Synthesis of \(\alpha,\gamma\)-Chiral Trifluoromethylated Amines through the Stereospecific Isomerization of \(\alpha\)-Chiral Allylic Amines

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General methods

All reagents were utilized without any further purification as obtained from commercial sources. Flash chromatography was performed with 60 Å (35-70 μm) silica gel (GC 60A 35-70 Micron, DAVISIL). Analytical TLC was performed on aluminum plates pre-coated (0-25 mm) with silica gel (Merck, Silica Gel 60 F254). Compounds were detected by exposure to UV light or by revealing the plates in a solution of 5% KMnO₄ in water. Melting points were recorded in metal block and are uncorrected. ¹H, ¹³C and ¹⁹F NMR spectra were recorded at 400 MHz, 100 MHz and 376 MHz respectively on a Bruker Advance spectrometer. Chemical shifts (d) are shown in ppm, using as a reference the residual peaks of CDCl₃ (dH 7.26 and dC 77.00). Coupling constants (J) are given in Hz. NMR yields were calculated using 1 equiv. of 1,2,4,5-tetrachloronitrobenzene as internal standard. High resolution mass spectra (HRMS) were recorded on Bruker microTOF mass spectrometer using APCI ionization. Herein, are reported the MS when they were possible to be detected. Enantiomeric excesses were determined using HPLC analysis on an Agilent 1200-series instrument with an autosampler and UV detection and using Chiralcel OD-H, Chiralpak AD-H and IF and Phenomenex Lux Cellulose 5 columns. Optical rotations were recorded on a RUDOLPH AUTOPOL IV with an automatic polarimeter. Microwave reactions were performed in an Initiator Classic microwave reactor from Biotage.

Allylic amines (compounds 4a-4q) decompose under HRMS conditions, we have identified the fragmentations of three of those compounds (4a, 4f, 4h). Although products 6a-6q could be identified by HRMS (6a, 6f, 6h), these compounds showed a higher stability when were Boc-protected. Therefore, we provide HRMS of all Boc-protected amines (both allylic amines 4’ and aliphatic amines 6’) and NMR (¹H NMR, ¹³C NMR and ¹⁹F NMR) data for non-protected amines

Instead, full characterization of boc-protected amines 4’ and 6’ are reported.
Optimization of reduction conditions

Table S1. Optimization of the one pot isomerization/diastereoselective synthesis of γ-trifluoromethylated aliphatic amines. a

| Entry | Reducing agent | Temp. (°C) | Time (h) | Conversion (%) b | Yield (%) b | d.r. b |
|-------|----------------|------------|----------|-----------------|-------------|--------|
| 1 c   | NaBH₄          | 25         | 2        | 99              | 99          | 50:50  |
| 2     | DIBAL-H        | 25         | 2        | 99              | 99          | 58:42  |
| 3     | BH₃·SMe       | 25         | 18       | 0               | 0           | -      |
| 4     | BH₃·THF       | 25         | 18       | 0               | 0           | -      |
| 5     | Et₃SiH/BCF₃   | 25         | 18       | 0               | 0           | -      |
| 6     | DIBAL-H       | 0          | 2        | 99              | 99          | 65:35  |
| 7     | DIBAL-H       | −78 °C     | 2        | 99              | 99          | 70:30  |
| 8     | L-Selectride  | −78 °C     | 2        | 99              | 13          | 92:8   |
| 9 d   | L-Selectride  | 25         | 2        | 99              | -           | -      |
| 10    | Super-hydride | −78 °C     | 2        | 99              | 81          | 56:44  |
| 11    | DIBAL-H       | −90 °C     | 2        | 99              | 99% (75%) c | 75:25  |
| 12 f  | DIBAL-H       | −90 °C     | 2        | 99              | 10          | -      |

a: Reactions were run using 4a (0.1 mmol) and 2 equiv. of reducing agent, 0.02M. b: Conversion and d.r. determined by ¹⁹F NMR spectroscopy. c: Toluene:MeOH (1:1) used as solvent. d: Decomposition of 4a was observed. e: Isolated yield in parenthesis. f: 1 equiv. of DIBAL-H used, ketone 5a observed as major product.
Control experiments performed on allylic amine 4a

\[
\text{Ph} \quad \text{NH}_2 \\ \text{Ph} \quad \text{NH}_2 \\ \text{F}_3\text{C} \quad \text{F}_3\text{C} \\
\begin{array}{c}
\text{H}_2 \text{(1 bar)} \\
Pd/C \text{(2 mol%)}
\end{array} \\
\begin{array}{c}
\text{MeOH}, 25 \degree C, 30 \text{ min}
\end{array}
\]

\[
\begin{array}{c}
\text{F}_3\text{C} \quad \text{Ph} \\
\text{NH}_2 \\
\text{Ph} \quad \text{NH}_2
\end{array} + \begin{array}{c}
\text{F}_3\text{C} \quad \text{Ph} \\
\text{NH}_2 \\
\text{Ph} \quad \text{NH}_2
\end{array}
\]

\[99\% \text{ NMR Yield} \quad \text{Not observed}\]

**Scheme S1.** Hydrogenation of 4a with Pd/C.

\[
\text{Ph} \quad \text{NH}_2 \\ \text{Ph} \quad \text{NH}_2 \\ \text{F}_3\text{C} \quad \text{F}_3\text{C} \\
\begin{array}{c}
\text{DIBAL-H} \text{(1 equiv.)}
\end{array} \\
\begin{array}{c}
\text{THF}, 0 \degree C, 2 \text{ h}
\end{array}
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{NH}_2 \\
\text{Ph}
\end{array}
\]

\[0\% \text{ conversion}\]

**Scheme S2.** Reduction of 4a with DIBAL-H.

**General procedure for the synthesis of enantioenriched allylic amines**

\[
\begin{array}{c}
\text{Ph} \\
\text{O}
\end{array} \\
\begin{array}{c}
\text{F}_3\text{C} \quad \text{F}_3\text{C} \\
\text{Ph} \quad \text{Ph}
\end{array}
\]

\[
\begin{array}{c}
\text{H}_2\text{N}^+\text{S}^- \quad \text{Ti(OEt)}_4
\end{array}
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{N}^+\text{S}^-
\end{array} \\
\begin{array}{c}
\text{F}_3\text{C} \quad \text{F}_3\text{C} \\
\text{Ph} \quad \text{Ph}
\end{array}
\]

\[
\begin{array}{c}
\text{1) DIBAL-H, 0 \degree C} \\
\text{2) HCl 3M}
\end{array} \\
\begin{array}{c}
\text{THF}
\end{array}
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{NH}_2 \\
\text{Ph}
\end{array}
\]

**Scheme S3.** Synthetic route for the synthesis of allylic amines 4.

**Allylic amines that could not be synthesized with this methodology**

![Allylic amines not accessible with the enantioselective synthetic pathway.](image1)

**Figure S1.** Allylic amines not accessible with the enantioselective synthetic pathway.

**Allylic amines that do not work under the isomerization reaction conditions**

![Allylic amines that don’t undergo isomerization reaction.](image2)

**Figure S2.** Allylic amines that don’t undergo isomerization reaction.
Possible stereochemical outcome of the base-catalyzed isomerization of allylic amines

Scheme S4. Different stereoisomeric products accessible under the isomerization conditions.

Above is explained how the stereochemical information of the starting material affect the stereochemical outcome of the products. The stereospecificity of the isomerization reaction not only depends on the stereochemistry of the α-carbon of the allylic amine, but also on the stereochemistry of the alkene. Therefore, R amines lead to different stereoisomers than S amines, as well as Z alkenes lead to different stereoisomers than E alkenes.

As a result of this stereodivergency, those substrates containing higher amounts of Z alkenes result in lower ee of the final chiral aliphatic amines.
General procedures

A Synthesis of allylic amines 4

The corresponding enone (5 mmol, 1 equiv.) was placed on a sealed MW vial with (R)-(+)2-methyl-2-propanesulfinamide (7.5 mmol, 1.5 equiv.) and titanium(IV) ethoxide (10 mmol, 2 equiv.) and the reaction was stirred at 100 °C for 2 h under neat conditions in the MW reactor. After completion of the reaction, the resulting imine was purified with FCC (pentane:EtOAc 9:1) to afford the pure imine. The imine was dissolved in THF (1M), the organic layers were washed with brine and dried over MgSO₄. The solvent was evaporated under reduced pressure and the amine was purified by FCC (pentane:EtOAc 8:2 to 6:4) to afford the pure allylic amines. 

(rac)-4 were obtained using the same protocol with (rac)-2-methyl-2-propanesulfinamide.

B Amine protection

To a solution of the corresponding amine (0.3 mmol, 1 equiv.) in CHCl₃ (3 mL, 0.1 M) at 0 °C a solution of di-tert-butyl dicarbonate (0.36 mmol, 1.2 equiv.) in CHCl₃ (3mL, 0.1 M) was added and the reaction was stirred overnight. Then, the protected amine was purified by FCC (pentane:EtOAc 97:3 to 9:1) to obtain the desired compounds.

C Isomerization and reduction of the allylic amines

The allylic amine (0.25 mmol, 1 equiv.) and TBD (0.012 or 0.025 mmol, 5 or 10 mol %) were charged on a pressure vial and purged with Ar. Dry Toluene (12.5 mL, 0.02 M) was added and the reaction mixture was stirred for 18 h at 60 or 120 °C on an oil bath. Then, the reaction mixture was allowed to reach room temperature and cooled to -90 °C. DIBAL-H (0.5 mmol, 2 equiv.) was added and stirred at that temperature for an additional 4 h. The reaction was allowed to reach room temperature and a solution of Rochelle’s salt was added and stirred for additional 30 min, the aqueous layer was extracted with EtOAc (3x15 mL), the organic layers were dried over MgSO₄, the solvent was removed under reduced pressure. The crude was then purified by FCC (pentane:EtOAc 7:3 to 0:1) to afford the pure amine.

Characterization of allylic amines 4 and 4'

(R,E)-4,4,4-Trifluoro-1,3-diphenylbut-2-en-1-amine (4a)

The title compound was obtained following GPA from (R,E)-4,4,4-trifluoro-1,3-diphenylbut-2-en-1-one (4.0 g, 14.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 42% yield over 3 steps (1.69 g, 6.1 mmol).

1H NMR (400 MHz. CDCl₃) δ 7.44 – 7.41 (m, 3H), 7.37 – 7.33 (m, 2H), 7.30 – 7.27 (m, 5H), 6.55 (dq, J = 9.5, 1.5 Hz, 1H), 4.48 (d, J = 9.5 Hz, 1H), 1.55 (bs, 2H).
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 142.8, 139.0 (Cq, $J_{CF} = 5.0$ Hz), 131.7, 130.5 (Cq, $J_{CF} = 30.0$ Hz), 129.6, 128.82, 128.80, 128.5, 127.6, 126.4, 123.3 (Cq, $J_{CF} = 273.5$ Hz), 53.0.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ −66.24 (s, CF$_3$).

HRMS (ESI) m/z: Fragmentation observed: 261.0906 [M − NH$_2$]$^+$ corresponding to C$_{16}$H$_{12}$F$_3^+$, C$_{16}$H$_{12}$F$_3$ requires 261.0886.

**tert-Butyl (R,E)-(4,4,4-trifluoro-1,3-diphenylbut-2-en-1-yl)carbamate (4a')**

\[
\text{Ph} \quad \text{NHBOC} \\
\text{F}_3\text{C} \quad \text{Ph}
\]

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-1,3-diphenylbut-2-en-1-amine (100.0 mg, 0.36 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a yellow oil in 40% yield over 3 steps (0.52 g, 1.8 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 95%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer $t_r = 10.2$ min, major enantiomer, $t_r = 7.6$ min.

[α]$_D^{25}$: −55.2 (c 1.00, CHCl$_3$, for the diastereomer mixture, d.r.: 97:3).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.41 − 7.39 (m, 3H), 7.33 − 7.27 (m, 5H), 7.17 − 7.15 (m, 2H), 6.54 (dd, $J = 9.5$, 2.0 Hz, 1H), 5.21 (bs, 1H), 4.96 (d, $J = 7.5$ Hz, 1H), 1.42 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 154.5, 140.2, 135.3 (Cq, $J_{CF} = 5.0$ Hz), 132.3, 131.1, 129.5, 128.92, 128.89, 128.5, 127.9, 126.6, 123.2 (Cq, $J_{CF} = 273.4$ Hz), 80.0, 52.6, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ −66.28 (s, CF$_3$).

HRMS (ESI) m/z: 400.1474 [M+Na]$^+$, C$_{21}$H$_{22}$F$_3$NNaO$_2^+$ requires 400.1495.

(R,E)-4,4,4-Trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-amine (4b)

\[
\text{Ph} \quad \text{NH}_2 \\
\text{F}_3\text{C} \quad \text{Ph}
\]

The title compound was obtained following GPA from (R,E)-4,4,4-trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-one (1.3 g, 4.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 40% yield over 3 steps (0.52 g, 1.8 mmol).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.43 − 7.40 (m, 3H), 7.34 − 7.32 (m, 1H), 7.28-7.25 (m, 2H); 7.16 (s, 3H), 6.53 (dq, $J = 10.0$, 1.5 Hz, 1H), 4.44 (d, $J = 10.0$ Hz, 1H), 2.35 (s, 3H), 1.51 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 139.9, 139.1 (Cq, $J_{CF} = 5.0$ Hz), 137.4, 131.7, 129.6, 129.5, 128.8, 128.5, 128.2, 126.6, 123.3 (Cq, $J_{CF} = 273.0$ Hz), 52.8, 21.0.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ −66.21 (s, CF$_3$).

**tert-Butyl (R,E)-(4,4,4-trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-yl)carbamate (4b')**
The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-amine (58.3 mg, 0.20 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 74% (57.9 mg, 0.15 mmol).

The enantiomeric excess (minor isomer: 96%, major isomer 90%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,Z) (minor diastereomer): minor enantiomer, t_r = 13.0 min, major enantiomer, t_r = 9.6 min, (1R,E) (major diastereomer): minor enantiomer t_r = 6.0 min, major enantiomer, t_r = 5.5 min.

[α]_D^25: –49.9 (c 0.85, CHCl₃, for the diastereomer mixture, d.r.: 84:16).

1H NMR (400 MHz, CDCl₃) δ 7.41 – 7.36 (m, 3H), 7.28 – 7.25 (m, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.05 (d, J = 7.9 Hz, 2H), 6.53 (dd, J = 9.5, 1.5 Hz, 1H), 5.16 (bs, 1H), 4.91 (d, J = 7.9 Hz, 1H), 2.34 (s, 3H), 1.42 (bs, 9H).

13C NMR (100 MHz, CDCl₃) δ 154.5, 137.7, 137.2, 135.5 (Cq, J_CF = 5.0 Hz), 131.2, 129.6, 129.57, 128.9, 128.5, 128.3, 126.5, 123.2 (Cq, J_CF = 273.5 Hz), 79.9, 52.4, 28.3, 21.0.

19F NMR (376 MHz, CDCl₃) δ –66.2 (s, CF₃).

HRMS (ESI) m/z: 414.1619 [M+Na]^+, C₂₂H₂₄F₃NaO₂ requires 414.1651.

(R,E)-4,4,4-Trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-amine (4c)

The title compound was obtained following GPA from (R,E)-4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-one (1.3 g, 4.2 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 31% yield over 3 steps (0.4 g, 1.3 mmol).

1H NMR (400 MHz, CDCl₃) δ 7.43 – 7.41 (m, 3H), 7.27 – 7.24 (m, 2H), 7.19 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.52 (dq, J = 9.6, 1.6 Hz, 1H), 4.42 (d, J = 9.6 Hz, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 1.50 (bs, 2H).

13C NMR (100 MHz, CDCl₃) δ 159.0, 139.3 (Cq, J_CF = 5.0 Hz), 135.0, 131.8, 130.1 (J_CF = 30.0 Hz) 129.7, 128.8, 128.5, 127.5, 123.3 (Cq, J_CF = 273.5 Hz), 114.2, 55.3, 52.5.

19F NMR (376 MHz, CDCl₃) δ –66.2 (s, CF₃).

tert-Butyl (R,E)-(4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-yl)carbamate (4c‘)
The title compound was obtained following GPB from \((R,E)\)-4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-amine (61.5 mg, 0.20 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 66% (53.8 mg, 0.13 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 94%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, \((1R,E)\) (major diastereomer): minor enantiomer \(t_e = 8.4\) min, major enantiomer, \(t_e = 7.8\) min.

\([\alpha]_D^{25}\): – 74.6 (c 1.01, CHCl₃, for the diastereomer mixture, d.r.: 94:6).

\(^1\text{H} \text{NMR}\) (400 MHz, CDCl₃) δ 7.39 – 7.35 (m, 3H), 7.27 – 7.25 (m, 2H), 7.06 (d, \(J = 9.0\) Hz, 2H), 6.85 (d, \(J = 9.0\) Hz, 2H), 6.52 (dq, \(J = 9.5, 1.5\) Hz, 1H), 5.13 (bs, 1H), 4.88 (d, \(J = 7.5\) Hz, 1H), 3.79 (s, 3H), 1.41 (s, 9H).

\(^{13}\text{C} \text{NMR}\) (100 MHz, CDCl₃) δ 159.2, 154.5, 135.6 (Cq, \(J_{CF} = 5.5\) Hz), 132.3 131.2, 129.5, 128.9, 128.4, 127.8, 127.3, 123.2 (Cq, \(J_{CF} = 273.5\) Hz), 114.3, 79.9, 55.2, 52.1, 28.3.

\(^{19}\text{F} \text{NMR}\) (376 MHz, CDCl₃) δ – 66.20 (s, CF₃).

HRMS (ESI) m/z: 430.1606 [M+Na]^+ , C₂₃H₂₄F₃NNaO₃ \(^+\) requires 430.1600.

\((R,E)-1-(4\text{-Bromophenyl})-4,4,4\text{-trifluoro-3-phenylbut-2-en-1-amine (4d)}\)

\[\text{F}_3\text{C} = \text{Ph} = \text{NH}_2\]

\[\text{Br}\]

The title compound was obtained following GPA from \((R,E)-1-(4\text{-bromophenyl})\)-4,4,4-trifluoro-3-phenylbut-2-en-1-one (5.0 g, 14.1 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 55% yield over 3 steps (2.7 g, 7.7 mmol).

\(^1\text{H} \text{NMR}\) (400 MHz, CDCl₃) δ 7.47 – 7.42 (m, 5H), 7.26 – 7.23 (m, 2H), 7.14 (d, \(J = 8.4\) Hz, 2H), 6.47 (dd, \(J = 9.7, 1.7\) Hz, 1H), 4.44 (d, \(J = 9.7\) Hz, 1H), 1.51 (bs, 2H).

\(^{13}\text{C} \text{NMR}\) (100 MHz, CDCl₃) δ 141.8, 138.5 (Cq, \(J_{CF} = 5.5\) Hz), 131.9, 131.5, 129.5, 128.9, 128.6, 128.2, 127.2, 123.1 (Cq, \(J_{CF} = 273.5\) Hz), 119.0, 52.6.

\(^{19}\text{F} \text{NMR}\) (376 MHz, CDCl₃) δ – 66.37 (s, CF₃).

\textit{tert}-Butyl \((R,E)-1-(4\text{-bromophenyl})-4,4,4\text{-trifluoro-3-phenylbut-2-en-1-yl} \text{carbamate (4d’)}\)

\[\text{F}_3\text{C} = \text{Ph} \quad \text{NHBoc}\]

\[\text{Br}\]

The title compound was obtained following GPB from \((R,E)-1-(4\text{-bromophenyl})\)-4,4,4-trifluoro-3-phenylbut-2-en-1-amine (71.2 mg, 0.20 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 90% (82.3 mg, 0.18 mmol) [m.p.: 110 – 112 °C].

