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β-(Phosphatoxy)alkyl and β-(Acyloxy)alkyl Radical Migrations Studied by Laser Flash Photolysis†

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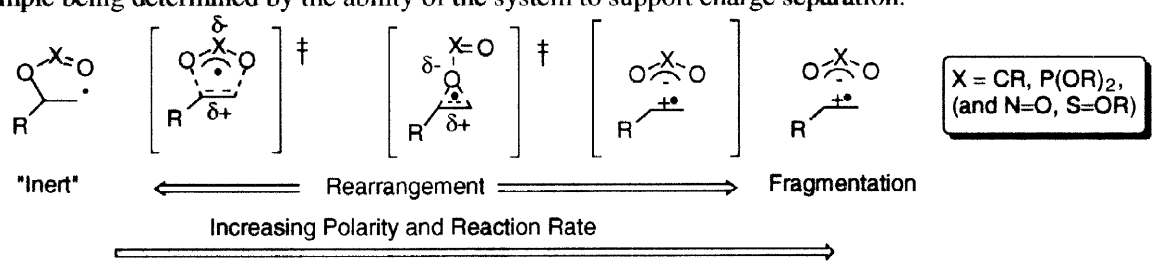
Abstract: A number of β-(phosphatoxy)alkyl and β-(acyloxy)alkyl radicals have been generated by laser flash photolysis of the corresponding Barton PTOC esters. Time resolved studies permitted the determination of rate constants and kinetic parameters for their rearrangement in benzene, THF, and acetonitrile. Migrations are accelerated by electron-donating groups on the alkyl moiety, electron-withdrawing groups on the migrating group, and more polar solvents. All reactions showed strictly first order kinetics. The results are interpreted in terms of concerted mechanisms occurring through three electron, three center and five electron, five center mechanisms. © 1999 Elsevier Science Ltd. All rights reserved.

Since their respective discoveries the β-(phosphatoxy)alkyl[1,2] and β-(acyloxy)alkyl[3,4] radical migrations have been subjected to considerable mechanistic scrutiny. As summarized in a recent review,[5] these rearrangements are intramolecular and extremely stereoselective. Isotopic and stereochemical labeling has demonstrated the existence of two manifolds, namely the 1,2-shift and the 2,3-shift and has focused attention on the differing proportions of the two extremes according to substitution pattern and medium.[5] Indirect kinetic studies, by both the tin hydride and benzeneselenol methods, have provided kinetic parameters for these reactions and have led to the advancement of polarized three electron, three center and five electron, five center cyclic transition states, resembling phosphate or carboxylate anions loosely bound to alkene radical cations, for the 1,2- and 2,3-shifts, respectively.[5] Most of the literature results may also be accommodated by a mechanism involving initial fragmentation to an alkene radical cation/phosphate or carboxylate pair followed by rapid, in-cage collapse to the product radical.[5] Experiments which differentiate between the concerted and cage manifolds have been conducted for certain examples[6,7] but these are necessarily very substrate specific and do not permit generalization. In the extreme case, when substituents or solvents provide sufficient stabilisation of charged species, results are observed which are consistent with the radical ionic fragmentation and cage escape. Such behaviour was observed originally by the Norman[8,9] and Schulte-Frohlinde[10,11] groups and is relevant to the cleavage of oligonucleotide C4' radicals[12-14] following hydrogen atom abstraction by the certain antitumor antibiotics[15-17] and hydroxyl radicals.[18] Beckwith, Crich and co-authors have reduced the available data to a continuum of mechanisms (Scheme 1) with the precise location of a given example being determined by the ability of the system to support charge separation.[5]



Scheme 1

† **Dedicated to the memory of our friend, colleague and mentor Derek H. R. Barton, F.R.S.**

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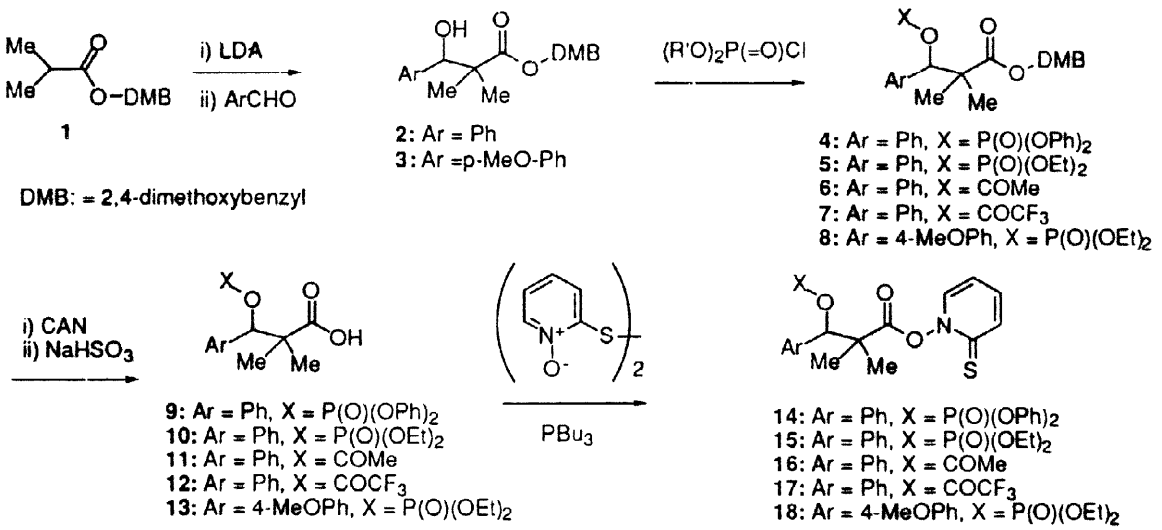
Here, we present in full[19] kinetic parameters, determined directly by the time resolved laser flash photolysis method, for a range of differentially substituted β-(phosphatoxy)alkyl and β-(acyloxy)alkyl rearrangements in solvents of differing polarity. The advantages of the direct LFP method over the indirect methods used previously derive from the ability to work over a considerable range of temperature, leading to meaningful Arrhenius parameters, and in a wide range of different solvents.

