o-Nitroaniline Derivatives. Part 11.[1] 4- and 7-Amino-1*H*-benzimidazole 3-Oxides

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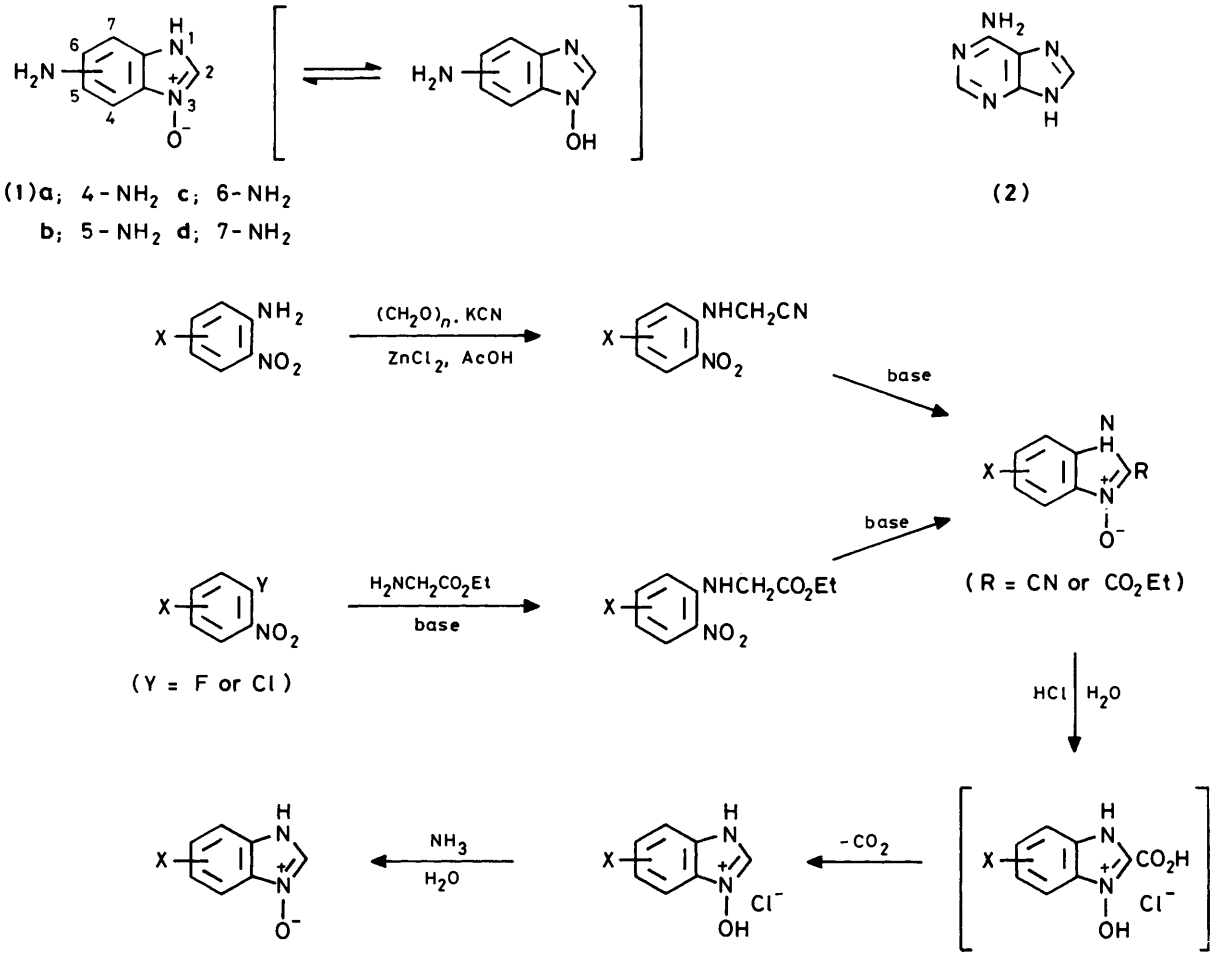
Of the two title compounds, the 4-amino isomer (**1a**) is easily obtained, either by reduction of the corresponding nitro compound, or in a five-step sequence from 2-nitro-1,3-phenylenediamine. The 7-amino isomer (**1d**) cannot be obtained by strictly analogous routes but it may be prepared in four steps from 2',3'-dinitroacetanilide. Attempts to cyanomethylate monoacylated 3-nitro-1,2-phenylenediamines (**8**) lead to 1-acyl-2,3-dihydro-4-nitrobenzimidazoles (**10**).

