Annulation of 2-Oxoalkylidenetriphenylphosphoranes with Enediones: A One-Step Synthesis of Substituted Cyclopentenones

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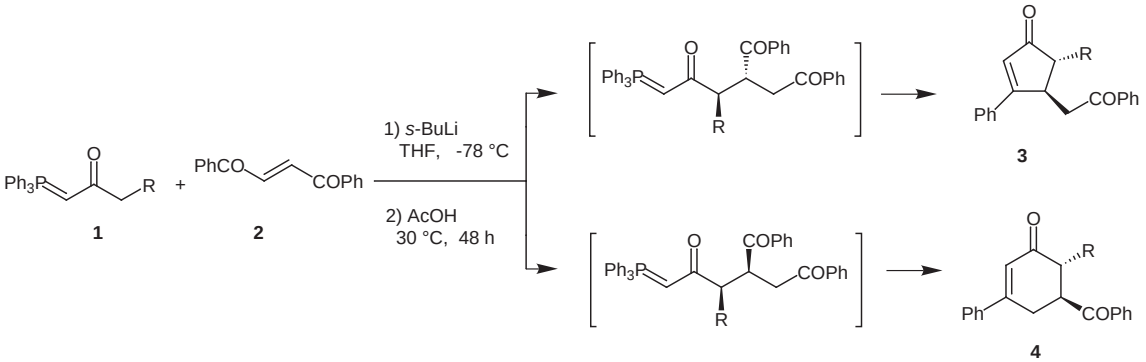
Abstract: 2-Oxoalkylidenetriphenylphosphoranes undergo [3+2] annulation with enediones to give cyclopentenones as major products along with cyclohexenones.

Key words: ylides, enediones, annulation, carbocycles, regioselectivity

Annulation to form 5-membered carbocycles is still an attractive subject of organic chemists, because there are many biologically active compounds bearing a 5-membered unit, such as prostaglandins, methylenomycin, and cyclopentanoid antibiotics.[2] We have demonstrated a useful method for this purpose using phosphoranes, such as allylidenetriphenylphosphoranes and 2-oxopropylidenetriphenylphosphoranes, which serve as versatile 1,3-bidentate reagents in the [3+2] pentaannulation leading to successful formation of a variety of cyclopentanoids.[3] For instance, 3-alkoxycarbonyl-2-oxopropylidenetriphenylphosphorane undergoes annulation with glyoxals and 1,2-diacylethylenes to afford 4-hydroxy- and 4-acylmethyl substituted cyclopentenones in good yields.[3c,d] Especially, in the latter case cyclopentenones were produced exclusively without attendant formation of other possible cyclohexenones.[4] The annulation proceeded smoothly in the presence or absence of base via carbanion formation at the 3-position of 3-alkoxycarbonyl-2-oxopropylidenetriphenylphosphorane, because the phosphorane has an active methylene at this position. In order to extend the scope of the reaction, we studied use of 2-oxopropylidenetriphenylphosphoranes with non electron-withdrawing substituents, such as alkyl and alkoxy, at the 3-position, which would provide a direct access to a variety of cyclopentenones.

2-Oxopropylidenetriphenylphosphorane (**1a**) was first examined as a simple model. When the phosphorane **1a** was treated at –78 °C with *s*-BuLi in THF followed by (*E*)-1,4-diphenylbut-2-ene-1,4-dione (**2**), Michael addition proceeded smoothly within 30 minutes. Warming the reaction mixture at 30 °C for 48 hours after neutralization with acetic acid effected the intramolecular Wittig reaction to afford the cyclopentenone **3a** and cyclohexenone **4a** in 79 and 10% yields, respectively (Scheme 1). Annulation of 3-alkyl and 3-methoxy substituted phosphoranes **1b**–**d** with **2** was then examined in a similar way. Reaction of 2-oxobutylidenetriphenylphosphorane (**1b)** with **2** gave the cyclopentenone **3b** and cyclohexenone **4b** in 43 and 27% yields, respectively. *trans*-Relationship of the substituents in both products was confirmed by NMR experiments and any *cis*-congeners were not detected. The ^{1}H NMR spectra of **3b** showed NOE (12%) between 5-Me and 4-H, whilst NOE (less than 1%) between 5-CH_3 and 4-CH_2. Assignment of the 5,6-*trans* orientation in **4b** was based on the observed H-H coupling constant ($J_{5,6}$ = 11.6 Hz). Quite similar results were obtained with 2-oxopentylidenetriphenylphosphorane (**1c**) which produced **3c** (43%) and **4c** (21%). Annulation of 3-methoxy-2-oxopropylidenetriphenylphosphorane (**1d**) also gave *trans*-5-methoxycyclopentenone (**3d**) in 21% yield along with *trans*-6-



Scheme 1

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methoxycyclohexenone (**4d**) (17% yield). Apparently, an increase of cyclohexenone formation was observed with alkyl and methoxy substituted phosphoranes **1b–d** in comparison to the annulation of phosphorane **1a** (Table 1, entry 1). This may be ascribed to the formation of a *syn-anti* isomeric mixture at the Michael addition stage in which the *anti*-isomer subsequently cyclizes to give **3** and the *syn*-isomer leads to **4**.

