Crystallographic and Oxygen-17 NMR Studies of Nitro Group Torsion Angles in a Series of 4-Alkylaminonitroquinolines Designed as Hypoxia-selective Cytotoxins

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Nitro group torsion angles have been determined by ^{17}O NMR spectroscopy for a series of 4-(alkylamino)nitroquinolines and their *ortho*-methyl-substituted analogues. Crystal structures were determined for two pairs of compounds, to further evaluate the validity of Boykin's equation. The crystallographic torsion angles were used to calculate a modified version of the equation, relating ^{17}O chemical shift values (δ) and nitro group torsion angles (θ), applicable to *N*-heterocyclic systems, as follows: $\theta = 1.18(\pm 0.13)\delta - 661$. This equation was then used to compute nitro group torsion angles for the nitroquinolines. Unhindered nitro groups were close to coplanar with the aromatic ring as expected, while addition of one *ortho* methyl group increased the torsion angle to *ca.* 30°. The 5-nitro derivative had a nitro group torsion angle of *ca.* 80°, due to *peri* interactions with the 4-aminoalkyl sidechain. The 8-nitroquinoline derivative is the first example of a nitroaromatic with a *peri* aromatic nitrogen substituent, and the torsion angle of 70–78° (measured by both NMR spectroscopy and X-ray crystallography) indicates the substantial steric effect of the nitrogen lone pair. Addition of a 7-methyl group in the other nitro *ortho* position of this compound results in the nitro group being virtually at right angles to the ring (torsion angle 86°). A comparison was made between the measured torsion angles and those calculated using the AM1 and PM3 methods. The former underestimates the nitro torsion angles in these systems, while the PM3 method significantly overestimates them. Overall, no simple relationship exists in the nitroquinolines between nitro group torsion angles and the reduction potentials of the compounds.

In studying a series of nitro-substituted 4-(alkylamino)-quinolines (Fig. 1) as potential hypoxia-selective cytotoxins, we noted[1] significant and variable changes in the one-electron reduction potentials of these compounds when a methyl substituent was added in a position *ortho* to the nitro group (Table 1). Since the nitro group reduction potential plays a critical role in the biological activity of these compounds, by dictating the rate of nitroreduction by cellular enzymes,[2] the ability to accurately predict these values from chemical structure is important in drug design. The major influences on reduction potential within a series are the electronic and steric properties of substituent groups. While electronic effects are relatively well understood,[3] the steric effects of neighbouring groups are less predictable, as evidenced by data from polycyclic aromatic hydrocarbons.[4]

Although the variable effects of an *ortho* methyl group on the reduction potentials of the above nitroquinolines were considered to be largely electronic (due to the concomitant changes in quinoline pK_a), the effects of altering the torsion angles of the nitro group with respect to the plane of the aromatic ring may also be considerable.[1] In the present paper we therefore study the nitro group torsion angles for representative compounds in this series by ^{17}O NMR spectroscopy and X-ray crystallography.

Results

Table 1 lists the ^{17}O resonances measured for the series of nitroquinolines, together with published[5] data for related nitroacridines. An empirical relationship between nitro group torsion angles (θ) and the chemical shift of the ^{17}O resonance of the nitro group (δ) in nitrobenzenoid aromatics has been well established by Boykin *et al.*[6] Eqn. (1) has been derived,

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

using a series of compounds in which the ^{17}O chemical shifts ranged from 575 to 637 ppm, and where the nitro group torsion angles (independently determined from X-ray diffraction data) varied from zero to nearly 90°.[6]

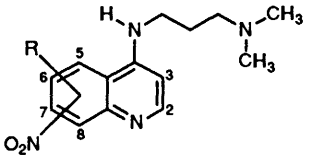
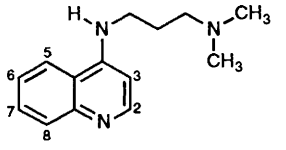


