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X-RAY AND VIBRATIONAL STUDIES OF THE COMPLEX BETWEEN *N-TERT*-BUTOXYCARBONYL-L-PHENYLALANINE AND PYRIDINE. ISOTOPE EFFECT

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The x-ray structure of the complex between *N-tert*-butoxycarbonyl-L-phenylalanine and pyridine shows that the crystals are held together by short hydrogen bonds between the OH group and the N atom of the pyridine ring [$R_{O(H)\cdots N}$ = 2·574(3) Å]. Deuteration of the OH and NH groups results in a small expansion of the unit cell associated with an elongation of the O···N distance [$R_{O(D)\cdots N}$ = 2·610(3) Å]. The infrared spectra show very broad stretching protonic bands in the range 2750–600 cm^{-1}. The isotopic ratio $\nu(OH\cdots H)/\nu(OD\cdots N)$ of nearly unity suggests a double minimum potential with a low barrier for the hydrogen bridge. The Raman and near-infrared spectra are discussed. The perturbation of the fundamental modes and of the overtones of pyridine suggests that the complex is not of the proton transfer type. The broad absorptions of the hydrogen bridge disappear in the near-infrared region. The perturbation of the pyridine overtones is discussed. © 1997 John Wiley & Sons, Ltd.

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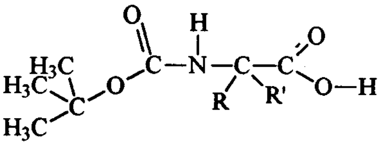
INTRODUCTION

N-Urethanylamino acids have been shown to be involved in enzymatic and synthetic reactions in which the molecular stereochemistry and the self-association may be important.[1, 2] One of the most widely used *N*-terminal protecting groups is the *tert*-butoxycarbonyl (Boc) group. Boc-amino acids of the general formula are often used as substrates, substrate analogues or competitive inhibitors or proteolytic enzymes. The study of their conformational preferences is important for an understanding of their interactions with enzymes. Structural parameters derived from x-ray crystallographic data show that the urethane amide bond can adopt both the *cis* and *trans* conformation. The *cis* urethane conformation is preferred in crystals of compounds with a tertiary nitrogen or in structures stabilized by strong intermolecular interactions.[3–5] As *N*-urethanylamino acids have two proton donors (the OH and NH groups) and two proton acceptors (the two carbonyl groups), it is interesting to investigate the relative strength of these sites from a fundamental point of view. Recently, *ab initio* calculations have been performed on the relative acidity and basicity of these different sites, taking the complex between *N*-methoxycarbonylglycine and water[6] as a model.



In this work, the interaction between *N-tert*-butoxycarbonyl-L-phenylalanine (R = H, R′ = $CH_2C_6H_5$) (BPA) and pyridine, which is often used as reference base in hydrogen bond studies, was investigated by x-ray diffraction and vibrational spectroscopy. Some differential scanning calorimetric (DSC) measurements were also made. The influence of ND–OD deuteration on the structural and spectroscopic properties is discussed.

EXPERIMENTAL

Materials. The complex between BPA and pyridine (BPA.Py) (**1**) was prepared by mixing equimolecular amount of BPA and pyridine in carbon tetrachloride. Suitable crystals for x-ray diffraction were obtained by slow evaporation of the solutions obtained by dissolving the precipitate in a 2 : 1 mixture of pyridine and carbon

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tetrachloride. The NH–OD deuterated complex (BPA_D.Py) (**2**) was obtained by dissolving BPA.Py in methanol-OD in a nitrogen atmosphere. The precipitate obtained was very sticky and suitable crystals for the x-ray diffraction were collected during the crystallization process. BPA from Sigma was used without further purification. Pyridine from Fluka was carefully dried.

Crystal data. $C_{19}H_{24}N_2O_4$ (**1**), $C_{19}H_{22}D_2N_2O_4$ (**2**). Orthorhombic, space group $P2_12_12_1$, $Z=4$ (by least-squares refinement on diffractometer angles of 30 centered reflections, $\lambda=0{\cdot}71073$ Å). Data for **1**: $a=9{\cdot}5470(10)$ Å, $b=10{\cdot}2980(10)$ Å, $c=19{\cdot}135(3)$ Å, $V=1881{\cdot}3(4)$ Å^3, $D=1{\cdot}216$ g cm^{-3}. Transparent crystals, $0{\cdot}60\times0{\cdot}30\times0{\cdot}20$ mm, $\mu(\text{Mo K}\alpha)=0{\cdot}086$ mm^{-1}. Data for **2**: $a=9{\cdot}641(3)$ Å, $b=10{\cdot}385(3)$ Å, $c=19{\cdot}340(8)$ Å, $V=1939{\cdot}4(11)$ Å^3, $D=1{\cdot}181$ g cm^{-3}. Transparent crystals, $0{\cdot}40\times0{\cdot}35\times0{\cdot}35$ mm, $\mu(\text{Mo K}\alpha)=0{\cdot}083$ mm^{-1}, temperature $=289(2)$ K.

Data collection and processing. The following were used: Siemens P4-PC diffractometer, graphite monochromatized Cu Kα radiation, θ–2θ mode, 2623 reflections collected for **1** and 2604 reflections for **2** (θ range for data collection between 2·11 and 25°, index range $-1\leqslant h\leqslant 11$, $-1\leqslant k\leqslant 12$, $-1\leqslant l\leqslant 22$, 2356 unique reflections ($R_{\text{merge}}=0{\cdot}034$) for **1** and 2422 unique reflections ($R_{\text{merge}}=0{\cdot}030$) for **2**.

Structure analysis and refinement. The structure was solved by direct methods and refined by full-matrix least-squares on F^2, with all non-hydrogen atoms anisotropic and hydrogens with isotropic temperature factors.[7,8] For **1**, final R indices were $R_1=0{\cdot}0345$, $wR_2=0{\cdot}077$ for $I>2\sigma(I)$ data and $R_1=0{\cdot}0486$, $wR_2=0{\cdot}0866$ for all data. For **2**, final R indices were $R_1=0{\cdot}0396$, $wR_2=0{\cdot}0891$ for $I>2\sigma(I)$ and $R_1=0{\cdot}0610$ and $wR_2=0{\cdot}0945$ for all data.

Atomic coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC).

