JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

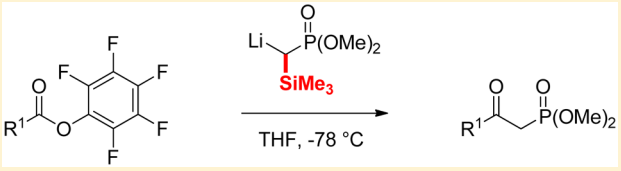
Chemoselective Synthesis of β-Ketophosphonates Using Lithiated α-(Trimethylsilyl)methylphosphonate

Simon Specklin* and Janine Cossy*

Laboratoire de Chimie Organique, Institute of Chemistry, Biology and Innovation (CBI)-UMR 8231-ESPCI ParisTech/CNRS/PSL Research University, 10 rue Vauquelin, 75231 Paris Cedex 05, France

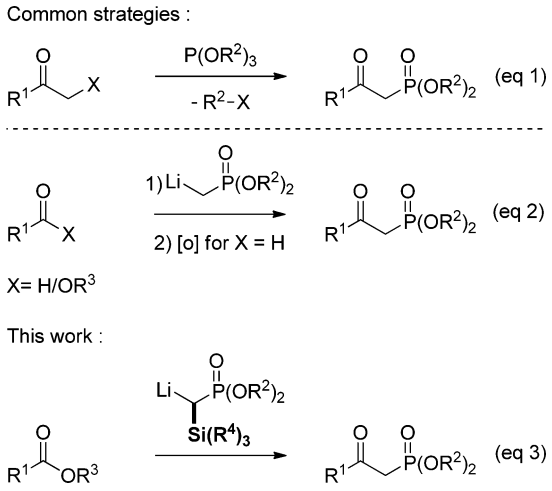
Supporting Information

ABSTRACT: A highly chemoselective synthesis of β-ketophosphonates from pentafluorophenyl esters and lithiated methyl α-(trimethylsilyl)methylphosphonate has been developed. This mild lithiated phosphonate reagent allows the synthesis of functionalized β-ketophosphonates in the presence of unactivated esters with high yields. This method has been compared with the standard lithiated methylphosphonate reagent.



The Horner−Wadsworth−Emmons (HWE) reaction[1] is a reliable and efficient method to synthesize α,β-unsaturated ketones, which is often used in total synthesis as a key step to construct *E*-olefins from functionalized reaction partners.[2] This highly stereoselective transformation requires β-ketophosphonates as precursors, making them a strategic class of compounds. The synthesis of β-ketophosphonates is generally realized according to two synthetic routes: the Michaelis−Arbuzov reaction[3] of an α-haloketone with a phosphite (Scheme 1, eq 1) or the addition of a lithiated methylphosphonate to esters, in order to directly access the β-ketophosphonates,[2c,d] or aldehydes followed by oxidation of the resulting alcohols (Scheme 1, eq 2).[2e,f] The requirement of an α-haloketone for the Arbuzov reaction and the competitive Perkov reaction makes this strategy less attractive than the condensation of lithiated methylphosphonates, particularly in the case of elaborated substrates. Although this latter method is usually preferred, several equivalents of lithiated methylphosphonate are often required to produce β-ketophosphonates in good yields. This is notably due to the latent instability of lithiated methylphosphonate toward self-condensation[4] or alkyl transfer, which could be limited by the order of addition of the reagents used for their generation.[5] Several other methods have also been developed to access β-ketophosphonates such as the Claisen condensation of several metalated methylphosphonates including copper,[6] cerium,[7] cobalt or magnesium derivatives,[8] practical procedures for the generation of the lithiated methylphosphonate reagent,[9] addition of the magnesium salt of diethyl phosphonoacetic acid to acid chlorides,[10] oxyphosphorylation of alkenes under oxidative conditions,[11] or addition of diazomethylphosphonates to aldehydes mediated by tin(II) chloride.[12] Besides the latter method, known as the Roskamp reaction which was very elegantly used on an advanced synthetic intermediate in a recent total synthesis of norhalichondrin B,[13] most of the other procedures either lead to low to moderate yields or have a limited range of applications.

Scheme 1. Synthetic Routes to β-Ketophosphonates



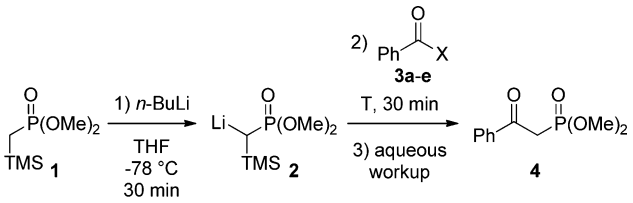
Herein, we report an efficient and chemoselective method for the generation of β-ketophosphonates based on the Claisen condensation of the lithiated α-(trimethylsilyl)methylphosphonate with activated esters (Scheme 1, eq 3). By taking advantage of the α-effect of the silicon[14] and the steric hindrance of the trimethylsilyl group, the reactivity of such phosphonate reagents could be modulated, thereby increasing the chemoselectivity and functional group tolerance in the substrates. α-(Trialkylsilyl)phosphonates have been extensively studied by Savignac et al.[15] and are mainly used as precursors of vinylphosphonates through the Peterson olefination.[16] However, to the best of our knowledge, only two reports were dealing with the use of those reagents for the synthesis of α-substituted β-ketophosphonates.[17,18] In one report, the conjugate addition of organolithium reagents to diethyl

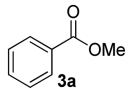
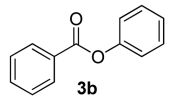
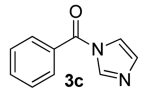
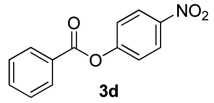
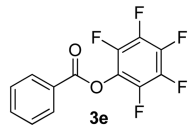
Received: January 7, 2015
Published: February 26, 2015

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

1-(trimethylsilyl)vinylphosphonate was achieved, and the resulting lithiated phosphonate intermediate was trapped with acyl chlorides to generate α-alkyl-β-ketophosphonates in good yields. However, only unfunctionalized organolithium reagents and acyl chlorides were used as partners.[17] The second report is dealing with α-(trimethylsilyl)methylphosphonate **1**, which produces β-ketophosphonates with acyl fluorides as intermediates for the HWE reaction.[18]

Table 1. Screening of Acyl Activating Groups[a]



entry	substrate **3**	T (°C)	yield (%)[b]
1	 **3a**	−78	0
2		−40	39
3		−20	78
4	 **3b**	−78	18
5	 **3c**	−78	94
6	 **3d**	−78	95
7	 **3e**	−78	99

[a]Reaction conditions: *n*-BuLi (0.66 mmol) was added to phosphonate **1** (0.69 mmol) in THF (1.5 mL) at −78 °C, and benzoic acid derivatives **3** (0.3 mmol) in THF (1.5 mL) were added after 30 min at the indicated temperature. [b]Isolated yields.

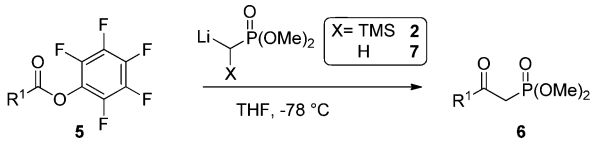
Our investigations started with the study of the reactivity of the lithiated α-(trimethylsilyl)methylphosphonate **2** (Table 1). This latter reagent was generated from α-(trimethylsilyl)methylphosphonate **1** by treatment with *n*-BuLi and then involved in a Claisen condensation with benzoic acid derivatives **3**. The electrophilic character of these derivatives was modulated by several classical acyl activating groups. When methyl ester **3a** was reacted with lithiated α-(trimethylsilyl)methylphosphonate **2**, no reaction occurred at −78 °C (Table 1, entry 1); however, raising the temperature to −40 or −20 °C afforded β-ketophosphonate **4** in 39% and 78% yield, respectively (Table 1, entries 2 and 3). It is also worth mentionning that β-ketophosphonate **4** was directly obtained after an aqueous workup with a saturated solution of ammonium chloride and that no traces of the α-trimethylsilyl-β-ketophosphonate intermediate were observed. The lability of the trimethylsilyl group after the condensation was of interest as this avoids an additional desilylation step to isolate the desired β-ketophosphonate. With a phenyl ester such as **3b** (Table 1, entry 4), a low conversion was noticed at −78 °C, suggesting that β-ketophosphonates could be obtained at that temperature if a better leaving group was used. To our delight, very high yields of β-ketophosphonate **4** were obtained at −78 °C with classical activated acyl donors derived from imidazole, *p*-nitrophenol, and pentafluorophenol (Table 1, entries 5 to 7). As the pentafluorophenyl ester **3e** led to a complete conversion and a quantitative yield of β-ketophosphonate **4**, this activating group was selected to generalize the reaction (Table 1, entry 7).

