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NMR STUDIES ON SOME N-NITRAMINES AND N-NITROSAMINES

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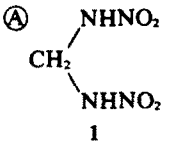
Abstract—The ^1H and ^{13}C NMR spectra of some N-nitramines and N-nitrosamines are reported. In general, the ^1H and ^{13}C NMR chemical shifts of the methylene groups of the N-nitramines are useful for the characterisation of these compounds. For N-nitrosamines, the effects due to the shielding anisotropy of the N-nitroso group are shown in the ^1H and ^{13}C NMR spectra.

INTRODUCTION

There are numerous reports concerning the ^1H NMR spectra of N-nitrosamines[1-4] and studies of the ^{13}C NMR spectra have also been reported.[5-6] However, there have been relatively few reports of the ^1H[7-9] and ^{13}C[10] NMR spectra of N-nitramines.

As part of a program dealing with the structures of N-nitramines and N-nitrosamines we have recorded the ^1H and ^{13}C NMR spectra of some primary and secondary N-nitramines and secondary N-nitrosamines. The examples chosen contain two or more N–NO_2 or N–NO groups per molecule, the majority are cyclic compounds.



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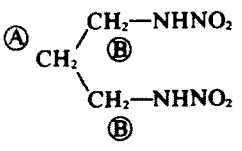

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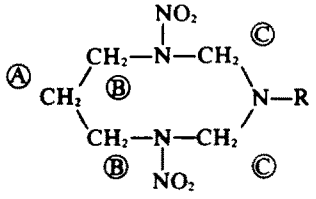

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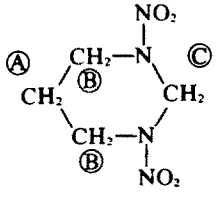

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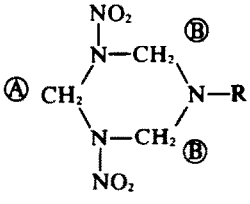

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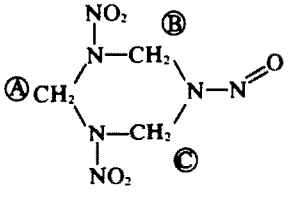
5a: R = NO_2
b: R = CH_2OCH_3



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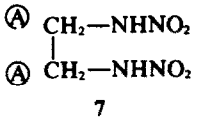

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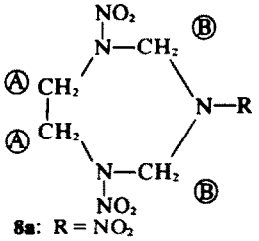
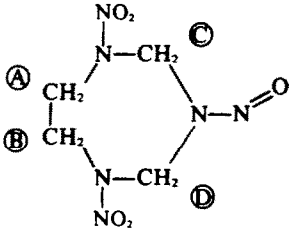


8a: R = NO_2
b: R = CH_2OCOCH_3
c: R = $CH_2N(NO_2)CH_3$



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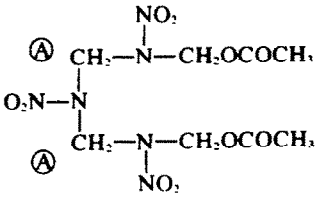

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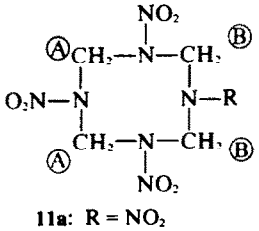
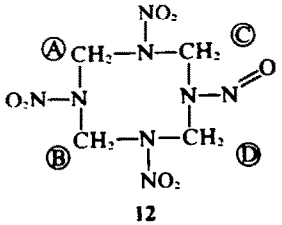


11a: R = NO_2
b: R = CH_2OCOCH_3



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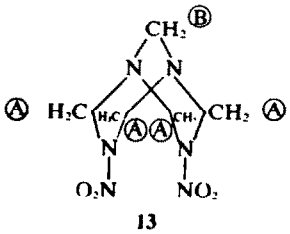

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Fig. 1.

RESULTS AND DISCUSSION

The N-nitramines considered (**1–13**) are illustrated in Fig. 1, including the mixed N-NO_2/N-NO compounds **6**, **9** and **12**. The ^{1}H NMR data are given in Table 1.

