Regio- and Stereoselective Addition of Perfluoroalkyl Iodides to Allenes Conjugated with Carbon–Oxygen or Phosphorus–Oxygen Double Bonds

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Abstract: In the presence of sodium dithionite, allenes conjugated with a carbon–oxygen or a phosphorus–oxygen double bond, such as allenic phosphonates, phosphine oxides and allenecarboxylates, reacted readily with perfluoroalkyl iodides at room temperature to give the corresponding addition products in moderate yields with complete regioselectivity and stereoselectivity. Perfluoroalkyl groups were introduced into the terminal position of allenes and addition products with the E-configuration were obtained selectively by the reaction.

Key words: perfluoroalkyl iodides, allenes, radical addition, stereoselectivity, regioselectivity

Recently, fluorine-containing compounds have drawn increasing interest owing to their unique properties and growing practical opportunities in crop protection, medicine, and diverse material applications. Accordingly, considerable effort has been devoted to the development of methodologies for the efficient and selective introduction of fluoroalkyl groups into organic molecules. Among various perfluoroalkylation methods, the addition of perfluoroalkyl halides to unsaturated carbon–carbon bonds is a practical and convenient route. The reaction usually takes place through a radical process and many effective initiating reagents have been developed. Although addition reactions of perfluoroalkyl halides to allenes or alkynes have been well-studied and widely used, the addition of perfluoroalkyl halides to allenes has been relatively less well investigated. As typical unsaturated hydrocarbons, allenes are important precursors in organic synthesis due to their high reactivity. Since there are three adjacent unsaturated carbons in the allene skeleton, the addition reaction of allenes may take place in different ways and different results may be obtained from their addition reaction depending on the structure of the allene, the radical source, and the reaction conditions.

Early studies in our laboratory showed that the reaction of perfluoroalkyl iodides and methoxyallene initiated by sodium dithionite, an effective initiator for perfluoroalkyl radical reactions, gave dimeric products with the ZZ-configuration (Scheme 1). In the reaction, the addition of the perfluoroalkyl radical occurred at the central carbon of the allene.

Scheme 1

Ogawa et al. reported that light could initiate the reaction of perfluoroalkyl iodides and allenes with alkyl substituents. The addition took place regioselectively at the less hindered terminal carbon of the allenes through a vinylic radical intermediate to give the corresponding perfluoroalkylated vinyl iodides as a Z/E mixture (Scheme 2).

Scheme 2

Very recently, the same reaction initiated by sodium dithionite was reported by Ma et al. and similar results were obtained. Obviously, the structure of allenes is very important for the addition pathway of allenes and perfluoroalkyl iodides. Although the addition reaction of perfluoroalkyl iodides and allenes with electron-donating groups such as alkyl and methoxy has been reported, similar reaction of allenes with electron-withdrawing substituents has been less well investigated. Due to its electrophilic nature, the addition of the perfluoroalkyl radical to an electron-deficient carbon–carbon unsaturated bond is generally more difficult compared to the addition to electron-rich carbon–carbon unsaturated bonds. To study the effects of substituents on the allene skeleton, the reaction of perfluoroalkyl iodides with various allenes initiated by sodium dithionite was recently investigated in our laboratory. It was found that some electron-deficient allenes conjugated with a carbon–oxygen or a phosphorus–oxygen double bond could react smoothly with perfluoroalkyl iodides to give the corresponding adducts regio- and stereoselectively (Scheme 3). The results are reported in this paper.

The reaction was carried out in aqueous acetonitrile. In the presence of sodium dithionite, allenes 1a–c reacted with perfluoroalkyl iodides readily at room temperature. NMR monitoring showed that only one isomer was
formed in the reaction. After workup compounds 3a–h were obtained in moderate yields. Spectral study and elemental analysis indicated that they were the corresponding 1:1 adducts of allenes and perfluoroalkyl iodides. Perfluoroalkyl groups were introduced into the terminal position of allenes regioselectively and adducts with the E-configuration were obtained stereoselectively. The structures of 3a–h were further proved by X-ray crystallography of 3a (Figure 1).7 The results are summarized in Table 1.

