Synthesis and NMR Characterization of New tert-Butyl Thiosemicarbazone Compounds and Corresponding Palladium Complexes

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Abstract

This work shows the synthesis and characterization of a new series of tert-Butyl thiosemicarbazone compounds, based on the 4-tert-Butyl-3-thiosemicarbazide substrate. The corresponding palladium complexes of this series of ligands were obtained via a reaction with Palladium(II) Chloride. After synthesis and purification, the ^{1}H NMR and ^{13}C NMR spectra were obtained using a 500 MHz NMR spectrometer to give evidence for the structures of these new compounds.

Experimental

[1] I-tBTSC

The product was collected: 0.6082 g which provided a 83.30% yield.

[2] MeI-tBTSC

In a 125 mL Erlenmyer flask equipped with a magnetic stir bar on a heat/stir plate, 50 mL isopropanol and 0.2283g (2.171 x 10^{-3} mol) of 1-tert-Butyl-3-thiosemicarbazide was added to 0.5030g (2.019 x 10^{-3} mol) 1-methylisatin at approximately 60°C and 150 centrigrade. One drop of concentrated sulfuric acid was added to catalyze the reaction. The reaction mixture was left to stir heated for 48 hours. After gravity-filtration, a yellow precipitate was recovered and dried.The product was collected: 0.7814 g which provided a 78.49% yield.

[3] PhI-tBTSC

The product was collected: 0.619g which provided a 81.67% yield.

[4] [Pd(I-tBTSC)Cl]

The product was collected: 0.208g which provided at 57.50% yield.

[5] [Pd(MeI-tBTSC)Cl]

In a 25 mL Erlenmyer flask equipped with a magnetic stir bar on a heat/stir plate, 20 mL ethanol and 0.0541g (1.94 x 10^{-4} mol) of newly synthesized methylisatin-tert-butyl thiosemicarbazone was added to 0.037g (2.09 x 10^{-4} mol) palladium dichloride at approximately 60°C and 150 centrigrade. The reaction mixture was left to stir heated for 48 hours. After gravity-filtration, a red precipitate was recovered and dried. The product was collected: 0.0456g which provided 51.24 % yield.

[6] [Pd(PhI-tBTSC)Cl]

The product was collected:0.129g which provided a 81.65% yield

Apparatus

All spectra were obtained on a Bruker Ascend-500 Multi-Nuclear NMR spectrometer.

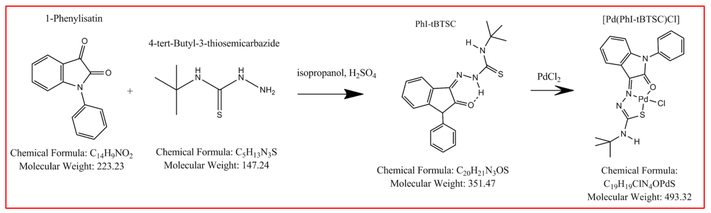

Figure 1. Synthesis of [Pd(PhI-tBTSC)Cl] characterized by the Bruker Ascend-500 Multi-Nuclear NMR Spectrometer.

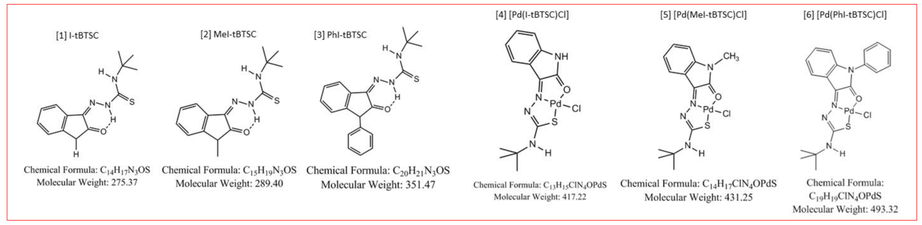

Figure 2. Structures of the Series of Compounds [1]-[6].

