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Synthesis and characterization of novel trifluoromethyl-containing alcohols with Ruppert's reagent

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ABSTRACT

Synthesis and characterization of novel new trifluoromethyl-containing alcohols using Ruppert's reagent [(trimethyl)trifluoromethylsilane] (**1**) are reported. The reactions of **1** with various ketones and aldehydes, such as tetraphenylcyclopentadienone (**2a**), 9,10-anthraquinone (**2b**), pyrenaldehyde (**2c**), 2,6-dimethyl-para-anisaldehyde (**2d**), and 2,3(methylenedioxy)benzaldehyde (**2e**) in the presence of a catalytic amount of tetrabutylammonium fluoride in THF led to the formation of the corresponding trifluoromethylated silyl ether derivatives **3a–e** in almost quantitative yields. Acid hydrolysis of **3a–e** gave the desired trifluoromethylated alcohol derivatives (**4a–e**) in excellent isolated yields. Compounds were characterized by IR, NMR (^{1}H, ^{19}F, ^{13}C NMR), GCMS, and elemental analysis. Single crystal X-ray structures of **4a** and **4b** support the proposed products.

1. Introduction

Fluorine is the most electronegative element. Therefore, the incorporation of trifluoromethyl group into an organic molecule changes dramatically its physical, chemical, and biological properties [1,2]. The concomitant changes in properties make these compounds suitable for diverse applications in material sciences, and agro chemistry, as well as in the pharmaceutical industry [3–6]. The biological activity [7,8] and numerous commercial applications [9–12] of organo fluorine compounds have encouraged interest in the development of synthetic methods for selective and efficient incorporation of trifluoromethyl groups into organic compounds under mild reaction conditions. Ruppert's reagent [(trimethyl)trifluoromethylsilane] is a well known nucleophilic trifluoromethylating reagent which allows introducing the trifluoromethyl group directly by reaction of substrates such as aldehydes, ketones, and esters. Earlier we and others have shown various applications of this methodology [13–21]. Here we report the synthesis and characterization of some novel trifluoromethylated alcohols using this reagent.

2. Results and discussion

Tetraphenylcyclopentadienone (**2a**) was reacted with 1.25 equivalent of Ruppert's reagent (**1**) in the presence of a catalytic amount of tetrabutylammonium fluoride in THF at room temperature (Scheme 1). The reaction was monitored by gas chromatography.

Based on NMR the yield of the trimethylsilyl ether intermediate (**3a**) was quantitative. Interestingly, **3a**, was found to be hydrolytically stable. Washing the reaction mixture with water and extracting the product with dichloromethane gave pure **3a** in 95% yield. The hydrolysis of **3a** was first attempted with a mixture of concentrated hydrochloric acid and THF (1:1) at room temperature for a few hours but no significant hydrolysis was observed (based on NMR). However, when the mixture was heated at 70 °C for 12 h, hydrolysis was found to be complete (Scheme 1). The product was extracted with dichloromethane and purified by crystallization with dichloromethane/hexane (2:1) to give pure **4a** in 90% yield. See crystal structure (Fig. 1).

Next the reaction of 9,10-anthraquinone (**2b**) was carried out with 2.25 equivalents of **1** in THF vide supra in order to make the bis(trifluoromethyl)diol derivative (**4b**). The formation of the trimethylsilyl ether intermediate (**3b**) was quantitative based on NMR. The hydrolysis of **3b** went smoothly with concentrated hydrochloric acid and THF at room temperature in 3 h (Scheme 2). The hydrolyzed derivative (**4b**) was extracted with dichloro-

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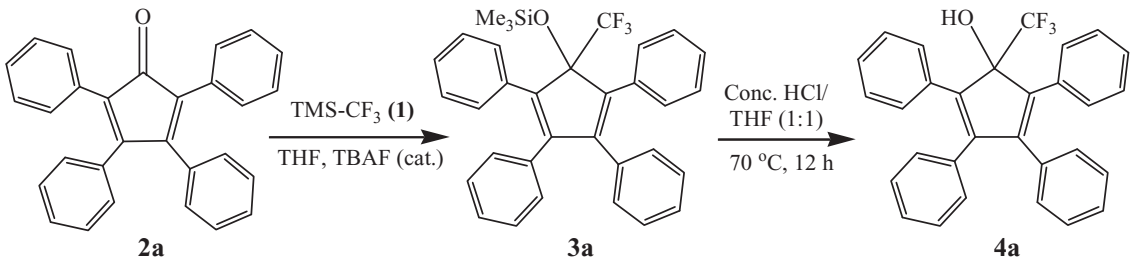


Scheme 1.

