JOC*Note*

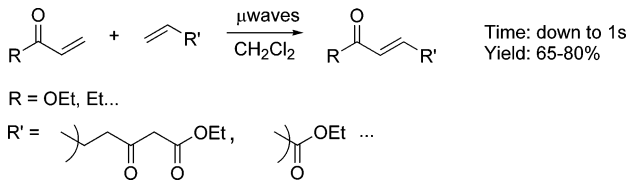
Cross-Metathesis Assisted by Microwave Irradiation

Frédéric C. Bargiggia and William V. Murray*

Johnson & Johnson Pharmaceutical Research and Development L.L.C., 1000 Route 202, P.O. Box 300, Raritan, New Jersey 08869

wmurray@prdus.jnj.com

Received July 14, 2005

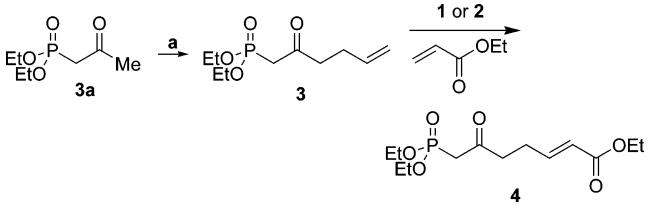


Microwave irradiation effectively accelerates cross-coupling metathesis reactions between deactivated olefins. Reactions have been carried out with the phosphine-free Hoveyda−Grubbs catalyst and the "second generation Grubbs' catalyst." While there have been reports that a "*microwave effect*" is observed in various transformations, the accelerations we observe are due to the efficient and rapid heating and increased pressure in the microwave apparatus.

Over the past two decades, metathesis reactions have been effectively utilized in organic and polymer synthesis.[1] Microwave-assisted reactions have also received considerable attention over the past few years. Microwave irradiation provides a practical and rapid way to reach reaction high temperatures. Use of microwave irradiation has enabled many practical advances, most notably, in aryl ring coupling reactions.[2] A few studies on microwave-assisted metathesis have been reported, but most refer to ring-closing metathesis.[2d−i]

The straightforward preparation of phosphonates such as **4** were key to our continued studies on aza-Diels−Alder reactions.[3] This type of ester can be assembled by a cross-metathesis reaction between a terminal olefin and an acrylate ester (Scheme 1). For this purpose, the phosphonate **3** was synthesized from the dianion of **3a** (Scheme 1).[4] A subsequent cross-metathesis reaction between **3** and ethyl acrylate afforded the desired phosphonate **4** (Scheme 1).

SCHEME 1. Cross-Coupling Metathesis with a Ketophosphonate[a]



[a] Key: (a) THF, NaH at 0 °C, then *n*-BuLi at 0 °C/allyl iodide.

In our hands, the cross-coupling between olefin **3** and excess ethyl acrylate does not proceed to completion at room temperature. When the coupling of **3** with ethyl acrylate is attempted using the "second generation Grubbs' catalyst" **1** (Figure 1), a 46% yield is achieved.[5a]

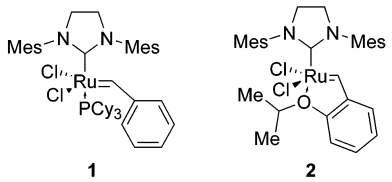


FIGURE 1. Metathesis catalysts.

Phosphine-free Hoveyda−Grubbs **2** affords a 30% yield for the same reaction[5b] (entries 1a and 2a, Table 1). When catalyst **1** is utilized at reflux in 1,2-dichloroethane, the reaction of **3** with ethyl acrylate is complete after 2 h in 70% yield. Catalyst **2** requires 6 h at reflux in dichloroethane and proceeds in 80% yield (entries 1b and 2b, Table 1). Olefin **6** is prepared by allylation of the dianion of ethylacteoacetate **5**. When olefin **6** and ethyl acrylate are subjected to cross-metathesis conditions using **1** or **2** at room temperature, the reaction does not proceed. When **6** is subjected to the reaction conditions used for **3**, the yields and the level of conversion are similar (Scheme 2). When the cross-metathesis of ethyl hept-7-enoate **8** with ethyl acrylate using catalyst **2** is carried out at room temperature, the conversion is complete in less than 2 h, in 83% yield (Scheme 2b).

