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Synthesis of 1-Alkyl-2-(trifluoromethyl)azetidines and Their Regiospecific Ring Opening toward Diverse α-(Trifluoromethyl)Amines via Intermediate Azetidinium Salts

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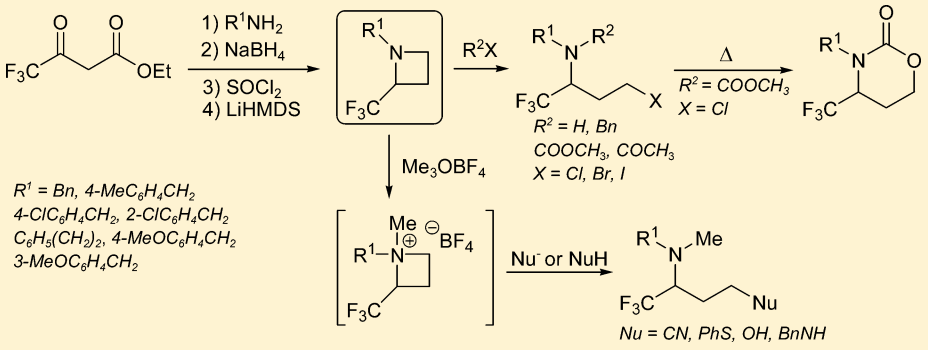
Supporting Information



ABSTRACT: A convenient approach toward nonactivated 1-alkyl-2-(trifluoromethyl)azetidines as a new class of constrained azaheterocycles was developed starting from ethyl 4,4,4-trifluoroacetoacetate via imination, hydride reduction, chlorination, and base-induced ring closure. Furthermore, the reactivity profile of these 2-CF_3-azetidines was assessed by means of quaternization and subsequent regiospecific ring opening at C4 of the azetidinium intermediates by oxygen, nitrogen, carbon, sulfur, and halogen nucleophiles, pointing to a clear difference in reactivity compared to azetidines bearing other types of electron-withdrawing groups at C2.

INTRODUCTION

Because of the unique chemical and physical properties of fluorine,[1] the interest in fluorinated compounds in organic and pharmaceutical chemistry has increased considerably over the years.[2] In that respect, particular attention has been paid to the introduction of a trifluoromethyl group, leading to numerous CF_3-containing drugs and drug-candidates[2c] such as fluoxetine (antidepressant),[3] celecoxib (anti-inflammatory activity),[4] and efavirenz (antiviral activity).[4] In general, fluorine-substituted amines are of high importance for the design of new drugs with a broad spectrum of biological activities.[5] The selective introduction of fluorine, for example, as a CF_3 group, can strongly alter the biological and pharmacological properties such as pK_a, lipophilicity, acute toxicity, and metabolic stability of bioactive compounds.[6] The synthesis of CF_3-containing structures can be accomplished by either the selective introduction of a CF_3 group using trifluoromethylating reagents or by the use of CF_3-containing building blocks. Trifluoromethylation in a late stage of the synthesis, however, often appears to be problematic,[7] and a building block approach can provide an efficient alternative.

Azetidines are an important class of four-membered azaheterocycles with a high ring strain energy (25.2 kcal/mol),[8] making them suitable precursors for a variety of functionalized amine derivatives.[9] Nevertheless, the chemistry of azetidines has not been explored as intensively as that of their lower homologues, aziridines, which already demonstrated their broad applicability as versatile building blocks through a variety of ring-opening and ring-transformation reactions.[10]

A potentially interesting subclass of these four-membered azaheterocycles involves the group of 2-(trifluoromethyl)-azetidines. The chemistry of 2-CF_3-azetidines comprises an unexplored field of research, both in terms of their synthesis and their reactivity. No reports regarding nonactivated 2-(trifluoromethyl)azetidines, i.e., 2-CF_3-azetidines bearing an electron-donating substituent at nitrogen, are available in the literature, and only one approach toward activated 4-trifluoromethyl-2-alkyl- and -2,3-dialkylazetidines has been described, involving Wittig reaction of a 4-CF_3-β-lactam followed by alkylation and hydrogenation.[11] Two other

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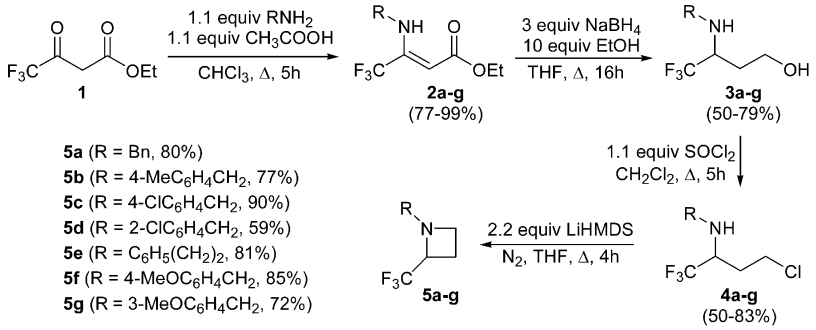
Scheme 1



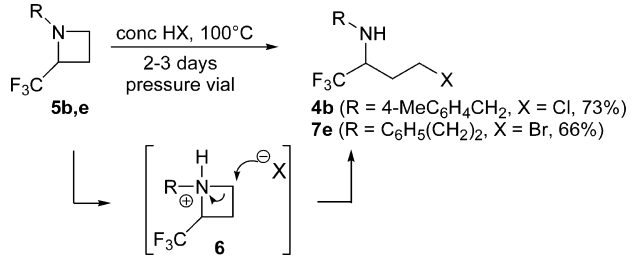
approaches toward (rather elusive) activated 2-CF_3-azetidines are based on either a cycloaddition reaction of a perfluorinated imine and an alkene to give 2,2-bis-(trifluoromethyl)-azetidines[12] or a cycloaddition reaction of a CF_3-imine and an alkene to furnish polysubstituted azetidines,[13] but both strategies do not provide selective and efficient entries into the class of 2-(trifluoromethyl)azetidines, as these compounds were obtained as side products or even only speculatively characterized by mass spectrometry. Moreover, no reports of monosubstituted 2-(trifluoromethyl)azetidines are available to date, except for two structures accommodating a 2-CF_3-azetidine unit as part of a large framework claimed in the patent literature.[14] In addition to the challenge to develop a convenient synthetic approach toward 2-(trifluoromethyl)-azetidines, the study of the unexplored reactivity of these synthons might provide new insights and opportunities from both a fundamental and an applied viewpoint. Therefore, in this paper, a straightforward synthetic method toward novel 1-alkyl-2-(trifluoromethyl)azetidines is evaluated starting from commercially available ethyl 4,4,4-trifluoroacetoacetate. Furthermore, important information concerning the reactivity of these novel small-ring azaheterocycles toward a variety of nucleophiles is acquired after initial quaternization of the azetidine moiety to the corresponding azetidinium intermediates, demonstrating a regiospecific C4 ring opening of 2-CF_3-azetidines as opposed to the behavior of azetidines bearing other types of electron-withdrawing groups at C2.

RESULTS AND DISCUSSION

At first, enamines **2a−g** (77−99%) were prepared through condensation of ethyl 4,4,4-trifluoroacetoacetate **1** upon treatment with a primary amine in the presence of acetic acid.[15] Reduction of these enamines **2a−g** using sodium borohydride (3 equiv) in EtOH (10 equiv) and THF as the solvent afforded the corresponding 3-alkylamino-4,4,4-trifluorobutan-1-ols **3a−g** in 50−79% yield (Scheme 1), and treatment of these γ-amino alcohols **3a−g** with thionyl chloride in dichloromethane under reflux for 5 h resulted in novel *N*-alkyl-4-chloro-1,1,1-trifluorobutan-2-amines **4a−g** (50−83%, Scheme 1). γ-Chloroamines **4a−g** were treated with two times 1.1 equiv of LiHMDS in THF under reflux for 4 h, affording 1-alkyl-2-(trifluoromethyl)azetidines **5a−g** in good to excellent yields (59−90%, Scheme 1).[16] The use of this strong base was required because of the reduced nucleophilicity of the nitrogen atom, caused by the strong electron-withdrawing effect of the trifluoromethyl substituent in α-position. It should be noted that the above-described method comprises a new and efficient approach for the construction of the α-CF_3-azetidine framework as a suitable template for further elaboration.

In the next part, the reactivity of these novel azetidines **5** was investigated toward ring-opening reactions with different nucleophiles in order to assess the influence of the strong electron-withdrawing trifluoromethyl group on the aptitude and selectivity of these transformations. Because of the presence of an electron-donating substituent at nitrogen, activation of the azetidine moiety to the corresponding azetidinium ion by means of protonation, alkylation, or acylation was required prior to ring opening. In a first approach, 2-CF_3-azetidines **5b,e** were dissolved in hydrochloric acid (37% solution in water) or hydrobromic acid (48% solution in water), which, after heating at 100 °C for 2−3 days, yielded 4-chloro-*N*-(4-methylbenzyl)-1,1,1-trifluorobutan-2-amine **4b** and 4-bromo-*N*-phenylethyl-1,1,1-trifluorobutan-2-amine **7e**, respectively (Scheme 2). The

Scheme 2



reaction occurred regiospecifically by nucleophilic attack of the halide (Cl^-, Br^-) at the less-hindered position of the intermediate azetidinium ions **6**. This observation was in accordance with previously reported results on the acid-induced ring opening of their smaller counterparts, 2-CF_3-aziridines.[16]

A regiospecific ring opening of 2-CF_3-azetidines **5b,e** was also accomplished using 1.5 equiv of acetyl chloride in dry CH_2Cl_2 at reflux for 4 h, resulting in the corresponding *N*-alkyl-*N*-[3-chloro-2-(trifluoromethyl)propyl]acetamides **9b,e** (68−85%, Scheme 3). Furthermore, in analogy with the ring opening of 1-alkyl-2-cyano- and 2-acyl-1-alkylazetidines with chloroformates,[17] 2-CF_3-substituted azetidines **5a,b,e** were treated with 3 equiv of methyl chloroformate in dry acetonitrile under reflux for 5 h, yielding methyl *N*-alkyl-*N*-[3-chloro-1-(trifluoromethyl)propyl]carbamates **10a,b,e** (63−70%, Scheme 3). It is noteworthy that the ring opening of the azetidinium ions **8** by chloride proceeds regiospecifically at the C4 position, whereas the ring opening of the azetidinium ions of 1-phenylethyl-2-acylazetidines by chloride is known to occur at the more electrophilic C2 position.[17] This difference could be explained by the steric hindrance and the electronic effect exerted by the trifluoromethyl group, rendering the less-electrophilic C4 position more accessible toward nucleophilic

