$Mn(OAc)_3$-Mediated Selective Free Radical Phosphonylation of Pyridinones and Pyrimidinones

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Received: 27.01.2013; Accepted after revision: 26.03.2013

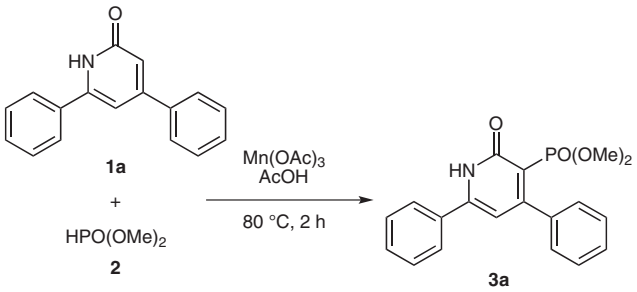
Abstract: The phosphonyl radical generated from the reaction of dimethyl phosphite with manganese(III) acetate adds selectively to the 3-position of pyridin-2-ones or the 5-position of pyrimidin-4-ones to afford phosphonylated products in good yields.

Key words: manganese(III) acetate, phosphonylation, pyridinone, pyrimidinone, dialkyl phosphite, free radical

Phosphonylated azaheterocycles such as pyridinones and pyrimidinones are associated with many biological active compounds and are important in organic, medicinal, and agricultural chemistry. Methods for the synthesis of pyrimidinylphosphonates include direct reaction of dichloropyrimidine with triethyl phosphite,[1] lithium 2,2,6,6-tetramethylpiperidide promoted rearrangement,[2] nucleophilic substitution,[3] lithium–halogen exchange followed by phosphonylation.[4] Oxidative diphosphonylation has been developed for 1,4-dihydropyridines and pyridinium salts.[5]

Manganese(III) acetate is a useful reagent in radical reactions. The Ishii group reported the first catalytic phosphonation of arenes with dialkyl phosphites using manganese(III) acetate/cobalt(II) acetate/oxygen as a redox couple.[6] We have recently reported mangangese(III)-promoted selective phosphonation of aryl,[7] heteroaryl,[8] and conjugated alkene systems.[9] This paper introduces first examples of manganese(III) acetate promoted direct phosphonation of pyridinones and pyrimidinones with a dialkyl phosphite.[10]

4,6-Diphenylpyridin-2(1*H*)-one (**1a**) was used as a substrate for the development of reaction conditions. After screening the reaction solvent, reagent ratio, reaction temperature, and time, it was found that acetic acid was a good solvent and the suitable reagent ratio was **1a**/dimethyl phosphite/manganese(III) acetate 1:2:3. It was also found that the addition of three equivalents of manganese(III) acetate in three portions gave the best results. The reaction at 80 °C for 120 minutes afforded phosphonylated product **3a** in 72% yield (Scheme 1).



Scheme 1 Phosphonylation of 4,6-diphenylpyridin-2(1*H*)-one

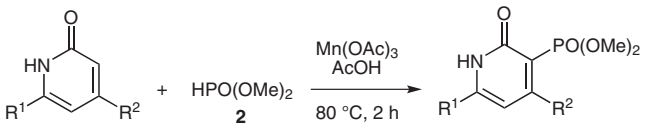
A series of 4,6-disubstituted pyridinones were employed to study the scope of this reaction. The results shown in Table 1 indicated that in all the cases 3-phosphonylated pyridinones were produced in moderate to good yields, and no 5-phosphonylated pyridinones or phenyl phosphonylated products were observed. It was found that aromatic substituents at the 4- and 6-positions of the pyridinone have no significant effect on the product yield. Pyridinone with methyl substitution at position 6 also produced the desired product (Table 1, entry 9).

The proposed mechanism for the phosphonylation of pyridinones is shown in Scheme 2. Electrophilic phosphonyl radical **6** generated from the reaction of manganese(III) acetate with dimethyl phosphite attacks the 3-position of pyridinones **1** to form radical **7** because this position has higher electron density than other sites.[10b] Radical **7** is oxidized by the second equivalent of manganese(III) acetate to form carbocation **8** followed by the deprotonation to give product **3**.

