

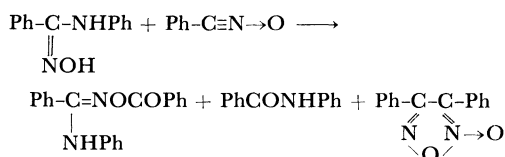
Reactions of Aromatic Hydroxamoyl Chlorides with Benzamidoxime Involving a Novel Synthesis of the 1,4-Dioxo-2,5-diazine Ring System<sup>1)</sup>

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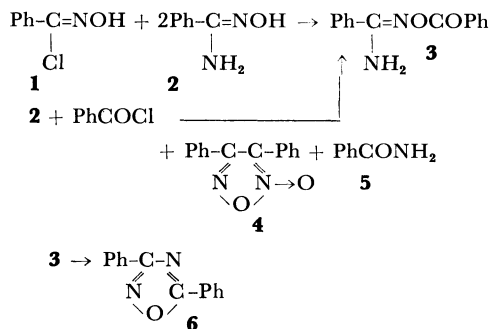
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*N*-Phenylbenzamidoxime is known to react with benzonitrile oxide to afford the *O*-benzoyl oxime as a major product together with small amounts of benzanilide and diphenylfuroxan, but without detailed documentation for the formation mechanism.<sup>2)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



In a previous paper,<sup>3)</sup> 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**,<sup>4)</sup> leading to the intermediate **7** or **8**, which was hydrolyzed<sup>5)</sup> 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  $1200\text{ cm}^{-1}$  presumably due to cyclic ether, and medium ones at  $1645$  and  $1610\text{ cm}^{-1}$  due to  $\text{-C=N-}$  instead of strong ones at  $1600\text{--}1625\text{ cm}^{-1}$  characteristic in furoxan structure,<sup>6</sup> while 13 manifested amino ( $3500$ ), hydroxyl ( $3225$ ) and carbonyl ( $1750\text{ cm}^{-1}$ ) absorptions, though the first amino absorption was slightly different from that of 3, in which two amino-absorptions at  $3450$  and  $3400\text{ cm}^{-1}$  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.*<sup>7</sup> 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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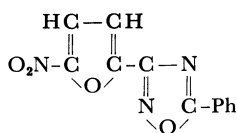
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5) Under anhydrous conditions, a hydrolysis cannot occur. We used commercially available ether directly.

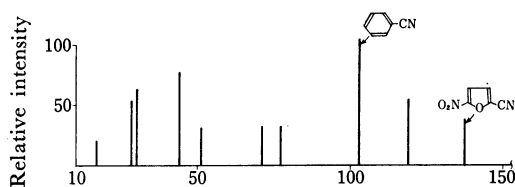
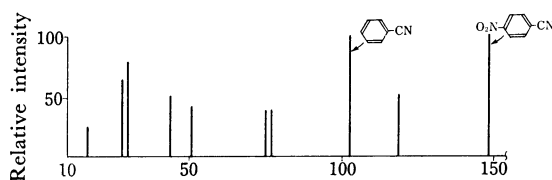
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Fig. 1. The mass spectrum of **12**.Fig. 2. The mass spectrum of **17**.

### Experimental<sup>9)</sup>

**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 (Na<sub>2</sub>SO<sub>4</sub>) 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.<sup>10)</sup> 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 C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub>: 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.<sup>11)</sup> mp 109°C).

**Reaction of 5-Nitro-2-furylhydroxamoyl Chloride with the Amidoxime.** A solution of 0.5 g of 5-nitro-2-furylhydroxamoyl chloride<sup>12)</sup> 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 $\mu$  ( $\epsilon$ ): 223 (20000) and 308 (8600).

Found: C, 53.19; H, 2.20; N, 15.55%. Calcd for C<sub>12</sub>H<sub>7</sub>O<sub>5</sub>N<sub>3</sub>: 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 C<sub>12</sub>H<sub>9</sub>O<sub>5</sub>N<sub>3</sub>: 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**)<sup>13)</sup> and benzoyl chloride as pale yellow crystals, mp 214–217°C.

Found: C, 52.43; H, 3.19; N, 15.05%. Calcd for C<sub>12</sub>H<sub>9</sub>O<sub>5</sub>N<sub>3</sub>: 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.<sup>11)</sup> mp 205°C).

**3-(p-Nitrophenyl)-6-phenyl-1,4-dioxo-2,5-diazine (17).** A solution of 1 g of *p*-nitrobenzhydroxamoyl chloride<sup>9)</sup> 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<sup>–1</sup> (–O–).

Found: C, 59.55; H, 3.31; N, 14.88%. Calcd for C<sub>14</sub>H<sub>9</sub>O<sub>4</sub>N<sub>3</sub>: 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 chloride<sup>9)</sup> (0.8 g) and benzamidoxime (1.5 g). IR (KBr): 1620 (–N=C–) and 1210 cm<sup>–1</sup> (–O–). Mass Spectrum *m/e* (rel. intensity): 103 (100) and 148 (100).

Found: C, 59.35; H, 2.92; N, 14.93%. Calcd for C<sub>14</sub>H<sub>9</sub>O<sub>4</sub>N<sub>3</sub>: 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 C<sub>12</sub>H<sub>8</sub>O<sub>5</sub>N<sub>2</sub>: 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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