A Convenient Synthesis of Methyl 1-Alkoxy-3-perfluoroalkyl-2-naphthoates[1]

Weiyu Ding,* Jiaqi Pu, Chunming Zhang
Department of Chemistry, Shanghai University of Science and Technology, Jiading, Shanghai 201800, People's Republic of China

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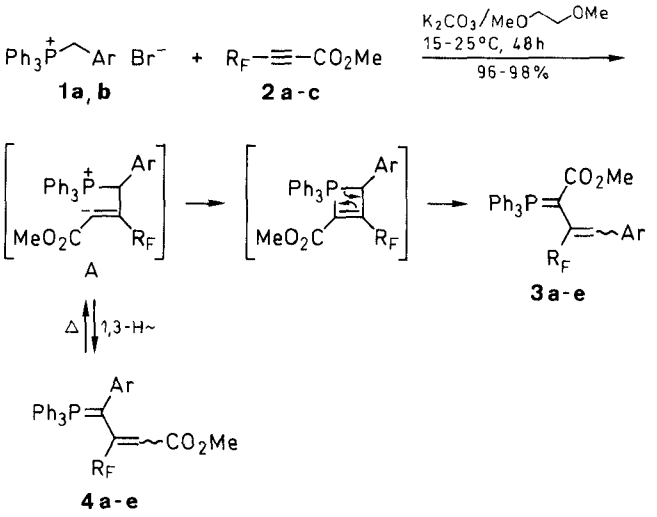
Methyl 1-alkoxy-3-perfluoroalkyl-2-naphthoates **5** were synthesized by heating appropriately substituted 2-triphenylphosphoranylidene-2-butenoates **3** in xylenes at 250 °C in a sealed tube. Compounds **3** were obtained via an intramolecular Wittig reaction of 2-alkoxycarbonylbenzyltriphenylphosphonium bromide (**1**) with methyl 2-perfluoroalkynoates **2** in the presence of potassium carbonate.

Polysubstituted aromatic compounds are useful intermediates in organic syntheses. However, their preparation by classical synthetic methods is restrained by the customary long synthetic routes and the difficult separation of positional isomers often formed. Besides, it was not possible to introduce a perfluoroalkyl group using the usual alkylation method. Thus, study of the preparation of specific positional polysubstituted fluorinated arenes is of interest.

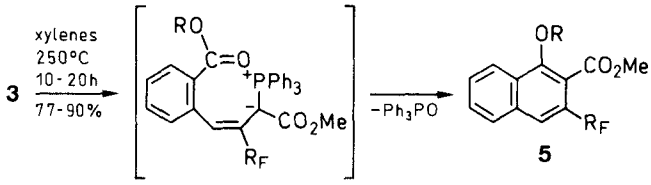
Bestmann et al. have reported the synthesis of unsaturated five- and six-membered ring compounds through an intramolecular Wittig reaction.[2] We have synthesized fluorinated aromatic compounds from acyclic precursors via the same reaction but using a different pathway.[3] The reaction of alkylidenetriphenylphosphoranes with dimethyl acetylenedicarboxylate[4] was further extended in our laboratory to synthesize the fluoro-containing phosphorous ylides possessing a six-carbon conjugated main chain and a terminal methoxycarbonyl group with methyl 2-perfluoroalkynoates **2a–c**. These acyclic precursors undergo intramolecular Wittig reaction to afford polysubstituted arenes.

In this paper a convenient synthesis of methyl 1-alkoxy-3-perfluoroalkyl-2-naphthoates **5a–e** is reported. The reaction of 2-alkoxycarbonylbenzyltriphenylphosphonium bromide **1a,b** with methyl 2-perfluoroalkynoates **2a–c** in anhydrous dimethoxyethane in the presence of potassium carbonate at room temperature gives two adducts, methyl 4-(2-alkoxycarbonylphenyl)-3-perfluoroalkyl-2-triphenylphopshoranylidene-3-butenoates **3a–e** and methyl 4-(2-alkoxycarbonylphenyl)-3-perfluoroalkyl-4-triphenylphosphoranylidene-2-butenoates **4a–e**[5] (Scheme 1). They cannot be separated by column chromatography, but when heated at 150–180 °C the mixture of **3** and **4** transforms solely to **3**. It may be explained that **3** is more stable than **4** at high temperature due to the long chain conjugation with the aromatic ring. 1-Alkoxy-3-perfluoroalkyl-2-naphthoates **5a–e** are formed when a mixture of **3a–e** and **4a–e** are heated in anhydrous xylenes in a sealed tube at 250 °C for 10–20 h (Scheme 2). The structures of **5a–e** are confirmed by analytical and spectral data (Table). As can be seen, the above mentioned synthetic method gives rise to a sole product in which the positions of the substituents are unambiguous. Besides, this route is short and the cyclization of **3** to products **5** proceeds with good yield.



