Spotlight

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

Petasis Reagent

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Introduction

The Petasis reagent1 (dimethyl titanocene, Cp₂TiMe₂) 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, relatively air- and water-stable, and can be used directly as a solution in toluene–THF.

The active olefinating reagent, Cp₂TiCH₂, 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.

Abstracts

(A) Aldehydes and ketones can be selectively methylenated in the presence of less electrophilic carbonyl groups such as esters14 and amides.6

(B) Reaction of dimethyl titanocene with heteroatom-substituted carbonyls,15 such as silylesters, 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 Cp₂TiMe₂ can be realized in good yields as long as the lactams are properly activated by N-protection.14
(F) Homologue dialkyltitanocene derivatives of the Petasis reagent can be prepared from titanocene dichloride and alkyllithium or Grignard reagents, 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 extension or contraction.

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

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

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

References