Conformation and circular dichroism of some *N*-nitropyrrolidines

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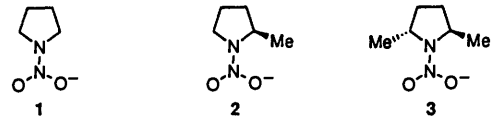
The results of a theoretical investigation (*ab initio* calculations) of the parent nitropyrrolidine 1 and its (*R*)-2-methyl and (*R,R*)-2,5-dimethyl derivatives 2, 3 are in good agreement with the CD, UV and ^{1}H NMR spectra of 2, 3 and the X-ray analysis of 3. In the ground state of nitropyrrolidines 1, 2 both nitrogen atoms of the nitroamino group are pyramidal and both nitrogen atoms of 3 are planar. In all cases, a small twisting of the nitroamino group about the N–N bond is observed. An envelope conformation with the C_4 atom at the tip is predicted for nitropyrrolidine 1 and the more stable isomer 2a, which has a pseudoaxial methyl group. The less stable isomer 2b, (with a pseudoequatorial methyl group) and both isomers of 3 (2,5-di-pseudoaxial 3a and 2,5-di-pseudoequatorial 3b) adopt a half-chair conformation. In solutions and the crystal state, 3 exists as isomer 3a. Four Cotton effects are observed in the CD spectra of 2, 3. The signs of the Cotton effect at 270, 240 and 200 nm (the n_O^+–π^*, π_N–π^* and π_O–π^* electronic transitions) are determined by the configuration of the α-carbon chiral centres. The intrinsic chirality of the nitroamine chromophore and the chirality of the five-membered ring influence, mostly, the Cotton effect of the n_O^-–π^* transition at 300 nm.

Introduction

From the stereochemical point of view, *N*-nitropyrrolidines are among the most interesting nitroamines. A study of these compounds permits one to broach simultaneously such basic problems as (*a*) local geometry of the nitroamino group (degree of nonplanarity of the nitrogen atoms and/or torsion about the N–N bond), (*b*) conformation of the five-membered ring (envelope or half-chair), (*c*) the influence of α-alkyl substituents on the geometry and conformation, and finally, (*d*) the influence of the local geometry of the nitroamine chromophore and of its spatial environment on the circular dichroism (CD), in particular on the signs of Cotton effects (CE) observed in the 200–300 nm region.[1,2a] The last can provide information for the first three problems because CD spectra are especially sensitive to conformational effects. For example, for the inherently nonplanar nitroamines-*N*-nitrosubstituted azetidines and aziridines, the sign of the longest wavelength Cotton effect was found[2] to depend directly on the intrinsic chirality of the nitroamine chromophore caused by *N–N* twisting.

From the few published works,[1,3,4] concerned with conformational problems of *N*-nitropyrrolidines a contradictory picture emerges. Indeed, Polonski and Prajer in their study[1] of the CD of 2-substituted *N*-nitropyrrolidines, assumed local C_{2v} symmetry of the nitroamino group and planarity of the pyrrolidine ring. On the basis of calculated data[3] at the RHF 3-21G level of theory, the parent nitropyrrolidine **1** has C_2 symmetry, *i.e.* it adopts a half-chair conformation with both nitrogen atoms planar and little twisting about the N–N bond. In the recent paper by Vilkov and co-workers,[4] the electron diffraction data of **1** were interpreted in terms of an envelope conformation of the ring with the pyramidal nitrogen atom being out of the plane of the remaining ring atoms and with a considerable N–N twisting. Thus, it is apparent that further investigation of stereochemistry of *N*-nitropyrrolidines is warranted.

In the present work, the parent nitropyrrolidine **1** has been studied at three levels of theory, *i.e.* RHF, DFT (Becke3LYP), and MP2. In each case, the 6-31G* basis set was employed because it was shown earlier[5] that split valence basis sets including polarization functions are needed for the correct description of the configurations of the nitrogen atoms in nitroamines. The influence of α-alkyl substituents on the local geometry of the nitroamino group and conformation of the five-membered ring is studied by the addition of one or two methyl groups. Thus, the conformers of methyl-substituted nitropyrrolidine **2**, **3**, were optimized at the Becke3LYP/6-31G* level. The excited singlet states of chiral conformations of nitropyrrolidines **1**–**3** were calculated by single point all-singles



1 **2** **3**

configuration interaction (CIS) calculations with the 6-31+G* basis set. The computed results are compared with experimental data which, for nitropyrrolidines **2** and **3**, were obtained in this work. These compounds were synthesized from the corresponding optically active *N*-nitrosopyrrolidines (see Experimental section).

Results and discussion

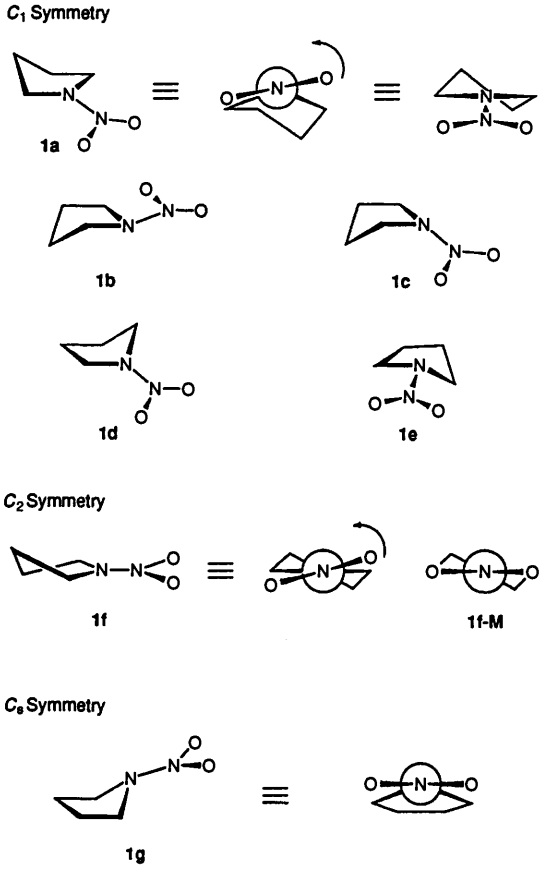
The most stable conformation of the parent nitropyrrolidine **1** is **1a** according to all three theoretical levels (RHF, Becke3LYP and MP2). The ring has an asymmetric envelope with a markedly pyramidal ring nitrogen (see out-of-plane angle α in Table 1). As in the case of other nitroamines,[5] the nitrogen atom of the nitro group of **1a** is slightly pyramidal (angle β in Table 1) in the direction which is opposite to the pyramidality of the ring nitrogen. Attempts to locate other possible conformations **1c–e** with C_1 symmetry led to conformer **1a** or its enantiomer **1b**.