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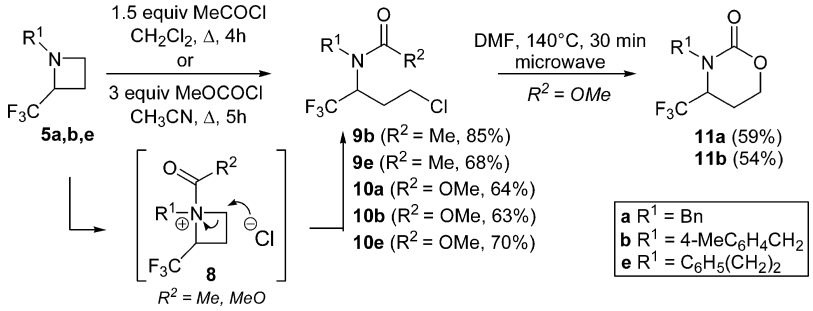
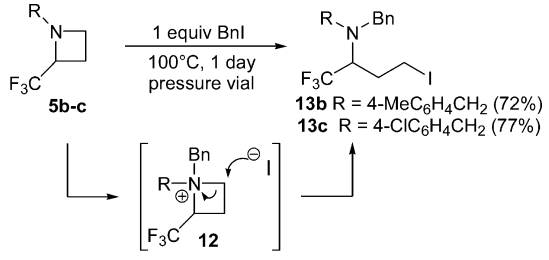
Scheme 3



attack. The corresponding methyl carbamates **10** showed to be valuable precursors for the synthesis of interesting CF_3-substituted 1,3-oxazinan-2-ones **11a,b**. When the latter methyl carbamates **10a,b** were heated in DMF under reflux, full conversion toward the corresponding 1,3-oxazinan-2-ones **11a,b** was achieved upon prolonged heating (>6 days). However, this drawback was easily overcome by the use of microwave irradiation, resulting in the corresponding 3-alkyl-4-trifluoromethyl-1,3-oxazinan-2-ones **11a,b** after heating of methyl carbamates **10a,b** at 140 °C (200 W) for 30 min (Scheme 3). Many drugs contain the 1,3-oxazinan-2-one substructure, and their derivatives exhibit important biological activities such as antibacterial,[18] anti-inflammatory,[19] and antitumor activities.[20]

In the next part, activation of the azetidine moiety was effected by alkylation of the nitrogen atom to produce quaternary ammonium salts. Treatment of 2-CF_3-azetidines **5b,c** with 1 equiv of benzyl iodide at 100 °C for 1 day in a pressure vial resulted in the corresponding γ-iodoamines **13b,c** in 72−77% yield through regioselective ring opening of azetidinium intermediates **12** at the C4 position (Scheme 4).

Scheme 4

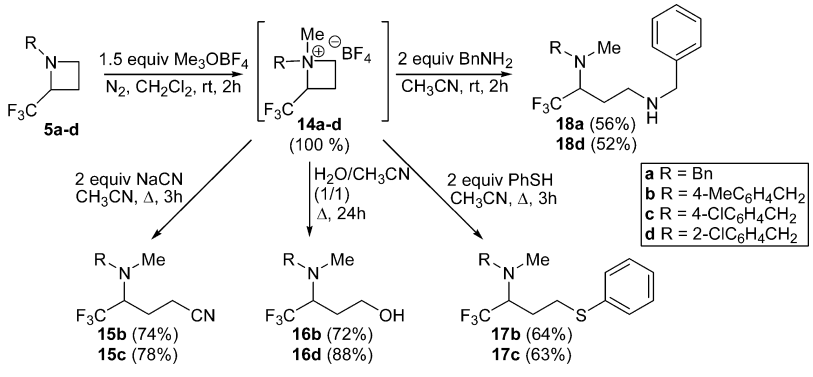


In analogy with the corresponding nonactivated 2-CF_3-aziridines, the ring opening of azetidines **5** by benzyl iodide affords primary iodides as the final products, pointing to a kinetically controlled reaction pathway.[16]

Alkylation of 2-CF_3-azetidines **5** was also performed utilizing 1.5 equiv of Me_3OBF_4 in dry CH_2Cl_2 at room temperature for 2 h, affording stable azetidinium salts **14a−d** in a quantitative way (Scheme 5). Afterward, these salts **14** were subjected to ring opening in a regiospecific way by using oxygen, nitrogen, carbon, and sulfur nucleophiles, thus providing a convenient entry into a variety of α-(trifluoromethyl)amines **15−18**. In a first experiment, azetidinium ions **14b,c** were treated with 2 equiv of sodium cyanide in CH_3CN under reflux for 3 h, resulting in 4-(*N*-alkyl-*N*-methyl)amino-5,5,5-trifluoropentanenitriles **15b,c** (74−78%, Scheme 5). In analogy, treatment of intermediates **14a−d** with thiophenol and benzylamine resulted in the corresponding 4-phenylthio-1,1,1-trifluorobutan-2-amines **17b,c** (63−64%, Scheme 5) and 4,4,4-trifluorobutan-1,3-diamines **18a,d** (52−56%, Scheme 5), respectively. In addition, 3-aminobutan-1-ols **16b,d** were obtained in good yields (72−88%, Scheme 5) by heating azetidinium salts **14b,d** in aq CH_3CN (1/1) for 24 h.

On the basis of all of the above-described transformations, it can be concluded that the ring opening of nonactivated 2-CF_3-azetidines proceeds regiospecifically at C4, independent of the type of activation and the nature of the nucleophile involved. Thus, a clear difference in reactivity between α-CF_3-azetidines and azetidines bearing other types of electron-withdrawing groups at C2 toward ring-opening reactions can be noted. For example, the Lewis acid-mediated ring opening of activated 2-aryl-1-tosylazetidines occurs regiospecifically at the more electrophilic C2 position,[9a,21] whereas nucleophilic ring opening of the azetidinium salts derived from nonactivated 2-acyl- or 2-cyano-1-alkylazetidines generally occurs regioselectively at the

Scheme 5



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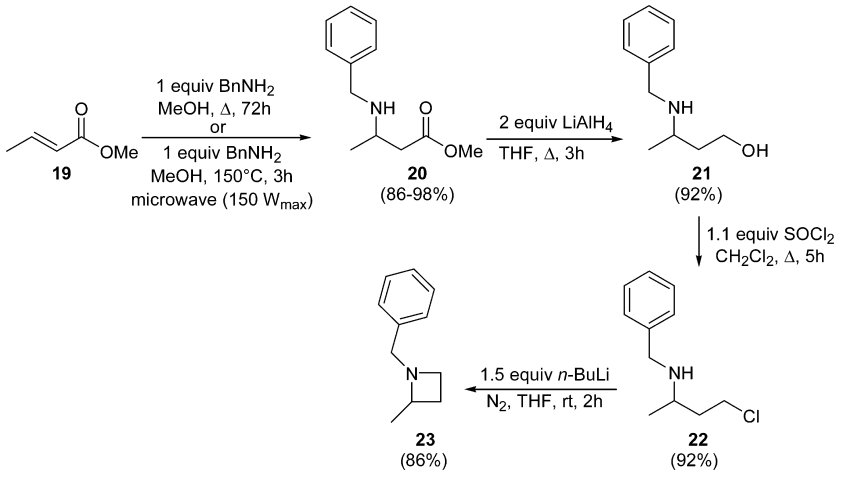
Scheme 6



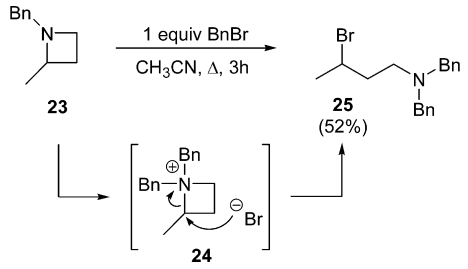
C4 position with formation of the C2 ring-opening products as minor constituents (2−25%, sometimes up to 63%),[9a,22] except for the ring opening with methyl chloroformate, which exclusively occurs at the C2 position. On the other hand, the ring opening of 2-CF_3-azetidines **5a−e** proved to be regiospecific in all cases, providing new insights into the chemistry of azetidines. In that respect, it is also fair to state that 2-CF_3-azetidines **5** are suitable substrates for efficient syntheses of a variety of novel acyclic α-trifluoromethylated amines (52−88%).

A final objective of this study comprised the assessment of the reactivity of 1-alkyl-2-(trifluoromethyl)azetidines **5** relative to that of their nonfluorinated analogues, i.e., 1-alkyl-2-methylazetidines, as very little information concerning the latter 2-methylazetidines is available in the literature.[23] In particular, nothing is known regarding their behavior toward alkyl halides, hence an effort was made in that respect in the present study.

In order to evaluate the reactivity of 1-alkyl-2-methylazetidines toward alkyl halides, 1-benzyl-2-methylazetidine **23** was chosen as a reference compound and was prepared in a four-step approach adapted from the literature starting from methyl 2-butenoate **19** (Scheme 6). In the first step, methyl 2-butenoate **19** was treated with benzylamine in methanol at reflux temperature to afford methyl 2-(benzylamino)butanoate **20** in excellent yield.[24] The use of microwave irradiation according to a literature protocol[25] afforded amino ester **20** after 3 h at 150 °C, albeit in a lower yield (86%). In the next step, methyl 2-(benzylamino)butanoate **20** was reduced by using $LiAlH_4$ in THF under reflux, resulting in the corresponding butan-1-ol **21**.[26] Treatment of this γ-amino alcohol **21** with thionyl chloride in dichloromethane under reflux resulted in *N*-benzyl-4-chlorobutan-2-amine **22**,[27] which was ring closed toward the desired 1-benzyl-2-methylazetidine **23**[28] by using 1.5 equiv of *n*-BuLi in THF at room temperature for 2 h.

In the next phase, 2-methylazetidine **23** was treated with 1 equiv of benzyl bromide in acetonitrile under reflux for 3 h to evaluate its behavior with respect to alkyl halides. As expected, this reaction resulted in the sole formation of the secondary bromide **25** (Scheme 7), which can be explained by ring opening of the intermediate azetidinium salt **24** at the substituted azetidine carbon atom under thermodynamic control. This result is in perfect agreement with different

Scheme 7



literature reports on the thermodynamically controlled ring opening of nonactivated 2-alkylaziridines by alkyl halides to produce secondary halides through ring opening at C2.[29]

It is clear that replacement of a methyl group by a trifluoromethyl group at the 2-position results in a complete switch of the reactivity of 1-alkylazetidines with respect to alkyl halides, providing secondary halides using the former and affording primary halides using the latter azetidines after ring opening. This profound difference in reactivity can be attributed to the strong electron-withdrawing property of the CF_3-substituent and is in line with the established reactivity of nonactivated 2-CF_3-aziridines.[16]

In conclusion, a straightforward four-step approach toward novel α-trifluoromethyl-substituted azetidines was developed starting from ethyl 4,4,4-trifluoroacetoacetate. Furthermore, activation of these 1-alkyl-2-(trifluoromethyl)azetidines via protonation, alkylation, or acylation and subsequent regiospecific ring opening of the intermediate azetidinium ions was achieved at the C4 azetidine carbon atom by means of oxygen, nitrogen, carbon, sulfur, and halogen nucleophiles, providing an entry into a broad variety of acyclic α-CF_3-amines. In addition, novel 4-CF_3-1,3-oxazinan-2-ones were obtained via cyclization of the corresponding methyl *N*-alkyl-*N*-[3-chloro-1-(trifluoromethyl)propyl]carbamates upon microwave irradiation.

