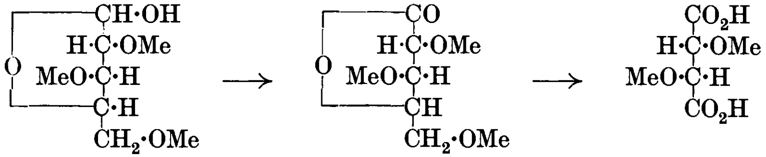
CCCXXV.—1 : 3 : 4 : 6-*Tetramethyl* (γ-)*Fructose and* 2 : 3 : 5-*Trimethyl* (γ-)*Arabinose. Oxidation of* d- *and* l-*Trimethyl* γ-*Arabonolactone.*

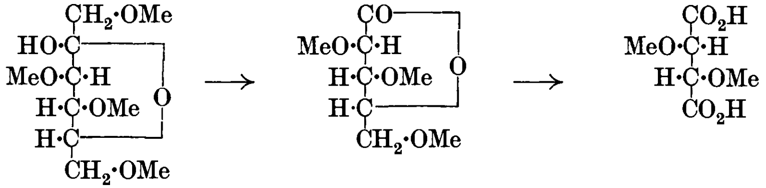
By WALTER NORMAN HAWORTH, EDMUND LANGLEY HIRST, and ABRAHAM LEARNER.

THE representative of the so-called γ-sugars in the arabinose series was first prepared as *l*-trimethyl γ-arabinose by Baker and Haworth (J., 1925, **127**, 365), who assigned a butylene-oxide structure to this sugar for the reason that it gave on oxidation with bromine water a crystalline trimethyl arabonolactone which was characterised as a γ-lactone. The latter conclusion was confirmed by Haworth and Nicholson (J., 1926, 1899), who showed that unsubstituted γ-arabonolactone prepared by oxidation of *l*-arabinose gave, on methylation, the same crystalline trimethyl derivative as Baker and Haworth had isolated by oxidation of trimethyl γ-arabinose (I).

The allocation of a butylene-oxide structure to both the lactone and the sugar was supported by the comparison of the rate of hydrolysis of the former with that of other γ-lactones (Charlton, Haworth, and Peat, J., 1926, 89; Drew, Goodyear, and Haworth, this vol., p. 1242). These conclusions have now been tested by degradation of *l*-trimethyl γ-arabonolactone by oxidative methods which are herein described.

In the meantime, the corresponding optical enantiomorph, *viz.*, *d*-trimethyl γ-arabonolactone, has also been isolated (Avery, Haworth, and Hirst, this vol., p. 2308) from the products of oxidation of tetramethyl γ-fructose. The crystalline form, melting point, and magnitude of specific rotation of the two specimens were identical, but the sign of rotation was opposite. It became evident that the final proof of the constitution of this lactone was an issue of considerable importance in the structural chemistry of the sugars, since the solution of the problem of the structure of sucrose rested upon this proof. Accordingly, the two enantiomorphous specimens of trimethyl γ-arabonolactone were submitted independently to oxidation with nitric acid (*d* 1·42). The product isolated from the *l*-trimethyl γ-arabonolactone (II) was recognised as *d*-dimethoxysuccinic acid (III), inasmuch as it gave a crystalline amide and a crystalline methylamide which were identical with authentic specimens specially prepared from *d*-tartaric acid.


(I.) (II.) (III.)


(IV.) (V.) (VI.)

Similarly, the *d*-variety of trimethyl γ-arabonolactone (V), which had been isolated from tetramethyl γ-fructose (IV), gave on oxidation *l*-dimethoxysuccinic acid (VI); this was characterised as the crystalline amide and methylamide, which were identified as before by direct comparison with authentic specimens prepared for this purpose from *l*-tartaric acid (Haworth and Jones, this vol., p. 2349).

These experimental results must be considered in relation to the structurally isomeric trimethyl δ-arabonolactone, which has been shown to be amylene-oxidic and to give rise on oxidation (Haworth and Jones, *loc. cit.*) to *l*-arabotrimethoxyglutaric acid, which was similarly characterised through the crystalline methylamide (compare Hirst and Robertson, J., 1925, **127**, 358). It was therefore demonstrated that whilst normal trimethyl arabinose contains an amylene-oxide ring, the trimethyl γ-arabinose, on the other hand, has a butylene-oxide structure; that *l*-trimethyl γ-arabonolactone derived from the latter sugar must be indexed as 2 : 3 : 5-trimethyl arabonolactone, and that to the *d*-isomeride isolated in the manner indicated above as a degradation product of the fructose residue in methylated sucrose is similarly to be assigned the constitution of *d*-2 : 3 : 5-trimethyl arabonolactone. These conclusions confirm in their entirety the inferences already drawn from the results of the earlier studies of the lactones and of the reference compounds herein described.

An additional point of interest which emerges from the further study of these lactones is that the two γ-lactones displayed great stability towards nitric acid, contrasting remarkably with the labile character of the corresponding δ-lactone of this series and also with other δ-lactones which have hitherto been submitted to oxidative degradation. This behaviour is in harmony with the distinctive properties of γ- and δ-lactones which have already been elucidated in the course of earlier work (Drew, Goodyear, and Haworth, *loc. cit.*).

EXPERIMENTAL.

