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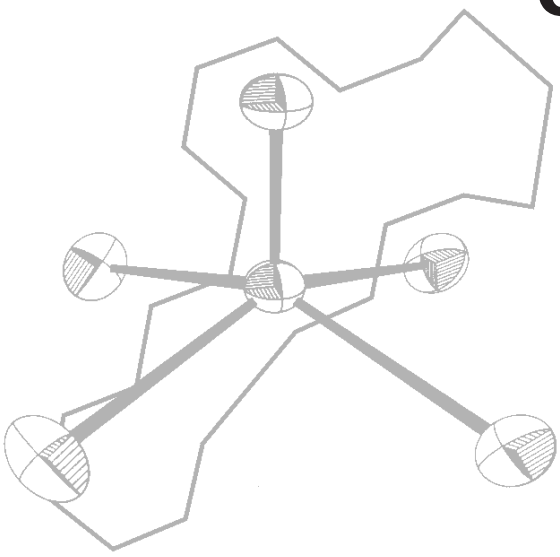

Volume 53, 2000

A journal for the publication of original research
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Aust. J. Chem., 2000, **53**, 715–722

Structural Studies of Some 1-Polymethyleneimino-2,4-dinitrobenzenes and Related Compounds; Crystal Structure of 1-(*cis*-2′,6′-Dimethylpiperidin-1′-yl)-2,4-dinitrobenzene

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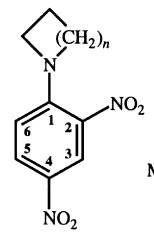
The ultraviolet and ^{1}H n.m.r. spectra of some 1-polymethyleneimino-2,4-dinitrobenzenes and related compounds are discussed. The effect of trifluoroacetic acid on these spectra was also investigated; with 1-azetidinyl-2,4-dinitrobenzene, acid-catalysed ring opening was observed. The solid-state conformation of 1-(*cis*-2′,6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene has been defined by single-crystal X-ray crystallography. Triclinic crystals belong to the space group $P\bar{1}$ with *a* 8.165(1), *b* 7.865(1), *c* 11.148(1) Å, α 95.23(1), β 106.00(1), γ 92.63(1)° and *Z* 2. The structure was refined to a final *R* of 0.048 for the 2222 observed data. In the crystal, the phenyl ring adopts a slight boat conformation, while the amino and *o*-nitro groups are significantly twisted from the mean plane of the ring.

Keywords. 2,4-Dinitroanilines; n.m.r.; ultraviolet spectroscopy; X-ray crystal structure.

Introduction

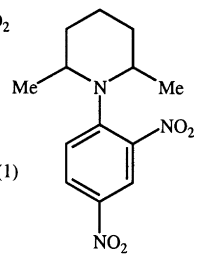
The 1-polymethyleneimino-2,4-dinitrobenzenes [general formula (1)] and the related 1-dialkylamino-2,4-dinitrobenzenes [general formula (2)] are coloured compounds (yellow to orange-red) in which the 2-nitro group, and the adjacent bulky polymethyleneimino group and the dialkylamino group respectively, are both twisted significantly out of the plane of the aryl ring. Evidence for this steric interaction has come from X-ray crystallographic studies conducted on several representatives of both classes of compounds [(1)[1,2] and (2)[3–6]].

In this communication, we describe the results of a spectroscopic investigation carried out on a series of 1-polymethyleneimino-2,4-dinitrobenzenes [general formula (1)]. We were particularly interested in the effect (if any) of *(a)* the size of the polymethyleneimino ring (3–8 members), and of *(b)* substituents on or in the ring (principally the six-membered ring) on the ultraviolet (in ethanol) and ^{1}H n.m.r. [in (D)chloroform] spectra of this class of compound. In addition, we recorded both types of spectra in trifluoroacetic acid solution in order to determine the extent of protonation (if any) by this acidic solvent. During our investigations, we verified an earlier report by Italian workers[7,8] that both 1-(*cis*-2′,6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1f) and its *trans* isomer (1g) showed anomalous ultraviolet and ^{1}H n.m.r. spectra (particularly so in the case of the *cis* isomer). This finding prompted us to determine the X-ray crystal structure of the *cis* isomer (1f); its structural details are described, and compared with the conclusions reached from our spectroscopic investigations, in the second part of this communication.

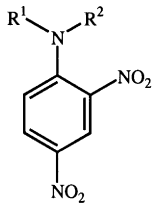


general formula (1)

(1a) $n = 0$
(1b) $n = 1$
(1c) $n = 2$
(1e) $n = 3$
(1m) $n = 4$
(1n) $n = 5$



cis isomer (1f)



general formula (2)

	R^1	R^2
(2a)	Me	Me
(2b)	Et	Et
(2c)	Pr^i	Pr^i
(2d)	cyclohexyl	cyclohexyl
(2e)	cyclohexyl	Pr^i

Results

In the following discussion, it will be convenient to refer to the compounds (1a–n) studied (see Tables 1 and 2) as the 2,4-dinitrophenyl (DNP) derivatives of the relevant secondary amines. They were all prepared by the reaction of 1-fluoro-2,4-dinitrobenzene with the appropriate aliphatic secondary amine in dimethyl sulfoxide solution in the presence of triethylamine as supporting base (cf.[9]). Many of these derivatives are known, but those which appeared to be new will be referred to by appropriate names in the Experimental section.

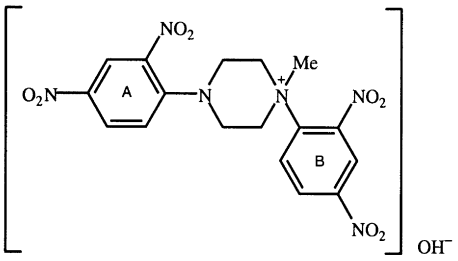
Manuscript received 1 June 2000 10.1071/CH00076 0004-9425/00/080715

Table 1. Ultraviolet absorption data of 2,4-dinitrophenyl derivatives of some secondary amines in various solvents

	2,4-Dinitrophenyl derivative of	Ring size[A]	λ_{max} ($\log \epsilon_{max}$)[B] EtOH	CF_3CO_2H
(1a)	aziridine	3	318 (4.16)	[C]
(1b)	azetidine	4	364 (4.29)	[D]
(1c)	pyrrolidine	5	368 (4.28)	383 (3.18)
(1d)	2,5-dimethylpyrrolidine	5	373 (4.33)	[E]
(1e)	piperidine	6	372 (4.19)	[E]
(1f)	*cis*-2,6-dimethylpiperidine	6	365 (3.19)	[E]
(1g)	*trans*-2,6-dimethylpiperidine	6	370 (3.76)	[F]
(1h)	morpholine	6	363 (4.05)	369 (3.87)
(1i)	thiomorpholine	6	366 (4.12)	[E]
(1j)	*N*-ethoxycarbonylpiperazine	6	362 (4.12)	348 (2.68)
(1k)	*N*-methylpiperazine	6	364 (4.14)	335 (4.15)
(1l)	*N*-phenylpiperazine	6	365 (4.19)	333 (4.03)
(1m)	azacycloheptane	7	372 (4.27)	[E]
(1n)	azacyclooctane	8	375 (4.28)	[E]

[A] Ring size of secondary amine. [B] λ_{max} value in nm.
[C] Insufficiently soluble; on heating, decomposition occurred.
[D] Acid-catalysed reaction occurred (see text). [E] No features.
[F] Not recorded.

