Benzimidazole *N*-Oxides: Photochemical Rearrangement and Reaction with Acylating Agents and Nucleophiles

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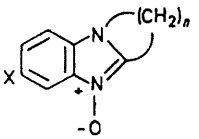
Summary 1,2-Polymethylenebenzimidazole *N*-oxides undergo substitution in the benzene ring by the combined action of an acid chloride and various nucleophiles (*e.g.* Cl, CN, SCN, and N_3) and rearrange to 1,3-polymethylenebenzimidazolones with tosyl chloride and sodium hydroxide or by photolysis of the *N*-oxide in methanol.

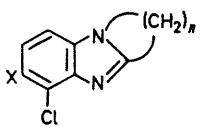
WE have recently shown[1] that benzimidazole *N*-oxides (I) are readily prepared by the action of boiling hydrochloric acid on *o*-nitro-*NN*-dialkyl anilines. We now find that prolonged action of hot hydrochloric acid gives instead of the *N*-oxide (I), a chloro-substituted benzimidazole (II).

The reaction is accelerated by heating the *N*-oxide hydrochloride in aqueous potassium chloride solution. This suggests that the process is a nucleophilic substitution with elimination of OH^- from the protonated *N*-oxide and it is reminiscent of an S_N2' mechanism in which the substrate is ·C : C·N·X, analogous to the allylic ·C : C·CR_2X. As expected, the reaction occurs even more readily when the *N*-oxide oxygen is made part of a better leaving group. Thus with phosphorus oxychloride in hot chloroform, the *N*-oxide (Ib; $n = 3$) gives the products (IIb and IIIb, $n = 3$; 30 and 69%, respectively), the latter predominating probably for steric reasons. The higher homologues (I; $n = 4$—7) produced corresponding results with this and other reagents such as tosyl chloride. For example,

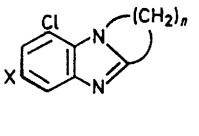
reaction of CN^- and SCN^- at room temperature with the *N*-oxide (Ib; $n = 5$) gave the products (IVa) (20%) and



(I)
a; X = H



(II)
b; X = NO_2

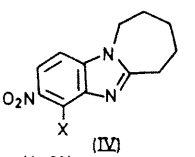


(III)
c; X = Cl

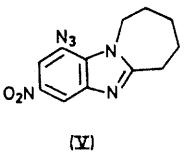
(IVb) (60%) while N_3^- produced the azide (V) (66%) and furoxan (VI) (33%). The latter arose presumably by concerted loss of nitrogen from the corresponding nitroazide. The furoxan (VI) was also obtained from the chloronitrobenzimidazole (IIb; $n = 5$) and sodium azide, substantiating this view. With Br^-, I^-, and EtS^-, reduction of the *N*-oxide was the sole reaction. However with OH^- as the nucleophile and tosyl chloride at room temperature a novel rearrangement was observed. Thus the *N*-oxides (I; $n = 5$—7) were transformed into the benzimidazolones (VII) some in good yield as shown in the Table, which also contains relevant spectral data. The high degree of strain in the benzimidazolones is borne out by the decrease in intensity of the highest-wavelength absorption in the u.v. spectrum, and increase in the carbonyl stretching frequency in the i.r. spectrum (*cf.* Table). The structures are further supported by the reduction product (VIII) obtained by action of lithium aluminium hydride on the benzimidazolone (VIIa; $n = 5$). No identifiable products were, however, obtained from the lower homologues (I; $n = 3$ and 4) under these conditions, but 2-ethyl-1-propylbenzimidazole 3-oxide gave 3-ethyl-1-propylbenzimidazolone (57%) by this method.

The mechanism of this rearrangement is best explained by attack of OH^- at the 2-position of the tosylated *N*-oxide (IX) followed by a concerted loss of the tosyloxy-group with rearrangement either directly to the benzimidazolone (path a) or *via* the oxaziridine (X) (path b).

