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Domino Reactions with Fluorinated Five-membered Heterocycles – Syntheses of Trifluoromethyl Substituted Butenolides and γ-Ketoacids#

Klaus Burger[1,*], **Lothar Hennig**[1], **Annett Fuchs**[2,*], **Dieter Greif**[2], **Jan Spengler**[3], and **Fernando Albericio**[3]

[1] Department of Organic Chemistry, University of Leipzig, D-04103 Leipzig, Germany
[2] Hochschule Zittau/Görlitz, Fachbereich Mathematik und Naturwissenschaften, D-02763 Zittau, Germany
[3] Institut de Recerca Biomédica de Barcelona, Parc Cientific Barcelona, 08028 Barcelona, Spain

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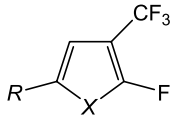
Summary. A new approach to trifluoromethyl substituted butenolides and their thioanalogues is described starting from 2-fluoro-3-trifluoromethylfurans and -thiophenes, respectively. The reaction sequence includes three steps – nucleophilic displacement reaction, *Claisen*, and finally *Cope* rearrangement – which can be run as domino reaction. A modification of the domino reaction (transesterification instead of *Cope* rearrangement) provides a concise access to α-trifluoromethyl-γ-ketoacids.

Keywords. 2-Fluoro-3-trifluoromethylthiophenes; 2-Fluoro-3-trifluoromethylfurans; Trifluoromethyl substituted butenolides; α-Trifluoromethyl-γ-keto acids; Domino reactions.

Introduction

Butenolides [2(5*H*)-furanones] [1, 2] are of interest to medicinal and agricultural chemists since decades due to their large abundance, their high structural diversity, and their broad biological activities. Compounds containing a butenolide substructure are considered *i.a.* as potential insecticides, bactericides, fungicides, antibiotics, anticancer agents, allergy inhibitors, antipsoriasis agents, and phospholipase A_2-inhibitors [3]. Furthermore, certain 3,4-disubstituted 2(5*H*)-furanones act as highly selective inhibitors of COX-1, involved in inflammation and other pain-inducing biological processes, allowing pain therapy without much

* Corresponding authors. E-mail: burger@organik.chemie.uni-leipzig.de, a.fuchs@hs-zigr.de
# Dedicated to Prof. Dr. *R. D. Chambers* on the occasion of his 70th birthday



1 *X* = S

1a *R* = C_6H_5
1b *R* = 4-Cl-C_6H_4
1c *R* = 4-Br-C_6H_4

4 *X* = O

4a *R* = 4-CH_3-C_6H_4
4b *R* = 4-Cl-C_6H_4
4c *R* = 4-Br-C_6H_4
4d *R* = 2-F-C_6H_4
4e *R* = 4-CH_3O-C_6H_4
4f *R* = 4-F-C_6H_4

Formula 1

of the unwanted side-effects of typical non-steroidal anti-inflammatory drugs (NSAIDs) [4].

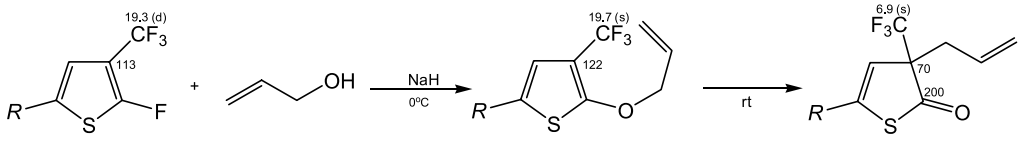
Consequently, numerous routes to this interesting class of compounds have been developed [5]. However, fluoromodified members are still rare, although modulation of pharmacokinetic properties by fluorine [6] and/or fluoroalkyl substitution [7, 8] has become a well established strategy for lead structure optimization and has resulted in a large number of fluorinated drugs in clinical use [9]. A number of properties, such as metabolic stability, lipophilicity, absorption, and transport rates [10] as well as permeability through certain body barriers like the blood/brain barrier can be affected in a favorable way [11].

In this paper we report on a new approach to trifluoromethyl substituted butenolides and their thioanalogues as well as to trifluoromethyl substituted γ-ketoacids *via* domino reactions [12, 13] starting from readily available 2-fluoro-3-trifluoromethylthiophenes **1a**–**1c** and -furans **4a**–**4f** [14] (Formula 1).

Results and Discussion

We have demonstrated that 5-fluoro-4-trifluoromethyl-1,3-azoles, 2-fluoro-3-trifluoromethyl-furans, and 2-fluoro-3-trifluoromethylthiophenes are useful building blocks in organofluorine chemistry [15, 16], because the fluorine atom adjacent to the trifluoromethyl group can be replaced by various N-, O-, and S-nucleophiles, and dinucleophiles under relatively mild conditions to give trifluoromethyl-substituted heterocyclic compounds of biological relevance [17] and materials [18] with interesting properties.

When NaH is added at 0°C to a solution of 2-fluoro-3-trifluoromethylthiophene **1a** and allyl alcohol (2 equivalents) in THF a nucleophilic displacement of the single fluorine readily takes place to give allyl ether **2** in excellent yield. The substitution process can be monitored by ^{19}F NMR spectroscopy (Scheme 1).



1

1a *R* = C_6H_5

2

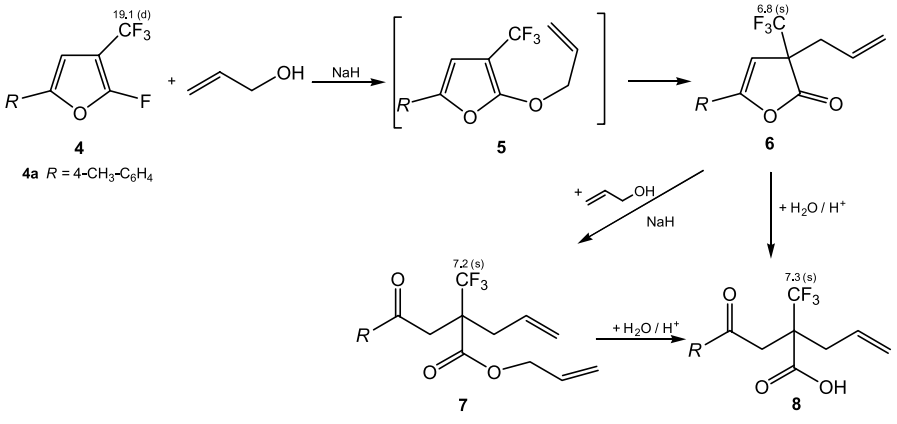
3

Scheme 1

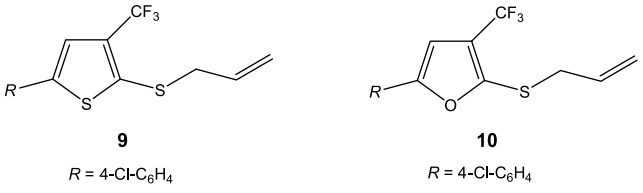
The trifluoromethyl group of the starting material which resonates as doublet at $\delta = 19.3$ ppm ($J = 11.7$ Hz) disappears, while a singlet ($\delta = 19.7$ ppm) emerges. Although compounds **2** turned out to be unstable on prolonged standing at room temperature they were fully characterized. The reason for the instability of allyl ethers of type **2** is the presence of a 1,5-hexadiene subunit, which is susceptible to undergo a *Claisen* rearrangement. *Claisen* and *Cope* rearrangements of fluorinated systems often proceed at surprisingly low temperatures [19]. The correct location of the trifluoromethyl group within the 1,5-hexadiene skeleton can result in a significant rate enhancement [20]. The final product which was formed quantitatively upon standing at room temperature after three weeks shows a singlet at $\delta = 6.9$ ppm, which indicates that the trifluoromethyl group is now placed at a sp^3 hybridized carbon atom. Structure **3** readily explains the spectroscopic data.

When 2-fluoro-3-trifluoromethylfuran **4a** [21] was treated with allyl alcohol in the presence of NaH under identical reaction conditions, a nucleophilic substitution product **5** could not be detected even on monitoring the reaction by ^{19}F NMR spectroscopy. As first product of the reaction sequence we identified the *Claisen* product **6** (Scheme 2). Compounds **6** are stable at room temperature, but in the presence of an alcoholate a rapid cleavage of the lactone moiety takes place. Therefore, in the presence of an excess of allyl alcohol and NaH α-trifluoromethyl substituted γ-ketoacid allylester **7** are the main products of the reaction sequence. On acidic hydrolysis compounds **7** are readily transformed into α-trifluoromethyl substituted γ-keto acids **8**.

In contrast, thioethers **9** or **10** obtained in very good yields on reaction of **1b** or **4b** with allyl mercaptane in the presence of NaH are thermally stable up to 140°C (Scheme 3). Above 140°C an uncontrolled decomposition starts to give a mixture



Scheme 2



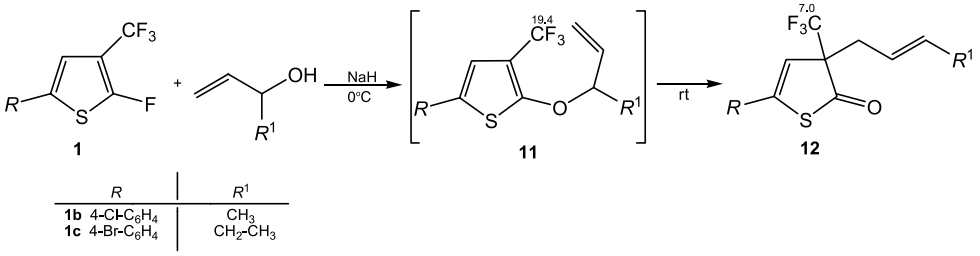
Scheme 3

of unidentified products. No evidence for a thio-*Claisen* rearrangement was found [22].

