Pergamon

Tetrahedron Letters, Vol. 37, No. 3, pp. 401-404, 1996

0040-4039/96 $15.00 + 0.00

0040-4039(95)02186-8

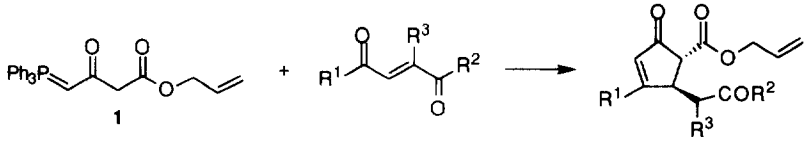
Single-Step Synthesis of Cyclopentenones from (3-Alkoxycarbonyl-2-oxo-propylidene)triphenylphosphorane and 1,2-Diacylethylenes

Minoru Hatanaka,* Akiharu Ishida, Yasuhiro Tanaka and Ikuo Ueda

The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki, Osaka 567, Japan

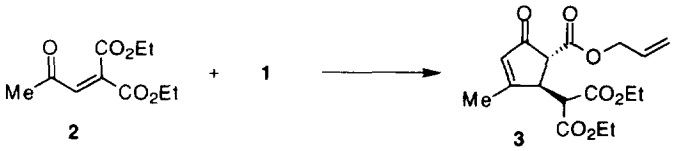
Abstract: (3-Alkoxycarbonyl-2-oxo-propylidene)triphenylphosphorane reacts with 1,2-diacylethylenes to give cyclopentenones in a single operation. Use of a chiral acylmethylenemalonate led to formation of optically active cyclopentenone in a highly diastereoselective fashion.

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 allylidenetriphenylphosphorane 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-alkoxycarbonyl-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 $LiClO_4$ 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 $NaHCO_3$, 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. Dibenzoylethylene (**4a**) reacted with **1** (1 equiv.) in a similar

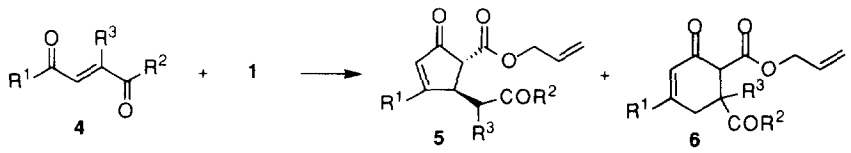


Scheme 1.

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	$LiCO_4$ (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.	*s*-BuLi (1 equiv.)	84

manner to give the cyclopentenone **5a** in 84% yield (entry 1). Diacetylethylene (**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-diacylethylenes.[7]



Scheme 2. For R^1, R^2 and R^3, see Table 2

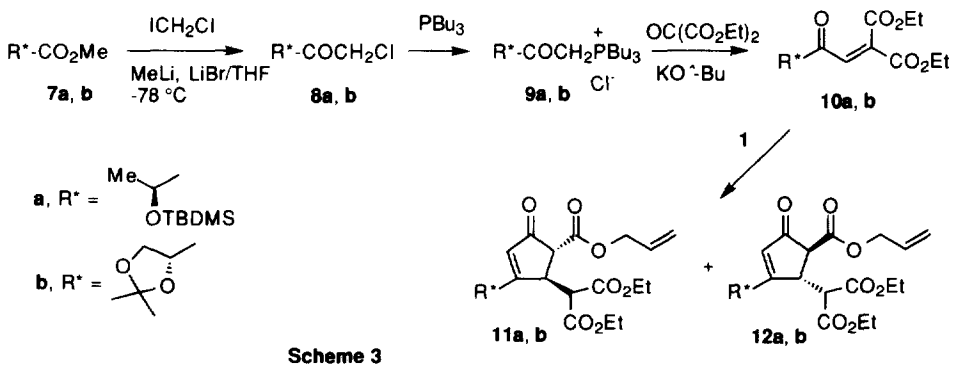
Table 2. Annulation of phosphorane **1** with 1,2-diacylethylenes **4**.[a]

Entry	No.	Substrate R^1	R^2	R^3	Cyclopentenone **5** Yield (%)[b]	Cyclohexenone **6** Yield (%)[b]
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	-

