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Preparation of Functionalized Cyclic Enol Phosphates by Halogen−Magnesium Exchange and Directed Deprotonation Reactions

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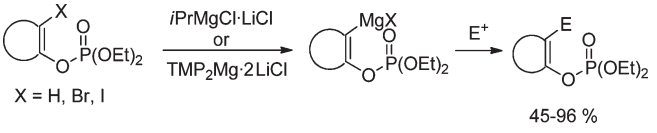
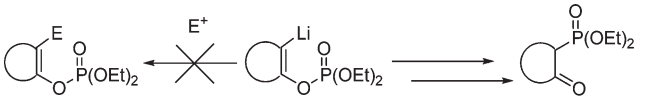


Cyclic enol phosphates were magnesiated by a halogen/magnesium exchange reaction or deprotonation using TMP-derived magnesium amide bases. The resulting magnesium reagents react readily with a wide range of electrophiles like allyl bromides and acid chlorides or can be used in Pd-catalyzed cross-coupling reactions. Several optically pure enol phosphates were prepared starting from readily available D-(+)-camphor derivatives.

1. Introduction

Enol phosphates have found applications as insecticides[1] and phosphatase inactivators.[2] Additionally, they can be used as versatile intermediates for the regioselective preparation of substituted double bonds. Several methods have been developed allowing efficient transition-metal-catalyzed cross-coupling reactions with these electrophiles.[3] In fact, enol phosphates are a useful synthetic alternative to the corresponding triflates since they are generally less expensive and more stable. Their preparation is conveniently performed starting either from enolizable ketones or α-halo carbonyl compounds.[1] The synthesis of lithiated enol phosphates of type 1 via halogen−lithium exchange or deprotonation using LDA has already been described by Wiemer.[4] However, these lithium reagents do not react with electrophiles (E^+) but rearrange to the corresponding β-keto phosphonates **2** in good yields (Scheme 1).

SCHEME 1. Rearrangement of Lithiated Enol Phosphates to the Corresponding β-Keto Phosphonate



As organomagnesium reagents are less reactive than organolithium reagents, it is expected that the corresponding magnesium reagents are more stable. In recent years, we have found that LiCl greatly facilitates the preparation of organomagnesium,[5] organozinc,[6] organoindium,[7] and other organometallic[8] reagents. Thus, *i*-PrMgCl·LiCl (**3**)[5a] allows the preparation of various alkenylmagnesium reagents starting from the corresponding alkenyl iodides.[9] Herein, we wish to report that

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(2) (a) Stowell, J. K.; Widlanski, T. S. *J. Am. Chem. Soc.* **1994**, *116*, 789. (b) Widlanski, T. S. US Patent 5,714,361.
(3) (a) Takai, K.; Sato, M.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 108. (b) Cahiez, G.; Gager, O.; Habiak, V. *Synthesis* **2008**, *16*, 2636. (c) Miller, J. A. *Tetrahedron Lett.* **2002**, *43*, 7111. (d) Larsen, U. S.; Martiny, L.; Begtrup, M. *Tetrahedron Lett.* **2005**, *46*, 4261.
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(5) (a) Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3333. (b) Krasovskiy, A.; Straub, B. F.; Knochel, P. *Angew. Chem., Int. Ed.* **2005**, *45*, 159. (c) Piller, F. M.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 6802. (d) Piller, F. M.; Metzger, A.; Schade, M. A.; Haag, B. A.; Gavryushin, A.; Knochel, P. *Chem.—Eur. J.* **2009**, *15*, 7192. (e) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 2958. (f) Clososki, G. C.; Rohbogner, C. J.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7681. (g) Rohbogner, C. J.; Clososki, G. C.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 1503. (h) Rohbogner, C. J.; Wirth, S.; Knochel, P. *Org. Lett.* **2010**, *12*, 1984.
(6) (a) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 6040. (b) Wunderlich, S. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7685.
(7) (a) Chen, Y.-H.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 7648. (b) Chen, Y.-H.; Sun, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 2236.
(8) Aluminum: (a) Wunderlich, S. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 1501. (b) Blümke, T. D.; Chen, Y.-H.; Knochel, P. *Nature Chem.* **2010**, *2*, 313. Manganese: (c) Wunderlich, S. H.; Kienle, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 7256. Iron: (d) Wunderlich, S. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 9717. (e) Wunderlich, S. H.; Knochel, P. *Chem.—Eur. J.* **2010**, *16*, 3304.
(9) (a) Ren, H.; Krasovskiy, A.; Knochel, P. *Org. Lett.* **2004**, *6*, 4215. (b) Ren, H.; Krasovskiy, A.; Knochel, P. *Chem. Commun.* **2005**, 543.

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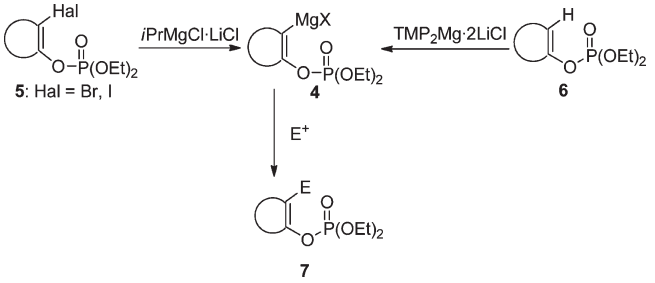
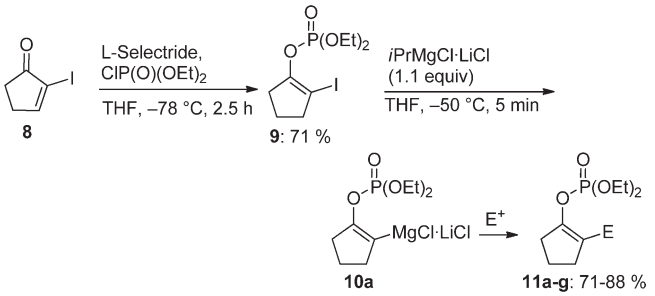
SCHEME 2. Strategy for the Functionalization of Enol Phosphates by Halogen/Magnesium Exchange or Deprotonation Reactions



SCHEME 3. Preparation and Reactions of the Magnesium Reagent 10a with Electrophiles



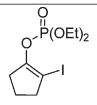
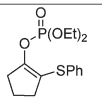
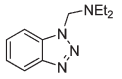
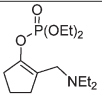
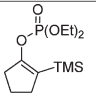
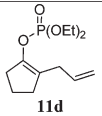
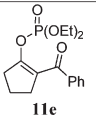
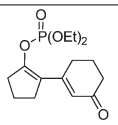
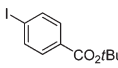
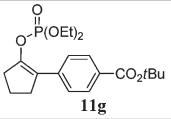
i-PrMgCl·LiCl (**3**) allows us to prepare magnesiated enol phosphates of type **4** starting from the corresponding bromides or iodides of type **5**. The presence of LiCl is essential since the use of *i*-PrMgCl does not lead to a convenient exchange reaction giving the Mg-species **4** at all. Furthermore, magnesium amide bases such as TMPMgCl·LiCl[5e] and TMP_2-Mg·2LiCl[5f–h] (TMP = 2,2,6,6-tetramethylpiperidyl) are able to directly metalate cycloalkenyl phosphates of type **6** providing an alternative preparation of enol phosphates of type **4**. After the addition of an electrophile (E^+), functionalized enol phosphates of type **7** can be obtained (Scheme 2).

2. Results and Discussion

Thus, starting from 2-iodocyclopent-2-enone (**8**), the 5-membered cyclic enol phosphate **9** was prepared by reduction with L-Selectride and quenching of the resulting enolate with diethyl chlorophosphate.[4b] The I/Mg-exchange reaction of **9** with *i*-PrMgCl·LiCl (**3**) proceeds smoothly and yields the alkenylmagnesium reagent **10a** within 5 min at −50 °C. Under these mild reaction conditions, no rearrangement to the β-keto phosphonate is observed. The magnesium reagent **10a** can then be reacted with various electrophiles and provides the corresponding 2-substituted cyclic enol phosphates **11a**−**g** in 71−88% yield (Scheme 3 and Table 1).

Thus, the magnesium reagent **10a** was reacted with $PhSO_2SPh$ to give the thioether **11a** in 83% yield (Table 1, entry 1). The treatment of the Grignard reagent **10a** with 1-(*N,N*-diethylamino)methylbenzotriazole[10] (−50 to 25 °C, 1 h) leads to the diethyl aminomethyl derivative **11b** in 82% yield (entry 2), while the reaction with TMS-CN (−50 to +25 °C, 3 h) affords the silylated product **11c** in 88% yield

TABLE 1. Products Obtained by the Reaction of 10a with Various Electrophiles

Entry	Substrate	Electrophile	Product	Yield [%][a]
1	 **9**	$PhSO_2SPh$	 **11a**	83
2	**9**		 **11b**	82
3	**9**	TMS-CN[b]	 **11c**	88
4	**9**		 **11d**	82[c]
5	**9**	PhCOCl	 **11e**	84[c]
6	**9**		 **11f**	71[c]
7	**9**		 **11g**	79[d]

[a]Yield of analytically pure product. [b]The use of TMSCl did not lead to the silylated compound. [c]Obtained after transmetalation with CuCN·2LiCl (20−100 mol %). [d]Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and $Pd(dba)_2$ (5 mol %) and tfp (10 mol %) catalyzed cross-coupling.

