6016 J. Am. Chem. Soc. 1990, 112, 6016-6021

Photochemistry of Phosphate Esters: An Efficient Method for the Generation of Electrophiles

Richard S. Givens,* Bogdan Matuszewski, Phillip S. Athey, and M. Robert Stoner

Contribution from the Department of Chemistry, The University of Kansas, Lawrence, Kansas 66045. Received January 22, 1990

Abstract: The photochemical cleavage of benzyl diethyl phosphates, **1a–g**, has been examined in *tert*-butyl alcohol, which produces the corresponding benzyl *tert*-butyl ether as the major solvolysis product upon direct irradiation. The multiplicity of the reactive excited state has been established as the singlet state. Evidence favoring an intermediate benzyl cation–phosphate ion pair formed from photofragmentation includes oxygen-18 scrambling, racemization of chiral benzyl phosphates, and substituent effects on the rate of reaction. The existence of an electrophilic intermediate is further supported by a linear free energy relationship for the rate of disappearance of **1**, k_{dis}, with Hammett σ, which gave a ρ value of –0.90 and for the rate of appearance of **2**, k_{app}, a Hammett ρ value of –0.97. Possible mechanisms including an electron transfer either before or after homolysis or simple heterolysis of the ester bond are evaluated.

Introduction

In an earlier communication,[1] we reported our discovery that benzyl, arylmethyl, and α-keto phosphates undergo efficient photochemically induced substitution reactions. We suggested at the time that the reaction occurs by heterolytic cleavage of the carbon–oxygen bond of the aryl or α-keto ester, producing a reactive electrophile. Efficient reactions of this carbocation with a nucleophilic solvent generally produce good yields of the substitution product. Prior to this study, little was known about the photochemistry of phosphate esters.[2]

We now report that this reaction is quite general and our results indicate that a heterolysis process rationalizes not only the product distribution, but also the effects of substituents on the reaction rates and the isotopic substitution for photolyzed labeled esters.

A seminal study of the substituent effect in a photosolvolysis reaction of benzyl derivatives was reported by Zimmerman et al. in 1963[3] and serves as a model for our investigation of the substituent effects on the phosphate reaction. In 1980, Cristol and Bindel[4] reported that the photosolvolysis of benzyl chlorides in *tert*-butyl alcohol proceeds by a triplet state, which favors bond heterolysis, whereas direct irradiation proceeds by homolysis of the carbon–chlorine bond raising the question of multiplicity for our reactions as well. Recently, Pincock et al.[5] found that the proportion of homolytic versus heterolytic cleavage from photosolvolysis of various nucleofuges depended on the nature of the leaving group. For a series of 1-naphthylmethyl derivatives, a semiquantitative trend of the photofugacities was established as $^{+}S(CH_3)_2 > Cl \simeq {}^{+}N(CH_3)_3 > O_2P(OEt)_2 > O_2CCH_3 > SO_2CH_3$. Homolysis, on the other hand, followed the order $Cl > {}^{+}S(CH_3)_2 \simeq Br > {}^{+}N(CH_3)_3 > O_2P(OEt)_2 \simeq SO_2CH_3 > O_2CCH_3$.[5] These results suggest that singlet-state photosolvolysis of 1-naphthylmethyl diethyl phosphate occurs primarily by a heterolytic route rather than by homolytic cleavage, in agreement with our earlier preliminary report.[1]

While the photochemistry of phosphates has received little notice,[2,5,6] the potential for generating a reactive electrophile under a variety of conditions was inviting. We report here the details of our investigation of oxygen-18 labeling studies, substituent effects, solvent effects, multiplicity, and stereochemical studies on the photochemistry of triesters of phosphoric acid.

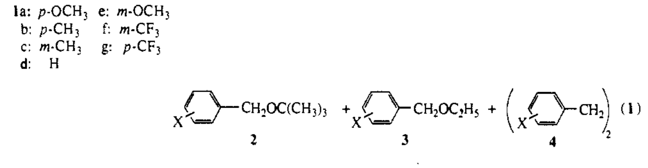
Table I. Percentage of Phosphate Conversion in Methanol and *tert*-Butyl Alcohol at 254 nm for 20 and 60 min, Respectively

ester 1		% in methanol		% in *tert*-butyl alcohol	
		irrad	control[a]	irrad	control[b]
a	*p*-OCH_3	95	88	47	0
d	H	43	0	26	0
e	*m*-OCH_3	35	0	28	0

[a] Monitored for 323 min. [b] Monitored for 12 h.

Results

Exploratory Photochemistry. A series of substituted benzyl diethyl phosphates (**1a–g**) were synthesized by a modification of known procedures.[7] Irradiation of each benzyl phosphate in *tert*-butyl alcohol resulted in the formation of a single major product, the substituted benzyl *tert*-butyl ether **2**, as determined by independent synthesis (eq 1).[3,8] *tert*-Butyl alcohol was chosen as the solvent because control studies indicated that phosphate **1a** was stable to nucleophilic substitution in the absence of light, in contrast with the situation when methanol was the solvent. Table I gives the comparison of relative photoreactivity along with control experiments for **1a**, **d**, and **e**.



In addition to **2**, minor amounts of benzyl ethyl ether **3** (<5%), arising from the loss of the elements of ethyl metaphosphate,[9] and 1,2-diphenylethane **4** (5%), a radical-derived coupling product, were isolated upon photolysis of **1d** (eq 1). Photolysis of the other substituted benzyl phosphates produced this characteristic reaction profile.

Oxygen-18 Labeled Ester. Benzyl diethyl phosphate-^{18}O (**1d**-^{18}O) was synthesized by esterification of the ^{18}O-labeled alcohol obtained by acid-catalyzed exchange of the aldehyde carbonyl of

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[2] (a) Arris, J.; Braddily, J.; Buchanan, J. G.; Thain, E. M. *J. Chem. Soc.* **1956**, 4968. (b) Clark, V. M.; Hobbs, J. B.; Hutchison, D. W. *J. Chem. Soc., Chem. Commun.* **1970**, 339. (c) Kaplan, J. H.; Forbush, B.; Hoffman, J. F. *Biochemistry* **1978**, *17*, 1929.

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[5] (a) Pincock, J. A.; Arnold, B.; Jurgens, A. *Can. J. Chem.* **1985**, *63*, 3140. (b) Pincock, J. A.; et al. *J. Am. Chem. Soc.* **1989**, *111*, 8948.

