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Partially Fluorinated Heterocycles from 4,4-Bis(trifluoromethyl)-hetero-1,3-dienes *via* C–F Bond Activation – Synthesis of 2-Fluoro-3-(trifluoromethyl)furans[#]

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Summary. An efficient synthesis of 2-fluoro-3-(trifluoromethyl)furans was developed. Keystep of the reaction sequence is a [4 + 1] cycloaddition reaction of tin(II)chloride to 4,4-bis(trifluoromethyl)-1-oxabuta-1,3-dienes. At elevated temperatures the tin heterocycles are transformed into 1-aryl-4,4-difluoro-3-(trifluoromethyl)but-3-en-1-ones which on treatment with sodium hydride in dry *DMF* give 2-fluoro-3-(trifluoromethyl)furans. The single fluorine bound to C-(2) can be readily replaced by various N-, O-, S-, and C-nucleophiles and dinucleophiles.

Keywords. [4 + 1] Cycloaddition; C–F Bond activation; 1-Aryl-4,4-difluoro-3-(trifluoromethyl)but-3-en-1-ones; Bridged 3-(trifluoromethyl)furans; 3-(Trifluoromethyl)tetrahydrocumaron.

Introduction

Incorporation of trifluoromethyl groups into strategical positions of biologically active compounds generally modifies the profile in a favorable way [1–3], by increasing metabolic stability and lipophilicity, enhancing *in vivo* absorption and transport rates, and improving permeability through certain body barriers. The number of publications and patents concerning fluorine-containing compounds in medicinal and agricultural chemistry as well as in material science is still growing [4]. The trifluoromethyl group is attractive since it is relatively non-toxic and somewhat more stable than the difluoromethyl and the monofluoromethyl group [5]. Originally the trifluoromethyl group was considered to be chemically inert [6]. The C–F bond is the strongest single bond connected to carbon [7]. Therefore, the development of new methodology for C–F bond activation is a challenge to preparative chemists. An arsenal of new fluorine-containing building blocks of broad structural variety will be the result, adding a new facette to preparative organofluorine chemistry [8, 9]. Recently, *Fuchibe* and *Akiyama* [10] reported on a low-valent niobium-mediated double activation strategy in which a C–F and a C–H bond in close proximity in the same molecule are jointly activated, leading to ring-closing and formation of polycyclic systems (Scheme 1). Differently substituted *o*-phenyl-α,α,α-trifluorotoluenes, $NbCl_5$ and $LiAlH_4$ were heated in *DME* under reflux for several hours to give fluorenes with variable substituent pattern in good yields [11].

Primary and secondary perfluoroalkyl amines are relatively unstable, but the situation is not as extreme as that of the corresponding alcohols [12].

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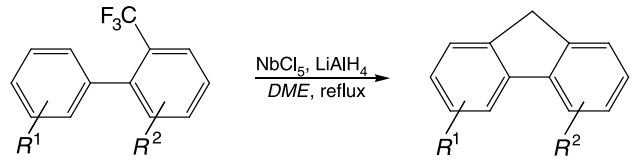
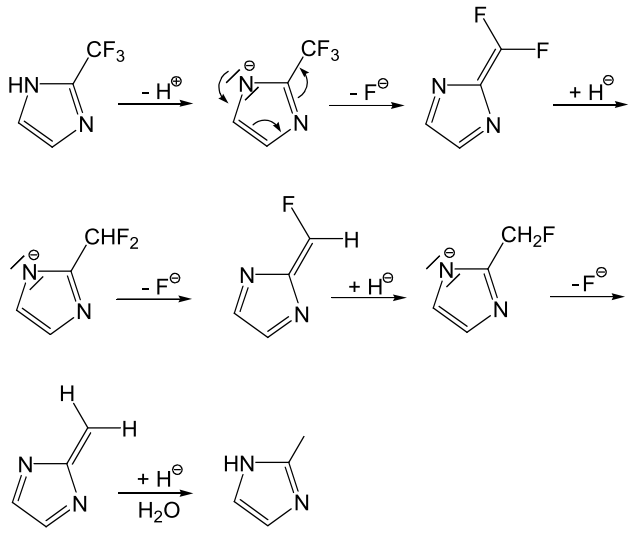
[#] Dedicated to Prof. Dr. *S. Hauptmann* on the occasion of his 75th birthday



Scheme 1



Scheme 2

In general, fluoroalkyl groups attached to skeleton atoms or heteroaromatic ring systems possessing acidic hydrogen atoms like trifluoromethanol and 3,3,3-trifluoroalanine or 2-trifluoromethylimidazole (Scheme 2) in basic media are readily transformed into anionic species [13]. Concomitantly, the C–F bonds are activated.

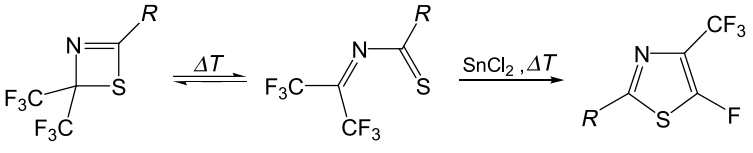
Activated trifluoromethyl groups react like ''*ortho*-fluorides'' and therefore can be applied as a synthetically useful functional group. This result is of interest, especially in the case of geminal trifluoromethyl groups. We found that the geminal pair of trifluoromethyl groups of 4,4-bis(trifluoromethyl)-1-oxa-3-azabuta-1,3-dienes after transfer of two electrons (anion activation *via* [4 + 1] cycloaddition of $SnCl_2$ or direct electron transfer from certain metals) react in a different way [14]. One trifluoromethyl group is degraded and finally its carbon atom is incorporated as skeleton atom into the newly formed ring system, while the second trifluoromethyl group remains unchanged being incorporated as CF_3-group. Thus, hexafluoroacetone can be applied as building block to introduce a single trifluoromethyl group into target molecules.

On the first view the ring transformation of 4,4-bis(trifluoromethyl)-2*H*-thiazetes into 5-fluoro-4-(trifluoromethyl)thiazoles on heating with $SnCl_2$ [15] (Scheme 3) is surprising. However, based on the knowledge that there exists a thermally mobile valence tautomeric equilibrium between the 4-membered heterocycle and the open-chain bis(trifluoromethyl) substituted hetero-1,3-diene [16], the mechanism of the ring enlargement can be readily explained. Now we report on the application of the $SnCl_2$-reaction to 4,4-bis(trifluoromethyl)-1-oxabuta-1,3-dienes, a hetero-1,3-diene with only one heteroatom in the 1,3-diene skeleton.

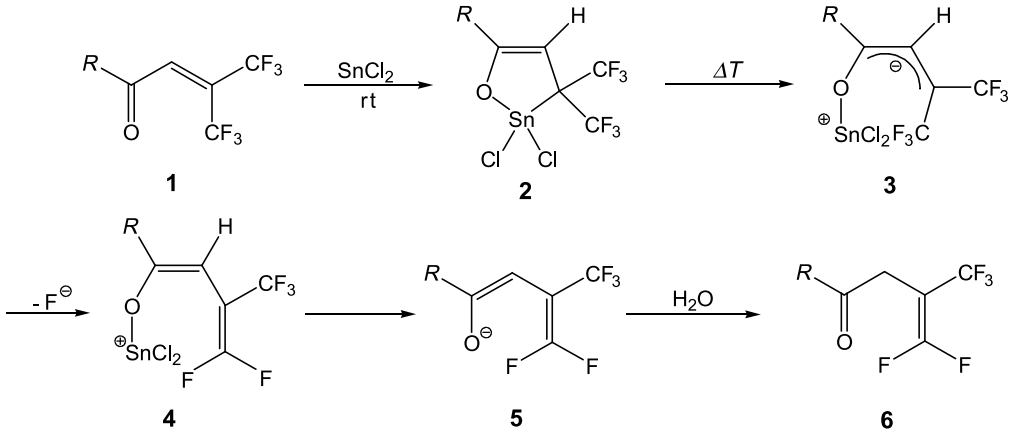
Results and Discussion

Enol ethers obtained from the reaction of methylketones and trimethylchlorosilane, react readily with hexafluoroacetone to give [1:1] adducts [17]. O-Deprotection can be achieved on treatment with methanolic HCl at room temperature. The aldol adducts are stable compounds and can be dehydrated with trifluoroacetic anhydride/pyridine at 0–20°C [18]. 4,4-Bis(trifluoromethyl)-1-oxa-1,3-dienes are stable against moisture and can be purified by distillation or column chromatography and stored at room temperature over months. Because of the structural similarity of 4,4-bis(trifluoromethyl)-1-oxabuta-1,3-dienes and 4,4-bis(trifluoromethyl)-1-oxa-3-azabuta-1,3-dienes we expected similar reaction behavior [19].

