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 $-\mathrm{C{\equiv}C}-$ bonds should make similar compounds more accessible. However neither anhydrous HF,[6] except when treated with $\mathrm{CF_3C{\equiv}CH}$,[7] nor amine–HF complexes investigated by Olah[8] and Yoneda[9] bring about this addition.

The $\mathrm{H_2F_3^-}$ ion, in which the H · · · F hydrogen bonds appear to be much weaker than in $\mathrm{HF_2^-}$,[10] might be expected to provide both the nucleophilic $\mathrm{F^-}$ and the electrophilic $\mathrm{H^+}$ species. We report here that $\mathrm{Bu^n{}_4N^+H_2F_3^-}$ and $\mathrm{P^+H_2F_3^-}$ ($\mathrm{P^+}$ = 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, $\mathrm{Bu^n{}_4N^+F^-}$ dissolved in 1,2-dichloroethane (DCE), or the solid resin $\mathrm{P^+F^-}$, are stirred in the presence of an aqueous saturated solution of HF–KF (2 : 1 ratio) (or HF–$\mathrm{KHF_2}$). 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 $\mathrm{P^+H_2F_3^-}$) after distillation of the water–DCE azeotrope.

$\mathrm{Bu^n{}_4N^+H_2F_3^-}$ and $\mathrm{P^+H_2F_3^-}$ react smoothly at moderate temperatures with bis-activated $\mathrm{A{-}C{\equiv}C{-}A}$ or mono-activated $\mathrm{R{-}C{\equiv}C{-}A}$ 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.

$$\begin{array}{c} \mathrm{A{-}C{\equiv}C{-}A} \\ \text{or} \\ \mathrm{R{-}C{\equiv}C{-}A} \end{array} \xrightarrow[\text{or } \mathrm{P^+H_2F_3^-}]{\mathrm{Bu^n{}_4N^+H_2F_3^-}} \begin{array}{c} \mathrm{A{-}CF{=}CH{-}A} \\ \text{or} \\ \mathrm{R{-}CF{=}CH{-}A} \end{array} \qquad (1)$$

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

The $\mathrm{H_2F_3^-}$ ion seems to play a fundamental role in this reaction. We have observed that Olah's reagent does not add HF to $\mathrm{MeO_2CC{\equiv}CCO_2Me}$ and that this ester is not readily transformed into *Z*-$\mathrm{MeO_2CCF{=}CHCO_2Me}$ (max. 10—15%) under the action of $\mathrm{Bu^n{}_4N^+HF_2^-}$. 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 $\mathrm{H_2F_3^-}$ 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 $\mathrm{H_2F_3^-}$ ion. The ester $\mathrm{Bu^nC{\equiv}CCO_2Me}$ 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.

	Reaction with $Bu^n{}_4N^+H_2F_3{}^{-a}$				Reaction with $P^+H_2F_3{}^{-\,b}$			
Acetylenic compound	Reaction time/h	Overall yield/%	*Z*-adduct/%	*E*-adduct/%	Reaction time/h	Overall yield/%	*Z*-adduct/%	*E*-adduct/%
$MeO_2CC\equiv CCO_2Me$	9	90	100	0	30	80	81	19
$PhC\equiv CCOPh$	50	53	100	0	—[c]	—	—	—
$C_7H_{15}C\equiv CCN$	7	95	70	30	30	95	34	66
$Bu^nC\equiv CCO_2Me$	24	90[d]	42	58	16	78[d]	35	65
$PhC\equiv CCO_2Me$	21	75	91	5	24	85	88	12
$PhC\equiv CCHO$	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, CCl_4 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 $Pr^nCH{=}CFCH_2CO_2Me$.

$Bu^nCF{=}CHCO_2Me$ and $Pr^nCH{=}CFCH_2CO_2Me$ (relative proportions 5 : 3); this last compound is likely to be formed by addition of HF to the allenic ester $Pr^nCH{=}C{=}CHCO_2Me$[11] after isomerization of $Bu^nC\equiv CCO_2Me$ through a well-known basic prototropy.[12] This product of this process is observed only as a trace amount from the nitrile $C_7H_{15}C\equiv CCN$.

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