Chlorination of 2-Thiophenecarboxylic Acid

BY J. F. BUNNETT, D. M. BACHMAN, L. P. SNIPPER AND J. H. MALONEY

Steinkopf and Kohler[1] reported that direct chlorination of 2-thiophenecarboxylic acid (I) in boiling water or cold glacial acetic acid gave traces of 4,5-dichloro-2-thiophenecarboxylic acid (II), the predominant products being chlorinated tetrahydrothiophenes resulting from a combination of chlorination, decarboxylation and addition of chlorine to double bonds. In a pamphlet published by the Socony-Vacuum Oil Co.,[2] substantially the same statement was made. A more recent publication[3] from the Socony-Vacuum Laboratories mentioned the use of direct chlorination for the preparation of II, but no experimental details were given on the preparation which apparently was on a rather small scale. The preparation of a monochloro-2-thiophenecarboxylic acid by direct chlorination has not been reported.

We have found that by addition of excess hydrochloric acid to an alkaline solution of I and hypochlorite, 5-chloro-2-thiophenecarboxylic acid (III) can be obtained in yield about 45% (using a hypochlorite to I ratio of 1.7:1), while when the ratio is 2.5:1, rather small yields (14%) of II result. Other procedures such as passing chlorine through a buffered solution of I or allowing a buffered solution of I and hypochlorite to react also gave III or II, but not in as good yield or quality.

In most chlorinations by various techniques oily by-products were observed. These by-products from a number of runs were combined and distilled. A considerable fraction of b. p. 160–165° and n^{16}_{D} 1.5624 was obtained. Nitration of this fraction gave a solid of m. p. 85–85.5°. This fraction was 2,5-dichlorothiophene (IV), since IV[3] has b. p. 162° and n^{20}_{D} 1.5626, and gives on nitration[4] 3,4-dinitro-2,5-dichlorothiophene of m. p. 88–91°. The by-product oil from another run in which hydrochloric acid was added to an alkaline solution of hypochlorite and I in 3:1 ratio appeared to be a mixture of chlorinated thiophenes, with IV the principal constituent.

We first encountered the chlorination method reported here when III was obtained by the hypochlorite oxidation of 2-acetylthiophene, using the household bleach "Clorox" as a source of hypochlorite. When the hypochlorite solution used was strongly alkaline, only normal oxidation to I occurred.

It is possible that modification of the procedures we report here might result in better yields. We report the work at this time because we do not intend to investigate the matter further.

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Experimental[5]

5-Chloro-2-thiophenecarboxylic Acid (III).—A solution of 3 g. (0.023 mole) of 2-thiophenecarboxylic acid, 0.042 mole of sodium hypochlorite and excess sodium hydroxide in a total volume of 400 ml. was prepared. To this solution (*p*H 11.0) at 48° were added with stirring 25 ml. of 6 *M* hydrochloric acid during six minutes. The temperature rose to 53°, the *p*H dropped to 1.3, and a white precipitate appeared. With continued stirring, an additional 5 ml. of acid and then 107 g. of sodium chloride were added. The solid obtained by filtration of the chilled solution weighed 1.75 g. (46%), m. p. 134–137°. After recrystallization and sublimation the m. p. was 149–150°. The mixed m. p. with a sample of III prepared by permanganate oxidation of 5-chloro-2-acetylthiophene was not depressed.

4,5-Dichloro-2-thiophenecarboxylic Acid (II).—The above procedure was followed, with 1.9 g. (0.015 mole) of I and 0.037 mole of sodium hypochlorite being employed. Four-tenths of a gram (14%) of II, m. p. 182–187° was obtained. After recrystallization from water, the m. p. was 194–194.5°. Steinkopf and Kohler[1] reported m. p. 196–197°.

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[1] Steinkopf and Kohler, *Ann.*, **532**, 250 (1937).

[2] "Thiophene Chemicals," Socony-Vacuum Oil Co., New York, N. Y., 1946, p. 17.

