

SYNLETT Spotlight 299

Petasis Reagent

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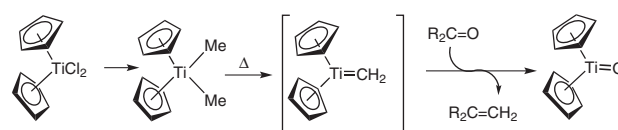


Introduction

The Petasis reagent¹ (dimethyl titanocene, Cp_2TiMe_2) is readily prepared by the reaction of methylmagnesium chloride² or methyllithium³ with titanocene dichloride. It is used for transforming carbonyl groups to terminal alkenes,⁴ like the Tebbe reagent or Wittig reaction. Unlike the Wittig reaction, the Petasis reagent can react with a wide range of carbonyls, such as aldehydes, ketones, esters, and lactones including enolizable and acid-labile substrates. The Petasis reagent is also non-pyrophoric, rel-

atively air- and water-stable, and can be used directly as a solution in toluene–THF.

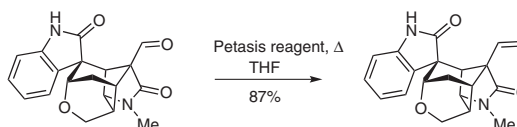
The active olefinating reagent, Cp_2TiCH_2 , can be prepared by heating the Petasis reagent in toluene or THF to 60–75 °C. The Petasis reaction can also be promoted by microwave irradiation.



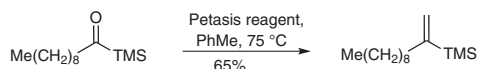
Scheme 1

Abstracts

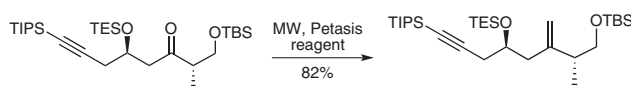
(A) Aldehydes and ketones can be selectively methylenated in the presence of less electrophilic carbonyl groups such as esters^{1a,5} and amides.⁶



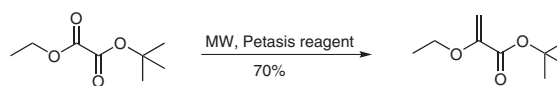
(B) Reaction of dimethyl titanocene with heteroatom-substituted carbonyls,^{1b} such as silyl esters, lactones,⁷ thioesters, selenoesters, and acylsilanes gives the corresponding heteroatom-substituted alkenes.



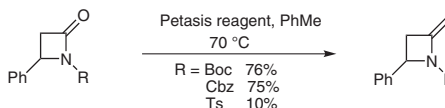
(C) Petasis methylenation can be accomplished in the presence of many protecting groups, like silyl ethers,⁸ benzyl ethers,⁹ and acetals.¹⁰ The reaction in the presence of an unprotected hydroxyl group¹¹ can also be efficient when an excess of the reagent is used.



(D) The selectivity of this reaction has been extended to unsymmetrical oxalates¹² and oxalate monoesters or monoamides. Improvement of the methylenation can be promoted by microwave irradiation.¹³



(E) The reaction of β -lactams with Cp_2TiMe_2 can be realized in good yields as long as the lactams are properly activated by N-protection.¹⁴



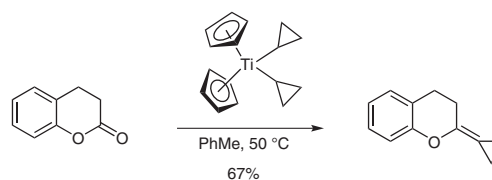
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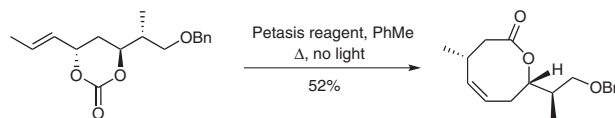
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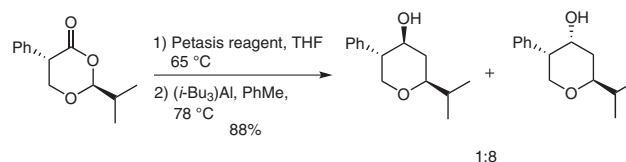
(F) Homologue dialkyltitanocene derivatives of the Petasis reagent can be prepared from titanocene dichloride and alkyllithium or Grignard reagents,¹⁵ with the exception of compounds that undergo facile β -hydride elimination.



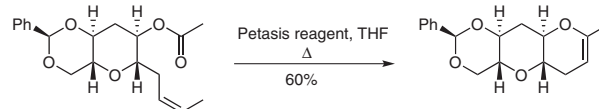
(G) The Petasis reagent has been utilized in a tandem methylenation–Claisen rearrangement to give ring extension¹⁶ or contraction.¹⁷



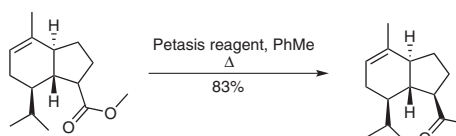
(H) One application of the Petasis reagent is the Petasis–Ferrier rearrangement,¹⁸ which involves methylenation of a 1,3-dioxan-4-one to give an enol ether which yields in the presence of a trialkylaluminum reagent a 2,6-*syn*-disubstituted tetrahydropyranone. This method has been utilized as an exceptional powerful tool for the total synthesis of complex natural product.¹⁹



(I) A one-pot methylenation–RCM procedure has been developed by Nicolaou²⁰ using Petasis reagent as both methylenation reagent and RCM catalyst.



(J) A one-carbon homologation was achieved using Petasis methylenation followed by acid hydrolysis.²¹



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