Spectrometers. FT-IR spectra were recorded on a Bruker Model 66 spectrometer at a resolution of 2 cm^{-1}. For the mid-infrared range a KBr beamsplitter and DTGS detector and for the near-infrared range a CaF_2 detector and InSb cooled detector were used. Raman spectra were measured on the same spectrometer equipped with an FRA-106 Raman module and a near-infrared YAG laser (200 mW) (CaF_2 beamsplitter and cooled Ge detector). Infrared spectra were measured using KBr pellets (concentration ratio for the mid-infrared range 3:300 and for the near-infrared range 30:300). All spectra were recorded at room temperature.

The centre of gravity of the broad protonic bands observed between 2700 and 600 cm^{-1} was calculated with the equation

$$\nu=\frac{\Sigma A_i\nu_i}{\Sigma A_i}$$

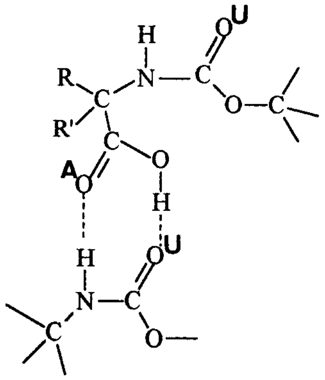
A being the intensities of the bands and ν their frequencies.

DSC measurements. DSC experiments were performed on a DuPont de Nemours instrument.

RESULTS AND DISCUSSION

X-ray structure of BPA.Py and BPA_D.Py

In crystals of uncomplexed BPA,[9,10] the molecules are held together in rows of asymmetric cyclic dimer motifs through intermolecular NH$\cdots{}^{A}$O=C and OH$\cdots{}^{U}$O=C hydrogen bonds, A and U denoting the acid and urethane carbonyl groups, respectively. The secondary amide group is in the unusual *cis* conformation and the carboxylic group is in the usual *syn* conformation:



There are two independent molecules in the asymmetric unit, the OH$\cdots$O distances being 2·59 and 2·62 Å and the NH$\cdots$O distances longer, 2·88 and 2·99 Å.

The atom numbering and ORTEP drawing for the BPA.Py complex are shown in Figure 1 and the packing of the molecules down the *b* axis is illustrated in Figure 2. Intramolecular bond lengths and bond angles for BPA.Py and BPA_D.Py_D are given in Table 1 and intermolecular distances in the hydrogen bonds in Table 2. In the pyridine complexes, the urethane group has the *trans* conformation theoretically predicted for the *tert*-methoxycarbonylglycine–water complex.[6] The hydrogen bond pattern is completely different from that of BPA. The molecules are held together by short hydrogen bonds [2·574(3) Å] between the acidic OH group and the basic pyridine N and weaker hydrogen bonds [3·015(3) Å] are formed between the N–H and the O(5) atom of the carboxyl group of the neighbouring molecule. The urethane carbonyl which normally has a more basic character than the carboxyl carbonyl is involved in a weak CH$\cdots$O interaction with one of the methyl groups of the *tert*-butylcarbonyl group, the

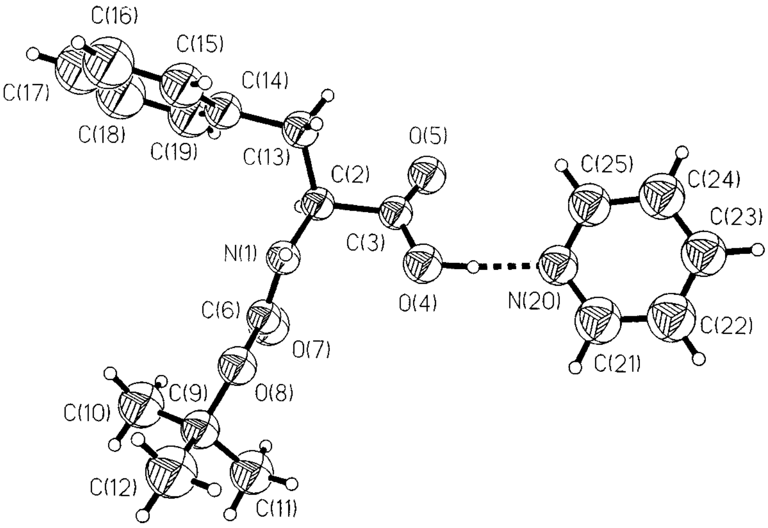


Figure 1. ORTEP drawing and atom numbering in the BPA.Py complex

C(10)H· · ·O(7) distance being 3·355(3) Å, the H· · ·O(7) distance 2·492(3) Å and the C(10)H· · ·O(7) angle 149·2(2)° (Figure 2).

The hydrogen bond pattern is thus very different in BPA and its pyridine complex, resulting in different distances for the functional groups. The $C{=}O^U$ distance is shorter in BPA.Py [1.206(3) Å] than in BPA (1·229 Å), where this group forms a strong hydrogen bond with the OH function and there is a marked decrease in the C(3)—O(4) distance (− 0·035 Å), and of the C(6)–N(1) distance (− 0·023 Å). As in BPA, the urethane N atom is in a nearly sp^2 hybridization state, the sum of the angles around N being 358·2°. The angle formed between the C(3)O(4)O(5) and the pyridine plane is 32·8°.

The crystals of BPA_D.Py are isomorphous with the complex BPA.Py. Deuteration results in a small expansion of the unit cell, associated with small elongations of the bonds [between 0·003 and 0·023 Å, only C(24)–C(25) is slightly shortened by 0·002 Å]. The angles are very similar in both complexes and the angle between the C(3)O(4)O(5) and the pyridine planes is now 33·6°. The O(D)· · ·N distance of 2·610(3) Å is 0·036 Å longer than in the non-deuterated complex.

These crystallographic studies show that the hydrogen atom is bound to the O atom and hence that there is no proton transfer in these complexes. Few data have been reported for strong OH· · ·N hydrogen bonds in crystals. In the pentachlorophenol–3-cyanopyridine complex, the O(H)· · ·N distance is longer (2·703 Å).[11] In the complex between 3,5-dinitrobenzoic acid and 3,5-dimethylpyridine,

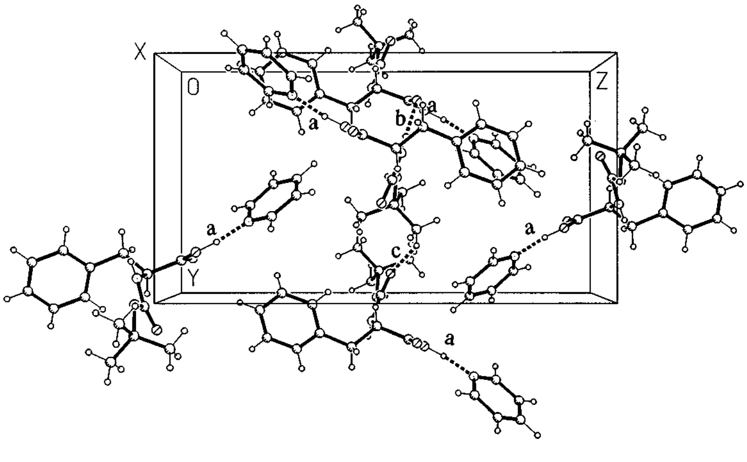


Figure 2. Packing of the BPA.Py complex in the unit cell showing the intermolecular hydrogen bonds. For letter codes, see Table 2

