diethyl dithioacetals: *aldehydo*-D-arabinose tetraacetate-d_{12} (II), m.p. 110.5–112°; and *aldehydo*-2-deoxy-D-glucose tetraacetate-d_{12}, m.p. 93–95.5°.

Acknowledgment.—The author would like to thank Professor K. Biemann for allowing him to use the mass spectrometer in his laboratories at the Massachusetts Institute of Technology. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Synthesis of L-*threo*-Pentulose and 3,4,5-Tri-*O*-benzoyl-1-deoxy-L-*threo*-pentulose[1]

M. L. WOLFROM AND R. B. BENNETT[2]

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received September 24, 1964

L-*threo*-Pentulose and 3,4,5-tri-*O*-benzoyl-1-deoxy-L-*threo*-pentulose were synthesized from 3,4,5-tri-*O*-acetyl- and 3,4,5-tri-*O*-benzoyl-1-deoxy-1-diazo-L-*threo*-pentulose, respectively. The diazomethyl ketones were prepared by acetylation or benzoylation of L-threonamide, deamination to the corresponding aldonic acids, conversion to the acyl halides, and reaction with diazomethane. The acetylated diazomethyl ketone was transformed into the sirupy *keto*-acetate which on deacetylation yielded the ketopentose. The benzoylated diazomethyl ketone was reduced to the corresponding 1-deoxy derivative. Although the aldonamides of higher carbon content mutarotate in aqueous solution, the amides of the aldotetronic acids do not show this property.

In continuation of our work on the general method for the preparation of ketoses from the acetylated sugar acids with one less carbon atom,[3] we report herein the application of this method to the synthesis of L-*threo*-pentulose (VII, "L-xylulose"); we also report the synthesis of 1-deoxy-L-*threo*-pentulose as the crystalline tribenzoate (XI).

L-*threo*-Pentulose has been isolated from the urine of humans with essential pentosuria,[4–8] the inborn error of metabolism discovered by Salkowski and Jastrowitz[9] in 1892. The definitive characterization of the urinary sugar was made by Levene and LaForge[4] in 1914. The role of this ketopentose in pentose metabolism and pentosuria has recently been reviewed.[10] L-*threo*-Pentulose was first synthesized by boiling L-xylose with pyridine, removing unchanged L-xylose by crystallization, and isolating the ketose as the *p*-bromophenylhydrazone.[11]

The starting point for our synthesis was L-threono-1,4-lactone prepared by the oxidative scission of L-ascorbic acid with *p*-toluenediazonium hydrogen sulfate.[12] The lactone was converted to L-threonamide[13] (I) with liquid ammonia.[14]

In contrast to other aldonamides,[15] L-threonamide was found by us to be hydrolytically stable at room temperature. No significant change in rotation occurred during 95 hr. and the amide was recovered unchanged after this period, as shown by melting point, infrared spectrum, and X-ray powder diffraction pattern. Crum[16] observed a similar hydrolytic behavior for D-erythronamide. This lack of mutarotation for the four-carbon aldonamides may be due to the nonformation of the postulated[15] glycosylamine intermediate, which in this case would be a furanosylamine.

Acetylation of L-threonamide with acetic anhydride and zinc chloride, conditions reported to produce *O*-acetylated aldonamides,[17] gave the fully acetylated amide, *N*-acetyl-2,3,4-tri-*O*-acetyl-L-threonamide (III), rather than the *O*-acetylated product. The fully acetylated amide was also prepared by acetylation of L-threonamide with the acetic anhydride–concentrated sulfuric acid procedure used to prepare other fully acetylated aldonamides.[17] Acetylation of L-threonamide in anhydrous pyridine with acetic anhydride gave only *O*-acetylation and produced 2,3,4-tri-*O*-acetyl-L-threonamide (II) in high yield.

Benzoylation of L-threonamide with benzoyl chloride in anhydrous pyridine, as described by Lake and Glattfeld[18] for benzoylation of DL-threonamide, gave 2,3,4-tri-*O*-benzoyl-L-threonamide (VIII). In one large run under the same (presumably) conditions, the product obtained was 2,3,4-tri-*O*-benzoyl-L-threononitrile (IV), the structure of which was proved unequivocally by its conversion to and synthesis from 2,3,4-tri-*O*-benzoyl-L-threonamide. In other runs under apparently the same conditions, only the benzoylated amide was obtained. It is interesting that the infrared absorption spectrum of 2,3,4-tri-*O*-benzoyl-L-threononitrile shows no nitrile absorption at 4.5 μ, apparently because of the "quenching" effect of oxygen in the molecule.[19]

The *O*-acetylated and the benzoylated amides were converted with dinitrogen trioxide ("nitrous anhy-

(1) Paper No. 21 in the series entitled "The Action of Diazomethane upon Acyclic Sugar Derivatives"; previous communication, M. L. Wolfrom, J. C. Crum, J. B. Miller, and D. I. Weisblat, *J. Am. Chem. Soc.*, **81**, 243 (1959).

(2) Charles F. Kettering Foundation Fellow, 1959–1960, 1961; National Science Foundation Summer Fellow, 1961; Goodyear Foundation Fellow, 1963–1964; Du Pont Grant-in-Aid Recipient, 1964.

(3) M. L. Wolfrom, R. L. Brown, and E. F. Evans, *J. Am. Chem. Soc.*, **65**, 1021 (1943), and other papers of the series (see ref. 1).

(4) P. A. Levene and F. B. LaForge, *J. Biol. Chem.*, **18**, 319 (1914).

(5) A. Hiller, *ibid.*, **30**, 129 (1917).

