Synthesis of Perfluoroalkyl-Substituted γ-Lactones and 4,5-Dihydropyridazin-3(2*H*)-ones *via* Donor–Acceptor Cyclopropanes

by **Daniel Gladow** and **Hans-Ulrich Reissig***

Institut für Chemie und Biochemie, Freie Universität Berlin, Takustrasse 3, DE-14195 Berlin
(fax: +49(30)83855367; e-mail: hans.reissig@chemie.fu-berlin.de)

Dedicated to Prof. *Dieter Seebach* on the occasion of his 75th birthday

$Rh_2(OAc)_4$-Catalyzed decomposition of diazo esters in the presence of perfluoroalkyl- or perfluoroaryl-substituted silyl enol ethers smoothly provided the corresponding alkyl 2-siloxycyclopropanecarboxylates in very good yields. The generated donor–acceptor cyclopropanes are equivalents of γ-oxo esters, which we demonstrated by their one-pot transformations to yield fluorine-containing heterocycles. A reductive procedure selectively afforded perfluoroalkyl-substituted γ-hydroxy esters or γ-lactones. The treatment of the donor–acceptor cyclopropanes with hydrazine or phenylhydrazine afforded a series of perfluoroalkyl- and perfluoroaryl-substituted 4,5-dihydropyridazin-3(2*H*)-ones.

1. Introduction. – The use of small-ring compounds in organic synthesis started to flourish in the 1970s [1]. Based on first results of *Wenkert* [2], our group introduced the concept of donor–acceptor cyclopropanes in 1980 [3] and subsequently published many examples of valuable synthetic transformations of this class of small-ring compounds[1]). More recently, a boost of new methods involving donor–acceptor cyclopropanes, in particular [3 + 2] and [3 + 3] cycloadditions, could be recorded, and many applications to the synthesis of natural products were reported [5].

We are currently interested in rarely explored perfluoroalkyl- and perfluoroaryl-substituted donor–acceptor cyclopropanes[2]) in order to explore their synthetic usefulness for the preparation of fluorine-containing products, in particular of heterocyclic compounds. Owing to the strong electron-withdrawing and hydrophobic properties of fluorine-containing substituents, their incorporation into organic molecules often leads to remarkable changes in their biological activity, degradability, and bioavailability. In detail, fluorinated compounds show different lipophilicity, volatility, acidity, and increased metabolic stability. As a consequence, *ca.* 20% of all presently used drugs and 30% of all agrochemicals on the market contain fluorine and the number is steadily increasing [7].

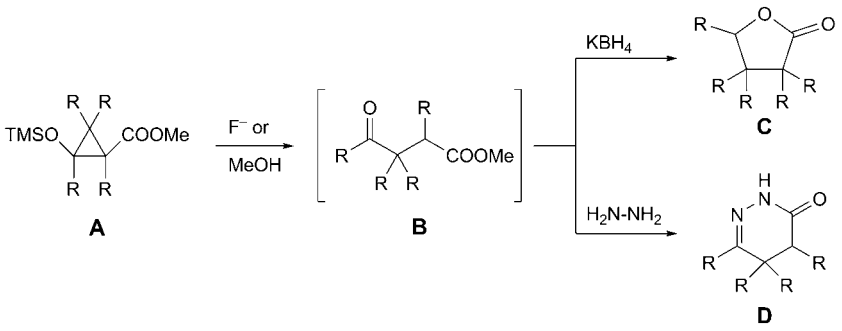
As first target product class, we were aiming to γ-lactones, since *ca.* 10% of all natural products with a biological profile, including antibiotic, antitumor, and

[1]) For reviews on donor–acceptor cyclopropanes, see [4a–4e]. For an interesting theoretical study on donor–acceptor cyclopropanes, see [4f].

[2]) For an excellent review on CF_3-substituted cyclopropanes, see [6a]. For recent original reports, see [6b–6g].

antifungal activities, contain this substructure [8]. The properties of their fluorinated analogs should, therefore, be of interest[3]). We also wanted to prepare pyridazin-3(2*H*)-ones, since they constitute an important class of N-containing heterocycles possessing various biological activities [10]. As early as 1886, *Fischer* set a common route towards these compounds by condensation of 4-oxoalkanoic acid derivatives with hydrazine and its derivatives, respectively [11]. In earlier publications, we reported that γ-lactones [12] and pyridazin-3(2*H*)-ones [13] are directly available from alkyl 2-silyloxycyclopropanecarboxylates **A** which are ring-opened in protic solvents, liberating the corresponding γ-oxo esters **B** (*Scheme 1*)[4]). These intermediates then rapidly undergo subsequent reactions either providing the γ-lactones **C** or pyridazin-3(2*H*)-ones **D**. We were curious to learn how perfluoroalkyl and perfluoroaryl substituents will influence these transformations. Recently, *Wan et al.* [15] investigated the reaction of various ω-fluoroalkylated keto esters (obtained by other methods) with hydrazine and phenylhydrazine, yielding fluoroalkyl-substituted heterocyclic 1,2-diaza 3-ones of different ring size.

Scheme 1. *One-Pot Transformations of Donor–Acceptor Cyclopropanes* **A** *to* γ*-Lactones* **C** *and 4,5-Dihydropyridazin-3(2*H*)-ones* **D**. TMS: Me_3Si.

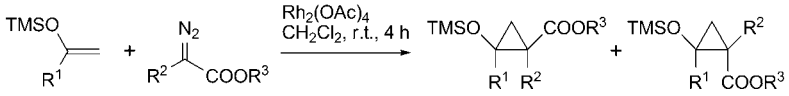


2. Results and Discussion. – 2.1. *Synthesis of Silyloxycyclopropanes.* The perfluoroalkyl- and perfluoroaryl-substituted silyl enol ethers **1a**–**1c** were prepared starting from the corresponding methyl ketones by standard methods. Their reactivity towards carbenium ions was recently studied in collaboration with the group of *Mayr*, and a dramatic decrease of rates was found; *e.g.*, perfluoroalkyl-substituted silyl enol ether **1b** is less reactive by eight orders of magnitude compared to its non-fluorinated counterpart [16]. We were very pleased to experience that this dramatically reduced nucleophilicity does not prevent cyclopropanations with diazo esters in the presence of suitable catalysts. Hence, addition by syringe pump of methyl diazoacetate **2a** to a soln. of silyl enol ethers **1a**–**1c** in CH_2Cl_2 in the presence of catalytic amounts of dirhodium tetraacetate ($Rh_2(OAc)_4$) at room temperature provided, after chromatographic purification, the desired silyloxycyclopropanes **3a**–**3c** in excellent yields (*Table 1*,

[3]) Trifluoromethyl-substituted lactones and functionalized alcohols are described in [9a–9i]. For the preparation of α-trifluoromethyl γ-lactones, see [9j] and references cited therein.

[4]) For other one-pot transformations of silyloxycyclopropanes, see [14].

Table 1. *Conversion of Silyl Enol Ethers* **1** *to Perfluoroalkyl- and Perfluoroaryl-Substituted 2-Silyloxycyclopropanes* **3**. TMS: Me_3Si.



1 **2** *cis*-**3** *trans*-**3**

Entry	**1**	**2**	R^1	R^2	R^3	**3**	Yield [%]	dr
1	**1a**	**2a**	C_5F_{11}	H	Me	**3a**	92	50 : 50
2	**1b**	**2a**	CF_3	H	Me	**3b**	84	25 : 75
3	**1c**	**2a**	C_6F_5	H	Me	**3c**	90	43 : 57
4	**1a**	**2b**	C_5F_{11}	CF_3	Et	**3d**	86	83 : 17
5	**1b**	**2b**	CF_3	CF_3	Et	**3e**	85	77 : 23[a])
6	**1d**	**2b**	H	CF_3	Et	**3f**	76	63 : 37

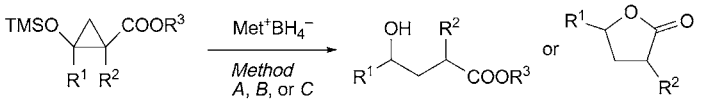
[a]) Compound *trans*-**3e** was found to be the major diastereoisomer as determined by NOE experiments.

Entries 1–3). We observed no or rather low *cis*/*trans* selectivity in these reactions and did not assign the configuration of the slightly preferred isomer of compound **3b**. Ethyl 3,3,3-trifluoro-2-diazopropanoate (**2b**) was employed to introduce a CF_3 group at C(1) of the silyloxycyclopropanes. The carbenoid addition was similarly performed as for **2a** and silyl enol ethers **1a** and **1b** were smoothly converted to cyclopropane derivatives **3d** and **3e**, respectively, bearing perfluoroalkyl groups at C(1) and C(2) (*Entries 4* and *5*). The diastereoselectivity of the reaction was moderate. For product **3e**, we could assign *trans*-configuration to the major isomer by NOE measurements. For comparison, we also prepared cyclopropane **3f** starting from the non-fluorinated silyl enol ether **1d** and diazo alkanoate **2b**. The compilation of *Table 1* illustrates that all cyclopropanations proceeded in excellent-to-good yields and with moderate-to-low diastereoselectivity. The missing diastereoselectivity is of no consequence for the subsequent transformations reported in this study, since the ring opening to intermediates of type **B** converts C(2) to a C=O group.

2.2. *Synthesis of γ-Lactones.* Perfluoroalkyl-substituted 2-silyloxycyclopropanes were then converted to γ-hydroxy esters **4** or γ-lactones **5**. Reaction of **3a**, **3b**, **3e**, and **3f** either with $NaBH_4$ or with KBH_4 in MeOH (*Methods A* and *B*, resp.) afforded the corresponding γ-hydroxy esters **4a**–**4d** in good yields (*Table 2*). These conditions induce desilylation of compounds **3** and their subsequent ring opening. The resulting γ-oxo esters are smoothly reduced by the hydride reagent to provide the alcohols **4**. Compared to their non-fluorinated analogs, these γ-hydroxy esters do not undergo spontaneous cyclization to the corresponding γ-lactones. Switching to *Method C*, which involves treatment with *para*-toluenesulfonic acid (TsOH) after the reduction step allowed the preparation of the desired perfluoroalkyl-substituted γ-lactones **5a**–**5d** in good yields. As expected, compounds **4c** and **5c** containing CF_3 groups at two stereogenic centers were formed as mixture of diastereoisomers.