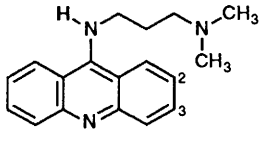
Fig. 1 Numbering in nitroquinolines

There are two points of interest arising from the data for the nitroquinolines (and related nicroacridines) in Table 1. Firstly, the range of ^{17}O NMR chemical shifts seen with these *N*-heterocyclic compounds covers a larger range (561–646 ppm) than for the nitroaromatics, so that direct use of the Boykin equation (1) to determine nitro group torsion angles was not satisfactory. Secondly, while most of the NMR-determined changes in torsion angle on addition of an *ortho* methyl group were in the expected range, two were not. In one of these (compounds **1** and **2**), addition of a 2-methyl group to a 3-nitro derivative led to a change in chemical shift of 85 ppm, indicating (by the Boykin equation) a change in nitro group torsion angle of $>90°$. In the other case (compounds **9** and **10**), addition of a 7-methyl group to an 8-nitroquinoline gave very little apparent change.

Table 1 Nitro group torsion angles for methyl-substituted nitroquinolines and isomeric nitroacridines



nitroquinolines



nitroacridines

Compound	Substituent	$E(1)^a$/ mV	δ^b	Torsion angles /° Calculated θ^c	Calculated θ^d	Calculated θ^e	Observed θ^f
Nitroquinolines							
1	3-nitro	−412	561	−15	0	7(1)	3.7
2	2-methyl-3-nitro	−453	646	94	100	63(69)	62.2
3	5-nitro	−286	628	71	79	82(83)	
4	6-methyl-5-nitro	−319	646	94	100	82(85)	
5	6-nitro	−310	569	−5	10	7(6)	
6	7-methyl-6-nitro	−453	596	30	42	14(58)	
7	7-nitro	−323	579	8	22	0(1)	
8	8-methyl-7-nitro	−423	612	50	60	10(79)	
9	8-nitro	−268	627	70	78	59(89)	70.6
10	7-methyl-8-nitro	−456	633	78	85	71(89)	86.4
Nitroacridines							
11	1-nitro	−303	605[g]	42	52	80(75)	63[h]
12	2-nitro	−376	567[g]	−7	7	1(12)	0[i]
13	3-nitro	−257	582[g]	11	25	0(1)	
14	4-nitro	−283	623[g]	65	73	45(87)	

[a] $E(1)$ determined by pulse radiolysis, from refs. 1 and 23. [b] ^{17}O NMR shift. [c] From NMR data and ref. 6. [d] Recalculated for heterocycles (see Discussion). [e] From AM1 calculation. PM3 calculation in parentheses. [f] From X-ray structure determination, this work. [g] From ref. 5. [h] From ref. 7. [i] From ref. 24.