(6) I. Greenwald, *ibid.*, **88**, 1 (1930).

(7) P. Bálint, *Biochem. Z.*, **274**, 305 (1934).

(8) O. Touster, R. H. Mayberry, and D. B. McCormick, *Biochim. Biophys. Acta*, **25**, 196 (1957).

(9) E. Salkowski and M. Jastrowitz, *Centr. med. Wiss.*, **30**, 337 (1892.)

(10) O. Touster, *Am. J. Med.*, **26**, 724 (1959).

(11) L. von Vargha, *Ber.*, **68**, 18 (1935).

(12) R. Weidenhagen, H. Wegner, K. H. Lung, and L. Nordström, *ibid.*, **72**, 2010 (1939).

(13) K. Gätzi and T. Reichstein, *Helv. Chim. Acta*, **20**, 1298 (1937).

(14) J. W. E. Glattfeld and D. Macmillan, *J. Am. Chem. Soc.*, **56** 2481 (1934).

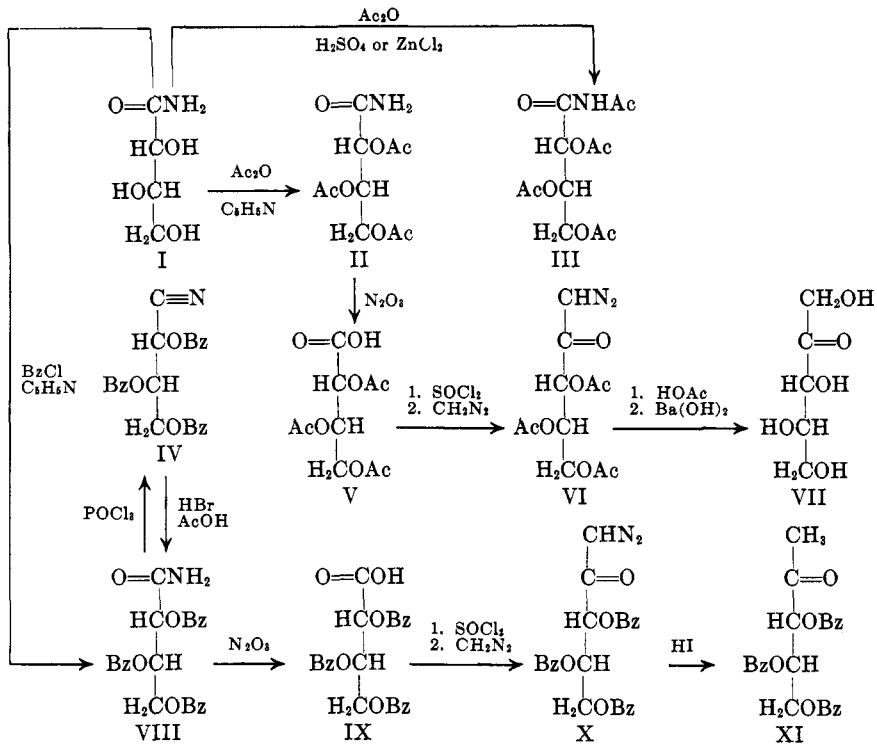
(15) M. L. Wolfrom, R. B. Bennett, and J. D. Crum, *ibid.*, **80**, 944 (1958).

(16) J. D. Crum, Ph.D. Thesis (The Ohio State University); University Microfilms, Ann Arbor, Mich., L. C. Card No. Mic. 58-3415; *Dissertation Abstr.*, **19**, 670 (1958).

(17) G. B. Robbins and F. W. Upson, *J. Am. Chem. Soc.*, **60**, 1788 (1938).

(18) W. W. Lake and J. W. E. Glattfeld, *ibid.*, **66**, 1091 (1944).

(19) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd. Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, pp. 265–266.



dride")[20] to 2,3,4-tri-*O*-acetyl-L-threonic acid (V) and 2,3,4-tri-*O*-benzoyl-L-threonic acid (IX), respectively, and then to 2,3,4-tri-*O*-acetyl-L-threonyl chloride (sirup) and 2,3,4-tri-*O*-benzoyl-L-threonyl chloride (sirup), respectively, with thionyl chloride. The sirupy acid chlorides were characterized as crystalline anilides. Reaction of the acid chlorides with diazomethane gave crystalline 3,4,5-tri-*O*-acetyl-1-deoxy-1-diazo-L-*threo*-pentulose (VI) and, after silicate column chromatography, crystalline 3,4,5-tri-*O*-benzoyl-1-deoxy-1-diazo-L-*threo*-pentulose (X).

Reaction of the acetylated diazomethyl ketone with glacial acetic acid and cupric acetate followed by reacetylation with acetic anhydride and zinc chloride yielded 1,3,4,5-tetra-*O*-acetyl-L-*threo*-pentulose (sirup). Deacetylation of the pentulose tetraacetate with barium hydroxide and preparative thin layer chromatography of the crude reaction product on microcrystalline cellulose[21] gave L-*threo*-pentulose (VII), characterized as the crystalline *p*-bromophenylhydrazone.[4] L-*threo*-Pentulose showed a particular sensitivity to alkali as indicated by the formation, during the deacetylation process, of several products as detected by thin layer chromatography.

