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Oxidative Cleavage of *o*-Hydroxyphenyl Phosphate by Iodobenzene Diacetate

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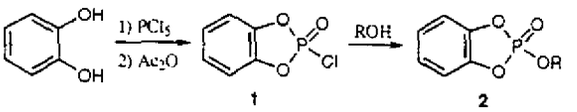
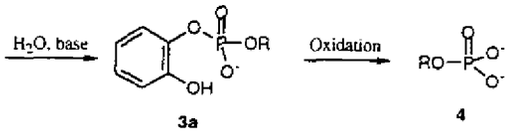
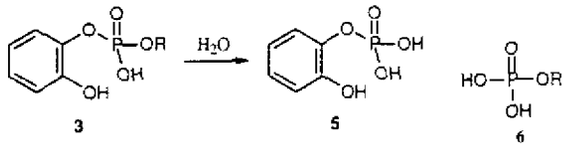
The protecting *o*-hydroxyphenyl group in the synthesis of mono- or dialkyl phosphates (**6** or **8**) could be removed by oxidative cleavage of mono- or dialkyl *o*-hydroxyphenyl phosphates (**3** or **7**) using iodobenzene diacetate.

Organic phosphoric acid esters play an important role in the biological processes and lubricant applications. The monoalkylphosphoric acid esters have been obtained as pure barium salt from alcohols in the presence of a suitable base and a suitable solvent by using catechol as the protecting group.[1] The phosphorylation of alcohols with *o*-phenylene phosphorochloridate (**1**), which was readily obtained from the reaction of catechol with phosphorus pentachloride followed by the addition of acetic anhydride, was proceeded to give monoalkyl *o*-phenylene phosphate **2**. The *o*-phenylene phosphate **2** was easily hydrolyzed to *o*-hydroxyphenyl phosphate **3a** during the alkaline work-up process. The removal of the *o*-hydroxyphenyl protector in **3a** yielded the corresponding monoalkyl phosphate **4** by hydrogenolysis or by treatment with bromine in neutral aqueous solution, periodic acid in aqueous solution, or lead tetraacetate in dioxan solution followed by alkaline hydrolysis.[2] We now wish to report that the monoalkyl *o*-hydroxyphenyl hydrogen phosphate **3** could rapidly be converted into the corresponding monoester **4** in good yield when **3** was treated with iodobenzene diacetate at room temperature.





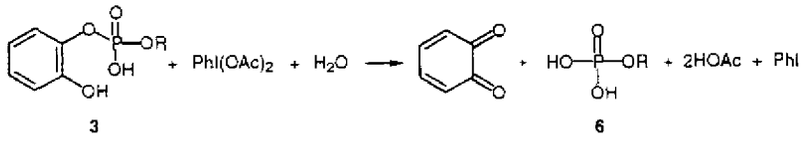
Usually, the relative hydrolysis rate of aryl phosphate was larger than that of alkyl phosphate.[3,4] An initial attempt was made to hydrolyze the *o*-hydroxyphenyl phosphate **3** under acidic or basic conditions.[2,5] Unfortunately, the hydrolyzed results showed that the cleavage between the P and O-alkyl bond to give **5** was much faster than that of the P and O-hydroxyphenyl bond to yield **6**.



This observation coupled with the known unstability of catechol[6] under the presence of oxidant prompted us to investigate the oxidative cleavage of the P and O-hydroxyphenyl bond. We have tried to use bromine as oxidant and work in acidic conditions to give the acid form of monoalkyl phosphate **6**, but the yield was not as good as before.

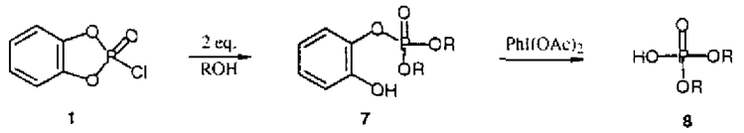
Hypervalent iodine agent, iodobenzene diacetate, was employed to oxidize alcohols,[7] enolizable ketone,[8] phenols,[9,10] or as a phenolic oxidative coupling agent,[11] iodonating agent.[12,13] Recently, some intramolecular cyclizations were effected via hypervalent iodine oxidation.[14,15] Thus, the reaction between **3** and iodobenzene diacetate using H_2O-CH_3CN as solvent successfully produced the desired monoalkyl phosphoric acid product **6** in good yield. This reaction should take place in the presence of water. A large amount of water caused a two phase reaction and gave the hydrolyzed product *o*-hydroxyphenyl phosphoric acid **5** instead of **6**. Acetonitrile was added as cosolvent. The optimum ratio of H_2O and CH_3CN was equal to 2:1. In order to shift the reaction toward the right, 6 equivalents of Na_2CO_3 were added. The physical and spectroscopic data of monoalkyl phosphoric acid **6** are summarized in Table 1.

