

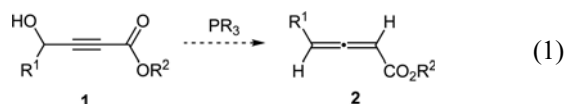
## A Convenient Method for the Synthesis of Allenates from 4-Hydroxyalk-2-ynoates with PPh<sub>3</sub>

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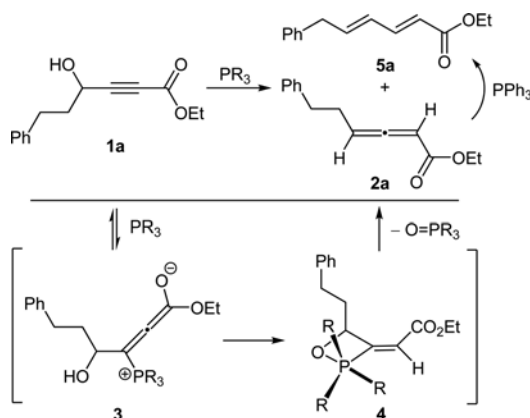
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Structurally unique allenyl substances are found in nature and play important biological and chemical roles.<sup>1</sup> Allenes become versatile building blocks in synthetic chemistry, the inherent instability associated with the cumulated double bond having been widely exploited for synthetic purposes. Recently allene moieties have been utilized as useful substrates for a variety of chemical transformations including many transition metal catalysis.<sup>2</sup> As a result, considerable attentions have been paid to develop synthetic methodologies for the compounds containing allenyl functionalities.<sup>3</sup> In particular, allenates have considered as an attractive substrate class showing diverse reactivity for Lewis base-catalyzed reactions with various electrophiles.<sup>4</sup> However, majority of known methods for the synthesis of allenates **2** are utilized the Wittig reaction<sup>5</sup> between phosphonium ylide and ketene from acyl chloride with base.<sup>6</sup>



As our continuous efforts to synthesize<sup>7</sup> and utilize<sup>8</sup> allenyl functionality to develop new stereoselective synthetic methods *via* catalysis, we became quite interested in designing a synthetic method to access allenate **2** from 4-hydroxyalk-2-ynoates **1** with phosphine as shown in Eq. (1). To provide direct access to the product **2** from **1**, we considered a aldehyde and corresponding propiolate as precursors which thought to be more convenient chemicals in terms of availability and practicability.



**Scheme 1.** General strategy.

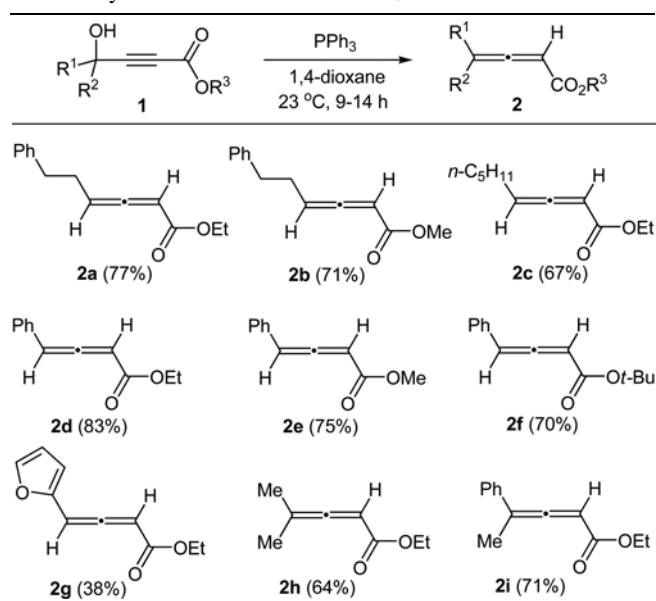
With this issue in mind, several 4-hydroxyalk-3-ynoates **1** were prepared from propiolates and aldehydes according to the modification of known procedure,<sup>9</sup> and our investigations began with **1a** ( $R^1 = \text{PhCH}_2\text{CH}_2$ ,  $R^2 = \text{Et}$ ) as a model substrate as shown in Scheme 1. Initial experiment on the conversion of **1a** with phosphine to **2a** afforded encouraging but marginal results. Treatment of **1a** with PPh<sub>3</sub> (1.2 equiv) at 23 °C for 14 h resulted in the formation of the allenate **2a** along with the 2,4-dienoate **5a** in a ratio of 72:29 as judged by the analysis of <sup>1</sup>H NMR spectrum of the crude products (entry 1 in Table 1). Although the desired allenate **2a** was produced, the formation of the 2,4-dienoate **5a** and low yield remained to be solved as shown in Scheme 1.

