

Highly stereoselective synthesis of substituted 1-pentafluorophenyl-1,3-dienes via arsonium ylides

Yanchang Shen ^{*}, Tielin Wang

Shanghai Institute of Organic Chemistry, Academia Sinica, 354 Fenglin Lu, Shanghai 200032, People's Republic of China

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Abstract

The highly stereoselective synthesis of substituted 1-pentafluorophenyl-1,3-butadienes via arsonium ylides in good to excellent yields is described. © 1997 Elsevier Science S.A. All rights reserved.

Keywords: Highly stereoselective synthesis; (3-Pentafluorophenyl)allylidetriphenylarsorane; (3-Pentafluorophenyl)allylidetriphenylphosphorane; Substituted 1-pentafluorophenyl-1,3-dienes

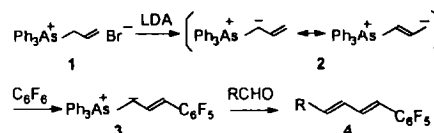
1. Introduction

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 [1]. Pentafluorophenyl alkenes are also useful intermediates for the synthesis of fluorine-containing organic compounds [2]. Recently, we reported that perfluorobenzene adds to allylidetriphenylphosphorane regioselectively, after transylation, to give (3-pentafluorophenyl)allylidetriphenylphosphorane, which reacts with aldehydes to afford 1-pentafluorophenyl-1,3-dienes [3]. However, in most cases, a mixture of 1E,3E and 1E,3Z isomers is obtained [3]. Furthermore, the phosphoranes react with ketones with low yields.

2. Results and discussion

As an extension of this study, we report a highly stereoselective synthesis of substituted 1-pentafluorophenyl-1,3-dienes via an arsonium ylide. The reaction sequence is shown in Scheme 1.

Allylidetriphenylarsorane **2**, generated from the corresponding arsonium salt and lithium diisopropylamide (LDA), reacts with hexafluorobenzene regioselectively at the 3-position, after transylation, to afford (3-pentafluorophenyl)allylidetriphenylarsorane **3**, which reacts with aldehydes to give substituted 1-pentafluorophenyl-1,3-dienes



Scheme 1.

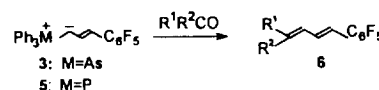
Table 1
The reaction of ylide **3** with aldehydes

Compound	R	Reaction time ^a (h)	Yield ^b (%)	1E,3E : 1E,3Z ^c
4a	C ₆ H ₅	2	96	100 : 0
4b	4-NO ₂ C ₆ H ₄	2	94	100 : 0
4c	4-ClC ₆ H ₄	2	91	100 : 0
4d	2,4-Cl ₂ C ₆ H ₃	1	93	100 : 0
4e	4-CH ₃ C ₆ H ₄	2	88	100 : 0
4f	4-CH ₃ OC ₆ H ₄	2	80	100 : 0
4g	<i>n</i> -C ₆ H ₁₃	3	92	100 : 0

^a Time of the reaction of **3** with aldehydes.

^b Isolated yields.

^c The 1E,3E stereoselectivity was ascertained on the basis of ¹⁹F NMR data.



Scheme 2.

with 1E,3E selectivity in 80%–96% yield. The results are summarized in Table 1.

Similarly, arsoranes **3** react with ketones highly stereoselectively with a longer reaction time (Scheme 2). The results are summarized in Table 2.

^{*} Corresponding author.

Table 2
The reaction of ylide **3** or **5** with ketones

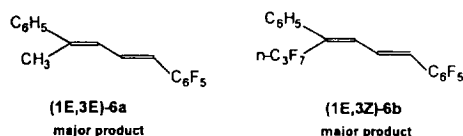
Compound	R ¹	R ²	Reaction time (h)	Method ^a	Yield ^b (%)	1E,3E : 1E,3Z ^c
6a	C ₆ H ₅	CH ₃	48	A	73	100 : 0
6a	C ₆ H ₅	CH ₃	48	B	29	63 : 37
6b	C ₆ H ₅	<i>n</i> -C ₃ F ₇	8	A	87	7 : 93 ^d
6b	C ₆ H ₅	<i>n</i> -C ₃ F ₇	36	B	59	30 : 70 ^d

^a Method A: arsorane **3** was used as reagent. Method B: phosphorane **5** was used as reagent.

^b Isolated yields.

^c The ratios of 1E,3E and 1E,3Z isomers were estimated on the basis of ¹⁹F NMR data.

^d According to the sequence rules, if the pentafluoropropyl group replaces the methyl group, the 3E isomer in **6a** becomes the 3Z isomer in **6b**. Therefore, in the case of **6b**, the 3Z isomer is the major product. For example:



The configuration of the products **4** and **6** was ascertained by comparison of the chemical shift of *o*-Ar-F with the data reported in the literature [3].

It is noteworthy that, as expected, arsoranones are more reactive than the corresponding phosphoranones [4], and good yields and high stereoselectivity are obtained.

