

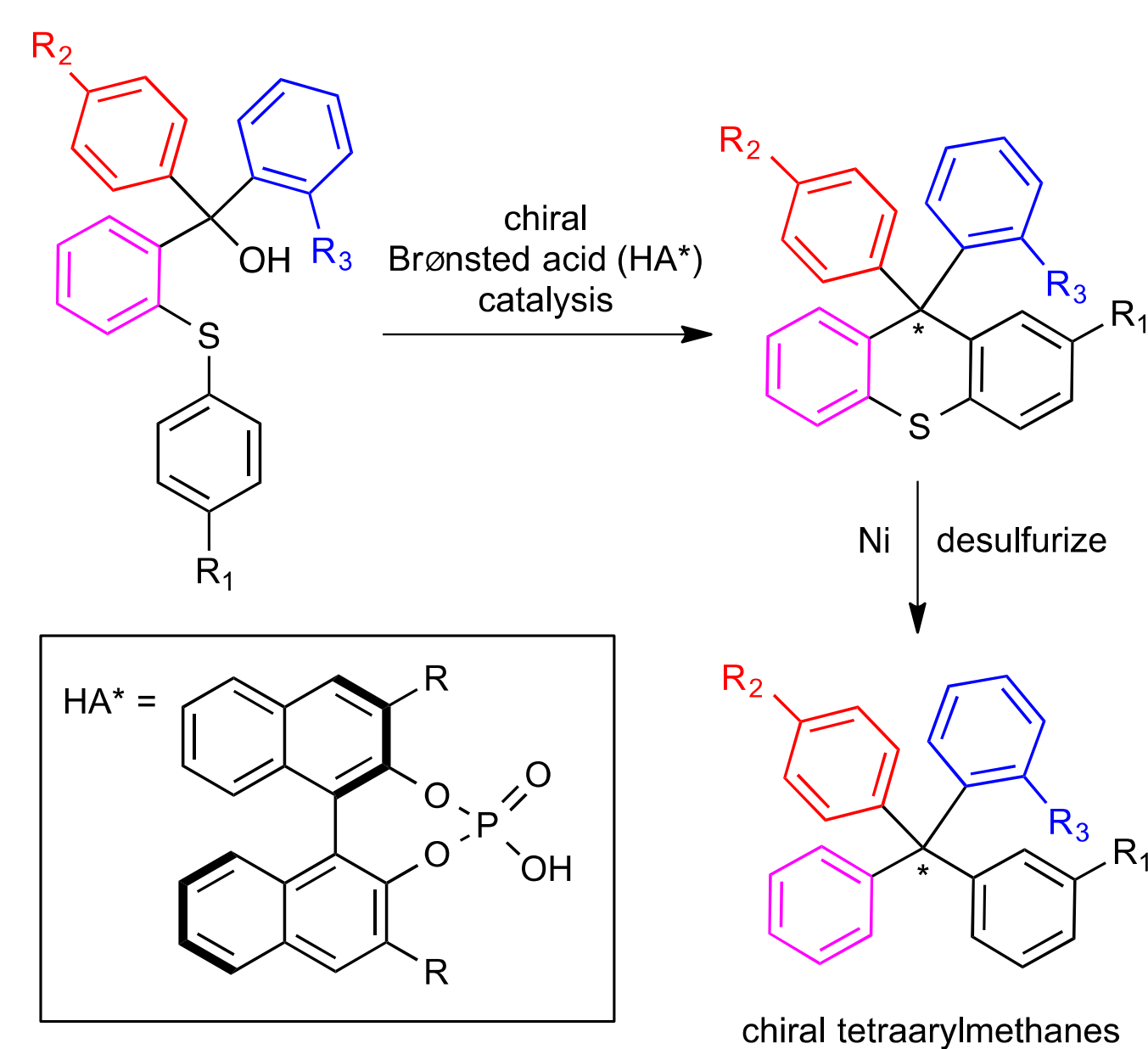
St. John T. Whittaker, Jake D. Selingo, and Dr. Arthur J. Catino

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Abstract

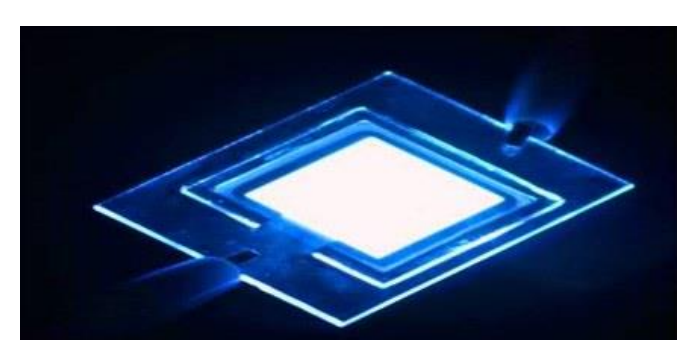
The synthesis of all-carbon quaternary stereocenters is a formidable challenge in organic chemistry. Catalytic enantioselective methods have been developed, but limitations arise as the steric demand of the substituents increases at carbon.

The aim of this research is to develop catalytic enantioselective reactions of 2-thioaryl-triarylmethanols for the preparation of quaternary stereocenters containing FOUR different aromatic groups on carbon. Subsequent desulfurization would give chiral tetraarylmethanes.