The enantiomeric excess (minor isomer: 92, major isomer 97%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, \((1R,Z)\) (minor diastereomer): minor enantiomer,
The enantiomeric excess (minor isomer: purified by FCC (pentane:EtOAc 95:5) as a white solid in (trifluoromethyl)phenyl)but
The title compound was obtained following GPB from (4e')
19 Cq, (d, 1H), 5.15 (bs, 1H), 4.97 (bs, 1H), 1.40 (s, 9H).
13 Cq, (Cq, JCF = 5.5 Hz), 132.1, 132.0, 130.9, 129.4, 129.1, 128.6, 128.2, 123.0 (Cq, JCF = 273.6 Hz), 121.8, 80.2, 52.2, 28.2.
19 F NMR (376 MHz, CDCl3) δ – 66.38 (s, CF3).
HRMS (ESI) m/z: 480.0637 [M+Na]+, C21H21BrF3NaO2 requires 480.0580.
(R,E)-4,4,4-Trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (4e)

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-one (3.7 g, 10.8 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 54% yield over 3 steps (2.0 g, 5.8 mmol).

1H NMR (400 MHz, CDCl3) δ 7.61 (d, J = 8.0 Hz, 2H), 7.46 – 7.44 (m, 3H), 7.40 (d, J = 8.0 Hz, 2H), 7.28 – 7.27 (m, 2H), 6.50 (dd, J = 9.5, 1.5 Hz, 1H), 4.55 (d, J = 9.5 Hz, 1H), 1.56 (bs, 2H).

13 Cq, (Cq, JCF = 30.0 Hz), 131.4, 129.9 (JCF = 32.4 Hz), 129.5, 129.0, 128.7, 126.9, 125.7 (Cq, JCF = 4.0 Hz), 124.0 (Cq, JCF = 272.0 Hz), 123.1 (Cq, JCF = 273.5 Hz), 52.8.

19 F NMR (376 MHz, CDCl3) δ – 66.55 (s, CF3), – 66.46 (s, CF3).

tert-Butyl (R,E)-(4,4,4-trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-yl)carbamate (4e')

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (86.3 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 88% (98.1 mg, 0.22 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 95%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer tR = 7.7 min, major enantiomer, tR = 13.9 min.

[α]D25: – 63.1 (c 0.99, CHCl3, for the diastereomer mixture, d.r.: 91:9).
The enantiomeric excess (minor isomer: (pentane:EtOAc 95:5) as a white solid in phenylbutyl ether). The title compound was obtained following GPB from tert-butyl (E)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-yl)carbamate (4f) as a yellow oil in phenylbutyl ether. The title compound was obtained following GPA from tert-butyl (4f) as a yellow oil in phenylbutyl ether. The protected allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 35% yield over 3 steps (0.8 g, 2.4 mmol).

\[\text{HRMS (ESI) } m/z: 468.1336 [M+Na]^+ \text{ requires } 468.1369.\]

\[\text{(R,E)-4,4,4-Trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-amine (4f)}\]

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-one (2.3 g, 7.1 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 35% yield over 3 steps (0.8 g, 2.4 mmol).

\[\text{HRMS (ESI) } m/z: 468.1336 [M+Na]^+ \text{ corresponding to } C_{20}H_{13}F^+. \]

\[\text{C_{20}H_{13}F^+ requires } 468.1369.\]

\[\text{tert-Butyl (R,E)-(4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-yl)carbamate (4f)}\]

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-amine (60.0 mg, 0.18 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 83% (65.2 mg, 0.15 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 97%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer \(t_r = 13.7 \text{ min}, \text{major enantiomer}, t_r = 9.6 \text{ min}.\)

\[\alpha]_{D}^{25} = -176.8 (c 1.00, CHCl_3, \text{for the diastereomer mixture, } d.r.: 97:3).\]

\[\text{HRMS (ESI) } m/z: 468.1336 [M+Na]^+ \text{ requires } 468.1369.\]
The enantiomeric excess (minor isomer: nd, major isomer 94%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (R,E) (major diastereomer): minor enantiomer \( t_r = 8.0 \) min, major enantiomer, \( t_r = 6.6 \) min.

\[ [\alpha]_D^{25} = -36.4 \text{ (c 0.77, CHCl}_3, \text{ for the diastereomer mixture, d.r.: 97:3).} \]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3) \delta 7.40 - 7.35 (m, 3H), 7.28 - 7.22 (m, 3H), 6.81 (dd, J = 8.3, 2.5 Hz, 1H), 6.74 (d, J = 7.7 Hz, 1H), 6.67 (s, 1H), 6.50 (dd, J = 9.3, 1.9, 1H), 5.16 (bs, 1H), 4.93 (d, J = 7.4 Hz, 1H), 3.77 (s, 3H), 1.41 (s, 9H). \]

\[^{13}C\text{ NMR (100 MHz, CDCl}_3) \delta 159.9, 154.5, 141.7, 135.2 (\text{Cq, } J_{CF} = 5.3 \text{ Hz}), 131.1, 130.0, 129.6, 128.9, 128.5, 123.1 (\text{Cq, } J_{CF} = 273.6 \text{ Hz}), 119.1, 118.6, 113.2, 112.4, 79.9, 55.2, 52.6, 28.3. \]

\[^{19}F\text{ NMR (376 MHz, CDCl}_3) \delta - 66.28 \text{ (s, CF}_{3}). \]

HRMS (ESI) \text{m/z: 430.1595 [M+Na]+, } C_{22}H_{24}F_3N\text{NaO}_{3}^+ \text{ requires 430.1600.}
**(R,E)-4,4,4-Trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)but-2-en-1-amine (4h)**

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-3-phenyl-1-(3-
(trifluoromethyl)phenyl)but-2-en-1-one (1.2 g, 3.5 mmol). The allylic amine was purified by FCC
(pentane:EtOAc 7:3) as a yellow oil in 66% yield over 3 steps (0.8 g, 2.3 mmol).

\[ \text{HRMS (ESI)} m/z: \text{Fragmentation observed: 329.0884} \]

\[ \text{HRMS (ESI)} m/z: \text{[M+Na]⁺ requires 468.1369.} \]

\[ \text{(R,E)-4,4,4-Trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-amine (4i)} \]

\[ \text{S14} \]
The title compound was obtained following GPA from \((E)\)-4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-one (2.7 g, 8.7 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 49% yield over 3 steps (1.3 g, 4.26 mmol).

\(^1\)H NMR (400 MHz. CDCl\(_3\)) \(\delta\) 7.41 – 7.39 (m, 3H), 7.24 – 7.23 (m, 3H), 7.07 (dd, \(J = 7.5, 1.3\) Hz, 1H), 6.91 (t, \(J = 7.8\) Hz, 1H), 6.87 (d, \(J = 8.3\) Hz, 1H), 6.76 (dd, \(J = 9.6, 1.2\) Hz, 1H), 4.54 (d, \(J = 9.7\) Hz, 1H), 3.79 (s, 3H), 1.77 (bs, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 156.9, 138.5 (Cq, \(J_{CF} = 5.3\) Hz), 132.0, 131.1, 130.1 (Cq, \(J_{CF} = 29.7\) Hz), 129.8, 128.63, 128.57, 128.3, 127.8, 123.5 (Cq, \(J_{CF} = 273.3\) Hz), 120.9, 110.9, 55.1, 50.7.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -66.06 (S, CF\(_3\)).

tert-Butyl (\(R,E\))-(4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-yl)carbamate (4i')

The title compound was obtained following GPB from (\(R,E\))-4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-amine (76.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 99% (100.5 mg, 0.25 mmol).

The enantiomeric excess (minor isomer: 94%, major isomer 75%) was determined by HPLC (CHIRACEL® IC), hexane/iPrOH 98/2, 1 mL/min, (1\(R,Z\)) (minor diastereomer): minor enantiomer, \(t_r = 12.8\) min, major enantiomer, \(t_r = 10.9\) min, (1\(R,E\)) (major diastereomer): minor enantiomer \(t_r = 9.3\) min, major enantiomer, \(t_r = 8.6\) min.

\([\alpha]_D^{25} = -24.3\) (c 0.76, CHCl\(_3\), for the diastereomer mixture, d.r.: 97:3).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.41 – 7.40 (m, 3H), 7.24 – 7.20 (m, 3H), 6.87 (d, \(J = 8.1\) Hz, 1H), 6.82 – 6.75 (m, 3H), 5.59 (bs, 1H), 5.30 (bs, 1H), 3.84 (s, 3H), 1.42 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 156.9, 154.4, 136.0, 131.4, 131.2 (Cq, \(J_{CF} = 30.1\) Hz), 129.8, 129.2, 128.7, 128.3, 127.9, 123.3 (Cq, \(J_{CF} = 273.3\) Hz), 120.9, 111.1, 79.5, 55.3, 51.5, 28.3.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -66.40 (s, CF\(_3\)).

HRMS (ESI) m/z: 430.1595 [M+Na]\(^+\), \(C_{25}H_{24}F_3NNaO_3\)\(^+\) requires 430.1600.

(\(S,E\))-5,5,5-Trifluoro-4-phenylpent-3-en-2-amine (4j)
The title compound was obtained following GPB from (E)-5,5,5-trifluoro-4-phenylpent-3-en-2-one (2.0 g, 9.3 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 30% yield over 3 steps (0.6 g, 2.8 mmol).

\[ ^1H \text{NMR} \] (400 MHz. CDCl\(_3\)) \( \delta \) 7.41 – 7.37 (m, 3H), 7.24 – 7.22 (m, 2H), 6.26 (dq, \( J = 9.5, 1.6 \) Hz, 1H), 3.44 (dt, \( J = 13.1, 6.6 \) Hz, 1H), 1.31 (bs, 2H), 1.14 (d, \( J = 6.6 \) Hz, 3H).

\[ ^{13}C \text{NMR} \] (100 MHz, CDCl\(_3\)) \( \delta \) 141.3 (Cq, \( J_{CF} = 5.1 \) Hz), 131.9, 129.8 (Cq, \( J_{CF} = 29.9 \) Hz), 129.5, 128.6, 128.5, 123.3 (Cq, \( J_{CF} = 273.1 \) Hz), 44.8, 23.1.

\[ ^{19}F \text{NMR} \] (376 MHz, CDCl\(_3\)) \( \delta \) -66.30 (s, CF\(_3\)).

**tert-Butyl (S,E)-(5,5,5-Trifluoro-4-phenylpent-3-en-2-yl)carbamate (4j')**

The title compound was obtained following GPB from (S,E)-5,5,5-trifluoro-4-phenylpent-3-en-2-amine (53.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 99% (69.4 mg, 0.22 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 28%) was determined by HPLC (CHIRACEL® OD-H), hexane/iPrOH 98/2, 1 mL/min, (1S,E) (major diastereomer): minor enantiomer \( t_r = 9.17 \) min, major enantiomer, \( t_r = 6.85 \) min.

\[ ^1H \text{NMR} \] (400 MHz, CDCl\(_3\)) \( \delta \) 7.42 – 7.38 (m, 3H), 7.32 – 7.31 (m, 2H), 6.47 (t, \( J = 6.7 \) Hz, 1H), 4.47 (bs, 1H), 4.17 (bs, 1H), 1.25 (bs, 2H).

\[ ^{13}C \text{NMR} \] (100 MHz, CDCl\(_3\)) \( \delta \) 154.6, 137.9, 131.4, 129.5, 128.7, 128.5, 127.2, 123.2 (Cq, \( J_{CF} = 273.2 \) Hz), 44.9, 28.3, 21.0.

\[ ^{19}F \text{NMR} \] (376 MHz, CDCl\(_3\)) \( \delta \) -66.46 (s, CF\(_3\)).

HRMS (ESI) \( m/z \): 338.1360 [M+Na]\(^+\), \( C_{16}H_{20}F_{3}NNaO_{2} \) requires 338.1338.

(E)-4,4,4-Trifluoro-3-phenylbut-2-en-1-amine (4k)

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-3-phenylbut-2-enal (0.7 g, 3.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 49% yield over 3 steps (0.35 g, 1.7 mmol).

\[ ^1H \text{NMR} \] (400 MHz, CDCl\(_3\)) \( \delta \) 7.42 – 7.38 (m, 3H), 7.24 – 7.22 (m, 2H), 6.47 (t, \( J = 6.7 \) Hz, 1H), 3.27 (dd, \( J = 6.9, 2.2 \) Hz, 2H), 1.25 (bs, 2H).

\[ ^{13}C \text{NMR} \] (100 MHz, CDCl\(_3\)) \( \delta \) 137.0 (Cq, \( J_{CF} = 5.3 \) Hz), 131.7, 131.3 (Cq, \( J_{CF} = 29.6 \) Hz), 129.4, 128.7, 128.5, 123.3 (Cq, \( J_{CF} = 273.1 \) Hz), 39.8.

\[ ^{19}F \text{NMR} \] (376 MHz, CDCl\(_3\)) \( \delta \) -66.01 (s, CF\(_3\)).
(R,E)-4,4,4-Trifluoro-1-phenyl-3-(p-tolyl)but-2-en-1-amine (4l)

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{F}_3C & \quad \quad \quad \quad \\
\end{align*}
\]

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-1-phenyl-3-(p-tolyl)but-2-en-1-one (1.6 g, 5.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 56% yield over 3 steps (0.9 g, 3.1 mmol).

\[\text{^1H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.34 - 7.33 (m, 2H), 7.30 - 7.27 (m, 3H), 7.24 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 6.51 (dd, J = 9.8, 1.7 Hz, 1H), 4.50 (d, J = 9.8 Hz, 1H), 2.40 (s, 3H), 1.56 (bs, 2H).\]

\[\text{^13C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 142.9, 138.8 (Cq, J_{CF} = 5.2 \text{ Hz}), 138.7, 130.5 (Cq, J_{CF} = 29.8 \text{ Hz}), 129.5, 129.2, 128.8, 128.7, 127.6, 126.4, 123.3 (Cq, J_{CF} = 273.3 \text{ Hz}), 53.0, 21.3.\]

\[\text{^19F NMR} \ (376 \text{ MHz, CDCl}_3) \delta -66.30 \text{ (s, CF}_3).\]

The enantiomeric excess (minor isomer: nd, major isomer 90%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer \(t_r = 6.9 \text{ min, major enantiomer, } t_r = 5.4 \text{ min.}\)

\[[\alpha]_D^{25}: -53.1 \text{ (c 0.98, CHCl}_3, \text{ for the diastereomer mixture, d.r.: 87:13).}\]

\[\text{^1H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.38 - 7.28 (m, 3H), 7.21 - 7.15 (m, 6H), 6.49 (dq, J = 9.4, 1.6 Hz, 1H), 5.22 (bs, 1H), 4.90 (d, J = 7.2 Hz, 1H), 2.38 (s, 3H), 1.41 (s, 9H).\]

\[\text{^13C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 154.5, 140.3, 138.8, 134.9 (Cq, J_{CF} = 4.7 \text{ Hz}), 129.4, 129.2, 128.9, 128.1, 127.9, 126.5, 123.2 (Cq, J_{CF} = 273.6 \text{ Hz}), 80.0, 52.6, 28.3, 21.3.\]

\[\text{^19F NMR} \ (376 \text{ MHz, CDCl}_3) \delta -66.32 \text{ (s, CF}_3).\]

HRMS (ESI) \(m/z: 414.1623 \text{ [M+Na]}^+, \text{ C}_{28}\text{H}_{22}\text{F}_3\text{NaN}_2\text{O}_2^+ \text{ requires 414.1651.}\)

tert-Butyl (R,E)-(4,4,4-trifluoro-1-phenyl-3-(p-tolyl)but-2-en-1-yl)carbamate (4l')

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
\text{F}_3C & \quad \quad \quad \quad \\
\end{align*}
\]

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-1-phenyl-3-(p-tolyl)but-2-en-1-amine (72.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 99% (93.2 mg, 0.24 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 90%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer \(t_r = 6.9 \text{ min, major enantiomer, } t_r = 5.4 \text{ min.}\)

\[[\alpha]_D^{25}: -53.1 \text{ (c 0.98, CHCl}_3, \text{ for the diastereomer mixture, d.r.: 87:13).}\]

\[\text{^1H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.38 - 7.28 (m, 3H), 7.21 - 7.15 (m, 6H), 6.49 (dq, J = 9.4, 1.6 Hz, 1H), 5.22 (bs, 1H), 4.90 (d, J = 7.2 Hz, 1H), 2.38 (s, 3H), 1.41 (s, 9H).\]

\[\text{^13C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 154.5, 140.3, 138.8, 134.9 (Cq, J_{CF} = 4.7 \text{ Hz}), 129.4, 129.2, 128.9, 128.1, 127.9, 126.5, 123.2 (Cq, J_{CF} = 273.6 \text{ Hz}), 80.0, 52.6, 28.3, 21.3.\]

\[\text{^19F NMR} \ (376 \text{ MHz, CDCl}_3) \delta -66.32 \text{ (s, CF}_3).\]

HRMS (ESI) \(m/z: 414.1623 \text{ [M+Na]}^+, \text{ C}_{28}\text{H}_{22}\text{F}_3\text{NaN}_2\text{O}_2^+ \text{ requires 414.1651.}\)

(R,E)-4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-amine (4m)
The title compound was obtained following GPA from (E)-4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-one (1.6 g, 5.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 56% yield over 3 steps (0.9 g, 3.1 mmol).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.37 – 7.33 (m, 2H), 7.29 – 7.27 (m, 3H), 7.19 (d, \(J = 8.6\) Hz, 1H), 6.94 (d, \(J = 8.6\) Hz, 1H), 6.51 (d, \(J = 9.7\) Hz, 1H), 4.50 (d, \(J = 9.7\) Hz, 1H), 3.85 (s, 3H), 1.55 (bs, 2H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.9, 143.0, 138.9 (Cq, \(J_{CF} = 5.1\) Hz), 130.9, 130.1 (Cq, \(J = 29.9\) Hz), 128.8, 127.6, 126.4, 123.7, 123.4 (Cq, \(J = 273.3\) Hz), 113.9, 55.2, 53.1.

\(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) – 66.40 (s, CF\(_3\)).

**tert-Butyl (R,E)-(4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-yl)carbamate (4m)**

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-amine (76.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 99% (86.2 mg, 0.21 mmol).

The enantiomeric excess (minor isomer: 98%, major isomer 93%) was determined by HPLC (CHIRACEL \(^\text{®}\) OD-H), hexane/iPrOH 98/2, 1 mL/min, (1R,Z) (minor diastereomer): minor enantiomer, \(t_r = 19.5\) min, major enantiomer, \(t_r = 12.0\) min, (1R,E) (major diastereomer): minor enantiomer \(t_r = 8.4\) min, major enantiomer, \(t_r = 6.3\) min.

[\(\alpha\)]\(_{D}^{25}\) = – 60.0 (c 0.98, CHCl\(_3\), for the diastereomer mixture, d.r.: 88:12).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38 – 7.27 (m, 4H), 7.21 – 7.17 (m, 3H), 6.92 (d, \(J = 8.7\) Hz, 2H), 6.50 (d, \(J = 9.2\) Hz, 1H), 5.24 (bs, 1H), 5.04 (bs, 1H), 3.82 (s, 3H), 1.42 (s, 9H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.9, 154.5, 140.3, 135.1 (Cq, \(J_{CF} = 5.5\) Hz), 130.8, 128.9, 127.8, 127.3, 126.5, 123.2 (Cq, \(J_{CF} = 273.5\) Hz), 123.2, 113.9, 79.9, 55.1, 52.6, 28.3.

\(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) – 66.36 (s, CF\(_3\)).

HRMS (ESI) \(m/z\): 430.1562 [M+Na]^+, \(C_{21}H_{22}F_{3}NaO_{2}\) requires 430.1600.

(R,E)-4,4,4-Trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (4n)
The title compound was obtained following GPA from \((E)-4,4,4\text{-trifluoro-1-phenyl-3-(4-}
\text{(trifluoromethyl)phenyl})\text{but-2-en-1-one}
\) \((0.8 \text{ g, } 2.3 \text{ mmol})\). The allylic amine was purified by FCC
\((\text{pentane:EtOAc } 7:3)\) as a yellow oil in 52\% yield over 3 steps
\((0.4 \text{ g, } 1.2 \text{ mmol})\).