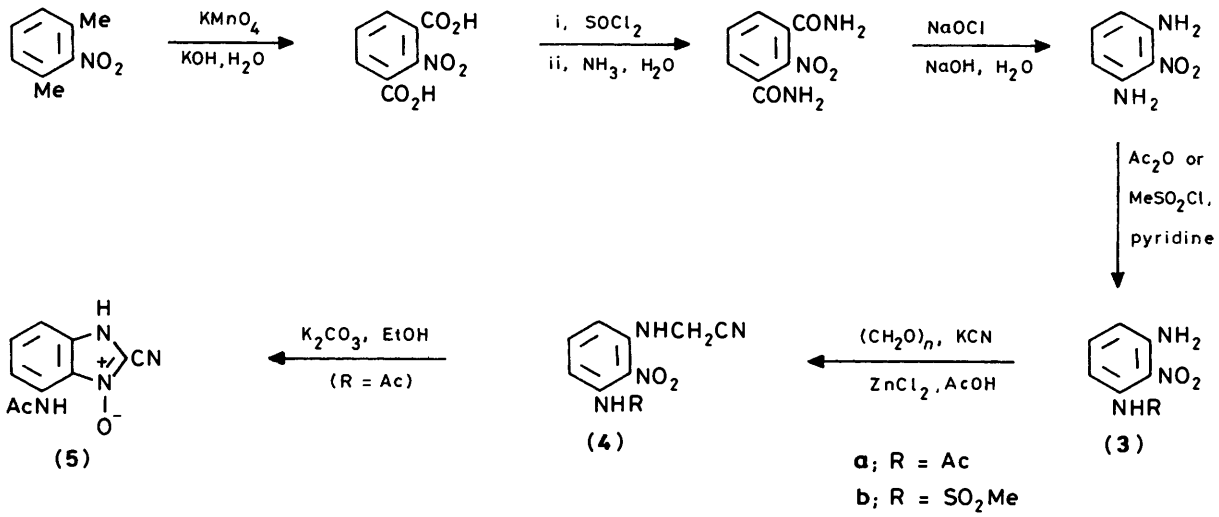
In Part 9,[2] we outlined a general synthetic route to 1*H*-benzimidazole 3-oxides which are unsubstituted at N-1 and C-2, and in Part 10[1] we showed how the method may be adapted to the synthesis of 5- and 6-aminobenzimidazole 3-oxides (**1b** and **c**). The two principal variants of the general method are shown in Scheme 1: both involve the base-induced cyclisation of an *N*-(O-nitrophenyl)glycine derivative (either an ester or a nitrile) to a 2-substituted benzimidazole oxide, followed by hydrolysis of the 2-substituent and decarboxylation. If the substituent X in the final product is amino, as in (**1b** and **c**), it must be protected (*e.g.* by acylation) in the early stages of the synthetic sequence.

We now describe the synthesis and characteristics of the 4- and 7-aminobenzimidazole oxides (**1a** and **d**), which are obvious structural relatives of adenine (**2**). The syntheses are less straightforward than those of the 5- and 6-amino isomers (**1b** and **c**), since they require vicinally trisubstituted benzenes as the substrates for the cyclisation step, and these are generally less accessible than their 1,2,4-trisubstituted analogues.

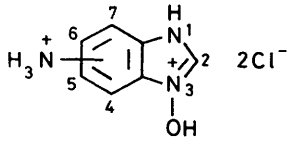
4-*Amino*-1H-*benzimidazole* 3-*Oxide* (**1a**).—(i) *From* 2-*nitro*-1,3-*phenylenediamine*. The diamine may be prepared in four steps, according to a published procedure (Scheme 2),[3,4] from 2-nitro-1,3-xylene. By careful control of the reaction conditions, monoacylation of the diamine may be achieved in reasonable yield, both the acetyl (**3a**) and the methylsulphonyl (**3b**) derivative being obtained; cyanomethylation of the other amino



Scheme 1.

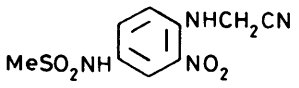


Scheme 2.



(6) a; 4-NH_3^+

b; 7-NH_3^+



(7)

group[5] then gives the nitriles (**4a** and **b**). The cyano acetamide (**4a**) is cyclised in base, under the standard conditions,[1,2] to give 4-acetamido-2-cyano-1*H*-benzimidazole 3-oxide (**5**), and the latter gives on hydrolysis the bis-hydrochloride (**6a**) and thence (**1a**).

The cyano sulphonamide (**4b**), on the other hand, does not undergo cyclisation on treatment with base; it appears merely to undergo deprotonation to give a water-soluble salt. This result may appear surprising at first, since the isomeric cyano sulphonamide (**7**) is cleanly and efficiently cyclised under these conditions.[1] However, we have previously demonstrated[1] that cyclisations of this type are inhibited by a powerful electron donor *para* to the nitro group, and compound (**4b**) in basic solution contains a powerful donor ($MeSO_2N^-$) *ortho* to the nitro group which may be expected to have a similar inhibiting effect.

(ii) *From* 4-*nitro*-1H-*benzimidazole* 3-*oxide*. We have previously noted[1] that catalytic hydrogenation of 5-nitro-1*H*-benzimidazole 3-oxide is unsatisfactory as a route to the 5-aminobenzimidazole oxide (**1b**), because of the low solubility of the nitro compound in most of the common solvents. This disadvantage does not apply, however, in the case of the 4-nitrobenzimidazole oxide,[2] which is readily soluble in ethanol. Hydrogenation of this nitro compound over palladium gives 4-aminobenzimidazole oxide (**1a**) directly and in good yield.

7-*Amino*-1H-*benzimidazole* 3-*Oxide* (**1d**).—This *N*-oxide is by far the least accessible of the four isomers of general formula (**1**). Neither of the methods already described for the preparation of (**1a**) is directly applicable to the preparation of (**1d**).

