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Solvent-free Fluorination of Electron Rich Aromatic Compounds with F-TEDA-BF_4 Reagent: Toward "Dry" Processes

Pavel A. Zaikin,*[a] Ok Ton Dyan,[a] Darya V. Evtushok,[c] Andrey N. Usoltsev,[c] Gennady I. Borodkin,[a, b] Elena V. Karpova,[a, b] and Vyacheslav G. Shubin[a]

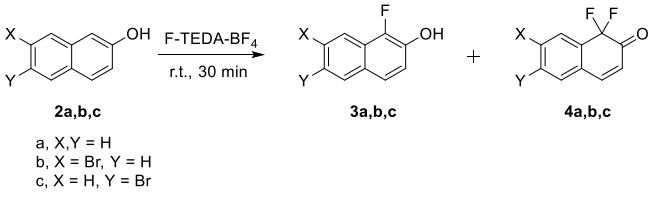
Abstract: Effective protocol of solvent-free fluorination of electron rich aromatic compounds with F-TEDA-BF_4 reagent is described. The protocol allows easy and efficient isolation of fluorinated products by vacuum sublimation without use of any solvent with high yields and purity and low E-factor values. Solid-state fluorination of naphthalene-2-ol was suggested by differential thermal analysis. Scanning electron microscopy is used to obtain evidences for the solid-state process. Crucial influence of alkali metal carbonates on the rate of solvent-free fluorination of hydroxynaphthalenes and estrone was demonstrated.

Introduction

Fluorination of aromatic compounds is of great practical importance as fluoroaromatic compounds constitute a class of widespread organic intermediates as well as fine chemicals with applications as pharmaceuticals, materials and dyes.[1,2]
Fluorinated aromatic compounds are of great importance for pharmaceutical industry[1-3] due to unique influence of fluorine substituent on biological properties.[4,5] As many as 30-40% agrochemicals and 20% of pharmaceuticals on the market are estimated to contain fluorine.[6] Development of new safe and environmentally benign methods of fluorination is on the agenda.[7] The development of electrophilic fluorinating agents of NF class to tame the reactivity of elemental fluorine resulted in great advancements in direct fluorination of C-H bonds.[8a,b,9] Turn from volatile organic solvents to more "green" alternatives is one of the most demanding areas of research.[10,11] Recent advances in "green" fluorination with NF-reagents includes reactions in room-temperature ionic liquids (IL), IL-alcohol,[12,13] supercritical carbon dioxide,[14] water[15,16] and PEG-400, H_2O-PEG-400[17,18] use of microwave irradiation for low energy consumption.[19-21] But possibly the most significant decrease of the environmental footprint of most industrial processes would be the complete elimination of the solvent. Avoiding the use of solvents is a crucial point for sustainability of organic synthesis.[22]
Despite the rapidly growing interest to the solvent-free and mechanochemical organic synthesis in last decade[23,24] only limited data concerning solvent-free aromatic fluorination has been published to date.[22, 25-29]
As a part of our ongoing effort to develop environmentally benign methods of electrophilic aromatic fluorination[12,15,28-30] we began to investigate a solvent-free fluorination of electron rich aromatic compounds with 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis (tetrafluoroborate) F-TEDA-BF_4 (Selectfluor™) reagent **1**.
Herein we describe a protocol of solvent-free fluorination of electron rich aromatic compounds with F-TEDA-BF_4 reagent. The protocol allows easy and efficient isolation of fluorinated products by vacuum sublimation without use of any solvent at any stage of the process. More effective conditions that could be achieved for this reaction are important for development of sustainable fluorine chemistry.

Results and Discussion

The first substrate we used was naphthalene-2-ol **2a** as one of the most reactive aromatic compounds in electrophilic fluorination.[31]
Fluorinated naphthalene derivatives were used in synthesis of nematic liquid crystals,[32] quinonoid molecules[33] and modern anticancer drugs.[34] For example, fluorination of 6-bromonaphthalene-2-ol with F-TEDA-BF_4 reagent in solvents was employed for preparation of fluorinated liquid crystals.[32]
Solvent-free fluorination of naphthalene-2-ol **2a** with equimolar quantity of F-TEDA-BF_4 resulted in formation of 1-fluoronaphthalene-2-ol **3a** and 1,1-difluoro-2(1*H*)-naphthalenone **4a** with 29 and 21% yield respectively (Scheme 1).



