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Mitsuyoshi Katayama
Takashi Ishihara
Hiroki Yamanaka

John T. Gupton
University of Richmond, jgupton@richmond.edu

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Efficient and General Synthesis of Novel β-Polyfluoroalkoxy Vinamidinium Salts

Koichiro Kase, Mitsuyoshi Katayama, Takashi Ishihara, Hiroki Yamanaka,* and John T. Gupton†

Department of Chemistry and Materials Technology, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606

+Department of Chemistry, The University of North Carolina at Asheville, Asheville, North Carolina 28804-3299, U. S. A.

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Novel β-polyfluoroalkoxy vinamidinium salts 3 and/or 4 were synthesized in good yields by the reaction of N-(2-polyfluoroalkoxy-3,3-difluoro-1-propenyl)trimethylammonium iodides (2), prepared from N-(2,3,3-trifluoro-1-propenyl)trimethylammonium iodide (1), with secondary amines in MeCN at 70 °C for 1 h. The salts were also obtainable in comparable yields by the one-pot reaction of 1 with sodium polyfluoroalkoxide followed by treatment with amines.

Vinamidinium (1,5-diazapentadienium) salts, vinylogs of amidinium compounds, are regarded as the alkenes stabilized by "push-pull" effects between the electron-donating amino group and the electron-withdrawing ammonium group, and thereby are susceptible to substitution rather than addition reactions. The salts are also characterized by their reactivities towards nucleophiles and electrophiles on the α- and β-carbons, respectively. These unique properties practically enable a wide range of their synthetic utility.1 Although many types of salts carrying various substituents have been developed and used in organic synthesis,2 there are few examples in the literature on the synthesis of fluorine-containing vinamidinium salts,3 which can serve as valuable intermediates for preparing fluorinated compounds of biological and material interest. Very recently we reported on the synthesis of β-monofluoro4 and β-trifluoromethyl5 vinamidinium salts and their applications to the preparation of fluorinated acroleins and heterocycles.5,6

In our continuing studies on the synthesis and reactions of fluorinated vinamidinium salts, we have found that N-(2-polyfluoroalkoxy-3,3-difluoro-1-propenyl)trimethylammonium iodides (2) smoothly react with secondary amines under mild conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. Herein we wish to describe an efficient and general conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. Herein we wish to describe an efficient and general conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. Herein we wish to describe an efficient and general conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. Herein we wish to describe an efficient and general conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. Herein we wish to describe an efficient and general conditions to afford β-polyfluoroalkoxyvinamidinium salts 3 in good yields. 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Polyfluoroalkoxy ammonium salts 2a-d7 were prepared in 76-79% yields by the reactions of N-(2-polyfluoroalkoxy-3,3-difluoro-1-propenyl)trimethylammonium iodide (1)8 with polyfluoroalcohols (1.1 equiv.) and NaH (1.1 equiv.) in MeCN at room temperature for 0.5 h.

When 2a was allowed to react with 5 equiv. of Et2NH in the presence of molecular sieves 4A (MS4A) in MeCN at 70 °C for 1 h, a symmetrical vinamidinium salt, 1,1,5,5-tetraethyl-1,5-diaza-3-(2,2,2-trifluoroethoxy)pentadienium iodide (3a-Et)9 and

Table 1. Synthesis of β-Polyfluoroalkoxy Vinamidinium Salts

<table>
<thead>
<tr>
<th>Entry</th>
<th>R2NH</th>
<th>Product 3 and/or 4 Yielda/% of 3 and/or 4 Ratio3/4</th>
<th>Yield3/% of 3 and/or 4</th>
<th>Ratio3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et2NH</td>
<td>OCH2CF3Et OCH2CF3Et</td>
<td>70</td>
<td>72 : 28</td>
</tr>
<tr>
<td>2</td>
<td>Et2NH</td>
<td>OCH2CF2CF3Et OCH2CF2CF3Et</td>
<td>69</td>
<td>69 : 31</td>
</tr>
<tr>
<td>3</td>
<td>Et2NH</td>
<td>OCH2CF3CF3H OCH2CF3CF3H</td>
<td>74</td>
<td>70 : 30</td>
</tr>
<tr>
<td>4</td>
<td>Et2NH</td>
<td>OCH2CF2CF2CF3H OCH2CF2CF2CF3H</td>
<td>68</td>
<td>69 : 31</td>
</tr>
<tr>
<td>5</td>
<td>i-Pr2NH</td>
<td>OCH2CF3H OCH2CF3H</td>
<td>82</td>
<td>0 : 100</td>
</tr>
<tr>
<td>6</td>
<td>NH</td>
<td>OCH2CF3H OCH2CF3H</td>
<td>74</td>
<td>100 : 0</td>
</tr>
<tr>
<td>7</td>
<td>NH</td>
<td>OCH2CF2CF3H OCH2CF2CF3H</td>
<td>68</td>
<td>100 : 0</td>
</tr>
<tr>
<td>8</td>
<td>NH</td>
<td>OCH2CF2CF2CF3H OCH2CF2CF2CF3H</td>
<td>79</td>
<td>100 : 0</td>
</tr>
<tr>
<td>9</td>
<td>NH</td>
<td>OCH2CF3CF3H OCH2CF3CF3H</td>
<td>72</td>
<td>100 : 0</td>
</tr>
<tr>
<td>10</td>
<td>NH</td>
<td>OCH2CF3CF2CF3H OCH2CF3CF2CF3H</td>
<td>69</td>
<td>100 : 0</td>
</tr>
<tr>
<td>11</td>
<td>NH</td>
<td>OCH2CF3CF2CF2CF3H OCH2CF3CF2CF2CF3H</td>
<td>67</td>
<td>100 : 0</td>
</tr>
</tbody>
</table>

* Isolated yields. Figures in parentheses are of the yields based on 2 in the stepwise preparation. 3 Determined by 19F NMR. Figures in parentheses are of the ratios in the stepwise preparation.

