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Transformation of alkynyl sulfones into alkynylphosphonates with trialkyl phosphites

Yasutaka Yatsumonji, Akitoshi Ogata, Akira Tsubouchi, Takeshi Takeda *

Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

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Abstract

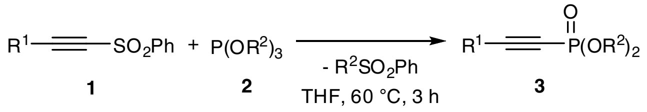
1-Alkynylphosphonates were obtained in good to high yields by simple heating of 1-alkynyl sulfones with trialkyl phosphites.

Keywords: Alkynylphosphonates; Alkynyl sulfones; Trialkyl phosphites; Arbuzov collapse

Dialkyl 1-alkynylphosphonates are useful synthetic intermediates as acetonyl equivalents,[1] Michael acceptors,[2] components of [2+2][3] and [2+2+2][4] cycloadditions and starting materials for certain cyclic compounds.[5] Two major approaches to these organophosphorous compounds have been investigated;[6] one is the reaction of alkynylmetals with electrophilic phosphorous reagents such as dialkyl chlorophosphates and the other is the nucleophilic displacement of alkynyl halides or related compounds with phosphorous nucleophiles such as trialkyl phosphites and sodium diethyl phosphite. Although the latter approach is advantageous over the former in that it requires no strongly basic reagents such as the Grignard reagents[7] or alkyllithiums,[8] its utility is largely restricted. For example, the nucleophilic displacement of 1-haloalkynes[9] with trialkyl phosphites suffers the limitation that only α-haloacetylenes bearing an electron-withdrawing or accommodating group can be employed. This limitation has been partially alleviated by the use of $NiCl_2$ as a catalyst.[10] 1-Alkynylphenyliodonium salts[11] are good alternatives for 1-haloalkynes but these starting materials are not easily accessible. Although the treatment of bromoalkynes with sodium dialkyl phosphites at low temperature affords alkynylphosphonates, it is pointed out that the purity of the products becomes a serious problem in certain cases.[6]

In connection with our study on the titanocene(II)-promoted cross-coupling of alkynes with unsaturated compounds,[12] we required a practical method for the preparation of various dialkyl 1-alkynylphosphonates. We then investigated a new method for their preparation without the difficulties associated with the use of haloalkynes or chlorophosphates. We took particular note of alkynyl sulfones as starting materials because these organosulfur compounds are readily available from terminal alkynes by simple procedures.

According to the method reported by Bieber,[13] alkynyl sulfides were prepared by the copper(I) iodide-catalyzed reaction of terminal alkynes with diphenyl disulfide in excellent yields. Oxidation of alkynyl phenyl sulfides with *m*-chloroperbenzoic acid produced alkynyl sulfones **1** quantitatively.[14] Treatment of phenyl 2-phenylethynyl sulfone (**1a**) with an equimolar amount of trimethyl phosphite (**2a**) at 60 °C for 3 h produced alkynylphosphonate **3a** in a high yield (Scheme 1, Table 1, entry 1). Although the



Scheme 1.

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* Corresponding author. Tel./fax: +81 42 388 7034.
E-mail address: takeda-t@cc.tuat.ac.jp (T. Takeda).

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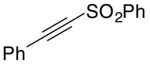
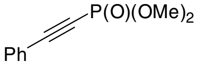
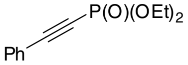
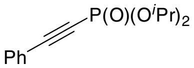
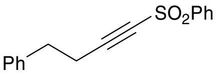
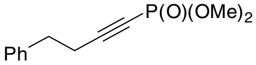
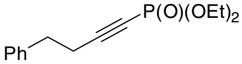
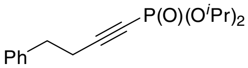
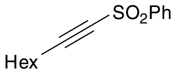
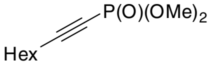
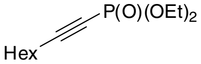
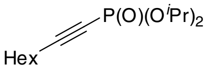
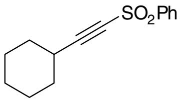
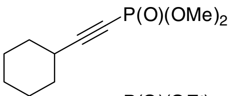
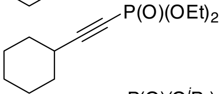
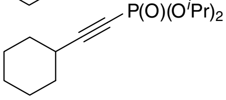
Table 1
Preparation of 1-alkynylphosphonates **3**

Entry	Alkynyl sulfone **1**	Trialkyl phosphite **2**	1-Alkynylphosphonate **3** (yield, %)[a]
1	 **1a**	$P(OMe)_3$ **2a**	 **3a** (96)
2	**1a**	$P(OEt)_3$ **2b**	 **3b** (98)
3	**1a**	$P(O^iPr)_3$ **2c**	 **3c** (71)
4	 **1b**	**2a**	 **3d** (93)
5	**1b**	**2b**	 **3e** (90, 88[b])
6	**1b**	**2c**	 **3f** (70)
7	 **1c**	**2a**	 **3g** (90)
8	**1c**	**2b**	 **3h** (95)
9	**1c**	**2c**	 **3i** (71)
10	 **1d**	**2a**	 **3j** (90)
11	**1d**	**2b**	 **3k** (95)
12	**1d**	**2c**	 **3l** (70)

