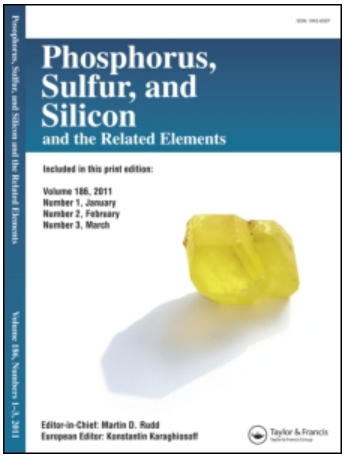

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FACTORS IN THE CONTROL OF PRODUCT COMPOSITION IN THE REACTIONS OF TRIALKYL PHOSPHITES WITH α-HALOGENOACETOPHENONES IN ALCOHOLIC MEDIA

György Keglevich[a]; Imre Petneházy[a]; László Tőke[a]; Harry R. Hudson[b]
[a] Department of Organic Chemical Technology, Technical University Budapest, Budapest [b] School of Chemistry, The Polytechnic of North London, London

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FACTORS IN THE CONTROL OF PRODUCT COMPOSITION IN THE REACTIONS OF TRIALKYL PHOSPHITES WITH α-HALOGENOACETOPHENONES IN ALCOHOLIC MEDIA

GYÖRGY KEGLEVICH, IMRE PETNEHÁZY and LÁSZLÓ TŐKE†
Department of Organic Chemical Technology, Technical University Budapest, 1521 Budapest

and

HARRY R. HUDSON†
School of Chemistry, The Polytechnic of North London, Holloway Road, London N7 8DB

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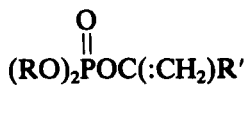
α-Hydroxyphosphonates are formed, in addition to vinyl phosphates and dehalogenated ketones, in the reactions of trimethyl phosphite (in methanol) or triethyl phosphite (in ethanol) with variously substituted α-chloro, α-bromo, and α,α-dichloro-acetophenones. Tri-isopropyl phosphite in propan-2-ol gives only the vinyl phosphate. Ketophosphonates are not detectable amongst the reaction products under the conditions used. Trends in product composition can be correlated with the leaving ability of halogen, substituent effects, structure of the phosphite, and reaction temperature. Additional products are obtained in the reactions of trimethyl phosphite in methanol with 4-nitro-α-chloroacetophenone, which gives the dehalogenated hydroxyphosphonate, and with the α,α-dichloroacetophenones which undergo monodehalogenation. Twenty three new α-hydroxyphosphonates are reported.

INTRODUCTION

It is well known that the reactions of α-halogenoketones with trialkyl phosphites in aprotic media give varying proportions of vinyl phosphates (**1**) and β-ketophosphonates (**2**) according to conditions.[1–3] Less information is available for the corresponding reactions in protic media. An early investigation by Chopard *et al.*[4] showed α-hydroxyphosphonates (**3**) to be formed in addition to vinyl phosphates, in the reactions of trimethyl phosphite with chloroacetone or with phenacyl chloride in methanol. Some hydroxyphosphonate was also obtained in the reaction of trimethyl phosphite with bromoacetone in acetic acid (but not in methanol). The results were in accord with the initial formation of a betaine intermediate (**4**), followed by protonation and dealkylation. Vinyl phosphate could thus have been formed *via* rearrangement of the betaine to the vinyloxyphosphonium intermediate (**5**), although direct nucleophilic attack of phosphorus on oxygen was not excluded.[4]

† To whom correspondence should be addressed.



