The Preparation of Dialkyl 1-Hydroxyalkylphosphonates in the Reaction of Trialkyl Phosphites with Oxonium Salts Derived from Aldehydes or Ketones

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Abstract: The reaction of trialkyl phosphites with aldehydes or ketones in the presence of hydrogen chloride gives dialkyl 1-hydroxyalkylphosphonates via Arbusov-like reaction of oxonium salts derived from aldehydes or ketones. This reaction is a very convenient instant method for the preparation of dialkyl 1-hydroxyalkylphosphonates with a good yield as an alternative to the well-known Abramov reaction.

Key words: Abramov reaction, nucleophilic addition, addition reactions, 1-hydroxyphosphonates

The synthesis of 1-hydroxyalkylphosphonates has been extensively studied and described in the literature. Searching common databases gives more than 500[1] papers devoted to the preparation of a broad spectrum of 1-hydroxyalkylphosphonates. However, most of them are just obvious modifications of the old method described for the first time in 1950[2] by Abramov[3] and independently by Pudovik[4] and Fields.[5] This method is based on the reaction of aldehydes or ketones with dialkyl phosphonates, in the presence of a catalytic amount of base (sodium alkoxides were applied by Abramov and Pudovik, and triethylamine by Fields). Except for some activated carbonyl compounds like hexafluoroacetone[6] or trichloroacetaldehyde,[7] the addition of base is essential for the Abramov reaction, since the reaction between dialkyl phosphonates and aldehydes or ketones does not start spontaneously because: (i) the phosphonate is too weakly acidic to activate the aldehyde or ketone, and (ii) the aldehyde (or ketone) is too weakly basic to activate the dialkyl phosphonates. Therefore, most methods devoted to the synthesis of 1-hydroxyalkylphosphonates concentrate on finding a better catalyst than reported previously.

Some of these catalysts were described in context of their usefulness for preparative applications. For example, Texier-Boullet et al.[8] described the convenient synthesis of 1-hydroxyalkylphosphonates from aldehydes and dialkyl phosphonates in the presence of potassium or ceasium fluorides, then on alumina,[9] and finally on potassium fluoride on alumina.[10] Baraldi et al.[11] described the preparation of several diethyl 1-hydroxyalkylphosphonates using triethylamine as catalyst. Gawron et al.[12] described an activation of diethyl phosphonate by ethylmagnesium bromide.

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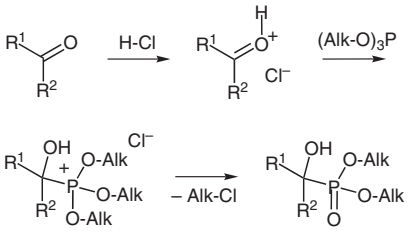
The activation of dialkyl phosphonates by bases causes two main problems. The first problem is the reversibility of the reaction of dialkyl phosphonates with aldehydes or ketones,[13] especially when a high temperature is necessary to distill the products. In this case instead of dialkyl 1-hydroxyalkylphosphonate, the substrates, namely a mixture of dialkyl phosphonate and the carbonyl compound, can be distilled from the reaction mixture when a base is present. The second problem is a well-known phosphonate–phosphate rearrangement, which gives the alkyl phosphates instead of the desired 1-hydroxyalkylphosphonates.[7,14] This problem exists especially when a strong base is applied as the catalyst in the Abramov reaction. Additionally, the anions of dialkyl phosphonates, obvious ambident nucleophiles, can react by their electron pair located on the phosphorus atom, as well as by those located on the oxygen, for example, when silver dialkyl phosphonates react with some halides, the alkylation on oxygen is observed predominantly.[15] Finally, the basic catalyst could also cause the well-known aldol reaction, and the products of the aldol reaction could react with dialkyl phosphonates to give a complex reaction mixture.

Studying the literature we found some precedents where acid catalysts like boron trifluoride etherate, aluminum trichloride or hydrogen chloride,[16] lithium perchlorate and diethyl ether[17] and TFA or TfOH,[18] were used for the activation of dialkyl phosphonates and aldehydes in the Abramov reaction, however, with moderate results.

