Supplementary Information

Synthesis of Chiral Tertiary Trifluoromethyl Alcohols by Asymmetric Nitroaldol Reaction with a Cu(II)-Bisoxazolidine Catalyst

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All commercially available reagents and solvents were used without further purification and all reactions were carried out under nitrogen. Anhydrous tetrahydrofuran was used as purchased and not dried any further. Trifluoromethyl ketones were purified by silica gel column chromatography prior to use. Flash chromatography was performed on Kieselgel 60, particle size 0.032-0.063 mm. NMR spectra were obtained at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) using $CDCl_3$ as solvent unless noted otherwise. Chemical shifts are reported in ppm relative to TMS.

General procedure for the Henry reaction of trifluoromethyl ketones

A solution of the bisoxazolidine ligand (37.0 mg, 0.10 mmol) and $Cu(OTf)_2$ (36.8mg, 0.10 mmol) in anhydrous THF (0.35mL) was stirred under nitrogen atmosphere at room temperature for 30 minutes. Then, nitromethane (610.0 mg, 10 mmol) was added, and the solution was stirred for an additional 30 minutes. This solution was transferred to a double-jacketed flask and cooled to -10 ^{o}C. After 10 minutes, tributylamine (37.0 mg, 0.20 mmol) was added followed by the addition of the freshly purified trifluoromethyl ketone (1.0 mmol). Upon completion, the reaction mixture was directly loaded on a silica gel column and purified by flash chromatography as described below.

Product purification and characterization

(*S*)-1,1,1-Trifluoro-3-nitro-2-phenylpropan-2-ol, **2**.[1]

Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 216.0 mg of a colorless oil (0.92 mmol, 92%, 86% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.61 (s, 1H), 4.98 (d, J = 13.6 Hz, 1H), 5.07 (d, J = 13.6 Hz, 1H), 7.40-7.44 (m, 3H), 7.56-7.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.2 (q, $J_{C\text{-}F}$ = 29.8 Hz), 77.5, 123.4 (q, $J_{C\text{-}F}$ = 284.6 Hz), 126.1, 128.9, 130.0, 133.0. The ee was determined by HPLC on a Daicel Chiralcel OJ column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 46.2 min, t_2 (minor) = 55.2 min, α = 1.21.

(*S*)-2-(4-Chlorophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **3**.[2]
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 245.0 mg of a colorless oil (0.91 mmol, 91%, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.65 (s, 1H), 4.99 (d, J = 13.6 Hz, 1H), 5.06 (d, J = 13.6 Hz, 1H), 7.42 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0 (q, $J_{C\text{-}F}$ = 29.9 Hz), 77.3, 123.2 (q, $J_{C\text{-}F}$ = 284.6 Hz), 127.6, 129.2, 131.4, 136.4. The ee was determined by HPLC on a Daicel Chiralcel OJ column using hexanes:IPA (93:7) as the mobile phase, t_1 (major) = 26.2 min, t_2 (minor) = 32.7 min, α = 1.29.

(*S*)-2-(4-Bromophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **4**.[2]
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 279.6 mg of a colorless oil (0.89 mmol, 89%, 80% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63 (s, 1H), 4.98 (d, J = 13.6 Hz, 1H), 5.05 (d, J = 13.6 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0 (q, $J_{C\text{-}F}$ = 29.8 Hz), 77.2, 123.1 (q, $J_{C\text{-}F}$ = 284.6 Hz), 124.6, 127.9, 132.0, 132.2. The ee was determined by HPLC on a Daicel Chiralcel OJ column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 20.1 min, t_2 (minor) = 25.4 min, α = 1.33.

(*S*)-1,1,1-Trifluoro-2-(4-fluorophenyl)-3-nitropropan-2-ol, **5**.[1]
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 235.5 mg of white crystals (0.93 mmol, 93%, 83% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.67 (s, 1H), 5.00 (d, J = 13.6 Hz, 1H), 5.07 (d, J = 13.6 Hz, 1H), 7.12 (t, J = 8.4 Hz, 2H), 7.58 (dd, J = 8.4, 5.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0 (q, $J_{C\text{-}F}$ = 29.9 Hz), 77.4, 116.0 (d, $J_{C\text{-}F}$ = 21.8 Hz), 123.3 (q, $J_{C\text{-}F}$ = 284.0 Hz), 128.3 (dd, $J_{C\text{-}F}$ = 8.6, 1.1 Hz), 128.7 (d, $J_{C\text{-}F}$ = 3.3 Hz), 163.5 (d, $J_{C\text{-}F}$ = 249.2 Hz). The ee was determined by HPLC on a Daicel Chiralcel OJ column using hexanes:IPA (94:6) as the mobile phase, t_1 (major) = 38.6 min, t_2 (minor) = 44.9 min, α = 1.18.

(*S*)-1,1,1-Trifluoro-3-nitro-2-(4-(trifluoromethyl)phenyl)propan-2-ol, **6**.
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 276.1 mg of a colorless oil (0.91 mmol, 91%, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.77 (s, 1H), 5.04 (d, J = 13.6 Hz, 1H), 5.11 (d, J = 13.6 Hz, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0 (q, $J_{C\text{-}F}$ = 29.9 Hz), 77.2, 123.1 (q, $J_{C\text{-}F}$ = 284.8 Hz), 123.5 (q, $J_{C\text{-}F}$ = 271.4 Hz), 125.9 (q, $J_{C\text{-}F}$ = 3.7 Hz), 126.8, 132.3 (q, $J_{C\text{-}F}$ = 32.8 Hz), 136.8. Anal. calcd. for $C_{10}H_7F_6NO_3$: C, 39.62; H, 2.33; N, 4.62. Found: C, 39.32; H, 2.46; N, 4.45. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 13.0 min, t_2 (minor) = 14.9 min, α = 1.21.

(*S*)-2-(4-*tert*-Butylphenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **7**.[1]
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 276.9 mg of white crystals (0.95 mmol, 95%, 86% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 9H), 4.60 (s, 1H), 4.98 (d, J = 13.6 Hz, 1H), 5.06 (d, J = 13.6 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.1, 34.6, 76.2 (q, $J_{C\text{-}F}$ = 29.7 Hz), 77.5,

123.5 (q, J_{C-F} = 284.5 Hz), 125.8, 125.9, 129.9, 153.1. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 9.8 min, t_2 (minor) = 19.4 min, α = 2.62.

(*S*)-1,1,1-Trifluoro-2-(4-methoxyphenyl)-3-nitropropan-2-ol, **8**.
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 228.2 mg of a colorless oil (0.86 mmol, 86%, 76% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H), 4.59 (s, 1H), 4.96 (d, *J* = 13.6 Hz, 1H), 5.06 (d, *J* = 13.6 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2, 76.1 (q, J_{C-F} = 29.7 Hz), 77.5, 114.3, 123.5 (q, J_{C-F} = 284.5 Hz), 124.7, 127.5, 160.7. Anal. calcd. for $C_{10}H_{10}F_3NO_4$: C, 45.29; H, 3.80; N, 5.28. Found: C, 44.95; H, 3.86; N, 5.03. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 28.8 min, t_2 (minor) = 32.1 min, α = 1.13.

(*S*)-1,1,1-Trifluoro-2-(4-methylthiophenyl)-3-nitropropan-2-ol, **9**.
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 253.3 mg of a colorless oil (0.90 mmol, 90%, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 4.58 (s, 1H), 4.96 (d, *J* = 13.6 Hz, 1H), 5.05 (d, *J* = 13.6 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.0, 76.1 (q, J_{C-F} = 29.8 Hz), 77.4, 123.4 (q, J_{C-F} = 284.5 Hz), 126.1, 126.5, 129.2, 141.5. Anal. calcd. for $C_{10}H_{10}F_3NO_3S$: C, 42.70; H, 3.58; N, 4.98. Found: C, 42.42; H, 3.67; N, 4.86. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 23.2 min, t_2 (minor) = 33.8 min, α = 1.55.

(*S*)-Ethyl 4-(1,1,1-trifluoro-2-hydroxy-3-nitro-2-propyl)benzoate, **10**.
Purification by flash chromatography (hexanes:ethyl acetate=8:2) gave 289.0 mg of a colorless oil (0.94 mmol, 94%, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, *J* = 7.2 Hz, 3H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.96 (s, 1H), 5.10 (d, *J* = 13.6 Hz, 1H), 5.14 (d, *J* = 13.6 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 61.4, 76.2 (q, J_{C-F} = 29.8 Hz), 77.4, 123.3 (q, J_{C-F} = 285.0 Hz), 126.4, 129.9, 131.9, 137.6, 165.9. Anal. calcd. for $C_{12}H_{12}F_3NO_5$: C, 46.91; H, 3.94; N, 4.56. Found: C, 46.57; H, 3.87; N, 4.62. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (93:7) as the mobile phase, t_1 (major) = 22.8 min, t_2 (minor) = 25.8 min, α = 1.16.

(*S*)-1,1,1-Trifluoro-3-nitro-2-(3-tolyl)propan-2-ol, **11**.
Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 226.8 mg of a colorless oil (0.91 mmol, 91%, 80% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H), 4.58 (s, 1H), 4.97 (d, *J* = 13.6 Hz, 1H), 5.06 (d, *J* = 13.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.28-7.36 (m, 2H), 7.40 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 76.2 (q, J_{C-F} = 29.7 Hz), 77.5, 123.1, 123.4 (q, J_{C-F} = 284.5 Hz), 126.7, 128.8, 130.7, 132.9, 138.9. Anal. calcd. for $C_{10}H_{10}F_3NO_3$: C, 48.20; H, 4.04; N, 5.62. Found: C, 47.83; H, 3.97; N, 5.76. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 11.8 min, t_2 (minor) = 18.9 min, α = 1.90.

(*S*)-4-(1,1,1-Trifluoro-2-hydroxy-3-nitro-2-propyl)benzonitrile, **12**.
Purification by flash chromatography (hexanes:ethyl acetate=8:2) gave 239.5 mg of white crystals (0.92 mmol, 92%, 75% ee). ^{1}H NMR (400 MHz, CD_3OD): δ 4.83 (s, 1H), 5.17 (d, *J* = 12.8 Hz, 1H), 5.50 (d, *J* = 12.8 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, CD_3OD): δ 75.8 (q, J_{C-F} = 29.9 Hz), 77.5, 112.7, 117.9, 124.0 (q, J_{C-F} = 285.9 Hz), 127.6, 131.8, 139.6. Anal. calcd. for $C_{10}H_7F_3N_2O_3$: C, 46.16; H, 2.71; N, 10.77. Found: C, 45.79; H, 2.87; N, 10.54. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (95:5) as the mobile phase, t_1 (major) = 67.3 min, t_2 (minor) = 73.7 min, α = 1.10.

(*S*)-2-Benzyl-1,1,1-trifluoro-3-nitropropan-2-ol, **13**.[1]
Purification by flash chromatography (hexanes:ethyl acetate=10:1) gave 216.9 mg of a colorless oil (0.87 mmol, 87%, 88% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92 (d, *J* = 14.4 Hz, 1H), 3.28 (d, *J* = 14.4 Hz, 1H), 4.22 (d, *J* = 13.2 Hz, 1H), 4.29 (s, 1 H), 4.63 (d, *J* = 13.2 Hz, 1H), 7.25-7.29 (m, 2H), 7.31-7.38 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 38.3, 74.8 (q, J_{C-F} = 28.6 Hz), 75.8, 124.5 (q, J_{C-F} = 286.0 Hz), 128.1, 128.8, 130.8, 132.0. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 10.9 min, t_2 (minor) = 14.0 min, α = 1.44.

(*S*)-1,1,1-Trifluoro-2-(nitromethyl)hexan-2-ol, **14**.
Purification by flash chromatography (CH_2Cl_2) gave 174.5 mg of a colorless oil (0.81 mmol, 81%, 80% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (t, *J* = 7.2 Hz, 3H), 1.26-1.43 (m, 3H), 1.52 (m, 1H), 1.66-1.95 (m, 2H), 3.97 (s, 1 H), 4.58 (d, *J* = 12.8 Hz, 1H), 4.67 (d, *J* = 12.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 22.7, 24.3, 32.6, 74.7 (q, J_{C-F} = 28.8 Hz), 76.3, 124.5 (q, J_{C-F} = 285.6 Hz). Anal. calcd. for $C_7H_{12}F_3NO_3$: C, 39.07; H, 5.62; N, 6.51. Found: C, 39.22; H, 5.47; N, 6.43. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (95:5) as the mobile phase, t_1 (major) = 8.9 min, t_2 (minor) = 10.3 min, α = 1.28.

(*S*)-3-Cyclohexyl-1,1,1-trifluoro-2-(nitromethyl)propan-2-ol, **15**.
Purification by flash chromatography (hexanes:CH_2Cl_2=3:1) gave 227.3 mg of a colorless oil (0.89 mmol, 89%, 91% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95-1.12 (m, 2H), 1.12-1.35 (m, 3H), 1.48-1.60 (m, 2H), 1.61-1.82 (m, 5H), 1.84-1.94 (m, 1H), 4.09 (s, 1 H), 4.60 (d, *J* = 12.8 Hz, 1H), 4.67 (d, *J* = 12.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.8, 26.0, 26.1, 32.4, 34.5, 34.9, 39.4, 75.2 (q, J_{C-F} = 28.5 Hz), 76.5, 124.5 (q, J_{C-F} = 285.8 Hz). Anal. calcd. for $C_{10}H_{16}F_3NO_3$: C, 47.06; H, 6.32; N, 5.49. Found: C, 46.83; H, 6.37; N, 5.54. The ee was determined by HPLC on a Daicel Chiralpak AS column using hexanes:IPA (97:3) as the mobile phase, t_1 (minor) = 8.7 min, t_2 (major) = 10.3 min, α = 1.33.

(*S*)-Ethyl 6,6,6-trifluoro-5-hydroxy-5-(nitromethyl)hexanoate, **16**.
Purification by flash chromatography (CH_2Cl_2) gave 246.0 mg of a colorless oil (0.90 mmol, 90%, 82% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, *J* = 7.2 Hz, 3H), 1.70-2.05 (m, 4H), 2.35-2.45 (m, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.63 (d, *J* = 12.4 Hz, 1H), 4.64 (s, 1 H), 4.69 (d,

J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 17.4, 31.5, 33.6, 60.8, 74.5 (q, J_{C-F} = 28.9 Hz), 76.2, 124.5 (q, J_{C-F} = 285.6 Hz), 173.4. Anal. calcd. for $C_9H_{14}F_3NO_5$: C, 39.57; H, 5.17; N, 5.13. Found: C, 39.16; H, 5.32; N, 5.25. The ee was determined by HPLC on a Daicel Chiralcel OJ column using hexanes:IPA (98:2) as the mobile phase, t_1 (major) = 36.3 min, t_2 (minor) = 42.4 min, α = 1.19.

Procedure for Henry reaction of 1,1,1-trifluoroacetophenone with nitroethane

A solution of the bisoxazolidine ligand (37.0 mg, 0.10 mmol) and $Cu(OTf)_2$ (36.8mg, 0.10 mmol) in anhydrous THF (0.35mL) was stirred under nitrogen atmosphere at room temperature for 30 minutes. Then, nitroethane (751.0 mg, 10 mmol) was added, and the solution was stirred for an additional 30 minutes. This solution was transferred to a double-jacketed flask and cooled to -10 ^{o}C. After 10 minutes, tributylamine (37.0 mg, 0.20 mmol) was added followed by the addition of the freshly purified 1,1,1-trifluoroacetophenone (1.0 mmol). Upon completion, the reaction mixture was directly loaded on a silica gel column and purified by flash chromatography as described below.

(2*S*,3*R*)-1,1,1-Trifluoro-3-nitro-2-phenylbutan-2-ol, **17**.[3]

Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 222.0 mg of white crystals (0.89 mmol, 89%, 91% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (d, *J* = 7.2 Hz, 3H), 4.73 (s, 1H), 5.51 (q, *J* = 7.2 Hz, 1H), 7.38-7.49 (m, 3H), 7.55-7.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 77.7 (q, J_{C-F} = 29.1 Hz), 83.7, 124.3 (q, J_{C-F} = 286.4 Hz), 125.6, 128.9, 129.6, 132.7. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (98:2) as the mobile phase, t_1 (minor) = 8.9 min, t_2 (major) = 10.5 min, α = 1.32.

(2*S*,3*S*)-1,1,1-Trifluoro-3-nitro-2-phenylbutan-2-ol, **21**.[3]

Purification by flash chromatography (hexanes:ethyl acetate=9:1) gave 12.6 mg of white crystals (0.05 mmol, 5%, 16% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.90 (d, *J* = 6.8 Hz, 3H), 4.14 (s, 1H), 5.31 (q, *J* = 6.8 Hz, 1H), 7.36-7.45 (m, 3H), 7.53-7.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.4, 77.8 (q, J_{C-F} = 28.8 Hz), 85.5, 123.3 (q, J_{C-F} = 284.5 Hz), 125.8, 128.8, 129.8, 134.8. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (97:3) as the mobile phase, t_1 (minor) = 10.0 min, t_2 (major) = 11.2 min, α = 1.20.

(2*S*,3*R*)-2-(4-Chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **18**.

Purification by flash chromatography (hexanes:ethyl acetate=10:1) gave 250.1 mg of white crystals (0.88 mmol, 88%, 83% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (d, *J* = 6.8 Hz, 3H), 4.78 (s, 1H), 5.27 (q, *J* = 6.8 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 77.5 (q, J_{C-F} = 29.3 Hz), 83.4, 124.0 (q, J_{C-F} = 286.5 Hz), 127.2, 129.2, 131.3, 136.0. Anal. calcd. for $C_{10}H_9ClF_3NO_3$: C, 42.35; H, 3.20; N, 4.94. Found: C, 41.93; H, 3.11; N, 4.78. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (96:4) as the mobile phase, t_1 (minor) = 17.4 min, t_2 (major) = 19.7 min, α = 1.17.

(2*S*,3*S*)-2-(4-Chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **22**.

Purification by flash chromatography (hexanes:ethyl acetate=10:1) gave 14.5 mg of white crystals (0.05 mmol, 5 %, 30% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.90 (d, *J* = 6.8 Hz, 3H), 4.16 (s, 1H), 5.45 (q, *J* = 6.8 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H). ^{13}C

NMR (100 MHz, $CDCl_3$): δ 15.3, 77.6 (q, J_{C-F} = 29.1 Hz), 85.3, 123.1 (q, J_{C-F} = 284.6 Hz), 127.4, 129.1, 133.3, 136.02. Anal. calcd. for $C_{10}H_9ClF_3NO_3$: C, 42.35; H, 3.20; N, 4.94. Found: C, 41.93; H, 3.11; N, 4.78. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (93:7) as the mobile phase, t_1 (minor) = 10.5 min, t_2 (major) = 11.8 min, α = 1.20.

(2*S*,3*R*)-2-Benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol, **19**.

Purification by flash chromatography (hexanes:ethyl acetate=15:1) gave 200.3 mg of colorless oil (0.76 mmol, 76%, 78% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74 (d, *J* = 6.8 Hz, 3H), 3.09 (d, *J* = 14.8 Hz, 1H), 3.38 (d, *J* = 14.8 Hz, 1H), 3.41 (s, 1 H), 5.00 (q, *J* = 6.8 Hz, 1H), 7.21-7.27 (m, 2H), 7.30-7.37 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 36.0, 76.1 (q, J_{C-F} = 27.0 Hz), 83.8, 124.6 (q, J_{C-F} = 287.0 Hz), 128.0, 128.8, 130.8, 131.9. Anal. calcd. for $C_{11}H_{12}F_3NO_3$: C, 50.19; H, 4.60; N, 5.32. Found: C, 49.94; H, 4.56; N, 5.23. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (90:10) as the mobile phase, t_1 (major) = 14.3 min, t_2 (minor) = 23.0 min, α = 1.83.

(2*S*,3*S*)-2-Benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol, **23**.

Purification by flash chromatography (hexanes:ethyl acetate=15:1) gave 26.5 mg of colorless oil (0.10 mmol, 10%, 21% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.70 (d, *J* = 7.2 Hz, 3H), 3.03 (d, *J* = 14.4 Hz, 1H), 3.28 (d, *J* = 14.4 Hz, 1H), 4.21 (s, 1 H), 4.57 (q, *J* = 7.2 Hz, 1H), 7.20-7.26 (m, 2H), 7.31-7.37 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 37.9, 76.7 (q, J_{C-F} = 27.0 Hz), 83.8, 124.7 (q, J_{C-F} = 287.0 Hz), 128.0, 128.7, 130.9, 132.1. Anal. calcd. for $C_{11}H_{12}F_3NO_3$: C, 50.19; H, 4.60; N, 5.32. Found: C, 49.94; H, 4.56; N, 5.23. The ee was determined by HPLC on a Daicel Chiralcel OD column using hexanes:IPA (94:6) as the mobile phase, t_1 (minor) = 16.5 min, t_2 (major) = 17.6 min, α = 1.08.

(2*S*,3*R*)-2-(Cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **20**.

Purification by flash chromatography (hexanes:CH_2Cl_2=4:1) gave 199.4 mg of colorless oil (0.74 mmol, 74%, 81% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85-1.05 (m, 2H), 1.05-1.19 (m, 2H), 1.18-1.35 (m, 2H), 1.49-1.82 (m, 6H), 1.66 (d, *J* = 7.2 Hz, 3H), 1.88 (m, 1H), 3.83 (s, 1 H), 4.86 (q, *J* = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 25.9, 26.1, 26.2, 32.3, 34.8, 34.9, 38.6, 76.7 (q, J_{C-F} = 27.7 Hz), 84.2, 124.9 (q, J_{C-F} = 286.8 Hz). Anal. calcd. for $C_{11}H_{18}F_3NO_3$: C, 49.07; H, 6.74; N, 5.20. Found: C, 49.46; H, 6.86; N, 4.83. The ee was determined by HPLC on a Daicel Chiralpak AS column using hexanes:IPA (96:4) as the mobile phase, t_1 (minor) = 10.1 min, t_2 (major) = 12.3 min, α = 1.35.

