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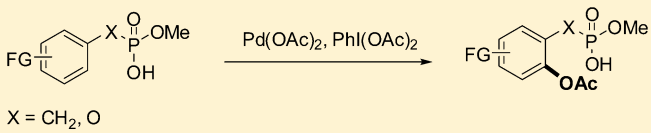
ortho-Acetoxylation of Phosphonic and Phosphoric Monoacids via Pd(II) Catalysis

Li Yan Chan, Xiangjian Meng, and Sunggak Kim*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

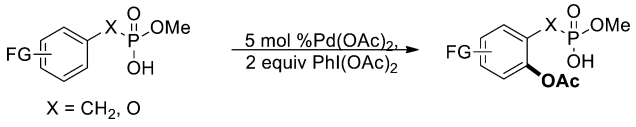
Supporting Information

ABSTRACT: A simple and efficient method is developed for Pd-catalyzed *ortho*-acetoxylation using organophosphates, namely, benzylic phosphonic and aryl phosphoric monoacids, as the directing group.



Transition-metal-catalyzed C−H functionalization is an attractive method in organic synthesis.[1] As such, this method has emerged as a powerful tool for introducing useful functionality via a coordinating directing group. Our recent reports exhibit the potential of organophosphate as the directing group, which is highly *ortho*-selective in various C−H activation reactions, especially in the area of alkenylation[2] and arylation.[3,4] Extensive mechanistic studies of C−O bond formation via Pd(II)/Pd(IV) catalytic cycle were done by Sanford's group[5] and have proven beneficial in Pd-catalyzed *ortho*-acetoxylation.[6,7] An alternative Pd(II)/Pd(III) redox catalysis with I(III) oxidants as demonstrated by Ritter's group offered another insight to the mechanism.[8] In our recent studies, we also proved the feasibility of *ortho*-arylation by Pd(II)/Pd(IV) catalysis, in the presence of various aryl iodonium salts.[3] Since organophosphates are well-known for their importance in biological activities and various organic synthetic aspects,[9,10] we are motivated to further explore the diversity of C−H functionalization using these aryl organophosphates. Herein, we report the versatility of such directing groups in *ortho*-acetoxylation of benzylic phosphonic and aryl phosphoric monoacids (Scheme 1).

Scheme 1. *ortho*-Acetoxylation of Benzylic Phosphonic and Aryl Phosphoric Monoacids



As summarized in Table 1, dimethyl 2-methylbenzylphosphonate (**1a**) was used for the preliminary studies in acetoxylation. No reaction occurred when **1a** was treated with 10 mol % $Pd(OAc)_2$ and 2 equiv of $PhI(OAc)_2$ at 110 °C for 15 h in either 1,2-dichloroethane or 1,4-dioxane (entries 1 and 2). The more reactive methyl hydrogen 2-methylbenzylphosphonate (**1b**) was then employed, and the reaction was performed under various solvents such as 1,4-dioxane, methanol, DMSO, DMF, AcOH, and toluene, but all gave low or no product (entries 3−8). Gratifyingly, 1,2-dichloroethane has proven to be the most ideal solvent in this *ortho*-acetoxylation (entries 9 and 10), and reducing the catalyst loading to 5 mol % did not hinder the reaction (entry 10). For facile purification, the crude **2b** was treated with TMS-diazomethane to afford methyl phosphonate ester **2a**, with 91% isolated yield.

Our continual research highlights the similarity of aryl phosphonic and phosphoric acid in the role of directing group in C−H activation,[2,3] and thus we postulate that this methodology can also be applied to phosphoric acid. Furthermore, the products obtained will be useful intermediates to synthesize catechol derivatives that are widely known to be the crucial moiety found in natural products and drugs.[11] As such, the optimized condition was used for methyl *o*-tolyl hydrogen phosphate (**1c**), but decomposition happened at the high temperature of 110 °C (entry 11). Apparently, phosphoric acid is more sensitive toward thermal conditions as it shows very different reactivity at 60, 80, and 110 °C (entries 11−13). To our delight, **1c** works well in 1,2-dichloroethane, dimethoxyethane, and 1,4-dioxane at 80 °C, giving high conversion to the desired acetoxylated **2c** (entries 12, 14, and 15). Increasing the amount of $PhI(OAc)_2$ to 3 equiv further improved the conversion to **2c** (entry 16), which gave 67% isolated yield of **2d** after methylation. The isolated yield was lower than expected because the acetoxy phosphate **2d** is relatively unstable and needed to be kept at −20 °C for storage after isolation. Compound **2d** decomposed and turned black after being left at ambient temperature for 3 days, unlike acetoxy phosphonic **2a**, which is stable at room temperature even after weeks. Expectedly, palladium catalyst is essential for reaction to take place (entry 17), and dimethyl *o*-tolyl phosphate **1d** is inert to this reaction condition (entries 18−20).

The scope of Pd-catalyzed *ortho*-acetoxylation of benzylic phosphonic acid is illustrated in Table 2. The reaction proceeded smoothly for alkyl or alkoxyl substitutents at the *ortho*- or *meta*-position (entries 1−5). However, further *ortho*-

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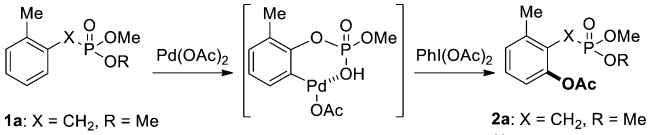
Table 1. Optimizing Reaction Conditions of *ortho*-Acetoxylation for 1[a]



1a: X = CH_2, R = Me
1b: X = CH_2, R = H
1c: X = O, R = H
1d: X = O, R = Me

2a: X = CH_2, R = Me
2b: X = CH_2, R = H
2c: X = O, R = H
2d: X = O, R = Me

entry	substrate	temp (°C)	solvent	conv (%)[b]
1	**1a**	110	DCE	0
2	**1a**	110	dioxane	0
3	**1b**	110	dioxane	0
4	**1b**	110	MeOH	0
5	**1b**	110	DMSO	0
6	**1b**	110	DMF	13
7	**1b**	110	AcOH	53
8	**1b**	110	toluene	56
9	**1b**	110	DCE	91
10[c]	**1b**	110	DCE	93 (91)[d]
11	**1c**	110	DCE	dec
12	**1c**	80	DCE	81
13	**1c**	60	DCE	0
14	**1c**	80	DME	83
15	**1c**	80	dioxane	90
16[e]	**1c**	80	dioxane	100 (67)[d]
17[e,f]	**1c**	80	dioxane	0
18	**1d**	110	dioxane	0
19	**1d**	110	DCE	0
20	**1d**	110	DME	0

