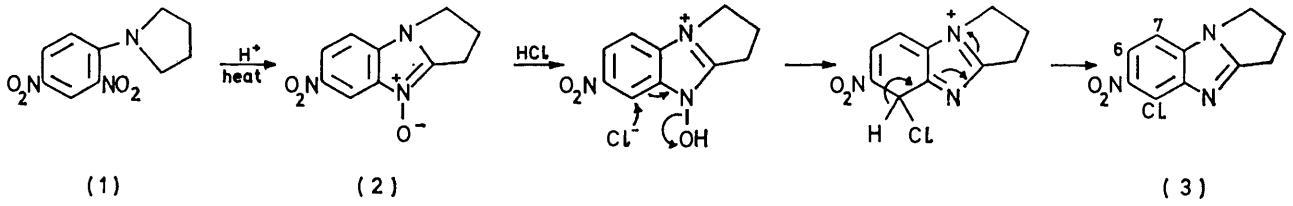
Syntheses of Heterocyclic Compounds. Part XXVII.[1] Substitution Reactions and Rearrangements of Benzimidazole *N*-Oxides

By **Rae Fielden, Otto Meth-Cohn,** and **Hans Suschitzky,*** Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, Lancashire

Treatment of benzimidazole *N*-oxides with a variety of nucleophiles results in ring substitution with concomitant loss of the *N*-oxide oxygen atom. Thus, reactions with HCl, KCl, $SOCl_2$, SO_2Cl_2, and various organic acid chlorides yield various chlorinated isomers. The co-action of toluene-*p*-sulphonyl chloride and the nucleophiles CN^-, SCN^-, N_3^-, butane-1-thiol, butylamine, or aniline results in ring substitution, whereas co-action with the nucleophiles Br, I, and butane-1-thiolate causes deoxygenation only. With toluene-*p*-sulphonyl chloride and alkali a novel rearrangement to *NN'*-polymethylenebenzimidazolones occurred in the case of some *N*-oxides. These reactions are rationalised and are shown to have considerable synthetic utility.

PREPARATION of benzimidazole *N*-oxides by treatment of *NN*-disubstituted *o*-nitroanilines [1a] with hot hydrochloric acid produced in one case a ring-chlorinated benzimidazole as a by-product. This was also formed from the *N*-oxide under the same reaction conditions oxidisable acid such as hydrobromic acid is used, halogenation is not observed and the major product from the *N*-oxide is the corresponding benzimidazole, obtained together with a small amount of the ring-brominated and reduced compound (6).



(1) (2) (3)

SCHEME 1

(Scheme 1). A chlorinated by-product (5) was also observed from the photocyclisation of an analogous pyridine derivative (4) (Scheme 2), and in all cases the reaction is conveniently rationalised in terms of an S_N2' nucleophilic substitution with all its modifications.[2] Thus, ring substitution by the chloride ion is concerted with loss of OH^- from the protonated *N*-oxide, as borne out by a closer investigation of the reaction in Scheme 1

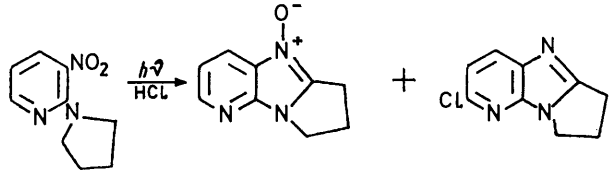
TABLE 1

Reactions of the pyrrolidine (1) and the benzimidazole *N*-oxide (2)

Substrate	Reagent	Time (h)	Yield (%) of (1)	(2)	(3)
(1)	Const. boiling HCl (110°)	20	46·5	32	11
(1)		92		44	35
(1)		144			64
(2)		144			78
(2), HCl	Water	168		80	20
(2), HCl	Sat. aqueous KCl	24		72	28

(Table 1). The amount of the chlorobenzimidazole (3) formed increases with reaction time at the expense of the *N*-oxide, and increasing the nucleophilicity of the solvent steps up the rate of *N*-oxide chlorination. The possibility that the chlorination is due to chlorine (produced through oxidation of the acid by the *N*-oxide) is discounted since the parent benzimidazole is unaffected after 168 h boiling in hydrochloric acid in the presence of pyridine *N*-oxide. When a more readily

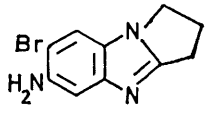
The availability of the chloronitrobenzimidazole (3) made a study of its synthetic potential attractive as



(4) (5)

SCHEME 2

illustrated by the synthesis of polyheterocycles in Scheme 3. The condensation of compound (3) with



