Manganese(III) Acetate Mediated Free-Radical Phosphonylation of Flavones and Coumarins

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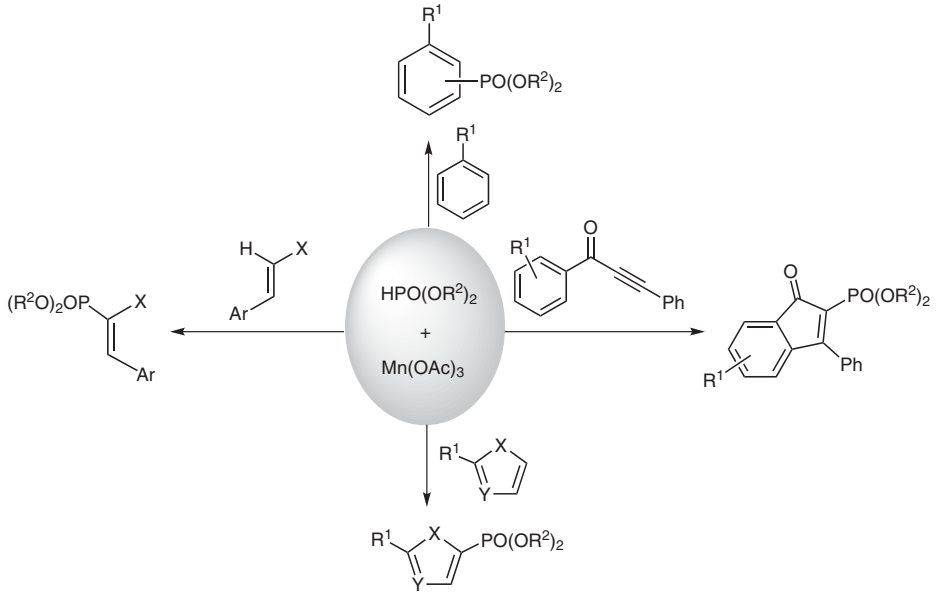
Received 29 December 2011; revised 13 February 2012

Abstract: The phosphonyl radical generated from the reaction of manganese(III) acetate with diethyl phosphonate selectively adds to the 3-position of flavones and coumarins to afford phosphonylated products in moderate to good yields.

Key words: manganese acetate, phosphonylation, flavones, coumarins, dialkyl phosphonate, free radical

The reaction of phosphorus radicals with sp^2 and sp C–H bond to form C–P bonds is a topic of current interest,[1] not only because of the broad biological utility of phosphorus compounds, but also for the development of novel heteroatom-based free-radical reactions. Manganese(III) acetate has been recently introduced as a new reagent for the generation of phosphorus radicals from the labile P–H bond. The Ishii group first reported the phosphonylation of monosubstituted benzenes with dialkyl phosphonates using manganese(II) acetate/cobalt(II) acetate/oxygen as a redox couple.[2] Our group has discovered that manganese(III) acetate can also efficiently generate phosphonyl radicals to react with benzene[3] and heteroaryl compounds such as thiazoles and furans,[4] to react with electron-withdrawing group substituted styrenes to give regio- and stereoselective phosphonylated products at the vinyl group,[5] and to react with 1,3-diarylpropynones to form phosphonylated indenones (Scheme 1).[6] We also found that the phosphinoyl radical could react with 5-arylpent-2-enoates to yield *trans*-disubstituted tetrahydronaphthalenes.[7] Reported in this paper are our recent efforts in the development of flavone and coumarin-based phosphonylation reactions.

Chromenes and coumarins are privileged rings for nature products. Among them, 2-phenyl-4*H*-chromen-4-ones (flavones) and coumarins have received special attention because of their widespread occurrence and interesting biological activity.[8] The phosphonyl group is an important functionality that can be used to regulate biological properties.[9] The development of efficient ways to introduce this moiety into flavones and coumarins could produce a range of new compounds for biological studies. To the



Scheme 1 Manganese(III) acetate promoted phosphonylations

SYNTHESIS 2012, 44, 1043–1050
Advanced online publication: 14.03.2012
DOI: 10.1055/s-0031-1289748; Art ID: M119611SS

best of our knowledge, only a few phosphonylated flavones and coumarins have been prepared by multistep synthesis.[10–13] We report here the first examples of the direct and selective phosphonylation of flavones and coumarins.

