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The Selective Dealkylation of Mixed Esters of Phosphoric Acid and Phenylphosphonic Acid Using Cation Exchange Resin

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Cation exchange resin (SO_3H) is a highly selective dealkylation reagent for mixed esters of phosphorus oxyacids bearing primary and secondary alkyl groups. The desired products which were produced by dealkylation of the secondary alkyl group were obtained in high yields under anhydrous and mild conditions.

Keywords——dealkylation; cation exchange resin; carbonium ion; phosphorus oxyacid ester; trialkyl phosphate; dialkyl phenylphosphonate; *p*-toluenesulfonic acid

We have recently reported that the reactions of carboxylic acid esters[1] and phosphorus oxyacid esters[2] with dehydrated *p*-toluenesulfonic acid (TsOH) afforded the corresponding *p*-toluenesulfonates (TsOR) in good yields. In particular, the reaction of secondary alkyl esters of phosphorus oxyacids with TsOH proceeded smoothly at a lower temperature (r.t.—40 °C) to afford TsOR^s in good yields. We have now turned our attention to the convenient and selective dealkylation of mixed esters bearing primary and secondary alkyl groups.

Protecting groups of phosphorus oxyacids play a very important role in the syntheses of oligonucleotides[3] and phosphonate analogues of natural phosphates.[4] A key reaction at the final stage of the syntheses is the selective dealkylation of fully esterified phosphorus oxyacids. The selectivity has been achieved by hydrogenolysis of the benzyl,[5] aryl,[6] and allyl[7] esters, by dealkylation of the 2-cyanoethyl group[8] under basic conditions, by reductive cleavage of the 2,2,2-trichloroethyl group,[9] through use of the base-labile phenylthio group,[10] and by treatment of the ethylthio group with iodine.[11] Several papers concerning dealkylation by use of bromotrimethylsilane have also been published.[12] Recently, Blackburn and Inglesen[13] showed that iodotrimethylsilane transforms alkyl esters of phosphorus oxyacids at room temperature into the corresponding trimethylsilyl esters, which can be treated with water to give dealkylated compounds, but the selective monodealkylation of dialkyl alkylphosphonates can not be achieved. Although a variety of dealkylation procedures have been reported to date, as described above, development of a readily available method for the mild and selective dealkylation of mixed esters of phosphorus oxyacids is still a subject of great interest.

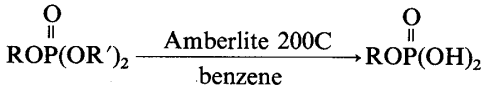
Our finding that TsOH exhibits greater reactivity towards secondary alkyl groups than primary alkyl groups prompted us to investigate its suitability for selective and partial dealkylation. However, since TsOH is soluble in water and thus the isolation of partially dealkylated products that are similarly soluble in water is troublesome, the use of TsOH seems to be unsuitable. Therefore, we investigated the application of a polymer-supported benzenesulfonic acid (cation exchange resin) in place of TsOH to the dealkylation of mixed esters of phosphorus oxyacids in order to isolate easily the products. Ion exchange resins have a wide range of uses in organic synthesis as catalysts[14] owing to the ease of product isolation, the simple work-up procedures, and the ease of regeneration and recycling. Although the

chemistry of the sulfonic acid moiety bound to the polymeric matrix is essentially unchanged from that exhibited by free mineral acids or TsOH, whether the reaction of phosphorus oxyacid esters with the resin gives the esterified resin or not is also a subject of interest.

In the present paper, we wish to report a highly selective dealkylation procedure for mixed esters of phosphorus oxyacids using cation exchange resin (SO_3H type).

These reactions were carried out by the general procedure, *i.e.*, dry cation exchange resin (Amberlite 200C) obtained by dehydration of commercial resin at 120 °C (1 mmHg) for 5 h was added to the solution of mixed esters of phosphorus oxyacids in benzene, and the mixture was stirred under appropriate reaction conditions, as shown in the tables. After removal of the resin by filtration, the resin was washed with water. The combined aqueous layer was evaporated under reduced pressure, and the residue was dissolved in chloroform. The solution was dried and concentrated under reduced pressure. When the crude product obtained was a

TABLE I. Dealkylation of Mixed Esters of Phosphoric Acid Bearing Two *sec*-Alkyl Groups Using Cation Exchange Resin



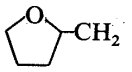
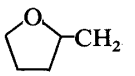
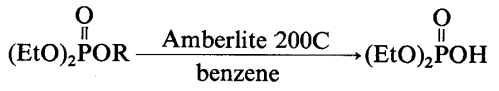
Compd. No.	R	R′	Reaction conditions		Yield (%)
			Temp. (°C)	Time (h)	
1	Ph	*sec*-C_4H_9	r.t.	48	88
2		iso-C_3H_7	40	96	50
3		*sec*-C_4H_9	40	72	99
4	iso-C_4H_9	*sec*-C_4H_9	40	72	93
5	C_2H_5	*sec*-C_4H_9	40	72	98

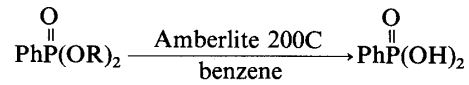
TABLE II. Dealkylation of Diethyl Alkyl Phosphates Using Cation Exchange Resin



