TABLE I

Base	Adduct	Calcd., N	Calcd., Anion	Anal., N	Anal., Anion	M.P.[a]
2-Aminopyridine	$C_5H_6N_2 \cdot HNO_3$	26.74	39.46	26.73	39.76	133–139
4-Aminopyridine	$C_5H_6N_2 \cdot HNO_3$	26.74	39.46	26.46	38.82	172–173
3-Aminopyridine	$C_5H_6N_2 \cdot HNO_3$	26.74	39.46	26.83	39.54	128–132
2-Amino-5-methylpyridine	$C_6H_8N_2 \cdot HNO_3$	24.55	36.29	25.25	36.06	139–140
2-Amino-6-methylpyridine	$C_6H_8N_2 \cdot HNO_3$	24.55	36.29	24.11	35.70	168–170[b]
2-Amino-4,6-dimethylpyridine	$C_7H_{10}N_2 \cdot HNO_3$	22.69	33.48	22.45	33.80	177–178
2-Aminopyridine	$C_5H_6N_2 \cdot HClO_4$	14.40		14.02		185–187
4-Aminopyridine	$C_5H_6N_2 \cdot HClO_4$	14.40		13.79		272–274
3-Aminopyridine	$C_5H_6N_2 \cdot HClO_4$	14.40		14.05		190–224
2-Amino-5-methylpyridine	$C_6H_8N_2 \cdot HClO_4$	13.43		13.51		99–103
2-Amino-6-methylpyridine	$C_6H_8N_2 \cdot HClO_4$	13.43		13.57		100–102
2-Amino-4,6-dimethylpyridine	$C_7H_{10}N_2 \cdot HClO_4$	12.58		12.70		186–187

[a] All melting points are uncorrected. [b] A m.p. of 168° was reported by Seide (ref. 4).

Experimental

Perchloric Acid Salts.—The perchloric acid addition salts were made by adding slowly 20 ml. of 70–72% perchloric acid to a solution of 4–5 g. of base in 20 ml. of alcohol. All reagents and the reaction vessel were kept cold in an ice bath. After allowing the mixture to stand in the ice bath for 1 hr., the salts were isolated by filtration and partially dried. They were recrystallized from glacial acetic acid or ethanol.[5]

Nitric Acid Salts.—The nitric acid salts were prepared by slowly adding 25 ml. of ice cold concd. nitric acid to 5 g. of cold anhydrous base. Excess nitric acid was removed by placing the sample in a wide flat dish and passing a gentle current of air over the sample overnight. If the salt were still moist, it was placed in a vacuum desiccator and the latter evacuated with a water pump intermittently. The salt was then recrystallized from commercial anhydrous ethyl alcohol. Occasionally, in order to avoid extensive decomposition, the nitric acid–base mixture was frozen and evaporated down to a thick slurry. An alternative method, especially when the pure monosalts were desired, was to add nitric acid to an ether solution of the free base.

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[5] Part of this method was suggested to us in a private communication from T. B. Joyner of the U. S. Naval Ordnance Test Station, China Lake, Calif.

D-Mannoheptulose 1-(N^1-Benzyl-N^1-phenyl)-2-(N^1-phenyl)osazone

LAWRENCE M. WHITE AND GERALDINE E. SECOR

Western Regional Research Laboratory, Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture, Albany 10, Calif.

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D-Mannoheptulose 1-(N^1-benzyl-N^1-phenyl)-2-(N^1-phenyl)osazone was synthesized in connection with a study on the identification of microgram amounts of D-mannoheptulose.[1] A detailed description of the preparation and structure of this new, characteristic, crystalline osazone is given here because very few hydrazine derivatives of this heptulose are known. The osazone is an acetic acid solvate when synthesized at room temperature, but washing and drying the crude product removes the acetic acid. Recrystallization from glacial acetic acid yields a solvate, but recrystallization from ethyl acetate or absolute ethanol yields the unsolvated osazone.

The osazone was recovered unaltered after attempted formazan formation in alkaline ethanol. The failure to react under these conditions establishes the point of attachment of the primary and secondary hydrazine groups to C-2 and C-1 of the sugar, respectively.[2] The assigned structure is in accord with the conclusions of Henseke and co-workers, who studied some pentose and hexose mixed osazones.[3,4]

Experimental

D-Mannoheptulose 1-(N^1-Benzyl-N^1-phenyl)-2-(N^1-phenyl)osazone (I).—A solution of 210 mg. (1 mmole) of D-mannoheptulose in 0.4 ml. of water was added with stirring to a mixture of 939 mg. (4 mmoles) of recrystallized 1-benzyl-1-phenylhydrazine hydrochloride, 289 mg. (2 mmoles) of ground recrystallized phenylhydrazine hydrochloride, 492 mg. (6 mmoles) of anhydrous sodium acetate, and 5 ml. of glacial acetic acid in a glass-stoppered weighing bottle.[5] After several hours, 2 ml. of glacial acetic acid was added with stirring. The product was removed by filtration after 20 hr.; washed with glacial acetic acid, ether, water, and ether; and air-dried. The yield was 289 mg. (60%). The dried, crude product contained no volatile acid. Recrystallization of 280 mg. of the crude sample from boiling absolute ethanol (7 mg. of sample per ml. of ethanol) gave 242 mg. (87% yield, two crops) of bright yellow, fine needles or filaments. The m.p. was 191–193° dec. (corrected) after two recrystallizations.

Anal. Calcd. for $C_{26}H_{30}N_4O_5$: C, 65.25; H, 6.39; N, 11.71. Found: C, 65.3; H, 6.35; N, 11.8.

