A One-Pot Synthesis of Doubly Unsaturated Trifluoromethyl Amines: Easy Access to CF_3-Substituted Piperidines

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A straightforward route to trifluoromethyl analogs of piperidines is described. These syntheses involve a Barbier-type allylation reaction of trifluoroacetaldimines, followed by *N*-allylation (one-pot), and ring-closing metathesis. An efficient asymmetric version is also reported (>98% *de*). Functionalized heterobicyclic compounds can also be obtained by a Pauson–Khand reaction.

Piperidines are an important class of compounds, and this heterocycle pattern is found in many therapeutic agents.[1] In this frame, the introduction of novel substituents on these heterocycles has been the focus of many investigations.[2] Among them, trifluoromethyl groups can greatly modify the biological properties of the target molecule.[3] The building-block strategy is a general approach to trifluoromethylated target compounds. Thus, aldimines derived from fluoral[4] in cycloaddition reactions have been shown to be a rich source of nitrogen heterocycles bearing a CF_3 group, especially β-lactams,[5] aziridines,[6] quinolines, and piperidinones.[7] An alternative route to the piperidine pattern involves ring-closing metathesis (RCM)[8] of doubly unsaturated amines. Recently, Billard and Langlois have successfully applied RCM to the preparation of nonchiral, CF_3-substituted piperidines.[9] However, a limitation of the methodology stemmed from the protection/deprotection steps required to access the substrates. In this context, a fast and general methodology to give the starting doubly unsaturated trifluoromethylamines would be highly desirable. Along these lines, we report here our investigations on a simple, one-pot methodology leading to doubly unsaturated trifluoromethylated amines, and their subsequent cyclization in RCM and Pauson–Khand reactions. The asymmetric synthesis of a nonracemic CF_3-containing piperidine (>98% *de*) is also described.

Results and Discussion

In a previous communication we disclosed the efficient synthesis of homoallyl trifluoromethylamines **4** and **5** by Barbier-type allylation of trifluoromethyl aldimines **1** and **2**, respectively (Scheme 1).[10,11] This reaction proceeds (75–97% yields) under mild conditions (at room temperature in DMF, or at reflux in THF) with allyl bromides as reaction partners and activated zinc (Zn*) as promoter.[12] Moreover, starting from the enantiopure aldimine **3**, the corresponding homoallylamines **4**–**6** were obtained with high *de* (up to 98%).[13] We also found that the propargylation reaction was successful under the same conditions (**4d**, **5d**).[14] Consequently, this approach allows the synthesis of a great diversity of substituted homoallyl (and homopropargyl) amines.

In order to access to doubly unsaturated amines, we studied the *N*-allylation reaction of homoallylamines **4a**–**d** and **5a**. Previous examples of *N*-allylation of α-trifluoromethylamines concerned only substrates with the nitrogen atom activated by an acyl group.[9] Nevertheless, the direct *N*-allylation of **4a**–**d** and **5a** was investigated under simple conditions: $NaHCO_3$ and allyl bromides, in refluxing acetonitrile, in the presence of a catalytic amount of KI (Table 1). Despite the fact that very long reaction times were required (3–5 days), very good yields of the expected products **7**, **9**, and **10** (79–80%) were obtained. The reaction was less efficient with the bulkier amine **4b**, yielding 42% of **8**, and even less so with aromatic amine **5a** (30% conversion after 10 days). In this latter case, replacing the previous base by NaH and performing the reaction overnight in DMF (100 °C) provided the corresponding product **11** in good yield (83%).

According to the mechanism of the Barbier-type reaction, a zinc amide should be the primary product of the Barbier allylation of aldimines. Such a species should exhibit a pronounced nucleophilic character. The *N*-allylation was thus attempted in situ (Table 2). This one-pot, Zn-mediated *C*-allylation/*N*-allylation sequence was performed

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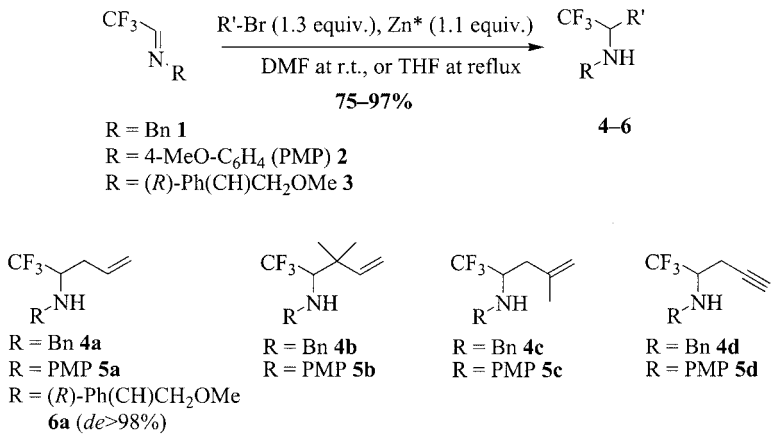
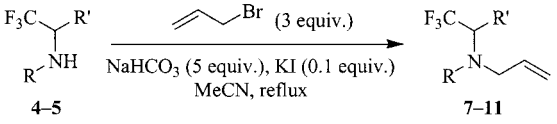
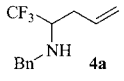
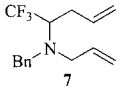
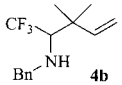
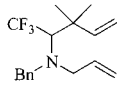
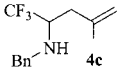
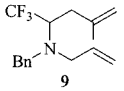
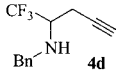
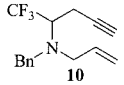
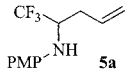
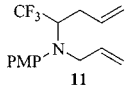


Scheme 1. Allylation and propargylation reaction of CF_3-containing aldimines **1**–**3**.

Table 1. Synthesis of doubly unsaturated amines **7**–**11**.



Entry	Amine	Time [d]	Conv. [%][a]	Product	Yield [%][b]
1	 **4a**	3	95	 **7**	80
2	 **4b**	5.5	58	 **8**	42
3	 **4c**	3.5	93	 **9**	80
4	 **4d**	4.5	87	 **10**	79
5[c]	 **5a**	0.7	91	 **11**	83

[a] Measured by GC analyses. [b] Yield of isolated product. [c] Reaction performed with NaH in DMF (100 °C).

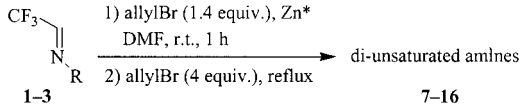
with aldimines **1**–**3** in DMF. In a preliminary experiment, the aldimine **1** was treated at room temperature in the presence of activated Zn (1.3 equiv.) with an excess of allyl bromide (5 equiv.), and the reaction medium was heated to reflux. Under these conditions, the allyl homoallylamine **7** was obtained in 70% yield (entry 1). Interestingly, this procedure also allowed the introduction of two different allyl substituents (entries 2–5, 7, and 8). The first step was performed at room temperature in DMF with 1.4 equiv. of allyl bromide and 1.5 equiv. of zinc, then the second allyl bromide (4 equiv.) was added to the mixture and the reaction was heated at reflux. With both methallyl bromide/allyl bromide (entry 2) and allyl bromide/propargyl bromide (entry 3), the corresponding amines **9** and **12** were obtained, after five hours, in good yields (63% and 65%, respectively). However, with other pairs of allyl bromides (entries 4–8) the reaction times were longer (12–18 h) and decomposition of both starting materials and expected adducts occurred, leading to a mixture of products. Nevertheless, we found that the reaction could be easily improved by simple addition of copper iodide (20 mol-%): the reaction times were shorter (1–3 h) and the corresponding amines were obtained in moderate to good yields (56–86%). To our delight, the reaction also gave good results with the chiral aldimine **3**. In this case, 1.5 equivalents of CuI was required, and the reaction had to be stopped before the total conversion of the homoallylamine intermediate in order to avoid complete decomposition of the product **16**. Nevertheless, **16** was obtained in 54% yield and with an excellent 98% *de* (entry 9).

