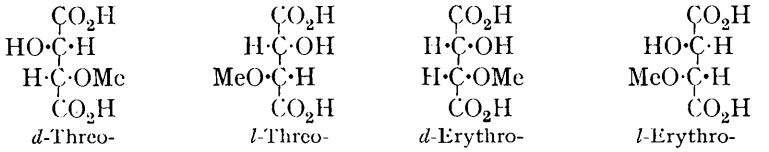
313. *Derivatives of Hydroxymethoxysuccinic Acids, and Some Related Amides.*

By R. Tecwyn Williams.

Methylation, with methyl sulphate and alkali, of *meso*-tartaric and racemic acid affords *dl*-erythro- and *dl*-threo-α-hydroxy-β-methoxysuccinic acid, respectively. The methyl esters, amides, and methylamides of these acids are described, together with the amides and methylamides of racemic, *meso*-tartaric, and *dl*-dimethoxysuccinic acids.

Methylation of *d*-tartaric acid with Haworth's reagents affords *l*-(+)threo-α-hydroxy-β-methoxysuccinic acid (*d*-hydroxymethoxysuccinic acid; Haworth, J., 1915, **107**, 15; Pryde and Williams, J., 1933, 642). Theoretically, six hydroxymethoxysuccinic acids (four active and two racemic) are possible, and these are related in configuration to the tetroses threose and erythrose.



Hydroxymethoxysuccinic acids.

In the present communication, derivatives of dl-*threo*- and dl-*erythro-hydroxymethoxysuccinic acids* are described, these being obtained respectively by methylation of racemic and of *meso*-tartaric acid with methyl sulphate and alkali. The yields of the monomethylated tartaric acids were small, and no evidence of the formation of dimethylated compounds was obtained, although methylation with Purdie's reagents or with diazomethane (Schmidt and Zeiser, *Ber.*, 1934, **67**, 2120) affords dimethylated tartaric acids. The *amides* and *methylamides* of racemic, *meso*-tartaric, and *dl*-dimethoxysuccinic acids have also been prepared.

Experimental.

Methylation of meso-*Tartaric Acid.—Methyl* dl-*erythro-α-hydroxy-β-methoxysuccinate.* 50 G. of *meso*-tartaric acid, obtained by oxidation of maleic acid with sodium chlorate and osmium tetroxide (cf. Hickinbottom, "Reactions of Organic Compounds," p. 12, London, 1936), were neutralised with potassium hydroxide and methylated with 130 c.c. of methyl sulphate and 76 g. of potassium hydroxide (in 100 c.c. of water) during 1 hour, followed by 2 hours' heating on a water-bath. Concentrated sulphuric acid (17 c.c.) was added to the solution, and the whole evaporated to dryness on a water-bath. The dry residue was powdered, and subjected to prolonged ether extraction (Soxhlet). The ether was evaporated, giving 52 g. of an almost colourless stiff syrup, containing a little sulphuric acid. The syrup was dissolved in 115 c.c.

of 1% methyl-alcoholic hydrogen chloride and boiled under reflux for 8 hours. After neutralisation with silver carbonate, filtration, drying over anhydrous magnesium sulphate, and evaporation of the solvent, the residue was extracted repeatedly with boiling benzene. The benzene extract was filtered and set aside to crystallise. Methyl *meso*-tartrate (m. p. 108—110°) which crystallised was separated, and the filtrate evaporated under diminished pressure. The residual pale yellow syrup on distillation in a vacuum gave 7 g. of *methyl* dl-*erythro-hydroxymethoxysuccinate* as a colourless thick liquid, b. p. 107—109° (bath temp.)/*ca.* 0·5 mm., $n_D^{14°}$ 1·4465, $[\alpha]_D$ 0° (in methyl alcohol) (Found : OMe, 49·6. $C_7H_{12}O_6$ requires OMe, 48·45%).

dl-*Erythro-α-hydroxy-β-methoxysuccindiamide*, obtained by treating the ester with ammonia in methyl alcohol, formed colourless stout needles, m. p. 195—196°, from ether–methyl alcohol (Found : N, 17·0; OMe, 19·3. $C_5H_{10}O_4N_2$ requires N, 17·3; OMe, 19·1%).

Treatment of the ester with a solution of methylamine in methyl alcohol gave the *bismethylamide*, which, after recrystallisation as above, formed tufts of closely-set, deliquescent needles, m. p. 125° (Found, in substance dried in a vacuum at 100° : C, 44·45; H, 7·35; N, 14·7; OMe, 16·5. $C_7H_{14}O_4N_2$ requires C, 44·2; H, 7·4; N, 14·7; OMe, 16·3%). On exposure to air, this compound takes up approximately $2\frac{1}{2}H_2O$, and the m. p. falls progressively during 1—2 hours to 69—70° (Found : C, 36·3; H, 7·9; N, 11·35. $C_7H_{14}O_4N_2,2\frac{1}{2}H_2O$ requires C, 35·8; H, 8·1; N, 11·9%); this *hydrate*, when heated at 100° in a vacuum, becomes anhydrous (Found : loss, 21·5%), then on exposure to air for 3 hours it regains its water (Found : gain, 20·3. $C_7H_{14}O_4N_2,2\frac{1}{2}H_2O$ requires $2\frac{1}{2}H_2O$, 19·1%).

Methylation of Racemic Acid.—Methyl dl-*threo-α-hydroxy-β-methoxysuccinate*. Racemic acid (30 g.), methylated with methyl sulphate (60 c.c.) and potassium hydroxide (74 g. in 100 c.c. of water), gave, after separation of methyl racemate (m. p. 85—88°) by means of benzene, 5 g. of the *ester* as a colourless, thick liquid, b. p. 140° (bath temp.) /2 mm., $n_D^{20°}$ 1·4409 (Found : OMe, 47·95%).

dl-*Threo-α-hydroxy-β-methoxysuccindiamide*, prepared in the usual manner, is microcrystalline, m. p. 192—193° (Found : C, 36·9; H, 6·3; N, 16·6; OMe, 19·4%). The *bismethylamide*, crystallised as for its isomer, forms large elongated prisms, m. p. 152—153° (Found : C, 43·8; H, 7·6; N, 14·2; OMe 16·1%).

The following amides were prepared by the action of ammonia in methyl alcohol on the corresponding methyl esters : dl-*Tartramide*, m. p. 226°, rectangular prisms from aqueous methyl alcohol (Found : N, 18·8. $C_4H_8O_4N_2$ requires N, 18·9%); meso-*tartramide*, similarly recrystallised, m. p. 189—190° (Found : N, 18·7%); dl-*dimethoxysuccindiamide*, elongated prisms, darkening at 150° and fusing (decomp.) at 268—272° (Found : OMe, 35·0. $C_6H_{12}O_4N_2$ requires OMe, 35·2%).

Also, the following bismethylamides were prepared by the action of methylamine in methyl alcohol on the methyl esters : dl-*Tartarobismethylamide*, flat wedges, m. p. 204—205°, from methyl alcohol (Found : N, 15·8. $C_6H_{12}O_4N_2$ requires N, 15·9%), meso-*tartarobismethylamide*, minute prisms, m. p. 182—183° (Found : N, 16·0. $C_6H_{12}O_4N_2$ requires N, 15·9%), from ether–methyl alcohol; dl-*dimethoxysuccinobismethylamide*, similarly recrystallised, rods, m. p. 194–195° (Found : OMe, 29·95. $C_8H_{16}O_4N_2$ requires OMe, 30·4%).

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