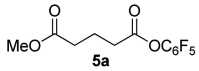
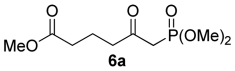
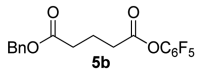
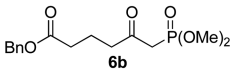
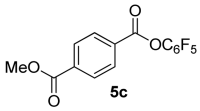
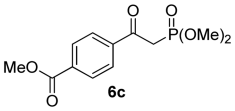
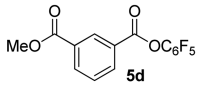
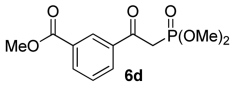
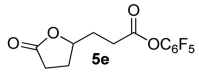
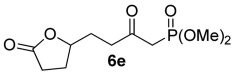
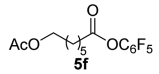
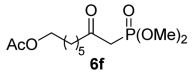
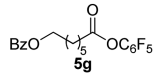
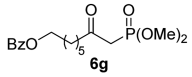
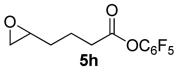
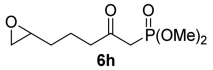
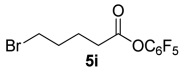
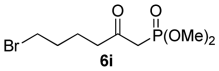
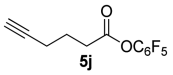
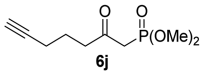
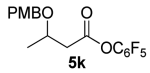
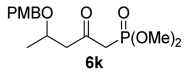
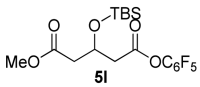
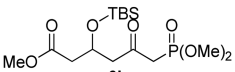
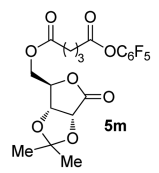
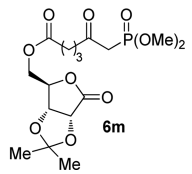
The substrate scope was evaluated with various pentafluorophenyl esters **5**, and the results are summarized in Table 2. These esters were easily prepared by a coupling reaction of the corresponding acid and the commercialy available pentafluorophenol mediated by dicyclohexylcarbodiimide (DCC) or *N*-(3-(dimethylamino)propyl)-*N*′-ethylcarbodiimide hydrochloride (EDCI). A control experiment was systematically performed with lithiated methylphosphonate **7** to assess the benefit of using the silylated phosphonate reagent **2** with activated esters. The amount of lithiated phosphonate reagent was set to 2.2 equiv, as one equivalent is directly consumed by deprotonation of the generated β-ketophosphonate. As shown in the previous screening of the acyl activating groups (Table 1), methyl ester **5a** and benzyl ester **5b** appeared to be fully compatible with reagent **2** at −78 °C, as well as methyl benzoates **5c**, **5d** and lactone **5e**. High yields of the corresponding β-ketophosphonates **6a**−**6e** were obtained. The use of lithiated methylphosphonate **7** with these substrates led to much lower yields due to incomplete conversion and formation of several unidentified byproducts (Table 2, entries 1−5). Similarly, the condensation of reagent **2** also occurred chemoselectively for substrates possessing an acetate or a benzoate (Table 2, entries 6−7). Not surprisingly, there were no significant differences between the lithiated phosphonates **2** and **7** for substrates bearing an epoxide (**5h**), a bromine (**5i**), or an alkyne (**5j**) (Table 2, entries 8−10). Since the formation of β-ketophosphonates from β-alkoxy esters could be difficult, considering the competitive β-elimination,[19] the less basic silyl phosphonate reagent **2** was tested with activated esters **5k** and **5l**. However, only a minor yield improvement was obtained with reagent **2** in comparison with lithium methylphosphonate **7** (Table 2, entries 11−12). One remarkable illustration of the chemoselectivity of lithiated phosphonate **2** is the reaction involving the functionalized sugar derivative **5m**. The corresponding β-ketophosphonate **6m** was obtained in 47% yield, whereas the reaction with lithiated methylphosphonate **7** gave rise to a complex mixture of compounds with no traces of **6m** (Table 2, entry 13).

In summary, we have described an efficient and chemoselective route to β-ketophosphonates from various pentafluorophenyl esters. It has been demonstrated that the combination of these activated esters with the lithiated silyl phosphonate reagent **2** provides a highly chemoselective method compatible with substrates containing unactivated esters. Moreover, these transformations proceed in high yields and only require a minimum amount of the lithium reagent **2**. This method constitutes an efficient tool for the introduction of a β-ketophosphonate moiety in polyfunctionalized substrates that should find applications in organic synthesis.

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

Table 2. Scope of the Reaction[a]



entry	pentafluorophenol esters **5**	phosphonate **6**	X (**2**/**7**)	yield (%)[b]
1	 **5a**	 **6a**	TMS	97
			H	45
2	 **5b**	 **6b**	TMS	92
			H	50
3	 **5c**	 **6c**	TMS	97
			H	40
4	 **5d**	 **6d**	TMS	91
			H	45
5	 **5e**	 **6e**	TMS	62
			H	28
6	 **5f**	 **6f**	TMS	81
			H	43
7	 **5g**	 **6g**	TMS	95
			H	70
8	 **5h**	 **6h**	TMS	96
			H	98
9	 **5i**	 **6i**	TMS	93
			H	81
10	 **5j**	 **6j**	TMS	90
			H	82
11	 **5k**	 **6k**	TMS	91
			H	85
12	 **5l**	 **6l**	TMS	51
			H	41
13	 **5m**	 **6m**	TMS	47
			H	0

[a]Reaction conditions: pentafluorophenyl esters **5** (0.30 mmol in 1.5 mL THF) were added to a solution of the corresponding lithiated methylphosphonate reagent **2** or **7** (0.66 mmol in 1.5 mL THF) at −78 °C. [b]Isolated yields.

EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C spectra were recorded with a 400 MHz spectrometer in $CDCl_3$ with TMS as internal standard. IR spectra were recorded on a ATX FT-IR spectrometer. High resolution mass spectra were obtained with an orbitrap mass analyzer by electrospray ionization. Low resolution mass spectra were recorded with a gas chromatography mass spectrometer with electronic impact (EI−MS). Dimethyl methylphosphonate was distilled from CaH_2 prior to use. The Grubbs-Hoveyda second generation catalyst was purchased from a chemical supplier and used as received. Compound **3c** was prepared according to a reported procedure and directly used without purification.[20]

Pentafluorophenyl Benzoate (3e)[21] (Representative Procedure for Esterification Mediated by EDCI). To a solution of benzoic acid (305 mg, 2.50 mmol) and pentafluorophenol (506 mg, 2.75 mmol, 1.1 equiv) in CH_2Cl_2 (12 mL) at 0 °C were added EDCI (719 mg, 3.75 mmol, 1.5 equiv) and DMAP (61 mg, 0.5 mmol, 0.2 equiv). The mixture was stirred at rt for 1 h, and a saturated solution of NH_4Cl was added. The mixture was extracted with EtOAc, and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (petroleum ether/EtOAc = 98:2) afforded 699 mg (97%) of the desired ester **3e** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.17 (m, 2H), 7.70 (br t, J = 7.4 Hz, 1H), 7.59−7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 141.4 (ddq$_{app}$, $^{1}J_{C-F}$ = 252 Hz, $^{2}J_{C-F}$ = 12.8 Hz and $^{3}J_{C-F}$ = 4.4 Hz, 2C), 139.5 (dtt, $^{1}J_{C-F}$ = 253 Hz, $^{2}J_{C-F}$ = 14.0 Hz and $^{3}J_{C-F}$ = 4.0 Hz), 138.0 (dm, $^{1}J_{C-F}$ ~ 254 Hz, 2C), 134.7, 130.7 (2C), 128.9 (2C), 126.9, 125.3.

