FT-IR and FT-Raman spectra of cimetidine and its metallocomplexes

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Abstract

We present vibrational spectra of three stable, well-reproducible, polymorphic forms of cimetidine (cim), a drug which is a powerful histamine H\(_2\)-receptor antagonist used in the treatment of peptic ulcer and the Zollinger–Ellison syndrome. Assignments of Raman and IR bands are made using semiempirical methods: MNDO, AM1 and PM3. We also describe the synthesis of Me(cim)\(_2\)(ClO\(_4\))\(_2\), where Me = Cu(II), Cd(II), Co(II) and Ni(II), and present their vibrational data. We show that the obtained complexes are isostructural, however a metal ion that occupies a center of octahedral unit introduces some distortions that can be seen in the spectra. We also make tentative assignment of metal–ligand stretching modes observed in low frequency range.

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Keywords: Cimetidine; Polymorphs; FT–IR; FT–Raman; Metallocomplexes

1. Introduction

\(N\)-cyano-\(N'\)-methyl-\(N''\)-2\([(5\text{-methyl-1-H-imidazol-4-yl})\text{thio}][\text{ethyl}]\text{guanidine, cimetidine (cim), developed and marketed by SmithKline and French, is a drug that has been used extensively as a powerful histamine H2-receptor antagonist in the treatment of peptic ulcer and the Zollinger–Ellison syndrome [1–3]. Its chemical formula together with the atomic numbering for convenience is shown in Fig. 1. The possible coexistence of polymorphs at certain temperature and pressure conditions has been of growing interest to pharmacists and chemists [4–10]. The extensive characterization of drug polymorphs is very important due to the relevance of crystal form to biological activity and due to the rheological properties of drug [11–14]. Sometimes, however, contamination of solvent molecules or amorphous phase has been taken mistakenly as different polymorphs because of their different crystal habits. Cim assumes different crystal forms depending on the solvent and method of crystallization. These polymorphs are formed through a variety of intra and/or intermolecular hydrogen bonds. For example, crystallization from aqueous solution under various conditions produces up to four polymorphs [15], while three other forms can be obtained by crystallization from organic or water/organic solvents [15,16]. However, it was found that two of these polymorphs can be well-reproduced during crystallization procedure only [15,17,18]. Hence, using similar crystallization conditions various cim polymorphic forms or their mixtures that often causes
confusion are obtained [15–27]. The crystal structure of these polymorphs was routinely characterized by powder X-ray analysis [4–10,15,16] as usually it was very difficult to grow suitable crystals. On the contrary, vibrational spectroscopy can be easily used to measure powder or polycrystalline samples for which even subtle changes in molecular structure can be detected [24]. To be more specific, changes in bond lengths as small as 0.001 Å can be detected. Somehow surprisingly, only few vibrational studies have been done on cim crystal forms thus far [15,16,21,25–27].

Cim is liable to coordinate to transition metal ions. Special interest has been devoted to its complexes with Cu(II), as a number of clinical observations supported the hypothesis that interaction of cim with copper ions played an important role in vivo [28–32]. Greenaway et al. [33] first reported X-ray, UV–vis, 1H and 13C NMR data on a “green” compound of copper-cimetidine complex. X-ray data on a single crystal showed that this complex, whose chemical formula can be written as Cu(II)(cim)2(ClO4)2, formed the cationic polymer in which Cu atoms occupied a crystallographic inversion center in the octahedral subunit. Additional data including magnetic moment, IR and EPR spectra were published few years later [34,35]. Then, it was shown that the crystal structure of Cu-cim complex could be modified by anion (ClO4−, NO3− versus SO42−) [36,37]. This structural modification was observed in Co(II) and Ni(II) cimetidine complexes for which some UV–vis, magnetic moment data and IR spectra were available [38–40]. Additionally, 1H NMR, spectrophotometric and potentiometric studies of zinc(II), platinum(II) and palladium(II) cimetidine complexes have been reported [41–43].