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Table II. Quantum Efficiencies of the Exchange (Φ_{exch}) of ^{18}O Label and Disappearance (Φ_{dis}) of **1d**-^{18}O during Photolysis in *n*-Butanol and Benzene at 254 nm

time	% conv	Φ_{dis} (±0.01)	excess label in $PhCH_2O^+$ obsd[a]	excess label in $PhCH_2O^+$ calcd diff[b]	% exch	Φ_{exch} (±0.02)
			In *n*-Butanol			
0	0	(0.26)[c]	9.17	2.1	0	(0.33)[c]
15 min	12	0.256	8.83	1.8	16 ± 1	0.301
30 min	22	0.235	8.56	1.5	29 ± 2	0.242
60 min	42	0.225	7.9	0.8	61 ± 5	0.189
			In Benzene[d]			
0	0	(0.030)[c]	9.17	2.1	0	(0.18)[c]
1 h	7	0.026	8.31	1.2	41	0.142
2 h	13	0.024	7.67	0.6	72	0.117
4 h	21	0.020	6.85	0.0	100	0.074
7 h	36		6.82	0.0	100	

[a] The total excess of ^{18}O of natural abundance in the ester of 14.16 ± 0.23% was determined from the integration of the mass spectral peaks between *m/e* 244 and 153. [b] The calculated difference between equilibrium of the exchanging oxygen functions (determined to be 6.8 ± 0.3%). [c] Extrapolated value. [d] >99.8% of the incident of irradiation was absorbed by benzene.

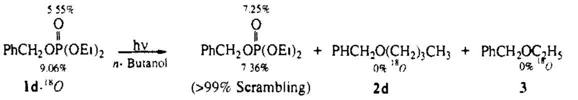
Table III. Quantum Efficiencies (Φ)[a] for Photolysis of Substituted Benzyl Esters **1a–g** at 254 nm in *tert*-Butyl Alcohol

ester 1		Φ_{dis}[b]	Φ_{app}[b]	ester 1		Φ_{dis}[b]	Φ_{app}[b]
a	*p*-OCH_3	0.42	0.14	**e**	*m*-OCH_3	0.18	0.065
b	*p*-CH_3	0.34	0.11	**f**	*m*-CF_3	0.027	(0.003)[c]
c	*m*-CH_3	0.13	0.10	**g**	*p*-CF_3	0.11	0.036
d	H	0.17	0.093				

[a] Disappearance of **1** and appearance of **2**. [b] Φ_{dis}, disappearance of **1**; Φ_{app}, appearance of **2**. [c] Experimental difficulties in analysis make this value questionable.

benzaldehyde with $H_2{}^{18}O$ followed by reduction with lithium aluminum hydride. Benzyl diethyl phosphate-^{18}O (**1d**-^{18}O) was obtained with 14.60 ± 0.73% enrichment of oxygen-18. Mass spectral analysis of the synthetic ester showed partial scrambling between the benzylic ether oxygen (9.06%) and phosphoryl oxygen (5.55%), which had occurred during the synthetic manipulations. Therefore, only 62% of the label introduced into **1d**-^{18}O was actually located at the benzylic ether position. The ester was shown to be stable in the dark to further ^{18}O scrambling.

The samples of unlabeled **1d** and oxygen-labeled **1d**-^{18}O benzyl diethyl phosphate were irradiated to 77% conversion, the products and ester were isolated, and ^{18}O distribution in the recovered ester and the two products **2d** and **3** was determined (eq 2). Quantum efficiencies for the ^{18}O-scrambling products were determined for **1d**-^{18}O in two solvents, *n*-butanol and benzene (Table II). As shown, the scrambling appears to be very efficient in both solvents. However, the efficiency of ^{18}O exchange is ~5 times more efficient in benzene than in *n*-butanol. The lower ϕ_{total} value of exchange and disappearance in benzene when compared with that in *n*-butanol is, in part, due to competitive absorption by benzene at 254 nm with concommitent inefficient singlet energy transfer. In the latter system, unlike the butanol experiments, greater than 99.8% of incident light at 254 nm was absorbed by benzene.



$$\underset{\mathbf{1d}\text{-}^{18}O}{PhCH_2\underset{9.06\%}{O}P\overset{\overset{5.55\%}{O}}{\|}(OEt)_2} \xrightarrow[n\text{-Butanol}]{h\nu} \underset{(>99\%\ \text{Scrambling})}{PhCH_2\underset{7.36\%}{O}P\overset{\overset{7.25\%}{O}}{\|}(OEt)_2} + \underset{\mathbf{2d}}{PHCH_2\underset{0\%\ ^{18}O}{O}(CH_2)_3CH_3} + \underset{\mathbf{3}}{PhCH_2\underset{0\%\ ^{18}O}{O}C_2H_5} \quad (2)$$

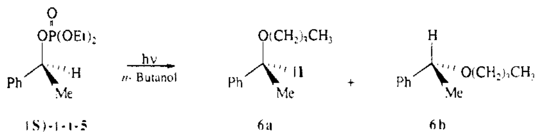
Chiral Ester. The synthesis of (*S*)-(−)-1-phenylethyl diethyl phosphate [(−)-**5**] from optically active (+)-1-phenylethanol was performed by utilizing the same procedure as for the benzyl esters **1a–g**. The optically active photoproduct, (+)-1-phenylethyl 1-butyl ether [(+)-**6**; $[\alpha]^5{}_D$ +49.8° (EtOH)], was also synthesized from (+)-1-phenylethyl alcohol (53% ee) in order to establish the chirality and enantiomeric excess of the major product from photolysis of (*S*)-(−)-1-phenylethyl diethyl phosphate [(*S*)-(−)-**5**] in *n*-butanol. Based on the optical purity of the alcohol, the maximum rotation of the optically pure ether (+)-**6** was estimated to be $[\alpha]^5{}_D$ +94.0° (EtOH), a value much higher than the previously reported value [$[\alpha]^{25}{}_D$ −53.8° (EtOH)].[10] The value obtained in this work was used for all calculations.

Table IV. Quantum Efficiencies for Quenched and Sensitized Photolysis of **1a**, **d**, and **g**

ester	sensitizer	quencher[a]	Φ_{dis}[b]	Φ_{app}[c]
1a	acetone		0.16	0.09
1a		*trans*-piperylene	0.42	0.14
1d	acetone		0.10	0.03
1g	acetone		0.03	0.0007

[a] A Corex filter was employed. [b] Φ_{dis}, disappearance of **1**. [c] Φ_{app}, appearance of **2**.

Recovered ester **5** was 28% racemized at 77% conversion. The major product, (*S*)-(−)-1-phenylethyl 1-butyl ether [(*S*)-(−)-**6a**], was formed with a small net retention of configuration (~5%) (eq 3).



