

Supporting Information

Asymmetric α -Hydroxylation of α -Aryl- δ -lactams with Molecular Oxygen under Phase-Transfer Conditions

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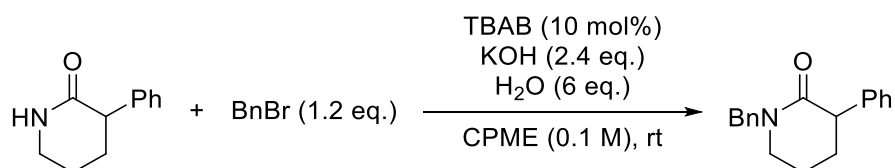
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General information

¹H NMR spectra were measured on JEOL JNM-ECA500 (500 MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane (in the case of CDCl₃) as an internal standard. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, and app = apparent), and coupling constants (Hz). ¹³C NMR spectra were recorded on JEOL JNM-ECA500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the solvent (CDCl₃) as an internal standard. ¹⁹F NMR spectra were measured on JEOL JNM-ECA500 (466 MHz) spectrometer. High performance liquid chromatography (HPLC) was performed on Shimadzu 20A instruments using Daicel CHIRALPAK IC or IC-3 4.6 mm × 25 cm column. The high-resolution mass spectra (HRMS) were performed on Thermo Scientific EXACTIVE PLUS. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout the work, Merck precoated TLC plates (silica gel 60 GF₂₅₄, 0.25 mm) were used. The products were purified by flash column chromatography on neutral silica gel 60N (Kanto Chemical Co. Inc., 40-50 μm). Dichloromethane (CH₂Cl₂), toluene, and tetrahydrofuran (THF) were purchased from Kanto Chemical Co. Inc. and Wako Pure Chemistry Co. Inc. as “Dehydrated”.

Chiral ammonium salt (*S*)-**1** was prepared by the procedure described in the literature.¹ The 3-arylpiperidin-2-ones (1-benzoyl-3-phenylpiperidin-2-one,² 1-(2,2-diphenylvinyl)-3-phenylpiperidin-2-one, **2a-2k**, and **2m**) were prepared by the procedure described in the literature.³

Preparation of 1-benzyl-3-phenylpiperidin-2-one.



To a test tube with a magnetic stir bar (cross type) were added 3-phenylpiperidin-2-one⁴ (87 mg, 0.5 mmol), tetrabutylammonium bromide (16 mg, 0.05 mmol), KOH (68 mg, 1.2 mmol), cyclopentyl methyl ether (5 mL), H₂O (0.054 mL, 3 mmol), and benzyl bromide (0.071 mL, 0.6 mmol) at 0 °C. The mixture was vigorously stirred at room temperature for 11 h. The resulting mixture was passed through silica gel pad (eluent: ethyl acetate, EtOAc) and concentrated in vacuo. Purification by flash column chromatography (hexane/EtOAc = 3/2) gave 1-benzyl-3-phenylpiperidin-2-one (66 mg, 0.25 mmol, 50%). The spectra accorded with the literature.² (¹H NMR (500 MHz, CDCl₃) δ 7.38-7.27 (m, 7H), 7.26-7.20 (m, 3H), 4.71 (d, *J* = 15.0 Hz, 1H), 4.64 (d, *J* = 15.0 Hz, 1H), 3.74 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.36 (ddd, *J* = 12.3, 8.0, 5.3 Hz, 1H), 3.30 (dt, *J*_d = 12.0 Hz, *J*_t = 5.8 Hz, 1H), 2.22-2.14 (m, 1H), 2.02-1.93 (m, 1H), 1.93-1.84 (m, 1H), 1.82-1.73 (m, 1H))

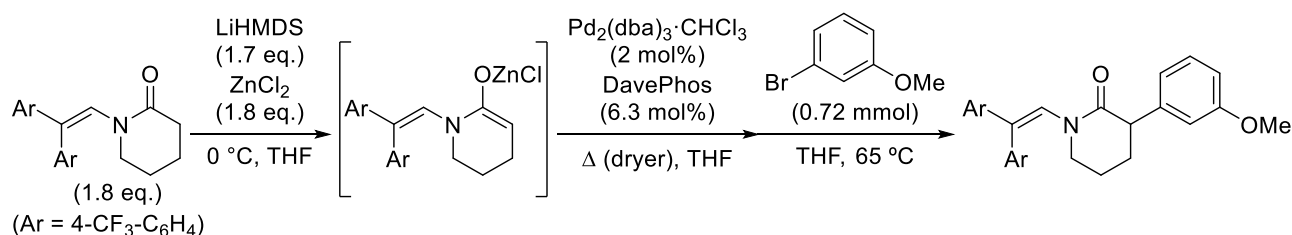
¹ T. Kano, Y. Hayashi, K. Maruoka *J. Am. Chem. Soc.* **2013**, *135*, 7134.

² A. de Filippis, D. G. Pardo, J. Cossy *Tetrahedron*, **2004**, *60*, 9757.

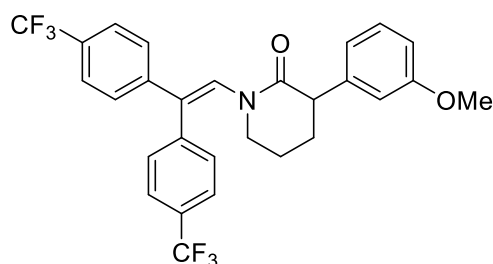
³ T. Inukai, T. Kano, K. Maruoka *Angew. Chem. Int. Ed.* **2020**, *59*, 2211.

⁴ S. Nunokawa, M. Minamisawa, K. Nakano, Y. Ichikawa, H. Kotsuki *Synlett*, **2015**, *26*, 2301.

Preparation of 1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)-3-(3-methoxyphenyl)piperidin-2-one (**2c**).



To a solution of 1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)piperidin-2-one³ (0.54 g, 1.3 mmol) in dry THF (3.6 mL) was added 0.53 M LiHMDS solution (2.3 mL, 1.2 mmol) at 0 °C. After stirring at 0 °C for 30 min, a solution of 2 M ZnCl₂ in 2-methyltetrahydrofuran (0.66 mL, 1.3 mmol) was added, and the mixture was stirred for 30 min at room temperature. Pd₂(dba)₃·CHCl₃ (16 mg, 0.015 mmol) and DavePhos (18 mg, 0.045 mmol) were dissolved in dry THF (1.6 mL) under an argon atmosphere. The Pd solution was heated by a hairdryer until the color changed from dark purple to dark brown. To the zinc enolate solution were added the Pd solution and 3-bromoanisole (0.091 mL, 0.72 mmol), and the mixture was heated at 65 °C (25 h, oil bath) under an argon atmosphere. The reaction mixture was cooled to room temperature, quenched with NH₄Cl solution and brine, and extracted with EtOAc. The organic phase was dried over Na₂SO₄ and concentrated.³ Purification by flash column chromatography (hexane/EtOAc = 3/1) gave **2c** (0.32 g, 0.61 mmol, 84%).



White solid.

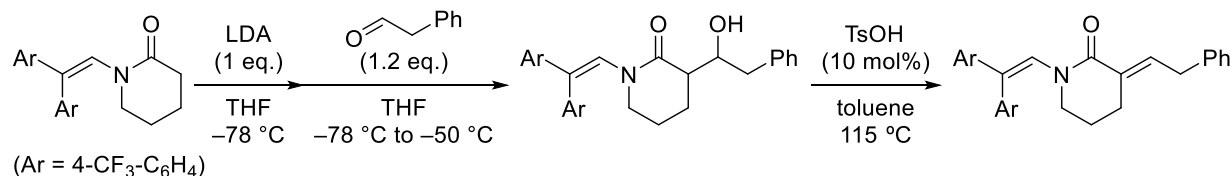
¹H NMR (500 MHz, CDCl₃) δ 7.68 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.38 (s, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.29-7.24 (m, 1H), 6.83-6.79 (m, 1H), 6.78-6.74 (m, 2H), 3.82 (s, 3H), 3.74 (dd, *J* = 8.3, 6.8 Hz, 1H), 3.12-3.08 (app t, 2H), 2.20-2.13 (m, 1H), 1.97-1.88 (m, 1H), 1.82-1.74 (m, 1H), 1.72-1.62 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 172.0, 159.8, 144.2, 142.5, 142.3, 130.8, 130.6, 130.3 (q, C-C-F₃, *J* = 32.3 Hz), 130.2, 129.7, 129.7 (q, C-C-F₃, *J* = 32.4 Hz), 128.2, 125.8 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.3 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 273.3 Hz), 124.1 (q, C-F₃, *J* = 274.1 Hz), 120.5, 114.7, 111.9, 55.3, 50.1, 49.1, 29.9, 21.6

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₂₄F₆NO₂ 520.1706; Found 520.1690.

Preparation of (*E*)-1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)-3-(2-phenylethylidene)piperidin-2-one (**2l**).



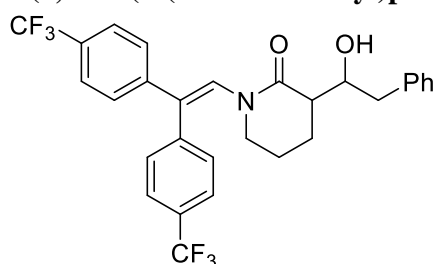
To a 0.77 M LDA solution (1.3 mL, 1.0 mmol) was added a solution of 1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)piperidin-2-one³ (0.41 g, 1.0 mmol) in dry THF (6 mL) at -78 °C. After stirring at -78 °C for 30 min, a solution of phenylacetaldehyde (0.14 mL, 1.2 mmol) in dry THF (2 mL) was added at -78 °C. The reaction mixture was warmed to -50 °C slowly, and quenched with 10% aqueous citric acid at -50 °C. After warming to room temperature, the mixture was extracted with EtOAc. The organic phase was washed with brine, dried over Na₂SO₄, and concentrated.⁵ Purification by flash column chromatography (hexane/EtOAc =

⁵ D. Lynch, R. E. Deasy, L.-A. Clarke, C. N. Slattery, U. B. R. Khandavilli, S. E. Lawrence, A. R. Maguire,

7/3 to 7/4) gave both diastereomers of 1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (0.32 g, 0.59 mmol, 59%, major/minor = 64/36).

A solution of 1-(2,2-bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (0.32 g, 0.59 mmol, major/minor = 64/36) and *p*-toluenesulfonic acid monohydrate (TsOH·H₂O, 11 mg, 0.060 mmol) in toluene (0.59 mL) was heated at 115 °C (oil bath) for 30 h under a nitrogen atmosphere. The reaction mixture was diluted with CH₂Cl₂, hexane, and EtOAc and charged to a silica gel column directly. Purification by flash-column chromatography (hexane/EtOAc = 9/2) gave **2I** (0.17 g, 0.32 mmol, 54%).

1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (major)



White solid.

¹H NMR (500 MHz, CDCl₃) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.33-7.29 (m, 4H), 7.28-7.22 (m, 4H), 4.39 (d, *J* = 3.0 Hz, 1H), 4.12-4.06 (m, 1H), 3.04-2.96 (m, 3H), 2.77 (dd, *J* = 13.8, 8.3 Hz, 1H), 2.49-2.42 (m, 1H), 2.05-1.99 (m, 1H), 1.75-1.69 (m, 1H), 1.64-1.49 (m, 2H)

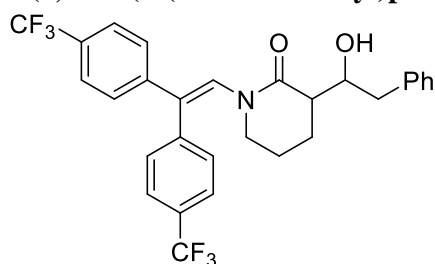
¹³C NMR (125 MHz, CDCl₃) δ 174.3, 143.9, 142.0, 138.4, 130.9, 130.4, 130.4 (q, C-C-F₃, *J* = 32.4 Hz), 129.9, 129.9 (q, C-C-F₃, *J* =

33.5 Hz), 129.7, 128.5, 128.3, 126.5, 125.8 (d, C-C-C-F₃, *J* = 3.5 Hz), 125.4 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 272.9 Hz), 124.0 (q, C-F₃, *J* = 272.9 Hz), 73.7, 49.4, 46.0, 40.5, 23.4, 22.2

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₉H₂₆F₆NO₂ 534.1862; Found 534.1859.

1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (minor)



White solid.

¹H NMR (500 MHz, CDCl₃) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.36-7.30 (m, 5H), 7.28-7.24 (m, 5H), 4.55-4.49 (m, 1H), 3.02-2.93 (m, 2H), 2.83 (dd, *J* = 13.8, 9.3 Hz, 1H), 2.74 (dd, *J* = 13.5, 5.5 Hz, 1H), 2.66 (d, *J* = 5.5 Hz, 1H), 2.59-2.53 (m, 1H), 1.99-1.92 (m, 1H), 1.85-1.73 (m, 2H), 1.65-1.57 (m, 1H)

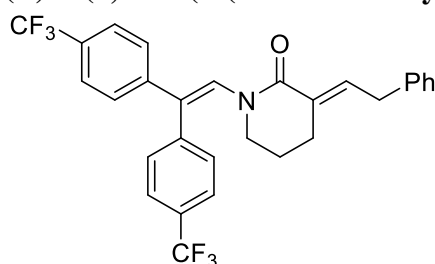
¹³C NMR (125 MHz, CDCl₃) δ 173.5, 144.2, 142.1, 138.5, 130.6, 130.4, 130.3 (q, C-C-F₃, *J* = 32.3 Hz), 130.1, 129.8 (q, C-C-F₃, *J* =

32.4 Hz), 129.3, 128.7, 128.3, 126.7, 125.8 (d, C-C-C-F₃, *J* = 3.5 Hz), 125.4 (d, C-C-C-F₃, *J* = 2.4 Hz), 124.2 (q, C-F₃, *J* = 274.5 Hz), 124.1 (q, C-F₃, *J* = 274.1 Hz), 72.7, 49.6, 46.7, 40.1, 22.6, 20.4

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₉H₂₆F₆NO₂ 534.1862; Found 534.1860.

(*E*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(2-phenylethylidene)piperidin-2-one (**2I**)



White solid.

¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.50 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.33-7.28 (app t, 2H), 7.27-7.16 (m, 6H), 3.50 (d, *J* = 8.0 Hz, 2H), 3.04-2.99 (app t, 2H), 2.56 (t, *J* = 5.5 Hz, 2H), 1.76-1.70 (m, 2H)

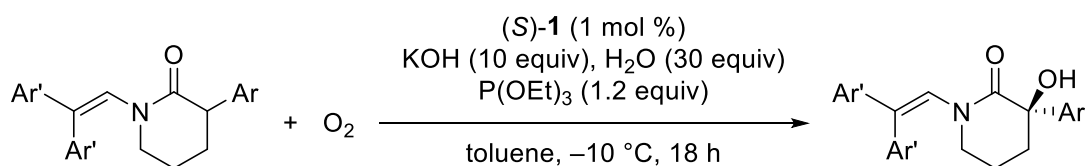
¹³C NMR (125 MHz, CDCl₃) δ 165.6, 144.6, 142.6, 139.7, 138.8, 131.4, 130.8, 130.2 (q, C-C-F₃, *J* = 32.3 Hz), 129.6 (q, C-C-F₃, *J* =

32.4 Hz), 128.9, 128.8, 128.7, 128.3 (2C), 126.6, 125.7 (d, C-C-C-F₃, *J* = 3.5 Hz), 125.4 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.3 (q, C-F₃, *J* = 273.3 Hz), 124.1 (q, C-F₃, *J* = 272.9 Hz), 50.0, 34.5, 24.7, 23.0

¹⁹F NMR (466 MHz, CDCl₃) δ -62.3 (s, 3F), -62.5 (s, 3F)

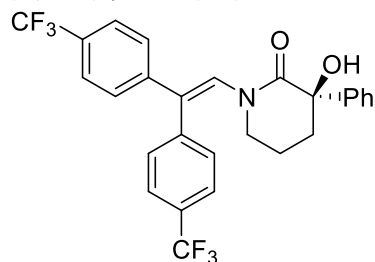
HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₉H₂₄F₆NO 516.1757; Found 516.1755.

Typical procedure of enantioselective hydroxylation of 3-arylpiperidin-2-one derivatives with molecular oxygen under phase-transfer conditions.



To a test tube with a magnetic stir bar (cross type) were added **2a** (49 mg, 0.10 mmol), (*S*)-**1** (1.1 mg, 0.0010 mmol), KOH (0.058 g, 1.0 mmol), dry toluene (1.0 mL), triethyl phosphite (0.021 mL, 0.12 mmol), and H₂O (0.054 mL, 3.0 mmol) at $-10\text{ }^{\circ}\text{C}$. The mixture was vigorously stirred (1350 rpm) under an oxygen atmosphere at $-10\text{ }^{\circ}\text{C}$ for 18 h. The resulting mixture was passed through silica gel pad (eluent: EtOAc) and concentrated in vacuo. Purification by flash column chromatography (hexane/CH₂Cl₂/EtOAc = 6/6/1) gave **3a** (46 mg, 0.090 mmol, 91%).⁶

(*R*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpiperidin-2-one (**3a**)



White solid.

¹H NMR (500 MHz, CDCl₃) δ 7.64 (d, $J = 8.5$ Hz, 2H), 7.57 (d, $J = 8.5$ Hz, 2H), 7.40-7.31 (m, 8H), 7.30 (d, $J = 8.5$ Hz, 2H), 3.92 (s, 1H), 3.10 (ddd, $J = 12.9, 8.4, 5.6$ Hz, 1H), 2.99 (dt, $J_d = 12.5$ Hz, $J_t = 5.8$ Hz, 1H), 2.35 (dt, $J_d = 13.8$ Hz, $J_t = 5.1$ Hz, 1H), 2.12 (ddd, $J = 13.6, 11.1, 4.9$ Hz, 1H), 1.76-1.68 (m, 1H), 1.60-1.51 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 174.6, 143.73, 143.70, 141.8, 132.5, 130.6

(q, C-C-F₃, $J = 32.8$ Hz), 130.5, 130.2 (q, C-C-F₃, $J = 32.4$ Hz), 129.5, 128.6, 128.31, 128.28, 125.9 (d, C-C-C-F₃, $J = 3.6$ Hz), 125.8, 125.5 (d, C-C-C-F₃, $J = 3.6$ Hz), 124.2 (q, C-F₃, $J = 272.9$ Hz), 124.0 (q, C-F₃, $J = 272.9$ Hz), 75.8, 49.7, 34.6, 19.3

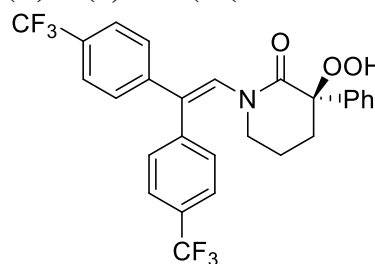
¹⁹F NMR (466 MHz, CDCl₃) δ -62.45 (s, 3F), -62.51 (s, 3F)

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₂₇H₂₂F₆NO₂ 506.1549; Found 506.1530.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 10.3 min (major) and 19.9 min (minor).

$[\alpha]_D^{29} = +9.1$ (c 2.0, CHCl₃, 95% ee)

(*R*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroperoxy-3-phenylpiperidin-2-one (**3a'**)



Performed using KOH (5 equiv) and H₂O (15 equiv) without triethyl phosphite for 72 h.

Eluent for column chromatography: CH₂Cl₂. 39 mg, 76%, colorless oil.

¹H NMR (500 MHz, CDCl₃) δ 10.50 (s, 1H), 7.63 (d, $J = 8.0$ Hz, 2H), 7.58 (d, $J = 8.5$ Hz, 2H), 7.45-7.39 (m, 3H), 7.38-7.33 (m, 4H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.26 (s, 1H), 3.06 (ddd, $J = 12.5, 9.5, 5.5$ Hz, 1H), 2.95 (dt, $J_d = 12.3$ Hz, $J_t = 5.1$ Hz, 1H), 2.36-2.26 (m, 2H), 1.77-1.69 (m, 1H), 1.57-1.49 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 173.2, 143.3, 141.5, 137.7, 133.9, 130.8 (q, C-C-F₃, $J = 33.5$ Hz), 130.4 (q, C-C-F₃, $J = 32.4$ Hz), 130.3, 129.2, 128.9, 128.7, 128.3, 127.3, 125.9 (d, C-C-C-F₃, $J = 3.5$ Hz), 125.5 (d, C-C-C-F₃, $J = 3.5$ Hz), 124.1 (q, C-F₃, $J = 274.1$ Hz), 123.9 (q, C-F₃, $J = 272.9$ Hz), 86.8, 48.9, 30.9, 19.2

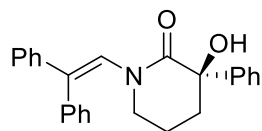
¹⁹F NMR (466 MHz, CDCl₃) δ -62.48 (s, 3F), -62.54 (s, 3F)

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₂₇H₂₂F₆NO₃ 522.1498; Found 522.1498.

Enantiomeric excess of **3a'** was determined after conversion to **3a** by reduction (PPh₃).

$[\alpha]_D^{30} = -1.0$ (c 1.0, CHCl₃, 93% ee)

⁶ 1 mmol scale: 0.49 g (**2a**), 0.44 g ((*R*)-**3a**, 87%, 94% ee)

(R)-1-(2,2-Diphenylvinyl)-3-hydroxy-3-phenylpiperidin-2-one

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 4/4/1. 12 mg, 33%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.41-7.21 (m, 15 H), 7.17 (s, 1H), 4.05 (s, 1H), 3.11 (ddd, *J* = 12.8, 8.8, 5.5 Hz, 1H), 3.00 (dt, *J*_d = 12.5 Hz, *J*_t = 5.5 Hz, 1H), 2.29 (dt,

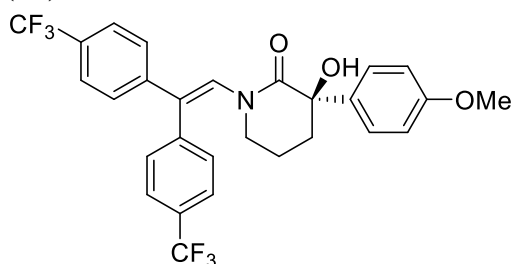
*J*_d = 13.8 Hz, *J*_t = 5.0 Hz, 1H), 2.09 (ddd, *J* = 13.4, 11.6, 4.9 Hz, 1H), 1.68-1.59 (m, 1H), 1.52-1.41 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 174.4, 144.2, 140.7, 138.6, 136.1, 130.1, 128.7, 128.5, 128.3, 128.2, 128.1, 128.03, 127.98, 126.9, 126.0, 75.8, 49.3, 34.7, 19.3

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₅H₂₄NO₂ 370.1802; Found 370.1792.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 18.4 min (major) and 31.0 min (minor).

[α]_D³⁰ = +26.0 (c 1.0, CHCl₃, 87% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(4-methoxyphenyl)piperidin-2-one**(3b)**

Performed for 72 h.

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 4/4/1. 47 mg, 88%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.29 (s, 1H), 7.22 (d, *J* = 9.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 3.90 (s, 1H), 3.83 (s, 3H), 3.09 (ddd, *J* = 12.8, 8.5, 5.8 Hz, 1H), 2.97 (dt, *J*_d = 12.5 Hz, *J*_t = 5.8 Hz, 1H), 2.35 (dt, *J*_d =

13.8 Hz, *J*_t = 5.0 Hz, 1H), 2.10 (ddd, *J* = 13.8, 11.3, 5.3 Hz, 1H), 1.75-1.66 (m, 1H), 1.58-1.48 (m, 1H)

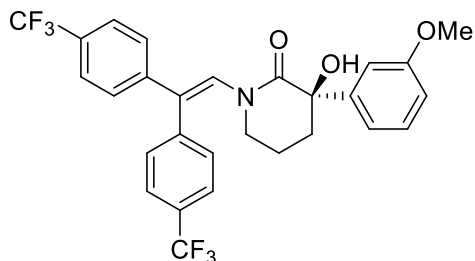
¹³C NMR (125 MHz, CDCl₃) δ 174.7, 159.5, 143.7, 141.8, 135.6, 132.6, 130.6 (q, C-C-F₃, *J* = 32.8 Hz), 130.4, 130.1 (q, C-C-F₃, *J* = 33.5 Hz), 129.5, 128.3, 127.2, 125.9 (d, C-C-C-F₃, *J* = 3.5 Hz), 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 272.9 Hz), 124.0 (q, C-F₃, *J* = 272.9 Hz), 113.9, 75.4, 55.4, 49.5, 34.3, 19.3

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₂₄F₆NO₃ 536.1655; Found 536.1635.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 16.1 min (major) and 28.4 min (minor).

[α]_D²⁹ = +8.3 (c 2.0, CHCl₃, 85% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-methoxyphenyl)piperidin-2-one**(3c)**

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 4/4/1. 51 mg, 96%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.32 (s, 1H), 7.31-7.27 (m, 3H), 6.98-6.95 (app t, 1H), 6.89-6.85 (m, 2H), 3.93 (s, 1H), 3.84 (s, 3H), 3.08 (ddd, *J* = 12.9, 8.6, 5.4 Hz, 1H), 2.98 (dt, *J*_d = 12.5 Hz, *J*_t = 5.8 Hz, 1H), 2.33 (dt, *J*_d = 13.7 Hz, *J*_t = 5.3 Hz, 1H), 2.11 (ddd, *J* = 13.9, 11.1, 5.1 Hz, 1H), 1.75-1.67 (m, 1H), 1.62-1.52 (m,

1H)

¹³C NMR (125 MHz, CDCl₃) δ 174.6, 159.9, 145.4, 143.7, 141.8, 132.4, 130.6 (q, C-C-F₃, *J* = 33.1 Hz), 130.5, 130.1 (q, C-C-F₃, *J* = 32.4 Hz), 129.64, 129.61, 128.3, 125.9 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 272.9 Hz), 124.0 (q, C-F₃, *J* = 274.1 Hz), 118.1, 113.0, 112.3, 75.8, 55.4, 49.7, 34.6, 19.4

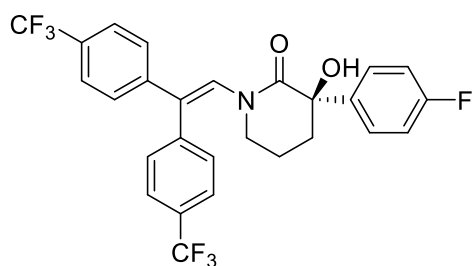
¹⁹F NMR (466 MHz, CDCl₃) δ -62.45 (s, 3F), -62.53 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₂₄F₆NO₃ 536.1655; Found 536.1633.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 14.1 min (major) and 30.9 min (minor).

$[\alpha]_{\text{D}}^{29} = +20.9$ (c 2.0, CHCl_3 , 95% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-fluorophenyl)-3-hydroxypiperidin-2-one (3d)



Performed for 72 h.

Eluent for column chromatography: hexane/ CH_2Cl_2 /EtOAc = 5/5/1. 25 mg, 47%, white solid.

^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.32-7.27 (m, 5H), 7.05 (t, J = 8.8 Hz, 2H), 3.87 (s, 1H), 3.12 (ddd, J = 12.6, 8.9, 5.4 Hz, 1H), 3.01 (dt, J_{d} = 12.5 Hz, J_{t} = 5.5 Hz, 1H), 2.28 (dt, J_{d} = 13.7 Hz, J_{t} = 5.1 Hz, 1H), 2.12 (ddd, J = 13.6, 11.4, 4.6 Hz, 1H), 1.77-

1.68 (m, 1H), 1.58-1.47 (m, 1H)

^{13}C NMR (125 MHz, CDCl_3) δ 174.3, 162.5 (d, C-F, J = 249.0 Hz), 143.6, 141.8, 139.8 (d, C-C-C-C-F, J = 3.5 Hz), 132.9, 130.7 (q, C-C-F₃, J = 32.4 Hz), 130.4, 130.3 (q, C-C-F₃, J = 32.7 Hz), 129.3, 128.3, 127.7 (d, C-C-C-F, J = 8.4 Hz), 125.9 (d, C-C-C-F₃, J = 3.5 Hz), 125.5 (d, C-C-C-F₃, J = 3.5 Hz), 124.2 (q, C-F₃, J = 272.9 Hz), 124.0 (q, C-F₃, J = 274.1 Hz), 115.5 (d, C-C-F, J = 21.6 Hz), 75.4, 49.8, 34.9, 19.3

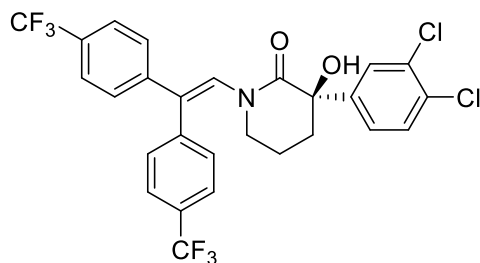
^{19}F NMR (466 MHz, CDCl_3) δ -62.47 (s, 3F), -62.52 (s, 3F), -113.7- -113.8 (m, 1F)

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{21}\text{F}_7\text{NO}_2$ 524.1455; Found 524.1434.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 207 nm, retention time: 8.3 min (major) and 11.3 min (minor).

