A Convenient Preparation of Arylmonofluoromethanes

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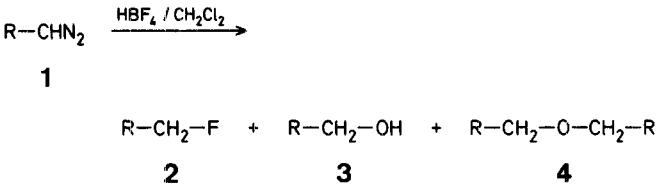
Considerable interest has been directed to the biological activities of fluorine compounds and their application in medicinal chemistry[1]. This has led to the development of several reactions for the preparation of organic fluorine compounds. Of these methods, the hydrofluorination of diazoalkanes has been applied to the preparation of fluoroalkanes using ethyl carbonofluoridate[2], potassium hydrogen difluoride[3], and 70% hydrogen fluoride/pyridine[4] as fluorinating agents. Furthermore, it has been well known that the Schiemann reaction[5] is an excellent method for the preparation of aromatic fluorine compounds from diazonium tetrafluoroborates. In order to prepare arylfluoromethanes, we have employed tetrafluoroboric acid, which is much easier to handle than hydrogen fluoride, and report now a convenient preparation of arylmonofluoromethanes **2** by the reaction of aryldiazomethanes **1** with tetrafluoroboric acid.



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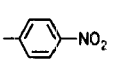
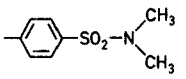
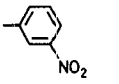
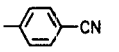
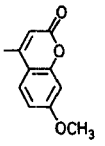
a		d	
b		e	
c		f	

Tetrafluoroboric acid reacted readily with aryldiazomethanes **1** having electron-negative groups, such as nitro[6], nitrile[7], sulfonamide[8], aza[9], and α,β-unsaturated carbonyl[10], in dichloromethane at room temperature for 10 min to afford the products **2** in 31–50% yield (Table). This reaction also gave the corresponding alcohols **3** and the symmetrical ethers **4** as by-products, which could be separated from **2** by means of thin-layer or column chromatography on silica gel. It is considered that **3** and **4** are formed by the acid hydrolysis of **1** and by the combination of **1** with the generated **3**, as reported in our previous paper[10] on the reaction of **1** with alcohols, respectively. The structures of **2**, **3**, and **4** were confirmed by I.R., ^{1}H-N.M.R., and mass spectra (Table). No products were obtained in the reaction of unsubstituted aryldiazomethanes with tetrafluoroboric acid. Furthermore, in a typical reaction the diazomethane derivative **1f** was reacted with the commercial 95%

