

A facile synthesis of dimethyl 4-(α -furyl)- and 4-(α -thienyl)-6-perfluoroalkylisophthalates via acyclic precursors¹

Weiguo Cao*, Weiyu Ding, Wenli Ding, Hui Huang

Department of Chemistry, Shanghai University, Shanghai 201800, China

Received 5 July 1996; revised 12 November 1996; accepted 26 November 1996

Abstract

In the presence of K_2CO_3 , reaction of methyl propynoate **2** with (α -furoyl)methyltriphenylphosphonium bromide **1a** or (α -thienacyl)methyltriphenylphosphonium bromide **1b** gave methyl 4-(α -furoyl)-2-(triphenylphosphoranylidene)but-3-enoate **4a** or methyl 4-(α -thienacyl)-2-(triphenylphosphoranylidene)but-3-enoate **4b** as the major product. Phosphorane **4a** or **4b** could react further with methyl perfluoroalkynoates **5a–b** to afford dimethyl 2-(α -furoyl-1-perfluoroalkylvinyl)-4-(triphenylphosphoranylidene)pent-2-enedioates **7a–b** or dimethyl 2-(α -thienacyl-1-perfluoroalkylvinyl)-4-(triphenylphosphoranylidene)pent-2-enedioates **7c–d**, respectively. Dimethyl 4-(α -furyl)-6-perfluoroalkylisophthalates **8a–b** or dimethyl 4-(α -thienyl)-6-perfluoroalkylisophthalates **8c–d** were prepared in high yields via intramolecular Wittig reaction of phosphoranes **7a–d** under heating in a sealed tube in xylenes. The structures of these compounds were confirmed by IR spectroscopy, mass spectrometry, 1H , ^{19}F and ^{13}C NMR spectra, and elemental analyses. Reaction mechanisms of the formation of compounds **4**, **6**, **7** and **8** were also proposed. © Elsevier Science S.A.

Keywords: Phosphoranes; Acyclic precursors; Intramolecular Wittig reaction; Dimethyl 4-(α -furyl)-perfluoroalkylisophthalates; 4-(α -Thienyl)-6-perfluoroalkylisophthalates

1. Introduction

Polysubstituted arenes have been synthesized traditionally through substitution of aromatic ring compounds. However, this method suffered from long synthetic routes and the presence of complicated positional isomers. The fluorinated analogues are more attractive as a result of their lipophilicity and the increment of activity [1,2]. Therefore, to study the convenient and efficient syntheses of polysubstituted arenes is valuable in organic synthetic methodology. Recently, we had designed a simple approach to the synthesis of fluorinated polysubstituted arenes through a nucleophilic addition of a phosphorane to an electrodeficient alkyne to produce a new phosphoric ylide which possesses a conjugated six-carbon main chain with a terminal carbonyl group. Under heating, this acyclic precursor gives rise to a polysubstituted arene via an intramolecular elimination of Ph_3PO . Several types of tri- or tetrasubstituted benzoates were synthesized via this method [3–8]. It is a preferable method owing to its simplic-

ity and the production of a sole product with definite positional functional groups.

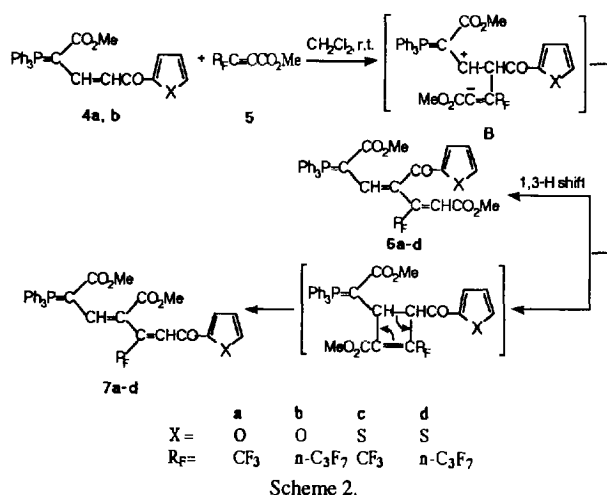
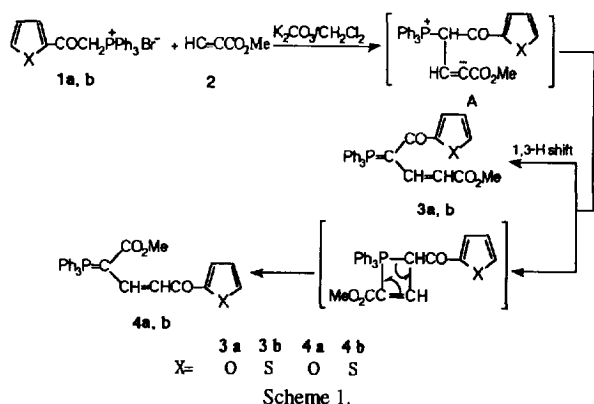
As a continuation of this study, a simple synthesis of tetrasubstituted benzenes—dimethyl 4-(α -furyl)-6-perfluoroalkylisophthalates **8a–b** and dimethyl 4-(α -thienyl)-6-perfluoroalkylisophthalates **8c–d**—will be reported in this paper.