[a]Conditions: 0.15 mmol of **1**, 2 equiv of $PhI(OAc)_2$, 10 mol % $Pd(OAc)_2$ in 1 mL of solvent for 15 h at 110 °C. [b]Conversion of starting material **1**, based on crude NMR. [c]5 mol % of $Pd(OAc)_2$ was used. [d]Isolated yield after methylation with $TMSCHN_2$. [e]3 equiv of $PhI(OAc)_2$ was used. [f]Blank test, without Pd catalyst.

acetoxylation was observed when using **3f** with methyl-substituted at the *para*-position (entry 6) and furnished 15% of diacetoxylated **4f′** as byproduct. The reaction also occurred nicely for naphthalene derivative (entry 7). Halogenated benzylic phosphonic acids were completely compatible in this optimized condition and gave the respective products in high yield (entries 8−13). Introduction of bulky groups to **3n**−**3p** (entries 14−16) did not hinder the reaction. Moreover, this also helps to suppress further diacetoxylation as seen in the unsubstituted example of **3p** (entry 16).

We then moved on to carry out *ortho*-acetoxylation on a variety of aryl phosphoric monoacids after using the fine-tuned optimized condition (Table 3). Similarly, alkyl, alkoxyl, and halogenated substitutions at the *ortho*- or *meta*-position are tolerant to the reaction conditions (entries 1−8). Biaryl phosphoric acid also proceeds well (entry 4). Surprisingly, when an even more electron-withdrawing ester group is present at the *ortho*-position, partial dephosphorylation to yield the corresponding phenol was noticed (**6i**:**6i′** = 53:24) as seen in entry 9. Similar diacetoxylated byproduct **6j′** was observed with unsubstituted **5j** (entry 10). When using an excess amount of $PhI(OAc)_2$ (5 equiv), diacetoxylated **6j′** was formed exclusively (entry 11).

When methyl hydrogen phenylphosphonate (**7**) was subjected to the conditions employed in the acetoxylation of **3**, the reaction was slow and did not go to completion, yielding 24% of **8** along with the recovery of **7** (59%) as dimethyl phenylphosphonate (Scheme 2). Elevating the reaction temperature to 110 °C led to decomposition to some extent without improving the yield.

In conclusion, we have shown that organophosphates are an excellent directing group for the Pd-catalyzed acetoxylation of benzyl phosphonic and aryl phosphoric monoacids, providing easy access to various acetoxy benzylic phosphonic acids along with catechol derivatives. The reaction is simple to handle and suitable to further diversify functional groups.

EXPERIMENTAL SECTION

General Methods. Chemical reagents were commercially purchased and used without further purification. NMR spectra were measured at 298 K on a 400 Fourier Transform NMR spectrometer. Chemical shifts were reported in δ (ppm), relative to the internal standard, TMS. The signals observed are described as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). The number of protons (n) for a given resonance are indicated as nH. Coupling constants are reported as J value in Hz. ^{13}C NMR is reported as δ (ppm) downfield from TMS and relative to the signal of chloroform-d (δ 77.00, triplet). Mass spectrometry was obtained using a Q-tof high resolution mass spectrometer.

General Procedure for *ortho*-Acetoxylation of 1, 3, or 5. $Pd(OAc)_2$ (5 or 10 mol %) and $PhI(OAc)_2$ (2 or 3 equiv) were carefully weighed into a vial equipped with a magnetic stirrer bar and a tightly screwed cap. Then **1**, **3**, or **5** (0.15 mmol; 1 equiv) in DCE or dioxane (1 mL) was added, stirred at 110 or 80 °C for 15 h, and cooled to rt. The mixture was filtered through Celite and concentrated *in vacuo*. TMS-diazomethane (5 equiv) was added to the crude product in MeOH (0.5 mL), and the mixture was stirred 30 min at rt, concentrated *in vacuo*, and purified by flash chromatography (CH_2Cl_2/acetone = 20:1) to afford the desired acetoxylated product **2**, **4**, or **6**.

2-((Dimethoxyphosphoryl)methyl)-3-methylphenyl Acetate (2a). Yield 37.2 mg, 91%; yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 7.9, 2.5 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 6.97 (d, J = 8.1 Hz, 1H), 3.64 (s, 3H), 3.62 (s, 3H), 3.23 (s, 1H), 3.17 (s, 1H), 2.41 (d, J = 1.4 Hz, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 149.1 (d, J = 6.4 Hz), 139.1 (d, J = 5.8 Hz), 127.8 (d, J = 3.5 Hz), 127.4 (d, J = 4.0 Hz), 122.3 (d, J = 9.8 Hz), 120.4 (d, J = 3.6 Hz), 52.9 (d, J = 6.9 Hz), 24.9 (d, J = 140.9 Hz), 21.1, 20.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.3; FTIR (NaCl, neat) ν 1768, 1471, 1208 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_5P$ $(M + H)^+$) calcd 273.0892, found 273.0894.

2-((Dimethoxyphosphoryl)oxy)-3-methylphenyl Acetate (2d). Yield 27.6 mg, 67%; yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 − 7.05 (m, 2H), 7.01 − 6.95 (m, 1H), 3.86 (d, J = 11.4 Hz, 6H), 2.38 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 142.0 (d, J = 3.0 Hz), 141.0 (d, J = 8.0 Hz), 132.0 (d, J = 4.0 Hz), 128.6 (d, J = 1.0 Hz), 125.4, 121.4 (d, J = 2.0 Hz), 55.0 (d, J = 6.0 Hz), 20.8, 16.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −3.9; FTIR (NaCl, neat) ν 1732, 1651, 1485, 1371, 1265 cm^{-1}; HRMS (ESI, $C_{11}H_{16}O_6P$ $(M + H)^+$) calcd 275.0685, found 275.0677.