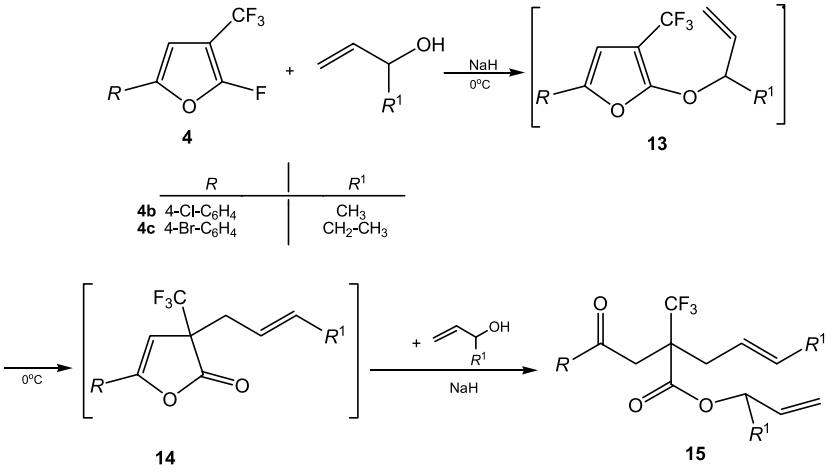
Although, both compounds **3** and **6** possess a 1,5-hexadiene subunit, products of a consecutive [3,3]-sigmatropic rearrangement have not been detected under the reaction conditions applied. To link both sigmatropic processes together in a domino reaction we decided to try to activate the final *Cope* rearrangement. We suggested that modification of the substituent pattern of the allyl alcohol is the easiest way to meet this goal.

First, we reacted secondary allyl alcohols ($HOCHR^1CH{=}CH_2$) and **1b** or **1c** at 0°C in the presence of NaH to give quantitatively the nucleophilic substitution product **11** within 1 h. ^{19}F NMR control of the nucleophilic substitution process reveals that already at room temperature the *Claisen* rearrangement starts to compete. A singlet at $\delta = 19.4$ ppm recorded in the ^{19}F NMR spectrum which is characteristic for the substitution product **11** disappears and upfield a new signal at $\delta = 7.0$ ppm appears (Scheme 4). From the ^1H NMR spectra of **12b** and **12c** a coupling constant of $^3J_{HH} = 15$ Hz can be extracted, characteristic for a *trans*-CC double bond, but no indication for a consecutive [3,3]-sigmatropic process was detected.

Compounds **4b**/**4c** and $HOCHR^1H{=}CH_2$ reacted to give trifluoromethyl substituted γ-keto esters **15** as stable products (Scheme 5). The logical precursors **13**



Scheme 4

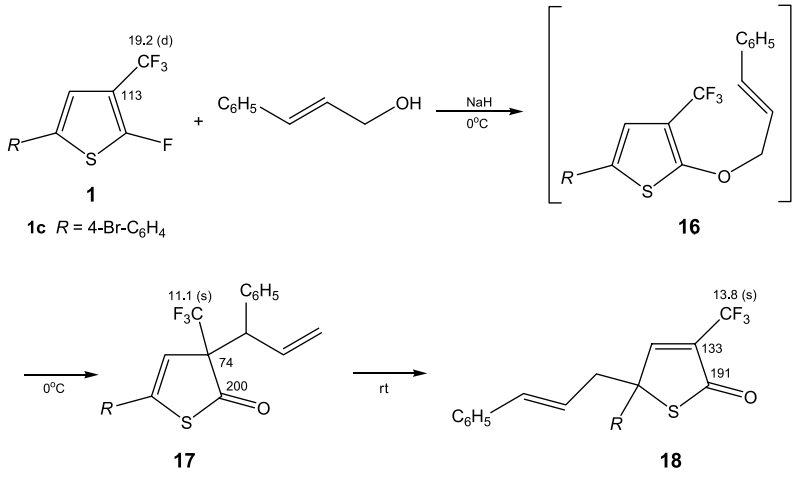


Scheme 5

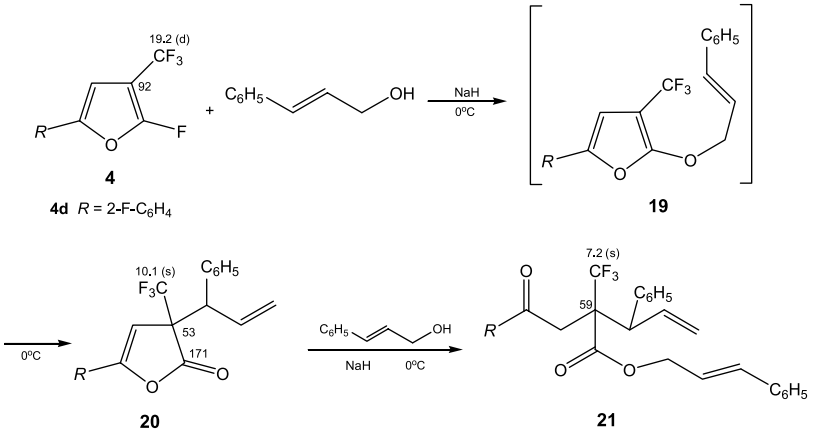
and **14** could not be isolated nor identified on monitoring the process by ^{19}F NMR spectroscopy. Furthermore, no evidence for a second [3,3]-sigmatropic process was obtained.

Therefore, we decided to introduce a phenyl group into C-(3) position of the allyl alcohol and found, that substitution reactions with cinnamic alcohol in the presence of NaH proceeded readily at 0°C and were complete within a few hours. The first compound we were able to isolate was the *Claisen* product **17**, which underwent already at room temperature a *Cope* rearrangement to give **18** (Scheme 6) on prolonged standing.

Domino reactions involving orbital symmetry controlled processes are known [12]. The combination of reaction types, such as *Diels-Alder* reactions [23], [3 + 2]-cycloaddition reactions [24], and *Mannich* reactions [25] represents a valuable synthetic tool for the construction of complex molecules, often in a stereoselective way [26]. Domino reactions including sequences like *Claisen*/*Cope* rearrangements [27] and *Claisen*/aza-*Claisen* rearrangements [28] have been successfully applied



Scheme 6



Scheme 7

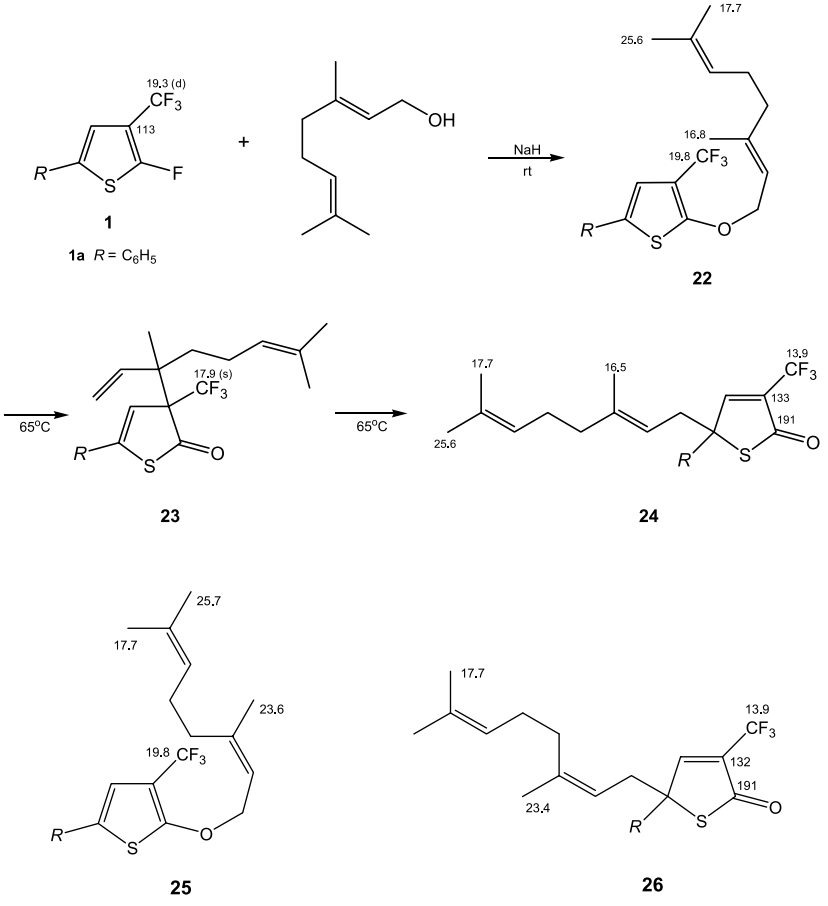
in organic synthesis. Remarkable for the above discussed reaction sequence **1c** → **16** → **17** → **18** is the low temperature necessary to start the domino process.