Flavone **1a** was used in a model reaction to optimize the manganese(III) acetate promoted phosphonylation reactions, including variation of the reaction solvent, reagent ratio, and reaction temperature and time. After screening a series of solvents such as acetic acid, ethanol, methanol, and acetonitrile, the best solvent was found to be ethanol. The most suitable ratio for the reagents was 1:2:3 **1a**/diethyl phosphonate/manganese(III) acetate. It was found that using less than two equivalents of manganese(III) acetate resulted in low product yields. It was also found that the addition of three equivalents of manganese(III) acetate in three portions gave the best results. The reaction temperature was varied from 20–80 °C and the reaction time from 60 to 120 minutes. Almost no reaction was observed below 60 °C. Under the optimized conditions of using 1:2:3 **1a**/diethyl phosphonate/manganese(III) acetate in ethanol and heating the mixture at 80 °C for 90 minutes, the reaction afforded phosphonylated product **3a** in 44% yield (Scheme 2 and Table 1, entry 1). A series of flavone analogues were employed to explore the scope and limitation of this reaction. It was found that different aromatic substituents at the 2-position of 4*H*-chromen-4-ones did not significantly change the product yield (Table 1). The structure of compound **3c** was confirmed by X-ray crystal structure analysis (Figure 1). We noticed that the isolated yields of phosphonylated products **3** were 20–30% lower than the conversions. Since byproducts were not isolated in major amounts, we believe some products were lost during flash chromatography purification.

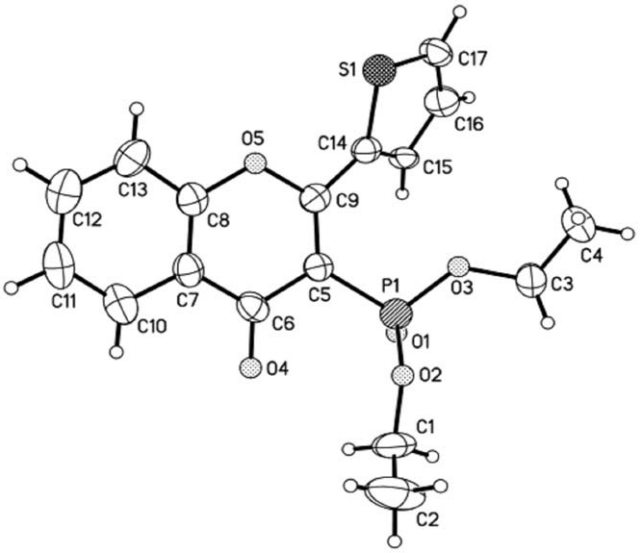


Figure 1 X-ray crystal structure of **3c**

We found that under the conditions described above, the starting materials were not fully consumed even using extended reaction times. The isolated product yields for the products listed in Table 1 were 42–68%. We proposed that this was a result of hindrance by the 2-phenyl group of flavone. 2-Methyl-4*H*-chromen-4-one (**1i**) was used as the substrate to test this hypothesis. The results shown in Table 2 indicate that only 6% phosphonylation was at the expected 3-position, while 60% phosphonylation occurred on the phenyl ring (Table 2, entry 1). The reaction of unsubstituted 4*H*-chromen-4-one (**1j**) gave a similar result (entry 2). The reaction of 2-styryl-substituted chromone **1k** produced a mixture of 3-position and vinyl phosphonylated products in the ratio of 1:1.6. No phosphonylation on the phenyl ring was observed (entry 3).

Table 1 Phosphonylation of Flavone Analogues **1**[a]

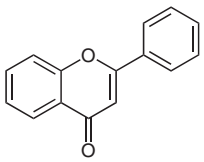
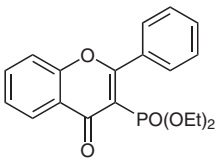
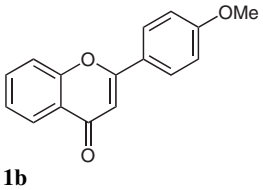
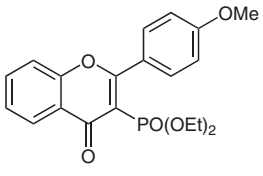
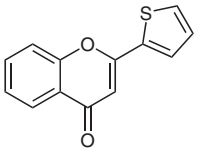
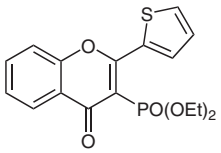
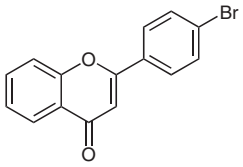
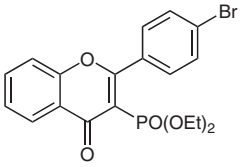
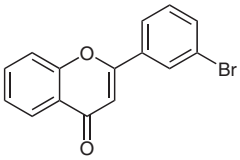
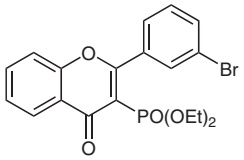
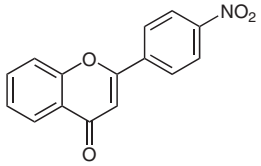
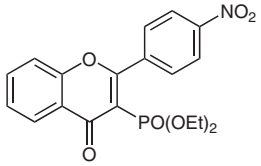
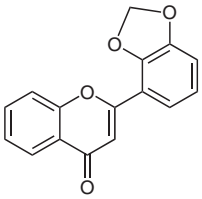
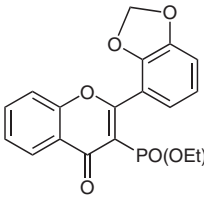
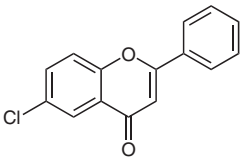
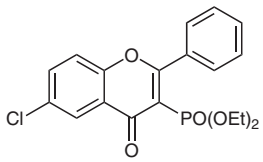
Entry	Substrate	Product	Conv.[b] (%)	Yield[c] (%)
1	 **1a**	 **3a**	75	44
2	 **1b**	 **3b**	78	46
3	 **1c**	 **3c**	75	62