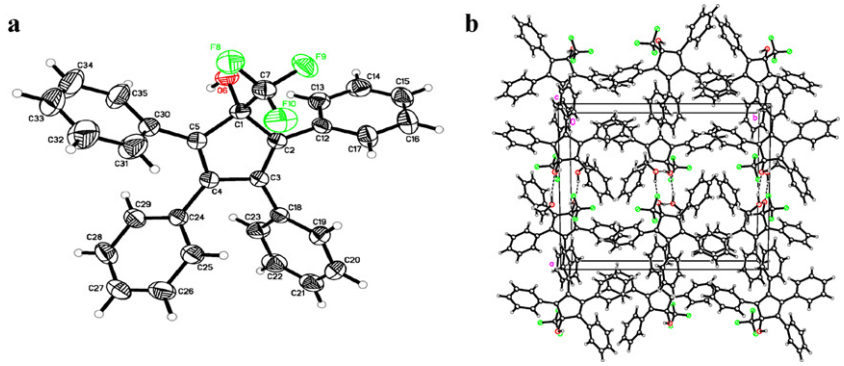
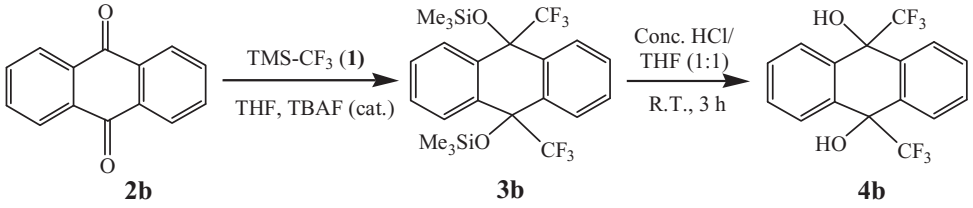


Fig. 1. (a) ORTEP diagram of compound **4a** and (b) crystal packing diagram of **4a**.



Scheme 2.

methane and purified by crystallization with dichloromethane/hexane (2:1) to afford pure **4b** in 88% yield. See crystal structure (Fig. 2).

2,2,2-Trifluoro-1-(1-pyrenyl)ethanol (**4c**) is a valuable compound as reported in the literature [22–24]. Earlier, the synthesis of this compound was reported [25] by the conversion of pyrene into 1-(trifluoroacetyl)pyrene in 65% yield by using $Me_2S{\cdot}BF_3$ in trifluoroacetic anhydride at −78 °C. However, reduction of the ketone group in 1-(trifluoroacetyl)-pyrene using sodium borohydride at 0 °C gave 2,2,2-trifluoro-1-(1-pyrenyl)ethanol (**4c**) in 95% yield (Scheme 3). In our present work, the aldehyde (**2c**) is reacted with 1.25 equivalent of Ruppert's reagent, **1**, and a catalytic amount of TBAF in THF at ambient temperature to yield the corresponding trimethylsilyl ether (**3c**) in quantitative yield (based on NMR). The hydrolysis of **3c** was carried out with concentrated hydrochloric acid and THF mixture (1:1) at room temperature for 3 h to achieve 2,2,2-trifluoro-1-(1-pyrenyl)ethanol (**4c**) in 96% isolated yield (Scheme 3).

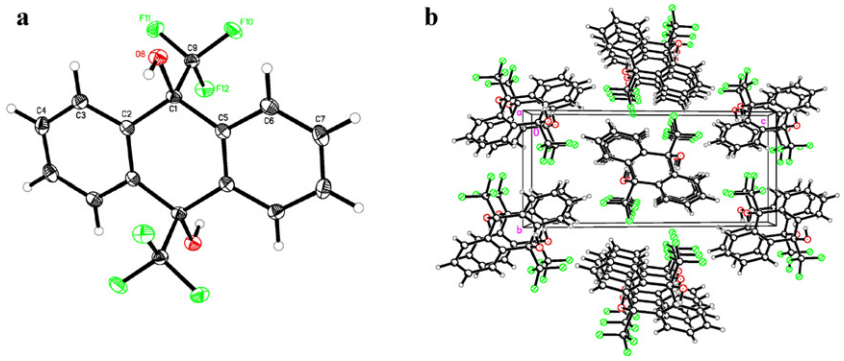
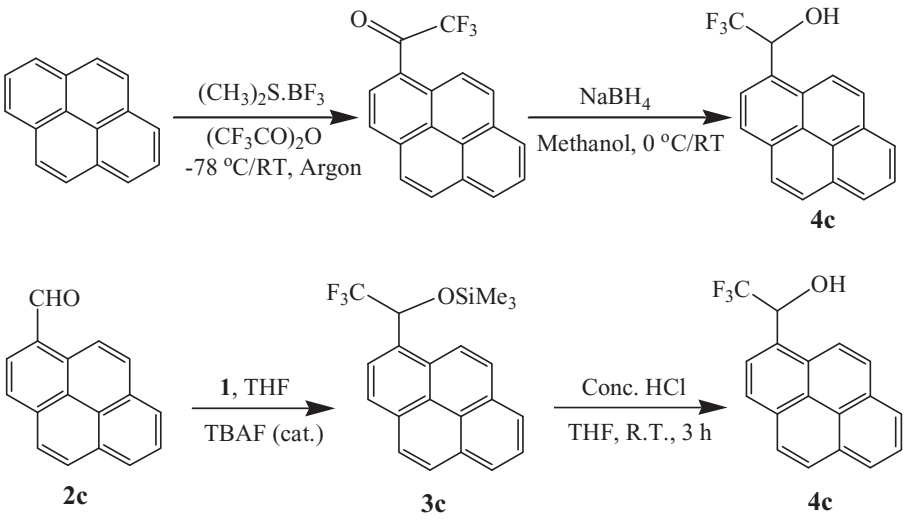