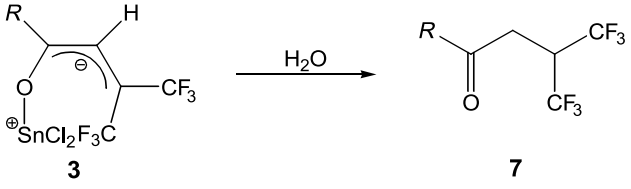
Indeed, the [4 + 1] cycloaddition of $SnCl_2$ (Scheme 4) works well already at room temperature (**1** → **2**). The Sn^{2+} species is oxidized to give a Sn^{4+} species. During the cycloaddition process two elec-



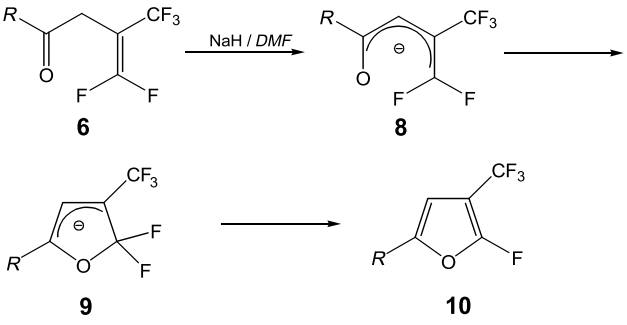
Scheme 3



Scheme 4



Scheme 5

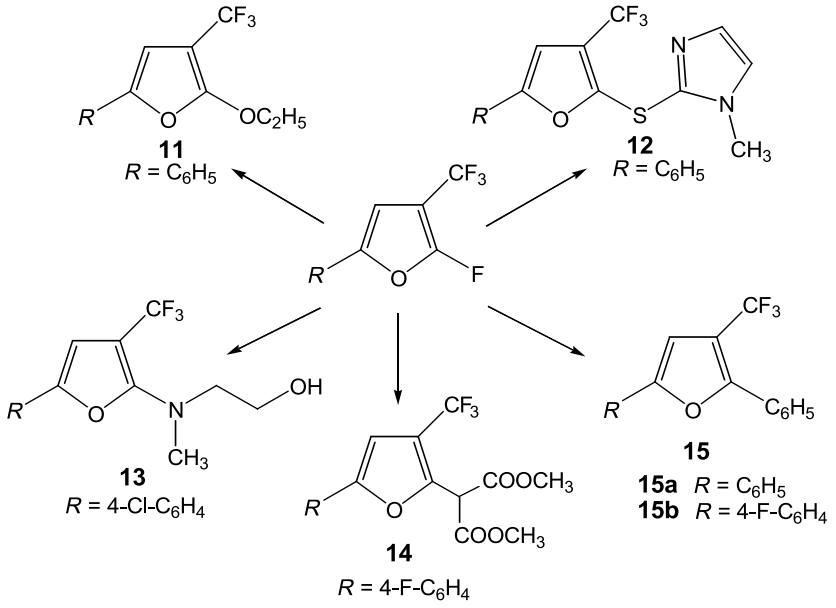


Scheme 6

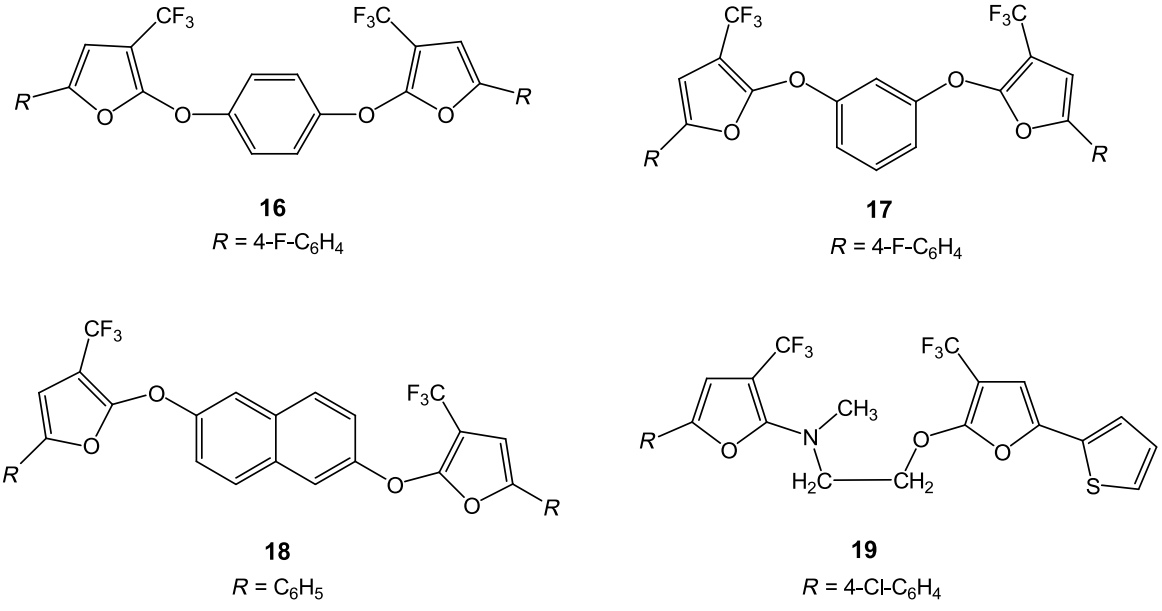
trons have been transferred from the metal centre to the hetero-1,3-diene skeleton. A by-product **7** (Scheme 5) isolated in 5–6% yield, which was fully characterized, indicates that a two electron transfer takes place in an early step of the reaction sequence, which is vital to ''switch on'' the activity of one of the trifluoromethyl groups.

At elevated temperatures the five-membered tin heterocycle undergoes a heterolytic ring cleavage to give a dipolar species (**2** → **3**), where the negative charge is accommodated in a bis(trifluoromethyl) substituted allylic anion substructure and the positive charge at the metal centre. The negative charge weakens the C–F bonds of the trifluoromethyl groups and fluoride elimination becomes possible (**3** → **4**) (Scheme 4). After splitting off the Sn fragment an oxapentadienyl anion **5** is formed. In the presence of water, protonation of **5** is much faster than the electrocyclic ring closure with elimination. Thus, protonation of **5** stops the reaction sequence and 1-aryl-4,4-difluoro-3-(trifluoromethyl)but-3-en-1-ones **6** were isolated in 70–90% yield. The perfluorinated fragment $F_3CC{=}CF_2$ can be readily identified with the help of the ^{13}C and ^{19}F NMR spectra. The transformation of **6** into partially fluorinated furans **10** has been achieved on treatment with sodium hydride or lithium diisopropylamide in dry polar aprotic solvents like *DMF* or *DMSO* at room temperature (Scheme 6). Heteroaromatization of the oxapentadienyl anion is the driving force for this reaction [20].

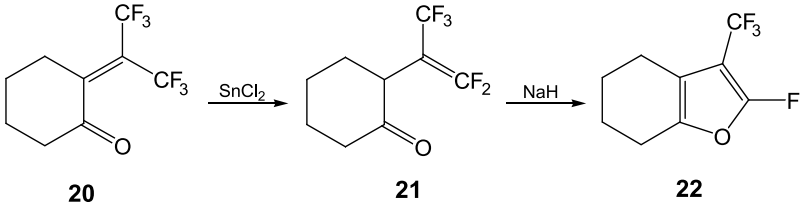
Structural diversity can be achieved on nucleophilic displacement reactions of the single fluorine bound to C-2 by N-, O-, S-, and C-nucleophiles [19, 21, 22] affording compounds of type **11**–**15**, *i.a.* arylation reactions with metal organic compounds like phenyl lithium and phenyl magnesium bromide proceed cleanly in good yields (Scheme 7). With dinucleophiles symmetrically **16**–**18** and unsymmetrically bridged heterocycles **19** are readily available (Scheme 8). From the NMR data it can be seen that the skeleton of the furan ring remains unchanged during the substitution procedures [23]. Therefore, the $SnCl_2$ reaction of bis(trifluoromethyl) substituted hetero-1,3-dienes represents a general, concise approach to trifluoromethyl substituted five-membered heterocycles, being well suited for the generation of ensembles.