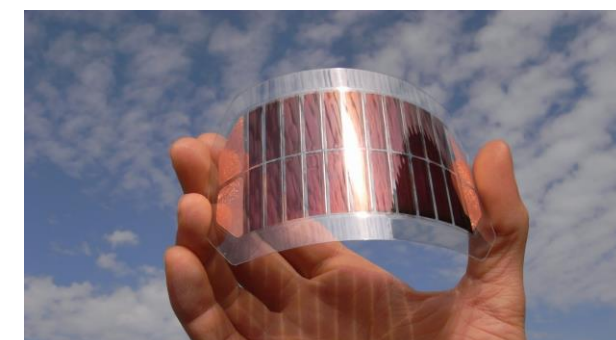


Applications of Tetraarylmethanes

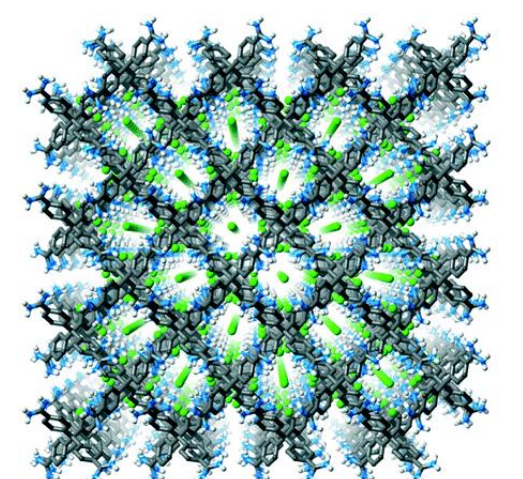
Tetraarylmethanes are utilized in numerous materials.



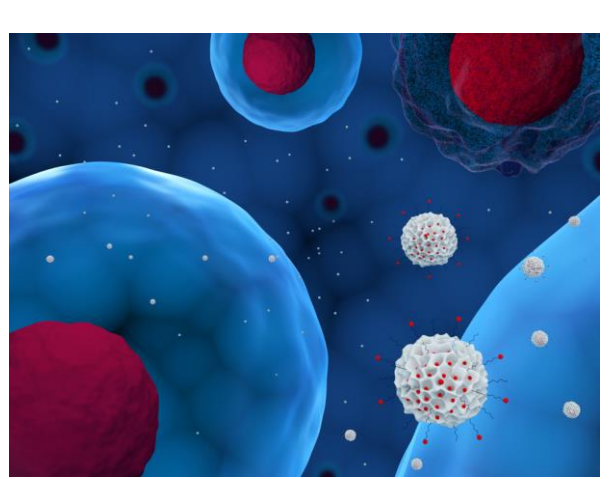
Organic LEDs (OLEDs)



Organic Solar Cells



Hydrogen Storage Materials

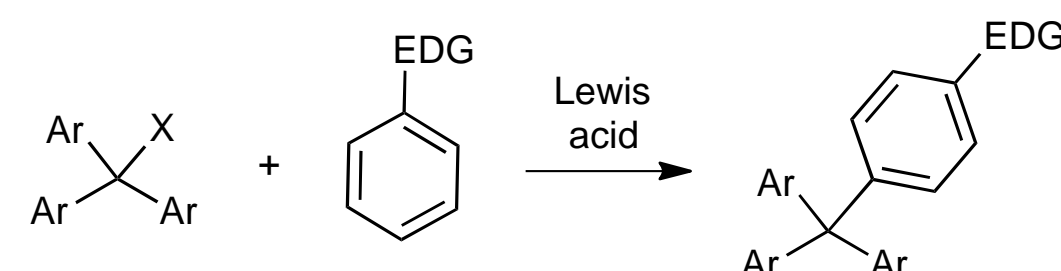


Drug Delivery/Transport Materials

** Chiral tetraarylmethanes that have never been reported and could exhibit interesting properties/applications.**

Synthesis of Tetraarylmethanes

One of the most commonly used methods to prepare tetraarylmethanes involves a Friedel-Crafts addition to triaryl halomethanes mediated by a Lewis acid.



Drawbacks:

