



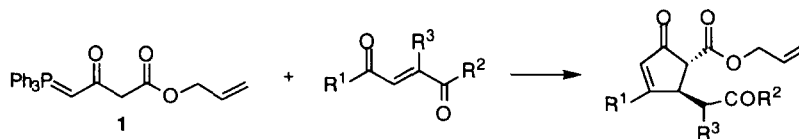
Single-Step Synthesis of Cyclopentenones from (3-Alkoxy carbonyl-2-oxo-propylidene)triphenylphosphorane and 1,2-Diacylethylenes

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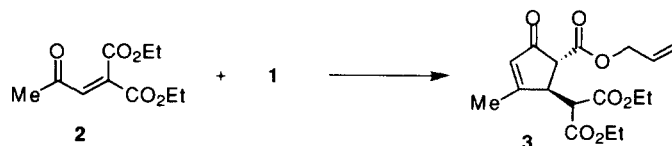
Abstract: (3-Alkoxy carbonyl-2-oxo-propylidene)triphenylphosphorane reacts with 1,2-diacylethylenes to give cyclopentenones in a single operation. Use of a chiral acylmethylenemalonate led to formation of optically active cyclopentenone in a highly diastereoselective fashion.

Short-step synthesis of substituted 5-membered carbocycles has been an attractive subject recently. Numerous interesting methodology have been documented for this purpose.¹ We have demonstrated that [3 + 2] annulation using allylidene triphenylphosphorane as a 3-carbon unit is powerful tool for the single-step preparation of substituted cyclopentadienes and cyclopentenones.² Recent paper has described that (3-alkoxy carbonyl-2-oxo-propylidene)phosphorane also proceeds [3 + 2] annulation with glyoxals to produce hydroxycyclopentenones in a single operation.³ In this context, we report herein an additional [3 + 2] annulation of the phosphorane with diacylethylenes, leading to one-step formation of substituted cyclopentenone in a highly regioselective fashion. Furthermore, this method provides a direct access to optically active cyclopentenone by using chiral acyl-methylenemalonate as a substrate.



At first, the reaction of the phosphorane with an active Michael acceptor, acylmethylenemalonate **2**, was examined (Scheme 1). Cyclopentenone formation occurred simply by stirring an equimolar mixture of **1** and **2** in THF at room temp. to give **3**⁴ in 14% yield (Table 1, entry 1). The annulation was found to be much accelerated by addition of lithium salts to the reaction mixture, of which LiClO₄ gave the best yield (84%, entry 2).⁵ Furthermore, anion formation at the 3-position of **1** by adding a base was also effective. The phosphorane **1** was allowed to react with *s*-BuLi (1 equiv.) followed by **2** (1 equiv.) in THF at -78 °C. After disappearance of **2**, the mixture was treated with acetic acid (1 equiv.) and aqueous NaHCO₃, and left at 30 °C for 2 days. Work-up of the mixture gave the cyclopentenone **3** in 84% yield (entry 5).

The procedure described above for entry 5 was applicable to annulation with various diacylethylenes **4** (Scheme 2). The results are illustrated in Table 2. Dibenzoyl ethylene (**4a**) reacted with **1** (1 equiv.) in a similar

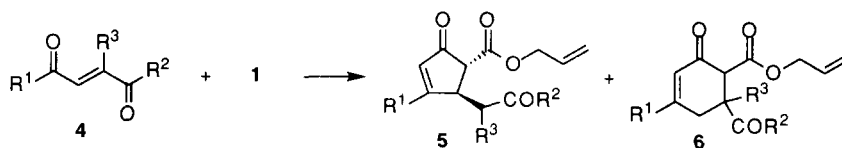


Scheme 1.

Table 1. Annulation of phosphorane **1** with **2**.

Entry	Conditions	Additive	Isolated yield (%) of 3
1	THF/rt./12 h	-	14
2	THF/rt./12 h	LiCO ₃ (1 equiv.)	84
3	THF/rt./12 h	LiBF ₄ (1 equiv.)	64
4	THF/rt./12 h	LiBr (1 equiv.)	57
5	THF/-78 °C to rt.	<i>s</i> -BuLi (1 equiv.)	84