Reduction of 3,4,5-tri-*O*-benzoyl-1-deoxy-1-diazo-L-*threo*-pentulose with hydriodic acid[22] and silicate column chromatography of the reaction product gave 3,4,5-tri-*O*-benzoyl-1-deoxy-L-*threo*-pentulose as a sirup which was crystallized under reaction conditions expected to effect debenzoylation to 1-deoxy-L-*threo*-pentulose. The barium hydroxide procedure usually used for deacetylation of acetylated ketoses is not generally practical for debenzoylation of benzoates in cold aqueous solutions. Therefore, the methanol–hydrochloric acid deacetylation procedure of Staněk and Černá[23] was chosen, but under these reaction conditions little or no debenzoylation occurred and instead the starting material began to crystallize after 1 week.

(20) C. D. Hurd and J. C. Sowden, *J. Am. Chem. Soc.*, **60**, 235 (1938).

(21) M. L. Wolfrom, D. L. Patin, and R. M. de Lederkremer, *Chem. Ind.* (London), 1065 (1964); *J. Chromatog.*, in press.

(22) M. L. Wolfrom and R. L. Brown, *J. Am. Chem. Soc.*, **65**, 1516 (1943).

Experimental[24]

2,3,4-Tri-*O*-acetyl-L-threonamide(II).— Oxidation of L-ascorbic acid with *p*-toluenediazonium hydrogen sulfate according to Weidenhagen and co-workers[12] gave L-threono-1,4-lactone of m.p. 75–76° and $[\alpha]^{25}D$ +30° (*c* 1.0 water). These data are in agreement with the values 74–76° and $[\alpha]D$ +30° cited by Hardegger and co-workers[25]; X-ray powder diffraction data[24]: 6.65 w, 5.46 m (2,2), 4.55 w, 4.21 s (1), 3.85 w, 3.49 m (2,2), 3.29 m (3), 3.13 m (2,2), 3.00 w, 2.79 (2,2), 2.70 w, 2.56 w, 2.31 w, 2.07 w, and 2.00 w. The action of liquid ammonia[14] upon the lactone gave L-threonamide (I), m.p. 105–107°, $[\alpha]^{20}D$ +56° (*c* 2.0, water), in agreement with the constants 105.5–107° and $[\alpha]^{21}D$ +56.0° reported by Gätzi and Reichstein[13]; X-ray powder diffraction data[24]: 12.77 w, 6.45 w, 4.64 s (2), 4.40 s (1), 3.79 w, 3.33 s (3,3), 3.17 w, 3.04 w, 2.88 m (3,3), 2.54 w, 2.38 w, 2.33 w, 2.29 w, 2.23 w, and 2.16 w. No mutarotation in aqueous solution was noted for this substance over an observation period of 95 hr. and unchanged material was recovered at the end of this period, identification being made by melting point, infrared spectrum, and X-ray powder diffraction pattern.

To 10 g. of L-threonamide, dissolved in 100 ml. of anhydrous pyridine and cooled to 0°, was added slowly, with stirring, 60 ml.

(23) J. Staněk and J. Černá, *Tetrahedron Letters*, 35 (1963).

(24) Thin layer chromatography was performed by the ascending technique on silica gel G (E. Merck, Darmstadt, Germany) activated at 100° or on Avirin (a microcrystalline cellulose produced by the American Viscose Co., Marcus Hook, Pa.; see ref. 21). Zones were located on silica gel plates by spraying with 1% potassium permanganate in 10% sodium hydroxide or by heating at 150° after spraying with concentrated sulfuric acid; zones were located on cellulose plates by the silver nitrate–sodium hydroxide procedure [W. E. Trevelyan, D. P. Proctor, and J. S. Harrison, *Nature*, **166**, 444 (1950)] or with resorcinol–hydrochloric acid reagent [L. Hough and J. K. N. Jones, *J. Chem. Soc.*, 4047 (1952)]. Melting points were determined on a Hershberg-type apparatus (A. Thompson and M. L. Wolfrom, in "Methods in Carbohydrate Chemistry," Vol. I, R. L. Whistler and M. L. Wolfrom, Ed., Academic Press Inc., New York, N. Y., 1962, p. 517). X-Ray powder diffraction data refer to interplanar spacing in Å. with Cu Kα radiation. Relative intensities were estimated visually: s, strong; m, medium; w, weak; v, very. The first three strongest lines are numbered (1, strongest); multiple numbers indicate approximately equal intensities.

(25) E. Hardegger, K. Kreis, and H. El Khadem, *Helv. Chim. Acta*, **34**, 2343 (1951).

of acetic anhydride. The reaction mixture was held at 0° for 1 hr., maintained overnight in a refrigerator, poured into ice–water, stirred intermittently for 1.5 hr., and exhaustively extracted with chloroform. The dried (magnesium sulfate) extract was evaporated under reduced pressure to a sirup which crystallized. Recrystallization from benzene gave 2,3,4-tri-*O*-acetyl-L-threonamide (II); yield 16.2 g. (84%). Two more recrystallizations from benzene gave pure material: m.p. 124–125°, $[\alpha]^{25}D$ −27° (*c* 3.0, chloroform); X-ray powder diffraction data[24]: 11.45 w, 8.95 m (3), 7.54 s (1), 5.74 w, 4.34 s (2), 4.01 m, 3.69 m, 3.34 m, and 3.17 m.

Anal. Calcd. for $C_{10}H_{15}NO_7$: C, 45.98; H, 5.79; N, 5.36, Found: C, 46.02; H, 5.86; N, 5.35.