\(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.60 \text{ (d, } J = 8.1 \text{ Hz, 2H), 7.45 – 7.44 \text{ (m, 3H), 7.40 \text{ (d, } J = 8.1 \text{ Hz, 2H), \)
\(7.27 – 7.26 \text{ (m, 2H), 6.50 \text{ (dd, } J = 9.7, 1.7 \text{ Hz, 1H), 4.55 \text{ (d, } J = 9.7 \text{ Hz, 1H), 1.56 \text{ (bs, 2H).}}\)

\(^{13}\text{C NMR (100 MHz, CDCl}_3\) \(\delta 146.7, 138.2 \text{ (Cq, } J_{\text{CF}} = 5.2 \text{ Hz), 131.5 \text{ (Cq, } J_{\text{CF}} = 30.2 \text{ Hz), 131.4 \text{, 129.9 \text{ (Cq, } J_{\text{CF}} = 32.5 \text{ Hz), 129.5 \text{, 129.0 \text{, 128.7, 126.9, 125.7 \text{ (Cq, } J_{\text{CF}} = 3.8 \text{ Hz), 124.0 \text{ (Cq, } J_{\text{CF}} = 272.0 \text{ Hz), \)
\(123.1 \text{ (Cq, } J_{\text{CF}} = 273.4 \text{ Hz), 52.8.}}\)

\(^{19}\text{F NMR (376 MHz, CDCl}_3\) \(\delta – 66.55 \text{ (s, CF}_3\), – 66.46 \text{ (s, CF}_3\)).

**tert-Butyl \((R,E)-(4,4,4\text{-trifluoro-1-phenyl-3-(4-}
\text{(trifluoromethyl)phenyl})\text{but-2-en-1-y1) carbamate (4n*)**

\(^{1}\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.66 \text{ (d, } J = 8.1 \text{ Hz, 2H), 7.41 \text{ (d, } J = 7.9 \text{ Hz, 2H), 7.36 – 7.30 \text{ (m, 3H), \)
\(7.15 – 7.12 \text{ (m, 2H), 6.61 \text{ (dd, } J = 9.4, 1.8 \text{ Hz, 1H), 5.13 \text{ (bs, 1H), 4.90 \text{ (d, } J = 7.4 \text{ Hz, 1H), 1.42 \text{ (s, 9H).}}\)

\(^{13}\text{C NMR (100 MHz, CDCl}_3\) \(\delta 154.5, 139.5, 136.6 \text{ (Cq, } J_{\text{CF}} = 4.4 \text{ Hz), 134.9, 131.13 \text{ (Cq, } J_{\text{CF}} = 32.5 \text{ Hz), 131.06 \text{ (Cq, } J_{\text{CF}} = 30.3 \text{ Hz), 130.2, 129.1, 128.2, 126.6, 125.5 \text{ (Cq, } J_{\text{CF}} = 3.8 \text{ Hz), 123.9 \text{ (Cq, } J_{\text{CF}} = 272.3 \text{ Hz), 122.8 \text{ (Cq, } J_{\text{CF}} = 273.5 \text{ Hz), 80.2, 52.7, 28.3.\)

\(^{19}\text{F NMR (376 MHz, CDCl}_3\) \(\delta – 62.85 \text{ (s, CF}_3\), – 66.14 \text{ (s, CF}_3\)).

HRMS (ESI) \(m/z: 468.1369 [M+Na]^+\), \(C_{22}H_{21}F_6\text{NNaO}_2^+\) requires 468.1369.

\((R,E)-4,4,4\text{-Trifluoro-1-phenyl-3-(m-tolyl})\text{but-2-en-1-amine (4o)}\)
The title compound was obtained following GPA from (E)-4,4,4-trifluoro-1-phenyl-3-(m-tolyl)but-2-en-1-one (2.0 g, 6.9 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 50% yield over 3 steps (1.0 g, 3.4 mmol).

\[ ^1H \text{NMR (400 MHz, CDCl}_3 \delta 7.38 - 7.27 \text{ (m, 6H), } 7.25 - 7.23 \text{ (m, 1H), } 7.08 - 7.06 \text{ (m, 2H), } 6.53 \text{ (dq, } J = 9.7, 1.6 \text{ Hz, 1H), } 4.49 \text{ (d, } J = 9.7 \text{ Hz, 1H), } 2.39 \text{ (s, 3H), } 1.56 \text{ (bs, 2H).} \]

\[ ^13C \text{NMR (100 MHz, CDCl}_3 \delta 142.9, 138.8 \text{ (Cq, } J_{CF} = 5.2 \text{ Hz), } 138.2, 131.6, 130.6 \text{ (Cq, } J_{CF} = 29.9 \text{ Hz), } 130.2, 129.6, 128.8, 128.4, 127.6, 126.7, 126.5, 123.3 \text{ (Cq, } J_{CF} = 273.3 \text{ Hz), } 53.0, 21.4. \]

\[ ^19F \text{NMR (376 MHz, CDCl}_3 \delta -66.18 \text{ (s, CF}_3). \]

**tert-Butyl (R,E)-(4,4,4-trifluoro-1-phenyl-3-(m-tolyl)but-2-en-1-yl)carbamate (4o')**

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (72.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 94% (92.3 mg, 0.24 mmol).

The enantiomeric excess (minor isomer: 93%, major isomer 89%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,Z) (minor diastereomer): minor enantiomer, t\(_r\) = 9.92 min, major enantiomer, t\(_r\) = 6.87 min, (1R,E) (major diastereomer): minor enantiomer t\(_r\) = 5.78 min, major enantiomer t\(_r\) = 4.93 min.

\[ [\alpha]_{D}^{25.} = -54.2 \text{ (c 1.00, CDCl}_3, \text{ for the diastereomer mixture, d.r.: 89:11).} \]

\[ ^1H \text{NMR (400 MHz, CDCl}_3 \delta 7.38 - 7.27 \text{ (m, 4H), } 7.22 - 7.20 \text{ (m, 1H), } 7.17 - 7.15 \text{ (m, 2H), } 7.08 - 7.05 \text{ (m, 2H), } 6.52 \text{ (dd, } J = 9.3, 1.9 \text{ Hz, 1H), } 5.21 \text{ (bs, 1H), } 4.99 \text{ (d, } J = 7.6 \text{ Hz, 1H), } 2.35 \text{ (s, 3H), } 1.42 \text{ (s, 9H).} \]

\[ ^13C \text{NMR (100 MHz, CDCl}_3 \delta 154.4, 140.4, 138.1, 135.1, 132.4 \text{ (Cq, } J_{CF} = 29.7 \text{ Hz), } 131.0, 130.2, 129.7, 128.8, 128.3, 127.8, 126.6, 126.5, 123.2 \text{ (Cq, } J_{CF} = 273.5 \text{ Hz), } 80.0, 52.6, 28.3, 21.3. \]

\[ ^19F \text{NMR (376 MHz, CDCl}_3 \delta -66.16 \text{ (s, CF}_3). \]

HRMS (ESI) m/z: 414.1652 [M+Na]^+, C\(_{21}\)H\(_{22}\)F\(_3\)NNaO\(_2\)^+ requires 414.1651.

\((R,Z)-4,4,4\text{-Trifluoro-1-phenyl-3-(thiophen-2-yl)but-2-en-1-amine (4p)}\)
The title compound was obtained following GPA from (Z)-4,4,4-trifluoro-1-phenyl-3-(thiophen-2-yl)but-2-en-1-one (1.5 g, 5.3 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 47% yield over 3 steps (0.7 g, 2.5 mmol).

$^1$H NMR (400 MHz. CDCl$_3$) $\delta$ 7.44 (d, $J = 4.8$ Hz, 1H), 7.40 – 7.29 (m, 5H), 7.11 – 7.09 (m, 2H), 6.62 (d, $J = 9.7$ Hz, 1H), 4.80 (d, $J = 9.7$ Hz, 1H), 1.60 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.4, 141.3 (Cq, $J_{CF} = 4.9$ Hz), 130.9, 129.5, 128.8, 127.7, 127.5, 127.2, 126.5, 123.7 (Cq, $J_{CF} = 31.2$ Hz), 122.7 (Cq, $J_{CF} = 273.5$ Hz), 53.1.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -66.58 (s, CF$_3$).

** tert-Butyl (R,Z)-(4,4,4-trifluoro-1-phenyl-3-(thiophen-2-yl)but-2-en-1-yl)carbamate (4p')**

The title compound was obtained following GPB from (R,E)-4,4,4-trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (70.8 mg, 0.25 mmol). The protected allylic amine was purified by FCC (pentane:EtOAc 95:5) as a white solid in 98% (94.4 mg, 0.24 mmol).

The enantiomeric excess (minor isomer: nd, major isomer 95%) was determined by HPLC (CHIRACEL $^R$ OD–H), hexane/iPrOH 98/2, 1 mL/min, (1R,E) (major diastereomer): minor enantiomer $t_r = 9.2$ min, major enantiomer, $t_r = 7.3$ min.

$[\alpha]_{D}^{25}$: -49.5 (c 1.00, CHCl$_3$, for the diastereomer mixture, d.r.: 96:4).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42 (dd, $J = 5.0$, 1.3 Hz, 1H), 7.38 – 7.28 (m, 3H), 7.24 – 7.23 (m, 2H), 7.09 (bs, 1H), 7.06 (dd, $J = 5.1$, 3.6 Hz, 1H), 6.58 (dd, $J = 9.2$, 0.8 Hz, 1H), 5.52 (bs, 1H), 4.95 (dd, $J = 7.7$ Hz, 1H), 1.42 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.5, 139.9, 137.0 (Cq, $J_{CF} = 5.5$ Hz), 130.4, 129.8, 129.0, 128.1, 127.8, 127.1, 126.7, 126.6, 122.7 (Cq, $J_{CF} = 273.9$ Hz), 80.2, 52.7, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -65.51 (s, CF$_3$).

HRMS (ESI) m/z: 406.1024 [M+Na]$^+$, C$_{19}$H$_{20}$F$_3$NNaO$_2$S$^+$ requires 406.1059.

** 4,4,4-Trifluoro-1-phenylbut-2-en-1-amine (4q)**

The title compound was obtained following GPA from (E)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (0.7 g, 3.5 mmol). The allylic amine was purified by FCC (pentane:EtOAc 7:3) as a yellow oil in 33% yield over 3 steps (0.3 g, 1.2 mmol).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 – 7.36 (m, 2H), 7.32 – 7.29 (m, 3H), 6.55 (ddq, $J = 15.7$, 5.5, 2.1 Hz, 1H), 5.92 (dq, $J = 15.7$, 6.4, 1.7 Hz, 1H), 4.65 (dp, $J = 4.5$, 2.2 Hz, 1H), 1.59 (bs, 2H).
13C NMR (100 MHz, CDCl3) δ 143.3 (Cq, JCF = 6.1 Hz), 142.3, 128.9, 127.9, 126.7, 123.3 (Cq, JCF = 269.4 Hz), 117.6 (Cq, JCF = 33.4 Hz), 56.2.

19F NMR (376 MHz, CDCl3) δ −63.79 (dt, J = 6.4, 2.1 Hz, CF3).

Characterization of amines 6 and 6’

HRMS of 6a-6q could not be obtained due to decomposition of the compounds. Instead, the HRMS of the 6a’-6p’ (protected amines) are reported. 6q HRMS could not be given, a fragmentation is observed. HPLC analysis and α values of 6a-6p is not reported here. Instead, the HPLC analysis and α values of 6a’-6p’ is reported.

4,4,4-Trifluoro-1,3-diphenylbutan-1-amine (6a)

The titled compound was obtained following GPC from 4a (69.3 mg, 0.25 mmol) as a colourless oil (83% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 75:25 in 80% isolated yield. Minor diastereomer (1S,3R)-6a isolated 20 mg (0.07 mmol) 28% yield, major diastereomer (1R,3R)-6a isolated 36 mg (0.13 mmol) 52% yield.

Minor diastereomer (configuration 1S, 3R)-6a

\[
\text{Ph} \quad \text{NH}_2 \\
\text{CF}_3 \quad \text{Ph} 
\]

1H NMR (400 MHz, CDCl3) δ 7.42 – 7.33 (m, 5H), 7.32 – 7.30 (m, 2H), 7.24 – 7.19 (m, 3H), 3.79 – 3.71 (m, 1H), 3.56 (t, J = 7.6 Hz, 1H), 2.24 – 2.50 (m, 2H), 1.40 (bs, 2H).

13C NMR (100 MHz, CDCl3) δ 146.4, 134.4 (Cq, JCF = 2,1 Hz), 129.2, 128.8, 128.7, 128.3, 127.2, 125.7, 124.3 (Cq, JCF = 272.8 Hz), 52.5, 47.3 (Cq, JCF = 26.7 Hz), 38.3 (Cq, JCF = 2.1 Hz).

19F NMR (376 MHz, CDCl3) δ −69.47 (d, J = 9.7 Hz, CF3).

Major diastereomer (configuration 1R, 3R)-6a

\[
\text{Ph} \quad \text{NH}_2 \\
\text{CF}_3 \quad \text{Ph} 
\]

1H NMR (400 MHz, CDCl3) δ 7.41 – 7.34 (m, 5H), 7.32 – 7.28 (m, 1H), 7.24 – 7.22 (m, 2H), 7.19 – 7.17 (m, 2H), 3.65 – 3.61 (m, 1H), 3.04 – 2.93 (m, 1H), 2.39 – 2.32 (m, 2H), 1.52 (bs, 2H).

13C NMR (100 MHz, CDCl3) δ 144.4, 134.3 (Cq, JCF = 2.0 Hz), 129.2, 128.8, 128.7, 128.3, 127.7, 126.8 (Cq, JCF = 278.0 Hz), 126.6, 53.6, 47.4 (Cq, JCF = 26.7 Hz), 37.9.

19F NMR (376 MHz, CDCl3) δ −69.91 (d, J = 9.5 Hz, CF3).

HRMS (ESI) m/z: 280.1336 [M+H]+, C16H17F3N+ requires 280.1308.

tert-Butyl 4,4,4-trifluoro-1,3-diphenylbutylcarbamate (6a’)

The titled compound was obtained following GPB from 6a and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer (1S,3R)-6a’, isolated yield 57% (15.1 mg, 0.04 mmol) from 20 mg (0.07 mmol) of (1S,3R)-6a. Major diastereomer (1R,3R)-6a’, isolated yield 72% (34.1 mg, 0.09 mmol) from 36 mg (0.13 mmol) of (1R,3R)-6a.
The enantiomeric excess (minor isomer: 94%, major isomer 90%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1S,3R (minor diastereomer): minor enantiomer, t_r = 7.2 min, major enantiomer, t_r = 5.9 min, 1R,3R (major diastereomer): minor enantiomer t_r = 6.1 min, major enantiomer, t_r = 7.8 min.

Minor diastereomer (configuration 1S, 3R)-6a’

![Structure]

[α]D 25: −5.4 (c 0.5, CHCl3, ee 94%).

^1H NMR (400 MHz, CDCl3) δ (Rotamers are observed) 7.38 – 7.29 (m, 8H), 7.16 – 7.14 (m, 2H), 4.99 – 4.76 (m, 1H), 4.50 – 4.28 (m, 1H), 3.47 (bs, 1H), 2.39 – 2.31 (m, 2H), 1.44 – 1.27 (m, 9H).

^13C NMR (100 MHz, CDCl3) δ 154.9, 142.2, 134.0, 129.1, 128.8, 128.7, 128.3, 127.5, 126.9 (Cq, JCF = 279.9 Hz), 125.9, 79.7, 51.5, 47.3 (Cq, JCF = 26.7 Hz), 36.8, 28.3.

^19F NMR (376 MHz, CDCl3) δ –69.31 (d, J = 9.7 Hz, CF3).

Major diastereomer (configuration 1R, 3R)-6a’

![Structure]

[α]D 25: −1.4 (c 0.71, CHCl3, ee 90%).

^1H NMR (400 MHz, CDCl3) δ 7.39 – 7.31 (m, 6H), 7.23 – 7.21 (m, 2H), 7.13 – 7.11 (m, 2H), 4.71 (d, J = 6.3 Hz, 1H), 4.36 (bs, 1H), 3.00 – 2.89 (m, 1H), 2.62 (bs, 1H), 2.35 (ddd, J = 13.7, 10.3, 3.6 Hz, 1H), 1.37 (bs, 9H).

^13C NMR (100 MHz, CDCl3) δ 154.6, 140.3, 133.3 (Cq, JCF = 2.1 Hz), 129.3, 129.0, 128.8, 128.5, 128.1, 126.6 (Cq, JCF = 278.0 Hz), 126.8, 79.6, 53.0, 47.2 (Cq, JCF = 27.9 Hz), 34.6, 28.3.

^19F NMR (376 MHz, CDCl3) δ –70.20 (bs, CF3).

HRMS (ESI) m/z: 402.1647 [M+Na]+, C21H24F3NNaO2+ requires 402.1651.

**4,4,4-Trifluoro-3-phenyl-1-(p-tolyl)butan-1-amine (6b)**

The titled compound was obtained following GPC from 4b (72.8 mg, 0.25 mmol) as a colourless oil (90% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 67:33 in 61% yield. Minor diastereomer could not be purified. Major diastereomer (1R,3R)-6b isolated 45 mg (0.15 mmol) 61% yield.

Major diastereomer (configuration 1R, 3R)-6b
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.38 – 7.35 (m, 3H), 7.23 – 7.22 (m, 2H), 7.16 (d, $J = 7.9$ Hz, 2H), 7.06 (d, $J = 7.9$ Hz, 2H), 3.57 (dd, $J = 8.7$, 6.4 Hz, 1H), 3.02 – 2.91 (m, 1H), 2.36 – 2.31 (m, 5H), 1.51 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 141.4, 137.3, 134.4 (q, $J = 2.1$ Hz), 129.5, 129.2, 128.7, 128.3, 126.8 (q, $J = 278.0$ Hz), 126.5, 53.3, 47.4 (Cq, $J_{CF} = 26.8$ Hz), 37.9, 21.1.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ – 69.91 (d, $J = 9.5$ Hz, CF$_3$).

*tert*-Butyl (4,4,4-trifluoro-3-phenyl-1-(p-tolyl)butyl)carbamate (6b’)

The titled compound was obtained following GPB from 6b and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6b’, isolated yield 56% (32.4 mg, 0.09 mmol) from 45 mg (0.15 mmol) of 6b.

The enantiomeric excess (minor isomer: nd, major isomer 67%) was determined by HPLC (CHIRALPAK® IF), hexane/iPrOH 98/2, 1 mL/min, $\lambda = 210$ nm, 1R,3R (major diastereomer): minor enantiomer tr = 7.1 min, major enantiomer, tr = 6.5 min.

**Major diastereomer (configuration 1R, 3R)-6b’**

[α]$_D^{25}$: – 7.8 (c 0.63, CHCl$_3$, ee 67%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.40 – 7.34 (m, 3H), 7.26 – 7.23 (m, 2H), 7.16 (d, $J = 7.8$ Hz, 2H), 7.00 (d, $J = 7.8$ Hz, 2H), 4.68 (bs, 1H), 4.31 (bs, 1H), 2.99 – 2.88 (m, 1H), 2.62 (bs, 1H), 2.36 – 2.29 (m, 4H), 1.37 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 154.7, 137.8, 137.3, 133.4, 130.8, 129.6, 129.3, 128.8, 128.4, 126.7, 126.65 (Cq, $J = 279.8$ Hz), 79.5, 52.7, 47.2 (Cq, $J = 26.9$ Hz), 34.6, 28.3, 21.1.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ – 70.18 (bs, CF$_3$).

HRMS (ESI) m/z: 416.1871 [M+Na]$^+$, C$_{22}$H$_{26}$F$_3$NNaO$_2$ requires 416.1871.