2.3. *Synthesis of Pyridazin-3(2*H*)-ones.* The reactions of perfluoroalkyl- and perfluoroaryl-substituted 2-silyloxycyclopropanes **3a**–**3c**, **3e**, and **3f** with $NH_2NH_2 \cdot H_2O$ in the presence of TsOH required heating to 65° for 24 to 48 h to provide the

Table 2. *Conversion of 2-Silyloxycyclopropanes* **3** *to γ-Hydroxy Esters* **4** *and γ-Lactones* **5**



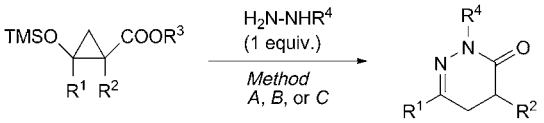
3 **4** **5**

Entry	**3**	R^1	R^2	R^3	**4**	Method[a])	Yield [%]	**5**	Method[a])	Yield [%]
1	**3a**	C_5F_{11}	H	Me	**4a**	*A*	89	**5a**	*C*	75
2	**3b**	CF_3	H	Me	**4b**	*A*	85	**5b**	*C*	57
3	**3e**	CF_3	CF_3	Et	**4c**	*B*	67[b])	**5c**	*C*	63[c])
4	**3f**	H	CF_3	Et	**4d**	*B*	69	**5d**	*C*	56

[a]) *Method A:* $NaBH_4$, MeOH, 0° to room temperature, 12 h; *Method B:* KBH_4, MeOH, 0°, 1 h; *Method C:* 1. KBH_4, MeOH, 0°, 10 min to 1 h, r.t., 0 to 16 h; 2. $TsOH \cdot H_2O$, CH_2Cl_2, 12 to 72 h. [b]) dr 56 : 44. [c]) dr 59 : 41

expected pyridazin-3(2*H*)-ones **6a**–**6e** in very good-to-moderate yields (*Table 3*, *Entries 1–5*). Again, the reaction conditions for the formation of the heterocyclic system are slightly harsher than for compounds without fluorinated substituents [13]. It is assumed that the transformation starts with a ring opening of the 2-silyloxycyclopropanes, followed by formation of the hydrazone of the produced γ-oxo esters. Cyclization by attack of the NHR^4 group to the alkoxycarbonyl group furnishes the heterocycle. This final step is apparently slower for products such as **6d** requiring higher reaction temperatures (*Entry 4*).

Table 3. *Conversion of 2-Silyloxycyclopropanes* **3** *to Pyridazin-3(2*H*)-ones* **6** *and* **7**



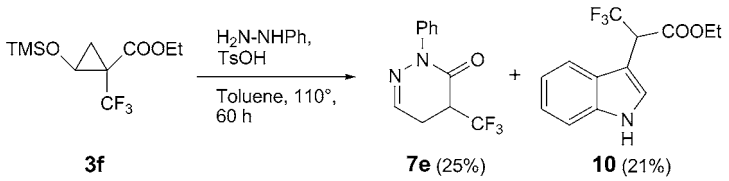
3 **6** or **7**

Entry	**3**	R^1	R^2	R^3	R^4	**6** or **7**	Method[a])	Yield [%]
1	**3a**	C_5F_{11}	H	Me	H	**6a**	*A*	72
2	**3b**	CF_3	H	Me	H	**6b**	*A*	87
3[b])	**3c**	C_6F_5	H	Me	H	**6c**	*B*	75
4[c])	**3e**	CF_3	CF_3	Et	H	**6d**	*B*	90
5	**3f**	H	CF_3	Et	H	**6e**	*A*	41
6	**3a**	C_5F_{11}	H	Me	Ph	**7a**	*C*	70
7	**3b**	CF_3	H	Me	Ph	**7b**	*C*	83
8[c])	**3c**	C_6F_5	H	Me	Ph	**7c**	*C*	90
9	**3e**	CF_3	CF_3	Et	Ph	**7d**	*C*	88
10	**3f**	H	CF_3	Et	Ph	**7e**	*C*	25[d])

[a]) *Method A:* $TsOH \cdot H_2O$, MeOH, 65°, 24 to 48 h; *Method B:* $TsOH \cdot H_2O$, toluene, 110°, 60 h; *Method C:* $TsOH \cdot H_2O$, toluene, 90°, 60 h. [b]) 2 Equiv. of NH_2NH_2 were used. [c]) 5 Equiv. of NH_2NH_2 were used. [d]) Indole **10** was formed as a by-product.

The reactions of the 2-silyloxycyclopropanes with $PhNHNH_2$ generally proceeded more sluggishly, but also afforded the desired Ph-substituted pyridazin-3(2*H*)-ones **7a**–**7d** in good-to-excellent yields (*Table 3*, *Entries 6–9*). Cyclopropane derivative **3f** with a CF_3 substituent at C(2) gave a unique result, as the expected pyridazin-3(2*H*)-one **7e** was formed in only 25% yield, and indole derivative **10** was isolated in similar quantities (21%). Obviously, the intermediate hydrazone derived from **3f** undergoes the expected intramolecular substitution to provide **7e**, but a *Fischer* indole synthesis competes under these acidic conditions furnishing **10** as second product (*Scheme 2*).

Scheme 2. *Competitive Cyclization and Indole Formation*



3f **7e** (25%) **10** (21%)

Conclusions. – In this work, we demonstrated that, despite of the low nucleophilicity of perfluoroalkyl- and perfluoroaryl-substituted silyl enol ethers, their dirhodium tetraacetate-catalyzed cyclopropanation with diazo esters provides the desired donor–acceptor cyclopropanes in excellent yields. These products undergo smooth ring-opening reactions to γ-oxo esters under mild conditions which was exploited for one-pot conversions into perfluoroalkyl-substituted γ-lactones, as well as perfluoroalkyl- and perfluoroaryl-substituted pyridazin-3(2*H*)-ones. Although rates of cyclization seem to be decreased by the fluorine-containing substituents the product yields were generally very good. The developed methods should also be applicable to the preparation of other fluorine-containing heterocycles with potential biological activity using fluorine-containing donor–acceptor cyclopropanes as key intermediates.

Experimental Part

General. Reactions were generally performed under Ar in flame-dried flasks. Solvents and reagents were added by syringes. Diazo esters were added with an infusion pump (*Precidor Type 8003*). Solvents were dried by standard procedures. *Methyl 2-diazoacetate* (**2a**) [17] and *ethyl 3,3,3-trifluoro-2-diazopropanoate* (**2b**) [18] were prepared according to literature procedures. Reagents were purchased and were used as received without further purification unless otherwise stated. Bulb-to-bulb distillations were performed with a *BÜCHI* glass oven (*B-585*). Column chromatography (CC): SiO_2 (230–400 mesh, *Merck* or *Fluka*) or Al_2O_3 (70–230 mesh, *Merck* or *Fluka*). Yields refer to anal. pure samples. M.p.: *Reichert* apparatus *Thermovar*; uncorrected. IR Spectra: *JASCO FT/IR-4100* spectrometer. NMR Spectra: *Bruker* (*AVIII 700*) and *JEOL* (*ECS 500*, *ECX 400*, and *Eclipse 500*) instruments; chemical shifts are reported relative to Me_4Si (δ(H) 0.00), $CDCl_3$ (δ(H) 7.26, δ(C) 77.2; δ(F), frequency calibrated lock with $\pm$1 ppm deviation) or CD_3OD (δ(H) 4.87, 3.31); all ^{13}C-NMR spectra are ^{1}H- or ^{19}F-decoupled; m_c, centered *multiplet*; coupling constants in Hz. HR-MS: *Agilent 6210* (ESI-TOF) instrument. Elemental analyses: *Perkin Elmer CHN-Analyzer 2400* and *Vario EL Elemental Analyzer*.

General Procedure (*GP*) *for the Cyclopropanations*. The silyl enol ether **1** was dissolved in CH_2Cl_2, and $Rh_2(OAc)_4$ was added. A soln. of the corresponding diazo ester **2** in CH_2Cl_2 was added to the mixture over 4 h using an infusion pump. After 30 min, the gas evolution decreased and the mixture was concentrated under reduced pressure. The residue was suspended in hexane to precipitate the catalyst,

and the supernatant soln. was concentrated under reduced pressure. The crude product was purified either by CC or distillation through a short *Vigreux* column (10 cm).

Methyl 2-[(Trimethylsilyl)oxy]-2-(undecafluoropentyl)cyclopropanecarboxylate (**3a**). According to *GP*, **1a** (2.99 g, 7.78 mmol), $Rh_2(OAc)_4$ (340 mg, 0.78 mmol), and **2a** (3.11 g, 31.1 mmol) gave, after CC (SiO_2; 0–5% AcOEt in hexane), **3a** (3.26 g, 92%, dr 50:50). Colorless liquid. IR (ATR): 3090–2760 (C–H), 1750 (C=O), 1235, 1200, 1140 (C–F). HR-ESI-TOF-MS: 479.0514 ($[M+Na]^+$, $C_{13}H_{15}F_{11}NaO_3Si^+$; calc. 479.0513). Anal. calc. for $C_{13}H_{15}F_{11}O_3Si$ (456.32): C 34.22, H 3.31; found: C 34.18, H 3.11.

Data of Diastereoisomer a. ^{1}H-NMR (700 MHz, $CDCl_3$): 3.73 (*s*, COOMe); 2.17 (*dd*, *J* = 10.2, 8.9, H–C(1)); 1.81 (*ddd*, *J* = 8.9, 7.2, *J*(H,F) = 1.7, 1 H of CH_2(3)); 1.42 (*ddd*, *J* = 10.2, 7.2, *J*(H,F) = 3.9, 1 H of CH_2(3)); 0.19 (*s*, Me_3Si). ^{13}C-NMR (176 MHz, $CDCl_3$): 168.1 (*d*, *J*(C,F) = 1.4, *C*OOMe); 117.6 (*tq*, *J* = 33.0, 288, $(CF_2)_4CF_3$); 114.6, 111.7, 110.7, 108.7 (4m_c, $(CF_2)_4CF_3$); 60.9 (*t*, *J*(C,F) = 30.5, C(2)); 52.5 (*q*, COO*Me*); 27.9 (m_c, C(1)); 15.9 (*td*, *J*(C,F) = 5.0, C(3)); 0.80 (*q*, Me_3Si). ^{19}F-NMR (470 MHz, $CDCl_3$): −80.8 (*t*, *J* = 9.6, $(CF_2)_4CF_3$); −114.5 to −127.3 (4*m*, $(CF_2)_4CF_3$).