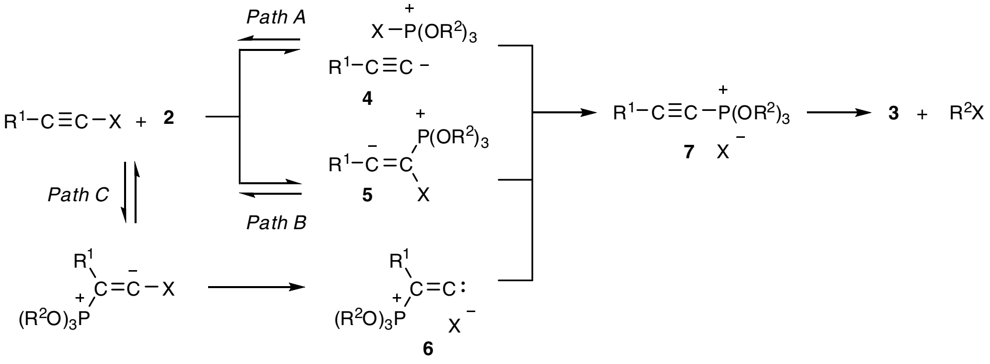
[a] Isolated yield.

[b] The reaction was carried out in 20 mmol scale and **3e** was isolated by distillation (170–175 °C/0.5 mmHg).

similar treatment of **1a** with triethyl phosphite (**2b**) gave phosphonate **3b** quantitatively (entry 2), the reaction using more bulky triisopropyl phosphite (**2c**) gave **3c** in a lower yield (entry 3). In a similar fashion, various 1-alkynylphosphonates **3** were obtained by the reaction of alkynyl phenyl sulfones **1** with trialkyl phosphites **2** in good to high yields.[15]

The preparation of alkynylphosphonates using alkynylphenyliodonium tosylates or 1-haloalkynes requires the use of excess phosphites and these starting materials are either rather unstable or explosive.[16] The present reaction enjoys advantages over these conventional methods in that the phosphonates are obtained in good to high yields using equimolar amounts of phosphites without aqueous workup. Indeed, phosphonate **3e** was obtained in a yield comparable to that obtained by a small scale reaction even when the reaction was carried out in gram scale and **3e** was isolated by the concentration of the reaction mixture and the distillation of the residue (entry 5).

Three reaction pathways have been proposed for the formation of 1-alkynylphosphonates by the reaction of alkynes having a leaving group (X) with phosphites (Scheme 2);[6] the formation of phosphonium salts with an acetylide counterion **4** by nucleophilic attack of phosphites to the leaving group (*Path A*), the addition of phosphites to the alkynes to form the twitter ions **5** (*Path B*) and the Michael-type addition of phosphites to the alkynes followed by the elimination of the leaving group to form alkylidenecarbenes **6** (*Path C*). The final step of all these pathways is the Arbuzov collapse of alkynylphosphonium salts **7**. Considering the strong electron-withdrawing and poor leaving abilities of phenylsulfonyl group, it is reasonable to assume that the present reaction follows *Path C* via the carbene intermediates **6**.



Scheme 2.

Acknowledgements

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15. *The typical procedure is as follows*: A THF (4 mL) solution of phenyl 4-phenyl-1-butynyl sulfone **1b** (540 mg, 2 mmol) and trimethyl phosphite **2a** (0.24 mL, 2 mmol) was heated at 60 °C for 3 h under argon. After cooling, the reaction mixture was concentrated. Chromatography of the residual oil on a silica gel (hexane–AcOEt = 2:1, v/v) gave dimethyl 4-phenyl-1-butynylphosphonate **3d** (443 mg, 93%) and methyl phenyl sulfone (248 mg, 73%). Compound **3d**: ^{1}H NMR δ 2.66 (dt, $J = 4.4$, 7.3 Hz, 2H), 2.90 (t, $J = 7.4$ Hz, 2H), 3.70 (d, $J = 12.3$ Hz, 6H), 7.18–7.35 (m, 5H); ^{13}C NMR δ 21.1, 21.2, 33.39, 33.41, 53.0, 53.1, 67.7, 71.7, 102.4, 103.1, 126.6, 128.2, 128.4, 139.1; ^{31}P NMR δ −2.7; IR (neat) 2931, 2857, 2204, 1459, 1276, 1184, 1033, 837, 783, 627 cm^{-1}. Anal. Calcd for $C_{12}H_{15}O_3P$: C, 60.50; H, 6.35. Found: C, 60.73; H, 6.66.
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