Synthesis of 2-Aryl-3 Fluoralkoxy-1-Pro-penes and Some Potentially Useful Reactions of These Systems

1987

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THE SYNTHESIS OF 2-ARYL-3-FLUOROALKOXY-1-PROPENES
AND SOME POTENTIALLY USEFUL REACTIONS OF THESE SYSTEMS

BY

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B.A., University of Louisville, 1982

THESIS
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ABSTRACT

This report discusses research involving the fluoroalkoxylation of 2-arylprop-1-en-3-yltrimethylammonium iodides and the useful synthetic application of the adducts formed. The present work includes: 1) reactions of several 2-arylprop-1-en-3-yltrimethylammonium iodides with the sodium salt of 2,2,2-trifluoroethanol; 2) reactions of several fluoroalkoxy alcohols with 2-(4-bromophenyl)prop-1-en-3-yltrimethylammonium iodide; and 3) the oxidation of 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene using the Lemieux/von Rudloff reagent. This report reveals the experimental conditions and procedures used as well as spectral and physical data of all new compounds synthesized. Explanation is offered for a possible mechanism for the formation of these compounds and recommendations for future research are given.
ACKNOWLEDGEMENTS

I would like to thank Dr. John T. Gupton III for his patience, encouragement and guidance during my graduate research. I am deeply indebted to him for the knowledge and experience I have acquired as a result of his expertise in the field of chemistry.

I am also grateful to Dr. Guy Mattson and Dr. Graeme Baker as members of my graduate committee for their time, input and encouragement.

Thanks also to my husband Kevin, my daughter Eleith, and parents for their patience, love and support during my college education. Finally, and most importantly, I thank God for continued strength and endurance during my college years (Phil. 4:13-15).
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LIST OF ABBREVIATIONS

bp  boiling point
°c  degrees Centigrade
cm⁻¹  wave number
δ  delta (NMR spectrum)
DMF  N,N-dimethyformamide
DMSO-d₆  deuterated dimethyl sulfoxide
EtOAc  ethyl acetate
g  grams
h  hours
Hz  Hertz (cycles per second)
IR  infrared
J  coupling constant (NMR spectrum)
m  multiplet
mg  milligrams
mL  milliliters
mp  melting point
mol  moles
M⁺  molecular ion
m/e  mass to charge ratio
NMR  nuclear magnetic resonance
ppm  parts per million
q    quartet
r.t.  room temperature
s    singlet
t    triplet
THF  tetrahydrofuran
TLC  thin layer chromatography
v/v  volume/volume
The synthetic utility of 2-arylvinamidinium salt systems has been of particular interest to our research group for the past several years.\textsuperscript{1-7} The foundation for the investigation of 2-arylvinamidinium salt systems was predicated by the previous chemistry which had been conducted on iminium and vinamidinium salt systems.\textsuperscript{8-12}

As illustrated in Figure 1, the preparation of arylvinamidinium salts is performed by reacting substituted phenylacetic acids with DMF and phosphorous oxychloride.\textsuperscript{3} The proposed mechanism by which this reaction occurs is that of a Vilsmeier-Haack type precursor.\textsuperscript{13}

Figure 1. Preparation of 2-Arylvinamidinium Perchlorates from Substituted Phenylacetic Acids, DMF, and Phosphorous Oxychloride.
Due to the considerable interest in the reduction of iminium salts\textsuperscript{14,15} by organic chemists and the potential application of the reaction products, our laboratory\textsuperscript{5} has pursued the investigation of 2-arylvinamidinium perchlorates (1) using sodium borohydride and sodium cyanoborohydride as the reducing agents. The reduction of simple iminium salt systems via sodium borohydride and cyanoborohydride has been extensively studied\textsuperscript{16-17}. Work in our laboratory has shown that N,N-dimethylallylic amines (2) are produced from the reduction of 2-arylvinamidinium perchlorates with sodium borohydride, as shown in Figure 2.

