162. *Acetone Derivatives of Gluconic Acid.*

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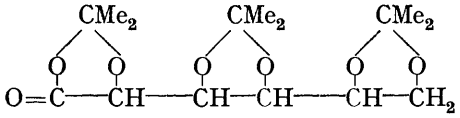
It should be possible theoretically to protect all the hydroxyl groups, including the carboxyl, in gluconic acid by condensation with acetone. Despite the *cis*- or *trans*-disposition of these groups with respect to one another in the conventional projection formula of gluconic acid it is clear that, allowing free rotation round the single-bonded carbon atoms, the addenda would take up appropriately *cis*-positions such as may be required for condensation with acetone. An atom model makes this point clear. This expectation is realised in the formation of both *gluconic acid diacetone* and *gluconic acid triacetone*, which are isolated as crystalline substances. The latter can also be converted into the former by mild hydrolytic agents. There can be little doubt that in the diacetone the positions 1 and 2 are unsubstituted, since 2-methyl gluconic acid was obtained by its methylation and subsequent hydrolysis. By the use of atom models it is shown that fifteen triacetone gluconic acids are theoretically possible, but, for the reasons stated on p. 797, only two of the models, namely, those showing the acetone groups at 1 : 2, 3 : 4, 5 : 6, or at 1 : 2, 3 : 5,

4 : 6, seem very probable structurally. On general grounds it would appear that the most likely formulation is that annexed.



Experimental.

Gluconic Acid Di- and Tri-acetone.—Finely powdered calcium gluconate (40 g.), anhydrous copper sulphate (35 g.), and acetone (800 c.c.) were intimately mixed and the calculated quantity of sulphuric acid (*d* 1·84) required to transform the calcium salt into gluconic acid was added. The mixture was shaken for 100 hours and was then filtered. The filtrate on concentration under diminished pressure gave a thin syrup, which partly crystallised. The solid was recrystallised from boiling light petroleum (1 l.), giving long white needles (2·4 g.) of *gluconic acid diacetone*, m. p. 154°, $[\alpha]_D^{18°}$ + 11° in ethyl alcohol (*c*, 1·84). This substance was soluble in water, alcohol and ether, the aqueous solution being distinctly acid in its reactions (Found : C, 52·2; H, 7·2; Me_2CO, 42·7. $C_{12}H_{20}O_7$ requires C, 52·2; H, 7·3; Me_2CO, 42·0%).

The petroleum mother-liquors were evaporated to a thin syrup, which partly crystallised. The solid on recrystallisation from light petroleum gave large colourless rhombic crystals of *gluconic acid triacetone* (1·6 g.), insoluble in water, easily soluble in alcohol and ether; m. p. 111°, $[\alpha]_D^{18°}$ + 31° in ethyl alcohol (*c*, 1·98) (Found : C, 57·1; H, 7·7; Me_2CO, 53·9. $C_{15}H_{24}O_7$ requires C, 57·0; H, 7·6; Me_2CO, 55·1%). An aqueous alcoholic solution was neutral to litmus.

Gluconic acid triacetone may be prepared more conveniently by the following method. Calcium gluconate (20 g.) was shaken with acetone (400 c.c.) containing concentrated sulphuric acid (3 c.c.) for 100 hours at room temperature. The filtered solution was neutralised with silver carbonate and concentrated under diminished pressure to a thin syrup, which partly crystallised. Recrystallisation of the solid from light petroleum gave gluconic acid triacetone (3·0 g.), m. p. 111°. The petroleum mother-liquors contained a small quantity (0·4 g.) of the diacetone derivative.

Gluconic acid diacetone may be obtained in very poor yield from the triacetone compound by careful hydrolysis in methyl alcohol containing 0·05% of hydrochloric acid. After 8 hours at 45°, when the rotation was $[\alpha]_D$ + 13° (initial value + 30°), the solution was neutralised (silver carbonate) and evaporated to a syrup, which slowly deposited crystals of gluconic acid diacetone, m. p. 154°.