Table 1. Selected bond lengths (Å) and angles (°) for **1** and **2**

	1	**2**
N(1)—C(6)	1·336(3)	1·343(3)
N(1)—C(2)	1·436(3)	1·450(3)
N(1)—H(1)	0·83(2)	0·84(3)
C(2)—C(3)	1·521(3)	1·535(4)
C(2)—C(13)	1·525(3)	1·531(4)
C(2(—H(2)	0·91(2)	0·95(3)
C(3)—O(5)	1·215(3)	1·224(3)
C(3)—O(4)	1·290(3)	1·313(3)
O(4)—H(4)	0·97(3)	1·04(3)
C(6)—O(7)	1·206(3)	1·217(3)
C(6)—O(8)	1·336(3)	1·346(3)
O(8)—C(9)	1·476(3)	1·492(3)
C(9)—C(10)	1·506(4)	1·510(5)
C(9)—C(11)	1·500(3)	1·520(4)
C(9)—C(12)	1·484(4)	1·510(4)
C(13)—C(14)	1·501(3)	1·517(4)
C(14)—C(15)	1·369(3)	1·377(4)
C(14)—C(19)	1·376(4)	1·379(5)
C(15)—C(16)	1·384(4)	1·396(5)
C(16)—C(17)	1·340)5)	1·355(6)
C(17)—C(18)	1·358(5)	1·376(6)
C(18)—C(19)	1·396(5)	1·403(5)
N(20)—C(25)	1·303(3)	1·321(4)
N(20)—C(21)	1·307(4)	1·328(4)
C(21)—C(22)	1·361(4)	1·365(5)
C(22)—C(23)	1·349(4)	1·365(5)
C(23)—C(24)	1·354(4)	1·368(5)
C(24)—C(25)	1·372(4)	1·370(5)
C(6)—N(1)—C(2)	120·8(2)	121·0(3)
C(6)—N(1)—H(1)	121·5(16)	121·5(19)
C(2)—N(1)—H(1)	115·9(16)	115·2(19)
N(1)—C(2)—C(3)	114·38(19)	114·4(2)
N(1)—C(2)—C(13)	110·82(19)	110·8(2)
C(3)—C(2)—C(13)	110·19(18)	110·2(2)
N(1)—C(2)—H(2)	107·02(13)	107·06(16)
C(3)—C(2)—H(2)	107·02(12)	107·06(16)
C(13)—C(2)—H(2)	107·02(13)	107·06(15)
O(5)—C(3)—O(4)	124·8(2)	124·5(3)
O(5(—C(3)—C(2)	120·6(2)	121·0(3)
O(4)—C(3)—C(2)	114·55(19)	114·5(2)
C(3)—O(4)—H(4)	114·6(15)	109·2(16)
O(7)—C(6)—N(1)	124·1(2)	123·8(2)
O(7)—C(6)—O(8)	125·2(2)	125·3(3)
N(1)—C(6)—O(8)	110·7(2)	110·7(3)
C(6)—O(8)—C(9)	120·43(19)	120·2(2)
O(8)—C(9)—C(10)	109·27(19)	109·5(2)
O(8)—C(9)—C(11)	109·9(2)	110·0(2)
O(8)–C(9)—C(12)	103·2(2)	102·7(3)
C(12)—C(9)—C(11)	110·9(2)	110·8(3)
C(12)—C(9)—C(10)	111·4(3)	111·5(3)
C(11)—C(9)—C(10)	111·8(2)	112·0(3)
C(14)—C(13)—C(2)	114·3(2)	114·5(2)
C(15)—C(14)—C(19)	117·7(3)	117·6(3)
C(15)—C(14)—C(13)	120·3(2)	120·5(3)
C(19)—C(14)—C(13)	122·0(2)	121·9(3)
C(14)—C(15)—C(16)	121·6(3)	121·7(4)
C(17)—C(16)—C(15)	120·0(4)	119·7(5)
C(16)—C(17)—C(18)	120·2(4)	120·3(5)
C(17)—C(18)—C(19)	120·2(4)	119·5(5)
C(14)—C(19)—C(18)	120·2(3)	121·1(4)
C(25)—N(20)—C(21)	117·4(3)	117·0(3)
N(20)—C(21)—C(22)	123·5(3)	123·7(4)
C(23)—C(22)—C(21)	118·9(3)	118·6(4)
C(22)—C(23)—C(24)	118·5(3)	118·5(4)
C(23)—C(24)—C(25)	118·8(3)	119·1(4)
N(20)—C(25)—C(24)	123·0(3)	123·1(4)

the O(H)···N distance is 2·550 Å and the O(D)···N distance 2·563 Å[12] and in the pentachlorophenol–4-methylpyridine complex the O(H)···N distance is 2·552 Å.[13] Interestingly, the crystals of pentachorophenol(OD)–4-methylpyridine that were studied are not isomorphous with the non-deuterated complex, and the O(D)···N distance is markedly longer (2·638 Å).[14] There may therefore be two polymorphs. These data indicate that the shortest observed O(H)···N distance lie between 2·53 and 2·56 Å. This distance seems to be associated with a double minimum potential with a low barrier.[15, 16] In the present complexes, the C(3)=O(5) and C(6)–O(7) distances of 1·215(3) and 1·290(3) Å respectively, and the O(5)C(3)O(4) angle of 124·8(2)° are not far from the Speakman's values[17] for the A type acid salts of carboxylic acids. Short intermolecular distances corresponding to a flat double minimum potential have also been observed for NH$^+$···O$^-$–proton transfer complexes, e.g. in the complex between 2,6-dichloro-4-nitrophenol and 3,4-dimethylpyridine where the O$^-$···(H$^+$)N distance of 2·532 Å[18] is in the same range.

