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PHOTOLYSIS OF SOME QUINOXALINE-1,4-DIOXIDES†

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Abstract—The photochemical rearrangement of 2,3-disubstituted quinoxaline-1,4-dioxides to 1,3-disubstituted benzimidazolones has been examined. Evidence against the previously reported mechanism is offered, and an alternative mechanism suggested. The scope of the reaction is increased to include new types. Furthermore, a new mode of rearrangement is recognized.

Several quinoxaline-1,4-dioxides and monoxides were successfully photolyzed to yield a variety of products depending on the structures of the substrates.[1-4] 2 - Aroyl - 3 - arylquinoxaline - 1,4 - dioxides (**1**, R_1 = Ar, R_2 = COAr) were reported to give 1,3-diaroylbenzimidazolones, **2**.[2,3] Analogous compounds with an alkyl group in place of an aryl group at positions 2 or 3 behave similarly (**1**, R_1 = alkyl, R_2 = COAr).[4] However, compounds which lack aryl substituents or a CO group as part of R_1 or R_2 failed to rearrange. The mechanism suggested[2-4] for the reaction is shown in Scheme 1A. This mechanism is incompatible with our findings in this study. In looking for support for the mechanism suggested above, a synthesis of the proposed intermediate **3b** was attempted, without success.[4] This result is in accord with the known resistance of 2-pyridones for N-acylation.[5]

In the present work, the photochemical reactions of the quinoxaline - 1,4 - dioxides (**1**, **a–d**) are studied

1a: $R_1 = CH_3$,	$R_2 = CH_2Ph$
1b: $R_1 = Ph$,	$R_2 = CH_2Ph$
1c: $R_1 = H$,	$R_2 = CH_2Ph$
1d: $R_1 = COPh$,	$R_2 = CH_2Ph$

The dominant features of these compounds are the presence of a benzyl substituent and (with the exception of **1d**) the lack of a CO group. Compounds with benzyl substituents were not previously investigated.

The essential feature of mechanism 1A is the migration of a CO carbon to an electron-defficient nitrogen e.g. an acyl or aroyl group migrates in the first stage. It is interesting to see if a benzyl group behaves similarly, knowing that 2,3-dialkyl or 2,3-diaryl analogues of **1** do not undergo the above type of rearrangement.

The results of the present work show that the benzyl group is capable of migration as anticipated. **1a** and **1b** on photolysis in methanol gave 1 - acetyl - 3 - benzylbenzimidazolone (**2a**) and 1 - benzoyl - 3 - benzylbenzimidazolone (**2b**). An accompanying product in each case was the hydrolysis product N-benzylbenzimidazolone (**4**).

In the case of **1d** the isolated product agrees with a higher migratory aptitude for a benzoyl compared with a benzyl substituent. The product **2c** hydrolyzes completely to the unsubstituted benzimidazolone instead of **4**.

Compound **1c** however did not behave similarly, but instead gave 1 - benzyl - 2,3 - quinoxalinedione (**5a**). Its structure is based on its elemental analysis and its IR and NMR spectra.

The rearrangement of **1b** can be explained by Scheme 1A.

The success of this reaction is important in that it provides a possibility of testing the proposed stepwise mechanism by a direct synthesis of intermediate **3c**. Benzylation of 3 - phenyl - 2 - quinoxalone - 4 - oxide(**3a**) is possible although its benzoylation failed. When intermediate **3c** was photolyzed under the same conditions used for **1b**, it failed to give **2b** and **4**, but instead gave **5b**. The structure of this unexpected product rests upon the following evidence: (i) Elemental analysis indicated a rearrangement. (ii) The IR spectrum showed no N–H and N→O bands. (iii) The presence of strong amide CO bands. (iv) Basic hydrolysis: The product of this treatment exhibited both an amide carbonyl and an N–H bands. From its spectroscopic properties (IR and NMR) and elemental analysis it was identified as *o*-(N-formyl-N-benzylamino) diphenylamine **6**.

