Relationships between Nitro Group Reduction Potentials and Torsion Angles in Di-*ortho*-substituted Nitrobenzenes; a Crystallographic and Oxygen-17 NMR Study

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A series of 3-nitro-4-alkylbenzamides has been prepared, and the effects of nitro group torsion angle on reduction potential studied. Nitro and carboxamide group torsion angles have been determined by ^{17}O NMR spectroscopy and X-ray crystallography, and one-electron reduction potentials by pulse radiolysis. ^{17}O Chemical shifts indicated similar amide torsion angles (from 35° to 45°) as the alkyl group varied from hydrogen to *tert*-butyl, but widely differing nitro group torsion angles; from 36° (hydrogen) to 92° (*tert*-butyl). Crystal structures of the isopropyl and *tert*-butyl derivatives indicate amide group torsion angles (50° and 64°) somewhat larger than those predicted by ^{17}O NMR, and nitro group torsion angles (59° and 65° respectively) considerably smaller than those predicted by ^{17}O NMR (75° and 92° respectively). These results support earlier data that ^{17}O chemical shifts predict for erroneously large nitro group torsion angles in non-rigid but sterically crowded molecules, because of additional contributions to the shift from van der Waals repulsions. The drop in reduction potential of 90 mV between the unsubstituted and *tert*-butyl derivatives is too large to be accounted for by the electronic effects of the alkyl groups, and indicates that increasing the nitro group torsion angle significantly lowers reduction potential.

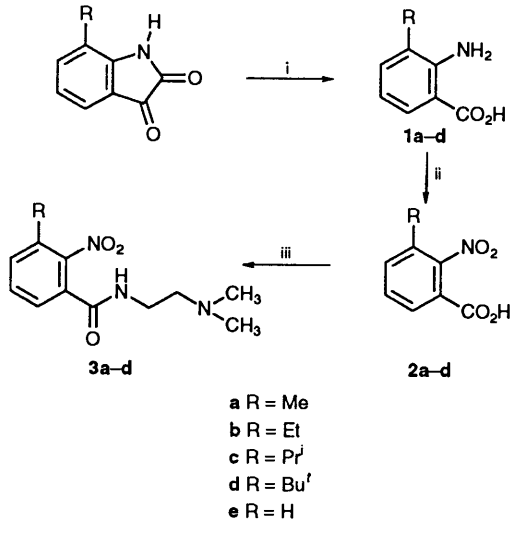
A fundamental problem in the development of nitroaromatic compounds as radiosensitisers of hypoxic tumour cells is the close correlation between two opposing biological effects; radiosensitising efficiency and cytotoxicity.[1] Each of these effects is principally determined by different but related properties of nitroaromatic compounds; the former by the ability to accept an electron from radiation-induced DNA radicals and the latter by the ease of reduction of the nitro group (to potentially-toxic species) by cellular enzymes. These two properties are similarly dependent on the reduction potential of the nitro group,[2] and therefore improving the therapeutic index of radiosensitisers (diverging radiosensitising efficiency and cytotoxicity) by simple variation of reduction potentials is difficult.

Fixation of radiation damage is an electron transfer reaction,[3] while reductive metabolism is enzymatic, with K_m values varying widely even for structurally-related compounds.[4] Since it is likely the latter process has more stringent steric requirements than the former, one possible strategy for improving therapeutic index is steric shielding of the nitro group. We have consequently been studying the conformation of sterically-crowded nitro groups in appropriate molecules. In a previous study of nitroquinolines,[5,6] we observed that *ortho* substitution by methyl groups lowered nitro group reduction potentials by varying but substantial amounts (from 30 to 180 mV). Although steric contributions could not be separated from concomitant electronic ones in these weak bases,[6] the former were considered to be significant.

There are few studies of nitro torsion angles in such environments. A study of various nitrobenzenes *ortho*-substituted by a planar group XYZ (including amide) concluded that, while the sum of the two torsion angles is usually close to 90°, the nitro and amide torsion angles can vary markedly and unpredictably. In the present paper, we report ^{17}O and X-ray crystallographic studies of the torsion angles of nitro groups in a series of 3-alkylsubstituted 2-nitrobenzamides, where the absence of pK_a effects was expected to simplify interpretation of the results.