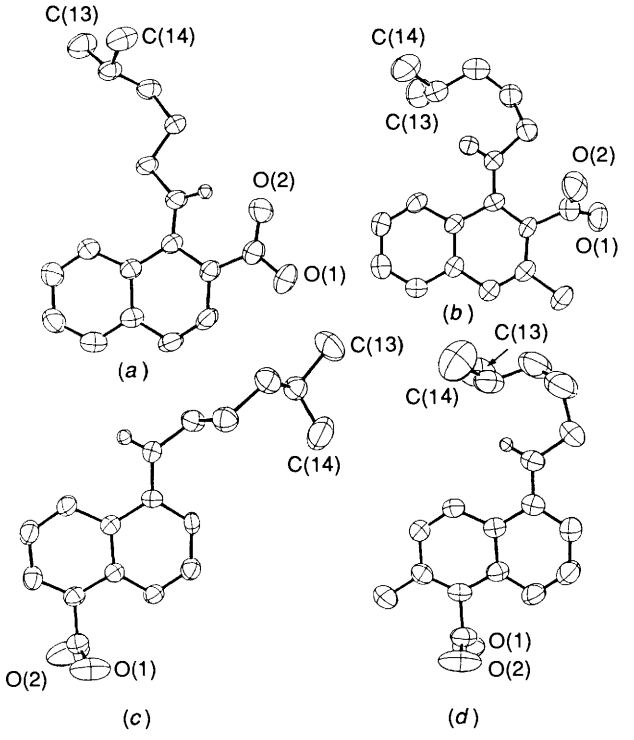


Fig. 2 Crystal structures of selected nitroquinolines of Table 1: (*a*) **1**, (*b*) **2**, (*c*) **9**, (*d*) **10**

In order to better understand these effects, and to verify the validity of the Boykin equation for *N*-heterocycles, X-ray crystal structures were determined for these two pairs of compounds (**1** and **2** and **9** and **10**) which showed the most extreme behaviour (Fig. 2). The numbering system common to all four molecules in the crystallographic study is shown in Fig. 3. The crystal data are given in Table 2, and the least squares planes used to calculate torsion angles are listed in Table 3. No structural anomalies were observed, with all bond lengths and angles considered normal. Hydrogen bond formation is seen from the amine proton. In compound **1** this is, as expected, to the *ortho* nitro group. In compounds **2** and **10** it occurs internally to the terminal NMe_2 of the side chain, and in compound **9** to the aromatic quinoline nitrogen of a symmetry related molecule.

Discussion

The crystallographic torsion angles (excluding that for compound **2**, which will be discussed later) and the ^{17}O chemical shifts of the four nitroquinolines, together with similar literature data for the two nitroacridines (**11** and **12**),[5,7] were used to calculate a θ/δ relationship [eqn. (2)] for these *N*-heterocyclic systems.

$$\theta = 1.18(\pm 0.13)\delta - 661 \qquad (2)$$

A plot of these data is compared with Boykin's original equation for nitroaromatics in Fig. 4. This shows that, while the correlation among the heterocyclic systems is not as good, the lines do have very similar slopes, differing mainly in their intercepts. The chemical shifts for the *N*-heterocyclic compounds are consistently displaced (by *ca.* 10 ppm) to higher field, consistent with increased shielding by the *N*-heterocycles.

It has been accepted for many years that unhindered aromatic nitro groups are close to coplanar with the aromatic ring, *i.e.* with a torsion angle of $< 15°$, as are those *ortho* to only a primary or secondary amine.[8] Thus planarity is expected for compounds **1**, **5** and **7**. The nitro groups of compounds **1** and **5** are indeed predicted by NMR spectroscopy to be within 10° of planarity

Table 2 Crystal structure for nitroquinolines

	3-Nitro	3-Nitro-2-methyl	8-Nitro	8-nitro-7-methyl
Molecular formula	$C_{14}H_{18}N_4O_2$	$C_{15}H_{20}N_4O_2$	$C_{14}H_{18}N_4O_2$	$C_{15}H_{20}N_4O_2$
M_r	274.3	288.4	274.3	288.4
Colour	yellow	yellow	red	yellow
Solvent	CH_3CN	light petroleum	CH_3CN	CH_3CN
Space group	triclinic	monoclinic	orthorhombic	monoclinic
	$P\bar{1}$	$P2_1/c$	P_{bca}	$P2_1/c$
a/Å	8.724(3)	9.458(1)	13.015(5)	11.288(2)
b/Å	8.862(3)	17.918(2)	13.178(3)	11.057(2)
c/Å	9.710(4)	9.012(2)	16.862(4)	12.699(9)
α/°	86.59(4)	90.0	90.0	90.0
β/°	111.67(3)	93.88(2)	90.0	91.37(3)
γ/°	92.65(3)	90.0	90.0	90.0
V/Å^3	696.1(5)	1523.7(5)	2891.7(14)	1584.4(12)
Z	2	4	8	4
D_c	1.307	1.257	1.260	1.209
μ/cm^{-1}	0.54	0.51	0.52	0.49
$F(000)$	292	616	1168	616
θ limit	25	28	27.5	25
Total no. of reflections	2235	1895	2317	2483
No. of observed reflections	1559	839	890	1838
Final R	0.0649	0.0377	0.0469	0.0579
Weighted R (R_w)	0.0693	0.0362	0.0495	0.0724
Weighting factor w	0.003 517	0.000 406	0.001 989	0.012 120

