Synthesis of 3-(Phosphorylmethyl)cycloalkenones by Forced Conjugate Addition of α-Phosphonate Carbanions to Cyclic Enones

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Abstract: Cycloalkenones were found to react with α-lithiated diethyl (phenylselanyl)methylphosphonate preferentially or exclusively at the carbonyl group giving 1,2-adducts. When complexes of cycloalkenones with aluminum tris(2,6-diphenylphenoxide) were used for this reaction, regioselective 1,4-addition was observed. Upon oxidation the thus-formed 1,4-adducts gave the corresponding 3-(phosphorylmethyl)cycloalk-2-enones. An alternative approach to the latter compounds involved 1,4-addition of diethyl lithiomethylphosphonate to 2-sulfinylcycloalk-2-enones followed by sulfoxide elimination.

Key words: conjugate addition, cycloalkenones, α-phosphonate carbanions, 3-phosphorylcycloalk-2-enones

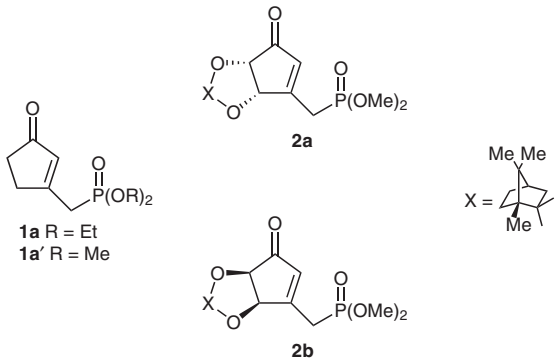
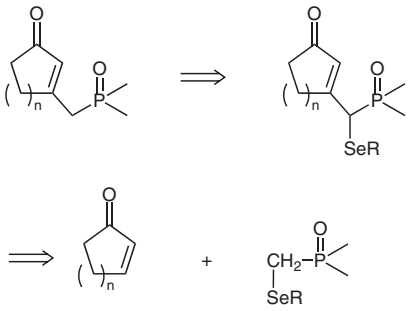


Figure 1

Cycloalkenones are valuable intermediates in a variety of synthetic transformations and useful building blocks in the synthesis of biologically active compounds. Among them, cyclopentenones are particularly interesting due to the presence of this structural motif in a wide range of important natural products, such as jasmonoids, cyclopentanoid antibiotics, and prostanoids. As part of our broad program on the application of phosphorus and sulfur reagents in organic synthesis,[1] we have also been engaged in the invention and development of general methods for the synthesis of functionalized cyclopentenones and cyclopentanones.[2] These endeavors resulted in the elaboration of new and efficient routes to racemic rosaprostol[3] and enantiomeric prostaglandin B_1 methyl esters[4] starting from 3-[(dimethoxyphosphoryl)methyl]cyclopent-2-enone (**1a′**) as a key intermediate and to both enantiomers of isoterrein[5] and neplanocin A[6] from the diastereomeric camphor protected 3-[(dimethoxyphosphoryl)methyl]-4,5-dihydroxycyclopent-2-enones **2a** and **2b**.

The starting cyclopentenones **1** and **2** (Figure 1) have been obtained by general methods for the synthesis of 3-(phosphorylmethyl)cycloalk-2-enones developed in our laboratory involving the reaction of dicarboxylic acid esters with α-phosphonate carbanions and subsequent intramolecular Horner reaction of bis(β-oxophosphonates), which were formed in the initial step.[7] This method complemented two other approaches to 3-(phosphorylmethyl)cycloalk-2-enones. The first employed oxidation of cyclic allylic alcohols obtained in the carbonyl addition of α-phosphonate anions to cycloalkenones,[8] while the second was based on substitution of the β-methoxy group in cyclic enones by α-lithiated alkylphosphonates.[9]

To gain further flexibility in the preparation of 3-(phosphorylmethyl)-substituted cycloalk-2-enones **1** and to overcome some limitations in the existing methods, we decided to devise a new strategy for the synthesis of these systems. According to our simple retrosynthetic analysis shown in Scheme 1, it should involve two steps: (a) conjugate addition of a phosphorylmethyl selenide to a cyclic enone and (b) oxidative selenide elimination.



