Thermal Fragmentation of Trihaloethyl and Hexafluoro-2-propyl (α-Hydroxyiminobenzyl)phosphonates. Solvent Effects and the Trapping of Metaphosphate

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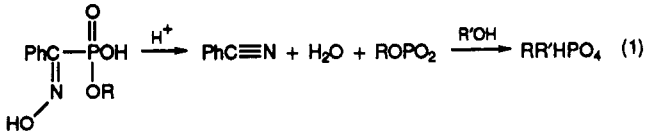
Received June 29, 1993•

Reactions of 2,2,2-trihaloethyl or 1,1,1,3,3,3-hexafluoro-2-propyl benzoylphosphonate anions **7** or **10** with hydroxylamine gave the corresponding (α-hydroxyiminobenzyl)phosphonates, **3** or **11**, respectively, as predominantly (*E*)-isomers. Refluxing (*E*)-**3a** or (*E*)-**3b** in EtOH or 2-PrOH caused them to fragment to benzonitrile and mixed phosphodiesters: ethyl trihaloethyl phosphate (**12**) or 2-propyl trihaloethyl phosphate (**13**), respectively. (*E*)-**3a** did not undergo any fragmentation in boiling water or MeOH. Refluxing (*E*)-**3a** in aprotic solvents led to the formation of benzonitrile and *P,P'*-bis-(2,2,2-trifluoroethyl)pyrophosphate (**4a**). The rate of fragmentation increased with solvent polarity. Similar behavior was exhibited by **11**. The fragmentation of anions **3** and **11** is interpreted in terms of a dissociative mechanism leading to the formation of metaphosphate in the first step. The lack of reactivity in water and methanol is rationalized by assuming stabilization of the starting material by H-bond formation, while the rate enhancement by polar solvent is attributed to stabilization of the transition state and solvation of the departing OH^- by the solvent. The metaphosphate formed in the thermal fragmentation of **3a** in MeCN was trapped by styrene oxide, as evidenced by the isolation and identification of 2-oxo-2-(2',2',2'-trifluoroethyl)-4-phenyl-1,3,2-dioxaphospholane as a mixture of diastereoisomers **18** and **19**.

Introduction

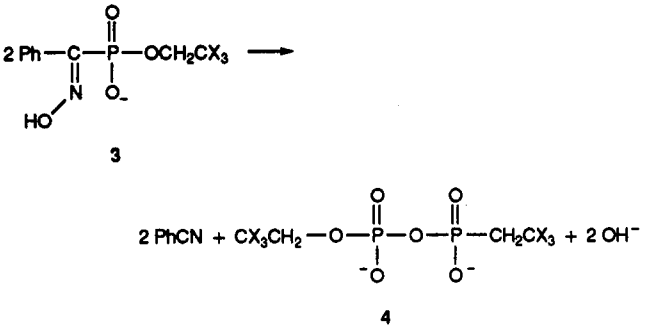
Previously we reported that (α-hydroxyiminophenyl)-phosphonic acids (e.g. **1**) and monoesters (**2**) undergo acid-catalyzed fragmentation to monomeric metaphosphoric acid[1] or ester,[2,3] respectively, and consequently may act as phosphorylating agents (eq 1).[1-4]



1, R = H
2, R = alkyl

In the course of our studies on the effect of structure on the behavior of this class of compounds, we examined a series of 2,2,2-trihaloethyl (α-hydroxyiminobenzyl)-phosphonates.[5] We found that, in contrast to the anion of methyl ester **2** (R = Me) which is thermally stable, the anion of 2,2,2-trifluoroethyl (α-hydroxyiminobenzyl)-phosphonate (**3a**) yields upon heating in acetonitrile a pyrophosphate derivative (**4a**) (Scheme I). Since this was interpreted in terms fragmentation of **3a** to a metaphosphate, we considered that phosphonates of type **3** could serve as starting materials to mixed phosphates containing 2,2,2-trihaloethyl groups. Such groups are useful for protection of phosphates and they are known to be easily removable under mild conditions.[6] In the present paper we wish to describe results of our studies aimed at determining the synthetic potential of compounds of type **3** under different conditions.

Scheme I[a]



[a] **a**, X = F; **b**, X = Cl.