2. Results and discussion

The reaction of (α -furoyl)methyltriphenylphosphonium bromide **1a** or (α -thienacyl)methyltriphenylphosphonium bromide **1b** with methyl propynoate **2** in the presence of K_2CO_3 in CH_2Cl_2 at room temperature afforded a mixture of compounds **3a**, **4a** or **3b**, **4b** respectively. Compounds **3** and **4** which could be separated by column chromatography were the products of 1,3-H migration and four-membered-ring rearrangement of the betaine **A**, respectively (Scheme 1). When the reaction of **1a** with **2** was carried out at 40 °C, compound **4a** was the major product, whereas when the reaction of **1b** with **2** was carried out at 90 °C, compound **4b** was

* Corresponding author.

¹ This paper is the 22nd report on our studies of the chemistry and application of phosphonium and arsonium ylides. For part XXI, see Ref. [8].



the major product (Table 1). Compound **4a** or **4b** could react further with methyl perfluoroalkynoates **5a–b** in methylene chloride at room temperature to produce compounds **6a–d** as minor products and **7a–d** as major products (Scheme 2). Compounds **6** and **7** could be separated by column chromatography. The phosphorus ylides **7a–d** possessing a conjugated six-carbon main chain with a terminal acyl group are acyclic precursors in the synthesis of aromatic compounds through an intramolecular Wittig reaction. Phosphoranones **7a–d** were heated in xylenes in a sealed tube at 150 °C for 3 h, whereupon an intramolecular Wittig reaction took place to form aromatic ring compounds **8a–d** in high yield (Scheme 3). The structures of **3**, **4**, **6**, **7** and **8** were confirmed

by IR, mass spectrometry (Table 1), ¹H NMR, ¹³C NMR, ¹⁹F NMR (Table 2) and microanalysis. Compound **8** is formed through elimination of a molecule of Ph₃PO from compound **7**; therefore the structure of compound **7** could be proposed from the structure of the isophthalate **8**. The spectral data for **7** are also in accord with the above proposition. Thus, the reaction mechanism of the formation of compounds **6** and **7** is suggested to be as follows: first, the C-4 of the phosphoranones **4** attacks β-C of esters **5** to give betaine **B**, which then undergoes a 1,3-H migration and a four-membered-ring rearrangement to form phosphoranones **6** and **7** (Scheme 2).


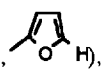



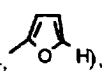









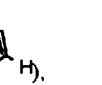


Table 1
Preparation of phosphoranones **3**, **4**, **6**, **7** and isophthalates **8**