(2*S*,3*S*)-2-(Cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **24**.

Purification by flash chromatography (hexanes:CH_2Cl_2=4:1) gave 21.7 mg of colorless oil (0.08 mmol, 8%, 26% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82-1.04 (m, 2H), 1.05-1.18 (m, 2H), 1.19-1.34 (m, 2H), 1.48-1.81 (m, 7H), 1.69 (d, *J* = 7.2 Hz, 3H), 1.90 (m, 1H), 3.92 (s, 1 H), 4.81 (q, *J* = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 25.9, 26.1, 26.2, 32.6, 34.9, 35.0, 39.9, 76.9 (q, J_{C-F} = 28.0 Hz), 85.0, 126.0 (q, J_{C-F} = 287.5 Hz). Anal. calcd. for $C_{11}H_{18}F_3NO_3$: C, 49.07; H, 6.74; N, 5.20. Found: C, 49.46; H, 6.86; N, 4.83. The ee was determined by HPLC on a Daicel Chiralpak AS column using hexanes:IPA (94:6) as the mobile phase, t_1 (minor) = 10.9 min, t_2 (major) = 13.5 min, α = 1.37.

Crystallographic Analysis of (2*S*,3*R*)-1,1,1-trifluoro-3-nitro-2-phenylbutan-2-ol, **17.**
Careful evaporation of a scalemic solution of **17** in diethyl ether gave a single crystal suitable for crystallographic analysis. Crystal structure data: $C_{10}H_{10}F_3NO_3$, M=249.19, colorless needle, 0.97 × 0.32 × 0.22 mm^3, monoclinic, space group $P2_1/n$ (No. 14), a = 12.8876(15) Å, b = 5.7106(7) Å, c = 14.2015(17) Å, α = 90.00°, β = 90.7800(10)°, γ = 90.00°, V = 1045.1(2) $Å^3$, Z = 4, D_c = 1.584 g/cm^3, F_{000} = 512, T = 100(2)K. Single crystal X-ray diffractions were performed at -100 ^oC using a Siemens platform diffractometer with graphite monochromated Mo-Ka radiation (λ = 0.71073 Å). Data were integrated with the Siemens SAINT program and corrected for the affects of absorption using SADABS. The structures were solved by direct methods and refined with full-matrix least square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameters and all hydrogen atoms were placed in calculated positions and refined with a riding model.

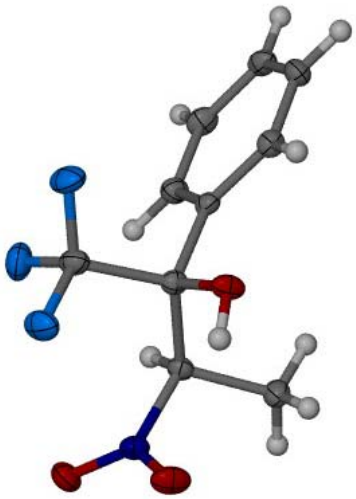
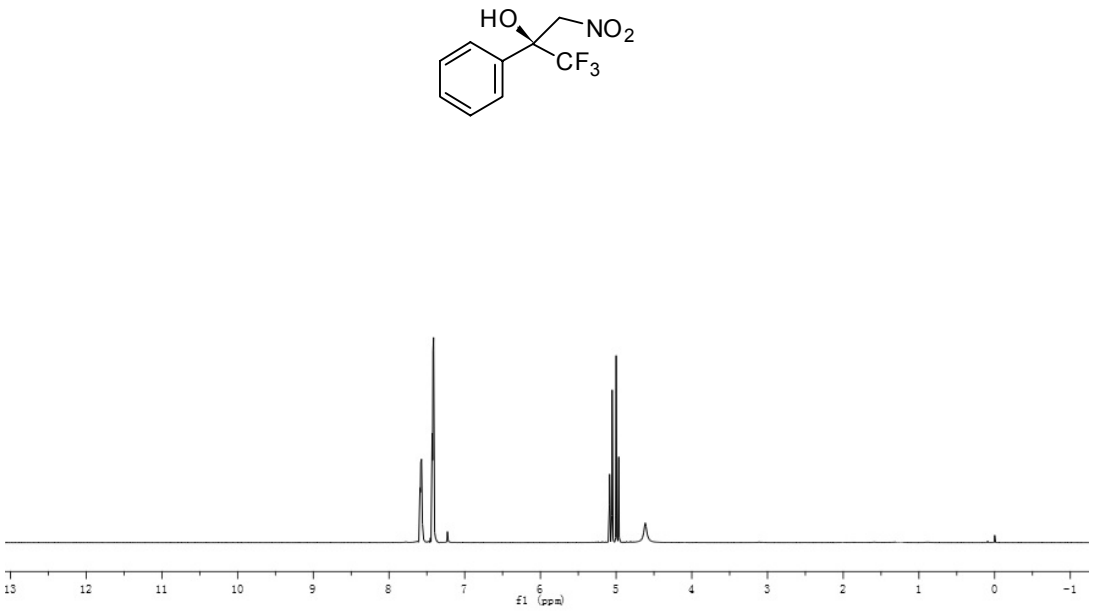


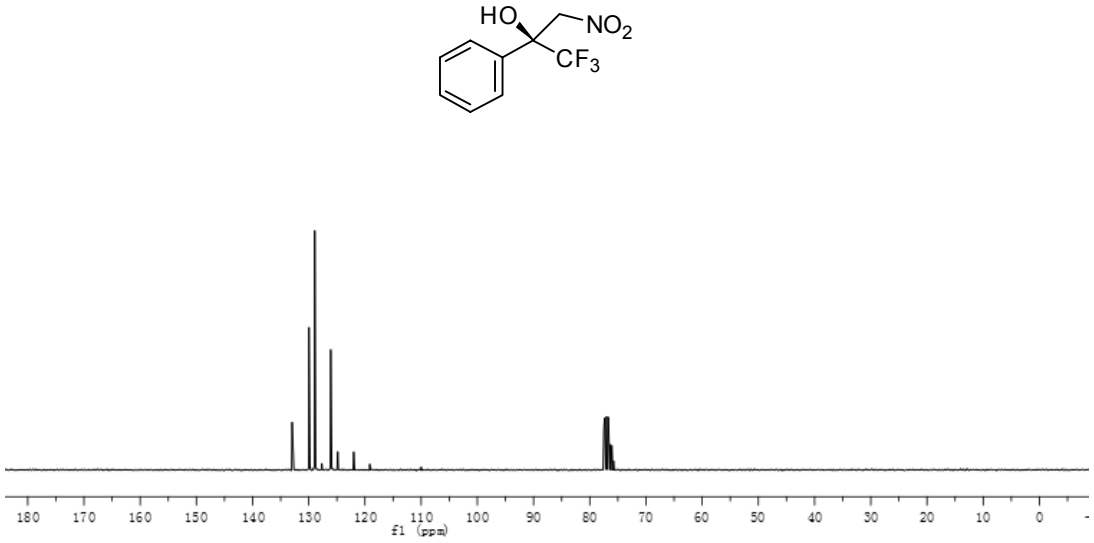
Figure 1. X-ray crystallographic structure of **17**. Ellipsoids drawn at the 50% probability level.

References

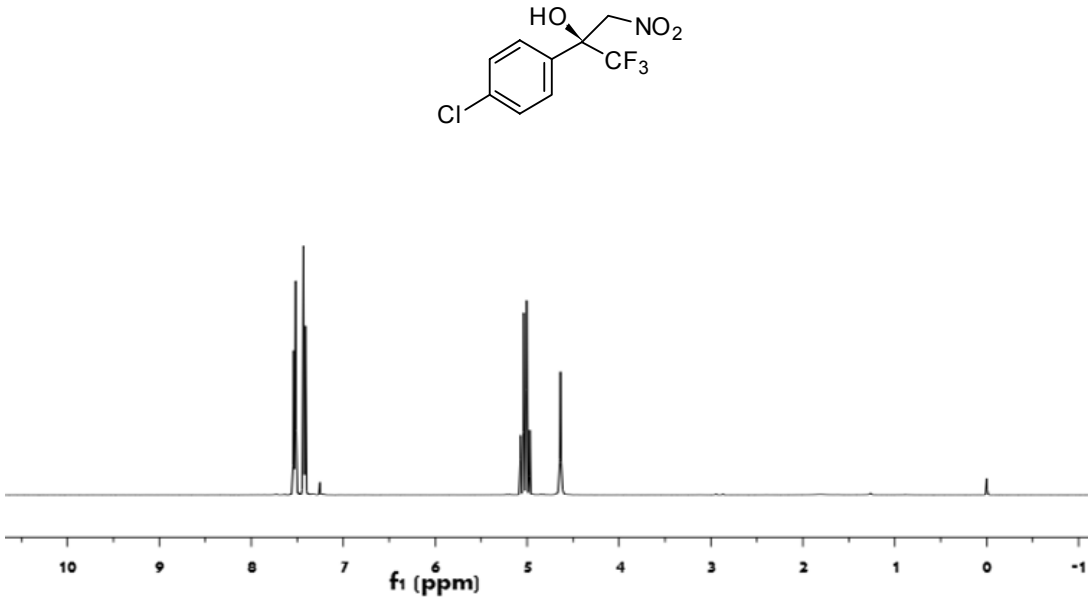
1. Tur, F.; Saá, J. M. *Org. Lett*. **2007**, *9*, 5079-5082.
2. Bandini, M.; Sinisi, R.; Umani-Ronchi, A. *Chem. Commun.* **2008**, 4360–4362.
3. Kingsbury, C. A.; Sopchik, A. E.; Underwood, G.; Rajan, S. *J. Chem. Soc., Perkin Trans.2* **1982**, 867-874.

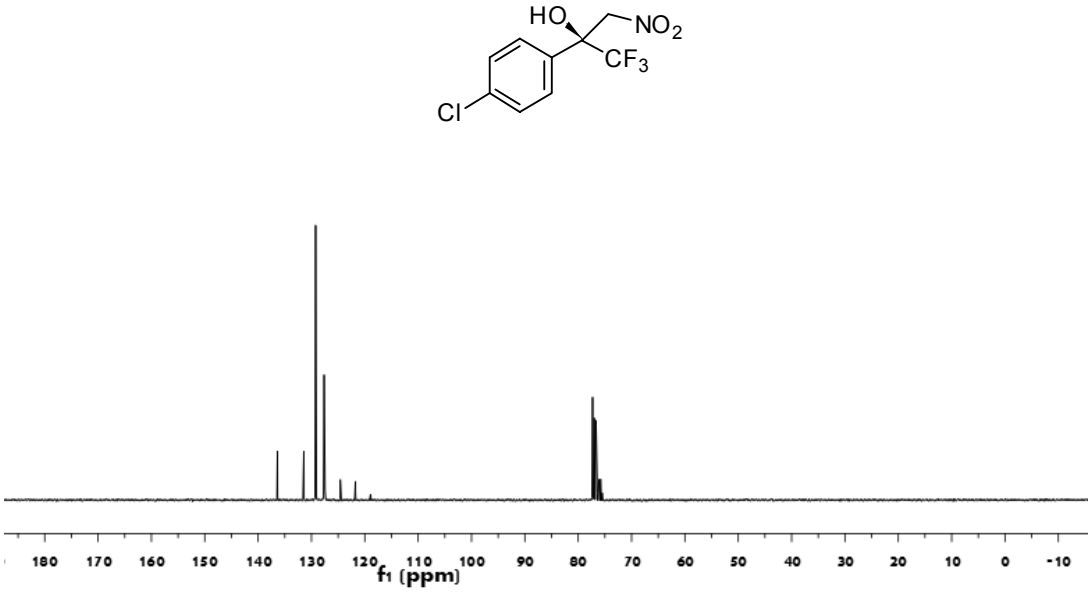
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-3-nitro-2-phenylpropan-2-ol, **2**, in $CDCl_3$:



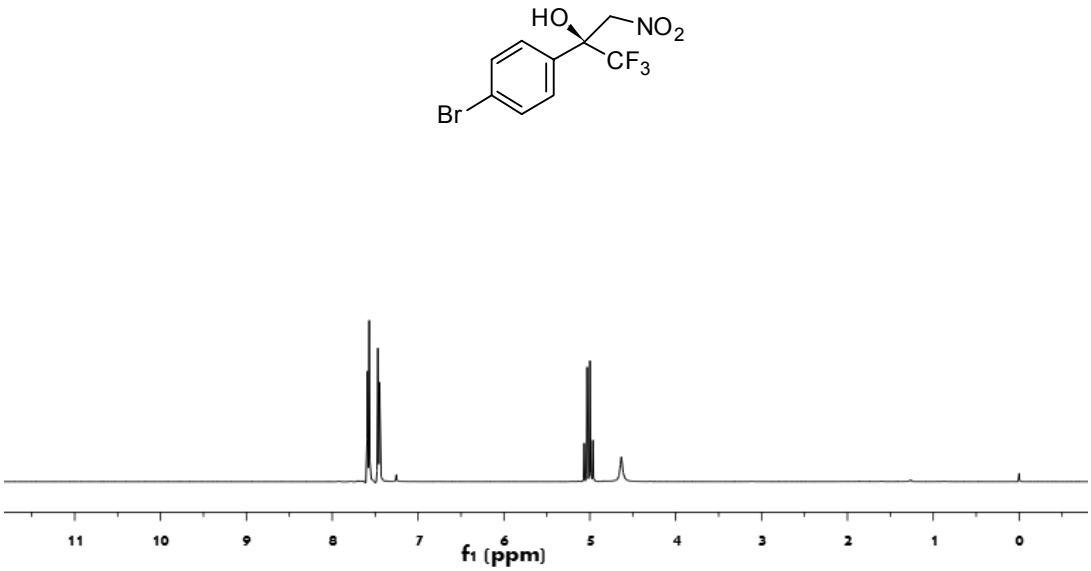


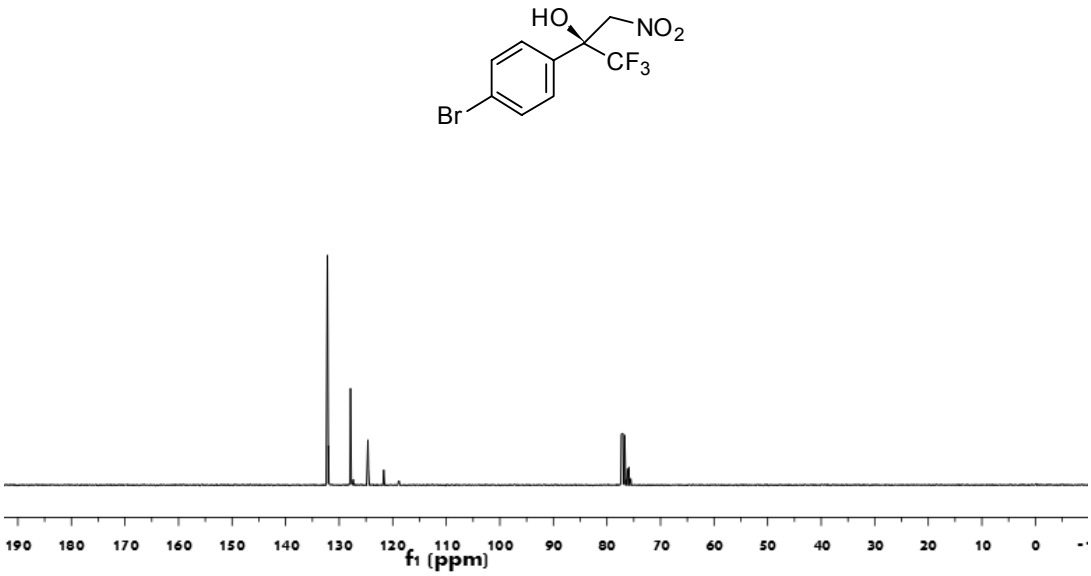
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **3**, in $CDCl_3$:



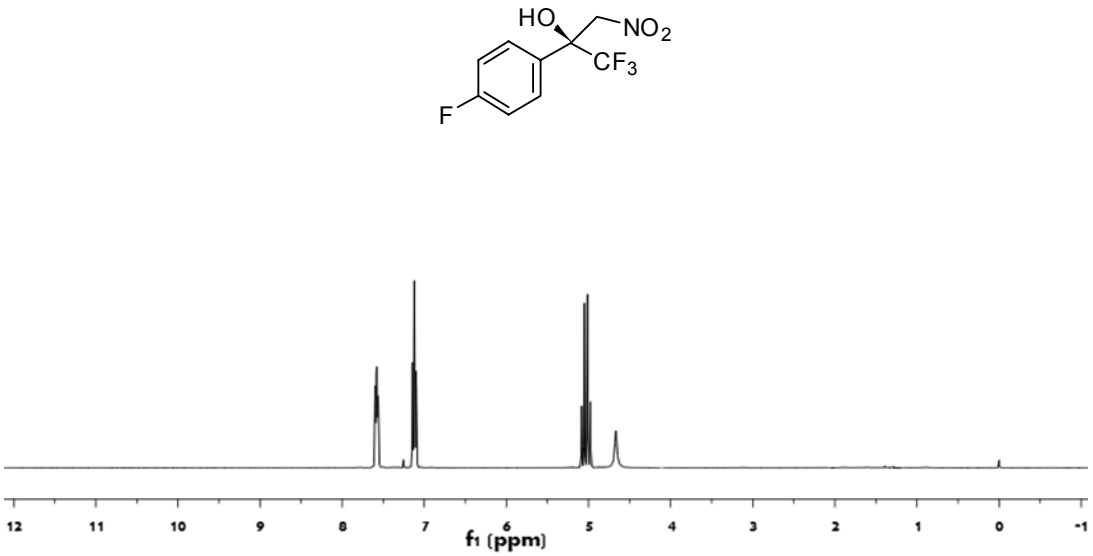


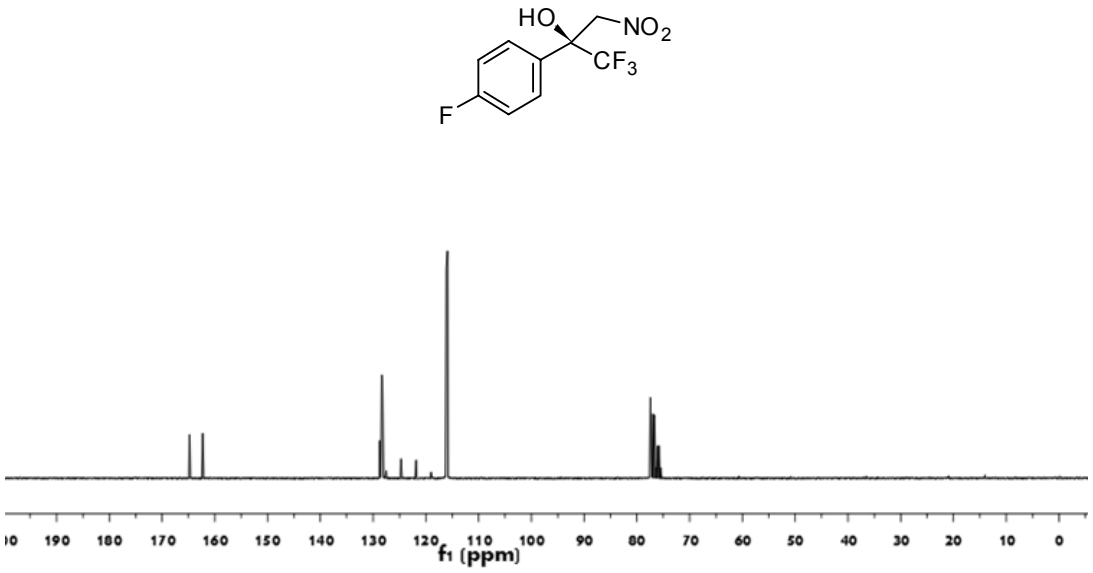
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-2-(4-bromophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **4**, in $CDCl_3$:



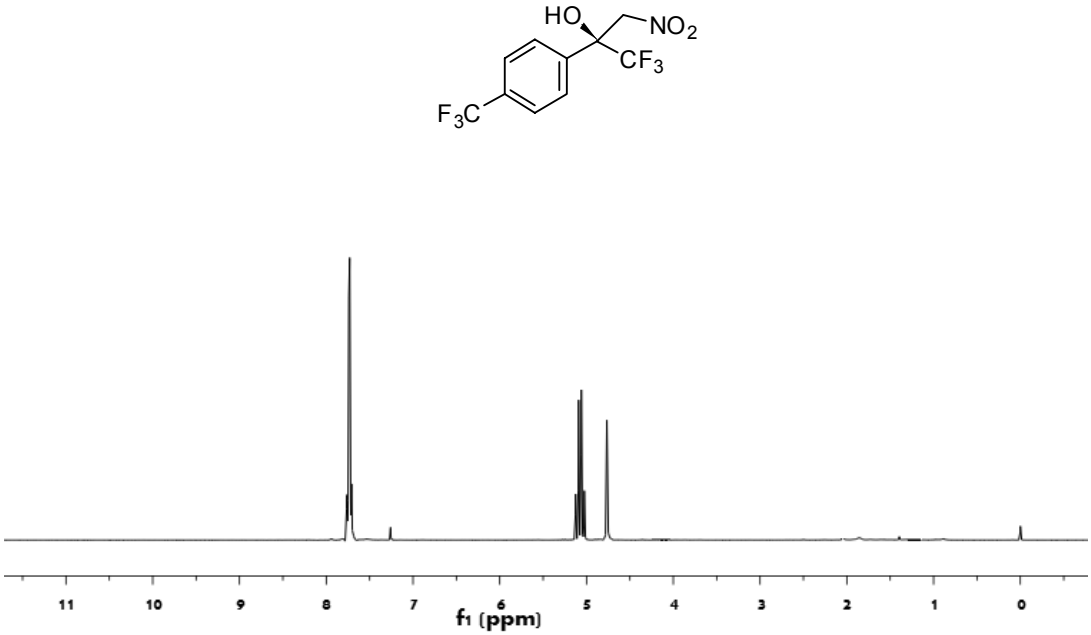


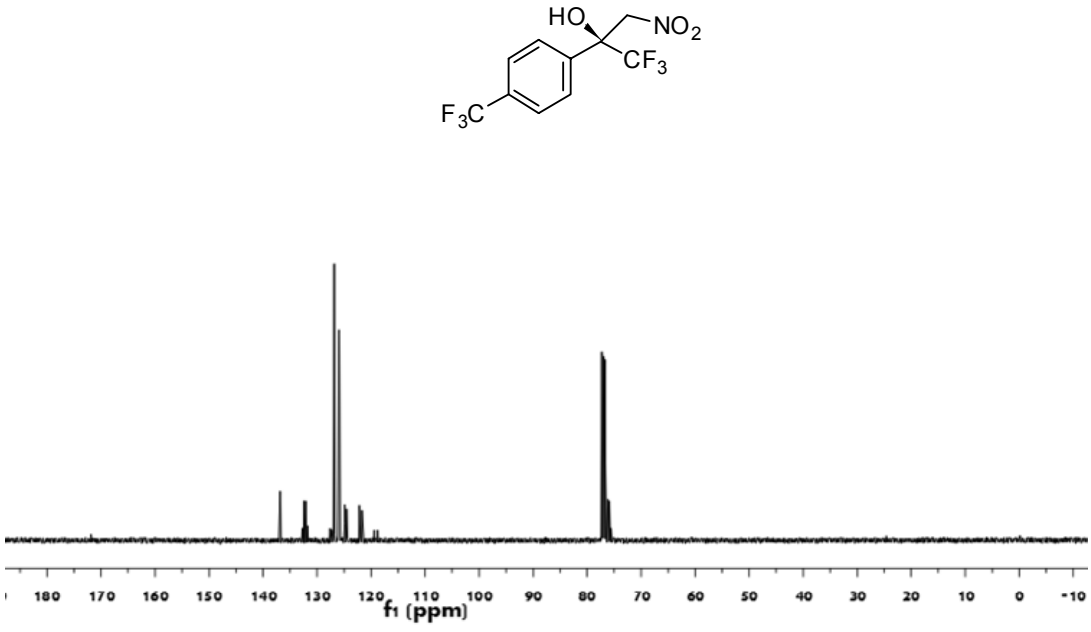
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-2-(4-fluorophenyl)-3-nitropropan-2-ol, **5**, in $CDCl_3$:



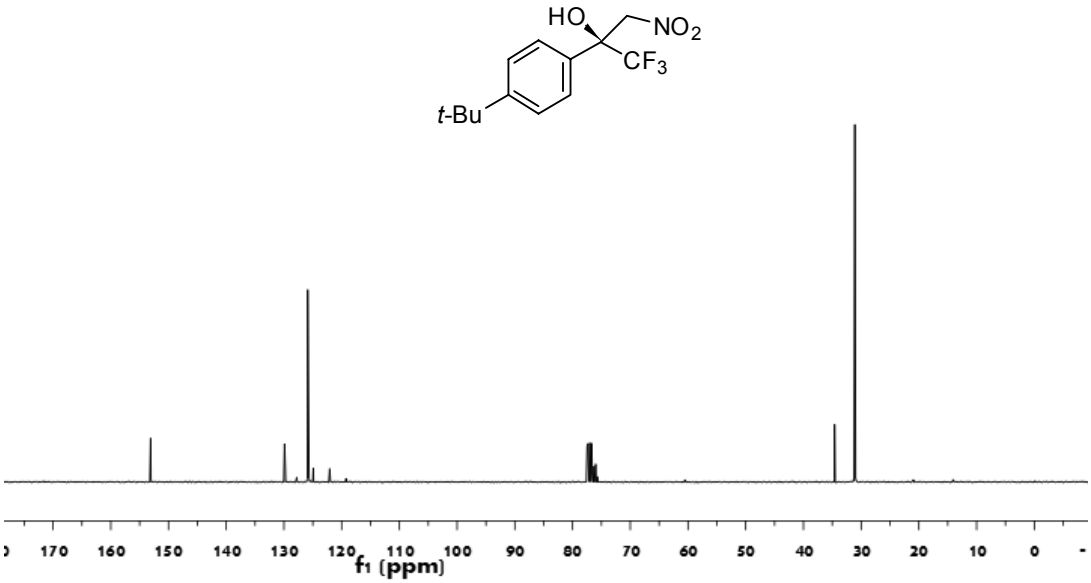


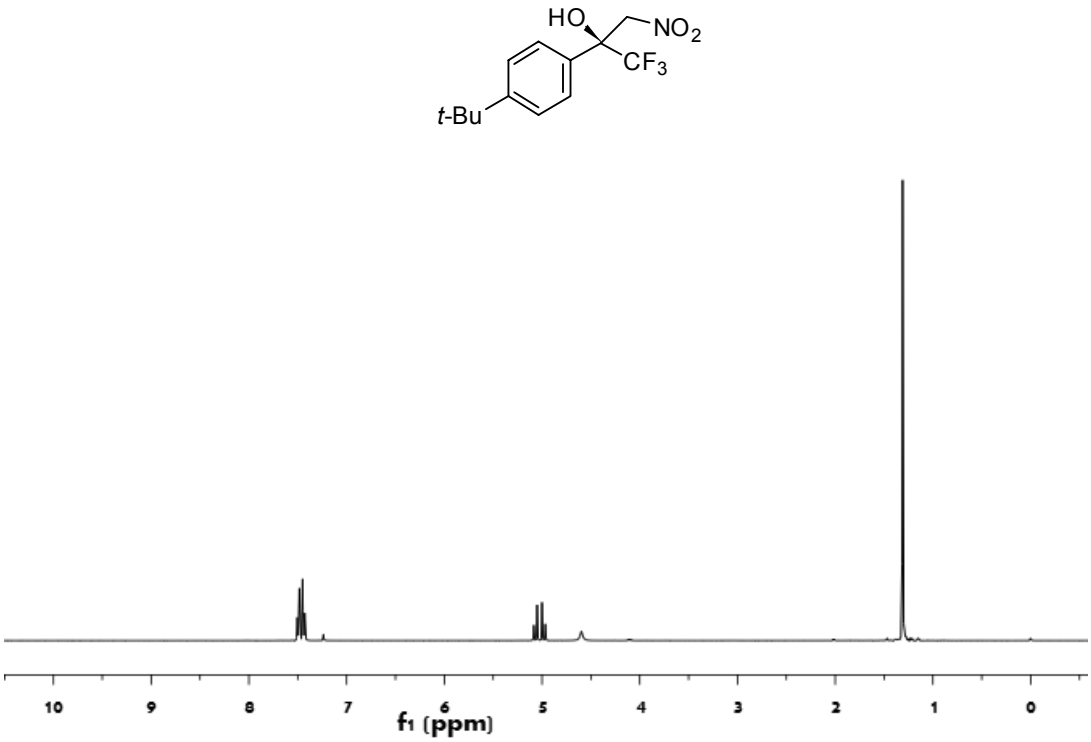
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-3-nitro-2-(4-(trifluoromethyl)phenyl)propan -2-ol, **6**, in $CDCl_3$:



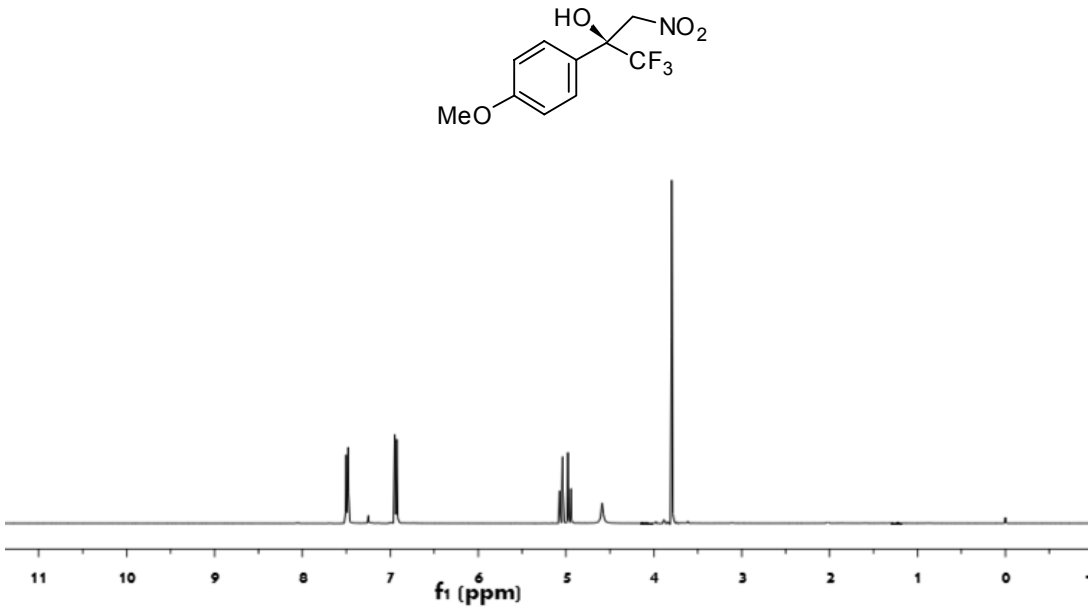


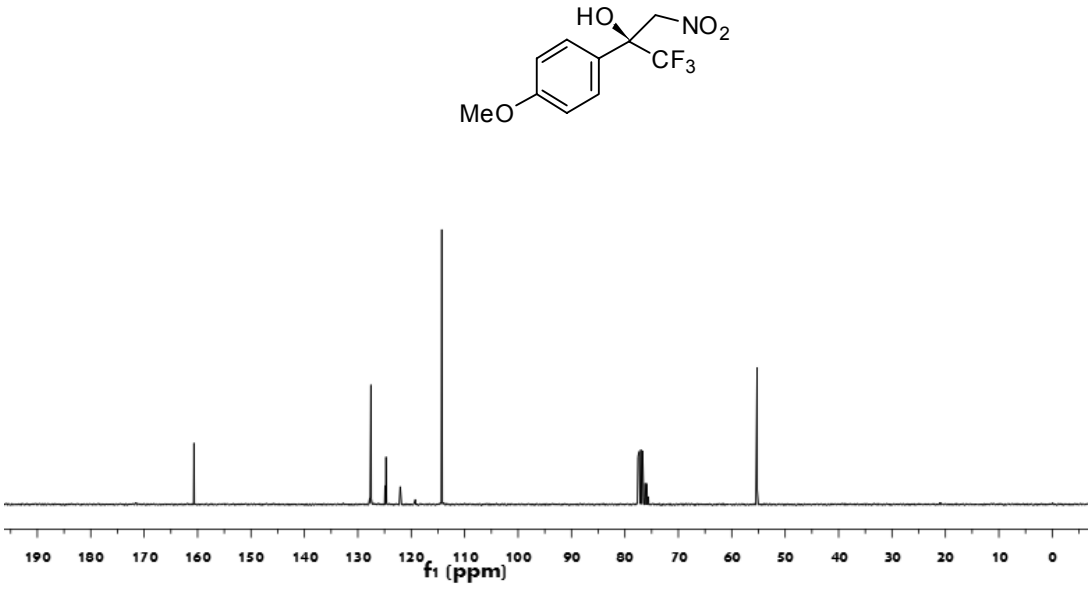
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-2-(4-*tert*-butylphenyl)-1,1,1-trifluoro-3-nitropropan-2-ol, **7**, in $CDCl_3$:



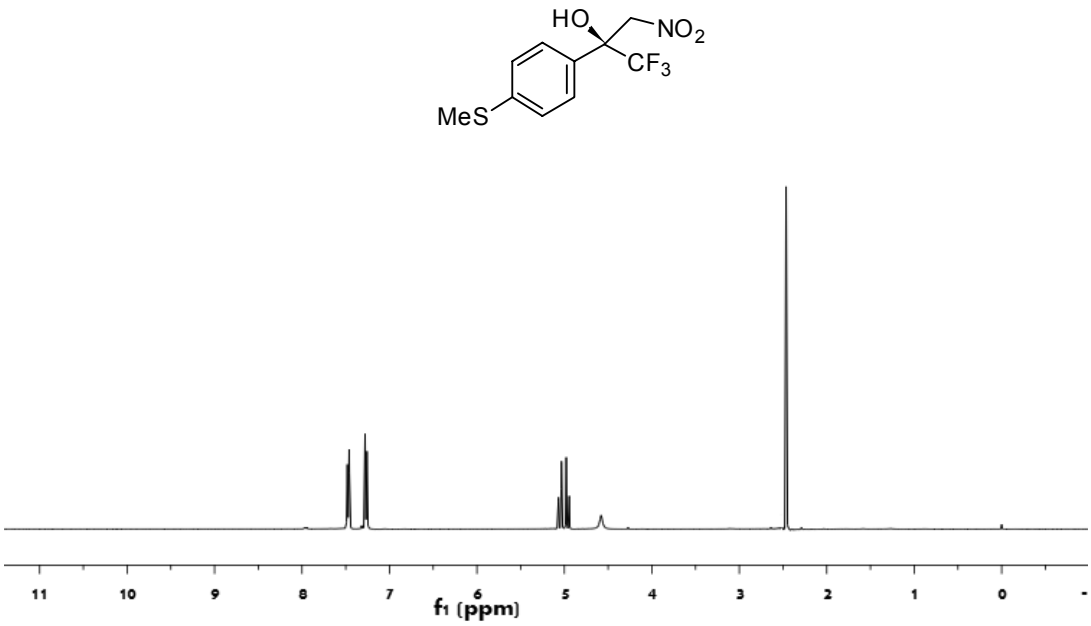


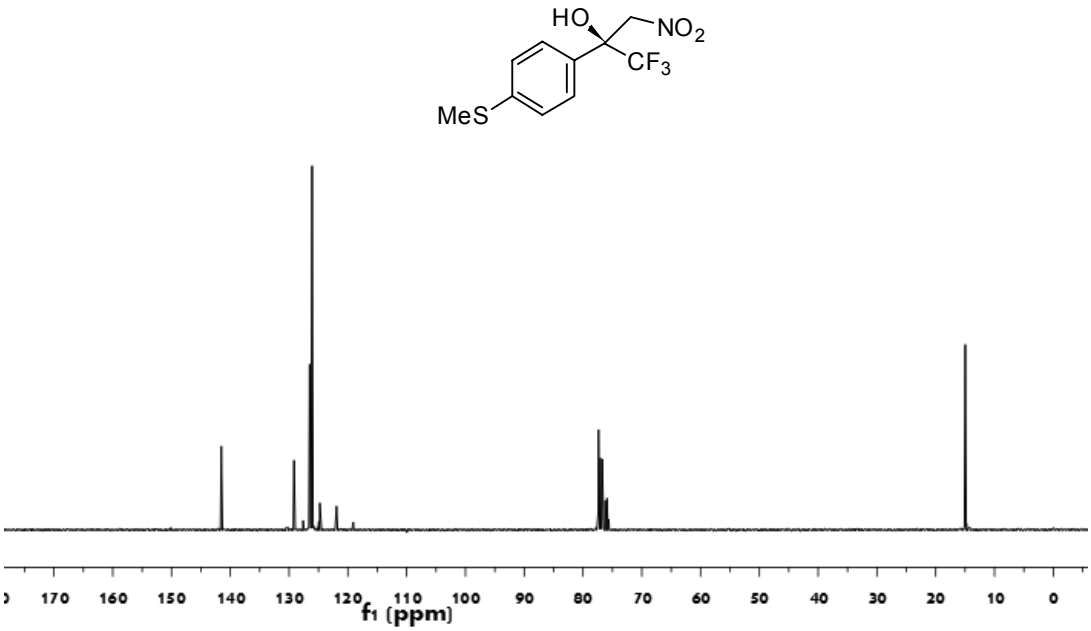
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-2-(4-methoxyphenyl)-3-nitropropan-2-ol, **8**, in $CDCl_3$:



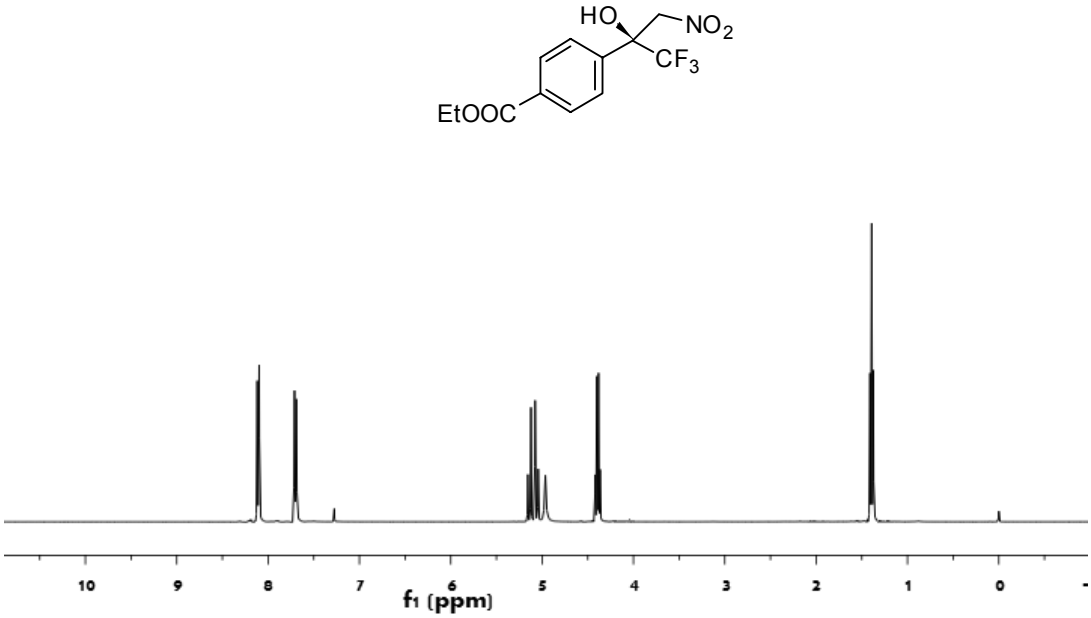


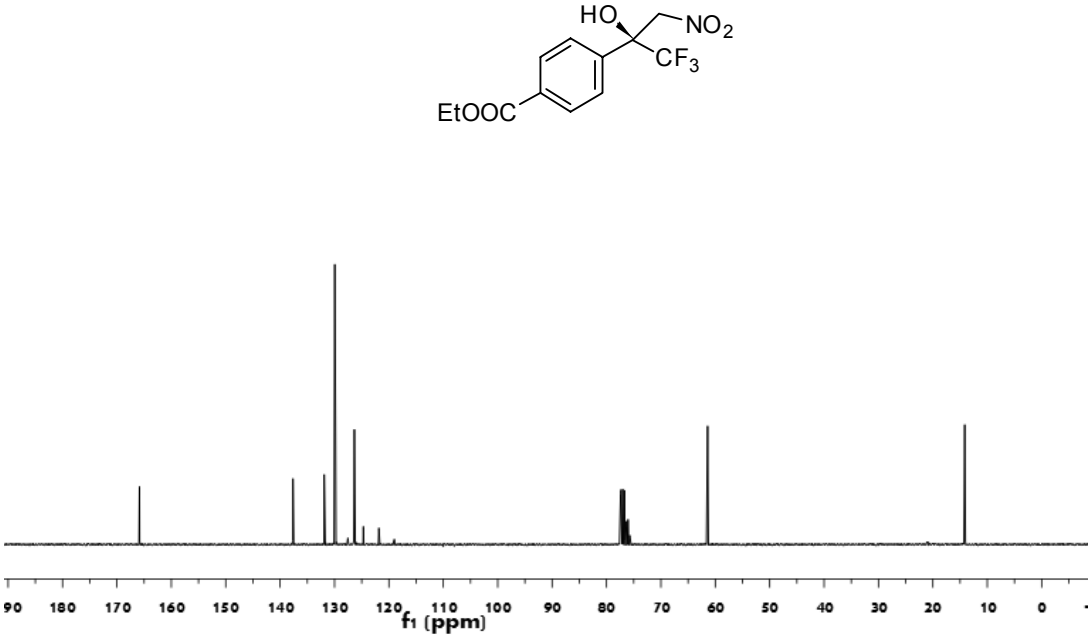
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-2-(4-methylthiophenyl)-3-nitropropan-2-ol, **9**, in $CDCl_3$:



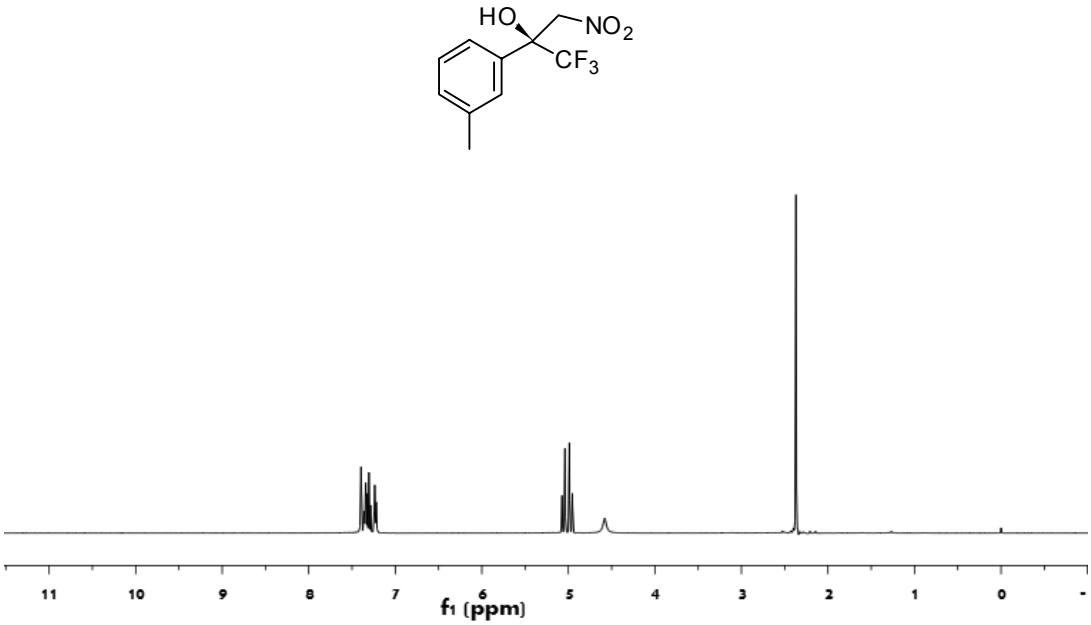


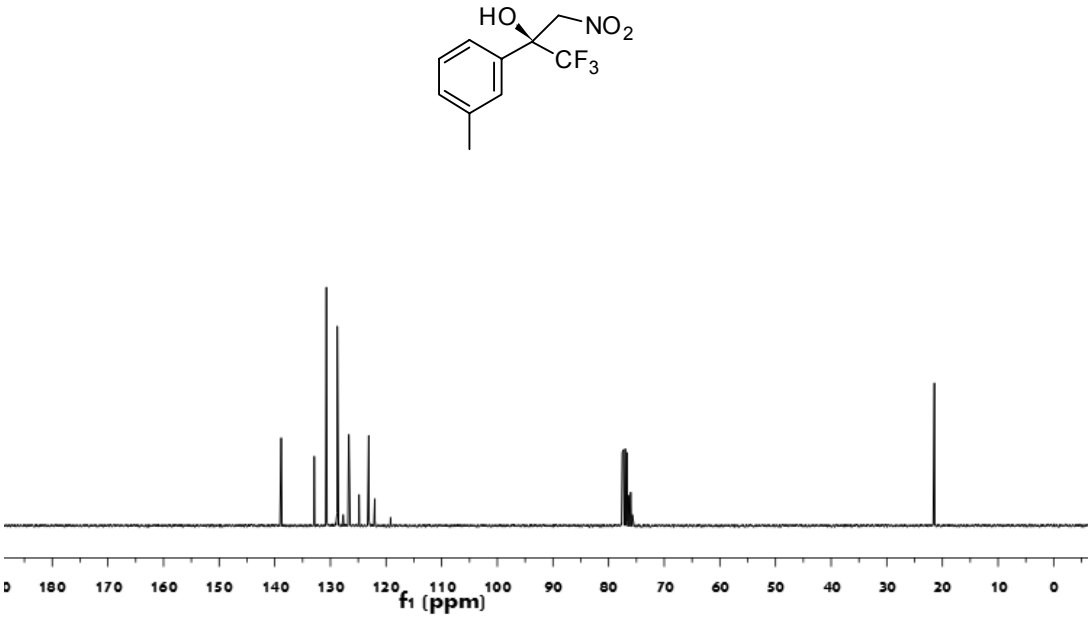
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-ethyl 4-(1,1,1-trifluoro-2-hydroxy-3-nitro-2-propyl)benzoate, **10**, in $CDCl_3$:



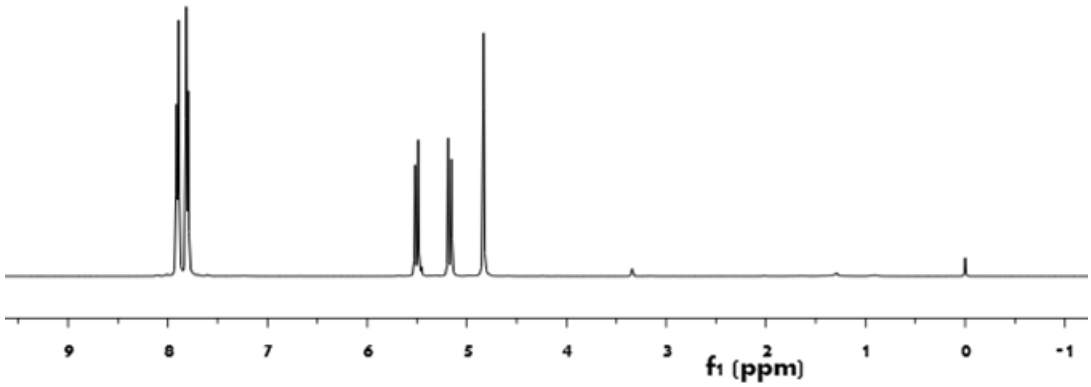


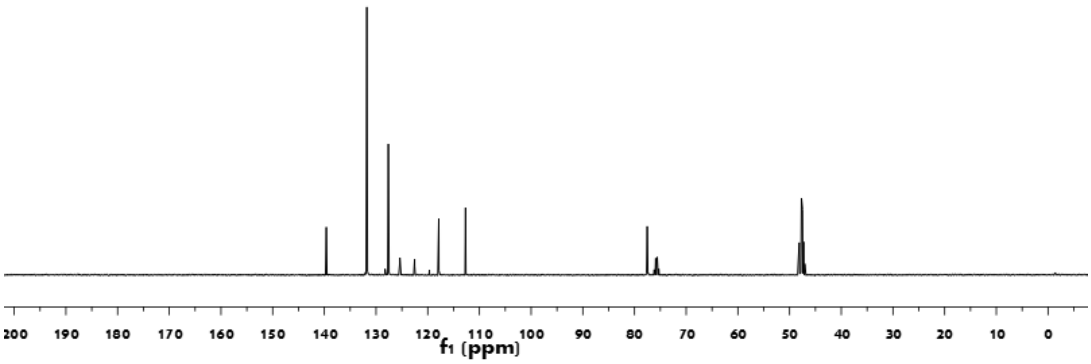
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-3-nitro-2-(3-tolyl)propan-2-ol, **11**, in $CDCl_3$:



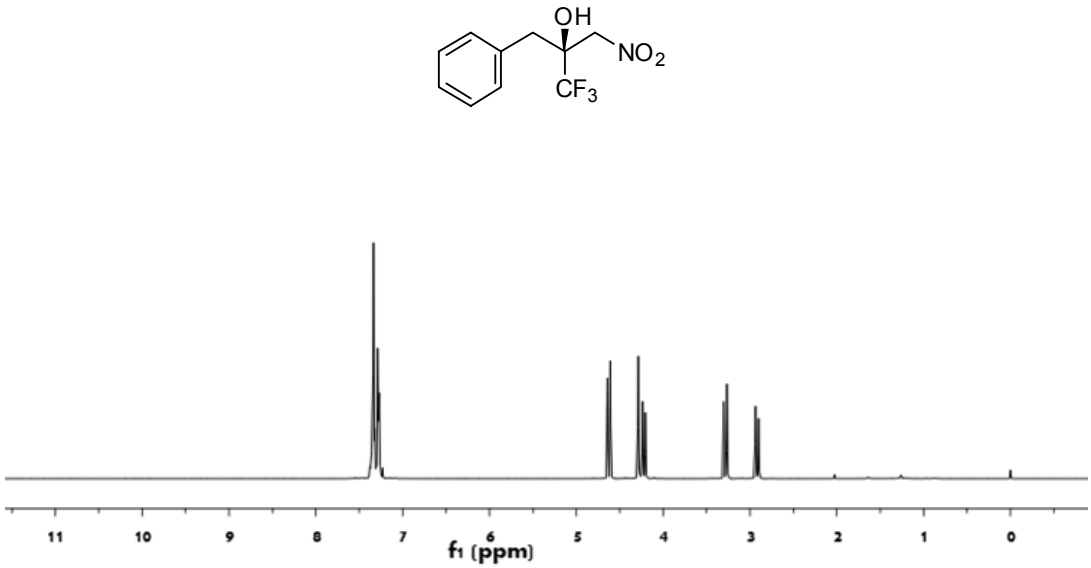


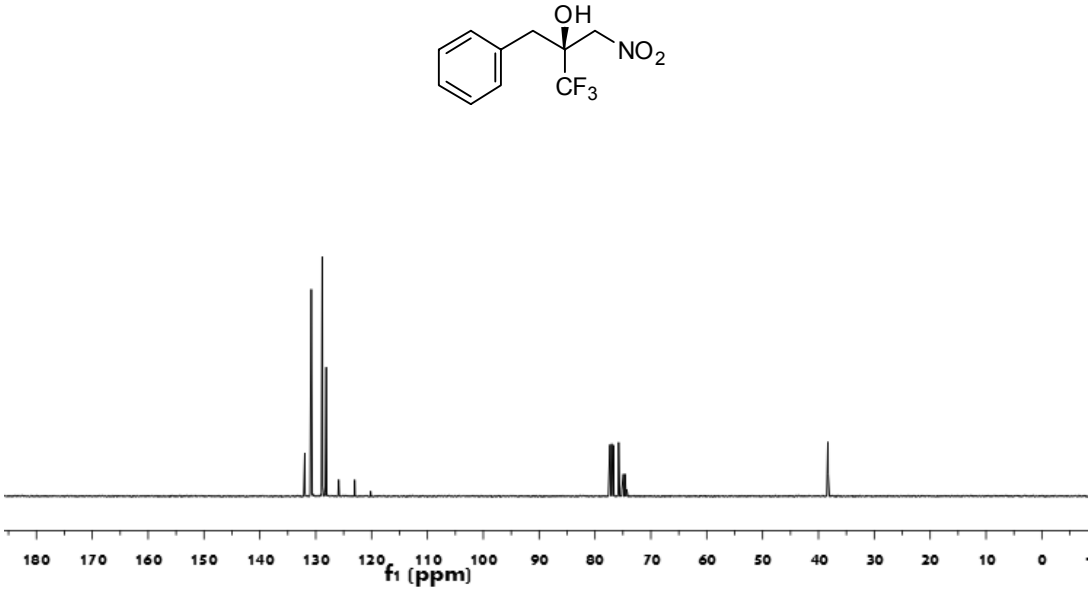
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-4-(1,1,1-trifluoro-2-hydroxy-3-nitro-2-propyl)benzonitrile, **12**, in CD_3OD:



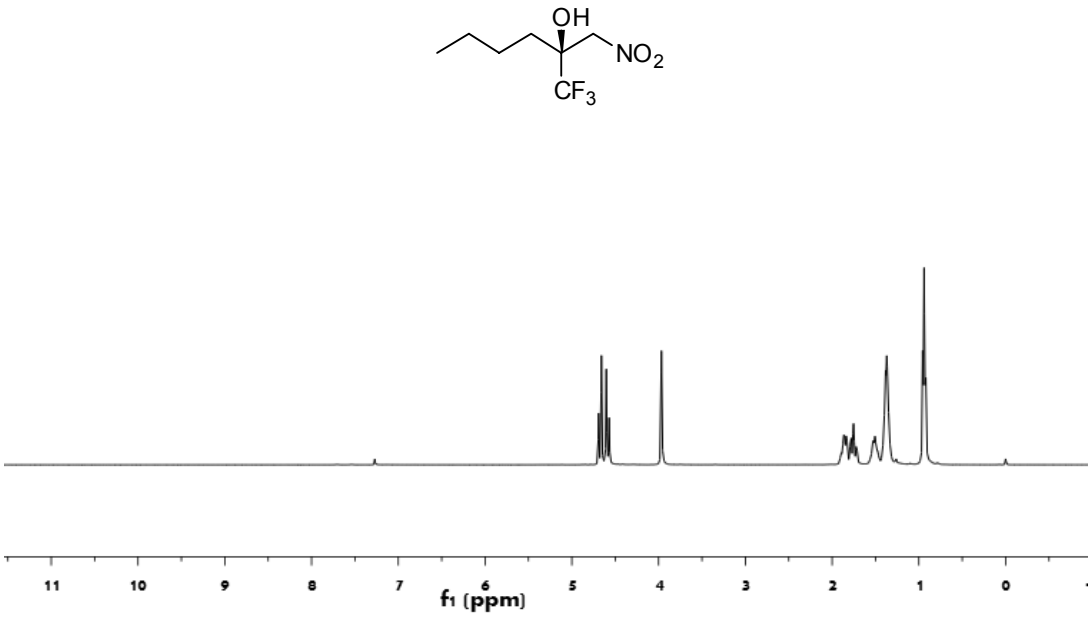


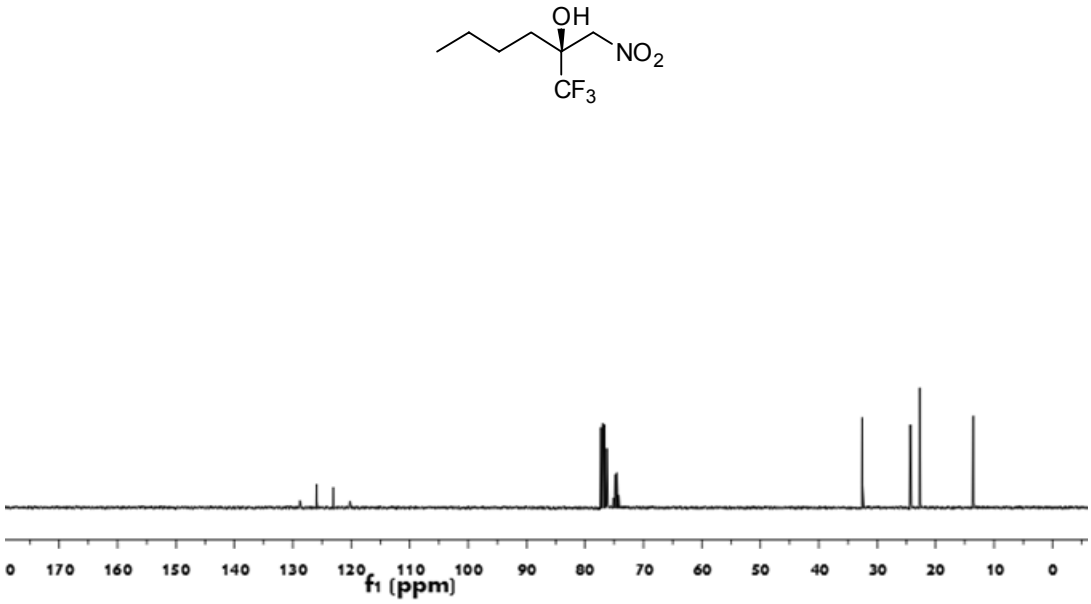
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-2-benzyl-1,1,1-trifluoro-3-nitropropan-2-ol, **13**, in $CDCl_3$:



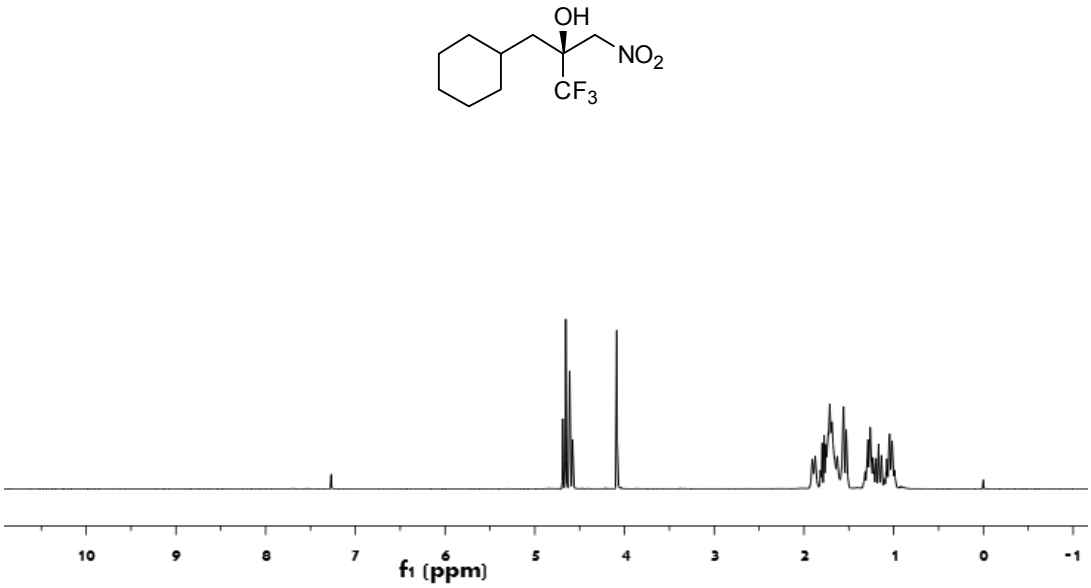


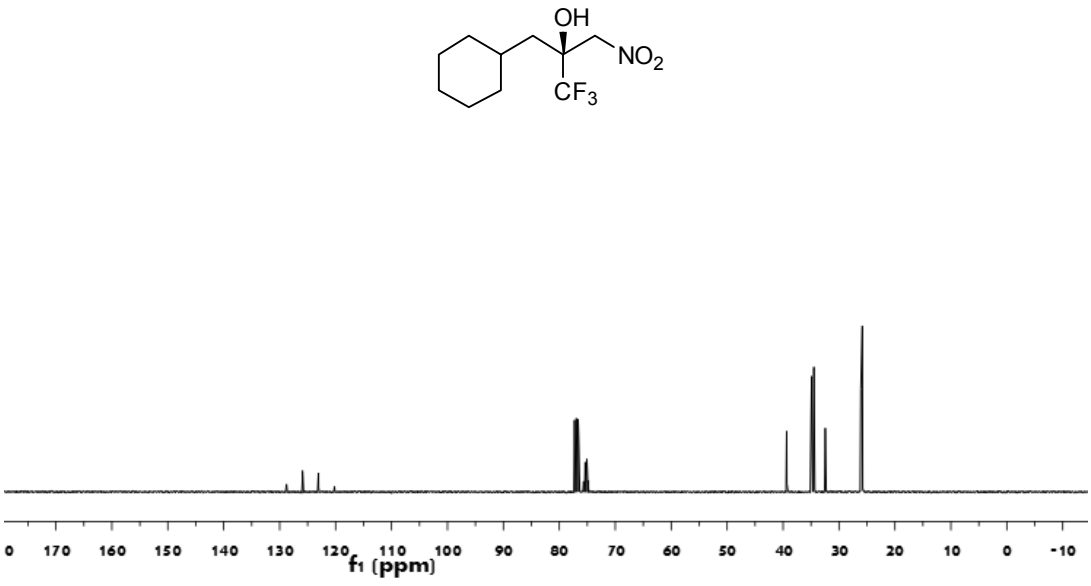
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-1,1,1-trifluoro-2-(nitromethyl)hexan-2-ol, **14**, in $CDCl_3$:



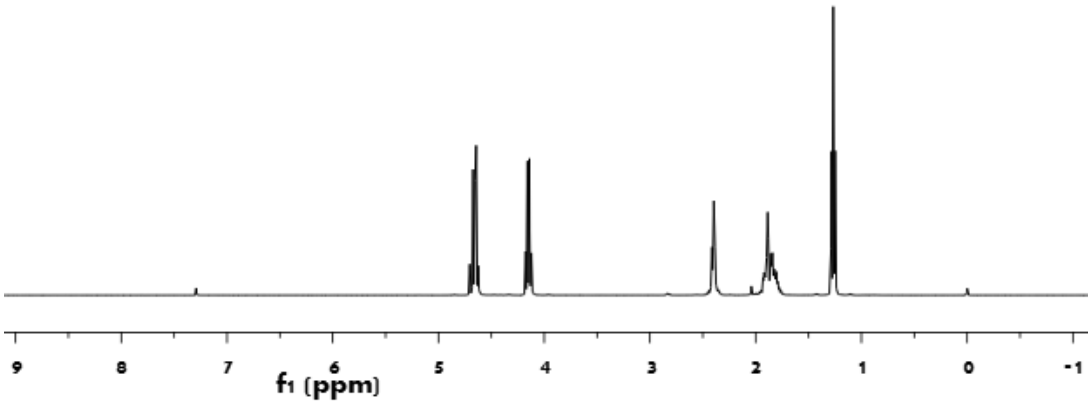


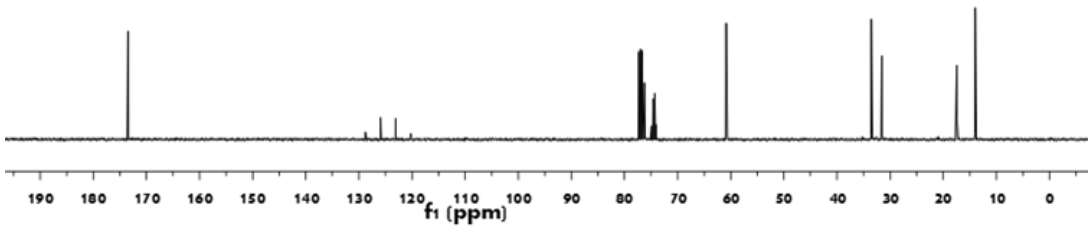
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-3-cyclohexyl-1,1,1-trifluoro-2-(nitromethyl)propan-2-ol, **15**, in $CDCl_3$:



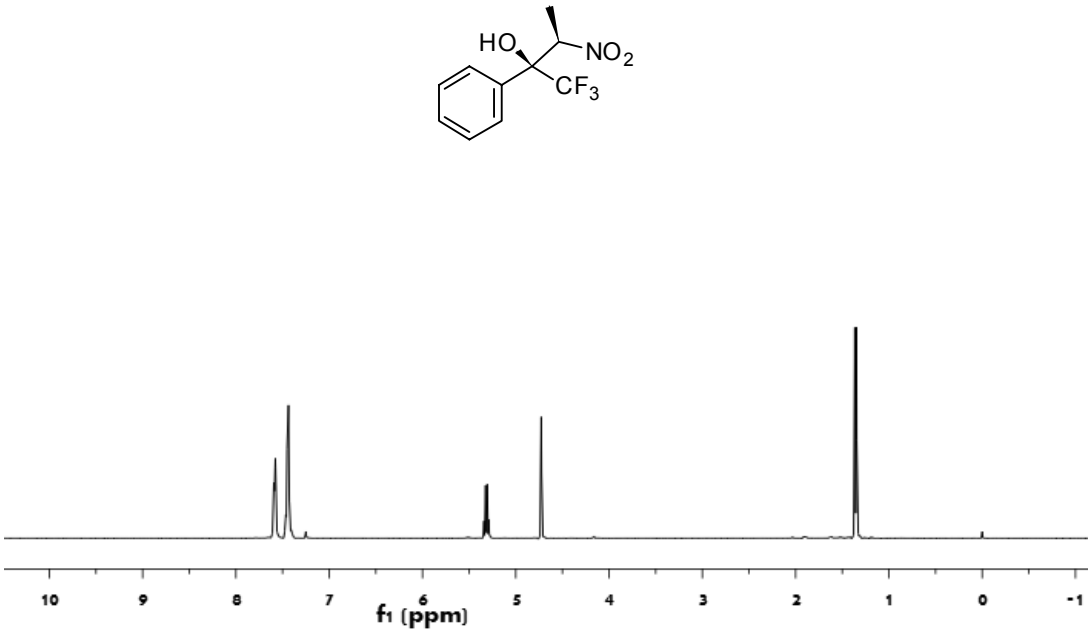


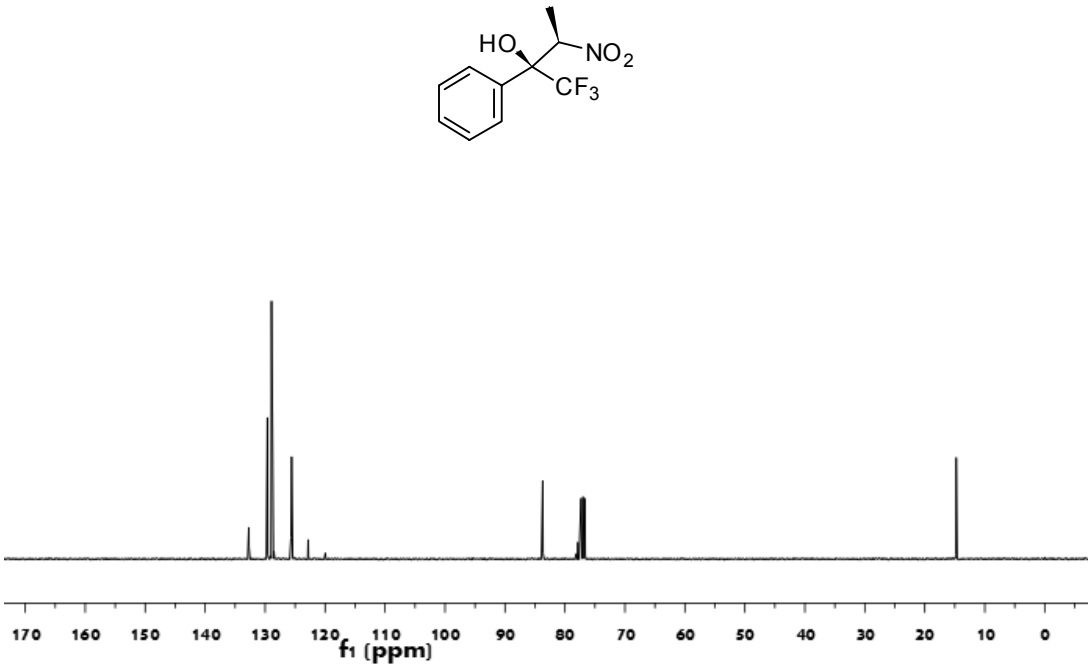
^{1}H NMR and ^{13}C NMR Spectra of (*S*)-ethyl 6,6,6-trifluoro-5-hydroxy-5-(nitromethyl)hexanoate, **16**, in $CDCl_3$:



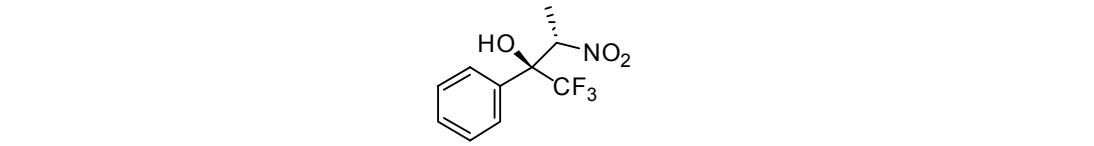


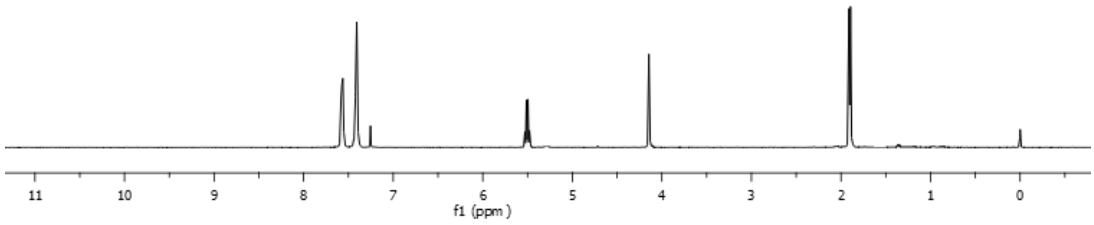
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*R*)-1,1,1-trifluoro-3-nitro-2-phenylbutan-2-ol, **17**, in $CDCl_3$:

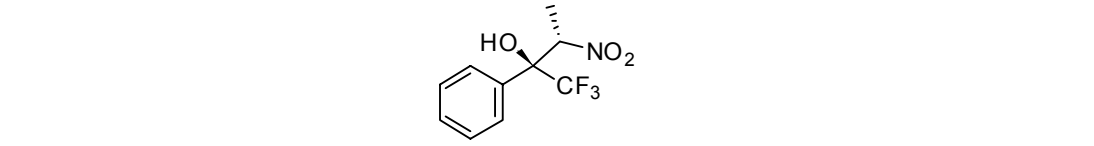


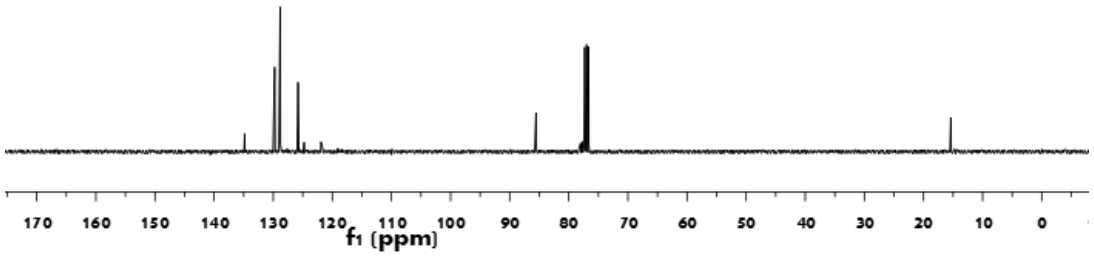


^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*S*)-1,1,1-trifluoro-3-nitro-2-phenylbutan-2-ol, **21**, in $CDCl_3$:

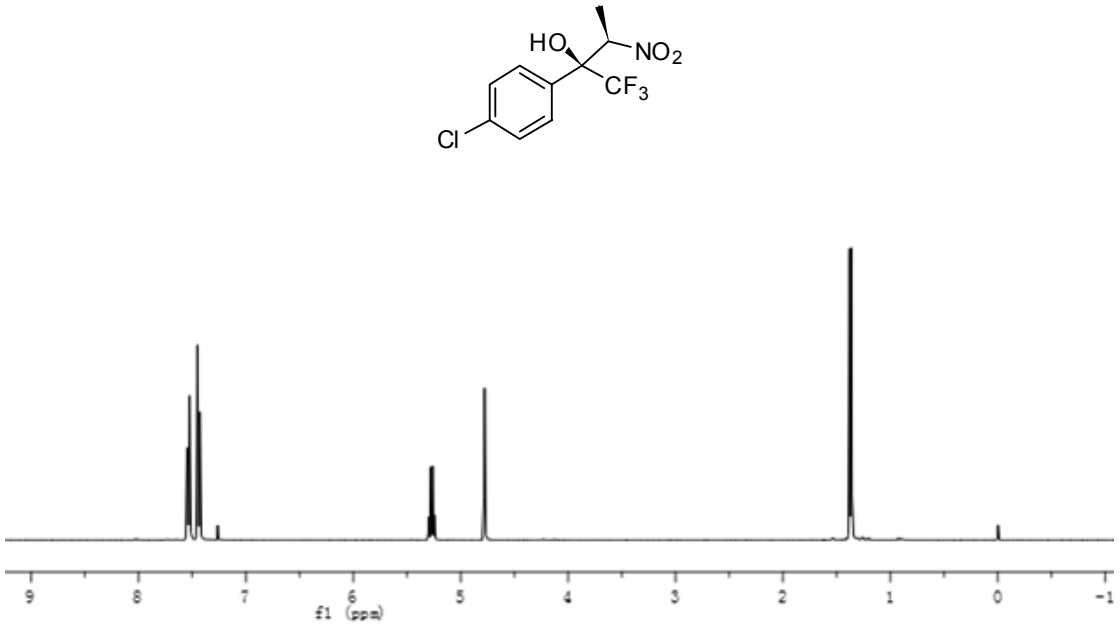


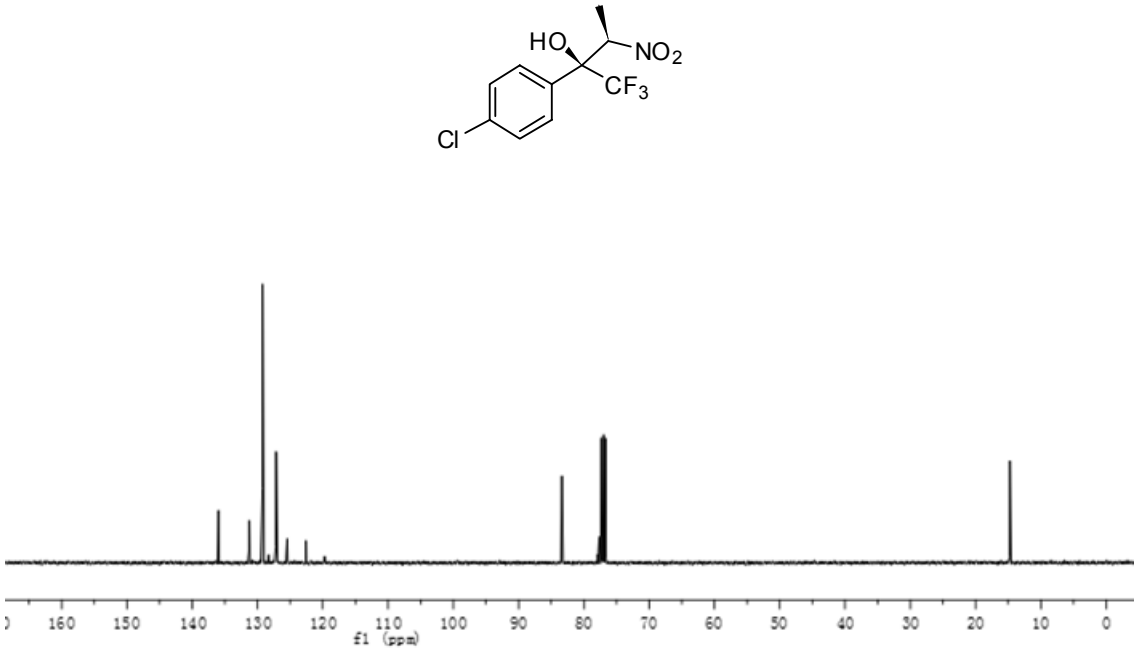




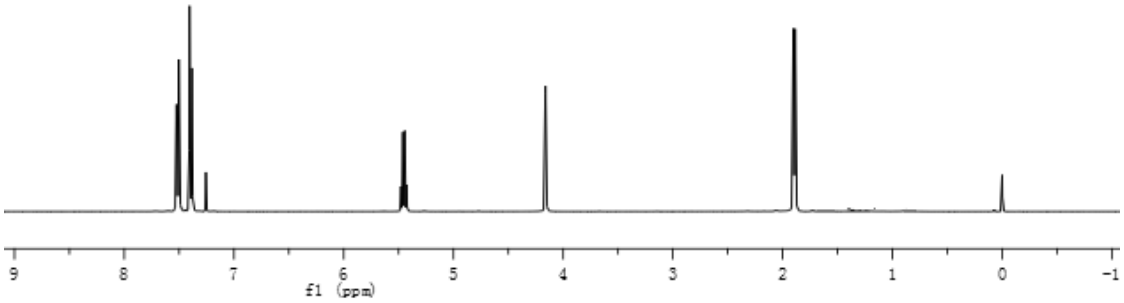


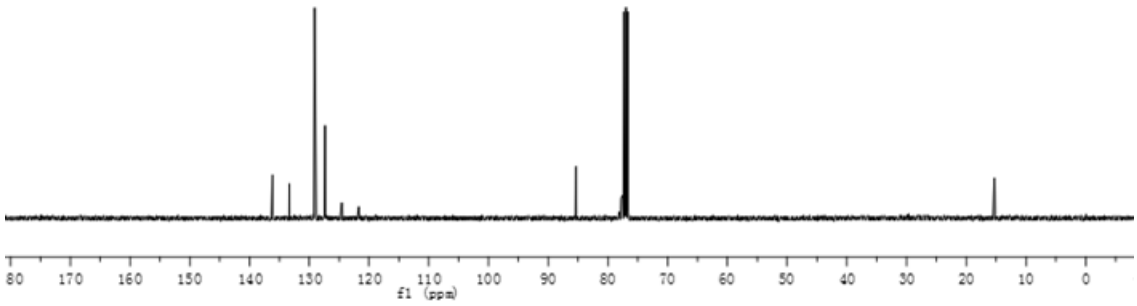
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*R*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **18**, in $CDCl_3$:



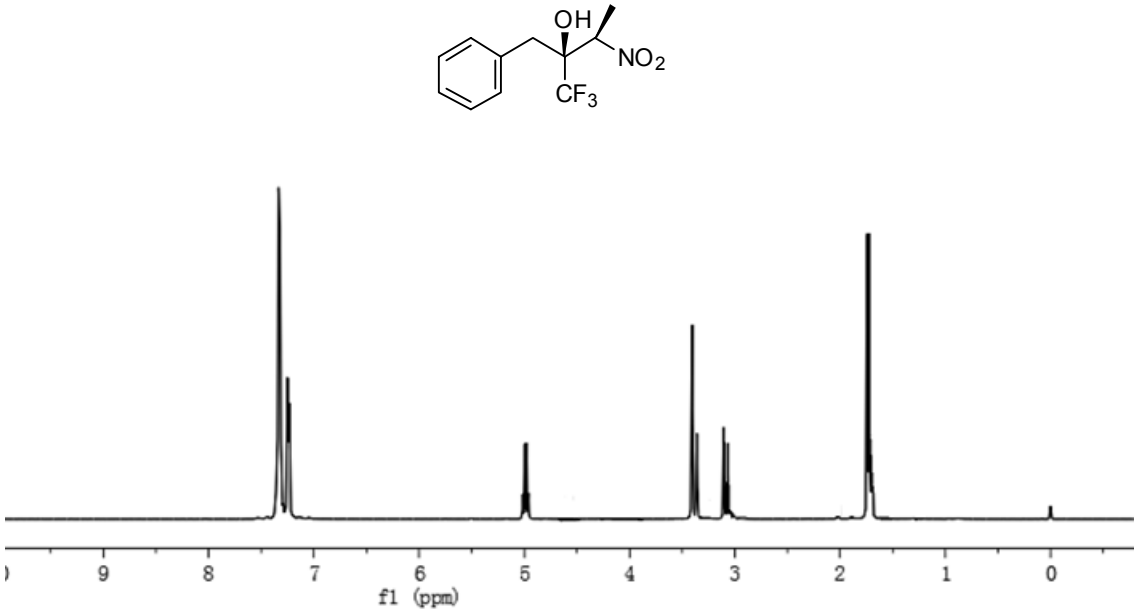


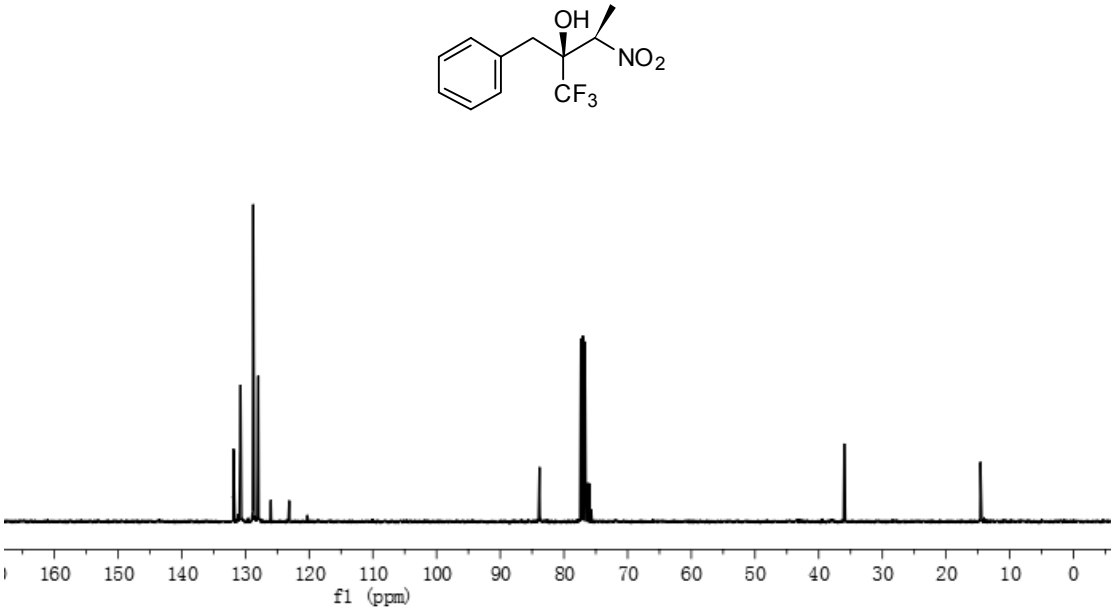
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*S*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **22**, in $CDCl_3$:



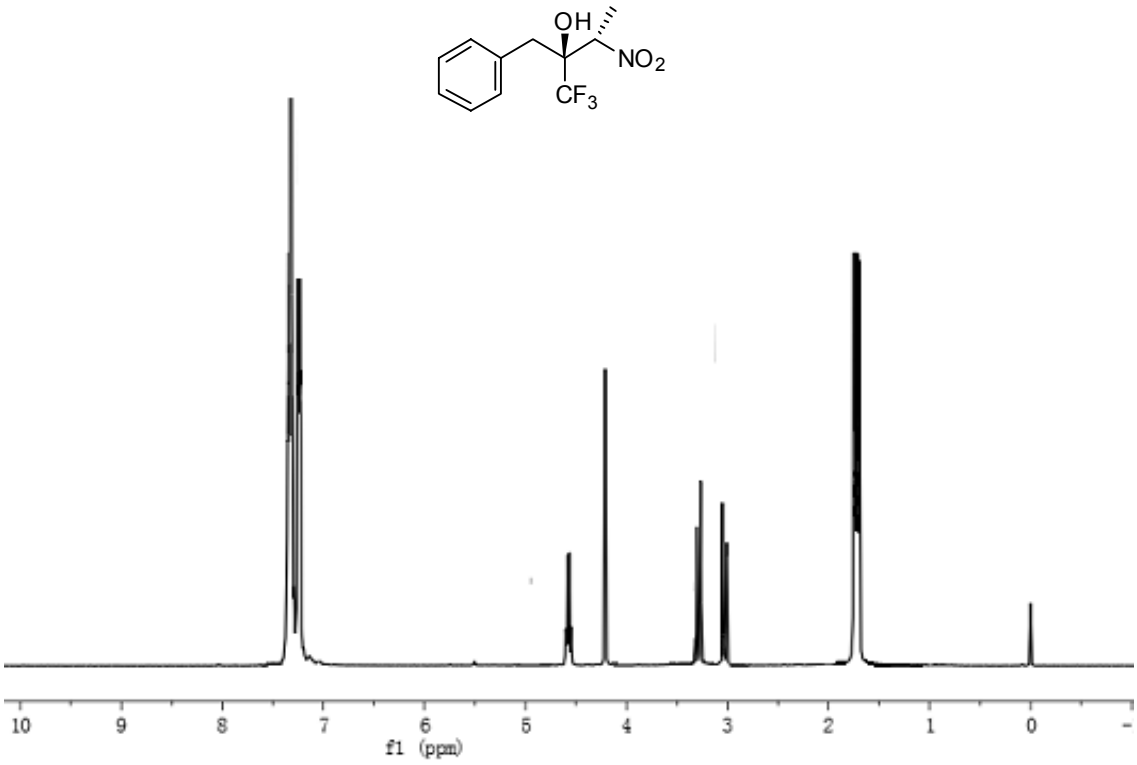


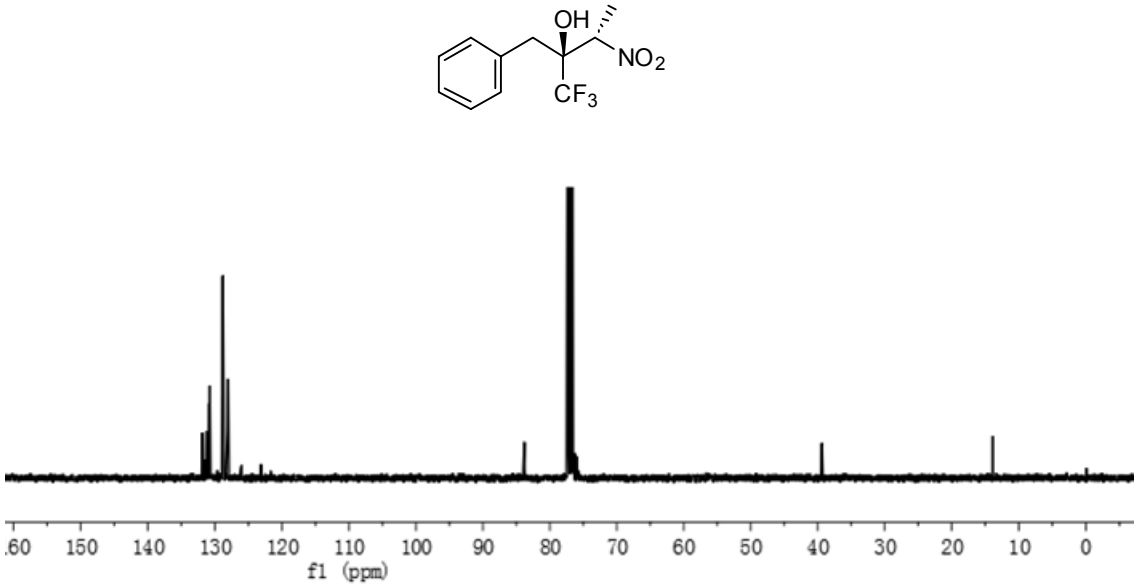
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*R*)-2-benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol, **19**, in $CDCl_3$:



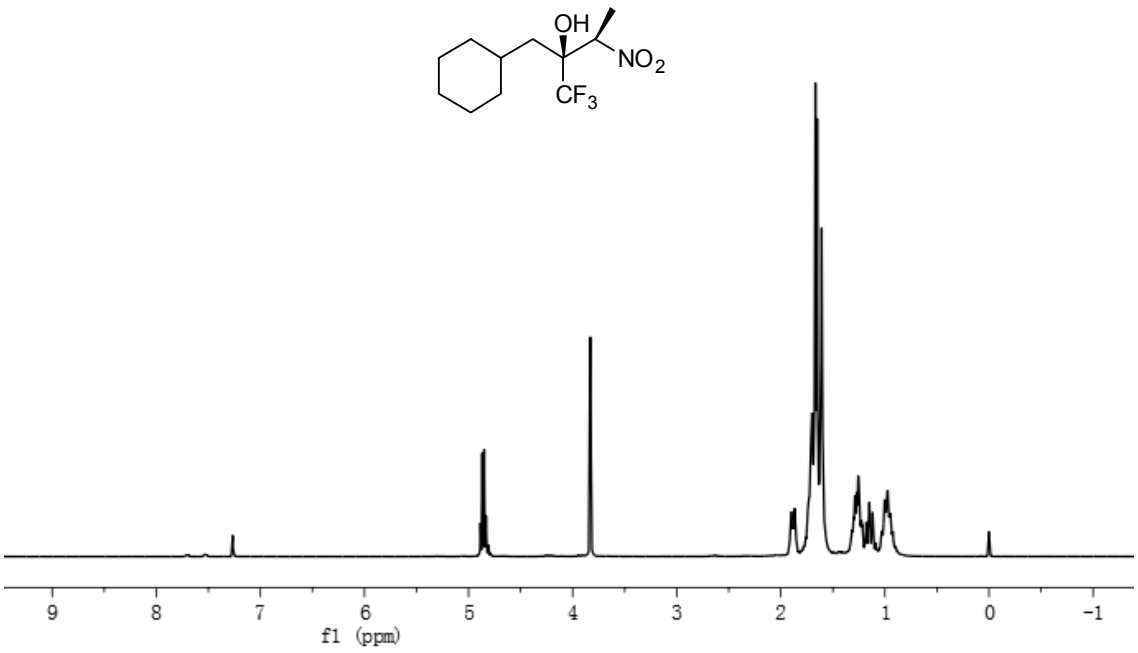


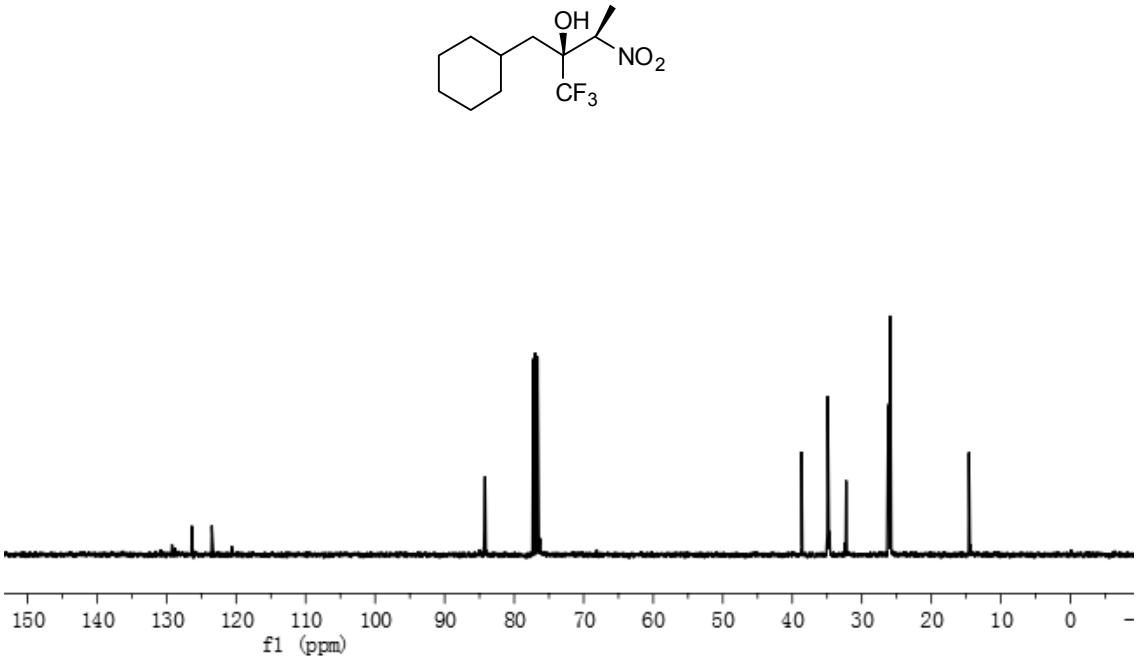
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*S*)-2-benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol, **23**, in $CDCl_3$:



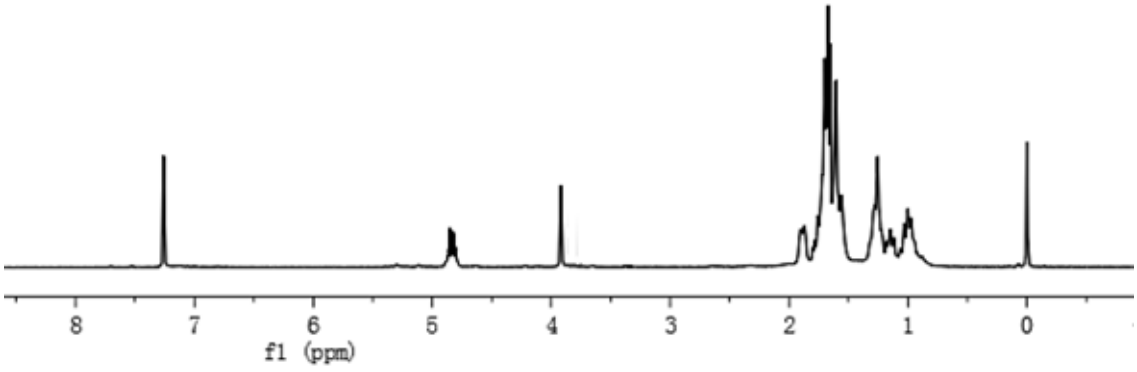


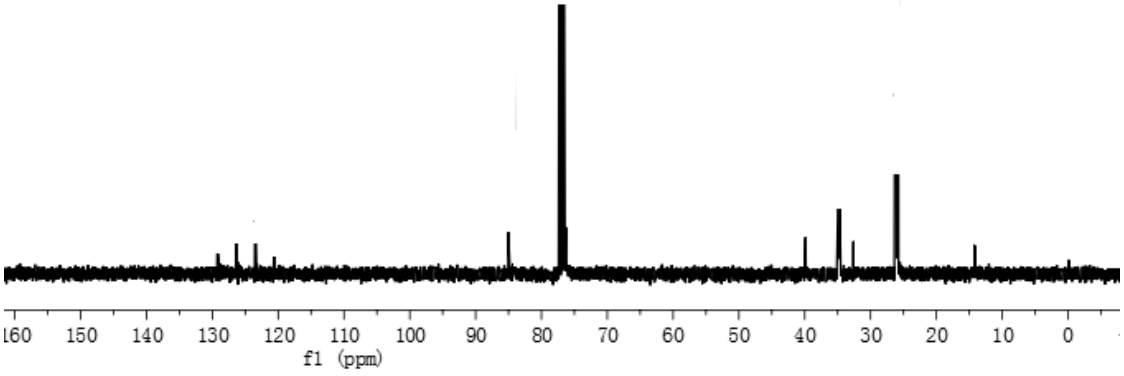
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*R*)-2-(cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **20**, in $CDCl_3$:



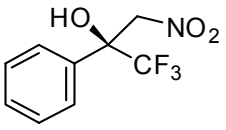


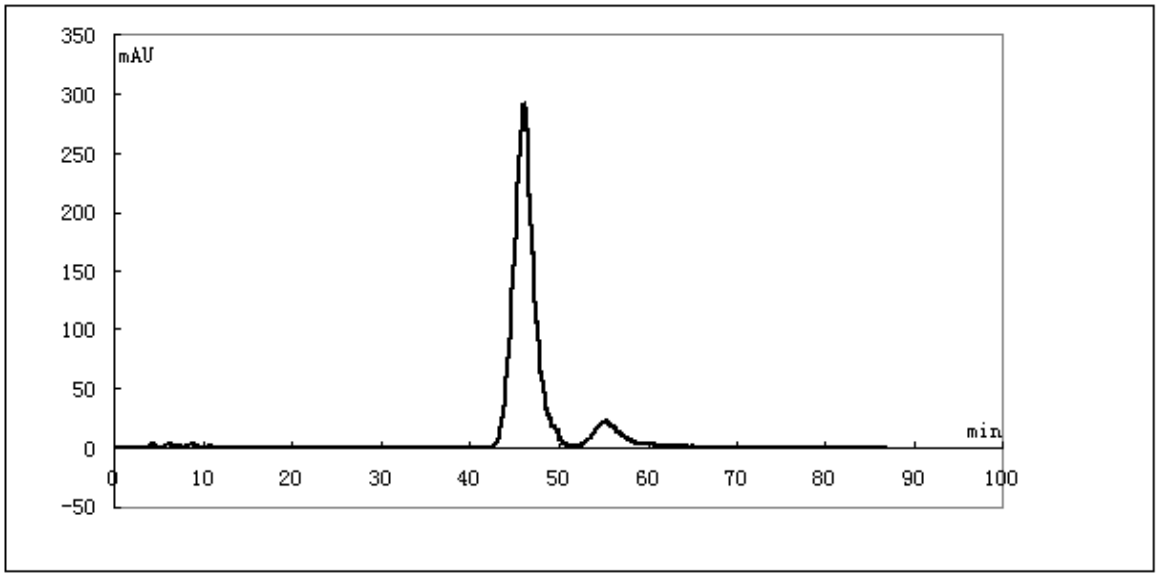
^{1}H NMR and ^{13}C NMR Spectra of (2*S*,3*S*)-2-(cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol, **24**, in $CDCl_3$:



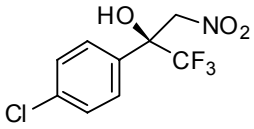


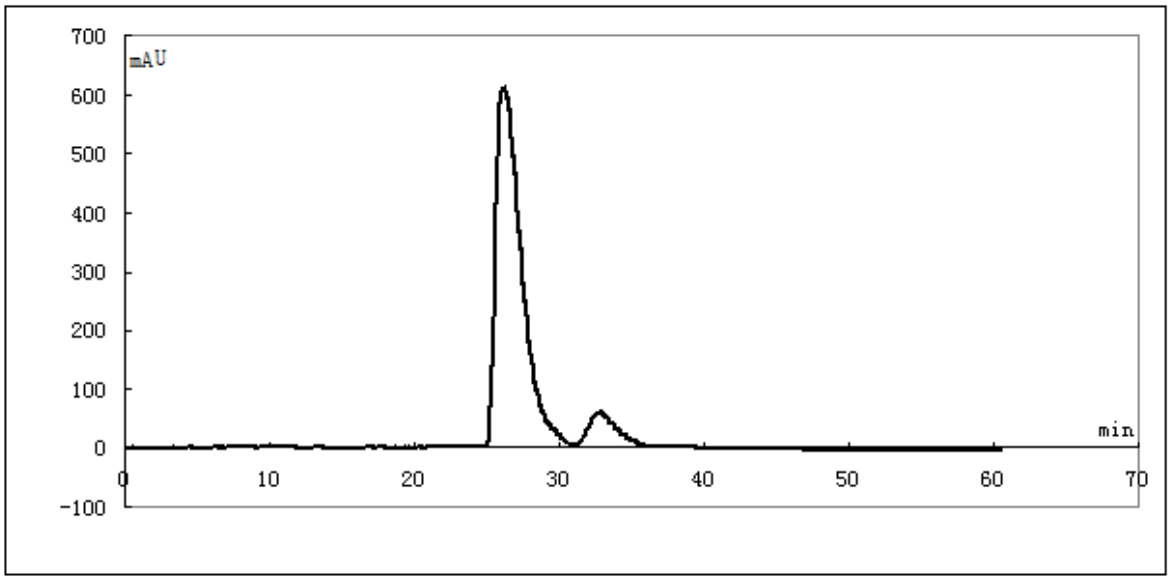
HPLC Analysis of (*S*)-1,1,1-trifluoro-3-nitro-2-phenylpropan-2-ol:
Daicel Chiralcel OJ column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 46.2 min, t_2 (minor) = 55.2 min, α = 1.21, 86% ee.



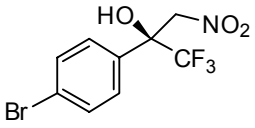


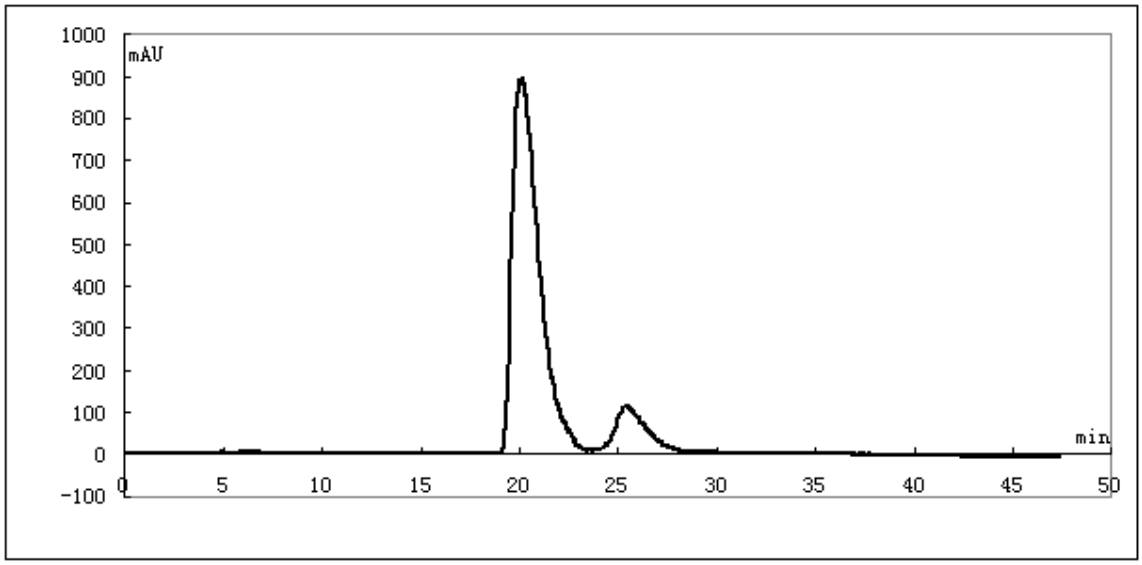
HPLC Analysis of (*S*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol:
Daicel Chiralcel OJ column, hexanes:IPA (93:7), 1 mL/min, λ= 214 nm, t_1 (major) = 26.2 min, t_2 (minor) = 32.7 min, α = 1.29, 84% ee.



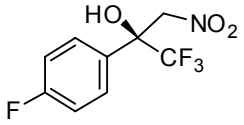


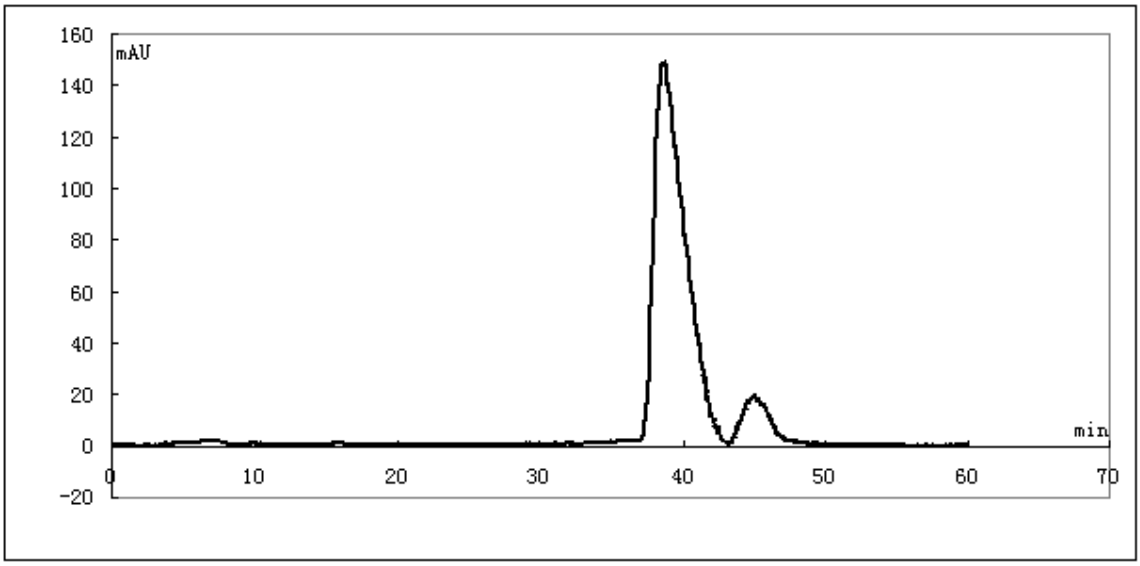
HPLC Analysis of (*S*)-2-(4-bromophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol:
Daicel Chiralcel OJ column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 20.1 min, t_2 (minor) = 25.4 min, α = 1.33, 80% ee.



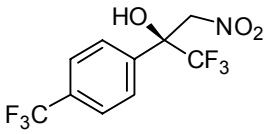


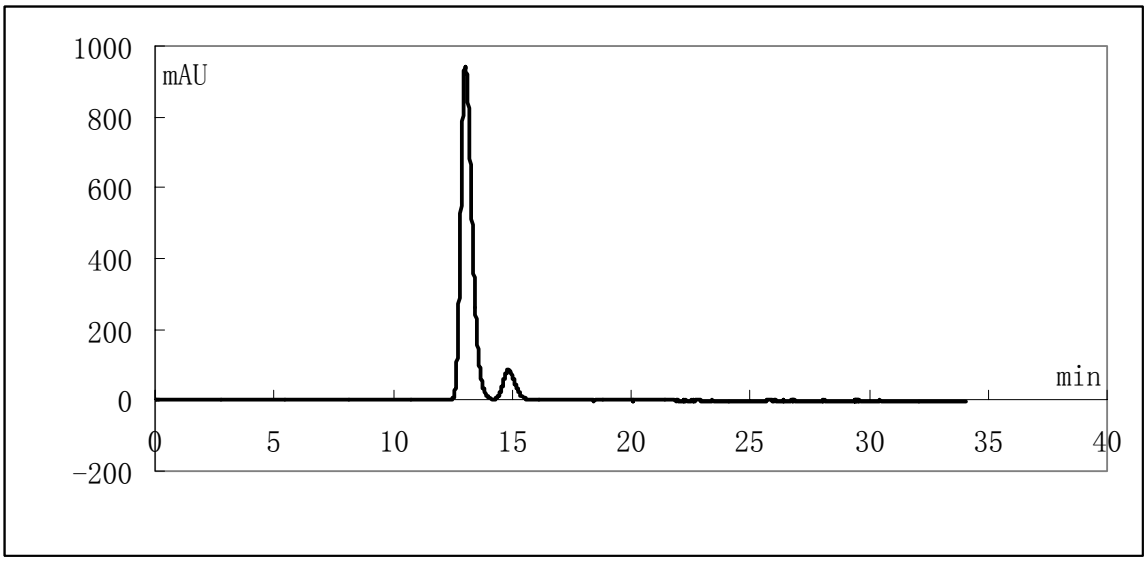
HPLC Analysis of (*S*)-1,1,1-trifluoro-2-(4-fluorophenyl)-3-nitropropan-2-ol:
Daicel Chiralcel OJ column, hexanes:IPA (94:6), 1 mL/min, λ= 214 nm, t_1 (major) = 38.6 min, t_2 (minor) = 44.9 min, α = 1.18, 83% ee.