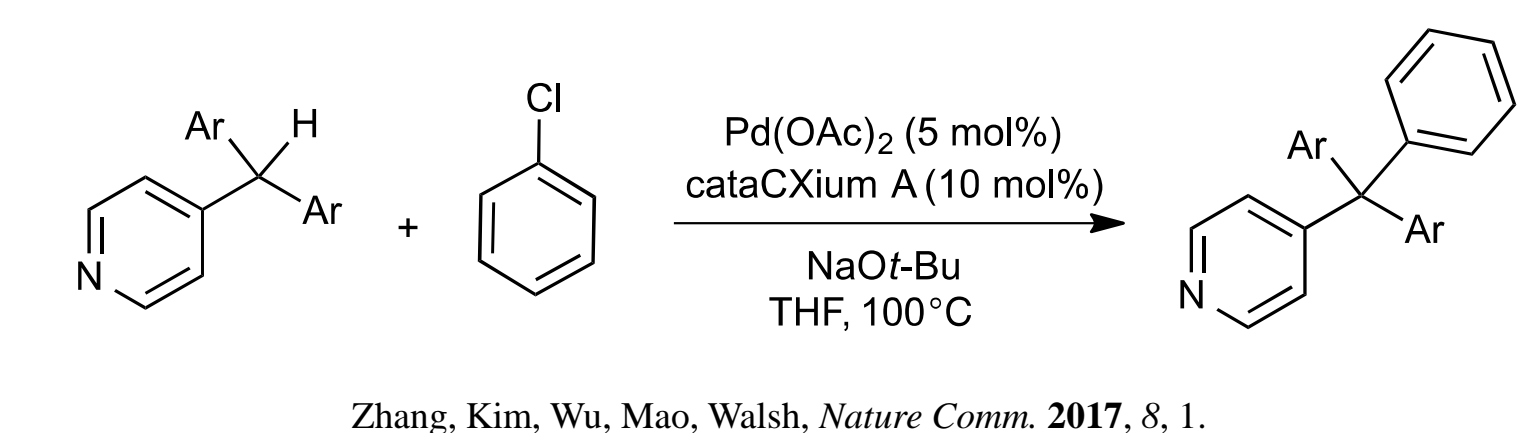
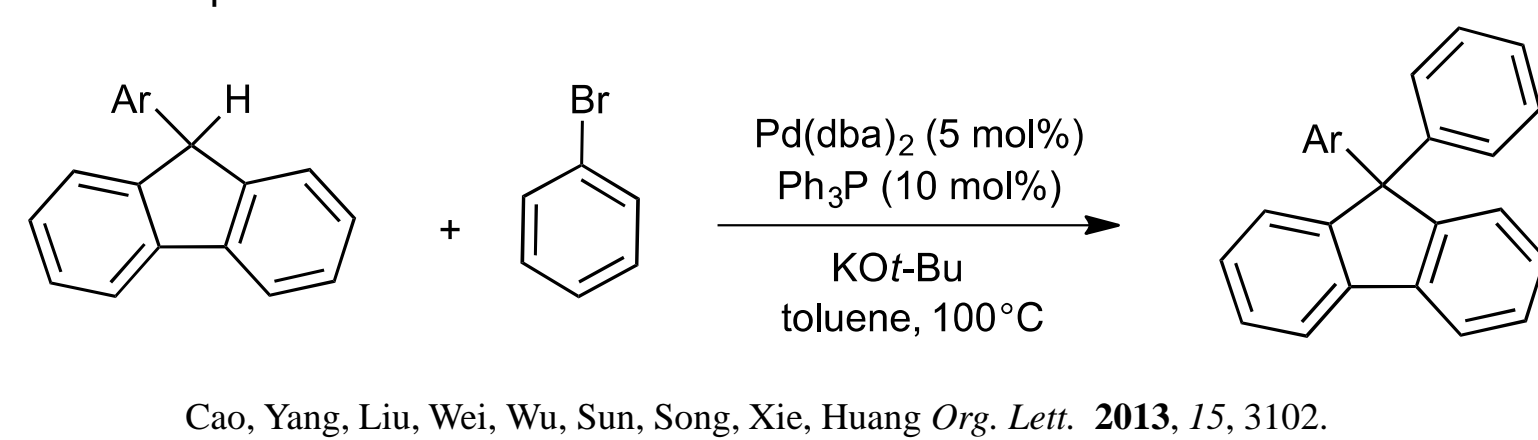
- 1) The aryl group must be substituted with a strong EDG group that is often unwanted and requires additional steps to remove.
- 2) Only *para*-substituted products can be obtained in these reactions.

For the synthesis of TPM, see: Zimmermann Müller *Synthesis* 2002, 2002, 1157.

Synthesis of Tetraarylmethanes (cont.)

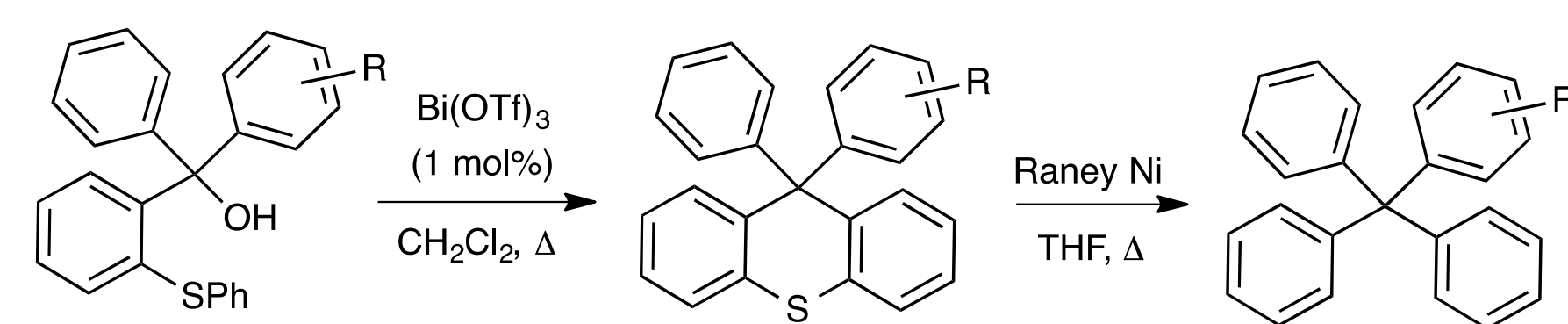
Recently, transition metal cross-coupling has become a viable strategy to prepare tetraarylmethanes.

Selected examples:



Our Strategy to Tetraarylmethanes

Our strategy is to perform an intramolecular Friedel-Crafts cyclization using a sulfur-tethered benzene group and then desulfurize to obtain the tetraarylmethane.