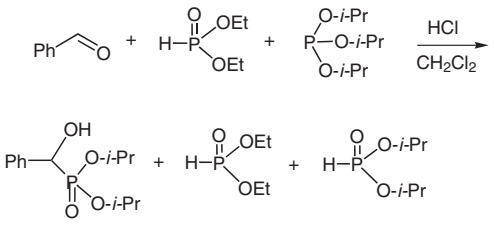
Surprisingly, we found very few reports describing the reactions of trialkyl phosphites with aldehydes or ketones, despite the fact that trialkyl phosphites are obviously much better nucleophiles than dialkyl phosphonates, and they are certainly P-nucleophiles because of their free electron pairs located only on the phosphorus atom. Abramov[19] reported that the reaction of trialkyl phosphites and aldehydes gives the corresponding dialkyl 1-alkoxyalkylphosphonates, though with rather low yields, and under very harsh reaction conditions (high temperature and pressure). Most aldehydes are unreactive towards trialkyl phosphites under neutral conditions at room temperature,[19] but if forced, by employing a high temperature and pressure, give complex reaction mixtures.[20] Also, 4-methyl-4-dichloromethylcyclohexadien-1-one,[21] acetone, and cyclohexanone were resistant to trialkyl phosphites, even when they were refluxed for a long time.[20b] The mixture of benzophenone and trimethylphosphite does not react at 160 °C even after several days.[20e]

Under such circumstances, we decided to apply the trialkyl phosphites with simultaneous in situ activation of the carbonyl group of aldehydes or ketones by an acid. We assumed that the strong acid, for example hydrogen chloride, would activate the carbonyl group by protonation of oxygen, to generate the corresponding oxonium salt. Then, the oxonium salt, a very strong electrophile, should react with nucleophilic trialkyl phosphite giving the intermediate phosphonium salt, which could be transformed to the final dialkyl 1-hydroxyalkylphosphonate analogously to the last step of the Arbuzov reaction (Scheme 1).



Scheme 1

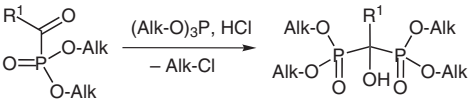
Indeed, when we examined the reaction of triethyl phosphite with benzaldehyde in the presence of a stoichiometric amount of hydrogen chloride in anhydrous diethyl ether at temperatures below –10 °C, we found by means of ^{31}P NMR spectroscopy that the crude reaction mixture contains as much as 88% of diethyl 1-hydroxy-1-phenylmethylphosphonate and a minor amount of diethyl phosphonate. To exclude the possibility that the triethyl phosphite was dealkylated by the hydrogen chloride to diethyl phosphonate (which could also give the final diethyl 1-hydroxy-1-phenylmethylphosphonate in the reaction with benzaldehyde), we accomplished the cross-experiment. Thus, when we mixed stoichiometric amounts of benzaldehyde, triisopropyl phosphite, diethyl phosphonate, and hydrogen chloride in diethyl ether –10 °C, we observed only diisopropyl 1-hydroxy-1-phenylmethylphosphonate in 94% yield (but not diethyl 1-hydroxy-1-phenylmethylphosphonate). We also recovered unreacted diethyl phosphonate with traces of diisopropyl phosphonate in about 6% yield (Scheme 2).



Scheme 2

After the reaction, the crystalline diisopropyl 1-hydroxy-1-phenylmethylphosphonate was isolated in 83% yield and its structure was confirmed. This double cross-experiment additionally shows that hydrogen chloride neither dealkylates the trialkyl phosphite nor activates dialkyl phosphite. Moreover, in a separate experiment we found that diethyl phosphonate does not react with benzaldehyde in the presence of equimolar amounts of hydrogen chloride.

To test the scope and limitation of this reaction we examined some representative carbonyl compounds under similar conditions. The reaction of acetone with triethyl phosphite gave diethyl 1-hydroxy-1-methylethylphosphonate in about 50% yield (by means of ^{31}P NMR spectroscopy), and diethyl phosphonate as a side-product derived from dealkylation of triethyl phosphite. However, when we used a 50% excess of triethyl phosphite, the yield increased to about 85%. Also in the case of aliphatic aldehydes, an excess of phosphites was useful. Benzophenone did not give 1-hydroxyphosphonate at all, which indicates that the dealkylation reaction of trialkyl phosphite is a few orders of magnitude faster than the reaction of triethyl phosphite with a sterically hindered oxonium salt. Therefore, the only product detected in the reaction mixture was diethyl phosphonate. Dialkyl 1-oxoalkylphosphonates react easily with an equimolar amount of trialkyl phosphites to give tetraalkyl 1-hydroxyalkylidenebisphosphonates in excellent yields (Scheme 3).



