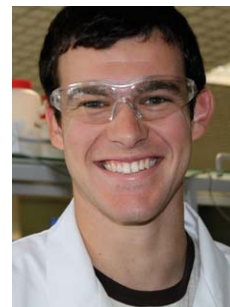


SYNLETT Spotlight 427

(Triphenylphosphoranylidene)ketene: The Bestmann Ylide

Compiled by Mark Bartlett



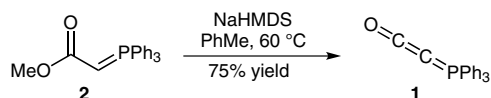
This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Mark Bartlett was born and schooled in New Zealand and ventured across the Pacific to undertake an undergraduate degree in Chemistry at Stanford University under the supervision of Professor Barry Trost. He subsequently worked as a medicinal chemist at Roche, Palo Alto, and has since returned to New Zealand, where he is pursuing a Ph.D. at Victoria University of Wellington under the guidance of Dr. Joanne Harvey. His research is focused on the total synthesis of natural products.

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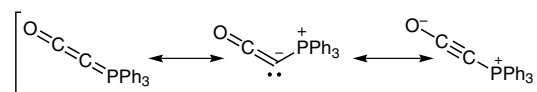
Introduction

(Triphenylphosphoranylidene)ketene (**1**), also known as the Bestmann ylide, is a reagent with intriguing properties and proven synthetic utility.¹ After early reports of this compound by others,² H. J. Bestmann popularized the use of **1** in the formation of a wide range of (triphenylphosphoranylidene)acyl derivatives.³ The Bestmann ylide (**1**) is now commercially available and used in a wide range of reactions. Alternatively, **1** can be prepared by the deprotonation of methyl (triphenylphosphoranylidene)acetate (**2**, Scheme 1),⁴ A variety of strong bases have been used to perform this transformation,⁵ with NaHMDS being particularly efficient and convenient.



Scheme 1 Preparation of the Bestmann ylide

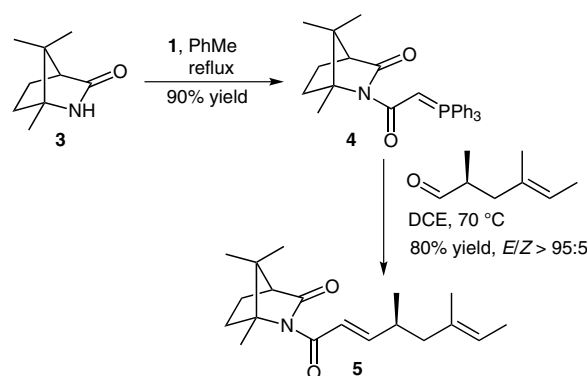
Interestingly, the X-ray crystal structure of **1** shows a 145.5° P=C=C bond angle and a remarkably short C=C bond length (1.21 Å).⁶ These properties are derived from the combination of three resonance structures (Scheme 2), which highlight the two overlapping, orthogonal π -systems that stabilize the molecule. This makes the reactivity of the Bestmann ylide significantly different from typical ketenes and phosphorus ylides. The Bestmann ylide is surprisingly stable and can be stored under inert atmosphere at ambient temperature for months.⁴



Scheme 2 Resonance structures of **1**

Abstracts

(A) Boeckman and co-workers have reported the use of the Bestmann ylide (**1**) as a linchpin in the assembly of highly functionalized α,β -unsaturated carbonyl motifs.⁷ Addition of the camphor-derived lactam **3** to the Bestmann ylide provided the desired imide **4** in excellent yield. Subsequent Wittig olefination enabled efficient access to the conjugated intermediate **5**. This reaction sequence ultimately led to the total synthesis of the bioactive natural product rasfonin.^{7a} Schobert and co-workers have also demonstrated that similar reaction sequences can be performed in a single pot.⁸ Additionally, the intermediate phosphorus ylide **4** can be α -alkylated with a range of different alkyl halides, ultimately giving rise to trisubstituted α,β -unsaturated carbonyls.^{7b} An analogous strategy has also been employed by Laschat and co-workers in the synthesis of (2*E*,4*Z*)-dienamides.⁹