Scheme 1. Fluorination of substituted naphthalene-2-ols with F-TEDA-BF_4.

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To improve the selectivity of 1,1-difluoro-2(1*H*)-naphthalenone formation we carried out fluorination of naphthalene-2-ol with 2.2 equivalents of fluorinating reagent. Increase of NF-reagent loading resulted in complete conversion of aromatic substrate and exclusive formation of 1,1-difluoro-2(1*H*)-naphthalenone. Direct fluorination is potentially very efficient in terms of utilization of reagents: the C–H is replaced directly with C–F.[35] Solvents account for 75-80% of the waste associated with the synthesis of active pharmaceutical ingredients and solvent waste disposal adds substantial cost to production of pharmaceutical ingredients.[7] Solventless reactions with high yield of pure product are the better choice. A true ‘‘solventless synthesis’’ must exclude any solvent when reactants interact to the pure product. This requires a quantitative reaction to one product without solvent-consuming chromatography after a stoichiometric reaction.[36] Efficiency of combination of solvent-free synthesis and solvent-free isolation by vacuum sublimation has been demonstrated on the synthesis of nitroso compounds.[37] We tried to implement solventless concept with the use of sublimation technique to obtain pure 1,1-difluoro-2(1*H*)-naphthalenone from the reaction mixture. The target naphthalenone was obtained in 70% yield. Even with large excess of fluorinating reagent the E-factor for this process could be estimated to 5,7 KgwasteKgprod-1. compare to the processes in manufacturing of fine chemicals in which a large amount of waste is produced (the E factor is 5–100 KgwasteKgproduct^{-1}).[38]

To prove the scalability of the reaction studied we carried out fluorination of naphthalene-2-ol on gram and 10-gram scale. Fluorination of 1 g of naphthalene-2-ol with 2.2-fold excess of F-TEDA-BF_4 followed by sublimation resulted in obtaining of target 1,1-difluoronaphthalen-2(1*H*)-one with exceptional purity of 99% by GC and 71% preparative yield. Fluorination on 10-gram scale resulted in formation of 1,1-difluoronaphthalen-2(1*H*)-one with slightly higher yield of 75%.

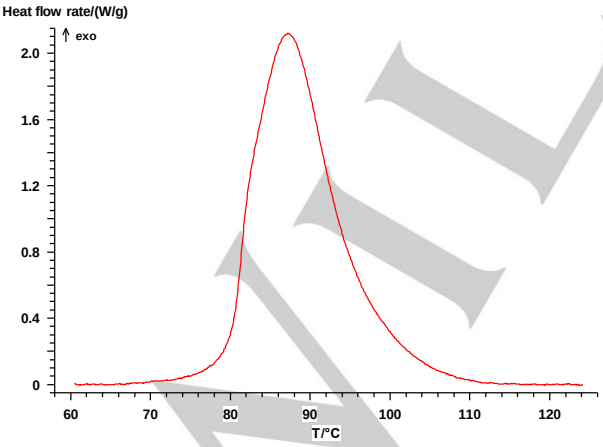


Figure 1. DSC curve obtained on 1:2 mixture of naphthalene-2-ol - F-TEDA-BF_4 at 6.7°C/min heating rate.

The possibility of truly solid-state reactions between two organic compounds is quite controversial.[39] Differential scanning calorimetry (DSC) have been proposed to be useful method of detection of formation of liquid eutectic melts during the solvent-free organic reactions.[40] To ensure that the fluorination of naphthalene-2-ol takes place without macroscopic melting we investigated reaction mixture with differential thermal analysis method (Figure 1). As one can see there was no endothermal effect corresponding to melting of reagents and formation of eutectic mixture

Scanning electron microscopy (SEM) is another tool to obtain evidences of solid-state process. SEM imaging could help us to fix any signs of macroscopic melting of the reaction mixture during mechanochemical reaction. We took series of images of reagents alone and the reaction mixture after 10, 15, 20 and 30 minutes of grinding (Figure 2, b, c, d and e,f respectively). As one could see during the reaction large particles of naphthalene-2-ol disappeared with formation of finely ground mixture without any signs of macroscopic melting.