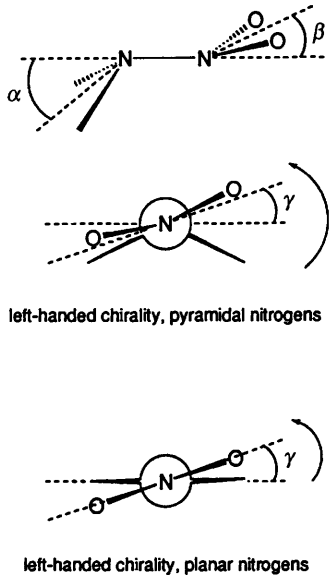
The C_2-symmetric conformation **1f** (half-chair) with planar nitrogen atoms ($\alpha = \beta = 0°$), which was assumed previously to be the ground state of the parent nitropyrrolidine, is, in fact, an inversion saddle point (one imaginary frequency). The vibrationless nitrogen inversion barriers of nitropyrrolidine, **1**, are predicted to be extremely low. The present values (RHF/6-31G*: 0.01 kcal mol^{-1} (1 cal = 4.184 J); MP2/6-31G*: 0.59 kcal mol^{-1}; Becke3LYP/6-31G*: 0.19 kcal mol^{-1}) are somewhat smaller than the barriers of dimethylnitroamine calculated at the same theoretical levels (RHF/6-31G*: 0.4 kcal mol^{-1}; MP2/6-31G*: 1.2 kcal mol^{-1}).[5c] In both molecules, addition of electron correlation leads to a slightly higher predicted barrier

Table 1 Selected geometrical parameters,[a] dipole moments[b] and relative energies[c] of the parent nitropyrrolidine stationary structures[d] calculated using the 6-31G* basis set

	1a			**1f**			**1g**	**1**
	RHF	Becke3LYP	MP2	RHF	Becke3LYP	MP2	Becke3LYP	Expt.[e]
O_1N_1	1.201	1.235	1.243	1.201	1.236	1.246	1.233	1.225
O_2N_2	1.201	1.235	1.244	1.201	1.236	1.246	1.233	1.225
N_1N_2	1.319	1.362	1.369	1.316	1.352	1.351	1.373	1.363
N_1C_2	1.460	1.471	1.472	1.457	1.462	1.457	1.467	1.477
N_1C_5	1.457	1.466	1.466	1.457	1.462	1.457	1.467	1.477
$O_1N_2O_2$	125.4	126.3	126.5	125.4	126.4	126.7	126.3	126.3
$O_1N_2N_1$	117.4	117.1	117.1	117.3	116.8	116.7	116.8	—
$O_2N_2N_1$	117.2	116.6	116.5	117.3	116.8	116.7	116.8	—
$N_2N_1C_2$	121.5	120.1	118.3	122.0	122.0	121.8	117.6	116.0
$N_2N_1C_5$	121.3	119.5	117.6	122.0	122.0	121.8	117.6	116.0
$C_2N_1C_5$	115.6	114.4	113.5	116.0	115.9	116.3	112.2	110.3
α[f]	6.5	23.5	31.2	0.0	0.0	0.0	33.7	39.9
β[f]	0.7	1.5	2.4	0.0	0.0	0.0	1.8	0.0[g]
$O_1N_2N_1C_2$	10.0	17.2	22.8	2.1	1.9	2.5	21.3	—
$O_2N_2N_1C_5$	−5.7	−13.1	−17.1	2.1	1.9	2.5	−21.3	—
$N_1C_2C_3C_4$	26.2	24.7	25.2	29.1	28.9	30.6	−17.0	—
$N_1C_5C_4C_3$	32.0	33.3	37.1	29.1	28.9	30.6	17.0	—
$C_2C_3C_4C_5$	−37.1	−36.7	−39.4	−37.1	−36.9	−39.2	0.0	0.0
γ[f]	2.1	1.9	2.6	2.1	1.9	2.5	0.0	1.68
μ	5.6574	5.2036	5.0003	5.7089	5.3752	5.3448	5.0200	—
$E_{rel.}$	0.00[h]	0.00[i]	0.00[j]	0.01	0.19 (0.04)	0.59	1.98 (1.93)	—

[a] Bond lengths (Å) angles (°). [b] In D (1D ≈ 3.335 64 × 10^{-30} cm). [c] In kcal mol^{-1}; relative energies including ZPVE are in parentheses. [d] See Fig. 2 for the atom numbering. [e] Ref. 4. [f] See structures. [g] Fixed parameter.[4] [h] E = −414.613 449 E_h. [i] E = −417.080 144 E_h. [j] E = −415.832 270 E_h (1 E_h ≈ 4.359 7482 × 10^{-18} J).





to inversion. The relative energy of another transition state-C_s-symmetric envelope **1g** with pyramidal nitrogens is at significantly higher energy than **1f** (Table 1). It can be regarded as the transition structure for the interconversion of the enantiomers **1a,b**.

The twisting about the N–N bond in isomers **1a,f** can be described by torsion angle γ (Table 1), *i.e.* by the angle of deviation of the nitro group from the ideal conformation with the coplanar arrangement of the n_N and π^*_{NO2} orbitals.[2] This angle is analogous to angle ψ_{NN} in ref. 4 or to angle α_t defined for dimethylnitroamine[6] as the angle of the projections along N–N of C–C and O–O.

