Acta Cryst. (1998). B**54**, 859–865

Solid-State Modeling. VI. 2,3-Diketopiperazine: the Integration of Crystallographic and Spectroscopic Evidence

A. T. H Lenstra,[a]* B. Bracke,[a] B. van Dijk,[a]† S. Maes,[a] C. Van Alsenoy,[a] Herman O. Desseyn[b] and Spiros P. Perlepes[b]

[a]*Department Structuurchemie, Antwerp University (UIA), Universiteitsplein 1, B-2610 Wilrijk, Belgium, and* [b]*Laboratorium Anorganische Scheikunde, Antwerp University (RUCA), Groenenborgerlaan 171, B-2020 Antwerpen, Belgium. E-mail: latifa@uia.ua.ac.be*

(*Received 26 June 1996; accepted 25 March 1998*)

Abstract

2,3-Diketopiperazine (2,3-piperazinedione) crystallizes in the monoclinic space group $P2_1/c$ with a = 5.941 (3), b = 10.080 (3), c = 8.282 (2) Å and β = 95.87 (3)°. The six-membered ring adopts a skew-boat conformation with Q = 0.467 (3) Å, θ = 64.6 (3)° and φ = 269.8 (4)°. *Ab initio* calculations show that the perfect skew-boat with its C_2 symmetry is broken by the formation of two intermolecular N—H···O bonds, involving only one of the C═O groups of the 2,3-diketopiperazine molecule. Vibrational spectra were recorded in solution and in the solid state. The assignment of the normal vibrations is proposed based on comparison with spectra of similar molecules and spectral changes due to deuteration. *Ab initio* calculations for the isolated molecule and the solid-state structure were used to calculate differences in the molecular geometry in the gas phase and crystalline state. Using these reference structures we calculated the stretching frequencies for the C═O groups. We predict an IR shift for C═O of 130 cm^{-1}, when the molecule goes from the gas phase to the solid state. The observed shift is 110 cm^{-1}. The differences between the C═O moieties in the solid state produce a calculated $\Delta\nu$ of 55 cm^{-1}, which matches satisfactorily the observed value of 49 cm^{-1}.

1. Introduction

In previous papers (Desseyn *et al.*, 1972, 1977, 1979; Desseyn & Van der Veken, 1975; Van der Veken *et al.*, 1977) we published the spectra of oxamides with *trans* secondary amide groups. 2,3-Diketopiperazine is a cyclic oxamide in which the oxamide unit is forced to adopt a *cis* conformation owing to the constraints of the ring system. This makes 2,3-diketopiperazine a useful model compound in the study of a *cis* secondary amide group.

The preparation of this compound has been reported by Vogl & Knight (1968).

Some spectral data have been reported by Granger *et al.* (1968) and Isaksson & Liljefors (1980). This work aims at a further elucidation of the *cis* secondary amide groups as these fundamentals are not well classified as characteristic group vibrations. The X-ray structure analysis (Lenstra *et al.*, 1998) showed that the symmetry typical for the molecule in its free form is broken in the solid state. Hydrogen-bond formation involves only one of the C═O groups in the 2,3-diketopiperazine molecule.

In §2 the IR and Raman spectra in the solid state as well as in a D_2O solution are analyzed. Vibrational frequencies and the proposed assignments are given.

Ab initio calculations were used to find the minimum energy conformer of 2,3-diketopiperazine. Its C_2 symmetry is lost in the solid state. With electrostatic crystal-field perturbed *ab initio* calculations we optimized the molecular geometry in the solid state.

The agreement between the theoretical and observed molecular geometry in the solid state was satisfactory. This encouraged us to continue the modeling exercise by exploiting the energy profile. The potential gradient is obviously linked to spectral frequencies. Since we already assigned spectral frequencies by comparison with similar molecules, a full frequency analysis by *ab initio* methods was not required. We decided to confine our efforts to the computation of the characteristic stretching frequencies of the C═O group. In this limited framework one avoids the extra complications in solid-state spectra caused by the mixing of molecular vibrations and lattice modes.