From the reaction of furan **4d** and cinnamic alcohol we were able to isolate and characterize the *Claisen* product **20** and the open-chain product **21** (Scheme 7). The yield of **21** depends on the amount of cinnamic alcohol used. These findings demonstrate that the cleavage of the lactone ring by the alcoholate is still faster than the *Cope* rearrangement.

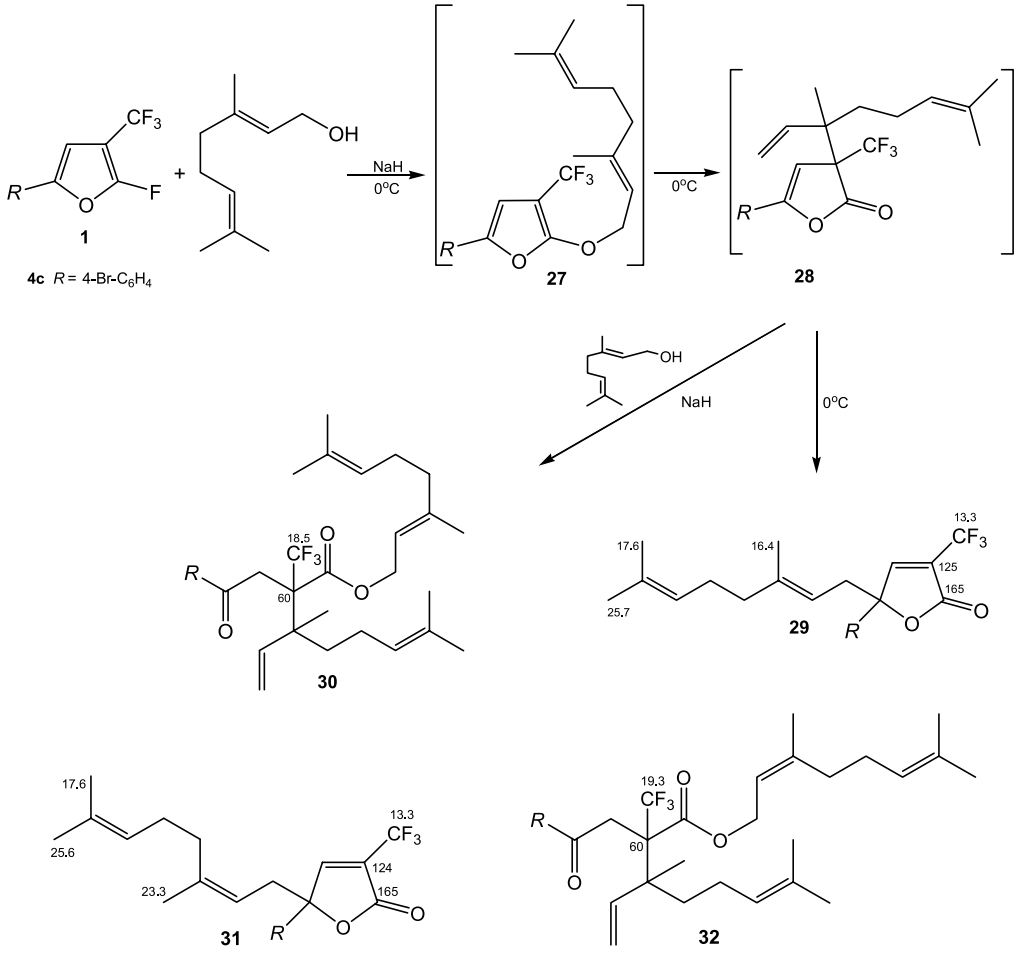
Finally, when we introduced two alkyl groups into 3-position of the allyl alcohol we succeeded in running the reaction consisting of nucleophilic substitution, *Claisen*, and Cope rearrangement as a domino reaction.

The development of methodology for incorporation of lipidic anchors into biologically relevant compounds is of current interest. Therefore, we tested the applicability of the new domino reaction for the introduction of lipidic side-chains using commercially available C-10 and C-15 building blocks like geraniol, nerol, and farnesol.

When compound **1a** was reacted with geraniol at room temperature due to the standard protocol the product of the nucleophilic substitution **22** was obtained in 78% yield (Scheme 8). The product is stable at room temperature, but on heating



Scheme 8

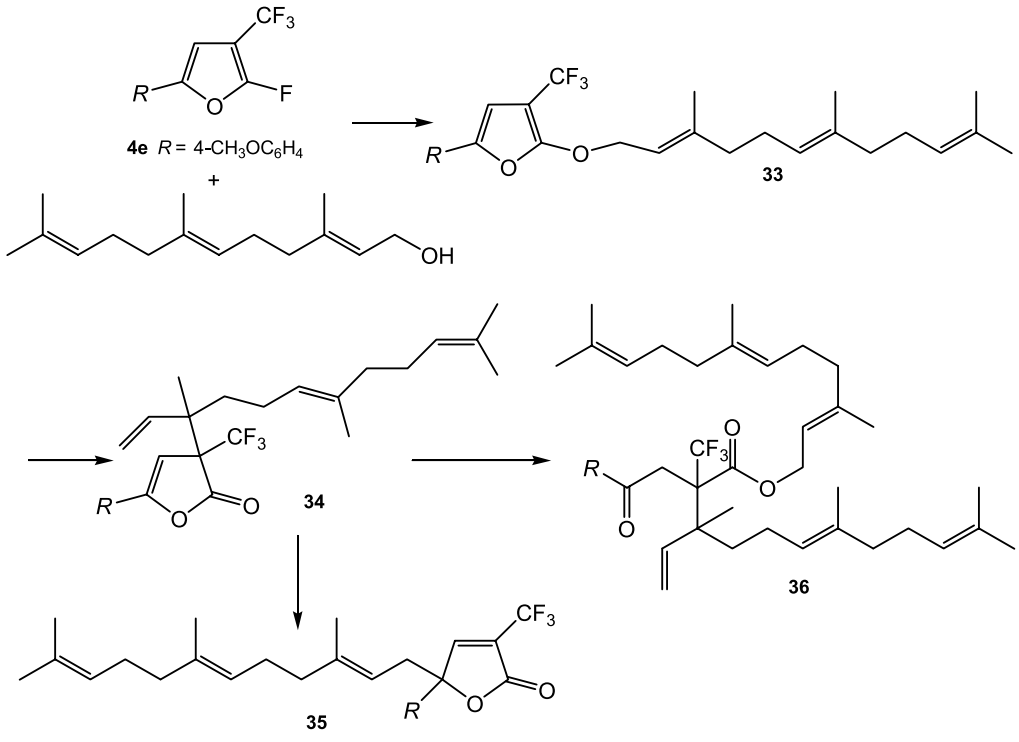


Scheme 9

up to *ca*. 65°C a consecutive reaction starts. *Via Claisen* product **23** (^{19}F NMR: $\delta = 17.9$ ppm) the *Cope* product **24** (^{19}F NMR: $\delta = 13.9$ ppm) was formed in 79% yield. Analogously, in the case of nerol compounds **25** and **26** were obtained and fully characterized.

The reaction of **4c** and geraniol at 0°C in the presence of NaH gave two main products: compound **29** (*Cope* product) and product **30** formed by alcoholytic ring opening of the *Claisen* product **28** (Scheme 9). Now, in the case of 3,3-dialkyl substituted allyl alcohols, the *Cope* rearrangement (**28** → **29**) successfully competes with the lactone cleavage (**28** → **30**). Analogously, with nerol compounds **31** and **32** were obtained.

Analogously farnesol reacts with **4e** to give 3-trifluoromethyl-2(5*H*)-furanones **35** with a lipidic C-15 tail and a head decorated with a lipophilic trifluoromethyl group (Scheme 10). Compounds of type **35** and their thioanalogues seem to be suitable model compounds to add drugs with poor pharmacokinetic properties across the *Michael* system to improve the transport rates [29–32], to dock them to membranes, and finally to guide them into cells. The presence of the

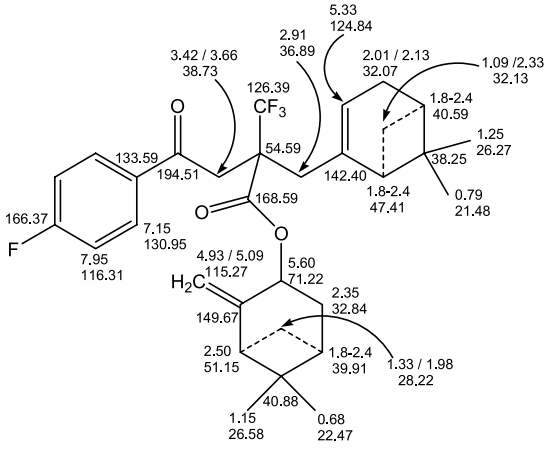


Scheme 10

trifluoromethyl group allows to monitor the binding procedure, the docking process, and the transport through the membrane by ^{19}F NMR spectroscopy.