Scheme 7



Scheme 8



Scheme 9

The thioanalogues, 2-fluoro-3-(trifluoromethyl)thiophenes, have been obtained from **6** *via* oxygen/sulfur exchange on heating with P_2S_5 without solvent [22]. Likewise, they are susceptible to nucleophilic exchange reactions at C-2, but the reaction rates of the nucleophilic fluorine substitution are considerably lower than in the furan series.

Starting the above discussed $SnCl_2$ reaction with the hetero-1,3-diene **20** provides compound **21** (Scheme 9). Finally, the annelated furan – 2-fluoro-3-(trifluoromethyl)-4,5,6,7-tetrahydrocumaron **22** – was obtained on treatment of **21** with NaH in dry *DMF* or *DMSO*.

2-Fluoro-3-(trifluoromethyl)furans **10** have been used as versatile building blocks for the synthesis of trifluoromethyl substituted butenolides and α-(trifluoromethyl)-γ-keto acids [24]. On further applications of trifluoromethyl substituted five-membered heterocycles as building blocks in organofluorine chemistry we report elsewhere [14].

Experimental

General

Solvents were purified and dried prior to use. Reagents were used as purchased. Flash chromatography was performed using silica gel (32–63 μm) with solvent systems given in the text. Melting points were determined with a *Tottoli* apparatus (Fa. Büchi). ^{1}H (200, 360 MHz), ^{13}C (50, 90 MHz), and ^{19}F (188, 282 MHz) NMR spectra were recorded on Bruker WP 200, Bruker AM 360, Jeol C 60 HL, and Jeol FX 90 Q spectrometers. *TMS* was used as reference for ^{1}H and ^{13}C NMR spectra (internal), and CF_3COOH for ^{19}F NMR spectra (external). IR spectra were obtained on Perkin Elmer 157 G and 257 spectrometers. Mass spectra were recorded on a Varian MAT CH 5 spectrometer at 70 eV. Elemental analyses were performed with a CHNO–S Rapid apparatus (Fa. Heraeus); their results agreed with calculated values.

1-Aryl-4,4-difluoro-3-(trifluoromethyl)but-3-en-1-ones (**6**)

4,4-Bis(trifluoromethyl)-1-oxabuta-1,3-diene (**1**) [14] (25 mmol) and 5.64 g $SnCl_2 \cdot 2H_2O$ (25 mmol) were heated in a solvent mixture of xylene (100 cm^3) and *THF* (30 cm^3) under reflux until the starting material was consumed (^{19}F NMR analysis; reaction time: 2–24 h). After filtration, the solution was concentrated *in vacuo* and the residue was purified by column chromatography (eluent: chloroform/hexanes, 1/1).

A second product was isolated in 5–6% yield on column chromatography and fully characterized in three cases. Based on the spectra data we ascribe the by-product the structure of 1-aryl-4,4,4-trifluoro-3-trifluoromethyl-1-butanones **7**.

4,4-Difluoro-1-phenyl-3-(trifluoromethyl)but-3-en-1-one (**6a**, $C_{11}H_7F_5O$)

Yield 5.38 g (86%), bp 50°C/0.1 Torr; IR (film): $\bar{\nu} = 3360$, 1750, 1690, 1600, 1580, 1455 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.85$ (dd, $J = 2.0$, 2.0 Hz, CH_2), 7.48 (m, 2Ar-H), 7.66 (m, Ar-H), 7.97 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.87$ (*C*H$_2$), 81.84 (ddq, $J = 14.0$, 29.0, 36.0 Hz, *C*=CF$_2$), 122.76 (ddq, $J = 5.0$, 13.0, 271.0 Hz, CF_3), 128.06, 128.79, 133.80, 135.50 (Ar-*C*), 157.39 (ddq, $J = 303.0$, 292.0, 4.0 Hz, =*C*F$_2$), 192.65 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -0.65$ (dtrq, $J = 16.0$, 2.0, 11.0 Hz, =C*F*$_a$), 3.29 (dtrq, $J = 16.0$, 2.0, 19.0 Hz, =C*F*$_b$), 16.76 (dd, $J = 19.0$, 11.0, CF_3) ppm; MS: $m/z = 231$ $[M-F]^+$, 203 $[231-CO]^+$, 183 $[203-HF]^+$, 145 $[M-C_6H_5CO]^+$, 105 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

4,4-Difluoro-1-(4-methylphenyl)-3-(trifluoromethyl)but-3-en-1-one (**6b**, $C_{12}H_9F_5O$)

Yield 6.00 g (91%), bp 58°C/0.1 Torr; IR (film): $\bar{\nu} = 3320$, 1750, 1690, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 2.44$ (s, CH_3), 3.83 (dd, $J = 2.0$, 2.0 Hz, CH_2), 7.30 (m, 2Ar-H), 7.88 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.55$ (*C*H$_3$), 32.77 (*C*H$_2$), 81.89 (ddq, $J = 14.0$, 28.0, 36.0 Hz, *C*=CF$_2$), 122.74 (ddq, $J = 7.0$, 12.0, 272.0 Hz, CF_3), 128.22, 129.49, 133.02, 144.88 (Ar-*C*), 157.37 (ddq, $J = 301.0$, 292.0, 5.0 Hz, =*C*F$_2$), 192.22 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -1.19$ (dtrq, $J = 16.0$, 2.0, 10.0 Hz, =C*F*$_a$), 3.12 (dtrq, $J = 16.0$, 2.0, 19.0 Hz, =C*F*$_b$), 16.77 (dd, $J = 19.0$, 10 Hz, CF_3) ppm; MS: $m/z = 264$ $[M]^+$, 245 $[M-F]^+$, 217 $[245-CO]^+$, 197 $[217-HF]^+$, 145 $[M-C_7H_7CO]^+$, 119 $[C_7H_7CO]^+$, 91 $[C_7H_7]^+$.

4,4-Difluoro-1-(2-methoxyphenyl)-3-(trifluoromethyl)but-3-en-1-one (**6c**, $C_{12}H_9,F_5O_2$)

Yield 4.90 g (70%), bp 56°C/0.1 Torr; IR (film): $\bar{\nu} = 3280$, 1750, 1675, 1600, 1485, 1470, 1440 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.86$ (dd, $J = 2.0$, 2.0 Hz, CH_2), 3.95 (s, OCH_3), 7.03 (m, 2Ar-H), 7.52 (m, Ar-H), 7.82 (m, Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 37.91$ (*C*H$_2$), 55.30 (O*C*H$_3$), 82.45 (ddq, $J = 13.0$, 29.0, 35.0 Hz, *C*=CF$_2$), 111.56, 120.73 (Ar-*C*), 121.42 (ddq, $J = 6.0$, 13.0, 271.0 Hz, CF_3), 126.0, 130.73, 134.56, (Ar-*C*), 157.28 (ddq, $J = 302.0$, 271.0, 4.0 Hz, =CF$_2$), 159.05 (Ar-*C*), 194.30 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -1.87$ (dtrq, $J = 17.0$, 2.0, 10.0 Hz, =C*F*$_a$), 2.26 (dtrq, $J = 17.0$, 2.0, 19.0 Hz, =C*F*$_b$), 16.78 (dd, $J = 19.0$, 10.0 Hz, CF_3) ppm; MS: $m/z = 280$ $[M]^+$, 221 $[M-CO-OCH_3]^+$, 135 $[C_7H_7OCO]^+$, 77 $[C_6H_5]^+$.

