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Reductive Amination/Cyclization of ω-Trifluoromethyl Keto Esters to Trifluoromethylated δ-Amino Alcohols and Lactams

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A reductive amination/cyclization approach towards biologically interesting trifluoromethylated four- to seven-membered ring lactams from simply prepared ω-trifluoromethyl keto esters in good to excellent yields has been developed. In addition, trifluoromethylated δ-amino alcohols were also obtained directly from an unexpected reduction of the corresponding γ-imino esters in the presence of an excess amount of $NaBH_4$.

Introduction

N-substituted δ-amino alcohol derivatives are of pharmacological interest for a variety of reasons. A few reported examples, such as 4-diethylamino-1-butanol and 4-[(4′-methoxyphenyl)amino]butan-1-ol, show more potent anesthetic activity than cocaine, and also exhibit antagonist activity in calcium T-type channels.[1] Likewise, naturally occurring lactams have biological significance, such as β- and γ-lactams that are subunits of alkaloids and toxins.[2] In light of these facts, the demand for simple and efficient methods for the synthesis of fluorinated δ-amino alcohol derivatives and lactams possessing medium-sized rings has attracted broad attention.[3]

The typical approach towards the construction of lactam rings is through a sequence of reductive amination and lactamization of a keto ester.[4] However, until now, few trifluoromethylated γ-lactams have been reported.[5] Other fluorinated analogs of medium-ring lactams and δ-amino alcohols still remain unknown. From our point of view, this may possibly be due to the lack of sources of fluoroalkyl-substituted keto esters and the proper synthetic methods.

Herein, we report a general and scalable method for the efficient synthesis of trifluoromethylated δ-amino alcohols and *N*-aryl 2-azetidinones (β-lactams), 2-pyrrolidinones (γ-lactams), 2-piperidinones (δ-lactams), and 2-azepanones (ε-lactams) through reductive amination of ω-trifluoromethyl keto esters followed by cyclization.

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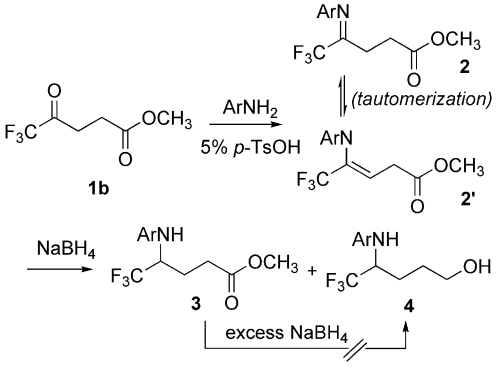
Results and Discussion

The starting trifluoromethylated γ-keto ester was produced by our optimized condensation of methyl trifluoroacetate with succinate at low temperature, followed by decarboxylation with H_3BO_3.[6] *p*-TsOH (5%)-catalyzed imination of γ-trifluoromethyl keto ester **1b** with arylamines in the presence of 4 Å molecular sieves resulted in the formation of iminoesters **2**, which were further tautomerized into their enamino ester forms (**2′**) at ambient temperature (Scheme 1).[7] Some of the enamine tautomers, such as the *N*-phenyl or *N*-*para*-fluorophenyl enamino esters, were isolable at room temperature, because of slow imine–enamine tautomerization. Imine tautomers **2** were found to be the predominant isomer according to ^{19}F NMR spectroscopic studies (see Experimental Section).

Subsequent reduction of a mixture of imino ester **2a** and enamine tautomer **2a′** with an excess amount of $NaBH_4$ in methanol provided *N*-phenylamino ester **3a** as the major product (Table 1).

It was quite interesting to find partial formation of unexpected δ-amino alcohol product **4a** when 1.0 equiv. of $NaBH_4$ was employed (Table 1, Entry 2). However, the use of an excess amount of $NaBH_4$ with a longer reaction time did not improve the yield of **4a** significantly (Table 1, Entries 8–10). Importantly, the reductive formation of amino alcohols was only observed in the cases of *N*-aryl-γ-imino (or enamino) esters **2a**–**f** (Table 2). It is clear that the chain length of the imino esters and enamino esters is the determining factor as to whether the corresponding amino alcohols are formed or not. This result provided us with a suggestion that the neighboring amino group could participate in the reduction of the ester to the alcohol. It was assumed that once amino ester intermediate **5a** was reductively formed, subsequent ring closure would occur due to the formation of pyrrolidine–borohydride complex **6a**. Subsequent intramolecular substitution of the methoxy



Ar		2/2'[a]
H	a	67:33
4-$MeOC_6H_4$	b	81:19
4-MeC_6H_4	c	76:24
3-MeC_6H_4	d	63:37
2-MeC_6H_4	e	72:28
4-FC_6H_4	f	68:32
4-$NO_2C_6H_4$	g	–[b]

[a] Determined by ^{19}F NMR spectroscopy.
[b] No desired products were obtained.

Scheme 1. Synthesis of *N*-aryl trifluoromethyl γ-amino esters **3** and δ-amino alcohols **4** from γ-trifluoromethyl keto ester **1b**.

Table 1. Optimization of the reduction of the imine tautomer of **2a**.[a]

Entry	Reductant	Reaction conditions	Yield of **3a** [%]	Yield of **4a** [%]
1	$NaBH_4$ (0.5 equiv.)	MeOH, 24 h	40	–
2	$NaBH_4$ (1.0 equiv.)	MeOH, 24 h	60	10
3	$NaBH_4$ (1.0 equiv.)	THF/MeOH (10:1), 24 h	55	–
4	$NaBH_4$ (1.0 equiv.)	$ZnCl_2$ (3 equiv.)/CH_2Cl_2, 24 h	65	–
5	$NaBH_4$ (2.0 equiv.)	MeOH, 24 h	65	15
6	$NaBH_4$ (5.0 equiv.)	THF, 24 h	30	–
7	$NaBH_3CN$ (5.0 equiv.)	MeOH, 24 h	32	–
8	$NaBH_4$ (10 equiv.)	MeOH, 24 h	68	18
9	$NaBH_4$ (10 equiv.)	MeOH, 48 h	72	18
10	$NaBH_4$ (20 equiv.)	MeOH, 48 h	75	20

[a] All reactions were carried out on a 2.0-mmol scale at room temperature. Yields are given for the isolated product.

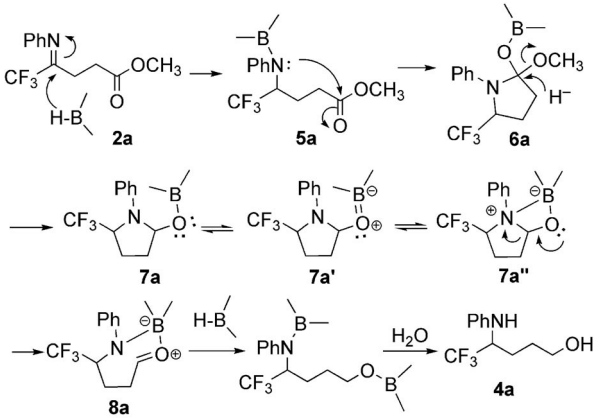
group by hydride followed by ring opening would result in the formation of δ-amino alcohols **4a** (Scheme 2).[8] The ring-closing reaction of **5a** to form five-membered pyrrolidine–borohydride complex **6a** should be a key step and kinetically favored in this sequence. Other imino esters with either shorter (β-) or longer chain lengths (δ-, ε-) would be kinetically disfavored for ring closure. This might be a possible reason why only trifluoromethyl δ-amino alcohols **4** were obtained from the reduction of γ-imino esters.

Table 2. Syntheses of trifluoromethylated *N*-aryl γ-amino esters **3** and δ-amino alcohols **4** from tautomers **2** and **2′**.

Entry[a]	**2** + **2′**	Ar	Product	Yield [%][b]
1	**a**	Ph	**3a** + **4a**	72 + 18
2	**b**	4-MeC_6H_4	**3b** + **4b**	75 + 20
3	**c**	4-MeC_6H_4	**3c** + **4c**	68 + 16
4	**d**	3-MeC_6H_4	**3d** + **4d**	55 + 19
5	**e**	2-MeC_6H_4	**3e** + **4e**	63 + 19
6	**f**	4-FC_6H_4	**3f** + **4f**	63 + 14
7	**g**	4-$NO_2C_6H_4$	**3g** + **4g**	–[c]

[a] All reactions were carried out on a 2.0-mmol scale by using an excess amount of $NaBH_4$ (10 equiv.) in MeOH at ambient temperature for 48 h. [b] Isolated yields. [c] Complex mixture.