Results and Discussion

Synthesis of Polyhaloalkyl (α-Hydroxyiminobenzyl)phosphonate Anions. The syntheses of compounds **3** are described in our previous paper. Two main approaches can be employed: (1) Demethylation of methyl 2,2,2-trihaloethyl (α-hydroxyiminobenzyl)phosphonates (**5**).[5] These compounds are obtained, usually as predominantly (*Z*)-isomers, by the reaction of the corresponding dialkyl acylphosphonates with hydroxylamine. The oxime stereochemistry is preserved in the dealkylation illustrated

• Abstract published in *Advance ACS Abstracts*, December 1, 1993.

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(3) Katzhendler, J.; Karaman, R.; Gibson, D.; Leader, H.; Breuer, E. *J. Chem. Soc., Perkin Trans. 2* **1989**, 589.

(4) Quin, L. D.; Wu, X.-P.; Breuer, E.; Mahajna, M. *Tetrahedron Lett.* **1990**, *31*, 6281.

(5) Breuer, E.; Mahajna, M. *Heteroat. Chem.* **1992**, *3*, 251.

(6) For use of 2,2,2-trichloroethyl group, see: Denharton, J. A.; Wijnands, R. A.; Van Boom, J. H. *J. Org. Chem.* **1981**, *46*, 2242. For 2,2,2-trifluoroethyl, see: Neilson, P. W.; Neilson, R. H. *Inorg. Chem. Soc.* **1980**, *19*, 1875. For 1,1,1,3,3,3-hexafluoro-2-propyl, see: Hosaka, H.; Suzuki, Y.; Sato, H.; Gug-Kim, S.; Takaku, H. *Nucleic Acids Res.* **1991**, *19*, 2935; and *Tetrahedron Lett.* **1991**, *32*, 785.

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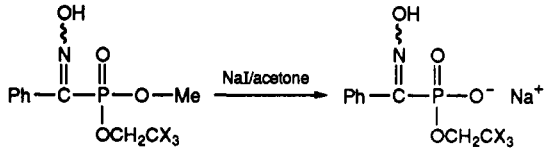
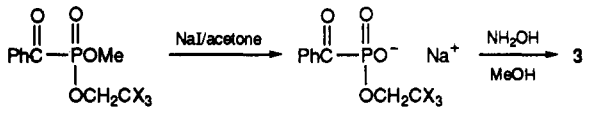
Scheme II[a]



5 3

[a] a, X = F; b, X = Cl.

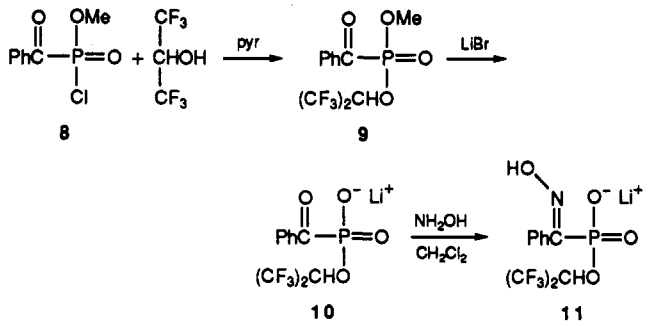
Scheme III[a]



6 7

[a] a, X = F, b, X = Cl.

Scheme IV



8 9 10 11

in Scheme II.[7] (2) Reaction of trihaloethyl benzoylphosphonate anions 7[5] with hydroxylamine. This synthetic route, which leads predominantly to (*E*)-isomers, is illustrated in Scheme III.

The latter approach was found applicable also for the preparation of lithium 1,1,1,3,3,3-hexafluoro-2-propyl (α-hydroxyliminobenzyl)phosphonate (**11**). Methyl benzoylphosphonochloridate (**8**)[8] was reacted with 1,1,1,3,3,3-hexafluoro-2-propanol in dichloromethane in the presence of pyridine. The resulting benzoylphosphonate mixed ester **9** was dealkylated by lithium bromide in acetonitrile, to yield ester salt **10**, which in turn was converted to the oxime **11** by hydroxylamine in dichloromethane (Scheme IV). In this case too, the product **11** formed was predominantly (*E*).