2-((Dimethoxyphosphoryl)methyl)-3,5-dimethylphenyl Acetate (4a). Yield 39.9 mg, 93%; yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 1H), 6.79 (s, 1H), 3.65 (s, 3H), 3.62 (s, 3H), 3.18 (s, 1H), 3.12 (s, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.29 (d, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 149.0 (d, J = 6.4 Hz), 138.7 (d, J = 5.8 Hz), 137.5 (d, J = 4.2 Hz), 128.8 (d, J = 3.6 Hz), 120.9 (d, J = 3.6 Hz), 119.1 (d, J = 9.9 Hz), 52.8 (d, J = 7.0 Hz), 24.6 (d, J = 141.3 Hz), 21.2, 21.0, 20.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.6; FTIR (NaCl, neat) ν 1767, 1368, 1209 cm^{-1}; HRMS (ESI, $C_{13}H_{20}O_5P$ $(M + H)^+$) calcd 287.1048, found 287.1048.

2-((Dimethoxyphosphoryl)methyl)-3-methoxyphenyl Acetate (4b). Yield 39.8 mg, 92%; yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 − 7.21 (m, 1H), 6.78 (s, 1H), 6.76 (s, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 3.64 (s, 3H), 3.29 (s, 1H), 3.24 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 158.2 (d, J = 5.7 Hz), 149.7 (d, J = 6.5 Hz), 127.9 (d, J = 3.9 Hz), 115.3 (d, J = 3.5 Hz), 113.2 (d, J = 10.5 Hz), 107.9 (d, J = 3.2 Hz), 56.0, 52.7 (d, J = 6.6 Hz),

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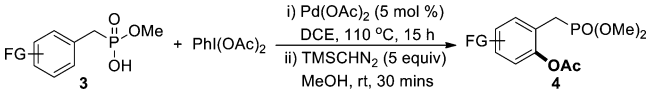
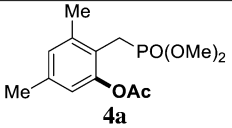
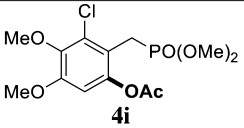
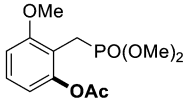
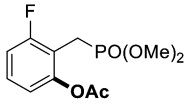
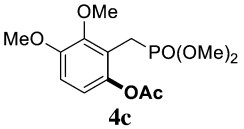
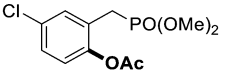
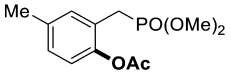
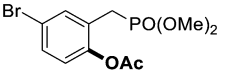
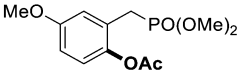
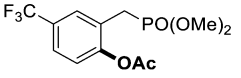
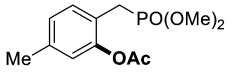
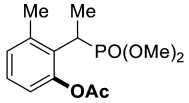
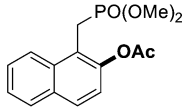
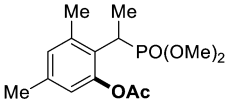
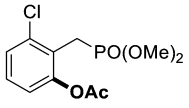
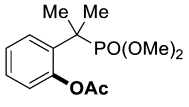
Table 2. Substrate Scope of the Benzylic Phosphonic Acid Directing Group in *ortho*-Acetoxylation[a]



entry	4	yield (%)[b]	entry	4	yield (%)[b]
1	 **4a**	93	9	 **4i**	95
2	 **4b**	92	10	 **4j**	81
3	 **4c**	94	11	 **4k**	82
4	 **4d**	85	12	 **4l**	93
5	 **4e**	83	13	 **4m**	91
6[c]	 **4f**	53, 15[d] (17)[e]	14	 **4n**	88
7	 **4g**	76	15	 **4o**	90
8	 **4h**	86	16	 **4p**	93

[a]Conditions: (i) 0.15 mmol of **3**, 2 equiv of $PhI(OAc)_2$, 5 mol % $Pd(OAc)_2$ in 1 mL of 1,2-dichloroethane for 15 h at 110 °C. (ii) 5 equiv of $TMSCHN_2$ in 0.5 mL of MeOH at rt for 30 min. [b]Isolated yield. [c]1.1 equiv of $PhI(OAc)_2$ was used. [d]Yield of diacetoxylated product. [e]Recovery yield of methylated starting material **3**.

21.3 (d, J = 141.2 Hz), 21.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.7; FTIR (NaCl, neat) ν 1767, 1606, 1369, 1209 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_6P$ (M + H)$^+$) calcd 289.0841, found 289.0837.

2-((Dimethoxyphosphoryl)methyl)-3,4-dimethoxyphenyl Acetate (4c). Yield 44.9 mg, 94%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, J = 1.5 Hz, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 3.27 (s, 1H), 3.22 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 150.4 (d, J = 3.4 Hz), 147.7 (d, J = 6.6 Hz), 142.5 (d, J = 5.8 Hz), 118.7 (d, J = 10.1 Hz), 117.7 (d, J = 3.3 Hz), 111.0 (d, J = 3.7 Hz), 60.8 (d, J = 1.6 Hz), 56.0, 52.8 (d, J = 6.7 Hz), 22.1 (d, J = 141.4 Hz), 21.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.2; FTIR (NaCl, neat) ν 1767, 1488, 1207 cm^{-1}; HRMS (ESI, $C_{13}H_{20}O_7P$ (M + H)$^+$) calcd 319.0947, found 319.0949.

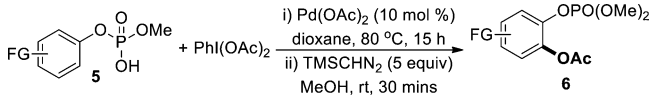
2-((Dimethoxyphosphoryl)methyl)-4-methylphenyl Acetate (4d). Yield 34.7 mg, 85%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (s, 1H), 7.08 (d, J = 8.3 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 3.68 (s, 3H), 3.65 (s, 3H), 3.13 (s, 1H), 3.08 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 146.6 (d, J = 7.4 Hz), 135.8 (d, J = 3.3 Hz), 131.9 (d, J = 5.5 Hz), 128.9 (d, J = 3.7 Hz), 123.1 (d, J = 9.2 Hz), 122.5 (d, J = 3.1 Hz), 52.9 (d, J = 6.8 Hz), 27.2 (d, J = 140.5 Hz), 21.0, 20.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.2; FTIR (NaCl, neat) ν 1761, 1500, 1370, 1218 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_5P$ (M + H)$^+$) calcd 273.0892, found 273.0897.

