The University of Manitoba

ALCOHOL TO ESTER REARRANGEMENTS IN PHOSPHORUS COMPOUNDS

by

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IN MEMORY OF MY FATHER

A B S T R A C T

The kinetics of the base-catalyzed rearrangement of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates, $(RO_2)P(O)C(OH)(CF_3)_2$, to 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates, $(RO)_2P(O)OCH(CF_3)_2$, where R = methyl, ethyl, and n-butyl have been studied by ^{19}F nmr techniques. Rate constants, energies of activation and entropies of activation have been calculated. A mechanism for the rearrangement is discussed in the light of the experimental evidence. The proposed mechanism is compared to mechanisms advanced for similar rearrangements involving phosphorus and other main group elements.

A mechanism is proposed to account for the formation of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates and 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates from the reaction of dialkyl phosphonates with hexafluoroacetone. Evidence from the kinetic study is used to account for the observed yield of each product.

A C K N O W L E D G E M E N T S

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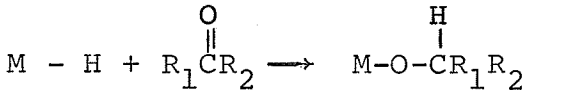
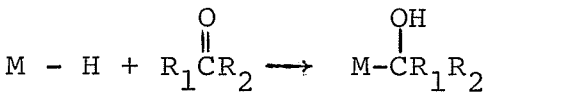
I N T R O D U C T I O N

The reactions of compounds containing metalloid-hydrogen bonds with unsaturated compounds have been extensively studied in the past three decades. Reactions between main group metal hydrides and compounds containing the carbonyl moiety have attracted a great deal of interest. It has been found that the reaction between these two classes of compound may proceed with the formation of the alkoxide or the alcohol or both,



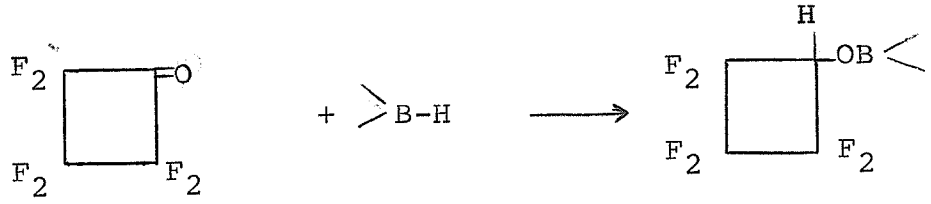
"alkoxide"



"alcohol"

where M is a main group element. Formation of the alkoxide or the alcohol was found to be dependent upon the substituents on the carbonyl group and the main group element involved.

Several workers have shown that boron hydrides add across carbonyl groups to yield the alkoxide product. Parshall (1) obtained the alkoxide product in the reaction of perfluorocyclobutanone with a boron hydride.



Kuhn and Doali (2) have investigated the kinetics of the reaction of acetone with diborane. The results of this vapor phase study suggest that the diborane and acetone react reversibly to form a 1:1 complex in which both bridged B-H bonds remain intact. This complex then reacts further with acetone to form diisopropoxyborane. The overall reaction may be illustrated as follows:

$$B_2H_6 + 4(CH_3)_2C{=}O \longrightarrow 2[(CH_3)_2CHO]_2BH$$

Janzen and Willis (3a) found that the reaction of silicon hydrides with hexafluoroacetone yielded the alkoxide.

$$(CH_3)_3SiH + O{=}C(CF_3)_2 \longrightarrow (CH_3)_3Si{-}O{-}\overset{H}{\overset{|}{C}}(CF_3)_2$$

These authors favored an ionic mechanism (3b) in which the first step is the abstraction of a hydride ion by hexafluoroacetone, giving a hexafluoroisopropoxide ion, $H{-}C(CF_3)_2O^-$, as an intermediate.

$$(CH_3)_3SiH + (CF_3)_2C{=}O \rightarrow (CH_3)_3Si^+ + HC(CF_3)_2O^-$$

$$HC(CF_3)_2O^- + (CF_3)_2C{=}O \rightarrow HC(CF_3)_2OC(CF_3)_2O^- \longrightarrow \text{product}$$

The polarization of the silicon hydrogen bond in this case is assumed to be $Si^+ - H^-$.

More recently Lapkin and Povarnitsyna (5) have verified the alkoxide formation from the addition of silicon hydrides

across carbonyl bonds.

$$RCH(=O) + HSiR_3' \rightarrow RHC(H)-OSiR_3'$$

$$RCOCH_2R' + HSiR_3'' \rightarrow RHC(H)-O-SiR_3''$$

Sheludyakov et al (4) reported that trialkylsilanes reacted with ketenes in a rapid exothermic reaction to form alkoxides.

$$(CF_3)_2C=C=O + (C_2H_5)_3SiH \rightarrow (CF_3)_2C=C(H)-O-Si(C_2H_5)_3$$

Cullen and Styan (6) reported that the hydrides of germanium and tin react with hexafluoroacetone in a manner analogous to the reaction of silicon with hexafluoroacetone (3) i.e. alkoxide formation.

$$(CH_3)_3M-H + (CF_3)_2C=O \rightarrow (CH_3)_3M-O-C(H)(CF_3)_2$$

M = Ge, Sn, Si

However, more recent work by Mironov et al (7) showed that trichlorogermane added to formaldehyde in the reverse direction that trichlorosilane adds to ketones and aldehydes (8), i.e. alcohol formation.

$$HCH(=O) + HGeCl_3 \rightarrow Cl_3Ge-CH_2(OH) \xrightarrow{CH_3MgCl} (CH_3)_3Ge-CH_2(OH)$$

The hydrides of group V elements have been found to undergo reaction with carbonyl containing compounds to yield the alcohol as product. For example, arsenic hydrides were found to react readily with hexafluoroacetone to form the

arsinopropinol in good yields as reported by Cullen and Styan (9).

$$(CH_3)_2As\text{-}H + (CF_3)_2C{=}O \longrightarrow (CF_3)_2\overset{OH}{\overset{|}{C}}\text{—}As(CH_3)_2$$

Krespan and Middleton's (10) recent review article illustrates that the reactions of hexafluoroacetone with a large variety of main group element hydrides proceeds with the formation of the alcohol.

Reactions of primary and secondary phosphines with compounds containing the carbonyl group are well known. In most cases the reaction product from these two classes of compounds is found to be the alcohol. Several of these reactions may be illustrated as follows:

$$(CF_3)_2C{=}O + R_1R_2PH \longrightarrow (CF_3)_2\overset{OH}{\overset{|}{C}}\text{—}PR_1R_2 \qquad (11)$$

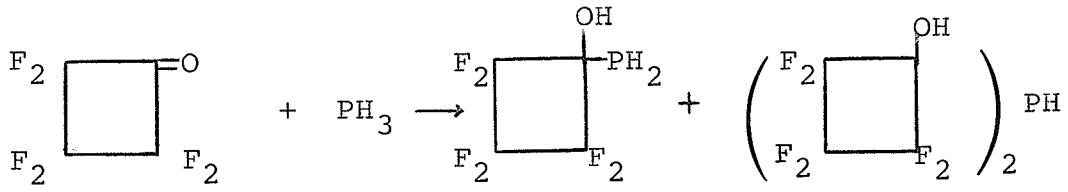
(a) $R_1 = R_2 = H$, (b) $R_1 = Me$, $R_2 = H$ (c) $R_1 = R_2 = Me$

Bruker et al (11) found that the ease of these reactions is dependent on the substituents on the phosphorus atom, the ease decreasing in the order dimethylphosphine > methylphosphine > phosphine. The same authors (12) have shown this tendancy to alcohol formation is followed also by the reaction of phosphine with 1,1,1-trifluoroacetone.

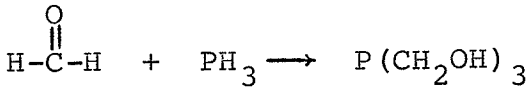
$$F_3C\overset{O}{\overset{\|}{C}}CH_3 + PH_3 \longrightarrow (CF_3)(CH_3)\overset{OH}{\overset{|}{C}}\text{—}PH_2$$

In several cases, a reaction between a carbonyl group

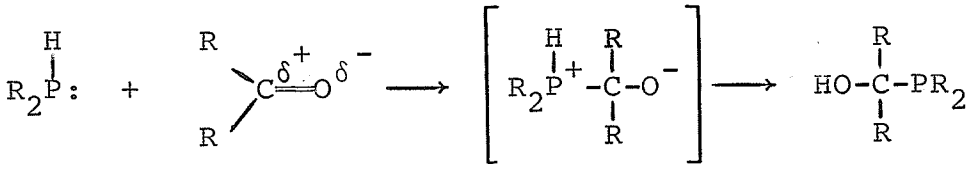
and more than one phosphorus hydrogen bond has been observed. Parshall (1) obtained both the mono and bis(1-hydroxyhexafluorocyclobutyl)phosphine from the reaction of phosphine and perfluorocyclobutanone.



The ratio of the product phosphines was determined by the ratio of the reactants. Grinshtein et al (18) reported the reaction between formaldehyde and phosphine yields the triol.



A mechanism which has been postulated for the reaction of trivalent phosphorus hydrides with carbonyl compounds involves, initially, the nucleophilic attack of the phosphorus lone pair electrons on the carbonyl carbon atom, which is expected to be slightly electron deficient.



The intermediate complex rearranges in a manner such that the proton moves from the positively charged phosphorus

atom to the negative oxygen yielding the observed alcohol as product. Thus the direction of addition is consistent with addition of an acidic P-H bond to the ketone.

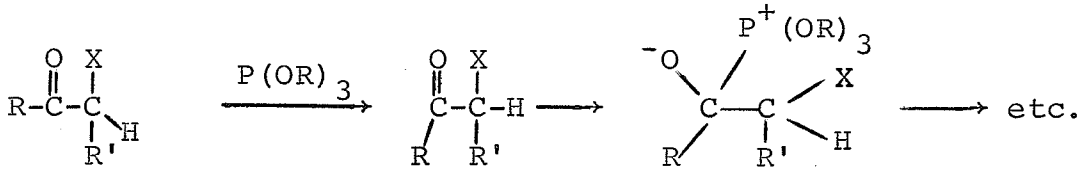
The nucleophilic properties of trivalent phosphorus compounds are well known. For example the Arbuzov reaction in which trialkyl phosphites, $P(OR)_3$, react with alkyl halides to produce phosphonate esters serves as an ideal model for the great number of nucleophilic reactions of trialkyl phosphites (13). The reaction proceeds in two steps:

$$(RO)_3P: + R'-X \longrightarrow (RO)_3P^+R' + X^-$$

$$(RO)_2\overset{R'}{\overset{|}{P^+}}-ORX^- \longrightarrow (RO)_2\overset{O}{\overset{\|}{P}}R' + RX$$

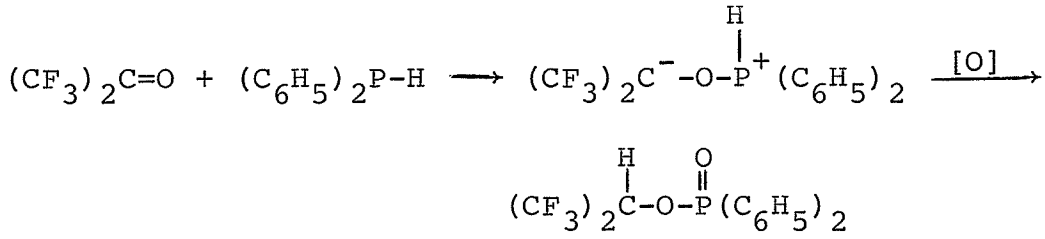
R = alkyl, R' = alkyl

The Perkow reaction also illustrates the nucleophilic properties of tertiary phosphines. By employing the nmr technique, Borowitz (19) has recently studied the mechanism of the Perkow reaction and found the initial step to be the nucleophilic attack of the phosphorus lone pair electrons on the carbonyl compound.

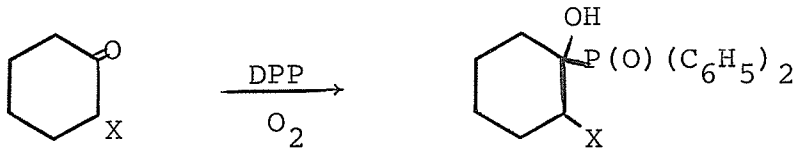


Until quite recently, the mechanism for the reaction of diphenylphosphine with various ketones has been somewhat

of an enigma. Stockel (14) reported that the reaction of diphenylphosphine with hexafluoroacetone proceeded by the following mechanism:

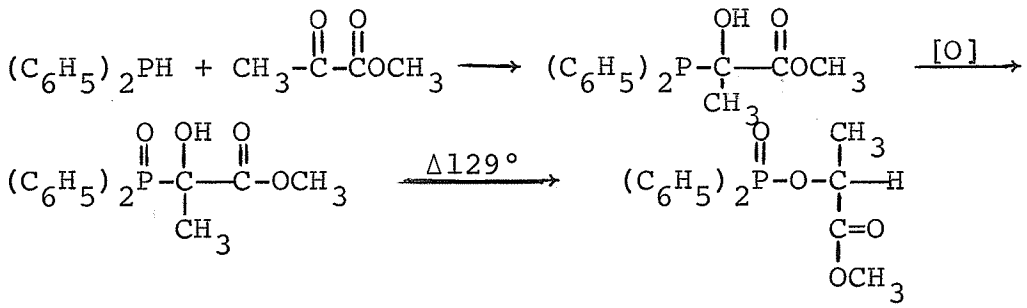


Several other workers have isolated the alcohol from the reaction of diphenylphosphine and ketones. Borowitz et al (16) have investigated the reaction of diphenylphosphine with various substituted cyclohexanones.



X = Cl, OSO_2CH_3, H

In these reactions the diphenylphosphine was allowed to oxidize to diphenylphosphinic acid by exposure to the atmosphere. Pudovik's (17) group recently studied the reaction of diphenylphosphine with methylpyruvate and concluded that the course of the reaction went as follows :



Thus it appears that the mechanism outlined above for the reaction of phosphines with carbonyl groups is quite general and it will be seen that this mechanism also has important implications in describing the reactions of phosphorus (V) hydrides.

The reactions of phosphorus (V) hydrides, such as those found in dialkyl phosphonates, $(RO)_2P(O)H$, and dialkyl phosphinous acids, $R_2P(O)H$, with systems containing the carbonyl moiety have also been extensively studied. For many years there has been considerable speculation as to whether compounds such as dialkyl phosphonates or dialkylphosphinous acids exist in a tautomeric equilibrium. This equilibrium for the dialkyl phosphonates may be represented as follows:

$$(RO)_2\overset{O}{\overset{\|}{P}}\text{-H} \rightleftharpoons (RO)_2\ddot{P}OH$$

phosphonate phosphite

Since the existence of the above tautomerism is important in explaining the production of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates, $(RO)_2P(O)C(OH)(CF_3)_2$, from the reaction of dialkyl phosphonates with hexafluoroacetone, the evidences for the presence of the phosphite tautomer will be discussed in some detail.

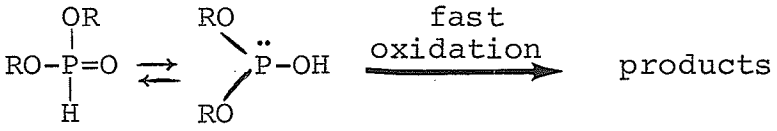
Evidence from physical methods such as Raman, ultraviolet and nuclear magnetic resonance spectral

studies (20) has shown that the esters of phosphorus acid exist primarily as the pentavalent or phosphonate tautomer. Several explanations have been advanced to account for the detection of only the phosphonate form. First of all, the stability of the phosphoryl bond (P=O) must be taken into consideration. The stability of this bond is attributable to the formation of two $p\pi$-$d\pi$ bonds at right angles to each other. The two lone pairs of electrons on oxygen overlap with the vacant 3d orbitals on the phosphorus atom, giving a phosphorus-oxygen bond whose strength approaches that of a triple bond. For this reason the phosphonate tautomer would be expected to be the most prevalent sending the above equilibrium far to the left. Secondly, as pointed out by Doak and Freedman, (20) none of the above physical techniques would be able to detect even a few percent of the phosphite tautomer if the tautomerism did exist.

More concrete evidence that the above tautomerism exists is revealed by the chemistry of dialkyl phosphonates. The fact that many reagents such as cuprous halides, diazomethane and phenylazide appear to react with the phosphonate form, the trivalent form being the reactive species, has been cited as evidence for the tautomeric equilibrium. Daasch (21) upon investigating the lithium, sodium, potassium and silver salts of the dialkyl phosphonates, reported a complete absence of

the phosphoryl (P=O) frequency in the infrared. These metal salts exhibited strong absorptions in the infrared characteristic of $P-O^{\ominus}$ and P-O-R linkages, thus suggesting the structure of the salt as being $(RO)_2PO^-M^+$. In addition ^{31}P nmr studies (22) of these salts indicated a triply connected structure, $(RO)_2\ddot{P}OM$. The chemical shift of the phosphorus in the salts was found to fall in the region of shifts expected for trialkylphosphites, $(RO)_3P$, i.e. δ = 150 ppm. Generally it has been observed that the ^{31}P chemical shifts in quadruply connected phosphorus compounds are much higher upfield. Thus on the basis of ^{31}P nmr a structure such as $(RO)_2\overset{O}{\overset{\|}{P}}{}^{\ominus}M^+$ does not seem likely for these salts. The research of Hunt and Saunders (23) showed that the tautomerism between the diphenylphosphinous acid $(C_6H_5)_2P(O)H$ and the trivalent $(C_6H_5)_2\ddot{P}OH$ does exist. These workers were able to prepare the silver salts of the phosphine compound, $(C_6H_5)_2POM$, and they observed that the formation of the salts is slow. The observation of the slow reaction implies that the trivalent phosphorus compound is probably the reactive species but the equilibrium is far to the left as would be expected. The formulation of the structure of the metal dialkyl phosphite salts as being trivalent, $(RO)_2\ddot{P}O^-M^+$, rather than pentavalent is also seen to have support in the reactions that these compounds undergo (24-27).