Results

The 3-alkyl-2-nitrobenzamides **3a–d** were synthesised as shown in Scheme 1. Oxidation of the appropriate 7-alkylisatins[8,9] with



Scheme 1 *Reagents:* i, H_2O_2–KOH, then H^+; ii, OXONE® (potassium peroxymonosulfate)–Me_2CO–CH_2Cl_2–H_2O; iii, CDI–DMF, then $H_2N[CH_2]_2NMe_2$

H_2O_2 gave the 2-aminobenzenecarboxylic acids **1a–d**. Further oxidation of these to the 2-nitrobenzenecarboxylic acids **2a–d** was conveniently carried out with dimethyldioxirane,[10] which gave greatly-improved yields over reported[11] methods. Coupling with 1,1′-carbonyldiimidazole[12] then gave the required benzamides **3a–d**.

Table 1 Reduction potentials, ^{17}O NMR and crystallographic data for compounds **3a–e**

					Torsion angle (°)				
			$\delta_{^{17}O}$		Calcd.			X-Ray	
No.	σ	$E(1)$/mV	NO_2	Amide	NO_2	$CONH_2$	$CON(Me)_2$	NO_2	Amide
4	0.0	−403	601	339	36	37	46		
3a	−0.17	−476	627	337	69	35	43		
3b	−0.15	−485	629	338	72	36	45		
3c	−0.15	−491	632	338	76	36	45		
3c (HCl salt)	—		631	341	75	39	50	59	50
3d	−0.16	−493	644	341	92	39	50	65	64

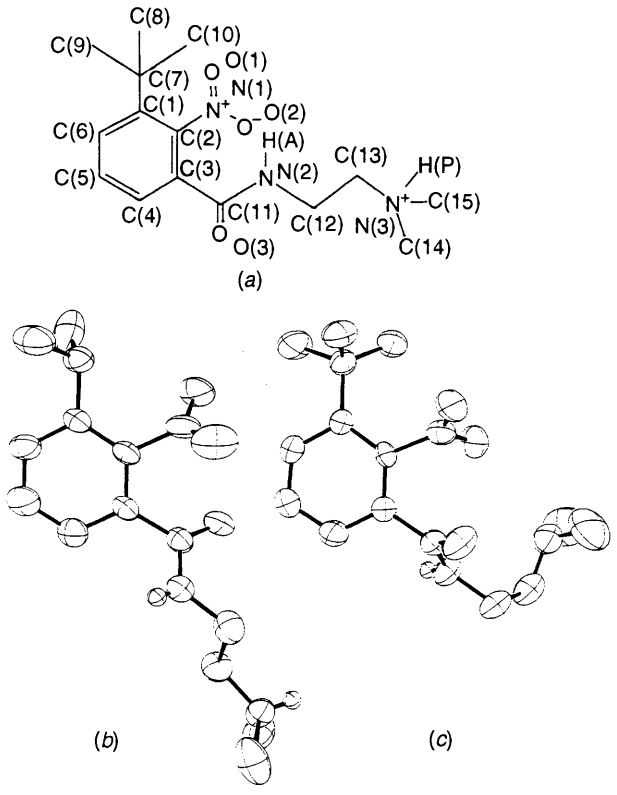


Fig. 1 (a) numbering for ORTEP diagrams; (*b*) ORTEP diagram of isopropylbenzamide **3c**; (*c*) ORTEP diagram of *tert*-butylbenzamide **3d**

The one-electron reduction potentials [$E(1)$] of these compounds were determined by pulse radiolysis, using methyl viologen [$E(1) = -447$ mV] as the reference sample. The ^{17}O resonances measured for the free bases of the 3-alkyl-2-nitrobenzamides **3a–d** and the analogous unsubstituted analogue **3e** are recorded in Table 1. Nitro and amide torsion angles (Θ), with respect to the aromatic ring plane, have been calculated from these shifts using the empirical equations established by Boykin *et al.*[13,14] [eqns. (1) and (2)], and are also in Table 1.