Data of Diastereoisomer b. ^{1}H-NMR (700 MHz, $CDCl_3$): 3.71 (*s*, COOMe); 2.14 (*ddt*, *J* = 9.5, 7.2, *J*(H,F) = 2.1, H–C(1)); 1.72 (*td*, *J*(H,F) = 2.9, *J* = 7.2, 1 H of CH_2(3)); 1.51 (*dd*, *J* = 7.2, 9.5, 1 H of CH_2(3)); 0.18 (*s*, Me_3Si). ^{13}C-NMR (176 MHz, $CDCl_3$): 167.6 (*s*, *C*OOMe); 117.6 (*tq*, *J*(C,F) = 33.0, 288, $(CF_2)_4CF_3$); 115.5, 111.7, 110.7, 108.7 (4m_c, $(CF_2)_4CF_3$); 60.5 (*t*, *J*(C,F) = 30.5, C(2)); 52.4 (*q*, COO*Me*); 24.2 (*td*, *J*(C,F) = 6.2, C(1)); 14.6 (*td*, *J*(C,F) = 3.4, C(3)); 0.75 (*qq*, *J*(C,F) = 1.8, Me_3Si). ^{19}F-NMR (470 MHz, $CDCl_3$): −80.8 (*t*, *J* = 9.6, $(CF_2)_4CF_3$); −114.5 to −127.3 (4*m*, $(CF_2)_4CF_3$).

Methyl 2-(Trifluoromethyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate (**3b**). According to *GP*, **1b** (4.00 g, 21.7 mmol), $Rh_2(OAc)_4$ (480 mg, 1.09 mmol), and **2a** (8.69 g, 87.0 mmol) gave, after CC (SiO_2, 20% Et_2O in pentane), **3b** (4.67 g, 84%, dr 75:25). Colorless liquid. IR (ATR): 3020–2810 (C–H), 1745 (C=O), 1330, 1280, 1250, 1170 (C–F). HR-ESI-TOF-MS: 279.0620 ($[M+Na]^+$, $C_9H_{15}F_3NaO_3Si^+$; calc. 279.0635).

Data of the Major Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.72 (*s*, COOMe); 2.14 (*dd*, *J* = 7.1, 9.7, H–C(1)); 1.74 (*qdd*, *J*(H,F) = 1.8, *J* = 6.9, 7.1, 1 H of CH_2(3)); 1.47 (*dd*, *J* = 6.9, 9.7, 1 H of CH_2(3)); 0.18 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.7 (*s*, *C*OOMe); 123.8 (*q*, *J*(C,F) = 277, CF_3); 60.3 (*q*, *J*(C,F) = 38.3, C(2)); 52.2 (*q*, COO*Me*); 23.5–23.2 (*m*, C(1)); 16.2–16.0 (*m*, C(3)); 0.5 (*qq*, *J*(C,F) = 0.8, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −76.5 (*s*, CF_3).

Data of the Minor Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.71 (*s*, COOMe); 2.14 (*dd*, *J* = 8.6, 10.0, H–C(1)); 1.76 (*dd*, *J* = 6.9, 8.6, 1 H of CH_2(3)); 1.37 (*qdd*, *J*(H,F) = 2.1, *J* = 6.9, 10.0, 1 H of CH_2(3)); 0.20 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 168.1 (*s*, *C*OOMe); 124.0 (*q*, *J*(C,F) = 277, CF_3); 60.4 (*q*, *J*(C,F) = 38.6, C(2)); 52.5 (*q*, COO*Me*); 27.9–27.6 (*m*, C(1)); 16.2–16.0 (*m*, C(3)); 0.6 (*qq*, *J*(C,F) = 0.8, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −71.8 (*s*, CF_3).

Methyl 2-(Pentafluorophenyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate (**3c**). According to *GP*, **1c** (10.3 g, 36.5 mmol), $Rh_2(OAc)_4$ (161 mg, 0.365 mmol), and **2a** (14.6 g, 146 mmol) gave, after flash chromatography (SiO_2; 15% Et_2O in pentane), **3c** (11.6 g, 90%, dr 57:43). Colorless liquid. IR (ATR): 3120–2730 (C–H), 1735 (C=O), 1655 (C=C); 1380, 1340, 1255, 1195, 1100 (C–F). HR-ESI-TOF-MS: 377.0591 ($[M+Na]^+$, $C_{14}H_{15}F_5NaO_3Si^+$; calc. 377.0608). Anal. calc. for $C_{14}H_{15}F_5O_3Si$ (354.34): C 47.45, H 4.27; found: C 46.66, H 4.30.

Data of the Major Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.62 (*s*, COOMe); 2.32 (*tdd*, *J*(H,F) = 1.1, *J* = 7.5, 9.6, H–C(1)); 1.76 (*dd*, *J* = 6.4, 9.6, 1 H of CH_2(3)); 1.71 (*tdd*, *J*(H,F) = 1.1, *J* = 6.4, 7.5, 1 H of CH_2(3)); 0.03 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 171.6 (*s*, *C*OOMe); 146.1, 141.6, 137.6, 112.8 (4m_c, Ar); 55.2 (m_c, C(2)); 52.1 (*q*, COO*Me*); 27.7 (m_c, C(1)); 21.8 (m_c, C(3)); 0.4 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −140.7, −140.9 (2*m*, 2 *o*-F); −153.6 (*m*, 1 *p*-F); −162.3 (*m*, 2 *m*-F).

Data of the Minor Diastereoisomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 3.77 (*s*, COOMe); 2.04 (*tdd*, *J*(H,F) = 0.8, *J* = 6.5, 7.3, 1 H of CH_2(3)); 1.97 (*dd*, *J* = 7.3, 9.0, 1 H of CH_2(3)); 1.49 (*tdd*, *J*(H,F) = 1.0, *J* = 6.5, 9.0, H–C(1)); 0.04 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 169.1 (*s*, *C*OOMe); 145.7, 141.6, 137.7, 115.7 (4m_c, Ar); 53.7 (m_c, C(2)); 52.1 (*q*, COO*Me*); 27.6 (*d*, C(1)); 19.6 (m_c, C(3)); 0.3 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −139.7 (m_c, 2 *o*-F); −153.1 (m_c, 1 *p*-F); −161.3 (m_c, 2 *m*-F).

Ethyl 1-(Trifluoromethyl)-2-[(trimethylsilyl)oxy]-2-(undecafluoropentyl)cyclopropanecarboxylate (**3d**). According to *GP*, **1a** (12.7 g, 32.9 mmol), $Rh_2(OAc)_4$ (97 mg, 0.22 mmol), and **2b** (4.00 g,

22.0 mmol) gave, after distillation (41–43°/12 mbar), **3d** (10.2 g, 86%, dr 83:17). Colorless liquid. IR (ATR): 3070–2830 (C–H), 1750 (C=O), 1330, 1240, 1200, 1160 (C–F). HR-ESI-TOF-MS: 561.0547 ($[M+Na]^+$, $C_{15}H_{16}F_{14}NaO_3Si^+$; calc. 561.0543). Anal. calc. for $C_{15}H_{16}F_{14}O_3Si$ (538.35): C 33.47, H 3.00; found: C 33.45, H 3.04.

Data of the Major Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.25, 4.17 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.2$, $J(A,B) = 10.9$, $COOCH_2Me$); 2.14 (*dt*, $J(H,F) = 1.9$, $J = 8.3$, 1 H of $CH_2(3)$); 1.86 (*ddd*, $J(H,F) = 0.5, 1.5$, $J = 8.3$, 1 H of $CH_2(3)$); 1.27 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.2$, $COOCH_2Me$); 0.19 (*s*, Me_3Si). ^{13}C-NMR (176 MHz, $CDCl_3$): 162.8 (*s*, *C*OOCH$_2$Me); 123.0 (*dq*, $J(C,F) = 1.3$, 276, CF_3); 117.5 (*tq*, $J(C,F) = 32.8$, 288, $(CF_2)_4CF_3$); 115.0, 111.4, 110.7, 108.7 ($4m_c$, $(CF_2)_4CF_3$); 62.9 (*t*, $J(C,F) = 32.2$, C(2)); 63.0 (*t*, COO*C*H$_2$Me); 38.4 (*dq*, $J(C,F) = 7.7$, 33.3, C(1)); 16.8 (*t*, C(3)); 13.5 (*q*, $COOCH_2Me$); 0.7 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −61.6 (*s*, CF_3); −80.7 (*tdd*, $J = 2.5, 8.6, 11.2$, $(CF_2)_4CF_3$); −106.6 to −128.2 (*m*, $(CF_2)_4CF_3$).

Data of the Minor Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.35 (*q*, $J = 7.1$, COOC*H*$_2$Me); 1.96 (*dd*, $J(H,F) = 1.7$, $J = 8.2$, 1 H of $CH_2(3)$); 1.51–1.48 (*m*, 1 H of $CH_2(3)$); 1.32 (*t*, $J = 7.1$, $COOCH_2Me$); 0.16 (*s*, Me_3Si). ^{13}C-NMR (176 MHz, $CDCl_3$): 163.3 (*s*, *C*OOCH$_2$Me); 122.8 (*q*, $J(C,F) = 276$, CF_3); 117.5 (m_c, $(CF_2)_4CF_3$); 115.0, 111.4, 110.7, 108.8 ($4m_c$, $(CF_2)_4CF_3$); 62.9 (*t*, $J(C,F) = 30.9$, C(2)); 62.9 (*t*, COO*C*H$_2$Me); 41.4 (*dq*, $J(C,F) = 6.8$, 37.0, C(1)); 17.1 (*t*, C(3)); 14.1 (*q*, $COOCH_2Me$); 0.7 (*q*, Me_3Si). $(CF_2)_4CF_3$ not resolved due to overlap with major diastereoisomer. ^{19}F-NMR (376 MHz, $CDCl_3$): −58.9 (*dd*, $J = 17.0$, 29.3, CF_3); −80.7 (overlapping with major diastereoisomer, $(CF_2)_4CF_3$); −106.6 to −128.2 (*m*, $(CF_2)_4CF_3$).