1	Ar	2	R_F	3,4	Ar	R_F
a	2-$MeO_2CC_6H_4$	a	CF_3	a	2-CO_2Me	CF_3
b	2-$EtO_2CC_6H_4$	b	C_2F_5	b	2-CO_2Me	C_2F_5
		c	n-C_3F_7	c	2-CO_2Me	n-C_3F_7
				d	2-CO_2Et	CF_3
				e	2-CO_2Et	n-C_3F_7

Scheme 1



5	R	R_F
a	Me	CF_3
b	Me	C_2F_5
c	Me	n-C_3F_7
d	Et	CF_3
e	Et	n-C_3F_7

Scheme 2

IR spectra were recorded on a 7400 spectrophotometer made in China. ^1H and ^{19}F NMR were taken on a AC-100 SC spectrometer and MS on a Finnigan-Mat 4510 spectrometer. Petroleum ether used refers to bp 60–90 °C.

2-Alkoxycarbonylbenzyltriphenylphosphonium Bromides 1a,b; General Procedure:

A solution of Ph_3P (5.25 g, 20 mmol) and methyl or ethyl 2-bromomethylbenzoate[6–8] (22 mmol) dissolved in anhydrous DMF (30 mL) was stirred for 12 h at 50–60 °C. After cooling, the mixture was diluted with EtOAc to give **1a** or **1b** respectively, as a white precipitate, which was recrystallized from $CHCl_3$/EtOAc. For the analytical and spectral data of 1a, see Ref. 5.

Table. Compound Mixture **3d,e** + **4d,e** and Compounds **5a–e** Prepared

Product	Yield (%)	mp (°C) or bp (°C)/mbar[a]	Molecular Formula[b]	IR (KBr) ν (cm^{-1})	MS (70 eV) m/z (%)	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{19}F NMR ($CDCl_3$/TFA) δ, J (Hz)
3d + **4d**	98	159–160	$C_{33}H_{28}F_3O_4P$ (576.5)	1712, 1610	576 (M^+, 14), 262 (100)	**3d**: 3.15 (*Z*-isomer) and 3.70 (*E*-isomer) (s, 3H, $=CCO_2CH_3$) **4d**: 1.40 (t, 3H, J = 7.1, CH_2CH_3), 3.53 (s, 3H, OCH_3), 4.36 (q, 2H, J = 7.1, OCH_2), 6.30 (s, 1H, C=CH), 7.1–8.4 (m, 19H_{arom})	**3d**: −10.1 (*Z*-isomer) and −10.4 (*E*-Isomer) (s, 3F, CF_3) **4d**: −18.0 (s, 3F, CF_3)
3e + **4e**	96	148–149	$C_{35}H_{28}F_7O_4P$ (676.5)	1720, 1612	676 (M^+, 4), 262 (100)	**3e**: 1.16–1.30 (m, 3H, CH_2CH_3), 3.06 (*Z*-isomer) and 3.62 (*E*-isomer) (s, 3H, $=CCO_2CH_3$), 4.05–4.16 (m, 2H, OCH_2), 7.1–7.9 (m, 20H, 19H_{arom} + C=CH) **4e**: 1.40 (t, 3H, J = 7.1, CH_2CH_3), 3.49 (s, 3H, $=CCO_2CH_3$), 4.38 (q, 2H, J = 7.1, OCH_2), 6.30 (br s, 1H, C=CH), 7.1–8.0 (m, 19H_{arom})	(*Z*)-**3e**: 3.8 (t, 3F, J = 11, CF_3), 29.8–30.5 (m, 2F, $=CCF_2$), 48.1 (s) and 47.7 (s) (2F, unequal CF_3CF_2) (*E*)-**3e**: 3.9 (t, 3F, J = 11, CF_3), 29.8–30.5 (m, 2F, $=CCF_2$), 48.4 (s) and 48.8 (s) (2F, unequal CF_3CF_2) **4e**: 4.4 (t, 3F, J = 11, CF_3), 23.5–24.4 (m, 2F, $=CCF_2$), 46.7 (s) and 46.9 (s) (2F, unequal CF_3CF_2) −16.4 (s, 3F, CF_3)
5a	90	94–95 (MeOH)	$C_{14}H_{11}F_3O_3$ (284.2)	1743	284 (M^+, 71), 253 (100)	4.00 (s, 3H, CO_2CH_3), 4.05 (s, 3H, $ArOCH_3$), 7.5–8.2 (m, 5H_{arom})	
5b	77	88–89 (MeOH)	$C_{15}H_{11}F_5O_3$ (334.2)	1745	334 (M^+, 51), 59 (100)	3.99 (s, 3H, CO_2CH_3), 4.04 (s, 3H, $ArOCH_3$), 7.5–8.2 (m, 5H_{arom})	7.6 (s, 3F, CF_3), 33.5 (s, 2F, CF_2)
5c	85	160–165/132	$C_{16}H_{11}F_7O_3$ (384.2)	1745	384 (M^+, 100), 353 (99)	3.97 (s, 3H, CO_2CH_3), 4.03 (s, 3H, $ArOCH_3$), 7.5–8.2 (m, 5H_{arom})	3.9 (t, 3F, J = 10, CF_3), 30.3 (q, 2F, J = 10, $=CCF_2$), 48.3 (s, 2F, CF_3CF_2) −16.5 (s, 3F, CF_3)
5d	81	150–155/132	$C_{15}H_{13}F_3O_3$ (298.2)	1745	298 (M^+, 25), 238 (100)	1.50 (t, 3H, J = 7.0, CH_2CH_3), 3.99 (s, 3H, $ArOCH_3$), 4.21 (q, 2H, J = 7.0, OCH_2), 7.5–8.2 (m, 5H_{arom})	
5e	90	48–50 (MeOH)	$C_{17}H_{13}F_7O_3$ (398.2)	1745	398 (M^+, 38), 338 (100)	1.50 (t, 3H, J = 7.0, CH_2CH_3), 3.97 (s, 3H, $ArOCH_3$), 4.20 (q, 2H, J = 7.0, OCH_2), 7.5–8.2 (m, 5H_{arom})	4.0 (t, 3F, J = 10, CF_3), 30.4 (q, 2F, J = 10, $=CCF_2$), 48.3 (s, 2F, CF_3CF_2)