![Figure 2. The Use of Sodium Borohydride in the Preparation of N,N-dimethylallylic Amines from 2-Arylvinamidinium Perchlorates.](image)

The proposed mechanism\textsuperscript{5} for the reduction with sodium borohydride follows a reduction-elimination-reduction sequence, which involves the addition of a hydride ion (nucleophilic attack) and the generation of a borane complex. The borane complex undergoes elimination followed by the addition of another hydride ion (Figure 3).
Figure 3. Postulated Mechanism for the Formation of N,N-dimethylallylic Amines from the Sodium Borohydride Reduction of 2-Arylvinaminidinium Perchlorates.
Organic chemists have shown interest for many years in allylic compounds. Magid,\textsuperscript{18} in his work with organometallic and nucleophilic displacement reactions of allylic compounds, pointed out that very few substitution reactions occur when the leaving group has the amino functionality. Gupton and coworkers\textsuperscript{19} decided it might be interesting and useful to examine the reaction of organolithium reagents with allylic amine systems, since the opportunity existed for metallation of the aromatic ring as well as possible addition to the alkene portion of the molecule. When a variety of 2-aryl-3-N,N-dimethylamino-1-propenes (2) were reacted with excess butyllithium at 0°C in anhydrous THF, the corresponding 3-butyl-2-aryl-1-propenes (3) were produced (Figure 4).

![Reaction Diagram](image)

**Figure 4.** The Preparation of 2-Aryl-3-substituted-1-propenes from 2-Aryl-3-N,N-dimethylamino-1-propenes and Butyllithium.

Mechanistically speaking, the overall reaction can be viewed as an $S_n2'$ process occurring by an addition-elimination process (Figure 5). The dimethylamino group is easily eliminated and this may indicate substantial coordination between the lithium and the amino group. These arylpropenes were produced cleanly and in relatively good yields.
Subsequent investigations examining 2-aryl-3-N,N-dimethylamino-1-propenes involving methylmagnesium bromide, with or without the incorporation of Cu(I) salts as a catalyst, were conducted by Gupton and coworkers. Since no reaction was observed in this case, they decided to investigate the corresponding allylic quaternary ammonium salts.

A number of nucleophiles such as phenylmagnesium bromide, various organometallic reagents, and sodium borohydride have been successfully reacted with these allylic quaternary ammonium iodides. Preparation of these quaternary ammonium iodides is accomplished by stirring a mixture of excess methyl iodide in THF with the appropriate 2-aryl-3-N,N-dimethylamino-1-propene (Figure 6).
The utility of other quaternary ammonium iodides has been seen in the synthesis of indole alkaloids\textsuperscript{22-24} and antitumor agents.\textsuperscript{25}

From the observations mentioned, it would be most interesting and worthwhile to investigate the reaction of several 2-arylprop-1-en-3-yltrimethylammonium iodides with other nucleophiles, namely fluorinated nucleophilic compounds.

Since the discovery of fluorinated refrigerants, commonly called "freons", the synthesis of fluorinated organic compounds has steadily increased.\textsuperscript{26} A variety of significant applications of fluorine derivatives are in the chemistry of polymers, propellants, blood substitutes, pharmaceuticals and pesticides.\textsuperscript{26-28} In this investigation specific interest is in fluorinated materials which incorporate the trifluoroethoxy (-OCH\textsubscript{2}CF\textsubscript{3}) moiety onto a hydrocarbon backbone.

The synthesis of fluoroalkoxy aromatics is particularly interesting in that they are found to be important intermediates for potentially effective pesticides and in the synthesis of pharmaceutical agents. For example, fluorinated DOWCO-416\textsuperscript{29-31} and Flecainide Acetate have been shown to be physiologically active (Figure 7).\textsuperscript{28,30}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fluoroalkoxy.png}
\caption{Fluoroethoxylated Organic Compounds: DOWCO-416 (5) and Flecainide Acetate (6).}
\end{figure}
In order to examine the reaction feasibility of various aryl substituted quaternary ammonium iodides with sodium fluoroalkoxides, we propose to investigate the following: 1) reactions of a variety of 2-arylprop-1-en-3-yltrimethylammonium iodides with 2,2,2-trifluoroethoxides; 2) reactions of several fluoroalkoxides with 2-(4-bromophenyl)prop-1-en-3-yltrimethylammonium iodide, and 3) reactions with 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene to produce the ketone adduct.
EXPERIMENTAL

Instrumentation and Equipment

Proton NMR spectra were obtained on a Varian EM-360A NMR spectrometer at 60 mHz. Solvent systems used in obtaining NMR spectra include CDCl₃ and DMSO-d₆. Chemical shifts were reported in ppm (δ) downfield from tetramethylsilane, which was used as an internal standard. Infrared spectra were recorded using a Perkin-Elmer 1420 ratio recording infrared spectrometer and absorptions are reported in cm⁻¹. Samples were run as thin films, nujol mulls, or CCl₄ solutions.