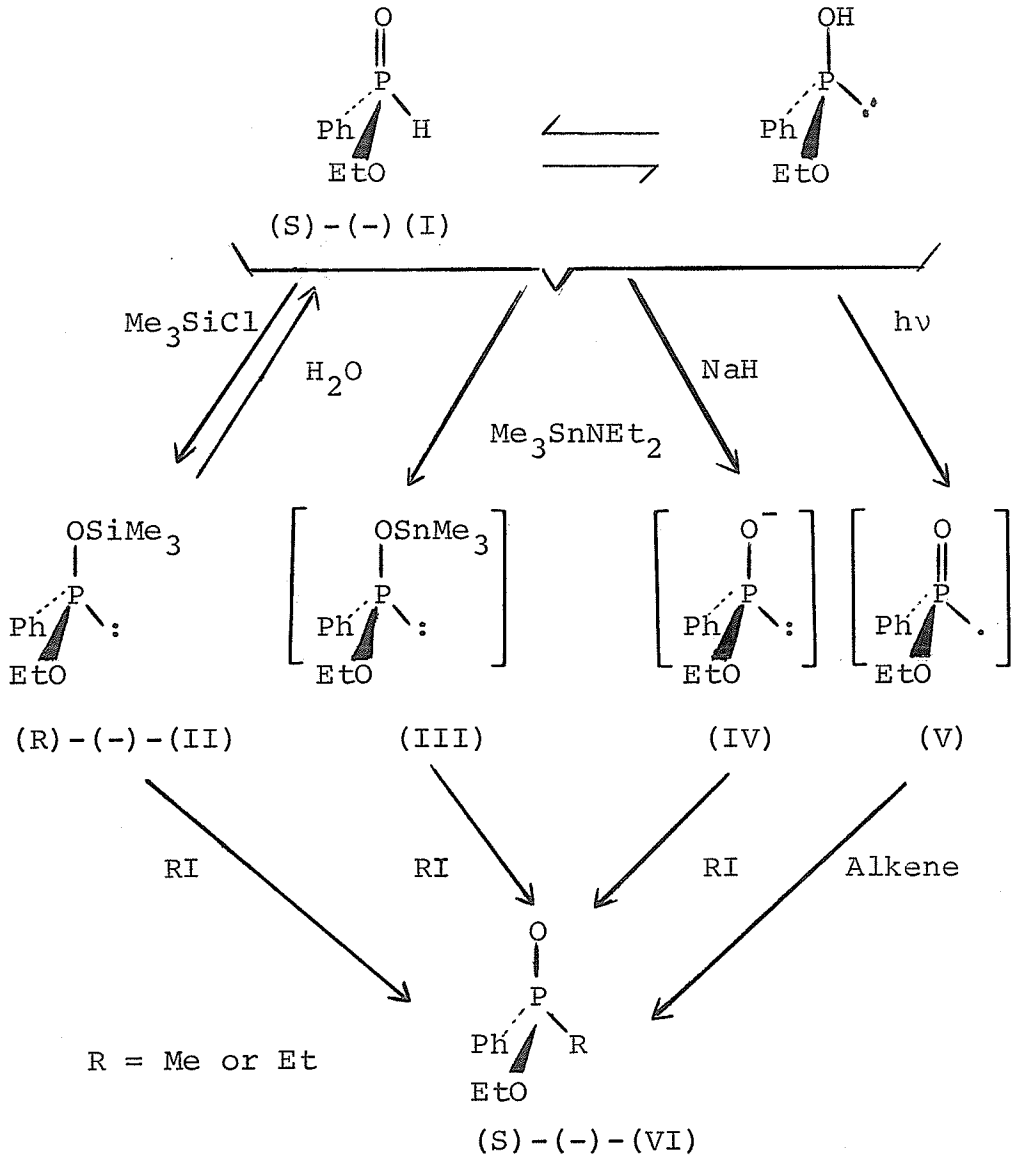
The most convincing evidence for the existence of the tautomerism comes from kinetic work involving dialkyl phosphonates. Nylen (28) noted that the oxidation of phosphonates to phosphates by halogens was independent of the concentration of the oxidant. He proposed a protropic rearrangement of the phosphonate to the phosphite, with the latter being the reactive species.



Nuclear magnetic resonance studies of the acid catalyzed exchange of the phosphorus bonded hydrogens in aqueous solutions of dialkyl phosphonates, led Luz and Silver (29) to suggest that the phosphite form of the dialkyl phosphonates serves as an intermediate for these exchange reactions. Significantly, Luz and Silver noted that the exchange rate of the phosphorus bonded hydrogen and the oxidation of dialkyl phosphonates, as studied by Nylen (28), followed an identical rate law indicating that the phosphite tautomer is the active species in both cases. Similar trends indicative of the phosphite tautomer were found by Hammond (30) and Bailey and Fox (31) in exchange reactions of dialkyl phosphonates.

Today it is generally accepted by many workers in organophosphorus chemistry, that in reactions of dialkyl

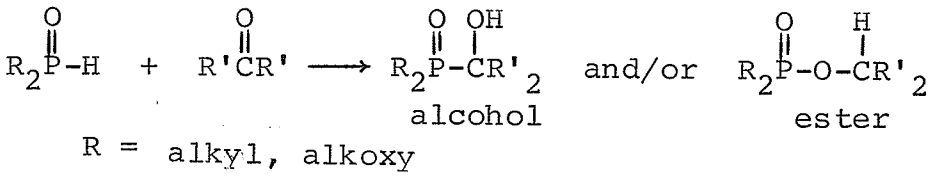
phosphonates, the phosphite tautomer is indeed the reactive species. Recently Van Den Berg (32) reported on the alkylation of optically active ethyl trimethyl phenylphosphonite which took place with retention of configuration. The reactive species was considered to be the phosphite tautomer as shown by the following reaction sequence.



Inspection of the literature shows many other instances where various authors working with dialkyl phosphonates or similar compounds consider the phosphite tautomer to be the reactive species (34-38,75).

In summary, it appears that there is little doubt that the phosphonate-phosphite tautomerism exists. It appears equally certain that the phosphite is normally present in very low concentrations, except in the compound $(CF_3)_2POH$, which has an infrared spectrum exhibiting an OH stretching absorption (40). The estimates as to how much of the tricovalent form exists vary from five percent (22) to 10^{-4} percent (20). Although the kinetic investigations of dialkyl phosphonates being oxidized and the investigations involving exchange reactions, as discussed above, were carried out in aqueous solution, several authors have stated that this tautomerism undoubtedly exists in nonaqueous solvents also (39).

It is well known that the addition of pentavalent phosphoryl hydrides to systems containing the carbonyl moiety may proceed with the formation of the alcohol or the ester.



The reactions of dialkyl phosphonates with aliphatic

or aromatic aldehydes was first reported by Craig and Hester (41) in the early 1950's.

$$(ClCH_2CH_2O)_2\overset{O}{\overset{\|}{P}}\text{-H} + Cl_3C\overset{O}{\overset{\|}{C}}H \longrightarrow (ClCH_2CH_2O)_2\overset{O}{\overset{\|}{P}}\text{-}\overset{OH}{\overset{|}{C}}HCCl_3$$

This reaction was found to be highly exothermic. A short time later Russian workers under Abramov (42) extended the investigation of reactions of dialkyl phosphonates with ketones, aldehydes and olefins.

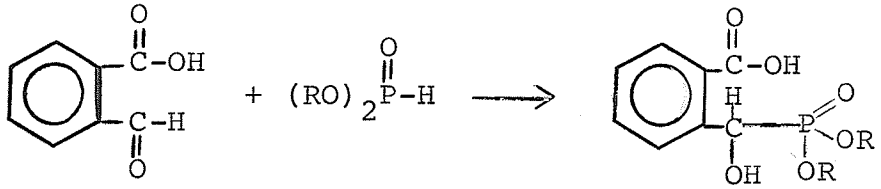
Barthel et al (43) found, in the absence of catalysts, that neutral dialkyl phosphonates reacted with chloral under moderate conditions producing the dialkyl 2,2,2-trichloro-1-hydroxyethylphosphonates in good yields.

$$(RO)_2\overset{O}{\overset{\|}{P}}\text{-H} + Cl_3C\overset{O}{\overset{\|}{C}}H \longrightarrow (RO)_2\overset{O}{\overset{\|}{P}}\text{-}\overset{OH}{\overset{|}{C}}HCCl_3$$

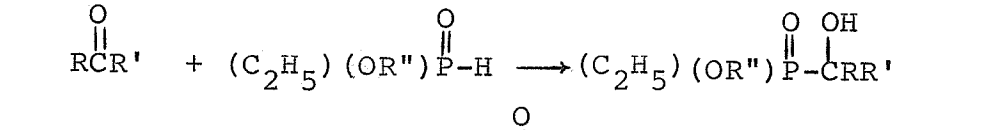
R = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7, C_4H_9 (43)

R = CH_3 (44)

Ramirez (45) obtained the alcohol from the reaction of diethyl phosphonate with the aldehydic carbonyl group of 1-carboxy benzaldehyde.

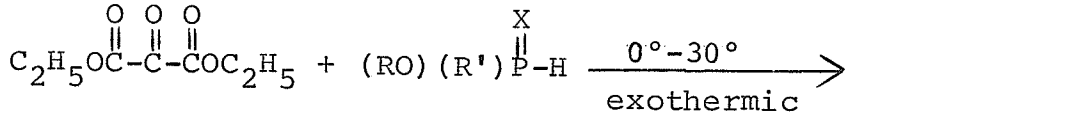


More recently Pudovik and coworkers extended the reactions of acid alkylphosphorus esters with α-carbonyl phosphoric esters and 2,3-butadione (46) and also with diethyl mesoxalate (38).



$R = CH_3$, C_6H_5; $R' = CH_3CO$, $\overset{O}{\overset{\|}{P}}\text{-}(OR")_2$; $R" = C_2H_5$, n-C_3H_7, i-C_3H_7, n-C_4H_9

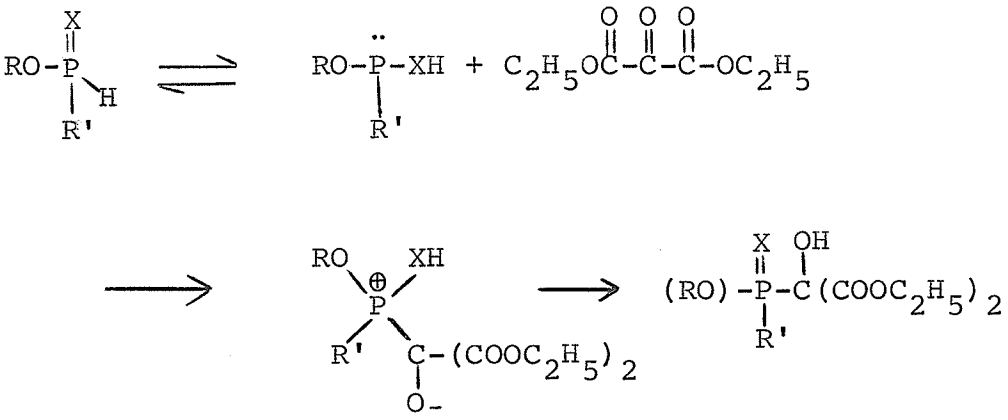
(46)



R = alkyl, R' = alkoxy, X = S,O

The literature shows many other instances where the reaction between phosphoryl hydrides, $R_1R_2P(O)H$, and compounds containing the carbonyl function yields the alcohol as outlined above (37,47(a-k)).

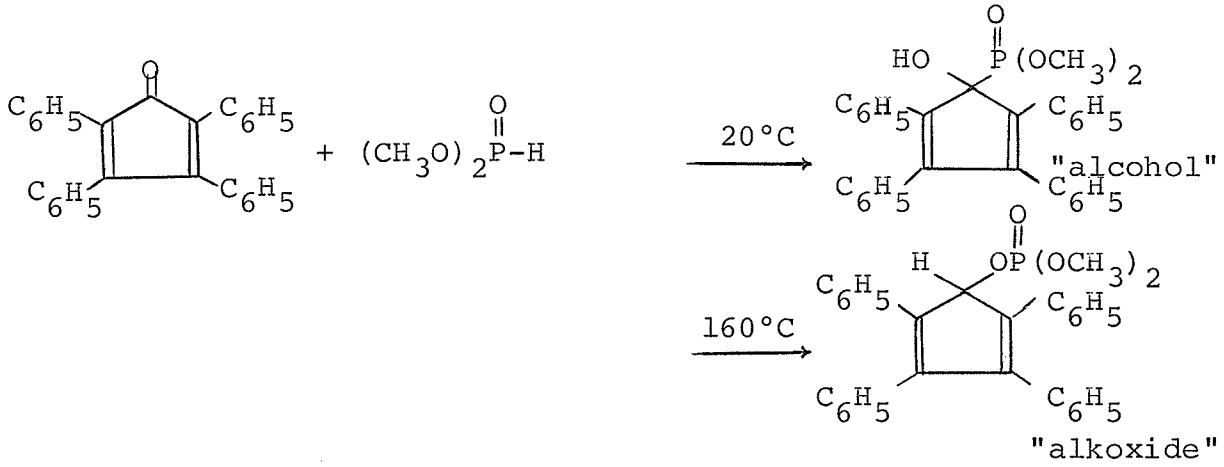
Pudovik (38) has proposed a mechanism to explain the alcohol formation in reaction between phosphoryl hydrides and carbonyl containing compounds. The mechanism may be illustrated by considering, as an example, the reaction of an acid phosphorus ester with diethyl mesoxalate.



R = alkyl, R' = alkoxy, X = S,O

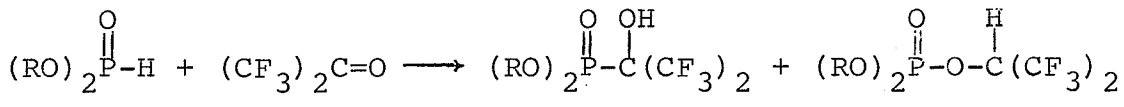
Pudovik's mechanism is seen to assume the existence of the tautomerism which interconverts the phosphoryl hydride to the phosphite. The phosphite tautomer is thought to be the active species as the phosphorus atom, which has a lone pair of electrons, attacks the carbon atom of the central carbonyl group. From this point on, the course of the reaction is quite similar to that discussed above for the reaction of phosphines with carbonyl groups. Proton rearrangement gives the alcohol.

There are several instances where the products of reactions between dialkyl phosphonates and carbonyl compounds have been found to be both the alcohol and the ester. Recently Miller (48) studied the reaction of dimethyl phosphonate with tetraphenylcyclopentadienone in ether at different temperatures. Miller attributed the



formation of the alcohol at 20°C to the attack of the phosphorus atom upon the carbonyl carbon of tetraphenylcyclopentadienone. At 160°C, however, he postulated that the formation of the ester product was due to the dimethyl phosphonate phosphorus atom attacking the carbonyl oxygen.

Recently Janzen and Pollitt (49) reinvestigated the reaction of several dialkyl phosphonates with hexafluoroacetone in the absence of solvent and found that the products included both the alcohol, dialkyl 2-hydroxy-



R = CH_3, C_2H_5 and n-C_4H_9

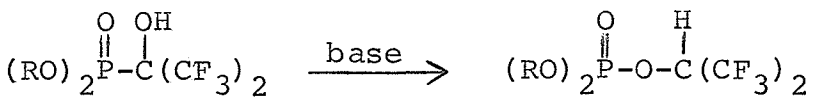
1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(RO)_2P(O)C(OH)(CF_3)_2$, and the ester, 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphate, $(RO)_2P(O)OCH(CF_3)_2$. Janzen and Pollitt showed that the yield of either the alcohol or the ester was

very dependent upon the nature of the substituent R with the amount of alcohol formation increasing in the order, R = CH_3, C_2H_5, and n-C_4H_9. Previously Ivin *et al* (50) had obtained only the ester product from the reaction of diethyl phosphonate with hexafluoroacetone.

The question now arises as to why a dual product formation results from the reaction of hexafluoroacetone and dialkyl phosphonates. Also of interest is the effect that the alkyl group R of the dialkyl phosphonate has on the ratio of the products formed.

A number of workers have reported base catalyzed "alcohol-ester" rearrangement involving phosphorus compounds (51(a-e)). A kinetic study of the thermally induced alcohol-ester rearrangement by Pudovik, employing the refractometric technique has been reported (52).

Since the alcohol-ester rearrangement was very well known, it seemed reasonable that the formation of the ester in the reaction of hexafluoroacetone with dialkyl phosphonate might be due to the rearrangement of the initially formed alcohol. To investigate this reaction further and determine under what conditions rearrangement does occur and what conditions give maximum yields of either alcohol or ester, a kinetic and mechanistic study was undertaken of the base catalyzed rearrangement, in which R, base, and temperature were systematically varied.



The mechanism postulated for the alcohol-ester rearrangement would also be of considerable interest since it could be compared to the mechanisms of base catalyzed rearrangements involving elements other than phosphorus. Thus one might conclude whether a general mechanism exists for a variety of elements undergoing the alcohol-ester rearrangement.

Apart from the actual kinetics of this investigation, the compounds themselves are of considerable interest. Related compounds such as chlorophase (43), show physiological activity. This alcohol, for example, has found wide application in various branches of agriculture as an insecticide of low toxicity toward warm-blooded animals.

General Procedure, Chemicals, and Instrumental

GENERAL

Conventional vacuum line techniques were used for handling all volatile materials. Reactions were carried out in thick walled Pyrex reaction vessels. Cold baths used in the preparations were liquid nitrogen (-196°C) and acetone-dryice (-78°C). Before hexafluoroacetone was introduced into the reaction tubes, the dialkyl phosphonates and solvent were degassed by using several freeze-pump-thaw cycles.

CHEMICALS

Hexafluoroacetone was purchased from Matheson of Canada. The hexafluoroacetone was purified by trap to trap distillation prior to use.

The dialkyl phosphonates (Eastman Organic Chemicals) were purified by vacuum distillation prior to use. The purity of the dialkyl phosphonates was checked by infrared and nuclear magnetic resonance spectroscopy.