There is no single report that fully describes the vibrational properties of either the cim ligand or its metallocomplexes. In this work, we present FT-IR and FT-Raman spectra of three polymorphic forms of cim crystallized from aqueous, methanol and/or isopropanol solutions. Additionally, we present vibrational data of copper(II), cadmium(II), cobalt(II) and nickel(II) perchlorate complexes of cim. As expected from earlier works [38–40,44], the FT-IR and FT-Raman spectra clearly show that all the obtained metallocomplexes are isomorphous. However, the influence of the cation on the distortion of octahedral environment is seen. The vibrational analysis of two polymorphic forms of cim for which X-ray data are available [15,19–23] and Me(II) complex is done based on the semiempirical methods: MNDO [45], AM1 [46] and PM3 (or PM3 TM) [47–49]. Thus, the calculated vibrational modes are assigned to match the experimental data and are found to be in agreement with the characteristic group frequencies [50].

2. Experimental

2.1. Compounds

The polycrystalline sample of cim was supplied by “Jelfa” Pharmaceuticals (Jelenia Góra). The C1 polymorphic form was prepared by dissolving 0.5 g of cim in 15 cm3 of distilled water at 85°C. The solution was set aside in a beaker, allowed to cool to room temperature and then placed in a fridge (4°C). After two days, the polycrystals were filtered out and washed twice with cold distilled water. The C2 polymorph was obtained by dissolving 0.5 g of cim in 2.5 cm3 of hot isopropanol (72°C) and allowed to cool to room temperature in a covered beaker. The crystalline form was obtained by slow evaporation of solvent. The precipitated crystals were collected and washed with isopropanol. The same crystalline form, i.e. C2, was obtained from a hot (54°C) methanol solution, saturated with cim, that was poured over the
ice. The C\textsubscript{3} form was prepared by dissolving 0.5 g of cim in a hot methanol (54°C) and allowed to cool to room temperature in a covered beaker. All samples were dried and stored in a dessicator over P\textsubscript{2}O\textsubscript{5}.

The metallocomplexes were obtained by using the following procedure: to a hot (85°C) aqueous solution of cimetidine (0.1 g in 30 cm\textsuperscript{3}), an aqueous solution (2 cm\textsuperscript{3}) of metal perchlorate was added dropwise while the solution was stirred. A final concentration ratio of cim to metal ions was 2.5:1. Thus, the obtained solutions (pH about 6) were allowed to cool to room temperature in covered beakers. After being at room temperature for a couple of days, the precipitates were filtered out, washed carefully with redistilled water and dried in a dessicator over P\textsubscript{2}O\textsubscript{5}/CaO mixture.

2.2. Spectral measurements

For the FT-Raman measurements, few milligrams of cim polymorph sample was placed in a capillary tube and measured directly (180° geometry). The metallocomplexes were diluted with spectroscopic grade KBr by a factor of 10 (w/w), then transferred to a capillary and measured. Typically, 512 and about 6000 scans were collected for cim ligands and metallocomplexes, respectively, with a resolution of 4 cm\textsuperscript{-1}. FT-MIR and FT-FIR spectra were run in KBr and low molecular weight polyethylene discs, respectively, by using standard procedures of sample preparation for these measurements. 128 and 512 scans were accommodated for all samples in MIR and FIR regions, respectively. The resolution was set at 4 cm\textsuperscript{-1} for MIR and 2 cm\textsuperscript{-1} for FIR measurements.

The FT-Raman spectra were recorded on a Bio-Rad step-scan spectrometer model FTS 6000 combined with a Bio-Rad model FTS 40 Raman Accessory. Excitation at 1064 nm was used from a Spectra-Physics model Topaz T10-106c cw Nd:YAG laser. Power at the sample was maintained at 200 mW. The FT-FIR spectra were measured on a Bio-Rad spectrometer model FTS 60V, while a Bruker spectrometer model IFS 48 was used to run the FT-MIR spectra. Accuracy of frequency reading for all presented spectra was ± 1 cm\textsuperscript{-1}.