Fig. 2. (a) ORTEP diagram of compound **4b** and (b) crystal packing diagram of **4b**.

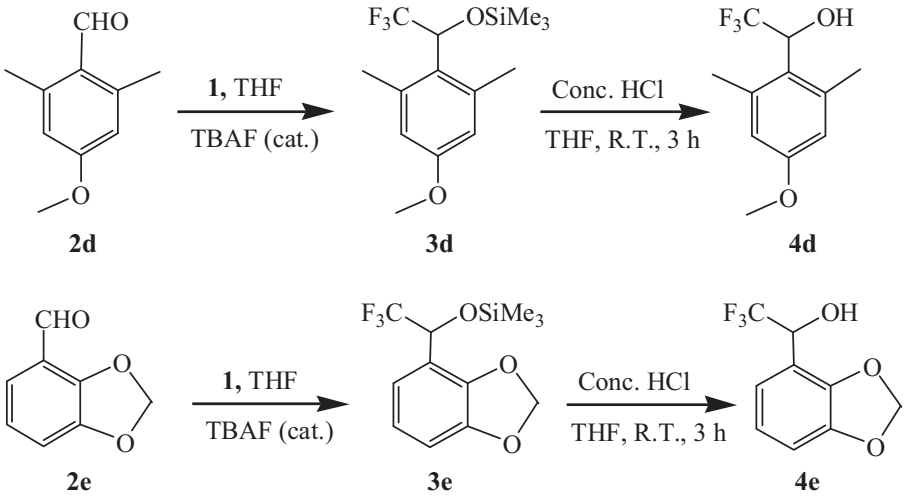


Scheme 3.

Using Ruppert's reagent, aldehydes, **2d–e** were also reacted. The reactions proceed well in THF in the presence of a catalytic amount of TBAF. Based on NMR spectral analyses, the intermediates, **3d–e**, were formed quantitatively. Hydrolysis of **3d–e** with concentrated hydrochloric acid in THF at room temperature produced trifluoromethylated products (**4d–e**) in excellent isolated yields (Scheme 4).

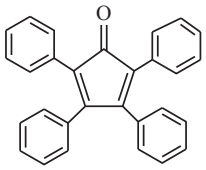
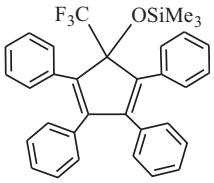
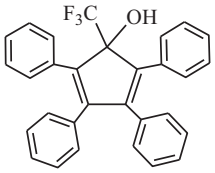
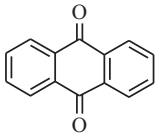
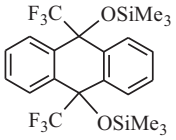
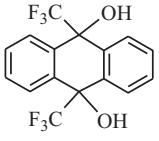
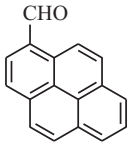
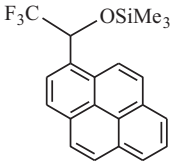
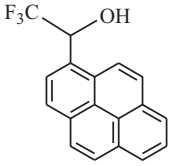
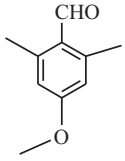
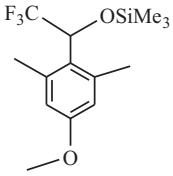
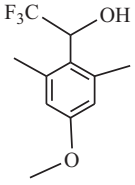
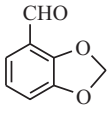
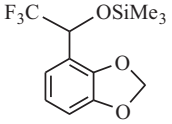
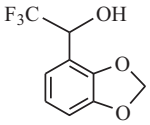
All trifluoromethylated alcohol derivatives (**4a–e**) were fully characterized by IR, NMR, GCMS, and elemental analysis. Some of the trimethylsilyl intermediates were also characterized by spectroscopic and elemental analysis to prove their structures. The characteristic peaks in the proton NMR spectra of the trifluoromethylated silyl ether intermediates (**3a–e**) showed a singlet resonance at about 0.1 ppm arising from the trimethylsilyl group. The CH proton bonded to the same carbon as the CF_3 group appeared as a quartet at 6.20 ppm in **3c**, 5.14 ppm in **3d**, and 5.18 ppm in **3e**, respectively. In the ^{19}F NMR spectra, signals due to the CF_3 group appeared as a singlet at −70.60 ppm in **3a**, −77.95 in **3b** whereas in **3c–e** it was seen as a doublet at -77 ± 1.6 ppm. In the ^{13}C NMR spectra, the CF_3 carbon appeared as a quartet at 125.0 ± 0.6 ppm with J values falling between 280 and 288 Hz in **3a–e**. For compounds **4a–e**, the characteristic peaks in the proton NMR spectra due to the hydroxyl proton appeared at 2.90 in **4a**, 5.21 ppm in **4b**, 2.78 ppm in **4c**, 3.26 ppm in **4d**, and 3.15 ppm in **4e**, respectively. In the ^{19}F NMR spectra, signals due to CF_3 group appeared as a singlet at −70.60 ppm in **4a**, −77.95 in **4b** where as in **3c–e** it appeared as a doublet at -77 ± 1.6 ppm. In ^{13}C NMR the CF_3 carbon appeared as a quartet at 125.0 ± 0.5 ppm with J values between 280 and 287 Hz in **4a–e**. The chemical shifts for CF_3 in the fluorine NMR spectra for compounds **3a–e** and **4a–e** are shown in Table 1.

