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One-pot synthesis of 1-pentafluorophenyl-1,3-dienes

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Abstract

Perfluorobenzene was added to allylidenetriphenylphosphorane regiospecifically, after transylidation, to give (3-pentafluorophenyl)allylidenetriphenylphosphorane, which reacted with aldehydes to afford 1-pentafluorophenyl-1,3-dienes in good to excellent yield.

Introduction

It has been shown that the introduction of pentafluorophenyl groups into biologically active compounds often brings about unique physiological activities [1]. Pentafluorophenyl alkenes are used as important intermediates for the synthesis of fluorine-containing organic compounds [2]. However, there have been only a few reports on their synthesis [2a] and the synthesis of pentafluorophenyl-1,3-dienes has not been reported previously. Hence, an effective method for their preparation would be valuable. We now wish to report a one-pot synthesis of the title compounds in good to excellent yield.

Results and discussion

The reaction sequence is as follows:

$$(C_6H_5)_3\overset{+}{P}{-}CH_2{-}CH{=}CH_2Br^- \xrightarrow{\text{n-BuLi}}$$

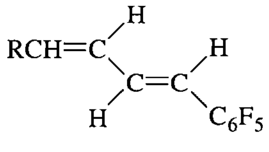
1

$$(C_6H_5)_3\overset{+}{P}{-}\overset{-}{C}H{-}CH{=}CH_2 \xrightarrow{C_6F_6}$$

2

$$(C_6H_5)_3\overset{+}{P}{-}\overset{-}{C}H{-}CH{=}CHC_6F_5 \xrightarrow{\text{RCHO}}$$

3

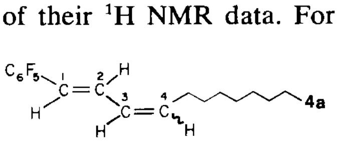


4

4a: R=n-C_6H_{13}
4b: R=4-$CH_3C_6H_4$
4c: R=2,4-$Cl_2C_6H_3$
4d: R=4-ClC_6H_4
4e: R=4-FC_6H_4
4f: R=4-$CH_3OC_6H_4$
4g: R=4-$NO_2C_6H_4$

We found recently that allylidenetriphenylphosphoranes can react regiospecifically with Me_3SiCl [3] and CF_3COOEt [4] at the 3-position. As an extension of this study, we found that **2** generated from the corresponding phosphonium salt and n-butyllithium reacted with hexafluorobenzene, also at the 3-position regiospecifically, after transylidation to give (3-pentafluorophenyl)allylidenetriphenylphosphorane (**3**), which reacted with aldehydes to afford 1-pentafluorophenyl-1,3-dienes in 87%–94% yield. The results are summarized in Table 1.

All products are new and were characterized by IR and NMR spectroscopy, and by mass spectrometry. The configuration of products **4** was ascertained on the basis of their ^1H NMR data. For example:



	H-2^a	H-4	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$^{a}
1*E*,3*E*	7.10 (dd)	5.69 (dt)	16.1	10.0	15.0	6.6
1*E*,3*Z*	7.35 (dd)	5.94 (dt)	16.1	10.0	10.0	6.6

^{a}Chemical shifts in ppm; coupling constants in Hz.

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TABLE 1. 1-Pentafluorophenyl-1,3-dienes prepared

Compound	Reaction time (h)	Yield[a] (%)	1*E*,3*E* 1*E*,3*Z*[b]
4a	6	90	78:22
4b	6	87	78:22
4c	4	93	79:21
4d	6	91	87:13
4e	6	90	86:14
4f	8	92	93:7
4g	6	94	100:0

[a] Isolated yield.
[b] Estimated on the basis of NMR spectra.

The coupling constants ($J_{1,2}=16.1$; $J_{3,4}=15.0$, 10.0 Hz) confirm that the double bond at the 1-position in **4** is exclusively in the *E* configuration and that that at the 3-position is in the *E* and *Z* configurations. The ^{19}F NMR spectra showed that the chemical shift of *o*-Ar−F in the 1*E*,3*E* isomer is upfield (64.7–66.3 ppm) and that of *o*-Ar−F in 1*E*,3*Z* isomer is downfield (60.3–61.3 ppm).