This methodology of reductive amination was also applied to compound **2f** (Ar = 4-FC_6H_4) and inseparable tautomers **2b**, **2c**, and **2d**. Our optimized conditions (Table 1, Entry 9) provided similar results to those obtained with **2a**, and excellent overall yields and partial formation of δ-amino alcohols were obtained (Table 2). The condensation

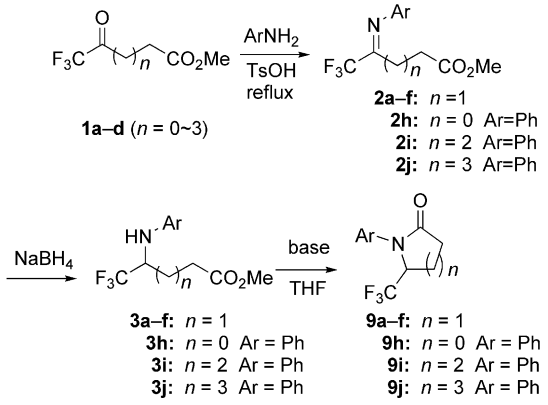


Scheme 2. Plausible reaction pathway for the conversion of γ-imino ester **2** into δ-amino alcohol **4**.

of **1b** with 4-$NO_2C_6H_4NH_2$ was clearly observed by TLC and ^{19}F NMR spectroscopy. Due to the instability of imino/enamino intermediate **2g** at ambient temperature, attempts to obtain desired amino ester **3g** and amino alcohol **4g** were tried with a one-pot condensation and reduction approach, without the separation and purification of **2g**. However, this one-pot approach failed to deliver **3g** and **4g**, and instead gave a complex mixture.

Desired trifluoromethylated 2-pyrrolidinone **9b** (Ar = 4-$CH_3OC_6H_4$) was also prepared through an intramolecular cyclization of **3b by** using a variety of bases at ambient tem-

perature (Scheme 3).[9] It was found that even after prolonged reaction times (up to 72 h), the conversion under weakly basic conditions, such as with DBU and Et_3N, was low. In contrast, stronger bases, such as NaH and *t*BuOK, were found to be effective. Moderate to excellent isolated yields of *N*-aryl 2-pyrrolidinones **9a**–**f** (n = 1) were obtained from corresponding γ-amino esters **3** by using optimized conditions of 1.1 equiv. of NaH in dry THF (Table 3). In addition, *t*BuOK was also applicable to this cyclization. The yields, however, were relatively lower. A single crystal of γ-lactam **9b** was obtained by slow evaporation from an EtOAc solution, and its structure (was unambiguously established by X-ray crystallographic analysis (Figure 1).



Scheme 3. Synthesis of four- to seven-membered lactams **9**.

Table 3. Cyclization of amino esters **3** to trifluoromethylated four- to seven-membered lactams **9**.

Entry	n	Ar	Product	Yield [%][a]
1	1	Ph	**9a**	94
2	1	4-$MeOC_6H_4$	**9b**	92
3	1	4-MeC_6H_4	**9c**	88
4	1	3-MeC_6H_4	**9d**	85
5	1	2-MeC_6H_4	**9e**	90
7	1	4-FC_6H_4	**9f**	93
8	0	Ph	**9h**	18
10	2	Ph	**9i**	91
11	3	Ph	**9j**	87

[a] Isolated yield after chromatography.

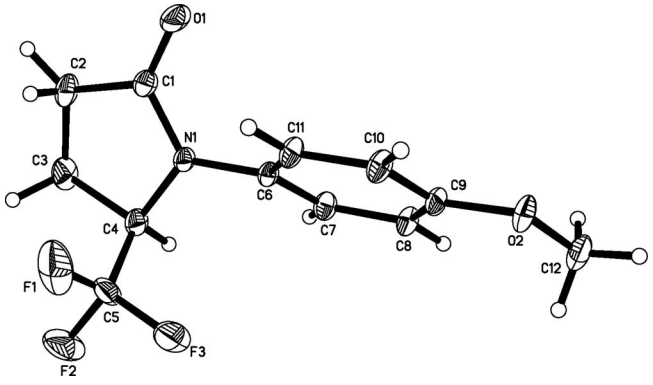
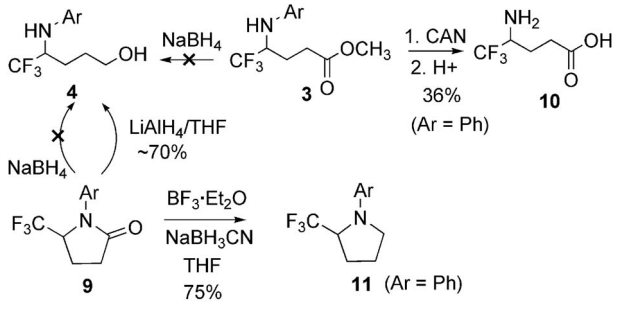


Figure 1. ORTEP drawing of the X-ray crystal structure of **9b**.

The ω-trifluoromethyl-substituted keto esters, including β-keto ester **1a** (n = 0), γ-keto ester **1b** (n = 1), δ-keto ester **1c** (n = 2), and ε-keto ester **1d** (n = 3), were recognized as important fluorine-containing building blocks that are generally applicable to the synthesis of trifluoromethylated lactams with four- to seven-membered ring sizes (Scheme 3) by using similar reaction conditions as described above. It should be pointed out that the use of an excess amount of $NaBH_4$ in the reduction of imino esters **2h**–**j** only afforded amino esters **3h**–**j** when the chain length was 0, 2, or 3. The formation of amino alcohols was not detected in these reactions. Lactams **9h**, **9i**, and **9j**, with four-, six-, and seven-membered rings, were successfully obtained through cyclization when NaH was employed to deprotonate the amino group.

To validate the hypothesis for the formation of δ-amino alcohols **4a**–**f** from the ring-opening reaction of 2-pyrrolidinones **9a**–**f** with an excess amount of $NaBH_4$, a large excess of $NaBH_4$ (30 equiv.) was added to the γ-lactams with various aryl substituents (**9a**–**f**) under the same conditions as for **2a**. However, no ring-opened product was detected, even at elevated temperatures or in polar aprotic solvents such as DMSO. This result implies that δ-amino alcohols are not directly obtainable from stable 2-pyrrolidinones, although Singaram reported the ring opening of *N*-phenyl-2-pyrrolidinones to 4-amino alcohols with LiH_3BNMe_2.[10] The ring-opening reaction of 2-pyrrolidinones **9a**–**f** took place when stronger reductants like $LiAlH_4$ were employed to afford desired δ-amino alcohols **4a**–**f** in about 70% yield (Scheme 4). A few reports have shown that some esters can be converted into alcohols by direct reduction with $NaBH_4$ without any additives such as I_2 or $InCl_3$.[11] However, our reduction of γ-amino esters **3a**–**f** with $NaBH_4$ in methanol did not occur, even at elevated temperatures. These results indicate that the mechanism of reduction of γ-imino esters into δ-amino alcohols should go through a pyrrolidinone–borohydride complex, such as **6** in our hypothesis in Scheme 2.



Scheme 4. Synthesis of trifluoromethylated γ-amino acid **10** and pyrrolidine **11**.

Furthermore, under standard conditions of N-deprotection in cerium ammonium nitrate (CAN) in CH_3CN/H_2O at room temperature, **3a** was converted into δ-fluorinated γ-amino acid **10**.[12] Corresponding fluorinated pyrrolidine

11 was also obtained from the reduction of 2-pyrrolidinones **9** by using $BF_3{\cdot}Et_2O$ and $NaBH_3CN$ in dry THF (Scheme 4).[13]

Conclusions

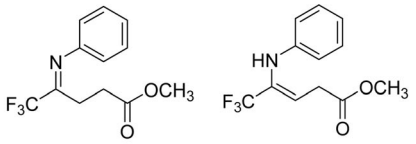
We have developed a simple, scalable, and convenient process for the synthesis of trifluoromethylated δ-amino alcohols and lactams containing four- to seven-membered rings through the reductive amination and cyclization of ω-trifluoromethylated keto esters. In addition, a possible mechanism for the formation of the δ-amino alcohols was proposed.