EXPERIMENTAL SECTION

Synthesis of Ethyl 3-Alkylamino-4,4,4-trifluorobut-2-enoates 2. As a representative example, the synthesis of ethyl 3-benzylamino-4,4,4-trifluorobut-2-enoate **2a** is described here. A solution of benzylamine (55.0 mmol) and CH_3COOH (55.0 mmol) in $CHCl_3$ (80 mL) was stirred at room temperature for 5 min, after which a solution of ethyl 4,4,4-trifluoroacetoacetate (50 mmol) in

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$CHCl_3$ (100 mL) was added. After stirring for 5 h under reflux, the solvent was evaporated under reduced pressure, and the residue was filtered through a short silica column using hexane to afford the desired ethyl 3-benzylamino-4,4,4-trifluorobut-2-enoate **2a**. The spectral data of enamines **2a** and **2f** were in full accordance with those available in the literature.[30]

Ethyl 3-(4-Methylbenzyl)amino-4,4,4-trifluorobut-2-enoate ***2b***. Transparent oil: yield 92% (13.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (3H, t, J = 7.2 Hz), 2.32 (3H, s), 4.12 (2H, q, J = 7.2 Hz), 4.41 (2H, d, J = 6.1 Hz), 5.15 (1H, s), 7.13−7.22 (4H, m), 8.40 (1H, s (broad)); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 14.3 (CH_3), 21.0 (CH_3), 48.0 (~d, J = 2.3 Hz, CH_2), 59.7 (CH_2), 85.2 (q, J = 5.8 Hz, CH), 120.6 (q, J = 277.3 Hz, C), 127.4 (CH), 129.6 (CH), 134.9 (C), 137.6 (C) 148.2 (q, J = 31.2 Hz, C), 169.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −67.09 (s); IR (cm^{-1}) ν_{NH} = 3228; ν_{CO} = 1670; $\nu_{C=C}$ = 1629; ν_{max} = 1150, 1286, 1214, 1200, 1130, 1035, 797, 759, 698, 662; MS (70 eV) m/z (%) 288 (M^+ + 1, 10), 224 (100); HRMS (ES-TOF) calcd for $C_{14}H_{17}F_3NO_2$ 288.1211 $[M + H]^+$, found 288.1193.

Ethyl 3-(4-Chlorobenzyl)amino-4,4,4-trifluorobut-2-enoate ***2c***. Pale yellow oil: yield 99% (15.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (3H, t, J = 7.2 Hz), 4.13 (2H, q, J = 7.2 Hz), 4.41 (2H, d, J = 6.1 Hz), 5.18 (1H, s), 7.20 and 7.30 (4H, 2 × d, J = 8.8 Hz), 8.46 (1H, s (broad)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (CH_3), 47.5 (~d, J = 3.2 Hz, CH_2), 59.94 (CH_2), 86.0 (q, J = 5.8 Hz, CH), 120.4 (q, J = 276.9 Hz, C), 128.7 (CH), 129.1 (CH), 133.8 (C), 136.5 (C), 148.1 (q, J = 31.2 Hz, C), 169.7 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −66.53 (s); IR (cm^{-1}) ν_{NH} = 3281; ν_{CO} = 1670, $\nu_{C=C}$ = 1631; ν_{max} = 1670, 1631, 1291, 1186, 1132, 1084, 797; MS (70 eV) m/z (%) 308/310 (M^+ + 1, 25), 264/6 (100); HRMS (ES-TOF) calcd for $C_{13}H_{14}ClF_3NO_2$ 308.0665 $[M + H]^+$, found 308.0663.

Ethyl 3-(2-Chlorobenzyl)amino-4,4,4-trifluorobut-2-enoate ***2d***. Transparent oil: R_f 0.55 (petroleum ether/EtOAc 95/5); yield 64% (9.8 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (3H, t, J = 7.2 Hz), 4.14 (2H, q, J = 7.2 Hz), 4.55 (2H, d, J = 6.6 Hz), 5.19 (1H, s), 7.18−7.26 and 7.29−7.38 (4H, m), 8.57 (1H, s (broad)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4 (CH_3), 45.9 (~d, J = 3.4 Hz, CH_2), 59.9 (CH_2), 85.9 (q, J = 5.8 Hz, CH), 120.4 (q, J = 276.9 Hz, C), 127.2 (CH), 128.9 (CH), 129.2 (CH), 129.8 (CH), 133.4 (C), 135.6 (C), 148.2 (q, J = 31.2 Hz, C), 169.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −66.90 (s); IR (cm^{-1}) ν_{NH} = 3283; ν_{CO} = 1670; $\nu_{C=C}$ = 1631; ν_{max} = 1446, 1305, 1288, 1184, 1131, 1037, 797, 750, 670; MS (70 eV) m/z (%) 308/310 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{13}H_{14}ClF_3NO_2$ 308.0665 $[M + H]^+$, found 308.0670.

Ethyl 3-(Phenylethyl)amino-4,4,4-trifluorobut-2-enoate ***2e***. Yellow oil: yield 78% (11.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (3H, t, J = 7.2 Hz), 2.86 (2H, t, J = 7.43), 3.51 (2H, q, J = 6.6 Hz), 4.13 (2H, q, J = 7.2 Hz), 5.09 (1H, s), 7.18−7.25 and 7.28−7.33 (5H, 2 × m), 8.24 (1H, s (broad)); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 14.4 (CH_3), 37.3 (CH_2), 45.7 (d, J = 2.3 Hz, CH_2), 59.7 (CH_2), 84.9 (q, J = 5.8 Hz, CH), 120.4 (q, J = 276.9 Hz, C), 126.9 (CH), 128.8 (CH), 128.9 (CH), 138.1 (C), 148.4 (q, J = 30.8 Hz, C), 169.9 (C) ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −67.27 (s); IR (cm^{-1}) ν_{NH} = 3282; ν_{CO} = 1670; $\nu_{C=C}$ = 1630; ν_{max} = 1473, 1455, 1287, 1181, 1131, 1090, 1039, 796, 698; MS (70 eV) m/z (%) 288 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{14}H_{17}F_3NO_2$ 288.1211 $[M + H]^+$, found 288.1217.

Ethyl 3-(3-Methoxybenzyl)amino-4,4,4-trifluorobut-2-enoate ***2g***. Yellow oil: R_f 0.74 (hexane/EtOAc 85/15); yield 94% (14.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, t, J = 7.1 Hz), 3.81 (3H, s), 4.14 (2H, q, J = 7.1 Hz), 4.45 (2H, d, J = 6.3 Hz), 5.17 (1H, s), 6.84 (2H, d, J = 6.2 Hz), 6.89 (1H, d, J = 7.5 Hz), 7.26−7.29 (1H, m), 8.44 (1H, s (broad)); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 14.3 (CH_3), 48.0 (d, J = 2.7 Hz, CH_2), 55.2 (CH_3), 59.7 (CH_2), 85.4 (q, J = 5.8 Hz, CH), 112.9 (CH), 113.2 (CH), 119.4 (CH), 120.3 (q, J = 277.0 Hz, C), 129.9 (CH), 139.3 (C), 148.1 (q, J = 31.0 Hz, C), 160.0 (C), 169.8 (C); IR (cm^{-1}) ν_{NH} = 3416; ν_{CO} = 1671; $\nu_{C=C}$ = 1633; ν_{max} = 1298, 1206, 1137, 1042, 613, 542; MS (70 eV) m/z (%)304 (M^+ + 1, 20), 282 (100); HRMS (ES-TOF) calcd for $C_{14}H_{17}F_3NO_3$ 304.1161 $[M + H]^+$, found 304.1137.

Synthesis of 3-Alkylamino-4,4,4-trifluorobutan-1-ols 3. As a representative example, the synthesis of 3-benzylamino-4,4,4-trifluorobutan-1-ol **3a** is described. To a solution of ethyl 3-benzylamino-4,4,4-trifluorobut-2-enoate **2a** (54 mmol) and EtOH (540 mmol) in THF (130 mL) at 0 °C was added $NaBH_4$ (54 mmol) in small portions while stirring. Subsequently, the reaction mixture was heated under reflux for 16 h, and every 5 h an extra equivalent of $NaBH_4$ was added (3 equiv in total). Afterward, the reaction mixture was quenched by a saturated solution of NH_4Cl (65 mL). Extraction with CH_2Cl_2 (3 × 40 mL), washing with brine (3 × 40 mL), drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded 3-benzylamino-4,4,4-trifluorobutan-1-ol **3a**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 7/3) in order to obtain an analytically pure sample.

3-Benzylamino-4,4,4-trifluorobutan-1-ol ***3a***. Pale yellow oil: R_f 0.29 (petroleum ether/EtOAc 7/3); yield 79% (9.9 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62−1.75 and 1.81−1.90 (2H, 2 × m), 2.76 (2H, s (broad)), 3.22−3.34 (1H, m), 3.71−3.79 (2H, m), 3.84 and 4.06 (2H, 2 × d, J = 12.7 Hz), 7.27−7.34 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.5 (CH_2), 51.7 (CH_2), 58.1 (q, J = 27.7 Hz, CH), 60.8 (CH_2), 126.5 (q, J = 280.0 Hz, C), 127.6 (CH), 128.5 (CH), 128.7 (CH), 139.0 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.58 (d, J = 6.6 Hz); IR (cm^{-1}) $\nu_{NH, OH}$ = 3337; ν_{max} = 1496, 1454, 1265, 1123, 1060, 1028, 740, 698; MS (70 eV) m/z (%) 234 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{14}F_3NO$ 234.1106 $[M + H]^+$, found 234.1104.

3-(4-Methylbenzyl)amino-4,4,4-trifluorobutan-1-ol ***3b***. Yellow oil: R_f 0.22 (petroleum ether/EtOAc 8/2); yield 77% (10.3 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59−1.72 and 1.78−1.87 (2H, 2 × m), 2.32 (3H, s), 3.19−3.29 (1H, m), 3.65−3.78 (2H, m), 3.78 and 3.99 (2H, 2 × d, J = 12.7 Hz), 7.13 and 7.19 (4H, d, J = 7.7, 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (CH_3), 30.7 (CH_2), 51.6 (CH_2), 57.7 (q, J = 27.7 Hz, CH), 60.4 (CH_2), 127.0 (q, J = 285.4 Hz, C), 128.5 (CH), 129.4 (CH), 136.3 (C), 137.3 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.63 (d, J = 6.6 Hz); IR (cm^{-1}) $\nu_{NH, OH}$ = 3338; ν_{max} = 1515, 1266, 1123, 1060, 1022, 806, 698; MS (70 eV) m/z (%) 248 (M^+ + 1, 72), 226 (100); HRMS (ES-TOF) calcd for $C_{12}H_{16}F_3NO$ 248.1262 $[M + H]^+$, found 248.1261.

3-(4-Chlorobenzyl)amino-4,4,4-trifluorobutan-1-ol ***3c***. Yellow oil: R_f 0.08 (petroleum ether/EtOAc 9/1); yield 57% (8.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60−1.72 and 1.81−1.91 (2H, 2 × m), 2.13 (1H, s (broad)), 3.19−3.31 (1H, m), 3.70−3.80 (2H, m), 3.80 and 4.00 (2H, 2 × d, J = 13.2 Hz), 7.22−7.30 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8 (CH_2), 51.1 (CH_2), 57.8 (q, J = 27.7 Hz, CH), 60.3 (CH_2), 126.8 (q, J = 285.0 Hz, C), 128.8 (CH), 129.8 (CH), 133.2 (C), 137.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.61 (d, J = 7.8 Hz); IR (cm^{-1}) $\nu_{NH, OH}$ = 3344; ν_{max} = 1492, 1265, 1123, 1090, 1060, 1015, 808; MS (70 eV) m/z (%) 268/70 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{13}ClF_3NO$ 268.0716 $[M + H]^+$, found 268.0711.

