ance of crystals, after which these were removed by filtration. These were crystals of *l*-fucononitrile tetraacetate; m. p. 176–177°. On further concentration, material was obtained which began to melt at about 115° and was a difficulty separable mixture of the cyclic-*l*-fucose oxime pentaacetate and the acetylated nitrile. Acetylation at −10° did not give crystals melting at 176°, but the nitrile was always present as the material isolated gave a faint nitrile reaction. Table I records the results of several experiments operated at different temperatures.

TABLE I

MILD ACETYLATION OF *l*-FUCOSE OXIME (0.5 G.) AT VARIOUS TEMPERATURES

Temp., °C.		−10	3	15	37	100
Wt., g., m. p.	115°	0.8	0.62	0.5	0.5	0.30
Wt., g., m. p.	176°	..	.12	.32	.36	.48

***l*-Fucononitrile Tetraacetate.**—The material from several of the preparations described above was combined and recrystallized from alcohol, from which it was obtained as rectangular plates; m. p. 177°, sp. rot. −22.4° (20°, D-line, *c* 5.0, $CHCl_3$, 2-dm.).

***l*-Fucose Oxime Pentaacetate.**—The product obtained by acetylation at −10° as described above, gave the nitrile test. Crystallization from alcohol did not separate the nitrile and the method of Deulofeu, Wolfrom and coworkers[3] for the purification of galactose oxime hexaacetate was employed. The crude preparation (1.5 g.) was recrystallized once from alcohol and this material was then boiled with 500 cc. of water, a portion dissolving. The mixture was cooled to 5°, maintained at this temperature for one hour, filtered and the filtrate extracted with chloroform. The crystalline material (plates) obtained on chloroform removal and recrystallization from alcohol gave a negative nitrile reaction; m. p. 116° (unchanged on further recrystallization), spec. rot. +44.9° (25°, D-line, *c* 3.35, $CHCl_3$, 1.894-dm.).

The acetylated oxime on heating at 135° for five minutes gave a sirup that crystallized on the addition of alcohol. The crystals melted at 115–116° and were the original substance. Unchanged material (m. p. 116°) also was returned on refluxing for fifteen minutes with acetic anhydride and sodium acetate.

Summary

1. A study has been made of the action of the reagent pyridine–acetic anhydride on the oximes of *d*-α-glucoheptose, *d*-glucosamine hydrochloride and *l*-fucose.

2. *d*-α-Glucoheptose oxime and *d*-glucosamine oxime react in an open-chain form to give the acetylated nitriles, even at low temperatures.

3. *l*-Fucose oxime reacts at low temperature in a cyclic form and cyclic-*l*-fucose oxime pentaacetate predominates among the substances obtained. At higher temperatures one part reacts in an open-chain form and *l*-fucononitrile tetraacetate is produced and predominates at 100°.

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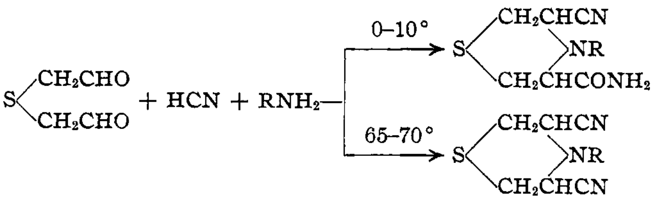
[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Studies in the Thiamorpholine Series. II. N-Alkyl Substituted Derivatives

BY HELEN I. MINER,[1] EDWIN O. HOOK[1] AND ROBERT D. COGHILL[2]

In the first paper of this series was described the reaction between thiodiacetaldehyde, hydrocyanic acid and ammonia to produce the half-amide, half-nitrile of thiamorpholine 3,5-dicarboxylic acid. The use of the Strecker reaction in this fashion for ring-closure in the thiamorpholine series has now been extended by using various aliphatic amines in place of the ammonia.

During the course of a study of the original synthesis in order to determine better reaction conditions, it was found that by allowing the reaction to proceed at temperatures of 65–70° instead of 0°, the dinitrile of the acid was obtained rather than the nitriloamide. This situation was also found to hold when methyl- or ethylamine was substituted for the ammonia, the dinitriles being formed at the elevated temperatures. These reactions can be expressed by the equations



In the cases of other amines, benzylamine formed only the dinitrile, while *n*-butyl-, *n*-amyl-, isoamyl- and *n*-heptylamine produced the nitriloamides. To date it has not been found possible to cause either reaction to take place with aniline.

Attempts have been made to hydrolyze these compound products to the corresponding N-alkyl

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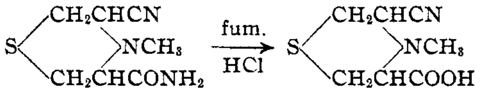
[1] This paper is constructed from the Dissertations of Helen I. Miner and Edwin O. Hook which were submitted in candidacy for the degree of Doctor of Philosophy at Yale University, June, 1939.