N-Acetyl-2,3,4-tri-*O*-acetyl-L-threonamide (III).—L-Threonamide (1 g.) was added with stirring to a cooled (0°) solution of 0.5 ml. of concentrated sulfuric acid and 10 ml. of acetic anhydride. The mixture was allowed to stand for 1 hr. at 0°, then at room temperature for 24 hr., and was poured with vigorous stirring into 40 ml. of ice–water; sodium hydrogen carbonate (2 g.) was carefully added. Chloroform extraction and removal of the dried (magnesium sulfate) chloroform under reduced pressure gave a sirup which, when repeatedly evaporated under reduced pressure from absolute ethanol solution, gave a crude product: yield 1.88 g. (84%), m.p. 119–121°. Three recrystallizations from benzene–petroleum ether (b.p. 30–60°) gave pure material: m.p. 120–122°, $[\alpha]^{25}D$ −25° (*c* 3.0, chloroform); X-ray powder diffraction data[24]: 9.38 w, 8.05 s (1), 7.47 w, 6.50 w, 5.25 m, 4.43 s (2), 4.14 m, 3.97 m, 3.84 m, 3.62 m, 3.36 m (3,3), 3.19 m (3,3), 3.08 w, 2.87 w, 2.81 m, and 2.66 m. The same product was obtained in 49% yield when freshly fused zinc chloride was used as catalyst (1 g. for each gram of amide) instead of concentrated sulfuric acid.

Anal. Calcd. for $C_{12}H_{17}NO_8$: C, 47.52; H, 5.65; N, 4.62. Found: C, 47.34; H, 5.40; N, 4.74.

2,3,4-Tri-*O*-benzoyl-L-threonamide (VIII). A. From L-Threonamide (I).—To 4.8 g. of L-threonamide, dissolved in 50 ml. of anhydrous pyridine and cooled to 0°, was added slowly, with stirring, 72 ml. of benzoyl chloride at such a rate that the temperature was maintained below 5°. After standing overnight in a refrigerator, the reaction mixture was poured with stirring into three times its volume of ice and water. The brown gum which formed was extracted with chloroform and the dried (magnesium sulfate) chloroform solution was concentrated under reduced pressure. Repeated evaporation under reduced pressure from toluene solution removed traces of pyridine and yielded a sirup which crystallized. One recrystallization from 90% ethanol gave a product: yield 12.6 g. (80%, two crops), m.p. 112–114°. Three recrystallizations from the same solvent gave pure material: m.p. 114–116°, $[\alpha]^{23}D$ −45° (*c* 3.1, chloroform); X-ray powder diffraction data[24]: 14.45 w, 10.92 s (2,2), 9.85 s (2,2), 7.35 w, 6.28 m, 5.44 w, 5.07 m, 4.82 s (1), 4.45 s (3,3), 4.16 w, 3.81 s (3,3), 3.63 m, 3.52 w, 3.41 w, 3.22 m, 2.95 m, and 2.74 m.

Anal. Calcd. for $C_{25}H_{21}NO_7$: C, 67.11; H, 4.73; N, 3.13. Found: C, 67.04; H, 4.75; N, 3.07.

B. From 2,3,4-Tri-*O*-benzoyl-L-threononitrile (IV).—Following the general procedure of Zemplén and Kiss[26] for converting acetylated aldononitriles to acetylated aldonamides, 2 ml. of glacial acetic acid saturated with hydrogen bromide was added to a mixture of 2,3,4-tri-*O*-benzoyl-L-threononitrile (1 g.), described below, in glacial acetic acid (1.5 ml.). The nitrile had completely dissolved after 15 min. The solution was allowed to stand overnight at room temperature and was then poured into 60 ml. of ice–water. The resulting solid material was filtered, washed with water, and recrystallized from 95% ethanol: yield 0.8 g. (77%). An additional recrystallization from the same solvent gave pure material: m.p. 114–116°, $[\alpha]^{25}D$ −44° (*c* 2.7, chloroform); X-ray powder diffraction data and the infrared spectrum were identical with those of a sample prepared from L-threonamide.

2,3,4-Tri-*O*-benzoyl-L-threononitrile (IV).—Following the general procedure of Ladenburg and co-workers[27] for preparing acetylated aldononitriles, a mixture of 0.5 g. of 2,3,4-tri-*O*-benzoyl-L-threonamide and 1.5 g. (1 ml.) of phosphorus oxychloride was heated at 80° for 30 min. Chloroform (10 ml.) was added to the reaction mixture and the solution was stirred cautiously into 30 ml. of ice and water. The organic layer was separated and the aqueous layer was extracted with three 10-ml. portions of chloroform. The combined chloroform extracts were washed with sodium hydrogen carbonate solution followed by water, dried (sodium sulfate), and concentrated under reduced pressure. The resulting sirup was twice evaporated under reduced pressure from absolute ethanol to give solid material: yield 0.29 g. (60%). Three recrystallizations from 90% ethanol gave pure material: m.p. 111–112°, $[\alpha]^{25}D$ +25° (*c* 0.7, chloroform); X-ray powder diffraction data[24]: 10.40 s, 9.14 m, 6.22 w, 5.49 s (1), 5.19 w, 4.84 m, 4.50 s (3), 4.15 s (2), 4.00 m, 3.84 w, 3.65 m, 3.47 s, 3.20 m, and 3.04 w. These constants and the infrared spectrum were identical with those of the product obtained in one experiment (which could not be duplicated under the same conditions) concerned with the benzoylation of a rather large amount of L-threonamide.

Anal. Calcd. for $C_{25}H_{19}NO_8$: C, 69.92; H, 4.46; N, 3.26. Found: C, 69.95; H, 4.72; N, 3.25.