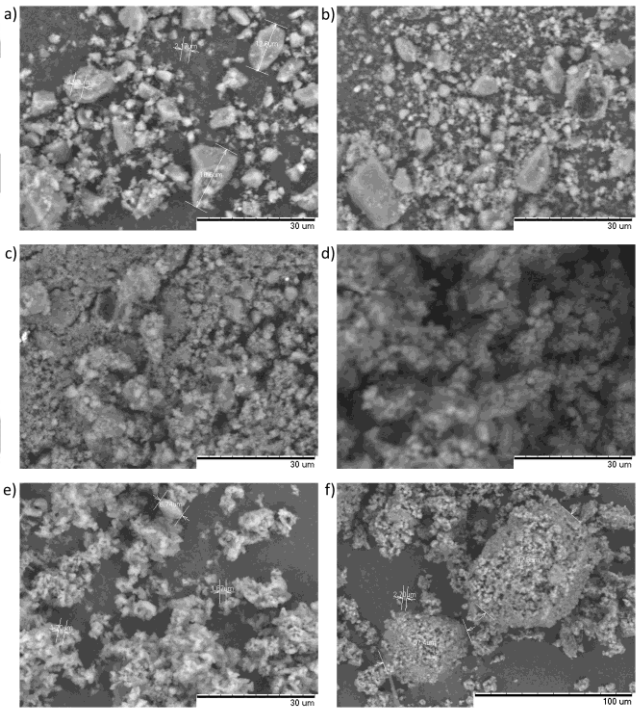


Figure 2. SEM images of the reaction mixture of naphthalene-2-ol – F-TEDA-BF_4 (1 : 2.2) during mechanochemical synthesis. Initial mixture (a), after 10 (b) 15 (c), 20 (d) and 30 (e x2500 ,f x1000) minutes of grinding.

It was a bit surprising that fluorination of naphthalene-2-ol proceeded even without continuous grinding. Holding of 1:2.2 mixture of naphthalene-2-ol and F-TEDA-BF_4 at room temperature without any additional grinding resulted in 75% conversion after a week and 85% conversion after 16 days (Figure 3).

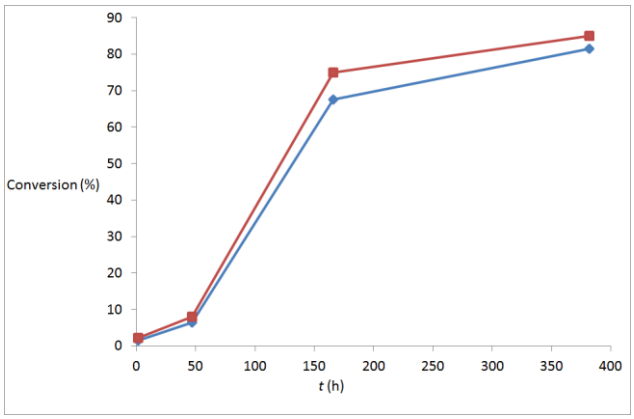


Figure 3. Dependence of conversion of reagents on holding time, red line: **1**, blue line: **2a**.

To obtain deeper insights into non-stimulated fluorination process we investigated the reaction mixture of naphthalene-2-ol with 2.2-fold excess of F-TEDA-BF_4 by *in situ* scanning electron microscopy (Figure 4). On the initial image large darker particle of 2-naphthalene-2-ol is surrounded by smaller lighter particles of F-TEDA-BF_4. After 60 h the naphthalene-2-ol particle transformed into conglomerate of much smaller particles of products similar as in grinding experiments (Figure 4,area *a*).

