Electronic supplementary information

First one-pot stereoselective synthesis of cis-2,3-dihydro-4-perfluoroalkyl-1H-1,5-benzodiazepines via a catalyst-free three-component reaction

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Experimental Section

General information

All reagents and solvents were purchased from commercial sources and used without further purification, except methyl 2-perfluoroalkynoates 2 were prepared according to reported literature. Melting points were uncorrected. 1H, 19F and 13C NMR spectra were recorded on 500MHz spectrometer. All chemical shifts are reported in parts per million downfield (positive) of the standard: C6F6 for 19F, TMS for 1H and 13C NMR spectra. IR spectras were obtained on a FT-IR spectrometer. Elemental analysis was performed on an elemental analysis instrument. MS (ESI) was run on a mass spectrometer and MS (EI) on a mass spectrometer. X-ray analysis was performed on an X-ray spectrometer.

Synthesis of product 3a.

A mixture of o-phenylenediamine 1 (0.5 mmol), methyl 2-perfluoroalkynoates 2a (0.5 mmol) in anhydrous ethanol (5 mL) was stirred at room temperature for about 30 min. The completion of the reaction was monitored by TLC. The solvent was removed under vacum. The residue was purified by silica gel column chromatography eluted with petroleum ether:ethyl acetate (v:v = 20:1) to give product 3a.

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

3a

(Z)-Methyl 3-(2-aminophenylamino)-4,4,4-trifluorobut-2-enoate 3a: Yellow solid. Yield: 88%. M.p.: 120.1~120.2℃. Anal. Calced. for C11H11F3N2O2: C, 50.77; H, 4.26; N, 10.77. Found C, 50.98; H, 4.47; N, 10.80. IR (KBr, cm⁻¹): ν 1669 (C=O), 2952 (CH), 3030 (Ar-H), 3386 (NH₂), 3473 (NH). 1H NMR (CDCl₃, ppm): δ 3.76 (s, 3H, OCH₃), 3.86 (s, 2H, NH), 5.39 (s, 1H, CH), 6.69-7.12 (m, 4H, ArH), 9.25 (s, 1H, NH). 13C NMR (CDCl₃, ppm): δ 170.2, 149.0 (q, CCF₃, 2J_C-F = 31.0 Hz), 144.1, 129.6, 129.5, 129.0, 123.8, 120.2 (q, CF₃, 1J_C-F = 276.0 Hz), 118.2, 115.8, 88.5 (q, C=CCF₃, 3J_C-F = 6.2 Hz), 51.5. 19F NMR (CDCl₃, ppm): δ -65.5 (s, CF₃). ESI-MS (m/z): 260 (M⁺).
**Synthesis of product 4a.**

A mixture of o-phenylenediamine 1 (0.5 mmol), methyl 2-perfluoroalkynoates 2a (0.5 mmol) in anhydrous ethanol (5 mL) was stirred at refluxing temperature for about 24h. The completion of the reaction was monitored by TLC. When the reaction finished, the solvent was removed by vaccum. The residue was purified by silica gel column chromatography eluted with petroleum ether:ethyl acetate (v:v = 10:1) to afford product 4a.

![Image of product 4a](image)

**(E)-4-(Trifluoromethyl)-1H-benzo[b][1,4]diazepin-2(3H)-one 4a:**

Yellow solid. Yield: 73%. M.p.: 188.9–190.4 °C. \( ^1 \)H NMR (CDCl3, ppm): \( \delta \) 3.36 (s, 2H, CH\(_2\)), 7.15-7.51 (m, 4H, ArH), 9.37 (s, 1H, NH).

**Synthesis of products 6.**

General method: A mixture of o-phenylenediamine 1 (0.5 mmol), aldehydes 5 (0.5 mmol) and methyl 2-perfluoroalkynoates 2 (0.5 mmol) in anhydrous ethanol (5 mL) was stirred at refluxing temperature for about 20–24h. The completion of the reaction was monitored by TLC. When the reaction finished, the solvent was removed by vaccum. And the residue was purified by silica gel column chromatography eluted with petroleum ether:ethyl acetate (v:v = 10:1) to get product 6. Further purification could be carried out by recrystallization from petroleum ether:ethyl acetate (v:v = 2:1).