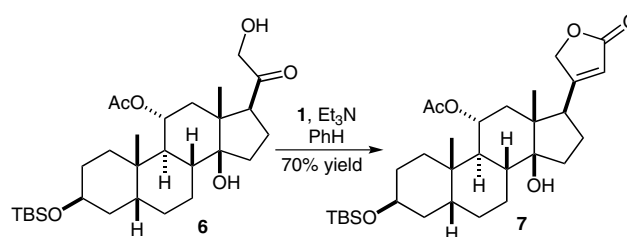
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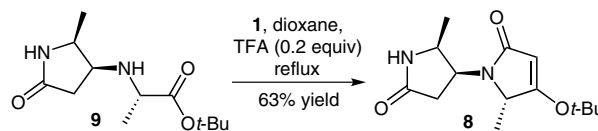
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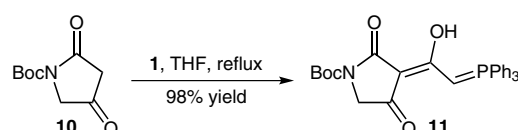
(B) Jung and Yoo recently reported the use of the Bestmann ylide to form a butenolide ring in the total synthesis of rhodexin A.¹⁰ Addition of the alcohol **6** to the electrophilic ketene carbon of **1**, followed by an intramolecular Wittig reaction gave rise to butenolide **7**. It is interesting to note that the primary alcohol is selectively acylated in the presence of a tertiary alcohol. This approach has been utilized in the synthesis of a number of butenolide-containing natural products and natural product analogues.¹¹



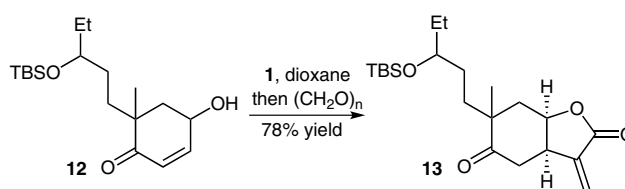
(C) Burgess and co-workers utilized the Bestmann ylide in the preparation of tetramic acid derivatives, such as **8**.¹² Addition of **1** to the amino ester **9**, in the presence of catalytic trifluoroacetic acid (TFA) provided conjugated enol ether **8** after an intramolecular Wittig reaction with the ester functional group.



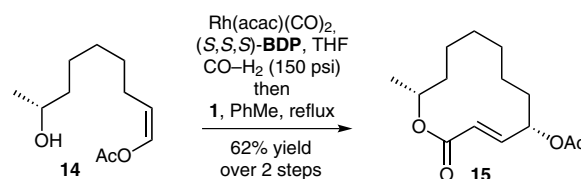
(D) Schobert and co-workers have shown that both tetramic and tetronic acids undergo selective acylation at C3 when treated with the Bestmann ylide.¹³ Tetramic acid **10** provided near-quantitative yield of the desired product **11**, which ultimately allowed the total synthesis of ravenic acid.



(E) Taylor and co-workers have developed a novel multi-component annulation using **1**.¹⁴ Acylation of a γ -hydroxy- α,β -unsaturated ketone, such as **12**, generates a nucleophilic phosphorus ylide and triggers an intramolecular Michael addition. A subsequent Wittig reaction with an exogenous aldehyde provides a rapid method of preparing α -alkylidene- γ -butyrolactones. This reaction was recently used to prepare **13**, an intermediate in the total synthesis of yomogin.^{14b}



(F) Burke and Risi recently reported a highly efficient enantioselective hydroformylation–macrocyclization cascade using the Bestmann ylide **1**.¹⁵ Enol ester **14** was subjected to a Rh(I)-catalyzed asymmetric hydroformylation using the (*S,S,S*)-bis(diazaphospholane) [(*S,S,S*)-BDP] ligand initially developed by Landis and co-workers.¹⁶



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