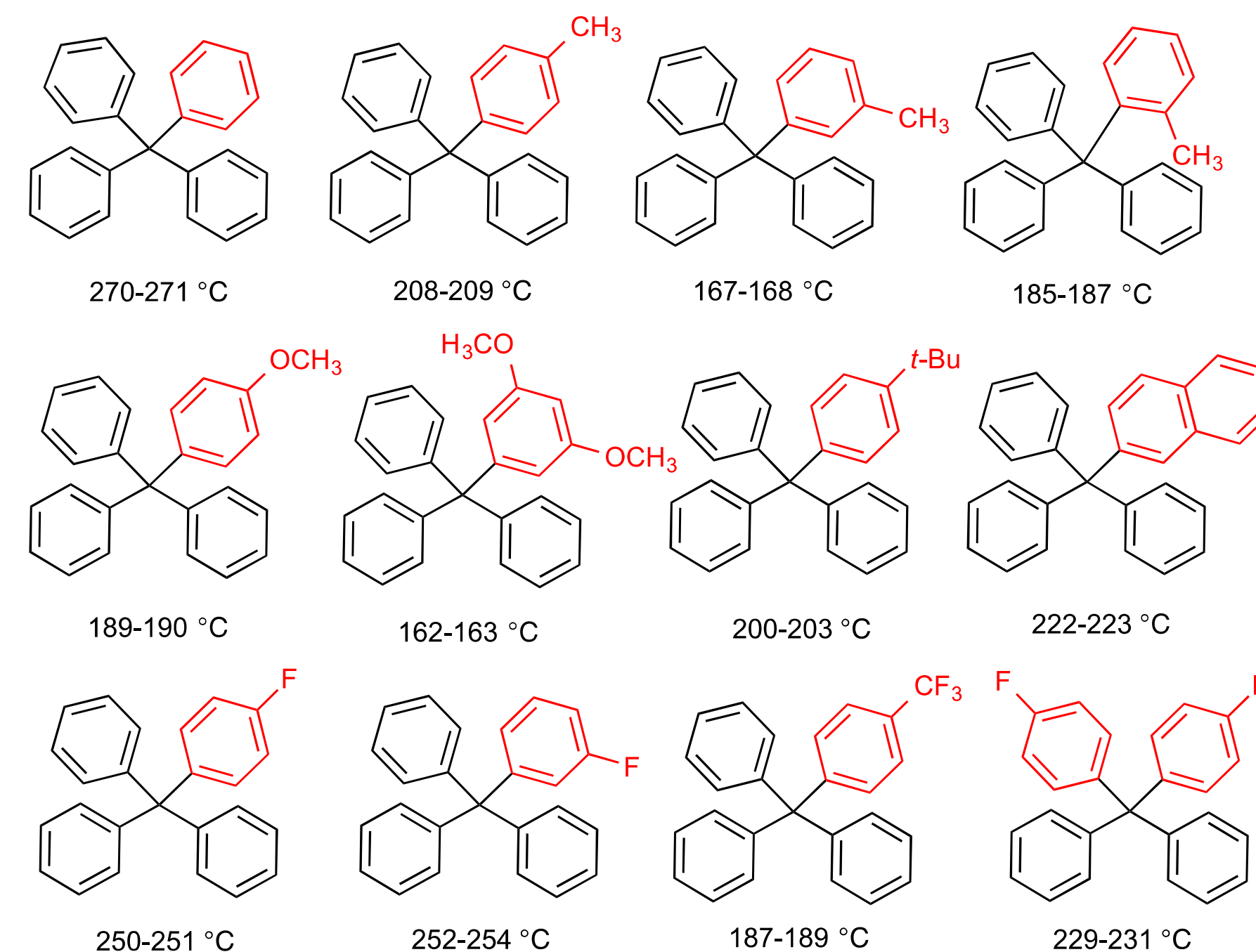


Griffin, P. J.; Fava, M. A.; Whittaker, S. T. T.; Kolonko, K. J.; Catino, A. J. Synthesis of Tetraarylmethanes via a Friedel-Crafts Cyclization/Desulfurization Strategy. *Tetrahedron Lett.* 2018, 59, 3999-4002.

Advantages:

- 1) There is no need for strong EDGs or harsh reaction conditions due to the close proximity of the tethered benzene and the formation of a thermodynamically favorable thioxanthene ring (center structure).
- 2) Access to tetraarylmethanes with all phenyl groups and/or polycyclic rings is possible.
- 3) Synthesis of tetraphenylmethanes with EDGs or EWGs that are *ortho*, *meta*, or *para* are also possible.
- 4) The 2-thiophenyl-triarylmethanols (right structure) are readily obtained from inexpensive starting materials.

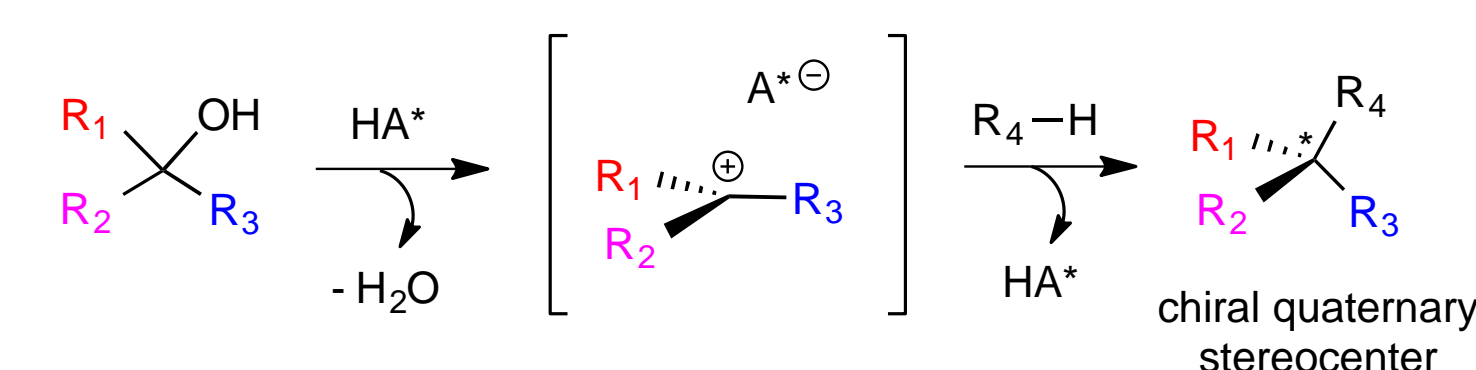
Examples of Tetraarylmethanes Prepared in our Lab