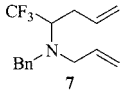
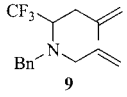
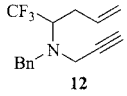
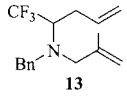
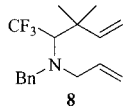
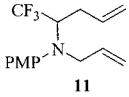
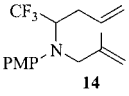
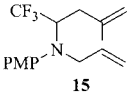
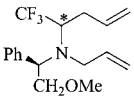
This process exhibits significant advantages over previous examples since various doubly unsaturated CF_3-containing amines can be prepared in a one-pot procedure and isolated in good yields (54–86% over 2 steps). Moreover, the reaction can be performed with commercially available allyl partners, which makes it suitable for larger scale preparation.

The products of the bis-allylation reaction **7**–**16** were then subjected to a ring-closing metathesis reaction (Table 3).

In the presence of Grubbs catalyst(5–10 mol-%), the allyl homoallyl adducts easily reacted, at room temperature, to afford the expected CF_3-containing dehydropiperidine derivatives in excellent yields (>89% in most cases). However, with the *N*-methallylamines **13** and **14**, the reaction required solvent reflux and longer reaction times to proceed (entries 4 and 6). The diastereo-enriched substrate **16** underwent the cyclization reaction to yield the corresponding dihydropiperidine derivative **24** (98% yield, 98% *de*).

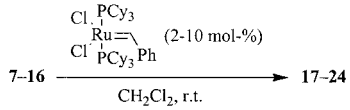
Table 2. One-pot synthesis of doubly unsaturated amines **7**–**16**.[a]

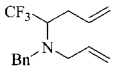
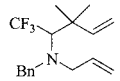
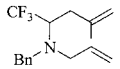
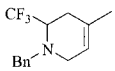
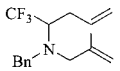
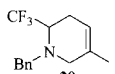
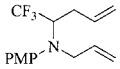
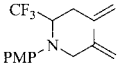
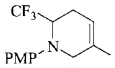
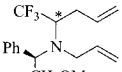
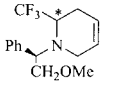
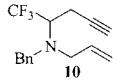
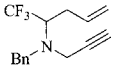
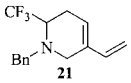


Entry	Imine	AllylBr	Time [h]	Product 7–16	Yield [%]
1	1	1) Br 2) Br	3	 **7**	70
2	1	1) Br 2) Br	5	 **9**	63
3	1	1) Br 2) Br	5	 **12**	65
4[b]	1	1) Br 2) Br	3	 **13**	56
5[b]	1	1) Br 2) Br	3	 **8**	57
6[b]	2	1) Br 2) Br	3	 **11**	61
7[b]	2	1) Br 2) Br	2	 **14**	56
8[b]	2	1) Br 2) Br	1	 **15**	86
9[c,d]	3	1) Br 2) Br	1	 **16**	54[e]

[a] Reactions performed on a 2 mmol scale. [b] 20 mol-% of CuI. [c] 1.5 equiv. of CuI. [d] 30% of homoallylamine **6c** was recovered. [e] 98% *de*.

Table 3. Cyclization of **7**–**16** by ring-closing metathesis.

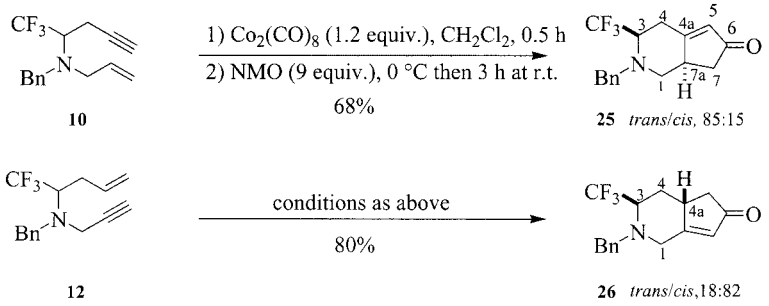


Entry	Diene	Cat [mol-%]	Time [h]	Product	Yield [%]
1	 **7**	5	2	 **17**	95
2	 **8**	5	2	 **18**	96
3	 **9**	5	2	 **19**	93
4	 **13**	10[a]	48	 **20**	89
5	 **11**	5	2	 **22**	90
6[b]	 **14**	6[a]	48	 **23**	41
7	 **16**	8[a]	3.5	 **24**	98[c]
8	 **10**	10	–	–	–
9	 **12**	5	12	 **21**	95

[a] Catalyst was added in three portions over the time indicated. [b] Reaction performed at reflux. [c] *de* > 98%.

The RCM was also studied with enynes as substrates, under similar conditions. Unfortunately, the homopropargyl allylamine **10** did not undergo cyclization, and starting material was recovered unchanged (entry 8). Heating the reaction to reflux or use of a second-generation Grubbs catalyst, also failed to give satisfactory results. Surprisingly, its isomer, the homoallyl propargylamine **12**, provided the piperidine **21** quantitatively (95% yield), leading to a dienic molecule (entry 9).

The enynes **10** and **12** can also be considered as good substrates for a Pauson–Khand reaction.[15] Under classical stoichiometric conditions [$Co_2(CO)_8$, followed by the addition of *N*-methylmorpholine oxide], both substrates **10** and **12** reacted very well, and in a similar fashion. The bicyclic products **25** and **26** resulting from the formal [2+2+1] cycloaddition were obtained in 68% (85:15 ratio of *trans*/*cis* stereoisomers) and in 80% yield (18:82 ratio of *trans*/*cis* stereoisomers), respectively (Scheme 2).[16] This transformation allows access to new, functionalized heterobicyclic molecules bearing a CF_3 group.



10 **25** *trans*/*cis*, 85:15

12 **26** *trans*/*cis*, 18:82

Scheme 2. Syntheses of CF_3-containing heterobicyclic compounds **25** and **26** by a Pauson–Khand reaction.

Conclusions

In summary, we have set up a simple and straightforward route to various trifluoromethyl-containing nitrogen heterocycles by ring-closing metathesis and Pauson–Khand reactions, including an asymmetric version (98% *de*). One of the strong features of this synthesis is the simple preparation of the substrates (doubly unsaturated trifluoromethylamines) by an original *C*-allylation/*N*-allylation one-pot procedure starting from easily accessible materials (CF_3-containing aldimines and allyl bromides).