2.3. Calculations

Calculations were carried out using MOPAC 6.0 [51] parameterized for the semiempirical hamiltonians: MNDO [45], AM1 [46] and PM3 [47–49]. We used HyperChem 4.5 and SPARTAN (PM3 TM) [52] programs to calculate the vibrations in which metal ion is involved. First we optimized the geometry of the molecule and compared it with the available X-ray structure [15,19–23,38–40]. Then, we calculated the frequencies of all the vibrational modes, assuming C\textsubscript{1} group symmetry. Thus calculated vibrational modes were assigned to match against experimental data and additionally checked to be in agreement with the characteristic group frequencies [50]. The match between the calculated and experimental frequencies in most cases is within 5%. Here we discuss that tentative assignment of bands has to be taken as preliminary results and starting data for further calculations.

3. Results and discussion

3.1. Polymorphic forms of cimetidine

As discussed in Section 1, cim appears in several polymorphic forms but only a few of them are well-reproducible [15,19–23]. Even slight changes in crystallization conditions, sometimes not noticeable, produce different crystal forms or their mixtures in an unpredictable manner. In some cases, obtained structures are identical, however their crystal parameters of the unit cell are somewhat different [15,20–22]. Additionally, inconsistent nomenclature of the polymorphic forms used by different authors is very common and makes discussion and comparison among polymorphs somehow confusing. Hence, we

<table>
<thead>
<tr>
<th>Given symbols</th>
<th>Reference</th>
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<tbody>
<tr>
<td>A B C D –</td>
<td>[15]</td>
</tr>
<tr>
<td>A – H – B</td>
<td>[16]</td>
</tr>
<tr>
<td>I – IV II III –</td>
<td>[20]</td>
</tr>
<tr>
<td>A – C? – B?</td>
<td>[22]</td>
</tr>
<tr>
<td>C\textsubscript{2} – C\textsubscript{1} – C\textsubscript{3}</td>
<td>This work</td>
</tr>
</tbody>
</table>
collected some of the data in Table 1 that makes our discussion easier to follow.

During our extensive studies [53,54], we have found that only three polymorphs can be obtained as pure crystalline phases under certain conditions, as described in Section 2. This is in agreement with Prodić-Kojić et al. [22], who showed that one pure form of \textit{cim} can be crystallized from water and two other from methanolic and isopropanolic solutions, only. Thus, based on the IR spectra, our C\textsubscript{1} form corresponds to form II of Prodić-Kojić et al. [22] and C\textsubscript{2} form is an anhydrous form of cimetidine reported as form I [22] and A [15]. We failed as others [15,22] to obtain four polymorphic forms from aqueous solution, as was reported by Shibata et al. [15]. By changing the \textit{cim} concentration in a wide range (from 2 to 150 mg/cm\textsuperscript{3}) and using various crystallization conditions, we were able to obtain only one pure form. This form corresponds to form C reported by Shibata et al. [15], that appeared to contain water molecule in the structure. In other cases we produced mixtures of different forms as reported by other authors as well [15,16,22]. Further, our FT-Raman spectra in the range of 500–800 cm\textsuperscript{-1} (data not shown) of C\textsubscript{1}, C\textsubscript{2} and C\textsubscript{3} forms are practically identical with those published for H, A, and B forms, respectively [16]. However, comparison of our data of C\textsubscript{1} form with H form of Jalovszky et al. [16] show that their H form is contaminated, most probably, with D form. This is based on the careful examination of Raman spectra of these forms and observation of two reminiscent bands of D form at 651 and around 740 cm\textsuperscript{-1} in the Raman spectrum of H form. In our case both these bands are missing in the Raman spectrum of C\textsubscript{1} form.