Experimental Section

General: Reactions were magnetically stirred in an appropriate round-bottomed flask with nitrogen protection. Thin-layer chromatography (TLC) was performed on silica gel. All melting points were taken with a WRS-1 digital melting point apparatus made by Shanghai physical instrument factory (SPOIF), China. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded with a Bruker AV-500 spectrometer. Chemical shifts for ^1H NMR spectra are reported in ppm downfield from TMS, chemical shifts for ^{13}C NMR spectra are reported in ppm relative to internal chloroform (δ = 77.2 ppm for ^{13}C), and chemical shifts for ^{19}F NMR spectra are reported in ppm downfield from internal fluorotrichloromethane ($CFCl_3$). The terms m, s, d, t, q refer to multiplet, singlet, doublet, triplet, quartet; br. refers to a broad signal. Infrared spectra (IR) were recorded with an AVATAR 370 FTIR spectrometer, absorbance frequencies are given at maximum of intensity in cm^{-1}. Elemental analyses were performed with an Elemental Vario EL III instrument. High-resolution mass spectra were obtained with a CONCEPT 1H spectrometer by using EI at 70 eV. Single-crystal XRD was performed with graphite-monochromated Mo-K_a radiation (λ = 0.71073 Å) with a Bruker Smart ApexII CCD diffractometer at T = 273(2) K. The structures were solved by direct methods with the SHELXS-97 program and refined by full-matrix least-squares on F^2 with the SHELXL-97 program. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were located and included at their calculated position.

General Procedure for the Condensation of ω-Trifluoromethylated Keto Esters with Aromatic Amines for the Preparation of Imino Esters 2 and Enamino Esters 2′: In a round-bottomed flask attached to a Dean–Stark trap, which was connected to a reflux condenser, was placed the amine (20 mmol), **1b** (10 mol), redistilled toluene (20 mL), and 4-methylbenzenesulfonic acid (0.1 g, 0.5 mmol). The flask was heated in an oil bath at about 140 °C, and the water that distilled out of the mixture with the refluxing toluene was removed at intervals. The mixture was hated at reflux until no more water separated (1.5 mL collected in about 60 h) and then for an additional 12 h. After the solution was cooled to room temperature, it was transferred to a 125-mL separatory funnel and washed with aqueous saturated $NaHCO_3$ (1 × 50 mL), water (5 × 50 mL), and brine (1 × 50 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated to provide a brown, free-flowing solid. The crude product was purified by flash column chromatography to afford title products **2** and **2′**. The ratio of **2** and **2′** was determined by ^{19}F NMR spectroscopy.

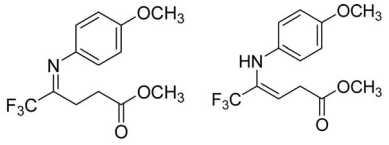
Methyl 5,5,5-Trifluoro-4-(phenylimino)pentanoate (2a) and Methyl 5,5,5-Trifluoro-4-(phenylamino)pent-3-enoate (2a′):



2a (*E* + *Z*) **2a'** (*E* + *Z*)

Ratio of **2a**/**2a′** = 67:33 (determined by ^{19}F NMR spectroscopy). Compound **2a** (*E* + *Z*; 1.50 g) was isolated as a pale-yellow oil in 58% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for (*E*)-**2a**: ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37 (t, J = 7.5 Hz, 2 H, Ar*H*), 7.16 (t, J = 7.5 Hz, 1 H, Ar*H*), 6.77 (d, J = 7.5 Hz, 2 H, Ar*H*), 3.62 (s, 3 H, OCH_3), 2.72 (t, J = 8.5 Hz, 2 H, CH_2), 2.51 (t, J = 8.5 Hz, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3, 158.8 (q, $^2J_{C,F}$ = 32.5 Hz), 147.2, 129.2, 125.1, 121.9 (q, $^1J_{C,F}$ = 278.8 Hz), 116.4, 51.9, 30.1, 23.7 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.87 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3064, 2955, 1742, 1686, 1596, 1485, 1194, 1132, 761, 698 cm^{-1}. Compound (*Z*)-**2a** was inseparable from (*E*)-**2a**. Data for (*Z*)-**2a**: ^1H NMR (500 MHz, $CDCl_3$): δ = 7.20, 7.10, 6.45 (m, Ar*H*), 3.70 (s, OCH_3) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –64.44 (s, CF_3) ppm. Ratio of (*E*)-**2a**/(*Z*)-**2a** = 94:6. Compound **2a′** (*E* + *Z*; 0.46 g) was also isolated as a pale-yellow oil in 18% yield by flash column chromatography (hexane/ethyl acetate, 8:1) on neutral aluminum oxide. Data for (*E*)-**2a′**: ^1H NMR (500 MHz, $CDCl_3$): δ = 7.22 (t, J = 7.5 Hz, 2 H, Ar*H*), 6.87–6.85 (m, 1 H, Ar*H*), 6.67 (d, J = 8.0 Hz, 1 H, Ar*H*), 6.32–6.29 (dd, J = 7 Hz, J = 0.5 Hz, 1 H, =C*H*), 4.98 (s, 1 H, N*H*), 3.68 (s, 3 H, OCH_3), 3.07–3.05 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 143.0, 129.6, 129.1 (q, $^2J_{C,F}$ = 32.5 Hz), 123.9 (q, $^1J_{C,F}$ = 273.3 Hz), 120.3, 119.9 (q, $^3J_{C,F}$ = 3.75 Hz), 114.9, 52.2, 32.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.06 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3367, 3030, 2656, 1735, 1601, 1500, 1122, 750, 694 cm^{-1}. Compound (*Z*)-**2a′** was inseparable from (*E*)-**2a′**. Data for (*Z*)-**3a**: ^1H NMR (500 MHz, $CDCl_3$): δ = 3.76 (s, OCH_3) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –74.66 (s, CF_3) ppm.

Methyl 5,5,5-Trifluoro-4-(*p*-methoxyphenylimino)pentanoate (2b) and Methyl 5,5,5-Trifluoro 4-(*p*-methoxyphenylamino)pent-3-enoate (2b′):

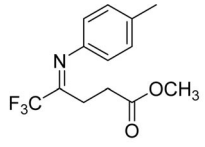


2b **2b'**

Ratio of **2b**/**2b′** = 81:19 (determined by ^{19}F NMR spectroscopy). Tautomers of imine and enamine **2b** and **2b′** (2.51 g) were obtained as a pale-yellow oil in 87% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for **2b**: ^1H NMR (500 MHz, $CDCl_3$): δ = 6.92 (d, J = 8.5 Hz, 2 H, Ar*H*), 6.76 (d, J = 8.5 Hz, 2 H, Ar*H*), 3.81 (s, 3 H, ArOCH_3), 3.64 (s, 3 H, OCH_3), 2.77 (t, J = 8.3 Hz, 2 H, CH_2), 2.51 (t, J = 8.3 Hz, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.4, 158.4 (q, $^2J_{C,F}$ = 32.5 Hz), 157.4, 140.1, 119.9, 119.3 (q, $^1J_{C,F}$ = 286.3 Hz), 114.9, 55.4, 52.0, 30.1, 23.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.71 (s, CF_3) for (*E*)-**2b**; –64.26 (s, CF_3) for (*Z*)-**2b** ppm. IR (KBr): $\tilde{\nu}$ = 3000, 2955, 1743, 1682, 1606, 1505, 1245, 1129, 842 cm^{-1}. Ratio of (*E*)-**2b**/(*Z*)-**2b** = 95:5. Compound **2b′** was in-

separable from **2b**. Data for **2b′**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.82 (m, Ar*H*), 6.70 (m, Ar*H*), 3.78 (s, ArOCH_3), 3.66 (s, OCH_3) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –70.89 for (*E*)-**2b′**; –79.88 (s, CF_3) for (*Z*)-**2b′** ppm.

