

Novel Synthesis of Conjugated Bisperfluoroalkyl Enynes

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Conjugated bisperfluoroalkyl enynes can be conveniently synthesized in 85–99% yield by vacuum pyrolysis of $\{[\alpha\text{-(perfluoroalkyl)vinyl}](\text{perfluoroacyl})\text{methylene}\}$ triphenylphosphoranes which were generated from the corresponding methylene triphenylphosphoranes *via* double perfluoroacylation in a one-pot reaction.

Conjugated enynes which belong to an important class of natural products have attracted much attention because of their biological activity.¹ They are capable of undergoing many useful synthetic transformations and are utilized as essential components in the total synthesis of some natural products.² Fluorinated enynes can be synthesized by Pd-catalysed coupling of either fluorine-containing vinyl iodides with terminal alkynylzinc reagents, or 1-halogenoalkynes with fluorinated vinyl zinc reagents.³ Recently Burton reported a simple method for the preparation of fluorinated enynes by direct Pd-catalysed coupling of fluorinated vinyl iodides with alk-1-ynes in the presence of copper(I) iodide and triethylamine.⁴ However, to the best of our knowledge, no report has appeared in the literature concerning the preparation of perfluoroalkylated enynes except our previous communication.⁵ These compounds would be expected to be useful intermediates for the synthesis of fluorine-containing biologically active compounds. Therefore to develop an effective method for the synthesis of the title compounds would be valuable.

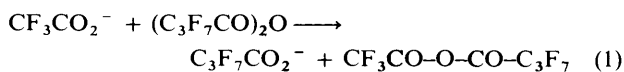
Results and Discussion

Recently we found that lithium acetylides could act as nucleophiles and attack fluorinated β -keto phosphonium salts, leading to the formation of perfluoroalkylated enynes.⁵ In an extension of this study, we now report a novel synthesis of conjugated bisperfluoroalkyl enynes by vacuum pyrolysis of $\{[\alpha\text{-(perfluoroalkyl)vinyl}](\text{perfluoroacyl})\text{methylene}\}$ triphenylphosphoranes which were generated from the corresponding parent methylenetriphenylphosphoranes *via* double perfluoroacylation in a one-pot reaction.

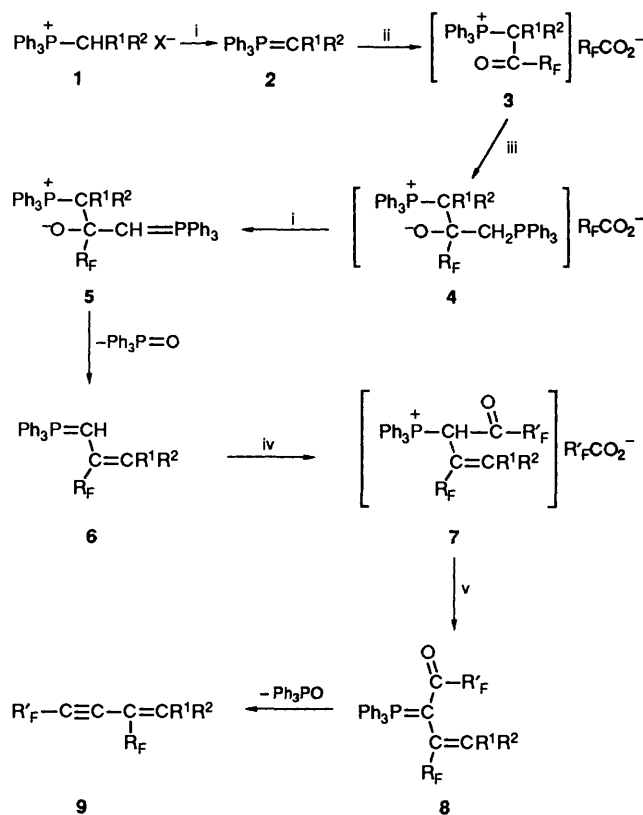
The reaction sequence is shown in Scheme 1.