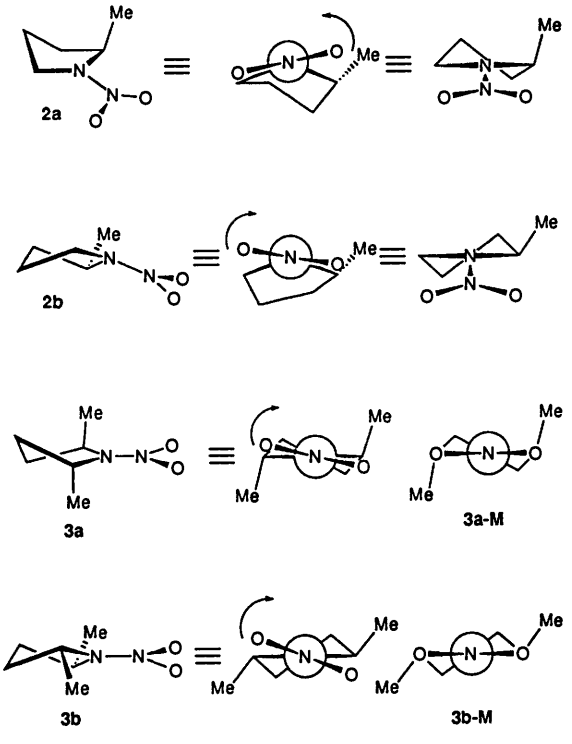
The direction of the twist of the nitro group is suitable for description of the intrinsic chirality of the nitroamino group:[2] a clockwise deviation (negative γ) corresponds to right-handed chirality and *vice versa*. Signs of torsion angles ONNC are not suitable for the role because these signs are opposite to one another in the case of nitroamines which have a pyramidal amine nitrogen. For the C_2-symmetric molecule **1f** with the planar ring nitrogen, angle γ coincides in its magnitude with torsion angles $O_1N_2N_1C_2$ and $O_2N_2N_1C_5$. However, the sign of these angles is opposite to the accepted direction of the N–N twisting.

The main cause of twisting of the nitroamino group about the

N–N bond in isomers **1a,f** is evidently a steric repulsion of the oxygen atoms with one (in the case of **1a**) or two (**1f**) pseudoequatorial α-hydrogens. The stereoelectronic effect of the σ_{CN}–π^*_{NO2} orbital interaction, was argued to play a role[2b] in determining the N–N torsional deformation of *N*-nitro-substituted azetidines and, especially, aziridines. This effect is apparently negligible for *N*-nitropyrrolidines because of a relatively poor electron donor ability of the unstrained CN bonds of the pyrrolidine ring.

The calculated inversion barrier of **1a** is very small, especially after inclusion of the zero point vibrational energy (Table 1). It disappears at the Hartree–Fock level but survives at higher levels. The bond lengths and valence angles of the nitroamino group of the C_1 symmetrical structure **1a** are close to the experimental electron diffraction data (Table 1). However, from the point of view of conformation, neither of structures **1a,f** are close to the model on the basis of which the experimental electron diffraction data were interpreted.[4] Previously,[7] it was noted that the conformation of five-membered rings $(CH_2)_4X$ depends, as a rule, on the local symmetry of the X group, *i.e.* compounds with C_{2v} or C_2 symmetry of this group adopt a half-chair conformation. The envelope conformation deduced by Vilkov and co-workers,[4] which is similar to **1g** but with the strongly twisted nitroamino group, is in disagreement with this general observation.[7]

For 2-methyl substituted nitropyrrolidine **2**, two stable conformers **2a,b** were found. Both conformers are characterized



by pyramidal N_1 and N_2 atoms and by a rather twisted nitro group which is in a *trans*-orientation with respect to the methyl group. It was established that 1,2-*cis*-isomers **2** are not stationary points of the potential energy surface of **2**. The steric interaction of the nitro group with the pseudoequatorial methyl group in **2b** is rather greater than with the pseudoaxial one in **2a** and, therefore, the ring nitrogen of **2b** is more pyramidal. In turn, this causes a greater repulsion between the O_2 atom and the pseudoequatorial hydrogen at C_5 and, consequently, the greater N–N torsional deformation of **2b**. Both factors, *i.e.* pyramidalization and N–N twisting, decrease the n_N–π^*_{NO2} conjugation in the nitroamino group of **2b** and, in this way, destabilize this conformer in comparison with **2a**. The difference in the calculated energies of conformers **2a,b** (Table 2) gives their ratio as 0.59:0.41 (at 20 °C, assuming $\Delta S^\circ = 0$). A preference for conformers with an axial orientation of α-alkyl groups was also observed earlier[8] for *N*-nitropiperidines.

The conformation of the five-membered ring of isomer **2a** is similar to the conformation **1a** of the parent nitropyrrolidine, *i.e.* it is an envelope with the C_4 atom at the tip. The conformation of the less stable isomer **2b** is closer to a half-chair than to an envelope since it is characterized by practically identical $N_1C_2C_3C_4$ and $N_1C_5C_4C_3$ (or $C_2N_1C_5C_4$ and $C_5N_1C_2C_3$) torsion angles (Table 2).

As in the case of nitropyrrolidine **2**, the existence of two stable conformers of 2,5-*trans*-dimethyl substituted **3**-di-pseudoaxial **3a** and di-pseudoequatorial **3b** could be supposed. In this case, it was evident that the steric interaction of the nitro group with two 2,5-*trans*-methyl groups must lead to a flattening of the ring nitrogen and, as a consequence, to a flattening of the nitro group nitrogen. Therefore, each conformer **3a** and **b** was optimized at the Becke3LYP level in two ways: (*i*) in C_1 symmetry (both the nitrogen atoms of the nitroamino group are pyramidal) and (*ii*) in C_2 symmetry (the nitrogen atoms are planar). The difference in energies of these structures in the case of **3a** is only 0.018 kcal mol^{-1} (with C_1-**3a** lower), indicating a highly deformable structure the average geometry of which is C_2 symmetry. The same is true also for **3b**, where C_2-**3b** is lower in energy by 0.008 kcal mol^{-1} than C_1-**3b**. Thus, one can say that both conformers **3a,b** are C_2-symmetrical in their ground states, *i.e.* are characterized by planar nitrogen atoms and a half-chair conformation (Scheme 3, Table 2). The di-pseudoaxial isomer **3a** is significantly more stable than the di-pseudoequatorial **3b**. It should be noted that all calculated structures (C_1 and C_2) of **3a,b** are twisted around the N–N bond because of the steric interaction of the oxygen atoms with the methyl groups. The most N–N twisting is observed for the di-pseudoequatorial isomer **3b** (Table 2). In nitropyrrolidine **2b** with one pseudoequatorial methyl group, such interaction is minimized owing to the *trans*-orientation of this group and the nitro group. Therefore, the difference in γ torsion angles and, correspondingly, the difference in the energies for the pair of conformers **2a,b** is substantially smaller than for the pair of **3a,b** (Table 2). The calculated ratio of conformers **3a,b** is equal to 0.98:0.02 (at 20 °C, assuming $\Delta S^\circ = 0$) in the gas phase.

The X-ray structure analysis of nitropyrrolidine **3** showed that this compound crystallizes as only the more stable conformer **3a** (Fig. 1). Good agreement of all calculated and experimental structural parameters is observed (Table 2).

