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Raman spectroscopic evidence of low temperature stability of D,L-glycolic and L-(+)-lactic acid crystals



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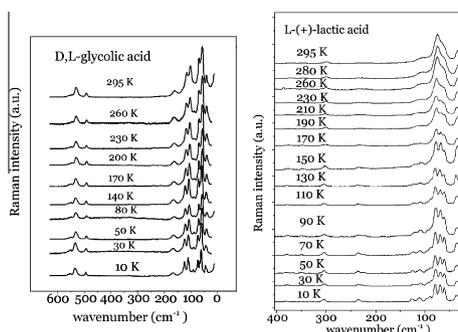
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HIGHLIGHTS

- Low temperature Raman spectra of glycolic and lactic acid are presented.
- Spectra show smooth temperature variation.
- No phase transitions are indicated in the 10–300 K interval.
- Vibrational analysis for free molecules and crystals is performed.

GRAPHICAL ABSTRACT

Temperature dependent Raman spectra of glycolic and lactic acid reveal great stability of crystal lattices from 295 K to 10 K. Four different hydrogen bonds exist in glycolic acid, and two types in lactic acid. Their strengths were estimated to be between 0.2 eV/mol and 0.34 eV/mol.



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ABSTRACT

Raman and infrared spectra of polycrystalline D,L-glycolic and L-(+) lactic acid are presented and assigned both by an *ab initio* calculation of normal modes of free conformers and by self-consistent-charge density-functional-theory computational program DFTB+. Temperature dependent Raman spectra from 295 K to 10 K reveal great stability of crystal lattices, since no soft modes and no band splittings that could be attributed to changes of the number of molecules per unit cell were observed. A semiempirical calculation with GULP program was used to estimate the strength of hydrogen bonds in crystals: in glycolic acid they have energies of -0.337 eV/mol, -0.329 eV/mol, -0.262 eV/mol and -0.242 eV/mol, while in lactic acid two hydrogen bonds have energies of -0.283 eV/mol and -0.202 eV/mol.

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Introduction

Biodegradable polymers on the basis of lactic (LA) and glycolic acid (GA) are among most frequently used synthetic polymers applied for medical sutures and devices, bioimplants and scaffolds in tissue engineering [1–5]. Among many applications, anti-tumor

drug coated with poly (lactic acid-co-glycolic acid), or PLGA, were made with intention of achieving continuous drug release during polymer degradation [6]. Such procedure has shown positive *in vivo* results for non-surgical treatment of prostate-confined cancer [7]. Detailed descriptions of PLGA uses as controlled drug delivery carrier can be found in [8].

Poly (glycolic acid) – PGA – was first synthesized by William Caruthers in 1930s. On heating, glycolic acid dimerizes into glycolide which is the starting monomer group for PGA polymerization.

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PGA in the crystalline form has melting point at 500 K [3], but degrades rapidly in water environment and therefore has to be stabilized by lactic acid polymers [9].

Production of poly (lactic acid), or PLA, uses two different routes: step-growth polymerization or polycondensation reaction for obtaining low molar mass oligomers which starts from monomers, and a ring-opening polymerization reaction of the lactide, lactic acid dimer, for high molar mass PLA [10,11]. The lactide ring is obtained as a product of backbiting reaction from low molar mass lactic acid oligomers [12]. At present, lactic acid monomers are produced on the industrial scale by microbial fermentation in order to obtain optically pure compounds [13].

In view of the roles temperature and water play in the polycondensation reaction, it seemed pertinent to follow the changes they produce on each of the starting materials. We chose to investigate temperature dependence of polycrystalline L-(+)-lactic acid and D,L-glycolic acid from room temperature to 10 K using Raman spectroscopy, already an established method for polymer characterization [14,15], to be followed by a vibrational study at the elevated temperatures later on. Previously published research focused on process of polymerization of water solutions of glycolic [16,17] and lactic acid [17,18]. Fekete et al. [19] and Losada et al. [20] studied conformational changes of LA in water solutions. Raman spectra of poly (lactic acid) in the form of monocrystal were analyzed by Aou and Hsu [21], while Lin et al. used density functional theory to calculate vibrational spectra of various crystalline poly(lactic acid)s [22]. To the best of authors' knowledge, complete vibrational spectra of polycrystalline glycolic and lactic acid were not presented so far.

In the following, full list of the observed bands for polycrystalline samples at room temperature and at 10 K will be presented. Lattice dynamics calculations performed using density functional tight binding approach allowed inspection of each of the calculated mode. Also, a semiempirical calculation of vibrations was undertaken in order to simulate hydrogen bond potential in order to provide an estimate of the hydrogen bond strength in the crystals.

Experimental

D,L-Glycolic acid, 99% pure, and L-(+)-lactic acid, 98% pure, were purchased from Sigma Aldrich and used without further purification. Each polycrystalline compound was transferred into a glass capillary having outer diameter of 2 mm, sealed and mounted on the sample holder of the optical CCS 350 cryostat made by Janis Research Company. Temperature in the range 10–295 K was controlled by Lake Shore 331 controller.

Raman spectra were recorded with HORIBA Jobin-Yvon T64000 Raman spectrometer equipped with liquid nitrogen cooled CCD detector and operating in triple subtractive mode. For excitation, both the 514.5 nm green line of the COHERENT INNOVA 400 argon laser and a 532 nm green line of the CNI solid state laser were used. For low wavenumber spectra "single window" operating option was chosen, while for the internal part of spectra (400–3700 cm^{-1}) a "multi-window" option was preferred. On cooling, one observed an increase of the fluorescent background, which was subtracted by fitting the background with a polynomial expression using LabSpec software.

Infrared spectra in the range 100–4000 cm^{-1} were obtained with a Nicolet iS50 FTIR spectrometer using an ATR module, taking one hundred scans at a resolution of 4 cm^{-1} .

Crystal packing and molecular conformation

Glycolic acid

Geometry optimization of the free glycolic acid and lactic acid molecules was performed with Gaussian03 [23], at the B3LYP/6-31++G(d,p) level of theory. Adopting the notation of Hollenstein

et al. [24], we denote the most stable glycolic acid conformation SSC. First letter refers to the torsional angle of the alcohol OH group with respect to the C–C bond (it is 0°), the second letter refers to the torsional angle of the C–O_a (alcohol oxygen) with respect to the C=O bond (and is 0°), and the third letter refers to the torsional angle of the carboxyl OH group with respect to the C–C bond (also 0°). The most stable conformer exhibits intramolecular hydrogen bond between alcoholic hydroxyl group and a carbonyl oxygen [25,26]. It differs from the two conformations found in the crystal motif mostly in the value of the torsional angle of the alcohol hydroxyl group $\tau(\text{OH})_a$ (Fig. S1). A comparison of the optimized geometry parameters and those found by diffraction methods [27,28] is given in the Supplementary Table S1.