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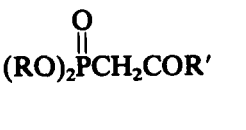

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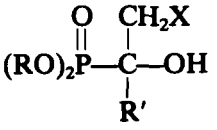

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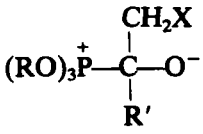

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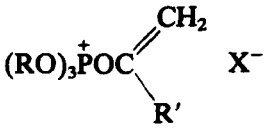

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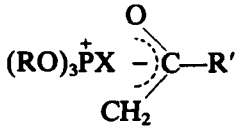

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Other investigations have generally shown the formation of vinyl phosphates to be favoured by protic media, especially acidic media such as acetic acid,[4-6] but in no cases have α-hydroxyphosphonates been reported as products. Dehalogenated ketones may also be formed together with trialkyl phosphates (presumably by solvolysis of the halogenophosphonium enolate, (**6**))[7] and are the only products in the reactions of triethyl phosphite with α,α-dibromo- or α-bromo-α-phenyl-acetophenones in acetic acid.[8,9] Dehalogenation is the principal reaction between trimethyl phosphite and certain sterically hindered α-bromo- and α,α-dihalogenoacetophenones in methanol.[10,11]

RESULTS AND DISCUSSION

We now present the results of a systematic investigation of the products obtained in the reactions of α-chloro-, α-bromo-, and α,α-dichloroaceto-phenones, having various substituents in the aromatic ring, with trimethyl, triethyl, and tri-isopropyl phosphite using the corresponding alcohols as reaction media. The phosphites were used in excess to ensure complete reaction of the halogenoketones and the products were analysed by gas chromatography (Tables I–VI).[12] In all reactions, except those of tri-isopropyl phosphite, the α-hydroxyphosphonate, (**3**, R′ = aryl) was formed, in addition to vinyl phosphate (**1**, R′ = aryl) and a smaller amount of the dehalogenated ketone, $ArCOCH_3$ (**7**). Ketophosphonates (**2**) were not detectable as products in any of the reactions studied.[13] The α-hydroxyphosphonates obtained in the present work are new compounds with the exception of one example (**3**, R = Me, X = Cl, R′ = Ph)[4] and were fully characterised. In certain cases, authentic samples were more conveniently prepared by reaction of the dialkyl phosphite with α-halogenoacetophenone on aluminia, as other products are not obtained by this procedure.[14] The vinyl phosphates (except the 4-fluro- and 4-iodo derivatives) are known compounds.[15]

The factors which control the various reaction pathways leading to the formation of α-hydroxyphosphonate, vinyl phosphate,[16] and dehalogenated ketone are complex but a number of trends can be observed. The better leaving

TABLE I

Reactions of trialkyl phosphites, $(RO)_3P$, with α-halogenoacetophenones, $PhCOCH_2X$, in ROH at 0°C

	Products (mole %)[a]					
	R = Me			R = Et		
X	1	3	7	1	3	7
Cl	55	35	10	85	11	4
Br	84	8	8	93	4	3

[a] R'(Ar) = Ph

properties of bromine compared to chlorine can be correlated with relatively greater formation of vinyl phosphate (Table I), whilst an increase in the electron-releasing propensity of the aromatic substituent (which may be expected to favour protonation of the betaine, 4), is paralleled by a tendency towards increasing formation of the hydroxy-phosphonate although the effect is small (Table II). The influence of the alkyl group of the phosphite ester on the course of reaction is shown by an increase in the relative amount of vinyl phosphate formed in the order $Me < Et < Pr^i$ (Table III). Assuming reversible formation of the α-hydroxyphosphonium intermediate (protonated (**4**)), the result may reflect the relative rates at which Arbuzov cleavage occurs.[4] Increasing stability would thus favour irreversible formation of the vinyloxyphosphonium ion (**5**) and hence vinyl phosphate. The relative pK_a values of the alcohols used as media for these reactions will also be of importance, as previously discussed,[4] and will favour a similar trend. From the point of view of preparative chemistry the effect of temperature is important, lower temperatures favouring the formation of hydroxyphosphonate to a significant extent (Table IV).