Figs. 2 and 3 show the FT-Raman and FT-IR spectra of three polymorphic forms of cimetidine: C\textsubscript{1}, C\textsubscript{2} and C\textsubscript{3}. The figures illustrate the vibrational modes of the cimetidine molecules in the different forms.
spectra, respectively, of three polymorphic forms of cim: C₁, C₂ and C₃ in the 1000–1700 cm⁻¹ range. Tudor et al. [25], while investigating Raman spectra of their three polymorphs that they named A, B and C, pointed out that the 1050–1250 and 1300–1500 cm⁻¹ regions were very useful to distinguish between these polymorphs. However, their spectra are not of high quality and many of the observed bands are not very well resolved due to low resolution of measurement conditions. Comparing the obtained Raman spectra with those of Tudor et al. [25], we can conclude that the spectrum of C₂ form resembles that of A, but our Raman spectra of C₁ and C₃ do not match well with those of polymorphs B and C.

As seen in Fig. 2, all the Raman spectra are quite complex and different in many features. Careful inspection of this figure allows us to find analytical bands that are unique for these forms. Thus, the Raman bands at 1084, 1194 and 1360 cm⁻¹ for C₁; 1094, 1202 and 1348 cm⁻¹ for C₂ and 1116, 1183 (doublet) and 1345 cm⁻¹ (doublet) for C₃ form can be used to identify a proper polymorph. This is in addition to the analytical bands suggested by Jalsovszky et al. [16] in the 500–800 cm⁻¹ range.

Similarly, analytical IR bands for the crystalline phases discussed here can be easily picked up in Fig. 3: 1057, 1084 and 1360 cm⁻¹ for C₁; 1078, 1158, 1202 and 1348 cm⁻¹ for C₂; and 1065 and 1183 cm⁻¹ for C₃ form. Also, Prodić-Kojić et al. [22] proposed several IR bands, that according to them are characteristic of the discussed polymorphs. Surprisingly, they listed several bands that are common for at least two phases, like 1500 and 1460 cm⁻¹ (phases I and II) or 1485, 1430 and doublet at 1370 cm⁻¹ (phases III and IV).

However, the best “fingerprint” region that show clear differences among all cim polymorphs is the 2100–2200 cm⁻¹ range, where the C≡N stretching vibrations appear [50]. This vibration is observed in the vibrational spectra with exactly the same frequency (Raman/IR frequency coincidence) at 2153, 2176 and 2166 cm⁻¹ (only Raman data are shown later in the paper in Fig. 5) for C₁, C₂ and C₃ forms, respectively. On the contrary, Tudor et al. [25] reported the Raman and IR frequencies of the ν(C≡N) vibrations that differ as much as 9–10 cm⁻¹ for the same compound. These demonstrate the existence of two non-equivalent CN groups in crystal structure or dipole–dipole interaction between two adjacent CN groups.

Based on the available crystal structures of C₁ and C₂ forms [15,19–23], we were able to calculate the frequencies and suggest tentative assignments of cim vibrational modes. Table 2 list the experimental and calculated IR and Raman frequencies of some characteristic bands of C₁ form only (data for C₂ form are not shown). Proposed assignment, shown in the last column of the table, is made by using AM1, PM3 and MNDO semiempirical methods and agrees well with the characteristic group frequencies. Also, our assignment agrees very well with that suggested by Bueno and Sabrinho [27], showing that despite the imperfections of the semiempirical methods to study such complex, non-rigid molecules, some clear-cut results can be obtained. It has to be emphasized that in most

![Fig. 4. FT-IR spectra of Me(cim)₂(ClO₄)₂, Me = Cu(II), Co(II), Cd(II), Ni(II), Fe(II) and Zn(II).]
cases the calculated frequencies differ from the experimental frequencies by less than 5%. It is also clear, from Table 2, that PM3 method is the most accurate method among those used in our calculations.

