2-Amino-2-deoxy-L-xylose[1,2]

M. L. WOLFROM, D. HORTON, AND A. BÖCKMANN

Department of Chemistry, The Ohio State University, Columbus 10, Ohio

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This work describes the synthesis of the last of the eight possible 2-amino-2-deoxypentoses, the L-*xylo* isomer, by alkaline epimerization of 2-acetamido-2-deoxy-L-lyxose[3] (I) followed by acid hydrolysis.

The first reported 2-amino-2-deoxypentose, the D-*xylo* isomer, was synthesized in this laboratory[4] by definitive C-5–C-6 degradation of a 2-amino-2-deoxy-D-glucose derivative. The L-*arabino* isomer was synthesized[5] by a similar route. The D-*ribo*,[6] L-*ribo*,[7] D-*lyxo*,[6] and L-*lyxo*[3] isomers were subsequently synthesized from suitably substituted pentose derivatives by hydrazinolysis and reduction. The D-*arabino* isomer was first prepared by Kuhn and Baschang[8] by a Strecker type synthesis from 2,4-*O*-ethylidene-D-erythrose.

None of the above procedures appeared to present a satisfactory route to 2-amino-2-deoxy-L-xylose, owing to the unavailability of suitable starting materials. However, the alkaline epimerization of 2-acetamido-2-deoxy-L-lyxose offered the possibility of an interconversion which could be predicted to favor the L-*xylo* isomer at equilibrium, on the basis of greater conformational stability of its pyranose ring form. In the *1C* conformation, 2-acetamido-2-deoxy-L-xylose (II) has equatorial substituents at C-2, C-3, and C-4, but the L-*lyxo* epimer (I) has an axial acetamido group. The epimerization procedure has been found useful for preparation of a number of examples of 2-acetamido-2-deoxyaldoses from their epimers[9,10]; the inductive effect of the acetamido group markedly accelerates[10] the epimerization reaction, in comparison with that of normal aldoses, and 2-ketoses cannot be formed when the acetamido group is present.

2-Acetamido-2-deoxy-L-lyxose (I), prepared as a sirup from crystalline 2-amino-2-deoxy-α-L-lyxose hydrochloride[3] by the Roseman–Ludowieg selective *N*-acetylation procedure,[11] was epimerized in 1 *N* ammonium hydroxide solution. The reaction, followed polarimetrically and by paper chromatography, is not a true equilibrium, since degradation products are simultaneously formed. Hence, the final specific rotation is not a measure of the proportions of the epimeric sugars in solution. The conditions described in the Experimental section are the result of a series of comparative experiments, and would appear optimal for conversion into a product without occurrence of undue degradation. 2-Acetamido-2-deoxy-α-L-xylose was obtained in crystalline condition; the L-*lyxo* enantiomorph[3] (I) again resisted all attempts to bring it to crystallization.

The two epimeric acetamido sugars were separated on borate-treated paper.[12] In the system used, the L-*lyxo* derivative (I) migrated more slowly than its epimer (II). It was shown that, even after removal of a 40% yield of crystalline 2-acetamido-2-deoxy-α-L-xylose, the mother liquors still contained some of the L-*xylo* epimer (II), present with the L-*lyxo* epimer (I) in the ratio 2:3. This supports the prediction made from considerations of relative conformational stability.

The crystalline 2-acetamido-2-deoxy-L-xylose showed upward mutarotation, indicative of an α-L-anomeric configuration, and provided an X-ray powder diffraction pattern identical with that of a reference sample of the D enantiomorph.[4] The infrared absorption in the 10.5–14-μ region showed strong absorptions at 12.90, 10.90, and 10.66 μ close to the corresponding values (13.16, 11.08, and 10.70 μ) reported[13] for α-D(or L)-xylopyranose and some related derivatives.

2-Acetamido-2-deoxy-α-L-xylose gave a positive Morgan–Elson[14] reaction, as did the D-enantiomorph. The statement[4] that 2-acetamido-2-deoxy-D-xylose gives a positive Elson–Morgan reaction is incorrect.

Hydrolysis of 2-acetamido-2-deoxy-α-L-xylose with 2 *N* hydrochloric acid gave crystalline 2-amino-2-deoxy-α-L-xylose hydrochloride, identical with the known D enantiomorph[4] in all respects except for the sign of the mutarotation curve. This compound gave a positive Elson–Morgan[15] reaction.

