

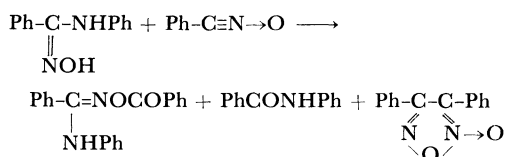
Reactions of Aromatic Hydroxamoyl Chlorides with Benzamidoxime Involving a Novel Synthesis of the 1,4-Dioxo-2,5-diazine Ring System¹⁾

Tadashi SASAKI, Toshiyuki YOSHIOKA and Yasuyuki SUZUKI

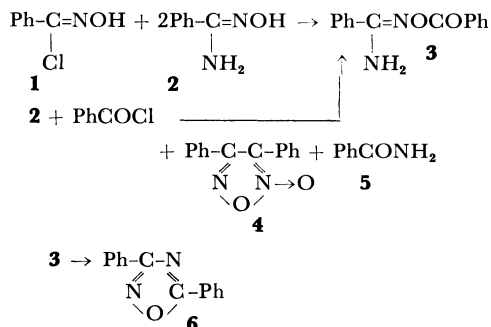
Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya

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N-Phenylbenzamidoxime is known to react with benzonitrile oxide to afford the *O*-benzoyl oxime as a major product together with small amounts of benzanilide and diphenylfuroxan, but without detailed documentation for the formation mechanism.²⁾



In a previous paper,³⁾ we have reported the 1,3-dipolar cycloaddition reactions of aromatic hydroxamoyl chlorides, a precursor to the nitrile oxides, with two equivalents amounts of basic dipolarophiles in ether at room temperature leading to the formation of five-membered heterocycles. Under similar conditions, we treated benzhydroxamoyl chloride (**1**) with benzamidoxime (**2**). Two products isolated from the ether-soluble part were characterized as *O*-benzoylbenzamidoxime (**3**) and diphenylfuroxan (**4**) together with benzamide (**5**) from the ether-insoluble part. Compound **3** was alternatively prepared from **2** and benzoyl chloride. When refluxed in toluene, **3** was converted to known 3,5-diphenyl-1,2,4-oxadiazole (**6**).



Considering that the types of these products are similar to those from the reaction of benzonitrile oxide with *N*-phenylbenzamidoxime, both reactions are concluded to proceed in the same manner as illustrated in Scheme 1; the nitrile oxide attacks to the hydroxyl, not to the amino group of **2**,⁴⁾ leading to the intermediate **7** or **8**, which was hydrolyzed⁵⁾ at (a) linkage to give *O*-benzoylbenzamidoxime or **3**, while the hydrolysis at (b) linkage afforded **4** and benzanilide or **5**. The results indicate that both types of the cleavage have occurred competitively.

Expecting similar results, 5-nitro-2-furyl-(9), *p*-(10) and *m*-nitrobenzhydroxamoyl chloride (11) were treated with 2 under similar conditions. From the reaction of 9 and 2, two crystalline products, 12 and 13, were isolated from the ether-soluble and insoluble part of the reaction mixture, respectively. The infrared spectrum (KBr) of 12 showed no absorptions due to amino and carbonyl but a strong one at 1200 cm^{-1} presumably due to cyclic ether, and medium ones at 1645 and 1610 cm^{-1} due to --C=N-- instead of strong ones at $1600\text{--}1625\text{ cm}^{-1}$ characteristic in furoxan structure,⁶⁾ while 13 manifested amino (3500), hydroxyl (3225) and carbonyl (1750 cm^{-1}) absorptions, though the first amino absorption was slightly different from that of 3, in which two amino-absorptions at 3450 and 3400 cm^{-1} indicate the presence of the primary amino group. The analysis of 12 supports a chemical formula $\text{C}_{12}\text{H}_7\text{O}_5\text{N}_3$, suggesting the so-called dimer-type structure of the nitrile oxide as expressed by 12' and 12''. Recently, Morrocchi *et al.*⁷⁾ have reported on the application of mass spectroscopy for distinguishing these isomeric dimers. We adopted this method for determining the structure. As depicted in Fig. 1, the most abundant peak corresponds to benzonitrile ion instead of disubstituted acetylene or aromatic carbonyl ions originated from 12'

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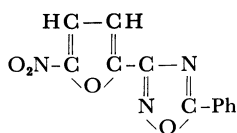
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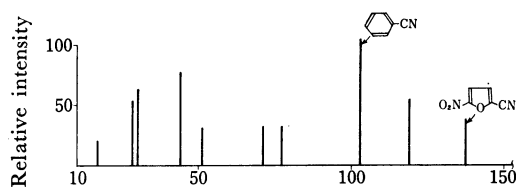
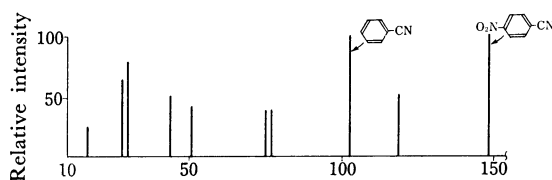
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Fig. 1. The mass spectrum of **12**.Fig. 2. The mass spectrum of **17**.

