CCL.—*The Structure of Lactones from Simple Sugars. Trimethyl γ-Arabonolactone and the Supposed β-Gluconolactone and β-Mannonolactone.*

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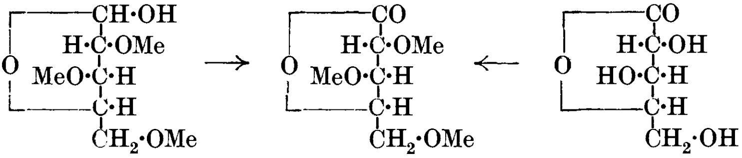
CONTINUING the work described in the communication on " A Revision of the Structural Formula of Glucose " by Charlton, Haworth, and Peat (this vol., p. 89), the present authors have prepared γ-arabonolactone from *l*-arabinose as indicated by Fischer and Piloty (*Ber.*, 1891, **24**, 4214) and Nef (*Annalen*, 1914, **403**, 204) and have isolated, by methylation of this lactone, the corresponding trimethyl γ-arabonolactone. This had previously been isolated by Baker and Haworth (J., 1925, **127**, 365) by the method of oxidising trimethyl γ-arabinose with nitric acid, and the identity of the two specimens is established by the following comparison of their properties :

	Trimethyl γ-arabonolactone	
	from trimethyl γ-arabinose.	from γ-arabonolactone.
Crystalline form	Long, colourless needles.	Long, colourless needles.
M. p.	32°	33° (and mixed m. p. 33°)
$[\alpha]_D$ in water, initial	−43·2°	−44·4°

This result confirms the constitution assigned by Baker and Haworth to trimethyl γ-arabinose (I), since the derived lactone (II) is identical with the product obtained by methylating the stable or γ-arabonolactone (III).


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

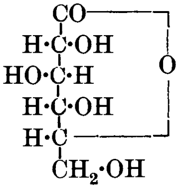
Nef (*loc. cit.*) outlined improved methods of preparing the ordinary stable γ-lactones from sugars, and suggested that simultaneously with the formation of these stable forms other lactones of a less stable character were also produced in varying but much smaller quantity. By a considerable modification of method, involving carefully graduated heating of the hydroxy-monocarboxylic acids over a prolonged period, or by low-temperature treatment in a vacuum, he succeeded in preparing, and isolating from their stable forms, two of these unstable lactones, which he described as β-gluconolactone and β-mannonolactone, the properties of which are given below for comparison with the predominant or stable γ-forms :

	γ-Gluconolactone.	"β"-Gluconolactone.
M. p.	133—135°	150—152°
$[\alpha]_D$ in water	+67·82°	+61·7° ⟶ 6·24°
	(little change in 22½ hours)	(in 26 hours)

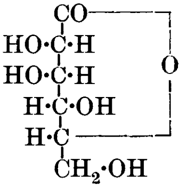
	γ-Mannonolactone.	"β"-Mannonolactone.
M. p.	151°	156°
$[\alpha]_D$ in water	+51·8°	+111·1° ⟶ 28·08°
	(no change in 4 days)	(in 24 hours)

Nef regarded the isolation of these two types of lactones as evidence of the structural rather than the stereochemical isomerism of α- and β-glucoses and of α- and β-methylglucosides, an inference which was strongly resisted by E. Fischer (*Ber.*, 1914, **47**, 1980). This unfortunate application of Nef's results has tended to obscure the real significance of the isolation of isomeric crystalline lactones from glucose and mannose.

We are of opinion, however, for the following reasons, that the unstable forms of glucono- and mannono-lactones are not β-lactones as supposed by Nef, but are in reality δ-lactones, containing a six-membered ring (1 : 5 oxide) corresponding to the normal or amylene-oxidic form of the parent sugars. If these were indeed β-lactones, then the lactone ring would be formed by engaging in each case hydroxyl groups on the left of the carbon chain and thus by Hudson's rule (*J. Amer. Chem. Soc.*, 1910, **32**, 345) the lactones should be lævorotatory or more lævorotatory respectively than gluconic or mannonic acid. This is not the case, since the rotations are strongly dextro and decline markedly to constant dextro values in 24 hours. The rotation changes, quoted in detail by Nef, are indeed comparable in all respects with those indicated in the graph published by Charlton, Haworth, and Peat (*loc. cit.*) for δ-lactones, and the figures given by Nef enable similar curves to be drawn which prove the similarity in behaviour to tetramethyl δ-gluconolactone, tetramethyl δ-galactonolactone, and trimethyl δ-arabonolactone (compare also the figures given for the corresponding tetramethyl δ-mannonolactone). We therefore assign the following structural formulæ to Nef's lactones:



δ-Gluconolactone.



δ-Mannonolactone.

If the usual method for the conversion of gluconic and mannonic acids into their lactones be adopted, the yield of the above unstable varieties would appear to be exiguous, and until 1914 the occurrence of these forms was unsuspected. The predominating lactone is invariably of the γ-type even in solution (compare Levene and Simms, *J. Biol. Chem.*, 1925, **65**, 31).

In discussing the formation of the lactone from 2 : 3 : 6-trimethyl gluconic acid, Charlton, Haworth, and Peat indicated for the above reasons that the choice was restricted to the γ-lactone by Hudson's hypothesis. We believe, however, that under experimental conditions resembling those described by Nef for the preparation of unstable lactones it will also be possible to isolate the 2 : 3 : 6-trimethyl δ-gluconolactone which, on methylation, should be identical with the lactone derived from normal tetramethyl glucose, and with the product obtained on methylating Nef's supposed "β"-gluconolactone, and this investigation is in progress.

Nef regarded the stable γ-lactones as the abnormal type, and the unstable lactones (δ-) as the normal variety. This accords with our views, since we consider the former to be related to the γ-aldoses and the latter to the normal aldoses of the pentose and hexose series.

EXPERIMENTAL.

Methylation of γ-Arabonolactone.—*l*-Arabinose was oxidised by bromine water to γ-arabonolactone following the conditions outlined by Kiliani (*Ber.*, 1886, **19**, 48; compare also Fischer and Piloty, Nef, *loc. cit.*). The lactone was methylated several times by Purdie's reagents, initially in presence of methyl alcohol and latterly with methyl iodide and silver oxide alone (Found: OMe, 51·8. Calc.: OMe, 48·9%). It was ascertained that this high methoxyl content was due to the presence of the corresponding methyl ester. The lactone was therefore purified by formation of the sodium salt in the cold, and the solid obtained on evaporation was extracted with warm ether. Thereafter an aqueous solution of the salt was acidified, evaporated to dryness under diminished pressure, and the resulting organic acid was extracted and heated at 100° for several hours in order to regenerate the lactone. Distillation of the latter at a bath temperature of 115° under 0·015 mm. pressure gave a colourless liquid which completely crystallised (m. p. 26—27°) on nucleation with a specimen of the trimethyl arabonolactone prepared by Baker and Haworth (*loc. cit.*). After being kept on porous tile in a desiccator, the crystals melted at 33°, and the m. p. was unchanged by recrystallisation of the substance from light petroleum. Baker and Haworth's specimen, originally quoted as m. p. 29°, was kept over phosphoric oxide in a vacuum and then melted at 32°. A mixture of the two specimens melted at 33° (Found: C, 50·6; H, 7·6; OMe, 46·3. Calc.: C, 50·5; H, 7·4; OMe, 48·9%). The specific rotation values in water ($c = 1·06$) were − 44·4°, after 5 mins.; 44·3°, 30 mins.; 44·1°, 1 hour; 43·8°, 2 hours; 43·4°, 4 hours; 40·0°, 24 hours.

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