Structural features and *in silico* prediction of the biological properties of a pyrazole-based coordination complex

Amani Direm 1,*, Brahim El Bali 2, Koray Sayin 3, Mohammed S. M. Abdelbaky 4, and Santiago García-Granda 4

1 Laboratory of Structure, Properties and Interatomic Interactions LASPI2A, Department of Matter Sciences, Faculty of Sciences and Technology, Abbes Laghrour University Khenchela, 40.000 Algeria. ORCID : 0000-0002-6347-9173;

2 Independent scientist, Oujda, Morocco; ORCID : 0000-0001-6926-6286.

3 Department of Chemistry, Faculty of Science, Cumhuriyet University 58140 Sivas – Turkey;

4 Departamento de Química Física y Analítica, Universidad de Oviedo-CINN, 33006 Oviedo, Spain.

* Corresponding author: amani_direm@yahoo.fr
Structural features and *in silico* prediction of the biological properties of a pyrazole-based coordination complex

Graphical Abstract
Abstract:
A pyrazole-based Co(II) complex, was synthesized and structurally characterized using single-crystal X-ray diffraction which showed that it crystallizes in the monoclinic C2/c space group with discrete [CoPz4Cl2] units held together via intra- and intermolecular hydrogen bonds. The structure was optimized, the MEP maps were obtained and the NLO properties estimated. Additionally, the optical properties were measured at room temperature by means of optical UV-visible absorption and photoluminescence spectroscopy, and the complex presented π→π*, n→π*, d→d and ligand-field transitions resulting in a predominant bright red photoluminescence. Furthermore, an in silico study was carried by estimating the binding ability of the cobalt complex with Staphylococcus aureus tyrosyl-tRNA synthetase and Pyrococcus kodakaraensis aspartyl-tRNA synthetase.

Keywords: Pyrazole-based complex, crystal structure, photoluminescence, in silico study, molecular docking.
Introduction
Pyrazole derivatives have been widely studied for their applications as analgesic [1], antibacterial [2], anti-hyperglycemic [3], anti-inflammatory [4], antipyretic [5], hypoglycaemic [6] and sedative hypnotic agents [18]. For instance, celecoxib, rimonabant, fomepizole and sildenafil were reported to be selective drugs [7]. In fact, celecoxib demonstrated an anti-inflammatory effect and inhibited Cox-2 [8], whereas rimonabant is considered as a cannabixiod receptor and is used for obesity treatment. On the other hand, Bindenafil and fomepizole are known for inhibiting phosphodiesterase and alcohol dehydrogenase, respectively [9]. Additionally, some pyrazole derivatives have non-nucleoside HIV-1 reverse transcriptase inhibitory activities [10-13], their metallic complexes are active metallobiomolecules and have shown excellent antibacterial and antifungal efficiency [14-16]. In order to contribute to the enrichment of these systems study, we will discuss the synthesis of a pyrazole-based cobalt(II) complex [17] together with its structural and physical properties. Furthermore, an in silico study of the complex was performed in order to estimate its biological activity towards Staphylococcus aureus tyrosyl-tRNA synthetase and Pyrococcus kodakaraensis aspartyl-tRNA synthetase using molecular docking calculations.
Results and discussion

Synthesis

\[
\begin{align*}
4 \text{HNN} + \text{CoCl}_2 & \quad \overset{\text{CH}_3\text{OH, H}_2\text{O}}{\text{HCl, 60°C}} \quad \text{NNNNN} \\
\end{align*}
\]
Results and discussion

Crystal structure

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Space Group</td>
<td>C2/c</td>
</tr>
<tr>
<td>a (Å)</td>
<td>13.6170(1)</td>
</tr>
<tr>
<td>b (Å)</td>
<td>9.2934(5)</td>
</tr>
<tr>
<td>c (Å)</td>
<td>14.9550(1)</td>
</tr>
<tr>
<td>β (°)</td>
<td>117.920(1)</td>
</tr>
<tr>
<td>R[F² &gt; 2σ(F²)]</td>
<td>0.0424</td>
</tr>
<tr>
<td>wR(F²)</td>
<td>0.0952</td>
</tr>
<tr>
<td>Δρ_{max}, Δρ_{min} (e Å⁻³)</td>
<td>0.36, –0.30</td>
</tr>
</tbody>
</table>
Results and discussion

Crystal structure
Results and discussion

Crystal structure

<table>
<thead>
<tr>
<th>D—H···A</th>
<th>D—H</th>
<th>H···A</th>
<th>D···A</th>
<th>D—H···A</th>
</tr>
</thead>
<tbody>
<tr>
<td>N2—H2N···Cl1\textsuperscript{ii}</td>
<td>0.86</td>
<td>3.05</td>
<td>3.739 (3)</td>
<td>139</td>
</tr>
<tr>
<td>N4—H4N···Cl1</td>
<td>0.86</td>
<td>2.53</td>
<td>3.138 (2)</td>
<td>129</td>
</tr>
<tr>
<td>C3—H3···Cl1</td>
<td>0.93</td>
<td>2.74</td>
<td>3.324 (2)</td>
<td>121</td>
</tr>
</tbody>
</table>
Results and discussion

