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

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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 $1.055 \text{ g}\cdot\text{cm}^{-3}$, 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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(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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