SYNTHESIS AND CHARACTERIZATION OF PT(II) COMPLEXES FOR ANTICANCER THERAPY

Mihaela A. Ciulei, McNair Scholar, Nutrition Sciences Major
Dr. Pradip K. Bhowmik, Department of Chemistry and Biochemistry

Introduction

The first platinum-based drug was discovered and approved by Food and Drug Administration (FDA) in 1978 as cis-diaminedichloroplatinum (II) (cisplatin or CDDP). Cisplatin is used for about 50% of the chemotherapeutic cancer treatments along with its two analogues carboplatin and oxaliplatin. So far these drugs have been used extensively as treatments along with its two analogues carboplatin and oxaliplatin. Due to these limitations other compounds have been synthesized. Specifically, our lab in conjunction with a biochemistry lab has recently published one article in this area. This project is a continuation to the discovery of novel platinum compounds with increased effectiveness and low toxic side effects.

Objective

This project’s objective is to synthesize a series of platinum Pt(II) complexes, I-IV, which will be tested for testing in different cell lines for their therapeutic effects in biochemistry lab facilities.

The structure-activity relationship will provide a rational basis for the discovery of novel platinum compounds with increased effectiveness and low toxic side effects.

Methodology

Results

Table 1. Elemental Analysis for Complex I

<table>
<thead>
<tr>
<th>Compound</th>
<th>C%</th>
<th>H%</th>
<th>N%</th>
<th>Pt%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calc</td>
<td>44.31</td>
<td>5.58</td>
<td>10.90</td>
<td>4.31</td>
</tr>
<tr>
<td>Found</td>
<td>44.41</td>
<td>5.61</td>
<td>-</td>
<td>4.37</td>
</tr>
<tr>
<td>Δ</td>
<td>0.1</td>
<td>0.93</td>
<td>-</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 2. Elemental Analysis for Complex II

<table>
<thead>
<tr>
<th>Compound</th>
<th>C%</th>
<th>H%</th>
<th>N%</th>
<th>Pt%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calc</td>
<td>51.64</td>
<td>7.14</td>
<td>8.97</td>
<td>3.54</td>
</tr>
<tr>
<td>Found</td>
<td>51.24</td>
<td>7.10</td>
<td>-</td>
<td>3.80</td>
</tr>
<tr>
<td>Δ</td>
<td>0.4</td>
<td>0.04</td>
<td>-</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Figure 3. (a) 1H NMR spectra of ligand I (left) and Pt(II)-complex I recorded in CDCl3 at room temperature. (b) 13C NMR spectra of ligand I and Pt(II)-complex I recorded in CDCl3 at room temperature.

Figure 4. (a) 1H NMR spectra of ligand II (L-C12) and Pt(II)-complex II (Pt-C12) recorded in CDCl3 at room temperature. (b) 13C NMR spectra of ligand II and Pt(II)-complex II recorded in CDCl3, at room temperature.

Conclusions

- Platinum complexes I and II were synthesized via a three-step reaction: demethylation, Sn2 (alkylation), and preparation of the platinum complex by coordination chemistry. The products were characterized by using 13C NMR, and elemental analysis.
- Unlike small organic compounds, ligands 3 and 5 showed broad melting endotherms at 72 and 99 °C, respectively. In contrast, I and II showed multiple endotherms in the first heating cycle, but in the second heating cycle they showed melting transitions at 174 and 152 °C, respectively.
- Ligand I was synthesized by a three-step reaction: oxidation, reduction, and demethylation. Additionally, ligand D will be synthesized by a three-step synthesis: oxidation, reduction, and demethylation.

Acknowledgments

We acknowledge the McNair Scholar Institute, University of Nevada Las Vegas (UNLV) for financial support, and are sincerely thankful to Ondita Tantmannatham, Jung Jae Koh, Di Van Vo, and Dr. Haesook Han for their generous help during the execution of this project.

References