Experimental Section

General Remarks: All reactions were performed in oven-dried glassware under an inert atmosphere of argon. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ on a 200 or a 400 MHz multinuclear spectrometer. ^{19}F NMR spectra are referenced to external $CFCl_3$, and ^{1}H and ^{13}C NMR spectra to TMS. In all NMR measurements $CDCl_3$ was used as a solvent. Elemental analyses were performed by the Service de Microanalyses at the Faculté de Pharmacie, Châtenay-Malabry. Diastereomeric ratios and diastereomeric excesses were determined by ^{19}F NMR spectroscopy and GC analysis.

Synthesis of Benzyl[1-(trifluoromethyl)but-3-ynyl]amine (4d):[17] The imine **1** (1.03 g, 5.5 mmol) and propargyl bromide (1.06 g, 7.16 mmol) were dissolved in DMF (10 mL). The solution was cooled to 0 °C, then coarse zinc powder[18] (467 mg, 7.16 mmol) was added, followed by 2 drops of TMSCl. The reaction mixture was then slowly warmed to room temperature. After 45 min (the reaction was monitored by GC) the medium was cooled to 0 °C and hydrolyzed with a saturated aqueous solution of NH_4Cl (20 mL), then extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$, filtered, and the solvents were evaporated. The residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt, 9:1) to afford compound **4d** as a colorless liquid (944 mg, 76%). ^{1}H NMR: δ = 2.0 (br. s, 1 H), 2.3 (t, J = 2.6 Hz, 1 H), 2.7 (ddd, J = 17.0, 7.6, 2.6 Hz, 1 H), 2.9 (ddd, J = 17.0, 4.8, 2.8 Hz, 1 H), 3.5 (m, 1 H), 4.2 (d, J = 13.0 Hz, 1 H), 4.3 (d, J = 13.0 Hz, 1 H), 7.4–7.6 (m, 5 H) ppm. ^{13}C NMR: δ = 19.3 (q, $^3J_{C,F}$ = 3.2 Hz, CF_3CHCH_2), 51.9, 57.1 (q, $^2J_{C,F}$ = 28.0, CF_3CH), 71.2, 78.6, 126.0 (q, $^1J_{C,F}$ = 284.0 Hz, CF_3), 127.3, 128.2, 128.4, 139.2 ppm. ^{19}F NMR: δ = –75.1 (d, $J_{H,F}$ = 7.0 Hz, CF_3) ppm. $C_{12}H_{12}F_3N$ (227.23): calcd. C 63.43, H 5.32, N 6.16; found C 63.80, H 5.52, N 6.01.

Synthesis of 4-Methoxyphenyl[1-(trifluoromethyl)but-3-ynyl]amine (5d): The imine **2** (1.12 g, 5.5 mmol) and propargyl bromide (1.06 g, 7.16 mmol) were dissolved in DMF (10 mL). The solution was cooled to 0 °C, then coarse zinc powder (467 mg, 7.16 mmol) was added, followed by 2 drops of TMSCl. The reaction was then slowly warmed to room temperature. After 45 min (the reaction was monitored by GC), the mixture was cooled to 0 °C and hydrolyzed with a saturated aqueous solution of NH_4Cl (20 mL), then extracted with Et_2O (3×20 mL). The organic layer was washed with brine (30 mL), dried with $MgSO_4$, filtered, and the solvents were evaporated. The residue was then purified by flash chromatography over silica gel (petroleum ether/AcOEt, 9:1) to afford compound **5d** as a colorless liquid (1.06 g, 79%).^{1}H NMR: δ = 2.1 (t, J = 2.6 Hz, 1 H), 2.6 (ddd, J = 17.0, 6.4, 2.6 Hz, 1 H), 2.8 (ddd, J = 17.0, 5.2, 2.8 Hz, 1 H), 3.7 (s, 3 H), 3.9 (m, 1 H), 6.7 (d, J = 9.2 Hz, 2 H), 6.8 (d, J = 9.2 Hz, 2 H) ppm; NH not observed. ^{13}C NMR: δ = 19.6 (q, $^3J_{C,F}$ = 2.5 Hz, CF_3CHCH_2), 55.4, 55.9 (q, $^2J_{C,F}$ = 29 Hz, CF_3CH), 71.7, 77.9, 114.8, 116.0, 125.5 (q, $^1J_{C,F}$ = 283 Hz, CF_3), 139.9, 153.5 ppm. ^{19}F NMR: δ = –69.5 (d, $J_{H,F}$ = 8.7 Hz, CF_3) ppm. $C_{12}H_{22}F_3NO$ (243.23): calcd. C 59.26, H 4.97, N 5.76; found C 58.95, H 4.81, N 5.52.

General Procedure for the *N*-Allylation Reaction. Synthesis of Compounds 7–11: The allyl bromide (3 mmol), $NaHCO_3$ (5 mmol), and KI (0.1 mmol) were added to a solution of homoallylic or homopropargylic amine **4**/**5** (1 mmol) in MeCN (3 mL), and the reaction mixture was heated at reflux (the reaction was monitored by GC). The mixture was then cooled to room temperature, brine was added (10 mL), and the mixture extracted with Et_2O (3×10 mL). The combined organic phases were dried with $MgSO_4$, and the solvents evaporated. The crude product was purified over silica gel (petroleum ether) to afford di-ω-unsaturated amine.

***N*-Allyl-*N*-benzyl[1-(trifluoromethyl)but-3-enyl]amine (7):** Amine **4a** (229 mg, 1 mmol), allyl bromide (363 mg, 3 mmol), $NaHCO_3$ (420 mg, 5 mmol), and KI (17 mg, 0.1 mmol) in MeCN (3 mL) were heated at reflux for 3 d. After purification, compound **7** was obtained as a colorless liquid (215 mg, 80%). ^{1}H NMR: δ = 2.6 (m, 2 H), 3.5 (m, 3 H), 3.9 (d, J = 14.0 Hz, 1 H), 4.2 (d, J = 14.0 Hz, 1 H), 5.3 (m, 4 H), 5.9 (m, 2 H), 7.3–7.5 (m, 5 H) ppm. ^{13}C NMR: δ = 30.9 (q, $^3J_{C,F}$ = 1.6 Hz), 53.1, 53.8, 59.3 (q, $^2J_{C,F}$ = 25.0 Hz), 117.2, 117.6, 127.0, 127.6 (q, $^1J_{C,F}$ = 291.0 Hz, CF_3), 128.2, 128.7, 134.5, 136.3, 139.3 ppm. ^{19}F NMR: δ = –69.5 (d, $J_{H,F}$ = 8.7 Hz, CF_3) ppm. $C_{15}H_{18}F_3N$ (269.31): calcd. C 66.90, H 6.74, N 5.20; found C 67.06, H 6.82, N 5.32.

***N*-Allyl-*N*-benzyl[2,2-dimethyl-1-(trifluoromethyl)but-3-enyl]amine (8):** Amine **4b** (257 mg, 1 mmol), allyl bromide (363 mg, 3 mmol), $NaHCO_3$ (420 mg, 5 mmol), and KI (17 mg, 0.1 mmol) in MeCN (3 mL) were heated at reflux for 5.5 d. After purification, compound **8** was obtained as a colorless liquid (124 mg, 42%). ^{1}H NMR: δ = 1.1 (m, 6 H), 3.1 (m, 2 H), 3.5 (q, $J_{H,F}$ = 8.0 Hz, 1 H), 3.7 (dq, J = 14, 1.5 Hz, 1 H), 4.1 (m, 1 H), 4.9 (dd, J = 15.2, 1.3 Hz, 2 H), 5.2 (dd, J = 15, 8 Hz, 2 H), 5.9 (m, 2 H), 7.2–7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 25.7, 26.1, 29.6, 40.3, 66.7 (q, $^2J_{C,F}$ = 22 Hz),

112.2, 117.6, 125.2, 128.1, 128.4 (q, $^1J_{C,F}$ = 294 Hz), 136.6, 144.4 ppm. ^{19}F NMR: δ = –59.5 (d, $J_{H,F}$ = 8.0 Hz, CF_3) ppm. $C_{17}H_{22}F_3N$ (297.37): calcd. C 68.67, H 7.46, N 4.71; found C 68.80, H 7.54, N 4.88.