2,3,4-Tri-*O*-acetyl-L-threonic Acid (V).—Following the general deamination procedure of Hurd and Sowden,[20] 2,3,4-tri-*O*-acetyl-L-threonamide (15.0 g.) was dissolved in 60 ml. of glacial acetic acid and the solution was cooled to 10° (bath temperature). Oxides of nitrogen, generated by the action of nitric acid (sp. gr. 1.35) on arsenic trioxide,[28] were bubbled into the acetic acid solution until a dark green color persisted whereupon the flow of gas was stopped and the solution was allowed to stand at room temperature for 3 hr. This process was repeated (two or three times) until thin layer chromatography on silica gel with chloroform–methanol (9:1 v./v.), using alkaline permanganate[24] as indicator, showed the absence of starting material (R_f 0.44). Evaporation of the solvent under reduced pressure at 45° gave a sirup which was repeatedly dissolved in toluene and concentrated under reduced pressure. On standing overnight the sirup crystallized: yield 11.2 g. (75%). Two recrystallizations from ether–petroleum ether gave pure material: m.p. 76–78°, $[\alpha]^{23}D$ −29° (*c* 2.0, chloroform); X-ray powder diffraction data[24]: 15.30 w, 7.67 s (2), 7.16 s (3), 5.57 m, 5.30 m, 5.18 w, 4.31 s (1), 4.15 m, 4.02 m, 3.92 w, 3.82 m, 3.70 m, 3.55 w, 3.42 m, 3.16 w, 3.06 w, 2.98 w, and 2.89 m.

Anal. Calcd. for $C_{10}H_{14}O_8$: C, 45.80; H, 5.38. Found: C, 45.98; H, 5.34.

2,3,4-Tri-*O*-benzoyl-L-threonic Acid (IX).—Oxides of nitrogen, generated as above for 2,3,4-tri-*O*-acetyl-L-threonic acid, were passed into a cooled (15°) solution of 2,3,4-tri-*O*-benzoyl-L-threonamide (8.4 g.) in 50 ml. of glacial acetic acid until a green color persisted. The reaction mixture stood overnight at room temperature and was then poured slowly into 98 g. of sodium hydrogen carbonate in 250 ml. of water. The resulting solution was acidified with 6 *N* hydrochloric acid to pH 4 and extracted with chloroform. The chloroform solution was dried (magnesium sulfate), treated with carbon, and concentrated under reduced pressure to a sirup which was repeatedly evaporated under reduced pressure from toluene to remove traces of acetic acid. Upon standing overnight the sirup crystallized to a solid mass which was recrystallized from benzene; yield 7.6 g. (90%), m.p. 121–122°. Further recrystallization from benzene gave pure material: m.p. 122–123°, $[\alpha]^{25}D$ −56° (*c* 3.0, chloroform); X-ray powder diffraction data[24]: 12.12 s (3), 7.43 m, 5.59 m, 5.23 s, (1), 4.91 m, 4.27 s (2), 3.68 m, 3.38 s, 3.23 m, 3.07 m, 2.84 s, and 2.67 w.

Anal. Calcd. for $C_{25}H_{20}O_8$: C, 66.96; H, 4.50. Found: C, 66.75; H, 4.51.

3,4,5-Tri-*O*-acetyl-1-deoxy-1-diazo-L-*threo*-pentulose (VI).—A solution of 2,3,4-tri-*O*-acetyl-L-threonic acid (6.0 g.) in dry benzene (50 ml.) and purified[29] thionyl chloride was refluxed for 2 hr., cooled, and maintained at room temperature overnight. The volatile material was removed by evaporation under reduced pressure at 40°. The resultant sirup was repeatedly dissolved in dry benzene and the solvent was evaporated under reduced pressure until all of the excess thionyl chloride had been removed.

The sirupy acid chloride (6.5 g.) in dry ether (100 ml.) was slowly added to a cooled (0°), anhydrous solution of diazomethane[30] (2 g.) in ether (200 ml.). The solution was allowed to stand at 0° for 2 hr. and was then permitted to warm gradually to room temperature. The solution was concentrated by a stream of dry air and the sirupy residue was dissolved in 120 ml. of

(26) G. Zemplén and D. Kiss, *Ber.*, **60**, 165 (1927).

(27) K. Ladenburg, M. Tishler, J. W. Wellman, and R. D. Babson, *J. Am. Chem. Soc.*, **66**, 1217 (1944).

(28) A. W. Dox, *Org. Syn.*, **4**, 27 (1925).

(29) D. L. Cottle, *J. Am. Chem. Soc.*, **68**, 1380 (1946).

(30) T. J. De Boer and H. J. Backer, *Org. Syn.*, **36**, 16 (1956).

benzene and 6 g. of Magnesol[31]–Celite[32] (5:1 w./w.) was added. The suspension was stirred for 30 min., filtered, and washed with 60 ml. of benzene. The filtrate and washings were evaporated under reduced pressure at 25° to a sirup which was diluted with a small amount of ether and placed in a refrigerator. Crystallization occurred within 2 days: yield 5.1 g. (77%). The material was recrystallized by dissolving in excess ether, concentrating, and cooling: m.p. 71–72°, $[\alpha]^{23}D$ +9° (*c* 2.0, chloroform); X-ray powder diffraction data[24]: 8.36 s (2,2), 7.59 m, 6.37 w, 5.17 s (1,1), 4.46 m, 4.29 s (2,2), 4.11 s (3), 3.88 w, 3.64 s (1,1), 3.45 w, 3.30 m, 3.13 m, 3.01 m, 2.81 w, 2.71 m, and 2.62 m.

Anal. Calcd. for $C_{11}H_{14}N_2O_7$: C, 46.15; H, 4.93; N, 9.79. Found: C, 46.28; H, 4.85; N, 9.87.