Product	Conditions	Yield (%) ^a	M.p. (°C)	Molecular formula (mass) ^b	MS (M ⁺)	IR (cm ⁻¹)
3a	0 °C, 24 h	73	209–210	C ₂₈ H ₂₃ O ₄ P (454.4)	454	1684, 1641
4a	0 °C, 24 h	19	188–189	C ₂₈ H ₂₃ O ₄ P (454.4)	454	1672, 1613
3a	15 °C, 20 h	60				
4a	15 °C, 20 h	32				
3a	40 °C, 14 h	31				
4a	40 °C, 14 h	61				
3b	15 °C, 24 h	62	213–214	C ₂₈ H ₂₃ O ₃ SP (470.5)	471	1683, 1640
4b	15 °C, 24 h	20	209–210	C ₂₈ H ₂₃ O ₃ SP (470.5)	471	1673, 1635
3b	40 °C, 6 h	44				
4b	40 °C, 6 h	44				
3b	90 °C, 3 h	30				
4b	90 °C, 3 h	60				
6a	25 °C, 20 h	2	160–161	C ₃₃ H ₂₆ O ₆ F ₃ P (606.4)	606	1742, 1632
7a	25 °C, 20 h	82	156–157	C ₃₃ H ₂₆ O ₆ F ₃ P (606.4)	606	1690, 1640
6b	25 °C, 30 h	40	176–177	C ₃₅ H ₂₆ O ₆ F ₇ P (706.4)	706	1730, 1654
7b	25 °C, 30 h	43	128–129	C ₃₅ H ₂₆ O ₆ F ₇ P (706.4)	706	1684, 1637
6c	25 °C, 20 h	12	169–170	C ₃₃ H ₂₆ O ₅ SF ₃ P (622.4)	622	1732, 1684
7c	25 °C, 20 h	87	176–177	C ₃₃ H ₂₆ O ₅ SF ₃ P (622.4)	622	1697, 1648
6d	25 °C, 30 h	53	189–190	C ₃₅ H ₂₆ O ₅ SF ₇ P (722.4)	722	1726, 1652
7d	25 °C, 30 h	32	124–125	C ₃₅ H ₂₆ O ₅ SF ₇ P (722.4)	722	1682, 1654
8a	150 °C, 3 h	95	77–78	C ₁₅ H ₁₁ O ₃ F ₃ (328.2)	328	1739
8b	150 °C, 3 h	98	43–44	C ₁₇ H ₁₁ O ₃ F ₇ (428.2)	428	1740
8c	150 °C, 3 h	95	60–61	C ₁₅ H ₁₁ O ₄ SF ₃ (344.3)	344	1736
8d	150 °C, 3 h	90	62–64	C ₁₇ H ₁₁ O ₄ SF ₇ (444.3)	444	1745

^a Based on isolated product.













^b Satisfactory microanalyses obtained: C ± 0.30, H ± 0.20.

Table 2
 ^1H , ^{13}C and ^{19}F NMR spectral data of phosphoranones 3, 4, 6, 7 and isophthalates 8

Product	^1H NMR (CDCl_3/TMS) δ (ppm), J (Hz)	^{13}C NMR (CDCl_3/TMS) δ (ppm) (C=O)	^{19}F NMR (CDCl_3) δ (ppm)
3a	3.56 (s, 3H, CO_2CH_3), 4.41 (d, 1H, $J=15.2$,  , =CH), 6.48 (dd, 1H, $J=3.1, 1.4$,  , 7.03 (d, 1H, $J=3.1$,  , 7.54–7.64 (m, 16H, $15\text{H}_{\text{arom}} +$  , 8.41 (dd, 1H, $J=32.0, 15.2$, =CH)	169.4 (s, $-\text{CO}_2-$), 177.7 (d, $J=8$ $-\text{CO}-$)	
4a	3.57 (s, 3H, CO_2CH_3),  , 6.48 (dd, 1H, $J=3.4, 1.4$,  , 7.07 (d, 1H, $J=3.4$,  , 7.43–7.78 (m, 18H, $15\text{H}_{\text{arom}} + 2 \times$ =CH + )	168.5 (d, $J=10.8$, $-\text{CO}_2-$), 177.9 (s, $-\text{CO}_2-$)	
3b	3.51 (s, 3H, CO_2CH_3), 4.41 (d, 1H, $J=15.4$,  , =CH), 7.04 (dd, 1H, $J=4.4, 1.9$,  , 7.37–7.80 (m, 17H, $15\text{H}_{\text{arom}} +$  , 8.18 (dd, 1H, $J=30.8, 15.4$, =CH)	169.4 (s, $-\text{CO}_2-$), 182.4 (d, $J=7.4$, $-\text{CO}-$)	
4b	3.45 (s, 3H, CO_2CH_3), 7.01 (dd, 1H, $J=4.0$,  , 1.5,  , 7.29–7.64 (m, 19H, $15\text{H}_{\text{arom}} + 2 \times$ =CH + )	168.6 (d, $J=10.1$, $-\text{CO}_2-$), 181.2 (s, $-\text{CO}-$)	
6a	3.33 (s, 3H, CO_2CH_3), 3.60 (s, 3H, CO_2CH_3),  , 6.14 (dd, 1H, $J=3.4, 1.7$,  , 6.43  , 6.51 (m, 2H,  , 7.01–7.21 (m, 2H, $2 \times$ =CH), 7.51–7.72 (m, 15H_{arom})	167.0 (d, $J=16.1$, $-\text{CO}_2-$), 164.9 (s, $-\text{CO}_2-$), 180.3 (s, $-\text{CO}-$)	12.08 (s, 3F CF_3)