2-*Methyl Gluconic Acid Diacetone.*—Gluconic acid diacetone (4·6 g.), dissolved in methyl iodide (40 c.c.) containing methyl alcohol (1 c.c.), was boiled for 3 hours with silver oxide (28 g.). The product was extracted by boiling ether and on removal of the solvent was obtained as a mobile syrup (5 g.), which was twice methylated by silver oxide and methyl iodide and then distilled, giving a mobile oil (4·7 g.), b.p. 105°/0·02 mm. This rapidly crystallised, giving *methyl 2-methylgluconate diacetone* in large plates, which were recrystallised from light petroleum; m. p. 44°, $[\alpha]_D^{19°}$ + 41° in water (*c*, 1·25). The ester was soluble in water and in organic solvents, and 0·1247 g. required for hydrolysis 4·3 c.c. of *N*/10-sodium hydroxide (calc., 4·1 c.c.) (Found : C, 55·4; H, 8·0; OMe, 20·7. $C_{14}H_{24}O_7$ requires C, 55·3; H, 8·0; OMe, 20·4%).

Methyl 2-methylgluconate diacetone was hydrolysed by heating its solution in 2% hydrochloric acid at 50° for 2 hours; the product was isolated in the usual way. 2-*Methyl γ-gluconolactone* was thus obtained as a colourless syrup which resisted crystallisation. The rotation data are therefore given with reserve : $[\alpha]_D$ + 45° (initial value), 37° (after 7 days; constant value) (Found : OMe, 14·8. $C_7H_{12}O_6$ requires OMe, 16·1%). The lactone (1·8 g.) was dissolved in methyl alcohol saturated at 0° with ammonia. No precipitate formed and the absence of gluconic acid was thereby established. After some hours at room temperature the solvent was evaporated, leaving a solid but extremely hygroscopic residue, which was recrystallised from dioxan (yield, 1·2 g.). 2-*Methyl gluconamide* was then obtained as a white microcrystalline powder, m. p. 139°, $[\alpha]_D^{18°}$ + 39° in water (*c*, 0·34). The amide was exceedingly hygroscopic and was freely soluble in water and in alcohol (Found : N, 6·6; OMe, 14·3. $C_7H_{15}O_6N$ requires N, 6·7; OMe, 14·8%).

When the amide was treated with aqueous sodium hypochlorite under the conditions prescribed by Weerman (*Rec. trav. chim.*, 1917, **37**, 16), several hours elapsed before there was a sensible diminution of the strength of the hypochlorite. The excess of hypochlorite was then removed and a solution of semicarbazide hydrochloride in concentrated aqueous sodium acetate

was added. No precipitate formed, even after several hours. In another experiment the solution, after reaction with the hypochlorite, was treated with hydrazine sulphate and neutralised, and benzaldehyde added. The resulting yellow precipitate (benzaldehydehydrazone) was completely soluble in ether and contained no benzaldehydesemicarbazone. The methoxy-group in the amide was therefore at position 2. Control experiments with gluconamide and the same solution of sodium hypochlorite gave copious yields of hydrazocarbonamide (m. p. 256°) and benzaldehydesemicarbazone (m. p. 220°) respectively.

X-*Ray Examination of Triacetone Gluconic Acid* (By E. G. Cox and C. J. Brown).

This substance forms large columnar crystals of orthorhombic symmetry, usually elongated parallel to the *c* axis. The forms *a*{100}, *m*{110}, and *o*{111} were observed. By means of *X*-ray measurements the unit-cell dimensions were found to be $a = 14{\cdot}62$, $b = 13{\cdot}22$ and $c = 8{\cdot}83$ A., so that there are four molecules in the unit cell and d (calc.) = 1·23 g./c.c. The birefringence is low, the mean refractive index for sodium light being 1·48.

Examination of models shows that at least eight of the fifteen theoretically possible triacetone gluconic acids can be obtained in strainless forms; of these, however, five involve seven-, eight-, or nine-membered rings. Of the remaining three, one (1 : 3, 2 : 4, 5 : 6) involves a somewhat improbably close juxtaposition of various atoms, so that it is very probable that triacetone gluconic acid has one of the remaining two structures, namely, 1 : 2, 3 : 4, 5 : 6 or 1 : 2, 3 : 5, 4 : 6. Unfortunately the *X*-ray data available do not enable a decision between these two to be made.

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