That it is not the isomeric **7** is shown by the appearance of singlets for both N–H and benzylic protons in the NMR spectrum. The more electrophilic carbonyl carbon at position 3 in 5b is preferentially attacked by hydroxide ion. The carbonyl carbon at position 2 interacts more effectively with the lone pair on the alkyl substituted nitrogen at position 1.

The results of photolysis of **3c** show that it cannot be an intermediate in the photolysis of **1b**, and that this photolysis does not proceed by the stepwise mechanism shown in Scheme 1A. This led us to suggest a more likely mechanism for the photolysis of compounds mentioned in Refs. 2 and 3 and the photolysis of **1a, b, c**. This mechanism involves the simultaneous excitation of both nitrone functions at positions 1 and 4, and leads from **1** to **2** as shown in Scheme 1B. This scheme can also account for the formation of **5a** from **1c**, by assuming a different mode of migration in the charged intermediate that leads to **2** in the normal reaction.

An analogy to the dioxaziridine intermediate of mechanism 1B is available in the literature.[6] A stable dioxaziridine (cis and trans forms) was reported to form upon irradiation of dinitrone **8**.

Finally the anisotropy of the CO group of the acetyl

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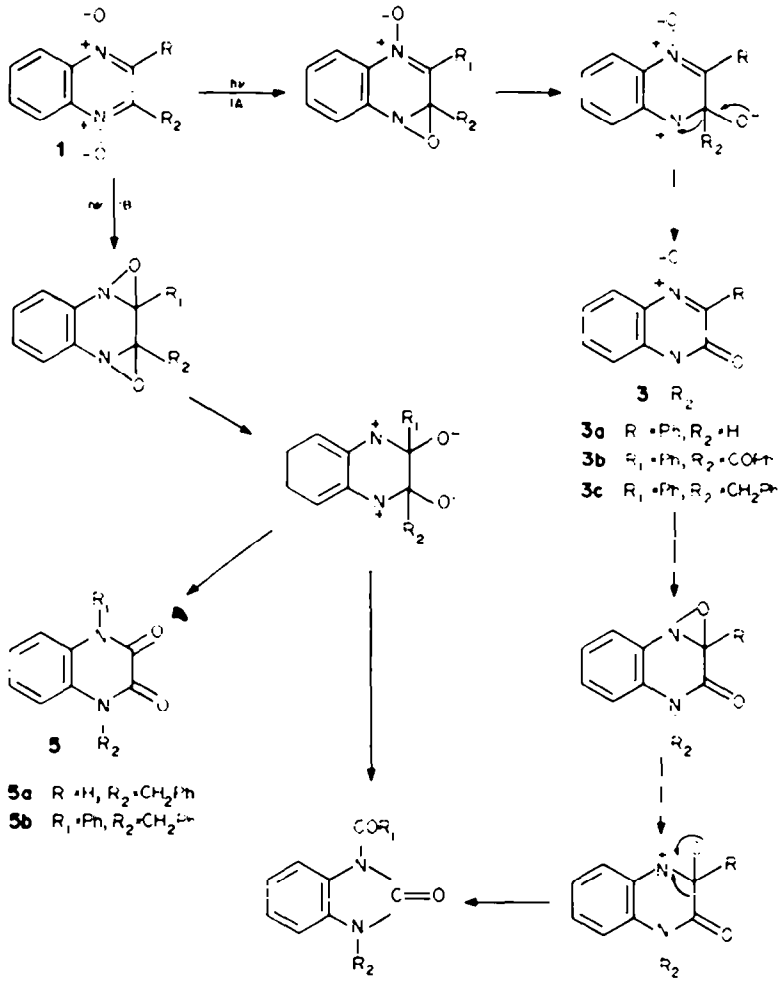
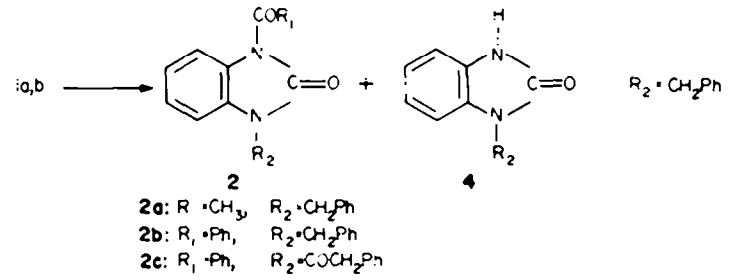
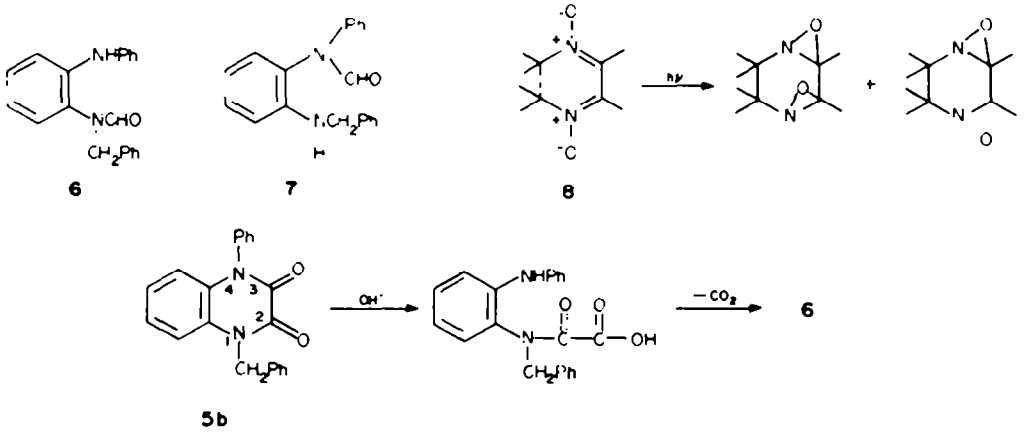