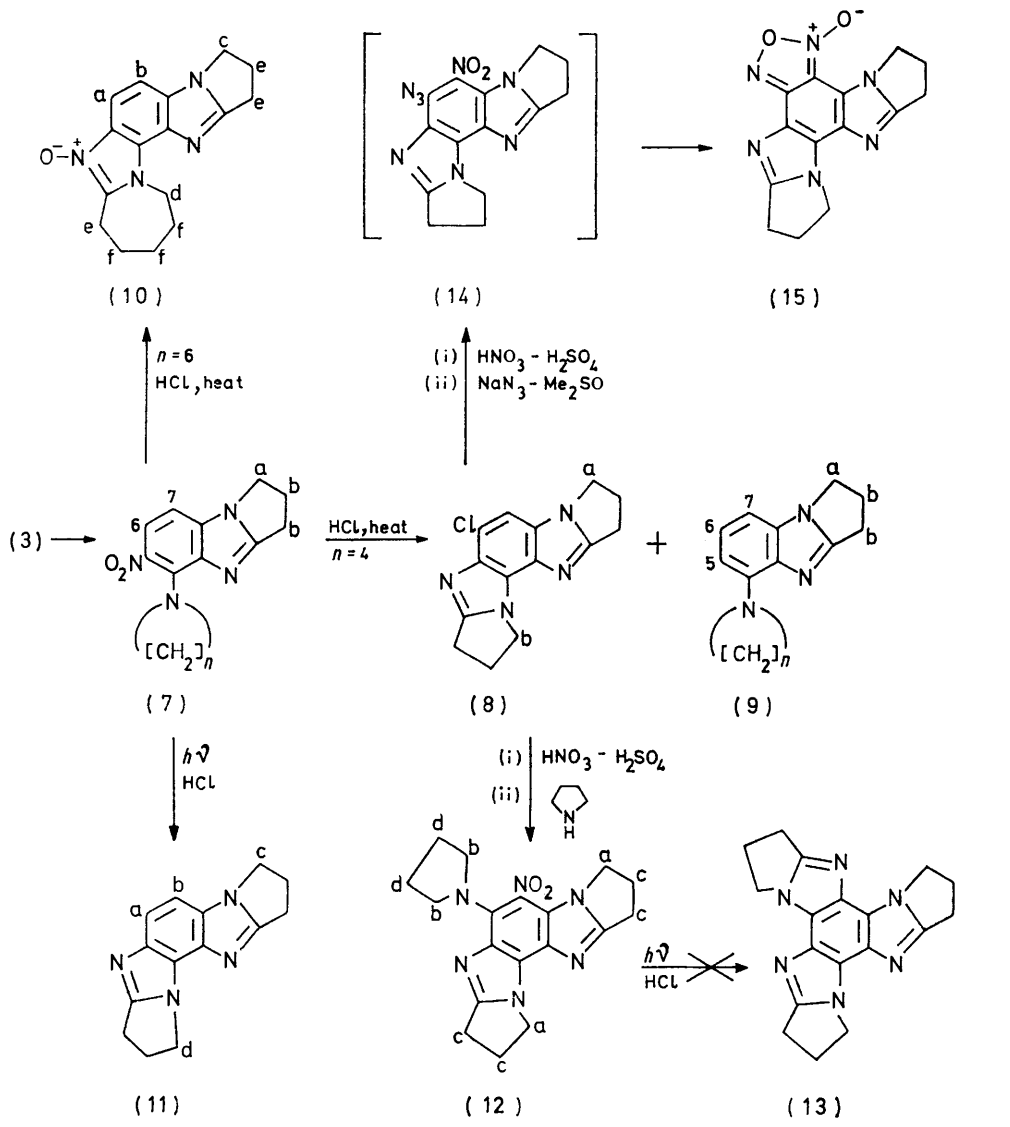
(6)

bases proceeded readily, as did the subsequent cyclisation, the thermal route giving the chloro-di-imidazole (8) directly with the pyrrolidine (7; $n = 4$); the perhydroazepinyl analogue gave the expected *N*-oxide (10). In both cases some denitration occurred [*e.g.* (9)]. Attempts to synthesise the tri-imidazole (13) were, however, unsuccessful at the last cyclisation stage. This difficulty was not due to annulation problems, since the furoxan (15) was formed readily when the chloro-nitro-di-imidazole was treated with sodium azide.

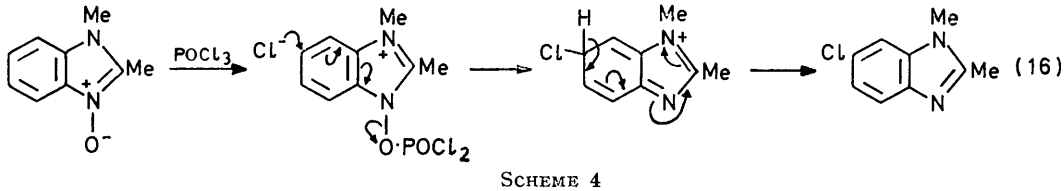
[1] (*a*) Part XXVI, preceding paper; (*b*) Part XXV, R. Fielden, O. Meth-Cohn, and H. Suschitzky, *J.C.S. Perkin I*, 1973, 696.

[2] F. G. Bordwell, *Accounts. Chem. Res.*, 1970, **9**, 281.

Examples of the S_N2'-type reaction of benzimidazole *N*-oxides have been briefly examined by Takahashi and Kano.[3] They observed, for example, that 1,2-dimethylbenzimidazole 3-oxide reacted with phosphoryl chloride



SCHEME 3



SCHEME 4

substitution is influenced considerably by the nature both of the substituent already in the ring and of the reagent used (Table 2). Thus whereas the unsubstituted or 5-chloro-compounds (expts. 1 and 2) underwent solely to give the 6-chlorobenzimidazole (16). We suggest that the reaction sequence may be rationalised according to Scheme 4. Since both nitrogen atoms are capable of bearing the formal charge, all the benzenoid ring positions are in principle capable of being substituted. This we have found to be the case and the position of 6-substitution with $POCl_3$, the 5-nitro-analogue (expt. 3) gave a mixture of 4- and 7-substituted products. Ring size of the saturated ring made little difference (*cf.* expts. 3 and 5) and a variety of inorganic acid chlorides

[3] S. Takahashi and H. Kano, *Chem. and Pharm. Bull.* (*Japan*), 1966, **14**, 1219.

gave similar proportions (*ca.* 2 : 1) of 7- to 4-substitution with the nitro-*N*-oxide (expts. 3, 5, 6, and 7). In each case, the reaction is best envisaged as occurring by attack of the reagent on the oxygen of the *N*-oxide, followed by subsequent reaction according to Scheme 4, the ease of reaction being particularly dependent upon $n = 5$) gave both a ring-substituted product (20; R = CN) (20%) and the α-benzoyloxylated product (19; R = NO_2, $n = 5$, X = BzO) (43%). When the benzoyl chloride was replaced by tosyl chloride the cyano-compound was isolated in similar yield with no other defined product. The action of other anions in conjunction with tosyl chloride was then considered. In every case the interaction of the reagents was accompanied by a transitory red colouration.

