

Enantioselective synthesis of allenic esters *via* an ylide route†

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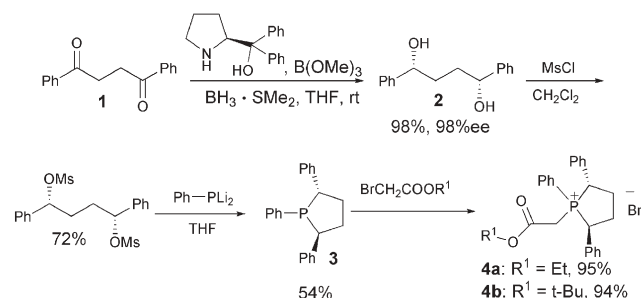
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Pseudo- C_2 -symmetric chiral phosphorus ylides have been designed and synthesized for the enantioselective preparation of allenic esters, and up to 92% ee has been achieved.

Chiral ylides have developed into excellent reagents for the synthesis of optically active epoxides,¹ cyclopropanes,² aziridines³ and olefins.⁴ Although the Wittig or Horner–Wadsworth–Emmons (HWE) reaction is good for the preparation of allenes,⁵ which are versatile building blocks⁶, as well as the basic units of numerous natural products and biologically-active compounds,⁷ only a few examples involve its asymmetric version.^{5c–g} Recently, Tanaka *et al.* described that optically-active 4,4-disubstituted allenecarboxylates could be prepared with binol-derived HWE reagents in 21–71% yields with 23–89% ee values.^{5e–5f} Pinho e Melo and his co-workers^{5g} documented that a phosphorus ylide bearing a 10-phenylsulfonyl-*iso*-borneol reacted with methylketene to give a penta-2,3-dienoic ester with excellent diastereoselectivity. In our studies of ylides in organic synthesis,⁸ we are interested in developing the chiral ylide-mediated syntheses of optically active allenes⁹ and have found that newly-designed chiral phosphorus ylides **7a** and **7b** could react with ketene very well to afford allenes with ee values up to 92%. In this communication, we wish to report the preliminary results.

Phosphonium salts **4a** and **4b** were readily available from the corresponding diketone on a gram scale (Scheme 1). The diketone **1** was reduced with a proline-derived chiral borane to give diol **2** in 98% yield with 98% ee.¹⁰ The diol was treated with methanesulfonyl chloride,¹⁰ followed by reaction with dilithium phenylphosphate to afford chiral phosphine **3**, which reacted with bromoacetate to give the desired phosphonium salts **4a** and **4b**. Gratifyingly, after deprotonation by NaHMDS, salt **4a** reacted



Scheme 1

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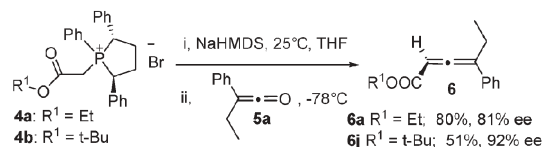
† Electronic Supplementary Information (ESI) available: Experimental details. See DOI: 10.1039/b603659g

smoothly with ethyl phenyl ketene at $-78\text{ }^\circ\text{C}$ to afford chiral allene **6a** with 81% ee in 80% yield. Further studies showed that the enantioselectivity could be improved to 92% ee when ethyl ester was replaced by *tert*-butyl ester (Scheme 2). This result encouraged us to study the generality of the reaction by investigating a variety of ketenes with different structures. As shown in Table 1, the substituents on the ketene proved to strongly influence both the yields and the enantioselectivities. For example, 2-aryl-1-buten-1-one gave 4-aryl-2,3-hexadienoic esters in high yields with high enantioselectivities (Table 1, entries 1 and 6–7), and up to 91% ee was obtained. Replacement of the ethyl group on ketene **5a** with other alkyl groups, such as *iso*-propyl, benzyl and allyl, decreased the enantiomeric excess greatly (Table 1, entries 2 and 4–5). As dialkyl ketene **5h** and monosubstituted ketene **5i** are not stable and could not be purified, as could ketenes **5a–5c**, we developed a one-pot strategy,¹¹ finding that in the presence of triethylamine, the reaction of acid chloride with phosphonium salt **4a** worked well, giving the desired allenic esters in good yields with moderate enantioselectivities (Table 1, entries 8–9).

