o-Nitroaniline Derivatives. Part V.[1] Cyclisation of *N*-Acylated Derivatives of *N*-Benzyl- and *N*-*p*-Nitrobenzyl-*o*-nitroaniline: a Comparison of Carboxamides and Sulphonamides

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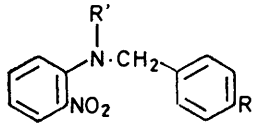
The *N*-acetyl and *N*-benzoyl derivatives of *N*-benzyl- and *N*-*p*-nitrobenzyl-*o*-nitroaniline are cyclised, by sodium methoxide in methanol, to 2-aryl-1-hydroxybenzimidazoles; however, in the corresponding reactions of the *N*-methylsulphonyl and *N*-*p*-tolylsulphonyl derivatives, cyclisation occurs only in the case of the *p*-nitrobenzyl compounds. Cyclisation of the *N*-benzyl-*o*-nitroaniline derivatives apparently involves deacylation as the first step, whereas kinetic evidence indicates that deacylation follows cyclisation in the reactions of the *N*-*p*-nitrobenzyl-*o*-nitroaniline derivatives.

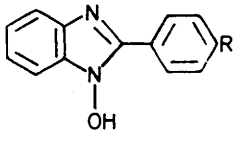
N-Ethoxycarbonyl-*N*-*p*-nitrobenzyl-*o*-nitroaniline is similarly cyclised by sodium ethoxide in ethanol. In the preparation of this compound, from ethyl *N*-*o*-nitrophenylcarbamate and *p*-nitrobenzyl bromide, 1-*p*-nitrobenzyloxy-2-*p*-nitrophenylbenzimidazole is obtained as a by-product.

The non-equivalence of the benzylic protons in the n.m.r. spectra of the title compounds is discussed.

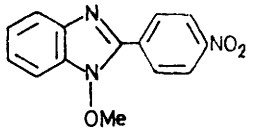
We have previously [2] described the cyclisation of *N*-*p*-nitrobenzyl-*N*-*p*-tolylsulphonyl-*o*-nitroaniline (1a), by methanolic sodium methoxide, to 1-hydroxy-2-*p*-nitrophenylbenzimidazole (3) and its *O*-methyl derivative (5). The mechanism proposed (Scheme 1) involves intramolecular base-catalysed condensation followed by detosylation of the intermediate 2-*p*-nitrophenyl-1-*p*-tolylsulphonylbenzimidazole 3-oxide (6). These steps lead to the anion of (3) and methyl toluene-*p*-sulphonate, and hence to the methylated compound (5).



(1) R = NO_2 (2) R = H
a; R' = $SO_2 \cdot C_6H_4Me$-*p*
b; R' = SO_2Me
c; R' = COPh
d; R' = COMe
e; R' = H
f; R' = CO_2Et



(3) R = NO_2
(4) R = H



(5)

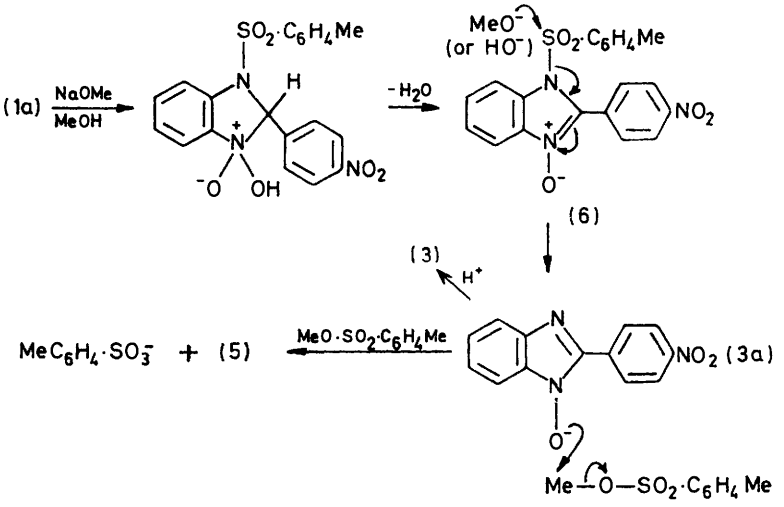
In an attempt to clarify further the mechanism of this cyclisation, and to provide additional evidence for the identity of the methylating agent, we have now examined the reactions of the two series of compounds (1a—e) and (2a—e) with sodium methoxide in methanol. If the reaction pattern for the tosyl compounds (1a) and (2a) [2] were to be followed throughout the series, and if the mechanism of Scheme 1 were correct, one might have expected the formation of the hydroxybenzimidazole (3) from each of the compounds (1a—e) and the methoxybenzimidazole (5) only in the reactions of the sulphonamides (1a and b) [since the reactions of (1c and d) would produce methyl carboxylates, which are not methylating agents]. One might also have expected the compounds (2), lacking a reactive methylene group, to have been unaffected by sodium methoxide, except perhaps for *N*-benzyl-*o*-nitroaniline (2e) itself, which is known [3,4] to be cyclised by bases to 1-hydroxy-2-phenylbenzimidazole (4).