Table 3 Equations for the crystallographic planes defining nitro group torsion angles

Compound	Nitro group	Aromatic ring
1 (3-nitro)	$-7.110(22)x + 4.141(21)y + 6.60(5)z = 3.19(6)$	$-6.774(8)x + 4.525(10)y + 6.710(10)z = 3.784(19)$
2 (3-nitro-2-methyl)	$3.25(7)x + 3.08(10)y + 8.09(4)z = 11.12(5)$	$-2.46(3)x + 15.38(3)y + 4.133(21)z = 13.736(16)$
9 (8-nitro)	$-5.86(16)x + 6.96(6)y + 12.14(11)z = 7.21(6)$	$3.36(3)x + 8.05(3)y - 12.62(3)z = 5.75(3)$
10 (8-nitro-7-methyl)	$6.27(5)x + 6.671(21)y - 7.43(5)z = 0.77(8)$	$-4.296(10)x + 8.333(7)y + 6.918(11)z = 3.261(11)$

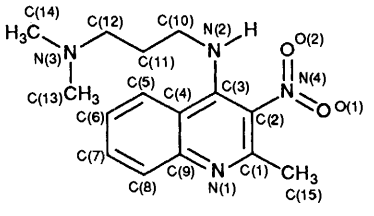


Fig. 3 Crystallographic numbering scheme for quinoline ring and side chain

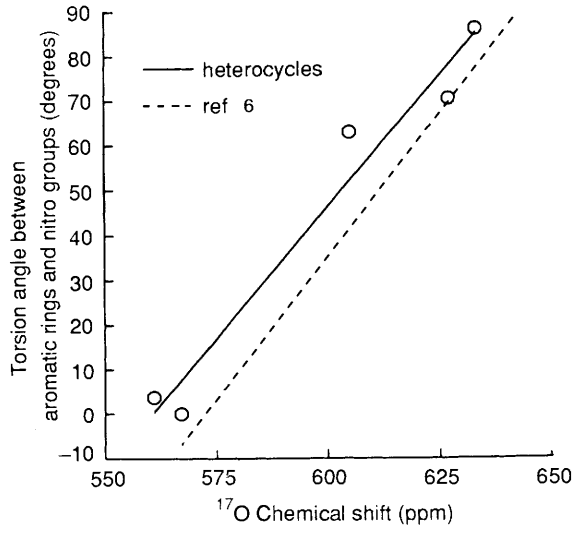


Fig. 4 Torsion angle/^{17}O chemical shift plots

with the ring. However, compound **7** is predicted to have a 20° torsion angle between the nitro group and the ring. This is similar to that predicted for the electronically similar 3-nitroacridine derivative (**13**), and while unexpected is not unprecedented, since torsion angles of up to 24° have been observed for other unhindered nitro aromatics,[8,9] showing that electronic and crystal packing effects cannot be ignored.

Addition of a methyl group *ortho* to an unhindered nitro group (compounds **6** and **8**) is expected[10] to increase the torsion angle by up to 30°, and the NMR data is in broad agreement with this. Compounds **3** and **9** also contain sterically-crowded nitro compounds, but not with an *ortho* methyl group. Compound **3** has the side chain in a position *peri* to the nitro group. Such *peri* interactions are known to cause large deviations from planarity in nitro torsion angles[11] and the NMR shift data for **3** support this.