X-ray quality crystals of compounds **4a** and **4b** were grown from a mixture of chloroform/hexane (1:1). Their structures are presented in Figs. 1 and 2. Selected bond lengths and bond angles are given in Tables 2 and 3, respectively. Crystallographic data are given in Table 4. Both, **4a** and **4b** are monoclinic and crystallize in the $P2_1/c$ space group. Compound **4b** shows an interesting hydrogen bonding pattern. The proposed structures of **4a** and **4b** are in agreement with X-ray analysis.



Scheme 4.

Table 1
Reaction of ketones (**2a**, **b**) and aldehydes (**2c**–**e**) with (trimethyl)trifluoromethylsilane.[a]

Substrate	Intermediate[b]	^{19}F NMR (δ)	Product	Yield (%)[c]	^{19}F NMR (δ)
 **2a**	 **3a**	−70.60	 **4a**	89	−72.88
 **2b**	 **3b**	−77.95	 **4b**	88	−78.65
 **2c**	 **3c**	−76.90	 **4c**	96	−77.33
 **2d**	 **3d**	−78.11	 **4d**	92	−78.49
 **2e**	 **3e**	−78.46	 **4e**	94	−77.78

[a] All the reactions were carried out with 5 mmol of substrate, 5.25 mmol of TMS-CF_3 and 0.1 mmol of TBAF in 10 mL of anhydrous THF (for **2b** 10.25 mmol of TMS-CF_3 was used).
[b] Yield of silylether intermediates is essentially quantitative based on ^{19}F NMR.
[c] Isolated yield.

Table 2
Selected bond lengths (Å) for compounds **4a** and **4b**.

4a		**4b**	
C(1)–O(6)	1.415(2)	C(1)–O(8)	1.4221(14)
C(1)–C(7)	1.528(3)	C(1)–C(5)	1.5223(17)
C(1)–C(5)	1.528(3)	C(1)–C(2)	1.5280(16)
C(1)–C(2)	1.533(3)	C(1)–C(9)	1.5549(16)
C(2)–C(3)	1.339(3)	C(2)–C(3)	1.4016(17)
C(2)–C(12)	1.483(3)	C(3)–C(4)	1.3907(18)
C(3)–C(18)	1.487(3)	C(3)–H(3)	0.9500
C(3)–C(4)	1.492(3)	C(4)–H(4)	0.9500
C(4)–C(5)	1.342(3)	C(5)–C(6)	1.4051(17)
C(4)–C(24)	1.478(3)	C(6)–C(7)	1.3858(19)
C(5)–C(30)	1.476(3)	C(6)–H(6)	0.9500
O(6)–H(6)	0.96(2)	C(7)–H(7)	0.9500
C(7)–F(10)	1.325(3)	O(8)–H(8)	0.8400
C(7)–F(9)	1.332(3)	C(9)–F(12)	1.3359(14)
C(7)–F(8)	1.333(2)	C(9)–F(11)	1.3411(14)

Table 3
Selected bond angles (°) for compounds **4a** and **4b**.