Pyrimidinone is a privileged ring that exists in many natural products and synthetic medicines. There are a wide variety of pharmacological properties and potential applications of pyrimidin-2(1*H*)-ones.[11–14] They could be suitable substrates for phosphonylation. Indeed, the reaction

SYNTHESIS 2013, 45, 1529–1533
Advanced online publication: 29.04.2013
DOI: 10.1055/s-0033-1338423; Art ID: SS-2013-M0082-OP

Table 1 Phosphonylation of Pyridinones **1**[a]

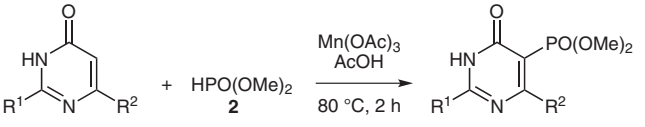


1a–i **3a–i**

Entry	Substrate	R^1	R^2	Product	Yield[b] (%)
1	**1a**	Ph	Ph	**3a**	72
2	**1b**	Ph	4-MeC_6H_4	**3b**	68
3	**1c**	4-$MeOC_6H_4$	Ph	**3c**	62
4	**1d**	4-BrC_6H_4	Ph	**3d**	69
5	**1e**	Ph	4-$MeOC_6H_4$	**3e**	66
6	**1f**	Ph	4-BrC_6H_4	**3f**	70
7	**1g**	4-BrC_6H_4	4-$MeOC_6H_4$	**3g**	63
8	**1h**	Ph	2-$MeOC_6H_4$	**3h**	60
9	**1i**	Me	Ph	**3i**	55

[a] Method: **1**/dimethyl phosphite/$Mn(OAc)_3$ (1:2:3), AcOH (5 mL), 80 °C, 2 h under air.
[b] Isolated yield.

Table 2 Phosphonylation of Pyrimidinones **4**[a]



4a–h **5a–h**

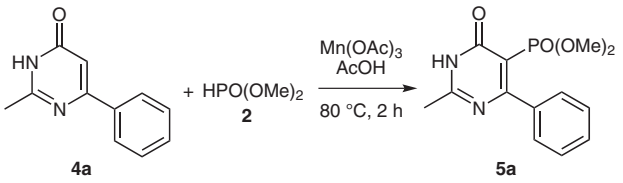
Entry	Substrate	R^1	R^2	Product	Yield[b] (%)
1	**4a**	Me	Ph	**5a**	65
2	**4b**	Me	4-$MeOC_6H_4$	**5b**	67
3	**4c**	Me	4-BrC_6H_4	**5c**	70
4	**4d**	Me	4-ClC_6H_4	**5d**	69
5	**4e**	Ph	Ph	**5e**	75
6	**4f**	Ph	4-MeC_6H_4	**5f**	70
7	**4g**	Ph	3-$MeOC_6H_4$	**5g**	65
8	**4h**	Ph	4-BrC_6H_4	**5h**	68

[a] Method: **4**/dimethyl phosphite/$Mn(OAc)_3$ (1:2:3), AcOH (5 mL), 80 °C, 2 h under air.
[b] Isolated yield.

of pyrimidinone **4a** with dimethyl phosphite afforded 5-phosphonylated pyrimidinone **5a** in 65% yield (Scheme 3). A series of substituted pyrimidinones were used for phosphonylation. Results shown in Table 2 indicate that substituents on the phenyl ring or at the 2-position of the pyrimidinone have no significant effect on product yields.