The *O*-acyl thiohydroxamates, or Barton PTOC esters, originally developed for synthetic purposes,[20,21] are ideal precursors for laser flash photolysis studies providing radicals cleanly and efficiently when irradiated in the visible and leaving a clear, unencumbered window for the observation of benzyl type radicals.[22,23] Their application to the problem in hand required the synthesis of β-aryl-β-hydroxypropionic acids for subsequent phosphorylation and/or acylation followed by transformation to the PTOC esters. Such acids may in principle be assembled by aldol condensation of an ester enolate with benzaldehyde followed by phosphorylation, or acylation, and release of the acid. In practice, it rapidly became obvious that the acid must be disubstituted at the α-position to prevent elimination on attempted phosphorylation or acylation. A more subtle problem involved choice of the ester group for the aldol/phosphorylation sequence. Numerous such groups were assayed but could not be released except under conditions which promoted solvolysis of the benzylic phosphate group, leading to the formation of a β-lactone. Ultimately, we settled on the 2,4-dimethoxybenzyl esters which could be cleaved oxidatively providing chromatographically unstable β-(phosphatoxy)propionic acids contaminated only by dimethoxybenzaldehyde, which could be removed extractively in the form of a bisulfite adduct. In this manner a series of β-(phosphatoxy) and β-(acyloxy)propionic acids were prepared (Scheme 2) and transformed into the corresponding PTOC esters with 2,2'-dipyridyl disulfide bis-*N*-oxide and tributylphosphine. This method of PTOC formation[24] was selected from the many available[21] as it enabled their rapid elution from silica gel ahead of any byproducts or reagents.



1

DMB: = 2,4-dimethoxybenzyl

2: Ar = Ph
3: Ar =p-MeO-Ph

4: Ar = Ph, X = P(O)(OPh)2
5: Ar = Ph, X = P(O)(OEt)2
6: Ar = Ph, X = COMe
7: Ar = Ph, X = COCF3
8: Ar = 4-MeOPh, X = P(O)(OEt)2

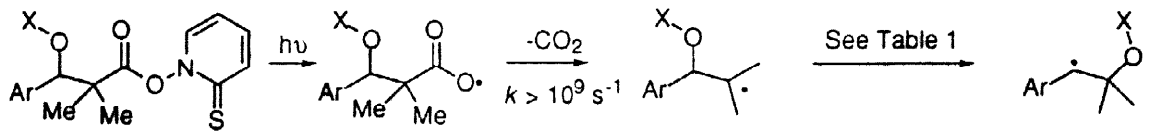
9: Ar = Ph, X = P(O)(OPh)2
10: Ar = Ph, X = P(O)(OEt)2
11: Ar = Ph, X = COMe
12: Ar = Ph, X = COCF3
13: Ar = 4-MeOPh, X = P(O)(OEt)2

14: Ar = Ph, X = P(O)(OPh)2
15: Ar = Ph, X = P(O)(OEt)2
16: Ar = Ph, X = COMe
17: Ar = Ph, X = COCF3
18: Ar = 4-MeOPh, X = P(O)(OEt)2

Scheme 2

In preparative scale experiments thiohydroxamate **14** was photolyzed in the presence of *tert*-butylmercaptan in benzene and acetonitrile solutions. In both instances examination of the crude reaction mixtures by ^{31}P-NMR spectroscopy revealed complete consumption of the substrate and formation of a single new phosphorus based product, diphenylphosphoric acid. From the photolysis in acetonitrile solution β,β-dimethylstyrene was isolated in 85% yield. In benzene the reaction was not so clean, as indicated by ^{1}H-NMR spectroscopy, nevertheless, β,β-dimethylstyrene was still the major product and was isolated in 50% yield.

Laser flash photolysis (LFP) kinetic studies were conducted with thiohydroxamates **14** - **18**. Photolysis of the PTOC ester with 355 nm light results in efficient cleavage of the weak N–O bond to give the pyridine-2-thiyl radical (λ_{max} = 490 nm) and an acyloxyl radical (Scheme 3). The acyloxyl radical decarboxylates "instantly" on the nanosecond time scale to give the desired β-ester radical (**19** - **23**). For the studies in Table 1, ester group migrations producing benzyl radicals (**24** - **28**) were apparent with the signals for benzylic radicals growing in at λ_{max} of about 320 nm.[25] Figure 1 shows some representative time-resolved spectra.



14: Ar = Ph, X = P(O)(OPh)$_2$
15: Ar = Ph, X = P(O)(OEt)$_2$
16: Ar = Ph, X = COMe
17: Ar = Ph, X = COCF$_3$
18: Ar = 4-MeOPh, X = P(O)(OEt)$_2$

19: Ar = Ph, X = P(O)(OPh)$_2$
20: Ar = Ph, X = P(O)(OEt)$_2$
21: Ar = Ph, X = COMe
22: Ar = Ph, X = COCF$_3$
23: Ar = 4-MeOPh, X = P(O)(OEt)$_2$

24: Ar = Ph, X = P(O)(OPh)$_2$
25: Ar = Ph, X = P(O)(OEt)$_2$
26: Ar = Ph, X = COMe
27: Ar = Ph, X = COCF$_3$
28: Ar = 4-MeOPh, X = P(O)(OEt)$_2$