Thermal Fragmentation of Polyhaloalkyl (α-Hydroxyiminobenzyl)phosphonate Anions. We examined the thermal behavior of monoanions **3a** in a series of refluxing solvents. The results are summarized in Table I. It is seen from the data in this table that there was no fragmentation observed in water and in methanol in 12–14 h. In contrast, when a solution of **3a** in ethanol or 2-propanol was refluxed, monitoring the reaction mixture by ^{31}P NMR spectroscopy revealed the gradual disappearance of the starting material and the evolvement of a new phosphorus-containing product. In ethanol the new peak was a quintet at 0.45 ppm and in 2-propanol it was a quartet at −0.33 ppm. These chemical shifts and splitting patterns indicate the formation of mixed phosphodiesters **12a** and **13a**, respectively (Scheme V). When the reaction was performed in a mixture of ethanol and 2-propanol (experiment 6, Table I), the formation of two mixed phosphodiesters, **12a** and **13a** was observed in the same ratio as the molar ratio of the two alcohols in the medium. The formation of two mixed phosphodiesters, **12a** and **13a**, in this experiment, in the same molar ratio as that of the two alcohols comprising the medium shows lack of selectivity among the two sterically different alcohols and confirms that the alcohols are not involved in the rate-determining step of the reaction. The absence of steric effect has been applied previously by several research groups as a diagnostic tool to distinguish between associative- and dissociative-type mechanisms.[9,10]

In all aprotic solvents examined the reactions yielded benzonitrile and a single phosphorus-containing product resonating at −11.3 ppm. This chemical shift is consistent with the bis(2,2,2-trifluoroethyl)pyrophosphate (**4a**) structure. We also examined, to a limited extent, the thermal behavior of 2,2,2-trichloroethyl (α-hydroxyiminobenzyl)-phosphonate (**3b**) and 1,1,1,3,3,3-hexafluoro-2-propyl (α-hydroxyiminobenzyl)phosphonate (**11**) anions. The results obtained for **3b** and **11** are summarized in Tables II and III, respectively. Thermal treatment of these compounds led to products of the same type as that of **3a**. Reflux of **3b** in 2-propanol gave mixed phosphodiester **13b**, while reflux in MeCN gave pyrophosphate **4b**. Similarly, heating 1,1,1,3,3,3-hexafluoro-2-propyl (α-hydroxyiminobenzyl)phosphonate (**11**) in EtOH or 2-PrOH gave hexafluoro-2-propyl ethyl or hexafluoro-2-propyl 2-propyl phosphates **15** and **16**, respectively (Scheme VI), while heating **11** in MeCN gave pyrophosphate **17** (Scheme VII).

Although these experiments were all carried out at different temperatures, and therefore cannot be viewed as kinetic studies, some trends are clearly apparent. From the results listed in Tables I–III, two points arise that deserve consideration. These are (i) the solvent effect on the reaction and (ii) the specificity of the (*E*)-oximes, as opposed to the (*Z*)-oximes, to undergo fragmentation.

(i) Effect of Solvent. The lack of fragmentation of **3a** in refluxing water and methanol can be attributed to stabilization of the starting material by solvent hydrogen bonding.[11] The variation of the reaction rate with the changing of the hydroxylic solvents in our case is, therefore, in accordance with a concerted dissociative mechanism involving the formation of metaphosphate (**14**, Scheme V) in the first step and its subsequent trapping by the solvent.

Although the solubilities of **3a** in the various aprotic solvents are different, as are the boiling points of the

(7) The assignment of the oxime stereochemistry is based on ^{31}P NMR shifts. For correlation of ^{31}P NMR shifts with stereochemistry in hydroxyiminophosphonates, see: Breuer, E.; Karaman, R.; Goldblum, A.; Gibson, D.; Leader, H.; Potter, B. V. L.; Cummins, J. H. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 3047.

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(9) (a) Freeman, S.; Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 3166; **1988**, *110*, 1268. (b) Cullis, P. M.; Nicholls, D. *J. Chem. Soc., Chem. Commun.* **1987**, 783. (c) Ramirez, F.; Marecek, J. F. *Tetrahedron* **1979**, *35*, 1581; **1980**, *36*, 3151. (d) Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 6126.

(10) The same type of test was applied to other metaphosphate analogs using amines of differing steric requirements: (a) Harger, M. J.; Smith, A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2507. (b) Coogan, M. P.; Harger, M. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1745.