(i) *Attempted synthesis* via 7-*nitro*-1H-*benzimidazole* 3-*oxide*. This fails because the nitro compound itself cannot be prepared by cyclisation of the *N*-(2,6-dinitrophenyl)glycine derivative (ester or nitrile)[6] according to the method of Scheme 1.

(ii) *Attempted synthesis from* 3-*nitro*-1,2-*phenylenediamine*. This diamine is best obtained by nitration of 2,1,3-benzoselenadiazole[7] followed by reductive ring-opening[8] (Scheme 3); as expected it undergoes selective monoacylation at N-1 to give the 2′-amino-3′-nitroanilides (**8a**—**c**). Attempted cyanomethylation of the second amino group, however, does not give the nitriles (**9a**—**c**); an intermediate in this process is apparently intercepted by the adjacent acylamino group, and the isolated products are dihydrobenzimidazoles (**10a**—**c**). In the case of the reaction involving the acetamido compound (**9a**), the cyclised nitrile (**11**) is also obtained as a by-product.

(iii) *Synthesis from* 2′,3′-*dinitroacetanilide*. It has been known for many years[9] that reaction of 2′,3′-dinitroacetanilide with dimethylamine results in displacement of the 3-nitro group. More recently, however, it has been shown[10] that with primary (*i.e.* less bulky) amines, it is the 2-nitro substituent which is preferentially displaced. As expected, therefore, reaction of 2′,3′-dinitroacetanilide with glycine ethyl ester gives the required *N*-(6-acetamido-2-nitrophenyl)glycine ester (**12**), and the latter is cyclised under the standard conditions giving the bis-hydrochloride (**6b**) and thence the *N*-oxide (**1d**) (Scheme 4).

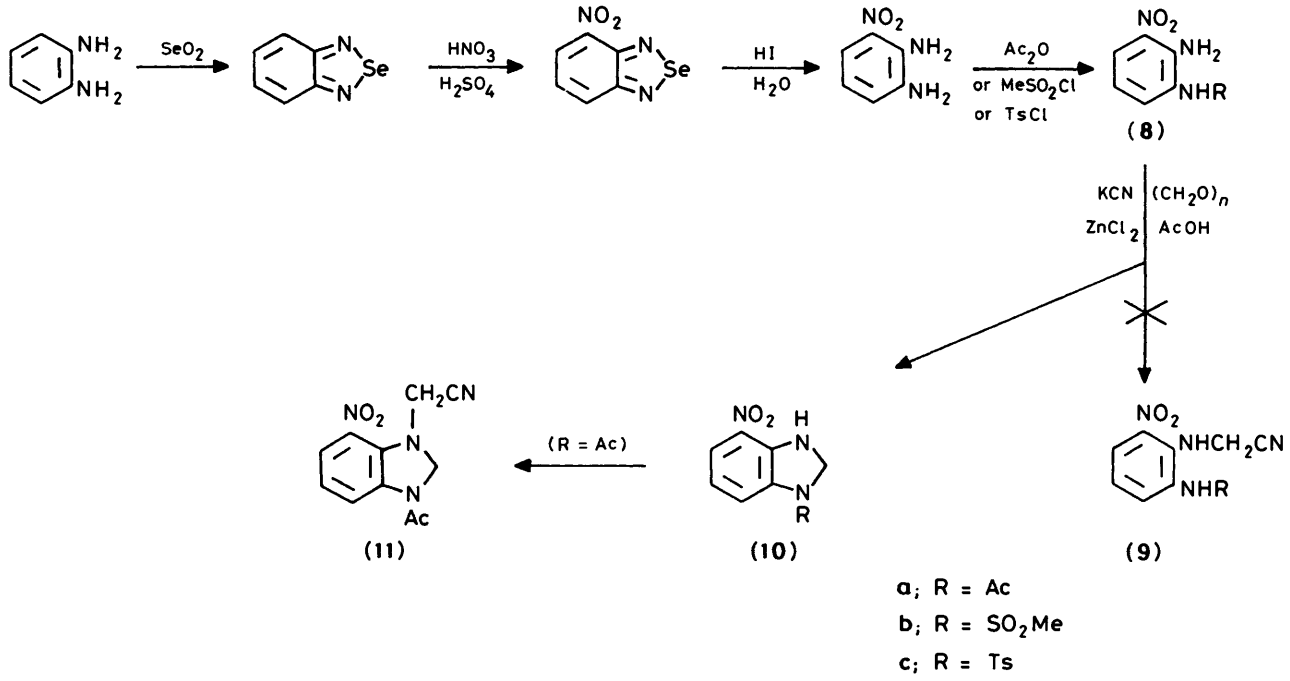
The two new *N*-oxides (**1a** and **d**) are similar in physical characteristics to the isomers (**1b** and **c**) described in Part 10.[1] Thus they crystallise out of aqueous media in the form of hydrates, and in consequence show no well defined N–H stretching absorption in their i.r. spectra. The 2-H resonance (low-field singlet) is the only diagnostic feature in their ^1H n.m.r. spectra; indeed throughout these reaction sequences the three adjacent protons in the carbocyclic ring seldom give first-order spectra.

We are now in the process of studying the selective alkylation of the *N*-oxides (**1a**—**d**), particularly with a view to synthesizing nucleoside analogues.

