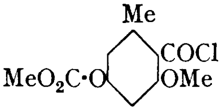
123. *Lichen Acids. Part V. A Synthesis of Methyl* O-*Tetramethylgyrophorate.*

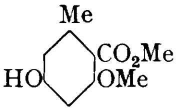
By Frederick W. Canter, Alexander Robertson, and Roy B. Waters.

The synthesis of *o*-diorsellinic acid by Fischer and Fischer (*Ber.*, 1913, **46**, 1138; 1914, **47**, 505) disproved the suggestion of Hesse (*J. pr. Chem.*, 1900, **62**, 463) that the lichen product gyrophoric acid, which occurs in the majority of species of *Gyrophora*, was a didepside isomeric with lecanoric acid. More recently, Asahina and his co-workers (*J. Pharm. Soc. Japan*, 1925, No. **519**, 1; *Ber.*, 1930, **63**, 3044; 1932, **65**, 983) have shown that the compound is a tridepside composed of three units of orsellinic acid, and, starting from lecanoric acid, have effected a synthesis of methyl tetramethylgyrophorate. In a similar manner, using the requisite diacetate of lecanoric acid, Koller (*Monatsh.*, 1932, **61**,

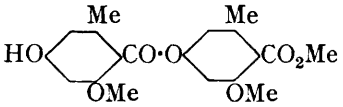
147) synthesised methyl tetra-acetylgyrophorate. The structure assigned to gyrophoric acid (V, R = H) by these authors has now been confirmed by the following synthesis of methyl *O*-tetramethylgyrophorate.



(I.)

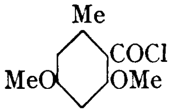


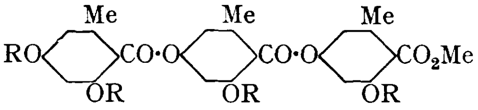
(II.)



(III.)

(IV.)





(V.)

The interaction of the acid chloride (I) and the ester (II) gave, on subsequent removal of the carbomethoxy-group, *methyl* O-*dimethyllecanorate* (III), and this compound on condensation with *O*-dimethylorsellinoyl chloride (IV) in the same manner yielded methyl *O*-tetramethylgyrophorate (V, R = Me), identical with the natural compound.

EXPERIMENTAL.

Methyl iso*Everninate* (II).—Methylation of *p*-monocarbomethoxyorsellinic acid (3 g.) with MeI (10 c.c.) and Ag_2O (6 g.) in boiling acetone for 12 hr. gave methyl carbomethoxy*iso*everninate (2 g.), m. p. 87° after crystn. from light petroleum (compare Fischer and Hoesch, *Annalen*, 1912, **391**, 371). If the Ag_2O is replaced by K_2CO_3, the carbomethoxy-group is removed in the reaction.

A solution of the carbomethoxy-derivative (8 g.) in EtOH (75 c.c.) was carefully treated with 20% alc. KOH (25 c.c.), kept for 1 hr., diluted with excess H_2O, acidified with dil. aq. HCl, and extracted with Et_2O. Evaporation of the dried extract left methyl *iso*everninate, which separated from C_6H_6 in needles (5 g.), m. p. 112°, and appeared to be identical with material obtained from methyl *O*-dimethylobtusate or methyl *O*-trimethyllecanorate by Asahina and Fuzikawa (*Ber.*, 1932, **65**, 580) (Found: C, 61·1; H, 6·1. Calc. for $C_{10}H_{12}O_4$: C, 61·2; H, 6·1%). It is readily sol. in H_2O, EtOH, $CHCl_3$ or acetone and does not give a $FeCl_3$ reaction.

*Carbomethoxy*iso*everninoyl Chloride* (I).—In the course of attempts to prepare *O*-acetyl*iso*everninic acid to be used in place of the carbomethoxy-derivative it was found that this compound could not be obtained either by the oxidation of *O*-acetyl*iso*everninaldehyde or by the acetylation of *iso*everninic acid.

Carbomethoxy*iso*everninic acid (3 g.) was treated in dry warm $CHCl_3$ (50 c.c. at 35—40°) with PCl_5 (3·1 g., added in portions), and the mixture kept at room temp. for ½ hr. and then at 50° for 10 min. to complete the reaction. The $CHCl_3$ and $POCl_3$ were removed in a vac. at 45°, the residue dissolved in a further quantity of $CHCl_3$, and the solution again evaporated. Repetition of this procedure finally removed the remaining traces of phosphorus compounds and left the chloride as a pale straw-coloured syrup which gradually crystallised in long needles, m. p. 45—48°. This compound, which was not further purified, rapidly decomposed in moist air. The *anilide* crystallised from 50% MeOH in regular laminated prisms which on drying appeared to lose solvent of crystn.; m. p. 149—150° (Found in material dried at 110°: C, 64·6; H, 5·4. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4%).