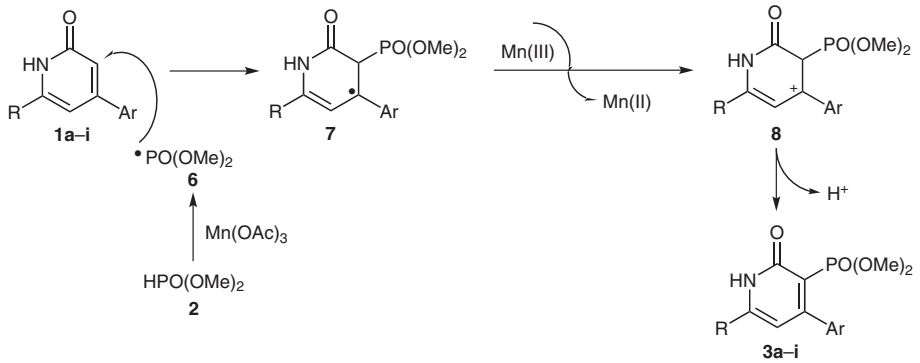
The phosphonylation reaction was further extended to other substrates. The reaction of pyrimidinedione **6a** afforded 5-phosphonylated product **7a** in 60% yield (Table 3, entry 1). Phosphonylation of 6-bromoquinolinone **6b** gave 3-phosphonylated product **7b** in 78% yield (Table 3, entry 2). Finally, direct phosphonylation was also applied to the reaction of triacetyl uridine **6c** to give the expected product **7c** in 70% yield (Table 3, entry 3). A multistep synthesis is required to make this kind of compound following reported procedures.[4]

In summary, we have developed a manganese(III)-mediated regioselective phosphonation reaction of pyridinones and pyrimidinones. The reactions are straightforward and efficient. This reaction extended further the synthetic utility of free-radical-based phosphonation of heterocyclic ring systems in the synthesis of biologically interesting compounds.



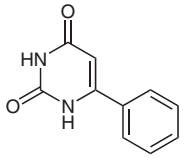
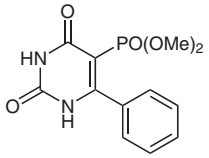
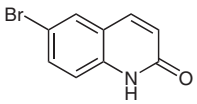
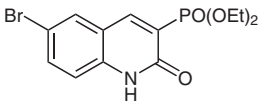
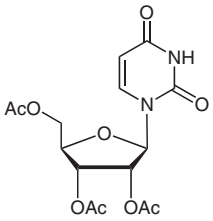
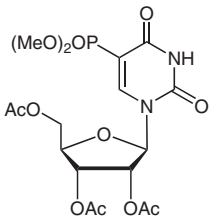
4a **5a**

Scheme 3 Phosphonylation of pyrimidinone



Scheme 2 Proposed mechanism for phosphonylation of pyridinones

Table 3 Phosphonylation of Other Azaheterocycles **6**[a]

Entry	Substrate	Product	Yield[b] (%)
1	 **6a**	 **7a**	60
2	 **6b**	 **7b**	78
3	 **6c**	 **7c**	70

[a] Method: **6**/dimethyl phosphite/Mn(OAc)$_3$ (1:2:3), AcOH (5 mL), 80 °C, 2 h under air.
[b] Isolated yield.

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 300 MHz or 400 MHz spectrometer and relative to internal TMS. HRMS were recorded on a MicroMass-TOF machine (EI). Column chromatography was performed with 200–300 mesh silica gel using flash column technique. All of the reagents were used directly as obtained commercially unless otherwise noted.

Dimethyl 2-Oxo-4,6-diphenyl-1,2-dihydropyridin-3-ylphosphonate (3a); Typical Procedure
To a mixture of pyridinone **1a** (0.25 g, 1.0 mmol), dimethyl phosphite (0.22 g, 2.0 mmol), and AcOH (5 mL) was added Mn(OAc)$_3$·2 H_2O (0.81 g, 3.0 mmol) in 3 portions; each portion was added when the red color of soln had faded. The resulting soln was heated at 80 °C for 2 h. To the resulting mixture was added H_2O (30 mL) and it was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (anhyd Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (acetone–petroleum ether 2:1) to afford **3a** as a yellow solid; yield: 0.26 g (72%); mp 174–176 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.54 (s, 1 H, NH), 7.90 (d, J = 6.3 Hz, 2 H, ArH), 7.55–7.35 (m, 8 H, ArH), 6.70 (s, 1 H, CH), 3.44 (d, J = 11.2 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.03, 164.65 (d, J_{PC} = 4.1 Hz), 152.80, 142.75, 135.03, 133.40, 131.72, 131.00, 130.38, 130.17, 129.86, 111.82 (d, J_{PC} = 12.8 Hz), 55.35.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{18}NO_4P$: 355.0973; found: 355.0974 (77%).

