l-Proline was prepared by the method of Bergmann.[6] Determination of C, H and N indicated a purity of 97 to 100%. This material is also very hygroscopic.

Taurine was prepared by the method of Cortese.[7] Determination of sulfur indicated a purity of 99%. The material was halide free.

The heat capacity data, in terms of the defined conventional calorie, are given in Table I. The purity of the citrulline and ornithine was not very high, nevertheless since these compounds are crystalline over the temperature range covered, we believe that the data are reasonably reliable.

The entropies of these compounds have been calculated by a graphical integration of a plot of C_p against ln T over the experimental range and by the extrapolation method of Parks, Kelley and Huffman[2] from 0 to 90°K. The molal entropies of these compounds are given in Table II.

(6) Bergmann, *J. Biol. Chem.*, **110**, 471 (1935).

(7) Cortese, THIS JOURNAL, **58**, 191 (1936).

TABLE II

ENTROPIES OF THE COMPOUNDS IN CAL. DEGREE^{-1} MOLE^{-1}

Substance	S_{90}	$\Delta S_{90-298.1}$	$S_{298.1}$
Creatine hydrate	16.39	39.62	56.0
dl-Citrulline	18.15	42.65	60.8
dl-Ornithine	13.16	33.08	46.2
l-Proline	13.40	27.38	40.8
Taurine	10.56	26.19	36.8

Summary

1. The experimentally determined heat capacities of creatine hydrate, *dl*-citrulline, *dl*-ornithine, *l*-proline and taurine are given over the range 90 to 298°K.

2. The entropies of the above compounds have been calculated.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Acyclic Derivatives of *d*-Lyxose

BY M. L. WOLFROM AND F. B. MOODY

To our knowledge, the only open-chain or acyclic derivative of *d*-lyxose is the *d*-lyxose diacetamide prepared by Wohl and List.[1] In the course of the past year we had in hand a small amount of this rare sugar and we have applied to it several of the reactions leading to acyclic products. The sugar formed a crystalline diethyl mercaptal which was water-soluble and which was isolated according to the general procedures established[2] previously in this Laboratory for the isolation of water-soluble sugar mercaptals. The crystalline diethyl mercaptals of *d*-xylose,[2] *d*-fructose[3] and *d*-lyxose are water-soluble. All the other known crystalline sugar mercaptals possess a low water solubility. From the diethyl mercaptal of *d*-lyxose its tetraacetate was obtained readily.

Demercaptalation of *d*-lyxose diethyl mercaptal tetraacetate failed to yield a crystalline *aldehydo*-tetraacetate but acetylation of the sirupy reaction product led to the crystallization of its 1,1-diacetate derivative, designated *aldehydo-d*-lyxose hexaacetate. This substance also was obtainable by the acetolysis of the acetylated mercaptal according to the general procedure of Pirie.[4]

We have thus obtained three new crystalline acyclic derivatives of this rare sugar. Several other reactions leading to acyclic products were attempted but this sugar structure, in common with most of the sugars possessing the *cis*-configuration on carbons two and three, showed a decided tendency to produce only sirups when submitted to such procedures.

(1) A. Wohl and E. List, *Ber.*, **30**, 3101 (1897).

(2) M. L. Wolfrom, Mildred R. Newlin and E. E. Stahly, THIS JOURNAL, **53**, 4379 (1931).

(3) M. L. Wolfrom and A. Thompson, *ibid.*, **56**, 880 (1934).

Experimental

***d*-Lyxose Diethyl Mercaptal.**—A solution of *d*-lyxose (10 g.) in 12 cc. of concentrated hydrochloric acid (d. 1.19) was treated, at 0° and under mechanical stirring, with ethyl mercaptan (12 cc.). After thirty minutes of stirring at 0°, the mixture was diluted with 50 cc. of water and lead carbonate was added until the solution was neutral to congo red. The lead salts were removed by filtration and washed with water. The filtrate was treated with hydrogen sulfide until no further precipitation occurred, aerated and filtered. The filtrate was shaken with an excess of silver carbonate, filtered and again treated with hydrogen sulfide. The colloidal silver sulfide precipitate was removed by adding Super-Cel (Johns Manville) and filtering through a bed of Super-Cel. The resultant solution was concentrated under reduced pressure (40°) until crystallization ensued at a

(4) N. W. Pirie, *Biochem. J.*, **30**, 374 (1936).

volume of about 50 cc. Further concentration yielded two additional crops; total yield 13.4 g., m. p. 100–104°. Pure material was obtained on recrystallization from absolute ethanol (20 parts) by the addition of an equal volume of petroleum ether; m. p. 103–104°, spec. rot. +41° (24°, *c* 5, H_2O).[5]

The substance crystallized in plates and was soluble in water, methanol, ethanol and acetone, moderately so in ether, and was practically insoluble in petroleum ether.

Anal. Calcd. for $C_5H_{10}O_4(SC_2H_5)_2$: C, 42.16; H, 7.86; S, 25.01. Found: C, 42.05; H, 7.66; S, 24.8.