Scheme 1

To realize our goal, the first reaction in the above scheme is crucial. However, addition of α-phosphonate carbanions to enones is a complex reaction that can follow different mechanistic pathways i.e. 1,2-addition, 1,4-addition, or addition–elimination, and the reaction outcome depends on the nature of α-phosphonate carbanion as well as on the substitution pattern of the enone.[9,10] Therefore, we initially examined the regioselectivity of the reaction

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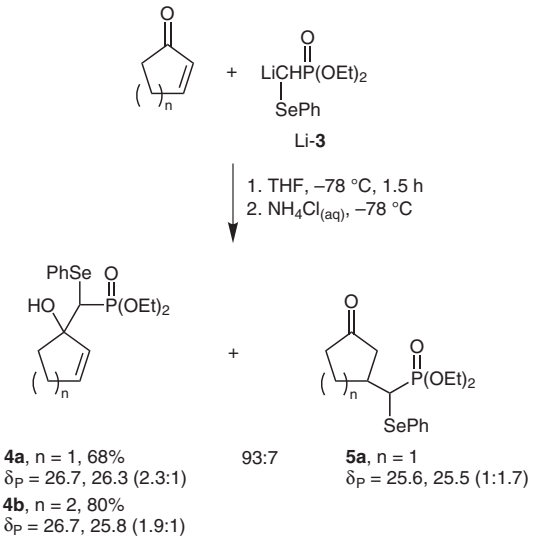
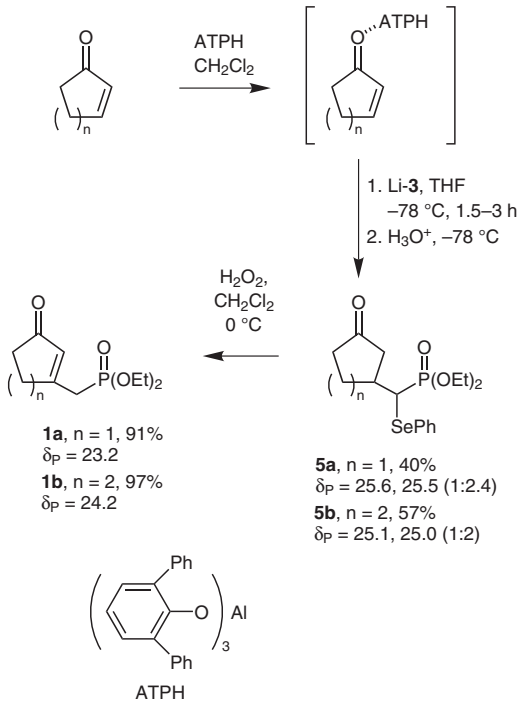
between cyclic enones and the lithium derivative of diethyl (phenylselanyl)methylphosphonate (**3**)[11] as a nucleophilic reaction partner. The addition of Li-**3** to cyclopent-2-enone afforded two adducts **4a** and **5a** in a 93:7 ratio; each of them is a mixture of two diastereomers. The major adduct **4a**, isolated in 68% yield, resulted from the addition of Li-**3** to the carbonyl group (1,2-addition) whereas **5a** was formed according to the 1,4-addition pattern. When the reaction was carried out in a mixture of tetrahydrofuran and hexamethylphosphoramide, a solvent preferring 1,4-addition, the **4a** to **5a** ratio was 69:31. With cyclohex-2-enone, the Li-**3** reacted exclusively in a 1,2-fashion affording the product **4b** (mixture of two diastereomers) in 80% yield (Scheme 2).