Dimethyl 2-Oxo-6-phenyl-4-*p*-tolyl-1,2-dihydropyridin-3-ylphosphonate (3b)
Yellow solid; yield: 0.25 g (68%); mp 164–166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.07 (s, 1 H, NH), 7.83 (d, J = 7.3 Hz, 2 H, ArH), 7.47–7.35 (m, 3 H, ArH), 7.25 (d, J = 7.7 Hz, 2 H, ArH), 7.15 (d, J = 7.8 Hz, 2 H, ArH), 6.55 (s, 1 H, CH), 3.35 (d, J = 11.4 Hz, 6 H, 2 CH_3), 2.31 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.90 (d, J_{PC} = 12.4 Hz), 162.26, 150.90, 138.76, 137.51 (d, J_{PC} = 4.3 Hz), 133.30, 131.04, 129.44, 128.79, 127.99, 127.56, 110.10, 53.05 (d, J_{PC} = 5.9 Hz), 21.57.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{20}NO_4P$: 369.1130; found: 369.1128 (69%).

Dimethyl 6-(4-Methoxyphenyl)-2-oxo-4-phenyl-1,2-dihydropyridin-3-ylphosphonate (3c)
White solid; yield: 0.24 g (62%); mp 178–180 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.80 (s, 1 H, NH), 7.93 (d, J = 8.0 Hz, 2 H, ArH), 7.32–7.46 (m, 5 H, ArH), 7.03 (d, J = 8.0 Hz, 2 H, ArH), 6.56 (s, 1 H, CH), 3.84 (s, 3 H, CH_3), 3.43 (d, J = 11.3 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.84 (d, J_{PC} = 12.6 Hz), 162.41 (d, J_{PC} = 6.8 Hz), 162.17, 150.46, 140.68 (d, J_{PC} = 4.1 Hz), 129.27, 128.70, 128.11, 127.95, 124.96, 114.89, 108.71 (d, J_{PC} = 13.2 Hz), 55.75, 53.02 (d, J_{PC} = 6.0 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{20}NO_5P$: 385.1079; found: 385.1075 (60%).

Dimethyl 6-(4-Bromophenyl)-2-oxo-4-phenyl-1,2-dihydropyridin-3-ylphosphonate (3d)
Yellow solid; yield: 0.30 g (69%); mp 188–190 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.21 (s, 1 H, NH), 7.96 (d, J = 7.2 Hz, 2 H, ArH), 7.59–7.48 (m, 5 H, ArH), 7.35 (d, J = 8.0 Hz, 2 H, ArH), 6.63 (s, 1 H, CH), 3.46 (d, J = 11.4 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.89 (d, J_{PC} = 12.3 Hz), 161.12, 151.72, 139.49 (d, J_{PC} = 4.5 Hz), 133.21, 131.50, 129.84, 129.72, 127.79, 123.31, 109.83, 53.32 (d, J_{PC} = 5.8 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{17}BrNO_4P$: 433.0079; found: 433.0070 (100%).