(entry 3). The transmetalation of the magnesium reagent **10a** with CuCN·2LiCl[11] (1.1 equiv, −20 °C, 30 min) provides an intermediate copper reagent which undergoes various Cu(I)-mediated reactions. Thus, when reacting this copper reagent with allyl bromide (25 °C, 1 h), the allylated enol phosphate **11d** is obtained in 82% yield (entry 4). Similarly, the reaction of this copper intermediate with benzoyl chloride (0 °C, 2 h) provides the expected ketone **11e** in 84% yield (entry 5). A 1,4-addition to 3-iodocyclohexenone also proceeds smoothly at 0 °C within 2 h, and the functionalized enol phosphate **11f** is obtained in 71% yield (entry 6). Additionally, a transmetalation with $ZnCl_2$ leads to a zinc reagent which undergoes a Pd-catalyzed Negishi cross-coupling reaction[12] by using $Pd(dba)_2$ (5 mol %) and tri(2-furyl)phosphine (tfp, 10 mol %)[13] as a catalytic

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(12) (a) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340. (b) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298. (c) Zeng, X.; Quian, M.; Hu, Q.; Negishi, E. *Angew. Chem., Int. Ed.* **2004**, *43*, 2259.

(13) (a) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *112*, 9585. (b) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905. (c) Klement, I.; Rottländer, M.; Tucker, C. E.; Majid, T. N.; Knochel, P.; Venegas, P.; Cahiez, G. *Tetrahedron* **1996**, *52*, 7201.

SCHEME 4. Preparation and Reactions of the Magnesium Reagent 10b with Electrophiles

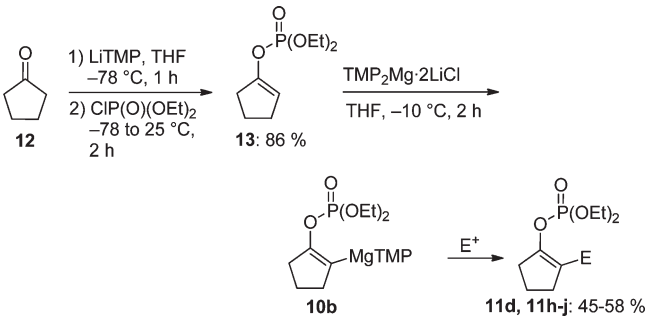


TABLE 2. Products Obtained by the Reaction of 10b with Various Electrophiles

Entry	Substrate	Electrophile	Product	Yield [%][a]
1	**13**	Br	**11d**	56[b]
2	**13**	Br	**11h**	45[b]
3	**13**	I, CO_2Et	**11i**	58[c]
4	**13**	CF_3, I	**11j**	58[c]

[a]Yield of analytically pure product. [b]Obtained after transmetalation with CuCN·2LiCl (20−100 mol %). [c]Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and $Pd(dba)_2$ (4 mol %) and tfp (12 mol %) catalyzed cross-coupling.

system. Thus, the reaction of the zinc reagent derived from **10a** with *tert*-butyl 4-iodobenzoate leads to the desired cross-coupling product **11g** in 79% yield (Table 1, entry 7).

Similar results were obtained by generating the magnesium reagent **10b** using the magnesium amide $TMP_2MgCl·2LiCl$.[5f−h] Deprotonation of cyclopentanone (**12**) with LiTMP (1.1 equiv, −78 °C, 1 h) and quenching the resulting enolate with diethyl chlorophosphate gives the enol phosphate **13** in 86% yield. The treatment of **13** with $TMP_2Mg·2LiCl$ (1.1 equiv) at −10 °C cleanly provides the corresponding magnesium reagent **10b** within 2 h due to the high coordinating effect of the phosphate group. The magnesium reagent **10b** readily undergoes Cu(I)-catalyzed allylation reactions[11] or palladium-catalyzed cross-coupling reactions[12] (after transmetalation to zinc) to give the products **11d**,**h**−**j** in 45−58% yield (Scheme 4 and Table 2).

This reaction sequence can also be extended to bicyclic systems. Starting from bicyclo[2.2.1]heptan-2-one (**14**), the bicyclic alkenyl phosphate **15** was prepared by deprotonation with LDA (1.1 equiv, −78 °C, 1.5 h) and quenching of the resulting enolate with diethyl chlorophosphate.[4a] The

SCHEME 5. Preparation and Reactions of the Magnesium Reagent 16 with Electrophiles

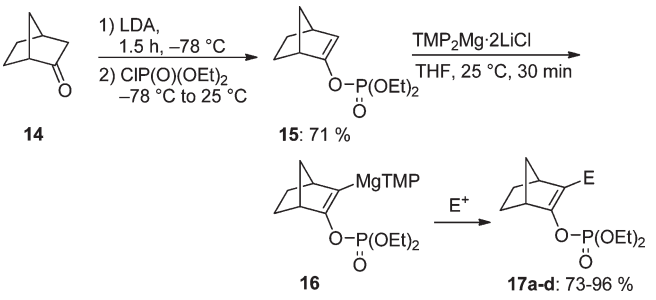


TABLE 3. Products Obtained by the Reaction of 16 with Various Electrophiles

Entry	Substrate	Electrophile	Product	Yield [%][a]
1	**15**	Br	**17a**	96[b]
2	**15**	PhCOCl	**17b**	75[b]
3	**15**	$PhSO_2SMe$	**17c**	73
4	**15**	I, CO_2Et	**17d**	75[c]

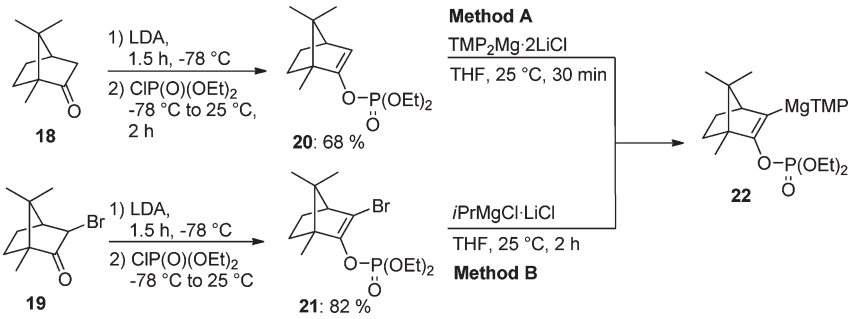
[a]Yield of analytically pure product. [b]Obtained after transmetalation with CuCN·2LiCl (20−100 mol %). [c]Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and $Pd(dba)_2$ (4 mol %) and tfp (12 mol %) catalyzed cross-coupling.

corresponding magnesium reagent **16** is then obtained by deprotonation of **15** with $TMP_2MgCl·2LiCl$ (1.1 equiv, 25 °C, 30 min). At this temperature, no rearrangement to the β-keto phosphonate is observed (see Scheme 1). After reaction of the Grignard reagent **16** with electrophiles such as allyl bromide, benzoyl chloride, *S*-methyl methanethiosulfonate, or ethyl 4-iodobenzoate in a Negishi cross-coupling[12] reaction (after transmetalation to zinc), the expected norbornene derivatives **17a**−**d** are given in 73−96% yield (Scheme 5 and Table 3).

Camphor derivatives are often used as chiral auxiliaries in stereoselective reactions.[14] Developing a functionalization of the camphor skeleton would therefore be a highly desirable process. Starting from D-(+)-camphor (**18**) or from commercially available D-(+)-bromocamphor (**19**), the enol phosphates **20** and **21** were prepared by deprotonation with LDA (1.1 equiv, −78 °C, 1.5 h) and quenching of the formed enolate with diethyl chlorophosphate in 68−82% yield. The corresponding magnesium reagent **22** was smoothly generated either by

(14) (a) Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969. (b) Chelucci, G. *Chem. Soc. Rev.* **2006**, *35*, 1230.

SCHEME 6. Preparation and Magnesiation of Enol Phosphates 20 and 21 via a Deprotonation Reaction (Method A) or a Br/Mg Exchange Reaction (Method B)



treatment of **20** with $TMP_2MgCl \cdot 2LiCl$[5f−h] (1.1 equiv, 25 °C, 30 min) or by the reaction of **21** with *i*-PrMgCl·LiCl[5a] (**3**: 1.1 equiv, 25 °C, 2 h, Scheme 6).

Interestingly, the bromo-enol phosphate **21** undergoes a fast Br/Mg-exchange reaction, therefore avoiding the use of the corresponding iodide. The magnesium reagent **22** has a similar reactivity, regardless of its preparation method. Thus, the Grignard reagent **22** generated by deprotonation with $TMP_2MgCl \cdot 2LiCl$ or Br/Mg exchange reacts with allylic bromides using a copper(I) catalysis,[11] giving the allylated products **23a**,**b** in 62−85% yield (Table 4, entries 1−3). Similarly, the cycloalkenylmagnesium reagent **22** undergoes acylation reactions with various acid chlorides using $CuCN \cdot 2LiCl$ (20 to 100 mol %),[11] and the expected ketones **23c**−**d** are provided in 67−82% yield (entries 4−6). Additionally, the use of ethyl cyanoformate allows the synthesis of the ester **23e** in 72% yield (entry 7). Thioethers are easily prepared by quenching the Grignard reagent **22** with thiosulfonates. Using $PhSO_2SMe$ or $PhSO_2SPh$ as electrophiles, the corresponding methyl and phenyl thioethers **23f** and **23g** were obtained in 65 and 73% yield (entries 8 and 9). After a transmetalation with $ZnCl_2$ (1.1 equiv), the resulting organozinc reagents undergo Negishi cross-coupling reactions.[12] Using $Pd(dba)_2$ (2 mol %) and tfp (4 mol %)[13] or $[Pd(PPh_3)_4]$ (4 mol %) as catalytic system, ethyl 4-iodobenzoate and 4-iodobenzonitrile are coupled to the camphor core in 58−74% yield (entries 10 and 11). Even the electron-rich 3-bromoanisole can be used in a cross-coupling reaction by using Buchwald's S-Phos ligand[15] (4 mol %) and $Pd(OAc)_2$ (2 mol %) yielding the arylated camphor derivative **23j** in 69% yield (entry 12).

