## MECHANISTIC PATHWAYS IN PHOSPHATE ESTER PHOTOCHEMISTRY

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ABSTRACT: Initial bond breaking processes (homolysis vs heterolysis) of phosphate ester photosolvolysis were probed by chemically trapping the reactive intermediates with a tethered 5-hexenyl group. The resulting mechanistic picture is a blend of homolytic and heterolytic pathways, where the heterolytic cleavage is dominant.

The importance of organophosphates in chemistry and biochemistry is well documented as exemplified by the wealth of information on the ground state reactions of phosphates, especially their hydrolysis and nucleophilic substitution reactions.<sup>1</sup> In contrast, photochemical reactions of this functional group are not well understood.<sup>2,3</sup> We report here our recent results on the photochemical reactions of phosphate esters which are tethered with a 5-hexenyl group to probe the nature and lifetime of the intermediate(s) generated upon photolysis.

## Photochemistry of Phosphate Esters,

Our earlier studies<sup>3</sup> of benzyl, arylmethyl and  $\alpha$ -keto phosphate photochemistry established that upon irradiation of these esters, the phosphate efficiently departed as a nucleofuge generating a reactive electrophile. The fate of the electrophile was highly solvent dependent and was controlled primarily by the nature of the nucleophiles present. In several cases small amounts of an ethyl ether and radical derived products were produced (Equation 1). In non-polar, hydrocarbon solvents like cyclohexane, dibenzyl and a complex mixture of solvent adducts derived by hydrogen-atom abstraction were observed.

$$ArCH_2OP(OC_2H_5)_2 \xrightarrow{hv} ArCH_2OR + ArCH_2OCH_2CH_3 + (ArCH_{2/2})_{5\%} (1)$$

What remains unanswered, however, is the question of the intervention of a radical pair precursor to the cation. Three likely processes are envisioned which yield the major substitution product as well as the hydrocarbon coupling products found in cyclohexane irradiations.<sup>3a</sup> For example, the reaction may be viewed as a combination of an initial homolysis followed by electron transfer (pathway a), electron transfer preceding any bond breaking (pathway c), or a direct heterolysis of the C-O bond (pathway b, Scheme 1).

Scheme 1. Mechanistic Pathways in Phosphate Ester Photochemistry.



As a test of the nature of the initially formed intermediate, chemical trapping of it through a "chemical clock"<sup>4</sup> experiment was an inviting probe of this mechanistic dilemma. The tethered 5-hexenyl group, originally developed by Ingold et al.<sup>4a</sup>, has been employed as a "chemical clock" for an intramolecular trapping of radicals with lifetimes of *ca.*  $10^{-5}$ s or longer through cyclization to 5-membered rings in competition with normal intermolecular processes.<sup>4</sup> The ground state version of our radical cyclization process was reported by Walling and co-workers<sup>6</sup> who found that reaction of 6-bromo-6-phenyl-1-hexene gave the mixture of cyclization products including a significant amount of the 5-membered ring product, 2-methyl-phenylcyclopentane, as the major product (Equation 2). The rate of cyclization (k<sub>c</sub>) of 5-hexenyl radical **H** was determined<sup>7</sup> to be *ca.*  $3x10^5$  s<sup>-1</sup>.



In contrast, solvolysis of 5-hexenyl *p*-nitrobenzenesulfonates in acetic acid with sodium acetate gave 5hexenyl and cyclohexenyl substitution products.<sup>5a</sup> A small amount (<4%) of unsaturated five membered ring products were also observed.<sup>5b,c,d</sup> Thus, the products from these two ground state reactions serve as the signatures for the reaction profiles of a "pure" radical and a "pure" carbocation intermediate.

Our primary objective, to determine the extent of the competing pathways for the initial bond cleavage process, was approached with the photolysis of phosphates 1 and 2 in methanol. These esters gave high quantum efficiencies for the disappearance of the phosphate of 0.26 and 0.10, respectively, in accord with our earlier results of substituted benzyl phosphates.<sup>3</sup> In fact the lower efficiency for the disappearance of the p-trifluoromethylbenzyl phosphate with its highly electron withdrawing substituent (e.g., CF<sub>3</sub>) correlates well with the results of our reported linear free energy relationship obtained for a series of substituted benzyl phosphates.<sup>3b,c</sup> The product distribution obtained from studies of a variety of reaction conditions is summarized in the Table. Changing the p-substitution from -H to -CF<sub>3</sub> has the following effect on the product distribution:

- a) a decrease in the formation of direct substitution products by 14%;
- b) a three-fold increase in the formation of elimination products;
- c) a decrease in the cyclization products by 30%.

