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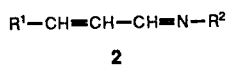
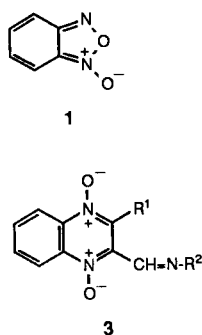
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Benzofuroxan reacts with imines derived from crotonaldehyde and cinnamaldehyde, to form 2-imino-methylquinoxaline 1,4-dioxides.

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The formation of quinoxaline di-*N*-oxides, by reaction of benzofuroxan (BFO) (**1**) with various reagents (ketone enolates, enamines, *etc.*) has been extensively investigated, and reviewed several times [1-4], since the reaction was first discovered in the mid-1960s [5]. The economic importance of the animal feed additive Carbadox (the carboxymethylhydrazone of 2-formylquinoxaline 1,4-dioxide), and the antibacterial properties of many compounds in this area [6], are responsible for the widespread interest in the reaction, the mechanism of which is still uncertain.

Lewis and Kluge reported the reaction of BFO with  $\alpha\beta$ -unsaturated aldehydes and ketones, with base (amine) catalysis, giving quinoxaline monoxides [7]. According to them, the product of the reaction depends on the base used. Thus, BFO reacts with *trans*-4-phenyl-3-buten-2-one in the presence of 1 equivalent of morpholine, in either benzene or acetonitrile at reflux, to give 3-phenylquinoxaline 1-oxide. Use of butylamine gives 3-acetyl-2-phenylquinoxaline 1-oxide, while with ammonia the product is the corresponding 1,4-dioxide.



	R <sup>1</sup>	R <sup>2</sup>
a	Ph	Ph
b	Ph	<i>p</i> -C <sub>6</sub> H <sub>4</sub> Me
c	Ph	<i>p</i> -C <sub>6</sub> H <sub>4</sub> OMe
d	Ph	Me
e	Ph	<i>t</i> Bu
f	Me	<i>t</i> Bu

We have investigated the behaviour of cinnamaldehyde and crotonaldehyde imines towards BFO. Interestingly, the normally inert C=C bond of these imines is involved in the reaction, giving quinoxaline 1,4-dioxide aldimines. The direct generation of aldehyde derivatives in a reaction of this type is, so far as we are aware, unprecedented, although there are many examples of 2-quinoxalinyll ketones being formed [7-9].

#### Results and Discussion.

The reaction between equimolar proportions of BFO (**1**) and cinnamylidene aniline (**2a**) was carried out by refluxing the reactants in dry benzene for one hour, followed by keeping the mixture for one week at room temperature. On work-up a yellow crystalline solid was obtained, mp 187-190° in 50% yield, along with a small amount of black polymeric material.

Analytical and spectral data (ir, nmr, ms) were all compatible with the quinoxaline dioxide structure (**3a**) for the yellow product. The ir showed bands at 1350 (N<sup>+</sup>-O<sup>-</sup>), 1600 (quinoxaline ring) and 1625 cm<sup>-1</sup> (C=N). The <sup>1</sup>H nmr spectrum showed a singlet at  $\delta$  8.86 for the azomethine proton, and a low-field 2H multiplet ( $\delta$  8.72) can be assigned to the overlapping signals of the protons (H-5,8) adjacent to the N-oxide functions. The mass spectrum showed a weak molecular ion (M<sup>+</sup>), another for (M<sup>+</sup>-17); the base peak was at (M<sup>+</sup>-33).

The reaction was extended to other conjugated imines **2b-d**, yielding the corresponding 3-phenylquinoxaline dioxide aldimines **3b-d**.

Although we were not able to isolate the unsaturated *N-t*-butyl aldimines **2e,f**, reaction *in situ* of cinnamaldehyde, *t*-butylamine and BFO gave the *t*-butyliminomethyl compound **3e** in 40% yield, and use of crotonaldehyde in place of cinnamaldehyde gave the corresponding 3-methyl aldimine **3f** (52%). Use of benzylamine and isopropylamine in place of the *t*-butylamine in the *in situ* reactions with BFO and crotonaldehyde or cinnamaldehyde led to no well-characterised product.

#### EXPERIMENTAL

Melting points were taken in open capillary tubes on a Büchi apparatus and are uncorrected. The nmr spectra were recorded in deuteriochloroform on a Varian 100 MHz spectrometer at the University of East Anglia; chemical shifts are recorded in  $\delta$  units (ppm relative to TMS as the internal standard). Mass spectra were determined on a Kratos MS25 instrument. The ir spectra were of samples in Nujol, measured using a Perkin-Elmer Model 297 IR spectrometer.

