Abnormal Oxidation of 3-Nitro-2-thenyl Bromide by Cupric Nitrate

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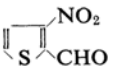
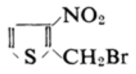
The present authors have reported the synthesis of 3-nitro-2-thiophenealdehyde (I): Oxidation of 3-nitro-2-methylthiophene by chromic trioxide in acetic anhydride followed by hydrolysis gave I (m. p. 52~53°C), but the yield was poor[1].

It has been found that oxidation of some aralkyl halides of benzyl halide type substituted by an electronwithdrawing group on the aromatic ring by cupric or lead nitrate, affords corresponding aromatic aldehydes[2] and also that this method is applicable to the thiophene series[1,3]. Therefore, an attempt was made for the synthesis of I by this method starting from 3-nitro-2-thenyl bromide (II).

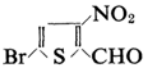
When II was heated in about 10% cupric nitrate solution (0.75 mol.) for 50 hr., two crystalline products melting at 78.5~79.5°C, and 81~82°C, respectively, were obtained. The low melting material (III) can be considered as an aldehyde from the method of separation of the products as described in the Experimental, but the infrared spectrum (Fig. 1) and the melting point of III are evidently different from those of I. The NMR spectrum of III (in acetone) shows a band of the aromatic hydrogen at 255.5 c. p. s., and a band due to the aldehyde hydrogen at 352.5 c. p. s., referred to cyclohexane. Gronowitz and Hoffman observed that the aldehyde hydrogen of thiophenealdehydes not substituted at the 5-position in the thiophene ring interacted with the hydrogen at the 5-position to split into two lines separated by about 1 c. p. s.[4], and this is also the case in some nitrothiophenealdehydes[1]. The splitting was not observed in the aldehyde hydrogen of III. In addition, III gave a positive test for the Beilstein test. These facts suggest that III is 5-bromo-3-nitro-2-thiophenealdehyde. Elemental analysis, in fact, gave corresponding values. III reacts with ordinary ketonic reagents, and with *p*-toluidine to yield the Schiff base.



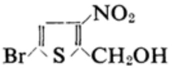
(I)



(II)



(III)



(IV)

The high melting material (IV) has infrared bands for OH group in the region of 3300~3100 cm^{-1} (Fig. 2). In the NMR spectrum of

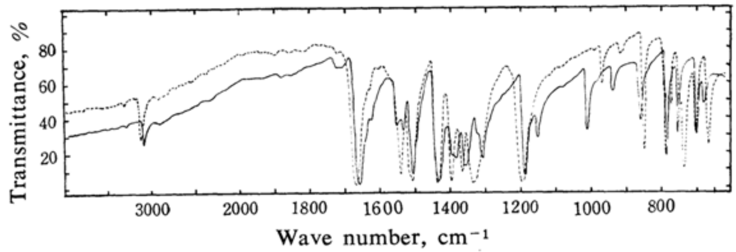


Fig. 1. Infrared spectra of I (----) and III (——) in KBr disk.

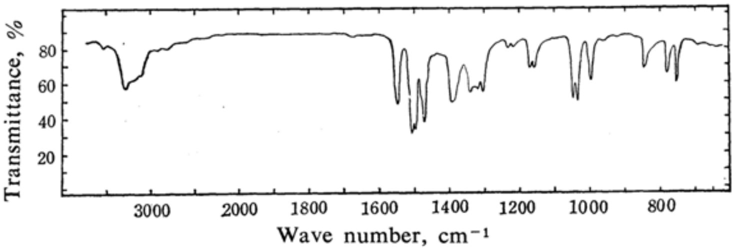


Fig. 2. Infrared spectrum of IV in KBr disk.

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[1] T. Sone and Y. Matsuki, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **83**, 496 (1962).

[2] Houben-Weyl, "Methoden der Organischen Chemie", Band VII, Teil 1, Georg Thieme Verlag, Stuttgart (1954), p. 193.

[3] E. Profft and H. Wolf, *Ann.*, **628**, 96 (1959).

[4] S. Gronowitz and R. A. Hoffman, *Acta Chem. Scand.*, **13**, 1687 (1959).

IV (in carbon tetrachloride), the chemical shifts (69, 145 and 240 c. p. s.) and the relative peak areas (approximately 1 : 2 : 1) of the bands suggest that they are due to a hydroxyl group, a methylene group and a ring hydrogen of trisubstituted thiophene, respectively. IV gave also a positive test for halogen. From these facts, it may be presumed that IV is 5-bromo-3-nitro-2-thenyl alcohol. Elementary analysis and the formation of the benzoate support this assumption. An attempt to synthesize the alcohol by nitration of 5-bromo-2-thenyl acetate followed by hydrolysis was unsuccessful, because the nitration product could not be hydrolyzed by either acid or alkaline solution. Starting material, II, is entirely free from other substances such as 5-bromo-3-nitro-2-thenyl bromide, for the coupling constant ($J=5.5$ c. p. s.) in the NMR spectrum indicates that II is a 2, 3-disubstituted thiophene[5], and the reaction of II with potassium thiocyanate gave 3-nitro-2-thenyl thiocyanate in 70% yield.

