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THE ISOMERISATION OF ANTHRAQUINONYL AMIDES TO OXAZIRIDINES - A REINVESTIGATION.

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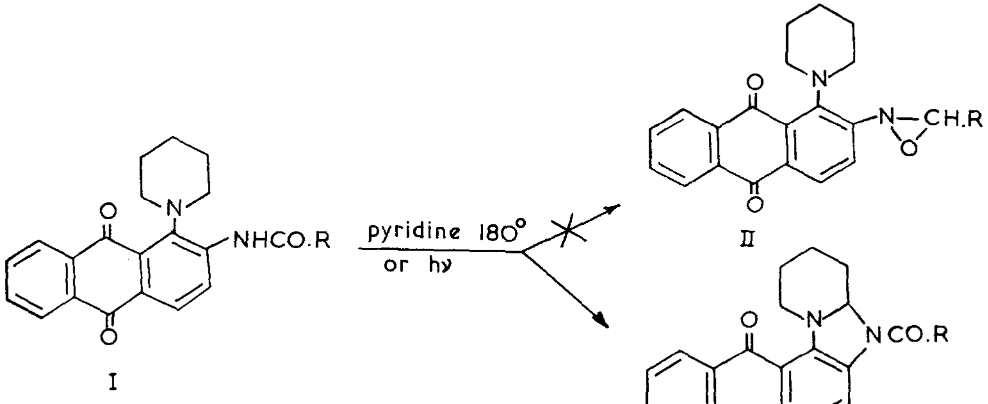
Russian workers[1] recently proposed a surprising new route to the oxaziridine system by the quantitative thermal or photochemical isomerisation of an amide. They substantiated their claim by empirical analysis, infrared spectroscopy, unambiguous synthesis and chemical reactivity of the products. The systems employed were the 1-piperidino-2-acylamino-anthraquinones (I). We now propose that the products are in fact the (non-isomeric) N-acyldihydroimidazoanthraquinones (III), not the oxaziridines (II).



a; R = CH_3
b; R = Ph

The same workers[2] had earlier demonstrated that under the above reaction conditions, the simple 1-dialkylaminoanthraquinones (e.g. IV) cyclise to the oxazines (V)*, for which we propose the mechanism shown (Scheme I) by analogy with numerous other reactions of

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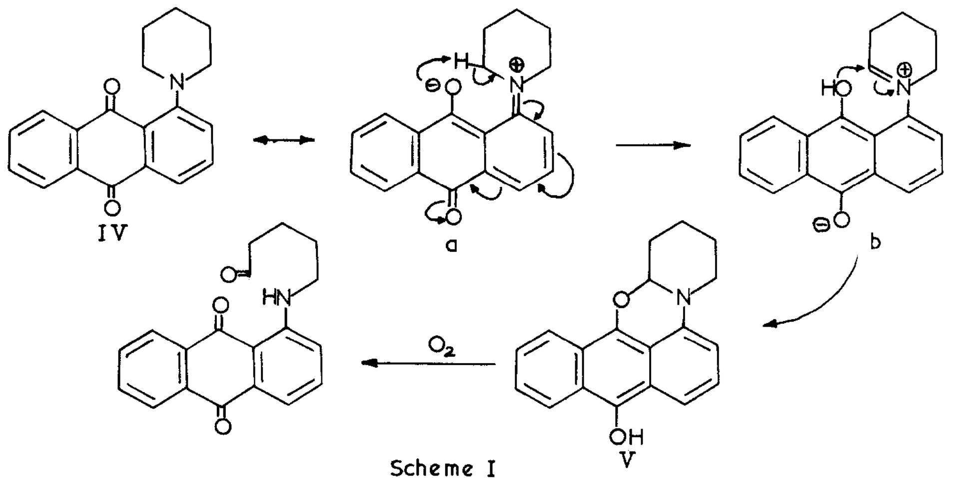
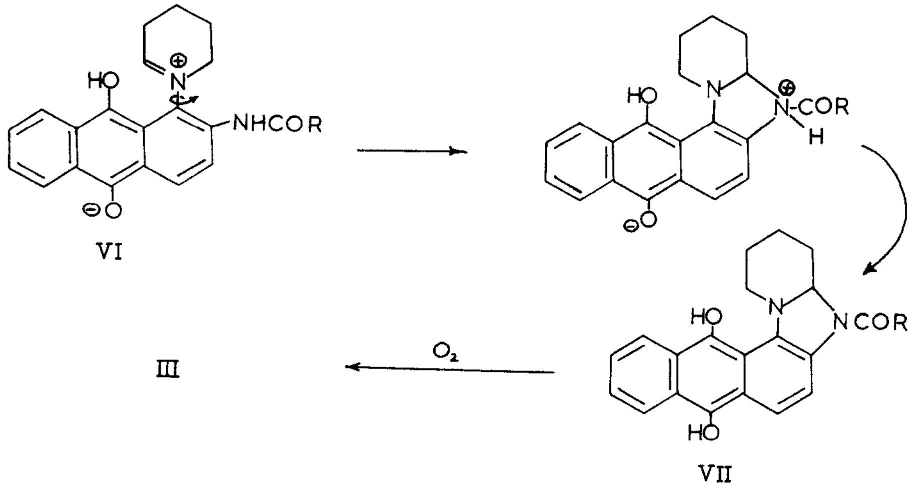
* Reports that the changes taking place in textiles dyed with this compound on exposure to light are due to photo-reduction, may need re-interpreting in the light of this observation.[4]