(3)

Determination of Quantum Efficiencies, Multiplicity, and Rate Constants. The quantum efficiencies for appearance of the benzyl *tert*-butyl ethers and for disappearance of the phosphates were determined by GLC analysis of aliquots taken at regular time intervals from samples irradiated in a Rayonet merry-go-round apparatus fitted with 4 × 2537 Å lamps (Table III). The light output was determined by ferrioxalate actinometry.[11] The *p*-methoxybenzyl ester, **1a**, proved to be the most reactive whereas the *m*- and *p*-(trifluoromethyl)benzyl esters, **1f** and **1g**, were the least reactive.

The multiplicity of the excited state was determined by sensitization and quenching experiments. Sensitization studies have generally proven to be difficult with benzyl esters because few useful triplet sensitizers are known that have sufficiently high energies for efficient energy transfer to these monosubstituted aromatics (E_T ~80 kcal/mol).[5] Acetone sensitization of **1a**, **d**, and **g** at a sufficiently high acetone concentration (0.6 M) in *tert*-butyl alcohol assured minimal competitive absorption by the aromatic chromophore while providing an adequately high triplet energy (E_T = 78 kcal/mol). In each case, the benzyl *tert*-butyl ethers were formed but at substantially lower efficiencies (Table IV), indicating only modest triplet reactivity.

Attempted quenching of **1a** with *trans*-piperylene at concentrations even as high as 0.14 mmol resulted in no diminution in the efficiency of phosphate disappearance or ether appearance. At this concentration of piperylene, quenching would be observed if as much as 10% reaction proceeded by way of a triplet state with a modest lifetime of 4.0 × 10^{-10} s. In addition, we[1] and Pincock[5] have shown that the corresponding naphthylmethyl phosphates can neither be sensitized nor be efficiently quenched, indicating essentially *no* triplet reactivity upon direct irradiated. Thus, the photosolvolysis of the benzyl phosphate esters are judged to proceed via the singlet manifold.

The rate constants for the singlet-state reactions were derived from a combined study of the reaction efficiencies and the fluorescence lifetime, i.e., through the relationship

$$\Phi_r = k_r \tau_S \quad (4)$$

Equation 4 relates the rate constant for the reaction, k_r, with the fluorescence lifetimes, τ_S, and the reaction efficiency, ϕ_r. The singlet lifetimes were determined directly in ethanol with an SLM Aminco Model 4800 polarization/subnanosecond lifetime spectrofluorometer and were used to obtain the rate constants for the

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(10) Kenyon, J.; Philips, H.; Taylor, F. M. H. *J. Chem. Soc.* **1933**, 173.

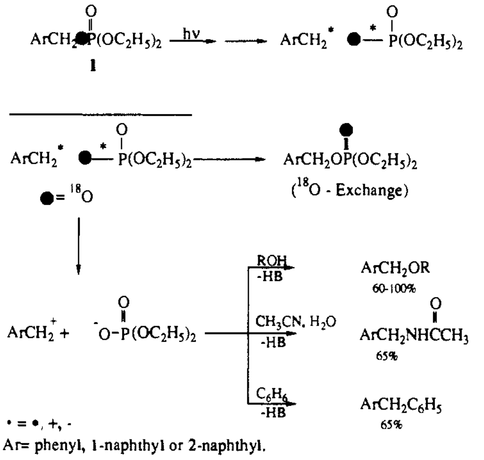
(11) Hatchard, C. G.; Parker, C. A. *Proc. R. Soc. London* **1956**, *A220*, 518.

Table V. Singlet Fluorescence Efficiencies, Lifetimes, and Rate Constants[a] for the Disappearance of **1a–g** and Their Product Appearance

ester 1		τ_S,[b] ns	$10^6 k_{dis}$, s^{-1}	$10^6 k_{app}$, s^{-1}	Φ_f[c]
a	*p*-OCH$_3$	4.2	100	33	0.19
b	*p*-CH$_3$	5.9	58	19	0.134
c	*m*-CH$_3$	6.9	19	15	0.045
d	H	2.5	67	37	0.048
e	*m*-OCH$_3$	4.9	37	13	0.027
f	*m*-CF$_3$	1.2	23	28	0.088
g	*p*-CF$_3$	6.7	16	5	0.09

[a] Rate constants (k_{app} and k_{dis}) were determined from the relationship $k_r = \Phi_r/\tau_S$ (τ_S, singlet-state fluorescence lifetimes). [b] Lifetimes were determined in ethanol with a SLM Aminco Lifetime spectrofluorometer. [c] Fluorescence efficiencies were determined in cyclohexane at 265 nm.

Scheme I. Photochemistry of Arylmethyl Esters

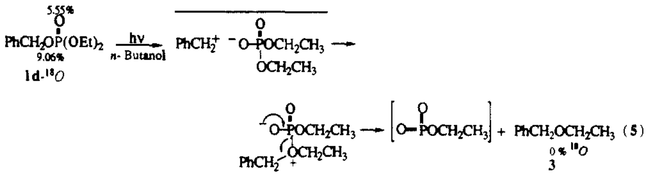


product appearance and reactant disappearance (Table V).

Discussion

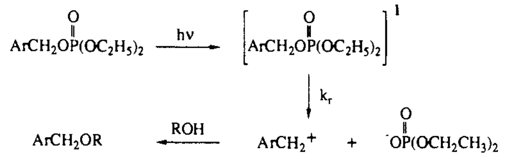
Early studies[2] on the photochemistry of phosphate esters were centered on the phosphate group as the absorbing chromophore. A number of years ago, we[12] embarked on the study of esters, including phosphates, in which the absorbing chromophore was one atom removed from the ester function. Unlike most of our studies on carbon or sulfur analogues, the phosphates gave primarily products resulting from nucleophilic substitution rather than free-radical reactions. Our current study, which we report here, has been directed toward understanding the nature of the photochemical process, the mechanism for the bond cleavage reaction, and the nature of the electrophilic benzyl cation intermediate.

The general photoreaction for benzyl phosphates is shown in Scheme I. Photolysis produces two major solvolysis products, i.e., solvent substitution for the leaving phosphate group, and diethyl phosphoric acid along with some polymeric material. One minor product, benzyl ethyl ether, was also identified when the reaction was carried out in alcoholic solvents other than ethanol. This may be a product of the extrusion of ethyl metaphosphate, as indicated in eq 5.

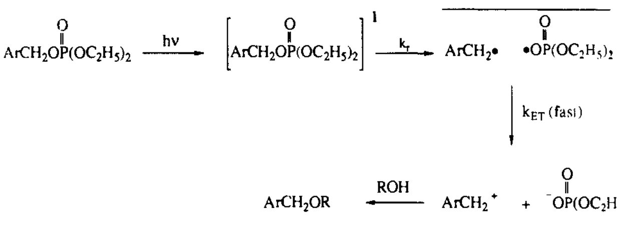


Our studies on the mechanism of triesters of phosphoric acid have considered the three possible routes outlined in Schemes II and III. In each mechanism, the penultimate intermediate is an electron-deficient benzyl cation paired with the departing phosphate ion.