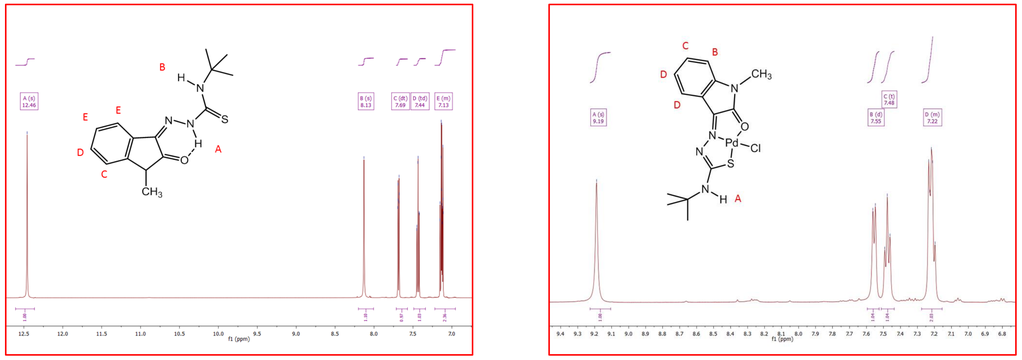

Figure 3. Downfield Portions of ^{1}H NMR Spectrum of MI-tBTSC and [Pd(MI-tBTSC)Cl]

Compound	Hydrazinic proton	Isatin Proton	Thioamide Proton	Aromatic Proton 1	Aromatic Proton 2	Aromatic Proton 3	Aromatic Proton 4	Tertbutyl protons
[Pd(PhI-tBTSC)Cl]	n/a	n/a	7.72 (d)	7.63 (dd)	7.42 (t)	7.28 (t)	6.87 (s)	1.44 (s)
PhI-tBTSC	12.46 (s)	n/a	8.24 s)	7.61 (m)	7.39 (td)	7.21 (t)	6.86 (d)	1.59 (s)
[Pd(I-tBTSC)Cl]	n/a	11.91 (s)	9.61 (s)	7.55 (d)	7.40 (t)	7.16 (t)	7.01 (d)	1.40 (s)
I-tBTSC	12.53 (s)	11.21 (s)	8.12 (s)	7.67 (dd)	7.35 (td)	7.07(d)	6.92 (d)	1.56 (s)
[Pd(MeI-tBTSC)Cl]	n/a	n/a	9.19 (s)	7.55 (d)	7.48 (t)	7.36 (m)	7.36 (m)	1.39 (s)
MeI-tBTSC	12.46 (s)	n/a	8.13 (s)	7.69 (dt)	7.44 (m)	7.14 (td)	7.12 (dt)	1.57 (s)

Table1. Important Downfield Resonances for the Six New Compounds

Results and Discussion

The synthesis shown in Figure 1. of these never-before-synthesized isatin tert-Butyl thiosemicarbazone ligands and metal complexes [1]-[6] goes into completion with huge success through the procedure stated in the experimental section. The yield of these products are relatively high and clean. The cleanliness of the newly synthesized compounds is shown through the Nuclear Magnetic Resonances. Since there is not enough room on this poster to include the NMR spectra for every compound in the series, we focused on compound [2], Methylisatin tert-Butyl-thiosemicarbazone, and it's metal complex, Palladium Methylisatin tert-Butyl-Thiosemicarbazone Chloride, to show results of the experiment. Figure 1. displays the synthesis of [6] [Pd(PhI-tBTSC)Cl]. Figure 2. shows the structures of all complexes [1]-[6] that were synthesized in this research. Figure 3. shows the ^{1}H NMR spectrum of compound [2] and compound [5] with several of the protons labeled with a structural representation. Table 1. includes the NMR condensed data collected from each compound [1]-[6] spectras.

Conclusions

The authors believe that this work has successfully produced three new thiosemicarbazone ligands and their corresponding palladium complexes. When these ligands are combined with copper (II) and palladium elements to form new complexes, research suggests that they have Topoisomerase IIa inhibiting factors. It is believed that this technique will be the next innovation in cancer-inhibiting chemotherapy drugs. In the future, this work hopes to extend into that field of complex addition to cancer cell lines in order to test this enzyme inhibition.

Acknowledgements

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References

(1) Muralisankar, Mathiyan, et al. "Synthesis, X-Ray Crystal Structure, DNA/Protein Binding and DNA Cleavage Studies of Novel Copper(Ii) Complexes of N-Substituted Isatin Thiosemicarbazone Ligands." *New Journal of Chemistry*, vol. 40, no. 3, 2016, pp. 2661–2679., doi:10.1039/c5nj02806j.
(2) Velasques, Jecika Maciel, et al. "Hirshfeld Analysis and Molecular Docking with the RDR Enzyme of 2-(5-Chloro-2-Oxoindolin-3-Ylidene)-N-Methylhydrazinecarbothioamide." *Acta Crystallographica Section E Crystallographic Communications*, vol. 73, no. 5, 2017, pp. 702–707., doi:10.1107/s2056989017005461.