Structure of 2,4-Dimethyl-1H-naphtho[2,3-b][1,4]diazepine Hydropicrate. Solid-state Assembly via C–H···O Hydrogen Bonding

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Crystal structure determination, semiempirical AM1 and PM3 calculations have been performed on 2,4-dimethyl-1H-naphtho[2,3-b][1,4]diazepine hydropicrate. The two molecules are almost planar apart from two NO_2 and CH_3 groups. The NO_2 plane makes an angle of 36.2° and 44.3° with the least squares plane of the 'phenyl' ring. The naphthodiazepine molecule and the picrate acid molecule are intermolecularly linked by one N–H···O and four C–H···O hydrogen bonds and form polar ribbons parallel to the [110] direction. The ribbons are linked by intermolecular C–H···O hydrogen bonds about a centre of inversion and the ensemble forms layers. These layers are weakly bound by van der Waals' interactions and undergo a reversible martensitic-type transition upon heating. During this transition the colour of the crystal changes from dark orange to yellow. AM1 and PM3 calculations on the dimers reproduce, with acceptable approximation, the main features of the structure.

A great number of diazepine analogues are used as anxiolytic, sedative-hypnotic or anticonvulsant drugs. Some of these, mainly 2,4-disubstituted compounds, have interesting chromogenic properties which are used for analytical purposes. For example, they are indicators of the action of free radicals in human pathology.

We recently reported the crystal structure of 2,4-Dimethyl-1H-naphtho[2,3-b][1,4]diazepine hydrochloride monohydrate ($[C_{15}N_2H_{15}]^+Cl^-\cdot H_2O$)[1] in which the seven membered ring diazepinium cation is essentially planar and the crystal is almost black. In this paper we report the crystal structure of 2,4-dimethyl-1H-naphtho[2,3-b][1,4]diazepine hydropicrate prepared by mixing picric acid with an ethanolic solution of the parent naphthodiazepine. This crystal is orange, and the colour of the crystal changes to pale yellow upon heating to above 150 °C. This colour change is accompanied by a solid-state phase transition.

The crystal structure reveals, in addition to classical N–H···O hydrogen bonds, several weak C–H···O hydrogen bonds involving nitro groups. As such C–H···O hydrogen bonds have recently aroused the interest of solid state chemists,[2-5] we attempted to analyse the C–H···O network using the semi-empirical computation methods AM1[6] and PM3.[7] In addition, the IR and FT-Raman spectra of the title compound were studied.

Experimental

2,4-Dimethyl-1H-naphtho[2,3-b][1,4]diazepine hydrochloride in ethanol was synthesised as reported.[1] The title compound was prepared by adding equimolar amounts of an ethanolic solution of picric acid to this ethanolic solution. The resulting orange precipitate was separated and dissolved in acetone. Single crystals were prepared by slow evaporation of the latter solution.

The crystal data are listed in Table 1. Intensities were collected on a CAD-4 ENRAF-NONIUS diffractometer. The lattice parameters were determined from 25 reflections having $12 \leq \theta/\text{deg} \leq 13$. 3464 independent reflections were observed using the $\omega/2\theta$ scan technique with scan width $s/\text{deg} = 0.08 + 0.345 \, \text{tg} \, \theta$ having $0.024 \leq (\sin \theta)/\lambda \leq 0.595 \, \text{Å}^{-1}$, $-9 \leq h \leq 9$, $-13 \leq k \leq 13$, $0 \leq l \leq 14$. From 3464 reflections, 1466 reflections with $(F_o)^2 > 3\sigma(F_o)^2$ were utilised. Two standard reflections $1\bar{4} \, 2$ and 1215) measured every 2 h were chosen to control the crystal stability and the crystal showed no deterioration during data collection. No correction for absorption was applied. The structure was solved using direct methods with the program SHELXS-86.[8] Hydrogen atoms were located from a Fourier difference map. Refined parameters were x, y, z and U_{ij}. Statistical weights, $w = 1$, were used and $S = 1.46$. The final difference electron density map showed $\Delta\rho_{max} = 0.24(4) \, \text{e} \, \text{Å}^{-3}$, $\Delta\rho_{min} = -0.18(4) \, \text{e} \, \text{Å}^{-3}$, $(\Delta/\sigma)_{max} = 0.01$; g (isotropic coefficient of secondary extinction) $= 49.7(1) \times 10^{-6}$. Atomic diffusion factors were taken from ref. 9. In the final cycles of full-matrix least-squares refinement, the SHELXL-93 system computer program was used.[10]

Single crystals of the title compound were examined by thermal analysis using a TA Instruments DSC 10 differential calorimeter equipped with a 9990/2100/2000 computer-analyser system, with a heating rate of 10 °C min⁻¹, under a nitrogen atmosphere.