From the equilibrium geometries in gas phase and solid state we calculated the stretching frequencies for the C═O groups. Theory predicts an IR shift of 130 cm^{-1} for ν(CO), when the molecule goes from the gas phase to the solid state. This matches gratifyingly well with an observed shift of 110 cm^{-1}.

The differences between the two C═O groups in the solid state, caused by the asymmetry in hydrogen bonding, produce a calculated $\Delta\nu$ of 55 cm^{-1}, which is close to the observed value of 49 cm^{-1}.

---

† ERASMUS exchange student from the Department of Crystal and Structural Chemistry, State University of Utrecht, Padualaan 8, The Netherlands.

2. Spectral analysis

The IR spectra were recorded on a Bruker 113v FT-IR instrument using KBr pellets in the 4000–400 cm^{-1} region and polyethylene pellets in the 400–10 cm^{-1} region. The Raman spectra were recorded on a SPEX 1403 using the 488 nm line of a Spectra Physics Ar-ion laser.

2.1. *Solid-state spectra*

The molecule as shown in Fig. 1 clearly exhibits two different *cis* secondary amide groups (O2—C6—N1—H) (*P*1) and (O1—C5—N4—H) (*P*2) caused by hydrogen bonds on the oxygen of the *P*2 peptide group. The X-ray geometry is summarized in Table 1.

The different bond distances indicate that for the *P*1 structure we can expect higher νCO, νNH and lower νCN, δNH, πNH, δCO and πCO modes.

The vibrational spectra in the solid state are interpreted in terms of these two different peptide groups; the further splitting of, for example, the carbonyl bands, where in the Raman spectra at least four bands can be identified, is due to the group splitting caused by interaction between the nonequivalent molecules in the unit cell ($Z = 4$). The complete vibrational spectrum can be interpreted in terms of the two different peptide groups, the ring system and the CH$_2$ group vibrations. The molecule belongs to the point group C_1 and the vibrational modes are classified as 36 *A* vibrations.

As the heavy atoms are almost co-planar and as we are mainly interested in the peptide functional group, it seems reasonable to neglect the CH$_2$ modes and consider these groups as point masses in a ten-atom molecule with C_s symmetry. The vibrational modes are $17A' + 7A''$, the A' modes being the in-plane and the A'' modes the out-of-plane motions.

The $17A'$ modes (10 stretching modes, two δNH, two δCO, three ring in-plane deformations) and the $7A''$ modes (two πCO, two πNH and three ring out-of-plane deformations) are assigned and given in Tables 2 and 3 for the normal and N-deuterated product.

The assignments are made by the isotopic study and in comparison with the literature data.

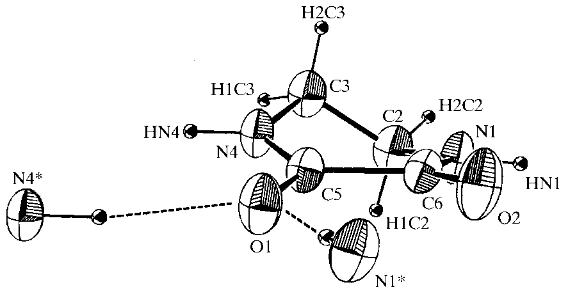

Fig. 1. *ORTEP* (Johnson, 1965) plot of 2,3-diketopiperazine including the hydrogen bonds with O1 as acceptor atom. Atomic numbering scheme of 2,3-diketopiperazine (50% probability level).

Table 1. *Bond distances (Å), valence angles (°) and torsion angles (°) in 2,3-diketopiperazine*