[a] Bath temperature of molecular distillation, uncorrected.

[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.1.

1b; yield: 90%; mp 205–206°C.

$C_{28}H_{26}BrO_2P$ (505.4) calc. C 66.54 H 5.18 found 66.29 5.16

IR (KBr): ν = 1695 (C=O), 1270 cm^{-1}.

^1H NMR (100 MHz, $CDCl_3$/TMS): δ = 1.15 (t, 3H, J = 7.1 Hz, CH_3), 3.91 (q, 2H, J = 7.1 Hz, OCH_2), 5.84 (d, 2H, J = 15 Hz, PCH_2), 7.3–7.9 (m, 19 H_{arom}).

MS (70 eV): m/z (%) = 521 ($M + O^+$, 4.8), 78 (100).

Methyl 4-(2-Alkoxycarbonylphenyl)-3-perfluoroalkyl-2-triphenylphosphoranylidene-3-butenoates 3 and Methyl 4-(2-Alkoxycarbonylphenyl)-3-perfluoroalkyl-4-triphenylphosphoranylidene-2-butenoates 4; General Procedure:

To a suspension of **1a,b** (2.0 mmol) and K_2CO_3 (0.5 g) in anhydrous dimethoxyethane (15 mL), was added the appropriate methyl 2-perfluoroalkynoate **2a–c**[9,10] (2.2 mmol) and the mixture was stirred at 15–25°C under N_2 for 48 h. The insoluble residue was filtered, the solvent distilled under reduced pressure and the residue was purified on a silica gel G column with EtOAc/petroleum ether (1:1) as eluent to give a mixture of **3a–e** and **4a–e** as a yellow solid. Recrystallization from $CHCl_3$/hexane gave light yellow crystals. Efforts to separate **3a–e** and **4a–e** were unsuccessful (Table). For the analytical data of the compound mixture of **3a** + **4a**, **3b** + **4b** and **3c** + **4c** see Ref. 5.

Methyl 1-Alkoxy-3-perfluoroalkyl-2-naphthoates 5a–e; General Procedure:

A solution of the compound mixture **3a–e** and **4a–e** (2 mmol) in anhydrous xylenes (3 mL) was heated in a sealed tube at 250°C for 10–15 h. After cooling, the mixture was separated on a silica gel G column with petroleum ether, petroleum ether/EtOAc and EtOAc as eluent to give product **5a–e** and Ph_3PO (Table).

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