Hydrolytic Cleavages of 7-Nitro-2-phenyl-1,2-benzisoxazol-3-one. Evidence for the Occurrence of a Benzidine-like Rearrangement of *N,O*-Diphenylhydroxylamines

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Preparation of the title compound **1** is described. Its treatment with base caused hydrolysis of the amide bond and subsequent benzidine-like rearrangement to give 4′-amino-3-carboxy-4-hydroxy-5-nitrobiphenyl (**4**). Acid treatment caused cleavage of the nitrogen-oxygen bond and rearrangement to 7-nitro-3-phenylbenzoxazol-2-one (**6**).

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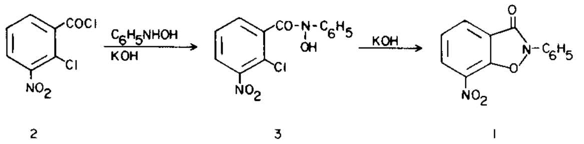
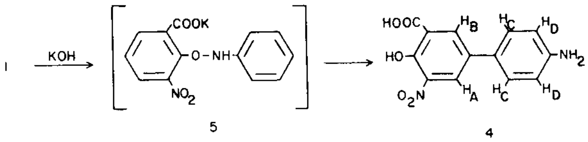
We were interested in cleavage reactions of the N-C_3 bond in *N*-phenylbenz-1,2-isoxazoles as a possible route to *N,O*-diphenylhydroxylamines. These hydroxylamines were proposed as intermediates in several processes which lead to biphenyls (1-4), and it has been assumed that a rearrangement which is an oxygen analogue of the benzidine rearrangement has taken place. We have recently described the synthetic utilization of the reaction for arylation of heterocycles (4) and also discussed some mechanistic aspects (5). However, in none of the reported cases hydroxylamine intermediates were isolated. Their intermediacy is still speculative and the formation of biphenyls is capable of a variety of other interpretations. The isoxazole ring cleavages mentioned above would show whether biphenyls are indeed formed from *N,O*-diphenylhydroxylamine precursors. Suitable substrates are the 2-phenyl-1,2-benzisoxazol-3-ones, in which the cleavage can be achieved by simple basic or acidic hydrolysis of the amide bond.

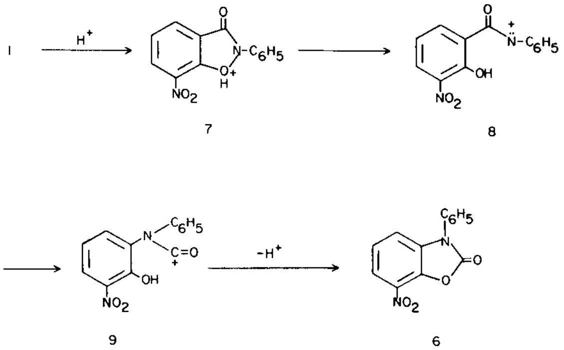
We have previously shown (6) that the only published (7) preparation of these benzisoxazolones is erroneous. We have however prepared the 7-nitro derivative (**1**) by reaction of 2-chloro-3-nitrobenzoyl chloride (**2**) with *N*-phenylhydroxylamine and cyclization of the resulting *N*-phenyl-2-chloro-3-nitrobenzohydroxamic acid (**3**) with ethanolic potassium hydroxide.



Treatment of compound **1** with aqueous-ethanolic potassium hydroxide caused precipitation of the potassium salt of **4**. The structure of the acid **4** (76% yield) was assigned as 4′-amino-3-carboxy-4-hydroxy-5-nitrobiphenyl. Structure proof includes the nmr spectrum which exhibited two 1H singlets at δ 8.25 and 8.18 (H_A and H_B respectively) and two 2H doublets at δ 7.53 and 7.00 (J = 8 Hz, H_C and H_D respectively). The infrared spectrum showed the presence of a primary amino group (3470 and 3375 cm^{-1}), a bonded carboxylic group (2600 and 1665 cm^{-1}) and the absence of a mono-substituted benzene ring. The formation of **4** from **1** *via* the hydrolysed intermediate **5** confirms the occurrence of the "oxabenzidine" rearrangement, as this is the first case of transformation of an isolable diarylhydroxylamine derivative to aminohydroxylbiphenyl.