$[\alpha]_{\text{D}}^{30} = +3.9$ (c 1.0, CHCl_3 , 88% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(3,4-dichlorophenyl)-3-hydroxypiperidin-2-one (3e)



Eluent for column chromatography: hexane/ CH_2Cl_2 /EtOAc = 6/6/1. 51 mg, 88%, white solid.

^1H NMR (500 MHz, CDCl_3) δ 7.70 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 2.5 Hz, 1H), 7.44 (d, J = 8.5 Hz, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.29 (s, 1H), 7.16 (dd, J = 8.5, 2.0 Hz, 1H), 3.87 (s, 1H), 3.15 (ddd, J = 12.6, 8.9, 4.9 Hz, 1H), 3.04 (dt, J_{d} = 12.5 Hz, J_{t} = 5.5 Hz, 1H), 2.21 (dt, J_{d} = 14.0 Hz, J_{t} = 5.4 Hz, 1H), 2.13 (ddd, J = 13.8, 10.8, 4.5 Hz,

1H), 1.78-1.70 (m, 1H), 1.54-1.46 (m, 1H)

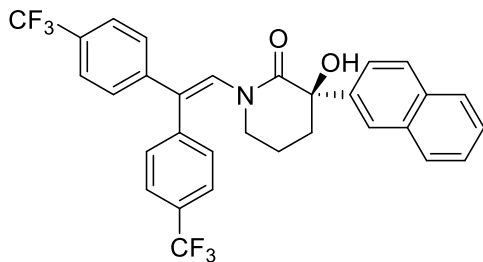
^{13}C NMR (125 MHz, CDCl_3) δ 173.6, 144.6, 143.5, 141.7, 133.4, 132.7, 132.4, 130.9 (q, C-C-F₃, J = 32.3 Hz), 130.6, 130.3, 130.3 (q, C-C-F₃, J = 33.5 Hz), 129.3, 128.3, 128.1, 126.1 (d, C-C-C-F₃, J = 3.6 Hz), 125.6 (d, C-C-C-F₃, J = 3.6 Hz), 125.3, 124.1 (q, C-F₃, J = 273.3 Hz), 123.9 (q, C-F₃, J = 274.0 Hz), 75.3, 49.9, 35.3, 19.3

^{19}F NMR (466 MHz, CDCl_3) δ -62.48 (s, 3F), -62.53 (s, 3F)

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{20}^{35}\text{Cl}_2\text{F}_6\text{NO}_2$ 574.0770; Found 574.0742.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 220 nm, retention time: 7.8 min (major) and 9.0 min (minor).

$[\alpha]_{\text{D}}^{28} = +39.1$ (c 2.0, CHCl_3 , 95% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(naphthalen-2-yl)piperidin-2-one (3f)

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 6/6/1. 51 mg, 91%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.90-7.83 (m, 3H), 7.76 (d, *J* = 1.0 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.56-7.51 (m, 2H), 7.49 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.41 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 4.05 (s, 1H), 3.10 (ddd, *J* = 12.5, 8.5, 5.5 Hz, 1H), 3.01 (dt, *J*_d = 12.5 Hz, *J*_t = 5.8 Hz, 1H), 2.48 (dt, *J*_d = 14.0 Hz, *J*_t = 5.3 Hz, 1H), 2.19 (ddd, *J* =

14.1, 10.6, 5.1 Hz, 1H), 1.79-1.70 (m, 1H), 1.63-1.53 (m, 1H)

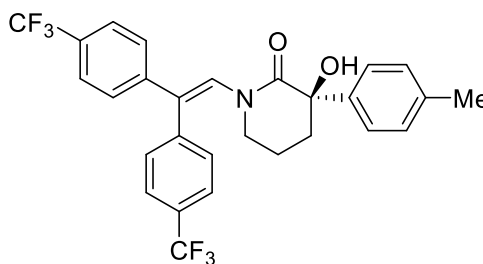
¹³C NMR (125 MHz, CDCl₃) δ 174.7, 143.8, 141.8, 140.9, 133.0, 132.9, 132.3, 130.6 (q, C-C-F₃, *J* = 33.5 Hz), 130.4, 130.1 (q, C-C-F₃, *J* = 33.5 Hz), 129.6, 128.7, 128.3, 128.2, 127.8, 126.7, 126.6, 125.9 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.0, 124.2 (q, C-F₃, *J* = 272.9 Hz), 123.9 (q, C-F₃, *J* = 274.0 Hz), 123.6, 76.0, 49.6, 34.4, 19.4

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.6 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₃₁H₂₄F₆NO₂ 556.1706 ; Found 556.1680.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 225 nm, retention time: 12.6 min (major) and 19.5 min (minor).

[α]_D²⁹ = +52.4 (c 2.0, CHCl₃, 95% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(*p*-tolyl)piperidin-2-one (3g)

Performed for 72 h.

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 6/6/1. 41 mg, 79%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.31 (s, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 3.90 (s, 1H), 3.08 (ddd, *J* = 12.5, 8.5, 5.5 Hz, 1H), 2.96 (dt, *J*_d = 13.0 Hz, *J*_t = 5.3 Hz, 1H), 2.37 (s, 3H), 2.35 (dt, *J*_d = 14.0

Hz, *J*_t = 5.3 Hz, 1H), 2.10 (ddd, *J* = 13.9, 11.1, 5.1 Hz, 1H), 1.75-1.66 (m, 1H), 1.59-1.49 (m, 1H)

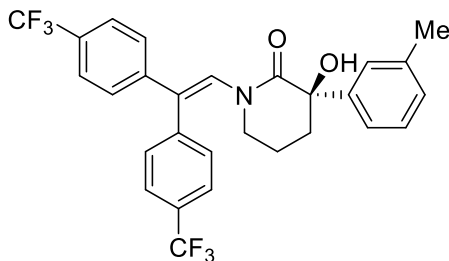
¹³C NMR (125 MHz, CDCl₃) δ 174.8, 143.7, 141.8, 140.6, 138.1, 132.4, 130.6 (q, C-C-F₃, *J* = 32.7 Hz), 130.5, 130.1 (q, C-C-F₃, *J* = 32.3 Hz), 129.6, 129.3, 128.3, 125.9 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.8, 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 274.1 Hz), 124.0 (q, C-F₃, *J* = 274.1 Hz), 75.6, 49.6, 34.3, 21.2, 19.3

¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₂₄F₆NO₂ 520.1706; Found 520.1685.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 11.2 min (major) and 32.2 min (minor).

[α]_D³⁰ = +17.1 (c 2.0, CHCl₃, 87% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(*m*-tolyl)piperidin-2-one (3h)

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 6/6/1. 40 mg, 78%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.35 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.28-7.24 (app t, 1H), 7.20 (s, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 3.91 (s, 1H), 3.07 (ddd, *J* = 12.9, 8.4, 5.6 Hz, 1H), 2.96 (dt, *J*_d = 12.5 Hz, *J*_t = 5.8 Hz, 1H), 2.40 (s, 3H), 2.36 (dt, *J*_d = 13.8 Hz, *J*_t = 5.3 Hz, 1H), 2.11 (ddd, *J* = 13.6, 10.9,

5.1 Hz, 1H), 1.75-1.66 (m, 1H), 1.59-1.49 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 174.8, 143.8, 143.6, 141.8, 138.4, 132.1, 130.6 (q, C-C-F₃, *J* = 32.3 Hz), 130.5, 130.1 (q, C-C-F₃, *J* = 33.5 Hz), 129.7, 129.1, 128.5, 128.3, 126.5, 125.9 (d, C-C-C-F₃, *J* = 3.5 Hz),

125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 272.9 Hz), 124.0 (q, C-F₃, *J* = 272.9 Hz), 122.9, 75.8, 49.6, 34.4, 21.8, 19.4

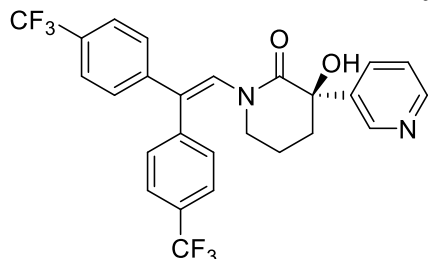
¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₂₄F₆NO₂ 520.1706; Found 520.1682.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 10.2 min (major) and 24.9 min (minor).

[α]_D²⁹ = +27.4 (c 2.0, CHCl₃, 95% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(pyridin-3-yl)piperidin-2-one (3j)



Eluent for column chromatography: EtOAc/CH₂Cl₂ = 3/1. 42 mg, 83%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 8.70-8.50 (br, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.69-7.65 (m, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.33-7.30 (m, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.30 (s, 1H), 3.97 (s, 1H), 3.15 (ddd, *J* = 12.5, 8.8, 5.3 Hz, 1H), 3.05 (dt, *J*_d = 12.5 Hz, *J*_t = 5.3 Hz, 1H), 2.28 (dt, *J*_d = 13.7 Hz, *J*_t = 5.3 Hz, 1H), 2.18 (ddd, *J* = 13.9, 11.4, 4.1 Hz, 1H), 1.80-1.72 (m, 1H), 1.59-1.48 (m, 1H)

¹³C NMR (125 MHz, CDCl₃) δ 173.5, 149.4, 147.4, 143.6, 141.7, 140.0, 133.7, 132.8, 130.8 (q, C-C-F₃, *J* = 33.5 Hz), 130.4, 130.2 (q, C-C-F₃, *J* = 33.6 Hz), 129.3, 128.3, 126.0 (d, C-C-C-F₃, *J* = 2.4 Hz), 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.1 (q, C-F₃, *J* = 272.9 Hz), 123.9 (q, C-F₃, *J* = 274.0 Hz), 123.5, 74.7, 50.0, 35.3, 19.3

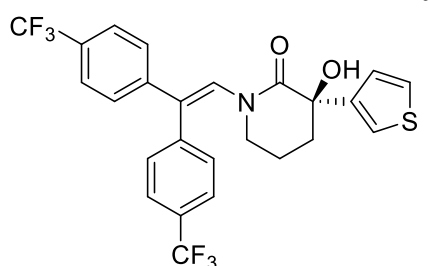
¹⁹F NMR (466 MHz, CDCl₃) δ -62.47 (s, 3F), -62.52 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₆H₂₁F₆N₂O₂ 507.1502; Found 507.1481.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 18.5 min (minor) and 40.8 min (major).

[α]_D³⁰ = +1.9 (c 2.0, CHCl₃, 77% ee)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-thienyl)piperidin-2-one (3k)



Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 4/4/1. 38 mg, 75%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.61 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.34 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.24 (s, 1H), 7.11 (dd, *J* = 3.0, 1.0 Hz, 1H), 7.07 (dd, *J* = 5.0, 1.5 Hz, 1H), 4.01 (s, 1H), 3.09 (ddd, *J* = 12.6, 9.1, 5.6 Hz, 1H), 2.97 (dt, *J*_d = 12.5 Hz, *J*_t = 5.5 Hz, 1H), 2.45 (dt, *J*_d = 13.8 Hz, *J*_t = 5.0 Hz, 1H), 2.12 (ddd, *J* = 13.6, 11.1, 5.1 Hz, 1H), 1.79-1.70

(m, 1H), 1.66-1.55 (m, 1H)

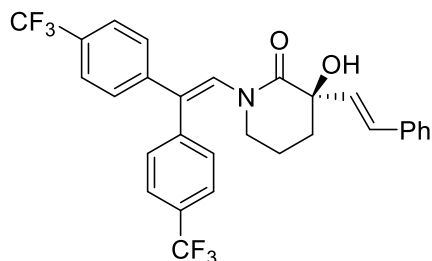
¹³C NMR (125 MHz, CDCl₃) δ 174.1, 144.4, 143.6, 141.7, 132.8, 130.6 (q, C-C-F₃, *J* = 32.4 Hz), 130.4, 130.2 (q, C-C-F₃, *J* = 32.4 Hz), 129.4, 128.3, 126.7, 125.9 (d, C-C-C-F₃, *J* = 3.6 Hz), 125.7, 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 274.1 Hz), 124.0 (q, C-F₃, *J* = 274.1 Hz), 122.4, 73.1, 49.5, 33.7, 19.6

¹⁹F NMR (466 MHz, CDCl₃) δ -62.46 (s, 3F), -62.51 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₅H₂₀F₆NO₂S 512.1113; Found 512.1093.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 11.6 min (major) and 20.0 min (minor).

[α]_D³⁰ = +1.5 (c 2.0, CHCl₃, 84% ee)

(*R,E*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-styrylpiperidin-2-one (3l)

Eluent for column chromatography: hexane/CH₂Cl₂/EtOAc = 6/6/1.
38 mg, 71%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.42-7.33 (m, 6H), 7.32-7.27 (m, 3H), 7.23 (s, 1H), 6.66 (d, *J* = 16.5 Hz, 1H), 6.26 (d, *J* = 16.0 Hz, 1H), 3.79 (s, 1H), 3.17-3.04 (m, 2H), 2.19 (dt, *J*_d = 13.5 Hz, *J*_t = 4.9 Hz, 1H), 2.02 (dt, *J*_d = 13.5 Hz, *J*_t = 8.0 Hz, 1H), 1.83-1.74 (m, 2H)

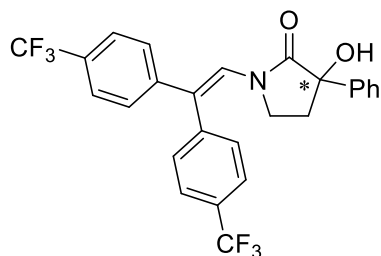
¹³C NMR (125 MHz, CDCl₃) δ 174.0, 143.7, 141.8, 136.1, 132.6, 131.5, 131.3, 130.6 (q, C-C-F₃, *J* = 32.4 Hz), 130.4, 130.2 (q, C-C-F₃, *J* = 33.5 Hz), 129.6, 128.9, 128.44, 128.36, 126.8, 125.9 (d, C-C-C-F₃, *J* = 3.5 Hz), 125.5 (d, C-C-C-F₃, *J* = 3.6 Hz), 124.2 (q, C-F₃, *J* = 272.9 Hz), 124.0 (q, C-F₃, *J* = 274.1 Hz), 73.8, 49.7, 33.2, 19.8

¹⁹F NMR (466 MHz, CDCl₃) δ -62.46 (s, 3F), -62.55 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₉H₂₄F₆NO₂ 532.1706; Found 532.1684.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 11.1 min (major) and 14.7 min (minor).