Experimental

All melting points and boiling point are reported uncorrected. IR spectra of solid products were obtained as KCl disks and of liquid products as films on a Shimadzu IR-440 spectrometer. NMR spectra (chemical shifts in ppm from TMS for ^{1}H NMR and from external TFA for ^{19}F NMR, positive for upfield shifts) were obtained on a Varian EM-360 (60 MHz) or XL-200 (200 MHz) spectrometer. Coupling constants are given in Hz. Mass spectra were measured on a Finnigan GC–MS 4021 spectrometer.

General procedure for the preparation of 1-pentafluorophenyl-1,3-dienes 4

n-Butyllithium (2 mmol) was added dropwise to a stirred suspension of allyltriphenylphosphonium bromide (2 mmol) and THF (10 ml) at −78 °C under nitrogen. After stirring at 0 °C for 0.5 h, ylide **2** was formed. Without isolation, hexafluorobenzene (1 mmol) was added slowly and the reaction mixture stirred at 20 °C for 2 h to form ylide **3**. Aldehydes were added and the mixture stirred at 20 °C for several hours (see Table 1). Diethyl ether (30 ml) was then added and the organic layer washed with water and dried. Evaporation of the solvent gave a residue which was purified by chromatography on silica gel eluting with petroleum ether (60–90 °C) and recrystallized from ethanol or distilled to afford product **4**.

1-Pentafluorophenyl-1,3-decadiene (**4a**): Yield 90%, b.p. 99 °C/1 Torr. Analysis: Calc. for $C_{16}H_{17}F_3$ (304.3): C, 63.15; H, 5.64%. Found: C, 63.40; H, 5.94%. MS *m/z* (rel. int.): 304 (M^+, 57); 233 ($M^+-C_5H_{11}$, 40). IR(film) (cm^{-1}): 1650; 1500; 1000; 960. ^{1}H NMR ($CDCl_3$/TMS) δ: 0.90 (t, 3H, $J=6.0$ Hz, CH_3); 1.20–1.30 (m, 8H, $-(CH_2)_4-$); 2.08–2.32 (m, 2H, H-5); 5.60–6.42 (m, 2H, H-1, H-3); 5.69 (dt, 0.78H, $J=15.0$, 6.6 Hz, 1*E*,3*E*-H-4); 5.94 (dt, 0.22H, $J=10.0$, 6.6 Hz, 1*E*,3*Z*-H-4); 7.10 (dd, 0.78H, $J=16.1$, 10.0 Hz, 1*E*,3*E*-H-2); 7.35 (dd, 0.22H, $J=16.1$, 10.0 Hz, 1*E*,3*Z*-H-2) ppm. ^{19}F NMR($CDCl_3$/TFA) δ: 60.3–61.3 (m, 0.44F, 1*E*,3*Z*-*o*-Ar−F); 64.7–66.3 (m, 1.56F, 1*E*,3*E*-*o*-Ar−F); 78.3–80.3 (m, 1F); 84.0–86.3 (m, 2F) ppm.

1-Pentafluorophenyl-4-(4-methylphenyl)-1,3-butadiene (**4b**): Yield 87%, m.p. 125–132 °C. Analysis: Calc. for $C_{17}H_{11}F_5$ (310.3): C, 65.81; H, 3.57%. Found: C, 66.17; H, 3.59%. MS *m/z* (rel. int.): 310 (M^+, 100); 295 (M^+-CH_3, 95). IR(KCl) (cm^{-1}): 1595; 1520; 995; 950. ^{1}H NMR ($CDCl_3$/TMS) δ: 2.33 (s, 3H, CH_3); 6.34 (d, 1H, $J=16$ Hz, H-1); 6.53–7.40 (m, 7H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 61.3–62.3 (m, 0.44F, 1*E*,3*Z*-*o*-Ar−F); 64.3–66.6 (m, 1.56F, 1*E*,3*E*-*o*-Ar−F); 78.3–79.6 (m, 1F); 84.0–85.6 (m, 2F) ppm.

1-Pentafluorophenyl-4-(2,4-dichlorophenyl)-1,3-butadiene (**4c**): Yield 93%, m.p. 155–156 °C. Analysis: Calc. for $C_{16}H_7Cl_2F_5$ (365.1): C, 52.63; H, 1.93%. Found: C, 52.68; H, 1.81%. MS *m/z* (rel. int.): 364 (m^+, 68); 329 (M^+-Cl, 68); 294 (M^+-Cl_2, 100). IR(KCl) (cm^{-1}): 1570; 1500; 990; 950. ^{1}H NMR ($CDCl_3$/TMS) δ: 6.56 (d, 1H, $J=16.0$ Hz, H-1); 6.75–7.65 (m, 6H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 60.3–62.0 (m, 0.42F, 1*E*,3*Z*-*o*-Ar−F); 64.3–65.0 (m, 1.58F, 1*E*,3*E*-*o*-Ar−F); 77.0–78.5 (m, 1F); 84.0–85.0 (m, 2F) ppm.