1-Methyl Pentafluorophenyl Pentanedioate (5a) (Representative Procedure for Esterification Mediated by DCC). To a solution of 5-methoxy-5-oxopentanoic acid (600 mg, 4.11 mmol) and pentafluorophenol (907 mg, 4.93 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL) at 0 °C were added DCC (1.27 g, 6.16 mmol, 1.5 equiv) and DMAP (50 mg, 0.41 mmol, 0.1 equiv). After 2.5 h stirring at rt, the resulting suspension was filtered (Et_2O) and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 90:10 then 80:20) to afford 1.23 g (96%) of ester **5a** as a pale yellow oil. IR 1788, 1737, 1517,1439, 1371, 1320, 1197, 1172, 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 3H), 2.77 (t, J = 7.2 Hz, 2H), 2.48 (t, J = 7.2 Hz, 2H), 2.10 (quintet, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 168.8, 141.1 (dm, $^{1}J_{C-F}$ ~ 251 Hz, 2C), 139.5 (dm, $^{1}J_{C-F}$ ~ 253 Hz), 137.9 (dm, $^{1}J_{C-F}$ ~ 256 Hz, 2C), 125.0 (m), 51.7, 32.5, 32.2, 19.8; EI−MS m/z (relative intensity) 281 (M − MeO$^+$, 7), 253 (M − CO_2Me^+, 4), 211 (7), 184 (3), 183 (4), 155 (8), 129 (M − $C_6F_5O^+$, 61), 101 (55), 97 (12), 69 (13), 59 (100), 55 (47). HRMS calcd for $C_{12}H_9O_4F_5Na$ (M + Na$^+$): 335.03132. Found: 335.03109.

*1-Benzyl Pentafluorophenyl Pentanedioate (**5b**).* Esterification of 5-(benzyloxy)-5-oxopentanoic acid[22] (1.00 g, 4.50 mmol) mediated by EDCI yielded **5b** after purification by flash chromatography (petroleum ether/EtOAc = 95:5 then 85:15) as a colorless oil (1.53 g, 88%). IR 1788, 1735, 1518, 1455, 1418, 1385, 1315, 1162, 1099, 991, 890, 737, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.29 (m, 5H), 5.15 (s, 2H), 2.76 (t, J = 7.3 Hz, 2H), 2.52 (t, J = 7.3 Hz, 2H), 2.11 (quintet, J = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 168.8, 141.1 (dm, $^{1}J_{C-F}$ ~ 252 Hz, 2C), 139.4 (dm, $^{1}J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^{1}J_{C-F}$ ~ 256 Hz, 2C), 135.7, 128.6 (2C), 128.3, 128.2 (2C), 124.9 (m), 66.4, 32.7, 32.2, 19.8; EI−MS m/z (relative intensity) 281 (M − BnO$^+$, 1), 253 (M − CO_2Bn^+, 1), 205 (M − $C_6F_5O^+$, 5), 91 (100). HRMS calcd for $C_{18}H_{13}O_4F_5Na$ (M + Na$^+$): 411.06262. Found: 411.06276.

*1-Methyl 4-Pentafluorophenyl Benzene-1,4-dicarboxylate (**5c**).* Esterification of monomethyl terephthalate (540 mg, 3.00 mmol) in a mixture of CH_2Cl_2/THF 3:1 (20 mL) mediated by DCC yielded **5c** after purification by flash chromatography (petroleum ether/EtOAc = 98:2 then 95:5) as a colorless solid (1.021 g, 98%). mp 106−108 °C; IR 1758, 1719, 1576, 1517, 1472, 1450, 1434, 1409, 1281, 1265, 1242, 1192, 1177, 1156, 1106, 1062, 1014, 993, 980 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (br d, J = 8.7 Hz, 2H), 8.21 (br d, J = 8.7 Hz, 2H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.9, 141.2

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

(dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.7 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.9 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 135.5, 130.7 (2C), 130.6, 129.9 (2C), 125.1 (m), 52.6; EI−MS *m*/*z* (relative intensity) 315 (M − MeO$^+$, 4), 183 (2), 163 (M − $C_6F_5O^+$, 100), 135 (M − $CO_2C_6F_5^+$, 29). Anal. Calcd for $C_{15}H_7F_5O_4$: C, 52.04; H, 2.04. Found: C, 52.44; H, 2.18.

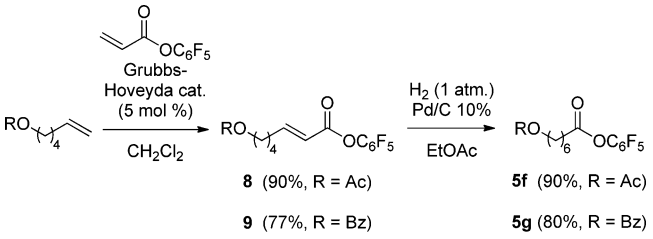
*1-Methyl 3-Pentafluorophenyl Benzene-1,3-dicarboxylate (**5d**).* Esterification of monomethyl isophthalate (360 mg, 2.00 mmol) in a mixture of CH_2Cl_2/THF 3:1 (12 mL) mediated by DCC yielded **5d** after purification by flash chromatography (petroleum ether/EtOAc = 98:2 then 95:5) as a colorless solid (640 mg, 92%). mp 97−99 °C; IR 1764, 1725, 1606, 1518, 1472, 1435, 1302, 1286, 1219, 1171, 1155, 1105, 1072, 1040, 1011, 989 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (t, *J* = 1.8 Hz, 1H), 8.39 (m, 1H), 8.37 (m, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 161.8, 141.3 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.7 (dm, $^1J_{C-F}$ ~ 254 Hz), 137.9 (dm, $^1J_{C-F}$ ~ 254 Hz, 2C), 135.5, 134.7, 131.7, 131.2, 129.2, 127.4, 125.1 (m), 52.6; EI−MS *m*/*z* (relative intensity) 315 (M − MeO$^+$, 6), 183 (2), 163 (M − $C_6F_5O^+$, 100), 135 (M − $CO_2C_6F_5^+$, 37). Anal. Calcd for $C_{15}H_7F_5O_4$: C, 52.04; H, 2.04. Found: C, 51.93; H, 2.01.

*Pentafluorophenyl 3-(5-Oxotetrahydrofuran-2-yl)propanoate (**5e**).* Esterification of 3-(5-oxotetrahydrofuran-2-yl)propanoic acid[23] (186 mg, 1.18 mmol) mediated by EDCI yielded **5e** after purification by flash chromatography (petroleum ether/Et_2O 50:50 then 30:70) as a colorless solid (333 mg, 87%). mp 75−77 °C; IR 1796, 1767, 1518, 1469, 1449, 1415, 1349, 1278, 1262, 1181, 1093, 1072, 1036, 989 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60 (m, 1H), 2.99−2.82 (m, 2H), 2.60 (dd, *J* = 9.5 Hz and *J* = 6.9 Hz, 2H), 2.43 (sextet$_{app}$, *J* = 6.9 Hz, 1H), 2.22−2.02 (m, 2H), 1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 168.7, 141.0 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.5 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 256 Hz, 2C), 124.8 (m), 78.9, 30.5, 29.4, 28.6, 27.9; EI−MS *m*/*z* (relative intensity) 184 (8), 183 (3), 167 (2), 155 (8), 141 (M − $C_6F_5O^+$, 84), 136 (7), 113 (60), 95 (20), 85 (100). HRMS calcd for $C_{13}H_9O_4F_5Na$ (M + Na$^+$): 347.03132. Found: 347.03115.

Pentafluorophenyl (2*E*)-7-(Acetoxy)hept-2-enoate (8, Scheme 2) (Representative Procedure for Cross-metathesis with Pentafluorophenyl Acrylate). To a solution of pentafluorophenyl acrylate[24] (509 mg, 2.14 mmol, 1 equiv) and hex-5-en-1-yl acetate[25] (304 mg, 2.14 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added the Grubbs-Hoveyda second generation catalyst (33 mg, 53 μmol, 0.025 equiv). After 8 h at rt, more Grubbs-Hoveyda catalyst (33 mg, 53 μmol, 0.025 equiv) was added. After a total of 23 h stirring at rt, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 95:5 then 90:10) to afford 612 mg (81%) of α,β-unsaturated ester **8** (*E*/*Z* 96/4) as a pale brown oil. This compound is contaminated by the dimer of hex-5-en-1-yl acetate (4.5 wt %, calculated by ^{1}H NMR) which could not be separated. IR 1761, 1738, 1649, 1518, 1471, 1366, 1236, 1127, 1103, 1024, 994 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dt, *J* = 15.7 Hz and *J* = 6.8 Hz, 1H), 6.09 (dt, *J* = 15.7 Hz and *J* = 1.6 Hz, 1H), 4.11 (t, *J* = 6.3 Hz, 2H), 2.38 (qd$_{app}$, *J* = 6.8 Hz and *J* = 1.6 Hz, 2H), 2.07 (s, 3H), 1.76−1.67 (m, 2H), 1.67−1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 161.9, 154.3, 141.2 (ddq$_{app}$, $^1J_{C-F}$ = 252 Hz, $^2J_{C-F}$ = 12.8 Hz and $^3J_{C-F}$ = 3.6 Hz, 2C), 139.4 (dtt, $^1J_{C-F}$ = 253 Hz, $^2J_{C-F}$ = 13.6 Hz and $^3J_{C-F}$ = 4.0 Hz), 137.3 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 125.1 (m), 118.3, 63.9, 32.1, 28.1, 24.2, 20.9; EI−MS *m*/*z* (relative intensity) 265(1), 252 (1), 237 (1), 183 (1), 169 (M − $C_6F_5O^+$, 5), 155 (2), 127 (81), 109 (12), 81 (100). HRMS calcd for $C_{15}H_{13}O_4F_5Na$ (M + Na$^+$): 375.06262. Found: 375.06251.