Dichloromethane (B.D.H. Laboratory Chemicals) was used without futher purification.

Pyridine, (Baker Analyzed Reagent) was purified by distillation and was stored over BaO (53) to keep it moisture free.

Aniline, N-methylaniline, N,N-dimethylaniline, and

dimethylsulfoxide were used as received.

n-Butyllithium was received as a 21.3 percent by weight solution in hexane and was used without further purification. Exposure to the atmosphere was minimized by handling the solution in an airtight syringe previously flushed with nitrogen.

INSTRUMENTAL

Infrared spectra were recorded with a Perkin Elmer 337 spectrophotometer using potassium bromide windows. Spectra of liquid compounds were recorded as neat liquid films. Infrared spectra were calibrated using a polystyrene film.

Nuclear magnetic resonance spectra were obtained on a Varian A56/60 spectrometer using 60 MHz and 56.4 MHz for proton and fluorine respectively. Tetramethylsilane and trichlorofluoromethane were used as internal proton and internal fluorine standards respectively. ^{19}F spectra were calibrated by generating side bands from the trichlorofluoromethane resonance at 0 ppm.

Mass spectra were obtained on a Finnigan 1015 quadrupole mass spectrometer.

E X P E R I M E N T A L

HEXAFLUOROACETONE AND DIALKYL PHOSPHONATES

Reaction of Dimethyl Phosphonate and Hexafluoroacetone in the Absence of Solvent and Without Temperature Control.

Dimethyl phosphonate (1.95 g, 17.72 mmole) was placed in a Pyrex reaction tube and degassed. Hexafluoroacetone (3.20 g, 19.27 mmole) was introduced into the reaction tube. The reaction tube was sealed under vacuum at -196°C. The reaction mixture was allowed to warm up to room temperature quickly. Then the reaction tube was opened and excess hexafluoroacetone was removed. Completion of the reaction was checked by ^{1}H nmr and infrared spectroscopy. The doublet due to the phosphoryl-hydrogen resonance, J_{P-H} = 752 Hz (literature value, J_{P-H} = 715 Hz) (22), characteristic of the dimethyl phosphonate, was found to have completely disappeared. The phosphorus-hydrogen stretching band at 2440 cm^{-1} of the dimethyl phosphonate was found to be absent in the infrared spectrum of the reaction product. ^{19}F nmr of the product showed a single doublet, J = 6 Hz, at +74.1 ppm. The infrared spectrum of the product showed no bands in the region expected for an oxygen-hydrogen stretch, i.e. approximately 3200 cm^{-1}. The infrared spectrum was identical to that reported by Janzen and Pollitt (49) for 1,1,1-3,3,3-hexafluoroisopropyldimethyl phosphate, $(CH_3O)_2P(O)-C(H)(CH_3)_2$. The yield was calculated to be 100% (4.89 g, 17.7 mmole).

Reaction of Dimethyl Phosphonate with Hexafluoroacetone in the Presence of a Solvent and with Temperature Regulation.

Dimethyl phosphonate (2.40 g, 21.8 mmole) and dichloromethane (10.0 ml) were introduced into a Pyrex reaction tube. After degassing, a slight excess of hexafluoroacetone (4.29 g, 25.8 mmole) was introduced into the ampoule which was then sealed under vacuum at -196°C. The reaction mixture was placed directly into an acetone-CO_2 bath at -78°C and then was allowed to warm to room temperature slowly as the acetone-CO_2 bath evaporated (24 h). After this time the reaction tube was opened and excess hexafluoroacetone was removed. ^1H nmr and infrared spectroscopy showed that the dimethyl phosphonate had reacted completely since the phosphoryl-hydrogen resonance, J_{P-H} = 752 Hz and the P-H stretching band at 2440 cm^{-1}, both indicative of the dimethyl phosphonate, had disappeared.

The products of this reaction have previously been identified as dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(CH_3O)_2P(O)C(OH)(CF_3)_2$, and 1,1,1,3-3,3-hexafluoroisopropyldimethyl phosphate, $(CH_3O)_2P(O)OCH(CF_3)_2$ (49). The ^{19}F nmr spectrum of the reaction mixture consisted of a doublet, J = 3 Hz, for the former at +70.3 ppm and a doublet J = 6 Hz for the latter at +74.1 ppm. The ^1H nmr spectrum was identical to that reported by Janzen and Pollitt (49). Integrated ^{19}F nmr signals of

the product mixture showed that the two products, the phosphonate and phosphate were formed in ratio 84:16. This ratio corresponds to a yield of the phosphonate (alcohol) of 5.06 g (84%) and the phosphate (ester) 0.96 g (16%).

Reaction of Diethyl Phosphonate with Hexafluoroacetone in the Absence of Solvent and Temperature Control.

Diethyl phosphonate (2.50 g, 18.11 mmole) was placed in a Pyrex reaction tube. Hexafluoroacetone (3.20 g, 19.27 mmole) was introduced into the reaction tube which was then sealed under vacuum at -196°C. The reaction mixture was then allowed to warm up to 25°C quickly. It was noted that the reaction vessel became very warm. The reaction tube was opened and excess hexafluoroacetone was removed. Total reaction of the diethyl phosphonate was verified by ^{1}H nmr and infrared spectroscopy as discussed in the reaction of dimethyl phosphonate with hexafluoroacetone. The doublet due to the phosphorus-hydrogen (J_{P-H} = 741 Hz) had completely disappeared as had the P-H stretching band at 2430 cm^{-1}. The infrared spectrum of the product showed no absorption in the area expected for the oxygen-hydrogen stretch in a hydroxyl group. The ^{19}F nmr spectrum showed a doublet (J = 6 Hz) at +73.9 ppm. The proton nmr spectrum was identical to that reported previously (49). On the basis

of ^{1}H and ^{19}F nmr spectroscopy the product was solely 1,1,1,3,3,3-hexafluoroisopropyldiethyl phosphate, $(C_2H_5O)_2P(O)-O-CH(CF_3)_2$ (5.50 g, 18.11 mmole).

Reaction of Diethyl Phosphonate with Hexafluoroacetone in the Presence of a Solvent and with Temperature Regulation.

Diethyl phosphonate (3.01 g, 21.8 mmole) and dichloromethane (10.0 ml) were mixed in a Pyrex reaction tube. A slight excess of hexafluoroacetone (4.29 g, 25.8 mmole) was introduced into the reaction ampoule. The reaction tube was sealed under vacuum at -196°C. The reaction mixture was immediately placed at -78°C and allowed to reach 25°C slowly over a period of 24 hours as the bath evaporated. After the warming up period, the reaction tube was opened and excess hexafluoroacetone was removed. As before ^{1}H and infrared spectroscopy were employed to verify that the diethyl phosphonate had completely reacted.

The products of this reaction had been previously identified (49) as diethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroiospropylphosphonate, $(C_2H_5O)_2P(O)C(OH)(CF_3)_2$, and 1,1,1,3,3,3-hexafluoroisopropyldiethyl phosphate, $(C_2H_5O)_2P(O)OCH(CF_3)_2$. ^{19}F and ^{1}H nmr and infrared spectroscopy of the reaction products was identical to the previous assignments.

On the basis of integrated ^{19}F nmr signals, the phosphonate and phosphate were formed in ratio 88:12. This ratio corresponds to respective yields of 5.38 g and 0.80 g.

Reaction of Di-n-butyl Phosphonate and Hexafluoroacetone in the Absence of Solvent and Without Temperature Control.

Di-n-butyl phosphonate (3.60 g, 18.55 mmole) was placed in a Pyrex reaction tube. Hexafluoroacetone (3.20 g, 19.27 mmole) was introduced into the ampoule. The reaction tube was sealed under vacuum at -196°C and then placed at room temperature, allowing the reaction mixture to warm to room temperature quickly. It was again noted that the reaction was highly exothermic. The reaction tube was then opened and excess hexafluoroacetone was removed. The lack of a P-H stretching band in the infrared spectrum and the absence of a doublet due to phosphorus-hydrogen coupling in the ^{1}H nmr spectrum confirmed that the di-n-butyl phosphonate had completely reacted.

The products of this reaction had previously been identified as di-n-butyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$, and 1,1,1,3,3,3-hexafluoroisopropyldi-n-butyl phosphate, $(n\text{-}C_4H_9O)_2P(O)O\text{-}CH(CF_3)_2$ (49). The ^{1}H and ^{19}F nmr spectra of the reaction products were identical to previous spectra.

On the basis of integrated ^{19}F nmr signals, the phosphonate and phosphate were formed in ratio 4:96. This ratio corresponds to respective yields of 0.26 g and 6.95 g.

Reaction of Di-n-butyl Phosphonate with the Hexafluoroacetone in the Presence of a Solvent and with Temperature Control.

Di-n-butyl phosphonate (4.23 g, 21.8 mmole) and dichloromethane (10.0 ml) were mixed in a Pyrex reaction tube and degassed. A slight excess of hexafluoroacetone (4.29 g, 25.8 mmole) was introduced in the reaction tube which was then sealed under vacuum at -196°C. The reaction mixture was transferred immediately to a bath at -78°C and allowed to warm up slowly to room temperature with the bath. This warming up process took approximately 24 hours. After this time, the reaction tube was broken and excess hexafluoroacetone was removed. That the di-n-butyl phosphonate had completely reacted was shown as usual by ^{1}H nmr and infrared spectroscopy.

The products of the reaction between di-n-butyl phosphonate and hexafluoroacetone had previously been identified by Janzen and Pollitt (49) as di-n-butyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$, and 1,1,1,3,3,3-hexafluoroisopropyldi-n-butyl phosphate, $(n\text{-}C_4H_9O)_2P(O)OCH(CF_3)_2$.

The ^{1}H and ^{19}F nmr spectra matched these previous assignments exactly.

^{19}F nmr spectroscopy showed that the phosphonate and the phosphate were formed in ratio 91:9. This ratio corresponds to respective yields of 7.14 g and 0.71 g.

preparation of Diphenyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate in Maximum Yield.

Diphenyl phosphonate (5.11 g, 21.8 mmole) and dichloromethane (10 ml) were mixed in a Pyrex reaction tube. A slight excess of hexafluoroacetone (4.29 g, 25.8 mmole) was introduced into the reaction tube which was then sealed under vacuum at -196°C. The reaction mixture was immersed immediately in a -78°C bath and was allowed to warm up to room temperature with the bath (24 hrs). After this time the reaction ampoule was opened and the excess hexafluoroacetone was removed. ^{1}H nmr and infrared spectroscopy were used to verify that the diphenyl phosphonate had completely reacted with the hexafluoroacetone.

The ^{19}F nmr spectrum exhibited two doublets, J = 3 Hz and J = 6 Hz at +72.1 ppm and +74.8 ppm respectively. Thus from the ^{19}F nmr spectrum and the expected similarity of the diphenyl phosphonate and the dialkyl phosphonates discussed above, the products of the reaction have been identified as diphenyl 2-hydroxy-1,1,1,3,3,3-

hexafluoroisopropylphosphonate, $(C_6H_5O)_2P(O)C(OH)(CF_3)_2$, and 1,1,1,3,3,3-hexafluoroisopropyldiphenyl phosphate, $(C_6H_5O)_2P(O)OCH(CF_3)_2$.

^{19}F nmr spectroscopy showed that the two products, the phosphonate and phosphate were formed in ratio 44:56. This ratio corresponds to respective yields of 3.85 g and 4.90 g.

Reaction of Diphenylphosphine with Hexafluoroacetone

Diphenyl phosphine (1.02 g, 5.4 mmole) and dichloromethane (10.0 ml) were introduced into a Pyrex reaction tube. A slight excess of hexafluoroacetone (1.00 g, 6.0 mmole) was added and the tube was sealed under vacuum at -196°C. The mixture was allowed to warm up to room temperature slowly from -78°C (24 hrs). The reaction tube was opened and excess hexafluoroacetone was removed. ^1H nmr spectroscopy was used to verify complete reaction of diphenylphosphine.

The ^{19}F spectrum consisted of two doublets. One doublet, centred at 70.2 ppm was characterized by a coupling constant, J = 19 Hz. The other doublet, centred at 72.2 ppm, was characterized by a coupling constant J = +6 Hz. On the basis of integrated ^{19}F nmr signals the products were formed in ratio 81:19 respectively. The ^1H nmr spectrum exhibited a complex multiplet, δ = 3.2

ppm and a symmetric 9 multiplet centred at δ = 3.7 ppm.

The sample was left in contact with the atmosphere and ^{19}F nmr spectra were recorded periodically.

KINETIC MEASUREMENTS

The rates of rearrangement of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates, $(RO)_2P(O)C(OH)(CF_3)_2$ (alcohol), to 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates, $(RO)_2P(O)OCH(CF_3)_2$ (ester), under the influence of a basic catalyst were measured by ^{19}F nmr techniques. The kinetics of the base catalyzed reactions were followed using ^{19}F nmr since the nine line multiplet of the 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphate which would be required to follow the rearrangement by ^{1}H nmr, seriously overlapped with the solvent resonance signals. The ^{19}F resonances of the phosphonate (alcohol) and the resulting phosphate (ester) were well separated, as was noted in the preparation of these compounds, so they were suitable for the kinetic studies. The ^{19}F spectrum of the alcohol product was found, as described in the preparations, to consist of a doublet, ($J = 3$ Hz) at approximately +70 ppm, and the ^{19}F spectrum of the esters consisted of a doublet ($J = 6$ Hz) approximately 4 ppm further upfield. The base catalyzed rearrangement was followed by observing both the disappearance of the doublet characteristic of the alcohol and the appearance of the doublet characteristic of the isomeric ester.

The nmr spectrometer was optimized by normal proceedures and was prepared for a kinetic run as follows.

A sample of the alcohol in a solution of dichloromethane in a standard nmr tube was inserted into the probe of the instrument and was allowed to reach the temperature of the probe. To ensure complete thermal equilibrium of the sample with the probe, the sample was left in the probe for a period of seven minutes. The frequency offset was adjusted to the CF_3 resonance region. The sweep offset control was adjusted such that the position of the doublet due to the alcohol was placed at the left side of the nmr chart paper. The spectrum amplitude was adjusted to give maximum deflection without exceeding full scale deflection.

The nmr tube containing the alcohol solution was withdrawn from the probe and a measured amount of base was injected, by means of a syringe, into the nmr tube. The mixture was shaken vigorously for several minutes to ensure thorough mixing. The tube was reinserted into the probe and allowed to reach thermal equilibrium. The signal due to the alcohol was scanned and the integral signal was recorded at regular time intervals, these time intervals depending on the rate of isomerization. That is, if the reaction was found to proceed very rapidly, integral signals were recorded every two minutes, and if the reaction rate was sufficiently slow, integrations were carried out every five minutes. The reactions were followed until about ten percent of the initial

alcohol concentration remained, except in certain cases where completion of the reaction was required. During the course of the kinetic runs, the integral heights of both the alcohol and ester were summed and these sums were compared at various times during the run to ensure that the alcohol was being converted only to the ester, i.e. the sums of the integral signals remain constant throughout the kinetic run.

Pseudo first order rate constants, k_1', were obtained from a plot of the natural logarithm of the integrated alcohol peak area (which is a measure of the alcohol concentration) *versus* time in seconds. A least squares program on a Hewlett-Packard 9100A calculator was employed to find the slope of the best straight line. The pseudo first order rate constant was the slope of the above linear plot. Second order rate constants, k_2, were obtained by dividing the pseudo first order rate constant, k_1', by the concentration of the base used in that particular kinetic run.

The Arrhenius energy of activation, E_a, was obtained by repeating the kinetic runs at several temperatures. From a plot of ln k_2 *versus* $T(°K)^{-1}$ the E_a was calculated. The entropy of activation was calculated from the equation $k_2 = \exp(kTh^{-1})\exp(\Delta S^{\ddagger}/R)\exp(-E_a/RT)$ (55) and A from $k_2 = A_e^{-E_a/RT}$ (ref. 55 p.53). The temperatures at which the reactions were carried out

were checked before and after every run to ensure that the temperature did not change during the course of the run. If, during the course of a run, the temperature was found to have changed, that particular run was discarded. An ethylene glycol, temperature versus shift chart was used to calibrate the temperature of the probe, and the temperatures are accurate to ± 1° (54).

Rearrangement of Dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(CH_3O)_2P(O)C(OH)(CF_3)_2$.

Dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosponate, $(CH_3O)_2P(O)C(OH)(CF_3)_2$, was prepared by the reaction of hexafluoroacetone with dimethyl phosphonate. Conditions, as described in the preparative section of the Experimental, were regulated to give maximum yield of the phosphonate (alcohol). From the ratio of the integral signals obtained from the ^{19}F spectrum, the concentration of the alcohol in the dichloromethane solution was calculated. The alcohol concentration in the dichloromethane solution was varied by the addition of dichloromethane. Base concentrations were regulated by adding calculated volumes of base to the alcohol solution.

Since the ratio of the $(CH_3O)_2P(O)C(OH)(CF_3)_2$ (alcohol) to $(CH_3O)_2P(O)OCH(CF_3)_2$ (ester) formed from the reaction mixture was very high, no attempt to separate the isomers was made prior to the kinetic runs.

Another reason why separation was not performed prior to a run was that the rearrangement product expected could be checked exactly by referring to the ^{19}F resonance signal of the ester already present in the sample.

In order to definitely establish the order of the kinetics of the alcohol to ester rearrangement reactions, various concentrations of the alcohol and the base (pyridine) were used. From these runs the pseudo first order rate constants were determined. The overall second order rate constants were then calculated from their respective pseudo first order rate constants. The second order rate constants were compared.

It was found, that during the course of the rearrangement of dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropyl-phosphonate to the ester 1,1,1,3,3,3-hexafluoroisopropyl-dimethyl phosphate, a peak of low intensity was buried under the ^{19}F resonance signal of the alcohol. This peak was carefully integrated numerous times after the signal due to the alcohol had vanished. The integral height of this peak was subtracted from each recorded alcohol integration height. It was assumed that the intensity of this peak remained constant throughout the kinetic run since its intensity did not diminish over a period of several days in excess pyridine. No attempt was made to characterize the source of this resonance signal. Throughout the kinetic runs, the sums of the integral heights of

the alcohol and the ester were compared to ensure that the alcohol was being converted to the ester.