Reaction of the series of compounds (1a—e) with sodium methoxide does indeed give 1-hydroxy-2-*p*-nitrophenylbenzimidazole (3) in every case. However, contrary to expectation, the methylated product (5) has been isolated only in the reaction of the *N*-tosyl compound (1a); in the reaction of the mesyl compound (1b) only a trace of (5) is formed (<1%; detected by mass spectrometry). This result is surprising, since methyl methanesulphonate is an efficient methylating agent for the anion of (3); but alkyl methanesulphonates are known [5] to be less reactive towards nucleophilic solvents (and hence are, presumably, more selective alkylating agents) than the corresponding toluene-*p*-sulphonates, and so it is conceivable that, during the cyclisation of the mesyl compound, when the anion (3a) and the methylating agent are being formed, slowly, in the presence of an excess of methoxide ion, it is the methoxide ion which is methylated almost exclusively at the expense of (3a).

As expected, the sulphonamides (2a and b) are unreactive towards sodium methoxide in methanol, but this is not true of the carboxamides (2c and d), which react to give *N*-benzyl-*o*-nitroaniline (2e) and 1-hydroxy-2-phenylbenzimidazole (4), the proportions of the products depending on the conditions. In dilute solutions, and with short reaction times, deacylation [giving (2e)] is the only reaction observed, but at higher concentrations and after longer periods the cyclisation product (4) is also obtained. Since (4) is also formed, in comparable yield, from *N*-benzyl-*o*-nitroaniline (2e) under similar conditions, it is reasonable to assume that

[1] Part IV, D. Johnston and D. M. Smith, *Org. Mass Spectrometry*, 1974, **9**, 789.
[2] H. McNab and D. M. Smith, *J.C.S. Perkin I*, 1973, 1310.
[3] G. W. Stacy, B. V. Ettling, and A. J. Papa, *J. Org. Chem.*, 1964, **29**, 1537.
[4] G. W. Stacy, T. E. Wollner, and T. R. Oakes, *J. Heterocyclic Chem.*, 1966, **3**, 51.
[5] R. K. Crossland and K. L. Servis, *J. Org. Chem.*, 1970, **35**, 3195.

the course of these reactions is: (2c) or (2d) ⟶ (2e) ⟶ (4), *i.e.* pathway A of Scheme 2. This is in accord with the apparently general rule [6] that base-induced cyclisations of *o*-nitro-compounds involving a feebly reactive β-methylene centre in the *ortho*-side chain occur only when the side chain also carries a mobile α-hydrogen atom; a rule which Stacy and his co-workers [4] have also exemplified by showing that *N*-benzyl-*N*-methyl-*o*-nitroaniline, unlike (2e), cannot be cyclised under a variety of basic conditions.