Pentafluorophenyl 7-(Acetoxy)heptanoate (5f, Scheme 2) (Representative Procedure for the Hydrogenation of the α,β-Unsaturated Ester). To a degassed solution of α,β-unsaturated ester **8** (306 mg, 0.87 mmol) in EtOAc (9 mL) was added palladium on carbon (10 wt %) (23 mg, 22 μmol, 0.025 equiv). The reaction mixture was stirred under an atmospheric pressure of hydrogen for 2 h at rt, the suspension was then filtered through Celite (EtOAc), and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/Et_2O = 95:5 then 90:10) to afford 277 mg (90%) of ester **5f** as a colorless oil. IR 1790, 1738, 1518, 1469, 1366, 1235, 1082, 1025, 992 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.05 (s, 3H), 1.79 (quintet$_{app}$, *J* = 7.5 Hz, 2H), 1.66 (quintet$_{app}$, *J* = 7.0 Hz, 2H), 1.51−1.37 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 169.4, 141.1 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.4 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 125.1 (m), 64.3, 33.2, 28.44, 28.36, 25.5, 24.6, 21.0; EI−MS *m*/*z* (relative intensity) 239 (1), 211 (1), 184 (2), 183 (2), 171 (M − $C_6F_5O^+$, 4), 155 (3), 129 (93), 127 (5),112 (4), 111 (52), 110 (3), 83 (48), 81 (8), 69 (21), 55 (100). HRMS calcd for $C_{15}H_{15}O_4F_5Na$ (M + Na$^+$): 377.07827. Found: 377.07825.

Scheme 2. Synthesis of 5f and 5g



*Pentafluorophenyl (2E)-7-(Benzoyloxy)hept-2-enoate (**9**, Scheme 2).* Cross-metathesis between pentafluorophenyl acrylate (596 mg, 2.50 mmol) and hex-5-en-1-yl benzoate[26] (511 mg, 2.50 mmol) using the Grubbs-Hoveyda second generation catalyst yielded **9** after purification by flash chromatography (petroleum ether/EtOAc = 95/5 then 90/10) as a colorless solid (796 mg, 77%). This compound is contaminated by the dimer of hex-5-en-1-yl benzoate (7.7 wt %, calculated by ^{1}H NMR) which could not be separated. mp 37−39 °C; IR 1764, 1708, 1651, 1518, 1470, 1451, 1335, 1315, 1273, 1140, 1103, 1071, 1051, 993, 961 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09−8.01 (m, 2H), 7.60−7.54 (m, 1H), 7.48−7.42 (m, 2H), 7.31 (dt, *J* = 15.7 Hz and *J* = 6.8 Hz, 1H), 6.10 (dt, *J* = 15.7 Hz and *J* = 1.6 Hz, 1H), 4.37 (t, *J* = 6.3 Hz, 2H), 2.42 (qd$_{app}$, *J* = 6.8 Hz and *J* = 1.6 Hz, 2H), 1.92−1.81 (m, 2H), 1.76−1.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 161.9, 154.3, 141.2 (dm, $^1J_{C-F}$ ~ 250 Hz, 2C), 139.3 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 255 Hz, 2C), 132.9, 130.2, 129.5 (2C), 128.4 (2C), 125.1 (m), 118.4, 64.3, 32.2, 28.3, 24.3. HRMS calcd for $C_{20}H_{15}O_4F_5Na$ (M + Na$^+$): 437.07827. Found: 437.07830.

*Pentafluorophenyl 7-(Benzoyloxy)heptanoate (**5g**, Scheme 2).* Hydrogenation of α,β-unsaturated ester **9** (400 mg, 0.97 mmol) yielded **5g** after purification by flash chromatography (petroleum ether/Et_2O = 95:5 then 90:10) as a pale yellow oil (322 mg, 80%). IR 1789, 1718, 1518, 1469, 1452, 1315, 1272, 1177, 1112, 1082, 1025, 992, 886, 711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−8.02 (m, 2H), 7.58−7.53 (m, 1H), 7.47−7.40 (m, 2H), 4.34 (t, *J* = 6.6 Hz, 2H), 2.68 (t, *J* = 7.3 Hz, 2H), 1.87−1.74 (m, 4H), 1.58−1.47 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 166.6, 141.1 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.4 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 253 Hz, 2C), 132.8, 130.4, 129.5 (2C), 128.3 (2C), 125.1 (m), 64.8, 33.2, 28.5 (2C), 25.7, 24.6. HRMS calcd for $C_{20}H_{17}O_4F_5Na$ (M + Na$^+$): 439.09392. Found: 439.09381.

*Pentafluorophenyl Hex-5-enoate (**10**).* Esterification of 5-hexenoic acid (685 mg, 6.00 mmol) mediated by EDCI yielded **10** after purification by flash chromatography (petroleum ether/EtOAc = 96:4) as a colorless oil (1.51 g, 90%). IR 1789, 1517, 1470, 1443, 1416, 1368, 1205, 1087, 1024, 991, 874 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.1 Hz, *J* = 10.2 Hz and *J* = 6.8 Hz, 1H), 5.12−5.02 (m, 2H), 2.68 (t, *J* = 7.3 Hz, 2H), 2.19 (q$_{app}$, *J* = 7.3 Hz, 2H), 1.88 (quintet$_{app}$, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 141.1 (ddq$_{app}$, $^1J_{C-F}$ = 252 Hz, $^2J_{C-F}$ = 12.4 Hz and $^3J_{C-F}$ = 3.6 Hz, 2C), 139.4 (dtt, $^1J_{C-F}$ = 253 Hz, $^2J_{C-F}$ = 13.6 Hz and $^3J_{C-F}$ = 3.6 Hz), 137.9 (dm, $^1J_{C-F}$ ~ 255 Hz, 2C), 136.9, 125.1 (m), 116.0, 32.7, 32.4, 23.8; EI−MS *m*/*z* (relative intensity) 184 (5), 183 (4), 167 (2), 155 (11), 136 (4), 117 (7), 97 (M − $C_6F_5O^+$, 80), 69 (100). The molecular ion of this compound is not observed by HRMS due to a very low ionization sensitivity.

*Pentafluorophenyl 4-(Oxiran-2-yl)butanoate (**5h**).* To a solution of ester **10** (300 mg, 1.07 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

m-CPBA (ca. 75 wt %, 360 mg, 1.61 mmol, 1.5 equiv). After 5 h at rt, a 25% solution of $Na_2S_2O_3$ and EtOAc was added. The layers were separated, and the organic phase was washed twice with a saturated solution of Na_2CO_3, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (pentane/EtOAc = 90:10 then 85:15) to afford 286 mg (90%) of epoxide **5h** as a colorless oil. IR 1788, 1517, 1415, 1368, 1204, 1119, 1079, 991 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.97 (dtd_{app}, J = 6.8 Hz, J = 4.3 Hz and J = 2.8 Hz, 1H), 2.83−2.70 (m, 3H), 2.51 (dd, J = 4.9 Hz and J = 2.8 Hz, 1H), 2.05−1.88 (m, 2H), 1.79 (m, 1H), 1.58 (ddt, J = 14.3 Hz, J = 8.3 Hz and J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 141.1 (ddq_{app}, $^1J_{C-F}$ = 251 Hz, $^2J_{C-F}$ = 12.4 Hz and $^3J_{C-F}$ = 3.6 Hz, 2C), 139.4 (dtt, $^1J_{C-F}$ = 253 Hz, $^2J_{C-F}$ = 13.6 Hz and $^3J_{C-F}$ = 4.0 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 254 Hz, 2C), 125.0 (m), 51.6, 46.7, 32.8, 31.4, 21.3; EI−MS *m*/*z* (relative intensity) 211 (1), 184 (5), 155 (8), 136 (4), 117 (7), 113 ($M - C_6F_5O^+$, 23), 85 (6), 83 (15), 55 (100). HRMS calcd for $C_{12}H_9O_3F_5Na$ ($M + Na^+$): 319.03641. Found: 319.03602.

