[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Carbohydrate C-Nitroalcohols: the Acetylated Nitroölefins

BY JOHN C. SOWDEN AND HERMANN O. L. FISCHER

In 1928, Schmidt and Rutz[1] discovered that the α-acetoxy primary nitroparaffins, when treated in ether solution with potassium bicarbonate, readily lose one mole of acetic acid to give rise to the corresponding primary nitroölefins.

We have now applied this reaction to the acetates of several recently reported[2] carbohydrate C-nitroalcohols and, in each instance, have obtained the corresponding acetylated carbohydrate C-nitroölefins in crystalline condition and in good yield. These acetylated carbohydrate C-nitroölefins were found to crystallize with extreme ease even from solutions containing large amounts of other acetylated carbohydrate material.

From a consideration of the formulas it is apparent that while any one sugar, I (D-arabinose), will give *two* nitroalcohols, II and III, when condensed with nitromethane, these in turn will give only *one* acetylated nitroölefin, IV, since the formation of the double bond destroys the asymmetry of carbon atom two of the nitroalcohols. Because of this loss of isomerism and the previously mentioned ease of crystallization, the isolation of the single acetylated nitroölefin, from the condensation of a sugar with nitromethane, is more easily accomplished than the isolation of the two nitroalcohols formed initially. Consequently, by converting the initial sirupy reaction products to the acetylated nitroölefins, we have been able to demonstrate conclusively for the first time that the *unsubstituted* aldose sugars will undergo the aldehyde–nitroparaffin condensation reaction with nitromethane in the presence of alkali.

When suspensions of D-xylose, L-xylose, D-ribose or D-arabinose[3] in methanol and nitromethane were shaken with sodium methoxide in methanol, the sugars dissolved rapidly and precipitation of the sodium derivatives of the resulting nitroalcohols then occurred. The sodium was removed from these precipitates by means of ion exchange, yielding sirupy mixtures of the nitroalcohols. Acetylation, followed by treatment in benzene solution with sodium bicarbonate, then gave the corresponding crystalline, acetylated nitroölefins in yields of from 20 to 40%.

When D-glucose was treated similarly with nitromethane and alkali in methanol, the sugar dissolved gradually but only a slight precipitation of the sodium nitroalcohols then occurred. Consequently, the entire reaction mixture was subjected to the remaining steps of the nitroölefin synthesis. The acetylated nitroölefin was isolated in a yield of only 5%. This low yield may be due to the solubility of the sodium nitroalcohols in the reaction mixture employed. It is known that while alkali catalyzes the aldehyde–nitroparaffin condensation, the reaction also reverses readily to the components.[4] Thus, in the homogeneous system containing D-glucose, nitromethane and alkali, an equilibrium may be reached with only a small amount of nitroalcohol present.

When the acetylated nitroölefin, IV, from D-arabinose was reduced in absolute ethanol with hydrogen and palladium black, one mole of hydrogen was rapidly taken up by the double bond, whereas the ensuing reduction of the nitro group was much slower. By interrupting the reduction after the absorption of the first mole of hydrogen, it was possible to isolate the acetylated 1,2-didesoxynitroalcohol, V, in good yield. When this substance was deacetylated with excess aqueous alkali and the resulting solution of sodium nitroalcohol was added to moderately concentrated sulfuric acid,[5,2] D-*arabo*-2-desoxyhexose,[6] ("2-desoxyglucose"), VI, could be isolated from the resulting solution as its benzylphenylhydrazone in 70% yield. This method of producing 2-desoxy sugars should prove of value as a supplement to the previous methods based on the hydration of glycals[7] and on the reductive cleavage of thioethers.[8]

The acetylated nitroölefins described herein have been given systematic names as derivatives of the corresponding aliphatic olefins, using the appropriate prefix to signify their carbohydrate configuration. Thus, IV is named D-*arabo*-tetraacetoxy-1-nitrohexene-1.

