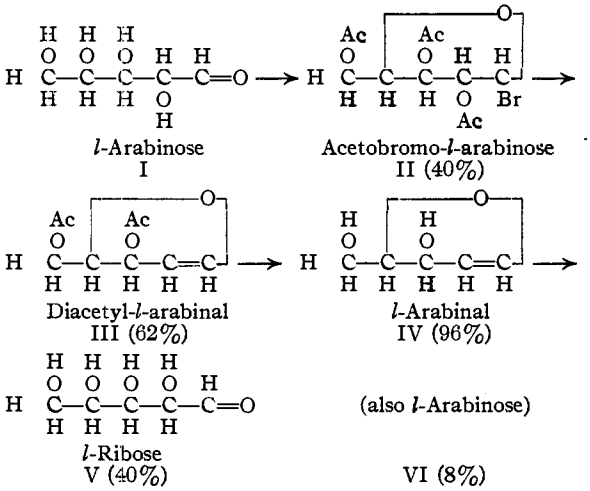
[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, LOYOLA UNIVERSITY SCHOOL OF MEDICINE]

The Preparation of *l*-Ribose[1,2,3]

BY W. C. AUSTIN AND FRED L. HUMOLLER

Recent investigations of two of the older known reactions of synthesis of *l*-ribose have demonstrated their impracticability.[4] The authors have, however so extended and improved the observations of Gehrke and Aicher[5] on a third method, originating from the studies of Bergmann and Shotte[6] on *d*-glucal, that they recently announced[7] the successful preparation of crystalline *l*-ribose. Although Gehrke and Aicher obtained no crystalline ribose, the authors have been able to convert *l*-arabinose to crystalline *l*-ribose in a yield of nearly 10% by the reactions indicated in the configurations I–VI, which offer the best known method for the preparation of this rare pentose. Under each configuration is given also the percentage yield obtained by the authors in the preparation of each substance from the preceding one. In this series of reactions the authors have made some improvements and adaptations in the many published directions for the preparation and oxidation of members of the class of glycals.



Experimental

In Table I there is shown the list of preparations made in these studies, together with yields, properties of products and citations of directions which have been either followed or adapted with success to the specific preparations. The description to follow will then be limited to the detail of the modifications of the authors.

The reduction of the acetobromo-*l*-arabinose in 50% acetic acid with pure zinc was never complete in five hours at 10° by the procedure of Levene and Mori. The reaction here was greatly improved by adding the 100 g. of acetobromo-*l*-arabinose in ten equal portions, at half-hour intervals, with each addition immediately followed by the introduction of 22 g. of zinc containing 5% of the copper–zinc couple of Straus.[13] The purified diacetyl-*l*-arabinal was a sirup, distilling at 75–82° at 0.03–0.05 mm. as described by Gehrke and Aicher and by Meisenheimer and Jung. It was saponified with almost quantitative yield to *l*-arabinal, recrystallized from benzene to the properties given. Recrystallization of this *l*-arabinal from chloroform, or exposure to air, caused decomposition detectable by lowering of rotation and melting point.

In the oxidation 59.5 g. of *l*-arabinal in 800 cc. of water

TABLE I

PREPARATIONS AND YIELDS IN THE CONVERSION OF *l*-ARABINOSE TO *l*-RIBOSE

	Preparation	Yield, g.	M. p., °C.	$[\alpha]_D^{20-25}$	Solvent	Methods used, adapted or modified
I	*l*-Arabinose	400	158	+102.3°	H_2O	Anderson and Sands[8]
II	Acetobromo-*l*-arabinose	365	139	+284.8°	$CHCl_3$	Meisenheimer and Jung[9]
III	Diacetyl-*l*-arabinal	135	sirup			Levene and Mori[10]
IV	*l*-Arabinal	75	81–82	−223.1°; −197.2°	$CHCl_3$; H_2O	Isbell,[11] Levene and Tipson[12]
V	*l*-Ribose	36.7	85–87	+ 22.6°	H_2O	Levene and Tipson[12]
VI	*l*-Arabinose	7.0	159	+104.6°	H_2O	Levene and Tipson[12]

(1) A portion of the results described here was given on the program of the meeting of the American Chemical Society in Washington, March 30, 1933, and on the program of the meeting of the American Society of Biological Chemists in Cincinnati, April 11, 1933.

(2) Through the coöperation of Dr. F. C. Koch, Professor of Physiological Chemistry and Pharmacology at the University of Chicago, this investigation will constitute a portion of the thesis of Mr. Humoller in partial fulfilment of the requirements for the degree of Doctor of Philosophy from the Division of the Biological Sciences of the University of Chicago.

(3) The progress of this investigation was greatly aided by the technical assistance of Mr. B. J. Gregory.

(4) (a) Austin, Smalley and Sankstone, THIS JOURNAL, **54**, 1933 (1932); (b) Austin and Humoller, *J. Biol. Chem.*, **27**, 10 (1933).

(5) Gehrke and Aicher, *Ber.*, **60**, 918 (1927).

(6) Bergmann and Schotte, *ibid.*, **54**, 450 (1921).

(7) Austin and Humoller, THIS JOURNAL, **54**, 4749 (1932).

(8) Anderson and Sands, "Organic Syntheses," 1928, Vol. VIII, p. 18.

(9) Meisenheimer and Jung, *Ber.*, **60**, 1462 (1927).

