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REVERSIBLE EQUILIBRIUM IN TERTIARY PHOSPHINE-FLUOROHALOMETHANE REACTIONS

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The generation of dihalomethylene ylides by the reaction of tertiary phosphines with carbon tetrahalides (halogen = Cl, Br) has been known for some time. Mechanistic studies have suggested that the initial step in the reaction sequence is the formation of an ion pair formed via attack of phosphorus on halogen.[1] Subsequent recombination of the ion pair (in the absence of a trapping agent) and dehalogenation of the resultant C-phosphonium salt form the ylide and the phosphorane observed (eq. 1).

(eq. 1)

$$R_3P + CX_4 \longrightarrow [R_3\overset{+}{P}X]CX_3^- \longrightarrow [R_3\overset{+}{P}\text{-}CX_3]X^- \xrightarrow{R_3P} R_3\overset{+}{P}\text{-}\overset{-}{C}X_2 + R_3PX_2$$

Recent work from our laboratory has shown that dihalodifluoromethanes also react with tertiary phosphines to similarly form stable difluoromethylene olefination solutions, which are synthetically useful in a wide range of applications.[2,3] In contrast to the stability exhibited by the pre-generated ylide solution formed by this method, ylide generation by the chlorodifluoroacetate-tertiary phosphine route can only be accomplished "in situ" and attempts to pregenerate a stable ylide solution by this route have met with repeated failure.[4] Since, presumably, the same ylide species is generated by either route, the unexplained difference in stability of these olefination solutions has remained an intriguing, puzzling question.

We now present evidence that the stability of the ylide solution formed from the reaction of tertiary phosphines and fluorohalomethanes is due to the formation of a mobile, dynamic equilibrium between phosphonium salt, phosphine, ylide, and phosphorane. In the reactions that we have examined, thus far, this equilibrium lies far to the side of phosphine and phosphonium salt (eq. 2). In the absence of a trapping agent for (III), the ylide recaptures

(eq. 2)

$$\underset{(I)}{[(C_6H_5)_3\overset{+}{P}CF_2Br]Br^-} + \underset{(II)}{(C_6H_5)_3P} \rightleftharpoons \underset{(III)}{(C_6H_5)_3\overset{+}{P}\text{-}\overset{-}{C}F_2} + \underset{(IV)}{(C_6H_5)_3PBr_2}$$

halogen from (IV) and regenerates (I) and (II).

In the chlorodifluoroacetate method, no phosphorane is generated and stabilization of the ylide solution <u>via</u> this type of equilibrium is prevented. Consequently, in the absence of such stabilization, ylide decomposition appears to be rapid and no <u>stable</u> olefination solution is formed.[4]

(eq. 3)

$$(C_6H_5)_3P + CF_2ClCO_2M \longrightarrow (C_6H_5)_3\overset{+}{P}\text{-}\overset{-}{C}F_2 + CO_2 + MCl$$

The reversibility of ylide formation (III) from (I) can be demonstrated by the following experiments. When (I)[5] is reacted with (II) in triglyme at 70°C for sixty hours, ^{19}F NMR analysis of an aliquot[7] of the reaction mixture shows <u>only</u> resonance due to (I). Addition of trifluoroacetophenone (V) to another aliquot of the same reaction mixture resulted in the rapid formation of a 74% yield of 2-phenylpentafluoropropene (VI). Control experiments ruled out a direct reaction between (I) and (V) to form (VI).[8]

In a similar experiment two equivalents of (II) were reacted with dibromodifluoromethane, (VII), in dry triglyme at 70°C for 41 hours. Subsequent filtration and purification of the precipitate gave a 98% isolated yield of (I) - identical in all respects to an authentic sample of (I). The filtrate from this reaction was treated with methyl iodide at 50° for 20 hours and gave an 85% isolated yield of methyltriphenylphosphonium iodide - identical in all respects to an authentic sample. Thus, in the absence of a trapping agent, recapture of bromine by (III) regenerates the original salt and phosphine. The high recovery of (I) and (II) demonstrate that this equilibrium lies to the left. In the presence of a trapping agent, (III) reacts and the equilibrium is shifted to the right.

Since (I) is not very soluble in triglyme and to rule out a possible solvent effect, the reaction between (I) and (II) was carried out in acetonitrile. In this solvent a homogeneous reaction solution is formed. After six hours at reflux, ^{19}F analysis of the reaction solution showed only the presence of (I) and a trace of $[(C_6H_5)_3\overset{+}{P}CF_2H]Br^-$, (VIII).[9] Addition of (V) gives a 53% yield of (VI) after six hours at 75-80°C. After 24 hours a 77% yield of (VI) is obtained and 22% (V) remains. Thus, even in a homogeneous solution the equilibrium lies to the left.