Oxidation of l-*Trimethyl* γ-*Arabonolactone.*—Arabonic acid, obtained in the usual way from arabinose by the action of bromine water, was purified by conversion into the cadmium salt, which could be readily recrystallised from water in place of alcohol as mentioned in the literature. After removal of the cadmium as sulphide, the lactone was obtained on concentrating the aqueous solution (Bauer, *J. pr. Chem.*, 1884, **30**, 367; 1886, **34**, 46). *l*-Trimethyl γ-arabonolactone was then obtained by methylating arabonolactone (Haworth and Nicholson, *loc. cit.*). It had m. p. 30—32° alone or mixed with specimens prepared from arabonolactone and from trimethyl γ-arabinose (Baker and Haworth, *loc. cit.*); $[\alpha]_D$ −44° in water (initial value) decreasing to −25° after 20 days. A solution containing 1·7 g. of this material in 17 c.c. of nitric acid (*d* 1·32) was heated on the water-bath until reaction commenced at 95°. At this temperature, evolution of nitrous fumes took place slowly, and the oxidation was allowed to proceed for 7 hours at 95—100°. Even then no definite end-point had been reached, but the rate of reaction had become extremely slow. 35 C.c. of distilled water were then added, and the nitric acid was removed by distillation under diminished pressure with frequent additions of water. The product was thus obtained as a colourless syrup, which was esterified by digestion for 8 hours with 40 c.c. of methyl alcohol containing 1·6 g. of hydrogen chloride. The mineral acid was neutralised in the usual way with silver carbonate, the solvent evaporated, and the esterified oxidation product purified by distillation, which proceeded smoothly only after a preliminary heating for 3 hours at 120°. This effected the transformation of some methyl trimethylarabonate into the lactone of the corresponding acid. During the preliminary heating, a small quantity of methyl oxalate was collected. The main fraction (A) distilled from a bath at 159—170°/16 mm., giving a colourless syrup (0·8 g.), n_D^{16} 1·4391; $[\alpha]_D^{16°}$ +41·5° in water (c = 1·1; initial value) (0·1041 G. required, as lactone, 2·0 c.c. of N/10-sodium hydroxide for neutralisation; for hydrolysis and neutralisation, 8·7 c.c.). These properties correspond with those required by a mixture containing approximately 65% of methyl *d*-dimethoxysuccinate and 35% of *l*-trimethyl arabonolactone. The presence of methyl *d*-dimethoxysuccinate was proved by the formation of the corresponding amide and methylamide. The distillate (A) (0·23 g.), dissolved in 2·3 c.c. of methyl-alcoholic ammonia, gave, after 40 hours, 0·07 g. of *d*-dimethoxysuccinamide, the identity of which was confirmed by comparison with an authentic specimen, melting to a dark liquid at 269°, decomposing rapidly at 283°; $[\alpha]_D$ +97° in water (c = 0·433) (Found: C, 40·7; H, 6·8; OMe, 33·7. Calc. for $C_6H_{12}O_4N_2$: C, 40·9; H, 6·8; OMe, 35·2%). Again, 0·13 g. of the distillate (A), dissolved in 1·3 c.c. of methyl alcohol saturated with methylamine, gave crystals on evaporation of the solvent after 3 days. These recrystallised from ethyl acetate as long needles (yield, 0·06 g.), m. p. 205—206°, alone or mixed with an authentic specimen of the methylamide of dimethoxysuccinic acid prepared from *d*-tartaric acid (Haworth and Jones, *loc. cit.*). No trace of the amide or methylamide of trimethoxyglutaric acid could be detected in the course of these experiments.

Oxidation of d-*Trimethyl* γ-*Arabonolactone*.—The *d*-trimethyl γ-arabonolactone was prepared from tetramethyl γ-fructose by the method described by Avery, Haworth, and Hirst (this vol., p. 2317); it had m. p. 33°; $[\alpha]_D$ +44·5° (initial value) in water $\longrightarrow$ +25·5° (after 20 days). This material (2·5 g.) was dissolved in 28 c.c. of nitric acid (d 1·42), the procedure thereafter being similar to that described above. A small quantity of oxalic acid (identified as methyl oxalate) was formed during the oxidation. The esterified product was distilled from a bath at 155—160°/13 mm., and gave 1·42 g. of colourless syrup (B), $n_D^{14°}$ 1·4400; $[\alpha]_D$ − 50° in methyl alcohol (c = 1·50) (0·0581 G. required 1·0 c.c. of N/10-sodium hydroxide for neutralisation, as lactone, and 4·9 c.c. of N/10-sodium hydroxide for complete hydrolysis and neutralisation). These figures correspond to a mixture containing 32% of methyl *l*-dimethoxysuccinate and 68% of *d*-trimethyl γ-arabonolactone. The amide [yield 0·202 g. from 0·50 g. of the product (B)], prepared in the usual way, was obtained as long needles, which melted after preliminary darkening at 245—250° to a dark liquid at 270° (rapid decomp. at 283°); $[\alpha]_D^{18°}$ − 94° in water (c = 0·9) (Found: C, 40·9; H, 6·8; N, 15·7; OMe, 33·2. Calc. for $C_6H_{12}O_4N_2$: C, 40·9; H, 6·8; N, 15·9; OMe, 35·2%). The corresponding methylamide was also prepared as long needles (from ethyl acetate), m. p. 204—205° alone or mixed with a specimen of the methylamide of *l*-dimethoxysuccinic acid prepared from *l*-tartaric acid (Haworth and Jones, *loc. cit.*).

No trace of the amide or methylamide of trimethoxyglutaric acid was found in the mother-liquors arising from these experiments.

The authors wish to express their thanks to the Department of Scientific and Industrial Research for a maintenance grant to one of them.

UNIVERSITY OF BIRMINGHAM,
EDGBASTON.

[*Received, August* 16*th*, 1927.]