4a		**4b**	
O(6)–C(1)–C(7)	104.32(16)	O(8)–C(1)–C(5)	112.86(10)
O(6)–C(1)–C(5)	114.53(16)	O(8)–C(1)–C(2)	112.46(10)
C(7)–C(1)–C(5)	110.76(18)	C(5)–C(1)–C(2)	114.05(10)
O(6)–C(1)–C(2)	113.87(16)	O(8)–C(1)–C(9)	102.75(9)
C(7)–C(1)–C(2)	110.26(17)	C(5)–C(1)–C(9)	106.91(9)
C(5)–C(1)–C(2)	103.24(15)	C(2)–C(1)–C(9)	106.80(9)
C(3)–C(2)–C(12)	128.75(17)	C(3)–C(2)–C(1)	118.48(11)
C(3)–C(2)–C(1)	108.68(17)	C(4)–C(3)–C(2)	120.77(12)
C(12)–C(2)–C(1)	122.54(16)	C(4)–C(3)–H(3)	119.6
C(2)–C(3)–C(18)	128.71(17)	C(2)–C(3)–H(3)	119.6
C(2)–C(3)–C(4)	109.62(16)	C(3)–C(4)–H(4)	120.1
C(18)–C(3)–C(4)	121.59(16)	C(6)–C(5)–C(1)	118.42(11)
C(5)–C(4)–C(24)	126.84(18)	C(1)–O(8)–H(8)	109.5
C(5)–C(4)–C(3)	109.94(17)	F(12)–C(9)–F(11)	107.63(10)
C(24)–C(4)–C(3)	123.19(16)	F(12)–C(9)–F(10)	107.31(10)
C(4)–C(5)–C(30)	127.28(19)	F(11)–C(9)–F(10)	105.96(9)
C(4)–C(5)–C(1)	108.49(17)	F(12)–C(9)–C(1)	110.32(10)
C(30)–C(5)–C(1)	124.11(17)	F(11)–C(9)–C(1)	112.68(10)
C(1)–O(6)–H(6)	109.4(14)	F(10)–C(9)–C(1)	112.63(10)

Table 4
Selected crystal data and refinement details for compounds **4a** and **4b**.

	4a	**4b**
Chemical formula	$C_{31}H_{25}F_3O_2$	$C_{16}H_{10}F_6O_2$
FW	486.51	348.24
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
Temperature (K)	293(2)	100(2)
a (Å)	14.237(2)	5.7441 (11)
b (Å)	17.734(3)	7.2930(14)
c (Å)	10.2900(16)	16.168(3)
α (°)	90	90
β (°)	99.136(3)	97.618(3)
γ (°)	90	90
V (Å^3)	2565.1(7)	671.3(2)
Z	4	2
Density (calculated) (mg/m^3)	1.620	1.723
μ (mm^{-1})	0.092	0.168
F(000)	1016	352
R_1	0.0475	0.0285
Crystal size (mm^3)	$0.21 \times 0.14 \times 0.06$	$0.37 \times 0.34 \times 0.28$
Reflections collected	23,154	5910
Independent reflections	5254	1361
$R_{int.}$	0.0457	0.0161
Observed [$I > 2s(I)$] reflections	2708	1609
No. of parameters	333	111
Goodness-of-fit	1005	1041

3. Conclusions

Application of Ruppert's reagent in the synthesis of some novel trifluoromethyl containing alcohol derivatives has been described by direct nucleophilic trifluoromethylation reactions from their corresponding ketones or aldehydes. The trimethylsilyl ether intermediates are formed in almost quantitative yield and their acid hydrolysis afforded the corresponding trifluoromethylated alcohols in excellent isolated yield. The proposed structures of 1-trifluoromethyl-2,3,4,5-tetraphenylcyclopentadiene-1-ol and 9,10-bis(trifluoromethyl)-9.10-dihydroxyanthracene have been confirmed by single crystal X-ray analysis.

4. Experimental

All the reactions were carried out in a dry nitrogen atmosphere. (Trifluoromethyl)-trimethylsilane and tetrabutylammonium fluoride (1 M solution in THF) were purchased from Aldrich. Sample preparation of all trimethylsilyl ether intermediates for spectroscopic measurements was carried out under nitrogen atmosphere and anhydrous solvents were used. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker spectrometer operating at 300, 282, and 76 MHz, respectively. Chemical shifts are reported in ppm relative to the appropriate standard, $CFCl_3$ for ^{19}F and TMS for ^{1}H and ^{13}C NMR spectra. Infrared spectra were recorded using a BIO-RAD FT spectrometer. For liquid compounds, a liquid film between KBr discs was used and for solids, KBr pellets were prepared. Melting points were obtained by using a Mel-Temp II apparatus. Mass spectra were recorded on a Shimadzu 5050 spectrometer. Elemental analyses were obtained by using a CE-440 elemental analyzer (EAI Exeter Analytical). Suitable single crystals for **4a** and **4b** were grown using a mixture of chloroform and hexane (1:1).

4.1. X-ray crystallographic details for compounds 4a and 4b

A colorless plate crystal (**4a**) of dimensions 0.21 mm × 0.14 mm × 0.06 mm, or an irregular colorless crystal (**4b**) of dimensions 0.37 mm × 0.34 mm × 0.28 mm was mounted on a MiteGen MicroMesh using a small amount of Cargille Immersion Oil. Data were collected on a Bruker three-circle platform diffractometer equipped with a SMART APEX II CCD detector. The crystals were irradiated using graphite monochromated MoKα radiation (λ = 0.71073). An Oxford Cobra low temperature device was used to keep the crystals at a constant 293(2) K (**4a**) or 100(2) K (**4b**) during data collection.