Experimental

1-Nitro-1-desoxy-D-mannitol Pentaacetate.—Three grams of 1-nitro-1-desoxy-D-mannitol[2a] was acetylated on the steam-bath for one-half hour with 20 cc. of acetic anhydride containing one drop of sulfuric acid. After cooling, the solution was poured onto ice and water and there resulted 5.26 g. (88%) of the crystalline pentaacetate. After recrystallization from a mixture of ether and petroleum ether the product melted at 88–89° and showed $[\alpha]^{23}\text{D}$ +37.8° in absolute chloroform, *c* 7.3.

Anal. Calcd. for $C_{16}H_{23}O_{12}N$ (421.3): C, 45.6; H, 5.50. Found: C, 45.7; H, 5.53.

Neither pyridine nor sodium acetate were found to be satisfactory acetylation catalysts for the nitroalcohol, both yielding dark colored sirups.

D-*arabo*-Tetraacetoxy-1-nitrohexene-1 (IV). From the Nitroalcohol Pentaacetate.—One gram of 1-nitro-1-

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[1] Schmidt and Rutz, *Ber.*, **61**, 2142 (1928).

[2] (a) Sowden and Fischer, THIS JOURNAL, **66**, 1312 (1944); (b) **67**, 1713 (1945); (c) **68**, 1511 (1946).

[3] The condensation of D- and L-arabinose with nitromethane, leading to the free, crystalline nitroalcohols, will be described in a forthcoming publication.

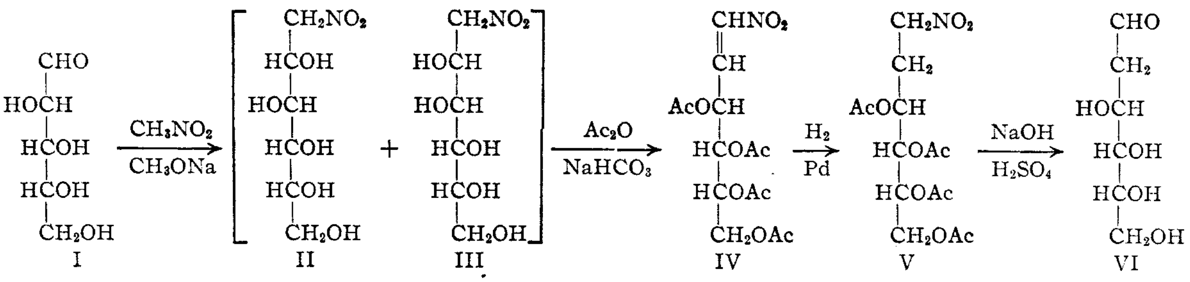
[4] Hass, *Ind. Eng. Chem.*, **35**, 1146 (1943); Hass and Riley, *Chem. Rev.*, **32**, 373 (1943).

[5] Nef, *Ann.*, **280**, 263 (1894).

[6] The name used here for this desoxy sugar follows the nomenclature proposed by Sowden, THIS JOURNAL, **69**, 1047 (1947).

[7] Bergmann, Schotte and Lechinsky, *Ber.*, **55**, 158 (1922).

[8] Jeanloz, Prins and Reichstein, *Helv. Chim. Acta*, **29**, 371 (1946).



desoxy-D-mannitol pentaacetate in 20 cc. of dry benzene was refluxed for two and one-half hours with 1 g. of sodium bicarbonate. The mixture was cooled, filtered and concentrated to dryness. The resulting crystalline residue on recrystallization from a mixture of ether and petroleum ether yielded 0.74 g. (86%) of the acetylated nitroölefin. The pure product melted at 115–116° and showed $[\alpha]^{23}D$ +32.4° in absolute chloroform, *c* 5.2.

Anal. Calcd. for $C_{14}H_{19}O_{10}N$ (361.3): C, 46.5; H, 5.30. Found: C, 46.4; H, 5.23.