(continued)

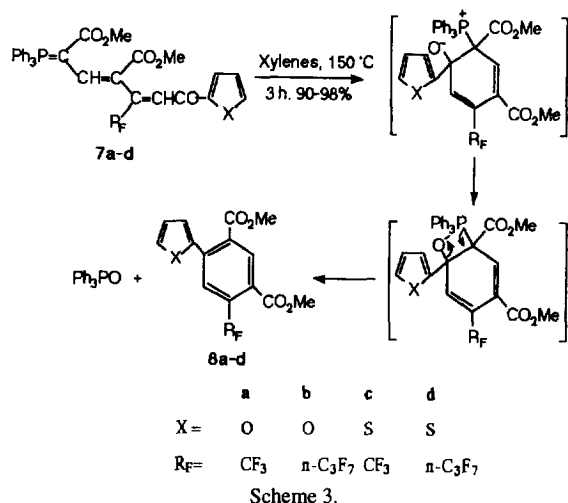
Table 2 (continued)

Product	¹ H NMR (CDCl ₃ /TMS) δ (ppm), J (Hz)	¹³ C NMR (CDCl ₃ /TMS) δ (ppm) (C=O)	¹⁹ F NMR (CDCl ₃) δ (ppm)
7a	3.27 (s, 3H, CO ₂ CH ₃), 3.48 (s, 3H, CO ₂ CH ₃), 6.50 (dd, 1H, J=3.4, 1.3, ) , 6.98 7.22 (m, 3H, 2×=CH+ ) , 7.52–7.67 (m, 16H, 15H _{arom} + )	167.2 (d, J=12.3, -CO ₂ -), 168.4 (s, -CO ₂ -), 177.8 (s, -CO-)	13.12 (s, 3F, CF ₃)
6b	3.44 (s, 3H, CO ₂ CH ₃), 3.72 (s, 3H, CO ₂ CH ₃), 6.16 (dd, 1H, J=3.0, 1.2, ) , 6.37 (d, 1H, J=3.0, ) , 6.55 (m, 1H, =CH), 7.10–7.35 (m, 2H, =CH ) , 7.46–7.80 (m, 15H _{arom})	167.8 (d, J=15.9, -CO ₂ -), 165.2 (s, -CO ₂ -), 180.2 (s, -CO-)	-3.54 (t, 3F, CF ₃) -35.18 (q, 2F, CF ₂) -49.24 (dd, 2F, CF ₂)
7b	3.40 (s, 3H, CO ₂ CH ₃), 3.50 (s, 3H, CO ₂ CH ₃), 6.62 (dd, 1H, J=3.4, 1.7, ) , 7.30 (s, 1H, =CH), 7.37 (s, 1H, =CH), 7.64– 7.82 (m, 17H, 15H _{arom} + )	168.5 (d, J=15.9, -CO ₂ -), 168.3 (s, -CO ₂ -), 177.7 (s, CO)	3.50 (t, 3F, CF ₃) 40.05 (q, 3F, CF ₂) 49.42 (dd, 2F, CF ₂)
6c	3.36 (s, 3H, CO ₂ CH ₃), 3.62 (s, 3H, CO ₂ CH ₃), 5.29 (s, 1H, =CH), 6.52 (s, 1H, =CH, 6.68– 7.27 (m, 3H, ) , 7.40–7.67 (m, 15H _{arom})	164.9 (s, -CO ₂ -), 167.2 (d, J=16.1, -CO ₂ -), 185.9 (s, -CO-)	11.85 (s, 3F, CF ₃)
7c	3.28 (s, 3H, CO ₂ CH ₃), 3.49 (s, 3H, CO ₂ CH ₃), 7.04–7.13 (m, 2H, 2×=CH), 7.47–7.78 (m, 18H, 15H _{arom} + )	166.9 (d, J=13.2, -CO ₂ -), 168.4 (s, CO ₂), 183.1 (s, -CO-)	13.11 (s, 3F, CF ₃)
6d	3.37 (s, 3H, CO ₂ CH ₃), 3.65 (s, 3H, CO ₂ CH ₃), 6.45–7.07 (m, 3H, 2×=CH, ) , 7.17– 7.67 (m, 17H, 15H _{arom} + )	166.9 (d, J=13.2, -CO ₂ -), 168.4 (s, -CO ₂ -), 185.3 (s, -CO-)	3.75 (t, 3F, CF ₃) 40.05 (q, 2F, CF ₂) -49.42 (dd, 2F, CF ₂)