TABLE II

Reactions of trialkyl phosphites, $(RO)_3P$, with aryl substituted α-halogenoacetophenones, $ArCOCH_2X$, in ROH at 0°C

		Products (mole %)[a]					
		R = Me			R = Et		
X	Ar	1	3	7	1	3	7
Cl	$3,4\text{-}Me_2C_6H_3$	52	41	7	83	13	4
	$4\text{-}MeC_6H_4$	53	39	8	83	13	4
	C_6H_5	55	35	10	85	11	4
	$4\text{-}FC_6H_4$	55	35	10	85	11	4
	$4\text{-}ClC_6H_4$	58	30	12	86	10	4
	$4\text{-}IC_6H_4$	59	29	12	87	9	4
Br	$4\text{-}MeC_6H_4$	83	10	7	93	4	3
	C_6H_5	84	8	8	93	4	3
	$4\text{-}FC_6H_4$	84	8	8	—	—	—
	$4\text{-}ClC_6H_4$	85	6	9	93	4	3

[a] R' = Ar

TABLE III

Reactions of trialkyl phosphites, $(RO)_3P$, with α-chloroacetophenone, $PhCOCH_2Cl$, in ROH at 26°C (or 15°C*)

	Products (mole%)[a]		
R	1	3	7
Me	70	23	7
Et	87*	10*	3*
Pr^i	100	0	0

[a] R′(Ar) = Ph, X = Cl

TABLE IV

Reactions of trialkyl phosphites, $(RO)_3P$, with α-chloroacetophenone, $PhCOCH_2Cl$, in ROH at various temperatures

Temp.	Products (mole%)[a]					
	R = Me			R = Et		
(°C)	1	3	7	1	3	7
0	55	35	10	85	11	4
26 (or 15*)	70	23	7	87*	10*	3*
52	84	11	5	95	5	0

[a] R′(Ar) = Ph, X = Cl

TABLE V

Reactions of trimethyl phosphite with 4-nitro-α-chloroacetophenone in methanol at 0°C

	Products (mole %)[a]			
Conditions	1	3	7	8
A	54	7	29	10
B	30	37	15	18
	(27	53.5	14.5	5)[b]

A. Reactants alone in methanol.
B. With α-hydroxyphosphonate (**3**) (1 mol. equiv.) added.
[a] R = Me, X = Cl, R′(Ar) = 4-$NO_2C_6H_4$
[b] Expected composition if **3** is inert.

Additional types of product to those referred to above were obtained in the reactions of trimethyl phosphite in methanol with 4-nitro-α-chloro-acetophenone (Table V) and with the α,α-dichloroacetophenones (Table VI). In the reaction with 4-nitro-α-chloroacetophenone the dehalogenated α-hydroxyphosphonate (**8**) was also formed, although this product cannot be accounted for by reaction of the phosphite with dehalogenated ketone (4-nitroacetophenone). Dehalogenation of

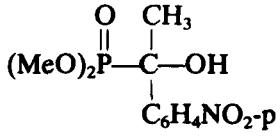
TABLE VI

Reactions of trimethyl phosphite with α,α-dichloroacetophenones, $ArCOCHCl_2$, in methanol at 0 or 52°C

Ar	Temp (°C)	Products (mole %)[a]					
		E−9	Z−9	10	1	3	7
C_6H_5	0	11	9	29	31	14	6
C_6H_5	52	34	27	14	25	0	0
4-ClC_6H_4	0	7	5	16	45	18	9
4-ClC_6H_4	52	27	20	7	39	3	4

[a] R = Me, X = Cl, R′ = Ar

the first-formed α-hydroxyphosphonate (**3**, R = Me, X = Cl, R′ = 4-$NO_2C_6H_4$) was, however, shown to occur under reaction conditions (see Table V) and appears to require the removal of positive chlorine, e.g. by an enolate anion (**6**), followed by protonation.[17] Reactions of the α,α-dichloroacetophenones were similar to those of the α-chloroacetophenones, giving the corresponding chlorovinyl phosphate (**9**), α,α-dichloro-α-hydroxyphosphonate (**10**) and monodehalogenated ketone (α-chloroacetophenone); the latter was not however detected as it reacted further with excess phosphite to give the expected products (**1**, **3**, and **7**) as described above. The extent of monodehalogenation was, however, considerably greater in the reactions of the α,α-dichloroacetophenones than in those of the α-chloroacetophenones. The dependence of product composition on temperature was similar for both systems.



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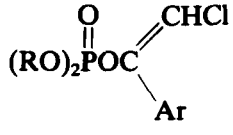

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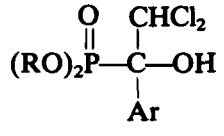

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EXPERIMENTAL

Reactions of the halogenoacetophenones (0.0025 mmol) with phosphites in excess (15–20 mole ratio) were carried out in the corresponding alcohols (40–60 ml) at the specified temperatures (Tables I–VI) and were monitored by g.l.c. until complete (ca. 1–20 h according to reactivity).