[α]_D³¹ = +24.4 (c 1.0, CHCl₃, 82% ee)

1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpyrrolidin-2-one (3m)

Eluent for column chromatography: CH₂Cl₂/EtOAc = 20/1. 40 mg, 82%, white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.47 (s, 1H), 7.44-7.33 (m, 7H), 7.29 (d, *J* = 8.0 Hz, 2H), 3.04 (s, 1H), 3.01 (ddd, *J* = 10.8, 7.0, 4.3 Hz, 1H), 2.89 (dt, *J*_d = 10.7 Hz, *J*_t = 7.6 Hz, 1H), 2.40-2.32 (m, 2H)

¹³C NMR (125 MHz, CDCl₃) δ 175.8, 144.0, 141.8, 141.2, 131.2, 130.6 (q, C-C-F₃, *J* = 33.5 Hz), 129.7 (q, C-C-F₃, *J* = 33.5 Hz), 129.0, 128.7,

127.8, 126.0, 125.6 (m, C-C-C-F₃, 2C), 125.3, 124.5, 124.2 (q, C-F₃, *J* = 273.0 Hz), 124.0 (q, C-F₃, *J* = 272.9 Hz), 78.0, 45.2, 36.3

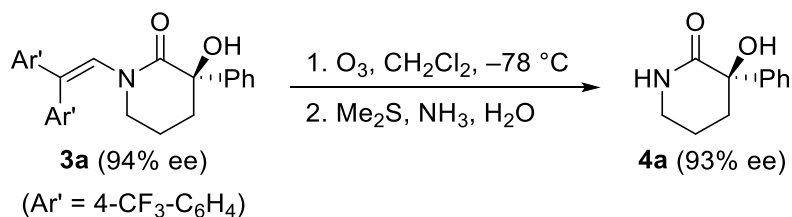
¹⁹F NMR (466 MHz, CDCl₃) δ -62.4 (s, 3F), -62.5 (s, 3F)

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₆H₂₀F₆NO₂ 492.1393; Found 492.1393.

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 7.8 min (major) and 10.4 min (minor).

[α]_D²⁸ = +9.0 (c 0.27, CHCl₃, 5% ee)

Deprotection with ozone.



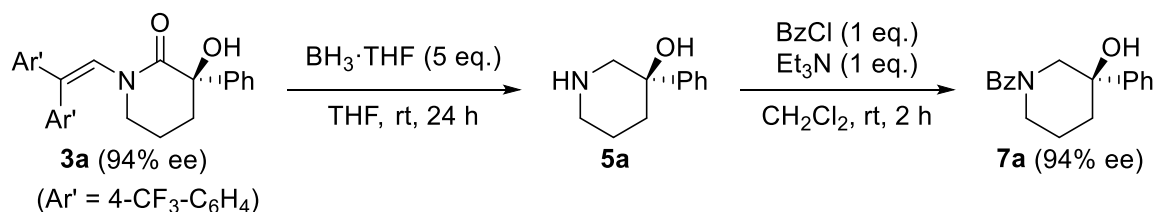
Ozone was bubbled into a solution of **3a** (42 mg, 0.083 mmol) in CH₂Cl₂ (8.3 mL) at -78 °C, and the ozonolysis was monitored by TLC. After the spot of **3a** was disappeared, nitrogen gas was bubbled until the blue color was disappeared. To the mixture was added dimethyl sulfide (0.030 mL, 0.41 mmol) at -78 °C, and the resulting mixture was warmed to room temperature slowly. The reaction mixture was washed with 2.2 M NH₃ solution completely, dried over Na₂SO₄, and concentrated in vacuo.⁷ Purification by flash column chromatography (EtOAc/CH₂Cl₂ = 9/1) gave **4a** (12 mg, 0.063 mmol, 76%).

(R)-3-Hydroxy-3-phenylpiperidin-2-one (4a)

White solid.
¹H NMR (500 MHz, CDCl₃) δ 7.50-7.42 (app d, 2H), 7.39-7.32 (app t, 2H), 7.32-7.26 (m, 1H), 6.74 (br, 1H), 4.06 (s, 1H), 3.44-3.31 (m, 2H), 2.24 (ddd, *J* = 16.8, 6.3, 5.0 Hz, 1H), 2.15 (td, *J*_t = 16.1 Hz, *J*_d = 4.5 Hz, 1H), 1.86-1.76 (m, 1H), 1.72-1.58 (m, 1H)
¹³C NMR (125 MHz, CDCl₃) δ 175.0, 144.4, 128.4, 128.0, 126.1, 75.5, 42.9, 35.8, 19.3
 HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₄NO₂ 192.1019; Found 192.1015.
 Daicel Chiralpak IC, 2-propanol, flow rate 0.4 mL/min, λ = 206 nm, retention time: 26.6 min (major) and 35.6 min (minor).
 [α]_D³¹ = -5.5 (c 0.50, CHCl₃, 93% ee)

⁷ J. M. Aizpurua, F. P. Cossio, B. Lecea, C. Palomo *Tetrahedron Lett.* **1986**, 27, 4359.

Deprotection and reduction with borane.



To a test tube were added **3a** (51 mg, 0.10 mmol) and dry THF (0.25 mL). To the test tube was added 1 M BH₃·THF in THF (0.50 mL, 0.50 mmol) over 10 min at 0 °C under a nitrogen atmosphere. After stirring at room temperature for 24 h, the test tube was cooled to 0 °C. To the mixture were added MeOH and 13.4 N NH₃ (NH₄⁺OH⁻) at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. After the organic solvents were removed under reduced pressure, to the residue were added water, brine, and NH₄⁺OH⁻. The crude mixture was extracted with CH₂Cl₂. The organic extracts were dried over Na₂SO₄ and concentrated in vacuo.³ Purification by flash column chromatography (CH₂Cl₂/MeOH/NH₄⁺OH⁻ = 9/1/0.2) gave **5a** (13 mg, 0.071 mmol, 71%). The spectra accorded with the literature.⁸

An analytical sample of **5a** (6.2 mg, 0.035 mmol) was dissolved into dry CH₂Cl₂ (0.47 mL), and triethylamine (5.4 μL, 0.038 mmol) was added. To the mixture was added benzoyl chloride (3.7 μL, 0.032 mmol). After the reaction was complete (room temperature, 2 h), the reaction mixture was diluted with CH₂Cl₂ and hexane, and the solution was charged to a silica gel column directly.³ Purification by flash column chromatography (CH₂Cl₂/EtOAc = 2/1) gave **7a** (9.3 mg, 0.033 mmol, 95%).

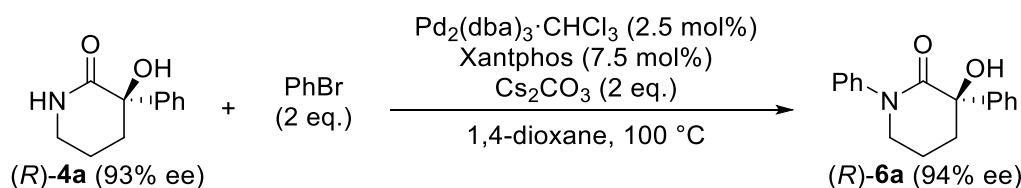
(R)-3-Phenylpiperidin-3-ol (5a)

White solid.
¹H NMR (500 MHz, CDCl₃) δ 7.53-7.50 (app d, 2H), 7.38-7.33 (app t, 2H), 7.29-7.24 (m, 1H), 3.12-3.05 (m, 1H), 2.88 (s, 2H), 2.63 (td, *J*_t = 12.0 Hz, *J*_d = 3.0 Hz, 1H), 2.05-1.60 (br, 2H), 2.00-1.81 (m, 3H), 1.67-1.61 (m, 1H)
¹³C NMR (125 MHz, CDCl₃) δ 146.3, 128.4, 127.1, 124.8, 70.7, 58.2, 46.4, 36.9, 22.5
 HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₆NO 178.1226; Found 178.1226.
 [α]_D²⁸ = -8.8 (c 0.50, CHCl₃, 94% ee)

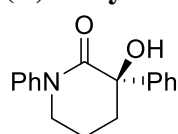
(R)-1-Benzoyl-3-phenylpiperidin-3-ol (7a)

White solid.
¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.53-7.44 (m, 4H), 7.42-7.36 (m, 3H), 7.37-7.32 (app t, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 4.70-3.70 (br, 2H), 3.29 (d, *J* = 14.0 Hz, 1H), 3.15-2.90 (br, 1H), 2.70-2.15 (br, 1H), 2.10-1.94 (m, 3H), 1.67-1.57 (br, 1H)
¹³C NMR (125 MHz, CDCl₃) δ 172.9, 172.0, 145.8, 145.1, 135.8, 130.04, 130.00, 128.6, 127.6, 127.5, 124.9, 72.9, 72.1, 58.2, 53.2, 48.6, 42.5, 37.1, 29.8, 22.5, 20.9 (mixture of amide rotamers)
 HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₀NO₂ 282.1489; Found 282.1487.
 Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 17.9 min (major) and 23.5 min (minor).
 [α]_D²⁸ = -46.9 (c 1.0, CHCl₃, 94% ee)

⁸ T. Wada, M. Shimizu (Chiralgen, Ltd.), Patent WO 12/039448, 2012.

Phenylation of **4a** and the determination of the absolute configuration of **6a**.

To a test tube with a magnetic stir bar were added **4a** (9.7 mg, 0.051 mmol), $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (1.2 mg, 0.0012 mmol), Xantphos (2.2 mg, 0.0038 mmol), Cs_2CO_3 (32 mg, 0.099 mmol), and 0.6 M bromobenzene in dry 1,4-dioxane (0.17 mL, 0.10 mmol). The mixture was heated at 100 °C (oil bath) for 54 h under a nitrogen atmosphere. The resulting mixture was passed through Celite[®] filter (eluent: CH_2Cl_2) and concentrated in vacuo.⁹ Purification by flash column chromatography (hexane/EtOAc = 3/2) gave **6a** (11 mg, 0.040 mmol, 79%). The spectra accorded with a literature.¹⁰

(R)-3-Hydroxy-1,3-diphenylpiperidin-2-one (6a)

Brown oil.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.56-7.52 (app d, 2H), 7.48-7.43 (app t, 2H), 7.42-7.35 (m, 4H), 7.35-7.30 (app t, 2H), 4.09 (s, 1H), 3.84 (ddd, $J = 12.4, 10.6, 5.6$ Hz, 1H), 3.69-3.63 (m, 1H), 2.45 (dt, $J_d = 13.2$ Hz, $J_t = 3.9$ Hz, 1H), 2.35 (td, $J_t = 13.3$ Hz, $J_d = 4.0$ Hz, 1H),

1.98-1.90 (m, 1H), 1.90-1.79 (m, 1H)

$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 173.4, 144.8, 142.5, 129.5, 128.6, 128.0, 127.5, 126.2, 126.0, 75.7, 51.9, 35.3, 19.5

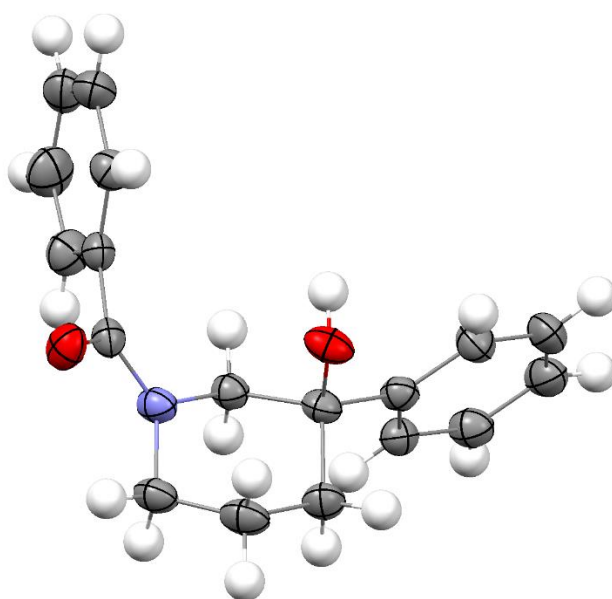
HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_2$ 268.1332; Found 268.1326.Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 27.8 min (major) and 48.1 min (minor). $[\alpha]_D^{29} = -38.6$ (c 0.58, CHCl_3 , 94% ee)

The absolute configuration was determined by comparison with optical rotation of the literature data, $[\alpha]_D^{22} = -60.0$ (c 0.58, CHCl_3 , 97% ee, (*R*)-isomer).¹⁰

⁹ J. Yin, S. L. Buchwald *J. Am. Chem. Soc.* **2002**, *124*, 6043.¹⁰ N. Ishida, D. Nečas, Y. Masuda, M. Murakami *Angew. Chem. Int. Ed.* **2015**, *54*, 7418.