Compound **9** is unique, in that the nitro group is *ortho* to the aromatic nitrogen. As previously mentioned, nitro groups *ortho* to primary or secondary amines are usually planar owing to hydrogen bonding. However, when the *ortho* group is a tertiary sp^3 nitrogen,[9,10,12] the torsion angle can increase by more than 40°, and changing the *ortho* group to an sp^2 nitrogen[13] can further increase the nitro group torsion angle by *ca.* 50°. However, no other structures where the *ortho* sp^2 nitrogen is aromatic have been studied, to our knowledge. It is shown here, by both NMR spectroscopy and X-ray crystallography, that the effect of the lone pair is substantial, increasing the torsion angle to 70–78°. Addition of a 7-methyl group in the other nitro *ortho* position of compound **9** gives **10**, where the nitro group is virtually at right angles to the ring (86°), as determined by both NMR spectroscopy and X-ray crystallography.

The two remaining compounds (**2** and **3**) show anomalously

Table 4 Aromatic proton resonances for compound **3** in $CDCl_3$ and D_2O at varying pH

		Chemical shift					
Solvent	pH	2	3	6	7	8	NH
$CDCl_3$		8.47	6.47	8.05	7.47	7.59	6.52
D_2O	2	8.47	7.11	8.29	8.02	8.17	—
	7	8.49	6.89	8.19	7.75	7.96	—

high ^{17}O chemical shifts which give unacceptably high torsion angles. While the X-ray structure of compound **2** does show a torsion angle of 65°, this is still much less than that predicted by the ^{17}O NMR data. We have observed a similar situation with other nitro compounds containing two substituents *ortho* to the nitro group.[14] In such cases, while the nitro group did not rotate to the full extent possible, contributions from the van der Waals repulsion of the *ortho* groups added significantly to the downfield shift of the ^{17}O resonance. This effect has been estimated to be 10–25 ppm for a methyl group,[15,16] while that of a secondary amine has not been previously measured. On the basis of the present results, the secondary amine effect can now be estimated at 0–15 ppm. Since the van der Waals repulsion effect of a *tert*-butyl group has been shown to range from 20–50 ppm,[15] this is not unreasonable.

The large calculated twist angle of 71° for the 5-nitro group in **3** has been explained by invoking considerable *peri* interaction with the 4-NHR group. In the analogous 1-nitroacridine (**11**), the crystal structure shows a nitro group twist of 63°, but this has been attributed[7] to the iminoacridan structure which the compound adopts both in the solid state[7] and as the free base in solution.[5] However, no evidence could be found for the 5-nitroquinoline (**3**) adopting a similar imino conformation. ^1H NMR data for compound **3** are given in Table 4. The chemical shifts of the protons at positions 6, 7 and 8 in both $CDCl_3$ and D_2O at pH 2 are very similar to those of nitracrine in its amino form.[5] In $CDCl_3$ solutions, coupling is seen (both in the 1-D spectrum and a COSY experiment) between the amine proton and the α-CH_2 of the side chain, confirming the amino configuration. In D_2O solution, when the pH changes from 2 to 7, the spectrum of nitracrine (which adopts the imino configuration at pH 7) shows dramatic upfield shifts (0.45–0.87 ppm) for all the aromatic protons.[5] No such shift is observed for compound **3**, confirming its amino structure and indicating that the *peri* interactions themselves are sufficient to account for the observed nitro twist of 71°.

It is of interest to compare the torsion angles measured from X-ray and NMR data with those calculated using the semi-empirical AM1 method[17] and the more recent PM3 parametrization,[18] Table 1. Full geometry optimizations of the nitroquinoline molecules studied here were made for both staggered and hydrogen-bonded conformations of the dimethylaminopropyl side chain. Both arrangements of the side chain corresponded to energy minima in the AM1 hypersurface.