In order to determine the activation parameters, the above rearrangement was studied at temperatures of 40.0°C and 45.5°C. The Arrhenius energy of activation, the entropy of activation, were calculated as described above.

During the rearrangement, it was found that the ester, $(CH_3O)_2P(O)OCH(CF_3)_2$, was unstable in the presence of pyridine. After an induction period of approximately 30 minutes the ester reacted with base to give a new product containing the grouping, $CH_3OPOCH(CF_3)_2$, as determined by ^1H and ^{19}F nmr. It was assumed that the reaction did not interfere with the kinetic analysis for several reasons. First of all, the rearrangement reactions were essentially complete within 30 minutes, i.e. before the ester had begun to react with the base. Secondly, if the reaction of the base and the ester did interfere with the kinetic results, deviations from linear plots would be expected. No such deviations were observed, however.

Rearrangement of Diethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(C_2H_5O)_2P(O)C(OH)(CF_3)_2$.

Diethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(C_2H_5O)_2P(O)C(OH)(CF_3)_2$, was prepared by the reaction of hexafluoroacetone and diethyl phosphonate in the

manner designed to yield maximum yields of the alcohol as discussed in the preparation section of Experimental. The concentration of the above alcohol in the solvent, dichloromethane, was calculated on the basis of the ratio of the alcohol ester integral signal heights which were measured directly after preparation. Exactly the same procedures were followed as with the methyl analogue in investigating the kinetics of the rearrangement to 1,1,1-3,3,3-hexafluoroisopropyldiethyl phosphate.

Since the rates of the rearrangement reactions had been found to follow second order kinetics in the methyl analogue, only two runs were carried out at 44.5°C with identical alcohol concentrations and different base concentrations in order to provide a check that the kinetics of the ethyl rearrangement followed second order kinetics as did its methyl analogue.

To determine the activation parameters for the rearrangement, kinetic runs using identical alcohol and base concentrations were carried out at 32.5°, 42.2°, 54.0° and 57.0°C. The activation parameters were calculated by methods outlined above.

It was noted that the ester, $(C_2H_5O)_2P(O)OCH(CF_3)_2$, was inert to base unlike the methyl analogue.

Rearrangement of Di-n-butyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate, $(n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$.

Di-n-butyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate was prepared by reaction of hexafluoroacetone with di-n-butyl phosphonate using reaction conditions designed to produce maximum yields of alcohol. The concentration of the alcohol in dichloromethane was calculated as in previous cases. Kinetic runs were carried out as outlined previously.

Using an identical alcohol concentrations and base concentrations, runs were also carried out at the following temperatures: 49.5°, 51.3°, 54.5°, 57.5° and 62°C. From the data obtained from these runs, the enthalpy and entropy of activation were calculated.

Rearrangement of Dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate Using Various Organic Bases

Dimethyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonate was prepared in maximum yields as described previously and the alcohol concentration in dichloromethane was calculated on the basis of ^{19}F nmr spectroscopy.

Using a constant alcohol concentration, the rearrangements were studied with the bases pyridine, aniline, N-methylaniline, N,N-dimethylaniline and dimethylsulfoxide at 33.0°C. The base concentration was 1.38 M in each case. The rate constants k_1' (pseudo first order rate constant) and k_2 (second order rate constant) were obtained and the rate of rearrangement as a function of

base strength were noted.

It was noted that when the strongly basic reagents diethylamine and piperidine were employed as the basic catalysts, the reaction rate was too fast to be measured by nmr techniques.

Attempted Wittig Type Rearrangement of 1,1,1,3,3,3-hexafluoroisopropyldimethyl phosphate, $(CH_3O)_2P(O)OCH(CF_3)_2$.

1,1,1,3,3,3-hexafluoroisopropyldimethyl phosphate (1.38 g, 5.0 mmole) was added slowly to an excess of n-butyl lithium with constant stirring. A gas, presumably butane was boiled off as the reaction occurred exothermically. After approximately 30 minutes, the mixture turned a dark brown color. Following neutralization with dilute HCl, the organic layer was separated from the aqueous layer. The ^{19}F nmr doublet of the ester, $(CH_3O)_2P(O)OCH(CF_3)_2$, was replaced by a singlet, as required for the carbanion, $(CH_3O)_2P(O)O\overset{\ominus}{C}(CF_3)_2$.

D I S C U S S I O N O F R E S U L T S

The rearrangement of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates, $(RO)_2P(O)C(OH)(CF_3)_2$, where R = methyl, ethyl, and n-butyl (referred to hereafter simply as alcohol "1", alcohol "2" and alcohol "3" as shown in Table I) to 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates, $(RO)_2P(O)OCH(CF_3)_2$, where R = methyl, ethyl and n-butyl, (ester "1", ester "2" and ester "3" as shown in Table I) in the presence of a Lewis base was studied by ^{19}F nuclear magnetic resonance spectroscopy.

$$\underset{\text{alcohol}}{(RO)_2P(O)C(OH)(CF_3)_2} \xrightarrow{\text{Lewis base}} \underset{\text{ester}}{(RO)_2P(O)OCH(CF_3)_2}$$

^{19}F nmr techniques are ideally suited to the kinetic study of rearrangement for several reasons. The ^{19}F resonance signal of the three alcohols appears as a doublet, J = 3 Hz, at approximately +72 ppm. This doublet is attributable to the ^{19}F resonance of the six magnetically equivalent fluorine nuclei of the two trifluoromethyl groups on the hydroxyl carbon atom, being split by the phosphorus nucleus which has spin, I = 1/2. The ^{19}F resonance signal of the three esters appears as a doublet at approximately +75 ppm. The doublet of the ester is due to the coupling between the six magnetically equivalent fluorine nuclei on the two trifluoromethyl groups and the proton on the carbon

TABLE I

Compounds Involved in the Alcohol to Ester Rearrangement

Dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroiospropylphosphonates	1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates
$(CH_3O)_2P(O)C(OH)(CF_3)_2$	$(CH_3O)_2P(O)OCH(CF_3)_2$
alcohol "1"	ester "1"
$(C_2H_5O)_2P(O)C(OH)(CF_3)_2$	$(C_2H_5O)_2P(O)OCH(CF_3)_2$
alcohol "2"	ester "2"
$(n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$	$(n\text{-}C_4H_9O)_2P(O)OCH(CF_3)_2$
alcohol "3"	ester "3"

in the P-O-C linkage. Since the doublets due to the alcohols and their respective esters are separated by 3 ppm, there is no problem of overlap of the resonance signals of either species. ^{19}F nmr techniques also have the advantage that using an instrument with a variable temperature probe allows for the facile determination of activation energies and entropies.

It was found experimentally that the rates of rearrangement of alcohol "1", alcohol "2" and alcohol "3" to their respective esters were first order in alcohol concentration. A typical plot of alcohol concentration (as measured by the integrated peak area beneath the ^{19}F resonance signal of the alcohols) versus the time (as measured from the time at which the Lewis base was added to the dichloromethane solution of the alcohol) was found to follow an exponential decrease, which is required for a reaction which is kinetically first order. Since the Lewis base, pyridine, is not consumed during the reaction, i.e. it is a catalyst, its concentration remains constant and the kinetics of the rearrangement appear as pseudo first order. Further evidence that the rearrangement of the alcohols to their respective esters is first order in alcohol concentration is revealed in the plot of the natural logarithm of the integrated alcohol peak area versus time. In all rearrangements studied, this plot was found to be linear within experimental error. The

errors calculated in the slope by the computer were found to be no more than three percent in any rearrangement.

That the alcohol to ester rearrangements are definitely second order overall, i.e. first order with respect to alcohol concentration and first order with respect to pyridine concentration of both the alcohol and pyridine. Table II shows that the rearrangements are first order in pyridine concentration since division of the pseudo first order rate constant, k_1', (as obtained from the slope of the plot of natural logarithm of the integrated peak area versus time) (Appendix I), by the pyridine concentration yields the second order rate constant, k_2, which is independent of the initial concentration of alcohol.

The most intensive study was carried out on the alcohol "1"-pyridine system at 32.6°C. At this temperature the rearrangement to ester "1" was essentially complete within forty minutes from the time the alcohol and the base were mixed. The concentration of alcohol "1" and pyridine was varied, as shown in Table II, and the values of k_2 were seen to be constant within experimental error. The average second order rate constant was calculated to be 3.04×10^{-4} ℓ mol^{-1} s^{-1}. The deviation from this mean value for any individual value of k_2 was

TABLE II

Rates of Rearrangement of $(RO)_2P(O)C(OH)(CF_3)_2$ by Pyridine in Dichloromethane

R	T(°C)	Initial Alcohol Conc.(M)	Initial Base Conc.(M)	$k_1'(s)^{-1}$	$k_2(\ell\ mol^{-1}\ s^{-1})$
CH_3	32.6	0.99	1.71	5.18×10^{-4}	3.03×10^{-4}
		0.49	1.71	5.15×10^{-4}	3.01×10^{-4}
		0.99	2.57	7.92×10^{-4}	3.08×10^{-4}
		0.49	2.57	7.82×10^{-4}	3.04×10^{-4}
C_2H_5	45.5	1.22	1.71	2.41×10^{-4}	1.41×10^{-4}
		1.22	2.57	3.42×10^{-4}	1.33×10^{-4}
$n\text{-}C_4H_9$	57.6	1.18	2.57	6.62×10^{-4}	2.42×10^{-4}
		1.18	1.71	4.10×10^{-4}	2.40×10^{-4}

found to be about one percent. Inspection of the reaction mixture after the alcohol had completely rearranged to the ester revealed that the formerly clear and colorless alcohol solution had acquired a light orange tint.

Using an initial alcohol "1" concentration of 0.99 M and an initial pyridine concentration of 2.57 M, the kinetic runs were repeated at 40.0° and 45.5° to yield respective rate constants of 4.89×10^{-4} ℓ mol^{-1} s^{-1} and 8.03×10^{-4} ℓ mol^{-1} s^{-1} as shown in Table III. Figure I shows the kinetic plots for these rearrangements. At 40.0°C the rearrangement was complete after 34 minutes whereas at 45.5°C the rearrangement was complete within twenty five minutes as would be expected. The Arrhenius energy of activation was found to be 14.6 kcal mol^{-1}. The entropy of activation was calculated to be -29.1 e.u. These activation parameters are listed in Table IV.

Based on the evidence of second order kinetics provided from the rearrangement of alcohol "1" to ester "1", it seemed likely that the rearrangement of alcohol "2" to ester "2" would similarly follow second order kinetics. This was confirmed by employing an initial alcohol "2" concentration of 1.22 M with pyridine concentrations of 1.71 M and 2.57 M at 45.5°C. Again excellent pseudo first order plots were obtained and are equal within experimental error as shown in Table II.

TABLE III

Rates of Rearrangement of $(RO)_2P(O)C(OH)(CF_3)_2$ by Pyridine in Dichloromethane

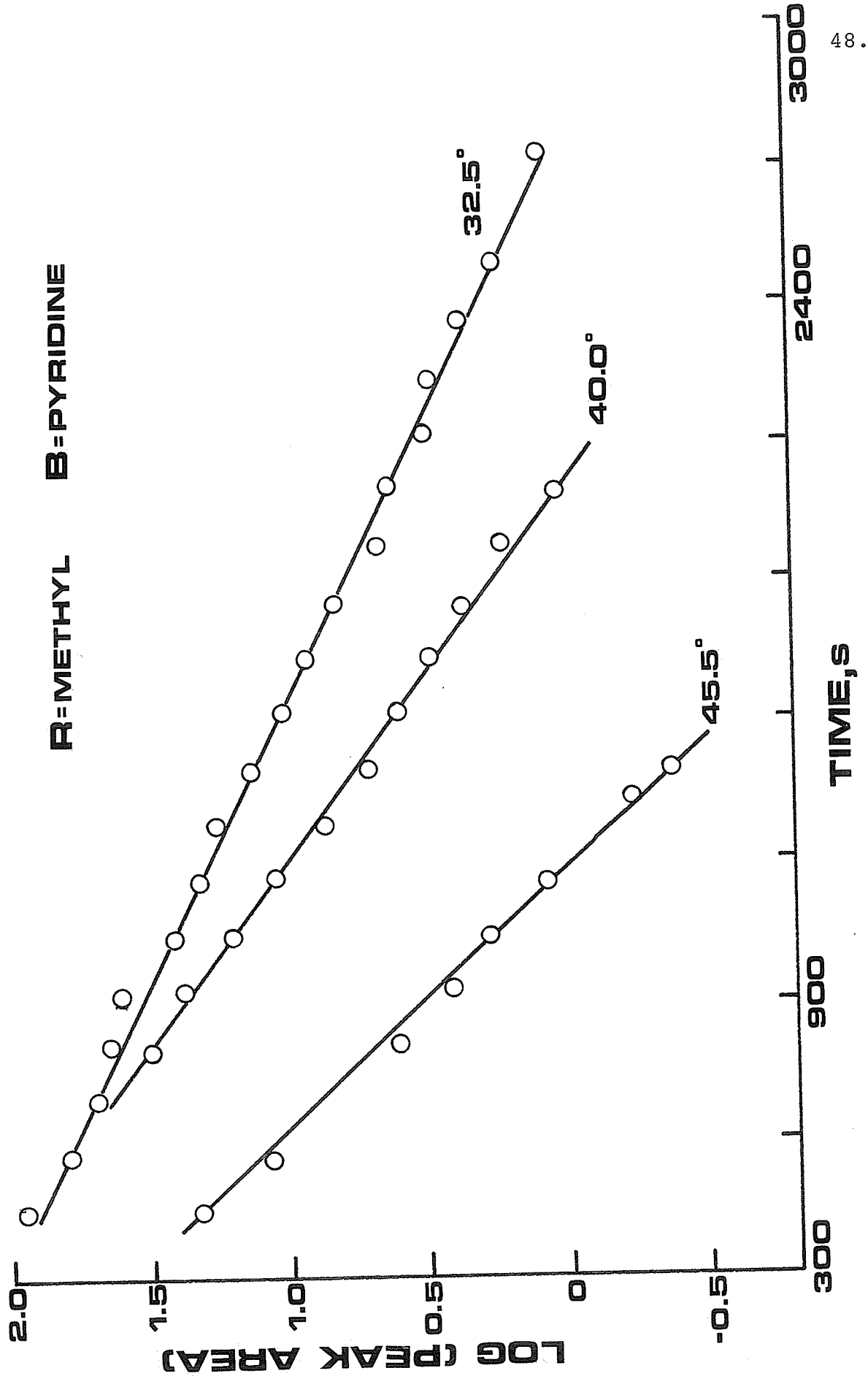
R	T(°C)	k_2(ℓ mol^{-1} s^{-1})
CH_3	32.6	3.03×10^{-4}
	40.1	4.89×10^{-4}
	45.6	8.03×10^{-4}
C_2H_5	32.6	3.96×10^{-5}
	42.3	1.07×10^{-4}
	44.6	1.33×10^{-4}
	54.1	3.15×10^{-4}
	57.1	3.80×10^{-4}
$n\text{-}C_4H_9$	51.4	1.27×10^{-4}
	54.6	1.60×10^{-4}
	57.6	2.42×10^{-4}
	58.0	3.01×10^{-4}
	62.1	4.07×10^{-4}

TABLE IV

Energy of Activation (E_a), Entropy of Activation ($\Delta S^{\ddagger}$) and Logarithm of Pre-exponent (Log A) for $(RO)_2P(O)C(OH)(CF_3)_2$ Rearrangement

R	E_a kcal/mol	$\Delta S^{\ddagger}$ cal/mol degree	Log A
CH_3	14.6	-29.1	6.87
C_2H_5	19.8	-15.9	9.75
n-C_4H_9	24.5	- 3.0	14.0

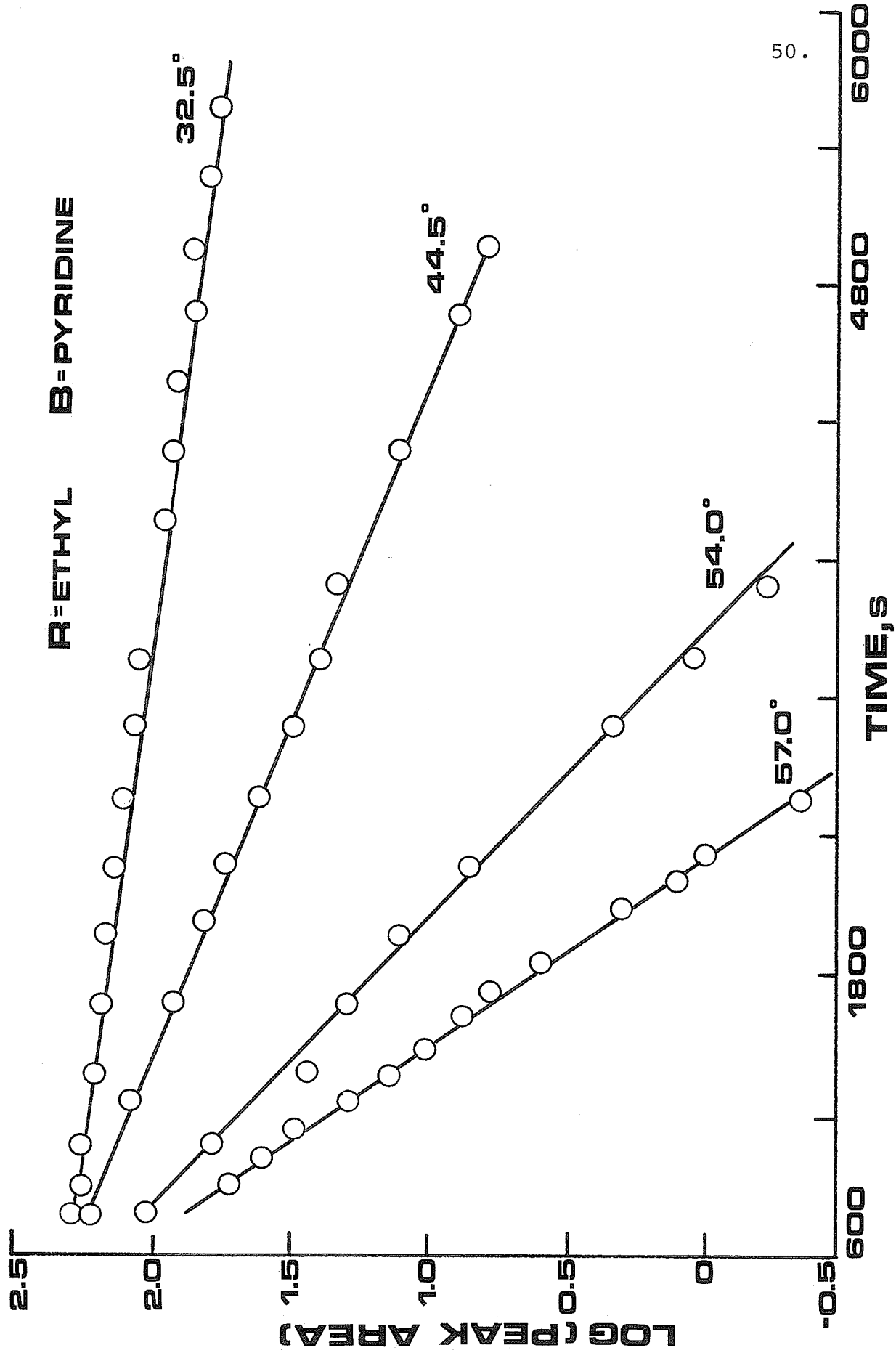
FIGURE I Plot of the log of peak area vs. time for the rearrangement of $(CH_3O)_2P(O)C(OH)(CF_3)_2$ (0.99 M) with pyridine (2.57 M) in dichloromethane at various temperatures.


