Stereochemical Studies of Monoterpene Compounds. Part XI.[1] Rearrangement of 2α-Hydroxypinan-3-one in the Presence of Anhydrous Oxalic Acid

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Treatment of (+)-2α-hydroxypinan-3-one (1) with anhydrous oxalic acid led to the formation of eucarvone (2), carvacrol (3), (+)-dihydro-β-campholenolactone (1,8,8-trimethyl-2-oxabicyclo[3,3,0]octan-3-one) (4), (−)-1,2-campholide (1,8,8-trimethyl-2-oxabicyclo[3,2,1]octan-3-one) (5), (±)-carvone (6), and (+)-α-campholenic acid (7). Conversion of (+)-2α-hydroxypinan-3-one (1) into the ketone (2) and the lactones (4) and (5) is a novel acid-catalysed rearrangement of the pinane skeleton. The mechanistic implications of the rearrangement are discussed.

TREATMENT of 2α-hydroxypinan-3-one (1)[2] † with anhydrous oxalic acid has been reported to afford carvacrol (3) and a terpene ketone, *p*-mentha-4(8),6-dien-2-one,[3] which was later shown to be eucarvone (2).[4] We now report the results of a more detailed examination of the reaction of (+)-2α-hydroxypinan-3-one (1) with anhydrous oxalic acid.

RESULTS AND DISCUSSION

The (+)-hydroxy-ketone (1) in acetone was treated with anhydrous oxalic acid as previously.[3] The product mixture consisted of carvacrol (3) (41%), (+)-dihydro-β-campholenolactone (1,8,8-trimethyl-2-oxabicyclo[3,3,0]-octan-3-one) (4)[5] (28%), eucarvone (2) (9·8%), (±)-carvone (6) (0·1%), (−)-1,2-campholide (1,8,8-trimethyl-2-oxabicyclo[3,2,1]octan-3-one) (5)[5] (0·05%), and unchanged hydroxy-ketone (1) (3·1%). The structures of the γ- and δ-lactones (4) and (5) were confirmed by their conversion into 2-(2-hydroxyethyl)-1,5,5-trimethylcyclopentanol (8) and 3-(2-hydroxyethyl)-1,2,2-trimethylcyclopentanol (9), respectively. The stereochemistry suggested[5] for the (+)-γ-lactone (4) and the (−)-δ-

† The αβ-notation has been used; the isopropylidene bridge has been considered to have the β-configuration.

[1] Part X, S. Watanabe, T. Suga, T. Shishibori, and T. Matsuura, *Bull. Chem. Soc. Japan*, 1971, **44**, 204.

[2] T. Kuwata, *J. Amer. Chem. Soc.*, 1937, **59**, 2509.

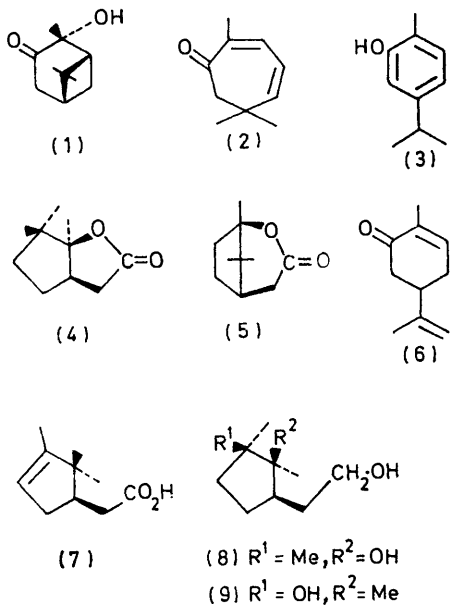
[3] T. Kuwata, *J. Soc. Chem. Ind., Japan*, 1937, **40**, 24.

[4] T. Suga, K. Mori, and T. Matsuura, *J. Org. Chem.*, 1965, **30**, 669.

[5] T. Hirata, T. Suga, and T. Matsuura, *Bull. Chem. Soc. Japan*, 1970, **43**, 2588.

lactone (5) was confirmed by application of the Snatzke lactone rule.[6]

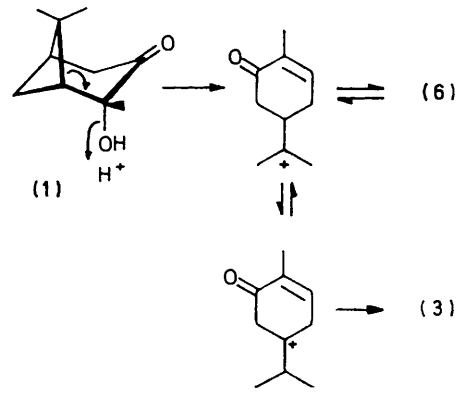
To establish the mechanism of the formation of lactones (4) and (5), the hydroxy-ketone (1) was treated with anhydrous oxalic acid for a shorter time. From this reaction the intermediate, (+)-α-campholenic acid (7),