Instrumentation and analysis

G.l.c. analyses were performed with a Packard 802 chromatograph using a column packed with Chromosorb G, impregnated with QF-1 silicone oil (2.5 or 5%). A column temperature of 180–210°C was used with hydrogen as the carrier gas and a thermal conductivity detector. The concentrations of α-halogenoacetophenones, vinyl phosphates, α-hydroxyphosphonates and acetophenones were determined from calibration graphs, the overall accuracy normally being within ±2%. Determination of the α-hydroxyphosphonate was possible on the basis of a reproducible quantitative decomposition to the corresponding halogenoacetophenone and dialkyl phosphite in the g.l.c. column. The halogenoacetophenone peak was used for calibration and for measurement of the hydroxyphosphonate. The dehalogenated hydroxyphosphonate (**8**) derived from 4-nitro-α-chloroacetophenone and the corresponding dehalogenated ketone (**7**, Ar = *p*-$NO_2C_6H_4$) to which it decomposes during g.l.c. were

readily distinguished by tlc, using Polygramm Sil G sheet with benzene-acetone (8:2); R_f values 0.2 and 0.82 respectively. Quantitative analysis was based on calibration graphs. Infrared spectroscopy was carried out on a Spektromom 2000 spectrometer. ^{1}H nmr spectra were recorded on a Perkin–Elmer 60 MHz instrument, and ^{31}P nmr spectra on a Bruker WP80 spectrometer operating at 32.4 MHz. Chemical shifts are given relative to TMS and to 85% H_3PO_4 respectively. Mass spectra were recorded on a Jeol JMS-01SG-2 instrument at 75 eV.

Starting materials and preparations

Commercially available trimethyl phosphite, triethyl phosphite, tri-isopropyl phosphite and acetophenones were used, the trialkyl phosphites being redistilled from sodium before use.[18] Vinyl phosphates were prepared from the α-halogenoacetophenones as described.[2,15] New vinyl phosphates, obtained in 50–60% yield, had the following properties: **1** (R = CH_3, R′ = 4-FC_6H_4) b.p. 122–4°C at 0.2 mmHg, n_D^{26} 1.5078, δ_H (CCl_4) 3.78 (CH_3O, d, 6 H, J_{POCH} 12 Hz), 5.16 (CH_2 d, 2H, J_{POCCH} 3 Hz), 6.80–7.68 (Ar, m, 4H), IR (film) ν_{POC} 1040, $\nu_{P=O}$1260, $\nu_{C=C}$1630 cm^{-1}; **1** (R = CH_3, R′ = 4 – IC_6H_4) b.p. 150–9°C/0.2–0.3 mmHg, n_D^{26} 1.5816, δ_H ($CDCl_3$) 3.77 (CH_3O, d, 6H, J_{POCH} 12 Hz), 5.2 (CH_2, m, 2H), 7.12–7.76 (Ar, m, 4 H), IR (film) ν_{POC} 1050, ν_{POC} 1050, $\nu_{P=O}$ 1270, $\nu_{C=C}$ 1630 cm^{-1}; **1** (R = C_2H_5, R′ = 4 – FC_6H_4) b.p. 126–8°C/0.1 mmHg, n_D^{26} 1.4980, δ_H (CCl_4) 1.28 (CH_3CH_2, tr, 6H, J_{HCCH} 7 Hz), 4.09 (CH_3CH_2, overlapping dq, six lines, 4 H, J_{POCH} 9 Hz, J_{PCCH} 7 Hz), 5.11 (CH_2, d, 2 H, J_{POCCH} 3 Hz), 6.78–7.68 (Ar, m, 4 H), IR (film) ν_{POC} 1020, $\nu_{P=O}$ 1260, $\nu_{C=C}$ 1625 cm^{-1}; **1** (R = C_2H_5, R′ = 4-IC_6H_4) b.p. 148–50°C/0.2 mmHg, n_D^{26} 1.5632, δ_H ($CDCl_3$) 1.32 (CH_3CH_2, overlapping dt, six lines, 6H, J_{HCCH} 7Hz, J_{POCCH} 1 Hz), 4.15 (CH_3CH_2, overlapping dq, five lines, 4H, J_{POCH} 9 Hz, J_{PCCH} 7 Hz), 5.18 (CH_2, d, 2H, J_{POCCH} 3 Hz), 7.11–7.77 (Ar, m, 4H), IR (film) ν_{POC} 1035, $\nu_{P=O}$ 1265, $\nu_{C=C}$ 1625 cm^{-1}.