![Image of product 6a](image)

**cis-Methyl 2-(2-bromophenyl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6a:** Yellow solid. Yield: 57%. M.p.: 150.9–153.5 °C. Anal. Calcd. for C\(_{18}\)H\(_{14}\)BrF\(_3\)N\(_2\)O\(_2\): C, 50.61; H, 3.30; N, 6.56. Found: C, 50.68; H, 3.24; N, 6.73. IR (KBr, cm\(^{-1}\)): \( v \) 1724 (C=O); 2953 (C-H); 3046 (Ar-H); 3427 (N-H). \( ^1 \)H NMR (CDCl3, ppm): \( \delta \) 3.56 (s, 3H, OCH\(_3\)), 4.46 (d, \( J = 4.5 \) Hz, 1H, CH), 4.62 (d, \( J = 6.0 \) Hz, 1H, NH), 4.83 (dd, \( J_1 = 6.0 \) Hz, \( J_2 = 4.5 \) Hz, 1H, CH), 6.75-7.67 (m, 8H, ArH). \( ^{13} \)C NMR (CDCl3, ppm): \( \delta \) 166.7, 145.4 (q, CCF\(_3\)), \( ^2 J_{C,F} = 34 \) Hz), 141.8, 138.1, 136.8, 133.8, 131.1, 130.3, 129.3, 128.0, 127.3, 120.5 (q, CF\(_3\)), \( ^1 J_{C,F} = 276 \) Hz), 119.9, 118.4, 117.6, 56.1, 55.3, 52.6. \( ^{19} \)F NMR (CDCl3, ppm): \( \delta \) -71.39 (s, CF\(_3\)). ESI-MS (m/z): 426 (M\(^+\)).
cis-Methyl 2-(4-bromophenyl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6b: Yellow solid. Yield: 73%. M.p.: 135.9~138.3°C. Anal. Calcd. for C_{18}H_{14}BrF_{3}N_{2}O_{2}: C, 50.61; H, 3.30; N, 6.56. Found: C, 50.90; H, 3.43; N, 6.81. IR (KBr, cm^{-1}): ν 1750 (C=O); 2957 (C-H); 3051 (Ar-H); 3329 (N-H). 1H NMR (CDCl_{3}, ppm): δ 3.58 (s, 3H, OCH_{3}), 4.44 (d, J = 4.5 Hz, 1H, CH), 4.94 (d, J = 6.0 Hz, 1H, CH), 5.44 (dd, J_{1} = 6.0 Hz, J_{2} = 4.5 Hz, 1H, CH), 6.76-7.44 (m, 8H, ArH). 13C NMR (CDCl_{3}, ppm): δ 167.6, 147.0 (q, CF_{3}, J_{C-F} = 34 Hz), 140.8, 139.8, 134.7, 131.9, 130.7, 130.3, 127.4, 121.9, 120.0 (q, CF_{3}, J_{C-F} = 276 Hz), 119.4, 118.3, 77.1, 60.6, 54.2, 53.1. 19F NMR (CDCl_{3}, ppm): δ -71.69 (s, CF_{3}). ESI-MS (m/z): 426 (M^+).

cis-Methyl 2-p-tolyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6c: Yellow solid. Yield: 90%. M.p.: 148.6~148.9°C. Anal. Calcd. for C_{19}H_{17}F_{3}N_{2}O_{2}: C, 62.98; H, 4.73; N, 7.73. Found: C, 62.81; H, 4.56; N, 7.82. IR (KBr, cm^{-1}): ν 1745 (C=O); 2957 (C-H); 3057 (Ar-H); 3329 (N-H). 1H NMR (CDCl_{3}, ppm): δ 2.27 (s, 3H, CH_{3}), 3.58 (s, 3H, OCH_{3}), 4.47 (d, J = 4.5 Hz, 1H, CH), 4.94 (d, J = 6.0 Hz, 1H, CH), 5.39 (dd, J_{1} = 6.0 Hz, J_{2} = 4.5 Hz, 1H, CH), 6.73-7.44 (m, 8H, ArH). 13C NMR (CDCl_{3}, ppm): δ 168.2, 147.0 (q, CF_{3}, J_{C-F} = 34 Hz), 141.6, 138.0, 137.8, 135.0, 130.8, 129.6, 125.7, 122.5, 120.7, 120.1 (q, CF_{3}, J_{C-F} = 267.5 Hz), 119.0, 118.4, 60.6, 54.9, 53.1, 21.2. 19F NMR (CDCl_{3}, ppm): δ -71.54 (s, CF_{3}). ESI-MS (m/z): 362 (M^+).