Compd. No.	R	Reaction conditions		Yield (%)
		Temp. (°C)	Time (h)	
6	iso-C_3H_7	r.t.	96	20
		40	72	43[a]
7	*sec*-C_4H_9	r.t.	48	75[b]
		r.t.	72	34[c]
8	*tert*-C_4H_9	r.t.	15	77
9	$PhCH_2$	r.t.	48	94
		r.t.	144	35[d]
10	$CH_2=CHCH_2$	40	72	91

a) The recovery of the unreacted ester was 56%. *b*) When dichloromethane was used as the solvent in place of benzene, the desired product was obtained in 35% yield under the same conditions, while the use of diethyl ether or ethanol gave no isolable product. *c*) A gel type resin (Amberlite IR-120B) was used as the cation exchange resin in place of Amberlite 200C. *d*) 1,2-Dichloroethane was used as the solvent.

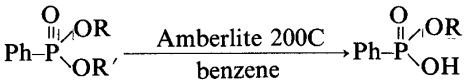
TABLE III. Dealkylation of Dialkyl Phenylphosphonates Using Cation Exchange Resin

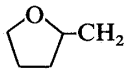


Compd. No.	R	Reaction conditions		Yield (%)
		Temp. (°C)	Time (h)	
11	iso-C_3H_7	r.t.	96	33[a]
		40	48	92
12	*sec*-C_4H_9	r.t.	48	97
		40	96	93[b]
13	iso-C_4H_9	40	48	—[c]
14	*cyclo*-C_6H_{11}	40	32	82
15	2-C_8H_{17}	40	72	85[d]
16	$PhCH_2$	r.t.	48	85
17	$CH_2=CHCH_2$	40	72	50[e]

a) Isopropyl hydrogen phenylphosphonate was isolated as the monodealkylated product in 40% yield. *b*) This reaction was carried out using 0.9 eq (SO_3H) of the resin. *c*) The recovery of the starting material (**13**) was 99%. *d*) Dichloromethane was used as the solvent in place of benzene. *e*) Complex products were formed.

TABLE IV. Dealkylation of Mixed Esters of Phenylphosphonates Using Cation Exchange Resin



Compd. No.	R	R′	Reaction conditions		Yield (%)
			Temp. (°C)	Time (h)	
18	CH_3	*sec*-C_4H_9	r.t.	48	93
19	CH_3	*cyclo*-C_6H_{11}	40	48	96
20		*sec*-C_4H_9	40	72	97

solid, the solid was purified by recrystallization. When the product was an oily substance, the pure product was isolated as its anilinium salt.

First, we chose di-*sec*-butyl phenyl phosphate (**1**) as a mixed triester, since phenyl dihydrogen phosphate is an easily isolable solid. The reaction of the di-*sec*-butyl ester (**1**) with the dry resin at room temperature for 48 h resulted in the formation of phenyl dihydrogen phosphate as a white powder (mp 87—90 °C) in 88% yield, while the use of wet resin led to the quantitative recovery of **1**. From this result, we found that the cation exchange resin also reacts with the mixed esters under anhydrous and mild conditions to give the desired dealkylation products. Subsequently, we examined the reaction of mixed esters of phosphoric acid bearing one primary and two secondary alkyl groups with the resin in order to obtain the monoalkyl esters, as shown in Table I. Further, we examined the reaction of mixed esters of phosphoric acid bearing one secondary and two primary alkyl groups with the resin in order to prepare the dialkyl esters, as shown in Table II. Di-*sec*-butyl tetrahydrofurfuryl phosphate (**3**), di-*sec*-butyl isobutyl phosphate (**4**), and di-*sec*-butyl ethyl phosphate (**5**) were selectively

dealkylated at 40 °C to give the corresponding dihydrogen phosphates in high yields. The tetrahydrofurfuryl substituent was selected as a simple model of the carbohydrate moiety in nucleotides. Dealkylation of diisopropyl tetrahydrofurfuryl phosphate (**2**) gave the desired dihydrogen phosphate in 50% yield along with a considerable amount of monodealkylated product (25%). The fact that the isopropyl group was very slowly dealkylated compared with the *sec*-butyl group is consistent with the result in the reaction using TsOH.[2] A similar tendency was also observed in the reactions of diethyl isopropyl phosphate (**6**) and diisopropyl phenylphosphonate (**11**) with the resin.

sec-Butyl, *tert*-butyl, benzyl, and allyl diethyl phosphates (**7**, **8**, **9**, and **10**) were also dealkylated to give high yields of diethyl hydrogen phosphate even at room temperature. It is expected that the *tert*-butyl and benzyl groups would be cleaved more smoothly than the *sec*-butyl group, because carbon-oxygen bond cleavage in protonated trialkyl phosphates is facilitated by the ability of the alkyl groups to leave as carbonium ions. In the case of the reaction of **9** with the resin in benzene, diphenylmethane was isolated in 60% yield from the organic layer after usual work-up. This result indicates clearly that this reaction involves a carbonium ion mechanism.[2] Further, in order to test the influence of variations in the solvents and resins on the yields we examined the behavior of **7** and **9**, as shown in Table II. From the results listed in Table II, it was found that benzene appears to be a preferable solvent, and when a gel-type resin (Amberlite IR-120B) was used in place of the macroporous resin (Amberlite 200C; surface area, 60 m^2/g), as might be expected, the reaction proceeded very slowly to give the dealkylation product in low yield, because the active sites are at the surface of the resin.