Vibrational spectra of BPA.Py and BPA$_D$.Py

The infrared spectra (3700–500 cm^{-1}) and the Raman spectra (3400–100 cm^{-1}) of BPA.Py and BAP$_D$.Py are shown in Figures 3 and 4. The absorption at 3200 cm^{-1} is due to the presence of water in KBr, which does not affect the isotopic exchange, the intensity of the ν(NH) absorption in BPA$_D$.Py being very weak. The spectrometric data and a tentative assignment of the vibrations are given in Table 3. In BPA.Py, two absorptions are observed at 2450 and 1910 cm^{-1} and in BPA$_D$ at 2470 and 1900 cm^{-1}. In the fingerprint region, both complexes show a broad absorption culminating at about 1200 and 1150 cm^{-1}, respectively. The centres of gravity of the three bands (usually called the B, C and D bands) are 1565 and 1545 cm^{-1}, giving an isotopic ratio of 1·015. Very few results on the isotopic ratio for very short O···N hydrogen bonds in crystals have been reported. For the interaction between 3,5-dinitrobenzoic acid and 3,5-dimethylpyridine, the isotopic ratio is close to unity.[12] Values of the isotopic ratios between 1·04 and 1·1 have also been observed for the complexes between trifluoroacetic acid and pyridine or methylated pyridines in benzene solution.[19] An anomalous isotopic ratio smaller than unity has been observed in the complex between pentachlor-

Table 2. Hydrogen bonding geometry for **1** and **2** (bond lengths in Å, angles in degrees)

D—X· · ·A[a]	Structure	D—X	X· · ·A	D· · ·A	D—X· · ·A	Letter in Figure 2
O(4)—H(4)· · ·N20^{i}	**1**	0·97(3)	1·61(3)	2·574(3)	173(2)	a
O(4)—D(4)· · ·N20^{i}	**2**	1·04(3)	1·58(3)	2·610(3)	171(3)	—
N(1)—H(1)· · ·O5^{ii}	**1**	0·83(2)	2·20(3)	3·015(3)	168(2)	b
N(1)—D(1)· · ·O5^{ii}	**2**	0·84(3)	2·22(3)	3·049(3)	168(3)	—
C(10)—H(10A)· · ·O(7)^{iii}	**1**	0·96(2)	2·49(1)	3·355(3)	149(1)	c
C(10)—H(10A)· · ·O(7)^{ii}	**2**	0·97(2)	2·52(2)	3·384(4)	148(1)	—

[a] Symmetry codes: (i) $-0{\cdot}5+x, 1{\cdot}5-y, -z$; (ii) $0{\cdot}5+x, 1{\cdot}5-y, -z$; (iii) $0{\cdot}5+x, 0{\cdot}5-y, -z$.

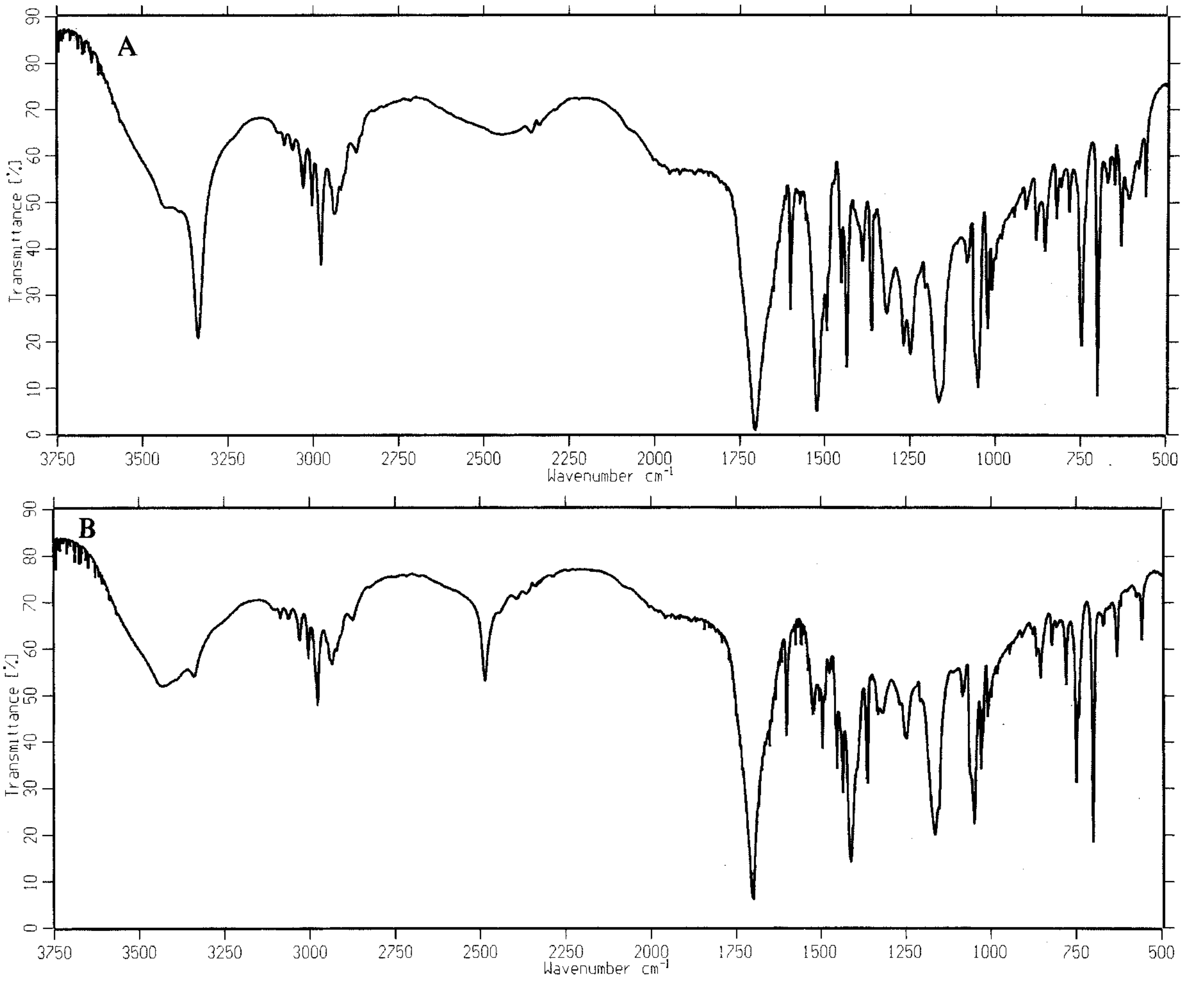


Figure 3. Infrared spectra (3700–500 cm^{-1}) of (A) BPA.Py and (B) BPA$_D$.Py

ophenol and 4-methylpyridine, but this is explained by drastic changes in the hydrogen bridge geometry.[14] Very short O(H)· · ·O hydrogen bonds (2·45–2·50 Å) are associated with an unsymmetrical double minimum potential energy curve with the barrier near the first excited level[20–24] and isotopic ratios close to unity are observed. The corresponding O(H)· · ·N distance is slightly longer (2·53–2·56 Å) with respect to the O(H)· · ·O distance. More experimental O(H)· · ·N/O(D)· · ·N distances should help to establish a correlation between distances and isotopic ratios.

