

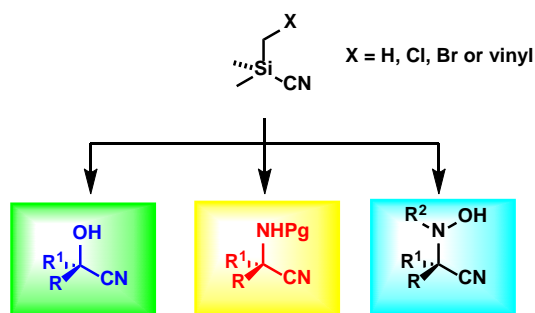
A journey in the Catalytic Enantioselective Cyanosilylation Reaction

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Catalytic enantioselective cyanosilylation of carbonyl derivatives such as ketones and ketimines are powerful for the synthesis of α -tertiary cyanohydrins, C^α -tetrasubstituted aminonitriles, and related versatile chiral synthons for a variety of value-added products.¹ Despite progress, it is still worthwhile to develop new catalyst systems, cyanating reagents and atom-economical processes to improve the scope of electrophiles of this methodology. For example, ketonitriles still present as problematic substrates for enantioselective cyanosilylation.

With our continuation in enantioselective cyanosilylation reactions, we found that bifunctional cinchona alkaloid derived (thio)urea could achieve excellent ee values in the cyanosilylation of activated ketones and ketimines.² During the mechanistic studies into the one-pot tandem Wittig-asymmetric cyanosilylation reaction, which we designed to recycle by-product Ph_3PO to activate TMSCN to facilitate the chiral (salen)AlCl complex mediated enone cyanosilylation,³ we found that phosphoranes could effectively activate (salen)AlCl for the cyanosilylation with a broad scope of ketones.⁴ We further designed a bifunctional cyanating reagent, $\text{Me}_2(\text{CH}_2\text{Cl})\text{SiCN}$, which was more active and enantioselective than TMSCN in the ketone cyanosilylation, allowing the one-pot sequential synthesis of tertiary alcohols featuring a chloromethyl ketone moiety.⁵ By phosphorane-(salen)AlCl catalyst, we developed the first highly diastereo- and enantioselective ketone cyanosilylation and kinetic resolution of α -branched aliphatic ketones. We also achieved a highly enantioselective cyanosilylation of ketonitriles using our bifunctional cyanating reagent.



Reference

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