D,L-Glycolic acid crystallizes in the $P2_1/c$ space group having cell parameters equal to $a = 8.9649(6) \text{ \AA}$, $b = 10.5634(7) \text{ \AA}$, $c = 7.8261(7) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 116.93^\circ$, $\gamma = 90^\circ$ and eight molecules in the conventional unit cell [28]. Two molecules forming the motif (denoted type I and type II) differ mainly in the angle $\tau(\text{OH})_a$ which is according to the X-ray diffraction study -88.35° and 85.94° for type I and type II [27], whereas neutron diffraction experiments gave values of -79.81° and -79.63° [28].

One intramolecular hydrogen bond existing in the SSC conformation (Fig. S1) is replaced with three medium strength intermolecular hydrogen bonds per molecule in the crystal (Fig. 1). The intermolecular oxygen–oxygen distances involved in the hydrogen bonds are 2.636 \AA , 2.646 \AA , 2.694 \AA and 2.715 \AA , creating a network in which alcohol OH_a group of the type I molecule binds to carbonyl oxygen from the type II molecule. The carboxylic OH group binds to alcohol oxygen belonging to another molecule of the same type.

Lactic acid

Similar to glycolic acid from which it differs by a methyl group, free lactic acid molecule also has an intramolecular hydrogen bond in the stable conformation [29]. In the crystal, alcohol hydroxyl group turns away to bind with neighboring carbonyl group and the conformation changes (the torsional angle CCO_aH being

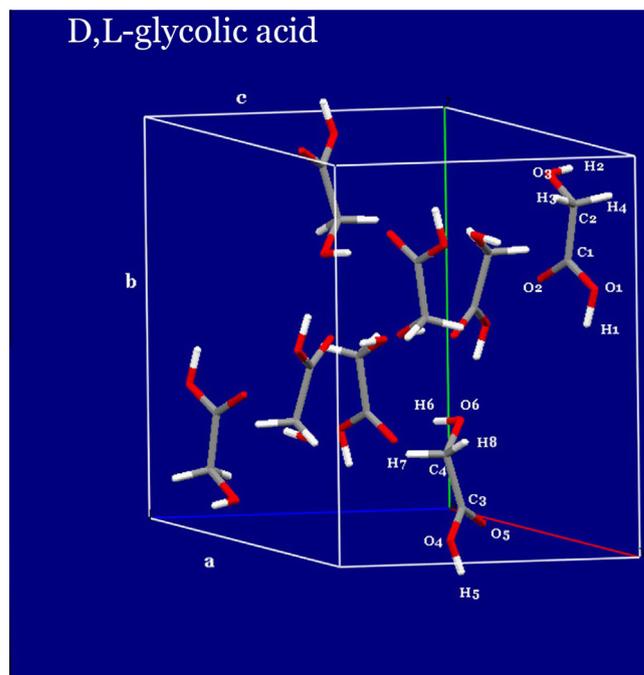


Fig. 1. Crystal structure of D,L-glycolic acid (figure prepared with Mercury 2.2 program, <http://www.ccdc.cam.ac.uk/mercury/>).

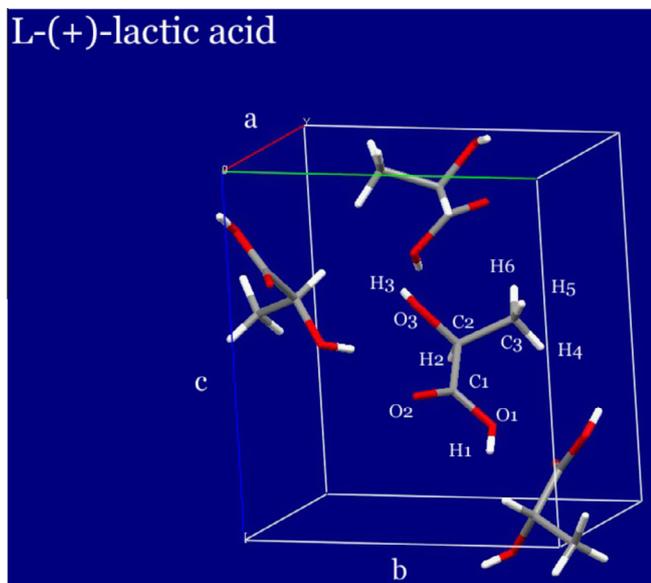


Fig. 2. Crystal structure of L-(+)-lactic acid (figure prepared with Mercury 2.2 program, <http://www.ccdc.cam.ac.uk/mercury/>).

–142.66°, see Fig. S2). L-(+)-lactic acid is an optically active compound – its crystal does not possess a center of inversion, but three mutually perpendicular screw axis, belonging to the $P2_12_12_1$ space group with $a = 5.4896(3)$ Å, $b = 8.4221(3)$ Å, $c = 9.3453(5)$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$ and four molecules per unit

cell (Fig. 2). A comparison of the optimized geometrical parameters and those determined by X-ray diffraction study [30] is given in the Supplementary Table S2. Two types of hydrogen bonds exist, $O_1H_1 \cdots O_3$ and $O_3H_2 \cdots O_2$, the first having oxygen separation equal to 2.634 Å, and the other equal to 2.713 Å (see Fig. 2).

Results

Since glycolic and lactic acid have rather similar chemical structure (one hydrogen from glycolic acid is replaced with a methyl group in lactic acid), the vibrational spectra of their polycrystalline phases are also rather similar (compare Fig. 3 with Fig. 4, and also Fig. 5 with Fig. 6).

