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Tributylphosphine [CAS: 998-40-3]

Application 140: Tributylphosphine-catalyzed Michael addition reactions

The non-trivial difference in the nucleophilicity parameter “N” between Bu₃P and Ph₃P (15.49 vs. 14.33) makes Bu₃P a much more effective catalyst for the Michael addition of activated olefins to electrophiles.

Bu₃P initially adds to an activated olefin such as acetonitrile to form a phosphonium β-ylid which then deprotonates an electrophile such as a diketone as the initiation step in the catalytic process.

This conjugated base of the diketone then adds to another equivalent of the activated olefin to

begin the propagation stage of the process which generates an intermediate carbanion, which in turn deprotonates a second equivalent of the diketone to form the final addition product and carry on the propagation (Figure 1).

Moreno-Mañas et al⁽¹⁾ have successfully used a 10% molar quantity of Bu₃P to generate high yields of addition products from diketones and a variety of activated olefins. Under similar conditions, Ph₃P was either relatively non-reactive or produced polymeric products.

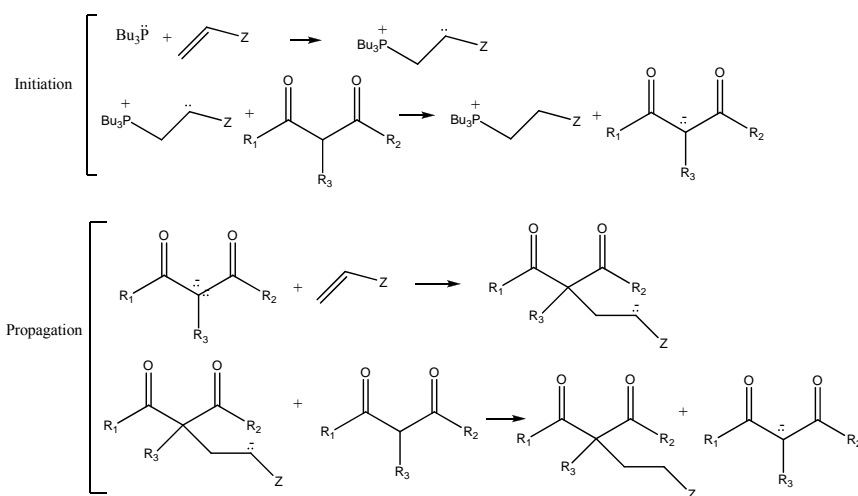


Figure 1

1) *Tetrahedron* 2005, 61, 8598-8605

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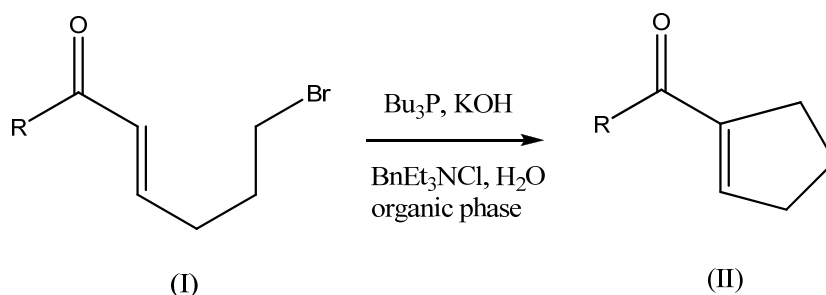
Application 490: Tri butylphosphine catalyzed alkylation via the Morita-Baylis-Hillman reaction

The Morita-Baylis-Hillman (MBH) reaction is typically an organo-amine catalyzed intermolecular addition of a β unsaturated ketone to a sp^2 hybridized aldehyde and as such is a useful synthetic tool. However, Krafft et al⁽¹⁾ have recently reported a variation of the MBH reaction in combination with PTC catalysis wherein the electrophile is now a tethered sp^3 hybridized alkylhalide.

The authors used an aqueous/organic phase system with $BnEt_3NCl$ as the PTC and Bu_3P as the MBH organo-catalyst to convert (I) via an intramolecular cyclization to (II) and obtained a yield of 84%. The chosen organic phase was t-butanol/ CH_2Cl_2 . In the absence of CH_2Cl_2 , the yields were considerably lower.

The possibility of simply a base catalyzed reaction was discounted when under the same conditions the reaction was carried out in the absence of the Bu_3P catalyst. The result was a 95% recovery of the starting material.

Five membered rings were readily formed even with only moderately activated enones ($R = \text{alkyl}$). However, when the length of the tether was extended to form six membered rings, the yields were low unless more highly activated enones were used – that is, where $R = \text{phenyl}$ or some other electronegative functional group.



1) *Synlett* 2006, No. 19, 3334-3336

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Tributylphosphine [CAS: 998-40-3]

Application 491: Tri butylphosphine catalyzed Morita-Baylis-Hillman reaction

The Morita-Baylis-Hillman (MBH) reaction is a very useful synthetic tool for the addition of aldehydes to β -unsaturated ketones. Traditionally, this reaction is catalyzed by tertiary amines but more recently tertiary alkylphosphines have been found to be much more effective.

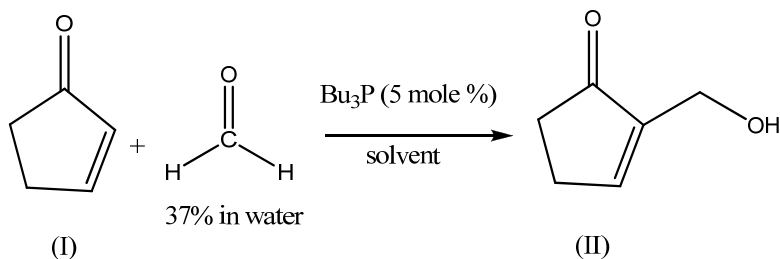
Previously reported synthesis of (II) from (I) using standard amine catalysts produced low yields (56%) with excessively long reaction times (72 h). Recently, Iguchi et al⁽¹⁾ dramatically improved the synthesis by using tertiary phosphines as the organo-catalyst. In particular, tri butylphosphine was most effective where the isolated yields were in the order of 95% in 2.5 hr at room temperature.

Dimethyl(phenyl)phosphine was also determined to be an effective catalyst. However, the

commercially available tri butylphosphine was marginally better under the same conditions. The yields were comparable but with shorter reaction times.

The authors also reported that the reaction solvent is also important with a combination of MeOH and CH₂Cl₂ providing a significant improvement over THF and dioxane.

The same protocol was used over a range of similar substrates such as six-membered ring 2-cyclohexene-1-ones having methyl substituents at positions 4,5 and 6. The corresponding 2-hydroxymethyl products were also recovered in high yields but with longer reaction times.



1) *Synthesis*, 2005, No. 18, 3035-3038