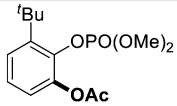
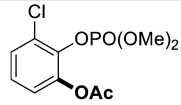
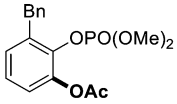
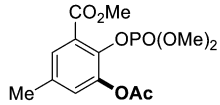
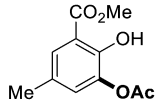
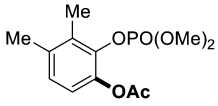
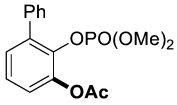
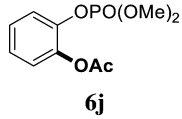
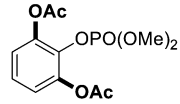
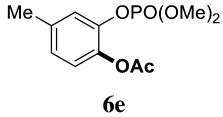
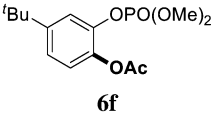
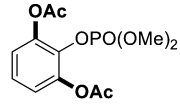
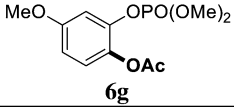
2-((Dimethoxyphosphoryl)methyl)-4-methoxyphenyl Acetate (4e). Yield 35.9 mg, 83%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, J = 8.9 Hz, 1H), 6.90 (t, J = 2.8 Hz, 1H), 6.80 (dt, J = 8.9, 2.6 Hz, 1H), 3.78 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 3.12 (s, 1H), 3.07 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.41, 157.1 (d, J = 3.4 Hz), 142.4 (d, J = 7.5 Hz), 124.5 (d, J = 9.1 Hz), 123.5 (d, J = 3.1 Hz), 116.3 (d, J = 5.5 Hz), 113.5 (d, J = 3.6 Hz), 55.6, 52.9 (d, J = 6.8 Hz), 27.4 (d, J = 140.5 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.8; FTIR (NaCl, neat) ν 1761, 1606, 1501, 1370, 1243 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_6P$ (M + H)$^+$) calcd 289.0841, found 289.0838.

2-((Dimethoxyphosphoryl)methyl)-5-methylphenyl Acetate (4f). Yield 21.6 mg, 53%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (q, J = 2.4 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 6.93 (s, 1H), 3.68 (d, J = 3.2 Hz, 3H), 3.65 (d, J = 3.2 Hz, 3H), 3.13 (s, 1H), 3.08 (s, 1H), 2.33 (d, J = 2.3 Hz, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 148.7 (d, J = 7.5 Hz), 138.4 (d, J = 3.8 Hz), 131.1 (d,

dx.doi.org/10.1021/jo4011188 | J. Org. Chem. 2013, 78, 8826−8832

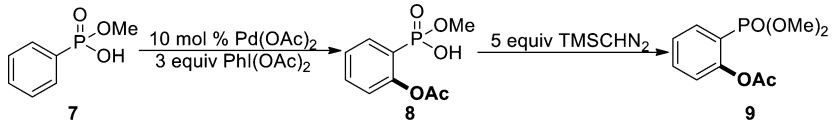
Table 3. Substrate Scope for *ortho*-Acetoxylation via Monophosphoric Acid Directing Group[a]



entry	6	yield (%)[b]	entry	6	yield (%)[b]
1	 **6a**	69	8	 **6h**	68
2	 **6b**	63	9	 **6i**  **6i'**	53, 24
3	 **6c**	72			
4	 **6d**	50	10	 **6j**  **6j'**	57, 8 (14)[c]
5	 **6e**	62			
6	 **6f**	66	11[d]	 **6j'**	67
7	 **6g**	64			

[a]Conditions: (i) 0.15 mmol of **5**, 3 equiv of $PhI(OAc)_2$, 10 mol % of $Pd(OAc)_2$ in 1 mL of 1,4-dioxane for 15 h at 80 °C. (ii) 5 equiv of $TMSCHN_2$ in 0.5 mL of MeOH at rt for 30 min. [b]Isolated yield. [c]Recovery yield of methylated starting material **5**. [d]5 equiv of $PhI(OAc)_2$ was used.

Scheme 2. *ortho*-Acetoxylation of Methyl Hydrogen Phenylphosphonate



J = 5.5 Hz), 127.0 (d, J = 3.3 Hz), 123.4 (d, J = 3.1 Hz), 120.3 (d, J = 9.3 Hz), 52.9 (d, J = 6.8 Hz), 26.8 (d, J = 140.9 Hz), 21.0 (d, J = 1.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.3; FTIR (NaCl, neat) ν 2955, 1751, 1636, 1211 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_5P$ (M + H)$^+$) calcd 273.0892, found 273.0890.

2-((Dimethoxyphosphoryl)methyl)-5-methylphenyl Acetate (4f'). Yield 7.4 mg, 15%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 2H), 3.65 (s, 3H), 3.62 (s, 3H), 3.15 (s, 1H), 3.10 (s, 1H), 2.34 (s, 3H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 149.3 (d, J = 6.2 Hz), 138.2 (d, J = 4.0 Hz), 121.0 (d, J = 3.4 Hz), 113.9 (d, J = 10.0 Hz), 52.9 (d, J = 6.9 Hz), 21.4 (d, J = 26.1 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.3; FTIR (NaCl, neat) ν 2953, 1770, 1761, 1626, 1369 cm^{-1}; HRMS (ESI, $C_{14}H_{20}O_7P$ (M + H)$^+$) calcd 331.0947, found 331.0951.