Scheme 2

To suppress the undesired 1,2-addition of the α-phosphonate carbanion derived from **3** to cycloalkenones, we took advantage of the fact that the reactivity of the carbonyl group in α,β-unsaturated carbonyl compounds can effectively be diminished by complexation with bulky aluminum reagents and that these complexes react with nucleophiles with 1,4-selectivity.[12]

Among many of such bulky Lewis acids designed by Yamamoto for selective organic synthesis,[12] aluminum tris(2,6-diphenylphenoxide) (ATPH) was selected for our study. It was gratifying to find that the addition reaction of Li-**3** to the freshly prepared complex of cyclopentenone and aluminum tris(2,6-diphenylphenoxide) resulted in exclusive formation of the 1,4-adduct **5a** (two diastereomers) in 60% yield as determined by ^{31}P NMR. Purification by column chromatography gave pure **5a** in 40% yield. A similar procedure with cyclohex-2-enone was more efficient; the 1,4-adduct **5b** was formed as the sole product in 80% yield (^{31}P NMR assay) and obtained in a pure state by column chromatography in 57% yield. Oxidation of compounds **5a** and **5b** with hydrogen peroxide afforded almost quantitatively the expected 3-(phosphorylmethyl)cycloalkenones **1a** and **1b**; spectroscopic data of **1a** and **1b** were consistent with those reported in the literature[7,9] (Scheme 3). There is no doubt that the selenoxides formed upon oxidation of **5a** and **5b** undergo spontaneous elimination of benzeneselenenic acid[13] and the 3-exocyclic C=C bond in the elimination products is transformed into the thermodynamically more stable endocyclic α,β-unsaturated system of **1**.



Scheme 3

It should be emphasized that, in addition to a simple access to **1**, another advantage of the present strategy is that both synthetic steps, i.e. conjugate addition and oxidation, may be performed as a one-pot reaction leading to higher yields of the final products **1a** and **1b** (55% and 78%, respectively).

In our further quest to develop a convenient approach to the synthesis of the title compounds, we were attracted by a series of papers by Posner et al.,[14] who demonstrated using many examples that 2-sulfinyl-substituted cycloalk-2-enones add organometallic reagents in a 1,4-fashion. In this case, the conjugate addition to cycloalkenone sulfoxides is forced by the presence of a sulfinyl substituent in position 2. On the other hand, it is well known that alkyl sulfoxides bearing a hydrogen at the β-carbon atom undergo thermal decomposition to form unsaturated compounds.[15] Having this in mind, we decided to investigate the reaction between easily available 2-(phenylsulfinyl)cyclopent-2-enone[16] with diethyl lithiomethylphosphonate as a key step in the synthesis of the title compounds. In fact, treatment of the above cyclopentenone sulfoxide with Li-**3** at –78 °C in tetrahydrofuran gave the expected 1,4-adduct **6a**, which was obtained in 40% yield after purification by column chromatography. The lower yield of **6a** is due to slow elimination of benzene-

sulfenic acid that takes place at room temperature. This elimination was preparatively carried out by heating **6a** in a benzene solution at 40 °C for two hours and the desired cyclopentenone **1a** was obtained in 80% yield (Scheme 4).

A similar reaction of lithiomethylphosphonate with 2-(phenylsulfinyl)cyclohex-2-enone[17] requires some additional comments (Scheme 4). As expected, it afforded the 1,4-adduct **6b** as a mixture of two diastereomers in a 2.5:1. However, the crude product was already contaminated with 3-(phosphorylmethyl)cyclohexenone **1b** (**6b**/**1b** 7:1). Attempts to purify **6b** by column chromatography led to a mixture of both compounds in a 2:1 ratio. Therefore, the conjugate addition and benzenesulfenic acid elimination were performed as a one-pot reaction, which gave **1b** in 87% yield.