(1) (a) Grubbs, R. H. *Handbook of metathesis*; Wiley-VCH: Weinheim, 2003; Vols. 1−3. (b) For reviews on metathesis, see: Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18−29. Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012−3043. Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450. Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117−7140. (c) For reviews on cross-metathesis, see: Chatterjee, A. K.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3171−3174. Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58−71. Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360−11370.

(2) (a) Loupy, A. In *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, 2002. (b) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225−9283. (c) Hayes, B. L. *Aldrichim. Acta* **2004**, *37*, 66−77. (d) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. *Org. Lett.* **2002**, *4*, 1567−1570. (e) Yang, C.; Murray, W. V.; Wilson, L. J. *Tetrahedron Lett.* **2003**, *44*, 1783−1786. (f) Salim, S. S.; Bellingham, R. K.; Brown, R. C. D. *Eur. J. Org. Chem.* **2004**, 800−806. (g) Appukkuttan, P.; Dehaen, W.; Van Der Eycken, E. *Org. Lett.* **2005**, *7*, 2723−2726. (h) Comer, E.; Organ, M. G. *J. Am. Chem. Soc.* **2005**, *127*, 8160−8167. (i) Garbacia, S.; Desai, B.; Lavastre, O.; Kappe, O. C. *J Org. Chem.* **2003**, *68*, 9136−9139. (j) De La Hoz, A.; Díaz-Ortiz Á.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164−178.

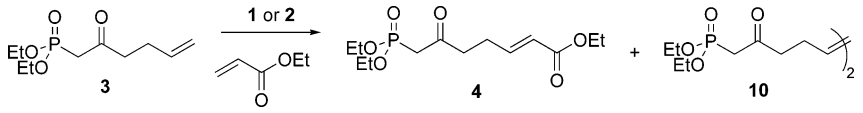
(3) (a) François, D.; Maden, A.; Murray, W. V. *Org. Lett.* **2004**, *6*, 1931−1934. (b) For reviews on aza-Diels−Alder reactions, see: Weinreb, S. M.; Staib R. R. *Tetrahedron* **1982**, *38*, 3087−3128. Boger D. L. *Tetrahedron* **1983**, *39*, 2869−2939. Behforouz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259−5288. Buonora, P.; Olsen J. C.; Oh, T. *Tetrahedron* **2001**, *57*, 6099−6138. Jayakumar, S.; Ishar, M. P. S.; Mahajan, M. P. *Tetrahedron* **2002**, *58*, 379−471.

(4) Grieco, P. A.; Pogonowski, C. S. *J. Am. Chem. Soc.* **1973**, *95*, 3071−3072.

(5) (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956. (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179

10.1021/jo0514624 CCC: $30.25 © 2005 American Chemical Society
Published on Web 10/20/2005

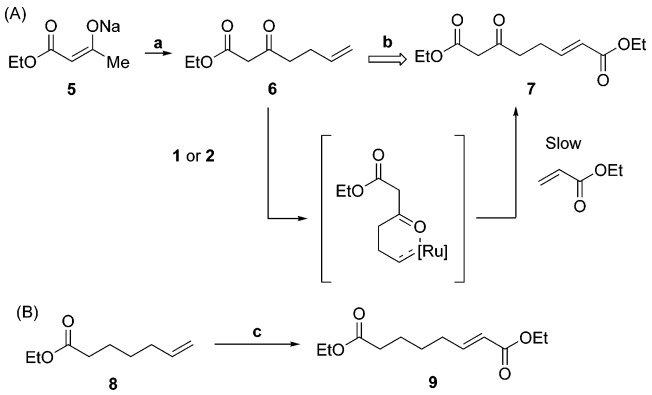
TABLE 1. Cross-Coupling Metathesis between Ethyl Acrylate and β-Ketophosphonate in Dichloromethane under Classical and Microwave Conditions