An unexpected reaction pathway was observed when reacting Grignard reagent **22** with aldehydes. The intermediate magnesium alcoholates of type **24** undergo a spontaneous elimination to give the α,β-unsaturated ketones **25a**−**c**[16] with an excellent *E*/*Z* selecitivity as shown by NMR analysis (see the Supporting Information). Thus, after the reaction of the Grignard reagent **22** with 4-cyanobenzaldehyde, the ketone **25a** is obtained in 72% yield and >98:2 *E*/*Z*-selectivity. Similarly, 4-bromobenzaldehyde gives a similar elimination and yields the unsaturated ketone **25b** in 68% yield and 98:2 *E*/*Z* selectivity. Aliphatic aldehydes react as well, and after the treatment of cyclohexane carboxyaldehyde with the magnesium reagent **22**, the elimination product **25c** is obtained in 70% yield and 96:4 *E*/*Z* selectivity (Scheme 7).

3. Conclusion

In summary, we have reported different procedures allowing an α-magnesiation of cyclic enol phosphates by a halogen/magnesium exchange reaction using *i*-PrMgCl·LiCl or a deprotonation reaction using $TMP_2MgCl \cdot 2LiCl$. The resulting magnesium reagents react readily with various electrophiles like sulfur electrophiles, allyl bromides, and acid chlorides or can be used in Pd-catalyzed cross-coupling reactions. Several optically pure enol phosphates were prepared starting from readily available D-(+)-camphor derivatives. Furthermore, the reaction of a camphor derived magnesium reagent with aldehydes furnishes, after an elimination, the corresponding α,β-unsaturated enones. Extensions of this work are currently underway in our laboratories.

4. Experimental Section

General Considerations. All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^1H NMR (25 °C) and capillary GC. Column chromatographical purifications were performed using SiO_2 (0.040−0.063 mm, 230−400 mesh ASTM). All reagents were obtained from commercial sources. TmpH, liquid aldehydes, and acid chlorides were distilled prior to use. The completion of the metalation was checked by GC analysis of reaction aliquots quenched with a solution of 3 drops of $CuCN \cdot 2LiCl$ (1 M in THF) and 5 drops of allyl bromide in 0.5 mL of THF. The analytical data for known compounds match the literature data. The stereochemistry of compounds **25** were determined by NOESY-NMR experiments.

Starting Materials and Organometallic Reagents. *i*-PrMgCl·LiCl (**3**) is commercially available. $TMP_2Mg \cdot 2LiCl$ was prepared according to the literature procedure.[5f,17] The enol phosphates **13**,[18] **15**,[4a] **20**,[4a] and **21**[4b] were prepared according to literature procedures. Enol phosphate **9** was prepared as follows:

2-Iodocyclopent-2-enone (**8**) (5.20 g, 25.0 mmol) dissolved in dry THF (30 mL) was cooled to −78 °C. L-Selectride (27.5 mL,

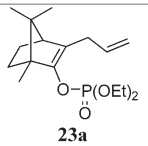
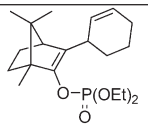
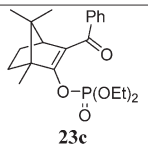
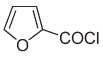
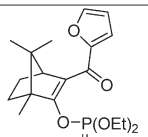
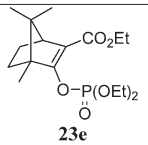
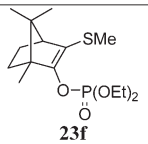
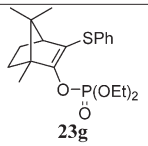
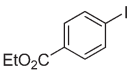
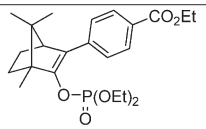
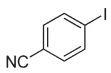
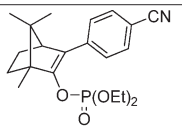
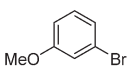
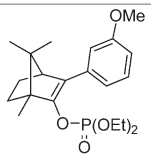
(15) (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (b) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *116*, 1907. (c) The use of less active catalytic systems like $Pd(PPh_3)_4$ or $Pd(dba)_2$/tfp did not lead to the corresponding cross-coupling products when aryl bromides were used instead of aryl iodides.

(16) Vashchenko, V.; Kutulya, L.; Krivoshey, A. *Synthesis* **2007**, *14*, 2125.

(17) Rohbogner, C. J.; Wagner, A. J.; Clososki, G. C.; Knochel, P. *Org. Synth.* **2009**, *86*, 374.

(18) Hayashi, T.; Fujiwa, T.; Okamoto, Y.; Katsuro, Y.; Kumada, M. *Synthesis* **1981**, 1001.

TABLE 4. Products Obtained by the Reaction of 22 with Various Electrophiles

Entry	Method	Electrophile	Product	Yield [%][a]
1	A		 **23a**	82[b]
2	B		**23a**	62[b]
3	A		 **23b**	85[b]
4	A	PhCOCl	 **23c**	82[b]
5	B		**23c**	67[b]
6	A		 **23d**	74[b]
7	B		 **23e**	72
8	A	$PhSO_2SMe$	 **23f**	73
9	B	$PhSO_2SPh$	 **23g**	65
10	A		 **23h**	74[c]
11	A		 **23i**	58[c]
12	B		 **23j**	69[c]

[a]Yield of analytically pure product. [b]Obtained after transmetalation with CuCN·2LiCl (20−100 mol %). [c]Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and Pd-catalyzed cross-coupling.

27.5 mmol, 1.0 M in THF) was then added dropwise. After 2 h of stirring at −78 °C, phosphorochloridic acid diethyl ester (5.6 g, 32.5 mmol) was added, and the mixture was allowed to warm to room temperature. After 1.5 h, the resulting mixture was quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1: 1) furnished the compound **9** (5.3 g, 17.7 mmol, 71%) as a yellowish oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.18 (dq, J = 14.2, J = 7.1 Hz, 4 H), 2.49−2.60 (m, 4 H), 1.98−2.08 (m, 2 H), 1.34 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 152.4 (d, J = 5.9 Hz), 74.2 (d, J = 11.1 Hz), 64.6 (d, J = 6.2 Hz, 2 C), 37.7, 30.1, 21.9, 16.0 (d, J = 6.7 Hz, 2 C); IR (film, cm^{-1}) $\tilde{\nu}$ = 2982 (m), 1722 (w), 1661 (s), 1280 (vs), 1224 (m), 1031 (vs), 963 (vs), 859 (s), 553 (w); MS (EI, 70 eV) m/z 346 (M^+, 19), 219 (61), 191 (46), 163 (100), 162 (20), 83 (45), 81 (22), 65 (28); HRMS (EI) calcd for $C_9H_{16}O_4PI$, 345.9831, found 345.9827.

Typical Procedures (TP). TP1: Metalation of Vinyl Phosphates. The corresponding phosphate (1.0 mmol) in THF (2.0 mL) reacted with freshly titrated TMP_2Mg·2LiCl (1.3 equiv, 2.36 mL, 0.55 M in THF) at the specified temperature and was stirred until the metalation was complete. The completion of the metalation was checked by GC analysis of reaction aliquots quenched with a solution of 3 drops of CuCN·2LiCl (1 M in THF) and 5 drops of allyl bromide in 0.5 mL of THF.

TP2: Transmetalation of Magnesium Reagents. To the Mg species that was prepared according to TP2 was added $ZnCl_2$ solution (1.0 M in THF, 1.1 mL, 1.1 equiv) at −20 °C, and the resulting mixture was stirred for 15 min.

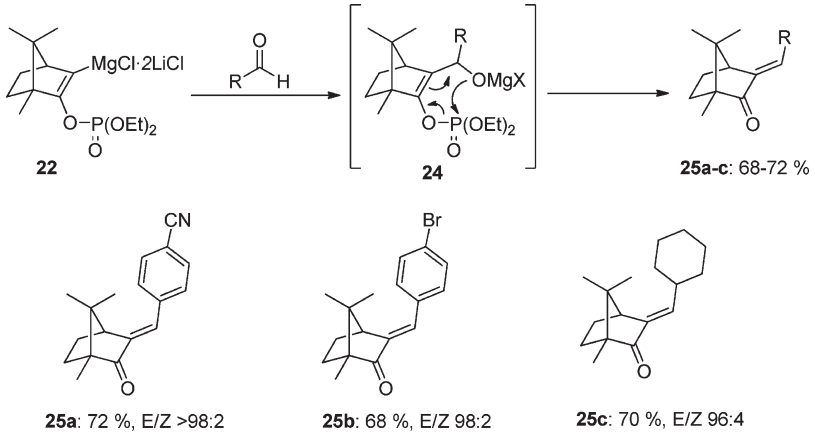
TP3: I/Mg Exchange on Phosphoric Acid 2-Iodocyclopent-1-enyl Ester Diethyl Ester (9). A solution of phosphoric acid 2-iodocyclopent-1-enyl ester diethyl ester (**9**) (346 mg, 1.0 mmol) in dry THF (1.0 mL) was cooled to −50 °C, *i*-PrMgCl·LiCl (0.96 mL, 1.1 mmol, 1.14 M in THF) was then added slowly, and the resulting mixture was stirred for 5 min at this temperature. Further functionalizations were performed as described below.

TP4: Br/Mg Exchange on 3-Bromo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-en-2-yl Diethyl Phosphate (21). To neat **21** (367 mg, 1.0 mmol) was added *i*-PrMgCl·LiCl (0.96 mL, 1.1 mmol, 1.14 M in THF) at 25 °C, and the resulting mixture was stirred for 2 h at this temperature. Further functionalizations were performed as described below.