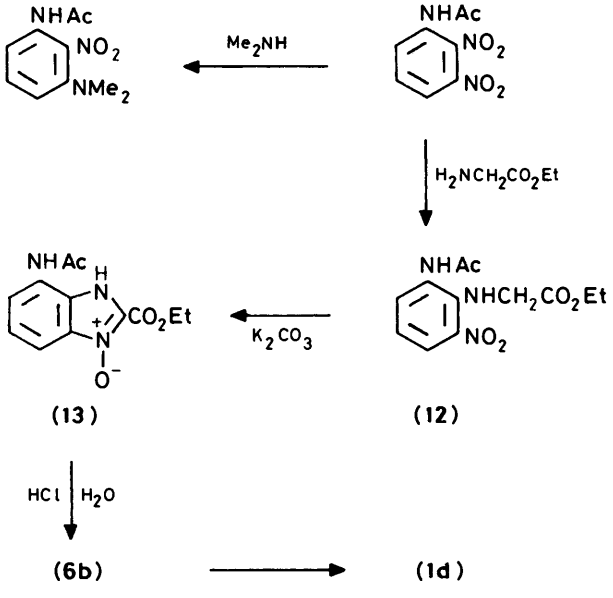
Experimental

I.r. spectra are those of Nujol mulls; ^1H n.m.r. spectra were recorded at 80 MHz for solutions in $(CD_3)_2SO$.

2-*Nitro*-1,3-*phenylenediamine*.—2-Nitro-1,3-xylene (30 g) was added to a solution of potassium permanganate (126 g) and potassium hydroxide (26.4 g) in water (1.2 l), and the mixture heated under reflux, with vigorous stirring, for 15 h. The manganese dioxide was filtered off, and the filtrate carefully neutralised (HCl) and refiltered to remove any monobasic acids,



Scheme 3.



Scheme 4.

and then acidified, giving 2-nitroisophthalic acid (26.3 g, 63%), m.p. 309—311 °C (from methanol–water; lit.,[3] 315 °C). The diacid was converted into the bis-acid chloride, m.p. 128—130 °C (lit.,[11] 125—127 °C), and the latter transformed into the diamide, m.p. 278—280 °C (from water; lit.,[4] 278—280 °C), essentially by the published procedure (yields 95 and 72%, respectively).

Sodium hypochlorite solution was prepared by passing chlorine into a solution of sodium hydroxide (25 g) in water (35 ml) until 19.2 g had been absorbed; the solution was then diluted to 200 ml with water. To this solution (45 ml), further diluted with water (260 ml) and cooled to 0 °C, the foregoing diamide (6.3 g, 0.03 mol) was added slowly, with stirring. After 1 h, the solution was filtered, if necessary, to remove unchanged diamide, and aqueous 1% sodium hydroxide (175 ml) was added to the filtrate. The Hofmann rearrangement was effected by allowing this solution to trickle slowly down the (steam-heated) spiral coil of a Quickfit (C3/12) condenser, as previously described.[4] 2-Nitro-1,3-phenylenediamine (3.2 g, 70%) crystallised from the cooled solution; it had m.p. 137—139 °C (from ethanol–water; lit.,[4] 141 or 145 °C); δ 6.20 (2 H, d, 4- and 6-H), 6.65 (4 H, br s, 2 × NH_2), and 7.12 (1 H, t, 5-H) ($J_{4,5} = J_{5,6}$ = 8 Hz).

3′-Amino-2′-nitroacetanilide (**3a**).—2-Nitro-1,3-phenylenediamine (5.11 g, 0.033 mol), acetic anhydride (7.7 g, 0.075 mol), benzene (600 ml), and pyridine (10 ml) were heated together, under reflux, for 4 h. More acetic anhydride (3.0 g) was added, the mixture was heated for a further 3 h, the solvents were evaporated off under reduced pressure, and the residue was extracted with chloroform. The insoluble portion was identified as 1,3-bisacetamido-2-nitrobenzene (0.72 g, 9%), m.p. 252—255 °C (lit.,[4] 256—258 °C), and the extract gave on evaporation 3′-amino-2′-nitroacetanilide (**3a**) (4.82 g, 74%), m.p. 113—114 °C (from propan-2-ol; lit.,[4] 114—114.5 °C); $\nu_{max.}$ 3 445, 3 290, and 3 160 (NH and NH_2), 1 690 (CO), and 1 540 and 1 315 cm^{-1} (NO_2); δ 2.00 (3 H, s, Me), 6.38 (2 H, br s, NH_2), 6.6—6.85 (2 H, m, 4- and 6-H), 7.1—7.35 (1 H, 4 lines, 5-H), and 9.89 (1 H, s, N*H*Ac).

N-(*3-Amino-2-nitrophenyl*)*methanesulphonamide* (**3b**).—Methanesulphonyl chloride (1.0 g, 8.7 mmol) was added to a solution of 2-nitro-1,3-phenylenediamine (1.2 g, 8.0 mmol) in pyridine (9 ml), and the mixture heated under reflux for 2 h. The pyridine was evaporated off under reduced pressure, and the residue dissolved in a little ethanol and added to ice–water. The precipitated *sulphonamide* (**3b**) (0.75 g, 41%) had m.p. 170—173 °C (from ethanol–water) (Found: C, 36.4; H, 3.8; N, 18.1. $C_7H_9N_3O_4S$ requires C, 36.4; H, 3.9; N, 18.2%); $\nu_{max.}$ 3 485, 3 360, and 3 240w (NH and NH_2), 1 510 and 1 330 (NO_2), and 1 305 and 1 150 cm^{-1} (SO_2); δ 3.05 (3 H, s, Me), 6.55—6.85 (4 H, m, 4- and 6-H and NH_2; simplified on addition of D_2O), 7.1—7.35 (1 H, 4 lines, 5-H), and 9.55 (1 H, br s, N*H*Ms).