Glycolic acid

In the case of D,L-glycolic acid, the space group is determined as $P2_1/c$, therefore an inversion operation is present which transforms D molecules into L ones and vice versa. Altogether there are eight molecules in the conventional unit cell disposing with 216 degrees of freedom. Reducible representation of atomic displacements spans following irreducible representations:

$$\Gamma = 54 A_g + 54 B_g + 54 A_u + 54 B_u.$$

Three acoustic modes $A_u + 2 B_u$ are to be extracted since their frequency linearly depends on wave vector and makes them unobservable in the experiments presented here. 54 A_g and 54 B_g modes are symmetric with respect to inversion and are Raman active, whereas 53 A_u and 52 B_u modes are infrared active. If one were

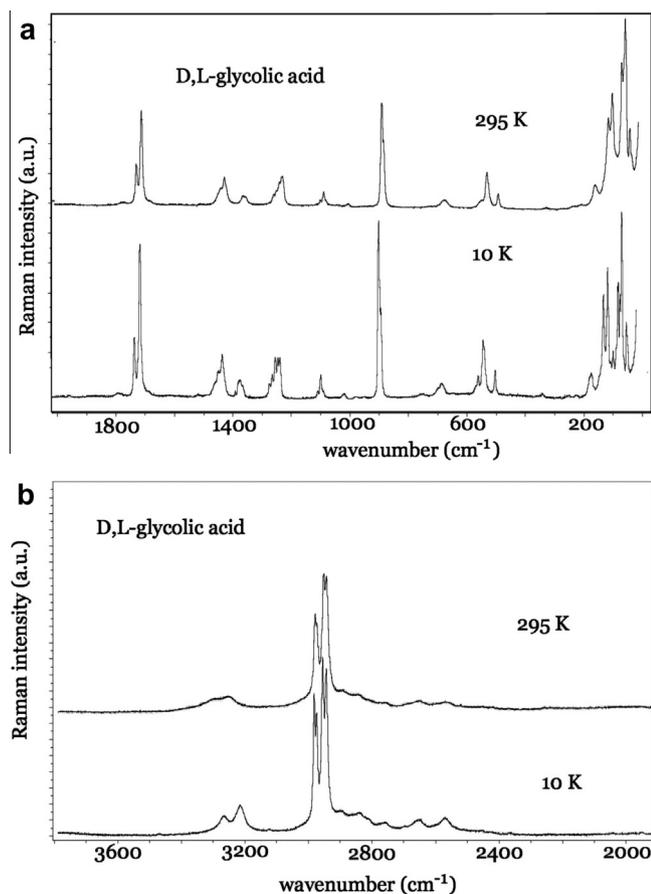


Fig. 3. Raman spectra of D,L-glycolic acid in the 20–1800 cm^{-1} interval (a) and in the 1800–3800 cm^{-1} interval (b). Upper spectra refer to room temperature, lower spectra refer to 10 K.

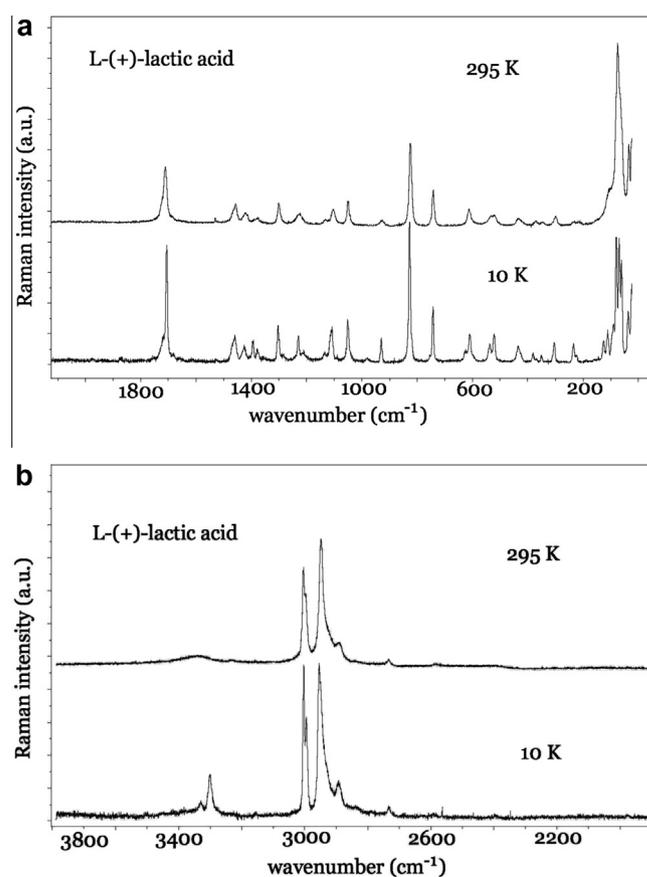


Fig. 4. Raman spectra of L-(+)-lactic acid in the 20–2000 cm^{-1} interval (a) and in the 2000–3800 cm^{-1} interval (b). Upper spectra refer to room temperature, lower spectra refer to 10 K.

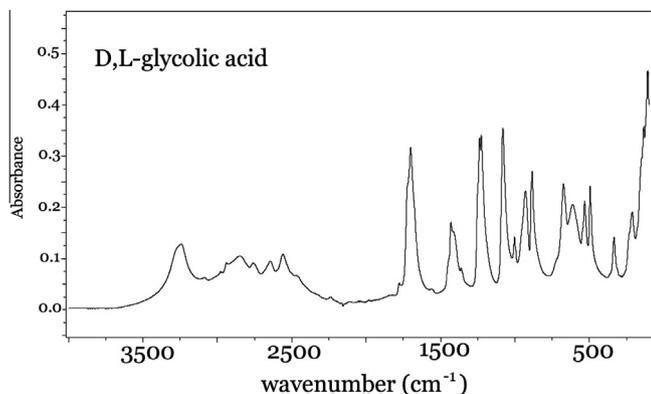


Fig. 5. Infrared and far-infrared spectrum of D,L-glycolic acid (100–4000 cm⁻¹).

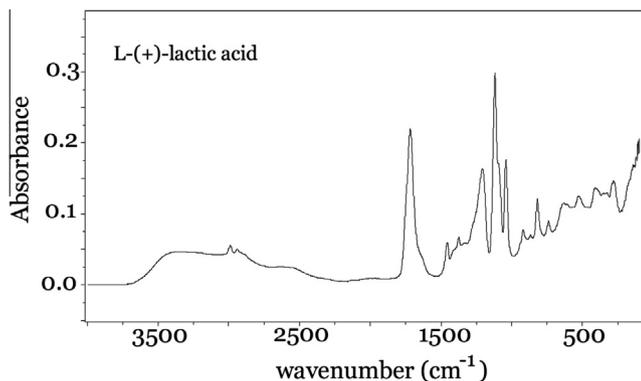


Fig. 6. Infrared and far-infrared spectrum of L-(+)-lactic acid (100–4000 cm⁻¹).