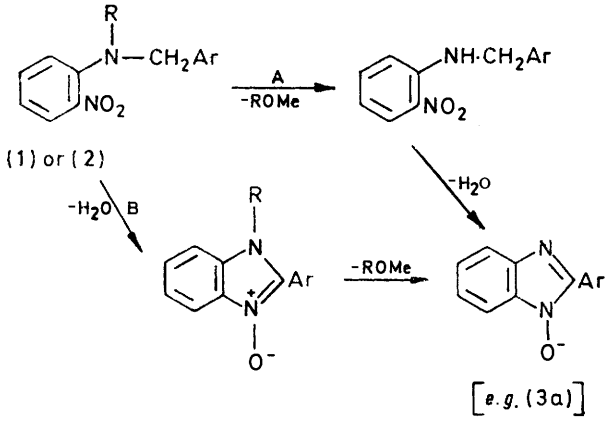


SCHEME 1

TABLE 1

Cyclisation of *N*-*p*-nitrobenzyl-*o*-nitroanilines

Compound	$\lambda_{max.}$ (MeOH)/nm (ε)	Yield (%) of (3)	Rate constant (k/s^{-1})	Isosbestic points (λ/nm)
(1a)	220, 265 (71 500, 53 300)	38 [+10% (5)][2]	4.05×10^{-5}	245, 297
(1b)	218, 266 (28 500, 30 400)	50	4.58×10^{-5}	256, 296
(1c)	211, 263 (22 300, 27 800)	42	1.61×10^{-5}	243, 288
(1d)	208, 271 (8 150, 6 200)	56	3.31×10^{-5}	252, 297
(1e)	232, 273, 415 (27 000, 17 800, 8 000)	37	1.54×10^{-5}	245, 297, 420



SCHEME 2

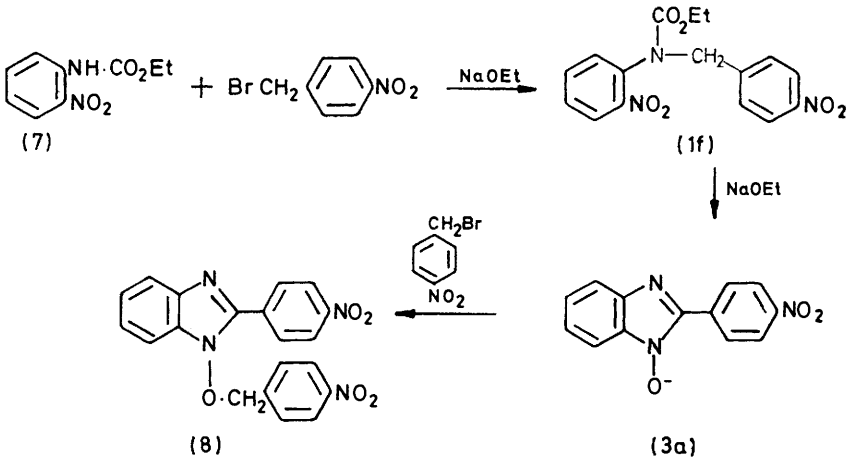
Thus, of the eight compounds (1a—d) and (2a—d), two (2a and b) are unreactive, two (2c and d) react *via* pathway A, and two (1a and b) react *via* pathway B (Scheme 2). The course of the reactions involving the remaining two, *viz.* (1c and d), is less easily determined, since both have a readily displaceable *N*-acyl substituent (facilitating pathway A) and a relatively reactive methylene group (permitting pathway B).

However, simple kinetic measurements on the overall reaction rates enable a distinction to be made. The reactions of *N*-*p*-nitrobenzyl-*o*-nitroaniline (1e) and its four derivatives (1a—d) with a large (200-fold) excess of sodium methoxide in methanol have been followed spectrophotometrically in the region 200—450 nm. For each reaction, superimposition of the series of spectra obtained as the reaction progresses reveals several isosbestic points; this indicates that each reaction involves only one slow rate-determining step.[7] The rate of formation of the final product (3a) may be measured by following the increase of absorbance at 355 nm. All the reactions under these conditions show first-order kinetics; the rate constants are collected in Table 1. The results show that not only do the sulphonamides react faster than the carboxamides, but (3a) is formed faster from all the *N*-substituted compounds than from the NH-compound (1e). This effectively rules out pathway A as a major pathway for all these substituted compounds, and so we believe that all four (1a—d) react mainly by pathway B, *i.e.* they undergo cyclisation prior to deacylation.

[6] J. D. Loudon and G. Tennant, *Quart. Rev.*, 1964, **18**, 389.
[7] M. D. Cohen and E. Fischer, *J. Chem. Soc.*, 1962, 3044; C. Chylewski, *Angew. Chem. Internat. Edn.*, 1971, **10**, 195.