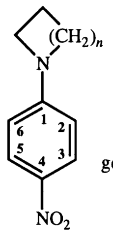
It was not established if the DNP derivative obtained from 2,5-dimethylpyrrolidine [(1d), see Table 1] was the *cis*- or *trans*-dimethyl isomer; in any event, unlike the *cis*- and *trans*-2,6-dimethylpiperidines (1f,g), this compound did not exhibit anomalous ultraviolet and ^{1}H n.m.r. spectra (see discussion below). Under the same reaction conditions, *N*-methylpiperazine gave the DNP derivative (1k) in good yield; however, the use of aqueous ethanol as solvent, with sodium acetate as supporting base, gave a different product which, on the basis of its microanalytical data and ^{1}H n.m.r. spectrum, is considered to be the salt (3) (see Experimental).



(3)

Ultraviolet Spectra

The spectra in ethanolic solution of each of the compounds studied showed only a single long-wavelength maximum (see Table 1), a feature which provides evidence that the *o*-nitro group has been pushed out of plane by the bulky substituent attached to the 1-position [cf. also the discussion[10] of the spectra of the DNP derivatives of dimethylamine (2a) and diethylamine (2b)]. From Table 1, it will be seen that, with the exception of DNP aziridine (1a), and of DNP *cis*- and *trans*-2,6-dimethylpiperidine [(1f) and (1g) respectively], the DNP polymethyleneimines studied show a long-wavelength maximum in about the same region of the spectrum, and with similar intensity, i.e., the size (4–8 members) of the polymethyleneimino ring has little effect on the ultraviolet spectrum. DNP aziridine (1a) absorbs at a significantly shorter wavelength than do any of the other DNP derivatives, an observation which implies that the rigid three-membered ring hinders delocalization of the anilino nitrogen lone-pair electrons into the DNP ring. This finding has a parallel with that found in a spectroscopic study (cf.[11]) of the corresponding 1-polymethyleneimino-4-nitrobenzenes [general formula (4)], where 1-aziridinyl-4-nitrobenzene (4a) absorbs at a significantly shorter wavelength than do the other 4-nitrophenyl derivatives studied. In the case of the two DNP 2,6-dimethylpiperidines (1f,g), their $\log \epsilon_{max}$ values were significantly less than those of the other DNP derivatives and, in particular, that of the parent piperidinyl derivative (1e) (cf.[7] also). This decreased intensity in colour suggests that the polymethyleneimino ring of these two compounds suffers greater twisting out of the plane of the DNP ring than is the case for the other DNP derivatives, and is greatest for DNP *cis*-2,6-dimethylpiperidine (1f). The corresponding spectra in carbon tetrachloride solution (data not shown) also showed a single maximum, but at shorter wavelengths (by 8–16 nm); the $\log \epsilon_{max}$ values obtained were practically identical to those found for ethanolic solutions.



general formula (4)
(4a) $n = 0$
(4b) $n = 1$

The ultraviolet spectra were also measured in trifluoroacetic acid solution (see Table 1). For many of the compounds, the spectra were featureless, a phenomenon which we ascribe to protonation of the anilino nitrogen atom by the solvent. Significantly, several compounds, namely the DNP derivatives of *N*-methyl- and *N*-phenyl-piperazine [(1k) and (1l) respectively], which contain other protonatable sites, retained their colour. So also did DNP morpholine (1h), presumably because its oxygen atom is preferentially protonated vis-a-vis the anilino nitrogen atom. Both DNP *N*-ethoxycarbonylpiperazine (1j) and, surprisingly, DNP pyrrolidine (1c) still retained some of their original colour. Finally, the spectrum of DNP azetidine (1b) changed quickly with time; this phenomenon, which is due to the occurrence of an acid-catalysed ring opening, was revealed also by ^{1}H n.m.r. spectroscopy (see next section).

^{1}H N.M.R. Spectra

^{1}H n.m.r. spectra were recorded for both (D)chloroform and trifluoroacetic acid solutions; selected spectroscopic data are presented in Table 2. With some minor differences, the respective dinitrophenyl ring protons (H 3, H 5 and H 6) of most of the compounds in (D)chloroform solution exhibited similar chemical shifts. However, DNP aziridine (1a) and DNP *cis*-2,6-dimethylpiperidine (1f) showed significant differences. On the one hand, the H 3 chemical shift of DNP

Table 2. ^{1}H n.m.r. chemical shifts of 2,4-dinitrophenyl derivatives of some secondary amines [general formula (1)]

	2,4-Dinitrophenyl derivative of	Ring size[A]	$CDCl_3$ solution H 3[B]	H 5[B]	H 6[B]	CF_3CO_2H solution H 3[C]	H 5[C]	H 6[C]
(1a)	aziridine	3	8.85	8.33	7.27	[D]	[D]	[D]
(1b)	azetidine	4	8.67	8.15	6.67	[E]	[E]	[E]
(1c)	pyrrolidine	5	8.62	8.17	6.90	9.18 (0.56)	8.78 (0.61)	8.12 (1.22)
(1d)	2,5-dimethylpyrrolidine	5	8.62	8.17	7.00	9.45 (0.83)	9.02 (0.85)	8.43 (1.43)
(1e)	piperidine	6	8.68	8.25	7.15	9.28 (0.60)	8.88 (0.63)	8.35 (1.22)
(1f)	*cis*-2,6-dimethylpiperidine	6	8.39	8.35	7.60	9.44 (1.05)	9.02 (0.67)	8.43 (0.83)
(1g)	*trans*-2,6-dimethylpiperidine	6	8.57	8.30	7.29	9.38 (0.81)	8.98 (0.68)	8.20 (0.93)
(1h)	morpholine	6	8.70	8.30	7.15	9.13 (0.43)	8.73 (0.43)	8.05 (0.90)
(1i)	thiomorpholine	6	8.65	8.27	7.15	9.34 (0.69)	8.94 (0.63)	8.45 (1.30)
(1j)	*N*-ethoxycarbonylpiperazine	6	8.68	8.30	7.17	9.30 (0.62)	8.78 (0.48)	8.08 (0.91)
(1k)	*N*-methylpiperazine	6	8.65	8.22	7.10	8.93 (0.28)	8.48 (0.26)	7.43 (0.33)
(1l)	*N*-phenylpiperazine	6	8.67	8.27	6.93	8.98 (0.31)	8.58 (0.31)	7.55 (0.62)
(1m)	azacycloheptane	7	8.55	8.13	7.03	9.28 (0.73)	8.90 (0.77)	8.32 (1.29)
(1n)	azacyclooctane	8	8.56	8.18	7.10	8.86 (0.30)	8.45 (0.27)	7.89 (0.77)