Next, we examined the reaction of dialkyl phenylphosphonates with the resin in order to obtain dihydrogen phenylphosphonate. As shown in Table III, di-*sec*-butyl, dicyclohexyl, di-2-octyl, dibenzyl, and diallyl phenylphosphonates (**12**, **14**, **15**, **16**, and **17**) gave the desired product in high yields. When diisobutyl ester (**13**) was used in the above reaction, no reaction occurred under these conditions. In the case of the reaction of diisopropyl ester (**11**), the desired product was obtained in 33% yield along with a monodealkylated product, isopropyl hydrogen phenylphosphonate (40%).

Finally, we examined the reaction of dialkyl phenylphosphonates bearing primary and secondary alkyl groups with the resin in order to obtain selectively monoalkylesters. As shown in Table IV, methyl *sec*-butyl, methyl cyclohexyl, and tetrahydrofurfuryl *sec*-butyl phenylphosphonates (**18**, **19**, and **20**) afforded quantitatively the desired products in which the secondary alkyl groups were selectively dealkylated. This result indicated that our reaction would provide an efficient procedure for the preparation of monoesters of phosphonic acids,[15] *e.g.*, lipophilic crown phosphonic acid monoalkyl esters, which are novel complexing agents.[16]

In conclusion, the features described above clearly demonstrate that the present method is potentially useful for the preparation of mono- and diesters of phosphorus oxyacids from the diesters or triesters in terms of high selectivity, and mild and facile work-up.

It remained unsettled whether the sulfonic acid function in the resin reacted with phosphorus oxyacid esters to form the esterified resin. In order to clarify the chemical behavior of the sulfonic acid function, we examined the exchange capacity of the resin before and after use. Surprisingly, the exchange capacity was unchanged (4.3 meq/g). This indicated that the esterified resin was not formed. Next, we found that when the resin after use was treated with toluene under reflux, the alkylated toluene which was expected from the reaction of TsOR with aromatic hydrocarbons was not obtained. Finally, we examined the presence of olefins, which were expected to be produced from carbonium ions generated *in situ* in the reaction mixture. Thus, when di-2-octyl phenylphosphonate (**15**) was treated with the resin, dihydrogen phenylphosphonate and a mixture of 1-octene and *trans*- and *cis*-2-octene were

isolated in 85 and 68% yields, respectively. Consequently, it is clear that when the resin was used in place of TsOH the carbonium ion was deprotonated to give the olefin,[17] and the resin remained in the parent form. This conclusion was also supported by the fact that treatment of **12** with a smaller amount of the resin at 40 °C gave dihydrogen phenylphosphonate in 93% yield (Table III). The reason why TsOH and cation exchange resin (SO_3H type) behave differently towards phosphorus oxyacid esters can not yet be explained. In any event, the synthetic utility value of our method was increased by the fact that the selective dealkylation of phosphorus oxyacid esters occurs even in the presence of a small amount of the resin to give high yields of the desired products.

Experimental

Melting points were determined on a Yanaco melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured on a JEOL JNH-MH-100 spectrometer using tetramethylsilane as an internal standard. Infrared (IR) spectra were obtained on a JASCO IR-2 spectrophotometer. Mass spectra (MS) were run on a JEOL JMS-D100 instrument. Column chromatography was carried out on silica gel (Kieselgel 60, 70—230 mesh, E. Merck) or on alumina (aluminiumoxid 90, 70—230 mesh, E. Merck). Amberlite 200C used was a sulfonated polystyrene copolymer with an exchange capacity of 4.3 meq/g.

Di-*sec*-butyl Phenyl Phosphate (1)——A solution of phenyl phosphorodichloridate (10.0 g, 47 mmol) in benzene (20 ml) was added dropwise to a solution of *sec*-butanol (7.1 g, 96 mmol) in pyridine (10 ml) under ice-cooling. The mixture was stirred at room temperature for 3 h, at 50 °C for 4 h, and then under reflux for 1 h. The reaction mixture was filtered to remove pyridinium chloride. The filtrate was diluted with benzene. The benzene layer was successively washed with 10% HCl, H_2O, sat. $NaHCO_3$, and then H_2O, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The resulting oil (16.1 g) was concentrated under reduced pressure (2 mmHg) to remove compounds with lower boiling point (bp *ca.* 100 °C). The resulting residue (13.2 g) was purified by column chromatography (alumina, $CHCl_3$) to give **1** (11.0 g, 82%) as a colorless oil. The spectra (NMR, IR, and MS) of the mixed esters shown below were consistent with their assigned structures. These esters seemed to be pure enough for the purpose of the dealkylation studies. NMR ($CDCl_3$) δ: 0.90, 0.96 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 1.32, 1.38 (6H, d, J=6 Hz, 2×$CHC\underline{H}_3$), 1.5—1.9 (4H, m, 2×$CHC\underline{H}_2CH_3$), 4.62 (2H, m, 2×$C\underline{H}CH_3$), 7.2—7.6 (5H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1272 (P=O), 1003 (P–O–C). MS (*m/e*): 286 (M^+).