Table. Compounds **2**, **3**, and **4** prepared

Product	Yield [%]	m.p. [°C] (solvent) b.p. [°C]/torr	Molecular formula[a] or Lit. Data	I.R. (KBr) ν [cm^{-1}]	M.S. m/e (M^+)	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
2a	50	37–38° (*n*-pentane)	38.2–38.5°[11]	1020 (C—F)	—	5.5 (d, 2H, J=48 Hz); 7.53 (d, 2H, J=8 Hz); 8.26 (d, 2H, J=8 Hz)
2b	49	102°/7	91°/3.5[11]	1080 (C—F)	—	5.45 (d, 2H, J=47 Hz); 7.5–8.4 (m, 4H)
2c	47	29–30° (*n*-pentane)	28°[12]	1014 (C—F)	—	5.45 (d, 2H, J=47 Hz); 7.43 (d, 2H, J=8 Hz); 7.7 (d, 2H, J=8 Hz)
2d	44	61–62° (*n*-pentane)	$C_9H_{12}FNO_2S$ (217.2)	990 (C—F)	—	2.71 (s, 6H); 5.43 (d, 2H, J=47 Hz); 7.5 (d, 2H, J=8 Hz); 7.8 (d, 2H, J=8 Hz)
2e	31	31–33° (*n*-pentane)	$C_{10}H_8FN$ (161.2)	1050 (C—F)	—	5.85 (d, 2H, J=47 Hz); 7.3–9.0 (m, 6H)
2f	33	152–154° (methanol)	$C_{11}H_9FO_3$ (208.2)	1065 (C—F)	—	3.9 (s, 3H); 5.55 (d, 2H, J=46 Hz); 6.36 (s, 1H); 6.9 (m, 2H); 7.33 (d, 1H, J=10 Hz)
3a	28	91–92° (benzene)	92–93°[13]	3470 (OH)	—	2.46 (br. s, 1H); 4.84 (s, 2H); 7.51 (d, 2H, J=8 Hz); 8.20 (d, 2H, J=8 Hz)
3b	24	26–27° (benzene)	27°[14]	3320 (OH)	—	2.7 (br. s, 1H); 4.83 (s, 2H); 7.2–8.6 (m, 4H)
3c	26	42–43° (benzene)	41–42°[15]	3400 (OH)	—	2.6 (br. s, 1H); 4.75 (s, 2H); 7.41 (d, 2H, J=9 Hz); 7.61 (d, 2H, J=9 Hz)
3d	29	82–83° (benzene)	83–84°[16]	3320 (OH)	—	2.66 (s, 6H); 3.1 (br. s, 1H); 4.73 (s, 2H); 7.43 (d, 2H, J=8 Hz); 7.66 (d, 2H, J=8 Hz)
3e	29	96–97° (methanol)	96–97°[17]	3200 (OH)	—	3.57 (br. s, 1H); 5.2 (d, 2H, J=6 Hz); 7.3 (m, 6H)
3f	40	183–185° (ethanol)	183–185°[18]	3340 (OH)	—	2.6 (br. s, 1H); 3.86 (s, 3H); 4.72 (d, 2H, J=6 Hz); 6.45 (s, 1H); 6.8 (m, 2H); 7.45 (d, 1H, J=10 Hz)
4a	7	98–99° (ethanol)	97–98°[13]	—	288	4.75 (s, 4H); 7.53 (d, 4H, J=8 Hz); 8.22 (d, 4H, J=8 Hz)
4b	6	96–97° (*n*-pentane)	$C_{14}H_{12}N_2O_5$ (288.3)	—	288	4.73 (s, 4H); 7.5–8.4 (m, 8H)
4c	12	97–98° (ethanol)	97–98°[15]	—	248	4.65 (s, 4H); 7.43 (d, 4H, J=8 Hz); 7.7 (d, 4H, J=8 Hz)
4d	8	141–142° (*n*-pentane)	$C_{18}H_{24}N_2O_5S_2$ (412.4)	—	412	2.73 (s, 12H); 4.7 (s, 4H); 7.53 (d, 4H, J=8 Hz); 7.8 (d, 4H, J=8 Hz)
4e	4	140–141° (*n*-pentane)	$C_{22}H_{18}O_7$ (394.4)	—	394	3.89 (s, 6H); 4.6 (s, 4H); 6.36 (s, 2H); 6.86 (m, 4H); 7.46 (d, 2H, J=10 Hz)

[a] Satisfactory microanalyses obtained: C ±0.42, H ±0.27, N ±0.13.

hydrogen fluoride/pyridine reagent in order to find out whether the high nucleophilicity of fluoride ion minimizes the formation of side products. The fluoroderivative **2f** was, however, obtained in 45% yield with some unknown by-products. *Moreover, the reaction occurred violently and thus caution is required in handling this reagent.*

Aryldiazomethanes 1:
These are prepared according to the literature procedures[6–10].

Arylmonofluoromethanes 2; General Procedure:
Tetrafluoroboric acid[19] (3.0 mmol) is added to a stirred solution of the appropriate diazoalkane **1** (1.0 mmol) in dichloromethane (10 ml). After 10 min, the mixture is shaken with additional dichloromethane (50 ml) and aqueous 5% sodium hydroxide (50 ml). The organic layer is separated, washed with water (10 ml), and dried with anhydrous sodium sulfate. The solvent is removed under reduced pressure and the residue separated by preparative T.L.C. or column chromatography on silica gel using benzene/ethyl acetate (9:1) as eluent.

Work-up procedure for **2f**: After 10 min, the reaction mixture is concentrated under reduced pressure and the product **2f** is isolated in the manner described above.

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