			microwave irradiation			classical conditions	
entry	catalyst[a]	ethyl acrylate (equiv)	conditions[b]	yield[c] of **4** (%)	yield[c] of **10** (%)	conditions	yield[c] of **4** (%)
1a	**1** (10)	4	100 °C/15min	70		rt/24 h	46 (5.3/1)[d]
1b						reflux/2 h	70
2a	**2** (10)	4	100 °C/15min	79		rt/24 h	30 (1.2/1)[d]
2b						reflux/6 h	80
3	**1** (10)	1.1	100 °C/15min	30 (4/1)[d]			
4	**2** (10)	1.1	100 °C/15min	65			
5	**1** (10)	1.1	100 °C/1min	30 (4/1)[d]			
6	**2** (10)	1.1	100 °C/1min	66			
7	**2** (10)	1.1	100 °C/10s	62	traces		
8	**2** (5)	1.1	100 °C/15min	81	traces		
9	**2** (1)	1.1	100 °C/15min	50	10		
10	**2** (10)	1.1	150 °C[e]/1 s	72			
11	**2** (10)	1.1	60 °C/15min	51	8		

[a] Catalyst proportion in mol %. [b] The time indicated does not consider ramp up (which requires about 30 s to reach 100 °C). [c] Isolated yields. [d] Crude NMR ^{1}H ratio between **4** and **3**. [e] In this case, 1,2-dichlorethane was used as solvent instead of dichloromethane.

SCHEME 2. Cross-Metathesis with an Olefin Bearing a γ,β-Dicarbonyl Grouping[a]



[a] Key: (a) THF, *n*-BuLi, 0 °C then allyl iodide (70%); (b) catalyst **2**, 10% per mol, ethyl acrylate (4 equiv), dichloromethane, 24 h (33% yield at rt (with 1/1 crude ^{1}H NMR ratio between **7** and **6**) and 64% yield (100% conversion in 2 h) at reflux); (c) catalyst **2**, ethyl acrylate (4 equiv), dichloromethane, rt, 2h, 83% yield.

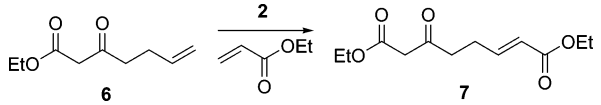
The reduced reactivity of these cross-couplings, where there is an β dicarbonyl grouping γ to the olefin, may be due to the ability of the carbonyl to chelate the catalyst when it is inserted in the terminal double bond of the reactant (Scheme 2). This intermediate is stable and can dramatically slow the reaction rate. Fürstner and Langemann have previously described this "unproductive chelated form."[6] One potential approach to circumvent this problem is the addition of 0.3 equiv of titanium(IV) isopropylate.[6] In fact, when the cross-coupling of **6** with ethyl acrylate was carried out as above with 0.3 equiv of titanium(IV) isopropylate, it reached complete conversion in 12 h at room temperature (77% yield).

The coupling between olefin **3** and ethyl acrylate has been carried out under microwave conditions with a dramatic increase in the rate of cross-coupling. When the reactions are run under microwave irradiation, using 4 equiv of ethyl acrylate and 10 mol % of metathesis catalyst **1** or **2** at 100 °C, the reaction is complete in less than 15 min. The yields are 70% with catalyst **1** and 79% with catalyst **2** (entries 1a and 2a, Table 1). An identical cross-coupling, using catalyst **2** in dichloromethane at reflux requires 6 h and proceeds in 80% yield. With catalyst **1** in dichloromethane at reflux, the cross coupling proceeds in 70% yield after 2 h (entry 1b, Table 1). It is clear that the higher reaction rates are driven by the ability to reach higher temperatures rapidly in the microwave apparatus. In addition to increased reaction rates, the microwave reaction can be carried out with significantly less ethyl acrylate (entries 3−11, Table 1). The rate enhancement is more pronounced for catalyst **2** than **1**. The reaction using **2** proceeds using a 1 min program in 66% yield, while catalyst **1** affords a 33% yield without complete conversion under similar conditions (Entries 5 and 6, Table 1). From these preliminary results, it appears that catalyst **2** may be more suitable for cross-coupling metathesis under microwave conditions. Using **2,** we can ultimately reduce the programmed peak reaction time to 10 s. This preparation affords a 62% yield of cross-coupled product with trace amounts of **10** present (entry 7, Table 1). The concentration of catalyst **2** could also be reduced to 1 mol % affording complete consumption of starting material and a yield of 50% (entry 9, Table 1). When 1 mol % of **2** is used, all the starting materials are consumed, but 10% of **10** appears in the product mixture. If the reaction temperature is increased to 150 °C using a 1 s peak program, the reaction proceeds to completion in 72% yield (entry 10, Table 1). At 60 °C, the reaction requires 15 min to reach completion (entry 11, Table 1).

