Characterisation of anticancer agents with Osmium's complex

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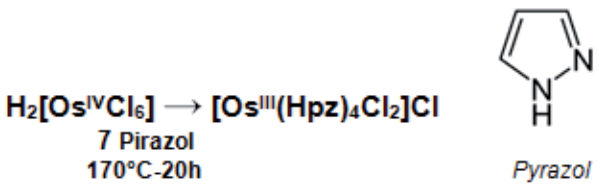
Introduction

A research project in Université Claude Bernard Lyon 1 tries to synthesize an osmium complex which contains the entity $[Os^{II}NO]^{3+}$ and at least four pyrazol heterocycles from the complex $H_2[Os^{IV}Cl_6]$. This complex is expected to have a very interesting antiproliferative activity against cancer cells due to the apoptosis property of the NO grouping and the bioactivation property of the pyrazol heterocycles. The research started with the substitution of four Chlorides from the complex $H_2[Os^{IV}Cl_6]$ with four pyrazoles and the characterization of the final complex with analytical methods.

Synthesis



In this reaction, seven equivalents of pyrazol were used. Indeed the synthesis needs four equivalents of pyrazol in order to substitute four chlorides, two others participate at the reduction of the $[Os^{IV}]$ to $[Os^{III}]$ and one more in excess which favors the reaction. The mixture of $H_2[Os^{IV}Cl_6]$ was boiled with seven equivalents of pyrazol at 170°C during twenty hours. After the end of the reaction the complex $[Os^{III}(Hpz)_4Cl_2]Cl$ crystallized as a red solid. An IR and a Mass Spectrometry analyses on positive mode were performed on the solid.

Analyses and results

- IR: The IR analysis was done with a FT-IR using the ATR mode. On the spectra (figure 1), a characteristic peak due to the N-H band (secondary amine) of the pyrazol is visible around 3300 cm^{-1}. The presence of two peaks around 1500 cm^{-1} (C=C) and 3126 cm^{-1} (C-H) demonstrates the presence of azole heterocycles. The band Osmium- pirazol is also visible with a peak at 570 cm^{-1}: Os-N.

- Mass Spectrometry : The mass spectrometry analyses were done in the positive ion-mode using an ESI source and a triple quadruple in the Q1MS mode. On the spectra (figure 2), four major ions are present. For our compound, an ion $[Os^{III}(Hpz)_4Cl_2]^+$ with a m/z at 534,0 Da was expected. This one is present on the spectra but with three other major peaks. One at 523.9 Da which corresponds to the ions $[Os^{III}(Hpz)_3Cl_2]Na+$, another at 1024.6 Da which corresponds to the multiple complex $[Os^3(Hpz)_3Cl_2][Os^{III}(Hpz)_3Cl_2]Na^+$, and the last one at 398.1 Da characteristic of the product ion $[Os^{III}(Hpz)_2Cl_2]^+$.

Figure 1: IR Spectra of Our compound
Figure 2: Mass spectra of our compound in positive Ion mode

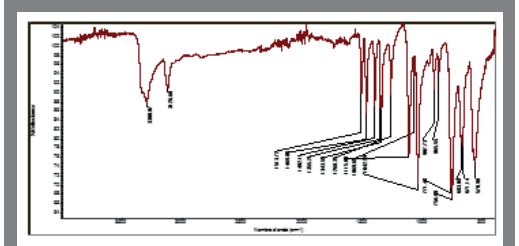


Figure 1

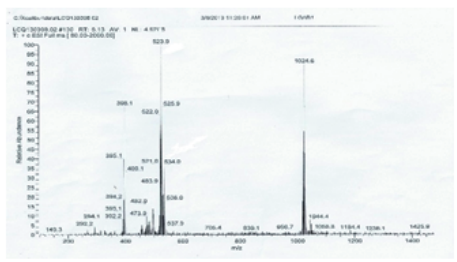


Figure 2

Conclusion

After this experimentation, the results demonstrate that the complex synthetized is not ready for the next step. Indeed, we have obtained a mixture of some Osmium's complex which contains three or four pirazoles and it is an obligation to have only four pirazoles on it. An improvement of the method is necessary. In order to make sure all the substitutions happen, the use of a bigger excess of pyrazol during the reaction is an option as much as the modification of the operational conditions during our synthesis (time and temperature of reaction,pH,matrix).

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