***N*-Allyl-*N*-benzyl[3-methyl-1-(trifluoromethyl)but-3-enyl]amine (9):** Amine **4c** (243 mg, 1 mmol), allyl bromide (363 mg, 3 mmol), $NaHCO_3$ (420 mg, 5 mmol), and KI (17 mg, 0.1 mmol) in MeCN (3 mL) were heated at reflux for 3.5 d. After purification, compound **9** was obtained as a colorless liquid (226 mg, 80%). ^{1}H NMR:δ = 1.7 (s, 3 H), 2.4 (dd, *J* = 14.5, 4.8 Hz, 1 H), 2.6 (dd, *J* = 14.5, 10 Hz, 1 H), 3.4 (m, 3 H), 3.7 (d, *J* = 14.0 Hz, 1 H), 4.1 (d, *J* = 14.0 Hz, 1 H), 4.85 (s, 1 H), 4.94 (s, 1 H), 5.20 (dq, *J* = 10.0, 1.3 Hz, 1 H), 5.24 (dq, *J* = 14.0, 1.3 Hz, 1 H), 5.7 (m, 1 H), 7.2–7.5 (m, 5 H) ppm. ^{13}C NMR: δ = 21.5, 34.9 (q, $^3J_{C,F}$ = 1.6 Hz), 53.0, 53.8, 57.3 (q, $^2J_{C,F}$ = 25 Hz), 114.1, 117.7, 127.1, 127.8 (q, $^1J_{C,F}$ = 291 Hz), 128.2, 128.8, 136.5, 139.4, 141.0 ppm. ^{19}F NMR: δ = –69.1 (d, $J_{H,F}$ = 8.3 Hz, CF_3) ppm. $C_{16}H_{20}F_3N$ (283.34): calcd. C 67.83, H 7.11, N 4.94; found C 68.05, H 7.20, N 5.02.

***N*-Allyl-*N*-benzyl[1-(trifluoromethyl)but-3-ynyl]amine (10):** Amine **4d** (227 mg, 1 mmol), allyl bromide (363 mg, 3 mmol), $NaHCO_3$ (420 mg, 5 mmol), and KI (17 mg, 0.1 mmol) in MeCN (3 mL) were heated at reflux for 4.5 d. After purification, compound **10** was obtained as a colorless liquid (211 mg, 79%). ^{1}H NMR: δ = 1.9 (t, *J* = 2.6 Hz, 1 H), 2.38 (ddd, *J* = 17.3, 5.4, 2.6 Hz, 1 H),2.5 (dd, *J* = 17.3, 2.6 Hz, 1 H), 3.2 (m, 2 H), 3.4 (m, 1 H), 3.6 (d, *J* = 13.8 Hz, 1 H), 3.8 (d, *J* = 13.8 Hz, 1 H), 5.0 (dq, *J* = 10.0, 1.5 Hz, 1 H), 5.05 (dq, *J* = 14.0, 1.5 Hz, 1 H), 5.6 (m, 1 H), 7.0–7.3 (m, 5 H) ppm. ^{13}C NMR: δ = 16.8 (q, $^3J_{C,F}$ = 2.2 Hz), 53.4, 53.9, 58.6 (q, $^2J_{C,F}$ = 26 Hz), 70.6, 80.0, 117.9, 126.5 (q, $^1J_{C,F}$ = 289 Hz), 127.1, 128.2, 128.6, 136.1, 139.0 ppm. ^{19}F NMR: δ = –71.0 (d, $J_{H,F}$ = 7.9 Hz, CF_3) ppm. $C_{15}H_{16}F_3N$ (267.30): calcd. C 67.40, H 6.03, N 5.24; found C 67.62, H 6.11, N 5.33.

***N*-Allyl-*N*-(4-methoxyphenyl)[1-(trifluoromethyl)but-3-enyl]amine (11):** NaH 60% (245 mg, 6.12 mmol) was slowly added to a solution of allyl bromide (987 mg, 8.16 mmol) and amine **5a** (500 mg, 2.05 mmol) in DMF (2 mL), under an argon atmosphere, at 0 °C in a sealed tube. The reaction was then heated to 100 °C. After 17 h, the solution was cooled to 0 °C, hydrolyzed with a saturated aq. NH_4Cl solution (30 mL), and extracted with Et_2O (3 × 30 mL). The combined organic phases were dried ($MgSO_4$) and the solvents evaporated. The crude product was purified over silica gel (petroleum ether/AcOEt, 70:30) to afford compound **11** as a brown oil (487 mg, 83%). ^{1}H NMR: δ = 2.5 (m, 2 H), 3.7 (s, 3 H), 3.9 (d, *J* = 5.4 Hz, 2 H), 4.1 (m, 1 H), 5.1 (m, 4 H), 5.8 (m, 2 H), 6.9 (m, 4 H) ppm. ^{13}C NMR: δ = 34.6, 48.2, 55.3, 62.7 (q, $^2J_{C,F}$ = 30 Hz), 114.2, 116.6, 118.0, 119.2, 126.4 (q, $^1J_{C,F}$ = 290 Hz), 133.3, 135.5, 143.9, 153.5 ppm. ^{19}F NMR: δ = –72.1 (d, $J_{H,F}$ = 7.9 Hz, CF_3) ppm. $C_{15}H_{18}F_3NO$ (285.30): calcd. C 63.15, H 6.36, N 4.91; found C 64.03, H, 6.21, N 4.95.

One-Pot Double Allylation Reaction. Synthesis of *N*-Allyl-*N*-benzyl[1-(trifluoromethyl)but-3-enyl]amine (7): Allyl bromide (1.3 g, 10.8 mmol), coarse zinc powder (196 mg, 3.0 mmol), and two drops of TMSCl were addedto a solution of imine **1** (374 mg, 2 mmol) in DMF (4 mL). After 1 h at room temperature, the mixture was refluxed for 3 h, then treated with a saturated aq. NH_4Cl solution(30 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and the solvents were evaporated. The residue was purified by chromatography over silica gel (petroleum ether/CH_2Cl_2, 8:2) to afford the amine **7** as a colorless liquid (377 mg, 70%).

Typical Procedure for the One-Pot Double Allylation Reaction. Synthesis of *N*-Allyl-*N*-benzyl[3-methyl-1-(trifluoromethyl)but-3-enyl]amine (9): Methallyl bromide (378 mg, 0.25 mL, 2.8 mmol), coarse zinc powder (195 mg, 3 mmol), and two drops of TMSCl were added to a solution of imine **1** (374 mg, 2 mmol) in DMF (3 mL). After 1 h, allyl bromide (968 mg, 8 mmol) was added. The mixture was then refluxed for 5 h, the solution was hydrolyzed with a saturated aqueous solution of NH_4Cl (30 mL), and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried with $MgSO_4$, the solvents were evaporated, and the residue was purified by chromatography over silica gel (petroleum ether/CH_2Cl_2, 3:1) to afford amine **9** as a colorless liquid (356 mg, 63%).