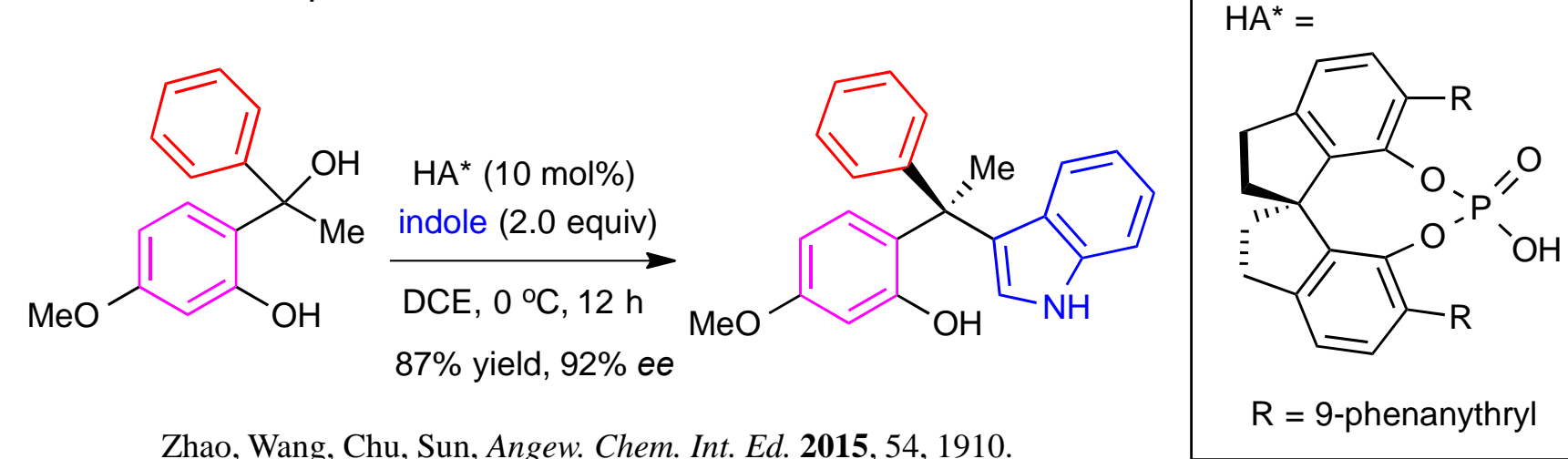
Catalytic Enantioselective Friedel-Crafts Reactions

Friedel-Crafts reactions of tertiary electrophiles catalyzed by chiral Brønsted acids (HA*) have recently emerged as a viable means to prepare highly congested quaternary stereocenters.

The general mechanism is outlined below:



Selected example:

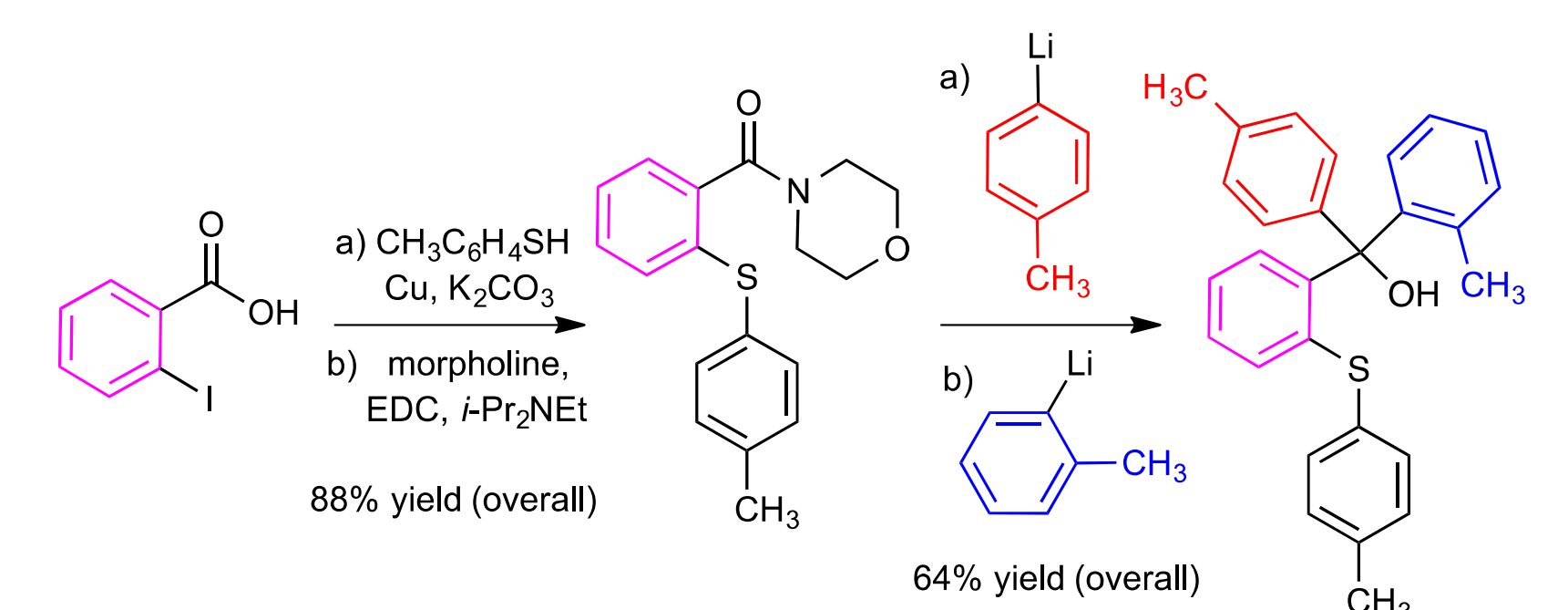


This method gives products with a quaternary stereocenter containing three aryl groups.

