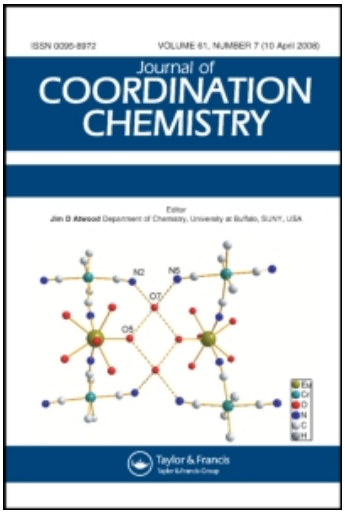



**Journal of Coordination Chemistry**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

# An Au(III) complex of glycyl-S-serine: a linear polarized IR and $^{1}$H- and $^{13}$C-NMR investigation

Tsonko Kolev[ab]; Bojidarka B. Ivanova[c]; Sonya Y. Zareva[c]
[a] Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria [b] Department of Organic Chemistry, Plovdiv University, 4000 Plovdiv, Bulgaria [c] Faculty of Chemistry, Sofia University "St. Kl. Ohridski", 1164 Sofia, Bulgaria

**To cite this Article** Kolev, Tsonko , Ivanova, Bojidarka B. and Zareva, Sonya Y.(2007) 'An Au(III) complex of glycyl-S-serine: a linear polarized IR and $^{1}$H- and $^{13}$C-NMR investigation', Journal of Coordination Chemistry, 60: 1, 109 — 115
**To link to this Article: DOI:** 10.1080/00958970600731620
**URL:** http://dx.doi.org/10.1080/00958970600731620

*Journal of Coordination Chemistry*
Vol. 60, No. 1, 10 January 2007, 109–115

Taylor & Francis
Taylor & Francis Group

# An Au(III) complex of glycyl-*S*-serine: a linear polarized IR and $^{1}$H- and $^{13}$C-NMR investigation

TSONKO KOLEV*†‡, BOJIDARKA B. IVANOVA§
and SONYA Y. ZAREVA§

†Institute of Organic Chemistry, Bulgarian Academy of Sciences,
Acad. G. Bonchev Str. build. 9, 1113 Sofia, Bulgaria
‡Department of Organic Chemistry, Plovdiv University,
Tzar Assen Str. 24, 4000 Plovdiv, Bulgaria
§Faculty of Chemistry, Sofia University "St. Kl. Ohridski",
1, J. Bourchier Blvd., 1164 Sofia, Bulgaria

(*Received in final form 18 January 2006*)



The structure of a mononuclear Au(III) complex of the dipeptide glycyl-*S*-serine (Gly-Ser) has been predicted using solid-state linear dichroic IR (IR-LD) spectroscopy, based on an orientation technique in a nematic liquid crystal suspension. Results are compared with data from $^{1}$H- and $^{13}$C-NMR, MS, elemental analysis, thermogravimetry and differential scanning calorimetry. The metal ion is coordinated as a tridentate through $NH_2$, N (from deprotonated amide) and O ($COO^-$) groups to form $[Au(C_5H_9N_2O_4)Cl]$, with the fourth position of the square-planar coordination sphere being completed by a $Cl^-$ ion.

*Keywords:* Gly-Ser dipeptide; Au(III); IR-LD spectroscopy; $^{1}$H- and $^{13}$C-NMR

## 1. Introduction

Full understanding of *in vivo* manner and mechanism of coordination of the Pt(II), Ru(III) and Au(III) metal ions with DNA requires a systematic investigation of their complexes with model systems for peptides and proteins [1–3]. The potential anticancer effects of some Pt(II) and Au(III) complexes of peptides also merits structural and spectroscopic study [4–6]. Conventional IR spectroscopy could be a fast, easy and cheap method for characterizing metal-peptide systems. However, the complicated IR spectra obtained require a significant level of interpretation. IR-LD spectroscopy using orientation techniques in nematic liquid crystal suspensions can circumvent some of the problems as well as giving additional structural information irrespective of whether the compound studied is crystalline or amorphous. This approach has been demonstrated for a series of peptides, their protonated forms or Au(III) complexes [6–12].

*Corresponding author. Email: kolev@orgchm.bas.bg

*Journal of Coordination Chemistry*
ISSN 0095-8972 print/ISSN 1029-0389 online © 2007 Taylor & Francis
DOI: 10.1080/00958970600731620

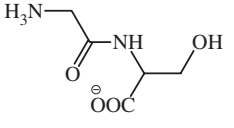
The present article deals with structural and IR characterization of an amorphous Au(III) complex of the dipeptide Gly-Ser (scheme 1). Data are compared with $^{1}$H- and $^{13}$C-NMR, MS, elemental analysis, TGV and DSC results.