Miscellaneous

Structural diversity can be generated by incorporating the double bond of the allyl alcohol into exo- and endocyclic positions of carbocyclic and heterocyclic systems



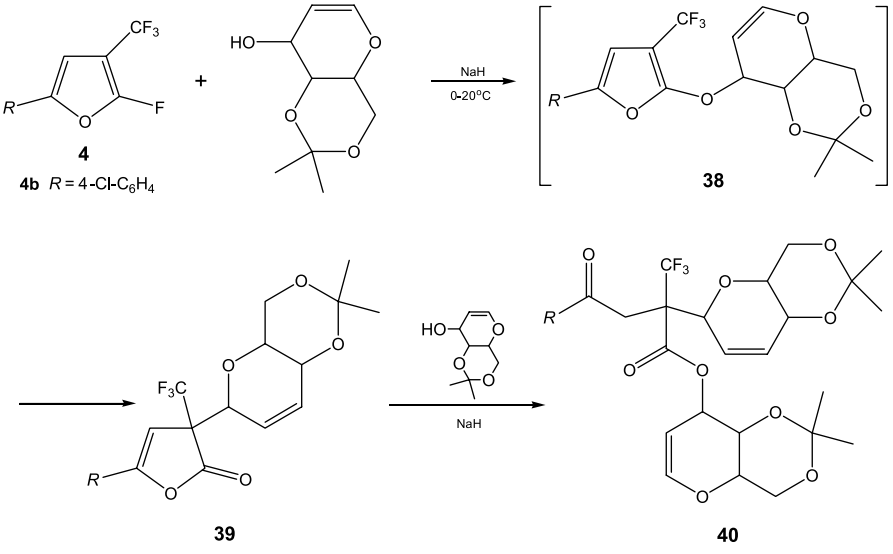
37

Scheme 11

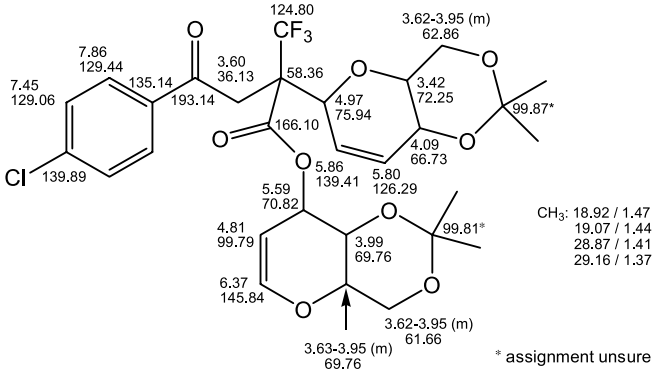
of different ring size as well as into aromatic and heteroaromatic species with variable substituent pattern. In addition, in the case of heteroaromatic and heterocyclic systems the skeleton can be modified considerably. Applying the new strategy, *i.a.* libraries of α-trifluoromethyl substituted γ-keto acids, C-glycosides, and amino acids become readily available *via* domino reactions in acceptable yields.

A typical example is the reaction of 2-fluoro-4-(4-fluorophenyl)-3-trifluoromethylfuran **4f** with (−)-*trans*-pinocarveol to give compound **37** in 31% yield (Scheme 11).

C-Glycosides are a class of compounds of current interest [33–35]. Now trifluoromethyl substituted members are readily available applying the above strategy. On addition of NaH to a solution of 5-(4-chlorophenyl)-2-fluoro-3-trifluoromethylfuran **4b** and 1,2-didesoxy-4,6-*O*-isopropylidene-*D*-arabino-1-hexapyranose [36, 37] in THF at 0°C a smooth reaction occurs. The product of a nucleophilic displacement immediately undergoes a *Claisen* rearrangement followed by an alcoholytic



Scheme 12



Scheme 13

cleavage of the lactone ring (Scheme 12). The formation of compounds **39** and **40** was unequivocally proved by ^{19}F NMR spectroscopy. The structure of the C-glycoside **40** which was obtained in 33% yield was identified by APT, H,H- and C,H-COSY spectra and homo decoupling experiments (Scheme 13).

On further applications of the new strategy, especially on the synthetic potential concerning α-trifluoromethylamino acids and their incorporation into peptides we report in due course.

Experimental

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). ^1H (200.04 MHz), ^{13}C (50.30 MHz), and ^{19}F (188.20 MHz) NMR spectra were recorded on a Varian Gemini 2000 spectrometer. TMS was used as reference for ^1H and ^{13}C NMR spectra (internal), and *TFA* 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); their results were within experimental errors.

*Reactions of **1** and **4** with Allyl Alcohols; General Procedure*

To an ice cold solution of **1** or **4** (2 mmol) [21, 38] and the corresponding allyl alcohol (4 mmol) in THF (5 cm^3), NaH (0.12 g, 5 mmol) was added. Then the reaction mixture was stirred at 0°C or room temperature (**3**, **9**, **10**, **18**, **22**, **25**, **35**, **36**, **40**) or at 65°C (**24**, **26**), respectively, 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: *DCM*/petroleum ether).

2-Allyloxy-5-phenyl-3-(trifluoromethyl)thiophene (**2**, $C_{14}H_{11}F_3OS$)

Yield 96%; oil; ^1H NMR ($CDCl_3$): $\delta = 4.65$ (dd, $^4J = 1.0$ Hz, $^3J = 6.0$ Hz, 2H), 5.35 (m, 1H), 5.46 (m, 1H), 6.01 (m, 1H), 7.06 (s, 1H), 7.23 (m, 1H), 7.35 (m, 2H), 7.43 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 76.2$, 112.7 (q, $^2J = 34.0$ Hz), 118.2 (q, $^3J = 3.0$ Hz), 119.7, 122.1 (q, $^1J = 270$ Hz), 125.1, 127.6, 129.0, 130.3, 131.2, 133.4, 163.6 (q, $^3J = 3.0$ Hz) ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.7$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 3400$, 1720, 1580, 1520, 1415 cm^{-1}; MS (EI): $m/z = 257$ $[M - C_2H_3]^+$, 244 $[M - C_3H_4]^+$, 216 $[244 - CO]^+$, 196 $[216 - HF]^+$, 77 $[C_6H_5]^+$.

3-Allyl-5-phenyl-3-trifluoromethyl-3H-thiophen-2-one (**3**, $C_{14}H_{11}F_3OS$)

Yield 100%; oil; ^1H NMR ($CDCl_3$): $\delta = 2.77$ (dd, $^2J = 14.0$ Hz, $^3J = 7.0$ Hz, 1H), 2.87 (dd, $^2J = 14.0$ Hz, $^3J = 8.0$ Hz, 1H), 5.16 (m, 1H), 5.55 (m, 1H), 5.67 (m, 1H), 6.10 (s, 1H), 7.35 (m, 3H), 7.48 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 36.7$ (q, $^4J = 2.0$ Hz), 69.4 (q, $^2J = 25.0$ Hz), 114.2, 121.0, 123.8 (q, $^1J = 284.0$ Hz), 126.5, 128.9, 129.0, 130.1, 132.2, 143.0, 200.2 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 6.9$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 3420$, 1720, 1450 cm^{-1}; MS (EI): $m/z = 284$ $[M]^+$, 257 $[M - C_2H_3]^+$, 256 $[M - CO]^+$, 243 $[M - C_3H_5]^+$, 215 $[243 - CO]^+$, 195 $[215 - HF]^+$, 121 $[C_6H_5CO]^+$, 77 $[C_6H_5]^+$.

3-Allyl-5-p-tolyl-3-trifluoromethyl-3H-furan-2-one (**6**, $C_{15}H_{13}F_3O_2$)

Yield 40%; mp 77°C; ^1H NMR ($CDCl_3$): $\delta = 2.39$ (s, 3H), 2.74 (dd, $^2J = 13.9$ Hz, $^3J = 6.2$ Hz, 1H), 2.85 (dd, $^2J = 13.9$ Hz, $^3J = 7.5$ Hz, 1H), 5.16 (d, $^3J_{cis} = 10.1$ Hz, 1H), 5.23 (d, $^3J_{trans} = 17.0$ Hz, 1H), 5.60 (m, 1H), 5.68 (s, 1H), 7.24 (m, 2H), 7.53 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.5$, 35.6, 58.7 (q, $^2J = 27.9$ Hz), 96.8, 121.4, 123.8 (q, $^1J = 282.2$ Hz), 124.2, 125.4, 129.2, 129.6, 144.2, 155.9,

171.4 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 5.9$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 1805$, 1652, 1288–1259, 1185–1165 cm^{-1}; MS (EI): m/z (%) = 282 $[M]^+$, 241 $[M - CH_2CH{=}CH_2]^+$ (100), 221 $[241 - HF]^+$, 193 $[241 - CO, -HF]^+$, 120 $[CH_3C_6H_4COH]^+$, 91 $[CH_3{-}C_6H_4]^+$.

