Testing Novel Phenolic Fluorophores as Palladium Sensors at Different Concentrations

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Introduction

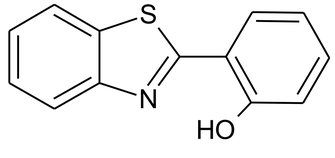
The ability of palladium metal complexes to be creatively designed has led to increased versatility and selectivity as catalysts and permitted relatively mild reaction conditions.[1] However, this has also led to an increased usage in the development of Active Pharmaceutical Ingredients (APIs). Palladium byproducts as a result of this synthesis are often difficult to remove and toxic to ingest. Therefore, it is of vital importance to efficiently and accurately identify the residual palladium catalyst in synthetic API compounds intended for use in biological studies, especially human consumption.[1]

One of the more innovative and successful approaches to sense palladium is through the installation of allyl groups onto phenolic fluorophores. The removal of this allyl group through a palladium-catalyzed substitution reaction, called the Tsuji-Trost reaction, results in a fluorescent molecule and a large increase in fluorescence as a result.[2] In most cases, a faster rate of this deallylation reaction indicates a more useful palladium sensor.

Our goal for this project was to utilize a set of phenolic fluorophores generously given to this lab in order to test their abilities at sensing palladium at different concentrations. The initial rates of the deallylation reaction can be graphed, which would tell us at what levels of palladium the compound can be distinguished from the blank and be considered an effective indicator. By using seven different concentrations of palladium, we will be able to divulge lower limits of detection for each of the novel fluorophores and determine what effects additional functional groups have on palladium sensing capabilities.

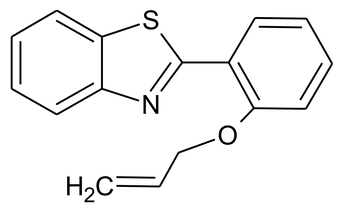
Procedure

- Prepared 10 mM solution of each compound to be tested in ~1mL DMSO
- 100 mM solutions of tri(2-furyl)phosphine (TFP) and $NaBH_4$
- Two cuvettes were prepared. One cuvette served as the blank with 2mL MeOH and one served as a sample with the following:
  - 1.9425 mL MeOH
  - 10 µL TFP (100 mM)
  - 25 µL $NaBH_4$ (100 mM)
  - 2.5 µL PM1_24A or other deallylated compound to be tested (10 mM)
  - 20 µL MeOH
- Carey Eclipse Fluorimeter used to find excitation and emission wavelengths, optimal PMT and slit widths, and background fluorescence
- Serial dilution of $Pd(allyl)_2Cl_2$ at 500 µM then 10 µM (Concentration 0). Using the the latter dilution, 1:2 dilutions were prepared down to 0.0137 µM (Concentrations 1-6).
- Two runs were performed for each trial: First the Blank, 0, 1, 2; then 3, 4, 5, and 6. The contents of these 4 cuvettes consisted of the following:
  - 1.9425 mL MeOH
  - 10 µL TFP (100 mM)
  - 25 µL $NaBH_4$ (100 mM)
  - 2.5 µL PM1_24A or other deallylated compound to be tested (10 mM)
  - 20 µL Corresponding Pd(II) concentration / MeOH (Blank)
- Fluorescence measured for 15 minutes; each compound performed in triplicate