Ethyl 1,2-Bis(trifluoromethyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate (**3e**). According to *GP*, **1b** (22.5 g, 122 mmol), $Rh_2(OAc)_4$ (359 mg, 0.813 mmol), and **2b** (14.8 g, 81.0 mmol) gave, after distillation (82–84°/12 mbar), **3e** (23.5 g, 85%, dr 77:23). Colorless liquid. IR (ATR): 3015–2925 (C–H), 1750 (C=O), 1335, 1300, 1260, 1165 (C–F). HR-ESI-TOF-MS: 377.0422 ($[M+K]^+$, $C_{11}H_{16}F_6KO_3Si^+$; calc. 377.0410).

Data of cis-**3e**. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.28, 4.24 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $J(A,B) = 10.8$, $COOCH_2Me$); 2.06, 1.83 (2*qd*, $J(H,F) = 1.7$, $J = 8.2$, $CH_2(3)$); 1.28 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $COOCH_2Me$); 0.16 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 163.1 (*q*, $J(C,F) = 2.2$, *C*OOCH$_2$Me); 123.0, 122.8 (2*q*, $J(C,F) = 278$ each, 2 CF_3); 65.5 (*t*, COO*C*H$_2$Me); 61.6 (*q*, $J(C,F) = 40.6$, C(1)); 40.0 (*q*, $J(C,F) = 37.2$, C(2)); 18.9 (m_c, C(3)); 14.1 (*q*, $COOCH_2Me$); 0.41 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −61.9 (*d*, $J(F,H) = 1.5$, CF_3); −73.3 (*s*, CF_3).

Data of trans-**3e**. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.30, 4.23 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $J(A,B) = 3.5$, COOC*H*$_2$Me); 2.16 (*qd*, $J(H,F) = 1.7$, $J = 8.0$, 1 H of $CH_2(3)$); 1.96 (*d*, $J = 8.0$, 1 H of $CH_2(3)$); 1.33 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $COOCH_2Me$); 0.20 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 163.0 (*q*, $J(C,F) = 1.4$, *C*OOCH$_2$Me); 122.9, 122.7 (2*q*, $J(C,F) = 276$, 275, 2 CF_3); 63.0 (*t*, COO*C*H$_2$Me); 61.4 (*q*, $J(C,F) = 39.0$, C(1)); 37.2 (*q*, $J(C,F) = 33.7$, C(2)); 18.2 (m_c, C(3)); 13.8 (*q*, $COOCH_2Me$); 0.41 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −71.9 (*q*, $J = 11.3$, CF_3); −59.5 (*qd*, $J(F,H) = 1.7$, $J = 11.3$, CF_3).

Ethyl 1-(Trifluoromethyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate (**3f**). According to *GP*, **1d** (19.1 g, 156 mmol), $Rh_2(OAc)_4$ (485 mg, 1.10 mmol), and **2b** (20.0 g, 110 mmol) gave, after distillation (80–82°/12 mbar), **3f** (22.5 g, 76%, dr 63:37). Colorless liquid. IR (ATR): 3010–2920 (C–H), 1740 (C=O), 1365, 1260, 1140, 1100 (C–F). HR-ESI-TOF-MS: 309.0544 ($[M+K]^+$, $C_{10}H_{17}F_3KO_3Si^+$; calc. 309.0531).

Data of the Major Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.25, 4.21 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $J(A,B) = 10.6$, $COOCH_2Me$); 3.87 (m_c, H–C(2)); 1.96 (*qdd*, $J(H,F) = 1.6$, $J = 5.3$, 7.0, 1 H of $CH_2(3)$); 1.48 (*t*, $J = 7.0$, 1 H of $CH_2(3)$); 1.27 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $COOCH_2Me$); 0.14 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 164.5 (*q*, $J(C,F) = 1.4$, *C*OOCH$_2$Me); 124.0 (*q*, $J(C,F) = 274$, CF_3); 61.8 (*t*, COO*C*H$_2$Me); 55.4 (*tq*, $J(C,F) = 2.5$, C(2)); 31.9 (*q*, $J(C,F) = 32.7$, C(1)); 18.4 (*dq*, $J(C,F) = 1.9$, C(3)); 14.2 (*q*, $COOCH_2Me$); −0.5 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): −65.2 (*s*, CF_3).

Data of the Minor Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.24, 4.20 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $J(A,B) = 10.6$, $COOCH_2Me$); 3.87 (m_c, H–C(2)); 1.76–1.62 (*m*, $CH_2(3)$); 1.28 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $COOCH_2Me$); 0.16 (*s*, Me_3Si). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.7 (*q*, $J(C,F) = 1.2$, *C*OOCH$_2$Me); 124.1 (*q*, $J(C,F) = 273$, CF_3); 61.9 (*t*, COO*C*H$_2$Me); 58.9 (*t*, C(2)); 34.0 (*q*,

J(C,F) = 33.4, C(1)); 19.6 (*dq*, *J*(C,F) = 1.8, C(3)); 14.2 (*q*, $COOCH_2$*Me*); – 0.5 (*q*, Me_3Si). ^{19}F-NMR (376 MHz, $CDCl_3$): – 60.3 (*s*, CF_3).

Methyl 5,5,6,6,7,7,8,8,9,9,9-Undecafluoro-4-hydroxynonanoate (**4a**). $NaBH_4$ (45 mg, 1.20 mmol) was added at 0° to a soln. of **3a** (500 mg, 1.10 mmol) in MeOH (2 ml). After stirring at r.t. for 12 h, the mixture was diluted with Et_2O (20 ml) and washed with sat. $NaHCO_3$ soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Bulb-to-bulb distillation (80°/0.5 mbar) afforded alcohol **4a** (378 mg, 89%). Colorless liquid. IR (ATR): 3880 – 3050 (O–H), 3050 – 2660 (C–H), 1725 (C=O), 1350, 1235, 1200, 1140, 1105 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.34 – 4.11 (*m*, H–C(4)); 3.71 (*s*, COOMe); 3.01 (*d*, *J* = 7.3, HO–C(4)); 2.65 (*ddd*, *J* = 5.9, 8.0, 17.5, 1 H of CH_2(2)); 2.57 (*ddd*, *J* = 6.0, 7.3, 17.5, 1 H of CH_2(2)); 2.10 (*tddd*, *J*(H,F) = 2.6, *J* = 5.4, 8.0, 13.4, 1 H of CH_2(3)); 2.07 – 1.91 (*m*, 1 H of CH_2(3)). ^{13}C-NMR (126 MHz, $CDCl_3$): 174.7 (*d*, *J*(C,F) = 0.8, C(1)); 117.4 (*tq*, *J*(C,F) = 33.5, 288, C(9)); 116.4 – 106.0 (4*m*, C(5), C(6), C(7), C(8)); 69.4 (*ddd*, *J*(C,F) = 23.0, 27.1, C(4)); 52.0 (*q*, COO*Me*); 29.6 (*t*, C(3)); 24.3 (*t*, C(2)). ^{19}F-NMR (376 MHz, $CDCl_3$): – 80.7 (*tt*, *J* = 2.5, 10.0, CF_3(9)); – 127.4 to – 120.5 (*m*, CF_2(5), CF_2(6), CF_2(7), CF_2(8)). HR-ESI-TOF-MS: 409.0290 ($[M + Na]^+$, $C_{10}H_9NaF_{11}O_3^+$; calc. 409.0274). Anal. calc. for $C_{10}H_9F_{11}O_3$ (386.16): C 31.10, H 2.35; found: C 31.34, H 2.39.

Methyl 5,5,5-Trifluoro-4-hydroxypentanoate (**4b**). $NaBH_4$ (49 mg, 2.1 mmol) was added at 0° to a soln. of **3b** (500 mg, 1.95 mmol) in MeOH (2 ml). After stirring at r.t. for 12 h the mixture was diluted with Et_2O (20 ml) and washed with sat. $NaHCO_3$ soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Bulb-to-bulb distillation (145°/15 – 20 mbar) afforded **4b** (308 mg, 85%). Colorless liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.07 – 3.92 (*m*, H–C(4)); 3.68 (*s*, COOMe); 3.67 – 3.58 (*m*, HO–C(4)); 2.59 – 2.49 (*m*, CH_2(2)); 2.03 (*dtd*, *J* = 3.2, 7.3, 14.5, 1 H of CH_2(3)); 1.90 (*dtd*, *J* = 6.7, 10.0, 14.5, 1 H of CH_2(3)). ^{13}C-NMR (101 MHz, $CDCl_3$): 174.4 (*s*, C(1)); 125.1 (*q*, *J*(C,F) = 282, C(5)); 69.7 (*dq*, *J*(C,F) = 31.3, C(4)); 52.2 (*q*, COO*Me*); 29.5 (*t*, C(2)); 24.7 (*tq*, *J*(C,F) = 1.7, C(3)). ^{19}F-NMR (376 MHz, $CDCl_3$): – 80.0 (*d*, *J*(F,H) = 6.3, F–C(5)). HR-ESI-TOF-MS: 209.0398 ($[M + Na]^+$, $C_6H_9F_3NaO_3^+$; calc. 209.0396). Enantiomerically pure (*R*)-ethyl 5,5,5-trifluoro-4-hydroxypentanoate was reported in [8], however, ^{13}C- and ^{19}F-NMR spectra have not been described.

Ethyl 5,5,5-Trifluoro-4-hydroxy-2-(trifluoromethyl)pentanoate (**4c**). KBH_4 (80 mg, 1.5 mmol) was added at 0° to a soln. of **3e** (500 mg, 1.48 mmol) in MeOH (5 ml). After stirring for 1 h, the mixture was diluted with CH_2Cl_2 (30 ml) and washed with 1M HCl soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. CC (SiO_2; 50% Et_2O in pentane) afforded **4c** (266 mg, 67%, dr 56 : 44). Colorless oil. IR (ATR): 3705 – 3050 (O–H), 3050 – 2720 (C–H), 1730 (C=O), 1270, 1165, 1105 (C–F). HR-ESI-TOF-MS: 291.0419 ($[M + Na]^+$, $C_8H_{10}F_6NaO_3^+$; calc. 291.0432). Anal. calc. for $C_8H_{10}F_6O_3$ (268.15): C 35.83, H 3.76; found: C 35.74, H 3.76.

