# Synthesis and NMR Characterization of a New Series of Thiazole-2-Carboxaldehyde Thiosemicarbozone Compounds [TZCA-TSC]

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## Abstract

This work will be the synthesis of a series of thiazole-carboxaldehyde-thiosemicarbazone ligands. After the synthesis and purification of these ligands, the new compounds went through analysis using the NMR spectrometer and obtaining data on $^{+}$H NMR, $^{13}$C NMR, HSQC (heteronuclear single quantum coherence) $^{1}$H-$^{13}$C NMR and HSQC $^{1}$H-$^{15}$N NMR, to obtain evidence for our predicted structures. After the analysis was complete, we reacted the new ligands with palladium to form their metal complexes.

## Experimental

**TZCA-tBTSC**

Initially, 0.9692 grams (8.566 mmol) of 1,3-thiazole-2-carboxaldehyde was added to a 125 mL Erlenmeyer flask while 1.2601 grams (8.558 mmol) of 4-tertbutyl-3-thiosemicarbazone was dissolved in about 20 mL of isopropanol. This solution was added dropwise to the 125 mL Erlenmeyer flask and the TZCA. A few drops of concentrated sulfuric acid were added as a catalyst. The solution was then heated at 70 oC and stirred for 24 hours. The pale yellow precipitate formed was gravity filtered using 15 cm qualitative 413 filter paper and set aside for air drying. **Yield:** 0.7080g (34%)

| | Ligand | Mass(g) | Percent Yield (%) |
|---|---|---|---|
| [1] | TZCA-TSC | 1.3070g | 89.6% |
| [2] | TZCA-MTSC | 0.7902g | 47.8% |
| [3] | TZCA-ETSC | 1.1308g | 77.5% |
| [4] | TZCA-tBTSC | 0.7059g | 34.0% |
| [5] | TZCA-bzTSC | 0.5635gg | 71.6% |
| [6] | TZCA-PTSC | 1.503g | 81.9% |
| [7] | TZCA-dMTSC | 1.4700g | 66.2% |

**[Pd(TZCA-tBTSC)Cl]**

Tetrachloropalladate, 0.2956 g (0.9056 mmol) was dissolved in about 5 mL methanol in a 20 mL scintillation vial. In a 50 mL two necked round bottom flask, a solution of TZCA-tbTSC was prepared by dissolving 0.1643 g (0.6780 mmol) in about 15 mL methanol. A small condenser was affixed to the vertical opening and the copper solution added dropwise as the ligand solution was stirred. This neck was then capped and allowed to reflux at 75 ° C overnight. The reaction appeared to proceed immediately, forming an ochre precipitate. The product was then gravity filtered using 15 cm qualitative 413 filter paper and set aside for air drying.
**Yield:** 0.2013 g (77.5%)

| | Ligands | Mass(g) | Percent Yield |
|---|---|---|---|
| [8] | [Pd(TZCA-TSC)Cl] | 1.3070g | (130.%) |
| [9] | [Pd(TZCA-tBTSC)Cl] | 0.2013g | (77.5%) |

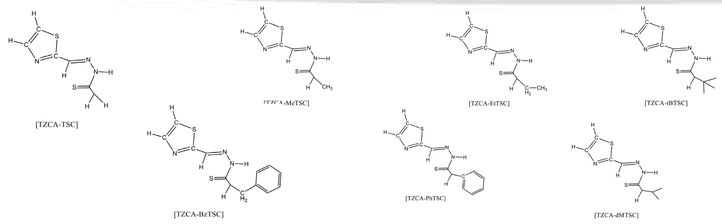



**Figure 1. Proposed structures for series of [TZCA-TSC] compounds**

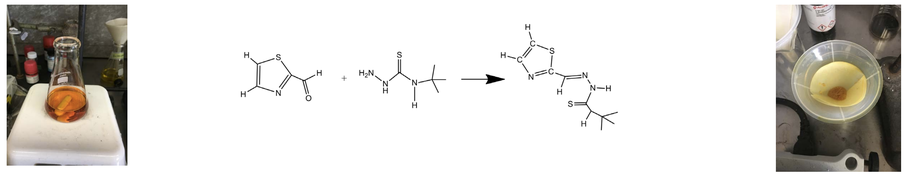
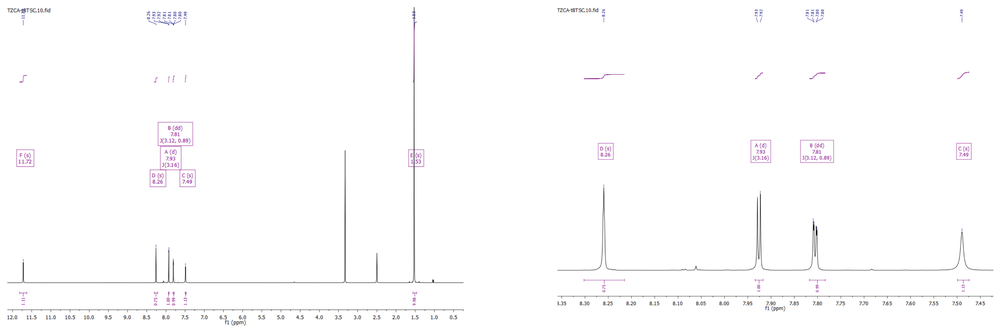