2-(2-Oxo-2-p-tolylethyl)-2-(trifluoromethyl)pent-4-enoic acid allylester (**7**, $C_{18}H_{19}F_3O_3$)
Yield 33%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 2.41$ (s, 3H), 2.89 (dd, $^2J = 14.0$ Hz, $^3J = 6.2$ Hz, 1H), 3.00 (dd, $^2J = 14.0$ Hz, $^3J = 7.4$ Hz, 1H), 3.42 (d, $^2J = 17.8$ Hz, 1H), 3.72 (d, $^2J = 17.8$ Hz, 1H), 4.70 (m, 2H), 4.98 (d, $^3J_{trans} = 17.2$ Hz, 1H), 4.99 (d, $^3J_{cis} = 10.5$ Hz, 1H), 5.22 (d, $^3J_{cis} = 10.5$ Hz, 1H), 5.31 (d, $^3J_{trans} = 17.2$ Hz, 1H), 5.65 (m, 1H), 5.87 (m, 1H), 7.25 (m, 2H), 7.81 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.6$, 34.3, 38.2, 53.5 (q, $^2J = 23.9$ Hz), 66.6, 118.5, 120.0, 126.1 (q, $^1J = 285.0$ Hz), 128.0, 129.4, 131.5, 132.3, 133.9, 144.5, 168.2, 194.7 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.2$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 1746$, 1688, 1298–1270, 1225–1188 cm^{-1}; MS (EI): m/z (%) = 340 $[M]^+$, 255 $[M - COOCH_2CH{=}CH_2]^+$, 134 $[C_9H_{10}O]^+$, 119 $[CH_3C_6H_4CO]^+$ (100), 91 $[CH_3C_6H_4]^+$.

2-(2-Oxo-2-p-tolylethyl)-2-(trifluoromethyl)pent-4-enoic acid (**8**, $C_{15}H_{15}F_3O_3$)
Yield 57%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 2.40$ (s, 3H), 2.91 (dd, $^2J = 14.0$ Hz, $^3J = 6.2$ Hz, 1H), 3.03 (dd, $^2J = 14.0$ Hz, $^3J = 7.4$ Hz, 1H), 3.47 (d, $^2J = 19.0$ Hz, 1H), 3.75 (d, $^2J = 19.0$ Hz, 1H), 4.98 (d, $^3J_{trans} = 17.2$ Hz, 1H), 5.03 (d, $^3J_{cis} = 10.7$ Hz, 1H), 5.79 (m, 1H), 7.45 (m, 2H), 7.81 (m, 2H), 7.92 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.4$, 34.3, 38.4, 53.2 (q, $^2J = 23.9$ Hz), 120.2, 126.1 (q, $^1J = 285.0$ Hz), 128.0, 129.4, 131.5, 133.9, 144.5, 172.2, 194.7 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.2$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 3020$, 1725, 1695, 1585, 1455, 1298–1270, 1225–1188 cm^{-1}; MS (EI): m/z (%) = 300 $[M]^+$, 258 $[M - C_3H_6]^+$, 257 $[M - C_3H_7]^+$, 231 $[M - CF_3]^+$, 119 $[CH_3C_6H_4CO]^+$ (100), 91$[CH_3C_6H_4]^+$.

2-Allylsulfanyl-5-(4-chlorophenyl)-3-(trifluoromethyl)thiophene (**9**, $C_{14}H_{10}ClF_3S_2$)
Yield 88%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.53$ (d, $^3J = 7.1$ Hz, 2H), 5.06 (m, 1H), 5.15 (m, 1H), 5.86 (m, 1H), 7.36 (m, 3H), 7.46 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 41.6$, 119.0, 121.8 (q, $^1J = 272.3$ Hz), 122.1 (q, $^3J = 3.3$ Hz), 126.8, 129.3, 131.3, 132.6, 134.4 (q, $^2J = 33.4$ Hz), 134.5, 136.1 (q, $^3J = 2.9$ Hz), 145.2 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 20.0$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 1493$, 1441, 1387, 1272–1226, 1167–1096 cm^{-1}; MS (EI): m/z (%) = 336/334 $[M]^+$, 295/293 $[M - CH_2CH{=}CH]^+$ (100), 231/229 $[295/293 - S_2]^+$, 40 $[CH_2CH{=}CH]^+$.

2-Allylsulfanyl-5-(4-chlorophenyl)-3-(trifluoromethyl)furan (**10**, $C_{14}H_{10}ClF_3OS$)
Yield 70%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.56$ (d, $^3J = 7.1$ Hz, 2H), 5.02 (m, 1H), 5.09 (m, 1H), 5.88 (m, 1H), 6.76 (s, 1H), 7.38 (m, 2H), 7.56 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 38.6$, 104.8 (q, $^3J = 2.5$ Hz), 118.5, 122.1 (q, $^1J = 267.8$ Hz), 123.1 (q, $^2J = 37.0$ Hz), 125.3, 127.7, 129.2, 133.0, 134.6, 145.9 (q, $^3J = 4.3$ Hz), 155.2 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.5$ (s, CF_3) ppm; IR (film): $\bar{\nu} =$ 1536, 1480, 1396, 1248, 1174, 1129 cm^{-1}; MS (EI): m/z (%) = 320/318 $[M]^+$, 280/278 $[M - CH_2CH{=}CH]^+$, 113/111 $[ClC_6H_4]^+$, 40 $[CH_2CH{=}CH]^+$ (100).

3-(But-2-enyl)-5-(4-chlorophenyl)-3-trifluoromethyl-3H-thiophen-2-one
(**12b**, $C_{15}H_{12}ClF_3OS$)
Yield 60%; mp 40°C; ^{1}H NMR ($CDCl_3$): $\delta = 1.61$ (dd, $^3J = 6.6$ Hz, $^4J = 1.5$ Hz, 3H), 2.67 (dd, $^2J = 13.7$ Hz, $^3J = 6.9$ Hz, 1H), 2.80 (dd, $^2J = 13.7$ Hz, $^3J = 7.9$ Hz, 1H), 5.30 (dt, $^3J_{trans} = 15.1$ Hz, $^3J = 7.7$, 6.8 Hz, 1H), 5.62 (dq, $^3J_{trans} = 15.1$ Hz, $^3J = 6.4$ Hz, 1H), 6.07 (s, 1H), 7.40 (s, 4H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.9$, 35.7, 69.9 (q, $^2J = 25.2$ Hz), 115.2, 121.1, 123.8 (q, $^1J = 284.1$ Hz), 127.7, 129.2, 130.8, 132.2, 136.0, 141.6, 199.9 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.0$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 1723$, 1489, 1263–1242, 1187–1173 cm^{-1}; MS (EI): m/z (%) = 334/332 $[M]^+$, 306/304 $[M - CO]^+$, 280/278 $[M - CHCH{=}CHCH_3]^+$, 260/258 $[280/278 - HF]^+$; 54 $[CHCH{=}CHCH_3]^+$ (100).

5-(4-Bromophenyl)-3-pent-2-enyl-3-trifluoromethyl-3H-thiophen-2-one
(**12c**, $C_{16}H_{14}BrF_3OS$)
Yield 64%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 0.88$ (t, $^3J = 7.4$ Hz, 3H), 1.96 (m, 2H), 2.67 (ddd, $^2J = 14.0$ Hz, $^3J = 8.0$ Hz, $^4J = 1.2$ Hz, 1H), 2.80 (ddd, $^2J = 14.0$ Hz, $^3J = 8.0$ Hz, $^4J = 0.8$ Hz, 1H), 5.26 (dt, $^3J_{trans} = 15.1$ Hz, 1H), 5.65 (dt, $^3J_{trans} = 15.1$ Hz, 1H), 6.08 (s, 1H), 7.35 (m, 2H), 7.56 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 13.6$, 25.5, 35.7, 70.0 (q, $^2J = 24.9$ Hz), 115.3, 118.9, 123.8 (q, $^1J = 284.3$ Hz), 124.3, 127.9, 131.2, 132.2, 139.3, 141.7, 199.9 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.0$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 1719$, 1487, 1263–1244, 1187–1149 cm^{-1}; MS (EI): m/z (%) = 392/390 $[M]^+$, 363/361 $[M - CH_3CH_2]^+$, 323/321 $[M - CH_3CH_2{-}CH{=}CHCH_2]^+$, 303/301 $[323/321 - HF]^+$, 69 $[CH_3CH_2CH{=}CHCH_2]^+$ (100).

2-[2-(4-Chlorophenyl)-2-oxoethyl]-2-(trifluoromethyl)hex-4-enoic acid 1-methylallyl ester (**15b**, $C_{19}H_{20}ClF_3O_3$)
Yield 46% (mixture of diastereomers); mp 29°C; ^{1}H NMR ($CDCl_3$): $\delta = 1.26/1.35$ (d, $^3J = 6.0$ Hz, 3H), 1.48 (d, $^3J = 4.0$ Hz, 3H), 2.80 (dd, $^2J = 18.0$ Hz, $^3J = 4.0$ Hz, 1H), 2.97 (dd, $^2J = 18.0$ Hz, $^3J = 6.0$ Hz, 1H), 3.38 (d, $^2J = 18.0$ Hz, 1H), 3.63 (d, $^2J = 18.0$ Hz, 1H), 5.0–5.3 (m, 2H), 5.3–5.4 (m, 2H), 5.4–5.5 (m, 1H), 5.7–5.9 (m, 1H), 7.44 (d, $^3J = 8.6$ Hz, 2H), 7.85 (d, $^3J = 8.0$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.7$, 19.3/19.4, 33.1, 38.0, 53.7 (q, $^2J = 23.7$ Hz), 72.8/72.9, 115.9/116.1, 124.7, 126.1 (q, $^1J = 285.1$ Hz), 128.9, 129.2, 130.9, 134.9, 136.8/136.9, 139.8, 167.5, 194.1 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.1$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 1742$, 1692, 1590, 1404, 1285–1264, 1213–1192 cm^{-1}; MS (EI): m/z (%) = 390/388 $[M]^+$, 335/333 $[M - CH_2CH{=}CHCH_3]^+$, 319/317 $[M - OCH_2CH{=}CHCH_3]^+$, 291/289 $[335/333 - CO_2]^+$, 271/268 $[291/289 - HF]^+$, 155/153 $[ClC_6H_4COCH_2]^+$, 141/139 $[ClC_6H_4CO]^+$, 54 $[C_4H_6]^+$ (100).