[A] Ring size of secondary amine. [B] H 3, d ($J \approx 2$ Hz); H 5, dd ($J \approx 2$ and 9 Hz); H 6, d ($J \approx 9$ Hz). Chemical shift data for aliphatic protons are omitted. [C] $\Delta\delta$ $CF_3CO_2H - CDCl_3$ are in parentheses. [D] Insufficiently soluble; on heating, decomposition occurred. [E] Acid-catalysed reaction occurred (see text and Experimental).

aziridine (1a), occurs at particularly low field, and therefore we deduce that, compared to the other DNP derivatives, its anilino nitrogen lone-pair electrons are less delocalized into the dinitrophenyl ring. On the other hand, the spectrum of DNP *cis*-2,6-dimethylpiperidine (1f) exhibits two anomalous features [previously reported by other workers (cf.[8])]. These are: its H 6 signal occurs at a lower field, and its H 3 signal occurs at a higher field than do the corresponding signals of all the other DNP derivatives, including the *trans* isomer (1g). The former feature implies that the polymethyleneimino ring of DNP *cis*-2,6-dimethylpiperidine (1f) is twisted out of the plane of the 2,4-dinitrophenyl ring to an even greater extent than it is in the other DNP derivatives. The latter feature prompts us to conclude that steric conflict forces the *o*-nitro group of the compound (1f) out of the plane of the DNP ring to such an extent that its electron-withdrawing ability has been significantly weakened.

The ^{1}H n.m.r. spectra in trifluoroacetic acid solution of many of the DNP derivatives revealed a very large downfield solvent shift [$\Delta\delta$ ($CF_3CO_2H - CDCl_3$) > 1.2 ppm] of the H 6 an observation which we regard as evidence that these particular derivatives are protonated at the anilino nitrogen atom. Those compounds, namely DNP morpholine, and DNP *N*-methyl-, DNP *N*-phenyl- and DNP *N*-ethoxycarbonyl-piperazine [(1h), (1k), (1l) and (1j) respectively], which have other protonatable sites, exhibited smaller downfield H 6 solvent shifts. Surprisingly, DNP azacyclooctane (1n) exhibited a smaller downfield solvent shift, i.e., was not completely protonated, than did the related DNP polymethyleneimines (1c,e,m) possessing smaller aliphatic rings. As was observed with the corresponding ultraviolet spectrum (see previous section), the ^{1}H n.m.r spectrum of DNP azetidine (1b) changed with time. Analysis of the changes by means of ^{1}H n.m.r. spectroscopy (see Experimental) has revealed that ring opening had occurred to give the trifluoroacetate (5b). 1-Azetidinyl-4-nitrobenzene (4b) reacted significantly more slowly (see Experimental).

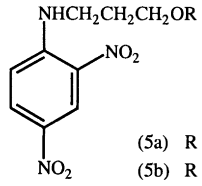
Interestingly, the ^{13}C n.m.r. chemical shifts of several of the DNP derivatives [in (D)chloroform solution] in our study have been reported elsewhere.[1,2,12] Of particular relevance to our work was the finding[12] that C 2 and C 6 of DNP 2,6-dimethylpiperidine [presumably the *cis* compound (1f), but not so specified] occur significantly further downfield than do the corresponding carbons of DNP piperidine (1e), DNP morpholine (1h) and DNP pyrrolidine (1c). The explanation[12] put forward for this downfield shift is that the dimethylpiperidinyl ring is twisted out of plane to a greater extent than are the polymethyleneimino rings of the other three DNP derivatives.

In summary, our spectroscopic investigations lead us to conclude that DNP *cis*-2,6-dimethylpiperidine (1f) has a structure in which both its polymethyleneimino and *o*-nitro groups are forced out of the plane of the phenyl ring to a significantly greater extent than are the corresponding groups of the other DNP derivatives, including the corresponding *trans* compound (1g), studied. It was therefore of interest to determine its X-ray crystal structure, and to compare it with the X-ray structures reported for the related compounds, DNP piperidine (1e),[1] DNP pyrrolidine (1c),[2] and DNP morpholine (1h).[2] Its molecular structure, which incidentally verified the *cis*-structure given to the compound by the Italian workers,[8] was successfully determined, and is discussed below.

Experimental

(a) General

All melting points are uncorrected. The elementary analyses were carried out by either the Australian Microanalytical Service,



(5a) R = H
(5b) R = $COCF_3$

Melbourne, or the Analytical Unit, Research School of Chemistry, Australian National University. Ultraviolet spectra were recorded either on a Beckman DK2 or on a Varian 235 spectrophotometer in ethanol, carbon tetrachloride (Merck Uvasol grade) and trifluoroacetic acid (Fluka grade) solutions. ^{1}H n.m.r. spectra were obtained in (D)chloroform and trifluoracetic acid with 0.4 M solutions either on a Varian A60D spectrometer or on a JEOL FX90 spectrometer. In order to avoid using large volumes of trifluoroacetic acid, solutions in this solvent were prepared directly by weighing out the sample (0.7–1.5 mg) in the cell (1 cm) and adding the solvent (3 ml). This procedure renders these $\log \epsilon_{max}$ values less accurate than those obtained with ethanol as solvent.

With the exception of *N*-ethoxycarbonylpiperazine and azetidine, the secondary amines used in this investigation were obtained from commercial sources. *N*-Ethoxycarbonylpiperazine, b.p. 102–104°C/5 mm, was prepared in 34% yield on the basis of starting piperazine hexahydrate by the literature procedure.[13] Azetidine was prepared as its solution in diglyme (cf.[14]) by the reaction of sodium naphthalenide with *N*-tosylazetidine; the azetidine content (33%) was determined by acidimetric titration with perchloric acid.