Data of the Major Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.30, 4.25 (*AB* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, *J*(*A*,*B*) = 10.9, COOC*H*$_2$Me); 4.17 – 3.97 (*m*, H–C(4)); 3.59 – 3.27 (*m*, CH_2(2)); 2.83 – 2.61 (*m*, HO–C(5)); 2.37 – 2.01 (*m*, CH_2(3)); 1.30 (*X* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, $COOCH_2$*Me*). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.6 (*q*, *J*(C,F) = 2.7, C(1)); 124.7, 124.5 (2*q*, *J*(C,F) = 280, 282, *C*F_3–C(2), *C*F_3–C(4)); 68.9 (*dq*, *J*(C,F) = 32.0, C(4)); 62.7 (*t*, COO*C*H$_2$Me); 47.2 (*dq*, *J*(C,F) = 28.2, C(2)); 26.6 – 26.4 (*m*, C(3)); 14.0 (*q*, $COOCH_2$*Me*). ^{19}F-NMR (376 MHz, $CDCl_3$): – 68.3 (*d*, *J*(F,H) = 8.6, CF_3–C(2)); – 80.3 (*d*, *J*(F,H) = 6.3, CF_3(5)).

Data of the Minor Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.32, 4.24 (*AB* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, *J*(*A*,*B*) = 10.7, COOC*H*$_2$Me); 4.17 – 3.97 (*m*, H–C(4)); 3.59 – 3.43 (*m*, 1 H of CH_2(2)); 3.43 – 3.27 (*m*, 1 H of CH_2(2)); 2.83 – 2.61 (*m*, HO–C(5)); 2.37 – 2.01 (*m*, CH_2(3)); 1.31 (*X* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, $COOCH_2$*Me*). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.1 (*q*, *J*(C,F) = 3.4, C(1)); 124.6, 124.50 (2*q*, *J*(C,F) = 282, 280, *C*F_3–C(2), *C*F_3–C(4)); 67.5 (*dq*, *J*(C,F) = 32.1, C(4)); 62.6 (*t*, COO*C*H$_2$Me); 46.1 (*dq*, *J*(C,F) = 28.5, C(2)); 26.2 – 26.0 (*m*, C(3)); 13.9 (*q*, $COOCH_2$*Me*). ^{19}F-NMR (376 MHz, $CDCl_3$): – 68.1 (*d*, *J*(F,H) = 8.2, CF_3–C(2)); – 80.4 (*d*, *J*(F,H) = 6.3, CF_3(5)).

Ethyl 4-Hydroxy-2-(trifluoromethyl)butanoate (**4d**). KBH_4 (100 mg, 1.85 mmol) was added at 0° to a soln. of **3f** (500 mg, 1.85 mmol) in MeOH (5 ml). After stirring for 1 h, the mixture was diluted with CH_2Cl_2 (30 ml) and washed with 1M HCl soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. CC (SiO_2, 20% AcOEt in hexane) afforded **4d** (256 mg, 69%). Colorless liquid. IR (ATR): 3715 – 3065 (O–H), 3060 – 2670 (C–H), 1740 (C=O), 1320,

1265, 1160, 1110 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.24, 4.21 (*AB* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $J(A,B) = 10.8$, COOCH_2Me); 3.78–3.71 (*m*, 1 H of CH_2(4)); 3.70–3.63 (*m*, 1 H of CH_2(4)); 3.44–3.26 (*m*, H–C(2)); 2.22–1.95 (*m*, CH_2(3)); 1.85 (*s*, HO–C(4)); 1.28 (*X* of *ABX*$_3$, $J(A,X) = J(B,X) = 7.1$, $COOCH_2Me$). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.9 (*q*, J(C,F) = 3.2, C(1)); 124.9 (*q*, J(C,F) = 280, CF_3); 62.0 (*t*, $COOCH_2$Me); 59.3 (*t*, C(4)); 47.3 (*dq*, J(C,F) = 27.8, C(2)); 29.0 (*tq*, J(C,F) = 2.0, C(3)); 13.9 (*q*, $COOCH_2Me$). ^{19}F-NMR (376 MHz, $CDCl_3$): −68.3 (*d*, J(F,H) = 8.4, CF_3). HR-ESI-TOF-MS: 223.0558 ($[M+Na]^+$, $C_7H_{11}F_3NaO_3^+$; calc. 223.0558). Anal. calc. for $C_7H_{11}F_3O_3$ (200.16): C 42.00, H 5.54; found: C 41.88, H 5.20.

*4,5-Dihydro-5-(undecafluoropentyl)furan-2(3*H*)-one* (**5a**). KBH_4 (59 mg, 1.10 mmol) was added at 0° to a soln. of **3a** (500 mg, 1.10 mmol) in MeOH (2 ml). After stirring for 1 h at 0° and 16 h at r.t., MeOH was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml), and $TsOH \cdot H_2O$ (140 mg, 0.736 mmol) was added. The mixture was heated under reflux for 48 h, in doing so every 12 h CH_2Cl_2 was evaporated and replaced. CH_2Cl_2 was removed under reduced pressure and CC (SiO_2; 50% Et_2O in pentane) of the crude material afforded γ-lactone **5a** (290 mg, 75%). Colorless liquid. IR (ATR): 3060–2690 (C–H), 1795 (C=O), 1230, 1195, 1140 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 5.09–4.84 (*m*, H–C(5)); 2.76–2.18 (*m*, CH_2(3), CH_2(4)). ^{13}C-NMR (101 MHz, $CDCl_3$): 174.9 (*s*, C(2)); 117.3 (*tq*, J(C,F) = 33.1, 288, $(CF_2)_4CF_3$); 114.8, 111.1, 110.5, 108.6 (4m_c, $(CF_2)_4CF_3$); 74.3 (*ddd*, J(C,F) = 22.2, 33.4, C(5)); 26.3 (*t*, C(3)); 20.9 (*t*, C(4)). ^{19}F-NMR (376 MHz, $CDCl_3$): −80.7 (*t*, J = 9.9, $(CF_2)_4CF_3$); −120.9 to −128.4 (*m*, $(CF_2)_4CF_3$). HR-ESI-TOF-MS: 377.0005 ($[M+Na]^+$, $C_9H_5F_{11}NaO_2^+$; calc. 377.0012). Anal. calc. for $C_9H_5F_{11}O_2$ (354.12): C 30.53, H 1.42; found: C 30.49, H 1.30.

*4,5-Dihydro-5-(trifluoromethyl)furan-2(3*H*)-one* (**5b**). KBH_4 (105 mg, 1.95 mmol) was added at 0° to a soln. of **3b** (500 mg, 1.95 mmol) in MeOH (2 ml). After stirring for 1 h at 0° and 16 h at r.t., MeOH was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml), and $TsOH \cdot H_2O$ (175 mg, 0.920 mmol) was added. The mixture was heated under reflux for 48 h, in doing so every 12 h CH_2Cl_2 was evaporated and replaced. CH_2Cl_2 was removed under reduced pressure and CC (SiO_2; 50% Et_2O in pentane) of the crude material afforded **5b** (171 mg, 57%). Colorless liquid. IR (ATR): 3060–2690 (C–H), 1795 (C=O), 1280, 1145, 1120 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.77 (*ddq*, J = 4.5, 8.3, J(H,F) = 6.5, H–C(5)); 2.80–2.20 (*m*, CH_2(3), CH_2(4)). ^{13}C-NMR (101 MHz, $CDCl_3$): 175.1 (*s*, C(2)); 123.7 (*q*, J(C,F) = 280, CF_3–C(5)); 75.0 (*dq*, J(C,F) = 34.4, C(5)); 26.2 (*t*, C(3)); 21.2 (*tq*, J(C,F) = 1.6, C(4)). ^{19}F-NMR (376 MHz, $CDCl_3$): −79.4 (*d*, J(F,H) = 6.5, CF_3–C(5)). HR-ESI-TOF-MS: 155.0313 ($[M+H]^+$, $C_5H_6F_3O_2^+$; calc. 155.0320). Known compound: **5b** has been prepared previously; however, NMR and MS data were not reported [15][19].

*4,5-Dihydro-3,5-bis(trifluoromethyl)furan-2(3*H*)-one* (**5c**). KBH_4 (160 mg, 2.96 mmol) was added at 0° to a soln. of **3e** (1.02 g, 2.96 mmol) in MeOH (10 ml). After stirring for 10 min at 0°, the mixture was diluted with CH_2Cl_2 (30 ml) and washed with 1M HCl soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 ml), and $TsOH \cdot H_2O$ (175 mg, 0.920 mmol) was added. The mixture was heated under reflux for 72 h, in doing so every 12 h CH_2Cl_2 was evaporated and replaced. After removing CH_2Cl_2 under reduced pressure, Na_2CO_3 (160 mg) was added to the crude product. Bulb-to-bulb distillation (55–60°/0.1 mbar) afforded **5c** (414 mg, 63%, dr 59:41). Colorless liquid.

Data of the Major Diastereoisomer. IR (ATR): 3050–2680 (C–H), 1805 (C=O), 1290, 1260, 1165, 1120 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.80 (*qdd*, J(H,F) = 5.5, J = 7.6, 8.8, H–C(5)); 3.61 (*qd*, J(H,F) = 8.3, J = 10.6, H–C(3)); 2.82 (*ddd*, J = 7.6, 10.4, 13.9, 1 H of CH_2(4)); 2.48 (*ddd*, J = 8.8, 10.8, 13.9, 1 H of CH_2(4)). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.0 (*q*, J(C,F) = 3.0, C(2)); 123.2, 122.6 (2*q*, J(C,F) = 280, 279, CF_3–C(3), CF_3–C(5)); 73.1 (*dq*, J(C,F) = 36.2, C(5)); 42.9 (*dq*, J(C,F) = 31.2, C(3)); 22.7 (*t*, C(4)). ^{19}F-NMR (376 MHz, $CDCl_3$): −68.8 (m_c, CF_3–C(3)); −79.1 (*qd*, J = 1.1, J(F,H) = 5.5, CF_3–C(5)). HR-ESI-TOF-MS: 245.0011 ($[M+Na]^+$, $C_6H_4F_6NaO_2^+$; calc. 245.0013). Anal. calc. for $C_6H_4F_6O_2$ (222.09): C 32.45, H 1.82; found: C 32.07, H 2.26.

Data of the Minor Diastereoisomer. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.87 (m_c, H–C(5)); 3.64–3.47 (*m*, H–C(3)); 2.82, 2.71 (2m_c, CH_2(4)). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.5 (*q*, J(C,F) = 3.1, C(2)); 123.5, 123.3 (2*q*, J(C,F) = 278 each, CF_3–C(3), CF_3–C(5)); 73.4 (*dq*, J(C,F) = 35.0, C(5)); 43.9 (*dq*, J(C,F) = 31.5, C(3)); 23.1 (*t*, C(4)). ^{19}F-NMR (376 MHz, $CDCl_3$): −69.0 (*d*, J(F,H) = 8.5, CF_3–C(3)); −79.3 (*d*, J(F,H) = 6.4, CF_3–C(5)).

