Synthetic pathways of platinum(IV) 2-phenylpyridine halogenic derivatives as potential anticancer agents

By Pierce Brooks

Introduction

Ever since the discovery of cisplatin’s inhibition of sarcoma 180 cells in mice, cisplatin has been a staple anticancer drug. However, literature has cited cisplatin resistance in sarcoma 180 cells in mice. Furthermore, the usage of this drug is held back by its side effects. Thus, further development of the field of platinum matallochemical anticancer research is needed. One promising avenue for this research is 2-phenylpyridine halogenic derivatives like Pt(IV)(ppy)Cl2, which has demonstrated anticancer properties. Therefore, I decided to try to synthesize halogenic variations of the form Pt(ppy)2X2 with the intention of testing and comparing the different derivatives’ anticancer properties. The scope of this poster and my research up until now has been to develop a synthetic pathway to create variations with iodine.

Future research is to include the compounds according to multiple different theoretical pathways. For conciseness, I have labeled these compounds according to overall order of synthesis (see “Synthesis” section). Characteristics reported to the right were attained by my experimentation. Of particular interest is Compound 4, the synthesis of which has not yet reported in the scientific literature.

Future research is to include further halogenic variation of the compounds.

Methods

Synthesis occurred according to multiple different theoretical pathways. Identities of products and reactants were determined the proton, 1H, and 195Pt NMR. Confirmation of a reaction’s success was also done by noting variation between spectra of reactants and products.

The Compounds

During my research, I dealt with multiple intermediates and multiple pathways. For conciseness, I have labeled these compounds according to overall order of synthesis (see “Synthesis” section). Characteristics reported to the right were attained by my experimentation. Of particular interest is Compound 4, the synthesis of which has not yet reported in the scientific literature.

Future research is to include further halogenic variation of the compounds.

Synthesis

Path Reagents Product Solution Duration, Temp. Wash Yield
A Compound 0, 2-phenylpyridine Compound 1 t:1 H2O/tert-butanol 24 hr, 80°C Vacuum filtration w/ methanol wash 76%
B Compound 1, NaI/NaBr Compound 2/5 Acetone/CHCl3+ methanol 24 hr, 25°C In vacuo evap., vacuum filtration w/ H2O wash 80%
C Compound 2, I2 Compound 3 CHCl3 24 hr, 25°C DMF washes, vacuum filtration w/ H2O wash 88%
D Compound 0, NaI K2PtI4 DI H2O 60 s, 25°C No wash, proceed to path E 75%
E K2Pt4, 2-phenylpyridine Compound 2 t:1 H2O/tert-butanol 24 hr, 75°C Vacuum filtration w/ methanol wash 75%
F Compound 1, I2 Compound 4 CHCl3 20 min, 25°C N/A

Table 1: labelling scheme and experimentally derived characteristics of experimental products and intermediates. Notice that Compounds 1-4 have different halogens. See “Synthesis” section for synthetic pathway.

Conclusions

- Pathways A-E are effective means of producing Compounds 1, 2, 3, and 5
- Pathway F is ineffective
- Many NaX’s do not effectively substitute NaI in pathway D, likely due to lowered free ion stability (as per Finkelstein reaction).
- Solvent variation of successful paths (example: Compound 5, Path B) appears to be an effective means of ligating other halogens
- The isolation process of Compound 2 is a substantial hazard to sanity
- Pathway A is highly effective and consistent
- Equilibrium may prove effective route to selective compound synthesis

Acknowledgements

Dr. Murphy for help with NMR, Dr. Howard for mentorship, Dr. Keller for help with WebMO, Shadrich Sitz for being a great lab partner, and Dr. Drew for guidance in research involvement.

References


Research reported in this publication was supported by an Undergraduate Research and Scholarship Activity funding by the University of Alaska Fairbanks.