Table 1 Phosphonylation of Flavone Analogues **1**[a] (continued)

Entry	Substrate	Product	Conv.[b] (%)	Yield[c] (%)
4	 **1d**	 **3d**	82	68
5	 **1e**	 **3e**	79	58
6	 **1f**	 **3f**	72	47
7	 **1g**	 **3g**	76	45
8	 **1h**	 **3h**	71	42

[a] Reaction conditions: flavone **1** (1 mmol), $HPO(OEt)_2$ (**2**, 2 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (3 mmol), EtOH (5 mL), air, 80 °C, 1–2 h; the crude product was purified by flash chromatography.
[b] Analyzed by HPLC.
[c] Isolated yield.

Table 2 Phosphonylation of 4*H*-Chromen-4-ones[a]

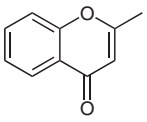
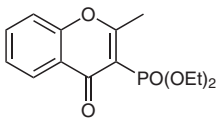
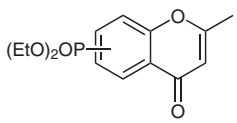
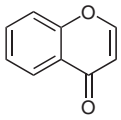
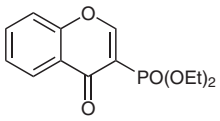
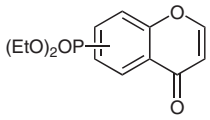
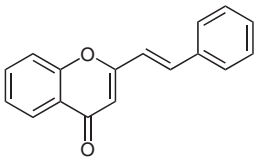
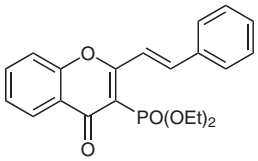
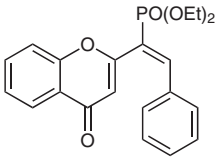
Entry	Substrate	Product	Conv.[b] (%)	Yield[c] (%)
1	 **1i**	 **3i**  **3i′**	69	6 60

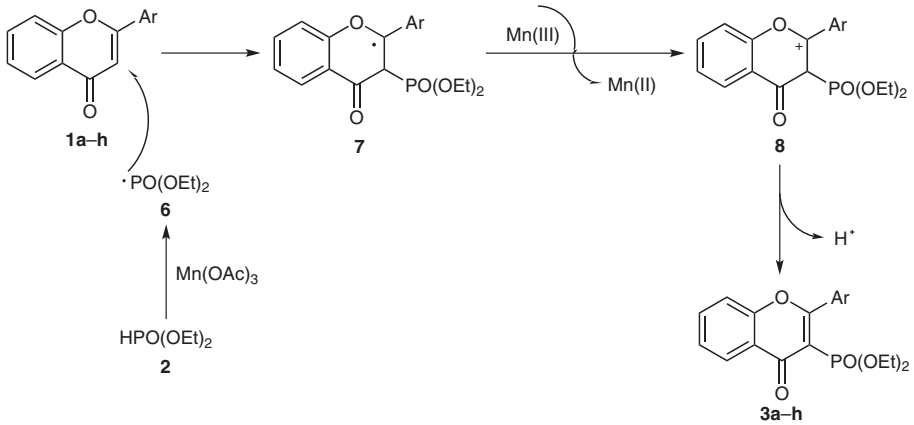
Table 2 Phosphonylation of 4*H*-Chromen-4-ones[a] (continued)

Entry	Substrate	Product	Conv.[b] (%)	Yield[c] (%)
2	 **1j**	 **3j**	65	5
		 **3j′**		58
3	 **1k**	 **3k**	75	27
		 **3k′**		42

[a] Reaction conditions: chromone **1** (1 mmol), $HPO(OEt)_2$ (**2**, 2 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (3 mmol), EtOH (5 mL), air, 80 °C, 1–2 h; the crude product was purified by flash chromatography.
[b] Analyzed by HPLC.
[c] Isolated yield.

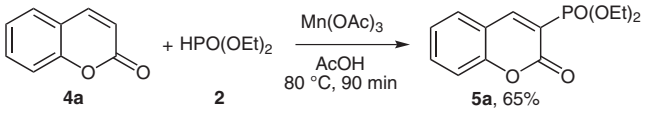
The results shown in Tables 1 and 2 indicate that the 2-phenyl group is responsible for the regioselectivity of the phosphonyl radical reaction of 4*H*-chromen-4-ones. A mechanism is proposed to explain the transformations (Scheme 2). Phosphonyl radical **6** generated by the reaction of manganese(III) acetate with diethyl phosphonate attacks the 3-position of flavone **1** to form benzyl radical **7**. It is then oxidized by manganese(III) acetate to carbocation **8** and then deprotonated to afford product **3**. There are two competitive pathways for the reaction of phosphonyl radical with compounds **1i**,**j**. The attack of phenyl ring is more favored than the 3-position of 4*H*-chromen-4-one because the later process does not generate a stable benzyl radical. The reaction of **1k** also has two competitive pathways. The formation of **3k′** is a major one because it is from the benzyl radical intermediate.

