Synthesis of 1-Hydroxyquinoxalin-2(1*H*)-one 4-*N*-Oxides

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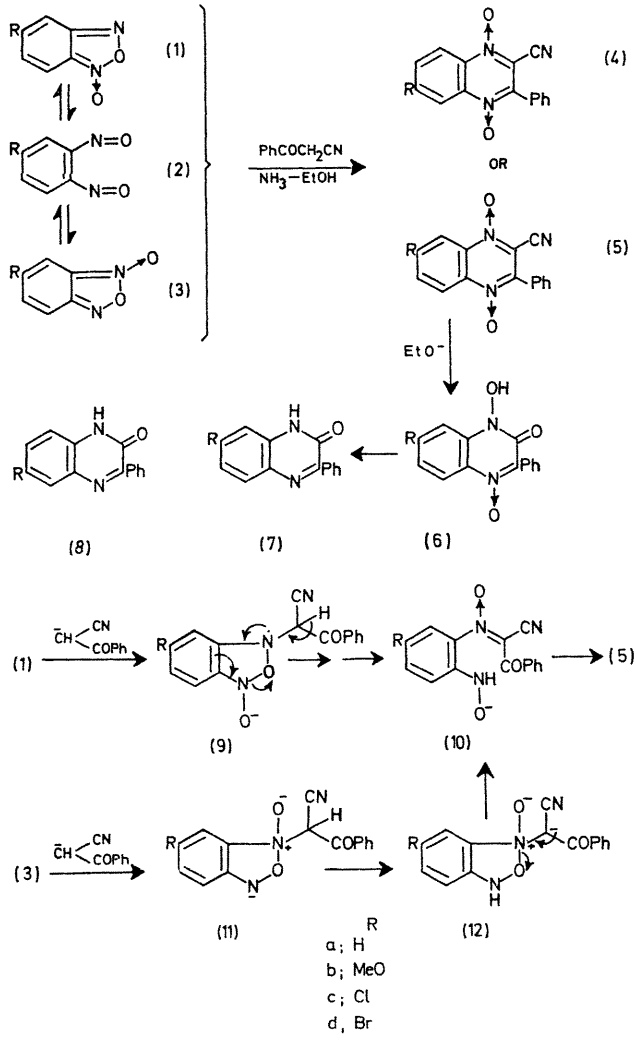
Summary Benzofuroxan and its 5-substituted derivatives condense with benzoylacetonitrile in ethanolic ammonia to yield the corresponding 2-cyano-3-phenylquinoxaline 1,4-di-*N*-oxides which are smoothly converted in warm ethanolic sodium ethoxide into 1-hydroxyquinoxalin-2-(1*H*)-one 4-*N*-oxides: the course of these reactions is discussed.

RECENTLY, two research groups[1,2] have reported an elegant general route to quinoxaline 1,4-di-*N*-oxides involving the base-catalysed condensation of benzofuroxans with active methylene compounds. The mechanisms of these interesting reactions have not been elucidated, but it might be



expected that, because of their tautomeric structure,[3] substituted benzofuroxans would afford an isomeric mixture of two quinoxaline di-*N*-oxides. We now describe a synthetic route to 1-hydroxyquinoxalin-2(1*H*)-one 4-*N*-oxides (required in connection with other studies[4]) which provides some information on this point.

Benzofuroxan (**1a**) condensed readily with benzoylacetonitrile in ethanolic ammonia at room temperature to give the quinoxaline di-*N*-oxide (**5a**) (Table). In accord with the assigned structure, warm ethanolic sodium ethoxide converted this product, with loss of the cyano-group,[5] into the cyclic hydroxamic acid (**6a**) (Table) which gave a deep red colour[5] with iron(III) chloride in ethanol and was converted in warm acetic anhydride into an acetoxy-derivative (**6a**; OAc for OH) with a characteristic[6] carbonyl i.r. band at 1800 cm^{-1} (cyclic :N·OAc). The substituted benzofuroxans (**1b—d**) also condensed readily with benzoylacetonitrile in ethanolic ammonia, but contrary to expectations a single product was formed (Table) in each case. A careful examination of the ^1H n.m.r. spectra of the crude products failed to reveal the presence of isomerides. The substituted di-*N*-oxides so obtained are formulated (Table) as (**5b—d**) rather than (**4b—d**) on the basis of their conversion (warm ethanolic sodium ethoxide) into the corresponding cyclic hydroxamic acids (**6b—d**) (Table) dithionite reduction of which afforded the quinoxalones (**7b—d**). The latter products were non-identical with the quinoxalones (**8b—d**) of established orientation[4,7] and showed ^1H n.m.r. absorption in accord with the assigned structures.

Quinoxaline di-N-oxides and 1-hydroxyquinoxalin-2(1H)-one 4-N-oxides[a]

	Yield(%)	M.p. (°)
(**5a**)	70	208
(**5b**)	74	223
(**5c**)	75	218
(**5d**)	59	216
(**6a**)	67	196
(**6b**)	76	243
(**6c**)	76	228
(**6d**)	81	231

[a] Satisfactory analyses and spectral data were obtained for all new compounds.

Ring-opening of adducts (**9**) formed by nucleophilic attack at N-3 in the benzofuroxans (**1**), and cyclisation of the resulting hydroxylamino-nitrone intermediates (**10**) is a possible course for formation of the di-*N*-oxides (**5**). This mechanism is in accord with reaction of a 5(6)-substituted benzofuroxan in the more stable[8] tautomeric form (**1**). An alternative course [(**3**) → (**11**) → (**12**) → (**10**)] initiated by nucleophilic attack at N-1 is also possible[1] but would require reaction of a 5(6)-substituted benzofuroxan in the less stable form (**3**). Preferential nucleophilic attack at the 3-nitroso-group in the dinitroso-tautomers (**2b—d**) would also account for the formation of the di-*N*-oxides (**5b—d**). However, it is unlikely that the implied deactivation of the 4-nitroso-group by the substituent would be sufficient—especially in the halogeno-tautomers (**2c—d**)—to account for the predominant attack at the 3-nitroso-group

demanded by the observed orientation (**5c—d**) in the products.

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