

SYNLETT Spotlight

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

Diethyl Vinylphosphonate

Compiled by Piotr Maria Zagórski

Piotr Maria Zagórski was born in Zgierz, Poland, in 1982. He obtained his M.Sc. (2009) in organic chemistry and synthesis from the University of Łódź, Poland. At the moment, he is pursuing his Ph.D. in synthetic organic chemistry at the same university under supervision of Professor Dr. Andrzej Józwiak and Dr. Dariusz Cal. His research is focused on the synthesis of isoindolinone derivatives functionalized with phosphonate substituents.

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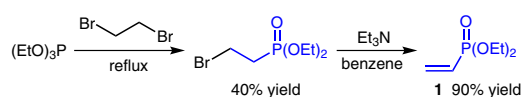
Dedicated to my best friends, Dr. Emilia Obijalska, M.Sc. Marcin Kowalski, M.Sc. Paweł Tokarz, and M.Sc. Aneta Wróblewska.



Introduction

Diethyl vinylphosphonate (**1**, vinyl phosphonic acid diethyl ester) is a colorless liquid with a characteristic odor, a density of 1.055 g·cm⁻³, and a boiling point of 50 °C at one Torr. The synthesis reported by Ford-Moore and Williams in 1947 is still the most convenient preparation.¹ The first step of this procedure consists of an Arbuzov reaction, followed by an elimination of the intermediate

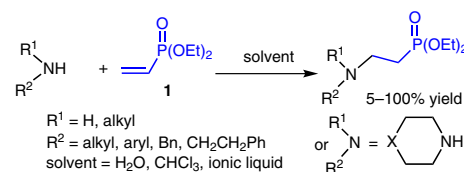
diethyl 2-bromoethanephosphonate. Diethyl vinylphosphonate is used in Michael-type additions, various metal-supported coupling reactions, cross-metathesis reactions, and in many types of cycloaddition reactions.



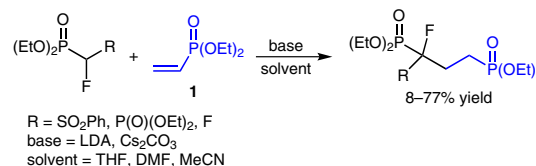
Scheme 1

Abstracts

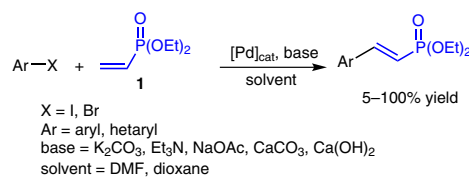
(A) The most commonly exploited reactions performed with **1** are Michael-type additions. These reactions can be applied in the synthesis of alkyl or aryl phosphonic amino esters, including cyclic ones. The reaction can be carried out in water^{2a,b} or ionic liquids,^{2c} in line with the trends of contemporary green chemistry.



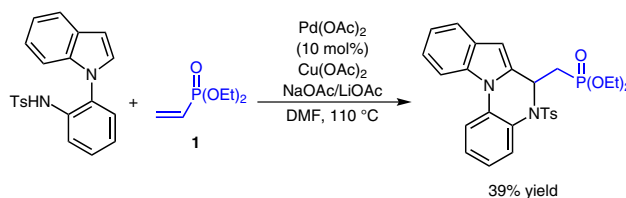
(B) Michael reactions, 1,4-additions of carbanions, lead to the formation of C–C bonds. For example, deprotonation of highly CH-acidic monofluorinated phosphonates, followed by addition to the **1**, yields substituted terminal bisphosphonates.^{3a-c}



(C) Diethyl vinylphosphonate (**1**) can be also be applied as a vinyl-ogous reagent in Heck-type coupling reactions. Diverse substituted mono- and polycyclic aromatic halides were treated with **1** in the presence of palladium catalysts. The yield of the reaction strongly depends on the type of the base used and varies for different aryl halides.^{4a,b}



(D) If an appropriate aromatic substrate is used, the palladium-catalyzed olefination can be followed by cyclization. Phosphonic, polycyclic derivatives of piperazine were prepared by this sequence.⁵



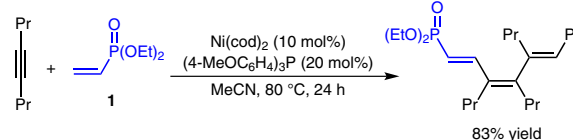
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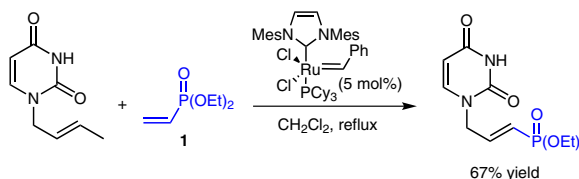
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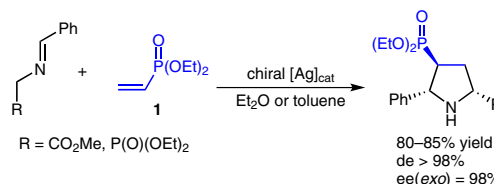
(E) Xiao and co-workers reported an interesting example of a cascade coupling using **1** and a substituted acetylene, forming a product with a conjugated system of double bonds. This cotrimerization was carried out under nickel catalysis.⁶



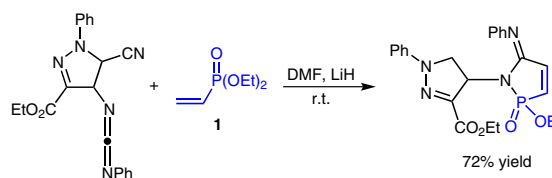
(F) The double bond of **1** can be exploited in ruthenium-mediated cross-metathesis reactions. Recently, it was applied in the synthesis of novel acyclic nucleoside phosphonates, structurally similar to known bioactive compounds, such as cidofovir.⁷



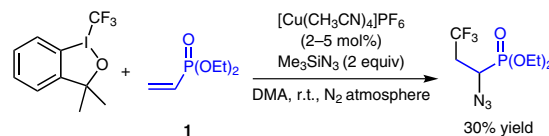
(G) Cycloaddition of diethyl vinylphosphonate (**1**) with carboxylic or phosphonic iminoesters afforded 3-phosphonylated 2,5-disubstituted pyrrolidines. The reaction was carried out in the presence of a chiral silver catalyst and with high enantio- and diastereoselectivity.^{8a-c}



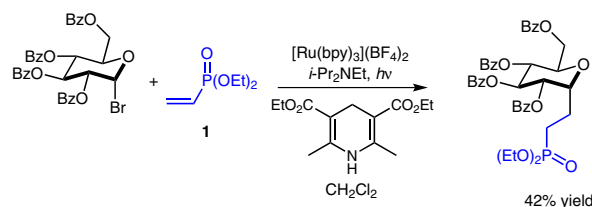
(H) Deprotonated **1** can react with carbodiimides. In the cyclized product, one of the C=N bonds and the C=C bond of **1** remained intact. The product contains a nitrogen atom and a phosphorus atom in the ring.⁹



(I) Electrophilic addition of a trifluoromethyl group was performed on substrate **1** using the *Togni Reagent II*. Subsequent addition of trimethylsilyl azide, followed by workup, yielded 1-azido-3,3,3-trifluoropropylphosphonate.¹⁰



(J) Radical addition of carboradicals derived from halides was also performed with **1**. Phosphonic derivatives of monosaccharides were synthesized in the presence of a ruthenium catalyst under irradiation with light.¹¹



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