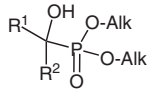
Scheme 3

For example, we prepared the tetraethyl 1-hydroxyethylidenebisphosphonate in over 95% yield, by the reaction of diethyl 1-oxoethylphosphonate with triethyl phosphite in the presence of hydrogen chloride. This seems to be a good method for the preparation of 1-hydroxybisphosphonates, which is competitive with those described in the literature.[22]

In summary, we have found that the reaction of trialkyl phosphites with aldehydes or ketones in the presence of hydrogen chloride[23] at a low temperature is a very good method for the preparation of dialkyl 1-hydroxyalkylphosphonates. This procedure is very simple, instant, and gives the final products in very good yields. Moreover, usually the final products are pure enough to be used directly for further steps, without the necessity of additional operations like chromatographic separation, for example. In many cases the products just crystallize directly out of the reaction mixture. The side products (volatile alkyl halides and dialkyl phosphonates) could be easily removed by simple evaporation. Also noteworthy is that the dialkyl 1-hydroxyalkylphosphonates obtained by our method neither decompose nor rearrange during their eventual distillation.

NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer in $CDCl_3$. FTIR spectra were measured on Perkin Elmer 2000 spectrometer as KBr pellets (1/200) for crystalline or as a film for liquid products. Melting points were determined on a Boetius microscope with electrical hot plate and were corrected. The carbo-

Table 1 Dialkyl 1-Hydroxyalkylphosphonates



R^1	R^2	Alk	$(AlkO)_3P/R^1R^2C=O$	Yield (%)	Mp (°C) or bp (°C/mmHg)
Ph	H	*i*-Pr	1:1	83	89–92[3b]
Ph	H	Et	1:1	74	78–80[2i,3b]
4-MeO-C_6H_4	H	Et	1:1	80	121–122[24]
Ph-CH=CH-	H	Et	1:1	79	104–107[24,13b,4b]
3-O_2N-C_6H_4	H	Et	1:1	80	93–94[3d,24]
Me	H	Et	3:2	72	148–156/15[a 3b,13b,5]
Et	H	Et	3:2	84	147–154/15[a, 3b,j,5]
i-Pr	H	Et	3:2	83	147–153/15[a, 13b]
Ph	Me	Et	3:2	41	73–75[10,14f]
Me	Me	Et	3:2	73	131–150/15[a 3b,13b,5]
Pr	Me	Et	3:2	66	140–160/15[a]
-$(CH_2)_5$-		Et	3:2	80	71–72[3b,10]
4-MeO-C_6H_4-	H	*i*-Pr	1:1	88	150–151
-$(CH_2)_5$-		*i*-Pr	3:2	79	97–98[3b]
Me	$P(O)(OEt)_2$	Et	1:1	98	Oil[14b]

[a] Bulb-to-bulb vacuum distillation, therefore the boiling ranges were very broad.

nyl compounds were acquired from a local supplier and were distilled before use. All reagents and solvents were of commercial quality and purchased from a local supplier. The procedures and isolations of products described in this paper were not optimized.

Cross-Experiment

To a cold (ca. –10 °C, ice–salt bath) solution of benzaldehyde (2.1 g, 0.020 mol), P(*i*-PrO)$_3$ (4.2 g, 0.020 mol) and O=PH(OEt)$_2$ (2.8 g, 0.020 mol), in CH_2Cl_2 (25 mL), a cold (ca. –10 °C) solution of HCl (5 M; 4 mL, 0.020 mol) in Et_2O was added dropwise. The reaction mixture was stirred for about 1 h at the same temperature, and then kept in the refrigerator (below –10 °C) overnight. Then, a sample (0.25 mL) was taken from the reaction mixture, evaporated to dryness in vacuo in a cold water bath, and the residue was dissolved in $CDCl_3$ (0.50 mL). ^{31}P and ^1H NMR spectroscopy gave only three peaks at 21.6 ppm (diisopropyl 1-hydroxy-1-phenylmethylphosphonate), 9.0 ppm (diethyl phosphonate), and traces of diisopropyl phosphonate at 6.1 ppm. The rest of the reaction mixture was concentrated in vacuo in a warm water bath (below 40 °C) to give an oily residue, which was crystallized, to give 4.5 g (83%) of diisopropyl 1-hydroxy-1-phenylmethylphosphonate.