[a]All reactions were carried out in THF in the presence of an equiv. of *s*-BuLi; see text. [b]Isolated 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 chloromethyllithium[8], (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 $LiClO_4$ 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

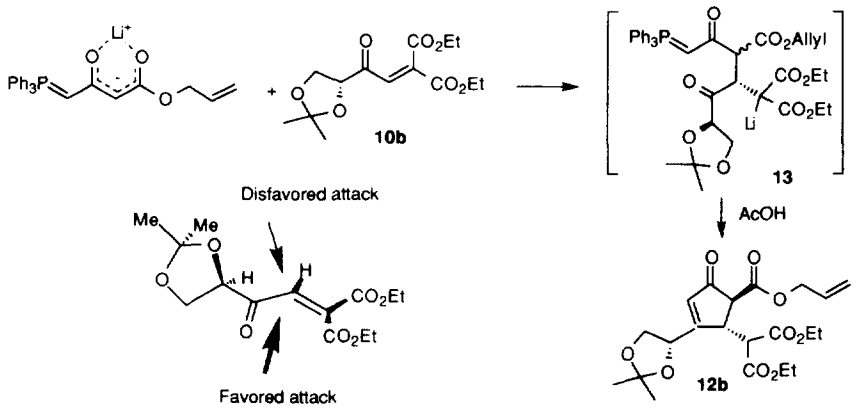
Table 3. Annulation of phosphorane **1** with chiral acylmethylenemalonates **10a** and **10b**.

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**	*s*-BuLi (1 equiv.)[c]	79 (7:3)
3	**10b**	*s*-BuLi (1 equiv.)[c]	72 (1:24)

[a]The ratio was estimated on the basis of their ^1H NMR spectra. [b]The reaction was carried out in THF at rt. for a day. [c]The 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 glyoxals[3] (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.

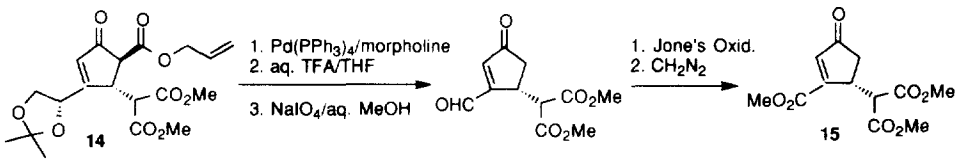
In summary, the [3 + 2] annulation between (3-alkoxycarbonyl-2-oxo-propylidene)triphenylphosphorane and 1,2-diacylethylenes provides an efficient method for the preparation of substituted cyclopentenones in a single operation. Furthermore this method is applicable for one-step preparation of optically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



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

References and Notes

1. For excellent reviews, see: Ramaiah, M. *Synthesis*, **1984**, 529. Little, R. D. *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I., Eds., Pergamon, Oxford, 1991, Vol. 5, 239. Habermas, K. L.; Denmark, S. E. *Org. React.* **1994**, *45*, 1.
2. Hatanaka, M.; Himeda, Y.; Ueda, I. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2269; Hatanaka, M.; Himeda, Y.; Imashiro, R.; Tanaka, Y.; Ueda, I. *J. Org. Chem.* **1994**, *59*, 111; Hatanaka, M.; Himeda, Y.; Tanaka, Y.; Ueda, I. *Tetrahedron Lett.*, **1995**, *36*, 3211.
3. Hatanaka, M.; Tanaka, Y.; Ueda, I. *Tetrahedron Lett.*, **1995**, *36*, 3719.
4. The cyclopentenones were obtained in a *trans* form. Spectral data for **3**: ^{1}H 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}.
5. ^{1}H NMR spectrum of **1** in 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.
6. Pietrusiewicz, K. M.; Monkiewicz, J.; Bodalski, R. *J. Org. Chem.* **1983**, *48*, 788. Pietrusiewicz, K. M.; Salammonczyk, I. *J. Org. Chem.* **1988**, *53*, 2837.
7. Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*, John Wiley & Sons, Ltd., London, 1976.
8. Barluenga, J.; Baragana, B.; Alonso, A.; Concellon, J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 969.
9. 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.



(*Received in Japan* 3 *October* 1995; *revised* 30 *October* 1995; *accepted* 17 *November* 1995)