Data collection was performed and the unit cell was initially refined using *APEX2* [v2010.3-0] [26]. Data Reduction was performed using *SAINT* [v7.60A] [27] and *XPREP* [v2008/2] [28]. Corrections were applied for Lorentz, polarization, and absorption effects using *SADABS* [v2008/1] [29]. The structure was solved and refined with the aid of the programs in the *SHELXTL-plus* [v2008/4] system of programs [30]. The full-matrix least-squares refinement on F^2 included atomic coordinates and anisotropic thermal parameters for all non-H atoms. The H atoms were included using a riding model.

4.2. 1-Trifluoromethyl-2,3,4,5-tetraphenylcyclopentadiene-1-trimethylsilylether (3a)

Tetraphenylcyclopentadienone (**2a**) (5 mmol) and (trimethyl)-trifluoromethylsilane (**1**) (5.25 mmol) were dissolved in tetrahydrofuran (10 mL) and a catalytic amount of tetrabutylammonium fluoride (0.1 mmol) was added at 10 °C. After 10 min stirring, the cold bath was removed and stirring was continued at 25 °C. for 24 h. Based on fluorine NMR, the yield of **3a** was quantitative. All of the volatile materials were removed at reduced pressure. The crude product was purified by crystallization using a dichloromethane/hexane mixture (2:1). Yield: 95%; IR (KBr pellet): 3056, 2959, 1599, 1490, 1443, 1254, 1171, 1097, 1072, 1029, 889, 844, 732, 697 cm^{-1}; ^{1}H NMR (CD_3CN): δ 0.12 (s, 9H), 6.82–7.50 (m, 20H); ^{19}F NMR (CD_3CN): δ −70.60 (s, 3F); ^{13}C NMR (CD_3CN): δ 1.88, 88.0 (q, J = 28.0 Hz), 124.7 (q, J = 287.4 Hz), 127.17, 127.31, 127.4, 127.69, 128.2, 129.6, 130.6; MS (EI) m/z: 526 (M^+), 457, 406, 289, 178, 77, 73; Elemental analysis calcd. for $C_{33}H_{29}F_3OSi$: C, 75.26; H, 5.55. Found: C, 74.51; H, 5.43.

4.3. 1-Trifluoromethyl-2,3,4,5-tetraphenylcyclopentadiene-1-ol (4a)

The silyl ether derivative **3a** (4 mmol) was dissolved in tetrahydrofuran (10 mL) and concentrated hydrochloric acid (10 mL) was added. The reaction mixture was heated at 70 °C for 20 h. It was cooled and mixed with dichloromethane (25 mL) and washed with water (2× 50 mL). The dichloromethane layer is separated and dried over anhydrous magnesium sulfate and filtered. Removal of solvent at reduced pressure gave **4a** as a white solid which was purified by crystallization with a dichloromethane/hexane mixture (2:1). Yield: 90%; IR (KBr pellet): 3541, 3055, 1599, 1489, 1440, 1253, 1169, 1144, 1071, 1028, 909, 731, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.90 (s, 1H), 6.85–7.40 (m, 20H); ^{19}F NMR ($CDCl_3$): δ 72.88 (s, 3F); ^{13}C NMR ($CDCl_3$): δ 89.1 (q, J = 28.2 Hz), 125.0 (q, J = 286.5 Hz), 127.5, 127.8, 127.9, 128.0, 128.2, 129.9, 130.7, 133.9, 140.0, 147.7; MS (EI) m/z (species, rel. int.): 454 (M^+, 100), 406, 385 (M^+-CF_3, 10), 279, 178, 105, 77 ($C_6H_5^+$, 15); Elemental analysis calcd. for $C_{30}H_{21}F_3O$: C, 79.28; H, 4.66. Found: C, 78.74; H, 4.70.

4.4. 9,10-Bis(trifluoromethyl)-9.10-bis(trimethylsiloxy)anthracene(3b)

The reaction was carried out as for **3a** using 9,10-anthraquinone (**2b**) (5 mmol) and (trimethyl)trifluoromethylsilane (**1**) (10.25 mmol). Based on fluorine NMR, the intermediate **3b** is formed quantitatively. IR (KBr pellets): 2968, 1674, 1601, 1447, 1409, 1319, 1260, 1174, 1076, 943, 875, 843, 763, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.06 (s, 18H), 7.4–7.6 (m, 4H), 7.8–8.1 (m, 4H); ^{19}F NMR ($CDCl_3$): δ −77.95 (s, 6F); ^{13}C NMR ($CDCl_3$): δ 2.5, 75.9 (q, J = 28 Hz), 125.6 (q, 288 Hz), 128.4, 129.6, 130.0, 130.5 (q, J = 3 Hz),

131.3, 133.8, 134.3149.0; MS (EI) *m*/*z*: 373 (M^+-F), 423 (M^+-CF_3), 353, 316, 288, 211, 73.