As part of another investigation, we have been studying the *N*-benzylation (and *p*-nitrobenzylation) of ethyl *N*-arylcarbamates, and have attempted the preparation of *N*-ethoxycarbonyl-*N*-*p*-nitrobenzyl-*o*-nitroaniline (1f) by the reaction of ethyl *N*-*o*-nitrophenylcarbamate (7) with sodium ethoxide followed by *p*-nitrobenzyl bromide. When approximately equimolar proportions of the reagents are used, a yellow, ethanol-insoluble, compound, $C_{20}H_{14}N_4O_5$, is produced (7%), and the ethanol-soluble mixture on chromatography yields unchanged carbamate (7) (50%) and *o*-nitroaniline (20%) as well as the required product (1f) (11%). The use of 2 mol. equiv. of *p*-nitrobenzyl bromide and base in the reaction gives an increased yield of (1f) (27%), but the yield of the yellow by-product (23%) is also increased.

This by-product was identified as 1-*p*-nitrobenzyloxy-2-*p*-nitrophenylbenzimidazole (8) on the basis of the n.m.r. spectrum, which shows two different *para*-disubstituted rings and a low-field methylene singlet (δ 5.60), and an alternative synthesis, from 1-hydroxy-2-*p*-nitrophenylbenzimidazole (3) and *p*-nitrobenzyl bromide. The structure (8) is preferred to the alternative *N*-oxide structure (9), despite the close resemblance of the n.m.r. spectrum to that of 1-*p*-nitrobenzyl-2-*p*-nitrophenylbenzimidazole, because of the known preference [2-4] of *N*-hydroxy-compounds like (3) for alkylation and acylation on oxygen; because the compound cannot be deoxygenated by phosphorus trichloride [8] (a standard reaction of *N*-oxides); and because the mass spectrum lacks an $(M - 16)^+$ ion. The most important fragment ion in the mass spectrum, $(M - 151)^+$, corresponds to the loss of *p*-nitrobenzaldehyde, a not unexpected thermolytic process for an *N*-*p*-nitrobenzyloxy-heterocycle.[9]



SCHEME 3

A scheme for the formation of the compound (8) is shown (Scheme 3). Each step has been independently verified; the intermediate (1f), like its *N*-acetyl and *N*-benzoyl analogues, is smoothly cyclised to (3a) in alkoxide solution.

A point of distinction between the carboxamides and the sulphonamides in both series [(1) and (2)] is apparent in their ^1H n.m.r. spectra. Whereas in the sulphonamides the methylene resonance is a singlet, in the carboxamides it is an AB quartet with J *ca.* 14—15 Hz (Table 2). Non-equivalence of methylene protons adjacent to an amidic nitrogen is well known,[10,11] and in the case of *N*-acyl-*N*-benzylanilines this has been attributed to restricted rotation about the aryl–nitrogen

TABLE 2

^1H N.m.r. data for benzylic resonances †

R′	Chemical shift (δ) at normal temperature: Compounds (1)	Chemical shift (δ) at normal temperature: Compounds (2)	Coalescence temperature (°C) ‡: Compounds (1)	Coalescence temperature (°C) ‡: Compounds (2)	Coalescence temperature (°C) ‡: Compounds (10)
$SO_2{\cdot}C_6H_4Me$	4.88	4.85	5 [$(CD_3)_2CO$]	0 [$(CD_3)_2CO$]	51 (pyridine)
SO_2Me	4.91	4.81	9 ($CDCl_3$) §	18 ($CDCl_3$) §	21 (pyridine)
COPh	4.56, 5.71 (J 14.5 Hz)	4.34, 5.76 (J 14 Hz)	68 ($CDBr_3$)	72 ($CDBr_3$)	98.5 ($PhNO_2$)
COMe	4.36, 5.33 (J 15 Hz)	4.15, 5.31 (J 14.5 Hz)	114 ($CDBr_3$)	112 ($CDBr_3$)	142 ($PhNO_2$)
H	4.68 (d, J 6 Hz)	4.48 (d, J 5 Hz)			
CO_2Et	4.78, 5.18br		50 ($CDBr_3$)		

† Data for compounds of series (10) are taken from ref. 12. ‡ ±1° for (1) and (2); ±2° for (10). § In $(CD_3)_2CO$ the protons are accidentally equivalent (singlet down to −85 °C).

[8] A. R. Katritzky and J. M. Lagowski, 'Chemistry of the Heterocyclic *N*-Oxides,' Academic Press, London and New York, 1971, p. 197.

[9] *Cf.* V. Dave and E. W. Warnhoff, *Tetrahedron*, 1975, **31**, 1255.

