Bis-perfluoroalkylation of aromatic compounds with sodium perfluoroalkanesulfinates

LIU, Jin-Tao* (刘金涛)   LU, He-Jun(吕贺军)
Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry,
Chinese Academy of Sciences, Shanghai 200032, China

Bis-perfluoroalkylation of aromatic compounds such as dimethoxybenzenes (2,4,6), anisole (8), pyridine (10) and quinoline (13) was accomplished by reaction with excess sodium perfluoroalkanesulfinates, R_FSO_2Na (1), in the presence of $Mn(OAc)_3 \cdot 2H_2O$ under mild conditions. The reaction provides a facile method for the synthesis of bis-perfluoroalkylated aromatic compounds.

Keywords   Sodium perfluoroalkanesulfinate, bis-perfluoroalkylation, aromatic compound

Introduction

Perfluoroalkylation of aromatic compounds by means of perfluoroalkyl free radical is an important way for the synthesis of fluorine-containing organic compounds, and many methods to generate perfluoroalkyl radicals have been developed.[1-5] Most perfluoroalkylation reactions gave mono-substituted products due to the electrophilic nature of perfluoroalkyl radicals and the strong electron-withdrawing effect of perfluoroalkyl groups. Poly-perfluoroalkylation of aromatic compounds was less studied. In 1996, Huang et al. reported the bis-perfluoroalkylation of para-substituted phenols using R_FI-$Na_2S_2O_4$ system.[6] Recently, poly-perfluoroalkylated coumarins were obtained in our laboratory by direct perfluoroalkylation of coumarin with sodium perfluoroalkanesulfinates in the presence of $Mn(OAc)_3 \cdot 2H_2O$.[7] In our continuous research on the reaction of sodium perfluoroalkanesulfinates, we found that the R_FSO_2Na-$Mn(OAc)_3 \cdot 2H_2O$ system could also be used for the bis-perfluoroalkylation of a series of other aromatic compounds.

Sodium perfluoroalkanesulfinates (1), readily available from perfluoroalkyl iodides through sulfinatodehalogenation reaction,[8] are good electron donors. They form the perfluoroalkyl radicals by oxidation with some single electron oxidants such as $Mn(OAc)_3 \cdot 2H_2O$ and $Ce(SO_4)_2$. The perfluoroalkyl radicals thus formed are very active and can react with various organic compounds including some electron-deficient aromatic compounds such as pyridine and methyl benzoate. The mono-perfluoroalkylation of benzene, pyridine and their derivatives with R_FSO_2Na-$Mn(OAc)_3 \cdot 2H_2O$ system was reported previously.[9-11] In this paper we report the bis-perfluoroalkylation of some aromatic compounds with this perfluoroalkylating reagent system.

Results and discussion

In the presence of $Mn(OAc)_3 \cdot 2H_2O$, the reaction of sodium perfluoroalkanesulfinates (1) with 1 equivalent or a little less 1,3-dimethoxybenzene (2) at 80—85℃ gave only mono-perfluoroalkylated products.[9] When 2-3 equivalents of 1 and excess $Mn(OAc)_3 \cdot 2H_2O$ were used, bis-perfluoroalkylation reaction took place readily under similar conditions. The reaction was carried out in $CH_3CN/AcOH/Ac_2O$ (5:1:1) at 80—85℃, giving o- and p-substituted bis-perfluoroalkylation products 3 in good yields (Scheme 1). The results are listed in Table 1.

Similarly, other aromatic compounds such as 1,2-dimethoxybenzene (4), 1,4-dimethoxybenzene (6) and anisole (8) could also react with excess 1 and

$Mn(OAc)_3 \cdot 2H_2O$ to give the corresponding o- and p-substituted bis-perfluoroalkylation products 5, 7 and 9 respectively in moderate to good yields depending on the substrate used (Scheme 2). A small amount of other bis-perfluoroalkylated isomers were formed as minor

products in some cases, but were not isolated and characterized. Mono-perfluoroalkylated products were found to be formed in these reactions and disappeared gradually during the reaction when enough 1 and $Mn(OAc)_3 \cdot 2H_2O$ were used.

