

# SYNLETT Spotlight 299

## Petasis Reagent

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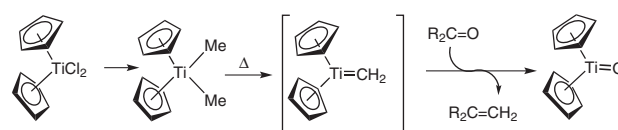
This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

### Introduction

The Petasis reagent<sup>1</sup> (dimethyl titanocene,  $\text{Cp}_2\text{TiMe}_2$ ) is readily prepared by the reaction of methylmagnesium chloride<sup>2</sup> or methyllithium<sup>3</sup> with titanocene dichloride. It is used for transforming carbonyl groups to terminal alkenes,<sup>4</sup> 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.

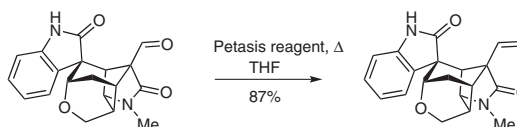
The active olefinating reagent,  $\text{Cp}_2\text{TiCH}_2$ , can be prepared by heating the Petasis reagent in toluene or THF to 60–75 °C. The Petasis reaction can also be promoted by microwave irradiation.



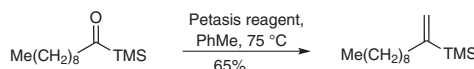
Scheme 1

### Abstracts

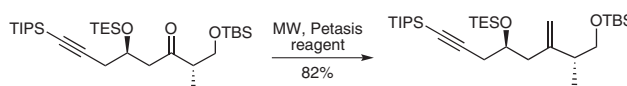
(A) Aldehydes and ketones can be selectively methylenated in the presence of less electrophilic carbonyl groups such as esters<sup>1a,5</sup> and amides.<sup>6</sup>



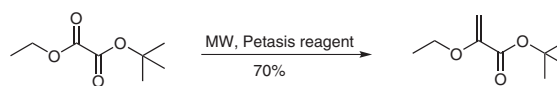
(B) Reaction of dimethyl titanocene with heteroatom-substituted carbonyls,<sup>1b</sup> such as silyl esters, lactones,<sup>7</sup> thioesters, selenoesters, and acylsilanes gives the corresponding heteroatom-substituted alkenes.



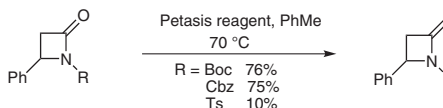
(C) Petasis methylenation can be accomplished in the presence of many protecting groups, like silyl ethers,<sup>8</sup> benzyl ethers,<sup>9</sup> and acetals.<sup>10</sup> The reaction in the presence of an unprotected hydroxyl group<sup>11</sup> can also be efficient when an excess of the reagent is used.



(D) The selectivity of this reaction has been extended to unsymmetrical oxalates<sup>12</sup> and oxalate monoesters or monoamides. Improvement of the methylenation can be promoted by microwave irradiation.<sup>13</sup>



(E) The reaction of  $\beta$ -lactams with  $\text{Cp}_2\text{TiMe}_2$  can be realized in good yields as long as the lactams are properly activated by N-protection.<sup>14</sup>



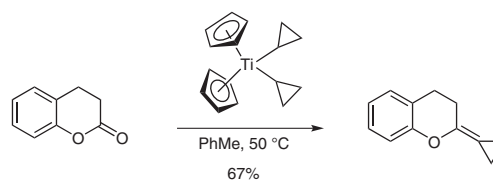
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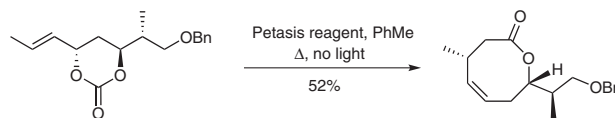
DOI: 10.1055/s-0029-1218382; Art ID: V30509ST

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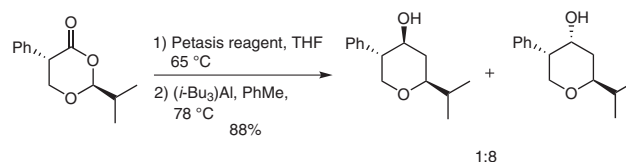
(F) Homologue dialkyltitanocene derivatives of the Petasis reagent can be prepared from titanocene dichloride and alkyl lithium or Grignard reagents,<sup>15</sup> with the exception of compounds that undergo facile  $\beta$ -hydride elimination.



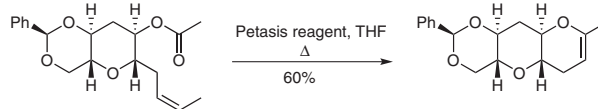
(G) The Petasis reagent has been utilized in a tandem methylenation–Claisen rearrangement to give ring extension<sup>16</sup> or contraction.<sup>17</sup>



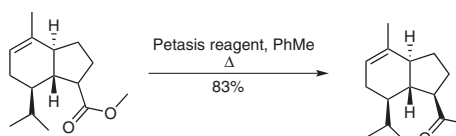
(H) One application of the Petasis reagent is the Petasis–Ferrier rearrangement,<sup>18</sup> which involves methylenation of a 1,3-dioxan-4-one to give an enol ether which yields in the presence of a trialkylaluminum reagent a 2,6-*syn*-disubstituted tetrahydropyranone. This method has been utilized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



(I) A one-pot methylenation–RCM procedure has been developed by Nicolaou<sup>20</sup> using Petasis reagent as both methylenation reagent and RCM catalyst.



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



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