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Domino Reactions with 2-Fluoro-3-trifluoromethylfurans and -thiophenes [1]

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Summary. The single fluorine atom of 2-fluoro-3-trifluoromethylfurans and -thiophenes can be readily replaced by various nucleophiles. Depending on the substituent pattern, certain products obtained upon nucleophilic substitution with benzyl alcohols are susceptible to [1,3]- and [1,5]-benzyl group migrations under very mild conditions. Therefore, these rearrangements can be integrated into domino reactions.

Keywords. 2-Fluoro-3-trifluoromethylfurans; 2-Fluoro-3-trifluoromethylthiophenes; 3-Trifluoromethyl-2(3*H*)-furanones; 3-Trifluoromethyl-2(3*H*)-thiophenones; 3-Trifluoromethyl-2(5*H*)-furanones; 3-Trifluoromethyl-2(5*H*)-thiophenones; [1,3]- and [1,5]-benzyl group migrations; Domino reactions.

Introduction

Due to their large abundance [2] and their broad biological activities, butenolides have been studied extensively and still constitute an area of current interest. Consequently, numerous synthetic pathways to this class of compounds have been developed [3,4]. Recently, we have demonstrated that 5-fluoro-4-trifluoromethyl-1,3-azoles [5], 2-fluoro-3-trifluoromethylfurans [6], and 2-fluoro-3-trifluoromethylthiophenes [7] are valuable building blocks for the synthesis of partially fluorinated heterocycles [8]. The single fluorine atom adjacent to the trifluoromethyl group can be replaced by various nucleophiles under relatively mild reaction conditions. This strategy provides ready access to trifluoromethyl substituted heterocycles with interesting substituent patterns [9].

In this paper we report on the synthesis of trifluoromethyl substituted butenolides and their thioanalogues *via* domino reactions [10] starting from 2-fluoro-3-trifluoromethylfurans and -thiophenes, respectively.

Results and Discussion

Already at room temperature, the fluorine atom at C-2 of 2-fluoro-3-trifluoromethylfurans **1** and -thiophenes **2** is susceptible to nucleophilic displacement reactions, *e.g.* by benzyl alcohols in the presence of sodium hydride, in high yields.

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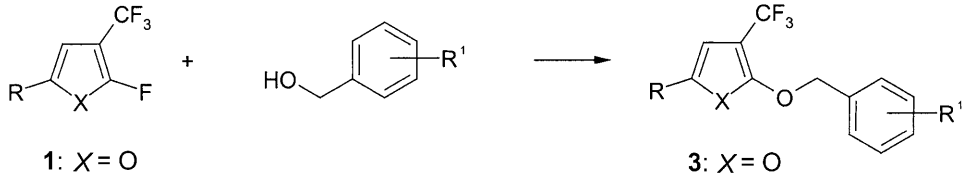


1: $X = O$
2: $X = S$

3: $X = O$
4: $X = S$

1a:	$R = C_6H_5$	**3a**:	$R = C_6H_5$ $R^1 = H$
1b:	$R = 4\text{-}CH_3C_6H_4$	**3b**:	$R = 4\text{-}ClC_6H_4$ $R^1 = H$
1c:	$R = 4\text{-}FC_6H_4$	**3c**:	$R = 4\text{-}FC_6H_4$ $R^1 = 4\text{-}Cl$
1d:	$R = 2\text{-}FC_6H_4$	**3d**:	$R = 4\text{-}BrC_6H_4$ $R^1 = 4\text{-}Cl$
1e:	$R = 4\text{-}ClC_6H_4$	**3e**:	$R = 2\text{-}FC_6H_4$ $R^1 = 4\text{-}Cl$
1f:	$R = 4\text{-}BrC_6H_4$	**3f**:	$R = 4\text{-}FC_6H_4$ $R^1 = 4\text{-}Br$
1g:	$R = 3,4,5\text{-}(CH_3O)_3C_6H_2$	**3g**:	$R = 4\text{-}ClC_6H_4$ $R^1 = 4\text{-}Br$
		3h:	$R = 4\text{-}ClC_6H_4$ $R^1 = 3,4,5\text{-}(CH_3O)_3$
2a:	$R = 4\text{-}ClC_6H_4$		
2b:	$R = 4\text{-}FC_6H_4$	**4**:	$R = 4\text{-}ClC_6H_4$ $R^1 = 4\text{-}Cl$

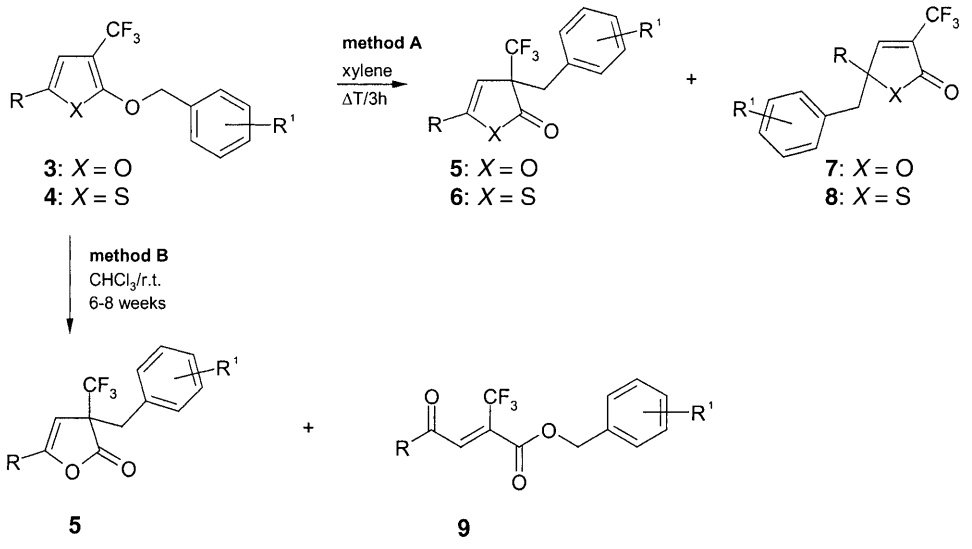
Scheme 1

Under these conditions the substitution products **3** are capable to react further. The reaction rate of the subsequent rearrangement depends strongly on the substituent pattern of the aromatic ring of the benzyl alcohol. Derivatives of 3,4,5-trimethoxy benzyl alcohol exhibit the strongest tendency to rearrange. In the case of the thioanalogues **4**, the rearrangement only occurs at elevated temperatures.

When a solution of compounds **3** and **4** in xylene is heated to 120°C (method A), after three hours no starting material can be detected by ^{19}F NMR spectroscopy. Two new products are formed. The compounds generated from **3** give rise to absorptions at $\nu = 1810$ and $1765\,cm^{-1}$ in their IR spectra which we assign to an isolated and a conjugated lactone moiety. The carbon atom C-3 bearing the trifluoromethyl group resonates at 60 ppm in the main product and at 125 ppm in the by-product, indicating that in the first case the trifluoromethyl group is bonded to a sp^3 carbon atom and in the latter case to an sp^2 hybridized carbon atom. The spectroscopic data of the products formed from **3** are in agreement with structures represented by formulae **5** and **7**, respectively. Analogously, the products of the rearrangement of the thioanalogues **4** can be identified as trifluoromethyl-2(3*H*)-thiophenones **6** and trifluoromethyl-2(5*H*)-thiophenones **8**.

Although compounds **3** and **4** can be classified as *Claisen* systems, no [3,3]-sigmatropic process can be observed. The isolated products are the result of [1,3]- and [1,5]-benzyl group migrations. Since a subsequent transformation of compounds **5** into **7** and compounds **6** into **8** cannot be achieved, the benzyl group migrations are obviously competing reactions. In all cases studied so far, the rate of the [1,3]-benzyl group migration is faster than the rate of the [1,5]-group migration. However, at elevated temperatures the yields of the by-products **7** and **8** increase.

A photochemically induced rearrangement of 3-benzyloxycholesta-3,5-diene to give 4-benzylcholest-4-en-3-one described in 1968 represents the first example of a

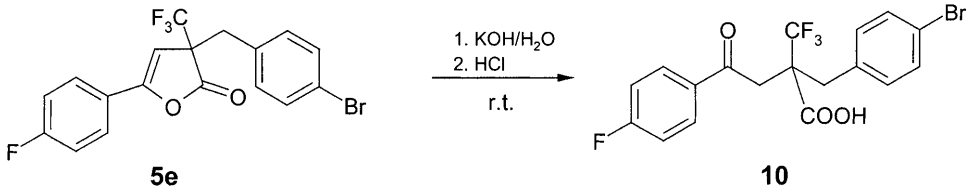


5a/7a:	$R = C_6H_5$	$R^1 = H$	**6/8**:	$R = 4\text{-}ClC_6H_4$	$R^1 = 4\text{-}Cl$
5b/7b:	$R = 2\text{-}FC_6H_4$	$R^1 = 4\text{-}Cl$			
5c/7c:	$R = 4\text{-}FC_6H_4$	$R^1 = 4\text{-}Cl$	**9a**:	$R = 4\text{-}FC_6H_4$	$R^1 = 4\text{-}Cl$
5d/7d:	$R = 4\text{-}BrC_6H_4$	$R^1 = 4\text{-}Cl$	**9b**:	$R = 4\text{-}BrC_6H_4$	$R^1 = 4\text{-}Cl$
5e/7e:	$R = 4\text{-}FC_6H_4$	$R^1 = 4\text{-}Br$	**9c**:	$R = 4\text{-}ClC_6H_4$	$R^1 = 4\text{-}Br$

Scheme 2

[1,3]-benzyl group migration from oxygen to carbon [12]. Furthermore, [1,3]-benzyl group migrations have been observed in anionic systems [13]. Examples for a competition of [1,3]- and [1,5]-migrations have been described by *W. Steglich et al.* in the 5-benzyloxyoxazole series [14].