We reasoned that coumarins could be more suitable substrates for phosphonylation because they have no steric hindered 2-aryl group compared to flavones, and they can generate stable benzyl radicals after the addition of phos-



Scheme 2 Proposed phosphonylation mechanism for flavones

phonyl radical at the 3-position. Indeed, the reaction of coumarin (**4a**) with diethyl phosphonate using acetic acid as a solvent afforded 3-phosphonylated coumarin **5a** in 65% yield (Scheme 3, and Table 3, entry 1), which is higher than that for 3-phosphonyl flavone **3a** (Table 1, entry 1). The reaction results for a series of coumarins **4** are shown in Table 3, which indicate that substituents on either the phenyl ring or at the 4-position have no significant impact on product yields.

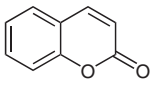
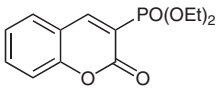
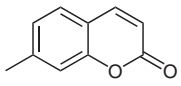
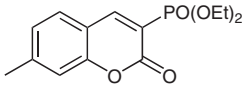
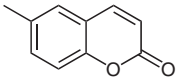
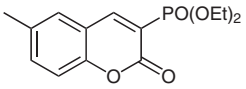
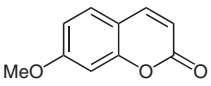
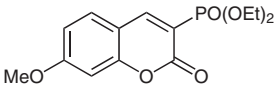
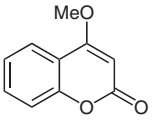
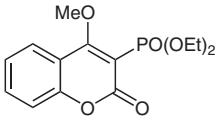
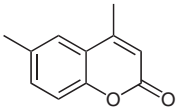
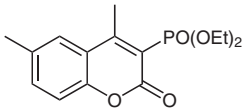
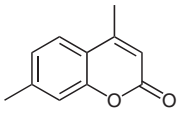
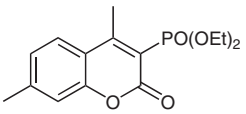
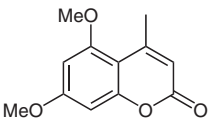
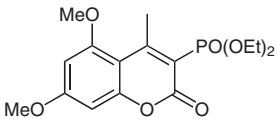


Scheme 3 Phosphonylation of coumarin

In summary, we have developed an efficient method for the direct phosphonylation of flavones and coumarins. Manganese(III) acetate induced phosphonyl radical reactions are regioselective at the 3-position of flavones and coumarins. This straightforward and selective method expands the synthetic utility of the free-radical-based phosphonylation of heteroaryl compounds.

All reactions were carried out under air. Solvents were dried by the standard procedures. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ on a Varian-Inova 300MHz or 400 MHz spectrometer referenced to internal TMS. HRMS were recorded on a MicroMass-TOF machine (EI). Flash column chromatography was performed using 200–300 mesh silica gel. All the commercial reagents were used directly for reactions unless otherwise noted.

Table 3 Phosphonylation of Coumarins **4**[a]

Entry	Coumarin	Product	Yield[b] (%)
1	 **4a**	 **5a**	65
2	 **4b**	 **5b**	65
3	 **4c**	 **5c**	74
4	 **4d**	 **5d**	78
5	 **4e**	 **5e**	63
6	 **4f**	 **5f**	75
7	 **4g**	 **5g**	87
8	 **4h**	 **5h**	72

[a] Reaction conditions: coumarin **4** (1 mmol), $HPO(OEt)_2$ (**2**, 2 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (3 mmol), AcOH (5 mL), air, 80 °C, 1–2 h; the crude product was purified by flash chromatography.
[b] Isolated yield.

Diethyl (4-Oxo-2-phenyl-4*H*-chromen-3-yl)phosphonate (3a); Typical Procedure for Phosphonylation of Flavones 1

To a stirred mixture of flavone **1a** (0.22 g, 1 mmol), $HPO(OEt)_2$ (**2**, 0.27 g, 2 mmol) in EtOH (5 mL) was added $Mn(OAc)_3{\cdot}2H_2O$ (0.81 g, 3 mmol) in 3 portions and the resulting soln was heated at 80 °C for 1.5 h. The mixture was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with sat. Na_2CO_3 soln, dried (anhyd Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (acetone–petroleum ether, 1:6) to afford **3a** (0.16 g, 44%).