4,4-Difluoro-1-(4-fluorophenyl)-3-(trifluoromethyl)but-3-en-1-one (**6d**, $C_{11}H_6F_6O$)

Yield 5.56 g (83%), bp 60°C/0.6 Torr; IR (film): $\bar{\nu} = 3340$, 1750, 1690, 1595, 1505, 1410 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.82$ (dd, $J = 2.0$, 2.0 Hz, CH_2), 7.17 (m, 2Ar-H), 8.00 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.81$ (*C*H$_2$), 81.73 (ddq, $J = 14.0$, 29.0, 36.0 Hz, *C*=CF$_2$), 115.97 (d, $J = 22.0$ Hz, Ar-*C3*,*C5*), 122.71 (ddq, $J = 6.0$, 13.0, 271 Hz, CF_3), 130.81 (d, $J = 10.0$ Hz, Ar-*C2*,*C6*), 131.97 (d, $J = 3.0$ Hz,

Ar-*C1*), 157.45 (ddq, $J = 303.0$, 292.0, 4.0 Hz, $=CF_2$), 166.15 (d, $J = 256.0$ Hz, Ar-*C4*), 191.12 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.02$ (m, Ar-F), −0.94 (dtrq, $J = 15.0$, 2.0, 11.0 Hz, $=CF_a$), 3.41 (dtrq, $J = 15.0$, 2.0, 19.0 Hz, $=CF_b$), 16.72 (dd, $J = 19.0$, 11.0 Hz, CF_3) ppm; MS: $m/z = 249$ $[M - F]^+$, 221 $[249 - CO]^+$, 201 $[221 - HF]^+$, 145 $[M - C_6H_4FCO]^+$, 123 $[C_6H_4FCO]^+$, 95 $[C_6H_4F]^+$, 75 $[95 - HF]^+$.

4,4-Difluoro-(4-chlorophenyl)-3-(trifluoromethyl)but-3-en-1-one (**6e**, $C_{11}H_6ClF_5O$)
Yield 6.26 g (88%), bp 56°C/0.1 Torr; IR (film): $\bar{\nu} = 3360$, 1750, 1690, 1590, 1575, 1405 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.82$ (dd, $J = 2.0$, 2.0 Hz, CH_2), 7.46 (m, 2Ar-H), 7.90 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.84$ (CH_2), 81.55 (ddq, $J = 14.0$, 29.0, 36.0 Hz, *C*=CF_2), 122.57 (ddq, $J = 5.0$, 13.0, 271.0 Hz, CF_3), 129.12, 129.46, 133.80, 140.38 (Ar-*C*), 157.34 (ddq, $J = 304.0$, 292.0, 5.0 Hz, $=CF_2$), 191.50 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -0.90$ (dtrq, $J = 15.0$, 2.0, 10.0 Hz, $=CF_a$), 3.42 (dtrq, $J = 15.0$, 2.0, 19.0 Hz, $=CF_b$), 16.70 (dd, $J = 19.0$, 10.0 Hz, CF_3) ppm; MS: $m/z = 267/265$ $[M - F]^+$, 239/237 $[267/265 - CO]^+$, 219/217 $[239/237 - HF]^+$, 182 $[219/217 - Cl]^+$, 141/139 $[C_6H_4ClCO]^+$, 113/111 $[C_6H_4Cl]^+$.

4,4-Difluoro-1-(5-methylfur-2-yl)-3-(trifluoromethyl)but-3-en-1-one (**6f**, $C_{10}H_7F_5O_2$)
Yield 4.39 g (69%), bp 49°C/0.1 Torr; IR (film): $\bar{\nu} = 3340$, 1750, 1675, 1590, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 2.41$ (s, CH_3), 3.67 (dd, $J = 2.0$, 2.0 Hz, CH_2), 6.21 (m, furyl-H), 7.19 (m, furyl-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 13.55$ (CH_3), 32.00 (CH_2), 81.37 (dtrq, $J = 13.0$, 29.0, 35.0 Hz, *C*=CF_2), 109.24, 119.66 (furyl-*C*), 122.65 (ddq, $J = 5.0$, 13.0, 271.0 Hz, CF_3), 150.16 (furyl-*C*), 157.42 (ddq, $J = 302.0$, 292.0, 4.0 Hz, $=CF_2$), 158.43 (furyl-*C*), 180.87 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -0.84$ (dtrq, $J = 15.0$, 2.0, 11.0 Hz, $=CF_a$), 3.37 (dtrq, $J = 15.0$, 2.0, 20.0 Hz, $=CF_b$), 16.71 (dd, $J = 20.0$, 11.0 Hz, CF_3) ppm; MS: $m/z = 254$ $[M]^+$, 235 $[M - F]^+$, 207 $[235 - CO]^+$, 187 $[207 - HF]^+$, 145 $[M - C_5H_5OCO]^+$, 109 $[C_5H_5OCO]^+$, 81 $[C_5H_5O]^+$, 53 $[81 - CO]^+$.

4,4-Difluoro-1-(thien-2-yl)-3-(trifluoromethyl)but-3-en-1-one (**6g**, $C_9H_5F_5OS$)
Yield 5.64 g (88%), 48°C/0.1 Torr; IR (film): $\bar{\nu} = 3360$, 1750, 1670, 1520, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.80$ (dd, $J = 2.0$, 2.0 Hz, CH_2), 7.17 (m, thienyl-H), 7.71 (m, thienyl-H), 7.78 (m, thienyl-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 33.22$ (CH_2), 81.62 (ddq, $J = 14.0$, 29.0, 36.0 Hz, *C*=CF_2), 122.66 (ddq, $J = 5.0$, 13.0, 271.0 Hz, CF_3), 128.33, 132.50, 134.64, 142.20 (thienyl-*C*), 157.54 (ddq, $J = 303.0$, 292.0, 4.0 Hz, $=CF_2$), 185.53 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -0.51$ (dtrq, $J = 15.0$, 2.0, 11.0 Hz, $=CF_a$), 3.31 (dtrq, $J = 15.0$, 2.0, 19.0 Hz, $=CF_b$), 16.73 (dd, $J = 19.0$, 11.0 Hz, CF_3) ppm; MS: $m/z = 256$ $[M]^+$, 237 $[M - F]^+$, 209 $[237 - CO]^+$, 189 $[208 - HF]^+$, 145 $[M - C_4H_3SCO]^+$, 111 $[C_4H_3SCO]^+$, 83 $[C_4H_3S]^+$.

1-(4-Fluorophenyl)-4,4,4-trifluoro-3-(trifluoromethyl)-1-butanone (**7d**, $C_{11}H_7F_7O$)
Yield 0.43 g (6%), bp 72°C/15 Torr; IR (film): $\bar{\nu} = 1690$, 1600, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.40$ (d, $J = 5.0$ Hz, CH_2), 4.17 (trsept, $J = 5.0$, 8.0 Hz, CH), 7.18 (m, 2Ar-H), 8.02 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.78$ (sept, $J = 2.0$ Hz, CH_2), 42.95 (sept, $J = 30.0$ Hz, CH), 123.67 (m, CF_3), 128.43, 132.77, 135.14, 142.05 (Ar-*C*), 185.47 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 9.90$ (d, $J = 8.0$ Hz, $CH(CF_3)_2$) ppm; MS: $m/z = 288$ $[M]^+$, 269 $[M - F]^+$, 249 $[M - F, HF]^+$, 123 $[C_6H_4FCO]^+$, 95 $[C_6H_4F]^+$, 75 $[95 - HF]^+$.

1-(4-Chlorophenyl)-4,4,4-trifluoro-3-(trifluoromethyl)-1-butanone (**7e**, $C_{11}H_7ClF_6O$)
Yield 0.38 g (5%), mp 59°C; IR (KBr): $\bar{\nu} = 3460$, 1700, 1600, 1578, 1495 cm^{-1}; ^{1}H NMR ($CDCl_3$): 3.39 (sept, $J = 5.0$ Hz, CH_2), 4.17 (trsept, $J = 5.0$, 8.0 Hz, CH), 7.49 (m, 2Ar-H), 7.92 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.46$ (sept, $J = 2.0$ Hz, CH_2), 43.03 (sept, $J = 30.0$ Hz, CH), 123.92 (m, CF_3), 129.42, 129.72, 133.75, 140.95 (Ar-*C*), 191.67 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 9.91$ (d, $J = 8.0$ Hz, $CH(CF_3)_2$) ppm; MS: $m/z = 306/304$ $[M]^+$, 267/265 $[M - F, -HF]^+$, 141/139 $[C_6H_4ClCO]^+$, 113/111 $[C_6H_4Cl]^+$.

