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A NEW SYNTHESIS OF PERFLUOROALKANEPHOSPHONATES

WENBIAO CEN and YANCHANG SHEN*

Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai 200032 (China)

SUMMARY

A new method for the synthesis of perfluoroalkanephosphonates, R_f-P(O)$(OC_2H_5)_2$ has been developed, involving the facile formation of R_f-P bond by the reaction of perfluoroalkyl Grignard reagents with diethyl chlorophosphate.

INTRODUCTION

Many phosphonic acids and their derivatives have been shown to exhibit biological activity [1]. It is well known that the introduction of a fluorine-containing group into molecules can greatly increase the biological activities of chemical compounds. Recently, because of their stability, strong acidity and high solubility, perfluoro and fluorinated phosphonic acids have aroused great interest[2]. Therefore, it was of value to develop a new synthetic method for the preparation of perfluoroalkanephosphonates.

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Because of the strong election-withdrawing effect, a perfluoroalkyl group causes electron-deficiency on the halogen atom of perfluoroalkyl halides. The usual synthetic method for phosphonates from the corresponding perfluoroalkyl halides cannot be applied to the synthesis of the title compounds.

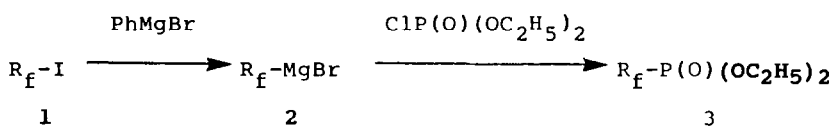
To the best of our knowledge, very few reports have appeared in the literature on the synthesis of perfluoroalkanephosphonates and halofluoroalkanephosphonates. Burton reported the formation of a $-CF_2-P$ bond and its application to the synthesis of bromodifluoromethanephosphonate from dibromodifluoromethane and triethyl phosphite [3]. The reaction mechanism might be via abstraction of positive bromine and formation of difluorocarbene rather than the Arbuzov reaction [4]. Thus, this reaction was only applicable for using perfluoroalkyl or halofluoroalkyl halides with one carbon atom. Kato reported the formation of a $-CF_2-P$ bond for the synthesis of perfluoroalkanephosphonates from tetraethyl pyrophosphite and perfluoroalkyl iodides via free radical initiation, but this method needed high temperature and use of an autoclave [5].

We now wish to report a general synthetic method for the preparation of perfluoroalkanephosphonates from readily available starting materials.

RESULTS AND DISCUSSION

Perfluoroalkyl Grignard reagents generated from exchange reaction of perfluoroalkyl iodides and phenylmagnesium

bromide could react with various electrophiles, such as diethyl chlorophosphate, at low temperature leading to the formation of $-CF_2-P$ bond and affording perfluoroalkanephosphonates (Scheme 1). The reaction was carried out in



Scheme 1.

ether at -50°C giving moderate yields of perfluoroalkanephosphonates. The results of the reactions are summarized in Table 1.

The products were isolated and characterized by ^1H, ^{19}F, ^{31}P NMR, IR and MS Spectroscopies. The data of 3a and 3e were in accord with published data. **Compounds** 3b, 3c and 3d are new giving satisfactory elemental analyses.

An ω-chloride in the R_f group did not interfere with the reaction. As we know, sulfonyl fluorides react with Grignard reagents in refluxing ether forming sulfones[6]. Due to the high reactivity of perfluoroalkyl Grignard reagents we could control the reaction temperature at -50°C to give the products exclusively.

TABLE 1

Preparation of Phosphonates (3)

Phosphonates	R_f	B.p(°C/mmHg)	Yield(%)
3a	$n\text{-}C_6F_{13}$	89/5	56
3b	$Cl(CF_2)_8$	95/0.8	45
3c	$Cl(CF_2)_6$	114/6	58
3d	$Cl(CF_2)_4$	101/11	36
3e	$FO_2S(CF_2)_2O(CF_2)_4$	119/0.8	31

EXPERIMENTAL

All boiling points were uncorrected. Infrared spectra of liquid product were obtained as films on a Shimadzu IR-440 Spectrometer. NMR spectra (chemical shifts in ppm from TMS for ^1H NMR, from external TFA for ^{19}F NMR, positive for upfield shifts and from external H_3PO_4 for ^{31}P NMR) were determined on a Varian EM-360 Spectrometer at 60 MHz or a JEOL FX-90Q Spectrometer at 90 MHz or at 36.2 MHz for ^{31}P. Mass spectra were recorded on a Finnigan GC-MS 4021 Mass Spectrometer.

