

# Gold(III) Complex of Caffeine: Synthesis, Isolation and Spectroscopic Characterization

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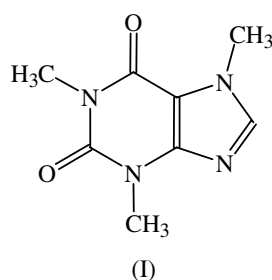
Received 01.02.2006

Au(III)-caffeine complex was synthesized and characterized by means of solid-state linear-dichroic infrared spectral analysis (IRLD),  $^1\text{H-NMR}$ , MS, DSC and TGA methods. The caffeine (*I*) is monodentate and coordinated with metal ion through its N9 atom at molar ratio metal to ligand 1:1. The other 3 positions in the Au(III) coordination sphere are occupied by  $\text{Cl}^-$ , thus forming  $[\text{Au}^{3+}(\text{C}_8\text{H}_{10}\text{N}_4\text{O}_2)\text{Cl}_3]$  complex. IR-characteristic band assignment in the  $4000\text{-}400\text{ cm}^{-1}$  IR region of pure ligand and corresponding Au(III) complex was performed.

**Key Words:** Caffeine, gold(III)-complex, IR-LD spectroscopy,  $^1\text{H-NMR}$ .

## Introduction

The metal complexes of purine and pyrimidine derivatives have been intensively studied because of their basic role in biochemical processes in the cell.<sup>1,2</sup> Binding of Ca(II) and Mg(II) cations to DNA and RNA as well as the Pt(II), Ru(II) and Au(III) metal ions, with a proposed antitumor effect, have been involved in some biological processes in vivo.<sup>3-6</sup> The study of the coordination ability of the last metals with purines and pyrimidines reveals in vitro the manner and mechanism of their coordination with DNA. Caffeine (3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione) could be used to examine the coordination ability on the N9 and O=(C6) positions as far as the N7 one is blocked by the  $-\text{CH}_3$  group (Scheme 1).<sup>3</sup> For these reasons, the present paper deals with the synthesis, and spectral and structural characterization of a new Au(III)-caffeine complex, applying the methods of  $^1\text{H-NMR}$ , MS and IRLD (IR spectral bands assignment and stereo-structural data) spectroscopies. The applicability of the last approach has been demonstrated already in a series of papers.<sup>7-10</sup>



## Experimental

### Synthesis

The Au(III) complex with caffeine [Au(III) (C<sub>8</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>)Cl<sub>3</sub>] was prepared as follows: 10 mL of methanol solutions of 0.0977 g of H<sub>2</sub>AuCl<sub>4</sub>·2H<sub>2</sub>O (Merck) and 0.0987 g of caffeine (Bachem Organics) corresponding to a molar ratio of methanol to ligand 1:1 are mixed. After 20 days, a yellow precipitation is formed, filtered, washed with methanol and dried over P<sub>2</sub>O<sub>5</sub> in air at 298 K. Yield: 22%. (Found: C, 19.26; H, 2.00; N, 11.32; Cl, 21.44%; Calc. for [Au(III) (C<sub>8</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>)Cl<sub>3</sub>]: C, 19.31; H, 2.03; N, 11.26; Cl, 21.38%). The most intensive signal in the mass spectrum of the protonated salt is the peak at *m/z* 496.51, characteristic of the singly charged [Au(III) (C<sub>8</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>)Cl<sub>3</sub>] cation with molecule weight 496.52. These data indicated the formation of mononuclear Au(III)-complex with caffeine at a molar ratio of metal to ligand 1:1.

### Methods

The IR spectra were measured on a Bomem-Michelson 100 FTIR-spectrometer (4000-400 cm<sup>-1</sup>, 2 cm<sup>-1</sup> 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. The oriented solid samples were obtained with a suspension in a nematic 4'-cyano-4'-alkylbicyclohexyl mixture (ZLI 1695, Merck), while its poor IR spectrum allows the recording of the guest-compound bands in the whole 4000-400 cm<sup>-1</sup> range. The presence of an isolated nitrile stretching IR band at about 2230 cm<sup>-1</sup> additionally serves as an orientation indicator. The effective orientation of solid samples was achieved through the following procedure: 5 mg of the compound studied was mixed with the liquid crystal substance until a slightly viscous suspension was obtained. The prepared phase was placed between 2 KBr plates, which were rubbed out in advance in one direction. The grinding of the prepared mull in the rubbing direction promotes an additional orientation of the sample.<sup>7-10</sup>