Table 1
Comparison of observed Raman and infrared bands of polycrystalline D,L-glycolic acid (GA) with those calculated for a free CSC conformer at the b3lyp/6-31++G(d,p) level of theory. Complete list of crystal vibrations calculated using DFTB+ program [32] is given in the Supplementary Table S3, while a selection is presented in Table 3.

Polycrystalline GA Raman		Polycrystalline GA infrared	Calculated normal modes of free CSC conformer	Assignment of calculated modes of the free CSC conformer
295 K	10 K	295 K		
3292 mw,sh	3268 mw	3275 m,sh	3752	v(OHacid)
3251 mw	3215 mw	3244 m	3740	v(OHalcohol)
	3122 vw	3086 w		
2979ms	2982 s			
2974 ms,sh	2974 s	2978 mw		
2952 s	2955 vs		3056	v(CH ₂) asym str.
2943 s	2943 vs	2939 mw	3028	v(CH ₂) sym. str.
	2896 mw			
2893 mw	2842 mw	2846 m,br		
2841 mw	2807 w,sh			
2802 w,sh	2759 w,sh	2760 m		
2757 w	2695 w,sh			
2649 w	2655 w	2644 m		
2568 w	2573 w	2559 m		
	2454 vw	2464 w		
	2365 vw			
1778 vw	1785 vw	1778 w		
1729 m	1728 m	1722 s,sh	1812	v(C=O)
1712 s	1709 s	1701 s		
		1553 w		
	1450 mw,sh	1447 w,sh	1493	δ(CH ₂) scissoring
1440 mw,sh	1439 mw,sh		1461	δ(CH ₂) bend
1429 m	1427 mw	1430 m		
		1412 m,br		
1365 w	1368 w	1361 w	1341	δ(C–Oacid–H)+ v(C–Oacid)
1354 w,sh	1357 w,sh			

(continued on next page)

to make a rigid molecule approximation, one could further divide the number of expected modes between internal (involving relative displacements of atoms within molecules) and external, described as translational and librational movements of the whole molecules:

$$\Gamma_{\text{int}} = 42 A_g + 42 B_g + 42 A_u + 42 B_u.$$

$$\Gamma_{\text{ext}} = 12 A_g + 12 B_g + 11 A_u + 10 B_u.$$

In Table 1, a comparison of the observed Raman and infrared modes obtained at room temperature is given, and low temperature Raman modes at 10 K listed as well. To facilitate the assignment, an *ab initio* calculation of vibrational normal modes with Gaussian03 program [23] was intended for a conformer with $\tau(\text{OH})_a$ equal to -89.6° (see Supplementary Fig. S1). During geometry optimization, however, conformation changed to the most stable one. Therefore calculated wavenumbers refer to the CSC stable conformation. The assignment was done using the Gaussview program and no scaling factors were introduced.

Lactic acid

Likewise, the list of all observed bands for L-(+)-lactic acid in the polycrystalline state is presented in Table 2, together with *ab initio* calculated values of normal modes for the conformer with CCO_aH torsional angle adopted in the crystal (-142.66°) depicted in the Supplementary Fig. S2. Here, one frequency was imaginary (torsion of the carboxylic group), indicating that this conformation does not correspond to a minimum in the potential energy surface.

L-(+)-Lactic acid crystallizes in $P2_12_12_1$ space group with four molecules in the unit cell [30]. The cell is orthorhombic and the three screw axis mutually orthogonal. The reducible

Table 1 (continued)

Polycrystalline GA Raman		Polycrystalline GA infrared	Calculated normal modes of free CSC conformer	Assignment of calculated modes of the free CSC conformer
295 K	10 K	295 K		
1260 w,sh	1265 w	1251 s,sh	1281	$\delta(\text{C-Oalcohol-H}) + \delta(\text{CH}_2)\text{wagg}$ $\delta(\text{CH}_2)$ twisting
1250 w,sh	1256 w		1248	
1240 mw,sh	1246 mw			
	1237 mw	1238 s		
1231 m	1230 mw	1226 s	1176	$\delta(\text{C-Oacid-H})$
1100 vw	1100 vw			
1089 w	1090 w			
	1080 vw	1082 s,br,asym	1114	$\nu(\text{C-Oalcohol}) + \nu(\text{C-Oacid})$
1042 vw	1042 vw			
1006 vw	1011 vw	1003 mw		
	969 vw	995 w,sh	1034	$\delta(\text{CH}_2)$ rocking
	941 vw	955 m,sh		
		930 ms,br		
890 s	893 s	890 s,sh		
884 ms	885 ms	884 s,asym	858	$\nu(\text{C-C})$
	743 vw			
		724 w,sh		
675 w	688 w			
	677 w	674 ms	644	$\delta(\text{O=C-O})$
		612 m,vbr	649	$\Upsilon(\text{OHacid})$ torsion
548 w,sh	558 w,sh	545 m,sh		
	550 w	532 m		
530 m	533 m	496 ms	503	out of plane carboxylic def.
492 w	492 mw	488 m,sh	470	$\delta(\text{C-C-Oacid})$ in plane
		362 w	307	$\Upsilon(\text{OHalcohol})$ torsion
328 vw	331 vw	335 mw		
		310 w,sh		
233 vw	244 vw	231 m,sh	277	In plane skeletal defor
210 vw	217 vw	213 m		
		200 m,sh		
	171 mw,sh	179 m,sh		
161 mw	165 mw			
		155 s,sh		
		148 s,sh		
	137 mw,sh	135 s		
	124 ms	124 s,sh		
		118 s,sh		
116 ms	110 s	110 vs		
	100 m,sh	107 vs		
103 s	91 m			
	82 m			
	74 ms			
	67 ms		65	Torsion around C-C
70 s	61 vs			
	53 mw,sh			
57 vs	45 m			
	43 m,sh			
43 ms	40 mw,sh			
34 m,ss				

ν -Stretching, δ -angle bending, Υ -torsion OH, τ -torsion.

Table 2

Comparison of observed Raman and infrared bands of polycrystalline L-(+)-lactic acid (LA) with calculated normal modes of the conformer found in the crystal (b3lyp/6-31++G(d,p)). Crystal vibrations calculated using DFTB+ program [32] are given in the Supplementary Table S4.