The ν(NH) and ν(ND) vibrations are observed at 3337 and 2487 cm^{-1}. The narrowness of the bands and the values of the isotopic ratio of 1·342 are characteristic features of weak hydrogen bonds.

In the Raman spectra, the B, C and D bands completely disappear.

The assignment of the vibrations in the fingerprint region is based on the comparison between the infrared and Raman spectra of BPA and *N-tert*-butoxycarbonyl-L-alanine (BA).

The vibrational bands of the aromatic ring are very weak in the infrared spectrum with the exception of the absorption at 701 cm^{-1} [ν(4) vibration]. The bands observed at 1605, 1586, 1033, 1005, 751 and 622 cm^{-1} in the Raman spectrum of BPA but not in the spectrum of BA are assigned to vibrations of the aromatic ring. The bands observed in BPA.Py and not in BPA are assigned to pyridine vibrations. The aromatic ring and pyridine modes 8a and 12 have nearly the same frequency in the Raman spectrum. Complex formation brings about frequency shifts of the normal modes of pyridine. The 8a, 8b, 19a and 1 modes are shifted upwards by 6, 3, 15 and 21 cm^{-1}, respectively, and the 12 and 6b modes are shifted downwards by 6 and 17 cm^{-1}. These shifts are smaller than those observed for the

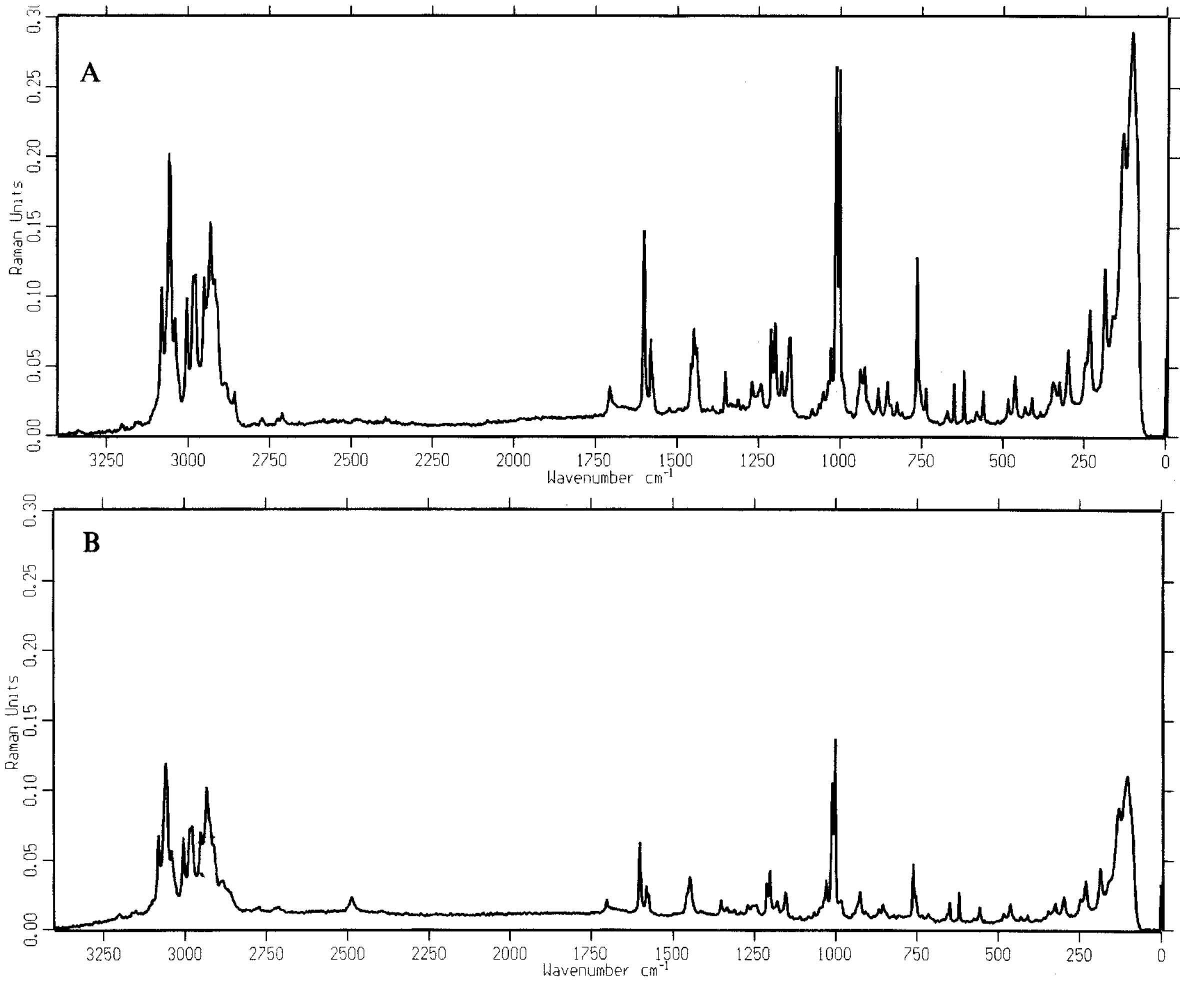


Figure 4. Raman spectra (3400–100 cm^{-1}) of (A) BPA.Py and (B) BPA$_D$.Py

Table 3. IR (1800–500 cm^{-1}) and Raman (1800–100 cm^{-1}) data for BPA.Py and BPA$_D$.Py in the solid state and tentative assignment of the vibrations[a]