cis-Methyl 2-(4-fluorophenyl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6d: Yellow solid. Yield: 54%. M.p.: 95.1~96.1°C. Anal. Calcd. for C_{18}H_{14}F_{4}N_{2}O_{2}: C, 59.02; H, 3.85; N, 7.65. Found: C, 59.09; H, 3.56; N, 7.82. IR (KBr, cm^{-1}): ν 1745 (C=O); 2959 (C-H); 3050 (Ar-H); 3335 (N-H). 1H NMR (CDCl_{3}, ppm): δ 3.55 (s, 3H, OCH_{3}), 4.44 (d, J = 4.5 Hz, 1H, CH), 5.09 (d, J = 6.5 Hz, 1H, CH), 5.44 (dd, J_{1} = 6.5 Hz, J_{2} = 4.5 Hz, 1H, CH), 6.73-7.43 (m, 8H, ArH). 13C NMR (CDCl_{3}, ppm): δ 167.7, 163.2, 161.2, 146.8 (q, CF_{3}, J_{C-F} = 34 Hz), 141.1, 136.8 (d, Ar-F, J_{C-F} = 2.5 Hz), 134.7, 130.7, 130.2, 127.4 (d, Ar-F, J_{C-F} = 7.5 Hz), 119.9 (q, CF_{3}, J_{C-F} = 276 Hz), 119.2, 118.3, 115.7, 115.6, 60.4, 54.5, 53.0. 19F NMR (CDCl_{3}, ppm): δ -71.67 (s, CF_{3}), -114.22 (m, ArF). ESI-MS (m/z): 366 (M^+).
cis-Methyl 2-(4-methoxyphenyl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6e: Yellow solid. Yield: 80%. M.p.: 110.7~111.2 ℃. Anal. Calcd. for C₁₉H₁₇F₃N₂O₃: C, 60.32; H, 4.53; N, 7.40. Found: C, 57.91; H, 4.43; N, 7.17. IR (KBr, cm⁻¹): ν 1736 (C=O); 2956 (C-H); 3004 (Ar-H); 3398 (N-H). ¹H NMR (CDCl₃, ppm): δ 3.58 (s, 3H, OCH₃), 3.73 (s, 3H, OCH₃), 4.44 (d, J = 4.5 Hz, 1H, CH), 4.95 (d, J = 4.0 Hz, 1H, CH), 6.74-7.44 (m, 8H, ArH). ¹³C NMR (CDCl₃, ppm): δ 168.0, 159.1, 146.8 (q, CF₃, J_C-F = 34 Hz), 141.6, 134.9, 133.0, 132.1, 130.7, 130.1, 126.9, 120.1 (q, CF₃, J_C-F = 276 Hz), 118.9, 118.3, 114.1, 114.5, 59.9, 55.2, 54.9, 53.0. ¹⁹F NMR (CDCl₃, ppm): δ -71.39 (s, CF₃). ESI-MS (m/z): 378 (M⁺).

cis-Methyl 2-(4-nitrophenyl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6f: Yellow solid. Yield: 50%. M.p.: 176.5~180.0 ℃. Anal. Calcd. for C₁₈H₁₄F₃N₃O₄: C, 54.97; H, 3.59; N, 10.68. Found: C, 54.99; H, 3.35; N, 10.89. IR (KBr, cm⁻¹): ν 1743 (C=O); 2971 (C-H); 3079 (Ar-H). ¹H NMR (CDCl₃, ppm): δ 3.61 (s, 3H, OCH₃), 4.36 (d, J = 4.0 Hz, 1H, CH), 4.65 (d, J = 6.0 Hz, 1H, CH), 4.70 (dd, J₁ = 6.0 Hz, J₂ = 4.0 Hz, 1H, CH), 6.78-8.31 (m, 8H, ArH). ¹³C NMR (CDCl₃, ppm): δ 166.4, 148.2, 146.4, 145.5 (q, CF₃, J_C-F = 34 Hz), 140.9, 136.4, 131.3, 129.6, 128.2, 124.4, 120.4, 120.3 (q, CF₃, J_C-F = 276 Hz), 120.1, 118.6, 113.4, 58.1, 56.6, 52.9. ¹⁹F NMR (CDCl₃, ppm): δ -71.57 (s, CF₃). ESI-MS (m/z): 393 (M⁺).

