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Phosphonic Systems. Part 12. Fragmentation-Rearrangement of Dialkyl 2-Acyloxyalkylphosphonates*

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ABSTRACT

Dialkyl esters of 2-acyloxyalkylphosphonic acids, $RCH(OAc)CH_2PO_3R'_2$, undergo thermolytic fragmentation to an alkene $RCH{=}CH_2$, a new ester AcOR', and an alkyl metaphosphate $R'OPO_2$. The reaction represents a new type of a process in which a metaphosphate species is generated from a neutral precursor and involves alkyl group (R') migration as a prerequisite for the reaction. Mechanistic studies indicate that the reaction involves interaction between the phosphoryl group and the electrophilic center of the Ac group, followed by the intramolecular dealkylation of the P–O–R' function and the subsequent fragmentation of the intermediate.

INTRODUCTION

The role of the monomeric metaphosphate ion, PO_3^-, as a key intermediate in numerous reactions of organophosphorus compounds is well established, and the earlier work in that field is a subject of a classical review by Westheimer [1]. It has also been demonstrated, first in the pyrolysis experiment by Clapp and Westheimer [2], that several phosphorus containing organic systems can serve as precursors for the *neutral* metaphosphate derivatives, $X–PO_2$. The most notable examples are the 2,3-oxaphosphabicyclo[2.2.2]octene system studied by Quin [3] and the monoalkyl esters of α-hydroxyiminophosphonic acids, whose fragmentation and phosphorylating properties were investigated in detail by Breuer and co-workers [4]. The same two groups of researchers introduced an ingenious method of trapping the intermediate metaphosphate species via the phosphorylation of the surface OH groups in silica gel [5]. Our own work showed that metaphosphate esters, $RO–PO_2$, can be extruded under mild conditions from 2-arylethylphosphorochloridates [6] or mixed amidophosphoric-carboxylic anhydrides [7]. In all the examples listed, the molecule of a precursor can be considered as a system in which the metaphosphate $X–PO_2$ has been "inserted" into a more complex molecular framework and can be "released" from that framework through the bond-breaking and bond-making fragmentation processes. In this work, we give full details of our recent report [8] on the reaction of the 2-acyloxyalkylphosphonic system, in which extrusion of a metaphosphate has to be accompanied by an intramolecular alkyl group migration.

RESULTS AND DISCUSSION

While investigating the applicability of the trifluoroacetoxy group as a potential leaving group in the Conant-Maynard-Swan reaction [9], we have found that the precursor for the free phosphonic acid, diethyl 2-trifluoroacetoxy-3-phenylpropylphosphonate (**1a**), decomposes upon distillation, yielding allylbenzene and ethyl trifluoroacetate. The reaction was found to be general for other dialkyl 2-acyloxyalkylphosphonic esters (**1**) which decom-

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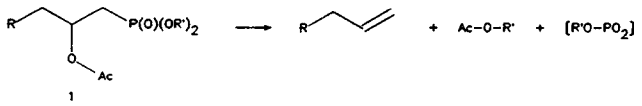
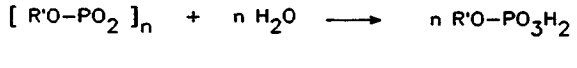


SCHEME 1

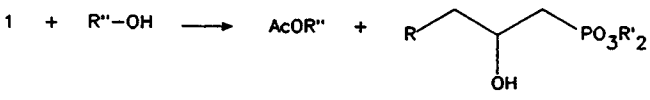
posed quantitatively when heated in polar, aprotic solvents according to Scheme 1.

Alkene and ester products of the reaction were identified and quantitatively determined by the combination of ^1H NMR spectroscopy, mass spectrometry, and gas chromatography using authentic samples of those products as standards. Metaphosphate esters were determined indirectly after the work up of the reaction products. When the crude reaction mixture was divided between an organic and an aqueous phase, the latter contained the corresponding mono-alkylphosphoric acid, $R'O-PO_3H_2$, formed by the hydrolysis of polymerized alkyl metaphosphate (Scheme 2) [10]. Alkylphosphoric acids were identified in solutions by ^{31}P NMR spectroscopy by adding samples of the independently prepared [11] compounds. Attempts to trap the monomeric metaphosphate esters as dialkyl phosphates by carrying out the reaction in the presence of alcohols (2-propanol, *t*-butyl alcohol) failed, since under those conditions, substrates **1** underwent transesterification rather than the usual fragmentation reaction (Scheme 3).

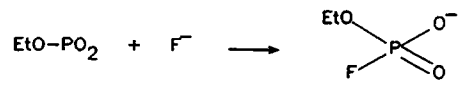
We have succeeded, however, in the direct trapping of the metaphosphate species by carrying out the fragmentation of **1a** in sulfolane containing lithium fluoride. After dilution of the reaction product with $CDCl_3$, NMR (^1H, ^{19}F, ^{31}P) spectroscopy revealed the formation of the ethyl phosphorofluoridate ion (Scheme 4), confirmed by the addition of the authentic N-methylanilinium ethyl phosphoro-fluoridate salt. We have demonstrated, therefore, that the F ion can be used for trapping



