of *t*-butyl chromate is probably initiated by donation of electrons from the *a*- and *b*-double bonds of the conjugated diene to the chromate, followed by reaction of the resulting carbonium ion with a chromate anion. Hydrolysis of the dichromate complex thus produced would afford the dione (3) and the α -hydroxy-enone (4). The enol lactone (8) is formed presumably by the simultaneous oxidative cleavage of both the *a*- and *b*-double bonds and cyclisation of oxo-carboxylic acid thus produced, followed by dehydration of the cyclised product.

EXPERIMENTAL

Measurements.—I.r. spectra were measured on a Hitachi 215 grating spectrophotometer for chloroform solutions or KBr discs. For OH-stretching data, i.r. spectra were recorded with a Perkin-Elmer 621 grating spectrometer for 0.0042M-solutions in carbon tetrachloride (at which concentration association of the solute may be avoided), with a salt absorption cell of 20 mm length. Sharp peaks were measured with an accuracy of ± 2 cm^{-1} . N.m.r. spectra were recorded with a Hitachi-Perkin-Elmer R-20 High Resolution Spectrometer at 60 MHz, with tetramethylsilane as internal standard in deuteriochloroform. U.v. spectra and optical rotations were measured on a Japan Spectroscopic Co. ORD/UV-5 automatically recording spectropolarimeter for ethanolic solutions, unless otherwise stated.

Occidentalol.—(+)-Occidentalol (1) was isolated from the milled heartwood of a mature Eastern white cedar tree

(*Thuja occidentalis* L.);¹⁶ m.p. 97.5–98°, $[\alpha]_D^{25} + 363.2^\circ$ (*c* 1.6 in CHCl_3).

Oxidation with *t*-Butyl Chromate.—A solution of *t*-butyl chromate was prepared¹ from chromium trioxide (15 g, 0.15 mol), *t*-butyl alcohol (28 g, 0.375 mol), benzene (150 ml), glacial acetic acid (30 ml), and acetic anhydride (20 ml). This solution was added dropwise with agitation at 25° to (+)-occidentalol (6.60 g, 0.03 mol) dissolved in benzene (50 ml), glacial acetic acid (20 ml), and acetic anhydride (5 ml) during 40 min. The mixture was maintained at room temperature for 24 h with stirring under nitrogen. Water (250 ml) and oxalic acid (45 g) were added, and the usual work-up^{1,2} gave a product (5.68 g). Chromatography of the product on a silica gel column with *n*-hexane-ethyl acetate-acetone-di-isopropyl ether (6:2:1:1 v/v) gave five fractions. The second (1.10 g) was a complex mixture and this was not further investigated. Unchanged occidentalol was not detected.

The first fraction (0.45 g) gave white needles of 3-(1-hydroxy-1-methylethyl)-6,9-dimethyl-8-oxabicyclo[4,3,0]non-9-en-7-one (8), m.p. 125.0–125.5° (from di-isopropyl ether), $[\alpha]_D^{25} + 30^\circ$ (*c* 0.248), λ_{\max} 227 nm (ϵ 40), ν_{\max} (CHCl_3) 3525 (OH), 1674 (C=C), and 1770 and 1235 (γ -lactone) cm^{-1} , δ 1.29 (6H, s, 2 \times Me), 1.32 (3H, s, Me), and 1.62 p.p.m. (3H, s, olefinic Me), *m/e* 224 (M^+) (0.7%) (Found: C, 69.7; H, 8.9. $\text{C}_{13}\text{H}_{20}\text{O}_3$ requires C, 69.6; H, 9.0%).

Ozonolysis of the lactone (8). The enolic lactone (8) (17 mg) in dichloromethane (2 ml) was ozonised with cooling (solid carbon dioxide-acetone) until the appearance of blue colour. Removal of the solvent in a stream of nitrogen afforded the ozonide, which was steam distilled. The distillate was treated with ethanolic 2,4-dinitrophenylhydrazine hydrochloride. T.l.c. of the mixture, after extraction with ethyl acetate, showed no acetone 2,4-dinitrophenylhydrazone to be present. In a control experiment with (+)-2-isopropylidene-5-methylcyclohexanone, acetone was detected as the 2,4-dinitrophenylhydrazone.