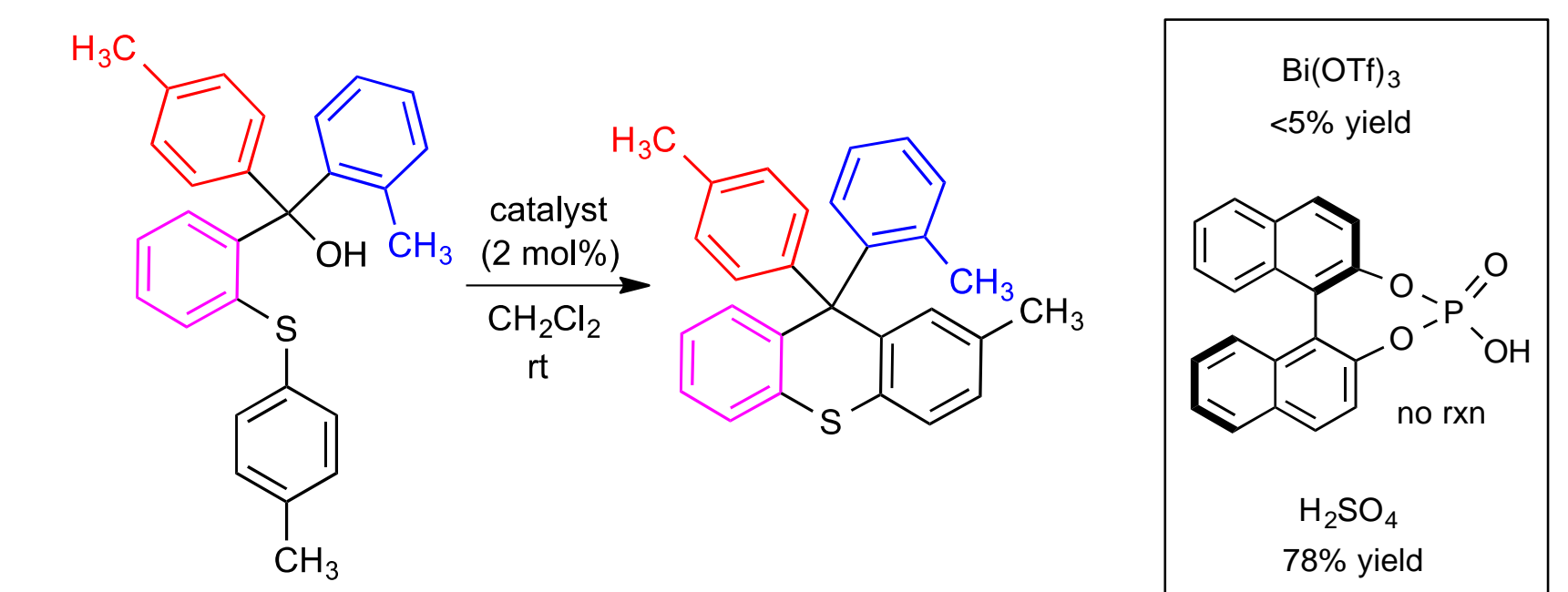
Note: A method that would give four aryl groups has not been reported.

Substrate Preparation

A 2-thioaryl-triarylmethanol substrate containing four different aryl groups was prepared in four steps from commercially available 2-iodobenzoic acid.