To make a comparison, the reaction of allenes 1d–f with alkyl or hydroxymethyl substituents was examined under similar conditions; the products 3i–k were all obtained as a Z/E mixture (Table 1, entries 9–11). This is consistent with the reported results.5,6

A possible mechanism is proposed for the reaction as shown in Scheme 4. The reaction of perfluoroalkyl iodides with the sulfur dioxide radical anion from the decomposition of sodium dithionite gives the R F radical. Addition of RF radical to the less hindered terminal carbon of allene affords radical intermediate M, which is stabilized by conjugation with the carbon–oxygen double bond. Subsequent abstraction of iodine from the perfluoroalkyl iodide results in the formation of 3 with the regeneration of the RF radical. The stereoselectivity may be rationalized by the stability of transition states in the reaction. Beckert et al.8 reported that the acrylate radical had a planar structure with all carbon atoms located in a plane. Comparing the two possible transition states, B is obviously disfavored due to steric effects and repulsion between the radical electron and the electron pair in oxygen. Therefore, only transition state A is involved in the reaction and adducts with E-configuration are obtained stereoselectively. In the case of an allene bearing an alkyl substituent, there is no obvious difference between the stabilities of the two transition states, hence the adducts are formed as a Z/E mixture.

In summary, the selective addition of perfluoroalkyl iodides to various allenes conjugated with a carbon–oxygen or a phosphorous–oxygen double bond has been achieved under mild conditions. Using sodium dithionite as initia-

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**Table 1 The Reaction of Allenes and Perfluoroalkyl Iodides**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Allene</th>
<th>R 1</th>
<th>R 2</th>
<th>R F</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Ratio E/Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>P(O)Ph2</td>
<td>2a</td>
<td>CF2CF2Cl</td>
<td>3a</td>
<td>63</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>P(O)Ph2</td>
<td>2b</td>
<td>(CF3)2CF2Cl</td>
<td>3b</td>
<td>68</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>P(O)Ph2</td>
<td>2c</td>
<td>(CF3)2CF</td>
<td>3c</td>
<td>49</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>P(O)Ph2</td>
<td>2d</td>
<td>(CF3)2CF</td>
<td>3d</td>
<td>40</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>5</td>
<td>1b</td>
<td>P(O)(OEt)2</td>
<td>2a</td>
<td>CF2CF2Cl</td>
<td>3e</td>
<td>62</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>6</td>
<td>1b</td>
<td>P(O)(OEt)2</td>
<td>2c</td>
<td>(CF3)2CF</td>
<td>3f</td>
<td>61</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>7</td>
<td>1c</td>
<td>COOEt</td>
<td>2b</td>
<td>(CF3)2CF2Cl</td>
<td>3g</td>
<td>69</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>8</td>
<td>1c</td>
<td>COOEt</td>
<td>2c</td>
<td>(CF3)2CF</td>
<td>3h</td>
<td>61</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>9</td>
<td>1d</td>
<td>Bu</td>
<td>2a</td>
<td>CF2CF2Cl</td>
<td>3i</td>
<td>78</td>
<td>34:66</td>
</tr>
<tr>
<td>10</td>
<td>1e</td>
<td>(CH3)3Me</td>
<td>2a</td>
<td>CF2CF2Cl</td>
<td>3j</td>
<td>82</td>
<td>31:69</td>
</tr>
<tr>
<td>11</td>
<td>1f</td>
<td>CH3OH</td>
<td>2b</td>
<td>(CF3)2CF2Cl</td>
<td>3k</td>
<td>82</td>
<td>46:54</td>
</tr>
</tbody>
</table>

* Isolated yield.
* Determined by NMR spectral analysis.
tor, the addition reaction took place at the terminal position of the allene to give stereoselectively the corresponding adducts with E-configuration, providing a convenient method for the synthesis of these special fluoro-containing compounds.

Melting points were measured with a Temp-Melt apparatus and were uncorrected. \(^1\)H and \(^13\)C NMR spectra were recorded in CDCl\(_3\) on Bruker AM-300 instruments with TMS as the internal standard. \(^19\)F NMR and \(^31\)P NMR spectra were recorded on the same spectrometer using CFCl\(_3\) and 85% H\(_2\)PO\(_4\) as external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. MS spectra were obtained on a Finnigen MAT-8430 instrument (EI, 70 eV). Elemental analyses were performed by this institute. All reactions, as well as column chromatography, were monitored routinely by TLC or \(^19\)F NMR spectroscopy. Start-

**Reactor of Perfluoroalkyl Iodide 2 with Allene 1; General Procedure**

To a mixture of allene \(1\) (2 mmol), perfluoroalkyl iodide \(2\) (3 mmol), H\(_2\)O (10 mL), and MeCN (10 mL) stirred magnetically at r.t., NaHCO\(_3\) (0.5 g, 6 mmol) was added. When the addition was complete, the mixture was stirred at r.t. until the reaction had finished (monitored by TLC). The mixture was poured into H\(_2\)O (20 mL) and extracted with EtO\(_2\) (3 × 20 mL). The combined organic layers were washed with sat. aq NaCl (3 × 20 mL), dried (anhyd Na\(_2\)SO\(_4\)), and evaporated in vacuo. The crude product was subjected to column chromatography to give 3. The results are given in Table 1.