These observations are reasonable when considering that the electron withdrawing trifluoromethyl group has a destablizing effect on the carbocation intermediate thus increasing its reactivity, in turn decreasing its selectivity. For example, in the competition between methanol and water as nucleophiles, the ratio of MeOH:H2O attack is 5.3:1 for R=CF3 and 13.4:1 for R=H. This particular effect may also be considered for the competition between elimination and cyclization pathways. As seen in the Table, there is a decrease in the direct substitution process relative to elimination for the p-CF3 substituent while the total of all elimination and substitution products remains nearly constant.

**TABLE**. Summary of Product Distribution for Photosolvolysis at 254 nm, Ground State Solvolysis and Radical Cyclization of 1-Aryl-5-hexenyl Derivatives.

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$\bigcup_{\text{hv or } \Delta} \frac{\text{solvent}}{\text{hv or } \Delta}$	$\langle \rangle$	$-\bigcirc$	$(\bigcirc$	$\bigcirc$	$\bigcirc$	$\langle \rangle$		-	-	-
	- <b>x</b>	гч	<b>⊢</b> צ	-2	-X	-2	≻≃	≻≃	≻≃	<u>≻</u> ∡
R=H: R=CF <sub>3</sub> ;	w 4	5,7 6,8	Ø	10 11	12 13	14 15	16	18	19	20
$X = (EtO)_2 PO_2^{-1};$ Solvent			Photolysis at	254 nm						
1; R = H; MeOH (moist)	67%	6%	2	10%	4%	5%	2%	2% (12:	2% 10:	<1% 5)
<b>2</b> ; $R = CF_3$ ; MeOH (moist)	53%	17%	i 1	6%	5%	10%	ţ	- %9>	•	
I; R = H; Benzene	ł	71%	10%	1	7%	ł	10%	2% (11:	1% 8:	6) 6
$X = NO_2C_6H_4CO_2$ ; Solvent	-		Refl	ux						
<b>21</b> ; R = H; MeOH (moist)	71%	9%9	1	12%	L	5%	6%	;	-	
X = Br'; Solvent			Bu <sub>3</sub> SnH,	AIBN, 70	ŝ	-				
<b>22</b> ; R = H; Benzene	ł	L t	ł	ł	1	1	ł	(l:	3:	<b>(</b> 9
* This work ** Ref. 6.								(1:	òċ	1)**

In a comparison of the effect of methanol and benzene as solvents, photolysis of phosphate 1 in benzene, gave predominantly elimination and a decrease in the cyclization. This change in product distribution is consistent with a competition between a poor "nucleophile" (benzene) and a weakly basic anion (phosphate) yielding primarily elimination products. Due to its much lower dielectric constant, the stability afforded the benzyl cation by benzene is considerably less than that by methanol rendering a much more reactive cation favoring elimination at expense of cyclization.

The photochemical product distribution of cyclized products compared very favorably with those obtained in the ground state solvolysis of 1-(1-phenyl)-5-hexenyl p-nitrobenzoate. The key products in this study, the sixmembered ring products arising from intramolecular "ene-cation" cyclization, account for *ca*. 15% of the GC volatile material. This similarity in product distribution strongly indicates that the carbocation is the major reactive intermediate in the photosolvolysis of phosphate esters. Supporting this is the comparison of the product distribution from the tributyltin hydride induced radical cyclization reaction of **22** with the photoproducts of phosphate **1** (Table). Furthermore, these results show that photochemical cyclization from the radical intermediate constitutes 5% of all GC volatile products. These results do confirm, however, that a small but measurable contribution of the cyclization does occur from a radical intermediate.

We conclude from the product distributions for the irradiations of phosphates 1 and 2 that it is reasonable to depict the mechanism as a blend of homolytic and heterolytic pathways where the latter predominates. It remains to be established whether electron transfer is competitive with either of the cyclizations reactions, however. Further studies toward the identification of these transient intermediates are in progress.

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