Diisopropyl Tetrahydrofurfuryl Phosphate (2)——Diisopropyl phosphorochloridate (1.8 g, 9.0 mmol) was added to a solution of tetrahydrofurfuryl alcohol (0.9 g, 8.8 mmol) and triethylamine (2 ml) in benzene (5 ml). The mixture was heated under reflux for 3 h. The resulting solution was filtered. The filtrate was diluted with benzene and then shaken with H_2O. The aqueous layer was separated and the benzene layer was successively washed with 10% HCl, H_2O, sat. $NaHCO_3$, and H_2O, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting oil (2.8 g) was purified by column chromatography (silica gel, ethyl acetate) to give **2** (1.3 g, 57%) as a colorless oil. NMR ($CDCl_3$) δ: 1.35 (12H, d, J=6 Hz, 4×CH_3), 1.5—2.2 (4H, m, CH_2CH_2), 3.6—4.2 (5H, m, OCH_2CHOCH_2), 4.66 (2H, m, 2×$C\underline{H}(CH_3)_2$). IR ν_{max}^{neat} cm^{-1}: 1260 (P=O), 995 (P–O–C). MS (*m/e*): 267 (M^++1).

Di-*sec*-butyl Tetrahydrofurfuryl Phosphate (3)——Di-*sec*-butyl phosphorochloridate (4.6 g, 20 mmol) was added to a solution of tetrahydrofurfuryl alcohol (2.1 g, 20 mmol), triethylamine (5 ml), and pyridine (1.8 g, 22 mmol) in benzene (20 ml). The mixture was heated under reflux for 3 h, then worked up as usual, and the resulting oil (5.4 g) was purified by column chromatography (silica gel, hexane–ethyl acetate 1 : 2) to give **3** (4.6 g, 81%) as a colorless oil. NMR ($CDCl_3$) δ: 0.94 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 1.34 (6H, d, J=6.5 Hz, 2×$CHC\underline{H}_3$), 1.4—2.2 (8H, m, 2×$C\underline{H}_2CH_3$, $C\underline{H}_2C\underline{H}_2$), 3.6—4.3 (5H, m, OCH_2CHOCH_2), 4.47 (2H, m, 2×$C\underline{H}CH_3$). IR ν_{max}^{neat} cm^{-1}: 1258 (P=O), 995 (P–O–C). MS (*m/e*): 295 (M^++1).

Di-*sec*-butyl Isobutyl Phosphate (4)——This compound was prepared from di-*sec*-butyl phosphorochloridate and isobutanol in the same way as described for **3**. The reaction mixture was worked up as described for **3**, and the resulting oil was subjected to column chromatography (silica gel, ethyl acetate). The oil obtained was distilled under reduced pressure to give **4** (37%) as a colorless oil, bp 93—94 °C (2 mmHg). NMR ($CDCl_3$) δ: 0.8—1.1 (12H, m, 2×$CH_2C\underline{H}_3$, $CH(C\underline{H}_3)_2$), 1.34 (6H, d, J=6 Hz, 2×$CHC\underline{H}_3$), 1.5—2.2 (5H, m, 2×$C\underline{H}_2CH_3$, $C\underline{H}(CH_3)_2$), 3.84 (2H, dd, J=7, 7 Hz, OCH_2), 4.50 (2H, m, 2×$OC\underline{H}CH_3$). IR ν_{max}^{neat} cm^{-1}: 1260 (P=O), 1005 (P–O–C). MS (*m/e*): 266 (M^+).

Di-*sec*-butyl Ethyl Phosphate (5)——This compound [bp 82—83 °C (2 mmHg)] was prepared in the same way as described for **4** in 75% yield. NMR ($CDCl_3$) δ: 0.98 (6H, t, J=7 Hz, 2×$CHCH_2C\underline{H}_3$), 1.35 (9H, d, J=6 Hz, 2×$CHC\underline{H}_3$ and t, J=7 Hz, $OCH_2C\underline{H}_3$), 1.64 (4H, m, $CHC\underline{H}_2$), 4.16 (2H, dq, J=8, 7 Hz, $OC\underline{H}_2CH_3$), 4.51 (2H, m, 2×$C\underline{H}CH_3$). IR ν_{max}^{neat} cm^{-1}: 1262 (P=O), 1000 (P–O–C). MS (*m/e*): 238 (M^+).

Diethyl isopropyl phosphate (**6**) and diethyl *sec*-butyl phosphate (**7**) prepared in the previous work[2] were used here. Diethyl benzyl phosphate (**9**) was prepared from diethyl phosphorochloridate and benzyl alcohol in the same

way as described for **3**. The crude **9** was obtained as a colorless oil, bp 124—129 °C (2 mmHg) [lit.,[20] bp 183—185 °C (18 mmHg)], which was purified by column chromatography (alumina, $CHCl_3$) to give a pure compound (74%). NMR ($CDCl_3$) δ: 1.30 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 4.07 (4H, dq, J=8, 7 Hz, 2×$C\underline{H}_2CH_3$), 5.06 (2H, d, J=8 Hz, CH_2Ph), 7.36 (5H, s, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1260 (P=O), 1020 (P–O–C). MS (*m/e*): 244 (M^+).