**(E)-5-Chloro-4,4,5,5-tetrafluoro-2-iodopent-1-ene(diphenyl)phosphine Oxide (3a)**

Colorless oil.

IR (KBr): 3080, 3025, 2981, 2928, 1594, 1484, 1438, 1342, 1347, 1289, 1255, 1240, 1213, 1194, 1131, 1115 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 4.46\) (t, J = 16.8 Hz, 2 H), 7.27 (d, J = 20.1 Hz, 1 H), 7.25–7.58 (m, 6 H), 7.67–7.72 (m, 4 H).

\(^19\)F NMR (282 MHz, CDCl\(_3\)): \(\delta = –71.35\) (m, 2 F), –112.14 (m, 2 F).

\(^31\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 23.27\).

MS (EI, 70 eV): m/z (%) = 374 (M\(^+\) – HI, 51), 201 (100).


**(E)-4,4,5,5,6,6,7,7-Octafluoro-2-iodohept-1-ene(diphenyl)phosphine Oxide (3b)**

Mp 94–95 °C.

IR (KBr): 3075, 3014, 2986, 2928, 1594, 1482, 1438, 1247, 1289, 1255, 1240, 1213, 1194, 1131, 1115 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 4.47\) (t, J = 15.0 Hz, 2 H), 7.30 (d, J = 21.1 Hz, 1 H), 7.48–7.57 (m, 6 H), 7.68–7.72 (m, 4 H).

\(^19\)F NMR (282 MHz, CDCl\(_3\)): \(\delta = –67.91\) (t, J = 13.2 Hz, 2 F), –112.26 (m, 2 F), –119.83 (m, 2 F), –122.63 (m, 2 F).

\(^31\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 23.25\).

MS (EI, 70 eV): m/z (%) = 568 (2), 476 (23), 200 (100).

Anal. Calcd for C\(_{23}\)H\(_{13}\)F\(_{17}\)IOP: C, 35.14; H, 1.67. Found: C, 35.28; H, 1.60.

**(E)-4,4,5,5,6,6,7,7-Nonafluoro-2-iodohept-1-ene(diphenyl)phosphine Oxide (3e)**

Mp 99–100 °C.

IR (KBr): 3034, 3014, 2986, 2928, 1594, 1482, 1438, 1247, 1289, 1255, 1240, 1213, 1194, 1131, 1115 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 4.48\) (t, J = 17.4 Hz, 2 H), 7.29 (d, J = 22.2 Hz, 1 H), 7.46–7.60 (m, 6 H), 7.67–7.71 (m, 4 H).

\(^19\)F NMR (282 MHz, CDCl\(_3\)): \(\delta = –80.95\) (t, J = 9.02 Hz, 3 F), –112.43 (m, 2 F), –124.25 (m, 2 F), –125.89 (m, 2 F).

\(^31\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 23.28\).

MS (EI, 70 eV): m/z (%) = 461 (43), 200 (100).


Reaction of Perfluoroalkyl Iodide 2 with Allene 1; General Procedure

To a mixture of allene \(1\) (2 mmol), perfluoroalkyl iodide \(2\) (3 mmol), H\(_2\)O (10 mL), and MeCN (10 mL) stirred magnetically at r.t. was added portionwise a mixture of Na\(_2\)S\(_2\)O\(_4\) (0.5 g, 3 mmol) and sat. aq Na\(_2\)CO\(_3\) (0.5 g, 6 mmol). When the addition was complete, the mixture was stirred at r.t. until the reaction had finished (monitored by TLC). The mixture was poured into H\(_2\)O (20 mL) and extracted with EtO\(_2\) (3 × 20 mL). The combined organic layers were washed with sat. aq NaCl (3 × 20 mL), dried (anhyd Na\(_2\)SO\(_4\)), and evaporated in vacuo. The crude product was subjected to column chromatography to give 3. The results are given in Table 1.

