tracted with 70 ml. of ether. After drying the combined organic solution over anhydrous magnesium sulfate, the ether was removed *in vacuo* and the residue distilled at 3 mm. pressure until the pot temperature reached 180°. Upon cooling, the residue solidified to yield the crude diethyl ester of cyclohexanone-2,6-dipropionic acid. This ester was recrystallized by dissolving in 50% ethanol, warming to *ca.* 50° and adding water until cloudy. After two recrystallizations, the diethyl cyclohexanone-2,6-dipropionate had m.p. 63–64°; yield, 145 g. (60%).

C.—The cyclohexanone-2,6-dipropionic acid (**8**) was prepared from the diethyl ester by refluxing with excess concentrated hydrochloric acid for 2 hr. Work-up in the usual manner gave the product acid (**8**) from water, m.p. 144–145° (lit.[8] m.p. 145°).

Wolff–Kishner Reduction of Cyclohexanone-2,6-dipropionic Acid.—In a 500-ml. three-necked flask equipped with a mechanical stirrer, thermometer, and reflux condenser was placed 21 g. (0.37 mole) of potassium hydroxide and 150 ml. of diethylene glycol. After stirring, with gentle heating, for 1 hr. the potassium hydroxide had dissolved. To the stirred warm solution there was added 18 g. (0.075 mole) of the keto diacid (**8**) and 5 ml. of 97% hydrazine. After heating for 2 hr. at 100–110° with stirring, the condenser was removed and heating was continued until the temperature had reached 180–190°. After heating for an additional 4 hr. the evolution of nitrogen had ceased and the reaction mixture was poured into 250 ml. of water. After acidification with hydrochloric acid the mixture was extracted with ether. The ethereal solution was extracted with saturated sodium bicarbonate solution, the bicarbonate extracts decolorized with charcoal, acidified with concentrated hydrochloric acid, and extracted with ether. After drying over anhydrous sodium sulfate the ether was removed *in vacuo* to yield a viscous oil which solidified to a white solid after standing overnight in the refrigerator. The yield of the mixed *cis*- and *trans*-dipropionic acids was *ca.* 12 g. (71%). Approximately 4 g. of the crude mixed acid material was added to water and heated to 50° at which temperature the acid began to oil and additional water was added until the total volume was 400 ml. The clear aqueous phase was separated from the residual oil while still hot. After cooling, the aqueous solution deposited *ca.* 1 g. of the crude *trans* acid (**6**) which, after four recrystallizations, had m.p. 94–95°. A mixture melting point of this material with the *trans*-dipropionic acid (**6**) obtained from the Arndt–Eistert reaction was undepressed and their infrared spectra were identical except for band intensities. Upon further standing, the aqueous solution deposited in very low yield, the *cis*-dipropionic acid (**5**) which, after three recrystallizations, had m.p. 97–98°. This acid had an infrared spectrum identical with the *cis*-dipropionic acid (**5**) obtained from the Arndt–Eistert reaction and a mixture melting point of the two acids was undepressed. A mixture melting point with the *trans*-dipropionic acid (**6**) was 77–81°.

The Addition of Amines to Carbohydrate α-Nitroolefins

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The addition of some aliphatic and aromatic amines to D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene in anhydrous methanol and some reactions of the resulting products are described. The addition of aniline yields two crystalline isomers both of which are converted to 3,4,5,6-tetra-*O*-acetyl-2-(*N*-phenylimino)-D-*arabino*-hexulosonitrile (VII) by treatment with acetic anhydride in pyridine.

The preparation of carbohydrate α-nitroolefins is well known.[2] Recently, O'Neill[3] and Sowden[4,5] have reported the addition of ammonia and methanol to D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene (I). Sowden obtained an epimeric pair of 2-acetamido-1,2-dideoxy-1-nitro-D-hexitols which were converted to D-mannosamine and D-glucosamine hydrochlorides *via* the Nef reaction.[6] The addition of amines to I, therefore, seemed a likely route to some interesting N-substituted amino derivatives of D-glucose and D-mannose.