TABLE 2

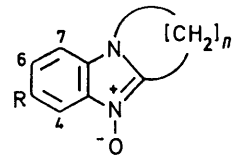
Products from reactions of benzimidazole *N*-oxides (17) with halides

	(17)			(18)			(19)	Others
Expt.	*n*	R	Reagent	4-Cl (%)	6-Cl (%)	7-Cl (%)	X (%)	(%)
1	3	H	$POCl_3$		100			
2	3	Cl	$POCl_3$		100			
3	3	NO_2	$POCl_3$	32		68		
4	3	NO_2	HCl	78				
5	5	NO_2	$POCl_3$	35		65		
6	5	NO_2	SO_2Cl_2	27		55		
7	5	NO_2	$SOCl_2$	35		65		
8	5	NO_2	AcCl				AcO (100)	
9	5	NO_2	BzCl	50			BzO (50)	
10	5	NO_2	4-MeO·C_6H_4·COCl	10			4-MeO·C_6H_4·CO_2 (84)	22 *
11	5	NO_2	TsCl	19		27		7 †
12	5	NO_2	$POBr_3$					‡

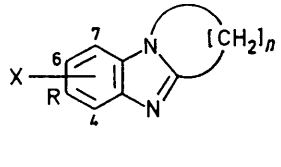
* *p*-Methoxybenzoic anhydride (R. K. Smalley and H. Suschitzky, *J. Chem. Soc.*, 1964, 755). † Compound (26). ‡ Deoxygenation is the sole result.

the leaving group. Organic acid chlorides bring about a second type of substitution [to give compounds of type (19)] which is well known in the pyridine series and has been studied by Takahashi and Kano [3] in the case of simple benzimidazole *N*-oxides. The extent of this reaction is clearly reduced in favour of ring substitution by increase in the anionic stability of the leaving group (see expts. 8—11). Thus *p*-methoxybenzoyl chloride gave a larger proportion (8·4 : 1) of α-attack compared to benzoyl chloride (1 : 1). Unfortunately, *p*-nitrobenzoyl chloride, which would be expected to favour ring substitution, gave only intractable tars. However toluene-*p*-sulphonyl chloride followed the expected trend in that no α-substitution was observed. The variation in the proportion of 4- to 7-ring substitution of the nitro-*N*-oxide with various reagents may be due to differences in the size of the leaving group. The smaller leaving groups such as OH allow substitution at the 4-position, where, presumably, electron density is lowest (between the charged ring and a nitro-group). However with larger groups this electronically preferred position is hindered and attack is directed to the less favoured 7-position. [The structure of the by-product (26) formed in the tosylation experiment was not established at this stage and will be discussed later.]

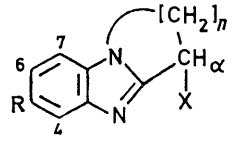
When a reagent with a good potential leaving group and a nucleophile better than the chloride ion is used, the reaction represents a general synthesis of substituted benzimidazoles from their *N*-oxides. This method is applicable to heteroaromatic *N*-oxides in general, and Takahashi and Kano [3] have exploited it with simple benzimidazole *N*-oxides. For example 1,2-dimethylbenzimidazole-*N*-oxide is substituted rapidly by the co-action of benzoyl chloride and potassium cyanide yielding 5-cyano-1,2-dimethylbenzimidazole in high yield. We found that the *N*-oxide (17; R = NO_2,



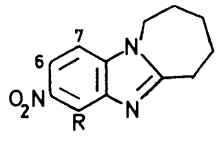
(17)



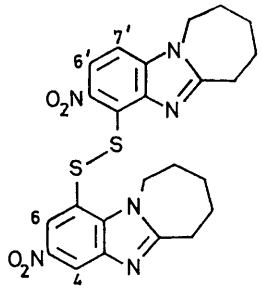
(18)



(19)



(20)



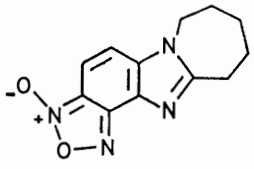
(21)

(22)

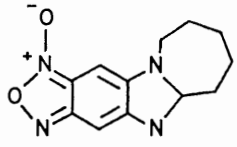
With thiocyanate ion the major product was the expected thiocyanate (20; R = SCN) (60%), obtained together with a yellow amorphous dimeric by-product

to which we have tentatively assigned structure (21) on the basis of its n.m.r. spectrum (see Experimental section). Giles and Parker[4] have shown that 2,4-dinitrofluorobenzene reacts with thiocyanate to give bis-(2,4-dinitrophenyl) disulphide.

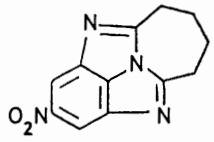
With the azide ion and tosyl chloride, the *N*-oxide (17; R = NO_2, $n = 5$) again gave two products, in the molar ratio 2 : 1, as with several earlier examples (Table 2). The major product was the 7-azidobenzimidazole (22; R = N_3) and the minor proved to be the furoxan (23) (the initially formed 4-azido-compound had cyclised with loss of nitrogen). This was confirmed by the



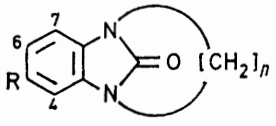
(23)



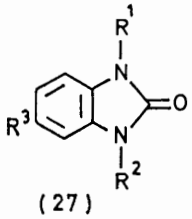
(24)



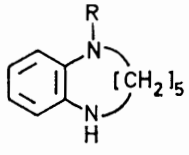
(25)



(26)



(27)

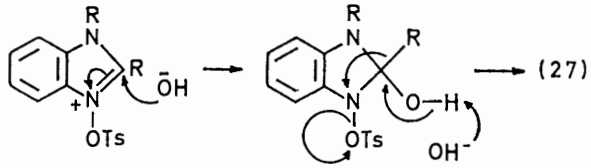


(28)

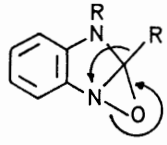
action of sodium azide on the corresponding 4-chloro-compound (20; R = Cl) (see Table 2) in dimethyl sulphoxide at 55°; the same furoxan (23) was formed. Recently the isomeric furoxan (24) has been described[5] and although the m.p. of our product was different from that reported the mass spectra were almost identical. In an attempt to prepare the elusive di-imidazole system (25), the azide (22; R = N_3) was thermally decomposed, liberating the necessary amount of nitrogen and producing a black intractable tar. This is in accord with the findings of Saunders, who obtained similar results from an analogous azide.[6]

With oxidisable anions such as bromide, iodide, and butane-1-thiolate, and tosyloxy as the potential leaving group, the *N*-oxide (17; R = NO_2, $n = 5$) underwent deoxygenation rather than ring substitution. However, butane-1-thiol and tosyl chloride caused only 6% deoxygenation and four other products were isolated, namely the 4-chloro- (20; R = Cl) (27%), the 4-butylthio- (20; R = SBu) (21%), and the 7-chloro-derivative (22; R = Cl) (14%), and an isomer of the *N*-oxide (10%) previously obtained in low yield (expt. 11, Table 2) whose structure is dealt with later. It is surprising that the chloride ion successfully competes against the more nucleophilic butanethiol to the extent of 2 : 1 in product ratio.