For the four crystal structures reported here, the O–N–ring torsion angles estimated from AM1 calculations are in reasonable agreement with the X-ray values. The largest deviation is 15° in compound **10**. A comparison of the torsion angles estimated from the NMR data, and those calculated from AM1 geometry optimisation also shows reasonable agreement for most compounds. However, it is clear that in certain cases there is a significant difference. For example, for compound **7**, the calculated structure gives a coplanar nitro group, but the NMR data predict a torsion angle of 20°. A more serious difference is seen in compounds **6** and **8** (NMR calculated 42° and 60° *vs.* AM1 calculation of 14° and 10°). A detailed study of the AM1 potential surface obtained by rotation of the NO_2 and CH_3 groups for the model nitromethylquinolines shows that in both cases **6** and **8**, the minimum geometry is found with the NO_2 groups coplanar with the quinoline rings. Calculations using the PM3 parametrization of Stewart[18] show more significant deviations between torsion angles measured by both NMR and X-ray methods, Table 1 (particularly for **6**, **8** and **10**, which all have methyl groups *ortho* to the nitro group). It thus appears that the AM1 method underestimates the nitro torsion angles in these systems, while the PM3 method significantly overestimates these angles. It is of interest that a similar study of 2-nitrotoluene by both the AM1 and PM3 methods predicts nitro torsion angles of 0.0 and 60° respectively, whilst *ab initio* molecular orbital calculations[19] give angles between 0 and 22°.

Finally, no simple relationships exists in the nitroquinolines between nitro group torsion angles and their reduction potentials. Addition of an *ortho* methyl group lowers reduction potentials in all cases, although by greatly differing amounts (33–188 mV: Table 1). The varying contributions to reduction potential of direct electronic effects of the methyl groups, their effects on pK_a, and their steric effects on nitro group torsion angles cannot be separately determined.

Experimental

Syntheses of the nitroquinolines studied here have been reported.[1] NMR studies were carried out on a Bruker 400 AM spectrometer equipped with an ASPECT 3000 data system. ^1H spectra were measured using a 5 mm $^1H/^{13}C$ dual probe. Solutions (0.05 mol dm^{-3} in $CDCl_3$ or 0.02 mol dm^{-3} in D_2O) were used with TMS ($CDCl_3$) or TSP (D_2O) internal reference. Data were collected and processed with the DISNMR program. COSY spectra[20] were acquired with 32 scans over 1024 data points and 4310.345 Hz for each of the 256 values of evolution time (t_1). The FIDs were zero-filled and a sine-bell window function was used before FT. Data were symmetrised prior to plotting. 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 to 1 and peak widths of 450 Hz were obtained with 100 000–300 000 scans and an exponential broadening of 25 Hz. Under these conditions, the ^{17}O resonance of nitrobenzene occurred at δ 575 (lit.[6] value δ 576).

Cuboid crystals of the four nitroquinolines were obtained by slow evaporation of the solvents indicated in Table 3. Lattice constants and intensity data were measured using Mo-Kα radiation, $\lambda = 0.710\,69$ Å, on a Nonius CAD-4 diffractometer in $\omega/2\theta$ scan mode. Three standard reflections were measured for every fifty reflections and no significant changes in the intensities of these reflections were observed.

All 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 all cases, refinement was halted when the largest shift/esd was less than 0.07 and maximum and minimum peaks in the final difference maps were less than 0.3 e $Å^{-3}$. The weighting function used was $1/[\sigma^2(F) + wF^2]$. Final positional parameters of the non-hydrogen atoms and the amine hydrogen are listed in Table 5. Tables of all positional parameters, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.*

* For details of the deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1992, issue 1.

Molecular orbital calcuations were carried out using the AM1 method with the program[18] MOPAC 5.0, implemented on the University of Auckland Computer Centre Silicon Graphics 4D/240S computer and the Auckland University Molecular Modelling Group Silicon Graphics 4D/30 Personal Iris computer. Full geometry optimizations were carried out for all molecules studied (dummy atoms in the centre of each aromatic ring were used). Differing conformations of functional groups attached to aromatic rings were investigated, particularly in the case of the dimethylaminopropyl side chain.

