Synthesis of INAP-ETSC and INAP-t-ButylTSC

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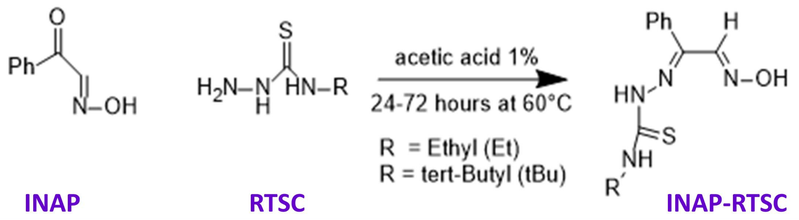
Abstract

Thiosemicarbazones are a class of organic compounds that function extremely well as ligands that bind to transition metals to form metal complexes with interesting biological properties. This presentation focuses on synthesis and characterization of a new series of monoxime thiosemicarbazone.

Two new compounds, namely α-isonitrosacetophenone ethyl thiosemicarbazone (INAP-ETSC) and α-isonitrosacetophenone tert-butyl thiosemicarbazone (INAP-tButyl), are synthesized and characterized by Nuclear Magnetic Resonance Spectroscopy (NMR). The synthesized compounds are further used to create the palladium-ligand complexes that can be tested for their anticancer properties by studying the inhibition of topo-isomerase 2α.

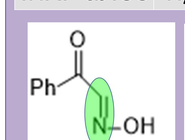
Synthesis of INAP Ligands

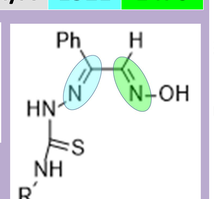


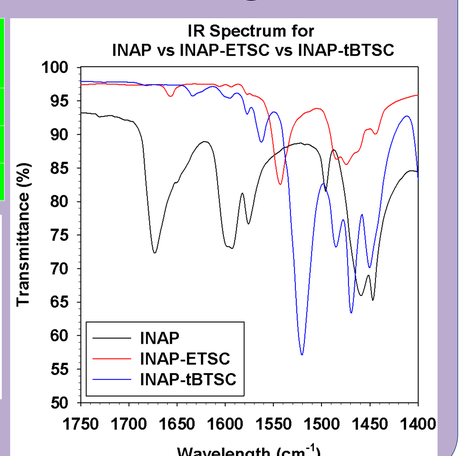
In a 50 mL Erlenmeyer Flask equipped with a magnetic stir bar, 1.15-13 mol of INAP and 1.15-13 mol of RTSC (RTSC = ETSC or tBuTSC), were added to 50 mL of 1% acetic acid. The obtained mixture was stirred at 60 °C on for 24 – 72 hours when a suspension was obtained. The solids were then filtered using gravity filtration and characterized using Infrared and Nuclear Magneti Resonance Spectroscopy.

Infrared Spectra for INAP Ligands

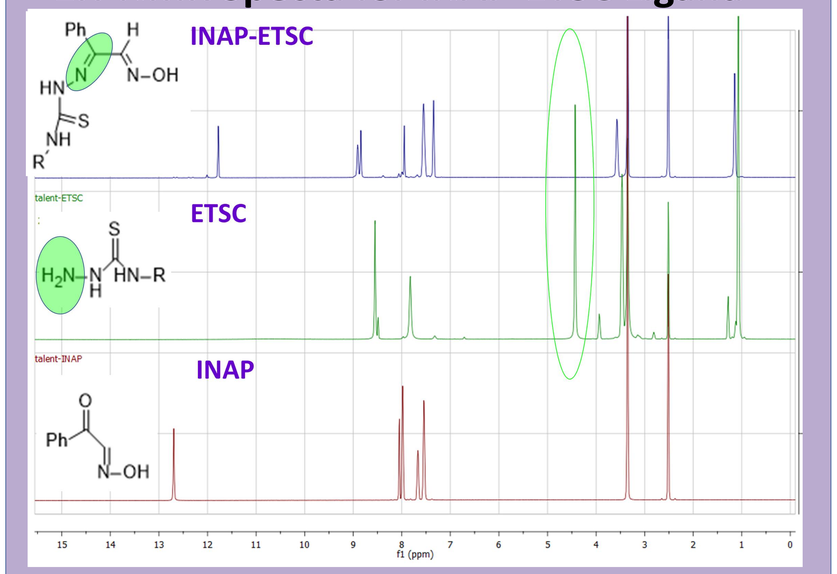
Compound	C=O	New C=N	Old C=N
INAP	1672	N/A	1595
INAP-ETSC	N/A	1583	1478
INAP-tbTSC	N/A	1521	1470