In an extension to the present work, 2-alkyl-substituted cyclopentenones **7** and **8** were also synthesized starting from the key intermediate **6a**. In this case, alkylation of the oxo sulfoxide anion generated from **6a** with potassium *tert*-butoxide in 1,3-dimethyl-2,3,4,5-tetrahydropyrimidin-2(1*H*)-one (DMPU) and elimination of benzenesulfenic acid under the conditions described above were performed in a one-pot procedure giving disubstituted cyclopentenones **7** and **8** in 60% and 48% yield, respectively. In this way we could overcome the problems connected with the poor C2-alkylation of the anion derived from 3-(phosphorylmethyl)cyclopent-2-enone **1a**, especially when reactive and long-chain aliphatic alkyl halides and sulfonates were used.

In conclusion, two simple synthetic routes were developed to access 3-(phosphorylmethyl)cycloalkenones. The key step in both procedures was the forced, conjugate addition of the appropriate α-phosphonate carbanion to a cycloalkenone or 2-sulfinylcycloalk-2-enone followed by oxidative elimination of selenide or sulfoxide. Facile accessibility of the starting alkenones as well as one-pot procedures make this method very attractive for the design and synthesis of functionalized biologically active cycloalkenones.

Melting and boiling points were uncorrected. THF was distilled over K/benzophenone, and benzene was distilled over Na wire, both immediately before use. CH_2Cl_2 was distilled over P_2O_5 and stored over anhyd Na_2CO_3. Reactions with organolithium reagents were carried out under dry argon. Column chromatography was performed using Merck $60F_{254}$ silica gel (70–230 mesh), and flash chromatography used Merck $60F_{254}$ silica gel (320–400 mesh). Reaction mixtures were analyzed by TLC using Merck $60F_{254}$ TLC plates. NMR spectra were recorded with Bruker AC 200 instrument at 200 MHz for ^1H, 80 MHz for ^{31}P, and 50 MHz for ^{13}C with $CDCl_3$ as solvent, unless noted otherwise. ^1H and ^{13}C chemical shifts are reported relative to TMS as an external standard. ^{31}P NMR downfield chemical shifts are expressed with a positive sign relative to an external standard of 85% H_3PO_4. HRMS were recorded on a Finnigan MAT 95 apparatus.

2-(Phenylsulfinyl)cyclohex-2-enone

Prepared by a literature procedure.[16]

White solid; yield: 9.5 g (87%); mp 56–57 °C (Et_2O).

^1H NMR (200 MHz, $CDCl_3$): δ = 1.82–2.13 (m, 2 H), 2.18–2.69 (m, 4 H), 7.31–7.47 (m, 3 H), 7.67–7.75 (m, 3 H).

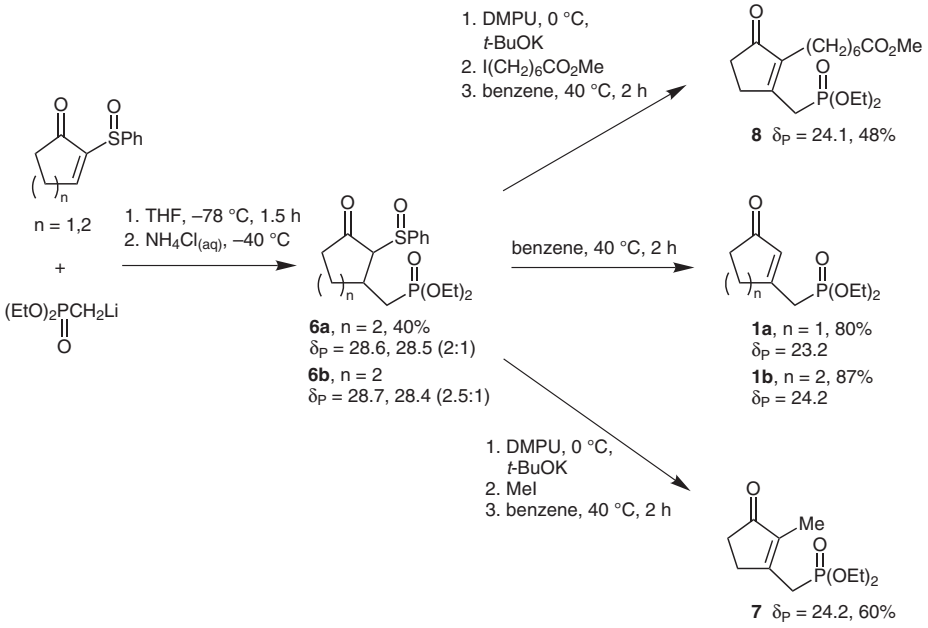
^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.02, 26.13, 38.29, 124.53, 125.18, 128.91, 131.09, 143.95 (d, *J* = 21.2 Hz), 149.18, 194.59.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{12}H_{12}SO_2$: 220.05540; found: 220.05580.