Scheme II



Scheme III

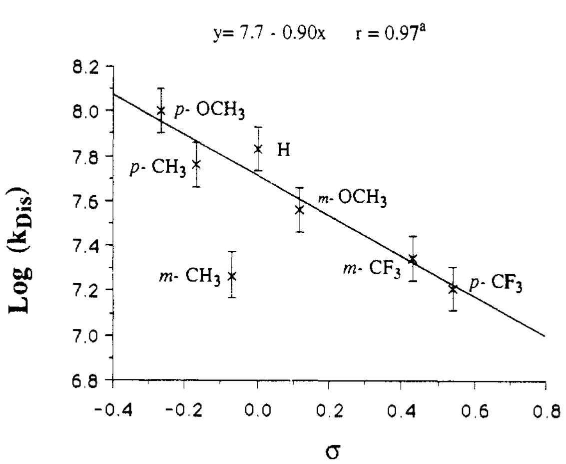


k$_{ET}$ = rate of electron transfer

Table VI. Correlation Coefficients (r) Derived from the Plot of Hammett Parameters versus log k_{dis} and log k_{app} (see Figures 1 and 2)

	r[a]	r[b]
σ	0.97	0.96
σ^+	0.81	0.84
σ^{ex}	0.72	0.90

[a] Based on the rate of disappearance of **1**. [b] Based on the rate of appearance of **2**.



a) *m*- CH$_3$ omitted. b) The error bars = ± 10 %.

Figure 1. log k_{dis} of **1** versus Hammett σ.

To elucidate the mechanism for the formation of the benzyl cation, we examined the substituent effects on the rate constant for the formation of products, which were correlated with Hammett σ values, applying the typical linear free energy approach for carbocation reactivity. The sensitivity constant (ρ) obtained from the correlation of rate constants for ester disappearance with σ also probed the nature of the fragmentation process.

Since the photosolvolysis result reported in this study involves a carbon–oxygen bond cleavage on an excited surface, it was anticipated that the transition state would be relatively nonpolar, that is, an early transition state. Therefore, the linear free energy correlation obtained from the photolysis of **1** should yield a small ρ value, on the order of −0.1 to −0.2. On the other hand, a more polar transition state such as that expected for a late transition state would be expected to yield a ρ of a greater magnitude, on the order of <−1.0, typically observed for ground-state heterolysis reactions. The latter is most frequently reported for ionization reactions in which the developing charge is in direct conjugation with the substituent on the aromatic ring. Indeed, in the extreme,

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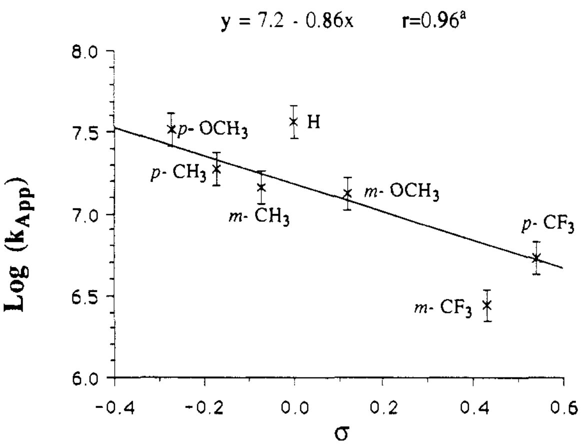
[12] Givens, R. S.; Matuszewski, B.; Levi, N.; Leung, D. *J. Am. Chem. Soc.* **1977**, *99*, 1896.



a) H and *m*- CF$_3$ omitted b) The error bars = ± 10 %.

Figure 2. log k_{app} of **2** versus Hammett σ.

direct conjugation would be better modeled by an Okomoto–Brown σ^+ relationship.[13]

In this study, we attempted LFER correlations with σ, σ^+, and σ^{ex} (Table VI). Our best fit was with Hammett σ, which gave ρ values of −0.90 ($r = 0.97$) and −0.86 ($r = 0.96$) for k_{dis} and k_{app}, respectively (see Figures 1 and 2). The extent to which the ground-state substituent values, σ, accurately represent the excited-state reaction is debatable. Indeed, attempts to fit our measured rate constants with the empirically derived excited-state parameter of Baldry,[15] σ^{ex}, gave a much poorer correlation ($r = 0.72$).

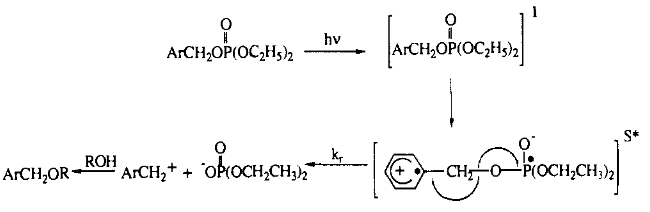
On the other hand, the values for ρ are intermediate between the two models given above, being somewhat smaller than the known heterolytic processes and considerably larger than those seen with nonpolar homolytic processes. We ascribe the smaller values to the low degree of bond breaking at an "early" transition state, as noted earlier in the evaluation of the suitability of various substituent models. These Hammett correlations were carried out using rate constants determined from the quantum efficiencies for disappearance of phosphate and appearance of product, which were not corrected for ion-pair return (vide infra).

The results of the ^{18}O-labeling experiments indicated that the scrambling of ^{18}O was essentially complete at 77% conversion, which is qualitatively consistent with the photoracemization of the chiral ester (*S*)-(−)-**5**. However, the oxygen-scrambling reaction of **1d**-^{18}O is more efficient than the racemization of the chiral ester (*S*)-(−)-**5**.

It is noteworthy that when labeled ester was irradiated no ^{18}O was incorporated in the substitution product (**2d**), clearly indicating that the ether oxygen in this product originated with the nucleophilic solvent. Likewise, no ^{18}O incorporation was found in the minor substitution product **3**. That this product could be formed through an intramolecular fragmentation followed by extrusion of "ethyl metaphosphate" (eq 5) is consistent with the absence of ^{18}O in ethyl ether **3**. These observations confirm the determination from mass spectral data that the label in the phosphate ester is located in either the arylmethyl ether or the phosphoryl position and not in the remaining two ethyl ether positions.