Scheme 3

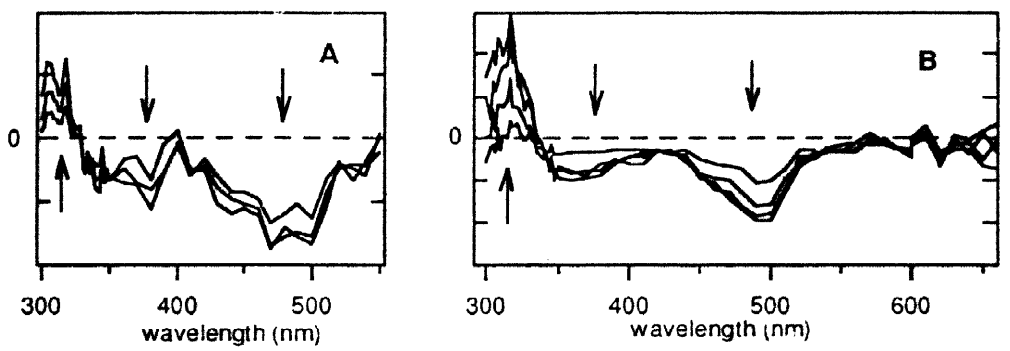


Figure 1. Time-resolved spectra. (A) Spectra from irradiation of **15** in acetonitrile at 20 °C at 6, 14, and 38 μs after the laser pulse. (B) Spectra from irradiation of **18** in THF at 20 °C recorded 2.5, 6.5, 14.5, and 29 μs after the laser pulse. The spectra have been "corrected" by subtraction of the observed signals immediately after the laser flash so that all signals evolve from the zero baseline. Benzylic product radicals are growing in at λ_{max} = 320 nm. Decaying signals are from bimolecular reactions consuming residual PTOC esters (centered at 360 nm) and depletion of the pyridine-2-thiyl radical (centered at 490 nm).

Fragmentations to give diffusively free radical cations and carboxylate or phosphate anions were readily excluded by the LFP results. Styrene radical cations have strong absorbances at ca. 350 nm and 600 nm,[26,27] but no transients with absorbances in these regions were observed to grow in with time. Further, the formation of benzylic radical products was first order in all cases. Finally, the rate constants in several cases exceeded 1×10^5 s^{-1} which is too fast for second order processes involving only transients produced by the laser flash; because the transients are produced in concentrations of $<5 \times 10^{-5}$ M, even diffusion-controlled couplings would have smaller pseudo first-order rate constants.

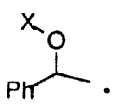
Either concerted migrations or fragmentations to radical cation--anion pairs that recombined are consistent with the observed behavior. Concerted ester migrations are expected to occur through polarized transitions states with partial charge separation (Scheme 1), whereas a fragmentation-recombination pathway for migration involves complete charge development. The kinetic results in Table 1 allow an evaluation of charge stabilizing

effects of the migrating ester group, the product radical center and solvent. All of these are consistent with some charge development in the transition states.

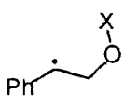
Table 1. Observed Rate Constants and Arrhenius Parameters

	Solvent	Arrhenius function[a]	k_{obs} (s^{-1})[b]	ε[c]
19 → **24**	benzene	-	1.2×10^6	2.27
19 → **24**	THF	$(10.9 \pm 0.3) - (6.2 \pm 0.5)/\theta$	1.5×10^6	7.58
19D → **24D**	THF	-	1.5×10^6	7.58
19 → **24**	MeCN	$(11.0 \pm 0.5) - (5.0 \pm 0.7)/\theta$	1.8×10^7	35.9
19D → **24D**	MeCN	$(11.0 \pm 0.3) - (5.0 \pm 0.4)/\theta$	1.8×10^7	35.9
20 → **25**	MeCN	-	$6\text{-}7 \times 10^4$	35.9
21 → **26**	MeCN	-	$< 1 \times 10^4$	35.9
22 → **27**	THF	$(10.7 \pm 0.5) - (6.2 \pm 0.6)/\theta$	1.2×10^6	7.58
22 → **27**	MeCN	$(11.2 \pm 0.3) - (5.9 \pm 0.4)/\theta$	6.2×10^6	35.9
23 → **28**	THF	$(12.1 \pm 0.8) - (9.7 \pm 1.2)\theta$	7×10^4	7.58

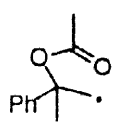
a: Errors are at 2σ; $\theta = 2.3RT$ (kcal/mol). b: Observed rate constant at 20 ± 1 °C unless stated; errors are <10%. c: Solvent dielectric constants in Debye units.[28]



29: X = P(O)(OPh)$_2$
30: X = P(O)(OEt)$_2$



31: X = P(O)(OPh)$_2$
32: X = P(O)(OEt)$_2$



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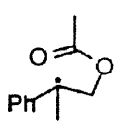

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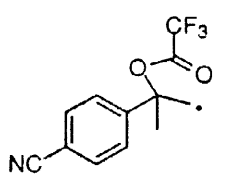

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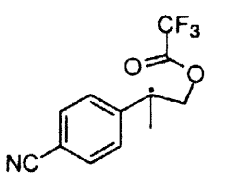