Determination of absolute configuration by X-ray analysis of (*R*)-1-benzoyl-3-phenylpiperidin-3-ol (7a**)****Crystal structure analysis of (*R*)-**7a****

Single crystals of (*R*)-**7a** for X-ray diffraction experiments were grown from ethyl acetate and hexane using vapor diffusion method at room temperature. The data were collected at $-160\text{ }^{\circ}\text{C}$ on a Rigaku R-Axis RAPID IP diffractometer with graphite-monochromated Cu $K\alpha$ radiation ($\lambda = 1.54187\text{ \AA}$). The crystal structure was solved by direct methods using SIR92,¹¹ and refined in SHELXL-2014/7¹² by full matrix least-squares using anisotropic thermal displacement parameters for all non-hydrogen atoms. Crystallographic data for (*R*)-**7a**: $\text{C}_{18}\text{H}_{19}\text{NO}_2$, colorless block, $0.68 \times 0.44 \times 0.29\text{ mm}^3$, orthorhombic, $P\ 2_1\ 2_1\ 2_1$ (No. 19), $a = 10.2229(3)$, $b = 10.4875(3)$, $c = 42.0759(12)\text{ \AA}$, $V = 4511.1(2)\text{ \AA}^3$, $\rho_{\text{calcd}} = 1.243\text{ g cm}^{-3}$, $Z = 12$, $2\theta_{\text{max}} = 136.42^{\circ}$, $\mu = 0.643\text{ mm}^{-1}$. A total of 47281 reflections were measured. $R = 0.0461$, and $R_w = 0.1370$ for 8131 observed reflections with $I > 2.0\sigma(I)$. Flack parameter = $0.96(8)$. CCDC-2020514 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



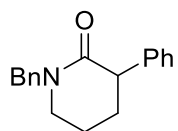
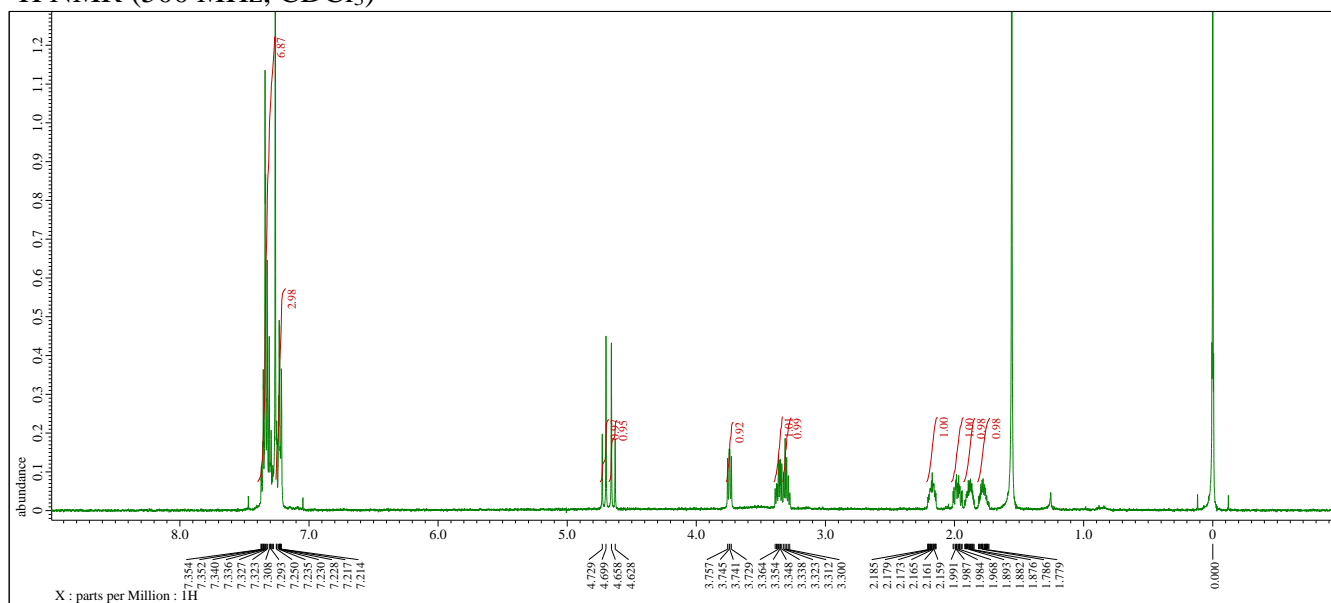
(*R*)-1-benzoyl-3-phenylpiperidin-3-ol (**7a**) (50% probability level)
Only one of three independent molecules is shown.

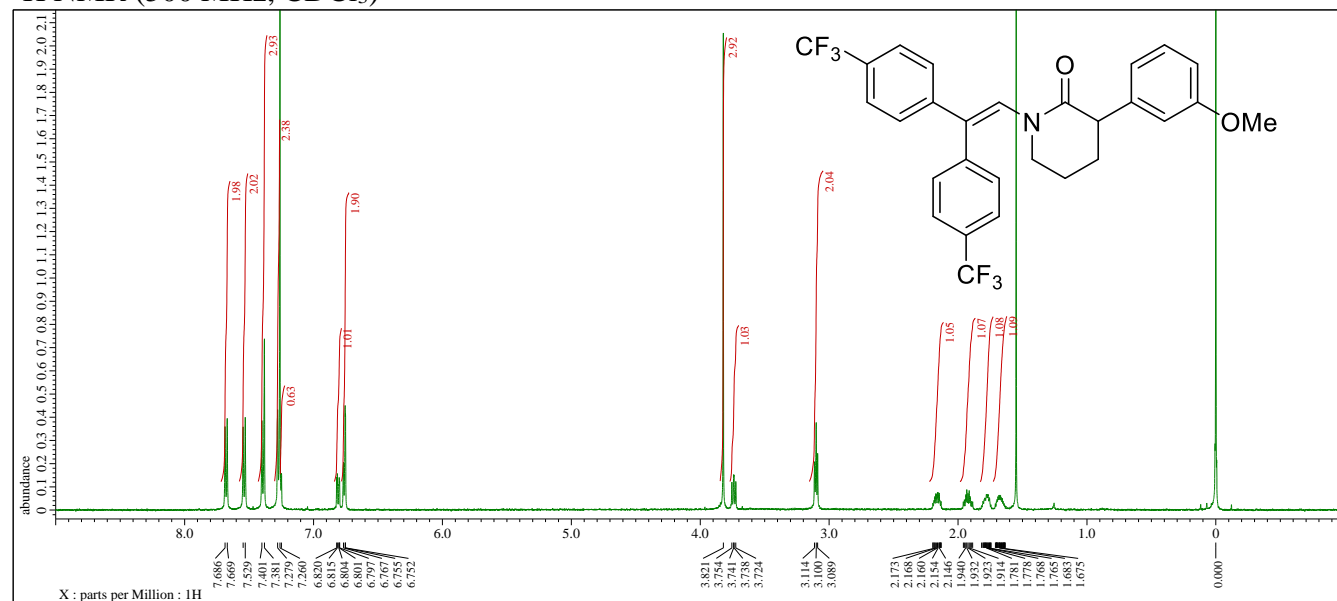
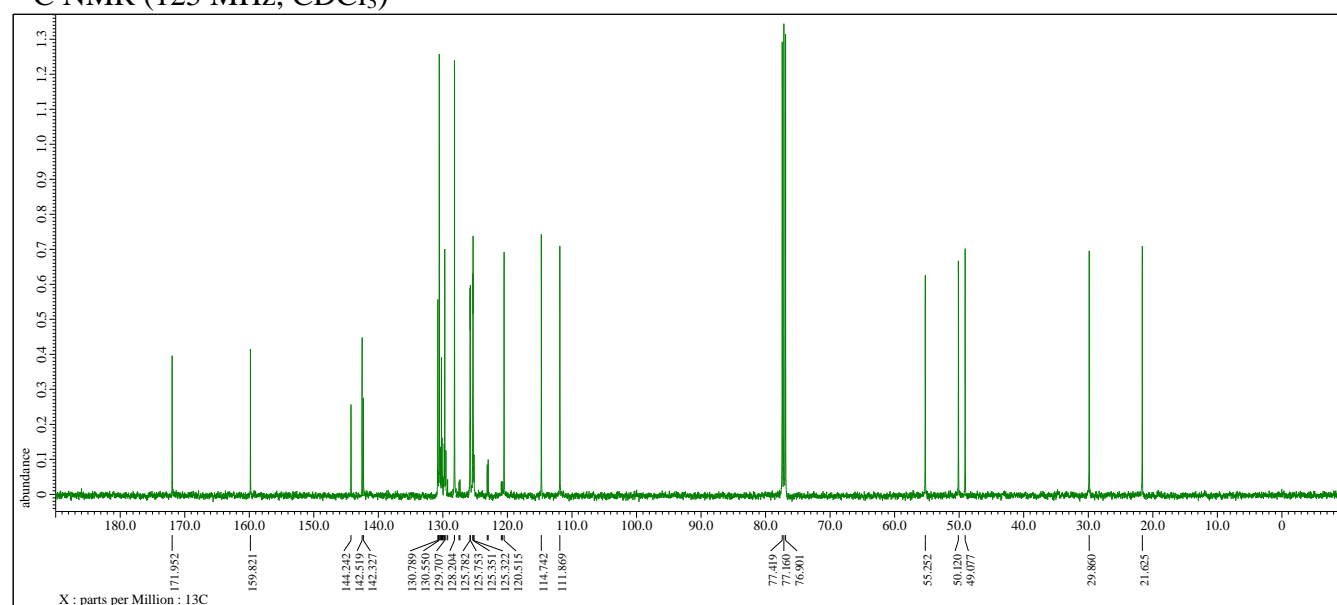
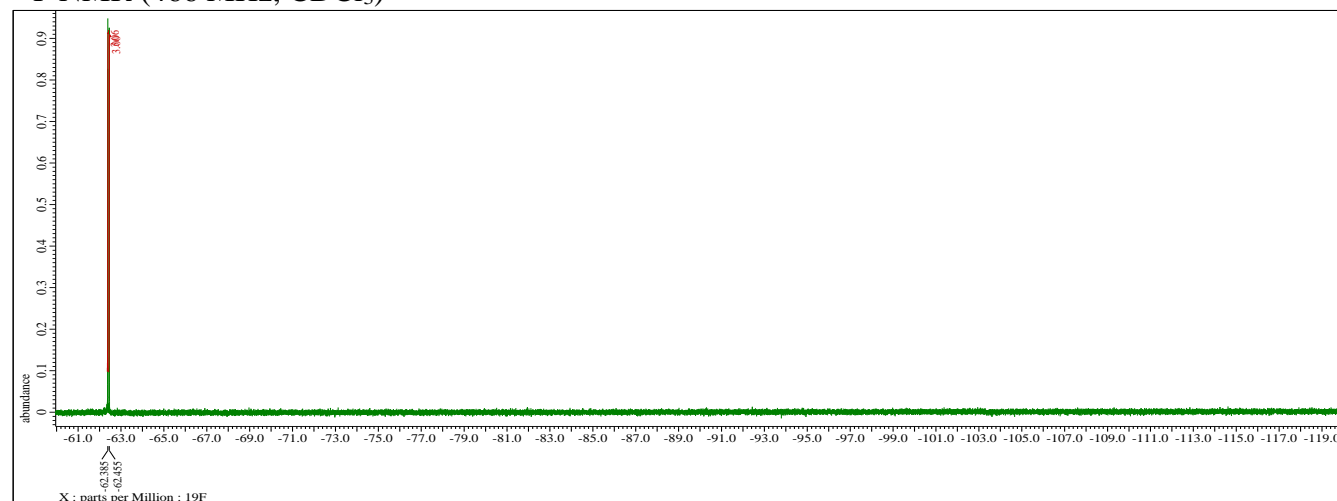
¹¹ SIR92, Program for the solution of crystal structures: Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.

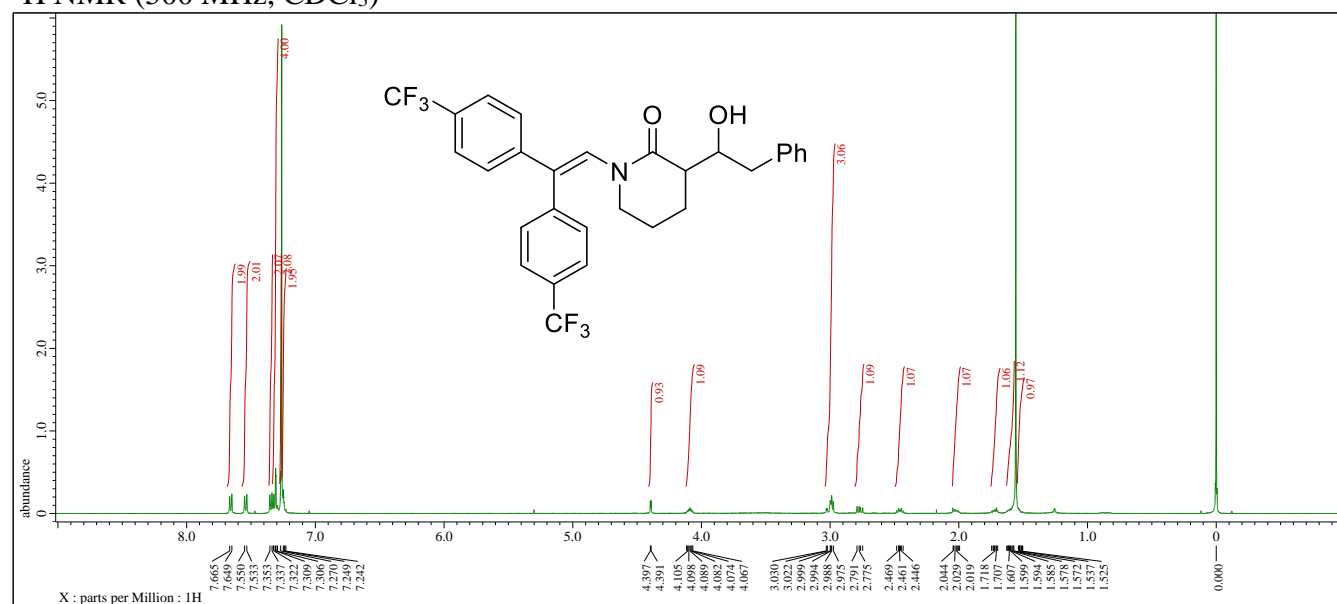
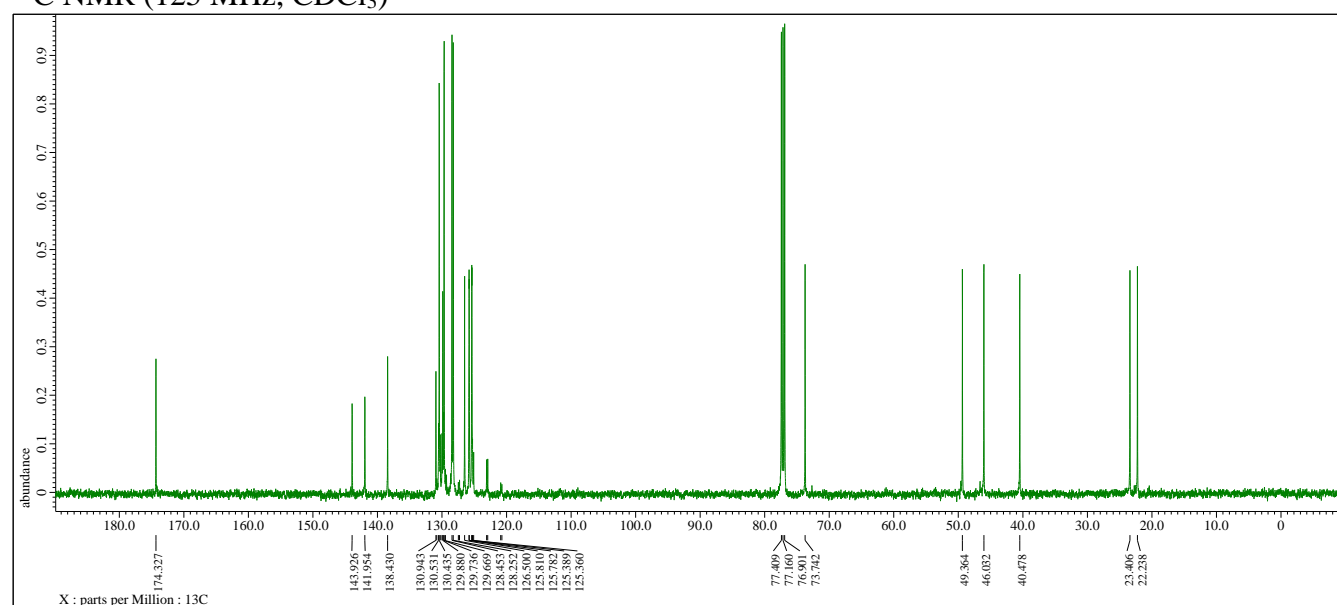
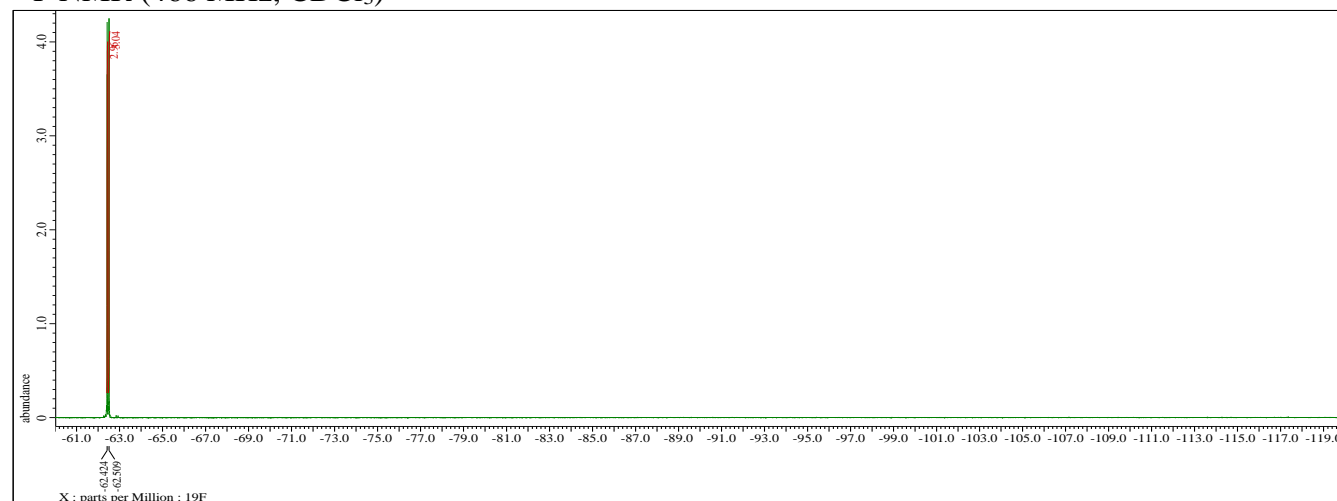
¹² Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112.

