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THE HYDROLYSIS OF BROMODIFLUOROMETHYLTRIPHENYLPHOSPHONIUM BROMIDE [1]

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SUMMARY

Hydrolysis of $[\text{Ph}_3\text{PCF}_2\text{Br}]^+\text{Br}^-$ afforded a high yield of bromodifluoromethane and triphenylphosphine oxide. Hydrolysis in the presence of a radioactive isotope of bromine or sodium iodide gave unequivocal evidence that the mechanism for this reaction proceeds through a difluorocarbene intermediate.

INTRODUCTION

Halo-F-methylphosphonium salts have been demonstrated to be useful synthetic intermediates for the transfer of either difluorocarbene [2] or the bromodifluoromethyl anion [3]. Although the classical work of Hine and co-workers [4] suggests that halodifluoromethyl carbanions $[\text{CF}_2\text{X}]^-$, where $\text{X} = \text{Cl}, \text{Br}, \text{I}$ have no appreciable lifetime in a hydroxylic solvent, recent work by Burton and Wheaton [5,6] and Buddrus [7] indicates that these types of methide ions possess some stability in a non-hydroxylic medium.

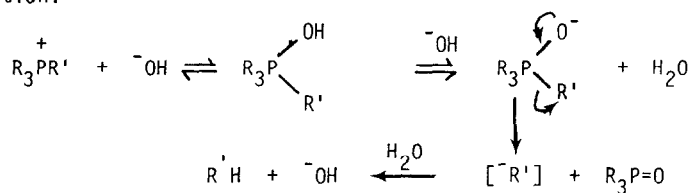
The hydrolysis of bromodifluoromethyltriphenylphosphonium bromide 1 under a variety of conditions gives bromodifluoromethane 2 in high yield. Mechanistic schemes can be written to rationalize the hydrolysis of 1 via the intermediate difluorocarbene 3 or the bromodifluoromethyl carbanion 4

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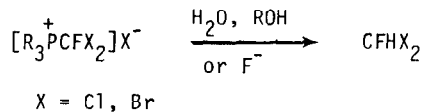
(cf. Scheme 1). The purpose of this investigation was to elucidate evidence which would distinguish between these two possible mechanistic pathways.

RESULTS AND DISCUSSION

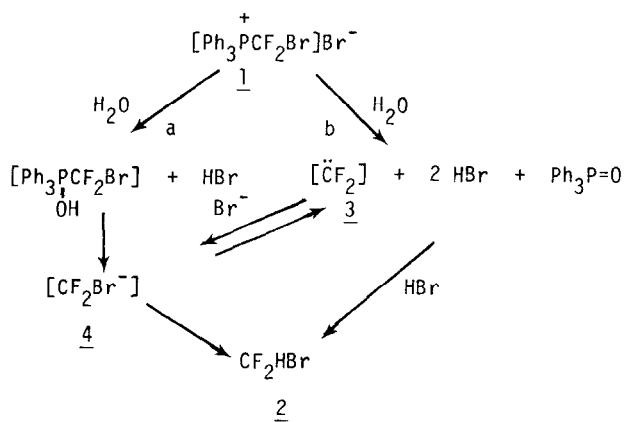
The generally accepted mode of hydrolysis of phosphonium salts is via nucleophilic attack on phosphorus with displacement of the most stable carbanion [8]. Protonation of the resultant carbanion completes the hydrolysis reaction.



Dichlorofluoromethylphosphonium [9] and dibromofluoromethylphosphonium [10] salts appear to undergo hydrolysis via this mechanistic pathway.



At first glance, it would appear that the hydrolysis of 1 proceeds via the same mechanism (path a in Scheme 1). Salt 1 is inert to HBr suggesting



Scheme 1. Hydrolysis of 1

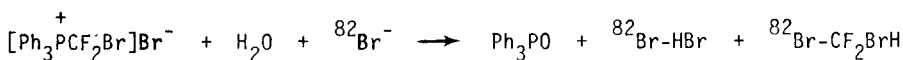
action sequence the carbon-bromine bond is severed. If 4 is the major reaction intermediate and undergoes rapid protonation to give 2, then the original carbon-bromine bond remains intact. Thus, if the hydrolysis of 1 is carried out in the presence of a radioactive isotope of bromine and the distribution of the isotope between 2 and HBr determined, a clear distinction between path a and b in Scheme 1 can be made.

If the carbon-bromine bond is cleaved to give 3, then all bromine atoms present in the reaction medium become equivalent. Hence, determination of the ratio of the activity of the CF_2HBr fraction to the HBr fraction provides a direct measure of the extent of this cleavage and hence conclusive evidence for the formation of 3. If 3 is the primary intermediate, the ratio of these activities would be 50/50.*

If the carbon-bromine bond is not cleaved to any significant extent, then all of the activity will remain as $^{82}\text{Br-HBr}$ in the reaction vessel. None of the activity would be found in 2.

When the hydrolysis of 1 was carried out in the presence of $^{82}\text{Br}^-$, labeled bromine was found in both 2 and HBr. The results of three separate hydrolysis experiments are summarized in Table I as a percentage of the total ^{82}Br activity.

TABLE 1



Trial	$^{82}\text{Br-HBr}(\%)$	$^{82}\text{Br-CF}_2\text{BrH}(\%)$
1	50	50
2	60	40
3	54	46

The average of the $^{82}\text{Br-CF}_2\text{BrH}$ activity in these three experiments is 45%. The result is in reasonable agreement with the theoretical result of 50% $^{82}\text{Br-CF}_2\text{BrH}$ expected for the quantitative hydrolysis of 1 via the difluorocarbene intermediate. Thus, 3 is the major transient intermediate in the hydrolysis of 1.