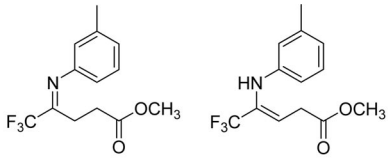
Methyl 5,5,5-Trifluoro-4-(*p*-tolylimino) pentanoate (2c):



2c

Ratio of **2c**/**2c′** = 76:24 (determined by ^{19}F NMR spectroscopy). Imine **2c** (*E* + *Z*; 1.99 g) was obtained as a pale-yellow oil in 73% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for (E)-**2c**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.5 Hz, 2 H, ArH), 6.70 (d, *J* = 8.5 Hz, 2 H, ArH), 3.65 (s, 3 H, -OCH_3), 2.76 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.53 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.36 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.5, 158.7 (q, $^2J_{C,F}$ = 32.5 Hz), 144.8, 134.9, 129.9, 118.3, 119.9 (q, $^1J_{C,F}$ = 277.5 Hz), 118.3, 52.1, 30.3, 23.6, 20.9 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.82 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3028, 2954, 1743, 1685, 1609, 1505, 1193, 1086, 828 cm^{-1}. Compound (*Z*)-**2c** was inseparable from (*E*)-**2c**. Data for (*Z*)-**2c**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 (d, ArH), 6.60 (d, ArH), 3.70 (s, OCH_3), 2.31 (s, $ArCH_3$) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –64.34 (s, CF_3) ppm. Ratio of (*E*)-**2c**/(*Z*)-**2c** = 94: 6.

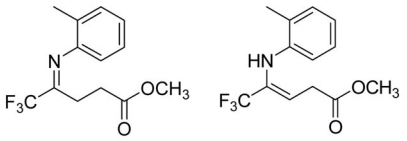
Methyl 5,5,5-Trifluoro-4-(*m*-tolylimino)pentanoate (2d) and Methyl 4-(*m*-toluidino)-5,5,5-trifluoropent-3-enoate (2d′)



2d **2d'**

Ratio of **2d**/**2d′** = 63:37 (determined by ^{19}F NMR spectroscopy). Imine **2d** (*E* + *Z*; 1.91 g) was obtained as a yellow oil in 70% yield by flash column chromatography (hexane/ethyl acetate, 6:1) on neutral aluminum oxide. Data for (*E*)-**2d**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (t, *J* = 7.5 Hz, 1 H, ArH), 6.99 (d, *J* = 7.5 Hz, 1 H, ArH), 6.59 (t, *J* = 7.5 Hz, 2 H, ArH), 3.66 (s, 3 H, OCH_3), 2.75 (t, *J* = 8.5 Hz, 1 H, CH_2), 2.53 (t, *J* = 8.5 Hz, 1 H, CH_2), 2.37 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.5, 158.7 (q, $^2J_{C,F}$ = 32.5 Hz), 147.3, 139.4, 129.2, 126.0, 119.9 (q, $^1J_{C,F}$ = 275 Hz), 118.7, 115.1, 52.1, 30.3, 23.7, 21.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.88 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3023, 2955, 1743, 1686, 1600, 1483, 1131, 1086, 787, 702 cm^{-1}. Compound (*Z*)-**2d** was inseparable from (*E*)-**2d**. Data for (*Z*)-**2d**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 (t, ArH), 6.90 (d, ArH), 6.50 (m, ArH), 3.70 (s, OCH_3), 2.98 (CH_2), 2.45 (s, $ArCH_3$) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –64.46 (s, CF_3) ppm. Ratio of (*E*)-**2d**/(*Z*)-**2d** = 94:6.

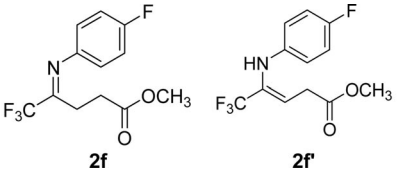
Methyl 5,5,5-Trifluoro-4-(*o*-tolylimino)pentanoate (2e) and Methyl 4-(*o*-toluidino)-5,5,5-trifluoropent-3-enoate (2e′):



2e **2e'**

Ratio of **2e**/**2e′** = 72:28 (determined by ^{19}F NMR spectroscopy). Imine **2e** (*E* + *Z*; 1.99 g) was obtained as a yellow oil in 73% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for (*E*)-**2e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.13–7.07 (m, 2 H, ArH), 6.99–6.67 (t, *J* = 7.5 Hz, 1 H, ArH), 6.50 (d, *J* = 7.5 Hz, 1 H, ArH), 3.52 (s, 3 H, OCH_3), 2.58 (t, *J* = 8.5 Hz, 2 H, CH_2), 2.37 (t, *J* = 8.5 Hz, 2 H, CH_2), 1.98 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.5, 158.6 (q, $^2J_{C,F}$ = 32.5 Hz), 146.0, 130.9, 126.7, 125.3, 119.8 (q, $^1J_{C,F}$ = 278.8 Hz), 116.9, 52.1, 29.9, 23.9, 17.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.75 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3069, 2954, 1743, 1686, 1581, 1484, 1234, 1133, 776, 750 cm^{-1}. Compound (*Z*)-**2e** was inseparable from (*E*)-**2e**. Data for (*Z*)-**2e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.08 (ArH), 6.80 (ArH), 6.45 (d, ArH), 3.60 (s, OCH_3), 2.90 (CH_2), 2.70 (CH_2), 1.90 (s, $ArCH_3$) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –66.07 (s, CF_3) ppm. Ratio of (*E*)-**2d**/(*Z*)-**2d** = 91:9.

Methyl 5,5,5-Trifluoro-4-(*p*-fluorophenylimino)pentanoate (2f) and Methyl 5,5,5-Trifluoro-4-(*p*-fluorophenylamino)pent-3-enoate (2f′):



2f **2f'**

Ratio of **2f**/**2f′** = 68:32 (determined by ^{19}F NMR spectroscopy). Imine **2f** (*E* + *Z*; 1.52 g) was obtained as a pale-yellow oil in 55% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for (*E*)-**2f**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.99 (m, *J* = 8.5 Hz, 2 H, ArH), 6.70–6.68 (m, *J* = 8.5 Hz, 2 H, ArH), 3.56 (s, 3 H, OCH_3), 2.65 (t, *J* = 8.5 Hz, 2 H,CH_2), 2.45 (t, *J* = 8.0 Hz, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 161.3 (d, $^1J_{C,F}$ = 235 Hz), 159.4 (q, $^2J_{C,F}$ = 32.5 Hz), 143.1 (d, $^4J_{C,F}$ = 3.75 Hz), 119.8 (d, $^3J_{C,F}$ = 7.5 Hz), 119.6 (q, $^1J_{C,F}$ = 277.5 Hz), 52.0, 29.6, 23.6 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.81 (s, CF_3), –118.21 (s, ArF) ppm. IR (KBr): $\tilde{\nu}$ = 3073, 2956, 1742, 1685, 1503, 1439, 1134, 1087, 1192, 847 cm^{-1}. Compound (*Z*)-**2f** was inseparable from (*E*)-**2f**. Data for (*Z*)-**2f′**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.90, 6.57 (m, ArH), 3.71 (s, OCH_3) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –64.39 (s, CF_3) ppm. Ratio of (*E*)-**2f**/(*Z*)-**2f** = 93:7. Compound **2f′** (*E* + *Z*; 0.36 g) was obtained as a pale-yellow oil in 13% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. Data for (*Z*)-**2f′**: ^{1}HNMR (500 MHz, $CDCl_3$): δ = 6.92 (d, *J* = 8.5 Hz, 2 H, ArH), 6.66–6.63 (m, 2 H, ArH), 6.26–6.23 (m, 1 H, =CH), 4.94 (s, 1 H, NH), 3.68 (s, 3 H, OCH_3), 3.04–3.02 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 157.3 (d, $^1J_{C,F}$ = 237.5 Hz), 139.2 (d, $^4J_{C,F}$ = 1.25 Hz), 129.7 (q, $^2J_{C,F}$ = 32.5 Hz), 121.73 (q, $^1J_{C,F}$ = 273.8 Hz), 119.0, 116.5 (d, $^3J_{C,F}$ = 7.6 Hz), 116.0 (d, $^2J_{C,F}$ = 23.75 Hz), 52.2, 32.3 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = 70.94 (s, CF_3), –123.80 (m, ArF) ppm. IR (KBr): $\tilde{\nu}$ = 3366, 3044, 2957, 1736, 1683, 1510, 1439, 1182, 1124, 827 cm^{-1}. Compound (*Z*)-**2f′**: was inseparable from (*E*)-**2f′**. Data for (*Z*)-**2f′**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.79 (s, OCH_3) ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.40 (s) ppm.