SCHEME 2



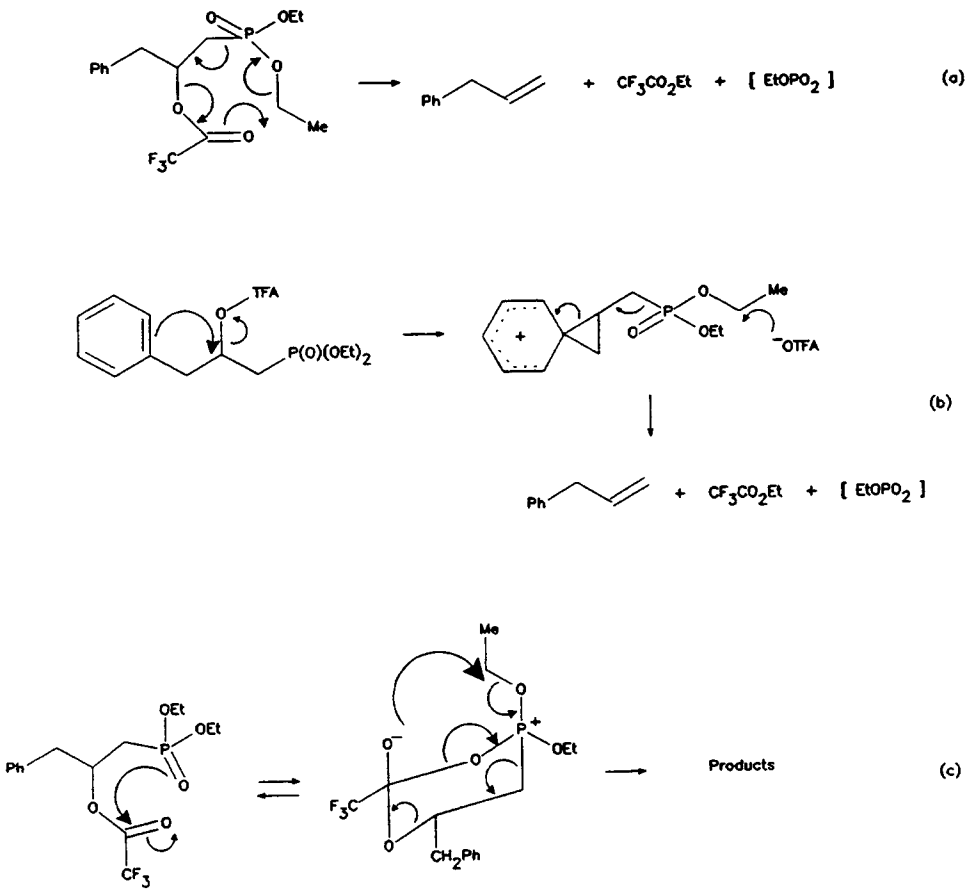
SCHEME 3



SCHEME 4

metaphosphate species, the driving force for the reaction in Scheme 4 being obviously the formation of an exceptionally strong P–F bond [12,13].

From a mechanistic point of view, the fragmentation reaction involves not only the fission of the C_α–P and the C_β–X bonds (as in the Conant-Maynard-Swan reaction) but also the migration of an alkyl group R′ from the phosphonate oxygen to the oxygen of the Ac function, in order to produce a new ester and to accommodate the bonding requirements of the metaphosphate derivative. Three major mechanistic schemes can be proposed to explain the reaction. In the first, the cleavage of one C–P and two C–O bonds, together with the formation of the carbonyl, metaphosphate, and olefinic functions, takes place in a concerted fashion, via an eight-membered, cyclic transition state. In the second, a two-step mechanism, a carbocation is formed via the initial C–OAc bond cleavage (with possible anchimeric assistance by an aromatic ring for R = Ar), followed by the dealkylation of the phosphonate group by the AcO^- ion, facilitated by the C–P bond cleavage and the release of the olefinic and metaphosphate products. Finally, the third mechanism involves the initial cyclization via the donor-acceptor interactions of the phosphoryl group with the electrophilic center of the Ac function, followed by the oxygen → oxygen alkyl transfer and a sequence of bond-breaking and bond-making processes yielding the final products. These three mechanistic patterns are shown (using substrate **1a** as an example) in Scheme 5 as equations (a), (b), and (c), respectively. In order to arrive at a reasonable mechanistic conclusion, the effect of the structural changes in substrates **1** and of the reaction conditions on the rate of the fragmentation was next studied. The reaction progress was followed by monitoring the disappearance of **1** by gas chromatography; in all cases, the reaction was first order with respect to **1** with *r* values in the range of 0.991–0.998. Table 1 gives the effect of the structural variations on the rate, with compound **1a** selected as a standard of reference. The mechanism involving the anchimerically assisted fission of the C–OAc bond (Scheme 5(b)) can be rejected after inspecting the effect of the position of the aromatic substituent (**1a** vs. **1c**) or of the electron-donating properties of the aromatic group (**1a** vs. **1b**) on the reaction rate. All three substrates showed very similar reactivity, while mechanism (b) (Scheme 5) requires **1c** to be much less and **1b** much more reactive than **1a** [14]. Relative reactivities of **1a**, **1b**, and **1c** clearly indicate that no significant carbocationic character is developed on the C(2) atom in the course of the reaction. In addition, for the reactions carried out in the presence of an alcohol (attempted trapping of a metaphosphate), a carbocationic intermediate should lead to the formation of an ether; transesterification of the substrate was observed instead.



SCHEME 5

TABLE 1 Structural Effects on the Rate of the Fragmentation of Phosphonic Derivatives in Sulfolane, 195°C

1	R′	Ac	R	10^4 k_{obs} (s^{-1})	k_{rel}
a	Et	$C(O)CF_3$	Ph	3.4	1.0
b	Et	$C(O)CF_3$	p-$MeOC_6H_4$	4.7	1.4
c	Et	$C(O)CF_3$	$PhCH_2$	4.0	1.2
d	Me	$C(O)CF_3$	Ph	10.0	2.9
e	Et	C(O)Me	Ph	≤0.7[a]	≤0.2
f	Et	SO_2Me	Ph	200[b]	59[b]
g	phosphonic amide: $P(O)(NEt_2)_2$	$C(O)CF_3$	Ph	—[c]	—[c]

[a]Upper limit; some other decomposition reactions contributed to the disappearance of **1e**.
[b]Approximate value.
[c]No reaction observed.