*Pentafluorophenyl 5-Bromopentanoate (**5i**).* Esterification of 5-bromopentanoic acid (362 mg, 2.00 mmol) mediated by EDCI yielded **5i** after purification by flash chromatography (petroleum ether/EtOAc = 95:5 then 90:10) as a colorless oil (587 mg, 85%). IR 1788, 1516, 1471, 1416, 1362, 1256, 1238, 1142, 1094, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.46 (t, J = 6.2 Hz, 2H), 2.73 (t, J = 7.1 Hz, 2H), 2.05−1.91 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 141.1 (ddq_{app}, $^1J_{C-F}$ = 252 Hz, $^2J_{C-F}$ = 12.4 Hz and $^3J_{C-F}$ = 3.6 Hz, 2C), 139.4 (dtt, $^1J_{C-F}$ = 253 Hz, $^2J_{C-F}$ = 13.2 Hz and $^3J_{C-F}$ = 4.0 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 255 Hz, 2C), 125.0 (m), 32.5, 32.3, 31.5, 23.2; EI−MS *m*/*z* (relative intensity) 267 ($M - Br^+$, 1), 225 (1), 184 (2), 183 (2), 165 ($M^{81}[Br] - C_6F_5O^+$, 10), 163 ($M^{79}[Br] - C_6F_5O^+$, 10), 155 (6), 137 (8), 135 (9), 117 (4), 55 (100). Anal. Calcd for $C_{11}H_8BrF_5O_2$: C, 38.07; H, 2.32. Found: C, 38.17; H, 2.32.

*Pentafluorophenyl 5-Hexynoate (**5j**).* Esterification of 5-hexynoic acid (336 mg, 3.00 mmol) mediated with DCC yielded **5j** after purification by flash chromatography (petroleum ether/EtOAc = 98:2 then 95:5) as a colorless oil (790 mg, 95%). IR 3310, 1786, 1655, 1516, 1471, 1370, 1308, 1196, 1099, 1069, 991 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.84 (t, J = 7.4 Hz, 2H), 2.36 (td, J = 6.9 Hz and J = 2.6 Hz, 2H), 2.03 (t, J = 2.6 Hz, 1H), 2.00 ($quintet_{app}$, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 141.1 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.4 (dm, $^1J_{C-F}$ ~ 253 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 254 Hz, 2C), 125.0 (m), 82.4, 69.7, 31.8, 23.3, 17.6; EI−MS *m*/*z* (relative intensity) 250 (1), 216 (1), 184 (4), 183 (3), 155 (6), 117 (4), 95 ($M - C_6F_5O^+$, 100). Anal. Calcd for $C_{12}H_7F_5O_2$: C, 51.81; H, 2.54. Found: C, 51.62; H, 2.62.

*Pentafluorophenyl 3-(4-Methoxybenzyloxy)butanoate (**5k**).* Esterification of 3-(4-methoxybenzyloxy)butanoic acid[27] (1.12 g, 5.00 mmol) mediated by EDCI yielded **5k** after purification by flash chromatography (petroleum ether/EtOAc = 95:5 then 90:10) as a colorless solid (1.68 g, 86%). mp 49−51 °C; IR 1785, 1614, 1586, 1519, 1470, 1459, 1415, 1377, 1367, 1342, 1295, 1246, 1176, 1129, 1077, 1053, 1033 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 4.54 (d, J = 11.0 Hz, 1H), 4.48 (d, J = 11.0 Hz, 1H), 4.11 (m, 1H), 3.80 (s, 3H), 2.95 (dd, J = 15.4 Hz and J = 7.7 Hz, 1H), 2.76 (dd, J = 15.4 Hz and J = 5.3 Hz, 1H), 1.34 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 159.2, 141.1 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.5 (dm, $^1J_{C-F}$ ~ 254 Hz), 137.9 (dm, $^1J_{C-F}$ ~ 257 Hz, 2C), 130.1, 129.3 (2C), 125.0 (m), 113.8 (2C), 71.2, 70.8, 55.3, 41.1, 19.7. HRMS calcd for $C_{18}H_{15}O_4F_5Na$ ($M + Na^+$): 413.07827. Found: 413.07877.

*1-Methyl Pentafluorophenyl 3-(tert-Butyldimethylsilyloxy)-pentanedioate (**5l**).* A solution of 3-(*tert*-butyldimethylsilyloxy)-glutaric anhydride (490 mg, 2.00 mmol) in MeOH (8 mL) was heated at reflux for 3.5 h. After cooling to rt, the solution was concentrated under reduced pressure, the crude acid was diluted in CH_2Cl_2 (10 mL), and pentafluorophenol (443 mg, 2.41 mmol, 1.2 equiv) was added. The solution was cooled to 0 °C, and EDCI (577 mg, 3.01 mmol, 1.5 equiv) and DMAP (49 mg, 0.40 mmol, 0.2 equiv) were subsequently added. After 4.5 h of stirring at rt, a saturated solution of NH_4Cl was added, and the mixture was extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc = 90:10) to afford 724 mg (82%) of ester **5l** as a colorless oil. IR 1791, 1740, 1519, 1472, 1439, 1376, 1256, 1174, 1094, 994 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.63 ($quintet_{app}$, J = 6.2 Hz, 1H), 3.70 (s, 3H), 2.95 (m, 2H), 2.66 (d, J = 6.2 Hz, 2H), 0.86 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 168.9, 141.1 (dm, $^1J_{C-F}$ ~ 252 Hz, 2C), 139.5 (dm, $^1J_{C-F}$ ~ 254 Hz), 137.9 (dm, $^1J_{C-F}$ ~ 253 Hz, 2C), 124.9 (m), 65.6, 51.7, 41.8, 41.2, 25.5 (3C), 17.8, −4.97, −5.04. HRMS calcd for $C_{18}H_{23}O_5F_5SiNa$ ($M + Na^+$): 465.11271. Found: 465.11262.

*5-{[(3aR,4R,6aR)-2,2-dimethyl-6-oxo-tetrahydro-2H-furo[3,4-d]-[1,3]dioxol-4-yl]methoxy}-5-oxopentanoic Acid (**5m**).* To a solution of 2,3-*O*-isopropylidene-D-ribono-1,4-lactone[28] (720 mg, 3.83 mmol, 1 equiv) and glutaric anhydride (873 mg, 7.65 mmol, 2 equiv) in CH_2Cl_2 (8 mL) were added Et_3N (1.07 mL, 7.65 mmol, 2 equiv) and DMAP (47 mg, 0.38 mmol, 0.1 equiv). The mixture was stirred overnight at rt and acidified to pH 1−2 with a 1 M HCl solution, and CH_2Cl_2 was added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude acid was diluted with CH_2Cl_2 (20 mL), and pentafluorophenol (1.41 g, 7.65 mmol, 2 equiv) was added. The solution was cooled to 0 °C, and EDCI (1.47 g, 7.65 mmol, 2 equiv) and DMAP (93 mg, 0.77 mmol, 0.2 equiv) were added. After 3 h of stirring at rt, a saturated solution of NH_4Cl was added, and the mixture was extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/Et_2O 50:50 then petroleum ether/EtOAc = 60:40) to afford 1.19 g (66%) of ester **5m** as a white solid. mp 109−112 °C; $[\alpha]_D$ −27.8 (*c* 1.88, $CHCl_3$); IR 1780, 1745, 1518, 1468, 1414, 1388, 1349, 1322, 1274, 1237, 1220, 1192, 1152, 1103, 1081, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.83−4.75 (m, 2H), 4.72 (d, J = 5.7 Hz, 1H), 4.44 (dd, J = 12.4 Hz and J = 3.0 Hz, 1H), 4.26 (dd, J = 12.4 Hz and J = 2.5 Hz, 1H), 2.77 (t_{app}, J = 7.1 Hz, 2H), 2.50 (t, J = 7.3 Hz, 2H), 2.09 (quintet, J = 7.3 Hz, 2H), 1.49 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 171.4, 168.7, 141.0 (dm, $^1J_{C-F}$ ~ 250 Hz, 2C), 139.5 (dm, $^1J_{C-F}$ ~ 254 Hz), 137.8 (dm, $^1J_{C-F}$ ~ 255 Hz, 2C), 124.8 (m), 113.8, 79.4, 77.7, 75.1, 63.6, 32.2, 32.0, 26.6, 25.4, 19.5. HRMS calcd for $C_{19}H_{17}O_8F_5Na$ ($M + Na^+$): 491.07358. Found: 491.07298.