[3] Coonradt, Hartough and Johnson, THIS JOURNAL, **70**, 2564 (1948).

[4] Steinkopf, "Die Chemie des Thiophens," Theodor Steinkopff, Dresden, 1941, p. 58.

[5] Melting points are uncorrected.

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N-Substituted 2,4:3,5-Dimethylene-D-gluconamides

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The structure of 2,4:3,5-dimethylene-D-gluconic acid has been the subject of two recent publications.[1,2] We take this opportunity of recording a modification of Zief and Scattergood's preparation of 2,4:3,5-dimethylene-D-gluconic acid and also the preparation of some N-substituted dimethylene gluconamides which appear to be new. Their properties are listed in Table I.

Experimental

2,4:3,5-Dimethylene-D-gluconic acid.—Dimethylene-D-gluconic acid was prepared by the method of Zief and Scattergood[2] which was modified by substituting calcium D-gluconate for D-glucono-δ-lactone. The calcium D-gluconate and the trioxane were dissolved completely by stirring. The yield of the acid was 64–66% of the theoretical. Using paraformaldehyde in essentially the same procedure, slightly higher yields were obtained (70%). The recrystallized acid had a m. p. of 219.4–220.8°; $[\alpha]^{27.5}_{\mathrm{D}}$ + 38.1° (*c*, 0.136; water).

Methyl 2,4:3,5-Dimethylene-D-gluconate.—The ester was prepared by the method of Mehltretter, *et al.*[1]

N-Substituted 2,4:3,5-Dimethylene-D-gluconamides.—The dimethylene gluconamides were prepared by treating the ester with the corresponding amine in either water or alcohol as solvent. The butyl, isobutyl and ethyl amide were obtained by treating in water at room temperature for several days. The cyclohexyl amide was prepared by refluxing in water while the allyl and the hydroxyethyl amides were prepared by refluxing in methanol. The methyl amide was obtained from methanol at 0°. The

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[1] Mehltretter, *et al.*, THIS JOURNAL, **69**, 2130 (1947).

[2] Zief and Scattergood, *ibid.*, **69**, 2132 (1947).

TABLE I

PHYSICAL AND ANALYTICAL DATA FOR THE N-SUBSTITUTED 2,4:3,5-DIMETHYLENE-D-GLUCONAMIDES

Amide	Yield, %	M. p., °C.	$[\alpha]_D$	Temp., °C.	c	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
N-Methyl	80	195.6–196.8	+92.7	29.6	1.48	$C_9H_{15}O_6N$	6.0	6.0
N-Ethyl	40	169.0–170.0	+77.5	29.0	1.64	$C_{10}H_{17}O_6N$	5.7	5.6
N-Allyl	69	191.2–192.8	+61.2	32.4	1.43	$C_{11}H_{17}O_6N$	5.4	5.4
N-*n*-Butyl	20	141.6–142.2	+64.2	30.8	1.04	$C_{12}H_{21}O_6N$	5.1	5.0
N-Isobutyl	15	158.6–159.0	+62.2	30.8	0.96	$C_{12}H_{21}O_6N$	5.1	5.0
N-β-Hydroxyethyl	40	176.8–178.0	+75.0	29.6	1.51	$C_{10}H_{17}O_7N$	5.3	5.5
Cyclohexyl	50	217.0–217.6	+34.9	29.6	4.0	$C_{14}H_{23}O_6N$	4.65	4.4

crude amides were recrystallized from methanol or methanol–benzene. All the N-substituted dimethylene gluconamides prepared were found to be soluble in water or methanol and insoluble in ether or benzene. The specific rotations were determined in water as solvent at the concentration and temperature indicated in Table I.

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The System Ammonium Sulfate–Ammonia

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Solvation of ammonium sulfate in liquid ammonia was first observed by Browne and Welsh.[1] Brief mention of this behavior also was made by Friedrichs[2] who stated that $(NH_4)_2SO_4 \cdot 3NH_3$, insoluble in liquid ammonia, was formed, and claimed that in a sealed tube this compound was stable up to 145°. The solubility was found to increase slightly with temperature.