Ethyl 4,4,4-Trifluoro-3-(phenylamino)but-2-enoate (2h): Compound **2h** (2.07 g) was obtained as a yellow oil in 80% yield by flash column chromatography (hexane/ethyl acetate, 8:1) on neutral aluminum oxide. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.92 (s, 1 H, NH),

7.37 (t, J = 7.5 Hz, 2 H, ArH), 7.28 (d, 1 H, ArH), 7.24 (t, J = 7.5 Hz, 2 H, ArH), 5.40 (s, 1 H, CH=C), 4.25 (q, J = 7.0 Hz, 2 H, OCH_2), 1.35 (t, J = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = δ175.2, 144.1, 131.0 (q, $^2J_{C,F}$ = 32.5 Hz), 129.4, 122.3 (q, $^1J_{C,F}$ = 271.3 Hz), 121.7, 113.8, 61.1, 52.7, 19.0 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.15 (d, J = 4.7 Hz, CF_3) ppm.

Methyl 6,6,6-Trifluoro-5-(phenylimino)hexanoate (2i): Compound **2i** (2.10 g) was obtained as a pale-yellow oil in 77% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on neutral aluminum oxide. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 (t, J = 7.5 Hz, 2 H, ArH), 7.15 (t, J = 7.5 Hz, 1 H, ArH), 6.75 (d, J = 7.5 Hz, 2 H, ArH), 3.56 (s, 3 H, OCH_3), 2.44 (t, J = 8.0 Hz, 2 H,CH_2), 2.20 (t, J = 8.0 Hz, 2 H, CH_2), 1.84 (t, J = 8.0 Hz, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.5, 160.2 (q, $^2J_{C,F}$ = 32.5 Hz), 147.4, 129.2, 125.0, 120.0 (q, $^1J_{C,F}$ = 277.5 Hz), 118.2, 51.6, 33.3, 27.8, 21.7 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.88 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3083, 2936, 1748, 1681, 1512, 1429, 1140, 1075, 847 cm^{-1}.

Methyl 7,7,7-Trifluoro-6-(phenylimino)heptanoate (2j): Compound **2j** (2.18 g) was obtained as a pale-yellow oil in 76% yield by flash column chromatography (hexane/ethyl acetate, 6:1) on neutral aluminum oxide. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 (t, J = 7.5 Hz, 2 H, ArH), 7.16 (t, J = 7.5 Hz, 1 H, ArH), 6.75 (d, J = 7.5 Hz, 2 H, ArH), 3.63 (s, 3 H, OCH_3), 2.40 (t, J = 7.5 Hz, 2 H, CH_2), 2.19 (t, J = 6.0 Hz, 2 H, CH_2), 1.52 (m, 4 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 160.8 (q, $^2J_{C,F}$ = 32.5 Hz), 147.7, 129.4, 125.1, 120.0 (q, $^1J_{C,F}$ = 278.8 Hz), 118.4, 51.7, 33.4, 28.4, 26.1, 24.8 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –71.89 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3092, 2938, 1750, 1688, 1501, 1434, 1142, 1077, 849 cm^{-1}.

General Procedure for the Synthesis of ω-Trifluoroarylamino Esters 3 and Trifluoroarylaminopentanol 4: To a solution of dry CH_3OH (20 mL) at 25 °C was added the corresponding tautomers imine and enamine **2** and **2′** (2.0 mmol). The resulting mixture was stirred at the same temperature for 1 h after $NaBH_4$ (1.0 mmol) was added. When TLC analysis showed no starting materials, the reaction was quenched with saturated ammonium chloride solution and extracted with dichloromethane (3 × 20 mL). The organic layers were combined, washed with brine, dried with anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure to provide the crude reaction mixture consisting of **3** and **4**. Purification was carried out on silica gel and eluted as indicated in each example.

Methyl 5,5,5-Trifluoro-4-(phenylamino)pentanoate (3a): Compound **3a** (0.375 g) was obtained as a pale-yellow oil in 72% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.10 (t, J = 7.5 Hz, 2 H, ArH), 6.71 (dd, J = 7.5 Hz, 1 H, ArH), 6.56 (d, J = 7.5 Hz, 2 H, ArH), 3.98–3.89 (m, 1 H, CH), 3.61 (m, 1 H, NH), 3.59 (s, 3 H, OCH_3), 2.48–2.37 (m, 2 H, CH_2), 2.16–2.11 (m, 1 H, CH_2), 1.86–1.79 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 146.5, 129.7, 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 119.1 (2 C), 113.5 (2 C), 55.2 (q, $^2J_{C,F}$ = 29.6 Hz), 52.0, 29.9, 24.4 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.26 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3389, 2961, 1732, 1603, 1516, 750, 694 cm^{-1}. $C_{12}H_{14}F_3NO_2$ (261.1): calcd. C 55.17, H 5.40, N 5.36; found C 55.31, H 5.17, N 5.10.

5,5,5-Trifluoro-4-(phenylamino)pentan-1-ol (4a): Compound **4a** (0.083 g) was obtained as a pale-yellow oil in 18% yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.13–7.10 (dd, J = 7.5 Hz, 2 H, ArH), 6.70 (t, J = 7.5 Hz, 1 H, ArH), 6.60 (d, J = 7.5 Hz, 2 H, ArH), 3.87–3.80 (m, 1 H, CH), 3.59 (t, J = 6.0 Hz, 1 H, CH_2), 1.97–1.92 (m, 1 H, CH_2) 1.74–1.63 (m, 1 H, 2 H, CH_2), 1.62–1.57 (m, 1 H, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.8, 129.4, 126.3 (q, $^1J_{C,F}$ = 282.5 Hz), 118.7, 113.3, 61.9, 55.6 (q, $^2J_{C,F}$ = 29.2 Hz), 28.4, 26.0 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.92 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3393, 2956, 2923, 1604, 1502, 1258, 1168, 1128, 755, 694 cm^{-1}. MS: m/z = 233.00 $[M]^+$.

Methyl 5,5,5-Trifluoro-4-(*p*-methoxyphenylamino)pentanoate (3b): Compound **3b** (0.436 g) was obtained as a yellow oil in 75% yield by flash column chromatography (hexane/ethyl acetate, 6:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.77 (d, J = 8.5 Hz, 2 H, ArH), 6.61 (d, J = 8.5 Hz, 2 H, ArH), 3.92–3.87 (m, 1 H, CH), 3.74 (s, 3 H, $ArOCH_3$), 3.65 (s, 3 H, $OCOCH_3$), 3.42 (m, 1 H, NH), 2.57–2.46 (m, 2 H, CH_2), 2.22–2.15 (m, 1 H, CH_2), 1.91–1.84 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.4, 153.0, 140.4, 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 114.9, 56.4 (q, $^2J_{C,F}$ = 28.75 Hz), 55.7, 51.9, 29.8, 24.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.17 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3386, 2927, 1731, 1617, 1512, 1464, 1180, 1097, 821 cm^{-1}. $C_{13}H_{16}F_3NO_3$ (291.1): calcd. C 53.61, H 5.54, N, 4.81; found C 53.36, H 5.27, N, 5.04.

5,5,5-Trifluoro-4-(*p*-methoxyphenylamino)pentan-1-ol (4b): Compound **4b** (0.105 g) was obtained as a yellow oil in 20% yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.82–6.79 (d, J = 8.5 Hz, 2 H, ArH), 6.67 (d, J = 8.5 Hz, 2 H, ArH), 3.77 (s, 3 H, OCH_3), 3.71 (t, J = 6.0 Hz, 2 H, CH), 2.06–1.99 (m, 1 H, CH_2), 1.85–1.79 (m, 1 H, CH_2), 1.79–1.72 (m, 1 H, CH_2), 1.69–1.63 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.2, 140.7, 126.4 (q, $^1J_{C,F}$ = 282.5 Hz), 115.3, 115.1, 62.3, 57.3 (q, $^2J_{C,F}$ = 28.75 Hz), 55.9, 28.6, 26.4 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.05 (d, J = 9.4 Hz, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3376, 3037, 2952, 1618, 1514, 1125, 1035, 821 cm^{-1}. $C_{12}H_{16}F_3NO_2$ (263.1): calcd. C 54.75, H 6.13, N 5.32; found C 54.56, H 5.97, N 5.04.