2-[2-(4-Bromophenyl)-2-oxoethyl]-2-(trifluoromethyl)hept-4-enoic acid 1-ethylallyl ester (**15c**, $C_{21}H_{24}BrF_3O_3$)
Yield 55% (mixture of diastereomers); oil; ^{1}H NMR ($CDCl_3$): $\delta = 0.65$ (t, $^3J = 7.6$ Hz, 3H), 0.78/0.90 (t, $^3J = 7.2$ Hz, $^3J = 7.2$ Hz, 2 × 3H), 1.56/1.66 (q, $^3J = 7.2$ Hz, $^3J = 7.2$ Hz, 2 × 2H), 1.77 (m, 2H), 2.76 (dd, $^2J = 16.1$ Hz, $^3J = 4.9$ Hz, 1H), 2.91 (dd, $^2J = 16.1$ Hz, $^3J = 6.4$ Hz, 1H), 3.34 (dd, $^2J = 17.7$ Hz, $J = 3.3$ Hz, 1H), 3.58 (d, $^2J = 17.7$ Hz, 1H), 5.13 (m, 1H), 5.19–5.28 (m, 2H), 5.32–5.37 (m, 2H), 5.64/5.72 (m, 2 × 1H), 7.70 (m, 2H), 7.53 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 9.56/9.61$, 13.9, 25.9, 27.4/27.5, 33.3, 38.4, 54.3 (q, $^2J = 23.6$ Hz), 78.4/78.6, 117.6/117.7, 123.0, 126.6 (q, $^1J = 285.2$ Hz), 129.1, 129.8, 132.4, 135.7, 135.84/135.88, 138.6, 168.1, 194.7 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 7.2$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 1742$, 1693, 1585, 1281–1265, 1210–1191 cm^{-1}; MS (EI): m/z (%) = 460 $[M - H]^+$, 393 $[M - C_5H_7]^+$, 376 $[M - C_5H_8O]^+$, 348 $[M - CH_2{=}CH{-}CH(CH_2CH_3)COO]^+$, 307 $[348 - CH_3CH_2CH]^+$, 287 $[307 - HF]^+$, 200/198 $[C_8H_7OBr]^+$ (100), 185/183 $[BrC_6H_4CO]^+$.

5-(4-Bromophenyl)-3-(1-phenylallyl)-3-trifluoromethyl-3H-thiophen-2-one (**17**, $C_{20}H_{14}BrF_3OS$)
Yield 51%; mp 85°C; ^{1}H NMR ($CDCl_3$): $\delta = 4.17$ (d, $^3J = 9.7$ Hz, 1H), 5.19 (d, $^3J_{cis} = 9.7$ Hz, 1H), 5.25 (d, $^3J_{trans} = 16.2$ Hz, 1H), 6.11 (m, 1H), 6.22 (s, 1H), 7.25–7.53 (m, 7H), 7.57 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 53.8$, 73.9 (q, $^2J = 23.6$ Hz), 113.5, 120.4, 123.4 (q, $^1J = 286.0$ Hz), 124.5, 127.9, 128.0, 128.7, 128.8, 131.1, 132.3, 132.9, 137.6, 143.1, 199.9 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 11.1$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 1710$, 1242, 1171 cm^{-1}; MS (EI): m/z (%) = 323/321 $[M - C_6H_5CH{=}CHCH_2]^+$, 214/212 $[M - C_6H_5C(CF_3)COCH{=}CH_2]^+$, 226 $[C_6H_5C(CF_3)COCH{=}CH_2]^+$, 117 $[C_6H_5CH{=}CHCH_2]^+$ (100).

5-(4-Bromophenyl)-5-(3-phenylallyl)-3-trifluoromethyl-5H-thiophen-2-one
(**18**, $C_{20}H_{14}BrF_3OS$)
Yield 29%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.25$ (m, 2H), 6.02 (dt, $^3J = 16.3$ Hz, $^3J = 6.5$ Hz, 1H), 6.55 (d, $^3J = 16.3$ Hz, 1H), 7.32 (m, 7H), 7.56 (m, 2H), 8.02 (q, $^3J = 1.1$ Hz) ppm; ^{13}C NMR ($CDCl_3$):

$\delta = 43.7$, 65.1, 120.0 (q, $^1J = 273.6$ Hz), 121.7, 122.9, 126.5, 128.2, 128.4, 128.7, 132.5, 133.0 (q, $^2J = 33.2$ Hz), 136.2, 136.4, 137.1, 161.7 (q, $^3J = 3.7$ Hz), 190.6 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.8$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 1696$, 1340, 1169–1147 cm^{-1}; MS (EI): m/z (%) = 440/438 $[M]^+$, 323/321 $[M - C_6H_5CH{=}CHCH_2]^+$, 117 $[C_6H_5CH{=}CHCH_2]^+$ (100).

5-(2-Fluorophenyl)-3-(1-phenylallyl)-3-trifluoromethyl-3H-furan-2-one (**20**, $C_{20}H_{14}F_4O_2$)
Yield 10%; mp 67°C; ^{1}H NMR ($CDCl_3$): $\delta = 4.20$ (d, $^3J = 9.3$ Hz, 1H), 5.21 (d, $^3J_{cis} = 10.3$ Hz, 1H), 5.32 (d, $^3J_{trans} = 16.8$ Hz, 1H), 6.08 (m, 1H), 6.17 (d, $^5J = 2.5$ Hz, 1H), 7.20–7.50 (m, 8H), 7.69 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 52.5$, 63.8 (q, $^2J = 26.3$ Hz), 102.2 (d, $^4J = 16.9$ Hz), 115.3 (d, $^2J = 11.2$ Hz), 116.2 (d, $^2J = 21.8$ Hz), 120.6, 123.3 (q, $^1J = 283.8$ Hz), 124.6 (d, $^3J = 3.5$ Hz), 126.4, 127.9, 128.5, 128.9, 132.0 (d, $^3J = 9.1$ Hz), 133.4, 137.2, 150.6 (d, $^3J = 3.6$ Hz), 160.8 (d, $^1J =$ 255.5 Hz), 170.5 ppm; ^{19}F NMR ($CDCl_3$): $\delta = -32.9$ (m, 1F, arom. F), 10.1 (s, 3F, CF_3) ppm; IR (KBr): $\bar{\nu} = 1814$, 1646, 1494, 1280–1255, 1248, 1172–1147 cm^{-1}; MS (EI): $m/z = 362$ $[M]^+$, 334 $[M - CO]^+$, 245 $[M - C_6H_5CH{=}CHCH_2]$, 117 $[C_6H_5CH{=}CHCH_2]$.

2-[2-(2-Fluorophenyl)-2-oxoethyl]-3-phenyl-2-(trifluoromethyl)pent-4-enoic acid 3-phenylallylic ester (**21**, $C_{29}H_{24}F_4O_3$)
Yield 51%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 3.72$ (d, $^2J = 18.3$ Hz, 1H), 3.81 (d, $^2J = 18.3$ Hz, 1H), 4.34 (d, $^3J = 10.0$ Hz, 1H), 4.95 (dd, $^2J = 6.5$ Hz, $^3J = 1.1$ Hz, 2H), 5.29 (m, 2H), 6.34 (m, 1H), 6.53 (m, 1H), 6.72 (d, $^3J = 15.9$ Hz, 1H), 7.19 (m, 2H), 7.32–7.50 (m, 11H), 7.83 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 45.3$, 53.9, 58.4 (q, $^2J = 22.6$ Hz), 66.4, 116.7 (d, $^2J = 23.9$ Hz), 119.1, 122.5, 124.7 (d, $^3J =$ 3.2 Hz), 125.4 (d, $^2J = 13.2$ Hz), 125.9 (q, $^1J = 284.9$ Hz), 126.8, 127.7, 128.2, 128.4, 128.7, 130.0, 130.8, 134.7, 135.0 (d, $^3J = 9.1$ Hz), 136.3, 138.4, 161.8 (d, $^1J = 252.9$ Hz), 167.9, 192.8 ppm; ^{19}F NMR ($CDCl_3$): $\delta = -30.7$ (m, 1F, arom. F), 14.2 (s, 3F, CF_3) ppm; IR (film): $\bar{\nu} = 1745$–1698, 1608, 1481, 1451, 1272, 1204–1179 cm^{-1}; MS (EI): $m/z = 379$ $[M - (CH_2CH{=}CHC_6H_5)]^+$, 315 $[M - COOCH_2CH{=}CHC_6H_5, -HF]^+$, 247 $[M - C_6H_5CH{=}CHCH_2, -OCH_2CH{=}CHC_6H_5 + H]^+$, 117 $[C_6H_5CH{=}CHCH_2]^+$.