Experimental⁹⁾

Reaction of Benzhydroxamoyl Chloride with Benzamidoxime. A solution of 1 g of benzamidoxime in 30 ml of ether was added to a solution of 0.5 g of benzhydroxamoyl chloride in 20 ml of ether at room temperature with stirring. The reaction mixture was allowed to stand for one month. The resulting precipitates were collected by filtration, washed with a small amount of cold water, and recrystallized from water to give benzamide, mp 130°C. The solvent was removed from the filtrate and the residual oil was extracted with ether (10 ml × 3). The ether extracts were dried (Na₂SO₄) and evaporated. The residue was chromatographed on silicic acid (Mallinckrodt, 100 mesh), using chloroform as the eluent. The first fraction (150 mg, 30%) was recrystallized from ethanol to give **4**, mp 118°C, which was identified by the infrared spectral comparison with a specimen.¹⁰⁾ The second fraction (300 mg, 40%) was recrystallized from benzene to afford **3** as colorless crystals, mp 153°C.

Found: C, 70.10; H, 4.94; N, 11.71%. Calcd for C₁₄H₁₂O₂N₂: C, 69.99; H, 5.03; N, 11.66%.

O-Benzoylbenzamidoxime (3). To a stirred solution of 1.3 g of benzamidoxime and 1.1 g of triethylamine in 60 ml of benzene was added dropwise 1.4 g of benzoyl chloride under cooling with ice-water.

After stirring for one day at room temperature, the resulting precipitates were collected by filtration, washed with water and recrystallized from ethanol to give 1.9 g (80%) of **3**, mp 153°C.

3,5-Diphenyl-1,2,4-oxadiazole (6). A solution of

0.7 g of **3** in 30 ml of toluene was refluxed for 12 hr. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol to give 0.6 g (85%) of **6**, mp 109°C (lit.¹¹⁾ mp 109°C).

Reaction of 5-Nitro-2-furylhydroxamoyl Chloride with the Amidoxime. A solution of 0.5 g of 5-nitro-2-furylhydroxamoyl chloride¹²⁾ and 1 g of benzamidoxime in 40 ml of ether was stirred at room temperature overnight. The precipitates were collected by filtration, washed with water, dried in the air and recrystallized from benzene to give 0.32 g (30%) of **12** as pale yellow crystals, mp 203–205°C (dec.). UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (ϵ): 223 (20000) and 308 (8600).

Found: C, 53.19; H, 2.20; N, 15.55%. Calcd for C₁₂H₇O₅N₃: C, 52.75; H, 2.58; N, 15.38%.

Ether was removed from the filtrate and the residue was recrystallized from benzene-ethanol to give 0.14 g (15%) of **13**, mp 191–194°C (dec.).

Found: C, 52.59; H, 3.39; N, 15.43%. Calcd for C₁₂H₉O₅N₃: C, 52.37; H, 3.30; N, 15.27%.

O-Benzoyl-5-nitro-2-furocarbamidoxime (14). This was prepared in 75% yield from 5-nitro-2-furocarbamidoxime (**15**)¹³⁾ and benzoyl chloride as pale yellow crystals, mp 214–217°C.

Found: C, 52.43; H, 3.19; N, 15.05%. Calcd for C₁₂H₉O₅N₃: C, 52.37; H, 3.30; N, 15.27%.

3-(5-Nitro-2-furyl)-5-phenyl-1,2,4-oxadiazole (16). Treatment of **14** similar to the preparation of **6** afforded 90% yield of **16**, mp 205°C (lit.¹¹⁾ mp 205°C).

3-(p-Nitrophenyl)-6-phenyl-1,4-dioxo-2,5-diazine (17). A solution of 1 g of *p*-nitrobenzhydroxamoyl chloride⁹⁾ and 1.4 g of benzamidoxime in 50 ml of ether was stirred at room temperature for several days. The resulting precipitates were collected by filtration, washed with water, dried in the air and recrystallized from benzene-ethanol to afford 0.52 g of **17** as yellow needles, mp 208–209°C (dec.). From the ethereal mother liquor, further 0.15 g of **17** was obtained. Total yield was 50%. IR (KBr): 1635 (–N=C–) and 1205 cm^{–1} (–O–).

Found: C, 59.55; H, 3.31; N, 14.88%. Calcd for C₁₄H₉O₄N₃: C, 59.36; H, 3.20; N, 14.84%.

3-(m-Nitrophenyl)-6-phenyl-1,4-dioxo-2,5-diazine (18). Similarly, 1 g (70%) of **18** was obtained as colorless crystals, mp 195°C (dec.), from *m*-nitrobenzhydroxamoyl chloride⁹⁾ (0.8 g) and benzamidoxime (1.5 g). IR (KBr): 1620 (–N=C–) and 1210 cm^{–1} (–O–). Mass Spectrum *m/e* (rel. intensity): 103 (100) and 148 (100).

Found: C, 59.35; H, 2.92; N, 14.93%. Calcd for C₁₄H₉O₄N₃: C, 59.36; H, 3.20; N, 14.84%.

Hydrolysis of 13 to N-benzoyl-5-nitro-2-furoylamide (19). A solution of **13** in ethanol was refluxed in the presence of 3% hydrochloric acid. The resulting precipitates after cooling were collected by filtration and recrystallized from ethanol-water to give 85% yield of **19**, mp 215°C.

Found: C, 55.45; H, 3.25; N, 10.65%. Calcd for C₁₂H₈O₅N₂: C, 55.39; H, 3.10; N, 10.77%.

9) Melting points are uncorrected. Infrared spectra were obtained on a Nippon-Bunko IR-S, ultraviolet spectra on a Nippon-Bunko ORD/UV-5 spectrometer. Mass spectra were measured on a Hitachi RMU-6D mass spectrometer at 70 eV.

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