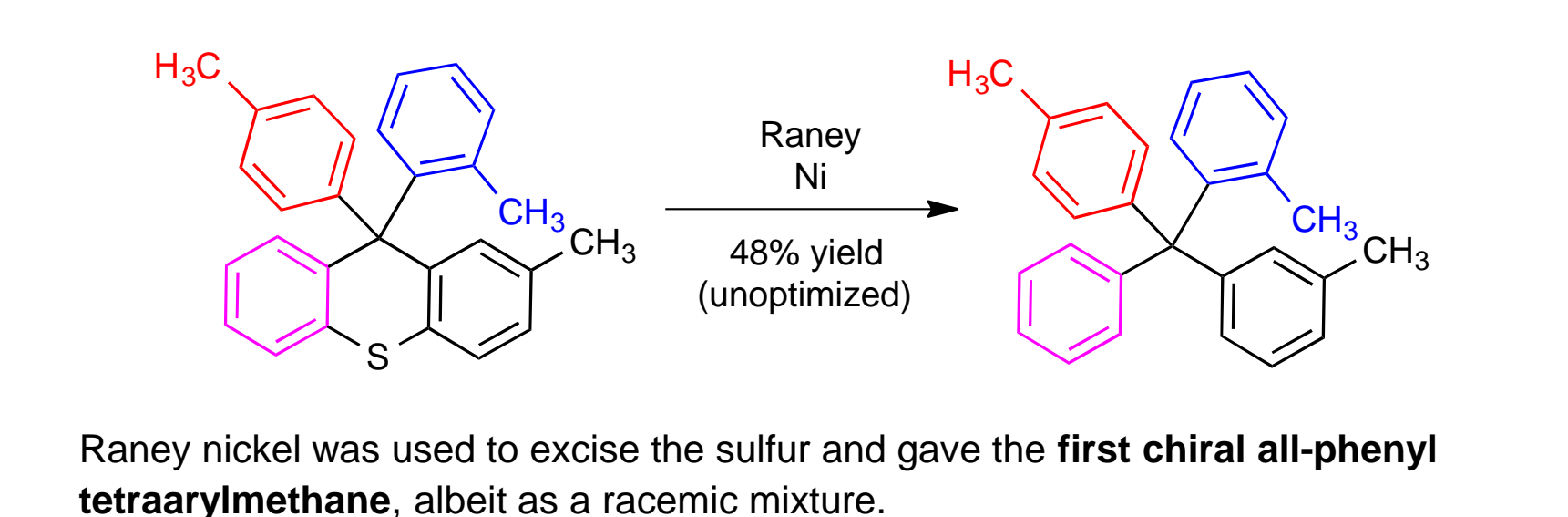


Catalyst Screen for the Friedel-Crafts Cyclization



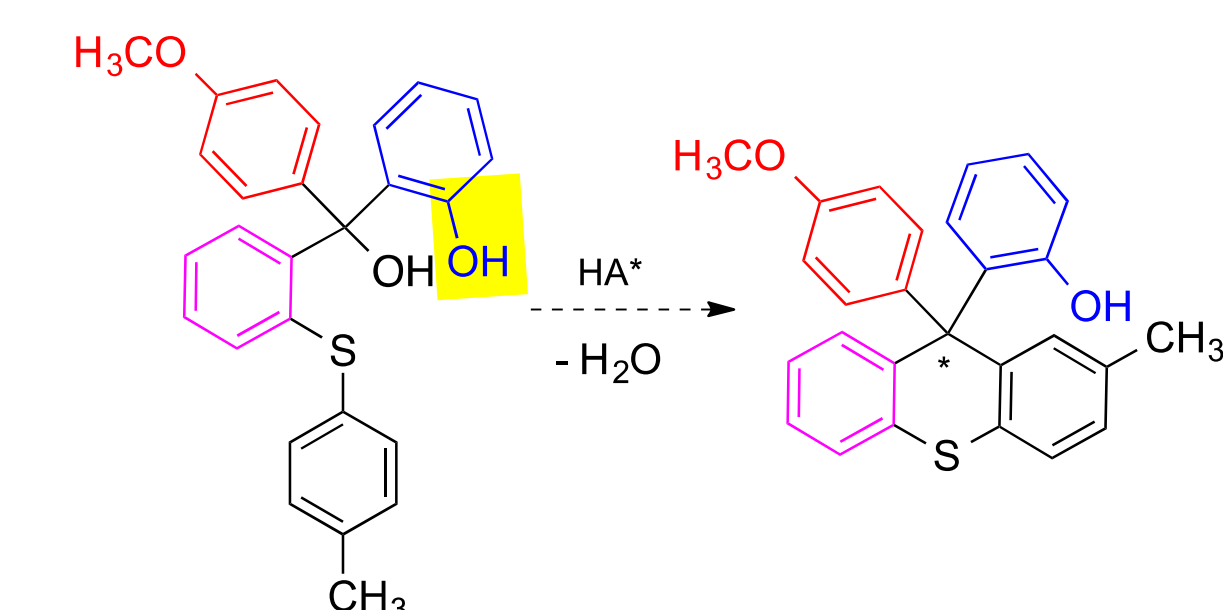
Neither bismuth triflate nor a chiral phosphoric acid (shown above) was able to catalyze the Friedel-Crafts cyclization. Only sulfuric acid was able to give the product.

Desulfurization

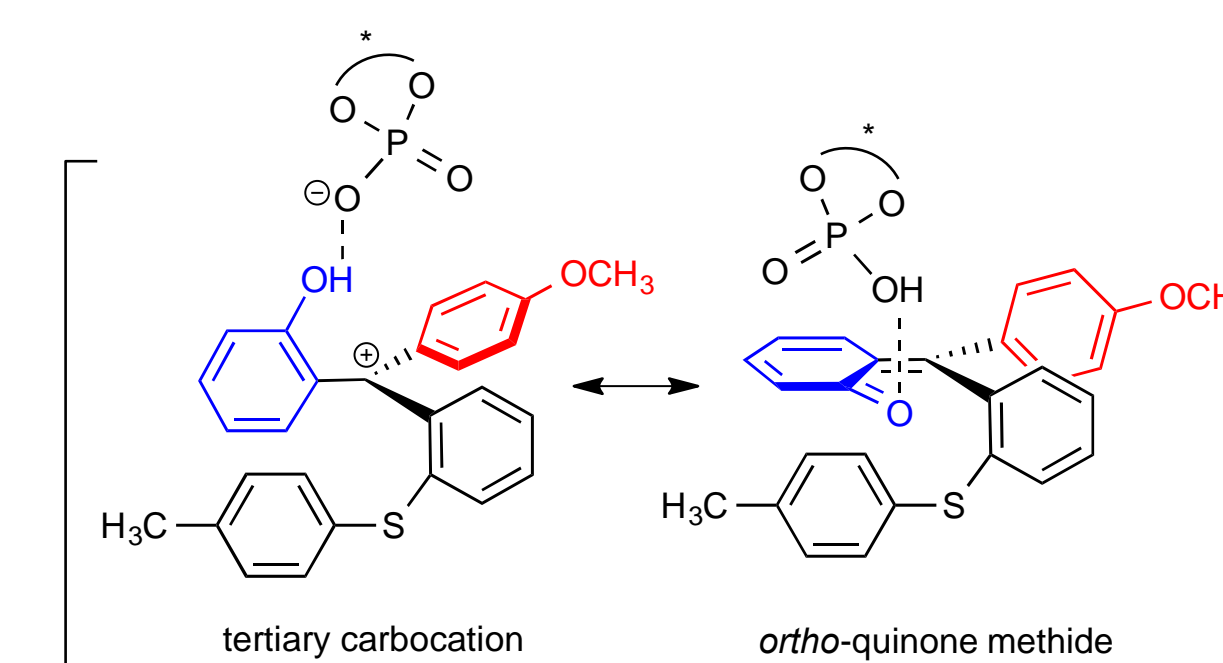


Catalysis via the *ortho*-Quinone Methide?

