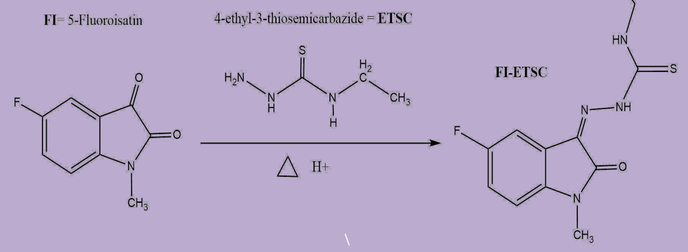
Synthesis of 5-Fluoroisatin and 7-Fluoroisatin Thiosemicarbazones

Emma K. Zachary, Bailey B. Talent, Dr. Edward C. Lisic

Tennessee Technological University, Cookeville, Tn 38501

Abstract

Isatin thiosemicarbazones have been known for a long time to have biological and medicinal properties and have been used for anti-tuberculosis drugs.[1-2] Recently, they have been used in the synthesis of metal complexes that have medicinal properties.[3] Therefore, we have investigated the synthesis and characterization of the 5-fluoroisatin and 7-fluoroisatin thiosemicarbazones, which have the NMR active fluorine. This work presents information on synthesis and NMR characterization of these ligands and reactions to form Pd(II) complexes.



Synthesis of 5-Fluoroisatin Ligands

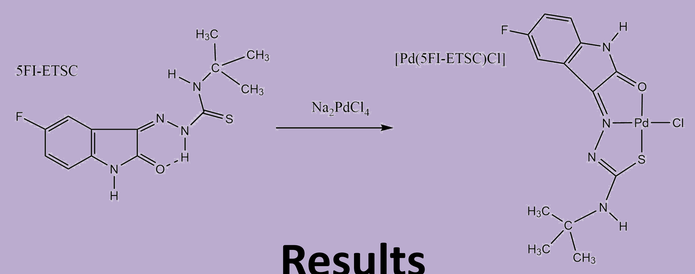
In a 125 mL flask equipped with a magnetic stir bar, (0.510-0.511g, $3.03x10^{-3}$ mol) of 5-Fluoroisatin and (0.361-0.448g, $3.03x10^{-3}$ mol) of ETSC were mixed with 50 mL of isopropanol and 2 drops of H_2SO_4. The mixture was heated to 75° Celsius and left to stir overnight. The next day, the yellow product was filtered out and left to dry. The dried product weighed 0.661-0.712g.

Synthesis of 7-Fluoroisatin Ligands

In a 50 mL flask equipped with a magnetic stir bar, (0.501-0.529g, $3.03x10^{-3}$ mol) of 7-Fluoroisatin and (0.316-0.416g, $3.03x10^{-3}$ mol) of ETSC were mixed with 30 mL of isopropanol and one drop of H_2SO_4. The mixture was heated to 75° Celsius and left to stir overnight. The next day, the powdered, yellow product was left to dry. The dried product weighed 0.633-0.747g.

Synthesis of [Pd(5-Fluoroisatin-ETSC)Cl]

In a 125 mL flask equipped with a magnetic stir bar, (0.100g, $3.57x10^{-4}$ mol) of 5-Fl-ETSC and (0.067g, $3.57x10^{-4}$ mol) of Na_2PdCl_4 were mixed with 50 mL of methanol. The mixture was heated to 60° Celsius and left to stir overnight. The next day, the powdered, red product was left to dry. The product weighed 0.130g.



Results

The compounds were synthesized in good yield. The proton NMR results were very consistent and provides evidence for our structure and assignments. The pertinent assignments are given in Table 1 below and the representative assignments are shown along with the structure for 5FI-ETSC in Figure 1. The ^{18}F NMR of each compound exhibits only one peak which couple to the nearest two aromatic hydrogens, as seen in Figure 2.

Table 1. NMR of the Four Thiosemicarbazones

Cmpd	Hydrazinic	Thioamide	Isatin	18F
5FI-ETSC	12.44 (s)	9.34 (t)	11.19 (s)	121.13 (td)
5FI-tBTSC	12.50 (s)	8.18 (s)	11.22 (s)	121.11 (td)
7FI-ETSC	12.52 (s)	9.37 (t)	11.73 (s)	132.09 (dd)
7FI-tBTSC	12.52 (s)	9.34 (s)	11.72 (s)	133.06 (dd)

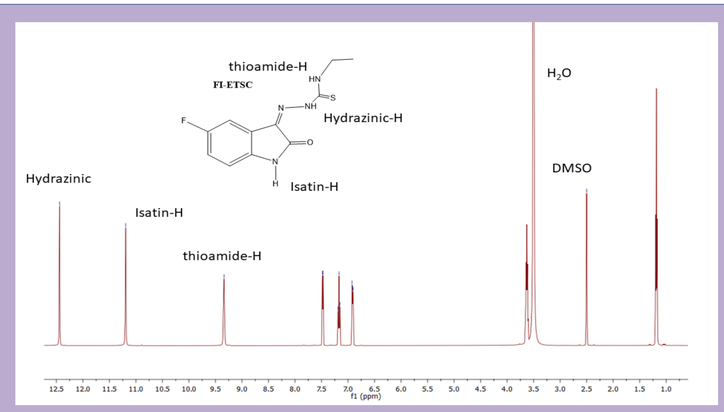


Figure 1. ^1H NMR Assignments with structure for 5-FI-ETSC

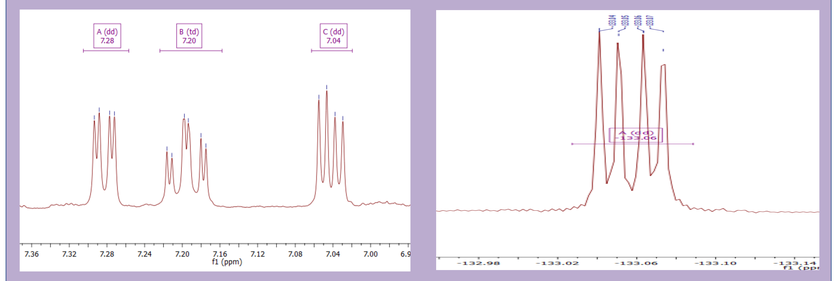


Figure 2. The ^1H NMR aromatic protons and the ^{18}F NMR peak for [Pd(7FI-tBTSC)Cl]

References

1. S. Padhye, and G.B. Kauffman. *Coord. Chem. Rev.*, 1985, 63, 127 -160.
2. J.S. Casas, M.S. Garcia-Tasende, and J. Sordo. *Coord. Chem. Rev.*, 2000, 209, 197-261.
3. A. N. Patange, Chem. Phys. Astron. 2015, 52, 22.

Acknowledgements

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