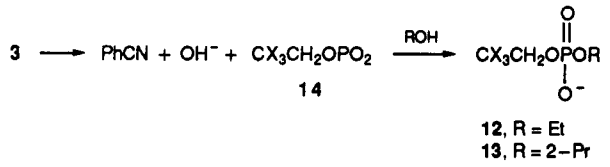
(11) A similar type of solvent effect was seen in the fragmentation of benzisoxazole-3-carboxylic acids. These undergo quantitative decarboxylation to salicylonitriles via a concerted mechanism. The rate constants of this fragmentation reaction were found to vary over a range of 10^8 from water to HMPA, water being the slowest: (a) Kemp, D. S.; Cox, D. D.; Paul, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 7312. (b) Kemp, D. S.; Paul, K. G. *Ibid.* **1975**, *97*, 7305. (c) Kemp, D. S.; Reczek, J.; Vellaccio, F. *Tetrahedron Lett.* **1978**, 741.

Table I. Summary of Results from Heating 3a in Different Solvents[a]

expt	E/Z ratio of 3a	solvent	temp, °C	time, h	products (yield, %)
1	90/10	water	100	14	s.m. recovered (100)
2	90/10	MeOH	64	12	s.m. recovered (100)
3	90/10	EtOH	78	12	**12a** (100) + PhCN (98)
4	90/10	2-PrOH	82	6	**13a** (100) + PhCN (N.D)
5	90/10	EtOH 2-PrOH 7:3	80	10	**12a** (65) + **13a** (35) + PhCN (95)
6	90/10	MeCN + 5 equiv of 2-PrOH	80	19	**13a** (100) + PhCN (100)
7	90/10	PhMe	111	72	s.m. (50) + **4a** (50) + PhCN (N.D.)
8	90/10	THF	67	24	s.m. (50) + **4a** (50) + PhCN (N.D.)
9	90/10	MeCN	80	14	**4a** (100) + PhCN (94)
10	90/10	EtCN	97	22	s.m. (27) + **4a** (73) + PhCN (N.D.)
11	20/80	2-PrOH	82	27	unreacted isomerized s.m. *E*:*Z* = 64:36
12	20/80	MeCN	80	5	isomerized s.m. (*E*:*Z* = 62:38)
13	20/80	MeCN	80	12	(*E*)-**3a** (50) + (*Z*)-**3a** (10) + **4a** (40)
14	20/80	MeCN	80	22	**4a** (100) + PhCN (99)

[a] Reaction mixtures were monitored by ^{31}P NMR spectroscopy. The durations of reactions given for 100% yields are accurate within 30 min. Chemical shifts of products: **4a** δ −11.3 (t); **12a** δ 0.45 (quint); **13a** δ −0.33 (q). Benzonitrile was determined by high performance liquid chromatography on a RP-18 column using methanol:water (60:40). s.m. = starting material. N.D. = not determined.

Scheme V[a]



[a] **a**, X = F; **b**, X = Cl.

Table II. Summary of Results from Heating 3b in Different Solvents[a]

expt	E/Z of 3b	solvent	temp, °C	time, h	products (yield, %)
1	75/25	2-PrOH	82	10	**13b** (100) + PhCN (95)
2	13/87	2-PrOH	82	44	(*E*)-**3b** (23) + **13b** (77) + PhCN (73)
3	75/25	MeCN	80	16	**4b** (100) + PhCN (97)
4	13/87	MeCN	80	15	(*E*)-**3b** (22) + (*Z*)-**3b** (29) **4b** (49) + PhCN (N.D.)
5	90/10	PhMe	111	72	s.m. (86) + **4b** (14) + PhCN

[a] Reaction mixtures were monitored by ^{31}P NMR spectroscopy. The durations of reactions given for 100% yields are accurate within 30 min. Chemical shifts of products: **4b** δ −12 (t); **13b** δ −1.9 (q). Benzonitrile was determined by high performance liquid chromatography on a RP-18 column using methanol:water (60:40). s.m. = starting material. N.D. = not determined.