3. Experimental details

All melting points (m.p.) and boiling points (b.p.) are uncorrected. The IR spectra of the solid products were obtained as KCl discs and the IR spectra of the liquid products were obtained as films on a Shimadzu IR-440 spectrometer. Nuclear magnetic resonance (NMR) spectra (chemical shifts in parts per million from tetramethylsilane (TMS) for ¹H NMR and from external trifluoro acetic acid (TFA) for ¹⁹F NMR, positive for upfield shifts) were obtained on Varian EM-360 (60 MHz) and XL-200 (200 MHz) spectrometers. Coupling constants are given in hertz. Mass spectra (MS) were measured on a Finnigan GC-MS 4021 spectrometer.

3.1. General procedure for the preparation of substituted 1-pentafluorophenyl-1,3-dienes **4** and **6**

Method A. LDA, generated from diisopropylamine (2 mmol), dry tetrahydrofuran (THF) (10 cm³) and *n*-butyllithium (2 mmol) at 0 °C, was added dropwise to a stirred suspension of allyltriphenylarsonium bromide (2 mmol) and THF (10 cm³) at -78 °C under nitrogen. After stirring at -78 to -20 °C for 0.5 h and at -20 °C for 0.5 h, ylide **2** was formed. Without isolation, hexafluorobenzene (1 mmol) was added slowly and the reaction mixture was stirred at -20 °C for 1 h and at 20 °C for 0.5 h to form ylide **3**. Carbonyl compounds (1 mmol) were added and the mixture was stirred at 20 °C for several hours (see Table 1). Diethyl ether (30 cm³) was then added and the organic layer was 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**.

Method B. A procedure similar to method A was used, but *n*-butyllithium was employed instead of LDA.

3.1.1. 1-Pentafluorophenyl-4-phenyl-1,3-butadiene (**4a**)

Yield, 96%; m.p., 141–142 °C (140–142 °C [5]). ¹H NMR (CDCl₃/TMS) δ: 6.20–6.95 (m, 4H), 7.10–7.50 (m, 5H). ¹⁹F NMR (CDCl₃/TFA) δ: 64.2–66.0 (m, 2F), 77.0–79.0 (m, 1F), 83.3–86.0 (m, 2F). MS *m/z* (relative intensity): 296 (M⁺, 100), 297 (21), 295 (17).

3.1.2. 1-Pentafluorophenyl-4-(4-nitrophenyl)-1,3-butadiene (**4b**)

Yield, 94%; m.p., 156–157 °C (156–157 °C [3]). IR (KCl) (cm⁻¹): 1600, 1520, 1000, 965. ¹H NMR (CDCl₃/TMS) δ: 6.51 (d, 1H, *J* = 16.0), 6.70–7.60 (m, 7H, ArH, vinyl H). ¹⁹F NMR (CDCl₃/TFA) δ: 64.0–65.0 (m, 2F), 77.0 (m, 1F), 84.0–85.0 (m, 2F).

3.1.3. 1-Pentafluorophenyl-4-(4-chlorophenyl)-1,3-butadiene (**4c**)

Yield, 91%; m.p., 133–134 °C (125–129 °C (1E,3E : 1E,3Z = 87 : 13) [3]). IR (KCl) (cm⁻¹): 1600, 1520, 1000, 965. ¹H NMR (CDCl₃/TMS) δ: 6.39 (d, 1H, *J* = 16.0), 6.54–7.25 (m, 7H, ArH, vinyl H). ¹⁹F NMR (CDCl₃/TFA) δ: 64.0–66.3 (m, 2F), 76.0–78.0 (m, 1F), 83.0–86.0 (m, 2F).

3.1.4. 1-Pentafluorophenyl-4-(2,4-dichlorophenyl)-1,3-butadiene (**4d**)

Yield, 93%; m.p., 162–163 °C (155–156 °C (1E,3E : 1E,3Z = 79 : 21) [3]). IR (KCl) (cm⁻¹): 1590, 1460, 995, 950. ¹H NMR (CDCl₃/TMS) δ: 6.56 (d, 1H, *J* = 16.0), 6.75–7.65 (m, 6H, ArH, vinyl H). ¹⁹F NMR

(CDCl₃/TFA) δ : 64.3–65.0 (m, 2F), 77.0–78.5 (m, 1F), 84.0–85.0 (m, 2F).

3.1.5. 1-Pentafluorophenyl-4-(4-methylphenyl)-1,3-butadiene (4e)

Yield, 88%; m.p., 152–153 °C (125–132 °C (1E,3E : 1E,3Z = 78 : 22) [3]). IR (KCl) (cm⁻¹): 1600, 1480, 1000, 960. ¹H NMR (CDCl₃/TMS) δ : 2.27 (s, 3H, CH₃), 6.36 (d, 1H, *J* = 16.0), 6.53–7.35 (m, 7H, ArH, vinyl H). ¹⁹F NMR (CDCl₃/TFA) δ : 64.3–66.6 (m, 2F), 78.3–79.6 (m, 1F), 84.5–85.6 (m, 2F).