36

Radical **19**, derived from the PTOC ester **14**, was found to rearrange in benzene solution with a rate constant of 1.2×10^6 s^{-1} at 20 °C. This is approximately one order of magnitude larger than that (1.2×10^5 s^{-1}) determined for the bis-nor analog (**29** → **31**) at 27 °C in benzene by the selenol trapping method.[29] The additional methyl groups in radical **19** better support charge separation and accelerate the reaction. On going to THF a modest acceleration in the rate constant for rearrangment of **19** was observed, while in acetonitrile an increase of an order of magnitude was found. These solvent effects further demonstrate charge development in the reaction. The deuterium labeled analog of **19**, **19D** with the two methyl groups fully deuterium labeled, rearranged with no significant kinetic isotope effect. This indicates that the β,β-dimethylstyrene observed in the preparative experiments must arise from a process subsequent to the rearrangement of **19** → **24** and not from any concerted elimination, of the type advocated by Zipse, leading directly to an 2-methyl-1-phenylallyl radical.[30]

The rearrangement of radical **20**, containing the diethylphosphatoxy group, was too slow to measure by LFP in THF and at the lower kinetic limit in acetonitrile. Nevertheless, an approximate rate constant for rearrangement of **20** of 6-7 x 10^4 s^{-1} in acetonitrile at room temperature was measured. This value nicely matches the rate constant observed for the migration of **30** → **32** in benzene at 27 °C by the selenol trapping method.[29] The reduced rate constant for rearrangement of **20** in comparison to **19** is consistent with the

reduced acidity of dialkyl phosphates relative to diphenyl phosphates and further indicative of charge separation in the reaction. When the phenyl group in **20** was replaced with the *p*-methoxyphenyl group in radical **23**, the rearrangement was accelerated due to the positive charge stabilizing effect of the methoxy group. Similar substituent effects were observed for the β-(acyloxy)alkyl rearrangements by Beckwith and Duggan.[31]

In LFP studies of acetoxy migrations, rearrangement of the β-(acetoxy)alkyl radical **21** was too slow to follow by the LFP method even in acetonitrile, although a weak benzyl radical signal was observed placing the rate constant between 1×10^3 and 1×10^4 s^{-1} at ambient temperature. As expected, the corresponding trifluoroacetoxyalkyl radical **22** underwent rearrangement to radical **27** several orders of magnitude more rapidly in both THF and acetonitrile. These results parallel those reported by Beckwith's group. The rate constant for the acetoxy migraption in **33** → **34** was 4.1×10^4 s^{-1} in benzene at 70 °C,[31,32] whereas the trifluoroacetoxy migration in **35** → **36** had a rate constant of 2.6×10^6 s^{-1} in benzene at 75 °C.[31,32]

Charge separation in the transition states for the rate-limiting processes in the ester group migrations is clearly indicated by qualitative evaluation of the kinetics, but a quantitative evaluation of the data suggests that the migration reactions are concerted rather than dissociative processes followed by recombination. For example, the kinetic solvent effects for **19** in proceding from benzene to THF to acetonitrile (k_{rel} = 1 : 1.2 : 15) are minor in comparison to those seen in ionic fragmentations (*e.g.* k_{rel} = 1 : 4 : 1400 for *t*-BuCl and k_{rel} = 1 : 3 : 800 for adamantyl tosylate), although they resemble the effects seen for benzyl chloride (k_{rel} = 1 : 2 : 12).[33] The log *A* terms in the Arrhenius functions indicate well organized transition states with negative entropies of activation. Ingold previously noted that log *A* = 13 for acetoxy migration (*i.e.* $\Delta S^{\ddagger} = 0$) was inconsistent with a dissociative process that should have a large positive entropy of activation,[34] and this would be the case even if the reactions involved ion pair formation in equilibrium followed by rate-limiting collapse to the final product.[35,36] A dissociative process giving ions can have a negative entropy of activation due to high solvent organization in the transition state, but this seems unlikely for the delocalized ions that would be formed and the relatively poor solvents THF and acetonitrile. Perhaps more important are the similarity of the log *A* terms for the phosphatoxy and acetoxy radicals and the invariance of log *A* when changing from THF to acetonitrile; both suggest that highly organized solvent is not the origin of the negative entropies of activation.

On balance, we believe the solvent effects and entropies of activation are most consistent with concerted phosphatoxy and acyloxy migrations. However, in all but two cases[31,37] previously studied, isotope-labeling and stereochemical studies show that both 3-center and 5-center reactions occur,[5] behavior readily explained by a dissociative process followed by recombination. Computations by Zipse indicate that concerted 3- and 5-centered migrations of β-(phosphatoxy)alkyl radicals will have similar barriers,[30] and it is possible that a combination of computational and experimental studies of specific systems will provide more complete mechanistic understanding of these interesting reactions.

Experimental Part

General. All solvents were dried and distilled prior by standard techniques. All NMR spectra were recorded in $CDCl_3$, unless otherwise stated. Chemicals shifts are in ppm downfield from tetramethylsilane (^1H and ^{13}C) or H_3PO_4 (^{31}P). Microanalyses were conducted by Midwest Microlabs, Indianapolis, IN.

2,4-Dimethoxybenzyl 2-Methylpropanoate (1). To a stirred solution of 2,4-dimethoxybenzyl alcohol (2.52 g, 15.0 mmol) and triethylamine (2.28 g, 22.5 mmol) in CH_2Cl_2 (20 mL), isobutyryl chloride (1.60 g, 15.0 mmol) was added dropwise at 0 °C. After stirring at room temperature for 2h, the precipitate was removed by filtration and the filtrate was concentrated to dryness. Column chromatography on silica gel (eluent: hexane/EtOAc 5:1) gave the title compound (3.28 g, 92%) as a colorless oil. ^1H NMR, δ: 1.15 (s, 3

H), 1.18 (s, 3 H), 2.57 (hept, J = 7.0 Hz, 1 H), 3.81 (s, 6 H), 5.08 (s, 2 H), 6.46 (m, 2 H), 7.23 (m, 1 H); ^{13}C NMR, δ: 19.2, 34.2, 52.4, 55.6, 61.7, 98.7, 104.1, 117.6, 131.2, 159.5, 161.8, 177.8. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.49; H, 7.31.