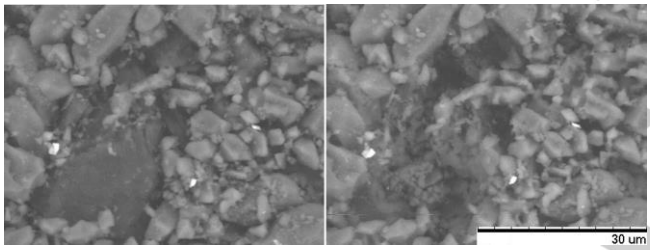
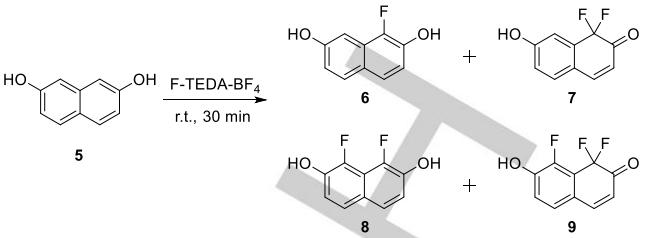


Figure 4. In situ SEM imaging of non-stimulated fluorination of 2-naphtol. Starting reaction mixture (left) and reaction mixture after 60 h (right).

Fluorination of 6-bromonaphthalene-2-ol with 2.2-fold excess of F-TEDA-BF_4 required longer reaction time. Full conversion of starting materials was achieved after 90 min of total grinding time leading to 95% NMR yield. Exploiting of the grinding-sublimation sequence on a gram scale allowed to obtain target 6-bromo-1,1-difluoronaphthalen-2(1*H*)-one in 84% isolated yield. The E-factor of 3.7, calculated for the fluorination of 6-bromonaphthalene-2-ol was even smaller than that for fluorination of naphthalene-2-ol.

Fluorination of more reactive naphthalene-2,7-diol with two-fold excess of F-TEDA-BF_4 led to formation of complex mixture, which contains besides of 1-fluoronaphthalene-2,7-diol and 7-hydroxy-1,1-difluoronaphthalene-2(1*H*)-one substantial amounts of 1,8-difluoronaphthalene-2,7-diol and 7-hydroxy-1,1,8-trifluoronaphthalene-2(1*H*)-one. Increase of excess of F-TEDA-BF_4 to 3 resulted in formation of mixture of only naphthalenones **7** and **9** in 1:0.93 ratio.



Scheme 2. Fluorination of naphthalene-2,7-diol with F-TEDA-BF_4.

Table 1. Solvent-free fluorination of phenols.

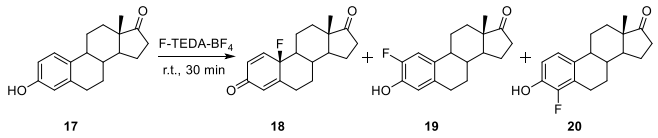
Entry	Substrate	ArH : NF molar ratio	Time, min	Products[a]
2	**2a**	1:1	30	1,1-difluoronaphthalen-2(1*H*)-one **4a** (21%), 1-fluoronaphthalene-2-ol **3a** (29%)
3	**2a**	1:2.2	30	1,1-difluoronaphthalen-2(1*H*)-one **4a** (94%, [70%][b]), 1-fluoronaphthalene-2-ol **3a** (1%)
4	**2c**	1:2.2	90	6-bromo-1,1-difluoro-2(1*H*)-naphthalenone **4b** (95%, [84%][b])
5	**5**	1:3	30	7-hydroxy-1,1-difluoronaphthalene-2(*1H*)-one **7** (47%), 7-hydroxy-1,1,8-trifluoronaphthalene-2(1H)-one **9** (44%)
6	**10**	1:1	30	2-fluoro-4-methylphenol **11** (41%), 4-fluoro-4-methylcyclohexa-2,5-diene-1-one **12** (16%)
7	**13**	1:1	30	3,4-dimethylcyclohexa-2,5-diene-1-one **14** (29%), 6-fluoro-3,4-dimethylphenol **15** (3%), 2-fluoro-3,4-dimethylphenol **16** (7%)
8	**17**	1:1	30	10β-fluoro-1,4-estradiene-3,17-dione **18** (21%), 2-fluoroestron **19** (2%), 4-fluoroestron **20** (2%)

