Syntheses of Heterocyclic Compounds. Part XXVI.[1] Photo-rearrangements of Benzimidazole *N*-Oxides and Related Systems

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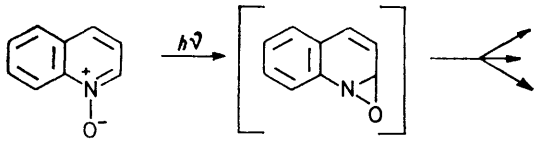
2,3-Dialkyl- and 2,3-polymethylene-benzimidazole 1-oxides are shown to rearrange when irradiated in neutral solution to give 1,3-dialkyl- and novel 1,3-polymethylene-benzimidazolones. The scope and mechanism of this rearrangement are discussed. Analogous 2,3-polymethylenequinoline 1-oxides and quinazolone 1-oxides react differently.

NUMEROUS reports of the photolysis of heteroaromatic *N*-oxides have appeared; in most cases these invoke an oxaziridine intermediate (*cf.* Scheme 1), although no

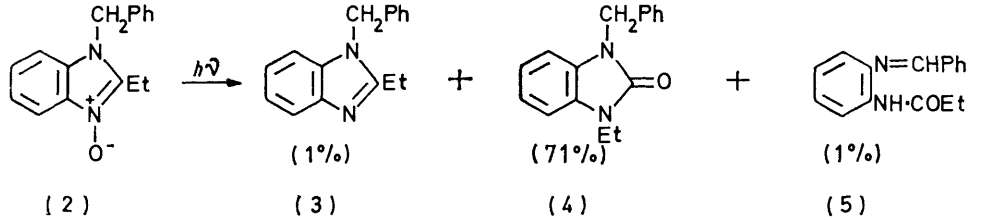


(1)

SCHEME 1

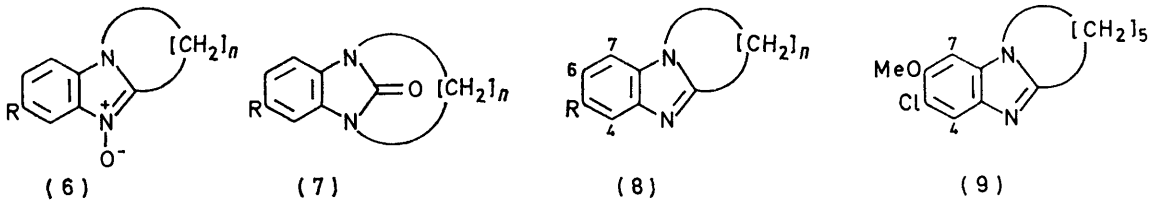
such intermediate has yet been isolated.[2] While our work on benzimidazole photolysis was in progress, Ogata and his co-workers [3] reported the formation of a benzimidazolone (4) together with traces of other products [(3) and (5)] from irradiation of the *N*-oxide (2). In view of our earlier results [1] we irradiated a range of benzimidazole *N*-oxides in pure methanol solution with a Hanovia medium-pressure lamp in a Pyrex cooling jacket. In general, reactions were complete within 24 h as judged by u.v. spectroscopy. Each of the benzimidazole *N*-oxides (6; R = H or Cl, $n = 5$—7) gave the corresponding benzimidazolone (7) in high yield together with some deoxygenated product (8) (Table). In one case (6; R = Cl, $n = 5$) ring substitution by the solvent, as described earlier,[1] was observed to a small extent to give compound (9). When *N*-oxides containing fewer than five methylene groups were irradiated they were generally unchanged. Also, while 1,2-dimethylbenzimidazole 3-oxide gave only tar on irradiation, the higher dialkyl *N*-oxide (10) gave the expected benzimidazolone (11) (55%).

The formation of the benzimidazolones follows the known type of rearrangement of *N*-oxides under irradiation and a reasonable mechanism is shown in Scheme 2. Thus, 2-methylquinoline *N*-oxide has been shown to give *N*-methylquinolin-2(1*H*)-one amongst the products,[4] and the cyclic analogues (12; $n = 3$ or 4) afforded

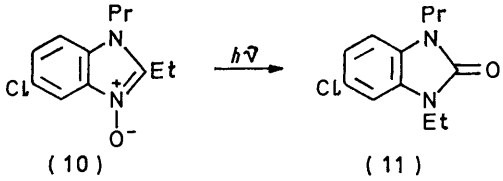


(1%) (71%) (1%)

(2) (3) (4) (5)



(6) (7) (8) (9)



(10) (11)

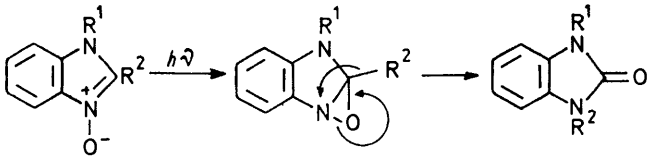
[1] Part XXV, preceding paper.