4,4,4-Trifluoro-1-(thien-2-yl)-3-(trifluoromethyl)-1-butanone (**7g**, $C_9H_6F_6OS$)
Yield 0.35 g (5%), oil; IR (film): $\bar{\nu} = 3280$, 1665, 1515, 1420, 1400 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.37$ (d, $J = 6.0$ Hz, CH_2), 4.12 (sept, $J = 6.0$, 8.0 Hz, CH), 7.19 (m, thienyl-H), 7.74 (m, thienyl-H), 7.80 (m, thienyl-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.78$ (sept, $J = 2.0$ Hz, CH_2), 42.95 (sept, $J = 30.0$ Hz, CH), 123.67 (m, CF_3), 128.43, 132.77, 135.14, 142.05 (thienyl-*C*), 185.47 (*C*=O) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 9.90$ (d, $J = 8.0$ Hz, $C(CF_3)_2$) ppm; MS: $m/z = 276$ $[M]^+$, 237 $[M - F–HF]^+$, 209 $[237 - CO]^+$, 145 $[M - C_4H_3SCO–HF]^+$, 111 $[C_4H_3SCO]^+$, 83 $[C_4H_3S]^+$.

5-Aryl-2-fluoro-3-(trifluoromethyl)furans (**10**)*; General Procedure*
To a stirred solution of 25 mmol **6** in 100 cm^3 dry *DMF* at 0°C 0.60 g NaH (25 mmol) were added in small portions. Stirring was continued at room temperature until ^{19}F NMR analysis indicates that the starting material was completely consumed (12–24 h). Then the reaction mixture was poured into 100 cm^3 ice-cold 1 *N* HCl. The mixture was extraced with 3×100 cm^3 ether. The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. Finally the residue was purified by column chromatography (eluent: hexanes).

2-Fluoro-5-phenyl-3-(trifluoromethyl)furan (**10a**, $C_{11}H_6F_4O$)
Yield 4.14 g (72%), bp 47°C/0.1 Torr; IR (film): $\bar{\nu} = 1665$, 1610, 1570, 1455, 1440 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 6.61$ (d, $J = 3.0$ Hz, furyl-H), 7.36 (m, 3Ar-H), 7.52 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 91.63$ (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 102.63 (m, furyl-*C4*), 121.20 (dq, $J = 5.0$, 266.0 Hz, CF_3), 123.39, 128.38, 128.50, 128.87 (Ar-*C*), 145.07 (furyl-*C5*), 153.86 (dq, $J = 285.0$, 5.0 Hz, furyl-*C2*) ppm; ^{19}F NMR

($CDCl_3$): $\delta = -30.08$ (dq, $J = 3.0$, 10.0 Hz, =C*F*), 19.36 (d, $J = 10.0$ Hz, CF_3) ppm; MS: $m/z = 230$ $[M]^+$, 211 $[M-F]^+$, 210 $[M-HF]^+$, 183 $[211-CO]^+$, 182 $[210-CO]^+$, 133 $[M-CO-CF_3]^+$.

2-Fluoro-5-(4-methylphenyl)-3-(trifluoromethyl)furan
(**10b**, $C_{12}H_8F_4O$)
Yield 4.15 g (68%), mp 53°C; IR (KBr): $\bar{\nu} = 3440$, 1675, 1595, 1505, 1450 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.36$ (s, CH_3), 6.55 (d, $J = 3.0$ Hz, furyl-H), 7.18 (m, 2Ar-H), 7.43 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.14$ (CH_3), 91.47 (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 101.85 (m, furyl-*C4*), 121.25 (dq, $J = 5.0$, 266.0 Hz, CF_3), 123.43 (d, $J = 1.0$ Hz), 125.74, 129.56, 138.63 (Ar-H), 145.37 (furyl-*C5*), 153.67 (dq, $J = 285.0$, 5.0 Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.36$ (dq, $J = 2.0$, 11.0 Hz, =CF), 19.22 (d, $J = 11.0$ Hz, CF_3) ppm; MS: $m/z = 244$ $[M]^+$, 225 $[M-F]^+$, 224 $[M-HF]^+$, 196 $[224-CO]^+$, 147 $[M-CO-CF_3]^+$.

2-Fluoro-5-(2-methoxyphenyl)-3-(trifluoromethyl)furan
(**10c**, $C_{12}H_8F_4O_2$)
Yield 4.42 g (68%), mp 39°C; IR (KBr): $\bar{\nu} = 3360$, 1670, 1605, 1495, 1460, 1450, 1430 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.93$ (s, OCH_3), 6.93 (d, $J = 3.0$ Hz, furyl-H), 6.99 (m, 2Ar-H), 7.31 (m, Ar-H), 7.65 (m, Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 55.24$ (OCH_3), 91.19 (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 107.71 (m, furyl-*C4*), 110.90, 117.27, 120.71 (Ar-*C*), 121.35 (dq, $J = 5.0$, 266.0 Hz, CF_3), 125.29, 129.08 (Ar-*C*), 141.85 (furyl-*C5*), 149.52 (dq, $J = 284.0$, 5.0 Hz, furyl-*C2*), 155.76 (d, $J = 2.0$ Hz, Ar-*C*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -31.47$ (dq, $J = 3.0$, 11.0 Hz, =CF), 19.40 (d, $J = 11.0$ Hz, CF_3) ppm; MS: $m/z = 260$ $[M]^+$, 241 $[M-F]^+$, 240 $[M-HF]^+$, 225 $[240-CH_3]^+$, 217 $[M-CH_3-CO]^+$, 197 $[225-CO]^+$, 169 $[197-CO]^+$, 163 $[M-CO-CF_3]^+$, 133 $[240-C_7H_7O]^+$.

2-Fluoro-5-(4-fluorophenyl)-3-(trifluoromethyl)furan
(**10d**, $C_{11}H_5F_5O$)
Yield 4.34 g (70%), bp 41°C/0.1 Torr; IR (film): $\bar{\nu} = 3350$, 1670, 1600, 1580, 1500, 1450, 1425 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 6.53$ (d, $J = 3.0$ Hz, furyl-H), 7.06 (m, 2Ar-H), 7.47 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 91.71$ (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 102.36 (dq, $J = 2.0$, 4.0 Hz, furyl-*C4*), 116.03 (d, $J = 22.0$ Hz, Ar-*C3*,*C5*), 121.15 (dq, $J = 5.0$, 266.0 Hz, CF_3), 124.76 (d, $J = 3.0$ Hz, Ar-*C1*), 125.31 (dd, $J = 1.0$, 9.0 Hz, Ar-*C2*, *C6*), 144.29 (furyl-*C5*), 153.87 (dq, $J = 285.0$, 5.0 Hz, furyl-*C2*), 162.84 (d, $J = 249.0$ Hz, Ar-*C4*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -34.29$ (m, =CF), -30.20 (dq, $J = 2.0$, 10.0 Hz, =CF), 19.26 (d, $J = 10.0$ Hz, CF_3) ppm; MS: $m/z = 248$ $[M]^+$, 229 $[M-F]^+$, 228 $[M-HF]^+$, 201 $[229-CO]^+$, 200 $[228-CO]^+$, 151 $[M-CO-CF_3]^+$.

5-(4-Chlorophenyl)-2-fluoro-3-(trifluoromethyl)furan
(**10e**, $C_{11}H_5ClF_4O$)
Yield 4.36 g (66%), mp 36°C; IR (KBr): $\bar{\nu} = 3440$, 1680, 1615, 1590, 1570, 1495, 1450, 1410 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 6.65$ (d, $J = 3.0$ Hz, furyl-H), 7.35 (m, 2Ar-H), 7.44 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 91.99$ (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 103.32 (m, furyl-*C4*), 121.11 (dq, $J = 5.0$, 266.0 Hz, CF_3). 124.78, 126.98, 129.30, 134.57 (Ar-*C*), 144.14 (furyl-*C5*), 154.04 (dq, $J = 286.0$, 5.0 Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -29.48$ (dq, $J = 2.0$, 11.0 Hz, =CF), 19.35 (d, $J = 11.0$ Hz, CF_3) ppm; MS: $m/z = 266/264$ $[M]^+$, 246/244 $[M-HF]^+$, 229 $[M-Cl]^+$, 218/216 $[246/244-CO]^+$, 201 $[229-CO]^+$, 182 $[201-F]^+$, 169/167 $[M-CO-CF_3]^+$, 132 $[167-Cl]^+$.

