Extremely Simple Route to β-Fluoro Vinamidinium Salts: A Novel Reaction of (Polyfluoro-1-propenyl)trimethylammonium lodides with Primary or Secondary Amines

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Abstract: (2,3,3-Trifluoro-1-propenyl)trimethylammonium iodide readily underwent demethylationallylic substitution followed by N-N exchange reaction at ambient temperature or at 70 °C by the action of various secondary amines or several primary amines to give the corresponding β fluorinated vinamidinium salts in good yields.

Vinamidinium, 1,5-diazapentadienium, salts¹ are a unique class of compounds regarded as vinylogs of amidinium compounds as well as push-pull stabilized alkenes. They are susceptible to substitution rather than addition reactions, and also capable of undergoing both electrophilic and nucleophilic substitution reactions. These characteristics have led to a wide range of their utilizations in organic synthesis,^{1b,2-4} particularly in the construction of a variety of carbocyclic and heterocyclic compounds.^{1b,3,4} Although the synthetic methods for various types of such useful vinamidinium salts have appeared in the literature,^{1b,5} there exist few or no methods for β -fluorinated salts,⁶ which will serve as valuable intermediates for preparing monofluoro cyclic compounds of biological interest.

In the course of our extensive studies on the chemistry and applications of polyfluorinated ammonium salts,⁷ we have found that (2,3,3-trifluoro-1-propenyl)trimethylammonium iodide (1) smoothly reacts with primary or secondary amines under very mild conditions to afford β -fluoro vinamidinium salts (3 or 4) in good yields. Herein we wish to report the preliminary results of this unique reaction which provides a very simple and efficient route to the salts 3 or 4.



The quaternary ammonium salts 1 and 2 empolyed in this study were easily prepared in 69% and 66% overall yields, respectively, by the four-step preparation starting from commercially available polyfluorinated alcohols.^{7b,8}



When 1 was allowed to react with 5 equiv. of diethylamine in anhydrous dimethyl sulfoxide (DMSO) at 70 °C for 1 h, a symmetrical salt, 1,1,5,5-tetraethyl-1,5-diaza-3-fluoropentadienium iodide (4b) was obtained in 74% yield (Entry 2), together with a small amount of β -(diethylamino)- α -fluoropropenal which resulted from hydrolysis of the salt 4b during a workup. Acetonitrile and *N*,*N*-dimethylformamide were usable as solvent in place of DMSO. The reactions between 1 and other secondary amines, such as dimethyl- (Entry 1), dipropylamine (Entry 3), pyrrolidine (Entry 5), and piperidine (Entry 6), also proceeded nicely under similar conditions to give the corresponding vinamidinium salts 4 in good yields, whereas the reaction with diisopropylamine provided an unsymmetrical salt, 1,1-diisopropyl-5,5-dimethyl-1,5-diaza-3-fluoropentadienium iodide (3d) in 56% yield (Entry 4). The results of these reactions are summarized in Table 1, along with some spectroscopic data for the products.⁹

Among the primary amines examined, like methyl-, ethyl-, butyl-, isobutyl-, *t*-butylamine, and aniline, the latter two amines participated in the reaction to yield the corresponding symmetrical salts 4 (Entries 7 and 8). The rest of the amines underwent different reactions leading preferentially to [2-(alkylimino)-3,3-difluoropropyl]trimethylammonium iodides.

The vinamidinium salts **3d** and **4** were found to be slightly sensitive to moisture. Once dried, however, these salts were storable for several months and were stable enough to be handled in air. Their ¹³C NMR spectra showed the resonance due to the α carbon at 144-152 ppm and the resonance due to the β carbon at 130-137 ppm. This tendency of the chemical shifts is typical of the alternation of electron density in push-pull alkenes.¹⁰ ¹⁹F NMR spectra of **3d** and **4** indicated that the coupling constants between the fluorine and vicinal protons fell in the range of 24-29 Hz, suggestive of the structure of these salts being an all-trans or W configuration. It should be noted that such electronic and structural features are analogous to those observed for other β -substituted vinamidinium salts.^{1b,10,11}

