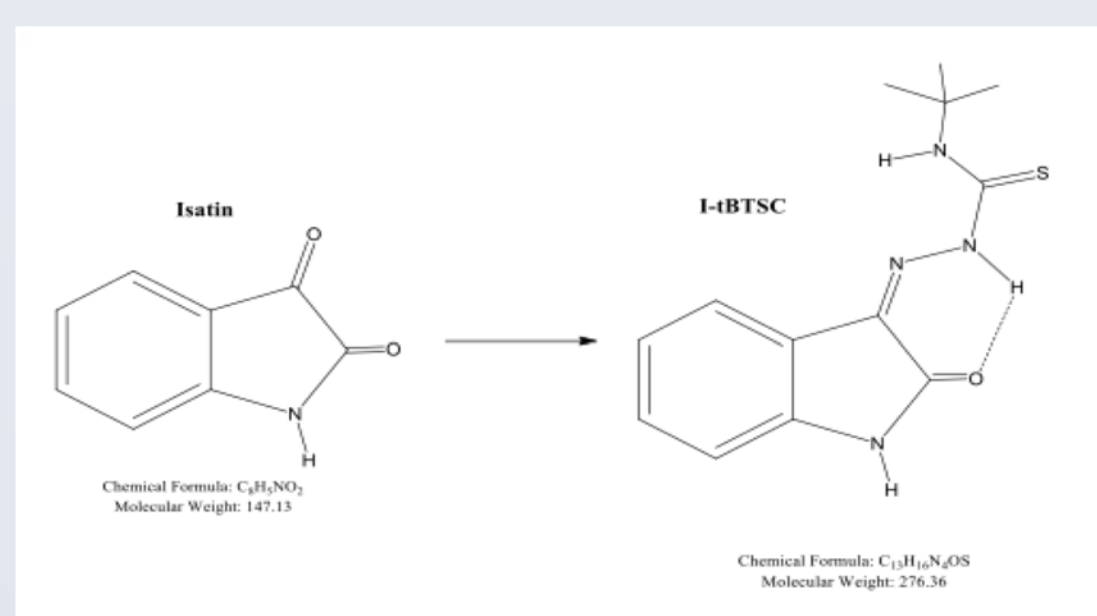


Abstract

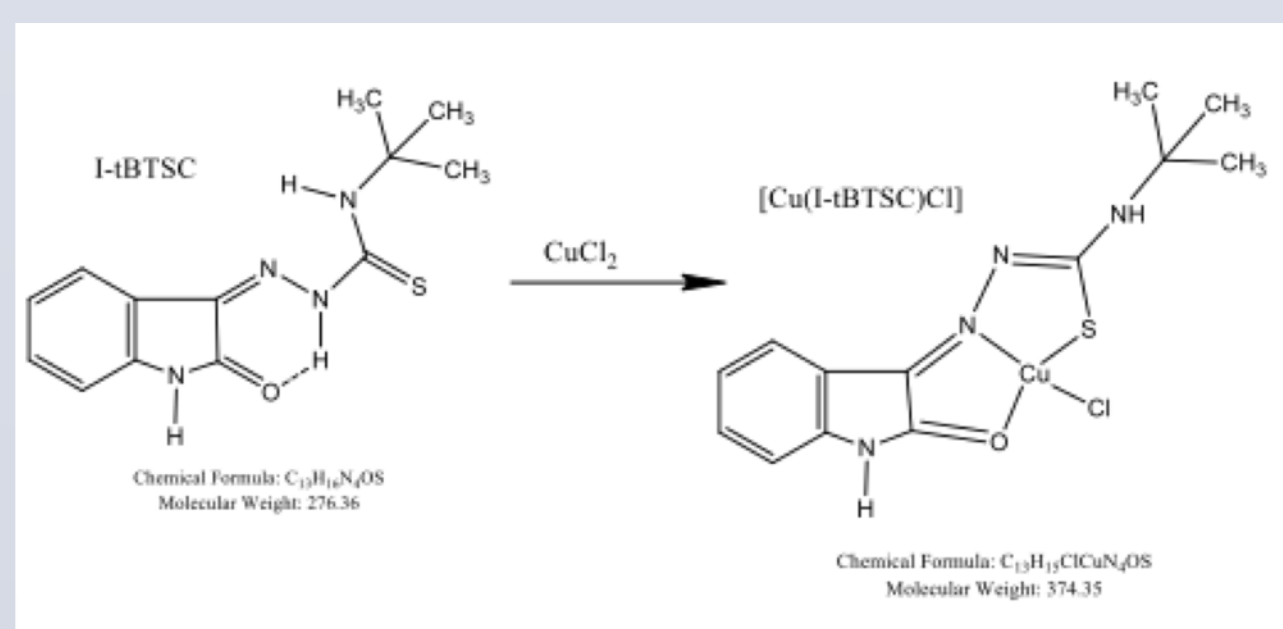
A new series of Isatin Thiosemicarbazone (I-TSC) ligands were synthesized. The ligands were synthesized with the following substituent groups: methyl thiosemicarbazone, ethyl thiosemicarbazone, tert-butyl thiosemicarbazone, phenyl thiosemicarbazone, and benzyl thiosemicarbazone. These ligands were then characterized by NMR spectroscopy in order to verify their structures. The following tests were run on the compounds: ^1H , ^{13}C , gradient selected COSY, ^1H - ^{13}C multiplicity, and ^1H - ^{13}C HMBC. The compounds were then reacted with CuCl_2 to form the metal complex $[\text{Cu}(\text{I-TSC})\text{Cl}]$. An inhibition assay study on these Isatin ligands and copper compounds for evidence of inhibition of Topoisomerase II α will be presented.

