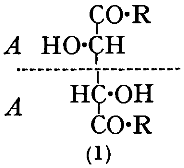
162. *New Derivatives of Hydroxymethoxysuccinic and Methoxymalonic Acids.*

By John Pryde and R. Tecwyn Williams.

An investigation of the structure of glucurone (the lactone of glucuronic acid) indicates that one product of the oxidation of trimethyl glucurone and trimethyl glucuralone (Pryde and Williams, *Nature*, 1931, **128**, 187; 1933, **131**, 57) is *d*-α-hydroxy-β-methoxysuccinic acid. Another possible oxidation product is methoxymalonic acid. Hydroxymethoxysuccinic acid has been prepared by Haworth (J., 1915, **107**, 15) by methylation of tartaric acid with methyl sulphate and alkali. Convenient crystalline reference compounds of this acid are d-α-*hydroxy*-β-*methoxysuccindiamide*, m. p. 190—191°, $[\alpha]_{5461}+129{\cdot}6°$ in water, and d-α-*hydroxy*-β-*methoxysuccinomethylamide*, m. p. 129°, $[\alpha]_{5461}+167{\cdot}4°$ in water. *Methyl* d-α-*hydroxy*-β-*methoxysuccinate* has $n_D^{17°}$ 1·4450, and $[\alpha]_{5461}+48{\cdot}1°$ in methyl alcohol.

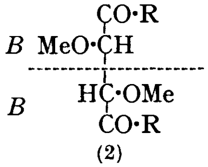
Haworth (*loc. cit.*) has pointed out that the specific rotation of hydroxymethoxysuccinic acid is the mean of the values recorded for tartaric acid and dimethoxysuccinic acid. The new data here recorded enable us to extend this generalisation to the corresponding methyl esters, amides, and methylamides. These are tabulated below.

The optical relations of d-*tartaric*, d-*dimethoxysuccinic*, *and* d-*hydroxymethoxysuccinic acids.*



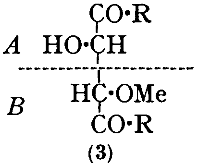
$$\begin{array}{ll} & \mathrm{CO{\cdot}R} \\ A & \mathrm{HO{\cdot}CH} \\ \hline A & \mathrm{HC{\cdot}OH} \\ & \mathrm{CO{\cdot}R} \end{array}$$

(1)



$$\begin{array}{ll} & \mathrm{CO{\cdot}R} \\ B & \mathrm{MeO{\cdot}CH} \\ \hline B & \mathrm{HC{\cdot}OMe} \\ & \mathrm{CO{\cdot}R} \end{array}$$

(2)



$$\begin{array}{ll} & \mathrm{CO{\cdot}R} \\ A & \mathrm{HO{\cdot}CH} \\ \hline B & \mathrm{HC{\cdot}OMe} \\ & \mathrm{CO{\cdot}R} \end{array}$$

(3)

If the rotation of (1) is $2A$ and of (2) is $2B$, then the rotation of (3) is $(A + B)$ or the mean of the rotations of (1) and (2).

Acids.	$[\alpha]_D$ found.	$A + B$ calc.	Dimethyl esters.	$[\alpha]_D$ found.	$A + B$ calc.
1	+15·52°	—	1	+ 2·16°	—
2	+76·63	—	2	+81	—
3	+45·5	+45·6°	3	+41	+41·58°

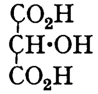
Diamides.	$[\alpha]_D$ found.	$A + B$ calc.	Methylamides.	$[\alpha]_D$ found.	$A + B$ calc.
1	+111·8°	—	1	+144·7°	—
2	+ 95	—	2	+132·6	—
3	+109·8	+103·4°	3	+141·9	+138·7°

All rotations are for the substances in aqueous solution except the methyl esters, which are in methyl-alcoholic solution.

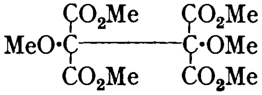
References: *Acids.* (1) Landolt, *Ber.*, 1873, **6**, 1075; (2) Purdie and Irvine, J., 1901, **79**, 962; (3) Haworth, *loc. cit.* *Esters.* (1) Richter, "Org. Chem.," Vol. 1, p. **604**, 1919; (2) Hirst, J., 1926, 350. *Amides.* (1) Clough, J., 1914, **105**, 60; (2) Haworth, Hirst, and Miller, J., 1927, 2436. *Methylamides.* (1) Frankland and Slator, J., 1903, **83**, 1360; (2) Haworth and Jones, J., 1927, 2349.

Several unsuccessful attempts to prepare methoxymalonic acid have been made. One of these methods, the methylation of tartronic acid (I) with silver oxide and methyl iodide, yielded *methyl* αβ-*dimethoxyethane*-ααββ-*tetracarboxylate* (II), from which it appears that in this instance silver oxide has brought about a condensation of the Wislicenus type:

(I.)



$$\begin{array}{c} CO_2H \\ | \\ CH\cdot OH \\ | \\ CO_2H \end{array}$$



$$\begin{array}{ccc} & CO_2Me & CO_2Me \\ & | & | \\ MeO\cdot & C\text{———}C & \cdot OMe \\ & | & | \\ & CO_2Me & CO_2Me \end{array}$$

(II.)

