Journal of Fluorine Chemistry, 27 (1985) 85–89

Received: June 5, 1984; accepted: July 18, 1984

A PRACTICAL SYNTHESIS OF FLUOROMETHYLTRIPHENYLPHOSPHONIUM SALTS

DONALD J. BURTON and DENISE M. WIEMERS

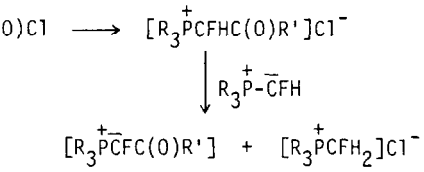
Department of Chemistry, University of Iowa, Iowa City, Iowa 52242 (U.S.A.)

SUMMARY

A practical synthesis of $[Ph_3\overset{+}{P}CH_2F]BF_4^-$ is reported *via* two routes, *via* fluorination of $[Ph_3\overset{+}{P}CH_2OH]BF_4^-$ with DAST or *via* hydrolysis of the phosphoranium salt, $[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Ph_3]Br^-$.

INTRODUCTION

In recent years fluorohalomethylene ylides have provided a useful and convenient entry to a variety of fluorohalomethylene olefins [1,2]. In theory, the most versatile of the ylides would be the fluoromethylene ylide itself ($R_3\overset{+}{P}\text{-}\overset{-}{C}FH$), since further alkylation, acylation, or arylation, followed by transylidation, would give a direct entry to α-fluoro substituted ylides (Scheme I).



Scheme I

The utility of such a synthetic sequence is predicated on a practical route to the ylide precursor - a fluoromethylphosphonium salt $[(R_3\overset{+}{P}CFH_2)X^-]$. The lack of a useful route to this required precursor has hampered progress in this area of fluorine-containing ylides.

0022-1139/85/$3.30

Schlosser has described the preparation of this precursor via the reaction of perchloryl fluoride with salt-free methylenetriphenylphosphorane [3]. However, the use of the precarious $FClO_3$ on a large scale has limited the utility of this approach and this method has attracted little attention. Burton and Greenlimb [4] reported the preparation of this precursor via the reaction of fluoroiodomethane with triphenylphosphine. Although an excellent yield of the phosphonium salt was obtained, the use of the expensive mercuric fluoride to prepare the fluoroiodomethane and the low yield (20%) of the fluoroiodomethane obtained via this route also limited the usefulness of this approach.

RESULTS AND DISCUSSION

Earlier work with the easily prepared hydroxymethyltriphenyl phosphonium salts and SF_4 also resulted in failure due to impurities present in the SF_4 [4,5]. However, we have now discovered that the use of diethylaminosulfur trifluoride (DAST) with hydroxymethyltriphenyl phosphonium tetrafluoroborate provides a clean high yield route to the fluoromethyltriphenyl phosphonium tetrafluoroborate (1).

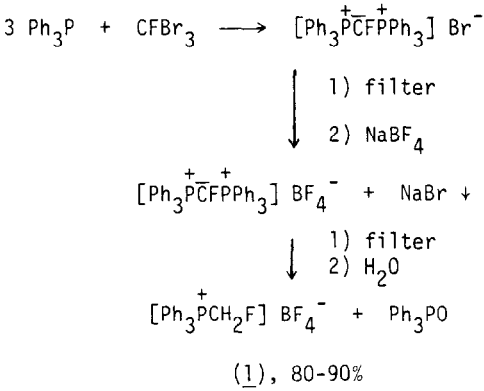
$$[Ph_3\overset{+}{P}CH_2OH]\ BF_4^- + Et_2NSF_3 \xrightarrow[CH_2Cl_2]{0°C} [Ph_3\overset{+}{P}CH_2F]\ BF_4^-$$

(1), 88%

With DAST we encountered none of the previous problems associated with the use of SF_4 [4,5]. This approach provides a useful synthesis of (1) from readily available precursors and is suitable for small scale preparations of (1). The only limitation of this route is the cost of DAST.

As an alternative to the use of DAST we have also developed a route to (1) from the recently reported fluorophosphoranium salts [6], which can be readily prepared from triphenylphosphine and fluorotribromomethane (Scheme II). Phosphoranium salt can be easily separated from the dibromotriphenylphosphorane by filtration. Anion exchange with sodium tetrafluoroborate* followed by hydrolysis and recrystallization gives (1) in 80-90% overall isolated yield. This preparation is readily amendable to scale up and is the method of choice when large quantities of (1) are required for further use.

*The fluoromethyl triphenylphosphonium tetrafluoroborate was easier to recrystallize and to handle than the analogous bromide salt.



Scheme II

The ready availability of (1) now provides the synthetic chemist with a useful and practical route to fluoromethylene olefins [3,4] via the fluoromethylene ylide, and a direct entry into other α-fluoro substituted ylides as outlined in Scheme I. Further work on this latter application is in progress in our laboratory and will be reported in due course.