cis-Methyl 2-phenyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6g: Yellow solid. Yield: 72%. M.p.: 113.8~114.2 ℃. Anal. Calcd. for C₁₈H₁₅F₃N₂O₂: C, 62.07; H, 4.34; N, 8.04. Found: C, 61.80; H, 4.12; N, 8.02. IR (KBr, cm⁻¹): ν 1742 (C=O); 2975 (C-H); 3075 (Ar-H). ¹H NMR (CDCl₃, ppm): δ 3.59 (s, 3H, OCH₃), 4.47 (d, J = 4.0 Hz, 1H, CH), 4.92 (d, J = 6.0 Hz, 1H, CH), 5.47 (dd, J₁ = 6.0 Hz, J₂ = 4.0 Hz, 1H, CH), 6.77-7.45 (m, 9H, ArH). ¹³C NMR (CDCl₃, ppm): δ 167.9, 146.8 (q, CF₃, J_C-F = 34 Hz), 141.4, 140.9, 138.4, 134.8, 130.7, 130.2, 128.8, 127.9, 125.6, 119.9 (q, CF₃, J_C-F = 276 Hz), 119.7, 119.0, 118.3, 60.8, 54.7, 53.0. ¹⁹F NMR (CDCl₃, ppm): δ -71.74 (s, CF₃). ESI-MS (m/z): 348 (M⁺).
cis-Methyl 2-(1H-indol-3-yl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6h: Yellow solid. Yield: 56%. M.p.: 149.4~152.0°C. Anal. Calcd. for C20H16F3N3O2: C, 62.01; H, 4.16; N, 10.85. Found: C, 61.74; H, 3.94; N, 10.87. IR (KBr, cm\(^{-1}\)): \(\nu\) 1747 (C=O); 2956 (C-H); 3063 (Ar-H); 3388 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 3.67 (s, 3H, OCH\(_3\)), 4.60 (d, \(J\) = 4.0 Hz, 1H, CH), 4.99 (d, \(J\) = 6.0 Hz, 1H, CH), 5.66 (dd, \(J_1\) = 6.0 Hz, \(J_2\) = 4.0 Hz, 1H, CH), 6.70-7.97 (m, 10H, ArH). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 168.6, 147.2 (q, CF\(_3\), \(J\)\(_{CF}\) = 34 Hz), 141.9, 136.6, 136.1, 135.4, 132.2, 131.1, 130.8, 129.1, 124.7, 120.4 (q, CF\(_3\), \(J\)\(_{CF}\) = 273 Hz), 120.2, 118.6, 115.9, 111.7, 54.9, 53.2, 52.9. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -71.34 (s, CF\(_3\)). ESI-MS (m/z): 387 (M\(^+\)).

6i

cis-Methyl 2-n-heptyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6i: Yellow oil. Yield: 56%. Anal. Calcd. for C\(_{19}\)H\(_{25}\)F\(_3\)N\(_2\)O\(_2\): C, 61.61; H, 6.80; N, 7.56. Found: C, 61.43; H, 6.67; N, 7.53. IR (KBr, cm\(^{-1}\)): \(\nu\) 1737 (C=O); 2928 (C-H); 3065 (Ar-H); 3398 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 0.84 (t, \(J\) = 7.0, 3H, CH\(_3\)), 1.19~1.28 (m, 12H, C\(_6\)H\(_{12}\)), 3.62 (s, 3H, OCH\(_3\)), 3.99 (m, 1H, CH), 4.17 (d, \(J\) = 4.0 Hz, 1H, CH), 4.89 (d, \(J\) = 5.5 Hz, 1H, CH), 6.64-7.56 (m, 4H, ArH). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 168.9, 144.5 (q, CF\(_3\), \(J\)\(_{CF}\) = 34 Hz), 141.0, 136.3, 131.0, 129.5, 120.5 (q, CF\(_3\), \(J\)\(_{CF}\) = 276 Hz), 118.7, 118.4, 117.4, 54.9, 53.0, 52.8, 32.7, 31.6, 29.0, 26.0, 22.6, 14.0. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -71.26 (s, CF\(_3\)). ESI-MS (m/z): 370 (M\(^+\)).

6j

cis-Methyl 2-cyclohexyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6j: Yellow solid. Yield: 68%. M.p.: 126.6~127.2°C. Anal. Calcd. for C\(_{18}\)H\(_{21}\)F\(_3\)N\(_2\)O\(_2\): C, 61.01; H, 5.97; N, 7.91. Found: C, 61.30; H, 6.01; N, 8.01. IR (KBr, cm\(^{-1}\)): \(\nu\) 1735 (C=O); 2960 (C-H); 3060 (Ar-H); 3403 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 0.88-1.76 (m, 11H, C\(_6\)H\(_{11}\)), 2.10 (dd, \(J_1\) = 4.0, \(J_2\) = 3.5, 1H, CH), 3.62 (s, 3H, CH\(_3\)), 4.39 (d, \(J\) = 4.0 Hz, 1H, CH), 4.90 (d, \(J\) = 3.5 Hz, 1H, CH), 6.64-7.54 (m, 4H, ArH). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 169.6, 144.8 (q, CF\(_3\), \(J\)\(_{CF}\) = 34 Hz), 141.0, 136.3, 131.0, 129.5, 120.5 (q, CF\(_3\), \(J\)\(_{CF}\) = 276 Hz), 118.7, 118.4, 117.4, 54.9, 53.0, 52.8, 32.7, 31.6, 29.0, 26.0, 22.6, 14.0. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -70.65 (s, CF\(_3\)). ESI-MS (m/z): 354 (M\(^+\)).