***N*-Allyl-*N*-benzyl[2,2-dimethyl-1-(trifluomethyl)but-3-enyl]amine (8):** From imine **1** (374 mg, 2 mmol), dimethylallyl bromide (417 mg, 2.8 mmol), allyl bromide (968 mg, 8 mmol), and CuI (76 mg, 0.4 mmol), **8** was obtained as a brown oil (338 mg, 57%).

***N*-Allyl-*N*-(4-methoxyphenyl)[1-(trifluoromethyl)but-3-enyl]amine (11):** From imine **2** (406 mg, 2 mmol), allyl bromide (1.3 g, 10.8 mmol), and CuI (76 mg, 0.4 mmol), **11** was obtained as a brown oil (347 mg, 61%).

***N*-Benzyl-*N*-prop-2-ynyl[1-(trifluoromethyl)but-3-enyl]amine (12):** From imine **1** (374 mg, 2 mmol), allyl bromide (339 mg, 2.8 mmol), and propargyl bromide (952 mg, 8 mmol), **12** was obtained as a brown oil (347 mg, 65%). ^{1}H NMR:δ = 2.2 (t, *J* = 2.4 Hz, 1 H), 2.4 (m, 1 H), 3.4 (d, *J* = 2 Hz, 2 H), 3.5 (m, 1 H), 3.7 (d, *J* = 13.6 Hz, 1 H), 4.0 (d, *J* = 13.6 Hz, 1 H), 5.1 (m, 2 H), 5.8 (m, 1 H), 7.1–7.3 (m, 5 H) ppm. ^{13}C NMR: δ = 30.7 (q, *J* = 1.7 Hz), 39.7 (q, *J* = 1.4 Hz), 53.6 (q, *J* = 1.2 Hz), 61 (q, $^2J_{C,F}$ = 26 Hz), 72.5, 117.5, 127.1 (q, $^1J_{C,F}$ = 289 Hz), 127.3, 128.4, 128.6, 134.2, 138.2 (q, *J* = 0.6 Hz) ppm. ^{19}F NMR: δ = –70.2 (d, *J* = 8.1 Hz, CF_3) ppm. $C_{15}H_{16}F_3N$ (267.30): calcd. C 67.40, H 6.03, N 5.24; found C 67.55, H 6.10, N 5.32.

***N*-Benzyl-*N*-(2-methylallyl)[1-(trifluoromethyl)but-3-enyl]amine (13):** From imine 1 (374 mg, 2 mmol), allyl bromide (339 mg, 2.8 mmol), methallyl bromide (1.08 g, 8 mmol), and CuI (76 mg, 0.4 mmol), **13** was obtained as a brown oil (317 mg, 56%). ^{1}H NMR: δ = 1.9 (s, 3 H), 2.6 (m, 2 H), 3.4 (s, 2 H), 3.5 (m, 1 H), 3.9 (d, *J* = 14.0 Hz, 1 H), 4.1 (d, *J* = 14.0 Hz, 1 H), 4.8 (m, 1 H), 4.9 (m, 1 H), 5.02 (d, *J* = 8.8 Hz, 1 H), 5.04 (d, *J* = 17.0 Hz, 1 H), 6.0 (m, 1 H), 7.4–7.5 (m, 5 H) ppm. ^{13}C NMR: δ = 20.3, 30.8, 54.0, 56.7, 58.6 (q, $^2J_{C,F}$ = 25 Hz), 114.3, 117.3, 127.1, 127.5 (q, $^1J_{C,F}$ = 291 Hz), 128.3, 129.0, 134.7, 139.0, 142.9 ppm. ^{19}F NMR: δ = –68.8 (d, *J* = 8.5 Hz, CF_3) ppm. $C_{16}H_{20}F_3N$ (283.34): calcd. C 67.83, H, 7.11, N 4.94; found C 67.76, H 7.17, N 4.85.

***N*-(4-Methoxyphenyl)-*N*-(2-methylallyl)[1-(trifluoromethyl)but-3-enyl]amine (14):** From imine **2** (406 mg, 2 mmol), allyl bromide (339 mg, 2.8 mmol), methallyl bromide (1.08 g, 8 mmol), and CuI (76 mg, 0.4 mmol), **14** was obtained as a brown oil (335 mg, 56%). ^{1}H NMR:δ = 1.7 (s, 3 H), 2.6 (m, 2 H), 3.76 (s, 3 H), 3.83 (s, 2 H), 4.1 (m, 1 H), 4.8 (m, 1 H), 4.9 (m, 1 H), 5.1 (dq, *J* = 9.2, 1.4 Hz, 1 H), 5.2 (dq, *J* = 17.1, 1.5 Hz, 1 H), 5.8 (m, 1 H), 6.8 (d, *J* = 9.4 Hz, 2 H), 6.9 (d, *J* = 9.4 Hz, 2 H) ppm. ^{13}C NMR: δ = 20.0, 31.4, 51.8, 55.3, 64.0 (q, $^2J_{C,F}$ = 27 Hz), 112.8, 114.1, 118.1, 120.1, 126.5 (q, $^1J_{C,F}$ = 288 Hz), 133.7, 141.7, 142.6, 153.9 ppm. ^{19}F NMR: δ = –71.7 (d, *J* = 7.6 Hz, CF_3) ppm. $C_{16}H_{20}F_3NO$ (299.33): calcd. C 64.20, H 6.73, N 4.68; found C 64.17, H 6.88, N 4.57.

***N*-Allyl-*N*-(4-methoxyphenyl)[3-methyl-1-(trifluoromethyl)but-3-enyl]amine (15):** From imine **2** (406 mg, 2 mmol), methallyl bromide (378 mg, 2.8 mmol), allyl bromide (968 mg, 8 mmol), and CuI (76 mg, 0.4 mmol), **15** was obtained as a brown oil (514 mg, 86%). ^{1}H NMR: δ = 1.6 (s, 3 H), 2.3 (dd, *J* = 15.2, 4.1 Hz, 1 H), 2.6 (dd, *J* = 15.2, 10.4 Hz, 1 H), 3.7 (s, 3 H), 3.9 (m, 2 H), 4.2 (dqd, *J* = 10.4, 8.0, 4.1 Hz, 1 H), 4.7 (m, 1 H), 4.8 (m, 1 H), 5.0 (d, *J* =

10.2 Hz, 1 H), 5.1 (d, *J* = 17.3 Hz, 1 H), 5.7 (m, 1 H), 6.8 (m, 4 H) ppm. ^{13}C NMR: δ = 21.9, 34.9, 47.9, 55.1, 61.0 (q, $^{2}J_{C,F}$ = 27.0 Hz), 114.0, 114.2, 116.4, 118.6, 126.7 (q, $^{1}J_{C,F}$ = 288 Hz), 135.6, 140.3, 142.3, 153.3 ppm. ^{19}F NMR: δ = –72.2 (d, *J* = 8.0 Hz, CF_3) ppm. $C_{16}H_{20}F_3NO$ (299.33): calcd. C 64.20, H 6.73, N 4.68; found C 63.98, H 6.91, N 4.52.