Diisopropyl 1-Hydroxy-1-phenylmethylphosphonate

IR: 3264 (OH), 3028, 2985, 2933, 2882, 1601, 1494, 1468, 1452, 1417, 1378, 1372, 1226 (P=O), 1207, 1186, 1143, 1107, 1080, 1046, 1024 (POC), 993 (POC), 937, 901, 892, 849, 789, 767, 746, 730, 701, 655, 630, 564, 545, 497, 458, 423 cm^{-1}.

^1H NMR: δ = 1.13 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.25 (d, *J* = 6.1 Hz, 3 H, CH_3), 1.27 (d, *J* = 5.5 Hz, 6 H, CH_3), 3.44 (br s, 1 H, OH), 4.62 (m, 2 H, CH), 4.95 (d, *J* = 10.9 Hz, 1 H, CHP), 7.28–7.37 (m, 3 H, *m*-,*p*-Ph), 7.47–7.50 (m, 2 H, *o*-Ph).

^{31}P NMR: δ = 21.5

Dialkyl 1-Hydroxyalkylphosphonates; General Procedure

To a cold (ca. –10 °C, ice–salt bath) solution of the carbonyl compound (0.020 mol) and trialkyl phosphite (0.020 mol for aromatic aldehydes, or 0.030 mol for aliphatic aldehydes or ketones), in CH_2Cl_2 (25 mL), a cold (ca. –10 °C) solution of HCl (0.020 or 0.030 mol, respectively) in Et_2O was added dropwise. The reaction mixture was stirred for about 1 h at the same temperature, and then kept in the refrigerator (below –10 °C) overnight. The solvent and volatile by-products were evaporated in vacuo in a warm water bath (below 40 °C) to give an oily residue, which was crystallized from Et_2O (20 mL) or from Et_2O–hexane (1:1, 20 mL). The crystallizing mixture was kept in the refrigerator at ca. –10 °C for about 1 h, and then the product was filtered, washed with cold Et_2O (3 × 5 mL) (or Et_2O–hexane), and dried. The liquid 1-hydroxyalkylphosphonates were distilled in vacuo. When the product is crystalline, the reaction could be performed in Et_2O–hexane, so the product crystallizes directly from the reaction mixture.

Diethyl 1-Hydroxy-1-phenylmethylphosphonate

IR: 3264 (OH), 2990, 2931, 2908, 2829, 1601, 1492, 1479, 1450, 1391, 1367, 1328, 1228 (P=O), 1205, 1187, 1083, 1051 (POC), 1026 (POC), 978, 961, 852, 788, 762, 727, 701, 659, 629, 560, 531, 478, 412 cm^{-1}.

^1H NMR: δ = 1.37 (t, *J* = 7.0 Hz, 6 H, CH_3), 1.63 (br s, 1 H, OH), 2.5 (d, *J* = 13.8 Hz, 1 H, CHP), 4.20 (dq, *J* = 7.0, 7.0 Hz, 4 H, OCH_2), 7.20 (t, *J* = 7.1 Hz, 1 H, *p*-Ph), 7.30 (t, *J* = 7.0 Hz, 2 H, *m*-Ph), 7.47 (d, *J* = 7.5 Hz, 2 H, *o*-Ph).

^{31}P NMR: δ = 28.4.

Diethyl 1-Hydroxy-1-(4-methoxyphenyl)methylphosphonate
IR: 3258 (OH), 2992, 2962, 2933, 2909, 2834, 1614, 1586, 1512, 1477, 1462, 1438, 1389, 1368, 1329, 1251, 1228 (P=O), 1196, 1171, 1109, 1065 (POC), 1029 (POC), 976, 964, 862, 838, 797, 757, 710, 669, 639, 596, 557, 534, 495, 422 cm^{-1}.