Olefin **6** was subjected to cross-metathesis under microwave conditions (Table 2). As expected, microwave irradiation dramatically increases the rate of the reaction. Using 10 mol % of **2**, 1.1 equiv of ethyl acrylate and

(6) Fürstner, A.; Langemann K. *J. Am. Chem. Soc.* **1997**, *119*, 9130−9136.

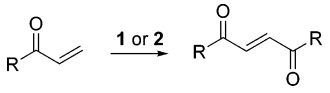
TABLE 2. Microwave Enhanced Cross-Coupling Metathesis between Ethyl Acrylate and γ-Keto Olefins



entry	catalyst[a] (%)	ethyl acrylate (equiv)	time[b]	T (°C)	yield[c] (%)
1	**2** (10)	1.1	15 min	100	75
2	**2** (1)	1.1	15 min	100	59
3	**2** (10)	1.1	10 s	100	71

[a] mol %. [b] The time indicated does not include ramp up time (which requires 30 s for 100 °C); see the Supporting Information. [c] Isolated yields.

TABLE 3. Homo-Cross-Coupling Metathesis between Acrylates or Vinyl Ketones under Microwave Irradiation



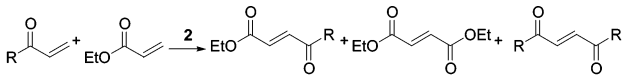
			microwave irradiation		classical conditions	
entry	catal[a] (%)	R	condns[b]	yield[c] (%)	condns	yield[c] (%)
1	**1** (5)	EtO	100 °C/15 min	19 (1/2)[d]	rt/24 h	20 (1/2)[d]
2	**1** (5)	EtO	100 °C/1 h	25 (1/1)[d]		
3	**2** (5)	EtO	100 °C/15 min	66	rt/24 h	18 (1/2)[d]
4	**2** (2.5)	EtO	100 °C/15 min	63		
5	**2** (0.5)	EtO	100 °C/15 min	23 (1/1)[d]		
6	**2** (5)	EtO	100 °C/1 min	20 (1/1.5)[d]		
7	**2** (5)	*t*-BuO	100 °C/15 min	87		
8	**2** (5)	Et	100 °C/15 min	>99		
9	**2** (5)	NH_2	100 °C/15 min	87		
10	**2** (2.5)	NH_2	100 °C/15 min	80		
11	**2** (0.5)	NH_2	100 °C/15 min	63		
12	**2** (5)	NMe_2	100 °C/15 min	<5		

[a] mol %. [b] The time indicated does not include ramp up time (which takes 30 s for 100 °C); see the Supporting Information. [c] Isolated yields. [d] Crude NMR ^{1}H ratio between the product (fumarate) and the starting material (acrylate).

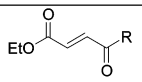
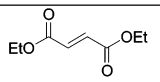
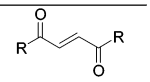
a 15 min program, the reaction proceeds to completion in 75% yield (entry 1, Table 2). With 1% of catalyst **2** under similar conditions, it proceeds to completion in 59% yield (entry 2, Table 2).