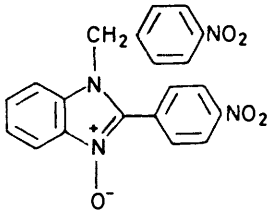
[10] M. B. Robin, F. A. Bovey, and H. Basch, in 'The Chemistry of Amides,' ed. J. Zabicky, Interscience, London and New York, 1970, p. 34.

[11] W. E. Stewart and T. H. Siddall, *Chem. Rev.*, 1970, **70**, 517.

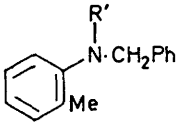
bond.[11] Evidently restricted rotation about the N–CO bond also plays a part, however, because the effect is less evident in sulphonamides, where rotation about the N–SO_2 bond is freer.[12]

Variable-temperature n.m.r. studies of the carboxamides and sulphonamides [(1) and (2)] indicate that in every case the methylene resonance is an AB quartet at low temperatures and a singlet at high temperatures. The coalescence temperatures for the carboxamides lie above room temperature, however, and those of the sulphonamides below room temperature.

Comparison of these coalescence temperatures with those of the corresponding *o*-toluidine derivatives (10) [12]



(9)



(10)

(Table 2) shows that the latter are substantially higher in almost every case. This result implies that there should be greater restriction to Ar–N bond rotation in each of the compounds (10) than in the corresponding members of series (1) and (2). This is an unexpected result, not only on steric but also on electronic grounds: one would expect a little additional restriction to rotation in the *o*-nitroaniline derivatives because of conjugation, however weak, between the amino- and the nitro-groups.

EXPERIMENTAL

I.r. spectra recorded were those of Nujol mulls. N.m.r. spectra were recorded with tetramethylsilane (normal or low temperature) or hexamethyldisiloxane (high temperature) as internal reference.

N-p-Nitrobenzyl-*N-p*-tolylsulphonyl-*o*-nitroaniline (1a),[2] m.p. 192—194°, *N*-benzyl-*N-p*-tolylsulphonyl-*o*-nitroaniline (2a),[13] m.p. 175—176°, and *N*-benzyl-*o*-nitroaniline (2e),[14] m.p. 75°, were prepared by the published methods.

N-*Methylsulphonyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1b).—*N*-Methylsulphonyl-*o*-nitroaniline [13] [m.p. 99—101° (lit., 101—102°)] (6.48 g) was dissolved in sodium ethoxide solution [from sodium (0.70 g) in ethanol (70 ml)] and to the warmed solution was added *p*-nitrobenzyl bromide (7.0 g). More ethanol (70 ml) was added, and the mixture was heated under reflux for 30 min, cooled to 0 °C, and filtered. The product was washed with water and recrystallised from acetic acid–ethanol; it formed almost colourless *plates* (7.95 g, 76%), m.p. 119—121° (Found: C, 47.9; H, 3.7; N, 12.1. $C_{14}H_{13}N_3O_6S$ requires C, 47.9; H, 3.7; N, 12.0%).

N-*Benzyl*-N-*methylsulphonyl*-o-*nitroaniline* (2b).—The sodium salt of *N*-methylsulphonyl-*o*-nitroaniline was prepared by dissolving the sulphonamide (2.16 g) in sodium methoxide solution [from sodium (0.23 g) in methanol (60 ml)] and removing the methanol *in vacuo*. To this salt, dissolved in dimethylformamide (20 ml), was added benzyl bromide (2.2 g), and the mixture was left overnight at room temperature. It was then added to crushed ice, and the precipitate was filtered off and recrystallised from methanol; m.p. 138—140° (lit.,[13] 139—140°); yield 2.21 g (73%).

N-p-*Nitrobenzyl*-o-*nitroaniline* (1e).—This was obtained, in 60% yield, by the direct reaction of *p*-nitrobenzyl bromide and *o*-nitroaniline in the presence of soda-lime,[15] or in 70% yield by hydrolysis of the *p*-tolylsulphonyl compound (1a) (4.27 g) with concentrated sulphuric acid (4 ml) and acetic acid (2 ml) at 100 °C for 2 h. It had m.p. 133—135° (from acetic acid–ethanol) (lit.,[15] 145°; lit.,[16] 138°); $\nu_{max.}$ 3 300 cm^{-1} (N–H), $\delta(CDCl_3)$ 4.68 (2 H, d, *J* 6 Hz, CH_2), 6.5—6.8 (2 H), 7.1—7.6 (3 H), 8.0—8.3 (3 H), and 8.50br (1 H, NH).