Addition of one equivalent of *p*-toluidine, benzylamine, cycloheptylamine, cyclohexylamine, ethanolamine, and isopropylamine to a solution of I in anhydrous methanol gave, in each case, only one of the two possible isomers in crystalline form. The yields and some physical constants of the adducts are reported in Table I.

The addition of aniline yielded both isomers in crystalline form. The higher melting 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-2-(*N*-phenylamino)-D-hexitol (V) was obtained in 28% yield, and the lower melting isomer in 44% yield. Sowden and Oftedahl[4] found that the addition of ammonia to nitroolefin gave *O*-deacetylated-*N*-acetylated derivatives. However, all the amine–nitroolefin adducts isolated in this study were fully *O*-acetylated. De-*O*-acetylation probably did not occur because only one equivalent of the amines was employed. Probably O → N acetyl migration did not take place because of the blocking effects of the alkyl and aryl groups attached to the amino groups. No such migration was observed in the case of the aromatic amines during reaction times (overnight) comparable to those used in the ammonia addition. The aliphatic amine adducts were isolated after 30 min. as they decomposed overnight giving brown solutions.

The absence of a band at 1600 cm.$^{-1}$ in the infrared spectra of the aniline and cyclohexylamine adducts proved that they are true addition products. The band was present in the spectrum of the nitroolefin and is characteristic of double bonds.[7] As mentioned before, the aliphatic amine adducts are unstable at room temperature, but the solids may be kept for several weeks at −10° without decomposition. The crystalline aromatic adducts are stable at room temperature. An attempt to stabilize the cycloheptylamine adduct by acetylation to the amide with acetic anhydride was unsuccessful, and nitroolefin was isolated in 80% yield. Acetic anhydride was without action on the higher-melting aniline adduct. Treatment of this adduct with acetic anhydride in pyridine gave a totally unexpected product which will be discussed later.

Hydrogenation of the amine–nitroolefin adducts in

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[1] Deceased April 14, 1963.

[2] J. C. Sowden and H. O. L. Fisher, *J. Am. Chem. Soc.*, **69**, 1048 (1947).

[3] A. N. O'Neill, *Can. J. Chem.*, **37**, 1747(1959).

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[6] J. U. Nef, *Ann. Chem.*, **280**, 263 (1894).

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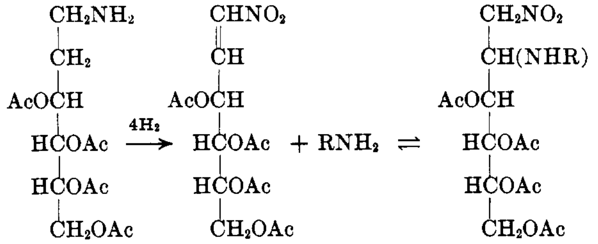
TABLE I

YIELDS, PHYSICAL CONSTANTS, AND ANALYSES OF AMINE–NITROOLEFIN ADDUCTS

Amine	Yield, % of crude product	M.p., °C.	$[\alpha]^{25}_D$ (CHCl$_3$)	Analytical data, % Calcd. C	H	N	Found C	H	N
p-Toluidine	48	104–105	+72.4 (*c* 7.8)	53.7	6.24	5.98	53.5	5.98	6.29
Benzylamine	75	94–95 dec.	+36.3 (*c* 7.2)	53.8	6.02	5.98	54.2	6.36	5.70
Cycloheptylamine	60	98–100 dec.	+38.6 (*c* 8.4)	53.1	7.22	5.91	53.9	7.13	5.88
Cyclohexylamine	63	104–105 dec.	+41.3 (*c* 7.8)	52.7	7.02	6.09	52.5	6.96	6.11
Ethanolamine	44	88–89 dec.	+44.7 (*c* 6.0)	45.5	6.20	6.63	45.6	6.30	6.59
IsoPropylamine	71	111–112	+47.3 (*c* 4.4)	48.6	6.66	6.66	48.2	6.50	6.86