6k

cis-Methyl 2-(naphthalen-1-yl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6k: Yellow solid. Yield: 85%. M.p.: 204.3~206.4°C. Anal. Calcd. for C\(_{22}\)H\(_{17}\)F\(_3\)N\(_2\)O\(_2\):
C, 66.33; H, 4.30; N, 7.03. Found: C, 66.07; H, 4.04; N, 7.15. IR (KBr, cm\(^{-1}\)): \(v\) 1739 (C=O); 2960 (C-H); 3059 (Ar-H); 3405 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 3.57 (s, 3H, OCH\(_3\)), 4.51 (d, \(J = 3.5\) Hz, 1H, CH), 4.76 (d, \(J = 6.0\) Hz, 1H, NH), 6.39 (dd, \(J_1 = 6.0\) Hz, \(J_2 = 3.5\) Hz, 1H, CH), 6.81-7.80 (m, 11H, ArH). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 167.8, 147.1 (q, CF\(_3\), \(J_{C-F} = 34\) Hz), 143.7, 138.8, 134.9, 134.8, 131.1, 130.4, 130.1, 129.4, 127.8, 126.7, 126.1, 124.6, 122.5, 120.9 (q, CF\(_3\), \(J_{C-F} = 275\) Hz), 119.3, 118.5, 60.3, 53.5, 20.8. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -71.39 (s, CF\(_3\)). ESI-MS (m/z): 398 (M\(^+\)).

\[\text{cis-Methyl 2-(furan-2-yl)-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6l:}\]
Yellow solid. Yield: 81%. M.p.: 88.1-89.7\(^\circ\)C. Anal. Calcd. for C\(_{16}\)H\(_{13}\)F\(_3\)N\(_2\)O\(_3\): C, 56.81; H, 3.87; N, 8.37. IR (KBr, cm\(^{-1}\)): \(v\) 1730 (C=O); 2959 (C-H); 3034 (Ar-H); 3412 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 3.65 (s, 3H, OCH\(_3\)), 4.66 (d, \(J = 4.0\) Hz, 1H, CH), 5.04 (d, \(J = 5.5\) Hz, 1H, NH), 5.33 (dd, \(J_1 = 5.5\) Hz, \(J_2 = 4.0\) Hz, 1H, CH), 5.92 (d, \(J_2 = 1.5\) Hz, 1H, Furan-H), 6.15 (dd, \(J_1 = 4\) Hz, \(J_2 = 1.5\) Hz, 1H, Furan-H), 6.72-7.47 (m, 4H, ArH), 7.46 (d, \(J = 4\) Hz, 1H, Furan-H). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 168.1, 151.9, 145.7 (q, CF\(_3\), \(J_{C-F} = 34\) Hz), 142.3, 141.1, 135.9, 131.1, 128.8, 120.4 (q, CF\(_3\), \(J_{C-F} = 275\) Hz), 119.7, 118.5, 113.1, 110.6, 107.4, 53.4, 52.6. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -71.40 (s, CF\(_3\)). ESI-MS (m/z): 338 (M\(^+\)).

\[\text{methyl 2-(4-methoxyphenyl)-7,8-dimethyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6m:}\]
Yellow solid. Yield: 62%. M.p.: 153.8-156.3\(^\circ\)C. Anal. Calcd. for C\(_{21}\)H\(_{21}\)F\(_3\)N\(_2\)O\(_3\): C, 62.06; H, 5.21; N, 6.89. IR (KBr, cm\(^{-1}\)): \(v\) 1747 (C=O); 2953 (C-H); 3038 (Ar-H); 3393 (N-H). 1H NMR (CDCl\(_3\), ppm): \(\delta\) 2.14 (s, 3H, CH\(_3\)), 2.18 (s, 3H, CH\(_3\)), 3.59 (s, 3H, OCH\(_3\)), 3.70 (s, 3H, OCH\(_3\)), 4.46 (d, \(J = 4.5\) Hz, 1H, CH), 4.87 (d, \(J = 5.5\) Hz, 1H, NH), 5.28 (dd, \(J_1 = 4.5\) Hz, \(J_2 = 5.5\) Hz, 1H, CH), 6.51-7.21 (m, 6H, ArH). 13C NMR (CDCl\(_3\), ppm): \(\delta\) 168.1, 159.0, 145.2 (q, CF\(_3\), \(J_{C-F} = 34\) Hz), 140.2, 139.3, 135.4, 133.1, 128.0, 127.2, 126.8, 120.2 (q, CF\(_3\), \(J_{C-F} = 276\) Hz), 118.9, 114.0, 59.0, 55.2, 54.8, 52.9, 19.6, 18.3. 19F NMR (CDCl\(_3\), ppm): \(\delta\) -71.24 (s, CF\(_3\)). ESI-MS (m/z): 406 (M\(^+\)).
**6n**