N-*Benzoyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1c).—A solution of *N-p*-nitrobenzyl-*o*-nitroaniline (7.8 g) and benzoyl chloride (4.1 g) in pyridine (20 ml) was heated under reflux for 4 h, cooled, and poured on to crushed ice, and the mixture was acidified with 5M-hydrochloric acid. The benzamide (1c), filtered off and recrystallised from acetic acid–ethanol (with charcoal), had m.p. 162—163° (Found: C, 64.0; H, 4.1; N, 10.95. $C_{20}H_{15}N_3O_5$ requires C, 63.7; H, 4.0; N, 11.1%); $\nu_{max.}$ 1 650 (C=O) and 1 510 and 1 335 cm^{-1} (NO_2); yield 4.25 g (40%).

N-*Benzoyl*-N-*benzyl*-o-*nitroaniline* (2c).—The above procedure, applied to *N*-benzyl-*o*-nitroaniline (6.84 g), benzoyl chloride (6.0 g), and pyridine (20 ml), gave the benzamide (2c) (7.50 g, 75%), m.p. 97—98° (lit.,[17] 97°) (Found: C, 72.0; H, 4.8; N, 8.1. Calc. for $C_{20}H_{16}N_2O_3$: C, 72.3; H, 4.85; N, 8.4%), $\nu_{max.}$ 1 650 (C=O) and 1 530 and 1 340 cm^{-1} (NO_2).

N-*Acetyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1d).—To a suspension of *N-p*-nitrobenzyl-*o*-nitroaniline (2.7 g) in acetic anhydride (7 ml) were added acetyl bromide (0.75 ml) and concentrated sulphuric acid (a few drops). The mixture was warmed gently until dissolution, then set aside for 24 h, and poured slowly into cold water. The *acetyl compound* (1d), filtered off and recrystallised from methanol, had m.p. 153—154° (Found: C, 56.9; H, 4.0; N, 13.1. $C_{15}H_{13}N_3O_5$ requires C, 57.1; H, 4.2; N, 13.3%); $\nu_{max.}$ 1 660 (C=O) and 1 510 and 1 340 cm^{-1} (NO_2); yield 2.04 g (68%).

N-Acetyl-*N*-benzyl-*o*-nitroaniline (2d), m.p. 82—83° (from methanol–water) (lit.,[17,18] 83—85°) was similarly obtained from *N*-benzyl-*o*-nitroaniline in 65% yield.

Cyclisation of the N-*Acyl*-N-p-*nitrobenzyl*-o-*nitroanilines* (1a—d).—The following procedure is typical. A solution of *N*-methylsulphonyl-*N-p*-nitrobenzyl-*o*-nitroaniline (1.75 g, 5 mmol) and sodium methoxide [from sodium (0.23 g, 10 mmol)] in methanol (50 ml) was heated under reflux for 2 h. The methanol was evaporated off *in vacuo* and the red residue extracted with benzene–water (1 : 1). Acidification (5M-H_2SO_4) of the aqueous layer gave 1-hydroxy-2-*p*-nitrophenylbenzimidazole [2] (3) (0.68 g, 50%), m.p. and

[12] B. J. Price, J. A. Eggleston, and I. O. Sutherland, *J. Chem. Soc.* (*B*), 1967, 922.
[13] J. L. Huppatz and W. H. F. Sasse, *Austral. J. Chem.*, 1963, **16**, 417.
[14] M. S. Gibson, *J. Chem. Soc.*, 1956, 1076.
[15] C. Paal and C. Benker, *Ber.*, 1899, **32**, 1251.
[16] E. Bamberger, *Ber.*, 1894, **27**, 359.
[17] P. Grammaticakis, *Bull. Soc. chim. France*, 1950, 158.
[18] S. Takahashi and H. Kano, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 1375.

mixed m.p. 243—245° (decomp.) (lit.,[2] 243—246°). Evaporation of the dried (Na_2SO_4) benzene layer, and chromatography of the residue on silica gel, gave a fraction (5 mg) eluted by chloroform, identified as 1-methoxy-2-*p*-nitrophenylbenzimidazole (5) by its mass spectrum.[2] The yields of (3) obtained from these cyclisations are recorded in Table 1.