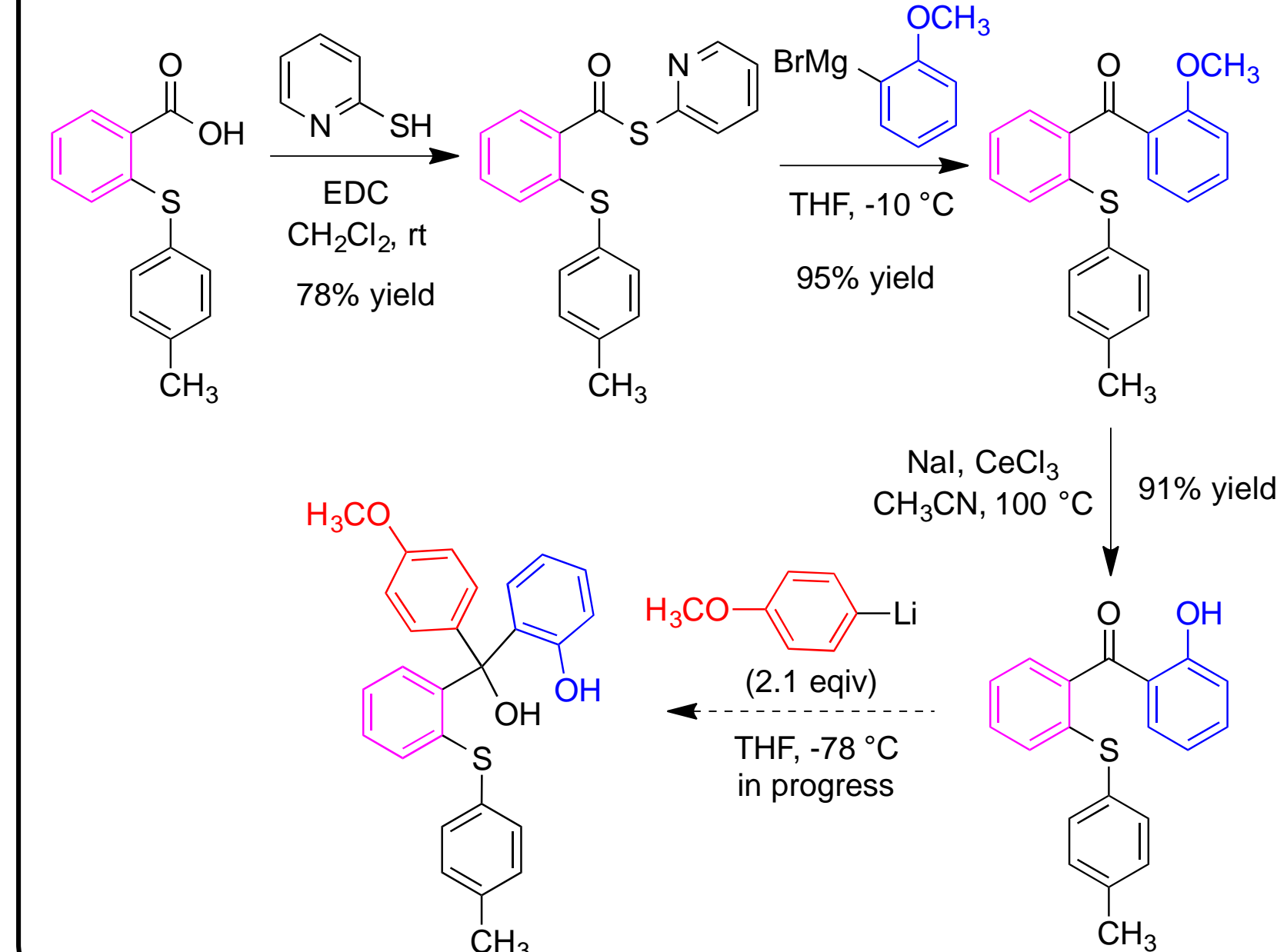
To enable us to use chiral phosphoric acids as catalysts, we suspect that a phenoxy-containing 2-thioaryl-triarylmethanol substrate would be needed.



Protonation of the tertiary alcohol and loss of H₂O would give a carbocation intermediate that would be stabilized as an *ortho*-quinone methide.



Substrate Preparation



Summary

We have reported general method to prepare tetraarylmethanes that contain all-phenyl groups and diverse substitution/electronics.

We have prepared the first chiral all-phenyl tetraarylmethane as a racemic mixture. This study revealed to us the importance of stabilizing the carbocation intermediate in the cyclization step.

Work is underway to prepare triarylmethanol substrates that would enable us to use chiral phosphoric acid catalysts in the Friedel-Crafts cyclization step.

Acknowledgements

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We are grateful to the University of Scranton for the financial and chemical supplies.