An Improved Procedure for the Synthesis of Perfluoroalkylacetylenes

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Abstract: A new and easy way to synthesize acetylene compounds is proposed. This synthesis is improved by including in one-pot, three reactions in a single step, with good yields. The reactants are commonly used compounds.

Key words: alkylation, radical reactions, fluorine

The preparation of perfluoroalkylacetylenes is of current interest due to their industrial applications as effective starting materials for the synthesis of valuable fluorinated molecules.1–11 In the early 1950’s, Haszeldine was among the first to describe the synthesis and characterization of a variety of fluorinated alkynes, corresponding to the general formula RF C≡CH.12 In the following twenty years, compounds containing perfluoroalkyl chains with one, two or three carbon atoms were of increasing interest.13–18 The extension to longer perfluoroalkyl chains appeared only in 1975 when De Pasquale et al.19 succeeded in implementing the reaction between a halogenated olefin and iodoperfluoroalkanes with up to eight carbon atoms. Still, the synthesis of such molecules is poorly described in the literature and procedures are multistep reactions involving low yields.20,21 Years later, Burton presented a synthesis of perfluoroalkylacetylenes using dechlorination of chlorofluoro compounds in the presence of zinc.22 In previous studies, our group presented an improved two-step procedure involving a free-radical initiator that was induced by either chemical or electrochemical reduction. These investigations resulted in higher yields as well as the opportunity to use a wider range of solvents.23,24 We report in this paper a novel single step perfluoroalkylation reaction using sodium hydroxide in its solid state. The addition of RFI (RF =CnF2n+1 with n = 4,6,8) to HC≡C–CR1R2OH (R1 = H, CH3; R2 = alkyl or aryl), in the presence of alkaline hydroxide, leads to the synthesis of RF C≡CH with elimination of the corresponding ketone. The reaction proceeds via the formation of RF C≡CCR1R2OH, which can be isolated. The main by-products of the reaction are RFRF and RFH (Scheme 1).

Based on the high quantity of superoxide ions that commercial alkaline hydroxides contain (used in previous work for the last elimination reaction step23,24), we assumed that they could be used as free-radical initiators. The successful reaction led to the formation of RF C≡CCR1R2OH (1a–c), followed by the elimination of the hydroxyalkyl moieties, to give RF C≡CH (2a–c) and the corresponding ketone. To our knowledge, this is the first example of a free-radical initiation using this type of base. In order to explain this result, we suggest that superoxide ions suspected to be present in the commercial bases could generate the radical according to the mechanism described (Scheme 2).

In order to determine the best reaction conditions, various parameters, including the nature of the alkaline hydroxide, the solvent and the reaction temperature were investigated in the case of the perfluorohexyl chain. All reactions were carried out in the presence of AIBN as it was previously observed that AIBN significantly improved the yields.25,26 The yields obtained for compounds 1b to 4b under different reaction conditions are presented in Table 1.

At a temperature of 10 °C, the best yields of perfluoroalkylacetylene were obtained with alkaline hydroxides in

Scheme 1 Single step synthesis of perfluoroalkylacetylenes
Table 1  Yields of Products According to the Different Reaction Parameters