Methyl 4-(*p*-Toluidino)-5,5,5-trifluoropentanoate (3c): Compound **3c** (0.374 g) was obtained as a pale-yellow oil in 68% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.99 (d, 2 H, J = 8.0 Hz, ArH), 6.56 (d, 2 H, J = 8.0 Hz, ArH), 3.96 (m, 1 H, CH), 3.64 (s, 3 H, OCH_3), 3.54 (m, 1 H, NH), 2.55–2.45 (m, 2 H, CH_2), 2.24 (s, 3 H, $ArCH_3$), 2.22–1.91 (m, 1 H, CH_2), 2.22–2.16 (m, 1 H, CH_2), 1.92–1.86 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.4, 144.1, 129.9, 128.2, 126.0 (q, $^1J_{C,F}$ = 282.5 Hz), 113.5, 55.5 (q, $^2J_{C,F}$ = 28.8 Hz), 51.8, 29.8, 24.5, 20.4 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.24 (d, J = 9.4 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3392, 3025, 2954, 1733, 1618, 1522, 1441, 1168, 1123, 809 cm^{-1}. $C_{13}H_{16}F_3NO_2$ (275.1): calcd. C 56.72, H, 5.86, N, 5.09; found C 56.54, H 5.90, N 5.26.

4-(*p*-Toluidino)-5,5,5-trifluoropentan-1-ol (4c): Compound **4c** (0.079 g) was obtained as a yellow oil in 16%yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.00 (d, J = 8.0 Hz, 2 H, ArH), 6.59 (d, J = 8.0 Hz, 2 H, ArH), 3.88–3.83 (m, 1 H, CH), 3.67 (t, J = 6.5 Hz, J = 5.5 Hz, 2 H, CH_2), 2.24 (s, 3 H, CH_3), 2.04–1.97 (m, 1 H, CH_2), 1.81–1.75 (m, 1 H, CH_2), 1.71–1.61 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.4, 129.0, 128.0 (q, $^1J_{C,F}$ = 282.5 Hz), 56.06 (q, $^2J_{C,F}$ = 28.75 Hz), 46.1, 29.7, 28.5, 20.4 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.15 (d, J = 4.7 Hz, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3389, 3027, 2925, 2871, 1618, 1521, 1251, 1165, 1126, 809 cm^{-1}. $C_{12}H_{16}F_3NO$ (247.1): calcd. C 58.29, H 6.52, N,5.66; found C 58.07, H 5.39, N 6.38.

Methyl 4-(*m*-Toluidino)-5,5,5-trifluoropentanoate (3d): Compound **3d** (0.303 g) was obtained as a yellow oil in 55% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H

NMR (500 MHz, $CDCl_3$): δ = 7.07 (t, J = 7.5 Hz, 1 H, ArH), 6.60 (d, J = 7.5 Hz, 1 H, ArH), 6.46 (d, J = 8.0 Hz, 2 H, ArH), 4.06–3.97 (m, 1 H, CH), 3.65 (s, 3 H, OCH_3), 3.61 (d, J = 10 Hz, 1 H, NH), 2.54–2.47 (m, 2 H, CH_2), 2.28 (s, 3 H, CH_3), 2.24–2.17 (m, 1 H, CH_2), 1.93–1.85 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.4, 146.4, 139.3, 129.3, 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 119.8, 114.2, 110.4, 55.0 (q, $^2J_{C,F}$ = 28.75 Hz), 51.9, 29.7, 24.5, 21.6 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.26 (d, J = 9.4 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3390, 2954, 1733, 1608, 1525, 1491, 1259, 1168, 1124, 772, 693 cm^{-1}. $C_{13}H_{16}F_3NO_2$ (275.1): calcd. C 56.72, H 5.86, N 5.09; found C 56.57, H 5.68, N 5.30.

4-(*m*-Toluidino)-5,5,5-trifluoropentan-1-ol (4d): Compound **4d** (0.094 g) was obtained as a yellow oil in 19% yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (t, J = 7.5 Hz, 1 H, ArH), 7.19–7.12 (d, J = 7.5 Hz, 1 H, ArH), 6.78–6.74 (d, J = 8.0 Hz, 2 H, ArH), 4.16 (m, 1 H, CH), 3.73 (m, 2 H, CH_2), 3.69 (m, 2 H, CH_2), 2.38 (s, 3 H, CH_3), 2.12–2.04 (m, 1 H, CH_2), 1.85–1.76 (m, 1 H, CH_2), 1.76–1.67 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.5, 130.6, 127.4, 126.3 (q, $^1J_{C,F}$ = 282.5 Hz), 122.9, 118.3, 110.8, 62.0, 55.4 (q, $^2J_{C,F}$ = 28.75 Hz), 28.4, 26.3, 17.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –79.71 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3419, 3303, 2921, 1615, 1563, 1493, 1136, 781, 691 cm^{-1}. $C_{12}H_{16}F_3NO$ (247.1): calcd. C 58.29, H 6.52, N 5.66; found C 58.35, H 6.35, N, 5.39.

Methyl 4-(*o*-Toluidino)-5,5,5-trifluoropentanoate (3e): Compound **3e** (0.347 g) was obtained as a yellow oil in 63% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.11 (t, J = 8.0 Hz, 1 H, ArH), 7.07 (d, J = 7.5 Hz, 1 H, ArH), 6.73 (t, J = 7.5 Hz, 1 H, ArH), 6.67 (d, J = 8.0 Hz, 1 H, ArH), 4.12 (br., 1 H, CH), 3.64 (s, 3 H, OCH_3), 3.53 (br., 1 H, NH), 2.52–2.49 (m, 2 H, CH_2), 2.27–2.17 (m, 1 H, CH_2), 2.17 (s, 3 H, $ArCH_3$), 1.98–1.93 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 144.4, 130.8, 127.3, 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 122.4, 118.6, 110.9, 54.9 (q, $^2J_{C,F}$ = 28.75 Hz), 51.9, 29.9, 24.7, 17.6 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.26 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3419, 2954, 1735, 1608, 1521, 1255, 1124, 748 cm^{-1}. $C_{13}H_{16}F_3NO_2$ (275.1): calcd. C 56.72, H 5.86, N 5.09; found C 56.90, H, 5.59, N 5.32.

4-(*o*-Toluidino)-5,5,5-trifluoropentan-1-ol (4e): Compound **4e** (0.094 g) was obtained as a yellow oil in 19% yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.18 (t, J = 7.5 Hz, 1 H, ArH), 7.13 (t, J = 7.5 Hz, 1 H, ArH), 6.78–6.74 (m, 2 H, ArH), 4.06–4.03 (m, 1 H, CH), 3.69 (t, 2 H, OCH_2), 2.23 (s, 3 H, CH_3), 2.11–2.06 (m, 1 H, CH_2), 1.83–1.76 (m, 1 H, CH_2), 1.76–1.67 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.5, 130.6, 127.4, 126.3 (q, $^1J_{C,F}$ = 282.5 Hz), 122.9, 118.3, 110.8, 62.0, 55.4 (q, $^2J_{C,F}$ = 28.75 Hz), 28.4, 26.3, 17.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.12 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3428, 2928, 1606, 1519, 1481, 1256, 1127, 748, 699 cm^{-1}. $C_{12}H_{16}F_3NO$ (247.1): calcd. C 58.29, H 6.52, N 5.66; found C 58.03, H 6.41, N 5.44.