(b) Preparation of the N-*2,4-Dinitrophenyl Derivatives*

All derivatives were crystallized from methylene chloride/light petroleum (60–80°). New compounds gave satisfactory microanalyses for nitrogen; their identities and purities were confirmed by their ^{1}H n.m.r. spectra in (D)chloroform solution. The chemical shift data for their DNP ring protons (H 3, H 5 and H 6) are presented in Table 2, and the chemical shifts, integration and appearance of the polymethyleneimino ring proton signals (not shown) were as expected. Their preparation is exemplified by the following preparation. Thus, a mixture of thiomorpholine (1.03 g, 10 mmol), 1-fluoro-2,4-dinitrobenzene (1.86 g, 10 mmol) and triethylamine (2.8 ml, 20 mmol) in dimethyl sulfoxide solution (20 ml) was stirred on a steam bath for 2 h before being poured into water to give *1-(thiomorpholin-4′-yl)-2,4-dinitrobenzene* (1i) (DNP thiomorpholine), m.p. 106–108°C, in 72% yield (Found: N, 15.9. $C_{10}H_{11}N_3O_4S$ requires N, 15.6%).

1-(2′,5′-Dimethylpyrrolidin-1′-yl)-2,4-dinitrobenzene (1d) (DNP 2,5-dimethylpyrrolidine) had m.p. 126–128°C (yield 74%) (Found: N, 15.8. $C_{12}H_{15}N_3O_4$ requires N, 15.8%).

1-(4′-Ethoxycarbonylpiperazin-1′-yl)-2,4-dinitrobenzene (1j) (DNP *N*-ethoxycarbonylpiperazine) had m.p. 119–121°C (yield 90%) (Found: N, 17.5. $C_{13}H_{16}N_4O_6$ requires N, 17.3%).

1-(Azacyclooctan-1′-yl)-2,4-dinitrobenzene (1n) (DNP azacyclooctane) had m.p. 104–105°C (yield 70%) (Found: N, 15.0. $C_{13}H_{17}N_3O_4$ requires N, 14.9%).

The corresponding reaction with *N*-methylpiperazine gave *1-(4′-methylpiperazin-1′-yl)-2,4-dinitrobenzene* (1k) (DNP 4-methylpiperazine), m.p. 77–79°C, in 84% yield (Found: N, 21.2. $C_{11}H_{14}N_4O_4$ requires N, 21.1%). However, reaction (steam bath; 4 h) of *N*-methylpiperazine (400 mg, 4 mmol) with 1-fluoro-2,4-dinitrobenzene (1.488 mg, 8 mmol) in a mixture of ethanol (32 ml) and water (8 ml) in the presence of sodium acetate (656 mg, 8 mmol) gave *1,4-bis(2,4-dinitrophenyl)-1-methylpiperazin-1-ium hydroxide* (3) as an orange solid (1.33 g; 74% yield) which crystallized from the mixture on cooling. The analytical sample (from ethanol/acetonitrile) had m.p. 195–197.5°C (Found: C, 45.1; H, 4.1; N, 18.5). $C_{17}H_{18}N_6O_9$ requires C, 45.3; H, 4.0; N, 18.7%). ^{1}H n.m.r. [$(CD_3)_2SO$]: δ 2.77, s, CH_3; 3.17 and 3.47, m, 2×NCH_2 (not assigned); 5.53, br s, OH (removed by the addition of deuterium oxide); 6.58, d (*J c*. 9 Hz), H 6 (ring A); 7.50, d (*J c*. 9 Hz), H 6 (ring B); 7.93, dd (*J c*. 2 and *c*. 9 Hz), H 5 (ring A); 8.33, dd (*J c*. 2 and *c*. 9 Hz), H 5 (ring B); 8.55 and 8.60, d (*J c*. 2 Hz), H 3 (signals not assigned).

The reaction (20 mmol scale; steam bath; 2 h) with 2,6-dimethylpiperidine (4 equiv.) (a mixture of *cis* and *trans* isomers) in the presence of triethylamine (4 equiv.) gave, after chromatography on silica gel, 1-(*cis*-2′,6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1f) (DNP *cis*-2,6-dimethylpiperidine), m.p. 82–84°C (lit.[8] 84–85°C), in 33% yield. The *trans*-2,6-dimethyl isomer (1g) could not be freed from unreacted 1-fluoro-2,4-dinitrobenzene; a small sample of this isomer was donated by Professor F. Pietra (see Acknowledgments).

1-Azetidinyl-2,4-dinitrobenzene (DNP azetidine) (1b) was prepared as follows. A diglyme solution (11.4 ml) containing approximately 20 mmol azetidine (cf.[14]) was stirred with a solution of 1-fluoro-2,4-dinitrobenzene (20 mmol) and triethylamine (0.28 ml, 2 equiv.) in dimethyl sulfoxide (10 ml) for 16 h at room temperature. The mixture was then poured into water, and extracted with ether to give a semisolid product which was purified by silica gel chromatography; elution with benzene/light petroleum (60–80°) (1 : 1) gave DNP azetidine (1b), m.p. 115–117°C, in 56% yield (Found: N, 18.7. $C_9H_{19}N_3O_4$ requires N, 18.8%).

1-Azetidinyl-4-nitrobenzene (4b) was prepared by a similar method, but with anhydrous potassium carbonate (2 equiv.) as the supporting base. Reaction (40 mmol scale; steam bath; 5 h) gave a yellow semisolid which was purified by chromatography on silica gel (30 g); elution with benzene/light petroleum (2:1) gave 1-azetidinyl-4-nitrobenzene (4b), m.p. 118–120°C (lit.[15] 119°C), in 29% yield. ^{1}H n.m.r. ($CDCl_3$): δ 2.45, quintet, CH_2; 4.05, t, NCH_2; 6.25, d (*J c*. 9 Hz), H 2/H 6; 8.05, d (*J c*. 9 Hz), H 3/H 5.

(c) The Reaction of DNP *Azetidine (1b) with Trifluoroacetic Acid*

Changes in the ^{1}H n.m.r spectrum occurred almost immediately after dissolution of the sample in trifluoroacetic acid. In addition to all the signals expected for DNP azetidine, other signals were also present. Significantly, the original two multiplets due to the azetidine ring protons had been joined by a third multiplet (upfield). After 30 min, all the original signals had been replaced by new signals. The original signals were located at δ 3.77, m, CH_2; 4.82, m, NCH_2; 7.83, d, H 6; 8.67, dd, H 5; 9.13, d, H 3. The new signals were located at δ 2.35, quintet, $CH_2\mathbf{CH_2}CH_2$; 3.77, t, NCH_2; 4.67, t, OCH_2; 7.13, d, H 6; 8.67, dd, H 5; 9.25, d, H 3. The nature of the reaction which had occurred was further revealed by removing the trifluoroacetic acid (by azeotropic treatment to dryness with benzene), and then recording the spectrum of the low-melting product in (D)chloroform solution. This spectrum showed signals located at δ 2.25, quintet, CH_2; 3.60, dt, NCH_2; 4.53, dt, OCH_2; 6.95, d, H 6; 8.33, dd, H 5; 8.58 br, NH; 9.13, d, H 3. Significantly, the H 5 signal showed fine splitting (*J c*. 0.7 Hz) which is due to long-range NH,H 5 coupling (cf.[9]). The broad signal at δ 8.58 was assigned to an aromatic NH group because it was absent in the trifluoroacetic acid spectrum.