Since the *o*-phenylene phosphate **2** has been proved to undergo ring-opening hydrolysis to *o*-hydroxyphenyl phosphate at a far greater rate,[17,18] dialkyl *o*-hydroxyphenyl phosphate **7** was obtained when the phosphorylation was proceeded in 2 equivalent excesses of alcohol. Similarly, the alcoholysis product **7** was subjected to oxidative cleavage with iodobenzene diacetate to give dialkyl phosphoric acid **8**. The physical and spectroscopic data of dialkyl phosphoric acid **8** are summarized in Table 2.



3 6

a: R = *n*-C_4H_9 f: R = $CH_2CH(CH_3)(CH_2)_2CH_3$
b: R = *sec*-C_4H_9 g: R = $CH(CH_3)CH_2(CH_3)_2$
c: R = *i*-C_4H_9 h: R = $CH_2CH_2C(CH_3)_3$
d: R = *n*-C_6H_{13} i: R = *n*-$C_{10}H_{21}$
e: R = $CH(CH_3)(CH_2)_3CH_3$ j: R = $(CH_2)_4CH{=}CH$



1 7 8

a: R = *n*-C_4H_9 f: R = $CH_2CH(CH_3)(CH_2)_2CH_3$
b: R = *sec*-C_4H_9 g: R = $CH(CH_3)CH_2(CH_3)_2$
c: R = *i*-C_4H_9 h: R = $CH_2CH_2C(CH_3)_3$
d: R = *n*-C_6H_{13} i: R = *n*-$C_{10}H_{21}$
e: R = $CH(CH_3)(CH_2)_3CH_3$ j: R = $(CH_2)_4CH{=}CH$

In this study, we described a convenient method for the preparation of monoalkyl and dialkyl phosphoric acid **5** and **8** including oxidative cleavage of P and O-hydroxyphenyl bond using iodobenzene diacetate.

Table 1. Selected Physical and Spectroscopic Data of Monoalkyl Phosphoric Acid **6**

Product	Yield %	Molecular formula[a]	^{1}H NMR ($CDCl_3$) δ, ppm	^{13}C NMR ($CDCl_3$) δ, ppm	^{31}P NMR ($CDCl_3$) δ, ppm
6a	75	$C_4H_{11}O_4P$	0.92 (3H, t, *J* = 7.2 Hz), 1.38 (2H, qt, *J* = 7.2, 6.5 Hz), 1.63 (2H, quintet, *J* = 6.5 Hz), 3.38 (br s, OH), 3.98 (2H, q, *J* = 6.5 Hz)	13.6, 18.7, 32.3, 67.0	-4.6
6b	79	$C_4H_{11}O_4P$	0.94 (3H, t, *J* = 7.4 Hz), 1.33 (3H, d, *J* = 6.3 Hz), 1.64 (2H, qd, *J* = 7.4, 6.3 Hz), 4.40 (1H, septet, *J* = 6.3 Hz), 6.87 (br s, OH)	9.3, 20.8, 30.2, 77.9	-4.6
6c	77	$C_4H_{11}O_4P$	0.95 (6H, d, *J* = 6.6 Hz), 1.97 (1H, nonatet, *J* = 6.6 Hz), 3.80 (2H, t, J = 6.6 Hz), 6.56 (br s, OH)	18.6, 29.0, 73.5	-4.3
6d	83	$C_6H_{15}O_4P$	0.89 (3H, t, *J* = 6.5 Hz), 1.31 (6H, m), 1.68 (2H, quintet, *J* = 6.5 Hz), 4.02 (2H, q, *J* = 6.5 Hz), 4.88 (br s, OH)	14.0, 22.5, 25.1, 30.2, 31.3, 67.7	-4.3
6e	81	$C_6H_{15}O_4P$	0.89 (3H, t, *J* = 6.4 Hz), 1.32 (3H, d, *J* = 5.4 Hz), 1.50 (6H, m), 4.44 (1H, septet, *J* = 5.4 Hz), 9.32 (br s, OH)	13.9, 21.3, 22.4, 27.1, 37.0, 77.0	-4.6
6f	81	$C_6H_{15}O_4P$	0.92 (6H, m), 1.35 (4H, m), 1.81 (1H, m), 3.86 (2H, m)	14.2, 16.3, 19.8, 33.5, 34.9, 72.7	-4.5
6g	72	$C_6H_{15}O_4P$	0.88 (3H, d, *J* = 6.3 Hz), 0.90 (3H, d, *J* = 6.3 Hz), 1.28 (1H, m), 1.30 (3H, d, *J* = 6.1 Hz), 1.70 (2H, m), 4.47 (1H, septet, *J* = 6.1 Hz), 7.43 (br s, OH)	21.7, 22.2, 22.8, 24.3, 46.7, 74.7	-5.7
6h	70	$C_6H_{15}O_4P$	0.92 (9H, s), 1.62 (2H, m), 4.07 (2H, m), 6.15 (br s, OH)	29.5, 43.1, 43.2, 65.4	-5.0
6i	82	$C_{10}H_{23}O_4P$	0.88 (3H, t, *J* = 6.6 Hz), 1.25 (14H, m), 1.62 (2H, m), 3.96 (2H, q, *J* = 6.5 Hz), 6.50 (br s, OH)	14.1, 22.7, 25.3, 29.2, 29.3, 29.6, 29.7, 30.1, 31.9, 68.3	-4.3
6j	78	$C_6H_{13}O_4P$	1.47 (2H, m), 1.70 (2H, m), 2.07 (2H, m), 4.04 (2H, q, *J* = 6.3 Hz), 5.00 (2H, m), 5.78 (1H, ddt, *J* = 17.0, 10.2, 6.6 Hz), 9.77 (br s, OH)	24.5, 29.4, 33.1, 67.9, 114.9, 138.2	-4.6