N-[3-(*Cyanomethylamino*)-2-*nitrophenyl*]*acetamide* (**4a**).—To 3′-amino-2′-nitroacetanilide (**3a**) (2.0 g, 10.2 mmol) were added, successively, paraformaldehyde (0.92 g, 30.6 mmol), potassium cyanide (1.99 g, 30.6 mmol), zinc chloride (5.04 g, 37 mmol), and acetic acid (50 ml) containing concentrated sulphuric acid (2 drops). The mixture was heated to 50 °C, with vigorous stirring, over *ca.* 30 min., and kept at this temperature for 7 h; it was then added to ice–water, and the product was filtered off and washed well with water. The *cyano acetamide* (**4a**) (1.34 g, 56%) had m.p. 222—224 °C (from acetic acid) (Found: C, 51.65; H, 4.4; N, 23.8. $C_{10}H_{10}N_4O_3$ requires C, 51.3; H, 4.3; N, 23.9%); $\nu_{max.}$ 3 360 and 3 270 (NH), 1 660 (CO), 1 530 and 1 340 cm^{-1} (NO_2) (no C≡N absorption observed); δ 2.00 (3 H, s, Me), 4.38 (2 H, d, CH_2), 6.7—6.95 (3 H, m, 4- and 6-H and N*H*CH_2), 7.35—7.6 (1 H, 3 lines, 5-H), and 10.00 (1 H, s, N*H*Ac)[*J*(CH_2NH) 6 Hz].

N-[3-(*Cyanomethylamino*)-2-*nitrophenyl*]*methanesulphonamide* (**4b**).—The *methanesulphonamide* (**4b**), m.p. 186—188 °C (from acetic acid–water), was similarly obtained (1.0 g, 41%) from the amino sulphonamide (**3b**) (2.1 g, 9.1 mmol), paraformaldehyde (0.82 g), potassium cyanide (1.78 g), zinc chloride (4.5 g), and acetic acid (45 ml) containing concentrated sulphuric acid (2 drops) (Found: C, 39.8; H, 3.7; N, 20.4. $C_9H_{10}N_4O_4S$ requires C, 40.0; H, 3.7; N, 20.7%); $\nu_{max.}$ 3 380 and 3 240 (NH), 2 235w (CN), 1 505 and 1 330 (NO_2), and 1 310 and 1 145 cm^{-1} (SO_2); δ 3.06 (3 H, s, Me), 4.38 (2 H, d, CH_2), 6.8—7.0 (3 H, m, 4- and 6-H and N*H*CH_2), 7.4—7.6 (1 H, 4 lines, 5-H), and 9.65 (1 H, br s, N*H*Ms) [*J*(CH_2NH) 6 Hz].

4-*Acetamido*-2-*cyano*-1H-*benzimidazole* 3-*Oxide* (**5**).—The cyano acetamide (**4a**) (0.4 g, 1.7 mmol), potassium carbonate (0.23 g, 1.7 mmol), and ethanol (30 ml) were heated together under reflux for 1.5 h; the solvent was then evaporated off under reduced pressure and the residue was dissolved in the minimum volume of water. Acidification of the aqueous solution (HCl) gave the N-*oxide* (**5**) (0.29 g, 78%), m.p. 220 °C (decomp.) (from methanol) (Found: C, 55.6; H, 3.7; N, 25.7. $C_{10}H_8N_4O_2$ requires C, 55.6; H, 3.7; N, 25.9%); $\nu_{max.}$ 3 310 (NH), 2 240 (CN), and 1 670 cm^{-1} (CO); δ 2.11 (3 H, s, Me), 7.25—7.9 (3 H, m, 5-, 6-, and 7-H), and 9.70 (1 H, br s, N*H*Ac).

4-*Amino*-1H-*benzimidazole* 3-*Oxide* (**1a**).—(*a*) A solution of 4-nitro-1*H*-benzimidazole 3-oxide (0.5 g) in ethanol (200 ml) was hydrogenated over palladium–charcoal (5%; 0.15 g). When the uptake of hydrogen was complete (*ca.* 45 min.), the catalyst was filtered off, the filtrate evaporated to dryness under reduced pressure, and the residue triturated with ether to induce crystallisation of the product. The *aminobenzimidazole* N-*oxide* (**1a**) (0.27 g, 58%) crystallised from water (with charcoal) as a *monohydrate*, m.p. 108—110 °C (Found: C, 49.9; H, 5.3; N, 24.9. $C_7H_7N_3O{\cdot}H_2O$ requires C, 50.3; H, 5.4; N, 25.1%); $\nu_{max.}$ 3 460, 3 320, and 3 130 cm^{-1} (NH); δ 5.38 (br, NH_2 + H_2O), 6.40 (1 H, 4 lines, 5-H), 6.65—7.10 (2 H, m, 6- and 7-H), and 8.23 (1 H, s, 2-H).