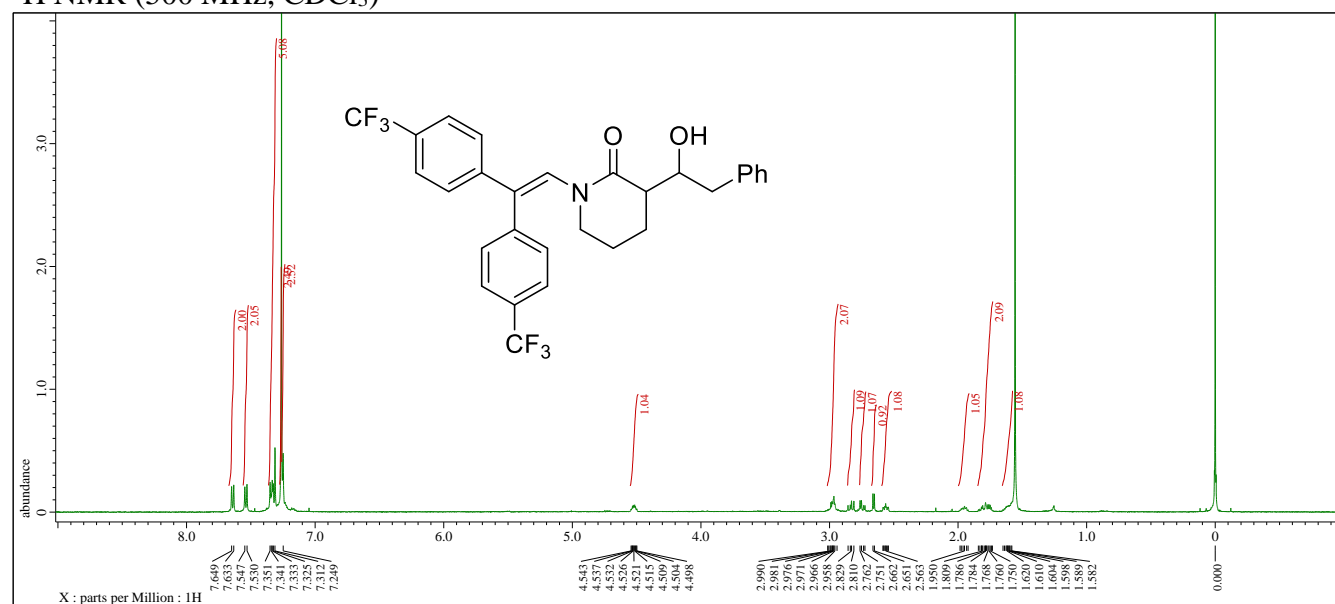
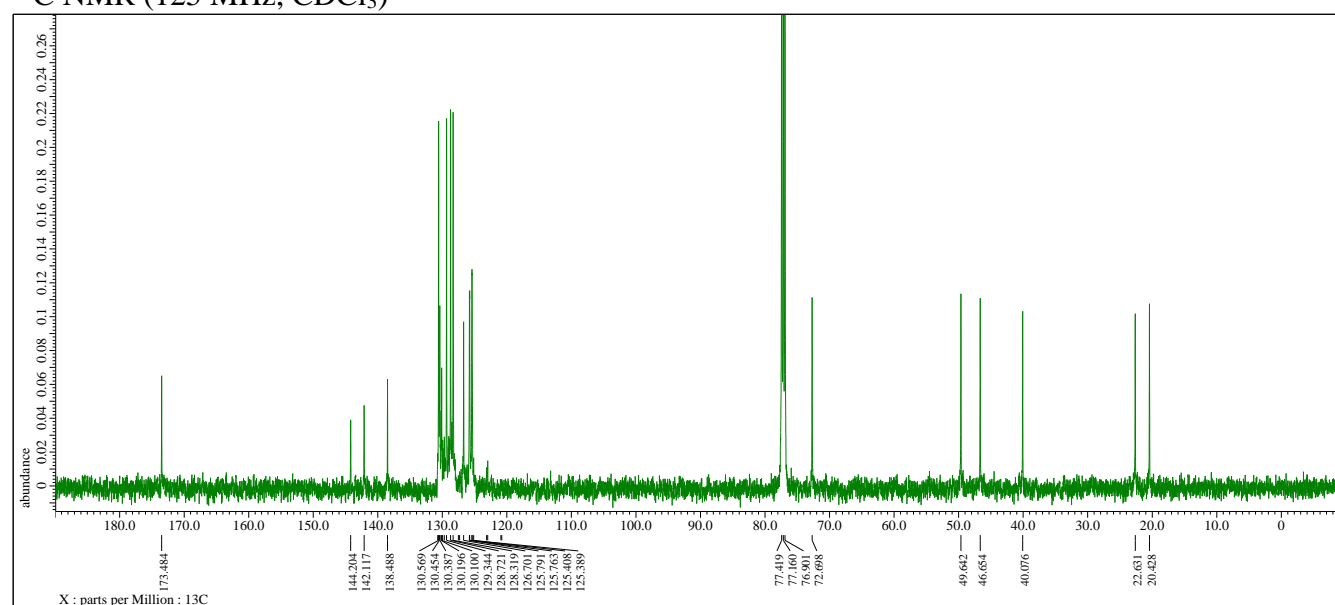
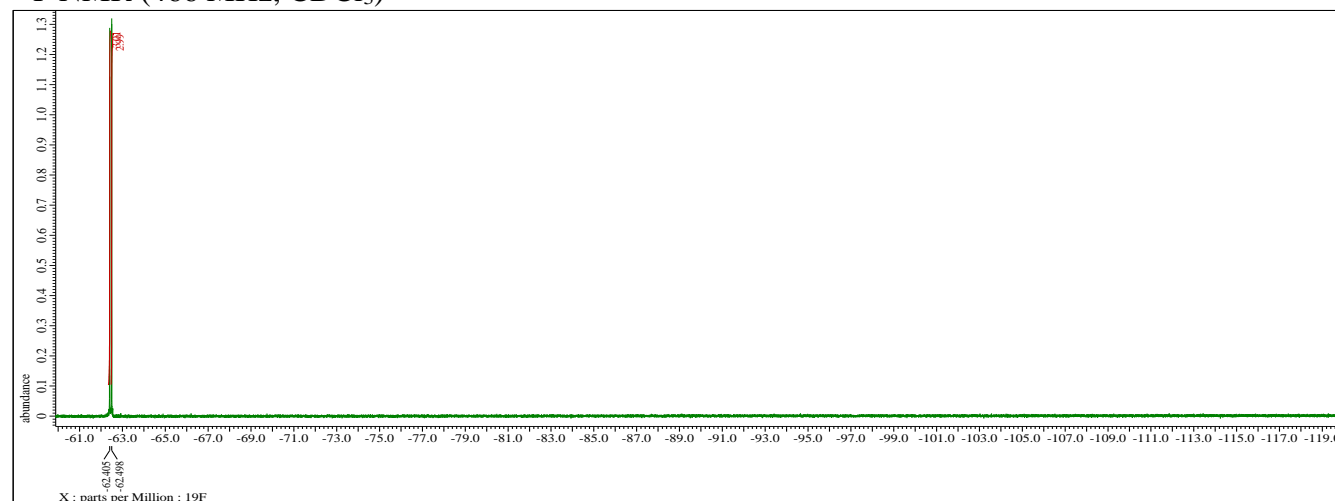
NMR spectra

1-Benzyl-3-phenylpiperidin-2-one.

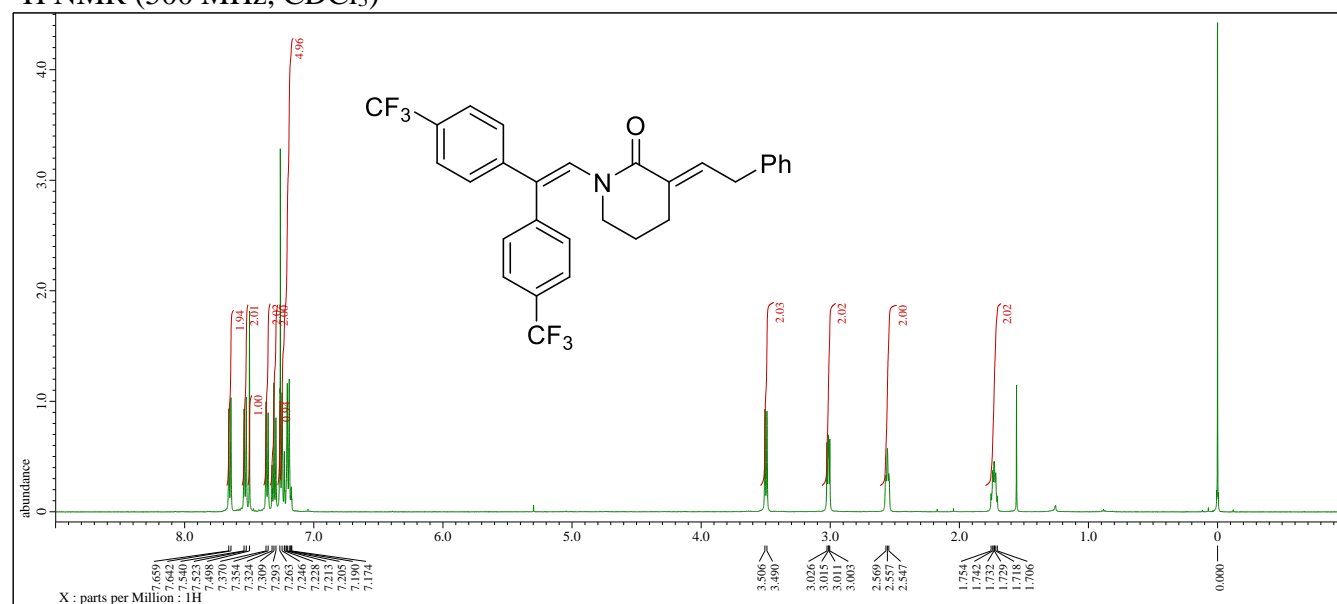
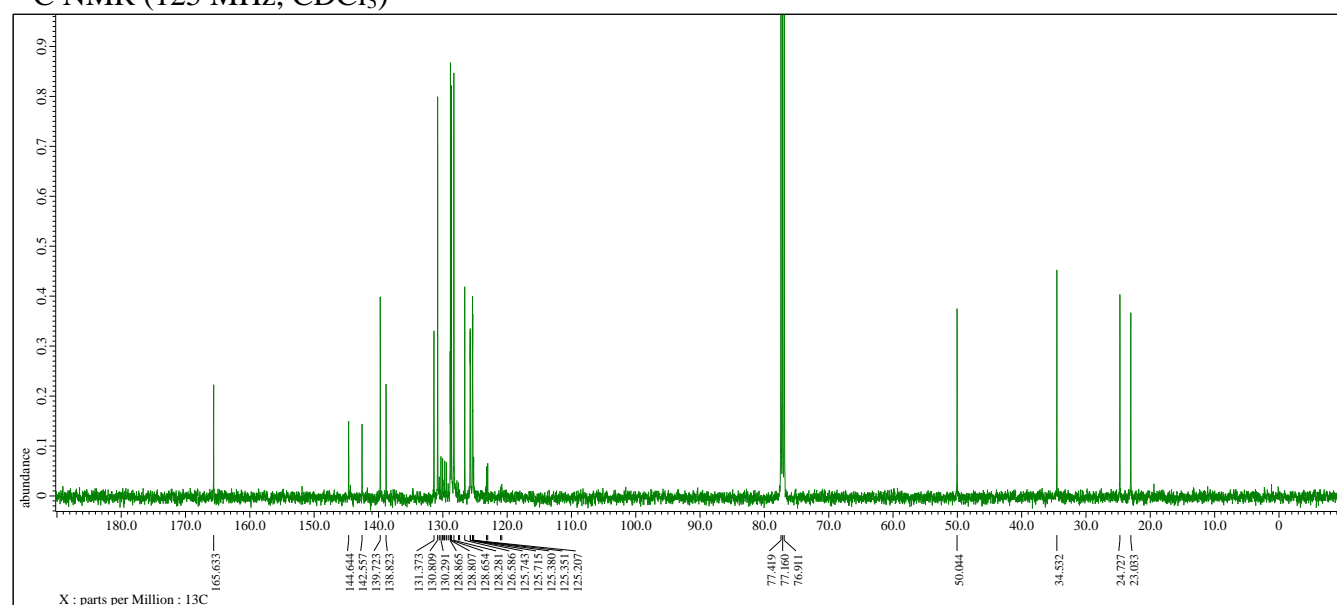
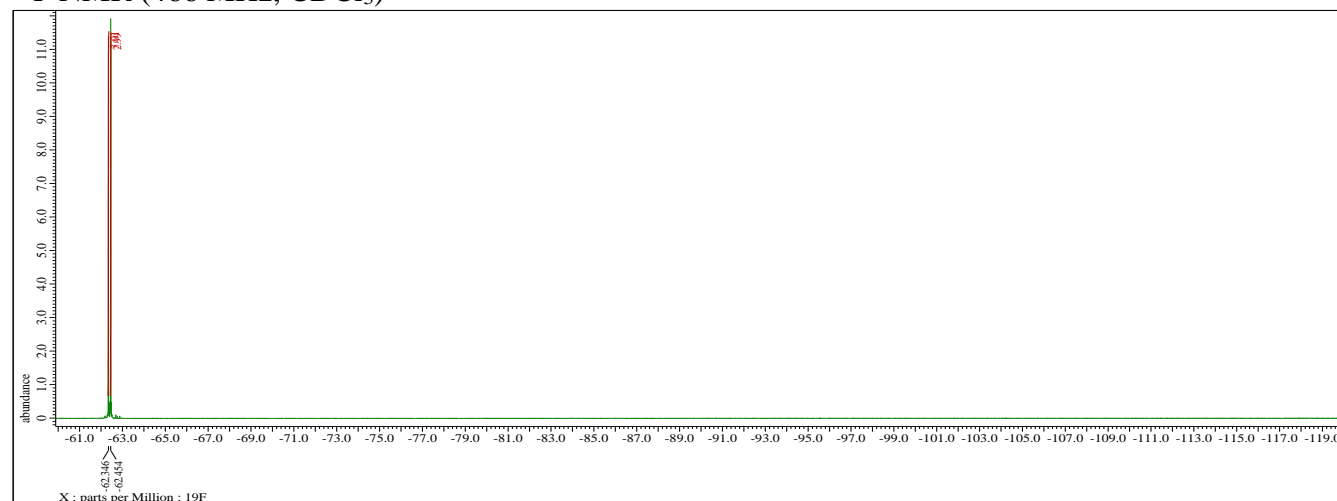
 ^1H NMR (500 MHz, CDCl_3)