*Dimethyl (Trimethylsilyl)methylphosphonate (**1**).*[29] To a solution of diisopropylamine (15 mL, 0.10 mol) in THF (50 mL) at −20 °C was added a solution of *n*-BuLi (40 mL, 2.5 M in hexanes, 0.10 mol). The mixture was then cooled to −78 °C, and a solution of dimethyl methylphosphonate (6.20 g, 50.0 mmol) in THF (10 mL) was added. After 20 min at −78 °C, trimethylsilyl chloride (6.6 mL, 52 mmol) was added, and the mixture was warmed to 0 °C over 30 min. The mixture was then cooled to −20 °C and acidified to pH 1 by dropwise addition of a 4 M solution of HCl. The layers were separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure (bp 67−70 °C/1 mmHg) to afford 6.51 g (66%) of phosphonate **1** as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 3.70 (d, $^3J_{H-P}$ = 11.0 Hz, 6H), 1.15 (d, $^2J_{H-P}$ = 22.0 Hz, 2H), 0.17 (s, 9H).

General Procedure A: Synthesis of β-Ketophosphonates Using Lithiated Dimethyl (Trimethylsilyl)methylphosphonate Reagent 2. To a solution of dimethyl (trimethylsilyl)methylphosphonate **1** (135 μL, 0.690 mmol, 2.3 equiv) in THF (1.5 mL) at −78 °C was added *n*-BuLi (0.26 mL, 2.5 M in hexanes, 0.66 mmol, 2.2 equiv). After 30 min of stirring at −78 °C, a solution of ester **5** (0.30 mmol, 1 equiv) in THF (1.5 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 30 min, and a saturated solution of NH_4Cl was added. The mixture was extracted with EtOAc, and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired phosphonate.

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

General Procedure B: Synthesis of β-Ketophosphonates Using Lithiated Dimethyl Methylphosphonate Reagent 7. To a solution of *n*-BuLi (0.26 mL, 2.5 M in hexanes, 0.66 mmol, 2.2 equiv) in THF (1.5 mL) at −78 °C was added dimethyl methylphosphonate (75 μL, 0.69 mmol, 2.3 equiv). After 30 min at −78 °C, a solution of activated ester (0.30 mmol, 1 equiv) in THF (1.5 mL) was added dropwise. The reaction mixture was stirred for 30 min at −78 °C, and a saturated solution of NH_4Cl was added. The mixture was extracted with EtOAc, and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired phosphonate.

*Dimethyl (2-Oxo-2-phenylethyl)phosphonate (**4**).*[9a] Yield 68.2 mg (99%) with procedure A (pentane/acetone = 75:25 then 60:40); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−7.98 (m, 2H), 7.64−7.57 (m, 1H), 7.53−7.46 (t_{app}, J = 7.4 Hz, 2H), 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.65 (d, $^2J_{H-P}$ = 22.6 Hz, 2H).

*Methyl 6-(Dimethoxyphosphoryl)-5-oxohexanoate (**6a**).*[30] Yield 73.6 mg (97%) with procedure A and 33.8 mg (45%) with procedure B (pentane/acetone = 60:40 then 40:60); pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.67 (s, 3H), 3.09 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.71 (t, J = 7.1 Hz, 2H), 2.35 (t, J = 7.1 Hz, 2H), 1.91 (quintet, J = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0 (d, $^2J_{C-P}$ = 6.4 Hz), 173.4, 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 51.5, 42.8, 41.3 (d, $^1J_{C-P}$ = 128.2 Hz), 32.6, 18.5.

*Benzyl 6-(Dimethoxyphosphoryl)-5-oxohexanoate (**6b**).* Yield 90.8 mg (92%) with procedure A and 49.0 mg (50%) with procedure B (petroleum ether/acetone = 70:30 then 50:50); pale yellow oil. IR 1714, 1497, 1455, 1386, 1253, 1168, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 5.11 (s, 2H), 3.77 (d, $^3J_{H-P}$ = 11.3 Hz, 6H), 3.07 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.69 (t, J = 7.2 Hz, 2H), 2.40 (t, J = 7.2 Hz, 2H), 1.93 (quintet, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0 (d, $^2J_{C-P}$ = 6.4 Hz), 172.8, 135.8, 128.5 (2C), 128.2 (3C), 66.2, 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 42.8, 41.3 (d, $^1J_{C-P}$ = 128.2 Hz), 32.8, 18.5; EI−MS m/z (relative intensity) 221 (M − BnO^+, 31), 194 (26), 179 (23), 166 (36), 151 (51), 91 (100). HRMS calcd for $C_{15}H_{21}O_6PNa$ (M + Na^+): 351.09680. Found: 351.09624.

*Methyl 4-[2-(Dimethoxyphosphoryl)acetyl]benzoate (**6c**).* Yield 83.2 mg (97%) with procedure A and 34.3 mg (40%) with procedure B (petroleum ether/acetone = 70:30 then 60:40); colorless solid: mp 57−60 °C; IR 2955, 2911, 2849, 1717, 1673, 1572, 1503, 1435, 1420, 1405, 1260, 1209, 1189, 1140, 1109, 1043, 1019, 1002, 959 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (br d, J = 8.7 Hz, 2H), 8.06 (br d, J = 8.7 Hz, 2H), 3.96 (s, 3H), 3.79 (d, $^3J_{H-P}$ = 11.3 Hz, 6H), 3.67 (d, $^2J_{H-P}$ = 22.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3 (d, $^2J_{C-P}$ = 6.4 Hz), 166.0, 139.4, 134.3, 129.8 (2C), 128.8 (2C), 53.2 (d, $^2J_{C-P}$ = 6.8 Hz, 2C), 52.5, 37.8 (d, $^1J_{C-P}$ = 131.4 Hz); EI−MS m/z (relative intensity) 286 (M^+, 10), 255 (M − MeO^+, 8), 226 (6), 198 (6), 190 (7), 163 (100), 151 (19), 135 (23), 109 (18). HRMS calcd for $C_{12}H_{15}O_6PNa$ (M + Na^+): 309.04985. Found: 309.04940.

*Methyl 3-[2-(Dimethoxyphosphoryl)acetyl]benzoate (**6d**).* Yield 78.1 mg (91%) with procedure A and 38.7 mg (45%) with procedure B (petroleum ether/acetone = 60:40); pale yellow oil. IR 2973, 2955, 2926, 2854, 1722, 1679, 1602, 1467, 1434, 1417, 1287, 1238, 1216, 1182, 1138, 1113, 1057, 1024, 978 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (t, J = 1.8 Hz, 1H), 8.27 (dt, J = 7.8 Hz and J = 1.8 Hz, 1H), 8.21 (dt, J = 7.8 Hz and J = 1.8 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 3.97 (s, 3H), 3.80 (d, $^3J_{H-P}$ = 11.3 Hz, 6H), 3.70 (d, $^2J_{H-P}$ = 22.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0 (d, $^2J_{C-P}$ = 6.8 Hz), 166.0, 136.5, 134.5, 133.0, 130.8, 130.0, 129.0, 53.2 (d, $^2J_{C-P}$ = 6.8 Hz, 2C), 52.4, 37.5 (d, $^1J_{C-P}$ = 131.4 Hz); EI−MS m/z (relative intensity) 255 (M − MeO^+, 3), 226 (13), 190 (3), 163 (100), 151 (12), 135 (26), 119 (14), 109 (21). HRMS calcd for $C_{12}H_{15}O_6PNa$ (M + Na^+): 309.04985. Found: 309.04926.

*Dimethyl [2-Oxo-4-(5-oxotetrahydrofuran-2-yl)butyl]phosphonate (**6e**).* Yield 49.4 mg (62%) with procedure A and 22.5 mg (28%) with procedure B (petroleum ether/acetone = 70:30 then 60:40); pale yellow oil. IR 2957, 2922, 2853, 1765, 1713, 1517, 1460, 1409, 1350, 1250, 1178, 1018 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 (m, 1H), 3.80 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.12 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.84 (t, J = 7.3 Hz, 2H), 2.58−2.51 (m, 2H), 2.42−2.32 (m, 1H), 2.03 (m, 1H), 1.94−1.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6 (d, $^2J_{C-P}$ = 6.4 Hz), 176.8, 79.5, 53.1 (d, $^2J_{C-P}$ = 6.8 Hz, 2C), 37.5 (d, $^1J_{C-P}$ = 128.6 Hz), 39.8, 29.1, 28.7, 27.9; HRMS calcd for $C_{10}H_{17}O_6PNa$ (M + Na^+): 287.06550. Found: 287.06531.