^1H NMR: δ = 1.14 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.20 (t, *J* = 7.1 Hz, 3 H, CH_3), 3.5 (br s, 1 H, OH), 3.73 (s, 3 H, OCH_3), 3.92–4.03 (m, 4 H, OCH_2), 4.87 (d, *J* = 9.9 Hz, 1 H, CHP), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-Ph), 7.33 (d, *J* = 8.7 Hz, 2 H, *m*-Ph).

^{31}P NMR: δ = 23.4.

Diethyl 1-Hydroxy-3-phenyl-2-propenylphosphonate
IR: 3255 (OH), 2982, 2929, 2910, 2866, 1599, 1519, 1495, 1478, 1447, 1392, 1369, 1292, 1226 (P=O), 1190, 1113, 1052 (POC), 1021 (POC), 970, 855, 793, 759, 730, 698, 660, 562, 527, 485, 418 cm^{-1}.

^1H NMR: δ = 1.31 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.32 (t, *J* = 7.1 Hz, 3 H, CH_3), 3.9 (br s, 1 H, OH), 4.18 (dq, *J* = 7.1, 7.1 Hz, 4 H, OCH_2), 4.66 (ddd, *J* = 12.9, 6.1, 1.4 Hz, 1 H, CHP), 6.31 (ddd, *J* = 15.9, 6.1, 6.0 Hz, 1 H, CHCP), 6.77 (ddd, *J* = 15.9, 4.8, 1.4 Hz, 1 H, PhCH), 7.23 (t, *J* = 7.4 Hz, 1 H, *p*-Ph), 7.30 (t, *J* = 7.4 Hz, 2 H, *m*-Ph), 7.30 (d, *J* = 7.4, 2 H, *o*-Ph).

^{31}P NMR: δ = 28.6.

Diethyl 1-Hydroxy-1-(3-nitrophenyl)methylphosphonate
IR: 3245 (OH), 2983, 2932, 2914, 2869, 1537 (NO_2), 1479, 1445, 1395, 1351 (NO_2), 1320, 1296, 1260, 1236, 1209 (P=O), 1189, 1166, 1091, 1044 (POC), 1020 (POC), 972, 906, 842, 810, 781, 738, 719, 687, 667, 568, 537 cm^{-1}.

^1H NMR: δ = 1.24 (t, *J* = 7.05 Hz, 3 H, CH_3), 1.28 (t, *J* = 7.05 Hz, 3 H, CH_3), 4.11 (m, 4 H, OCH_2), 5.15 (d, *J* = 11.5 Hz, 1 H, PCH), 5.7 (br s, 1 H, OH), 7.5 (t, *J* = 7.8 Hz, 1 H, *m*-Ph), 7.79 (d, *J* = 7.8 Hz, 1 H, *o*-Ph), 8.12 (d, *J* = 7.8 Hz, 1 H, *p*-Ph), 8.39 (s, 1 H, *o*-Ph).

^{31}P NMR: δ = 21.6.

Diethyl 1-Hydroxyethylphosphonate
IR: 3317 (OH), 2983, 2935, 2911, 2873, 1651, 1479, 1445, 1393, 1369, 1220 (P=O), 1164, 1114, 1100, 1053 (POC), 1028 (POC), 968, 902, 867, 795, 692, 553, 474 cm^{-1}.

^1H NMR: δ = 1.30 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.31 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.4 (dd, *J* = 17.5, 7.2 Hz, 3 H, CH_3CP), 3.9 (br s, 1 H, OH), 4.00 (dq, *J* = 14.2, 7.2 Hz, 1 H, CHP), 4.13 (dq, *J* = 7.2, 7.2 Hz, 2 H, OCH_2), 4.14 (dq, *J* = 7.1, 7.1 Hz, 1 H, OCH*H*), 4.15 (dq, *J* = 7.0, 7.0 Hz, 1 H, OC*H*H).

^{31}P NMR: δ = 32.8.

Diethyl 1-Hydroxypropylphosphonate
IR: 3312 (OH), 2981, 2935, 2878, 1470, 1444, 1393, 1369, 1215 (P=O), 1165, 1119, 1091, 1053 (POC), 1028 (POC), 968, 792, 619, 566, 506 cm^{-1}.