(*b*) The nitrile (**5**) (1.24 g) was heated under reflux with concentrated hydrochloric acid (24 ml) for 4 h. The cooled solution deposited the *bis-hydrochloride* (**6a**) (0.50 g), and concentration of the mother liquor yielded a further crop (0.50 g: total yield 78%). Compound (**6a**) had m.p. 190—192 °C (decomp.) (from conc. HCl) (Found: C, 38.2; H, 4.1; N, 19.1. $C_7H_7N_3O{\cdot}2HCl$ requires C, 37.9; H, 4.1; N, 18.9%); δ 6.90—7.25 (2 H, 8 lines, 5- and 7-H), 7.46 (1 H, t, 6-H), 8.60 (br, NH and OH), and 9.85 (1 H, s, 2-H). The bis-hydrochloride (0.3 g) was added in portions to aqueous ammonia (*d* 0.88; 6 ml) at 0 °C; the solution was stirred at 0 °C for 30 min and evaporated under reduced pressure at 50 °C. The residue was triturated with a little ice–water. The amino *N*-oxide (**1a**) (0.1 g, 44%) was spectroscopically identical with the product from (*a*).

Attempted Cyclisation of the Cyano Sulphonamide (**4b**).—The cyano sulphonamide (**4b**) (0.75 g, 2.8 mmol) was dissolved, as far as possible, in boiling ethanol (50 ml). Potassium carbonate (0.39 g, 2.8 mmol) was added, and the mixture heated under reflux for 1.5 h, dissolution being achieved after *ca.* 30 min. The solvent was evaporated off under reduced pressure, the residue dissolved in water, and the solution acidified (HCl); the product was identical (m.p., i.r., and ^{1}H n.m.r. spectra) with the starting compound (**4b**). The recovery was 0.45 g (60%); no other product was detected.

[Under identical conditions, the isomeric sulphonamide (**7**) underwent cyclisation in 92% yield.[1]]

3-*Nitro*-1,2-*phenylenediamine*.—1,2-Phenylenediamine (36.6 g, 0.34 mol) and selenium dioxide (41.3 g, 0.37 mol) in boiling ethanol (210 ml) gave, after 10 min, 2,1,3-benzoselenadiazole (47.2 g, 76%), m.p. 70—73 °C (from water; lit.,[12] 75 °C). This was nitrated with concentrated nitric and sulphuric acids according to the published method[7] to give the 4-nitro derivative (75%), m.p. 216—218 °C (from dimethylformamide; lit.,[7] 219—221 °C). Reduction of the selenadiazole ring was effected with hydroiodic acid (*d* 1.7) at 50 °C, again by a published procedure;[8] 3-nitro-1,2-phenylenediamine, obtained in 68% yield, had m.p. 157—158 °C (from propan-2-ol; lit.,[8] 158—159 °C).

2′-*Amino*-3′-*nitroacetanilide* (🦢).—3-Nitro-1,2-phenylenediamine (5 g, 0.033 mol), acetic anhydride (3.4 g, 0.033 mol), and benzene (300 ml) were heated together under reflux for 30 min. The solution was then cooled and the product filtered off; it had m.p. 158—160 °C (from ethanol; lit.,[10] 165—167 °C); yield 4.61 g (72%); $\nu_{max.}$ 3 435 (NH), 3 325 and 3 300 (NH_2), 1 670 (CO), and 1 520 and 1 325 cm^{-1} (NO_2); δ 2.10 (3 H, s, Me), 6.67 (1 H, dd, 5-H), 7.08 (2 H, br s, NH_2), 7.51 (1 H, br d, 6-H), 7.92 (1 H, dd, 4-H), and 9.32 (1 H, s, N*H*Ac) ($J_{4.5}$ 8.5, $J_{5.6}$ 7.5, $J_{4.6}$ 1.5 Hz).

N-(2-*Amino*-3-*nitrophenyl*)*methanesulphonamide* (**8b**).—Methanesulphonyl chloride (6.9 g, 0.06 mol) was added carefully to a solution of 3-nitro-1,2-phenylenediamine (9 g, 0.059 mol) in dry pyridine (90 ml), and the mixture was heated under reflux for 30 min. The pyridine was evaporated off under reduced pressure, water was added to the residue, and the product was filtered off and washed with water. The *sulphonamide* (**8b**) (11.6 g, 85%) had m.p. 221—222 °C (from 4:1 ethanol–dimethylformamide) (Found: C, 36.1; H, 3.85; N, 18.1. $C_7H_9N_3O_4S$ requires C, 36.4; H, 3.9; N, 18.2%); $\nu_{max.}$ 3 470 (NH), 3 360 and 3 160 (NH_2), 1 510 (NO_2), 1 315 (NO_2 and SO_2), and 1 125 cm^{-1} (SO_2); δ 3.10 (3 H, s, Me), 6.80 (1 H, dd, 5-H), 7.25 (2 H, br s, NH_2), 7.63 (1 H, dd, 6-H), 8.15 (1 H, dd, 4-H), and 9.33 (1 H, s, N*H*Ms) ($J_{4.5}$ 9, $J_{5.6}$ 8, $J_{4.6}$ 2 Hz).