2,4-Dimethoxybenzyl 3-Hydroxy-2,2-dimethyldihydrocinnamate (2). To a stirred solution of **1** (0.476 g, 2.0 mmol) in THF (10.0 mL) at - 78 °C was added LDA (0.5 M in THF, 4.8 mL, 2.4 mmol). After 20 min, benzaldehyde (0.245 mL, 2.4 mmol) was introduced with a syringe and the reaction mixture warmed to room temperature over 1 h before saturated aqueous NH_4Cl (15.0 mL) and EtOAc (30 mL) were added. The reaction mixture was extracted with EtOAc (3 x 15 mL) and the combined organic extracts washed with water and brine, dried (Na_2SO_4) and concentrated to dryness. Column chromatography on silica gel (eluent: hexane/EtOAc 1:1) afforded the title compound (0.57 g, 82%) as a colorless oil. ^{1}H NMR, δ: 7.26 (m, 5 H), 7.22 (d, J = 8.9 Hz, 1 H), 6.47 (m, 2 H), 5.14 (AB quart, J = 34.8, 12.0 Hz, 2 H), 4.86 (d, J = 4.7 Hz, 1 H), 3.82 (s, 6 H), 3.37 (d, J = 4.7 Hz, 1 H), 1.12 (s, 6 H); ^{13}C NMR, δ: 177.5, 161.5, 159.0, 140.0, 131.5, 127.9, 116.6, 104.2, 98.9, 78.9, 62.9, 55.7, 48.3, 23.5, 19.3. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.62; H, 7.05.

2,4-Dimethoxybenzyl 2,2-Dimethyl-3-(diphenylphosphatoxy)dihydrocinnamate (4). To a stirred solution of **2** (1.67 g, 7.0 mmol) in THF (10 mL) at -78 °C was added LDA (1.0 M in THF, 8.4 mL). After 30 mins, benzaldehyde (1.11 g, 10.5 mmol) was introduced via syringe and the reaction mixture was stirred at -78 °C for 1.5 h. Then diphenyl chlorophosphate (2.26 g, 8.4 mmol) was added dropwise and the reaction mixture was stirred for another 1.5 h. The reaction was worked up by addition of saturated NH_4Cl solution (20 mL) and EtOAc (40 mL), extracted with EtOAc (3 x 20 mL), washed with brine (2 x 10 mL), dried over Na_2SO_4 and concentrated to dryness. Chromatography on silica gel (eluent: hexane/EtOAc 3:1) gave the title compound (3.08 g, 77%) as a colorless oil. ^{1}H NMR, δ: 1.08 (s, 3 H), 1.26 (s, 3 H), 3.78 (d, J = 7.1 Hz, 6 H), 5.00 (AB quart, J = 59.3, 12.1 Hz, 2 H), 5.89 (d, J = 8.0 Hz, 1 H), 6.42 (m, 2 H), 6.91 (d, J = 8.2 Hz, 2 H), 7.08-7.30 (m, 14 H); ^{13}C NMR, δ: 20.9, 21.0, 40.9, 52.4, 55.5, 62.5, 85.7, 98.6, 104.1, 116.7, 120.1, 120.3, 125.2, 125.4, 127.9, 128.1, 128.6, 129.7, 131.4, 136.1, 151.5, 159.6, 162.0, 175.5; ^{31}P NMR, δ: -12.24. Anal. Calcd for $C_{32}H_{33}O_8P$: C, 66.66; H, 5.77. Found: C, 66.84; H, 5.88.

2,4-Dimethoxybenzyl 2,2-Dimethyl-3-(diethylphosphatoxy)dihydrocinnamate (5). To a stirred solution of **2** (0.833 g, 3.5 mmol) in THF (8.0 mL) at -78 °C was added LDA (0.5 M in THF, 8.4 mL). After 30 min, benzaldehyde (0.556 g, 5.25 mmol) was introduced via syringe and the reaction mixture was stirred at -78 °C for 45 min. Then diethyl chlorophosphate (0.725 g, 4.2 mmol) was added dropwise and the reaction mixture was stirred for another 3.0 h. The reaction was worked up by adding saturated NH_4Cl solution (15 mL) and EtOAc (30 mL), extraction with EtOAc (3 x 15 ml), washing with brine (2 x 10 mL), drying over Na_2SO_4 and concentration to dryness. Column chromatography on silica gel (eluent: hexane/EtOAc 3:1 to 1:1) gave the title compound (1.36 g, 81%) as a colorless oil. ^{1}H NMR, δ: 7.26-7.29 (m, 5 H), 7.22 (d, J = 8.8 Hz, 1 H), 6.46 (m, 2 H), 5.61 (d, J = 8.2 Hz, 1 H), 5.08 (AB quart, J = 44.0, 12.1 Hz, 2 H), 4.06-3.77 (m, 10 H), 1.29 (s, 3 H), 1.17 (dt, J = 7.1, 1.1 Hz, 3 H), 1.09 (dt, J = 7.1, 1.1 Hz, 3 H), 1.08 (s, 3 H); ^{31}P NMR, δ: -1.29. Anal. Calcd for $C_{24}H_{33}O_8P$: C, 59.99; H, 6.92. Found: C, 59.92; H, 7.03.

