Synthesis and NMR Characterization of New Isatin Thiosemicarbazone Derivatives

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Abstract

In this research the main focus of the presentation is the synthesis of several different isatin thiosemicarbazone derivatives and their structural determination given by a 500-MHz NMR. Isatin-5-sulfonic acid-TSC was chosen because of water-soluble properties exhibited by the sulfonic acid group compared to the phenyl and methyl analogs. The molecular structures of these new compounds will be confirmed using 1H NMR, 13C NMR, 1H-13C HSQC (Heteronuclear Single Quantum Coherence Nuclear Magnetic Resonance), and 1H-15N HSQC spectrum. These new isatin thiosemicarbazone compounds unique intramolecular forces, i.e. hydrogen bonding, that will be illustrated utilizing various NMR spectroscopic methods.

Experimental

[1] I-tBTSC
The product was collected: 0.7814 g which provided a 78.49% yield.

[2] MeI-tBTSC
The product was collected: 0.8075g which provided a 79.24% yield.

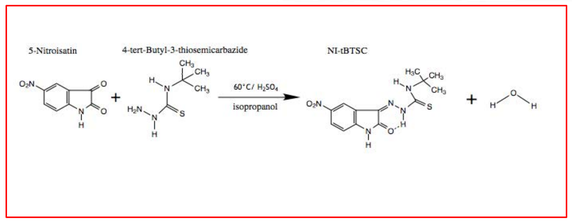
[3] PhI-tBTSC
The product was collected: 0.6810g which provided a 84.78% yield.

[4] NI-tBTSC
In a 50 mL Erlenmeyer flask equipped with a magnetic stir bar on a heat/stir plate containing approximately 25 mL of isopropanol (2-propanol) and 0.5167g (2.689 x10-3 mol) of 5-Nitroisatin was added to 0.3990 g 4-tert-butyl-3-thiosemicarbazone (2.710 x 10-3 mol) at approximately 60° C and 150 centigrade. A drop of concentrated sulfuric acid was added as a catalyst, and reaction was carried out at 60° C. The reaction mixture was stirred overnight, and the resulting yellow precipitate was vacuum-filtered and thoroughly dried. The product was collected: 0.6738g which provided a 74.26% yield.

[5] ISA-tBTSC
The product was collected: 0.6927g which provided a 100% yield. Contains water.

Apparatus

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



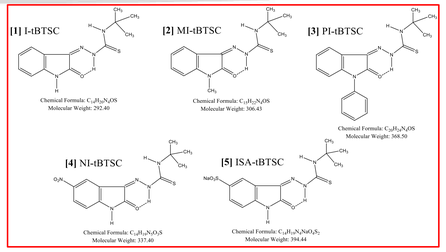
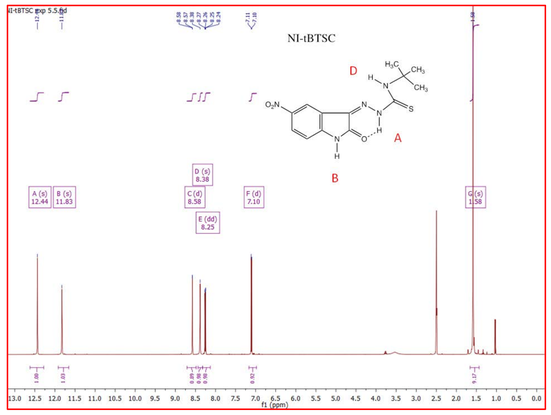


Figure 1. Synthesis of the NI-tBTSC Ligand and Structures of Compounds [1]-[5]



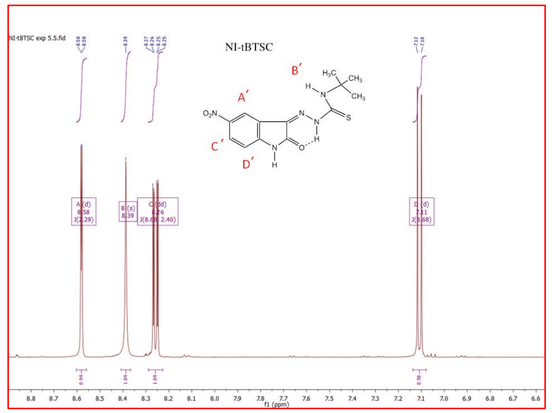


Figure 2. The Full and Downfield Portion ^{1}H NMR Spectrum of NI-tBTSC

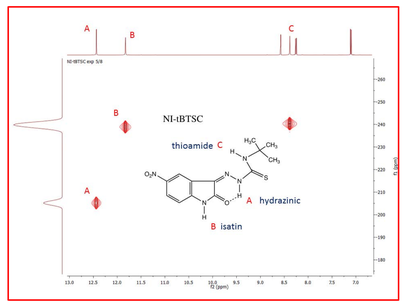


Figure 3.The 2-D 1H,15N Heteronuclear Single Quantum Coherence NMR Spectrum of NI-tBTSC obtained on Bruker Ascend-500 Multi-Nuclear NMR Spectrometer

Compound	(A) Hydrazinic Proton (ppm)	(F)Isatin Proton (ppm)	(B) Thioamide Proton (ppm)	(C) Aromatic 1 (ppm)	(D) Aromatic 2 (ppm)	(E) Aromatic 3 (ppm)	(F) Aromatic 4 (ppm)
[1]I-tBTSC	12.54	11.22	8.13	7.68 (dd)	7.36 (td)	7.08 (td)	6.93 (dt)
[2]MeI-tBTSC	12.46	na	8.23	7.68 (dd)	7.44 (m)	7.14 (td)	7.12 (dt)
[3]PhI-tBTSC	12.46	na	8.24	7.61 (m)	7.39 (td)	7.21 (td)	6.86 (dt)
[4]NI-tBTSC	12.44	11.83	8.38	8.58 (d)	8.39 (s)	7.11 (d)	na
[5]ISA-tBTSC	12.55	11.28	8.24	7.90 (d)	7.62 (dd)	6.86 (d)	na

Table1. Important Downfield Resonances for the Five New Compounds

Results and Discussion

The synthesis of the new never-before-synthesized isatin thiosemicarbazone compounds [1]-[5], (as shown in Figure 1) proceeds easily under the reaction conditions stated in the experimental section, and results in high yields of clean products. The proof for the clean products was obtained through NMR data. Since there is not enough room on this poster to include all of the NMR spectra for compounds [1]-[5], we focused on compound [4], Nitroisatin thiosemicarbazone as an example. Figure 1 presents the synthesis of [4] NI-tBTSC. Figure 2. shows not only the full ^{1}H NMR spectrum of compound [4] with several of the protons labelled with a structural representation, but also a zoomed in portion of the aromatic region of the spectrum. We assigned protons as seen in Table 1 to the hydrazinic protons, the isatin protons (which are only seen in compounds [1],[4], and [5] because compounds [2] and [3] have a methyl and a phenyl substituent respectively in that position), the thioamide protons, and the aromatic protons on the isatin ring. The Figure 3 shows the 2-D 1H, 15N Heteronuclear Single Quantum Coherence NMR Spectrum of NI-tBTSC, and supports our assignment of the N-H protons in Table 1 and in Figure 2.

Conclusions

We believe that we have synthesized cleanly and in good yield five new compounds. These compounds are of the type of thiosemicarbazones which have been identified in the literature as potential ligands for copper (II) complexes that can act as Topoisomerase IIa inhibitors. To that end, future work will be to extend the series of ligands and metal complexes, and to test all the compounds against Topoisomerase IIa enzyme.

Acknowledgements

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