Solid state linear-dichroic infrared (IR-LD) spectroscopic characterization of α- and β- glycine polymorphs

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Abstract: IR-LD spectroscopic analysis using nematic liquid crystal suspension as a solid-state orientation technique and the reducing-difference procedure for polarized spectra interpretation are applied to the α- and β-polymorphs of glycine. Both structural analysis and detailed IR band assignments were carried out.

Keywords: α- and β- glycine polymorphs, solid state IR-LD analysis

1 Introduction

Polymorphism is an important problem in modern pharmaceutical science. Glycine, for example, has three (α, β and γ) polymorphs [1-7] differing in how \( +\text{NH}_3\text{-CH}_2\text{-COO}^- \) zwitterions are linked together in the solid [1-3, 8, 9]. α and β are monoclinic (α, \( P2_1/n \); β, \( P2_1 \)), while the γ-form is trigonal (\( P3_1 \)). Their stabilities decrease \( \alpha > \beta > \gamma \) [1-7, 9, 10]. The \( \beta \to \alpha \) transition depends on factors such as temperature, solvent polarity, pressure etc. [10]. The γ-modification can crystallize from β- or α-forms under 3 - 23 GPa pressure.

Powder and X-ray diffraction, DSC, and TG are powerful methods of polymorph investigation which have been applied to glycine [1-7, 9, 10]. IR spectroscopy is also useful [1, 10]. However, linear-dichroic IR-spectroscopy using an orientation technique...
such as nematic liquid crystal suspension has been used relatively rarely on polymorphs. It has been applied to polymorphs of paracetamol [11] for structural analysis and detailed IR band assignment, using a reduction procedure for polarized spectra interpretation.

The present work applies IR-LD spectroscopy to the α- and β-polymorphs of glycine, giving detailed characterization of their IR spectra and structures.

2 Experimental

2.1 Synthesis

α-glycine (99 %) was obtained from Sigma-Aldrich. Crystals of β-glycine were grown by a liquid diffusion method described in [1, 10]. Ethanol (5 ml) was carefully added dropwise to 10 ml of a saturated aqueous solution of α-glycine at 25 °C, forming small crystals of the β-form. The solid was filtered, washed with ethanol, and dried over P₂O₅ at 25 °C. β-glycine was identified using standard polymorph IR spectra.

2.2 Methods

IR-spectra were measured on a Bomem-Michelson 100 FTIR spectrometer (4000 – 400 cm⁻¹, 2 cm⁻¹ resolution, 150 scans) equipped with a Perkin Elmer wire-grid polarizer. The non-polarized solid state IR spectra were recorded using the KBr disk technique. Oriented samples were obtained as a suspension in a nematic 4′-cyano-4′-alkylbicyclohexyl mixture (ZLI 1695, Merck), mesomorphic at room temperature. Its poor IR spectrum allows recording the guest compound bands over the whole 4000 - 400 cm⁻¹ range. The isolated nitrile stretch at 2236 cm⁻¹ additionally serves as an orientation indicator. Effective orientation of solid state samples was achieved as follows: 5 mg of compound was mixed with the liquid crystal until a slightly viscous suspension was obtained. Two KBr plates were abraded in the same direction with fine sandpaper. The suspension was placed between the plates and they were rubbed together in the direction of their abrasion, promoting sample orientation [12, 13].

IR-LD spectroscopy principles and in particular the difference-reduction procedure used for polarized IR spectra interpretation are described in [14–17]. It consists in subtraction of the perpendicular spectrum, (IRₚ, resulting from a 90° angle between the polarized light beam electric vector and the orientation of the sample) from the parallel one (IRₛ) obtained with collinear mutual orientation. The recorded difference (IRₚ−IRₛ) spectrum converts the corresponding parallel (Aₚ) and perpendicular (Aₛ) absorbances of each band into positives originating from transition moments which form an average angle with the orientation direction (n) between 0° and 54.7° (magic angle), and negative ones corresponding to transition moments between 54.7° and 90°. Next, the perpendicular spectrum multiplied by the parameter c is subtracted from the parallel one; c is varied until a band or set of bands are eliminated. The simultaneous disappearance of bands in the reduced IR-LD spectrum obtained (IRₚ−cIRₛ) indicates collinearity of the corre-
sponding transition moments, thus giving information regarding the mutual disposition of the molecular fragments. This is done graphically using the IR software.

The IR-LD spectral interpretation of both glycine polymorphs required noting the absorption regions of the liquid crystal medium. Fig. 2 shows the difference IR-LD spectra of α– and β–polymorphs with an indication of the liquid crystal absorption bands. A significant degree of orientation of both glycine forms was established as well.

