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1,4-Unsubstituted 2-phosphorylated vinylacetylenes as valuable phosphorus-containing dipolarophiles

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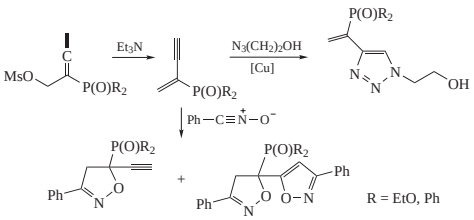
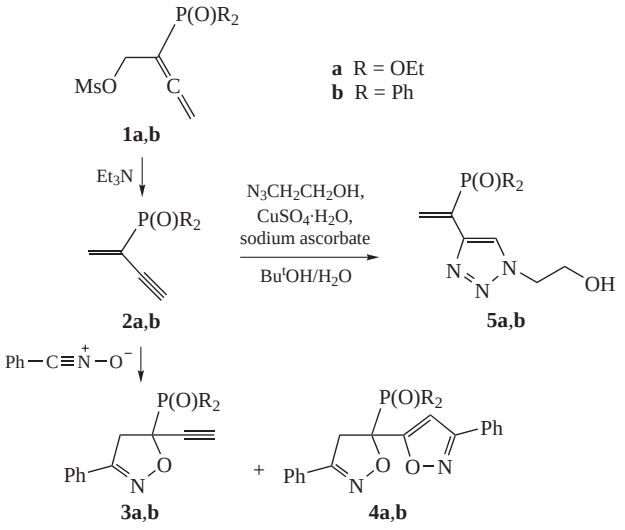
2-(Diethoxyphosphoryl)- and 2-(diphenylphosphoryl)but-2-en-3-ynes, accesible from 4-mesyloxy-3-phosphorylbuta-1,2-dienes, undergo [2 + 3] cycloaddition with benzonitrile *N*-oxide or azides to afford isoxazole or 1,2,3-triazole derivatives, respectively.



Vinyl-[1] and ethynylphosphonates[2] are widely used as building blocks in the synthesis of various organophosphorus compounds. Phosphorus compounds containing vinylacetylene fragment are virtually unstudied although they may be of interest as synthons with large synthetic capabilities. Few examples of substituted phosphorylated vinylacetylenes were reported,[3] however, the promising representatives with terminal $=CH_2$ and $\equiv CH$ groups are not described. 4-Chlorobuta-1,2-dienyl-2-phosphonates were shown to be useful for preparing 4-diethoxyphosphorylbut-2-en-4-yne,[3(d)] vinylacetylene containing phosphoryl group at the acetylene carbon atom. In continuation of our studies in the field of unsaturated organophosphorus compounds, we intended to access unsubstituted phosphorylated vinylacetylenes with the use of phosphorylated allenes and to demonstrate their reactivity as dipolarophiles in [2 + 3] cycloaddition reactions.

It was shown previously that 2-phosphorylbuta-2,3-dienyl mesylates **1a**,**b** were highly reactive towards nucleophiles affording substituted allenes or alka-1,3-dienes.[4] In this study we discovered that treatments of mesylates **1a**,**b** with triethylamine at ambient temperature for 45 min caused 1,4-elimination of methanesulfonic acid and formation of previously unknown vinylacetylenes **2a**,**b** (Scheme 1)† in yields of 90–94%. Their structure was established by spectral methods and by results of their chemical transformations, in particular, in reactions with 1,3-dipoles.