[a] NMR yield determined by addition of weight standard are given in parenthesis. [b] Isolated yield

Fluorination of *para*-cresol **10** resulted in 41% conversion and formation of 2-fluoro-4-methylphenol **11** with 16% yield along with trace amounts of 4-fluoro-4-methylcyclohexa-2,5-diene-1-one **12** – product of *ipso*-attack of electrophilic fluorine at 4-position. *Ipso*-fluorination became mainstream in the case of 3,4-dimethylphenol **13**, which reacted with equimolar amount of

F-TEDA-BF_4 upon grinding for 30 min with formation of 4-fluoro-3,4-dimethylcyclohexa-2,5-diene-1-one **14** with 29% yield along with 7% of 6-fluoro- and 3% of 2-fluoro isomers **15** and **16** respectively. Similarly, formation of large amounts of *ipso*-fluorinated product was observed in fluorination of such a substrate in solutions.[41] Solvent-free fluorination leads to relatively larger amount of 2-fluoro-4-methylphenol compare to fluorination in acetonitrile and close to *ipso*-/*ortho*- ratio obtained in MeOH.[41]

Estrone **17** undergone fluorination similarly to its analog - 5,6,7,8-tetrahydro-2-naphthol[42] with formation of main product of electrophilic *ipso*-attack – ketone **18** along with substantially lower amounts of *ortho*-fluorinated products **19** and **20** (Scheme 3).



Scheme 3. Fluorination of estrone.

Table 2. Effect of alkali metal carbonates.

Entry	Substrate	Products[a]
1	Naphthalene-1-ol/K_2CO_3[b]	2-fluoronaphthalene-1-ol (1%), 4-fluoronaphthalene-1-ol (1%), 2,4-difluoronaphthalene-1-ol (1%), 2,2-difluoronaphthalen-1(2*H*)-one (19%), 4,4-difluoronaphthalen-1(4*H*)-one (2%)
2	Estrone/Li_2CO_3	10β-fluoro-1,4-estradiene-3,17-dione (18%), 2-fluoroestrone (1%), 4-fluoroestrone (1%)
3	Estrone/Na_2CO_3	10β-fluoro-1,4-estradiene-3,17-dione (12%), 2-fluoroestrone (1%), 4-fluoroestrone (1%)
4	Estrone/K_2CO_3	10β-fluoro-1,4-estradiene-3,17-dione (32%), 2-fluoroestrone (3%), 4-fluoroestrone (3%)
5	Estrone/Rb_2CO_3	10β-fluoro-1,4-estradiene-3,17-dione (12%), 2-fluoroestrone (<1%), 4-fluoroestrone (<1%)
6	Estrone/Cs_2CO_3	Complex mixture
7	6-bromonaphthalene-2-ol /Cs_2CO_3	6-bromo-1,1-difluoro-2(1*H*)-naphthalenone (76%)
8	7-bromonaphthalene-2-ol /Cs_2CO_3	7-bromo-1,1-difluoro-2(1*H*)-naphthalenone (78%)

[a] NMR yield determined by addition of weight standard are given in parenthesis.

In contrast to naphthalenols studied 7-bromonaphthalene-2-ol **2b** and naphthalene-1-ol reacted with F-TEDA-BF_4 only in little extent. To improve the yields of fluorinated products we attempted to enhance reactivity of phenols by complexing with alkali metal carbonates. It has been previously shown that complexation of phenols with potassium carbonate in DMF resulted in considerable increase of nucleophilicity of such substances.[43]

Grinding of unreactive naphthalene-1-ol with equimolar amount of potassium carbonate for 10 min. followed by typical fluorination procedure led to activation of the substrate and formation of mixture of products (see Table 2).

In case of 7-bromonaphthalene-2-ol 10-min. advance grinding with cesium carbonate led to substantial increase of activity of aromatic substrate and formation of 7-bromo-1,1-difluoro-2(*1H*)-naphthalenone with 78% yield.