[2] (*a*) G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev.*, 1970, **70**, 231; (*b*) C. Kanecko, *J. Synth. Org. Chem.* (*Japan*), 1968, 758.

[3] M. A. Ogata, H. Matsumoto, S. Takahashi, and H. Kano, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 964.

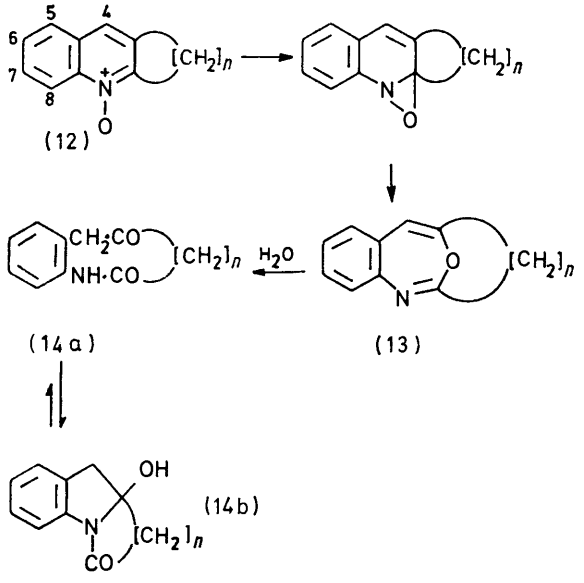
[4] M. Ishikawa, S. Yamada, H. Hotta, and C. Kanecko, *Chem. and Pharm. Bull.* (*Japan*), 1966, **14**, 1102.

products (14a and b) the formation of which was rationalised in terms of an intermediate oxaziridine and



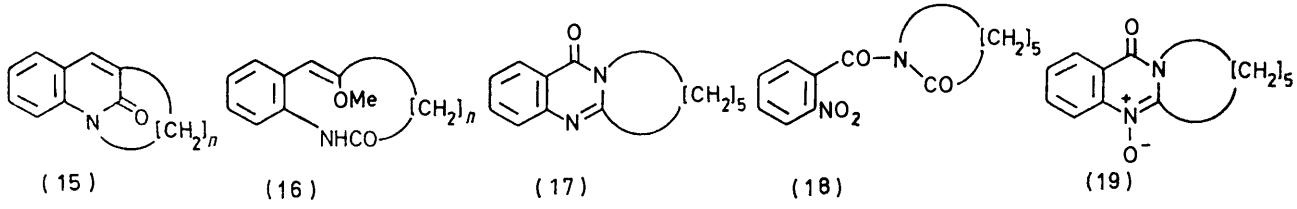
SCHEME 2

the oxazepine (13)[5] (Scheme 3). Because of our results we prepared the analogue (12; $n = 6$) in the



SCHEME 3

hope that photoisomerisation to the polymethylenequinolone (15) could be induced. The starting material was readily formed by a Pfitzinger-type condensation[6] of isatin with cyclo-octanone and subsequent decarboxylation of the acid so formed to give the 2,3-hexamethylenequinoline, which readily formed the *N*-oxide (12; $n = 6$) with peracetic acid. Irradiation did not yield the cyclophane (15) but gave the two products (14a; $n = 6$) and (16), which probably result from the action of water or methanol on the intermediate oxazepine (13; $n = 6$). As a closer analogue of the benzimidazole *N*-oxide system we prepared the quinazolone (17) from isatoic anhydride and ε-caprolactam by Späth's procedure.[7] This compound was not convertible into its *N*-oxide by use of a variety of oxidising methods, which consistently gave *N*-(2-nitrobenzoyl)-ε-caprolactam (18). However, hydrogenation of the nitro-compound (18) over palladium–charcoal in the presence of 1 mol. equiv. of hydrochloric acid produced the required *N*-oxide (19). Irradiation of this compound gave only the quinazolone (17).



EXPERIMENTAL

Photo-reactions were conducted with a Hanovia 200 W medium-pressure lamp with a Pyrex cooling jacket (AnalaR methanol as solvent). I.r. spectra were obtained with a Perkin-Elmer 137 or 337, n.m.r. with a Varian A60A or HA100, and mass spectra with an A.E.I. MS12 instrument. Column chromatography was performed with type H alumina (Hopkin and Williams). Light petroleum was the fraction of b.p. 60—80°.