	X-ray r_α	Isolated *ab initio* r_g	Solid-state *ab initio* r_α
C5—O1	1.230 (4)	1.212	1.235
C6—O2	1.215 (4)	1.212	1.224
C6—N1	1.338 (4)	1.378	1.350
C5—N4	1.322 (4)	1.378	1.347
C5—C6	1.532 (4)	1.541	1.568
C2—C3	1.490 (4)	1.529	1.534
C2—N1	1.451 (4)	1.485	1.490
C3—N4	1.458 (4)	1.485	1.499
N1—HN1	0.87 (4)	1.027	1.037
N4—HN4	0.90 (4)	1.027	1.034
C2—H21	1.02 (3)	1.114	1.103
C2—H22	0.97 (3)	1.110	1.107
C3—H31	0.98 (3)	1.114	1.106
C3—H31	0.98 (3)	1.110	1.105
O1—C5—C6	119.2 (2)	120.2	118.9
O1—C5—N4	123.5 (2)	123.9	124.2
O2—C6—C5	119.1 (2)	120.2	118.1
O2—C6—N1	124.9 (3)	123.9	124.7
N1—C6—C5	116.0 (2)	115.9	117.2
N4—C5—C6	117.3 (3)	115.9	116.9
C2—N1—C6	122.8 (3)	124.2	124.9
C3—N4—C5	122.9 (3)	124.2	123.2
O1—C5—C6—O2	−15.4 (4)	−13.57	−7.78
C3—N4—C5—O1	175.6 (2)	173.97	167.29
C2—N1—C6—O2	177.1 (3)	173.97	175.91
O1—C5—C6—N1	165.4 (2)	166.41	172.41
O2—C6—C5—N4	163.5 (2)	166.41	170.94
N4—C5—C6—N1	−15.6 (3)	−13.60	−8.88
N1—C2—C3—N4	−52.0 (3)	−53.77	−48.38
C3—N4—C5—C6	−3.3 (4)	−6.02	−11.35
N4—C5—C6—N1	−15.6 (4)	−13.60	−8.8
C5—C6—N1—C2	−3.8 (4)	−6.02	−4.29
C6—N1—C2—C3	38.6 (4)	40.69	33.78
N1—C2—C3—N4	−52.6 (3)	−53.77	−48.38
C2—C3—N4—C5	37.9 (4)	40.69	40.50

D—H···*A*	*D*—H	H···*A*	*D*—*A*	*D*—H···*A*
N1—HN1···O1^{i}	0.87 (3)	2.08 (3)	2.951	177 (3)
N4—HN4···O1^{ii}	0.90 (3)	2.01 (3)	2.906	174 (3)

Applied corrections (Popelier *et al.*, 1989)

	δ (Å)	*K* (Å)
C—C	0.002	0.002
C═O	0.000	0.004
C—N	0.020	0.007
N—H	0.031	0.010

Symmetry codes: (i) $-x, -y, -z$; (ii) $1 - x, \frac{1}{2} + y, \frac{1}{2} - z$.

The νNH vibrations are situated in the complex broad band in the 3200 cm^{-1} region in the IR spectrum. A rather broad and weak band with a maximum at 3200 cm^{-1} and shoulders on both sides is observed in the Raman spectrum.

In this region we always expect the overtones and combination bands of the carbonyl modes. Fermi resonance strongly influences the position and intensity of these bands, but from the deuterated compound, where

Table 2. *The vibrational frequencies (cm^{-1}) and proposed assignments of normal 2,3-diketopiperazine*