Diethyl (4,7-Dimethyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5g); Typical Procedure for Phosphonylation of Coumarins 4

To a stirred mixture of coumarin **4g** (0.17 g, 1 mmol), $HPO(OEt)_2$ (**2**, 0.27 g, 2 mmol) in AcOH (5 mL) was added $Mn(OAc)_3{\cdot}2H_2O$ (0.81 g, 3 mmol) in 3 portions and the resulting soln was heated at 80 °C for 1.5 h. The mixture was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with sat. Na_2CO_3 soln, dried (anhyd Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (acetone–petroleum ether, 1:4) to afford **5g** (0.27 g, 87%).

Diethyl (4-Oxo-2-phenyl-4*H*-chromen-3-yl)phosphonate (3a)

Yellow liquid; yield: 0.16 g (44%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.7 Hz, 1 H, ArH), 7.74 (d, *J* = 7.4 Hz, 2 H, ArH), 7.66 (t, *J* = 7.7 Hz, 1 H, ArH), 7.38–7.56 (m, 5 H, ArH), 4.09–3.98 (m, 4 H, 2 CH_2), 1.16 (t, *J* = 6.6 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8 (d, J_{P-C} = 3.9 Hz), 171.6 (d, J_{P-C} = 19.8 Hz), 155.9, 134.8, 134.3, 131.6, 129.8, 128.4, 126.3, 123.6 (d, J_{P-C} = 7.6 Hz), 118.3, 112.6 (d, J_{P-C} = 195.0 Hz), 63.0 (d, J_{P-C} = 5.8 Hz), 16.4 (d, J_{P-C} = 6.5 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{19}O_5P$: 358.0970; found: 358.0974.

Diethyl [2-(4-Methoxyphenyl)-4-oxo-4*H*-chromen-3-yl]phosphonate (3b)

White liquid; yield: 0.18 g (46%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.9 Hz, 1 H, ArH), 7.73 (d, *J* = 8.1 Hz, 2 H, ArH), 7.63 (t, *J* = 8.3 Hz, 1 H, ArH), 7.33–7.40 (m, 2 H, ArH), 6.95 (d, *J* = 8.1Hz, 2 H, ArH), 3.97–4.11 (m, 4 H, 2 CH_2), 3.82 (s, 1 H, CH_3), 1.09 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0 (d, J_{P-C} = 3.3 Hz), 171.5 (d, J_{P-C} = 19.8 Hz), 162.6, 155.9, 134.6, 131.9, 126.4, 126.3, 126.1, 123.6 (d, J_{P-C} = 7.6 Hz), 118.1, 113.7, 111.5 (d, J_{P-C} = 195.7 Hz), 63.0 (d, J_{P-C} = 6.2 Hz), 55.9, 16.5 (d, J_{P-C} = 6.7 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{21}O_6P$: 388.1076; found: 388.1085.

Diethyl [4-Oxo-2-(thiophen-2-yl)-4*H*-chromen-3-yl]phosphonate (3c)

White crystals; yield: 0.23 g (62%); mp 122–124 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 7.8 Hz, 1 H, ArH), 8.01 (d, *J* = 3.3 Hz, 1 H, ArH), 7.66 (t, 2 H, ArH), 7.37–7.43 (m, 2 H, ArH), 7.15 (t, *J* = 4.0 Hz, 1 H, ArH), 4.09–4.16 (m, 4 H, 2 CH_2), 1.17 (t, *J* = 7.0 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8 (d, J_{P-C} = 4.8 Hz), 165.1 (d, J_{P-C} = 19.1 Hz), 155.6, 135.4, 134.8, 134.2, 131.9, 128.0, 126.4, 126.3, 123.7 (d, J_{P-C} = 6.8 Hz), 118.2, 63.3 (d, J_{P-C} = 6.0 Hz), 16.6 (d, J_{P-C} = 6.7 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{17}O_5PS$ 364.0534; found: 364.0534.

Diethyl [2-(4-Bromophenyl)-4-oxo-4*H*-chromen-3-yl]phosphonate (3d)

Yellow liquid; yield: 0.30 g (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.9 Hz, 1 H, ArH), 7.66 (t, *J* = 7.5 Hz, 1 H, ArH), 7.58 (s, 4 H, ArH), 7.38 (t, *J* = 7.5 Hz, 2 H, ArH), 4.12–3.98 (m, 4 H, 2 CH_2), 1.09 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 170.5 (d, J_{P-C} = 19.7 Hz), 155.9, 134.9, 133.2, 131.6, 131.4, 126.5, 126.4, 123.5 (d, J_{P-C} = 7.4 Hz), 118.3, 112.9 (d, J_{P-C} = 194.8 Hz), 63.1 (d, J_{P-C} = 6.0 Hz), 16.5 (d, J_{P-C} = 6.6 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{18}{}^{79}BrO_5P$: 436.0075; found: 436.0074.