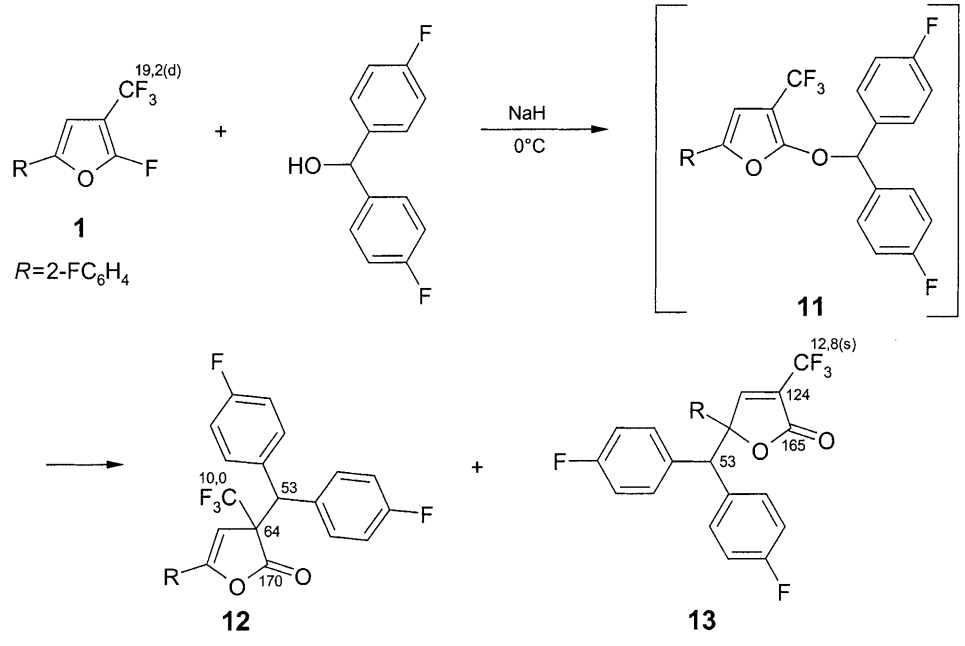
Performing the rearrangement of compounds **3** at room temperature (method B), ^{19}F NMR analysis revealed that extremely long reaction times are necessary (6–8 weeks). Surprisingly, 3-trifluoromethyl-2(3*H*)-furanones **5** are only formed as by-products in this case, and 3-trifluoromethyl-2(5*H*)-furanones **7** cannot be detected even spectroscopically. For the new main product, IR absorptions at $\nu = 1737$ and $1680\,cm^{-1}$ are recorded, which are in agreement with the presence of a conjugated ester and a conjugated keto function. The ^{13}C NMR spectrum of compound **9a** shows absorptions at 128.6 $(q, {}^2J_{CF} = 32.2\,Hz, =CCF_3)$ and 141.5 ppm $(q, {}^3J_{CF} = 4.9\,Hz, =CH)$, which is characteristic for a -CH=CCF_3-substructure. Resonance lines at 160.2 and 189.9 ppm confirm the information already extracted from the IR spectra, *i.e.* that both ester and keto function are in conjugation with a C=C double bond. The spectroscopic data are in agreement with a structure depicted by formula **9**. α,β-Unsaturated γ-keto acid derivatives of type **9** represent valuable trifluoromethyl substituted building blocks with a multifunctional array of functional groups [15]. Their formation can be explained *via* a hydrolytic ring opening of substitution products **3** followed by oxidation on air. Detailed mechanistic studies are in progress. In contrast, the corresponding 2-benzyloxy-3-trifluoromethylthiophenes **4** are stable under similar reaction conditions. Hydrolysis



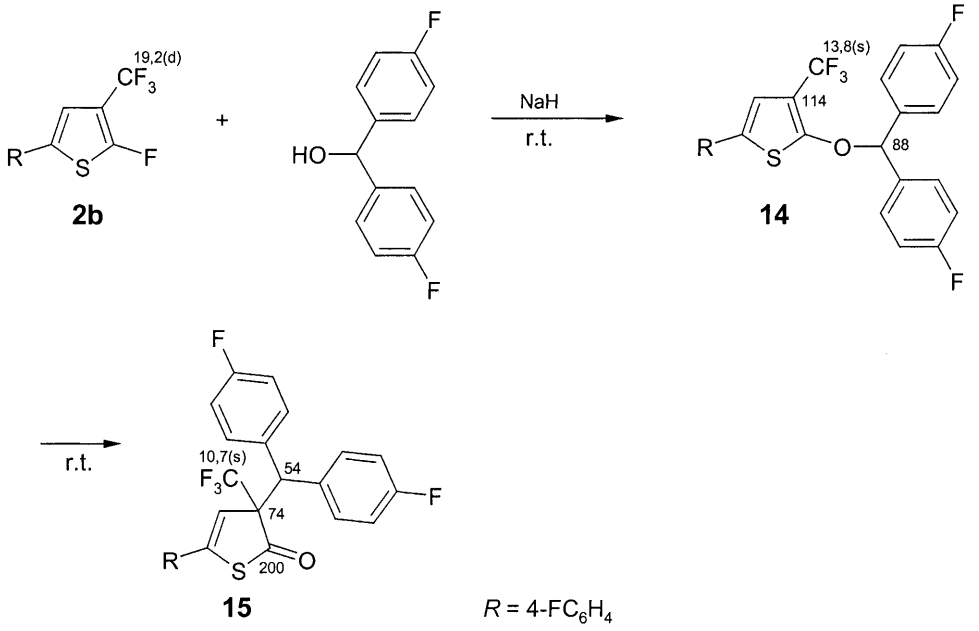
Scheme 3

of **5e** results in the formation of the aryl substituted 3,3,3-trifluoromethylpropionic acid **10**. Compounds of type **10** represent interesting building blocks; they can be used as starting materials for the synthesis of GABA derivatives [15]. α-Arylpropionic acids (*e.g.* ibuprofen) are a class of non-steroid antiinflammatories which exhibit growing potential in treatment of polyarthritis, arthrosis, and rheumatic diseases [16]. Because of the structural similarity, modification of compounds **10** could be of interest in developing new selective COX-2 inhibitors [17].

Reactions of 2-fluoro-3-trifluoromethylfurans **1** and -thiophenes **2** with secondary benzyl alcohols, *e.g.* 4,4′-difluorobenzhydrol, in the presence of sodium hydride are complete within a few hours at room temperature (^{19}F NMR analysis). The second aryl group lowers the activation barrier of the rearrangement. When **1** was reacted, the successive [1,3]- and [1,5]-rearrangements are fast compared to the nucleophilic substitution process. Therefore, the intermediacy of **11** could not be proved even by ^{19}F NMR spectroscopy. Similar benzhydryl group migrations have been described in the literature: 4-benzhydryloxy-5-methoxy[1,2]benzoquinone



Scheme 4



Scheme 5

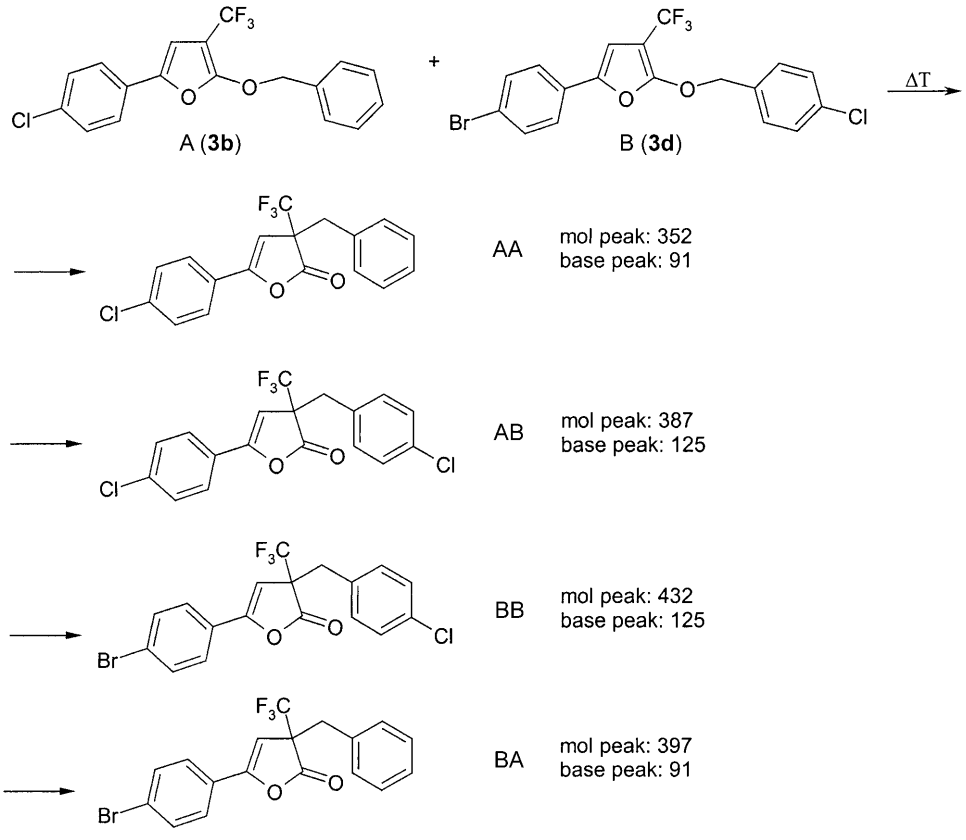
→ 3-benzhydryl-2-hydroxy-5-methoxy[1,4]benzoquinone [18] and 4-bromo-3-benzhydryloxy-1,5-diphenyl-2,5-dihydropyrrol-2-one → 4-benzhydryl-1,5-diphenyl-2,3-dihydro-2,3-pyrroldione [19].

When thiophene **2b** was reacted with 4,4′-difluorobenzhydrol, we were able to isolate and characterize the substitution product **14** which at room temperature slowly rearranges (**2** → **14** → **15**). A competition of a [1,5]-migration could not be detected under the reaction conditions applied. Compounds **12**, **13**, and **15** show two sets of signals for two diastereotopic 4-fluorophenyl groups in their ^{13}C and ^{19}F NMR spectra.

Repeatedly, [1,3]-benzyl group migrations from oxygen to carbon have been classified as sigmatropic processes [20]. In earlier investigations on the mechanism of benzyl group migrations we could prove that in the case of 5-benzyloxy-4-trifluoromethyloxazoles a multi-step procedure is operating, consisting of a separate bond-breaking and bond-forming process [21]. To clarify the mechanism of the above discussed [1,3]- and [1,5]-benzyl group migrations, we performed intercrossing experiments.

A mixture of equimolar amounts of the two substitution products **3b** and **3d** was heated to 120°C in xylene. Then, the composition of the reaction mixture obtained was analyzed by GC/MS. In the case of a multi-step procedure, the formation of four products should be expected (AA, BB, AB, BA), whereas for a concerted process only the products AA and BB should be obtained.

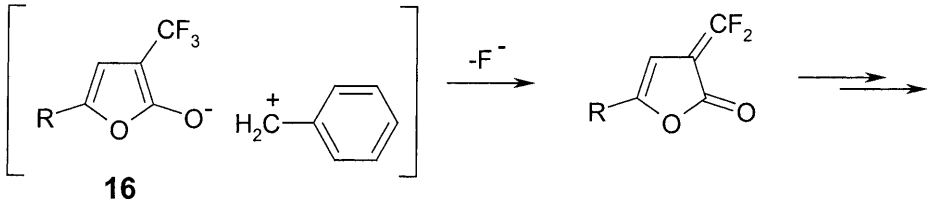
Unequivocally, four compounds could be detected and characterized by mass spectrometry *via* mol peak and base peak. The intercrossing products AB and BA are only formed in minor amounts and could not be isolated. As an additional argument for a multi-step procedure we interprete the formation of products **7** and **8**



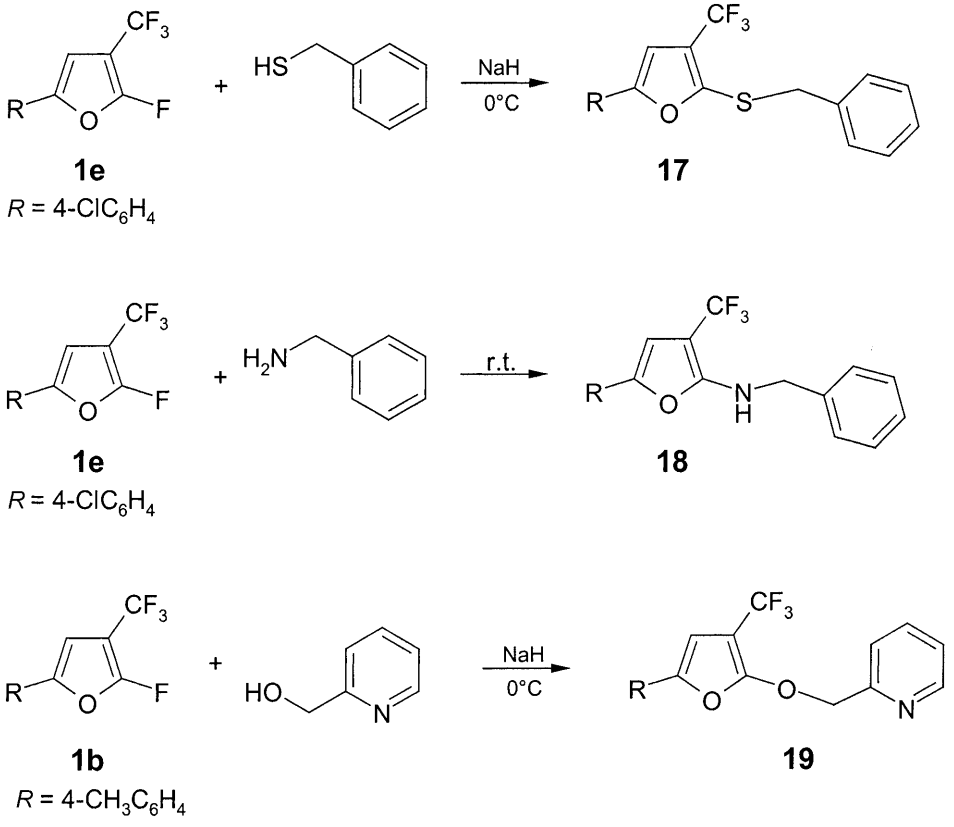
Scheme 6

via a [1,5]-benzyl group migration. For this process, a sequence of two [1,3]-migration steps can be ruled out.