In the case of the cyclic N-nitramines **5**, **6**, **8**, **9**, **11** and **12**, the ring methylene protons give singlet spectra (Table 1). At first sight the methylene protons might be expected to exhibit "AB" patterns due to geminal proton interaction. However, the N-nitramine group may be considered to be conjugated, with the C_2N-NO_2 grouping essentially planar.[11, 12] This implies some sp^2 character for the amino N atom of the N-nitramine grouping. For the cyclic N-nitramines **4**, **5a**, **8a** and **11a** this is expected to lead to a flattening of the ring and thus the existence of fast ring inversion; the planarity of the N-nitramine grouping also implies minimal nitrogen inversion for these molecules. These processes render the ring methylene protons magnetically equivalent. For the compounds **3a**, **5b**, **8b**, **8c** and **11b**, where the R groups are not considered to be conjugative, nitrogen inversion has to be considered for the amino N atom to which the R group is attached. In order to account for the fact that all of the ring methylene protons in these compounds exhibit singlet spectra, fast nitrogen inversion at this particular N atom is thought to occur in addition to fast ring inversion. For these molecules the methyl or methylene protons in the respective side-chains (R) appear to be equivalent (Table 1). This possibly arises as a consequence of the fast ring and nitrogen inversion which is proposed for these molecules, and as a result of rotation about the N–C and C–C bonds in the side-chains.

For the mixed N-NO_2/N-NO compounds **6**, **9** and **12**,

Table 1. ^{1}H NMR data for some primary and secondary N-nitramines

Compound	Type	δ(—CH_2—) ppm*	Others
1	A	5·05(s)	12·5(b)(—NH—)
2	A	1·80(q, 2H) (J = 6 Hz)	12·8(b)(—NH—)
	B	3·50(t, 4H)	
3a	A	2·00(q, 2H) (J = 5 Hz)	2·70(s, 3H)(N—CH_3)
	B	4·00(t, 4H)	
	C	5·00(s, 4H)	
4	A	1·90(q, 2H) (J = 5 Hz)	
	B	4·00(t, 4H)	
	C	5·90(s, 2H)	
5a	A(B)	6·09(s)	
5b†	A	6·08(s, 2H)	4·15(s, 2H)(>N—CH_2—)
	B	5·20(s, 4H)	2·97(s, 3H)(—OCH_3)
6	A	6·20(s)‡	
	B	5·82(s)	
	C	6·42(s)‡	
7	A	3·82(s)	12·0(b)(—NH—)
8a†	A	4·26(s)	
	B	6·04(s)	
8b	A	4·21(s, 4H)	5·00(s, 2H)(>N—CH_2—)
	B	5·28(s, 4H)	1·77(s, 3H)(—$COCH_3$)
8c	A	4·24(s, 4H)	4·88(s, 2H)(>N—CH_2—)
	B	5·22(s, 4H)	3·40(s, 3H)(—CH_3)
9	A(B)	4·26(s, 4H)	
	C	5·68(s, 2H)	
	D	6·20(s, 2H)	
10	A	5·88(s, 4H)‡	5·78(s, 4H)(>N—CH_2—)‡
			2·05(s, 6H)(—$COCH_3$)
11a	A(B)	6·04(s)	
11b†	A	6·00(s, 4H)	5·11(s, 2H)(>N—CH_2—)
	B	5·28(s, 4H)	1·85(s, 3H)(—$COCH_3$)
12	A	6·03(s)‡	
	B	6·14(s)‡	
	C	5·71(s)	
	D	6·36(s)‡	
13	A	4·96(d, 4H) 5·52(d, 4H) (J = 13 Hz)	
	B	4·14(s, 2H)	

*Spectra were recorded on a Varian HA 100 instrument in $(CD_3)_2SO$ with TMS as internal standard.

†Spectra recorded on a Perkin Elmer R10 instrument at 60 MHz in $(CH_3)_2SO$ with TMS as internal standard.

‡Assignments may possibly be reversed: s, singlet; d, doublet; t, triplet; q, quintet; b, broad. Chemical shifts are given in units of δ ppm with respect to TMS as internal standard. Shifts to higher frequency are considered positive.

the N–NO group may be considered to be conjugated due to a planar C_2N–NO grouping,[13, 14] a situation analogous to that of the closely related N–NO_2 grouping. For these molecules the ring methylene protons exhibit singlet spectra (Table 1), which are consistent with fast ring inversion and minimal nitrogen inversion. The effects of the magnetic anisotropy of the N–NO group and restricted rotation about the N–N bond are also observed. This is exemplified by the fact that the methylene protons *cis* and *trans* to the nitroso O atom give individual signals.