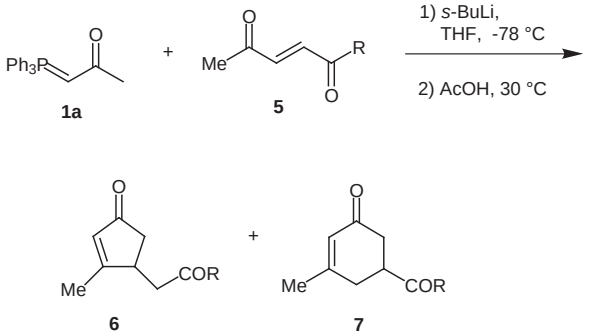
Table 1 Annulation of Phosphoranes **1** with *trans*-1,4-Diphenylbut-2-ene-1,4-dione (**2**)

Entry	**1**	R	Yield of **3** (%)[a]	Yield of **4** (%)[a]
1	**a**	H	79	10
2	**b**	Me	43	27
3	**c**	Et	43	21
4	**d**	MeO	21	17

[a] The yields are based on **2**.

Annulation of phosphorane **1a** with various unsymmetrical enediones **5** was next investigated and the results are depicted in Table 2. Thus, (*E*)-1-phenylpent-2-ene-1,4-dione (**5a**) reacted with **1a** under the same conditions as described above to give cyclopentenone **6a** in 59% yield along with cyclohexenone **7a** (4% yield) (Scheme 2). Each product was single and the corresponding regioisomer was not detected. It is evident that **6a** is formed via the initial Michael addition at the 3-position of **5a** followed by the intramolecular Wittig reaction with the 4-keto group, whilst **7a** arises from the Michael addition at the 2-position and subsequent Wittig reaction with the 4-keto group. Attempted efforts to improve the yield with additives including TMEDA and CuCN·2LiCl were unsuccessful and resulted in lowering the yield. Several substituents were then introduced on the phenyl group in order to test attendant changes of the product distribution (Table 2, entries 2–4). However, the accompanied formation of cyclohexenones was observed at an analogous rate in all cases although somewhat improvement of the yield was achieved with **5b** (entry 2). Nevertheless, cyclopentenones were mainly produced and could be purified readily by column chromatography. With (*E*)-hex-3-ene-2,5-dione, poor yields of cyclization products were obtained and a large amount of the enedione was recovered, probably implying that proton transfer occurred in preference to Michael addition. However, thioester **5e** was found to give cyclopentenone **6e** as a sole cyclization product in a moderate yield.

We have described in a previous publication a highly diastereoselective annulation of 3-allyloxycarbonyl-2-oxopropylidenetriphenylphosphorane with a chiral triacyl substrate to form an optically active cyclopentenone in 91% de.[3c] However, the phosphorane showed a low level of both the diasteroselectivity (less than 50% de) and the regioselectivity with chiral enediones such as **8**. This



Scheme 2

Table 2 Annulation of Phosphorane **1a** with Unsymmetrical Enediones **5**

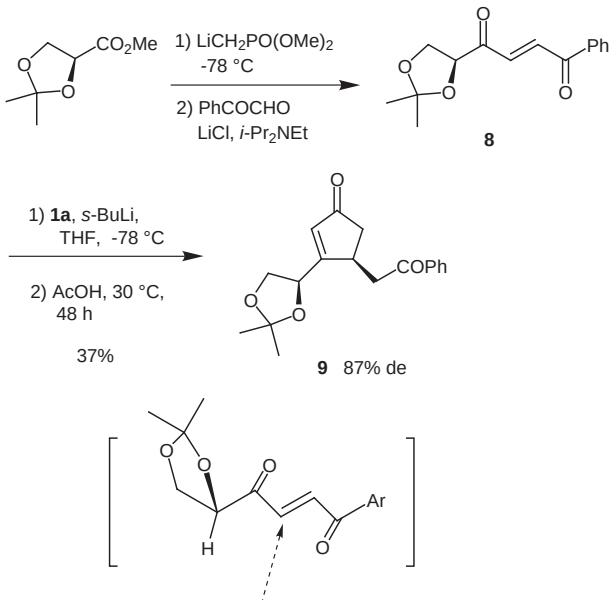
Entry	**5**	R	Yield of **6** (%)[a]	Yield of **7** (%)[a]
1	**a**	Ph	59	4
2	**b**	4-$MeOC_6H_4$	63	6
3	**c**	4-FC_6H_4	57	5
4	**d**	2,4-$Me_2C_6H_3$	44	4
5	**e**	SEt	33	–

[a] The yields are based on the starting enediones **5**.

asymmetric induction was therefore studied using phosphorane **1a**. Thus, methyl (*S*)-(–)-2,2-dimethyl-1,3-dioxolane-4-carboxylate was converted into enedione **8** by treatment with dimethyl methylphosphonate in the presence of BuLi followed by phenylglyoxal.[5] When **1a** was allowed to react with chiral enedione **8**, cyclopentenone **9** was obtained as the main product in a moderate yield, but with high diastereoselection (87% de). Recrystallization of the diastereomeric mixture afforded **9** as a single diastereomer (Scheme 3). The stereochemistry of **9** was estimated from the previous results.[3c] In the initial Michael addition, the carbanion of **1a** may attack preferentially from the less hindered bottom face of the s-*cis*-oriented double bond to the carbonyl group.

