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

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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.

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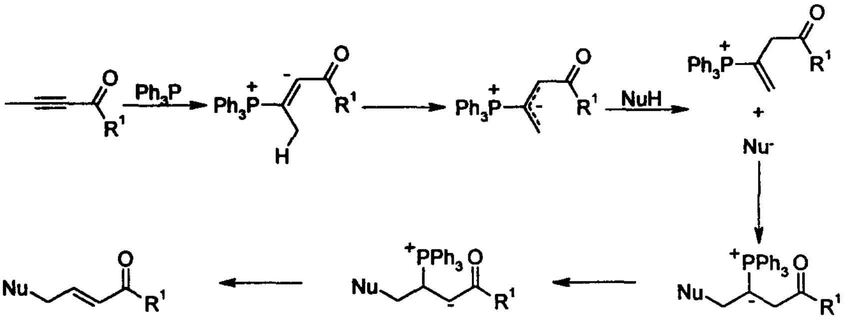
Phosphines are able to promote the addition of nucleophiles to the γ-position of alkynes bearing conjugated electron-withdrawing groups (Trost's reaction, Scheme 1).



Scheme 1.

Carbon pronucleophiles for which $pK_a < 16$ have served satisfactorily in this reaction.[1] Heteronucleophiles, nitrogen-[2] and oxygen[3]-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

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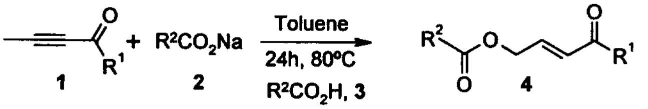
nucleophiles. Therefore, we report herein our results in the intermolecular addition of carboxylates to the γ-position of alkynes **1**, as a means of synthesizing potentially useful functionalized allyl carboxylates (Scheme 2).[6] The results are gathered in Table 1.



1a, $R^1 = OCH_3$
1b, $R^1 = {}^tBu$

2a, 3a, $R^2 = CH_3$
2b, 3b, $R^2 = Ph$
2c, 3c, $R^2 = Et$
2d, 3d, $R^2 = PhCH_2$

4a, $R^1 = OCH_3$, $R^2 = CH_3$
4b, $R^1 = OCH_3$, $R^2 = Ph$
4c, $R^1 = OCH_3$, $R^2 = Et$
4d, $R^1 = OCH_3$, $R^2 = PhCH_2$
4e, $R^1 = {}^tBu$, $R^2 = CH_3$
4f, $R^1 = {}^tBu$, $R^2 = Ph$
4g, $R^1 = {}^tBu$, $R^2 = Et$
4h, $R^1 = {}^tBu$, $R^2 = PhCH_2$

Scheme 2.

Treatment of **1a** (1.0 mol) with sodium acetate (**2a**, 1.0 mol) and acetic acid (**3a**, 1.0 mol) in the presence of Ph_3P (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 carboxylates[7] **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

Table 1
Addition of carboxylates **2** to the γ-position of alkynes **1**

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	**1a**	**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)

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

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7. Sodium phenylacetate (**2b**) was prepared by treatment of the corresponding acid **3b** (1.0 mol) with Na (1.0 mol) in Et_2O solution.
8. Typical experimental procedure: A mixture of the alkyne (**1**, 2.0 mmol), Ph_3P (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).
9. All compounds **4** were obtained as single *E*-isomers, as evidenced by the magnitude of the vinylic coupling constant in their ^1H NMR ($CDCl_3$, 300 MHz) spectra.
10. 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.