Experimental[16]

2-Acetamido-2-deoxy-α-L-xylose.—A solution of sirupy 2-acetamido-2-deoxy-L-lyxose[3] (I, 1.00 g.) in 1 *N* ammonium hydroxide (100 ml.) was stored for 51 hr. at 20°, during which time the specific rotation changed from −12.8 to −7.1°. The solution was evaporated to dryness, traces of water were removed by

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[1] Preliminary communication: M. L. Wolfrom, D. Horton, and A. Böckmann, *Chem. Ind.* (London), 41 (1963).

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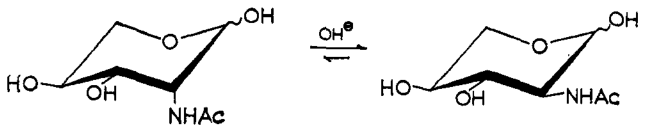
[16] Melting points were determined on a Fisher-Johns apparatus. Optical rotations were measured in a 4-dm. tube. Microanalyses were performed by W. N. Rond. Infrared spectra were determined with a Perkin-Elmer Model 137 ("Infracord") spectrophotometer, and the pellets were pressed from a finely ground mixture of the product with dried, analytical reagent grade potassium bromide. Paper chromatography was performed by the descending technique, with detection of zones by the silver nitrate–sodium hydroxide procedure of W. E. Trevelyan, D. P. Proctor, and J. S. Harrison [*Nature*, **166**, 444 (1950)]. Borate-treated[12] Whatman No. 1 chromatography paper was stored at least 1 week in contact with the atmosphere before use. Photodensitometric determinations were made with a Photovolt Model 52-C-501A photometric densitometer. Paper-chromatographic mobilities, R_x, are relative to 2-acetamido-2-deoxyxylose.



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codistillation with ethanol and toluene, and the remaining sirup was dissolved in ethanol, whereupon 2-acetamido-2-deoxy-α-L-xylose crystallized (first nuclei were obtained by cellulose-column chromatography); yield 0.40 g. (40%). Recrystallization from ethanol gave pure material; yield 0.33 g.; m.p. 194–195° dec.; $[\alpha]^{19}\text{D}$ −58, initial, extrapolated, → −7.1°, 4 hr., equil. (*c* 0.5, water); $\lambda_{\max}^{\text{KBr}}$ 3.00 (OH), 6.10, 6.50 (NHAc), 12.90, 10.90, and 10.66 μ; X-ray powder diffraction data[17]: 8.98 vw, 6.86 vs (2), 5.09 s (3), 4.67 w, 4.27 vs (1), 3.95 m, 3.80 m, 3.51 m, 3.44 vw, 3.36 vw, 3.17 vw, 3.10 m; Morgan-Elson[14] reaction (+).

Anal. Calcd. for $C_7H_{13}NO_5$: C, 43.97; H, 6.85; N, 7.33. Found: C, 44.34; H, 7.15; N, 7.59.

The D enantiomorph has been reported[4] to have m.p. 186–189° dec., $[\alpha]\text{D}$ +56 → +9°. The X-ray powder diffraction pattern of the D enantiomorph was found to be identical with that recorded herein for the L-enantiomorph.

Paper chromatography of the residual mother liquors on borate-treated paper[12] with a 6:4:3 butanol–pyridine–water system, gave two principal zones, R_x value[16] 0.72 and 1.00 in the intensity ratio, determined densitometrically, of 3 to 2, together with proportions of slower moving components. The zone R_x 0.72 corresponded to starting material (I); the faster zone corresponded to the product (II). 2-Acetamido-2-deoxy-D-xylose[4] was indistinguishable from its enantiomorph on paper chromatograms. A further yield of (sirupy) 2-acetamido-2-deoxy-L-xylose (II) was obtainable by isolative paper chromatography, to raise the total yield to 62%. The two epimers were not separable on untreated Whatman No. 1 paper.