2,4-Dimethoxybenzyl 3-Acetoxy-2,2-dimethyldihydrocinnamate (6). Acetylation of **2** with acetic anhydride under standard conditions gave **6** in 96% yield. ^{1}H NMR, δ: 7.24 (m, 6 H), 6.47 (m, 2 H), 6.02 (s, 1 H), 5.12 (s, 2 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 1.94 (s, 3 H), 1.20 (s, 3 H), 1.11 (s, 3 H); ^{13}C NMR, δ: 175.7, 169.6, 161.4, 159.2, 137.2, 131.5, 128.8, 128.1, 128.0, 127.7, 116.9, 104.1, 98.6, 79.4, 62.2, 55.6, 47.2, 22.2, 21.0, 20.1. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.30; H, 6.70.

2,4-Dimethoxybenzyl 2,2-Dimethyl-3-(trifluoroacetoxy)dihydrocinnamate (7). Trifluoroacetylation of **2** with trifluoroacetic anhydride under standard conditions gave **7** in 100% yield. ^{1}H NMR, δ: 7.26-7.34 (m, 6 H), 6.47 (m, 2 H), 6.22 (s, 1 H), 5.11 (s, 2 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 1.26 (s, 3 H), 1.13

(s, 3 H); ^{13}C NMR, δ: 174.8, 161.6, 159.3, 134.6, 131.7, 129.0, 128.4, 127.6, 116.4, 104.1, 98.7, 83.2, 62.9, 55.6, 47.4, 22.1, 19.7; ^{19}F NMR, δ: -2.83. Anal. Calcd for $C_{22}H_{23}F_3O_6$: C, 60.00; H, 5.26. Found: C, 59.86; H, 5.44.

2,4-Dimethoxybenzyl 2,2-Dimethyl-3-(diethylphosphatoxy)dihydro-*p*-methoxycinnamate (8). Prepared analogously to **5** in 73% isolated yield by condensation of **2** with p-anisaldehyde and diethyl chlorophosphate without isolation of the intermediate aldol **3**. ^{1}H NMR, δ: 7.22 (m, 3 H), 6.79 (d, J = 8.6 Hz, 1 H), 6.45 (m, 2 H), 5.56 (d, J = 8.1 Hz, 1 H), 5.08 (AB quart, J = 39.2, 12.2 Hz, 2 H), 4.0 (m, 2 H), 3.88 (m, 2 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.76 (s, 3 H), 1.33 (s, 3 H), 1.19 (dt, J = 7.1, 1.0 Hz, 3 H), 1.10 (dt, J = 7.0, 1.0 Hz, 3 H), 1.08 (s, 3 H); ^{13}C NMR, δ: 175.1, 161.0, 159.3, 158.7, 130.9, 129.0, 116.6, 113.0, 103.8, 98.3, 83.3 (d), 63.5 (t), 61.9, 55.3, 55.1, 52.1, 48.5 (d), 20.8, 20.5, 15.9 (t); ^{31}P NMR, δ: -1.25. Anal. Calcd for $C_{25}H_{35}O_9P.0.5H_2O$: C, 57.79; H, 6.98. Found: C, 58.03; H, 6.88.

General Protocol for the Oxidative Cleavage of 2,4-Dimethoxybenzyl Esters. 2,2-Dimethyl-3-(diphenylphosphatoxy)hydrocinnamic Acid (9). A solution of **4** (3.46 g, 6.0 mmol) in a mixture of MeCN and H_2O (10/1 v/v, 120 mL) was treated with CAN (7.25 g, 13.23 mmol) and the resulting mixture stirred at room temperature for 1 h. Water (200 mL) and EtOAc (100 mL) were then added and the reaction mixture extracted with EtOAc (3 x 70 mL). The combined organic extracts were concentrated to dryness. Examination by ^{1}H NMR spectroscopy indicated complete conversion of the starting ester with clean formation of the title acid and dimethoxybenzaldehyde. This mixture was taken up in EtOAc (100 mL), and shaken vigorously 15% $NaHSO_3$ (10 x 25 mL), water (15 mL) and brine (2 x 10 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The title acid (> 95% pure by ^{1}H and ^{31}P NMR spectroscopy) was obtained essentially quantitavely in this way and was used for the preparation of the PTOC ester without further purification. ^{1}H NMR, δ: 1.10 (s, 3 H), 1.28 (s, 3 H), 5.90 (d, J = 8.1 Hz, 1 H), 6.92 (d, J = 8 5 Hz, 2 H), 7.10-7.32 (m, 13 H); ^{13}C NMR, δ: 19.5, 21.9, 48.5, 85.6, 120.0, 120.1, 120.4, 120.4, 125.3, 125.5, 128.1, 128.2, 128.8, 129.8, 129.8, 135.7, 151.5, 178.5; ^{31}P NMR, δ: -12.53.

3-(Diethylphosphatoxy)-2,2-dimethyldihydrocinnamic acid (10). Prepared from ester **5** by the standard protocol. After extraction with $NaHSO_3$, the acid (> 95% purity ^{1}H and ^{31}P NMR) was obtained quantitatively and was used in the next step without further purification. ^{1}H NMR, δ: 7.35 (m, 5 H), 5.74 (d, J = 8.2 Hz, 1 H), 3.98 (m, 4 H), 1.22 (m, 6 H), 1.02 (s, 3 H), 0.98 (dt, J = 7.1, 1.0 Hz, 3 H); ^{13}C NMR, δ: 178.6, 136.5, 128.6, 128.0, 83.9 (d), 64.2 (dd), 48.2, 22.5, 18.8, 16.1 (dd); ^{31}P NMR, δ: -1.80.

3-Acetoxy-2,2-dimethyldihydrocinnamic acid (11). Prepared from ester **6** by the standard method. After extraction with $NaHSO_3$, the acid (> 95% purity ^{1}H NMR) was obtained quantitatively and was used in the next step without further purification. ^{1}H NMR, δ: 7.31 (m, 5 H), 6.06 (s, 1 H), 2.08 (s, 3 H), 1.23 (s, 3 H), 1.14 (s, 3 H); ^{13}C NMR, δ: 181.9, 169.8, 136.7, 128.3, 128.1, 127.9, 79.1, 47.1, 22.5, 21.2, 19.5.