The conformational equilibrium of nitropyrrolidine **3** in a solution is also practically shifted towards dipseudoaxial conformer **3a**. Indeed, the experimental values of the vicinal spin–spin coupling constants of the α-protons, 7.5 and 0.9 Hz, are quite close to the constants $^3J_{ea}$ 7.48 and $^3J_{ee}$ 1.99 Hz obtained from an extended Karplus equation[9] on the basis of the calculated structural parameters of **3a**. The geometry of less preferable dipseudoequatorial conformer **3b** gives substantially different calculated coupling constants for these protons: $^3J_{aa}$ 10.34, $^3J_{ae}$ 4.07 Hz.

It should be noted that the values of the vicinal constants, 7.0 and 3.9 Hz, observed for the proton at C_2 in the ^{1}H NMR spectrum of mono-methylsubstituted nitropyrrolidine **2** manifest the presence of isomer **2b** with a pseudoequatorial methyl group. This is an indirect confirmation of the calculated data on the close population of conformers **2a,b**. Additional supporting evidence of correctness of the conformational analysis of nitropyrrolidine **2** as well as **3** has been obtained from the theoretical and experimental data on the optical activity (circular dichroism) of these compounds. Unlike **2**, **3**, the parent nitropyrrolidine **1** cannot exist in an optically active form under normal conditions owing to the low barrier of the interconversion of the enantiomers **1a,b**. Therefore, the optical

Table 2 Selected geometrical parameters,[a] dipole moments[b] and relative energies[c] of conformers of methyl-substituted nitropyrrolidines[d] **2**, **3** at the Becke3LYP/6-31G* level

			3a		
	2a	**2b**	Calc.	Expt[e]	**3b**
O_1N_2	1.236	1.235	1.237	1.246(4)	1.236
O_2N_2	1.235	1.234	1.237	1.251(4)	1.236
N_1N_2	1.364	1.371	1.354	1.331(4)	1.358
N_1C_2	1.483	1.484	1.475	1.472(5)	1.481
N_1C_5	1.467	1.475	1.475	1.469(6)	1.481
$O_1N_2O_2$	126.0	125.7	125.6	124.0(4)	125.3
$O_1N_2N_1$	117.3	117.0	117.2	118.7(4)	117.4
$O_2N_2N_1$	116.7	117.3	117.2	117.2(4)	117.4
$N_2N_1C_2$	119.8	118.8	121.8	121.6(4)	121.9
$N_2N_1C_5$	118.7	118.4	121.8	122.3(3)	121.9
$C_2N_1C_5$	114.6	113.8	116.5	115.9(4)	116.3
α	25.4	28.9	0.00	2.7	0.00
β	1.5	1.6	0.00	1.2	0.00
$O_1N_2N_1C_2$	18.0	14.2	−2.9	−5.1(6)	−13.9
$O_2N_2N_1C_5$	−14.3	−22.4	−2.9	−0.5(6)	−13.9
$N_1C_2C_3C_4$	24.7	−29.6	29.6	33.1(5)	−27.4
$N_1C_5C_4C_3$	33.7	−29.6	29.6	29.0(4)	−27.4
$C_2C_3C_4C_5$	−37.1	37.5	−38.2	−40.4(4)	35.4
γ	1.7	−4.0	−2.9	−2.8	−13.9
μ	5.0415	4.9335	5.0823		5.0300
$E_{rel.}$	0.00[f]	0.22	0.00[g]		2.29

[a] Bond lengths (Å) angles (°). [b] In D. [c] In kcal mol^{-1}. [d] See Fig. 1 for the atom numbering. [e] Present work. [f] $E = -456.397\,742\ E_h$. [g] $E = -495.713\,344\ E_h$.

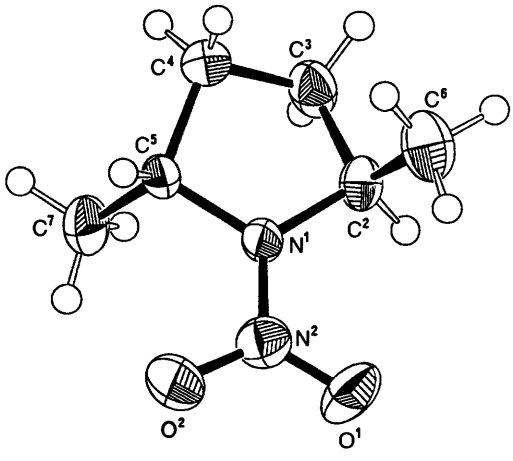


Fig. 1 ORTEP drawing of the X-ray structure of nitropyrrolidine **3**

activity of the conformations of this compound are studied only theoretically.

The calculations of chiroptical properties connected with the first four excited states of nitropyrrolidines **1**–**3** were performed with the CIS/6-31 + G* method implemented in G92. The excited states of the parent nitropyrrolidine **1** were also calculated with the PCI method (see Computational methods). In the main, a good conformity of the signs and magnitudes of the rotational strengths of the electronic transition of **1** calculated with both methods is observed (Table 3).

Examination of the molecular orbitals involved in the first four electronic transitions (Fig. 2) shows the following features of nitroamino group spectroscopy. The first four transitions are to valence excited states. Each transition originated from a different occupied orbital but terminates to the same antibonding π* orbital of the nitroamino group. The antisymmetrical combination (n_O^-) of the non-bonding orbitals of the oxygen atoms is the initial orbital of the first transition and the symmetrical combination (n_O^+) of these orbitals of the second one. The initial orbitals of the third and fourth transitions have π-symmetry and might be designated as π_N and π_O, correspondingly, in accordance with their principal components. Such description is not significantly different from the descriptions which were made for pyramidal *N*-nitroazetidines[2b] at the same theoretical level, and for *N*-nitropiperidines[11] calculated with a semiempirical method assuming local C_{2v} symmetry of the nitroamine chromophore.

The first two transitions, *i.e.* $n_O^- - \pi^*$ and $n_O^+ - \pi^*$, are electric dipole forbidden (in C_{2v} symmetry) and are not revealed in the UV spectra of the parent nitropyrrolidine[12] and its methyl derivatives **2**, **3** in the background of the intense bands of the allowed $\pi_N - \pi^*$ and $\pi_O - \pi^*$ transitions at *ca.* 240 and 200 nm, correspondingly (Fig. 3). Owing to their magnetic dipole allowed character, the n–π* transitions are observed in the CD spectra of nitropyrrolidines **2**, **3** in the region 303–270 nm, nevertheless the π–π* transitions dominate also in these spectra (Table 4, Fig. 3).