From D-Arabinose.—A suspension of 10 g. of D-arabinose in 50 cc. of absolute methanol and 50 cc. of nitromethane was shaken with 75 cc. of methanol containing 2.1 g. of sodium. The sugar dissolved rapidly and an amorphous precipitate of the sodium nitroalcohols began to appear after a few minutes. After shaking for twenty hours, the mixture was diluted with 60 cc. of dry ether and the precipitate was filtered and washed successively with cold methanol, ether and petroleum ether. After drying over phosphorus pentoxide, the light colored powder weighed 15.3 g. and contained 9.05% of sodium. The powder was dissolved in 100 cc. of water and immediately passed through a column containing about 250 g. of moist Amberlite-IR-100-AG. Concentration of the effluent at reduced pressure and thorough drying over phosphorus pentoxide yielded 11 g. of light yellow sirup. Acetylation of this sirup on the steam-bath for one hour with 120 cc. of acetic anhydride containing one drop of sulfuric acid yielded 20 g. of the sirupy acetates. Treatment of this sirup in 250 cc. of benzene with 20 g. of sodium bicarbonate, as described above, followed by concentration of the resulting filtered solution then gave 9.7 g. (40%) of the acetylated nitroölefin. After recrystallization from absolute ethanol, the product melted at 115–116°.

L-*xylo*-Tetraacetoxy-1-nitrohexene-1. From 6-Nitro-6-desoxysorbitol.[2b]—Ten grams of the nitroalcohol was acetylated for twenty-four hours at room temperature with 50 cc. of acetic anhydride containing one drop of sulfuric acid. The acetylation mixture was then poured onto ice and water and the resulting sirup extracted with chloroform. Concentration of the extract yielded a colorless sirup which failed to crystallize. Treatment of this sirup in benzene solution with sodium bicarbonate, as described above, gave 14.9 g. (87%) of the crystalline acetylated nitroölefin, m. p. 115–116°. For analysis, the product was recrystallized from absolute ethanol. It then melted at 115–116° and showed $[\alpha]^{22}D$ −9.8° in absolute chloroform, *c* 5.4.

Anal. Calcd. for $C_{14}H_{19}O_{10}N$ (361.3): C, 46.5; H, 5.30; N, 3.88. Found: C, 46.5; H, 5.26; N, 3.69.

From L-Xylose.—When 7 g. of L-xylose[9] was treated exactly as described above for D-arabinose there was obtained 3.55 g. (21%) of the crystalline, acetylated nitroolefin. After recrystallization from absolute ethanol, the product melted at 115–116°.

D-*gluco*-Pentaacetoxy-1-nitroheptene-1

From 1-Nitro-1-desoxy-D-α-glucoheptitol.[2c]—Acetylation of 1 g. of 1-nitro-1-desoxy-D-α-glucoheptitol with acetic anhydride and sulfuric acid yielded 1.54 g. (75%) of the crude, crystalline hexaacetate, m. p. 72–75°. The hexaacetate contained a small amount of the acetylated nitroölefin, m. p. 106–107°, described below and purification by recrystallization was found to be very difficult. Accordingly, the crude material was converted directly to the acetylated nitroölefin by treatment in benzene solution with sodium bicarbonate. The product, obtained in 81% yield from the hexaacetate, was recrystallized from absolute ethanol and then melted at 106–107° and showed $[\alpha]^{20}D$ +18° in absolute chloroform, *c* 4.2.

Anal. Calcd. for $C_{17}H_{23}O_{12}N$ (433.4): C, 47.1; H, 5.35; N, 3.23. Found: C, 46.8; H, 5.12; N, 3.57.