Our results show that the most prominent changes observed in the vibrational spectra (Figs. 2 and 3) are those associated with chain vibrations. All the analytical bands discussed earlier in the paper are due to either $\delta(C_{\text{I}}\text{–H})$ of methylthioethyl fragment or $\nu(N_{13}\text{–C}_{14})$, $\nu(N_{13}\text{–C}_{12})$ and $\delta(N_{1\text{r}}\text{–H})$ of amidine group and not imidazole vibrations [55,56]. This is as expected since the spatial orientation of amidine side chain with respect to the imidazole ring depends on the conformation of methylthioethyl chain. As was shown, this conformation is different in all cim polymorphs [15,19–23] and its model compounds [57] and strongly influences biological activity of the drug.

### Table 2

Experimental and calculated IR and Raman of some characteristic frequencies and their assignment by using semiempirical methods (C\text{1 crystal form of cimetidine})

<table>
<thead>
<tr>
<th>IR</th>
<th>R</th>
<th>AM1</th>
<th>PM3</th>
<th>MNDO</th>
<th>Assignment</th>
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<tr>
<td>2153</td>
<td>2153</td>
<td>2499</td>
<td>2390</td>
<td>2524</td>
<td>$\nu(C_{16}\text{–N}_{17})$</td>
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<tr>
<td>1592</td>
<td>1592</td>
<td>1760</td>
<td>1689</td>
<td>1851</td>
<td>$\nu(C_{12}\text{–N}_{13})$</td>
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<tr>
<td>1498</td>
<td>1498</td>
<td>1610</td>
<td>1480</td>
<td>1695</td>
<td>$\nu(C_{12}\text{–N}_{11})$</td>
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<tr>
<td>1449</td>
<td>1449</td>
<td>1512</td>
<td>1460</td>
<td>1572</td>
<td>$\nu(C_{4}\text{–C}_{3})$</td>
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<tr>
<td>1360</td>
<td>1360</td>
<td>1404</td>
<td>1331</td>
<td>1415</td>
<td>$\nu(N_{13}\text{–C}_{14})$</td>
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<tr>
<td>1301</td>
<td>1301</td>
<td>1378</td>
<td>1378</td>
<td>1430</td>
<td>$\delta(C_{6}\text{–H})$</td>
</tr>
<tr>
<td>1374</td>
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<td>1284</td>
<td></td>
<td>1434</td>
<td>$\delta(C_{10}\text{–H})$</td>
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<tr>
<td>1370</td>
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<td>1434</td>
<td>$\delta(C_{14}\text{–H})$</td>
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<td>1278</td>
<td>1278</td>
<td>1340</td>
<td>1257</td>
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<td>$\delta(C_{9}\text{–H})$</td>
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<td>1383</td>
<td>$\delta(C_{7}\text{–H})$</td>
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<td>1071</td>
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<td>$\delta(C_{6}\text{–H})$</td>
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3.2. Metallocomplexes of cimetidine

In a green complex, Cu(cim)$_2$(ClO$_4$)$_2$, copper(II) ion occupies a crystallographic inversion center in the octahedral subunit [33,34]. In this structure, cim acts as a bidendate ligand through $N_{\text{imidazole}}$ and $S_{\text{ether}}$ atoms. Two other $N_{\text{nitrile}}$ atoms from two neighboring cim molecules coordinate as axial ligands to fulfill an octahedral environment around Cu(II) ion and form the cationic polymer. Perchlorate anions, placed in the polymer network, act as counter ions to balance the positive charge of the Cu(II) ions.