Light petroleum refers to the fraction bp 60-80°.

## Preparation of Conjugated Imines.

Cinnamylidene arylamines **2a-c** were prepared by warming ethanolic solutions of equimolar quantities of freshly distilled cinnamaldehyde with the arylamines. The imines separated on cooling, in ca 90% yield, and were recrystallised from ethanol.

Cinnamylidene methylamine (**2d**).

Equimolar proportions of cinnamaldehyde and methylamine (33% ethanolic solution) were mixed at 0°, and the reaction mixture was kept at 5-10° for 4 hours. Evaporation of the ethanol under reduced pressure left a syrupy liquid which was distilled under vacuum (120°/2 mm Hg). The distillate solidified to a crystalline mass, mp 43-45° (20%). Much high-boiling/polymeric material remained in the distillation flask; <sup>1</sup>H nmr: δ 3.25 (3H, d, J 1.6 Hz, N-CH<sub>3</sub>), 6.5-7.2 (7H, m, PhCH=CH), 7.70 (1H, dq, J 6.5, 1.6 Hz, CH=N). The spectrum always showed traces of an aldehyde peak at δ 9.43 (d, J 7 Hz); a satisfactory analysis was not obtained.

Reaction Between BFO (**1**) and Cinnamylideneaniline (**2a**). 3-Phenyl-2-(phenyliminomethyl)quinoxaline 1,4-Dioxide (**3a**).

BFO (1.36 g, 0.01 mole) and cinnamylideneaniline (2.07 g, 0.01 mole) were heated under reflux in dry benzene (30 ml) for 1 hour. The mixture was then allowed to stand at room temperature for one week. Black polymeric material which separated out during this period was filtered off. On removal of benzene under vacuum, a dark brown sticky mass was obtained. This was triturated several times with dry ether (5 x 10 ml). The ether extracts were combined and the solvent was removed, to leave a brown solid which after repeated crystallisation from benzene-light petroleum gave a yellow crystalline solid (1.70 g, 50%), mp 187-190°; <sup>1</sup>H nmr: 6.87 (2H, m), 7.27 (3H, m), 7.52 (5H, m), 7.93 (2H, m), 8.72 (2H, m), 8.86 δ (1H, s); ms: m/z 341 (3%, M<sup>+</sup>), 324 (31), 308 (100); ir: 1350, 1600, 1625 cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>: C, 73.8; H, 4.5; N, 12.3. Found: C, 73.9; H, 4.4; N, 12.3.

2-(4-Methylphenyliminomethyl)-3-phenylquinoxaline 1,4-Dioxide (**3b**).

The reaction was carried out as above, using equimolar proportions of BFO and cinnamylidene-*p*-toluidine, but with an initial reflux period of ½ hour. Crystallisation from benzene-light petroleum gave the yellow dioxide (1.92 g, 52%), mp 189-191°; <sup>1</sup>H nmr: δ 2.32 (3H, s); 6.83 (2H, m), 7.13 (2H, m), 7.53 (5H, m), 7.96 (2H, m), 8.75 (2H, m), 8.92 (1H, s); ms: m/z 355 (2%, M<sup>+</sup>), 338 (17.5), 322 (100); ir: 1348, 1599, 1622 cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>22</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>: C, 74.4; H, 4.8; N, 11.8. Found: C, 74.3; H, 4.8; N, 11.9.

2-(4-Methoxyphenyliminomethyl)-3-phenylquinoxaline 1,4-Dioxide (**3c**).

Equimolar proportions of cinnamylidene-*p*-anisidine and BFO were refluxed ½ hour in benzene (30 ml), and then allowed to stand 4 days at room temperature. Crystallisation from benzene-light petroleum gave the yellow imine (1.93 g, 50%), mp 193-194°; <sup>1</sup>H nmr: δ 4.9 (3H, s), 6.88 (2H, m), 7.10 (2H, m), 7.52 (5H, m), 7.94 (2H, m), 8.70 (2H, m), 8.90 (1H, s); ir: 1352, 1600, 1625 cm<sup>-1</sup>; ms: m/z 371 (5%, M<sup>+</sup>), 355 (15), 354 (18), 330 (100).

*Anal.* Calcd. for C<sub>22</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: C, 71.2; H, 4.6; N, 11.3. Found: C, 71.0; H, 4.6; N, 11.4.

2-(Methyliminomethyl)-3-phenylquinoxaline 1,4-Dioxide (**3d**).