4,4,4-Trifluoro-1-(4-methoxyphenyl)-3-phenylbutan-1-amine (6c)

The titled compound was obtained following GPC from 4e (76.8 mg, 0.25 mmol) as a colourless oil (68% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 65:35 in 35% yield. Minor diastereomer could not be purified. Major diastereomer (1R,3R)-6c isolated 27 mg (0.09 mmol) 35% yield.

**Major diastereomer (configuration 1R, 3R)-6c**

S24
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.40 – 7.33 (m, 3H), 7.23 – 7.21 (m, 2H), 7.09 (d, \(J = 8.7\) Hz, 2H), 6.89 (d, \(J = 8.7\) Hz, 2H), 3.82 (s, 3H), 3.57 (dd, \(J = 9.6, 5.4\) Hz, 1H), 2.94 (ddq, \(J = 14.2, 9.6, 4.8\) Hz, 1H), 2.34 (m, 2H), 1.50 (bs, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.0, 136.3, 134.3 (Cq, \(J = 1.9\) Hz), 129.2, 128.7, 128.3, 127.7, 126.8 (Cq, \(J = 279.7\) Hz), 114.2, 55.3, 52.9, 47.4 (Cq, \(J = 26.8\) Hz), 38.0.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) – 69.92 (d, \(J = 9.5\) Hz, CF\(_3\)).

tert-Butyl (4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbutyl)carbamate (6c’)

The titled compound was obtained following GPB from 6c and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6c’, isolated yield 85% (30.0 mg, 0.08 mmol) from 27 mg (0.15 mmol) of 6c.

The enantiomeric excess (minor isomer: nd, major isomer 90%) was determined by HPLC (CHIRACEL® OD-H), hexane/iPrOH 98/2, 1 mL/min, \(\lambda = 210\) nm, 1R,3R (major diastereomer): minor enantiomer \(t_r = 9.2\) min, major enantiomer, \(t_r = 10.4\) min.

Major diastereomer (configuration 1R, 3R)-6c’

1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.40 – 7.33 (m, 3H), 7.22 – 7.02 (m, 2H), 7.03 (d, \(J = 8.5\) Hz, 2H), 6.88 7.03 (d, \(J = 8.5\) Hz, 2H), 4.65 (bs, 1H), 4.28 (bs, 1H), 3.82 (s, 3H), 2.97 – 2.87 (mm, 1H), 2.62 (bs, 1H), 2.30 (ddt, \(J = 13.6, 10.7, 3.3\) Hz, 1H), 1.37 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.3, 154.6, 133.3, 132.3, 129.3, 128.8, 128.4, 128.0, 126.7 (Cq, \(J = 279.6\) Hz), 114.3, 79.6, 55.3, 52.3, 47.2 (Cq, \(J = 26.4\) Hz), 34.5, 28.3.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) – 70.18 (d, \(J = 9.3\) Hz, CF\(_3\)).

HRMS (ESI) \(m/z\): 432.1757 [M+Na]\(^+\), \(C_{22}H_{26}F_3\)NaO\(_3\)\(^+\) requires 432.1785.

1-(4-Bromophenyl)-4,4,4-trifluoro-3-phenylbutan-1-amine (6d)

The titled compound was obtained following GPC from 4d (89 mg, 0.25 mmol) as a colourless oil (67% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 74:26 in 67% yield. Minor diastereomer could not be purified. Major diastereomer (1R,3R)-6d isolated 39.6 mg (0.09 mmol) 44% yield.

Reaction 1g scale

The titled compound was obtained following GPC from 4d (1.0 g, 2.81 mmol) as a colourless oil (73% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 70:30 in 68% yield. Minor diastereomer could not be purified. Major diastereomer (1R,3R)-6d isolated 387.5 mg (1.08 mmol) 38% yield.

Major diastereomer (configuration 1R, 3R)-6d
The titled compound was obtained following GPB from 6d and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6d', isolated yield 91% (46.1 mg, 0.10 mmol) from 39.6 mg (0.11 mmol) of 6d.

The enantiomeric excess (minor isomer: nd, major isomer 86%) was determined by HPLC (CHIRACEL® OD-H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1R,3R (major diastereomer): minor enantiomer tᵣ = 9.0 min, major enantiomer, tᵣ = 12.4 min.

**Major diastereomer (configuration 1R, 3R)-6d'**

![Chemical Structure](image)

[α]D²⁵: −37.1 (c 0.93, CHCl₃, ee 86%).

**1H NMR** (400 MHz, CDCl₃) δ 7.48 (d, J = 8.4 Hz, 2H), 7.41 – 7.37 (m, 3H), 7.22 – 7.20 (m, 2H), 7.00 (d, J = 8.1 Hz, 2H), 4.70 (d, J = 7.4 Hz, 1H), 4.32 (bs, 1H), 2.92 (dt, J = 18.3, 9.2, 4.6 Hz, 1H), 2.55 (bs, 1H), 2.30 (ddd, J = 13.7, 10.2, 3.6 Hz, 1H), 1.36 (s, 9H).

**13C NMR** (100 MHz, CDCl₃) δ 154.5, 139.6, 133.1, 132.1, 129.2, 128.9, 128.6, 128.5, 126.5 (Cq, J = 279.8 Hz), 121.9, 79.9, 52.4, 47.15 (Cq, J = 29.4 Hz), 34.6, 28.3.

**19F NMR** (376 MHz, CDCl₃) δ −70.22 (d, J = 9.2 Hz, CF₃).

HRMS (ESI) m/z: 480.0733 [M+Na]^+. C₂₁H₂₃F₅BrNNaO₂⁺ requires 480.0756.

**4,4,4-Trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)butan-1-amine (6e)**

The titled compound was obtained following GPC from 4e (86.3 mg, 0.25 mmol) as a colourless oil (60% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained
in a ratio 65:35 in 54% yield. Minor diastereomer could not be purified. Major diastereomer (1R,3R)-6e isolated 28.0 mg (0.08 mmol) 32% yield.

**Major diastereomer (configuration 1R, 3R)-6e**

![Structure](image)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.61 (d, $J$ = 8.0 Hz, 2H), 7.40 – 7.37 (m, 3H), 7.30 (d, $J$ = 8.0 Hz, 2H), 7.23 – 7.21 (m, 2H), 3.75 (dd, $J$ = 8.8, 6.1 Hz, 1H), 2.97 (pd, $J$ = 9.4, 5.3 Hz, 1H), 2.42 – 2.30 (m, 2H), 1.54 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.4, 134.0 (Cq, $J$ = 1.8 Hz), 130.0 (Cq, $J$ = 32.4 Hz), 129.1, 128.9, 128.5, 127.0, 126.6, 125.8 (Cq, $J$ = 3.7 Hz), 124.0 (d, $J$ = 272.1 Hz), 53.3, 47.3 (d, $J$ = 27.1 Hz), 37.9.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ – 62.51 (s, CF$_3$), – 70.00 (d, $J$ = 9.2 Hz, CF$_3$).

**tert-Butyl (4,4,4-trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)butyl)carbamate (6e')**

The titled compound was obtained following GPB from 5e and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6e', isolated yield 78% (27.8 mg, 0.106 mmol) from 28.0 mg (0.08 mmol) of 6e.

The enantiomeric excess (minor isomer: nd, major isomer 87%) was determined by HPLC (CHIRACEL® OD-H), hexane/iPrOH 98/2, 1 mL/min, $\lambda$ = 210 nm, 1R,3R (major diastereomer): minor enantiomer $t_r$ = 10.8 min, major enantiomer, $t_r$ = 7.8 min.

**Major diastereomer (configuration 1R, 3R)-6e’**

![Structure](image)

[$\alpha$]$_D^{25}$: – 16.0 (c 0.45, CHCl$_3$, ee 87%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J$ = 8.0 Hz, 2H), 7.42 – 7.38 (m, 3H), 7.26 – 7.21 (m, 4H), 4.75 (d, $J$ = 7.5 Hz, 1H), 4.46 (bs, 1H), 2.95 (dtd, $J$ = 18.4, 9.2, 3.7 Hz, 1H), 2.56 (bs, 1H), 2.36 (ddd, $J$ = 13.6, 9.7, 3.8 Hz, 1H), 1.36 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.6, 144.8, 133.2, 133.0 (Cq, $J$ = 35.7 Hz), 129.1, 129.0, 128.7, 127.1, 126.4 (d, $J$ = 279.8 Hz), 125.9 (Cq, $J$ = 3.6 Hz), 123.9 (d, $J$ = 272.1 Hz), 80.0, 52.7, 47.2 (Cq, $J$ = 27.8 Hz), 34.8, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ – 62.56 (s, CF$_3$), – 70.23 (bs, CF$_3$).

HRMS (ESI) $m/z$: 470.1551 [M+Na]$^+$, C$_{22}$H$_{23}$F$_6$NNaO$_2$$^+$ requires 470.1525.

**4,4,4-Trifluoro-1-(naphthalen-2-yl)-3-phenylbutan-1-amine (6f)**

The titled compound was obtained following GPC from 4f (81.8 mg, 0.25 mmol) as a colourless oil (86% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The
diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 75:25 in 87% yield. Minor diastereomer (1S,3R)-6f isolated 23 mg (0.07 mmol) 28 % yiled. Major diastereomer (1R,3R)-6f isolated 46.0 mg (0.14 mmol) 56% yield.

Minor diastereomer (configuration 1S, 3R)-6f

\[
\text{CF}_3 \quad \text{Ph} \quad \text{NH}_2
\]

\(^1\text{H} \text{NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \ 7.83 - 7.78 \ (m, 3H), 7.64 \ (s, 1H), 7.50 - 7.46 \ (m, 2H), 7.41 - 7.37 \ (m, 5H), 7.33 \ (dd, J = 8.6, 1.8 \text{ Hz, } 1H), 3.82 - 3.73 \ (m, 2H), 2.32 \ (dd, J = 8.2, 6.5 \text{ Hz, } 2H), 1.49 \ (bs, 2H).

\(^{13}\text{C} \text{NMR} \ (100 \text{ MHz, CDCl}_3) \ \delta \ 143.7, 134.5 \ (\text{Cq, } J = 2.0 \text{ Hz}), 133.4, 132.3, 129.2, 128.8, 128.5, 128.3, 127.7, 127.6, 126.2, 125.8, 124.2, 124.1, 52.6, 47.3 \ (\text{Cq, } J = 26.7 \text{ Hz}), 38.2.

\(^{19}\text{F} \text{NMR} \ (376 \text{ MHz, CDCl}_3) \ \delta \ -69.39 \ (d, J = 9.6 \text{ Hz, CF}_3).

Major diastereomer (configuration 1R, 3R)-6f

\[
\text{CF}_3 \quad \text{Ph} \quad \text{NH}_2
\]

\(^1\text{H} \text{NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \ 7.89 - 7.79 \ (m, 3H), 7.53 - 7.48 \ (m, 3H), 7.41 - 7.38 \ (m, 4H), 7.26 - 7.23 \ (m, 2H), 3.81 \ (t, J = 7.5 \text{ Hz, } 1H), 2.99 \ (pd, J = 9.3, 6.6 \text{ Hz, } 1H), 2.45 \ (dd, J = 8.4, 6.7 \text{ Hz, } 2H), 1.61 \ (bs, 2H).

\(^{13}\text{C} \text{NMR} \ (100 \text{ MHz, CDCl}_3) \ \delta \ 141.6, 134.3 \ (\text{Cq, } J = 1.9 \text{ Hz}), 133.3, 133.0, 129.2, 128.9, 128.7, 128.3, 127.8, 127.7, 126.7 \ (\text{Cq, } J = 279.8 \text{ Hz}), 126.3, 126.0, 125.8, 124.1, 53.7, 47.4 \ (\text{Cq, } J = 26.8 \text{ Hz}), 37.7.

\(^{19}\text{F} \text{NMR} \ (376 \text{ MHz, CDCl}_3) \ \delta \ -69.93 \ (d, J = 9.6 \text{ Hz, CF}_3).

HRMS (ESI) m/z: 330.1482 [M+H]^+, \text{C}_{20}\text{H}_{19}\text{F}_3\text{N}^+ \text{requires } 330.1464.

tert-Butyl (4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbutyl)carbamate (6f')

The titled compound was obtained following GPB from 5f and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer (1S,3R)-6f', isolated yield 25% (7.5 mg, 0.06 mmol) from 23.0 mg (0.08 mmol) of 5f. Major diastereomer (1R,3R)-6f', isolated yield 55% (33.1 mg, 0.08 mmol) from 46.0 mg (0.14 mmol) of 6f.

The enantiomeric excess (minor isomer: 93%, major isomer 95%) was determined by HPLC (CHIRACEL OD-H), hexane/iPrOH 98/2, 1 mL/min, \( \lambda = 210 \text{ nm} \), 1S,3R (minor diastereomer): minor enantiomer, \( t_r = 21.5 \text{ min}, \) major enantiomer, \( t_r = 16.7 \text{ min} \), 1R,3R (major diastereomer): minor enantiomer \( t_r = 13.2 \text{ min} \), major enantiomer, \( t_r = 10.9 \text{ min} \).

Minor diastereomer (configuration 1S, 3R)-6f'

\[
\text{CF}_3 \quad \text{Ph} \quad \text{NH}_{\text{Boc}}
\]
$\alpha_D^{25}$: $-21.0$ (c 0.20, CHCl$_3$, ee 93%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 – 7.77 (m, 3H), 7.60 (s, 1H), 7.49 – 7.46 (m, 2H), 7.38 – 7.34 (m, 5H), 7.26 – 7.25 (m, 1H), 5.00 – 4.85 (m, 1H), 4.66 – 4.43 (m, 1H), 3.51 (bs, 1H), 2.46 – 2.40 (m, 2H), 1.44 – 1.27 (m, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.0, 139.5, 134.0, 133.3, 132.7, 129.1, 128.9, 128.6, 128.5, 127.8, 127.6, 126.9 (Cq, $J$ = 278.0 Hz), 126.3, 126.0, 125.5, 124.5, 124.2, 79.8, 51.7, 47.4 (Cq, $J$ = 27.0 Hz), 36.6, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -69.25 (d, $J$ = 9.6 Hz, CF$_3$).

Major diastereomer (configuration 1R, 3R)-6f

![Diastereomer Structure]

$\alpha_D^{25}$: $-43.5$ (c 1.00, CHCl$_3$, ee 95%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 – 7.84 (m, 2H), 7.80 – 7.78 (m, 1H), 7.52 – 7.50 (m, 3H), 7.40 – 7.39 (m, 3H), 7.28 (d, $J$ = 8.4 Hz, 1H), 7.23 – 7.21 (m, 2H), 4.86 (d, $J$ = 6.6 Hz, 1H), 4.54 (bs, 1H), 2.95 (ddt, $J$ = 18.5, 12.7, 6.3 Hz, 1H), 2.68 (bs, 1H), 2.46 (ddd, $J$ = 13.7, 10.2, 3.6 Hz, 1H), 1.37 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.7, 137.6, 133.3, 133.2, 133.0, 129.3, 129.0, 128.8, 128.5, 128.0, 127.9, 127.7, 126.6 (Cq, $J$ = 279.9 Hz), 126.4, 126.2, 124.1, 79.6, 53.1, 47.2 (Cq, $J$ = 26.7 Hz), 35.5, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.16 (s, CF$_3$).

HRMS (ESI) $m/z$: 452.1826 [M+Na]$^+$, C$_{25}$H$_{26}$F$_3$NNaO$_2$ requires 452.1808.

4,4,4-Trifluoro-1-(3-methoxyphenyl)-3-phenylbutan-1-amine (6g)

The titled compound was obtained following GPC from 4g (76.8 mg, 0.25 mmol) as a colourless oil (99% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 66:33 in 99% yield. Minor diastereomer (1S,3R)-6g isolated 24 mg (0.08 mmol) 31 % yield. Major diastereomer (1R,3R)-6g isolated 48.0 mg (0.16 mmol) 62% yield.

Minor diastereomer (configuration 1S, 3R)-6g

![Diastereomer Structure]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.41 – 7.33 (m, 5H), 7.23 (t, $J$ = 7.9 Hz, 1H), 6.80 – 6.73 (m, 3H), 3.80 (s, 3H), 3.75 – 3.51 (m, 1H), 2.23 – 2.19 (m, 2H), 1.49 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.9, 148.2, 134.4 (Cq, $J$ = 1.9 Hz), 129.7, 129.2, 128.8, 128.3, 127.1 (Cq, $J$ = 279.6 Hz), 118.0, 112.2, 111.7, 55.2, 52.5, 47.3 (Cq, $J$ = 26.7 Hz), 38.2.
\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta - 69.47\) (d, \(J = 9.6\) Hz, CF\(_3\)).

Major diastereomer (configuration 1\(R\), 3\(R\))-6g

-\(\begin{array}{c}
\text{CF}_3 \\
\text{NH}_2 \\
\text{OMe}
\end{array}\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.40 - 7.36\) (m, 3H), 7.29 - 7.23 (m, 3H), 6.84 (dd, \(J = 8.3, 2.5\) Hz, 1H), 6.75 (d, \(J = 7.6\) Hz, 1H), 6.71 (bs, 1H), 3.81 (s, 3H), 3.61 - 3.58 (m, 1H), 3.06 - 2.95 (m, 1H), 2.36 - 2.32 (m, 2H), 1.68 (bs, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 159.9, 146.0, 134.3\) (Cq, \(J = 1.9\) Hz), 129.9, 129.2, 128.7, 128.1, 126.7 (Cq, \(J = 279.7\) Hz), 118.8, 113.1, 112.1, 55.2, 53.6, 47.3 (Cq, \(J = 26.8\) Hz), 37.8.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta - 69.47\) (d, \(J = 9.6\) Hz, CF\(_3\)).

\textit{tert}-Butyl (4,4,4-trifluoro-1-(3-methoxyphenyl)-3-phenylbutyl)carbamate (6g')

The titled compound was obtained following GPB from 6g and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer (1\(S\),3\(R\))-6g', isolated yield 60% (19.7 mg, 0.05 mmol) from 24.0 mg (0.08 mmol) of 6g. Major diastereomer (1\(R\),3\(R\))-6g', isolated yield 88% (57.7 mg, 0.14 mmol) from 48.0 mg (0.16 mmol) of 6g.

The enantiomeric excess (minor isomer: 86%, major isomer 89%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, \(\lambda = 210\) nm, 1\(R\),3\(R\) (major diastereomer): minor enantiomer \(t_r = 9.5\) min, major enantiomer, \(t_r = 7.7\) min.

Minor diastereomer (configuration 1\(S\), 3\(R\))-6g'

-\(\begin{array}{c}
\text{CF}_3 \\
\text{Ph} \\
\text{NHBOc} \\
\text{OMe}
\end{array}\)

\([\alpha]_D^{25}: - 43.5\) (c 1.00, CHCl\(_3\), ee 95%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.41 - 7.37\) (m, 3H), 7.31 - 7.30 (m, 2H), 7.22 (t, \(J = 7.9\) Hz, 1H), 6.78 (dd, \(J = 8.3, 2.4\) Hz, 1H), 6.74 (d, \(J = 7.7\) Hz, 1H), 6.68 (s, 1H), 4.71 (d, \(J = 9.3\) Hz, 1H), 4.41 (bs, 1H), 3.77 (s, 3H), 3.46 (bs, 1H), 2.37 - 2.27 (m, 2H), 1.43 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 159.8, 154.9, 143.9, 134.0, 129.8, 129.1, 128.8, 128.5, 126.9\) (Cq, \(J = 279.3\) Hz), 118.1, 112.7, 112.0, 79.7, 55.2, 51.5, 47.3 (Cq, \(J = 27.0\) Hz), 36.7, 28.3.

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta - 69.31\) (d, \(J = 9.5\) Hz, CF\(_3\)).