**Scheme 4** Proposed mechanism for the reaction of ethyl allene carboxylate and perfluoroalkyl iodides
MS (EI, 70 eV): m/z (%) = 311 (M⁺ – I, 47), 109 (100).

Diethyl (E)-4,4,5,5,6,6,7,7,7,7,7,7,7,7,7,7-Nonafluoro-2-iodohept-1-ethylphosphonate (3f)
Colorless oil.
IR (KBr): 2959, 2930, 2859, 1635, 1460, 1424, 1380, 1255, 1205, 1154, 1094, 938 cm⁻¹.
¹H NMR (CDCl₃): δ (E-isomer) = 0.88–0.89 (m, 3 H), 1.26–1.53 (m, 8 H), 2.13–2.20 (m, 2 H), 3.38 (t, J = 16.8 Hz, 2 H), 6.61 (t, J = 2.7 Hz, 1 H); δ (Z-isomer) = 0.88–0.89 (m, 3 H), 1.26–1.53 (m, 8 H), 2.13–2.20 (m, 2 H), 3.38 (t, J = 16.8 Hz, 2 H), 5.82 (t, J = 6.6 Hz, 1 H).
¹³C NMR (75 MHz, CDCl₃): δ = 13.75, 13.89, 22.20, 22.71, 29.75, 30.97, 31.45, 36.75, 39.34 (t, Jₑₑₑₑ = 62.60 Hz), 45.25 (t, Jₑₑₑₑ = 62.04 Hz), 79.15, 87.06, 150.00, 150.25.
¹⁹F NMR (282 MHz, CDCl₃): δ (E-isomer) = –71.26 (m, 2 F), –112.61 (m, 2 F); δ (Z-isomer) = –70.74 (m, 2 F), –112.92 (m, 2 F).
MS (EI, 70 eV): m/z (%) = 358 (M⁺, 13), 302 (10), 55 (100).

Ethyl (E)-8-Chloro-5,5,6,6,7,7,8,8-octafluoro-3-iodo-2-enedioate (3g)
Colorless oil.
IR (KBr): 2986, 2940, 1602, 1394, 1240, 1199, 1169, 1135, 1053, 1026, 972 cm⁻¹.
¹H NMR (CDCl₃): δ = 1.33 (t, J = 7.5 Hz, 6 H), 4.08–4.26 (m, 6 H), 6.68 (d, J = 8.4 Hz, 1 H).
¹³P NMR (162 MHz, CDCl₃): δ = 10.89.
MS (EI, 70 eV): m/z (%) = 525 (8), 394 (52), 109 (100).

1-Chloro-1,1,2,2-tetrafluoro-4-iodonon-4-ene (3i)
Colorless oil.
IR (KBr): 2985, 2930, 2859, 1635, 1460, 1424, 1380, 1255, 1205, 1154, 1094, 938 cm⁻¹.
¹H NMR (CDCl₃): δ (E-isomer) = 1.26–1.53 (m, 8 H), 2.13–2.20 (m, 2 H), 3.38 (t, J = 16.8 Hz, 2 H), 6.61 (t, J = 2.7 Hz, 1 H); δ (Z-isomer) = 0.88–0.89 (m, 3 H), 1.26–1.53 (m, 8 H), 2.13–2.20 (m, 2 H), 3.38 (t, J = 16.8 Hz, 2 H), 5.82 (t, J = 6.6 Hz, 1 H).
¹³C NMR (75 MHz, CDCl₃): δ = 14.02, 14.10, 22.72, 22.73, 27.86, 28.05, 28.78, 28.92, 31.77, 31.97, 34.20, 37.04, 39.35 (t, Jₑₑₑₑₑₑₑₑₑₑ = 62.12 Hz), 45.23 (t, Jₑₑₑₑₑₑₑₑₑₑ = 60.77 Hz), 79.15, 87.06, 145.04, 150.29.
¹⁹F NMR (282 MHz, CDCl₃): δ (E-isomer) = –71.39 (m, 2 F), –113.05 (m, 2 F); δ (Z-isomer) = –70.91 (m, 2 F), –112.67 (m, 2 F).
MS (EI, 70 eV): m/z (%) = 386 (M⁺, 6), 302 (9), 69 (68), 41 (100).
HRMS: m/z [M⁺] calcd for C₁₀H₈ClI₂: 357.9608; found: 357.9604.

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References
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(7) The crystal structure of 3a has been deposited as supplementary publication No. CCDC-619205 at the Cambridge Crystallographic Data Centre. Copies of the data can be obtained free of charge on application to: CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk.