## 2. Experimental

### 2.1. *Materials and methods*

Gly-Ser was purchased from Bachem and $HAuCl_4 \cdot 3H_2O$ from Acros Organics. Conventional IR (KBr pellets) and IR-LD spectra were recorded between 4000 and 400 $cm^{-1}$ on a Bomem-Michelson 100 FTIR spectrophotometer equipped with a Perkin-Elmer wire-grid polarizer. Some150 scans were performed for each spectrum with a resolution of 4 $cm^{-1}$. A 4-cyano-4′-alkylbicyclohexyl mixture (ZLI-1695, Merck) was used for orientation of the solid sample as a nematic liquid crystal suspension [6–14]. Its IR spectrum makes it possible to record guest compound bands over the whole 4000–400 $cm^{-1}$ range. Effective orientation of the solid sample was achieved by means of procedures described elsewhere [6–14]. The difference-reduction procedure for polarized spectra interpretation consists of subtraction of the perpendicular spectrum (IRs), measured at 90° to the polarized light beam electric vector and the orientation of the sample, from the parallel one (IRp) obtained with a co-linear mutual orientation. The recorded difference (IRp-IRs) spectrum divides the corresponding parallel (Ap) and perpendicular (As) integrated 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 negatives, corresponding to transition moments between 54.7 and 90° [15–18]. The perpendicular spectrum multiplied by the parameter $c$, is subtracted from the parallel one and $c$ varied until a band or set of bands are eliminated. The simultaneous disappearance of these bands in the obtained (IRp-cIRs) reduced IR-LD spectrum indicates a co-linearity of the corresponding transition moments, thus giving information regarding the mutual disposition of the molecular fragments involved.

$^{1}$H- and $^{13}$C-NMR measurements, referenced to sodium TSS, were made at 298 K with a Bruker DRX-400 spectrometer using 5 mm tubes and $D_2O$ as solvent. *Elemental analysis* was performed according to classical methods: C and H as $CO_2$ and $H_2O$, N using Duma's method and chlorine by titration with $Hg(NO_3)_2$ after wet digestion of the sample. Molecular weight was determined from FAB mass spectra, measured on a Fusion VG Autospect instrument employing 3-nitrobenzyl alcohol as matrix. Thermogravimetric (TGV) measurements were performed using a Perkin-Elmer TGS2 apparatus. DSC runs were recorded on a Perkin-Elmer DSC-2C system under argon.




Scheme 1. The dipeptide Gly-Ser.

### 2.2. *Synthesis*

A methanol solution (10 $cm^3$) of $HAuCl_4 \cdot 3H_2O$ (204.4 mg) was added to a 10 $cm^3$ solution of the dipeptide (195.9 mg) in same solvent. Dilute aqueous NaOH was then added at a mol ratio of Au : L : NaOH = 1 : 1 : 1. After 30 days the yellow precipitate that had formed was filtered off, washed with methanol and dried in air at 298 K. Yield: 71%. Anal. Calcd for $[Au(C_5H_9N_2O_4)Cl]$ (%): C, 15.3; H, 2.3; N, 7.1; Cl, 9.0. Found: C, 15.1; H, 2.1; N, 7.0; Cl, 8.8. The most intense signal in the mass spectrum was $m/z$ 358.02, corresponding to $[Au(C_5H_9N_2O_4)]^+$ ($m = 358.10$). TGV and DSC data in the 300 to 600 K range confirmed the absence of any molecular solvent in the Au(III) complex.

## 3. Results and discussion

### 3.1. *IR-LD data*

IR-LD analysis started with interpretation of polarized spectra of Gly-Ser. Characteristic IR bands of both ligand and complex are presented in table 1. The non-polarized IR-spectrum of Gly-Ser (figure 1.1) has a broad maximum in the 3100–2300 $cm^{-1}$ region assigned to asymmetric and symmetric $\nu_{NH3+}$ modes. Intense peaks at 3300 and 3170 $cm^{-1}$ belong to $\nu_{NH}$ and $\nu_{OH}$ modes. The low frequency shift of the latter is explained by participation of the OH group in the serine side chain in strong intermolecular interactions; crystallographic studies of the peptide reveal an intermolecular OH···O hydrogen bond of length 2.598 Å [19]. The 1700–1400 $cm^{-1}$ contains series of maxima characteristic of $NH_3^+$, $COO^-$ and amide groups as assigned in table 1. Confirmation is obtained by IR-LD analysis. Simultaneous reduction of the 3315 and 1660 $cm^{-1}$ peaks (figure 1.2) in the reduced IR-LD spectrum of Gly-Ser indicated their character as $\nu_{NH}$ and $\nu_{C=O}$ (Amide I) modes as well as a *transoid* configuration of the amide. The data correlate well with crystallographic information;