INAP

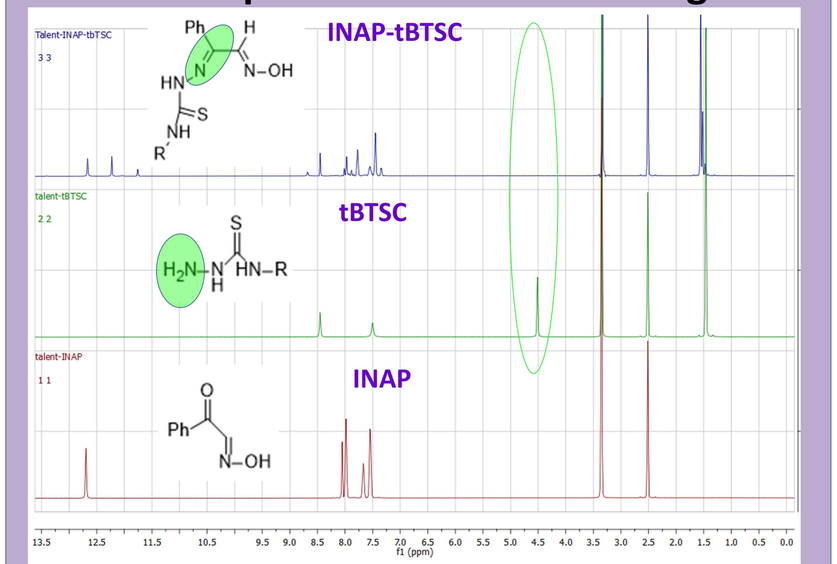

INAP-RTSC



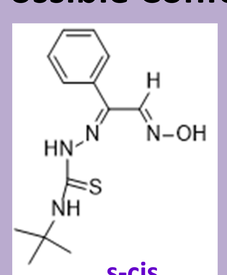
1H-NMR Specta for INAP-ETSC Ligand

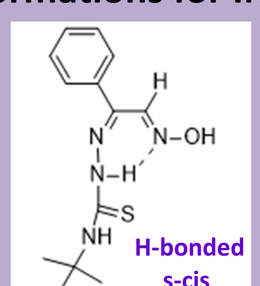


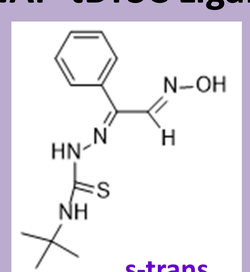
1H-NMR Spectra for INAP-tBTSC Ligand



Possible Conformations for INAP-tBTSC Ligand


s-cis conformation


H-bonded s-cis conformation


s-trans conformation

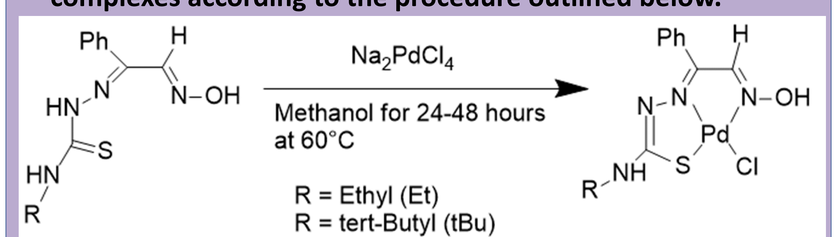
Results and Discussions

- <u>INAP-ETSC Ligand</u>:
  - The hydrogens from NH_2 group in ETSC (4.42 ppm) are not present in the INAP-ETSC ligand; this is consistent with the conversion of this group into C=N group.
  - The hydrogen from oxime group in INAP (12.69 ppm) is shifted upfield in the INAP-ETSC ligand (11.77 ppm).

- <u>INAP-tBTSC Ligand</u>:
  - The hydrogens from NH_2 group in tBTSC (4.51 ppm) are not present in the INAP-tBTSC ligand, which is consistent with the conversion of this group into a C=N group.
  - The hydrogen from oxime group in INAP is shifted upfield in the INAP-tBTSC ligand. However, the presence of three acidic peaks in the 11.75-12.66 ppm region suggests the presence of 3 conformers.

Conclusions and Future work

- The INAP-ETSC ligand was synthesized under the reaction conditions used. However, a mixture of 3 conformers was obtained in the INAP-tBTSC synthesis. Optimization of the synthesis of INAP-tBuTSC ligand will be performed and the pure ligands will be used in the synthesis of Pd(II) complexes according to the procedure outlined below.



References

Lisic, E. C., Rand, V. G., Ngo, L., Kent, P., Rice, J., Gerlach, D., Papish, E. T. and Jiang, X. H. (2018) Cu(II) Propionyl-Thiazole Thiosemicarbazone Complexes: Crystal Structure, Inhibition of Human Topoisomerase IIα, and Activity against Breast Cancer Cells. Open Journal of Medicinal Chemistry, 8, 30-46. https://doi.org/10.4236/ojmc.2018.82004

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