An overall mechanistic picture that may be constructed from these studies suggests that the rate-determining step is cleavage directly from the singlet excited state to an ion pair with rate constant k_r, as shown in Scheme II. The homolytic cleavage mechanism to a radical pair, formed directly from the singlet excited state of the phosphate, which subsequently undergoes a rapid electron transfer to the ion pair (Scheme III), poses a second, less likely alternative. Rate-determining homolysis would require a polar activated complex to explain the large magnitude of the ρ value observed in our study. In this mechanism, the final product mixture requires that electron transfer leading to the benzyl ethers be much more efficient than diffusion of the radical pair to yield the minor bibenzyl products.

Scheme IV



An alternative charge-transfer mechanism (Scheme IV) in which the singlet excited state undergoes rapid intramolecular electron transfer to a charge-transfer state (CTI) is also possible. The CTI then suffers homolytic cleavage, forming the benzyl cation. This mechanism is kinetically indistinguishable from the mechanism in Scheme I and cannot be ruled out at this time.

In each of these mechanisms, the process of recombination of the ion pair to the original benzyl diethyl phosphate **1** would be expected to compete with solvolytic reactions. Indeed, that recombination is an important pathway was demonstrated by scrambling of ^{18}O-labeled **1d** upon irradiation in *n*-butanol, ($\Phi_{recombination} = 0.29$; $\Phi_{ether} = 0.23$). While the extent of recombination in *tert*-butyl alcohol was not determined, it is reasonable to expect similar results. Accordingly, the measured quantum efficiencies for product formation and for disappearance of **1** do not account for the entire chemical process. In evaluating the linear free energy relationship for the rate of disappearance of **1**, as in Figure 1, it has been assumed that the ratio of recombination and product formation from the ion pair is a constant for the series of the benzyl derivatives of **1**. In other words, the relative selectivity for nucleophilic attack by phosphate ion or *tert*-butyl alcohol is assumed to be insensitive to the nature of the aryl substituent.

Even when the competing recombination process is taken into account, these results favor a singlet-state heterolytic process to the ion pair. These results confirm our earlier assertion that the photochemistry of arylmethyl phosphates proceeds through ionic intermediates, which contrasts with most of the other nucleofugal groups that have been the object of photosolvolysis studies. The high yield of products from electrophile generated in these photolysis reactions has encouraged further studies on phosphate ester photochemistry for photoinitiation and photoprotecting group applications and will be reported at a later date.

Experimental Section

General Methods. A Varian 1400 (with a CDS 111 integrator) or a Varian 3300 gas chromatograph (capillary column, with a Varian 4270 integrator) was used for the assays of **1a–e,g** and a Shimadzu GC-9AM (with a Shimadzu Chromatopic integrator) was used for **1b,f** and the quenching photolysis of **1a**. Four columns were used for the assays: a 0.125 in. by 6 ft 10% Carbowax 20M on Chromosorb W for **1d**; a 0.125 in. by 6 ft 10% SE30 on Chromosorb W for **1c,e,g**; a 25QC2/SE30 capillary column (0.22 mm × 25 m) for **1a**; and an Altech RS2-150 (15 m × 0.53 mm) microbore column for **1b,f**. In each case temperature programs were utilized: 90 °C (3 min), 90–190 °C at 10 °C/min, 90 °C (5 min) for **1a**; 120–220 °C, 220 °C at 10 °C/min (5 min) for **1b,f**; 50–180 °C, 180 °C at 8 °C/min (5 min) for **1c,e,g**; 50–180 °C, 180 °C at 8 °C/min (9 min) for **1d**.

Proton magnetic resonance spectra were determined for deuterated chloroform solutions with TMS as the internal standard on a Varian EM-360 or XL-300 spectrometer. IR spectra were obtained on a Beckman Acculab 3 IR. The elemental analysis were performed at the University of Kansas in the Medicinal Chemistry Department. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. GC–MS was obtained with a DB1 capillary column eluting into a Nermag R 10-10C mass spectrometer. Irradiations were carried out with a Rayonet photochemical reactor equipped with a merry-go-round sample holder. Either 4 RPR 254-nm or 16 RPR 300-nm lamps were used. Actinometry was accomplished by the potassium

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[13] Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.

[14] Russell, G. A. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 1, p 295.

[15] Baldry, P. J. *J. Chem. Soc., Perkin Trans. 2* **1979**, 951.

ferrioxalate method of Hatchard and Parker.[11]

Pyridine was distilled and stored over KOH. *tert*-Butyl alcohol and acetone were Fischer Certified grade and were distilled and stored over 4-Å molecular sieves. Diethyl chlorophosphate used in the preparation of the phosphate esters was used without further purification. *trans*-Piperylene was passed through a small alumina column (0.5 cm × 5 cm) immediately before use.

(A) Syntheses. Synthesis of Benzyl *tert*-Butyl Ethers.[4b,16] The ethers were synthesized either by acid-catalyzed dehydration of the two alcohols (ethers **2a,e–g**) or by the Williamson method[8a] (ethers **2a,c,e**). All were purified by distillation followed by flash chromatography.

(+)-1-Phenylethyl *n*-Butyl Ether [(+)-6]. The Williamson synthesis, similar to that described by Kenyon and co-authors,[10] was employed. The workup procedure was modified and the unreacted alcohol was separated from the reaction mixture by column chromatography. Optically active (+)-1-phenylethyl alcohol (95% pure by GLC) was obtained by resolution of the racemic material using the procedure described previously.[10] From the optical rotation, $[\alpha]^{25}_{D}$ +24.1° (c = 2.42, MeOH), the optical purity of the 1-phenylethanol was determined to be 53% based on $[\alpha]_D$ −45.5° for the (−)-enantiomer.[17] (+)-1-Phenylethanol (0.5067 g, 4.15 mmol) was mixed with 0.16 g (4.09 mol) of potassium in 5 mL of anhydrous diethyl ether for several hours until potassium metal had mostly disappeared. Next, 0.4261 g (3.11 mmol) of *n*-butyl bromide was added and the mixture refluxed for 2 h. The solution was then washed with 20 mL of 2% HCl, the ether layer was separated, washed with water and brine, and dried, and the residue obtained after evaporation of the solvent was chromatographed on a silica gel (SilicAR CC-7, 1.5 × 50 cm column, fraction volume 25 mL) giving in fractions 10–19 (1–3% ether–hexane) 112.7 mg (20% isolated yield) of (+)-1-phenylethyl 1-butyl ether [(+)-**6**], 99.9% pure by GLC, and 131.9 mg (1.08 × 10^{-3} mol) of unreacted (+)-1-phenylethanol with the same optical rotation as the starting material in fractions 37–41 (20% ether–hexane). NMR and IR spectra of (+)-**6** were identical with the racemic **6** isolated from the photolysis of 1-phenylethyl diethyl phosphate (**5**) in *tert*-butyl alcohol. Optical rotations for (+)-**6** were $[\alpha]^{25}_{D}$ +55.1° (c = 1.073, ether) and +49.8° (c = 1.133, absolute ethanol). Assuming the complete retention at the chiral carbon during the ether synthesis, the optical rotation of (+)-**6** obtained in this work corresponds to 53% optical purity. Therefore, the material with 100% optical purity should exhibit the optical rotation $[\alpha]^{25}_{D}$ +94.0° (EtOH). This contrasts with the report by Kenyon et al., who found that (−)-**6** obtained from (−)-1-phenylethanol had a rotation of −53.8°.[10] In fact, the optical purity of their product must be less than 57%. Apparently extensive racemization occurred during the synthesis. The optical rotation $[\alpha]^{25}_{D}$ +94.0° (EtOH) for optically pure (+)-**6**, which we obtained from our synthesis, was used for the calculation of the optical purity of (−)-**6** obtained during photolysis of phosphate (*S*)-(−)-**5** in *n*-butanol.