manner to give the cyclopentenone **5a** in 84% yield (entry 1). Diacetylene (**4b**) also underwent cyclization to afford **5b** (entry 2). Thus, the symmetrical ethylenes underwent [3 + 2] annulation exclusively without being accompanied by [3 + 3] annulation.⁶ On the other hand, methyl 4-oxo-2-pentenoate (**4c**) and ethyl 2-methyl-4-oxo-2-pentenoate (**4d**) produced cyclohexenones **6c** and **6d**, in 65 and 54% yields, respectively (entries 3, 4). Interestingly, *S*-ethyl 4-oxo-2-pentenethioate (**4e**) gave **5e** via a regioselective Michael addition at the 3-position of **4e**. An unsymmetrical ethylene, 1-phenyl-2-propen-1,4-dione (**4f**), also gave **5f** selectively in 88% yield. The observed regioselective outcomes of the initial Michael addition agreed with those anticipated from the electron population in LUMO of 1,2-diacetylenes.⁷

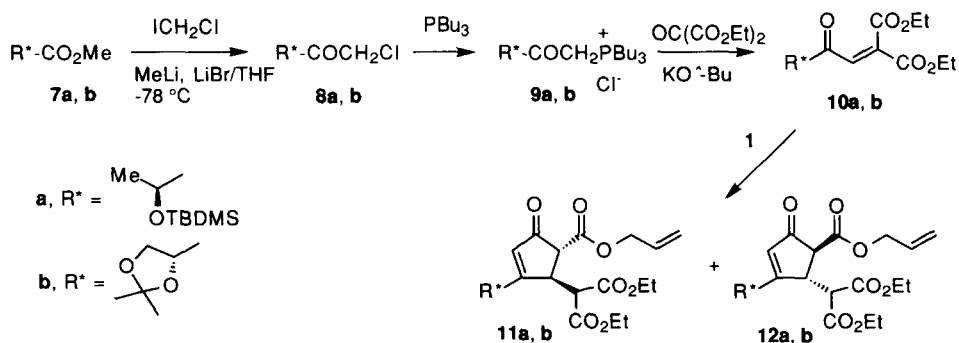
Scheme 2. For R¹, R² and R³, see Table 2Table 2. Annulation of phosphorane **1** with 1,2-diacetylenes **4**.^a

Entry	No.	Substrate			Cyclopentenone 5 Yield (%) ^b	Cyclohexenone 6 Yield (%) ^b
		R ¹	R ²	R ³		
1	4a	Ph	Ph	H	84	-
2	4b	Me	Me	H	55	-
3	4c	Me	OMe	H	-	65
4	4d	Me	OEt	Me	-	54
5	4e	Me	SEt	H	74	-
6	4f	Me	Ph	H	88	-

^aAll reactions were carried out in THF in the presence of an equiv. of *s*-BuLi; see text. ^bIsolated yield.

Next, an enantioselective synthesis of cyclopentenones was investigated with chiral acylmethylene-malonates. Chiral substrates **10a** and **10b** were prepared from the corresponding esters **7a** and **7b** in 45% and

52% overall yields, respectively, by straightforward sequences involving (i) addition of chloromethylithium⁸, (ii) treatment with tributylphosphine, and then (iii) Wittig reaction with diethyl ketomalonate. Compound **10a** was treated with **1** in THF in the presence of 1 equiv. of LiClO₄ at room temp. to give 1:1 mixture of **11a** and **12a** in 35% total yield. Significant 1,3-asymmetric induction was observed under the conditions using *s*-BuLi in which initial Michael addition underwent at -78 °C and finally **11a** and **12a** were obtained in a 7:3 ratio in 79% yield. In a similar fashion, high level of asymmetric induction was accomplished by use of **10b** as a substrate, which led to formation of **11b** and **12b** in a 1:24 ratio in 72% yield. The stereochemistry of the major product **12b** was determined to be 4*R* configuration by deriving it to known compound.⁹



Scheme 3

Table 3. Annulation of phosphorane **1** with chiral acylmethylenemalonates **10a** and **10b**.

