DI-TERT-ALKYLPHOSPHINE SYNTHESIS AND INVESTIGATION OF CHEMOENZYMATIC SYNTHESIS OF THEIR PRECURSORS - TERTIARYACETATES

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Bulky di-*tert*-alkylbiaryl phosphines are used in palladium catalysed cross-coupling reactions (Buchwald amination, Suzuki-Miyaura cross coupling, Heck reaction, etc) [1]. More efficient catalysts may be developed by modifying steric and electronic properties of these ligands. However, synthesis of di-alkyl phosphines involves multiple steps [2] and toxic, highly reactive reagents [3]. Our newly developed method eliminates some of these challenges using easier to handle tris(trimethylsilyl)phosphine ($P(TMS)_3$) (Fig.1). Phosphine nucleophile generated *in situ* from $P(TMS)_3$ and triflic acid reacts with an electrophylic tertiary carbocation. The final product of this umpolung (P^-/C^+) reaction is an easily isolatable air-stable phosphine triflate salt.

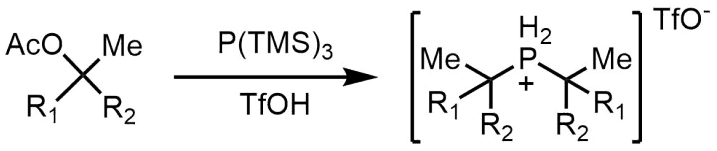

Fig. 1. Synthesis of di-*tert*-alkyl phosphine salts using $P(TMS)_3$

Currently tertiary acetates are synthesised chemically, however chemoenzymatic reactions present a greener, more energy-efficient, and in some cases, less labour-intensive means to synthesize organic molecules in comparison to traditional methods [4]. In our study a wide variety of esterases were tested for acetylation and hydrolysis of tertiary alcohols and esters (Fig. 2). Most efficient enzymes were selected for further investigations.

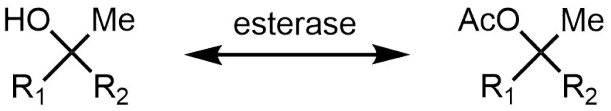

Fig. 2. Chemoenzymatic synthesis of tertiary acetates

[1] Surry, D.S.; Buchwald, S.L. Biaryl phosphane ligands in palladium-catalyzed amination. Angew. Chem. Int. Ed. 2008, 47 (34), 6338-6361
[2] Kendall, A.J.; Tyler, D.R. The synthesis of heteroleptic phosphines. Dalton Trans. 2015, 44 (28), 12473-12483
[3] Barber, T.; Argent, S.P.; Ball, T.L. Expanding Ligand Space: Preparation, Characterization, and Synthetic Applications of Air Stable, Odorless Di-tert-alkylphosphine Surrogates. ACS Catalysis, 2020, 10 (10), 5454-5461
[4] Roddan, R.; Carter, E.M., Thair, B.; Hailes, H.C. Chemoenzymatic approaches to plant natural product inspired compounds. Nat. Prod. Rep. 2022, 39 (7), 1375-1382