Synthesis of I-ETSC



Initially, 0.4845 g (0.0041 mol) of 4-Ethyl-3-thiosemicarbazide and 0.5863g (0.0040 mol) Isatin were weighed into a 125 mL Erlenmeyer flask with a magnetic stir bar and 50 mL isopropanol. A drop of sulfuric acid was added to the solution as a catalyst. The solution was stirred overnight at 65° C. The solution was gravity filtered with isopropanol and left to dry. The final product was 0.9268 g, which provided a 93.7% percent yield. The same procedure was performed to synthesize the other ligands.

Synthesis of $[\text{Cu}(\text{I-tBTSC})\text{Cl}]$ metal complex



I-tBTSC, 0.2508g (9.07×10^{-4} mol) and 0.1512 g (8.86×10^{-4} mol) CuCl_2 dihydrate were weighed into separate vials. The vial of CuCl_2 was filled with 3.0 mL of ethanol, dissolved and then pipetted into a 50 mL Erlenmeyer flask. The CuCl_2 was set on a heating plate at 60° C and stirred with a magnetic stir bar. Next, the I-tBTSC dissolved in 15 mL of ethanol was added to the flask of CuCl_2 . The solution turned dark brown immediately. The solution was left at 65° C overnight. The product was filtered and dried. The final product was 0.3037g (8.11×10^{-4} mol) which provided a 91.5% percent yield.