3,4,5-Tri-*O*-benzoyl-1-deoxy-1-diazo-L-*threo*-pentulose (X).—2,3,4-Tri-*O*-benzoyl-L-threonic acid (7.6 g.) was converted to the sirupy acid chloride (8.0 g.) as described above for the acetylated derivative. The isolated sirupy product was converted with diazomethane (2 g.) to the diazomethyl ketone in the manner described above. The crude, sirupy product (8.5 g.) was dissolved in 40 ml. of benzene and chromatographed in 20-ml. portions on two 75 × 250 mm. columns of Magnesol[31]–Celite[32] (5:1 w./w.) using 1 l. (for each column) of benzene–*t*-butyl alcohol (100:1 v./v.) as developer. An alkaline permanganate streak[33] showed a large zone 130–170 mm. from the top of the extruded column. The excised zones from the two columns were combined, eluted with acetone, and the eluate was evaporated under reduced pressure to a sirup which crystallized from ether–petroleum ether: yield 4.4 g. (55%). Recrystallization from ether–petroleum ether gave pure material: m.p. 76–78°, $[\alpha]^{28}D$ −20° (*c* 1.0, chloroform); X-ray powder diffraction data[24]: 11.02 m, 9.94 m, 7.67 w, 7.08 w, 6.49 w, 5.04 s (1), 4.68 s (2), 4.40 m (3), 4.16 m, 3.80 m, 3.63 m, 3.49 m, 3.32 m, and 3.08 m.

Anal. Calcd. for $C_{26}H_{20}N_2O_7$: C, 66.10; H, 4.27; N, 5.93. Found: C, 66.27; H, 4.35; N, 5.93.

2,3,4-Tri-*O*-acetyl-L-threonanilide.—Aniline (1 ml.) was added to a solution of sirupy 2,3,4-tri-*O*-acetyl-L-threonyl chloride (0.3 g.) in ether (10 ml.). The reaction mixture was allowed to stand at room temperature for 1 hr. and then was diluted with ether (10 ml.). The ether solution was washed once with water, twice with 3 *N* hydrochloric acid, and once again with water. Concentration of the dried (magnesium sulfate) ether solution gave a crystalline product: yield 0.23 g. The material was recrystallized by dissolving in excess ether, concentrating, and cooling: m.p. 139–140°, $[\alpha]^{23}D$ +6° (*c* 1.0, chloroform); X-ray powder diffraction data[24]: 11.49 s (1), 8.69 w, 7.77 s (3), 7.26 vw, 6.68 w, 5.93 w, 5.42 w, 4.78 m, 4.68 s (2), 4.57 m, 4.17 m, 4.04 m, 3.98 m, 3.82 m, 3.72 m, 3.56 m, and 3.32 w.

Anal. Calcd. for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 57.48; H, 5.75; N, 4.35.

2,3,4-Tri-*O*-benzoyl-L-threonanilide.—Sirupy 2,3,4-tri-*O*-benzoyl-L-threonyl chloride (0.1 g.) was converted to the anilide as described above for the acetylated compound; three recrystallizations from 95% ethanol gave pure material: m.p. 136–136.5°, $[\alpha]^{26}D$ −29° (*c* 1.0, chloroform); X-ray powder diffraction data[24]: 11.72 s (1), 9.63 w, 7.80 w, 5.80 w, 5.10 s (2), 4.66 m, 4.39 s (3), 4.10 s, 3.87 m, 3.65 m, 3.49 m, and 3.33 m.

Anal. Calcd. for $C_{31}H_{25}NO_7$: C, 71.12; H, 4.81; N, 2.68. Found: C, 71.19; H, 4.90; N, 2.31.

L-*threo*-Pentulose (VII).—A solution of 3,4,5-tri-*O*-acetyl-1-deoxy-1-diazo-L-*threo*-pentulose (2.0 g.) in glacial acetic acid (35 ml.), to which had been added 7 mg. of cupric acetate and a trace of powdered copper, was allowed to stand at room temperature for 2 hr. and was then heated at 80–90° for 15 min. The reaction mixture was cooled and then concentrated under reduced pressure at 35° to a sirup which was dissolved in 30 ml. of chloroform. The chloroform solution was washed twice with water, dried (magnesium sulfate), treated with carbon, and evaporated under reduced pressure to a sirup: yield 2.0 g. The sirup (2.0 g.) was reacetylated by dissolving in 25 ml. of acetic anhydride containing 0.25 g. of freshly fused zinc chloride. After standing overnight at room temperature, the acetic anhydride was hydrolyzed with ice and water. The acetate was extracted with chloroform; the chloroform solution was washed with water, dried (magnesium sulfate), and evaporated under reduced pressure to a sirup: yield 1.8 g., which gave a positive Pacsu[34] *keto*-acetate test. A thin layer chromatogram of the sirup on silica gel with benzene–methanol (9:1 v./v.) showed the presence of one major spot (R_f 0.58) and a faint trace of some other material (R_f 0.37).

The above sirup (1.6 g.) was cooled to 0° and deacetylated by adding a solution of barium hydroxide octahydrate (6 g.) in 75 ml. of water also at 0°, and stirring for 2 hr. at 0°. The solution was saturated with carbon dioxide and the precipitated barium carbonate was removed by filtration through Celite.[32] The filtrate was decolorized with carbon and then passed through a 24 × 120 mm. column of Amberlite[35] IR-120 (H^+ resin). The resin was washed with distilled water until the eluate failed to reduce hot Benedict reagent. The washings were combined with the original eluate and the resulting solution was concentrated under reduced pressure at 35° to a sirup: yield 0.65 g. A thin layer chromatogram of the sirup on Avirin[24] with 40:11:19 1-butanol–ethanol–water, when detected with silver nitrate–sodium hydroxide,[24] showed a main spot (R_f 0.54, R_{xylose} 1.17), a smaller component (R_f 0.43), and a faint spot (R_f 0.61). A similar chromatogram sprayed with resorcinol–hydrochloric acid[24] gave a single blue spot (R_f 0.53, $R_{sorbose}$ 1.32), characteristic of a ketopentose.