From D-Glucose.—When 10 g. of powdered, anhydrous D-glucose was treated with nitromethane and alkali in methanol, as described above for D-arabinose, the sugar gradually dissolved but only a slight precipitation of sodium nitroalcohols occurred. This precipitate redissolved when the mixture was acidified with 6 cc. of glacial acetic acid. The resulting solution was concentrated to a sirup at reduced pressure, water was added, and sodium was removed, as before, by means of ion-exchange. Acetylation of the sirup obtained by concentration of the aqueous solution then gave about 25 g. of sirupy acetates. Treatment in benzene solution with sodium bicarbonate then gave a nearly colorless sirup. Fractional crystallization of this sirup from ether gave 1.2 g. (5%) of the acetylated nitroölefin, m. p. 106–107°. Further amounts of crystalline material were obtained by the gradual addition of petroleum ether to the ether solution, but all showed negative tests for the presence of the nitro group when treated with the Greiss–Ilosvay reagent.[10]

D-*xylo*-Tetraacetoxy-1-nitrohexene-1.—Ten grams of D-xylose, when treated as described above for D-arabinose, yielded 8.45 g. (35%) of the corresponding acetylated nitroölefin. After recrystallization from absolute ethanol, the product melted at 115–116° and showed $[\alpha]^{25}D$ +10.2° in absolute chloroform.

Anal. Calcd. for $C_{14}H_{19}O_{10}N$ (361.3): C, 46.5; H, 5.30; N, 3.88. Found: C, 46.5; H, 5.30; N, 3.80.

D-*ribo*-Tetraacetoxy-1-nitrohexene-1.—Ten grams of D-ribose, when treated as described above for D-arabinose, yielded 5.15 g. (21%) of the corresponding acetylated nitroölefin. Recrystallized from absolute ethanol, the product melted at 86–87° and showed $[\alpha]^{28}D$ +17° in absolute chloroform, *c* 5.

Anal. Calcd. for $C_{14}H_{19}O_{10}N$ (361.3): C, 46.5; H, 5.30; N, 3.88. Found: C, 46.5; H, 5.28; N, 3.87.

Unlike the acetylated nitroölefins described above, which were all very pale yellow in color, the product from D-ribose was colorless.

1-Nitro-1,2-didesoxy-D-*arabo*-hexitol Tetraacetate (V).—Two grams of the acetylated nitroölefin, IV, in 20 cc. of absolute ethanol was shaken with hydrogen at room temperature and pressure in the presence of 0.2 g. of palladium black.[11] One mole of hydrogen was absorbed in twelve minutes and the rate of reduction then dropped sharply. Concentration and cooling of the filtered solution yielded 1.58 g. (79%) of the acetylated didesoxynitroalcohol, m. p. 81–86°. Recrystallization from absolute ether gave the pure product, m. p. 91–92° and $[\alpha]^{26}D$ +29.4° in absolute chloroform, *c* 2.5.

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(9) Prepared from 2,4-benzylidene sorbitol by the method of v. Vargha, *Ber.*, **68**, 18 (1935).

(10) Bose, *Analyst*, **56**, 504 (1931).

(11) Tausz and Putnoky, *Ber.*, **52**, 1573 (1919).

Anal. Calcd. for $C_{14}H_{21}O_{10}N$ (363.3): C, 46.3; H, 5.83. Found: C, 46.8; H, 5.88.

D-*arabo*-2-**Desoxyhexose** ("2-Desoxyglucose").[6]—One gram of the crude acetylated didesoxynitroalcohol, m. p. 84–86°, described above was dissolved at room temperature in 15 cc. of 1 *N* sodium hydroxide solution and allowed to stand for one hour. The solution was then added to a stirred mixture of 3 cc. of water and 2.1 cc. of sulfuric acid at room temperature. The solution was diluted and neutralized by stirring with barium carbonate. After centrifuging and filtering, the solution was treated with a few drops of acetic acid and was concentrated to dryness at reduced pressure. Treatment of the resulting sirup with 0.6 cc. of benzylphenylhydrazine in 10 cc. of 75% ethanol then yielded 0.68 g. (71%) of D-*arabo*-2-desoxyhexose benzylphenylhydrazone.[12] After recrystallization from ethyl acetate, the hydrazone melted at 158–159° and showed $[\alpha]^{25}D$ +7.6° in methanol, *c* 1.2.