Irradiation of Benzimidazole N-Oxides (6).[1] The *N*-oxide (1 g) in AnalaR methanol (300 ml) was irradiated in a nitrogen atmosphere for 24 h. The solution was evaporated to dryness; the residue was taken up in a little benzene and chromatographed on alumina with first benzene, then chloroform, as eluant. Details are given in the Table.

2,3-Hexamethylenequinoline N-Oxide (7,8,9,10,11,12-Hexahydrocyclo-octa[b]quinoline N-Oxide) (12; $n = 6$).—Isatin (3 g), cyclo-octanone (2·65 g), and potassium hydroxide (6 g) in water (20 ml) and ethanol (20 ml) were boiled under reflux for 12 h. The solution was poured into water (200 ml) and acidified, and the white precipitate of 2,3-hexamethylenequinoline-4-carboxylic acid (4·2 g) was filtered off, washed, and dried. The crude acid was decarboxylated by heating at 280° for 10 min. The residue was extracted with ether and the extract dried, treated with charcoal, and filtered. Sublimation of the product (2·8 g) *in vacuo* gave 2,3-hexamethylenequinoline, m.p. 57° (lit.,[6] 59°). The quinoline (2·11 g, 0·01 mol) in acetic acid (3 ml) and hydrogen peroxide (0·9 ml; 28%) was heated at 70° for 6 h. More hydrogen peroxide (0·8 ml) was added and the solution was maintained at 70° for a further 6 h. The resulting mixture was poured into water (30 ml), neutralised with sodium hydrogen carbonate, and extracted with chloroform (5 × 30 ml). Evaporation of the extract gave the N-*oxide* (12; $n = 6$) (1·9 g) as needles (from aqueous ethanol), m.p. 114° (Found: C, 76·8; H, 7·7; N, 5·8. $C_{15}H_{17}NO,0{\cdot}5H_2O$ requires C, 76·3; H, 7·7; N, 5·9%), τ ($CDCl_3$) 1·14 (dd, *J* 9·0 and 2·0 Hz, H-8), 2·02—2·59 (H-4 to H-7), 6·57 (t, *J* 6·5 Hz, 2-CH_2), 7·09 (t, *J* 6·5 Hz, 3-CH_2), and 7·79—8·83 ($[CH_2]_4$).

Irradiation of 2,3-Hexamethylenequinoline N-Oxide (12; $n = 6$).—The *N*-oxide (1·5 g) in methanol (300 ml) was

[5] (*a*) C. Kanecko, S. Yamada, and M. Ishikawa, *Chem. and Pharm. Bull. (Japan)*, 1969, **17**, 1290; (*b*) C. Kanecko, S. Yamada, I. Yokoe, and M. Ishikawa, *Tetrahedron Letters*, 1967, 1873.

[6] P. Jacquignon and N. P. Buu-Hoï, *J. Org. Chem.*, 1957, **22**, 72.

[7] E. Späth and M. Platzner, *Ber.*, 1935, **68B**, 935, 2221.

irradiated for 24 h and the oily residue obtained on evaporation chromatographed on alumina. Elution with benzene gave 3,4,5,6,7,8-*hexahydro*-9-*methoxy*-1-*azabenzocyclododecin*-2(1H)-*one* (16; $n = 6$) (0·37 g, 22%), m.p. 97°, white needles (from light petroleum), $\nu_{max.}$ (Nujol) 3360 (NH) and 1720 (CO) cm^{-1} (Found: C, 73·9; H, 8·3; N, 5·1. $C_{16}H_{21}NO_2$ requires C, 74·1; H, 8·2; N, 5·4%), τ ($CDCl_3$) 2·25—3·02 (4H, m, aromatic), 1·60—2·11br (NH), 3·72 (1H, s, =CH), 6·32 (3H, s, OMe), 7·12—7·50 (2H, m, $CO{\cdot}CH_2$), 7·51—7·94 (2H, m, $=C{\cdot}CH_2$), and 8·00—9·32 (8H, m, $[CH_2]_4$). Further elution with ethyl acetate gave 1,3,4,5,6,7,8,10-*octahydro*-1-*azabenzocyclododecin*-2,9-*dione* (14a; $n = 6$) (1·2 g, 75%) as white crystals (from ethyl acetate), m.p. 226° (Found: C, 73·0; H, 8·1; N, 5·4. $C_{15}H_{19}NO_2$ requires C, 73·5; H, 7·8; N, 5·7%), τ ($CDCl_3$) 2·52—2·83 (4H, m, aromatic), 2·76—3·02br (NH), 5·97 (2H, s, $ArCH_2$), 7·29—7·76 (4H, m, 2 × $CO{\cdot}CH_2$), and 7·91—8·83 (8H, m, $[CH_2]_4$).