Anal. Calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found: C, 65.19; H, 5.75.

Addition of Diethyl (Phenylselanyl)methylphosphonate (3) to Cycloalkenones; General Procedure

A soln of 2.4 M BuLi in hexane (1.3 mol equiv) in THF (3 mL per mmol of **3**) was cooled to –78 °C. To this soln was added dropwise with stirring a soln of diethyl (phenylselanyl)methylphosphonate[11]



Scheme 4

(**3**, 1 mol equiv, typically 3 mmol) in THF (1 mL per 1 mmol of **3**) and the resulting soln was stirred at –78 °C for 0.5 h. Then, a soln of enone (1.3 mol equiv) in THF (1 mL per 1 mmol of enone) was added, and the mixture was stirred for 1.5 h. Sat. aq NH_4Cl soln (10 mL) was added at –78 °C and the mixture was allowed to warm to r.t. The mixture was extracted with Et_2O (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. The crude adducts were purified by column chromatography (hexane–acetone, 2:1). The major adducts **4a** (68% yield) and **4b** (80% yield) were obtained in an analytically pure state as mixtures of two stereoisomers and characterized.

Diethyl (1-Hydroxycyclopent-2-enyl)(phenylselanyl)methylphosphonate (4a)
Colorless oil; yield: 0.79 g (68%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.1 Hz, 6 H), 2.10 (m, 2 H), 2.42 (m, 2 H), 3.35 (d, *J* = 14.8 Hz, 1 H), 4.02–4.25 (m, 4 H), 4.51 (br s, 1 H), 5.62 (m, 1 H, minor isomer), 5.94 (m, 1 H, major isomer), 7.25 (m, 3 H), 7.55 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.4 (d, *J* = 5.8 Hz), 31.1, 31.3, 39.8 (d, *J* = 10.1 Hz), 48.5 (d, *J* = 138.2 Hz), 49.78 (d, *J* = 139.5 Hz), 61.8 (d, *J* = 6.3 Hz), 61.8 (d, *J* = 6.3 Hz), 83.3 (d, *J* = 5.2 Hz), 126.9, 127.5, 128.8, 129.3, 130.2, 133.5, 136.2 (d, *J* = 9.7 Hz), 152.1.

^{31}P NMR (80 MHz, $CDCl_3$): δ = 26.7, 26.3 (2.3:1).

Anal. Calcd for $C_{16}H_{23}O_4PSe$: C, 49.37; H, 5.96; P, 7.96. Found: C, 49.20; H, 5.68; P, 7.72.

Diethyl (1-Hydroxycyclohex-2-enyl)(phenylselanyl)methylphosphonate (4b)
Colorless oil; yield: 0.96 g (80%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.33 (m, 6 H), 1.55–2.1 (m, 6 H), 3.21 (d, *J* = 15.5 Hz, 1 H), 4.05–4.28 (m, 4 H), 4.45 (br s, 1 H), 5.45 (m, 1 H, minor isomer) and 5.90 (m, 1 H, major isomer), 7.25 (m, 3 H), 7.57 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.7 (d, *J* = 4.7 Hz), 17.9 (d, *J* = 9.4 Hz), 23.4, 24.3 (d, *J* = 10.6 Hz), 32.9, 34.5 (d, *J* = 5.9 Hz), 49.1 (d, *J* = 138.1 Hz), 50.9 (d, *J* = 139.9 Hz), 62.5 (2q, *J* = 7.1 Hz, *J* = 19.2 Hz), 70.3, 71.6, 127.0, 127.5, 128.5, 129.1, 129.3, 130.4 (d, *J* = 5.4 Hz), 130.7, 131.0, 132.2, 133.6.