Polycrystalline LA Raman		Polycrystalline LA infrared	Calculated normal modes of the conformer found in the crystal	Assignment of calculated bands
295 K	10 K	295 K		
3383 mw,br	3329 w		3802	$\nu(\text{OH acid})$
		3255 mw,vbr		
3284 vw	3300 m	3200 mw,vbr,sh	3731	$\nu(\text{OH alcohol})$
3003 vs	3003 s		3135	$\nu(\text{CH}_3)$ asym. str.
2998 s,sh	2995 m	2988 mw	3123	$\nu(\text{CH}_3)$ asym. str.
	2954 s,sh			
2948 s	2948 s,sh		3049	$\nu(\text{CH}_3)$ sym.str.
2924 m,sh	2931 m,sh	2941 mw	2975	$\nu(\text{CH})$
2891 w	2890 m,br	2892 mw,sh		
2733 vw	2734 w			
		2635 w,br		

(continued on next page)

Table 2 (continued)

Polycrystalline LA Raman		Polycrystalline LA infrared	Calculated normal modes of the conformer found in the crystal	Assignment of calculated bands
295 K	10 K	295 K		
2583 vw		2552 w,br,sh		
1725 m,sh	1718 mw	1746 m,sh	1822	$\nu(\text{C}=\text{O})$
1711 s	1706 s	1717 vs		
1685 w,sh	1683 vw			
		1642 w,sh	1504	Traces of H ₂ O
			1496	$\delta(\text{CH}_3)$ asym. bend.
1466 mw,sh	1468 m			$\delta(\text{CH}_3)$ asym. bend.
1457 m	1459 m,asym,br	1456 mw	1439	$\delta(\text{CH})$
	1433 w,sh		1415	$\delta(\text{CH}_3)$ sym. bend
1421 w	1425 w,asym	1408 w,sh		
1389 vw,sh	1395 w			
1377 w	1378 w	1375 mw	1346	$\delta(\text{CH}) + \nu(\text{C}-\text{C})$
1300 m	1303 s	1333 w	1319	$\delta(\text{C}-\text{Oalcohol}-\text{H}) + \nu(\text{C}-\text{Oacid})$
	1284 vw	1271 m,sh,br	1290	$\delta(\text{HC}_2\text{C}_1)$
1226 mw,br	1230 mw			
	1214 w	1207 s,br	1196	$\delta(\text{C}-\text{Oacid}-\text{H}) + \nu(\text{C}-\text{Oalcohol})$
1132 w	1134 w		1133	$\nu(\text{C}-\text{Oacid}) + \delta(\text{C}-\text{Oacid}-\text{H})$
	1114 m,sh	1118 vs		
1104 m	1110 m	1095 s,sh	1087	$\nu(\text{C}-\text{CH}_3)$ stretching
1050 m	1051 m	1041 s	1053	$\delta(\text{CH}) + \delta(\text{CH}_3)$ rocking
	1038 w,sh			
	982 vw			
927 w	930 mw	938 w,sh	924	$\nu(\text{C}-\text{CH}_3) + \nu(\text{C}_1-\text{C}_2)$
		920 m		
		868 mw		
825 ms	828 s	819 ms	796	$\nu(\text{C}-\text{COOH})$
	820 w,sh			
	755 w,sh			
742 ms	742 m	741 m	719	Carboxylic carbon out of pl.def.
	625 w			
612 m	610 m	634 m,br	604	$\delta(\text{O}=\text{C}-\text{C})$
	599 w	609 m		
532 w	537 mw	567 m		
522 w	522 m	527 m,br	531	$\gamma(\text{OH acid})$
432 w,asym		469 m	476	$\delta(\text{Oacid}-\text{C}-\text{C}) + \delta(\text{Oalc}-\text{C}-\text{C})$
372 w	434 mw,br			
	381 w	410 s,br,asym	410	$\delta(\text{Oalc}-\text{C}-\text{C})$
	369 vw			
347 vw	351 w			
		355 m	332	$\gamma(\text{OHalcohol})$
300 w	305 mw	326 m	317	CH_3 in plane bend.
		290 s,sh		
		280 s,br	248	$\gamma(\text{CH}_3)$ out of plane bend
		247 m,sh		
234 vw	235 mw		226	$\tau(\text{CH}_3)$
212 vw	225 w,sh	227 m		
		201 m,sh		
	190 vw	179 ms,sh		
148 mw		168 ms,sh		
		152 s		
		142 s		
	126 mw	133 s		
104 m,br	111 m	122 s		
	95 m,sh	111 s		
	90 m	106 s	- ^a	Torsion around C-C
74 vs	80 s			
64 s,sh	70 s			
34 s	61 s			
	36 m			

^a Torsional frequency was imaginary.

representation of all atomic displacements in the unit cell spans following irreducible representations:

$$\Gamma = 36 A + 36 B_1 + 36 B_2 + 36 B_3.$$

Using the fact that molecules are placed on a general site with C₁ symmetry, one can use correlation tables to determine the sym-

metry of the internal and external modes. Translations of the crystal as a whole belong to B₁ + B₂ + B₃ representations and are exempt from further consideration.

$$\Gamma_{\text{int}} = 30 A + 30 B_1 + 30 B_2 + 30 B_3$$

$$\Gamma_{\text{ext}} = 6 A + 5 B_1 + 5 B_2 + 5 B_3.$$

Table 3

Comparison of selected Raman and infrared bands observed in the spectra of D,L-glycolic acid (GA) at room temperature with values calculated by GULP and DFTB + program (3ob parameterization).

Polycrystalline GA 295 K		Calculated phonons and their symmetry		Assignment of modes
Raman	Infrared	GULP	DFTB+	
	1785 vw	1590 A _u	1653,1650	ν(C=O)
	1728 m	1584 B _u	1641,1635	
1778 vw		1571 B _g	1630,1625	
1729 m		1570 A _g	1625,1612	
	1709 s	1544 A _u ,B _u		
1712 s		1543 A _g ,B _g		
1365 w	1361 w	1232 B _u	1345,1344	δ(COH)alcohol
1354 w,sh		1227 A _u	1344,1341	
		1225 B _g	1338,1336	
		1216 A _g	1336,1333	
1260 w,sh		1202 A _u	1277,1275	δ(COH) acid
1250 w,sh	1251 s,sh	1190 B _u	1271,1270	
1240 mw	1238 s	1183 A _g	1266,1263	
1231 m	1226 s	1182 B _g	1261,1259	
1100 vw		1142 B _g	1024	ν(C–O) alcohol
		1129 A _u	1022	
		1110 B _u	1013	
		1100 B _g	1012	
		1095 B _u	1012	
	1082 s	1091 A _u	1011	
		1091 B _g	1007	
		1090 A _g	1004	
1089 w				

All modes are Raman active, while only B modes are infrared active.