The IR spectrum of Cu(cim)$_2$(ClO$_4$)$_2$ in the range of 1000–1700 cm$^{-1}$ is shown in Fig. 4 together with Cd(II), Co(II) and Ni(II) complexes. What is immediately seen from the figure is that all the spectra are identical. This shows that all the studied metallocomplexes are isostructural and there is only slight
influence of the metal ion on the structure of the complex that will be discussed further in the paper. Moreover, the pattern of the IR bands of these metallocomplexes is different from the respective patterns recorded for any of the polymorphic forms presented in Fig. 3. This should be obvious as after coordination to metal ion, free chain of cim ligand anchors to the metal center and becomes “more rigid” as it assumes a certain position dictated by coordination. In such a structure, torsional and dihedral angles of the chain appear to be almost the same in all the studied metallocomplexes. However, careful inspection of Figs. 3 and 4 shows that the IR pattern in the 1350–1650 cm\(^{-1}\) range of metallocomplexes is very similar to the C\(_3\) polymorph. In this range characteristic doublet is assigned to the imidazole vibration (higher frequency) and \(\nu(C_{12}-N_i)\) of the aminidine group [54]. This is in agreement with Sancho et al. [34] who assigned the band at 1605 cm\(^{-1}\) to the imidazole asymmetric C=N–C=C stretching vibration. They assigned the stretching C=N–C=C vibration of the imidazole fragment to the band at 1440 cm\(^{-1}\). Our calculations show, however, that this band is mainly due to \(\nu(C_4-C_5)\) mixed with \(\delta_{ip}(C_4-H)\), \(\delta_{ip}(C_5-H)\) and \(\delta_{ip}(N_3-H)\), in agreement with the results obtained by Harada and coworkers [55,56]. Other bands in this range are mainly due to \(\nu(N_{13}-C_3)\), \(\nu(N_{11}-C_3)\) mixed with \(\delta_{ip}(N_{13}\ or \ N_{11}-H)\) and \(\delta_{ip}(C_4-H)\), where \(x = 6,10\) and 12. Surprisingly, \(\delta_{ip}(C_4-H)\), where \(x = 6.7\) and 9, are observed below 1250 cm\(^{-1}\). The 1212 cm\(^{-1}\) band can be assigned to \(\nu(N_1-C_2)\) and \(\nu(N_3-C_2)\) mixed with \(\delta_{ip}(N_3-H_{19})\) of the imidazole ring.

Fig. 5. FT-IR and FT-Raman spectra of polymorphic forms of cimetidine (C\(_1\), C\(_2\), C\(_3\)) and metallocomplexes Me(cim)\(_2\)(ClO\(_4\))\(_2\), Me = Cu(II), Co(II), Cd(II), Ni(II), in the range of the \(\nu(CN)\) vibrations.
The metallocomplexes studied here also show two broad and complex bands at around 1095 (Fig. 4) and 630 cm\(^{-2}\) (not shown). These bands are assigned to \(\nu_3\) and \(\nu_4\) of the ClO\(_4\)\(^-\) anion, respectively \[58\]. Observation of all four vibrations of this anion, expected in the Raman spectra \[54\], confirms that the ClO\(_4\)\(^-\) anion retains T\(_d\) symmetry in these complexes. The \(\nu_{(CN)}\) vibrations is found at 2171 cm\(^{-1}\) for Cd(II), 2188 cm\(^{-1}\) for Cu(II) and Co(II), and 2194 cm\(^{-1}\) for Ni(II) complexes as shown in Fig. 5. However, Borras and coworkers \[34,36\] reported that the \(\nu_{(CN)}\) frequency was the same for Me(cim)\(_2\)(ClO\(_4\))\(_2\) complexes, where Me stands for Co(II), Ni(II) and Cu(II), and was located at 2200 cm\(^{-1}\). It has to be emphasized that there is a coincidence in frequency of the \(\nu_{(CN)}\) vibration in Raman and IR spectra as expected for the molecule with C\(_1\) group symmetry. Thus, this vibration is observed at the same frequency in both spectra. Observation of only one \(\nu_{(CN)}\) indicates that both CN bonds have the same bond lengths upon ligation to a central metal ion, implying that two metal–CN bonds also have the same bond length. As also seen in this figure, the \(\nu_{(CN)}\) frequency increases compared to the corresponding vibration of C\(_1\) and C\(_3\) polymorphic forms (left side of Fig. 5). This behavior is expected, as upon coordination to metal center electron density on the CN \(\pi^+\) antibonding orbital decreases concomitantly, thereby strengthening the C≡N bond \[58\]. Thus, the high frequency of \(\nu_{(CN)}\) of C\(_2\) form, i.e. 2176 cm\(^{-1}\), indicates that the CN group of this polymorphic form is involved in strong hydrogen bonding that is in agreement with crystallographic data \[15,22\]. Additionally, this vibration is observed at 2172 cm\(^{-1}\) in 0.1 HCl aqueous solution that is consistent with the involvement of CN group in hydrogen bonding.