General procedure for preparation of perfluoroalkanephosphonates (3)

A solution of perfluoroalkyl iodide (8 mmol) in diethyl ether (20 ml) was added dropwise with stirring

over 15 min to a solution of phenylmagnesium bromide (8 mmol) in ether (40 ml) at -50°C. The reaction mixture was stirred for 0.5 h at -50°C and a solution of diethyl chlorophosphate (8 mmol) in ether (20 ml) was slowly added with stirring. After addition the mixture was allowed to stir for another 1 h and warm to 0°C, 30% aqueous solution of HCl (20 ml) was added. The organic layer was separated and dried (Na_2SO_4). Evaporation of the solvent gave a residue which was isolated by column chromatography on silica gel eluting with petroleum ether/ethyl acetate (9:1) as product (3).

3a: 56% yield; b.p. 89°C/5mmHg [Lit data 60°C/1.5mmHg] [5]; IR(film): 1290(s), 1020(s) cm^{-1}; ^1H NMR($CDCl_3$): δ 1.33(t,6H, $^3J_{H-H}$=8.0Hz), 4.29(m, 4H); ^{19}F NMR($CDCl_3$): δ 4.4(s, 3F), 43.7-47.0 (m, 8F), 49.5(m, 2F); ^{31}P NMR($CDCl_3$): δ -0.19 (t,$^2J_{P-F}$=90.2Hz). MS m/e: 457(M^++1), 137[$^+P(O)(OC_2H_5)_2$], 109[$^+P(O)(OH)(OC_2H_5)$].

3b: 45% yield; b.p. 95°C/0.8mmHg; IR(film): 1290(s),1020(s) cm^{-1}; ^1H NMR($CDCl_3$): δ 1.40(t,6H,$^3J_{H-H}$=8.0Hz), 4.36(m,4H); ^{19}F NMR($CDCl_3$): δ -6.9(s, 2F), 42.6-46.1(m, 14F); ^{31}P NMR ($CDCl_3$): δ -0.15(t,$^2J_{P-F}$=92.0Hz); MS m/e: 573(M^++1), 137 [$^+P(O)(OC_2H_5)_2$], 109[$^+P(O)(OH)(OC_2H_5)$]; Analysis: Calcd for $C_{12}H_{10}ClF_{16}O_3P$: C,25.15, H,1.75; Found: C,24.84, H,1.75%.

3c: 58% yield; b.p. 114°C/6mmHg; IR(film): 1290(s),1040(s) cm^{-1}; ^{1}H NMR($CDCl_3$): δ 1.30(t,6H, $^{3}J_{H-H}$=8.0Hz), 4.15(m,4H); ^{19}F NMR($CDCl_3$): δ -8.3(s, 2F), 44.0-46.3(m, 10F); ^{31}P NMR ($CDCl_3$): δ -0.12(t, $^{2}J_{P-F}$=89.3Hz); MS m/e: 473(M^{+}+1), 137 [$^{+}P(O)(OC_2H_5)_2$], 109[$^{+}P(O)(OH)(OC_2H_5)$]; Analysis: Calcd for $C_{10}H_{10}ClF_{12}O_3P$: C,25.40, H,2.12; Found: C,25.17, H,2.01%.

3d: 36% yield; b.p. 101°C/11mmHg; IR(film): 1290(s), 1020 (s)cm^{-1}; ^{1}H NMR($CDCl_3$): δ1.30(t, 6H, $^{3}J_{H-H}$=8.0Hz); 4.23(m, 4H); ^{19}F NMR($CDCl_3$): δ -8.3(s, 2F), 43.3(m, 4F), 45.3(d, 2F); ^{31}P NMR($CDCl_3$): δ -0.15(t,$^{2}J_{P-F}$=89.3Hz); MS m/e: 373 (M^{+}+1),137[$^{+}P(O)(OC_2H_5)_2$],109[$^{+}P(O)(OH)(OC_2H_5)$]; Analysis: Calcd for $C_8H_{10}ClF_8O_3P$: C,25.77, H,2.68; Found: C,25.53, H,2.49%.

3e: 31% yield; b.p. 119°C/0.8mmHg [Lit data 133°C/1.1mmHg] [2]; IR(film): 1290(s), 1020(s)cm^{-1}; ^{1}H NMR($CDCl_3$): δ1.37 (t,6H,$^{3}J_{H-H}$=8.0Hz), 4.30(m,4H); ^{19}F NMR($CDCl_3$): δ-121.3(s, 1F), 5.0-6.0(m, 4F), 35.5(s, 2F), 44.0-46.3(m,4F), 48.3(s, 2F); ^{31}P NMR($CDCl_3$): δ-0.32(t, $^{2}J_{P-F}$=89.3Hz); MS m/e: 537 (M^{+}+1), 137[$^{+}P(O)(OC_2H_5)_2$], 109[$^{+}P(O)(OH)(OC_2H_5)$].

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