(–)-*N*-Allyl-*N*-(2-methoxy-1-phenylethyl)[1-(trifluoromethyl)but-3-enyl]amine (16): From imine **3** (462 mg, 2 mmol), allyl bromide (1.3 g, 10.8 mmol), and CuI (571 mg, 3 mmol), **16** was obtained as a brown oil (338 mg, 54%). $[\alpha]_D^{25}$ = –32.4 (*c* = 1.02 in MeOH). ^{1}H NMR: δ = 2.1 (m, 2 H) 3.2 (s, 3 H), 3.3 (m, 3 H), 3.6 (d, *J* = 6.4 Hz, 2 H), 4.1 (t, *J* = 6.4 Hz, 1 H), 4.80 (d, *J* = 16.7 Hz, 1 H), 4.83 (d, *J* = 10.3 Hz, 1 H), 5.0 (d, *J* = 10.0 Hz, 1 H), 5.1 (d, *J* = 17.0 Hz, 1 H), 5.4 (ddt, *J* = 17.0, 10.3, 6.9 Hz, 1 H), 5.7 (ddt, *J* = 16.8, 10.0, 6.2 Hz, 1 H), 7.2 (m, 5 H) ppm. ^{13}C NMR: δ = 31.5, 50.2, 58.7, 59.1 (q, *J* = 27.0 Hz), 61.7, 73.8, 116.8, 117.0, 127.1 (q, *J* = 287.0 Hz), 127.4, 128.3, 128.4, 134.4, 137.3, 139.7 ppm. ^{19}F NMR: δ = –71.7 (d, *J* = 8.3 Hz, CF_3) ppm. $C_{17}H_{22}F_3NO$ (313.36): calcd. C 65.16, H 7.08, N 4.47; found C 65.22, H 7.09, N 4.21.

General Procedure for the Ring-Closing Metathesis. Synthesis of Compounds 17–24: Di-ω-dienes **7**–**16** and the Grubbs catalyst (5–10 mol-%) were dissolved in CH_2Cl_2 under an argon atmosphere. After 2–48 h (monitored by GC), the solvent was evaporated and the crude mixture was purified over silica gel (petroleum ether/AcOEt, 9:1) to afford **17**–**24**.

1-Benzyl-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (17): Starting from **7** (121 mg, 0.45 mmol) and the Grubbs catalyst (18 mg, 5 mol-%), compound **17** was obtained as a clear, brown liquid (103 mg, 95%). ^{1}H NMR: δ = 2.2 (m, 1 H), 2.5 (m, 1 H), 3.1 (d, *J* = 16 Hz, 1 H), 3.3 (d, *J* = 16 Hz, 1 H), 3.4 (m, 1 H), 3.7 (d, *J* = 14 Hz, 1 H), 3.9 (d, *J* = 14 Hz, 1 H), 5.7 (d, *J* = 2.0 Hz, 2 H), 7.2–7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 24.2 (q, $^{3}J_{C,F}$ = 2.0 Hz), 44.1, 56.1 (q, $^{2}J_{C,F}$ = 26 Hz), 59.1, 121.5, 125.1, 125.3 (q, $^{1}J_{C,F}$ = 293 Hz), 127.1, 128.3, 128.4, 138.7 ppm. ^{19}F NMR: δ = –68.6 (d, $J_{H,F}$ = 9.0 Hz, CF_3) ppm. $C_{13}H_{14}F_3N$ (241.26): calcd. C 64.72, H 5.85, N 5.81; found C 64.99, H, 5.78, N 5.88.

1-Benzyl-3,3-dimethyl-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (18): Starting from **8** (134 mg, 0.45 mmol) and the Grubbs catalyst (18 mg, 5 mol-%), compound **18** was obtained as a clear, brown liquid (116 mg, 96%). ^{1}H NMR: δ = 1.1–1.3 (m, 6 H), 3.0 (q, *J* = 9.0 Hz, 1 H), 3.2 (m, 2 H), 4.0 (m, 2 H), 5.4 (m, 1 H), 5.6 (td, *J* = 3.1, 10 Hz, 1 H), 7.3–7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 24.8, 31.4, 46.3, 60.4, 66.7 (q, $^{2}J_{C,F}$ = 23 Hz), 122.3, 127.1, 128.0 (q, $^{1}J_{C,F}$ = 297 Hz), 128.2, 128.5, 133.1, 139.0 ppm. ^{19}F NMR: δ = –62.2 (d, $J_{H,F}$ = 9.0 Hz, CF_3) ppm. $C_{15}H_{18}F_3N$ (269.31): calcd. C 66.90, H 6.74, N 5.20; found C 66.58, H, 6.69, N 5.31.

1-Benzyl-4-methyl-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (19): Starting from diene **9** (127 mg, 0.45 mmol) and the Grubbs catalyst (18 mg, 5 mol-%), compound **19** was obtained as a clear, brown liquid (107 mg, 93%). ^{1}H NMR: δ = 1.4 (s, 3 H), 2.0 (m, 1 H), 2.4 (m, 1 H), 3.1 (m, 2 H), 3.5 (m, 1 H), 3.9 (qd, *J* = 14.0, 1.6 Hz, 1 H), 4.0 (d, *J* = 14.0 Hz, 1 H), 5.4 (m, 1 H), 7.2–7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 22.7, 28.6 (q, $^{3}J_{C,F}$ = 2.0 Hz), 47.3, 56.7 (q, $^{2}J_{C,F}$ = 26.0 Hz), 58.7, 119.9, 127.1, 127.7 (q, $^{1}J_{C,F}$ = 292 Hz), 128.3, 128.4, 128.9, 138.7 ppm. ^{19}F NMR ($CDCl_3$): δ = –68.8 (d, $J_{H,F}$ = 9.0 Hz, CF_3) ppm. $C_{14}H_{16}F_3N$ (255.29): calcd. C 65.87, H 6.32, N 5.49; found C 65.06, H 6.25, N 5.58.

1-Benzyl-5-methyl-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (20): Starting from **13** (160 mg, 0.6 mmol) and the Grubbs catalyst (44 mg, 20 mol-%), compound **20** was obtained as a clear, brown liquid (128 mg, 89%). ^{1}H NMR: δ = 1.5 (s, 3 H), 2.1 (d, *J* = 17.8 Hz, 1 H), 2.4 (d, *J* = 17.8 Hz, 1 H), 2.9 (d, *J* = 15.9 Hz, 1 H), 3.1 (d, *J* = 15.9 Hz, 1 H), 3.3 (qt, *J* = 9.1, 2.3 Hz, 1 H), 3.8 (dq, *J* = 13.6, 1.6 Hz, 1 H), 3.9 (d, *J* = 13.6 Hz, 1 H), 5.3 (s, 1 H), 7.1–7.3 (m, 5 H) ppm. ^{13}C NMR: δ = 20.6, 24.1, 51.4, 55.9 (q, $^{2}J_{C,F}$ = 25.0 Hz), 58.9, 115.8, 127.2, 127.8 (q, $^{1}J_{C,F}$ = 292 Hz), 128.4, 128.5, 132.1, 138.8 ppm. ^{19}F NMR: δ = –68.5 (d, *J* = 9.0 Hz, CF_3) ppm. $C_{14}H_{16}F_3N$ (255.29): calcd. C 65.87, H 6.32, N 5.49; found C 65.80, H 6.66, N 5.41.

