Synthesis of Pentafluorophenyl or Chlorotetrafluorophenyl Allenes†

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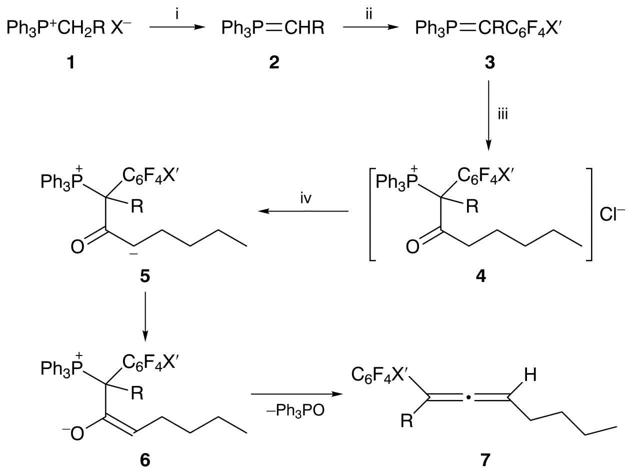
The sequential reaction of phosphonium salt **1** with *n*-butyllithium, hexafluorobenzene or chloropentafluorobenzene, hexanoyl chloride and triethylamine affords pentalfuorophenyl or chlorotetrafluorophenyl allenes in 82–95% yields.

Allenes have attracted much attention as they are potentially useful intermediates in a variety of synthetic transformations and as components of various natural products.[1] More interesting is that they have emerged as reactive intermediates in the radical cyclization of the antitumor natural product neocarzinostatin and related compounds.[2] A variety of methods have been reported for their preparation[1a,b,3] involving the rearrangement of bonds in an existing three-carbon skeleton. In addition, the introduction of a pentafluorophenyl group into biologically active compounds often leads to unique physiological activities, and organofluorine compounds are increasingly being applied in pharmaceuticals, agrochemicals and other fields.[4] Pentafluorophenyl alkenes are also useful intermediates for the synthesis of fluorine-containing organic compounds.[5] Therefore, it is of interest to develop an effective method for the preparation of the title compounds since they would be expected to be useful intermediates for the synthesis of fluorine-containing biologically active compounds.

In previous papers[6] the sequential reaction of phosphonium or arsonium salts has been applied to the synthesis of pentafluorophenylated 1,3-dienes. As an extension of this study, we report that the sequential reaction of phosphonium salts can be applied to the synthesis of pentafluorophenyl or chlorotetafluorophenyl allenes. The reaction sequence is shown in Scheme 1.

Phosphoranes **2**, generated from the corresponding phosphonium salts **1** and butyllithium in tetrahydrofuran (THF), were allowed to react with hexafluorobenzene or chloropentafluorobenzene to phosphoranes **3**, which, in the reaction medium, were treated with hexanoyl chloride to give the phosphonium salts **4**. Deprotonation of the latter by base (triethylamine) gave **5** which was converted into **6** *via* electron transfer. Triphenylphosphine oxide was then eliminated spontaneously to give the product **7**. The results are summarized in Table 1. All compounds are new and have been characterized by microanalyses, IR, NMR and mass spectroscopy.



Scheme 1 *Reagents and conditions*: i, Bu^nLi, THF, –20 to 0 °C; ii, C_6F_5X' (X′ = F, Cl), 0–20 °C; iii, hexanoyl chloride, 0 °C; iv, triethylamine

Table 1 Preparation of substituted fluorinated 1,2-dienes

Entry	R	X′	Yield (%)[a]
7a	H	F	93
7b	CH_3	F	94
7c	C_2H_5	F	86
7d	n-C_3H_7	F	92
7e	n-C_4H_9	F	86
7f	n-C_5H_{11}	F	82
7g	H	Cl[b]	95
7h	CH_3	Cl[b]	92

[a]Isolated yields. [b]At *para* position.

Table 2 The effect of base on the yield of **7a**

Entry	Base (equiv.)	**7a** (%)[a]
1	Et_3N	93
2	$Bu^n{}_3N$	85
3	DBU[b]	40
4	Pyridine	37
5	NaH	Trace
6	K_2CO_3	Trace

[a]Isolated yields. [b]DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

The effect of base has been investigated in more detail with **4a** as reactant. The results are summarized in Table 2.