2-Fluoro-5-(5-methylfur-2-yl)-3-(trifluoromethyl)furan
(**10f**, $C_{10}H_6F_4O_2$)
Yield 3.51 g (60%), bp 39°C/0.1 Torr; IR (film): $\bar{\nu} = 1680$, 1615, 1590, 1570, 1450, 1410 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.33$ (s, CH_3), 6.03 (m, furyl-H), 6.43 (d, $J = 3.0$ Hz, furyl-H), 6.45 (d, $J = 3.0$ Hz, furyl-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 13.48$ (*C*H_3), 91.27 (dq, $J = 7.0$, 40.0 Hz, furyl-*C3*), 101.59 (m, furyl-*C4*), 107.61, 107.73 (furyl-*C*), 121.06 (dq, $J = 5.0$, 266.0 Hz, CF_3), 138.05 (furyl-*C*), 142.09 (furyl-*C5*), 153.08 (furyl-*C*), 153.33 (dq, $J = 285.0$, 5.0 Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.36$ (dq, $J = 2.0$, 11.0 Hz, =CF), 19.28 (d, $J = 11.0$ Hz, CF_3) ppm; MS: $m/z = 234$ $[M]^+$, 219 $[M-CH_3]^+$, 215 $[M-F]^+$, 214 $[M-HF]^+$, 191 $[219-CO]^+$, 187 $[215-CO]^+$, 186 $[214-CO]^+$, 171 $[191-HF]^+$, 163 $[191-CO]^+$, 137 $[M-CO-CF_3]^+$, 109 $[C_5H_5OCO]^+$.

2-Fluoro-5-(thien-2-yl)-3-(trifluoromethyl)furan
(**10g**, $C_9H_4F_4OS$)
Yield 3.72 g (63%), bp 35°C/0.1 Torr; IR (film): $\bar{\nu} = 1665$, 1450, 1425 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 6.46$ (d, $J = 3.0$ Hz, furyl-H), 7.02 (m, thienyl-H), 7.22 (m, thienyl-H), 7.26 (m, thienyl-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 91.66$ (dq, $J = 7.0$, 40.0 Hz, furyl-*C5*), 102.62 (m, furyl-*C4*), 121.06 (dq, $J = 5.0$, 266.0 Hz, CF_3), 124.09 (d, $J = 2.0$ Hz), 125.46, 127.73, 130.74 (thienyl-*C*), 140.86 (furyl-*C5*), 153.42 (dq, $J = 286.0$, 5.0 Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.30$ (dq, $J = 3.0$, 11.0 Hz, =CF), 19.31 (d, $J = 11.0$ Hz, CF_3) ppm; MS: $m/z = 236$ $[M]^+$, 217 $[M-F]^+$, 216 $[M-HF]^+$, 208 $[M-CO]^+$, 189 $[217-CO]^+$, 188 $[216-CO]^+$, 139 $[M-CO-CF_3]^+$.

2-Ethoxy-5-phenyl-3-(trifluoromethyl)furan (**11**, $C_{13}H_{11}F_3O_2$)
To a solution of the freshly prepared alcoholate (6 mmol) in dioxane 0.70 g **10a** (3 mmol) were added. After *ca* 60 min the reaction was complete (^{19}F NMR analysis). Water (20 cm^3) was added and the reaction mixture was extracted with 3×20 cm^3 CH_2Cl_2. After drying the organic phase with $MgSO_4$ the solvent was evaporated under reduced pressure and the residue was purified by column chromatography. Yield 0.74 g (96%), mp 47°C; IR (KBr): $\bar{\nu} = 3400$, 1635, 1600, 1560, 1460, 1440 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.44$ (tr, $J = 7.0$ Hz, CH_3), 4.41 (q, $J = 7.0$ Hz, OCH_2), 6.61 (s, furyl-H), 7.24 (m, Ar-H), 7.35 (m, 2Ar-H), 7.52 (m, 2Ar-H) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 15.66$ (*C*H_3), 69.59 (O*C*H_2), 94.16 (q, $J = 38.0$ Hz, furyl-*C3*), 104.30 (q, $J = 2.0$ Hz, furyl-*C4*), 123.47 (q, $J = 266.0$ Hz, CF_3), 123.77, 128.26, 129.59, 130.46 (Ar-*C*), 145.24 (furyl-*C5*), 157.43 (q,

$J = 4.0$ Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.38$ (s, CF_3) ppm; MS: $m/z = 256$ $[M]^+$, 228 $[M - CO]^+$, 227 $[M - C_2H_5]^+$, 209 $[228 - F]^+$, 208 $[M - HF]^+$, 180 $[209 - C_2H_5]^+$, 179 $[208 - C_2H_5]^+$, 105 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

2-(N-Methylimidazol-2-ylthio)-5-phenyl-3-(trifluoromethyl)furan (**12**, $C_{18}H_{11}F_3OS$)

To a solution of 0.72 g **10a** (3 mmol) and the corresponding thio compound (0.70 g, 6 mmol) in 25 cm^3 dioxane 0.07 g NaH (3 mmol) were added. After the reaction was complete, the mixture was quenched with 20 cm^3 water and extracted with 3×25 cm^3 ether. After drying the organic phase with $MgSO_4$, the solvent was evaporated *in vacuo* and the residue was purified by column chromatography. Yield 0.98 g (94%), mp 133°C; IR (KBr): $\bar{\nu} = 3420$, 1610, 1595, 1540, 1485, 1460, 1400 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.81$ (s, CH_3), 6.76 (s, furyl-H), 7.03 (d, $J = 1.0$ Hz, imidazolyl-H), 7.12 (d, $J = 1.0$ Hz, imidazolyl-H), 7.34 (m, 3Ar-H), 7.56 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 33.90$ (CH_3), 104.29 (q, $J = 2.0$ Hz, furyl-*C4*), 121.70 (q, $J = 268.0$ Hz, CF_3), 122.00 (q, $J = 38.0$ Hz, furyl-*C3*), 124.02, 124.15, 128.55, 128.72, 128.85, 130.36, 134.48 (Ar-*C*, imidazolyl-*C*), 141.19 (q, $J = 4.0$ Hz, furyl-*C2*), 156.82 (furyl-*C5*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.69$ (s, CF_3) ppm; MS: $m/z = 324$ $[M]^+$, 305 $[M - F]^+$, 255 $[M - CF_3]^+$, 219 $[M - C_6H_5CO]^+$, 183 $[M - C_4H_5N_2S{-}CO]^+$, 105 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

5-(4-Chlorophenyl)-2-[(2-hydroxyethyl)methylamino]-3-(trifluoromethyl)furan (**13**, $C_{14}H_{13}ClF_3NO_2$)

A solution of equimolar amounts of **10e** (0.80 g, 3 mmol) and 2-(methylamino)ethanol (0.23 g, 3 mmol) in 20 cm^3 dioxane was stirred until the reaction was complete (^{19}F NMR analysis). After quenching the mixture with 20 cm^3 water the organic phase was extracted with 3×20 cm^3 ether. Further work-up as above. Yield 0.90 g (94%), mp 69°C; IR (KBr): $\bar{\nu} = 3320$, 3230, 1600, 1465, 1430 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.74$ (s, OH), 3.09 (q, $J = 1.0$ Hz, NCH_3), 3.51 (tr, $J = 6.0$ Hz, NCH_2), 3.85 (tr, $J = 6.0$ Hz, OCH_2), 6.65 (s, furyl-H), 7.31 (m, 2Ar-H), 7.41 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 38.83$ (q, $J = 2.0$ Hz, NCH_3), 54.96 (NCH_2), 60.20 (OCH_2), 93.74 (q, $J = 37.0$ Hz, furyl-*C3*), 105.75 (q, $J = 3.0$ Hz, furyl-*C4*), 123.43 (q, $J = 265.0$ Hz, CF_3), 123.72, 128.40, 128.86, 132.27 (Ar-*C*), 142.95 (furyl-*C5*), 155.75 (q, $J = 4.0$ Hz, furyl-*C2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 25.87$ (d, $J = 1.0$ Hz, CF_3) ppm; MS: $m/z = 321/319$ $[M]^+$, $290/288$ $[M - OCH_3]^+$, $219/217$ $[M - C_3H_8NO{-}CO]^+$, $141/139$ $[ClC_6H_4CO]^+$, $113/111$ $[ClC_6H_4]^+$.