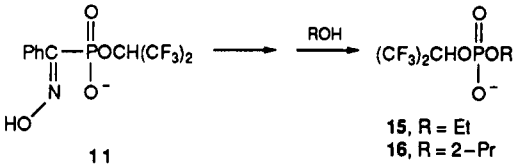
Table III. Summary of Results from Heating 11 (*E*/*Z* = 93:7) in Different Solvents[a]

expt	solvent	temp, °C	time, h	products (yield, %)
1	EtOH	78	21	s.m. (35) + PhCN (66) + **15** (65)
2	2-PrOH	82	6	**16** (100) + PhCN (92)
3	MeCN	80	21	s.m. (42) + **17** (58) + PhCN (N.D.)

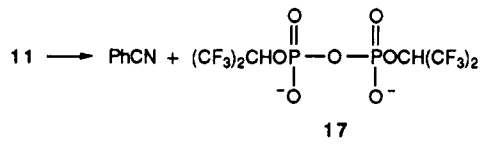
[a] Reaction mixtures were monitored by ^{31}P NMR spectroscopy. The durations of reactions given for 100% yields are accurate within 30 min. Chemical shifts of products: **17** δ −11.2 (d); **15** δ −1.0 (m); **16** δ −1.9 (q). Benzonitrile was determined by high performance liquid chromatography on a RP-18 column using methanol:water (60:40). s.m. = starting material. N.D. = not determined.

solvents, the results in Table I illustrate the dependence of rate on the polarity of the medium. For example, from the data listed in Table I it appears that **3a** undergoes complete fragmentation in acetonitrile several hundreds times faster (taking into account the difference in boiling points between the two solvents) than in toluene. It appears that in polar solvents the reaction rate is enhanced. This rate enhancement is likely to be the result of increased stabilization of the transition state leading to fragmentation and of better solvation of the leaving hydroxy group

Scheme VI



Scheme VII



by the more polar solvents. In aprotic solvents, in the absence of reactive compounds, dimerization of the metaphosphate is observed, as seen in the fragmentation of other types of metaphosphate precursors in such conditions.[8,12,13]

(ii) Stereospecificity. Examination of Table I reveals that the predominantly (*Z*)-**3a** does not undergo fragmentation in 2-propanol in 27 h. On the other hand, heating (*Z*)-**3a** in acetonitrile causes first a slow isomerization to the (*E*)-isomer, which is then followed by fragmentation. Similarly it can be seen in Table II that predominantly (*E*)-**3b** undergoes complete fragmentation in refluxing 2-propanol in 10 h, while the predominantly (*Z*)-**3b** gives in the same solvent in 44 h 77% fragmentation and 23% isomerization to the (*E*)-isomer. A similar trend is seen in refluxing acetonitrile. Thus, it appears that the fragmentation is a specific characteristic of the (*E*)-isomers.

It was noted earlier in our laboratory that the acid-catalyzed fragmentation of methyl hydrogen (α-hydroxyiminobenzyl)phosphonate is specific for the (*E*)-isomer.[3] This was interpreted in terms of stereoelectronic assistance by the nonbonding electron pairs of the P–O oxygens in the C–P bond-breaking process.[3] It appears that the present reaction too can be rationalized in similar trends. Additional analogy can be found between the present fragmentation and the Beckmann fragmentation of oximes.[14] Such fragmentation, which occurs when the

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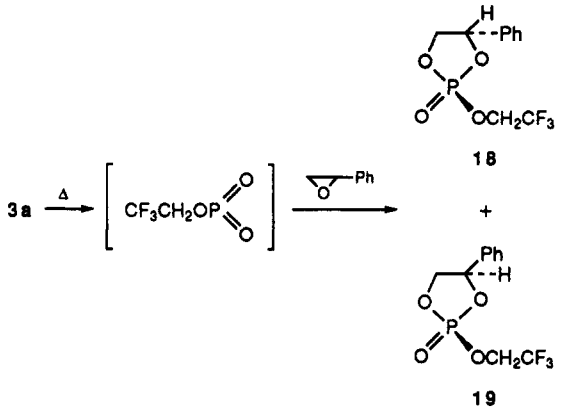
(13) Ramirez, F.; Marecek, J. F.; Yemul, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1345.

(14) Deslongchamps, P. *Stereoelectronic effects in organic chemistry*; Pergamon Press: Oxford, 1983; pp 298–9, and references cited therein.