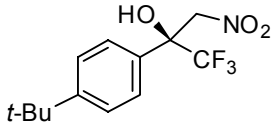


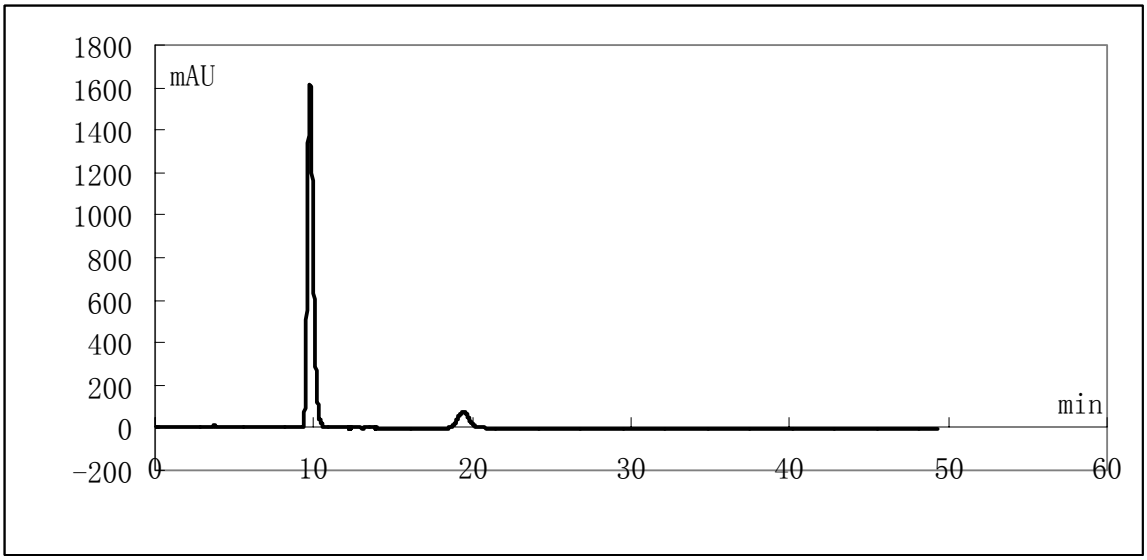
HPLC Analysis of (*S*)-1,1,1-trifluoro-3-nitro-2-(4-(trifluoromethyl)phenyl)propan-2-ol: Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 13.0 min, t_2 (minor) = 14.9 min, α = 1.21, 84% ee.



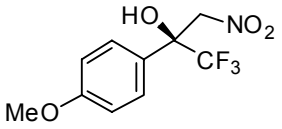


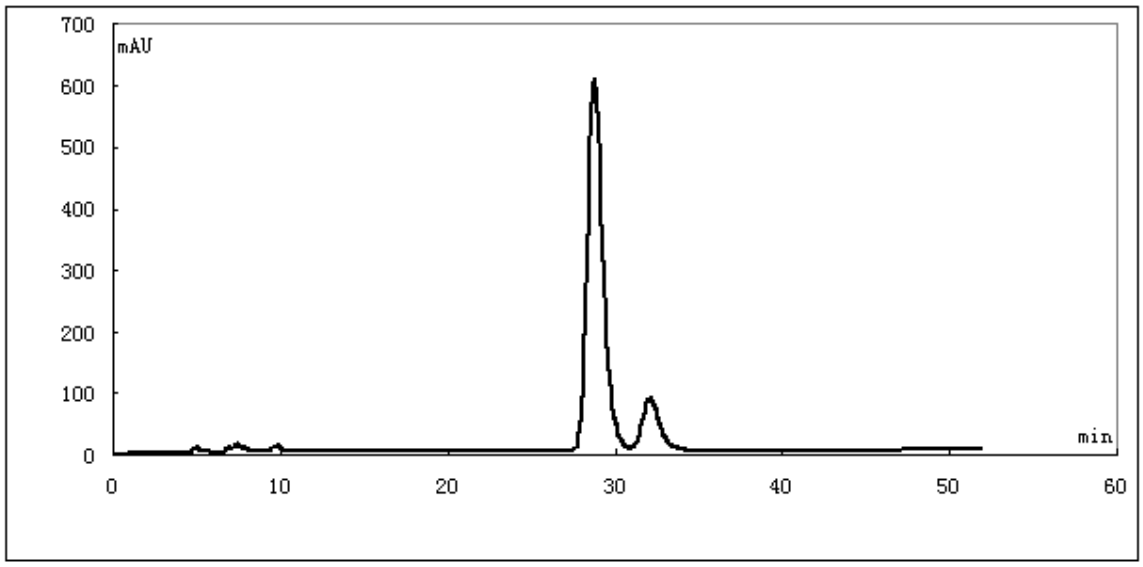
HPLC Analysis of (*S*)-2-(4-*tert*-butylphenyl)-1,1,1-trifluoro-3-nitropropan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 9.8 min, t_2 (minor) = 19.4 min, α = 2.62, 86% ee.



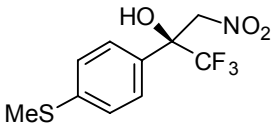


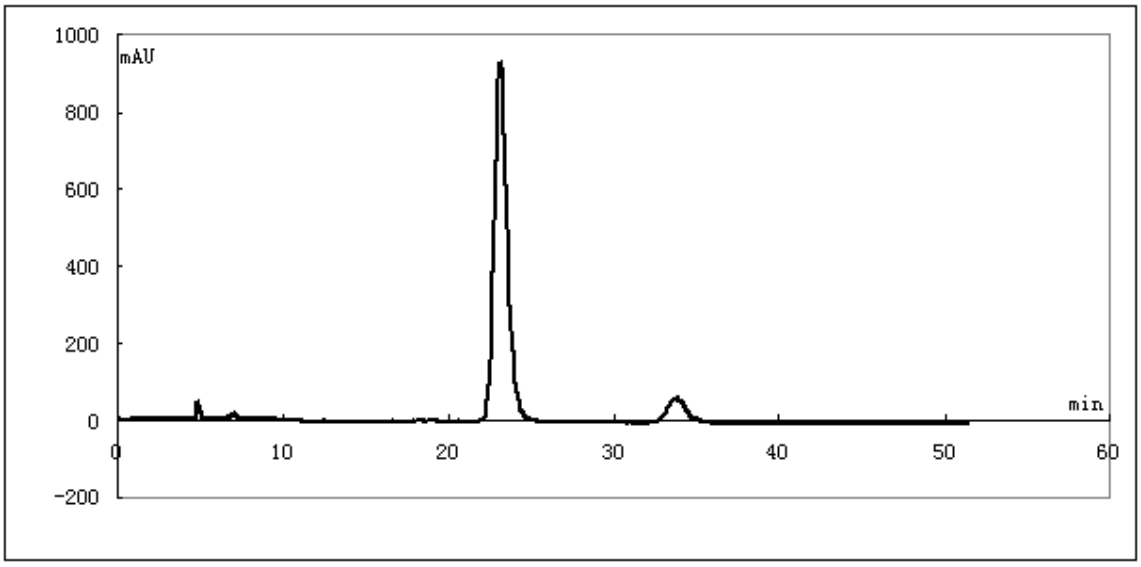
HPLC Analysis of (*S*)-1,1,1-trifluoro-2-(4-methoxyphenyl)-3-nitropropan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 28.8 min, t_2 (minor) = 32.1 min, α = 1.13, 76% ee.



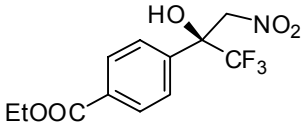


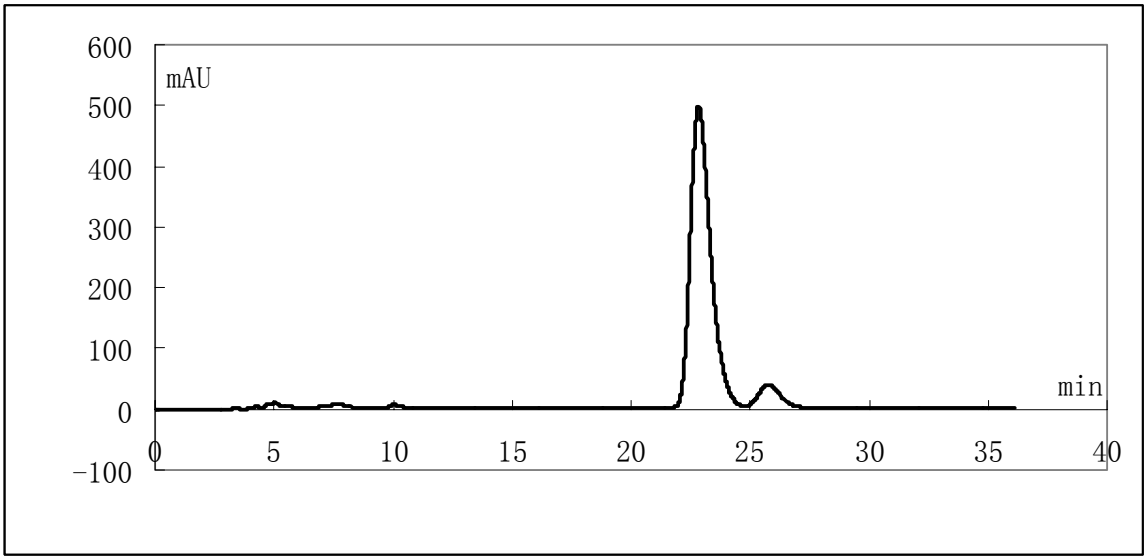
HPLC Analysis of (*S*)-1,1,1-trifluoro-2-(4-methylthiophenyl)-3-nitropropan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 23.2 min, t_2 (minor) = 33.8 min, α = 1.55, 84% ee.


HO
NO2
CF3
MeS


1000
mAU
800
600
400
200
0
min
0
10
20
30
40
50
60
-200

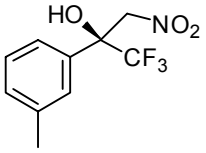
HPLC Analysis of (*S*)-ethyl 4-(1,1,1-trifluoro-2-hydroxy-3-nitro-2-propyl)benzoate: Daicel Chiralcel OD column, hexanes:IPA (93:7), 1 mL/min, λ= 214 nm, t_1 (major) = 22.8 min, t_2 (minor) = 25.8 min, α = 1.16, 84% ee.

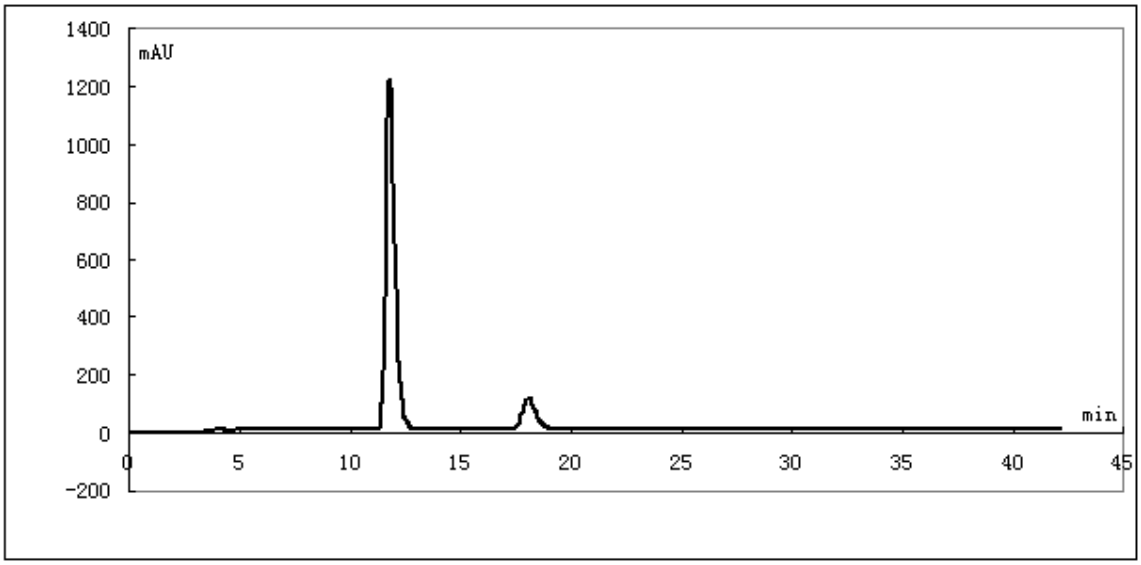




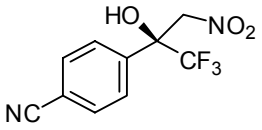
HPLC Analysis of (*S*)-1,1,1-trifluoro-3-nitro-2-(3-tolyl)propan-2-ol:

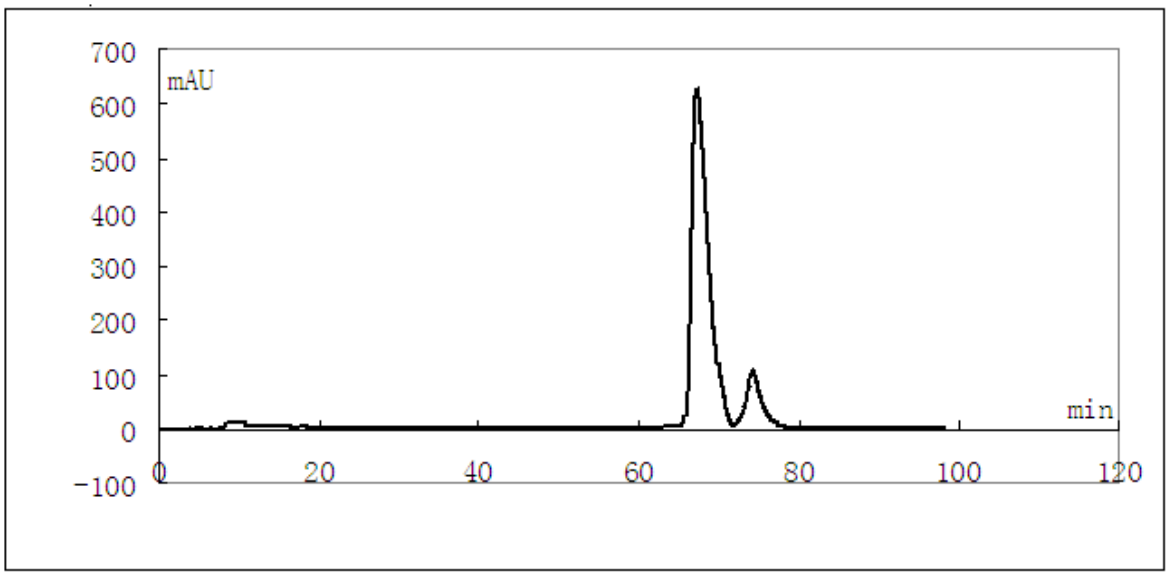
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 11.8 min, t_2 (minor) = 18.9 min, α = 1.90, 80% ee.





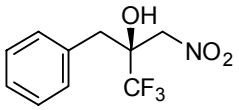
HPLC Analysis of (*S*)-4-(1,1,1-trifluoro-2-hydroxy-3-nitro-2-propyl)benzonitrile:
Daicel Chiralcel OD column, hexanes:IPA (95:5), 1 mL/min, λ= 214 nm, t_1 (major) = 67.3 min, t_2 (minor) = 73.7 min, α = 1.10, 75% ee.

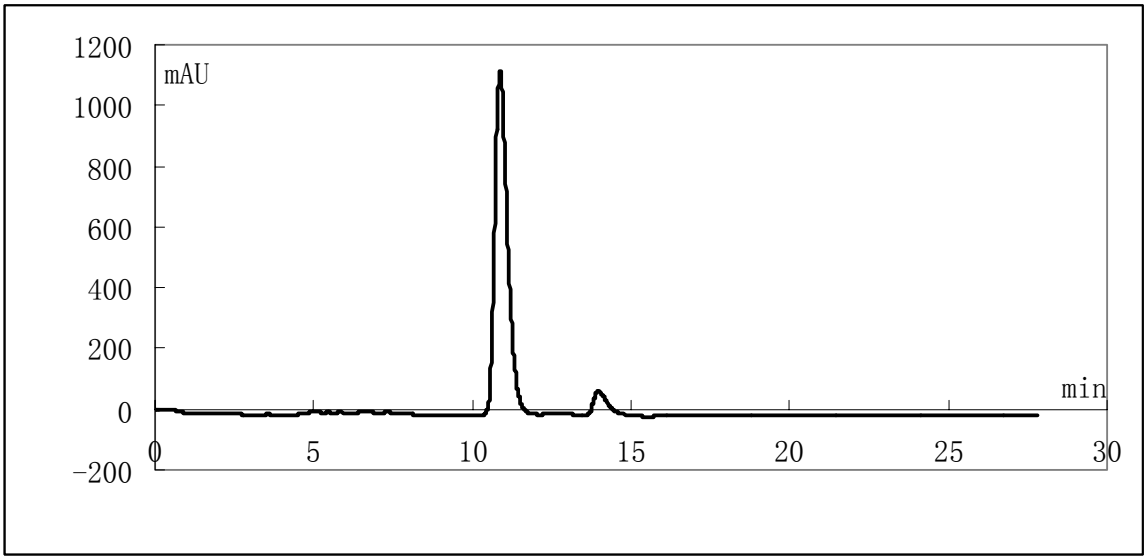




HPLC Analysis of (*S*)-2-benzyl-1,1,1-trifluoro-3-nitropropan-2-ol:

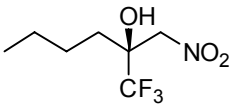
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) = 10.9 min, t_2 (minor) = 14.0 min, α = 1.44, 88% ee.

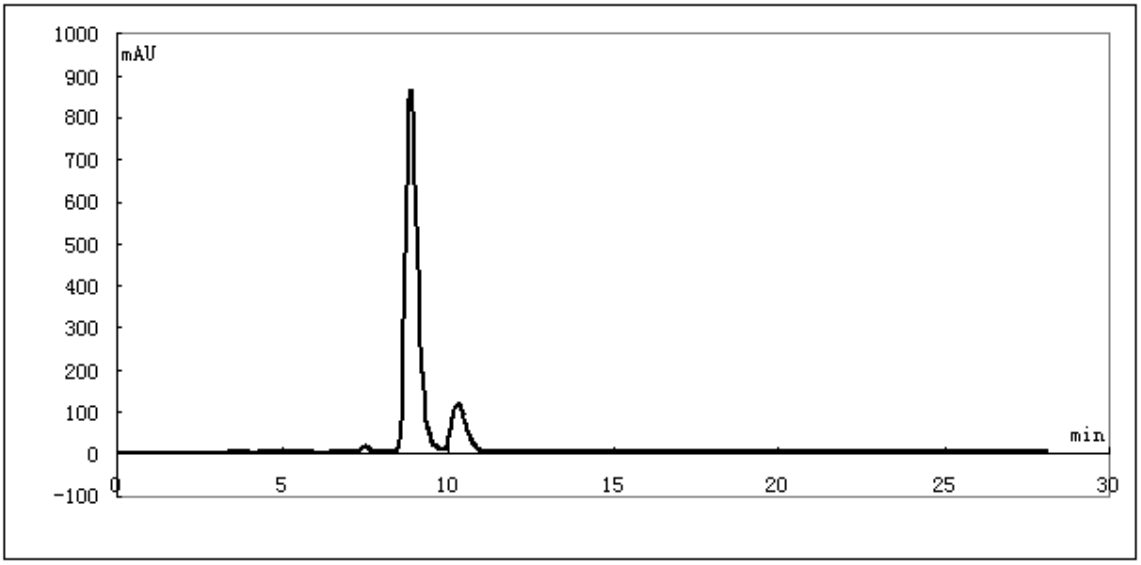




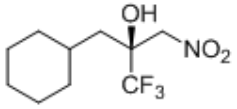
HPLC Analysis of (*S*)-1,1,1-trifluoro-2-(nitromethyl)hexan-2-ol:

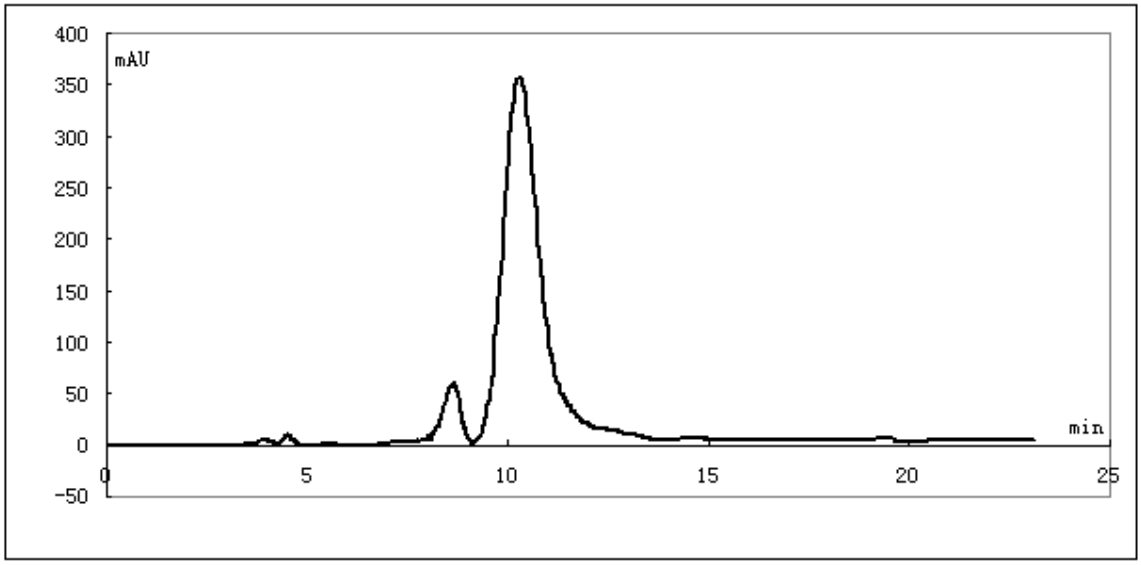
Daicel Chiralcel OD column, hexanes:IPA (95:5), 1 mL/min, λ= 214 nm, t_1 (major) = 8.9 min, t_2 (minor) = 10.3 min, α = 1.28, 80% ee.



