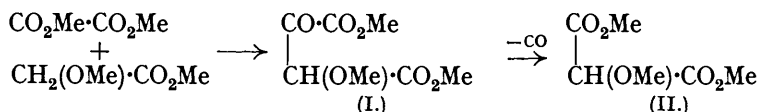


385. *New Derivatives of Methoxymalonic Acid.*

By JOHN PRYDE and R. TECWYN WILLIAMS.

A POSSIBLE oxidation product of trimethyl glucurone and of trimethyl glucuralone (Pryde and Williams, *Biochem. J.*, 1933, **27**, 1205) is methoxymalonic acid (see also Levene and Harris, *J. Biol. Chem.*, 1932, **97**, 11), no derivative of which has hitherto been described.

Several attempts to prepare one were made without success. For instance, methylation of hydroxymalonic acid (tartronic acid) with silver oxide and methyl iodide gave methyl $\alpha\beta$ -dimethoxyethane- $\alpha\alpha\beta\beta$ -tetracarboxylate (Pryde and Williams, this vol., p. 642); and treatment of potassium tartronate with methyl sulphate and alkali caused no appreciable methylation, since suitable treatment of the products gave methyl tartronate and tartronamide, m. p. 196° (Pinner, *Ber.*, 1885, **18**, 753, gives m. p. 192—196°). Success was eventually achieved by adopting the "carbon monoxide cleavage" method used by Wislicenus and Münzesheimer (*Ber.*, 1898, **31**, 552) for the preparation of ethoxymalonic acid. *Methyl α -keto- β -methoxysuccinate* (I) was prepared by condensing methyl methoxyacetate with methyl oxalate in dry ether in the presence of sodium (compare Wislicenus, *Annalen*, 1897, **295**, 347), and this, by loss of carbon monoxide, yielded *methyl methoxymalonnate* (II) :



Methyl α -keto- β -methoxysuccinate possesses an asymmetric carbon atom, but no attempt was made in this investigation to resolve it. Owing to a troublesome contamination with products which we ascribe to "acid" and "ketone" cleavage of methyl α -keto- β -methoxysuccinate, neither the latter nor methyl methoxymalonnate was obtained in a pure state, but the following crystalline derivatives were prepared, purified, and analysed: *methoxymalondiamide*, m. p. 203—204° (slight decomp.), and *methoxymalonnemethylamide*, m. p. 115° (without decomp.).

EXPERIMENTAL.

Methyl Methoxyacetate.—Methyl glycolate, prepared by refluxing glycollic acid with 4% hydrogen chloride in methyl alcohol, was methylated with silver oxide and methyl iodide and ethereal extracts of the products were dried over anhydrous sodium sulphate. After removal of the ether, the resulting methyl methoxyacetate was distilled; b. p. 129.5—130.5°/767 mm., n_D^{20} 1.3972 (Fölsing, *Ber.*, 1884, **17**, 484, gives b. p. 127°/727 mm.; Karvonen, *Chem. Zentr.*, 1919, III, 811, b. p. 129.6—130.2°/756 mm.; and Palomaa, *ibid.*, 1913, II, 1959, n_D^{20} 1.39636).

Methyl α -Keto- β -methoxysuccinate.—Methyl methoxyacetate (35 g.) was added from a dropping-funnel to a solution of 34 g. of dry methyl oxalate in 400 c.c. of dry ether containing 6.64 g. of sodium wire. After effervescence had ceased (1½ days; at room temperature under reflux condenser with protection from moisture), the ether was decanted, the red-brown solid, which contained the sodium salt of the enolic form of methyl α -keto- β -methoxysuccinate, was dissolved in the minimum amount of water, and dilute sulphuric acid was added to the solution under ether until the reaction was just acid to Congo-red paper. The free methyl ester was then extracted from the aqueous layer with ether. In decomposing the sodium salt it is important

to avoid an excess of sulphuric acid, since the latter cannot be removed from the ethereal layer by washing with dilute aqueous sodium carbonate or bicarbonate, owing to the ease with which the sodium salt is re-formed in the presence of these carbonates. The ethereal extract was dried by standing for 24 hours over calcium chloride and then evaporated on a water-bath. The dark brown syrupy residue (8 g.) was distilled in a high vacuum and the crude *methyl* ester distilled as a pale yellow, viscous liquid (5 g.) at a bath temperature of 110—120°/1 mm.; it had $n_D^{19.5}$ 1.4465, but it was not further purified (Found : OMe, 42.6. $C_7H_{10}O_6$ requires OMe, 48.95%). There was a considerable amount of a black solid residue.

The following reactions show the ester to be a ketonic compound : it forms a silver mirror with ammoniacal silver nitrate; it reduces Fehling's solution on warming; it decolorises aqueous permanganate; it gives a port-wine red colour with ferric chloride; it gives a green precipitate with normal copper acetate solution (compare oxalacetic and acetoacetic esters).

Methyl Methoxymalonate.—The crude methyl ketomethoxysuccinate (2.3 g.) was distilled at 745.5 mm. Vigorous evolution of gas took place and the expected *methyl methoxymalonate* distilled at 215° as a pleasant-smelling, slightly yellow liquid (1.34 g.), leaving a black solid residue. It gave none of the reactions of methyl ketomethoxysuccinate, except immediate decoloration of aqueous permanganate in the cold. The quantity obtained was small and did not allow of further purification (Found : OMe, 53.9. $C_6H_{10}O_5$ requires OMe, 57.4%).

Methoxymalondiamide.—A solution of methyl methoxymalonate (0.23 g.) in 3 c.c. of dry methyl alcohol was saturated with ammonia at 0°; it developed a deep yellow colour and crystals began to appear after $\frac{1}{2}$ hour. After 12 hours, the crystals were separated, washed with a little methyl alcohol and then with dry ether, and dried. On solution in a little methyl alcohol and addition of an excess of ether, *methoxymalondiamide* was precipitated in colourless, microscopic, blunt-ended needles, m. p. 203—204° (slight decomp.), slightly soluble in methyl alcohol and insoluble in ether (Found : C, 36.5; H, 6.2; N, 21.1; OMe, 23.5. $C_4H_8O_3N_2$ requires C, 36.4; H, 6.1; N, 21.2; OMe, 23.5%).

Methoxymalonomethylamide.—Dry methylamine was passed into a solution of the crude ester (1 g.) in 5 c.c. of dry methyl alcohol at 0°. The solution was kept over-night in a desiccator. Long needle-shaped crystals of oxobismethylamide separated, m. p. 213—214° (Found : C, 41.4; H, 6.7; N, 24.8. Calc. for $C_4H_8O_2N_2$: C, 41.4; H, 6.9; N, 24.1%). The solution was decanted and allowed to evaporate to dryness, whereby a yellow crystalline mass, containing mostly methoxymalonomethylamide contaminated with oxobismethylamide, was obtained. By repeated crystallisation from benzene (decolorising with "norite" charcoal) pure *methoxymalonomethylamide* was obtained as colourless feathery needles, m. p. 115° (without decomp.) (Found : C, 45.0; H, 7.5; N, 17.5; OMe, 19.4. $C_6H_{12}O_3N_2$ requires C, 45.0; H, 7.5; N, 17.5; OMe, 19.4%).

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