4.5. 9,10-Bis(trifluoromethyl)-9.10-dihydroxyanthracene(4b)

Compound **3b** is dissolved in 10 mL of THF and concentrated hydrochloric acid (10 mL) was added. It was stirred at 25 °C for 3 h, and treated as for **4a**. **4b** is a white solid which was crystallized with chloroform/hexane (2:1) mixture. Yield: 88%; IR (KBr pellets): 3534, 2444, 1483, 1446, 1328, 1211, 1172, 1030, 911, 773, 694, 627 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.21 (s, 2H), 7.61 (s, 4H), 8.03 (s, 4H); ^{19}F NMR ($CDCl_3$): δ −78.65 (s, 3F); ^{13}C NMR ($CDCl_3$): δ 73.7 (q, J = 27 Hz), 118.1, 125.5 (q, 286 Hz) 129.31 (q, J = 2.8 Hz), 130.1; MS (EI) *m*/*z* (species, rel. int.): 348 (M^+, 1), 279 (M^+-CF_3, 55), 210 (M^+-2CF_3, 100), 181 [$M^+-(2CF_3 + COH)$, 25], 152 [$M^+-(2CF_3 + 2COH)$, 20], 105 ($C_6H_4COH^+$, 20), 76 (C_6H_4, 15), 69 (CF_3^+, 10); Elemental analysis calcd. for $C_{16}H_{10}F_6O_2$: C, 55.18; H, 2.89. Found: C, 55.05; H, 2.84.

4.6. 2,2,2-Trifluoro-1-trimethylsiloxy-1-pyrene (3c)

The reaction was carried out as for **3a** using pyrenaldehyde (**2c**) (5 mmol). Based on fluorine NMR, the intermediate white solid **3c** was formed quantitatively. ^1H NMR ($CDCl_3$): δ 0.24 (s, 9H), 6.20 (q, 1H, J = 6.5 Hz), 8.0–8.5 (m, 9H), ^{19}F NMR ($CDCl_3$): δ −76.90 (d, 3F, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$): δ −0.06, −70.4 (q, J = 32.2 Hz), 122.4, 124.8 (q, 285 Hz), 125.1, 125.6, 125.9, 126.3, 126.4, 127.5, 128.24, 128.8, 129.1, 130.6, 131.5, 132.1; MS (EI) *m*/*z*: 372 (M^+), 303 (M^+-CF_3), 233, 201, 73.

4.7. 2,2,2-Trifluoro-1-pyreneethanol (4c)

Compound **3c** is treated as for **4b**. Removal of solvent at reduced pressure gave **4c** as white solid which was crystallized from dichloromethane. Yield: 96%; IR (KBr pellets): 1302, 1249, 11991116, 1080, 887, 839, 755, 694 cm^{-1} ^1H NMR ($CDCl_3$): δ 2.78 (d, 1H, J = 4.5 Hz), 6.18 (dq, 1H, J = 11 Hz, J = 6.3 Hz), 8.0–8.35 (m, 9H), ^{19}F NMR ($CDCl_3$): δ −77.33 (d, 3F, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$): δ 69.58 (q, J = 30.3 Hz), 122.2, 124.8, 124.9, 125.0 (q, J = 280 Hz), 125.1, 125.2, 125.8, 126.1, 126.5, 128.4, 128.8, 129.4, 130.6, 131.5, 132.3; MS (EI) *m*/*z*: 300 (M^+), 231, 203, 202, 100, 69. Elemental analysis calcd. for $C_{16}H_{10}F_6O_2$: C, 72.00; H, 3.69; Found: C, 71.84; H, 3.63.

4.8. 2,2,2-Trifluoro-1-(2,6-dimethyl-4-methoxyphenyl)trimethylsilylether (3d)

The reaction is carried out as for **3a** using 2,6-dimethyl-4-methoxybenzaldehyde (**2d**) with stirring at 25 °C for 5 h. All the solvents were removed at reduced pressure. The resulting liquid is mixed with ether and hexane (10 mL, 1:1 mixture) and filtered through a small pipette of silica gel to remove TBAF. Removal of solvent at reduced pressure gave the desired trimethylsilyl ether derivative (**3d**) as a liquid. Yield: 90%; IR (liquid): 2958, 1614, 1506, 1254, 1177, 1133, 1035, 880, 843 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.11 (s, 9H), 2.26 (s, 3H), 3.82 (s, 3H), 5.14 (q, 1H, J = 6.7 Hz), 6.60 (s, 1H), 7.35 (s, 1H); ^{19}F NMR ($CDCl_3$): δ −78.11 (d, 3F, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$): δ −0.08, 16.2, 55.3, 69.5 (q, J = 32.0 Hz), 111.7, 119.4, 124.5 (q, 281.0 Hz) 130.6, 158.1; MS (EI) *m*/*z* (species, rel. int.): 306 (M^+, 50), 237, 163, 77, 73; Elemental analysis calcd. for $C_{14}H_{21}F_3O_2Si$: C, 54.88; H, 6.91. Found: C, 54.71; H, 6.94.