R=METHYL
B=PYRIDINE
32.5°
40.0°
45.5°
LOG (PEAK AREA)
TIME, S
2.0
1.5
1.0
0.5
0
-0.5
300
900
2400
3000

In contrast to the relatively short time period required for the rearrangement of alcohol "1", ie approximately 60 minutes at 32.5°C, the complete rearrangement of alcohol "2" required approximately 5 hours. Due to the fact that the rearrangements of alcohol "2" took a long time at lower temperatures, rearrangement studies to find the activation parameters were carried out at significantly higher temperatures. Using initial alcohol "2" and pyridine concentrations of 1.22 M and 2.57 M, the rearrangements were followed at 32.5°, 42.3°, 54.1° and 57.1°C. The derived second order rate constants are listed in Table III. Figure II shows the kinetic plots at the various temperatures. The Arrhenius energy of activation and the entropy of activation for the rearrangement of alcohol "2" are listed in Table IV. The significant increase in the energy of activation for rearrangement of alcohol "2" over that obtained for alcohol "1", i.e. 19.8 kcal mol^{-1} and 14.9 kcal mol^{-1} respectively, is at once reflected in the large differences in the second order rate constants of the two rearrangements.

As was found with the rearrangement of alcohol "1", the rearrangement of alcohol "2" occurred with the formation of a light orange tint in the reaction mixture. However unlike ester "1", ester "2" was found to be stable in the presence of pyridine even though ester "2" was kept in contact with pyridine for a period of one week at room

FIGURE II Plot of log of peak area *vs.* time for the rearrangement of $(C_2H_5O)_2P(O)C(OH)-(CF_3)_2$ (1.22 M) with pyridine (2.57 M) in dichloromethane at various temperatures.

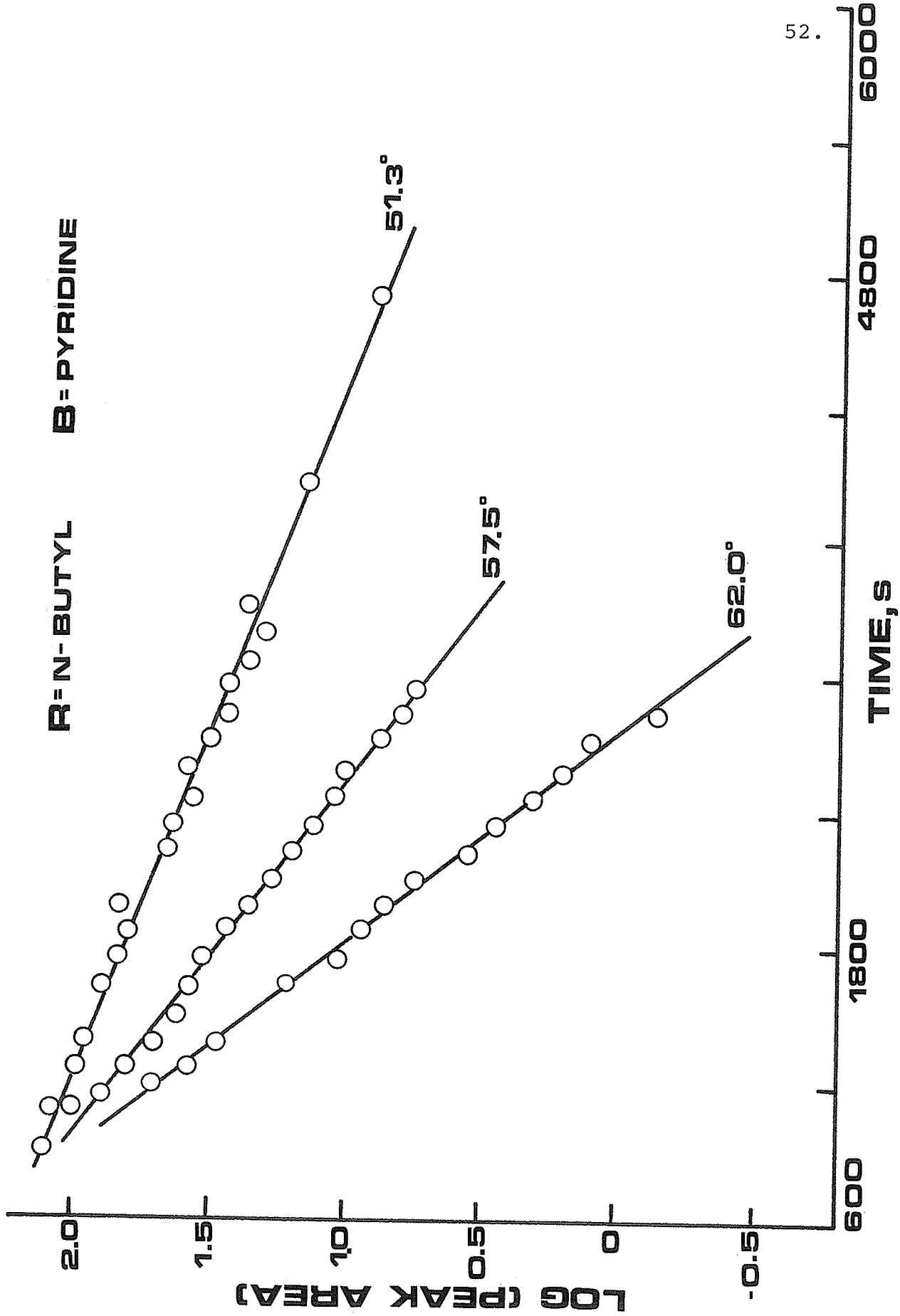

R=ETHYL B=PYRIDINE
32.5°
44.5°
54.0°
57.0°
LOG (PEAK AREA)
TIME, S
2.5
2.0
1.5
1.0
0.5
0
-0.5
600
1800
4800
6000

temperature.

The rearrangement of alcohol "3" to ester "3" was found to be first order both in alcohol and pyridine as shown in Table II. The rate constants, k_2, are seen to be equal within experimental error. The excellent agreement of these two second order rate constants coupled with the expected similarity of the rearrangements of alcohol "1" and alcohol "2" was considered acceptable evidence that the rearrangement of alcohol "3" to ester "3" followed second order kinetics.

The activation parameters of alcohol "3" were determined and are outlined in Table IV. The kinetic plots are shown in Figure III. The rearrangement of alcohol "3" was carried out at much higher temperatures than were used for the other two cases in the determination of the activation parameters. At lower temperatures, the alcohol "3" to ester "3" transition was too slow to be studied accurately by nmr techniques. The accuracy of the nmr instrument was not sufficient to detect very small decreases in the peak area of the alcohol. The natural logarithm of peak area versus time plot for 51.3°C as shown in Figure III shows an erratic behavior for this reason. At higher temperatures, as is evident from the kinetic plots at 57.5°C and 62.0°C in Figure III where the rearrangement rate is much faster, this erratic behavior is not as apparent. Analogously to alcohols "1" and "2", the rearrangement of

FIGURE III Plot of log of peak area vs. time for the rearrangement of $(n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$ (1.18 M) with pyridine (2.57 M) in dichloromethane at various temperatures.


R= N-BUTYL
B= PYRIDINE
51.3°
57.5°
62.0°
LOG (PEAK AREA)
2.0
1.5
1.0
0.5
0
-0.5
600
1800
4800
6000
TIME, s

alcohol "3" was also accompanied by the appearance of an orange color. Ester "3" showed no sign of decomposition in the presence of pyridine after an extended period of time.

The effect of varying the base strength on the rate of rearrangement of alcohol "1" is shown in Table V. It was generally found that as the base strength increased, i.e. greater values of pK_b (60), the rates of rearrangement increased also with the exception of the N,N-dimethylaniline case. When diethylamine or piperidine were employed as basic catalysts, the rate of rearrangement was much too fast to be measured by nmr techniques since the rearrangement reaction was complete within a matter of seconds from the time the base and alcohol were brought into contact. Figure IV shows that plotting log k_2 against the respective log base dissociation constants, pK_b, yields a near linear plot, although the existence of such a linear plot has been previously questioned (74).

Summary of Results

Inspection of Table II shows that the rate of rearrangement of the three alcohols to their respective esters is extremely sensitive to the nature of the alkyl groups involved. The rates of rearrangement are seen to decrease in the order methyl > ethyl > n-butyl with

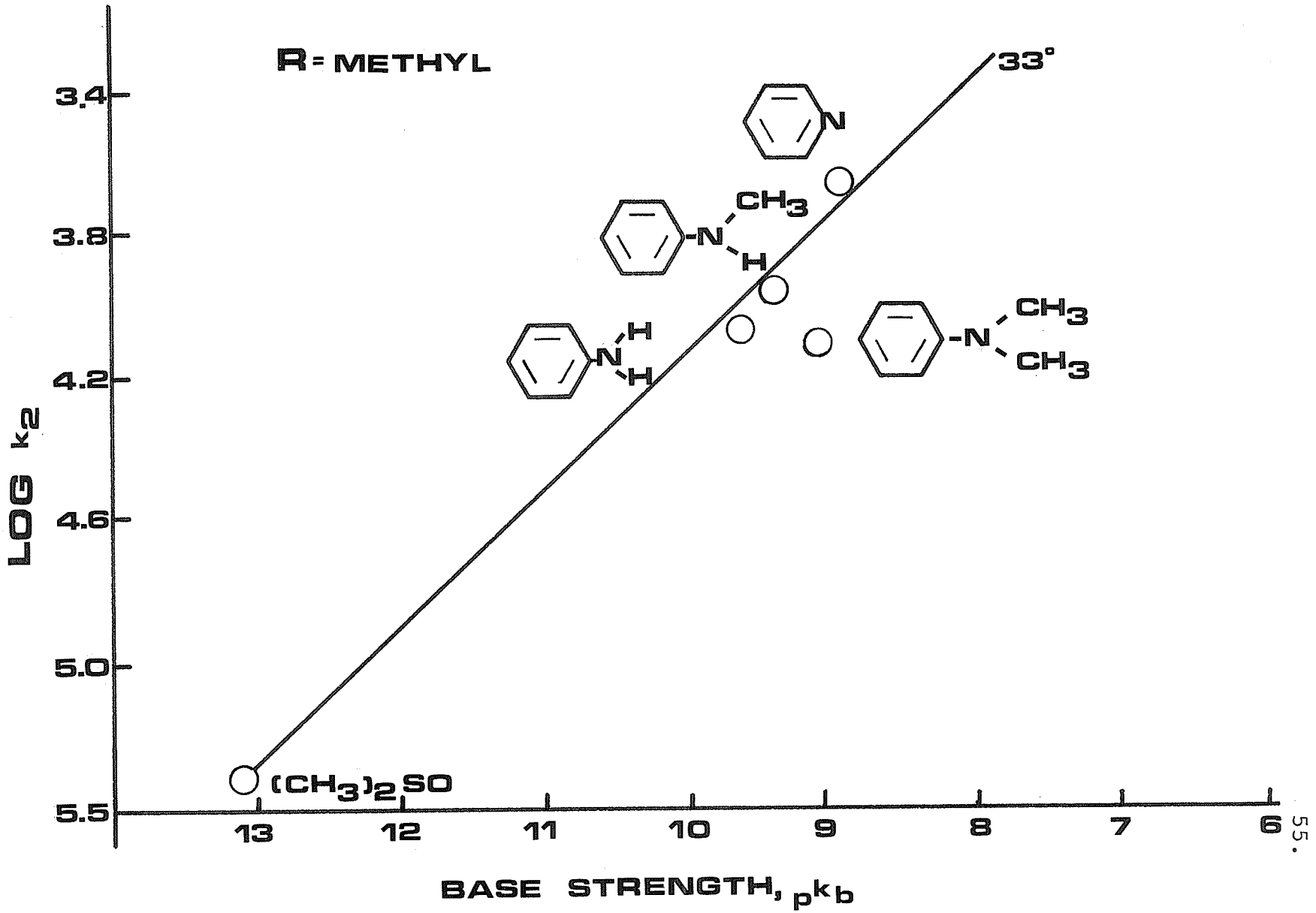
TABLE V

Effect of Base Catalyst (1.38 M) on Rearrangement of $(CH_3O)_2P(O)C(OH)(CF_3)_2$ (1.10 M) in Dichloromethane at 33°C

Base	pK_b	k_2 (ℓ mol^{-1} s^{-1})
Dimethylsulfoxide	13	7×10^{-6}
Aniline	9.37	1.11×10^{-4}
N-Methylaniline	9.15	1.47×10^{-4}
N,N-Dimethylaniline	8.85	1.02×10^{-4}
Pyridine	8.75	3.00×10^{-4}
Diethylamine	3.51	†
Piperidine	2.88	†

† To fast for measurement by nmr techniques.

FIGURE IV Plot of log k_2 *vs.* pK_b of base (1.38 M) for the rearrangement of $(CH_3O)_2P(O)C(OH)(CF_3)_2$ (1.10 M) in dichloromethane at 33°C.

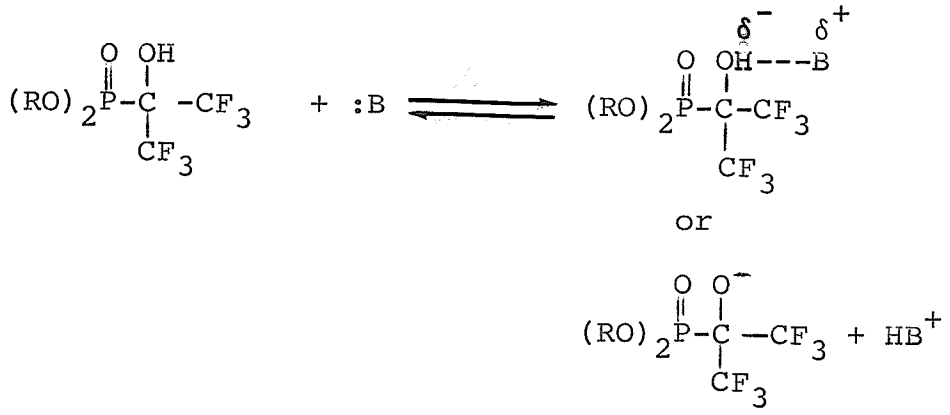

R = METHYL
33°
3.4
3.8
4.2
4.6
5.0
5.5
LOG k_2
13
12
11
10
9
8
7
6
$(CH_3)_2SO$
BASE STRENGTH, pK_b

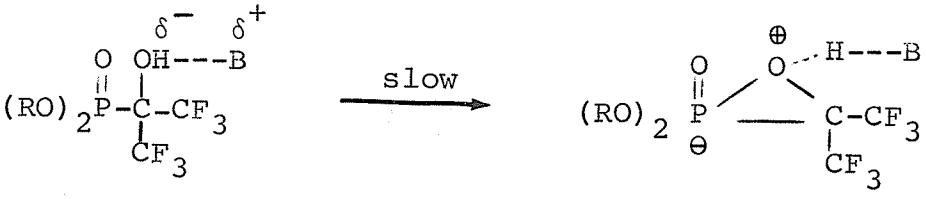
respective rate constants being 8.03×10^{-4} ℓ mol^{-1} s^{-1} (45.5°C), 3.15×10^{-4} ℓ mol^{-1} s^{-1} (54.0°C) and 1.60×10^{-4} ℓ mol^{-1} s^{-1} (54.0°C). Accompanying this trend in decreasing rearrangement rates, the activation energies increase in the order, methyl < ethyl < n-butyl with respective values of 14.6 kcal mol^{-1}, 19.8 kcal mol^{-1} and 24.5 kcal mol^{-1}. The entropies of activation similarly decrease in the order methyl > ethyl > n-butyl with respective values of -29.1 e.u., -15.9 e.u., and -3.0 e.u. The rates of rearrangement are seen to be dependent on the base strength also. The implications involved in the experimentally determined second order rate constants and activation parameters with respect to the mechanism of rearrangement will be discussed fully in the following section.