3-(2-Chlorobenzyl)amino-4,4,4-trifluorobutan-1-ol ***3d***. Yellow oil: R_f 0.36 (petroleum ether/EtOAc 9/1); yield 60% (8.7 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62−1.74 and 1.84−1.93 (2H, 2 × m), 3.26−3.36 (1H, m), 3.37 (1H, s (broad)), 3.67−3.80 (2H, m), 3.90 and 4.16 (2H, 2 × d, J = 13.2 Hz), 7.18−7.27 and 7.33−7.39 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.7 (CH_2), 49.7 (CH_2), 58.3 (q, J = 27.7 Hz, CH), 60.3 (CH_2), 126.7 (q, J = 285.0 Hz, C), 127.1 (CH), 129.0 (CH), 129.8 (CH), 130.5 (CH), 134.0 (C), 136.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.90 (d, J = 7.8 Hz); IR (cm^{-1}) $\nu_{NH, OH}$ = 3342; ν_{max} = 1574, 1444, 1265, 1121, 1055, 1038, 752, 698; MS (70 eV) m/z (%) 268/70 (M^+ + 1, 72), 300/2 (100); HRMS (ES-TOF) calcd for $C_{11}H_{13}ClF_3NO$ 268.0716 $[M + H]^+$, found 268.0716.

3-(Phenylethyl)amino-4,4,4-trifluorobutan-1-ol ***3e***. Transparent oil: R_f 0.21 (petroleum ether/EtOAc 7/3); yield 71% (9.5 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (1H, s (broad)), 1.57−1.74 and 1.78−1.85 (2H, 2 × m), 2.78 (2H, t, J = 6.9 Hz), 2.92−2.98 (1H, m), 3.23−3.31 (2H, m), 3.74−3.78 (2H, m), 7.19−7.26 and 7.29−7.34 (5H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1 (CH_2), 37.0 (CH_2), 48.8 (CH_2), 59.8 (q, J = 25.4 Hz, CH), 61.2 (CH_2), 126.4 (q, J = 286.1 Hz, C), 126.5 (CH), 128.7 (CH), 139.1 (C); ^{19}F NMR (282 MHz,

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$CDCl_3$) δ −74.92 (d, J = 7.9 Hz); IR (cm^{-1}) $\nu_{NH, OH}$ = 3332; ν_{max} = 1454, 1264, 1125, 1099, 1060, 1030, 749, 698; MS (70 eV) m/z (%) 248 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{16}F_3NO$ 248.1262 $[M + H]^+$, found 248.1259.

3-(4-Methoxybenzyl)amino-4,4,4-trifluorobutan-1-ol ***3f***. Yellow oil: R_f 0.18 (hexane/EtOAc 9/1); yield 60% (8.6 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.71−1.77 and 1.84−1.89 (2H, 2 × m), 2.31 (2H, s (broad)), 3.29−3.33 (1H, m), 3.71−3.76 (2H, m), 3.80 (3H, s), 3.81 and 4.03 (2H, 2 × d, J = 13.7 Hz), 6.88 and 7.25 (2H, d, J = 8.6, 7.1 Hz); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 30.3 (CH_2), 51.0 (CH_2), 55.3 (CH_3), 57.9 (q, J = 27.1 Hz, CH), 60.9 (CH_2), 114.1 (CH), 125.9 (q, J = 284.0 Hz, C), 129.8 (CH), 130.4 (C) and 159.2 (C); IR (cm^{-1}) $\nu_{NH, OH}$ = 3351; ν_{max} = 1607, 1514, 1250, 1129, 1033, 834, 466; MS (70 eV) m/z (%) 264 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{16}F_3NO_2$ 264.1211 $[M + H]^+$, found 264.1229.

3-(3-Methoxybenzyl)amino-4,4,4-trifluorobutan-1-ol ***3g***. Yellow oil: R_f 0.20 (hexane/EtOAc 8/2); yield 50% (7.1 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.86−1.90 and 1.99−2.04 (2H, 2 × m), 2.74 (2H, s (broad)), 3.42−3.48 (1H, m), 3.87−3.99 (2H, m), 3.95 (3H, s), 3.98 and 4.20 (2H, 2 × d, J = 12.9 Hz), 6.96−6.98, 7.03−7.06 and 7.38−7.41 (4H, 3 × m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 30.5 (CH_2), 51.6 (CH_2), 55.2 (CH_3), 57.9 (q, J = 27.4 Hz, CH), 60.8 (CH_2), 113.2 (CH), 113.9 (CH), 120.7 (CH), 129.7 (CH), 126.6 (q, J = 285.9 Hz, C), 140.3 (C), 159.9 (C); IR (cm^{-1}) $\nu_{NH, OH}$ = 3360; ν_{max} = 1602, 1492, 1267, 1134, 1055, 700; MS (70 eV) m/z (%) 264 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{16}F_3NO_2$ 264.1211 $[M + H]^+$, found 264.1250.

Synthesis of *N*-Alkyl-4-chloro-1,1,1-trifluorobutan-2-amines 4. As a representative example, the synthesis of *N*-benzyl-4-chloro-1,1,1-trifluorobutan-2-amine **4a** is described. To an ice-cooled solution of 3-benzylamino-4,4,4-trifluorobutan-1-ol **3a** (31.0 mmol) in dry CH_2Cl_2 (100 mL), $SOCl_2$ (34.1 mmol) was added dropwise. After heating under reflux for 5 h, the reaction mixture was neutralized by a saturated solution of $NaHCO_3$ (50 mL). Extraction with CH_2Cl_2 (3 × 30 mL), washing with brine (3 × 30 mL), drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded *N*-benzyl-4-chloro-1,1,1,-trifluorobutan-2-amine **4a**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 98/2) in order to obtain an analytically pure sample.

N-Benzyl-4-chloro-1,1,1-trifluorobutan-2-amine ***4a***. Orange oil: R_f 0.16 (petroleum ether/EtOAc 98/2); yield 70% (5.4 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (1H, s (broad)), 1.79−1.91 and 2.05−2.16 (2H, 2 × m), 3.30−3.42 (1H, m), 3.65−3.81 (2H, m), 3.85 and 4.07 (2H, 2 × d, J = 12.9 Hz), 7.34−7.39 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.2 (CH_2), 41.0 (CH_2), 51.8 (CH_2), 55.9 (q, J = 27.7 Hz, CH), 127.1 (q, J = 285.8 Hz, C), 127.4 (CH), 128.3 (CH), 128.5 (CH), 139.6 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.83 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{NH} = 3354; ν_{max} = 1454, 1261, 1145, 1117, 870, 741, 698, 663; MS (70 eV) m/z (%) 252/4 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{13}ClF_3N$ 252.0767 $[M + H]^+$, found 252.0762.

4-Chloro-N-(4-methylbenzyl)-1,1,1-trifluorobutan-2-amine ***4b***. Orange oil: yield 88% (7.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (1H, s (broad)), 1.75−1.87 and 2.02−2.13 (2H, 2 × m), 2.33 (3H, s), 3.27−3.36 (1H, m), 3.61−3.73 (2H, m), 3.78 and 4.00 (2H, 2 × d, J = 12.7 Hz), 7.11−7.14 and 7.18−7.30 (4H, 2 × m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 21.2 (CH_3), 32.3 (CH_2), 41.1 (CH_2), 51.6 (CH_2), 56.0 (q, J = 27.7 Hz, CH), 127.3 (q, J = 285.4 Hz, C), 128.4 (CH), 129.3 (CH), 136.8 (C), 137.1 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.82 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{NH} = 3347; ν_{max} = 1515, 1261, 1152, 1117, 871, 806, 663; MS (70 eV) m/z (%) 266/8 (M^+ + 1, 15), 226 (100); HRMS (ES-TOF) calcd for $C_{12}H_{15}ClF_3N$ 266.0923 $[M + H]^+$, found 266.0918.

4-Chloro-N-(4-chlorobenzyl)-1,1,1-trifluorobutan-2-amine ***4c***. Yellow oil: R_f 0.31 (petroleum ether/EtOAc 9/1); yield 50% (4.4 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (1H, s (broad)), 1.73−1.84 and 2.00−2.12 (2H, 2 × m), 3.28−3.33 (1H, m), 3.59−3.72 (2H, m), 3.77 and 3.98 (2H, 2 × d, J = 13.2 Hz), 7.24 (4H, s (broad)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.2 (CH_2), 41.0 (CH_2), 51.1 (CH_2), 56.0 (q, J = 27.7 Hz, CH), 127.2 (q, J = 285.4 Hz, C), 128.7 (CH), 129.7 (CH), 133.1 (C), 138.4 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.82 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{NH} = 3358; ν_{max} = 1492, 1260, 1147, 1178, 1090, 810, 663; MS (70 eV) m/z (%) 286/88/90 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{12}Cl_2F_3N$ 286.0377 $[M + H]^+$, found 286.0365.

4-Chloro-N-(2-chlorobenzyl)-1,1,1-trifluorobutan-2-amine ***4d***. Orange oil: R_f 0.36 (petroleum ether/EtOAc 99/1); yield 83% (7.3 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (1H, s (broad)), 1.78−1.89 and 2.04−2.18 (2H, 2 × m), 3.31−3.43 (1H, m), 3.60−3.75 (2H, m), 3.88 and 4.16 (2H, 2 × d, J = 13.2 Hz), 7.18−7.27 and 7.32−7.42 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.2 (CH_2), 40.9 (CH_2), 49.6 (CH_2), 56.1 (q, J = 27.7 Hz, CH), 127.0 (q, J = 285.0 Hz, C), 127.0 (CH), 128.8 (CH), 129.7 (CH), 130.4 (CH), 134.0 (C), 137.1 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −75.11 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{NH} = 3363; ν_{max} = 1574, 1444, 1261, 1153, 1116, 1051, 752, 682; MS (70 eV) m/z (%) 286/88/90 (M^+ + 1, 42), 248 (100); HRMS (ES-TOF) calcd for $C_{11}H_{12}Cl_2F_3N$ 286.0377 $[M + H]^+$, found 286.0373.

4-Chloro-N-(phenylethyl)-1,1,1-trifluorobutan-2-amine ***4e***. Pale yellow oil: R_f 0.15 (petroleum ether/EtOAc 98/2); yield 73% (6.0 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (1H, s (broad)), 1.71−1.82 and 1.99−2.11 (2H, 2 × m), 2.73−2.82 (2H, m), 2.89−2.97 and 3.14−3.23 (2H, m), 3.26−3.36 (1H, m), 3.59−3.63 (1H, m), 7.20−7.33 (5H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.0 (CH_2), 37.0 (CH_2), 41.0 (CH_2), 49.0 (CH_2), 57.0 (q, J = 27.3 Hz, CH), 127.0 (q, J = 285.0 Hz, C), 126.3 (CH), 128.5 (CH), 128.7 (CH), 139.57 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −75.21 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{NH} = 3367; ν_{max} = 1603, 1454, 1261, 1142, 1117, 748, 698; MS (70 eV) m/z (%) 266/8 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}ClF_3N$ 266.0923 $[M + H]^+$, found 266.0919.