Diethyl *tert*-Butyl Phosphate (8)——Diethyl phosphorochloridate (17.3 g, 100 mmol) was added dropwise to a solution of potassium *tert*-butoxide (12.4 g, 110 mmol) in petroleum ether (250 ml) under ice-cooling. After standing overnight at room temperature, the reaction mixture was filtered. The filtrate was evaporated under reduced pressure to give a yellow oil (20.8 g), which purified by column chromatography (alumina, $CHCl_3$) to give the desired product (17.3 g, 82%). NMR ($CDCl_3$) δ: 1.35 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 1.53 (9H, s, 3×CH_3), 4.12 (4H, dq, J=9, 7 Hz, 2×$C\underline{H}_2CH_3$). IR ν_{max}^{neat} cm^{-1}: 1260 (P=O), 1000 (P–O–C). MS (*m/e*): 210 (M^+).

Diethyl Allyl Phosphate (10)——This compound was obtained as a colorless oil (38%), bp 110—111 °C (11 mmHg) [lit.,[21] bp 63 °C (0.5 mmHg)], from diethyl phosphorochloridate and allyl alcohol in the same way as described for **6**. NMR ($CDCl_3$) δ: 1.33 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 4.08 (4H, dq, J=8, 7 Hz, 2×$C\underline{H}_2CH_3$), 4.48 (2H, m, $C\underline{H}_2CH=CH_2$), 5.20 (1H, d, J=10 Hz, *cis*-H of $=CH_2$), 5.32 (1H, d, J=15 Hz, *trans*-H of $=CH_2$), 5.7—6.1 (1H, m, $C\underline{H}=CH_2$). IR ν_{max}^{neat} cm^{-1}: 1262 (P=O), 1025 (P–O–C). MS (*m/e*): 194 (M^+).

General Procedure for The Preparation of Dialkyl Phenylphosphonates——A solution of phenylphosphonodichloridate (50 mmol) in benzene (50 ml) was added dropwise to a solution of an appropriate alkanol (110 mmol) in pyridine (10 ml) under ice-cooling with stirring. After standing overnight at room temperature with stirring, the reaction mixture was filtered to remove pyridinium chloride. The filtrate was diluted with benzene. The benzene layer was successively washed with 10% HCl, H_2O, sat. Na_2HCO_3, and H_2O, dried over anhydrous Na_2SO_4, and then evaporated under reduced pressure to give an oil. The oily residue was purified by column chromatography (alumina, $CHCl_3$) to give the desired product.

Diisopropyl phenylphosphonate (**11**) was obtained as a colorless oil (20%). NMR ($CDCl_3$) δ: 1.25, 1.40 (12H, d, J=6 Hz, 2×$CH(C\underline{H}_3)_2$), 4.76 (2H, m, 2×CH), 7.4—7.6 (3H, m, aromatic H), 7.7—8.0 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1438 (P–Ph), 1238 (P=O), 980 (P–O–C). MS (*m/e*): 242 (M^+).

Di-*sec*-butyl phenylphosphonate (**12**) was obtained as a colorless oil (95%). NMR ($CDCl_3$) δ: 0.81, 0.97 (6H, t, J=7 Hz, 2×$CH_2C\underline{H}_3$), 1.21, 1.39 (6H, d, J=6.5 Hz, 2×$CHC\underline{H}_3$), 1.60 (4H, m, 2×CH_2), 4.55 (2H, m, 2×CH), 7.4—7.6 (3H, m, aromatic H), 7.7—8.0 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1438 (P–Ph), 1245 (P=O), 975 (P–O–C). MS (*m/e*): 270 (M^+).

Diisobutyl phenylphosphonate (**13**) was obtained as a colorless oil (92%). NMR ($CDCl_3$) δ: 0.93 (12H, d, J=7 Hz, 2×$CH(C\underline{H}_3)_2$), 1.92 (2H, m, 2×$CH_2C\underline{H}$), 3.76 (4H, m, OCH_2), 7.4—7.6 (3H, m, aromatic H), 7.7—8.0 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1438 (P–Ph), 1250 (P=O), 1010 (P–O–C). MS (*m/e*): 270 (M^+).

Dicyclohexyl phenylphosphonate (**14**) was obtained as a colorless oil (87%). NMR ($CDCl_3$) δ: 1.0—2.4 (20H, m, 10×CH_2), 4.47 (2H, m, 2×OCH), 7.4—7.7 (3H, m, aromatic H), 7.8—8.1 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1440 (P–Ph), 1248 (P=O), 990 (P–O–C). MS (*m/e*): 322 (M^+).

Di-2-octyl phenylphosphonate (**15**) was obtained as a colorless oil (95%). NMR ($CDCl_3$) δ: 0.7—1.0 (6H, m, 2×$CH_2C\underline{H}_3$), 1.0—2.0 (26H, m, 2×$C\underline{H}_3CH(CH_2)_5$), 4.48 (2H, m, 2×CH), 7.3—7.5 (3H, m, aromatic H), 7.6—7.9 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1438 (P–Ph), 1250 (P=O), 980 (P–O–C). MS (*m/e*): 382 (M^+).