Distillations were performed under high vacuum (0.2-0.5 mmHg) using a Kugelrohr distillation apparatus. Melting points were determined on purified materials using a Fisher-Johns melting point apparatus. A Buchi Rotovapor-R rotary evaporator was used for the removal of solvents in vacuo with a thermostatically controlled hot water bath. Analytically pure samples were prepared by using either Kugelrohr distillation or a Harrison Research Chromatotron (preparative, accelerated thin-layer chromatograph).

A. Feasibility Study for the Preparation of 2-Aryl-3-fluoroalkoxy-1-propenes from 2-Arylprop-1-en-3-yltrimethylammonium Iodides.

\[
\text{Ar} = \text{N(CH₃)}_3, \quad \text{I}^- + \text{NaOCH₂CF₃} \xrightarrow{\Delta, 1,4\text{ dioxane}} \text{ArOR}^f
\]
<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>$R_f$</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>bp (°C)</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>76</td>
<td>55-61</td>
<td>0.4 mmHg</td>
</tr>
<tr>
<td>2</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>57</td>
<td>88-104</td>
<td>0.4 mmHg</td>
</tr>
<tr>
<td>3</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>52</td>
<td>60-90</td>
<td>0.3 mmHg</td>
</tr>
<tr>
<td>4</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>83</td>
<td>75-100</td>
<td>0.4 mmHg</td>
</tr>
<tr>
<td>5</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>71</td>
<td>68-80</td>
<td>0.3 mmHg</td>
</tr>
<tr>
<td>6</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>69</td>
<td>80-110</td>
<td>0.3 mmHg</td>
</tr>
<tr>
<td>7</td>
<td><img src="" alt="image" /></td>
<td>CH₂CF₃</td>
<td>31</td>
<td>40-60</td>
<td>0.4 mmHg</td>
</tr>
</tbody>
</table>

<sup>a</sup>The yields refer to products purified by vacuum distillation. Calculations are based on the theoretical conversion of starting material to product.

<sup>b</sup>Spectral information follows the experimental procedure.
\( ^{13} \text{CNMR (CDCl}_3 \) \( \delta \) 3.90 (q, J=9Hz, 2H), 4.53 (s, 2H), 5.32 (s, 1H), 5.55 (s, 1H) and 7.01 (m, 3H); IR (thin film) 1625, 1600, 1580, 1525, 1460, 1410, 1330, 1305, 1280, 1225, 1160, 1120, 1025, 965, 910, 855, 810 and 770 cm\(^{-1}\); mass spectrum m/e 276 (M\(^+\)).

\( ^{19} \text{dNMR (CDCl}_3 \) \( \delta \) 3.84 (q, J=9Hz, 2H), 4.53 (s, 2H), 5.35 (s, 1H), 5.60 (s, 1H) and 7.63 (m, 4H); IR (thin film) 1495, 1315, 1280, 1165, 1128, 1100, 1014, 965, 917 and 834 cm\(^{-1}\).

\( ^{23} \text{eNMR (CDCl}_3 \) \( \delta \) 3.80 (m, 5H), 4.58 (s, 2H), 5.30 (s, 1H), 5.55 (s, 1H), 6.90 (d, J=8Hz, 2H) and 7.50 (d, J=8Hz, 2H); IR (thin film) 1610, 1511, 1305, 1280, 1250, 1165, 1125, 1100, 1032, 961 and 832 cm\(^{-1}\).

\( ^{27} \text{fNMR (CDCl}_3 \) \( \delta \) 3.90 (q, J=9Hz, 2H), 4.53 (s, 2H), 5.40 (s, 1H), 5.62 (s, 1H) and 7.44 (m, 4H); IR (thin film) 1630, 1589, 1490, 1430, 1395, 1310, 1280, 1160, 1125, 1100, 1070, 1000, 965, 915 and 835 cm\(^{-1}\); mass spectrum m/e 294, 296 (M\(^+\)).

\( ^{29} \text{gNMR (CDCl}_3 \) \( \delta \) 3.85 (q, J=9Hz, 2H), 4.43 (s, 2H), 5.39 (s, 1H), 5.75 (s, 1H) and 7.28-8.20 (m, 7H); IR (thin film) 1640, 1589, 1574, 1505, 1450, 1430, 1400, 1335, 1305, 1275, 1160, 1125, 1063, 1018, 1000, 965, 920, 850, 825, 805, 780, 735, 710 and 665 cm\(^{-1}\); mass spectrum m/e 266 (M\(^+\)).