Major diastereomer (configuration 1\(R\), 3\(R\))-6g'

-\(\begin{array}{c}
\text{CF}_3 \\
\text{Ph} \\
\text{NHBOc} \\
\text{OMe}
\end{array}\)
$[\alpha]_D^{25} - 0.8$ (c 1.00, CHCl$_3$, ee 89%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.41 – 7.36 (m, 3H), 7.29 – 7.23 (m, 3H), 6.85 (dd, $J = 8.3$, 2.4 Hz, 1H), 6.72 (d, $J = 7.5$ Hz, 1H), 6.63 (s, 1H), 4.74 (d, $J = 7.3$ Hz, 1H), 4.33 (bs, 1H), 3.78 (s, 3H), 2.97 (ddt, $J = 18.7$, 12.6, 6.3 Hz, 1H), 2.62 (bs, 1H), 2.33 (ddd, $J = 13.7$, 10.3, 3.5 Hz, 1H), 1.38 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.9, 154.7, 141.9, 133.3, 130.1, 129.3, 128.8, 128.5, 126.6 (Cq, $J = 279.8$ Hz), 118.8, 113.5, 112.5, 79.6, 55.2, 52.9, 47.1 (Cq, $J = 26.8$ Hz), 35.6, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ –70.19 (s, CF$_3$), –69.54 (d, $J = 9.6$ Hz, CF$_3$).

HRMS (ESI) m/z: 432.1761 [M+Na]$^+$, C$_{22}$H$_{26}$F$_3$NaNaO$_3$ requires 432.1757.

4,4,4-Trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butan-1-amine (6h)

The titled compound was obtained following GPC from 4h (86.3 mg, 0.25 mmol) as a colourless oil (80% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 75:25 in 80% yield. Minor diastereomer (1$^S$,3$^R$)-6h isolated 15 mg (0.04 mmol) 17 % yiled. Major diastereomer (1$^R$,3$^R$)-6h isolated 45.0 mg (0.13 mmol) 52% yield.

Minor diastereomer (configuration 1$^S$, 3$^R$)-6h

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.49 (d, $J = 7.6$ Hz, 1H), 7.45 – 7.33 (m, 8H), 3.77 – 3.67 (m, 1H), 3.65 – 3.61 (m, 1H), 2.24 – 2.20 (m, 2H), 1.51 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.3, 134.0 (Cq, $J = 1.9$ Hz), 131.0 (Cq, $J = 32.1$ Hz), 129.3, 129.1, 128.9, 128.6, 128.4, 127.0 (Cq, $J = 276.8$ Hz), 126.7 (Cq, $J = 279.6$ Hz), 124.1 (Cq, $J = 3.8$ Hz), 122.6 (Cq, $J = 3.8$ Hz), 52.4, 47.3 (Cq, $J = 26.9$ Hz), 38.2.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ –62.59 (s, CF$_3$), –69.54 (d, $J = 9.6$ Hz, CF$_3$).

HRMS (ESI) m/z: 348.1137 [M+H]$^+$, C$_{17}$H$_{16}$F$_6$N Na$^+$ requires 348.1181.

Major diastereomer (configuration 1$^R$, 3$^R$)-6h

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.56 (d, $J = 7.6$ Hz, 1H), 7.48 (t, $J = 7.7$ Hz, 1H), 7.42 – 7.36 (m, 5H), 7.22 – 7.20 (m, 2H), 3.76 (dd, $J = 9.2$, 5.6 Hz, 1H), 2.96 (pd, $J = 9.4$, 4.7 Hz, 1H), 2.42 – 2.29 (m, 2H), 1.56 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.4, 134.0 (Cq, $J = 1.9$ Hz), 131.0 (Cq, $J = 32.2$ Hz), 129.9, 129.3, 129.1, 128.9, 128.5, 126.6 (d, $J = 279.8$ Hz), 124.0 (Cq, $J = 272.3$ Hz), 124.6 (Cq, $J = 3.8$ Hz), 123.7 (Cq, $J = 3.8$ Hz), 53.4, 47.3 (Cq, $J = 26.9$ Hz), 38.0.
$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ = −62.67 (s, CF$_3$), −69.99 (d, $J$ = 9.4 Hz, CF$_3$).

**tert-Butyl (4,4,4-trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butyl)carbamate (6h’)**

The titled compound was obtained following GPB from 6h and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer (1S,3R)-6h’, isolated yield 96% (17.1 mg, 0.04 mmol) from 15.0 mg (0.04 mmol) of 6h. Major diastereomer (1R,3R)-6h’, isolated yield 93% (54.1 mg, 0.12 mmol) from 45.0 mg (0.13 mmol) of 6h.

The enantiomeric excess (minor isomer: 77%, major isomer 90%) was determined by HPLC (CHIRACEL® OD-H), hexane/iPrOH 98/2, 1 mL/min, $\lambda$ = 210 nm, 1S,3R (minor diastereomer): minor enantiomer, $t_r$ = 7.6 min, major enantiomer, $t_r$ = 10.8 min, 1R,3R (major diastereomer): minor enantiomer $t_r$ = 16.5 min, major enantiomer, $t_r$ = 10.3 min.

**Minor diastereomer (configuration 1S, 3R)-6h’**

\[
\begin{align*}
\text{CF}_3 & \quad \text{NHBOc} \\
\text{Ph} & \\
\text{CF}_3
\end{align*}
\]

$[\alpha]_D^{25}$: −9.9 (c 0.63, CHCl$_3$, ee 77%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (d, $J$ = 7.7 Hz, 1H), 7.44 – 7.26 (m, 8H), 4.77 (bs, 1H), 4.51 (bs, 1H), 3.48 (bs, 1H), 2.37 – 2.27 (m, 2H), 1.43 – 1.26 (m, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.8, 143.4, 133.5, 131.1 (Cq, $J$ = 27.6 Hz), 129.54, 129.47, 129.23, 129.16, 129.0, 128.7, 124.4 (Cq, $J$ = 3.7 Hz), 122.6, 80.2, 51.3, 47.4 (Cq, $J$ = 27.6 Hz), 36.5, 28.2.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ = −62.66 (s, CF$_3$), −69.38 (d, $J$ = 9.5 Hz, CF$_3$).

**Major diastereomer (configuration 1R, 3R)-6h’**

\[
\begin{align*}
\text{CF}_3 & \quad \text{NHBOc} \\
\text{Ph} & \\
\text{CF}_3
\end{align*}
\]

$[\alpha]_D^{25}$: −7.8 (c 0.90, CHCl$_3$, ee 90%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58 (d, $J$ = 7.7 Hz, 1H), 7.49 (t, $J$ = 7.7 Hz, 1H), 7.40 – 7.33 (m, 5H), 7.21 – 7.20 (m, 2H), 4.76 (d, $J$ = 7.4 Hz, 1H), 4.46 (bs, 1H), 2.99 – 2.88 (m, 1H), 2.56 (bs, 1H), 2.35 (ddd, $J$ = 13.6, 9.6, 3.9 Hz, 1H), 1.36 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.6, 141.8, 133.1, 131.18 (Cq, $J$ = 32.3 Hz), 130.0, 129.5, 129.0, 128.7, 127.8, 126.44 (Cq, $J$ = 279.9 Hz), 124.86 (Cq, $J$ = 3.6 Hz), 123.9 (d, $J$ = 272.5 Hz), 123.7, 80.0, 52.9, 47.2 (d, $J$ = 25.8 Hz), 34.9, 28.2.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ = −62.70 (s, CF$_3$), 70.22 (s, CF$_3$).

HRMS (ESI) $m/z$: 470.1531 [M+Na]$^+$, C$_{22}$H$_{23}$F$_6$NNaO$_2^+$ requires 470.1525.

4,4,4-Trifluoro-1-(2-methoxyphenyl)-3-phenylbutan-1-amine (6i)
The titled compound was obtained following GPC from 4i (76.8 mg, 0.25 mmol) as a colourless oil (78% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 66:34 in 56% yield. Minor diastereomer (1S,3R)-6i isolated 18.6 mg (0.06 mmol) 24% yield. Major diastereomer (1R,3R)-6i isolated 20.2 mg (0.17 mmol) 26% yield.

Minor diastereomer (configuration 1S, 3R)-6i

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{CF}_3 & \quad \text{MeO}
\end{align*}
\]

\[\text{H NMR} (400 MHz, CDCl}_3) \delta 7.40 - 7.33 (m, 5H), 7.20 (t, J = 7.8 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 6.91 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 3.85 - 3.73 (m, 5H), 2.32 - 2.19 (m, 2H), 1.59 (bs, 2H).
\]

\[\text{C NMR} (100 MHz, CDCl}_3) \delta 156.6, 134.5 (Cq, J = 1.9 Hz), 134.4, 129.5, 128.4, 128.0, 127.9, 127.3 (Cq, J = 277.6 Hz), 126.1, 120.6, 110.6, 55.0, 48.6, 47.3 (q, J = 26.5 Hz), 35.8.
\]

\[\text{F NMR} (376 MHz, CDCl}_3) \delta -69.58 (d, J = 9.7 Hz, CF}_3).
\]

Major diastereomer (configuration 1R, 3R)-6i

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{CF}_3 & \quad \text{MeO}
\end{align*}
\]

\[\text{H NMR} (400 MHz, CDCl}_3) \delta 7.36 - 7.31 (m, 3H), 7.27 - 7.19 (m, 3H), 6.97 - 6.88 (m, 3H), 3.81 - 3.74 (m, 4H), 3.02 (pd, J = 9.8, 3.7 Hz, 1H), 2.63 (ddd, J = 13.6, 9.8, 3.8 Hz, 1H), 2.32 (ddd, J = 13.5, 11.1, 5.5 Hz, 1H), 1.83 (m, 2H).
\]

\[\text{C NMR} (100 MHz, CDCl}_3) \delta 157.3, 134.7 (Cq, J = 1.8 Hz), 131.9, 129.3, 128.5, 128.4, 128.1, 126.9 (Cq, J = 277.7 Hz), 120.7, 111.0, 55.1, 50.8, 47.8 (Cq, J = 26.6 Hz), 35.9.
\]

\[\text{F NMR} (376 MHz, CDCl}_3) \delta -69.84 (d, J = 9.4 Hz, CF}_3).
\]

tert-Butyl (4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbutyl)carbamate (6i')

The titled compound was obtained following GPB from 6i and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer (1S,3R)-6i', isolated yield 84% (20.6 mg, 0.05 mmol) from 18.6 mg (0.06 mmol) of 6i. Major diastereomer (1R,3R)-6i', isolated yield 89% (25.5 mg, 0.06 mmol) from 20.2 mg (0.07 mmol) of 6i.

The enantiomeric excess (minor isomer: 69%, major isomer 72%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1S,3R (minor diastereomer): minor enantiomer, tr = 7.9 min, major enantiomer, tr = 7.3 min, 1R,3R (major diastereomer): minor enantiomer tr = 9.6 min, major enantiomer, tr = 8.6 min.

Minor diastereomer (configuration 1S, 3R)-6i'}
[α]D<sup>25</sup>: −26.9 (c 0.70, CHCl₃, ee 69%).

**1H NMR** (400 MHz, CDCl₃) δ (Rotamers are observed) 7.40 – 7.28 (m, 5H), 7.20 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.87 – 6.80 (m, 2H), 5.33 (d, J = 10.0 Hz, 1H), 4.59 (td, J = 10.2, 3.7 Hz, 1H), 3.78, 3.52 – 3.40 (m, 1H), 2.48 – 2.42 (m, 1H), 2.30 – 2.23 (m, 1H), 1.43 – 1.26 (m, 9H).

**13C NMR** (100 MHz, CDCl₃) δ 156.8. 155.0, 134.1, 129.8, 129.4, 128.6, 128.5, 128.2, 127.9, 120.7, 110.9, 79.3, 55.1, 47.5 (Cq, J = 28.2 Hz), 35.3, 28.4.

**19F NMR** (376 MHz, CDCl₃) δ – 69.43 (d, J = 9.8 Hz, CF₃).

Major diastereomer (configuration 1R, 3R)-6i’

[α]D<sup>25</sup>: +8.7 (c 0.50, CHCl₃, ee 72%).

**1H NMR** (400 MHz, CDCl₃) δ (Rotamers are observed) 7.39 – 7.34 (m, 3H), 7.30 – 7.26 (m, 1H), 7.22 – 7.21 (m, 2H), 6.91 (d, J = 8.2 Hz, 1H), 6.86 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 7.0 Hz, 1H), 5.42 (d, J = 8.7 Hz, 1H), 4.57 (q, J = 8.8 Hz, 1H), 3.86 (s, 3H), 2.95 – 2.86 (m, 1H), 2.65 – 2.59 (m, 1H), 2.60 – 2.42 (m, 1H), 1.39 (s, 9H).

**13C NMR** (100 MHz, CDCl₃) δ 157.3, 154.9, 133.6, 130.0, 129.4, 129.1, 128.6, 128.3, 127.4, 126.8 (Cq, J = 279.9 Hz), 120.7, 111.1, 79.2, 55.3, 51.7, 47.6 (q, J = 27.0 Hz), 33.1, 28.4.

**19F NMR** (376 MHz, CDCl₃) δ – 70.28 (d, J = 9.5 Hz, CF₃).

HRMS (ESI) m/z: 432.1736 [M+Na]<sup>+</sup>, C₂₂H₂₆F₃NNaO₃<sup>+</sup> requires 432.1757.

**5,5,5-Trifluoro-4-phenylpentan-2-amine (6j)**

The final compound was not isolated due to low conversion. Conversion to the mixture of E and Z diastereomers was determined by integration of the CF₃ of both starting material and product by <sup>19</sup>F NMR (Shown below). <sup>19</sup>F NMR (376 MHz, CDCl₃) δ – 66.28 (s, CF₃, Allylic amine 4j), – 69.55 - – 70.01 (d, CF₃, diastereomeric mixture of 6j).
4,4,4-Trifluoro-3-phenylbutan-1-amine (6k)

The final compound could not be separated from the starting material. The conversion to the mixture of E and Z diastereomers was determined by integration of the CF₃ of both starting material and product by $^{19}$F NMR (Shown below). $^{19}$F NMR (376 MHz, CDCl₃) δ – 66.00 – 66.04 (s, CF₃, Allylic amine 4k), – 69.63 – 69.66 (s, CF₃, 6k).
The titled compound was obtained following GPC from 4l (72.8 mg, 0.25 mmol) as a colourless oil (90% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 67:33 in 90% yield. Minor diastereomer could not be isolated. Major diastereomer (1R,3R)-6l isolated 44.0 mg (0.15 mmol) 60% yield.

Major diastereomer (configuration 1R, 3R)-6l

\[ \text{Ph} \quad \text{NH}_2 \]

\[ \text{CF}_3 \]

\[ \text{Ph} \quad \text{NH}_2 \]

\[ \text{Ph} \quad \text{NH}_2 \]

\[ \text{Ph} \quad \text{NH}_2 \]

\[ \text{Ph} \quad \text{NH}_2 \]

**$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 7.37 – 7.27 (m, 3H), 7.19 – 7.17 (m, 4H), 7.11 (d, $J = 7.9$ Hz, 2H), 3.64 – 3.61 (m, 1H), 2.93 (dq, $J = 18.5$, 9.3 Hz, 1H), 2.37 (s, 3H), 2.35 – 2.31 (m, 2H), 1.55 (bs, 2H).

**$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ 144.5, 138.1, 131.22 (Cq, $J = 1.9$ Hz), 129.4, 129.0, 128.8, 127.7, 126.6, 126.8 (Cq, $J = 279.7$ Hz), 53.6, 47.0 (Cq, $J = 26.8$ Hz), 37.9, 21.1.

**$^{19}$F NMR** (376 MHz, CDCl$_3$) $\delta$ – 70.09 (d, $J = 9.6$ Hz, CF$_3$).

**tert-Butyl (4,4,4-trifluoro-1-phenyl-3-(p-tolyl)butyl)carbamate (6l')**

The titled compound was obtained following GPB from 6l and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6l’, isolated yield 87% (51.3 mg, 0.13 mmol) from 44.0 mg (0.15 mmol) of 6l.
The enantiomeric excess (minor isomer: nd, major isomer 70%) was determined by HPLC (CHIRACEL\textsuperscript{®} OD–H), hexane/iPrOH 98/2, 1 mL/min, \( \lambda = 210 \) nm, 1\textit{R},3\textit{R} (major diastereomer): minor enantiomer \( t_r = 6.9 \) min, major enantiomer, \( t_r = 5.1 \) min.

**Major diastereomer (configuration 1\textit{R}, 3\textit{R})-6l’**

![diagram]

\([\alpha]_D^{25}: \) – 15.8 (c 0.70, CHCl\textsubscript{3}, ee 70%).

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\textsubscript{3}) \( \delta \) 7.37 – 7.29 (m, 3H), 7.19 (d, \( J = 7.8 \) Hz, 2H), 7.13 – 7.10 (m, 4H), 4.72 (d, \( J = 6.5 \) Hz, 1H), 4.35 (bs, 1H), 2.95 – 2.85 (m, 1H), 2.59 (bs, 1H), 2.37 – 2.29 (m, 4H), 1.38 (s, 9H).

\(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\textsubscript{3}) \( \delta \) 154.6, 140.4, 138.2, 130.2, 129.5, 129.1, 128.9, 128.0, 126.8, 126.7 (Cq, \( J = 279.7 \) Hz), 79.5, 52.9, 46.7 (Cq, \( J = 27.4 \) Hz), 34.7, 28.3, 21.1.

\(^{19}\text{F} \text{NMR} \) (376 MHz, CDCl\textsubscript{3}) \( \delta \) – 70.33 (d, \( J = 9.4 \) Hz, CF\textsubscript{3}).

HRMS (ESI) \( m/z \) 416.1871 [M+Na]\textsuperscript{+}, C\textsubscript{22}H\textsubscript{26}F\textsubscript{3}NNaO\textsubscript{2}\textsuperscript{+} requires 416.1808.

**4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenylbutan-1-amine (6m)**

The titled compound was obtained following GPC from 4m (76.8 mg, 0.25 mmol) as a colourless oil (73% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 65:35 in 73% yield. Minor diastereomer could not be isolated.

**Major diastereomer (configuration 1\textit{R}, 3\textit{R})-6m**

![diagram]

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\textsubscript{3}) \( \delta \) 7.38 – 7.33 (m, 2H), 7.31 – 7.27 (m, 1H), 7.18 – 7.13 (m, 4H), 6.90 (d, \( J = 8.8 \) Hz, 2H), 3.83 (s, 3H), 3.64 – 3.61 (m, 1H), 2.96 – 2.85 (m, 1H), 2.33 – 2.30 (m, 2H), 1.62 (bs, 2H).

\(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\textsubscript{3}) \( \delta \) 159.5, 144.4, 130.2, 128.8, 127.7, 126.8 (Cq, \( J = 278.0 \) Hz), 126.6, 126.2 (Cq, \( J = 2.2 \) Hz), 114.1, 55.2, 53.6, 46.6 (Cq, \( J = 26.9 \) Hz), 37.9.

\(^{19}\text{F} \text{NMR} \) (376 MHz, CDCl\textsubscript{3}) \( \delta \) – 70.34 (d, \( J = 9.4 \) Hz, CF\textsubscript{3}).

*tet*-Butyl (4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbutyl)carbamate (6m’)*
The titled compound was obtained following GPB from 6m and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6m’, isolated yield 64% (28.8 mg, 0.07 mmol) from 35.0 mg (0.11 mmol) of 6m.

The enantiomeric excess (minor isomer: nd, major isomer 81%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1R,3R (major diastereomer): minor enantiomer t_r = 10.4 min, major enantiomer, t_r = 6.9 min.

Major diastereomer (configuration 1R, 3R)-6m’

\[
\text{OMe} \\
\text{CF}_3 \\
\text{NHBoc} \\
\text{Ph}
\]

([α]_D^{25} = -22.9 (c 0.85, CHCl₃, ee 81%).

