Studies on Synthetic Pyrethroid

Part XI.* Another Evidence for the trans-Configuration of \( \alpha\beta \)-Dimethylsorbic Acid

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Methyl \( \alpha\beta \)-dimethylsorbate, when submitted to the selective oxidation sequence by the actions of perbenzoic acid, mineral acid, lead tetaacetate and peracetic acid in this order, finally gives \( \beta \)-monomethyl mesaconate, which is converted after hydrolysis to mesaconic acid of the well-defined trans-configuration. The reaction sequence involves no process likely to invert the configuration, and thus another cogent chemical evidence for the trans-configuration of \( \alpha\beta \)-dimethylsorbic acid is obtained in agreement with the physico-chemical conclusion, previously reported.

The assignment of the trans-configuration to \( \alpha\beta \)-dimethylsorbic acid has been provided by physico-chemical processes in our previous paper\(^1\), in which the selective semi-hydrogenation of this acid and ultra-violet, infra-red absorption spectra and acid dissociation constant of the hydrogenated product were dealt.

Another cogent chemical evidence for this configuration is presented in this paper.

Heinanen\(^2\), reported that the selective epoxydation occurred at the \( \gamma\delta \)-double bond of methyl sorbate by the action of perbenzoic acid in the cold, giving methyl \( \gamma\delta \)-epoxy-\( \Delta_6 \)-hexenoate.

Epoxydation of methyl \( \alpha\beta \)-dimethylsorbate (II) by perbenzoic acid gave methyl \( \gamma\delta \)-epoxy-\( \alpha\beta \)-dimethyl-\( \Delta_6 \)-hexenoate (III) as was expected, one atom of oxygen being taken up. The \( \gamma\delta \)-epoxy structure of III, can reasonably be deduced from the subsequent processes. Conversion of the epoxy-ester into the dihydroxy-compound was easily effected by treatment with dilute sulphuric acid, yielding

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\begin{align*}
\text{Me}_2\text{C} = \text{CH} - \text{CH} = \text{C(Me)CO}_2\text{H} & \xrightarrow{\text{CH}_2\text{N}_2} \text{Me}_2\text{C} = \text{CH} - \text{CH} = \text{C(Me)CO}_2\text{Me} \xrightarrow{\text{BzO}_2\text{H}} \text{(II)} \\
\text{Me}_2\text{C} - \text{CH} - \text{CH} = \text{C(Me)CO}_2\text{Me} & \xrightarrow{\text{dil. H}_2\text{SO}_4} \xrightarrow{\text{Pb(}\text{AcO})_4} \xrightarrow{\text{KOH}} \quad \text{OH} \quad \text{OH} \\
\text{Me}_2\text{C} - \text{CH} - \text{CH} = \text{C(Me)CO}_2\text{Me} & \text{(III)} \\
\xrightarrow{\text{AcO}_2\text{H}} \xrightarrow{\text{H}_2\text{O}} \text{HO}_2\text{C} - \text{CH} = \text{C(Me)CO}_2\text{Me} \quad \text{HO}_2\text{C} - \text{CH} = \text{C(Me)CO}_2\text{H} \xrightarrow{\text{H}_2\text{O}_2} \text{(I)} \\
\end{align*}
\]

\( \gamma\delta \)-dihydroxy-\( \alpha\beta \)-dimethyl-\( \Delta_6 \)-hexenoate (IV).

Lead tetaacetate cleaved the glycolic carbon-carbon linkage of IV and gave \( \beta \)-monomethyl mesaconaldehyde (V), which

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was characterized by 2, 4-dinitrophenylhydrazone m.p. 204-4.5°.

β-Monomethyl mesaconaldehydate was then oxidized with peracetic acid to β-monomethyl mesaconate (VI) m.p. 82-3°, which, as well as the amide m.p. 117° derived therefrom, was completely consistent with the literature3).

Cold saponification of β-monomethyl mesaconate gave mesaconic acid (VII) m.p. 202-3°, not depressed by the mixed melting point comparison with an authentic specimen.

Since the oxidation sequence involves no process likely to invert the geometrical configuration of the double bond, the retention of the configuration in the parent compound can reasonably be concluded. Thus, the final formation of mesaconic acid of the well-established trans-configuration unambiguously shows the trans-configuration of the αβ-double bond of the parent methyl αβ-dimethylsorbate.

Direct peroxidation of αβ-dimethylsorbic acid also gave mesaconic acid in an inferior yield.

The chemical evidence mentioned above is in agreement with the physico-chemical conclusion described in our previous paper.

EXPERIMENTAL

All melting and boiling points were uncorrected. Microanalyses were by the Microanalytical Division of Mitsui Laboratory, Kyoto University. Before analyses, samples were completely dried over P2O5 in vacuo at an appropriate temperature for each.

Methyl αβ-dimethylsorbate (II) To a 4.5 g quantity of αβ-dimethylsorbic acid4) (I, m.p. 134-5°, 0.032 mole) dissolved in 200 ml of dry ether and chilled at -15°, were added dropwise 1.3 g of diazomethane in ether (0.032 mole) under an effective stirring and chilling. The reaction mixture was washed with saturated sodium bicarbonate solution and dried over anhydrous sodium sulphate. After removal of ether, the residue was distilled under a reduced pressure to give methyl αβ-dimethylsorbate*. b.p. 85-6°/7 mm., nD20 1.5242, yield 4.1 g (85%).