The only alkoxy-derivative of malonic acid of the type $RO\cdot CH(CO_2H)_2$ that has been prepared is ethoxymalonic acid, $EtO\cdot CH(CO_2H)_2$ (Wislicenus and Munzesheimer, *Ber.*, 1898, **31**, 552), which was obtained crystalline, m. p. 123—125°, from ethoxyoxalacetic ester. Further attempts to prepare methoxymalonic acid are in progress.

EXPERIMENTAL.

Methyl d-α-*Hydroxy*-β-*methoxysuccinate.*—A solution of hydroxymethoxysuccinic acid (Haworth, *loc. cit.*, $[\alpha]_{5461}$ + 51·66°, c = 0·87) (3 g.) in 30 c.c. of dry MeOH containing 4% HCl was boiled under reflux for 6 hr. and then neutralised with Ag_2CO_3, MeOH was removed from the filtered liquid under diminished press., and the resulting syrup distilled in a high vac. The *ester* was thus obtained as a colourless viscous liquid, b. p. 119—122°/1·6 mm., $n_D^{17^\circ}$ 1·4450, $[\alpha]_{5461}^{22^\circ}$ + 48·1° (c = 0·988 in MeOH) (Found: OMe, 47·7. $C_7H_{12}O_6$ requires OMe, 48·45%).

d-α-*Hydroxy*-β-*methoxysuccindiamide.*—A solution of the ester (1 g.) in 10 c.c. of dry MeOH was saturated with dry NH_3 at 0° and then kept at room temp. for 19 hr. The stout colourless needles obtained (0·675 g.; 80% of theo. amount) were washed with Et_2O containing a little MeOH; they had m. p. 190—191° (to a bright yellow melt), $[\alpha]_{5461}^{18^\circ}$ + 129·6° (c = 1·103 in H_2O) (Found: C, 36·6; H, 6·15; N, 17·3; OMe, 19·3. $C_5H_{10}O_4N_2$ requires C, 37·0; H, 6·2; N, 17·3; OMe, 19·1%).

d-α-*Hydroxy*-β-*methoxysuccinomethylamide.*—The ester (0·6 g.) was dissolved in 6·5 c.c. of a sat. solution of dry NH_2Me in MeOH and kept for 11 days at room temp.; the solution was then concentrated to a syrup, which deposited crystals when Et_2O was added. The mixture of syrup and crystals was taken up in MeOH and Et_2O, and further addition of Et_2O caused a slight pptn. It was then set aside to crystallise in a warm place. The *methylamide* separated in clusters of closely-set fine needles, m. p. 129° forming a clear melt without decomp., $[\alpha]_{5461}^{12^\circ}$ + 167·4° (c = 0·675 in H_2O) (Found: C, 44·0; H, 7·4; N, 14·8. $C_7H_{14}O_4N_2$ requires C, 44·2; H, 7·4; N, 14·7%).

Preparation of Hydroxymalonic (*Tartronic*) *Acid.*—This acid was prepared from dihydroxytartaric acid (cf. Fenton, J., 1898, **73**, 73). Dihydroxytartaric acid (5 g.) was dissolved in the minimum quantity of H_2O, and the solution heated at 80° until the evolution of CO_2 had ceased. On cooling, the product formed a cryst. mass. It was triturated several times with dry Et_2O, whereby coloured impurities and unchanged dihydroxytartaric acid were removed. The residue of pure tartronic acid, after drying in warm air, had m. p. 152—155° (cf. Behrend and Prüsse, *Annalen*, 1918, **416**, 233).

Methylation of Hydroxymalonic Acid. Isolation of Methyl αβ-*Dimethoxyethane*-ααββ-*tetracarboxylate.*—Tartronic acid (2 g.) was dissolved in the minimum quantity of dry MeOH, and the solution mixed with 10 g. of dry Ag_2O and 15 c.c. of MeI. After 12 hr. the liquid was filtered and the residues were extracted with MeOH. From the united filtrate and extracts, MeOH was removed in vac., and the resulting syrup was methylated under reflux at 45—50° with 10 g. of Ag_2O and 15 c.c. of MeI. After 8 hrs.' methylation, the residue was extracted several times with MeOH, filtered, and concentrated in vac. to a viscous water-clear syrup, which crystallised completely on standing over-night in the refrigerator. The crystals formed large, flat, elongated prisms and after thorough washing with Et_2O, or recrystn. from hot H_2O, had m. p. 76° (Found: C, 44·7; H, 5·6; OMe, 56·3. $C_{12}H_{18}O_{10}$ requires C, 44·7; H, 5·6; OMe, 57·8%).

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