*4,5-Dihydro-3-(trifluoromethyl)furan-2(3*H*)-one* (**5d**). KBH_4 (200 mg, 3.70 mmol) was added at 0° to a soln. of **3f** (1.00 g, 3.70 mmol) in MeOH (10 ml). After stirring for 30 min at 0°, the mixture was diluted with CH_2Cl_2 (30 ml) and washed with 1M HCl soln. (20 ml). The org. layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 ml), and $TsOH \cdot H_2O$ (352 mg, 1.85 mmol) was added. The mixture was heated under reflux for 12 h, in doing so every 12 h CH_2Cl_2 was evaporated and replaced. CH_2Cl_2 was removed under reduced pressure and CC (SiO_2, 10–50% Et_2O in pentane) of the crude material afforded **5d** (320 mg, 56%). Colorless liquid. IR (ATR): 3070–2740 (C–H), 1780 (C=O), 1260, 1170, 1120 (C–F). ^{1}H-NMR (500 MHz, $CDCl_3$): 4.49–4.29 (*m*, CH_2(5)); 3.44–3.28 (*m*, H–C(3)); 2.63–2.44 (*m*, CH_2(4)). ^{13}C-NMR (101 MHz, $CDCl_3$): 169.8 (*q*, *J*(C,F) = 3.5, C(2)); 124.1 (*q*, *J*(C,F) = 278, CF_3–C(3)); 66.5 (*t*, C(5)); 44.0 (*dq*, *J*(C,F) = 30.4, C(3)); 23.5 (*tq*, *J*(C,F) = 2.0, C(4)). ^{19}F-NMR (470 MHz, $CDCl_3$): −68.6 (*s*, CF_3–C(3)). HR-ESI-TOF-MS: 177.0149 ($C_5H_5F_3NaO_2^+$; $[M+Na]^+$, calc. 177.0139). Anal. calc. for $C_5H_5F_3O_2$ (154.09): C 38.97, H 3.27; found: C 38.97, H 3.31.

*4,5-Dihydro-6-(undecafluoropentyl)pyridazin-3(2*H*)-one* (**6a**). A soln. of **3a** (500 mg, 1.10 mmol), $TsOH \cdot H_2O$ (42 mg, 0.20 mmol), and $NH_2NH_2 \cdot H_2O$ (55 mg, 1.1 mmol) in MeOH (5 ml) was heated under reflux for 24 h. All volatiles were removed under reduced pressure and the crude product was purified by CC (SiO_2; 30% AcOEt in hexane) to afford **6a** (288 mg, 72%). Colorless crystals. M.p. 110–112°. IR (ATR): 3770–3040 (N–H), 3040–2675 (C–H), 1655 (C=O), 1450, 1410 (C=N), 1240, 1205, 1110 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 10.48 (*s*, NH); 5.81 (*t*, *J* = 8.4, CH_2(4)); 5.63 (*t*, *J* = 8.4, CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.0 (*s*, C(3)); 140.8 (*t*, *J*(C,F) = 26.8, C(6)); 117.3 (*tq*, *J*(C,F) = 32.9, 289, $(CF_2)_4CF_3$); 112.8, 111.2, 110.6, 108.8 (4m_c, $(CF_2)_4CF_3$); 25.2 (*t*, C(4)); 20.4 (*t*, C(5)). ^{19}F-NMR (376 MHz, CD_3OD): −82.4 (*t*, *J* = 10.1, $(CF_2)_4CF_3$); −115.8 (*tt*, *J*(F,H) = 2.7, *J* = 13.5, 2 F of $(CF_2)_4CF_3$); −122.9 to −127.6 (*m*, 6 F of $(CF_2)_4CF_3$). HR-ESI-TOF-MS: 389.0093 ($[M+Na]^+$, $C_9H_5F_{11}N_2NaO^+$; calc. 389.0124). Anal. calc. for $C_9H_5F_{11}N_2O$ (366.13): C 29.52, H 1.38, N 7.65; found: C 29.50, H 1.60, N 7.69.

*4,5-Dihydro-6-(trifluoromethyl)pyridazin-3(2*H*)-one* (**6b**). A soln. of **3b** (500 mg, 1.95 mmol), $TsOH \cdot H_2O$ (74 mg, 0.390 mmol), and $NH_2NH_2 \cdot H_2O$ (98 mg, 2.00 mmol) in MeOH (5 ml) was heated under reflux for 48 h. All volatiles were removed under reduced pressure, and the crude product was purified by CC (neutral Al_2O_3, 20% AcOEt in hexane) to give **6b** (282 mg, 87%). Colorless crystals. M.p. 89–91°.^{1}H-NMR (400 MHz, $CDCl_3$): 9.23 (*s*, NH); 2.76, 2.62 (2*t*, *J* = 8.3, CH_2(4), CH_2(5)). Known compound: NMR data are consistent with reported values; m.p. 75–77° [15].

*4,5-Dihydro-6-(pentafluorophenyl)pyridazin-3(2*H*)-one* (**6c**). A soln. of **3c** (500 mg, 1.41 mmol), $TsOH \cdot H_2O$ (1.34 g, 7.06 mmol), and $NH_2NH_2 \cdot H_2O$ (353 mg, 7.06 mmol) in toluene (30 ml) was heated under reflux for 60 h. All volatiles were removed under reduced pressure, and the crude product was purified by flash chromatography (FC; SiO_2; 40% AcOEt in hexane) to afford **6c** (278 mg, 75%). Colorless crystals. M.p. 158–160°. IR (ATR): 3730–3170 (N–H), 3170–2740 (C–H), 1690 (C=O), 1525, 1495 (C=N), 1340, 1295, 1215, 1130 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 9.72 (*s*, NH); 2.86, 2.64 (2*t*, *J* = 8.2, CH_2(4), CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.2 (*s*, C(3)); 141.7 (*s*, C(6)); 144.6, 141.7, 137.9, 112.3 (*s*, 3*d*, Ar); 26.2 (*t*, C(4)); 26.0 (*m*, C(5)). ^{19}F-NMR (376 MHz, $CDCl_3$): −141.2 (m_c, 2 F); −152.2 (m_c, 1 F); −161.0 (m_c, 2 F). HR-ESI-TOF-MS: 265.0387 ($[M+H]^+$, $C_{10}H_6F_5N_2O^+$; calc. 265.0400). Anal. calc. for $C_{10}H_5F_5N_2O$ (264.15): C 45.47, H 1.91, N 10.61; found: C 45.48, H 1.95, N 10.61.

*4,5-Dihydro-4,6-bis(trifluoromethyl)pyridazin-3(2*H*)-one* (**6d**). A soln. of **3e** (500 mg, 1.48 mmol), $TsOH \cdot H_2O$ (562 mg, 2.96 mmol), and $NH_2NH_2 \cdot H_2O$ (148 mg, 2.96 mmol) in toluene (7 ml) was heated under reflux for 60 h. All volatiles were removed under reduced pressure, and the crude product was purified by FC (SiO_2; AcOEt) to give **6d** (310 mg, 90%). Colorless crystals. M.p. 72–74°. IR (ATR): 3620–3055 (N–H), 3055–2750 (C–H), 1660 (C=O), 1480, 1440 (C=N), 1300, 1250, 1200, 1180, 1140, 1120 (C–F). ^{1}H-NMR (500 MHz, $CDCl_3$): 9.11 (*s*, NH); 3.40 (*X* of *ABX*, H–C(4)); 3.16–2.87 (*AB* of *ABX*, *J*(*A*,*B*) = 18.4, CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 160.3 (*q*, *J*(C,F) = 2.2, C(3)); 139.7 (*q*, *J*(C,F) = 37.3, C(6)); 123.9, 112.0 (2*q*, *J*(C,F) = 280, 273, CF_3–C(6), CF_3–C(3)); 40.3 (*dq*, *J*(C,F) = 28.9, C(4)); 20.5 (*tq*, *J*(C,F) = 2.5, C(5)). ^{19}F-NMR (471 MHz, $CDCl_3$): −68.9 (*d*, *J*(F,H) = 8.4, CF_3–C(4)); −71.3 (*s*, CF_3–C(6)). HR-ESI-TOF-MS: 257.0136 ($[M+Na]^+$, $C_6H_4F_6N_2NaO^+$; calc. 257.0126). Anal. calc. for $C_6H_4F_6N_2O$ (234.10): C 30.78, H 1.72, N 11.97; found: C 31.05, H 1.96, N 12.37.

*4,5-Dihydro-4-(trifluoromethyl)pyridazin-3(2*H*)-one* (**6e**). A soln. of **3f** (500 mg, 1.85 mmol), $TsOH \cdot H_2O$ (70 mg, 0.37 mmol), and $NH_2NH_2 \cdot H_2O$ (93 mg, 1.85 mmol) in MeOH (5 ml) was heated under reflux for 48 h. All volatiles were removed under reduced pressure, and the crude product was purified by FC (neutral Al_2O_3; 20% AcOEt in hexane) to furnish **6e** (127 mg, 41%). Colorless crystals. M.p. 82–84°. IR (ATR): 3745–3035 (N–H), 3035–2710 (C–H), 1670 (C=O), 1430, 1400 (C=N), 1310, 1260, 1190, 1155, 1120 (C–F). ^{1}H-NMR (500 MHz, $CDCl_3$): 9.51 (*s*, NH); 7.19 (*s*, H–C(6)); 3.36–3.14 (*m*, H–C(4)); 2.91–2.62 (*m*, CH_2(5)). ^{13}C-NMR (126 MHz, $CDCl_3$): 160.5 (*q*, *J*(C,F) = 1.9, C(3)); 142.7 (*d*, C(6)); 124.3 (*q*, *J*(C,F) = 280, CF_3); 40.6 (*dq*, *J*(C,F) = 28.4, C(4)); 22.9 (*tq*, *J*(C,F) = 2.7, C(5)). ^{19}F-NMR (471 MHz, $CDCl_3$): −68.7 (*d*, *J*(F,H) = 8.2, CF_3). HR-ESI-TOF-MS: 189.0258 ($[M + Na]^+$, $C_5H_5F_3N_2NaO^+$; calc. 189.0246). Anal. calc. for $C_5H_5F_3N_2O$ (166.10): C 36.15, H 3.03, N 16.87; found: C 36.24, H 3.04, N 16.87. The ^{1}H-NMR data are consistent with reported values; however, additional anal. data were not reported [20].