\( ^{31} \text{hNMR (CDCl}_3 \) \( \delta \) 3.90 (q, J=9Hz, 2H), 4.55 (s, 2H), 5.35 (s, 1H), 5.65 (s, 1H) and 7.42 (m, 5H); IR (thin film) 1281, 1164, 965, 775 and 710 cm\(^{-1}\).

**Preparation of 2-(p-Methylphenyl)-3-(2,2,2-trifluoroethoxy)-1-propene**

To a 250 mL three-neck round bottom flask equipped with a thermometer, a condenser, magnetic stirrer and a rubber septum were
added 0.568 g (0.148 mol) of sodium hydride, (60% by weight in mineral oil) and 20 mL of distilled hexane. This mixture was allowed to stir under nitrogen for 30 minutes. Stirring was discontinued and the sodium hydride was allowed to settle. The hexane-oil layer was then removed by suction. Sixty mL of dry dioxane was added to the flask followed by 1.48 g (0.0148 mol) of 2,2,2-trifluoroethanol and the mixture was allowed to stir until the evolution of hydrogen ceased. Subsequently 1.5 g (0.0047 mol) of 2-(p-methylphenyl)prop-1-en-3-yltrimethylammonium iodide was added in one portion, heated and allowed to stir for 24 h. The reaction mixture was allowed to cool to room temperature and the solvent removed in vacuo. The crude product was dissolved in water (75 mL) and extracted with chloroform (3 x 50 mL) and then dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the chloroform removed in vacuo. The residue was then distilled (Kugelrohr 55-61°C at 0.3 mm Hg) to yield a clear liquid weighing 0.69 g (76% yield). NMR (CDCl₃) δ 2.40 (s,3H), 3.95 (q,J=9Hz,2H), 4.62 (s,2H), 5.42 (s,1H), 5.70 (s,1H), 7.33 (d,J=9Hz,2H), 7.95 (d,J=9 Hz,2H); IR (thin film) 1515, 1308, 1280, 1164, 1125, 1100, 1020, 966, 910 and 825 cm⁻¹.

B. Preparation of 2-(4-Bromophenyl)-3-fluoroalkoxy-1-propenes from 2-(4-Bromophenyl)prop-1-en-3-yltrimethylammonium Iodides.

\[
\begin{align*}
\text{Br} & \quad \text{I}^- \\
\text{H} & \quad \text{N} \quad \text{(CH₃)}_3 \\
\text{H} & \quad \text{H} & \quad \text{H} \\
\end{align*}
\]

\[
\xrightarrow{1,4\text{-Dioxane}}
\]

\[
\begin{align*}
\text{Br} & \quad \text{OR}_f \\
\text{H} & \quad \text{H} \\
\end{align*}
\]
Table II
Experimental Data for the Preparation of 2-(4-Bromophenyl)-3-fluoroalkoxy-1-propenes\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>R\textsubscript{f}</th>
<th>% Yield\textsuperscript{b}</th>
<th>bp (°C) (0.3 mmHg)</th>
<th>t (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-CH\textsubscript{2}CF\textsubscript{3}</td>
<td>71\textsuperscript{c}</td>
<td>68-80</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>-CH\textsubscript{2}CF\textsubscript{2}CF\textsubscript{2}CF\textsubscript{3}</td>
<td>52\textsuperscript{d}</td>
<td>65-90</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>-CH\textsubscript{2}CF\textsubscript{2}CF\textsubscript{3}</td>
<td>31\textsuperscript{e}</td>
<td>75-100</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>-CH\textsubscript{3}</td>
<td>28\textsuperscript{f}</td>
<td>75-100</td>
<td>20</td>
</tr>
</tbody>
</table>

\textsuperscript{a}The reaction procedure is the same as performed for the preparation of 2-(p-methylphenyl)-3-(2,2,2-trifluoroethoxy)-1-propene.

\textsuperscript{b}Yields reported refer to products purified by vacuum distillation. Calculations are based on the theoretical conversion of starting material to product.

\textsuperscript{c}NMR (CDCl\textsubscript{3}) \(\delta\) 3.90 (q,\textit{J}=9Hz,2H), 4.53 (s,2H), 5.40 (s,1H), 5.62 (s,1H) and 7.44 (m,4H); IR (thin film) 1630, 1589, 1490, 1430, 1395, 1310, 1280, 1160, 1125, 1100, 1070, 1000, 965, 915, and 835 cm\textsuperscript{-1}; mass spectrum m/e 294, 296 (M\textsuperscript{+}).