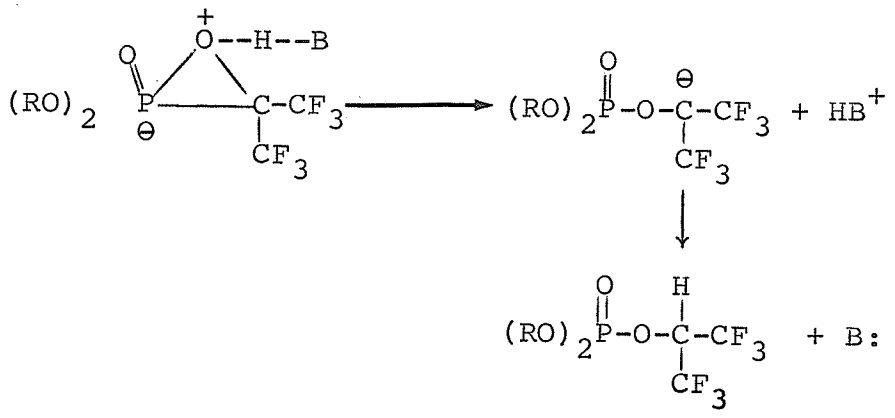
MECHANISM OF REARRANGEMENT

In proposing a mechanism for the rearrangement of dialkyl 2-hydroxy-1,1,1,3,3,3-hexafluoroisopropylphosphonates to 1,1,1,3,3,3-hexafluoroisopropyldialkyl phosphates, i.e. alcohol to ester, it is essential that such a mechanism be compatible with the second order kinetics observed for the rearrangement. In addition, this mechanism must be consistent with the experimentally determined energies of activation and entropies of activation and must also explain how the nature of R would influence the observed activation parameters.

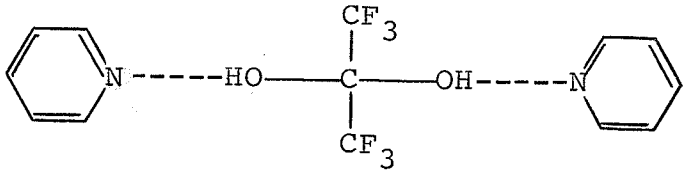
A mechanism, based on the transition state concept (Appendix I), which is consistent with the observed second order kinetics is outlined in equations [1] - [3].

[1] 

[2] 

[3] 

The first step involves the polarization of the hydroxyl oxygen of the alcohol through hydrogen bonding between the hydroxyl proton and the Lewis base. Hydrogen bonding between the alcohol and the pyridine would be expected to be particularly strong due to the presence of the two trifluoromethyl groups. Middleton and Lindsey (58) have reported that the hydrogen bonding with pyridine in the following diol is so strong that the adduct can be distilled.



Infrared spectroscopy has shown that the hydrogen bond between the phosphoryl oxygen and the hydroxyl group is expected to be of a very small magnitude (59), hence such a bond would not act as a barrier to hydrogen bonding with the pyridine.

It is postulated that step [1] involves a rapid reversible proton exchange between the alcohol and the basic catalyst. If this is the case the effect of increasing base strength would be to shift the equilibrium to the right, i.e. in the direction of increased ionization. This was verified experimentally by varying the Lewis base strengths in the rearrangement of alcohol "1". As discussed earlier, increasing the value of pK_b caused an increase in the magnitude of the rate constant with the exception of N,N-dimethylaniline. The cause of the deviation for this particular Lewis base may lie in steric effects. The tendency of the Lewis base and the hydroxyl group to form a hydrogen bond is a function of the ability of the lone pair of electrons on the nitrogen to come into fairly close contact with the hydroxyl proton. For the bases, aniline, N-methylaniline and pyridine, steric hindrance would have little effect on hydrogen bond formation. On the other hand, N-N-dimethylaniline has two methyl groups on the nitrogen atom. It is conceivable that the presence of these two methyl groups will inhibit hydrogen bond formation because of the steric interactions with the two trifluoromethyl groups of the alcohol.

Step [2] of the proposed mechanism must then represent the rate determining step. Step [2] involves the intramolecular nucleophilic attack of the negatively charged hydroxyl oxygen on the phosphorus atom. It is reasonable

to postulate that the phosphorus atom will have a slight electron deficiency due to the presence of the electronegative oxygen atoms of the alkoxy groups, OR, as well as the electron withdrawing influence of the two highly electronegative trifluoromethyl groups situated on the carbon atom adjacent to the phosphorus atom. This implies that any substituent on the phosphorus atom which may either release electron density to phosphorus or interfere with the necleophilic attack of the oxygen upon the phosphorus will cause an increase in the energy barrier to the transition state. Any variation in the energy barrier to the transition state will be reflected in the observed values of the energy of activation. The inductive (electron releasing) effect of the alkyl groups is generally assumed to follow the order butyl > ethyl > methyl. This series indicates that the positive charge on the phosphorus atom will decrease in the order methyl > ethyl > n-butyl. Therefore, the tendency of the negative oxygen atom to attack the phosphorus will decrease in the order methyl > ethyl > n-butyl due to the electron releasing abilities of these alkyl groups. Inspection of the activation energies as shown in Table IV reveals this to be exactly the case with the respective activation energies being 14.6 kcal mol^{-1} (R = methyl), 19.8 kcal mol^{-1} (R = ethyl) and 24.5 kcal mol^{-1} (R = n-butyl).

The amount of electron density on the phosphorus atom and the observed effects on the activation energy may be

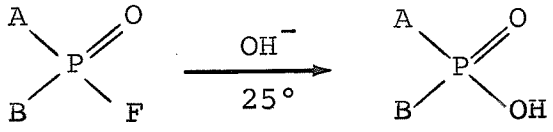
rationalized as follows. pπ-dπconjugation between the alkoxy groups, OR, and phosphorus is well known (61-64). This bond arises from the flow of the unpaired 2p electrons of the oxygen to the vacant, energetically favorable 3d orbitals of the phosphorus atom. Thus in the R-O-P linkage there exists two mutually opposing effects which affect the electron density on the phosphorus atom in different ways. These are, firstly, a negative inductive effect leading to the displacement of σ electrons along the P-O bond, and secondly, pπ-dπ conjugation as discussed above. Since the inductive effect of the alkyl group follows the order n-butyl > ethyl > methyl, the degree of pπ-dπ bonding between the oxygen and the phosphorus will follow the order n-BuO > EtO > MeO. Therefore, the amount of negative charge present on the phosphorus atom will decrease in the order $(CH_3O)_2P(O)C(OH)(CF_3)_2 < (C_2H_5O)_2P(O)C(OH)(CF_3)_2 < (n\text{-}C_4H_9O)_2P(O)C(OH)(CF_3)_2$.

The nucleophilic attack of the negative oxygen atom on the partially positive phosphorus as outlined in step [2] will be facilitated by the formation of pπ-dπ bonds between the attacking oxygen and the vacant 3d orbitals on phosphorus. It has been shown (65,66) that the formation of pπ-dπ bonds in such compounds is very sensitive to change in the charge on the phosphorus atom. More specifically, as the amount of electron density on the phosphorus atom increases, there will be a reduced tendency for this stabilizing pπ-dπ bond formation between the nucleophilic oxygen and the phosphorus

atom. Since the negative charge on the phosphorus atom in the alcohols has been shown to increase in the order n-Bu > Et > Me, it follows that this stabilizing $p\pi$-$d\pi$ bond formation will increase in the order Me > Et > n-Bu.

One can draw certain analogies to this step of the alcohol to ester rearrangement with other areas of phosphorus chemistry. For example, Dostrovsky and Halmann (67) studied the solvolysis of phosphoryl halides in 100% ethyl alcohol at 0°C and Table VI shows some pertinent results which have certain similarities to this work. As the alkyl group is varied from methyl to ethyl the rate of reaction decreases. Similar variation of the alkyl group raises the activation energy. The kinetic order of these solvolysis reactions together with the position of bond fission established that the oxygen attacks the phosphorus atom in the rate controlling step as is postulated in this work.

Knunyants' group studied the alkaline hydrolysis of phosphorus acid fluorides (68).



In these alkaline hydrolysis reactions the rate determining step is assumed to be the nucleophilic attack of the hydroxide ion on the phosphorus atom. As the R group is varied from methyl to ethyl and then butyl, the values of the second order rate constant are shown to decrease in value as shown

TABLE VI

Pseudo-Unimolecular Rate Constants for the Solvolysis of Phosphoryl Halides in Neutral Oxygen Solvents

Compound	k sec^{-1}	E kcal/mol	log A sec^{-1}
$(CH_3O)_2POCl$	5.6×10^{-5}	12.0	5.4
$(C_2H_5O)_2POCl$	2.3×10^{-5}	13.4	6.1

in Table VII. A similar variation of the alkyl groups yields increasing values of the activation energy. These trends qualitatively match those found for this work. Knunyants has found similar trends in the reaction rates and energies of activation for the hydrolysis of phosphonochloridic esters (69) and also the alkaline hydrolysis of dialkyl-S-methyl thiophosphates (71) as shown in Table VIII.

As well as the differing inductive effects of the alkyl groups on the alcohols, the size of the alkyl group may also have an effect on the magnitude of the activation energies of the rearrangement. As the bulkiness of the alkoxy group attached to the phosphorus atom increases, the tendency for nucleophilic attack by the oxygen upon the phosphorus will decrease because of steric hindrance. The observed activation energies which have been shown to follow the order n-butyl > ethyl > methyl substantiate this arguement. A direct analogy may be made to nucleophilic attack at a carbon center. It is well known that for nucleophilic substitution the order of reactivity is CH_3>1°>2°>3°, and that crowding of the reaction center raises the energy of the transition state and slows down the reaction (70).

Consideration of the experimentally determined entropies of activation also give some insight into the mechanism of the base catalyzed rearrangements since $\Delta S^{\ddagger}$ provides one of the best indications of the nature of the transition state. A decrease in entropy corresponds to a

TABLE VII

Data on the Alkaline Hydrolysis of Phosphorus Acid Fluorides

A	B	k_2 $\ell\ mol^{-1}\ s^{-1}$	E kcal/mol	log A
CH_3O	CH_3O	12.9	11.61	9.60
C_2H_5O	C_2H_5O	2.8	11.64	9.10
$n\text{-}C_4H_9O$	$n\text{-}C_4H_9O$	1.26	12.04	8.93

TABLE VIII

Values for Arrhenius Equation Parameters, A, and E in the Alkaline Hydrolysis of $(CH_3S)P(O)(OR)_2$

R	E kcal/mol	log A
CH_3	11.2	6.69
C_2H_5	12.0	6.40
iso-C_3H_7	16.0	7.77

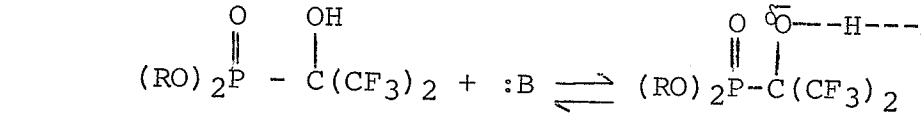
more ordered or less random molecular configuration. The large negative entropies found in the methyl case, $\Delta S^{\ddagger} = -29.1$ e.u. and in the ethyl case, $\Delta S^{\ddagger} = -15.9$ e.u. favor a highly oriented transition state.

In the transition state theory $\Delta S^{\ddagger}$ is defined as the change in entropy from the reactants to the transition state complex. According to the reaction scheme outlined in equations [] - [3].

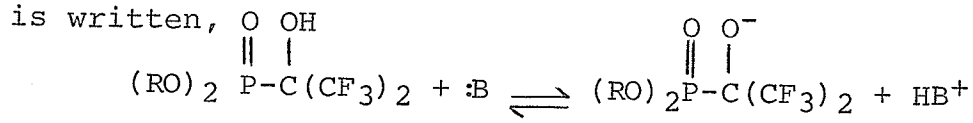
$$\Delta S^{\ddagger} = \Delta S^{\circ}_{E} + \Delta S_{2}^{\ddagger}$$

where ΔS°_{E} is the change in entropy for the equilibrium step and $\Delta S_{2}^{\ddagger}$ is the entropy change for step [2].

Thus, if the equilibrium step is represented as,



then it would be expected that ΔS°_{E} would make a negative contribution to $\Delta S^{\ddagger}$. In this case two participants are combining to form a one participant complex, i.e. a less random molecular configuration. However, if the equilibrium step is written,

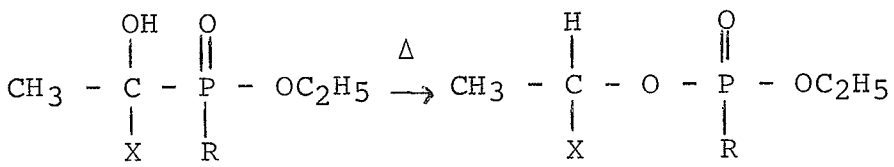


ΔS°_{E} would make a small positive or small negative contribution to $\Delta S^{\ddagger}$ since in this case two reacting species yield two product species and there is no net creation of order in the system. It must be realized, however, that these possible contributions of ΔS°_{E} to the overall value of $\Delta S^{\ddagger}$ are only speculative since kinetic studies do not give any

information about fast equilibria which occur before the rate determining step.

As stated above, the rate determining step is considered to be the nucleophilic attack of the negative oxygen on the phosphorus atom as outlined in step [2]. It is postulated that this rate determing step involves the formation of a cyclic transition state (the point at which the transition occurs from the starting material side to the product side). The formation of such a transition state would give highly negative values of $\Delta S^{\ddagger}$ since the rotational freedom of the molecule would be decreased. The oxygen bridge between the phosphorus and carbon atoms would severely hinder rotation about the phosphorus-carbon bond.

Evidence that the rate determining step involves a cyclic transition state comes from the studies of Pudovik et al. (52) who studied the thermal rearrangements of esters of some α-hydroxyalkylphosphinic acids, $(R)(OC_2H_5)P(O)-C(OH)(CH_3)X$.



The results are outlined in Table IX.

In this investigation the refractometric method was used to follow the kinetics since a linear dependence was found to exist between the refractive index and the composition of the mixture composed of the α-hydroxyalkylphosphinic

TABLE IX

Activation Parameters for the Thermal Rearrangement of Esters of α-hydroxyalkylphosphonic Acids

X	R	E kcal/mol	log A	$\Delta S^{\ddagger}$ e.u.
$COOC_2H_5$	C_2H_5O	25.6	8.97	-18.1
$COOC_2H_5$	C_2H_5	26.6	10.5	-11.1
CN	C_2H_5	27.3	10.8	- 9.63

acid and the rearrangement product. As was observed in the present work, Pudovik found the entropies of activation to be highly negative even in the absence of a basic catalyst. The rate determining step as proposed by these authors involves a cyclic transition state resulting from the attack of the oxygen atom of the hydroxyl group upon the phosphorus. This nucleophilic attack leads to the synchronous cleavage of the O-H and C-P bonds and rearrangement is completed by the formation of the C-O-P and C-H linkages. Pudovik's values for the entropy of activation are highly negative, as shown in Table IX and are indicative of a cyclic transition state. Thus it is reasonable to postulate that such a cyclic transition state as proposed in this work would similarly yield a highly negative contribution to $\Delta S^{\ddagger}$.

On the other hand, the entropy of activation for the alcohol to ester rearrangement for the n-butyl compound was found to be only -3.0 e.u. A small negative entropy of activation such as this suggests that the entropy of the transition state in the rearrangement of alcohol "3" is approximately the same as the base polarized molecule and further suggests that perhaps the proposed cyclic transition state may not be the most energetically favorable in this case. Evidence that the rearrangement of alcohol "3" also proceeds by a cyclic three membered transition state comes from the presence of an isokinetic relationship (72). The isokinetic relation has been successfully applied to many series of

reactions in which the solvent or structural change does not change the mechanism of the reaction or the nature of the transition state. In a series of related reactions involving moderate changes in structure or solvent, the enthalpy of activation and the entropy of activation vary but not usually independently. Large values of $\Delta H^{\ddagger}$ tend to accompany large values of $\Delta S^{\ddagger}$. At times this tendency attains the precision of a linear relationship between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. This relationship may be defined by the following linear equation called the isokinetic relationship.

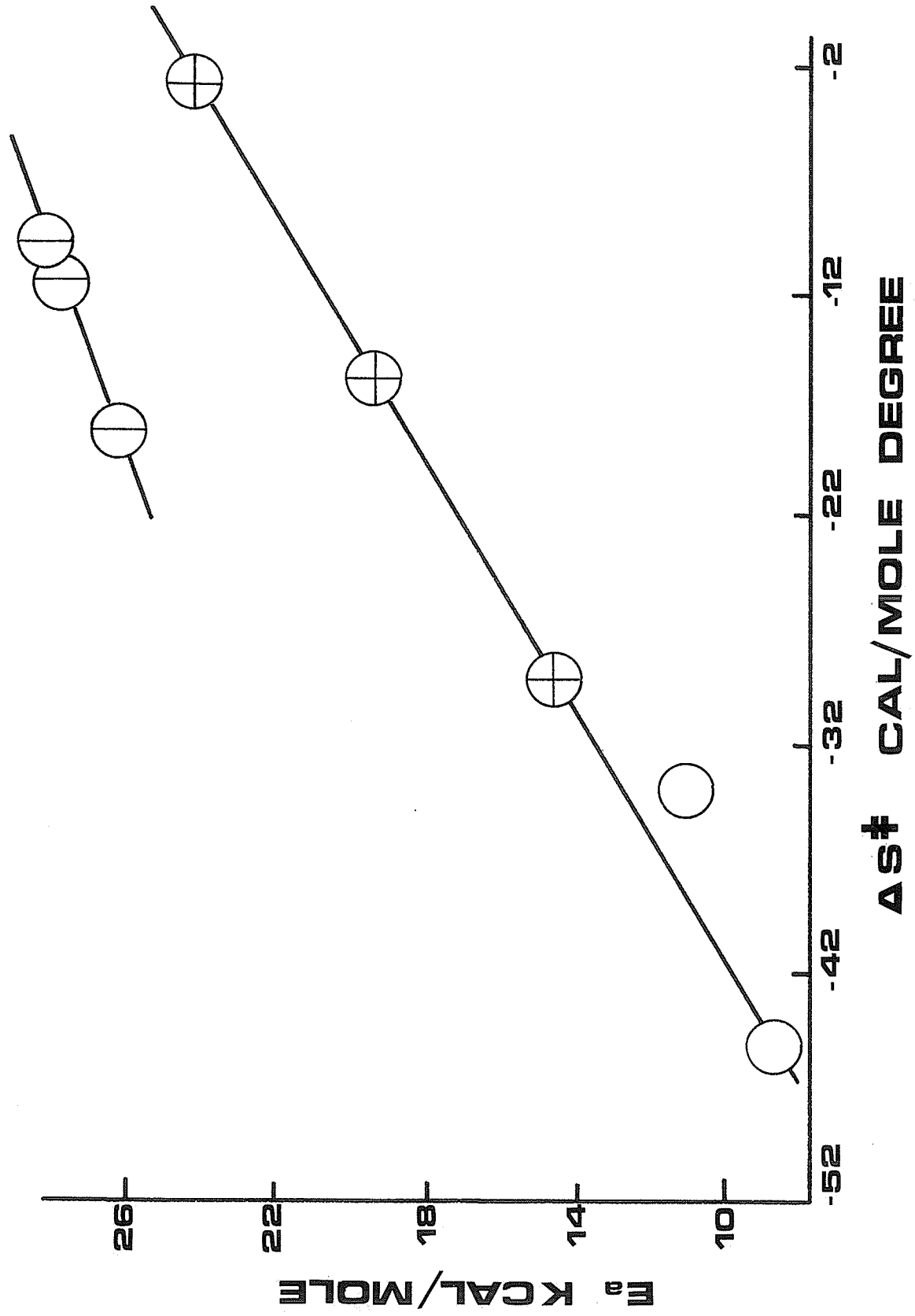
$$\Delta H^{\ddagger} = \Delta H^{\ddagger}_{o} + B\Delta S^{\ddagger}$$

The existence of this relationship has been considered in many cases to be evidence favoring a constant mechanism for a related series of reactions.