Structures and ^1H NMR Data

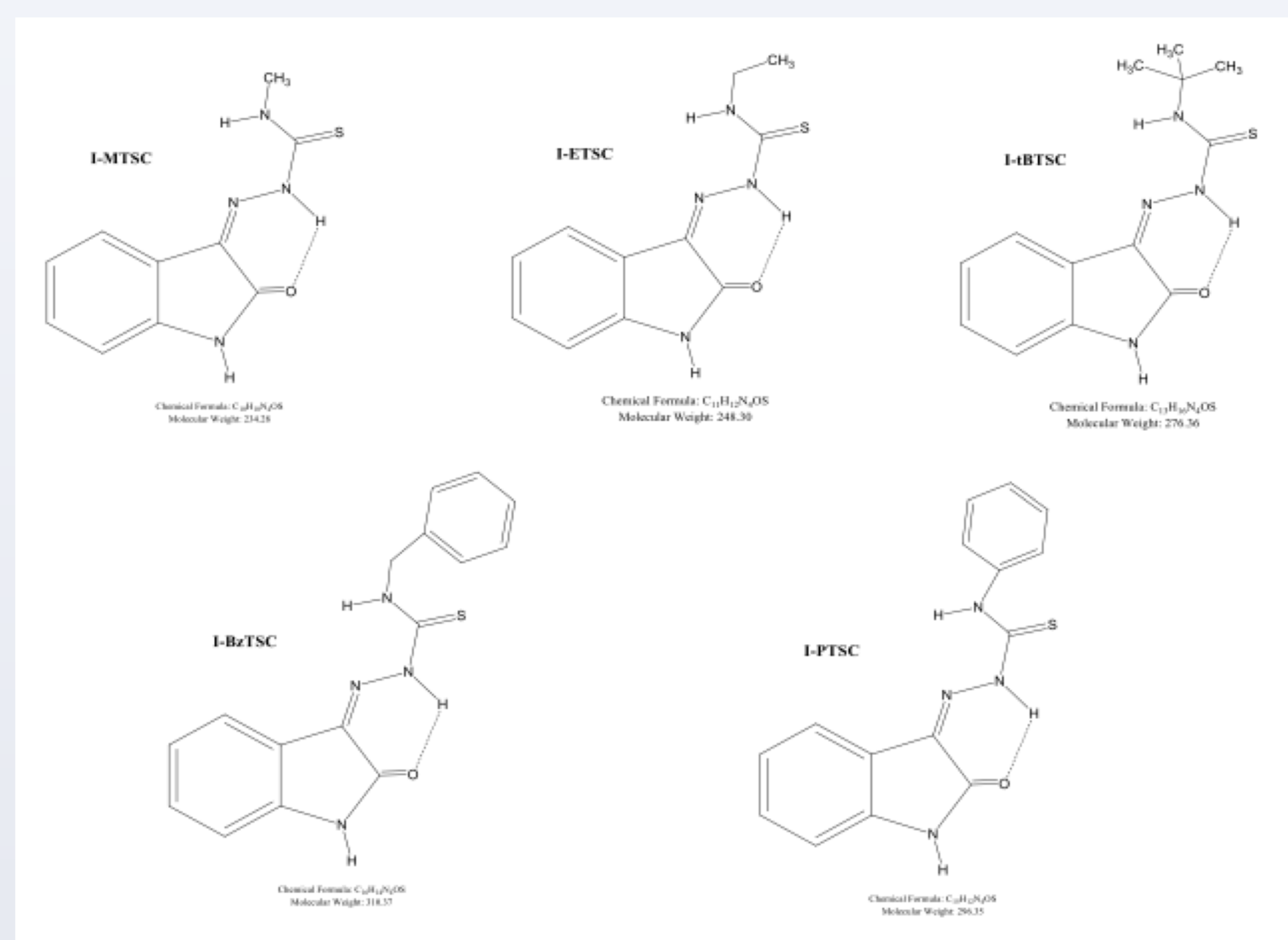


Figure 1. Thiosemicarbazone ligands

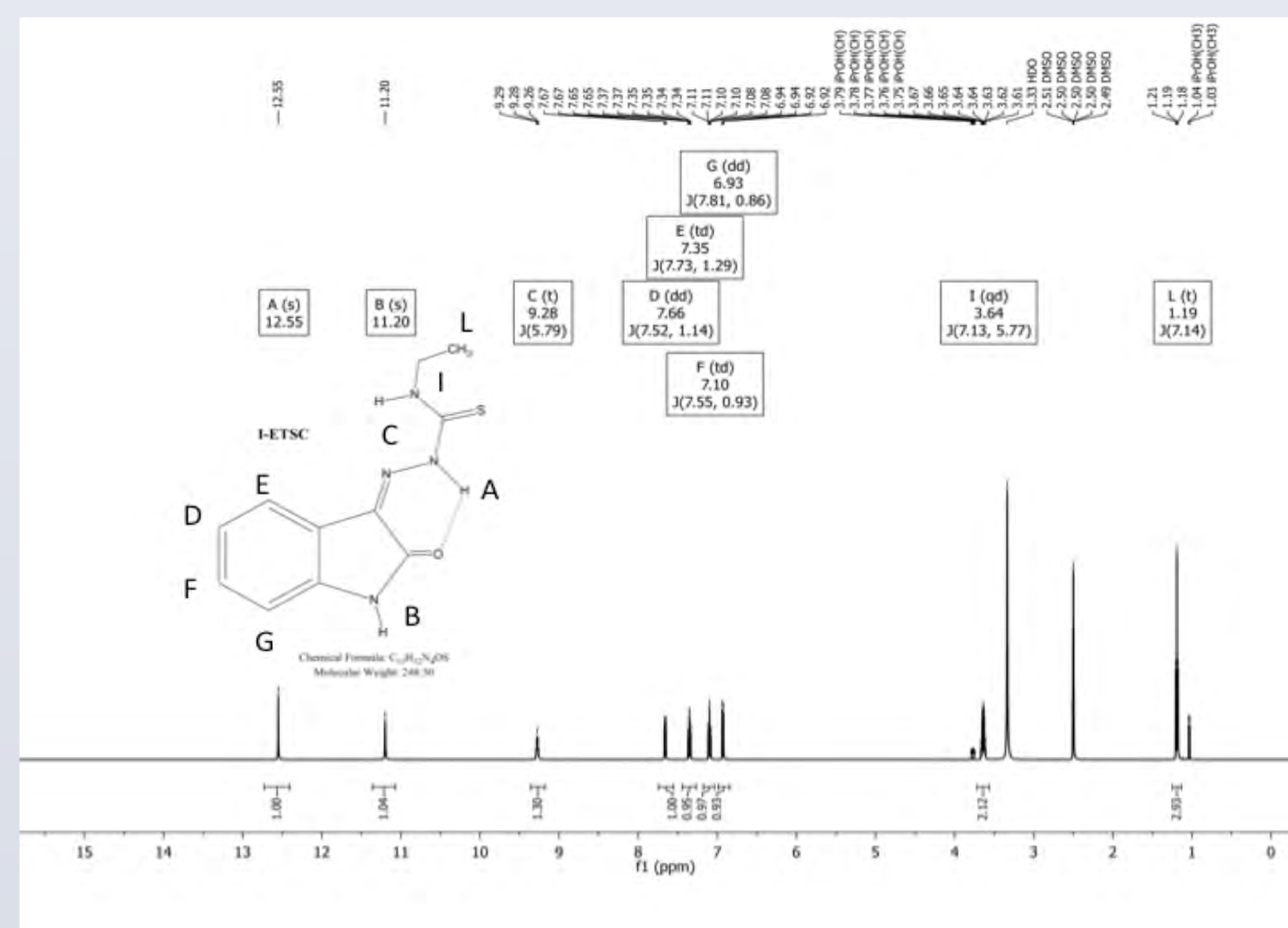


Figure 2. ^1H NMR Full view spectrum of I-ETSC

Thiosemicarbazone ligand yields

- The synthesis of I-MTSC produced 0.994g (4.2×10^{-3} mol) of product, yielding 93.8%.
- The synthesis of I-ETSC produced 0.9268g (3.7×10^{-3} mol) of product, yielding 93.7%.
- The synthesis of I-tBTSC produced 0.6499g (2.35×10^{-3} mol) of product, yielding 72.4%.
- The synthesis of I-BzTSC produced 0.9636g (3.1×10^{-3} mol) of product, yielding 94.5%.
- The synthesis of I-PTSC produced 0.8044g (2.7×10^{-3} mol) of product, yielding 93.6%.