5-(4-Fluorophenyl)-2-bis(methoxycarbonyl)methyl-3-(trifluoromethyl)furan (**14**, $C_{12}H_{10}F_4N_2O$)

To a solution of 0.49 g **10d** (2 mmol) and 0.53 g dimethyl malonate (4 mmol) in 10 cm^3 *THF* 0.12 g NaH (5 mmol) were added portionwise with cooling (0°C). After 1 h the temperature was risen to 50°C. When the reaction was complete (^{19}F NMR analysis) it was quenched with 1 *N* HCl at 0°C and extracted with 3×25 cm^3 ether. After drying the organic phase ($MgSO_4$) the solvent was removed under reduced pressure and the residue was purified by column chromatography (eluent: CH_2Cl_2). Yield 0.40 g (55%), mp 67°C; IR (KBr); $\bar{\nu} = 1766$–1739, 1498, 1311 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta =$ 3.83 (s, 2× CH_3), 5.06 (s, CH), 6.70 (s, furyl-H), 7.09 (m, 2Ar-H), 7.63 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 50.5$ (CH), 53.4 (2× OCH_3), 103.0 (furyl-*C4*), 116.0 (d, $J =$ 22.3 Hz, Ar-*C3*,*C5*), 117.8 (q, $J = 37.5$ Hz, furyl-*C3*), 122.2 (q, $J = 267.5$ Hz, CF_3), 125.4 (d, $J = 3.2$ Hz, Ar-*C1*), 126.2 (d, $J = 8.0$ Hz, Ar-*C2*,*C6*), 144.0 (furyl-*C5*), 154.2 (furyl-*C2*), 162.9 (d, $J = 249.5$ Hz, Ar-*C4*) 165.4 (2× CO_2CH_3) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -34.2$ (m, 1F), 19.7 (s, CF_3) ppm; MS: $m/z = 360$ $[M]^+$, 340 $[M - HF]^+$, 301 $[M - CO_2CH_3]^+$, 59 $[CO_2CH_3]^+$.

2,5-Diphenyl-3-(trifluoromethyl)furan (**15a**, $C_{17}H_{11}F_3O$)

To a stirred solution of 2 mmol **10** in 20 cm^3 *THF* a 2.0 *M* phenyl lithium solution in *THF* (3.0 cm^3, 6 mmol) was added at room temperature. After 1 h the reaction is complete (^{19}F NMR analysis). The mixture was quenched with 20 cm^3 1 *N* HCl at 0°C and extracted with 3×10 cm^3 ether. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (eluent: hexanes). Yield 0.38 g (66%), oil; IR ($CHCl_3$): $\bar{\nu} = 3400$, 1625, 1600, 1555, 1485, 1450, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 6.88$ (s, furyl-H), 7.32 (m, 2Ar-H), 7.44 (m, 4Ar-H), 7.72 (m, 2Ar-H), 7.79 (m, 2Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 105.22$ (q, $J = 3.0$ Hz, furyl-*C4*), 114.21 (q, $J = 37.0$ Hz, furyl-*C3*), 122.82 (q, $J = 267.0$ Hz, CF_3), 123.98, 127.13 (q, $J = 2.0$ Hz), 128.34, 128.62, 128.72, 128.82, 128.25, 129.37 (Ar-*C*), 151.82 (q, $J = 4.0$ Hz, furyl-*C2*), 152.92 (furyl-*C5*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 21.39$ (s, CF_3) ppm; MS: $m/z = 288$ $[M]^+$, 269 $[M - F]^+$, 191 $[M - CO{-}CF_3]^+$, 183 $[M - CO{-}C_6H_5]^+$, 144 $[183 - HF{-}F]^+$, 105 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

5-(4-Fluorophenyl)-2-phenyl-3-(trifluoromethyl)furan (**15b**, $C_{17}H_{10}F_4O$)

Yield 0.39 g (63%), oil; IR (film): $\bar{\nu} = 1605$, 1600, 1560, 1505, 1495, 1450, 1430, 1410 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 6.82$ (s, furyl-H), 7.11 (m, 2Ar-H), 7.47 (m, 3Ar-H), 7.72 (m, 4Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 104.90$ (q, $J = 2.0$ Hz, furyl-*C4*), 114.27 (q, $J = 38.0$ Hz, furyl-*C3*), 116.00 (d, $J = 22.0$ Hz, Ar-*C3*,*C5*), 122.80 (q, $J = 267.0$ Hz, CF_3), 125.76 (d, $J =$ 3.0 Hz, Ar-*C4*), 125.88 (d, $J = 8.0$ Hz, Ar-*C2*,*C6*), 127.08 (d, $J = 2.0$ Hz), 128.67, 129.35 (Ar-*C*), 151.87 (q, $J = 5.0$ Hz, Hz, furyl-*C2*), 152.12 (furyl-*C5*), 162.68 (d, $J = 249.0$ Hz, Ar-*C4*) ppm; ^{1}H NMR ($CDCl_3$): $\delta = -34.58$ (m, Ar-F), 21.26 (s, CF_3) ppm; MS: m/z 306 $[M]^+$, 287 $[M - F]^+$, 209 $[M - CO{-}CF_3]^+$, 183 $[M - CO{-}C_6H_4F]^+$, 105 $[C_6H_5CO]^+$, 95 $[C_6H_4F]^+$, 77 $[C_6H_5]^+$.

1,4-Bis[5-(4-fluorophenyl)-3-(trifluoromethyl)fur-2-yloxy]benzol (**16**, $C_{28}H_{14}F_8O_4$)

A mixture of 2 mmol **10** 1 mmol of the corresponding dinucleophile, and 0.12 g KOH (2 mmol) in 20 cm^3 dioxane was stirred at 80°C until the reaction was complete (8–12 h, ^{19}F NMR analysis). The reaction mixture was quenched with

20 cm^3 1 *N* HCl and extracted with $3 \times 20\,cm^3$ CH_2Cl_2. After drying the organic phase with $MgSO_4$, the solvent was removed *in vacuo*. Finally the residue was purified by column chromatography (eluent: chloroform/hexanes, 1/3). Yield 1.48 g (87%), mp 132°C; IR (KBr): $\bar{\nu} = 3440$, 1650, 1605. 1575, 1500, 1440 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 6.66$ (s, 2furyl-H), 7.06 (m, 4Ar-H), 7.10 (s, 4Ar-H), 7.51 (m, 4Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 99.75$ (q, $J = 39.0$ Hz, furyl-*C3*), 102.73 (q, $J = 2.0$ Hz, furyl-*C4*), 115.98 (d, $J = 22.0$ Hz, Ar-*C3*,*C5*), 118.33 (Ar-*C2*,*C3*), 121.77 (q, $J = 267.0$ Hz, CF_3), 125.27 ($J = 4.0$ Hz, Ar-*C1*), 125.41 (d, $J = 8.0$ Hz, Ar-*C2*,*C6*), 146.21 (furyl-*C5*), 152.43 (q, $J = 5.0$ Hz, furyl-*C2*), 152.80 (C-1, Ar-*C1*,*C4*), 162.59 (d, $J = 249.0$ Hz, Ar-*C4*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -34.58$ (m, 2F), 19.44 (s, 2× CF_3) ppm; MS: $m/z = 566$ $[M]^+$, 547 $[M-F]^+$, 321 $[M - C_{11}H_5O_2F_4]^+$, 245 $[C_{11}H_5O_2F]^+$, 123 $[FC_6H_4CO]^+$, 95 $[FC_6H_4]^+$.

1,3-Bis[5(4-fluorophenyl)-3-(trifluoromethyl)fur-2-yloxy] benzene (**17**, $C_{28}H_{14}F_8O_4$)

Yield 0.56 g (50%), oil; IR (film): $\bar{\nu} = 3400$, 1655, 1600, 1570, 1505, 1485, 1445, 1415 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 6.65$ (s, 2furyl-H), 6.87 (s, Ar-H), 6.89 (m, 2Ar-H), 7.04 (m, 4Ar-H), 7.33 (m, Ar-H), 7.49 (m, 4Ar-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 100.35$ (q, $J = 39.0$ Hz, furyl-*C3*), 102.07 (q, $J = 2.0$ Hz, furyl-*C4*), 112.68 (Ar-*C*), 115.97 (d, $J = 22.0$ Hz, Ar-*C3*,*C5*), 121.69 (q, $J = 267.0$ Hz, CF_3), 125.21 (d, $J = 3.0$ Hz, Ar-*C4*), 125.46 (q, $J = 8.0$ Hz, Ar-*C-2*,*C6*), 130.90 (Ar-*C*), 146.55 (furyl-*C5*), 151.78 (q, $J = 5.0$ Hz, furyl-*C2*), 157.80 (Ar-*C*), 162.66 (d, $J = 249.0$ Hz, Ar-*C4*) ppm; MS: $m/z = 566$ $[M]^+$, 547 $[M-F]^+$, 321 $[M - C_{11}H_5O_2F_4]^+$, 245 $[C_{11}H_5O_2F_4]^+$, 123 $[FC_6H_4CO]^+$, 95 $[C_6H_4F]^+$.