D-Mannoheptulose 1-(N^1-Benzyl-N^1-phenyl)-2-(N^1-phenyl)osazone Acetic Acid Solvate.—Recrystallized I was dissolved in hot glacial acetic acid (8 mg. of I per ml. of acid), and the solution was allowed to cool slowly. The fine yellow needles that formed were removed by filtration and washed with cold glacial acetic acid without allowing them to become dry. A thin layer of wet crystals on platinum foil was exposed to air and their weight was recorded at timed intervals. When the weight loss per unit of time decreased

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[1] L. M. White and G. E. Secor, *Anal. Chem.*, **33**, 1287 (1961).

[2] L. Mester, *J. Am. Chem. Soc.*, **77**, 4301 (1955).

[3] G. Henseke and H.-J. Binte, *Chimia*, **12**, 103 (1958).

[4] G. Henseke and W. Liebenow, *Ber.*, **87**, 1068 (1954).

[5] The same mixed osazone was obtained when total hydrazine ranged from 3 moles to 9 moles per mole of sugar and with 1 or 2 moles of 1-benzyl-1-phenylhydrazine hydrochloride per mole of phenylhydrazine hydrochloride.

abruptly, samples were taken for the determination of volatile acid.

Anal. Calcd. for $C_{26}H_{30}N_4O_5 \cdot 2^1/_2\ HC_2H_3O_2$: weight loss, 23.88; volatile acid, 23.88. Found: weight loss at 100° (in vacuo), 23.4; volatile acid as acetic, 23.5.

The direction of vibration of the slower component was lengthwise of the crystal in crude I before washing and drying and also in I recrystallized from glacial acetic acid, but the direction of vibration of the slower component was crosswise of the crystal in I recrystallized from ethanol.

Attempted Formazan Formation.—Recrystallized I (from absolute ethanol) was recovered unchanged after attempted formazan formation,[2] as evidenced by comparison of elemental analyses, melting points, and X-ray powder patterns of the original and recovered osazones. Under the same conditions, sugar osazones having a phenylhydrazine group on C-1 underwent a marked color change to produce typical sugar formazans.

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Polyfunctional Aliphatic Compounds. I. The Preparation of 3-Hydroxyglutaronitriles

FRANCIS JOHNSON, J P. PANELLA, AND A. A. CARLSON

The Dow Chemical Co., Eastern Research Laboratory, Framingham, Mass.

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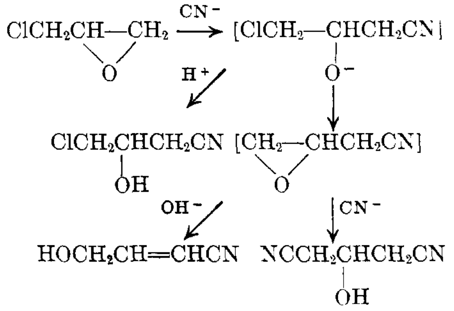
The necessity of obtaining large quantities of the base-sensitive 3-hydroxyglutaronitrile and related three-substituted homologs for cyclization studies has prompted us to re-examine the methods of preparation for these compounds. Previous syntheses of 3-hydroxyglutaronitrile itself have relied on the reaction of aqueous potassium cyanide with 1,3-dichloropropanol-2[1–4] and on the action of a concentrated solution of potassium cyanide on 4-chloro-3-hydroxybutyronitrile.[5,6] Of these only the latter appeared to merit any attention as a preparative method, but even here the reported yields were low (35–40%). This reaction proved to be highly exothermic and required careful control but when the operating temperature was kept around 40°, yields as high as 51.5% were obtained. Nevertheless on a large scale, the difficulties of manipulation and extraction prohibited the use of this method.

We now have found that the required 3-hydroxyglutaronitriles can be prepared by allowing an epichlorohydrin to react with an aqueous solution of potassium cyanide buffered by magnesium sulfate to a pH of approximately 9.5. The best yields were obtained by carrying out these mildly exothermic reactions at 10 to 11° followed by ethyl acetate extraction.

Epichlorohydrin, itself, in this reaction led to 3-hydroxyglutaronitrile in 60% yield accompanied by smaller amounts (18%) of 4-chloro-3-hydroxybutyronitrile and 4-hydroxycrotononitrile. The latter materials, being considerably more volatile, were easily separated by distillation. These two components were the only materials that could be isolated when magnesium sulfate was omitted from the reaction.[7] The various products probably arise according to the scheme shown below.



However, on no occasion did we isolate any 3,4-epoxybutyronitriles from our reaction products. Culvenor, Davies, and Haley[7] have commented on the instability to base of epoxy systems of this type, and it appears that they are attacked faster by nucleophiles than the corresponding chloro epoxides.

The use of 1,3-dichloropropanol-2 or 4-chloro-3-hydroxybutyronitrile in the buffered system led to poorer yields of 3-hydroxyglutaronitrile.

The action of the buffered potassium cyanide solution on 2-methyl-, 2-ethyl-, and 2-phenylepichlorohydrin was also examined. The latter two materials were prepared in high yield by the reaction of the appropriate Grignard reagent with 1,3-dichloroacetone at −60°, followed by treatment of the resultant 1,3-dichloroisopropanol with strong base. Under the conditions described above, 2-methyl-, and 2-ethylepichlorohydrin afforded exclusively the corresponding 3-hydroxy-3-alkylglutaronitriles in 71 and 77% yield. However, the reaction with 2-phenylepichlorohydrin did not proceed at any measurable rate. In this case modest yields of the crystalline 3-hydroxy-3-phenylglutaronitrile were realized by employing a mixture of potassium carbonate and bicarbonate (1:1 molar ratio) as the buffering agent.

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(1) M. Simpson, *Ann.*, **133**, 74 (1864).

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(3) M. H. Dreifuss and C. K. Ingold, *J. Chem. Soc.*, **123**, 2964 (1923).

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