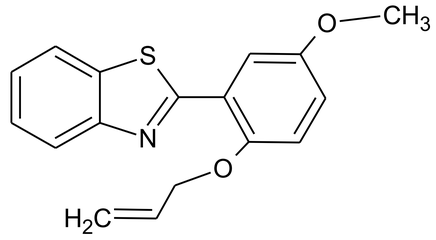


PM1_24A

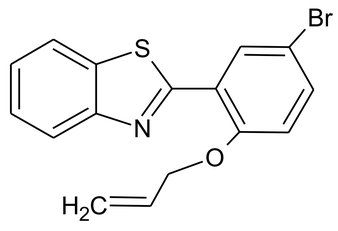
Preliminary Results



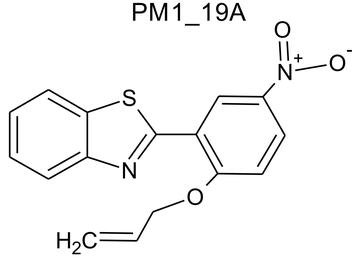
PM1_23A



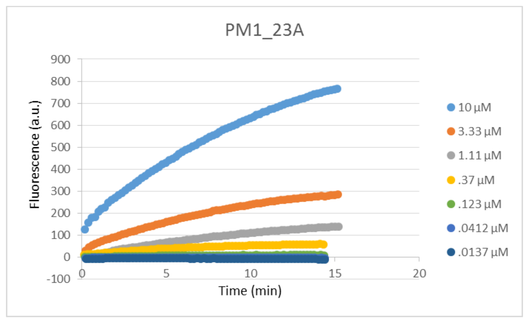
PM1_22A

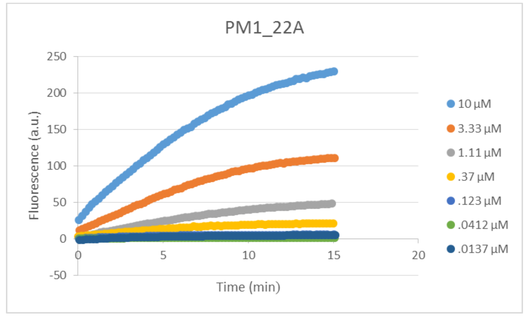


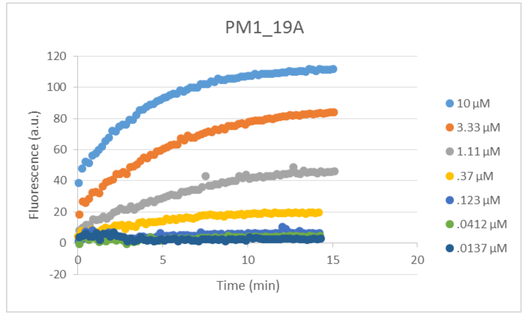
PM1_19A



PM1_17B

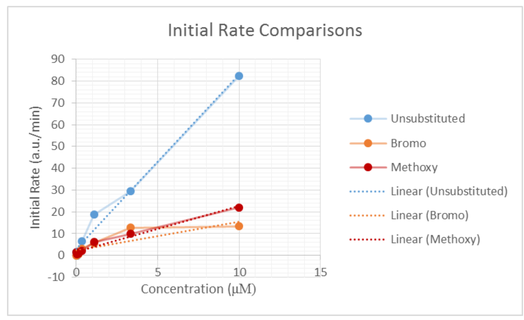






First trial of PM1_17B showed sporadic changes in background fluorescence. The instability of the compound resulted in poor results that forced us to discontinue analysis.

Analysis and Discussion



- Substituents had a negative effect on compounds viability as sensors
  - EWG (-NO2) made compound react with water to fluoresce without presence of palladium
  - EDG made the rate of fluorescence slower and had poor background fluorescence
- Unsubstituted compound (PM1_23A) seemed to work the best as a palladium sensor, though other substituents could be used to maximize if the above effects could be avoided

Future Work

The initial analysis of these compounds did not show much promise for this group of fluorescent dyes as palladium sensors. The compounds in previous research had better results. Still, there are some things that might be able to maximize the efficiency of the unsubstituted compounds success:

- Weaker electron withdrawing groups
  - Carbonyl functional groups
  - Nitrile group
  - Amine

The next logical step is to report the findings our contributor and determine if there are any other tests that should be done or if a new library of compounds should be used

References

1. Wysocki, Laura M.; Cloyd, Ryan A.; Kitley, Weston R.; Santa Maria, Peter J. Synthesis of high contrast fluorescein-diethers for rapid bench-top sensing of palladium. *Chem. Commun.*, 2015, 51, 8520-8523.
2. B. M. Trost and T. J. Fullerton, *J. Am. Chem. Soc.*, 1973, 95, 292.

Acknowledgements

We thank Wabash College for generous support through the Department of Chemistry. We would also like to thank Andrew Korich from Grand Valley State University for providing the compounds for this research.