176. *Oxomanoyl Oxide.*

By P. K. Grant.

The position of the carbonyl group in oxomanoyl oxide has been confirmed. The six-membered oxide ring shows two characteristic infrared absorption bands, at 1117—1120 and 1076—1080 cm.$^{-1}$.

Hosking and Brandt[1] assigned structure (I) to oxomanoyl oxide. This compound yielded a hydroxymethylene derivative (presumably the mono-derivative) on treatment with ethyl formate, despite the presence of two methylene groups adjacent to the ketonic group, but their isolation of 1 : 2 : 5 : 7-tetramethylnaphthalene on selenium dehydrogenation of its methyl Grignard derivative proved the 3-position of the keto-group.

Since this investigation, no other diterpene has been shown conclusively to be oxygenated in ring A, but all similarly oxygenated triterpenes have the oxygen atom, usually as hydroxyl, adjacent to the *gem.*-dimethyl group. By analogy the possibility that oxomanoyl oxide was oxygenated in the 2-position warranted investigation. The 2-position also offered the possibility of a different biosynthetic process,[2] namely cyclisation by OH^+ (as for triterpenes) of the necessary isoprenoid units rather than the normal H^+-cyclisation of diterpenes.

Chemical and physical studies were undertaken to distinguish between the two alternative structures of oxomanoyl oxide. Catalytic reduction of the oxide gave dihydrooxomanoyl oxide which with sodium borohydride gave the two stereoisomers of dihydrohydroxymanoyl oxide; these were also prepared *via* hydroxymanoyl oxide by treatment with these reducing agents in the reverse order.

Since the A/C ring-junction in the manoyl oxide series is *trans*,[3] a 3-hydroxyl group in the more stable equatorial conformation would have the α-configuration, whereas an equatorial 2-hydroxyl group would have the β-configuration. The stereoisomeric dihydrohydroxymanoyl oxides were separated chromatographically, the major component showing a C–O stretching band at 1039 cm.$^{-1}$, a frequency consistent with an equatorial hydroxyl group,[4] but the axial epimer showed an unusually high C–O stretching frequency (1030 cm.$^{-1}$).

The location of the hydroxyl group was shown by the standard reaction sequence[5] previously applied to triterpenes with 3β-hydroxy-groups (cf. II): dehydration with phosphorus oxychloride of such compounds is accompanied by ring contraction involving retropinacolinic rearrangement, and ozonolysis of the dehydration product (III) then yields acetone and the corresponding A-nor-ketone (IV). Now, dehydration of both

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[1] Hosking and Brandt, *Ber.*, 1935, **68**, 286.

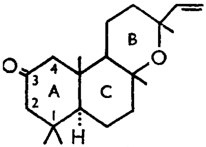
[2] Ruzicka, *Experientia*, 1953, **9**, 357.

[3] Jeger, Durst, and Buchi, *Helv. Chim. Acta*, 1947, **30**, 1853.

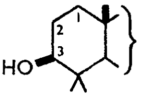
[4] Cole, Jones, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571.

[5] Ruzicka, Montavon, and Jeger, *Helv. Chim. Acta*, 1948, **31**, 818; Dorée, McGhie, and Kurzer, *J.*, 1949, S167.

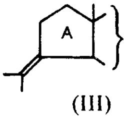
epimers of dihydrohydroxymanoyl oxide gave the same product, which showed a C:C stretching band at 1663 cm.$^{-1}$ but no band for a hydroxyl-group. A strong absorption band at 964 cm.$^{-1}$, together with lack of end absorption in the ultraviolet region,[6] strongly suggested the presence of a disubstituted ethylenic double bond: the dehydration product thus has a CH:CH group at position 2 : 3 or 3 : 4 in a six-membered ring A, consistent with structure (I) for oxomanoyl oxide and inconsistent with a 2-oxo-group, for in the latter case the dehydration product (III) would contain a tetrasubstituted ethylenic linkage. Ozonolysis of the dehydration product gave no acetone or other volatile carbonyl product, and the ozonolysis product, although not crystalline, showed absorption bands at 1703 and 1723 cm.$^{-1}$, possibly corresponding to expectations for an aldehydic carboxylic acid. The absence of a carbonyl band in the 1740 cm.$^{-1}$ region eliminated the possibility that the ozonolysis product was a *cyclo*pentanone (IV), the end product from a 2-ketone in this reaction sequence.