Scheme VIII



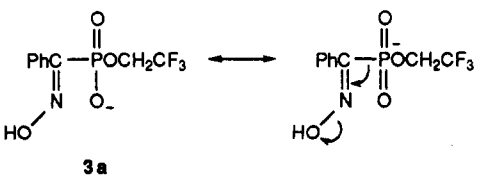
potential migrating group, oriented *anti* to the N–OH group, can form a relatively stable carbonium ion,[15] also yields the corresponding nitrile.

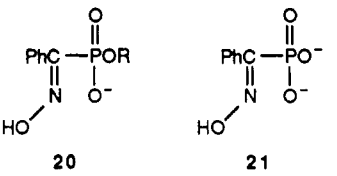
Trapping of Metaphosphate by Styrene Oxide. Metaphosphates are highly electrophilic species in solution.[16,17] In addition to their capacity to phosphorylate amines[10] and hydroxy compounds,[1-5,9,13,16] they have also been shown to perform electrophilic substitutions on activated aromatic rings, such as anilines[18] and *N*-methylpyrrole.[19] On the other hand, it has been established that some low-coordination phosphorus compounds react with epoxides with ring opening followed by subsequent formation of cyclic or polymeric products.[20] Recently, successful trapping of metaphosphate by epoxide was reported.[21] When we carried out the fragmentation of **3a** in the presence of 5 equiv of styrene oxide by reflux in dry acetonitrile, a solid product was formed. Examination of this product by ^{31}P NMR revealed only two signals in the range 17.6–17.8 ppm,[22] consistent with the formation of structures **18** and **19** in the reaction (Scheme VIII). The product (a mixture of two diastereoisomers which were not separated) was isolated and the structures were also confirmed by ^{1}H NMR and mass spectrometry.

Conclusion

In order to rationalize the thermal behavior of compounds of type **3** described here, we consider the contrast in behavior between the α-hydroxyimino phosphonic cids and monoesters. While simple monoester anions **20** were stable for 30 h in refluxing acetonitrile, dianions **21** exhibit a tendency to undergo fragmentation.[1]

Scheme IX





This indicates that one negative charge on the phosphonate group is insufficient, but two charges are adequate to provide electrons for the C–P bond fission and the departure of the oxime hydroxy group. It seems therefore reasonable to assume that the polyhaloalkyl and similar groups (e.g. *p*-chlorophenyl[23]) exert their influence through their electron-withdrawing effect. We assume that the contribution of hexavalent phosphorus resonance forms (Scheme IX) would result in an increase in the electron density on the phosphorus, which in turn would assist in the C–P bond breaking (as indicated) and the departure of the hydroxide leaving group.

The results presented indicate that α-hydroxyimino phosphonate esters with electron-withdrawing polyhaloalkoxy groups have the potential to phosphorylate hydroxy groups under neutral conditions and to yield 2,2,2-trihaloethyl or 1,1,1,3,3,3-hexafluoro-2-propyl phosphates. Since such groups are known to be useful phosphate protecting groups,[6] it appears that phosphonates of type **3** and **11** have the potential of becoming useful reagents.

Experimental Section

General. For the instruments used and for the preparation of compounds **3a** and **3b** see ref 5.

1,1,1,3,3,3-Hexafluoro-2-propyl Methyl Benzoylphosphonate (9). To a solution of methyl benzoylphosphonochloridate (8,[8] 21.8 g, 0.1 mol) in dry dichloromethane (70 mL) was added dropwise with stirring at 0 °C under nitrogen a solution of pyridine (9 mL, 0.11 mol) and 1,1,1,3,3,3-hexafluoro-2-propanol (16.8 g, 0.1 mol) in dry dichloromethane (70 mL). After the reaction mixture had been stirred for 2 h at ambient temperature, the solvent was removed at reduced pressure and the residue was taken up in anhydrous ester. Pyridinium chloride was removed by filtration and evaporation of the ether yielded 31 g (0.088 mol, 88%) of crude **9** as an oil: ^{31}P NMR (CH_2Cl_2) δ −1.3 (quint); IR (neat) CH 3055, C=O 1650, C=C 1592, P=O 1260 cm^{-1}. This product was used immediately without further purification for the synthesis of compound **10**.