The IRLD spectroscopy grounds and polarized IR-spectra interpretation for the difference-reduction procedure are shown in the literature.<sup>12-15</sup> The method consists of subtraction of a perpendicular spectrum, (IR<sub>s</sub>), 90° angle rotation between the polarized light beam electric vector and the orientation of the sample from a parallel one (IR<sub>p</sub>), obtained with a co-linear mutual orientation. The recorded difference (IR<sub>p</sub>-IR<sub>s</sub>) spectrum divided the parallel (A<sub>p</sub>) and perpendicular (A<sub>s</sub>) integrated absorbance of each band into positives, originating from transition moments that form average angles with the orientation direction (**n**) between 0° and 54.7°, and negative ones, corresponding to transition moments between 54.7° and 90°. After that, the perpendicular spectrum multiplied by the parameter *c* is subtracted from the parallel one and *c* has to vary until the elimination of a band or set of bands. The simultaneous disappearance of the bands in

the obtained ( $IR_p - cIR_s$ ) reduced IRLD spectrum indicates a co-linearity of the corresponding transition moments, thus giving rise to information regarding the mutual disposition of the molecular fragments. This elimination method is graphically carried out using a subtracting procedure attached to the program for the processing of IR spectra.

The  $^1H$ -NMR measurements were obtained at 298 K with a Bruker DRX-400 spectrometer using 5 mm tubes and  $D_2O$  as solvent. The chemical shift reference was sodium 3-(trimethylsilyl)tetradeuteriopropionate.

The elemental analysis was performed by standard procedures for C, H (as  $CO_2$ , and  $H_2O$ ), and N by Duma's method and Cl by titration with  $Hg(NO_3)_2$  after wet digestion of the sample. The FAB mass spectra for the molecule weight determination were recorded on a Fisons VG Autospect instrument employing 3-nitrobenzyl alcohol as a matrix.

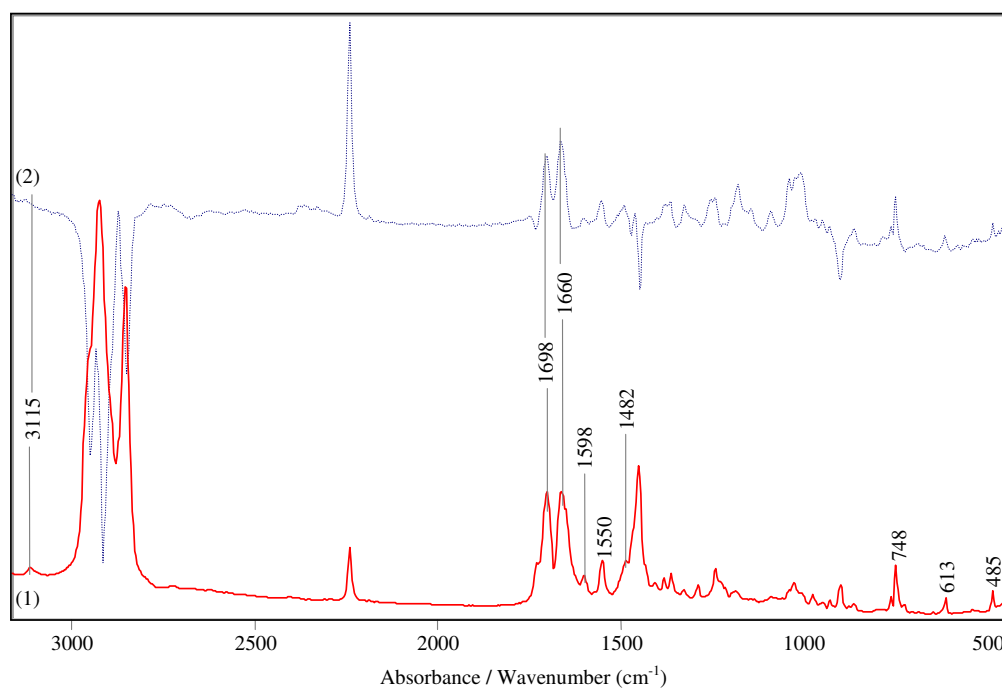
The thermogravimetric study was performed using Perkin-Elmer TGS2 apparatus. The calorimetric ones are performed on DSC-2C Perkin-Elmer equipment in argon.

