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LETTERS

A one-pot procedure for the synthesis of alkynes and bromoalkynes from aldehydes

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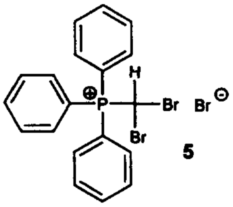
Abstract

Alkynes R-C≡CH were obtained in good yield through a one-pot procedure by a sequence of reactions starting from a Wittig-type condensation of the aldehydes RCHO with the ylide derived from dibromomethyltriphenylphosphonium bromide **5**. The same reactions could also be used to prepare the intermediate dibromoalkenes RCH=CBr$_2$, and in certain cases, the bromoalkynes R-C≡CBr. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: alkynes; bromoalkynes; dibromomethyltriphenylphosphonium bromide; ylids.

The Corey–Fuchs conversion[1] of an aldehyde RCHO (**1**) into an alkyne R-C≡CH (**2**) necessitates two steps, one in methylene chloride for the generation of the ylide by a slight modification of Ramirez method[2,3] and the formation of the dibromoalkene **3**, and a second one in THF for the elimination of HBr and the reduction of the bromoalkyne **4**.



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Using a known reagent, dibromomethyltriphenylphosphonium bromide (**5**),[4] we have developed a new and efficient method avoiding the intermediate step (Scheme 1). Furthermore, the same one-pot procedure, if stopped at different stages, may be used to obtain the dibromoalkenes **3**, and in some cases, the bromoalkynes **4**.

The reagent **5** was easily prepared by Wolkoff's method.[4b] In fact, the recrystallization step was found to be unnecessary, so that the crude compound could be stored and used as such.

The alkynes were prepared as shown in Table 1.

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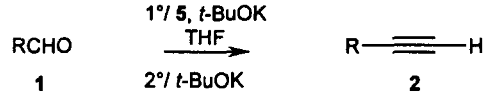
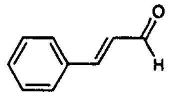
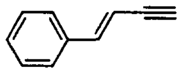
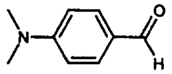
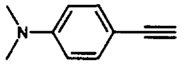
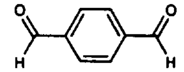
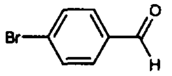
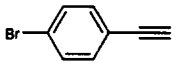
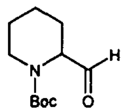
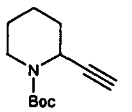
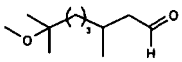
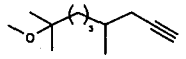
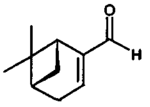
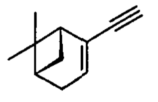
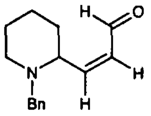
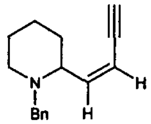


Scheme 1.

Table 1

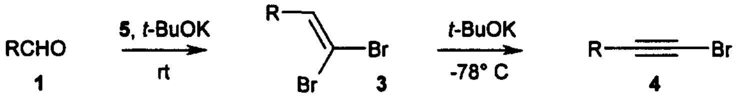
	1	2	Temperature(a)	Yield (%)(b)
a			-78° C	94
b			-78° C(c)	66
c			-78° C	85(d)
d			rt	66
e			-78° C	84(e)
f			rt	97
g			rt	42
h			rt	54

(a) Temperature of the second addition of *t*-BuOK; (b) isolated yield; (c) or at room temperature; (d) four equivalents of **5** were used; (e) BuLi was used instead of *t*-BuOK

The dibromomethylenetriphenylphosphorane was generated by reaction of *t*-BuOK in THF on a slight excess of **5**. A yellow-brown colour was immediately observed, indicating the formation of the ylide. The aldehyde **1** was then added at room temperature. After less than 5 min under stirring, the dibromoalkene **3** was formed (TLC). The THF solution was then cooled to the appropriate temperature and *t*-BuOK was added. (For the conversion of the aldehyde **1e**, a solution of BuLi was used at −78°C in order to prevent a reaction between the carbamate and the acetylide functions). As indicated in Table 1, different temperatures were tested for this second addition: with aromatic substrates (i.e. **1a**, **1b** and **1c**), reduction of the intermediate bromoalkyne occurred readily at −78°C, while with other substrates (i.e. **1f**, **1g** and **1h**), a higher temperature was necessary (see below), so that *t*-BuOK was added at room temperature. Finally, and still at the same temperature, the reaction mixture was hydrolyzed with brine (when pure water was used instead of a saturated sodium chloride solution, a separation between the organic and the aqueous layers could not be observed; it is thus very important to use this saturated solution in the workup). It was concluded from these experiments that in the addition of *t*-BuOK, the low temperature was not necessary for the synthesis of the alkynes **2**: the whole reaction can be effected at room temperature.