Oxidation of 7,8,9,10-*Tetrahydro*-6H-*azepino*[2,1-b]*quinazolin*-12-*one* (17).—(*a*) The quinazolinone [7] (1 g) in acetic acid (5 ml) at 60° was treated with two successive portions of hydrogen peroxide (1 ml; 28%) at six-hourly intervals and worked up as before to give only starting material. (*b*) When 90% hydrogen peroxide was employed, work-up gave *N*-(*o*-nitrobenzoyl)-ε-caprolactam (18) as a pale yellow solid (0·55 g), m.p. 118°, as needles from ethanol (lit.,[8] 119·5—120°).

Reduction of N-(o-*Nitrobenzoyl*)-ε-*caprolactam*.—The lactam [8] (2·62 g) and hydrochloric acid (5 ml; d 1·18) in ethanol (60 ml) containing palladium–charcoal (1 g; 5%) was hydrogenated at room temp. and pressure (uptake 448 ml, 2 mol. equiv.). The mixture was filtered and the filtrate evaporated to dryness. The residue was treated with saturated aqueous sodium hydrogen carbonate and extracted with chloroform (3 × 20 ml). The extract (2·5 g) was chromatographed on alumina. Elution with benzene gave the quinazolinone (17) (0·4 g); elution with ethyl acetate gave starting material (0·3 g). Finally, elution with chloroform gave the *quinazolinone* N-*oxide* (19) (1·6 g), m.p. 176° (from acetone) (Found: C, 67·8; H, 6·4; N, 12·3. $C_{13}H_{14}N_2O_2$ requires C, 67·8; H, 6·1; N, 12·2%), τ ($CDCl_3$) 1·31 (1H, dd, J 9·0 and 2·0 Hz, H-4), 1·48—2·48 (3H, m, H-1, -2, -3), 6·02—6·33 (2H, m, $N{\cdot}CH_2$), 6·28—6·63 (2H, m, $C{\cdot}CH_2$), and 7·82—8·32 (6H, m, $[CH_2]_3$).

Irradiation of the Quinazolinone N-*Oxide* (19).—The *N*-oxide (1·5 g) in methanol (300 ml) was irradiated for 96 h in the usual way. Work-up gave the quinazolinone (17) (1·3 g).

Products from the irradiation of the benzimidazole *N*-oxides (6)

N-Oxide (6) R	*n*	Product	Yield (%)	M.p. (°C)	ν_{CO}(Nujol)/ cm^{-1}	U.v.(MeOH) $\lambda_{max.}$	ε	Found (%) C	H	N	Required (%) C	H	N	M^+	τ($CDCl_3$) (J in Hz)
Cl	4	(6)	20 *												
H	5	(6)	42												
		(7)	25	81	1735	215	17,410	70·9	6·7	13·4	71·3	7·0	13·9	202	†
		(8)	32	124 [a]		281	2816								
Cl	5	(6)	12												
		(7)	44	112	1735	219	22,210	60·4	5·3	11·8	60·9	5·5	11·9	236/238	†
		(9)	15	164		289	3181	61·8	6·0	11·1	62·3	6·0	11·2		2·29 (s, H-4), 3·22 (s, H-7), 5·78—6·06 ($N{\cdot}CH_2$), 6·79—71·0 ($C{\cdot}CH_2$), 7·90—8·47 ($[CH_2]_3$), 6·03 (OMe).
		(8)	16	107 [b]											†
Cl	6	(7)	66	105	1730	221	21,270	62·1	5·8	11·1	62·3	6·0	11·2	250/252	
		(8)	22	117		293	5303	66·1	6·6	12·1	66·5	6·4	11·9		2·24 (s, H-4), 2·75 (s, H-6, -7), 5·72 (t, J 6·0, $N{\cdot}CH_2$) 6·94 (t, J 6·0, $C{\cdot}CH_2$), 7·85—8·94 ($[CH_2]_4$).
Cl	7	(7)	low	143				64·0	6·0	10·2	63·5	6·5	10·6	264/266	†

* Much tar formed. † See following paper. ‡ K. H. Saunders, *J. Chem. Soc.*, 1955, 3275.
[a] Lit.,‡ 125—126°. [b] Lit.,‡ 107—109°.

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[8] G. Reinisch, *Faserforsch. Textiltech.*, 1962, **13**, 549.

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