A Novel Degradation of Bromomethyl 5-Nitro-2-furyl Ketone

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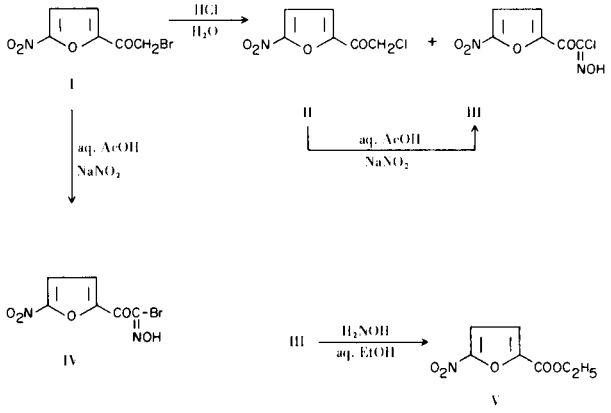
The preparation of chloromethyl 5-nitro-2-furyl ketone (II) from bromomethyl 5-nitro-2-furyl ketone (I) has been reported (1). During the purification of II by recrystallization from carbon tetrachloride, an insoluble higher melting material III was obtained which differed greatly from II. The structure of III and its independent synthesis is described.

The results of elemental analysis and molecular weight determinations of III indicated an empirical formula of $C_6H_3ClN_2O_5$. The infrared spectrum showed the presence of a NO_2, C=O and an NH or OH group together with a furan ring. The nmr spectrum indicated the presence of the two furan protons and an exchangeable proton at δ = 14.03 together with the absence of the two methylene protons which were present in II. These observations indicate that the 5-nitro-2-furoyl portion is still intact in III but that the methylene group no longer is present. Furthermore, the loss of one H and the gain of N and O indicates nitrosation at an active methylene site. The nitrosation of the active methylene group of phenacyl chlorides to yield stable arylglyoxylohydroxamyl chlorides has been reported (2). The nitrous acid probably arises from the acidic displacement of the nitro group of either I or II. There are several references to the release of nitrite ion by the alkaline degradation of nitrofurans (3); although the formation of nitrous acid by the decomposition of nitrofurans under acidic conditions is not as well documented (4), it was reported that the formation of nitrite from nitrofurans is slower in acidic solutions (4b).

In order to check the structure of III, the nitrosation of II was carried out in aqueous acetic acid using sodium nitrite. The product obtained was identical in all respects (*i.e.*, m.p. and infrared and nmr spectra) to III. The treatment of I under the same conditions yielded the corresponding bromo derivative IV.

When III was treated with hydroxylamine hydrochloride in aqueous ethanol, the only product isolated was ethyl 5-nitro-2-furoate (V). Although the exact mechanism for the formation of V has not been determined, it has been reported that the treatment of arylglyoxylohydroxamyl chlorides with dilute sulfuric acid resulted in the formation of the corresponding benzoic acid (2).



EXPERIMENTAL (5)

5-Nitro-2-furylglyoxyloyl Chloride 1-Oxime (III) (6).

A. From the preparation of chloromethyl 5-nitro-2-furyl ketone (II).

A mixture of I (7) (5.0 g.) and concentrated hydrochloric acid (125 ml.) was heated on a steam bath at about 80° with stirring for approximately 10 minutes. A clear solution was obtained which was cooled in ice and filtered. The solid was washed with cold water and dried to yield crude II (2.1 g., m.p. 80-83°). The filtrate was diluted to 250 ml. with cold water and cooled in an ice bath for 15 minutes to yield an additional amount of II (0.9 g.). The crude II was dissolved in boiling carbon tetrachloride and filtered hot to give III (0.1 g.) m.p. 158-164° dec. The insoluble material was recrystallized from 2-propanol with the aid of decolorizing carbon to yield an analytical sample, m.p. 178-179° dec.

The nmr spectrum contained signals at δ = 7.67 and 7.80 (2 furan protons, 2 doublets, J = 4 cps) and 14.03 (=NOH, exchangeable).