1-Benzyl-2-trifluoromethyl-5-vinyl-1,2,3,6-tetrahydropyridine (21): Starting from **12** (267 mg, 1 mmol) and the Grubbs catalyst (44 mg, 10 mol-%), compound **21** was obtained as a clear, brown liquid (253 mg, 95%). ^{1}H NMR: δ = 2.3 (d, *J* = 19.0 Hz, 1 H), 2.6 (d, *J* = 19.0 Hz, 1 H), 3.3 (dq, *J* = 9.0, 2.2 Hz, 1 H), 3.8 (d, *J* = 13.6 Hz, 1 H), 4.0 (d, *J* = 13.6 Hz, 1 H), 4.83 (d, *J* = 17.6 Hz, 1 H), 4.84 (d, *J* = 11.0 Hz, 1 H), 5.7 (s, 1 H), 6.2 (dd, *J* = 17.6, 11.0 Hz, 1 H), 7.4–7.5 (m, 5 H) ppm. ^{13}C NMR: δ = 24.5 (q, $^{3}J_{C,F}$ = 2.0 Hz), 46.5 (q, $^{3}J_{C,F}$ = 0.6 Hz), 56.0 (q, $^{2}J_{C,F}$ = 25.8 Hz), 59.1, 110.8, 123.1, 127.3, 127.6 (q, $^{1}J_{C,F}$ = 292 Hz), 128.4, 128.5, 134.2 (q, *J* = 0.7 Hz), 136.9, 138.5 (q, *J* = 0.5 Hz) ppm. ^{19}F NMR: δ = –68.8 (d, *J* = 9.0 Hz, CF_3) ppm. $C_{15}H_{16}F_3N$ (267.29): calcd. C 67.40, H 6.03, N 5.23; found C 67.38, H 6.02, N 5.32.

1-(4-Methoxyphenyl)-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (22): Starting from **11** (57 mg, 0.45 mmol) and the Grubbs catalyst (18 mg, 5 mol-%), compound **22** was obtained as a clear, brown liquid (104 mg, 90%). ^{1}H NMR: δ = 2.3 (m, 2 H), 2.6 (m, 2 H), 3.7 (s, 3 H), 4.3 (quint, *J* = 9.0 Hz, 1 H), 5.8 (s, 2 H), 6.8 (m, 4 H) ppm. ^{13}C NMR: δ = 24.0, 44.2, 54.4 (q, $^{2}J_{C,F}$ = 30.0 Hz), 55.4, 114.5, 116.7, 121.1, 124.4, 126.7 (q, $^{1}J_{C,F}$ = 290 Hz), 143.5, 153.2 ppm. ^{19}F NMR: δ = –70.8 (d, $J_{H,F}$ = 8.5 Hz, CF_3) ppm. $C_{13}H_{14}F_3NO$ (257.29): calcd. C 60.70, H 5.49, N 5.44; found C 60.59, H 5.51, N 5.45.

1-(4-Methoxyphenyl)-5-methyl-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (23): Starting from **14** (136 mg, 0.45 mmol) and the Grubbs catalyst (21 mg, 7 mol-%), compound **23** was obtained as a brown liquid (47 mg, 41%). ^{1}H NMR: δ = 1.8 (s, 3 H), 2.4 (d, *J* = 17.9 Hz, 1 H), 2.7 (d, *J* = 17.9 Hz, 1 H), 3.5 (d, *J* = 16.9 Hz, 1 H), 3.7 (d, *J* = 16.9 Hz, 1 H), 3.8 (s, 3 H), 4.4 (q, *J* = 8.3 Hz, 1 H), 5.5 (m, 1 H), 6.8–6.9 (m, 4 H) ppm. ^{13}C NMR: δ = 20.6, 24.1 (q, $^{3}J_{C,F}$ = 1.6 Hz), 48.3, 54.1 (q, $^{2}J_{C,F}$ = 27.0 Hz), 55.5, 114.6, 115.7, 116.9, 126.9 (q, $^{1}J_{C,F}$ = 292 Hz), 131.4, 143.4, 153.3 ppm. ^{19}F NMR: δ = –70.8 (d, *J* = 8.3 Hz, CF_3) ppm. $C_{14}H_{16}F_3NO$ (271.28): calcd. C 61.98, H 5.94, N, 5.16; found C 61.82, H 6.06, N 5.04.

(–)-1-(2-Methoxy-1-phenylethyl)-2-trifluoromethyl-1,2,3,6-tetrahydropyridine (24): Starting from **16** (258 mg, 0.82 mmol) and the Grubbs catalyst (56 mg, 7 mol-%), compound **24** was obtained as a brown liquid (214 mg, 98%). $[\alpha]_D^{25}$–26.4 (*c* = 0.265 in MeOH). ^{1}H NMR: δ = 2.1 (d, *J* = 18.0 Hz, 1 H), 2.5 (d, *J* = 18.0 Hz, 1 H), 3.0 (d, *J* = 17.6 Hz, 1 H), 3.1 (d, *J* = 17.6 Hz, 1 H), 3.2 (s, 3 H), 3.62 (d, *J* = 5.7 Hz, 1 H), 3.63 (d, *J* = 4.4 Hz, 1 H), 3.7 (m, 1 H), 4.0 (t, *J* = 5.2 Hz, 1 H), 5.5–5.7 (m, 2 H), 7.2–7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 24.1, 44.8, 53.8 (q, $^{2}J_{C,F}$ = 27.0 Hz), 58.8, 66.0, 75.0, 121.7, 125.5, 127.4, 127.9 (q, $^{1}J_{C,F}$ = 292 Hz), 127.9, 128.3, 141.0 ppm. ^{19}F NMR: δ = –69.6 (d, *J* = 9.0 Hz, CF_3) ppm. $C_{15}H_{18}F_3NO$ (285.30): calcd. C 63.15, H 6.36, N 4.91; found C 63.26, H 6.52, N 4.98.

Synthesis of 2-Benzyl-3-trifluoromethyl-1,2,3,6,7,7a-hexahydro-[2]pyrindin-6-one (25): $Co_2(CO)_8$ (261 mg, 0.76 mmol) was added to a solution of **10** (170 mg, 0.64 mmol) in CH_2Cl_2 (4 mL) under an argon atmosphere. After disappearance of the starting material (0.5 h; monitored by TLC), the reaction mixture was cooled to 0 °C, and *N*-methylmorpholine *N*-oxide monohydrate (774 mg, 5.7 mmol) was added in several portions over 15 min. The reaction

mixture was then allowed to warm to room temp. After 3 h (monitored by TLC), the mixture was filtered through silica gel. The solvent was then evaporated and the crude product was purified by chromatography over silica gel (petroleum ether/AcOEt, 1.5:1) to afford compound **25** (109 mg, 58% of *trans* and 19 mg, 10% of *cis*) as yellow oils.