The formation of only small amounts of the intercrossing products suggests that the rearrangement proceeds *via* close radical or ion pairs. Experiments to trap the radical species were unsuccessful so far as were ESR experiments. On the other hand, the rate of the rearrangements turned out to be independent of the polarity of the solvents used. As a strong argument against an ionic pathway we interpret the fact that no degradation products of the trifluoromethyl group could be detected which should be expected if anionic intermediates of type **16** are formed. Detailed mechanistic studies are in progress.



Scheme 7



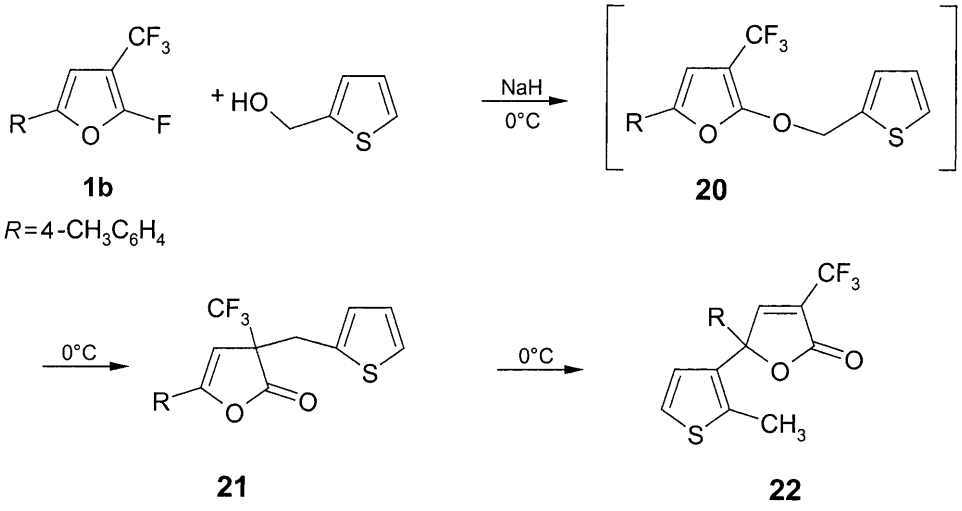
Scheme 8

Upon reaction of **1e** with benzyl mercaptane and benzylamine, stable substitution products **17** and **18** are formed. Experiments to initiate [1,3]- and [1,5]-benzyl group migrations by heating have been unsuccessful so far. The compounds are stable up to 140°C; above this temperature an undefined decomposition process starts. Similar reaction behaviour is exhibited by compounds **19**, readily obtainable from **1e** and 2-hydroxymethyl pyridine.

In contrast, **1b** reacts with 2-hydroxymethyl thiophene in the presence of sodium hydride already at 0°C. We were not able to isolate the expected substitution product **20**. Under the reaction conditions applied, **20** reacts further to give **21**, the product of a [1,3]-thenyl group migration, which turned out to be unstable even at 0°C and slowly rearranges to give a *Cope* product which spontaneously undergoes heteroaromatization (**21** → **22**). The domino reaction, the transformation of 2-fluoro-3-trifluoromethylfurans into 3-trifluoromethylbutenolides includes four separate steps:

1) a nucleophilic substitution,
2) a [1,3]-thenyl group migration,
3) a *Cope* rearrangement, and
4) finally a rearomatization process

The complete reaction sequence can be performed already at 0°C. Compounds of type **22** represent preparatively interesting *Michael* systems.



Scheme 9

To the best of our knowledge this is the first example of a domino reaction including a thenyl group migration.

Experimental

General

Solvents were purified and dried prior to use. Reagents were used as purchased. Melting points (uncorrected) were determined on a Boetius heating table. Mass spectra were recorded on a VG 12-250 and a MAT 212 (Masslab) electron ionization spectrometer (EI-MS, EI = 70 eV). IR spectra were obtained with a FTIR spectrometer (Genesis ATI Mattson/Unicam) and a Specord M 80 (Fa. Carl Zeiss, Jena). ^{1}H (200 MHz), ^{13}C (50 MHz), and ^{19}F (188 MHz) NMR spectra were recorded on a Varian Gemini 2000 spectrometer. *TMS* was used as reference for ^{1}H and ^{13}C NMR spectra (internal), and CF_3CO_2H for ^{19}F NMR spectra (external). Flash chromatography was performed using silica gel (32–63 μm). Elemental analyses were performed with a CHNO-S-Rapid apparatus (Fa. Heraeus).

1 → **3** *and* **2** → **4**; *general procedure*

To an ice cold solution of **1** [6] or **2** [7] (2 mmol) and of the corresponding benzyl alcohol (4 mmol) in *THF* (5 cm^3), NaH (0.12 g, 5 mmol) was added. Then the reaction mixture was stirred at room temperature until the starting material was consumed (^{19}F NMR analysis). The reaction mixture was treated with an ice/water mixture and extracted with ether. After drying the organic phase with $MgSO_4$, the solvent was evaporated *in vacuo*. The remaining crude product was purified by column chromatography (eluent: CH_2Cl_2/petrol ether).

2-Benzyloxy-5-phenyl-3-trifluoromethylfuran (**3a**; $C_{18}H_{13}F_3O_2$)

Yield: 77%; colourless oil; ^{1}H NMR ($CDCl_3$): δ = 5.22 (s, 2H, OCH_2), 6.50 (s, 1H, CH_{furan}), 7.29 (m, 10H, arom.) ppm; ^{13}C NMR ($CDCl_3$): δ = 74.0 (OCH_2), 93.7 (q, ^{2}J = 39.0 Hz, C-3$_{furan}$), 103.5 (q, ^{3}J = 2.0 Hz, C-4$_{furan}$), 122.6 (q, ^{1}J = 266.0 Hz, CF_3), 122.9, 127.4, 128.1, 128.6, 128.7 (2x), 129.4,

134.9 (arom.), 144.6 (C-5_{furan}), 156.2 (q, $^3J = 4.0$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.7$ (s, 3F, CF_3) ppm; IR (film) $\nu = 1675, 1600, 1500, 1455, 1445\,cm^{-1}$; MS (EI): $m/z = 318$ $[M]^+$, 228 $[M–C_7H_6]^+$, 208 $[M–C_7H_7, –F]^+$, 107 $[C_7H_7O]^+$, 105 $[C_6H_5CO]^+$, 91 $[C_7H_7]^+$, 77 $[C_6H_5]^+$.

2-Benzyloxy-5-(4-chlorophenyl)-3-trifluoromethylfuran (**3b**; $C_{18}H_{12}ClF_3O_2$)

Yield: 93%; mp.: 47°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.32$ (s, 2H, OCH_2), 6.56 (s, 1H, CH_{furan}), 7.35 (m, 9H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 74.3$ (OCH_2), 94.1 (q, $^2J = 39$ Hz, C-3_{furan}), 104.1 (q, $^3J = 2$ Hz, C-4_{furan}), 122.4 (q, $^1J = 266$ Hz, CF_3), 124.2, 127.9, 128.0, 128.2, 128.9, 129.0, 133.2, 134.9 (arom.), 143.6 (C-5_{furan}), 156.4 (q, $^3J = 4$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.4$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1640$, 1600, 1580, 1555, 1455, 1445, $1405\,cm^{-1}$; MS (EI): $m/z = 354/352$ $[M]^+$, 263/261 $[M–C_7H_7]^+$, 141/139 $[C_7H_4ClO]^+$, 91 $[C_7H_7]$, 77 $[C_6H_5]^+$.

2-(4-Chlorobenzyloxy)-5-(4-fluorophenyl)-3-trifluoromethylfuran (**3c**; $C_{18}H_{11}ClF_4O_2$)

Yield: 65%; mp.: 56°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.33$ (s, 2H, OCH_2), 6.55 (s, 1H, CH_{furan}), 7.09 (m, 3H, arom.), 7.38 (m, 3H, arom.), 7.49 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 73.7$ (OCH_2), 94.5 (q, $^2J = 38.2$ Hz, C-3_{furan}), 103.2 (q, $^3J = 2.1$ Hz, C-4_{furan}), 115.8 (d, $^2J = 22.3$ Hz, C-3, C-$5_{fluorophenyl}$), 122.3 (q, $^1J = 266.0$ Hz, CF_3), 124.9 (d, $^3J = 8.0$ Hz, C-2, C-$6_{fluorophenyl}$), 125.8 (d, $^4J = 3.3$ Hz, C-$1_{fluorophenyl}$), 128.9, 129.5, 129.8, 134.9 (arom.), 144.1 (C-5_{furan}), 155.9 (C-2_{furan}), 162.3 (d, $^1J = 247.5$ Hz, C-$4_{fluorophenyl}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -35.7$ (m, 1F, *p*-FC_6H_4), 20.1 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1650$, 1610, 1590, 1450, $1360\,cm^{-1}$; MS (EI): $m/z = 370/372$ $[M]^+$, 245 $[M–C_7H_6Cl]^+$, 226 $[M–C_7H_6Cl, -F]^+$, 197 $[M–C_7H_6Cl, –F, –CO]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

5-(4-Bromophenyl)-2-(4-chlorobenzyloxy)-3-trifluoromethylfuran (**3d**; $C_{18}H_{11}BrClF_3O_2$)

Yield: 87%; mp.: 65°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.33$ (s, 2H, OCH_2), 6.63 (s, 1H, CH_{furan}), 7.38 (m, 5H, arom.), 7.51 (m, 3H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 73.6$ (OCH_2), 94.5 (q, $^2J = 39.6$ Hz, C-3_{furan}), 104.2 (q, $^3J = 2.3$ Hz, C-4_{furan}), 121.4 (arom.), 122.2 (q, $^1J = 266.2$ Hz, CF_3), 124.5, 128.3, 129.0, 129.5, 132.0, 133.2, 134.9 (arom.), 143.8 (C-5_{furan}), 156.2 (q, $^3J = 4.6$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.1$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1650$, 1600, 1580, 1450, $1360\,cm^{-1}$; MS (EI): $m/z = 430/432/434$ $[M]^+$, 305/307 $[M–C_7H_6Cl]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