4-Chloro-N-(4-methoxybenzyl)-1,1,1-trifluorobutan-2-amine ***4f***. Dark orange oil: R_f 0.50 (hexane/EtOAc 8/2); yield 50% (4.4 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (1H, s (broad)), 1.83−1.89 and 2.07−2.14 (2H, 2 × m), 3.33−3.37 (1H, m), 3.66−3.70 and 3.72−3.78 (2H, 2 × m), 3.81 (3H, s (broad)), 3.80 and 4.00 (2H, 2 × d, J = 12.3 Hz), 6.86−6.89 and 7.26−7.28 (4H, 2 × m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 32.2 (CH_2), 41.0 (CH_2), 51.2 (CH_2), 55.3 (CH_3), 55.7 (q, J = 27.4 Hz, CH), 113.9 (CH), 127.1 (q, J = 285.8 Hz, C), 129.5 (CH), 139.6 (C), 159.0 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.79 (s (broad)); IR (cm^{-1}) ν_{NH} = 3356; ν_{max} = 1610, 1519, 1253, 1122, 1039, 828; MS (70 eV) m/z (%) 282/4 (M^+ + 1, 13), 278 (100).

4-Chloro-N-(3-methoxybenzyl)-1,1,1-trifluorobutan-2-amine ***4g***. Dark orange oil: R_f 0.56 (hexane/EtOAc 8/2); yield 50% (4.4 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72 (1H, s (broad)), 1.97−2.04 and 2.22−2.29 (2H, 2 × m), 3.48−3.54 (1H, m), 3.81−3.85 and 3.89−3.94 (2H, 2 × m), 3.96 (3H, s (broad)), 3.98 and 4.19 (2H, 2 × d, J = 13.2 Hz), 6.95−6.97, 7.07−7.08 and 7.38−7.41 (4H, 3 × m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 32.2 (CH_2), 40.9 (CH_2), 51.7 (CH_2), 55.2 (CH_3), 55.9 (q, J = 27.5 Hz, CH), 112.9 (CH), 113.8 (CH), 120.5 (CH), 129.5 (CH), 127.0 (q, J = 285.7 Hz, C), 141.1 (C), 159.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −74.84 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{NH} = 3355; ν_{max} = 1597, 1487, 1265, 1124, 1047, 875; MS (70 eV) m/z (%) 282/4 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}ClF_3NO$ 282.0873 $[M + H]^+$, found 282.0903.

Synthesis of 1-Alkyl-2-(trifluoromethyl)azetidines 5. As a representative example, the synthesis of 1-benzyl-2-(trifluoromethyl)-azetidine **5a** is described. In a flame-dried flask under N_2 atmosphere, *N*-benzyl-4-chloro-1,1,1-trifluorobutan-2-amine **4a** (17.0 mmol) was dissolved in dry THF (50 mL). The resulting mixture was then cooled to 0 °C, and LiHMDS (18.7 mmol) was added dropwise via a syringe. After stirring at reflux temperature for 2 h, the reaction was again cooled to 0 °C, and an additional 1.1 equiv of LiHMDS (18.7 mmol) was added. The reaction mixture was stirred for another 2 h at reflux temperature. Afterward, the reaction mixture was quenched with a saturated solution of NH_4Cl (25 mL), extracted with EtOAc (3 × 15 mL), and washed with brine (3 × 15 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded 1-benzyl-2-(trifluoromethyl)azetidine **5a**, which was purified by means of column

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chromatography on silica gel (petroleum ether/EtOAc 95/5) to obtain an analytically pure sample.

1-Benzyl-2-(trifluoromethyl)azetidine ***5a***. Transparent oil: R_f 0.25 (petroleum ether/EtOAc 95/5); yield 80% (2.9 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05−2.17 and 2.25−2.37 (2H, 2 × m), 2.93 (1H, ∼q, J = 8.1 Hz), 3.27−3.33 (1H, m), 3.52 and 3.91 (2H, 2 × d, J = 12.7 Hz), 3.59−3.71 (1H, m), 7.23−7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (∼d, J = 3.5 Hz, CH_2), 50.3 (CH_2), 61.9 (CH_2), 63.4 (q, J = 33.5 Hz, CH), 125.5 (q, J = 278.1 Hz, C), 127.5 (CH), 128.5 (CH), 128.9 (CH), 137.2 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.66 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1397, 1283, 1159, 1125, 1092, 984, 701; MS (70 eV) m/z (%) 216 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{12}F_3N$ 216.1000 $[M + H]^+$, found 216.1000.

1-(4-Methylbenzyl)-2-(trifluoromethyl)azetidine ***5b***. Yellow oil: R_f 0.26 (petroleum ether/EtOAc 95/5); yield 77% (3.0 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03−2.13 and 2.23−2.35 (2H, 2 × m), 2.33 (3H, s), 2.92 (1H, ∼q, J = 8.1 Hz), 3.24−3.30 (1H, m), 3.47 and 3.87 (2H, 2 × d, J = 12.7 Hz), 3.57−3.69 (1H, m), 7.11−7.18 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (∼d, J = 2.3 Hz, CH_2), 21.1 (CH_3), 49.9 (CH_2), 61.3 (CH_2), 63.1 (q, J = 32.3 Hz, CH), 125.2 (q, J = 278.1 Hz, C), 128.8 (CH), 129.1 (CH), 133.8 (C), 136.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.57 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1515, 1397, 1283, 1159, 1136, 1125, 1091, 984, 810, 693; MS (70 eV) m/z (%) 230 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}F_3N$ 230.1157 $[M + H]^+$, found 230.1160.

1-(4-Chlorobenzyl)-2-(trifluoromethyl)azetidine ***5c***. Yellow oil: R_f 0.31 (petroleum ether/EtOAc 95/5); yield 90% (3.8 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03−2.13 and 2.22−2.34 (2H, 2 × m), 2.86 (1H, ∼q, J = 8.1 Hz), 3.23−3.29 (1H, m), 3.44 and 3.83 (2H, 2 × d, J = 13.2 Hz), 3.55−3.67 (1H, m), 7.18−7.28 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (∼d, J = 2.3 Hz, CH_2), 50.4 (CH_2), 61.2 (CH_2), 63.5 (q, J = 32.3 Hz, CH), 125.2 (q, J = 278.1 Hz, C), 128.6 (CH), 130.1 (CH), 133.1 (C), 135.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.71 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1491, 1282, 1159, 1137, 1098, 814, 692; MS (70 eV) m/z (%) 250/2 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{12}ClF_3N$ 250.0610 $[M + H]^+$, found 250.0610.

1-(2-Chlorobenzyl)-2-(trifluoromethyl)azetidine ***5d***. Yellow oil: R_f 0.36 (petroleum ether/EtOAc 99/1); yield 59% (2.5 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08−2.18 and 2.26−2.38 (2H, 2 × m), 2.96 (1H, ∼q, J = 8.1 Hz), 3.36−3.42 (1H, m), 3.72 and 3.94 (2H, 2 × d, J = 14.3 Hz), 3.68−3.80 (1H, m), 7.13−7.24, 7.31−7.34 and 7.39−7.42 (4H, 3 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5 (∼d, J = 3.5 Hz, CH_2), 51.1 (CH_2), 58.7 (CH_2), 63.6 (q, J = 32.7 Hz, CH), 125.2 (q, J = 278.1 Hz, C), 126.9 (CH), 128.5 (CH), 129.5 (CH), 130.2 (CH), 133.8 (C), 135.1 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.90 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1574, 1444, 1398, 1283, 1161, 1131, 1091, 751, 693; MS (70 eV) m/z (%) 250/2 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{11}H_{12}ClF_3N$ 250.0610 $[M + H]^+$, found 250.0607.

1-(2-Phenylethyl)-2-(trifluoromethyl)azetidine ***5e***. Yellow oil: R_f 0.33 (petroleum ether/EtOAc 99/1); yield 81% (3.2 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00−2.13 and 2.22−2.34 (2H, 2 × m), 2.54−2.75 (3H, m), 2.83−2.96 (2H, m), 3.40−3.59 (2H, m), 7.15−7.18 and 7.23−7.28 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3 (∼d, J = 3.5 Hz, CH_2), 34.0 (CH_2), 51.0 (CH_2), 60.2 (CH_2), 64.3 (q, J = 32.3 Hz, CH), 125.2 (q, J = 277.7 Hz, C), 126.2 (CH), 128.5 (CH), 128.7 (CH), 139.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.66 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1604, 1397, 1283, 1158, 1135, 1125, 1094, 748, 696; MS (70 eV) m/z (%) 230 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}F_3N$ 230.1157 $[M + H]^+$, found 230.1151.

1-(4-Methoxybenzyl)-2-(trifluoromethyl)azetidine ***5f***. Orange oil: yield 85% (3.5 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03−2.13 and 2.23−2.36 (2H, 2 × m), 2.92 (1H, ∼q, J = 8.1 Hz), 3.23−3.29 (1H, m), 3.45 and 3.84 (2H, 2 × d, J = 13.2 Hz), 3.56−3.68 (1H, m), 3.80 (3H, s), 6.83−6.88 and 7.17−7.22 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (∼d, J = 3.5 Hz, CH_2), 49.8 (CH_2), 55.2 (CH_3), 61.0 (CH_2), 63.0 (q, J = 32.3 Hz, CH), 113.8 (CH), 125.2 (q, J = 278.1 Hz, C), 128.9 (C), 130.1 (CH), 158.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.56 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1613, 1512, 1283, 1247, 1158, 1135, 1125, 1090, 1035, 984, 824, 814, 694; MS (70 eV) m/z (%) 246 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}F_3NO$ 246.1106 $[M + H]^+$, found 246.1103.

1-(3-Methoxybenzyl)-2-(trifluoromethyl)azetidine ***5g***. Orange oil: yield 72% (3.0 g); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06−2.20 and 2.25−2.37 (2H, 2 × m), 2.94 (1H, ∼q, J = 8.1 Hz), 3.29−3.34 (1H, m), 3.49 and 3.88 (2H, 2 × d, J = 13.2 Hz), 3.59−3.71 (1H, m), 3.81 (3H, s), 6.79−6.87 and 7.20−7.32 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4 (∼d, J = 2.3 Hz, CH_2), 50.2 (CH_2), 55.2 (CH_3), 61.7 (CH_2), 63.2 (q, J = 32.3 Hz, CH), 112.8 (CH), 114.3 (CH), 121.1 (CH), 125.2 (q, J = 278.1 Hz, C), 129.4 (CH), 138.5 (C), 158.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −77.64 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{max} = 1601, 1586, 1489, 1283, 1265, 1146, 1136, 1125, 1091, 1044, 777, 707, 691; MS (70 eV) m/z (%) 246 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{15}F_3NO$ 246.1106 $[M + H]^+$, found 246.1108.

Synthesis of 4-Chloro-*N*-(4-methylbenzyl)-1,1,1-trifluorobutan-2-amine 4b. In a 10 mL pressure vial, 1-(4-methylbenzyl)-2-(trifluoromethyl)azetidine **5b** (0.44 mmol) was dissolved in a 37% solution of HCl in water (2 mL). The reaction mixture was stirred at 100 °C for 3 days. Afterward the reaction mixture was neutralized by using a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded 4-chloro-*N*-(4-methylbenzyl)-1,1,1-trifluorobutan-2-amine **4b**. The spectral data were in accordance with those described above.