Scheme I

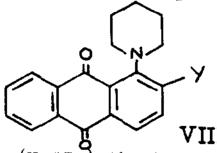
this general type.[3] We now conclude that the present reaction is basically analogous to that shown in scheme 1 but that the mesomeric immonium ion (VI) is capable of reaction with the ortho substituent (the acylamino group) instead of the anthraquinone oxygen. In the sealed-tube reactions the oxidation (VII→III) only takes place on opening the tube to the atmosphere when very rapid aerial oxidation is observed. Thus the benzoyl compound gives a bright red precipitate of VII which on short exposure to the atmosphere rapidly becomes purple with oxidation to the anthraquinone (III).



The n.m.r. spectra of the products were unequivocal. Thus in the acetyl compound (IIIa) (Figure) the methyl absorption was a singlet (not a doublet as would be the case in (IIa)) and the remaining nine aliphatic protons clearly showed that the piperidine ring was substituted in the 2-position. The 2-axial and 6-equatorial and 6-axial protons were distinct from the remaining six protons and the proposed assignments were substantiated by double irradiation experiments. The 6-equatorial proton is considerably deshielded by its proximity to the carbonyl group. Similar results were obtained with the benzoyl compound.

We found that the thermal reactions did not give quantitative conversions under the conditions quoted by the Russian workers, which may account for their erroneous empirical analysis* and some of their chemical reactions designed to prove the oxaziridine structure. Thus the lithium aluminium hydride reduction was reported to give the 2-benzylamino derivative. However the properties of dihydroimidazoles is such[5] that the benzylamino compound could result from acid-catalysed disproportionation of the N-benzyldihydroimidazole during work up.

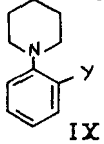
The Russian workers endeavoured to prove the oxaziridine structure (II) by the well-known peracid oxidation of the corresponding anil (VIIIa) with 20% peracetic acid in pyridine, giving the required compound in 22% yield. In our hands careful separation(PLC) of the products from this reaction (using three different mixtures of 20% peracetic acid each having variable amounts of water/acetic acid) gave only very low yields of III and no oxaziridine II and up to nine other products including benzaldehyde, benzoic acid, the amine (VIIIb) the benzoyl compound (Ib) and the acetyl compound (Ia)! The sterically hindered anil (VIIIa) hydrolysed very readily and gave the amine as the major product in aqueous conditions while the benzoyl derivative (Ib) (probably derived by hydrolysis of the true oxaziridine) was the main product under anhydrous conditions. Both the anil[6] (IXa) and the benzoyl[7] derivative (IXb) have been shown to undergo cyclisations to benzimidazoles (X) with peracid and the trace of cyclised compound could arise in an analogous way. However the benzoyl derivative (Ib) was unchanged on treatment with peracid under the above conditions.



VIII

a; Y = N=CHPh

b; Y = NH_2



IX

a; = Y = N=CHPh

b; Y = NHCOPh

Finally, this reaction is capable of considerable utility by varying the ortho substituent (Y in VIII) with different nucleophiles. Thus the amine (VIIIb) on heating in

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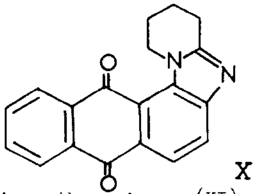
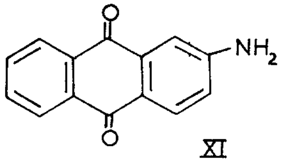
*Their analysis for the cyclised benzoyl compound is better for the structure (IIIb) than (IIb) pyridine at 180° for 10 hrs. was converted quantitatively into a mixture of the benzimidazole



X



XI

(X) and 2-aminoanthraquinone (XI), the latter product possibly arising by action of the dihydroimidazole intermediate (known to be powerful reducing agents[5]) on the starting compound. These reactions are under active investigation.

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