Electrophilicity of the phosphonate ester group has, on the other hand, a bearing on the reaction rate. The methyl ester (**1d**) is about three times more reactive than the diethyl substrate (**1a**); it is known [15] that, in the nucleophilic dealkylation of phosphate esters, the methyl derivatives show superior reactivity over other alkyl analogues. As expected, changing the phosphonic diester group $P(O)(OR')_2$ for the tetraalkyldiamide function (substrate **1g**) resulted in the loss of the observed reactivity due to the negligible electrophilicity of the alkyl groups in the amide function.

The rate of the reaction was found to depend most strongly on the nature of the 2-acyloxy group OAc. In a series of 2-acetyloxy- (**1e**), 2-trifluoroacetyloxy- (**1a**), and 2-methylsulfonyloxy- (**1f**) substituted phosphonates, the relative rate increased in the order <0.2, 1.0, and ≈60, respectively. In fact,

1e was found to react too slowly and **1f** too fast for the determination of the respective rate constants to be achieved with greater than approximate accuracy using our kinetic methodology. In the reaction of ring-substituted benzoyl chlorides with aniline, the electron-withdrawing substituents show a moderate rate-enhancing effect (ρ = 1.18 [16]); in the cases of substrates **1**, the changes in the structure of the entire acyl group should have a much more pronounced effect. Mechanism (b) (Scheme 5) implies that the presence of external nucleophiles should accelerate the second step of the reaction. Fragmentation carried out in the presence of NaI (possible nucleophilic deethylation by I^-) resulted in only slight ($k_{rel} \approx 2$) increase of the rate.

The results presented here led us to favor the mechanism in which a cyclization to a dipolar intermediate is a prerequisite for the fragmentation-rearrangement (Scheme 5c). In contrast to the concerted mechanism (a), such a two-step mechanism involving a dipolar intermediate should be affected by the polarity of the reaction medium. In agreement with that, the rate of the reaction of **1a** in diglyme was found to be only about half of that in sulfolane, while we were not able to observe any significant reaction in refluxing 1,1,2,2-tetrachloroethane, the respective solvent polarity parameters, E_T decreasing in the order 44.0, 38.6, and 31.9 [17]. The formation of a cyclic intermediate postulated in mechanism (c) should be reflected by a negative entropy of activation, typical for reactions involving loss of internal rotational degrees of freedom in the substrate's molecule [18]. We have measured the rate of reaction of **1a** in sulfolane at three temperatures (178°C, 195°C, and 212°C) and obtained the value of $\Delta S^{\neq} = -103$ J mol^{-1} K^{-1}. Pyrolytic elimination of sulfoxides involving a cyclic, six-membered arrangement of the reactive skeleton was reported to yield the entropy of activation values in the range of -50 to -60 J mol^{-1} K^{-1} [19]. A cyclic intermediate formed according to our proposed mechanism (Scheme 5c) can undergo further fragmentation in a concerted, or stepwise, fashion. Further experiments aimed at the more detailed elucidation of the reaction mechanism are in progress.

EXPERIMENTAL

Solvents and commercially available reagents were purified and dried by conventional methods immediately before use. Reactions involving organometallic reagents were carried out under an atmosphere of dry nitrogen. Bulb to bulb distillations were carried out using a Buchi GKR-50 apparatus. For column chromatography, Merck-Kieselgel 60 (0.063–0.200 mm) was used as a stationary phase. NMR spectra were recorded on a Bruker AC300 spectrometer using $CDCl_3$ solutions, and the chemical shifts are reported relative to TMS (^{1}H, ^{13}C) as an internal standard and 85% H_3PO_4 (^{31}P) as an external standard. Mass spectra were recorded on a Varian MAT-212 double focusing direct inlet spectrometer at an ionization potential of 70 eV. IR spectra were recorded on a Bomem-Michelson 100 spectrophotometer as CCl_4 solutions. Only values of selected MS ion peaks and IR bands, most relevant to structural determination, are reported.

Preparation of Substrates and Standards

Diethyl 2-oxo-3-phenylpropylphosphonate was prepared from phenylacetyl chloride and lithiated diethyl methylphosphonate [20]. Oil (89%); n_D^{16} 1.5079. ^{1}H NMR δ 1.28 (t, J = 7.1 Hz, 6H), 3.04 (d, J = 22.7 Hz, 2H), 3.85 (s, 2H), 4.09 (m, 4H), 7.21 (m, 5H); ^{13}C NMR δ 16.1 (d, J = 6.7 Hz), 41.2 (d, J = 128 Hz), 50.6 (s), 62.5 (d, J = 7.0 Hz), 126.8 (s), 128.6 (s), 129.8 (s), 133.3 (s), 199.4 (d, J = 6.1 Hz); ^{31}P NMR δ 20.3; IR ν (cm^{-1}) 1254 (P=O), 1719 (C=O), 2985 (C–H); MS m/z 270 (M$^+$, 97%), 179 (90), 151 (69), 137 (23), 123 (67), 91 (100), 109 (57).

Dimethyl 2-oxo-3-phenylpropylphosphonate was prepared in the same way from dimethyl methylphosphonate and was purified by bulb-to-bulb distillation (oven temperature 203–205°C (0.5 mm)). Oil (53%); n_D^{23} 1.5146. ^{1}H NMR δ 3.09 (d, J = 22.6 Hz, 2H), 3.74 (d, J = 11.3 Hz, 6H), 3.85 (s, 2H), 7.27 (m, 5H); ^{13}C NMR δ 39.8 (d, J = 130 Hz), 40.9 (s), 53.0 (d, J = 6.4 Hz), 127.0 (s), 128.5 (s), 129.4 (s), 133.0 (s), 200.3 (s); ^{31}P NMR δ 23.5; IR ν (cm^{-1}) 1219 (P=O), 1720 (C=O), 2998 (C–H); MS m/z 242 (M$^+$, 63%), 151 (100), 124 (62), 109 (88), 105 (44), 91 (91).