For nitro groups

$$\Theta = 1.29\delta - 739 \quad (1)$$

For unsubstituted amides

$$\Theta = 0.84\delta - 308 \quad (2)$$

For *N*,*N*-dialkylamides

$$\Theta = 0.6\delta - 313 \quad (3)$$

The chemical shifts for the amide oxygen varied very little across the series (δ 338–341), suggesting the amide torsion angle to be largely unaffected by variations in the size of the 3-substituent. Two Θ/δ eqns. (2) and (3) have been derived by Boykin, for carboxamides and *N*,*N*-dialkylcarboxamides respectively; a similar equation for *N*-monoalkyl compounds has not been derived, because of problems with hydrogen-bonding.[14] However, the two available equations suggest an amide torsion angle for the present *N*-monoalkylcarboxamides **3a–d** of between about 35° and 45°. The amide torsion angle of *ortho*-substituted *N*-monoalkylamides can range from near planar to near perpendicular depending on the hydrogen bonding that occurs. When there is no hydrogen bonding, a torsion angle of *ca.* 50° is not unusual.[15]

In contrast, the ^{17}O chemical shifts of the nitro groups vary significantly with the nature of the 3-substituent. Data for the unsubstituted compound **3e** suggest a nitro group torsion angle of 36°, comparable to that seen in other mono-*ortho*-substituted nitrobenzenes.[16] The presence of a 3-methyl substituent in **3a** increases the apparent torsion angle of the nitro group, now placed between two ortho substituents, to 69°. Replacement of methyl by ethyl or isopropyl (compounds **3b**, **c**) does not increase the apparent torsion angle much more, whereas a 3-*tert*-butyl group (in **3d**) results in a further apparent increase, to 92°.

To obtain an independent measure of nitro group torsion angles, X-ray structure determinations of the isopropyl and *tert*-butyl analogues (**3c** and **d**) were carried out. A diagram of the compounds involved, and the numbering scheme used, is shown in Fig. 1. The *tert*-butyl compound (**3d**) crystallised well as the free base, but the isopropyl analogue (**3c**) did not, and the crystal structure determination was carried out on the hydrochloride salt. The ^{17}O NMR chemical shifts of both the nitro and amide groups were essentially identical in both the free base and the hydrochloride salt, indicating no significant change in geometry between the two forms in solution.

Discussion

The effects of steric crowding on the torsion angles of aromatic nitro groups are of interest in medicinal chemistry, since the significant deconjugation expected at large torsion angles can be expected to have an influence on their reduction potentials.[17] *ortho*-Substitution by methyl groups lowers nitro group reduction potentials of 4-alkylaminonitroquinolines by varying but substantial amounts (from 30 to 180 mV).[5,6] Although steric contributions could not be separated from concomitant electronic ones in these weak bases,[6] the former were considered to be significant.

The compounds studied here possess nitro groups flanked by both alkyl and amide functions. The drop in reduction potential of 73 mV between the unsubstituted and 3-methyl compounds (**3e** and **a**) is too large to be accounted for by the electronic effects of the methyl group, which are estimated by eqn. (4),

$$E(1)/\text{mV} = 163\sigma^- - 492 \quad (4)$$

relating reduction potentials in substituted nitrobenzenes to substituent electronic effects,[18] as only *ca.* 25 mV. Thus the increase in nitro group torsion angle (from 36° to 69° as determined by ^{17}O NMR) appears to have a significant effect on reduction potential. As the 3-substituent is altered from methyl to isopropyl in compounds **3a–c** there are small increases in nitro group torsion angles, but on going to *tert*-butyl (compound **3d**) another large apparent increase is seen (to 92°). This is not unreasonable on steric grounds, because methyl, ethyl and isopropyl groups can orient similarly to minimise non-bonded interactions with the nitro, whereas *tert*-butyl cannot. However, the reduction potential of **3d** is unchanged; since the electronic properties of the substituent alkyl groups are similar, this is at odds with such a large torsion angle.

Analyses of the crystal structures of a number of systems with a nitro group *ortho* to non-hydrogen substituents of similar size (including amides),[7,19] showed that although the nitro and amide torsion angle can vary markedly, the sum of the two angles is usually close to 90°. When a third group is positioned in the other *ortho* position to the nitro group, the sum of the amide and nitro torsion angles increases to between 95° and 130°.[7] The sum of the nitro and amide torsion angles (determined by ^{17}O NMR) for compounds **3a–c** fit this pattern, but those for **3d** exceed this limit.