Synthesis of Substituted Benzyl Diethyl Phosphates. The substituted benzyl diethyl phosphates used in the study were prepared by previously reported methods.[7] The general procedure is illustrated by the preparation of phospate **1d**.

Benzyl Diethyl Phosphate (1d). A 50-mL three-necked flask was fitted with an addition funnel, a mechanical stirrer, and a thermometer. Benzyl alcohol (3.24 g, 30 mmol) and 4.03 g (51 mmol) of pyridine were mixed and the solution was cooled to 0 °C; 5.18 g (30 mmol) of diethyl chlorophosphate was added slowly over the course of 2 h so that the temperature never exceeded 5 °C. The solution was then stirred an additional 4 h at 0 °C. Water (50 mL) was added and the mixture extracted with ether (3 × 50 mL). The organic layer was washed with 1 N H_2SO_4 (2 × 50 mL), 5% sodium bicarbonate (1 × 50 mL), water (3 × 50 mL), and brine (1 × 50 mL), dried over $MgSO_4$, and filtered. Removal of the ether and distillation under reduced pressure gave 4.2 g (45% yield) of benzyl diethyl phosphate: ^{1}H NMR ($CDCl_3$) δ 1.3 (t, J = 7.5 Hz, 6 H), 3.97 (m, J = 7.5 Hz, 4 H), 4.95 (d, J = 8.5 Hz, 2 H), 7.3 (s, 5 H); mass spectrum, m/e (rel intensity) 246 (2.2), 245 (15.6), 244 (29.2), 215 (15.5), 188 (15.7), 187 (24.7), 153 (10.3), 125 (25.9), 107 (78.6), 91 (100). Anal. Calcd for $C_{11}H_{17}PO_4$: C, 54.10; H, 7.02. Found C, 54.40; H, 7.20.

***p*-Methoxybenzyl Diethyl Phosphate (1a).**[8c] By use of the same procedure as for **1d**, 2.03 g (12 mmol) of diethyl chlorophosphate was added to a solution containing 1.47 g (19 mmol) of pyridine and 1.51 g (10.9 mmol) of *p*-methoxybenzyl alcohol. The aqueous workup was omitted. The crude reaction mixture was purified directly by flash chromatography. A second flash chromatography was performed for final purification to yield *p*-methoxybenzyl diethyl phosphate (**1a**): 0.96 g (48%); ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.5 Hz, 6 H), 3.7 (s, 3 H), 3.9 (m, J = 7.5 Hz, 4 H), 4.9 (d, J = 8.5 Hz, 2 H) 6.8 (d, 2 H), 7.3 (d, 2 H); mass spectrum, m/e (rel intensity) 274 (17), 245 (21), 217 (11), 137 (30), 121 (100), 91 (27).

***p*-Methylbenzyl Diethyl Phosphate (1b).** By use of the procedure for **1d**, a solution of 1.52 g (12.5 mmol) of *p*-methylbenzyl alcohol and 1.96 g (24.7 mmol) of pyridine was reacted with 2.38 g (13.8 mmol) of diethyl chlorophosphate. The product was purified by silica gel flash chromatography to yield 2.1 g (66%) of *p*-methylbenzyl diethyl phosphate (**1b**): ^{1}H NMR ($CDCl_3$) δ 1.3 (t, J = 7.5 Hz, 6 H), 2.3 (s), 4.0 (m, J = 7.5 Hz, 4 H), 4.9 (d, J = 8.5 Hz, 2 H), 7.5 (m, 4 H); mass spectrum, m/e (rel intensity) 258 (22), 229 (25), 201 (35), 132 (35), 121 (88), 105 (100), 91 (55). Anal. Calcd for $C_{12}H_{19}O_4P$: C, 55.81; H, 7.42. Found: C, 55.28; H, 7.50.

***m*-Methylbenzyl Diethyl Phosphte (1c).** Phosphate **1c** was obtained in 59% yield from the reaction of 2.50 g (20.5 mmol) of *m*-methylbenzyl alcohol using the same procedure used for **1a** or **1d**. The phosphate ester was purified by silica gel flash chromatography: ^{1}H NMR (CCl_4) δ 1.27 (t, J = 7.5 Hz, 6 H), 2.37 (s, 3 H), 4.00 (m, J = 7.5 Hz, 4 H), 4.92 (d, J = 8.5 Hz, 2 H), 7.16 (m, 4 H); mass spectrum, m/e (rel intensity) 258 (27), 132 (48), 121 (100), 105 (97), 104 (57), 81 (45), 77 (54). Anal. Calcd for $C_{12}H_{19}O_4P$: C, 55.81; H, 7.42. Found: C, 55.61; H, 7.50.

***m*-Methoxybenzyl Diethyl Phosphate (1e).**[8c] Phosphate **1e** was prepared by the procedure used for **1d** or **1a** in 55.5% yield from 3.46 g (25 mmol) of *m*-methoxybenzyl alcohol. The product was purified by silica gel flash chromatography: ^{1}H NMR (CCl_4) δ 1.27 (t, J = 7.5 Hz, 6 H), 3.80 (s, 3 H)8 4.00 (m, J = 7.5 Hz, 4 H), 4.93 (d, J = 8.5 Hz, 2 H), 6.7–7.3 (m, 4 H); mass spectrum, m/e (rel intensity) 274 (39), 245 (12), 217 (15), 137 (42), 121 (100), 91 (53).