(10) Levene and Mori, *J. Biol. Chem.*, **83**, 803 (1929).

(11) Isbell, *Bur. Stds. J. Res.*, **5**, 1179 (1930).

(12) Levene and Tipson, *J. Biol. Chem.*, **93**, 631 (1931).

(13) Houben, "Die Meth. d. org. Chem.," 3d Ed., 1925, Vol. II, p. 304.

was added with vigorous stirring to 85 g. of benzoic peracid in 1000 cc. of ethyl acetate at 0°. The temperature was never allowed to rise above 8°. After four hours, when the consumption of the peracid had ceased, the aqueous layer was separated and with additional aqueous extracts again extracted with chloroform. After clarification and concentration to 500 cc., analysis by Goebel's method showed 59.9 g. of aldopentose.[14]

The above solution was evaporated to a sirup which was then mixed with 25 cc. of methyl alcohol, 240 cc. of absolute alcohol and 40 cc. of ether. After twenty-four hours 6 g. of crystallized *l*-arabinose was removed and recrystallized, giving the properties in VI of the table. The filtrate containing the *l*-ribose was combined with a similar one (previously prepared by the oxidation of 9 g. of *l*-arabinal, followed by the removal of 1 g. of crystalline *l*-arabinose). These combined filtrates were again reduced to a sirup, which crystallized spontaneously after three weeks, giving 28 g. of *l*-ribose. The remaining sugar in the mother liquor formed the *p*-bromophenylhydrazone of *l*-ribose, which was recrystallized from alcohol by the addition of ether to 35.5 g., with m. p. 170–172° and $[\alpha]_D^{25}$ −10.67°, in absolute alcohol. The corresponding derivative, prepared from pure *l*-arabinose, melted at 161–162°, had $[\alpha]_D^{20-25}$ +10.23° in absolute alcohol, and was much less soluble in the solvents of purification. The decomposition of the above derivative of *l*-ribose by the method of van Ekenstein and Blanksma[15] with benzaldehyde afforded 8.7 g. more of crystalline *l*-ribose. None of the *l*-ribose exhibited mutarotation at 20°, although Phelps, Isbell and Pigman[16] have more recently observed the unusual mutarotation of this sugar at 1°. It was recrystallized from absolute alcohol to a product of the properties given in the table.

(14) Goebel, *J. Biol. Chem.*, **72**, 801 (1927).

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Summary

Improved directions have been given for the preparation of *l*-ribose by the Bergmann reaction, involving the preparation of *l*-arabinal and its oxidation to a product containing approximately five parts of *l*-ribose to one part of *l*-arabinose. By this reaction *l*-ribose has been prepared in pure crystalline form from *l*-arabinose with a yield of nearly 10%.

(15) Van Ekenstein and Blanksma, *Chem. Weekblad*, **22**, 373 (1909).

(16) Phelps, Isbell and Pigman, THIS JOURNAL, **56**, 747 (1934).

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[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, LOYOLA UNIVERSITY SCHOOL OF MEDICINE]

The Preparation of Two New Crystalline Aldohexoses, *l*-Allose and *l*-Altrose, from *l*-Ribose by the Cyanohydrin Reaction[1,2,3]

BY W. C. AUSTIN AND FRED L. HUMOLLER

After having announced the preparation of crystalline *l*-ribose by improved methods, the authors[3] reported the preparation of crystalline *l*-allonolactone, calcium *l*-altronate and β-*l*-allose. To these preparations have now been added the sirupy *l*-altronolactone and crystalline β-*l*-altrose, and the authors describe herewith in more detail their studies of the substances made from *l*-ribose after the cyanohydrin reaction. These investigations have been guided, in large measure, by the valuable contribution of Levene and Jacobs,[4] who prepared from *d*-ribose the corresponding enantiomorphous substances and obtained the *d*-allose and *d*-altrose as uncrystallizable sirups.

The β-*l*-allose and β-*l*-altrose complete the list of the sixteen theoretically possible aldohexoses which have been prepared, although they are only the seventh and eighth which have been crystallized.[5] The reactions of preparation, with structures, of the new substances from *l*-ribose are indicated in the configurations I–V. Under each configuration is given also the percentage yield obtained by the authors in the preparation of each substance from the preceding one.

(1) Through the coöperation of Dr. F. C. Koch, Professor of Physiological Chemistry and Pharmacology at the University of Chicago, this investigation will constitute a portion of the thesis of Mr. Humoller in partial fulfilment of the requirements for the degree of Doctor of Philosophy from the Division of the Biological Sciences of the University of Chicago.

(2) The progress of this investigation was greatly aided by the technical assistance of Mr. B. J. Gregory.

(3) Austin and Humoller, THIS JOURNAL, **54**, 4749 (1932); **55**, 2167 (1933); **56**, 1152 (1934).

(4) Levene and Jacobs, *Ber.*, **43**, 3141 (1910).

(5) In the short communication by Austin and Humoller[3] the β-*l*-allose was termed the sixth crystalline aldohexose, *l*-mannose having been omitted from the list. The authors have since received a personal communication from Professor J. J. Blanksma, calling their attention to the description in *Chem. Zentr.*, II, 1265 (1914), of his synthesis of crystalline *l*-mannose. The authors take this opportunity to express their regret at the unintentional omission and make the necessary correction. The previously crystallized aldohexoses are *d*- and *l*-glucose, mannose and galactose.