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## Cyanomethylenetriethylphosphorane, a powerful reagent for the Wittig olefination of esters, lactones and imides

Tetsuto Tsunoda,\* Harue Takagi, Daiki Takaba, Hiroto Kaku and Shô Itô

*Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima 770-8514, Japan*

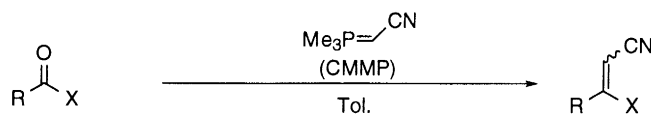
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### Abstract

Cyanomethylenetriethylphosphorane (CMMP) reacted with esters, lactones, *N*-Boc lactam, and cyclic imide to give the corresponding Wittig products in excellent yield. © 1999 Elsevier Science Ltd. All rights reserved.

*Keywords:* Wittig reactions; phosphoranes; esters; lactones; imides; nitriles; enol ethers.

The Wittig reaction is the most important and the most popular chemical transformation for the olefination of simple carbonyl compounds, aldehydes and ketones.<sup>1</sup> Compared with this, the similar reaction, conveniently called the ‘non-classical’ Wittig reaction, of carboxylic acid derivatives, such as esters, thioesters, lactones, anhydrides and imides, is by far less popular than the classical Wittig reaction, because of the reduced carbonyl reactivity toward phosphoranes,<sup>2</sup> although some improvements have been reported.<sup>3,4</sup> In the course of the evaluation of new Mitsunobu reagents,<sup>5</sup> we found that cyanomethylenetriethylphosphorane (CMMP) underwent the non-classical Wittig reaction with these functional groups in good to excellent yields (Scheme 1). Some representative examples are described herein.<sup>6</sup>



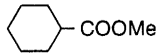
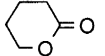
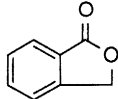
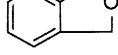
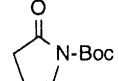
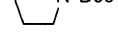
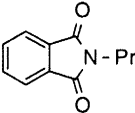
Scheme 1.

The intermolecular reaction of a simple ester with a phosphorane has only rarely been reported.<sup>3</sup> The reaction of methyl benzoate with CMMP does not occur in toluene at room temperature, but it proceeds smoothly at 100°C to give the corresponding enol ether (a 0.9: 1 mixture of *E*- and *Z*-isomers) in 89% yield as shown in Table 1. The use of cyanomethylenetriethylphosphorane (CMBP) for the same transformation afforded 61% of the enol ether along with the starting ester even at 150°C (entry 2),

\* Corresponding author. Fax: +81 88 655 3051; e-mail: tsunoda@ph.bunri-u.ac.jp (T. Tsunoda)

suggesting that the bulkier the alkyl groups on phosphorus, the less reactive the mediator is for the non-classical Wittig reaction (entry 1 versus 2). Methyl octanoate is less reactive than methyl benzoate, thus requiring 4 equivalents of CMMP to give a comparable yield of the product (entry 5). Also shown is the steric effect of the alkyl group on either end (entries 3, 4 and 6). On the contrary, the olefination of lactones,<sup>3</sup> *N*-Boc lactam, and imide occurs easily at room temperature (entries 7, 8, 10 and 12) but, in some cases, the best yield of product is obtained at 100°C (entries 9 and 11). However, the reaction of simple amides did not proceed. In all cases presented herein, the mixtures of *E*- and *Z*-isomers obtained probably reflects the steric situation of the substrates. The poor selectivity for these products may be overcome when the enol ethers are hydrolyzed to the corresponding ketones.

Table 1  
Wittig olefination of carbonyl compounds with CMMP

entry	carbonyl compound	equiv. of CMMP	temp. (°C)	period (h)	yield (%)	<i>E</i> / <i>Z</i> ratio
1	PhCOOMe	2	100	48	89	0.9 / 1
2		2 <sup>a</sup>	150	48	61	1.1 / 1
3	PhCOOEt	2	100	48	61	0.8 / 1
4	PhCOOBu <sup>t</sup>	2	150	24	trace	
5	<i>n</i> -C <sub>7</sub> H <sub>15</sub> COOMe	4	100	48	83	1.6 / 1
6		4	120	48	67	0.5 / 1
7		2	r.t.	48	93	3.7 / 1
8		2	r.t.	48	35	0.4 / 1
9		2	100	24	93	0.6 / 1
10		2	r.t.	48	79	2.7 / 1
11		2	100	48	92	3 / 1
12		2	r.t.	48	96	1.3 / 1

<sup>a</sup>: CMBP was used as a reagent.

Thus, CMMP was shown to be active enough to undergo the non-classical Wittig reaction and, therefore, provides a valuable new methodology for the preparation of the enol ethers or the corresponding ketones from carboxylic acid derivatives at various stages of organic synthesis.

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6. Experimental conditions: CMMP (2.0–4.0 mmol) was added to a dry toluene solution (5 mL) of an ester (1 mmol) with stirring under argon atmosphere. For the reactions at a higher temperature, the mixture of the reactants was heated in an Ace pressure tube (Ace Glass Inc., max. 200 psi), after careful manipulation under argon atmosphere. After completion of the reaction, the solvent was evaporated in vacuo and the product was purified by silica gel column chromatography. The configuration at the double bond was assigned on the basis of the chemical shifts and/or NOESY NMR experiments.