## Results and Discussion

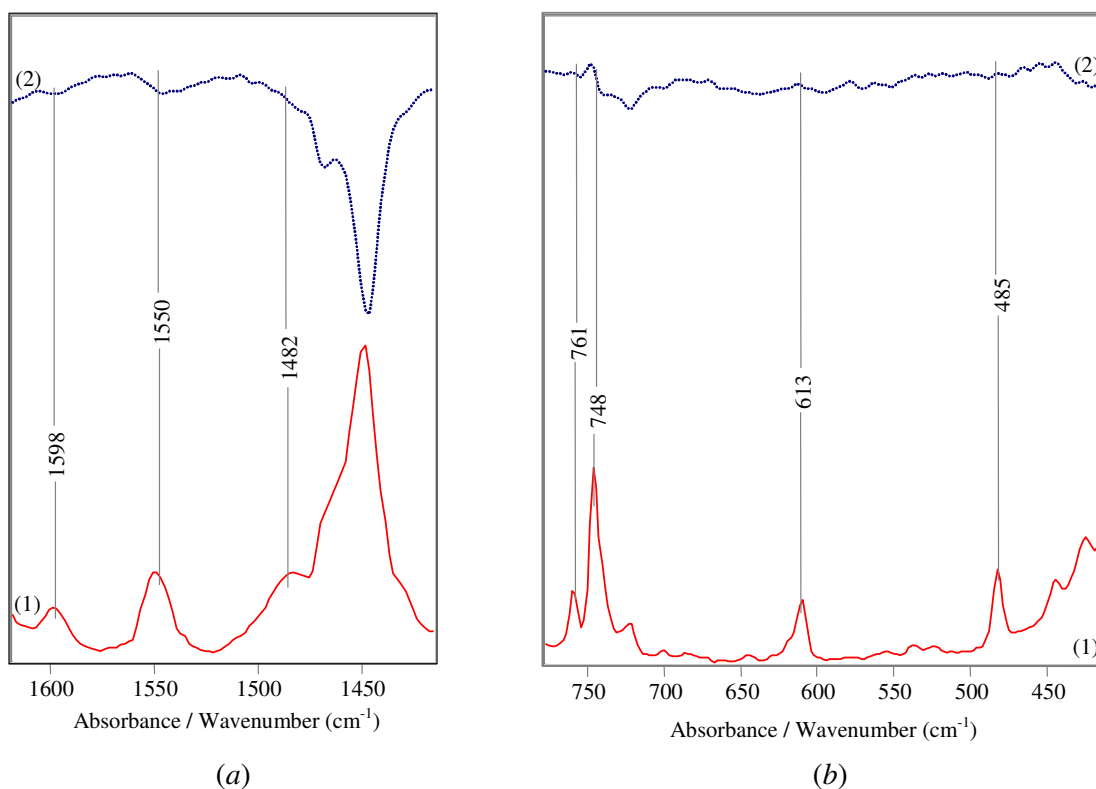
### IRLD spectral analysis of caffeine and its Au(III)-complex

The non-polarized IR-spectrum of caffeine (Figure 1.1) shows strong intensive peaks at 1698 and 1660  $cm^{-1}$  assigned as  $\nu_{C=O}$  and  $\nu_{C=O} + \nu_{ring(imidazole)}$  modes.<sup>15-17</sup> The multiple characters could be explained by crystal field splitting. The 1598 and 1550  $cm^{-1}$  peaks are assigned to  $\nu_{ring(imidazole)} + \nu_{ring(primidine)}^{16-18}$  and the 1482  $cm^{-1}$  one to  $\nu_{C=N(imidazole)}$ . The observed maxima at 761 and 748  $cm^{-1}$  correspond to  $\gamma_{ring}$  (out of plane) +  $\delta_{C=O}$  (in plane) and  $\gamma_{ring}$  modes.<sup>16-18</sup> The other relatively intensive maxima at 613 and 485  $cm^{-1}$  should be assigned to  $\gamma_{ring}$  and  $\gamma_{C=O}$ , both out-of plane maxima. The application of the reducing-difference procedure for polarized IRLD spectra interpretation experimentally assigned and revealed the character of the corresponding peaks. The elimination of the relatively intensive  $\nu_{CH}$  peak at 3115  $cm^{-1}$  (Figure 1.2) does not provoke the vanishing of in-plane (i.p.) ring maxima (see below), similarly observed in other symmetric substituted heterocyclic derivatives,<sup>19</sup> thus indicating the deviation of the main i.p. (ring) mode axis (*II*).