Diethyl [2-(3-Bromophenyl)-4-oxo-4*H*-chromen-3-yl]phosphonate (3e)

Yellow liquid; yield: 0.25 g (58%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.1 Hz, 1 H, ArH), 7.86 (s, 1 H, ArH), 7.71–7.65 (m, 3 H, ArH), 7.44 (d, *J* = 8.0 Hz, 2 H, ArH), 7.37 (t, *J* = 7.9 Hz, 1 H, ArH), 4.17–4.02 (m, 4 H, 2 CH_2), 1.13 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 169.9 (d, J_{P-C} = 19.0 Hz), 155.9, 136.2, 135.0, 134.5, 132.3, 129.9, 128.7, 126.5 (2 peaks), 123.6 (d, J_{P-C} = 7.7 Hz), 122.3, 118.3, 112.3, 63.1 (d, J_{P-C} = 6.0 Hz), 16.5 (d, J_{P-C} = 6.7 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{18}{}^{79}BrO_5P$: 436.0075; found: 436.0076.

Diethyl [2-(4-Nitrophenyl)-4-oxo-4*H*-chromen-3-yl]phosphonate (3f)

Yellow liquid; yield: 0.19 g (47%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (s, 2 H, ArH), 8.23 (s, 1 H, ArH), 7.92 (s, 2 H, ArH), 7.73 (t, *J* = 7.4 Hz, 1 H, ArH), 7.48 (s, 2 H, ArH), 4.16–4.10 (m, 4 H, 2 CH_2), 1.13 (m, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2 (d, J_{P-C} = 18.7 Hz)., 155.8, 149.3, 140.0, 135.0, 130.7, 126.6, 126.4, 123.3, 118.1, 63.2, 16.4.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{18}NO_7P$: 403.0821; found: 403.0828.

Diethyl [2-(1,3-Benzodioxol-5-yl)-4-oxo-4*H*-chromen-3-yl]phosphonate (3g)

Yellow liquid; yield: 0.18 g (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 7.8 Hz, 1 H, ArH), 7.66 (t, *J* = 7.8 Hz, 1 H, ArH), 7.43–7.38 (m, 2 H, ArH), 7.34 (d, *J* = 8.1 Hz, 1 H, ArH), 7.22 (s, 1 H, ArH), 6.89 (d, *J* = 7.9 Hz, 1 H, ArH), 6.04 (s, 2 H, CH_2), 4.14–4.05 (m, 4 H, 2 CH_2), 1.19 (t, *J* = 6.5 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (d, J_{P-C} = 2.9 Hz), 170.9 (d, J_{P-C} = 19.9 Hz), 155.5, 150.5, 147.5, 134.4, 127.5, 126.0, 125.9, 125.3, 123.3 (d, J_{P-C} = 7.5 Hz), 117.9, 111.5 (d, J_{P-C} = 195.6 Hz), 109.7, 108.0, 101.9, 62.7 (d, J_{P-C} = 6.2 Hz), 16.3 (d, J_{P-C} = 7.2 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{19}O_7P$: 402.0868; found: 402.0868.

Diethyl (6-Chloro-4-oxo-2-phenyl-4*H*-chromen-3-yl)phosphonate (3h)

Yellow liquid; yield: 0.16 g (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 2.5 Hz, 1 H, ArH), 7.75 (d, *J* = 7.1 Hz, 2 H, ArH), 7.63 (dd, *J* = 2.5, 8.9 Hz, 1 H, ArH), 7.58–7.48 (m, 3 H, ArH), 7.42 (d, *J* = 8.9 Hz, 1 H, ArH), 4.16–3.98 (m, 4 H, 2 CH_2), 1.08 (t, *J* = 7.0 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1, 161.0 (d, J_{P-C} = 11.6 Hz), 156.8, 150.7, 150.6, 134.2, 133.7 (d, J_{P-C} = 20.0 Hz), 130.8, 130.1, 129.0, 126.0, 125.7, 124.2, 121.7, 118.3, 113.4, 63.1 (d, J_{P-C} = 5.3 Hz), 16.6 (d, J_{P-C} = 6.1 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{18}ClO_5P$: 392.0580; found: 392.0580.

Diethyl (2-Methyl-4-oxo-4*H*-chromen-3-yl)phosphonate (3i)
Yellow liquid; yield: 0.018 g (6%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.0 Hz, 1 H, ArH), 7.66 (t, *J* = 7.8 Hz, 1 H, ArH), 7.40 (d, *J* = 7.9 Hz, 2 H, ArH), 4.29–4.15 (m, 4 H, 2 CH_2), 2.87 (s, 3 H, CH_3), 1.36 (t, *J* = 7.0 Hz, 6 H, 2 CH_3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}O_5P$: 296.0814; found: 296.0813.

Diethyl (4-Oxo-4*H*-chromen-3-yl)phosphonate (3j)
Yellow liquid; yield: 0.014 g (5%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 7.9 Hz, 1 H, 2-H), 8.22 (d, *J* = 9.6 Hz, 1 H, ArH), 7.72 (t, *J* = 7.8 Hz, 1 H, ArH), 7.51–7.44 (m, 2 H, ArH), 4.32–4.19 (m, 4 H, 2 CH_2), 1.37 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}O_5P$: 282.0657; found: 282.0658.