2-(3,7-Dimethylocta-2,6-dienyloxy)-5-phenyl-3-(trifluoromethyl)thiophene (**22**, $C_{21}H_{23}F_3OS$)
Yield 78%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.64$ (s, 3H), 1.71 (s, 3H), 1.79 (s, 3H), 2.17 (s, 4H), 4.74 (d, $^3J = 6.8$ Hz, 2H), 5.12 (m, 1H), 5.55 (t, $^3J = 6.6$ Hz, 1H), 7.11 (s, 1H), 7.29 (m, 1H), 7.38 (m, 2H), 7.50 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 16.8$, 17.7, 25.6, 26.2, 39.6, 72.6, 112.6 (q, $^2J = 34.5$ Hz), 117.8, 118.3 (q, $^3J = 3.0$ Hz), 122.3 (q, $^1J = 269.9$ Hz), 123.6, 125.1, 127.0, 129.0, 130.1, 132.0, 133.6, 144.4, 164.0 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.8$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2966$–2857, 1708, 1338, 1258, 1152 cm^{-1}; MS (EI): m/z (%) = 243 $[M - (CH_3)_2C{=}C(CH_2)_2C(CH_3){=}CHCH_2]^+$, 137 $[(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$, 82 $[C_6H_{10}]^+$, 69 $[(CH_3)_2C{=}CHCH_2]^+$ (100).

5-(2,7-Dimethylocta-2,6-dienyl)-5-phenyl-3-trifluoromethyl-5H-thiophen-2-one (**24**, $C_{21}H_{23}F_3OS$)
Yield 79%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.61$ (s, 3H), 1.63 (s, 3H), 1.71 (s, 3H), 2.04 (m, 4H), 3.10 (dd, $^2J = 7.3$ Hz, $^3J = 2.1$ Hz, 2H), 5.06 (m, 2H), 7.35–7.42 (m, 5H), 8.02 (q, $^4J = 1.3$ Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 16.5$, 17.6, 25.6, 26.4, 38.9, 39.7, 66.1, 117.0, 120.2 (q, $^1J = 273.1$ Hz), 123.8, 126.6, 128.6, 129.2, 131.8, 132.6 (q, $^2J = 33.2$ Hz), 138.3, 141.4, 162.5 (q, $^3J = 2.9$ Hz), 191.3 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.9$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2969$–2856, 1707, 1446, 1339, 1285, 1149 cm^{-1}; MS (EI): m/z (%) = 380 $[M]^+$, 243 $[M - (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$, 137 $[(CH_3)_2C{=}CH{-}(CH_2)_2C(CH_3){=}CHCH_2]^+$, 82 $[C_6H_{10}]^+$, 69 $[(CH_3)_2C{=}CHCH_3]^+$ (100).

2-(3,7-Dimethylocta-2,6-dienyloxy)-5-phenyl-3-(trifluoromethyl)thiophene (**25**, $C_{21}H_{23}F_3OS$)
Yield 6%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.67$ (s, 3H), 1.75 (s, 3H), 1.86 (s, 3H), 2.20 (s, 4H), 4.72 (d, $^3J = 6.9$ Hz, 2H), 5.17 (m, 1H), 5.58 (t, $^3J = 7.4$ Hz, 1H), 7.13 (s, 1H), 7.31 (m, 1H), 7.40 (m, 2H), 7.52 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.7$, 23.6, 25.7, 26.6, 32.5, 72.4, 112.5 (q, $^2J = 34.8$ Hz),

118.3 (q, $^3J = 2.7$ Hz), 118.7, 122.3 (q, $^1J = 269.5$ Hz), 123.5, 125.1, 127.5, 129.0, 130.0, 132.5, 133.6, 144.4, 164.0 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.8$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2965–2857$, 1708, 1515, 1410, 1286–1261, 1156–1124 cm^{-1}; MS (FAB): m/z (%) = 380 $[M]^+$, 243 $[M - (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$, 137 $[(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$ (100).

5-(3,7-Dimethylocta-2,6-dienyl)-5-phenyl-3-trifluoromethyl-5H-thiophen-2-one
(**26**, $C_{21}H_{23}F_3OS$)
Yield 61%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.61$ (s, 3H), 1.69 (s, 6H), 2.03 (m, 4H), 3.06 (dd, $^2J = 7.3$ Hz, $^3J = 2.6$ Hz, 2H), 5.06 (m, 2H), 7.36–7.42 (m, 5H), 7.95 (q, $^4J = 1.9$ Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.7$, 23.4, 25.7, 26.2, 32.3, 38.4, 65.7, 117.5, 120.1 (q, $^1J = 273.1$ Hz), 123.7, 126.6, 128.6, 129.2, 132.2, 132.3 (q, $^2J = 33.2$ Hz), 138.3, 141.4, 162.4 (q, $^3J = 3.7$ Hz), 191.3 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.9$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2967–2858$, 1706, 1339, 1150 cm^{-1}; MS (EI): m/z (%) = 380 $[M]^+$; 243 $[M - (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH]^+$, 137 $[(CH_3)_2C{=}CH(CH_2)_2{-}C(CH_3){=}CHCH_2]^+$, 82 $[C_6H_{10}]^+$, 69 $[(CH_3)_2C{=}CHCH_2]^+$ (100).

5-(4-Bromophenyl)-5-(3,7-dimethylocta-2,6-dienyl)-3-trifluoromethyl-5H-furan-2-one
(**29**, $C_{21}H_{22}BrF_3O_2$)
Yield 33%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.54$ (s, 3H), 1.56 (s, 3H), 1.67 (s, 3H), 1.98 (s, 4H), 2.74 (dd, $^2J = 15.0$ Hz, $^3J = 7.4$ Hz, 1H), 2.85 (dd, $^2J = 14.7$ Hz, $^3J = 7.7$ Hz, 1H), 4.94 (t, $^3J = 8.0$ Hz, 1H), 5.00 (m, 1H), 7.26 (m, 2H), 7.52 (m, 2H), 7.94 (q, $^3J = 1.6$ Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 16.4$, 17.6, 25.7, 26.5, 38.5, 39.7, 89.5, 114.5, 119.5 (q, $^1J = 270.6$ Hz, CF_3), 123.1, 123.7, 124.7 (q, $^2J = 37.1$), 126.9, 132.2, 132.0, 136.1, 142.8, 158.4 (q, $^3J = 3.5$ Hz), 164.7 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.3$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2968–2855$, 1774, 1359, 1152 cm^{-1}; MS (EI): m/z (%) = 444/442 $[M]^+$, 362/360 $[M - C_6H_{10}]^+$, 321/319 $[M - (CH_3)_2C{=}CH{-}(CH_2)_2C(CH_3){=}CH_2]^+$, 307/305 $[M - (CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$, 137 $[(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2]^+$, 82 $[C_6H_{10}]^+$, 69 $[(CH_3)_2C{=}CHCH_3]^+$ (100).

2-[2-(4-Bromophenyl)-2-oxoethyl]-3,7-dimethyl-2-trifluoromethyl-3-vinyloct-6-enoic acid 3,7-dimethylocta-2,6-dienyl ester (**30**, $C_{31}H_{40}BrF_3O_3$)
Yield 23%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.26$ (m, 4H), 1.54 (s, 3H), 1.58 (s, 3H), 1.65 (s, 6H), 1.70 (s, 6H), 2.07 (m, 4H), 3.45 (d, $^2J = 16.6$ Hz, 1H), 3.57 (d, $^2J = 16.6$ Hz, 1H), 4.70 (dd, $^2J = 12.0$ Hz, $^3J = 6.0$ Hz, 1H), 4.81 (dd, $^2J = 12.0$ Hz, $^3J = 6.0$ Hz, 1H), 5.02 (m, 1H), 5.07 (m, 1H), 5.11 (d, $^3J_{trans} = 17.9$ Hz, 1H), 5.26 (d, $^3J_{cis} = 10.5$ Hz, 1H), 5.40 (dd, $^3J = 7.0$ Hz, 1H), 6.01 (dd, $^3J = 10.5$ Hz, $^3J = 16.9$ Hz, 1H), 7.56 (m, 2H), 7.72 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 16.4$, 17.6–17.7 ($4 \times CH_3$), 23.1, 25.6, 26.3, 36.1, 39.1, 39.5, 45.9, 59.8 (q, $^2J = 21.9$ Hz), 62.3, 116.1, 117.7, 123.7, 124.0, 126.3 (q, $^1J = 287.2$ Hz), 128.3, 129.5, 131.7, 131.9, 135.8, 143.1, 167.7, 194.2 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 18.5$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2968–2927$, 1738, 1696, 1584, 1210–1174 cm^{-1}; MS (FAB): m/z (%) = 463/461 $[M - C_{10}H_{15}]^+$; 445/443 $[M - C_{10}H_{17}O]^+$, 306 $[463/461 - C_6H_4Br]^+$, 185/183 $[BrC_6H_4CO]^+$, 153 $[OCH_2CH{=}C(CH_3)CH_2CH_2CH{=}C(CH_3)_2]^+$ (100).