Scheme 1


a, $R_F=Cl(CF_2)_4$;　b, $R_F=Cl(CF_2)_6$;　c, $R_F= F(CF_2)_6$
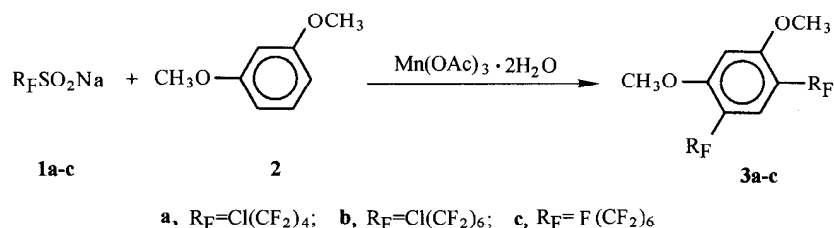
These bis-perfluoroalkylated aromatic compounds could be isolated by column chromatography and were identified by their spectral data and elemental analyses. Taking ^1H NMR spectra as an example: The ^1H NMR

spectrum of compound 3 showed two singlet signals (C2-H, C5-H) for aromatic protons, while only one singlet signal appeared in the ^1H NMR spectrum of compounds 5 and 6, indicating that the chemical environment of the

Scheme 2
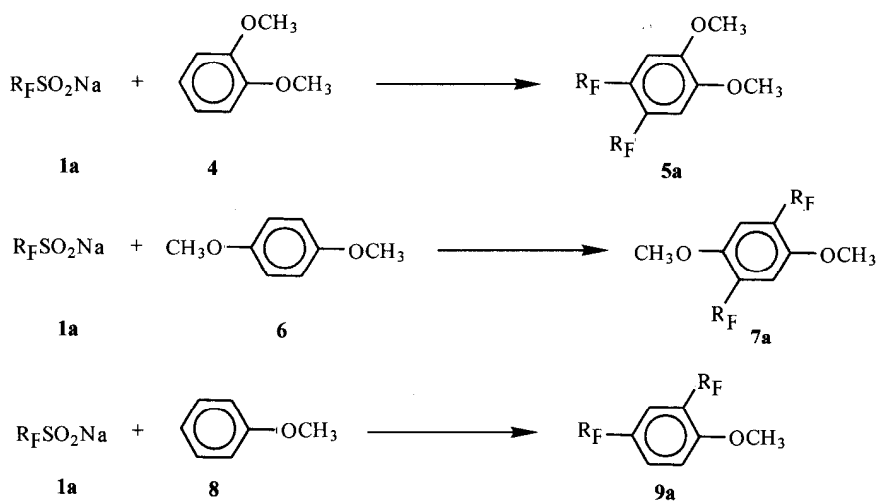
two aromatic protons in the latter two compounds was the same. The fact that no 2,4-bis-perfluoroalkylated 1,3-dimethoxybenzene was isolated from the reaction of 1 and 2 indicated that steric factor played an important role in the bis-perfluoroalkylation reaction, and thus ruled out the possibility of the formation of 2,6-bis(per-fluoroalkyl)-1,3-dimethoxybenzene as major product in the bis-perfluoroalkylation reaction of 6. This is in consistent with the reported result of the mono-perfluoroalkylation of 1,3-dimethoxybenzene, in which 4-per-

fluoroalkyl-1,3-dimethoxybenzene was formed predominantly over 2-perfluoroalkyl-1,3-dimethoxybenzene.[9]

Mono-perfluoroalkylation of pyridine with R_FI-$HOCH_2SO_2Na^{12}$ or R_FSO_2Na-$Mn(OAc)_3 \cdot 2H_2O^{11}$ gave a mixture of 2-, 3- and a small amount of 4-substituted isomers. When pyridine was allowed to react with excess 1 and $Mn(OAc)_3 \cdot 2H_2O$, 2,5-bis(perfluoroalkyl)pyridine (11) and 2,4-bis(perfluoroalkyl)pyridine (12) were obtained as major products (Scheme 3), no 2,3-bis(perfluoroalkyl)pyridine was obtained. In the case of