The α-hydroxyphosphonates were prepared by the reaction (24 h) of the corresponding α-halogenoacetophenones (0.07 mol) with trialkyl phosphite (0.21 mol) in the appropriate alcohol (100–300 cm^3) at 26°C or at −20°C (method 1 or 2 respectively) or by the reaction of an α-halogenoacetophenone (0.05 mol) with a dialkyl phosphite (0.1 mol) on the surface of aluminium oxide, using the method of Foucaud[6] (method 3). Products were recrystallised from methanol or ethanol.[19]

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = Ph) (method 1):
yield 32%; (Found: C, 45.3; H, 5.4. $C_{10}H_{14}ClO_4P$ requires: C, 45.4; H, 5.4%), m.p. 155 °C (lit.[4] m.p. 144–6°C, δ p($CDCl_3$) + 21.5 ppm, δ_H ($CDCl_3$) 3.49 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.71(CH_3O, d, 3H, J_{POCH} 11 Hz), 4.16(CH_2X, m, 2H), 7.15–7.70 (Ar, m, 5H), m/z 264 (3%, M^+), 110 (100%), IR (KBr disc) ν_{POC} 1030, $\nu_{P=O}$ 1210, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 3,4-$Me_2C_6H_3$) (method 2):
yield 65% (Found: C, 49.2; H, 6.2. $C_{12}H_{18}ClO_4P$ requires: C, 49.3; H, 6.2%), m.p. 177 °C, δp ($CDCl_3$) + 21.8 ppm, δ_H ($CDCl_3$) 2.24 (CH_3, s, 6H), 3.50, (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.72 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.14 (CH_2X, m, 2H), 7.06–7.36 (Ar, m, 3H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1200, ν_{OH} 3220 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 4-$CH_3C_6H_4$) (method 1):
yield 27%; (Found: C, 47.2; H, 5.7. $C_{11}H_{16}ClO_4P$ requires: C, 47.4; H, 5.8%), m.p. 154°C, δ_P ($CDCl_3$) + 21.6 ppm, δ_H ($CDCl_3$) 2.35 (CH_3, s, 3H), 3.53, (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.74 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.16 (CH_2X, m, 2H), 7.04–7.59 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1205, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 4-FC_6H_4) (method 3):
yield 56%; (Found: C, 42.9; H, 5.1. $C_{10}H_{13}ClFO_4P$ requires: C, 42.5; H, 4.6%), m.p. 134°C, δ_H ($CDCl_3$) 3.54, (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.75 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.13 (CH_2X, m, 2H), 6.83–7.73 (Ar, m, 4H), IR (KBr disc) ν_{POC}, 1010, $\nu_{P=O}$ 1220, ν_{OH} 3200 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 4-ClC_6H_4) (method 1):
yield 31%; (Found: C, 40.0; H, 4.4. $C_{10}H_{13}Cl_2O_4P$ requires: C, 40.2; H, 4.4%), m.p. 142°C, δ_P ($CDCl_3$) + 21.0 ppm, δ_H ($CDCl_3$) 3.53 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.70 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.10 (CH_2X, m, 2H), 7.15–7.60 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1200, ν_{OH} 3220 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 4-IC_6H_4) (method 2):
yield 49%; (Found: C, 30.5; H, 3.2. $C_{10}H_{13}ClIO_4P$ requires: C, 30.8; H, 3.4%), m.p. 172–3°C, δ_P (dmso-d_6) + 21.2 ppm, δH (DMSO-d_6) 3.54 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.71 (CH_3O, d, 3H, J_{POCH}