^1H NMR (400 MHz, CDCl₃) δ 7.37 – 7.29 (m, 3H), 7.15 – 7.11 (m, 4H), 6.91 (d, J = 8.6 Hz, 2H), 4.72 (d, J = 4.8 Hz, 1H), 4.34 (bs, 1H), 3.83 (s, 3H), 2.92 – 2.28 (m, 1H), 2.59 (bs, 1H), 2.31 (ddd, J = 13.6, 10.6, 3.4 Hz, 1H), 1.38 (s, 9H).

^13C NMR (100 MHz, CDCl₃) δ 159.6, 154.7, 140.3, 130.3, 129.0, 128.1, 126.9, 126.7 (Cq, J = 279.7 Hz), 125.1, 114.2, 79.5, 55.2, 52.9, 46.3 (Cq, J = 26.4 Hz), 34.6, 28.3.

^19F NMR (376 MHz, CDCl₃) δ -70.58 (s, CF₃).

HRMS (ESI) m/z: 432.1764 [M+Na]^+ requires 432.1757.

4,4,4-Trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)butan-1-amine (6n)

The titled compound was obtained following GPC from 4n (86.3 mg, 0.25 mmol) as a colourless oil (55% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 85:15 in 55% yield. Minor diastereomer could not be isolated. Major diastereomer (1R,3R)-6n isolated 37.0 mg (0.11 mmol) 43% yield.

Major diastereomer (configuration 1R, 3R)-6n

\[
\text{CF}_3 \\
\text{CF}_3 \\
\text{NH}_2 \\
\text{Ph}
\]

^1H NMR (400 MHz, CDCl₃) δ 7.64 (d, J = 8.0 Hz, 2H), 7.38 – 7.29 (m, 5H), 7.15 (d, J = 7.3 Hz, 2H), 3.60 (dd, J = 9.1, 6.0 Hz, 1H), 3.09 (pd, J = 9.4, 4.9 Hz, 1H), 2.43 – 2.31 (m, 2H), 1.56 (bs, 2H).

^13C NMR (100 MHz, CDCl₃) δ 148.4, 134.0, 130.0 (Cq, J = 32.4 Hz), 129.1, 128.9, 128.5, 127.0, 126.6 (Cq, J_CF = 279.8 Hz), 125.8 (Cq, J_CF = 3.7 Hz), 124.0 (Cq, J_CF = 272.0 Hz), 53.3, 47.3, 37.9.

^19F NMR (376 MHz, CDCl₃) δ -62.71 (s, CF₃), -69.73 (d, J = 9.1 Hz, CF₃).
**tert-Butyl (4,4,4-trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)butyl)carbamate (6n’)**

The titled compound was obtained following GPB from 6n and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6n’, isolated yield 82% (40.4 mg, 0.09 mmol) from 37.0 mg (0.11 mmol) of 6n.

The enantiomeric excess (minor isomer: nd, major isomer 70%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1R,3R (major diastereomer): minor enantiomer t_r = 9.0 min, major enantiomer, t_r = 6.1 min.

**Major diastereomer (configuration 1R, 3R)-6n’**

![Diastereomer Structure](image)

[α]_D^{25} = −1.8 (c 0.55, CHCl₃, ee 70%).

**1H NMR** (400 MHz, CDCl₃) δ 7.66 (d, J = 8.1 Hz, 2H), 7.39 – 7.33 (m, 5H), 7.11 (dd, J = 7.8, 1.7 Hz, 2H), 4.68 (d, J = 7.0 Hz, 1H), 4.31 (bs, 1H), 3.02 (ddq, J = 18.2, 9.1, 4.5, 3.4 Hz, 1H), 2.69 (bs, 1H), 2.39 (ddd, J = 13.7, 10.3, 3.5 Hz, 1H), 1.38 (s, 9H).

**13C NMR** (100 MHz, CDCl₃) δ 154.7, 139.8, 137.4, 130.8 (Cq, J = 32.6 Hz), 129.8, 129.2, 128.4, 126.8, 126.2 (Cq, J = 278.0 Hz), 125.8 (Cq, J = 3.7 Hz), 123.9 (Cq, J = 272.2 Hz), 79.8, 53.0, 47.1 (Cq, J = 27.2 Hz), 34.2, 28.3.

**19F NMR** (376 MHz, CDCl₃) δ −62.73 (s, CF₃), −70.09 (d, J = 8.7 Hz, CF₃).

HRMS (ESI) m/z: 470.1548 [M+Na]⁺, C₂₂H₂₃F₈NNO₂⁺ requires 470.1525.

**4,4,4-Trifluoro-1-phenyl-3-(m-tolyl)butan-1-amine (6o)**

The titled compound was obtained following GPC from 4o (72.8 mg, 0.25 mmol) as a colourless oil (81% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 75:25 in 75% yield. Minor diastereomer could not be isolated.

Major diastereomer (configuration 1R, 3R)-6o isolated 39.0 mg (0.13 mmol) 53% yield.

**Major diastereomer (configuration 1R, 3R)-6o**

![Diastereomer Structure](image)

**1H NMR** (400 MHz, CDCl₃) δ 7.38 – 7.34 (m, 2H), 7.31 – 7.29 (m, 1H), 7.28 – 7.24 (m, 1H), 7.19 – 7.16 (m, 3H), 7.04 – 7.00 (m, 2H), 3.63 (dd, J = 8.2, 6.8 Hz, 1H), 2.95 (dq, J = 18.6, 9.4 Hz, 1H), 2.37 (s, 3H), 2.35 – 2.32 (m, 2H), 1.62 (bs, 2H).

**13C NMR** (100 MHz, CDCl₃) δ 144.5, 138.4, 134.3 (Cq, J = 1.9 Hz), 129.7, 129.0, 128.8, 128.5, 128.2, 127.7, 126.8 (Cq, J = 278.0 Hz), 126.6, 126.4, 53.6, 47.3 (Cq, J = 26.7 Hz), 38.0, 21.4.
**19F NMR** (376 MHz, CDCl₃) δ – 69.83 (d, J = 9.5 Hz, CF₃).

**tert-Butyl (4,4,4-trifluoro-1-phenyl-3-(m-tolyl)butyl)carbamate (6o’)**

The titled compound was obtained following GPB from 6o and purified by FCC using (pentane:EtOAc 95:5). Major diastereomer (1R,3R)-6o’, isolated yield 71% (36.3 mg, 0.09 mmol) from 39.0 mg (0.11 mmol) of 6o.

The enantiomeric excess (minor isomer: nd, major isomer 83%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, λ = 210 nm, 1R,3R (major diastereomer): minor enantiomer tᵣ = 6.8 min, major enantiomer, tᵣ = 5.2 min.

**Major diastereomer (configuration 1R, 3R)-6o’**

\[
\begin{align*}
\text{CF}_3 & \quad \text{NHBoc} \\
\text{Ph} &
\end{align*}
\]

[α]D²⁵: – 1.1 (c 0.90, CHCl₃, ee 70%).

**1H NMR** (400 MHz, CDCl₃) δ 7.40 – 7.31 (m, 3H), 7.27 – 7.25 (m, 1H), 7.18 – 7.13 (m, 3H), 7.03 (d, J = 7.7 Hz, 1H), 6.99 (s, 1H), 4.70 (bs, 1H), 4.38 (bs, 1H), 2.98 – 2.88 (m, 1H), 2.55 (bs, 1H), 2.37 – 2.31 (m, 4H), 1.37 (s, 9H).

**13C NMR** (100 MHz, CDCl₃) δ 154.7, 140.6, 138.4, 133.4, 130.0, 129.2, 128.7, 128.0, 126.8, 126.2, 79.5, 53.0, 47.0, 35.0, 28.3, 21.4.

**19F NMR** (376 MHz, CDCl₃) δ – 70.06 (s, CF₃).

HRMS (ESI) m/z: 416.1803 [M+Na]+, C₂₂H₂₆F₃NNaO₂⁺ requires 416.1808.

**4,4,4-Trifluoro-1-phenyl-3-(thiophen-2-yl)butan-1-amine (6p)**

The titled compound was obtained following GPC from 4p (72.8 mg, 0.25 mmol) as a colourless oil (99% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4). The diastereomers were obtained in a ratio 73:27 in 99% yield. Minor diastereomer (1S,3S)-6p isolated 19.0 mg (0.07 mmol) 27% yield. Major diastereomer (1R,3S)-6p isolated 46.0 mg (0.16 mmol) 64% yield.

**Minor diastereomer (configuration 1S, 3S)-6p**

\[
\begin{align*}
\text{CF}_3 & \quad \text{NH}_2 \\
\text{Ph} &
\end{align*}
\]

**1H NMR** (400 MHz, CDCl₃) δ 7.35 – 7.31 (m, 3H), 7.26 – 7.22 (m, 3H), 7.09 (d, J = 2.9 Hz, 1H), 7.05 (dd, J = 5.1, 3.5 Hz, 1H), 4.12 (dqd, J = 10.8, 9.2, 4.1 Hz, 1H), 3.67 (dd, J = 10.2, 4.1 Hz, 1H), 2.24 – 2.11 (m, 2H), 1.51 (bs, 2H).

**13C NMR** (100 MHz, CDCl₃) δ 146.3, 136.34 (Cq, J = 2.1 Hz), 128.7, 127.9, 127.2, 127.0, 126.3 (Cq, J = 279.5 Hz), 125.7, 125.6, 52.4, 42.8 (Cq, J = 28.4 Hz), 39.7.
$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ – 70.67 (d, $J$ = 8.9 Hz, CF$_3$).

**Major diastereomer (configuration 1R, 3S)-6p**

![Diagram of 1R, 3S-6p]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 – 7.29 (m, 4H), 7.24 – 7.22 (m, 2H), 7.03 (dd, $J$ = 5.1, 3.5 Hz, 1H), 6.96 (d, $J$ = 3.3 Hz, 1H), 3.75 (dd, $J$ = 10.0, 5.1 Hz, 1H), 3.28 (dt, $J$ = 17.8, 8.9, 4.5 Hz, 1H), 2.40 – 2.25 (m, 2H), 1.58 (bs, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.1, 136.4 (q, $J$ = 2.0 Hz), 128.9, 127.8, 127.7, 127.3, 126.9, 125.9 (Cq, $J$ = 279.7 Hz), 125.7, 53.6, 42.9 (q, $J$ = 28.5 Hz), 39.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ – 71.09 (d, $J$ = 8.9 Hz, CF$_3$).

**tert-Butyl (4,4,4-trifluoro-1-phenyl-3-(thiophen-2-yl)butyl)carbamate (6p')**

The titled compound was obtained following GPB from 6p and purified by FCC using (pentane:EtOAc 95:5). Minor diastereomer ($^{1}$S,3$^{R}$)-6p', isolated yield 99% (27.0 mg, 0.07 mmol) from 19.0 mg (0.07 mmol) of 6p. Major diastereomer ($^{1}$R,3$^{S}$)-6p', isolated yield 65% (40.1 mg, 0.10 mmol) from 46.0 mg (0.16 mmol) of 6p.

The enantiomeric excess (minor isomer: 86%, major isomer 90%) was determined by HPLC (CHIRACEL® OD–H), hexane/iPrOH 98/2, 1 mL/min, $\lambda$ = 210 nm, $^{1}$S,3$^{S}$ (minor diastereomer): minor enantiomer, $t_r$ = 6.1 min, major enantiomer, $t_r$ = 7.5 min, $^{1}$R,3$^{S}$ (major diastereomer): minor enantiomer $t_r$ = 8.3 min, major enantiomer, $t_r$ = 6.1 min.

**Minor diastereomer (configuration 1$^{S}$, 3$^{S}$)-6p’**

![Diagram of 1S, 3S-6p]

[\[\alpha\]]$_D^{25}$ = – 37.0 (c 0.30, CHCl$_3$, ee 86%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34 – 7.30 (m, 3H), 7.27 – 7.24 (m, 1H), 7.19 (d, $J$ = 7.3 Hz, 1H), 7.06 – 7.04 (m, 2H), 4.77 (d, $J$ = 9.4 Hz, 1H), 4.60 (bs, 1H), 3.83 (bs, 1H), 2.35 (t, $J$ = 11.2 Hz, 1H), 2.25 (t, $J$ = 11.5 Hz, 1H), 1.43 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.0, 142.1, 135.6 (Cq, $J$ = 2.0 Hz), 128.8, 128.5, 127.5, 127.0, 126.0, 125.8, 79.8, 51.5, 42.9 (Cq, $J$ = 28.3 Hz), 38.2, 28.3.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ – 70.63 (d, $J$ = 9.0, CF$_3$).

**Major diastereomer (configuration 1$^{R}$, 3$^{S}$)-6p’**

S41
[α]D25: +5.3 (c 0.94, CHCl3, ee 90%).

1H NMR (400 MHz, CDCl3) δ 7.39 – 7.30 (m, 4H), 7.18 (d, J = 7.2 Hz, 2H), 7.05 – 7.00 (m, 2H), 4.75 (d, J = 4.8 H, 1H), 4.49 (bs, 1H), 3.24 (tt, J = 11.9, 8.8 Hz, 1H), 2.55 (bs, 1H), 2.37 (ddd, J = 13.5, 10.3, 3.3 Hz, 1H), 1.38 (s, 9H).

13C NMR (100 MHz, CDCl3) δ 154.6, 140.2, 135.2, 129.1, 128.2, 127.9, 127.2, 127.0, 126.8, 126.0, 125.8 (Cq, J = 279.8 Hz), 79.7, 53.0, 42.6 (Cq, J = 28.7 Hz), 36.0, 28.3.

19F NMR (376 MHz, CDCl3) δ – 71.25 (d, J = 8.9 Hz, CF3).

HRMS (ESI) m/z: 408.1197 [M+Na]+, C19H22F3NNaO2S requires 408.1216.

4,4,4-Trifluoro-1-phenylbutan-1-amine (6q)

The titled compound was obtained following GPC from 4q (50.3 mg, 0.25 mmol) as a colourless oil (99% NMR yield). The diastereomers were purified by FCC using (pentane:EtOAc 8:2 to 6:4).

\[
\text{CF}_3^{\text{NH}}_2^{\text{Ph}}
\]

Isolated yield 86% (40.1 mg, 0.22 mmol).

1H NMR (400 MHz, CDCl3) δ 7.38 – 7.34 (m, 2H), 7.29 – 7.25 (m, 3H), 3.94 (t, J = 6.8 Hz, 1H), 2.19 – 1.87 (m, 4H), 1.50 (bs, 2H).

13C NMR (100 MHz, CDCl3) δ 145.1, 128.8, 127.4, 127.2 (Cq, J = 274.3 Hz), 126.1, 55.1, 31.4 (Cq, J = 2.5 Hz), 30.86 (Cq, J = 28.7 Hz).

19F NMR (376 MHz, CDCl3) δ – 66.19 (t, J = 10.7 Hz, CF3).

HRMS (ESI) m/z: 187.0735 [M+H]+, C10H10F3+ requires 187.0729.
NMR of allylic amines 4 and 4’

\((R,E)-4,4,4\text{-Trifluoro-1,3-diphenylbut-2-en-1-amine (4a)}\)

\[
\begin{align*}
F_3C & \quad \text{Ph} & \quad \text{NH}_2 \\
\text{Ph} & & 
\end{align*}
\]

\((R,E)-4a\)

\(^1\text{H NMR, CDCl}_3, 400 \text{ MHz}\)

\[
\begin{align*}
\text{H} & \quad \text{ppm} \\
7.48 & \quad 7.35 & \quad 7.33 & \quad 7.29 & \quad 6.88 & \quad 6.76 & \quad 6.74 & \quad 6.68 & \quad 4.49 & \quad 2.91
\end{align*}
\]

\[(R,E)-4a\]

\(^{13}\text{C NMR, CDCl}_3, 100 \text{ MHz}\)

\[
\begin{align*}
\text{C} & \quad \text{ppm} \\
150 & \quad 140 & \quad 130 & \quad 120 & \quad 110 & \quad 100 & \quad 90 & \quad 80 & \quad 70 & \quad 60 & \quad 50 & \quad 40 & \quad 30 & \quad 20 & \quad 10 & \quad 0
\end{align*}
\]
tert-Butyl \((R,E)-(4,4,4\text{-trifluoro-1,3-diphenylbut-2-en-1-yl})\) carbamate (4a’)

\[
\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{F}_3\text{C} & \quad \text{Ph}
\end{align*}
\]

\((R,E)-4a’\)

\(^1\text{H NMR, CDCl}_3, 400\text{ MHz}\)

\[
\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{F}_3\text{C} & \quad \text{Ph}
\end{align*}
\]

\((R,E)-4a’\)

\(^{13}\text{C NMR, CDCl}_3, 100\text{ MHz}\)
(R,E)-4,4,4-Trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-amine (4b)

\[
\text{F}_3\text{C} \begin{array}{c}
\text{NH}_2 \\
\text{Ph}
\end{array} 
\]

(R,E)-4b

$^1$H NMR, CDCl$_3$, 400 MHz

\[
\begin{array}{c}
\text{F}_3\text{C} \\
\text{NH}_2 \\
\text{Ph}
\end{array} 
\]

(R,E)-4b

$^{13}$C NMR, CDCl$_3$, 100 MHz
**tert-Butyl (R,E)-(4,4,4-trifluoro-3-phenyl-1-(p-tolyl)but-2-en-1-yl)carbamate (4b')**

(R,E)-4b

$^1$H NMR, CDCl$_3$, 400 MHz

(R,E)-4b'

$^{13}$C NMR, CDCl$_3$, 100 MHz
(R,E)-4,4,4-Trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-amine (4c)

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{NH}_2 \\
\text{Ph} & \quad \text{OMe}
\end{align*}
\]

(R,E)-4c

\(^1\)H NMR, CDCl\textsubscript{3}, 400 MHz

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{NH}_2 \\
\text{Ph} & \quad \text{OMe}
\end{align*}
\]

(R,E)-4c

\(^{13}\)C NMR, CDCl\textsubscript{3}, 100 MHz
tert-Butyl (R,E)-(4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbut-2-en-1-yl)carbamate (4c‘)

(R,E)-4c‘

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
(R,E)-1-(4-Bromophenyl)-4,4,4-trifluoro-3-phenylbut-2-en-1-amine 4d

$\text{F}_3\text{C}=\text{C}($\text{Ph}$)\text{NH}_2\text{Ph}$

(R,E)-4d

$^1$H NMR, CDCl$_3$, 400 MHz

$\text{F}_3\text{C}=\text{C}($\text{Ph}$)\text{NH}_2\text{Ph}$

(R,E)-4d

$^{13}$C NMR, CDCl$_3$, 100 MHz
tert-Butyl (R,E)-(1-(4-bromophenyl)-4,4,4-trifluoro-3-phenylbut-2-en-1-yl)carbamate (4d')

$\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{F}_3\text{C} & \quad \text{Br}
\end{align*}$

$\text{(R,E)-4d'}$

$^1\text{H}$ NMR, $\text{CDCl}_3$, 400 MHz

$\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{F}_3\text{C} & \quad \text{Br}
\end{align*}$

$\text{(R,E)-4d'}$

$^{13}\text{C}$ NMR, $\text{CDCl}_3$, 100 MHz

S53
(R,E)-4d'

| Peak | RetTime | Type | Width | Area         | Height | Area       |
|------|---------|------|-------|--------------|--------|------------|
| 1    | 6.907   | MF   | 0.2355 | 4723.09619  | 334.29535 | 48.7371   |
| 2    | 7.718   | FM   | 0.2738 | 3700.70605  | 225.22873 | 38.1872   |
| 3    | 12.835  | MM   | 0.4564 | 690.65741   | 25.22265  | 7.1268    |
| 4    | 16.704  | MM   | 0.6539 | 576.50079   | 14.69383  | 5.9489    |

| Peak | RetTime | Type | Width | Area         | Height | Area       |
|------|---------|------|-------|--------------|--------|------------|
| 1    | 6.791   | MM   | 0.2388 | 1.73989e4    | 1214.15039 | 87.6811   |
| 2    | 7.607   | MM   | 0.2176 | 290.86615    | 22.28024  | 1.4658    |
| 3    | 12.737  | MM   | 0.4546 | 2072.23926   | 75.97820  | 10.4430   |
| 4    | 16.833  | MM   | 0.8601 | 81.39301     | 1.57716   | 0.4102    |
(R,E)-4,4,4-Trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (4e)