The reaction of (2,3,3,3-tetrafluoro-1-propenyl)trimethylammonium iodide (2) with diethylamine (5 equiv.) at 70 °C for 3 h furnished 74% combined yield of a 26 : 74 mixture of (*Z*)-(2,3,3,3-tetrafluoro-1-propenyl)dimethyl- and -diethylamine, which are the compounds corresponding to 5 and 6 ($R^1 = R^2 = Et$), respectively. On treatment of 1 with a small excess (2 equiv.) of diethylamine at 70 °C for 1 h, not only the symmetrical salt 4b but also the unsymmetrical salt 3b resulted in a ratio of 70 to 30. Interestingly, the symmetrical salt 4a was converted with diethylamine into the symmetrical salt 4b. These facts strongly suggest that the present reaction of 1 involves the formation of intermediates 5 and 6 as well as an N-N exchange¹² process. Thus, a possible mechanism of the reaction is as follows: The salt 1 may undergo a facile demethylation to form 5,

Entry	Amine	Temp/°C Time/h	Product 3 or 4	Yield/% ^a	¹³ C NMR ^b δ (J, Hz)	¹⁹ F NMR ^c δ (<i>J</i> , Hz)
1	Me ₂ NH	r.t. 3	H H Me ₂ N F (4a)	63 (16)	149.6 (s) 132.4 (d, <i>J</i> =234.4)	-83.5 (tqq, <i>J</i> =26.4, 5.3, 5.3)
2	Et₂NH	70 1	H H Et ₂ N F (4b)	74 (8)	146.1 (s) 129.9 (d, <i>J</i> =235.9)	-84.5 (tm, <i>J</i> =28.0)
3	Pr ₂ NH	70 1	$\begin{array}{c} H & H \\ H & H \\ Pr_2 N & H \\ F \\ F \\ (4c) \end{array}$	73 (10)	149.3 (s) 131.8 (d, <i>J</i> =235.8)	-82.3 (tm, <i>J=</i> 27.7)
4	<i>i</i> -Pr₂NH	70 1.5	H H F Pr ₂ N ⁺ F (3d)	56 (25)	146.1 (s) (α-C) 152.0 (s) (α-C) 133.2 (d. J=235.9)	-78.7 (ddm, <i>J</i> =28.4, 27.2)
5	NH	70 1		73 (12)	145.7 (d, <i>J</i> =3.6) 133.1 (d, <i>J</i> =231.7)	-85.3 (ttt, <i>J</i> =26.7, 8.3, 8.3)
6	NH	70 1		58 (27)	148.1 (s) 131.9 (d, <i>J</i> =236.7)	-78.3 (tm, <i>J</i> =27.3)
7	t-BuNH ₂	r.t. 24	(4f) H H F H F (4g)	80	146.0 (d, <i>J</i> =5.8) 135.6 (d, <i>J</i> =231.5)	-76.9 (tm, <i>J</i> =23.6)
8	PhNH ₂	70 1	H H PhHN HPh F (4h)	71	143.6 (d, <i>J</i> =4.7) 137.4 (d, <i>J</i> =236.6) ^d	-72.4 (im, <i>J</i> =24.6) ^d

Table 1. Yields and Spectroscopic Data for β-Fluoro Vinamidinium Salts 3 and 4

a) Yields are of pure isolated products. Values in parentheses refer to β -(dialkylamino)- α -fluoropropenal. b) Determined in chloroform-*d* with tetramethylsilane as internal standard. The upper values represent the chemical shifts for the α carbon and the lower values for the β carbon. c) Measured in chloroform-*d* with external trifluoroacetic acid. d) Measured in DMSO-*d*₆.

which is transformed into 6 via the N-N exchange reaction. The intermediate 6 will be subject to allylic substitution with amine to produce the product 4. Concurrently, 4 may also be formed through the allylic substitution of 5 with amine followed by the N-N exchange reaction.

Further studies on the synthetic applications of 4-6 and related compounds are being pursued.

References and Notes

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