The result of plotting the enthalpy of activation or the energy of activation, E_a ($\Delta H^{\ddagger}$ and E_a related by the expression $\Delta H^{\ddagger} = E_a - RT$ (83) and since $RT << E_a$, then $\Delta H^{\ddagger} \simeq E_a$) versus the entropy of activation is shown in Figure V, ⊕. The existence of this perfectly linear plot implies that all three of the alcohols rearrange to their respective esters with the same mechanism.

Construction of space filling molecular models show that slight steric interactions are present between the rotating n-butyl groups and the trifluoromethyl groups of alcohol "3". Rotation about the P-C bond in alcohols "1" and "2" is much freer. Thus in the rearrangement of alcohol

FIGURE V Plot of E_a *vs.* $\Delta S^{\ddagger}$ for the alcohol to ester rearrangement: this work, ⊕; Brook *et al*, O; and Pudovik *et al*, ◐.


E_a KCAL/MOLE
26
22
18
14
10
-52
-42
-32
-22
-12
-2
$\Delta S^{\ddagger}$ CAL/MOLE DEGREE

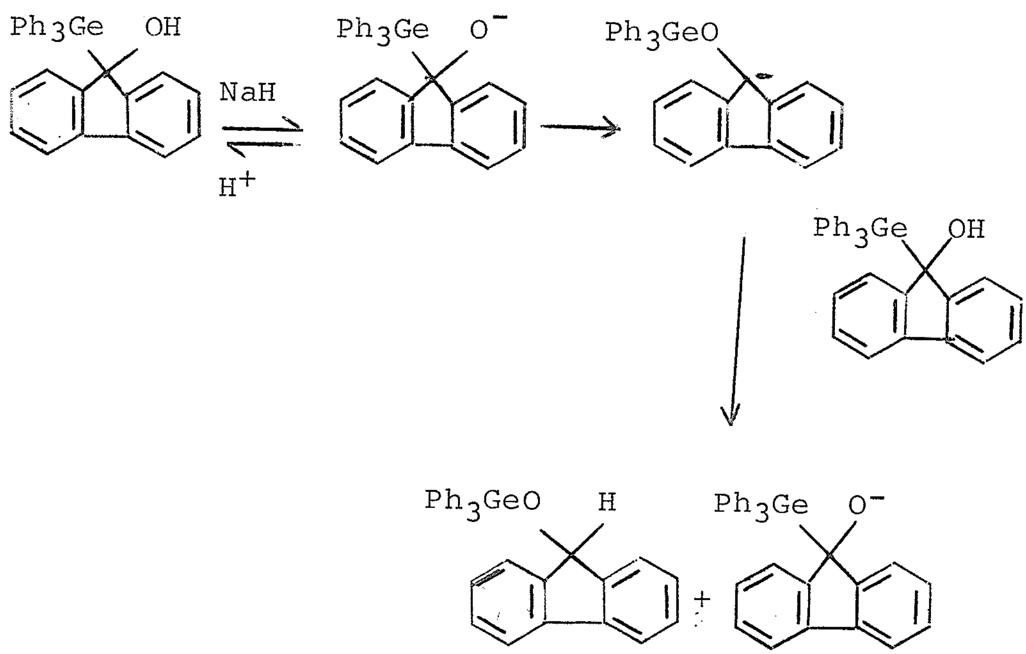
"3", passage through the transition state would be expected to involve only a slight increase in the restriction on the freedom of rotation about the P-C bond. However, for $R = CH_3$ and to a lesser extent for $R = C_2H_5$ the value of $\Delta S^{\ddagger}$ would be much larger since there would be a greater increase in the restriction on the freedom of rotation about the P-C bond.

Step [3] of the mechanism is considered to involve a rapid collapse of the cyclic transition state to yield the ester $(RO)_2P(O)OCH(CF_3)_2$. This step could proceed either through an intermediate carbanion followed by proton transfer from the protonated base or by direct formation of the product by simultaneous cleavage of the P-C bond and formation of the C-H bond.

It would be useful to compare the results of the alcohol to ester rearrangement in phosphorus compounds with similar rearrangements in other systems. Peddle and Ward have reported the rearrangement of germyl alcohols to germyl ethers (73).

One can see certain qualitative similarities between this rearrangement of the germyl alcohol to the germyl ether and the alcohol to ester rearrangement in the phosphorus compounds. The formation of the alkoxide in both cases is brought about by the initial abstraction of the hydroxyl proton followed by the nucleophilic attack of the oxygen atom on the main group element. Peddle and Ward also reported

that the attempted alkoxide to alcohol reaction using n-butyl lithium was unsuccessful. This investigation by these authors did not include any kinetic results, however.



Brook et al. recently carried out the kinetic investigation of the base catalyzed rearrangements of α-silyl alcohols to silyl ethers (74).

$$R_3Si\underset{\displaystyle OH}{C}R'R'' \xrightarrow{B:} R_3SiOCHR'R''$$

Using 'H nmr techniques, Brook showed that the above rearrangement was second order overall, i.e. first order in the amine catalyst and first order in the α-silyl alcohol Brook observed that as the substituents on the silicon atom were made more electronegative the rates of rearrangement were enhanced as for example with

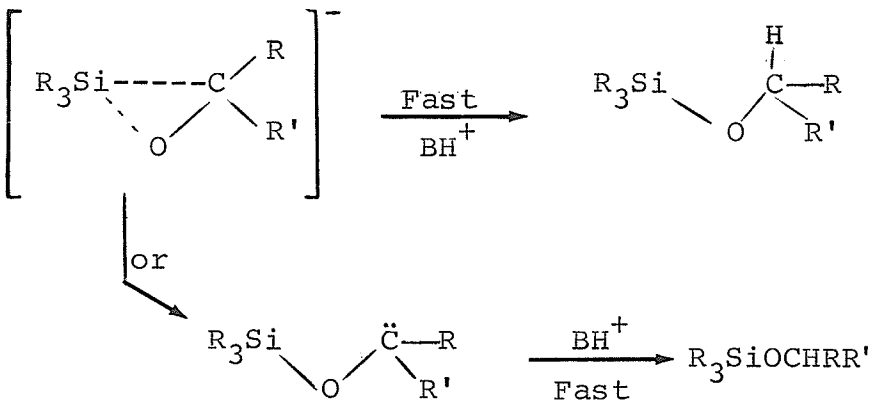
$R = C_6H_5$, $R' = R'' = C_6H_5$, $k_2 = 6.10 \times 10^{-3}$ whereas for $R = CH_3$, $R' = R'' = C_6H_5$, $k_2 = 0.25 \times 10^{-4}$. Similar trends were found for the alcohol to ester rearrangements in the phosphorus compounds. Table X shows the activation parameters for several rearrangement reactions involving silicon compounds. Again the values for the entropy of activation are very low and they are consistent with a highly oriented, sterically crowded transition state in which there may be considerable restriction to free rotation about single bonds as in a cyclic transition state. The values of the energies of activation for the silicon compounds are much smaller than those found in the rearrangement of the phosphorus compounds.

Brook, in this publication, makes no attempt to separate possible inductive or steric factors and attributes the variation in the activation energy solely to the inductive effects of the substituents on the silicon atom. The mechanism proposed by Brook for the rearrangement of the silicon compounds is indeed very similar to that postulated for the alcohol to ester rearrangement of phosphorus compounds.

[1] $$R_3Si-\underset{\displaystyle OH}{\overset{\displaystyle R}{\underset{|}{\overset{|}{C}}}}-R' + :B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_3Si-\underset{\displaystyle O^-}{\overset{\displaystyle R}{\underset{|}{\overset{|}{C}}}}-R' + BH^+$$

[2] $$R_3Si-\underset{\displaystyle O^-}{\overset{\displaystyle R}{\underset{|}{\overset{|}{C}}}}-R' \longrightarrow \left[R_3Si\text{-----}C\begin{matrix} R \\ O \\ R' \end{matrix} \right]^-$$

[3]



Furthermore, a common mechanism of rearrangement for phosphorus and silicon compounds is suggested in Figure V, the isokinetic plot. The points for compounds listed in Table X have been plotted, O. Extension of the line through the points for the rearrangement of the phosphorus compounds, ⊕ shows that the line passes very close to Brook's points.

Figure V also contains the plot of the activation parameter reported by Pudovik (52) for the thermal rearrangement discussed earlier. The fact that Pudovik did not use a solvent or a base catalyst as in this work suggests that there should be some differences in the two systems. Figure V shows that the points for Pudovik's compounds O lie considerably above the plot for this work. This vertical displacement is attributable to the absence of solvent and base catalyst. It is of interest to note that the vertical displacement in the isokinetic plot of Pudovik's work, O, from the isokinetic plot of this work, ⊕, is consistent with the generalization that catalysts decrease the energy of activation

TABLE X

Activation Parameter for Isomeric Silylalcohols

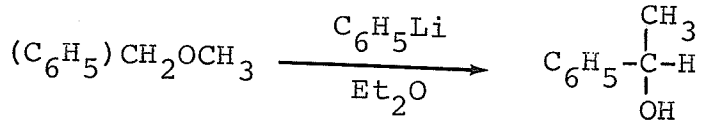
Silylalcohol	E_a kcal/mol	$\Delta S^{\ddagger}$ e.u.
$(C_6H_5)_3SiC(OH)(CH_3)(C_6H_5)$	11.16	-34.3
$(C_6H_5)_2(CH_3)SiC(OH)(C_6H_5)_2$	8.65	-45.6

of a reaction. The similarity in the magnitude of the activation entropies for the two systems is good evidence for a cyclic three membered transition state which has been postulated in both cases.

Thus it appears that it is possible that a variety of elements undergo the alcohol to ester rearrangement by way of a general mechanism as formulated for the alcohol to ester rearrangement in the phosphorus compounds. Janzen's group have recently investigated the alcohol to ester rearrangement in sulfur compounds and it will be interesting to see if this rearrangement follows a similar pathway (15).

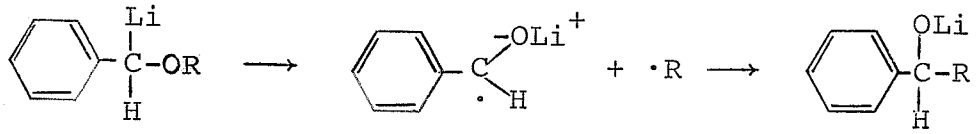
ATTEMPTED ALKOXIDE TO ALCOHOL REARRANGEMENT

Alkoxide to alcohol rearrangements in compounds containing main group elements are well known. Perhaps the most important rearrangement of this type found in organic chemistry is the Wittig rearrangement (76) as illustrated by the following reaction.

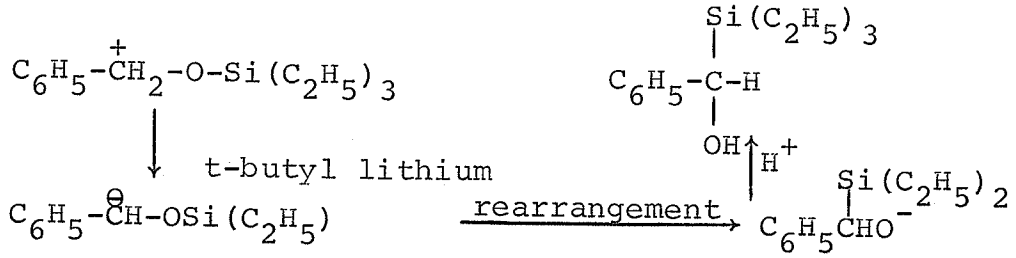


"alkoxide" "alcohol"

Recent mechanistic studies by Lansbury et al suggest that the Wittig rearrangement proceeds by a cleavage-recombination mechanism involving free radical pairs (79).



Rearrangements, analogous to the Wittig rearrangement, have been discovered recently by West and coworkers (78) in silicon compounds.



An intramolecular mechanism, involving a pentacoordinate silicon intermediate has been invoked to explain product formation.

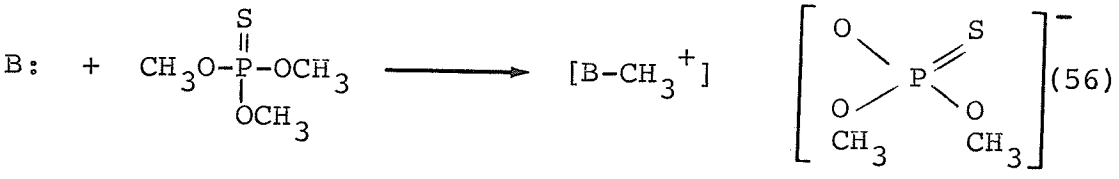
The treatment of ester "1" with n-butyl lithium, followed by acidification did not give an ^{19}F nmr spectrum indicative of alcohol "1". A singlet possibly due to the carbanion $(MeO)_2P(O)O\overset{\ominus}{C}(CF_3)_2$ was obtained. Rearrangement to the alcohol would involve cleavage of the P-O bond. As discussed earlier the P-O bond has two components which make the bond very strong. These two components are the σ bond and the $p\pi$-$d\pi$ conjugation between the oxygen lone pair electrons and the phosphorus 3d orbitals. Thus it is proposed that the ester to alcohol rearrangement goes no further than the carbanion formation due to the inherent stability of the P-O bond.

SPECULATION ON THE FATE OF ESTER "1" IN THE PRESENCE OF PYRIDINE

As outlined in the Experimental section, ester "1" was found to be unstable in the presence of the basic catalyst pyridine. After approximately 30 minutes from the start of the rearrangement a doublet, J = 6 Hz, appeared at 0.25 ppm downfield from the ^{19}F resonance signal of ester "1". The intensity of this new signal increased with time even after the ^{19}F resonance signal of alcohol "1" had vanished. That the compound producing

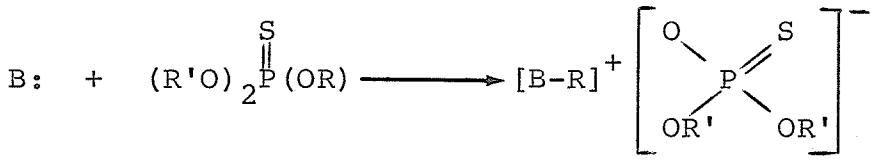
this new doublet was formed from ester "1" was proven by the simultaneous increase in the ^{19}F signal of the new compound and the decrease in the ^{19}F signal intensity of ester "1". The increase in the peak intensity of the new doublet was accompanied exactly by a decrease in the ^{19}F signal intensity of the ester. After approximately 24 hours, the signals were of equal intensity, thus showing that the reaction of ester "1" was very slow in comparison to the rearrangement reaction. Since the appearance of this new doublet was shown to occur at the expense of ester "1" and not alcohol "1", it was assumed that this reaction did not affect the disappearance of alcohol "1", and hence did not interfere with the kinetic study.

Although the product of the reaction between ester "1" and pyridine was not investigated, it is interesting to speculate what the product may be. This product was found to contain the grouping $CH_3OP(O)CH(CF_3)_2$ as determined by ^{1}H and ^{19}F nmr. Several workers have investigated the reactions between phosphates (esters) and organic bases.



(56)

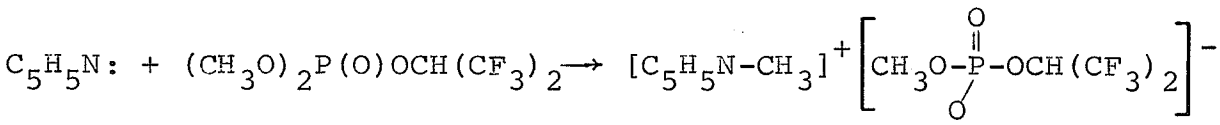
B: = tertiary organic base



(57)

R = lower alkyl, R' = aryl or larger alkyl, B = heterocyclic amine.

In light of these reactions and on the basis of the ^{19}F and ^{1}H nmr, it appears reasonable that ester "1" may react with pyridine as follows:



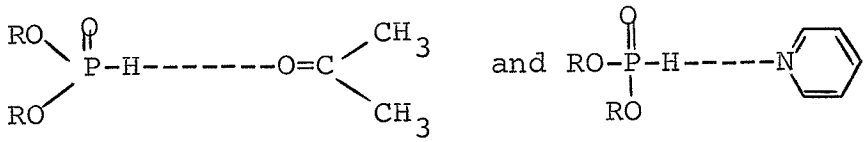
Besides being unstable in pyridine, ester "1" was also unstable in Lewis bases such as diethylaniline and aniline. Ester "2" and ester "3" were found to be stable in pyridine as no reaction occurred after a week. Mel'nikov et al found in their studies that only esters with methyl groups reacted with base (56). Therefore on the basis of the similarity between the two systems, it seems reasonable that the decomposition of ester "1" follows the path indicated above.