Grubbs described a study on the cross-coupling metathesis between two deactivated olefins which required 3 h at reflux in dichloromethane to reach completion.[7a] This led us to examine the cross-coupling of ethyl acrylate to diethyl fumarate. We found that after 24 h at room temperature neither **1** or **2** afforded more than a 20% of the fumarate (entries 1 and 3, Table 3). Using **2** under microwave conditions and a 100 °C program, the conversion to diethyl fumarate is complete in 15 min affording a 66% yield (entry 3, Table 3). Under similar conditions, the *tert*-butyl acrylate ester cross-coupling proceeds to di-*tert*-butyl fumarate in 87% yield (entry 7, Table 3). Using a 100 °C program for 15 min and catalyst **2** the ethyl vinyl ketone cross coupling proceeds to *E*-3,6-dioxo-4-octene in quantitative yield (entry 8, Table 3). Acrylamide is also highly reactive with catalyst load as low as 0.5%. The reaction proceeds to completion in 80% and 63% yields using 0.025 and 0.005 equiv of catalyst **2** respectively (entry 9−11, Table 3). This high conversion is probably driven by the precipitation of the fumaric acid diamide from the mixture. The precipitation also lowers the possibility of decomposition of the product. *N*,*N*-Dimethylacrylamide does not react at all (entry 12, Table 3). We believe this is due to the dimethylamino intermediate forming a more stable chelate than the primary amine.[7b]

TABLE 4. Hetero-Cross-Coupling Ratios of Acrylates or Vinyl Ketones under Microwave Irradiation



Conditions: dichloromethane, microwave 15 minutes at 100°C and 10% per mole of catalyst.

Entry	(eq)	 (Yield[a] %)	 (Yield[a] %)	 (Yield[a] %)
1	R = t-BuO (1)	2 (32)	1 (11)	1 (9)
2	R = Et (1)	5 (36)	2 (16)	1 (7)
3	R = Et (0.25)	6 (45)	2.5 (20)	1 (8)
4	R = NH_2 (1)	-	1 (35)	1 (37)

[a] Isolated yield. The ratios were calculated from the ^{1}H NMR of the crude using anisol or 1,2-xylene as an internal standard.

Hetero-cross-coupling metathesis between ethyl acrylate and a deactivated double bond can also be carried out under microwave irradiation (Table 4). When a 1/1 mixture of ethyl acrylate and *tert*-butyl acrylate is treated with microwaves in the presence of catalyst **2**, the statistical distribution 1/1/2 (diethyl fumarate)/(di-*tert*-butyl fumarate)/(*tert*-butyl ethyl fumarate) is observed (entry 1, Table 4). When a 1/1 mixture of ethyl vinyl ketone and ethyl acrylate is treated under microwave conditions with catalyst **2**, a 1/2/5 distribution {(diethyl fumarate)/(*E*-3,6-dioxo-4-octene)/(ethyl *E*-4-oxo-2-hexenoate) is observed (entry 2, Table 4). When a 1/4 mixture ethyl vinyl ketone/ethyl acrylate is irradiated the ratio becomes 2.5/1/6 (diethyl fumarate)/(*E*-3,6-dioxo-4-octene)/(*E*-ethyl 4-oxo-2-hexenoate) (entry 3, Table 4). When a vinyl ketone and an acrylic ester are mixed together in the presence of the metathesis catalyst, the ruthenium complex should insert into the double bond of the vinyl ketone before the olefin of ethyl acrylate. In this case, the quantity of free ethyl ester remaining is higher than that of the vinyl ketone. If this were the case, the cross-coupling should proceed favoring the mixed dimer. While it was possible that secondary cycloaddition reactions of the dioxooctene reduce the level of diketone, we see no evidence of those products by ^{1}HNMR or mass spec. When a 1:1 mixture of acrylamide and ethyl acrylate is irradiated, no traces of the hetero dimer were observed. Only the fumaric acid diamide in 35% yield and the diethyl fumarate in 37% yield were isolated (entry 4, Table 4).