1-Pentafluorophenyl-4-(4-chlorophenyl)-1,3-butadiene (**4d**): Yield 91%, m.p. 125–129 °C. Analysis: Calc. for $C_{16}H_8ClF_5$ (330.7): C, 58.12; H, 2.44%. Found: C, 58.30; H, 2.37%. MS *m/z* (rel. int.): 320 (M^+, 60); 295 (M^+-Cl, 100). IR(KCl) (cm^{-1}): 1600, 1520, 985, 960. ^{1}H NMR ($CDCl_3$/TFA) δ: 6.39 (d, 1H, $J=16.0$ Hz, H-1); 6.54–7.50 (m, 7H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 61.0–62.0 (m, 0.26F, 1*E*,3*Z*-*o*-Ar−F); 64.0–66.3 (m, 1.74F, 1*E*,3*E*-*o*-Ar−F); 76.0–78.0 (m, 1F); 83.0–86.0 (m, 2F) ppm.

1-Pentafluorophenyl-4-(4-fluorophenyl)-1,3-butadiene (**4e**): Yield 90%, m.p. 132–134 °C. Analysis: Calc. for $C_{16}H_8F_6$ (314.2): C, 61.53; H, 2.78%. Found: C, 61.12; H, 2.57%. MS *m/z* (rel. int.): 314 (M^+, 80); 294 (M^+-HF, 8). IR(KCl) (cm^{-1}): 1600, 1520, 1000, 960. ^{1}H NMR ($CDCl_3$/TMS) δ: 6.60–7.60 (m, 8H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 34.0 (m, 1F, C_6H_4F); 60.1–62.0 (m, 0.28F, 1*E*,3*Z*-*o*-Ar−F); 65.0–66.0 (m, 1.72F, 1*E*,3*E*-*o*-Ar−F); 78.0–79.0 (m, 1F); 84.0–85.5 (m, 2F) ppm.

1-Pentafluorophenyl-4-(4-methoxyphenyl)-1,3-butadiene (**4f**): Yield 92%, m.p. 126–128 °C. Analysis: Calc. for $C_{17}H_{11}F_5O$ (326.3): C, 62.58; H, 3.40%. Found: C, 62.24; H, 3.21%. MS *m/z* (rel. int.): 326 (M^+, 100); 295 ($M^+ - OCH_3$, 15); 159 ($M^+ - C_6F_5$, 34). IR (KCl) (cm^{-1}): 1600; 1510; 990; 960. ^1H NMR ($CDCl_3$/TMS) δ: 3.80 (s, 3H, OCH_3); 6.49 (d, 1H, $J = 16.0$ Hz, H-1); 6.71–7.63 (m, 7H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 61.0–62.9 (m, 0.14F, 1*E*,3*Z*-*o*-Ar−F); 65.6–67.0 (m, 1.86F, 1*E*,3*E*-*o*-Ar−F); 79.6–80.0 (m, 1F); 84.0–86.3 (m, 2F) ppm.

1-Pentafluorophenyl-4-(4-nitrophenyl)-1,3-butadiene (**4g**): Yield 94%, m.p. 156–157 °C. Analysis: Calc. for $C_{16}H_8F_5NO_2$ (341.2): C, 56.32; H, 2.36; N, 4.10%. Found: C, 56.52; H, 2.23; N, 4.32%. MS *m/z* (rel. int.): 341 (M^+, 86); 294 ($M^+ - HNO_2$, 57); 127 ($M^+ - HNO_2 - C_6F_5$, 100). IR (KCl) (cm^{-1}): 1600; 1520; 1000; 965. ^1H NMR ($CDCl_3$/TMS) δ: 6.51 (1H, d, $J = 16.0$ Hz); 6.70–7.60 (m, 7H, ArH, vinyl H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 64.0–65.0 (m, 2F); 77.0 (m, 1F); 84.0–85.0 (m, 2F) ppm.

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