Density-functional tight-binding approach involving self-consistent-charge density (SCC-DFTB) [31–33] was used for optimizing crystal lattice geometries and calculation of phonons for both glycolic and lactic acid. Because of large number of calculated modes (213 for GA, 141 for LA) only a selection of modes is presented and compared to the position of observed bands and the wavenumbers of phonons calculated by General Utility Lattice program (GULP, v. 4.0) [34] in Tables 3 and 4, while complete list of modes is given for three different DFTB parametrizations in the Supplementary Tables S3 and S4. Outputs are available from authors on request.

Discussion

Assignment of the crystalline bands is facilitated by previous matrix isolation studies. Free glycolic acid has 21 normal modes,

and free lactic acid has 30 vibrational modes. Neither molecule has any symmetry element present beside identity, which means that all modes of free molecules are infrared and Raman active and could be observed in e.g. matrix isolation experiments like those conducted by Hollenstein et al. [24,25] or Reva et al. [26] on glycolic acid and by Borba et al. [29] on lactic acid.

Most intense and prominent infrared bands observed in matrix-isolated glycolic acid are bands involving motions of alcoholic hydroxyl and carbonyl groups such as the band at 3561 cm⁻¹ belonging to the stretching O_a–H, the band at 1774 cm⁻¹ associated with the stretching of carbonyl bond ν(C=O), the band at 1332 cm⁻¹ corresponding to the bending of alcohol hydroxyl group δ(C–O_a–H), the band at 1143 cm⁻¹ corresponding to the bending of acid hydroxyl group δ(C–O–H), the band at 1090 cm⁻¹ corresponding to the stretching ν(C–O_a), and the band at 281 cm⁻¹ involving the torsion τ(O_aH), where O_a is the oxygen atom in the alcohol hydroxyl group [24]. All of these transitions refer to the conformer

Table 4

Comparison of selected Raman and infrared bands observed in the spectra of L(+)-lactic acid (LA) at room temperature with values calculated by GULP and DFTB+ program (3ob).

Polycrystalline LA 295 K		Calculated phonons		Assignment of modes
Raman	Infrared	GULP	DFTB+	
1725 m,sh	1746 m,sh			ν(C=O)
1711 s	1717 vs	1599 B ₁	1625	
1685 w,sh		1596 A	1620	
	1642 w,sh	1594 B ₃	1606	
		1507 A	1244,1234	δ(COH)acid
1300 m		1490 B ₁	1211,1188	
		1419 B ₂		
	1271 m,sh,br	1365 B ₃		δ(COH) alcohol
1226 mw,br		1281 B ₃	1169,1155	
	1207 s,br	1272 B ₁	1145,1144	
			1071,1061	δ(CH ₃) + δ(COH) alcohol
1132 w	1118 vs	1083 B ₁	1064,1061	
	1095 s,sh	1087 B ₃		ν(C–O) alcohol
1104 m		1070 A		
		1058 B ₂	925,920	
	1041 s		920,915	

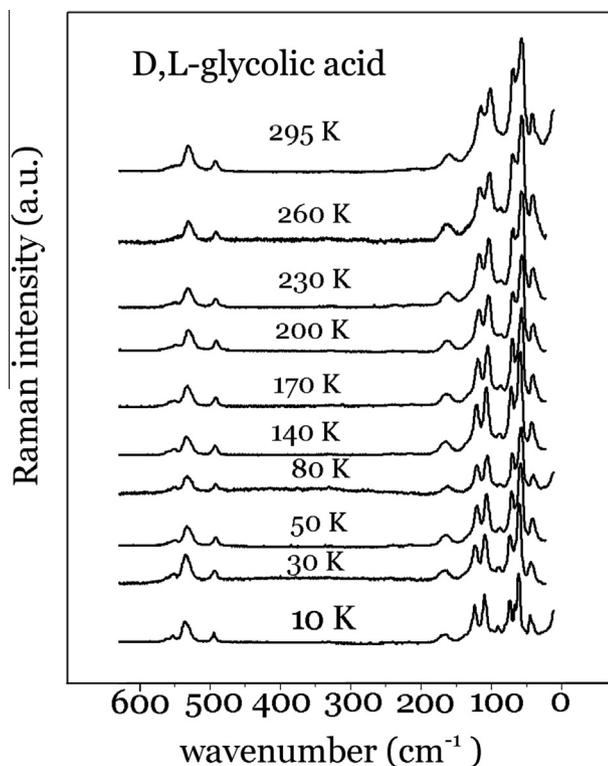


Fig. 7. Temperature dependence of low frequency spectra of glycolic acid from 295 K to 10 K.

where O_aH is in *cis* position with respect to the carbonyl group to which it is bonded via intramolecular hydrogen bond. Likewise, in the infrared spectrum of matrix isolated lactic acid, the $\delta(C-O_a-H)$ bending is assigned at higher wavenumbers (1376 cm^{-1}) than the $\delta(C-O-H)$ deformation of the carboxyl OH group (attributed to sequence of bands ranging from 1328 cm^{-1} to 1265 cm^{-1}), while the band corresponding to the $\nu(C-O_a)$ stretching is observed at 1119 cm^{-1} [29].

Cassanas and coworkers studied glycolic [16] and lactic acid [18] in solution and in the process of polymerization. Acid hydroxyl group bending vibration is attributed to the 1410 cm^{-1} band in GA solution, and to the 1420 cm^{-1} band in the LA solution, while the $\delta(C-O_a-H)$ of alcohol O_a-H group is assigned to 1230 cm^{-1} band in the GA solution and to the 1285 cm^{-1} band in the lactic acid solution.