Diethyl 2-oxo-3-(4-methoxyphenyl)propylphosphonate was prepared in the same way using *p*-methoxyphenylacetyl chloride and was purified by bulb-to-bulb distillation (oven temperature 231–233°C (0.45 mm)). Oil (68%); n_D^{16} 1.5029. ^{1}H NMR δ 1.28 (t, J = 7.0 Hz, 6H), 3.03 (d, J = 22.7 Hz, 2H), 3.73 (s, 3H), 3.78 (s, 2H), 4.07 (m, 4H), 6.81 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H); ^{13}C NMR δ 16.2 (d, J = 6.6 Hz), 41.0 (d, J = 128 Hz), 49.8 (s), 55.1 (s), 62.6 (d, J = 7.0 Hz), 114.0 (s), 130.1 (s), 130.5 (s), 158.7 (s), 199.8 (d, J = 6.1 Hz); ^{31}P NMR δ 20.3; IR ν (cm^{-1}) 1250 (P=O), 1718 (C=O), 2956 (C–H); MS m/z 300 (M$^+$, 5%), 121 (100), 152 (37), 135 (71).

Diethyl 2-oxo-4-phenylbutylphosphonate was prepared in the same way from 3-phenylpropionyl chloride. Oil (99%); n_D^{15} 1.5060. ^{1}H NMR δ 1.25 (t, J = 7.0 Hz, 6H), 2.88 (m, 4H), 3.01 (d, J = 22.8 Hz, 2H), 4.05 (m, 4H), 7.16 (m, 5H); ^{13}C NMR δ 16.0 (d, J = 6.4 Hz), 29.2 (s), 42.2 (d, J = 127 Hz), 45.1 (s), 62.3 (d, J = 6.5 Hz), 125.8 (s), 128.1 (s), 128.2 (s), 140.4 (s), 200.8 (d, J = 6.0 Hz); ^{31}P NMR δ 20.4; IR ν (cm^{-1}) 1254 (P=O), 1720 (C=O), 2963 (C–H); MS m/z 284 (M$^+$, 11%), 257 (11), 229 (19), 152 (35), 91 (100).

Dialkyl 2-hydroxyalkylphosphonates were pre-

pared from the corresponding 2-oxoalkylphosphonates according to the following general procedure. To a suspension of sodium borohydride (13 g, 0.33 mol) in ethanol (100 mL) cooled to 0°C, a solution of a ketophosphonate (0.11 mol) in ethanol (30 mL) was added dropwise. The mixture was then stirred at room temperature for 2 hours, poured into dil hydrochloric acid (100 mL), and neutralized with solid sodium bicarbonate. Extraction with chloroform, drying ($MgSO_4$), and evaporation of the solvent yielded the product as a colorless oil.

Diethyl 2-hydroxy-3-phenylpropylphosphonate (80%); n_D^{15} 1.5137. ^{1}H NMR δ 1.25 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.87 (m, 2H), 2.81 (m, 2H), 4.04 (m, 4H), 4.19 (m, 1H), 7.15 (m, 5H); ^{13}C NMR δ 16.3 (d, J = 5.8 Hz), 32.6 (d, J = 139 Hz), 44.4 (d, J = 16.7 Hz), 61.8 (d, J = 7.8 Hz), 67.5 (d, J = 4.1 Hz), 126.5 (s), 128.4 (s), 129.5 (s), 137.6 (s); ^{31}P NMR δ 30.3; IR ν (cm^{-1}) 1240 (P=O), 2928 (C–H), 3363 (O–H); MS m/z 254 (11), 181 (86), 153 (39), 125 (100), 91 (40).

Diethyl 2-hydroxy-3-(4-methoxyphenyl)propylphosphonate (79%); n_D^{16} 1.5072. ^{1}H NMR δ 1.27 (t, J = 7.0 Hz, 6H), 1.89 (m, 2H), 2.75 (m, 2H), 3.75 (s, 3H), 3.99–4.15 (m, 5H), 6.81 (d, J = 8.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H); ^{13}C NMR δ 16.1 (d, J = 5.8 Hz), 32.4 (d, J = 139 Hz), 43.2 (d, J = 16.4 Hz), 54.9 (s), 61.5 (d, J = 4.3 Hz), 67.5 (d, J = 4.8 Hz), 113.6 (s), 129.5 (s), 130.2 (s), 158.1 (s); ^{31}P NMR δ 30.9; IR ν (cm^{-1}) 1236 (P=O), 2951 (C–H), 3384 (O–H); MS m/z 302 (M^+, 2%), 284 (40), 181 (21), 147 (63), 125 (47), 121 (100).

Diethyl 2-hydroxy-4-phenylbutylphosphonate (78%); n_D^{15} 1.5069. ^{1}H NMR δ 1.30 (t, J = 7.1 Hz, 6H), 1.85 (m, 4H), 2.70 (m, 2H), 3.63 (br s, 1H), 4.07 (m, 5H), 7.21 (m, 5H); ^{13}C NMR δ 16.4 (d, J = 6.7 Hz), 31.7 (s), 33.6 (d, J = 138 Hz), 39.7 (d, J = 17.1 Hz), 61.9 (d, J = 8.0 Hz), 65.8 (d, J = 6.3 Hz), 125.8 (s), 128.3 (s), 128.4 (s), 141.7 (s); ^{31}P NMR δ 30.9; IR ν (cm^{-1}) 1230 (P=O), 2948 (C–H), 3357 (O–H); MS m/z 268 (34), 181 (30), 125 (52), 117 (81), 104 (81), 91 (100).