2-Amino-2-deoxy-α-L-xylose Hydrochloride.—A solution of 2-acetamido-2-deoxy-α-L-xylose (123 mg.) in 2 *N* hydrochloric acid (50 ml.) was heated for 2 hr. at 100°. The solution then was evaporated, and traces of acid were removed by codistillation with 2-propanol and ethanol. The residue was crystallized from ethanol–acetone; yield 80 mg. (68%), m.p. 164–168° dec. Recrystallization was effected, with little loss, from ethanol–acetone–ether; m.p. 165–169° dec.; $[\alpha]^{23}\text{D}$ −78, initial, extrapolated, → −46.4 ± 0.5°, 3 hr., equil. (*c* 0.5, water); $\lambda_{\max}^{\text{KBr}}$ 3.0–3.3 (OH, NH_3^+), 6.25, 6.61 (NH_3^+), 10.98, 11.30, and 13.25 μ; X-ray powder diffraction data[17]: 8.01 m, 6.03 s, 4.54 s (2), 4.37 s (3), 4.06 s, 3.41 s (1), 3.23 s, 3.06 w, 2.95 w, 2.78 w, 2.69 w, 2.61 m, 2.51 m, 2.37 m, 2.33 m, 2.26 m, 2.21 s; Elson–Morgan[15] reaction (+).

Anal. Calcd. for $C_5H_{12}ClNO_4$: Cl, 19.10. Found: Cl, 18.76.

For 2-amino-2-deoxy-α-D-xylose hydrochloride, Wolfrom and Anno[4] report m.p. 160–165° dec.; $[\alpha]\text{D}$ +80, initial, extrapolated → +40° (*c* 0.8, water, final).

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[17] Interplanar spacing, Å., Cu Kα radiation. Relative intensity estimated visually: s, strong; m, medium; w, weak; v, very. First three strongest lines are numbered (1, strongest).

Mercaptan–Disulfide Interchange Reactions. II. Some Equilibrium Constants[1]

GARY DALMAN, JOHN MCDERMED, AND GEORGE GORIN[2]

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma

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Equilibrium constants have been determined for the interchange reactions between two organic disulfides and/or between a mercaptan and a disulfide for the following cases: *n*-hexyl–phenyl, *n*-hexyl–β-hydroxyethyl, *n*-hexyl–(β-diethylamino)ethyl, *n*-propyl–*sec*-butyl, and *n*-butyl–*t*-butyl. The constants differ from the statistically predicted values by a factor of two or less, except for the reactions of phenyl mercaptan with hexyl phenyl disulfide and of *t*-butyl mercaptan with *n*-butyl *t*-butyl disulfide, which have smaller constants. These data and others indicate that the interchange reactions are not sensitive to the effect of substituent groups, except ones that interfere sterically.

Mercaptans and organic disulfides can react with one another in appropriate conditions. Such reactions occur in diverse chemical systems and may have consequences of considerable importance; examples may be found in petroleum,[3] polysulfide rubber,[4] and living organisms.[5] In organic chemistry, reactions which proceed to a measurable equilibrium state are comparatively rare, and the mercaptan–disulfide interchange reactions to be described are interesting from this point of view also. The present paper will be concerned with some general aspects of the problem and with reactions taking place in an organic medium. Paper III of this series, which follows,[6] will consider reactions of water-soluble compounds in buffered aqueous medium.

The reaction of two symmetrical disulfides to give the unsymmetrical, or "mixed," disulfide may be represented by eq. 1a. Unsymmetrical disulfides also may

$$\text{RSSR} + \text{R'SSR'} \rightleftarrows 2\text{RSSR'} \qquad (1a)$$

result from the reaction of RSSR with a mercaptan, according to eq. 2a. The reaction may then proceed further, according to eq. 3a.

$$\text{RSSR} + \text{R'SH} \rightleftarrows \text{RSSR'} + \text{RSH} \qquad (2a)$$

$$\text{RSSR'} + \text{R'SH} \rightleftarrows \text{R'SSR'} + \text{RSH} \qquad (3a)$$

The corresponding equilibrium expressions are

$$K_1 = (\text{RSSR'})^2/(\text{RSSR})(\text{R'SSR'}) \qquad (1b)$$

$$K_2 = (\text{RSSR'})(\text{RSH})/(\text{RSSR})(\text{R'SH}) \qquad (2b)$$

$$K_3 = (\text{R'SSR'})(\text{RSH})/(\text{RSSR'})(\text{R'SH}) \qquad (3b)$$

where the quantities in parentheses are the activities of the respective chemical species. The product K_2K_3 measures the equilibrium constant for reaction 4a.

$$\text{RSSR} + 2\text{R'SH} \rightleftarrows \text{R'SSR'} + 2\text{RSH} \qquad (4a)$$

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