\textsuperscript{d}NMR (CDCl\textsubscript{3}) \(\delta\) 3.93 (t,\textit{J}=14Hz,2H), 4.53 (s,2H), 5.40 (s,1H), 5.64 (s,1H) and 7.20-7.60 (m,4H); IR (thin film) 1625, 1585, 1486, 1390, 1350, 1340, 1225, 1200, 1180, 1120, 1095, 1070, 1008, 960, 915, 830, 780, 755 and 735 cm\textsuperscript{-1}; mass spectrum m/e 394, 396 (M\textsuperscript{+}).
$\delta$ NMR (CDCl$_3$) $\delta$ 3.90 (t, $J=14$ Hz, 2H), 4.53 (s, 2H), 5.42 (s, 1H), 5.65 (s, 1H) and 7.25-7.68 (m, 4H); IR (thin film) 1625, 1585, 1485, 1465, 1390, 1370, 1350, 1255, 1200, 1145, 1125, 1080, 1044, 1022, 1008, 955, 938, 915, 830, 778, 755 and 728 cm$^{-1}$; mass spectrum m/e 344, 346 (M$^+$).

$\delta$ NMR (CDCl$_3$) $\delta$ 1.50, (d, $J=4$ Hz, 3H), 3.85 (hept, $J=6$ Hz, 1H), 4.40 (d, $J=12$ Hz, 1H), 4.60 (d, $J=12$ Hz, 1H), 5.40 (s, 1H), 5.60 (s, 1H) and 7.25-7.60 (m, 4H); IR (thin film) 1625, 1585, 1488, 1450, 1385, 1275, 1175, 1155, 1099, 1070, 1008, 915, 830, 775, 755, 735 and 675 cm$^{-1}$; mass spectrum m/e 308, 310 (M$^+$).

C. Oxidation and Optimization Study for the Preparation of (4-Chlorophenyl)-(2,2,2-trifluoroethoxymethyl) Ketone from 2-(4-Chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene.

Table III
Experimental Data for the Preparation of (4-Chlorophenyl)-(2,2,2-trifluoroethoxymethyl) Ketone

<table>
<thead>
<tr>
<th>Entry</th>
<th>Molar ratio$^a$</th>
<th>Temp °C</th>
<th>Time (h)</th>
<th>% Yield$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60:1</td>
<td>r.t.</td>
<td>24</td>
<td>(36) 4$^c$</td>
</tr>
<tr>
<td>2</td>
<td>60:2</td>
<td>r.t.</td>
<td>24</td>
<td>(16) 8</td>
</tr>
<tr>
<td>3</td>
<td>60:8</td>
<td>r.t.</td>
<td>48</td>
<td>(76) 48</td>
</tr>
<tr>
<td>4</td>
<td>60:8</td>
<td>r.t.</td>
<td>72</td>
<td>(92) 61$^d$</td>
</tr>
<tr>
<td>5</td>
<td>60:8</td>
<td>55</td>
<td>24</td>
<td>(52) 33</td>
</tr>
</tbody>
</table>
The molar ratio refers to that of sodium meta periodate to potassium permanganate respectively dissolved in 50 mL of deionized water with heating.

Percent yields refer to the crude product yields (in parentheses) followed by their purified yields. Calculations are based on the theoretical conversion of starting material to product.

To purify this material, 0.178 g of crude material was chromatographed on a Harrison chromatotron to give 0.023 g pure sample (eluent: 90/10, v/v, hexane/EtOAc).

The following preparation procedure is indicative of the preparation of a sample at the highest attained yield.

Preparation of 2-(4-chlorophenyl)-(2,2,2-trifluoroethoxymethyl) ketone

A 250 mL three-necked, round bottom flask was equipped with a reflux condenser, a magnetic stirrer and two glass stoppers. To the flask were added 0.50 g (0.002 mol) of 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene and 50 mL of t-butanol. Sodium meta periodate (1.02 g, 0.0048 mol), along with potassium permanganate (0.013 g, 0.0023 mol) was dissolved in 50 mL of water with heating. (See Table III for periodate-permanganate molar ratios.) The reaction was stopped after the desired time by adding 0.765 g of sodium bisulfite was added to kill any excess oxidizing agent. The mixture was filtered and the solvent removed in vacuo. The reaction mixture was diluted with 75 mL of water and extracted with 3 x 50 mL washings of CHCl₃. The CHCl₃ layer was dried over anhydrous magnesium sulfate with the addition of norite
to decolorize the solution. The drying agent and norite were removed by gravity filtration and the solution concentrated in vacuo to leave a white semisolid. In order to prepare an analytically pure sample, the crude material was distilled (Kugelrohr) at a bp 70-110°C (0.4 mmHg) to yield a white solid: mp 58-72°C; NMR (CDCl₃, DMSO-d₆) δ 4.10 (q, J=9Hz, 2H), 4.93 (s, 2H), 7.50 (d, J=9Hz, 2H) and 9.40 (d, J=9Hz, 2H); IR (nujol) 2925, 1700, 1688, 1580, 1485, 1395, 1359, 1300, 1280, 1225, 1160, 1135, 1090, 1055, 1012, 990, 960, 830 and 660 cm⁻¹, mass spectrum m/e 252 (M⁺).
DISCUSSION OF RESULTS