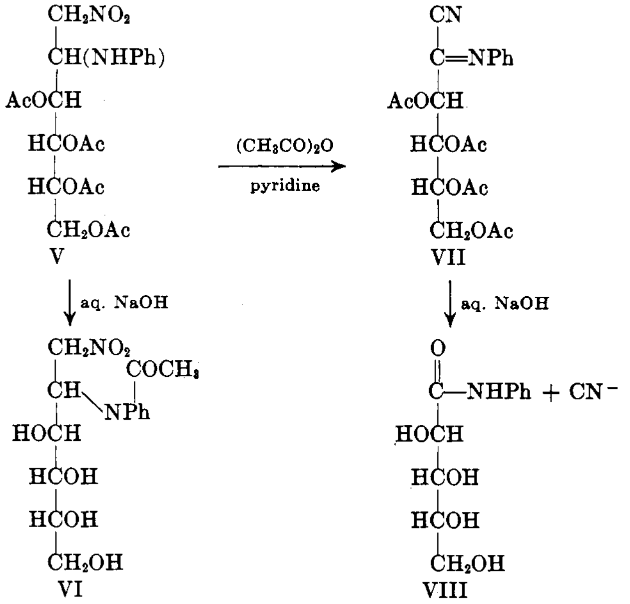
the presence of Adam's platinum oxide catalyst required four moles of hydrogen, whereas simple reduction of the nitro group should take only three moles. The results are explained if it is assumed that the adducts are in equilibrium with amine and nitroolefin, and the latter is reduced to a 1-amino-2-deoxy derivative[8] (IV). Chromatograms of the reduction products of the aniline adduct and of the nitroolefin were identical in agreement with this explanation.



IV I II III

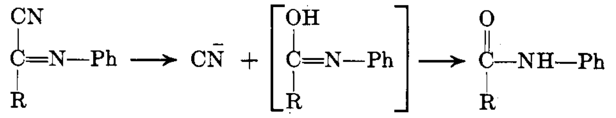
It was not possible to prepare the N-substituted hexosamines by application of the Nef reaction to III; the higher-melting aniline adduct gave only starting material. The possibility of deacetylating before applying the Nef reaction was investigated. Treatment of the same adduct with dry ammonia in methanol was not satisfactory, because the only crystalline product isolated was a small amount of 2-acetamido-1,2-dideoxy-1-nitro-D-mannitol.[4] The action of dilute aqueous sodium hydroxide solution did, however, give a low yield (23%) of 1,2-dideoxy-1-nitro-2(*N*-phenylacetamido)hexitol (VI). A Nef reaction was carried out on this product, but paper chromatography indicated a complex mixture of products. An attempt was made to improve the yield of VI by preparing the fully acetylated adduct before deacetylating. The higher melting aniline adduct was treated with acetic anhydride in pyridine, which is the usual method for preparing *N*-acetyl compounds. A white crystalline compound was isolated in 48% yield, but it was not the expected *N*-acetate. Evidence indicates that the compound is 3,4,5,6-tetra-*O*-acetyl-2-(*N*-phenylimino)-D-*arabino*-hexulosononitrile (VII). (See col. 2.)

Elemental analysis of the crystalline compound gave results in agreement with the empirical formula ($C_{20}H_{22}O_8N_2$) required by this structure. A strong absorption in the ultraviolet (λ_{max} 235, 340 mμ) indicated that the phenyl group was still present. When the lower-melting aniline adduct was treated under identical conditions the same product was obtained, although in much lower yield (11%). The destruction of asymmetry on C-2 agrees with the formation of an imino group. The infrared spectrum of the compound also indicated the presence of an imino group. The spectrum has a strong band at 1660 cm.$^{-1}$. Compounds which are known to contain this group have an absorption in this region.[9] The infrared spectrum also confirms the other structural features of the compound. There are no –NH or nitro bands. The cyano group would be expected to give a strong absorption in the 2220–2260-cm.$^{-1}$ region,[9] but there is only a very weak band at 2260 cm.$^{-1}$ However, cyano compounds which also contain oxygen often have reduced nitrile absorptions. Kuhn[10] found that a similar compound, N-phenyl-D-glucosamic acid nitrile, has only a weak cyanide band at 2230 cm.$^{-1}$.