Equimolar proportions of BFO (1.36 g) and *N*-cinnamylidene-methylamine (**2d**) (1.45 g) were kept at 20° in dry diethyl ether (50 ml) for 5 days. The product **3d** separated as a yellow crystalline solid (1.72 g, 62%), mp 172-173° after recrystallization from benzene-light petroleum; <sup>1</sup>H nmr: δ 3.33 (3H, d), 7.47 (5H, m), 7.92 (2H, m), 8.88 (2H, m), 8.54 (1H, q); ir: 1348, 1600, 1648 cm<sup>-1</sup>; ms: m/z 281 (19%, M<sup>+</sup>), 266 (27), 249 (84), 234 (100%).

*Anal.* Calcd. for C<sub>16</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>: C, 68.8; H, 4.7; N, 15.05. Found: C, 68.8; H, 4.6; N, 15.1%.

Reaction Between Cinnamaldehyde, *t*-Butylamine, and Benzo-furoxan. 2-(*t*-Butyliminomethyl)-3-phenylquinoxaline 1,4-Dioxide (**3e**).

Cinnamaldehyde (0.87 g, 6.6 mmoles) was stirred for 5 hours at 20° with *t*-butylamine (0.44 g, 6 mmoles) in dried diethyl ether (40 ml), over molecular sieves (14 g). The solution was decanted off and cooled to 0°, and to it was added BFO (0.56 g, 4.1 mmoles). The reaction mixture was kept for 3 days at room temperature. The yellow solid which separated was recrystallised (carbon tetrachloride-light petroleum), providing 2-(*t*-butyliminomethyl)-3-methylquinoxaline 1,4-dioxide (**3e**) as yellow crystals, mp 175-177° (0.53 g, 40%); <sup>1</sup>H nmr: δ 1.92 (9H, s), 7.57 (5H, m), 7.90 (2H, m), 8.85 (2H, m), 8.49 (1H, s); ir: 1350, 1600, 1648 cm<sup>-1</sup>; ms: m/z 321 (2%, M<sup>+</sup>), 305 (12), 304 (16), 77 (100).

*Anal.* Calcd. for C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>: C, 71.0; H, 5.9; N, 13.1. Found: C, 71.2; H, 5.8; N, 13.1.

2-(*t*-Butyliminomethyl)-3-methylquinoxaline 1,4-Dioxide (**3f**).

The reaction was carried out using molar proportions as above, but with crotonaldehyde (0.46 g) in place of the cinnamaldehyde, and the reaction mixture was kept for 1 week at 5-10°. The yellow product (0.56 g, 53%, from carbon tetrachloride-light petroleum) had mp 145-147°; <sup>1</sup>H nmr: δ 1.96 (9H, s), 2.96 (3H, s), 7.85 (2H, m), 8.16 (2H, m), 8.46 (1H, s); ir: 1349, 1600, 1648 cm<sup>-1</sup>; ms: m/z 259 (18%, M<sup>+</sup>), 244 (9), 243 (10), 78 (100).

*Anal.* Calcd. for C<sub>14</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>: C, 64.9; H, 6.6; N, 16.2. Found: C, 64.6; H, 6.6; N, 16.2%.

No product was isolated when benzylamine or isopropylamine were used as the amine in the above reaction.

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## REFERENCES AND NOTES

- [1] A. J. Boulton and P. B. Ghosh, *Adv. Heterocyclic Chem.*, **10**, 12 (1969).
- [2] K. Ley and F. Seng, *Synthesis*, 415 (1975).
- [3] M. J. Haddadin and C. H. Issidorides, *Heterocycles*, **4**, 767 (1976).
- [4] A. Gasco and A. J. Boulton, *Adv. Heterocyclic Chem.*, **29**, 306 (1981).
- [5] M. J. Haddadin and C. H. Issidorides, *Tetrahedron Letters*, 3253 (1965).
- [6] J. K. Landquist, *J. Chem. Soc.*, 2816 (1953); J. K. Landquist and G. J. Stacey, *ibid.*, 2822 (1953).
- [7] G. S. Lewis and A. F. Kluge, *Tetrahedron Letters*, 2491 (1977).
- [8] M. J. Haddadin, M. U. Taha, A. A. Jarrar, and C. H. Issidorides, *Tetrahedron*, **32**, 719 (1976).
- [9] A. F. Kluge, M. L. Maddox, and G. S. Lewis, *J. Org. Chem.*, **45**, 1909 (1980); *ibid.*, **46**, 2603 (1981).