3 Results and discussion

3.1 IR-LD spectral analysis of α-Glycine

The solid-state IR-spectrum of α-glycine (Fig. 1.1) shows a broad absorption maximum with the highest NH stretching peak at 3093 cm\(^{-1}\), characteristic of the α–modification [1, 10]. According to theory [18] the 1700 – 1200 cm\(^{-1}\) region includes maxima at 1664 cm\(^{-1}\), 1633 cm\(^{-1}\) (\(\delta_{\text{NH3}^+}\)), at 1596 cm\(^{-1}\) (\(\nu_{\text{COO}^-}\)), at 1570 cm\(^{-1}\) (\(\delta_{\text{NH3}^+} + \nu_{\text{COO}^-}\)), at 1504 cm\(^{-1}\) (\(\delta_{\text{NH3}^+}\)), at 1419 cm\(^{-1}\) (\(\nu_{\text{COO}^-}\)), at 1334 cm\(^{-1}\) (\(\omega_{\text{CH2}} + \nu_{\text{COO}^-}\)) and at 1321 cm\(^{-1}\) (\(\rho_{\text{NH3}} + \omega_{\text{CH2}}\)). The observed peak at 1043 cm\(^{-1}\) belongs to (\(\nu_{\text{CN}} + \nu_{\text{CC}}\)), 929 cm\(^{-1}\) to (\(\rho_{\text{CH2}} + \rho_{\text{NH3}} + \omega_{\text{COO}^-}\)), 688 cm\(^{-1}\) to (\(\delta_{\text{COO}^-} + \rho_{\text{CH2}} + \nu_{\text{CC}}\)) and 503 cm\(^{-1}\) is assigned to \(\tau_{\text{CN}}\) [24] or to (\(\delta_{\text{CCO}} + \nu_{\text{CC}}\)) [18].

Assignment and confirmation of the experimental IR bands is carried out by IR-LD spectral analysis below and compared with the crystallographic structure for α-glycine [1–10].

**Fig. 1** Solid state IR-spectra (KBr-pellets) of α- (1) and β- (2) glycine.
According to [1] the crystal structure of $\alpha$-glycine (Scheme 1a) contains head-to-tail chains of zwitterions linked via bifurcated NH...O hydrogen bonds in double antiparallel layers (N...O$_I$ and N...O$_{II}$ distances are 2.768, 2.850 and 2.949, 3.074 Å, respectively [4]). The interactions between these double layers are van-der-Waals and hydrogen bonds [9]. This leads to collinearity of the separated $\nu^\prime$$_{COO^-}$, $\nu^\prime$$\prime$$_{COO^-}$, $\delta^s$$_{NH3^+}$, $\delta^as$$_{NH3^+}$ and $\delta$$_{COO^-}$-transition moments in the frame of each glycine molecule and in the overall crystal structure as shown in Scheme 1a. In addition the collinear average mutual orientation of $\delta^s$$_{NH3^+}$ and $\delta^as$$_{NH3^+}$ is also characteristic of the $\alpha$-glycine crystal structure (Scheme 1a).

![Scheme 1](image)

**Scheme 1** Crystal structure of $\alpha-$ (a) and $\beta-$ polymorphs of glycine.

Application of the stepwise reduction procedure discussed above leads to the following: elimination of the 1334 cm$^{-1}$ peak (Fig. 2.2) provoked the disappearance of a series of maxima at 1664 cm$^{-1}$, 1575 cm$^{-1}$, 1411 cm$^{-1}$, 1324 cm$^{-1}$, 686 cm$^{-1}$, 613 cm$^{-1}$ and 503 cm$^{-1}$. Because the $\omega$$_{CH2}$, $\delta^s$$_{NH3^+}$, $\delta^as$$_{NH3^+}$ and $\delta$$_{COO^-}$-transition moments are nearly collinearly oriented in the frames, not only of one molecule but of the overall crystal structure as well (Scheme 1), this result allows the assignment of 1570 cm$^{-1}$ to $\delta^as$$_{NH3^+}$, 1411 cm$^{-1}$ to $\nu^s$$_{COO^-}$, 1324 cm$^{-1}$ to $\rho^\prime$$_{NH3}$, 688 cm$^{-1}$ to $\delta$$_{COO^-}$, and 508 cm$^{-1}$ to $\delta$CCO, respectively. The identification of the 1664 cm$^{-1}$ peak with the $\delta^as$$_{NH3^+}$ mode [18], agrees well with the assignment published in [18–22].