Dibenzyl phenylphosphonate (**16**) was obtained as a colorless oil (61%). NMR ($CDCl_3$) δ: 5.24 (4H, d, J=8 Hz, 2×OCH_2Ph), 7.5—7.7 (3H, m, aromatic H), 7.55 (10H, s, aromatic H), 7.8—8.1 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1440 (P–Ph), 1248 (P=O), 995 (P–O–C). MS (*m/e*): 338 (M^+).

Diallyl phenylphosphonate (**17**) was obtained as a colorless oil (65%), bp 119—120 °C (0.7 mmHg) [lit.,[22] bp 128 °C (1 mmHg)]. NMR ($CDCl_3$) δ: 4.54 (4H, m, 2×OCH_2), 5.16 (2H, d, J=10 Hz, 2×*cis*-H of $=CH_2$), 5.32 (2H, d, J=15 Hz, 2×*trans*-H of $=CH_2$), 5.7—6.1 (2H, m, 2×$C\underline{H}=CH_2$), 7.3—7.6 (3H, m, aromatic H), 7.7—8.0 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1439 (P–Ph), 1248 (P=O), 1010 (P–O–C). MS (*m/e*): 238 (M^+).

Methyl *sec*-Butyl Phenylphosphonate (18)——A solution of *sec*-butanol (1.9 g, 25.6 mmol) in pyridine (2.1 ml) was added dropwise to a solution of phenylphosphonodichloridate (5.0 g, 25.6 mmol) in benzene (20 ml) under ice-cooling. Stirring was continued for 0.5 h, then a solution of methanol (1.0 g, 31 mmol) and pyridine (2.1 ml) was added to the reaction mixture. After standing overnight at room temperature, the whole was worked up as usual. The resulting oil (5.9 g) was purified by column chromatography (silica gel, hexane–ethyl acetate, 2 : 1) to give the desired product (3.0 g, 51%) along with di-*sec*-butyl phenylphosphonate (0.6 g) and dimethyl phenylphosphonate (1.2 g). NMR ($CDCl_3$) δ: 0.82, 0.96 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.23, 1.38 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 1.60 (2H, m, $C\underline{H}_2CH_3$), 3.65, 3.76 (3H, d, J=11 Hz, OCH_3), 4.54 (1H, m, CH), 7.4—7.6 (3H, m, aromatic H), 7.6—7.9 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1440 (P–Ph), 1240 (P=O), 990 (P–O–C). MS (*m/e*): 228 (M^+).

Methyl Cyclohexyl Phenylphosphonate (19)——A solution of cyclohexyl alcohol (2.9 g, 29 mmol) in pyridine (2.4 ml) was added dropwise to a solution of phenylphosphonodichloridate (5.7 g, 29 mmol) in dry ether (50 ml) under ice-cooling, and the mixture was stirred for 0.5 h. Then, a solution of methanol (1.0 g, 31 mmol) in pyridine (2.4 ml) was added dropwise to the mixture. After standing overnight at room temperature, the reaction mixture was worked up as usual. The resulting oil (7.3 g) was purified by column chromatography (silica gel, hexane–ethyl acetate, 3 : 1) to give the desired product (2.5 g, 34%) along with dicyclohexyl phenylphosphonate (0.5 g) and dimethyl phenylphos-

phonate (1.1 g). NMR ($CDCl_3$) δ: 1.0—2.1 (10H, m, $5\times CH_2$), 3.63 (3H, d, $J=11$ Hz, OCH_3), 4.39 (1H, m, OCH), 7.2—7.5 (3H, m, aromatic H), 7.5—7.8 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1440 (P–Ph), 1250 (P=O), 995 (P–O–C). MS (*m/e*): 254 (M^+).

***sec*-Butyl Tetrahydrofurfuryl Phenylphosphonate (20)**——A solution of tetrahydrofurfuryl alcohol (2.6 g, 25.6 mmol) and pyridine (2.1 ml) in benzene (10 ml) was added dropwise to a solution of phenylphosphonodichloridate (5.0 g, 25.6 mmol) in benzene (20 ml) under ice-cooling. Stirring was continued for 1 h, and then *sec*-butanol (2.0 g, 27 mmol) in pyridine (2.1 ml) was added dropwise. After standing overnight at room temperature, the reaction mixture was worked up as usual. The resulting oil (8.5 g) was purified by column chromatography (silica gel, hexane–ethyl acetate, 1 : 1) to give a colorless oil (4.6 g, 60%). NMR ($CDCl_3$) δ: 0.82, 0.95 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.23, 1.36 (3H, d, $J=6$ Hz, $CHC\underline{H}_3$), 1.5—2.1 (6H, m, $C\underline{H}_2CH_3$, $C\underline{H}_2C\underline{H}_2$), 3.6—4.2 (5H, m, OCH_2CHOCH_2), 4.49 (1H, m, OCH), 7.3—7.5 (3H, m, aromatic H), 7.6—7.9 (2H, m, aromatic H). IR ν_{max}^{neat} cm^{-1}: 1438 (P–Ph), 1245 (P=O), 985 (P–O–C). MS (*m/e*): 299 ($M^+ + 1$).