***m*-(Trifluoromethyl)benzyl Diethyl Phosphate (1f).** By use of the procedure for **1d**, a solution of 1.02 g (5.8 mmol) of *m*-(trifluoromethyl)benzyl alcohol and 0.956 g (12.1 mmol) of pyridine was reacted with 0.84 g (4.9 mmol) of diethyl chlorophosphate. The product was purified by silica gel flash chromatography to yield 0.563 g (38%) of *m*-(trifluoromethyl)benzyl diethyl chlorophosphate (**1f**): ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 6 H), 4.05 (m, 4 H), 5.05 (d, 2 H), 7.4–7.7 (m, 4 H); mass spectrum, m/e (rel intensity) 313 (10), 312 (16), 236 (33), 175 (83), 159 (100), 125 (54), 109 (33), 82 (40). Anal. Calcd for $C_{12}H_{16}F_3O_4P$: C, 46.16; H, 5.17. Found: C, 45.80; H, 5.30.

***p*-(Trifluoromethyl)benzyl Diethyl Phosphate (1g).** The same procedure was followed that was employed for **1d**. A solution containing 1.17 g (6.66 mmol) of *p*-(trifluoromethyl)benzyl alcohol and 1.05 g (13.3 mmol) of pyridine was cooled to 0 °C before 1.14 g of (6.66 mmol) of diethyl chlorophosphate was slowly added. The compound was purified by flash chromatography on silica gel. A yield of 1.51 g (72%) of *p*-(trifluoromethyl)benzyl diethyl phosphate was achieved: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.5 Hz, 6 H), 4.0 (m, J = 7.5 Hz, 4 H), 5.0 (d, J = 8.5 Hz, 2 H), 7.5 (m, 4 H); mass spectrum, m/e (rel intensity) 312 (10), 175 (100), 159 (77), 145 (55), 125 (78). Anal. Calcd for $C_{12}H_{16}F_3O_4P$: C, 46.16; H, 5.17. Found: C, 45.88; H, 5.30.

Benzyl Alcohol-^{18}*O*. The labeled compound was synthesized by $LiAlH_4$ reduction of the labeled aldehyde, according to the method described previously.[12] The benzaldehyde, was reacted with a 1.5 g of 97.5% ^{18}O-enriched water (Isotec, Inc.). Benzyl alcohol-^{18}*O*, 710 mg (86%), with 16.24% enrichment was obtained from 813 mg (7.66 mmol) of benzaldehyde.

Benzyl Diethyl Phosphate-^{18}*O* (1d-^{18}*O*). The ester was prepared from the ^{18}O-labeled alcohol by using the same general method of synthesis described previously by reaction of diethyl chlorophosphate and the alcohol in the pyridine solution at 0 °C. From 448.8 mg (4.16 × 10^{-3} mol) of benzyl alcohol-^{18}*O* (16.237% ^{18}O enrichment) was obtained 736.3 mg (73%) of crude **1d**-^{18}*O*, 98.6% pure by GLC. This material (710 mg) was chromatographed on silica gel column (SilicAR CC-7, 1.5 × 45 cm, fraction volume 50 mL) giving in fractions 29–40 (60–80% ether–hexane) 612 mg (61%) of **1d**-^{18}*O*, >99.9% pure by GLC. The total ^{18}O content of the ester was calculated from the intensities of the mass spectral peaks in the molecular ion peak region (m/e 244). It was also possible to determine the ^{18}O content in the $PhCH_2O^+$ (m/e 107) and $^+OP(O)(OEt)_2$ (m/e 153) fragments. The total ^{18}O enrichment in **1d**-^{18}*O* was 15.02% or 14.19% based on the analysis of the molecular ion (m/e 244) or the fragment (m/e 153) peak regions. The ^{18}O enrichment in the $PhCH_2O^+$ fragment was calculated to be equal to 9.06%, indicating that not all of the oxygen-18 incorporated into **1d**-^{18}*O* was preserved in the ether (C—O—P) position but was substantially scrambled during the synthesis. The remaining amount of the label (5.548 ± 0.729%) was in the P═O position in the ester molecule.

(B) Photochemistry. Direct Photolysis of Phosphates 1a–g in *tert*-Butyl Alcohol. A solution containing 0.4 mmol of the phosphate and the appropriate internal standard (*n*-heptadecane for **1a,b,d,e** and *n*-pentadecane for **1c,f,g**) in 10 mL of *tert*-butyl alcohol was placed in a quartz tube. The solution was degassed for 15–20 min with nitrogen, followed

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Table VII. Specific Rotations and Optical Purity ($[\alpha]^{25}$) for (*S*)-(−)-**1**-Phenylethyl Diethyl Phosphate [(*S*)-(−)-**5**] and (*S*)-(−)-**1**-Phenylethyl *n*-Butyl Ether [(*S*)-(−)-**6**] Before and After Photolysis

	concn, g/100 mL	specific rotation, deg 589 nm	546 nm	436 nm	% opt purity
ester (*S*)-(−)-**5**					
before irrad	1.267[a]	39.7	46.9	83.0	87[b]
after irrad	1.240[a]	28.5	34.1	59.6	62
ether (*S*)-(−)-**6**					
after irrad	0.840[c]	4.1	5.5	8.5	4.4[d]

[a] In ether. [b] Based on $[\alpha]_{589}$ −45.9° (ether) for optically pure (*S*)-(−)-**5**. This value was calculated from the $[\alpha]_{589}$ −41.3° for (*S*)-(−)-**5** obtained after synthesis from 90% optically pure (*S*)-(−)-**1**-phenylethyl alcohol. In absolute ethanol. [d] Based on $[\alpha]_{589}$ +94.0° (absolute ethanol) calculated for optically pure (+)-enantiomer from ethers synthesized in this work (see Experimental Section).

by irradiation with four RPR 254-nm lamps. Throughout the photolysis, aliquots of ca. 0.10 mL were removed with a syringe at regular intervals, stored in the cold, and analyzed by GLC. Relative response factors for the *tert*-butyl ethers and the phosphates were determined from standard solutions of known concentrations. Quantum efficiencies were determined by a regression analysis with light outputs from potassium ferrioxalate actinometry.[11] Results are given in Table III.