4.9. 2,2,2-Trifluoro-1-(2,6-dimethyl-4-methoxyphenyl)ethanol (4d)

The silylether derivative (**3d**) (4 mmol) was treated as for **4b**. Removal of solvent at reduced pressure gave **4d** which was purified by silica-gel chromatography using ethylacetate/hexane (1:3) mixture. Yield: 92%; IR (neat on KBr window): 3410, 2951, 1616, 1512, 1463, 1294, 1258, 1166, 1124, 1100, 843, 758, 685 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.21 (s, 3H), 3.26 (broad, s, 1H), 3.85 (s, 3H), 5.25 (dq, 1H, J = 13.0 Hz, J = 6.6 Hz), 6.65 (s, 2H); ^{19}F NMR ($CDCl_3$): δ −77.78 (d, 3F, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$): δ 16.7, 56.2, 69.4 (q, J = 32.0 Hz), 112.9, 124.7 (q, 280.5 Hz), 129.9, 36.1, 159.0; MS (EI) *m*/*z*: 234 (M^+), 165, 137, 122, 91, 69; Elemental analysis calcd. for $C_{11}H_{13}F_3O_2$: C, 56.41; H, 5.59. Found: C, 54.95; H, 6.02.

4.10. 2,2,2-Trifluoro-1-(2,3-methylenedioxyphenyl)ethanol (4e)

The reaction is carried out as for **3a** using 2,3-methylenedioxyphenyl benzaldehyde (**2e**) with stirring at 25 °C for 5 h. Based on NMR the trimethylsilylether intermediate (**3e**) is formed quantitatively. An aliquot was drawn from the reaction mixture and the solvent was removed at reduced pressure and spectroscopic data were collected for **3e**. To the remainder of the reaction mixture, concentrated hydrochloric acid (10 mL) was added and the reaction mixture was stirred at 25 °C for 3 h. It was mixed with dichloromethane (10 mL) and washed with water (2× 25 mL). The dichloromethane layer is separated and dried over magnesium sulfate and filtered. Removal of solvent at reduced pressure gave **4e** as liquid product which was purified by silica-gel chromatography using ethyl acetate/hexane mixture (1:3).

4.11. 2,2,2-Trifluoro-1-(2,3-methylenedioxyphenyl)trimethylsilylether (3e)

IR (neat on KBr disc): 2963, 2901, 1464, 1365, 1243, 1176, 1130, 1055, 991, 933, 873, 845, 731 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.18 (q, 1H, J = 6.5 Hz), 5.97 (d, 1H, J = 1.5 Hz), 6.00 (1H, J = 1.5 Hz), 6.8–6.91, m, (2H), 7.07 (d, J = 7.5 Hz); ^{19}F NMR ($CDCl_3$): δ −78.46 (d, 3F, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$): δ 67.75 (q, J = 33.4 Hz), 101.4, 109.2, 120.9, 121.9, 124.4 (q, J = 280.5 Hz), 145.7, 147.4; MS (EI) *m*/*z*: 234 (M^+), 165 (M+–CF_3), 137, 122, 105, 91, 77, 69.

4.12. 2,2,2-Trifluoro-1-(2,3-methylenedioxyphenyl)ethanol (4e)

Yield: 94%; IR (liquid): 3455, 2904, 1605, 1466, 1359, 1249, 1175, 1128, 1049, 980, 930, 835, 796, 771, 731, 689 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.15 (d, 1H, J = 6.6 Hz), 5.10 (dq, 1H, J = 13.4 Hz, J = 6.7 Hz), 5.96 (d, 2H, J = 6.0 Hz), 6.70–6.95 (m, 3H); ^{19}F NMR ($CDCl_3$): δ −78.49 (d, 3F, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$): δ 69.1 (q, J = 33.0 Hz), 101.5, 109.6, 115.9, 120.5, 122.2, 124.5 (q, 280.8 Hz), 145.8, 147.7; MS (EI) *m*/*z*: 220 (M^+, 40), 151, 123, 93, 75, 65; Elemental analysis calcd. for $C_9H_7F_3O_3$: C, 49.10; H, 3.20. Found: C, 49.17; H, 3.23.

Supplementary data

Crystallographic data for compounds **4a** and **4b** have been deposited with the Cambridge Crystallographic Data Center allocated deposit numbers CCDC 831455 and 831456. A copy of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223 336033, e mail: deposit@ccdc.ac.uk.

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