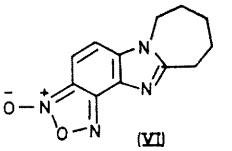
To test the feasibility of route (b) we subjected the *N*-oxides (I) to photolysis in methanol, when by analogy



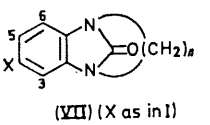
(IV)
a; X = CN
b; X = SCN



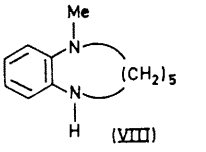
(V)



(VI)



(VII) (X as in I)



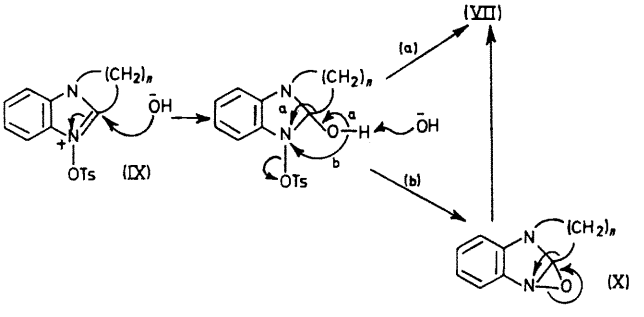
(VIII)

with other heteroaromatic *N*-oxides, the oxaziridine could be invoked as the intermediate of any further reaction.[2] In fact, Ogata, Matsumoto, Takahashi, and Kano[3] have very recently photolysed a 1,2-dialkylbenzimidazole *N*-oxide and isolated, amongst other products a 1,3-dialkylbenzimidazolone. Photolysis of the *N*-oxides (I) gave as expected the corresponding benzimidazolones (VII) with comparable yields (see Table) to those obtained from the previous method.

Properties of the benzimidazolones (VII) *derived from the* N-*oxide* (I) *with tosyl chloride and* NaOH (i) *or by photolysis* (ii)

Compound	M.p.	Yield (%) (i)	Yield (%) (ii)	I.r. (Nujol)[a] ν_{max} (CO) (cm^{-1})	U.v. (MeOH)[a] λ_{max} (nm)	ϵ	N.m.r. (τ, $CDCl_3$)[b]
(VIIc; $n=5$)	112°	35	41[c]	1735	219	22,210	Ar H's, 2·7—3·0; *N*-CH_2's, 5·60 br. tr. and 6·22 br.d;
					289	3181	$(CH_2)_3$, 8·1—9·2
(VIIc; $n=6$)	105°	85	66[d]	1730	221	21,270	Ar H's, 2·75—3·15; *N*-CH_2's 5·75c and 6·3c; $(CH_2)_4$,
					293	5303	7·8—9·8c.
(VIIc; $n=7$)	143°	13	low	1710	221	23,090	Ar H's, 2·7—3·15; *N*-CH_2's 5·5 br. and 6·2 br.d;
					293·5	6336	$(CH_2)_5$, 8·1—8·8.
(VIIb; $n=5$)	131°	55	—	1750	228	14,980	Ar H's: H-3, 1·97d (J 2Hz); H-5, 1·77 dd (J 8·5 and
					318	6494	2 Hz) H-6, 2·70d (J 8·5 Hz); *N*-CH_2's, 5·52 br. tr. and 6·1 br. d; $(CH_2)_3$ 8·1 —8·8.
(VIIa; $n=5$)	81°	23	—	1735	215	17,410	Ar H's: 2·98; *N*-CH_2's, 5·75 br. tr. and 6·35 br.d;
					281	2816	$(CH_2)_3$, 8·3—8·9.

[a] *Cf.* 1-Ethyl-3-propylbenzimidazolone which shows a band at 1700 cm^{-1} (CO), and in the u.v., bands at 219 (18,670) and 292 nm (6974).
[b] br = broad; c = complex; d = doublet; tr = triplet.
[c] Together with 16% (IIc; $n=5$) and 15% 5-chloro-6-methoxy-1,2-pentamethylenebenzimidazole.
[d] Together with 22% (IIc; $n=6$).



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[2] M. Ogata, H. Matsumoto, S. Takahashi, and H. Kano, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 964.
[3] C. Kanecko, *J. Synth. Org. Chem.* (*Japan*), 1968, 758.