1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(3-methoxyphenyl)piperidin-2-one (2c)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

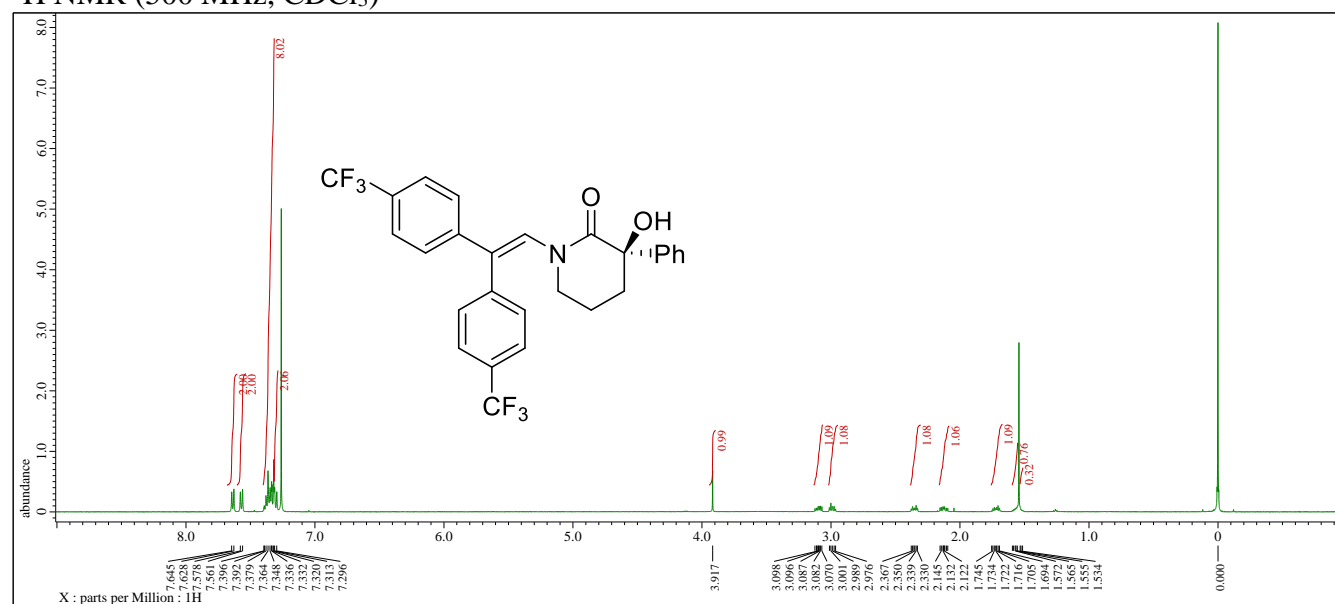
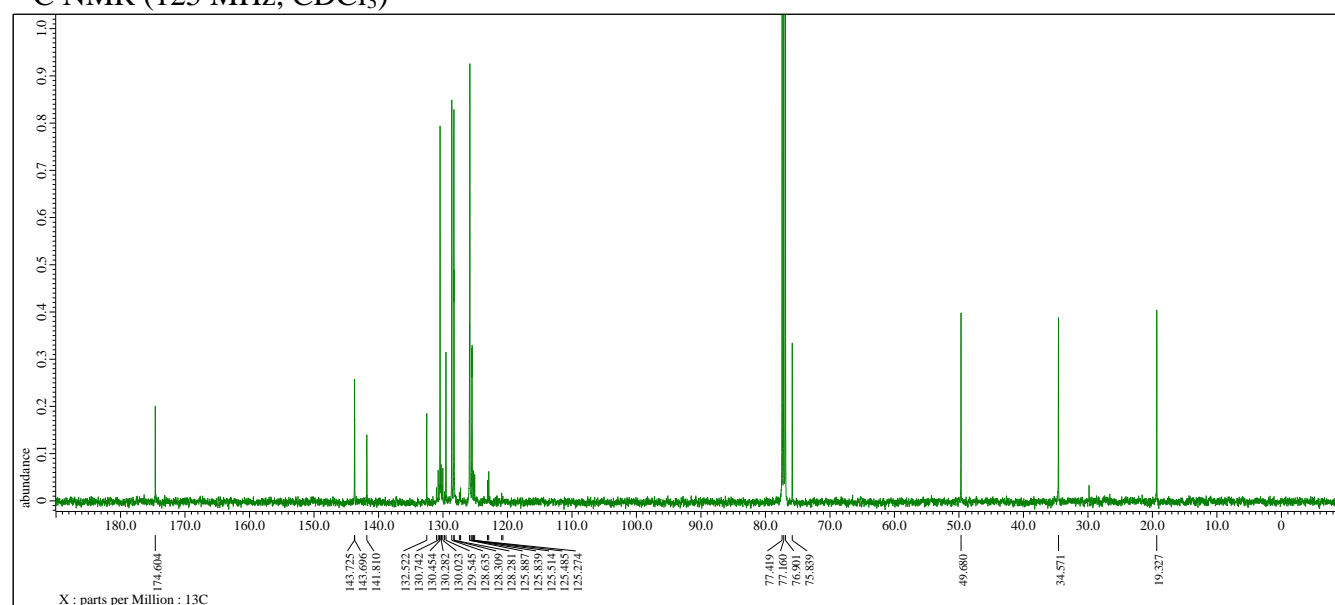
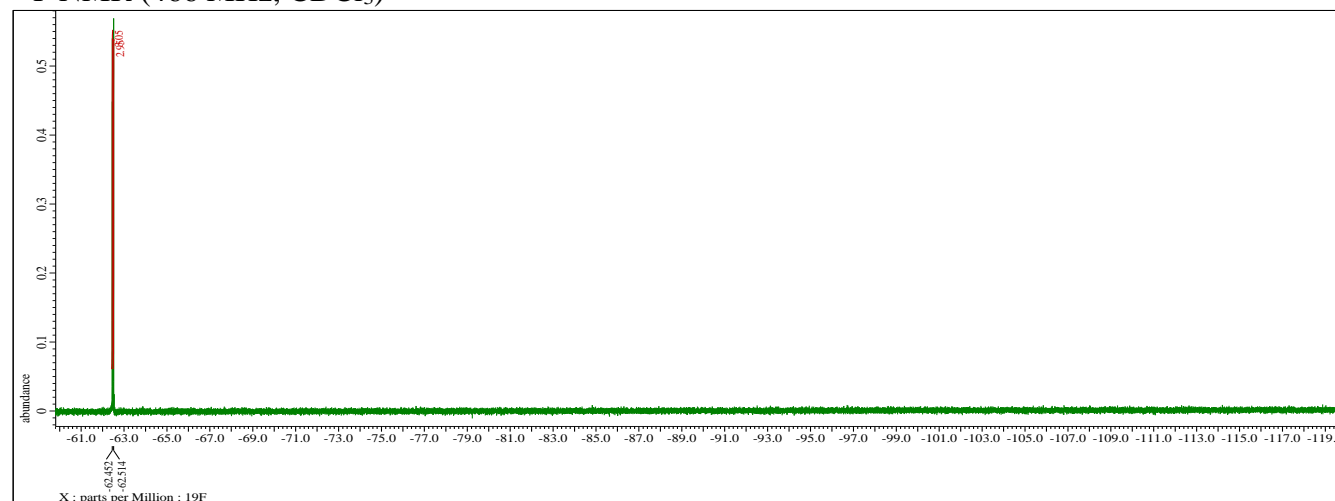
1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (major)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