Scheme 1.





substituent in **2a** is seen to cause a downfield shift of 1.2 ppm equivalent to one aromatic proton. This agrees with previous results on the conformations of N-acyl-benzimidazolones.[7]

A lower shift of 0.6 ppm is observed in **2c**, but none in **2b**. The shifts are measured relative to the main aromatic signal, and are believed to result from the predominence of the *endo* conformation.

EXPERIMENTAL

(A) *Preparation of quinoxaline-1,4-dioxides.* These were prepared by the reaction of benzofurazan-1-oxide (BFO) with a ketone or diketone in the presence of a suitable base.[8]

2 - *Benzyl* - 3 - *methylquinoxaline* - 1,4 - *dioxide* (**1a**). Benzylacetone (25 ml, 0.1 mole) in MeOH (25 ml) and BFO (13.6 g, 0.1 mole) in MeOH (25 ml) were mixed. n-Butylamine (10 ml) was added dropwise with stirring at room temp. and the mixture was left overnight, yield: 83%, m.p. 159–60° (MeOH) (Lit.[9] 155°).

2 - *Benzyl* - 3 - *phenylquinoxaline* - 1,4 - *dioxide* (**1b**). Dibenzylketone (10.5 g, 0.05 mole) in dry ether (50 ml) and powdered sodamide (3 g) were mixed. BFO (6.8 g, 0.05 mole) in dry ether (100 ml) was then added *dropwise with stirring*. Water was then cautiously added to destroy excess sodamide, and more water up to 150 ml was added, yield: 52%, m.p. 176–7°.