The phosphoranes **2**, generated from the corresponding phosphonium salts **1** and phenyllithium, were acylated upon addition of perfluoroalkanoic anhydrides to give the fluorinated β -keto phosphonium salts **3**, which in the reaction medium were attacked by methylenetriphenylphosphorane to give the salts **4**. Deprotonation (to give zwitterions **5**) and elimination of triphenylphosphine oxide gave fluorinated phosphoranes **6**. Without isolation, fluorinated phosphoranes **6** in the reaction medium were acylated again by the addition of a perfluoroalkanoic anhydride to give salts **7**; subsequently deprotonation gave $\{[\alpha\text{-(perfluoroalkyl)vinyl}](\text{perfluoroacyl})\text{methylene}\}$ triphenylphosphoranes **8**, which were pyrolysed under diminished pressure (10 mmHg) to give conjugated bisperfluoroalkyl enynes **9** (Tables 1 and 2).

In the second perfluoroacylation of phosphoranes **6**, if R'_F is different from R_F , an anion exchange would take place to give a mixed perfluoroalkanoic anhydride **10** [eqn. (1)], which could



10



Scheme 1 Reagents: i, PhLi; ii, (R_FCO)₂O; iii, Ph₃P=CH₂; iv, (R'_FCO)₂O; v, 6

react with a second molecule of fluorinated phosphorane **6** to afford a mixture of phosphoranes [e.g., eqn. (2)]. Therefore, in case **h**, compound **8h** was obtained in 30% yield, together with compound **8d** (30%).

Experimental

All m.p.s and b.p.s are uncorrected. IR spectra of all products were obtained on a Perkin-Elmer 683 spectrometer. ¹H NMR and ¹⁹F NMR spectra were recorded on a Varian EM-360 (60 MHz) of Varian XL-200 (200 MHz) spectrometer with SiMe₄ and CF₃CO₂H (positive for upfield shifts) as external reference, respectively. *J*-Values are given in Hz. Mass spectra were measured on a GC-MS-4021 spectrometer.

General Procedure.—*Preparation of compounds 8.* A solution of phenyllithium (7.0 mmol) in Et₂O (15 cm³) was added dropwise to a stirred suspension of the phosphonium salt **1** (7.0 mmol) in absolute tetrahydrofuran (THF) (40 cm³) at -20 °C under nitrogen. The mixture was stirred for 30 min at -20 °C and was then cooled to -78 °C, and the perfluoroalkanoic

Table 1 Preparation of fluorinated phosphoranes **8**

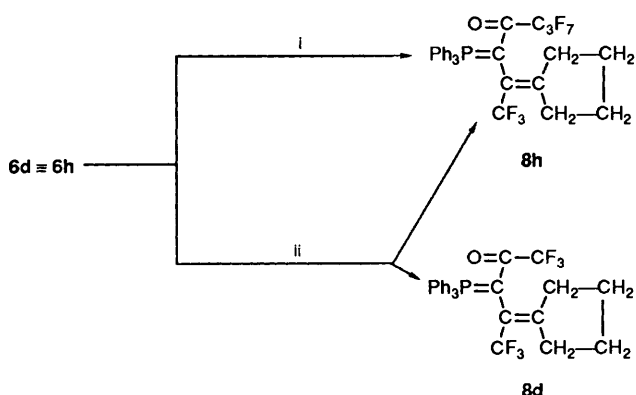
Compound	R ¹	R ²	R _F	R _F '	Yield (%) ^a
8a	Me	Me	CF ₃	CF ₃	44
8b	Me	Me	C ₂ F ₅	C ₂ F ₅	52
8c	Me	Me	C ₃ F ₇	C ₃ F ₇	48
8d	-[CH ₂] ₄ -		CF ₃	CF ₃	50
8e	-[CH ₂] ₄ -		C ₂ F ₅	C ₂ F ₅	52
8f	-[CH ₂] ₄ -		C ₃ F ₇	C ₃ F ₇	58
8g	-[CH ₂] ₅ -		CF ₃	CF ₃	42
8h	-[CH ₂] ₄ -		CF ₃	C ₃ F ₇	30 ^b

^a Isolated yields. All compounds were characterized by microanalyses, and IR, NMR and mass spectroscopy. ^b Accompanied by a 30% yield of compound **8d**.