Dimethyl 2-hydroxy-3-phenylpropylphosphonate (76%); n_D^{23} 1.5009. ^{1}H NMR δ 1.91 (m, 2H), 2.72 (d, J = 6.8 Hz, 2H), 3.68 (d, J = 11.0 Hz, 6H), 4.20 (m, 1H), 7.25 (m, 5H); ^{13}C NMR δ 31.7 (d, J = 139 Hz), 32.0 (s), 44.4 (d, J = 16.1 Hz), 52.2 (d, J = 6.3 Hz), 67.3 (d, J = 4.7 Hz), 126.4 (s), 128.3 (s), 129.3 (s), 137.5 (s); ^{31}P NMR δ 33.4; IR ν (cm^{-1}) 1227 (P=O), 2949 (C–H), 3381 (O–H); MS m/z 226 (100), 153 (94), 117 (79), 91 (78).

N,N,N',N'-tetraethyl 2-hydroxy-3-phenylpropylphosphonodiamidate was prepared from (2,3-epoxypropyl)benzene and the anion of *N,N,N',N'*-tetraethyl-hydrogenphosphonate. A solution of $(Et_2N)_2P(O)H$ (4.0 g, 21 mmol) in THF (10 mL) was cooled to −94°C, and BuLi (1.5 M solution in hexane, 21 mmol) was added dropwise with stirring. Stirring was continued for 20 minutes, (2,3-epoxypropyl)benzene (prepared from allylbenzene and MCPBA, 2.5 g, 19 mmol) was added, and the mixture was allowed to warm to room temperature over the period of 2 hours. Sat. aq NH_4Cl (20 mL) was added, the mixture was extracted with ether (3 × 20 mL), and the ether solution was dried ($MgSO_4$) and evaporated. The product was obtained as a pale yellow oil (4.8 g, 79%); n_D^{25} 1.5072. ^{1}H NMR δ 0.78 (t, J = 7.1 Hz, 6H), 0.94 (t, J = 7.1 Hz, 6H), 1.68 (ddd, J = 14.9, 12.9, 2.0 Hz, 1H), 1.78 (ddd, J = 14.8, 12.0, 10.0 Hz, 1H), 2.48–2.97 (m, 10H), 3.99 (m, 1H), 5.31 (br s, 1H), 7.12 (m, 5H); ^{13}C NMR δ 13.5 (s), 13.9 (s), 31.5 (d, J = 114 Hz), 38.1 (d, J = 4.6 Hz), 44.2 (d, J = 17.1 Hz), 67.7 (d, J = 3.7 Hz), 126.0 (s), 127.9 (s), 129.0 (s), 137.6 (s); ^{31}P NMR δ 38.3; IR ν (cm^{-1}) 1208 (P=O), 2927 (C–H), 3364 (O–H); MS m/z 326 (M^+, 4%), 254 (20), 235 (49), 191 (100), 120 (14), 91 (13), 72 (23).

2-Trifluoroacetoxyalkylphosphonates **1a**, **1b**, **1c**, **1d**, **1g** were prepared from the corresponding alcohols and trifluoroacetic anhydride [21]. Trifluoroacetic anhydride (1.6 mL, 12 mmol) was added with stirring to a solution of the alcohol (7.3 mmol) in THF (10 mL), and the mixture was stirred at room temperature for 15 minutes. Volatile components were evaporated under reduced pressure, and the crude products were purified by bulb-to-bulb distillation.

Diethyl 2-trifluoroacetoxy-3-phenylpropylphosphonate (**1a**) (84%), oven temp 160–170°C (0.08 mm); n_D^{15} 1.4425. ^{1}H NMR δ 1.25 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 2.11 (ddd, J = 19.1, 15.6, 5.6 Hz, 1H), 2.19 (ddd, J = 18.2, 15.6, 7.1 Hz, 1H), 3.02 (m, 2H), 4.06 (m, 4H), 5.46 (m, 1H), 7.16 (m, 5H); ^{13}C NMR δ 16.0 (s), 29.8 (d, J = 143 Hz), 40.8 (d, J = 10.7 Hz), 62.2 (d, J = 7.8 Hz), 74.0 (d, J = 3.2 Hz), 114.9 (q, J = 299 Hz), 127.2 (s), 128.6 (s), 129.3 (s), 134.9 (s), 158.7 (q, J = 40.5 Hz); ^{31}P NMR δ 25.6; IR ν (cm^{-1}) 1228 (P=O), 1773 (C=O), 2985 (C–H); MS m/z 254 (56), 117 (56), 91 (33), 69 (97), 45 (100). Anal. calcd for $C_{15}H_{20}F_3O_5P$: C, 48.9; H, 5.5. Found: C, 49.1; H, 5.4.

Diethyl 2-trifluoroacetoxy-3-(p-methoxyphenyl)-propylphosphonate (**1b**) (88%), oven temperature 234–235°C (0.6 mm); n_D^{16} 1.4643. ^{1}H NMR δ 1.27 (t, J = 7.0 Hz, 6H), 2.07 (m, 2H), 2.98 (m, 2H), 3.76 (s, 3H), 4.07 (m, 4H), 5.45 (m, 1H), 6.81 (d, J = 8.6 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H); ^{13}C NMR δ 16.0 (s), 29.7 (d, J = 142 Hz), 39.9 (d, J = 10.7 Hz), 54.9 (s), 61.9 (d, J = 6.7 Hz), 74.2 (d, J = 3.0 Hz), 113.9 (s), 126.8 (s), 130.4 (s), 158.7 (s), 114.3 (q, J = 286 Hz), 156.2 (q, J = 42.3 Hz); ^{31}P NMR δ 25.6; IR ν (cm^{-1}) 1236 (P=O), 1785 (C=O), 2985 (C–H); MS m/z 284 (68), 147 (100), 121 (45). Anal. calcd for $C_{16}H_{22}F_3O_6P$: C, 48.2; H, 5.6. Found: C, 48.7; H, 5.4.