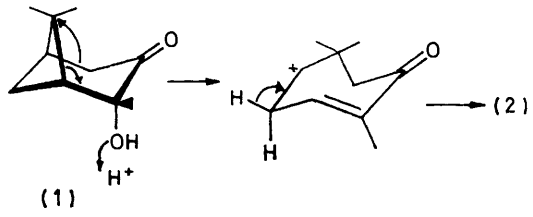
was isolated in addition to the other products. The acid-catalysed reaction of (+)-α-campholenic acid (7) with anhydrous oxalic acid gives the lactones (4) and (5) in 74 and 25% yield, respectively,[5] although only the γ-lactone (4) is formed in the reaction of the acid (7) with sulphuric acid.[7] This indicates that α-campholenic acid (7) is an intermediate in the formation of lactones (4) and (5) from the hydroxy-ketone (1).

Treatment of compound (6) with anhydrous oxalic acid afforded only the phenol (3), and no trace of the ketone (2) could be detected.

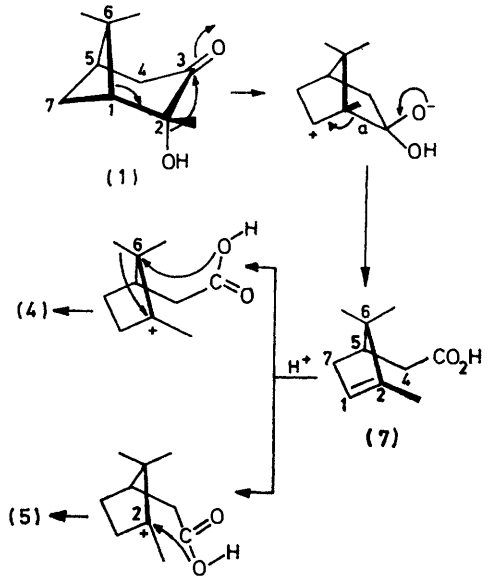
Reaction Mechanism.—The formation of the products is explained in terms of the following processes: (*a*) alteration of the bicyclic skeleton to a monocyclic system, (*b*) ring-expansion to a seven-membered ring, and (*c*) lactone formation involving a Wagner–Meerwein rearrangement. The formation of carvacrol (3) and carvone (6) involves pathway (*a*). The initial loss of the tertiary hydroxy-group, followed by ring-opening, results in the formation of the phenol (3) and the ketone (6) (Scheme 1). Pathway (*b*) is responsible for the formation of eucarvone (2), by ring-expansion involving concerted migration of bonds (Scheme 2). The formation of lactones (4) and (5) involves a Wagner–Meerwein rearrangement (Scheme 3). This rearrangement is initiated by protonation of the carbonyl group. Concerted migration of the hydroxy-group and the bridge, followed by migration of bond a, affords the acid (7) as an intermediate. The acid (7) is then protonated and a 1,2-shift of a methyl group, followed by lactone formation between the carboxy-group and



SCHEME 1



SCHEME 2



SCHEME 3

C-6 gives the γ-lactone (4). The δ-lactone (5) is formed by direct lactone formation between the carboxy-group and C-2.

EXPERIMENTAL

N.m.r. spectra were recorded with a Varian A-60 spectrometer using tetramethylsilane as internal standard. O.r.d. and c.d. curves were obtained at 25° with a JASCO ORD/UV-5 automatically recording spectropolarimeter equipped with

[6] G. Snatzke, H. Ripperger, C. Horstmann, and K. Schreiber, *Tetrahedron*, 1966, **22**, 3103.
[7] R. R. Sauers, *J. Amer. Chem. Soc.*, 1959, **81**, 925.

a c.d. attachment. G.l.c. analyses were performed with a Perkin-Elmer F6-D gas chromatograph. Identities of products were confirmed by comparison with authentic materials.

2α-Hydroxypinan-3-one (1).—(−)-Pin-2-ene, b.p. 71·0° at 51 mmHg, $[\alpha]_D^{25}$ −39·9°, was oxidized [2] with potassium permanganate in aqueous 90% acetone for 8·5 h at −5° to give (+)-2α-hydroxypinan-3-one (1) (24%), m.p. 34—35° (lit.,[8] 34·5—35·3°), $[\alpha]_D^{25}$ +23·3° (*c* 4·64 in EtOH) [lit.,[2] −18·56° (*c* 14·44 in EtOH)].