BPA.Py		BPA$_D$.Py		
IR	Raman	IR	Raman	Assignment
1707s,br	1708vw	1700s,br	1704vw	$\nu_{C=O^A} + \nu_{C=O^U}$
1603m	1603m	1603m	1603m	Py(8a) + Raman AR(8a)
	1583m		1583m	AR(8a)
1576w		1576w		Py(8b)
1525s	1526vw	1414s	1416vw	Amide II
1497m		1497m		Py(19a)
1454m	1458sh	1454m	1458sh	$\delta(CH_3)$
	1450m		1449	$\delta(CH_3)$
1437m	1442sh	1437m		Py(19b)
1392m		1325w	1334vw	$\delta(OH,OD) + \delta(CH_3)$
1367m		1367m		$w(CH_2)$ or $\delta(CH)$
	1353w		1353w	$\delta(CH)$
1321m		1319m		$w(CH_2)$ or $t(CH_2)$
1271m	1271w	1156[b]	1156w	Amide III
1250m	1244w	1250m	1244w	$\nu_{C—O^A}$
	1213m		1213m	Py(9a)
	1201m		1203m	AR(9a)
1180sh	1180w	1180sh	1180vw	$r(CH_3)$
1168s,br		1164		$\nu_{C—O^U}$
	1155m		1155m	AR
1086w		1086w		Py(18a)
1052s,br		1051s		$r(CH_3)$
1024s	1030m	1030s	1030m	Py(12) + AR(12)
1012m	1014s	1012m	1012s	Py(1)
	1003vs		1003vs	AR(1)
984w	984w	984w	984w	ν(C—C)
	940w			
	927m		927m	
884m		884w		
857m	857m	857w	857w	
824m	824vw	824m	824vw	
786m		781		$\delta(O—C=O^U)$
	766m		763m	AR(4)
748s		751s		Py(4)
702vs		702vs		Py and AR(11)
673w	672w	673w		
652w	652w	652w	652w	Py(6a)
633m		633m		$\gamma(C—C—O^A)$
	622m		622m	AR(6a)
611m,br				Amide V
582vw	582vw	573vw	577vw	out-of-plane skeletal deformation and torsional modes
562m	563w	559m	559w	
	486w		486w	
	465m		465m	
	348		347	
	328		326	
	301w		300w	
	234m		232m	Intermolecular modes
	188m		187m	
	133m		131m	

[a] ν = Stretching, δ = in-plane deformation, γ = out-of-plane deformation, w = wagging, t = twisting, r = rocking, Py = pyridine vibration, AR = aromatic vibration, vs = very strong, s = strong, m = medium, w = weak, br = broad, sh = shoulder.

[b] Overlap with the vibration at 1167 cm^{-1}.

pyridinium ion[25] in pyridinium chloride or in the ionic complexes between oxalic acid and pyridine.[26] This feature, and also the fact that the typical carboxylate bands are absent, confirm the non-ionic structure of the OH· · ·N hydrogen bridge. It is worth mentioning that in the pentachlorophenol–4-methylpyridine complex, very deep Evans holes at 1011 and 816 cm^{-1} have been observed. These holes have been assigned to strong resonance coupling between the pyridine ring vibrations and the stretching and out-of-plane deformation vibrations.[14] They were not observed in the present complexes, but a very sharp minimum coinciding with the Raman frequency of the $\nu(12)$ vibration is observed at 1030 cm^{-1}. In the pentachlorophenol–4-methylpyridine complex, the O· · ·N distance is slightly shorter and the departure from the linearity somewhat smaller, the OH· · ·N angle being 176°. This shows that a small shortening of the hydrogen bridge in this critical range may have a great influence on the shape of the infrared spectra.

As shown by recent *ab initio* calculations on *N*-methoxycarbonylglycine,[6] the vibrational modes of amino acids are strongly coupled, and the assignment given in Table 3 is only tentative. The $\nu(C{=}O^A)$ and $\nu(C{=}O^U)$ vibrations at 1712 and 1648 cm^{-1} in BPA appear as a single broad absorption in the complex. This may be due to the fact that the two carbonyl distances are very different in BPA but become similar in the complex (see above). The amide II and III vibrations are easily identified at 1525 and 1271 cm^{-1} in BPA.Py and at 1414 and 1156 cm^{-1} in BPA$_D$.Py. Their intensities are very weak in the Raman spectra. The in-plane deformation mode γ(OH· · ·N) could not be identified and probably overlaps with the pyridine 1 and 12 modes, as in the pentachlophenol–4-methylpyridine complex.[14]

The near-infrared spectra (6250–3750 cm^{-1}) of BPA.Py and BPA$_D$.Py are shown in Figure 5. These spectra show that the absorptions in the deuterated complex are stronger than in the non-detuerated complex; we have no explanation for this.

The broad bands observed in the mid-infrared disappear in the near-infrared region. This is in agreement with the theory of Bernard-Houplain and Sandorfy,[27] predicting the