In summary, this paper describes the annulation using readily available 2-oxoalkylidenetriphenylphosphoranes, which react with enediones in the presence of *s*-BuLi to give 3,4-di- and 3,4,5-trisubstituted cyclopentenones as major products. Further studies on the applications of the reaction to synthesis of enantiomerically enriched cyclopentanoids are now in progress.

All mps were measured on a Yanagimoto hot stage apparatus and are uncorrected. IR spectra were recorded on a Hitachi 270-30 spectrometer. ^{1}H NMR spectra were measured at 500 MHz in $CDCl_3$ on a JEOL Lambda 500 spectrometer, using $SiMe_4$ as the internal standard. *J*-Values are given in Hz. ^{13}C NMR spectra were recorded at 125 MHz on the spectrometer and solvent peak ($CDCl_3$: δ_C 77.0) was used for the internal standard. Mass spectra were recorded on a



Scheme 3

Shimadzu GCMS-QP5000 spectrometer or a JEOL JMS-700T spectrometer. HPLC data was obtained on a JASCO TRI ROTAR-VI instrument. All reactions were carried out under Ar in dried glassware. Flash chromatography was performed on Wakogel C-300. Extracts were dried over $MgSO_4$ and evaporated under reduced pressure. THF was distilled from sodium benzophenone ketyl under Ar prior to use. (*E*)-1-phenylpent-2-ene-1,4-dione (**5a**) and *S*-ethyl (*E*)-4-oxopent-2-enethioate (**5e**) were prepared according to literature procedures.[6,7] The phosphoranes **1b**–**d** were prepared according to the literature procedures.[8,9] All other commercially available reagents were used as received.

Annulation of Phosphoranes 1 with Enediones 2; 4-(2-Oxo-2-phenylethyl)-3-phenylcyclopent-2-en-1-one (3a) and 3-Phenyl-5-benzoylcyclohex-2-en-1-one (4a); Typical Procedure (TP-1)

To a solution of **1a** (159 mg, 0.5 mmol) in THF (8 mL) was added a 1.0 M solution of *s*-BuLi in hexane (0.5 mL) at –78 °C. The reaction mixture was stirred for 30 min at that temperature. To the mixture was added dropwise a solution of **2** (58 mg, 0.33 mmol) in THF (1 mL). After stirring for 1 h at –78 °C, the mixture was treated with AcOH (29 μL, 0.5 mmol) and sat. aq $NaHCO_3$ (1 mL) and the stirring was then continued for 48 h at r.t. The mixture was poured into brine and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc, 8:1) to give **3a** (72 mg, 79%) and **4a** (9 mg, 10%).

3a

Colorless solid; mp 109–110 °C (hexane–EtOAc).

IR (Nujol): 1684, 1596, 1360, 1180, 762, 752, 692 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.14 (dd, 1 H, *J* = 18.9, 1.5 Hz), 3.01 (dd, 1 H, *J* = 18.0, 6.6 Hz), 3.02 (dd, 1 H, *J* = 18.9, 11.2 Hz), 3.36 (dd, 1 H, *J* = 18.0, 2.4 Hz), 4.17 (m, 1 H), 6.52 (d, 1 H, *J* = 1.2 Hz), 7.43 (br t, 2 H, *J* = 8.2 Hz), 7.48 (m, 3 H), 7.56 (br t, 1 H, *J* = 8.2 Hz), 7.59 (m, 2 H), 7.88 (br d, 2 H, *J* = 8.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.67, 197.82, 177.12, 136.42, 133.53, 133.17, 131.08, 129.27, 129.24, 128.72, 128.02, 127.18, 43.79, 43.50, 36.06.

EIMS: *m*/*z* (%) = 276 (M^+, 67), 171 (100), 105 (82), 77 (38).

Anal. Calcd for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.83; H, 5.83.

4a

Colorless solid; mp 107–108 °C (hexane–EtOAc).

IR (Nujol): 1686, 1664, 1348, 1252, 754, 708, 686 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.73 (m, 2 H), 3.01 (dd, 1 H, *J* = 18.0, 4.6 Hz), 3.15 (ddd, 1 H, *J* = 18.0, 10.4, 2.1 Hz), 4.22 (m, 1 H), 6.51 (d, 1 H, *J* = 2.1 Hz), 7.42 (m, 3 H), 7.51 (br t, 2 H, *J* = 7.3 Hz), 7.55 (m, 2 H), 7.62 (br t, 1 H, *J* = 7.3 Hz), 7.98 (br d, 2 H, *J* = 7.3 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.82, 197.60, 157.71, 138.19, 135.12, 133.73, 130.34, 129.03, 128.90, 128.47, 126.18, 125.03, 42.54, 39.71, 30.71.

EIMS: *m*/*z* (%) = 171 (M^+ – COPh, 63), 105 (100), 77 (44).

Anal. Calcd for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.31; H, 6.04.

(4*S,5*S**)-5-Methyl-4-(2-oxo-2-phenylethyl)-3-phenylcyclopent-2-en-1-one (3b) and (5*R**,6*S**)-6-Methyl-3-phenyl-5-benzoylcyclohex-2-en-1-one (4b)**

Synthesized according to TP-1 by the reaction of **1b** with **2**. The crude product was purified by flash chromatography (hexane–EtOAc, 8:1) to give **3b** in 43% yield as a colorless oil and **4b** in 27% yield as a colorless solid.