The band assignment for polycrystalline samples was facilitated by the DFTB+ computational program. In glycolic acid, the carbonyl stretching $\nu(C=O)$ is attributed to Raman bands at 1729 and 1712 cm^{-1} and to infrared bands at 1728 and 1709 cm^{-1} , the $\delta(C-O_a-H)$ bending to 1365 and 1354 cm^{-1} Raman bands and to infrared band at 1361 cm^{-1} ; the $\delta(C-O-H)$ bending to four Raman bands observed at 1260 , 1252 , 1240 and 1231 cm^{-1} , and three infrared bands at 1251 , 1238 and 1226 cm^{-1} . The band corresponding to the $\nu(C-O_a)$ stretching vibration appears at 1100 and 1089 cm^{-1} in Raman and at 1082 cm^{-1} in the infrared spectrum of GA crystal, having a position quite similar to the band of matrix isolated GA observed at 1090 cm^{-1} . For crystalline L-(+)-lactic acid there is a reverse order of bending vibrations involving hydroxyl groups: it is the acidic $\delta(C-O-H)$ bending vibration that lies at higher wavenumbers (1300 cm^{-1} in the Raman, 1271 cm^{-1} in the infrared spectrum) compared to the $\delta(C-O_a-H)$ bending (1226 cm^{-1} in the Raman and 1207 cm^{-1} in the infrared spectrum).

Semiempirical calculation of crystal vibrations was performed by GULP program [34]. Optimization of crystal structures was achieved with potential energy expressed as a sum of intra- and

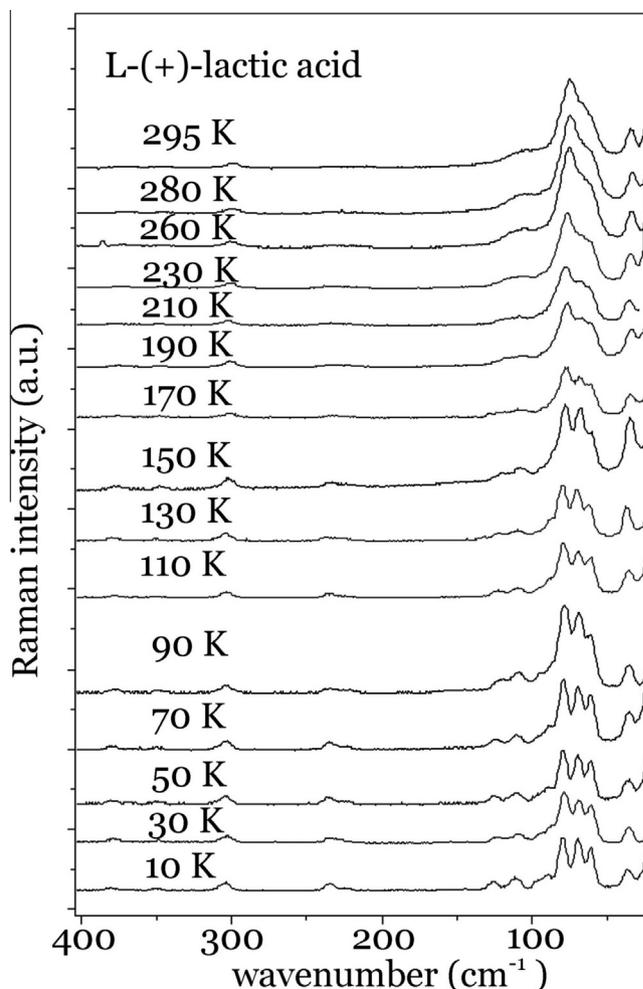


Fig. 8. Temperature dependence of low frequency spectra of lactic acid from 295 K to 10 K.

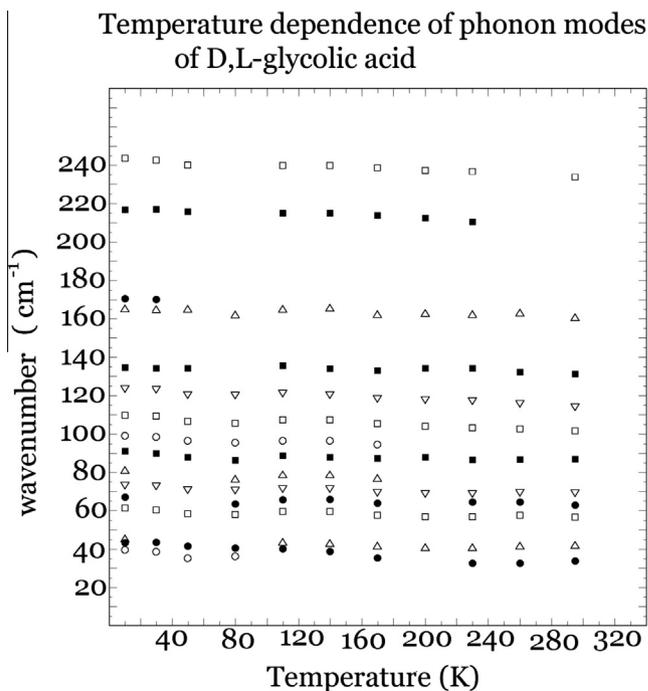


Fig. 9. Temperature dependence of phonon modes of glycolic acid from 295 K to 10 K.

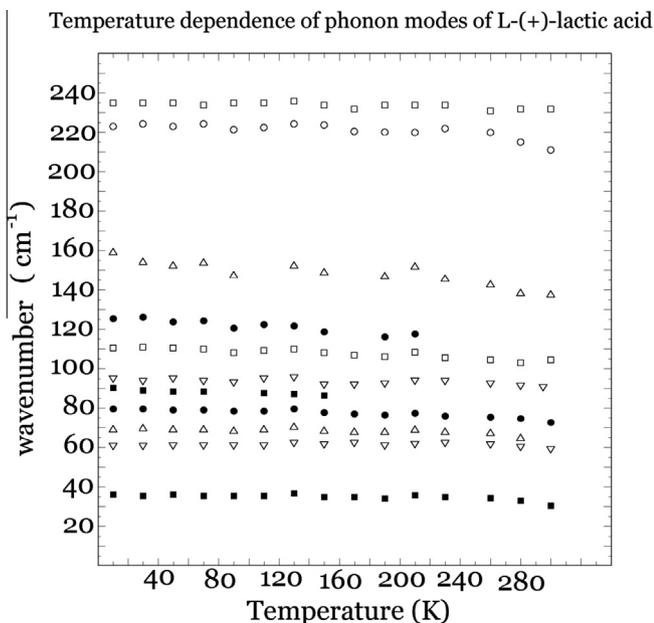


Fig. 10. Temperature dependence of phonon modes of lactic acid from 295 K to 10 K.

inter-molecular interactions presented in Supplementary Tables S5 and S6. The strength of hydrogen bonding in glycolic acid is -0.337 eV/mol for $O_1H_1 \cdots O_3$ bond, -0.329 eV/mol for $O_4H_5 \cdots O_6$, -0.262 eV/mol for $O_3H_2 \cdots O_5$ bond, and -0.242 eV/mol for $O_6H_6 \cdots O_2$ bond. For lactic acid, there are two types of hydrogen bonds: $O_3H_3 \cdots O_2$ bond estimated to be -0.283 eV/mol and $O_1H_1 \cdots O_3$ bond estimated to be -0.202 eV/mol.