The above sirup was chromatographed in 25-mg. portions on 8 × 8 in. plates of Avirin[24] with 40:11:19 1-butanol–ethanol–water. The main ketose zone, detected by spraying the edges and center of each plate with silver nitrate–sodium hydroxide,[24] was scraped from each plate and eluted with distilled water. The solution was concentrated under reduced pressure at 35° to a sirup (0.25 g.), $[\alpha]^{21}D$ +31° (*c* 1.0, water). Levene and LaForge[4] report $[\alpha]^{25}D$ +33°. The sirup migrated as a single spot on Avirin[24] thin layer chromatograms developed with 40:11:19 1-butanol–ethanol–water and sprayed with silver nitrate–sodium hydroxide.[24]

A portion (80 mg.) of the sirup was converted to the *p*-bromophenylhydrazone[4]: yield 75 mg., m.p.127– 128°, $[\alpha]^{20}D$ −20 (10 min.) → +22° (5 hr., *c* 0.5, ethanol); Levene and LaForge[4] report m.p. 128–129°, $[\alpha]D$ −20.0 (5 min.) → +22.4° (5 hr., *c* 10, ethanol); X-ray powder diffraction data[24]: 8.09 w, 6.83 m, 5.47 s, 4.60 w, 4.36 s (1), 4.14 s, 3.95 m, 3.76 s (2), 3.49 s (3), 3.28 m, 3.16 m, 3.06 m, and 2.99 m.

3,4,5-Tri-*O*-benzoyl-1-deoxy-L-*threo*-pentulose (XI).—3,4,5-Tri-*O*-benzoyl-1-deoxy-1-diazo-L-*threo*-pentulose (2 g.), dissolved in 50 ml. of chloroform, was shaken in a separatory funnel with 8 ml. of 47% aqueous hydriodic acid. After cessation of the slow nitrogen evolution, water was added and the separated chloroform layer was washed successively with water, dilute aqueous sodium thiosulfate (until free of iodine), and again with water. The dried (magnesium sulfate) chloroform solution was evaporated to a sirup: yield 1.95 g.

The sirupy product was dissolved in 20 ml. of benzene and chromatographed on a 53 × 190 mm. column of Magnesol[31]–Celite[32] (5:1 w./w.) using 600 ml. of benzene–*t*-butyl alcohol (100:1 v./v.) as developer. An alkaline permanganate streak[33] showed the main zone at 100–130 mm. from the top of the extruded column. The excised zone was eluted with acetone and the acetone solution was concentrated under reduced pressure to a sirup: yield 0.8 g. The sirup migrated as a single zone on silica gel thin layer chromatograms with benzene–methanol (9:1 v./v.).

The above sirup was dissolved in methanol (2 ml.) containing 1 drop of concentrated hydrochloric acid. The reaction mixture was allowed to stand at room temperature for 1 week at which time crystals began to deposit. After standing 2 more weeks in a refrigerator, the crystals were filtered and washed with cold methanol: yield 0.42 g. (22%). After recrystallization once from methanol and twice from ethanol–water, pure material was obtained: m.p. 78–80°, $[\alpha]^{22}D$ −68° (*c* 1.02, chloroform); X-ray powder diffraction data[24]: 11.83 m, 8.58 m, 7.40 w, 6.57 vw, 5.73 m, 5.07 s (1), 4.58 m, 4.43 s (3), 4.25 m, 4.00 m. 3.87 w, 3.76 w, 3.67 s (2), 3.53 w, 3.36 w, 3.18 w, and 3.05 m.

The substance gave a positive iodoform test. The n.m.r. spectrum (Varian A-60 n.m.r. spectrometer) of the above prod-

(31) A synthetic magnesium silicate that had been produced by the Westvaco Chemical Division of the Food Machinery and Chemical Corp., South Charleston, W. Va.; see M. L. Wolfrom, R. M. de Lederkremer, and L. E. Anderson, *Anal. Chem.*, **35**, 1357 (1963).

(32) No. 535, Johns-Manville Co., New York, N. Y.

(33) W. H. McNeely, W. W. Binkley, and M. L. Wolfrom, *J. Am. Chem. Soc.*, **67**, 527 (1945).

(34) E. Pacsu and F. V. Rich, *ibid.*, **55**, 3018 (1933); F. B. Cramer and E. Pacsu, *ibid.*, **59**, 1467 (1937).

(35) A product of the Rohm and Haas Co., Philadelphia, Pa.

uct, taken in chloroform solution at 60° and 60 M c.p.s. with a tetramethylsilane internal reference standard, included a singlet at τ 7.76 attributable to the terminal deoxy group. The n.m.r. spectra of other terminal deoxy sugars have been shown[36] to possess similar high field signals.

(36) M. L. Wolfrom, K. Matsuda, F. Komitsky, Jr., and T. E. Whiteley, *J. Org. Chem.*, **28**, 3551 (1963).

Anal. Calcd. for $C_{26}H_{22}O_7$: C, 69.95; H, 4.97; sapon. value, 6.72 ml. of 0.01 *N* NaOH/10 mg. Found: C, 69.79; H, 5.15; sapon. value, 6.81 ml. of 0.01 *N* NaOH/10 mg.