Dimethyl 4-(4-Methoxyphenyl)-2-oxo-6-phenyl-1,2-dihydropyridin-3-ylphosphonate (3e)
Yellow solid; yield: 0.25 g (66%); mp 196–198 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.80 (s, 1 H, NH), 7.90 (d, J = 6.6 Hz, 2 H, ArH), 7.59–7.48 (m, 3 H, ArH), 7.41 (d, J = 7.6 Hz, 2 H, ArH), 6.96 (d, J = 7.6 Hz, 2 H, ArH), 6.65 (s, 1 H, CH), 3.86 (s, 3 H, CH_3), 3.48 (d, J = 11.3 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.93, 160.09, 150.57, 135.17, 132.84, 132.36, 130.90, 129.42, 129.21, 127.27, 113.32, 109.93, 55.32, 52.88.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{20}NO_5P$: 385.1079; found: 385.1075 (60%).

Dimethyl 4-(4-Bromophenyl)-2-oxo-6-phenyl-1,2-dihydropyridin-3-ylphosphonate (3f)
White solid; yield: 0.30 g (70%); mp 184–186 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.66 (s, 1 H, NH), 7.93 (d, J = 6.7 Hz, 2 H, ArH), 7.50–7.57 (m, 5 H, ArH), 7.32 (d, J =7.7 Hz, 2 H, ArH), 6.59 (s, 1 H, CH), 3.47 (d, J = 11.0 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.69, 152.68, 140.83, 134.25, 132.80, 131.13, 131.04, 129.08, 124.60, 110.92, 54.61 (d, J_{PC} = 5.4 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{17}BrNO_4P$: 433.0079; found: 433.0080 (100%).

Dimethyl 6-(4-Bromophenyl)-4-(4-methoxyphenyl)-2-oxo-1,2-dihydropyridin-3-ylphosphonate (3g)
Yellow solid; yield: 0.29 g (63%); mp 194–196 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.27 (s, 1 H, NH), 7.86 (d, *J* = 8.0 Hz, 2 H, ArH), 7.67 (d, *J* = 7.9 Hz, 2 H, ArH), 7.39 (d, *J* = 8.1 Hz, 2 H, ArH), 6.97 (d, *J* = 8.1 Hz, 2 H, ArH), 6.71 (s, 1 H, CH), 3.87 (s, 3 H, OCH_3), 3.50 (d, *J* = 11.3 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.26, 161.70, 160.34, 132.62, 132.34, 129.63, 129.14, 125.72, 113.56, 110.74, 55.57, 53.07 (d, J_{PC} = 5.6 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{19}BrNO_5P$: 463.0184; found: 463.0185 (55%).

Dimethyl 4-(2-Methoxyphenyl)-2-oxo-6-phenyl-1,2-dihydropyridin-3-ylphosphonate (3h)
Yellow solid; yield: 0.23 g (60%); mp 168–170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.36 (s, 1 H, NH), 7.95 (d, *J* = 7.3 Hz, 2 H, ArH), 7.55–7.45 (m, 3 H, ArH), 7.37 (t, *J* = 7.6 Hz, 1 H, ArH), 7.22 (d, *J* = 7.1 Hz, 1 H, ArH), 7.02 (t, *J* = 7.3 Hz, 1 H, ArH), 6.95 (d, *J* = 8.2 Hz, 1 H, ArH), 6.59 (s, 1 H, CH), 3.81 (s, 3 H, OCH_3), 3.51 (d, *J* = 11.4 Hz, 3 H, CH_3), 3.43 (d, *J* = 11.3 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.75 (d, J_{PC} = 11.7 Hz), 162.90, 159.21, 156.05, 150.78, 133.18, 130.88, 130.01, 129.36, 127.62, 120.28, 110.63, 55.69, 52.97 (d, J_{PC} = 28.5 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{20}NO_5P$: 385.1079; found: 385.1082 (15%).

Dimethyl 6-Methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-ylphosphonate (3i)
Yellow solid; yield: 0.16 g (55%); mp 190–192 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.64 (s, 1 H, NH), 7.40 (s, 5 H, ArH), 6.08 (s, 1 H, CH), 3.53 (d, *J* = 11.0 Hz, 6 H, 2 CH_3), 2.42 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.75, 162.78, 149.67, 140.44, 128.63, 128.04, 127.82, 110.47 (d, J_{PC} = 13.5 Hz), 53.00 (d, J_{PC} = 5.2 Hz), 19.42.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{16}NO_4P$: 293.0817; found: 293.0816 (100%).