Methyl 5,5,5-Trifluoro-4-(*p*-fluorophenylamino)pentanoate (3f): Compound **3f** (0.374 g) was obtained as a pale-yellow oil in 67%yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.89 (t, 2 H, ArH), 6.60–6.58 (m, 2 H, ArH), 3.96–3.89 (m, 1 H, CH), 3.65 (s, 3 H, OCH_3), 3.60 (d, 1 H, NH), 2.57–2.45 (m, 2 H, CH_2), 2.22–2.16 (m, 1 H, CH_2), 1.93–1.85 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.4, 156.6 (d, $^1J_{C,F}$ = 235 Hz), 142.8 (d, $^4J_{C,F}$ = 2.5 Hz), 126.1 (q, $^1J_{C,F}$ = 282 Hz), 115.9 (d, $^2J_{C,F}$ = 22.5 Hz), 114.5 (d, $^3J_{C,F}$ = 7.5 Hz), 56.1 (q, $^2J_{C,F}$ = 29.2 Hz), 51.9, 29.8, 24.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.26 (d, J = 9.4 Hz, CF_3), –126.27 (m, ArF) ppm. IR (KBr): $\tilde{\nu}$ = 3392, 3039, 2955, 1729, 1614, 1511, 1441, 1168, 1124, 824, 769 cm^{-1}. $C_{12}H_{13}F_4NO_2$ (279.1): calcd. C 51.62, H 4.69, N 5.02; found C 51.41, H 4.55, N 5.31.

5,5,5-Trifluoro-4-(*p*-fluorophenylamino)pentan-1-ol (4f): Compound **4f** (0.070 g) was obtained as a yellow oil in 14% yield by flash column chromatography (hexane/ethyl acetate, 1:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.90 (t, 2 H, ArH), 6.55–6.62 (m, 2 H, ArH), 3.83 (m, 1 H, CH), 3.69 (t, 2 H, CH_2), 2.44 (br., 2 H, NH, OH), 2.04–1.99 (m, 1 H, CH_2), 1.76–1.17 (m, 1 H, CH_2), 1.82–1.65 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.6 (d, $^1J_{C,F}$ = 236.25 Hz), 143.0 (d, $^4J_{C,F}$ = 1.25 Hz), 125.2 (q, $^1J_{C,F}$ = 281 Hz), 116.0 (d, $^2J_{C,F}$ = 22.5 Hz),114.7 (d, $^3J_{C,F}$ = 7.5 Hz), 62.2, 56.8 (q, $^2J_{C,F}$ = 28.75 Hz), 28.5, 26.3 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.01 (d, J = 9.4 Hz, 3 F), 126.08 (m, ArF) ppm. IR (neat): $\tilde{\nu}$ = 3445, 2984, 2937, 1733, 1041, 1565, 127, 1026, 860, 776 cm^{-1}. M.p. 113.4–113.8 °C. MS: m/z = 266.00 $[M]^+$. $C_{11}H_{13}F_4NO$ (251.1): calcd. C 52.59, H 5.22, N 5.58; found C 52.68, H 5.45, N 5.45.

General Procedure for the Synthesis of Trifluoromethylated *N*-Aryl Lactams 9: To a solution of **3** (1.0 mmol) in THF (10 mL) was added NaH (1.1 mmol) under a nitrogen atmosphere at room temperature. After the reaction mixture was stirred for 2 h, the mixture was poured into saturated aqueous NH_4Cl solution and extracted with AcOEt (4 × 30 mL). The EtOAc extract was successively washed with saturated aqueous $NaHCO_3$ solution and brine, dried with $MgSO_4$, concentrated. Purification of the residue by column chromatography gave lactam **9**.

1-Phenyl-5-(trifluoromethyl)pyrrolidin-2-one (9a): Compound **9a** (0.215 g) was obtained as a colorless solid in 94% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 (t, J = 7.5 Hz, 2 H, ArH), 7.34–7.30 (m, 3 H, ArH), 7.29 (d, J = 7.5 Hz, 2 H, ArH), 4.65–4.59 (m, 1 H, CF_3CH), 2.83–2.76 (m, 1 H, CH), 2.60–2.45 (m, 2 H, CH_2), 2.35–2.29 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.5, 137.1, 129.3, 128.7, 125.3 (q, $^1J_{C,F}$ = 282.5 Hz), 121.9 (2 C), 61.0 (q, $^2J_{C,F}$ = 28.1 Hz), 29.7, 19.4 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.13 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3064, 2941, 1699, 1593, 1500, 1457, 762, 697 cm^{-1}. $C_{11}H_{10}F_3NO$ (229.2): calcd. C 57.64, H 4.40, N 6.11; found C 57.87, H 4.41, N 6.24.

1-(*p*-Methoxyphenyl)-5-(trifluoromethyl)pyrrolidin-2-one (9b): Compound **9b** (0.238 g) was obtained as a colorless solid in 92% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, J = 9.0 Hz, 2 H, ArH), 6.93 (d, J = 9.0 Hz, 2 H, ArH), 4.52–4.46 (m, 1 H, CF_3CH), 3.81 (s, 3 H, OCH_3), 2.79–2.72 (m, 1 H, CH_2), 2.58–2.43 (m, 2 H, CH_2), 2.33–2.28 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.8, 158.6, 129.8, 126.9, 125.3 (q, $^1J_{C,F}$ = 281.25 Hz), 114.6, 61.5 (q, $^2J_{C,F}$ = 31.25 Hz), 55.5, 29.5, 19.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.09 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3381, 2963, 1695, 1611, 1515, 1409, 837 cm^{-1}. M.p. 128.6–130.1 °C. MS: m/z = 259.00. $C_{12}H_{12}F_3NO_2$ (259.0): calcd. C 55.60, H 4.67, N 5.40; found C 55.87, H 4.51, N 5.21.

1-(*p*-Methylphenyl)-5-(trifluoromethyl)pyrrolidin-2-one (9c): Compound **9c** (0.214 g) was obtained as a colorless solid in 88% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.22–7.17 (m, 4 H, ArH), 4.58–4.52 (m, 1 H, CF_3CH), 2.78–2.71 (m, 1 H, CH), 2.56–2.43 (m, 2 H, CH), 2.34 (s, 3 H, CH_3), 2.30–2.238 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.8, 137.3, 134.6, 129.9, 127.7 (q, $^1J_{C,F}$ = 282.5 Hz), 125.2, 61.3 (q, $^2J_{C,F}$ = 31.25 Hz), 29.7, 21.1,

19.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.12 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3070, 2925, 1697, 1614, 1517, 1407, 1122, 834 cm^{-1}. M.p. 114.5–116.4 °C. $C_{12}H_{12}F_3NO$ (243.1): calcd. C 59.26, H 4.97, N 5.76; found C 59.50, H 5.14, N 5.51.

1-(*m*-Methylphenyl)-5-(trifluoromethyl)pyrrolidin-2-one (9d): Compound **9d** (0.207 g) was obtained as a colorless solid in 85% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.29 (t, J = 7.5 Hz, 1 H, ArH), 7.14 (s, 1 H, ArH), 7.10 (d, J = 7.5 Hz, 2 H, ArH), 4.62–4.56 (m, 1 H, CF_3CH), 2.82–2.74 (m, 1 H, CH_2), 2.59–2.44 (m, 2 H, CH_2), 2.37 (s, 3 H, CH_3), 2.34–2.29 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.5, 139.2, 136.9, 130.9, 128.2, 125.9, 125.3 (q, $^1J_{C,F}$ = 282.5 Hz), 122.1, 61.2 (q, $^2J_{C,F}$ = 31.25 Hz), 29.7, 21.4, 19.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –75.14 (d, J = 9.4 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3472, 2923, 1713, 1606, 1589, 1451, 1255, 1163, 1124, 797 cm^{-1}. $C_{12}H_{12}F_3NO$ (243.1): calcd. C 59.26, H 4.97, N 5.76; found C 59.17, H 5.08, N 5.84.

1-(*o*-Methylphenyl)-5-(trifluoromethyl)pyrrolidin-2-one (9e): Compound **9e** (0.218 g) was obtained as a pale-yellow oil in 90% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.12–7.06 (m 2 H, ArH), 6.73–6.66 (m, 2 H, ArH), 4.14–4.10 (m, 1 H, CF_3CH), 2.55 (t, J = 5.5 Hz, 1 H, CH_2), 2.25–2.20 (m, 1 H, CH_2), 2.16 (s, 3 H, CH_3), 1.96–1.91 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.6, 144.3, 130.8, 127.2, 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 122.5, 118.7, 110.9, 54.8 (q, $^2J_{C,F}$ = 29.2 Hz), 45.4, 29.9, 24.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.22 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3415, 2927, 1712, 1606, 1589, 1451, 1255, 1163, 1124, 749 cm^{-1}. $C_{12}H_{12}F_3NO$ (243.1): calcd. C 59.26, H 4.97, N 5.76; found C 59.08, H 4.80, N 5.54.

