Tetrabutylammonium and Polymer-supported Dihydrogentrifluoride: New Hydrofluorinating Reagents for Electrophilic Alkynes

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Tetrabutylammonium and polymer-supported dihydrogentrifluoride are readily accessible reagents which allow addition of HF to activated carbon-carbon triple bonds, thus leading to functional fluoroalkenes in good yields.

Functionalised fluoroalkenes, which are attractive molecules owing to their biological activity,^{1,2} are generally obtained in multi-step sequences.^{3—5} The addition of HF to activated $-C\equiv C$ - bonds should make similar compounds more accessible. However neither anhydrous HF,⁶ except when treated with CF₃C \equiv CH,⁷ nor amine–HF complexes investigated by Olah⁸ and Yoneda⁹ bring about this addition.

The $H_2F_3^-$ ion, in which the $H \cdots F$ hydrogen bonds appear to be much weaker than in HF_2^{-} ,¹⁰ might be expected to provide both the nucleophilic F⁻ and the electrophilic H⁺ species. We report here that $Bu^n_4N^+H_2F_3^-$ and $P^+H_2F_3^-$ (P⁺ = a polymeric cation from a macroreticular anion-exchange resin, *e.g.* Amberlyst A 26 or Amberlite IRA 900) can be used as efficient hydrofluorinating reagents towards electrophilic alkynes.

These stable and easily handled new dihydrogentrifluoride salts are obtained using a very simple method. The corresponding fluorides, Bun_4N+F^- dissolved in 1,2-dichloroethane (DCE), or the solid resin P+F⁻, are stirred in the presence of an aqueous saturated solution of HF-KF (2:1 ratio) (or HF-KHF₂). HF phase-transfer occurs and leads to the dihydrogentrifluoride salts which, after separation of the aqueous layer, are isolated from DCE (this solvent being added in the case of P+H₂F₃⁻) after distillation of the water-DCE azeotrope.

 $Bu^{n}_{4}N^{+}H_{2}F_{3}^{-}$ and $P^{+}H_{2}F_{3}^{-}$ react smoothly at moderate temperatures with bis-activated A-C=C-A or mono-activated

R-C=C-A acetylenic bonds, generating the desired addition of HF according to equation (1). In all cases the reaction stops at the alkene stage; generally a mixture of the Z- and E-isomers of the fluoro-adduct A-CF=CH-A or R-CF=CH-A is obtained in good yields, a bigger proportion of syn-adduct being formed from the polymer-supported reagent. The results are summarized in Table 1.

$$\begin{array}{ccc} A-C\equiv C-A & \xrightarrow{Bu^n_4N^+H_2F_3^-} & A-CF=CH-A \\ or & \xrightarrow{or P^+H_2F_3^-} & or & (1) \end{array}$$

R = alkyl or phenyl; A = nitrile, ester, ketone, aldehyde

The $H_2F_3^-$ ion seems to play a fundamental role in this reaction. We have observed that Olah's reagent does not add HF to MeO₂CC=CCO₂Me and that this ester is not readily transformed into Z-MeO₂CCF=CHCO₂Me (max. 10—15%) under the action of Bun₄N+HF₂⁻. On the other hand, the dihydrogentrifluoride salts do not induce any addition of HF to simple alkynes which easily produce *gem*-difluoro alkanes by reaction with pyridine–HF, (1:10 mol. ratio).⁸ These results may be explained by the good nucleophilicity of the H₂F₃⁻ ion, and the relatively weak H · · · F hydrogen bonds in this species.

In the aliphatic mono-activated series, a side-reaction occurs which is probably due to the slightly basic power of the $H_2F_3^-$ ion. The ester BunC=CCO₂Me leads to the two isomers

Table 1. Formation of fluoro-adducts A-CF=CH-A and R-CF=CH-A from acetylenic compounds A-C=C-A and R-C=C-A.

Acetylenic compound	Reaction with $Bu^n_4N^+H_2F_3^{-a}$				Reaction with $P^+H_2F_3^{-b}$			
	Reaction time/h	Overall yield/%	Z-adduct/%	E-adduct/%	Reaction time/h	Overall yield/%	Z-adduct/%	E-adduct/%
MeO ₂ CC=CCO ₂ Me	9	90	100	0	30	80	81	19
PhCECCOPh	50	53	100	0	c			
C ₇ H ₁₅ C=CCN	7	95	70	30	30	95	34	66
Bu ⁿ C=CCO ₂ Me	24	90d	42	58	16	78d	35	65
PhC=CCO ₂ Me	21	75	91	5	24	85	88	12
PhC=CCHO	4.5	75	91	9	4	62	83	17

^a After the preparation of $Bu^n_4N^+H_2F_3^-$ most of the DCE is evaporated under vacuum, the alkyne is added (onium salt: alkyne 2:1), then this mixture is heated (60 °C for the dimethyl butynedioate, 110–120 °C for the other alkynes). ^b P+H_2F_3: alkyne 2:1 molar ratio, CCl₄ as solvent with dimethyl butynedioate (60 °C) and n-octane as solvent with the other alkynes (110–120 °C); the concentration of the alkyne was 1 M. No difference is observed between the Amberlyst A 26 or the Amberlite IRA 900 resins. ^c This ketone does not add HF when P+H_2F_3⁻ is used. ^d This yield includes the formation of the ester PrnCH=CFCH₂CO₂Me.

BuⁿCF=CHCO₂Me and PrⁿCH=CFCH₂CO₂Me (relative proportions 5:3); this last compound is likely to be formed by addition of HF to the allenic ester PrⁿCH=C=CHCO₂Me¹¹ after isomerization of BuⁿC=CCO₂Me through a well-known basic prototropy.¹² This product of this process is observed only as a trace amount from the nitrile C₇H₁₅C=CCN.

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