^1H NMR: δ = 1.04 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2CH), 1.30 (t, *J* = 7.1 Hz, 6 H, CH_3CH_2O), 1.70 (m, 1 H, OCH*H*CH_3), 1.77 (m, 1 H, OC*H*HCH_3), 3.7 (ddd, br s, *J* = 13.7, 4.1 Hz, 2 H, CHP, OH), 4.13 (dq, *J* = 7.1, 7.1 Hz, 2 H, OCH_2), 4.132 (dq, *J* = 7.1, 7.1 Hz, 1 H, OC*H*H), 4.137 (dq, *J* = 7.1, 7.1 Hz, 1 H, OCH*H*).

^{31}P NMR: δ = 32.2.

Diethyl 1-Hydroxy-2-methylpropylphosphonate
IR: 3313 (OH), 2982, 2934, 2910, 2875, 1645, 1470, 1445, 1392, 1368, 1216 (P=O), 1165, 1130, 1097, 1050 (POC), 1030 (POC), 968, 851, 799, 708, 624, 564, 515, 455 cm^{-1}.

^1H NMR: δ = 1.037 (d, *J* = 6.8 Hz, 3 H, CH_3CH), 1.042 (d, *J* = 7.1 Hz, 3 H, CH_3CH), 1.31 (t, *J* = 7.1 Hz, 6 H, CH_3), 2.06 (m, 1 H, CH), 3.0 (br s, 1 H, OH), 3.62 (dd, *J* = 6.05, 6.05 Hz, 1 H, CHP), 4.14 (dq, *J* = 7.1, 7.1 Hz, 2 H, CH_2O), 4.15 (dq, *J* = 6.9, 6.9 Hz, 2 H, CH_2O).

^{31}P NMR: δ = 32.0.

Diethyl 1-Hydroxy-1-phenylethylphosphonate
IR: 3289 (OH), 2978, 2934, 2907, 1603, 1496, 1452, 1390, 1371, 1289, 1220 (P=O), 1200, 1186, 1162, 1139, 1126, 1098, 1051 (POC), 1026 (POC), 963, 946, 912, 833, 790, 762, 746, 698, 685, 658, 584, 562, 508, 471 cm^{-1}.

^1H NMR: δ = 1.18 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.24 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.80 (d, *J* = 15.4 Hz, 3 H, CH_3CP), 3.42 (br s, 1 H, OH), 3.95 (m, 2 H, OCH_2), 4.07 (m, 2 H, OCH_2), 7.27 (dd, *J* = 7.2, 1.6 Hz, 1 H, *p*-Ph), 7.33 (d, *J* = 7.9 Hz, 1 H, *o*-Ph), 7.36 (d, *J* = 7.4 Hz, 1 H, *o*-Ph), 7.59 (m, 2 H, *m*-Ph).

^{31}P NMR: δ = 30.9.

Diethyl 1-Hydroxy-1-methylethylphosphonate
Crystallizes in the refrigerator and melts at r.t.

IR: 3315 (OH), 2982, 2934, 2911, 1699, 1445, 1393, 1375, 1237 (P=O), 1193, 1136, 1162, 1139, 1126, 1098, 1050 (POC), 1028 (POC), 971, 857, 792, 762, 666, 529, 436 cm^{-1}.

^1H NMR: δ = 1.27 (t, *J* = 7.2 Hz, 6 H, CH_3), 1.38 (d, *J* = 15.3 Hz, 6 H, CH_3CP), 4.1 (dq, br s, *J* = 7.2, 7.2 Hz, 5 H, 2 × CH_2O, OH).

^{31}P NMR: δ = 34.5.

Diethyl 1-Hydroxy-1-methylbutylphosphonate
IR: 3316 (OH), 2981, 2963, 2935, 2911, 2875, 1699, 1645, 1468, 1457, 1445, 1393, 1369, 1292, 1227 (P=O), 1167, 1135, 1098, 1031 (POC), 967 (POC), 912, 848, 794, 766, 711, 670, 570, 520 cm^{-1}.