### 3.2 IR-LD spectral analysis of $\beta-$Glycine

Crystallography [1, 7, 9, 10] shows the monoclinic $\beta$-polymorph to be very similar to $\alpha$, also forming head-to-tail chains of zwitterions linked by NH...O hydrogen bonds (N...O$_I$ and N...O$_{II}$ distances are 2.758, 3.002 and 2.833, 3.022 Å, respectively [4]). In the $\beta$-form individual parallel polar layers are linked via hydrogen bonds in a three-dimensional network [1, 7, 9, 10] (see Schemes 1a and 1b). However, the departure of the N-atom from the plane containing the COO$^-$-fragment is larger in the $\beta$-polymorph (Scheme 1b). This difference affects the interlayer hydrogen bonds to both oxygen atoms (i.e. the crystallographically determined different N...O interatomic distances) and the
Fig. 2 1750 – 400 cm\(^{-1}\) non-polarized (1) and reduced IR-LD spectrum of \(\alpha\)-glycine in ZLI 1695 suspension after elimination of the 1334 cm\(^{-1}\) peak (2).

IR bands characteristic of the polymorphs.

The solid state IR spectrum of \(\beta\)-glycine shows a high-frequency shifted N-H stretching maximum at 3189 cm\(^{-1}\) (Fig. 1.2), in contrast to \(\alpha\)-glycine, where it is at 3093 cm\(^{-1}\) (compare Figs. 3.1 and 3.2). The result is explained by the weaker hydrogen bonds in \(\beta\)-glycine. The same phenomenon causes the low-frequency shift of the \(\delta''_{\text{NH}_3^+}\) peak in \(\alpha\)-glycine (1575 cm\(^{-1}\)) to 1525 cm\(^{-1}\) in \(\beta\)-glycine (see Figs. 1.1 and 1.2). Other major differences between the IR spectra of \(\alpha\)- and \(\beta\)-glycine are: the doublet character of the 928 cm\(^{-1}\) peak in the \(\beta\)-form; high-frequency shifting of the \(\delta_{\text{COO}^-}\) to 703 cm\(^{-1}\) and multiple bands in the 530 – 470 cm\(^{-1}\) range (Fig. 1.2). Elimination of the 1334 cm\(^{-1}\) maximum (Fig. 3.2) by the stepwise reduction procedure produced the following results for the \(\alpha\)-form: peaks at 1666 cm\(^{-1}\), 1525 cm\(^{-1}\), 1401 cm\(^{-1}\), 929 cm\(^{-1}\)/914 cm\(^{-1}\) doublet, 703 cm\(^{-1}\), 605 cm\(^{-1}\) and the multiple band between 550 – 450 cm\(^{-1}\) (Fig. 3.2) simultaneously disappeared. Because the X-ray structures for both monoclinic forms are similar, these results make possible exact peak assignments for \(\beta\)-glycine as well. It can be concluded that: the 1525 cm\(^{-1}\) and 1401 cm\(^{-1}\) peaks correspond to \(\delta''_{\text{NH}_3^+}\) and \(\nu_{\text{COO}^-}\) bending and stretching modes respectively, and \(\delta'_{\text{as}_{\text{NH}_3^+}}\) describes the 1666 cm\(^{-1}\) peak. The departure of the N-atom from the COO\(^{-}\)-plane leads to simultaneous elimination of the 928 cm\(^{-1}\)/914 cm\(^{-1}\) doublet with the 1334 cm\(^{-1}\) and the assignment of the doublet to a \((\rho_{\text{CH}_2} + \rho''_{\text{NH}_3} + \omega_{\text{COO}^-})\) mixed mode, in contrast to \(\alpha\)-glycine (see above). The maximum at 703 cm\(^{-1}\) is assigned to \(\delta_{\text{COO}^-}\), as in the \(\alpha\)-form, where the corresponding value is 688 cm\(^{-1}\) (Scheme 1b).
Fig. 3 1750 – 400 cm\(^{-1}\) non-polarized (1) and reduced IR-LD spectrum of β-glycine in ZLI 1695 suspension after elimination of the 1334 cm\(^{-1}\) peak (2).