Experimental Procedures and Analytical Data. Diethyl 2-(Phenylthio)cyclopent-1-en-1-yl Phosphate (11a). (2-Iodo-cyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. The mixture was cooled to −50 °C, benzenethiosulfonic acid *S*-phenyl ester (300 mg, 1.2 mmol) was then added, and the resulting mixture was allowed to stir at 25 °C for 3 h. The mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:2) furnished the compound **11a** (273 mg, 0.83 mmol, 83%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.15−7.33 (m, 5 H), 4.00 (dq, J = 14.1 Hz, J = 7.1 Hz, 4 H), 2.70−2.77 (m, 2 H), 2.29−2.38 (m, 2 H), 1.91−2.01 (m, 2 H), 1.34 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 150.6 (d, J = 6.9 Hz), 134.0, 130.0, 128.8, 126.4, 114.2 (d, J = 9.4 Hz), 64.6 (d, J = 6.2 Hz), 32.1, 31.9, 16.0 (d, J = 6.8 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2982, 1649, 1478, 1283, 1032, 985, 873, 745, 692; MS (70 eV, EI) m/z 328 (73) [M^+], 219 (100), 191 (46), 173 (40), 163 (62), 147 (17), 109 (19), 91 (17), 83 (15), 81 (20); HRMS (EI) calcd for $C_{15}H_{21}O_4PS$ 328.0898, found 328.0895.

2-[(Diethylamino)methyl]cyclopent-1-en-1-yl Diethyl Phosphate (11b). (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. A mixture of benzotriazol-1-ylmethyldiethylamine and

SCHEME 7. Reaction of Magnesium Reagent 22 with Various Aldehydes Leading to α,β-Unsaturated Ketones of Type 25



benzotriazol-2-ylmethyldiethylamine (245 mg, 1.2 mmol) was then added at −50 °C, and the resulting mixture was allowed to warm to 25 °C. After addition of THF (4 mL), the mixture was stirred for an additional 1 h at 25 °C, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:2) furnished the compound **11b** (251 mg, 0.82 mmol, 82%) as a colorless oil: ^{1}H NMR (C_6D_6, 300 MHz) δ = 3.97 (dq, J = 8.5 Hz, J = 7.1 Hz, 4 H), 3.20 (s, 2 H), 2.68−2.78 (m, 2 H), 2.46 (q, J = 7.1 Hz, 4 H), 2.29−2.40 (m, 2 H), 1.64−1.74 (m, 2 H), 1.03 (td, J = 7.1 Hz, J = 0.9 Hz, 6 H), 1.00 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (C_6D_6, 75 MHz) δ = 145.8 (d, J = 7.2 Hz), 122.6 (d, J = 8.5 Hz), 63.9 (d, J = 5.8 Hz), 49.4, 47.4, 32.3, 31.1, 20.0, 16.2 (d, J = 6.4 Hz), 12.3; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2935, 1698, 1446, 1336, 1274, 10237, 966, 907; MS (70 eV, EI) m/z 276 (100) [M$^+$], 170 (24), 141 (30), 136 (20), 123 (22), 122 (34), 99 (13), 81 (17), 79 (13), 72 (18); HRMS (EI) calcd for $C_{14}H_{28}NO_4P$ 305.1756, found 305.1734.

Diethyl 2-(Trimethylsilyl)cyclopent-1-en-1-yl Phosphate (11c). (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. The mixture was cooled to −50 °C, and TMSCN (109 mg, 1.2 mmol) was added. The solution was allowed to warm to −20 °C and stirred for 3 h at this temperature. The reaction mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:1) furnished the compound **11c** (258 mg, 0.88 mmol, 88%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 4.14 (dq, J = 14.2 Hz, J = 7.1 Hz, 4 H), 2.60−2.68 (m, 2 H), 2.27−2.35 (m, 2 H), 1.85−1.97 (m, 2 H), 1.34 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H), 0.10 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 156.6 (d, J = 6.7 Hz), 119.8 (d, J = 10.1 Hz), 64.0 (d, J = 6.0 Hz), 33.2, 32.0, 22.3, 16.1 (d, J = 6.8 Hz), 1.39; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2982, 2957, 1635, 1249, 1034, 993, 890, 840, 756; MS (70 eV, EI) m/z 292 (12) [M$^+$], 221 (17), 203 (15), 171 (13), 155 (100), 83 (29), 75 (14); HRMS (EI) calcd for $C_{12}H_{25}O_4PSi$ 292.1260, found 292.1266.

2-Allylcyclopent-1-en-1-yl Diethyl Phosphate (11d). (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) was then added, and the resulting mixture was stirred for 10 min and then cooled to −50 °C. Allyl bromide (145 mg, 1.2 mmol) was then added dropwise, and the mixture was stirred at 25 °C for 1 h. The reaction mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:1) furnished the compound **11d** (213 mg, 0.82 mmol, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 5.71 (ddt, J = 16.9 Hz, J = 10.0 Hz, J = 6.7 Hz, 1 H), 4.94−5.05 (m, 2 H), 4.00 (dq, J = 14.2 Hz, J = 7.1 Hz, 4 H), 2.81−2.83 (m, 2 H), 2.52−2.60 (m, 2 H), 2.18−2.24 (m, 2 H), 1.80−1.90 (m, 2 H), 1.32 (td, J = 7.1 Hz, J = 0.9 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 143.0 (d, J = 7.8 Hz), 135.0, 121.5 (d, J = 8.6 Hz), 115.6, 64.1 (d, J = 6.0 Hz), 31.4, 30.8, 30.7, 19.4, 16.0 (d, J = 6.7 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2981, 1698, 1274, 1192, 1030, 981, 908, 819, 566; MS (70 eV, EI) m/z 260 (43) [M$^+$], 231 (26), 155 (26), 127 (28), 106 (46), 105 (100), 99 (50), 91 (55), 81 (25), 79 (27); HRMS (EI) calcd for $C_{12}H_{21}O_4P$ 260.1177, found 260.1197.

2-Benzoylcyclopent-1-en-1-yl Diethyl Phosphate (11e). (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. The solution was cooled to −50 °C, CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) and benzoyl chloride (169 mg, 1.2 mmol) were then added, and the resulting mixture was stirred at 0 °C for 2 h. The mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:7) furnished the compound **11e** (273 mg, 0.84 mmol, 84%) as a yellowish oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.77 (d, J = 6.9 Hz, 2 H), 7.38−7.51 (m, 3 H), 3.67−3.85 (m, 4 H), 2.84−2.89 (m, 2 H), 2.71−2.77 (m, 2 H), 1.96−2.07 (m, 2 H), 1.13 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 193.2, 154.4 (d, J = 6.0 Hz), 138.8, 132.0, 128.9, 128.1, 121.8 (d, J = 9.0 Hz), 64.5 (d, J = 6.4 Hz), 33.3, 30.3, 19.6, 15.8 (d, J = 7.0 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2983, 1641, 1448, 1362, 1278, 1037, 986, 897, 724; MS (70 eV, EI) m/z 324 (70) [M$^+$], 170 (24), 169 (64), 155 (43), 142 (38), 141 (30), 128 (47), 105 (100), 81 (17), 77 (41); HRMS (EI) calcd for $C_{16}H_{21}O_5P$ 324.1127, found 324.1158.

Diethyl 2-(3-oxocyclohex-1-en-1-yl)cyclopent-1-en-1-yl phosphate (11f). (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. CuCN·2LiCl (1.1 mL, 1.1 mmol, 1.0 M in THF) was then added at −30 °C, and the mixture was stirred at this temperature for 1 h. 3-Iodocyclohex-2-enone (169 mg, 1.2 mmol) in 1 mL of THF was then added at −30 °C, and the mixture was allowed to warm to 0 °C and stirred for 2 h. The reaction mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (Et_2O) furnished the compound **11f** (223 mg, 0.71 mmol, 71%) as a colorless oil: ^{1}H NMR (C_6D_6, 300 MHz) δ = 6.07 (s, 1 H), 3.90 (dq, J = 14.4 Hz, J = 7.1 Hz, 4 H), 2.73 (t,

J = 7.0 Hz, 2 H), 2.50 (t, J = 5.7 Hz, 2 H), 2.16−2.21 (m, 2 H), 2.05−2.10 (m, 2 H), 1.54−1.65 (m, 2 H), 1.41−1.51 (m, 2 H), 0.99 (td, J = 7.1 Hz, J = 0.8 Hz, 6 H); ^{13}C NMR (C_6D_6, 75 MHz) δ = 198.02, 153.4, 151.9 (d, J = 6.5 Hz), 125.9, 120.5 (d, J = 9.0 Hz), 64.4 (d, J = 5.8 Hz), 37.7, 34.0, 30.2, 27.9, 23.1, 19.2, 16.1 (d, J = 6.4 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2982, 2944, 1665, 1625, 1278, 1188, 1032, 968, 892, 518; MS (70 eV, EI) m/z 314 (52) [M$^+$], 160 (100), 159 (72), 155 (44), 145 (40), 131 (29), 127 (42), 117 (26), 99 (34), 91 (43), 81 (23), 77 (26); HRMS (EI) calcd for $C_{15}H_{23}O_5P$ 314.1283, found 314.1288.