Temperature stability of crystal lattices is demonstrated by smooth dependence of phonons positions at various temperatures (Figs. 5 and 6). At 10 K, one expects twenty four bands for glycolic acid and twenty one band for lactic acid, but only sixteen modes for glycolic and eleven modes for lactic acid are found (see Figs. 7–10).

Conclusions

Raman and infrared spectra of polycrystalline D,L-glycolic and L-(+) lactic acid are presented for the first time, and assigned with the help of *ab initio* computations for free conformers and with the self-consistent-charge density-functional-theory computational program DFTB+. Temperature dependent Raman spectra reveal great stability of crystal lattices since there are no soft modes observed and no band splittings observed that could be attributed to changes of the number of molecules per unit cell. A semiempirical calculation with GULP program was used to estimate the strength of hydrogen bonds in crystals: in glycolic acid hydrogen bonds have energies of -0.337 eV/mol, -0.329 eV/mol, -0.262 eV/mol and -0.242 eV/mol, while in lactic acid two hydrogen bonds have energies of -0.283 eV/mol and -0.202 eV/mol.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.saa.2014.12.048>.

References

- [1] D.A. Stout, B. Basu, T.J. Webster, *Acta Biomater.* 7 (2011) 3101.
- [2] H. Liu, T.J. Webster, *Biomaterials* 28 (2007) 354.
- [3] D.W. Huttmacher, J.C.H. Goh, S.H. Teoh, *Ann. Acad. Med. Singapore* 30 (2001) 183.
- [4] Chan-Zen Wang, Mei-Ling Ho, Wem-Chang Chan, et al., *Mater. Sci. Eng. C31* (2011) 1343.
- [5] Min Woo Sa, Jong Yong Kim, *Int. J. Precis. Manuf.* 14 (2013) 1.
- [6] T.W.J. Steele, C.L. Huang, E. Widjaja, F.Y.C. Boey, J.S.C. Loo, S.S. Venkatraman, *Acta Biomater.* 7 (2011) 1973.
- [7] S.C.J. Loo, Z.Y.S. Tan, S.L.I. Lin, *J. Pharm. Sci.* 99 (2010) 3060.
- [8] H.K. Makadia, J. Siegel, *Polymers* 3 (2011) 1377.
- [9] D.J. Mooney, C.L. Mazzoni, C. Breuer, K. Mc Namara, D. Hern, J.P. Vaccanti, P. Langer, *Biomaterials* 17 (1996) 115.
- [10] D.A.S. Marques, S. Jarmelo, C.M.S. Baptista, M.H. Gil, *Macromol. Symp.* 296 (2010) 63.
- [11] F. Achmad, K. Yamane, S. Quan, T. Kokugan, *Chem. Eng. J.* 151 (2009) 342.
- [12] S. Inkinen, M. Hakkarainen, A.-C. Albertsson, A. Södergård, *Biomacromolecules* 12 (2011) 523.
- [13] A. Trontel, A. Batušić, I. Gusić, A. Slavica, B. Šantek, S. Novak, *Food Technol. Biotechnol.* 49 (2011) 75.
- [14] G. Kister, G. Cassanas, M. Vert, *Spectrochim. Acta A* 53 (1997) 1399.
- [15] G. Kister, G. Cassanas, M. Vert, B. Pauvert, A. Térol, *J. Raman Spectrosc.* 26 (1995) 307.
- [16] G. Cassanas, M. Morssli, E. Fabrègue, L. Bardet, *J. Raman Spectrosc.* 22 (1991) 11.
- [17] G. Cassanas, G. Kister, E. Fabrègue, M. Morssli, L. Bardet, *Spectrochim. Acta A* 49A (1993) 271.
- [18] G. Cassanas, M. Morssli, E. Fabrègue, L. Bardet, *J. Raman Spectrosc.* 22 (1991) 409.
- [19] Z.A. Fekete, T. Körtvélyesi, J. Andor, I. Pálínkó, *J. Mol. Struct. THEOCHEM* 666–667 (2003) 159.
- [20] M. Losada, Ha Tran, Yunjie Xu, *J. Chem. Phys.* 128 (2008) 014508.
- [21] K. Aou, S. Ling Hsu, *Macromolecules* 39 (2006) 3337–3344.
- [22] T. Lin, X.-Y. Liu, C. He, *J. Phys. Chem. B* 116 (2012) 1524.
- [23] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Ste-fanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. John-son, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian03, Revision C.02, Gaussian Inc, Wallingford, CT, 2004.
- [24] H. Hollenstein, T.-K. Ha, H.S.H. Günthard, *J. Mol. Struct.* 146 (1986) 289.
- [25] H. Hollenstein, R.W. Schär, N. Schwizgebel, G. Grassi, H.S.H. Günthard, *Spectrochim. Acta A* 39 (1983) 193.
- [26] I.D. Reva, S. Jarmelo, L. Lapinski, R. Fausto, *Chem. Phys. Lett.* 389 (2004) 68.
- [27] W.P. Pijper, *Acta Cryst. B27* (1971) 344.
- [28] R.D. Ellison, C.K. Johnson, H.A. Levy, *Acta Cryst. B27* (1971) 333.
- [29] A. Borba, A. Gómez-Zavaglia, L. Lapinski, R. Fausto, *Phys. Chem. Chem. Phys.* 6 (2004) 2101.
- [30] A. Schouten, J.A. Kanters, J. van Krieken, *J. Mol. Struct.* 323 (1994) 165–168.
- [31] M. Elstner, D. Porezag, J. Jungnickel, M. Elstner, T. Haugk, Th. Frauenheim, S. Suhai, G. Seifert, *Phys. Rev. B* 58 (1998) 7260.
- [32] M. Gaus, A. Goetz, M. Elstner, *J. Chem. Theory Comput.* 9 (2013) 338.
- [33] M. Witek, S. Irle, K. Morokuma, *J. Chem. Phys.* 121 (2004) 5163.
- [34] J.D. Gale, A.L. Rohl, *Mol. Simul.* 29 (2003) 291.