1^H NMR, CDCl₃, 400 MHz

13^C NMR, CDCl₃, 100 MHz
tert-Butyl \((R,E)-(4,4,4\text{-trifluoro-3-phenyl-1-}(4\text{-}(trifluoromethyl)phenyl)but-2-en-1-yl)\)carbamate (4e')

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
\text{CF}_3 & \quad \text{CF}_3
\end{align*}
\]

\((R,E)-4e'\)

\(^1\text{H NMR, CDCl}_3, 400 \text{ MHz}\)

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
\text{CF}_3 & \quad \text{CF}_3
\end{align*}
\]

\((R,E)-4e'\)

\(^{13}\text{C NMR, CDCl}_3, 100 \text{ MHz}\)
(R,E)-4,4,4-Trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-amine (4f)

$\text{Ph} \quad \text{NH}_2$

$\text{F}_3\text{C} \quad \text{NH}_2$

(R,E)-4f

$^1$H NMR, CDCl$_3$, 400 MHz

13C NMR, CDCl$_3$, 100 MHz

S58
**tert-Butyl (R,E)-(4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbut-2-en-1-yl)carbamate (4f')**

1H NMR, CDCl3, 400 MHz

13C NMR, CDCl3, 100 MHz
(R,E)-4,4,4-Trifluoro-1-(3-methoxyphenyl)-3-phenylbut-2-en-1-amine (4g)

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{F}_3\text{C} & \quad \text{\text{OMe}}
\end{align*}
\]

(R,E)-4g

\(^1\)H NMR, CDCl\(_3\), 400 MHz

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{F}_3\text{C} & \quad \text{\text{OMe}}
\end{align*}
\]

(R,E)-4g

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz
tert-Butyl (R,E)-(4,4,4-trifluoro-1-(3-methoxyphenyl)-3-phenylbut-2-en-1-yl)carbamate (4g')

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
\begin{array}{c}
\text{F}_3\text{C} \\
\end{array} & \begin{array}{c}
\text{Ph} \\
\end{array} & \begin{array}{c}
\text{OMe} \\
\end{array}
\end{align*}
\]

\((R,E)-4g'\)

\(^1\)H NMR, CDCl\(_3\), 400 MHz

\[
\begin{align*}
199.99 & \quad 154.48 \\
141.72 & \quad 135.78 \\
129.86 & \quad 128.22 \\
121.96 & \quad 121.96 \\
117.83 & \quad 118.08 \\
117.63 & \quad 117.63 \\
73.95 & \quad 73.95 \\
61.98 & \quad 61.98 \\
55.19 & \quad 55.19 \\
25.36 & \quad 25.36 
\end{align*}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
\begin{array}{c}
\text{F}_3\text{C} \\
\end{array} & \begin{array}{c}
\text{Ph} \\
\end{array} & \begin{array}{c}
\text{OMe} \\
\end{array}
\end{align*}
\]

\((R,E)-4g'\)

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz

\[
\begin{align*}
199.99 & \quad 154.48 \\
141.72 & \quad 135.78 \\
129.86 & \quad 128.22 \\
121.96 & \quad 121.96 \\
117.83 & \quad 118.08 \\
117.63 & \quad 117.63 \\
73.95 & \quad 73.95 \\
61.98 & \quad 61.98 \\
55.19 & \quad 55.19 \\
25.36 & \quad 25.36 
\end{align*}
\]
### (R,E)-4g

![Chemical Structure](image)

### Chromatogram Data

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 6.483   | BB   | 0.2139| 2.37795e4| 1779.48376| 50.3735 |
| 2    | 7.816   | VB   | 0.2431| 1.86578e4| 1201.85327| 39.5240 |
| 3    | 12.747  | VV   | 0.3940| 2637.63428| 101.88622 | 5.5875  |
| 4    | 15.539  | VV   | 0.4991| 2131.39990| 64.23135  | 4.5151  |

### Chromatogram Data

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 6.642   | MM   | 0.2102| 1.30041e4| 1031.17188| 97.0618 |
| 2    | 8.012   | MM   | 0.2600| 393.64725 | 25.23112  | 2.9382  |

S63
(R,E)-4,4,4-Trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)but-2-en-1-amine (4h)

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{CF}_3 & \\
\end{align*}
\]

(R,E)-4h

\(^1\)H NMR, CDCl\(_3\), 400 MHz

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{CF}_3 & \\
\end{align*}
\]

(R,E)-4h

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz
tert-Butyl \((R,E)-(4,4,4\text{-trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)but-2-en-1-yl})carbamate\) (4h‘)

\[
\text{Ph} \quad \text{NHBoc} \quad \text{CF}_3
\]

\((R,E)-4h'\)

\(^1\text{H} \text{NMR, CDCl}_3, 400 \text{ MHz}\)

\[
\text{Ph} \quad \text{NHBoc} \quad \text{CF}_3
\]

\((R,E)-4h'\)

\(^{13}\text{C} \text{NMR, CDCl}_3, 100 \text{ MHz}\)
(R,E)-4,4,4-Trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-amine (4i)

\[
\begin{align*}
\text{Ph} & \quad \text{NH}_2 \\
\text{F}_3\text{C} & \quad \text{MeO}
\end{align*}
\]

\(\text{(R,E)-4i}\)

\(^1\text{H NMR, CDCl}_3, 400 \text{ MHz}\)

\[
\begin{align*}
&\text{13C NMR, CDCl}_3, 100 \text{ MHz}\n\end{align*}
\]

\(\text{(R,E)-4i}\)
**tert-Butyl (R,E)-(4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbut-2-en-1-yl)carbamate (4i')**

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOC} \\
F_3C & \quad \text{MeO} \\
\end{align*}
\]

(R,E)-4i'

\[^1H\text{NMR, CDCl}_3, 400 \text{ MHz}\]

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOC} \\
F_3C & \quad \text{MeO} \\
\end{align*}
\]

(R,E)-4i'

\[^{13}C\text{NMR, CDCl}_3, 100 \text{ MHz}\]
(S,E)-5,5,5-Trifluoro-4-phenylpent-3-en-2-amine (4j)

$\text{Ph} \quad \text{NH}_2$

(S,E)-4j

$^1$H NMR, CDCl$_3$, 400 MHz

$\text{Ph} \quad \text{NH}_2$

(S,E)-4j

$^{13}$C NMR, CDCl$_3$, 100 MHz
**tert-Butyl (S,E)-(5,5,5-Trifluoro-4-phenylpent-3-en-2-yl)carbamate (4j')**

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
F_3\text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C}
\end{align*}
\]

\[\textcolor{red}{(S,E)-4j'}\]

\[^1\text{H} \text{ NMR, CDCl}_3, 400 \text{ MHz}\]

\[
\begin{align*}
\text{Ph} & \quad \text{NHBOc} \\
F_3\text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C} & \quad \text{C} = \text{C}
\end{align*}
\]

\[\textcolor{red}{(S,E)-4j'}\]

\[^{13}\text{C} \text{ NMR, CDCl}_3, 100 \text{ MHz}\]

---

S71
(E)-4,4,4-Trifluoro-3-phenylbut-2-en-1-amine (4k)

(\(\text{Ph}\))

\[
\text{F}_3\text{C} \equiv \text{NH}_2
\]

\((R,E)-4k\)

\(^1\text{H} \text{ NMR, CDCl}_3, 400 \text{ MHz}\)

(\(\text{Ph}\))

\[
\text{F}_3\text{C} \equiv \text{NH}_2
\]

\((R,E)-4k\)

\(^{13}\text{C} \text{ NMR, CDCl}_3, 100 \text{ MHz}\)
(\textit{R,E})-4,4,4-Trifluoro-1-phenyl-3-(\textit{p}-tolyl)but-2-en-1-amine (4l)

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\includegraphics[width=0.8\textwidth]{structure}};
\end{tikzpicture}
\end{center}

$^{1}H$ NMR, CDCl$_3$, 400 MHz

$^{13}C$ NMR, CDCl$_3$, 100 MHz
**tert-Butyl (R,E)-(4,4,4-trifluoro-1-phenyl-3-(p-tolyl)but-2-en-1-yl)carbamate (4l')**

(R,E)-4l'

$^1$H NMR, CDCl$_3$, 400 MHz

(R,E)-4l'

$^{13}$C NMR, CDCl$_3$, 100 MHz
\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{NHBoc} \\
\text{Ph} & \\
(R,E)-4\text{I}'
\end{align*}
\]

| Peak | RetTime | Type | Width | Area     | Height | Area % |
|------|---------|------|-------|----------|--------|--------|
| 1    | 5.458   | MM   | 0.2300| 8718.00586| 631.83197| 53.4617 |
| 2    | 7.029   | MM   | 0.2578| 7589.01953| 490.53333| 46.5383 |

| Peak | RetTime | Type | Width | Area     | Height | Area % |
|------|---------|------|-------|----------|--------|--------|
| 1    | 5.383   | MM   | 0.2299| 1.14998e4| 833.57446| 95.8861 |
| 2    | 6.915   | MM   | 0.2567| 493.38300| 32.03526| 4.1139  |
(R,E)-4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-amine (4m)

\[ \text{OMe} \quad \text{NH}_2 \quad \text{Ph} \]

(R,E)-4m

$^1$H NMR, CDCl$_3$, 400 MHz

\[ \text{OMe} \quad \text{NH}_2 \quad \text{Ph} \]

(R,E)-4m

$^1$H NMR, CDCl$_3$, 400 MHz
**tert-Butyl (R,E)-(4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbut-2-en-1-yl)carbamate (4m’)**

\[
\begin{align*}
\text{OMe} & \\
\text{F}_3\text{C} & \text{NHBoc} \\
\text{Ph} & \\
\end{align*}
\]

(R,E)-4m’

\[\text{\textsuperscript{1}H NMR, CDCl}_3, 400 MHz\]

\[
\begin{align*}
\text{OMe} & \\
\text{F}_3\text{C} & \text{NHBoc} \\
\text{Ph} & \\
\end{align*}
\]

(R,E)-4m’

\[\text{\textsuperscript{1}H NMR, CDCl}_3, 400 MHz\]
(R,E)-4,4,4-Trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-amine (4n)

(R,E)-4n

^1H NMR, CDCl_3, 400 MHz

(R,E)-4n

^13C NMR, CDCl_3, 100 MHz
*tert*-Butyl \((R,E)-(4,4,4\text{-trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl})\)carbamate (4n’)

\[
\begin{align*}
\text{CF}_{3} & \quad \text{NHBoc} \\
\text{F}_{3}\text{C} & \quad \text{Ph}
\end{align*}
\]

\((R,E)-4n’\)

\(^1\)H NMR, CDCl\(_3\), 400 MHz

\[
\begin{align*}
\text{CF}_{3} & \quad \text{NHBoc} \\
\text{F}_{3}\text{C} & \quad \text{Ph}
\end{align*}
\]

\((R,E)-4n’\)

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz
(R,E)-4n'

**Peak RetTime Type Width Area Height Area %**

| #  | [min] | [min] | [mAU*s] | [mAU] | %     |
|----|-------|-------|---------|-------|-------|
| 1  | 5.024 | 0.2559| 4523.22705 | 294.54364 | 58.0993 |
| 2  | 7.069 | 0.2803| 3262.11377 | 193.94978 | 41.9007 |

**Peak RetTime Type Width Area Height Area %**

| #  | [min] | [min] | [mAU*s] | [mAU] | %     |
|----|-------|-------|---------|-------|-------|
| 1  | 5.051 | 0.3152| 3.81342e4 | 2016.45679 | 96.9799 |
| 2  | 6.914 | 0.2698| 1187.57690 | 73.35021 | 3.0201 |

S82
(R,E)-4,4,4-Trifluoro-1-phenyl-3-(m-tolyl)but-2-en-1-amine (4o)

(R,E)-4o

$^1$H NMR, CDCl$_3$, 400 MHz

13C NMR, CDCl$_3$, 100 MHz
**tert-Butyl (R,E)-(4,4,4-trifluoro-1-phenyl-3-(m-tolyl)but-2-en-1-yl)carbamate (4o')**

\[\text{(R,E)-4o'}\]

**1H NMR, CDCl₃, 400 MHz**

\[\text{13C NMR, CDCl₃, 100 MHz}\]

---

**S84**
(R,Z)-4,4,4-Trifluoro-1-phenyl-3-(thiophen-2-yl)but-2-en-1-amine (4p)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl (R,Z)-(4,4,4-trifluoro-1-phenyl-3-(thiophen-2-yl)but-2-en-1-yl)carbamate (4p')

(R,E)-4p'

$^1$H NMR, CDCl$_3$, 400 MHz

(R,E)-4p'

$^{13}$C NMR, CDCl$_3$, 100 MHz
NMR of compounds 6 and 6’

(1S,3R)-4,4,4-Trifluoro-1,3-diphenylbutan-1-amine – minor diastereomer (6a)

$^1$H NMR, CDCl$_3$, 400 MHz

$^{13}$C NMR, CDCl$_3$, 100 MHz

$^{13}$C NMR, CDCl$_3$, 100 MHz
**tert-Butyl ((1S,3R)-4,4,4-trifluoro-1,3-diphenylbutyl)carbamate – minor diastereomer (6a’)**

\[ \text{Ph} \quad \text{NHBoc} \]
\[ \text{CF}_3 \]
\[ \text{Ph} \]

**1S,3R-6a’**

\[ ^1\text{H NMR, CDCl}_3, 400 \text{ MHz} \]

\[ ^{13}\text{C NMR, CDCl}_3, 100 \text{ MHz} \]
(1R,3R)-4,4,4-Trifluoro-1,3-diphenylbutan-1-amine – major diastereomer (6a)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl ((1R,3R)-4,4,4-trifluoro-1,3-diphenylbutyl) carbamate – major diastereomer (6a’)

$1R,3R-6a'$

$^1$H NMR, CDCl$_3$, 400 MHz

$13^C$ NMR, CDCl$_3$, 100 MHz
1R,3R-6a’

---|-----|-----|------------------|------------------|-----|-----|
1 6.056 BV 0.1990 5949.37158 472.04483 55.5792
2 7.807 BV 0.2499 4754.93506 298.41345 44.4208

---|-----|-----|------------------|------------------|-----|-----|
1 6.056 MM 0.2069 1.63019e4 1313.05225 95.1749
2 7.848 MM 0.2527 826.45880 54.50021 4.8251
(1R,3R)-4,4,4-Trifluoro-3-phenyl-1-(p-tolyl)butan-1-amine – major diastereomer (6b)

13C NMR, CDCl3, 100 MHz
**tert-Butyl ((1\text{R},3\text{R})-4,4,4-trifluoro-3-phenyl-1-(p-tolyl)butyl)carbamate – major diastereomer (6b')**

\[
\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{CF}_3 & \\
\end{align*}
\]

1\text{R},3\text{R}-6b'

\[\text{\textsuperscript{13}C NMR, CDCl}_3, 100 \text{ MHz}\]

---

\[
\begin{align*}
\text{Ph} & \quad \text{NHBoc} \\
\text{CF}_3 & \\
\end{align*}
\]

1\text{R},3\text{R}-6b'

\[\text{\textsuperscript{13}C NMR, CDCl}_3, 100 \text{ MHz}\]
| Peak | RetTime | Type | Width | Area  | Height | Area   | %      |
|------|---------|------|-------|-------|--------|--------|--------|
| 1    | 6.610   | BV   | 0.2083| 1.05567e4 | 798.36798 | 54.4745 |        |
| 2    | 7.258   | VV   | 0.2353| 8822.41699 | 587.30841 | 45.5255 |        |

---

| Peak | RetTime | Type | Width | Area  | Height | Area   | %      |
|------|---------|------|-------|-------|--------|--------|--------|
| 1    | 6.489   | BV   | 0.2812| 2.76891e4 | 1605.84692 | 83.4816 |        |
| 2    | 7.102   | VV   | 0.2719| 5478.82080 | 319.71326 | 16.5184 |        |
(1R,3R)-4,4,4-Trifluoro-1-(4-methoxyphenyl)-3-phenylbutan-1-amine – major diastereomer (6c)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
**tert-Butyl ((1R,3R)-4,4,4-trifluoro-1-(4-methoxyphenyl)-3-phenylbutyl)carbamate – major diastereomer (6c’)**

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
1R,3R-6c'

| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|-------------------|-------------|--------------|--------------|--------|
| 1                 | 8.788 BV    | 0.2756       | 476.69098    | 56.0823|
| 2                 | 10.130 VB   | 0.3233       | 315.91843    | 43.9177|

| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|-------------------|-------------|--------------|--------------|--------|
| 1                 | 9.164 MM    | 0.2992       | 41.58955     | 5.2305 |
| 2                 | 10.372 BV   | 0.3397       | 617.15686    | 94.7695|
(1R,3R)-1-(4-Bromophenyl)-4,4,4-trifluoro-3-phenylbutan-1-amine – major diastereomer (6d)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
**tert-Butyl (1\(R\),3\(R\))-1-(4-bromophenyl)-4,4,4-trifluoro-3-phenylbutyl)carbamate – major diastereomer (6d’)**

1\(R\),3\(R\)-6d’

\(^1\)H NMR, CDCl\(_3\), 400 MHz

1\(R\),3\(R\)-6d’

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz
| Peak | Ret Time | Type  | Width | Area   | Height | Area % |
|------|----------|-------|-------|--------|--------|--------|
| 1    | 7.760    | MM    | 0.2838| 9609.80762 | 564.44696 | 57.2907 |
| 2    | 10.351   | MM    | 0.3713| 7163.97168  | 321.60458  | 42.7093 |

| Peak | Ret Time | Type  | Width | Area   | Height | Area % |
|------|----------|-------|-------|--------|--------|--------|
| 1    | 9.004    | BV    | 0.3245| 1.07869e4 | 518.95776 | 92.9500 |
| 2    | 12.432   | BV    | 0.4319| 818.16278  | 28.08563  | 7.0500  |
(1S,3R)-4,4,4-Trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)butan-1-amine – major diastereomer (6e)

\[ \text{CF}_3 \text{Ph} \text{NH}_2 \text{CF}_3 \]

\( ^1H \text{NMR, CDCl}_3, 400 \text{ MHz} \)

\[ \text{CF}_3 \text{Ph} \text{NH}_2 \text{CF}_3 \]

\( ^13C \text{NMR, CDCl}_3, 100 \text{ MHz} \)
tert-Butyl ((1R,3R)-4,4,4-trifluoro-3-phenyl-1-(4-(trifluoromethyl)phenyl)butyl)carbamate – major diastereomer (6e')

\[ \text{Ph} \quad \text{NHBOc} \]

\[ \text{CF}_3 \quad \text{CF}_3 \]

1H NMR, CDCl\textsubscript{3}, 400 MHz

\[ \text{Ph} \quad \text{NHBOc} \]

\[ \text{CF}_3 \quad \text{CF}_3 \]

13C NMR, CDCl\textsubscript{3}, 100 MHz
(1S,3R)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbutan-1-amine – minor diastereomer (6f)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl ((1S,3R)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbutyl)carbamate – minor diastereomer (6f')

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
### 1S,3R-6f'

![Chemical Structure](image)

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 15.479  | BV   | 0.5814| 4568.28809 | 117.54218 | 64.8386 |
| 2    | 20.277  | VV   | 0.6730| 2477.34546 | 45.66288  | 35.1614 |

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 16.749  | MM   | 0.7586| 1.46960e4 | 322.86279 | 96.7179 |
| 2    | 21.497  | MM   | 1.0989| 498.71426 | 7.56412  | 3.2821  |
(1R,3R)-4,4,4-Trifluoro-1-(naphthalen-2-yl)-3-phenylbutan-1-amine – major diastereomer (6f)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
*tert*-Butyl ((1*R,3*R)-4,4,4-trifluoro-1-(naphthalen-2-yl)-3-phenylbutyl)carbamate – major diastereomer (6f')