***tert*-Butyl 4-[2-[(Diethoxyphosphoryl)oxy]cyclopent-1-en-1-yl]-benzoate (11g).** (2-Iodocyclopent-1-enyl)phosphonic acid diethyl ester (**9**) (346 mg, 1.0 mmol) was treated with *i*-PrMgCl·LiCl according to TP3. $ZnCl_2$ solution (1.1 mL, 1.1 mmol, 1.0 M in THF) was then added, and the mixture was allowed to warm to 25 °C. Pd(dba)$_2$ (29 mg, 5 mol %) and P(2-furyl)$_3$ (23 mg, 10 mol %) dissolved in THF (2 mL) and mixed with ethyl *tert*-butyl 4-iodobenzoate (335 mg, 1.1 mmol) were then transferred via cannula to the reaction mixture. The resulting mixture was stirred at 25 °C for 2.5 h, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 1:5) furnished the compound **11g** (312 mg, 0.79 mmol, 79%) as a light brown oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 7.55 (d, J = 8.7 Hz, 2 H), 7.00 (d, J = 8.7 Hz, 2 H), 4.06−4.18 (m, 4 H), 2.80−2.86 (m, 2 H), 2.66−2.72 (m, 2 H), 1.91−2.04 (m, 2 H), 1.34 (s, 9H), 1.31 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 177.0, 149.5, 144.8 (d, J = 7.2 Hz), 132.1, 127.9, 121.0, 119.4 (d, J = 9.1 Hz), 64.3 (d, J = 6.0 Hz), 39.0, 32.9, 31.3, 27.1, 19.2, 16.0 (d, J = 6.8 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2980, 2935, 1753, 1600, 1507, 1205, 1168, 1115, 1033, 898; MS (70 eV, EI) m/z 396 (55) [M$^+$], 313 (16), 312 (100), 284 (18), 283 (35), 174 (13), 158 (31),157 (36), 57 (50); HRMS (EI) calcd for $C_{20}H_{29}O_6P$ 396.1702, found 396.1679.

2-Allylcyclopent-1-en-1-yl Diethyl Phosphate (11d). Cyclopent-1-en-1-yl diethyl phosphate **13** (220 mg, 1.0 mmol) reacted at −10 °C for 2 h according to TP1 and was then transmetalated according to TP2. CuCN·2LiCl (1 M solution in THF, 0.4 mL) and allyl bromide (600 mg, 5.0 mmol) were then added dropwise, and the reaction mixture was stirred at −20 °C for 3 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc 5:1) furnished the compound **11d** (150 mg, 0.56 mmol, 56%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80−5.67 (m, 1 H), 5.06−4.96 (m, 2 H), 4.15 (p, J = 7.9 Hz, 4 H), 2.84 (d, J = 5.7 Hz, 2 H), 2.60−2.55 (m, 2 H), 2.24 (s, 2 H), 1.87 (p, J = 7.9 Hz, 2 H), 1.34 (td, J = 7.1 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0 (d, J = 7.7 Hz), 135.0, 121.6 (d, J = 8.6 Hz), 115.7, 64.1 (d, J = 6.1 Hz), 31.5, 30.7, 19.5, 16.1 (d, J = 6.1 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2976, 2917, 2851, 1698, 1444, 1382, 1350, 1337, 1274, 1191, 1166, 1118, 1061, 1024, 979, 964, 907, 872, 819, 802, 753, 663, 566; MS (70 eV, EI) m/z 260 (58) [M$^+$], 231 (54), 203 (29), 106 (100), 79 (27); HRMS (EI) calcd for $C_{12}H_{21}O_4P$ 260.1177, found 260.1183.

2-Cyclohex-2-en-1-ylcyclopent-1-en-1-yl Diethyl Phosphate (11h). Cyclopent-1-en-1-yl diethyl phosphate **13** (220 mg, 1.0 mmol) reacted at −10 °C for 2 h according to TP1 and was then transmetalated according to TP2. CuCN·2LiCl (1 M solution in THF, 0.4 mL) and 3-bromocyclohexene (800 mg, 5.0 mmol) were then added dropwise, and the reaction mixture was stirred at −20 °C for 3 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 4:1) furnished the compound **11h** (130 mg, 0.45 mmol, 45%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.57−5.68 (m, 1 H), 5.45−5.39 (m, 1 H), 4.20−4.05 (m, 4 H), 3.32−3.26 (m, 1 H), 2.60−2.53 (m, 2 H), 2.25−2.16 (m, 2 H), 2.00−1.93 (m, 2 H), 1.89−1.66 (m, 4 H), 1.62−1.40 (m, 2 H), 1.37−1.31 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (d, J = 7.7 Hz), 129.6, 127.8, 127.1 (d, J = 8.8 Hz), 64.1 (d, J = 6.2 Hz), 33.1, 31.5, 28.2, 27.1, 24.8, 22.0, 19.6, 16.1 (t, J = 6.7 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2256, 2980, 2931, 2857, 2301, 1990, 1724, 1692, 1478, 1444, 1393, 1333, 1243, 1186, 1164, 1098, 1019, 972, 904, 868, 817, 801, 748, 722, 671, 640, 617, 611; MS (70 eV, EI) m/z 300 (18) [M$^+$], 163 (6), 155 (38), 146 (100), 131 (28), 117 (22), 99 (10); HRMS (EI) calcd for $C_{15}H_{25}O_4P$ 300.1490, found 300.1503.

Ethyl 4-[2-[Ddiethoxyphosphoryl)oxy]cyclopent-1-en-1-yl]benzoate (11i). Cyclopent-1-en-1-yl diethyl phosphate **13** (220 mg, 1.0 mmol) reacted at −10 °C for 2 h according to TP1 and was then transmetalated according to TP2. Pd(dba)$_2$ (23 mg, 4 mol %), P(2-furyl)$_3$ (28 mg, 12 mol %), and ethyl-4-iodobenzoate (360 mg, 1.3 mmol, 1.3 equiv) were then added to the reaction mixture. The resulting mixture was stirred at −10 °C overnight, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 3:1) furnished the compound **11i** (210 mg, 0.58 mmol, 58%) as a yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (J = 8.7 Hz, 2 H), 7.60 (d, J = 8.7 Hz, 2 H), 4.36 (q, J = 7.2 Hz, 2 H), 4.19−4.09 (m, 4 H), 2.88−2.85 (m, 2 H), 2.75−2.71 (m, 2 H), 2.04−1.99 (m, 2 H), 1.38 (t, J = 7.0 Hz, 3 H), 1.32 (td, J = 7.0 Hz, J = 1.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 147.1, 139.1, 129.3, 128.6, 126.7, 119.4, 64.5 (d, J = 5.7 Hz), 60.8, 33.1, 31.1, 19.3, 16.1 (d, J = 7.2 Hz), 14.3; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2982, 2934, 2907, 1711, 1651, 1601, 1477, 1444, 1409, 1393, 1367, 1340, 1271, 1182, 1103, 1018, 957, 877, 855, 773, 702; MS (70 eV, EI) m/z 368 (22) [M$^+$], 322 (100), 294 (63), 265 (33), 203 (11), 185 (79), 169 (26), 157 (13), 141 (51), 129 (22), 115 (50), 102 (21), 80 (24); HRMS (EI) calcd for $C_{18}H_{25}O_6P$ 368.1389, found 368.1387.

Diethyl 2-[3-(Trifluoromethyl)phenyl]cyclopent-1-en-1-yl Phosphate (11j). Cyclopent-1-en-1-yl diethyl phosphate **13** (220 mg, 1.0 mmol) reacted at −10 °C for 2 h according to TP1 and was then transmetalated according to TP2. Pd(dba)$_2$ (29 mg, 5 mol %), P(2-furyl)$_3$ (24 mg, 10 mol %) and trifluoro-3-iodobenzene (360 mg, 1.3 mmol, 1.3 equiv) were then added to the reaction mixture. The resulting mixture was stirred at −10 °C overnight, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 4:1) furnished the compound **11j** (210 mg, 0.58 mmol, 58%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1 H), 7.65−7.60 (m, 1 H), 7.45−7.39 (m, 2 H), 4.19−4.09 (m, 4 H), 2.91−2.82 (m, 2 H), 2.75−2.67 (m, 2 H), 2.0 (p, J = 7.5 Hz, 2 H), 1.31 (tq, J = 7.0 Hz, J = 0.49 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.5 (d, J = 6.7 Hz) 135.4 (d, J = 1.54 Hz), 130.4 (q, J = 32.0 Hz), 130.0, 128.6, 126.1, 123.4 (dq, J = 49.2 Hz, J = 3.9 Hz), 118.8 (d, J = 9.3 Hz), 64.4 (dd, J = 18.6 Hz, J = 6.2 Hz), 33.0, 31.0, 20.9, 19.3, 16.0 (d, J = 7.0 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2990, 2169, 2911, 2852, 1659, 1486, 1446, 1393, 1370, 1342, 1323, 1277, 1221, 1196, 1180, 1163, 1115, 1091, 1073, 1026, 968, 884, 808, 754, 701, 663, 647, 633, 610, 604; MS (70 eV, EI) m/z 364 (44) [M$^+$], 316 (44), 267 (15), 190 (100), 151 (11); HRMS (EI) for Calcd $C_{16}H_{20}F_3O_4P$ 364.1051, found 364.1045.

3-Allylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (17a). The bicyclic enol phosphate **15** (250 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. CuCN·2LiCl (1 M solution in THF, 0.4 mL) and allyl bromide (600 mg, 5.0 mmol) were then added dropwise, and the reaction mixture was stirred at 0 °C for 1 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over

anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 2:1) furnished the compound **17a** (260 mg, 0.96 mmol, 96%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82−5.69 (m, 1 H), 5.08−4.94 (m, 2 H), 4.19−4.09 (m, 4 H), 3.0 (s, 1 H), 2.93−2.86 (m, 1 H), 2.74−2.60 (m, 2 H), 1.74−1.61 (m, 2 H), 1.54−1.48 (m, 1 H), 1.46−1.38 (m, 1 H), 1.33 (td, J = 7.1 Hz, J = 0.98 Hz, 6 H), 1.15−1.09 (m, 1 H), 1.04 (td, J = 8.0 Hz, J = 1.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0 (d, J = 7.2 Hz), 135.4, 124.8 (d, J = 8.5 Hz), 115.5, 64.2 (d, J = 3.6 Hz), 46.1, 43.6 (d, J = 1.0 Hz), 29.1 (d, J = 1.3 Hz), 26.0 (d, J = 10.6 Hz), 16.1 (d, J = 7.0 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2977, 2874, 1732, 1674, 1639, 1475, 1445, 1394, 1370, 1334, 1270, 1219, 1204, 1160, 1097, 1026, 986, 950, 908, 868, 818, 762; MS (70 eV, EI) m/z 286 (60) [M^+], 258 (100), 155 (5), 104 (9), 91 (1); HRMS (EI) calcd for $C_{14}H_{23}O_4P$ 286.1334, found 286.1307.