MECHANISM OF THE REACTION OF HEXAFLUOROACETONE WITH DIALKYL PHOSPHONATES

In their investigation of the reaction of hexafluoroacetone and dialkyl phosphonates, Janzen and Pollitt (49) suggested that perhaps the formation of both the alcohol

and the ester may be due to a variable polarization of the P-H bond. These authors argue that the polarization $P^{\delta+}-H^{\delta-}$ should decrease in the order $CH_3O > C_2H_5O > C_4H_9O$ since the inductive effect of the alkyl group decreases in the order $C_4H_9 > C_2H_5 > CH_3$. They postulated that the polarization of the phosphorus hydrogen bond in di-n-butyl phosphonate may be $P^{\delta-}-H^{\delta+}$. A polarization, $P^{\delta+}-H^{\delta-}$ for the dimethyl and diethyl phosphonate would explain the ester formation in major yields since an analogy could be drawn to the reaction of silicon hydrides and hexafluoroacetone in which the alkoxide product is formed. In the silicon hydrides, the polarization of the silicon hydrogen bond is also considered to be $M^{\delta+}-H^{\delta-}$ (3,6).

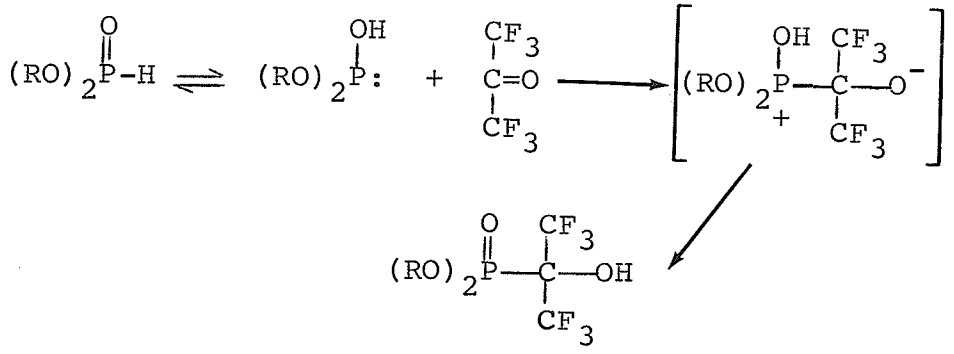
However, infrared studies of dialkyl phosphonates show that the existence of a $P^{\delta+}-H^{\delta-}$ type polarization is somewhat questionable. Workers (79) have shown that in both acetone and pyridine, which are both electron donors, significant shifts (11-20 cm^{-1}) of the P-H stretch occur. This shift has been attributed to hydrogen bonding interactions.



R = Me, Et and n-Bu.

These studies indicate that a polarization in the direction $P^{\delta-}-H^{\delta+}$ must be present to explain the hydrogen bonding. Therefore it seems that assuming a polarization $P^{\delta+}-H^{\delta-}$ is not adequate to explain the ester formation in these reactions.

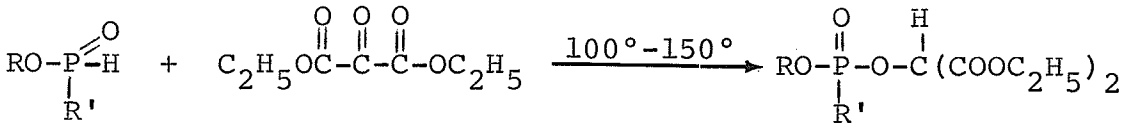
By accepting the validity of the phosphonate-phosphite tautomerism, as discussed in the Introduction, one can propose a reasonable mechanism to account for the high yields of the alcohols (84%), R = CH_3; 88%, R = C_2H_5; and 90%, R = n-C_4H_9 as found in this work. This mechanism may subsequently be extended to account for the formation of the lower yields of the esters (16%, R = CH_3; 12%, R = C_2H_5; and 10%, R = C_4H_9).



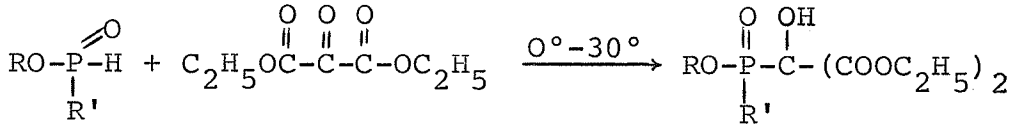
Such a mechanism is very similar to that put forward by Pudovik (38). The reactive species is seen to be the phosphite tautomer. The nucleophilic phosphorus atom of the phosphite tautomer attacks the carbonyl carbon of hexafluoroacetone forming the ionic intermediate which undergoes a proton rearrangement to yield the alcohol.

However, while such a mechanism does account for the high yields of the alcohol, it fails to show why the formation of the ester takes place. In order to explain the ester formation one must consider both the experimental conditions of the reactions as well as the tendency of the alcohols to rearrange as discussed previously.

The literature contains many examples of heat induced rearrangements of alcohol compounds to their respective esters. In addition, it has been found that the reaction of phosphoryl hydrides with carbonyl containing compounds occurs with the liberation of heat. For example, Pudovik and coworkers (38) have found that the reactions of acid phosphorus esters with diethyl mesoxalate were highly exothermic as the temperature of the reaction mixture rose to 100-150° after a short induction period.



Failure to regulate the reaction temperature yielded the ester as the sole product. However, if the temperature of the reaction mixture was kept at 30°C, the alcohol was the sole product.



Hence it appeared that the heat liberated in the formation

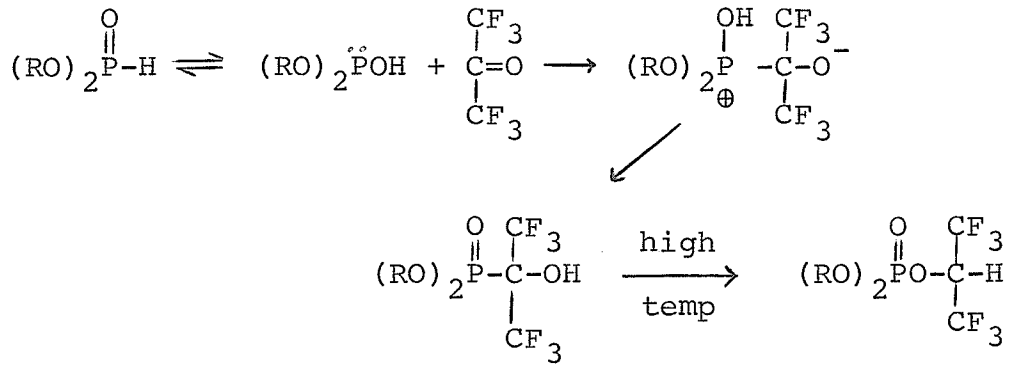
of the alcohol was sufficient to cause the thermal rearrangement of the alcohol to its corresponding ester.

Work in this laboratory and elsewhere has shown that the reaction of dialkyl phosphonates with highly fluorinated ketones is highly exothermic. The reaction of chloropentafluoroacetone with dialkyl phosphonates has been found to be violently exothermic. Ivin (80) has reported that the reaction of 1,3-dichlorotetrafluoroacetone with dialkyl phosphonate proceeds with considerable evolution of heat. When mixtures of hexafluoroacetone and dialkyl phosphonates were placed at room temperature immediately after mixing, the reaction mixture became very warm. In this experiment, the yields of methyl, ethyl, and n-butyl alcohols were found to be 0%, 0%, and 4% respectively, and the ester yields were found to be 100%, 100%, and 96% respectively. Thus it appeared that the heat liberated from the reaction of hexafluoroacetone and dialkyl phosphonates was sufficient to cause the thermal rearrangement of the initially formed phosphonates.

To test this theory, the reactions were carried out with temperature control and in the presence of a solvent. Keeping the reaction mixture cool, i.e. allowing it to warm up slowly from -78°C over a period of 24 hours, yielded the methyl, ethyl, and n-butyl alcohols in respective yields of 84%, 88% and 90%.

Such results are consistent with the postulate that

the formation of the esters, $(RO)_2P(O)OCH(CF_3)_2$, are caused by the thermal rearrangement of the initially formed alcohols and a reaction scheme explaining the formation of both the alcohol and the ester is as follows:



The formation of small amounts of ester at lower temperatures is probably due to the thermal rearrangement caused by isolated local heating effects in the reaction mixture or by the reaction of remaining dialkyl phosphonate and hexafluoroacetone occurring after the reaction mixture has warmed up considerably.

It should be noted that the formation of the small amounts of ester even at lower temperatures is consistent with the results of the base catalyzed rearrangements discussed earlier. The tendency of the alcohols to rearrange in the presence of a basic catalyst has been found to decrease in the order methyl > ethyl > n-butyl. Hence, the ability of the initially formed alcohol to undergo rearrangement, would be expected to follow the same order since the thermal rearrangement would proceed by a similar

mechanism involving nucleophilic attack by the oxygen upon the phosphorus atom.

This argument may be extended to explain the yields of the alcohol and ester in the reaction of diphenyl phosphonate with hexafluoroacetone. The yields are 44% and 56% respectively. The positive charge on the phosphorus atom in $(C_6H_5O)_2P(O)C(OH)(CF_3)_2$ would be greater than on the methyl, ethyl or n-butyl analogues because the lone pairs on the oxygen atom of the phenoxy group conjugate with the aromatic ring. Since the lone pairs are not as available to form $p\pi$-$d\pi$ bonds with the phosphorus, the inductive effect of the oxygen predominates rather than the π effect found in the alkoxy groups (63). Thus it would be expected that the amount of ester product formed will be greater than in the methyl, ethyl, or n-butyl case. Even though a kinetic study of the alcohol to ester rearrangement was not carried out in the phenyl case, it seems reasonable that such a rearrangement would occur faster, and with a lower activation energy than the compounds which have been investigated.

REACTION OF DIPHENYLPHOSPHINE WITH HEXAFLUOROACETONE

The reactions of diphenylphosphine with various carbonyl containing compounds has been discussed fully in the Introduction, and a general mechanism for these reactions has been given. It was also shown that the

reaction mechanism proposed by Stockel for the reaction of diphenylphosphine with hexafluoroacetone was inconsistent with the general mechanism as Stockel's mechanism did not assume initial alcohol formation (14).

The reaction of hexafluoroacetone with diphenylphosphine was repeated. The ^{19}F spectrum of the product showed a predominant doublet, J = 19 Hz, at +70.2 ppm. This product was assigned the structure, $(C_6H_5)_2P\text{-}C(OH)(CF_3)_2$, for several reasons. In the first place, this structure by analogy to other reactions of diphenylphosphine, is expected. Secondly, the structure is assigned on the basis of ^{19}F nmr. It is established that P-C-C-F coupling may vary from about 20-40 Hz. For example, in the compound $(CHF_2CF_2)PCl_2$, J_{PF_β} has a value of 26 Hz (81). In other systems J_{PF_β} has been found to be in the area of 20 Hz (82). As the reaction product was exposed to air, the doublet at +70.2 ppm decreased in intensity whereas the previously minor doublet, J = 6 Hz, at +72.2 ppm increased in intensity. Based on previous work the doublet, J=6 Hz is indicative of a H-C-C-F linkage. Evidence that the compound contained a $P(O)OCH(CF_3)_2$ grouping was based on the doublet of septets present in the ^1H nmr spectrum (49).

Hence it is proposed that the initially formed alcohol rearranges upon oxidation as follows:

$$(C_6H_5)_2PH + (CF_3)_2C{=}O \longrightarrow (C_6H_5)_2P\text{-}\underset{\displaystyle OH}{\overset{\displaystyle |}{C}}\text{-}(CF_3)_2 \xrightarrow{[O]} (C_6H_5)_2P(O)OCH(CF_3)_2$$

After this work was completed, Janzen and Vaidya reinvestigated this reaction in more detail and also found that the initially formed alcohol rearranges to the ester upon air oxidation. Thus it appears that the general mechanism outlined previously for the reaction of diphenylphosphine with carbonyl compounds is valid for the reaction of diphenylphosphine with hexafluoroacetone.

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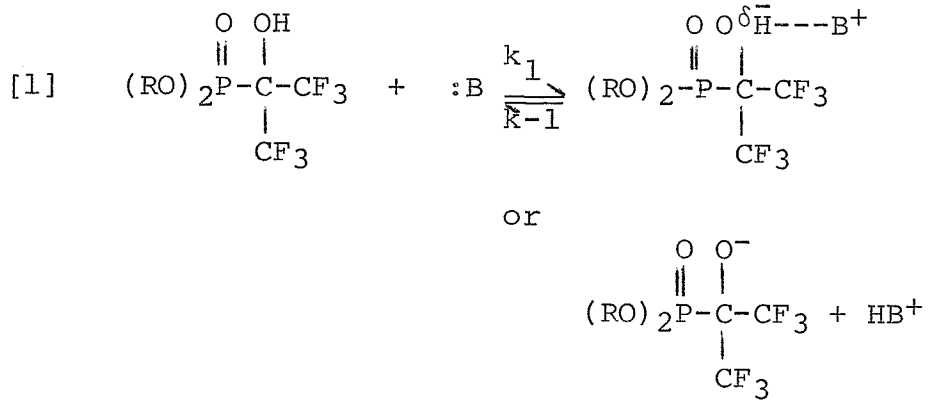
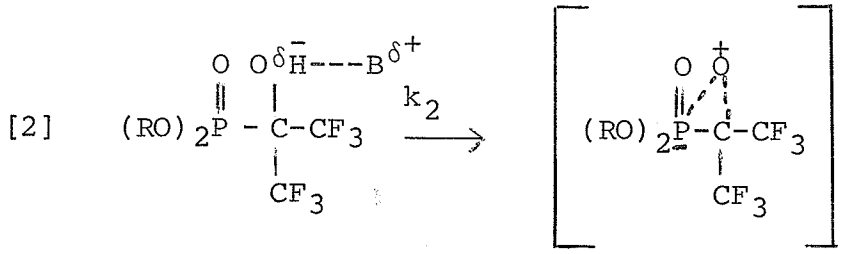
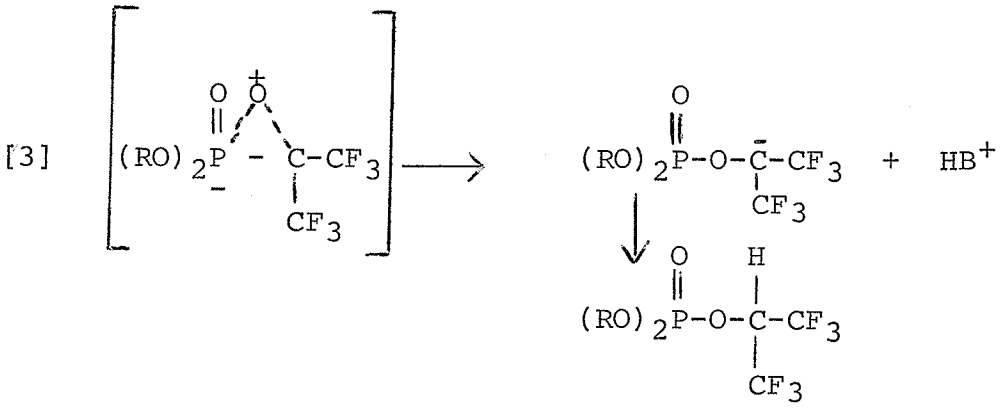
APPENDIX I

Derivation of the rate equation for the alcohol to ester rearrangement in phosphorus compounds.

The proposed mechanism for the alcohol to ester rearrangement is as follows.







Letting

$$A = (RO)_2\overset{\overset{O}{\|}}{P}-\overset{\overset{OH}{|}}{C}(CF_3)_2$$

B = Lewis Base

$$C = (RO)_2\overset{\overset{O}{\|}}{P} - \overset{\overset{OH^{\delta+}---B^{\delta-}}{|}}{C}(CF_3)_2$$

$$F = (RO)_2\overset{\overset{O}{\|}}{P}-O-\bar{C}(CF_3)_2$$

$$H = (RO)_2\overset{\overset{O}{\|}}{P}-O-\overset{\overset{H}{|}}{C}(CF_3)_2$$

The rate of formation of the ester depends only on the difference in free energy between the starting materials, alcohol and Lewis base, and the activated complex at the transition state of step [2].

$$\Delta G^{\ddagger} = \Delta G_E^{\circ} + \Delta G_2^{\ddagger}$$

Thus the rate of the reaction is described in terms of an equilibrium between starting materials and the activated complex, all other equilibria or reaction steps being ignored.

$$\text{Rate of product formation} = \frac{d[F]}{dt} = k_2[C]$$

$$\frac{d[C]}{dt} = k_1[A][B] - k_{-1}[C] - k_2[C]$$

By the stationary state approximation $\frac{d[C]}{dt} = 0$

Therefore

$$k_2[C] + k_{-1}[C] = k_1[A][B]$$

$$[C]\ (k_2 + k_{-1}) = k_1[A][B]$$

$$[C] = \frac{k_1[A][B]}{k_2+k_{-1}}$$

$$\text{Rate} = k_2[C] = \frac{k_2k_1[A][B]}{k_2+k_{-1}}$$

$$= \frac{k_1[A][B]}{1 + \frac{k_{-1}}{k_2}}$$

Since $k_2 << k_{-1}$, $\frac{k_{-1}}{k2} >> 1$

$$\text{Rate} = \frac{k_1[A][B]}{\frac{k_{-1}}{k_2}}$$

$$= \frac{k_2k_1}{k_{-1}}[A][B]$$

$$\text{Rate} = k_2K_{eq}[A][B]$$

Hence

$k_{obs} = k_1'$(pseudo first order rate constant) $= k_2K_{eq}[B]$

$\text{Rate} = k_1'[A]$

$$\frac{-d[A]}{dt} = k_1'[A]$$

$$\frac{d[A]}{[A]} = -k_1'dt$$

Integrating

$$\ln A = -k_1't + C$$

Therefore a plot of ln A against t yields a straight line of slope $-k_1'$.

Division of k_1' by [B] the catalyst concentration yields the observed second order rate constant.

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