Table 1. Solid-state IR data for Gly-Ser and the Au(III) complex.

| | $\nu$ ($cm^{-1}$) | |
|---|---|---|
| Assignment | Gly-Ser | $Au^{3+}$-dipeptide complex |
| $\nu_{OH}$ | 3170 | 3490 |
| $\nu_{NH3+}$ | 3100–2300 broad | |
| $\nu_{NH}$ (Amide fragment) | 3315 | |
| $\nu^{as}_{NH2}$,$\nu^{s}_{NH2}$ | | 3345, 3210, 3100 |
| $\nu_{C=O}$ | | 1718 |
| $\delta^{as}_{NH3+}$,$\delta^{as'}_{NH3+}$ | 1693, 1623 | |
| $\delta_{NH2}$ | | 1681 |
| $\nu_{C=O}$ (Amide I) | 1660 | 1645 |
| $\delta^{s}_{NH3+}$ | 1590 | |
| $\delta_{NH}$ (Amide II) | 1555 | |
| $\nu^{as}_{COO^-}$ | 1515 | |
| $\nu^{s}_{COO^-}$ | 1405 | |
| $\delta_{C=O}$ (Amide IV) | 721 | 624 |
| $\gamma_{NH}$ (Amide V) | 668 | |
| $\gamma_{C=O}$ (Amide VI) | 624 | 574 |

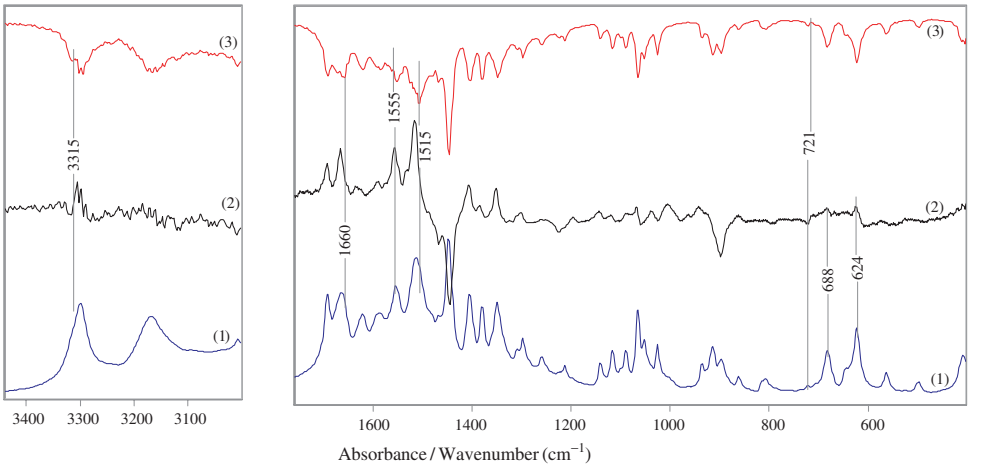
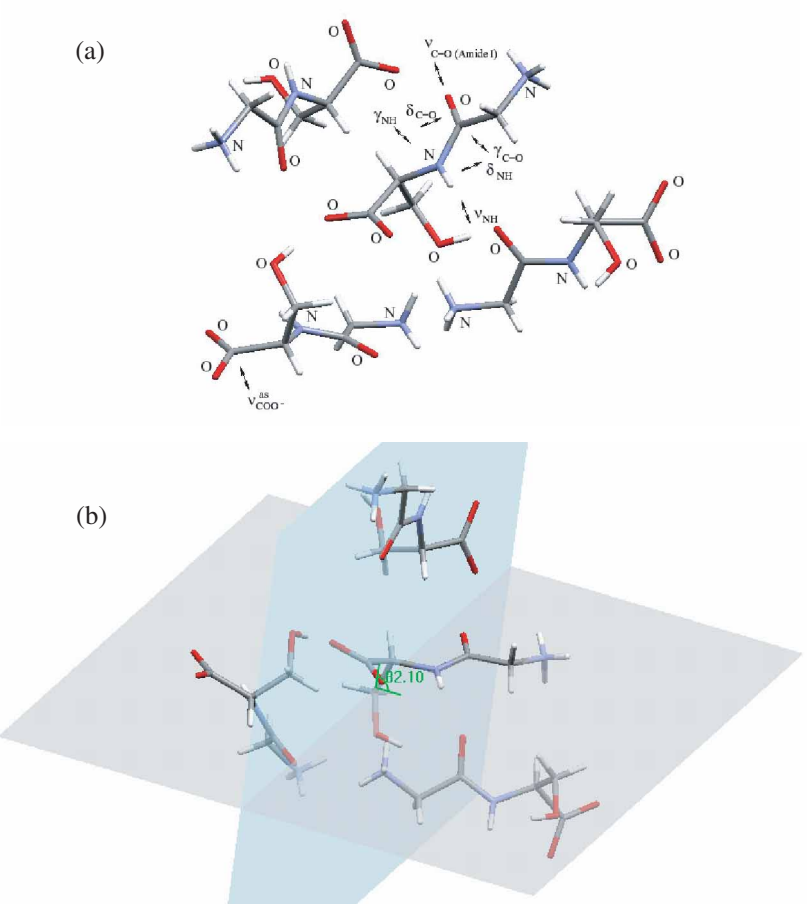