3-Benzoylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (17b). The bicyclic enol phosphate **15** (250 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1. The resulting mixture was cooled to −20 °C, CuCN·2LiCl (1 M solution in THF, 1.1 mL) was added, and the reaction mixture was stirred at this temperature for 30 min. Benzoyl chloride (350 mg, 2.5 mmol) was then added, and the mixture was allowed to warm fast to 25 °C for 1 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL) and aq NH_3, and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 2:1) furnished the compound **17b** (260 mg, 0.75 mmol, 75%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76−7.72 (m, 2 H), 7.49−7.35 (m, 3 H), 3.86−3.71 (m, 4 H), 3.36 (s, 2 H), 1.98−1.92 (m, 2 H), 1.77−1.70 (m, 1 H), 1.60−1.46 (m, 2 H), 1.26−1.20 (m, 1 H), 1.18−1.10 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.7, 160.3 (J = 5.7 Hz), 139.3, 131.8, 128.9, 128.0, 125.6 (d, J = 9.0 Hz), 64.6 (d, J = 6.5 Hz), 45.9, 44.8 (d, J = 1.3 Hz), 43.3, 26.2 (d, J = 31.2 Hz), 15.8 (d, J = 7.0 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2981, 2877, 1633, 1598, 1578, 1476, 1447, 1365, 1282, 1268, 1220, 1204, 1168, 1115, 1024, 992, 949, 933, 892, 846, 819, 802, 787, 774, 749, 714, 694, 675; MS (70 eV, EI) m/z 350 (46) [M^+], 168 (100), 105 (37), 77 (25); HRMS (EI) calcd for $C_{18}H_{23}O_5P$ 350.1283, found 350.1268.

Diethyl 3-(Methylthio)bicyclo[2.2.1]hept-2-en-2-yl Phosphate (17c). The bicyclic enol phosphate **15** (250 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1. Benzenethiosulfonic acid *S*-methyl ester (570 mg, 3.0 mmol) was then added dropwise, and the reaction mixture was warmed to 30 °C for 3 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 4:1) furnished the compound **17c** (160 mg, 0.73 mmol, 73%) as a yellowish oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24−4.12 (m, 4 H), 3.11 (s, 1 H), 2.94 (s, 1 H), 2.24 (s, 3 H), 1.79−1.65 (m, 2 H), 1.54−1.42 (m, 2 H), 1.34 (tp, J = 7.1 Hz, J = 0.97 Hz, 6 H), 1.29−1.19 (m, 1 H), 1.12−1.08 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5 (d, J = 6.4 Hz), 119.9 (d, J = 9.5 Hz), 64.4 (t, J = 6.2 Hz), 44.5 (d, J = 3.6 Hz), 26.3 (d, J = 1.0 Hz), 26.0 (d, J = 1.8 Hz), 16.1 (d, J = 4.9 Hz), 15.1; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2979, 2925, 2872, 1619, 1478, 1444, 1393, 1370, 1315, 1276, 1216, 1198, 1155, 1124, 1098, 1054, 1023, 965, 947, 936, 917, 850, 818, 796, 758, 734; MS (70 eV, EI) m/z 292 (29) [M^+], 277 (37), 264 (29), 236 (67), 218 (22), 208 (55), 123 (46), 110 (100); HRMS (EI) calcd for $C_{12}H_{21}O_4PS$ 292.0898, found 292.0889.

Ethyl 4-[3-[(Diethoxyphosphoryl)oxy]bicyclo[2.2.1]hept-2-en-2-yl]benzoate (17d). The bicyclic enol phosphate **15** (250 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. $Pd(dba)_2$ (24 mg, 4 mol %), P(2-furyl)$_3$ (28 mg, 12 mol %), and ethyl-4-iodobenzoate (360 mg, 1.3 mmol, 1.3 equiv) were then added to the reaction mixture. The resulting mixture was stirred at 25 °C for 2 h, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 1:1) furnished the compound **17d** (300 mg, 0.75 mmol, 75%) as a yellowish oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 8.6 Hz, 2 H), 7.53 (d, J = 8.6 Hz, 2 H), 4.34 (q, J = 7.3 Hz, 2 H), 4.25−4.06 (m, 4 H), 3.32 (d, J = 9.7 Hz, 2 H), 1.93−1.82 (m, 2 H), 1.72−1.67 (m 1 H), 1.62−1.50 (m, 1 H), 1.39−1.30 (m, 8 H), 1.26−1.16 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 152.6 (d, J = 6.5 Hz), 137.9 (d, J = 1.5 Hz), 129.5, 127.7, 126.0, 123.8 (d, J = 9.5 Hz), 64.5 (t, J = 5.9 Hz), 60.7 (d, J = 32.2 Hz), 45.4 (d, J = 7.5 Hz), 26.5 (d, J = 29 Hz), 21.0, 16.0 (q, J = 4.4 Hz), 14.3 (d, J = 11.6 Hz); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2979, 2873, 1711, 1628, 1605, 1562, 1508, 1476, 1446, 1412, 1393, 1367, 1345, 1270, 1213, 1183, 1166, 1103, 1050, 1020, 969, 950, 916, 856, 818, 799, 779, 761, 703; MS (70 eV, EI) m/z 394 (45) [M^+], 366 (100), 320 (40), 292 (26), 264 (10), 230 (7), 184 (6), 80 (5); HRMS (EI) calcd for $C_{20}H_{27}O_6P$ 394.1545, found 394.1549.

3-Allyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (23a). Method A. The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. CuCN·2LiCl (1 M solution in THF, 0.2 mL) and allyl bromide (605 mg, 5.0 mmol) were then added dropwise, and the reaction mixture was allowed to warm slowly to 25 °C overnight. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 6:1) furnished the compound **23a** (270 mg, 0.82 mmol, 82%) as a colorless oil.

Method B. The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. CuCN·2LiCl (1 M solution in THF, 0.2 mL) and allyl bromide (132 mg, 1.1 mmol) were then added dropwise, and the reaction mixture was stirred for 1 h at 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/ EtOAc = 6:1) furnished the compound **23a** (203 mg, 0.62 mmol, 62%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83−5.69 (m, 1 H), 5.10−4.97 (m, 2 H), 4.20−4.10 (m, 4 H), 3.07−2.99 (m, 1 H), 2.79−2.69 (m, 1 H), 2.18 (d, J = 3.7 Hz, 1 H), 1.85−1.74 (m, 1 H), 1.62−1.53 (m, 1 H), 1.47−1.39 (m, 1 H), 1.34 (tq, J = 7.1 Hz, J = 1.0 Hz, J = 0.51 Hz, 6 H), 1.11−1.03 (m, 1 H), 1.00 (s, 3 H), 0.89 (s, 3 H), 0.72 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4, 124.6 (d, J = 6.4 Hz), 115.8, 64.2, 55.1, 54.4, 52.4 (d, J = 1.4 Hz), 32.5 (d, J = 1.7 Hz), 30.2 (d, J = 1.7 Hz), 25.4 (d, J = 5.6 Hz), 19.7 (d, J = 28.8 Hz), 16.2 (d, J = 6.9 Hz), 10.2; MS (70 eV, EI) m/z 328 (2) [M^+], 111 (54), 97 (70), 85 (44), 83 (67), 71 (65), 69 (69), 57 (100), 55 (55), 43 (50); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2954, 2873, 1672, 1639, 1476, 1444, 1388, 1368, 1319, 1271, 1211, 1167, 1133, 1054, 1028, 1008, 977, 928, 858, 820, 756, 647, 603; HRMS (EI) calcd for $C_{17}H_{29}O_4P$ 328.1803, found 328.1784.

3-Cyclohex-2-en-1-yl-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (23b). The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. CuCN·2LiCl (1 M solution in THF, 0.2 mL) and 3-bromocyclohexene (805 mg, 5.0 mmol) were then added dropwise, and the reaction mixture was allowed to warm slowly to 25 °C overnight. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 7:1) furnished the

compound **23b** (313 mg, 0.85 mmol, 85%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77−5.66 (m, 1 H), 5.52−5.41 (m, 1 H), 4.21−4.08 (m, 4 H), 3.43−3.34 (m, 1 H), 2.24−2.19 (m, 1 H), 2.02−1.95 (m, 2 H), 1.89−1.71 (m, 3 H), 1.63−1.39 (m, 5 H), 1.34 (tq, J = 7.0 Hz, J = 0.97 Hz, 5 H), 1.18−1.09 (m, 1 H), 1.0 (s, 3 H), 0.89 (s, 3 H), 0.71 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1 (d, J = 11.5 Hz), 129.9 (d, J = 6.7 Hz), 128.8 (d, J = 2.0 Hz), 127.6, 64.1 (t, J = 6.5 Hz), 55.6, 54.2 (d, J = 1.7 Hz), 50.6 (d J = 1.4 Hz), 32.7 (d J = 1.7 Hz), 31.9 (d,J = 1.7 Hz), 27.6 (d, J = 2.5 Hz), 26.3 (d J = 3.7 Hz), 24.8, 21.7, 19.7, 19.4, 16.2 (d, J = 7.0 Hz), 10.2; MS (70 eV, EI) m/z 368 (5) [M$^+$], 214 (67), 199 (100), 186 (49), 171 (40), 155 (22), 145 (17), 129 (9), 115 (4), 105 (7), 91 (7); IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2931, 1670, 1476, 1444, 1386, 1366, 1271, 1212, 1166, 1126, 1054, 1028, 1009, 961, 929, 896, 825, 803, 751, 721, 686; HRMS (EI) calcd for $C_{20}H_{33}O_4P$ 368.2116, found 368.2088.