3b

IR (neat): 3098, 3005, 1686, 1594, 1448, 1356, 1328, 1186, 768, 754, 690 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.42 (d, 3 H, *J* = 7.3 Hz), 2.20 (br q, 1 H, *J* = 7.3 Hz), 3.02 (dd, 1 H, *J* = 18.0, 11.0 Hz), 3.35 (dd, 1 H, *J* = 18.0, 2.4 Hz), 3.75 (d, 1 H, *J* = 11.0 Hz), 6.47 (br s, 1 H), 7.44 (br t, 2 H, *J* = 7.9 Hz), 7.47 (m, 3 H), 7.56 (br t, 1 H, *J* = 7.9 Hz), 7.60 (m, 2 H), 7.89 (br d, 2 H, *J* = 7.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 210.99, 197.98, 175.74, 136.47, 133.46, 133.23, 131.04, 129.18, 128.70, 127.99, 127.56, 127.19, 49.44, 44.56, 43.67, 17.72.

EIMS: *m*/*z* (%) = 290 (M^+, 15), 185 (51), 170 (23), 105 (100), 77 (72).

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.70; H, 6.22.

4b

Mp 75–76 °C (hexane–EtOAc).

IR (Nujol): 1664, 1612, 1594, 1360, 1266, 1234, 1200, 758, 708, 692 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.16 (d, 3 H, *J* = 6.7 Hz), 2.99 (m, 2 H), 3.06 (ddd, 1 H, *J* = 18.0, 10.7, 2.4 Hz), 4.04 (dt, 1 H, *J* = 11.0, 4.8 Hz), 6.50 (d, 1 H, *J* = 2.4 Hz), 7.40 (m, 3 H), 7.51 (m, 2 H), 7.52 (br t, 2 H, *J* = 7.9 Hz), 7.62 (br t, 1 H, *J* = 7.9 Hz), 8.02 (br d, 2 H, *J* = 7.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.80, 200.40, 155.64, 137.97, 136.33, 133.79, 130.17, 128.99, 128.84, 128.44, 126.03, 124.54, 48.26, 42.58, 31.77, 13.34.

EIMS: *m*/*z* (%) = 185 (M^+ – COPh, 91), 157 (15), 105 (100), 77 (71).

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.95; H, 6.28.

(4*S,5*S**)-5-Ethyl-4-(2-oxo-2-phenylethyl)-3-phenylcyclopent-2-enone (3c) and (5*R**,6*S**)-6-Ethyl-3-phenyl-5-benzoylcyclohex-2-enone (4c)**
Synthesized according to TP-1 by reaction of **1c** with **2**. The crude product was purified by flash chromatography (hexane–EtOAc, 8:1) to give **3c** in 43% yield as a colorless oil and **4c** in 21% yield as a colorless solid.

3c
IR (neat): 2960, 2928, 1684, 1598, 1574, 1352, 1330, 1218, 766, 752, 692 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, 3 H, *J* = 7.3 Hz), 1.42 (dq, 2 H, *J* = 7.3, 1.8 Hz), 2.20 (dt, 1 H, *J* = 5.8, 1.2 Hz), 3.06 (dd, 1 H, *J* = 17.7, 10.4 Hz), 3.30 (dd, 1 H, *J* = 17.7, 2.4 Hz), 3.86 (dt, 1 H, *J* = 10.4, 1.2 Hz), 6.47 (br d, 1 H, *J* = 0.9 Hz), 7.43 (br t, 2 H, *J* = 8.2 Hz), 7.46 (m, 3 H), 7.55 (br t, 1 H, *J* = 8.2 Hz), 7.62 (m, 2 H), 7.88 (br d, 2 H, *J* = 8.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 210.51, 197.97, 176.14, 136.50, 133.38, 133.05, 131.02, 129.13, 128.63, 128.15, 127.96, 127.11, 55.45, 43.67, 41.91, 25.39, 10.58.

EIMS: *m*/*z* (%) = 304 (M^+, 11), 199 (39), 184 (65), 105 (100), 77 (93).

Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.92; H, 6.80.

4c
Mp 97–98 °C (hexane–EtOAc).

IR (Nujol): 1664, 1610, 1596, 1576, 1306, 1258, 1212, 760, 690 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.6 Hz), 1.68 (dq, 1 H, *J* = 7.6, 0.9 Hz), 1.84 (dq, 1 H, *J* = 4.8, 1.8 Hz), 2.93 (dq, 1 H, *J* = 4.8, 1.2 Hz), 3.03 (d, 2 H, *J* = 7.3 Hz), 4.21 (m, 1 H), 6.45 (t, 1 H, *J* = 1.5 Hz), 7.33 (m, 3 H), 7.50 (m, 2 H), 7.51 (br t, 2 H, *J* = 8.2 Hz), 7.62 (br t, 1 H, *J* = 8.2 Hz), 8.00 (br d, 2 H, *J* = 8.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.66, 199.92, 155.03, 137.95, 135.84, 133.67, 130.09, 128.99, 128.80, 128.39, 126.03, 124.96, 48.22, 45.05, 30.76, 21.24, 11.29.