*4,5-Dihydro-2-phenyl-6-(undecafluoropentyl)pyridazin-3(2*H*)-one* (**7a**). A soln. of **3a** (200 mg, 0.438 mmol), $TsOH \cdot H_2O$ (83 mg, 0.440 mmol), and $PhNHNH_2$ (47 mg, 0.440 mmol) in toluene (15 ml) was stirred at 90° for 60 h. A colorless precipitate was filtered off, and all volatiles were removed under reduced pressure. The crude product was purified by CC (SiO_2; 15% AcOEt in hexane) to afford **7a** (136 mg, 70%). Yellow wax. IR (ATR): 3765–3185 (C=C–H), 3185–2725 (C–H), 1715 (C=O), 1495, 1430 (C=N), 1375, 1360, 1305, 1230, 1195, 1140, 1105 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.52–7.25 (*m*, 5 arom. H); 2.96–2.74 (*m*, CH_2(4), CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 164.3 (*s*, C(2)); 141.7 (*t*, *J*(C,F) = 27.2, C(6)); 140.2, 128.8, 127.5, 124.7 (*s*, 3*d*, Ph); 117.4 (*tq*, *J*(C,F) = 33.1, 288, $(CF_2)_4CF_3$); 115.3–107.5 (4*m*, $(CF_2)_4CF_3$); 27.2 (*t*, C(4)); 21.3 (*t*, C(5)). ^{19}F-NMR (376 MHz, $CDCl_3$): −80.6 (*tt*, *J* = 2.5, 9.9, $(CF_2)_4CF_3$); −114.7 (*tt*, *J* = 3.1, 13.6, 2 F of $(CF_2)_4CF_3$); −126.4 to −121.3 (3*m*, 6 F of $(CF_2)_4CF_3$). HR-ESI-TOF-MS: 465.0443 ($[M + Na]^+$, $C_{15}H_9F_{11}N_2NaO^+$; calc. 465.0437). Anal. calc. for $C_{15}H_9F_{11}N_2O$ (442.23): C 40.74, H 2.05, N 6.33; found: C 40.62, H 2.22, N 6.34.

*4,5-Dihydro-2-phenyl-6-(trifluoromethyl)pyridazin-3(2*H*)-one* (**7b**). A soln. of **3b** (200 mg, 0.780 mmol), $TsOH \cdot H_2O$ (148 mg, 0.780 mmol), and $PhNHNH_2$ (84 mg, 0.78 mmol) in toluene (15 ml) was stirred at 90° for 60 h. A colorless precipitate was filtered off, and all volatiles were removed under reduced pressure. The crude product was purified by CC (SiO_2, 15% AcOEt in hexane) to give **7b** (157 mg, 83%). Yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.51–7.36 (*m*, 4 arom. H); 7.33–7.27 (*m*, 1 arom. H); 2.93–2.73 (*m*, CH_2(4), CH_2(5)). The compound was reported as a chocolate brown solid, and NMR data are consistent with reported values [15].

*4,5-Dihydro-6-(pentafluorophenyl)-2-phenylpyridazin-3(2*H*)-one* (**7c**). A soln. of **3c** (500 mg, 1.41 mmol), $TsOH \cdot H_2O$ (1.34 g, 7.06 mmol), and $PhNHNH_2$ (763 mg, 7.06 mmol) in toluene (15 ml) was stirred at 90° for 60 h. A colorless precipitate was filtered off, and all volatiles were removed under reduced pressure. The crude product was purified by CC (SiO_2; 30% AcOEt in hexane) to furnish **7c** (430 mg, 90%). Colorless crystals. M.p. 164–166°. IR (ATR): 3725–3125 (C=C–H), 3125–2745 (C–H), 1690 (C=O), 1525, 1490 (C=N), 1330, 1295, 1230, 1150, 1120 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.53–7.23 (*m*, 5 arom. H); 3.07–2.96, 2.93–2.81 (2*m*, CH_2(4), CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 164.6 (*s*, C(3)); 142.6 (m_c, C(6)); 140.5, 128.7, 127.1, 124.8 (*s*, 3*d*, Ph); 144.6, 141.7, 137.9, 112.3 (4m_c, Ar); 27.7 (*t*, C(4)); 26.5 (m_c, C(5)). ^{19}F-NMR (376 MHz, $CDCl_3$): −140.9 (m_c, 2 F); −151.7 (m_c, 1 F); −160.6 (m_c, 2 F). HR-ESI-TOF-MS: 363.0551 ($[M + Na]^+$, $C_{16}H_9F_5N_2NaO^+$; calc. 363.0527). Anal. calc. for $C_{16}H_9F_5N_2O$ (340.25): C 56.48, H 2.67, N 8.23; found: C 56.50, H 2.71, N 8.47.

*4,5-Dihydro-2-phenyl-4,6-bis(trifluoromethyl)pyridazin-3(2*H*)-one* (**7d**). A soln. of **3e** (500 mg, 1.48 mmol), $TsOH \cdot H_2O$ (287 mg, 1.48 mmol), and $PhNHNH_2$ (160 mg, 1.48 mmol) in toluene (50 ml) was stirred at 90° for 60 h. A colorless precipitate was filtered off, and all volatiles were removed under reduced pressure. The crude product was purified by CC (SiO_2; 20% AcOEt in hexane) to yield **7d** (404 mg, 88%). Colorless crystals. M.p. 88–90°. IR (ATR): 3735–3150 (C=C–H), 3050–2785 (C–H), 1710 (C=O), 1495, 1430 (C=N), 1290, 1260, 1210, 1170, 1120 (C–F). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.53–7.31 (*m*, 5 arom. H); 3.56 (*m*, H–C(4)); 3.23–3.06 (*m*, CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 157.8 (*q*, *J*(C,F) = 2.1, C(3)); 139.2 (*q*, *J*(C,F) = 37.3, C(6)); 139.6, 129.0, 128.2, 125.0 (*s*, 3*d*, Ph); 124.0, 119.9 (2*q*, *J*(C,F) = 281, 274, CF_3–C(6), CF_3–C(4)); 41.5 (*dq*, *J*(C,F) = 28.6, C(4)); 21.1 (*t*, C(5)). ^{19}F-NMR (471 MHz, $CDCl_3$): −68.9 (*d*, *J*(F,H) = 8.2, CF_3–C(6)); −71.0 (*s*, CF_3–C(4)). HR-ESI-TOF-MS:

333.0437 ([M + Na]$^+$, $C_{12}H_8F_6N_2NaO^+$; calc. 333.0439). Anal. calc. for $C_{12}H_8F_6N_2O$ (310.20): C 46.46, H 2.60, N 9.03; found: C 46.37, H 2.53, N 8.96.

*4,5-Dihydro-2-phenyl-4-(trifluoromethyl)pyridazin-3(2*H*)-one* (**7e**). A soln. of **3f** (1.00 g, 3.70 mmol), $TsOH \cdot H_2O$ (704 mg, 3.70 mmol), and $PhNHNH_2$ (400 mg, 3.70 mmol) in toluene (50 ml) was stirred at 90° for 60 h. A colorless precipitate was filtered off, and all volatiles were removed under reduced pressure. The crude product was purified by CC (SiO_2; 20% AcOEt in hexane) to afford **7e** (222 mg, 25%). Orange oil. IR (ATR): 3735–3160 (C=C–H), 3160–2735 (C–H), 1690 (C=O), 1495, 1430 (C=N), 1350, 1290, 1260, 1190, 1140 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.50–7.00 (*m*, H–C(6), 5 arom. H); 3.47–2.94 (*m*, H–C(4), CH_2(5)). ^{13}C-NMR (101 MHz, $CDCl_3$): 158.4 (*q*, *J*(C,F) = 2.1, C(3)); 140.3 (*d*, C(6)); 124.5 (*q*, *J*(C,F) = 280, *C*F_3–C(4)); 143.1, 128.8, 127.5, 125.1 (*s*, 3*d*, Ph); 41.8 (*dq*, *J*(C,F) = 28.2, C(4)); 23.5 (*tq*, *J*(C,F) = 2.5, C(5)). ^{19}F-NMR (376 MHz, $CDCl_3$): −68.5 (*d*, *J*(F,H) = 8.7, CF_3–C(4)). HR-ESI-TOF-MS: 265.0568 ([M + Na]$^+$, $C_{11}H_9F_3N_2NaO^+$; calc. 265.0565). Anal. calc. for $C_{11}H_9F_3N_2O$ (242.20): C 54.55, H 3.75, N 11.57; found: C 54.52, H 3.82, N 11.40.

*Ethyl 3,3,3-Trifluoro-2-(1*H*-indol-3-yl)propanoate* (**10**). During the preparation of **7e**, **10** was isolated (207 mg, 21%). Brown solid. M.p. 82–84°. IR (ATR): 3645–3150 (N–H), 3150–2780 (C–H), 1745, 1720 (C=O), 1340, 1265, 1240, 1150, 1110 (C–F). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.31 (*s*, NH); 7.67 (*d*, *J* = 7.8, H–C(2′)); 7.44–7.15 (*m*, 4 arom. H); 4.67 (*q*, *J* = 8.5, H–C(2)); 4.25, 4.22 (*AB* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, *J*(*A*,*B*) = 10.8, COOC*H*$_2$Me); 1.26 (*X* of *ABX*$_3$, *J*(*A*,*X*) = *J*(*B*,*X*) = 7.1, COOCH$_2$*Me*). ^{13}C-NMR (101 MHz, $CDCl_3$): 167.2 (*q*, *J*(C,F) = 2.5, C(1)); 124.4 (*q*, *J*(C,F) = 280, CF_3); 135.9, 126.5, 124.9, 122.8, 120.5, 118.7 (2*s*, 4*d*, Ph); 111.7 (*d*, C(2′)); 104.0 (*q*, *J*(C,F) = 2.0, C(3′)); 62.2 (*t*, COO*C*H$_2$Me); 47.7 (*dq*, *J*(C,F) = 30.1, C(2)); 13.9 (*q*, COOCH$_2$*Me*). ^{19}F-NMR (376 MHz, $CDCl_3$): −67.9 (*d*, *J*(F,H) = 8.3, CF_3). HR-ESI-TOF-MS: 294.0720 ([M + Na]$^+$, $C_{13}H_{14}F_3NNaO_2^+$; calc. 294.0718).