Table 2 Preparation of bisperfluoroalkyl enynes **9**

Compound	R ¹	R ²	R _F	R _F '	Yield (%) ^a
9a	Me	Me	CF ₃	CF ₃	94
9b	Me	Me	C ₂ F ₅	C ₂ F ₅	94
9c	Me	Me	C ₃ F ₇	C ₃ F ₇	90
9d	-[CH ₂] ₄ -		CF ₃	CF ₃	99
9e	-[CH ₂] ₄ -		C ₂ F ₅	C ₂ F ₅	85
9f	-[CH ₂] ₄ -		C ₃ F ₇	C ₃ F ₇	86
9g	-[CH ₂] ₅ -		CF ₃	CF ₃	96
9h	-[CH ₂] ₄ -		CF ₃	C ₃ F ₇	90

^a Isolated yields. All compounds were characterized by microanalyses, and IR, NMR and mass spectroscopy.



Reagents: i, (C₃F₇CO)₂O; ii, C₃F₇CO-O-COCF₃

anhydride (6.7 mmol) was slowly added until the characteristic brown ylidic colour had disappeared. The mixture was then stirred at -78 °C for 30 min and a solution of methyl-triphenylphosphorane [generated from methyltriphenylphosphonium bromide (7 mmol) and phenyllithium (7 mmol) in Et₂O (30 cm³) at 25 °C for 30 min] was added. After addition of phenyllithium (6.7 mmol) to the mixture at -78 °C the mixture was stirred at -78 °C for 1 h, and then at 25 °C for 2 h. Then another portion of perfluoroalkanoic anhydride (4.0 mmol) was added at 25 °C and the mixture was stirred for a further 2 h. Filtration, and evaporation of the filtrate, gave a residue, which was purified by column chromatography on silica gel with light petroleum (b.p. 60–90 °C)-ethyl acetate (7:3) as eluent to give the product **8**. The calculation of the yield of product **8** is based on the molar ratio in Scheme 1. Because 1 mol of (R_FCO)₂O needs to react with 2 mol of the phosphorene **6**, the theoretical yield of product **8** is 3.35 mmol from 6.7 mmol of reactant **6**. For example; in the case of compound **8a**, 1.48 mmol was obtained (44%); in case of compound **8b**, 1.74 mmol was obtained (52%).

Preparation of compounds 9. A phosphorane **8** (0.5 mmol) was pyrolysed in a distillation vessel at 250–260 °C/10 mmHg.

The pyrolysate was collected in a solid CO₂-ethanol trap. Redistillation afforded the corresponding pure product **9**.

The following products **8** and **9** were thus obtained.

3-Methyl-1-trifluoroacetyl-2-trifluoromethylbut-2-en-1-ylidene(triphenyl)phosphorane 8a was obtained in 44% yield; m.p. 132–134 °C; δ_H(CDCl₃) 7.10–7.80 (15 H, m) and 1.50–2.20 (6 H, m); δ_F(CDCl₃) -21.9 (3 F, s) and -5.7 (3 F, s); ν_{max}/cm⁻¹ 1680s, 1585s and 1570s; m/z 494 (M⁺, 74%), 479 (M⁺ - CH₃, 100), 425 (M⁺ - CF₃, 24) and 262 (PPh₃, 34) (Found: C, 63.75; H, 4.35. C₂₆H₂₁F₆OP requires C, 63.16; H, 4.28%).