The co-action of an acyl halide and hydroxide ion on the *N*-oxide (17; R = NO_2, $n = 5$) was of particular interest. With benzoyl chloride the expected α-benzoyloxy-product (62%) was again obtained, together with a by-product (33%). This by-product was the sole product when tosyl chloride was used with sodium hydroxide, and was identical with the minor compound from the action of tosyl chloride alone and the action of tosyl chloride with butanethiol (see before). It was isomeric with the parent *N*-oxide, showed i.r. carbonyl absorption (1750 cm^{-1}) and was monomeric as shown by both mass spectroscopy and a Menzies-Wright ebullioscopic molecular weight determination. The n.m.r. spectrum (see Table 5) supported the novel benzimidazolone structure (26; R = NO_2, $n = 5$). The same type of product was obtained from a series of *N*-oxides having 1,2-dialkyl or 1,2-polymethylene substituents (containing at least five CH_2 units) (Table 5). The structure (26; R = H, $n = 5$) was confirmed by alkaline hydrolysis to give the known[7] *NN'*-pentamethylene-*o*-phenylenediamine (28; R = H) and by reduction with lithium aluminium hydride to the *N*-methyl analogue (28; R = Me). The considerable strain involved in these structures is indicated by both the u.v. and the i.r. spectra.[1b] With decreasing ring size, the carbonyl absorption frequency increases, demonstrating the steric



(29) (30) (27)



(31) (27)

inhibition of amide mesomerism; this is also shown by a progressive drop in the intensity of the highest wavelength absorption in the u.v. spectrum. In the n.m.r. spectrum the N·CH_2 groups show non-equivalence of the hydrogen atoms, indicating that conformational 'flipping' is slow, and no change was observed up to 120°.

The formation of these novel benzimidazolones can best be rationalised by invoking the tosyloxy-inter-

[4] D. E. Giles and A. J. Parker, *Austral. J. Chem.*, 1970, **23**, 1581.

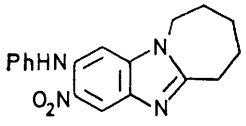
[5] R. C. Perera, R. K. Smalley, and L. G. Rogerson, *J. Chem. Soc. (C)*, 1971, 1348.

[6] K. H. Saunders, *J. Chem. Soc.*, 1955, 3275.

[7] H. Stetter, *Chem. Ber.*, 1953, **86**, 197.

mediate (29), which is attacked by OH^- at the 2-position rather than on the benzene ring. The rearrangement of the 2-substituent is then encouraged by the ready loss of the tosylate anion. Alternatively the intermediate (30) could form the oxaziridine (31), which could then rearrange to the benzimidazolone (27). The step (29) ⟶ (30) is analogous to the well known ring opening of benzimidazoles by the action of an acyl halide and hydroxide.[8]

Finally, the action of amines and tosyl chloride on the *N*-oxide (17; $n = 5$) was investigated. The use of butylamine at room temperature gave a mixture of the 4-butylaminobenzimidazole (20; R = NHBu) (60%) and the benzimidazolone (26; R = NO_2, $n = 5$). With



the weaker base, aniline, no benzimidazolone was formed but a mixture of the 4-anilino- (20; R = NHPh) (90%) and the 6-anilino-benzimidazole (32) (10%) was obtained. This unexpected substitution orientation could arise by means of the hydrogen-bonded assistance by the nitro-group. As mentioned previously, the incoming nucleophile may, in principle, take up any position in the benzene ring; the outcome appears to depend on a delicate balance of electronic, steric, and other factors. The same products were obtained in similar proportions by the action of phenyl isocyanate [3] on the *N*-oxide.

EXPERIMENTAL

Spectra were obtained as in the preceding papers; experimental methods were as previously described.[1]

4-Chloro-1,2-trimethylene-5-nitrobenzimidazole (*5-Chloro-2,3-dihydro-6-nitro-1H-pyrrolo*[1,2-a]*benzimidazole*) (3).—*N*-(2,4-dinitrophenyl)pyrrolidine (1), the *N*-oxide (2), or the hydrochloride of the latter was treated with the appropriate reagent (about seven times the weight of substrate) according to the conditions in Table 1. The reaction mixture was evaporated to dryness, water was added, and the solution was neutralised with sodium hydrogen carbonate. Extraction with chloroform (4 × 100 ml) gave a dark brown product which was chromatographed on alumina. Elution with benzene gave any unchanged material followed by the *chloro-nitro-benzimidazole* (3), recrystallised as yellow needles (from ethyl acetate), m.p. 184° (Found: C, 50·5; H, 3·6; N, 17·5. $C_{10}H_8ClN_3O_2$ requires C, 50·5; H, 3·4; N, 17·7%), M^+ 237/239, τ ($CDCl_3$) 2·20 (d, *J* 9·0 Hz, H-6), 2·77 (d, *J* 9·0 Hz, H-7), 5·78 (t, *J* 7·0, N·CH_2), and 6·68—7·36 (m, CH_2·CH_2).