1-((Dimethoxyphosphoryl)methyl)naphthalen-2-yl Acetate (4g). Yield 35.1 mg, 76%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.80 (dd, J = 9.0, 2.1 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 9.0 Hz, 1H), 3.68 (s, 1H), 3.63 (s, 1H), 3.60 (s, 3H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 147.0 (d, J = 8.5 Hz), 132.6 (d, J = 4.3 Hz), 131.8 (d, J = 3.0 Hz), 128.6 (d, J = 3.6 Hz), 128.6, 126.8, 125.6, 124.4 (d, J = 1.9 Hz), 121.8 (d, J = 4.2 Hz), 118.3 (d, J = 10.4 Hz), 52.9 (d, J = 6.9 Hz), 24.0 (d, J = 141.8 Hz), 21.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.6; FTIR (NaCl, neat) ν 2955, 1763, 1630, 1516, 1205 cm^{-1}; HRMS (ESI, $C_{15}H_{18}O_5P$ (M + H)$^+$) calcd 309.0892, found 309.0900.

3-Chloro-2-((dimethoxyphosphoryl)methyl)phenyl Acetate (4h). Yield 37.8 mg, 86%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.1 Hz, 1H), 7.23 (dd, J = 8.1, 2.4 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.44 (s, 1H), 3.38 (s,

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1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 149.8 (d, J = 6.1 Hz), 135.3 (d, J = 6.8 Hz), 128.1 (d, J = 3.9 Hz), 126.9 (d, J = 3.4 Hz), 123.2 (d, J = 10.3 Hz), 121.8 (d, J = 3.5 Hz), 52.9 (d, J = 6.8 Hz), 25.6 (d, J = 141.3 Hz), 21.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.7; FTIR (NaCl, neat) ν 1776, 1451, 1201 cm^{-1}; HRMS (ESI, $C_{11}H_{15}ClO_5P$ (M + H)$^+$) calcd 293.0344, found 293.0349.

3-Chloro-2-((dimethoxyphosphoryl)methyl)-4,5-dimethoxyphenyl Acetate (4i). Yield 50.3 mg, 95%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (s, 1H), 3.84 (d, J = 1.5 Hz, 6H), 3.68 (s, 3H), 3.66 (s, 3H), 3.35 (s, 1H), 3.29 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 152.4 (d, J = 3.6 Hz), 145.2 (d, J = 6.3 Hz), 143.6 (d, J = 3.4 Hz), 129.4 (d, J = 6.1 Hz), 115.3 (d, J = 10.3 Hz), 106.3 (d, J = 3.5 Hz), 60.7, 56.1, 52.9 (d, J = 6.8 Hz), 25.4 (d, J = 142.5 Hz), 21.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.2; FTIR (NaCl, neat) ν 1768, 1485, 1205 cm^{-1}; HRMS (ESI, $C_{13}H_{19}ClO_7P$ (M + H)$^+$) calcd 353.0557, found 353.0559.

2-((Dimethoxyphosphoryl)methyl)-3-fluorophenyl Acetate (4j). Yield 33.6 mg, 81%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 − 7.24 (m, 1H), 6.98 (t, J = 8.0 Hz, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.25 (d, J = 1.5 Hz, 1H), 3.20 (d, J = 1.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 161.2 (d, J = 247.6 Hz), 149.7 (d, J = 6.1 Hz), 128.2 (dd, J = 9.9, 3.8 Hz), 118.8 (t, J = 3.4 Hz), 112.8 (d, J = 3.3 Hz), 112.6 (d, J = 3.3 Hz), 52.9 (d, J = 6.6 Hz), 21.8 (d, J = 3.2 Hz), 21.0 (s), 20.4 (d, J = 3.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.8; ^{19}F NMR (162 MHz, $CDCl_3$) δ −114.00 (d, J = 4.5 Hz); FTIR (NaCl, neat) ν 1775, 1469, 1205 cm^{-1}; HRMS (ESI, $C_{11}H_{15}FO_5P$ (M + H)$^+$) calcd 277.0641, found 277.0646.

4-Chloro-2-((dimethoxyphosphoryl)methyl)phenyl Acetate (4k). Yield 36.0 mg, 82%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, J = 2.6 Hz, 1H), 7.25 (d, J = 7.9 Hz, 1H), 7.07 (d, J = 8.7 Hz, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.14 (s, 1H), 3.08 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 147.3 (d, J = 7.3 Hz), 131.3 (d, J = 3.8 Hz), 131.2 (d, J = 5.6 Hz), 128.3 (d, J = 3.6 Hz), 125.6 (d, J = 9.4 Hz), 124.2 (d, J = 3.1 Hz), 53.0 (d, J = 6.9 Hz), 27.2 (d, J = 140.9 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.0; FTIR (NaCl, neat) ν 1767, 1486, 1204 cm^{-1}; HRMS (ESI, $C_{11}H_{15}ClO_5P$ (M + H)$^+$) calcd 293.0346, found 293.0355.

4-Bromo-2-((dimethoxyphosphoryl)methyl)phenyl Acetate (4l). Yield 47.0 mg, 93%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, J = 2.5 Hz, 1H), 7.39 (dt, J = 8.6, 2.3 Hz, 1H), 7.00 (d, J = 8.6 Hz, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 3.13 (s, 1H), 3.07 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 147.9 (d, J = 7.2 Hz), 134.1 (d, J = 5.6 Hz), 131.2 (d, J = 3.7 Hz), 126.0 (d, J = 9.3 Hz), 124.6 (d, J = 3.1 Hz), 118.9 (d, J = 3.9 Hz), 53.0 (d, J = 6.8 Hz), 27.2 (d, J = 140.9 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.0; FTIR (NaCl, neat) ν 1767, 1484, 1203 cm^{-1}; HRMS (ESI, $C_{11}H_{15}BrO_5P$ (M + H)$^+$) calcd 336.9840, found 336.9837.

2-((Dimethoxyphosphoryl)methyl)-4-(trifluoromethyl)-phenyl Acetate (4m). Yield 44.5 mg, 91%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.56 (d, J = 8.6 Hz, 1H), 7.27 (d, J = 6.9 Hz, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.23 (s, 1H), 3.17 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 151.3 (d, J = 6.0 Hz), 128.6 (dd, J = 5.4, 3.8 Hz), 125.3 (t, J = 3.6 Hz), 125.0 (d, J = 9.4 Hz), 123.6 (d, J = 3.0 Hz), 53.0 (d, J = 6.8 Hz), 27.4 (d, J = 141.0 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.29; FTIR (NaCl, neat) ν 2957, 1771, 1425, 1335, 1267 cm^{-1}; HRMS (ESI, $C_{12}H_{15}F_3O_5P$ (M + H)$^+$) calcd 327.0609, found 327.0615.