The CE signs in the CD spectra of nitropyrrolidine **2** coincide with the signs of the rotational strengths (−0.3, +4.9, −27.2 and −22.5) which can be predicted for the equilibrium mixture of conformers **2a**,**b** on the basis of their calculated ratio (0.59:0.41) and parameters of the first four electronic transitions of each conformer (Table 3). Conformity between the experimental and theoretical CE signs is mainly observed also for nitropyrrolidine **3** with the assumption that the conformational equilibrium is entirely shifted towards the dipseudoaxial isomer **3a**. Some apparent disagreement is connected with the CE of the $n_O^+ - \pi^*$ transition, the intensity of which, according to the calculations, should be greater than the intensity of the CE of the $n_O^- - \pi^*$ transition (Table 3). In reality, the CE of the $n_O^+ - \pi^*$ transition is revealed in the CD spectrum of **3** only in acetonitrile as the very low-intensity band at 270 nm [Fig. 3(*a*), Table 4]. The theoretical method may simply overestimate the relative rotational strength of the second electronic transition of **3a**. However, the discrepancy may only be apparent. It is possible that the positive CE of this transition is not revealed in the CD spectra of **3** in heptane and methanol because of an overlap with the much more intense negative CE of the third ($\pi_N - \pi^*$) transition. Unlike nitropyrrolidine **2**, the smaller predicted difference in energies of the corresponding transitions of **3a** (0.61 *vs.* 0.87 eV for **2a** and 0.89 eV for **2b**) suggests a greater overlapping of these CE in the CD spectra of **3**. Nevertheless, the intensity and position of the CE of the $n_O^+ - \pi^*$ transition in the CD spectra of nitropyrrolidine **2** are also distorted because of a partial

Table 3 Calculated parameters[a] for the first four electronic transitions of stationary and model structures[b] of nitropyrrolidines **1–3** with CIS/6-31+G*[c]

	1a	**1f**	**1f-M**	**2a**	**2b**	**3a**	**3a-M**	**3b**	**3b-M**
Chirality of:									
first sphere[d]	left	left	—	left	right	right	—	right	—
second sphere[d]	left	left	left	left	right	left	left	right	right
third sphere[d]	—	—	—	2*R*	2*R*	2*R*,5*R*	2*R*,5*R*	2*R*,5*R*	2*R*,5*R*
$S_0 \longrightarrow S_1$ (n_O^-–π*)									
E	5.86 (6.11)	5.95	5.95	5.84	5.81	5.92	5.92	5.82	5.87
[*R*]	+5.54 (+6.74)	+6.28	+4.21	+4.53	−7.22	−0.34	+3.10	−22.02	−4.63
f	0.0002 (0.0003)	0.0003	0.0001	0.0002	0.0003	0.0000	0.0001	0.0028	0.0001
$S_0 \longrightarrow S_2$ (n_O^+–π*)									
E	6.55 (6.84)	6.66	6.66	6.52	6.51	6.63	6.63	6.56	6.62
[*R*]	−2.43 (+0.98)	−1.17	−1.11	+2.09	+8.89	+7.04	+7.10	+13.93	+11.89
f	0.0062 (0.0024)	0.0009	0.0009	0.0065	0.0053	0.0009	0.0009	0.0009	0.0011
$S_0 \longrightarrow S_3$ (π_N–π*)									
E	7.43 (7.78)	7.38	7.38	7.39	7.41	7.24	7.25	7.18	7.29
[*R*]	−14.33 (−21.58)	−16.07	−8.63	−39.56	−9.35	−33.81	−45.71	+34.82	−25.37
f	0.3055 (0.2512)	0.3482	0.3478	0.2846	0.2837	0.2933	0.2961	0.2660	0.2906
$S_0 \longrightarrow S_4$ (π_O–π*)									
E	7.79 (8.29)	7.85	7.85	7.76	7.74	7.78	7.78	7.71	7.77
[*R*]	+3.58 (+2.61)	+3.65	+3.80	−18.22	−29.31	−57.70	−56.84	−71.84	−54.42
f	0.2417 (0.1053)	0.2401	0.2399	0.2357	0.2332	0.2205	0.2205	0.2267	0.2310

[a] The transition energies (*E*) are given in eV, the rotational strengths ([*R*]) in cgs × 10^{-40}, the oscillator strengths (*f*) in cgs. [b] Becke3LYP/6-31G* geometries (Tables 1, 2). [c] The 6-31+G* basis set, values shown for **1a** in parentheses were derived with PCI method, see Computational methods for explanation. [d] See text for definition of the chiral spheres.

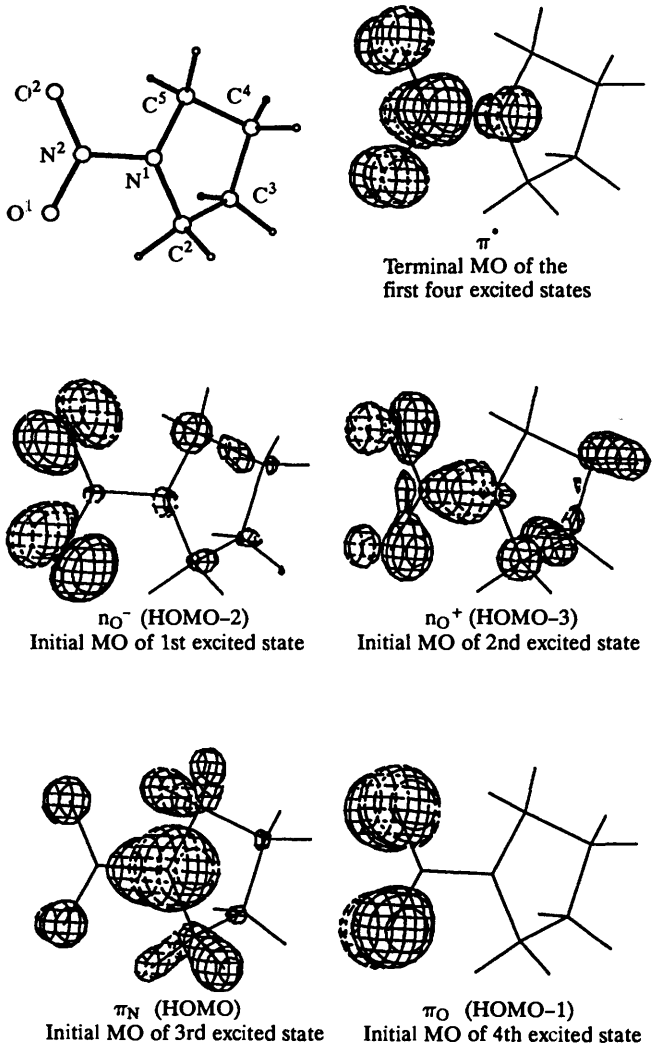


Fig. 2 The Becke3LYP/6-31G* structure **1a** of the parent nitropyrrolidine and the four upper occupied molecular orbitals and the terminal orbital (contour 0.075) involved in the first four electronic transitions of **1a**