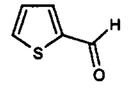
This method is a convenient way to convert in a one-pot procedure an aldehyde into the corresponding alkyne. It is more tolerant than the Corey–Fuchs procedure, because of the absence of superfluous PPh_3Br_2 (or $ZnBr_2$ when metallic zinc is added) formed upon reaction of PPh_3 with CBr_4. Moreover, in the case of α,β-unsaturated aldehydes, this conversion takes place without isomerization of the double bond[5] (i.e. **2a**, **2g** and **2h**).

The reagent **5** was also used to prepare the dibromoalkenes **3a**, **3b** and **3e** (Scheme 2, Table 2).



Scheme 2.

Table 2

1	3 yield (%)(a)	4 yield(%)(a)
a	98	(b)
b	68	(b)
e	87	91
g		48
 i		62

(a) Isolated yield; (b) the bromoalkyne was not obtained, see text

Some bromoalkynes **4** could also be obtained in a one-pot procedure by quenching the reaction between the dibromoalkene **3** and *t*-BuOK[6] at −78°C (Table 2). However, the formation of these bromoalkynes strongly depends upon the nature of the aldehyde: although, as previously mentioned, the aromatic bromoalkynes[7] derived from **3a** and **3b** could not be isolated because they were immediately reduced even at this temperature, this was not the case with the aromatic 2-thiophenecarboxaldehyde **1i**, which was smoothly converted to **4i**.

General procedure: Under an argon atmosphere, **5** (4 mmol) and *t*-BuOK (3.8 mmol) were dissolved in THF (20 mL). The solution was stirred for a few minutes, and the aldehyde (2 mmol) was then added. After 10 min, *t*-BuOK (10 mmol) was added at room temperature. The solution was quenched with saturated brine (30 mL) and extracted twice with 30 mL of ether. The organic layers were dried over Na_2SO_4 and concentrated. Chromatography on silica gel afforded the corresponding alkyne, identified through their ^{13}C NMR spectra.[8]

Acknowledgements

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6. A conversion of a dibromoalkene to the bromoalkyne by *t*-BuOK has been reported: de Meijere, A.; Kozhushkov, S.; Haumann, T.; Boese, R.; Puls, C.; Cooney, M. J.; Scott, L. T. *Chem. Eur. J.* **1995**, *1*, 124–131.
7. A general method for the preparation of the analogous iodoalkynes is described in the accompanying communication: Michel, P.; Rassat, A. *Tetrahedron Lett.* **1999**, *40*, 8579–8581.
8. **2a** ($CDCl_3$, 50 MHz): 79.3, 83.1, 106.9, 126.1, 126.2, 128.6, 128.8, 135.7, 142.9; **2b** ($CDCl_3$, 50 MHz): 39.9, 74.7, 84.8, 108.5, 111.5, 133.0, 150.2; **2c** ($CDCl_3$, 50 MHz): 79.1, 83.0, 122.5, 132.0; **2d** ($CDCl_3$, 50 MHz): 78.3, 82.5, 121.0, 123.1, 131.6, 133.5; **2e** ($CDCl_3$, 50 MHz): 19.4, 24.8, 27.7, 29.9, 39.8, 43.5, 71.6, 79.3, 81.4, 153.8; **2f** ($CDCl_3$, 50 MHz): 19.3, 21.2, 24.9, 25.7, 32.3, 36.4, 39.9, 49.0, 69.0, 74.4, 83.2; **2g** ($CDCl_3$, 50 MHz): 20.9, 26.0, 31.3, 32.0, 37.9, 40.1, 46.8, 76.7, 84.4, 129.1, 132.6; **2h** ($CDCl_3$, 50 MHz): 23.8, 25.7, 32.0, 52.0, 60.2, 62.2, 80.0, 82.7, 108.5, 126.6, 128.0, 129.0, 139.0, 149.1.