2-(4-Chlorobenzyloxy)-5-(2-fluorophenyl)-3-trifluoromethylfuran (**3e**; $C_{18}H_{11}ClF_4O_2$)

Yield: 81%; mp.: 48°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.36$ (s, 2H, OCH_2), 6.84 (d, $^5J = 3$ Hz, CH_{furan}), 7.21 (m, 4H, arom.), 7.39 (m, 3H, arom.), 7.60 (m, 1H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 73.5$ (OCH_2), 94.5 (q, $^2J = 39.2$ Hz, C-3_{furan}), 108.9 (d, $^4J = 10.3$ Hz, C-4_{furan}), 116.1 (d, $^2J = 21.3$ Hz, C-$3_{fluorophenyl}$), 117.9 (d, $^2J = 12.2$ Hz, C-$1_{fluorophenyl}$), 122.4 (q, $^1J = 266.2$ Hz, CF_3), 124.4 (d, $^3J = 3.4$ Hz, C-$6_{fluorophenyl}$), 125.1 (d, $^4J = 2.8$ Hz, C-$5_{fluorophenyl}$), 128.6 (d, $^3J = 8.3$ Hz, C-$4_{fluorophenyl}$), 129.0, 129.5, 133.3, 134.9 (arom.), 139.3 (d, $^3J = 2.3$ Hz, C-5_{furan}), 156.0 (C-2_{furan}), 158.5 ($^1J = 250.7$ Hz, C-$2_{fluorophenyl}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -36.6$ (m, 1F, *o*-FC_6H_4), 20.1 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1650$, 1620, 1580, 1480, 1470, 1430, $1360\,cm^{-1}$; MS (EI): $m/z = 370/372$ $[M]^+$, 245 $[M–C_7H_6Cl]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

2-(4-Bromobenzyloxy)-5-(4-fluorophenyl)-3-trifluoromethylfuran (**3f**; $C_{18}H_{11}BrF_4O_2$)

Yield: 82%; mp.: 58°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.31$ (s, 2H, OCH_2), 6.55 (s, 1H, CH_{furan}), 7.08 (m, 2H, arom.), 7.31 (m, 2H, arom.), 7.51 (m, 4H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 73.7$ (OCH_2),

94.5 (q, $^2J = 38.9$ Hz, C-3_{furan}), 103.2 (m, C-4_{furan}), 115.8 (d, $^2J = 22.4$ Hz, C-3, C-$5_{fluorophenyl}$), 122.3 (q, $^1J = 265.9$ Hz, CF_3), 123.0 (arom.), 124.9 (d, $^3J = 8$ Hz, C-2, C-$6_{fluorophenyl}$), 125.8 (d, $^4J = 3.3$ Hz, C-$1_{fluorophenyl}$), 129.8, 131.9, 133.9 (arom.), 144.2 (C-5_{furan}), 159.9 (C-2_{furan}), 162.3 (d, $^1J = 248$ Hz, C-$4_{fluorophenyl}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -35.6$ (m, 1F, *p*-FC_6H_4), 20.1 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1650$, 1600, 1590, 1450, 1360 cm^{-1}; MS (EI): $m/z = 414/416$ $[M]^+$, 245 $[M–C_7H_6Br]^+$, 217 $[M–C_7H_6Br, –CO]^+$, 197 $[M–C_7H_6Br, –CO, –HF]^+$, 169/171 $[C_7H_6Br]^+$ (100).

2-(4-Bromobenzyloxy)-5-(4-chlorophenyl)-3-trifluoromethylfuran (**3g**; $C_{18}H_{11}BrClF_3O_2$)

Yield: 62%; mp.: 63°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.32$ (s, 2H, OCH_2), 6.62 (s, 1H, CH_{furan}), 7.40 (m, 6H, arom.), 7.55 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 73.6$ (OCH_2), 94.5 (q, $^2J = 38.3$ Hz, C-3_{furan}), 104.1 (C-4_{furan}), 123.1, 124.3 (arom.), 125.8 (q, $^1J = 264.7$ Hz, CF_3), 127.9, 129.1, 129.8, 131.9, 133.4, 133.8 (arom.), 143.9 (C-5_{furan}), 156.1 (q, $^3J = 3.9$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.3$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1650$, 1600, 1580, 1450, 1360 cm^{-1}; MS (EI): $m/z = 430/432/434$ $[M]^+$, 261/263 $[M–C_7H_6Br]^+$, 242/244 $[M–C_7H_6Br, –F]^+$, 213/215 $[M–C_7H_6Br, –HF, –CO]^+$, 169/171 $[C_7H_6Br]^+$ (100).

5-(4-Chlorophenyl)-2-(3,4,5-trimethoxybenzyloxy)-3-trifluoromethylfuran (**3h**; $C_{21}H_{18}ClF_3O_5$)

Yield: 81%; mp.: not detectable due to rearrangement; ^{1}H NMR ($CDCl_3$): $\delta = 3.85$ (s, 9H, $3 \times OCH_3$), 5.30 (s, 2H, OCH_2), 6.61 (s, 1H, CH_{furan}), 6.67 (s, 2H, arom.), 7.33 (m, 2H, arom.), 7.43 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 56.1$ ($2 \times OCH_3$), 60.8 (OCH_3), 74.4 (OCH_2), 94.2 (q, $^2J = 38.7$ Hz, C-3_{furan}), 104.0 (q, $^3J = 2.4$ Hz, C-4_{furan}), 105.3 (arom.), 122.4 (q, $^1J = 266.6$ Hz, CF_3), 124.2, 127.9, 129.0, 130.3, 133.3, 138.5 (arom.), 143.7 (C-5_{furan}), 153.5 (arom.), 156.3 (q, $^3J = 4.6$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.2$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1633$, 1600, 1462, 1453, 1369 cm^{-1}; MS (EI): $m/z = 441/443$ $[M]^+$, 260/262 $[M–C_7H_4(OCH_3)_3]^+$, 181 $[C_7H_4(OCH_3)_3]^+$ (100).

2-(4-Chlorobenzyloxy)-5-(4-chlorophenyl)-3-trifluoromethylthiophene (**4**; $C_{18}H_{11}Cl_2F_3OS$)

Yield: 80%; mp.: 120°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.18$ (s, 2H, OCH_2), 7.06 (s, 1H, $CH_{thiophene}$), 7.36 ppm (m, 8H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 76.6$ (OCH_2), 113.5 (q, $^2J = 34.8$ Hz, C-$3_{thiophene}$), 118.7 (q, $^3J = 3.2$ Hz, C-$4_{thiophene}$), 122.0 (q, $^1J = 270.2$ Hz, CF_3), 126.3, 129.0, 129.1, 129.2 (arom.), 129.5 (C-$5_{thiophene}$), 131.8, 133.2, 133.5, 134.8 (arom.), 163.3 (q, $^3J = 3.4$ Hz, C-$2_{thiophene}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.5$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1579$, 1512, 1421, 1374 cm^{-1}; MS (EI): $m/z = 403/405$ $[M]^+$, 276/278 $[M–C_7H_6Cl]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

3 → 5 + 7 *and* **4 → 6 + 8**; *general procedure*

Method A: A solution of **3** (2 mmol) or **4** (2 mmol) in xylene (5 cm^3) was heated to 120°C until the starting material was consumed (^{19}F NMR analysis). The reaction mixture was poured into an ice/water mixture and extracted with ether. After drying the organic phase with $MgSO_4$, the solvent was evaporated *in vacuo*. Finally, the crude product was purified by column chromatography (eluent: petrolether/CH_2Cl_2, elution sequence: **5**, **7** and **6**, **8**, respectively).

3 → 5 + 9; *general procedure*

Method B: A solution of **3** (2 mmol) in $CHCl_3$ (5 cm^3) or in xylene (5 cm^3) was stirred at room temperature until the starting material was completely consumed (^{19}F NMR analysis). Work-up: see above; elution sequence: **5**, **9**.

3-Benzyl-5-phenyl-3-trifluoromethyl-2(3H)-furanone (**5a**; $C_{18}H_{13}F_3O_2$); *5-Benzyl-5-phenyl-3-trifluoromethyl-2(5H)-furanone* (**7a**; $C_{18}H_{13}F_3O_2$)

5a: yield: 70%; mp.: 84°C; ^{1}H NMR ($CDCl_3$): $\delta = 3.18$ (d, $^2J = 13$ Hz, 1H, CH_2^a), 3.42 (d, $^2J = 13$ Hz, 1H, CH_2^b), 5.66 (s, 1H, $CH_{furanone}$), 7.12 (m, 5H, arom.), 7.34 (m, 5H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 37.3$ (CH_2), 60.2 (q, $^2J = 28$ Hz, C-3$_{furanone}$), 98.0 (C-4$_{furanone}$), 123.9 (q, $^1J = 283$ Hz, CF_3), 125.3, 126.9, 127.8, 128.5, 128.7, 130.0, 130.7, 132.7 (arom.), 155.7 (C-5$_{furanone}$), 171.4 (C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 6.2$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1805$, 1660, 1500, 1455 cm^{-1}; MS (EI): $m/z = 318$ $[M]^+$, 227 $[M–C_7H_7]^+$, 179 $[M–C_7H_7$, –CO, –HF$]^+$, 91 $[C_7H_7]^+$, 77 $[C_6H_5]^+$.
7a: yield: 14%; mp.: 133°C; ^{1}H NMR ($CDCl_3$): $\delta = 3.38$ (d, $^2J = 14.0$ Hz, 1H, CH_2^a), 3.47 (d, $^2J = 14.0$ Hz, 1H, CH_2^b), 7.05 (m, 2H, arom.), 7.24 (m, 3H, arom.), 7.40 (m, 5H, arom.), 8.03 (q, $^4J = 2.0$ Hz, 1H, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 46.5$ (CH_2), 89.4 (C-5$_{furanone}$), 119.3 (q, $^1J = 270$ Hz, CF_3), 124.5 (q, $^2J = 37.0$ Hz, C-3$_{furanone}$), 125.2, 127.2, 128.5, 129.0, 129.1, 130.3, 132.6, 136.7 (arom.), 158.7 (q, $^3J = 4.0$ Hz, C-4$_{furanone}$), 164.8 (C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.0$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1765$, 1500, 1455 cm^{-1}; MS (EI): $m/z = 227$ $[M–C_7H_7]^+$, 91 $[C_7H_7]^+$, 77 $[C_7H_7]^+$.