Beyond the thermal side of microwave irradiation, a number of investigators have reported nonthermal effects.[2j] Kiddle et al proposed that there is a nonthermal effect in ring-closing metathesis.[2d] To study this hypothesis, we have carried out reactions in parallel under microwave conditions and in a sealed vial heated in an oil bath. When olefin **6** is irradiated or heated in a sealed tube

(7) (a) Choi, T. L.; Lee, C. W.; Chatterjee, A. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 10417−10418. (b) Choi, T. L.; Chatterjee, A. K.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2001** *40*, 1277−1279.

with ethyl acrylate in dichloromethane using 10% of **2** the difference in conversion and yield is not notably different. Likewise, when a solution of ethyl acrylate and 5% of **2** was irradiated or heated in dichloroethane in a sealed tube, the yield and conversion were similar. In these two cases, the difference between classical and microwave conditions was not significant. Garbacia came to similar conclusions in studies on ring-closing metathesis.[2i] In our studies, the rate acceleration seems to be due to the high temperature, higher pressure, and the ease to which microwave irradiation reaches them.

In conclusion, microwave irradiation is a convenient way to generate high temperatures and somewhat elevated pressures (4−5 Barr) rapidly. This can drive the cross-metathesis reaction to proceed in short reaction times with low catalyst load. In the case of coupling between a terminal olefin and an unactivated double bond or between two unactivated double bonds the yields or the selectivity of the reactions are not changed.

Experimental Section

General Procedure for Cross-Metathesis under Microwave Irradiation. To a solution of olefin in dichloromethane was added the acrylate ester (or vinyl ketone) followed by the catalyst. To ensure a homogeneous system, all of the batches were prestirred for 15 s before the irradiations were initiated. The vial was sealed and irradiated in a microwave reactor at the desired temperature for the appropriate time (see Tables 2−4). All of the microwave irradiations were carried out with a Personal Chemistry, Emrsy Optimiser 1−300 W. All of the experiments were carried out at a 10^{-1}M concentration. The program information is available in the Supporting Information. When the vial was removed from the apparatus, the solvent was evaporated under vacuum, and the crude was analyzed by ^{1}H NMR and subsequently purified via silica gel chromatography.

Diethyl (2-Oxohex-5-enyl)phosphonate 3. To a suspension of sodium hydride in 60% mineral oil (480 mg, 24.00 g/mol, 1 equiv) in dried THF (0.4 M) was added, at 0 °C, the diethyl (2-oxopropyl)phosphonate **3a** (3.8 mL, 194.17 g/mol, 1 equiv). The resulting mixture was stirred for 1 h at 0 °C. Then, a solution of *n*-butyllithium in hexanes (8.8 mL, 2.5 M, 1.1 equiv) was added dropwise to the mixture at 0 °C and stirred for 1 h at 0 °C. The allyl iodide (2.2 mL, 167.98 g/mol, 1.2 equiv) was then added, the resulting mixture was allowed to reach room temperature and stirred during 3 h. The reaction was quenched with 5% aqueous HCl, and the product was extracted with chloroform. The system was dried over $MgSO_4$, and the solvents were removed under vacuum. The crude was purified by silica gel chromatography to afford pure **3** in 75% yield.

$C_{10}H_{19}O_4P$. Mol wt: 234.23 g/mol. ^{1}H NMR (300 MHz $CDCl_3$): δ 5.81 (ddt; ^3J = 16.9, 10.2, 6.5 Hz; 1H); 5.05 (dd, ^3J = 16.9, 1.5 Hz; 1H); 4.98 (dd, ^3J = 10.2, 1.5 Hz; 1H); 4.15 (dq; ^3J = 7.2, 7.2 Hz; 4H); 3.09 (d; ^2J_P = 22.8 Hz; 2H); 2.74 (t; ^3J = 7.2 Hz; 2H); 2.34 (pq; ^3J = 7.2 Hz; 2H); 1.34 (t; ^3J = 7.2 Hz; 6H). **^{13}C NMR** (75.45 MHz; $CDCl_3$): δ 200.0 (C); 135.9 (CH); 114.3 (CH_2); 61.6 (CH_2); 61.5 (CH_2); 42.0 (CH_2), 41,4 (d; ^2J_P = 126 Hz; CH_2); 26.5 (CH_2); 15.4 (CH_3); 15.3 (CH_3). IR: ν^{-1} 2980; 2910; 1720; 1640; 1400; 1260; 1020; 960. MS *m/z* (relative intensity): 235 M + H$^+$ [27]; 257 M + Na$^+$ [7]; 468 2M + Na$^+$ [100]. Anal. Calcd: C, 51.28; H, 8.18. Found: C, 51.65; H, 8.32. HRMS: calcd 235.1099, found 235.1111.