As mentioned in the introduction, the purpose of this work was to first react a variety of 2-arylprop-1-en-3-yltrimethylammonium iodides with 2,2,2-trifluoroethanol, then react 2-(4-bromophenyl)-prop-1-en-3-yltrimethylammonium iodide with several fluoroalkoxy alcohols, and finally to react 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene to produce the ketone adduct.

The reactions of sodium 2,2,2-trifluoroethoxide with a variety of 2-arylsubstituted allylic quaternaryammonium salts in refluxing dioxane, produced the anticipated fluoroalkoxy ethers in good yield. The types of compounds examined were the p-methylphenyl, p-methoxyphenyl, dimethoxyphenyl, p-chlorophenyl, p-bromophenyl, a-naphthyl, and the unsubstituted phenyl allylic quaternaryammonium salts. The products were characterized by NMR, IR and mass spectroscopy. Purification was accomplished by distillation or chromatotron separation of the crude products. Low yields reported may be attributed to decomposition of products due to conditions of temperature and pressure during vacuum distillation or physical loss.

Interestingly enough, four of the 2-aryl-3-(2,2,2-trifluoroethoxy)-1-propenes were found in the literature to have been synthesized in good yields by Gassman and Harrington. They reacted 2,2,2-trifluoroethanol with 2-aryltosylates in a
buffered solution of 2,6-lutidine, blanketed with argon in a sealed tube (Figure 8).

![Chemical structure](image)

Figure 8. Trifluoroethanolysis of 2-Arylallyl Tosylates.

Gassman and Harrington\textsuperscript{33} characterized the p-methylphenyl, p-chlorophenyl, p-methoxyphenyl and the unsubstituted phenyl compounds and found the quartet representing two protons in the NMR at about 3.84 ppm (J=9Hz) corresponding to the protons in the -OCH\textsubscript{2}CF\textsubscript{3} group. Their spectral data for both NMR and IR agreed with ours. The disappearance of the broad singlet at 3.35 ppm in the proton NMR spectrum, which corresponds to the -N(CH\textsubscript{3})\textsubscript{3} group and the upfield shift of the -CH\textsubscript{2}-OR\textsubscript{f} hydrogens to 4.53 ppm from 4.95 ppm gave additional evidence for the formation of our 2-aryl-3-trifluoroalkoxy-1-propenes. Please see Figure 9 for an example of the designation of protons in the NMR spectrum of 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene.

The IR spectra of these compounds consistently revealed the strong absorption of the CF\textsubscript{3} group in the 1350-1120 cm\textsuperscript{-1} region. Absorption bands in the 1280-1200 cm\textsuperscript{-1} and 1075-1020 cm\textsuperscript{-1} regions were attributed respectively to the asymmetrical and symmetrical aryl alkyl ether stretches. Only one spot was seen for the TLC
analysis of each compound using different solvent systems indicating a high level of purity.

Mass spectral data of the three trifluoroethoxy ethers not reported by Gassman\textsuperscript{33} were consistent with the molecular ion peaks of the dimethoxy (M$^+$ 276), bromophenyl (M$^+$ 294,296), and the α-naphthyl (M$^+$ 266) compounds.

The low yield for 2-phenyl-3-(2,2,2-trifluoroethoxy)-1-propene, entry 7 of Table I, may be attributed to decomposition of the product under conditions of temperature and pressure during vacuum distillation. The temperature range and pressure for the distillation of this product was 40-60°C and 0.4 mm Hg, respectively. Physical losses may also have had an effect on the amount of purified product obtained.

The experimental data represented in Table II demonstrates the versatility of 2-arylprop-1-en-3-yltrimethylammonium iodides by their reaction with a variety of fluoroalkoxide nucleophiles. The bromine substituted phenyl quaternaryammonium iodide was used in these reactions and reacted in good to fair yields. The procedure for the preparation of these fluoroalkoxy propenes was the same as that performed for the preparation of the compounds in Table I.