EIMS: *m*/*z* (%) = 199 (M^+ – COPh, 92), 171 (35), 105 (100), 77 (62).

Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.60; H, 6.54.

(4*R,5*S**)-5-Methoxy-4-(2-oxo-2-phenylethyl)-3-phenylcyclopent-2-enone (3d) and (5*R**,6*S**)-6-Methoxy-3-phenyl-5-benzoylcyclohex-2-enone (4d)**
Synthesized according to TP-1 by reaction of **1d** with **2**. The crude product was purified by flash chromatography (hexane-EtOAc, 8:1) to give **3d** in 21% yield as a colorless solid and **4d** in 17% yield as a colorless solid.

3d
Mp 109–110 °C (hexane–EtOAc).

IR (Nujol): 1700, 1596, 768, 692 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.15 (dd, 1 H, *J* = 17.7, 9.5 Hz), 3.37 (dd, 1 H, *J* = 17.7, 3.1 Hz), 3.63 (s, 3 H), 3.66 (d, 1 H, *J* = 1.5 Hz), 3.98 (dq, 1 H, *J* = 9.5, 1.5 Hz), 6.47 (br d, 1 H, *J* = 1.2 Hz), 7.44 (br t, 2 H, *J* = 7.9 Hz), 7.46 (m, 3 H), 7.56 (br t, 1 H, *J* = 7.9 Hz), 7.58 (m, 2 H), 7.88 (br d, 2 H, *J* = 7.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.56, 204.96, 175.21, 133.55, 132.98, 131.37, 129.20, 128.73, 127.99, 127.37, 126.81, 100.05, 85.20, 58.53, 42.99, 40.77.

EIMS: *m*/*z* (%) = 306 (M^+, 12), 201 (10), 186 (27), 105 (100), 77 (64).

Anal. Calcd for $C_{20}H_{18}O_3$: H, 5.92; C, 78.41. Found: H, 5.73; C, 78.70.

4d
Mp 99–100 °C (hexane–EtOAc).

IR (Nujol): 1676, 1654, 762, 708 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.02 (dd, 1 H, *J* = 17.7, 3.7 Hz), 3.16 (ddt, 1 H, *J* = 18.0, 5.2, 2.7 Hz), 3.58 (s, 3 H), 4.31 (m, 2 H), 6.47 (d, 1 H, *J* = 2.4 Hz), 7.33 (m, 3 H), 7.49 (br t, 2 H, *J* = 8.1 Hz), 7.50 (m, 2 H), 7.61 (br t, 1 H, *J* = 8.1 Hz), 8.03 (br d, 2 H, *J* = 8.1 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.86, 198.25, 156.11, 137.46, 136.46, 133.71, 130.42, 128.88, 128.80, 128.71, 126.11, 123.81, 81.99, 60.78, 47.97, 31.71.

EIMS: *m*/*z* (%) = 201 (M^+ – COPh, 9), 105 (55), 77 (51).

Anal. Calcd for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92. Found: C, 78.49; H, 5.71.

Enediones; (*E*)-1-(4-Methoxyphenyl)pent-2-ene-1,4-dione (5b); Typical Procedure (TP-2)
A solution of **1a** (159 mg, 0.5 mmol) and 4-methoxyphenylglyoxal (91 mg, 0.5 mmol) in THF (10 mL) was stirred at r.t. for 3 h. The solvent was evaporated and the residue was purified by column chromatography (hexane–EtOAc, 20:1) to give **5b** (77 mg, 76%) as pale yellow crystals; mp 65–66 °C.

IR (Nujol): 1676, 1654, 1302, 1280, 1210, 1180, 836 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 3.90 (s, 3 H), 6.98 (br d, 2 H, *J* = 8.9 Hz), 7.08 (br d, 1 H, *J* = 15.6 Hz), 7.71 (br d, 1 H, *J* = 15.6 Hz), 7.99 (br d, 2 H, *J* = 8.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.96, 188.35, 164.22, 137.69, 134.08, 131.26, 129.76, 114.11, 55.56, 29.05.

EIMS: *m*/*z* (%) = 204 (M^+, 23), 189 (11), 173 (4), 161 (12), 135 (100), 107 (12), 92 (14), 77 (26).

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.37; H, 5.88.

(*E*)-(4-Fluorophenyl)-4-methylbut-2-ene-1,4-dione (5c)
Synthesized according to TP-2 by reaction of **1a** with 4-fluorophenylglyoxal. The crude product was purified by flash chromatography (hexane–EtOAc, 20:1) to give **5c** in 94% yield as a yellow solid; mp 64–65 °C (hexane–EtOAc)

IR (Nujol): 1678, 1654, 1596, 1570, 1326, 1210, 838 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 7.10 (br d, 1 H, *J* = 15.9 Hz), 7.20 (dd, 2 H, *J* = 8.6, 8.5 Hz), 7.68 (br d, 1 H, *J* = 15.9 Hz), 8.03 (dd, 2 H, *J* = 8.6, 8.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.68, 188.61, 167.24, 165.20, 138.47, 133.49, 131.62, 116.25, 29.17.

EIMS: *m*/*z* (%) = 192 (M^+, 8), 177 (26), 164 (7), 149 (18), 123 (100).

Anal. Calcd for $C_{11}H_9O_2F$: C, 68.74; H, 4.72. Found: C, 68.66; H, 5.01.