Ethyl 5-Oxohept-2-enoate 6. To a solution of enolate (3 g, 152.13 g/mol, 1 equiv) in dried THF (100 mL, 0.2 M) was added dropwise, at 0 °C, *n*-butyllithium in hexanes (8.7 mL, 2.5 M, 1.1 equiv). The allyl iodide (2.0 mL, 167.98 g/mol, 1.1 equiv) was then added, and the resulting mixture was allowed to reach room temperature and stirred for 1.5 h. The reaction was quenched with a saturated solution of ammonium chloride, and the product was extracted 3 times with diethyl ether. The organic layers were combined, washed with brine, and dried over $MgSO_4$, and the solvents were removed under vacuum. The crude was purified by silica gel chromatography to afford pure **6** in 70% yield.

$C_9H_{14}O_3$. Mol wt: 170.21 g/mol. ^{1}H NMR (300 MHz $CDCl_3$): δ 5.80 (ddt, ^3J = 16.8, 10.2, 6.5 Hz; 1H); 5.03 (dd, ^3J = 16.8, 1.5 Hz; 1H); 4.97 (dd, ^3J = 10.2, 1.5 Hz; 1H); 4.17 (q; ^3J = 7.2 Hz; 2H); 3.45 (s; 2H); 2.66 (t; ^3J = 7.2 Hz; 2H); 2.33 (pq; ^3J = 7.2 Hz; 2H); 1.27 (t; ^3J = 7.2 Hz; 3H). Enolic proton: 12.14 (s; 0.08H). ^{13}C NMR (75.45 MHz; $CDCl_3$): δ 201.6 (C); 166.6 (C); 136.2 (CH); 114.8 (CH_2); 60.6 (CH_2); 48.7 (CH_2); 41.4 (CH_2), 26.9 (CH_2); 13.5 (CH_3). IR: ν^{-1} 3080; 2980; 2920; 1750; 1730; 1710; 1640; 1410; 1370; 1320; 1240; 1030; 920. MS *m/z* (relative intensity): 171 M + H$^+$ [100]; 193 M + Na$^+$ [30]. HRMS: calcd 171.1021, found 171.1017.

Ethyl 7-(Diethoxyphosphoryl)-6-oxohept-2-enoate 4. $C_{13}H_{23}O_6P$. Mol wt: 306.29 g/mol. ^{1}H NMR (300 MHz $CDCl_3$): δ 6.92 (dt; ^3J = 15.7, 6.7 Hz; 1H); 5.84 (d; ^3J = 15.7 Hz; 1H); 4.19 (q; ^3J = 7.2 Hz; ^3J_P = 7.2 Hz; 4H); 4.14 (q; ^3J = 7.2 Hz; 2H); 3.09 (d, ^2J_P = 22.8 Hz; 2H); 2.81 (t; ^3J = 7.2 Hz; 2H); 2.49 (pq; ^3J = 7.0 Hz; 2H); 1.34 (t; ^3J = 7.2 Hz; 6H); 1.28 (t; ^3J = 7.2 Hz; 3H). Enolic proton: 12.14 (s, 0.15H). ^{13}C NMR (100.6 MHz; $CDCl_3$): δ 199.2 (C); 166.0 (C); 146.5 (CH); 121.8 (CH); 62.4 (CH_2); 62.3 (CH_2); 59.9 (CH_2), 42.1 (d; ^2J_P = 127 Hz; CH_2); 41.5 (CH_2); 25.3 (CH_2); 16.0 (CH_3); 15.9 (CH_3); 13.9 (CH_3). IR: ν^{-1} 2980; 2940; 2910, 1720; 1650; 1310; 1270; 1180; 1040. MS *m/z* (relative intensity): 307 M + H$^+$ [100]; 329 M + Na$^+$ [95]; 635 2M + Na$^+$ [60]. HRMS: calcd 307.1310, found 307.1312. Anal. Calcd: C, 50.98; H, 7.58. Found: C, 51.36; H, 7.61.

