

SYNTHESIS OF FUNCTIONALISED *m*-TERPHENYLS AND CHEMOENZYMATIC SEPARATION OF ATROPISOMER

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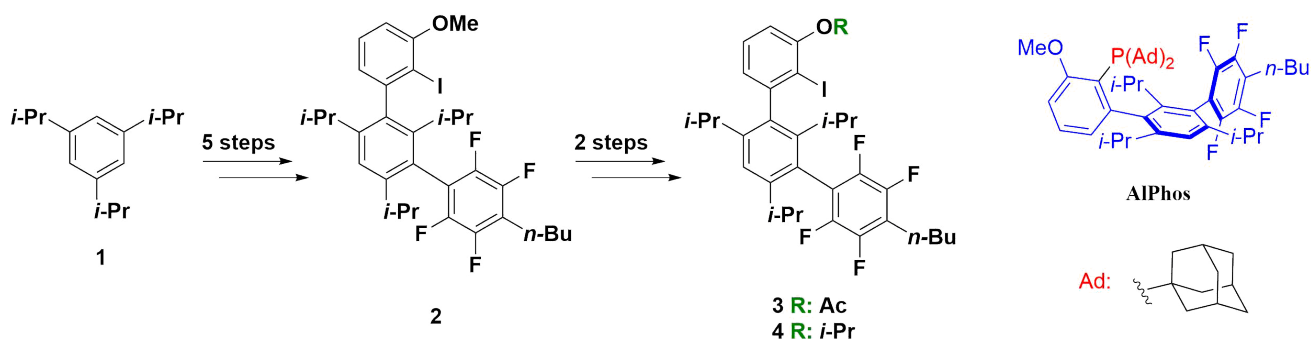


Fig. 1. General scheme for *m*-terphenyl synthesis. Structure of phosphine ligand **AlPhos**

Fluorinated aromatic substances are widely used in medicine¹ and agriculture². However, their synthesis remains complicated with commonly used methods being non-selective, requiring harsh conditions and resulting in modest product yields for sensitive substrates. A possible solution to these problems is the use of transition-metal catalysis. Its application in C-F bond formation remained elusive until relatively recently and is still requiring more research to be done.³ Thus, our team is developing new ligands, based on the structure of **AlPhos**⁴ (Fig. 1. right side), for palladium (0/II) catalysed C-F cross-coupling reactions, with the aim of expanding the (hetero)aromatic substrate range of these reactions. These ligands consist of a di-*tert*-alkylphosphine (Fig. 1. colored red) coupled with a *m*-terphenyl backbone (Fig. 1. colored blue). My work covers the synthesis and modification of the *m*-terphenyl backbone.

Furthermore, these *m*-terphenyl backbones possess axial chirality. Synthetic methods for atropisomer separation are usually difficult, require specialised equipment and reagents.⁵ Different esterases have been successfully used to separate (hetero)biaryl atropisomers with high enantioselectivity and good yields, although *m*-terphenyl compounds have yet to be studied.⁶ This work will bring a better understanding on how different esterases interact with highly hydrophobic atropisomeric substrates such as acetate **3**.

[1] Gillis, E. P.; Eastman, K. J.; Hill, M. D.; Donnelly, D. J.; Meanwell, N. A.; J. Med. Chem. 2015, 58, 8315-8359

[2] Jeschke, P.; ChemBioChem 2004, 5, 570-589

[3] Campbell, M. G.; Ritter, T.; Chem. Rev. 2015, 115, 612-633

[4] Sather, A. C.; Lee, H. G.; Valentina, R.; Yang, Y.; Müller, P.; Buchwald, S. L.; J. Am. Chem. Soc. 2015, 137, 13433-13438

[5] Carlsson, A.; Karlsson, S.; Munday, R. H.; Tatton, M. R.; Acc. Chem. Res. 2022, 55 (20), 2938-2948

[6] Olivia; Berreur, J.; Beatrice; Clayden, J.; Acc. Chem. Res. 2022, 55 (23), 3362-3375