*8-(Dimethoxyphosphoryl)-7-oxooctyl Acetate (**6f**).* Yield 71.5 mg (81%) with procedure A and 38.1 mg (43%) with procedure B (pentane/acetone = 65:35 then 50:50); yellow oil. IR 1733, 1715, 1462, 1367, 1239, 1184, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.04 (t, J = 6.7 Hz, 2H), 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.09 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.63 (t, J = 7.2 Hz, 2H), 2.05 (s, 3H), 1.67−1.54 (m, 4H), 1.41−127 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.8 (d, $^2J_{C-P}$ = 6.0 Hz), 171.1, 64.3, 53.0 (d, $^2J_{C-P}$ = 6.8 Hz, 2C), 43.9, 41.2 (d, $^1J_{C-P}$ = 127.8 Hz), 28.4, 28.3, 25.6, 23.1, 20.9; EI−MS m/z (relative intensity) 235 (M − OAc^+, 2), 234 (2), 221 (1), 207 (1), 193 (2), 179 (M − $C_6H_{11}O_2^+$, 19), 166 (M − $C_7H_{12}O_2^+$, 100), 151 (M − $C_8H_{15}O_2^+$, 79), 147 (8), 124 (100), 119 (9), 109 (43). HRMS calcd for $C_{12}H_{23}O_6PNa$ (M + Na^+): 317.11245. Found: 317.11184.

*8-(Dimethoxyphosphoryl)-7-oxooctyl Benzoate (**6g**).* Yield 101.3 mg (95%) with procedure A and 74.4 mg (70%) with procedure B (petroleum ether/acetone = 60:40 then 50:50); yellow oil. IR 1713, 1601, 1452, 1399, 1315, 1271, 1177, 1113, 1024 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−8.01 (m, 2H), 7.56 (m, 1H), 7.48−7.41 (br t, J = 7.3 Hz, 2H), 4.31 (t, J = 6.7 Hz, 2H), 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.09 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.63 (t, J = 7.3 Hz, 2H), 1.77 ($quintet_{app}$, J = 6.7 Hz, 2H), 1.62 (quintet, J = 7.3 Hz, 2H), 1.51−1.42 (m, 2H), 1.41−1.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.8 (d, $^2J_{C-P}$ = 6.0 Hz), 166.6, 132.8, 130.4, 129.5 (2C), 128.3 (2C), 64.8, 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 43.9, 41.2 (d, $^1J_{C-P}$ = 128.2 Hz), 28.5 (2C), 25.8, 23.1. HRMS calcd for $C_{17}H_{25}O_6PNa$ (M + Na^+): 379.12810. Found: 379.12770.

*Dimethyl [5-(Oxiran-2-yl)-2-oxopentyl]phosphonate (**6h**).* Yield 68.0 mg (96%) with procedure A and 68.4 mg (98%) with procedure B (petroleum ether/acetone = 60:40 then 40:60); yellow oil. IR 1713, 1457, 1406, 1374, 1253, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.10 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.91 (dtd, J = 6.8 Hz, J = 4.3 Hz and J = 2.8 Hz, 1H), 2.75 (dd, J = 4.9 Hz and J = 4.3 Hz, 1H), 2.71 (t, J = 6.9 Hz, 2H), 2.47 (dd, J = 4.9 Hz and J = 2.8 Hz, 1H), 1.82−1.71 (m, 2H), 1.68−1.58 (m, 1H), 1.48 ($quintet_{app}$, J = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3 (d, $^2J_{C-P}$ = 6.4 Hz), 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 51.8, 46.7, 43.4, 41.3 (d, $^1J_{C-P}$ = 128.2 Hz), 31.4, 19.7; EI−MS m/z (relative intensity) 166 (M − $C_4H_6O^+$, 14), 151 (M − $C_5H_9O^+$, 100), 124 (84), 109 (94). HRMS calcd for $C_9H_{17}O_5PNa$ (M + Na^+): 259.07058. Found: 259.06989.

*Dimethyl (6-Bromo-2-oxohexyl)phosphonate (**6i**).* Yield 79.7 mg (93%) with procedure A and 69.4 mg (81%) with procedure B (petroleum ether/acetone = 60:40 then 40:60); yellow oil. IR 1713, 1449, 1403, 1373, 1253, 1183, 1021 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (d, $^3J_{H-P}$ = 11.2 Hz, 6H), 3.41 (t, J = 6.6 Hz, 2H), 3.10 (d, $^2J_{H-P}$ = 22.9 Hz, 2H), 2.67 (t, J = 6.9 Hz, 2H), 1.91−1.83 (m, 2H), 1.79−1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2 (d, $^2J_{C-P}$ = 6.0 Hz), 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 42.8, 41.3 (d, $^1J_{C-P}$ = 128.2 Hz), 33.1, 31.6, 21.8; EI−MS m/z (relative intensity) 207 (M − Br^+, 41), 179 (26), 151 (M − $C_4H_8Br^+$, 96), 124 (52), 119 (17), 109 (100), 94 (64), 79 (69). HRMS calcd for $C_8H_{16}O_4BrPNa$ (M^{79}[Br]+Na^+): 308.98618. Found: 308.98630; calcd for $C_8H_{16}O_4BrPNa$ (M^{81}[Br]+Na^+), 310.98413. Found: 310.98348.

*Dimethyl (2-Oxohept-6-yn-1-yl)phosphonate (**6j**).*[31] Yield 58.9 mg (90%) with procedure A and 53.7 mg (82%) with procedure B (petroleum ether/acetone = 60:40); pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (d, $^3J_{H-P}$ = 11.3 Hz, 6H), 3.11 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.78 (t, J = 6.9 Hz, 2H), 2.24 (td, J = 6.9 Hz and J = 2.6 Hz, 2H), 1.97 (t, J = 2.6 Hz, 1H), 1.81 (quintet, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2 (d, $^2J_{C-P}$ = 6.8 Hz), 83.4, 69.1, 53.1 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 42.5, 41.4 (d, $^1J_{C-P}$ = 128.2 Hz), 22.0, 17.5.

*Dimethyl {4-[(4-Methoxyphenyl)methoxy]-2-oxopentyl}phosphonate (**6k**).* Yield 89.7 mg (91%) with procedure A and 84.0 mg (82%) with procedure B (petroleum ether/acetone = 70:30 then 50:50); pale yellow oil. IR 1713, 1613, 1514, 1462, 1374, 1301, 1246, 1177, 1137, 1111, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (br

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308

d, J = 8.6 Hz, 2H), 6.86 (br d, J = 8.6 Hz, 2H), 4.50 (d, J = 11.1 Hz, 1H), 4.38 (d, J = 11.1 Hz, 1H), 4.02 (m, 1H), 3.79 (s, 3H), 3.77 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.76 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.12 (dd, $^2J_{H-P}$ = 22.6 Hz and J = 18.7 Hz, 1H), 3.09 (dd, $^2J_{H-P}$ = 22.6 Hz and J = 18.7 Hz, 1H), 2.90 (dd, J = 16.2 Hz and J = 7.5 Hz, 1H), 2.69 (dd, J = 16.2 Hz and J = 5.1 Hz, 1H), 1.23 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5 (d, $^2J_{C-P}$ = 6.4 Hz), 159.1, 130.4, 129.3 (2C), 113.7 (2C), 71.0, 70.4, 55.2, 53.0 (d, $^2J_{C-P}$ = 6.4 Hz, 2C), 50.9, 42.1 (d, $^1J_{C-P}$ = 127.8 Hz), 19.6. HRMS calcd for $C_{15}H_{23}O_6PNa$ (M + Na^+): 353.11245. Found: 353.11161.

*Methyl 3-[(tert-Butyldimethylsilyl)oxy]-6-(dimethoxyphosphoryl)-5-oxohexanoate (**6l**).* Yield 58.7 mg (51%) with procedure B (petroleum ether/acetone = 60:40 then 50:50); yellow oil. IR 1737, 1717, 1463, 1438, 1373, 1253, 1184 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (quintet$_{app}$, J = 6.1 Hz, 1H), 3.793 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.789 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.67 (s, 3H), 3.12 (d, $^2J_{H-P}$ = 22.6 Hz, 2H), 2.89 (d, J = 6.1 Hz, 2H), 2.55 (dd, J = 15.0 Hz and J = 5.7 Hz, 1H), 2.47 (dd, J = 15.0 Hz and J = 6.3 Hz, 1H), 0.84 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9 (d, $^2J_{C-P}$ = 6.4 Hz), 171.3, 65.3, 53.00 (d, $^2J_{C-P}$ = 6.0 Hz), 52.95 (d, $^2J_{C-P}$ = 6.0 Hz), 51.5, 51.0, 42.3 (d, $^1J_{C-P}$ = 128.2 Hz), 42.1, 25.6 (3C), 17.8, −4.9, −5.1. HRMS calcd for $C_{15}H_{31}O_7PSiNa$ (M + Na^+): 405.14689. Found: 405.14676.