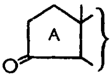
(I)



(II)

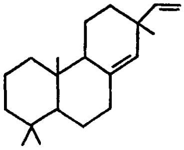


(III)

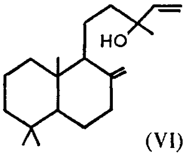


(IV)

From a study of the infrared spectra of these derivatives of manoyl oxide and of the closely related compounds rimuene (V) and tetrahydrorimuene it has been possible to attribute a characteristic frequency to the oxide ring in the manoyl oxide type compounds. The series manoyl oxide, dihydromanoyl oxide, oxomanoyl oxide, dihydro-oxomanoyl oxide, hydroxymanoyl oxide, dihydrohydroxymanoylol oxide, and the dehydration product of dihydrohydroxymanoyl oxide all showed two strong bands, at 1117—1120 and 1076—1080 cm.$^{-1}$ respectively, both of which were absent from the spectra of rimuene, tetrahydrorimuene, and manool (VI) where the oxide ring is not present. The former band, the characteristic C–O stretching band, is in the range 1150—1060 cm.$^{-1}$ attributed to alkyl ethers.[7] The doublet is also present in the ozonolysis product.



(V)



(VI)

It was hoped that by measuring the peak intensity of the band resulting from methylene groups adjacent to the oxo-group [8] of oxomanoyl oxide a physical proof of the position of this group could be obtained. Measurements were carried out on dihydro-oxomanoyl oxide in order to eliminate the interference of the 1418 cm.$^{-1}$ CH_2 in-plane deformation band of the vinyl side chain, but the intensity of the " perturbed CH_2 vibration " at 1422 cm.$^{-1}$ showed little correlation with the intensities of similar bands in the reference compounds cholestanone, lanostenone, and β-amyrone.

EXPERIMENTAL

M. p.s are corrected. Unless otherwise stated, light petroleum had b. p. 40—60°.

Fractional distillation, under reduced pressure, of an acetone extract of the heartwood of *Dacrydium colensoi* yielded oxomanoyl oxide, b. p. 170—180°/0·4 mm. The ether–light petroleum eluate from a chromatogram of this oil on alumina (grade 1) gave oxomanoyl oxide,

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[6] Halsall, *Chem. and Ind.*, 1951, 867.

[7] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1955, p. 101.

[8] Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648.

m. p. 77—78° (from aqueous methanol) (lit., b. p. 174—178°/0·5 mm.; m. p. 76—77°), $\nu_{max.}$ (in Nujol) 3044w, 1703s, 1635, 1419, 1348w, 1310w, 1295w, 1282s, 1264, 1224, 1212, 1190w, 1166, 1155, 1140, 1120s, 1097, 1080s, 1041s, 1023, 1016, 996, 985, 968, 923s, 892w, 863, 847 cm.$^{-1}$.

Dihydro-oxomanoyl Oxide.—Oxomanoyl oxide (200 mg.) in methanol (25 c.c.) was hydrogenated in the presence of Adams catalyst (uptake 15·4 c.c. at 20°/766 mm., equiv. to one double bond). Removal of the methanol in a vacuum and chromatography of a light petroleum solution of the product yielded dihydro-oxomanoyl oxide (150 mg.), m. p. 91—92° (from aqueous methanol) (lit., 89—90°), $\nu_{max.}$ (in Nujol) 2720w, 1703s, 1345w, 1314w, 1299w, 1284s, 1265w, 1224, 1208, 1196w, 1177w, 1120s, 1109w, 1080s, 1056w, 1035, 996s, 988w, 960, 957, 912w, 891w, 863w, 840, 777w, 754w, 722, 705w, 690w cm.$^{-1}$, (in CCl_4) 1485, 1466s, 1422, 1394s, 1376s, 1369sh cm.$^{-1}$.

Dihydrohydroxymanoyl Oxide.—Dihydroxy-oxomanoyl oxide (1·77 g.) in methanol (30 c.c.) was reduced with sodium borohydride, the excess of hydride being destroyed with a few drops of glacial acetic acid. After dilution and removal of the methanol in a vacuum the mixture was extracted with ether to give a clear glass (1·87 g.). A light petroleum solution of the product was chromatographed on alumina (grade 1). A light petroleum–ether (5 : 1) eluate gave a colourless oil which on recrystallization from aqueous methanol yielded needles of dihydrohydroxymanoyl oxide (axial epimer), m. p. 79·5—80·5°. A light petroleum–ether (2 : 1) eluate gave needles of *dihydrohydroxymanoyl oxide* (*equatorial epimer*), m. p. 51—52° after recrystallisation from aqueous methanol (Found: C, 77·85; H, 11·7. $C_{20}H_{36}O_2$ requires C, 77·85; H, 11·8%), $\nu_{max.}$ (in Nujol) 3370s, 1348w, 1314w, 1295w, 1225, 1200w, 1192, 1150w, 1140w, 1119s, 1093w, 1080s, 1039s, 1005, 994, 956, 929w, 909w, 889w, 835, 812 cm.$^{-1}$.