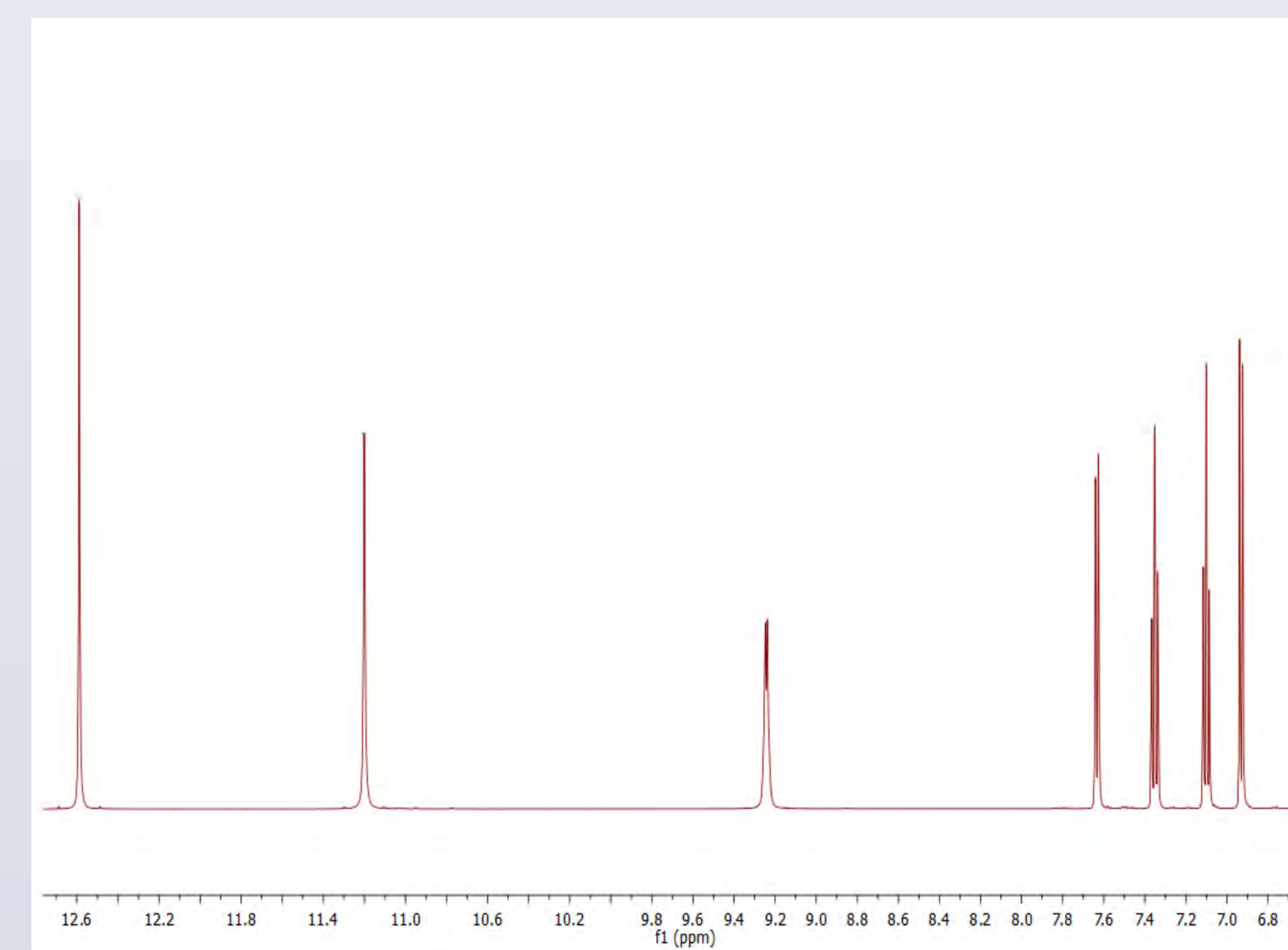


Figure 3. ^1H NMR Downfield View spectrum of I-MTSC

Copper (II) metal complex yields

- The synthesis of $[\text{Cu}(\text{I-MTSC})\text{Cl}]$ produced 0.3296g (9.92×10^{-4} mol) of product, yielding 92.6%.
- The synthesis of $[\text{Cu}(\text{I-ETSC})\text{Cl}]$ produced 0.3127g (9.03×10^{-4} mol) of product, yielding 89.4%.
- The synthesis of $[\text{Cu}(\text{I-tBTSC})\text{Cl}]$ produced 0.3037g (8.11×10^{-4} mol) of product, yielding 91.5%.
- The synthesis of $[\text{Cu}(\text{I-BzTSC})\text{Cl}]$ produced 0.2486g (6.09×10^{-4} mol) of product, yielding 75.4%.
- The synthesis of $[\text{Cu}(\text{I-PTSC})\text{Cl}]$ produced 0.3172g (8.04×10^{-4} mol) of product, yielding 95.3%.