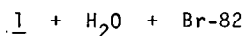
* Since the hydrolysis generally gives 90-95% 2, the 50/50 ratio is the ratio expected for quantitative hydrolysis. In reality, the ratio is expected to approach this value depending on the yield of 2.

CONCLUSIONS

Both the chemical and radiolabel evidence support the formation of difluorocarbene as the primary intermediate in the hydrolysis of $[\text{Ph}_3\text{P}^+\text{CF}_2\text{Br}]\text{Br}^-$. Although no statement can be made regarding the origin of the carbene---i.e., whether it is formed in a concerted reaction from the salt or via loss of bromide from the CF_2Br^- ion---the formation of difluorocarbene as the reaction intermediate in the hydrolysis sequence has been unequivocally demonstrated.

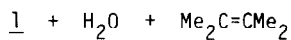
EXPERIMENTAL

The ^{19}F NMR spectra were recorded on a Varian HA-100 Spectrometer operating at 94.075 MHz, and the chemical shifts are reported in ϕ^* values upfield from internal CFC_3 reference. Br-82 (as bromide) was obtained in a 1.0 M NH_4OH solution with an initial activity of 1.0 m Ci/ml upon shipment from New England Nuclear. All experiments involving Br-82 were carried out behind 4 x 8 x 16 cm lead bricks. Measurement of Br-82 activity was accomplished by use of a Capintec Radioisotope Calibrator.

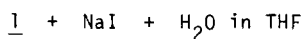


All Br-82 reactions were carried out in identical sets of apparatus. One representative experiment is as follows. An aliquot (0.3 ml) of the Br-82 solution (0.29 mg Br/ml) was placed in a 30 ml brown serum bottle equipped with a magnetic stir-bar and sealed with a rubber septum. The aqueous solution was evaporated to dryness under a stream of argon. No activity was lost to the atmosphere during this evaporation. A solution of $\underline{1}$ (0.43 g, 0.911 mmole) in 8 ml of dry CH_2Cl_2 was added and the reaction vessel connected via plastic tubing to an identical serum bottle cooled in dry ice/isopropanol. After stirring for ten minutes at ambient temperature, water (0.064 ml, 3.55 mmole) was added, and the resulting mixture stirred for twenty minutes to complete the hydrolysis. Approximately 6 ml of the solvent were then distilled directly into the cooled receiver.* The serum bottles were then removed and the Br-82 content of each determined in the radioisotope calibrator.

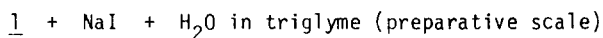
*Previous experiments with unlabeled material showed that all of the volatile CF_2BrH distilled under these conditions and that none of the co-product HBr distilled. Other control experiments demonstrated: (a) under the conditions of the radioactive hydrolysis experiment, but in the absence of $\underline{1}$, no activity was observed to distil with the CH_2Cl_2 ; (b) addition of an aqueous solution of HBr to a suspension of the bromide-Br-82 in CH_2Cl_2 , followed by distillation, gave no Br-82 activity in the distillate.



Into a tared 5 mm NMR tube were placed 1 (0.189 g, 0.401 mmole), 2,3-dimethyl-2-butene (0.067 g, 0.801 mmole) and 0.5 ml dry triglyme. Water (0.2 ml, 11.1 mmoles) was added. The homogeneous solution which resulted was shown by ^{19}F NMR analysis to contain only 2 and 1,1-difluorotetramethylcyclopropane in a 78/22 ratio.



To a 100 ml three neck round bottom flask, equipped with a septum port and magnetic stir bar, and protected by a flow of dry nitrogen, was added 2.52 g (5.34 mmoles) of 1, 12 ml dry THF, and 3.42 g (22.8 mmoles) of dry sodium iodide. The slurry was cooled with an ice water bath and 1.0 ml (55 mmoles) water was added in one portion. The mixture was stirred for three hours at 0°C and then analyzed by ^{19}F NMR (using PhCF_3 as an internal standard for integration purposes). The ^{19}F NMR analysis showed 92% CF_2IH (ϕ^* 67.9 ppm, d, $J = 55$ Hz) and 3% CF_2BrH (ϕ^* 68.3 ppm, d, $J = 60$ Hz). The NMR sample was spiked with an authentic sample of CF_2BrH to confirm the assignment of the minor doublet. A similar hydrolysis experiment of 1 in triglyme with added NaI gave 96% CF_2IH .



To a 250 ml three neck round bottom flask, equipped with a septum port, magnetic stir bar and reflux condenser, was added 33.9 (71.8 mmoles) 1 and 150 ml of dry triglyme. The reaction mixture was stirred under a nitrogen atmosphere to give a slurry of 1. Then, 23.3 g (155 mmoles) NaI was added, followed by 19.9 ml (1.1 moles) H_2O while cooling the reaction mixture with an ice bath. The mixture became homogeneous within a few minutes.

After stirring at room temperature for two hours, all volatile material was distilled under vacuum (0.1 torr) into a receiver cooled in liquid nitrogen. The distillate contained two layers. ^{19}F NMR and ^1H NMR analysis showed the organic layer to contain CF_2IH with small amounts of 2, CH_3I , and triglyme. Trap-to-trap distillation of the organic layer gave 8.5 g (66%) of CF_2IH . ^{19}F NMR analysis showed the ratio of 5/2 was 94/6. ^1H NMR δ 7.67 (t), $J = 56$ Hz.

Mass Spectrum: m/e 178 (100%) CF_2IH^+ , 159 (30%) CFIH^+ , 127 (68%) I^+ , 51 (21%) CF_2H^+ .

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