Palladium-Catalyzed Enantioselective Synthesis of $P$-Stereogenic Compounds via C–H Arylation

Chiral phosphine compounds are extremely useful ligands in catalysis. However, phosphorus ($P$)-chiral ligands have not been explored as extensively in catalytic reactions as axially chiral, carbon ($C$)-chiral, or planar-chiral compounds such as binap, diop, or josiphos. This is probably because $P$-chiral compounds are less easily available and more difficult to synthesize than other types of chiral compounds. Asymmetric catalysis has the potential to provide a more direct and efficient synthetic route compared to traditional resolution methods of constructing $P$-chiral compounds.
C–H bond functionalization has been an extremely popular topic over the past decade, and numerous methods based on a C–H bond activation strategy have been developed to build diverse complex molecules from unfunctionalized materials. The group of Professor Wei-Liang Duan at the Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (P. R. of China) has a longstanding interest in both the asymmetric synthesis of chiral phosphorus compounds (J. Am. Chem. Soc. 2010, 132, 5562; Org. Chem. Front. 2014, 1, 541) and C–H bond functionalization reactions (J. Am. Chem. Soc. 2013, 135, 16754). Professor Duan said: “We asked ourselves the question of whether the enantioselective C–H arylation strategy could be utilized for the synthesis of useful P-stereogenic compounds (Scheme 1).”

Professor Duan explained: “Initially, ortho-bromophenyl diphenylphosphinate was chosen as the model substrate for palladium-catalyzed intramolecular C–H arylation reactions; however, formation of racemic products – with no enantiocontrol – was observed with several ligands examined (Synthesis 2014, 46, 1067).” He continued: “Then, diarylphosphinic amides were prepared and investigated under palladium catalysis and using various chiral phosphine ligands. Finally, the use of a Taddol-based dimethylaminophosphoramidite ligand successfully generated an array of P-stereogenic compounds with up to 93% ee (Scheme 2).”

It is worth pointing out that the P–N bond of the products can be cleaved with alkyllithium reagents, and P-chiral monophosphine oxides were obtained without erosion of enantioselectivity (Scheme 3).

Professor Duan concluded: “Now, we are trying to synthesize P-chiral biaryl monophosphine ligands based on the developed protocols, and we hope that the resulting P-chiral phosphines can be utilized as efficient ligands in some asymmetric reactions.”

About the authors

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