Methyl O-*Dimethyllecanorate* (III).—The afore-mentioned acid chloride (from 3 g. of acid) was added to a solution of methyl *iso*everninate (0·9 g.) in dry pyridine (10 c.c.), and the mixture agitated for several hr., kept at room temp. for 4 days and then at 40° for ½ hr., and poured into 3% aq. AcOH (200 c.c.). An ethereal solution of the semi-solid ppt. was washed with H_2O and then with aq. $NaHCO_3$, dried and evaporated. A solution of the residual gum in acetone (10 c.c.) was treated with 4% aq. NaOH (25 c.c.) and after ½ hr. the *ester* was carefully pptd. with dil. aq. HCl, washed with H_2O, and crystallised from MeOH, forming thick colourless needles (1·6 g.), m. p. 142° (Found: C, 63·2; H, 5·7. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%). This compound is sol. in aq. NaOH and insol. in aq. $NaHCO_3$, and does not give a $FeCl_3$ reaction.

2 : 4-*Dimethoxy*-6-*methylbenzanilide*.—The prepn. of *O*-dimethylorsellinic acid by the oxidation of *O*-dimethylorcylaldehyde, m. p. 67°, has been more fully investigated (cf. Robertson

and Robinson, J., 1927, 2200, who record m. p. of this aldehyde 64—65°) and it has been found that oxidation of the aldehyde (10 g.) in acetone (100 c.c.) with $KMnO_4$ (12 g. in 200 c.c. of H_2O) at 40—45° gave the acid (6·8 g., plates from C_6H_6, m. p. with decomp. 145—146°) and unchanged aldehyde (1·5 g.).

The acid (1 g.) was converted into the chloride (IV) with PCl_5 (1·1 g.) in dry $CHCl_3$ (15 c.c.) by the procedure used in the case of carbomethoxy*iso*everninoyl chloride (cf. Asahina and Fuzikawa, *Ber.*, 1932, **65**, 983). This compound was finally obtained as a straw-coloured gum, and on treatment with $PhNH_2$ (4 c.c.) gave rise to the *anilide*, which separated from 50% MeOH in needles (1·2 g.), m. p. 131° (Found : C, 70·8; H, 6·1. $C_{16}H_{17}O_3N$ requires C, 70·9; H, 6·3%).

Methyl O-*Tetramethylgyrophorate* (V, R = Me).—A mixture of *O*-dimethylorsellinoyl chloride (from 4 g. of acid), methyl *O*-dimethyllecanorate (3·8 g.), and dry pyridine (40 c.c.) was kept for 3 days at room temp., heated at 50° for 1 hr., and poured into 6% aq. AcOH (300 c.c.). The ppt. was washed with aq. $NaHCO_3$ and H_2O and on crystn. from acetone formed microscopic prisms (5 g.), m. p. 194°. Recryst. from xylene and then from acetone, it had m. p. 195° (Found : C, 64·6; H, 5·6. Calc. for $C_{29}H_{30}O_{10}$: C, 64·7; H, 5·6%).

O-*Acetyl*iso*everninaldehyde.*—On methylation with MeI (6 c.c.) and Ag_2O (4 g.) in boiling acetone (50 c.c.) during 4 hr., *p*-monocarbomethoxyorcylaldehyde (Hoesch, *Ber.*, 1913, **46**, 886) (3 g.) gave rise to carbomethoxy*iso*everninaldehyde (2·5 g.), m. p. 81° after crystn. from light petroleum (cf. Hirst, J., 1927, 2490). 20% Alc. KOH (25 c.c.) was added to a solution of this compound (9·5 g.) in EtOH (75 c.c.) and after 1 hr. the mixture was diluted with H_2O (500 c.c.) and acidified with HCl aq., yielding *iso*everninaldehyde (5·7 g.), m. p. 196° after crystn. from 50% MeOH (cf. Gattermann, *Annalen*, 1907, **357**, 346; St. Pfau, *Helv. Chim. Acta*, 1928, **11**, 864). Acetylation of *iso*everninaldehyde (4 g.) with Ac_2O (20 c.c.) and AcONa (6 g.) on the steam-bath for 2 hr. gave the *acetate*, which separated from light petroleum in colourless prisms (4·4 g.), m. p. 85° (Found : C, 63·6; H, 5·7. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). This compound is readily sol. in EtOH or AcOEt and is phototropic, becoming deep yellow on exposure to light and colourless again in the dark.

2 : 4-*Diacetoxy*-6-*methylbenzylidene Diacetate.*—In the course of attempts to obtain orcylaldehyde diacetate it was found that acetylation of the aldehyde (5 g.) with Ac_2O (25 c.c.) and AcONa (10 g.) on the steam-bath for 3 hr. gave rise to the *benzylidene diacetate* (9 g.), which separated from light petroleum (b. p. 60—80°) in tiny colourless prisms, m. p. 95—96° (Found : C, 57·0; H, 5·3. $C_{16}H_{18}O_8$ requires C, 56·8; H, 5·3. Calc. for orcylaldehyde diacetate, $C_{12}H_{12}O_5$: C, 61·0; H, 5·1%). This substance is readily sol. in Et_2O, AcOEt, C_6H_6, or EtOH and does not give a $FeCl_3$ reaction.

The use of pyridine in place of AcONa yielded the same compound. On oxidation with $KMnO_4$ this substance did not give *O*-diacetylorsellinic acid.

One of us (F. W. C.) is indebted to the Dixon Fund of London University for a grant and to the Department of Scientific and Industrial Research for a maintenance grant.

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[*Received, April* 3*rd*, 1933.]