V VII VI VIII

Deacetylation of VII with ammonia or sodium methoxide in methanol gave only dark sirups. Treatment of the compound with dilute sodium hydroxide solution gave a white crystalline compound in 29.2% yield. This compound was identified as the anilide of D-arabinonic acid by comparison with authentic material prepared from arabinonic-γ-lactone and aniline.[11] The reaction mixture gave a positive picric acid test[12] indicating that cyanide ions were liberated during the deacetylation. The amount of cyanide liberated was estimated by precipitation with silver nitrate. A 33.8% yield of silver cyanide gave evidence that equimolecular amounts of the anilide and cyanide are pro-



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[8] J. C. Sowden, *Advan. Carbohydrate Chem.*, **6**, 315 (1951).

[9] L. J. Bellamy, ref. 7, p. 263.

[10] R. Kuhn and W. Kirschenlohr, *Ann. Chem.*, **600**, 126 (1956).

[11] W. J. van Marle, *Rec. trav. chim.*, **39**, 549 (1920).

[12] G. Gutzeit, *Helv. Chim. Acta*, **12**, 713 (1929).

duced. This reaction resembles the hydrolysis of acid halides by base.

The imino-nitrile is formed from the aniline adducts under conditions which would normally give the *N*-acetyl derivatives of the adducts. However, these conditions are also dehydrating, and acetic anhydride in pyridine is commonly used for the dehydration of oximes to cyanides. The over-all reaction in the conversion of adduct to imino-nitrile is essentially one in which two moles of water are lost from each mole of adduct.

Experimental

All melting points are uncorrected. Chromatography was carried out in the upper phase of 1-butanol–ethanol–water (4:1:5, v./v.)[13] using Whatman No. 1 paper. Alkaline silver nitrate[14] and ninhydrin sprays[15] were used to detect the various compounds. Infrared spectra were measured on Nujol mull samples with a Perkin-Elmer Model 137 Infracord recording spectrophotometer. Ultraviolet spectra were obtained on the compounds in ethanol solution with a Cary 14 recording spectrophotometer.

General Procedure for the Preparation of Amine–Nitroolefin Adducts.—The nitroolefin (I) was suspended in methanol (4–5 ml. of methanol per gram of olefin), and one equivalent of amine in a small volume of methanol was added slowly. Crystallization occurred when the solvent was evaporated, except in the case of ethanolamine. In this case crystallization was induced by cooling the solution to −20°. The crystalline adducts were collected by covering the solid with warm petroleum ether (b.p. 63–69°) and adding warm ethanol to dissolve the mixture. The cooled solution deposited crystalline needles which were collected by filtration. Yields, physical constants, and elemental analyses of the adducts are shown in Table I.

Aniline–Nitroolefin Adducts (V).—A solution of 5.15 g. of redistilled aniline in a small volume of methanol was added to a suspension of 20 g. of nitroolefin (I) in 80 ml. of methanol. The solid dissolved on standing and after 0.5 hr. at room temperature the solvent was evaporated to give a pale green sirup. The sirup was dissolved in the minimum amount of hot ethanol. The solution was seeded and allowed to stand at 5°. The crystals were filtered off to give 16 g. (64%) of crude product. From the filtrate another 9 g. (34%) of material having a wide melting range was obtained. Fractional crystallization of the combined solids from ethanol gave two pure isomers. The higher melting isomer was obtained in 28% yield, m.p. 123–124° and $[\alpha]^{25}\mathrm{D}$ +10.5° (*c* 12, chloroform).

Anal. Calcd. for $C_{20}H_{26}O_{10}N_2$: C, 52.9; H, 5.76; N, 6.17. Found: C, 52.6; H, 5.74; N, 6.17.

The other isomer was obtained in 44% yield, m.p. 104–105° and $[\alpha]^{25}\mathrm{D}$ +71.3° (*c* 3.8, chloroform).

Anal. Found: C, 52.91; H, 5.77; N, 6.48.