2-(1-(Dimethoxyphosphoryl)ethyl)-3-methylphenyl Acetate (4n). Yield 37.8 mg, 88%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 7.8, 1.8 Hz, 1H), 7.05 (d, J = 7.5 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 3.71 (d, J = 10.7 Hz, 3H), 3.60 − 3.49 (m, 1H), 3.46 (d, J = 10.5 Hz, 3H), 2.38 (s, 3H), 1.63 (dd, J = 18.5, 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 149.9 (d, J = 5.2 Hz), 138.5 (d, J = 8.3 Hz), 128.1 (d, J = 5.9 Hz), 127.8 (d, J = 1.9 Hz), 127.5 (d, J = 3.0 Hz), 122.2 (d, J = 2.9 Hz), 53.0 (dd, J = 117.3, 7.1 Hz), 32.4 (d, J = 141.3 Hz), 21.7, 20.8, 13.7 (d, J = 4.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.9; FTIR (NaCl, neat) ν 1767, 1464, 1368, 1206 cm^{-1}; HRMS (ESI, $C_{13}H_{20}O_5P$ (M + H)$^+$) calcd 287.1048, found 287.1041.

2-(1-(Dimethoxyphosphoryl)ethyl)-3,5-dimethylphenyl Acetate (4o). Yield 40.5 mg, 90%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.77 (s, 1H), 3.70 (d, J = 10.7 Hz, 3H), 3.47 (d, J = 10.5 Hz, 3H), 3.47 − 3.45 (m, 1H), 2.36 (s, 3H), 2.33 (s, 3H), 2.28 (d, J = 1.3 Hz, 3H), 1.60 (dd, J = 18.5, 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 149.7 (d, J = 5.1 Hz), 138.1 (d, J = 8.3 Hz), 137.5 (d, J = 3.2 Hz), 128.8 (d, J = 1.8 Hz), 125.0 (d, J = 5.9 Hz), 122.7 (d, J = 2.9 Hz), 53.5 (d, J = 6.9 Hz), 52.4 (d, J = 7.3 Hz), 32.1 (d, J = 141.3 Hz), 21.8, 20.8 (d, J = 12.0 Hz), 13.8 (d, J = 4.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 32.1; FTIR (NaCl, neat) ν 1761, 1447, 1208 cm^{-1}; HRMS (ESI, $C_{14}H_{22}O_5P$ (M + H)$^+$) calcd 301.1205, found 301.1201.

2-(2-(Dimethoxyphosphoryl)propan-2-yl)phenyl Acetate (4p). Yield 39.9 mg, 93%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 3.50 (s, 3H), 3.48 (s, 3H), 2.28 (s, 3H), 1.67 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 149.7 (d, J = 5.4 Hz), 132.4 (d, J = 4.6 Hz), 129.8 (d, J = 5.6 Hz), 128.1 (d, J = 3.1 Hz), 125.6 (d, J = 2.4 Hz), 124.9 (d, J = 2.8 Hz), 53.4 (d, J = 7.4 Hz), 39.2 (d, J = 138.0 Hz), 24.7 (d, J = 4.5 Hz), 21.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 33.3; FTIR (NaCl, neat) ν 2955, 1767, 1370, 1211 cm^{-1}; HRMS (ESI, $C_{13}H_{20}O_5P$ (M + H)$^+$) calcd 287.1048, found 287.1053.

3-(*tert*-Butyl)-2-((dimethoxyphosphoryl)oxy)phenyl Acetate (6a). Yield 32.7 mg, 69%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 − 7.22 (m, 1H), 7.10 (t, J = 8.0 Hz, 1H), 7.02 (dd, J = 8.0, 1.5 Hz, 1H), 3.86 (d, J = 11.5 Hz, 6H), 2.38 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 142.3 (d, J = 6.0 Hz), 142.2 (d, J = 8.0 Hz), 141.6, 124.7, 124.6, 121.9, 54.9 (d, J = 6.0 Hz), 35.1, 30.1, 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ −5.1; FTIR (NaCl, neat) ν 1769, 1643, 1469, 1368, 1269 cm^{-1}; HRMS (ESI, $C_{14}H_{22}O_6P$ (M + H)$^+$) calcd 317.1154, found 317.1147.

3-Benzyl-2-((dimethoxyphosphoryl)oxy)phenyl Acetate (6b). Yield 33.1 mg, 63%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 − 7.25 (m, 2H), 7.24 − 7.16 (m, 3H), 7.13 − 6.99 (m, 2H), 6.93 (d, J = 7.6 Hz, 1H), 4.12 (s, 2H), 3.80 (d, J = 11.4 Hz, 6H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 141.9 (d, J = 3.0 Hz), 140.6, 139.2, 134.7 (d, J = 5.0 Hz), 129.0, 128.5, 128.2, 126.3, 125.5, 122.0 (d, J = 1.0 Hz), 55.1 (d, J = 7.0 Hz), 35.7, 20.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.1; FTIR (NaCl, neat) ν 1769, 1601, 1470, 1371, 1267 cm^{-1}; HRMS (ESI, $C_{17}H_{20}O_6P$ (M + H)$^+$) calcd 351.0998, found 351.0996.

2-((Dimethoxyphosphoryl)oxy)-3,4-dimethylphenyl Acetate (6c). Yield 31.1 mg, 72%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 8.3 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 3.85 (d, J = 11.4 Hz, 6H), 2.33 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 140.6 (d, J = 8.0 Hz), 139.8 (d, J = 3.0 Hz), 136.0, 130.3 (d, J = 4.0 Hz), 130.3, 126.6, 120.3, 55.0 (d, J = 6.0 Hz), 20.8, 19.9, 13.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ −3.8; FTIR (NaCl, neat) ν 1769, 1614, 1487, 1371, 1273 cm^{-1}; HRMS (ESI, $C_{12}H_{18}O_6P$ (M + H)$^+$) calcd 289.0841, found 289.0842.