3-Benzoyl-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (23c). Method A. The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min after TP1. The resulting mixture was cooled to −20 °C, CuCN·2LiCl (1 M solution in THF, 1.1 mL) was added, and the reaction mixture was stirred at this temperature for 30 min. Benzoyl chloride (351 mg, 2.5 mmol) was then added, and the mixture was allowed to warm fast to 25 °C for 1 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 2: 1) furnished the compound **23c** (332 mg, 0.82 mmol, 82%) as a yellow oil.

Method B. The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, CuCN·2LiCl (1 M solution in THF, 0.2 mL) was added, and the reaction mixture was stirred at this temperature for 30 min. Benzoyl chloride (155 mg, 1.1 mmol) was then added, and the mixture was allowed to warm to 25 °C overnight. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 2:1) furnished the compound **23c** (263 mg, 0.67 mmol, 67%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83−7.79 (m, 2 H), 7.50−7.37 (m, 3 H), 3.76−3.53 (m, 4 H), 2.82 (d, J = 3.4 Hz, 1 H), 2.06−1.95 (m, 1 H), 1.77−1.62 (m, 2 H), 1.49−1.41 (m, 1 H), 1.09 (m, 12 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.8 (d, J = 2.6 Hz), 158.5 (d, J = 12.4 Hz), 139.0, 132.0, 129.1, 128.0, 64.3 (t, J = 6.7 Hz), 56.8, 55.1, 52.8, 31.5 (d, J = 2.1 Hz), 26.0 (d, J = 3.1 Hz), 19.4 (d, J = 6.7 Hz), 15.9 (q, J = 3.1 Hz), 9.8; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2964, 2879, 1638, 1614, 1578, 1478, 1450, 1341, 1317, 1283, 1276, 1251, 1204, 1168, 1127, 1107, 1032, 1010, 977, 921, 894, 880, 827, 820, 775, 723, 703, 694, 657, 621; MS (70 eV, EI) m/z 392 (32) [M$^+$], 238 (23), 223 (34), 210 (33), 195 (38), 167 (13), 155 (13), 105 (100), 91 (9), 77 (34); HRMS (EI) calcd for $C_{21}H_{29}O_5P$ 392.1753, found 392.1746.

Diethyl 3-(2-Furoyl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Phosphate (23d). The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1. The resulting mixture was cooled to −20 °C, CuCN·2LiCl (1 M solution in THF, 1.1 mL) was added, and the reaction mixture was stirred at this temperature for 30 min. 2-Furoyl chloride (326 mg, 2.5 mmol) was then added, and the mixture was allowed to warm fast to 25 °C for 1 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 2:1) furnished the compound **23d** (285 mg, 0.74 mmol, 74%) as a yellowish oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (q, J = 1.0 Hz, 1 H), 7.16 (dd, J = 3.7 Hz, J = 0.73 Hz, 1 H), 6.5 (q, J = 2.0 Hz, 1 H), 4.05−3.91 (m, 4 H), 2.84 (d, J = 3.7 Hz, 1 H), 2.07−1.97 (m, 2 H), 1.80−1.62 (m, 2 H), 1.52−1.44 (m, 1 H), 1.27−1.15 (m, 5 H), 1.11 (s, 3 H), 0.98 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4 (d, J = 2.6 Hz), 159.8 (d, J = 12.4 Hz), 152.9, 146.0, 127.2 (d, J = 6.2 Hz), 118.0, 111.9, 64.7 (t, J = 6.7 Hz), 56.6 (d, J = 2.1 Hz), 55.6, 52.7 (d, J = 1.0 Hz), 31.2 (d, J = 2.1 Hz), 26.0 (d, J = 3.1 Hz), 19.2 (d, J = 11.3 Hz), 16.0 (d, J = 1.6 Hz), 9.9; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2961, 1634, 1565, 1466, 1392, 1336, 1315, 1276, 1213, 1164, 1131, 1024, 976, 918, 875, 824, 800, 754, 683; MS (70 eV, EI) m/z 382 (78) [M$^+$], 354 (33), 228 (56), 213 (67), 200 (81), 185 (45), 172 (30), 95 (100); HRMS (EI) calcd for $C_{19}H_{27}O_6P$ 382.1545, found 382.1541.

Ethyl 3-[(Diethoxyphosphoryl)oxy]-4,7,7-trimethylbicyclo[2.2.1]-hept-2-ene-2-carboxylate (23e). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, ethyl cyanoformate (109 mg, 1.1 mmol) was added, and the reaction mixture was slowly warmed to 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 3:1) furnished the compound **23e** (260 mg, 0.72 mmol, 72%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ = 4.26−4.14 (m, 6H), 2.70 (d, J = 3.5 Hz, 1H), 1.95−1.90 (m, 1H), 1.68−1.64 (m, 1H), 1.53−1.49 (m, 1H), 1.34 (td, J = 7.1 Hz, J = 1.1 Hz, 6H), 1.28 (t, J = 7.1 Hz, 3H), 1.26−1.22 (m, 1H), 1.07 (s, 3H), 0.91 (s, 3H), 0.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ = 163.6, 162.6 (d, J = 11.2 Hz), 120.0 (d, J = 6.7 Hz), 64.6, 59.9, 56.6, 55.3, 50.9, 31.3 (d, J = 2.2 Hz), 25.6, 19.4, 19.1, 16.1 (d, J = 7.3 Hz), 14.3, 9.8; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2978, 1703, 1635, 1392, 13709, 1339, 1275, 1246, 1186, 1025, 921; MS (70 eV, EI) m/z 360 (10) [M$^+$], 332 (14), 314 (95), 286 (82), 258 (37), 230 (38), 178 (100); HRMS (EI) calcd for $C_{17}H_{29}O_6P$ 360.1702, found 360.1708.

Diethyl 1,7,7-Trimethyl-3-(methylthio)bicyclo[2.2.1]hept-2-en-2-yl Phosphate (23f). The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1. Benzenethiosulfonic acid *S*-methyl ester (377 mg, 2.0 mmol) was then added dropwise, and the reaction mixture was warmed to 30 °C for 2 h. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 4:1) furnished the compound **23f** (246 mg, 0.73 mmol, 73%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25−4.10 (m, 4 H), 2.44 (d, J = 3.7 Hz, 1 H), 2.20 (s, 3 H), 1.88−1.82 (m, 1 H), 1.65−1.60 (m, 1 H), 1.52−1.48 (m, 1 H), 1.37−1.32 (m, 6 H), 1.28−1.18 (m, 1 H), 1.03 (s, 3 H), 0.93 (s, 3 H), 0.76 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3 (d, J = 11.9 Hz), 119.5 (d, J = 7.7 Hz), 64.2 (t, J = 6.2 Hz), 55.5 (d, J = 1.6 Hz), 53.9, 53.5, 32.3 (d, J = 2.1 Hz), 25.3 (d, J = 3.6 Hz), 19.3 (d, J = 57 Hz), 18.9, 15.9 (d, J = 8.8 Hz), 14.6 (d, J = 1.6 Hz), 9.90; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2954, 2872, 1623, 1476, 1442, 1388, 1367, 1314, 1273, 1204, 1166, 1133, 1097, 1053, 1026, 1003, 959, 917, 822, 764, 697, 652; MS (70 eV, EI) m/z 334 (24) [M$^+$], 319 (100), 165 (88), 152 (98), 105 (32), 81 (11), 55 (21); HRMS (EI) calcd for $C_{15}H_{27}O_4PS$ 334.1368, found 334.1372.

Diethyl 1,7,7-Trimethyl-3-(phenylthio)bicyclo[2.2.1]hept-2-en-2-yl Phosphate (23g). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, benzenethiosulfonic acid *S*-phenyl ester (275 mg, 1.1 mmol) was added, and the reaction mixture was slowly warmed to 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by

flash chromatography (pentane/Et_2O = 3:1) furnished the compound **23g** (257 mg, 0.65 mmol, 65%) as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ = 7.40−7.37 (m, 2H), 7.28−7.15 (m, 3H), 4.26−4.16 (m, 4H), 2.19 (d, J = 3.5 Hz, 1H), 1.81−1.71 (m, 1H), 1.67−1.59 (m, 1H), 1.53−1.45 (m, 1H), 1.36−1.30 (m, 6H), 1.25−1.16 (m, 1H), 1.07 (s, 3H), 0.99 (s, 3H), 0.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 155.1 (d, J = 11.1 Hz), 134.9, 130.7, 128.7, 126.5, 117.7 (d, J = 7.6 Hz), 64.5, 55.99, 54.2, 53.2, 32.9, 25.8, 19.4, 16.0 (d, J = 7.1 Hz), 10.0; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2958, 16919, 1477, 1440, 1280, 1133, 1034, 965, 823; MS (70 eV, EI) m/z 396 (75) [M^+], 368 (71), 319 (80), 287 (87), 214 (93), 105 (100); HRMS (EI) for $C_{20}H_{29}O_4PS$ 396.1524, found 396.1532.