Synthesis of 4-Bromo-*N*-phenylethyl-1,1,1-trifluorobutan-2-amine 7e. In a 10 mL pressure vial, 1-phenylethyl-2-(trifluoromethyl)azetidine **5e** (0.44 mmol) was dissolved in a 48% solution of HBr in water (2 mL). The reaction mixture was stirred at 100 °C for 2 days. Afterward, the reaction mixture was neutralized by using a saturated solution of $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded 4-bromo-*N*-phenylethyl-1,1,1-trifluorobutan-2-amine **7e**.

4-Bromo-N-phenylethyl-1,1,1-trifluorobutan-2-amine ***7e***. Yellow oil: yield 66% (89.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (1H, s (broad)), 1.79−1.91 and 2.05−2.16 (2H, 2 × m), 2.72−2.79 (2H, m), 2.89−2.97 and 3.14−3.23 (2H, 2 × m), 3.25−3.34 (1H, m), 3.43−3.47 (2H, m), 7.19−7.23 and 7.27−7.35 (5H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.4 (CH_2), 32.0 (CH_2), 36.9 (CH_2), 48.8 (CH_2), 57.7 (q, J = 27.7 Hz, CH), 126.9 (q, J = 285.4 Hz, C), 126.3 (CH), 128.5 (CH), 128.7 (CH), 139.5 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −75.09 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{NH} = 3352; ν_{max} = 1603, 1454, 1257, 1148, 1114, 1088, 873, 749, 698; MS (70 eV) m/z (%) 310/312 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{16}BrF_3N$ 310.0418 $[M + H]^+$, found 310.0419.

Synthesis of *N*-Alkyl-*N*-[3-chloro-1-(trifluoromethyl)propyl]-acetamides 9. As a representative example, the synthesis of *N*-[3-chloro-1-(trifluoromethyl)propyl]-*N*-(4-methylbenzyl)acetamide **9b** is described. In a flame-dried flask under N_2 atmosphere, 1-(4-methylbenzyl)-2-(trifluoromethyl)azetidine **5b** (0.44 mmol) was dissolved in dry CH_2Cl_2 (3 mL). Acetyl chloride (0.66 mmol) was added via a syringe, and the resulting mixture was stirring under reflux for 4 h. Afterward, the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded *N*-[3-chloro-1-(trifluoromethyl)propyl]-*N*-(4-methylbenzyl)acetamide **9b**, which was purified by means of preparative TLC (petroleum ether/EtOAc 95/5) to obtain an analytically pure sample. In ^{1}H and ^{13}C NMR, two rotamers were observed because of hindered rotation.

N-[3-Chloro-1-(trifluoromethyl)propyl]-N-(4-methylbenzyl)-acetamide ***9b***. Pale yellow oil: R_f 0.06 (petroleum ether/EtOAc 99/1); yield 68% (91.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09−2.17 (4H, m), 2.29 and 2.32 (12H, 2 × s (broad)), 3.01−3.09 and 3.30−3.34 (2H, 2 × m), 3.43−3.45 (2H, m), 4.05 and 5.14 (2H, 2 × d, J = 15.4 Hz), 4.51 and 4.63 (2H, 2 × d, J = 18.2 Hz), 4.66 (1H, s (broad)), 5.60 (1H, s (broad)) 7.09−7.15 (8H, m); ^{13}C NMR (75

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MHz, $CDCl_3$) δ 21.0 (2 × CH_3), 22.1 (CH_3), 22.4 (CH_3), 29.2 (CH_2), 29.4 (CH_2), 40.0 (CH_2), 40.4 (CH_2), 45.3 (2 × CH_2), 57.1 (q, J = 30.0 Hz, 2 × CH), 125.3 (q, J = 283.4 Hz, 2 × C), 125.8 (2 × CH), 127.6 (2 × CH), 129.4 (2 × CH), 129.7 (2 × CH), 133.7 (C), 135.2 (C), 137.1 (C), 137.5 (C), 172.6 (C), 173.3 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −71.89 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{CO} = 1665; ν_{max} = 1516, 1407, 1273, 1230, 1166, 1153, 1121, 1048, 1020, 796, 735; MS (70 eV) m/z (%) 308/10 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{14}H_{18}ClF_3NO$ 308.1029 $[M + H]^+$, found 308.1033.

N-[3-Chloro-2-(trifluoromethyl)propyl]-N-(2-phenylethyl)-acetamide ***9e***. Pale yellow oil: R_f 0.14 (petroleum ether/EtOAc 95/5); yield 61% (82.4 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11−2.29 (4H, m), 2.27 (6H, 2 × s), 2.72−2.81 (1H, m), 2.84−2.96 (2H, m), 2.99−3.11 (1H, m), 3.20−3.31 (3H, m), 3.35−3.63 (5H, m), 4.49−4.64 (1H, m), 5.50 (1H, s (broad)), 7.17−7.36 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6 (CH_3), 22.2 (CH_3), 28.9 (CH_2), 29.1 (CH_2), 34.0 (CH_2), 36.2 (CH_2), 39.8 (CH_2), 40.1 (CH_2), 44.8 (2 × CH_2), 56.3 (q, J = 30.0 Hz, 2 × CH), 125.2 (q, J = 283.8 Hz, 2 × C), 126.6 (CH), 127.1 (CH), 128.6 (2 × CH), 128.7 (2 × CH), 128.9 (2 × CH), 129.0 (2 × CH), 137.7 (C), 139.2 (C), 171.9 (C), 172.2 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −72.72 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{CO} = 1662; ν_{max} = 1413, 1271, 1227, 1167, 1149, 1122, 741, 700; MS (70 eV) m/z (%) 308/310 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{14}H_{18}ClF_3NO$ 308.1029 $[M + H]^+$, found 308.1032.

Synthesis of Methyl *N*-Alkyl-*N*-[3-chloro-1-(trifluoromethyl)-propyl]carbamates 10. As a representative example, the synthesis of methyl *N*-benzyl-*N*-[3-chloro-1-(trifluoromethyl)propyl]carbamate **10a** is described. In a flame-dried flask under N_2 atmosphere, 1-benzyl-2-(trifluoromethyl)azetidine **5a** (2.3 mmol) was dissolved in dry CH_3CN (10 mL). Methyl chloroformate (6.9 mmol) was added via a syringe, and the resulting mixture was stirred under reflux for 5 h. Afterward, the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (5 mL), extracted with EtOAc (3 × 5 mL), and washed with brine (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded pure methyl *N*-benzyl-*N*-[3-chloro-1-(trifluoromethyl)propyl]carbamates **10a**. In ^{1}H and ^{13}C, two rotamers were observed because of hindered rotation.

Methyl N-Benzyl-N-[3-chloro-1-(trifluoromethyl)propyl]-carbamate ***10a***. Orange oil: yield 64% (455.0 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14−2.17 (4H, m), 3.16 (2H, m), 3.31 (2H, m), 3.80 (6H, s (broad)), 4.37 and 4.67 (4H, 2 × d, J = 16.0 Hz), 4.87 (1H, m), 5.02 (1H, m), 7.31−7.36 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.4 (2 × CH_2), 40.1 (2 × CH_2), 48.0 (2 × CH_2), 53.6 (2 × CH_3), 55.4 (q, J = 27.7 Hz, 2 × CH), 125.4 (q, J = 284.6 Hz, 2 × C), 127.6 (2 × CH), 128.7 (8 × CH), 137.8 (2 × C), 157.5 (2 × C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −72.07 (s (broad)); IR (cm^{-1}) ν_{CO} = 1708; ν_{max} = 1451, 1335, 1268, 1233, 1167, 1126, 1115, 733, 699; MS (70 eV) m/z (%) 310/2 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{13}H_{16}ClF_3NO_2$ 310.0822 $[M + H]^+$, found 310.0812.

Methyl N-[3-Chloro-1-(trifluoromethyl)]propyl-N-(4-methylbenzyl)carbamate ***10b***. Pale orange oil: R_f 0.17 (petroleum ether/EtOAc 99/1); yield 63% (468.2 mg); ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$) δ 2.09−2.14 and 2.20−2.25 (4H, 2 × m), 2.31 (6H, s), 3.18−3.26 and 3.28−3.36 (4H, 2 × m), 3.78 (6H, s), 4.31 and 4.67 (4H, 2 × d, J = 14.6 Hz), 4.92 (2H, m), 7.10−7.16 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (2 × CH_3), 29.4 (2 × CH_2), 40.1 (2 × CH_2), 47.8 (2 × CH_2N), 53.5 (2 × CH_3), 55.3 (q, J = 28.8 Hz, 2 × CH), 125.3 (q, J = 283.8 Hz, 2 × C), 129.4 (8 × CH), 134.7 (2 × C), 137.3 (2 × C), 157.5 (2 × C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −72.10 (s (broad)); IR (cm^{-1}) ν_{CO} = 1710; ν_{max} = 1451, 1330, 1268, 1232, 1167, 1117, 1025, 774; MS (70 eV) m/z (%) 324/6 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{14}H_{18}ClF_3NO_2$ 324.0978 $[M + H]^+$, found 324.0969.

Methyl N-[3-Chloro-1-(trifluoromethyl)]propyl-N-(phenylethyl)-carbamate ***10e***. Yellow oil: yield 70% (520.2 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14−2.21 (4H, m), 2.80−2.94 (3H, m), 2.96−3.09 (1H, m), 3.21−3.34 (2H, m), 3.37−3.53 (2H, m), 3.79 (3H, s), 3.82 (3H, s), 5.00 (2H, m), 7.17−7.24 and 7.28−7.33 (10H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.1 (2 × CH_2), 34.6 (CH_2), 35.6 (CH_2), 39.9 (2 × CH_2), 45.9 (2 × CH_2), 53.3 (CH_3), 53.5 (CH_3), 54.8 (q, J = 28.8 Hz, 2 × CH), 125.3 (q, J = 283.4 Hz, 2 × C), 126.7 (2 × CH), 128.7 (2 × CH), 128.8 (2 × CH), 128.9 (2 × CH), 138.65 (C), 138.89 (C), 156.47 (C), 157.49 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −72.98 (s, minor), −72.71 (s, major); IR (cm^{-1}) ν_{CO} = 1708; ν_{max} = 1454, 1275, 1229, 1168, 1127, 1113, 1031, 774, 748, 700; MS (70 eV) m/z (%) 324/6 (M^+ + 1, 100).

Synthesis of 3-Alkyl-4-trifluoromethyl-1,3-oxazinan-2-ones 11. As a representative example, the synthesis of 3-benzyl-4-trifluoromethyl-1,3-oxazinan-2-one **11a** is described. In a 10 mL thick-walled Pyrex reaction vessel, methyl *N*-benzyl-*N*-[(3-chloro-1-(trifluoromethyl)propyl]carbamate **10a** (0.49 mmol) was dissolved in DMF (4 mL). The mixture was heated to 140 °C for 30 min under microwave irradiation (200 W). Afterward, the reaction mixture was dissolved in Et_2O (4 mL) and washed with brine (4 × 2 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent afforded 3-benzyl-4-trifluoromethyl-1,3-oxazinan-2-one **11a**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 8/2).