Photolysis of (*S*)-(−)-5 in *n*-Butanol. A solution of 202.6 mg (0.785 mmol) of (*S*)-(−)-1-phenylethyl diethyl phosphate [(*S*)-(−)-**5**, 87% optically pure] in 15 mL of *n*-butanol was placed in a quartz tube, degassed with nitrogen, and irradiated for 220 min with 16 RPR 2537-Å lamps. GLC analysis showed ~77% conversion. After careful removal of solvent the residue was chromatographed on silica gel (SilicAR CC-7, 1.5 × 30 cm column, fraction volume 25 mL) giving in fractions 1–10 (hexane) 37.9 mg of mostly main product (*S*)-(−)-**6**, and in fractions 48–56 (60–70% ether–hexane) 45.5 mg of starting phosphate (77% conversion). The remainder, approximately 50% at this high coversion, was elimination products or polymers. The material from fractions 1–10 was purified further by silica gel chromatography (1 × 10 cm column, fraction volume 10 mL) giving in fraction 14 (1% ether–hexane) 19.3 mg of (*S*)-(−)-**6** (18% isolated yield). The specific rotations of the major product (*S*)-(−)-**6** and of the recovered (*S*)-(−)-**5** were measured in ethanol and ether, respectively, and the results are shown in Table VII.

Quantum Yield of Oxygen-18 Exchange of 1d-^{18}*O*. Solutions of approximately the same concentration of the unlabeled and oxygen-18 labeled ester, each in 10 mL of solvent, were placed in quartz tubes, degassed with nitrogen, and irradiated with four RPR 2537-Å lamps. Light output was monitored by potassium ferrioxalate actinometry.[11] Aliquots of unlabeled ester were removed at intervals and analyzed by GLC, using cyclodecane as an internal standard. The results of at least five GLC analyses were averaged and are given. The aliquots of the unlabeled and labeled ester were removed next from the irradiated tubes, both before and after partial photolysis, and were subjected to GC–MS analysis. The ^{18}O content in the ester and in the $PhCH_2O^+$ fragment region was calculated as described previously. The total ^{18}O content in the labeled ester before photolysis and recovered after irradiation remained essentially the same. However, the excess of ^{18}O in the $PhCH_2O^+$ fragment decreased steadily with time of irradiation. From these data, the percent scrambling of ^{18}O label was calculated at various irradiation times (or percent conversion) of the ester. The results obtained during irradiation in *n*-butanol are shown in Table II. The concentration of the ester with the scrambled label and the quantum yields of scrambling at different ester conversions were calculated from the amount of the ester remaining in the irradiated mixture and percent scrambling. These results are presented in Table II. Extrapolation of these values to 0% conversion gave the desired quantum efficiency of scrambling (ϕ_{scramb}). Quantum yields of **1d**-^{18}*O* disappearance for photolysis in *n*-butanol were also measured and are given in Table II. The following samples were used:

In *n*-Butanol. Two samples were prepared: a solution of 80.4 mg (0.330 mmol) of **1d**-^{18}*O* and 83.4 mg (0.342 mmol) of **1**, each in 10 mL of *n*-butanol. Cyclodecane (30.8 mg) was added to the sample with unlabeled ester **1**. Aliquots were removed before and after 15, 30, and 60 min of irradiation and analyzed as described previously. Light output was measured as equal to 0.616 ± 0.010 meinstein/h. The results are presented in Table **II**.

In Benzene. Solutions of 56.0 mg (0.230 mmol) of **1**-^{18}*O* and 56.5 mg (0.232 mmol) of unlabeled **1**, containing 28.5 mg (0.204 mmol) and 29.8 mg (0.213 mmol) of cyclodecane, respectively, each in 10 mL of benzene, were degassed and irradiated. Aliquots were removed before and after 1, 2, 4, and 7 h of photolysis and analyzed as before. Light output was measured as in *n*-butanol. The results are presented in Table II. Here, the scrambling was much faster than ester disappearance.

Acetone-Sensitized Photolysis of Phosphates 1a,d,g in *tert*-Butyl Alcohol. Solutions of phosphates **1a**,**d**, and **g** were prepared as in the direct photolysis except that acetone was added. Relative concentrations of the esters and acetone were chosen such that greater than 90% of the light would be absorbed by the acetone. A parallel set of phosphate ester solutions without sensitizer was also prepared. The solutions were placed in Pyrex tubes, degassed with nitrogen for 15 min, and then irradiated with 16 RPR 300-nm lamps. Quantum efficiencies were determined from analyses of aliquots taken at regular intervals. Analysis of the three directly irradiated samples in the control study showed no sign of ether formation for phosphates **1d** and **1g**. However, for phosphate **1a**, a conversion of 2% of the phosphate to the ether was noted. This was well below the conversion noted in the sensitized run for the same time interval. Results are given in Table IV.

Quenching of Phosphate 1a. A stock solution was prepared containing 1.64 mmol of phosphate **1a** and 0.5933 mmol of *n*-heptadecane diluted to 5 mL with *tert*-butyl alcohol (stock solution A). A second stock solution was prepared containing 13.7 mmol of *trans*-piperylene diluted to 10 mL with *tert*-butyl alcohol (stock solution B). A third stock solution was prepared containing 9.48 mmol of acetophenone diluted to 25 mL with *tert*-butyl alcohol (stock solution C). Pyrex tube 1 contained 1 mL of stock solution A (0.328 mmol of **1a**), 0.2 mL of solution B (0.273 mmol of *trans*-piperylene), and 1.8 mL of *tert*-butyl alcohol. Pyrex tube 2 contained 0.2 mL of solution B (0.273 mmol of *trans*-piperylene) and 2.8 mL of *tert*-butyl alcohol. Pyrex tube 3 contained 1 mL of solution A (0.328 mmol of **1a**) and 2 mL of *tert*-butyl alcohol. Pyrex tube 4 contained 0.2 mL of solution B (0.273 mmol of *trans*-piperylene), 1 mL of solution C (0.379 mmol of acetophenone), and 1.8 mL of *tert*-butyl alcohol. The four Pyrex tubes each containing a total of 3.0 mL were degassed with N_2 for 5.0 min and irradiated in a Hanovia medium-pressure merry-go-round apparatus fitted with a Corex filter. Aliquots were removed at 0, 60, 210, 384, 744, and 2130 min and analyzed on the Shimadzu GC-9AM. Results are given in Table IV.

Determination of Lifetimes τ. The lifetimes of the phosphates **1a**,**d**,**f**, and **g** were measured on a SLM Aminco Model 4800 polarization/subnanosecond lifetime spectrofluorometer with a 0.5-nm slit excitation monochromator. The filter employed was a SCHOTT 240–330 nm; type UG11; melt 540341; size 50.8 × 50.8 mm; thickness 3 mm. The phosphates were dissolved in absolute ethanol. A *para*-terphenyl solution was utilized as the reference. Results are given in Table V. Ferrioxalate actinometry[11] was used to determine the light output.

Acknowledgment. We thank Professor Ken Audus for the generous use of his SLM Aminco Model 4800 spectrofluorometer. We also acknowledge the generous financial support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, Kansas University Biomedical grants from NIH, and Kansas University General Research Fund Grants.