From the above ^{1}H n.m.r. evidence, it seemed likely that the product of the acidic reaction was the trifluoroacetate (5b). This deduction was confirmed in the following way. *3-[(2′,4′-Dinitrophenyl)amino]propan-1-ol* (5a), m.p. 73–75°C, was prepared in 80% yield by the reaction of 3-aminopropan-1-ol with 1-fluoro-2,4-dinitrobenzene in dimethyl sulfoxide solution in presence of triethylamine as described in section *(b)* (Found: N, 17.1. $C_9H_{11}N_3O_5$ requires N, 17.4%). ^{1}H n.m.r. ($CDCl_3$): δ 2.07, quintet, $CH_2\mathbf{CH_2}CH_2$; 2.12, s, OH (removed by the addition of deuterium oxide); 3.62, dt, NCH_2; 3.98, t, OCH_2; 6.98, d, H 6; 8.25, dd, H 5; 8.85, br, NH (removed by the addition of deuterium oxide); 9.07, d, H 3. The H 5′ signal showed long-range NH,H 5 coupling (*J c*. 0.7 Hz). The trifluoroacetate (5b) was prepared by stirring a solution of the parent alcohol (5a) (1.94 g) in chloroform (20 ml) with trifluoroacetic anhydride at room temperature for 1 h. The solvent was removed on a rotary evaporator to give a yellow oil (2.67 g; 98% crude yield) which solidified in the fridge. Crystallization from pentane cooled in dry ice gave *3-[(2′,4′-dinitrophenyl)amino]propyl trifluoroacetate* (5b), m.p. 48–50°C (Found: C, 39.0; H, 2.9; N, 12.6. $C_{11}H_{10}F_3N_3O_5$ requires C, 39.2; H, 3.0; N, 12.5%). ν_{max} (C=O) 1780 cm^{-1}. The ^{1}H n.m.r spectra of this compound in both (D)chloroform and trifluoroacetic acid solutions were identical with the corresponding spectra (see above) of the product obtained from the reaction of DNP azetidine (1b) with trifluoroacetic acid.

The action of trifluoroacetic acid on 1-azetidinyl-4-nitrobenzene (4b) was also briefly studied. The ^{1}H n.m.r spectrum of a solution (0.4 M) of this compound in trifluoroacetic acid changed very slowly. After 3 days, partial ring opening was observed; complete reaction was not achieved, however, because decomposition appeared to occur thereafter.

*(d) Crystallographic Study of 1-(*cis*-2′,6′-Dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1f)*

Crystals suitable for an X-ray structure analysis were obtained by slow evaporation of a hexane solution at room temperature. Accurate cell dimensions were determined at 18(2)°C by least-squares refinement of 25 automatically centred reflections in the range $35 < 2\theta < 63°$ measured with Cu Kα (graphite-monochromatized) radiation (λ = 1.5418 Å).

Crystal data. $C_{13}H_{17}N_3O_4$, *M* 279.3, triclinic, space group $P\bar{1}$, *a* 8.165(1), *b* 7.865(1), *c* 11.148(1) Å, α 95.23(1), β 106.00(1), γ 92.63(1)°, *V* 683.4(2) Å^3, D_c 1.357 (*Z* = 2) g cm^{-3}, *F*(000) 296, μ(Cu Kα) 8.53 cm^{-1}.

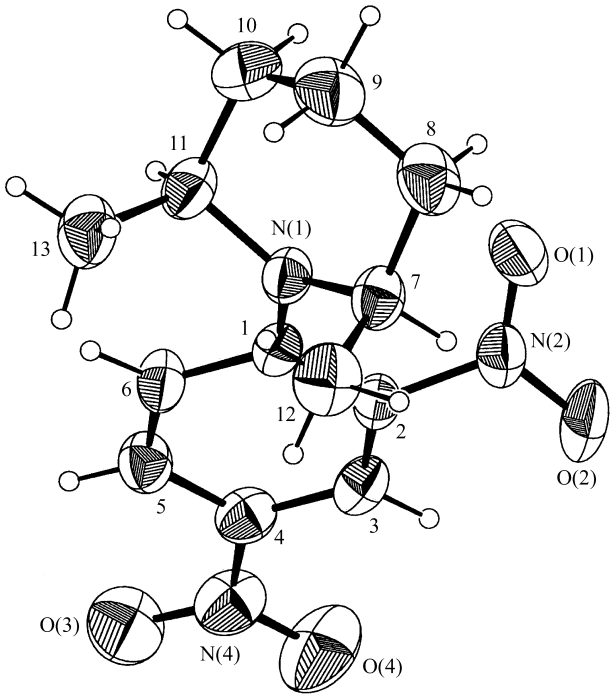


Fig. 1. Perspective view of 1-(*cis*-2′,6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1f) with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms are represented by circles of arbitrary radius. Carbon atoms are denoted by numerals only.

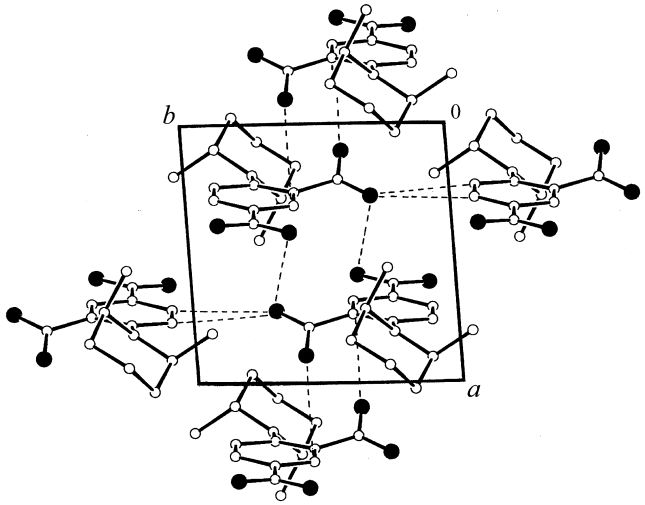


Fig. 2. The crystal packing of 1-(*cis*-2′,6-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1f) as viewed down the crystal *c*-axis. The large filled circles are oxygen.

* $R = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ and $wR = [\Sigma[w(F_o)^2-(F_c)^2]/\Sigma[w(F_o)^2]]^{1/2}$.