The FT-IR spectra of Me(cim)\(_2\)(ClO\(_4\))\(_2\), where Me = Cu(II), Cd(II), Co(II) and Ni(II), in the 100–500 cm\(^{-1}\) range are shown in Fig. 6. In general, this region should provide direct information about the structure and bonding of the metal–ligand (M–L) linkage. However, often it is difficult, or in many cases impossible, to assign unequivocally M–L vibrations due to the appearance of ligand deformation vibrations in the same ranges. Also, the presence of a strong mixing or vibrational coupling between M–L and ligand deformation modes can complicate the definitive assignments of bands appearing in the low-frequency spectra to certain vibrations. Additional complication in the solid state spectra can be caused by the appearance of the lattice modes. The obvious choice in assigning M–L vibrations in the simple coordination compounds is to use metal isotopes as the magnitude of metal isotope–ligand shift for pure vibration is of the order of 2–10 for stretching and up to 2 cm\(^{-1}\) for bending modes \[58\]. However, when a metal ion occupies the center of highly symmetrical units, it practically does not move during the symmetric stretching vibrations and no metal isotope shift is expected. Additionally, if several different donors, like in our case coordinate the metal ion, isotope ligand labeling is necessary in order to distinguish between different M–L stretching vibrations.

As seen in Fig. 6, the IR band pattern of Co(II) and Ni(II) complexes is practically the same, however,
almost all IR bands of Ni(cim)$_2$(ClO$_4$)$_2$ are elevated by few wavenumbers compared to those of Co(II) compound. Also, the IR spectrum of Cu(cim)$_2$(ClO$_4$)$_2$ resembles that described above. By contrast, the IR spectrum of Cd(II) complex is slightly different, but careful examination of the figure shows that all these bands have their counterpart that can be found in IR spectra of Cu(II), Co(II) and Ni(II) complexes. These data clearly show that all these compounds are isostructural, however, central metal ion introduces some distortion of the octahedral unit, which is in agreement with the crystallographic data [34–37].

There is no direct correlation between the mass of the metal ion and the IR frequencies observed in this region. This observation points out that M–L vibrations mix strongly with deformation modes of the ligand, as expected. Our calculations performed for few selected M–L modes show that the metal isotope shift expected for $^{63}$Cu/$^{65}$Cu will be of the order of 0.2–0.4 cm$^{-1}$ due to mode mixing (vide supra). Hence, we gave up to make metal isotope labeling complexes, as these experiments would be too expensive and the predicted isotope shifts too small to be observed. Our calculations suggest that bands at 450 cm$^{-1}$ have substantial participation from metal–CN stretching vibration (coordination through the cyano nitrogen). Surprisingly, Sancho et al. [36] assigned the IR band at 450 cm$^{-1}$ in Me(cim)$_2$(ClO$_4$)$_2$ complexes to the $\nu$(C–S) vibration changing their previous assignment [34], where they observed the $\nu$(C–S) mode at around 700 cm$^{-1}$. The latter assignment is in agreement with our calculations as well as other available data on a free ligand [25,27,53,54]. The bands at 300–350 cm$^{-1}$ are strongly influenced by $\nu$(metal–S), while the bands below 300 cm$^{-1}$ can be assigned to $\nu$(metal–N) mixed with deformation modes. The $\nu$(metal–N$_{imidazole}$) is probably observed at around 200–230 cm$^{-1}$. More extensive studies by using DFT methods are currently in progress in our laboratory. However, these calculations are expensive and time consuming.

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