The infrared spectrum showed absorption maxima at 3250 (OH), 1660 (C=O), 1530 and 1390 (NO_2), 1040 and 970 (nitrofuran) cm^{-1}.

Anal. Calcd. for $C_6H_3ClN_2O_5$: C, 32.97; H, 1.38; Cl, 16.22; N, 12.81; Mol. Wt., 218.5. Found: C, 33.04; H, 1.59; Cl, 16.26; N, 12.50; Mol. Wt., 219 (formamide).

B. Synthesis from II.

A stirred solution of II (9.0 g., 0.05 mole) in acetic acid (150 ml.) and water (10 ml.) was kept at $< 10°$ while sodium nitrite (15 g., 0.22 mole) was added in small portions. After stirring for 1 hour, the reaction mixture was cooled and filtered. The crude product was washed with water and dried to yield

5.0 g. (45.5%), m.p. 173-175° dec.

An analytical sample was prepared by recrystallization from 2-propanol, m.p. 178-180° dec.

The infrared spectrum contained absorption maxima at 3250 (OH), 1660 (C=O), 1530 and 1390 (NO_2), 1040 and 970 (nitrofuran) cm^{-1}.

The nmr spectrum contained signals at δ = 7.67 and 7.80 (2 furan protons, 2 doublets, J = 4 cps) and at 14.03 (=NOH, exchangeable).

Anal. Calcd. for $C_6H_3ClN_2O_5$: C, 32.97; H, 1.38; N, 12.81; N, 12.81; Cl, 16.22. Found: C, 33.18: N, 1.52; N, 12.31; Cl, 16.37.

5-Nitro-2-furylglyoxyloyl Bromide 1-Oxime (IV).

A stirred solution of bromomethyl 5-nitro-2-furyl ketone (117.0 g., 0.5 mole) (7) in acetic acid (1500 ml.) and water (100 ml.) was kept at approximately 15° while sodium nitrite (150 g., 2.2 moles) was added in small portions. After stirring for 1 hour, the reaction mixture was cooled and filtered. The crude material was recrystallized from benzene with the aid of decolorizing carbon to yield 30.0 g. (22.7%), m.p. 151-152° dec.

The infrared spectrum contained absorption maxima at 330 (OH), 1650 (C=O), 1525 and 1340 (NO_2), 1030 and 970 (nitrofuran) cm^{-1}.

The nmr spectrum contained signals at δ 7.68 and 7.81 (2 furan protons, 2 doublets, J = 4 cps) and 14.16 (=NOH, exchangeable).

Anal. Calcd. for $C_6H_3BrN_2O_5$: C, 27.40; H, 1.15; Br, 30.39. Found: C, 27.47; H, 1.28; Br, 30.34.

Reaction of III with hydroxylamine hydrochloride.

A solution of III (11 g., 0.05 mole) in 95% ethanol (400 ml.) was added to a solution of hydroxylamine hydrochloride (7 g., 0.1 mole) in water (200 ml.). The resulting solution was diluted with water (200 ml.), allowed to stand overnight at room temperature, and filtered to yield 2.0 g. of recovered III. The filtrate was evaporated to near-dryness under reduced pressure and a yellow-orange solid collected. The gummy solid was washed with water and dried *in vacuo* over potassium hydroxide to yield 4.3 g. which was crystallized from aqueous 2-propanol to give V (2.0 g.), m.p. 92-93°, identical with an authentic sample of ethyl 5-nitro-2-furoate (8).

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(5) The melting points, obtained in open capillaries on a Mel-Temp melting point apparatus, are uncorrected. The infrared spectra were obtained as Nujol mulls on the Perkin-Elmer Infracord Model 137. The nmr spectra were determined on a Varian Model A-60A spectrometer using deuterated DMSO with TMS as an internal standard.

(6) This compound has been reported recently as being prepared from methyl 5-nitro-2-furyl ketone, m.p. 188-189° (methanol), N. O. Saldabol, B. S. Velovich, L. N. Alekseeva, B. A. Brizga, and L. V. Kruzmetra, *K Khim. Farm. Zhur.*, 3 (9), 16 (1969); *Chem. Abstr.*, 72, 31749s (1970).

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