Methyl 7,8-dichloro-2-(4-methoxyphenyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6n: Yellow oil. Yield: 60%. Anal. Calcd. for C_{19}H_{15}Cl_2F_3N_2O_3: C, 51.03; H, 3.38; N, 6.26. Found: C, 51.22; H, 3.40; N, 6.28. IR (KBr, cm^{-1}): v 1738 (C=O); 2956 (C-H); 3064 (Ar-H); 3392 (N-H). 1H NMR (CDCl_3, ppm): δ 3.63 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 4.52 (d, J = 5.0 Hz, 1H, CH), 5.31 (dd, J_1 = 5.0 Hz, J_2 = 5.5 Hz, 1H, CH), 5.41 (br-s, 1H, NH), 6.76-7.53 (m, 6H, ArH). 13C NMR (CDCl_3, ppm): δ 167.6, 159.4, 148.2, 141.2, 136.1, 132.2, 130.6, 129.3, 126.7, 121.4, 119.8, 118.9, 114.4, 60.6, 58.9, 55.4, 53.3, 21.2, 14.3. 19F NMR (CDCl_3, ppm): δ -71.79 (s, CF_3). ESI-MS (m/z): 446 (M^+).

![Chemical Structure Image]

**6o**

cis-Methyl 2-(4-nitrophenyl)-4-(pentafluoroethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6o: Yellow solid. Yield: 31%. M.p.: 150.4~151.1 °C. Anal. Calcd. for C_{19}H_{14}F_5N_3O_4: C, 51.48; H, 3.18; N, 9.48. Found: C, 51.24; H, 3.34; N, 9.57. IR (KBr, cm^{-1}): v 1741 (C=O); 2956 (C-H); 3080 (Ar-H); 3421 (N-H). 1H NMR (CDCl_3, ppm): δ 3.59 (s, 3H, OCH_3), 4.53 (d, J = 4.5 Hz, 1H, CH), 5.03 (d, J = 6.5 Hz, 1H, NH), 5.66 (dd, J_1 = 6.5 Hz, J_2 = 4.5 Hz, 1H, CH), 6.82-8.14 (m, 8H, ArH). 13C NMR (CDCl_3, ppm): δ 167.4, 148.2, 147.5, 147.2, 146.9, 140.4, 134.9, 131.2, 130.6, 126.9, 124.1, 120.0, 119.7, 118.3, 118.2 (qt, CF_3), 61.3, 53.9, 53.3. 19F NMR (CDCl_3, ppm): δ -80.77 (s, CF_3), -114.19 (m, CF_2). ESI-MS (m/z): 443 (M^+).

![Chemical Structure Image]