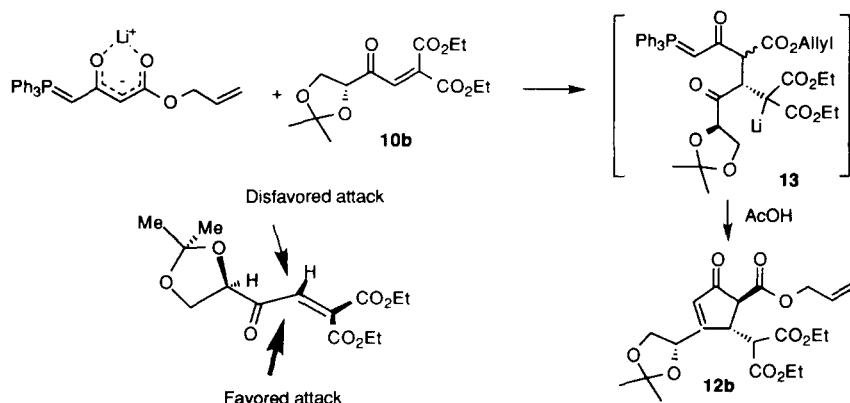
Entry	Substrate No.	Additive	Yield (%) of Cyclopentenone (Ratio of 11 to 12) ^a
1	10a	LiCO ₄ (1 equiv.) ^b	35 (1:1)
2	10a	<i>s</i> -BuLi (1 equiv.) ^c	79 (7:3)
3	10b	<i>s</i> -BuLi (1 equiv.) ^c	72 (1:24)

^aThe ratio was estimated on the basis of their ¹H NMR spectra. ^bThe reaction was carried out in THF at rt. for a day.

^cThe reaction was carried out in THF at -78 °C for 8 h and then at 30 °C for 2 days after quenching with AcOH.

The observed high level of 1,3-asymmetric induction may be rationalized by assuming a similar transition-state model reported previously for the formation of chiral 4-hydroxycyclopentenones from **1** and chiral glyoxals³ (Scheme 4). The annulation must undergo stepwise, that is an initial Michael addition of **1** to **10b** followed by an intramolecular Wittig reaction. In the first step, the carbanion of **1** attacks preferentially from the less hindered bottom face of the *s-cis* oriented double bond on a Felkin-Anh model to give **13**. The observed high level of diastereoselection implied usefulness of 1,3-asymmetric induction based on this model. Final Wittig cyclization gave **12b** in which the carboxyl ester adopted thermodynamically stable *trans* configuration.

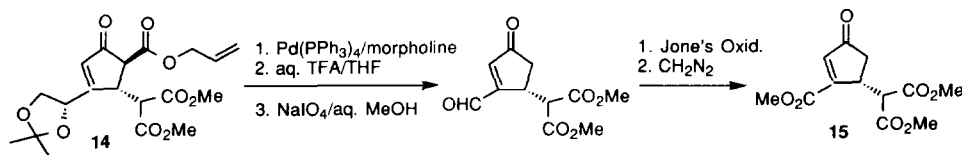
In summary, the [3 + 2] annulation between (3-alkoxycarbonyl-2-oxo-propylidene)triphenylphosphorane and 1,2-diacylethylenes provides an efficient method for the preparation of substituted cyclopentenones in a single operation. Furthermore this method is applicable for one-step preparation of optically active cyclopentenone by using chiral acylmethylenemalonates as a substrate.



Scheme 4. Plausible mechanism for the formation of **12b**

References and Notes

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- The cyclopentenones were obtained in a *trans* form. Spectral data for **3**: ^1H NMR (CDCl_3 , 270 MHz,) δ 7.86 (d, $J=7.3$ Hz, 2H), 7.62-7.39 (m, 8H), 6.46 (d, $J=1.2$ Hz, 1H), 6.06-5.92 (m, 1H), 5.42 (dd, $J=17.2$, 1.3 Hz, 1H), 5.27 (dd, $J=10.6$, 1.3 Hz, 1H), 4.77 (d, $J=5.6$ Hz, 2H), 4.47 (broad d, $J=11.2$ Hz, 1H), 3.50 (dd, $J=18.5$, 2.6 Hz, 1H), 3.31 (d, $J=2.0$ Hz, 1H), 3.03 (dd, $J=18.5$, 11.2 Hz, 1H); IR (CH_2Cl_2) 1740, 1697, 1600 cm^{-1} .
- ^1H NMR spectrum of **1** in $\text{THF}-d_8$ was changed remarkably by addition of an equiv. of LiClO_4 , implying the generation of reactive species. The detail will be discussed in a full paper.
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- In order to determine the stereochemistry of the major product, the cyclopentenone dimethyl ester **14** (de. 91%) was prepared in a similar manner from the corresponding dimethyl ester of **10b**. Compound **14** was converted via the following sequences into the cyclopentenone **15** which showed identical physical data with these reported previously; Klunder, A. J. H.; Huizinga, W. B.; Sessink, P. J. M.; Zwanenburg, B. *Tetrahedron Lett.*, **1987**, *28*, 357.



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