Dimethyl 2-Methyl-6-oxo-4-phenyl-1,6-dihydropyrimidin-5-ylphosphonate (5a); Typical Procedure
To a mixture of pyrimidinone **4a** (0.19 g, 1.0 mmol), dimethyl phosphite (0.22 g, 2.0 mmol), and AcOH (5.0 mL) was added $Mn(OAc)_3{\cdot}2\,H_2O$ (0.81 g, 3.0 mmol) in 3 portions and the resulting soln was heated at 80 °C for 2 h. To the resulting mixture was added H_2O (30.0 mL) and it was extracted with EtOAc (3 × 10.0 mL). The combined organic layers were dried (anhyd Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (acetone–petroleum, 2:1) to afford **5a** as a white solid; yield: 0.19 g (65%); mp 191–192 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.4 (br s, 1 H), 7.61–7.68 (m, 2 H), 7.41–7.47 (m, 3 H), 3.56 (d, *J* = 10.1 Hz, 6 H), 2.56 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7 (d, *J* = 5.0 Hz), 161.7, 139.6, 130.7, 129.5, 128.5, 53.8 (d, *J* = 2.9 Hz), 22.6.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{16}N_2O_4P$: 294.0769; found: 295.0842.

Dimethyl 4-(4-Methoxyphenyl)-2-methyl-6-oxo-1,6-dihydropyrimidin-5-ylphosphonate (5b)
White solid; yield: 0.22 g (67%); mp 189–191 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.30 (br s, 1 H), 7.65 (d, *J* = 8.6 Hz, 2 H), 6.90 (d, *J* = 8.6 Hz, 2 H), 3.79 (s, 3 H), 3.55 (d, *J* = 11.4 Hz, 6 H), 2.47 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (d, *J* = 8.0 Hz), 165.7, 162.0, 161.0, 131.8, 131.7, 113.7, 108.7 (d, *J* = 201.7 Hz), 55.9, 53.6 (d, *J* = 6.1 Hz), 22.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{18}N_2O_5P$: 324.0875; found: 325.0944.

Dimethyl 4-(4-Bromophenyl)-2-methyl-6-oxo-1,6-dihydropyrimidin-5-ylphosphonate (5c)
White solid; yield: 0.26 g (70%); mp 212–214 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.16 (br s, 1 H), 7.55 (d, *J* = 8.1 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 3.60 (d, *J* = 11.4 Hz, 6 H), 2.51 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9 (d, *J* = 8.6 Hz), 164.6, 161.7, 138.0, 131.2, 130.8, 124.9, 109.8 (d, *J* = 200.5 Hz), 53.5 (d, *J* = 6.0 Hz), 22.0.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{15}BrN_2O_4P$: 371.9876; found: 372.9960.

Dimethyl 4-(4-Chlorophenyl)-2-methyl-6-oxo-1,6-dihydropyrimidin-5-ylphosphonate (5d)
White solid; yield: 0.23 g (69%); mp 219–220 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.3 (br s, 1 H), 7.59 (d, *J* = 8.2 Hz, 2 H), 7.38 (d, *J* = 8.2 Hz, 2 H), 3.60 (d, *J* = 11.0 Hz, 6 H), 2.49 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0 (d, *J* = 6.1 Hz), 161.5, 137.7, 136.4, 130.6, 128.2, 53.4 (d, *J* = 4.6 Hz), 22.1.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{15}ClN_2O_4P$: 328.0380; found: 328.0460.

