

**REACTION OF LITHIUM ALKYNOLATES WITH ACID CHLORIDES:
A CONVENTIONAL APPROACH TO THE PREPARATION OF YNOL ESTERS**

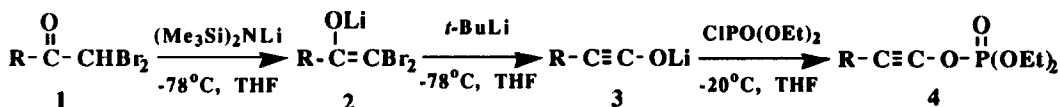
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Summary. Lithium alkynolates ($R-C\equiv COLi$, $R = CH_3, n-C_4H_9, t-C_4H_9, Ph$), generated in situ from dibromomethylketones and a strong base, react with electrophiles (diethyl chlorophosphate or benzoyl chloride) with the formation of the corresponding ynol esters.

Alkynyl ethers¹ and esters² represent an important class of functionalized acetylenes—derivatives of the hypothetical alkynols,³ $RC\equiv COH$. Acetylenic ethers, which have been known for almost 100 years,¹ are usually synthesized by a conventional dehydrohalogenation reaction.¹ However, numerous attempts to apply such an obvious approach to the preparation of alkynol esters failed.⁴ The only known synthesis of the alkynyl carboxylate, phosphate, and sulfonate esters to date involves alkynyliodonium salts as the precursors.² In view of the highly useful properties of alkynyl esters² development of a more conventional and inexpensive synthetic approach to these compounds is highly desirable.

We have found, that lithium alkynolates **3**, which can be easily prepared in situ from readily available dibromomethylketones **1** by a known procedure,⁵ react with acid chlorides resulting in the corresponding alkynyl esters as major products. The best results are obtained by the reaction of lithium alkynolates with diethyl chlorophosphate as electrophile in THF at low temperature forming the corresponding alkynyl phosphate esters in 30-56% isolated yields.

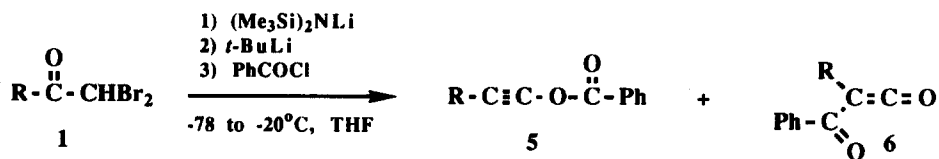


4a: R = Me (56%), 4b: R = n-Bu (42%), 4c: R = t-Bu (39%), 4d: R = Ph (30%)

General procedure for the preparation of alkynyl(diethyl)phosphates 4. A 2.5 M *n*-butyllithium solution in hexane (0.84 ml, 2.1 mmol) was added dropwise to a solution of hexamethyldisilazane (0.43 ml, 2.2 mmol) in 5 ml of dry THF at -78°C under nitrogen. To this cold stirred mixture a solution of 2 mmol of the corresponding dibromomethylketone in 2 ml THF was added. The reaction mixture was briefly warmed to 0°C , then recooled to -78°C and a 1.7 M solution of *tert*-butyllithium in pentane (3.9 ml, 6.6 mmol) was

added. The reaction mixture was stirred for 10-15 min at -78°C and then 0.58 ml (4 mmol) of $\text{ClPO}(\text{OEt})_2$ was added. The resulting solution was stirred for 8-12h at -15 to -20°C , then filtered through silicagel (5g), which was additionally washed with 20 ml of a 1:1 mixture CH_2Cl_2 - acetone. The combined organic solutions were evaporated to give crude products **4** as slightly yellow oils. The pure products **4** were obtained by flash column chromatography on silicagel using a 10:1 mixture of CH_2Cl_2 - acetone as the eluent. The spectral data and properties of products **4** were identical to the previously reported data.⁶

According to spectral data of the crude reaction mixtures, phosphate esters **4** are the only products observed in the reaction of **3** with diethyl chlorophosphate and the possible isomeric ketenes the result of C-attack of the electrophile have not been detected. In contrast in the reaction of lithium alkynolates with benzoyl chloride both products **5** (O-acylation) and **6** (C-acylation) have been found. In most cases products **5,6** are not stable enough to survive chromatographic separation, however, we were able to isolate **5b** and **6a**;⁷ products **5a**⁸ and **6b** were identified by spectral means.



5a: R = *t*-Bu (<10%), **5b:** R = Ph (45%), **6a:** R = *t*-Bu (53%), **6b:** R = Ph (unstable)

In conclusion, the reaction of lithium ynolates with diethyl chlorophosphate gives alkynyl phosphate esters in moderate isolated yield, whereas the analogous reaction with benzoyl chloride gives both products of O- and C-acylation of the alkynolate anion.

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References and Notes

1. Reviews: L. Brandsma, H.J.T. Bos, J.F. Arens in "Chemistry of Acetylenes", Marsel Dekker: New York, 1969, Chapter 2, p. 751; S.I. Radchenko, A.A. Petrov, *Russian Chemical Reviews* **1989**, *58*, 948.
2. For a review see: P.J. Stang, *Acc. Chem. Res.* **1991**, *24*, 304.
3. A.J. Kresge, *Acc. Chem. Res.* **1990**, *23*, 43.
4. For a brief review on early attempts for the preparation of alkynyl esters see: P.J. Stang, B.W. Surber, Z.-C. Chen, K.A. Roberts, A.G. Robertson, *J. Am. Chem. Soc.* **1987**, *109*, 228.
5. C.J. Kowalski, K.W. Fields, *J. Am. Chem. Soc.* **1982**, *104*, 321.
6. P.J. Stang, T. Kitamura, M. Boehshar, H. Wingert, *J. Am. Chem. Soc.* **1989**, *111*, 2225.
7. Selected spectral data for **5b**: oil; IR (neat): 3062, 2251 ($\text{C}\equiv\text{C}$), 1700, 1225 cm^{-1} ; ^1H NMR (CDCl_3 , δ): 8.0-7.3 (m, 2Ph); ^{13}C NMR (CDCl_3 , δ): 188.7, 134.4, 134.2, 133.4, 130.2, 129.4, 129.1, 128.9, 128.1, 116.5, 46.5; CI HRMS m/z 222.06713 $[\text{M}]^+$, calcd for $\text{C}_{15}\text{H}_{10}\text{O}_2$: 222.06807. For **6a**: oil; IR (neat): 3063, 2961, 2103 ($\text{C}=\text{C}=\text{O}$), 1775, 1714 cm^{-1} ; ^1H NMR (CDCl_3 , δ): 7.6-7.4 (m, 5H, Ph), 1.3 (s, 9H, *t*-Bu); ^{13}C NMR (CDCl_3 , δ): 193.2, 173.4, 140.5, 135.1, 131.2, 128.7, 126.7, 29.2, 28.9; CI HRMS m/z 202.09788 $[\text{M}]^+$, calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: 202.09937.
8. P.J. Stang, M. Boehshar, H. Wingert, T. Kitamura, *J. Am. Chem. Soc.* **1988**, *110*, 3272.

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