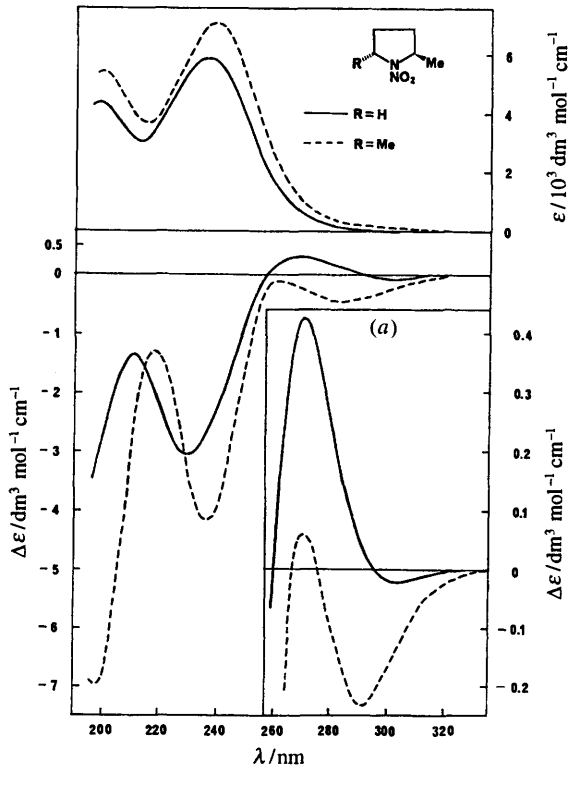


Fig. 3 UV and CD spectra of nitropyrrolidines **2**, **3** in heptane; (*a*) the long wavelength regions of the CD spectra of these compounds in acetonitrile

overlapping with the CE of the more intense adjacent π_N–π* transition. The absence of a hypsochromic shift of the CE of the n_O^+–π* transition of **2** in methanol and moreover the bathochromic shift of this CE (Table 4) are apparently explained by this circumstance. A similar anomaly is also observed for the CE of the n_O^-–π* transition in the CD spectra of nitropyrrolidine **3**. The band of the π_N–π* transition itself exhibits the normal (for bands of π–π* transitions) bathochromic shift in CD and UV spectra of nitropyrrolidines **2**, **3** in the polar solvents (Table 4).

Table 4 CD and UV spectra of nitropyrrolidines **1–3**

Compound	Method	Solvent	λ_{max}, nm ($\Delta\varepsilon$ or ε)			
			$n_O^+-\pi^*$	$n_O^--\pi^*$	$\pi_N-\pi^*$	$\pi_O-\pi^*$
1[a]	UV	Hexane			235 (7030)	
2	CD	Heptane	303 (−0.028)	267 (0.309)	230 (−3.050)	200n[b]
		MeCN	302 (−0.020)	271 (0.427)	236 (−3620)	200n[b]
		MeOH	300 (−0.024)	270 (0.288)	237 (−3.649)	200n[b]
	UV	Heptane			236 (5850)	197 (4350)
		MeOH			240 (6050)	199 (4000)
3	CD	Heptane	284 (−0.438)		236 (−4.176)	198 (−6.96)
		MeCN	291 (−0.228)	270 (0.058)	239 (−7.506)	199 (−8.49)
		MeOH	290 (−0.198)		239 (−6.124)	199 (−6.51)
	UV	Heptane			239 (7070)	200 (5400)
		MeOH			243 (8300)	202 (5530)

[a] Ref. 12. [b] Negative CD without a maximum.

According to a concept due to Snatzke,[13] a chiral molecule can be divided into chiral 'spheres', every one of which influences in its own way the optical activity of the molecule. This idea provides a convenient method of characterizing the optical activity of nitropyrrolidines if one regards the intrinsically chiral nitroamino chromophore as the first sphere, the chiral conformation of the five-membered ring as the second, and the α-methyl group(s) (in the case of substituted nitropyrrolidines **2**, **3**) as the third. For estimation of the contribution of these spheres, we used the data of the calculations of model compounds **1f-M**, **3a-M**, **3b-M** (Table 3) equally with calculated data of stationary structures **1a,f**, **2a,b**, **3a,b**. These models (**-M**) differ from closest stationary structures **1f**, **3a,b** by forced planarity (local C_{2v} symmetry) of the nitroamino group. Other structural parameters were optimized. Removal of the chiral first sphere in this way causes a very small increase of energy relative to the slightly N–N twisted nitropyrrolidines **1f**, **3a** (0.013 and 0.031 kcal mol^{-1}, correspondingly) and a rather more noticeable increase (1.18 kcal mol^{-1}) for the more deformed **3b**.

Model compound **1f-M** is homochiral, *i.e.* it contains only the second chiral sphere. From the calculated rotational strengths of **1f-M** (Table 3), one may conclude that this sphere influences mainly the $n_O^--\pi^*$ (first) and $\pi_N-\pi^*$ (third) transitions. The left-handed half-chair conformation as in compounds **1f**, **1f-M**, **3a** and **3a-M** must make a positive contribution in the CE of the $n_O^--\pi^*$ transition and a negative one in the CE of the $\pi_N-\pi^*$ transition.

Correspondingly, contributions to the CEs of the right-handed half-chair of **2b**, **3b** and **3b-M** have the opposite signs, assuming the model data is transferable. The envelope conformation with the left-handed intrinsic chirality in nitropyrrolidines **1a**, **2a** has the same effect, evidently, as the left-handed half-chair. At least for **1a**, it is confirmed by the same signs and close magnitudes of the rotational strengths of all the electronic transitions of isomers **1a,f** and **1f-M**.

The comparison of the rotational strength magnitudes of model compounds **1f-M** and **3a,b-M** shows, nevertheless, that the second chiral sphere cannot compete with the combined effect of two α-methyl groups in their influence on the $\pi_N-\pi^*$ transition. These groups have undoubtedly a dominant effect upon the $n_O^+-\pi^*$ and $\pi_O^-\pi^*$ transitions also. The same conclusion can be made with regard to one α-methyl group in conformers **2a,b**. These conformers are characterized by the same (*R*) configuration of the α-carbon chiral centre and by the opposite chiralities of the first and second spheres. These conformers differ by the rotational strength signs of only the first transition.