2,2-Dimethyl-3-(trifluoroacetoxy)dihydrocinnamic acid (12). Prepared from ester **7** by the standard method. After extraction with $NaHSO_3$, the acid (> 95% purity ^{1}H NMR) was obtained quantitatively and was used for preparation of the PTOC ester without further purification. yield. ^{1}H NMR, δ: 7.30-7.39 (m, 5 H), 6.23 (s, 1 H), 1.30 (s, 3 H), 1.18 (s, 3 H); ^{13}C NMR, δ: 181.7, 181.6, 134.3, 129.3, 128.6, 127.7, 82.8, 47.2, 22.5, 19.0; ^{19}F NMR, δ: -2.91.

3-(Diethylphosphatoxy)-2,2-dimethyldihydro-*p*-methoxycinnamic acid (13). Prepared from ester **8** by the standard protocol. After extraction with $NaHSO_3$, the acid (> 95% purity ^{1}H and ^{31}P NMR) was obtained in 70% yield together with 30% of recovered substrate. It was used for preparation of the PTOC ester without further purification. ^{1}H NMR, δ: 7.26 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 5.62 (d, J = 8.1 Hz, 1 H), 4.02 (m, 2 H), 3.87 (m, 2 H), 3.78 (s, 3 H), 1.22 (s, 3 H), 1.18 (t, J = 6.9 Hz, 3 H), 1.06 (dt, J = 7.2, 0.9 Hz, 3 H), 1.04 (s, 3 H); ^{13}C NMR, δ: 179.1, 159.7, 129.4, 128.7, 113.2, 83.7 (d), 64.0, 62.2, 55.4, 48.1 (d), 22.0, 19.2, 16.0 (t); ^{31}P NMR, δ: -1.81.

General Protocol for the Formation of PTOC Esters. (1*H*)-2-Thioxo-1-pyridyl 2,2-Dimethyl-3-(diphenylphosphatoxy)dihydrocinnamate (14). To a solution of **9** (0.424 g, 1.0 mmol) and 2,2'-dipyridyl disulfide bis-*N*-oxide (0.278 g, 1.1 mmol) in dry CH_2Cl_2 (10 mL) in a flask covered with aluminum foil was added tributylphosphine (0.268 g, 1.1 mmol) at 0 °C under Ar. The reaction was stirred at room temperature for 2 h before aqueous Na_2CO_3 (10 %, 20 mL) was added. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were washed with brine (2 x 10 mL), dried (Na_2SO_4), and concentrated to dryness. Column chromatography on silica gel (eluent: hexane/EtOAc 2:1) in the dark gave the PTOC ester (0.38 g, 71 %) as a yellow solid. ^{1}H NMR, δ: 1.41 (s, 3 H), 1.42 (s, 3 H), 5.99 (d, *J* = 8.2 Hz, 1 H), 6.42 (dt, *J* = 7.0, 1.6 Hz, 1 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 7.10-7.36 (m, 14 H), 7.63 (dd, *J* = 7.4, 1.6 Hz, 1 H), 7.84 (d, *J* = 7.0 Hz, 1 H); ^{13}C NMR, δ: 17.8, 23.3, 49.5, 85.0, 112.8, 119.9, 119.9, 120.6, 125.5, 126.0, 128.3, 128.4, 129.3, 129.9, 130.0, 133.8, 134.4, 137.3, 138.9, 150.8, 170.5, 176.1; ^{31}P NMR, δ: -11.74. Anal. Calcd for $C_{28}H_{26}NO_6PS$: C, 62.80; H, 4.89. Found: C, 62.68; H, 5.10.

(1*H*)-2-Thioxo-1-pyridyl 3-(Diethylphosphatoxy)-2,2-dimethyldihydrocinnamate (15). A yellow oil prepared in 71% yield from **10** by the standard protocol. ^{1}H NMR, δ: 8.32 (d, *J* = 5.87 Hz, 1 H), 7.68 (dd, *J* = 8.8, 1.4 Hz, 1 H), 7.39 (m, 5 H), 7.19 (m, 1 H), 6.64 (dt, *J* = 6.90, 1.8 Hz, 1 H), 5.73 (d, *J* = 8.6 Hz, 1 H), 4.06 (m, 2 H), 3.80 (m, 2 H), 1.40 (s, 3 H), 1.38 (s, 3 H), 1.26 (dt, *J* = 7.1, 1.1 Hz, 3 H), 0.99 (dt, *J* = 7.1, 1.1 Hz, 3 H); ^{13}C NMR, δ: 176.5, 175.5, 171.2, 139.2, 137.3, 135.6, 133.9, 129.2, 128.3, 112.9, 83.3 (d), 65.0 (2 x d), 49.0, 23.1, 17.8, 16.5 (2 x d); ^{31}P NMR, δ: -1.46. Anal. Calcd for $C_{20}H_{26}NO_6PS$: C, 54.66; H, 5.96. Found: C, 54.59; H, 5.92.

(1*H*)-2-Thioxo-1-pyridyl 3-Acetoxy-2,2-dimethyldihydrocinnamate (16). An unstable yellow oil prepared in 55-65 % yield from **11** by the standard protocol. ^{1}H NMR, (C_6D_6) δ: 1.32 (s, 3 H), 1.36 (s, 3 H), 1.61 (s, 3 H), 5.44 (dt, *J* = 1.5, 6.6 Hz, 1 H), 5.99 (dt, *J* = 1.8, 8.7 Hz, 1 H), 6.33 (s, 1 H), 7.00 (s, 5 H), 7.08 (dd, mixed with benzene signal, 1 H), 7.39 (dd, *J* = 1.5, 9.0 Hz, 1 H); ^{13}C NMR, (C_6D_6) δ: 18.8, 20.2, 22.5, 47.3, 78.4, 110.8, 128.3, 169.5, 171.5.

