RING CONTRACTION OF 2-AZIDOQUINOLINE- AND QUINOXALINE-1-OXIDES

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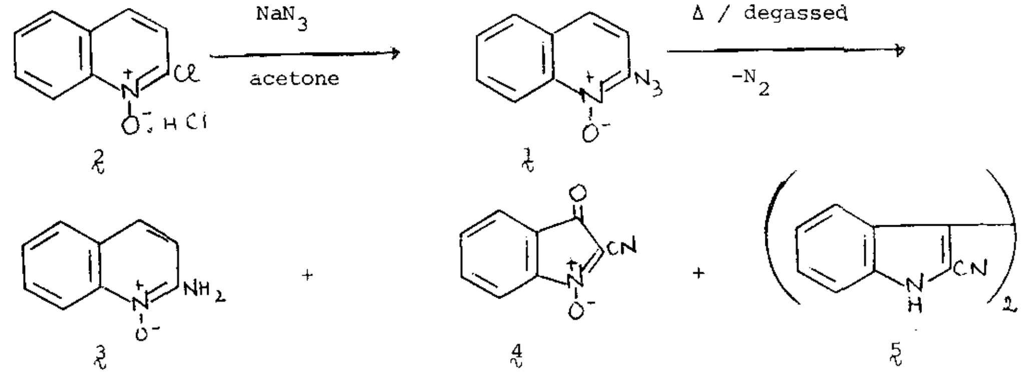
2-Azidoquinoline-1-oxide undergoes thermal ring-opening, intermolecular nucleophilic addition and ring contraction to give 2-aminoquinoline-1-oxide, 2-cyanoisatogen (**4**), and 2,2'-dicyano-3,3'-bisindole (**5**). If the 4-position in the quinoline is blocked then the expected ring-contractions take place: 2-azidolepidine-1-oxide gives 2-cyano-*N*-hydroxy-3-methylindole, while 2-azidoquinoxaline-1-oxide gives 2-cyano-1-hydroxybenzimidazole. Syntheses of authentic **4** and **5** are reported.

We have recently shown[1] that thermolysis of 2-azido-pyridine- and pyrazine-1-oxides in benzene gives the corresponding 2-cyano-*N*-hydroxy-pyrroles and imidazole in good yields. The reaction proceeds *via* an open chain unsaturated intermediate which has been intercepted by nucleophilic solvents. We now report extensions of this ring-contraction to bicyclic systems. These are of particular interest since *N*-hydroxyindole derivatives are of potential value in medicinal chemistry.

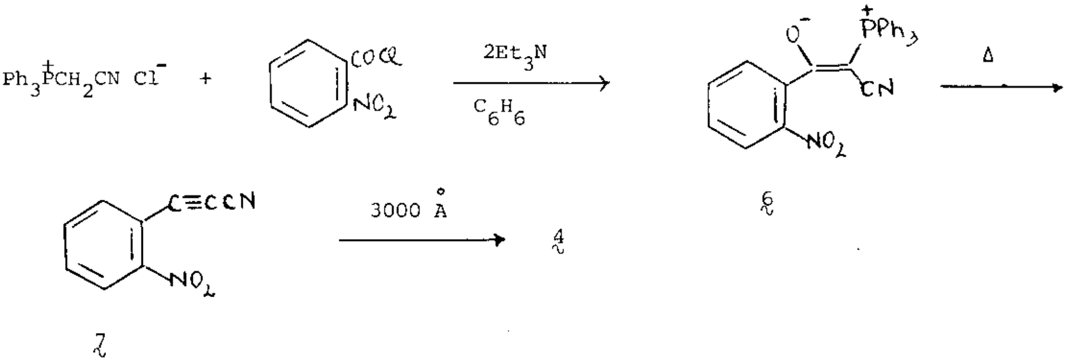
The preparation of 2-azidoquinoline-1-oxide (**1**) (as its hydrate) from

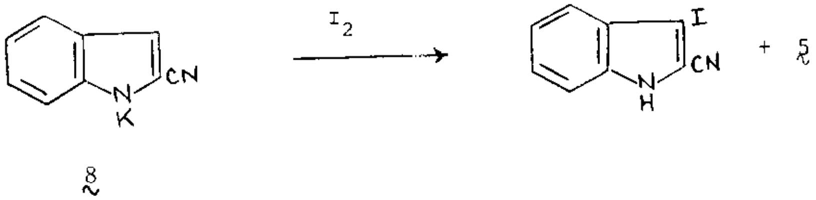
2-chloroquinoline-1-oxide (2) in hot methanol has been reported.[2] Repetition of this procedure led to a mixture of azide and mainly decomposition products, as expected on the basis of our previous work.[1] Reaction of 2 hydrochloride with azide ion in aqueous acetone at 25° did give pure 1 (58%) (not a hydrate), mp 103-104°. Thermolysis of 1 in toluene at 100° gave a mixture of 2-aminoquinoline-1-oxide (3) (22%), mp 155-157°,[3] 2-cyanoisatogen (4) (21%), mp 199-201° (dec.), and 2,2'-dicyano-3,3'-bisindole (5) (21%), mp 184° (dec.). Thermolysis of 1 in boiling methanol readily gave 3 (32%), 4 (15%), and 5 (28%). The structures of the products followed from their analytical and spectroscopic properties and were confirmed by the synthesis of authentic samples.[4]