(+)-2 α -Hydroxy-9-(1-hydroxy-1-methylethyl)-2 β ,6 α -dimethylbicyclo[4,4,0]dec-4-en-3-one (4).—The third fraction (0.65 g) gave white crystals, m.p. 150.0–151.5° (from di-isopropyl ether), $[\alpha]_D^{25} + 244^\circ$ (*c* 0.107 in CCl_4), λ_{\max} 234 (lit.,¹⁷ 227 nm) and 342 nm (ϵ 8520 and 63, respectively), ν_{\max} (CHCl_3) 3600 and 3400 (OH), 1670 (conjugated ketone), and 832 (C=C) cm^{-1} , δ 1.11 (6H, s, 2 \times Me), 1.34 (3H, s, Me), 1.42 (3H, s, Me), 2.23br (s, disappeared on treatment with D_2O , OH), 5.95 (1H, d, *J* 10.5 Hz, vinyl), and 6.59 p.p.m. (1H, dd, *J* 10.5 and 2.0 Hz, vinyl), *m/e* 252 (M^+) (1.9%) (Found: C, 71.0; H, 9.4. $\text{C}_{15}\text{H}_{24}\text{O}_3$ requires C, 71.4; H, 9.6%).

Acetylation of the Enone (4).—A mixture of compound (4) (30 mg), toluene-*p*-sulphonic acid (21 mg), and acetic anhydride (1 ml) was kept at room temperature overnight and then poured into water and extracted with ether. The ether solution was washed with water and then dried (Na_2SO_4). Removal of the solvent gave the diacetate (5) (20 mg) as an oil, $[\alpha]_D^{25} - 12^\circ$ (*c* 0.336), λ_{\max} 236 and 327 nm (ϵ 5950 and 69), ν_{\max} (CHCl_3) 1729 (OAc), 1685 (conjugated ketone), and 1260 and 1245 (OAc) cm^{-1} , δ 1.34 (9H, s, 3 \times Me), 1.54 (3H, s, Me), 1.92 (3H, s, OAc), 1.99 (3H, s, OAc), 5.98 (1H, d, *J* 10.5 Hz, vinyl), and 6.50 p.p.m. (1H, dd, *J* 10.5 and 2.0 Hz, vinyl). Its 2,4-dinitrophenylhydrazone failed to crystallise, but showed λ_{\max} 385 nm (ϵ 24,530).

8-(1-Hydroxy-1-methylethyl)-1,5-dimethylbicyclo[4,4,0]dec-

¹⁶ E. von Rudloff and H. Erdtman, *Tetrahedron*, 1962, **18**, 1315.

4-ene-2,3-dione (3).—The fourth fraction (2.79 g) was further separated into two [fractions (a) and (b)] by column chromatography as before. Fraction (a) gave a yellow oil (1.50 g), λ_{\max} 273, 365, and 435 nm (ϵ 3320, 827, and 24), ν_{\max} (CHCl₃) 3450 (OH), 1725 (ketone), 1670 (conjugated ketone), and 1620 (C=C) cm⁻¹, δ 1.06 (3H, s, Me), 1.15 (3H, s, Me), 1.21 (3H, s, Me), 2.14 (3H, d, *J* 2.0 Hz, vinylic Me), and 6.22br p.p.m. (1H, s, vinyl), *m/e* 250 (*M*⁺) (5.8%). This compound was relatively labile to silica gel.

(+)-3-[2-Carboxy-5-(1-hydroxy-1-methylethyl)-2-methylcyclohexyl]but-2-enoic Acid (6).—Fraction (b) (see preceding paragraph) gave white crystals of the acid (6) (1.28 g), m.p. 171.5° (decomp.) (from ethanol), $[\alpha]_D^{25} + 51^\circ$ (*c* 0.148), λ_{\max} 224 nm (ϵ 4580) (lit.,¹⁷ 217 nm), ν_{\max} (KBr) 3300 (OH), 2550 and 1690 (CO₂H), and 1630 (C=C) cm⁻¹, δ [(CD₃)₂CO] 1.15 (9H, s, 3 × Me), 1.86 (3H, d, *J* 1.5 Hz, vinylic Me), and

5.75br p.p.m. (1H, s, vinyl), *m/e* 284 (*M*⁺) (0.5%) (Found: C, 63.4; H, 8.7. C₁₅H₂₄O₅ requires C, 63.4; H, 8.5%).

Methylation of the acid (6). To a solution of the acid (6) (30 mg) in ethanol (1 ml), an ethereal solution of diazomethane was added dropwise until the appearance of yellow colour. Removal of the solvents gave the dimethyl ester (7) (20 mg) as an oil, $[\alpha]_D^{25} + 64^\circ$ (*c* 0.312), λ_{\max} 230 nm (ϵ 9450), ν_{\max} (CHCl₃) 3500 (OH), 1720 (ester), 1632 (C=C), and 1150 (ester) cm⁻¹, δ 1.15 (3H, s, Me), 1.20 (6H, s, 2 × Me), 1.71 (3H, d, *J* 1.5 Hz, vinylic Me), 3.66 (6H, s, 2 × CO₂Me), and 5.72 p.p.m. (1H, d, *J* 1.5 Hz, vinyl).

[1/1598 Received, 2nd September, 1971]

¹⁷ A. I. Scott, in 'Interpretation of the Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, pp. 58 and 79.