$\text{Ph} \quad \text{NHBOC} \quad \text{CF}_3$

$\text{1}R,\text{3}R-6f'$

$^1$H NMR, CDCl$_3$, 400 MHz

$\text{Ph} \quad \text{NHBOC} \quad \text{CF}_3$

$\text{1}R,\text{3}R-6f'$

$^{13}$C NMR, CDCl$_3$, 100 MHz
### Peak RetTime Type Width Area Height Area

| #  | RetTime   | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|----|-----------|------|-------------|--------------|--------------|--------|
| 1  | 10.692    | BV   | 0.3884      | 2.05084e4    | 812.80261    | 64.8635|
| 2  | 12.735    | VV   | 0.4781      | 1.11093e4    | 359.93011    | 35.1365|

### Peak RetTime Type Width Area Height Area

| #  | RetTime   | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|----|-----------|------|-------------|--------------|--------------|--------|
| 1  | 10.871    | MM   | 0.4292      | 2.85714e4    | 1109.36584   | 97.3738|
| 2  | 13.162    | MM   | 0.5435      | 770.59174    | 23.63230     | 2.6262 |
(1S,3R)-4,4,4-Trifluoro-1-(3-methoxyphenyl)-3-phenylbutan-1-amine – minor diastereomer (6g)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
*tert*-Butyl ((1*S,3R)-4,4,4-trifluoro-1-(3-methoxyphenyl)-3-phenylbutyl)carbamate—minor diastereomer (6g')

**1H NMR, CDCl₃, 400 MHz**

**13C NMR, CDCl₃, 100 MHz**
**1S,3R-6F**

![Chemical Structure](image_url)

| Peak RetTime | Width | Area [mAU*s] | Height [mAU] | Area [%] |
|--------------|-------|--------------|--------------|---------|
| 1            | 12.399| 3308.19751   | 55.91677     | 41.6459 |
| 2            | 19.691| 4635.42969   | 61.59345     | 58.3541 |

| Peak RetTime | Width | Area [mAU*s] | Height [mAU] | Area [%] |
|--------------|-------|--------------|--------------|---------|
| 1            | 12.574| 732.01520    | 12.49027     | 7.1791  |
| 2            | 19.859| 9464.41211   | 128.07130    | 92.8209 |
(1R,3R)-4,4,4-Trifluoro-1-(3-methoxyphenyl)-3-phenylbutan-1-amine – major diastereomer (6g)

$^{1}H$ NMR, CDCl$_3$, 400 MHz

$^{13}$C NMR, CDCl$_3$, 100 MHz
**tert-Butyl ((1R,3R)-4,4,4-trifluoro-1-(3-methoxyphenyl)-3-phenylbutyl)carbamate – major diastereomer (6g')**

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
| Peak | Ret Time | Type | Width | Area | Height | Area % |
|------|----------|------|-------|------|--------|-------|
| 1    | 7.714    | MM   | 0.2774| 1.72279e4| 1035.24622 | 56.0796 |
| 2    | 9.379    | MM   | 0.3435| 1.34925e4| 654.59137  | 43.9204 |

| Peak | Ret Time | Type | Width | Area | Height | Area % |
|------|----------|------|-------|------|--------|-------|
| 1    | 7.743    | MM   | 0.2611| 8724.56250| 557.00623  | 94.3413 |
| 2    | 9.464    | MM   | 0.3294| 523.30811| 26.47727    | 5.6587  |

1R,3R-6g’
(1S,3R)-4,4,4-Trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butan-1-amine – minor diastereomer (6h)

1H NMR, CDCl$_3$, 400 MHz

13C NMR, CDCl$_3$, 100 MHz
tert-Butyl (1S,3R)-4,4,4-trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butyl)carbamate – minor diastereomer (6h’)

\[ \text{1S,3R-6h'} \]

\(^1\)H NMR, CDCl\(_3\), 400 MHz

\[ \text{1S,3R-6h'} \]

\(^{13}\)C NMR, CDCl\(_3\), 100 MHz
| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------------------|-------------|--------------|--------------|--------|
| 1                | 0.5645      | 4053.77100   | 97.22186     | 43.4633|
| 2                | 0.6677      | 5273.12109   | 126.13394    | 56.5367|

| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------------------|-------------|--------------|--------------|--------|
| 1                | 0.6001      | 4758.38721   | 113.26289    | 11.5296|
| 2                | 0.6418      | 3.65128e4    | 910.68823    | 88.4704|
(1R,3R)-4,4,4-Trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butan-1-amine – major diastereomer (6h)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl (\((1R,3R)\)-4,4,4-trifluoro-3-phenyl-1-(3-(trifluoromethyl)phenyl)butyl)carbamate – major diastereomer \((6h')\)

\[\text{1H NMR, CDCl}_3, 400 MHz}\]

\[\text{13C NMR, CDCl}_3, 100 MHz]\]
**1R,3R-6h**

![Chemical Structure]

### Peak RetTime Type Width Area Height Area

| #  | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|----|---------------|------|-------------|--------------|--------------|--------|
| 1  | 9.622         | VV   | 0.5197      | 5738.3750    | 176.31398    | 56.4385 |
| 2  | 16.094        | VB   | 0.6646      | 4429.10303   | 102.00723    | 43.5615 |

### Peak RetTime Type Width Area Height Area

| #  | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|----|---------------|------|-------------|--------------|--------------|--------|
| 1  | 3.876         | VB   | 0.0626      | 19.13806     | 4.59840      | 5.6458 |
| 2  | 10.256        | BB   | 0.5126      | 319.83951    | 9.96070      | 94.3542 |
(1S,3R)-4,4,4-Trifluoro-1-(2-methoxyphenyl)-3-phenylbutan-1-amine - minor diastereomer (6i)

$^{1}$H NMR, CDCl$_3$, 400 MHz

$^{13}$C NMR, CDCl$_3$, 100 MHz
tert-Butyl ((1S,3R)-4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbutyl)carbamate – minor diastereomer (6i')

1H NMR, CDCl3, 400 MHz

13C NMR, CDCl3, 100 MHz

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**1S,3R-6i'**

**Table 1**

| #  | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|----|---------------|------|-------------|--------------|--------------|---------|
| 1  | 7.129         | VV   | 0.2209      | 3949.51587   | 279.38400    | 54.1906 |
| 2  | 7.730         | VB   | 0.2418      | 3338.67139   | 211.86257    | 45.8094 |

**Table 2**

| #  | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|----|---------------|------|-------------|--------------|--------------|---------|
| 1  | 7.229         | VV   | 0.2236      | 1.24736e4    | 868.37579    | 84.5006 |
| 2  | 7.887         | VB   | 0.2486      | 2287.95801   | 140.07599    | 15.4994 |
(1\textit{R},3\textit{R})-4,4,4-Trifluoro-1-(2-methoxyphenyl)-3-phenylbutan-1-amine – major diastereomer (6i)

\textbf{1H NMR, CDCl\textsubscript{3}, 400 MHz}

\textbf{13C NMR, CDCl\textsubscript{3}, 100 MHz}
tert-Butyl ((1R,3R)-4,4,4-trifluoro-1-(2-methoxyphenyl)-3-phenylbutyl)carbamate – major diastereomer (6i')

\[ \text{Ph} \quad \text{CF}_3 \quad \text{NHBoc} \]

\[ \text{MeO} \]

1H NMR, CDCl\textsubscript{3}, 400 MHz

\[ \text{Ph} \quad \text{CF}_3 \quad \text{NHBoc} \]

\[ \text{MeO} \]

13C NMR, CDCl\textsubscript{3}, 100 MHz
| Peak | RetTime | Type | Width | Area     | Height | Area  | %    |
|------|---------|------|-------|----------|--------|-------|------|
| 1    | 8.785   | MF   | 0.3095| 1.65488e4| 891.15698 | 53.8248 |
| 2    | 9.819   | FM   | 0.3600| 1.41969e4| 657.23694 | 46.1752 |

| Peak | RetTime | Type | Width | Area     | Height | Area  | %    |
|------|---------|------|-------|----------|--------|-------|------|
| 1    | 8.575   | MF   | 0.2810| 1.53710e4| 911.81726 | 85.8995 |
| 2    | 9.611   | FM   | 0.3308| 2.52316089| 127.14045 | 14.1005 |
(1R,3R)-4,4,4-Trifluoro-1-phenyl-3-(p-tolyl)butan-1-amine diastereomer 2 – major diastereomer (6l)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
**tert-Butyl ((1R,3R)-4,4,4-trifluoro-1-phenyl-3-(p-tolyl)butyl)carbamate – major diastereomer (6l')**

\[ \begin{align*}
\text{CF}_3 & \quad \text{NHBOc} \\
\text{Ph} & \\
\end{align*} \]

**1R,3R-6l'**

\(^1\)H NMR, CDCl\(_3\), 400 MHz

**13C NMR, CDCl\(_3\), 100 MHz**
$1R,3R-6l'$

| Peak | RetTime | Type | Width | Area      | Height | Area   | %    |
|------|---------|------|-------|-----------|--------|--------|------|
| 1    | 5.124   | MM   | 0.175 | 9509.138 | 904.209| 54.644|      |
| 2    | 6.941   | MM   | 0.235 | 7892.728 | 557.831| 45.356|      |

| Peak | RetTime | Type | Width | Area      | Height | Area   | %    |
|------|---------|------|-------|-----------|--------|--------|------|
| 1    | 5.116   | VV   | 0.174 | 1.39353e4 | 1286.579| 85.046|      |
| 2    | 6.940   | VB   | 0.219 | 2450.124 | 173.172| 14.953|      |
(1R,3R)-4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenylbutan-1-amine – major diastereomer (6m)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl ((1R,3R)-4,4,4-trifluoro-3-(4-methoxyphenyl)-1-phenylbutyl)carbamate – major diastereomer (6m')

$\text{OMe}$

\[
\begin{align*}
\text{CF}_3 & \quad \text{NHBoc} \\
\text{Ph} &
\end{align*}
\]

1R,3R-6m'

$^1$H NMR, CDCl$_3$, 400 MHz

$\text{13C NMR, CDCl}_3$, 100 MHz
(1R,3R)-4,4,4-Trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)butan-1-amine – major diastereomer (6n)

$^{1}H$ NMR, CDCl$_3$, 400 MHz

$^{13}C$ NMR, CDCl$_3$, 100 MHz
**tert-Butyl ((1R,3R)-4,4,4-trifluoro-1-phenyl-3-(4-(trifluoromethyl)phenyl)butyl)carbamate – major diastereomer (6n’)**

\[
\text{CF}_3 \\
\text{NHBoc} \\
\text{Ph}
\]

1\(R,3R\)-6n’

\(^1\text{H} \text{NMR, CDCl}_3, 400 \text{ MHz}\)

\[
\text{CF}_3 \\
\text{NHBoc} \\
\text{Ph}
\]

1\(R,3R\)-6n’

\(^{13}\text{C} \text{NMR, CDCl}_3, 100 \text{ MHz}\)
(1R,3R)-4,4,4-Trifluoro-1-phenyl-3-(m-tolyl)butan-1-amine – major diastereomer (6o)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
*tert*-Butyl ((1R,3R)-4,4,4-trifluoro-1-phenyl-3-(m-tolyl)butyl)carbamate – major diastereomer (6o’)

\[ \text{CF}_3 \text{NHBOc} \]

**1R,3R-6o’**

$^1$H NMR, CDCl$_3$, 400 MHz

\[ \text{CF}_3 \text{NHBOc} \]

**1R,3R-6o’**

$^{13}$C NMR, CDCl$_3$, 100 MHz
### Peak RetTime Type Width Area Height Area %

| # | [min] | [min] | [mAU*s] | [mAU] | %      |
|---|-------|-------|---------|-------|--------|
| 1 | 5.231 | MM    | 0.1792  | 3295.30908 | 306.51895 | 57.2553 |
| 2 | 6.772 | MM    | 0.2319  | 2460.15430 | 176.84816 | 42.7447 |

### Peak RetTime Type Width Area Height Area %

| # | [min] | [min] | [mAU*s] | [mAU] | %      |
|---|-------|-------|---------|-------|--------|
| 1 | 5.241 | MM    | 0.2149  | 2.05743e4  | 1595.82104 | 91.3214 |
| 2 | 6.813 | MM    | 0.2309  | 1955.25659 | 141.10260 | 8.6786  |
(1S,3S)-4,4,4-Trifluoro-1-phenyl-3-(thiophen-2-yl)butan-1-amine – minor diastereomer (6p)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl ((1S,3S)-4,4,4-trifluoro-1-phenyl-3-(m-tolyl)butyl)carbamate – minor diastereomer (6p’)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
| Peak | RetTime | Type | Width | Area   | Height | Area %  |
|------|---------|------|-------|--------|--------|---------|
| 1    | 6.100   | MM   | 0.2064| 4628.16504 | 373.68042 | 42.7449 |
| 2    | 7.528   | MM   | 0.2559| 6199.23682 | 403.77646 | 57.2551 |

| Peak | RetTime | Type | Width | Area   | Height | Area %  |
|------|---------|------|-------|--------|--------|---------|
| 1    | 6.138   | MM   | 0.1984| 274.54715 | 23.06816 | 7.1650  |
| 2    | 7.534   | MM   | 0.2583| 3557.21191 | 229.51276 | 92.8350 |
(1R,3S)-4,4,4-Trifluoro-1-phenyl-3-(thiophen-2-yl)butan-1-amine – major diastereomer (6p)

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
tert-Butyl ((1R,3S)-4,4,4-trifluoro-1-phenyl-3-(thiophen-2-yl)butyl)carbamate – major diastereomer (6p')

1H NMR, CDCl₃, 400 MHz

13C NMR, CDCl₃, 100 MHz
1R,3S-6p'
4,4,4-Trifluoro-1-phenylbutan-1-amine (6q)

\[ \text{F}_3 \text{C} \quad \text{NH}_2 \quad \text{Ph} \]

\[ 6q \]

$^1$H NMR, CDCl$_3$, 400 MHz

$^{13}$C NMR, CDCl$_3$, 100 MHz
Crystal structure determination

Single crystal X-ray diffraction data on suitable crystals of compounds 4d’ and (1R,3R)-6d’ were collected using Cu Kα radiation on a Bruker D8 VENTURE diffractometer equipped with a PHOTON 100 detector. The dataset was reduced and absorption correction was applied using the APEX3 suite. The crystal structures were solved and refined by SHELXT and SHELXL respectively. The crystal structures were refined using full-matrix least-squares based on \( F^2 \) with all non-hydrogen atoms anisotropically defined. All hydrogen atoms were either located in the difference Fourier maps or placed using a riding model. A summary of the crystallographic data and refinement parameters are provided in Tables S2 and S3.

CCDC 2129456-2129457 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via http://www.ccdc.cam.ac.uk/structures.

Compound 4d’ crystallizes in the Sohnecke space group \( P_2_1_2_1_2_1 \) with four molecules in the asymmetric unit and 16 molecules per unit cell. All molecules in the crystal had the same right-handed stereocenters (R configuration) and enantiopurity was confirmed by the low Flack parameter. Hydrogen-bonding occurs between the amine and carbonate groups on neighbouring molecules forming a 1D hydrogen-bonded network along the c-axis.

Compound (1R,3R)-6d’ also crystallizes in the same Sohnecke space group \( P_2_1_2_1_2_1 \) but with only one molecule per asymmetric unit and four per unit cell. All molecules in the crystal had the same right-handed stereocenters (R,R configuration) and enantiopurity was confirmed by the low Flack parameter.

Both crystals 4d’ and 6d’ were grown by diffusion crystallization using a mixture pentane:CH\(_2\)Cl\(_2\) (ca 97:3) as solvent system.

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1. G. Sheldrick, Acta Cryst., 2008, A64, 112-122
Figure S1. Structure of 4d’ (CCDC 2129456) as determined by single crystal X-ray diffraction. Thermal ellipsoids are displayed with 50% probability. Atom are colored as the following: carbon (grey), oxygen (red), nitrogen (blue), fluorine (green), bromine (brown), hydrogen (white spheres).
**Table S2: Crystallographic data and refinement details for compound 4d’**

| Property                              | Value                                      |
|---------------------------------------|--------------------------------------------|
| **Empirical formula**                 | C21 H21 Br F3 N O2                         |
| **formula weight**                    | 456.30                                    |
| **temperature**                       | 296 K                                     |
| **wavelength**                        | 1.54178 Å                                 |
| **crystal system**                    | orthorhombic                              |
| **space group**                       | P2₁2₁2₁ (No. 19)                         |
| **unit cell dimensions**              |                                          |
| a                                     | 13.2581 (3) Å                            |
| b                                     | 19.2734 (5) Å                            |
| c                                     | 34.5735 (9) Å                            |
| **volume**                            | 8834.5 (4) Å³                            |
| **Z**                                 | 16                                        |
| **density (calculated)**              | 1.372 g/cm³                               |
| **absorption coefficient**            | 2.893 mm⁻¹                                |
| **F(000)**                            | 3712                                      |
| **θ range for data collection**       | 2.556° to 70.344°                        |
| **index ranges**                      | -16 ≤ h ≤ 16, -22 ≤ k ≤ 23, -33 ≤ l ≤ 41 |
| **reflections collected**             | 16766                                     |
| **independent reflections**           | 8392 [R(int) = 0.1144]                    |
| **absorption correction**             | multi-scan                                |
| **data / restraints / parameters**    | 16766 / 0 / 1038                         |
| **goodness-of-fit on F²**             | 1.014                                     |
| **final R indices [I>2σ(I)]**         | R1 = 0.0575, wR2 = 0.1270                 |
| **largest diff. peak and hole**       | 0.244 and −0.261 e/Å³                    |
| **Flack parameter**                   | 0.126 (13)                                |
Figure S2. Structure of (1R,3R)-6d’ (CCDC 2129457) as determined by single crystal X-ray diffraction. Thermal ellipsoids are displayed with 50% probability. Atom are colored as the following: carbon (grey), oxygen (red), nitrogen (blue), fluorine (green), bromine (brown), hydrogen (white spheres).
**Table S3:** Crystallographic data and refinement details for compound (1R,3R)-6d'

| Property                      | Value                                           |
|-------------------------------|-------------------------------------------------|
| Empirical formula            | C21 H22 Br F3 N O2                              |
| formula weight               | 457.30                                          |
| temperature                  | 296 K                                           |
| wavelength                   | 1.54178 Å                                       |
| crystal system               | orthorhombic                                    |
| space group                  | \(P2_12_12_1\) (No. 19)                        |
| unit cell dimensions         | \(a = 5.4631 \text{ Å}\)                       |
|                              | \(b = 17.5350 \text{ Å}\)                      |
|                              | \(c = 22.3359 \text{ Å}\)                      |
| volume                       | 2139.7 (3) \text{ Å}³                          |
| \(Z\)                        | 4                                               |
| density (calculated)         | 1.420 g/cm³                                     |
| absorption coefficient       | 2.987 mm\(^{-1}\)                              |
| \(F(000)\)                   | 932                                             |
| \(\theta\) range for data collection | 3.204° to 68.471°                     |
| index ranges                 | \(-6 \leq h \leq 5, -20 \leq k \leq 21, -17 \leq l \leq 26\) |
| reflections collected        | 3795                                            |
| independent reflections      | 1813 [\(R\text{(int)} = 0.2085\)]               |
| absorption correction       | multi-scan                                      |
| data / restraints / parameters | 3795 / 0 / 261                               |
| goodness-of-fit on \(F^2\)   | 0.983                                           |
| final R indices \([I>2\sigma(I)]\) | \(R1 = 0.1083, \text{ wR}2 = 0.2572\)          |
| largest diff. peak and hole  | 0.961 and \(-0.912 \text{ e/Å}³\)              |
| Flack parameter              | 0.09 (6)                                        |