We investigated the influence of alkali metal cation on the reactivity of estrone. Fluorination of estrone in the presence K_2CO_3 led to approximately 1.5-fold increase of products yields comparing to fluorination without carbonate wheares in the case of sodium or rubidium carbonates approximately two-fold decrease of products yields is observed. It has been previously shown that the nature of the alkali metal cation influenced the transformation of F-TEDA-BF4, the highest being with Li^+, Na^+ Cs^+ and the lowest with K^+.[44]

Conclusions

Efficient and ecologically benign method of fluorination of activated aromatic compounds was developed. Solventless fluorination of naphthalene-2-ols was performed by implication of vacuum sublimation for isolation of fluorinated products with high yields and purity. Solid-state fluorination of naphthalene-2-ol was suggested by differential thermal analysis and scanning electron microscopy. The influence of alkali metal carbonates on the rate of solvent-free fluorination of naphthalenols and estrone was demonstrated.

Experimental Section

^1H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$ or acetone-d_6 on Bruker AV-300 and AV-400 spectrometers and chemical shifts are given in ppm relative to TMS and $CFCl_3$ respectively with C_6F_6 (^{19}F, -162.9 ppm) or residual solvent signals (^1H, ^{13}C) as secondary external standards. GC/MS spectra were recorded on an Agilent instrument operating at 70eV. High resolution mass spectra (HRMS) were measured using DFS instrument. IR spectra were recorded on Bruker Vector 22 spectrometer and UV-Vis spectra were recorded on Varian Cary 5000 spectrophotometer (lgε is indicated in brackets). Elemental analysis was performed on EA-3028 analyzer. SEM images were obtained on Hitachi TM-1000 instrument, DTA analysis was performed on Netzsch STA 409 thermoanalyser. Melting points were recorded on Mettler-Toledo FP81. All reactants were obtained from commercial sources and used without further purification. Spectral data of products obtained were consistent with literature data (see Supporting Information).

General procedure for room-temperature fluorination of phenols with F-TEDA-BF_4. A mixture of aromatic substrate (0.5 mmol) and fluorination reagent was ground in agate mortar for the time indicated in Table 1. Reaction mixture was then extracted with ether and the solvent was removed in vacuo to yield crude products which were analyzed by ^1H, ^{19}F NMR spectroscopy and GC/MS. Yields were determined by

integration of signals of products in NMR spectra with comparison of signal intensity of weight standard ($PhCF_3$) added.

General procedure for fluorination of naphthalene-2-ols with F-TEDA-BF_4 followed by vacuum sublimation. Naphthalene-2-ol (1.00 g, 7 mmol) and F-TEDA-BF_4 (5.46 g, 10 mmol) were ground in mortar at room temperature for 30 min. the mixture was maintained at room temperature overnight and then sublimed in vacuo at 70˚C to yield 1,1-difluoronaphthalen-2(1*H*)-one as yellow needles (0.88 g, 70%). mp 51˚C (cf. 50˚C [45]).

General procedure for fluorination of naphthalenols and estron with F-TEDA-BF_4 in the presence of alkali metal carbonates. A mixture of phenol (0.5 mmol) and metal carbonate (0.5 mmol) was ground in agate mortar for 10 min. Then fluorination reagent (0.5 mmol) was added and the reaction mixture was ground for additional 30 min., then was extracted with ether, the solvent was removed in vacuo to yield a crude product. Residue was dissolved in $CDCl_3$ or acetone-d_6 and directly analyzed by ^1H, ^{19}F NMR spectroscopy and GC/MS. Yields were determined by integration of signals of products in NMR spectra with comparison of signal intensity of weight standard added (α,α,α-trifluorotoluene, $PhCF_3$, or C_6F_6 for ^{19}F, CH_2Br_2 for ^1H).