**6p**

cis-Methyl 4-(pentafluoroethyl)-2-p-tolyl-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6p: Yellow solid. Yield: 61%. M.p.: 109.6~112.2 °C. Anal. Calcd. for C_{20}H_{17}F_5N_2O_2: C, 58.25; H, 4.16; N, 6.79. Found: C, 58.34; H, 4.34; N, 6.81. IR (KBr, cm^{-1}): v 1720 (C=O); 2955 (C-H); 3037 (Ar-H); 3381 (N-H). 1H NMR (CDCl_3, ppm): δ 2.27 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 4.51 (d, J = 4.5 Hz, 1H, CH), 4.95 (d, J = 6.0 Hz, 1H, NH), 5.41 (dd, J_1 = 6.0 Hz, J_2 = 4.5 Hz, 1H, CH), 6.72-7.42 (m, 8H, ArH). 13C NMR (CDCl_3, ppm): δ 168.1, 147.5, 147.2, 141.5, 138.1, 137.7, 135.2, 130.8, 129.4, 125.6, 122.5, 119.6, 118.9, 118.1, 118.8 (qt, CF_3), 19F NMR (CDCl_3, ppm): δ -80.78 (s, CF_3), -114.14 (m, CF_2). ESI-MS (m/z): 412 (M^+).
cis-Methyl 2-(4-methoxyphenyl)-4-(pentafluoroethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6q: Yellow solid. Yield: 51%. M.p.: 100.3~103.3℃. Anal. Calcd. for C_{20}H_{17}F_{5}N_{2}O_{3}: C, 56.08; H, 4.00; N, 6.54. Found: C, 56.26; H, 4.22; N, 6.58. IR (KBr, cm⁻¹): ν 1728 (C=O); 2957 (C-H); 3076 (Ar-H); 3335 (N-H). ¹H NMR (CDCl₃, ppm): δ 3.58 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 4.47 (d, J = 5.0 Hz, 1H, CH), 4.96 (d, J = 6.0 Hz, 1H, NH), 5.40 (dd, J₁ = 6.0 Hz, J₂ = 5.0 Hz, 1H, CH), 6.73-7.43 (m, 8H, ArH). ¹³C NMR (CDCl₃, ppm): δ 168.1, 159.2, 147.6, 147.4, 141.4, 135.1, 133.3, 130.8, 126.9, 125.6, 124.1, 118.9, 118.8 (qt, CF₃, J_C-F = 259 Hz, J_C-F = 36 Hz), 118.2, 110.4 (m, CF₂), 60.4, 55.3, 54.8, 52.9. ¹⁹F NMR (CDCl₃, ppm): δ -80.79 (s, CF₃), -114.16 (m, CF₂). ESI-MS (m/z): 428 (M⁺).

cis-Methyl 2-(4-bromophenyl)-4-(pentafluoroethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6r: Yellow solid. Yield: 71%. M.p.: 113.0~114.2℃. Anal. Calcd. for C_{19}H_{14}BrF₅N₂O₂: C, 47.82; H, 2.96; N, 5.87. Found: C, 47.96; H, 3.02; N, 5.96. IR (KBr, cm⁻¹): ν 1724 (C=O); 2953 (C-H); 3096 (Ar-H); 3340 (N-H). ¹H NMR (CDCl₃, ppm): δ 3.55 (s, 3H, OCH₃), 4.49 (d, J = 4.5 Hz, 1H, CH), 5.07 (d, J = 6.5 Hz, 1H, NH), 5.42 (dd, J₁ = 6.5 Hz, J₂ = 4.5 Hz, 1H, CH), 6.73-7.41 (m, 8H, ArH). ¹³C NMR (CDCl₃, ppm): δ 167.8, 147.4, 147.2, 140.5, 135.0, 131.9, 130.7, 128.7, 128.4, 127.5, 127.2, 126.1, 120.1, 118.7 (qt, CF₃), J_C-F = 285 Hz, J_C-F = 36 Hz), 118.2, 110.4 (m, CF₂), 60.6, 54.2, 53.1. ¹⁹F NMR (CDCl₃, ppm): δ -80.73 (s, CF₃), -114.10 (m, CF₂). ESI-MS (m/z): 476 (M⁺).