Cyclisation of N-p-*Nitrobenzyl*-o-*nitroaniline* (1e).—The amine (0.82 g, 3 mmol), dissolved in methanol (30 ml), was treated with sodium methoxide [from sodium (0.14 g, 6 mmol)] in methanol (5 ml), and the mixture was heated under reflux for 6 h and then concentrated *in vacuo*. 1-Hydroxy-2-*p*-nitrophenylbenzimidazole (0.26 g, 37%) was isolated as described in the preceding paragraph.

Kinetic measurements. These were carried out with a Unicam SP 500 spectrophotometer, operating at 355 nm. Methanolic solutions of sodium methoxide (6.6×10^{-2}M; 0.3 ml) and the nitro-compound (3.3×10^{-4}M; 0.3 ml) were added, successively, to methanol (1.4 ml) in a 10 mm cell. The solution was shaken and placed in the thermostatted (25 °C) cavity of the spectrophotometer. Absorbance measurements were made (automatically) at 10- or 15-min intervals over 12 h, and again after 1—2 days when the reaction was complete. The rate constant, k, was determined by plotting $\log_{10}(A - A_t)$ against t (A being the final absorbance and A_t the absorbance at time t); the gradient of this line is $-k/2.303$.

Reactions of N-*Benzyl*-o-*nitroaniline* (2e) *and its Derivatives* (2c *and* d) *with Sodium Methoxide*.—The procedure was identical with that described above for the cyclisation of (1a—d). Acidification of the aqueous layer gave 1-hydroxy-2-phenylbenzimidazole (4), identified by comparison with an authentic sample,[3,4] or as its benzoyl derivative, m.p. 112—114° (lit.,[3] 116—118°). Evaporation of the organic layer gave *N*-benzyl-*o*-nitroaniline (2e), which was purified, if necessary, by chromatography on silica gel, with ether–petroleum (1 : 3) as eluant. The products obtained by reaction of the nitro-compounds (5 mmol) and sodium methoxide (10 mmol) under various conditions are tabulated (Table 3).

TABLE 3

Compd.	Conditions: 50 ml MeOH, 2 h	50 ml MeOH, 6 h	15 ml MeOH, 2 h
(2c)	70% (2e), 3% (4)	72% (2e), 21% (4)	82% (2e), 12% (4)
(2d)	73% (2e), 0% (4)	74% (2e), 17% (4)	81% (2e), 8% (4)
(2e)	(2e) recovered almost quantitatively	70% (2e), 23% (4)	69% (2e), 21% (4)

Methylation of the Hydroxybenzimidazole (3).—Methyl methanesulphonate [prepared (17%) from methanesulphonyl chloride, methanol, and triethylamine by an adaptation of Crossland and Servis' method,[5] b.p. 38—40° at 0.5 mmHg (lit.,[19] 101—102° at 26 mmHg), $\delta(CDCl_3)$ 3.10 (3 H, s, CH_3S) and 4.00 (3 H, s, CH_3O)] (0.15 g) was added to a solution of the hydroxy-compound (3) (0.44 g) and sodium methoxide [from sodium (0.04 g)] in methanol (5 ml). The mixture was boiled for 2 h, the methanol was evaporated off *in vacuo*, and the residue was extracted into benzene–water (1 : 1). The benzene layer was dried (Na_2SO_4) and evaporated, giving 1-methoxy-2-nitrophenylbenzimidazole (5),[2] m.p. and mixed m.p. 148—150° (lit.,[2] 154—156°); yield 0.15 g (32%).

Ethyl N-o-*Nitrophenylcarbamate* (7).—This was prepared [20] from *o*-nitroaniline (13.8 g), ethyl chloroformate (20.2 g), and pyridine (8.1 ml) in carbon tetrachloride (130 ml); yield 17.3 g (83%); m.p. 54—55° (from ethanol) (lit.,[21] 55—56°); $\nu_{max.}$ 3 370 (N–H) and 1 745 cm^{-1} (C=O); $\delta(CCl_4)$ 1.38 (3 H, t, CH_3), 4.20 (2 H, q, CH_2), 7.03 (1 H, dt), 7.57 (1 H, dt), 8.13 (1 H, dd), 8.57 (1 H, dd), and 9.70br (1 H, s, NH) (J_{Et} 7, J_{ortho} 8, J_{meta} 2 Hz).