IR solid	Raman solid	Raman D_2O solution		Assignments
3354w				CO overtones
3289ms				$\nu(N_1H)$
3194vs	3210 (3)br	3200 (1)br		
3150sh	3143 (1)			
3060vs				$\nu(N_4H)$
	3006 (5)	3004 (3)		
2988m	2999 (4)			
2948mw	2972 (1)	2952 (2)*P*		
2921m	2925 (2)		νCH_2	
2891m		2900 (2)*P*		
2966m	2883 (3)			
2847sh				
1698sh	1715 (2)			
1690vs	1694 (2)	1690 (7)br$P(A_1)$		$\nu(C_6O_2)$
1669vs	1661 (3)	1664sh(B_1)		$\nu(C_5O_1)$
1626sh	1645 (1)			
1490m	1487 (7)	1494 (9)$P(A_1)$		Ring str. $\nu(C_5N_4)$
1475ms				
1469ms	1469 (3)	1471 (5)(B_1)		Ring str. $\nu(C_6N_1)$
1431ms	1442 (2)	1440 (2)		$\delta(N_4H)$
1418sh	1435 (2)		δCH_2	
1378m	1387 (3)	1387 (3)		
1361ms	1355 (2)	1367 (4)*P*		
1354s	1351 (2)		ωCH_2	
1298m	1305 (1)	1305br (1)*P*		$\delta(N_1H)$
1288sh				
1260w	1259 (3)	1255 (5)$P(A_1)$		Ring str. $\nu(C_2N_1)$
1236w	1238 (2)	1240sh(B)	νCH_2	Ring str. $\nu(C_3N_4)$
1093w	1089 (1)	1091 (1)		
1039m	1045 (1)	1034 (1)		
1034m				
974mw	971 (1)	971 (2)$P(A_1)$	ρCH_2	Ring str. $\nu(C_2C_3)$
966mw				
918w	919 (2)	919 (3)$P(A_1)$		Ring str. $\nu(C_5C_6)$
835msbr				$\pi(N_4H)$
813m	816 (1)	818br(2)		$\delta(C_5O_1)$
761msbr	770 (1)			$\pi(N_1H)$
730s	734 (10)	733 (10)$P(A_1)$		Ring in-plane deformation
702w				$\delta(C_6O_2)$
681w				Ring in-plane deformation
583m	585 (1)	580 (1)		$\pi(C_5O_1)$
514mw	517 (5)	514 (2)		$\pi(C_6O_2)$
475w	480 (1)			Ring in-plane deformation
432mw	437 (1)			Ring deformation
385mw	378 (1)			Ring deformation
325mw	327 (2)			Ring deformation
194w	200 (3)			$\nu(NH\cdots O)$
		7 (3)		
141mw	133 (5)			Lattice vibration
113mw	114 (9)			Lattice vibration
105mw				Lattice vibration
85mw	95 (8)			Lattice vibration
73w	58 (5)			Lattice vibration

possible Fermi resonance in the 2400 cm^{-1} region is not obvious, we clearly observe two different νND vibrations of approximately equal intensity, assignable to the two different peptide groups.

The νCO modes are clearly the intense IR bands in the 1680 cm^{-1} region, showing the expected doublet due to the two different carbonyl groups and the further factor group splitting, especially in the Raman spectra. Cheam & Krimm (1984) also suggested that the splitting of the carbonyl bands in similar molecules can be caused by Fermi resonance. The slightly decreased frequencies observed for the deuterated compounds are typical for these carbonyl modes and can be explained by a weak coupling with the δNH modes and the mass effect. These bands have the same characteristics as the amide (I) band in *trans* secondary amides.

The 1500–1350 cm^{-1} region has been the subject of much controversy. In this region we expect the two νCN

Table 3. *The vibrational frequencies* (cm^{-1}) *and proposed assignments of deuterated 2,3-diketopiperazine*

IR solid	Raman solid	Raman D_2O solution		Assignments
3345vw				CO overtones
	3005 (5)	3003 (3)		
2990m	2997 (4)			
2945w	2970 (1)	2948 (2)*P*	νCH_2	
2928w	2924 (2)			
2891m	2892 (4)	2903 (2)*P*		
2395s	2367 (3)	(2380)		$\nu(N_1D)$
2340s	2329 (2)			$\nu(N_4D)$
1699sh	1703 (2)			
1677vs	1681 (3)	1679 (7)br$P(A_1)$		$\nu(C_6O_2)$
1659vs	1637 (4)	1650sh(B)		$\nu(C_5O_1)$
1627s	1624 (2)			
1488m	1484 (10)	1488 (8)$P(A)$		Ring str. $\nu(C_5N_4)$
1473m	1477 (3)			
1448ms	1458 (10)	1465 (9)		Ring str. $\nu(C_6N_4)$
1404m	1405 (2)	1411 (1)	δCH_2	
1358s	1359 (2)	1372 (4)*P*		
1326ms	1330 (1)		ωCH_2	
1265w	1270 (5)	1270 (6)$P(A_1)$		Ring str. $\nu(C_2N_1)$
1231w	1234 (2)	1240sh(B_1)	τCH_2	Ring str. $\nu(C_3N_4)$
1142ms	1149 (1)			$\delta(N_4D)$
1093w	1089 (1)			
965mw	967 (1)	970 (2)$P(A_1)$	ρCH_2	Ring str. $\nu(C_2C_3)$
930m	935 (1)	910 (1)$P(A_1)$		$\delta(N_1D)$ ring str. $\nu(C_5C_6)$
815m	815 (1)	839 (1)br		$\delta(C_5O_1)$
710mbr	715 (9)	715 (10)$P(A_1)$		$\pi(N_4D)$ ring in-plane deformation + $\delta(C_6O_2)$
634m	613 (1)			$\pi(N_1D)$ ring in-plane deformation
569ms	561 (1)	560 (1)		$\pi(C_5O_1)$
505mw	506 (4)	510 (1)		$\pi(C_6O_2)$
470mw	470 (1)			Ring deformation
407mw	420 (1)			Ring deformation
383mw	376 (1)			Ring deformation
323mw	324 (2)			Ring deformation
192w	196 (3)	183 (3)		$\nu(ND\cdots O)$
140mw	132 (6)			Lattice vibration
111mw	113 (9)			Lattice vibration
104mw				Lattice vibration
86m	94 (9)			Lattice vibration
71w	58 (5)			Lattice vibration