Diethyl 2-trifluoroacetoxy-4-phenylbutylphosphonate (**1c**) (56%), oven temperature 207–209°C (0.2 mm); n_D^{15} 1.4608. ^{1}H NMR δ 1.27 (t, J = 7.0 Hz, 6H), 2.13 (m, 4H), 2.65 (m, 2H), 4.08 (m, 4H), 5.32 (m, 1H), 7.20 (m, 5H); ^{13}C NMR δ 15.4 (d, J = 5.4 Hz), 29.9 (d, J = 142 Hz), 30.4 (s), 35.6 (d, J = 8.8

Hz), 61.6 (d, J = 6.9 Hz), 73.0 (s), 114.0 (q, J = 286 Hz), 125.7 (s), 127.7 (s), 128.0 (s), 139.5 (s), 156.0 (q, J = 42.2 Hz); ^{31}P NMR δ 25.1; IR ν (cm^{-1}) 1208 (P=O), 1776 (C=O), 2958 (C–H); MS m/z 268 (40), 91 (100). Anal. calcd for $C_{16}H_{22}F_3O_5P$: C, 50.3; H, 5.8. Found: C, 50.0; H, 5.6.

Dimethyl 2-trifluoroacetoxy-3-phenylpropylphosphonate (**1d**) (57%), oven temperature 192–194°C (0.4 mm); n_D^{24} 1.4534. ^{1}H NMR δ 2.15 (m, 2H), 3.05 (m, 2H), 3.71 (d, J = 9.0 Hz, 6H), 5.49 (m, 1H), 7.27 (m, 5H); ^{13}C NMR δ 28.8 (d, J = 152 Hz), 40.7 (d, J = 11.2 Hz), 52.4 (d, J = 6.7 Hz), 73.8 (d, J = 3.5 Hz), 114.2 (q, J = 286 Hz), 127.2 (s), 128.5 (s), 129.3 (s), 134.8 (s), 156.1 (q, J = 42.3 Hz); ^{31}P NMR δ 28.1; IR ν (cm^{-1}) 1226 (P=O), 1785 (C=O), 2955 (C–H); MS m/z 226 (71), 117 (72), 91 (65), 69 (100), 45 (99). Anal calcd for $C_{13}H_{16}F_3O_5P$: C, 45.9; H, 4.7. Found: C, 45.6; H, 4.5.

N,N,N',N'-Tetraethyl 2-trifluoroacetoxy-3-phenylpropylphosphonodiamidate (**1g**) (100%), not distilled; n_D^{24} 1.4270. ^{1}H NMR δ 1.02 (t, J = 7.1 Hz, 6H), 1.09 (t, J = 7.1 Hz, 6H), 2.35 (m, 2H), 2.88–3.22 (m, 10H), 5.50 (m, 1H), 7.32 (m, 5H); ^{13}C NMR δ 13.7 (s), 29.4 (d, J = 118 Hz), 38.7 (d, J = 3.9 Hz), 41.1 (d, J = 8.8 Hz), 74.8 (s), 114.4 (q, J = 286 Hz), 127.5 (s), 128.6 (s), 129.5 (s), 135.3 (s), 159.5 (q, J = 39.8 Hz); ^{31}P NMR δ 34.2; IR ν (cm^{-1}) 1183 (P=O), 1783 (C=O), 2942 (C–H); MS m/z 308 (1), 191 (10), 117 (100), 91 (33), 72 (29). Anal. calcd for $C_{19}H_{30}F_3N_2O_3P$: C, 54.0; H, 7.2; N, 6.6. Found: C, 53.6; H, 7.0; N, 6.5.

Diethyl 2-acetoxy-3-phenylpropylphosphonate (**1e**) was prepared from the corresponding alcohol by acetylation with acetic anhydride (30-fold molar excess, 2 hours of reflux). After extraction with chloroform, drying, and evaporation, crude product was purified by bulb-to-bulb distillation (40%), oven temperature 232–234°C (0.4 mm); n_D^{15} 1.4922. ^{1}H NMR δ 1.26 (t, J = 7.0 Hz, 6H), 2.00 (m, 2H), 1.97 (s, 3H), 2.96 (d, J = 6.0 Hz, 2H), 4.05 (m, 4H), 5.29 (m, 1H), 7.28 (m, 5H); ^{13}C NMR δ 16.3 (d, J = 6.9 Hz), 21.0 (s), 30.0 (d, J = 141 Hz), 40.9 (d, J = 9.6 Hz), 61.7 (d, J = 6.5 Hz), 69.6 (s), 126.7 (s), 128.4 (s), 129.5 (s), 136.6 (s), 169.9 (s); ^{31}P NMR δ 27.2; IR ν (cm^{-1}) 1241 (P=O), 1738 (C=O), 2962 (C–H); MS m/z 254 (88), 117 (84), 91 (60), 43 (100). Anal. calcd for $C_{15}H_{23}O_5P$: C, 57.3; H, 7.4. Found: C, 57.0; H, 7.4.