cis-Methyl 2-(naphthalen-1-yl)-4-(n-heptafluoropropyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6s: Yellow solid. Yield: 74%. M.p.: 129.5~130.0℃. Anal. Calcd. for C_{24}H_{17}F₇N₂O₂: C, 57.84; H, 3.44; N, 5.62. Found: C, 57.99; H, 3.67; N, 5.76. IR (KBr, cm⁻¹): ν 1728 (C=O); 2956 (C-H); 3063 (Ar-H); 3381 (N-H). ¹H-NMR (CDCl₃, ppm): δ 3.58 (s, 3H, OCH₃), 4.75 (d, J = 4.5 Hz, 1H, CH), 4.99 (d, J = 6.0 Hz, 1H, NH), 6.35 (dd, J₁ = 6.0 Hz, J₂ = 4.5 Hz, 1H, CH), 6.76-8.04 (m, 11H, ArH). ¹³C NMR (CDCl₃, ppm): δ 168.0, 149.0, 141.4, 137.3, 136.9, 134.6, 133.8, 131.2, 130.3, 129.6, 129.1, 127.3, 126.0, 125.5, 124.2, 123.4, 121.6, 120.2 (qt, CF₃), J_C-F = 286 Hz, J_C-F = 35 Hz), 119.6, 118.5, 110.4 (m, CF₂), 108.7 (m, CF₂), 61.3, 52.9. ¹⁹F NMR (CDCl₃, ppm): δ -79.65 (t, J = 9.4 Hz, CF₃), -112.95 (m, CF₂), -125.08 (m, CF₂). ESI-MS (m/z): 498 (M⁺).
cis-Methyl 2-(4-bromophenyl)-4-(n-heptafluoropropyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6t: Yellow oil. Yield: 70%. Anal. Calcd. for C$_{20}$H$_{14}$BrF$_7$N$_2$O$_2$: C, 45.56; H, 2.68; N, 5.31. Found: C, 45.87; H, 2.88; N, 5.45. IR (KBr, cm$^{-1}$): v 1753 (C=O); 2960 (C-H); 3097 (Ar-H); 3345 (N-H). $^1$H NMR (CDCl$_3$, ppm): δ 3.50 (s, 3H, OCH$_3$), 4.53 (d, $J$ = 4.5 Hz, 1H, CH), 5.28 (d, $J$ = 6.5 Hz, 1H, NH), 5.39 (dd, $J_1 = 6.5$ Hz, $J_2 = 4.5$ Hz, 1H, CH), 6.71-7.41 (m, 8H, ArH). $^{13}$C NMR (CDCl$_3$, ppm): δ 167.7, 147.5, 147.2, 141.2, 140.3, 134.9, 131.6, 131.0, 130.5, 128.7, 127.5, 118.8, 117.9, 115.5 (qt, CF$_3$, $^1$J$_{C-F}$ = 303 Hz, $^2$J$_{C-F}$ = 36 Hz), 113.6, 110.6 (m, CF$_2$), 109.5 (m, CF$_2$), 60.5, 54.7, 52.9. $^{19}$F NMR (CDCl$_3$, ppm): δ -79.67 (t, $^1$J$_{C-F}$ = 9.4 Hz, CF$_3$), -111.78 (m, CF$_2$), -124.64 (m, CF$_2$). ESI-MS (m/z): 526 (M$^+$).

Methyl 2-(4-methoxyphenyl)-6-methyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6u and Methyl 2-(4-methoxyphenyl)-9-methyl-4-(trifluoromethyl)-2,3-dihydro-1H-benzo[b][1,4]diazepine-3-carboxylate 6u': Yellow oil. Yield: 64%. Anal. Calcd. for C$_{20}$H$_{19}$F$_3$N$_2$O$_3$: C, 61.22; H, 4.88; N, 7.14. IR (KBr, cm$^{-1}$): v 1739 (C=O); 2956 (C-H); 3003 (Ar-H). $^1$H NMR (CDCl$_3$, ppm): δ 2.38 (s, 3H, CH$_3$), 3.53 (s, 3H, OCH$_3$), 3.77 (s, 3H, OCH$_3$), 4.17 (d, $J$ = 4.5 Hz, 1H, CH), 4.36 (br-s, 1H, NH), 5.46 (dd, $J_1 = 5$ Hz, $J_2 = 4.5$ Hz, 1H, CH), 6.60-7.35 (m, 7H, ArH). $^1$H NMR (CDCl$_3$, ppm): δ 2.26 (s, 1H, CH$_3$), 3.58 (s, 1H, OCH$_3$), 3.74 (s, 1H, OCH$_3$), 4.46 (d, $J$ = 4.5 Hz, 0.3H, CH), 4.74 (d, $J$ = 5.5 Hz, 0.3H, NH), 5.50 (dd, $J_1 = 4.5$ Hz, $J_2 = 5.5$ Hz, 0.3H, CH), 6.60-7.35 (m, 2.1H, ArH). $^{13}$C NMR (CDCl$_3$, ppm): δ 168.3, 168.2, 159.4, 159.3, 148.4 (q, CF$_3$, $^2$J$_{C-F}$ = 35 Hz), 147.0 (q, CF$_3$, $^2$J$_{C-F}$ = 34 Hz), 140.7, 140.3, 139.7, 133.5, 133.2, 132.2, 131.8, 131.5, 131.1, 129.8, 127.9, 127.4, 126.9, 124.6, 122.4, 120.1 (q, CF$_3$, $^1$J$_{C-F}$ = 276 Hz), 117.6, 114.5, 114.3, 114.2, 60.9, 60.6, 55.4, 55.3, 54.7, 54.2, 53.0, 52.9, 21.2, 19.2, 18.4, 14.4. $^{19}$F NMR (CDCl$_3$, ppm): δ -71.25 (t, $^1$J$_{C-F}$ = 9.4 Hz, CF$_3$), -111.78 (m, CF$_2$), -124.64 (m, CF$_2$). ESI-MS (m/z): 392 (M$^+$).
6d
6i
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