3-Benzyl-4-trifluoromethyl-1,3-oxazinan-2-one ***11a***. White crystals: mp 73−75 °C: yield 59% (74.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00−2.13 and 2.15−2.21 (2H, 2 × m), 3.72−3.81 (1H, m), 4.06 and 5.53 (2H, 2 × d, J = 15.5 Hz), 4.29−4.34 and 4.42−4.50 (2H, 2 × m), 7.27−7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9 (CH_2), 51.5 (CH_2), 53.2 (q, J = 30.0 Hz, CH), 63.6 (CH_2), 125.3 (q, J = 285.0 Hz, C), 128.3 (CH), 128.4 (CH), 129.1 (CH), 135.6 (C), 152.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.46 (d, J = 6.5 Hz); IR (cm^{-1}) ν_{CO} = 1679; ν_{max} = 1456, 1264, 1232, 1163, 1156, 1148, 1128, 1049, 704, 694; MS (70 eV) m/z (%) 260 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{13}F_3NO_2$ 260.0898 $[M + H]^+$, found 260.0903.

3-(4-Methylbenzyl)-4-trifluoromethyl-1,3-oxazinan-2-one ***11b***. Pale yellow oil: R_f 0.17 (petroleum ether/EtOAc 9/1); yield 54% (72.3 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97−2.12 and 2.14−2.21 (2H, 2 × m), 2.35 (3H, s), 3.74−3.79 (1H, m), 4.00 and 5.52 (2H, 2 × d, J = 14.9 Hz), 4.27−4.36 and 4.42−4.51 (2H, 2 × m), 7.11−7.23 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (CH_3), 21.7 (CH_2), 51.1 (CH_2), 52.8 (q, J = 30.0 Hz, CH), 63.5 (CH_2), 125.2 (q, J = 285.0 Hz, C), 128.4 (CH), 129.7 (CH), 132.4 (C), 137.3 (C), 152.9 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −72.39 (d, J = 6.6 Hz); IR (cm^{-1}) ν_{CO} = 1678; ν_{max} = 1457, 1262, 1129, 1218, 1162, 1148, 1127, 1049, 762, 642; MS (70 eV) m/z (%) 274 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{13}H_{15}F_3NO_2$ 274.1055 $[M + H]^+$, found 274.1055.

Synthesis of *N*-Alkyl-*N*-benzyl-4-iodo-1,1,1-trifluorobutan-2-amines 13. As a representative example, the synthesis of *N*-benzyl-*N*-(4-methylbenzyl)-4-iodo-1,1,1-trifluorobutan-2-amine **13b** is described. In a 10 mL pressure vial, 1-(4-methylbenzyl)-2-(trifluoromethyl)azetidine (1.31 mmol) and benzyl iodide (1.31 mmol) was heated at 100 °C under neat conditions for 1 day, affording *N*-benzyl-*N*-(4-methylbenzyl)-4-iodo-1,1,1-trifluorobutan-2-amine **13b**, which was purified by means of column chromatography on silica gel (hexane) to obtain an analytically pure sample.

N-Benzyl-N-(4-methylbenzyl)-4-iodo-1,1,1-trifluorobutan-2-amine ***13b***. Transparent oil: R_f 0.35 (hexane); yield 75% (439.2 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99−2.12 and 2.17−2.31 (2H, 2 × m), 2.34 (3H, s), 2.96−3.05 (1H, m), 3.20−3.33 (2H, m), 3.61−3.69 (2H, m), 3.89 and 3.93 (2H, 2 × d, J = 12.4 Hz), 7.10−7.22 and 7.23−7.37 (9H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.3 (CH_2), 21.2 (CH_3), 31.2 (CH_2), 53.9 (CH_2), 54.1 (CH_2), 59.0 (q, J = 25.4 Hz, CH), 127.4 (q, J = 291.9 Hz, C), 127.4 (CH), 128.6 (CH), 129.0 (CH), 129.1 (CH), 129.3 (CH), 135.4 (C), 137.1 (C), 138.6 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −69.96 (d, J = 9.2 Hz); IR (cm^{-1}) ν_{max} = 1514, 1495, 1454, 1249, 1142, 1111, 1091, 801, 735, 698; MS (70 eV) m/z (%) 448 (M^+ + 1, 80), 320 (100); HRMS (ES-TOF) calcd for $C_{19}H_{22}F_3IN$ 448.0749 $[M + H]^+$, found 448.0740.

N-Benzyl-N-(4-chlorobenzyl)-4-iodo-1,1,1-trifluorobutan-2-amine ***13c***. Pale yellow oil: R_f 0.33 (hexane); yield 75% (458.8 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00−2.12 and 2.16−2.28 (2H, 2 × m), 2.33 (3H, s), 3.03 (1H, ~q, J = 8.3 Hz), 3.20−3.33 (2H, m), 3.66 and 3.86 (2H, 2 × d, J = 13.8 Hz), 3.66 and 3.89 (2H, 2 × d, J = 13.2 Hz), 7.20−7.36 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.1 (CH_2), 31.0 (CH_2), 53.7 (CH_2), 54.3 (CH_2), 59.3 (q, J = 25.0 Hz, CH), 127.3

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(q, J = 291.5 Hz, C), 127.6 (CH), 128.7 (CH), 128.8 (CH), 129.0 (CH), 130.4 (CH), 133.26 (C), 137.03 (C), 138.28 (C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −67.38 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{max} = 1491, 1454, 1248, 1142, 1112, 1089, 1073, 802, 736, 698; MS (70 eV) m/z (%) 468 (M^+ + 1, 91), 415 (100); HRMS (ES-TOF) calcd for $C_{18}H_{19}ClF_3IN$ 468.0203 $[M + H]^+$, found 468.0205.

Synthesis of 1-Alkyl-1-methyl-2-(trifluoromethyl)-azetidinium Tetrafluoroborates 14. As a representative example, the synthesis of 1-methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)-azetidinium tetrafluoroborate **14b** is described. In a flame-dried flask under N_2 atmosphere, Me_3OBF_4 (1.95 mmol) was added to an ice-cooled solution of 1-(4-methylbenzyl)-2-(trifluoromethyl)azetidine **5b** (1.30 mmol) in dry CH_2Cl_2 (4 mL). After stirring for 2 h at room temperature, the solvent was evaporated, affording 1-methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)azetidinium tetrafluoroborate **14b**, which was used as such in the following step without prior purification. In order to confirm the structure, the spectral data are reported below.

*1-Methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)azetidinium Tetrafluoroborate **14b**.* Orange oil: yield 100% (430.5 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.37 (3H, s), 2.90 (2H, ∼q, J = 8.4 Hz), 3.21 (3H, s), 4.03−4.11 (1H, m), 4.67 and 4.72 (2H, 2 × d, J = 13.8 Hz), 4.87 (1H, q, J = 9.9 Hz), 5.33−5.47 (1H, m), 7.18−7.30 and 7.34−7.42 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0 (CH_2), 21.2 (CH_3), 44.2 (CH_3), 63.3 (CH_2), 68.2 (q, J = 35.8 Hz, CH), 69.5 (CH_2), 121.3 (q, J = 279.2 Hz, C), 123.6 (C), 130.3 (CH), 132.0 (CH), 141.6 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −69.96 (d, J = 6.6 Hz), −150.19 (s); IR (cm^{-1}) ν_{max} = 1708, 1473, 1379, 1280, 1184, 1052, 1037, 1017, 815, 691.

Synthesis of 4-(*N*-Alkyl-*N*-methylamino)-5,5,5-trifluoropentanenitriles 15. As a representative example, the synthesis of 4-[*N*-methyl-*N*-(4-methylbenzyl)amino]-5,5,5-trifluoropentanenitrile **15b** is described. To a solution of 1-methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)azetidinium tetrafluoroborate **14b** (0.90 mmol) in CH_3CN (8 mL) was added NaCN (1.80 mmol). After stirring for 3 h under reflux, the reaction mixture was poured out in a saturated solution of $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 × 5 mL), and washed with brine (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded 4-[*N*-methyl-*N*-(4-methylbenzyl)amino]-5,5,5-trifluoropentanenitrile **15b**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 98/2) to obtain an analytically pure sample.

*4-[N-Methyl-N-(4-methylbenzyl)amino]-5,5,5-trifluoropentanenitrile **15b**.* Transparent oil: R_f 0.16 (petroleum ether/EtOAc 98/2); yield 74% (179.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.86−2.06 (2H, m), 2.34 (6H, s), 2.37−2.57 (2H, m), 3.18−3.31 (1H, m), 3.76 and 3.85 (2H, 2 × d, J = 13.2 Hz), 7.11−7.22 (4H, m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 14.1 (CH_2), 21.2 (CH_3), 22.4 (CH_2), 35.8 (CH_3), 59.4 (CH_2), 61.9 (q, J = 25.4 Hz, CH), 119.1 (C), 127.2 (q, J = 292.3 Hz, C), 128.8 (CH), 129.4 (CH), 135.4 (C), 137.3 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.47 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{max} = 2859, 1514, 1457, 1258, 1166, 1144, 1085, 1110, 1046, 805, 700; MS (70 eV) m/z (%) 271 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{14}H_{18}F_3N_2$ 271.1422 $[M + H]^+$, found 271.1453.

*4-[N-(4-Chlorobenzyl)-N-methylamino]-5,5,5-trifluoropentanenitrile **15c**.* Transparent oil: R_f 0.10 (petroleum ether/EtOAc 98/2); yield 78% (203.6 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90−2.08 (2H, m), 2.32 (3H, d, J = 1.7 Hz), 2.42−2.59 (2H, m), 3.22−3.35 (1H, m), 3.79 and 3.87 (2H, 2 × d, J = 13.8 Hz), 7.22−7.24 and 7.30−7.33 (4H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1 (CH_2), 22.3 (CH_2), 35.5 (CH_3), 59.1 (CH_2), 62.5 (q, J = 25.4 Hz, CH), 119.1 (C), 127.2 (q, J = 292.3 Hz, C), 128.8 (CH), 130.2 (CH), 133.1 (C), 137.3 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.56 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{max} = 1598, 1579, 1491, 1258, 1166, 1110, 1088, 1045, 1015, 851, 824, 803, 700; MS (70 eV) m/z (%) 291/3 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{13}H_{15}ClF_3N_2$ 291.0876 $[M + H]^+$, found 291.0881.

Synthesis of 3-(*N*-Alkyl-*N*-methylamino)-4,4,4-trifluorobutan-1-ols 16. As a representative example, the synthesis of 3-[*N*-methyl-*N*-(4-methylbenzyl)amino]-4,4,4-trifluorobutan-1-ol **16b** is described. 1-Methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)-azetidinium tetrafluoroborate **14b** (0.80 mmol) was dissolved in 4 mL of H_2O/CH_3CN (1/1). After stirring for 24 h under reflux, the reaction mixture was poured out in a saturated solution of $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 × 5 mL), and washed with brine (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded 3-[*N*-methyl-*N*-(4-methylbenzyl)-amino]-4,4,4-trifluorobutan-1-ol **16b**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 98/2) to obtain an analytically pure sample.