The simultaneous disappearance of 1598, 1550 and 1482  $cm^{-1}$  maxima (Figure 2.(a).2) confirmed their  $\nu_{ring}$  assignment. The elimination of the 761  $cm^{-1}$  peak (Figure 2.(b).2) lead with peaks at 748, 613  $cm$  and 485  $cm^{-1}$  proved their out-of-plane origin. The reduction of all of the multiple components in the 1700-1650  $cm^{-1}$  region confirmed their origin as crystal field splitting bands.

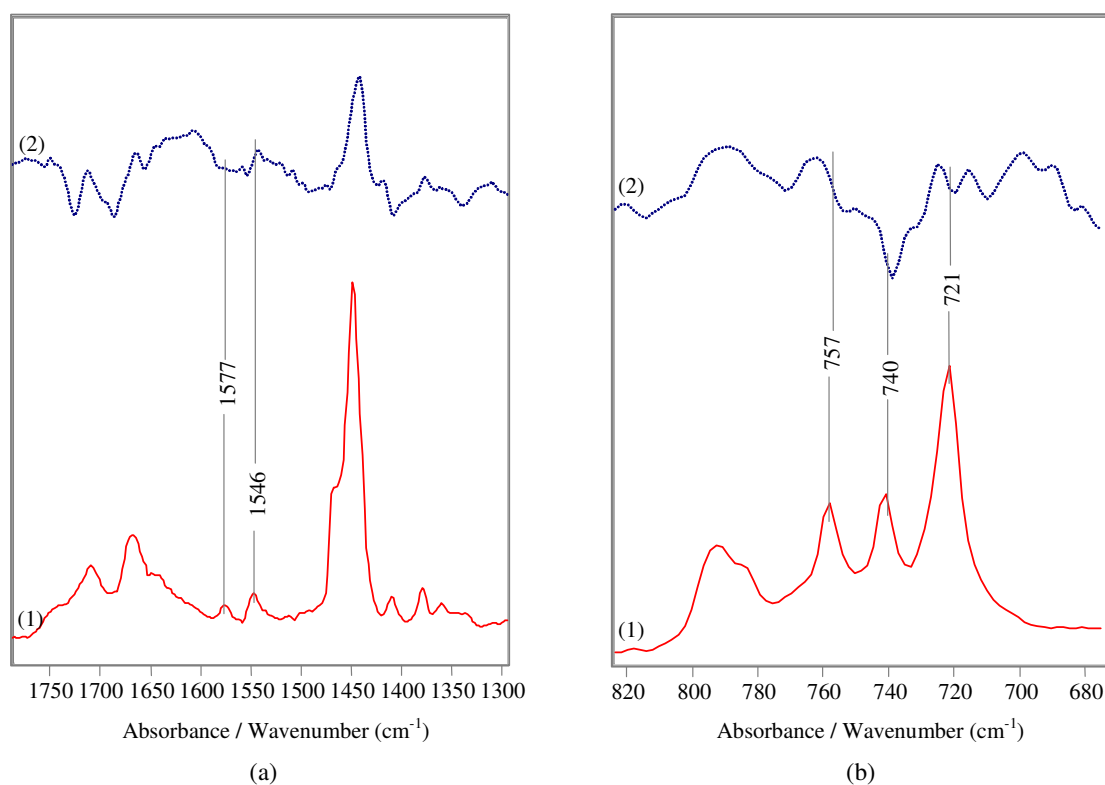


**Figure 1.** Non-polarized IR-(1) and reduced IR-LD (2) spectrum of caffeine after elimination of the  $3115\text{ cm}^{-1}$  peak.