Reaction of the Benzimidazole (3) *with Bases.*—To the chloro-nitro-compound (4·75 g, 0·02 mol) in ethanol (25 ml) and benzene (25 ml) under reflux, pyrrolidine, piperidine, or perhydroazepine (0·044 mol) was added during 0·5 h. The solution was boiled for 12 h, poured into water (120 ml), and extracted with chloroform (3 × 40 ml). Evaporation of the extract gave the product (7) as an orange solid (95—100%). Recrystallisation from ethanol gave (*a*) the *4-pyrrolidin-1-yl derivative* (7; $n = 4$), m.p. 155° (Found: C, 61·6; H, 5·7; N, 20·3. $C_{14}H_{16}N_4O_2$ requires C, 61·7; H, 5·9; N, 20·6%), τ ($CDCl_3$) 2·27 (d, *J* 9·0 Hz, H-6), 3·45 (d, *J* 9·0 Hz, H-7), 5·92 (t, *J* 7·0 Hz, H_a), 6·21 (t, *J* 7·0 Hz, $N[CH_2]_2$), 6·82—7·46 (m, H_b), and 7·89—8·19 (m, $[CH_2]_2$); (*b*) the *4-piperidino-derivative* (7; $n = 5$), m.p. 193° (Found: C, 63·0; H, 5·9; N, 19·1. $C_{15}H_{18}N_4O_2$ requires C, 62·9; H, 6·3; N, 19·6%), τ ($CDCl_3$) 2·32 (d, *J* 9·0 Hz, H-6), 3·21 (d, *J* 9·0 Hz, H-7), 5·88 (t, *J* 7·0 Hz, H_a), 6·40—6·62 (m, $N[CH_2]_2$), 6·73—7·36 (m, H_b), and 8·14—8·37 (m, $[CH_2]_2$); (*c*) the *4-perhydroazepin-1-yl derivative* (7; $n = 6$), m.p. 131° (Found: C, 63·6; H, 6·7; N, 18·3. $C_{16}H_{20}N_4O_2$ requires C, 64·0; H, 6·7; N, 18·7%), τ ($CDCl_3$) 2·45 (d, *J* 9·0 Hz, H-6), 3·30 (d, *J* 9·0 Hz, H-7), 5·97 (t, *J* 7·0 Hz, H_a), 6·31—6·58 (m, $N[CH_2]_2$), 6·79—7·52 (m, H_b), and 8·07—8·52 (m, $[CH_2]_2$).

2,3,9,10-Tetrahydro-1H,8H-benzo[1″,2″:5,4:3″,4″:5′,4′]*bis-(imidazo*[1,2-a]*pyrrole*) (11).—The pyrrolidine (7; $n = 4$) (3 g) in AnalaR methanol (300 ml) was irradiated with a Hanovia 200 W medium-pressure lamp in a Pyrex cooling jacket for 120 h. Evaporation of the methanol gave the *di-imidazole* (2·9 g) as a white solid, m.p. 303° (from water) (Found: C, 70·4; H, 6·0; N, 23·5. $C_{14}H_{14}N_4$ requires C, 70·6; H, 5·9; N, 23·5%), M^+ 238, τ ($CDCl_3$) 2·38 (d, *J* 8·5 Hz, H_a), 2·83 (d, *J* 8·5 Hz, H_b), 5·47 (t, *J* 7·0 Hz, H_d), 5·84 (t, *J* 7·0 Hz, H_c), and 6·6—7·47 (8H, m).

Acidolysis of the Pyrrolidine (7; $n = 4$) *and the Perhydroazepine* (7; $n = 6$).—The compound (7) (5 g) in hydrochloric acid (50 ml; *d* 1·18) was boiled for 48 h. The solution was evaporated to dryness and water (50 ml) was added. The solution was basified with sodium hydrogen carbonate solution and extracted with chloroform (4 × 60 ml). The extract was dried and evaporated and the residue chromatographed on alumina. From the pyrrolidine (7; $n = 4$), elution with benzene gave first *2,3-dihydro-4-pyrrolidin-1-yl-1H-pyrrolo*[1,2-a]*benzimidazole* (9; $n = 4$) (0·3 g, 7%) as white needles, m.p. 187° (from light petroleum) (Found: C, 73·9; H, 7·4; N, 18·3. $C_{14}H_{17}N_3$ requires C, 74·0; H, 7·5; N, 18·5%), τ ($CDCl_3$) 2·88 (t, *J* 7·5 Hz, H-6), 3·36 (dd, *J* 7·5 and 1·5 Hz, H-7), 3·68 (dd, *J* 7·5 and 1·5 Hz, H-5), 6·00 (t, *J* 7·0 Hz, H_a), 6·21 (t, *J* 7·0 Hz, $N[CH_2]_2$), 6·79—7·56 (m, H_b), and 7·87—8·18 (m, $[CH_2]_2$); then *6-chloro-2,3,9,10-tetrahydro-1H,8H-benzo*[1″,2″:5,4:3″,4″:5′,4′]*bis-(imidazo*[1,2-a]*pyrrole*) (8) (1·9 g, 38%), as white clusters from benzene, m.p. 239° (Found: C, 6·17; H, 4·9; N, 21·0. $C_{14}H_{13}ClN$ requires C, 61·7; H, 4·8; N, 20·5%), τ ($CDCl_3$) 2·77(s), 5·52 (t, *J* 7·0 Hz, H_b), 5·86 (t, *J* 7·0 Hz, H_a), and 6·57—7·55 (8H, m, $[CH_2]_2$).

From the perhydroazepine (7; $n = 6$), elution with benzene gave *2,3-dihydro-4-perhydroazepino-1-yl-1H-pyrrolo-*[1,2-a]*benzimidazole* (9; $n = 6$) (0·4 g, 9%) as white needles, m.p. 111° (from light petroleum) (Found: C, 75·3; H, 8·1; N, 16·1. $C_{16}H_{21}N_3$ requires C, 75·2; H, 8·3; N, 16·5%), τ ($CDCl_3$) 2·94 (t, *J* 7·5 Hz, H-6), 3·42 (dd, *J* 7·5 and 1·5 Hz, H-7), 3·56 (dd, *J* 7·5 and 1·5 Hz, H-5), 6·11br (t, H_a), 6·11br (t, $N[CH_2]_2$), 6·90—7·68 (4H, m, H_b), and 7·96—8·63 (4H, m, $[CH_2]_2$). Elution with chloroform gave *2,3,9,10,11,12-hexahydro-1H,8H-azepino*[1,2-a]*pyrrolo-*[2′,1′:2,3]*imidazo*[4,5-g]*benzimidazole 7-oxide* (10) (2·3 g, 41%) as white clusters (from ethyl acetate), m.p. 188° (Found: C, 60·9; H, 6·8; N, 17·9. $C_{16}H_{18}N_4O,H_2O$ requires C, 60·4; H, 7·0; N, 17·6%), τ ($CDCl_3$) 2·27 (d, *J* 9·0 Hz, H_a), 2·62 (d, *J* 9·0 Hz, H_b), 4·93—5·22 (m, H_d), 5·77 (t, *J* 7·0 Hz, H_c), 6·56 (6H, m, H_c), and 7·91—8·23 (6H, m, H_f).