Cleavage of the hydrazone with benzaldehyde according to the directions of Bergmann, Schotte and Lechinsky[7] gave the crystalline D-*arabo*-2-desoxyhexose, $[\alpha]^{23}D$ +46.6° (one hour) in water, *c* 2.

The desoxy sugar apparently was obtained as a mixture predominating in the α-form since its initial melting point of 128–129° was lowered to 123–125° on recrystallization and a slight downward mutarotation was evident in its aqueous solution: $[\alpha]^{23-25}D$ +53.8°, ten minutes; +50.3°, twenty minutes; +48°, thirty minutes; +46.6°, one hour (constant).

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Summary

Treatment of the acetylated carbohydrate C-nitroalcohols in benzene solution with sodium bicarbonate produces the corresponding acetylated nitroölefins in good yield.

Several unsubstituted sugars have been shown to condense with nitromethane in the presence of alkali. The products were isolated in crystalline form by conversion to the corresponding acetylated nitroölefins.

The acetylated nitroölefin arising from D-arabinose and nitromethane, D-*arabo*-tetraacetoxy-1-nitrohexene-1, was reduced catalytically to the acetylated 1,2-didesoxynitroalcohol. Deacetylation of this substance followed by treatment of the sodium nitroalcohol with sulfuric acid gave rise to D-*arabo*-2-desoxyhexose, ("2-desoxyglucose") in good yield. This new method of synthesis for 2-desoxy aldoses should prove valuable as a supplement to the previously known procedures for preparing this rare type of sugar.

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[12] Bergmann and Schotte, *Ber.*, **54**, 440 (1921).

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The Action of Copper Sulfate on the Phenylosazones of the Sugars. IV. The Phenylosotriazoles of Some Heptoses

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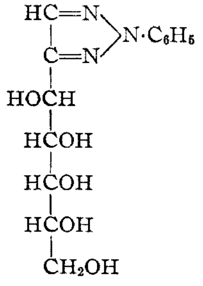
In previous articles[1] we have described the phenylosotriazoles of the pentoses and hexoses; the present article deals with the preparation of the phenylosotriazoles from four heptoses, namely, sedoheptulose (D-altroheptulose), D-mannoheptulose, D-gluco-D-*gulo*-heptose and D-gala-L-*gluco*-heptose and some of their acetyl and benzoyl derivatives. All of these heptose phenylosotriazoles crystallized readily and exhibited relatively low aqueous solubilities, especially D-*gala*-heptose phenylosotriazole, which has so low a solubility in water that it is comparable in this respect with D-*arabo*-hexose[2] phenylosotriazole. The new phenylosotriazoles, like the previous ones, are colorless very stable substances that possess sharp melting points and freedom from mutarotation, properties which make them valuable reference substances for establishing the identity of the respective phenylosazones.

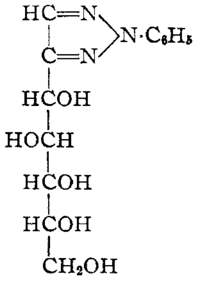
Oxidation of the heptose phenylosotriazoles by sodium metaperiodate produced in each instance a high yield (92–96%) of 2-phenyl-4-formyl-2,1,3-triazole (V) together with the appropriate amounts of formic acid and formaldehyde; these results show that the 4-substituted 2-phenyl-2,1,3-triazole structure that has been shown to be present in the pentose and hexose phenylosotriazoles also occurs in the heptose phenylosotriazoles.

The structures of the new phenylosotriazoles that have been proved by the oxidation of the substances with periodate are shown in the formulas.



I

Sedoheptulose phenylosotriazole (D-*altro*-Heptose phenylosotriazole)



II

D-*gluco*-Heptose phenylosotriazole

[1] Hann and Hudson, THIS JOURNAL, **66** 735 (1944); (II) Haskins, Hann and Hudson, *ibid.*, **67**, 939 (1945); (III) Haskins, Hann and Hudson, *ibid.*, **68**, 1766 (1946).

[2] There is here used the systematic nomenclature recently proposed by Sowden, *ibid.*, **69**, 1047 (1947).