In the case of **6** and **9** the appearance of three line spectra suggests that the influence of the N–NO group in these molecules only extends to the α methylene groups. However, for **12**, the appearance of a four line spectrum implies that the influence of the N–NO group extends throughout the whole molecule. The spectrum of **3** (R=NO)[7] is consistent with this proposal.

For the linear N-nitramines **1**, **2**, **7** and **10** the protons in the respective methylene groups appear to be equivalent. This is presumably due either to an averaging mechanism, such as molecular tumbling, or to the existence of a favourable molecular environment.

For the molecules containing the trimethylenedinitramine system (**2**, **3**, **4**) the methylene protons A and B (Fig. 1) are vicinally coupled (J = 5–6 Hz), geminal coupling appears to be absent.

The molecule **13** is an example of a cyclic N-nitramine which possesses a fixed molecular structure. It exists in a flattened chair-chair form (Fig. 1). The equivalent bridge methylene protons appear as a singlet and the inequivalent axial and equatorial α methylene protons exhibit an "AB" quartet (J = 13 Hz) in its ^{1}H NMR spectrum.[15]

From Table 1 it is apparent that the respective methylene protons associated with particular types of N-nitramine groupings fall into comparatively narrow chemical shift ranges. For example, a consideration of the cyclic secondary N-nitramines, excluding the mixed N–NO_2/N–NO compounds, shows that the protons in the –(NO_2)N–CH_2–N(NO_2)– methylene group resonate within the range $\delta = 5{\cdot}90 - 6{\cdot}20$, the –$(NO_2)$N–$CH_2$–N(R)– ($R \neq NO_2$, NO) protons appear within the range $\delta = 5{\cdot}00 - 5{\cdot}28$, and the –$(NO_2)$N–$CH_2$–C< protons occur within the range $\delta = 4{\cdot}00 - 4{\cdot}26$ ppm.

The ^{13}C NMR data for some of the N-nitramines shown in Fig. 1 are given in Table 2.

The assignments presented for the C atoms in these compounds are fairly straightforward, with the exception of the mixed N–NO_2/N–NO compounds **6**, **9** and **12**. Although the resonances for these compounds have not been unambiguously assigned, their ^{13}C NMR spectra confirm the proposal that the influence of the N–NO group extends over the whole molecule. The assignments for these compounds have been made on the basis that the methylene C atoms *cis* to the nitroso O atom are shielded relative to the *trans* methylene C atoms.[5]

There are interesting chemical shift changes on passing from the linear dinitramines **1**, **2** and **7** to the cyclic N-nitramines containing the dinitramine units. The methylene carbon atom of type A in **1** undergoes a shift of 8 ppm to higher frequency on passing from **1** to **4** and **5a**, which predominently reflects the change from primary to secondary N-nitramine. There is a shift of 10 ppm to higher frequency on passing from **1** to **11a**, which indicates that the nature and size of the ring also influences the chemical shift. On passing from **7** to **8b** and **8c** the carbon atoms of type A in **7** experience a shift of 4 ppm to higher frequency. The methylene carbon atom of Type A in **2** shifts from 24·0 → 24·9 ppm in **3a** and from 24·0 → 21·2 ppm in **4**, while the C atoms of type B shift from 42·9 → 50·9 ppm in **3a** and from 42·9 → 47·2 ppm in **4**. On passing from the linear primary N-nitramine **1** to the linear secondary N-nitramine **10** the C atom of type A in **1** shifts from 53·5 to 64·9 ppm.

As with ^{1}H NMR spectra the respective methylene C atoms connected with particular types of N-nitramine groupings fall into comparatively narrow chemical shift ranges. For the cyclic N-nitramines the –(NO_2)N–CH_2–N(NO_2)– Catoms resonate within the range 61·4 – 64·2 ppm, the –(NO_2)N–CH_2–N(R)– ($R \neq NO_2$, NO) C atom resonances occur within the range 66·5 – 72·0 ppm, and the –(NO_2)N–CH_2C– C atoms appear within the range 46·2 – 50·9 ppm.

