

Chlorination of 2-Thiophenecarboxylic Acid

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Steinkopf and Kohler¹ 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 publication³ 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_D^{16} 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 IV³ has b. p. 162° and n_D^{20} 1.5626, and gives on nitration⁴ 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.

(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 Steinkopf, Dresden, 1941, p. 58.

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Experimental⁵

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 (pH 11.0) at 48° were added with stirring 25 ml. of 6 *M* hydrochloric acid during six minutes. The temperature rose to 53°, the pH 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 Kohler¹ reported m. p. 196–197°.

(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 Scattergood² 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°; $[\alpha]_D^{27.5} + 38.1^\circ$ (c, 0.136; water).

Methyl 2,4:3,5-Dimethylene-D-gluconate.—The ester was prepared by the method of Mehlretter, *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

(1) Mehlretter, *et al.*, *THIS JOURNAL*, **69**, 2130 (1947).

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