1,2-Dideoxy-1-nitro-2-(*N*-phenylacetamido)-D-hexitol (VI).—A solution of 1.32 g. of sodium hydroxide in 50 ml. of water was cooled to 0° and added slowly to a solution of 3.0 g. of the high-melting aniline adduct. The reaction mixture was stirred and kept at 0° during the addition. The resulting solution was freed of sodium ions by passing over a column of Dowex (H^+) resin. The column was washed successively with one volume of 50% ethanol and one volume of 95% ethanol. The combined eluates were evaporated to a sirup which crystallized on standing. The crystals were filtered off with the aid of a little ethanol to yield 0.50 g. of crude product, m.p. 167–168°. Recrystallization from 1-butanol gave 0.28 g. (13%) of pure 1,2-dideoxy-1-nitro-2-(*N*-phenylacetamido)-D-hexitol, m.p. 173–174° dec. and $[\alpha]^{25}\mathrm{D}$ −54.2° (*c* 1.6, pyridine).

Anal. Calcd. for $C_{14}H_{20}O_7N_2$: C, 51.30; H, 6.13; N, 8.54. Found: C, 51.16; H, 6.31; N, 8.34.

3,4,5,6-Tetra-*O*-acetyl-2-(*N*-phenylimino)-D-*arabino*-hexulosonitrile (VII). A. From V (High-Melting Isomer).—To a solution of 5.0 g. of high-melting isomer V in 50 ml. of dry pyridine was added 7.5 ml. of acetic anhydride. The solution was allowed to stand at room temperature overnight and then poured into 200 ml. of ice and water. After a few hours at 0° the resulting solid was filtered off and washed with water and then ethanol to give 2.4 g. of crude product. Recrystallization from ethanol yielded 2.22 g. (48.5%) of pure VII, m.p. 117–118° and $[\alpha]^{25}\mathrm{D}$ +16.5° (*c* 3.3, chloroform).

Anal. Calcd. for $C_{20}H_{22}O_8N_2$: C, 57.40; H, 5.30; N, 6.69. Found: C, 57.4; H, 5.42; N, 6.81.

B. From V (Low-Melting Isomer).—To a solution of 0.5 g. of the isomer in 5 ml. of dry pyridine was added 0.75 ml. of acetic anhydride. After 2 hr. at room temperature the mixture was poured into 50 ml. of ice and water. The oil, which formed, only partially crystallized after standing for 3 hr. at 0°. The mixture was extracted with three 20-ml. portions of chloroform and the extract washed successively with *N* sulfuric acid, saturated sodium bicarbonate solution, and water. The chloroform layer was dried over calcium chloride and evaporated to a sirup. The sirup was dissolved in hot ethanol. Cooling and filtration gave 0.05 g. (11%) of crude product, m.p. 116–117°. Recrystallization from ethanol raised the melting point to 117–118°. The mixture melting point with the product obtained from the higher melting isomer was not depressed.

Reaction of VII with Sodium Hydroxide Solution.—Three grams of VII was dissolved in 100 ml. of acetone and the solution cooled to 0°. The solution was stirred, and a cold solution of 1.2 g. of sodium hydroxide in 100 ml. of water was added slowly. After 15 min. sodium ions were removed by passing the solution over a column of Dowex 50 (H^+) resin. The column was washed with an acetone-water mixture (1:1). Evaporation of the combined eluates gave a crystalline solid. The crystals were slurried with ethanol and filtered off to give 0.50 g. (29.2%) of crude product, m.p. 195–197°. Recrystallization from 80% ethanol yielded 0.16 g. of pure anilide, m.p. 201–202° and $[\alpha]^{25}\mathrm{D}$ −84.2° (*c* 1.0, pyridine). The compound was compared with authentic D-arabinonic acid anilide prepared by the method of Marle,[12] m.p. 201–202° and $[\alpha]^{25}\mathrm{D}$ −84.4° (*c* 1.1, pyridine).

An accurately weighed sample of VII (0.203 g.) was treated with sodium hydroxide solution as described before. The eluate from the deionization was run directly into a solution of 0.08 g. of silver nitrate in 100 ml. of water. The precipitated silver cyanide weighed 0.0221 g. (33.8%).

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