We subsequently speculated that the formation of **5a** was attributed to an isomerization of **2a** with excess PPh<sub>3</sub>. Control experiments supported this claim: i) reaction of **2a** with PPh<sub>3</sub> (10 mol %) at 23 °C for 14 h afforded **5a** in 70% isomerization. ii) the isomerization was reduced in the presence of *t*-BuOH (30 mol %) under same conditions in 20% conversion. Consequently, reduced usage of PPh<sub>3</sub> resulted in diminishing the isomerization of **2a** to **5a** (entry 2 in Table 1). However, low chemical yields were still problematic. Several attempts in different solvents such as EtCN, toluene, and THF indicated that the conversion to **2a** could also not be satisfied mainly due to an isomerization and low yields as indicated in Table 1. The use of ether turned out to be a limited outcome. We observed the formation of **2a** in 67% yield with only 5% of isomerization (entry 8). Unfortunately,

**Table 1.** Preliminary Investigations for **1a** to **2a** in Scheme 1<sup>a</sup>

Entry	PR <sub>3</sub> (equiv)	Solvent	t/h	<b>2a</b> : <b>5a</b> <sup>b</sup>	Yield (%) <sup>c</sup>
1	PPh <sub>3</sub> (1.2)	CH <sub>2</sub> Cl <sub>2</sub>	14	71:29	38
2	PPh <sub>3</sub> (0.9)	CH <sub>2</sub> Cl <sub>2</sub>	12	82:18	44
3	PMe <sub>3</sub> (0.9)	CH <sub>2</sub> Cl <sub>2</sub>	12	83:17	38
4	PBu <sub>3</sub> (0.9)	CH <sub>2</sub> Cl <sub>2</sub>	12	82:18	44
5	PPh <sub>3</sub> (0.8)	EtCN	8	63:37	34
6	PPh <sub>3</sub> (0.9)	Toluene	12	83:17	41
7	PPh <sub>3</sub> (0.9)	THF	12	88:12	58
8	PPh <sub>3</sub> (0.9)	Ether	12	95:5	67
9	PPh <sub>3</sub> (0.9)	1,4-Dioxane	12	>99:1	77
10	P(OEt) <sub>2</sub> ONa <sup>d</sup>	THF	12	NA	NR

<sup>a</sup>All reactions were carried out at 22–25 °C (rt). <sup>b</sup>Ratios were determined by <sup>1</sup>H NMR spectra of crude products. <sup>c</sup>Yields are referred as purified yield for **2a**. <sup>d</sup>Run reaction at 23–67 °C.

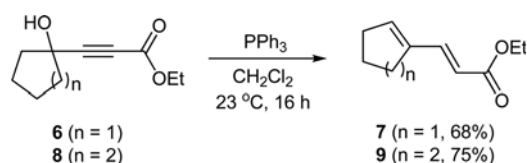
**Table 2.** Synthesis of **2** from **1** with PPh<sub>3</sub><sup>a</sup><sup>a</sup>Same conditions as described in Table 1.

reaction did not take place with P(OEt)<sub>2</sub>ONa under various conditions. Finally, we were delighted to find that 1,4-dioxane could be a proper solvent for this transformation. Under optimal conditions, the reaction was conducted by an addition of PPh<sub>3</sub> (0.9 equiv) in 1,4-dioxane at 23 °C to a solution of **1a** (1 equiv) in 1,4-dioxane (entry 9).

With the notion that this approach might lead to a general and convenient method for the synthesis of allenoates **2** as shown in Table 2, we set out to determine the scope to produce various products. Indeed, the method is successful with a variety of aldehydes to yield the allenoates **2a-i** in moderate to high yields with high purity as it can be seen in Table 2. It is worthy of note that the reaction produced none or only trace amounts of isomerized 2,4-dienoate **5** (less than 3%) according to the analysis of <sup>1</sup>H NMR spectra of crude products.

Although the exact mechanistic aspects of this transformation have not been rigorously elucidated, Scheme 1 illustrates possible chemical route. Reaction must be initiated by the addition of PPh<sub>3</sub> to a 4-hydroxyalk-3-ynoate **1** to form an enolate **3**. After transfer of anionic charge in **3** into more acidic hydroxyl group, the formation of an oxaphosphetane **4** followed by its decomposition result in the formation of an allenoate **2** as depicted in Scheme 1.

However, reaction of cyclic substrates **6** and **8** gave only 2,4-dienoates **7** and **9** respectively in 1,4-dioxane (40%) or CH<sub>2</sub>Cl<sub>2</sub> as shown in Scheme 2. We could not observe any

**Scheme 2.** Formation of 2,4-dienoates.

formation of corresponding allenoates presumably due to an exocyclic strain.

In summary, this paper describes a practical and convenient synthesis of allenoates **2** from 4-hydroxyalk-3-ynoates **1** with PPh<sub>3</sub> in 1,4-dioxane. We observed a significant solvent effect to retard significantly an isomerization of allenoates **2** to corresponding 2,4-dienoates **5**. Application of this method into an asymmetric route with enantiomerically enriched 4-hydroxyalk-3-ynoates **1**<sup>10</sup> to establish chiral allenoates **2** are in progress.

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