Because of the above conflicting results, X-ray crystal structures of both **3c** and **d** were undertaken; these showed amide group torsion angles of 50° and 64° respectively. The value for **3c** agrees tolerably well with that predicted by ^{17}O NMR using eqn. (3) (*ca.* 45°), but that for **3d** is much larger than predicted, suggesting that the (admittedly limited) Θ/δ relationship for amides underpredicts torsion angles in very crowded molecules. This variation in amide torsion angle was particularly surprising when the virtually identical ^{17}O chemical shifts are considered. Fig. 1 shows the ORTEP diagrams of the two structures. It is not inconceivable that the amide torsion angle of the hydrochloride salt of the isopropyl compound is in fact close to that of the *tert*-butyl in solution, but the presence of the potentially hydrogen bonding NH^+ group at the terminus of the amide side chain has led to a marked difference in the conformation of this part of the molecule in the solid state.

In contrast, the nitro group torsion angles for both **3c** and **d** (56 and 65° respectively) are much smaller than those predicted by ^{17}O NMR using the Boykin Θ/δ eqn. (1).

We have previously observed[5] that this equation predicts erroneously large nitro group torsion angles for nitroquinolines containing two *ortho* groups, because in these circumstances the ^{17}O chemical shift is also affected by van der Waals repulsions. Boykin *et al.*[20] have investigated the ^{17}O chemical shifts in a number of species containing a rigid carbonyl fragment, and have classified compounds into two groups; those with relatively unconstrained groups, where the main contribution to chemical shift is torsion angle, and rigid systems where the main contribution arises from in-plane bond distortions and repulsive van der Waals interactions.

It is clear from both the present and previous[5] data, that in non-rigid but sterically crowded molecules contributions to chemical shift come from both factors. 2,4,6-Tri-*tert*-butylnitrobenzene has also been shown to exhibit a substantial additional downfield shift.[13] In general, the effect of a *tert*-butyl group as one *ortho* substituent in *ortho*-disubstituted nitroaromatics is to produce an additional downfield shift in the ^{17}O NMR spectrum, due to van der Waals interactions, of at least 25 ppm over and above that due to the effects on nitro group torsion angle, while that of an isopropyl group can produce an additional shift of more than 10 ppm.

Experimental

N-[12-(*Dimethylamino*)*ethyl*]-3-*alkyl*-2-*nitrobenzamides*.—N-[2-(*Dimethylamino*)*ethyl*]-3-*methyl*-2-*nitrobenzamide hydrochloride* (**3a**). A mixture of commercial 3-methyl-2-nitrobenzoic acid (**2a**) (3.0 g, 16.6 mmol) and 1,1′-carbonyldiimidazole[12] (CDI) (4.03 g, 24.9 mmol) in dry dimethylformamide (DMF) (20 cm^3) was stirred at 50 °C for 15 min. The mixture was cooled to 20 °C, 2-(dimethylamino)ethylamine (5.50 cm^3, 49.8 mmol) was added. The reaction was stirred at 20 °C for a further 90 min before being quenched with ice-cold aq. Na_2CO_3 (2 mol dm^{-3}) and extracted into EtOAc. Work-up of the organic layer gave the benzamide **3a** (3.8 g, 90%). The HCl salt had m.p. 200–201 °C (from MeOH–EtOAc–HCl) (Found: C, 50.1; H, 6.2; N, 14.5; Cl, 12.3. $C_{12}H_{17}N_3O_3$·HCl requires: C, 50.08; H, 6.30; N, 14.60; Cl, 12.32%); $\delta_H[(CD_3)_2SO]$ 11.00 (br, D_2O exch., 1 H, HCl), 9.22 (t, *J* 6.0, D_2O exch., 1 H, CONH), 7.83 (dd, *J* 6.7, 2.3, 1 H, 6-H), 7.61 (dd, *J* 6.7, 2.3, 1 H, 4-H), 7.58 (t, *J* 6.7, 1 H, 5-H), 3.60 (q, *J* 6.0, collapse to t with D_2O, 2 H, $CONHCH_2$), 3.23 (t, *J* 6.0, 2 H, $CONHCH_2CH_2$), 2.80 [s, 6 H, $N(CH_3)_2$] and 2.30 (s, 3 H, CH_3).