Dimethyl 6-Oxo-2,4-diphenyl-1,6-dihydropyrimidin-5-ylphosphonate (5e)
White solid; yield: 0.27 g (75%); mp 195–197 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.6 (br s, 1 H), 8.31–8.55 (m, 2 H), 7.71–7.84 (m, 2 H), 7.35–7.62 (m, 6 H), 3.51 (d, *J* = 11.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4 (d, *J* = 8.7 Hz), 158.2, 139.6, 133.2, 131.3, 130.4, 129.6, 129.3, 128.9, 127.9, 53.3 (d, *J* = 4.6 Hz).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{18}N_2O_4P$: 356.0926; found: 357.1014.

Dimethyl 6-Oxo-2-phenyl-4-*p*-tolyl-1,6-dihydropyrimidin-5-ylphosphonate (5f)
White solid; yield: 0.26 g (70%); mp 189–190 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.63 (br s, 1 H), 8.44 (d, *J* = 7.3 Hz, 2 H), 7.73 (d, *J* = 7.8 Hz, 2 H), 7.54–7.57 (m, 3 H), 7.27 (d, *J* = 7.9 Hz, 2 H), 3.55 (d, *J* = 11.4 Hz, 6 H), 2.42 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6 (d, *J* = 8.0 Hz), 158.2, 141.1, 136.9, 133.4, 131.6, 131.6, 130.0, 129.5, 129.1, 128.9, 53.5 (d, *J* = 6.1 Hz), 22.0.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{20}N_2O_4P$: 370.1082; found: 371.1157.

Dimethyl 4-(3-Methoxyphenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-ylphosphonate (5g)
White solid; yield: 0.25 g (65%); mp 192–193 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.65 (br s, 1 H), 8.44 (d, *J* = 7.6 Hz, 2 H), 7.54–7.62 (m, 3 H), 7.35–7.41 (m, 3 H), 7.01–7.06 (m, 1 H), 3.88 (s, 3 H), 3.55 (d, *J* = 11.4 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (d, *J* = 8.6 Hz), 159.2, 140.8, 133.3, 131.8 (d, *J* = 9.4 Hz), 129.3, 129.2, 129.1, 129.1 (d, *J* =176.2 Hz), 128.9, 122.0, 116.8, 114.5, 110.0, 55.7, 53.5 (d, *J* = 6.1 Hz).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{20}N_2O_5P$: 386.1032; found: 387.1103.

Dimethyl 4-(4-Bromophenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-ylphosphonate (5h)
White solid; yield: 0.30 g (68%); mp 240–241 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 13.45 (br s, 1 H), 8.31–8.51 (m, 2 H), 7.50–7.71 (m, 7 H), 3.57 (d, *J* = 14.0 Hz, 6 H).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{17}BrN_2O_4P$: 434.0031; found: 435.0105.

Dimethyl 2,4-Dioxo-6-phenyl-1,2,3,4-tetrahydropyrimidin-5-ylphosphonate (7a)
White solid; yield: 0.18 g (60%); mp 210–213 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1 H, NH), 8.16 (s, 1 H, NH), 7.46–7.57 (m, 5 H), 3.55 (d, *J* = 10.7 Hz, 6 H).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}N_2O_5P$: 296.0562; found: 297.0635.

Diethyl 6-Bromo-2-oxo-1,2-dihydroquinolin-3-ylphosphonate (7b)
Yellow powder; yield: 0.28 g (78%); mp 120–122 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.68 (br s, 1 H, NH), 8.48 (d, *J* = 17.4 Hz, 1 H, ArH), 7.81 (s, 1 H, ArH), 7.67 (d, *J* = 8.7 Hz, 1 H, ArH), 7.27 (s, 1 H, CH), 4.50–4.10 (m, 4 H, 2 CH_2), 1.40 (t, *J* = 6.7 Hz, 6 H, 2 CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.10, 150.01, 140.19, 136.71, 132.19, 122.31, 121.13, 120.92, 118.96, 116.54, 64.12 (d, J_{PC} = 5.8 Hz), 17.48 (d, J_{PC} = 6.3 Hz).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{15}BrNO_4P$: 358.9922; found: 358.9922.