[a] All compounds were analyzed by high resolution mass spectral measurement for the quasimolecular ion $[M+H]^+$.

Table 2. Selected Physical and Spectroscopic Data of Dialkyl Phosphoric Acid **8**

Product	Yield %	Molecular formula[a]	^{1}H NMR ($CDCl_3$) δ, ppm	^{13}C NMR ($CDCl_3$) δ, ppm	^{31}P NMR ($CDCl_3$) δ, ppm
8a	72	$C_8H_{19}O_4P$	0.94 (6H, t, J = 7.3 Hz), 1.42 (4H, sextet, J = 7.3 Hz), 1.69 (4H, tt, J = 7.3, 6.6 Hz), 4.07 (4H, q, J = 6.6 Hz), 8.38 (br s, OH)	13.5, 18.6, 32.0, 67.9	-5.2
8b	75	$C_8H_{19}O_4P$	0.94 (6H, t, J = 7.5 Hz), 1.32 (6H, d, J = 6.2 Hz), 1.75 (4H, m), 4.39 (2H, septet, J = 6.3 Hz), 10.76 (br s, OH)	9.4, 20.8, 30.2, 77.1	-5.7
8c	72	$C_8H_{19}O_4P$	0.95 (12H, d, J = 6.7 Hz), 1.97 (2H, m), 3.80 (4H, t, J = 6.4 Hz), 7.57 (br s, OH)	18.6, 29.0, 73.6	-4.5
8d	79	$C_{12}H_{27}O_4P$	0.89 (6H, t, J = 6.7 Hz), 1.32 (12H, m), 1.65 (4H, m), 4.03 (4H, q, J = 6.7 Hz), 7.00 (br s, OH)	13.9, 22.5, 25.0, 30.0, 31.3, 68.0	-4.4
8e	74	$C_{12}H_{27}O_4P$	0.90 (6H, t, J = 7.2 Hz), 1.33 (6H, d, J = 6.3 Hz), 1.50 (12H, m), 4.43 (2H, septet, J = 6.3 Hz), 6.47 (br s, OH)	13.9, 21.4, 22.4, 27.1, 37.1, 76.5	-6.1
8f	75	$C_{12}H_{27}O_4P$	0.90 (6H, t, J = 7.1 Hz), 0.94 (6H, d, J = 6.7 Hz), 1.30 (8H, m), 1.80 (2H, m), 3.85 (4H, m), 8.55 (br s, OH)	14.2, 16.3, 19.8, 33.5, 34.9, 72.4	-4.6
8g	72	$C_{12}H_{27}O_4P$	0.90 (6H, d, J = 5.9 Hz), 0.93 (6H, d, J = 6.0 Hz), 1.20 (2H, m), 1.33 (6H, d, J = 6.2 Hz), 1.70 (4H, m), 4.50 (2H, septet, J = 6.2 Hz), 6.53 (br s, OH)	22.1, 22.2, 22.9, 24.3, 46.7, 74.7	-5.8
8h	75	$C_{12}H_{27}O_4P$	0.93 (18H, s), 1.63 (4H, t, J = 7.4 Hz), 4.09 (4H, q, J = 7.4 Hz), 6.95 (br s, OH)	29.6, 43.3, 43.4, 65.5	-4.7
8i	78	$C_{20}H_{43}O_4P$	0.88 (6H, t, J = 6.4 Hz), 1.26 (24H, m), 1.66 (4H, m), 4.02 (4H, q, J = 6.5 Hz), 6.20 (br s, OH)	14.1, 22.7, 25.5, 29.1, 29.3, 29.5, 29.6, 30.3, 31.9, 67.7	-6.1
8j	81	$C_{12}H_{23}O_4P$	1.44 (4H, m), 1.70 (4H, m), 2.08 (4H, m), 4.02 (4H, q, J = 6.6 Hz), 5.00 (4H, m), 5.79 (2H, ddt, J = 17.0, 10.2, 6.6 Hz), 9.83 (br s, OH)	24.7, 29.5, 33.1, 67.4, 114.8, 138.2	-4.9