The reaction proceeds best with triethylamine as a base while the yield of the reaction was poor when NaH or K_2CO_3 was used as a base.

Thus, this one-pot synthesis is very convenient for the synthesis of the title compounds with good to excellent yields starting from commercially available substances.

Experimental

All boiling points are uncorrected. The IR spectra of products were obtained as films on a Perkin-Elmer 983 spectrometer. ^1H NMR spectra were recorded on a Bruker AM-300 (300 MHz) spectrometer (δ values in ppm from tetramethylsilane, in $CDCl_3$, J values are given in Hz). ^{19}F NMR spectra were taken on a Varian EM-360 960 MHz) spectrometer (δ in ppm from external trifluoroacetic acid, in $CDCl_3$, positive for upfield shifts). Mass spectra were measured on a Finnigan GC-MS-4021 mass spectrometer. All allenes are racemic.

General Procedure for the Synthesis of Pentafluorophenyl or Chlorotetrafluorophenyl Allenes 7.—Butyllithium (4 mmol in 2 ml of hexane) was added dropwise with stirring to a suspension of triphenylphosphonium salt (4 mmol) in absolute THF (10 ml) at –20 °C under nitrogen. The reaction mixture was stirred for 30 min at –20 to 0 °C and hexafluorobenzene or chloropentafluorobenzene (2 mmol) was slowly added. The mixture was allowed to warm to 20 °C, stirred for 1 h and recooled to 0 °C. Hexanoyl chloride (0.27 g, 2 mmol) and then triethylamine (0.2 g, 2 mmol) were slowly added. After these additions, the mixture was stirred at 20 °C for

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3 h. and then water (20 ml) was added. The reaction mixture was extracted with diethyl ether (3 × 25 ml). The combined organic layer was washed with brine (30 ml) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue which was purified by flash chromatography on silica gel eluting with light petroleum (bp 60–90 °C) to give the product **7**.

1-Pentafluorophenylhepta-1,2-diene **7a**. Bp: 90 °C at 2 mmHg. ν_{max}/cm^{-1}: 2960, 2860, 1950, 1640; δ_H 0.95 (t, 3H, *J* 7.1), 1.31–1.51 (m, 4H), 2.10–2.17 (m, 2H), 5.60 (dt, 1H, *J* 6.8, 6.8), 6.10–6.15 (m, 1H); δ_F 66.0 (m, 2F), 81.0 (m, 1F), 86.5 (m, 2F); *m/z* 220 ($M^+ + 1 - C_3H_7$, 79%), 181 (29), 151 (38), 57 (100), 43 (57) (Found: C, 59.31; H, 4.10. $C_{13}H_{11}F_5$ requires C, 59.55; H, 4.23%).

2-Pentafluorophenylocta-2,3-diene **7b**. Bp: 98 °C at 2 mmHg. ν_{max}/cm^{-1}: 2970, 2940, 1960, 1640; δ_H 0.85 (t, 3H, *J* 7.1), 1.18–1.37 (m, 4H), 1.94–2.20 (m, 2H), 1.95 (d, 3H, *J* 2.6), 5.19–5.25 (m, 1H); δ_F 65.0 (m, 2F), 81.0 (m, 1F), 86.5 (m, 2F); *m/z* 234 ($M^+ + 1 - C_3H_7$, 19%), 220 (17), 219 (100), 181 (44), 169 (22) (Found: C, 60.81; H, 4.74. $C_{14}H_{13}F_5$ requires C, 60.87; H, 4.74%).

3-Pentafluorophenylnona-3,4-diene **7c**. Bp: 110 °C at 2 mmHg. ν_{max}/cm^{-1}: 2970, 1960, 1650; δ_H 0.90 (t, 3H, *J* 7.1), 1.05 (t, 3H, *J* 7.4), 1.25–1.47 (m, 4H), 2.10 (q, 2H, *J* 7.2), 2.25–2.33 (m, 2H), 5.35–5.42 (m, 1H); δ_F 64.0 (m, 2F), 80.0 (m, 1F), 86.0 (m, 2F); *m/z* 248 ($M^+ + 1 - C_3H_7$, 11%), 233 (27), 220 (11), 219 (100), 181 (38). (Found: C, 62.51; H, 5.51. $C_{15}H_{15}F_5$ requires C, 62.07; H, 5.21%).