Optimized structure

Quantum chemical calculations were performed by GaussView 5.0.9 [18] and Gaussian 09 AS64L-G09RevD.01 [19] programs, by using HF and B3LYP methods with 6-31+G(d)(LANL2DZ) mix basis sets in gas phase.
Results and discussion

Optimized structure

Bond Lengths in HF Method

\[ y = 0.9917x \]
\[ R^2 = 0.7268 \]

Bond Lengths in B3LYP Method

\[ y = 1.0331x \]
\[ R^2 = 0.9348 \]

Bond Angles in HF Method

\[ y = 0.9998x \]
\[ R^2 = 0.9985 \]

Bond Angles in B3LYP Method

\[ y = 0.9998x \]
\[ R^2 = 0.998 \]
Results and discussion

MEP map

-4.920 \times 10^{-2} \quad +4.920 \times 10^{-2}
Results and discussion

SOMO and LUMO contour diagram

\[ E_{\text{GAP}} = 4.433 \text{ eV} \]
## Results and discussion

### Estimated NLO properties

<table>
<thead>
<tr>
<th>Compound</th>
<th>$E_{\text{HOMO}}$</th>
<th>$E_{\text{LUMO}}$</th>
<th>$I$</th>
<th>$A$</th>
<th>$E_{\text{GAP}}$</th>
<th>$\eta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co complex</td>
<td>-6.118</td>
<td>-1.685</td>
<td>6.118</td>
<td>1.685</td>
<td>4.433</td>
<td>2.216</td>
</tr>
<tr>
<td>Urea</td>
<td>-7.314</td>
<td>-0.372</td>
<td>7.314</td>
<td>0.372</td>
<td>6.942</td>
<td>3.471</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\sigma^b$</th>
<th>$\sigma_O^b$</th>
<th>$\chi^a$</th>
<th>CP$^a$</th>
<th>$\Delta N_{\text{Max}}$</th>
<th>$\alpha^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co complex</td>
<td>0.451</td>
<td>0.226</td>
<td>3.902</td>
<td>-3.902</td>
<td>1.760</td>
<td>245.662</td>
</tr>
<tr>
<td>Urea</td>
<td>0.288</td>
<td>0.144</td>
<td>3.843</td>
<td>-3.843</td>
<td>1.107</td>
<td>32.505</td>
</tr>
</tbody>
</table>

*a in eV  
b in eV$^{-1}$  
c in a.u.
Results and discussion

Optical properties

The 7th International Electronic Conference on Medicinal Chemistry
01–30 November 2021 | ONLINE
Results and discussion

Photoluminescence properties
Results and discussion

Molecular docking

Molecular docking calculations were done against *Staphylococcus aureus* tyrosyl-tRNA synthetase and *Pyrococcus kodakaraensis* aspartyl-tRNA synthetase by using Maestro 12.2 program [20-25]. The related proteins were selected from protein data bank web tool (*1JIL* [26] and *1B8A* [27]).

<table>
<thead>
<tr>
<th>Protein</th>
<th>Docking Score</th>
<th>van der Waals Energy</th>
<th>Coulomb Energy</th>
<th>Total Interaction Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1JIL</td>
<td>-2.690</td>
<td>-27.127</td>
<td>0.000</td>
<td>-27.127</td>
</tr>
<tr>
<td>1B8A</td>
<td>-3.072</td>
<td>-31.415</td>
<td>0.000</td>
<td>-31.415</td>
</tr>
</tbody>
</table>
Results and discussion

Molecular docking

1JIL
Results and discussion

Molecular docking
Conclusions

The X-ray crystal structure of the pyrazole Co(II) complex showed the presence of weak inter- and intramolecular N—H···Cl and C—H···Cl hydrogen bonds. The optimized structure results showed a very good agreement with the experimental ones and the molecular electrostatic potential maps exhibited the complex active regions. The analysis of the optical properties of the cobalt complex investigated at room temperature using optical absorption UV-visible and photoluminescence spectroscopy showed its interesting photoluminescence behavior with a particular bright red relaxation. The estimated NLO properties suggested that the complex could be a candidate for NLO applications. On the other hand, the molecular docking calculations showed that the material displays an inhibition activity against *Pyrococcus kodakaraensis* aspartyl-tRNA synthetase.
References

Acknowledgments

The financial support from Abbes Laghrour University of Khenchela (Algeria), TUBITAK ULAKBIM, High Performance and Grid Computing Center (TR-Grid e-Infrastructure), Spanish MINECO (MAT2016-78155-C2-1-R), Gobierno del Principado de Asturias (GRUPIN-IDI/2018/000170) are acknowledged. This work is supported by the Scientific Research Project Fund of Sivas Cumhuriyet University under the project number RGD-020.