(*E*)-4-Methyl-1-(2,4-dimethylphenyl)but-2-ene-1,4-dione (5d)
Synthesized according to TP-2 by reaction of **1a** with 2,4-dimethylphenylglyoxal. The crude product was purified by flash chromatography (hexane–EtOAc, 20:1) to give **5d** in 94% yield as a yellow oil.

IR (neat): 3236, 2924, 1662, 1610, 1260, 816 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.40 (s, 3 H), 2.48 (s, 3 H), 6.84 (br d, 1 H, *J* = 15.9 Hz), 7.09 (d, 1 H, *J* = 7.9 Hz), 7.11 (s, 1 H), 7.41 (br d, 1 H, *J* = 15.9 Hz), 7.51 (d, 1 H, *J* = 7.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.19, 193.91, 142.76, 139.02, 138.31, 137.57, 134.00, 132.84, 129.76, 126.33, 28.56, 21.44, 20.97.

EIMS: *m*/*z* (%) = 202 (M^+, 5), 159 (100), 133 (46), 105 (34).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.39; H, 6.88.

(*RS*)-3-Methyl-4-(2-oxo-2-phenylethyl)cyclopent-2-enone (6a)
Synthesized according to TP-1 by reaction of **1a** with **5a**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **6a** in 59% yield as a colorless solid and 3-methyl-5-benzoylcyclohex-2-enone (**7a)** in 4% yield as a colorless oil.

6a
Mp 91–92 °C (hexane–EtOAc).

IR (Nujol): 1678, 1614, 1596, 1364, 1182, 756, 690 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.06 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.15 (s, 3 H), 2.82 (dd, 1 H, *J* = 18.9, 6.4 Hz), 2.99 (dd, 1 H, *J* = 17.1, 9.8 Hz), 3.40 (dd, 1 H, *J* = 17.1, 4.0 Hz), 3.44 (m, 1 H), 5.97 (s, 1 H), 7.50 (br t, 2 H, *J* = 7.3 Hz), 7.61 (br t, 1 H, *J* = 7.3 Hz), 7.94 (br d, 2 H, *J* = 7.3 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.17, 197.79, 179.77, 136.55, 133.54, 131.74, 128.80, 128.02, 43.10, 41.84, 39.91, 17.49.

EIMS: *m*/*z* (%) = 214 (M^+, 15), 109 (88), 105 (100), 77 (72).

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.23; H, 6.89.

7a
IR (neat): 3052, 2982, 1710, 1668, 1578, 1356, 1250, 760, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.01 (s, 3 H), 2.48 (dd, 1 H, *J* = 18.0, 4.3 Hz), 2.61 (m, 2 H), 2.72 (dd, 1 H, *J* = 18.0, 10.1 Hz), 4.09 (m, 1 H), 5.97 (s, 1 H), 7.50 (br t, 2 H, *J* = 7.3 Hz), 7.61 (br t, 1 H, *J* = 7.3 Hz), 7.95 (br d, 2 H, *J* = 7.3 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.71, 197.32, 157.68, 138.14, 135.15, 128.93, 128.88, 125.07, 47.84, 38.76, 33.28, 24.35.

HRMS(FAB): *m*/*z* calcd for $C_{14}H_{15}O_2$ [MH^+]: 215.1072, found 215.1040.

(*RS*)-4-[2-(4-Methoxyphenyl)-2-oxoethyl]-3-methylcyclopent-2-enone (6b)
Synthesized according to TP-1 by reaction of **1a** with **5b**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **6b** in 63% yield as a colorless solid and 3-methyl-5-(4-methoxybenzoyl)cyclohex-2-enone (**7b**) in 6% yield as a colorless oil.

6b
Mp 125–127 °C (hexane–EtOAc).

IR (Nujol): 1696, 1672, 1616, 1600, 1310, 1264, 1174, 840 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.05 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.13 (s, 3 H), 2.80 (dd, 1 H, *J* = 18.9, 6.7 Hz), 2.92 (dd, 1 H, *J* = 17.1, 10.1 Hz), 3.32 (dd, 1 H, *J* = 17.1, 4.0 Hz), 3.44 (m, 1 H), 3.88 (s, 3 H), 5.99 (t, 1 H, *J* = 1.2 Hz), 6.95 (br d, 2 H, *J* = 8.9 Hz), 7.94 (br d, 2 H, *J* = 8.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.30, 196.26, 180.03, 163.82, 131.65, 130.34, 129.66, 113.92, 55.54, 43.11, 41.43, 40.07, 17.50.

EIMS: *m*/*z* (%) = 244 (M^+, 76), 150 (32), 135 (100), 109 (45).

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.38; H, 6.53.

7b
IR (neat): 3052, 2982, 1710, 1666, 1598, 758, 690 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.01 (s, 3 H), 2.44 (dd, 1 H, *J* = 18.3, 4.1 Hz), 2.59 (m, 2 H), 2.73 (dd, 1 H, *J* = 18.3, 10.4 Hz), 3.89 (s, 3 H), 4.03 (m, 1 H), 5.96 (s, 1 H), 6.96 (d, 2 H, *J* = 8.9 Hz), 7.94 (d, 2 H, *J* = 8.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.26, 197.64, 163.94, 160.56, 130.76, 128.10, 126.34, 114.12, 55.56, 41.98, 39.63, 33.49, 24.39.