3.1.6. 1-Pentafluorophenyl-4-(4-methoxyphenyl)-1,3-butadiene (4f)

Yield, 80%; m.p., 146–147 °C (126–128 °C (1E,3E : 1E,3Z = 93 : 7) [3]). IR (KCl) (cm⁻¹): 1570, 1460, 995, 950. ¹H NMR (CDCl₃/TMS) δ : 3.80 (s, 3H, OCH₃), 6.49 (d, 1H, *J* = 16.0), 6.71–7.63 (m, 7H, ArH, vinyl H). ¹⁹F NMR (CDCl₃/TFA) δ : 65.6–67.0 (m, 2F), 79.6–80.6 (m, 1F), 84.0–86.3 (m, 2F).

3.1.7. 1-Pentafluorophenyl-1,3-decadiene (4g)

Yield, 92%; b.p., 110 °C/1 Torr (99 °C/1 Torr (1E,3E : 1E,3Z = 78 : 22) [3]). IR (film) (cm⁻¹): 1640, 1500, 1000, 980. ¹H NMR (CDCl₃/TMS) δ : 5.40–7.47 (m, 4H), 2.08–2.32 (m, 2H), 1.20–1.30 (m, 8H), 0.85 (t, 3H, *J* = 6.0). ¹⁹F NMR (CDCl₃/TFA) δ : 64.0–66.3 (m, 2F), 78.3–80.3 (m, 1F), 84.0–86.3 (m, 2F).

3.1.8. 1-Pentafluorophenyl-4-phenyl-1,3-pentadiene (6a)

Method A. Yield, 73%; m.p., 155–156 °C. IR (KCl) (cm⁻¹): 1490, 1480, 998, 955. ¹H NMR (CDCl₃/TMS) δ : 7.00–7.65 (m, 6H), 6.10–6.65 (m, 2H), 2.30 (s, 3H). ¹⁹F NMR (CDCl₃/TFA) δ : 65.1–66.9 (m, 2F), 9.5–80.5 (m, 1F), 85.3–87.9 (m, 2F).

Method B. Yield, 29%; m.p., 144–145 °C. IR (KCl) (cm⁻¹): 1500, 1480, 990, 965. ¹H NMR (CDCl₃/TMS) δ : 7.00–7.70 (m, 6H), 6.30–6.80 (m, 2H), 2.30 (s, 3H). ¹⁹F NMR (CDCl₃/TFA) δ : 65.1–61.8–64.5 (m, 0.37 × 2F, 1E,3Z), 65.0–67.0 (m, 0.63 × 2F, 1E,3E), 76.6–81.0 (m, 1F), 83.6–87.3 (m, 2F). Analysis: calculated for C₁₇H₁₁F₅

(310.3): C, 65.81%; H, 3.57%; found: C, 65.94%; H, 3.82%. MS *m/z* (relative intensity): 310 (M⁺, 25), 295 (100), 275 (20), 129 (42).

3.1.9. 1-Pentafluorophenyl-5,5,6,6,7,7,7-heptafluoro-1,3-heptadiene (6b)

Method A. Yield, 87%; m.p., 58–59 °C. IR (KCl) (cm⁻¹): 1505, 1490, 999, 950. ¹H NMR (CDCl₃/TMS) δ : 6.90–7.35 (m, 6H), 6.35–6.75 (m, 2H). ¹⁹F NMR (CDCl₃/TFA) δ : 3.5–4.5 (m, 3F), 24.7 (s, 0.07 × 2F, 1E,3E), 28.5 (s, 0.93 × 2F, 1E,3Z), 47.4–48.6 (m, 2F), 63.8–64.1 (m, 0.07 × 2F, 1E,3E), 64.2–64.9 (m, 0.93 × 2F, 1E,3Z), 75.6–76.9 (m, 1F), 85.9–86.9 (m, 2F).

Method B. Yield, 59%; b.p., 112 °C/0.5 Torr. IR (film) (cm⁻¹): 1505, 1490, 999, 950. ¹H NMR (CDCl₃/TMS) δ : 6.90–7.35 (m, 6H), 6.35–6.75 (m, 2H). ¹⁹F NMR (CDCl₃/TFA) δ : 3.5–4.5 (m, 3F), 24.7 (s, 0.30 × 2F, 1E,3E), 28.5 (s, 0.70 × 2F, 1E,3Z), 47.4–48.6 (m, 2F), 63.8–64.1 (m, 0.3 × 2F, 1E,3E), 64.2–64.9 (m, 0.7 × 2F, 1E,3Z), 75.6–76.9 (m, 1F), 85.6–86.9 (m, 2F). Analysis: calculated for C₁₉H₈F₁₂ (464.3): C, 49.16%; H, 1.74%; found: C, 49.15%; H, 1.67%. MS *m/z* (relative intensity): 465 (M⁺ + 1, 23), 295 (100), 275 (27).

Acknowledgements

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