General Procedure for the Dealkylation of Mixed Esters of Phosphorus Oxyacids with Cation Exchange Resin (Amberlite 200C)——Dry Amberlite 200C (5.0 g, 21.5 mmol SO_3H), which was obtained by treatment of commercial resin at 120 °C (1 mmHg) for 5 h, was added to a solution of a mixed ester of phosphorus oxyacid (5 or 10 mmol) in dry benzene (10 ml). In the dealkylation of mixed esters having two labile alkyl groups, *ca.* 4 eq of the resin was used, while in the case of one labile alkyl group, *ca.* 2 eq of the resin was used. The mixture was stirred under the conditions (temperature and time) shown in the tables. After removal of the resin by filtration, the resin was washed with H_2O. The filtrate (benzene solution) was extracted twice with H_2O. The combined aqueous layer was evaporated under reduced pressure. The residue was dissolved in $CHCl_3$. The solution was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. When the residue was a solid, the solid was purified by recrystallization. When the residue was an oil, the pure product was isolated as its anilinium salt.

Dealkylation of Di-*sec*-butyl Phenyl Phosphate (1)——Phenyl dihydrogen phosphate was obtained as a white powder, mp 87—90 °C ($CHCl_3$) (lit.,[23] mp 94 °C), in 88% yield. NMR (DMSO-d_6) δ: 6.81 (2H, br s, $2\times$OH, D_2O-exchangeable), 7.1—7.6 (5H, m, aromatic H).

Dealkylation of Diisopropyl Tetrahydrofurfuryl Phosphate (2)——The dealkylated product (75%) was obtained as a mixture of the desired dihydrogen compound and isopropyl tetrahydrofurfuryl hydrogen phosphate (2 : 1) (from NMR data).

Dealkylation of Di-*sec*-butyl Tetrahydrofurfuryl Phosphate (3)——Tetrahydrofurfuryl dihydrogen phosphate was obtained as a pale yellow oil in 99% yield. NMR ($CDCl_3$) δ: 1.5—2.2 (4H, m, $CH_2C\underline{H}_2C\underline{H}_2CH$), 3.4—4.3 (5H, m, CH, $2\times OCH_2$), 10.68 (2H, br s, $2\times$OH, D_2O-exchangeable).

The pale yellow oil was dissolved in 95% EtOH and treated with aniline. The precipitated anilinium salt (95%), mp 121—125 °C, was collected. An analytical sample was obtained by recrystallization from EtOH, mp 125—128 °C. *Anal.* Calcd for $C_{11}H_{18}NO_5P$: C, 48.00; H, 6.59; N, 5.09. Found: C, 47.72; H, 6.64; N, 5.07.

Dealkylation of Di-*sec*-butyl Isobutyl Phosphate (4)——Isobutyl dihydrogen phosphate was obtained as a pale yellow oil in 93% yield. NMR ($CDCl_3$) δ: 0.98 (6H, d, $J=7$ Hz, $C\underline{H}_3CHC\underline{H}_3$), 2.01 (1H, m, CH), 3.94 (2H, m, OCH_2), 10.70 (2H, br s, $2\times$OH, D_2O-exchangeable). Its anilinium salt was obtained as colorless prisms, mp 145—148 °C (iso-PrOH) (lit.,[24] mp 155—156 °C), in the same way as described above. *Anal.* Calcd for $C_{10}H_{18}NO_4P$: C, 48.58; H, 7.34; N, 5.67. Found: C, 48.30; H, 7.50; N, 5.50.

Dealkylation of Di-*sec*-butyl Ethyl Phosphate (5)——Ethyl dihydrogen phosphate was obtained as a pale yellow oil in 98% yield. Its anilinium salt was isolated as colorless needles, mp 155—158 °C (EtOH) (lit.,[25] mp 160—162 °C), in the same way as described above. *Anal.* Calcd for $C_8H_{14}NO_4P$: C, 43.84; H, 6.44; N, 6.39. Found: C, 43.89; H, 6.65; N, 6.48.

Dealkylation of Diethyl Isopropyl Phosphate (6)——Diethyl hydrogen phosphate was obtained as a colorless oil in 20—43% yields. NMR ($CDCl_3$) δ: 1.38 (6H, t, $J=7$ Hz, $2\times CH_2C\underline{H}_3$), 4.18 (4H, dq, $J=8$, 7 Hz, $2\times C\underline{H}_2CH_3$), 10.26 (1H, br s, OH, D_2O-exchangeable).

$PbCO_3$ (2.0 g) was added to a solution of diethyl hydrogen phosphate (0.5 g) in 95% ethanol (10 ml). The mixture was stirred at 70 °C for 1 h. The resulting solution was filtered while hot. After cooling, the precipitate was collected by filtration and washed with EtOH to give the lead salt as colorless needles (0.7 g), mp 181—183 °C (lit.,[26] mp 182—183 °C). The structure of the dealkylated product was also identified by comparison of its NMR data with those of an authentic sample prepared by hydrolysis of diethyl phosphorochloridate.

Dealkylation of Diethyl *sec*-Butyl Phosphate (7)——Diethyl hydrogen phosphate was obtained as a colorless oil in 75% yield. The structure was identified by NMR comparison with the dealkylated product of **6**.