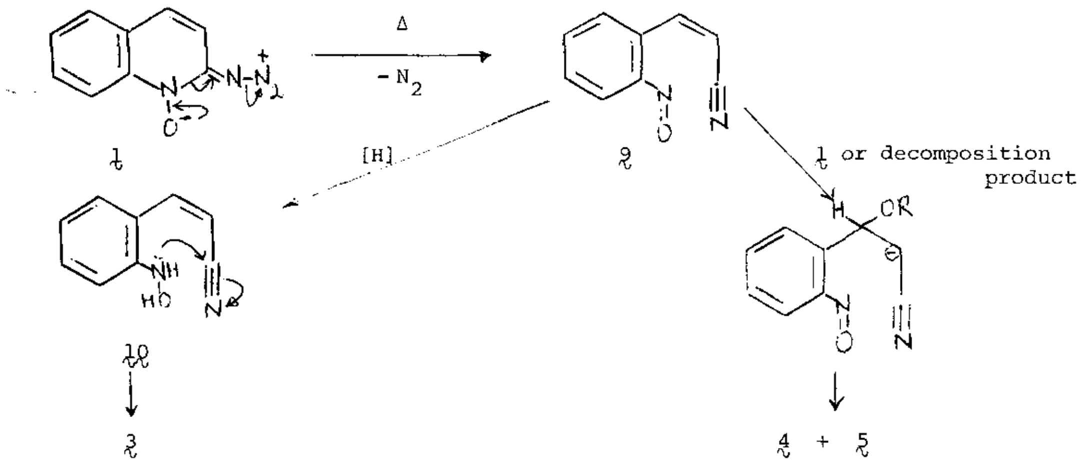
Treatment of α-cyanomethyltriphenylphosphonium chloride with o-nitrobenzoyl chloride and two equivalents of triethylamine in benzene gave α-cyanotriphenylphosphonium-o-nitrophenacylide (6) (87%), mp 128° (dec.), which, on pyrolysis at 260°/5mm, gave o-nitrophenylpropiolonitrile (7) (18%) (yellow oil). Irradiation of 7 with 3000 Å light (Pyrex filter) gave 4 (48%) as a bright red solid, identical with the product obtained from 1.

Potassio-2-cyanoindole (8) was treated with iodine to give a mixture of *5 (22%) and a trace of 2-cyano-3-iodoindole.* The bisindole 5 was identical with the product obtained from the azide.

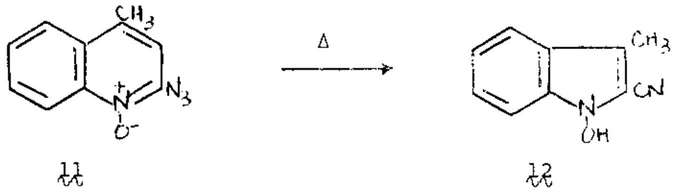


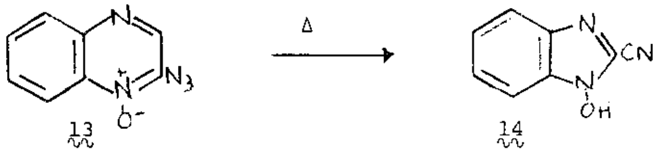


The mechanism for the formation of 3, 4, and 5 from 1 will be discussed in the full paper. We do not believe, however, that a free nitrene is formed in this or the related decompositions of 2-azidopyridine-1-oxides, in view of the low thermolysis temperature required. The amine 3, which is the expected product of hydrogen-abstraction by a 2-nitreno derivative, probably arises by the reduction of the intermediate open-chain unsaturated nitroso-derivative (9) to the hydroxylamine (10), followed by recyclization to give 3. A number of possible pathways can be written leading from 9 to 4 and 5 *via* a dihydro-intermediate which serves as the reducing agent for 9 to 10. It appears reasonable that a nucleophilic addition of an oxygen atom (from the starting *N*-oxide, nitroso-derivative, or ring-contracted product) to the α,β-unsaturated nitrile system in 9 leads to the formation of 4 (there is no other source of oxygen), and that this addition competes very effectively with the electrocyclic ring-closure of 9 (destruction of aromaticity of the benzene ring in the transition state) so that no 2-cyano-*N*-hydroxyindole



was formed. If, then, such a nucleophilic addition could be slowed down, intramolecular cyclization should occur readily. This has now been achieved. 2-Azidolepidine-1-oxide (**11**), mp 99-100° gave, on thermolysis in toluene, 2-cyano-*N*-hydroxy-3-methylindole (**12**) (45%), mp 130-131°, and no product related to **3**, **4** or **5**. Similarly,[5] thermolysis (or even recrystallization) of 2-azidoquinoxaline-1-oxide (**13**) gave 2-cyano-1-hydroxybenzimidazole (**14**), mp 236°, (*O*-tosylate, mp 112-114°), identical with a sample prepared by the procedure of Livingstone and Tennant.[6]





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3 A.R. Katritzky, *J. Chem. Soc.*, 4385 (1957).

4 All new compounds gave satisfactory microanalytical and spectral data.

5 A group at ICI, Plant Protection Division, Jealott's Hill, England, has achieved the same ring-contraction of **13** (Private communication to R.A.A.).

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