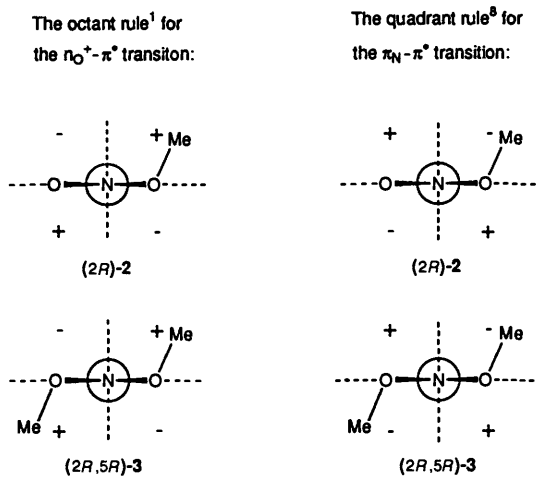
The strong increase of the negative rotational strength of the $n_O^-\pi^*$ transition and the alteration of the sign of the rotational strength of the $\pi_N-\pi^*$ transition by N–N twisting of the chromophore in nitropyrrolidine **3** (transformation of **3a** into **3b**) indicate that the first chiral sphere, like the second, has an effect mainly on the CEs of the first and third electronic transitions. Like the second sphere, the first one with the left-handed chirality makes a positive contribution in the CE of the $n_O^-\pi^*$ transition and a negative contribution in the CE of the $\pi_N-\pi^*$ transition. In fact, the removal of the left-handed first chiral sphere in nitropyrrolidine **1f** (transformation of **1f** into **1f-M**) leads to a decrease of the positive rotational strength of the first transition and of the negative rotational strength of the third one. Also, the predicted changes of the signs and magnitudes of the rotational strengths of these transitions take place upon removal of the right-handed first sphere in nitropyrrolidines **3a,b**, *i.e.* upon transformation of these into **3a,b-M** (Table 3). In the case of nitropyrrolidine **2**, the opposite signs of the rotational strengths of the $n_O^-\pi^*$ transition of conformers **2a,b** are caused by the opposite chiralities of both the nitroamine chromophore and the five-membered ring. An obvious predominance of the first chiral sphere over the second one in the case of the $n_O^-\pi^*$ transition and over the third sphere in the case of the $\pi_N-\pi^*$ transition is possible only after considerable N–N twisting of the chromophore such as is observed for nitropyrrolidine **3b**. It should be noted that the connection of the sign of the rotational strength of the $n_O^-\pi^*$ transition with the intrinsic chirality of the nitroamine chromophore is the same as it has been found[2] for *N*-nitro-substituted azetidines and aziridines.

Sector rules have been offered connecting the CE signs in CD spectra of *N*-nitropyrrolidines[1] and *N*-nitropiperidines[8] with the absolute stereochemistry of these compounds. These rules, *i.e.* an octant rule[1] for the CE at 270 nm (the $n_O^+-\pi^*$ transition) and a quadrant rule[8] for the CE at 240 nm (the $\pi_N-\pi^*$ transition), are based on the assumption of strict C_{2v} local symmetry of the nitroamine chromophore. As was shown by us (see above) and others,[4–6] in reality *N*-nitroamines do not possess such symmetry of the chromophore in their ground state. Nevertheless, with the assumption[1] of local C_{2v} symmetry of the nitroamino group and planarity of the pyrrolidine ring, the signs of the CEs of the $n_O^+-\pi^*$ and $\pi_N-\pi^*$ transitions observed in the CD spectra of nitropyrrolidines **2**, **3** (Fig. 3, Table 4) are consistent with these octant and quadrant rules, respectively.

This takes place only owing to the decisive influence of the α-methyl groups (the third chiral sphere) on the rotational strengths of these transitions and to the relatively insignificant N–N twisting in **2a,b** and **3a**. One must suppose though that a blind application of these rules for other nitroamines could lead to erroneous conclusions.

Conclusions

The nitroamino group and five-membered ring are interdependent, conformationally labile, fragments of *N*-nitropyrrolidines.



The local geometry of the nitroamino group is mainly determined by the closest spatial environment (*i.e.* by steric effects). In the ground state, the parent nitropyrrolidine is characterized by a shallow pyramidal configuration of both nitrogen atoms of the nitroamino group. The pyramidality of the ring nitrogen is much greater than the pyramidality of the nitro group, and increases upon introduction of an α-methyl group *trans*-oriented with respect to the nitro group. However, the ring nitrogen becomes planar (and as a consequence, the nitro group becomes planar as well) in the presence of two mutually *trans*-oriented 2,5-methyl groups. Minimization of the steric interaction of the oxygen atoms with the pseudoequatorial α-hydrogens or methyl groups leads to N–N twisting of the nitroamino group. Such a deformation decreases the n_N–π^*_{NO2} conjugation and leads to relative destabilization of the conformers with pseudoequatorial α-methyl groups.

The local symmetry of the nitroamino group is connected to the conformation of the five-membered ring as observed for the parent nitropyrrolidine **1**. The ground state **1a** has the C_1-symmetric nitroamino group and a C_4-envelope. The saddle structures with local C_2 and C_s symmetry of the nitroamino group are characterized by half-chair and N_1-envelope conformations, respectively. The half-chair conformation of the isomers of 2,5-*trans*-dimethyl-substituted nitropyrrolidine **3** is associated with the C_2-symmetric local geometry of the nitroamino group. 2-Methyl-substituted nitropyrrolidine **2** occupies an intermediate position: the more preferable isomer with the pseudoaxial methyl group adopts the envelope conformation which is similar to **1a**; the conformation of the second isomer with the pseudoequatorial methyl group is close to a half-chair.

The CEs of four electronic transitions, *i.e.* n_O^-–π^*, n_O^+–π^*, π_N–π^* and π_O–π^*, can be as a rule observed in the CD spectra of *N*-nitropyrrolidines in solutions. The signs of the last three transitions at *ca.* 270, 240 and 200 nm are determined by the absolute configuration of the α-carbon chiral centres. The first (chromophore intrinsic chirality) and second (ring chirality) chiral spheres influence, mainly, the CE of the first transition at *ca.* 300 nm. The first chiral sphere dominates in the CEs of the n_O^-–π^* and π_N–π^* transitions if N–N twisting is large. The sign of the rotational strength of the n_O^-–π^* transition induced by the chromophore intrinsic chirality obeys a spiral rule established previously[2] for other non-planar nitroamines-*N*-nitrosubstituted azetidines and aziridines.