Reaction of 2α-Hydroxypinan-3-one (1) *with Anhydrous Oxalic Acid.*—(a) *For 6 h.* (+)-2α-Hydroxypinan-3-one (1) (200 g) and anhydrous oxalic acid (333 g) in acetone (266 ml) were heated under reflux for 6 h. After removal of acetone under reduced pressure, the mixture was poured into saturated sodium chloride solution and extracted with light petroleum. The extract was washed with 5% potassium hydroxide solution to give the acidic product, carvacrol (3) (82·8 g), b.p. 111·5—112·0 at 9 mmHg; phenylurethane, m.p. 134—135°. Removal of solvent from the residue gave the neutral fraction (98·9 g) which was distilled and then chromatographed on silica gel (ethyl acetate–n-hexane) to give five components: (i) eucarvone (2) (19·6 g), b.p. 82—84° at 10 mmHg, n_D^{25} 1·5055, d^{25} 0·9445; $\lambda_{max.}$ (MeOH) 303 nm (log ε 3·81); 2,4-dinitrophenylhydrazone, m.p. 151—152°; (ii) (±)-carvone (6) (0·2 g), $\lambda_{max.}$ (MeOH) 235 nm (log ε 3·80); 2,4-dinitrophenylhydrazone, m.p. 187—187·5°; (iii) (+)-dihydro-β-campholenolactone (4) (60 g); (iv) (−)-1,2-campholide (5) (0·1 g); and (v) the unchanged hydroxy-ketone (1) (6·2 g).

The (+)-γ-lactone (4) had m.p. 32—33° (lit.,[9] 32°); $[\alpha]_D^{25}$ +16·10° (*c* 10·0 in EtOH); $\nu_{max.}$ (CCl_4) 1774 (lactone C=O), 1442 (CH_2), 1392, 1371, and 1178 cm^{-1} (*gem*-Me_2); δ (CCl_4) 0·85 (3H, s), 1·00 (3H, s), and 1·20 p.p.m. (3H, s); $\lambda_{max.}$ (MeOH) 210sh nm (log ε 1·65); *m/e* 168 (M^+); o.r.d. (*c* 2·64 in MeOH) $[\phi]_{400}$ +272°, $[\phi]_{225}$ +1550°, and $[\phi]_{210}$ +2000°; c.d. (*c* 2·64 in MeOH) $[\phi]_{250}$ 0°, $[\theta]_{210}$ +328°, and $[\theta]_{200}$ +300°.

The (−)-δ-lactone (5) had m.p. 162—163° (lit.,[7] 168·5—171·5°); $[\alpha]_D^{25}$ −35·0° (*c* 1·0 in EtOH) (lit.,[7] −37°); $\nu_{max.}$ (CCl_4) 1729 cm^{-1} (lactone C=O); δ ($CDCl_3$) 1·00 (3H, s), 1·07 (3H, s), and 1·29 p.p.m. (3H, s); $\lambda_{max.}$ (MeOH) 215sh nm (log ε 1·98); o.r.d. (*c* 1·62 in MeOH) $[\phi]_{400}$ −250, $[\phi]_{227}$ −4010, $[\phi]_{208}$ −1770, and $[\phi]_{200}$ −2970; c.d. (*c* 1·62 in MeOH) $[\theta]_{242}$ 0, $[\theta]_{215}$ −4270, and $[\theta]_{200}$ −3200.

(b) *For 3 h.* The hydroxy-ketone (1) was treated as above for 3 h. The reaction mixture in light petroleum was first washed with sodium hydrogen carbonate solution to give (+)-α-campholenic acid (7) (6·2%), b.p. 116—118° at 3 mmHg, n_D^{25} 1·4705, d^{25} 1·0058, $[\alpha]_D^{25}$ +7·4° (*c* 10 in EtOH); $\nu_{max.}$ (film) 1711 cm^{-1} (CO_2H), and then with sodium hydroxide solution to give carvacrol (3) (15·2%). The neutral fraction was composed of eucarvone (2) (2·2%), carvone (6) (16·6%), (+)-γ-lactone (4) (7·8%), δ-lactone (5) (trace), and unchanged hydroxy-ketone (1) (15·2%).

Reaction of Carvone (6) *with Anhydrous Oxalic Acid.*—Carvone (50 g) and anhydrous oxalic acid (95 g) in acetone (80 ml) were heated under reflux for 6 h to give carvacrol (3) (19%) and unchanged carvone (77%).

Reduction of Dihydro-β-campholenolactone (4).—(+)-γ-Lactone (4) (0·30 g) in ether (50 ml) was refluxed with lithium aluminium hydride (0·3 g) for 7 h to yield the glycol (8) (0·24 g), m.p. 147—148° (lit.,[9] 147°), $[\alpha]_D^{25}$ +38·9° (*c* 1·49 in EtOH); $\nu_{max.}$ (CCl_4) 3626 (OH, free) and 3462 cm^{-1} (OH, bonded) (Found: C, 69·85; H, 11·95. Calc. for $C_{10}H_{20}O_2$: C, 69·7; H, 11·7%).

Reduction of 1,2-Campholide (5).—Reduction of the (−)-δ-lactone (5) (0·2 g) with lithium aluminium hydride (0·2 g) in ether (100 ml) gave the glycol (9) (0·09 g), m.p. 92—93° (lit.,[7] 91—93°), $[\alpha]_D^{25}$ +72·4° (*c* 1·85 in EtOH); $\nu_{max.}$ (CCl_4) 3624 cm^{-1} (OH, free) (Found: C, 70·0; H, 11·7%).

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[9] M. Harispe and D. Mea, *Bull. Soc. chim. France*, 1962, 1340.