Structure determination. Intensity data were measured at 18(2)°C with Cu Kα radiation from a cleaved specimen of dimensions *c*. 0.36 by 0.36 by 0.22 mm aligned on a Rigaku–AFC four-circle diffractometer, recorded by an ω–2θ scan with 2θ scan rate 2.0° min^{-1}, and 10 s stationary background counts. Three reference reflections monitored every 100 reflections indicated no decay. Data to a $2\theta_{max}$ 130° yielded a total of 2301 unique terms (R_{merg} = 0.015); corrections for Lorentz and polarization effects were applied: analytical absorption corrections were made with SHELX-76[16] (transmission factors 0.758–0.856). The structure was solved by direct methods with SHELX-76[16] and least-squares refinements were carried out with SHELXL-93[17] on a VAX8800 computer with 2222 unique terms ($I > 2\sigma I$). Full-matrix least-squares refinements [on $(F_o)^2$], with anisotropic factors given to the non-hydrogen atoms and isotropic given to the hydrogen atoms, gave residuals* for the 2222 data of *R* 0.048 and *wR* 0.146 with *S* = 1.093 (250 variables). The function minimized in the refinements was $\Sigma w[(F_o)^2-(F_c)^2]^2$ with $w = [\sigma^2(F_o^2) + (0.0783P)^2 + 0.2909P]^{-1}$ where $P = [\max(F_o^2,0) + 2F_c^{2/3}]$. The maximum and minimum residual electron-density peak heights were +0.18 and –0.24 e Å^{-3}. An extinction parameter was applied to the F_c terms with SHELXL-93;[17] the extinction coefficient was $0.073(5) \times 10^{-6}$.

Results. The results are presented in Tables 3–7, and Figs 1 and 2. The latter were prepared from the output of ORTEPII.[18] Material deposited: anisotropic thermal parameters, hydrogen atom parameters, and observed and calculated structure amplitudes; copies are available (until 31 December 2005) from the Australian Journal of Chemistry, P.O. Box 1139, Collingwood, Vic. 3066.

Discussion of the Crystal Structure

A perspective view of the 1-(*cis*-2′6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene molecule (1f) is given in Fig. 1. The piperidinyl ring adopts a fairly regular chair conformation with asymmetry parameter,[19] ΔC_s^{N1}, 3.0°. Interestingly, the two methyl groups on the ring are both in the axial position, that is the less stable orientation expected for such substituents [the two torsion angles C(1)–N(1)–C(7)–C(12) and C(1)–N(1)–C(11)–C(13) are close to 90° (see Table 6)]. The C(7),N(1),C(11) plane is twisted by 36.2(2)° from the mean plane of the phenyl ring of the DNP moiety, and the *o*-nitro group by 29.5(2)°. This twisting minimizes steric interaction between the substituents on the anilino nitrogen atom at C(1) and the *o*-nitro group. The interplanar angle of 36.2(2)° indicates a twisting of the polymethyleneimino ring from the plane of the DNP moiety in the *cis*-2,6-dimethylpiperidine derivative (1f), which is much greater than that reported[2] for DNP pyrrolidine (1c), in which the corresponding angles range from 16.1(5) to 20.5(5)°, and somewhat greater than that [31.5(2)°] reported[1] for the parent piperidinyl structure (1e). This finding is therefore consistent with the molecular picture which we derived from our analysis of the spectroscopic properties (see above) of the DNP *cis*-2,6-dimethylpiperidine (1f). However, in the case of DNP morpholine (1h), which does not exhibit anomalous spectroscopic properties (see Tables 1 and 2, and ref. 12), the interplanar angle is reported to be 41.4(2)°, i.e., its polymethyleneimino ring is twisted to an even greater extent from the phenyl ring plane than it is in compound (1f). Furthermore, in the case of several DNP *N*,*N*-dialkylanilines[3–6] [general formula (2)] (see

also Table 7), the CNC plane of the dialkylamino group is twisted from the mean phenyl ring by values ranging from 29.9(5) to 38.8(2)°. We conclude therefore that there is no simple correlation between the size of the substituents on the anilino nitrogen and the magnitude of this angle.

The twisting of the *o*-nitro group in compound (1f) from the phenyl ring plane by 29.5(2)° is the major difference between the molecular structure of the DNP *cis*-2,6-dimethylpiperidine (1f), and the structures of a number of other related DNP compounds[1–6] (for structures, see Table 7), in which the *o*-nitro groups are twisted from the associated ring planes by much larger values [from 38.6(2) and 55.5(5)°]. These findings indicate that there is no simple correlation between the size of the substituent on the anilino nitrogen atom, and the deviation of the *o*-nitro group from planarity with the phenyl ring (see also our discussion above concerning the phenyl/dialkylamino interplanar angles of these molecules). A similar finding has already been noted by previous workers (cf.[2,6]). In 2,4-dinitroaniline, which has no substituents on the anilino nitrogen, both the amino and *o*-nitro groups have been found[20] to lie close to the phenyl ring plane, a finding which indicates there is an intramolecular hydrogen bond between the amino and the *o*-nitro group. This no doubt prevents rotation of the *o*-nitro group from the ring plane.

As in the structures of the related DNP molecules, the phenyl ring of DNP *cis*-2,6-dimethylpiperidine (1f) exhibits deviations from C_{6mmm} symmetry (see also Tables 4 and 5). This ring adopts a slight boat conformation, with C(1) and C(4) lying on one side of the mean plane at distances of 0.031(1) and 0.019(1) Å respectively, whilst the other ring atoms lie on the opposite side [mean deviation 0.010(1) Å]. Although the phenyl ring in 2,4-dinitroaniline[20] is planar to within experimental limit, the slight boat conformation persists in the other DNP molecules.[1–6] Here the deviations are not as pronounced as those reported for four of the compounds.* This distortion from planarity of the aromatic ring is considered to be due to the *ortho* effect. The N(1) and N(2) atoms lie significantly from the phenyl ring, and on opposite sides of it in all the molecules listed in Table 7. This is reflected in the torsion angle N(1)–C(1)–C(2)–N(2) of –18.5(3)° obtained for our compound (1f), which lies between that [–8.1(3)°] found for DNP morpholine (1h)[2] and that [–21.4(6)°] found for DNP dicyclohexylamine (2d);[5] the value in 2,4-dinitroaniline is only –1.9(7)°. However, it should be noted that, in the DNP *cis*-2,6-dimethyl compound (1f), the endocyclic angle at C(1) of 114.6(2)° is significantly less than the regular trigonal value (120°), and is accompanied by an enlargement of the endocyclic angles at C(2) and C(6) to 122.5(2) and 122.8(2)° respectively. This may be due to a combination of the electron-releasing property of the amino group and the electron withdrawal by the *o*-nitro group. The C(1)–C(2) and C(1)–C(6) bonds of 1.423(2) and 1.422(3) Å respectively are significantly elongated compared to the regular aromatic C–C length of 1.397

Table 3. Fractional atomic coordinates and equivalent isotropic temperature factors of the non-hydrogen atoms