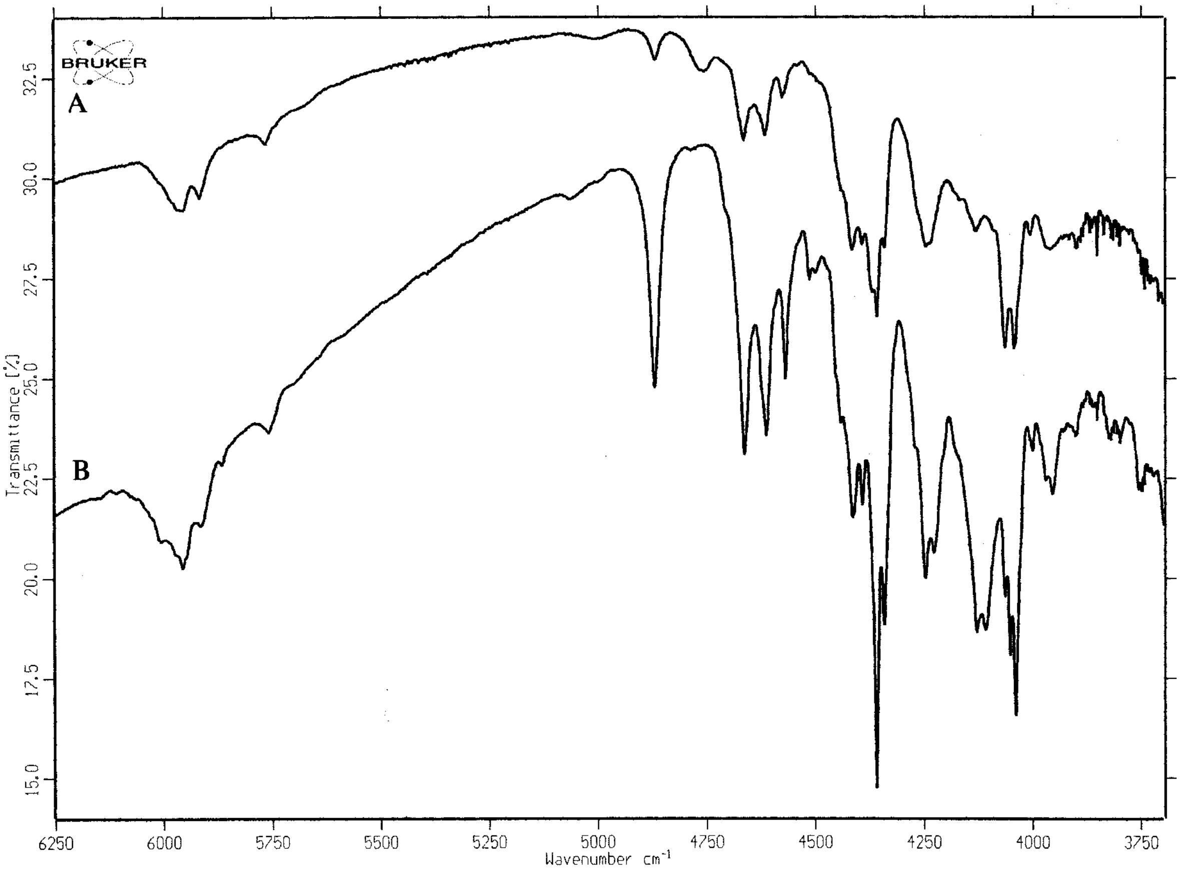


Figure 5. Near-infrared spectra (6250–3750 cm^{-1}) of (A) BPA.Py and (B) BPA$_D$.Py

same band shape in the near-infrared and Raman spectra of hydrogen-bonded systems. No data on the overtone spectra of *N-tert*-Boc-amino acids are available in the literature, and for the pyridine derivatives only the overtones of the ν(CH) vibrations observed between 5830 and 6000 cm^{-1} have been investigated.[28] These overtones are observed at 5957 and 5767 cm^{-1} in the BPA complexes. More interesting are the spectroscopic data observed between 5000 and 4000 cm^{-1}, summarized in Table 4. This table also gives the frequencies of free pyridine and of the pyridinium ion as determined recently.[29] The trio of bands between 4670 and 4570 cm^{-1} are characteristic of pyridine and are combinations of the ν(CH) and pyridine ring vibrations. In the BPA.Py complex these three overtones are shifted upwards. As for the fundamentals, the shifts are smaller than those observed in the pyridinium ion. The same holds for the overtone observed at 4131 cm^{-1}, which is probably due to a combination $2\times\nu(8b)+\nu(1)$. As for the fundamentals, the frequencies of these combinations are very insensitive to deuteration. This is not the case for the 4758 cm^{-1} absorption, which is shifted to 4516 cm^{-1} on deuteration. This absorption is assigned to the combination $\nu(C{=}O^{U})+2\times$amide II, observed in aliphatic amides.[30, 31] Finally, the strong absorption at 4360 cm^{-1}, observed in other *N-tert*-Boc-amino acids,[32] is assigned to a $\nu(CH_3)+\delta(CH_3)$ combination of the *tert*-Boc group. Combinations involving the ν(NH,ND) vibrations and the amide I or amide II vibrations usually observed in aliphatic amides between 4900 and 4700 cm^{-1}[30, 31] were not observed for the present molecule.

The intense infrared absorption at 3337 cm^{-1} is thus assigned to the fundamental ν(NH) vibration. One of the referees requested some comments on the inelastic neutron scattering study of crystalline amides such as *N*-methylacetamide and polyglycine that have shown that the 1575 cm^{-1} mode must be attributed to the ν(NH) vibration rather than the 3250 cm^{-1} mode, which was assigned to the 2ν(NH) overtone.[33, 34] This lower frequency was interpreted as a strong NH bond weakening by proton transfer to the neighbouring oxygen. At room temperature, the relevant picture becomes $N^{-}\cdots H^{+}\cdots O^{-}$, similar to strong $O^{-}\cdots H^{+}\cdots O^{-}$ hydrogen bonds. The proton transfer dynamics can be described by a symmetric double minimum potential function. At low temperature, there is a dynamic proton exchange between amidic C(=O)NH and imidic C(OH)=N forms. In our opinion, this interpretation is very questionable. As pointed out by Perrin,[35] the hydrogen equally likely on the N and O atoms seems doubtful owing to the very different energies (12 kcal mol^{-1}) of the two resonance forms. Also, the acidities of the two proton donor bonds are badly mismatched. The deprotonation energies (in the gas phase) of the NH and OH bonds in *N*-methylacetamide and in imidic acids are 362·6[36] and 351·2[37] kcal mol^{-1}, respectively, and this makes the proton transfer very unlikely. Spectroscopic arguments also make the assignment of Kearley *et al.*[34] very doubtful. The infrared spectrum reproduced in Ref. 33 does not show the characteristics of strong hydrogen bonds as in

Table 4. Near-infrared data (cm^{-1}) for the BPA.Py and BPA$_D$.Py complexes and assignment of the vibrations[a]

BPA.Py	BPA$_D$.Py	Pyridine[b]	Pyridinium ion[a]	Assignment	
4758vw				$\nu_{C=O^U}$ + 2amide II	1706 + 3052
	4516vw			$\nu_{C=O_U}$ + 2amide II	1700 + 2818
4667m		4656	4711	ν(CH) + Py(8a)	3085 + 1603
	4663m				3084 + 1603
4617m		4598	4663	ν(CH) + Py(8b)	3060 + 1576
	4615				3059 + 1576
4578w		4555	4618	ν(CH) + Py(19a)	3029 + 1497
	4571w				3028 + 1497
4417m				$\nu(CH_3)+\delta(CH_3)$	2877 + 1454
	4415m				2876 + 1454
4360s				$\nu(CH_3)+\delta(CH_3)$	2934 + 1454
	4360s				2932 + 1454
4248m				$\nu(CH_2)+w(CH_2)$	2934 + 1367
	4248m				2034 + 1367
4131w		4115	4129	2Py(8b) + Py(1)	3152 + 1012
	4131m				3152 + 1012
4065m[b,c]				?	
4044				ν(CH) + AR(1)	3048 + 1003
	4040				3044 + 1003

[a] ν = Stretching, δ = in-plane deformation, w = wagging, Py = pyridine vibration, AR = aromatic vibration, s = strong, m = medium, w = weak.

[b] From Ref. 28.

[c] The band disappeared upon deuteration and could not be assigned.