EXPERIMENTAL

Preparation of hydroxymethyl triphenylphosphonium tetrafluoroborate

This phosphonium salt was prepared by modification of the method of Wittig [7]. Into a one liter one-necked flask, fitted with a stir bar and a water-cooled reflux condenser, was charged 131.3 g (0.5 mole) of triphenylphosphine, 15.0 g (0.5 mole) of paraformaldehyde, and 500 ml of anhydrous ether. The solution was moderately stirred as 172 ml of 48% fluoroboric acid (112.3 g, 1.27 moles) was slowly added. An exothermic reaction ensued and a large quantity of precipitate formed. After the addition of the fluoroboric acid was completed, the reaction mixture was stirred at room temperature for five days.

The reaction mixture was filtered through a medium-fritted funnel and the precipitate washed with ether and with cold water. The product was dried under vacuum in a vacuum desiccator to give 97.0 g (0.26 mole, 51%) of hydroxymethyl triphenylphosphonium tetrafluoroborate, m.p. 127.5-130.4 (lit. [7] 128-130°, decomp.). ^{1}H NMR ($CDCl_3$), TMS (internal reference): broad singlet at δ = 4.2 (1H), broad singlet at δ = 5.3 (2H) and a

multiplet at δ = 7.6-7.7 (15H); ^{31}P NMR ($CDCl_3$), H_3PO_4 (external reference) δ = 22.1 (s).

Preparation of (1) from hydroxymethyltriphenylphosphonium tetrafluoroborate

A 125 ml polypropylene bottle was charged with 3.8 g (10 mmoles) of hydroxymethyltriphenyl phosphonium tetrafluoroborate and 10 ml of methylene chloride. This solution was cooled to 0°C with an ice-bath and 1.2 ml (10 mmoles) of DAST was slowly added via syringe to the cooled solution. The reaction mixture was warmed to room temperature, and then periodically shaken at room temperature for one hour, and then diluted with 20 ml of water. The organic layer was separated and dried over anhydrous magnesium sulfate. After filtration to remove $MgSO_4$, ether was added to precipitate the phosphonium salt (1). Recrystallization with Et_2O/CH_2Cl_2 gave 3.36 g (88%) isolated yield of (1), m.p. 112-113°C. ^{19}F NMR ($CDCl_3$), $CFCl_3$ (internal reference): ϕ^* = -244.3 ppm (d,t), $J_{F,P}$ = 55 Hz, $J_{F,H}$ = 47 Hz; ^{31}P NMR ($CDCl_3$), H_3PO_4 (external reference): δ = 15.5 (d); ^1H NMR ($CDCl_3$), TMS (internal reference): $CF\underline{H}_2$ δ = 6.5 (d); aromatic hydrogens 7.7-7.8 (m); ^{13}C NMR, $CDCl_3$ (internal reference): $\underline{C}FH_2$ δ = 76.7 (d,d), $J_{F,C}$ = 195 Hz, $J_{P,C}$ = 65 Hz.

Preparation of (1) from phosphoranium salts

A three-neck one liter flask equipped with a water condenser, N_2 tee, septum and stopper was charged with 500 ml of dry methylene chloride. Then 393 g (1.5 moles) of triphenylphosphine was dissolved in the methylene chloride, the resultant solution cooled to 0°C, and 49.0 ml (0.5 mole) of $CFBr_3$ slowly added. The reaction mixture was then stirred at 0°C for one hour and then at room temperature for six hours. The reaction mixture was then pressure filtered under nitrogen through a medium-fritted Schlenk funnel into a one liter flask (to remove the insoluble Ph_3PBr_2). The solid phosphorane was washed with 40 ml of dry methylene chloride and the methylene chloride solutions combined. To the resultant solution was added 66.0 g (0.6 mole) of sodium tetrafluoroborate and the mixture was stirred at room temperature for eight hours; followed by pressure filtration through a fine-fritted Schlenk funnel under nitrogen (to remove the insoluble NaBr). The precipitated sodium bromide was washed with 30 ml of dry methylene

chloride, the methylene chloride fractions were combined and cooled to 0°C. Addition of 9 ml of water to this cooled solution leads to the formation of (1). The resultant homogeneous solution was stirred overnight at room temperature, then dried over anhydrous magnesium sulfate, filtered, and Et_2O added to precipitate (1). Recrystallization with Et_2O/CH_2Cl_2 resulted in 153 g to 172 g (80-90%) isolated yields of (1), m.p. 112-113°C. Analysis: Calc'd: C, 59.7%; H, 4.45%. Found: C, 60.2%, H, 4.46%.

ACKNOWLEDGEMENT

We wish to thank the National Science Foundation and the Air Force Office of Scientific Research for generous support of our programs.

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