peptide modes, the two δNH and the CH_2 deformations. The 1490 cm^{-1} band shifts only slightly to lower frequency on deuteration, cannot exhibit δNH character and its frequency is too high for a possible δCH_2 mode. De Prospo & McDermott (1987) studied the amide bond stretching in cyclic amides and concluded that the bands arising in the 1450–1500 cm^{-1} region exhibit a high νCN character. Therefore, the highest frequency at 1490 cm^{-1} is attributed to the ring stretching mode with high $\nu(C_5N_4)$ character; the $\nu(C_6N_1)$ mode is observed at slightly lower frequency (1470 cm^{-1}). These bands are practically uninfluenced by deuteration, indicating that the coupling between δNH and νCN, which causes the amide (II) and amide (III) bands in *trans* secondary amides, is absent in the *cis* configuration. The relatively broad bands appearing in the 1430 and 1300 cm^{-1} region in the IR spectra are practically undetectable in the Raman spectra and shift to 1140 and 930 cm^{-1} in the deuterated compounds. These bands can be easily assigned to the two different δNH and δND modes. The δNH/δND ratio again confirms the fact that the coupling between the δNH and νCN modes, which is enormous in the *trans* configuration, is practically nonexistent in the *cis* compounds. The high intensity of the 1500 cm^{-1} band and the very weak intensity of the δNH mode also prove that we can consider rather pure νCN and δNH modes in these peptides groups. The further splitting in this region must be ascribed to the factor group splitting and the CH_2 deformations.

The πNH and πND modes for *cis* secondary amides are expected at slightly higher frequency, compared with the amide (V) bands of *trans* secondary amides. The broad and intense IR bands appearing at 835 and 761 cm^{-1}, shifted to 710 and 634 cm^{-1} in the deuterated compound, must have πNH and πND character. These bands are very weak in Raman spectra, as expected.

The δCO modes appear as relatively intense bands at 813 and 730 cm^{-1}. The πCO modes are, in comparison with the data obtained for 2,5-diketopiperazine (Van der Veken *et al.*, 1977), assigned to the 580 and 515 cm^{-1}

bands. These bands only shift slightly to lower frequency on deuteration and compare very well with the amide (IV) (δCO) and amide (VI) (πCO) bands of the *trans* secondary amides. The deformations of the carbonyl group involved in the hydrogen bonding (C5O1) consequently appear at higher frequency compared with the C6O2 deformations.

The ring stretching modes with mainly νC2N1 and νC3N4 character appear as weak IR and more intense Raman bands at 1260 and 1236 cm^{-1}, respectively; these bands are practically uninfluenced by deuteration. The ring vibrations with high νC2C3 and νC5C6 character are located as relatively weak IR and slightly more intense Raman bands at 974 and 918 cm^{-1}, respectively.

The ring in-plane deformations are situated in the 750–450 cm^{-1} region and the remaining $3A''$ modes, compared with 2,5-diketopiperazine (Cheam & Krimm, 1984), can be assigned to the weak IR and Raman bands in the 410–300 cm^{-1} region.