2-((Dimethoxyphosphoryl)oxy)-[1,1′-biphenyl]-3-yl Acetate (6d). Yield 25.2 mg, 50%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 − 7.46 (m, 2H), 7.43 (t, J = 7.4 Hz, 2H), 7.38 − 7.33 (m, 1H), 7.29 − 7.21 (m, 3H), 7.19 − 7.15 (m, 1H), 3.42 (d, J = 11.5 Hz, 6H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 142.3, 139.7, 136.9, 136.2 (d, J = 4.0 Hz), 129.6, 128.4, 128.2, 127.7, 125.6, 123.1, 54.5 (d, J = 6.0 Hz), 20.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.5; FTIR (NaCl, neat) ν 1769, 1599, 1470, 1371, 1254 cm^{-1}; HRMS (ESI, $C_{16}H_{18}O_6P$ (M + H)$^+$) calcd 337.0841, found 337.0840.

2-((Dimethoxyphosphoryl)oxy)-4-methylphenyl Acetate (6e). Yield 25.5 mg, 62%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 1H), 7.03 − 6.95 (m, 2H), 3.85 (d, J = 11.4 Hz, 6H), 2.34 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 141.8, 138.9 (d, J = 7.0 Hz), 137.2, 126.2, 123.3, 121.6 (d, J = 3.0 Hz), 55.0 (d, J = 6.0 Hz), 21.0, 20.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.4; FTIR (NaCl, neat) ν 1769, 1595, 1510, 1371, 1279 cm^{-1}; HRMS (ESI, $C_{11}H_{16}O_6P$ (M + H)$^+$) calcd 275.0685, found 275.0680.

4-(*tert*-Butyl)-2-((dimethoxyphosphoryl)oxy)phenyl Acetate (6f). Yield 31.3 mg, 66%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.19 (dd, J = 8.5, 2.2 Hz, 1H), 7.05 (dd, J = 8.5, 1.0 Hz,

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1H), 3.85 (d, J = 11.4 Hz, 6H), 2.32 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 150.5, 141.6 (d, J = 7.0 Hz), 138.7, 123.0, 122.6, 118.5 (d, J = 2.0 Hz), 55.0 (d, J = 6.0 Hz), 34.7, 31.2, 20.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.4; FTIR (NaCl, neat) ν 1769, 1591, 1504, 1368, 1269 cm^{-1}; HRMS (ESI, $C_{14}H_{22}O_6P$ $(M + H)^+$) calcd 317.1154, found 317.1158.

2-((Dimethoxyphosphoryl)oxy)-4-methoxyphenyl Acetate (6g). Yield 27.9 mg, 64%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 8.9 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 6.71 (dd, J = 8.9, 2.8 Hz, 1H), 3.85 (d, J = 11.4 Hz, 6H), 3.79 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 157.9, 142.6 (d, J = 7.0 Hz), 134.8, 123.9, 110.8, 107.2 (d, J = 3.0 Hz), 55.8, 55.0 (d, J = 6.0 Hz), 20.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.5; FTIR (NaCl, neat) ν 1769, 1620, 1514, 1371, 1285 cm^{-1}; HRMS (ESI, $C_{11}H_{16}O_7P$ $(M + H)^+$) calcd 291.0634, found 291.0634.

3-Chloro-2-((dimethoxyphosphoryl)oxy)phenyl Acetate (6h). Yield 30.1 mg, 68%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 7.8 Hz, 1H), 7.18 − 7.07 (m, 2H), 3.92 (d, J = 11.5 Hz, 6H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 143.1 (d, J = 3.0 Hz), 139.6 (d, J = 7.0 Hz), 127.8, 127.5 (d, J = 5.0 Hz), 125.7 (d, J = 1.0 Hz), 122.7, 55.4 (d, J = 6.0 Hz), 20.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.7; FTIR (NaCl, neat) ν 1779, 1587, 1470, 1371, 1265 cm^{-1}; HRMS (ESI, $C_{10}H_{13}ClO_6P$ $(M + H)^+$) calcd 295.0138, found 295.0159.

Methyl 3-Acetoxy-2-((dimethoxyphosphoryl)oxy)-5-methylbenzoate (6i). Yield 25.3 mg, 53%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 1.9 Hz, 1H), 7.13 (d, J = 2.0 Hz, 1H), 3.89 (d, J = 12.1 Hz, 6H), 3.85 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 165.1, 142.4 (d, J = 3.0 Hz), 139.2 (d, J = 7.0 Hz), 135.6 (d, J = 2.0 Hz), 129.1, 128.3 (d, J = 2.0 Hz), 125.0 (d, J = 3.0 Hz), 55.2 (d, J = 6.0 Hz), 52.3, 20.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.2; FTIR (NaCl, neat) ν 1778, 1732, 1614, 1485, 1371, 1323 cm^{-1}; HRMS (ESI, $C_{13}H_{18}O_8P$ $(M + H)^+$) calcd 333.0739, found 333.0734.

Methyl 3-Acetoxy-2-hydroxy-5-methylbenzoate (6i′). Yield 8.1 mg, 24%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 7.54 (d, J = 1.3 Hz, 1H), 7.07 (d, J = 2.0 Hz, 1H), 3.94 (s, 3H), 2.34 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 168.9, 151.3, 138.8, 129.5, 128.2, 127.2, 113.4, 52.4, 20.6, 20.4; FTIR (NaCl, neat) ν 3165, 1771, 1682, 1620, 1479, 1443, 1346 cm^{-1}; HRMS (ESI, $C_{11}H_{13}O_5$ $(M + H)^+$) calcd 225.0763, found 225.0772.

2-((Dimethoxyphosphoryl)oxy)phenyl Acetate (6j). Yield 22.2 mg, 57%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.5 Hz, 1H), 7.25 − 7.11 (m, 3H), 3.85 (d, J = 11.4 Hz, 6H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 142.3 (d, J = 6.0 Hz), 141.3, 126.9, 125.6, 123.8, 121.1 (d, J = 3.0 Hz), 55.0 (d, J = 6.0 Hz), 20.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.4; FTIR (NaCl, neat) ν 1769, 1599, 1495, 1371, 1285 cm^{-1}; HRMS (ESI, $C_{10}H_{14}O_6P$ $(M + H)^+$) calcd 261.0528, found 261.0542.