IR spectra were recorded from 4000 to 600 cm⁻¹ using a 257 Perkin-Elmer spectrometer. Samples for IR studies were prepared as fused KBr discs using spectral-grade potassium bromide. FT Raman spectra were recorded using a IFS66/FRA 106 FT spectrometer. The excitation source was a continuous wave Nd:Yag laser operating at 1064 nm. A laser power of 270 mW was used and 100 scans at a nominal resolution of 2 cm⁻¹ were collected. A Ge-diode detector covered the spectral range 50–3500 cm⁻¹.

The AM1 and PM3 calculations were done on Silicon Graphics Indigo R4000, with the MOPAC-6.00 program, as available within INSIGHT II.[11] Geometries were fully optimised starting from the crystal geometry, without applying any constraints, down to a gradient of 1 with the standard BFGS algorithm then down to a gradient of 0.01 using the EF algorithm.

Fig. 1 presents the ORTEP II[12] molecular structure and atomic numbering of the naphthodiazepine hydropicrate. A MolDraw[13] stereoview of all molecules as packed into the unit cell is shown in Fig. 2.
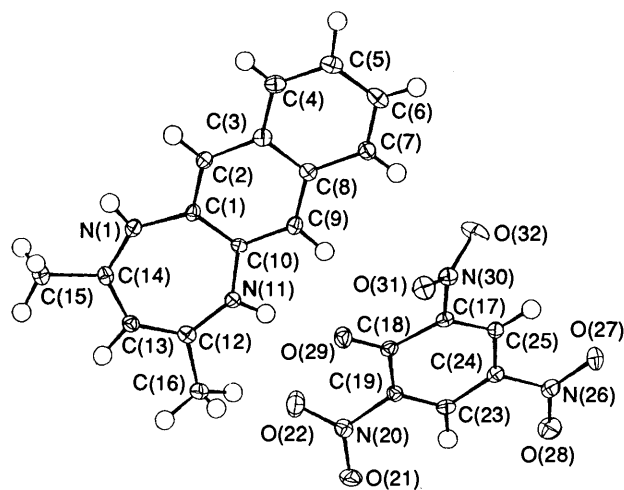
The observed wavenumber (cm⁻¹) of bands in the FT-Raman

Fig. 1 The title molecule with atom numbering

and IR spectra of two naphthodiazepinium salts are collected in Table 2.

Lists of fractional atomic coordinates, bond distances, angles, structure factors, anisotropic thermal parameters, H atom parameters, selected torsion angles, and distances of atoms from least-squares planes have been deposited at the Cambridge Crystallographic Data Centre. For details of the CCDC deposition scheme, see 'Instructions for Authors (1994)', *J. Chem. Soc., Perkin Trans. 2*, 1994, issue 1.