Acid treatment of **1** did not afford **4**, but caused another type of rearrangement which led to 7-nitro-3-phenylbenzoxazol-2-one (**6**). In acid medium heterolysis of the nitrogen-oxygen bond in the protonated species **7** is probably faster than hydrolysis of the amide bond. Aryl migration to the electron deficient nitrogen in the acylnitrenium ion **8** and cyclization of **9** result in the benzoxazolone **6**.



EXPERIMENTAL

Melting points (uncorrected) were taken on a Thomas-Hoover apparatus. Nmr spectra (in DMSO) were recorded on Varian T-60 or El-360 spectrometers and ir spectra (in Nujol mulls) on Perkin-Elmer 257 spectrometer.

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N-Phenyl-2-chloro-3-nitrobenzohydroxamic Acid (**3**).

To a solution of *N*-phenylhydroxylamine (10.9 g., 0.1 mole) in ether (200 ml.), potassium carbonate (12.6 g.) and water (4 ml.) were added and the mixture was vigorously stirred with cooling (ice-bath). The chloride **2** (22 g., 0.1 mole) in ether (400 ml.) was added dropwise during 1 hour. After an additional hour the ethereal layer was separated, washed twice with 0.1*N* hydrochloric acid and then with water, concentrated and dried (sodium sulfate). Addition of petroleum-ether (b.p. 40-60°) caused precipitation of the product. Crystallization from ether-petroleum ether (b.p. 40-60°) gave 21.7 g. (74%) of **3**, m.p. 125°; ir: 3200 (OH) 1630 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_9N_2ClO_4$: C, 53.35; H, 3.08; N, 9.54; Cl, 12.14. Found: C, 53.60; H, 3.41; N, 9.63; Cl, 11.84.

7-Nitro-2-phenyl-1,2-benzisoxazol-3-one (**1**).

Compound **3** (2.93 g., 0.01 mole) was dissolved in ethanolic potassium hydroxide (1*N*, 10 ml.) and was left at room temperature. After 48 hours it was cooled, the precipitate formed was collected and crystallized from ethanol to give 2.3 g. (90%) of **1** as colorless needles, m.p. 147-148°; ir: 1700 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_8N_2O_4$: C, 60.93; H, 3.12; N, 10.93. Found: C, 61.00; H, 3.18; N, 10.87.

4-Amino-3-carboxy-4-hydroxy-5-nitrobiphenyl (**4**).

To a solution of compound **3** (0.256 g., 1 mmole) in ethanol (30 ml.), aqueous potassium hydroxide (1*N*, 3 ml.) was added. After stirring overnight the red precipitate was collected and suspended in 0.1*N* hydrochloric acid solution in which its colour changed to yellow. Filtration and cyrstallization from DMF-water afforded **4** (0.222 g., 76%), m.p. >300°. For spectral properties see text.

Anal. Calcd. for $C_{13}H_{10}N_2O_5 \cdot H_2O$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.36; H, 3.85; N, 9.49.

7-Nitro-3-phenylbenzoxazol-3-one (**6**).

A solution of compound **4** (0.5 g.) in acetic acid (10 ml.) and concentrated hydrochloric acid (5 ml.) was refluxed for 24 hours. The precipitate formed on cooling was collected and crystallized from ethanol to give 0.25 g. (50%) of **6**, m.p. 254°; ir: 1780 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_8N_2O_4$: C, 60.93; H, 3.12; N, 10.93. Found: C, 60.80; H, 2.92; N, 10.65.

REFERENCES AND NOTES

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