$O^- \cdots H^+ \cdots O^-$ systems where very broad bands are observed. The overlapping of the 2ν(OH) and the 2ν(NH) (?) bands at about 3200 cm^{-1} also seems very doubtful and the same remark also holds for the high intensity of the overtone compared with the fundamental (?) at 1550 cm^{-1}. One also obtains an unrealistic value of the anharmonicity constant for the ν(NH) vibration; at room temperature, where the bands are observed at 3100 and 1550 cm^{-1}, this constant is strictly zero, contradicting all classical theories of hydrogen bonds. The isotopic ratio of the band at 3200 cm^{-1} of 1·33 reflects also a characteristic hydrogen bond of medium strength and not a very strong hydrogen bond. Lastly, it must be mentioned that the near-infrared spectrum of *N*-methylacetamide in $CCl_3F–C_2Br_2F_4$ shows at low temperature a strong absorption at 6280 cm^{-1}. These absorptions were assigned by Bernard-Houplain and Sandorfy[38] to the first overtone of the ν(NH) vibration of self-associated species, the fundamental being observed at 3250 cm^{-1}. The anharmonicity takes the realistic value of -110 cm^{-1}. The assignment made by Kearley *et al.*[34] should predict the *third* overtone of the ν(NH) vibration at about 6200 cm^{-1}. This assignment cannot account for the high intensity of the band observed at this wavenumber.

DSC measurements

The melting temperature and the melting enthalpy are $117 \pm 0{\cdot}1$ °C and $146 \pm 0{\cdot}3$ J g^{-1} for BPA.Py and $111 \pm 0{\cdot}4$ °C and $109 \pm 0{\cdot}1$ J g^{-1} for BPA$_D$.Py. These results are in line with the expansion of the crystalline lattice on deuteration. No phase transition was observed.

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REFERENCES

1. E. L. Becker, H. E. Bleich, A. R. Day, R. I. Frear, J. A. Ghasel and J. Vinsintainer, *Biochemistry* **16**, 4656 (1979).
2. M. N. James, D. G. Brayer, L. T. Delbaire, A. R. Sielecki and A. Gertler, *J. Mol. Biol.* **139**, 423 (1980).
3. E. Benedetti, C. Pedone, C. Toniolo, G. Nemethy, M. S. Pottle and H. A. Scheraga, *Int. J. Pept. Protein Res.* **16**, 156 (1980).
4. G. Valle, G. M. Bonora and C. Toniolo, *Gazz. Chim. Ital.* **114**, 341 (1984).
5. L. Van Meervelt, K. Dewael and Th. Zeegers-Huyskens, *J. Mol. Struct.* **356**, 183 (1995).
6. M. T. Nguyen, K. Dewael and Th. Zeegers-Huyskens, *J. Phys. Chem.* **99**, 9739 (1995).
7. *SHELXTL PC Manual Version 4.1.* Siemens Analytical X-Ray Instruments, Madison, WI (1990).
8. G. M. Sheldrick, *SHELXL-93, a Fortran-77 Program for the Refinement of Crystal Structures from Diffraction Data.* University Göttingen, Göttingen (1993).
9. J. W. Bates, H. Fuess, H. Kessler and R. Schuk, *Chem. Ber.* **113**, 520 (1980).
10. E. Benedetti, B. Di Blasio, V. Pavone, C. Pedone, C. Toniolo and G. M. Bonora, *Int. J. Biol. Macromol.* **2**, 217 (1980).
11. Z. Malarski, I. Majerz and T. Lis, *Acta Crystallogr., Sect. C* **43**, 1766 (1987).
12. L. B. Jerykiewicz, Z. Malarski, L. Sobczyk, T. Lis and E. Grech, personal communication.
13. Z. Malarski, I. Majerz and T. Lis, *J. Mol. Struct.* **158**, 360 (1987).
14. I. Majerz, Z. Malarski and T. Lis, *J. Mol. Struct.* **240**, 47 (1990).
15. Th. Zeegers-Huyskens and L. Sobczyk, *J. Mol. Liq.* **46**, 263 (1990).
16. J. Kalenik, I. Majerz, Z. Malarski and L. Sobczyk, *Chem. Phys. Lett.* **165**, 15 (1990).
17. J. C. Speakman, *Acid Salts of Carboxylic Acids. Crystals with Some Very Short Hydrogen Bonds. Structure and Bonding,* p. 141. Berlin (1972).
18. I. Majerz, W. Sawka-Dobrowolska and L. Sobczyk, *J. Mol. Struct.* **319**, 1 (1994).
19. Z. Daga-Szafran and E. Dulewicz, *Adv. Mol. Relaxation Interaction Processes* **21**, 207 (1981).
20. A. Novak, *Struct. Bonding* **18**, 177 (1974).
21. H. Romanowski and L. Sobczyk, *Chem. Phys.* **19**, 361 (1977).
22. N. D. Sokolov and V. A. Savelev, *Chem. Phys.* **22**, 383 (1977).
23. R. Janoschek, A. Hayd, E. G. Weidemann, M. Leuchs and G. Zundel, *J. Chem. Soc., Faraday Trans. 2* **74**, 1938 (1978).
24. Y. Guissani and H. Ratajczak, *Chem. Phys.* **62**, 161 (1981).
25. F. R. Dollish, W. G. Fateley and F. F. Bentley, *Characteristic Raman Frequencies of Organic Compounds.* Wiley, New York (1973).
26. Y. Belabbes and A. Lautie, *J. Raman Spectrosc.* **24**, 237 (1993).
27. M. C. Bernard-Houplain and C. Sandorfy, *Chem. Phys. Lett.* **27**, 154 (1974).
28. D. L. Snavely, J. A. Overly and V. A. Walters, *Chem. Phys. Lett.* **201**, 567 (1995).
29. G. Bator and Th. Zeegers-Huyskens, *Spectrosc. Lett.* **30**, 321 (1997).
30. S. E. Krikorian and M. Mahpour, *Spectrochim. Acta, Part A* **29**, 1233 (1973).
31. S. E. Krikorian, *Spectrochim. Acta Part A* **37**, 745 (1981).
32. K. Dewael, PhD Thesis, University of Leuven (1996).
33. F. Fillaux, J. P. Fontaine, M. H. Baron, G. J. Kearley and J. Tomkinson, *Chem. Phys.* **176**, 249 (1993).
34. G. J. Kearley, F. Fillaux, M. H. Baron, S. Bennington and J. Tomkinson, *Science* **264**, 1285 (1994).
35. C. L. Perrin, *Science* **266**, 1665 (1994).
36. M. Meot-Ner (Mautner), *J. Am. Chem. Soc.* **110**, 3071 (1988).
37. M. J. S. Dewar and K. M. Dieter, *J. Am. Chem. Soc.* **108**, 8075 (1986).
38. M. C. Bernard-Houplain and C. Sandorfy, *Can. J. Chem.* **51**, 3640 (1973).