N-[2-(*Dimethylamino*)*ethyl*]-3-*ethyl*-2-*nitrobenzamide hydrochloride* (**3b**). 2-Amino-3-ethylbenzoic acid[11] (**1b**) (2.7 g, 16.4 mmol) was dissolved in a two-phase mixture of Me_2CO (160 cm^3), CH_2Cl_2 (160 cm^3), aq. $NaHSO_4$ (84 cm^3, 67 mmol; 0.8 mol dm^{-3}), aq. tetraethylammonium hydroxide (0.6 cm^3, 0.8 mmol; 20% w/v) and water (246 cm^3). The mixture was stirred vigorously at 20 °C, and solid potassium peroxymonosulfate (32.8 g, 53.3 mmol) was added portionwise over 90 min, with the solution being maintained at *ca.* pH 8 by the occasional addition of aq. KOH (2 mol dm^{-3}).[10] The mixture was stirred for a further 2 h at 20 °C, then acidified with HCl and extracted with EtOAc. The organic layer was washed with water and worked-up to give 3-ethyl-2-nitrobenzoic acid (**2b**) (3.0 g, 94%), m.p. 201–203 °C (from CH_2Cl_2–EtOAc) (lit.,[11] m.p. 206–207 °C); $\delta_H(CDCl_3)$ 7.98 (dd, *J* 7.7, 1.4, 1 H, 6-H), 7.60 (dd, *J* 7.7, 1.4, 1 H, 4-H) 7.54 (t, *J* 7.7, 1 H, 5-H), 6.62 (br, D_2O exch., 1 H, CO_2H), 2.64 (q, *J* 7.5, 2 H, CH_2) and 1.28 (t, *J* 7.5, 3 H, CH_3). Coupling of **2b** with 2-(dimethylamino)ethylamine as above gave the benzamide hydrochloride (**3b**) (75% yield), m.p. 158–160 °C (from MeOH–EtOAc–HCl) (Found: C, 51.8; H, 6.8; N, 14.2; Cl, 11.9. $C_{13}H_{19}N_3O_3$·HCl requires: C, 51.76; H, 6.68; N, 13.93, Cl, 11.75%); $\delta_H[(CD_3)_2SO]$ 10.76 (br, D_2O exch., 1 H, HCl), 9.19 (t, *J* 6.0, D_2O exch., 1 H, CONH), 7.83 (dd, *J* 6.4, 2.5, 1 H, 6-H), 7.63 (m, 2 H, 4-, 5-H), 3.59 (q, *J* 6.0, collapse to t with D_2O, 2 H, $CONHCH_2$), 3.22 (t, *J* 6.0, 2 H, $CONHCH_2CH_2$) 2.80 [s, 6 H, $N(CH_3)_2$], 2.58 (q, *J* 7.5, 2 H, CH_2CH_3) and 1.17 (t, *J* 7.5, 3 H, CH_2CH_3).