[a] All compounds were analyzed by high resolution mass spectral measurement for the quasimolecular ion $[M+H]^+$.

EXPERIMENTAL SECTION

General

IR spectra were recorded on a Nicolet Magna FT-IR spectrometer as thin films. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200 FT-NMR spectrometers; all chemical shifts are reported in ppm from tetramethylsilane as an internal standard. ^{31}P NMR spectra were recorded on Bruker AMX-400 FT-NMR spectrometers; all chemical shifts are reported in ppm from phosphoric acid as an external standard. MS and HRMS spectra were recorded on a VG 70-250S spectrometer.

The general procedure for the preparation of monoalkyl *o*-hydroxyphenyl phosphate 3

o-Phenylene phosphorochloridate (**1**) was prepared according to standard procedures.[7] Alcohol (5 mmol) was added slowly to a solution of **1** (0.95 g, 5 mmol) in anhydrous diethyl ether (20 mL). The reaction mixture was stirred at room temperature for 1 h and poured into a solution of pyridine (1.19 g, 15 mmol) in diethyl ether (20 mL). This solution was extracted with water (30 mL × 3). The aqueous layer was washed with EtOAc (10 mL × 2) and acidified with 4 N HCl and extracted with diethyl ether (30 mL × 3). The combined organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give pure monoalkyl *o*-hydroxyphenyl phosphate **3**.

The general procedure for the preparation of dialkyl *o*-hydroxyphenyl phosphate 7

Alcohol (10 mmol) was added slowly to a solution of *o*-phenylene phosphorochloridate (**1**, 0.95 g, 5 mmol) in anhydrous diethyl ether (20 mL). The reaction mixture was stirred at room temperature for 1 h. This solution was extracted with water (10 mL × 3). The combined organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give pure dialkyl *o*-hydroxyphenyl phosphate **7**.

The general procedure for the oxidative cleavage of mono- or dialkyl *o*-hydroxyphenyl phosphate 3 or 7 to mono- or dialkyl phosphate 6 or 8

Mono- or dialkyl *o*-hydroxyphenyl phosphate **3** or **7** (1 mmol) together with iodobenzene diacetate (0.39 g, 1.2 mmol) were added to a mixed solvent of acetonitrile—H_2O

(2:1, total 3 mL). The reaction mixture was stirred at room temperature for 1 h, then, Na_2CO_3 (0.64 g, 6 mmol) was added and stirred for another 1 h. The resulting solution was poured into H_2O (15 mL). The aqueous layer was washed with EtOAc (10 mL × 2) and acidified with 4 N HCl and extracted with EtOAc (20 mL × 3). The combined organic layer was decolored with charcoal, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give pure *o*-hydroxyphenyl phosphate **6** or **8**. The physical and spectroscopic data are shown in Tables 1 and 2.

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Key Words

Monoalkyl phosphoric acid; Dialkyl phosphoric acid; *o*-Hydroxyphenyl phosphate; Iodobenzene diacetate; Oxidative cleavage.

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