One band in the low-frequency region shifts slightly to lower frequency on deuteration; this 200 cm^{-1} band can be tentatively assigned to the ν(NH$\cdots$O) mode, generally appearing in this region for molecules exhibiting intermolecular NH$\cdots$O hydrogen bonds.

The other vibrations appearing in the low-frequency region can be regarded as lattice vibrations. These five IR and four Raman bands are practically uninfluenced by deuteration.

The ν_{as}, ν_s and δCH$_2$ modes can be regarded as pure vibrations and result in absorption frequencies at 3000, 2950 and 1450 cm^{-1}, which can be correlated.

The twisting, wagging and rocking modes depend strongly on the rest of the molecule and, as a result, these frequencies are spread out over a region. They are assigned by comparison with the data obtained for 2,5-diketopiperazine (Rey-Lafon & Forel, 1970; Rey-Lafon *et al.*, 1973).

The δCH$_2$ expected in the 1450 cm^{-1} region overlaps with δN$_4$H and is observed at ~1410 cm^{-1} in the deuterated compound. The wagging CH$_2$ is observed as a more intense band in the 1350 cm^{-1} region, where the ring stretching νCN modes are situated. The CH$_2$ rocking mode is situated in the νCC region and probably has some coupling effect with the ν(C$_3$C$_2$) vibration.

2.2. *Solution spectra*

In the Raman solution spectra we can no longer distinguish between the two peptide groups and the molecule can then be considered, regarding the CH$_2$ groups as point masses, with C_{2v} symmetry resulting in $9A_1 + 4A_2 + 8B_1 + 3B_2$ vibrations.

The $9A_1$ and $8B_1$ modes are in-plane vibrations and only the totally symmetric A_1 modes can be polarized from the out-of-plane A_2 and B_2 modes: the $4A_2$ vibrations are only Raman active.

Most A_1 vibrations could be identified and are also given in Tables 2 and 3.

The νNH and νND modes appear as very weak bands, overlapped by the rather intense and broad water bands. The ν_{as}CH$_2$ band appears nonpolarized at 3004 cm^{-1}. It is noteworthy that this band appears at an unusually high frequency. Two polarized bands of equal intensity are observed at 2952 and 2900 cm^{-1}; these bands must have ν_sCH$_2$ character.

The relatively high νCO at 1690 (A_1) and the shoulder at 1665 cm^{-1} (B_1) shift slightly to lower frequency on deuteration.

From the solution spectra it is clear that the νCN, the peptide band, must be situated at ~1500 cm^{-1}. The polarized 1494 cm^{-1} band has A_1 symmetry; the other νCN can be assigned to the 1471 cm^{-1} band. These bands also shift slightly to lower frequency on deuteration. The rather polarized band of medium intensity at 1367 cm^{-1} also appears in the deuterated species at 1372 cm^{-1}, so this band cannot exhibit δNH character and must originate from a CH$_2$ deformation. The weak and broad band at 1305 cm^{-1}, which disappears on deuteration, has δNH character. The δND mode is too weak to be observed. The polarized 1255 cm^{-1} (A_1) band and the shoulder at 1242 cm^{-1} (B_1) are ring-stretching vibrations with high νCN character. The intense 733 cm^{-1} band is strongly polarized and must be a symmetric in-plane ring deformation.

The other bands in the spectrum are all too weak to be analyzed or discussed.

3. *Ab initio* modeling in the gas phase and solid state

3.1. *Geometry*

2,3-Diketopiperazine contains two CH$_2$—NH—C=O subunits, which are identical in the free molecule. This identity is lost in the solid state owing to hydrogen-bond formation. This is quite an interesting feature, which made us decide to examine the molecule using the alternative procedure of '*ab initio*' modeling.