Diethyl (*E*)-(4-Oxo-2-styryl-4*H*-chromen-3-yl)phosphonate (3k)
Yellow liquid; yield: 0.10 g (27%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (d, *J* = 15.9 Hz, 1 H, α-H), 8.19 (dd, *J* = 1.5, 7.9 Hz, 1 H, ArH), 7.80 (d, *J* = 15.9 Hz, 1 H, β-H), 7.71–7.70 (m, 3 H, ArH), 7.54 (d, *J* = 8.3 Hz, 1 H, ArH), 7.44–7.40 (m, 4 H, ArH), 4.33–4.17 (m, 4 H, 2 CH_2), 1.38 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.1, 167.8 (d, J_{P-C} = 24.8 Hz), 155.0, 140.5, 135.4, 134.4, 130.4, 129.1, 128.6, 126.2, 125.7, 123.4 (d, J_{P-C} = 7.7 Hz), 120.0, 117.6, 109.4 (d, J_{P-C} = 187.6 Hz), 62.9 (d, J_{P-C} = 5.8 Hz), 16.6 (d, J_{P-C} = 6.4 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{21}H_{21}O_5P$: 384.1127; found: 384.1126.

Diethyl (*E*)-[1-(4-Oxo-4*H*-chromen-2-yl)-2-phenylvinyl]phosphonate (3k′)
Yellow liquid; yield: 0.16 g (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (dd, *J* = 1.5, 8.0 Hz, 1 H, ArH), 7.89 (d, *J* = 23.5 Hz, 1 H, β-H), 7.66–7.62 (m, 1 H, ArH), 7.42 (t, *J* = 7.5 Hz, 2 H, ArH), 7.32–7.30 (m, 3 H, ArH), 7.28–7.25 (m, 2 H, ArH), 6.47 (d, *J* = 2.3 Hz, 1 H, C_3-H), 4.23–4.16 (m, 4 H, 2 CH_2), 1.34 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.5, 171.5 (d, J_{P-C} = 19.6 Hz), 154.0, 134.7, 133.7, 131.9, 131.5, 129.5, 128.1, 126.5, 125.4, 124.2 (d, J_{P-C} = 7.5 Hz), 119.8, 112.5 (d, J_{P-C} = 195.6 Hz), 107.9, 62.8 (d, J_{P-C} = 5.8 Hz), 16.1 (d, J_{P-C} = 6.4 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{21}H_{21}O_5P$: 384.1127; found: 384.1127.

Diethyl (2-Oxo-2*H*-chromen-3-yl)phosphonate (5a)
White powder; yield: 0.18 g (65%); mp.65–66 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, $^3J_{PH}$ = 17.2 Hz, 1 H, C_4-H), 7.63–7.58 (m, 2 H, ArH), 7.36–7.31 (m, 2 H, ArH), 4.32–4.20 (m, 4 H, 2 CH_2), 1.37 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (d, J_{P-C} = 14.6 Hz), 155.3, 153.5 (d, J_{P-C} = 6.4 Hz), 134.4, 129.5, 125.1, 118.0 (d, J_{P-C} = 14.1 Hz), 117.9 (d, J_{P-C} = 197.1 Hz), 116.9, 63.5 (d, J_{P-C} = 5.7 Hz), 16.5 (d, J_{P-C} = 6.1 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}O_5P$: 282.0657; found: 282.0657.

Diethyl (7-Methyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5b)
Yellow powder; yield: 0.19 g (65%); mp 62–64 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1 H, C_4-H), 7.39 (d, *J* = 7.5 Hz, 1 H, ArH), 7.06 (d, *J* = 7.4 Hz, 2 H, ArH), 4.19 (m, 4 H, 2 CH_2), 2.40 (s, 3 H, 7-CH_3), 1.30 (s, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 155.6, 153.7, 146.4, 129.3, 126.4, 117.1, 115.8, 106.6 (d, J_{P-C} = 200.7 Hz), 63.5, 22.3, 16.6.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}O_5P$: 296.0814; found: 296.0815.

Diethyl (6-Methyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5c)
Yellow powder; yield: 0.22 g (74%); mp 74–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 17.1 Hz, 1 H, 4-H), 7.38 (d, *J* = 8.5 Hz, 1 H, ArH), 7.30 (s, 1 H, ArH), 7.17 (d, *J* = 8.5 Hz, 1 H, ArH), 4.23–4.17 (m, 4 H, 2 CH_2), 2.35 (s, 3 H, 6-CH_3), 1.31 (t, *J* = 7.0 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0 (2 peaks), 158.9 (2 peaks), 153.7, 153.6, 135.6, 135.0, 129.2, 117.9 (2 peaks), 117.8 (2 peaks), 116.8, 63.6, 20.9, 16.6.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}O_5P$: 296.0814; found: 296.0814.