Estimated standard deviations are in parentheses: U_{eq} (Å^2) were calculated from the refined anisotropic temperature parameters

Atom	*x*	*y*	*z*	U_{eq}
C(1)	0.7716(2)	0.2536(2)	0.8917(2)	0.0356(4)
C(2)	0.7390(2)	0.4044(2)	0.9594(2)	0.0358(4)
C(3)	0.6880(2)	0.4007(2)	1.0675(2)	0.0422(5)
C(4)	0.6745(2)	0.2474(2)	1.1154(2)	0.0429(5)
C(5)	0.7145(3)	0.0978(3)	1.0579(2)	0.0435(5)
C(6)	0.7630(3)	0.1016(2)	0.9503(2)	0.0420(5)
N(2)	0.7888(2)	0.5772(2)	0.9362(2)	0.0438(4)
N(4)	0.6208(3)	0.2441(3)	1.2288(2)	0.0569(5)
O(1)	0.8985(2)	0.5971(2)	0.8822(2)	0.0554(5)
O(2)	0.7235(3)	0.6978(2)	0.9791(2)	0.0707(5)
O(3)	0.6145(3)	0.1064(3)	1.2721(2)	0.0757(6)
O(4)	0.5843(3)	0.3784(3)	1.2771(2)	0.0861(7)
N(1)	0.8082(2)	0.2474(2)	0.7791(1)	0.0385(4)
C(7)	0.7186(3)	0.3506(3)	0.6791(2)	0.0445(5)
C(8)	0.8415(4)	0.4150(3)	0.6090(2)	0.0584(6)
C(9)	0.9381(4)	0.2723(4)	0.5660(3)	0.0654(7)
C(10)	1.0317(3)	0.1835(3)	0.6778(2)	0.0594(6)
C(11)	0.9096(3)	1.1089(3)	0.7452(2)	0.0456(5)
C(12)	0.5565(3)	0.2529(4)	0.5930(2)	0.0591(6)
C(13)	0.8074(4)	–0.0532(3)	0.6716(3)	0.0598(6)

Table 4. Bond lengths (Å) involving the non-hydrogen atoms

Estimated standard deviations are in parentheses

Atoms	Distance	Atoms	Distance
C(1)–C(2)	1.423(2)	N(4)–O(4)	1.228(3)
C(1)–C(6)	1.422(3)	N(1)–C(1)	1.365(2)
C(2)–C(3)	1.381(3)	N(1)–C(7)	1.485(2)
C(2)–N(2)	1.467(2)	N(1)–C(11)	1.482(2)
C(3)–C(4)	1.374(3)	C(7)–C(8)	1.527(3)
C(4)–N(4)	1.450(3)	C(7)–C(12)	1.528(3)
C(4)–C(5)	1.384(3)	C(8)–C(9)	1.518(4)
C(5)–C(6)	1.365(3)	C(9)–C(10)	1.519(4)
N(2)–O(1)	1.221(2)	C(10)–C(11)	1.530(3)
N(2)–O(2)	1.232(2)	C(11)–C(13)	1.526(3)
N(4)–O(3)	1.230(3)		

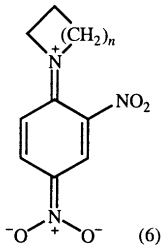
Table 5. Bond angles (degrees) involving the non-hydrogen atoms

Estimated standard deviations are in parentheses

Atoms	Angle	Atoms	Angle
N(1)–C(1)–C(2)	125.1(2)	O(3)–N(4)–C(4)	118.2(2)
N(1)–C(1)–C(6)	120.3(2)	C(4)–N(4)–O(4)	118.6(2)
C(2)–C(1)–C(6)	114.6(2)	O(3)–N(4)–O(4)	123.2(2)
C(1)–C(2)–C(3)	122.5(2)	C(1)–N(1)–C(7)	121.3(1)
C(1)–C(2)–N(2)	123.9(2)	C(1)–N(1)–C(11)	119.1(2)
N(2)–C(2)–C(3)	113.5(2)	C(7)–N(1)–C(11)	118.2(2)
C(2)–C(3)–C(4)	119.4(2)	N(1)–C(7)–C(8)	110.3(2)
C(3)–C(4)–C(5)	120.7(2)	N(1)–C(7)–C(12)	111.5(2)
C(3)–C(4)–N(4)	119.2(2)	C(8)–C(7)–C(12)	113.5(2)
N(4)–C(4)–C(5)	120.2(2)	C(7)–C(8)–C(11)	112.2(2)
C(4)–C(5)–C(6)	119.7(2)	C(10)–C(9)–C(12)	109.8(2)
C(1)–C(6)–C(5)	122.8(2)	C(9)–C(10)–C(11)	120.0(2)
O(1)–N(2)–C(2)	119.6(2)	N(1)–C(11)–C(10)	108.5(2)
C(2)–N(2)–O(2)	117.6(2)	N(1)–C(11)–C(13)	116.0(2)
O(1)–N(2)–O(2)	122.7(2)	C(1)–C(11)–C(13)	120.0(2)

* Errors were noted in the planarities reported for the structures of DNP piperidine (1e),[1] DNP diisopropylamine (2c),[3] DNP dicyclohexylamine (2d),[5] and DNP cyclohexyl(isopropyl)amine (2e).[4] The recalculated values have been deposited.

Å. However, these values lie within the range reported for the related DNP derivatives.[1–6] The C(1)–N(1) bond length of 1.365(2) Å is suggestive of some double-bond character, and the N(1)–C(7) and N(1)–C(11) bond lengths of 1.485(2) and 1.482(2) Å respectively are significantly longer than the values of 1.354(2), 1.466(2) and 1.460(2) Å found for these bonds in the parent piperidinyl molecule (1e).[1] The dimensions in the *cis*-dimethyl molecule (1f) suggest a stabilization of the resonance structure as shown in formula (6). This feature is also evident in the other DNP molecules,[1–6] and has been in fact already suggested by previous workers (cf.[2]).



(6)

There are clearly differences between the structure of the molecule (1f) as suggested by spectroscopic data (obtained in solution) and the solid-state structure defined by the X-ray analysis. We believe that these differences are a consequence of the greater mobility of the molecules in solution as opposed to the molecules in the solid state which are packed and held together in the crystal lattice. The anomaly concerning the disposition of the *o*-nitro group, which is not twisted to such an extent from the associated phenyl ring in (1f) as it is in the other DNP molecules,[1–6] could have arisen as a consequence of intermolecular forces in the crystal. The forces in all these molecules are to a large extent dependent on the packing modes of the molecules in the crystal, and therefore will differ in the structures studied. As in the crystal structure of the parent molecule [DNP piperidine (1e)],[1] there are several C–H···O intermolecular contacts in the crystal structure of DNP *cis*-2,6-dimethylpiperidine (1f) shown in Fig. 2, which are less than the sum of the van der Waals radii of the involved atoms, and can be interpreted as attractive interactions.[21,22] Two of the interactions, C(5)···O(2) [*x*,–1+*y*,*z*] 3.198(3) Å and C(6)···O(2) [*x*,–1+*y*,*z*] 3.231(3) Å, link the molecules into infinite chains along the crystal *b*-axis, whilst the other two interactions, C(3)···O(2) [1–*x*,1–*y*,2–*z*] 3.299(3) Å and C(3)···O(1) [2–*x*,1–*y*,2–*z*] 3.265(3) Å, link the molecules across centres of symmetry into infinite chains extending along the *a*-axis. When considered as a whole, the four unique interactions link the molecules into layers parallel to the crystal *ab* plane.