Hydroxymanoyl Oxide.—Oxomanoyl oxide (0·7 g.) in methanol (25 c.c.) was reduced with sodium borohydride, and the mixture worked up as before. The product was purified by chromatography on alumina but separation into stereoisomers was not attempted at this stage.

Recrystallisation of the product (0·6 g.) from aqueous methanol gave colourless needles of *hydroxymanoyl oxide*, m. p. 80—81° (a mixed m. p. with oxomanoyl oxide gave a 20° depression) (Found: C, 78·3; H, 10·9. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2%), $\nu_{max.}$ (in Nujol) 3400s, 3062w, 1644, 1490, 1413, 1365, 1321, 1311w, 1289, 1256, 1222, 1198, 1190, 1168w, 1136, 1117s, 1100s, 1076s, 1041w, 1025s, 1000sh, 944s, 928w, 918s, 904, 887, 837s, 810, 797w, 745w, 721w, 703, 668w, 652 cm.$^{-1}$. Hydrogenation of this oxide (122 mg.) in methanol (20 c.c.) in the presence of Adams catalyst (uptake 7·6 c.c., 20°/764 mm., equiv. to one double bond) gave, after removal of the methanol in a vacuum and chromatography of the product on alumina (grade 1), the epimeric dihydrohydroxymanoyl oxides, m. p. and mixed m. p. 79° and 51° respectively.

Dehydration of Dihydrohydroxymanoyl Oxide.—Phosphorus oxychloride (10 c.c.) was added dropwise to a solution of dihydrohydroxymanoyl oxide (0·52 g.) in pyridine (30 c.c.). The mixture was heated on a water-bath for ¼ hr., kept overnight, and re-heated on a water-bath for ½ hr. Dilution with water and ether-extraction gave sticky crystals which were chromatographed on alumina (grade 1) in light petroleum. A light petroleum eluate gave colourless needles of the dehydration product (0·32 g.), m. p. 83—84° after recrystallisation from methanol (Found: C, 82·4; H, 11·7. $C_{20}H_{34}O$ requires C, 82·65; H, 11·8%), $\lambda_{max.}$ 205, 210, 215, 220, 223 mμ (ε 708, 152, 54, 38, 30), $\nu_{max.}$ (in Nujol) 1660, 1359, 1324w, 1305, 1277w, 1262, 1236w, 1222, 1199, 1166, 1120s, 1077s, 1068w, 1038s, 1005, 994s, 984s, 964, 954, 946, 928w, 910w, 903, 887, 847s, 807w, 774w, 760w, 733s, 724s cm.$^{-1}$.

The following spectra were also recorded:

Manoyl oxide, m. p. 29°, $\nu_{max.}$ (film) 2934s, 2872, 1649, 1469s, 1446, 1389s, 1366, 1336w, 1311w, 1295w, 1250, 1224w, 1206w, 1193w, 1175w, 1151, 1126w, 1119s, 1102, 1079s, 1045, 1030, 1018, 995, 988, 973, 963w, 918s, 859w, 841w, 814w, 700w, 683w, 669w cm.$^{-1}$.

Dihydromanoyl oxide, m. p. 19°, $\nu_{max.}$ (film) 2926s, 2864, 1463, 1387, 1374, 1352w, 1338w, 1311, 1294, 1275w, 1264, 1243w, 1212w, 1202, 1188, 1146, 1117s, 1090, 1080s, 1070w, 1054w, 1044, 1035, 1025w, 1005s, 985w, 970s, 959s, 931, 903w, 887w, 857, 844, 831w, 814w, 782w, 699, 673 cm.$^{-1}$.

Manool, m. p. 53°, $\nu_{max.}$ (in Nujol) 3390s, 1643, 1409w, 1345w, 1315w, 1271w, 1254w, 1222w, 1202, 1190, 1138w, 1115w, 1101, 1037, 988s, 913s, 888s, 735, 675 cm.$^{-1}$.

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