1-(*p*-Fluorophenyl)-5-(trifluoromethyl)pyrrolidin-2-one (9f): Compound **9f** (0.23 g) was obtained as a colorless solid in 93% yield by flash column chromatography (hexane/ethyl acetate, 2:1) on silica gel. ^1H NMR (500 MHz, CD_3COCD_3): δ = 7.51–7.49 (m, 2 H, ArH), 7.19 (t, 2 H, ArH), 5.12–5.06 (m, 1 H, CF_3CH), 2.70–2.58 (m, 2 H, CH_2), 2.51–2.47 (m, 1 H, CH_2), 2.31–2.24 (m, 1 H, CH_2) ppm. ^{13}C NMR (125 MHz, CD_3COCD_3): δ = 173.7, 160.6 (d, $^1J_{C,F}$ = 242.5 Hz), 134.3 (d, $^4J_{C,F}$ = 2.5 Hz), 126.8 (d, $^3J_{C,F}$ = 8.75 Hz), 126.1 (q, $^1J_{C,F}$ = 282.5 Hz), 115.4 (d, $^2J_{C,F}$ = 22.5 Hz), 60.2 (q, $^2J_{C,F}$ = 30 Hz), 18.7 ppm. ^{19}F NMR (470 MHz, CD_3COCD_3): δ = –75.83 (d, J = 4.7 Hz, CF_3), –117.30 (m, ArF) ppm. IR (KBr): $\tilde{\nu}$ = 3428, 2924, 1699, 1605, 1513, 1409, 1161, 1119, 838 cm^{-1}. MS: m/z = 247.00. $C_{11}H_9F_4NO$ (247.1): calcd. C 53.45, H 3.67, N 5.67; found C 53.25, H 3.84, N 5.87.

1-Phenyl-4-(trifluoromethyl)azetidin-2-one (9h): Compound **9h** (0.042 g) was obtained as a colorless solid in 18% yield by flash column chromatography (hexane/ethyl acetate, 6:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.20 (t, J = 7.5 Hz, 2 H, ArH), 6.78 (t, J = 7.5 Hz, 1 H, ArH), 6.67 (d, 2 H, ArH), 3.90–3.84 (m, 1 H, CF_3CH), 2.53–2.40 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.4, 137.1, 132.7, 129.5, 126.2, 125.2 (q, $^1J_{C,F}$ = 281.3 Hz), 60.8 (q, $^2J_{C,F}$ = 31.3 Hz), 31.6 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –74.35 (d, J = 9.4 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3075, 2932, 1691, 1587, 1489, 1453, 751, 692 cm^{-1}. $C_{10}H_8F_3NO$ (215.2): calcd. C 55.82, H 3.75, N 6.51; found C 55.70, H 3.64, N 6.76.

1-Phenyl-6-(trifluoromethyl)piperidin-2-one (9i): Compound **9i** (0.238 g) was obtained as a colorless solid in 91% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.20 (t, J = 7.5 Hz, 2 H, ArH), 6.78 (t, J = 7.5 Hz, 1 H, ArH), 6.67 (d, J = 8.0 Hz, 2 H, ArH), 3.89–3.89 (m, 1 H, CF_3CH), 2.43–2.39 (m, 2 H, CH_2), 1.97–1.90 (m, 2 H, CH_2), 1.75–1.58 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.2, 140.1, 128.8, 127.4, 124.9, 120.4 (q, $^1J_{C,F}$ = 272.5 Hz), 55.5 (q, $^2J_{C,F}$ = 28.8 Hz), 30.9, 26.9, 20.2 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.26 (d, J = 9.4 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3047, 2947, 1689, 1588, 1499, 1447, 750, 696 cm^{-1}. $C_{12}H_{12}F_3NO$ (243.2): calcd. C 59.26, H 4.97, N 5.76; found C 59.35, H 4.80, N, 5.89.

1-Phenyl-7-(trifluoromethyl)azepan-2-one (9j): Compound **9j** (0.239 g) was obtained as a colorless solid in 87% yield by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.19 (t, J = 7.5 Hz, 2 H, ArH), 6.77 (t, J = 7.5 Hz, 1 H, ArH), 6.66 (d, J = 7.5 Hz, 2 H, ArH), 3.88–3.84 (m, 1 H, CF_3CH), 2.35 (t, J = 7.5 Hz, 2 H, CH_2), 1.94–1.81 (m, 1 H, CH), 1.69–1.56 (m, 4 H, CH_2), 1.47–1.43 (m, 1 H, CH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 179.0, 146.6, 129.4, 126.1 (q, $^1J_{C,F}$ = 281.3 Hz), 118.8, 113.3, 55.5 (q, $^2J_{C,F}$ = 28.8 Hz), 33.5, 29.3, 25.0, 24.2 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –76.12 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 3037, 2937, 1688, 1590, 1492, 1429, 752, 688 cm^{-1}. $C_{13}H_{14}F_3NO$ (257.3): calcd. C 60.70, H 5.49, N 5.44; found C 60.91, H 5.62, N 5.59.

4-Amino-5,5,5-trifluoropentanoic Acid (10): To a 100-mL, three-necked, round-bottomed flask was added **3a** (78 mg, 0.3 mmol), CH_3CN (5 mL), H_2O (5 mL), and ammonium ceric nitrate (0.015 mmol). After the reaction mixture was stirred for 2 h, concentrated HCl (5 mL) was added, and the reaction mixture was stirred for another 1 h. Once the reaction was complete, the mixture was poured into H_2O (10 mL) and anhydrous ether (20 mL), extracted with saturated aqueous NaCl solution (3 × 30 mL), dried with $MgSO_4$, and concentrated. The residue was then purified by column chromatography (methanol/ethyl acetate, 1:1) to give product **10** (18 mg, 36% yield). ^1H NMR (500 MHz, [D_6]acetone): δ = 7.57 (br., 1 H, NH), 4.34 (m, 1 H, CF_3CH), 2.49 (m, 1 H, CH_2), 2.39 (m, 1 H, CH_2), 2.27 (m, 2 H, $COCH_2$) ppm. ^{13}C NMR (125 MHz, [D_6]acetone): δ = 177.63, 126.1 (q, $^1J_{C,F}$ = 277 Hz), 54.56 (q, $^2J_{C,F}$ = 31 Hz), 28.1, 20.3 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –78.71 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3323, 2929, 2857, 1717, 1400, 1173, 842 cm^{-1}. MS (EI, 70 eV): m/z (%) = 171 (20) $[M]^+$. HRMS: calcd. for $C_5H_8F_3NO_2$ [M + 1] 171.0507; found 171.0506.

1-Phenyl-2-(trifluoromethyl)pyrrolidine (11): To a solution of **9a** (10 mmol) in dry THF (20 mL) was added $NaBH_3CN$ (80 mmol) and $BF_3{\cdot}Et_2O$ (100 mmol) under a nitrogen atmosphere, and the mixture was stirred at reflux for 4 h. Once the reaction was complete, the mixture was poured into saturated aqueous NH_4Cl solution and extracted with AcOEt (4 × 30 mL). The AcOEt extract was successively washed with saturated aqueous $NaHCO_3$ solution and brine, dried with $MgSO_4$, and concentrated. Purification of the residue by flash column chromatography (hexane/ethyl acetate, 4:1) on silica gel gave **11** a colorless solid (1.61 g, 75% yield). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.26 (t, 2 H, ArH), 6.80 (q, 2 H, ArH), 4.24–4.18 (m, 1 H, CF_3CH), 3.63 (t, 1 H, CH), 3.21 (q, 1 H, CH), 2.24–2.19 (m, 2 H, CH_2), 2.08–1.99 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.6, 129.2, 126.9 (q, $^1J_{C,F}$ = 282.5 Hz), 118.0, 113.1, 59.9 (q, $^2J_{C,F}$ = 30 Hz), 50.0, 27.0, 23.6 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = –73.8 (d, J = 4.7 Hz, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 2927, 1478, 1398, 1159, 1132, 842 cm^{-1}. $C_{11}H_{12}F_3N$ (215.2): calcd. C 61.39, H 5.62, N 6.51; found C 61.08, H 5.47, N 6.69.

CCDC-704555 (for **9b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H, ^{13}C, and ^{19}F NMR spectra for the prepared compounds; references for known compounds.

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