**Figure 2. Reaction of [TZCA-tBTSC]**



**The $^{1}$H NMR spectra were determined using a Varian Mercury VX 300MHz NMR.**

**Figure 3. $^{1}$H NMR and Downfield Expansion for [TZCA-tBTSC]**

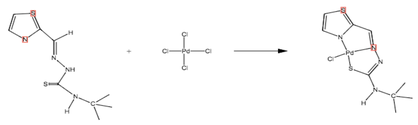


**Figure 4. Reaction of [Pd(TZCA-tBTSC)Cl]**

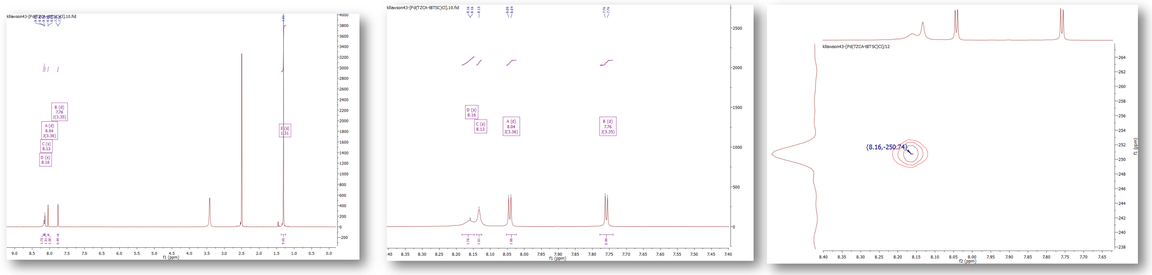


**Figure 5. $^{1}$H NMR, Downfield Expansion and HSQC spectra for [Pd (TZCA-tBTSC)Cl]**

## Results and Discussion

**For this project, a series of thiazole-2-carboxaldehyde thiosemicarbazones were synthesized, reacted with a palladium complex and spectroscopy tests($^{1}$H NMR and HSQC) were obtained. For example purposes, I chose the tert-butyl derivative of the ligand and its palladium complex. Some differences were observed in the ligand and its metal complex. In the ligand spectra, there is evidence of a hydrazinic proton that is present near 11.7 ppm in the $^{1}$H spectra. After the tert-butyl ligand was reacted with the palladium starting material, as shown in figure 4, the hydrazinic proton disappeared. We knew from the predicted reaction a thioamide group would be present in the final result. In figure 5, the 2D $^{1}$H, $^{15}$N HSQC spectrum shows evidence of the thioamide group in the final product, and where that peak is located in the $^{1}$H NMR spectrum. Multiple palladium complexes were synthesized from the ligands that are mentioned in the chart to the left. However, the only palladium complexes that showed clean $^{1}$H NMR spectra after reaction with the ligands was the [Pd(TZCA-tBTSC)Cl] complex shown here, and the [Pd(TZCA-TSC)Cl] complex. For future work, the remaining ligands that showed unclean NMR data will be recrystallized and will once again be reacted with other palladium starting materials in hopes of a cleaner result.**

## Conclusions

Now that we have successfully synthesized the whole series of the TZCA compounds, we determined that the ligands do react with the potassium tetrachloropalladate starting material but not as predicted. For future experimentation, new and cleaner ways of reacting these ligands with palladium (II) will be investigated.

## Acknowledgements

Funding was provided in part by the Tennessee Technological University URECA! Travel Grant and Chapter 606.

## References

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**[2] Huang, H., Chen, Q., Ku, X., Meng, L., Lin, L., Wang, X., ... & Liu, H. (2010). A series of α-heterocyclic carboxaldehyde thiosemicarbazones inhibit topoisomerase IIα catalytic activity. *Journal of medicinal chemistry*, *53*(8), 3048-3064.**