3-(4-Chlorobenzyl)-5-(2-fluorophenyl)-3-trifluoromethyl-2(3H)-furanone (**5b**; $C_{18}H_{11}ClF_4O_2$); *5-(4-Chlorobenzyl)-5-(2-fluorophenyl)-3-trifluoromethyl-2(5H)-furanone* (**7b**; $C_{18}H_{11}ClF_4O_2$)

5b: yield: 52% (method A), 14% (method B); oil; ^{1}H NMR ($CDCl_3$): δ: 3.27 (d, $^2J = 13.4$ Hz, 1H, CH_2^a), 3.48 (d, $^2J = 13.4$ Hz, 1H, CH_2^b), 6.02 (d, $^5J = 2.5$ Hz, $CH_{furanone}$), 7.14 (m, 4H, arom.) 7.20 (m, 2H, arom.) 7.40 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 36.4$ (CH_2), 60.1 (q, $^2J = 28.2$ Hz, C-3$_{furanone}$), 103.5 (d, $^4J = 13.6$ Hz, C-4$_{furanone}$), 115.1 (d, $^2J = 11.3$ Hz, C-1$_{fluorophenyl}$), 116.1 (d, $^2J = 20.7$ Hz, C-3$_{fluorophenyl}$), 123.7 (q, $^1J = 283.0$ Hz, CF_3), 124.5 (d, $^4J = 3.9$ Hz, C-6$_{fluorophenyl}$), 127.7 (C-5$_{fluorophenyl}$), 128.7, 131.1, 131.5 (arom.), 132.0 (q, $^3J = 9.0$ Hz, C-4$_{fluorophenyl}$), 133.9 (arom.), 150.3 (d, $^3J = 2.3$ Hz, C-5$_{furanone}$), 160.6 (d, $^1J = 252.5$ Hz, C-2$_{fluorophenyl}$), 170.3 (q, $^3J = 2.3$ Hz, C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -33.3$ (m, 1F, *o*-FC_6H_4), 6.0 (s, 3F, CF_3) ppm; IR (Film): $\nu = 1813$, 1649, 1493, 1453 cm^{-1}; MS (EI): $m/z = 370/372$ $[M]^+$, 246 $[M–C_7H_6Cl]^+$, 217 $[M–C_7H_6Cl$, -CO$]^+$, 125/127 $[C_7H_6Cl]^+$ (100).
7b: yield: 6%; mp.: 111°C; ^{1}H NMR ($CDCl_3$): $\delta = 3.33$ (d, $^2J = 14.0$ Hz, 1H, CH_2^a), 3.46 (d, $^2J = 14$ Hz, 1H, CH_2^b), 7.01 (m, 2H, arom.), 7.18 (m, 4H, arom.), 7.37 (m, 2H, arom.), 8.25 (q, $^4J = 1.6$ Hz, 1H, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 43.8$ (CH_2), 87.4 (d, $^3J = 4.2$ Hz, C-5$_{furanone}$), 116.1 (d, $^2J = 21.7$ Hz, C-3$_{fluorophenyl}$), 119.3 ($^1J = 270.3$ Hz, CF_3), 123.8 (d, $^2J = 12.2$ Hz, C-1$_{fluorophenyl}$), 124.7 (q, $^2J = 38.0$ Hz, C-3$_{furanone}$), 125.4 (d, $^3J = 3.3$ Hz, C-6$_{fluorophenyl}$), 127.7 (d, $^4J = 3.2$ Hz, C-5$_{fluorophenyl}$), 128.6, 131.2 (arom.), 131.2 (d, $^3J = 8.4$ Hz, C-4$_{fluorophenyl}$), 131.6, 133.8 (arom.), 158.5 (d, $^1J = 244.9$ Hz, C-2$_{fluorophenyl}$), 164.3 (C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -36.9$ (m, 1H, *o*-FC_6H_4), 12.9 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1775$, 1489, 1361 cm^{-1}; MS (EI): $m/z = 370/372$ $[M]^+$, 245 $[M–C_7H_6Cl]^+$, 197 $[M–C_7H_6Cl$, –CO$]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

3-(4-Chlorobenzyl)-5-(4-fluorophenyl)-3-trifluoromethyl-2(3H)-furanone (**5c**; $C_{18}H_{11}ClF_4O_2$); *5-(4-Chlorobenzyl)-5-(4-fluorophenyl)-3-trifluoromethyl-2(5H)-furanone* (**7c**; $C_{18}H_{11}ClF_4O_2$)

5c: yield: 60% (method A), 18% (method B); mp.: 73°C; ^{1}H NMR ($CDCl_3$): $\delta = 3.22$ (d, $^2J = 13.5$ Hz, 1H, CH_2^a), 3.45 (d, $^2J = 13.5$ Hz, 1H, CH_2^b), 5.65 (s, 1H, $CH_{furanone}$), 7.09 (m, 4H, arom.), 7.22 (m, 2H, arom.), 7.48 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 36.5$ (CH_2), 60.1 (q, $^2J = 27.6$ Hz, C-3$_{furanone}$), 97.1 (C-4$_{furanone}$), 116.2 (d, $^2J = 22.4$ Hz, C-3, C-5$_{fluorophenyl}$), 122.9 (d, $^4J = 3.2$ Hz, C-1$_{fluorophenyl}$), 123.8 (q, $^1J = 283.1$ Hz, CF_3), 127.5 (d, $^3J = 8.5$ Hz, C-2, C-6$_{fluorophenyl}$), 128.8, 131.2, 131.3, 133.9 (arom.), 155.1 (C-5$_{furanone}$), 164.1 (d, $^1J = 252$ Hz, C-4$_{fluorophenyl}$), 170.8 (q, $^3J = 2.3$ Hz, C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.3$ (m, 1F, *p*-FC_6H_4), 5.9 (s, 3F, CF_3)

ppm; IR (KBr): $\nu = 1811, 1659, 1601, 1508, 1493\,cm^{-1}$; MS (EI): $m/z = 370/372$ $[M]^+$, 245 $[M–C_7H_6Cl]^+$, 217 $[M–C_7H_6Cl, –CO]^+$, 125/127 $[C_7H_6Cl]^+$ (100).
7c: yield: 15%; mp.: 148°C; ^1H NMR ($CDCl_3$): $\delta = 3.29$ (d, $^2J = 14.1\,Hz$, 1H, CH_2^a), 3.39 ($d, J = 14.1\,Hz$, 1H, CH_2^b), 6.95 (m, 2H, arom.), 7.09 (m, 2H, arom.), 7.28 (m, 4H, arom.), 7.99 (q, $^4J = 1.5\,Hz$, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 45.9$ (CH_2), 88.7 (C-$5_{furanone}$), 116.2 (d, $^2J = 22.1\,Hz$, C-3, C-$5_{fluorophenyl}$), 119.2 (q, $^1J = 271\,Hz$, CF_3), 125.0 (q, $^2J = 37.8\,Hz$, C-$3_{furanone}$), 127.2 (d, $^3J = 8.1\,Hz$, C-2, C-$6_{fluorophenyl}$), 128.7, 130.9, 131.6 (arom.), 132.2 (d, $^4J = 3.4\,Hz$, C-$1_{fluorophenyl}$), 134.0 (arom.), 158.1 (q, $^3J = 3.5\,Hz$, C-$4_{furanone}$), 162.9 (d, $^1J = 249.6\,Hz$, C-$4_{fluorophenyl}$), 164.5 (C-$2_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -33.9$ (m, 1F; p-FC_6H_4), 13.0 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1765, 1513, 1491, 1368\,cm^{-1}$; MS (EI): $m/z = 370/372$ $[M]^+$, 245 $[M–C_7H_6Cl]^+$, 197 $[M–C_7H_6Cl, –F, –CO]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

5-(4-Bromophenyl)-3-(4-chlorobenzyl)-3-trifluoromethyl-2(3H)-furanone (**5d**; $C_{18}H_{11}BrClF_3O_2$);
5-(4-Bromophenyl)-5-(4-chlorobenzyl)-3-trifluoromethyl-2(5H)-furanone (**7d**; $C_{18}H_{11}BrClF_3O_2$)

5d: yield: 50% (method A), 20% (method B); mp.: 92°C; ^1H NMR ($CDCl_3$): $\delta = 3.22$ (d, $^2J = 13.5\,Hz$, 1H, CH_2^a), 3.46 (d, $^2J = 13.5\,Hz$, 1H, CH_2^b), 5.73 (s, 1H, $CH_{furanone}$), 7.08 (m, 2H, arom.), 7.22 (m, 2H, arom.), 7.34 (m, 2H, arom.), 7.53 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 36.5$ (CH_2), 60.1 (q, $^2J = 27.6\,Hz$, C-$3_{furanone}$), 98.1 (C-$4_{furanone}$), 123.6 (q, $^1J = 282.9\,Hz$, CF_3), 125.4, 125.5, 126.8, 128.8, 131.0, 131.1, 132.2, 134.0 (arom.), 155.1 (C-$5_{furanone}$), 170.7 (C-$2_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 6.0$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1811, 1652, 1592, 1490\,cm^{-1}$; MS (EI): $m/z = 430/432/434$ $[M]^+$, 305/307 $[M–C_7H_6Cl]^+$, 257/259 $[M–C_7H_6Cl, –CO, –HF]^+$, 125/127 $[C_7H_6Cl]^+$ (100).
7d: yield: 6%; mp.: 172°C; ^1H NMR ($CDCl_3$): $\delta = 3.28$ (d, $^2J = 14.2\,Hz$, 1H, CH_2^a), 3.39 (d, $^2J = 14.2\,Hz$, 1H, CH_2^b), 6.95 (m, 2H, arom.), 7.20 (m, 2H, arom.), 7.24 (m, 2H, arom.), 7.53 (m, 2H, arom.), 7.98 (q, $^4J = 1.4\,Hz$, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 45.7$ (CH_2), 88.7 (C-$5_{furanone}$), 119.2 (q, $^1J = 270.5\,Hz$, CF_3), 123.4 (arom.), 125.0 (q, $^2J = 37.8\,Hz$, C-$3_{furanone}$), 126.9, 128.8, 130.8, 131.7, 132.4, 134.0, 135.4 (arom.), 157.9 ($q, J = 3.6\,Hz$, C-$4_{furanone}$), 164.3 (C-$2_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.0$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1766, 1491, 1367\,cm^{-1}$; MS (EI): $m/z = 430/432/434$ $[M]^+$, 305/307 $[M–C_7H_6Cl]^+$, 257/259 $[M–C_7H_6Cl, –HF, –CO]^+$, 183/185 $[C_6H_4BrCO]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

3-(4-Bromobenzyl)-5-(4-fluorophenyl)-3-trifluoromethyl-2(3H)-furanone (**5e**; $C_{18}H_{11}BrF_4O_2$);
5-(4-Bromobenzyl)-5-(4-fluorophenyl)-3-trifluoromethyl-2(5H)-furanone (**7e**; $C_{18}H_{11}BrF_4O_2$)