^1H NMR: δ = 0.9 (t, *J* = 7.2 Hz, 3 H, C*H*$_3$CH$_2$), 1.3 (t, *J* = 7.2 Hz, 6 H, C*H*$_3$CH$_2$O), 1.35 (d, *J* = 15.9 Hz, 3 H, C*H*$_3$CHP), 1.45 (m, 2 H, CH$_3$C*H*$_2$CH), 1.65 (m, 2 H, C*H*$_2$CHP), 3.1 (br s, 1 H, OH), 4.13 (dq, *J* = 7.2, 7.2 Hz, 2 H, OCH_2), 4.14 (dq, *J* = 7.2, 7.2 Hz, 2 H, OCH_2).

^{31}P NMR: δ = 34.4.

Diethyl 1-Hydroxycyclohexylphosphonate
IR: 3259 (OH), 2984, 2936, 2865, 2849, 1484, 1444, 1397, 1367, 1320, 1262, 1220 (P=O), 1163, 1139, 1071, 1047, 1024, (POC), 970 (POC), 957, 932, 911, 902, 847, 802, 760, 699, 582, 520, 502, 491, 452 cm^{-1}.

^1H NMR: δ = 1.29 (t, *J* = 7.1 Hz, 6 H, CH_3), 1.5 (m, 2 H, 4-CH_2), 1.6 (m, 6 H, 2-,3-,5-,6-CH_2), 1.8 (m, 2 H, 2-,6-CH_2), 3.08 (br s, 1 H, OH), 4.13 (dq, *J* = 7.1, 7.1 Hz, 4 H, OCH_2).

^{31}P NMR: δ = 33.6.

Diisopropyl 1-Hydroxy-1-(4-methoxyphenyl)methylphosphonate
IR: 3268 (OH), 2978, 2937, 2898, 2873, 2837, 1613, 1584, 1511, 1460, 1438, 1389, 1377, 1357, 1344, 1300, 1249, 1226 (P=O), 1202, 1190, 1170, 1143, 1107, 1063, 1028 (POC), 995, 900, 891, 856, 786, 757, 737, 712, 673, 638, 596, 559, 546, 511, 471, 433, 418 cm^{-1}.

^1H NMR: δ = 1.13 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.27 (d, *J* = 6.2 Hz, 6 H, CH_3), 1.28 (d, *J* = 6.2 Hz, 3 H, CH_3), 3.56 (br d, *J* = 3.6 Hz, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.61 (m, 2 H, CH), 4.87 (d, *J* = 10.0 Hz, 1 H, CHP), 6.88 (d, *J* = 8.7 Hz, 2 H, *o*-Ph), 7.41 (d, *J* = 8.7 Hz, 1 H, *m*-Ph), 7.42 (d, *J* = 8.7 Hz, 1 H, *m*′-Ph).

^{31}P NMR: δ = 21.7.

Diisopropyl 1-Hydroxycyclohexylphosphonate
IR: 3275 (OH), 2991, 2978, 2946, 2858, 1759, 1471, 1448, 1407, 1384, 1358, 1259, 1227 (P=O), 1176, 1159, 1141, 1105, 1070,

1037, 996 (POC), 982 (POC), 933, 915, 896, 881, 763, 756, 699, 681, 581, 538, 494, 426 cm^{-1}.

^1H NMR: δ = 1.33 (d, *J* = 6.2 Hz, 12 H, CH_3), 1.53 (m, 2 H, 4-CH_2), 1.58–1.77 (m, 6 H, 2-, 3-5-,6-CH_2), 1.83 (m, 2 H, 2-,6-CH_2), 2.27 (br s, 1 H, OH), 4.75 (dsept, *J* = 6.2, 12.4 Hz, 2 H, CHO).

^{31}P NMR: δ = 26.8.

Tetraethyl 1-Hydroxyethylidenediphosphonate

IR: 3250 (OH), 2985, 2934, 2911, 2871, 1479, 1445, 1393, 1368, 1251, (P=O), 1165, 1098, 1027 (POC), 973 (POC), 842, 797, 734, 639, 542 cm^{-1}.

^1H NMR: δ = 1.21 (t, *J* = 7.1 Hz, 12 H, CH_3CO), 1.53 (t, *J* = 16.2 Hz, 3 H, CH_3CP), 3.94–4,15 (m, br s, 9 H, 4 × CH_2, OH).

^{31}P NMR: δ = 27.2.

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References

(1) Since citation of more than 500 papers in this short article is not appropriate we will send a copy of a text file with the citations to interested readers.