Table 5 Atomic co-ordinates for the X-ray crystallographic structures of Fig. 2

Atom	*x/a*	*y/b*	*z/c*
Compound 1 (3-nitro)			
O(1)	−0.337 9(4)	0.364 2(4)	−0.031 3(4)
O(2)	−0.208 1(4)	0.575 5(3)	−0.024 0(3)
N(1)	−0.067 6(4)	0.207 8(3)	0.367 8(3)
N(2)	0.050 6(4)	0.633 8(3)	0.211 6(3)
N(3)	0.382 3(3)	1.029 1(3)	0.265 4(3)
N(4)	−0.225 0(4)	0.451 5(3)	0.035 6(3)
C(1)	−0.151 9(5)	0.268 4(4)	0.238 6(4)
C(2)	−0.114 8(4)	0.407 3(4)	0.179 6(3)
C(3)	0.022 9(4)	0.498 7(3)	0.263 9(3)
C(4)	0.123 3(4)	0.430 2(3)	0.406 4(3)
C(5)	0.273 8(4)	0.492 9(4)	0.503 1(4)
C(6)	0.363 7(5)	0.424 2(4)	0.636 6(4)
C(7)	0.312 5(5)	0.286 1(4)	0.680 4(4)
C(8)	0.168 3(5)	0.217 8(4)	0.588 1(4)
C(9)	0.073 5(4)	0.286 3(4)	0.452 5(4)
C(10)	0.163 8(4)	0.760 3(4)	0.280 1(4)
C(11)	0.104 0(5)	0.902 2(4)	0.182 5(4)
C(12)	0.210 2(5)	1.041 3(4)	0.247 3(4)
C(13)	0.481 2(6)	1.149 8(6)	0.357 4(5)
C(14)	0.404 1(6)	1.036 7(5)	0.123 7(5)
HA	−0.027(5)	0.647(5)	0.117(5)
Compound **2** (3-nitro-2-methyl)			
O(1)	1.367 2(4)	0.636 56(17)	−0.015 0(5)
O(2)	1.240 3(4)	0.735 36(18)	−0.001 6(5)
N(1)	1.090 7(5)	0.557 95(19)	0.299 9(7)
N(2)	0.968 5(6)	0.649 6(2)	−0.117 2(7)
N(3)	0.714 3(5)	0.677 3(2)	−0.301 9(6)
N(4)	1.259 3(4)	0.668 7(2)	0.016 1(5)
C(1)	1.185 0(6)	0.593 9(2)	0.225 3(8)
C(2)	1.148 3(6)	0.625 0(2)	0.084 3(7)
C(3)	1.013 4(6)	0.622 4(2)	0.015 4(7)
C(4)	0.910 0(6)	0.583 2(2)	0.099 9(8)
C(5)	0.766 2(9)	0.575 8(3)	0.047 9(9)
C(6)	0.672 4(8)	0.538 7(3)	0.129 6(10)
C(7)	0.717 2(8)	0.508 8(3)	0.266 7(9)
C(8)	0.854 0(8)	0.515 5(3)	0.320 3(9)
C(9)	0.955 9(6)	0.553 2(2)	0.238 3(8)
C(10)	1.047 3(8)	0.676 4(3)	−0.242 9(9)
C(11)	0.960 4(8)	0.664 4(4)	−0.384 3(9)
C(12)	0.818 9(11)	0.709 0(4)	−0.398 1(10)
C(13)	0.655 4(11)	0.609 0(4)	−0.362 0(13)
C(14)	0.598 2(10)	0.733 5(5)	−0.2907(13)
C(15)	1.327 1(7)	0.602 9(4)	0.301 8(9)
HA	0.875(7)	0.648(3)	−0.153(9)
Compound **9** (8-nitro)			
O(1)	0.014 2(4)	−0.065 4(5)	0.064 9(4)
O(2)	−0.005 2(4)	−0.198 0(5)	0.131 6(5)
N(1)	0.066 5(3)	0.028 1(4)	0.223 2(3)
N(2)	0.353 1(4)	0.089 1(4)	0.329 2(3)
N(3)	0.338 5(4)	0.352 3(4)	0.489 0(3)
N(4)	0.042 5(4)	−0.125 5(5)	0.113 1(4)
C(1)	0.080 2(5)	0.101 0(5)	0.276 0(4)
C(2)	0.173 5(4)	0.123 1(5)	0.312 3(4)
C(3)	0.261 9(4)	0.068 9(4)	0.295 3(3)
C(4)	0.250 4(4)	−0.013 4(4)	0.240 1(3)
C(5)	0.330 4(5)	−0.080 0(5)	0.219 1(4)
C(6)	0.315 5(5)	−0.156 8(5)	0.165 7(4)
C(7)	0.220 9(5)	−0.172 7(5)	0.131 5(4)
C(8)	0.143 3(4)	−0.108 1(4)	0.150 8(4)
C(9)	0.151 5(4)	−0.027 8(4)	0.205 0(3)
C(10)	0.369 8(5)	0.164 9(5)	0.389 3(4)
C(11)	0.078 0(6)	0.272 4(5)	0.358 0(4)
C(12)	0.407 7(6)	0.349 9(5)	0.421 5(5)
C(13)	0.382 7(8)	0.418 7(8)	0.549 9(5)
C(14)	0.235 1(7)	0.385 8(8)	0.468 5(7)
HA	0.406(4)	0.047(4)	0.319(3)