(continued)

Table 2 (continued)

Product	¹ H NMR (CDCl ₃ /TMS) δ (ppm), <i>J</i> (Hz)	¹³ C NMR (CDCl ₃ /TMS) δ (ppm) (C=O)	¹⁹ F NMR (CDCl ₃) δ (ppm)
7d	3.30 (s, 3H, CO ₂ CH ₃), 3.50 (s, 3H, CO ₂ CH ₃), 7.07–7.29 (m, 3H, 2×=CH, ) , 7.54– 7.86 (m, 17H, 15H _{arom} + )	167.5 (d, <i>J</i> =13.2, –CO ₂ –), 164.9 (s, –CO ₂ –), 197.3 (s, –CO–)	–3.49 (t, 3F, CF ₃) –35.44 (q, 2F, CF ₂) –49.35 (dd, 2F, CF ₂)
8a	3.91 (s, 3H, CO ₂ CH ₃), 3.95 (s, 3H, CO ₂ CH ₃), 6.52 (dd, 1H, <i>J</i> =3.4, 1.7, ) , 6.81 (d, 1H, <i>J</i> =3.4, ) , 7.55 (d, 1H, <i>J</i> =1.7, ) , 8.05 (s, 1H _{arom}), 8.08 (s, 1H _{arom})	165.7 (s, –CO ₂ –), 167.7 (s, –CO ₂ –)	17.01 (s 3F, CF ₃)
8b	3.92 (s, 3H, CO ₂ CH ₃), 3.92 (s, 3H, CO ₂ CH ₃), 6.54 (dd, 1H, <i>J</i> =3.5, 1.8, ) , 6.80 (d, 1H, <i>J</i> =3.5, ) , 7.57 (d, 1H, <i>J</i> =1.8, ) , 7.90 (br. s, 2H _{arom})		–3.70 (t, 3F, CF ₃) 29.03 (q, 2F, CF ₂) 46.88 (s, 2F, CF ₂)
8c	3.60 (s, 3H, CO ₂ CH ₃), 3.96 (s, 3H, CO ₂ CH ₃), 7.05–7.18 (m, 2H, ) , 7.45 (d, 1H, <i>J</i> =1.5, ) , 7.68 (s, 1H _{arom}), 8.16 (s, 1H _{arom})	166.1 (s, –CO ₂ –), 167.6 (s, –CO ₂ –)	16.47 (s, 3F, CF ₃)
8d	3.61 (s, 3H, CO ₂ CH ₃), 3.94 (s, 3H, CO ₂ CH ₃) 7.08–7.20 (m, 2H, ) , 7.45 (d, 1H, <i>J</i> =1.6, ) , 7.74 (s, 1H _{arom}), 7.98 (s, 1H _{arom})		3.70 (t, 3F, CF ₃) 29.13 (q, 2F, CF ₂) 46.87 (s, 2F, CF ₂)



3. Experimental

M.p.s and b.p.s are uncorrected. M.p.s were measured with WRS-1 digital melting point apparatus made by Shanghai Physical Optical Instrument Factory (SPOIF), China. IR spectra were recorded on a 7400 spectrometer (Shanghai Analytical Instrument Factory, China) for samples as KBr discs or liquid films. NMR spectra were determined with an AC-100SC spectrometer for solutions in CDCl₃ with tetramethylsilane as internal standard for ¹H NMR, and trifluoroacetic acid as the external reference for ¹⁹F NMR. *J* values are given in hertz. Mass spectra were run on a Finnigan-Mat 4510 spectrometer. Petroleum ether refers to the fraction boiling in the range 60–90 °C.