*3-[N-Methyl-N-(4-methylbenzyl)]amino-4,4,4-trifluorobutan-1-ol **16b**.* Pale yellow oil: R_f 0.37 (petroleum ether/EtOAc 8/2); yield 72% (150.4 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.63−1.72 and 1.95−2.08 (2H, 2 × m), 2.34 (3H, s), 2.42 (3H, q, J = 2.0 Hz), 3.29−3.42 (1H, m), 3.66−3.82 (2H, m), 3.77 and 3.88 (2H, 2 × d, J = 13.2 Hz), 7.14−7.23 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2 (CH_3), 27.5 (CH_2), 36.3 (CH_3), 59.7 (CH_2), 61.2 (CH_2), 62.1 (q, J = 25.4 Hz, CH), 127.1 (q, J = 291.9 Hz, C), 129.0 (CH), 129.4 (CH), 135.0 (C), 137.4 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.47 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{OH} = 3362; ν_{max} = 1514, 1456, 1262, 1161, 1107, 1052, 805, 701; MS (70 eV) m/z (%) 262 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{13}H_{19}F_3NO$ 262.1419 $[M + H]^+$, found 262.1420.

*3-[N-(2-Chlorobenzyl)-N-methylamino]-4,4,4-trifluorobutan-1-ol **16d**.* Yellow oil: R_f 0.23 (petroleum ether/EtOAc 8/2); yield 88% (197.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.68−1.77 and 1.91−2.05 (2H, 2 × m), 2.42 (3H, s), 3.05−3.06 and 3.66−3.75 (2H, 2 × m), 3.37−3.50 (1H, m), 3.93 and 4.00 (2H, 2 × d, J = 13.8 Hz), 7.20−7.27, 7.32−7.37 and 7.38−7.41 (4H, 3 × m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 28.0 (CH_2), 35.6 (CH_3), 58.0 (CH_2), 60.7 (CH_2), 62.7 (q, J = 25.4 Hz, CH), 126.9 (CH), 129.1 (CH), 127.3 (q, J = 291.9 Hz, C), 130.0 (CH), 131.3 (CH), 134.7 (C), 135.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.47 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{OH} = 3366; ν_{max} = 1444, 1260, 1149, 1164, 1091, 1107, 1054, 751, 702, 683; MS (70 eV) m/z (%) 282/284 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{12}H_{16}ClF_3NO$ 282.0873 $[M + H]^+$, found 282.0875.

Synthesis of *N*-Alkyl-*N*-methyl-4-phenylthio-1,1,1-trifluorobutan-2-amines 17. As a representative example, the synthesis of *N*-methyl-*N*-(4-methylbenyl)-4-phenylthio-1,1,1-trifluorobutan-2-amine **17b** is described. To a solution of 1-methyl-1-(4-methylbenzyl)-2-(trifluoromethyl)azetidinium tetrafluoroborate **14b** (1 mmol) in CH_3CN (5 mL) was added thiophenol (2 mmol). After stirring for 3 h under reflux, the reaction mixture was poured out in a saturated solution of $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 × 5 mL), and washed with brine (3 × 5 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded *N*-methyl-*N*-(4-methylbenyl)-4-phenylthio-1,1,1-trifluorobutan-2-amine **17b**, which was purified by means of column chromatography on silica gel (hexane) to obtain an analytically pure sample.

*N-Methyl-N-(4-methylbenyl)-4-phenylthio-1,1,1-trifluorobutan-2-amine **17b**.* Pale orange oil: R_f 0.17 (hexane); yield 64% (226.0 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76−1.88 and 1.94−2.06 (2H, 2 × m), 2.31 (3H, ∼q, J = 1.8 Hz), 2.34 (3H, s), 2.91−3.01 and 3.12−3.20 (2H, 2 × m), 3.34−3.49 (1H, m), 3.72 and 3.84 (2H, 2 × d, J = 13.5 Hz), 7.10−7.23 and 7.25−7.37 (9H, 2 × m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (CH_3), 25.7 (CH_2), 30.3 (CH_2), 36.1 (CH_3), 59.2 (CH_2), 62.0 (q, J = 25.0 Hz, CH), 127.6 (q, J = 291.9 Hz, C), 126.3 (CH), 128.6 (CH), 129.0 (CH), 129.1 (CH), 129.7 (CH), 135.8 (C), 136.0 (C), 136.8 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.57 (d, J = 9.2 Hz); IR (cm^{-1}) ν_{max} = 1584, 1480, 1256, 1154, 1105, 1079, 803, 737, 690; MS (70 eV) m/z (%) 354 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{19}H_{23}F_3NS$ 354.1503 $[M + H]^+$, found 354.1509.

*N-(4-Chlorobenyl)-N-methyl-4-phenylthio-1,1,1-trifluorobutan-2-amine **17c**.* Pale orange oil: R_f 0.19 (hexane); yield 63% (235.0 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78−1.90 and 1.94−2.06 (2H, 2 × m), 2.28 (3H, d, J = 1.7 Hz), 2.92−3.02 and 3.11−3.19 (2H, 2 × m), 3.36−3.51 (1H, m), 3.73 and 3.84 (2H, 2 × d, J = 13.8 Hz), 7.18−7.37 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6 (CH_2),30.4 (CH_2), 35.9 (CH_3), 58.8 (CH_2), 62.2 (q, J = 25.4 Hz, CH), 127.5 (q, J = 291.9 Hz,), 126.4 (CH), 128.5 (CH), 129.1 (CH), 129.8 (CH), 132.9 (C), 135.6 (C), 137.6 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ

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−68.66 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{max} = 1490, 1256, 1154, 1107, 1088, 844, 802, 738, 690; MS (70 eV) m/z (%) 374/6 (M^+ + 1, 30), 230 (100); HRMS (ES-TOF) calcd for $C_{18}H_{20}ClF_3NS$ 374.0957 [M + H]$^+$, found 374.0959.

Synthesis of N^3-Alkyl-N^1-benzyl-N^3-methyl-4,4,4-trifluorobutan-1,3-diamines 18. As a representative example, the synthesis of N^1,N^3-dibenzyl-N^3-methyl-4,4,4-trifluorobutan-1,3-diamine **18a** is described. To a solution of 1-benzyl-1-methyl-2-(trifluoromethyl)-azetidinium tetrafluoroborate **14a** (0.65 mmol) in CH_3CN (4 mL) was added benzylamine (1.30 mmol). After stirring for 2 h at room temperature, the reaction mixture was poured out in a saturated solution of $NaHCO_3$ (4 mL), extracted with CH_2Cl_2 (3 × 2 mL) and washed with brine (3 × 2 mL). Drying ($MgSO_4$), filtration of the drying agent, and evaporation of the solvent yielded N^1,N^3-dibenzyl-N^3-methyl-4,4,4-trifluorobutan-1,3-diamine **18a**, which was purified by means of column chromatography on silica gel (petroleum ether/EtOAc 8/2) to obtain an analytically pure sample.

N^1,N^3-Dibenzyl-N^3-methyl-4,4,4-trifluorobutan-1,3-diamine ***18a***. Yellow oil: R_f 0.11 (petroleum ether/EtOAc 8/2); yield 56% (122.4 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (1H, s (broad)), 1.69−1.80 and 1.84−1.96 (2H, 2 × m), 2.34 (3H, ∼d, J = 1.7 Hz), 2.73−2.86 (2H, 2 × m), 3.26−3.39 (1H, m), 3.76 and 3.81 (2H, 2 × d, J = 13.2 Hz), 3.75 and 3.88 (2H, 2 × d, J = 13.8 Hz), 7.21−7.36 (10H, m); ^{13}C NMR (75 MHz, ref =$CDCl_3$) δ 26.5 (CH_2), 36.6 (CH_3), 45.9 (CH_2), 54.0 (CH_2), 59.5 (CH_2), 61.7 (q, J = 25.4 Hz, CH), 127.2 (CH), 127.3 (CH), 127.9 (q, J = 291.9 Hz, C), 128.3 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 139.4 (C), 140.3 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.81 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{NH}= 3308; ν_{max}= 1494, 1454, 1260, 1150, 1106, 733, 696; MS (70 eV) m/z (%) 337 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{19}H_{24}F_3N_2$ 337.1893 [M + H]$^+$, found 337.1897.

N^1-Benzyl-N^3-(2-chlorobenzyl)-N^3-methyl-4,4,4-trifluorobutan-1,3-diamine ***18d***. Transparent oil: R_f 0.09 (petroleum ether/EtOAc 8/2); yield 52% (125.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.69−1.80 and 1.84−1.96 (2H, 2 × m), 2.37 (3H, ∼d, J = 1.7 Hz), 2.74−2.79 (2H, ∼t, J = 3.4 Hz), 3.31−3.44 (1H, m), 3.71 and 3.77 (2H, 2 × d, J = 13.2 Hz), 3.89 and 3.95 (2H, 2 × d, J = 14.9 Hz), 7.14−7.41 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.5 (CH_2), 36.0 (CH_3), 45.8 (CH_2), 53.9 (CH_2), 57.1 (CH_2), 62.0 (q, J = 24.6 Hz, CH), 126.6 (CH), 127.0 (CH), 127.8 (q, J = 291.9 Hz, C), 128.1 (CH), 128.4 (CH), 129.6 (CH), 130.5 (CH), 134.4 (C), 136.5 (C), 140.29 (C); ^{19}F NMR (282 MHz, $CDCl_3$, ref = $CFCl_3$) δ −68.67 (d, J = 7.9 Hz); IR (cm^{-1}) ν_{NH} = 3302; ν_{max} =1453, 1444, 1257, 1150, 1107, 750, 736, 697, 683; MS (70 eV) m/z (%) 371 (M^+ + 1, 100); HRMS (ES-TOF) calcd for $C_{19}H_{23}ClF_3N_2$ 371.1502 [M + H]$^+$, found 371.1506.

Synthesis of *N,N*-Dibenzyl-3-bromobutan-1-amine 25. To a solution of 1-benzyl-2-methylazetidine **23**[28] (3.10 mmol) in CH_3CN (10 mL) was added benzyl bromide (3.10 mmol). After stirring for 3 h under reflux, the solvent was evaporated affording *N,N*-dibenzyl-3-bromobutan-1-amine **25**, which was purified by means of column chromatography on silica gel (hexane).

N,N-Dibenzyl-3-bromobutan-1-amine ***25***. Yellow oil: R_f 0.38 (petroleum ether/EtOAc 95/5); yield 52% (530 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (3H, d, J = 7.2 Hz), 1.83−1.94 and 1.97−2.09 (2H, 2 × m), 2.56−2.61 (2H, m), 3.56 (4H, s) 4.15−4.26 (1H, m), 7.20−7.37 (10H, m); ^{13}C NMR (75 MHz, ref = $CDCl_3$) δ 26.5 (CH_3), 39.1 (CH_2), 49.6 (CH), 51.9 (CH_2), 58.8 (CH_2), 127.2 (CH), 128.4 (CH), 129.1 (CH), 139.7 (C); IR (cm^{-1}) ν_{max} = 2922, 2780, 1494, 1452, 1376, 1192, 1147, 1126, 1074, 1028, 965, 744, 732, 697; MS (70 eV) m/z (%) 332/334 (M^+ + 1, 25), 252 (100).

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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