Figure 1. Non-polarized IR (1) and reduced IR-LD spectra of Gly-Ser after elimination of peaks at 3315 (2) and 1555 $cm^{-1}$ (3).



a –C(=O)–NH torsion angle of 171.9(5)° has been refined [19]. The $\nu^{as}_{COO^-}$ peak at 1515 $cm^{-1}$ is not observed, in accordance with single crystal X-ray data [19], indicating that the Gly-Ser unit cell contains four molecules oriented as shown in scheme 2(a) and supposing the mutual co-linear disposition of Amide I and $\nu^{as}_{COO^-}$ modes between neighbouring molecules (scheme 2a). On the other hand a reduction of both Amide V and Amide VI peaks (table 1) in the same dichroic ratio as obtained in figure 1.2 confirmed their assignment as $\gamma_{NH}$ and $\gamma_{C=O}$ out-of-plane frequencies. It is interesting to note that the discussed elimination led to the observation of maxima at 3300, 1665 and 1520 $cm^{-1}$, assigned to $\nu_{NH}$, $\nu_{C=O}$ (Amide I) and $\nu^{as}_{COO^-}$ (figure 1.2). This is explained by the presence in the unit cell of molecules of Gly-Ser that are almost perpendicular to each other (scheme 2b). Elimination of the 1555 $cm^{-1}$ peak (figure 3) caused the disappearance of that at 721 $cm^{-1}$; these are assigned to $\delta_{NH}$ (Amide II) and $\delta_{C=O}$ (Amide IV) as a result of their co-linearity (scheme 2a).

Comparison of the IR spectra (figures 1.1 and 2.1) of the ligand and the Au(III) complex gives the following main differences. The 3300 $cm^{-1}$ peak ($\nu_{NH}$) disappears and $\nu_{OH}$ shifts to 3490 $cm^{-1}$ in the complex. The relatively high frequency of the latter points to the absence of intermolecular OH interactions. The former is associated with coordination of the deprotonatedpeptide to Au(III) via the amide N atom. New peaks at 3345, 3210 and 3100 $cm^{-1}$ in the complex are typical of $\nu^{as}_{NH2}$ and Fermi-resonance splitting of $\nu^{s}_{NH2}$ of the primary $NH_2$ group, when asymmetric HNH···X interactions are present [20]. The disappearance of all bending ($\delta_{NH3^+}$) maxima of $NH_3^+$ group in the 1700–1400 $cm^{-1}$ region and observation of $\delta_{NH2}$ at 1681 $cm^{-1}$ is consistent with coordination to Au(III) by $NH_2$. The fact that the $\nu_{C=O}$ (Amide I) peak is significant shifted to low frequency and $\delta_{NH}$ (Amide II) disappears in the IR spectrum of the complex means that the metal ion is coordinated through the amide N atom (scheme 3). The observation of $\nu_{C=O}$ at 1718 $cm^{-1}$ with the disappearance of $\nu^{as}_{COO^-}$ and $\nu^{s}_{COO^-}$ at 1515 and 1407 $cm^{-1}$ in the complex indicates coordination of the $COO^-$ group. Deprotonation of the –C(=O)–NH-amide group in the complex




Scheme 2. Orientation of Gly-Ser in the crystalline state.

causes the disappearance of $\gamma_{NH}$ and low frequency shifting of $\delta_{C=O}$ and $\gamma_{C=O}$ modes (table 1).