N-(2-*Amino*-3-*nitrophenyl*)*toluene*-p-*sulphonamide* (**8c**).—The *sulphonamide* (**8c**), m.p. 192—193 °C (from ethanol), was similarly obtained from 3-nitro-1,2-phenylenediamine (4 g) and toluene-*p*-sulphonyl chloride (5.5 g) in pyridine (40 ml); the yield, after treatment with charcoal, was 4.1 g (43%) (Found: C, 50.4; H, 4.2; N, 13.6. $C_{13}H_{13}N_3O_4S$ requires C, 50.8; H, 4.3; N, 13.7%); $\nu_{max.}$ 3 480 (NH), 3 370 and 3 250 (NH_2), 1 510 and 1 340 (NO_2), and 1 325 and 1 155 cm^{-1} (SO_2); δ 2.37 (3 H, s, Me), 6.62 (1 H, dd, 5-H), 7.05 (1 H, dd, 6-H), 7.0—7.25 (2 H, br, NH_2), 7.4—7.9 (4 H, AA′BB′, Me$C_6H_4SO_2$), 8.05 (1 H, dd, 4-H), and 10.80 (1 H, s, N*H*Ts) ($J_{4.5}$ 8, $J_{5.6}$ 7, $J_{4.6}$ 2 Hz).

Attempted Cyanomethylation of the Amino Amides (**8a**—**c**).—(a) *The acetamide* (**8a**). 2′-Amino-3′-nitroacetanilide (2 g), paraformaldehyde (0.92 g), potassium cyanide (1.99 g), and zinc chloride (5.04 g) were treated as described for the preparation of (**4a**). The crude product was fractionally recrystallised from acetic acid. The less soluble fraction (0.91 g) had m.p. 244—246 °C and was identified as 1-*acetyl*-2,3-*dihydro*-4-*nitrobenzimidazole* (**10a**) (Found: C, 52.1; H, 4.35; N, 19.9. $C_9H_9N_3O_3$ requires C, 52.2; H, 4.4; N, 20.3%) *m/z* ($M^{+\cdot}$) 207; $\nu_{max.}$ 3 340br (NH), 1 665 (CO), and 1 510 and 1 325 cm^{-1} (NO_2); δ 2.13 (3 H, s, Me), 5.60 (2 H, s, ring CH_2), 6.56 (1 H, dd, 6-H), 7.43 (1 H, dd, 5-H), 7.85 (1 H, dd, 7-H), and 8.51 (1 H, br s, NH) ($J_{5,6}$ 9, $J_{6,7}$ 7, $J_{5,7}$ 1.5 Hz). The more soluble fraction (0.20 g), m.p. 179—180 °C (from dimethylformamide—water), was identified as 1-*acetyl*-3-*cyanomethyl*-2,3-*dihydro*-4-*nitrobenzimidazole* (**11**) (Found: C, 54.0; H, 4.1; N, 22.45. $C_{11}H_{10}N_4O_3$ requires C, 53.7; H, 4.1; N, 22.75%); *m/z* ($M^{+\cdot}$) 246; $\nu_{max.}$ 1 670 (CO) and 1 515 and 1 335 cm^{-1} (NO_2), (no C≡N absorption observed); δ 2.18 (3 H, s, CH_3), 4.53 (2 H, s, CH_2CN), 5.54 (2 H, s, ring CH_2), 6.98 (1 H, dd, 6-H), 7.60 (1 H, dd, 5-H), and 8.10 (1 H, dd, 7-H) ($J_{5,6}$ 9, $J_{6,7}$ 7.5, $J_{5,7}$ 1.5 Hz). The yields of (**10a**) and (**11**) were 43 and 20%, respectively.

(b) *The methanesulphonamide* (**8b**). Compound (**8b**) (2 g), paraformaldehyde (0.78 g), potassium cyanide (1.69 g), and zinc chloride (4.3 g) similarly give 2,3-*dihydro*-1-*methylsulphonyl*-4-*nitrobenzimidazole* (**10b**) (1.2 g, 57%), m.p. 171—172 °C (from acetic acid) (Found: C, 39.3; H, 3.6; N, 17.2. $C_8H_9N_3O_4S$ requires C, 39.5; H, 3.7; N, 17.3%); *m/z* ($M^{+\cdot}$) 243; $\nu_{max.}$ 3 435 (NH), 1 510 and 1 350 (NO_2), and 1 305 and 1 140 cm^{-1} (SO_2); δ 3.20 (3 H, s, Me), 5.55 (2 H, s, ring CH_2), 6.78 (1 H, dd, 6-H), 7.38 (1 H, dd, 7-H), 7.70 (1 H, dd, 5-H), and 8.57 (1 H, s, N*H*Ms) ($J_{5,6}$ 9, $J_{6,7}$ 7, $J_{5,7}$ 2 Hz). No second product was isolated.