5-(4-Bromophenyl)-5-(3,7-dimethylocta-2,6-dienyl)-3-trifluoromethyl-5H-furan-2-one
(**31**, $C_{21}H_{22}BrF_3O_2$)
Yield 53%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.57$ (s, 3H), 1.67 (s, 6H), 1.97 (s, 4H), 2.77 (dd, $^2J = 15.0$ Hz, $^3J = 7.5$ Hz, 1H), 2.83 (dd, $^2J = 15.0$ Hz, $^3J = 7.5$ Hz, 1H), 4.93 (t, $^3J = 8.0$ Hz, 1H), 5.03 (m, 1H), 7.27 (m, 2H), 7.51 (m, 2H), 8.03 (q, $^3J = 1.6$ Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.6$, 23.3, 25.6, 26.2, 31.9, 38.0, 89.5, 115.1, 119.6 (q, $^1J = 270.2$ Hz), 123.0, 123.6, 124.3 (q, $^2J = 38.2$ Hz), 126.9, 132.0, 132.2, 136.1, 142.3, 159.2 (q, $^3J = 3.5$ Hz), 165.0 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.3$ (s, CF_3) ppm; IR (film): $\bar{\nu} = 2968–2858$, 1777, 1359, 1152 cm^{-1}; MS (EI): m/z (%) = 444/442 $[M]^+$, 362/360 $[M - C_6H_{10}]^+$, 321/319 $[M - (CH_3)_2C{=}CH(CH_2)_2{-}C(CH_3){=}CH_2]^+$, 307/305 $[M - C_{10}H_{17}]^+$, 137 $[(CH_3)_2C{=}CH{-}(CH_2)_2C(CH_3){=}CHCH_2]^+$, 82 $[C_6H_{10}]^+$, 69 $[(CH_3)_2C{=}CHCH_2]^+$ (100).

2-[2-(4-Bromophenyl)-2-oxoethyl]-3,7-dimethyl-2-trifluoromethyl-3-vinyloct-6-enoic acid 3,7-dimethylocta-2,6-dienyl ester (**32**, $C_{31}H_{40}BrF_3O_3$)
Yield 14%; mp 41°C; ^{1}H NMR ($CDCl_3$): $\delta = 1.26$ (m, 4H), 1.56 (s, 3H), 1.58 (s, 3H), 1.65 (s, 6H), 1.74 (s, 6H), 2.09 (m, 4H), 3.40 (d, $^2J = 16.0$ Hz, 1H), 3.60 (d, $^2J = 16.0$ Hz, 1H), 4.75 (m, 2H), 5.07 (m, 2H), 5.11 (d, $^3J_{trans} = 17.4$ Hz, 1H), 5.26 (d, $^3J_{cis} = 10.5$ Hz, 1H), 5.40 (dd, $^3J = 7.0$ Hz, 1H), 5.81 (dd, $^3J = 10.5$ Hz, $^3J = 17.4$ Hz, 1H), 7.56 (m, 2H), 7.72 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 17.6$, 17.7, 18.4, 23.4 ($2 \times CH_3$), 23.4, 25.7, 26.6, 32.1, 35.8, 38.1, 45.9, 60.5 (q, $^2J = 22.4$ Hz), 62.2, 116.3, 118.6, 123.6, 124.1, 126.2 (q, $^1J = 287.2$ Hz), 128.3, 129.6, 131.7, 131.9, 135.9, 142.9, 167.6, 194.5 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 19.3$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 2967$–2925, 1734, 1687, 1584, 1212–1172 cm^{-1}; MS (FAB): m/z (%) = 463/461 $[M - C_{10}H_{15}]^+$, 445/443 $[M - C_{10}H_{17}O]^+$, 306 $[463/461 - C_6H_4Br]^+$, 185/183 $[BrC_6H_4–CO]^+$, 153 $[OCH_2CH=C(CH_3)CH_2CH_2CH=C(CH_3)_2]^+$ (100).

5-(4-Methoxyphenyl)-5-(3,7,11-trimethylduodeca-2,6,10-trienyl)-3-trifluoromethyl-5H-furan-2-one (**35**, $C_{27}H_{33}F_3O_3$)
Yield 47%; oil; ^{1}H NMR ($CDCl_3$: $\delta = 1.55$ (s, 3H), 1.60 (s, 3H), 1.68 (s, 3H), 1.81 (s, 3H), 2.03 (m, 8H), 2.94 (m, 2H), 3.84 (s, 3H), 4.72 (m, 2H), 5.42 (m, 1H), 6.50 (m, 2H), 7.71 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 15.9$, 16.3, 17.7, 25.8, 26.4, 26.8, 31.9, 39.8, 40.1, 55.6, 90.3 (m), 104.7, 111.6, 116.2, 119.9 (q, $J = 284.2$ Hz), 123.9, 124.4, 124.5 (m), 127.5, 132.6, 135.4, 141.8, 156.2, 159.7, 161.4 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 13.9$ (s, CF_3) ppm; MS (EI) $m/z = 462$ $[M]^+$.

2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-ylmethyl)-4-(4-fluorophenyl)-4-oxo-2-trifluoromethylbutyric acid 6,6-dimethyl-2-methylenebicyclo[3.1.1]hept-3-yl ester (**37**, $C_{31}H_{36}F_4O_3$)
Yield 31%; oil; ^{1}H NMR ($CDCl_3$): $\delta = 0.68$ (s, 3H), 0.79 (s, 3H), 1.09 (d, $^2J = 8.5$ Hz, 1H), 1.15 (s, 3H), 1.25 (s, 3H), 1.33 (d, $^2J = 10.2$ Hz, 1H), 1.8–2.4 (m, 9H), 2.5 (m, 1H), 2.91 (s, 2H), 3.42 (d, $^2J = 18.0$ Hz, 1H), 3.66 (d, $^2J = 18.0$ Hz, 1H), 4.92 (s, 1H), 5.09 (s, 1H), 5.33 (m, 1H), 5.60 (m, 1H), 7.15 (m, 2H), 7.95 (dd, $^3J = 9.8$ Hz, $^3J = 8.8$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.5$, 22.5, 26.2, 26.6, 28.2, 32.07, 32.1, 32.8, 36.9, 38.2, 38.7, 39.9, 40.6, 40.9, 47.4, 51.1, 54.6 (q, $^2J = 23.1$ Hz), 71.2, 115.3, 116.3 (d, $^2J = 22.1$ Hz), 124.8, 126.4 (q, $^1J = 285.4$ Hz), 130.9 (d, $^3J = 9.5$ Hz), 133.6 (d, $^4J = 3.0$ Hz), 142.4, 149.6, 166.4 (d, $^1J = 255.4$ Hz), 168.6, 194.5 ppm; ^{19}F NMR ($CDCl_3$): $\delta = -26.8$ (m, 1F), 8.7 (s, CF_3); IR (film): $\bar{\nu} = 2930$, 1737, 1692, 1598, 1409, 1226–1161 cm^{-1}; MS (EI): m/z (%) = 532 $[M]^+$, 380 $[M - C_{10}H_{15}O]^+$, 41 $[C_3H_5]^+$ (100).

4-(4-Chlorophenyl)-2-(2,2-dimethyl-4,4a,6,8a-tetrahydropyrano[3,2-d][1,3]dioxin-6-yl)-4-oxo-2-(trifluoromethyl)butyric acid 2,2-dimethyl-4,4a,8,8a-tetrahydropyrano[3,2-d][1,3]-dioxin-8-yl ester (**40**, $C_{29}H_{32}ClF_3O_9$)
Yield 33%; mp 160°C; ^{1}H NMR ($CDCl_3$): $\delta = 1.36$ (s, 3H), 1.40 (s, 3H), 1.43 (s, 3H), 1.46 (s, 3H), 3.3–4.1 (m, 10H), 4.81 (dd, $^3J = 6.0$ Hz, $^3J = 2.0$ Hz, 1H), 4.97 (m, 1H), 5.58 (dd, $^3J = 7.7$ Hz, $^3J = 1.8$ Hz, 1H), 5.79 (dt, $^2J = 10.6$ Hz, $J = 2.0$ Hz, 1H), 5.86 (d, $^2J = 10.6$ Hz, 1H), 6.36 (dd, $^3J = 6.1$ Hz, $^4J = 1.5$ Hz, 1H), 7.46 (d, $^3J = 9.6$ Hz, 2H), 7.85 (d, $^3J = 8.8$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 18.9$, 19.0, 28.8, 29.1, 36.1, 58.5 (q, $^2J = 24.2$ Hz), 61.6, 62.8, 66.7, 69.7, 70.8, 72.2, 75.9, 99.8, 99.9, 124.8 (q, $^1J = 285.8$ Hz), 126.3, 129.0, 129.4, 130.4, 135.1, 139.8, 145.8, 166.0, 193.1 ppm; ^{19}F NMR ($CDCl_3$): $\delta = 12.6$ (s, CF_3) ppm; IR (KBr): $\bar{\nu} = 1750$, 1698, 1640, 1590, 1375, 1230–1199, 1108 cm^{-1}; MS (FAB): m/z (%) = 639 $[M + Na]^+$, 617 $[M + H]^+$, 559 $[M - C_3H_5O]^+$, 447 $[M - C_9H_{13}O_3]^+$, 169 $[C_9H_{13}O_3]^+$ (100).

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