Investigations in this Laboratory have verified the existence of ammonium sulfate 3-ammoniate. A pressure–concentration isotherm at −32.5° and vapor pressure data for this compound were determined. No other ammoniates were formed over the temperature range −33 to +8°.

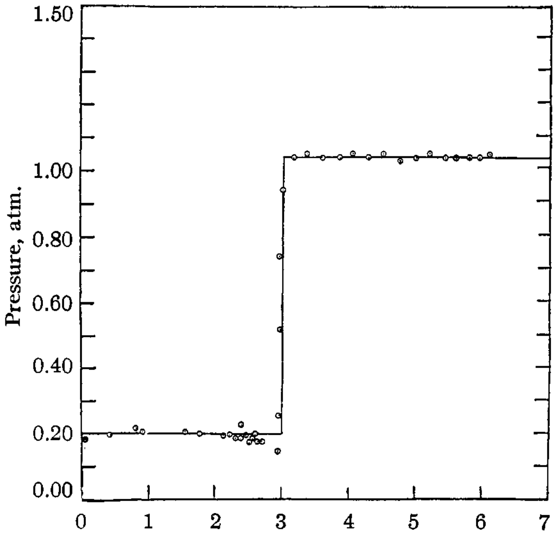

Fig. 1.—Pressure–concentration isotherm (−32.5°) of the system ammonium sulfate–ammonia.

Experimental

The apparatus employed in this investigation was similar to the equipment described by Howard, Friedrichs and Browne[3] for the study of binary systems having one volatile component. Commercial anhydrous ammonia was dried by passing the gas through a tube containing potassium hydroxide and then through a tube containing fine sodium wire. Ammonium sulfate (J. T. Baker C.P.) was purified further by recrystallization.

The pressure–concentration isotherm shown in Fig. 1 was obtained by adding a measured excess of ammonia to a weighed sample of ammonium sulfate and then withdrawing small increments of the gas. Pressure readings were taken when the system reached equilibrium, usually after twenty-four hours. Vapor pressure data for ammonium sulfate 3-ammoniate which are shown graphically in Fig. 2, were determined in the same apparatus. These data may be summarized by the equation $\log p$ (mm. Hg) = $10.2737 - 1934.4/T°K$.

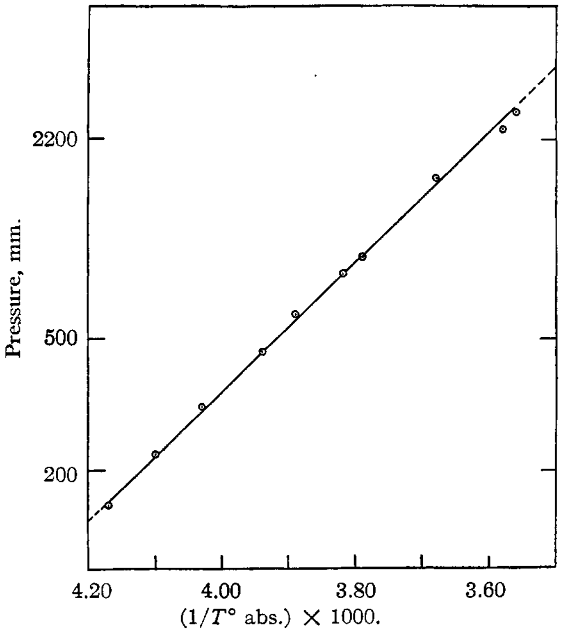

Fig. 2.—Vapor pressure of ammonium sulfate 3-ammoniate.

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[1] Browne and Welsh, THIS JOURNAL, **33**, 1728 (1911).

[2] Friedrichs, *ibid.*, **35**, 1866 (1913); *Z. anorg. allgem. Chem.*, **84**, 373 (1914).

[3] Howard, Friedrichs, and Browne, *ibid.* **56**, 2332 (1934).