(*RS*)-4-[2-(4-Fluorophenyl)-2-oxoethyl]-3-methylcyclopent-2-enone (6c)
Synthesized according to TP-1 by reaction of **1a** with **5c**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **6c** in 57% yield as a colorless solid and 3-methyl-5-(4-fluorobenzoyl)cyclohex-2-enone (**7c**) in 5% yield as a colorless oil.

6c
Mp 92–93 °C (hexane–EtOAc).

IR (Nujol): 1676, 1616, 1594, 1234, 828 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.04 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.14 (s, 3 H), 2.82 (dd, 1 H, *J* = 18.9, 6.7 Hz), 2.93 (dd, 1 H, *J* = 17.4, 10.1 Hz), 3.37 (dd, 1 H, *J* = 17.4, 4.0 Hz), 3.44 (m, 1 H), 6.00 (t, 1 H, *J* = 1.2 Hz), 7.16 (br d, 2 H, *J* = 8.3 Hz), 7.98 (br d, 2 H, *J* = 8.3 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.01, 196.11, 179.50, 166.98, 164.95, 131.80, 130.71, 115.83, 43.05, 41.73, 39.83, 17.45.

EIMS: *m*/*z* (%) = 232 (M^+, 69), 123 (81), 109 (100), 95 (83).

Anal. Calcd for $C_{14}H_{13}O_2F$: C, 72.40; H, 5.64. Found: C, 72.73; H, 5.57.

7c
IR (neat): 2956, 2920, 1726, 1680, 1596, 1260, 818, 736 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.01 (s, 3 H), 2.45 (dd, 1 H, *J* = 18.6, 4.9 Hz), 2.60 (m, 2 H), 2.72 (dd, 1 H, *J* = 18.6, 11.3 Hz), 4.05 (m, 1 H), 5.97 (s, 1 H), 7.17 (d, 2 H, *J* = 8.6 Hz), 7.98 (d, 2 H, *J* = 8.6 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.56, 197.12, 167.77, 160.27, 132.09, 130.89, 126.41, 116.06, 42.26, 38.75, 33.26, 22.99.

HRMS (FAB): *m*/*z* calcd for $C_{14}H_{14}O_2F$ [MH^+]: 233.0978, found 233.0977.

(*RS*)-4-[2-(2,4-Dimethylphenyl)-2-oxoethyl]-3-methylcyclopent-2-enone (6d)
Synthesized according to TP-1 by reaction of **1a** with **5d**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **6d** in 44% yield as a colorless solid and 3-methyl-5-(2,4-dimethylbenzoyl)cyclohex-2-enone (**7d**) in 4% yield as a colorless oil.

6d
Mp 74–75 °C (hexane–EtOAc).

IR (Nujol): 1676, 1612, 818, 712 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.04 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.13 (s, 3 H), 2.39 (s, 3 H), 2.50 (s, 3 H), 2.79 (dd, 1 H, *J* = 18.9, 6.4 Hz), 2.89 (dd, 1 H, *J* = 17.1, 9.8 Hz), 3.31 (dd, 1 H, *J* = 17.1, 4.0 Hz), 3.40 (m, 1 H), 5.97 (t, 1 H, *J* = 1.2 Hz), 7.07 (br d, 1 H, *J* = 8.2 Hz), 7.09 (br s, 1 H), 7.57 (br d, 1 H, *J* = 8.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.22, 200.84, 180.03, 142.56, 138.97, 134.29, 133.16, 131.63, 129.03, 126.45, 44.28, 42.99, 40.28, 21.64, 21.39, 17.48.

EIMS: *m*/*z* (%) = 242 (M^+, 89), 227 (23), 133 (100), 109 (78).

Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.62; H, 7.68.

7d

IR (neat): 2976, 2908, 1726, 1690, 1378, 816, 724 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.99 (s, 3 H), 2.36 (s, 3 H), 2.42 (s, 3 H), 2.43 (dd, 1 H, *J* = 18.0, 4.9 Hz), 2.55 (m, 2 H), 2.62 (dd, 1 H, *J* = 18.0, 10.1 Hz), 3.91 (m, 1 H), 5.94 (s, 1 H), 7.07 (br d, 1 H, *J* = 7.9 Hz), 7.09 (br s, 1 H), 7.48 (br d, 1 H, *J* = 7.9 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.28, 197.59, 160.35, 142.21, 138.87, 133.58, 133.05, 128.20, 126.46, 122.35, 44.69, 39.05, 33.13, 24.33, 21.36, 21.14.

HRMS(FAB): *m*/*z* calcd for $C_{16}H_{19}O_2$ [MH^+]: 243.1385, found 243.1387.

(*RS*)-4-(2-Ethylthio-2-oxoethyl)-3-methylcyclopent-2-enone (6e)

Synthesized according to TP-1 by reaction of **1a** with **5e**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **6e** in 33% yield as a colorless oil.