Figure 9 is representative of the proton peak assignments for the NMR spectrum of entry 1 (Table II). For entry 1, the quartet at 3.90 ppm represents the protons of the -OCH$_2$CF$_3$ group. A triplet at 3.93 ppm corresponds to the protons in the -OCH$_2$CF$_2$CF$_2$CF$_3$ group of entry 2 and a triplet at 3.90 ppm corresponds to the protons in the -OCH$_2$CF$_2$CF$_3$ group of entry 3.
For entry 4, a heptet at 3.85 ppm, J=6Hz, corresponds to the hydrogen on the chiral carbon in the CF$_3$CH-CH$_3$ group. The chiral carbon of this fluoropropoxy group causes the two allylic hydrogens (-CH$_2$O-R$_f$) to be non-equivalent giving a doublet at 4.40 ppm, J=12Hz, and a doublet at 4.60 ppm, J=12Hz (Figure 10).

In the IR spectra for all four compounds the absorption band seen in the region of 1280-1200 cm$^{-1}$ was due to the aryl alkyl ether (C-O-C) asymmetrical stretching. Strong absorptions in the region of 1350-1120 cm$^{-1}$ indicated the presence of the CF$_3$ and/or CF$_2$ groups stretch. The mass spectra of the reaction products were also consistent with the anticipated results. (See Experimental section, Part B.).

<table>
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<tr>
<th>Peak Assignments</th>
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<tr>
<td>Protons</td>
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<td>b</td>
<td>4.53 (s,2H)</td>
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<tr>
<td>c</td>
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Figure 9. Protons Responsible for the Peaks in the NMR Spectrum of 2-(4-Chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene.
Peak Assignments
Chemical Shifts

Proton  ppm
a   1.50 (d, 3H)
b   3.85 (hept, 1H)
c   4.40 (d, 1H)
d   4.60 (d, 1H)
e   5.40 (s, 1H)
f   5.60 (s, 1H)
g   7.25-7.60 (m, 4H)

Figure 10. Protons Responsible for the Peaks in the NMR Spectrum of 2-(4-Bromophenyl)-3-(1,1,1-trifluoroprop-2-oxy)-1-propene.

Figure 11. Proposed Mechanism for the Formation of 2-Aryl-substituted-3-fluoroalkoxy-1-propenes in an Addition-Elimination Sequence.
The mechanism in Figure 11 is proposed to explain the formation of 2-arylsubstituted-3-fluoroalkoxy-1-propenes by an $S_{N2}'$ process occurring by an addition-elimination sequence. This mechanism has been proposed by Gupton\textsuperscript{19} and others,\textsuperscript{3} showing the attack of a nucleophile on the pi system of the vinylidene group.

After the synthesis of these 2-aryl-3-fluoroalkoxy-1-propenes, we thought it would be most interesting to perform an oxidation reaction involving cleavage of the styrene double bond of 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene. In a review by March\textsuperscript{13}, the cleavage under mild conditions and with good yield, with periodic acid was addressed.

Periodic acid and its sodium and potassium salts have been used by organic chemists as an oxidizing agent for many years.\textsuperscript{35} Oxidations with periodates have been used in carbohydrate chemistry\textsuperscript{36} and in the nucleic acid field.\textsuperscript{37} Fatiadi in his work describes the use of the Lemieux/von Rudloff reagent, sodium meta periodate and potassium permanganate, to cleave \( \Delta^4 \)-3-ketosteroids to 5-keto-4-norsteroid-3-carboxylic acids in approximately 70-90% yield in t-butyl alcohol and water (Figure 12).

\[ \text{NaIO}_4 / \text{KMnO}_4 \rightarrow \text{CH}_3 \]

Figure 12. The Cleavage of \( \Delta^4 \)-3-Keto-steroids to 5-Keto-norsteroid-3-carboxylic acid by Sodium Meta Periodate-potassium Permanganate.
Lemieux and von Rudloff, who developed the reagent for the oxidative fission of olefinic double bonds, used aqueous sodium meta periodate and potassium permanganate at a pH of 7.7 in a molar ratio of 60:1. This reagent has been of particular value and usefulness in the analysis of oils and fats, the esterification of fragment acids from unsaturated lipids, in the oxidative degradation of terpenes, and reactions with steroids. Bernassau and Fetizon used Lemieux/von Rudloff reagent to improve the method of degradation of the side chain of the steroid lanosterol (Figure 13).