5e: yield: 60% (method A), 34% (method B); mp.: 91°C; ^1H NMR ($CDCl_3$): $\delta = 3.20$ (d, $^2J = 13.5\,Hz$, 1H, CH_2^a), 3.44 (d, $^2J = 13.5\,Hz$, 1H, CH_2^b), 5.65 (s, 1H, $CH_{furanone}$), 7.06 (m, 4H, arom.), 7.37 (m, 2H, arom.), 7.48 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 36.5$ (CH_2), 59.9 (q, $^2J = 27.6\,Hz$, C-$3_{furanone}$), 97.0 (C-$4_{furanone}$), 116.1 (d, $^2J = 22.3\,Hz$, C-3, C-$5_{fluorophenyl}$), 122.0 (arom.), 122.9 (d, $^4J = 3.3\,Hz$, C-$1_{fluorophenyl}$), 123.8 (q, $^1J = 283.3\,Hz$, CF_3), 127.5 (d, $^3J = 8.9\,Hz$, C-2, C-$6_{fluorophenyl}$), 131.7, 131.8 (arom.), 155.1 (C-$5_{furanone}$), 162.6 (d, $^1J = 251\,Hz$, C-$4_{fluorophenyl}$), 170.8 (q, $^3J = 2.3\,Hz$, C-$2_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.3$ (m, 1F, p-FC_6H_4), 5.9 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1810, 1650, 1600, 1500, 1480\,cm^{-1}$; MS (EI): $m/z = 414/416$ $[M]^+$, 245 $[M–C_7H_6Br]^+$, 197 $[M–C_7H_6Br, –CO, –F]^+$, 169/171 $[C_7H_6Br]^+$ (100), 123 $[FC_6H_4CO]^+$.
7e: yield: 16%; mp.: 152°C; ^1H NMR ($CDCl_3$): $\delta = 3.28$ (d, $^2J = 14.0\,Hz$, 1H, CH_2^a), 3.37 (d, $^2J = 14.0\,Hz$, 1H, CH_2^b), 6.88 (m, 2H, arom.), 7.09 (m, 2H, arom.), 7.34 (m, 2H, arom.), 7.40 (m, 2H, arom.), 8.01 (q, $^4J = 1.8\,Hz$, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 45.9$ (CH_2), 88.7 (C-$5_{furanone}$), 116.2 (d, $^2J = 21.9\,Hz$, C-3, C-$5_{fluorophenyl}$), 119.2 (q, $^1J = 270\,Hz$, CF_3), 122.0 (arom.), 124.8 (q, $^2J = 37.8\,Hz$, C-$3_{furanone}$), 127.2 (d, $^3J = 8.2\,Hz$, C-2, C-$6_{fluorophenyl}$), 131.5, 131.7, 132.0 (arom.), 132.2 (d, $^4J = 3.3\,Hz$, C-$1_{fluorophenyl}$), 158.3 (q, $^3J = 3.2\,Hz$, C-$4_{furanone}$), 162.9 (d, $^1J = 249.6\,Hz$,

C-4$_{fluorophenyl}$), 164.4 (C-2$_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -33.9$ (m, 1F, p-FC_6H_4), 13.0 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1764$, 1512, 1367 cm^{-1}; MS (EI): $m/z = 415/417$ $[M]^+$, 245 $[M–C_7H_6Br]^+$, 197 $[M–C_7H_6Br, –CO, –HF]^+$, 169/171 $[C_7H_6Br]^+$ (100), 123 $[FC_6H_4CO]^+$.

3-(4-Chlorobenzyl)-5-(4-chlorophenyl)-3-trifluoromethyl-2(3H)-thiophenone (**6**; $C_{18}H_{11}Cl_2F_3OS$); *5-(4-Chlorobenzyl)-5-(4-chlorophenyl)-3-trifluoromethyl-2(5H)-thiophenone* (**8**; $C_{18}H_{11}Cl_2F_3OS$)

6: yield: 48%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.22$ (d, $^2J = 13.2$ Hz, 1H, CH_2^a), 3.46 (d, $^2J = 13.2$ Hz, 1H, CH_2^b), 6.07 (s, 1H, $CH_{thiophenone}$), 7.09 (m, 2H, arom.) 7.22 (m, 4H, arom.), 7.34 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 37.6$ (CH_2), 70.5 (q, $^2J = 25.2$ Hz, C-3$_{thiophenone}$), 114.5 (C-4$_{thiophenone}$), 123.8 (q, $^1J = 284.7$ Hz, CF_3), 127.6, 128.5, 129.3, 130.4, 131.0, 131.5, 133.7, 136.2 (arom.), 142.6 (C-5$_{thiophenone}$), 200.0 (C-2$_{thiophenone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.0$ (s, 3F, CF_3) ppm; IR (Film): $\nu = 1713$, 1491 cm^{-1}; MS (EI): $m/z = 402/404/406$ $[M]^+$, 278 $[M–C_7H_6Cl]^+$, 214 $[M–C_7H_6Cl, –HF, –CS]^+$, 125/127 $[C_7H_6Cl]^+$ (100).
8: yield: 6%; mp.: 130°C; ^{1}H NMR ($CDCl_3$): $\delta = 3.55$ (s, 2H, CH_2), 6.88 (m, 2H, arom.), 7.22 (m, 2H, arom.), 7.27 (m, 2H, arom.), 7.37 (m, 2H, arom.), 7.99 (q, $^4J = 1.2$ Hz, 1H, $CH_{thiophenone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 46.9$ (CH_2), 65.2 (C-5$_{thiophenone}$), 119.7 ($^1J = 273$ Hz, 3F, CF_3), 128.2, 128.5, 129.3, 131.7 (arom.), 132.3 (arom.), 133.3 (q, $^2J = 33.3$ Hz, C-3$_{thiophene}$), 134.0, 134.9, 136.6 (arom.), 160.5 (q, $^3J = 3.8$ Hz, C-4$_{thiophenone}$), 189.5 (C-2$_{thiophenone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.7$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1679$, 1491, 1345 cm^{-1}; MS (EI): $m/z = 402/404/406$ $[M]^+$, 278/280 $[M–C_7H_6Cl]^+$, 214/216 $[M–C_7H_6Cl, –HF, –CS]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

4-(4-Fluorophenyl)-4-oxo-2-trifluoromethyl-2-butenoic acid (4-chlorobenzyl)-ester (**9a**; $C_{18}H_{11}ClF_4O_3$)

Yield: 40% (method B); mp.: 38°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.06$ (s, 2H, CH_2), 7.06 (m, 2H, arom.), 7.14 (m, 2H, arom.), 7.24 (m, 2H, arom.), 7.44 (q, $^4J = 1.5$ Hz, 1H, = CH), 7.80 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 67.3$ (OCH_2), 116.2 (d, $^2J = 22.0$ Hz, C-3, C-5$_{fluorophenyl}$), 120.9 (q, $^1J = 273.9$ Hz, CF_3), 128.6 (q, $^2J = 32.2$ Hz, C-2), 128.7 (arom.), 128.9 (C-1$_{fluorophenyl}$), 129.8 (arom.), 131.4 (d, $^3J = 10.3$ Hz, C-2, C-6$_{fluorophenyl}$), 132.4, 134.6 (arom.), 141.5 (q, $^3J = 4.9$ Hz, = CH), 160.2 (CO$_{ester}$), 166.4 (d, $^1J = 258.1$ Hz, C-4$_{fluorophenyl}$), 188.9 (CO$_{ketone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -24.2$ (m, 1F, *p*-FC_6H_4), 12.7 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1737$, 1681, 1597, 1507, 1494 cm^{-1}; MS (EI): $m/z = 386/388$ $[M]^+$, 246 $[M–OCH_2C_6H_4Cl]^+$, 226 $[M–OCH_2C_6H_4Cl, –HF]^+$, 141/143 $[OCH_2C_6H_4Cl]^+$, 125/127 $[C_7H_6Cl]^+$ (100).

4-(4-Bromophenyl)-4-oxo-2-trifluoromethyl-2-butenoic acid (4-chlorobenzyl)-ester (**9b**; $C_{18}H_{11}BrClF_3O_3$)

Yield: 21% (method B); oil; ^{1}H NMR ($CDCl_3$): $\delta = 5.05$ (s, 2H, CH_2), 7.05 (m, 2H, arom.), 7.24 (m, 2H, arom.), 7.41 (q, $^4J = 1.5$ Hz, 1H, =CH), 7.45 (m, 2H, arom.), 7.71 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 67.4$ (CH_2), 120.9 (q, $^1J = 274.3$ Hz, CF_3), 128.6 (q, $^2J = 29.6$ Hz, C-2), 128.7, 129.0, 129.8, 129.9, 132.3, 132.5, 133.6, 134.7 (arom.), 141.4 (q, $^3J = 4.7$ Hz, =CH), 160.1 (CO$_{ester}$), 189.5 (CO$_{ketone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 12.7$ (s, 3F, CF_3) ppm; IR (film): $\nu = 1737$, 1679, 1586, 1494, 1384, 1366 cm^{-1}; MS (EI): $m/z = 446/448/450$ $[M]^+$, 305/307 $[M–C_7H_6ClO]^+$, 285/287 $[M–C_7H_6ClO, –HF]^+$, 183/185 $[C_7H_6BrO]$, 125/127 $[C_7H_6Cl]^+$ (100).

4-(4-Chlorophenyl)-4-oxo-2-trifluoromethyl-2-butenoic acid (4-bromobenzyl)-ester (**9c**; $C_{18}H_{11}BrClF_3O_3$)

Yield: 47% (method B); mp.: 82°C; ^{1}H NMR ($CDCl_3$): $\delta = 5.03$ (s, 2H, CH_2), 6.98 (m, 2H, arom.), 7.37 (m, 2H, arom.), 7.41 (m, 3H, arom., =CH), 7.68 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$):

$\delta = 67.4$ (OCH_2), 120.9 (q, $^1J = 273.9$ Hz, CF_3), 128.6 (q, $^2J = 33.0$ Hz, C-2), 122.8, 129.3, 129.9, 130.1, 131.7, 132.8, 133.1, 141.1 (arom.), 141.5 (q, $^3J = 4.7$ Hz, =CH), 160.1 (CO_{ester}), 189.3 (CO_{ketone}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 12.7$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1738$, 1667, 1587, 1489, 1348 cm^{-1}; MS (EI): $m/z = 446/448/450$ $[M]^+$, 261/263 $[M–C_7H_6BrO]^+$, 241/243 $[M–C_7H_6BrO, –HF]^+$, 185/187 $[C_7H_6BrO]^+$, 169/171 $[C_7H_6Br]^+$ (100).

2-(4-Bromobenzyl)-4-(4-fluorophenyl)-4-oxo-2-trifluoromethyl butanoic acid (**10**; $C_{18}H_{13}BrF_4O_3$)

To a solution of **5e** (0.83 g, 2 mmol) in dioxane (5 cm^3), an aqueous solution of KOH (5 cm^3, $pH = 10$) was added. The mixture was stirred at room temperature until the starting material was completely consumed (^{19}F NMR analysis). Then, diluted HCl was added with ice cooling until the reaction mixture attained *pH* 1. The mixture was extracted with CH_2Cl_2, and the organic phase was dried over $MgSO_4$. Finally, the solvent was evaporated *in vacuo*, and the remainig crude material was purified by column chromatography (eluent: $CHCl_3$:CH_3OH:CH_3COOH = 85:10:5).
Yield: 35%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.18$ (d, $^2J = 13.5$ Hz, 1H, CH_2^a), 3.46 (d, $^2J = 10.5$ Hz, 1H, CH_2^a), 3.63 (d, $^2J = 10.5$ Hz, 1H, CH_2^b), 3.70 (d, $^2J = 13.5$ Hz, 1H, CH_2^b), 6.95 (m, 2H, arom.), 7.14 (m, 2H, arom.), 7.31 (m, 2H, arom.), 7.92 (m, 2H, arom.), 9.52 (s, br, COOH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 34.4$ (CH_2), 37.8 (CH_2CO), 54.3 (q, $^2J = 23.4$ Hz, C-2), 116.1 (d, $^2J = 22.6$, C-3, C-$5_{fluorophenyl}$), 121.5 (arom.), 125.5 (q, $^1J = 285.7$ Hz, CF_3), 130.7 (d, $^3J = 9.2$ Hz, C-2, C-$6_{fluorophenyl}$), 131.5, 132.4, 134.0 (arom.), 166.2 (d, $^1J = 256.4$ Hz, C-$4_{fluorophenyl}$), 173.9 (q, $^3J = 2.1$ Hz, CO_{acid}), 194.3 (CO_{ketone}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -25.7$ (m, 1F, *p*-FC_6H_4), 8.7 (s, 3F, CF_3) ppm.