To enumerate an equilibrium geometry for the isolated molecule we used the program *BRABO* (Van Alsenoy, 1988) and a 4-21G basis set. The choice of the basis set is dictated by the existence of empirical corrections δ, which enables us to extrapolate the *ab initio* r_e geometry into a more practical r_g geometry *via* $r_g = r_e(\text{4-21G}) + \delta$. δ eliminates the artefacts of the 4-21G basis set on the r_e distance and at the same time δ overrules the rigidity constraint typical in *ab initio* modeling. To compare the bond distance r_g with the r_α bond length, which is the characteristic result of an X-ray analysis, a second correction K is required. This large amplitude correction is necessary to translate the average distance between two atoms into a distance between the two mean atomic positions. The *ab initio* r_e value is related to the crystallographic r_α distance by

$$r_\alpha \simeq r_e(\text{4-21G}) + \delta - K.$$

Two starting models for 2,3-diketopiperazine were used: (*a*) a planar geometry for the non-H atoms and (*b*) a twisted form with a twofold axis through the midpoints of C5—C6 and C1—C2. The twist form appeared to be the lowest-energy conformer. The energy of the optimized planar entity is 28.89 kJ mol^{-1} higher. The extrapolated r_g geometry of the skew-boat conformer is shown in Table 1.

To calculate the solid-state geometry we included an electrostatic perturbation in the *ab initio* computations. This crystal-field potential represents the solid-state neighbors. For a detailed description of the iterative analysis we refer to Popelier *et al.* (1989). The r_e geometry of the isolated skew-boat entity served as a starting point in the solid-state optimization. The extrapolated r_α geometry inferred from the r_e (4-21G; solid state) structure is summarized in Table 1.

When we compare the structure of the free molecule with its solid-state adjusted geometry it is clear that intermolecular interactions do influence the molecular structure. Looking at the differences between 'equivalent' bond lengths, the solid-state model shows an asymmetry which parallels the observed structure. The calculated difference between C5═O1 and C6═O2 is 0.011 Å, which corresponds to an observed difference of 0.015 (6) Å. A similar correspondence is found in C3—N4 *versus* C2—N1 and C6—N1 *versus* C5—N4. It is also remarkable that C2—C3, a real Csp^3—Csp^3 distance, is smaller than C5—C6, which could be regarded as a Csp^2—Csp^2 distance. Here too, observation and model calculations arrive at a similar variation in distances.

The *ab initio* geometries in the gas phase and solid state show that the peptide bonds C6—N1 and C5—N4 decrease by 0.03 Å in the solid state owing to the formation of hydrogen bonds. The nonpeptide bonds C2—N1 and C3—N4 show the opposite effect, *viz.* an increase of ~0.01 Å related to the gas–solid phase transition. A similar increase is observed at C6═O2, which demonstrates that the C═O bond length in the absence of hydrogen bonds is not necessarily phase invariant.

With regard to the torsion angles, the observed structure is closer to the 'gas-phase' model than to the 'solid-state' model. This can be easily understood. The torsional force constants in 2,3-diketopiperazine have a value of ~83.74 J mol^{-1} deg^2. The molecule has a B value of 4 Å^2. A molecular movement (translation or rotation) in the lattice has the force constant f. Since $U \simeq RT/2f$, a molecular libration force constant can be estimated from B; this gives $f \simeq$ 104.67 J mol^{-1} (deformation)^2. This suffices to show that it is extremely difficult to strike the correct balance between intra- and intermolecular deformations. Our crystal-field model does not include 'steric hindrance', because it does not look at a repulsive/attractive overlap between the electron clouds of adjacent molecules. These effects are included when the wave function includes not only the central molecule, but also its nearest neighbors. The supermolecule approach to 2,3-diketopiperazine in the solid state has been investigated (Peeters *et al.*, 1993). Whereas our electrostatic model gives an r.m.s. torsion (obs.–calc.) of 6.0°, the supermolecule results in a molecular geometry with an r.m.s. torsion of 1.5°.

3.2. *Spectroscopy*

So far we have looked at geometrical indications to judge the results of our crystal-field *ab initio* calculations. Another quality check is possible *via* the spectroscopic evidence. Here we look at the energy profile close to the equilibrium position. The increase in molecular energy owing to an elongation or shortening of 0.01 Å on *e.g.* the C═O bond length is calculated. In the harmonic approximation the calculated energy difference between the deformed entity and its equilibrium form can be written as $\Delta E = k(\text{deformation})^2$, in which k, the force constant of that deformation, is linked to the deformation frequency ω *via* $\omega = 1/2\pi(k^{1/2})/\mu$, with μ as the reduced mass.