11 Hz), 4.13 (CH_2X, m, 2H), 7.16–7.82 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1210, ν_{OH} 3220 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = Ph) (method 3):
yield 49%; (Found C, 49.9; H, 6.7. $C_{12}H_{18}ClO_4P$ requires: C, 49 2; H, 6.2%), m.p. 81–2°C, δ_P ($CDCl_3$) + 19.3 ppm, δ_H (CCl_4) 1.22 (CH_3, tr, 6H, J_{HCCH} 7 Hz), 4.05 (CH_2O and CH_2Cl, m, 6H), 7.06–7.62 (Ar, m, 5H), IR (KBr disc) ν_{POC} 1010, 965, $\nu_{P=O}$ 1210, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = 3,4-$Me_2C_6H_3$) (method 2):
yield 26%; (Found: C, 52.1; H, 6.7. $C_{14}H_{22}ClO_4P$ requires: C, 52.6; H, 6.9%), m.p. 115°C, δ_P ($CDCl_3$) + 19.5 ppm, δ_H ($CDCl_3$) 1.10 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 1.25 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 2.25 (CH_3, s, 6H), 4.05 (CH_2O and CH_2X, m, 6H), 7.00–7.43 (Ar, m, 3H), IR (KBr disc) ν_{POC} 1010, 960, $\nu_{P=O}$ 1200, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = 4-$CH_3C_6H_4$) (method 2):
yield 19%; (Found: C, 51.2; H, 6.5. $C_{13}H_{20}ClO_4P$ requires: C, 50.9; H, 6.6%), m.p. 110°C, δ_P ($CDCl_3$) + 19.5 ppm, δ_H ($CDCl_3$) 1.16 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 1.28 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 2.33 (CH_3, s, 3H), 3.90 (CH_2O and CH_2Cl, m, 6H), 7.00–7.58 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, 970, $\nu_{P=O}$ 1210, ν_{OH} 3260 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = 4-FC_6H_4) (method 3):
yield 34%; (Found C, 46.2; H 5.5. $C_{12}H_{17}ClFO_4P$ requires: C, 46.4; H, 5.5), m.p. 95–7°C, δ_H ($CDCl_3$) 1.23 ($\underline{CH_3}CH_2$, tr, 6H, J_{HCCH} 7 Hz), 4.0 (CH_2O and CH_2Cl, m, 6H), 6.75–7.65 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1010, $\nu_{P=O}$ 1210, ν_{OH} 3220 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = 4-ClC_6H_4) (method 3):
yield 53% (Found: C, 44.2; H, 5.1. $C_{12}H_{17}Cl_2O_4P$ requires: C, 44.0; H, 5.2%), m.p. 115°C, δ_P ($CDCl_3$) + 18.8 ppm, δ_H ($CDCl_3$) 1.16 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 1.25 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 4.05 (CH_2O and CH_2X, m, 6H), 7.12–7.57 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1010, 965, $\nu_{P=O}$ 1210, ν_{OH} 3250 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Cl, R′ = 4-IC_6H_4) (method 3):