quinoline, bis-perfluoroalkylation took place on C-5 and

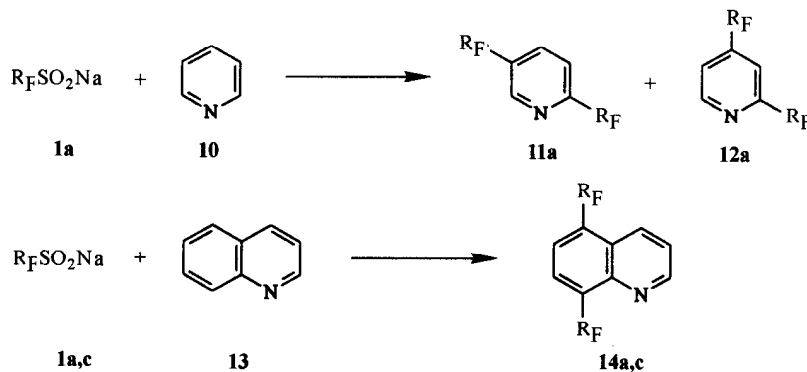C-8 positions to give compound **14** predominantly.

Scheme 3

Table 1   Bis-perfluoroalkylation of aromatic compounds

R_FSO_2Na	ArH	Product	Yield $(\%)^a$
1a	**2**	**3a**	80
1b	**2**	**3b**	74
1c	**2**	**3c**	78
1a	**4**	**5a**	54
1a	**6**	**7a**	67
1a	**8**	**9a**	55
1b	**10**	**11b**	33
		12b	25
1a	**13**	**14a**	70
1c	**13**	**14c**	65

^{a} Isolated yield based on ArH.

In general, 2—3 equivalent or more sodium perfluoroalkanesulfinates and a 1:1.5—2 mole ratio of **1** to $Mn(OAc)_3 \cdot 2H_2O$ were used in the above reactions for a better conversion. TLC monitoring showed that the bis-perfluoroalkylation reaction took place step by step. It was confirmed by the reaction of 4-(4-chloro-octafluorobutyl)-1,3-dimethoxybenzene with **1a** and $Mn(OAc)_3 \cdot 2H_2O$, in which **3a** was obtained as expected.

Experimental

Melting points were uncorrected. All reagents were chemically pure or of analytical grade. $Mn(OAc)_3 \cdot 2H_2O$ was prepared using the reported procedure.[13] IR spectra were recorded on an IR-440 spectrometer, using liquid films and KBr pellets for solids. ^1H NMR spectra were measured on FX-90Q (90 MHz) or Bruker AM 300 (300 MHz) spectrometers, using TMS as internal standard. ^{19}F NMR spectra were recorded on a Varian EM-

360L spectrometer (56.4 MHz) using TFA as external standard . The values reported were $\delta_{CFCl_3} = \delta_{TFA} +$ 76.8, positive for upfield. Mass spectra were taken on a Finnigan GC-MS 4021 spectrometer. Column chromatography was performed using silica gel H, particle size 10—40 μm.

Typical procedure

To a solution of 20 mL of acetonitrile, 4 mL of acetic acid and 4 mL of acetic anhydride , was added 0.189 g (1.37 mmol) of **2**, 1.69 g (4 mmol) of **1b** and 2.14 g (8 mmol) of $Mn(OAc)_3 \cdot 2H_2O$. The mixture was stirred at 80—85 °C for 5—6 h (monitored by TLC). After being cooled, the mixture was filtered and the solid was washed with diethyl ether. Water (30 mL) was added to the combined filtrate and the resulting mixture was extracted with ether (3 × 20 mL). The ethereal solution was washed with aqueous $NaHCO_3$ solution and water to neutral, and dried over anhydrous Na_2SO_4. After the removal of ether, the crude product was purified by column chromatography using petroleum-ethyl acetate as eluant to give 0.82 g of **3b** as a colorless liquid. ν_{max}: 1620, 1580, 1470, 1305, 1200, 1140, 1020 cm^{-1}. $\delta_H(CDCl_3)$: 7.59(s, 1H, ArH), 6.56 (s, 1H, ArH), 3.93 (s, 6H, CH_3O). $\delta_F(CDCl_3)$: 67.5 (t,4F,$ClCF_2$),107.1(t,4F,$ArCF_2$),120.1—121.5 (m, 16F, CF_2). m/z: 808, 806(M^+), 771($M^+ -$ Cl),521($M^+ - ClC_5F_{10}$). Anal. $C_{20}H_8Cl_2F_{24}O_2$. Calcd: C,29.76; H,1.00; F,56.49. Found: C,29.91; H, 1.07; F, 56.46.