The absolute configurations of **6a** and **6e** were assigned as *S* by chemical transformations.¹¹ Very recently, Aggarwal and his co-workers developed an elegant dipole–dipole interaction model to account for the selectivity of the reaction of stabilized phosphorus ylides with aldehydes.¹² Based on their mechanistic insights, as well as the current experimental results, a stereochemical model, shown in Scheme 3, has been developed to explain the configuration of the allenic esters formed. This reaction was proposed to proceed *via* a $\pi_2s + \pi_2a$ cycloaddition, affording the oxaphosphetane, which then decomposed into the corresponding phosphine oxide and chiral allene. The ketene approached the *re* face of ylide **7a** preferentially due to the steric hindrance between the substituents of the ketene and the ylide. Thus allenes with *S*-configurations were obtained, consistent with the experimental results.¹¹

One of the advantages of the current reaction is that the chiral phosphine oxide could be recycled and reused. For example, **8** was recovered in 81% yield and was readily reduced by LiAlH_4 into phosphine **3** in 90% yield (Scheme 4).¹¹

In summary, we have developed an efficient method for the preparation of optically-active 4,4-disubstituted and 4-mono-substituted allenic esters in good yields. The easily available phosphonium salts, good to high enantioselectivity and, in particular, the recovery and the reuse of the phosphine oxide

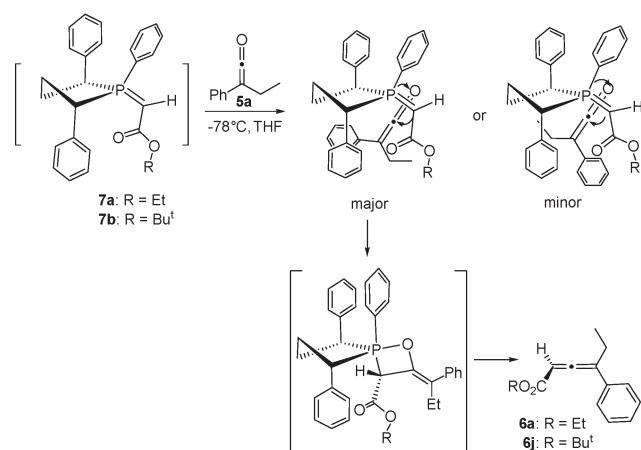


Scheme 2

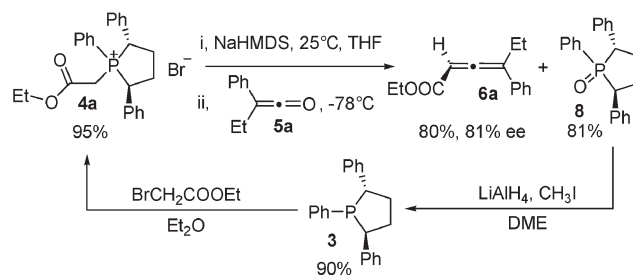
Table 1 Asymmetric synthesis of allenes **6** from phosphonium salts **4**¹¹

Entry	Ketene	4	6	Yield (%) ^a	ee (%) ^b
1				80	81
2				76	71
3				71	85
4 ^c				46	61
5 ^c				51	52
6				78	91
7				75	85
8 ^d				51	63
9 ^d				52	55
10				51	92

^a Isolated yield. ^b Determined by chiral HPLC. ^c Ketene prepared *in situ*. ^d One-pot reaction.



Scheme 3



Scheme 4

make the present method potentially useful. Studies on further improving the enantioselectivity and understanding the mechanism are in progress in our laboratory.

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