We gratefully acknowledge support by the *Deutsche Forschungsgemeinschaft* (GRK 1582 '*Fluorine as Key Element*') and *Bayer HealthCare*. Dr. *Reinhold Zimmer* is thanked for his assistance during preparation of this manuscript, and *Anette Semisch* for preliminary experiments dealing with the cyclopropanations employing ethyl 3,3,3-trifluoro-2-diazopropanoate.

REFERENCES

[1] D. Seebach, *Angew. Chem.* **1979**, *91*, 259; D. Seebach, *Angew. Chem., Int. Ed.* **1979**, *18*, 239; D. Wendisch, 'Carbocyclic Three-Membered Ring Compounds', in 'Methods in Organic Chemistry (Houben-Weyl)', Vol. 4/3, 4th edn., Ed. E. Müller, Thieme, Stuttgart, 1971, p. 879; D. Seebach, S. Beckmann, H. Geiger, 'Isocyclic Four-Membered Ring Compounds', in 'Methods in Organic Chemistry (Houben-Weyl)', Vol. 4/4, 4th edn., Ed. E. Müller, Thieme, 1971, p. 567; S. Danishefsky, *Acc. Chem. Res.* **1979**, *12*, 66; H.-U. Reissig, 'The Chemistry of the Cyclopropyl Group', in 'Organic Synthesis via Cyclopropanes – Principles and Applications', Ed. Z. Rappoport, John Wiley and Sons, London, 1987, pp. 375–443; H. N. C. Wong, M. Y. Hon, C. W. Tse, Y. C. Yip, J. Tanko, T. Hudlicky, *Chem. Rev.* **1989**, *89*, 165; A. de Meijere, 'Carbocyclic Three- and Four-Membered Ring Compounds', in 'Methods in Organic Chemistry (Houben-Weyl)', Vol. E17a–d, Thieme, Stuttgart, 1997; A. de Meijere, S. I. Kozhushkov, 'Product Class 2: Cyclopropanes', in 'Alkanes', 'Science of Synthesis', Vol. 48, Ed. I. Fleming, Thieme, Stuttgart, 2009, pp. 477–613; R. Kostikov, M. S. Baird, in 'Product Class 3: Cyclobutanes', in 'Alkanes', 'Science of Synthesis', Vol. 48, Ed. I. Fleming, Thieme, Stuttgart, 2009, pp. 615–646.

[2] E. Wenkert, *Acc. Chem. Res.* **1980**, *13*, 27.

[3] H.-U. Reissig, E. Hirsch, *Angew. Chem.* **1980**, *92*, 839; H.-U. Reissig, E. Hirsch, *Angew. Chem., Int. Ed.* **1980**, *19*, 813.

[4] a) H.-U. Reissig, *Top. Curr. Chem.* **1988**, *144*, 73; b) H.-U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151; c) F. Gnad, O. Reiser, *Chem. Rev.* **2003**, *103*, 1603; d) M. Yu, B. L. Pagenkopf, *Tetrahedron* **2005**, *61*, 321; e) F. De Simone, J. Waser, *Synthesis* **2009**, 3353; f) T. F. Schneider, D. B. Werz, *Org. Lett.* **2011**, *13*, 1848; g) M. Y. Mel'nikov, E. M. Budynina, O. A. Ivanova, I. V. Trushkov, *Mendeleev Commun.* **2011**, *21*, 293.

[5] C. A. Carson, M. A. Kerr, *Chem. Soc. Rev.* **2009**, *38*, 3051; M. J. Campbell, J. S. Johnson, A. T. Parsons, P. D. Pohlhaus, S. D. Sanders, *J. Org. Chem.* **2010**, *75*, 6317; T. F. Schneider, J. Kaschel, S. I. Awan, B. Dittrich, D. B. Werz, *Chem. – Eur. J.* **2010**, *16*, 11276; T. P. Lebold, M. A. Kerr, *Pure Appl. Chem.* **2010**, *82*, 1797.

[6] a) O. O. Grygorenko, O. S. Artamonov, I. V. Komarov, P. K. Mykhailiuk, *Tetrahedron* **2011**, *67*, 803; b) B. Morandi, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 950; c) B. Morandi, E. M. Carreira, *Angew. Chem., Int. Ed.* **2010**, *49*, 938; d) B. Morandi, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 4390; e) B. Morandi, E. M. Carreira, *Angew. Chem., Int. Ed.* **2010**, *49*, 4294; f) B. Morandi, J. Cheang, E. M. Carreira, *Org. Lett.* **2011**, *13*, 3080; g) V. R. Petrov, W. Marshall, *J. Fluorine Chem.* **2012**, *133*, 61.

[7] T. Hiyama, 'Organofluorine Compounds: Chemistry and Applications', Springer, Berlin Heidelberg, 2000; P. Kirsch, 'Modern Fluoroorganic Chemistry', Wiley-VCH, Weinheim, 2005; K. Müller, C. Fäh, F. Diederich, *Science* **2007**, *317*, 1881; D. O' Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308; T. Yamazaki, T. Taguchi, I. Ojima, in 'Fluorine in Medicinal Chemistry and Chemical Biology', Ed. I. Ojima, Wiley-Blackwell, Chichester, 2009, pp. 3 – 46; A. A. Gakh, L. K. Kirk, 'Fluorinated Heterocycles', American Chemical Society, Washington, 2009; V. A. Petrov, 'Fluorinated Heterocyclic Compounds: Synthesis, Chemistry, and Applications', John Wiley & Sons, Hoboken, 2009.

[8] S. Gil, M. Parra, P. Rodriguez, J. Segura, *Mini-Rev. Org. Chem.* **2009**, *6*, 345; M. Seitz, O. Reiser, *Curr. Opin. Chem. Biol.* **2005**, *9*, 285; E. M. Maier, in 'Three Carbon-Heteroatom Bonds: Esters and Lactones; Peroxyacids and R(CO)OX Compounds; R(CO)X, X = S, Se, Te', 'Science of Synthesis, Houben-Weyl Methods of Molecular Transformations', Eds. J. S. Panek, E. N. Jacobsen, Thieme, Stuttgart, 2006, Vol. 20b, pp. 1421 – 1551.

[9] a) W. Adam, J.-C. Liu, O. Rodriguez, *J. Org. Chem.* **1973**, *38*, 2269; b) T. Kitazume, N. Ishikawa, *Chem. Lett.* **1984**, *13*, 1815; c) D. Seebach, P. Renaud, W. B. Schweizer, M. F. Züger, M.-J. Brienne, *Helv. Chim. Acta* **1984**, *67*, 1843; d) D. Seebach, P. Renaud, *Helv. Chim. Acta* **1985**, *68*, 2342; e) M. Acs, C. von dem Bussche, D. Seebach, *Chimia* **1990**, *44*, 90; f) C. von dem Bussche-Hünnefeld, C. Cescato, D. Seebach, *Chem. Ber.* **1992**, *125*, 2795; g) M. Gautschi, W. B. Schweizer, D. Seebach, *Chem. Ber.* **1994**, *127*, 565; h) A. R. Sting, D. Seebach, *Tetrahedron* **1996**, *52*, 279; i) H. Angert, R. Czerwonka, H.-U. Reissig, *Liebigs Ann.* **1997**, 2215; j) F.-L. Qing, Z.-X. Jiang, *Tetrahedron Lett.* **2001**, *42*, 5933.

[10] M. Tišler, B. Stanovnik, *Adv. Heterocycl. Chem.* **1968**, *9*, 211; F. R. Rittig, R. Becker, H. Bleiholder, F. Feichtmayr, E. Haedicke, J. B. S. John, *Pestic. Sci.* **1983**, *14*, 299; P. Máatyus, *J. Heterocycl. Chem.* **1998**, *35*, 1075; S.-G. Lee, J.-J. Kim, H.-K. Kim, D.-H. Kweon, Y.-J. Kang, S.-D. Cho, S.-K. Kim, Y.-J. Yoon, *Curr. Org. Chem.* **2004**, *8*, 1463.

[11] E. Fischer, *Justus Liebigs Ann. Chem.* **1886**, *236*, 126.

[12] E. L. Grimm, H.-U. Reissig, *J. Org. Chem.* **1985**, *50*, 242.

[13] I. Reichelt, H.-U. Reissig, *Synthesis* **1984**, 786.

[14] E. L. Grimm, R. Zschiesche, H.-U. Reissig, *J. Org. Chem.* **1985**, *50*, 5543; A. Ullmann, J. Schnaubelt, H.-U. Reissig, *Synthesis* **1998**, 1052; R. Zimmer, A. Ziemer, M. Gruner, I. Brüdgam, H. Hartl, H.-U. Reissig, *Synthesis* **2001**, 1649; P. K. Patra, H.-U. Reissig, *Eur. J. Org. Chem.* **2001**, 4195; I. Veljkovic, R. Zimmer, H.-U. Reissig, I. Brüdgam, H. Hartl, *Synthesis* **2006**, 2677; H. Özbek, I. S. Veljkovic, H.-U. Reissig, *Synlett* **2008**, 3145.

[15] W. Wan, J. Hou, H. Jiang, Y. Wang, S. Zhu, H. Deng, J. Hao, *Tetrahedron* **2009**, *65*, 4212.

[16] H. A. Laub, D. Gladow, H.-U. Reissig, H. Mayr, *Org. Lett.* **2012**, *14*, 3990.

[17] E. B. Womack, A. B. Nelson, *Org. Synth., Coll. Vol.* **1955**, *3*, 392; E. B. Womack, A. B. Nelson, *Org. Synth.* **1944**, *24*, 56.

[18] G. Shi, Y. Xu, *J. Chem. Soc., Chem. Commun.* **1989**, 607.

[19] R. H. Groth, *J. Org. Chem.* **1959**, *24*, 1709; M. Hanack, H. Meyer, *Justus Liebigs Ann. Chem.* **1968**, *720*, 81.

[20] R. E. Brown, F. Burkamp, V. A. Doughty, S. R. Fletcher, G. J. Hollingworth, B. A. Jones, T. J. Sparey, WO2004074290A1, 2004.

Received August 3, 2012