2 - *Benzyl* - 3 - *benzoylquinoxaline* - 1,4 - *dioxide* (**1d**). 1,4 - Diphenyl - 1,3 - butanedione (5.9 g, 0.05 mole) in triethylamine (30 ml) and BFO (3.4 g, 0.025 mole) in triethylamine (50 ml) were mixed and left at room temp. for 24 hr. The tar-like product, left after evaporation of the solvent, was triturated with cold MeOH (50 ml) to give a yellow crystalline solid, yield: 21%, m.p. 165°; IR(KBr) 1675, 1595, 1350, 1045, 845, 650 cm^{-1}; NMR ($CDCl_3$) δ 4.18 (2H, s), 6.8 (14H,m), 8.3–8.6 (2H, m). (Found: C, 73.41; H, 4.43; N, 7.64. Calc. for $C_{22}H_{16}N_2O_3$: C, 74.16; H, 4.49; N, 7.86%).

2 - *Benzylquinoxaline* - 1,4 - *dioxide* (**1c**). **1d** (4 g, 0.01 mole) was dissolved in 2% methanolic KOH (180 ml). It was then heated on the steam bath with stirring for 15 min, during which a blue color appeared. The solid formed on cooling was crystallized from MeOH, yield: 93%, m.p. 178–180°; IR(KBr) 1605, 1535, 1370, 1290, 820, 705, 650 cm^{-1}; NMR ($CDCl_3$) δ 4.32 (2H, s), 7.3 (5H, s), 7.8 (2H, m), 8.0 (1H, s), 8.5 (2H, m). (Found: C, 70.80; H, 4.86; N, 11.01. Calc. for $C_{15}H_{12}N_2O_2$: C, 71.43; H, 4.76; N, 11.11%).

(B) 3 - *Phenyl* - 2(1H) - *benzylquinoxalone* - 4 - *oxide* (**3c**). Compound **3a**[10] (8 g, 0.034 mole), benzyl-bromide (17.6 g, 0.1 mole) and anhyd. Na_2CO_3 (6.72 g) in freshly distilled methyl ethyl ketone (300 ml) were refluxed for 24 hr. Filtration and evaporation of the solvent produced a solid from which excess benzyl bromide was removed by washing with petroleum spirit, yield: 45%; m.p. 196–8° (petroleum spirit 60–80°); IR(KBr) 1650, 1370, 1235, 1170, 1025, 870, 760, 690 cm^{-1}; NMR($CDCl_3$) δ 5.47 (2H, s), 7.3 (11H, m), 7.8 (2H, m), 8.45 (1H, m); (Found: C, 76.88; H, 4.87; N, 8.27. Calc. for $C_{21}H_{16}N_2O_2$: C, 76.83; H, 4.88; N, 8.54%).

(C) *Photolysis.* Methanolic solns (400 ml) of the substrate (1 g sample) was irradiated with UV light from a Hanovia 679A36 lamp with a Pyrex filter, or exposed to bright sunlight in a Pyrex flask. The mixture was stirred and was monitored by TLC to the disappearance of the starting material.

The soln was evaporated to about 25 ml and left to crystallize. The main product was separated, and the mother liquor was concentrated and left to crystallize whereupon a new product or further amounts of the first product were obtained.

3 - *Acetyl* - 1 - *benzylbenzimidazolone* (**2a**) *and* 1-*benzylbenzimidazolone* (**4**) *from* **1a**. The first crop was mainly **2a**. Concentration of the mother liquor and cooling produced mainly **4**. time: 18 hr (lamp); Yields: **2a** (25%), **4** (7%); 50 hr (sun); Yields: **2a** (30%), **4** (18%).

Compound **2a**: m.p. 110–112°; IR(KBr) 1730, 1610, 1490, 1380, 1020, 760, 650 cm^{-1}; NMR ($CDCl_3$) δ Singlets 2.73 (3H), 4.97 (2H, 7.23(5H), multiplets 6.97 (3H), 8.12 (1H). (Found: C, 71.33; H, 5.22; N, 10.48. Calc. for $C_{16}H_{14}N_2O_2$: C, 72.18; H, 5.26; N, 10.53%).