*[(3aR,4R,6aR)-2,2-Dimethyl-6-oxo-tetrahydro-2H-furo[3,4-d]-[1,3]dioxol-4-yl]methyl 6-(dimethoxyphosphoryl)-5-oxohexanoate (**6m**).* Yield 57.0 mg (47%) with procedure A (petroleum ether/acetone = 60:40 then 50:50); yellow oil. $[\alpha]_D$ −34.3 (c 1.34, $CHCl_3$); IR 1786, 1741, 1714, 1456, 1378, 1242, 1176, 1152, 1081, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81 (d, J = 5.7 Hz, 1H), 4.78 (t$_{app}$, J = 2.7 Hz, 1H), 4.74 (d, J = 5.7 Hz, 1H), 4.40 (dd, J = 12.4 Hz and J = 2.8 Hz, 1H), 4.23 (dd, J = 12.4 Hz and J = 2.4 Hz, 1H), 3.792 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.788 (d, $^3J_{H-P}$ = 11.2 Hz, 3H), 3.10 (d, $^2J_{H-P}$ = 22.7 Hz, 2H), 2.78−2.63 (m, 2H), 241−2.32 (m, 2H), 1.89 (quintet$_{app}$, J = 7.1 Hz, 2H), 1.49 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9 (d, $^2J_{C-P}$ = 6.4 Hz), 173.5, 171.9, 113.7, 79.5, 77.7, 75.1, 63.4, 53.1 (d, $^2J_{C-P}$ = 6.8 Hz), 53.0 (d, $^2J_{C-P}$ = 7.6 Hz), 42.4, 41.3 (d, $^1J_{C-P}$ = 127.4 Hz), 32.5, 26.6, 25.5, 18.2. HRMS calcd for $C_{16}H_{25}O_{10}PNa$ (M + Na^+): 431.10775. Found: 431.10746.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*(S.S.) E-mail: simon.specklin@espci.fr.

*(J.C.) E-mail: janine.cossy@espci.fr.

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) (a) Horner, L.; Hoffmann, H.; Wippel, H. *Chem. Ber.* **1958**, *91*, 61−63. (b) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733−1738. (c) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87−99. (d) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927. (e) Edmonds, M.; Abell, A. In *Modern Carbonyl Olefination*; Takeda, T., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2003; pp 1−17.

(2) (a) Bisceglia, J. A.; Orelli, L. R. *Curr. Org. Chem.* **2012**, *16*, 2206−2230. (b) Nicolaou, K. C.; Härter, M. W.; Gunzner, J. L.; Nadin, A. *Liebigs Ann./Recl.* **1997**, 1283−1301. For selected examples, see (c) Uenishi, J.; Iwamoto, T.; Tanaka, J. *Org. Lett.* **2009**, *11*, 3262−3265. (d) Shing, T. K. M.; Cheng, H. M. *J. Org. Chem.* **2007**, *72*, 6610−6613. (e) Nicolaou, K. C.; Aversa, R. J.; Jin, J.; Rivas, F. *J. Am. Chem. Soc.* **2010**, *132*, 6855−6861. (f) Paterson, I.; Burton, P. M.; Cordier, C. J.; Housden, M. P.; Mühlthau, F. A.; Loiseleur, O. *Org. Lett.* **2009**, *11*, 693−696.

(3) (a) Michaelis, A.; Kaehne, R. *Chem. Ber.* **1898**, *31*, 1048−1055. (b) Arbuzov, A. E. *J. Russ. Phys. Chem. Soc.* **1906**, *38*, 687. (c) Bhattacharya, A. K.; Thyagarajan, G. *Chem. Rev.* **1981**, *81*, 415−430. For recent exemples, see (d) Ho, S.; Bucher, C.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2013**, *52*, 6757−6761. (e) Rajeshwaran, G. G.; Nandakumar, M.; Sureshbabu, R.; Mohanakrishnan, A. K. *Org. Lett.* **2011**, *13*, 1270−1273. (f) Perumal, S. K.; Adediran, S. A.; Pratt, R. F. *Bioorg. Med. Chem.* **2008**, *16*, 6987−6994. (g) Mandal, M.; Yun, H.; Dudley, G. B.; Lin, S.; Tan, D. S.; Danishefsky, S. J. *J. Org. Chem.* **2005**, *70*, 10619−10637.

(4) Teulade, M. P.; Savignac, P.; Aboujaoude, E. E.; Collignon, N. *J. Organomet. Chem.* **1986**, *312*, 283−295.

(5) Yasuda, N.; Hsiao, Y.; Jensen, M. S.; Rivera, N. R.; Yang, C.; Wells, K. M.; Yau, J.; Palucki, M.; Tan, L.; Dormer, P. G.; Volante, R. P.; Hughes, D. L.; Reider, P. J. *J. Org. Chem.* **2004**, *69*, 1959−1966.

(6) Mathey, F.; Savignac, P. *Tetrahedron* **1978**, *34*, 649−654.

(7) Blades, K.; Lequeux, T. P.; Percy, J. M. *Tetrahedron* **1997**, *53*, 10623−10632.

(8) Orsini, F.; Di Teodoro, E.; Ferrari, M. *Synthesis* **2002**, 1683−1688.

(9) (a) Maloney, K. M.; Chung, J. Y. L. *J. Org. Chem.* **2009**, *74*, 7574−7576. (b) Milburn, R. R.; McRae, K.; Chan, J.; Tedrow, J.; Larsen, R.; Faul, M. *Tetrahedron Lett.* **2009**, *50*, 870−872.

(10) Corbel, B.; L'hostis-Kervella, I.; Haelters, J.-P. *Synth. Commun.* **2000**, *30*, 609−618.

(11) Wei, W.; Ji, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 9097−9099.

(12) Holmquist, C. R.; Roskamp, E. J. *Tetrahedron Lett.* **1992**, *33*, 1131−1134.

(13) Jackson, K. L.; Henderson, J. A.; Motoyoshi, H.; Phillips, A. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 2346−2350.

(14) Wetzel, D. M.; Brauman, J. I. *J. Am. Chem. Soc.* **1988**, *110*, 8333−8336.

(15) (a) Iorga, B.; Savignac, P. *Synlett* **2001**, 447−457. (b) Aboujaoude, E. E.; Liétjé, S.; Collignon, N.; Teulade, M. P.; Savignac, P. *Synthesis* **1986**, 934−937. (c) Savignac, P.; Teulade, M.-P.; Collignon, N. *J. Organomet. Chem.* **1987**, *323*, 135−144.

(16) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780−784.

(17) Hong, S.; Chang, K.; Ku, B.; Oh, D. Y. *Tetrahedron Lett.* **1989**, *30*, 3307−3308.

(18) Umezawa, T.; Seino, T.; Matsuda, F. *Org. Lett.* **2012**, *14*, 4206−4209.

(19) Menche, D.; Hassfeld, J.; Li, J.; Mayer, K.; Rudolph, S. *J. Org. Chem.* **2009**, *74*, 7220−7229.

(20) Zaramella, S.; Strömberg, R.; Yeheskiely, E. *Eur. J. Org. Chem.* **2002**, 2633−2639.

(21) Babadzhanova, L. A.; Kirij, N. V.; Yagupolskii, Y. L.; Tyrra, W.; Naumann, D. *Tetrahedron* **2005**, *61*, 1813−1819.

(22) Peng, L.; DeSousa, J.; Su, Z.; Novak, B. M.; Nevzorov, A. A.; Garland, E. R.; Melander, C. *Chem. Commun.* **2011**, *47*, 4896−4898.

(23) Grayson, D. H.; McCarthy, Ú.; Roycroft, E. D. *Org. Biomol. Chem.* **2003**, *1*, 1930−1937.

(24) Jochum, F. D.; Theato, P. *Macromolecules* **2009**, *42*, 5941−5945.

(25) Vilaça, G.; Rubio, C.; Susperregui, J.; Latxague, L.; Déléris, G. *Tetrahedron* **2002**, *58*, 9249−9256.

(26) Schleicher, K. D.; Jamison, T. F. *Org. Lett.* **2007**, *9*, 875−878.

(27) Eh, M.; Schomburg, D.; Schicht, K.; Kalesse, M. *Tetrahedron* **1995**, *51*, 8983−8992.

(28) Bennis, K.; Calinaud, P.; Gelas, J.; Ghobsi, M. *Carbohydr. Res.* **1994**, *264*, 33−44.

(29) Hamada, A.; Braunstein, P. *Organometallics* **2009**, *28*, 1688−1696.

(30) Wenkert, E.; Guo, M.; Lavilla, R.; Porter, B.; Ramachandran, K.; Sheu, J. H. *J. Org. Chem.* **1990**, *55*, 6203−6214.

(31) Batsomboon, P.; Gold, B.; Alabugin, I.; Dudley, G. *Synthesis* **2012**, 1818−1824.

DOI: 10.1021/acs.joc.5b00039
J. Org. Chem. 2015, 80, 3302−3308