

Tetrahedron Letters 40 (1999) 8465-8467

TETRAHEDRON LETTERS

Carboxylates as pronucleophiles in the phosphine-catalyzed y-addition reaction

Carlos Alvarez-Ibarra,* Aurelio G. Csákÿ and Cristina Gómez de la Oliva

Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain

Received 7 July 1999; accepted 14 September 1999

Abstract

Carboxylates have been used as pronucleophiles in the phosphine-catalyzed γ -addition reaction to alkynes bearing electron-withdrawing groups (Trost's reaction) giving rise to functionalized allyl carboxylates. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: addition reaction; carboxylic acids; carboxylic acid derivatives; phosphines; sodium; sodium compounds.

Phosphines are able to promote the addition of nucleophiles to the γ -position of alkynes bearing conjugated electron-withdrawing groups (Trost's reaction, Scheme 1).



Scheme 1.

Carbon pronucleophiles for which $pK_a < 16$ have served satisfactorily in this reaction.¹ Heteronucleophiles, nitrogen-² and oxygen³-based, have also been used in this reaction. It has been reported that alcohols are better donors than carbon nucleophiles in this isomerization–addition reaction, in contrast to the Michael reaction.⁴ However, as far as we know, only the intramolecular version of the Trost's reaction with alcohols as nucleophiles, i.e. cyclization to afford tetrahydrofurans, has been described.^{3,5} In order to extend the scope of the process, we have been exploring the intermolecular version with other oxygen

^{*} Corresponding author.

nucleophiles. Therefore, we report herein our results in the intermolecular addition of carboxylates to the γ -position of alkynes 1, as a means of synthesizing potentially useful functionalized allyl carboxylates (Scheme 2).⁶ The results are gathered in Table 1.





Treatment of **1a** (1.0 mol) with sodium acetate (**2a**, 1.0 mol) and acetic acid (**3a**, 1.0 mol) in the presence of Ph₃P (0.1 mol) afforded, after isolation and purification of the reaction crude, the corresponding allyl acetate **4a** in moderate yield (entry 1). On the other hand, when the reaction was carried out with a two-fold excess of **1a**, a high yield of compound **4a** was obtained (entry 2). These reaction conditions were extended to the reaction of alkynes **1a**,**b** with carboxylates⁷ **2a**–**d**, which allowed for the synthesis of the allyl carboxylates **4b**–**h** (entries 3–9).^{8,9}

In conclusion, the Trost reaction, which is characterized by its simplicity and mildness, has been extended to the preparation of functionalized allyl carboxylates 4. The presence of an α , β -unsaturated

| Entry | 1 | 2, 3 | Molar ratio 1 : 2 : 3 | 4 (%) ^a |
|--|------------|--------|-----------------------|---------------------------|
| 1 | 1a | 2a, 3a | 1.0 : 1.0 : 1.0 | 4a (60) |
| 2 | 1a | 2a, 3a | 2.0 : 1.0 : 1.0 | 4a (90) |
| 3 | 1a | 2b, 3b | 2.0 : 1.0 : 1.0 | 4b (75) |
| 4 | 1 a | 2c, 3c | 2.0 : 1.0 : 1.0 | 4c (75) |
| 5 | 1a | 2d, 3d | 2.0 : 1.0 : 1.0 | 4d (70) |
| 6 | 1b | 2a, 3a | 2.0 : 1.0 : 1.0 | 4e (80) |
| 7 | 1b | 2b, 3b | 2.0 : 1.0 : 1.0 | 4f (70) |
| 8 | 1b | 2c, 3c | 2.0 : 1.0 : 1.0 | 4g (70) |
| 9 | 1b | 2d, 3d | 2.0 : 1.0 : 1.0 | 4h (70) |
| (a) Isolated yield after silica gel chromatography (hexane - ethyl acetate, 90 : 10) | | | | |

Table 1 Addition of carboxylates 2 to the y-position of alkynes 1

carbonyl compound in the reaction product together with the allyl carboxylate functionality offers a great opportunity for further structural elaboration.¹⁰

Acknowledgements

DGCYT (project PB96-0009) is gratefully acknowledged for financial support and the predoctoral grant for one of the authors (C.G.). We also thank UCM (MS, RMN and the Elemental Analysis services).

References

- 1. Trost, B. M.; Li, C.-J. J. Am. Chem. Soc. 1994, 116, 3167-3168.
- 2. Trost, B. M.; Dake, G. R. J. Org. Chem. 1994, 62, 5670-5671.
- 3. Trost, B. M.; Li, C.-J. J. Am. Chem. Soc. 1994, 116, 10819-10820.
- For reviews on conjugate additions, see: (a) Perlmutter, P. In Conjugate Addition Reactions in Organic Synthesis: Pergamon Press: Oxford, 1992; pp. 1–127. (b) Jung, M. E. In Comprehensive Organic Synthesis; Trost, B. M.; Fleming, I.; Semmelhack, M. F., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp. 1–67.
- 5. For the conjugate addition of alcohols to α , β -unsaturated alkynoates catalyzed by Ph₃P, see: Inanaga, J.; Baba, Y.; Hanamoto, T. Chem. Lett. **1993**, 241–244.
- 6. For previous synthesis of γ-hydroxy-α,β-unsaturated carbonyl compounds, see: (a) Suryawanshi, S. N.; Fuchs, P. L. Tetrahedron Lett. 1981, 22, 4201-4204. (b) Reich, H. J.; Clark, M. C.; Willis Jr., W. W. J. Org. Chem. 1982, 47, 1618-1623. (c) Nokami, J.; Nishimuri, A.; Sunami, M.; Wakabayashi, S. Tetrahedron Lett. 1987, 28, 644-650.
- 7. Sodium phenylacetate (2b) was prepared by treatment of the corresponding acid 3b (1.0 mol) with Na (1.0 mol) in Et₂O solution.
- 8. Typical experimental procedure: A mixture of the alkyne (1, 2.0 mmol), Ph₃P (0.1 mmol), the sodium carboxylate (2, 1.0 mmol) and the corresponding carboxylic acid (3, 1.0 mmol) in toluene (5 mL) was heated at 80°C for 24 h under Ar. Upon cooling, the mixture was filtered and the solid was washed with ether. The combined organic fractions were concentrated and the residue was purified by silica gel chromatography (hexane:ethyl acetate, 90:10).
- All compounds 4 were obtained as single E-isomers, as evidenced by the magnitude of the vinylic coupling constant in their ¹H NMR (CDCl₃, 300 MHz) spectra.
- For synthetic uses of γ-hydroxy-α,β-unsaturated carbonyl compounds, see, for example: (a) Trost, B. M.; Toste, F. D. J. Am. Chem. Soc. 1999, 121, 3543-3544; (b) Nokami, J.; Nishimuri, A.; Sunami, M.; Wakabayashi, S. Tetrahedron Lett. 1987, 28, 644-650, and references cited therein.