(*c*) *The toluene*-p-*sulphonamide* (**9c**). This compound (1.5 g), paraformaldehyde (0.45 g), potassium cyanide (0.96 g), and zinc chloride (5.1 g) gave, after 5 h, 2,3-*dihydro*-4-*nitro*-1-p-*tolylsulphonylbenzimidazole* (**10c**) (0.95 g, 60%), m.p. 145—146 °C (from acetic acid) (Found: C, 52.8; H, 4.1; N, 13.2. $C_{14}H_{13}N_3O_4S$ requires C, 52.7; H, 4.1; N, 13.2%); $\nu_{max.}$ 3 380 (NH), 1 510 and 1 330 (NO_2), and 1 310 and 1 160 cm^{-1} (SO_2); δ 2.40 (3 H, s, Me), 5.57 (2 H, s, ring CH_2), 6.82 (1 H, dd, 6-H), 7.50—8.0 (6 H, m, ArH), and 8.40 (1 H, s, NH) ($J_{5,6}$ 8.5, $J_{6,7}$ 7 Hz).

N-(6-*Acetamido*-2-*nitrophenyl*)*glycine Ethyl Ester* (**12**).—2′,3′-Dinitroacetanilide[13] (7 g, 0.031 mol), glycine ethyl ester hydrochloride (3.92 g, 0.028 mol), sodium hydrogen carbonate (4.76 g, 0.056 mol), and dimethyl sulphoxide (120 ml) were heated, with stirring, for 1.5 h at 60 °C. More glycine ethyl ester hydrochloride (3.92 g) was then added, and heating was continued for 2.5 h. T.l.c. showed the presence of unchanged 2′,3′-dinitroacetanilide, and so two further portions of hydrochloride (each 3.92 g) were added, with a 2 h interval between the additions. When all the dinitroacetanilide had reacted (total reaction time 8.5 h), the mixture was poured onto ice, giving the *ester* (**12**) (5.0 g, 57%), m.p. 118—119 °C (from ethanol) (Found: C, 51.35; H, 5.3; N, 15.0. $C_{12}H_{15}N_3O_5$ requires C, 51.2; H, 5.4; N, 14.9%); $\nu_{max.}$ 3 355 and 3 220 (NH), 1 740 (ester CO), 1 650 (amide CO), and 1 540 and 1 340 cm^{-1} (NO_2); δ 1.16 (3 H, t, *Me*CH_2), 2.08 (3 H, s, MeCO), 4.10 (4 H, overlapping d + q, 2 × CH_2), 6.92 (1 H, t, 4-H), 7.35 (1 H, br t, N*H*CH_2), 7.57 and 7.91 (2 H, 2 × br dd, 3- and 5-H), and 9.55 (1 H, br s, N*H*Ac) [$J(CH_3CH_2)$ 7, $J_{3,4} = J_{4,5}$ = 8 Hz].

Ethyl 7-*Acetamido*-1H-*benzimidazole*-2-*carboxylate* 3-*Oxide* (**13**).—The nitro ester (**12**) (4.53 g, 0.016 mol), potassium carbonate (2.26 g, 0.016 mol), and ethanol (170 ml) were heated together under reflux for 2 h. The ethanol was evaporated off under reduced pressure and the residue extracted with water. Acidification (HCl) of the extract gave the *ester* (**13**) (1.83 g, 43%), m.p. 98—99 °C (from ethanol–water); this compound retains water tenaciously and requires prolonged drying (Found: C, 54.5; H, 5.0; N, 15.9. $C_{12}H_{13}N_3O_4$ requires C, 54.75; H, 5.0; N, 16.0%); $\nu_{max.}$ 3 340w (NH), 1 730 (ester CO), and 1 665 cm^{-1} (amide CO); δ 1.40 (3 H, t, *Me*CH_2), 2.27 (3 H, s, MeCO), 4.47 (2 H, q, C*H*$_2$Me), 7.2—7.55 (2 H, m, 4- and 5-H), 8.07 (1 H, 4 lines, 6-H), and 10.06 (1 H, s, N*H*Ac) [$J(CH_3CH_2)$ 7 Hz].

7-*Amino*-1H-*benzimidazole* 3-*Oxide* (**1d**).—The acetamido ester (**13**) (2 g) was heated with concentrated hydrochloric acid (20 ml), under reflux, for 4 h. The solution was concentrated and the brown residue recrystallised from concentrated hydrochloric acid (with charcoal), giving the *bis-hydrochloride* (**6b**) (1.15 g, 68%), m.p. 224—226 °C (from HCl). (Found: C, 38.0; H, 4.1; N, 18.95. $C_7H_7N_3O$·2HCl requires C, 37.9; H, 4.1; N, 18.9%); δ 6.75—7.15 (2 H, m), 7.37 (1 H, approx. t), 9.50 br (NH and OH), and 9.78 (1 H, s, 2-H). Reaction of the bis-hydrochloride (0.2 g) with ammonia, as described for the isomer (**6a**), gave the 7-*aminobenzimidazole oxide* (**1d**), m.p. 118—120 °C (from water) (Found: C, 50.5; H, 5.4; N, 25.2. $C_7H_7N_3O$·H_2O requires C, 50.3; H, 5.4; N, 25.1%); yield 0.091 g (61%); $\nu_{max.}$ 3 500sh, 3 400, 3 310, 3 210sh, 3 115, and 3 095 cm^{-1} (NH and OH); δ 5.70 (br, NH and H_2O), 6.42 and 6.70 (2 H, 2 × br d, 4- and 6-H), 7.01 (1 H, t, 5-H), and 8.17 (1 H, s, 2-H) ($J_{4,5} = J_{5,6}$ = 7.5 Hz).

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