6-bromo-1,1-difluoro-2(1H)-naphthalenone. m.p. 67.4-68.3°C; ^1H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=6.28 (dt, J=10.2, 2.7 Hz, 1H, H_3) 7.57 (d, J=10.2 Hz, 1H, H_4) 7.63 - 7.88 (m, 3H, $H_{5,7,8}$); ^{13}C NMR (126 MHz, $CDCl_3$, 25°C, TMS) δ=105.1 (t, J=245.3 Hz, C_1) 124.5 (t, J=2.4 Hz, C_8) 126.4 (t, J=2.5 Hz, C_6) 129.1 (t, J=3.3 Hz, C_3) 131.7 (t, J=23.9 Hz, C_{8a}) 131.9 (t, J=5.5 Hz, C_{4a}) 132.5 (s, C_5) 133.6 (t, J=1.8 Hz, C_7) 143.9 (s, C_4) 186.6 (t, ^2J(C,F)=25.1 Hz, C_2) ^{19}F (282 MHz, $CDCl_3$, 25°C, $CFCl_3$): δ -101.4 (s); IR (KBr): ν = 1699 cm^{-1} (C=O); UV/Vis ($CHCl_3$): λ_{max} (ε, $mol^{-1}dm^3cm^{-1}$) 240 (300), 320 nm (54); elemental analysis: calcd (%) for $C_{10}H_5BrF_2O$ (259.1): C 46.36, H 1.95, F 14.67, Br 30.85; found: C 46.07, H 1.80, F 14.64, Br 31.01.

7-bromo-1,1-difluoro-2(1H)-naphthalenone. R_f=0.54 (SiO_2, $CHCl_3$); m.p. 92.2-96.7°C; ^1H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=6.28 (dt, ^3J(H,H)=10.2 Hz, ^4J(H,F)=2.7 Hz, 1H, H_3), 7.24-7.28 (m, 1H, H_5), 7.42 (d, ^3J(H,H)=10.2 Hz, 1H, H_4), 7.66-7.75 (m, 1H, H_6), 7.95-8.01 (m, 1H, H_8); ^{13}C (101 MHz, $CDCl_3$, 25°C, TMS): δ=104.8 (t, ^1J(C,F)=246.4 Hz, C_1), 123.7 (t, J(C,F)=2.4 Hz, C_3), 125.7 (t, J(C,F)=2.3 Hz, C_7), 129.1 (t, J(C,F)=5.6 Hz, C_{4a}), 131.0 (t, J(C,F)=3.6 Hz, C_8), 131.1 (s, C_5), 134.7 (t, ^2J(C,F)=23.6 Hz, C_{8a}), 135.4 (t, J(C,F)=2.0 Hz, C_6), 144.7 (t, J(C,F)=1.5 Hz, C_4), 186.4 (t, ^2J(C,F)=24.6 Hz, C_2); ^{19}F (282 MHz, $CDCl_3$, 25°C, $CFCl_3$): δ=-101.4 (s); IR (KBr): ν=1693 cm^{-1} (C=O); UV/Vis ($CHCl_3$): λ_{max} (ε)=240 (300), 320 nm (54 $mol^{-1}dm^3cm^{-1}$); elemental analysis: calcd (%) for $C_{10}H_5BrF_2O$ (259.1): C 46.36, H 1.95, F 14.67, Br 30.85; found: C 46.40, H 1.99, F 14.39, Br 31.00.

1,1-difluoro-7-hydroxy-2(1H)-naphthalenone. mp 147.1-147.2°C; ^1H NMR (300 MHz, $CDCl_3$, 25°C, TMS): δ=6.06 (dt, ^3J(H,H)=10.0 Hz, ^4J(H,F)=2.7 Hz, 1H, H^3) 6.41 (br. s, 1H, OH) 6.90 - 6.97 (m, 1H, H^6) 7.20 - 7.26 (m, 1H, H^5) 7.26 - 7.30 (m, 1H, H^8) 7.37 (d, ^3J(H,H)=10.0 Hz, 1H, H^4); ^{13}C (101 MHz, $CDCl_3$, 25°C, TMS): 105.3 (t, J(C,F)=245.6 Hz, C^1) 115.8 (t, J(C,F)=3.5 Hz, C^8) 118.7 (t, J(C,F)=1.7 Hz, C^6) 120.9 (t, J(C,F)=2.3 Hz, C^3) 123.4 (t, J(C,F)=5.2 Hz, C^{4a}) 132.1 (s, C^5) 135.7 (t, J(C,F)=23.5 Hz, C^{8a}) 146.1 (s, C^4) 158.6 (t, J(C,F)=1.7 Hz, C^7) 187.8 (t, J(C,F)=24.1 Hz, C^2); ^{19}F (282 MHz, $CDCl_3$, 25°C, $CFCl_3$): -102.0 (s, 2F).; IR (KBr): 3354; 2924; 1684; 1612; 1558; 1510; 1346; 1315; 1250; 1227; 1190; 1149; 1041; 883; 845 cm^{-1}; UV-Vis (MeOH): λ_{max}, nm (lgε) = 249 (4.18), 376 (4.75); HRMS found m/z 196.0329 [M+]. Calc. for $C_{10}H_6F_2O_2$. M = 196.0336; elem. anal. found, %: C 61.31, H 3.06; F 19.20. calc. for $C_{10}H_6F_2O_2$, %: C 61.23; H 3.08; F 19.37.

