Synthesis of 1-Hydroxyalkanephosphonic Esters on Alumina

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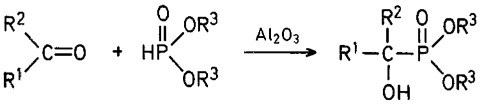
Alumina can act as base to catalyze organic reactions under mild conditions[1-4]. We describe here a new and easy synthesis of dialkyl 1-hydroxyalkanephosphonates (**3**) from carbonyl compounds (**1**) and dialkyl hydrogen phosphites (**2**) on an alumina surface, without solvent. 1-Hydroxyalkanephosphonic esters (**3**) have been prepared from the same components using potassium or caesium fluorides as catalysts[5,7]; our present method may be a useful alternative.



1 **2** **3**

On stirring with a sufficient amount of alumina, the reaction components **1** and **2** are completely adsorbed. The product **3** can then be eluted with dichloromethane; it is usually of high purity. Woelm basic chromatographic alumina was used; Merck 60 basic chromatographic alumina gives practically the same yields.

Diethyl hydroxymethanephosphonate (**3h**), which is a useful reagent for the synthesis of enol ethers[6], can be easily prepared by our alumina method; it cannot be prepared, however, using potassium fluoride as catalyst.

It is interesting to note that under the conditions used by us silica gel does not act as catalyst for the addition of carbonyl compounds (**1**) to dialkyl phosphites (**2**).

Dialkyl 1-Hydroxyalkanephosphonates (3); General Procedure:
Commercial aluminum oxide (3-5 g, see Table) is added to a stirred mixture of the dialkyl phosphite (**2**; 10 mmol) and the carbonyl compound (**1**; 10 mmol) at room temperature. The reagents are completely adsorbed on the alumina. After a reaction time of 2-72 h (see Table), the alumina is extracted with dichloromethane (2 x 25 ml). The extract is evaporated under reduced pressure to give the crude phosphonic ester **3** which may be purified by bulb-to-bulb distillation or by recrystallization (for example, from cyclohexane).

Diethyl Hydroxymethanephosphonate (3h):
Merck 60 neutral alumina (3 g) is added to a stirred mixture of diethyl phosphite (1.38 g, 10 mmol) and paraformaldehyde (0.3 g, 10 mmol). This mixture is heated at ~100 °C for 1.5 h and then allowed to cool to room temperature. The phosphonate **3h** is extracted with dichloromethane (2 x 25 ml), then the solvent is removed in vacuo to give pure **3h**; yield: 1.31 g (78%); b.p. 150 °C (bath)/0.3 torr.

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 1.35$ (t, 6 H, 2 O—CH_2—$C\underline{H}_3$, $J = 7$ Hz); 3.90 (d, 2 H, $C\underline{H}_2$—P, $J_{PH} = 6$ Hz); 4.16 (m, 4 H, 2 O—$C\underline{H}_2$—CH_3); 4.87 ppm (1 H, O$\underline{H}$, varies with dilution).

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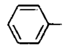
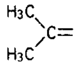
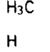
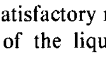
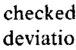
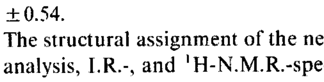
Table. Dialkyl 1-Hydroxyalkanephosphonates (**3**) from Carbonyl Compounds (**1**) and Dialkyl Hydrogen Phosphites (**2**) on Alumina

3	R^1	R^2	R^3	Amount of alumina [g]	Reaction time [h]	Yield [%]	m.p. [°C] or b.p. [°C]/torr	Molecular formula or Lit. m.p. or b.p./torr	I.R. (Nujol) ν_{OH} [cm^{-1}]
a		H	C_2H_5	$3^{a,b}$	2	96^c	83°	83-83.2°[7,8]	3239
b		H	i-C_3H_7	5^b	24	90^c	93°	92°[7], 96°[8]	3250
c		H	CH_3	$5^{a,b}$	48	78	101° (c-C_6H_{12})	101°[7,9]	3288
d	 $H_3C-\overset{O}{\overset{\parallel}{C}}-$	CH_3	C_2H_5	5^b	24	95^c	150°/0.3^d	138-140°/10[10]	3402 3303
e	CH_3	 $H_3C-\underset{Cl}{\underset{\vert}{C}H}-$	C_2H_5	$5^{a,b}$	72	79^c	150°/0.03^d	$C_8H_{18}ClO_4P^{e,f}$ (244.7)	3275
f		$Cl-CH_2-$	C_2H_5	5^b	65	84	80° (c-C_6H_{12})	82.5-84°[11] 80°[7]	3245
g		H	CH_3	5^b	48	92^c	210°/0.03^d	$C_{12}H_{25}O_4P^{e,g}$ (264.2)	3400
h	H	H	C_2H_5	3	1.5^i	78^c	150°/0.3^{d,h}	120°/0.1[6]	3300

[a] Merck 60 basic chromatographic alumina.
[b] Woelm basic chromatographic alumina.
[c] Yield of crude product which gave a satisfactory microanalysis.
[d] Bulb-to-bulb distillation. The purity of the liquid products was checked by microanalyses which showed the following maximum deviations from the calculated values: C, ±0.28; H, ±0.10; P, ±0.54.
[e] The structural assignment of the new compounds is based on microanalysis, I.R.-, and ^{1}H-N.M.R.-spectral data.
[f] ^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 1.31$ (t, 6 H, 2 O—CH_2—$C\underline{H}_3$, $J_{HH} = 7$ Hz); 1.51 (d, 3 H, P—C—$C\underline{H}_3$, $J_{PH} = 16$ Hz); 1.64 (d, 3 H, $\underline{H}_3C$—CHCl, $J_{HH} = 6.5$ Hz); 4.2 ppm (6 H, 2 O—$C\underline{H}_2$—CH_3, C$\underline{H}$Cl, O$\underline{H}$).
[g] ^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.97$, 0.90 (2 d, 3 H, $\underline{H}_3C$—CH, $J_{HH} = 5$ Hz); 1.60, 1.67 [2 s, 6 H, $(C\underline{H}_3)_2C=$]; 1.1-2.1 (m, 13 H); 3.78 [d, 6 H, $P(OC\underline{H}_3)_2$, $J_{PH} = 10$ Hz]; 4.07 (m, 2 H, C$\underline{H}$—OH); 5.08 ppm (m, 1 H, C=C$\underline{H}$).
[h] M.S.: $m/e = 168.0553$ (M^+) (calc. 168.0551).
[i] Reaction temperature: 100 °C.

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