<table>
<thead>
<tr>
<th>Entry No</th>
<th>Nature of R&lt;sup&gt;1&lt;/sup&gt; and R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Base</th>
<th>T (°C)</th>
<th>Solvent</th>
<th>% 1b</th>
<th>% 2b</th>
<th>% 3b</th>
<th>% 4b</th>
<th>% Other Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH pellets</td>
<td>10</td>
<td>–</td>
<td>11</td>
<td>31</td>
<td>5</td>
<td>53</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH pellets</td>
<td>10</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;OH</td>
<td>–</td>
<td>–</td>
<td>63</td>
<td>15</td>
<td>22 alkenes</td>
</tr>
<tr>
<td>3</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH pellets</td>
<td>10</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;</td>
<td>28</td>
<td>41</td>
<td>9</td>
<td>22</td>
<td>–</td>
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<tr>
<td>4</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH pellets</td>
<td>10</td>
<td>ClCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;Cl</td>
<td>23</td>
<td>47</td>
<td>10</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH beads</td>
<td>10</td>
<td>ClCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;Cl</td>
<td>23</td>
<td>47</td>
<td>10</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH powder</td>
<td>10</td>
<td>ClCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;Cl</td>
<td>Highly Exothermic Reaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>KOH pellets</td>
<td>10</td>
<td>ClCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;Cl</td>
<td>19</td>
<td>51</td>
<td>10</td>
<td>20</td>
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<tr>
<td>8</td>
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<td>KOH beads</td>
<td>10</td>
<td>ClCH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;Cl</td>
<td>22</td>
<td>48</td>
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<td>9</td>
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<td>KOH powder</td>
<td>10</td>
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<td>Highly Exothermic Reaction</td>
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</tr>
<tr>
<td>10</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH pellets</td>
<td>80</td>
<td>–</td>
<td>0</td>
<td>60</td>
<td>40</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH beads</td>
<td>80</td>
<td>–</td>
<td>0</td>
<td>95</td>
<td>5</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>12</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>NaOH powder</td>
<td>80</td>
<td>–</td>
<td>0</td>
<td>63</td>
<td>37</td>
<td>0</td>
<td>–</td>
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<td>NaOH beads</td>
<td>80</td>
<td>–</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100 R&lt;sub&gt;f&lt;/sub&gt;l</td>
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<tr>
<td>14</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H</td>
<td>NaOH beads</td>
<td>80</td>
<td>–</td>
<td>–</td>
<td>53</td>
<td>35</td>
<td>–</td>
<td>12 R&lt;sub&gt;f&lt;/sub&gt;l</td>
</tr>
<tr>
<td>15</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H</td>
<td>NaOH beads</td>
<td>80</td>
<td>–</td>
<td>–</td>
<td>34</td>
<td>23</td>
<td>–</td>
<td>43 R&lt;sub&gt;f&lt;/sub&gt;l</td>
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<td>NaOH beads</td>
<td>80</td>
<td>–</td>
<td>–</td>
<td>76</td>
<td>22</td>
<td>–</td>
<td>2 R&lt;sub&gt;f&lt;/sub&gt;l</td>
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</tbody>
</table>
pellets or beads in 1,2-dichloroethane (entries 4, 5, 7, 8). A better reactivity was observed when using potassium hydroxide (entries 7, 8) than sodium hydroxide, as already described by others in the synthesis of various perfluoroalkyl compounds. Under near conditions, the main product was RF C ≡ C H, as a result of a terminal coupling reaction between two perfluoroalkyl radicals (entry 1). Also, the use of a protic solvent such as methanol did not lead to the expected acetylenic products. Instead, RF H (3a–c) was obtained as the major product (entry 2). Powdered potassium or sodium hydroxide led to a highly exothermic reaction and the characterization of the final products was not possible (entries 6 and 9). Heating to a temperature of 80 °C, in order to thermodynamically activate the reaction, was also tried. Under near conditions, RF C ≡ C H and RF H were the only products observed (entries 10 to 12). RF C≡C(CH 3 ) 2 OH (1a–c), which was identified as a stable intermediate at 10 °C could not be isolated this time and the reaction went to completion. The best yields (95%) were obtained when sodium hydroxide beads were employed (entry 11). When potash was used in these same conditions, very violent reactions were observed along with the destruction of products and reactants.

The reaction was extended to a few analogues with different substituents on the acetylenic alcohol. As shown in entries 13–16, similar results were obtained. However the ratio between the formation of perfluoroalkylacetylene and that of perfluoralkane was not as good and reactions never went to completion. Also, no reaction was observed in the case of propargylic alcohol (entry 13). Several other bases were investigated such as Al 2 O 3 (beads), Ba(OH) 2 (powder) or Ba(OH) 2 ⋅ 8H 2 O (recrystallized), giving unsuccessful perfluoroalkylations. Attempts to extend the reaction to other alkyl or perfluoroalkylhalides according to the same procedure were performed but the reactions did not lead to the formation of the expected products. Thus, bromoperfluoroalkane didn’t react with 2-methylbut-3-yn-2-ol, which could be explained by the higher energy required to break a C–Br bond (bond energy: 276 kcalmol–1) compared to that of a C–I bond (bond energy: 217 kcalmol–1). Also, the lack of reaction between iodo-pentane and 2-methylbut-3-yn-2-ol suggests that hydrogenated compounds are not suitable for undergoing such radical addition.

Although this reaction didn’t reveal itself to be very flexible, it provides an efficient one-step procedure involving easy set-up, cheap and readily accessible reactants and high yields of perfluoroalkylacetylenes.

The 1 H NMR spectra and 19 F NMR spectra were recorded with a Bruker AC 250MHz spectrometer. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer.

Starting acetylenic derivatives were purchased from Aldrich®, and alkali bases from SDS®.