N-[2-(*Dimethylamino*)*ethyl*]-3-*isopropyl*-2-*nitrobenzamide hydrochloride* (**3c**). Oxidation of 7-isopropylisatin[9] with H_2O_2 gave 2-amino-3-isopropylbenzoic acid (**1c**) (64% yield), m.p. 98–99 °C (from EtOAc–light petroleum); $\delta_H(CDCl_3)$ 7.82 (dd, *J* 8.0, 1.5, 1 H, 6-H), 7.30 (dd, *J* 8.0, 1.5, 1 H, 4-H), 6.68 (t, *J* 8.0, 5-H), 2.89 (sept, *J* 6.8, 1 H, CH) and 1.27 (d, *J* 6.8, 6 H, 2 × CH_3) (Found: C, 67.3; H, 7.3; N, 8.0. $C_{10}H_{13}NO_2$ requires: C, 67.0; H, 7.3; N, 7.8%). Oxidation of **1c** with dimethyldioxirane as above gave 3-isopropyl-2-nitrobenzoic acid (**2c**) (81% yield), m.p. 185–187 °C (from CH_2Cl_2) (Found: C, 57.75; H, 5.15; N, 6.7. $C_{10}H_{11}NO_4$ requires: C, 57.41; H, 5.30; N, 6.69%); $\delta_H(CDCl_3)$ 7.98 (dd, *J* 7.8, 1.3, 1 H, 6-H), 7.69 (dd, *J* 7.8, 1.3, 1 H, 4-H), 7.57 (t, *J* 7.8, 1 H, 5-H), 4.10 (br, D_2O exch., 1 H, CO_2H), 2.93 (sept, *J* 6.8, 1 H, CH) and 1.28 (d, *J* 6.8, 6 H, 2 × CH_3). Coupling of **2c** with 2-(dimethylamino)ethylamine as above gave the benzamide hydrochloride (**3c**) (69% yield), m.p. 189–191 °C (from MeOH–EtOAc–HCl) (Found: C, 53.35; H, 6.9; N, 13.55; Cl, 11.5. $C_{14}H_{21}N_3O_3$·HCl requires: C, 53.24; H, 7.02; N, 13.33, Cl, 11.22%); $\delta_H[(CD_3)_2SO]$ 10.60 (br, D_2O exch., 1 H, HCl), 9.15 (t, *J* 6.0, D_2O exch., 1 H, CONH), 7.82 (dd, *J* 7.7, 1.2, 1 H, 6-H), 7.76 (dd, *J* 7.7, 1.2, 1 H, 4-H), 7.66 (t, *J* 7.7, 1 H, 5-H),

Table 2 Crystal structure data for compounds **3c** and **d**

	3c	**3d**
Formula	$C_{14}H_{21}N_3O_3$·HCL	$C_{15}H_{23}N_3O_3$
M	315.69	293.27
Colour	white	yellow
Solvent	EtOAc–MeOH	EtOAc–light petroleum
Space group	orthorhombic, $Pna2_1$	orthorhombic, *Pbca*
a/Å	28.954(7)	9.343(3)
b/Å	5.428(3)	22.193(3)
c/Å	10.733(2)	15.735(5)
α(°)	90.0	90.0
β(°)	90.0	90.0
γ(°)	90.0	90.0
V/Å^3	1686.9(1.2)	3263.5(1.6)
Z	4	8
D_c/g cm^{-3}	1.243	1.195
μ/mm^{-1}	0.24	0.80
F(000)	672	1264
θ limit	25	28
Total no. reflections	1514	2592
No. observed reflections	1393	1036
Final *R*	0.035 6	0.040 6
Weighted *R* (R_w)	0.040 1	0.039 6
Weighting factor *w*	0.004 102	0.000 723

3.59 (q, *J*, 6.0, collapse to t with D_2O, 2 H, CONHCH_2), 3.21 (t, *J* 6.0, 2 H, $CONHCH_2CH_2$), 2.74–2.87 [m, 7 H, $N(CH_3)_2$, $CH(CH_3)_2$] and 1.22 (d, *J* 6.8, 6 H, $CH(CH_3)_2$).