3-(4,4′-Difluorobenzhydryl)-5-(2-fluorophenyl)-3-trifluoromethyl-2(3H)-furanone (**12**; $C_{24}H_{14}F_6O_2$); *5-(4,4′-Difluorobenzhydryl)-5-(2-fluorophenyl)-3-trifluoromethyl-2(5H)-furanone* (**13**; $C_{24}H_{14}F_6O_2$)

To a solution of **1d** (0.49 g, 2 mmol) or **2b** (0.52 g, 2 mmol) and 4,4′-difluoro-benzhydrol (0.88 g, 4 mmol) in *THF* (5 cm^3), NaH (0.12 g, 5 mmol) was added at 0°C. The reaction mixture was stirred at room temperature until complete conversion of the starting materials (^{19}F NMR analysis), poured into ice/water, and extracted with ether. The organic phase was separated and dried over $MgSO_4$. The crude material remaining after evaporation of the solvent *in vacuo* was purified by column chromatography (eluent: petrolether: CH_2Cl_2 = 1:1; elution sequence: **12, 13** and **14, 15**, respectively.
12: yield: 47%; mp.: 117°C; ^{1}H NMR ($CDCl_3$): $\delta = 4.86$ (s, 1H, CH), 6.40 (d, $^5J = 2.4$ Hz, $CH_{furanone}$), 6.90 (m, 2H, arom.), 7.06 (m, 3H, arom.), 7.25 (m, 2H, arom.), 7.50 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 52.6$ (CH), 63.9 (q, $^2J = 26.2$ Hz, C-$3_{furanone}$), 102.4 (d, $^4J = 14.9$ Hz, C-$4_{furanone}$), 115.2 (d, $^2J = 10.7$ Hz, C-$1_{2\text{-fluorophenyl}}$), 115.7 (d, $^2J = 21.4$ Hz, C-$3_{4\text{-fluorophenyl}}$), 115.9 (d, $^2J = 21.4$ Hz, C-$3_{4\text{-fluorophenyl}}$), 116.3 (d, $^2J = 21.1$ Hz, C-$3_{2\text{-fluorophenyl}}$), 123.4 (q, $^1J = 284.5$ Hz, CF_3), 124.8 (d, $^3J = 3.7$ Hz, C-$6_{2\text{-fluorophenyl}}$), 127.9 (d, $^4J = 2.0$ Hz, C-$5_{2\text{-fluorophenyl}}$), 130.5 (d, $^3J = 8.0$ Hz, C-$2_{4\text{-fluorophenyl}}$), 130.6 (d, $^3J = 5.8$ Hz, C-$2_{4\text{-fluorophenyl}}$), 132.4 (d, $^3J = 8.9$ Hz, C-$4_{2\text{-fluorophenyl}}$), 133.2 (d, $^4J = 3.2$ Hz, C-$1_{4\text{-fluorophenyl}}$), 133.7 (d, $^4J = 3.5$ Hz, C-$1_{4\text{-fluorophenyl}}$), 151.5 (d, $^3J = 3.3$ Hz, C-$5_{furanone}$), 160.8 (d, $^1J = 254.5$ Hz, C-$2_{2\text{-fluorophenyl}}$), 162.3 (d, $^1J = 247.7$ Hz, C-$4_{4\text{-fluorophenyl}}$, 2x) 170.1 (d, $^5J = 2.3$ Hz, C-$2_{furanone}$) ppm; ^{19}F- NMR ($CDCl_3$): $\delta = -36.5$ (m, 1F, *p*-FC_6H_4), -36.2 (m, 1F, *p*-FC_6H_4), -33.5 (m, 1F, *o*-FC_6H_4), 10.0 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1815$, 1646, 1605, 1509 cm^{-1}; MS (EI): $m/z = 245$ $[M–CH(C_6H_4F)_2]^+$, 225 $[M–CH(C_6H_4F)_2, –HF]^+$, 203 $[CH(C_6H_4F)_2]^+$ (100).
13: yield: 16%; mp.: 174°C; ^{1}H NMR ($CDCl_3$): $\delta = 4.95$ (s, 1H, CH), 6.82–7.09 (m, 6H, arom.), 7.24–7.45 (m, 6H, arom.), 8.18 (q, $^4J = 1.6$ Hz, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 56.4$ (d, $^4J = 4.3$ Hz, CH), 89.5 (d, $^3J = 5.1$ Hz, C-$5_{furanone}$), 115.5 (d, $^2J = 21.0$ Hz, C-$3_{4\text{-fluorophenyl}}$), 115.8 (d, $^2J = 21.5$ Hz, C-$3_{4\text{-fluorophenyl}}$), 116.1 (d, $^2J = 22.6$ Hz, C-$3_{2\text{-fluorophenyl}}$), 119.1 (q, $^1J = 270.6$ Hz, CF_3), 123.4 (d, $^2J = 11.9$ Hz, C-$1_{2\text{-fluorophenyl}}$), 124.5 (q, $^2J = 37.9$ Hz, C-$3_{furanone}$), 125.2 (d,

$^3J = 3.2$ Hz, C-$6_{2\text{-fluorophenyl}}$), 127.8 (d, $^4J = 3.3$ Hz, C-$5_{2\text{-fluorophenyl}}$), 131.0 (d, $^3J = 8.0$ Hz, C-$2_{4\text{-fluorophenyl}}$), 131.1 (d, $^3J = 10.8$ Hz, C-$4_{2\text{-fluorophenyl}}$), 132.3 (d, $^4J = 3.4$ Hz, C-$1_{4\text{-fluorophenyl}}$), 133.4 (d, $^4J = 3.4$ Hz, C-$1_{4\text{-fluorophenyl}}$), 158.3 (d, $^1J = 244.1$ Hz, C-$2_{2\text{-fluorophenyl}}$), 158.3 (m, C-$4_{\text{furanone}}$), 162.0 (d, $^1J = 247.0$ Hz, C-$4_{4\text{-fluorophenyl}}$), 162.4 (d, $^1J = 248.5$ Hz, C-$4_{4\text{-fluorophenyl}}$), 164.7 (C-$2_{\text{furanone}}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -36.9$ (m, 1F, *p*-FC_6H_4), -36.8 (m, 1F, *p*-FC_6H_4), -35.9 (m, 1F, *o*-FC_6H_4), 12.8 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1790, 1508, 1361\ cm^{-1}$; MS (EI): $m/z = 429$ $[M–F]^+$, 245 $[M–CH(C_6H_4F)_2]^+$, 203 $[CH(C_6H_4F)_2]^+$ (100).

2-(4,4′-Difluorobenzhydryloxy)-5-(4-fluorophenyl)-3-trifluoromethylthiophene (**14**; $C_{24}H_{14}F_6OS$)

Yield: 62%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.14$ (s, 1H, CH), 7.0 (s, 1H, $CH_{\text{thiophene}}$), 7.02–7.15 (m, 6H, arom.), 7.31–7.45 (m, 6H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 87.8$ (CH), 114.4 (q, $^2J = 34.7$ Hz, C-$3_{\text{thiophene}}$), 115.8 (d, $^2J = 21.6$ Hz, C-3, C-$5_{\text{fluorophenyl}}$), 116.0 (d, $^2J = 21.9$ Hz, C-3, C-$5_{\text{fluorophenyl}}$), 117.8 (C-$4_{\text{thiophene}}$), 122.2 (d, $^1J = 270.3$ Hz, CF_3), 127.0 (d, $^3J = 8.0$ Hz, C-2, C-$6_{\text{fluorophenyl}}$), 129.0 (d, $^3J = 8.5$ Hz, C-2, C-$6_{\text{fluorophenyl}}$), 129.5 (d, $^4J = 3.3$ Hz, C-$1_{\text{fluorophenyl}}$), 130.7 (C-$5_{\text{thiophene}}$), 135.0 (d, $^4J = 3.0$ Hz, C-$1_{\text{fluorophenyl}}$), 161.9 (q, $^3J = 3.5$ Hz, C-$2_{\text{thiophene}}$), 162.5 (d, $^1J = 248.0$ Hz, C-$4_{\text{fluorophenyl}}$), 162.9 (d, $^1J = 248$ Hz, C-$4_{\text{fluorophenyl}}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -36.0$ (m, 1F, *p*-FC_6H_4), -34.9 (m, 2F, *p*-FC_6H_4), 19.8 (s, 3F, CF_3) ppm; IR (film): $\nu = 1604, 1575, 1515, 1421, 1400\ cm^{-1}$; MS (EI): $m/z = 464$ $[M]^+$, 261 $[M–CH(C_6H_4F)_2]^+$, 203 $[CH(C_6H_4F)_2]^+$ (100), 183 $[CH(C_6H_4F)_2, –HF]^+$.

3-(4,4′-Difluorobenzhydryl)-5-(4-fluorophenyl)-3-trifluoromethyl-2(3H)-thiophenone (**15**; $C_{23}H_{14}F_6OS$)

Yield: 8%; mp.: 129°C; ^{1}H NMR ($CDCl_3$): $\delta = 4.84$ (s, 1H, CH), 6.41 (s, 1H, $CH_{\text{thiophenone}}$), 6.86–7.25 (m, 6H, arom.), 7.34–7.53 (m, 6H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 53.7$ (CH), 74.2 (q, $^2J = 23.6$ Hz, C-$3_{\text{thiophenone}}$), 112.5 (C-$4_{\text{thiophenone}}$), 115.7 (d, $^2J = 21.1$ Hz, C-3, C-$5_{\text{fluorophenyl}}$), 115.8 (d, $^2J = 21.7$ Hz, C-3, C-$5_{\text{fluorophenyl}}$), 116.5 (d, $^2J = 22.5$ Hz, C-3, C-$5_{\text{fluorophenyl}}$), 123.6 (q, $^1J = 286.7$ Hz, CF_3), 128.4 (d, $^4J = 3.2$ Hz, C-$1_{\text{fluorophenyl}}$), 128.5 (d, $^3J = 8.8$ Hz, C-2, C-$6_{\text{fluorophenyl}}$), 130.5 (d, $^3J = 8.0$ Hz, C-2, C-$6_{4\text{-fluorophenyl}}$), 130.8 (d, $^3J = 8.0$ Hz, C-2, C-$6_{\text{fluorophenyl}}$), 133.5 (d, $^4J = 3.6$ Hz, C-$1_{\text{fluorophenyl}}$), 134.5 (d, $^4J = 3.4$ Hz, C-$1_{\text{fluorophenyl}}$), 144.7 (C-$5_{\text{thiophenone}}$), 162.2 (d, $^1J = 247.8$ Hz, C-$4_{\text{fluorophenyl}}$), 163.9 (d, $^1J = 252.5$ Hz, C-$4_{\text{fluorophenyl}}$), 199.9 (C-$2_{\text{thiophenone}}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = -36.4$ (m, 2F, *p*-FC_6H_4), -31.1 (m, 1F, *p*-FC_6H_4), 10.7 (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1716, 1604, 1508\ cm^{-1}$; MS (EI): $m/z = 464$ $[M]^+$, 261 $[M–CH(C_6H_4F)_2]^+$, 203 $[CH(C_6H_4F)_2]^+$ (100), 183 $[CH(C_6H_4F)_2, –HF]^+$.

2-Benzylmercapto-5-(4-chlorophenyl)-3-trifluoromethylfuran (**17**; $C_{18}H_{12}ClF_3OS$)

To a solution of **1e** (0.53 g, 2 mmol) and benzyl mercaptane (0.50 g, 4 mmol) in *THF* (5 cm^3) at 0°C, NaH (0.12 g, 5 mmol) was added. The mixture was stirred at 0°C until complete conversion of **1e** (^{19}F NMR analysis), treated with ice/water, and extracted with ether. The organic phase was dried over $MgSO_4$. After evaporation of the solvent, the remaining crude product was purified by column chromatography (eluent: CH_2Cl_2/petrol ether).