^{31}P NMR (80 MHz, $CDCl_3$): δ = 26.7, 25.8 (1.9:1).

Anal. Calcd for $C_{17}H_{25}O_4PSe$: C, 50.63; H, 6.25; P, 7.68. Found: C, 50.38; H, 6.42; P, 7.55.

Addition of Diethyl (Phenylselanyl)methylphosphonate (3) to Cycloalkenone–Aluminum Tris(2,6-diphenylphenoxide) Complexes; General Procedure
A soln of 2 M Me_3Al in hexane (0.75 mL, 1.5 mmol) was added dropwise to magnetically stirred soln of 2.6-diphenylphenol (1.1 g, 4.5 mmol) in CH_2Cl_2 (10 mL) at r.t. and the soln was stirred for 0.5 h to furnish aluminum tris(2,6-diphenylphenoxide). In the next step, this soln was cooled to –78 °C and cycloalkenone (1 mmol) was added at this temperature. To a soln of the complex obtained was added a soln of Li-**3** (2 mmol) [prepared by treatment of diethyl (phenylselanyl)methylphosphonate (**3**, 0.643 g, 2.1 mmol) dissolved in THF (10 mL) with 2 M BuLi in hexane (1 mL, 2 mmol) at –78 °C]. The whole mixture was stirred at –78 °C for 2 h and allowed to warm to r.t. Then, the mixture was quenched with 10% aq HCl (15 mL). The aqueous phase was extracted with Et_2O (5 × 10 mL) and the combined organic phases were dried ($MgSO_4$) and evaporated under reduced pressure. The crude products **5a** and **5b** formed as mixtures of two diastereomers were purified by column chromatography (silica gel, hexane–acetone, 2:1) and characterized.

3-[(Diethoxyphosphoryl)(phenylselanyl)methyl]cyclopentanone (5a)
Colorless oil; yield: 0.16 g (40%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (m, 6 H), 1.57–2.52 (m, 6 H), 2.64–2.86 (m, 1 H), 3.12 (dd, *J* = 17 Hz, *J* = 5.1 Hz, 1 H, minor isomer), 3.16 (dd, *J* = 17 Hz, *J* = 4.4 Hz, 1 H, major isomer), 4.04–4.26 (m, 4 H), 7.24 (m, 3 H), 7.58 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.5 (d, *J* = 5.7 Hz), 28.1, 28.3, 37.6, 38.4, 43.4 (d, *J* = 9.2 Hz), 45.0 (d, *J* = 149.6 Hz), 62.8 (d, *J* = 7.2 Hz), 63.1 (d, *J* = 7.2 Hz), 128.1, 129.0, 133.9, 208.2.

^{31}P NMR (80 MHz, $CDCl_3$): δ = 25.6, 25.5 (1:2.4).

MS (EI, 70 eV): *m*/*z* (%) = 390 (100) $[M + H]^+$, 308 (28), 233 (22), 157 (19).

Anal. Calcd for $C_{16}H_{23}O_4PSe$: C, 49.37; H, 5.96. Found: C, 49.25; H, 5.72.

3-[(Diethoxyphosphoryl)(phenylselanyl)methyl]cyclohexanone (5b)
Colorless oil; yield: 0.23 g (57%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.0 Hz, 3 H), 1.32 (t, *J* = 7.0 Hz, 3 H), 1.65 (m, 2 H), 1.86–2.20 (m, 2 H), 2.25–2.85 (m, 5 H), 3.0 (dd, *J* = 2.5 Hz, *J* = 18.2 Hz, 1 H, minor isomer), 3.17 (dd, *J* = 2.1 Hz, *J* = 18.2 Hz, 1 H, major isomer), 4.07–4.27 (m, 4 H), 7.26 (m, 3 H), 7.60 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.25 (d, *J* = 5.8 Hz), 24.4, 29.6, 39.5, 40.7 (d, *J* = 6.5 Hz), 46.7 (d, *J* = 143.5 Hz), 48.7, 63.2, 127.9, 129.2, 130.1, 133.6, 210.3.