Diethyl 6-Oxo-oct-2-enedioate 7. $C_{12}H_{18}O_5$. Mol wt: 242.27 g/mol. ^{1}H NMR (300 MHz $CDCl_3$): δ 6.92 (dt; ^3J = 15.7, 6.8 Hz; 1H); 5.84 (d; ^3J = 15.7 Hz; 1H); 4.19 (q; ^3J = 7.2 Hz; 2H); 4.17 (q; ^3J = 7.2 Hz; 2H); 3.47 (s, 2H); 2.76 (t; ^3J = 7.1 Hz; 2H); 2.49 (pq; ^3J = 7.0 Hz; 2H); 1.28 (t; ^3J = 7.2 Hz; 3H); 1.27 (t; ^3J = 7.2 Hz; 3H). Enolic proton: 12.14 (s, 0.15H). ^{13}C NMR (75.45 MHz; $CDCl_3$): δ 200.5 (C); 166.3 (C); 165.2 (C); 146.2 (CH); 121.2 (CH); 60.3 (CH_2); 59.2 (CH_2); 48.2 (CH_2), 39.8 (CH_2); 24.8 (CH_2); 13.3 (CH_3); 13.2 (CH_3). IR: ν^{-1} 2970; 2920; 1710; 1650; 1310; 1270; 1190; 1040. MS *m/z* (relative intensity): 243 M + H$^+$ [58]; 260 [100]; 265 M + Na$^+$ [34]. HRMS: calcd 243.1233, found 243.1240. Anal. Calcd: C, 59.49; H, 7.49. Found: C, 59.66; H, 7.66.

Diethyl Oct-2-enedioate 9. $C_{12}H_{20}O_4$. Mol wt: 228.28 g/mol. ^{1}H NMR (300 MHz $CDCl_3$): δ 6.57 (dt; ^3J = 15.6, 6.9 Hz; 1H); 5.46 (d; ^3J = 15.6 Hz; 1H); 3.79 (q; ^3J = 6.9 Hz; 2H); 3.74 (q; ^3J = 6.9 Hz; 2H); 1.95 (t; ^3J = 7.0 Hz; 2H); 1.87 (pq; ^3J = 6.9 Hz; 2H); 1.29 (pp; ^3J = 7.0 Hz; 2H); 1.15 (pp; ^3J = 7.0 Hz; 2H); 0.90 (t; ^3J = 6.9 Hz; 3H); 0.88 (t; ^3J = 6.9 Hz; 3H). ^{13}C NMR (100.6 MHz; $CDCl_3$): δ 172.1 (C); 165.3 (C); 147.6 (CH); 120.9 (CH); 59.4 (CH_2); 59.1 (CH_2); 33.0 (CH_2); 31.0 (CH_2), 27.8 (CH_2); 23.6 (CH_2); 13.4 (CH_3); 13.3 (CH_3). IR: ν^{-1} 2980; 2930; 2870; 1720; 1650; 1400; 1270; 1180; 1040. MS *m/z* (relative intensity): 229 M + H$^+$ [100]; 71 M + Na$^+$ [7]; 328 [95]. HRMS: calcd 229.1440, found 229.1432. Anal. Calcd: C, 63.14; H, 8.83. Found: C, 62.77; H, 8.45.

Supporting Information Available: General experimental procedures, microwave programs, CAS numbers for known compounds, and ^{1}H and ^{13}C spectra for compounds **3**, **4**, **6**, **7**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0514624