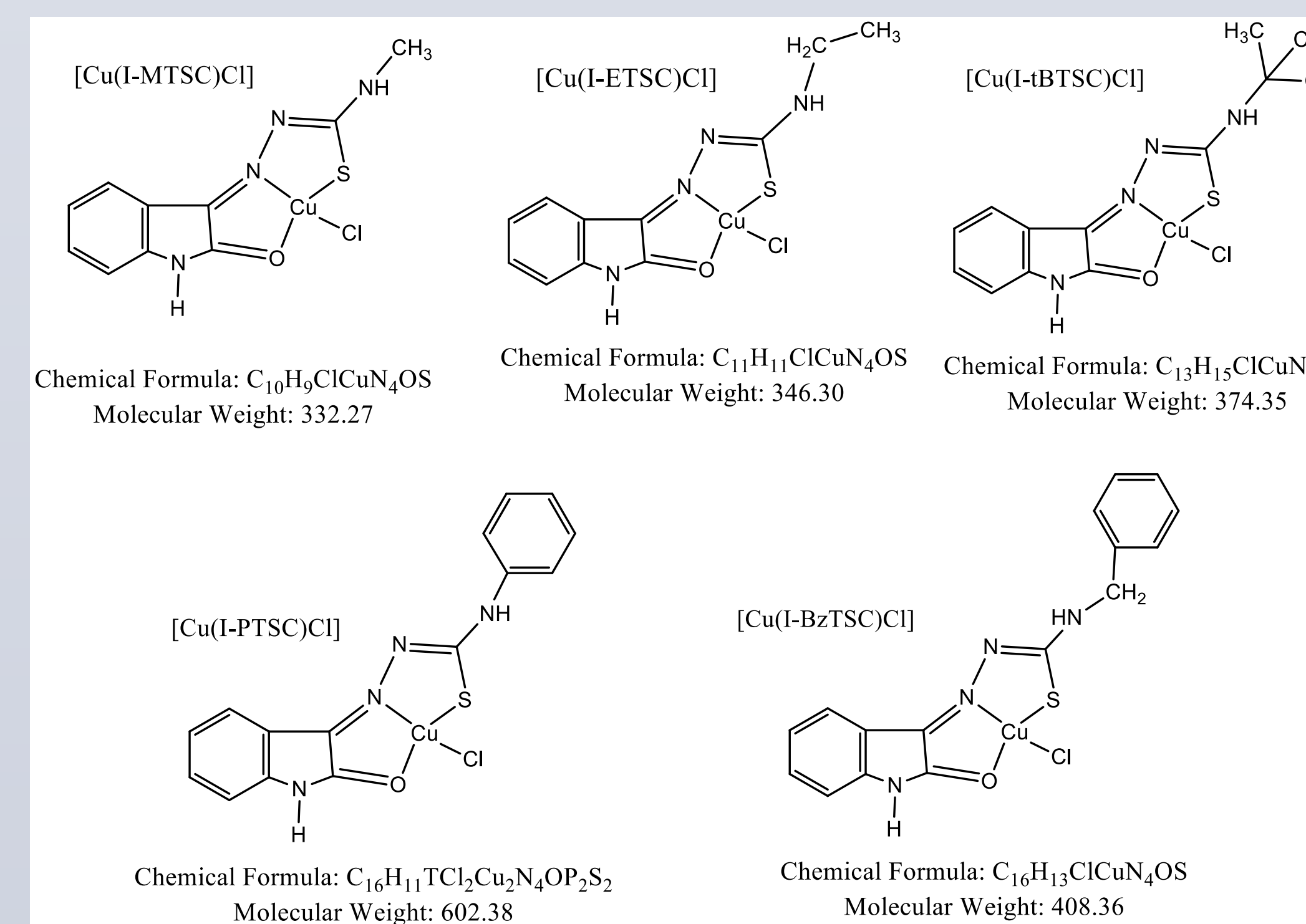
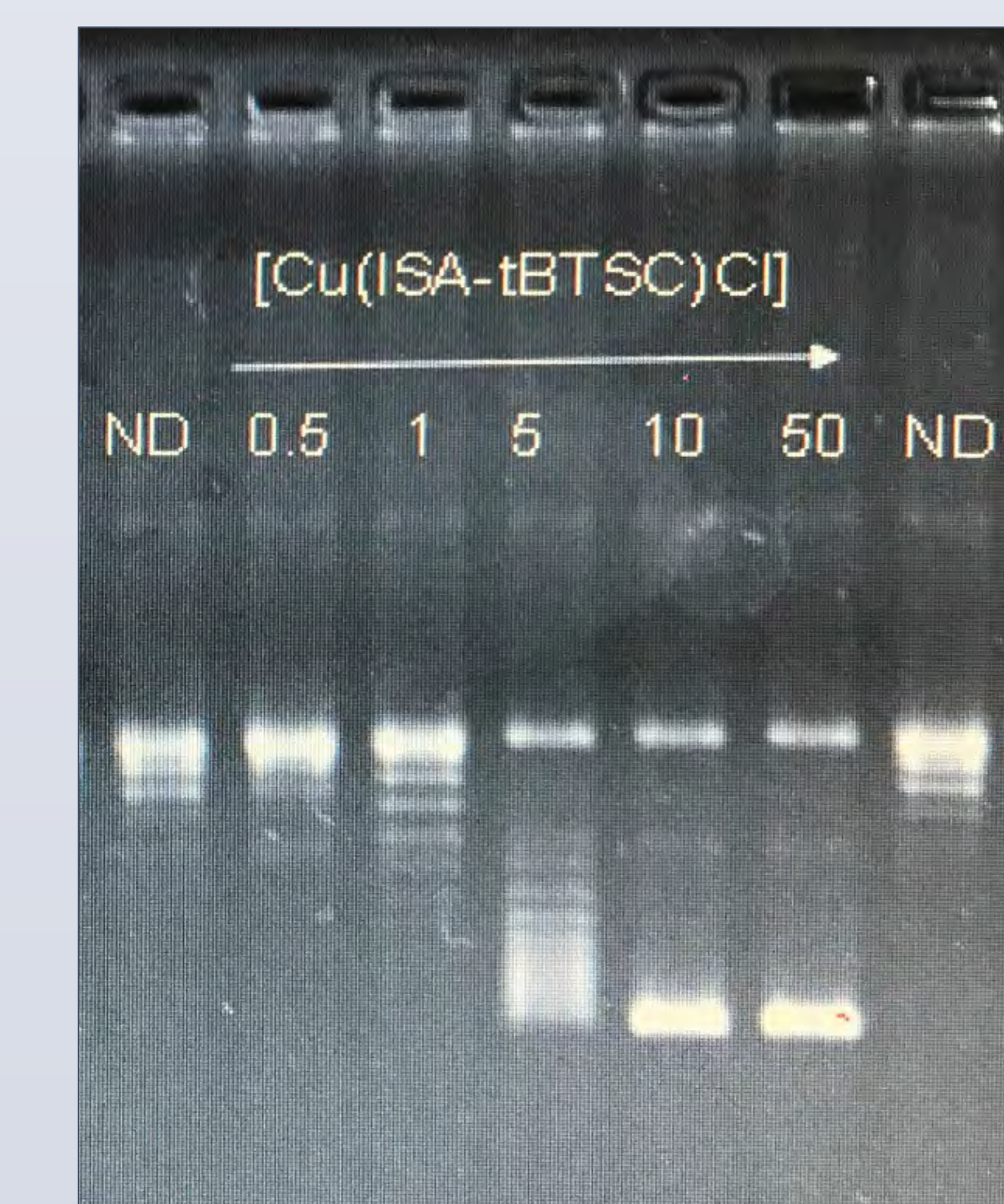


Figure 4. Copper (II) complexes

Discussion

After the Isatin-Thiosemicarbazone ligands, in figure 1, were synthesized and characterized by the NMR, the ^1H proton NMR data (see figures 2 and 3) of the ligands all present peaks for the aromatic ring protons, the hydrazinic proton, the thioamide proton, and the amine proton. The NMR data was compared to data from other studies in order to confirm structure.² The substituent groups for each ligands were all displayed as predicted. This can be seen when comparing figure 2 and figure 3.

The five thiosemicarbazone ligands, in figure 1, were then used to synthesize the $[\text{Cu}(\text{I-TSC})\text{Cl}]$ metal complexes (see figure 4). Studies have shown evidence of Copper(II) metal complexes as possible anticancer agents.¹ The $[\text{Cu}(\text{I-tBTSC})\text{Cl}]$ was selected out of the complexes shown in Figure 4 to run an Inhibition assay study. The study was completed in order to see if the metal complex displayed any inhibitory behavior against Topoisomerase II α . The study, displayed below, revealed that these compounds possessed the predicted qualities and is therefore a strong candidate for further research.



References

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