Results and Discussion

Molecular Structure and Crystal Packing.—(a) 2,4-*Dimethyl-*1H-*naphtho*[2,3-b][1,4]*diazepinium ion.* Experimental bond lengths and bond angles are similar to those observed for related compounds. The two molecules are roughly planar, except for the NO_2 and CH_3 groups. However, in the present compound we found substantial deviation of the seven-membered diazepinium ring from planarity with torsion angles varying from −6.28° to 7.38° (mean = 4.5°). In the previously studied naphthodiazepine hydrochloride,[1] the analogous torsion angles were respectively, between −2.6° and 1.7° (mean = 1.3°). A search of the Cambridge Structural Data Base revealed two similar structures involving the benzodiazepinium ring system: in refcode #MDZAP (2,4-dimethyl-1,5-benzodiazepinium
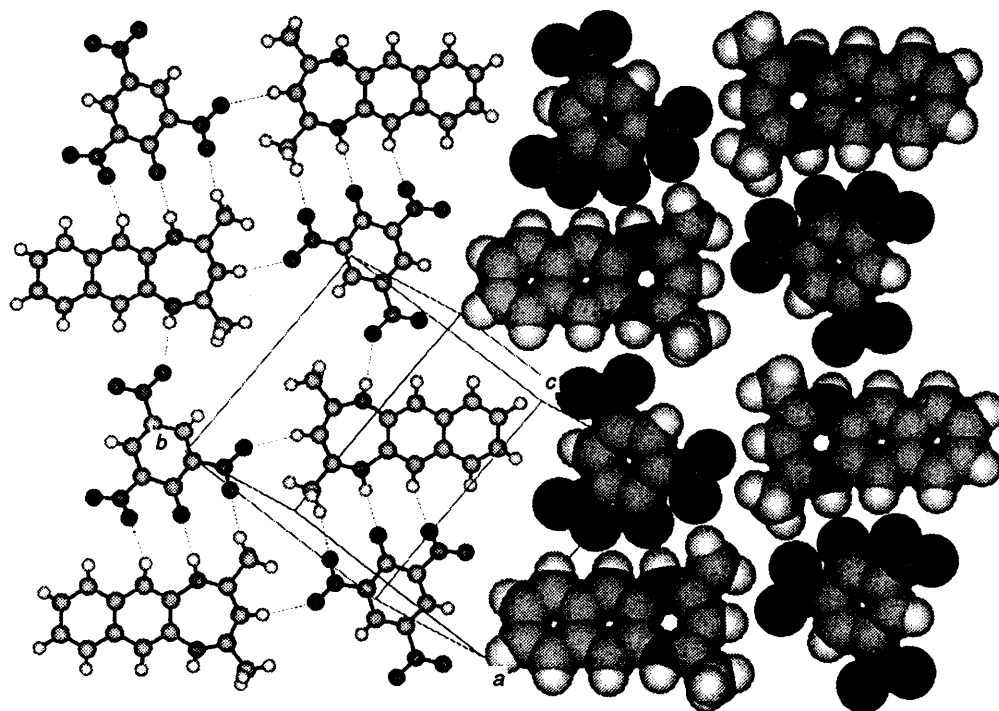

Fig. 2 View of the lattice molecules in the unit cell; dotted lines represent hydrogen bonds

Table 1 Crystal data for 2,4-dimethyl-1H-naphtho[2,3-b][1,4]diazepine hydropicrate

Parameter		Parameter	
Molecular formula	$C_{21}H_{15}N_2^+C_6H_2N_3O_7^-$	$D_{cal}/Mg\ m^{-3}$	1.51
Space group	$P\bar{1}$	Crystal size/mm	0.26 × 0.22 × 0.05
$F(000)$	468	Morphology	Orange platelets
Z	2	Radiation, Å	Mo-Kα, λ = 0.710 69
μ/mm^{-1}	1.08	T/K	294
$a/Å$	7.936(1)	Reflections used	1466 $(F_o)^2$ > 3σ $(F_o)^2$
$b/Å$	11.378(2)	R factor	0.034
$c/Å$	12.071(2)	R_w factor (weighted, w = 1)	0.040
α/deg	100.49(1)	No. of parameters refined	299
β/deg	98.28(1)	$V/Å^3$	996(5)
γ/deg	107.99(1)	M	523

Table 2 Observed FT-Raman and IR bands (cm⁻¹)[a]

FT-Raman	IR	Assignment[b]
—	710m	CH out-of-plane
750vw	740m	CH out-of-plane (picrate)
766vw	765m	C–N–C str. (diaz. ring)
—	785m	C–N–C str. (diaz. ring)
819s	820m	NO_2 def. (scissoring)
890vw	890m	N–C–C str. (diaz. ring)
900vw	900m	C–N–C str.
913vw	910m	CH in-plane (picrate)
1021w	1030w	CH in-plane
1078w	1075m	C–H in-plane (picrate)
1152w	1150m	C–N str.
1166w	1165m	C–O str.
1262m (sh)	1262m	C–H in-plane def. (diaz. ring)
1272 (sh)	1272m (sh)	C=C str.
1284vvs	1285s	NO_2 str. sym.
1345s	1345m	Ring breathing (diaz.)
1364ms	1360s	NO_2 str. sym.
1397m	1400w	C–CH_3 (conj.) def.
1482s	1480m	C=C and C=N str.
1515mw	1515ms	N–H def.
1564m	1550ms	NO_2 str. asym.
1600m (sh)	1610s	C=C str.
1628w	1630vs	C=N str.
1928w		CH_3 str.
3060w		CH ar. str.
	2000 to 3400 (br)	NH^+ str. and hydrogen bonding
	3280m	NH str. hydrogen bonding
	3320m	NH^+ str. (free)

[a] Relative intensities are denoted by v = very, s = strong, w = weak, m = medium, sh = shoulder, br = broad. [b] str. = strench, diaz. = naphthodiazepinium, sym. = symmetric, asym. = asymmetric.

chloride dihydrate)[14] these torsion angles are between −1.72° and +1.95° (mean = 1.5°), whereas in refcode #JILTED (2,4-dimethylbenzo[1,5]diazepinium hexafluorophosphate)[15] they are between −26.91° and +26.91° (mean = 16.4°).