2,6-Bis[5-phenyl-3-(trifluoromethyl)fur-2-yloxy]naphthaline (**18**, $C_{32}H_{18}F_6O_4$)

Yield 0.48 g (41%), mp 187°C; IR (KBr): $\bar{\nu} = 3440$, 1660, 1600, 1570, 1520, 1455, 1440 cm^{-1}; ^1H NMR (acetone-d_6): $\delta = 7.21$ (s, 2furyl-H), 7.35 (m, 2Ar-H), 7.42 (m, 4Ar-H), 7.50 (m, 2Ar-H), 7.69 (m, 4Ar-H), 7.73 (m, 2Ar-H), 8.06 (m, 2Ar-H) ppm; ^{13}C NMR (acetone-d_6): $\delta = 100.26$ (q, $J = 39.0$ Hz, furyl-*C3*), 104.29 (q, $J = 2.0$ Hz, furyl-*C4*), 113.50, 119.46 (Ar-*C*), 123.09 (q, $J = 266.0$ Hz, CF_3), 124.42, 129.25, 129.81, 129.86, 130.97, 132.34, Ar-*C*), 148.37 (furyl-*C5*), 153.44 (q, $J = 4.0$ Hz, furyl-*C2*), 154.80 (Ar-*C*) ppm; ^{19}F NMR (acetone-d_6): $\delta = 19.87$ (s, 2× CF_3) ppm; MS: $m/z = 580$ $[M]^+$, 561 $[M-F]^+$, 353 $[M - C_{11}H_6F_3O_2]^+$, 227 $[C_{11}H_6F_3O_2]^+$, 179 $[227 - HF{-}CO]^+$, 126 $[C_{10}H_6]^+$, 105 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

2-[Methyl[5-(4-chlorophenyl)-3-(trifluoromethyl)fur-2-yl]amino]1-[5-(thien-2-yl)-3-(trifluoromethyl)fur-2-yl oxyl]ethane (**19**, $C_{23}H_{16}ClF_6NO_3S$)

To a solution of 0.96 g **13** (3 mmol) and 0.71 g **10g** (3 mmol) in dioxane were stirred at 80°C until the reaction was complete (^{19}F NMR analysis). After quenching with water (20 cm^3) work-up as described before. The residue was purified by column chromatography (eluent: CHC_3/hexanes, 1/1). Yield 0.61 g (38%, oil; IR (film): $\bar{\nu} = 1650$, 1600, 1455 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.17$ (q, $J = 1.0$ Hz, NCH_3), 3.79 (tr, $J = 5.0$ Hz, NCH_2), 4.56 (tr, $J = 5.0$ Hz, OCH_2), 6.44 (s, furyl-H), 6.62 (s, furyl-H), 6.98 (m, thienyl-H), 7.10 (m, thienyl-H), 7.19 (m, thienyl-H), 7.26 (m, 2Ar-H), 7.35 (m, 2thienyl-H) ppm; ^{13}C NMR ($CDCl_3$). $\delta = 38.95$ (q, $J = 2.0$ Hz, NCH_2), 51.90 (NCH_2), 70.59 (OCH_2), 92.66 (q, $J = 38.0$ Hz, furyl-*C3*), 93.20 (q, $J = 39.0$ Hz, furyl-*C3*), 103.57 (q, $J = 2.0$ Hz, furyl-*C4*), 106.01 (q, $J = 3.0$ Hz, furyl-*C4′*), 122.21 (q, $J = 267.0$ Hz, CF_3), 122.76 (thienyl-*C*), 123.46 (q, $J = 265.0$ Hz, CF_3), 123.69 (Ar-C), 124.40, 127.63 (thienyl-*C*), 128.39, 128.84, 131.90, 132.20 (Ar-*C*, thienyl-*C*), 140.44 (furyl-*C5*), 142.78 (furyl-*C5*), 154.92 (q, $J = 4.0$ Hz, furyl-*C2*), 155.43 (q, $J = 4.0$ Hz, furyl-*C2*) ppm; MS: $m/z = 537/535$ $[M]^+$, 518/516 $[M-F]^+$, 320/318 $[M - C_9H_4F_3OS]^+$, 304/302 $[M - C_9H_4F_3O_2S]^+$, 276/274 $[304/302 - C_2H_4]^+$, 233 $[C_9H_4F_3O_2S]^+$, 217 $[C_9H_4F_3OS]^+$, 141/139 $[ClC_6H_4]^+$, 113/111 $[ClC_6H_4]^+$.

2-(1,1,3,3,3-Pentafluoropropen-2-yl)cyclohexanone (**21**, $C_9H_9F_5O$)

4.92 (20 mmol) 2-(1,1,1,3,3,3-hexafluoroisopropyliden)cyclohexanone **20** [18c] and $SnCl_2 \cdot 2H_2O$ (4.52 g, 20 mmol) were heated for 6 h under reflux in a solvent mixture (xylene 60 cm^3, THF 6 cm^3). After filtration the product was purified by distillation *in vacuo*. Yield 3.60 g (79%), 69°C/15 Torr; IR (film): $\bar{\nu} = 1745$, 1715, 1445 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.73$ (m, CH_2), 1.90 (m, CH_2), 2.01 (m, CH_2), 2.13 (m, CH_2), 2.23 (m, CH_2), 2.35 (m, CH_2), 2.56 (m, CH_2), 3.19 (m, CH_2) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 25.15$, 26.37, 31.73 (m), 41.34, 47.17, 85.51 (ddq, $J = 7.0$, 11.0, 34.0 Hz, $C{=}CF_2$), 122.98 (ddq, $J = 5.0$, 14.0, 271.0 Hz, CF_3), 156.96 (ddq, $J = 293.0$, 304.0, 4.0 Hz, $C{=}CF_2$), 204.11 ($C{=}O$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 2.04$ (m, $=CF_a$), 3.52 (m, $=CF_b$), 17.97 (dd, $J = 10.0$, 22.0 Hz, CF_3) ppm; MS: $m/z = 228$ $[M]^+$, 200 $[M - CO]^+$, 184 $[M - C_2H_4O]^+$, 158 $[M - C_3H_6CO]^+$, 115 $[184 - CF_3]^+$, 89 $[158 - CF_3]^+$, 69 $[CF_3]^+$, 55 $[C_4H_7]^+$, 42 $[C_3H_6]^+$, 41 $[C_3H_5]^+$.

2-Fluoro-3-(trifluoromethyl)-4,5,6,7-tetrahydrocumaron (**22**, $C_9H_8F_4O$)

To a solution of 4.56 g **21** (20 mmol) in 100 cm^3 *DMSO* 0.48 g NaH (20 mmol) were added slowly at 0°C with stirring. Stirring was continued until the starting material was consumed (^{19}F NMR analysis). Then the reaction mixture was poured into 30 cm^3 ice-cold 1 *N* HCl and the mixture was extracted with $3 \times 30\,cm^3$ pentane. The organic phase was dried ($MgSO_4$) filtered, and concentrated *in vacuo*. Yield 0.88 g (21%), oil; IR (film): $\bar{\nu} = 3440$, 1675, 1450 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.79$ (m, 2× CH_2), 2.46 (m, 2× CH_2) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.43$, 21.86, 22.02, 22.29 (*C-4* − *C-7*), 115.91 (m, *C-3′*), 116.71 (m, *C-3*), 121.81 (dq, $J = 5.0$, 266.0 Hz, CF_3), 141.76 (*C-7′*), 153.65 (dq, $J = 284.0$, 5.0 Hz, *C-2*) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -34.03$ (q, $J = 12.0$ Hz, =CF), 19.22 (d, $J = 12.0$ Hz, CF_3) ppm.

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