The 4-21G calculated force constant locates the C═O stretching mode at 1841 cm^{-1} for the free molecule. A gas-phase spectrum shows a symmetric and antisymmetric C═O stretch at the average wave number 1770 cm^{-1}. This shows that our '*ab initio*' force constant is reasonably accurate. For a 4-21G basis set and a stretching frequency, a scale factor of ~0.96 usually connects the theoretical value with the experimental one (Geise & Pyckhout, 1988).

For the molecule in the crystalline phase we calculated the force constants for C5═O1 and C6═O2. The enumerated wave numbers are 1685 and 1740 cm^{-1}, respectively, which fit the observed frequencies of 1638 and 1687 cm^{-1} *via* the scale factor of 0.96 obtained above. Therefore, we calculate an overall IR shift of 130 cm^{-1} for C═O in 2,3-diketopiperazine, when the molecule goes from the gas phase to the solid state. This value matches gratifyingly well with the observed shift of 110 cm^{-1}.

The frequency difference between C5═O1 and C6═O2 is 54 cm^{-1} in our solid-state model description. This difference, induced by hydrogen bonding, is in keeping with the observed difference of 49 cm^{-1}. Therefore, the local potential field in our solid-state description, which combines the intramolecular forces *via* the wave function and the intermolecular forces by an electrostatic crystal field, is apparently an adequate representation of the true crystalline potential. The minimum energy position gives a good estimate for the solid-state geometry; the potential gradient is clearly good enough to arrive at proper values for spectroscopic frequencies or frequency differences.

References

Cheam, T. C. & Krimm, S. (1984). *Spectrochim. Acta Part A*, **40**, 481–503.

De Prospo, A. M. & McDermott, D.P. (1987). *Spectrochim. Acta Part A*, **43**, 587.

Desseyn, H. O., Jacob, W. A. & Herman, M. A. (1972). *Spectrochim. Acta Part A*, **28**, 1329–1334.

Desseyn, H. O. & Van der Veken, B. J. (1975). *Spectrochim. Acta Part A*, **31**, 641–646.

Desseyn, H. O., Van der Veken, B. J. & Herman, M. A. (1977). *Spectrochim. Acta Part A*, **33**, 633–641.

Desseyn, H. O., Van Riel, W. & Van der Veken, B. J. (1979). *Can. J. Spectrosc.* **24**, 98–104.

Geise, H. J. & Pyckhout, W. (1988). *Stereochemical Applications of Gas-Phase Electron Diffraction*, edited by I. Hargittai & M. Hargittai. New York: VCH Publishers.

Granger, R., Onzelesi, H. & Roble, Y. (1968). *Trav. Soc. Pharm. Montpellier*, **28**, 65–71.

Isaksson, R. & Liljefors, T. (1980). *J. Chem. Soc. Perkin Trans.* 2, pp. 1815–1820.

Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

Lenstra, A. T. H., Bracke, B., van Dijk, B., Maes, S., Vanhulle, C. & Desseyn, H. O. (1998). *Acta Cryst.* B**54**, 851–858.

Peeters, A., Van Alsenoy, C., Lenstra, A. T. H. & Geise, H. J. (1993). *Int. J. Quantum Chem.* **46**, 73–80.

Popelier, P., Lenstra, A. T. H., Van Alsenoy, C. & Geise, H. J. (1989). *J. Am. Chem. Soc.* **111**, 5658–5660.

Rey-Lafon, M. & Forel, M. T. (1970). *J. Chim. Phys.* **67**, 757–772.

Rey-Lafon, M., Forel, M. T. & Garrigou-Lagrange, C. (1973). *Spectrochim. Acta Part A*, **29**, 471–490.

Van Alsenoy, C. (1988). *J. Comput. Chem.* **9**, 620–626.

Van der Veken, B. J., Desseyn, H. O. & Herman, M. A. (1977). *Z. Naturforsch. Teil A*, **32**, 775–779.

Vogl, O. & Knight, A. C. (1968). *Macromolecules*, **1**, 311–315.