DMF is known to react rapidly with (IV).[10] Consequently, pre-generation of (III) in DMF might be expected to exhibit little stability to the olefination solution if (IV) is rapidly destroyed - thereby preventing formation of the equilibrium proposed. Indeed, when (II) and (VII) are reacted in DMF at 50°C, the olefination solution shows little or no stability. Ylide formation and capture can be demonstrated by the "in situ" reaction of (II), (VII), and (V) to give an 81% yield of (VI).[11]

(eq. 4)

$$2(C_6H_5)_3P + CF_2Br_2 \xrightarrow{50^\circ} [\text{olefinating solution}] \xrightarrow{C_6H_5COCF_3} 1\%\ (VI)$$

(eq. 5)

$$2(C_6H_5)_3P + CF_2Br_2 + \underset{(V)}{C_6H_5COCF_3} \xrightarrow{50^\circ} \underset{(VI)}{C_6H_5(CF_3)C{=}CF_2} \quad 81\%$$

A similar equilibrium (which again lies far to the left) is established when bromodifluoromethyl-<u>tris</u>-(dimethylamino)phosphonium bromide (IX) is reacted with <u>tris</u>-(dimethylamino)phosphine in triglyme. Filtration of this reaction mixture after 23 hours gave a 90% recovery of (IX) and a 73% isolated yield of $[(CH_3)_2N]_3\overset{+}{P}CH_3I^-$ after treatment of the filtrate with methyl iodide.[12] Under similar conditions reaction with acetophenone gave a 81% yield of $C_6H_5(CH_3)C{=}CF_2$ in 1.5 hours.

(eq. 6)

$$\underset{(IX)}{[[(CH_3)_2N]_3\overset{+}{P}CF_2Br]Br^-} + [(CH_3)_2N]_3P \rightleftharpoons [(CH_3)_2N]_3\overset{+}{P}\text{-}\overset{-}{C}F_2 + [(CH_3)_2N]_3PBr_2$$

Thus, in the bromodifluoromethylphosphonium salt/tertiary phosphine reactions, stabilization of the olefination solution is provided by the establishment of a mobile equilibrium. Extention to other ylide solutions from CCl_4, CBr_4, $CFCl_3$ and $CFBr_3$ to establish the generality of this phenomenon and the position of equilibrium is in progress.

NOTES AND REFERENCES

1. Cf. H. Teichmann, *Z. Chem.*, **14**. Jg. (1974), 216-222 for a recent general review of tertiary phosphine-polyhalogen compound chemistry.
2. D. G. Naae and D. J. Burton, *J. Fluorine Chem.*, **1**, 123 (1971/1972).
3. D. G. Naae and D. J. Burton, *Synthetic Comm.*, **3**, 197 (1973).
4. D. J. Burton and F. E. Herkes, *J. Org. Chem.*, **32**, 1311 (1967) and **33**, 1854 (1968).
5. (I), mp = 178-181°C, ^{19}F NMR[6], ϕ^* = +50.4 ppm (d), J_{CPF} 84.5 Hz.
6. All ^{19}F NMR spectra were obtained on a Varian HA-100 spectrometer operated at 97.075 MHz. Chemical shifts are reported in ppm *upfield* from internal $CFCl_3$.
7. A small amount of $CHCl_3$ was added to solubilize the heterogeneous reaction mixture.
8. When (I) is reacted with (V) in triglyme at 70° for 48 hours, glpc analysis showed no (VI) and a 94% recovery of (V). Similarly, the intensity and position of the carbonyl band of (V) remain unchanged when (I) and (V) are dissolved in triglyme.
9. Reaction of (III) with solvent (proton capture) forms (VIII). In acetonitrile this reaction is slow. Even after 24 hrs. at reflux, addition of (V) gave 77% (VI), a 22% recovery of (V), and only 11% (VIII).

   (VIII), mp. 175-180°C, showed a doublet of doublets in the ^{19}F NMR, ϕ^* 126.2 ppm, J_{CPF} 79.7 Hz, J_{HCF} 46.6 Hz. ^{1}H NMR showed two absorptions, δ7.97, multiplet (aromatic protons) and δ9.60 doublet of triplets, J_{PCH} 30.5 Hz, J_{HCF} 46.5. Analysis: Calc'd. $C_{19}H_{16}BrF_2P$: %C 58.03, %H 4.10. Found: %C 57.86, %H 4.23.
10. T. Dahl, R. Stevenson, and N. S. Bhacca, *J. Org. Chem.*, **36**, 3243 (1971).
11. (I) is rapidly formed "in situ" from (II) and (VII) and the mechanism is unchanged.
12. (IX), showed a doublet in the ^{19}F NMR, ϕ^* 49.3 ppm, J_{CPF} 90 Hz. ^{1}H NMR showed doublet δ2.95 (methyl protons), J_{PCH} 10.0 Hz. $[(CH_3)_2N]_3\overset{+}{P}CH_3I^-$ was characterized by carbon and hydrogen analysis. Analysis: Calc'd. for $C_7H_{21}IP$: %C 27.55, %H 6.94, %N 13.77. Found: %C 27.52, %H 6.97, %N 13.65.