Elimination of the 1681 $cm^{-1}$ peak in the IR spectrum of the complex (figure 2.2) caused the disappearance of the 3210 and 3100 $cm^{-1}$ peaks assigned to $\delta_{NH2}$ and $\nu^{s}_{NH2}$, whose transition moments are co-linear in the frame of an $NH_2$ group (scheme 3). Simultaneous elimination of $\nu_{OH}$, $\nu_{C=O}$ and $\nu_{C=O}$ (Amide I) peaks at 3490, 1718 and 1645 $cm^{-1}$ in the reduced IR-LD spectrum of the complex indicates their mutual co-linear orientation (scheme 3; figure 2.3). As in the IR-LD spectra of the ligand alone, pairs of peaks at 3500, 1724 and 1650 $cm^{-1}$ arise. Co-linearity of $\nu_{C=O}$ and $\nu_{C=O}$ (Amide I) transition moments is not realized in an isolated but related molecules in a poorly ordered solid may be responsible for the effect. Similar data were obtained for other peptide systems [6–12].

### 3.2. *NMR data*

Significant differences between $^{1}H$- and $^{13}C$-NMR data for the dipeptide and the complex are evident and are consistent with IR-LD data with respect to coordination

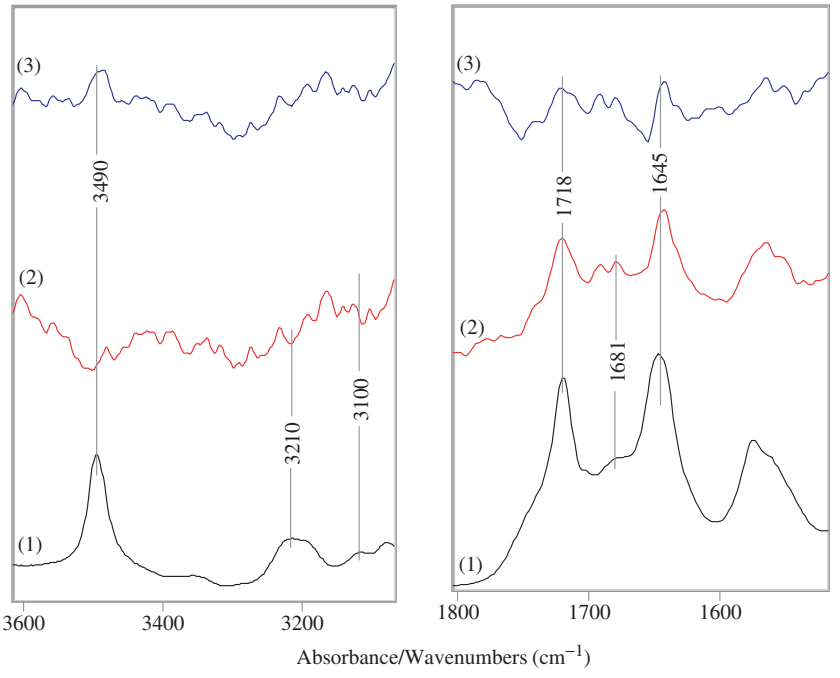
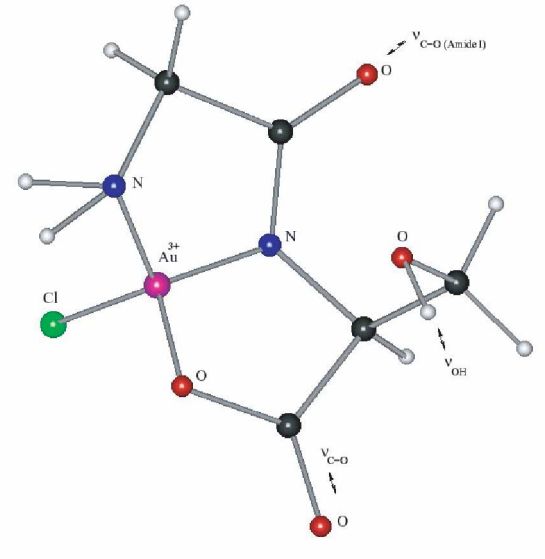



Figure 2. Non-polarized IR (1) and reduced IR-LD spectra of the Au(III) complex after elimination of peaks at 1681 (2) and 3490 cm$^{-1}$ (3).