3-Methyl-2-pentafluoroethyl-1-pentafluoropropionylbut-2-en-1-ylidene(triphenyl)phosphorane 8b was obtained in 52% yield; m.p. 166–167 °C; δ_H(CDCl₃) 7.10–8.10 (15 H, m), 1.96 (3 H, q, J 4.0) and 1.70 (3 H, q, J 4.0); δ_F(CDCl₃) 4.6 (3 F, s), 5.0–6.5 (3 F, m), 31.0–31.4 (2 F, m) and 39.7–41.3 (2 F, m); ν_{max}/cm⁻¹ 1577s and 1545s; m/z 594 (M⁺, 16%), 579 (M⁺ - CH₃, 46), 475 (M⁺ - C₂F₅, 17) and 262 (PPh₃, 100) (Found: C, 56.7; H, 3.4. C₂₈H₂₁F₁₀OP requires C, 56.59; H, 3.53%).

1-Heptafluorobutyl-2-heptafluoropropyl-3-methylbut-2-en-1-ylidene(triphenyl)phosphorane 8c was obtained in 48% yield; m.p. 168–169 °C; δ_H(CDCl₃) 7.16–7.80 (15 H, m) and 1.56–2.09 (6 H, m); δ_F(CDCl₃) 1.3–3.6 (6 F, m), 21.3–23.1 (2 F, m), 36.0–37.4 (2 F, m) and 35.8–36.7 (4 F, m); ν_{max}/cm⁻¹ 1624s, 1576s and 1543s; m/z 694 (M⁺, 14%), 679 (M⁺ - CH₃, 12) and 262 (PPh₃, 100) (Found: C, 52.3; H, 2.9. C₃₀H₂₁F₁₄OP requires C, 51.70; H, 3.02%).

2-Cyclopentylidene-1-trifluoroacetyl-2-trifluoromethylethylidene(triphenyl)phosphorane 8d was obtained in 50% yield; m.p. 216–218 °C; δ_H(CDCl₃) 6.87–8.17 (15 H, m) and 1.07–2.67 (8 H, m); δ_F(CDCl₃) -17.5 (3 F, s) and -5.8 (3 F, s); ν_{max}/cm⁻¹ 1644s, 1577s and 1561s; m/z 520 (M⁺, 18%), 491 (M⁺ - F, 37), 451 (M⁺ - CF₃, 19) and 262 (PPh₃, 77) (Found: C, 65.0; H, 4.4. C₂₈H₂₃F₆OP requires C, 64.64; H, 4.42%).

2-Cyclopentylidene-2-pentafluoroethyl-1-pentafluoropropionylethylidene(triphenyl)phosphorane 8e was obtained in 52% yield; m.p. 206–207 °C; δ_H(CDCl₃) 6.80–8.17 (15 H, m) and 1.17–2.60 (8 H, m); δ_F(CDCl₃) 3.0 (3 F, s), 5.2 (3 F, s), 28.6–30.4 (2 F, m) and 39.2–40.4 (2 F, m); ν_{max}/cm⁻¹ 1640s and 1560s; m/z 619 (M⁺ - 1, 15%), 591 (M⁺ - F, 12) and 262 (PPh₃, 100) (Found: C, 57.8; H, 3.5. C₃₀H₂₃F₁₀OP requires C, 58.08; H, 3.71%).

2-Cyclopentylidene-1-heptafluoropropionyl-2-heptafluoropropylethylidene(triphenyl)phosphorane 8f was obtained in 58% yield; m.p. 182–183 °C; δ_H(CDCl₃) 7.10–8.52 (15 H, m) and 1.10–2.80 (8 H, m); δ_F(CDCl₃) 2.7 (6 F, t, J 10), 24.0–26.0 (2 F, m), 35.6–37.4 (2 F, m), 45.0–46.0 (2 F, m) and 47.0–48.0 (2 F, m); ν_{max}/cm⁻¹ 1627s, 1575s and 1549s; m/z 719 (M⁺ - 1, 72%), 690 (M⁺ - F - 1, 66), 550 (M⁺ - CF₃ - 1, 53) and 262 (PPh₃, 100) (Found: C, 52.9; H, 3.0. C₃₂H₂₃F₁₄OP requires C, 53.33; H, 3.19%).