3a　ν_{max}: 1620, 1580, 1470, 1310, 1215, 1180, 1115, 810 cm^{-1}. δ_H(CDCl$_3$): 7.59(s, 1H, ArH), 6.56(s, 1H, ArH), 3.92(s, 6H, CH$_3$O). δ_F (CDCl$_3$): 67.1(t, 4F, ClCF$_2$), 107.1(t, 4F, ArCF$_2$), 119.8—120.5(m, 8F, CF$_2$). m/z: 608, 606 (M$^+$), 571(M$^+$ − Cl), 421(M$^+$ − ClC$_3$F$_6$). Anal. C$_{16}$H$_8$Cl$_2$F$_{16}$O$_2$. Calcd: C, 31.65; H, 1.33. Found: C, 31.62; H, 1.11.

3c　Mp: 45—46℃. ν_{max}: 1620, 1580, 1470, 1310,1210,1140,1110,1080,1020cm^{-1}. δ_H(CDCl$_3$): 7.58(s, 1H, ArH), 6.55(s, 1H, ArH), 3.93(s, 6H, CH$_3$O). δ_F(CDCl$_3$): 80.1(t, 6F, CF$_3$), 107.1 (t, 4F, ArCF$_2$), 121.5—125.8(m, 8F, CF$_2$). m/z: 774(M$^+$), 755(M$^+$ − F), 505(M$^+$ − C$_5$F$_{11}$). Anal. C$_{20}$H$_8$F$_{26}$O$_2$. Calcd: C, 31.03; H, 1.04. Found: C, 31.20; H, 1.00.

5a　ν_{max}: 1620, 1580, 1510, 1470, 1310, 1215,1180,1115,1080,1020cm^{-1}. δ_H(CDCl$_3$):7.13 (s, 2H, ArH), 3.97(s, 6H, CH$_3$O). δ_F(CDCl$_3$): 66.8(t, 4F, ClCF$_2$), 102.1(t, 4F, ArCF$_2$), 117.1— 119.5(m, 8F, CF$_2$). m/z: 608, 606(M$^+$), 571 (M$^+$ − Cl), 421(M$^+$ − ClC$_3$F$_6$). HRMS: Calcd. for C$_{16}$H$_8$Cl$_2$F$_{16}$O$_2$: 605.9646. Found: 605.9600.

7a　Mp: 76—78℃. ν_{max}: 1518, 1470, 1402, 1240, 1220, 1182, 1130, 1090, 1065, 1035, 750, 710, 680, 640 cm^{-1}. δ_H (CDCl$_3$): 7.11 (s, 2H, ArH), 3.85(s, 6H, CH$_3$O). δ_F(CDCl$_3$): 66.8(t, 4F, ClCF$_2$), 107.8(t, 4F, ArCF$_2$), 119.6(m, 8F, CF$_2$). m/z: 608, 606(M$^+$), 571(M$^+$ − Cl), 421 (M$^+$ − ClC$_3$F$_6$). Anal. C$_{16}$H$_8$Cl$_2$F$_{16}$O$_2$. Calcd : C, 31.65; H, 1.33; F, 50.08. Found: C, 31.32; H, 1.17; F, 50.14.

9a　ν_{max}: 1620, 1512, 1465, 1280, 1180, 1130, 1020, 840, 820, 765 cm^{-1}. δ_H(CDCl$_3$): 7.71 (d, J = 8.0Hz,1H,ArH),7.69(s,1H,ArH),7.10 (d, J = 8.0 Hz, 1H, ArH), 3.92(s, 3H, CH$_3$O). δ_F (CDCl$_3$): 68.3(t, 4F, ClCF$_2$), 108.6(t, 2F, ArCF$_2$), 110.8(t, 2F, ArCF$_2$), 121.0(m, 8F, CF$_2$). m/z: 576 (M$^+$), 541 (M$^+$ − Cl), 391 (M$^+$ − ClC$_3$F$_6$). Anal. C$_{15}$H$_6$Cl$_2$F$_{16}$O. Calcd: C, 31.22; H, 1.04. Found: C, 30.92; H, 0.93.