IR (neat): 2968, 2924, 1680, 1618, 1438, 1410, 1184, 1044, 1024, 986 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, 3 H, *J* = 7.3 Hz), 2.21 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.11 (s, 3 H), 2.52 (dd, 1 H, *J* = 15.6, 9.8 Hz), 2.65 (dd, 1 H, *J* = 18.9, 6.7 Hz), 2.91 (q, 2 H, *J* = 7.3 Hz), 2.96 (dd, 1 H, *J* = 15.6, 4.6 Hz), 3.27 (m, 1 H), 5.97 (t, 1 H, *J* = 1.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.56, 197.32, 178.83, 131.85, 46.59, 41.71, 41.05, 23.62, 17.32, 14.67.

EIMS: *m*/*z* (%) = 198 (M^+, 23), 137 (30), 109 (100), 95 (38).

Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.58; H, 7.12. Found: C, 60.36; H, 7.39.

(*E*)-1-[(4*S*)-2,2-Dimethyl-1,3-dioxolane-4-yl]-4-phenylbut-2-ene-1,4-dione (8)

Methyl (*S*)-(–)-2,2-dimethyl-1,3-dioxolane-4-carboxylate was converted into dimethyl 2-[(*S*)-2,2-dimethyl-1,3-dioxolane-4-yl]-2-oxoethylphosphonate in 87% yield by treatment with dimethyl methylphosphonate in the presence of BuLi according to the procedure reported by Yamanoi et al. To a stirred suspension of LiCl (27 mg, 0.63 mmol) in anhyd MeCN (6 mL) was added a solution of this phosphonate (159 mg, 0.63 mmol) in MeCN (1 mL) followed by the addition of *i*-Pr_2NEt (68 mg, 0.53 mmol) at r.t. The mixture was cooled to –30 °C and treated with a solution of phenylglyoxal (80 mg, 0.53 mmol) in MeCN (1 mL). After stirring for 10 min at r.t., the mixture poured into brine and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc, 20:1) to give **8** (133 mg, 81%) as a yellow solid; mp 45–47 °C (hexane–EtOAc); $[\alpha]_D^{25}$ –41.3 (*c* = 1.17, $CDCl_3$)

IR (Nujol): 1698, 1662, 1330, 1294, 1264, 1060, 690 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.44 (s, 3 H), 1.49 (s, 3 H), 4.15 (dd, 1 H, *J* = 8.9, 5.2 Hz), 4.26 (dd, 1 H, *J* = 8.9, 7.6 Hz), 4.68 (dd, 1 H, *J* = 7.6, 5.2 Hz), 7.52 (dd, 1 H, *J* = 8.2, 7.3 Hz), 7.53 (br d, 1 H, *J* = 15.6 Hz), 7.63 (tt, 1 H, *J* = 7.3, 1.2 Hz), 7.90 (br d, 1 H, *J* = 15.6 Hz), 8.01 (dd, 2 H, *J* = 8.2, 1.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.93, 189.81, 136.69, 135.26, 133.91, 133.46, 128.89, 128.85, 111.44, 79.99, 66.38, 26.03, 25.11.

EIMS: *m*/*z* (%) = 245 (M^+ – Me, 8), 159 (87), 105 (36), 101 (100), 77 (51).

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 68.97; H, 6.50.

(4*S*)-3-[(4*R*)-2,2-Dimethyl-1,3-dioxolane-4-yl]-4-(2-oxo-2-phenylethyl)cyclopent-2-enone (9)

Synthesized according to TP-1 by reaction of **1a** with **8**. The crude product was purified by flash chromatography (hexane–EtOAc, 5:1) to give **9** in 37% yield as a colorless solid, which was estimated to have 87% de on the basis of the vinyl proton signals in the ^{1}H NMR spectra. Recrystallization of the solid afforded **9** in a single diastereomeric form. The ee of the the cyclopentenone was determined to be 96% (HPLC conditions: Daisel Chiralcel OD-H, 45 × 250 mm, λ = 254 nm, hexane–propan-2-ol, 8:2, t_{major} = 37.1 min, t_{minor} = 34.2 min); mp 103–104 °C (hexane–EtOAc); $[\alpha]_D^{21}$ –3.6 (*c* = 0.36, $CDCl_3$).

IR (Nujol): 1676, 1616, 1374, 760, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (s, 3 H), 1.45 (s, 3 H), 2.14 (dd, 1 H, *J* = 18.9, 2.1 Hz), 2.88 (dd, 1 H, *J* = 19.2, 6.7 Hz), 3.08 (dd, 1 H, *J* = 17.7, 8.2 Hz), 3.46 (dd, 1 H, *J* = 17.7, 5.2 Hz), 3.55 (m, 1 H), 3.84 (dd, 1 H, *J* = 8.2, 6.4 Hz), 4.36 (dd, 1 H, *J* = 8.2, 7.0 Hz), 4.84 (dd, 1 H, *J* = 7.0, 6.4 Hz), 6.27 (t, 1 H, *J* = 1.5 Hz), 7.49 (br t, 2 H, *J* = 8.2 Hz), 7.60 (br t, 1 H, *J* = 8.2 Hz), 7.94 (br d, 2 H, *J* = 8.2 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.06, 197.53, 179.85, 136.26, 133.71, 129.84, 128.81, 127.98, 110.41, 74.17, 68.45, 43.24, 42.49, 36.28, 26.18, 25.33.

EIMS: *m*/*z* (%) = 285 (M^+ -Me, 14), 270 (19), 226 (15), 105 (100).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.93; H, 6.46.

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