Dealkylation of Diethyl *tert*-Butyl Phosphate (8)——Diethyl hydrogen phosphate was obtained as a colorless oil in 77% yield. The structure was identified by NMR comparison with the dealkylated product of **6**.

Dealkylation of Diethyl Benzyl Phosphate (9)——Diethyl hydrogen phosphate was obtained as a colorless oil in 94% yield. The structure was identified by NMR comparison with the dealkylated product of **6**.

Dealkylation of Diethyl Allyl Phosphate (10)——Diethyl hydrogen phosphate was obtained as a colorless oil in 91% yield. The structure was identified by NMR comparison with the dealkylated product of **6**.

Dealkylation of Diisopropyl Phenylphosphonate (11)——The residual solid obtained from the aqueous layer was

dissolved in hot ethyl acetate. The hot solution was dried over anhydrous Na_2SO_4, and filtered to remove Na_2SO_4 while hot. The filtrate was evaporated to give dihydrogen phenylphosphonate as a white powder in 92% yield. The powder was recrystallized from hexane–ethyl acetate to give colorless prisms, mp 162—164 °C (lit.,[27] mp 162.5—163 °C). The structure of the dihydrogen compound was identified by comparison of its NMR spectrum with that of a commercial sample (Aldrich Chemical Co.). NMR (DMSO-d_6) δ: 7.4—7.6 (3H, m, aromatic H), 7.7—7.9 (2H, m, aromatic H), 8.00 (2H, br s, 2 × OH, D_2O-exchangeable).

Dealkylation of Di-*sec*-butyl Phenylphosphonate (12)——Dihydrogen phenylphosphonate was quantitatively obtained. The structure was identified by NMR comparison with the dealkylated product of **11**.

Dealkylation of Dicyclohexyl Phenylphosphonate (14)——Dihydrogen phenylphosphonate was obtained in 82% yield. The structure was identified by NMR comparison with the dealkylated product of **11**.

Dealkylation of Di-2-octyl Phenylphosphonate (15)——The reaction was carried out by using dichloromethane in place of benzene as a solvent to give dihydrogen phenylphosphonate in 85% yield.

Isolation of octene: Amberlite 200C (10.0 g, 43 mmol) was added to a solution of **15** (5.0 g, 13 mmol) in dichloromethane (50 ml). The mixture was heated under reflux with stirring for 72 h. After cooling, the reaction mixture was filtered to remove the resin. The resin was washed with dichloromethane (100 ml). The filtrate and washings were combined, and the combined solution was concentrated to give the residue (20 ml), which was distilled to afford octene (2.0 g, 68%), bp 121—122 °C. The octene was shown by its NMR spectrum to be a mixture of 1-octene and *trans*- and *cis*-2-octene.

Dealkylation of Dibenzyl Phenylphosphonate (16)——Dihydrogen phenylphosphonate was obtained in 85% yield. Diphenylmethane (60%) was isolated from the organic layer according to the general procedure. Its identity was confirmed by NMR comparison with an authentic sample.

Dealkylation of Diallyl Phenylphosphonate (17)——Dihydrogen phenylphosphonate was obtained in 50% yield along with complex materials.

Dealkylation of Methyl *sec*-Butyl Phenylphosphonate (18)——Methyl hydrogen phenylphosphonate was obtained as a colorless oil in 93% yield. NMR ($CDCl_3$) δ: 3.66 (3H, d, J=11.5 Hz, OCH_3), 7.2—7.6 (3H, m, aromatic H), 7.6—7.9 (2H, m, aromatic H), 10.63 (1H, br s, OH, D_2O-exchangeable). MS (*m/e*): 172 (M^+). The product was treated with diazomethane in the usual way to give dimethyl phenylphosphonate, which was identified by comparison of its NMR data with those of an authentic sample prepared from phenylphosphonodichloridate and methanol according to the general procedure for the preparation of dialkyl phenylphosphonates.

Dealkylation of Methyl Cyclohexyl Phenylphosphonate (19)——Methyl hydrogen phenylphosphonate was obtained as a colorless oil in 96% yield.

Dealkylation of *sec*-Butyl Tetrahydrofurfuryl Phenylphosphonate (20)——Tetrahydrofurfuryl hydrogen phenylphosphonate was obtained as a colorless oil in 97% yield. NMR ($CDCl_3$) δ: 1.5—2.1 (4H, m, CH_2CH_2), 3.6—3.8 (2H, m, OCH_2), 3.8—4.2 (3H, m, CH, OCH_2), 7.2—7.5 (3H, m, aromatic H), 7.6—7.9 (2H, m, aromatic H), 11.32 (1H, br s, OH, D_2O-exchangeable). IR ν_{max}^{neat} cm^{-1}: 2270 (P–OH), 1438 (P–Ph), 1200 (P=O). The oil was dissolved in 95% EtOH and treated with aniline. The precipitated anilinium salt (95%), mp 84—90 °C, was collected. An analytical sample was obtained by recrystallization from benzene–diisopropyl ether, mp 93—95 °C. *Anal.* Calcd for $C_{17}H_{22}NO_4P$: C, 60.89; H, 6.61; N, 4.18. Found: C, 60.61; H, 6.70; N, 4.00.

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