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References

[1] Y. Iitaka: “The crystal structure of β-glycine”, Acta Crystallogr., Vol. 13, (1960), pp. 35–45.
[2] Y. Iitaka: “The crystal structure of γ-glycine”, Acta Crystallogr., Vol. 14, (1961), pp. 1–10.
[3] R.E. Marsh: “A refinement of the crystal structure of glycine”, Acta Crystallogr., Vol. 11, (1958), pp. 654–663.
[4] P.-G. Jonsson and A. Kvick: “Precision neutron diffraction structure determination of protein and nucleic acid components. III. The crystal and molecular structure of the amino acid glycine”, Acta Crystallogr., Vol. 28B, (1958), pp. 1827–1833.
[5] J. Almlof, A. Kvick and J.O. Thomas: “Glycine-polymorphs”, J. Chem. Phys., Vol. 59, (1973), pp. 3901–3905.
[6] L.F. Power, K.E. Turner and F.H. Moore: “The crystal and molecular structure of α-glycine by neutron diffraction - a comparison”, Acta Crystallogr., Vol. 32B, (1976), pp. 11–16.
[7] T.N. Drebushchak, E.V. Boldyreva and E.S. Shutova: “β-Glycine, Acta Crystallogr., Vol. E58, (2002), pp. 0634–0636.
[8] E.V. Boldyreva, T.N. Drebushchak, E.S. Shutova: “Crystal structure of beta and gamma glycine”, Z. Kristallogr., Vol. 218, (2003), p.p. 366 - 374.
[9] E.V. Boldyreva, T.N. Drebushchak, T.P. Shakhtshneider, H. Sowa, H. Ahsbahs, S.V. Goryainov, S.N. Ivashevskaya, E.N. Kolesnik, V.A. Drebushchak and E.B. Burgina: “Variable-temperature and variable-pressure studies of smallmolecule organic crystals”, ARKIVOC, Vol. 12, (2004), pp. 128–155.
[10] E.S. Ferrari, R.J. Davey, W.I. Cross, A.L. Gillon and Ch.T. Towler: “Crystallization in Polymorphic Systems: The Solution-Mediated Transformation of β to α-Glycine”, Crystal Growth Design, Vol. 3, (2003) pp. 53–60.
[11] B.B. Ivanova: “Monoclinic and orthorhombic polymorphs of paracetamol—solid state linear dichroic infrared spectral analysis”, J. Mol. Struct., Vol. 738, (2005), pp. 233–238.
[12] B.B. Ivanova, M.G. Arnaudov and P.R. Bontchev: “Linear-dichroic infrared spectral analysis of Cu(I)–homocysteine complex”, Spectrochim. Acta, Vol. 60A, (2004), pp. 855–864.
[13] M.G. Arnaudov, B.B. Ivanova and Sh. Dinkov: “A solid-state linear dichroic infrared spectral study of 4-aminopyridine”, Vibr. Spectrosc., Vol. 37, (2005), pp. 145–148.
[14] B. Jordanov, R. Nentchovska and B. Schrader: “FT-IR linear dichroic solute spectra of nematic solutions as a tool for IR band assignment“, J. Mol. Struct., Vol. 297, (1993), pp. 401–406.
[15] B. Jordanov and B. Schrader: “Reduced IR-LD spectra of substances oriented as nematic solutions”, J. Mol. Struct., Vol. 347, (1995), pp. 389–398.
[16] J. Michl and E.W. Thulstrup: Spectroscopy with Polarized Light. Solute alignment by photoselection, in liquid crystals, polymers, and membranes, VCH Publishers, New York, 1986.
[17] E.W. Thulstrup and J.H. Eggers: “Moment directions of the electronic transitions of fluoranthene”, Chem. Phys. Lett., Vol. 1, (1996), pp. 690–694.
[18] M.T. Rosado, M.T.S. Duarte and R. Fausto: “Vibrational spectra of acid and alkaline glycine salts”, Vibr. Spectrosc., Vol. 16, (1998), pp. 35–54.
[19] K. Furic, V. Mohacek, B. Bonifacic and I. Stefanić: “Raman spectroscopic study of H2O and D2O water solutions of glycine”, J. Mol. Struct., Vol. 267, (1992), pp. 39–44.
[20] R.W. Williams: “A scaled quantum mechanical force field and vibrational analysis for the gamma glycine crystal polymorph: Hydrogen bond stretching modes observed”, J. Mol. Struct. Theochem, Vol. 685, (2004), pp. 101–107
[21] S.V. Goryainov, E.N. Kolesnik and E.V. Boldyreva: Missing title of the article, Phys. B, Vol. 357, (2005), pp. 340–347.
[22] J. Baran and H. Ratajczak: “Polarised IR and Raman spectra of the γ-glycine single crystal”, Spectrochim. Acta, Vol. A61, (2005), pp. 1611–1626.