2-Cyclohexylidene-1-trifluoroacetyl-2-trifluoromethylethylidene(triphenyl)phosphorane 8g was obtained in 42% yield; m.p. 185–187 °C; δ_H(CDCl₃) 7.20–7.90 (15 H, m), 1.90–2.60 (4 H, m) and 1.30–1.60 (6 H, m); δ_F(CDCl₃) -22.5 (3 F, s) and -5.5 (3 F, s); ν_{max}/cm⁻¹ 1622s and 1560s; m/z 534 (M⁺, 8%), 465 (M⁺ - CF₃, 10) and 262 (PPh₃, 100) (Found: C, 65.0; H, 4.8. C₂₉H₂₅F₆OP requires C, 65.23; H, 4.68%).

2-Cyclopentylidene-1-heptafluorobutyl-2-trifluoroacetyl-ethylidene(triphenyl)phosphorane 8h was obtained in 30% yield; m.p. 178–180 °C; δ_H(CDCl₃) 7.15–7.86 (15 H, m) and 1.21–2.76 (8 H, m); δ_F(CDCl₃) -17.0 (3 F, s), 2.01 (3 F, t, J 10), 36.2–38.0 (2 F, m) and 47.3 (2 F, s); ν_{max}/cm⁻¹ 1640s and 1560s; m/z 620 (M⁺, 33%), 601 (M⁺ - F, 11), 451 (M⁺ - CF₃, 89) and 262 (PPh₃, 100) (Found: C, 58.1; H, 3.6. C₃₀H₂₃F₁₀OP requires C, 58.08; H, 3.71%).

6,6,6-Trifluoro-2-methyl-3-trifluoromethylhex-2-en-4-yne 9a was obtained in 94% yield; b.p. 132 °C; δ_H(CDCl₃) 1.98–2.10 (6

H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ -22.0 (3 F, s) and -19.0 (3 F, s); $\nu_{\text{max}}/\text{cm}^{-1}$ 2250w and 1630s; m/z 216 (M^+ , 10%), 197 ($\text{M}^+ - \text{F}$, 14), 147 ($\text{M}^+ - \text{CF}_3$, 7) and 43 (C_3H_7 , 100) (Found: C, 44.8; H, 3.0. $\text{C}_8\text{H}_6\text{F}_6$ requires C, 44.26; H, 2.80%).

6,6,7,7,7-Pentafluoro-2-methyl-3-pentafluoroethylhept-2-en-4-yne **9b** was obtained in 94% yield; b.p. 135 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.86–2.06 (6 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ 9.0 (3 F, s), 10.0 (3 F, t, *J* 10), 26.5 (2 F, s) and 33.7 (2 F, s); $\nu_{\text{max}}/\text{cm}^{-1}$ 2242w and 1623s; m/z 316 (M^+ , 12%), 297 ($\text{M}^+ - \text{F}$, 14), 247 ($\text{M}^+ - \text{CF}_3$, 34) and 43 (C_3H_7 , 100) (Found: C, 37.8; H, 1.85. $\text{C}_{10}\text{H}_6\text{F}_{10}$ requires C, 38.00; H, 1.90%).

6,6,7,7,8,8,8-Heptafluoro-3-heptafluoropropyl-2-methyloct-2-en-4-yne **9c** was obtained in 90% yield; b.p. 152 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.00–2.23 (6 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ 5.2 (3 F, t, *J* 10), 5.5 (3 F, t, *J* 10), 23.0–24.0 (2 F, m) 29.3–30.3 (2 F, m), 50.5 (2 F, s) and 51.2 (2 F, t, *J* 10); $\nu_{\text{max}}/\text{cm}^{-1}$ 2241w and 1621s; m/z 416 (M^+ , 4%), 397 ($\text{M}^+ - \text{F}$, 8) and 43 (C_3H_7 , 57) (Found: C, 34.2; H, 1.3. $\text{C}_{12}\text{H}_6\text{F}_{14}$ requires C, 34.64; H, 1.44%).