Reactions with Solvent; Typical Procedure

In a typical procedure, NaOH (12 g, 0.3 mol) and AIBN (0.05 g, 3 × 10–4 mol) were dissolved in CH 2 Cl 2 (20 mL) and introduced into an Erlenmeyer (250 mL) with a ground glass joint fitted with a pressurizer equalizing dropping funnel (250 mL) topped with a water condenser. To this dropping funnel was added CF 3 I (34.6 g), CF 3 Br (44.6 g) or CF 3 Cl (54.6 g, 0.1 mol) and 2-methyl-3-butyn-2-ol (8.41 g, 0.1 mol). The soln in the Erlenmeyer was stirred, cooled down with an ice bath and the mixture in the dropping funnel was added dropwise during 25 min. The ice bath was then removed and the reaction mixture was allowed to warm to r.t. The reaction was complete after 3 h. The reaction mixture was then filtered through a Büchner funnel, the filtrate was washed with H 2 O (3×100 mL), dried over anhyd Na 2 SO 4 and the solvent was evaporated. The resulting brownish oil was analyzed without further purification.

Reactions without Solvent; Typical Procedure

In a typical procedure, NaOH beads (12 g, 0.3 mol) and AIBN (0.05 g, 3 × 10–4 mol) were introduced into a Erlenmeyer (250 mL) with a ground glass joint fitted with a pressure equalizing dropping funnel (250 mL) topped with a water condenser. To the dropping funnel were added CF 3 I (34.6 g), CF 3 Br (44.6 g) or CF 3 Cl (54.6 g, 0.1 mol) and 2-methyl-3-butyn-2-ol (8.41 g, 0.1 mol). The solid mixture in the Erlenmeyer was stirred and heated to 80 °C and the soln in the dropping funnel was quickly added in order to maintain abundant reflux. After 15 min, the products were trapped in the dropping funnel by closing the stopcock. The lower layer, corresponding to the product, was washed with H 2 O (3 × 100 mL), dried over anhyd Na 2 SO 4 , providing pure perfluoroalkylacetylene as a colourless liquid.

IR and NMR spectroscopy were used to characterize the compounds by comparing the values with previously published data.

1a

Yield: 25%; bp 136 °C.
IR: 2256 (C≡C).
1 H NMR: δ = 1.6 (s, 6 H, CH 3 ), 4.8 (s, 1 H, OH).
19 F NMR: δ = –83.5 (s, 3 F, CF 3 ), –97.5 (s, 2 F, CF 2 –C≡C), –125.5, –127.4 (br s, 4 F, CF 2 ).

1b

Yield: 28%; bp 174 °C.
IR: 2256 (C≡C).
1 H NMR: δ = 1.6 (s, 6 H, CH 3 ), 4.8 (s, 1 H, OH).
19 F NMR: δ = –83.4 (s, 3 F, CF 3 ), –97.8 (s, 2 F, CF 2 –C≡C), –123.2, –127.6 (br s, 8 F, CF 3 ).

1c

Yield: 28%; bp 216 °C.
IR: 2256 (C≡C).
1 H NMR: δ = 1.6 (s, 6 H, CH 3 ), 4.8 (s, 1 H, OH).
19 F NMR: δ = –83.2 (s, 3 F, CF 3 ), –97.8 (s, 2 F, CF 2 –C≡C), –122.9, –123.8 (br s, 12 F, CF 3 ).

2a

Yield: 90%; bp 42 °C.
IR: 2131 (C≡C).
1 H NMR: δ = 2.9 (t, J = 5.9 Hz, 1 H, CH).
19 F NMR: δ = –99.5 (s, 2 F, CF 2 –C≡C), –125.5, –127.4 (s, 4 F, CF 2 ), –83.5 (s, 3 F, CF 3 ).

2b

Yield: 95%; bp 94 °C.
IR: 2131 (C≡C).
1 H NMR: δ = 2.9 (t, J = 5.9 Hz, 1 H, CH).
19F NMR: $\delta = -83.4$ (s, 3 F, CF$_3$), $-99.5$ (s, 2 F, CF$_2$-C≡), $-123.2$, $-127.6$ (br s, 8 F, CF$_2$).

2c Yield: 95%; bp 147 °C.

IR: 2131 (C≡).

1H NMR: $\delta = 2.9$ (t, $J = 5.1$ Hz, 1 H, CH).

19F NMR: $\delta = -83.2$ (s, 3 F, CF$_3$), $-99.5$ (s, 2 F, CF$_2$-C≡), $-122.9$, $-123.8$ (br s, 12 F, CF$_2$).

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References
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