(1*H*)-2-Thioxo-1-pyridyl 2,2-Dimethyl-3-Trifluoroacetoxydihydrocinnamate (17). An unstable yellow oil prepared in 55-65 % yield from **12** by the standard protocol. ^{1}H NMR, (C_6D_6): δ 1.22 (s, 3 H), 1.27 (s, 3 H), 5.38 (dt, *J* = 1.8, 6.9 Hz, 1 H), 5.99 (dt, *J* = 1.5, 8.7 Hz, 1 H), 6.29 (s, 1 H), 6.67 (dd, *J* = 1.8, 6.9 Hz, 1 H), 6.95 (s, 5 H), 7.33 (dd, *J* = 1.8, 7.2 Hz, 1 H); ^{13}C NMR, (C_6D_6) δ: 18.3, 22.7, 47.1, 82.8, 111.1, 128.3, 129.1, 132.1, 136.3, 137.4, 149.3 (the CF_3 carbon and 4 other carbons are unidentified due to diluted sample and overlapping with benzene-d_6).

(1*H*)-2-Thioxo-1-pyridyl 3-(Diethylphosphatoxy)-2,2-dimethyldihydro-p-methoxycinnamate (18). An unstable yellow oil prepared in 55-65 % yield from **13** by the standard protocol. ^{1}H NMR, δ: 1.00 (dt, *J* = 0.9, 7.2 Hz, 3 H), 1.24 (dt, *J* = 1.1, 7.0 Hz, 3 H), 1.35 (s, 3 H), 1.36 (s, 3 H), 3.72 - 3.80 (pentet, *J* = 7.5 Hz, 2 H), 3.81 (s, 3 H), 3.90 - 4.10 (m, 2 H), 5.66 (d, *J* = 8.4 Hz, 1 H), 6.62 (dt, *J* = 1.8, 7.2 Hz, 1 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 7.20 (dt, *J* = 1.5, 6.6 Hz, 1 H), 7.26 (d, *J* = 8.7 Hz, 2 H), 7.63 (dd, *J* = 1.8, 8.7 Hz, 2 H), 8.30 (d, *J* = 5.7 Hz, 1 H); ^{13}C NMR, δ: 15.7 (d, *J* = 6.7 Hz), 15.9 (d, *J* = 6.6 Hz), 17.5, 22.8, 48.6 (d, *J* = 7.7 Hz), 55.3, 64.0 (d, *J* = 5.6 Hz), 64.2 (d, *J* = 5.6 Hz), 82.6 (d, *J* = 5.5 Hz), 112.6, 113.4, 127.1, 129.2, 133.6, 137.1, 139.0, 159.9, 170.5, 175.9.

Photolysis of 14 in the Presence of *tert*-Butylmercaptan. Isolation of 2-Methyl-1-phenyl-1-propene. A solution of **14** (0.181 g, 0.34 mmol) and *tert*-butylthiol (76.7 μL, 0.68 mmol) in MeCN (10.0 mL) in a Pyrex flask was photolyzed at room temperature with a 250 W sunlamp for 1.5 h under argon. After removal of the volatiles under vacumn, ^{1}H and ^{31}P NMR spectroscopy indicated a clean reaction and complete conversion of **14** with essentially quantitative formation of diphenyl phosphate (^{31}P NMR, δ: -10.36). Purification by preparative TLC (eluent: hexane/EtOAc 10:1) gave 2-methyl-1-phenyl-1-propene (38 mg, 85%) as the major product.[38] ^{1}H NMR, δ: 7.18-7.34 (m, 5 H), 6.27 (s, 1 H), 1.91 (d, *J* = 1.2 Hz, 3 H),

1.86 (d, J = 1.2 Hz, 3 H). When the reaction was carried out with **14** (0.195 g, 0.37 mmol) and *tert*-BuSH (82.5 μL, 0.728 mmol) in benzene-d_6 (8 mL), it was not as clean as in MeCN. Nevertheless, from the ^{31}P NMR spectrum of the crude photolysate about 95% conversion of **14** to the diphenyl phosphate was observed. The ^{1}H NMR spectrum of the photolysate indicated approximately 50% formation of the alkene along with other unidentified products.

Laser Flash Photolysis studies were conducted on a modified Applied Photophysics LK-50 kinetic spectrometer using the Applied Photophysics software for instrument control and data analysis. A Spectron Nd-YAG laser operating at a nominal power rating of 40 mJ (355 nm) was used for photolysis. Hammamatsu 1P28 photomultiplier tubes and a Hewlett-Packard 54522 oscilloscope were employed. Solutions of the desired precursor with an absorbance of 0.4-0.5 at the laser wavelength were sparged with helium and thermally equilibrated in a jacketed addition funnel by circulation of a water/ethylene glycol solution from a thermally-regulated bath. For reactions conducted below 0 °C, the flow cell was positioned in a nitrogen-filled box fitted with quartz windows. The solutions were allowed to flow through a quartz flow cell with an 8 mm × 8 mm ID. Temperatures were measured with a thermocouple placed in the flowing stream approximately 1 cm above the irradiation zone. Multiple runs (5-15) at a given temperature were averaged. The observed temperature variation over the course of multiple runs was ± 0.2 °C. Observed rate constants had standard errors of 1-5%.

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