For structures calculated using the AM1 method, the torsion angles vary between −34.0° and +34.0° (mean = 19.3°) and using the PM3 method they vary between −37.2° and +36.8° (mean = 20.5°). Semi-empirical structures are gas-phase structures in which packing forces are not taken into account by the calculations. These packing forces tend to flatten the cation in the crystal, unless large counter ions such as PF_6 or other molecules such as picrate with nitro groups twisted out of the benzene ring are present in the lattice. This might provide an explanation of the observation that the naphthodiazepinum picrate is less intensely coloured (orange) than the naphthodiazepinium chloride (black).

(b) *Picrate ion.* The geometry of the picrate ion is normal. The ring angle at C(18) is typically low at 110.9(4)°, the bonds C(18)–(19) and C(17)–C(18) are long, 1.443(7) Å and 1.445(7) Å, respectively, while the bond C(18)–O(29) is short, 1.246(6) Å, (quasi-double C=O bond). The average N–O bond length, 1.225 Å, and the average ONO angle, about 123°, are comparable to those usually observed (1.22 Å and 120.1°, respectively) for nitro groups of picrate ions.[16,17]

The nitro groups are twisted out of the plane of the six-membered ring by varying amounts: for the *ortho* nitro groups, the torsion angles are C(18)–C(19)–N(20)–O(22) = 36.2° and C(25)–C(17)–N(30)–O(32) = 44.3°, while the *para* nitro group, C(25)–C(24)–N(26)–O(27) = 2.9°, is almost coplanar with the benzene ring.

(c) *Hydrogen-bond network.* The more important interactions between the naphthodiazepinium and picrate ions are the following: two classical intermolecular hydrogen bonds: N(11)–H(11)···O(29): 2.938(4) Å, 174.0(5)° and N(1)–H(1)···O(28ⁱ): 2.990(4) Å, 143(4)° (symmetry code *i*: x, 1 + y, 1 + z); two C–H···O interactions, C(9)–H(9)···O(31):

3.299(4) Å, 152.0(4)° and C(16)–H(163)···O(22): 3.268(4) Å, 169.0(5)°. These hydrogen bonds and C–H···O interactions link the naphthodiazepinium and picrate ions into polar ribbons along the [110] direction (the angle between the mean planes of each ion is 18.3°).

These ribbons are linked about a centre of inversion by similar C–H···O hydrogen bonds, C(13)–H(13)···O(21ⁱⁱ), 3.366(4) Å, 166.0(5)° (symmetry code *ii*: −x, 1 − y, z) to form sheets (Fig. 2) approximately parallel to the (100) plane. In each sheet one naphthodiazepinuim ion is surrounded by four picrate ions and *vice versa*.

Between the parallel sheets there are phenyl–phenyl interactions, for example, between picrate–picrate ions: C(18)···C(23ⁱⁱⁱ) = 3.380(4) Å, C(17)···C(23ⁱⁱⁱ) = 3.471(4) Å and between naphthodiazepinium–naphthodiazepinium ions: C(8)···C(10ⁱᵛ) = 3.461(4) Å (symmetry codes *iii*: −x, −y, −z, *iv*: 1 − x, 1 − y, 1 − z).

Vibrational Mode Analysis.—The vibration mode analysis given in Table 2 was made qualitatively using the data found for related compounds.[18-23] We were particularly interested in two frequency regions: 1600–800 cm⁻¹ (corresponding to NO_2 vibration bands) and 3500–2000 cm⁻¹ (NH vibration bands).