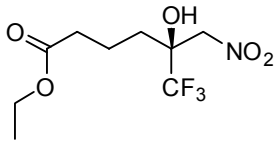


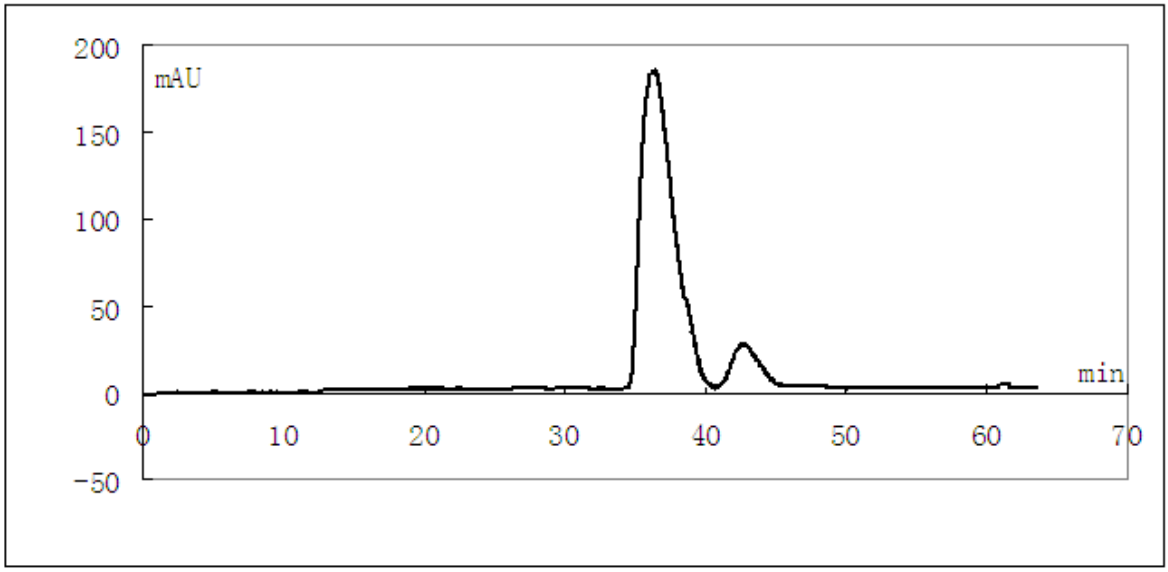
HPLC Analysis of (*S*)-3-cyclohexyl-1,1,1-trifluoro-2-(nitromethyl)propan-2-ol:
Daicel Chiralpak AS column, hexanes:IPA (97:3), 1 mL/min, λ= 214 nm, t_1 (minor) = 8.7 min, t_2 (major) = 10.3 min, α = 1.33, 91% ee.



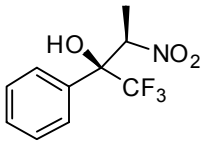


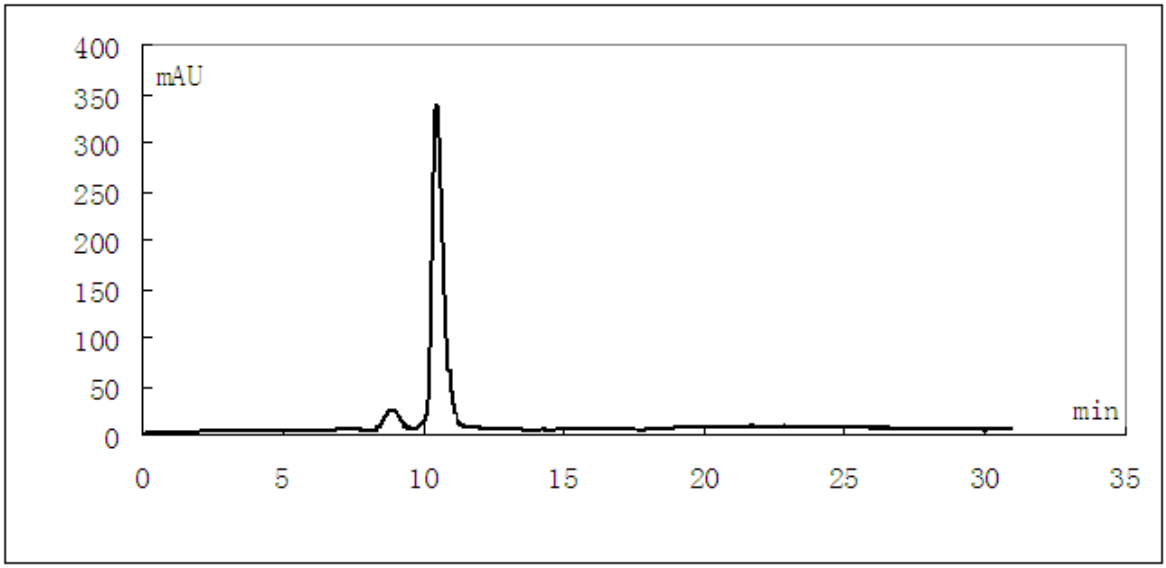
HPLC Analysis of (*S*)-ethyl 6,6,6-trifluoro-5-hydroxy-5-(nitromethyl)hexanoate:
Daicel Chiralcel OJ column, hexanes:IPA (98:2), 1 mL/min, λ= 214 nm, t_1 (major) = 36.3 min, t_2 (minor) = 42.4 min, α = 1.19, 82% ee.



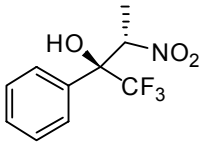


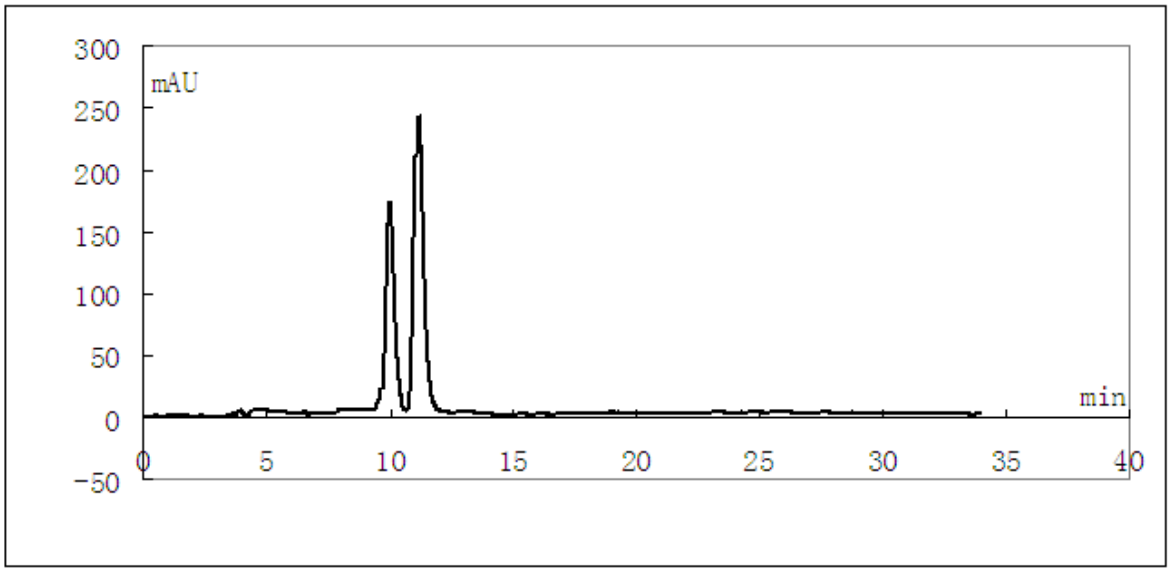
HPLC Analysis of (2*S*,3*R*)-1,1,1-trifluoro-3-nitro-2-phenylbutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (98:2), 1 mL/min, λ= 214 nm, t_1 (minor) = 8.9 min, t_2 (major) = 10.5 min, α = 1.32, 91% ee.



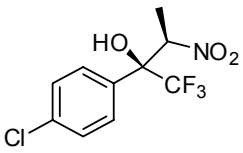


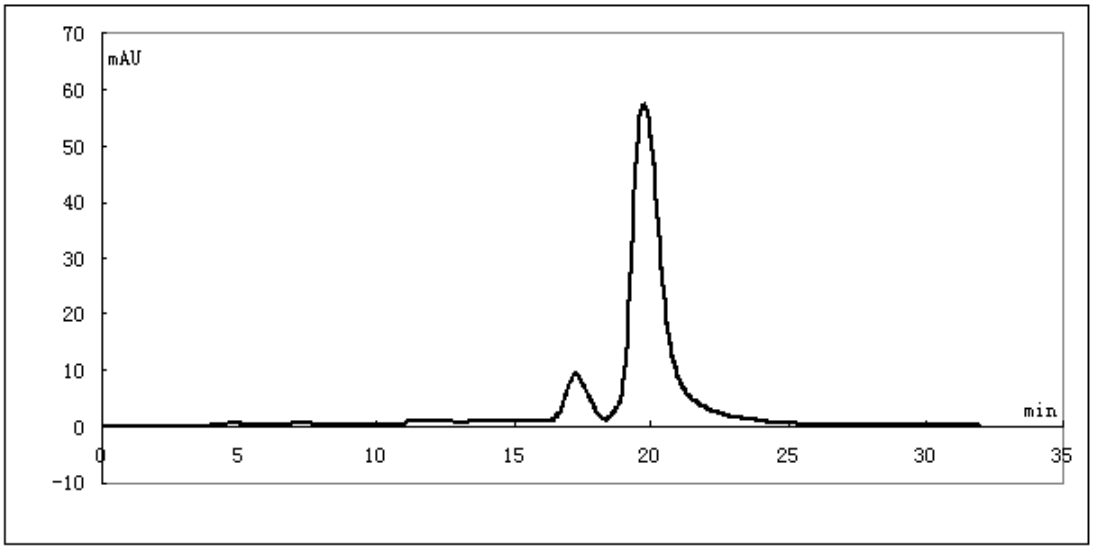
HPLC Analysis of (2*S*,3*S*)-1,1,1-trifluoro-3-nitro-2-phenylbutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (97:3), 1 mL/min, λ= 214 nm, t_1 (minor) = 10.0 min, t_2 (major) = 11.2 min, α = 1.20, 16% ee.



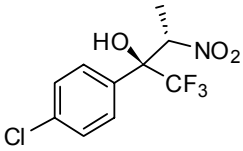


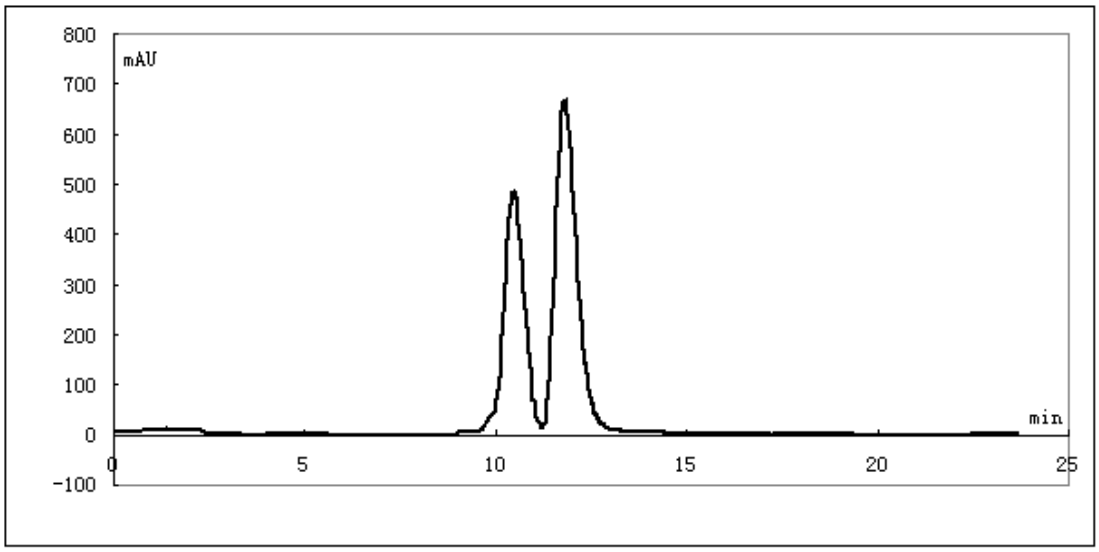
HPLC analysis of (2*S*,3*R*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (96:4), 1 mL/min, λ= 214 nm, t_1 (minor) = 17.4 min, t_2 (major) = 19.7 min, α = 1.17, 83% ee.



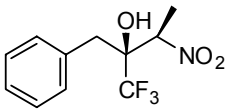


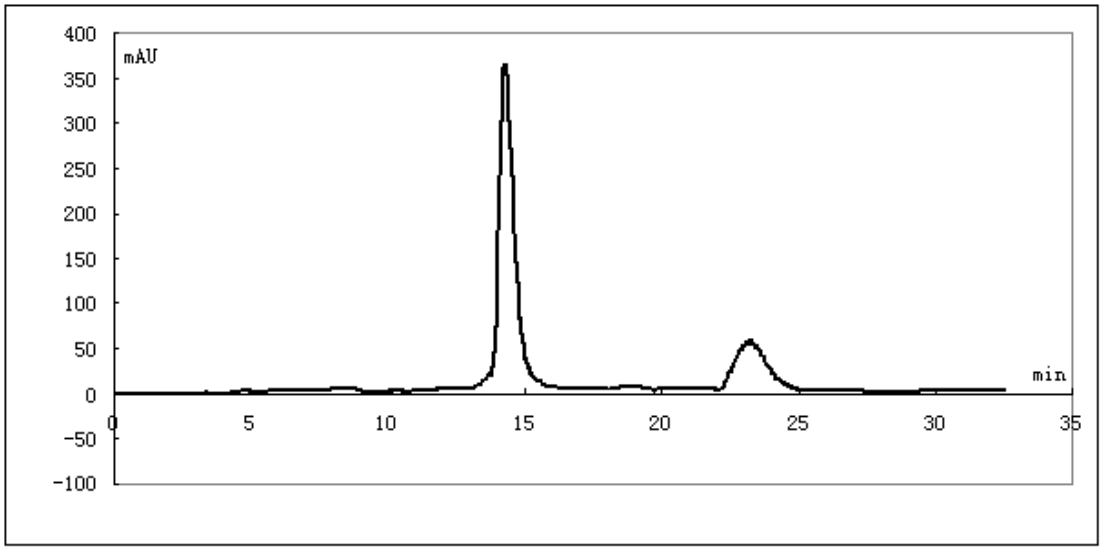
HPLC analysis of (2*S*,3*S*)-2-(4-chlorophenyl)-1,1,1-trifluoro-3-nitrobutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (93:7), 1 mL/min, λ= 214 nm, t_1 (minor) = 10.5 min, t_2 (major) = 11.8 min, α = 1.20, 30% ee.



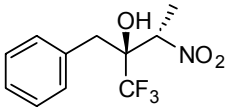


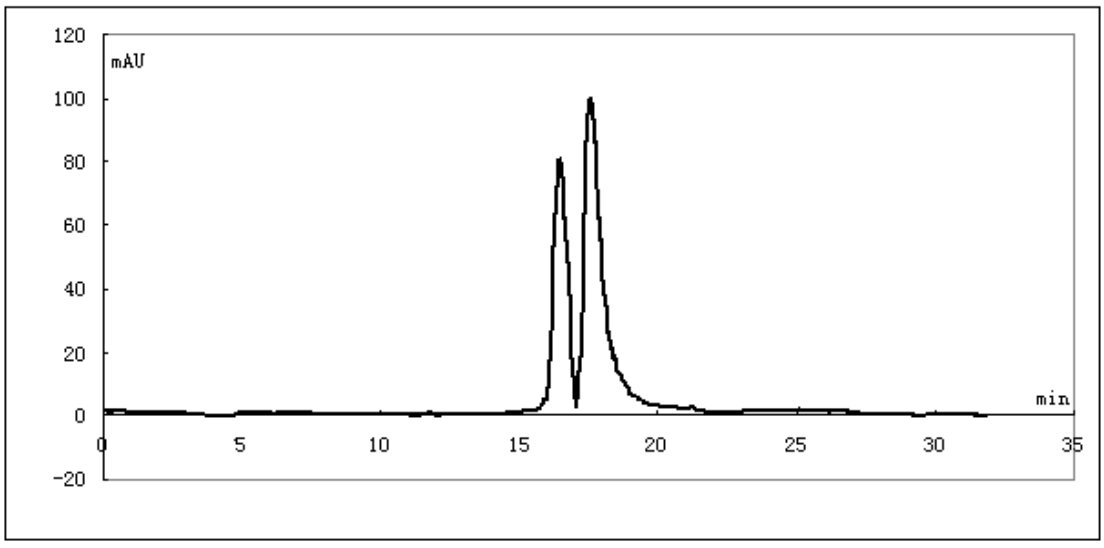
HPLC analysis of (2*S*,3*R*)-2-benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (90:10), 1 mL/min, λ= 214 nm, t_1 (major) =14.3 min, t_2 (minor) = 23.0 min, α = 1.83, 78% ee.





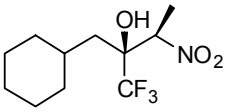
HPLC analysis of (2*S*,3*S*)-2-benzyl-1,1,1-trifluoro-3-nitrobutan-2-ol:
Daicel Chiralcel OD column, hexanes:IPA (94:6), 1 mL/min, λ= 214 nm, t_1 (minor) =16.5 min, t_2 (major) = 17.6 min, α = 1.08, 21% ee.

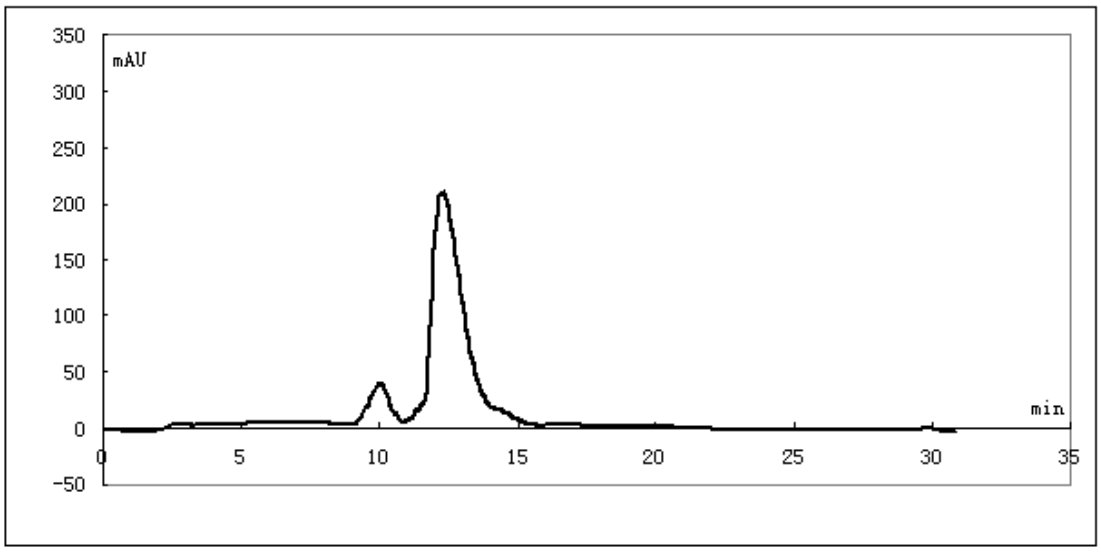




HPLC analysis of (2*S*,3*R*)-2-(cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol:

Daicel Chiralpak AS column, hexanes:IPA (96:4), 1 mL/min, λ= 214 nm, t_1 (minor) =10.1 min, t_2 (major) = 12.3 min, α = 1.35, 81% ee.





HPLC analysis of (2*S*,3*S*)-2-(cyclohexylmethyl)-1,1,1-trifluoro-3-nitrobutan-2-ol:
Daicel Chiralpak AS column, hexanes:IPA (94:6), 1 mL/min, λ= 214 nm, t_1 (minor) =10.9 min, t_2 (major) = 13.5 min, α = 1.37, 26% ee.