1,1,8-trifluoro-7-hydroxy-2(1H)-naphthalenone. ^1H NMR (300 MHz, CD_3CN, 25°C, TMS): δ=6.09 (dt, J=10.2, 3.0 Hz, 1H, H^3) 7.11 - 7.24 (m, 2H, $H^{5,6}$) 7.54 (dd, J=10.2, 2.1 Hz, 1H, H^4) 8.13 (br. s., 1H, OH); ^{13}C (101 MHz, CD_3CN, 25°C, TMS): δ= 105.7 (td, J=244.6, 1.8 Hz, C^1) 121.1 (td, J=22.3, 9.3 Hz, C^{8a}) 121.5 (td, J=2.5, 0.8 Hz, C^3) 121.7 (dt, J=3.8, 1.6 Hz, C^6) 124.1 (td, J=5.4, 1.8 Hz, C^{4a}) 128.6 (d, J=3.2 Hz, C^5) 147.7 (dt, J=3.4, 1.6 Hz, C^4) 149.0 (dt, J=12.7, 2.0 Hz, C^7) 152.6 (dt, J=254.5, 2.0 Hz, C^8) 186.9 (t, J=24.0 Hz, C^2); ^{19}F (282 MHz, $CDCl_3$, 25°C, $CFCl_3$): -102.5 (d, 2F, J = 15 Hz), -150.5 (dt, 1F, J_1 = 15 Hz, J_2 = 8 Hz). UV-vis (CH_3OH), λ_{max} nm, (lg ε): 243 (4.26), 266 (4.18), 459 (3.98). IR (KBr, cm^{-1}): $\bar{\nu}$= 3325 (OH); 1672 (C=O); 1603; 1572; 1514; 1473; 1317; 1289; 1214; 1173; 1119; 1063; 1007; 853. HRMS: calcd. for $C_{10}H_5F_3O_2$ *m/z*= 214.0242, found: *m/z* 214.0240 [M^+].

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Keywords: Aromatic substitution • Electrophilic substitution • Fluorine • Solid-state reactions • Sustainable Chemistry

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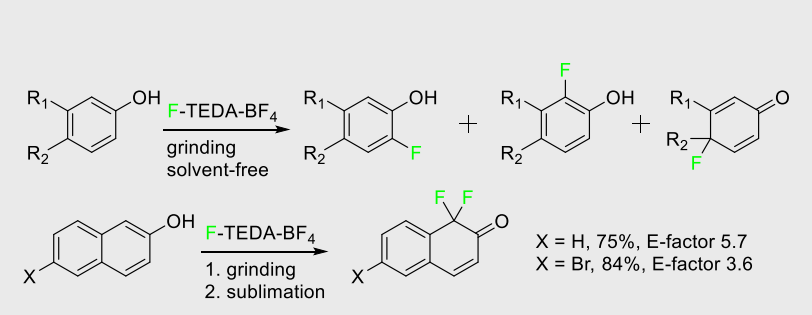

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Solvent-free Fluorination of Electron Rich Aromatic Compounds with F-TEDA-BF$_4$ Reagent: Toward "Dry" Processes

Efficient and ecologically benign method of fluorination of activated aromatic compounds was developed. Solventless fluorination of naphthalene-2-ols was performed by implication of vacuum sublimation for isolation of fluorinated products with high yields and purity.

Key Topic
Green Chemistry; Fluorination