4-Cyclopentylidene-1,1,1,5,5,5-hexafluoropent-2-yne **9d** was obtained in 99% yield; b.p. 132 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.35–2.91 (4 H, m) and 1.60–2.05 (4 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ -25.4 (3 F, s) and -14.8 (3 F, s); $\nu_{\text{max}}/\text{cm}^{-1}$ 2242w and 1635s; m/z 242 (M^+ , 15%), 223 ($\text{M}^+ - \text{F}$, 49), 173 ($\text{M}^+ - \text{CF}_3$, 79) and 67 (C_5H_7 , 100) (Found: C, 49.3; H, 3.35. $\text{C}_{10}\text{H}_8\text{F}_6$ requires C, 49.61; H, 3.30%).

5-Cyclopentylidene-1,1,1,2,2,6,6,7,7,7-decafluorohept-3-yne **9e** was obtained in 85% yield; b.p. 165 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.37–2.90 (4 H, m) and 1.53–2.03 (4 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ 8.9 (3 F, s), 9.9 (3 F, s), 26.2 (2 F, s) and 35.8 (2 F, s); $\nu_{\text{max}}/\text{cm}^{-1}$ 2240w and 1626s; m/z 342 (M^+ , 2%), 273 ($\text{M}^+ - \text{CF}_3$, 7) and 67 (C_5H_7 , 47) (Found: C, 42.4; H, 2.4. $\text{C}_{12}\text{H}_8\text{F}_{10}$ requires C, 42.13; H, 2.34%).

6-Cyclopentylidene-1,1,1,2,2,3,3,7,7,8,8,9,9,9-tetradecafluoronon-4-yne **9f** was obtained in 86% yield; b.p. 190 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.34–2.97 (4 H, m) and 1.47–2.04 (4 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ 3.1 (3 F, t, *J* 10), 3.3 (3 F, t, *J* 10), 21.0–22.1 (2 F, m), 35.0–36.2 (2 F, m), 49.1 (2 F, s) and 49.3 (2 F, t, *J* 10); $\nu_{\text{max}}/\text{cm}^{-1}$ 2240w and 1624s;

m/z 441 ($\text{M}^+ - 1$, 11%), 273 ($\text{M}^+ - \text{C}_3\text{F}_7$, 7) and 67 (C_5H_7 , 80) (Found: C, 38.4; H, 1.7. $\text{C}_{14}\text{H}_8\text{F}_{14}$ requires C, 38.03; H, 1.81%).

4-Cyclohexylidene-1,1,1,5,5,5-hexafluoropent-2-yne **9g** was obtained in 96% yield; b.p. 126 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.30–2.75 (4 H, m) and 1.51–1.97 (6 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ -27.4 (3 F, s) and -20.9 (3 F, s); $\nu_{\text{max}}/\text{cm}^{-1}$ 2245w and 1618s; m/z 256 (M^+ , 4%), 237 ($\text{M}^+ - \text{F}$, 19) and 187 ($\text{M}^+ - \text{CF}_3$, 20) (Found: C, 51.6; H, 3.5. $\text{C}_{11}\text{H}_{10}\text{F}_6$ requires C, 51.56; H, 3.91%).

2-Cyclopentylidene-1,1,1,5,5,6,6,7,7,7-decafluorohept-3-yne **9h** was obtained in 90% yield; b.p. 108 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.14–2.74 (4 H, m) and 1.34–1.98 (4 H, m); $\delta_{\text{F}}(\text{CDCl}_3)$ -14.3 (3 F, s), 5.0 (3 F, t, *J* 10), 22.7–23.7 (2 F, m) and 51.0 (2 F, t, *J* 10); $\nu_{\text{max}}/\text{cm}^{-1}$ 2240w and 1636s; m/z 342 (M^+ , 80%), 322 ($\text{M}^+ - \text{F} - 1$, 91) and 67 (C_5H_7 , 27) (Found: C, 41.6; H, 2.2. $\text{C}_{12}\text{H}_8\text{F}_{10}$ requires C, 42.12; H, 2.34%).

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