3.1. Methyl 4-(α-furoyl)-2-(triphenylphosphoranylidene)-but-3-enoate **4a** and methyl 4-(α-thienacyl)-2-(triphenylphosphoranylidene)but-3-enoate **4b**: general procedure

To a suspension of **1a** or **1b** [9] (2 mmol) in CH₂Cl₂ (20 ml) was added methyl propynoate **2** [10] (2.4 mmol) and K₂CO₃ (3 mmol) and the mixture was stirred at 40 °C (**1a** + **2**) or 90 °C (**1b** + **2**) for 14 or 3 h respectively. After filtration of insoluble material, the solvent was removed under reduced pressure and the residue was separated on a silica gel G column with EtOAc/petroleum ether (1:2–1:1) as eluent to give compounds **3a**, **4a** and compounds **3b**, **4b** respectively. Further purification was by recrystallization from EtOAc/petroleum ether.

3.2. Dimethyl 2-(α-furoyl-1-perfluoroalkylvinyl)-4-(triphenylphosphoranylidene)pent-2-enedioates **6a–b** and dimethyl 2-(α-thienacyl-1-perfluoroalkylvinyl)-4-(triphenylphosphoranylidene)pent-2-enedioates **6c–d**: general procedure

To a solution of compound **4a** or **4b** (1.0 mmol) in anhydrous methylene dichloride (15 ml) was added a methyl perfluoroalkynoate **5a** or **5b** [11] (1.5 mmol) and the mixture was stirred at room temperature for 20 h. The solvent was removed, and the residue was purified by column chromatography on silica gel and elution with EtOAc/petroleum ether (1:1). Further purification by recrystallization from EtOAc/petroleum ether gave compounds **6a–d** and **7a–d** respectively.

3.3. Dimethyl 4-(α-furyl)-6-perfluoroalkylisophthalates **8a–b** and dimethyl 4-(α-thienyl)-6-perfluoroalkylisophthalates **8c–d**: typical procedure

A solution of **6a–d** (1.5 mmol) in anhydrous xylenes (10 ml) was heated in a sealed tube at 150 °C for 3 h. After cooling, the solution was passed through a silica gel column and eluted with EtOAc/petroleum ether (1:9) to separate the product **8a–d** from triphenylphosphine oxide. The product **8a–d** was further purified by recrystallization from light petroleum.

Acknowledgements

Thanks are due to the National Natural Science Foundation of China for the partial financial support.

References

- [1] R.E. Banks (Ed.), *Organofluorine Chemicals and their Industrial Application*, Ellis Harwood, 1979.
- [2] J.T. Welch, *Tetrahedron* 43 (1987) 3123.
- [3] W.Y. Ding, P.S. Zhang, W.G. Cao, *Tetrahedron Lett.* 28 (1987) 81.
- [4] W.Y. Ding, J.Q. Pu, C.M. Zhang, *Synthesis* (1992) 635.
- [5] W.Y. Ding, W.G. Cao, Z.R. Xu, Z.J. Shi, Y. Yao, *Chin. J. Chem.* 11 (1993) 81.
- [6] W.Y. Ding, W.G. Cao, Z.R. Xu, Y. Yao, Z.J. Shi, Z.H. Han, *J. Chem. Soc. Perkin Trans. 1* (1993) 855.
- [7] W.Y. Ding, W.G. Cao, Y. Yao, Z.M. Zhu, *Chin. J. Chem.* 13 (1995) 468.
- [8] W.G. Cao, W.Y. Ding, T. Yi, Z.M. Zhu, *J. Fluorine Chem.* 81 (1997) 153.
- [9] W.T. Tao, H.F. Pu, *YOUJI HUAXUE* (1983) 129.
- [10] D.S. James, P.E. Fanta, *J. Org. Chem.* 27 (1962) 3346.
- [11] Y.Z. Huang, Y.C. Shen, G.D. Chen, S.Q. Wang, *Acta Chim. Sin.* 37 (1979) 47.