yield 21%; (Found: C, 34.1; H, 4.0. $C_{12}H_{17}ClIO_4P$ requires: C, 34.4; H, 4.1%), m.p. 99–100°C, δ_H ($CDCl_3$) 1.17 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 1.28 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 4.06 (CH_2O and CH_2X, m, 6H), 7.02–7.82 ppm (Ar, m, 4H), IR (KBr disc) ν_{POC} 1010, 970, $\nu_{P=O}$ 1210, ν_{OH} 3250 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Br, R′ = Ph) (method 3):
yield 61%; (Found: C, 39.1; H, 4.7. $C_{10}H_{14}BrO_4P$ requires: C, 38.9; H, 4.6%), m.p. 149–50°C, δ_P ($CDCl_3$) + 20.1 ppm, δ_H ($CDCl_3$) 3.48 (CH_3O, d, 3H, J_{POCH} 10 Hz), 3.73 (CH_3O, d, 3H, J_{POCH} 10 Hz), 4.08 (CH_2X, d, 2H, J_{PCCH} 7 Hz), 7.13–7.63 (Ar, m, 5H), m/z 308 (1%, M^+), 110 (100%), IR (KBr disc) ν_{POC} 1030, $\nu_{P=O}$ 1220, ν_{OH} 3250 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Br, R′ = 4-$CH_3C_6H_4$) (method 3):
yield 12%; (Found: C, 41.1; H, 5.1. $C_{11}H_{16}BrO_4P$ requires: C, 40.9; H, 5.0%), m.p. 149–151°C, δ_P ($CDCl_3$) + 20.2 ppm, δ_H ($CDCl_3$) 2.34 (CH_3, s, 3H), 3.53 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.75 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.09 (CH_2X, d, 2H, J_{PCCH} 7 Hz), 7.04–7.56 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1040, $\nu_{P=O}$ 1215, ν_{OH} 3200 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Br, R′ = 4-FC_6H_4) (method 3):
yield 50%; (Found: C, 40.0; H, 4.1, $C_{10}H_{13}BrFO_4P$ requires: C, 36.7; H, 4.0%), m.p. 139–40°C, δ_H ($CDCl_3$) 3.58 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.77 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.08 (CH_2X, d, 2H, J_{PCCH} 6 Hz), 6.89–7.75 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1210, ν_{OH} 3220 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Br, R′ = 4-ClC_6H_4) (method 3):
yield 50%; (Found; C, 35.1; H, 3.8. $C_{10}H_{13}BrClO_4P$ requires: C, 35.0; H, 3.8%), m.p. 137–40°C, δ_P ($CDCl_3$) + 19.6 ppm, δ_H ($CDCl_3$) 3.58 (CH_3O, d, 3H, J_{POCH} 10 Hz), 3.72 (CH_3O, d, 3H, J_{POCH} 10 Hz), 4.02 (CH_2X, d, 2H, J_{PCCH} 6 Hz), 7.16–7.59 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1040, $\nu_{P=O}$ 1210, ν_{OH} 3200 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Br, R′ = Ph) (method 3):
yield 25%; (Found: C, 42.5; H, 5.2. $C_{12}H_{18}BrO_4P$ requires: C, 42.7; H, 5.4%), m.p. 92–93°C, δ_P ($CDCl_3$) + 18.0 ppm, δ_H ($CDCl_3$) 1.19 (CH_3CH_2, tr, 3H, J_{HCCH} 7 Hz), 1.27 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH}