[8] O. Meth-Cohn, *J. Chem. Soc.*, 1964, 5245.

2,3,9,10-*Tetrahydro*-5-*nitro*-6-*pyrrolidin*-1-*yl*-1H,8H-*benzo*-[1″,2″:5,4:3″,4″:5′,4′]*bis*(*imidazo*[1,2-a]*pyrrole*) (12).—The chlorodi-imidazole (8) (1·8 g) was added slowly to a mixture of sulphuric acid (2 ml; *d* 1·84) and fuming nitric acid (2 ml) at 0°. The mixture was then allowed to reach room temperature and poured on ice. Basification with sodium hydrogen carbonate precipitated the 6-*chloro*-5-*nitro*-*di*-*imidazole* (14; Cl for N_3), which gave yellow needles (1·8 g), m.p. 320° (from aqueous acetic acid) (Found: C, 52·9; H, 4·0; N, 21·8. $C_{14}H_{12}ClN_5O_2$ requires C, 52·9; H, 3·8; N, 22·0%). To pyrrolidine (1 ml) in ethanol (10 ml) was added the chloro-nitro-di-imidazole (0·8 g). The mixture was refluxed for 8 h, then poured into water, precipitating the magenta *imidazole* (12) (0·8 g), which crystallised as needles (from ethanol), m.p. >300° (Found: C, 60·7; H, 5·8; N, 23·7. $C_{18}H_{20}N_6O_2$ requires C, 61·3; H, 5·7; N, 23·9%), τ ($CDCl_3$) 5·40—5·76 (4H, m, H_a), 6·16 (t, *J* 6·5 Hz, H_b), 6·79—7·54 (8H, m, H_c), and 7·85—8·16 (4H, m, H_d).

2,3,10,11-*Tetrahydro*-1H,9H-*bis*(*pyrrolo*[1″,2″:1,2]*imid*-*azo*)[4,5-e:4′,5′-g]*benzofurazan* 5-*Oxide* (15).—The chloro-nitro-di-imidazole (14; Cl for N_3) (1·0 g) and sodium azide (1·0 g) were heated in dimethyl sulphoxide (5 ml) at 90°. Slow gas evolution was observed during 6 h and after 12 h the mixture was poured into water and the yellow precipitate (1·0 g) collected and washed with water. Recrystallisation from ethyl acetate–chloroform gave yellow *needles*, m.p. 268° (decomp.) (Found: C, 51·1; H, 4·6; N, 25·1. $C_{14}H_{12}N_6O_2,2H_2O$ requires C, 50·6; H, 4·9; N, 25·3%), M^+ 296, τ ($CDCl_3$) 5·54 (t, *J* 6·5 Hz, N·CH_2) and 6·62—7·46 (m, CH_2·CH_2).

Reaction of the Benzimidazole N-*Oxides* (17) *with Acid Halides*.—The *N*-oxide [1] (17) (1·5 g) in chloroform (25 ml) was treated with the appropriate acid halide (1·1 mol. equiv.) and the solution was boiled for 4 h. The mixture was washed with saturated sodium hydrogen carbonate solution, the combined washings were further extracted with chloroform, and the chloroform layer was examined by t.l.c. If only one component was present the solvent was removed and the residue recrystallised. If more than one component was present the evaporated material was subjected to chromatography on alumina and eluted with ethyl acetate–carbon tetrachloride (4 : 1). The products are recorded in Table 2 and their properties in Table 3.

The Co-action of an Acid Chloride and a Nucleophile on the N-*Oxides* (17).—The *N*-oxide (1·5 g) in chloroform (10 ml) was treated successively with the appropriate nucleophile (2 g) in water (20 ml) and an acid chloride (1·1 mol. equiv.); the mixture was stoppered and vigorously shaken at 10° for about 10 min. The aqueous phase was separated and extracted with chloroform (3 × 20 ml) and the combined chloroform extracts were dried ($MgSO_4$) and evaporated; the residues were chromatographed on alumina. The products are recorded in Table 4 together with their properties.

Unambiguous Synthesis of 8,9,10,11-*Tetrahydro*-7H-*aze*-*pino*[1′,2′:1,2]*imidazo*[4,5-e]*benzofurazan* 3-*Oxide* (23).—A mixture of 1-chloro-7,8,9,10-tetrahydro-2-nitro-6*H*-azepino-[1,2-*a*]benzimidazole (20; R = Cl) (0·2 g), sodium azide (0·2 g), and dimethyl sulphoxide (2 ml) was heated at 55° for 12 h with slow evolution of nitrogen. The mixture was poured into water (15 ml) and the yellow precipitate filtered off, washed with water, and recrystallised from ethanol; m.p. 216°. The product was identical (m.p., mixed m.p., i.r. spectrum) with that reported in Table 4.

Reactions of the Benzimidazole N-*Oxides* (17) *with an Acid Chloride and Sodium Hydroxide*.—The *N*-oxide (1·0 g) in chloroform (10 ml) was treated successively with aqueous sodium hydroxide (2M; 20 ml) and an acid chloride (1·1 mol. equiv.); the mixture was shaken vigorously at ambient temperature for 10 min and extracted with chloroform (3 × 20 ml). The dried ($MgSO_4$) extract was chromatographed on alumina to give the products recorded in Table 5. 5-Chloro-2-ethyl-1-propylbenzimidazole 3-oxide under these conditions, with toluene-*p*-sulphonyl chloride, gave 5-*chloro*-3-*ethyl*-1-*propylbenzimidazole* (48%), m.p. 61° as white needles (by sublimation) (Found: C, 59·8; H, 6·2; N, 11·8. $C_{12}H_{15}ClN_2O$ requires C, 60·3; H, 6·4; N, 11·7%), τ (CCl_4) 3·00—3·17 (3H, m, aromatic), 6·13 (q, *J* 7·5 Hz, N·CH_2Me), 8·70 (t, *J* 7·5 Hz, N·CH_2·CH_3), 6·22 (t, *J* 7·5 Hz, N·CH_2·CH_2Me), 8·27 (sextet, *J* 7·5 Hz, N·CH_2·CH_2), and 9·06 (t, *J* 7·5 Hz, N[CH_2]$_2$·CH_3).