2-((Dimethoxyphosphoryl)oxy)-1,3-phenylene Diacetate (6j′). Yield 32.0 mg, 67%; yellow solid; mp 73 − 75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 − 7.16 (m, 1H), 7.07 (d, J = 8.3 Hz, 2H), 3.85 (d, J = 11.5 Hz, 6H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 143.0 (d, J = 4.0 Hz), 134.9 (d, J = 7.0 Hz), 125.0, 121.2, 55.2 (d, J = 7.0 Hz), 20.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −4.4; FTIR (NaCl, neat) ν 1769, 1605, 1472, 1368, 1271 cm^{-1}; HRMS (ESI, $C_{12}H_{16}O_8P$ $(M + H)^+$) calcd 319.0583, found 319.0559.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sgkim@ntu.edu.sg.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected recent reviews, see: (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (c) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (e) McMurray, L.; Hara, F. O.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (f) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (g) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (h) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (i) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (j) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588. (k) Wencel-Delord, J.; Glorius, F. *Nature Chem.* **2013**, *5*, 369. (l) Shang, Y.; Jie, X.; Zhou, J.; Hu, P.; Huang, S.; Su, W. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 1299.

(2) (a) Chan, L. Y.; Kim, S.; Ryu, T.; Lee, P. H. *Chem. Commun.* **2013**, *49*, 4682. (b) Meng, X. J.; Kim, S. *Org. Lett.* **2013**, *15*, 1910.

(3) (a) Chan, L. Y.; Cheong, L. L.; Kim, S. *Org. Lett.* **2013**, *15*, 2186. (b) Chary, B. C.; Kim, S.; Park, Y.; Kim, J.; Lee, P. H. *Org. Lett.* **2013**, *15*, 2692.

(4) For Pd(II)-catalyzed *ortho*-arylation using a phosphate directing group, see: Jeon, W. H.; Lee, T. S.; Kim, E. J.; Moon, B.; Kang, J. *Tetrahedron* **2013**, *69*, 5152.

(5) (a) Dick, A. R.; Kampf, J. W.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 12790. (b) Hull, K. L.; Lanni, E. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 14047. (c) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 9651. (d) Racowski, J. A.; Dick, A. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 10974. (e) Racowski, J. A.; Nicholas, D. B.; Sanford, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 18022.

(6) For selected Sanford reports on *ortho*-acetoxylation, see: (a) Dick, A. R.; Hull, K. L.; Sanford, M. S. J. *Am. Chem. Soc.* **2004**, *126*, 2300. (b) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542. (c) Kalyani, D.; Sanford, M. S. *Org. Lett.* **2005**, *7*, 4149. (d) Desai, L. V.; Malik, H. A.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 1141. (e) Neufeldt, S. R.; Sanford, M. S. *Org. Lett.* **2010**, *12*, 532.

(7) For additional recent *ortho*-C-H oxidations, see: (a) Wang, D.-H.; Hao, X.-S.; Wu, D.-F.; Yu, J.-Q. *Org. Lett.* **2006**, *8*, 3387. (b) Wang, G.-W.; Yuan, T.-T.; Wu, X.-L. *J. Org. Chem.* **2008**, *73*, 4717. (c) Zhang, J.; Khaskin, E.; Anderson, N. P.; Zavalij, P. Y.; Vedernikov, A. N. *Chem. Commun.* **2008**, 3625. (d) Zhang, Y. H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654. (e) Chernyak, N.; Dudnik, A. S.; Huang, C.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 8270. (f) Huang, C.; Ghavtadze, N.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 17630. (g) Wang, C.; Ge, H. *Chem.—Eur. J.* **2011**, *17*, 14371.

(8) (a) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302. (b) Powers, D. C.; Lee, E.; Ariafard, A.; Sanford, M. S.; Yates, B. F.; Canty, A. J.; Ritter, T. *J. Am. Chem. Soc.* **2012**, *134*, 12002.

(9) (a) Khandelwal, A.; Lukacova, V.; Comez, D.; Kroll, D. M.; Raha, S.; Balaz, S. *J. Med. Chem.* **2005**, *48*, 5437. (b) de Garavilla, L.; Greco, M. N.; Sukumar, N.; Chen, Z.-W.; Pineda, A. O.; Mathews, F. S.; Di Cera, E.; Giardino, E. C.; Wells, G. I.; Haertlein, B. J.; Kauffman, J. A.; Corcoran, T. W.; Derian, C. K.; Eckardt, A. J.; Damiano, B. P.; Andrade-Gordon, P.; Maryanoff, B. E. *J. Biol. Chem.* **2005**, *280*, 18001. (c) Dang, Q.; Kasibhatla, S. R.; Jiang, T.; Fan, K.; Liu, Y.; Taplin, F.; Schulz, W.; Cashion, D. K.; Reddy, K. R.; van Poelje, P. D.; Fujitaki, J. M.; Potter, S. C.; Erion, M. D. *J. Med. Chem.* **2008**, *51*, 4331. (d) Metcalf, W. W.; van der Donk, W. A. *Annu. Rev. Biochem.* **2009**, *78*, 65. (e) Verbrugghen, T.; Cos, P.; Maes, L.; Van Calenbergh, S. *J. Med. Chem.* **2010**, *53*, 5342.

(10) For reviews, see: (a) Wardworth, W. S., Jr. *Org. React.* **1977**, *25*, 73. (b) Stec, W. J. *Acc. Chem. Res.* **1983**, *16*, 411. (c) Terada, M. *Synthesis* **2010**, *12*, 1929. (d) Bisceglia, J. A.; Orelli, L. R. *Curr. Org. Chem.* **2012**, *16*, 2206.

(11) (a) Gustafson, K. R.; Cardellina, J. H., II; McMahon, J. B.; Pannell, L. K.; Cragg, G. M.; Boyd, M. R. *J. Org. Chem.* **1992**, *57*, 2809. (b) Nicolaou, K. C.; Vourloumis, D.; Winssinger, N.; Baran, P. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 44. (c) Yang, D. P.; Ji, H. F.; Tang, G. Y.; Ren, W.; Zhang, H. Y. *Molecules* **2007**, *12*, 878.