trans-**25** (major): ^{1}H NMR: δ = 1.96 [dd, J = 19.0, 2.5 Hz, 1 H, C(7)-H], 2.47 [dd, J = 19.0, 6.4 Hz, 1 H, C(7)-H], 2.71 [tq, J = 11.0, 2.4 Hz, 1 H, C(1)-H], 2.84 [ddd, J = 15.0, 7.0, 0.4 Hz, 1 H, C(4)-H], 2.98 [m, 1 H, C(7a)-H], 3.04 [d, J = 15 Hz, 1 H, C(4)-H], 3.12 [dd, J = 11.0, 6.6 Hz, 1 H, C(1)-H], 3.64 [m, 1 H, C(3)-H], 3.93 (dq, J = 14.0, 1.7 Hz, 1 H, CH_2Ph), 4.07 (d, J = 14 Hz, 1 H, CH_2Ph), 6.01 [m, 1 H, C(5)-H], 7.2–7.4 (m, 5 H, Ph) ppm. ^{13}C NMR: δ = 28.6 [q, $^3J_{C,F}$ = 2.0 Hz, C(4)], 38.7 C(7), 38.8 C(7a), 52.2 C(1), 58.8 [q, $^2J_{C,F}$ = 26 Hz, C(2)], 59.3 (CH$_2$Ph), 127.2 (q, $^1J_{C,F}$ = 293 Hz), 127.5 (Ph), 128.1 (Ph), 128.7 (Ph), 138.3 (Ph), 177.0 (C=CH), 207.2 (CO) ppm. ^{19}F NMR: δ = –65.9, (d, J = 8.6 Hz, CF_3) ppm. $C_{16}H_{16}F_3NO$ (295.31): calcd. C 65.08, H 5.46, N 4.74; found C 65.22, H 5.52, N 4.79.

cis-**25** (minor): ^{1}H NMR: δ = 1.84 [dd, J = 18.7, 2.4 Hz, 1 H, C(7)-H], 1.96 [t, J = 12 Hz, 1 H, C(1)-H], 2.46 [dd, J = 18.7, 6.6 Hz, 1 H, C(7)-H], 2.77 [m, 1 H, C(4)-H], 2.95 [m, 1 H, C(7a)-H], 3.07 [m, 1 H, C(4)-H], 3.24 [m, 1 H, C(3)-H], 3.25 [m, 1 H, C(1)-H], 3.54 (d, J = 13.5 Hz, 1 H, CH_2Ph), 4.16 (d, J = 13.5 Hz, 1 H, CH_2Ph), 6.00 [s, 1 H, C(5)-H], 7.2–7.4 (m, 5 H, Ar) ppm. ^{13}C NMR: δ = 28.5 [q, ^3J = 2.0 Hz, C(4)], 38.1 [C(7)], 38.2 [C(7a)], 55.0 (CH$_2$Ph), 56.5 [C(1)], 62.8 [q, $^2J_{C,F}$ = 26 Hz, C(2)], 128.5 (×2, Ph), 129.2 (×2, Ph), 129.3 [q, $^1J_{C,F}$ = 293 Hz, C(9)), 138.3 (Ph), 178.0 [C(8)], 208.0 [C(6)] ppm. ^{19}F NMR: δ = –69.2, (d, J = 7.3 Hz, CF_3) ppm. $C_{16}H_{16}F_3NO$ (295.31): calcd. C 65.08, H 5.46, N 4.74; found C 65.11, H 5.47, N 4.77.

Synthesis of 2-Benzyl-3-trifluoromethyl-1,2,3,4,4a,5-hexahydro-[2]pyrindin-6-one (26): $Co_2(CO)_8$ (261 mg, 0.76 mmol) was added to a solution of **12** (170 mg, 0.64 mmol) in CH_2Cl_2 (4 mL) under an argon atmosphere. After disappearance of the starting material (0.5 h; monitored by TLC), the reaction mixture was cooled to 0 °C, and *N*-methylmorpholine *N*-oxide monohydrate (774 mg, 5.7 mmol) was added in several portions over 15 min. The reaction mixture was then allowed to warm to room temp. After 3 h (monitored by TLC), the mixture was filtered through silica gel. The solvent was then evaporated and the crude product was purified by chromatography over silica gel (petroleum ether/AcOEt, 1.5:1) to afford compound **26** (193 mg, 65.6% of *cis* and 42 mg, 14.4% of *trans*) as yellow oils.

cis-**26** (major): ^{1}H NMR: δ = 1.74 [td, J = 13.6, 5.7 Hz, 1 H, C(4)-H], 2.04 [dd, J = 18.7, 2.6 Hz, 1 H, C(5)-H], 2.42 [ddd, J = 12.6, 6.0, 4.6 Hz, 1 H, C(4)-H], 2.67 [dd, J = 18.6, 6.4 Hz, 1 H, C(5)-H], 3.13 [d, J = 13.0 Hz, 1 H, C(4a)-H], 3.45 [qdd, J = 9.5, 5.7, 1.4 Hz, 1 H, C(3)-H], 3.65 [d, J = 14.2 Hz, 1 H, C(1)-H], 3.80 [d, J = 14.2 Hz, 1 H, C(1)-H], 3.88 (d, J = 13.8 Hz, 1 H, CH_2Ph), 4.04 (d, J = 13.8 Hz, 1 H, CH_2Ph), 5.9 [m, 1 H, C(7)-H], 7.2–7.4 (m, 5 H, Ph) ppm. ^{13}C NMR: δ = 30.5 [C(4)], 36.0 [C(4a)], 42.0 [C(5)], 48.0 [C(1)], 57.5 [q, $^2J_{C,F}$ = 26 Hz, C(3)], 59.0 (CH$_2$Ph), 125.4 [q, $^1J_{C,F}$ = 293 Hz, C(9)], 128.3 [C(7)], 128.5 (×3, Ph), 137.5 (Ph), 175.3 [C(8)], 207.5 [C(6)] ppm. ^{19}F NMR: δ = –65.2 (d, J = 9.5 Hz, CF_3) ppm. $C_{16}H_{16}F_3NO$ (295.31): calcd. C 65.08, H 5.46, N 4.74; found C 65.20, H 5.50, N 4.69.

trans-**26** (minor): ^{1}H NMR: δ = 1.70 [td, J = 12.7, 10.1 Hz, 1 H, C(4)-H], 2.13 [dd, J = 18.6, 2.1 Hz, 1 H, C(5)-H], 2.44 [dt, J = 13.0, 5.8 Hz, 1 H, C(4)-H], 2.69 [dd, J = 18.6, 6.6 Hz, 1 H, C(5)-H], 3.03 [m, 1 H, C(4a)-H], 3.47 [d, J = 16.4 Hz, 1 H, C(1)-H], 3.65 [dqd, J = 10.1, 8.2, 5.1 Hz, 1 H, C(3)-H], 3.76 (d, J = 13.4 Hz, 1 H, CH_2Bn), 3.80 [d, J = 16.4 Hz, 1 H, C(1)-H], 3.89 (d, J = 13.4 Hz, 1 H, CH_2Bn), 5.94 [m, 1 H, C(7)-H], 7.2–7.4 (m, 5 H, Ar) ppm. ^{13}C NMR: δ = 29.5 [C(4)], 38.0 [C(4a)], 41.5 [C(5)], 50.5 [C(1)], 54.7 (CH$_2$Ph), 60.5 [C(3)], 125.5 [q, $^1J_{C,F}$ = 290 Hz, C(9)], 128.45 [C(7)], 128.5 (×3, Ar), 137.0 (Ph), 176.5 [C(8)], 207.5 [C(6)] ppm. ^{19}F NMR: δ = –70.1 (d, J = 8.2 Hz, CF_3) ppm. $C_{16}H_{16}F_3NO$ (295.31): calcd. C 65.08, H 5.46, N 4.74; found C 65.10, H 5.47, N 4.68.

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