N-[2-(*Dimethylamino*)*ethyl*]-3-tert-*butyl*-2-*nitrobenzamide hydrochloride* (**3d**). Oxidation of 7-*tert*-butylisatin[9] with H_2O_2 gave 2-amino-3-*tert*-butylbenzoic acid (**1d**) (93% yield), m.p. 190–192 °C (from CH_2Cl_2–light petroleum) (Found: C, 68.65; H, 7.6; N, 7.4. $C_{11}H_{15}NO_2$ requires: C, 68.37; H, 7.82; N, 7.25%); $\delta_H(CDCl_3)$ 7.90 (dd, *J* 8.0, 1.6, 1 H, 6-H), 7.42 (dd, *J* 8.0, 1.6, 1H, 4-H), 6.63 (t, *J* 8.0, 1 H, 5-H), 5.50 (br, D_2O exch., 3 H, NH_2, CO_2H) and 1.45 [s, 9 H, $C(CH_3)_3$]. Oxidation of **1d** with dimethyldioxirane as above gave 3-*tert*-butyl-2-nitrobenzoic acid (**2d**) (72% yield), m.p. 177–179 °C (from CH_2Cl_2–light petroleum) (Found: C, 59.4; H, 5.9; N, 6.7. $C_{11}H_{13}NO_4$ requires: C, 59.18; H, 5.87; N, 6.28%); $\delta_H(CDCl_3)$ 7.97 (dd, *J* 8.0, 1.3, 1 H, 6-H), 7.83 (dd, *J* 8.0, 1.3, 1 H, 4-H), 7.51 (t, *J* 8.0, 1 H, 5-H), 5.50 (br, D_2O exch., 1 H, CO_2H) and 1.45 [s, 9 H, $C(CH_3)_3$]. Coupling of **2d** with 2-(dimethylamino)ethylamine as above gave the benzamide hydrochloride (**3d**) (80% yield), m.p. 223–225 °C (from MeOH–EtOAc–HCl) (Found: C, 54.8; H, 7.25; N, 12.9; Cl, 10.6. $C_{15}H_{23}N_3O_3$·HCl requires: C, 54.62; H, 7.33; N, 12.74; Cl, 10.75%); $\delta_H[(CD_3)_2SO]$ 10.78 (br, D_2O exch., 1 H, HCl), 9.08 (t, *J* 6.0, D_2O exch., 1 H, CONH), 7.81 (dd, *J* 7.8, 1.2, 1 H, 6-H), 7.76 (dd, *J* 7.8, 1.2, 1 H, 4-H), 7.61 (t, *J* 7.8, 1 H, 5-H), 3.57 (q, *J* 6.0, collapse to t with D_2O, 2 H, CONHCH_2), 3.20 (t, *J* 6.0, 2 H, $CONHCH_2CH_2$), 2.80 [s, 6 H, $N(CH_3)_2$] and 1.35 [s, 9 H, $C(CH_3)_3$].

Reduction Potentials.—These were measured by pulse radiolysis, using a 1.8 MV Linac delivering *ca.* 3 Gy in 0.2 μs to a 2 cm pathlength cell, essentially as discussed previously.[5] Solutions were 3 mmol dm^{-3} in phosphate buffer at pH 7, using either isopropanol or isopropanol–acetone mixtures as co-solvent. The redox indicator used was methyl viologen [$E(1) = -447$ mV].

NMR Spectroscopy.—NMR studies were carried out on a Bruker 400 AM spectrometer equipped with an ASPECT 3000 data system. ^1H Spectra were measured in $CDCl_3$ with Me_4Si internal reference using a 5 mm $^1H/^{13}C$ dual probe. *J*-Values are given in Hz. Data were collected and processed with the DISNMR program. Natural abundance ^{17}O spectra were measured at 54.23 MHz in 10 mm tubes with a tuneable broad-band probe. Solutions were *ca.* 100 mmol dm^{-3} in CH_3CN, containing 30% CD_3CN to provide a lock signal. The probe temperature was 70 °C, and the spectra were referenced to external D_2O at 70 °C over a spectral width of 8000 Hz, using 4K data points. The pulse width was 15 μs, with an acquisition time of 0.25 s. Signal-to-noise ratios of 5–10:1 and peak widths of 450 Hz were obtained with (1–3) × 10^5 scans and an exponential broadening of 25 Hz. Under these conditions, the ^{17}O resonance of nitrobenzene occurred at δ 575 (lit.,[13] δ 576).

X-Ray Crystallography.—Crystals of the nitroamides (**3c** and **d**) were obtained by slow evaporation of the solvents indicated in Table 2. Lattice constants and intensity data were measured using Mo-Kα radiation, λ = 0.710 69 Å, on a Nonius CAD-4 diffractometer in $\omega/2\Theta$ scan mode. Three standard reflections were measured for every 50 reflections and no significant changes in the intensities of these reflections were observed.

The structures were solved by direct methods using SHELX-S,[21] and refined with SHELX-76.[22] Hydrogen atoms were found from difference maps and their positional parameters and isotropic thermal parameters were refined. In both cases, refinement was halted when the largest shift/esd was less than 0.09 and maximum and minimum peaks in the final difference maps were less than 0.25 e Å^{-3}. The weighting function used was $1/[\sigma^2(F) + wF^2]$. All positional and thermal parameters and bond lengths and angles have been deposited with the Cambridge Crystallographic Data Centre.*

Acknowledgements

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* For details of the CCDC deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1994, issue 1.

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