![Figure 13. The Steroid Lanosterol.](image)

To produce the desired ketone adduct of 2-(4-chlorophenyl)-3-(fluoroethoxy)-1-propene, we decided to utilize the Lemieux/von Rudloff reagent adapting the procedure performed by Bernassau and Fetizon. (See procedure in Experimental section, Part C).

The successful preparation of the trifluoroethoxyethanone in low yield led to our hopes of maximizing the process. To do this, we varied the sodium periodate to potassium permanganate molar
ratio and also varied the reaction time (see Table III). The reaction was monitored over a 24 h period by TLC to determine if starting material was present in the reaction mixture. At the 60:8 molar ratio a good yield was achieved after a period of 72 h (entry 4). Analytically pure samples were obtained by either distillation, recrystallization or the use of a chromatotron separation.

The (4-chlorophenyl)-(2,2,2-trifluoroethoxymethyl) ketone compound was characterized by NMR, IR and mass spectroscopy. The proton NMR revealed a quartet still remaining at 4.10 ppm corresponding to the -OCH₂CF₃ group and the disappearance of the two vinylic protons at 5.35 and 5.60 ppm (Figure 14). The appearance of the C=O stretch at 1700 cm⁻¹ and the disappearance of the vinylidene absorption band between 895-885 cm⁻¹ was consistent with the anticipated structure.

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Figure 14. Protons Responsible for the Peaks in the NMR Spectrum of (4-Chlorophenyl)-(2,2,2-trifluoroethoxymethyl) Ketone.
CONCLUSIONS

The fluoroalkoxylation of 2-arylprop-1-en-3-yltrimethylammonium iodides has been successfully investigated. These reactions have increased our fundamental understanding of reaction with quaternaryammonium systems. The preparation of 2-aryl-3-(2,2,2-trifluoroethoxy)-1-propenes was shown to proceed smoothly under mild conditions and in fair to good yields.

2-(4-Bromophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene was found to react smoothly with the following fluorinated alcohols: 2,2,2-trifluoroethanol; 2,2,3,3,3-pentafluoropropanol; 2,2,3,3,4,4,4-heptafluorobutanol; and 1,1,1-trifluoropropanol-2. These reactions gave relatively good yields thereby demonstrating the versatility of quaternaryammonium iodides reacting with various fluorinated nucleophiles.

Additionally, 2-(4-chlorophenyl)-3-(2,2,2-trifluoroethoxy)-1-propene was chosen to react with Lemieux/von Rudloff reagent, aqueous sodium periodate and potassium permanganate, and was oxidized to (4-chlorophenyl)-(2,2,2-trifluoroethoxymethyl) ketone. The yield of (4-chlorophenyl)-(2,2,2-trifluoroethoxy-methyl) ketone was optimized (Table III). The most favorable results were obtained using a molar ratio of 60:8 for the reagent, sodium periodate to potassium permanganate respectively, a reaction time of 72 h at r.t.
RECOMMENDATIONS

The following recommendations are suggested for further research involving 2-arylprop-1-en-3-yltrimethylammonium iodides and their corresponding fluoroalkoxy adducts.

1. Additional conditions should be investigated concerning the reactions of 2-arylprop-1-en-3-yltrimethylammonium iodide to produce the ketone adduct presented in this report. Complete optimization of the procedure conditions for the synthesis of the oxidation product is recommended before future studies of this system are conducted. Suggestions for optimization conditions studies may also include:
   a) further study of the effect of the molar ratio of the Lemieux/von Rudloff reagent, reaction time and temperature on the purified yield.
   b) the effect of pH on the rate of permanganate oxidation.
   c) Fatiadi\textsuperscript{38} reported the use of other solvents such as 1-4-dioxane and pyridine which give good results for reactions with water-insoluble alkenes.

2. Further reactions should be performed using the other fluoroalkoxy propenes reported in Tables I and II. to produce their ketone adducts.
3. Duranceau\textsuperscript{3} produced a variety of sulfonylhydroxyacetates from the corresponding arylallyl sulfides using excess sodium perborate and glacial acetic acid. It would be most interesting to examine the conversion of a variety of 2-aryl substituted fluoroalkoxy ethers to the corresponding hydroxyacetate.

4. It may prove interesting to react (4-chlorophenyl)-(2,2,2-trifluoroethoxymethyl) ketone with a variety of aldehydes in an aldol type condensation reaction.
REFERENCES


16. Lane, C. Aldrichimica Acta (1975), 8, 3.