Yield: 91%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.15$ (s, 2H, CH_2), 6.73 (s, 1H, CH_{furan}), 7.27 (m, 5H, arom.) 7.37 (m, 2H, arom.), 7.49 (m, 2H, arom.) ppm; ^{13}C NMR: $\delta = 40.4$ (CH_2), 104.8 (q, $^3J = 2.4$ Hz, C-4_{furan}), 122.0 (q, $^1J = 268.5$ Hz, CF_3), 123.1 (q, $^2J = 37.6$ Hz, C-3_{furan}), 125.3, 127.6, 127.7, 128.6, 128.9, 129.1, 134.6, 136.7 (arom.), 145.9 (C-2_{furan}), 155.2 (C-5_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.4$ (s, 3F, CF_3) ppm; IR (film): $\nu = 1536, 1480, 1396\ cm^{-1}$; MS (EI): $m/z = 368/370$ $[M]^+$, 277/279 $[M–C_7H_7]^+$, 246 $[M–C_7H_7S]^+$, 91 $[C_7H_7]^+$ (100).

2-(Benzylamino)-5-(4-chlorophenyl)-3-trifluoromethylfuran (**18**; $C_{18}H_{13}ClF_3NO$)

A solution of **1e** (0.53 g, 2 mmol) and benzyl amine (0.43 g, 4 mmol) in *THF* (5 cm^3) was stirred at room temperature until **1e** was completly consumed (^{19}F NMR analysis), treated with ice/water, and extracted with ether. The organic phase was separated, dried over $MgSO_4$, and evaporated to dryness. The remaining crude product was recrystallized from petrol ether.
Yield: 81%; mp. 79°C; ^1H NMR ($CDCl_3$): $\delta = 4.57$ (d, $^3J = 5.7$ Hz, 2H, CH_2), 4.74 (s, br, 1H, NH), 6.60 (s, 1H, CH_{furan}), 7.26–7.41 (m, 9H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 47.6$ (CH_2), 89.2 (q, $^2J = 37.8$ Hz, C-3_{furan}), 104.6 (C-4_{furan}), 123.6 (arom.), 124.0 ($^1J = 264.4$ Hz, CF_3), 127.5, 127.8, 128.6, 128.8, 128.9, 132.1, 138.3 (arom.), 143.5 (C-5_{furan}), 154.5 (q, $^3J = 3.5$ Hz, C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 21.6$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 3485$, 1637, 1603, 1472 cm^{-1}; MS (EI): $m/z = 351/353$ $[M]^+$, 332/334 $[M–F]^+$, 260/262 $[M–C_7H_7]^+$, 91 $[C_7H_7]^+$ (100).

5-(4-Methylphenyl)-2-(2-pyridylmethoxy)-3-trifluoromethylfuran (**19**; $C_{18}H_{14}F_3NO_2$)

To a solution of **1b** (0.49 g, 2 mmol) and 2-hydroxymethyl pyridine (0.44 g, 4 mmol) in *THF* (5 cm^3) at 0°C, NaH (0.12 g, 5 mmol) was added. Stirring was continued at 0°C until the reaction was complete (^{19}F NMR analysis). The reaction mixture was treated with ice/water and extracted with ether. The organic phase was dried over $MgSO_4$, evaporated to dryness, and the residue was purified by column chromatography (eluent: CH_2Cl_2/petrol ether).

Yield: 78%; mp.: 84°C; ^1H NMR ($CDCl_3$): $\delta = 2.35$ (s, 3H, CH_3), 5.52 (s, 2H, CH_2), 6.58 (s, 1H, CH_{furan}), 7.16 (m, 2H, arom.) 7.29 (m, 1H, H-$5_{pyridine}$), 7.40 (m, 2H, arom.), 7.56 (m, 1H, H-$3_{pyridine}$), 7.78 (m, 1H, H-$4_{pyridine}$), 8.60 (m, 1H, H-$6_{pyridine}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.2$ (CH_3), 74.1 (CH_2), 93.5 (q, $^2J = 38.9$ Hz, C-3_{furan}), 102.7 (q, $^3J = 2.3$ Hz, C-4_{furan}), 121.3 (arom.), 122.5 (q, $^1J = 265.7$ Hz, CF_3), 123.0, 123.2, 126.7, 129.5, 137.0, 137.6 (arom.), 145.2 (C-5_{furan}), 149.3, 155.3 (arom.), 155.6 (C-2_{furan}) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.3$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1649$, 1443 cm^{-1}; MS (EI): $m/z = 333$ $[M]^+$, 241 $[M–C_6H_6N]^+$ (100), 221 $[M–C_6H_6N, –HF]^+$, 214 $[M–CH_3C_6H_4CO]^+$, 193 $[M–C_6H_6N, –HF, –CO]^+$, 119 $[CH_3C_6H_4CO]^+$, 92 $[C_6H_6N]^+$.

5-(4-Methylphenyl)-3-(2-thienyl)-3-trifluoromethyl-2(3H)-furanone (**21**; $C_{17}H_{13}F_3O_2S$);
5-(4-Methylphenyl)-5-(2-methylthien-3-yl)-3-trifluoromethyl-2-(5H)-furanone (**22**; $C_{17}H_{13}F_3O_2S$)

To a stirred solution of **1b** (0.49 g, 2 mmol) and 2-hydroxymethyl thiophene (0.46 g, 4 mmol) in *THF*, NaH (0.12 g, 5 mmol) was added at 0°C. Stirring was continued until the reaction was complete (^{19}F NMR analysis). The reaction mixture was treated with ice/water and extracted with ether. The organic phase was dried over $MgSO_4$ and evaporated to dryness. Compound **21** can be separated from the reaction mixture by column chromatography with a cooled column (eluent: CH_2Cl_2/petrol ether). Compound **21** rearranges upon standing at room temperature to give quantitatively **22**.

21: yield: 5%; mp.: 90°C; ^1H NMR ($CDCl_3$): $\delta = 2.37$ (s, 3H, CH_3), 3.43 (d, $^2J = 14.0$ Hz, 1H, CH_2^a), 3.75 (d, $^2J = 14.0$ Hz, 1H, CH_2^b), 5.73 (s, 1H, $CH_{furanone}$), 6.88 (m, 2H, arom.), 7.18 (m, 3H, arom.), 7.42 (m, 2H, arom.) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.5$ (CH_3), 31.4 (q, $^3J = 2.4$ Hz, CH_2), 60.0 (q, $^2J = 27.4$ Hz, C-$3_{furanone}$), 96.8 (C-$4_{furanone}$), 123.7 (q, $^1J = 282.9$ Hz, CF_3), 124.1, 125.4, 125.7, 127.0, 128.1, 129.5, 133.9, 141.2 (arom.), 156.7 (C-$5_{furanone}$), 171.1 (C-$2_{furanone}$) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 6.0$ (s, 3F, CF_3) ppm; IR (KBr): $\nu = 1804$ cm^{-1}; MS (EI): $m/z = 338$ $[M]^+$, 241 $[M–C_5H_5S]^+$, 221 $[M–C_5H_5S, –HF]^+$, 193 $[M–C_5H_5S, –CO]^+$, 97 $[C_5H_5S]^+$ (100).

22: yield: 46%; oil; ^1H NMR ($CDCl_3$): $\delta = 2.38$ (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 6.64 (d, $^3J = 3.2$ Hz, 1H, $CH_{thiophene}$), 6.70 (d, $^3J = 3.2$ Hz, 1H, $CH_{thiophene}$), 7.23 (m, 2H, arom.) 7.33 (m, 2H, arom.), 8.20 (q, $^3J = 1.6$ Hz, 1H, $CH_{furanone}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 15.3$ (CH_3), 21.2 (CH_3), 87.9 (C-$5_{furanone}$), 119.7 (q, $^1J = 270.4$ Hz, CF_3), 123.2 (q, $^2J = 37.4$ Hz, C-$3_{furanone}$), 125.3, 126.0, 127.6, 129.7, 133.9, 137.8, 139.7, 143.0 (arom.), 158.1 (C-$4_{furanone}$), 164.9 (q, $^3J = 2.8$ Hz, C-$2_{furanone}$)

ppm; ^{19}F- NMR ($CDCl_3$): $\delta = 13.4$ (s, 3F, CF_3) ppm; IR (film): $\nu = 1786$, 1359 cm^{-1}; MS (EI): $m/z = 338$ $[M]^+$, 119 $[CH_3C_6H_4CO]^+$ (100).

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References

[1] Part 2; Part 1: Burger K, Fuchs A, Hennig L, Helmreich B (2001) Tetrahedron Lett **42**: 1657
[2] a) Rao YS (1964) Chem Rev **64**: 353; b) Rao YS (1976) Chem Rev **76**: 625; c) Knight DW (1994) Contemp Org Synth **1**: 287
[3] Tyvorskii VI, Kukharev AS, Kulinkovich OG, De Kimpe N, Abbaspour-Tehrani K (1998) Tetrahedron **54**: 1801
[4] Shengming M, Zhangjie S (1998) J Org Chem **63**: 6387 and literature cited therein
[5] a) Ottlinger R, Burger K, Goth H, Firl J (1978) Tetrahedron Lett **50**: 5003; b) Burger K, Ottlinger R, Goth H, Firl J (1982) Chem Ber **115**: 2494
[6] Burger K, Helmreich B (1992) J Prakt Chemie **334**: 311
[7] Burger K, Helmreich B, Popkova VY, German LS (1994) Heterocycles **39**: 819
[8] Burger K, Wucherpfennig U, Brunner E (1994) Fluoro Heterocycles with Five-Membered Rings. In: Katritzky AR (ed) Advances of Heterocyclic Chemistry, vol 60. Academic Press, p1
[9] a) Burger K, Höß E, Geith K (1990) Synthesis 360; b) Hübl D, Ganzer M, Arndt F, Rees R, Ger Offen DE (1988) 3 614 229; (1988) CA **109**: 12441c
[10] Tietze L (1996) Chem Rev **96**: 115 and literature cited therein
[11] Fuchs A (1999) PhD Thesis, Universität Leipzig
[12] Pinhey JT, Schaffner K (1968) Aust J Chem **21**: 2265
[13] Arnold RT, Kulenovic ST (1980) J Org Chem **45**: 891
[14] a) Steglich W, personal communication; b) Lomar R (1980) PhD Thesis, Universität Bonn
[15] Unpublished results
[16] Beuck M (1999) Angew Chem **111**: 663; (1999) Angew Chem Int Ed **39**: 631
[17] Zhao D, Xu F, Chen C, Tillyer RD, Grabowski EJJ, Reider PJ (1999) Tetrahedron **55**: 6001
[18] Reinaud O, Capdevielle P, Maumy M (1987) Tetrahedron **43**: 4167
[19] Andreichikov YS, Gein VL, Ivanenko OI, Brigadnova EV, Maslivets AN (1988) J Org Chem USSR (Engl Transl) **24**: 1007
[20] Gilchrist TL, Storr R (1979) Organic Reactions and Orbital Symmetry, 2nd ed. Cambridge University Press, Cambridge, p 257 and literature cited therein
[21] Burger K, Gaa K, Geith K, Schierlinger C (1989) Synthesis 850

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