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 Redox-Neutral Organocatalytic Mitsunobu Reactions
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A Newly Designed Catalyst for Additive-Free Mitsunobu Reactions

Category

Organo- and Biocatalysis

Key words

Mitsunobu reaction

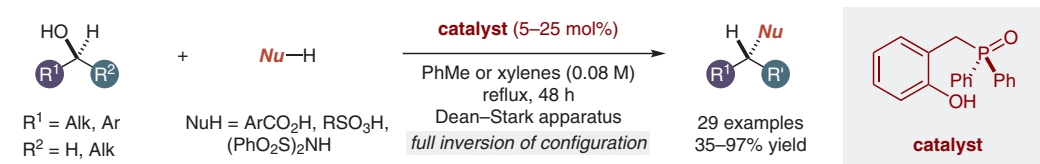
nucleophilic substitution

organophosphorus catalysis

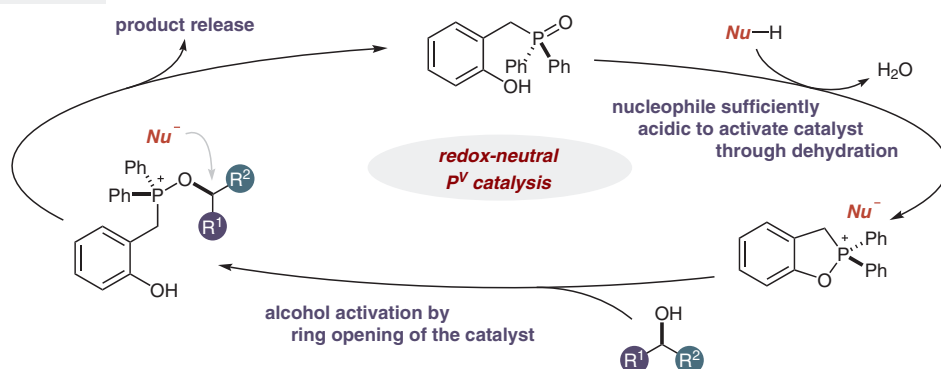
alcohols

carboxylic acids

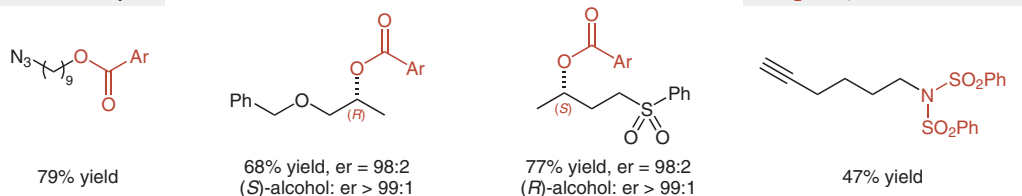
Synfact
of the
Month



Catalytic cycle:



Selected examples:



Significance: The Denton group reports a redox-neutral P(V)-catalyzed Mitsunobu reaction. Upon activation by dehydration, the newly designed phosphine oxide catalyst is converted into the corresponding dihydrobenzoxaphospholium ion, which activates an alcohol for nucleophilic attack. By this method, a variety of sufficiently acidic nucleophiles gave the corresponding substitution products in moderate to very good yields with almost complete inversion of configuration.

Comment: Mitsunobu reactions are redox condensations that are among the most valuable organic transformations because of their high degree of reliability and stereospecificity. However, they are also generally wasteful. The development of this completely catalytic version not only overcomes problems such as the use of toxic diazo compounds or the production of phosphine oxide waste, but also avoids the use of additional oxidants or reductants by operating exclusively in the P(V) regime. An orthogonal activation mode of the catalyst to permit the use of less-acidic nucleophiles would expand the generality of this method.

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