Diethyl 2-methylsulfonyloxy-3-phenylpropylphosphonate (**1f**) was prepared from the corresponding alcohol by sulfonylation with methanesulfonyl chloride in pyridine at 0°C. After adding cold, dilute aq HCl and extraction with ether, **1f** was obtained as a pale yellow oil (83%). The product was not further purified because of its thermal instability; the ^{31}P NMR spectrum showed, however, that only one phosphorus containing compound was present in the product. n_D^{25} 1.4952; ^{1}H NMR δ 1.26 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H), 2.23 (m, 2H), 2.51 (s, 3H), 3.08 (m, 2H), 4.03 (m, 4H), 4.93 (m, 1H), 7.18 (m, 5H); ^{13}C NMR δ 16.0 (d, J = 5.9 Hz), 31.3 (d, J = 139 Hz), 37.3 (s), 41.4 (d, J = 6.2 Hz), 62.0 (s), 62.1 (s), 79.0 (s), 127.0 (s), 128.5 (s), 129.6 (s), 135.8 (s); ^{31}P NMR δ 25.5; IR ν (cm^{-1}) 1208 (P=O), 2985 (C–H); MS m/z 255 (100), 117 (22), 91 (36), 79 (46). Anal. calcd for $C_{14}H_{23}O_6SP$: C, 48.0; H, 6.6. Found: C, 47.3; H, 6.3.

Allylbenzene was prepared from phenylmagnesium bromide and allyl bromide in THF. 84%; bp 152–157°C; n_D^{16} 1.5183 (Ref. [22] n_D^{15} 1.5145); ^{1}H NMR δ 3.42 (d, J = 6.7 Hz, 2H), 5.12 (m, 2H), 6.00 (m, 1H), 7.30 (m, 5H).

4-Methoxyallylbenzene was prepared in the same way from 4-bromoanisole; 74%; bp 198–201°C; n_D^{16} 1.5268 (Ref. [23] n_D^{18} 1.5230); ^{1}H NMR δ 3.38 (d, J = 6.7 Hz, 2H), 3.82 (s, 3H), 5.11 (m, 2H), 6.00 (m, 1H), 6.90 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H).

4-Phenyl-1-butene was prepared in the same way from benzyl chloride; 73%; bp 91–93°C (15 mm); n_D^{22} 1.5098; ^{1}H NMR δ 2.44 (m, 2H), 2.78 (t, J = 7.8 Hz, 2H), 5.07 (m, 2H), 5.92 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 7.30 (m, 5H).

Ethyl and methyl trifluoroacetate were prepared by acylation of an alcohol with trifluoroacetic anhydride in the presence of pyridine; ethyl ester (62%), bp 58–59°C; ^{1}H NMR δ 1.33 (t, J = 7.2 Hz, 3H), 4.35 (q, J = 7.2 Hz, 2H). Methyl ester (65%), bp 39–40°C; ^{1}H NMR δ 3.91 (s).

Ethyl methanesulfonate was prepared from ethanol and mesyl chloride in the presence of pyridine (70%), n_D^{24} 1.4170 (Ref. [24] n_D^{15} 1.4194); ^{1}H NMR δ 1.28 (t, J = 7.0 Hz, 3H), 2.88 (s, 3H), 4.16 (q, J = 7.0 Hz, 2H).

N-Methylanilinium ethylphosphorofluoridate was prepared according to the literature procedure [25]; white powder; ^{1}H NMR δ 1.24 (t, J = 7.0 Hz, 3H), 2.89 (s, 3H), 4.01 (m, 2H), 7.37 (m, 5H); ^{31}P NMR δ −6.3 (d, J_{PF} = 932 Hz); ^{19}F NMR δ (*rel* to $CFCl_3$) −83.6 (d, J_{FP} 931 Hz).

Product Identification. A solution of **1** in a chosen solvent (usually sulfolane) was heated in a sealed tube for a required period of time. Part of the solution was diluted with $CDCl_3$, D_2O was added, and after shaking, both organic and aqueous solutions were examined by NMR spectroscopy. Individual products were identified by addition of the authentic samples to the solutions. Products contained in the organic phase were, after evaporation of the solvent, additionally identified by mass spectrometry. Another part of the reaction mixture was injected into a Carlo Erba Fractovap 2150 gas chromatograph attached to a Spectra-Physics SP42 90 integrator. Nitrogen (1 kg cm^{-2}) was used as a carrier gas, oven temperature being varied from sample to sample, and the following two columns were used. Column A: 2 m with 3 mm inner diameter, packed with 90–100 mesh Chromosorb WHP-SP using 5% by weight of SE-30 (GCG) as

TABLE 2 Retention Times of the Components of the Reaction Mixtures for the Fragmentation of Substrates **1**

Column	Column Temperature (°C)	Compound	R_T (min)
A	180	**1a**	9.29–9.32
		allylbenzene	1.03
		sulfolane	1.60–1.61
		CF_3CO_2Et	0.73–0.75
	193	**1d**	6.39–6.44
		allylbenzene	0.83–0.84
		sulfolane	1.39
		CF_3CO_2Me	0.59–0.63
	196	**1f**	8.68–8.77
		allylbenzene	0.83–0.85
		sulfolane	1.29–1.30
		$MeSO_3Et$	0.61–0.62
B	190	**1a**	4.81–4.84
		allylbenzene	0.67–0.69
		sulfolane	1.50–1.52
		CF_3CO_2Et	0.42
		diglyme	0.53–0.55
	220	**1b**	5.07–5.16
		allylanisole	0.63–0.67
		sulfolane	0.96–0.98
		CF_3CO_2Et	0.43
	210	**1c**	4.11–4.17
		4-phenylbutene	0.54–0.55
		sulfolane	1.08
		CF_3CO_2Et	0.43–0.45
	210	**1e**	6.90–7.05
		allylbenzene	0.51–0.52
		sulfolane	1.08
		$MeCO_2Et$	0.43–0.44

liquid phase; Column B: 1.9 m with 3 mm inner diameter, packed with 80–100 mesh WHP-SP using 3% by weight of OV-17 as liquid phase. Retention times of substrates and products are given in Table 2. Nonphosphorus products were identified by addition of authentic samples to the mixture.