11b　Mp: 86—88℃. ν_{max}: 1605, 1580, 1400, 1320, 1290, 1180, 1080, 980, 675, 655 cm^{-1}. δ_H(CDCl$_3$): 9.00(s, 1H), 8.13(d, J = 8.3 Hz, 1H), 7.87(d, J = 8.3 Hz, 1H). δ_F(CDCl$_3$): 67.5

(t, 4F, ClCF$_2$), 111.5(t, 2F, ArCF$_2$), 113.8(t, 2F, ArCF$_2$), 120.3—121.3(m, 16F, CF$_2$). m/z: 747(M$^+$), 712(M$^+$ − Cl), 462(M$^+$ − ClC$_5$F$_{10}$). Anal. C$_{17}$H$_3$Cl$_2$F$_{24}$N. Calcd: C, 27.29; H, 0.40; N, 1.87. Found: C, 27.29; H, 0.60; N, 1.78.

12b　Mp: 90-91℃. ν_{max}: 1600, 1585, 1400, 1320, 1290, 1170, 1080, 1060, 980, 770 cm^{-1}. δ_H (CDCl$_3$): 8.96(d, J = 4.8 Hz, 1H), 7.85(s, 1H), 7.70(d, J = 4.8 Hz, 1H). δ_F(CDCl$_3$): 67.0(t, 4F, ClCF$_2$), 112.0(t, 2F, ArCF$_2$), 113.0(t, 2F, ArCF$_2$),120.3—121.3(m,16F,CF$_2$). m/z:747(M$^+$),712(M$^+$ − Cl),462(M$^+$ − ClC$_5$F$_{10}$). Anal. C$_{17}$H$_3$Cl$_2$F$_{24}$N. Calcd: C, 27.29; H, 0.40; N, 1.87. Found: C, 27.40; H, 0.30; N, 2.01.

14a　Mp: 56—58℃. ν_{max}: 1585, 1500, 1310, 1290, 1160, 1080, 1015, 790, 720 cm^{-1}. δ_H (CDCl$_3$): 9.10(d, J = 3.8 Hz, 1H), 8.59(d, J = 8.6 Hz, 1H), 8.14(d, J = 8.0 Hz, 1H), 7.98(d, J =8.0 Hz, 1H), 7.60(dd, J_1 = 8.6 Hz, J_2 = 3.8 Hz, 1H). δ_F(CDCl$_3$): 66.5(t, 4F, ClCF$_2$), 103.8 (t, 4F, ArCF$_2$), 117.1—118.8(m, 8F, CF$_2$). m/z: 599, 597(M$^+$), 562(M$^+$ − Cl), 412(M$^+$ − ClC$_3$F$_6$). Anal. C$_{17}$H$_7$Cl$_2$F$_{16}$N. Calcd: C, 34.14; H, 0.84; N, 2.34. Found: C, 33.93; H, 0.66; N, 2.26.

14c　Mp: 62—64℃. ν_{max}: 1610, 1585, 1505, 1290, 1170, 1040, 1010, 800, 710 cm^{-1}. δ_H (CDCl$_3$): 9.10(d, J = 3.8 Hz, 1H), 8.59(d, J = 8.6 Hz, 1H), 8.14(d, J = 8.0 Hz, 1H), 7.97(d, J =8.0 Hz, 1H), 7.59(dd, J_1 = 8.6 Hz, J_2 = 3.8 Hz, 1H). δ_F(CDCl$_3$): 80.1(t, 6F, CF$_3$), 104.5(t, 4F, ArCF$_2$), 118.1—125.8(m, 16F, CF$_2$). m/z: 765(M$^+$), 746(M$^+$ − F), 496(M$^+$ − C$_5$F$_{11}$). Anal. C$_{21}$H$_5$F$_{26}$N. Calcd: C, 32.96; H, 0.66; N, 1.83. Found: C, 32.55; H, 0.61; N, 2.08.

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(E9909137   JIANG, X.H.; DONG, L.J.)