Table 2. ^{13}C NMR data for some primary and secondary N-nitramines

Compound	Type	$\delta(^{13}CH_2—)$ ppm*	Others
1	A	53·5	
2	A	24·0	
	B	42·9	
3a	A	24·9	41·4(>N—CH_3)
	B	50·9	
	C	72·0	
4	A	21·2	
	B	47·2	
	C	61·6	
5a	A(B)	61·4	
6	A	62·5†	
	B	52·4	
	C	63·2†	
7	A	42·4	
8b	A	46·2	67·4(>N—CH_2—)
	B	66·5	21·2(—CH_3)
			169·4(>C=O)
8c	A	46·3	67·4(>N—CH_2—)
	B	67·1	38·5(—CH_3)
9	A	46·9	
	B	49·1†	
	C	59·5†	
	D	63·5	
10	A	64·9	72·2(—CH_2—)
			20·5(—CH_3)
			170·4(>C=O)
11a	A(B)	63·2	
12	A	63·3†	
	B	63·6†	
	C	55·1	
	D	65·2†	
13	A	68·5	
	B	64·9	

*Spectra were run on a Bruker WH-90 FT instrument, operating at 22·64 MHz, with broad band proton decoupling employed for all samples. The samples were run in 10 mm o.d. NMR tubes in $(CD_3)_2SO$ with TMS as internal standard. Chemical shifts are given in units of δ ppm (±0·1) with respect to TMS. Shifts to higher frequency are considered positive.

†Assignments may possibly be reversed.

For the ^{1}H NMR spectra the relative shielding of the respective methylene protons is in the order

$$-(NO_2)N-CH_2-C< > (NO_2)N-CH_2-N(R)- > -(NO_2)-CH_2-N(NO_2)-$$

whereas in the ^{13}C NMR spectra the relative shielding of the respective methylene C atoms is

$$-(NO_2)N-CH_2-C< > -(NO_2)N-CH_2-N(NO_2)- > -(NO_2)N-CH_2-N(R)-$$

This indicates that on passing from $>$N-R (R=CH_2R') to $>$N-NO_2 the NO_2 group relatively deshields the methylene group protons and shields the methylene group C atom compared to the R group.

It is, however, apparent from Tables 1 and 2 that the ^{1}H and ^{13}C chemical shift data may be considered useful for the characterisation of N-nitramines, in particular cyclic N-nitramines.

The ^{1}H NMR spectra of some cyclic secondary N-nitrosamines **14–17** (Fig. 2) are reported in Table 3.

The molecules **14–16** have spectra which are consistent with fast ring inversion and minimal nitrogen inversion, together with the effects of the magnetic anisotropy of the N–NO groups and restricted rotation about the N–N bonds. Rotation about the N–N bonds in these molecules appears to be sufficiently slow to enable the observation of individual signals from all of the possible conformational isomers and these are illustrated in Fig. 2. Although all of the possible *syn/anti* conformational isomers appear experimentally to be present, they are not found in their expected statistical proportions. This indicates the presence of unfavourable steric or electronic effects which may determine the observed isomer ratios. It seems that a *cis/cis* orientation (**14C**, **15D** and **16F**) is relatively unfavourable in these molecules. The assignments given in Table 3 are relatively straightforward for **15** and **16**, but for **14** a complex spectrum is obtained. The assignments are made by comparison of the spectrum with those of 1,4-dinitroso-piperazine (**14**) and 1,3-dinitroso-1,3-diazacyclohexane, the spectrum of which has been assigned by Evans.[16]

The bicyclic N-nitrosamine **17** is an example of an N-nitrosamine with a fixed molecular structure. This molecule is considered to exist in a flattened chair-chair conformation, and the complex ^{1}H NMR spectrum may be interpreted on the basis of the involvement of the *syn* and *anti* forms **17(H)** and **(I)** (Fig. 2).[15] The assignments given in Table 3 are substantiated by decoupling experiments and a consideration of the integrated spectrum.