(2) The chemistry of 1-hydroxyalkylphosphonic acids is of course much older. 1-Hydroxyalkylphosphonic acids were prepared in the 19th and 20th centuries by Marie and Fossek: (a) Marie, C. *C. R. Hebd. Seances Acad. Sci.* **1902**, *135*, 107. (b) Marie, C. *C. R. Hebd. Seances Acad. Sci.* **1903**, *136*, 48. (c) Marie, C. *Ann. Chim. (Paris)* **1904**, *8*, 335. (d) Fossek, W. *Monatsh. Chem.* **1884**, *5*, 121. (e) Fossek, W. *Monatsh. Chem.* **1886**, *5*, 627. (f) Fossek, W. *Monatsh. Chem.* **1886**, *7*, 20. Later, Conant described the preparation of some 1-hydroxyalkylphosphonic acids in the reaction of phosphorous (phosphonic) acid or phosphorus trichloride with aldehydes or ketones: (g) Conant, J. B. *J. Am. Chem. Soc.* **1917**, *39*, 2679. (h) Conant, J. B.; Cook, A. A. *J. Am. Chem. Soc.* **1920**, *42*, 830. (i) Conant, J. B. *J. Am. Chem. Soc.* **1921**, *43*, 1705.

(3) This reaction is commonly called the Abramov reaction. For the most representative Abramov papers, see: (a) Abramov, V. S. *Dokl. Akad. Nauk SSSR* **1950**, *73*, 487; *Chem. Abstr.* **1951**, *45*, 2855h. (b) Abramov, V. S. *Zh. Obshch. Khim* **1952**, *22*, 647; *Chem. Abstr.* **1953**, *47*: 5351e. (c) Abramov, V. S.; Semenowa, L. P. *Sb. Statei Obshch. Khim.* **1953**, *1*, 393; *Chem. Abstr.* **1955**, *49*, 838g. (d) Abramov, V. S. *Zh. Obshch. Khim.* **1957**, *27*, 169; *Chem. Abstr.* **1957**, *51*, 12878e. (e) Abramov, V. S.; Pall, S. *Zh. Obshch. Khim.* **1957**, *27*, 172; *Chem. Abstr.* **1957**, *51*, 12878g. (f) Abramov, V. S.; Kapustina, A. S. *Zh. Obshch. Khim.* **1957**, *27*, 173; *Chem. Abstr.* **1957**, *51*, 12878h. (g) Abramov, V. S.; Dimitrieva, R. V.; Kapustina, A. S. *Zh. Obshch. Khim.* **1953**, *23*, 257; *Chem. Abstr.* **1954**, *48*, 2572c. (h) Abramov, V. S.; Khairullin, V. K. *Zh. Obshch. Khim.* **1956**, *26*, 811; *Chem. Abstr.* **1956**, *50*: 14606b. (i) Abramov, V. S.; Khairullin, V. K. *Zh. Obshch. Khim.* **1959**, *29*, 1222; *Chem. Abstr.* **1960**, *54*, 1347b. (j) Abramov, V. S.; Il'ina, N. A. *Zh. Obshch. Khim.* **1954**, *24*, 124; *Chem. Abstr.* **1955**, *49*; 2997g. (k) Abramov, V. S.; Kapustina, A. S. *Zh. Obshch. Khim.* **1954**, *24*, 311; *Chem. Abstr.* **1955**, *49*; 4507a. (l) Abramov, V. S.; Nazmutdinova, A. S. *Zh. Obshch. Khim.* **1955**, *25*, 1141; *Chem. Abstr.* **1956**, *50*, 3214b. (m) Abramov, V. S.; Kuznetsov, N. S. *Sb. Statei Obshch. Khim.* **1953**, *1*, 398; *Chem. Abstr.* **1955**, *49*, 839a. (n) Abramov, V. S.; Bochkova, Yu. A.; Polyakova, A. D. *Zh. Obshch. Khim.* **1953**, *23*, 1013; *Chem. Abstr.* **1954**, *48*, 8169d. (o) Khairullin, V. K.; Ledeneva, A. I.; Abramov, V. S. *Zh. Obshch. Khim.* **1959**, *29*, 2551; *Chem. Abstr.* **1960**, *54*, 10835g.

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