Unfortunately, the region near to 1600 cm⁻¹ is also characterised by the frequencies of the naphthalene and the diazepine rings, as shown in the spectra of some other benzodiazepines.[19,20] Therefore, an intense FT-Raman band near 1340 cm⁻¹ and a group of strong bands near 1500 cm⁻¹ as well as IR bands near 1600 cm⁻¹ and 1480 cm⁻¹ were attributed to the frequencies of the naphthalene and the diazepine rings. The strong FT-Raman bands at 1550, 1360, 1285 and 820 cm⁻¹ and IR bands at 1564, 1364, 1284 and 819 cm⁻¹ must be attributed, respectively, to the asymmetric, symmetric stretching and the scissoring deformation of the NO_2 groups.[18,21-23]

Note that the bands at 1284 and 1360 cm⁻¹, attributed to NO_2 symmetric stretching show a bathochromic shift relative to usual NO_2 frequencies.[19,22,23] In our opinion, the shift of the frequency at 1284 cm⁻¹ and the weaker shift at 1360 cm⁻¹ may be caused, respectively, by the N–H···O_2N hydrogen bond interaction and the weaker C–H···O_2N hydrogen bond interaction.

The IR spectra show two frequencies at 3280 and 3320 cm⁻¹ which can be assigned to the NH stretching associated with the NH^+ stretching band.[22,23] These bands undergo a bathochromic shift relative to usual secondary amine NH band.[22,23] This shift is similar to that displayed by some nitroamines[18,22,23] and nitrobenzodiazepines[19,20] and may be due to strong hydrogen bonding (N–H···O) with the NO_2 group.[18,22]

Thus, the vibrational analysis results are in good agreement with the crystal structure of the title compound where the N···O contact and the NH···O contact are, respectively, shorter than 3.1 Å and 2.5 Å and in good agreement with the literature relating to hydrogen bonding of nitroamines.[18]

AM1 and PM3 Calculations.—For the simulation of C–H···O hydrogen bonds, the super molecule comprising the whole content of the unit cell (two naphthodiazepine + two picrate molecules related by an inversion centre of symmetry −x, −y, −z) was calculated. As packing forces are not present in the calculation, the final distances between the centres of the picrate rings (AM1, 6.18 Å; PM3, 5.67 Å) are much longer than in the crystal (3.51 Å). However, we did not hope to reproduce the weak van der Waals interaction between benzene rings but only the stronger hydrogen bonds between picrate ion and diazepinium ion. The final dipole moment of the super molecule (AM1, 0.03 D; PM3, 0.01 D) and the overall symmetry of the geometry are good indications of the quality of minimisation, as no symmetry constraints were imposed. Several thousand

Table 3 Comparison of observed and AM1 and PM3 calculated hydrogen bonds geometries for the $-x$, $-y$, $-z$ dimer of naphthodiazepinium picrate

Distance or angle	X-Ray	AM1	PM3
N(11)···O(29)	2.938(4) Å	2.89 Å	2.76 Å
C(9)···O(31)	3.299(4) Å	3.37 Å	2.91 Å
C(16)···O(22)	3.268(4) Å	3.18 Å	3.49 Å
N(11)–H(11)···O(29)	174.0(5)°	136°	160°
C(9)–H(9)···O(31)	151.7(4)°	150°	159°
C(16)–H(163)···O(22)	168.9(5)°	140°	146°
H(11)···O(29)	2.04(4) Å	2.06 Å	1.78 Å
H(9)···O(31)	2.41(5) Å	2.37 Å	1.84 Å
H(163)···O(22)	2.25(5) Å	2.24 Å	2.52 Å
H(11)···O(22)	3.64(5) Å	2.19 Å	3.80 Å
H(9)···O(29)	2.64(5) Å	2.15 Å	3.27 Å
H(7)···O(31)	2.79(5) Å	2.38 Å	3.53 Å

iterations were required and, as usual, there is no guarantee that the global energy minimum was located.

AM1 and PM3 calculations are known to reproduce with variable success the hydrogen-bond features.[24,25] The results obtained for the title compound are listed in Table 3 and compared with the observed geometries. AM1 gives good geometries for the hydrogen bonds but establishes more hydrogen bonds than are really observed: six hydrogen bonds instead of three hydrogen bonds in the crystal. PM3 gives hydrogen bonds that are too short and does not reproduce the observed C–H ··· O interaction between one nitro group and a hydrogen on the methyl group. This is usual behaviour for these two Hamiltonians.