Identification of Ethyl Phosphate Formed after the Work up of a Product of the Fragmentation. **1a** (0.76 g) was dissolved in sulfolane (0.5 mL), and the solution was heated at 210°C for 23 hours. After cooling, a 40% solution of NaOD in D_2O (1 mL) was added and the mixture was stirred for 10 minutes. $CDCl_3$ (1 mL) was added, and, after shaking, the D_2O layer was separated and examined by NMR (^1H and ^{31}P) spectroscopy. ^1H NMR δ 1.15 (t, J = 7.1 Hz, 3H), 3.81 (q, J = 7.1 Hz, 2H); ^{31}P NMR δ 1.24. Authentic anilinium ethylphosphate [11] was then added, and the NMR spectra were recorded again. No new signal appeared in the ^{31}P spectrum, and in the ^1H spectrum, only the signals of the anilinium ion were observed in addition to the signals derived from the ethyl group.

Trapping of ethyl metaphosphate by fluoride ion. A mixture of **1a** (0.14 g, 0.38 mmol), LiF (0.01 g, 0.4 mmol), and sulfolane (0.1 mL) was heated at 220°C for 5 hours. After cooling, $CDCl_3$ (1 mL) was added and the solution was divided into two parts. Authentic N-methyl anilinium ethylphosphorofluoridate (0.042 g, 0.19 mmol) was added to one of the solutions, and both solutions were examined by NMR spectroscopy. Both spectra were practically identical, and no new signals were observed, except for the signals of the N-methyl anilinium ion present in the spectrum of the sample containing the standard. ^{31}P NMR δ −6.8 (d, J = 935 Hz); ^{19}F NMR δ −83.8 (d, J = 931 Hz).

Rate Measurements. A concentrated solution of **1** in a given solvent was placed in micro test tubes (typically 12 tubes per run); the tubes were sealed and immersed in a thermostatted oil bath. Individual tubes were removed at time intervals, cooled in ice water, and opened, and the content was analyzed by GC. Reaction progress was measured by monitoring the decrease of the substrate peak relative to the solvent peak, and the values of k_{obs} were obtained from the plots of ln (X_0/X_t) vs. time, where X_0 is the initial ratio of the area of the peak of the substrate and the peak of the solvent and X_t is the same ratio for a sample removed from an oil bath after time t. Good first-order kinetic plots were obtained with $r > 0.99$. Each kinetic run was carried out in duplicate, and the content of each tube was injected to the chromatograph three times so the average value of the peak ratio was used.

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REFERENCES AND NOTES

[1] F. H. Westheimer, *Chem. Rev., 81*, 1981, 313.
[2] C. H. Clapp, F. H. Westheimer, *J. Am. Chem. Soc., 96*, 1974, 6710.
[3] R. Bodalski, L. D. Quin, *J. Org. Chem., 56*, 1991, 2666 and the references cited therein.
[4] J. Katzhendler, R. Karaman, D. Gibson, E. Breuer, *J. Chem. Soc. Perkin Trans., 2*, 1989, 589.
[5] L. D. Quin, X-P Wu, E. Breuer, M. Mahajna, *Tetrahedron Lett., 31*, 1990, 6281.
[6] S. Cocks, T. A. Modro, *Tetrahedron Lett., 26*, 1985, 945.
[7] J. Symes, T. A. Modro, *Can. J. Chem., 64*, 1986, 1702.
[8] C. P. de Jongh, T. A. Modro, *J. Chem. Soc., Chem. Commun.*, 1992, 1003.
[9] J. B. Conant, E. L. Jackson, *J. Am. Chem. Soc., 46*, 1924, 1003 and the preceeding articles of this series; J. A. Maynard, J. M. Swan, *Aust. J. Chem., 16*, 1963, 596.
[10] Direct determination of the polymer was difficult because of the solubility problems.

[11] A. M. Modro, T. A. Modro, *Org. Prep. Proc. Int., 24,* 1992, 57.
[12] D. E. C. Corbridge: *Phosphorus. An Outline of its Chemistry, Biochemistry and Technology,* 4th Ed., Elsevier, Amsterdam, p. 44 (1990).
[13] As the Referee pointed out, F^- ion could also add to the phosphonium intermediate (Scheme 5c). We have found, however, that fluoride ions do not change the rate of the fragmentation.
[14] In the fragmentation which does involve anchimeric assistance, we have found the *p*-methoxyphenyl substituted substrate to be at least 50 times more reactive than the phenyl derivative [6].
[15] M. D. Gray, D. J. Smith, *Tetrahedron Lett., 21,* 1980, 859.
[16] H. Maskill: *The Physical Basis of Organic Chemistry,* Oxford University Press, Oxford, p. 451 (1985).
[17] C. Reichardt: *Solvent Effects in Organic Chemistry,* Verlag Chemie, Weinheim, p. 270 (1979).
[18] B. K. Carpenter: *Determination of Organic Reaction Mechanisms,* Wiley-Interscience, New York, ch. 7.2 (1984).
[19] D. W. Emerson, A. P. Craig, I. W. Potts, *J. Org. Chem., 32,* 1967, 102.
[20] F. Mathey, P. Savignac, *Tetrahedron, 34,* 1978, 649.
[21] A. M. M. M. Phillips, M. J. Mphahlele, A. M. Modro, T. A. Modro, A. Zwierzak, *Phosphorus, Sulfur, and Silicon, 71,* 1992, 165.
[22] G. Berti, *J. Chem. Soc.,* 1954, 1213.
[23] *The Merck Index,* 11th ed., Merck & Co., Rahway, p. 3657 (1989).
[24] W. C. J. Ross, W. Davis, *J. Chem. Soc.,* 1957, 2420.
[25] C. Stolzer, A. Simon, *Chem. Ber., 93,* 1960, 1323.