Dimethyl 2,4-Dioxo-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-1,2,3,4-tetrahydropyrimidin-5-ylphosphonate (7c)[4]
Yellow oil; yield: 0.34 g (70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.36 (br, 1 H, NH), 8.25 (d, *J* = 13.5 Hz, 1 H), 5.95 (d, *J* = 5.1 Hz, 1 H), 5.43–5.38 (m, 1 H), 5.36–5.33 (m, 1 H), 4.33–4.29 (m, 3 H), 3.78 (d, *J* = 2.4 Hz, 3 H, OCH_3), 3.75 (d, *J* = 2.4 Hz, 3 H, OCH_3), 2.08 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3).

Acknowledgement

J.P.Z. thanks the National Natural Science Foundation of China for financial support (No. 20772088, 21172163) and A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions.

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

References

(1) Pavlenko, N. G.; Kukhar, V. P. *Ukr. Khim. Zh. (Russ. Ed.)* **1982**, *48*, 395.
(2) Stansfield, I.; Avolio, S.; Colarusso, S.; Gennari, N.; Narjes, F.; Pacini, B.; Ponzi, S.; Harper, S. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5085.
(3) Onysko, P. P.; Golobov, Y. G.; Remennikov, G. Y.; Cherkasov, V. M. *Zh. Obshch. Khim.* **1980**, *50*, 1230.
(4) Maruyama, T.; Honjo, M. *Nucleosides, Nucleotides Nucleic Acids* **1988**, *7*, 203.
(5) Lavilla, R.; Spada, A.; Bosch, J. *Org. Lett.* **2000**, *2*, 1533.
(6) Kagayama, T.; Nakano, A.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2006**, *8*, 407.
(7) Xu, W.; Zou, J.-P.; Zhang, W. *Tetrahedron Lett.* **2010**, *51*, 2639.
(8) (a) Mu, X.-J.; Zou, J.-P.; Qian, Q.-F.; Zhang, W. *Org. Lett.* **2006**, *8*, 5291. (b) Zhou, P.; Jiang, Y.-J.; Zou, J.-P.; Zhang, W. *Synthesis* **2012**, *44*, 1043.
(9) (a) Pan, X.-Q.; Zou, J.-P.; Zhang, G.-L.; Zhang, W. *Chem. Commun.* **2010**, *46*, 1721. (b) Pan, X.-Q.; Wang, L.; Zou, J.-P.; Zhang, W. *Chem. Commun.* **2011**, *47*, 7875.
(10) Reviews on P–C bond formation by radical ractions: (a) Van der Jeught, S.; Stevens, C. V. *Chem. Rev.* **2009**, *109*, 2672. (b) Leca, D.; Fensterbank, L.; Lacote, E.; Malacria, M. *Chem. Soc. Rev.* **2005**, *34*, 858. (c) Marque, S.; Tordo, P. *Top. Curr. Chem.* **2005**, *250*, 43.
(11) Atwal, K. S.; Rovnyak, G. C.; Schwartz, J.; Moreland, S.; Hedberg, A.; Gougoutas, J. Z.; Malley, M. F.; David, M. F. *J. Med. Chem.* **1990**, *33*, 1510.
(12) Yamaguchi, M.; Wakasugi, K.; Saito, R.; Adachi, Y.; Yoshikawa, Y.; Sakurai, H.; Katoh, A. *J. Inorg. Biochem.* **2006**, *100*, 260.
(13) Sadanandam, Y. S.; Shetty, M. M.; Diwan, P. V. *Eur. J. Med. Chem.* **1992**, *27*, 87.
(14) Wright, C. M.; Chovatiya, R. J.; Jameson, N. E.; Turner, D. M.; Zhu, G.; Werner, S.; Huryn, D. M.; Pipas, J. M.; Day, B. W.; Wipf, P.; Brodskya, J. L. *Bioorg. Med. Chem.* **2008**, *16*, 3291.