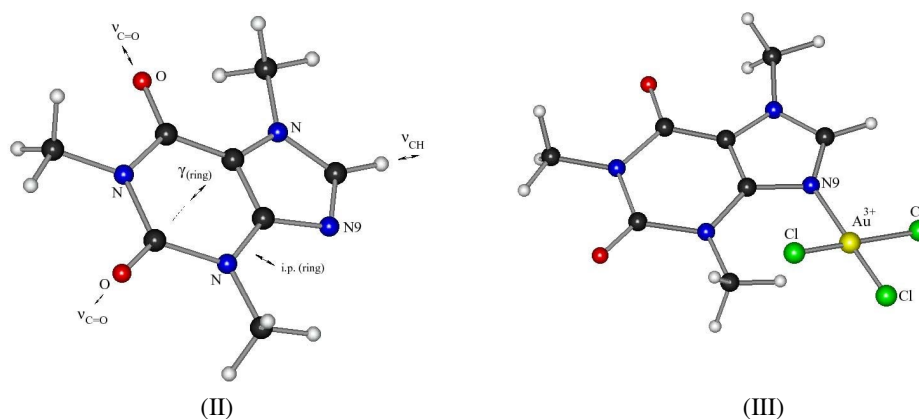


**Figure 2.** Non-polarized IR (1) and reduced IR-LD (2) spectra of caffeine after elimination of the peaks at (1)  $1598\text{ cm}^{-1}$  and (2)  $748\text{ cm}^{-1}$ .

The IR spectrum of the Au(III)-caffeine complex (Figure 3.1) is characterized by insignificant high frequency shifting of pairs of  $\nu_{C=O}$  maxima to 1710 and 1666  $\text{cm}^{-1}$  with a keeping of their multiple character. Similar behavior has been observed in  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  complexes with caffeine,<sup>3</sup> but the changes cannot correspond to the participation of O=C groups in coordination with  $\text{Au}^{3+}$  ion. In our case, the significant changes were connected with the  $\nu$  ring in plane and  $\gamma_{(ring)}$  peaks after complexation (compared to Figures 1.1 and 3.1). The 1598 and 1550  $\text{cm}^{-1}$  maxima in the ligand (Figure 1.1) are low frequency shifted to 1577 and 1546  $\text{cm}^{-1}$  in the complex (Figure 3.1). The low-intensive peak of  $\nu_{C=N(imidazole)}$  in the ligand practically disappears in the complex. On the other hand, the 810-770  $\text{cm}^{-1}$  region of the IR spectrum of the complex is characterized by a series of peaks at 791, 757, 740 and 721  $\text{cm}^{-1}$ . These data assumed a monodentate coordination of caffeine through its N9 atom (*III*). A similar  $\text{Zn}^{2+}$ -complex has been obtained and crystallographically refined.<sup>20</sup> In addition, the peak at 3115  $\text{cm}^{-1}$  practically disappears in the corresponding complex. The IRLD analysis yields the following results: (i) The elimination of the 1577  $\text{cm}^{-1}$  peak (Figure 3.(a).2) with the 1546  $\text{cm}^{-1}$  one, both i.p. modes; (ii) The disappearance of the 757, 791 and 721  $\text{cm}^{-1}$  peaks (Figure 3.(b).2), all out-of-plane frequencies. (iii) Like in the IR spectrum of pure ligand the multiple character of the peak in the 1700-1600  $\text{cm}^{-1}$  region confirmed their crystal field splitting origin.



**Figure 3.** Non-polarized IR (1) and reduced IR-LD (2) spectra of Au(III)-caffeine complex after elimination of the peaks at (1) 1577  $\text{cm}^{-1}$  and (2) 757  $\text{cm}^{-1}$ .



### <sup>1</sup>H-NMR data

The <sup>1</sup>H-NMR spectrum of caffeine in D<sub>2</sub>O solution showed 4 relatively low intensive peaks at 3.30, 3.54, 3.90 and 7.76 ppm corresponding to the 3 CH<sub>3</sub>-groups and CH, respectively.<sup>21,22</sup> The analogous spectrum of the Au(III)-caffeine complex is characterized by peaks at 3.28, 3.77, 3.98 and 7.66 ppm.

### TGA and DSC data

The thermogravimetric and DSC data in the 300-500 K range indicated an absence of any solvent molecules included in the coordination spheres of obtained Au(III)-complex with caffeine.

### Conclusion

The application of mass spectral and elemental analysis data indicated a quantitative amount of new complex as [Au(III) (C<sub>8</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>)Cl<sub>3</sub>] (*III*) with a metal to ligand molar ratio 1:1. Both spectroscopic <sup>1</sup>H-NMR and IRLD data indicated a monodentate coordination of caffeine though N9 with metal ion. In addition, 3 Cl<sup>-</sup> anions are coordinated through Au(III), thus forming a square planar geometry of AuNCl<sub>3</sub> chromophore.

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