7 Hz), 4.00 (CH_2O and CH_2X, m, 6H), 7.20–7.50 (Ar, m, 5H), IR (KBr disc) ν_{POC} 1020, 970, $\nu_{P=O}$ 1205, ν_{OH} 3200 cm^{-1}

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Br, R′ = 4-$CH_3C_6H_4$) (method 3):
yield 27%; (Found: C, 44.2; H, 5.5. $C_{13}H_{20}BrO_4P$ requires: C, 44.5; H, 5.7%), m.p. 128–130°C, δ_P ($CDCl_3$) + 18.1 ppm, δ_H ($CDCl_3$) 1.15 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 1.28 ($\underline{CH_3}CH_2$, tr, 3H, J_{HCCH} 7 Hz), 2.34 (CH_3, s, 3H), 4.03 (CH_2O and CH_2X, m, 6H), 7.00–7.54 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1030, 975, $\nu_{P=O}$ 1220 ν_{OH} 3250 cm^{-1}.

α-Hydroxyphosphonate **3** (R = C_2H_5, X = Br, R′ = 4-ClC_6H_4) (method 3):
yield 48%; (Found: C, 38.5; H, 4.6. $C_{12}H_{17}BrClO_4P$ requires: C, 38.8; H, 4.6%), m.p. 132–4°C, δ_P ($CDCl_3$) + 17.5 ppm, δ_H ($CDCl_3$) 1.22 (CH_3CH_2, m, 6H), 4.10(CH_2O and CH_2X, m, 6H), 7.16–7.62 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1030, 980, $\nu_{P=O}$ 1215, ν_{OH} 3200 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = Cl, R′ = 4-$NO_2C_6H_4$) (method 3):
yield 58%; (Found: C, 39.8; H, 4.2; N, 4.5. $C_{10}H_{13}ClNO_6$ requires: C, 38.8, H, 4.2; N, 4.5%), m.p. 148°C, δ_H ($CDCl_3$) 3.62 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.78 (CH_3O, d, 3H, J_{POCH} 11 Hz), 4.15 (CH_2X, m, 2H), 7.58–8.38 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1220, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **3** (R = CH_3, X = H, R′ = 4-$NO_2C_6H_4$) (method 2, from 4-nitro-α-chloroacetophenone):
yield 12%; (Found C, 43.8; H, 5.2; N, 5.0. $C_{10}H_{14}NO_6$ requires: C, 43.6; H, 5.1; N 5.1%), m.p. 164–6°C δ_H ($CDCl_3$), 1.85 (CH_3, d, 3H, J_{PCCH} 16 Hz), 3.72 (CH_3O, d, 3H, J_{POCH} 10 Hz), 3.77 (CH_3O, d, 3H, J_{POCH} 10 Hz), 7.25 (OH, s, 1H), 7.65–8.36 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1030, $\nu_{P=O}$ 1220, ν_{OH} 3240 cm^{-1}.

α-Hydroxyphosphonate **10** (R = CH_3, Ar = Ph) (method 3:)
yield 19%; (Found: C, 42.9; H, 5.1. $C_{10}H_{13}Cl_2O_4P$ requires: C, 44.0; H, 5.2%), m.p. 92–93°C, δ_H ($CDCl_3$) 3.32 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.74 (CH_3O, d, 3H, J_{POCH} 11 Hz), 6.41 (CH, d, 1H, J_{PCCH} 1 Hz), 7.14–7.76 (Ar, m, 5H), m/z 298 (4%, M^+), 110 (100%), IR (KBr disc) ν_{POC} 1030, $\nu_{P=O}$ 1210, ν_{OH} 3770 cm^{-1}.

α-Hydroxyphosphonate **10** (R = CH_3, Ar = 4-MeC_6H_4) (method 3):
yield 11%; (Found: C, 42.7; H, 4.9. $C_{11}H_{15}Cl_2O_4P$ requires: C, 42.2; H, 4.8%), m.p. 109°C, δ_H ($CDCl_3$) 2.33 (CH_3, s, 3H), 3.34 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.73 (CH_3O, d, 3H, J_{POCH} 11 Hz), 6.38 (CH, d, 1H, J_{PCCH} 1 Hz), 7.0–7.6 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1240, ν_{OH} 3285 cm^{-1}.

α-Hydroxyphosphonate **10** (R = CH_3, Ar = 4-ClC_6H_4) (method 3):
yield 29%; (Found: C, 36.3; H 3.7. $C_{10}H_{12}Cl_3O_4P$ requires: C, 36.0; H, 3.6%), m.p. 149–50°C, δ_H ($CDCl_3$) 3.39 (CH_3O, d, 3H, J_{POCH} 11 Hz), 3.72 (CH_3O, d, 3H, J_{POCH} 11 Hz), 6.33 (CH, d, 1H, J_{PCCH} 1 Hz), 7.13–7.68 (Ar, m, 4H), IR (KBr disc) ν_{POC} 1020, $\nu_{P=O}$ 1240, ν_{OH} 3280 cm^{-1}.

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12. Results are quoted for 15–20:1 mole ratios of phosphite to α-halogenoacetophenone (see Experimental) and demonstrate trends in product composition for various changes in reaction parameters. $(RO)_2PHO$ and $(RO)_2P(O)Me$ are also formed as by-products. It should be noted that the absolute values of the yields obtained are influenced by the reactant ratios, higher percentages of α-hydroxyphosphonate being formed with more nearly equivalent quantities of reactants (see e.g. preparations by methods 1 or 2 in the experimental section).
13. Ketophosphonates have previously been reported as minor products in the reactions of certain α-bromo-ketones with phosphite esters in alcoholic media (cf. refs. 4, 6, 8). Such products were not detectable under the conditions of our experiments, which were carried out at lower temperatures. It is likely that protonation of carbonyl oxygen (or at least coordination to the alcoholic proton) will be favoured under these conditions and that phosphite addition to the carbonyl group, leading to hydroxyphosphonate or vinyl phosphate formation, will be preferred.
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