4-Pentafluorophenyldeca-4,5-diene **7d**. Bp: 120 °C at 2 mmHg. ν_{max}/cm^{-1}: 2961, 2940, 1960, 1650; δ_H 0.94 (t, 3H, *J* 7.2), 0.95 (t, 3H, *J* 7.2), 1.25–1.48 (m, 6H), 2.05 (q, 2H, *J* 6.9), 2.24–2.30 (m, 2H), 5.31–5.37 (m, 1H); δ_F 65.0 (m, 2F), 80.0 (m, 1F), 85.0 (m, 2F); *m/z* 262 ($M^+ + 1 - C_3H_7$, 41%), 233 (43), 219 (100), 181 (73), 57 (23) (Found: C, 63.18; H, 5.57. $C_{16}H_{17}F_5$ requires C, 63.16; H, 5.63 %).

5-Pentafluorophenylundeca-5,6-diene **7e**. Bp: 90 °C at 2 mmHg. ν_{max}/cm^{-1}: 2960, 2930, 1960, 1650; δ_H 0.90 (t, 6H, *J* 7.2), 1.27–1.44 (m, 8H), 2.10 (q, 2H, *J* 7.0), 2.25–2.29 (m, 2H), 5.30–5.37 (m, 1H); δ_F 64.5 (m, 2F), 81.0 (m, 1F), 86.5 (m, 2F); *m/z* 276 ($M^+ + 1 - C_3H_7$, 29%), 261 (29), 233 (72), 220 (50), 219 (100), 181 (71) (Found: C, 64.20; H, 6.07. $C_{17}H_{19}F_5$ requires C, 64.14; H, 6.02%).

6-Pentafluorophenylodeca-6,7-diene **7f**. Bp: 140 °C at 2 mmHg. ν_{max}/cm^{-1}: 2930, 1960, 1650; δ_H 0.86–0.94 (m, 6H), 1.29–1.46 (m, 10H), 2.06 (q, 2H, *J* 7.1), 2.25–2.30 (m, 2H), 5.30–5.37 (m, 1H); δ_F 64.5 (m, 2F), 81.0 (m, 1F), 86.5 (m, 2F); *m/z* 290 ($M^+ + 1 - C_3H_7$, 21%), 276 (71), 275 (51), 261 (67), 247 (59), 219 (100), 233 (99) (Found: C, 65.06; H, 6.39. $C_{18}H_{21}F_5$ requires C, 65.06; H, 6.37%).

1-Chlorotetrafluorophenylhepta-1,2-diene **7g**. Bp: 120 °C at 2 mmHg. ν_{max}/cm^{-1} 2960, 2930, 1950, 1630; δ_H 0.90 (t, 3H, *J* 7.1), 1.31–1.51 (m, 4H), 2.10–2.18 (m, 2H), 5.51–5.62 (m, 1H), 6.13–6.20 (m, 1H); δ_F 65.0 (s, 4F); *m/z* 249 ($M^+ - C_2H_5$, 12%), 236 (60), 221 (19), 216 (42), 201 (100) (Found: C, 55.86; H, 3.85. $C_{13}H_{11}ClF_4$ requires C, 56.03; H, 3.98%).

2-Chlorotetrafluorophenylocta-2,3-diene **7h**. Bp: 125 °C at 2 mmHg. ν_{max}/cm^{-1}; 2960, 2930, 1960, 1630; δ_H 0.90 (t, 3H, *J* 7.3), 1.30–1.47 (m, 4H), 2.01–2.10 (m, 2H), 5.27–5.35 (m, 1H); δ_F 63.0–64.0 (m, 2F), 64.6–65.6 (m, 2F); *m/z* 250 ($M^+ + 1 - C_3H_7$, 24%), 237 (40), 235 (100), 215 (25), 200 (63), 197 (42) (Found: C, 57.61; H, 4.46. $C_{14}H_{13}ClF_4$ requires C, 57.45; H, 4.48%).

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