[2] Northern Regional Research Laboratory, U. S. Department of Agriculture, Peoria, Ill.

TABLE I

3,5-Dinitrilothiamorpholine	Formula	M. p., °C. corr.	Analyses, % C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found	S Calcd.	S Found
N-Methyl-	$C_7H_9N_3S$	178	50.2	50.0	5.4	5.4	25.1	24.9	19.2	19.4
N-Ethyl-	$C_8H_{11}N_3S$	137	53.0	53.1	6.1	6.2	23.2	23.1	17.7	18.0
N-Benzyl-	$C_{13}H_{13}N_3S$	170	64.2	64.0	5.4	5.3	17.3	16.9		
Nitrilothiamorpholine-5-carboxamide										
N-Methyl-3-	$C_7H_{11}ON_3S$	208d	45.3	45.1	6.0	6.2	22.6	22.3	17.3	17.5
N-Ethyl-3-	$C_8H_{13}ON_3S$	177d	48.2	48.3	6.6	6.8	21.1	20.8	16.1	16.5
N-*n*-Butyl-3-	$C_{10}H_{17}ON_3S$	192d	52.8	52.7	7.5	7.7	18.5	17.3	14.1	14.5
N-*n*-Amyl-3-	$C_{11}H_{19}ON_3S$	174d	54.7	54.8	7.9	7.9	17.4	16.4	13.3	12.9
N-iso-Amyl-3-	$C_{11}H_{19}ON_3S$	192d	54.7	54.7	7.9	8.1	17.4	16.3	13.3	13.4
N-*n*-Heptyl-3-	$C_{13}H_{23}ON_3S$	181d	57.9	58.1	8.6	8.8	15.6	14.7	11.9	12.2

thiamorpholine-3,5-dicarboxylic acids, but so far with very meager success. The compounds are unstable and decompose under most of the reaction conditions used. The odor of hydrocyanic acid becomes quite pronounced and the material rapidly transforms into red or black tars. In one case, however, using cold fuming hydrochloric acid, the amide group of the N-methyl derivative was hydrolyzed to a carboxyl.



This nitrilo acid, when subjected to more strenuous conditions, also gave rise to colored tar-like products. Further attempts are being made to accomplish this hydrolysis in a satisfactory manner.

Experimental

All melting points are corrected.

3,5-Dinitrilothiamorpholine.—Fifty-three grams of acetalyl sulfide was hydrolyzed and the resulting solution of thiodiacetaldehyde concentrated to 100 cc. as previously described.[3] To this solution, held at a temperature of 0°, were added 4 drops of piperidine and 16 cc. of liquid hydrogen cyanide. After standing ten minutes 7 g. of ammonia gas was led in without cooling. The temperature rapidly rose to 70° and a crystalline material separated. This was filtered off, washed with ice-water and dried; yield, 13.9 g. or 43%. After recrystallization from 95% alcohol the product was obtained as four-sided plates which melted with decomposition at 214°.

Anal. Calcd. for dinitrile, $C_6H_7N_3S$: C, 47.0; H, 4.6; N, 27.4; S, 20.9. Found: C, 47.0; H, 4.5; N, 26.8; S, 21.0.

N-Alkyl Dinitrilothiamorpholines.—These were prepared as described above except for the substitution of methyl-, ethyl- and benzylamines for the ammonia. Table I portrays the melting points and analyses of these substances.

N - Alkyl - 3 - nitrilothiamorpholine - 5 - carboxamides.—These compounds were prepared as described for the dinitriles, except that during the addition of the amines the temperatures were kept below 10°. Liquid amines were added slowly from a dropping funnel. The melting points and analyses of these substances are given in Table I.

N-Methyl-3-nitrilothiamorpholine-5-carboxylic Acid.—Five grams of N-methyl-3-nitrilothiamorpholine carboxamide was dissolved in 50 cc. of cold fuming hydrochloric acid and allowed to stand for five days at 10° and an additional five days at room temperature. After removal of the hydrochloric acid *in vacuo* at low temperature the residue was taken up in 50 cc. of cold water, which dissolved the tarry material and left some crystals in suspension. These were filtered off, washed, and recrystallized from boiling water. They melted at 184–185° and decomposed aqueous sodium bicarbonate; yield, 0.6 g. (12%).

Anal. Calcd. for $C_7H_{10}O_2N_2S$: C, 45.15; H, 5.41. Found: C, 45.06; H, 5.35.

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Summary

Several new N-alkyl substituted thiamorpholines have been prepared and described.

NEW HAVEN, CONN. RECEIVED APRIL 24, 1940

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[3] R. D. Coghill, THIS JOURNAL, **59**, 801 (1937).