Acknowledgment.—The authors are grateful to M. P. Puterbaugh and J. D. Crum for preliminary work on this problem and to F. Komitsky, Jr., for obtaining and interpreting the n.m.r. spectrum.

The Anomeric Pair of Phenyl Sedoheptulosides (Phenyl α- and β-D-*altro*-Heptulopyranosides) and Their Marked Lability toward Acid and Alkali

EMMANUEL ZISSIS AND NELSON K. RICHTMYER

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Public Health Service, U. S. Department of Health, Education, and Welfare, Bethesda, Maryland 20014

Received September 29, 1964

The condensation of sedoheptulose hexaacetate and phenol, with zinc chloride as catalyst, has furnished us for the first time with an anomeric pair of phenyl heptuloside pentaacetates and, after deacetylation, the phenyl α- and β-sedoheptulosides (phenyl α- and β-D-*altro*-heptulopyranosides). These sedoheptulosides are hydrolyzed very readily by acids, even at room temperature. They are extremely sensitive toward alkalies: methanolic sodium methoxide converts then into methyl α-sedoheptuloside (which was synthesized independently for comparison) and dilute aqueous potassium hydroxide converts them very rapidly at room temperature into sedoheptulose and phenol. New data on the behavior of other phenyl heptulosides and hexosides toward alkali are reported; several new sedoheptulosan derivatives are described, together with n.m.r. data used in proving their structures; and some brief comments on the mechanism of the alkaline degradation of phenyl glycosides are added.

Earlier studies in this laboratory have been concerned with the biologically important sedoheptulose (D-*altro*-heptulose),[1] with the formation of nonreducing anhydro sugars by the action of acid on reducing sugars,[2] and with the degradation of phenyl glycosides to nonreducing anhydro sugars under the influence of alkalies.[3] This paper relates to all three of those topics.

Haskins, Hann, and Hudson[4] have described an isopropylidenesedoheptulosan. Through n.m.r. spectra we have established that the *O*-isopropylidene group is attached to C-4 and C-5, as expected; also that in the new monotosyl derivative of this compound the *O*-*p*-tolylsulfonyl group is attached at C-1, also as expected. The pertinent data are given in the Experimental section, together with descriptions of the ditosyl derivative of isopropylidenesedoheptulosan, of a high-melting modification of tetratosylsedoheptulosan, and of a crystalline sedoheptulosan 1,3,5-triacetate whose structure has been established through its n.m.r. spectrum.

Although the heptuloses and their derivatives, such as the penta- and hexaacetates, acetylated glycosyl halides, glycosides, etc., should be capable of existing in both α- and β-forms, no one to our knowledge has ever isolated previously anything but the α-anomer (α based on the optical rotation).[5] Although the *galacto*- and *talo*-heptuloses show mutarotation, it is not known what other species of sugar besides the α-anomer may exist in the equilibrium mixture.[6]

Starting with sedoheptulose hexaacetate,[1] phenol, and fused zinc chloride, by a modification of the Helferich and Schmitz-Hillebrecht synthesis,[7] we have succeeded in preparing phenyl α-sedoheptuloside pentaacetate in 84% yield and also, in very small yield, the phenyl β-sedoheptuloside pentaacetate, with rotations in chloroform of $[\alpha]^{20}D$ +60.7 and −94.6°, respectively. Careful deacetylation yielded the unique pair of crystalline phenyl α-sedoheptuloside (I) and phenyl β-sedoheptuloside with rotations in water of $[\alpha]^{20}D$ +121 and −145°, respectively. The pyranoside ring structures of these glycosides were established through the consumption of 2 moles of periodate and the liberation of 1 mole of acid/mole of compound.

The phenyl sedoheptulosides are extremely sensitive to acids and even a 5-min. contact at room temperature with the strongly acidic ion-exchange resin Amberlite IR-120(H^+) was sufficient to afford a detectable amount of sedoheptulose while longer contact converted the liberated sugar into sedoheptulosan.

The phenyl sedoheptulosides are labile also toward alkalies. For example, the deacetylation of phenyl α-sedoheptuloside pentaacetate with methanolic sodium methoxide at 20° led to the isolation not only of phenyl α-sedoheptuloside but also of methyl α-sedoheptuloside. The latter was made independently through the Koenigs–Knorr synthesis and its pyranoside structure proved by oxidation with periodate. When the deacetylation was carried out at 65° the product appeared to be exclusively the methyl α-

(1) For the preceding paper on sedoheptulose, see N. K. Richtmyer and J. W. Pratt, *J. Am. Chem. Soc.*, **78**, 4717 (1956).

(2) For the preceding paper in this series, see L. C. Stewart, E. Zissis, and N. K. Richtmyer, *J. Org. Chem.*, **28**, 1842 (1963).

(3) For an earlier paper in this series, see E. Zissis and N. K. Richtmyer, *ibid.*, **26**, 5244 (1961).

(4) W. T. Haskins, R. M. Hann, and C. S. Hudson, *J. Am. Chem. Soc.*, **74**, 2198 (1952).

(5) This refers, of course, to the 2-heptuloses only, for R. Schaffer [*J. Org. Chem.*, **29**, 1473 (1964)] has described a levorotatory, mutarotating β-D-*manno*-3-heptulose.

(6) See R. S. Tipson and H. S. Isbell [*J. Res. Natl. Bur. Std.*, **66A**, 31 (1962)] for a study of the infrared absorption spectra of such equilibrium mixtures.

(7) B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933); E. M. Montgomery, N. K. Richtmyer, and C. S. Hudson, *J. Am. Chem. Soc.*, **64**, 690 (1942).