Synthesis and NMR Characterization of New Isatin Sulfonic Acid Thiosemicarbazone Compounds

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Introduction

Isatin thiosemicarbazone compounds have been described in the literature, and are important medicinal compounds.[1,2] This work shows the synthesis and characterization of a series of isatin sulfonic acid thiosemicarbazone compounds, based on the 5-isatin-3-sulfonic acid (ISA) substrate. After synthesis and purification, the ^{1}H NMR and ^{13}C NMR spectra were obtained using a 500 MHz NMR spectrometer. Experimental data was observed using 2D NMR techniques, such as, HSQC (heteronuclear single quantum coherence) ^{1}H-^{13}C NMR and HSQC ^{1}H-^{15}N NMR to give evidence for the structures of these new compounds.

Experimental

[1] ISA-MTSC

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 4-methyl-3-thiosemicarbazide was added to 0.5030g (2.019 x 10^{-3} mol) 5- Isatin Sulfonic acid 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: 0.6082g which provided a 83.30% yield.

[2] ISA-BzTSC

The product was collected: 0.7883g which provided a 96.37% yield.

[3] ISA-ETSC

The product was collected: 0.6164g which provided a 97.95% yield.

[4] ISA-tBTSC

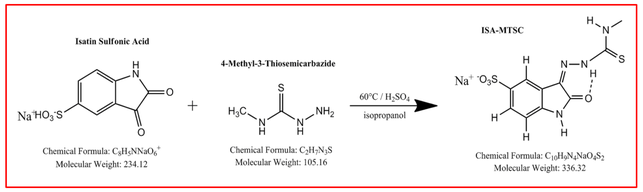
The product was collected: 0.522g which provided a 83.83% yield.

[5] ISA-PTSC

The product was collected: 0.588g which provided a 71.97% yield.

Apparatus

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



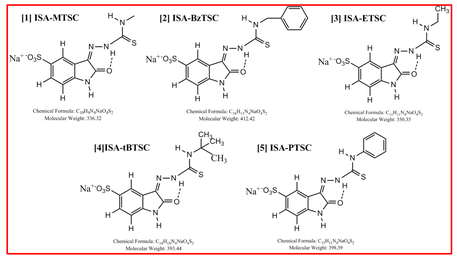


Figure 1. Synthesis of the ISA-MTSC Ligand and Structures of Compounds [1]-[5]

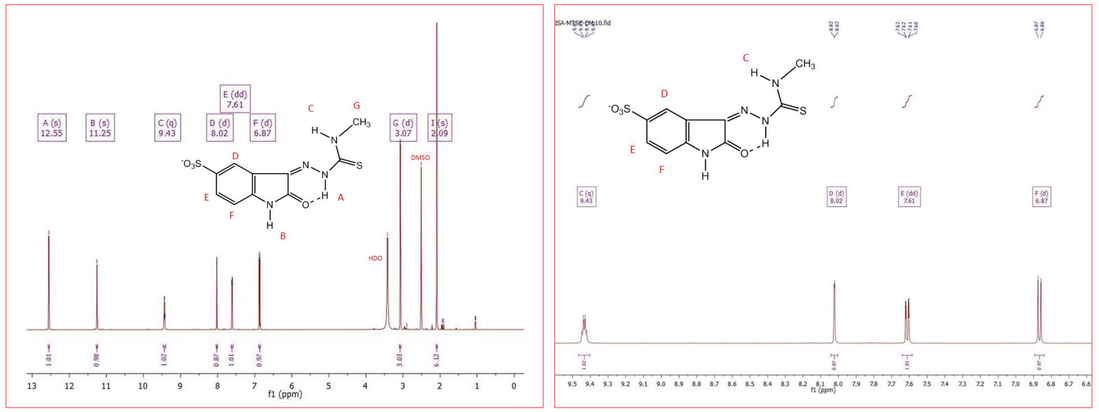


Figure 2. The Full and Downfield Portion ^{1}H NMR Spectrum of ISA-MTSC

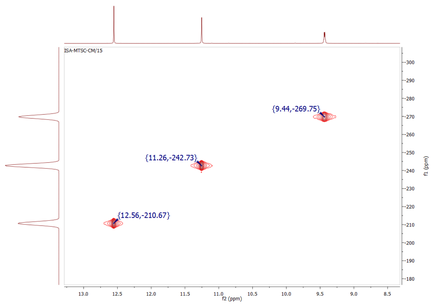


Figure 3.The 2-D 1H,15N Heteronuclear Single Quantum Coherence NMR Spectrum of ISA-MTSC obtained on Bruker Ascend-500 Multi-Nuclear NMR Spectrometer

Table1. Important Downfield Resonances for the Five New Compounds

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)
[1]ISA-MTSC	12.55	11.25	9.43 (q)	8.02 (d)	7.61 (dd)	6.87 (d)
[2]ISA-BzTSC	12.60	11.26	10.03 (t)	8.03 (d)	7.61 (dd)	6.86 (d)
[3]ISA-ETSC	12.49	11.25	9.48 (d)	8.03 (d)	7.61 (dd)	6.87 (dd)
[4]ISA-tBTSC	12.56	11.28	7.90 (d)	8.25 (d)	7.62 (dd)	6.87 (d)
[5]ISA-PTSC	12.77	11.31	11.01 (s)	8.16 (d)	7.64 (dd)	6.89 (d)

Results and Discussion

The synthesis shown in Figure 1. of these never-before-synthesized isatin sulfonic acid thiosemicarbazone compounds [1]-[5] 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 Resonance spectra. Since there is not enough room on this poster to include the NMR spectra for every compound in the series, we focused on compound [1], Isatin sulfonic acid methyl-thiosemicarbazone to show results of the experiment. Figure 1. displays the synthesis of [1] ISA-MTSC. Figure 2. shows the ^{1}H NMR spectrum of compound [1] with several of the protons labeled with a structural representation, along with a condensed view of the aromatic region within the compound. Figure 3. shows the 2-D 1H, 15N Heteronuclear Single Quantum Coherence NMR Spectrum of ISA-MTSC. Table 1. includes the ^{1}H NMR condensed data collected from each compound [1]-[5].

Conclusions

The authors believe that this work has successfully produced five new thiosemicarbazone ligands. 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) Bell, T., Mayes, R., Lawson, R., and Edward C. Lisic, “Synthesis of a Series of Isatin-3- thiosemicarbazone-5-sulfonic Acid Compounds and Structural Characterization Using NMR Spectroscopy,” Journal of Undergraduate Chemistry Research, 2004, 1, pp. 39-45.

(2) Hall, M. D., Salam, N. K., Hellawell, J. L., Fales, H. M., Kensler, C. B., Ludwig, J. A., . . . Gottesman, M. M. (2009, May 28). Synthesis, activity and pharmacophore development for isatin-β-thiosemicarbazones with selective activity towards multidrug resistant cells.