The ^{13}C NMR data for the compounds **14–17** are also given in Table 3. The number of lines obtained for each molecule confirm that all possible conformational isomers are present. For **15** and **16** the assignments given in Table 3 are based on the expected shielding effect of the N–NO groups[5,6] and on the intensities. The ^{13}C NMR intensities are in qualitative agreement with the ^{1}H NMR intensities substantiating the isomer ratios indicated for these molecules (Table 3). **14** and **17** give 11 and 6 line spectra respectively, for both of these compounds the assignments given in Table 3 are tentative. For **14** the

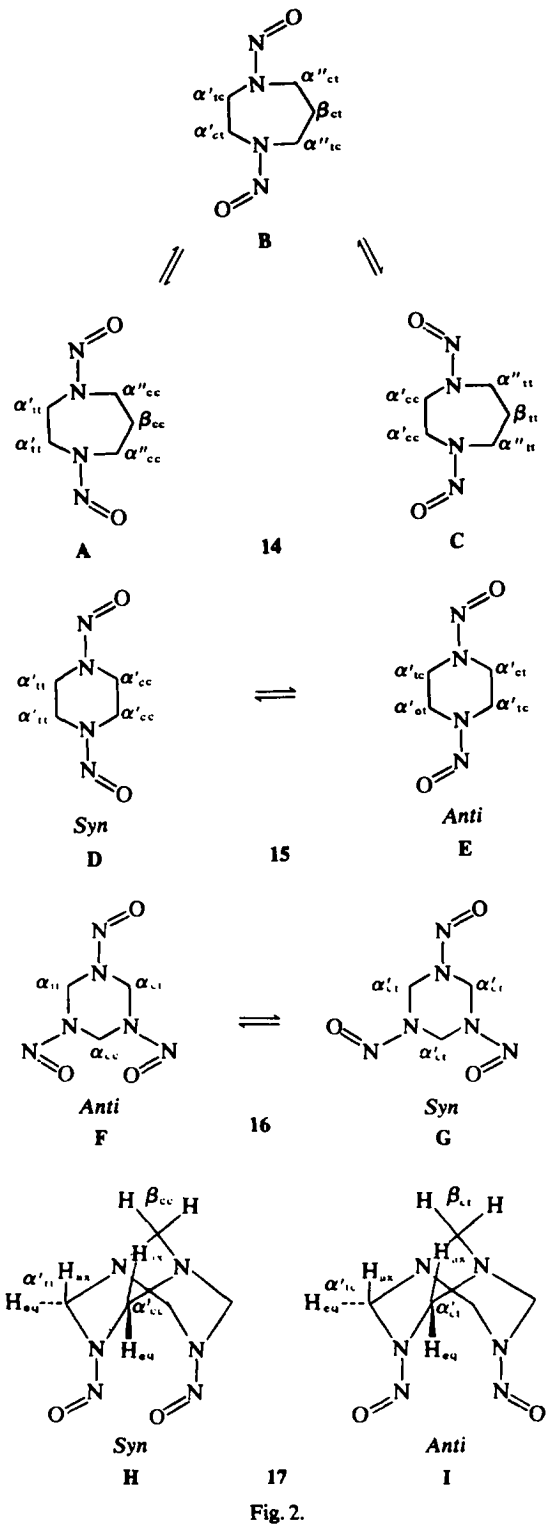

Fig. 2.

assignments are made from comparison with the spectrum of **15**, from a consideration of the intensities of the lines, and by using the relationships (a)–(c) found for the proton shieldings

$$\alpha'_{tt} > \alpha'_{tc} > \alpha'_{ct} > \alpha'_{cc} \quad \text{(a)}$$

$$\alpha''_{tt} > \alpha''_{tc} > \alpha''_{ct} > \alpha''_{cc} \quad \text{(b)}$$