Table 5 (*continued*)

Compound **10** (8-nitro-7-methyl)			
O(1)	0.884 2(2)	0.244 1(3)	0.861 42(18)
O(2)	0.937 3(3)	0.092 8(3)	0.770 4(3)
N(1)	0.665 3(2)	0.055 8(2)	0.820 05(17)
N(2)	0.373 83(19)	0.076 1(2)	0.606 7(2)
N(3)	0.252 8(2)	0.221 9(2)	0.455 4(2)
N(4)	0.871 1(2)	0.174 5(2)	0.787 93(19)
C(1)	0.567 0(3)	−0.007 7(3)	0.831 2(2)
C(2)	0.468 9(3)	−0.007 0(3)	0.762 8(2)
C(3)	0.467 6(2)	0.068 2(3)	0.674 7(2)
C(4)	0.571 4(2)	0.140 1(2)	0.658 42(17)
C(5)	0.586 3(2)	0.217 6(2)	0.571 74(19)
C(6)	0.687 9(2)	0.282 4(2)	0.559 0(2)
C(7)	0.784 7(2)	0.273 0(2)	0.631 27(19)
C(8)	0.770 3(2)	0.194 3(2)	0.713 69(17)
C(9)	0.666 8(2)	0.127 3(2)	0.732 86(18)
C(10)	0.264 4(3)	0.008 2(4)	0.619 3(3)
C(11)	0.182 9(4)	0.024 2(4)	0.525 2(4)
C(12)	0.151 8(4)	0.151 2(5)	0.502 0(6)
C(13)	0.222 0(5)	0.347 4(4)	0.471 1(6)
C(14)	0.271 8(9)	0.200 8(6)	0.345 9(5)
C(15)	0.896 3(3)	0.344 9(4)	0.616 1(3)
HA	0.373(3)	0.135(3)	0.550(2)

Note added in proof—We omitted to state that P. Balakrishnan and D. W. Boykin (*J. Heterocycl. Chem.*, 1986, **23**, 191) reported identical ^{17}O chemical shifts for unsubstituted 8-nitro- and 7-methyl-8-nitro-quinoline to those we report in Table 1 for the corresponding 4-$NH(CH_2)_3NMe_2$ analogues **9** and **10**. These authors also commented on the substantial lone pair–nitro group interaction indicated by their results.

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