Methyl γδ-epoxy-αβ-dimethyl-δα-hexenoate (III) Four grams of methyl αβ-dimethylsorbate, (0.027 mole) were dissolved in 5 ml of dry chloroform and to this were added 147 ml of 3.5% perbenzoic acid in chloroform (0.038 mole). The mixture was kept at 0° and the consumption of the active oxygen was estimated by means of iodometry on a small portion drawn from the reaction mixture at intervals. After 5 days' standing, 0.03 atom of oxygen was taken up, then the excess of perbenzoic acid was decomposed with sodium sulphite, removed by washing with sodium carbonate and dried over anhydrous sodium sulphate. After removal of the solvent, the residue was distilled under a reduced pressure to give methyl γδ-epoxy-αβ-dimethyl-δα-hexenoate, b.p. 91-2°/6 mm., nD20 1.4672, yield 3.7 g (84%).

Methyl γδ-dihydroxy-αβ-dimethyl-δα-hexenoate (IV) To a 1.5 g quantity of epoxy-ester (III), was added 0.5 ml of 5% sulphuric acid, kept at room temperature and after several hour it turned homogeneous. This was then extended in 100 ml of alcohol-free ether and was completely dried over anhydrous sodium sulphate. Removal of ether gave methyl γδ-dihydroxy-αβ-dimethyl-δα-hexenoate in a quantitative yield. plates, (from methanol and benzene) m.p. 50-1° (Anal. Found : C, 57.40; H, 8.46. Calcd. for C9H16O4: C, 57.43 ; H, 8.57).

Methyl γδ-mesaconaldehydate (V) The dihydroxy-ester (IV, 1.48 g., 0.0079 mole) was dissolved in 100 ml of dry benzene and to this were added 3.9 g of freshly prepared lead tetraacetate (0.0087 mole) in three portions. The mixture was stirred at 50° for 2 hrs. and then at 60° for 2 hrs. After the duration, excess of lead tetraacetate was decomposed with water and lead oxide formed was removed by filtration. The filtrate was dried over anhydrous sodium sulphate and the solvent was distilled off. Distillation of the residue in vacuo gave β-monomethyl mesaconaldehydate, b.p. 76-8°/12 mm., nD20 1.4680 (0.75 g., 75%). 2, 4-Dinitrophenylhydrazone, orange needles (from methanol), m.p. 204-4.5° (decomp.) (Anal. Found : C, 46.73 ; H, 3.92; N, 18.21. Calcd. for C12H12O6N4: C, 46.76 ; H, 3.92 ; N, 18.18).

*This ester is completely identical with that obtained by the dehydration of the corresponding Reformatski ester.1) This reconversion of the free acid into the original ester excludes the stereomutation during the hydrolysis and provides further certification for the homogeneity of the trans-ester used in our total synthesis of chrysanthemum dicarboxylic acid.

\(\beta\)-Monomethyl mesaconate (VI) The aldehyde ester (V, 0.3 g., 0.0024 mole.) was dissolved in 2.7 ml of 13.3\% peracetic acid (0.0047 mole) and the mixture was kept cold for 36 hrs. Then the mixture was diluted with water and dried up in vacuo to yield a crystalline mass. The residue was crystallized from petroleum ether (b.p. 40–50°) to give \(\beta\)-monomethyl mesaconate (0.31 g), needles, m.p. 82–3° (Anal. Found C, 50.04; H, 5.61; Calcd. for C\(_6\)H\(_8\)O\(_4\), C, 50.00; H, 5.60) Amide, needles (from ether-petroleum ether), m.p. 115.5–6.5° (Anal. Found : C, 50.39; H, 6.51; N, 9.72; Calcd. for C\(_6\)H\(_8\)O\(_3\)N : C, 50.34; H, 6.34, N, 9.79). These were perfectly consistent with the literature3).

Mesaconic acid (VII) \(\beta\)-Monomethyl mesaconate (VI, 0.1 g) was hydrolysed with cold 5\% ethanolic potassium hydroxide, dried up in vacuo and acidified with dilute sulphuric acid. This was extended in ether, dried over anhydrous sodium sulphate and the removal of ether gave mesaconic acid, cubes (from water) m.p. 202–3° (Anal. Found : C, 46.07; H, 4.60; Calcd. for C\(_6\)H\(_6\)O\(_4\) : C, 46.16; H, 4.65). The melting point was not depressed by the mixed melting point comparison with an authentic specimen prepared by recorded method\(^5\). bis-p-Phenylphenacyl ester, fine needles (from chloroform), m.p. 204–5° (Anal. Found : C, 76.35; H, 5.14; Calcd. for C\(_{33}\)H\(_{26}\)O\(_6\) : C, 76.43; H, 5.05).

**Peroxidation of \(\alpha\beta\)-dimethylsorbic acid (I)** \(\alpha\beta\)-Dimethylsorbic acid (0.3 g) was dissolved in 10 ml of dilute acetic acid, and to this were added 5 ml of 30\% hydrogen peroxide. The mixture was warmed on a water bath for about 10 hrs. with additional peroxide at intervals. At the end of this time, the solution was dried up in vacuo and the solid residue was extracted with cold ether. To the remaining residue were added a drop of dilute sulphuric acid and 2 ml of water, and it was warmed on a water bath. Reduction of the volume gave mesaconic acid (19 mg), which melted at 201–3° after recrystallization from water. The melting point was not depressed by admixture with an authentic specimen. Further reduction of the filtrate gave a less pure product (ca. 25 mg).

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