$$\beta_{tt} > \beta_{ct} > \beta_{cc} \quad \text{(c)}$$

Table 3. ^1H and ^{13}C NMR data for some cyclic secondary N-nitrosamines

Compound	Solvent	Isomer	Isomer Ratio	Type of —CH_2—	(^1H)*	(^{13}C)†
14	$CDCl_3$	A	‡	α'_{tt}	4·66(s)	51·1
				α''_{cc}	3·76(t) (J = 6 Hz)	43·1
				β_{cc}	1·93(q)	22·0
		B	‡	α'_{tc}	4·5(m)	43·6
				α''_{tc}	4·5(m)	51·5
				α'_{ct}	4·1(m)	42·4
				α''_{ct}	3·8(m)	49·3
				β_{ct}	2·0(m)	25·9
		C	‡	α'_{cc}	3·8(m)	41·0
				α''_{tt}	4·5(m)	53·3
				β_{tt}	2·0(m)	29·9
15	$CDCl_3$	D	5	α'_{tt}	4·71(s)	49·6
				α'_{cc}	3·83(s)	37·7
		E	8	α'_{ct}	4·0(m)	40·5
				α'_{tc}	4·4(m)	47·0
16	$(CD_3)_2SO$	F	2	α_{cc}	5·62(s)	45·9
				α_{ct}	6·26(s)	56·4
				α_{tt}	6·90(s)	64·6
		G	1	α'_{ct}	6·22(s)	55·0
17	$(CD_3)_2SO$	H	3	α'_{tt}	5·23(d), 5·45(d) (J = 13 Hz)	69·7
				α'_{cc}	4·22(d), 5·46(d) (J = 14 Hz)	59·5
				β_{cc}	4·46(bs)	68·1
		I	2	α'_{tc}	5·35(d), 5·77(d) (J = 13 Hz)	69·0
				α'_{ct}	4·29(d), 5·76(d) (J = 14 Hz)	60·3
				β_{ct}	4·46(bs)	67·8

s, singlet; d, doublet; t, triplet; q, quintet; m, multiplet; bs, broad singlet.

*Spectra in $CDCl_3$ were run on a Bruker WH-90 FT instrument, operating at 90 MHz. Spectra in $(CD_3)_2SO$ were run on a Varian HA 100 instrument. Chemical shifts are given in units of δ ppm with respect to TMS as internal standard. Shifts to higher frequency are considered positive.

†Spectra were recorded on a Bruker WH-90 FT instrument, operating at 22·64 MHz, with broad band proton decoupling employed for all samples. The samples were run in 10 mm o.d. NMR tubes with TMS as internal standard. Chemical shifts are given in units of δ ppm with respect to TMS (±0·1), shifts to higher frequency are considered positive.

‡Could not be estimated with certainty.

For **17** the assignments are made from a consideration of the intensities and the suggestion that the *syn* isomer might produce a greater chemical shift difference between the methylene C atoms α to the N–NO group than would the *anti* isomer.

The chemical shift differences between the α methylene C atoms *cis* and *trans* to the N–NO group are of the order 7–12 ppm, except for the compound **16**. This compound contains methylene carbons of the type –(NO)–N–CH_2–N(NO)–, and the chemical shift difference between each type of C atom in the unsymmetrical isomer (**F**) is $\alpha_{cc} \rightarrow \alpha_{ct} = 10{\cdot}5$ ppm, $\alpha_{ct} \rightarrow \alpha_{tt} = 8{\cdot}2$ ppm and $\alpha_{cc} \rightarrow \alpha_{tt} = 18{\cdot}7$ ppm; this latter large difference reflects the situation where each C atom experiences the shielding effect of two adjacent N–NO groups.

EXPERIMENTAL

Compounds **1**, **2**, **3a**, **4**, **5a**, **5b**, **7**, **8a**, **8b**, **8c**, **11a**, **11b** and **13** were supplied by E.R.D.E., Waltham Abbey, Essex. The compounds **6**, **9**, **10** and **12** were prepared by the procedures of Bell and Dunstan[7] (from **5b**, **8b**, **5b** and **11b** respectively).

The compound **14** was prepared by nitrosation of the parent diamine (Commercially available from Aldrich Chemical Co.) with $NaNO_2/H_2O$/dil H_2SO_4 at 10°C, after the method of Bell and Dunstan.[18]

Cold 1,4-diazacycloheptane (1 g) was quickly added to a cold soln (ice-water bath) containing $NaNO_2$(2 g) in 10 ml water and 10 ml dil H_2SO_4 with stirring. A light yellow ppt settled on top of the soln. The soln was stirred at 10° for a further 10 min, then filtered and dried in a dessicator, yield: 0·4 g (25%) m.p 91–92°C (recryst MeOH). (Found: C, 37·98; H, 6·36; N, 35·62. Calc. for $C_5H_{10}N_4O_2$: C, 37·97; H, 6·33; N, 35·44%; Mass spec. m/e = 158 (M^+)).

The compound **15** was commercially available (Eastman Kodak), and **16** and **17** were prepared after the method of Bachmann and Deno.[19]

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