^{31}P NMR (80 MHz, $CDCl_3$): δ = 25.09, 24.97 (1:2).

MS (EI, 70 eV): *m*/*z* (%) = 404 (32) $[M + H]^+$, 403 (100) $[M]^+$, 308 (66), 247 (38), 157 (35).

Anal. Calcd for $C_{17}H_{25}O_4PSe$: C, 50.63; H, 6.25. Found: C, 50.56; H, 6.51.

3-[(Diethoxyphosphoryl)methyl]cyclopent-2-enone (1a);[7,9] Typical Procedure
To a soln of selenide **5a** (0.389 g, 1 mmol) in CH_2Cl_2 (5 mL) was added 30% aq H_2O_2 (0.125 mL, 1.1 mmol) at 0 °C and the mixture was stirred vigorously for 2 h. Then, H_2O (5 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), and evaporated. The crude product was purified by column chromatography (silica gel, hexane–acetone, 2:1) to give **1a** as a colorless oil; yield: 0.21 g (91%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 6 H), 2.40–2.45 (m, 2 H), 2.70–2.76 (m, 2 H), 3.0 (d, *J* = 23.5 Hz, 2 H), 4.1 (dq, *J* = 7.1 Hz, *J* = 11.0 Hz, 4 H), 6.1 (m, 1 H).

^{31}P NMR (80 MHz, $CDCl_3$): δ = 23.2.

3-[(Diethoxyphosphoryl)methyl]cyclohex-2-enone (1b)[7,9]
Oxidation of selenide **5b** (0.40 g, 1 mmol) according to the procedure described above gave **1b** as a colorless oil; yield: 0.24 g (97%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.1 Hz, 6 H), 1.98 (q, *J* = 6.1 Hz, 2 H), 2.34–2.48 (m, 4 H), 2.80 (d, *J* = 23.5 Hz, 2 H), 4.1 (dq, *J* = 7.1 Hz, *J* = 11.2 Hz, 4 H), 5.93 (br d, *J* = 5.6 Hz, 1 H).

^{31}P NMR (80 MHz, $CDCl_3$): δ = 24.2.

3-[(Diethoxyphosphoryl)methyl]-2-(phenylsulfinyl)cyclopentanone (6a)
A 2.5 M soln of BuLi in hexane (1.58 mL, 3.96 mmol) was diluted with THF (10 mL). To this soln, cooled to –78 °C, was added dropwise a soln of diethyl methylphosphonate (0.548 g, 3.6 mmol) in THF (4 mL) and stirring was continued for 0.5 h. A soln of 2-(phenylsulfinyl)cyclopentenone[16] (0.816 g, 3.96 mmol) in THF (4 mL)

was then added and the resulting mixture was stirred at –78 °C for 1.5 h. It was then warmed to –40 °C and sat. aq NH_4Cl (10 mL) was added. The aqueous phase was extracted with Et_2O (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography (hexane–acetone, 2:1) to give the pure **6a** (mixture of two diastereomers) as a colorless liquid; yield: 0.51 g (40%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.34 (m, 6 H), 1.54–2.52 (m, 6 H), 3.34 (br d, *J* = 8.3 Hz, 1 H, minor isomer), 3.67 (br d, *J* = 8.3 Hz, 1 H, major isomer), 3.86–4.02 (m, 1 H), 4.1–4.18 (m, 4 H), 7.48–7.64 (m, 5 H).

^{31}P NMR (80 MHz, $CDCl_3$): δ = 28.6, 28.5 (2:1).

FAB-MS: *m*/*z* (%) = 359 (100) $[M + H]^+$.