Acknowledgments

The authors wish to thank Mrs Judi Rosevear for technical assistance, and Professor Francesco Pietra, Chemistry Department, University of Trento, Italy, for a gift of 1-(*trans*-2′,6′-dimethylpiperidin-1′-yl)-2,4-dinitrobenzene (1g).

References

[1] Ellena, J., Punte, G., Rivero, B. E., Remedi, M. V., de Vargas, E. B., and de Rossi, R. H., *J. Chem. Crystallogr.*, 1995, **25**, 801.

Table 6. Selected torsion angles (degrees)
Estimated standard deviations are in parentheses

Atoms	Angle	Atoms	Angle
C(1)–C(2)–N(2)–O(1)	–19.4(3)	C(1)–N(1)–C(11)–C(13)	91.6(2)
C(3)–C(2)–N(2)–O(2)	–27.1(2)	N(1)–C(7)–C(8)–C(9)	50.3(3)
C(3)–C(4)–N(4)–O(4)	2.0(3)	C(7)–C(8)–C(9)–C(10)	–56.0(3)
C(5)–C(4)–N(4)–O(3)	0.9(3)	C(8)–C(9)–C(10)–C(11)	58.6(3)
N(2)–C(2)–C(1)–N(1)	–18.5(3)	C(9)–C(10)–C(11)–N(1)	–54.5(3)
C(2)–C(1)–N(1)–C(7)	–39.8(3)	C(10)–C(11)–N(1)–C(7)	51.7(2)
C(6)–C(1)–N(1)–C(11)	–26.6(3)	C(11)–N(1)–C(7)–C(8)	–50.1(2)
C(1)–N(1)–C(7)–C(12)	–89.5(2)		

Table 7. Selected dimensions for 1-X-2,4-dinitrobenzenes

X substituent	Interplanar angles (degrees) Phenyl/amino	Phenyl/*o*-NO_2	N(1)–C(1)–C(2)–N(2)[A] (degrees)	Ref.
Piperidin-1-yl (1e)	31.5(3)	38.9(3)	–19.0(2)	1
Pyrrolidin-1-yl (1c)	18.7(5)	42.5(5)	–9.8(8)	2
	16.1(5)	55.5(5)	–10.1(9)	2
	20.5(5)	45.2(5)	–16.7(8)	2
Morpholin-4-yl (1h)	41.4(2)	44.5(2)	–8.1(3)	2
Diisopropylamino (2c)	29.9(5)	40.7(4)	–16.7(5)	3
Cyclohexyl(isopropyl)amino (2e)	36.5(5)	55.2(5)	–15.5(4)	4
Dicyclohexylamino (2d)	38.8(2)	38.6(2)	–19.8(6)	5
	30.8(2)	47.0(2)	–21.4(6)	5
cis-2,6-Dimethylpiperidin-1-yl (1f)	36.2(2)	29.5(1)	–18.5(3)	this work
Amino (2,4-dinitroaniline)	2.7(5)	4.3(4)	–1.9(7)	20

[A] The values refer to the same mirror image isomer as for DNP *cis*-2,6-dimethylpiperidine (1f) (see Fig. 1).

[2] Remedi, M. V., Bujan, E. L., Baggio, R., and Garland, M. T., *J. Phys. Org. Chem*., 1998, **11**, 895.
[3] Punte, G., Rivero, B. E., Socolovsky, S. E., and Nudelman, N. S., *Acta Crystallogr*., *Sect. C*, 1989, **45**, 1952.
[4] Punte, G., Rivero, B. E., Socolovsky, S. E., and Nudelman, N. S., *Acta Crystallogr*., *Sect. C*, 1991, **47**, 1222.
[5] Punte, G., and Rivero, B. E., *Acta Crystallogr*., *Sect. C*, 1991, **47**, 2118.
[6] Low, J. N., Doidge-Harrison, S. M. S. V., and Cobo, J., *Acta Crystallogr*., *Sect. C*, 1996, **52**, 964.
[7] Pietra, F., and del Cima, F., *J. Org. Chem*., 1968, **33**, 1411.
[8] Pietra, F., and del Cima, F., *Tetrahedron Lett*., 1966, 1925.
[9] Gale, D. J., and Wilshire, J. F. K., *Aust. J. Chem*., 1972, **25**, 2145.
[10] Kamlet, M. J., Adolph, H. G., and Hoffsommer, J. C., *J. Am. Chem. Soc*., 1964, **86**, 4018.
[11] Eastes, J. W., Aldridge, M. H., Minesinger, R. R., and Kamlet, M. J., *J. Org. Chem*., 1971, **36**, 3847.
[12] Al-Rawi, J. M. A., Khuthier, A.-H., and Hanna, S. Y., *Spectrosc. Lett*., 1988, **21**, 249.
[13] Moore, T. S., Boyle, M., and Thorn, V. M., *J. Chem. Soc*., 1929, 39.
[14] White, J., and McGillivray, S., *J, Org. Chem*., 1974, **39**, 1973.
[15] Deady, L. W., Leary, G. J., Topsom, R. D., and Vaughan, J., *J. Org. Chem*., 1963, **28**, 511.
[16] Sheldrick, G. M., SHELX-76, Program for Crystal Structure Determination. University of Cambridge, England, 1976.
[17] Sheldrick, G. M., SHELXL-93, Program for Crystal Structure Refinement, University of Göttingen, Germany, 1993.
[18] Johnson, C. K., ORTEPII, Report ORNL-5138, Oak Ridge National Laboratories, Tennessee, U.S.A., 1976.
[19] Duax, W. L., and Norton, D. A., 'An Atlas of Steroid Structure' pp. 18–19 (Plenum Press: New York 1975).
[20] Prasad, I., Gabe, E. J., and Page, Y. Le., *Acta Crystallogr*., *Sect. B*, 1982, **38**, 674.
[21] Taylor, R., and Kennard, O., *J. Am. Chem. Soc*., 1982, **104**, 5063.
[22] Desiraju, G. R., *Acc. Chem. Res*., 1991, **24**, 290.