From 1,2-dimethylbenzimidazole 3-oxide under the above conditions only tar was formed.

Reduction of 1,3-*Pentamethylenebenzimidazol*-2(3H)-*one* (26; R = H, *n* = 5).—To the title compound (0·2 g) in dry benzene (5 ml) was added sodium bis-(2-methoxy-ethoxy)aluminium hydride [68·5% w/w solution in benzene (Aldrich); 0·9 g] and the solution was set aside for 4 h.

TABLE 3

Properties of the benzimidazoles (18) and (19) (see Table 2)

Product				M.p. (°C)	Found (%)			Required (%)			τ(CDCl₃) (*J* in Hz)						
	n	R	X		C	H	N	C	H	N	4-H	5-H	6-H	7-H	N·CH_2	C·CH_2	[CH_2]$_n$	X
(18)	3	H	6-Cl	136	62·1	4·8	14·8	62·3	4·7	14·6	2·38 (d, 9·0)	2·82 (dd, 9·0 and 2·0)		2·74 (d, 2·0)	5·99 (t, 7·0)	6·78—7·52 (m)		
(18)	3	Cl	6-Cl	211	53·1	3·5	12·4	52·9	3·6	12·3	2·22 (s)			2·64 (s)	5·94 (t, 7·0)	6·73—7·47 (m)		
(18)	3	NO_2	4-Cl	184	50·5	3·6	17·5	50·5	3·4	17·7			2·20 (d, 9·0)	2·77 (d, 9·0)	5·78 (t, 7·0)	6·68—7·36 (m)		
(18)	3	NO_2	7-Cl	162	50·8	3·5	17·8	50·5	3·4	17·7	1·50 (d, 8·0)		1·87 (d, 2·0)		5·48 (t, 7·0)	6·68—7·23 (m)		
(18)	5	NO_2	4-Cl	162	54·2	4·6	15·3	54·2	4·6	15·8			2·05 (d, 9·0)	2·72 (d, 9·0)	5·62—5·86 (m)	6·66—6·91 (m)	7·94—8·28 (m)	
(18)	5	NO_2	7-Cl	136	54·7	4·6	15·9	54·2	4·6	15·8	1·53 (d, 2·0)		1·89 (d, 2·0)		5·05—5·31 (m)	6·68—6·97 (m)	7·90—8·30 (m)	
(19)	5	NO_2	OAc	204 [a]														
(19)	5	NO_2	OBz	179	64·6	4·8	11·5	65·0	4·9	12·0	1·22 (d, 2·0)		1·62—1·96 (m)	2·27—2·69 (m)	5·39—5·63 (m)	3·25—3·45 (m)	7·40—8·21 (m)	1·62—1·96 (m) 2·27—2·69 (m)
(19)[b]	5	NO_2	O·C_6H_4·OMe-*p*	155	62·5	5·0	10·8	63·0	5·0	11·0	1·40 (d, 2·0)		1·73 (dd, 9·0 and 2·0)	2·19 (d, 9·0)	5·18—5·47 (m)	3·38—3·58 (m)	7·73—8·12 (m)	1·84 (d, 9·0) 2·93 (d, 9·0) 6·07 (s, OMe)

[a] Lit., 205° [R. K. Grantham and O. Meth-Cohn, *J. Chem. Soc.* (*C*), 1969, 70]. [b] N.m.r. in hexadeuterioacetone.

Water was then added, the benzene layer was separated, dried, and evaporated and the oily residue was chromatographed on alumina with carbon tetrachloride to give *N-methyl-NN'-pentamethylene-o-phenylenediamine* (28; R = Me) (0·15 g) as an oil (Found: C, 75·2; H, 9·6; N, 14·8. $C_{12}H_{18}N_2$ requires C, 75·7; H, 9·5; N, 14·8%), τ (CCl_4) 86°, identical (m.p., mixed m.p., and i.r. spectrum) with a sample made by the method of Stetter.[7]

Action of Phenyl Isocyanate on the N-*Oxide* (17; R = NO_2, *n* = 5).—Phenyl isocyanate (0·48 g) was added dropwise to a solution of the *N*-oxide (1 g) in chloroform (10 ml). A vigorous reaction occurred on each addition, yielding a bright red solution. The solution was evaporated and the residue chromatographed on alumina with 1 : 4 ethyl acetate–carbon tetrachloride as eluant to give the anilinobenzimidazoles (20; R = NHPh) (1·2 g, 90%) and (32) (0·14 g, 10%), identical with the products recorded in Table 4.

TABLE 4

Properties of the products of the co-action of an acid chloride and a nucleophile on the *N*-oxide (17; R = NO_2, *n* = 5)