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an unsymmetrical salt, 1,1-diethyl-5,5-dimethyl-1,5-diaza-3-(2,2,2-trifluoroethoxy)pentadinium iodide (4a-Et) was obtained in 59% and 26% yields, respectively (Entry 1). Either elongation of the reaction time (10 h) or use of excess amine (10 equiv.) reduced the yield of the unsymmetrical salt to less than 5%. The absence of MS4A resulted in the formation of considerable amounts of β-(diethylamino)- and β-(dimethylamino)-α-(trifluoroethoxy)propenals, which may arise from the hydrolysis of \textit{in-situ} formed vinamidinium salts.\(^\text{10}\) The reactions of other polyfluoroalkoxy ammonium salts 2b-d with Et\(_2\)NH also took place nicely under similar conditions to afford the corresponding salts 3b-d-Et\(^7\) and 4b-d-Et\(^7\) (Entries 2-4). Interestingly, the yields and ratios of 3-Et and 4-Et were almost the same, irrespective of the length of polyfluoroalkyl group.

\[
\text{CH}_2\text{F} \quad \text{H} \quad \text{Et}_{\text{N}} \quad \text{C}=\text{O} \quad \text{R} \quad \text{O} \quad \text{C} \quad \text{F} \\
\text{RICH}_2 \quad \text{O} \quad \text{NMe}_3 \quad \text{I} \quad \text{MeCN} \quad \text{OCH}_2\text{Rf} \quad \text{OCH}_2\text{Rf} \\
2a-d \quad 3a-d\text{-Et} \quad 4a-d\text{-Et} \\
\]

To simplify the procedure for the synthesis of the vinamidinium salts, we examined the one-pot reaction starting from 1 are summarized in Table 1. The ammonium salts 4a-d-R in good yields. The results of these one-pot secondary amines under the same conditions led to the corresponding symmetrical 3a-d-R and/or unsymmetrical vinamidinium salts 4a-d-R in good yields. The results of these one-pot syntheses starting from 1 are summarized in Table 1.

\[
\text{CH}_2\text{F} \quad \text{H} \quad \text{Et}_{\text{N}} \quad \text{C}=\text{O} \quad \text{R} \quad \text{O} \quad \text{C} \quad \text{F} \\
\text{RICH}_2 \quad \text{O} \quad \text{NMe}_3 \quad \text{I} \quad \text{MeCN} \quad \text{OCH}_2\text{Rf} \quad \text{OCH}_2\text{Rf} \\
1 \quad 3a-d\text{-R} \quad 4a-d\text{-R} \\
\]

It should be noted that the ratio of 3 to 4 is strongly dependent on the secondary amine employed. Et\(_2\)NH afforded a mixture of 3a-d-Et and 4a-d-Et in a ratio of around 70:30 (Entries 1-4). Disopropylamine, a bulky amine, gave only unsymmetrical salt 4a-i-Pr (Entry 5). In contrast, cyclic amines such as pyrrolidine, piperidine, and morpholine yielded only symmetrical salts 3a-d-Py, 3a-Pi, and 3a-Mo, respectively (Entries 6-11). The salt 4a-Et was converted into the symmetrical salt 3a-Et on treating with Et\(_2\)NH at 70 °C for 1 h in MeCN, whereas the treatment of 4a-i-Pr with disopropylamine did not give any 3a-i-Pr. These facts suggest that an N-N exchange process takes part in determining the ratio of 3 to 4, where the bulkiness of the amine rather than its basicity or nucleophilicity plays a dominant role.

Further studies on the synthetic applications of 3 and 4, including elucidation of their reactivities relative to β-fluoro and β-trifluoromethyl vinamidinium salts, are in progress.

References and Notes


7 All isolated products gave satisfactory spectroscopic and analytical data.


9 3a-Et: Mp 103.5-104.7 °C; IR (KBr, cm\(^{-1}\)) 2978, 1654, 1597, 1443, 1315, 1265, 1061, 988; 
\(\text{\text{H}}\) NMR (CDCl\(_3\), TMS, 300 MHz) \(\delta = 1.29\) (t, \(J = 7.2\) Hz, 6H), 1.40 (t, \(J = 7.2\) Hz, 6H), 3.69 (q, \(J = 7.2\) Hz, 8H), 8.30 (q, \(J = 8.2\) Hz, 2H), 8.51 (s, 2H); 
\(\text{\text{F}}\) NMR (CDCl\(_3\), CCF\(_3\), 90 MHz) \(\delta = -73.75\) (s, \(J = 8.2\) Hz, 3F); SIMS (2M+I). 4a-Et: Mp 131.5-132.5 °C; IR (KBr, cm\(^{-1}\)) 2978, 1663, 1612, 1312, 1269, 1061, 964; 
\(\text{\text{H}}\) NMR (CDCl\(_3\), TMS, 300 MHz) \(\delta = 1.30\) (t, \(J = 7.2\) Hz, 3H), 1.40 (t, \(J = 7.2\) Hz, 3H), 3.48 (s, 1H); 
\(\text{\text{F}}\) NMR (CDCl\(_3\), CCF\(_3\), 90 MHz) \(\delta = -73.42\) (s, \(J = 8.3\) Hz, 3F). SIMS (2M+I).

10 The propenals were obtained in 90% yield when the reaction was conducted in 20% aqueous MeCN.