Lithium 1,1,1,3,3,3-Hexafluoro-2-propyl Benzoylphosphonate (10). A solution of **9** (17.5 g, 0.05 mol) in dry acetonitrile (100 mL) was added to a solution of lithium bromide (4.8 g, 0.055 mol) in dry acetonitrile (30 mL). After the reaction mixture was stirred overnight at room temperature, the precipitated salt was filtered off, washed with dry acetonitrile, and dried in air: yield 95%; IR (KBr) 3050, 1650, 1594, 1260, 1090 cm^{-1}; ^{31}P NMR (D_2O) δ −2.0 (d, J = 11 Hz); ^{1}H NMR (D_2O) δ 8.17 (2H), 7.7 (1H, t), 7.58 (2H, t), 5.41 (1H, m). Anal. Calcd for $C_{10}H_6F_6O_4PLi$: C, 35.1, H, 1.75. Found: C, 35.4, H, 2.03.

(15) Although carbonium ions and metaphosphates[16] are very different from the standpoint of electronic configuration, there are certain features common to both types of these reactive intermediates. They both are frequently formed in dissociative-type reactions, they both are electrophilic, planar, and they both are intermediates leading to racemizations.

(16) (a) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313. (b) Regitz, M.; Maas, G. *Top. Curr. Chem.* **1981**, *97*, 71. (c) Calvo, K. C.; Westheimer, F. H. *J. Am. Chem. Soc.* **1984**, *106*, 4205. (d) Ramirez, F.; Marecek, J.; Minore, J.; Srivastava, S.; le Noble, W. *J. Am. Chem. Soc.* **1986**, *108*, 348. (e) Meisel, M. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M., Scherer, O. J., Eds.; Thieme: Stuttgart, 1990; pp 415–442.

(17) On the other hand, metaphosphates are quite stable and unreactive in the gas phase: (a) Henchman, M.; Viggiano, A. A.; Paulson, J. F. *J. Am. Chem. Soc.* **1985**, *107*, 1453. (b) Keesee, R. G.; Castleman, A. W. *Z. Naturforsch.* **1987**, *42b*, 1585.

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Lithium 1,1,1,3,3,3-hexafluoro-2-propyl (α-Hydroxyiminobenzyl)phosphonate (11). Hydroxylamine free base was prepared by neutralizing hydroxylamine hydrochloride (8.34 g, 0.12 mol) in methanol (50 mL) with sodium methoxide freshly prepared by dissolving sodium (2.8 g, 0.12 mol) in methanol. After the precipitated sodium chloride was filtered off, the solvent was removed under reduced pressure and the residue was dissolved in dry dichloromethane (50 mL) was added to a suspension of **10** (34 g, 0.1 mol) in dry dichloromethane (150 mL). After the reaction mixture was stirred at room temperature for 3 h, the solvent was removed at reduced pressure and the residue salt was washed several times with dry acetonitrile and dried in air; yield 85%; IR (KBr) 3050, 1640, 1594, 1260, 1090 cm^{-1}; ^{31}P NMR (D_2O) δ 4.24 (d, J = 11 Hz) (93%, (*E*)-11), −0.5 (d, J = 11 Hz) (7%, (*Z*)-11); ^1H NMR (D_2O) δ 7.51–7.35 (5H, m), 5.3 (1H, m). No good analysis could be obtained for this compound. The low values obtained for C, H, and N, together with the good ^{31}P and ^1H NMR spectra, indicate the probable presence of an inorganic impurity, which could not be removed.

Thermal Fragmentation of 3 and 11. A suspension of **3** (100 mg) in dry solvent (10 mL) was heated to reflux. The progress of the reaction was monitored by ^{31}P NMR spectroscopy. After removal of the solvent the residue was also analyzed by IR and HPLC for benzonitrile.

Trapping of Metaphosphate by Styrene Oxide. A suspension of **3a** (360 mg, 1.25 mmol) and styrene oxide (0.7 mL, 6 mmol) in dry acetonitrile (15 mL) was refluxed for 15 h. The reaction mixture was cooled in an ice bath. The white precipitate was filtered, washed several times with dry acetone and dry acetonitrile, and dried to yield 280 mg (80%) of **18** and **19** as a mixture of diastereoisomers: MS m/z 282 (M^+); ^{31}P NMR ($CDCl_3$) δ 17.6, 17.8 (1:1); ^1H NMR ($CDCl_3$) δ 7.54–7.43 (5H, m), 5.5 (1H, m), 4.55 (2H, m), 4.15 (2H, m).