Compound **4**: Obtained directly from photolysis or by warming **2a** in 5% methanolic KOH for 20 min, evaporation and treatment of the residue with H_2O, yield of hydrolysis 90%, m.p. 197–198°; IR(KBr) 3200–2700, 1690, 1480, 1390, 1350, 1190, 880, 750, 700, 630 cm^{-1}; NMR($CDCl_3$) δ Singlets 4.98 (2H), 7.22 (5H), 10.58 (1H), multiplet 6.85 (4H).

3 - *Benzoyl* - 1 - *benzylbenzimidazolone* (**2b**) *and* **4** *from* **1b**. The products were separated by fractional crystallization as in **1a** above. time: 8 hr (lamp); yields: **2b** (29%), **4** (12%); 45 hr (sun); yields: **2b** (37%), **4** (15%). **2b**: m.p. 146–7°; IR(KBr) 1740, 1690, 1370, 1160, 875, 750, 695, 665 cm^{-1}; NMR ($CDCl_3$) δ 4.93 (2H, s), 7.35 (14H,m). (Found: C, 77.03; H, 4.77; N, 8.52. Calc. for $C_{21}H_{16}N_2O_2$: C, 76.83; H, 4.88; N, 8.54%). Hydrolysis of **2b** by the same method used for **2a** produced **4** in 90% yield.

1 - (α - *Phenylacetyl*) 3-*benzoylbenzimidazolone* (**2c**) *from* **1d**. time: 3.5 hr (lamp); yield: **2c** (9%); 24 hr (sun); yield: **2c** (10%). m.p.: 150°; IR(KBr) 1740, 1690, 1470, 1320, 1160, 1050, 765, 690 cm^{-1}; NMR($CDCl_3$) δ Singlet 4.4 (2H), multiplets 7.33 (10H), 7.66(3H), 8.21 (1H). (Found: C, 73.54; N, 4.40; H, 7.77. Calc. for $C_{22}H_{16}N_2O_3$: C, 74.16; H, 4.49; N, 7.86%). Hydrolysis in 5% methanolic KOH produced benzimidazol-2-one.

1 - *Benzyl* - 2,3 - *quinoxalinedione* (**5**, R_1 = H, R_2 = CH_2Ph) *from* **1c**. time: 2.5 hr; yield: 21%; m.p.: 270–272°; IR(KBr) 3550–3350, 1680, 1600, 1300, 710 cm^{-1}; NMR ($CDCl_3$) δ singlets 5.37(2H), 7.1 (4H), 7.27 (5H), 12.03 (1H). (Found: C, 70.86; H, 4.83; N, 10.96. Calc. for $C_{15}H_{12}N_2O_2$: C, 71.43; H, 4.76; N, 11.11%).

1 - *Benzyl* - 4 - *phenyl* - 2,3 - *quinoxalinedione* (**5b**) *from* **3c** (R_2 = CH_2Ph in both). time: 14 hr; yield: 17%; m.p.: 262–4°; IR(KBr) 1660, 1590, 1490, 1350, 1320, 810, 760, 665 cm^{-1}; NMR ($CDCl_3$) δ singlet 5.48 (2H), multiplet 7.05 (14H). (Found: C, 76.13; H, 4.77; N, 8.27. Calc. for $C_{21}H_{16}N_2O_2$: C, 76.83; H, 4.88; N, 8.54%).

o - (N - *Formyl* - N - *benzylamino*)*diphenylamine* (**6**) *from* **5b**. Hydrolysis of **5b** (R_1 = Ph, R_2 = CH_2Ph) in 5% methanolic KOH (30 ml) for 20 min on the steam bath produced **6**; yield: 82%; m.p. 110–111° (petroleum spirit 60–80°); IR(KBr) 3295, 1665, 1595, 1480, 1360, 1270, 1080, 915, 830, 740, 700 cm^{-1}; NMR($CDCl_3$) singlets 4.8 (2H, broad), 5.39 (1H), 8.13 (1H), multiplet 6.97 (14H) (Found: C, 79.60; H, 6.20; N, 9.29. Calc. for $C_{20}H_{18}N_2O$: C, 79.47; H, 5.96; N, 9.27%).

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