Such an abnormal oxidation of aralkyl halides by a heavy metal nitrate, giving halogenated aldehyde and alcohol, has not been observed as far as the authors know. As it has been suggested that the normal oxidation involves the formation of a nitrate[6] as an intermediate and cupric halide[2] which can be used as a halogenating agent[7], the mechanism of the reaction presented here probably consists in the bromination of intermediate nitrate by cupric bromide to yield 5-bromo-3-nitro-2-thenyl nitrate, which subsequently gives III by elimination and IV by nucleophilic substitution.

Experimental

All melting points are uncorrected. The infrared spectra were measured with a Perkin-Elmer model 21 infrared spectrometer. The NMR spectra were obtained with a Varian Associates Model V-4300B spectrometer at 40 Mc. and cyclohexane was used as an internal reference.

3-Nitro-2-theyl Bromide (II).—Prepared according to the procedure described by Snyder et al.[8], m. p. 60∼61°C (reported m. p. 60∼62°C; Found: C, 27.04; H, 1.77; N, 6.18%). The chemical shifts are 141.5 (methylene protones), 231 (doublet) and 243.5 c. p. s. (doublet) (ring protons) and the coupling constant is $J=5.5$ c. p. s., characteristic of 2,3-disubstituted thiophenes ($J_{23}=5.4\pm0.6$[5a], 5.4 c. p. s.[5b]).

Reaction of II with Potassium Thiocyanate.—A mixture of II (0.22 g.) and potassium thiocyanate (0.15 g.) in ethanol was warmed at 60∼65°C for 30 min. The resulting solution was poured into water and the precipitates were collected and recrystallized from ethanol to form 3-nitro-2-thenyl thiocyanate as pale yellow needles, m. p. 109∼110°C. Yield 0.14 g.

Found: C, 36.20; H, 1.73; N, 13.79. Calcd. for $C_6H_4N_2O_2S_2$: C, 35.98; H, 2.01; N, 13.99%.

Oxidation of II by Cupric Nitrate.—A mixture of II (4.4 g.) and a cupric nitrate solution ($Cu(NO_3)_2\cdot3H_2O$, 3.6 g.; H_2O, 30 ml.) was gently refluxed for 50 hr. After cooling, the reaction products were extracted with ether and the ether extracts were washed with water and then shaken with excess of saturated sodium bisulfite solution to form the addition product; this was collected and dissolved in water, and the solution was acidified with hydrochloric acid and steam-distilled. The crystals precipitated in the distillate amounted to 1.23 g., m. p. 67∼72°C, which, after recrystallization from petroleum ether, gave 5-bromo-3-nitro-2-thiophenealdehyde (III) as pale yellow needles, m. p. 78.5∼79.5°C.

Found: C, 25.63; H, 0.89; N, 6.01; Br, 32.92. Calcd. for $C_5H_2BrNO_3S$: C, 25.44; H, 0.85; N, 5.93; Br, 33.85%.

The infrared spectrum showed absorption for the carbonyl group at 1658 cm^{-1}.

Semicarbazone.—Yellow crystals, m. p. 269°C (decomp.) (from dioxane).

Found: N, 18.98. Calcd. for $C_6H_5BrN_4O_3S$: N, 19.11%.

2, 4-Dinitrophenylhydrazone.—Orange needles, m. p. 252∼253°C (from ethyl acetate).

Found: C, 31.59; H, 1.28; N, 16.46. Calcd. for $C_{11}H_6BrN_5O_6S$: C, 31.74; H, 1.45; N, 16.82%.

Reaction of III with p-Toluidine.—A mixture of III (0.1 g.) and *p*-toluidine (0.1 g.) in methanol (5 ml.) was left on standing at room temperature for two days. The yellow crystals precipitated were collected and recrystallized from ethanol to form the Schiff base as yellow needles, m. p. 129°C. Yield, 0.13 g.

Found: N, 8.44. Calcd. for $C_{12}H_9BrN_2O_2S$: N, 8.61%.

The ether solution, after separation of the addition product, was washed with water and dried. Evaporation of ether yielded 0.87 g. of crystals, m. p. 80.5∼82°C, which were recrystallized from a mixture of ether and petroleum ether to give 5-brom-3-nitro-2-thenyl alcohol (IV) as colorless needles, m. p. 81∼82°C.

Found: C, 25.25; H, 1.61; N, 6.01; Br, 33.73. Calcd. for $C_5H_4BrNO_3S$: C, 25.22; H, 1.69; N, 5.88; Br, 33.56%.

Benzoate.—Pale brown needles, m. p. 119∼120°C (from ethanol).

Found: C, 42.18; H, 2.51; N, 4.01. Calcd. for $C_{12}H_8BrNO_4S$: C, 42.12; H, 2.35; N, 4.09%.

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[5] a) S. Gronowitz and R. A. Hoffman, *Arkiv Kemi*, 13, 279 (1958); b) K. Takahashi, Y. Matsuki, T. Mashiko and G. Hazato, This Bulletin, 32, 156 (1959).

[6] D. J. Cram and G. S. Hammond, "Organic Chemistry", McGraw-Hill, New York (1959), p. 384.

[7] For example, Fort brominated β-naphthol by using cupric bromide in methanol-water at room temperature. A. W. Fort, *J. Org. Chem.*, 26, 765 (1961).

[8] H. R. Snyder, L. A. Carpino, J. F. Zack., Jr, and J. F. Mills, *J. Am. Chem. Soc.*, 79, 2556 (1957).

his infrared spectral measurements and Miss Yoko Endo and Miss Yukiko Endo for microanalyses.

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