Reagents		Products				Yield	M.p.	νmax./ cm⁻¹	Found (%)			Required (%)			τ ($CDCl_3$) (*J* in Hz)			
A	B		*n*	R	X	(%)	(°C)	(Nujol)	C	H	N	C	H	N	Aromatic	N·CH_3	C·CH_2	$[CH_2]_3$
BzCl	CN^-	(19)	5	NO_2	BzO	43	See Table 3											
		(20)		CN		20	205	2230	61·1	4·7	61·1	60·9	4·7	21·9	1·62 (d, 9·0, H-6), 2·16 (d, 9·0, H-7)	5·62—5·90 (m)	6·67—7·02 (m)	81·2—8·48 (m) [a]
TsCl	CN^-	(20)		CN		20	205	2230										
TsCl	SCN^-	(20)		SCN		60	142	2165	53·9	4·3	18·9	54·2	4·2	19·4	1·84 (d, 9·0, H-6), 2·54 (d, 9·0, H-7), 1·27—1·91 (m, 4·4)	5·55—5·84 (m)	6·57—6·96 (m)	7·81—8·30 (m)
TsCl	SCN^-	(21)				20	300								1·27—1·91 (4H, m)	4·92—5·32 (2H, m) 5·62—5·95 (2H, m)	6·62—7·12 (4H, m)	7·90—8·28 (12H, m)
TsCl	N_3^-	(22)		N_3		66	154 *	2130	53·1	4·5	31·1	53·0	4·5	30·9	1·74 (d, 2·0, H-4), 2·14 (d, 2·0, H-6)	5·41—5·62 (m)	6·70—7·03 (m)	7·65—8·10 (m)
TsCl	N_3^-	(23)				33	218		59·2	4·8	22·7	59·0	5·0	22·9	2·70—2·83 (m)	5·62—5·91 (m)	6·65—7·01 (m)	7·89—8·41 (m)
TsCl	BunSH	(20)		Cl		27												
TsCl	BunSH	(20)		SBu		21	71·2		59·9	6·7	13·3	60·1	6·6	13·2	2·14 (d, 9·0, H-6), 2·80 (d, 9·0, H-7)	5·62—5·92 (m)	6·30—6·65 (m)	6·65—7·03 (2H, m) 7·91—9·34 (13H, m) [b]
TsCl	BunSH	(22)		H		6	173 [c]											
TsCl	BunSH	(22)		Cl		14	See Table 3											
TsCl	BunSH	(26)	5	NO_2		10	See Table 5											
TsCl	OH⁻	(26)	5	NO_2		See Table 5												
TsCl	$BunNH_2$	(20)		NHBu		60	99		66·3	7·0	18·3	63·6	7·3	18·5	1·92 (d, 9·0, H-6), 3·52 (9·0, H-7)	5·45—6·09 (m)	6·81—7·11 (4H, m)	7·94—9·26 (13H, m) [b]
TsCl	$BunNH_2$	(26)	5	NO_2		20	See Table 5											
TsCl	$PhNH_2$	(20) †		NHPh		90	150		63·5	5·6	16·0	63·5	5·9	16·5	1·88 (d, 9·0, H-6) 2·86, (d, 9·0, H-7), 2·65—2·83 (Ph)	5·51—5·73 (m)	6·91—7·20 (m)	7·90—8·41 (m) [d]
TsCl	$PhNH_2$	(32)				10	198		67·0	5·8	17·4	67·1	5·6	17·4	1·41 (s, H-4), 3·00 (s, H-7), 2·50—2·67 (Ph)	5·89—6·71 (m)	6·80—7·11 (m)	7·95—8·37 (m)

[a] N.m.r. in C_5D_5N. [b] Includes Bun. [c] Saunders [6] reports 174—175°. [d] N.m.r. in $(CD_3)_2CO$.
* Decomp. † Monohydrate.

TABLE 5

Products from the co-action of an acid chloride and sodium hydroxide on the *N*-oxides (17)

N-Oxide		Acid	Products				Yield	M.p.	Found (%)			Required (%)			τ($CDCl_3$) (*J* in Hz)
n	R	chloride	No.	*n*	R	Others	(%)	(°C)	C	H	N	C	H	N	
3	NO_2	TsCl	(3)			H for Cl	10	210 [a]							
4	Cl	TsCl	Tar												
5	H	TsCl	(26)	5	H		23	81 [b]							2·98 (s, ArH), 5·48—6·01br (t, N·CH_A), 61·5—6·54br (d, N·CH_B), 8·36—8·80 (m, $[CH_2]_3$)
5	Cl	TsCl	(26)	5	Cl		35	112 [b]							2·77—2·93 (m, ArH), 5·33—5·88br (t, N·CH_A), 6·01—6·42br (d, N·CH_B), 8·18—9·10 (m, $[CH_2]_3$)
5	Cl	BzCl	(26)	5	Cl		27	112 [b]							
			(19)	5	Cl	X = BzO	36	171	66·4	5·0	8·2	67·0	5·0	8·2	2·21 (H-4), 1·75—1·98 (4H, m), 2·31—2·76 (2H, m), 5·49—5·74 (m, N·CH_2), 3·28—3·48br (d, CH), 7·71—8·23 (m, $[CH_2]_3$)
5	NO_2	TsCl	(26)	5	NO_2		55	131	58·3	5·6	16·6	58·3	5·3	17·0	1·69 (d, 2·0, H-4), 1·90 (dd, 9·0 and 2·0, H-6), 2·72 (d, H-7, 9·0), 5·28—5·82br (t, N·CH_A), 5·89—6·30br (d, N·CH_B), 8·11—8·61 (m, $[CH_2]_3$)
6	Cl	TsCl	(26)	6	Cl		85	105 [b]							2·86—3·03 (m, ArH), 5·47—6·02 (dt, N·CH_A), 6·0—6·61 (dt, N·CH_B), 7·72—9·60 (m $[CH_2]_4$)
7	Cl	TsCl	(26)	7	Cl		63	143 [b]							2·85—3·01 (m, ArH), 5·18—5·82br (t, N·CH_A), 5·96—6·39 (d, N·CH_B), 8·08—8·80 (m, $[CH_2]_5$)

[a] Lit., 210° (M. D. Nair and R. Adams, *J. Amer. Chem. Soc.*, 1961, **83**, 3518). [b] See preceding paper for i.r., u.v., and mass spectral and analytical data.

3·03—3·38 (m, aromatic), 5·10br (NH), 6·60—6·82 and 6·88—7·13 (each 2H, m, N·CH_2), 7·31 (s, Me), and 2·24—2·64 (m, $[CH_2]_3$).

Hydrolysis of 1,3-*Pentamethylenebenzimidazol*-2(3H)-*one* (26; R = H, *n* = 5).—The benzimidazolone (0·6 g) was boiled with saturated ethanolic potassium hydroxide (15 ml) for 12 h; the product was poured into water and the precipitate was filtered off, washed with water, and dried to give, after recrystallisation from light petroleum, *NN'*-pentamethylene-*o*-phenylenediamine (28; R = H), m.p.

We thank the S.R.C. for a grant (to R. F.).

[2/2400 *Received*, 20*th October*, 1972]