N-*Ethoxycarbonyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1f) *and* 1-p-*Nitrobenzyloxy*-2-p-*nitrophenylbenzimidazole* (8).—Sodium ethoxide [from sodium (0.46 g)] in ethanol (25 ml) was added to a solution of ethyl *N*-*o*-nitrophenylcarbamate (7) (2.10 g) in ethanol (35 ml). *p*-Nitrobenzyl bromide (4.32 g) was added, over 10 min, to the resulting red solution, and the mixture was stirred at room temperature overnight. It was then filtered, and the yellow residue was recrystallised from dimethylformamide–water to give 1-p-*nitrobenzyloxy*-2-p-*nitrophenylbenzimidazole* (8) (0.88 g, 23%), m.p. 223—224° (Found: C, 61.1; H, 3.5; N, 13.95. $C_{20}H_{14}N_4O_5$ requires C, 61.5; H, 3.6; N, 14.35%); $\nu_{max.}$ 1 505 and 1 310 cm^{-1} (NO_2); $\delta(CF_3{\cdot}CO_2H)$ 5.60 (2 H, s, CH_2) and 7.3—8.7 (12 H, m, aromatic; 2 AA'BB' patterns visible); *m/e* 390 (M^+, 18%), 270 (42), 239 (35),* 150 (98), 136 (97), 104 (99), 78 (98), and 51 (100).

The ethanolic filtrate was evaporated, and the organic portion of the residue extracted into ether. Evaporation of the extract and chromatography of the residue on silica gel, with chloroform as eluant, gave unchanged carbamate (7) (0.45 g, 23%) and then N-*ethoxycarbonyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1f) (0.88 g, 27%), m.p. 85—87° (from ethanol–water) (Found: C, 55.6; H, 4.5; N, 12.1. $C_{16}H_{15}N_3O_6$ requires C, 55.65; H, 4.4; N, 12.2%); $\nu_{max.}$ 1 700 (C=O) and 1 510 and 1 340 cm^{-1} (NO_2); $\delta(CDCl_3)$ 1.14br (3 H, t, CH_3),* 4.15br (2 H, $CH_3{\cdot}CH_2$),† 4.78 and 5.18 (2 H, ABq, $N{\cdot}CH_2$; *cf.* Table 2), and 6.9—8.3 (8 H, m, aromatic).

The benzimidazole derivative (8) was also obtained (yield 57%) by adding *p*-nitrobenzyl bromide (0.42 g) to a solution of 1-hydroxy-2-*p*-nitrophenylbenzimidazole (3) (0.51 g) and sodium ethoxide [from sodium (0.046 g)] in ethanol (40 ml), and stirring the resulting mixture at room temperature overnight.

Cyclisation of N-*Ethoxycarbonyl*-N-p-*nitrobenzyl*-o-*nitroaniline* (1f).—A solution of (1f) (0.53 g) and sodium ethoxide [from sodium (0.07 g)] in ethanol (20 ml) was heated under reflux for 2 h, then worked up as for the other cyclisations described above. The yield of 1-hydroxy-2-*p*-nitrophenylbenzimidazole (3) was 0.27 g (71%).

1-p-*Nitrobenzyl*-2-p-*nitrophenylbenzimidazole*.—This material, m.p. 209—210° (lit.,[22] 212°), was prepared [22] from

* Found: 239.068 560. $C_{13}H_9N_3O_2$ requires 239.069 472).

† At higher temperatures (>70 °C) the CH_3 and $CH_2{\cdot}CH_3$ signals are simplified to a normal triplet and quartet respectively (J 7 Hz) whereas at lower temperatures (<0 °C) the signals are resolved into two triplets and two quartets respectively. These are each separated by 0.18 p.p.m. and are not of equal intensity; they presumably result from two conformers of (1f) which interconvert slowly because of restricted rotation about the N–CO bond.

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[21] J. M. Prokipcak, P. A. Forte, and D. D. Lennox, *Canad. J. Chem.*, 1969, **47**, 2482.
[22] N. V. Subba Rao and C. V. Ratnam, *Proc. Indian Acad. Sci.*, 1956, **43***A*, 173.

p-nitrobenzaldehyde and *o*-phenylenediamine, and showed $\delta(CDCl_3)$ 5.57 (2 H, s, CH_2) and 7.2—8.5 (12 H, m, aromatic).

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