Phase Transition Studies.—DSC measurements show that title compound undergoes a reversible phase transformation at 414 K with $\Delta H = 4.5$ kJ mol⁻¹, $\Delta S = 10.9$ J K⁻¹ mol⁻¹. During this transition the colour of the crystal changes from orange to pale yellow. After cooling, the single crystals remain intact and revert to the original orange colour. The colour change may be related to the deformation of the diazepinium ring as has already been proposed[14] for similar compounds. As the crystal is not destroyed during this process and the ΔH is very low we favour a martensitic transition between the weakly bound layers.

Conclusions

The solid-state structure of the title compounds shows that the C–H ··· O hydrogen-bond network contributes notably to the arrangement of the molecules in parallel layers. Despite the low energy associated with these C–H ··· O hydrogen bonds, their presence in higher proportion relative to classical N–H ··· O hydrogen bonds (4:1) makes them a major contributor to the

stabilisation of the crystal. These layers are weakly bonded by van der Waals interactions and undergo a reversible martensitic-type transition upon heating. The vibrational analysis confirms the existence of the C–H ··· O and N–H ··· O hydrogen bonds in the crystal structure. AM1 and PM3 calculations of dimers reproduce with acceptable approximation the main features of the structure.

References

1 N. Rodier, V. Agafonov, P. Dubois, M. Mariaud, P. Levillain and J. M. Cense, *Acta Crystallogr., Sect. C*, 1993, **49**, 156.
2 R. Taylor and O. Kennard, *J. Am. Chem. Soc.*, 1982, **104**, 5063.
3 L. Berkovitch-Yellin and L. Leiserovitz, *Acta Crystallogr., Sect. B*, 1984, **40**, 159.
4 K. Biragha, C. V. K. Sharma, K. Panneerselvam, L. Shimoni, H. L. Carell, D. E. Zacharias and G. R. Desiraju, *J. Chem. Soc., Chem. Commun.*, 1993, 1473.
5 C. B. Aakeröy and K. R. Seddon, *Chem. Soc. Rev.*, 1993, 397.
6 J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.
7 J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 221.
8 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, **46**, 1990, 467.
9 *International Tables for X-Ray Crystallography*, Tome IV, Kynoch Press, Birmingham, 1974 pp. 99 and 149.
10 G. M. Sheldrick, SHELXL-93. *A Program for Crystal Structure Determination*, University of Göttingen, FRG, 1993.
11 Biosym Technologies, 10065 Barnes Canyon Road, San Diego, CA 92121, USA.
12 C. K. Johnson, ORTEP II, Report 5138, Oak Ridge National Laboratory, Tennessee, USA 1976.
13 J. M. Cense, *Tetrahedron Comput. Methodol.*, 1989, **2**, 65.
14 J. C. Speakman and F. B. Wilson, *Acta Crystallogr., Sect. B*, 1976, **32**, 622.
15 A. J. Blake, M. Schroder and R. J. Sorbie, *Z. Kristallogr.*, 1991, **194**, 148.
16 M. D. Walkinshow, *Acta Crystallogr., Sect. C*, 1986, **42**, 246.
17 M. Botoshansky, F. H. Herbstein and M. Kapon, *Acta Crystallogr., Sect. B*, 1994, **50**, 191.
18 T. W. Panunto, Z. Urbanczyk-Lipkowska, R. Johnson and M. C. Etter, *J. Am. Chem. Soc.*, 1987, **109**, 7786.
19 G. A. Neville, H. D. Beckstead and H. F. Shurvell, *Vibrational Spectroscopy*, 1991, **1**, 287.
20 G. A. Neville and H. F. Shurvell, *J. Raman Spectrosc.*, 1990, **21**, 9.
21 B. Brzezinski, T. Glowiak, E. Grech, Z. Malarski, W. Sawka-Dobrowolska and L. Sobczyk, *J. Mol. Struct.*, 1993, **299**, 1.
22 D. Lin-Vien, N. B. Colthup, W. G. Fateley and J. G. Grosselli, *Handbook of Infrared and Raman Characteristic Fequencies of Organic Molecules*, Academic Press, New York, 1991.
23 L. J. Bellamy, *The Infrared Specta of Complex Molecules*, Chapman and Hall, New York, 1975.
24 J. J. Dannenberg and E. M. Evleth, *Int. J. Quantum Chem.*, 1993, **44**, 869.
25 H. Bock, R. Dienelt, H. Schödel and Z. Havlas, *J. Chem. Soc., Chem. Commun.*, 1993, 1792.