Scheme 3. Proposed structure of the complex.

of Au(III) by $COO^-$, amide and $NH_2$ groups. $^1$H- and $^{13}$C-NMR spectra of Gly-Ser showed chemical shifts involving the glycyl fragment at 3.67 (d) ($CH_2$), 43.19 (*C*O) and 165.34 ppm ($CH_2$–). The chemical shift in $^{13}$C-NMR of $COO^-$ in the serine side chain is at 207.13 ppm. Data correlate well with those of similar glycyl and serine peptides [21–24]. The complex is characterized by the following changes. The glycyl ($CH_2$) signal is shifted to high field [4.02 ppm (m)] and *C*O and *C*$OO^-$ signals shift, respectively, to 57.61 and 179.13 ppm.

## 4. Conclusions

IR-LD spectroscopy based on orientation techniques, and $^1$H- and $^{13}$C-NMR data, have been used to predict the coordination geometry of the amorphous complex $[Au(C_5H_9N_2O_4)Cl]$. The dipeptide Gly-Ser coordinates as a doubly deprotonated tridentate via $NH_2$, $COO^-$ amide (N) groups. Square-planar geometry is completed by coordination of a $Cl^-$ ion.



## References

[1] J. Reedjik. *J. Chem Soc., Chem. Commun*., 801 (1996).
[2] D.B. Zambe, S.J. Lippard. *Trends Biochem. Sci*., **20**, 435 (1995).
[3] J. Reedjik. *Inorg. Chim. Acta*, **198**, 837 (1994).
[4] K.J. Barnham, M.I. Djuran, P. Del Soccoro Murrdoch, P.J. Sadler. *J. Chem. Soc., Chem. Commun*., 721 (1994).
[5] B.B. Ivanova, M. Mitewa. *J. Coord. Chem*., **57**, 217 (2004).
[6] B.B. Ivanova. *J. Coord. Chem*., **58**, 587 (2005).
[7] B.B. Ivanova, St.T. Todorov, M.G. Arnaudov. *J. Coord. Chem*. (In press).
[8] B.B. Ivanova, M.G. Arnaudov, S.T. Todorov, W.S. Sheldrick, H. Mayer-Figge. *Struct. Chem*., (In press).
[9] B.B. Ivanova. *Spectrochim. Acta, Part A* (In press).
[10] B.B. Ivanova, M.G. Arnaudov. *Spectrochim. Acta, Part A* (In press).
[11] B.B. Ivanova. *J. Mol. Struct*. (In press).
[12] B.B. Ivanova, Ts. Kolev, S. Zareva. *Struct. Chem*. (Submitted for publication).
[13] B.B. Ivanova, M.G. Arnaudov, P.R. Bontchev. *Spectrochim. Acta*, **60A**, 855 (2004).
[14] M.G. Arnaudov, B.B. Ivanova, S. Dinkov. *Vibr. Spectroscopy*, **37**, 145 (2005).
[15] J. Michl, E.W. Thulstrup. *Spectroscopy with Polarized Light. Solute Alignment by Photoselection in Liquid Crystals, Polymers and Membranes*, VCH Publishers, New York (1986).
[16] E.W. Thulstrup, H.H. Eggers. *Chem. Phys. Lett*., **1**, 690 (1996).
[17] B. Jordanov, R. Nentchovska, B. Schrader. *J. Mol. Struct*., **297**, 2922 (1993).
[18] B. Jordanov, B. Schrader. *J. Mol. Struct*., **347**, 389 (1995).
[19] C.H. Gorbitz. *Acta Crystallogr*., **55B**, 1090 (1999).
[20] M.G. Arnaudov, B.B. Ivanova, St.T. Todorov, S.I. Zareva. *Spectrochim. Acta, Part A* (In press).
[21] R.S. Dickins, A.S. Batsanov, J.A.K. Howard, D. Parker, H. Puschmann, S. Salamano. *J. Chem. Soc., Dalton Trans*., **1**, 70 (2004).
[22] T. Asakura, J.M. Yao. *Protein Sci*., **11**, 2706 (2002).
[23] R.N. Gursoy, D.S.S. Jois, T.J. Siahaan. *J. Pept. Res*., **53**, 422 (1999).
[24] P. Whiteman, A.K. Downing, R. Smallridge, P.R. Winship, P.A. Handford. *J. Biolog. Chem*., **273**, 7807 (1998).