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SOLVENT EFFECTS ON THE STEREOCHEMISTRY OF SOME REACTIONS OF PHENYLMETHYLPROPYLPHOSPHINE. (1).

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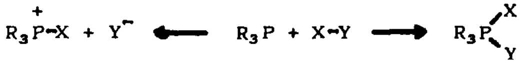
The mechanisms of nucleophilic displacement reactions by phosphorus containing nucleophiles are potentially much more complex than those of the more common nucleophiles. This complexity arises because of the ability of phosphorus to form pentasubstituted compounds or intermediates. Thus displacement reactions can proceed to form ions, I, or a pentacovalent compound, II (2).



$$R_3\overset{+}{P}{-}X + Y^- \longleftarrow R_3P + X{-}Y \longrightarrow R_3P\begin{smallmatrix}X\\Y\end{smallmatrix}$$

I II

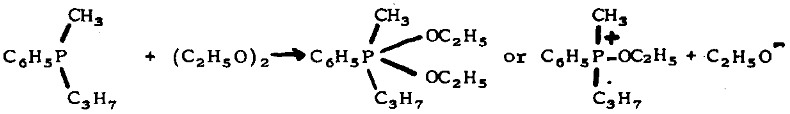
In an earlier study (3) it was found that the stereochemistry of the conversion of optically active phenylmethylpropylphosphine, III, to its oxide, IV, by reaction with t-butyl hypochlorite depended on the solvent used in the reaction. It has now been found that this is also true for the reactions of III with diethyl peroxide and diethyl bromomalonate. The results are presented in Table I.

TABLE I

Series	Reactant	Oxide, $[\alpha]_D$[b]	Solvent
A[a]	$(CH_3)_3COOH$	+16.8°	Pentane
A	$(C_2H_5O)_2$	-0.1	Benzene
A	$(C_2H_5O)_2$	0.0	Ethanol
B	$(CH_3)_3COOH$	+17.6	Pentane
B	$(C_2H_5O)_2$	-11.7	$H_2O\cdot THF(1:4)$
C	$(CH_3)_3COOH$	-19.0	Pentane
C	$BrCH(CO_2C_2H_5)_2$	+ 1.4	Methanol
C	$BrCH(CO_2C_2H_5)_2$	+12.6	$H_2O\cdot THF(1:5)$

[a] In each series the maximum possible rotation of the phosphine oxide was determined by allowing the phosphine to react with t-butyl hydroperoxide. It is assumed that this reaction proceeds with complete retention of configuration. [b] Rotations were taken on methanol solutions of the oxide. In each case the n.m.r. and infrared spectra of the oxide samples were identical to those of an authentic sample.

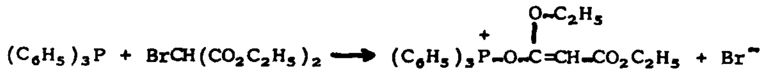
The reactions of triphenyl and phenyldipropylphosphine with diethyl peroxide in oxygen-18 labeled ethanol have been shown to lead to extensive incorporation of oxygen-18 into the phosphine oxides (4). The complete racemization found when III was allowed to react with diethyl peroxide in ethanol is in accord with this finding. The displacement process can be envisioned as leading to either V or VI. Formation of VI should occur with re-



tention of configuration and for racemization and exchange to occur V or a transition state similar to V would have to be formed in a subsequent step. This would have to occur considerably more rapidly than the competing decomposition to the phosphine oxide. This path cannot be ruled out in either the reaction in ethanol or benzene. It seems more reasonable to suggest that in benzene V is formed directly, and that it is formed as a dl-pair or alternatively undergoes racemization by internal motion after its formation.

The results obtained in water-tetrahydrofuran are particularly striking and show quite conclusively that this change in medium has had a profound effect on the overall stereochemistry of the reaction. The rotation of the oxide corresponds to 66% inversion. Inversion is most easily accounted for by stereospecific formation of VI, i.e. retention, followed by hydrolysis with inversion at phosphorus (5). There are several ways in which racemization can arise and they cannot be distinguished at this time.

The reaction of diethyl bromomalonate with triphenylphosphine in the absence of hydroxylic solvents has been shown to give the enol-phosphonium salt, VII (6). Solvolysis of the salt yields



$$(C_6H_5)_3P + BrCH(CO_2C_2H_5)_2 \longrightarrow (C_6H_5)_3\overset{+}{P}-O-\overset{\overset{O-C_2H_5}{|}}{C}=CH-CO_2C_2H_5 + Br^-$$

VII

triphenylphosphine oxide and diethyl malonate. When the reaction is conducted in methanol or water these products are obtained directly. The results of the present experiments show though that the stereochemistry of the reaction is a function of the medium, with methanol giving a small amount of inversion and water leading to 61% inversion. These results can be fitted into mechanistic schemes involving ions and pentasubstituted phosphorus compounds. Unfortunately these various paths cannot be distinguished at the present time.

The important thing to be noted from these experiments is that stereochemical results in one medium are only definitive for that particular medium and thus generalizations from these kinds of experiments must be made with extreme caution. The understanding of the role of pentasubstituted intermediates vs ions in organophosphorus chemistry remains as a major key to future mechanistic generalization.

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