Diethyl (7-Methoxy-2-oxo-2*H*-chromen-3-yl)phosphonate (5d)
Yellow oil; yield: 0.24 g (78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60–8.20 (m, 1 H, ArH), 7.47 (d, *J* = 8.6 Hz, 1 H, ArH), 6.84 (dd, *J* = 1.6, 34.0 Hz, 1 H, ArH), 6.79 (d, *J* = 2.0 Hz, 1 H, ArH), 4.23–4.22 (m, 4 H, 2 CH_2), 3.88 (s, 3 H, 7-OCH_3), 1.37–1.34 (t, *J* = 5.7 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 157.9, 154.0 (d, J_{P-C} = 17.6 Hz), 130.9, 113.8, 112.1 (d, J_{P-C} = 12.4 Hz), 108.7 (d, J_{P-C} = 189.7 Hz), 101.0, 63.6 (d, J_{P-C} = 3.1 Hz), 56.4, 16.8 (d, J_{P-C} = 4.9 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}O_6P$: 312.0763; found: 312.0762.

Diethyl (4-Methoxy-2-oxo-2*H*-chromen-3-yl)phosphonate (5e)
Yellow oil; yield: 0.20 g (63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.1 Hz, 1 H, ArH), 7.57 (t, *J* = 7.8 Hz, 1 H, ArH), 7.26 (d, *J* = 7.0 Hz, 2 H, ArH), 4.26 (s, 3 H, 3-OCH_3), 4.23–4.19 (m, 4 H, 2 CH_2), 1.32 (t, *J* = 7.0 Hz, 6 H, 2 CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 160.9 (d, J_{P-C} = 10.3 Hz), 154.3, 134.6, 125.0, 124.6, 117.1, 103.4 (d, J_{P-C} = 195.6 Hz), 65.5, 63.5 (d, J_{P-C} = 6.2 Hz), 16.6 (d, J_{P-C} = 6.7 Hz).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}O_6P$: 312.0763; found 312.0762.

Diethyl (4,6-Dimethyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5f)
Yellow powder; yield: 0.23 g (75%); mp 30–32 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (s, 1 H, ArH), 7.39 (d, *J* = 8.4 Hz, 1 H, ArH), 7.18 (d, *J* = 8.4 Hz, 1 H, ArH), 4.28–4.17 (m, 4 H, 2 CH_2), 2.95 (d, *J* = 2.4 Hz, 3 H, 4-CH_3), 2.41 (s, 3 H, 7-CH_3), 1.34 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.4 (d, J_{P-C} = 9.8 Hz), 158.8 (d, J_{P-C} = 14.9 Hz), 151.8, 135.0, 134.3, 125.9, 119.7 (d, J_{P-C} = 15.5 Hz), 116.8, 115.0 (d, J_{P-C} = 194.5 Hz), 63.1 (d, J_{P-C} = 5.9 Hz), 21.2, 17.3 (d, J_{P-C} = 4.0 Hz), 16.5 (d, J_{P-C} = 6.3 Hz).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{19}O_5P$: 310.0970; found: 310.0969.

Diethyl (4,7-Dimethyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5g)

Yellow liquid; yield: 0.27 g (87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.2 Hz, 1 H, ArH), 7.13 (d, *J* = 8.3 Hz, 1 H, ArH), 7.10 (s, 1 H, ArH), 4.29–4.18 (m, 4 H, 2 CH_2), 2.94 (d, *J* = 2.5 Hz, 3 H, 4-CH_3), 2.45 (s, 3 H, 7-CH_3), 1.37 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.3 (d, J_{P-C} = 9.7 Hz), 158.7 (d, J_{P-C} = 16.2 Hz), 153.6, 145.5, 125.8, 117.5 (d, *J* = 15.5 Hz), 116.9, 116.6, 113.8 (d, J_{P-C} = 195.0 Hz), 62.9 (d, J_{P-C} = 5.7 Hz), 21.7, 17.1 (d, J_{P-C} = 3.8 Hz), 16.5 (d, J_{P-C} = 6.3 Hz).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{19}O_5P$: 310.0970; found: 310.0969.

Diethyl (5,7-Dimethoxy-4-methyl-2-oxo-2*H*-chromen-3-yl)phosphonate (5h)

Yellow powder; yield: 0.26 g (72%); mp 84–86 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.39 (d, *J* = 2.3 Hz, 1 H, ArH), 6.30 (d, *J* = 2.3 Hz, 1 H, ArH), 4.26–4.18 (m, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.03 (d, $^4J_{PH}$ = 2.4 Hz, 3 H, CH_3), 1.36 (t, *J* = 7.1 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (d, J_{P-C} = 11.2 Hz), 164.6, 160.6, 158.8 (d, J_{P-C} = 15.8 Hz), 157.3, 110.3 (d, J_{P-C} = 199.4 Hz), 105.6 (d, J_{P-C} = 15.4 Hz), 96.1, 93.2,, 62.8 (d, J_{P-C} = 6.0 Hz), 56.2, 56.1, 22.7 (d, J_{P-C} = 5.3 Hz), 16.6 (d, J_{P-C} = 6.6 Hz).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{21}O_7P$: 356.1025; found: 356.1025.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Acknowledgement

J.P.Z. thanks the National Natural Science Foundation of China for financial support (No. 20772088, 21172163).

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