Ethyl 4-[3-[(Diethoxyphosphoryl)oxy]-4,7,7-trimethylbicyclo-[2.2.1]hept-2-en-2-yl]benzoate (23h). The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. $Pd(dba)_2$ (11.3 mg, 2 mol %), P(2-furyl)$_3$ (9.3 mg, 4 mol %), and ethyl-4-iodobenzoate (359 mg, 1.3 mmol) were then added to the reaction mixture. The resulting mixture was stirred at 25 °C for 9 h, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 6: 1) furnished the compound **23h** (326 mg, 0.74 mmol, 74%) as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2 H), 7.52 (d, J = 8.1 Hz, 2 H), 4.35 (q, J = 7.1 Hz, 2 H), 4.15−3.87 (m, 4 H), 2.69 (d, J = 3.7 Hz, 1 H), 2.06−1.95 (m, 1 H), 1.73 (t, J = 6.1 Hz, 2 H), 1.38 (t, J = 7.1 Hz, 3 H), 1.34−1.28 (m, 1 H), 1.24 (td, J = 7.1 Hz, J = 1.2 Hz, 3 H), 1.14 (s, 3 H), 1.13 (td, J = 7.1 Hz, J = 1.2 Hz, 3 H), 0.96 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 152.6 (d, J = 11.9 Hz), 139.0 (d, J = 2.5 Hz), 129.4, 128.0, 126.6 (d, J = 1.1 Hz), 126.1 (d, J = 7.7 Hz), 64.3, 60.8, 56.0 (d, J = 20.5 Hz), 53.3, 32.3 (d, J = 1.9 Hz), 25.8 (d, J = 3.6 Hz), 19.6 (d, J = 28.5 Hz), 16.0 (t, J = 6.6 Hz), 14.3, 10.2; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2975, 2917, 2872, 1716, 1635, 1607, 1445, 1368, 1321, 1271, 1180, 1105, 1028, 1003, 980, 930, 857, 826, 763, 712; MS (70 eV, EI) m/z 436 [M^+] (16), 408 (12), 390 (13), 363 (22), 254 (100), 282 (20), 214 (13), 209 (29), 181 (16); HRMS (EI) calcd for $C_{23}H_{33}O_6P$ 436.2015, found 436.2005.

3-(4-Cyanophenyl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Diethyl Phosphate (23i). The bicyclic enol phosphate **20** (288 mg, 1.0 mmol) reacted at 25 °C for 30 min according to TP1 and was then transmetalated according to TP2. $Pd(dba)_2$ (11.3 mg, 2 mol %), P(2-furyl)$_3$ (9.3 mg, 4 mol %), and 4-iodobenzonitrile (298 mg, 1.3 mmol) were then added to the reaction mixture. The resulting mixture was stirred at 25 °C overnight, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 3:1) furnished the compound **23i** (227 mg, 0.58 mmol, 58%) as a yellowish oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.58−7.52 (m, 4 H), 4.16−3.87 (m, 4 H), 2.66 (d, J = 3.64 Hz, 1 H), 2.05−1.95 (m, 1 H), 1.79−1.65 (m, 2 H), 1.36−1.23 (m, 1 H), 1.25 (td, J = 7.1 Hz, J = 1.2 Hz, 3 H), 1.14 (td, J = 7.1 Hz, J = 1.2 Hz, 3 H), 1.13 (s, 3 H), 0.94 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8 (d, J = 12.1 Hz), 139.0 (d, J = 3.1 Hz), 131.9, 127.2 (d, J = 1.4 Hz), 125.3 (d, J = 7.9 Hz), 119.2, 109.3, 64.4 (t, J = 4.5 Hz), 56.2 (d, J = 1.4 Hz), 55.8, 53.1, 32.3 (d, J = 2.3 Hz), 25.6 (d, J = 3.6 Hz), 19.3 (d, J = 47.0 Hz), 16.0 (q, J = 7.0 Hz), 10.2; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2976, 2927, 2854, 2227, 1633, 1605, 1444, 1381, 1351, 1277, 1118, 1032, 1004, 963, 913, 844, 750; MS (70 eV, EI) m/z 389 (12) [M^+], 235 (20), 220 (23), 207 (100), 192 (16), 167 (19), 155 (17), 140 (3), 127 (6); HRMS (EI) calcd for $C_{21}H_{28}NO_4P$ 389.1756, found 389.1742.

Diethyl 3-(3-Methoxyphenyl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl Phosphate (23j). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4 and was then transmetalated according to TP2. $Pd(OAc)_2$ (4.5 mg, 2 mol %), S-Phos (16.5 mg, 4 mol %), and 3-bromoanisole (281 mg, 1.5 mmol) were then added to the reaction mixture. The resulting mixture was stirred at 25 °C overnight, quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/EtOAc = 3:1) furnished the compound **23j** (273 mg, 0.69 mmol, 69%) as a yellowish oil: ^1H NMR ($CDCl_3$, 600 MHz) δ = 7.21 (t, J = 7.9 Hz, 1H), 7−07−7.02 (m, 2H), 6.73 (dd, J = 7.9 Hz, J = 2.2 Hz, 1H), 4.11−3.90 (m, 4H), 3.81 (s, 3H), 2.65 (d, J = 3.7 Hz, 1H), 2.13 (brs, 1H), 1.99−1.94 (m, 1H), 1.70 (t, J = 6.3 Hz, 2H), 1.35−1.27 (m, 1H), 1.22 (td, J = 7.2 Hz, J = 1.0 Hz, 3H), 1.15 (td, J = 7.2 Hz, J = 1.0 Hz, 3H), 1.13 (s, 3H), 0.97 (s, 3H), 0.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ = 159.4, 150.7 (d, J = 12.0 Hz), 135.7 (d, J = 2.8), 129.0, 126.3 (d, J = 7.6 Hz), 119.4, 112.4, 112.2, 64.2, 55.7, 55.5, 55.2, 53.5, 32.4, 25.8 (d, J = 3.7 Hz), 19.5 (d, J = 43.8 Hz), 15.9, 10.3; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2953, 1636, 1597, 1483, 1271, 1161, 1129, 1025, 1003, 960, 922, 875, 784, 686; MS (70 eV, EI) m/z 394 (22) [M^+], 240 (30), 225 (33), 212 (100), 197 (17); HRMS (EI) calcd for $C_{21}H_{31}O_5P$ 394.1909, found 394.1908

4-[(*E*)-(4,7,7-Trimethyl-3-oxobicyclo[2.2.1]hept-2-ylidene)methyl]-benzonitrile (25a). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, 4-cyanobenzaldehyde (144 mg, 1.1 mmol) was added, and the reaction mixture was slowly warmed to 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 3:1) furnished the compound **25a** (191 mg, 0.72 mmol, 72%) as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ = 7.65 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.18 (s, 1H), 3.03 (d, J = 4.5 Hz, 2H), 2.25−2.13 (m, 1H), 1.86−1.76 (m, 1H), 1.63−1.47 (m, 2H), 1.02 (s, 3H), 1.00 (s, 3H), 0.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 207.4, 145.1, 140.3, 132.3, 130.09, 125.1, 118.6, 111.8, 57.1, 49.2, 46.6, 30.4, 25.9, 20.6, 18.2, 9.2; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 3436, 2959, 2228, 1724, 1648, 1504, 1324, 1295, 1064, 1016, 837; MS (70 eV, EI) m/z 265 (100) [M^+], 250 (58), 222 (57), 183 (59), 154 (54); HRMS (EI) for $C_{18}H_{19}NO$: (265.1467) 265.1492.

(3*E*)-3-(4-Bromobenzylidene)-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-one (25b). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, 4-bromobenzaldehyde (204 mg, 1.1 mmol) was added, and the reaction mixture was slowly warmed to 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether (3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 4:1) furnished the compound **25b** (220 mg, 0.68 mmol, 68%) as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ = 7.50 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.14 (s, 1H), 3.03 (d, J = 4.0 Hz, 1H), 2.22−2.09 (m, 1H), 1.84−1.73 (m, 1H), 1.59−1.46 (m, 2H), 1.02 (s, 3H), 0.99 (s, 3H), 0.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 207.9, 142.8, 134.6, 131.9, 131.1, 126.2, 122.8, 57.1, 49.2, 46.7, 30.6, 25.9, 20.6, 18.3, 9.2; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 3420, 2957, 1720, 1641, 1586, 1491, 1323, 1071, 1064, 1008, 796; MS (70 eV, EI) m/z 320 (100) [M^+], 318 (98) [M^+], 303 (37), 275 (22), 249 (19), 236 (38), 196 (21), 128 (37); HRMS (EI) calcd for $C_{17}H_{19}OBr$ 318.0619, found 318.0621

(3*E*)-3-(Cyclohexylmethylene)-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-one (25c). The bicyclic enol phosphate **21** (367 mg, 1.0 mmol) was reacted at 25 °C for 2 h according to TP4. The reaction mixture was cooled to −20 °C, cyclohexylcarbaldehyde (123 mg, 1.1 mmol) was added, and the reaction mixture was slowly warmed to 25 °C. The resulting mixture was then quenched with a satd aq NH_4Cl solution (30 mL), extracted with diethyl ether

(3 × 50 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/Et_2O = 4:1) furnished the compound **25c** (173 mg, 0.70 mmol, 70%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 6.18 (d, J = 8.9 Hz, 1H), 2.67 (d, J = 4.4 Hz, 1H), 2.22−2.10 (m, 1H), 2.03−1.93 (m, 1H), 1.72−1.56 (m, 6H), 1.42−1.07 (m, 7H), 0.93 (s, 3H), 0.92 (s, 3H), 0.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 208.0, 141.0, 135.5, 57.7, 47.7, 46.0, 37.99, 32.3, 32.2, 30.09, 26.8, 25.8, 25.5, 20.5, 18.3, 9.2; IR (ATR) $\tilde{\nu}$ (cm^{-1}) 2848, 1725, 1662, 1446, 1257, 1109, 1065, 940; MS (70 eV, EI) m/z 246 (95) [M^+], 231 (98), 218 (81), 203 (100), 95 (94); HRMS (EI) calcd for $C_{17}H_{26}O$ 246.1984, found 246.1963.

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Supporting Information Available: NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.