3-[(Diethoxyphosphoryl)methyl]cyclopent-2-enone (1a)[7,9]

Cyclopentanone sulfoxide **6a** (0.25 g, 0.7 mmol) was dissolved in anhyd benzene (5 mL) and the soln was stirred at 40 °C for 2 h. Then, benzene was evaporated and the residue was chromatographed (hexane–acetone, 2:1) to give **1a** as a colorless liquid; yield: 0.13 g (80%).

3-[(Diethoxyphosphoryl)methyl]cyclohex-2-enone (1b)[7,9]

A 2.4 M soln of BuLi in hexane (2.1 mL, 4.95 mmol) in THF (10 mL) was cooled to – 78 °C and diethyl methylphosphonate (0.82 g, 5.4 mmol) in THF (5 mL) was added dropwise. The mixture was stirred at this temperature for 0.5 h and then a soln of 2-(phenylsulfinyl)cyclohex-2-enone (1.1 g, 4.95 mmol) in THF (8 mL) was added and the resulting mixture was stirred for 1.5 h. The reaction soln was warmed to –40 °C and treated with sat. aq NH_4Cl (15 mL). The aqueous phase was extracted with Et_2O (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography (hexane–acetone, 2:1) to give a colorless liquid consisting of the adduct **6b** {MS (CI): *m*/*z* = 373.3 $[M + H]^+$} and **1b** {MS (CI): *m*/*z* = 247.2 $[M + H]^+$}, in a 3:1 ratio.

The crude product was dissolved in anhyd benzene (15 mL) and the soln was stirred at 40 °C for 2 h. After evaporation of benzene the residue was purified by column chromatography (hexane–acetone, 2:1) to give **1b** as a colorless liquid; yield: 1.05 g (87%).

2-Alkyl-Substituted 3-(Phosphorylmethyl)cyclopent-2-enones 7 and 8; General Procedure

To a stirred soln of *t*-BuOK (1.2 equiv) in freshly distilled DMPU (2 mL per mmol) cooled to –10 °C was added a soln of **6a** (1 mol equiv) in DMPU (1 mL per mmol) and the resulting soln was stirred at –10 °C for 1 h. Then, alkyl iodide (1.8 equiv) was added and the mixture was stirred at 0 °C for 48 h. The mixture was quenched with 10% aq HCl (10 mL) and extracted with $CHCl_3$ (3 × 15 mL). The combined organic phases were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was dissolved in benzene (5 mL) and the resulting soln was stirred at 40 °C for 2 h. After evaporation of benzene, the crude product was purified by column chromatography (hexane–acetone, 2:1).

3-[(Diethoxyphosphoryl)methyl]-2-methylcyclopent-2-enone (7)[9]

Colorless oil; yield: 0.066 g (60%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 6 H), 1.73 (t, *J* = 2.1 Hz, 3 H), 2.16 (m, 2 H), 2.55 (m, 2 H), 2.96 (d, *J* = 23.9 Hz, 2 H), 4.10 (d, *J* = 7.1 Hz, *J* = 11.1 Hz, 4 H).

^{31}P NMR (80 MHz, $CDCl_3$): δ = 24.2.

Methyl 7-{2-[(Diethoxyphosphoryl)methyl]-5-oxocyclopent-1-enyl}heptanoate (8)[3]

Colorless oil; yield: 0.08 g (48%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.1 Hz, 6 H), 1.20–1.50 (m, 6 H), 1.50–1.75 (m, 4 H), 2.16 (m, 2 H), 2.29 (t, *J* = 27.3 Hz, 2 H), 2.60 (m, 2 H), 2.96 (d, *J* = 24.0 Hz, 2 H), 3.65 (s, 3 H), 4.12 (q, *J* = 7.1 Hz, 4 H).

^{31}P NMR (80 MHz, $CDCl_3$): δ = 24.1.

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(17) The starting cyclohexenyl sulfoxide was prepared by oxidation of the corresponding sulfide according to ref. 16. However, our product was crystalline and not an oil as reported. For full spectroscopic and analytical data, see the experimental part.