***d*-Lyxose Diethyl Mercaptal Tetraacetate.**—*d*-Lyxose diethyl mercaptal (11.4 g.) was acetylated at room temperature (initial cooling) for twelve hours with pyridine (50 cc.) and acetic anhydride (100 cc.) and the crystalline product (18.5 g.) that separated on pouring the acetylation mixture into ice and water (one liter) was obtained pure from the minimum amount of ether by the addition of two volumes of petroleum ether; m. p. 36–37°, spec. rot. +40.5° (28°, *c* 5, abs. $CHCl_3$).

The substance crystallized in soft prisms and was soluble in the common solvents except water and petroleum ether.

Anal. Calcd. for $C_5H_6O_4(CH_3CO)_4(SC_2H_5)_2$: S, 15.10; CH_3CO, 9.42 cc. 0.1 *N* NaOH per 100 mg. Found: S, 14.83; CH_3CO, 9.46 cc.

This substance also was prepared directly from the sugar without the isolation of the mercaptal. *d*-Lyxose (13.5 g.) was mercaptalated as described previously and the hydrochloric acid was neutralized at 0° (addition of ice) by the cautious addition of concentrated ammonium hydroxide. The dried mixture of ammonium chloride and lyxose mercaptal obtained on solvent removal under reduced pressure was acetylated as described above and the product was isolated in the same manner; yield 23 g.

***aldehydo-d*-Lyxose Hexaacetate.**—Demercaptalation of *d*-lyxose diethyl mercaptal tetraacetate in moist acetone with mercuric chloride and cadmium carbonate according to the improved procedure of Wolfrom and Konigsberg[6] yielded only sirups that were not amenable to crystallization. An amount of 2 g. of such a sirup was acetylated for fifteen hours at room temperature (initial cooling) with pyridine (25 cc.) and acetic anhydride (50 cc.). The mixture obtained on pouring the brown solution into ice and water (300 cc.) was extracted with chloroform and the sirup obtained on solvent removal from the washed (successively with 5% sulfuric acid, aqueous sodium bicarbonate, and water) and dried extract was crystallized from methanol by the addition of water; yield 0.41 g. Pure material was obtained on further crystallization effected in the same manner; m. p. 87–88°, spec. rot. +13° (29°, *c* 3.6, U. S. P.[7] $CHCl_3$).

Anal. Calcd. for $C_5H_6O_6(CH_3CO)_6$: C, 48.57; H, 5.76; CH_3CO, 14.3 cc. 0.1 *N* NaOH per 100 mg. Found: C, 48.70; H, 5.64; CH_3CO, 14.2 cc.

This substance also was obtainable by acetolysis of the acetylated mercaptal according to the general procedure of Pirie.[4] *d*-Lyxose diethyl mercaptal tetraacetate (2 g.) was treated for eighteen hours at room temperature (initial cooling) with 35 cc. of acetic anhydride containing 1 cc. of concentrated sulfuric acid. The yellow sirup obtained on pouring the reaction mixture into ice and water (200 cc.) crystallized on standing overnight at ice-box temperature; yield 1.1 g. Pure material was obtained on purification from methanol–water; m. p. 87–88°, spec. rot. +13° (U. S. P. $CHCl_3$).

Summary

1. The synthesis is reported of three acyclic derivatives of *d*-lyxose: *d*-lyxose diethyl mercaptal, *d*-lyxose diethyl mercaptal tetraacetate, *aldehydo-d*-lyxose hexaacetate.

(5) All rotations are recorded to the D-line of sodium light; 24° is the temperature; *c* is the concentration in g. per 100 cc. soln.

(6) M. L. Wolfrom and M. Konigsberg, THIS JOURNAL, **61**, 574 (1939).

(7) United States Pharmacopoeia.

COLUMBUS, OHIO RECEIVED OCTOBER 17, 1940

[CONTRIBUTION FROM THE VEADER LEONARD LABORATORY OF EXPERIMENTAL THERAPEUTICS]

Alkyl Ethers of 2,4-Dinitrophenol as Stimulants of the Metabolic Rate

BY LAURENCE G. WESSON

The fatalities resulting from a rapid hyperthermia in isolated cases of dinitrophenol poisoning led us, in 1934, to attempt to develop derivatives of dinitrophenol that would have a more gradual and moderate action on the metabolism of the body. One such attempt that was apparently successful in so far as this particular phase is concerned, consisted in the preparation and testing of a series of new alkyl ethers of dinitrophenol. The ether that gave the greatest promise of usefulness was the isopropyl ether. This compound was characterized by a low degree of toxicity and a protracted increase of the metabolic rate under its influence, as well as favorable melting point and ease and cheapness of its preparation.

The first preparation of an alkyl ether of 2,4-dinitrophenol was that of Cahours[1] in 1850 who obtained the ethyl ether by the nitration of phenetol. In 1867, Gruner[2] used the alkyl iodide–

(1) A. Cahours, *Ann.*, **74**, 315 (1850).

(2) H. Gruner, *J. prakt. Chem.*, **102**, 222 (1867).