Computational methods

The structure of the parent nitropyrrolidine **1** was fully optimized at the Hartree–Fock (RHF), second order Moller–Plesset (MP2) and density functional (DFT) theoretical levels, all with the internal 6-31G* basis set, using procedures implemented in the GAUSSIAN 92/DFT system of programs.[14] In the case of the MP2 calculations, the frozen core approximation was used. The full geometry optimization of methylsubstituted nitropyrrolidines **2**, **3** as well as the partial geometry optimization of the model compounds **1f**-M, **3a,b-M** were performed at the DFT/6-31G* theoretical level. For the DFT calculations, the 'Becke 3LYP' non-local exchange functional approximation,[15a] which uses Becke's 88 non-local functional,[15b] Lee–Yang–Parr's gradient corrected correlation functional,[15c] and the local correlation functional of Vosko, Wilk and Nusair,[15d] was employed. All calculations were carried out with INT = FINEGRID specified. Harmonic frequency analysis verified the nature of the stationary points as minima (all real frequencies) or as transition structures (one imaginary frequency) and was used to provide an estimate of the zero-point vibrational energies (ZPVE) of **1**. For the purpose of Boltzmann analyses, entropy differences between conformations were assumed to be zero.

For all species, chiroptical properties were calculated using the GAUSSIAN 92 (G92/CIS) and PCI (only for **1a**) programs, and the 6-31+G* basis set at the Becke3LYP/6-31G* geometries. The use of diffuse s and p functions designated by the '+' is desired for a more accurate description of the excited singlet states. The G92/CIS method, as implemented in the GAUSSIAN 92 package,[14] uses a window of all valence-occupied and -unoccupied orbitals, but, unlike PCI, does not include the ground state correlation contribution. An all singles CI calculation is carried out for a specified number of electronic states and values of electric and magnetic dipole transition moments are calculated. The magnetic dipole transition moments are for a ground state to excited state transition and must be reversed in sign when used to calculate rotational strengths. The results for **1a** correspond to PCI values prior to addition of the ground state correlation term. The PCI theory is described in detail elsewhere[16] and the method has been extensively used [See ref. 2(*b*) and references cited therein], but for small molecules like **1a** or smaller because, for technical reasons, the PCI program is limited to a window of 15 occupied and 50 unoccupied orbitals. The PCI program can carry out extensive analysis of the excited state wavefunctions in terms of post-CI orbitals. Molecular orbitals of the ground and excited states of **1a** are displayed as modified Jorgensen–Salem plots.[17]

Experimental

N-Nitropyrrolidines **2**, **3** were prepared from the corresponding *N*-nitrosopyrrolidines by oxidation with trifluoroperacetic acid according to the procedure of Emmons.[18] (2*R*)-2-Methyl-1-nitrosopyrrolidine has been described by Gaffield and co-workers.[19] The procedure developed by these authors was used in the present work for nitrosation of (2*R*, 5*R*)-2,5- dimethylpyrrolidine hydrochloride[20] {$[\alpha]_D^{20}$ +5.30 (*c* 1.4, CH_2Cl_2)}.

(2*R*,5*R*)-2,5-Dimethyl-1-nitrosopyrrolidine

The nitrosopyrrolidine was purified by flash chromatography (silica gel 60, 30% EtOAc in light petroleum) and distilled, yield 88%, bp 60 °C (1 mmHg) [lit.,[21] bp 57 °C (1 mmHg), racemate], $[\alpha]_D^{20}$ −61.6 (*c* 1.2, heptane); $\delta_H(CDCl_3)$ 1.21 (3 H, d, *J* 6.5 Hz, Me), 1.57 (3 H, d, *J* 6.5 Hz, Me), 1.50–1.72 (2 H, m), 2.07–2.36 (2 H, m) and 4.43 (2 H, m).

(2*R*)-2-Methyl-1-nitropyrrolidine 2

The nitropyrrolidine **2** was purified by flash chromatography (silica gel 60, 20% EtOAc in light petroleum), yield 87%, $[\alpha]_D^{20}$ −84.2 (*c* 1.2, $CHCl_3$); $\delta_H(CDCl_3)$ 1.38 (3 H, d, *J* 6.4 Hz, Me), 1.68–1.80 (1 H, m), 1.95–2.30 (3 H, m), 3.88 (2 H, m, 5, 5-H) and 4.43 (1 H, m, *J* 7.0, 6.4, 3.9 Hz, 2-H) (Anal. calcd. for $C_5H_{10}N_2O_2$: C, 46.1; H, 7.75; N, 21.5. Found: C, 45.8; H, 7.6; N, 21.8%).

(2*R*,5*R*)-2,5-Dimethyl-1-nitropyrrolidine 3

The nitropyrrolidine **3** was purified by recrystallization from pentane (at 0 °C), yield 86%, mp 57–58 °C, $[\alpha]_D^{20}$ −165.7 (*c* 1.1, $CHCl_3$); $\delta_H(CDCl_3)$ 1.33 (6 H, d, *J* 6.4 Hz, 2, 5-Me), 1.70 (2 H, m), 2.30 (2 H, m) and 4.46 (2 H, m, *J* 7.5, 6.4, 0.9 Hz, 2, 5-H) (Anal. calcd. for $C_6H_{12}N_2O_2$: C, 50.0; H, 8.4; N, 19.4. Found: C. 49.8; H, 8.3; N, 19.5).

Crystal Structure Determination

A colourless needle-shaped crystal of **3** ($C_6H_{12}N_2O_2$) having approximate dimensions of 0.15 × 0.13 × 0.45 mm was used for data collection on a Rigaku AFC6S diffractometer with graphite monochromated Mo-Kα radiation at 200(1) K. Tetragonal space group $P4_1$ (No. 76) with a = 6.434(1), c = 18.267(3) Å, V = 756.2(3) Å^3, Z = 4, F_W = 144.17 and D_c = 1.27 g cm^{-3}. The structure was solved by direct methods[22] and refined by full-matrix least squares calculations. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final values for R and wR were 0.033 and 0.022, respectively, for 482 observed data. All calculations were performed using the TEXSAN[23] crystallographic software package of Molecular Structure Corporation.

Supplementary material available: Tables of X-ray crystallographic data for **3** including details of data collection, atomic coordinates, bond lengths and angles, and anisotropic thermal parameters have been deposited with the Cambridge Crystallographic Data Centre (CCDC). For details of the CCDC deposition scheme, see 'Instructions for Authors' (1996), *J. Chem. Soc., Perkin Trans. 2*, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 188/12.

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