Scheme 1

The thus prepared vinylacetylenes **2a**,**b** were reacted with benzonitrile oxide. The latter was generated *in situ* by treatment of *N*-hydroxybenzenecarboximidoyl chloride with triethylamine in the presence of reactants **2a**,**b** in diethyl ether at –40 °C.[5] The [2 + 3] cycloaddition in general resulted in two adducts: products of addition at the double bond only (compounds **3a**,**b**) and products of addition at both multiple bonds (compounds **4a**,**b**). No products of addition at the only triple bond were detected. This fact agrees with the previous data on the reaction of vinylacetylene with nitrile oxides,[6] which indicate that the double bond in vinylacetylene is more reactive. Reaction optimization by varying the ratio of the reactants allowed us to raise considerably the yield of monoadducts **3a**,**b** (**3** : **4** ~ 9 : 1).‡ Raising amounts of benzonitrile oxide mostly caused formation of bis-adducts **4**.§

Cycloaddition at the triple bond can be anticipated when azides are used as dipoles.‡ The [2 + 3] cycloaddition of 2-azido-

† *Compounds* **2a**,**b** *(general procedure)*. A mixture of phosphorylated allene **1a** or **1b** (5 mmol) and Et_3N (5 drops) in CH_2Cl_2 (10 ml) was stirred at room temperature for 45 min. Water and CH_2Cl_2 were added, the organic phase was separated, the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, filtered and evaporated on a rotary evaporator to give a crude product as an oil. The product was purified by column chromatography using gradient elution $CHCl_3$–MeOH mixtures (gradient 10 : 0.3). Evaporation of the appropriate fractions gave the desired compounds as light yellow liquids.

‡ *Compounds* **3a**,**b** *(general procedure)*. Vinylacetylene **2a** or **2b** (3 mmol) was dissolved in Et_2O (10 ml). *N*-Hydroxybenzenecarboximidoyl chloride (1 mmol) in Et_2O (5 ml) was added at –40 °C. Triethylamine (4 mmol) was added dropwise over 2 h. Stirring was continued at –40 °C for 3 h and at room temperature for 2 h. The mixture was then quenched with NH_4Cl (aq. sat., 10 ml), extracted with Et_2O and concentrated. The residue was purified by column (l = 30 cm, d = 2 cm) chromatography using $CHCl_3$–MeOH (10 : 0.4) as an eluent. Evaporation of the appropriate fractions afforded the desired compounds as viscous liquids.

§ Compounds **4a**,**b** were obtained similarly from vinylacetylenes **2a**,**b** (1 mmol) and *N*-hydroxybenzenecarboximidoyl chloride (2 mmol) in Et_2O (5 ml); Et_3N (4 mmol) was then added dropwise over 2 h. Column chromatography ($CHCl_3$–MeOH, 10 : 0.4) and evaporation of appropriate fractions afforded the desired compounds as viscous liquids.

ethanol with vinylacetylenes **2a**,**b** was conducted in the presence of copper sulfate and sodium ascorbate according to the reported procedure[7] to afford triazole adducts **5a**,**b**.¶ The structure of new compounds **2**–**5** was proved by multinuclear NMR spectroscopy and elemental analysis (see Online Supplementary Materials).

In conclusion, the efficient method for preparing phosphorylated vinylacetylenes, new promising phosphorus-containing building blocks, has been developed. Vinylacetylenes **2a**,**b** have been demonstrated to be efficient dipolarophiles, which readily undergo [2 + 3] cycloaddition with nitrile oxides or azides. It has been shown that the regioselectivity of cycloaddition is dependent on the dipole used.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.11.031.

¶ *Compounds* **5a**,**b** *(general procedure)*. $CuSO_4 \cdot 5H_2O$ (5 M aq., 0.62 ml, 0.05 mmol) and sodium ascorbate (0.2 mmol) were added to a stirred solution of vinylacetylene **2a**,**b** (1 mmol) and 2-azidoethanol (1.1 mmol) in a mixture of *tert*-butanol (5 ml) and H_2O (2 ml). The yellow mixture was stirred at room temperature for 24 h (TLC monitoring). When the reaction mixture turned greenish, more sodium ascorbate was added until the mixture turned yellow again. The solvents were evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 (30 ml), stirred and filtered. The colourless solution was evaporated to dryness and the residue was purified by column (l = 30 cm, d = 2 cm) chromatography on silica gel using $CHCl_3$–MeOH (10 : 0.4) as an eluent. Evaporation of appropriate fractions resulted in the desired compounds as viscous liquid.

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