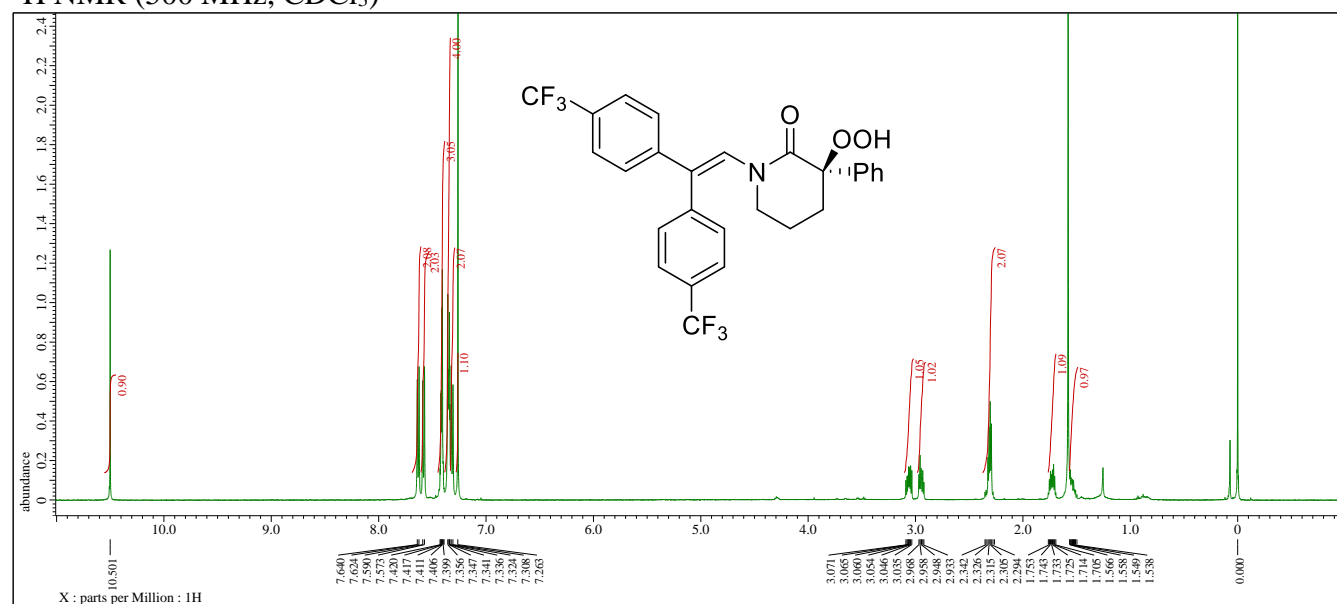
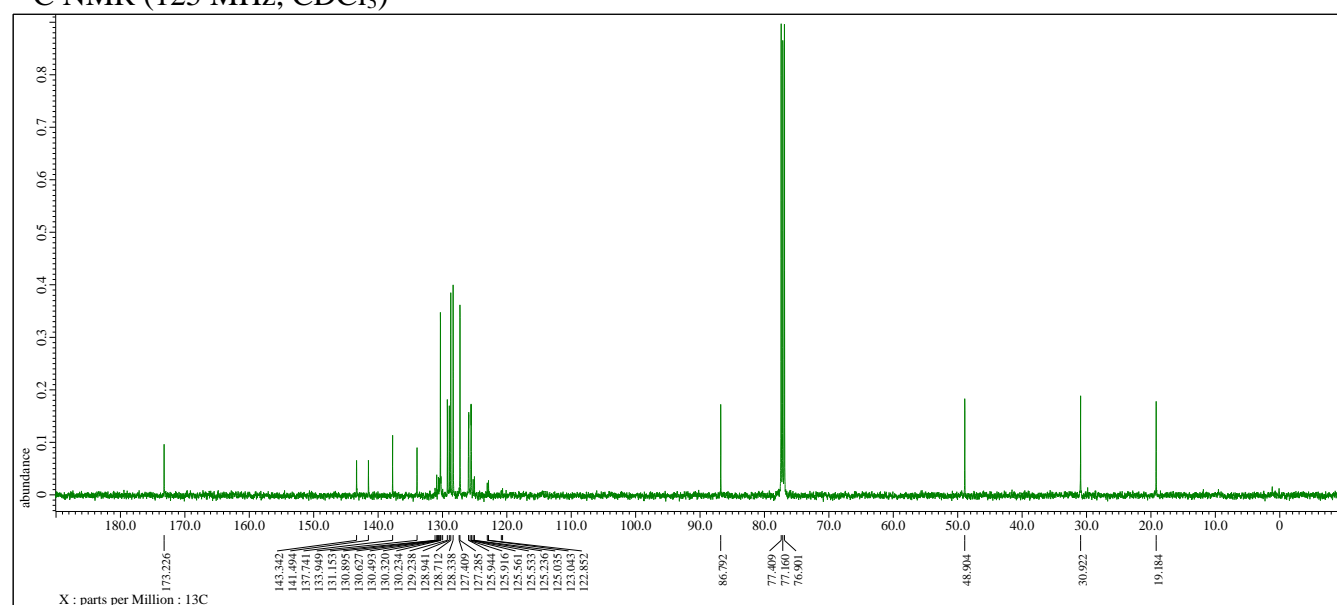
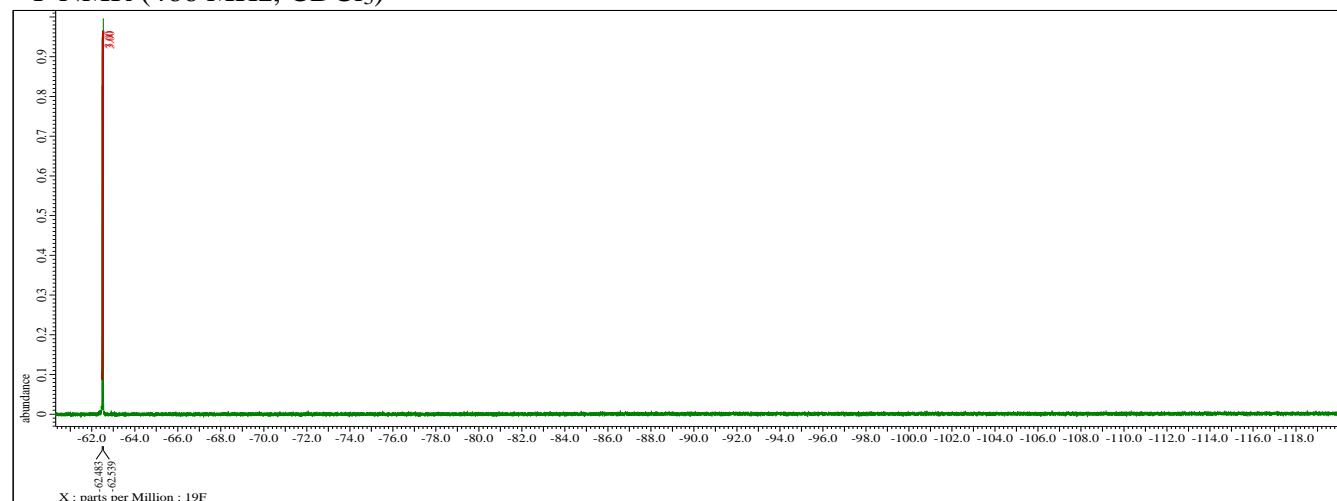
1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(1-hydroxy-2-phenylethyl)piperidin-2-one (minor)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

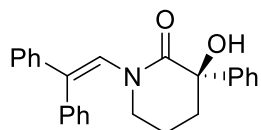
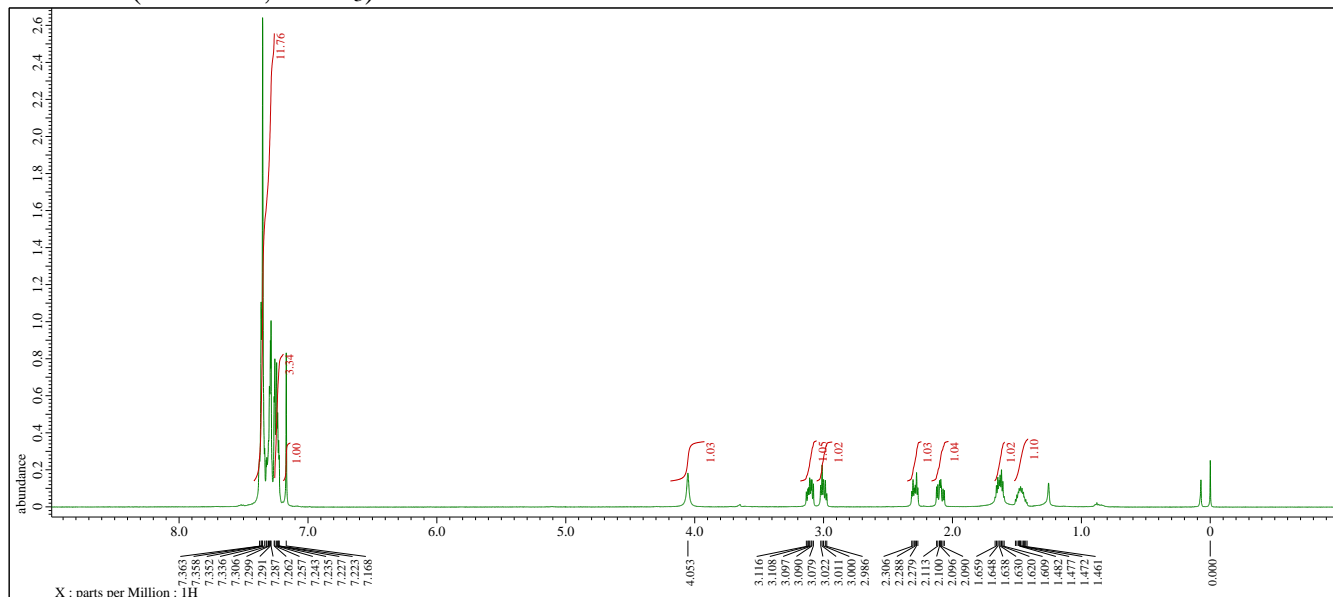
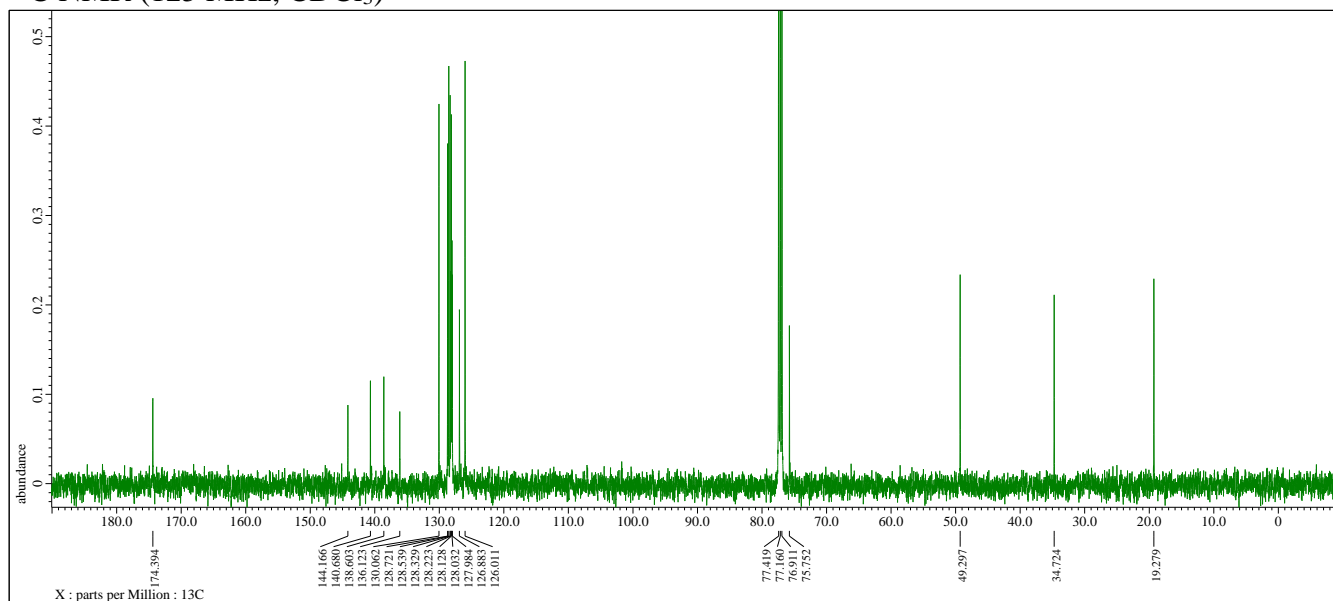
SUPPORTING INFORMATION

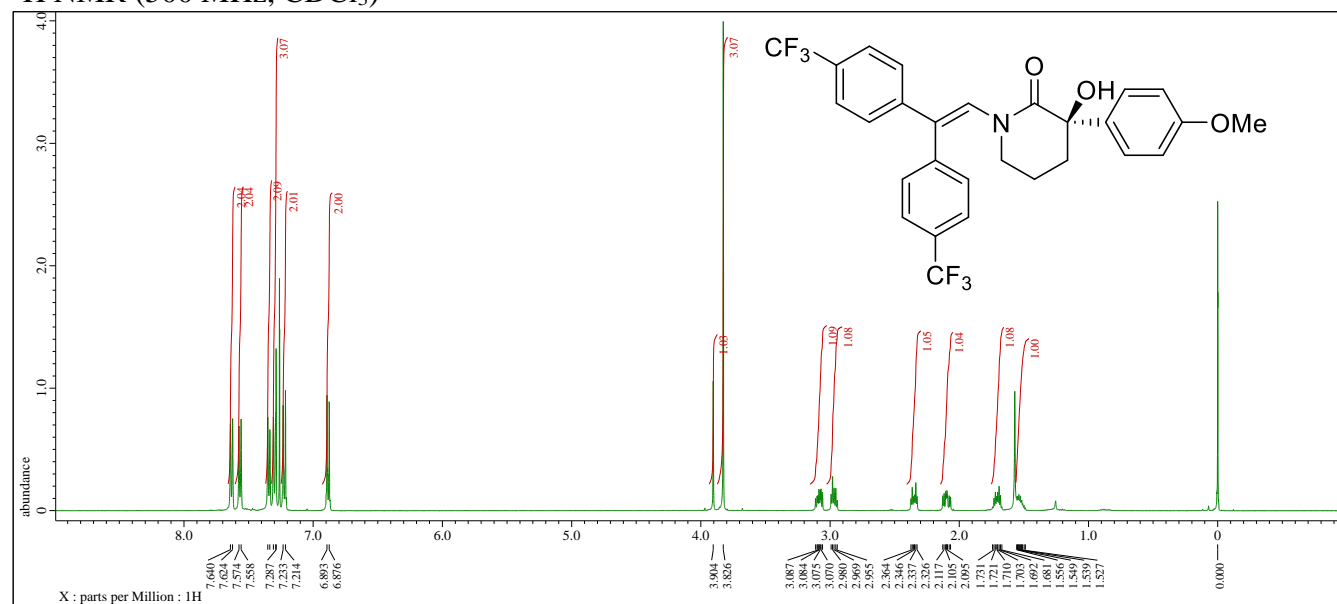
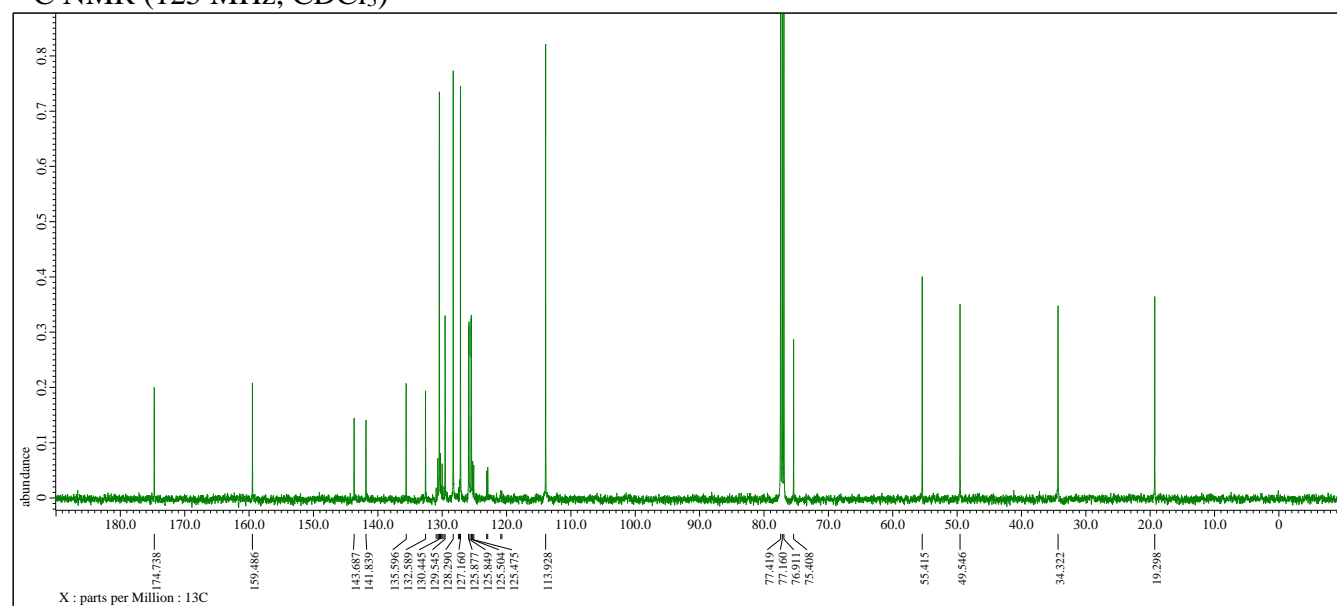
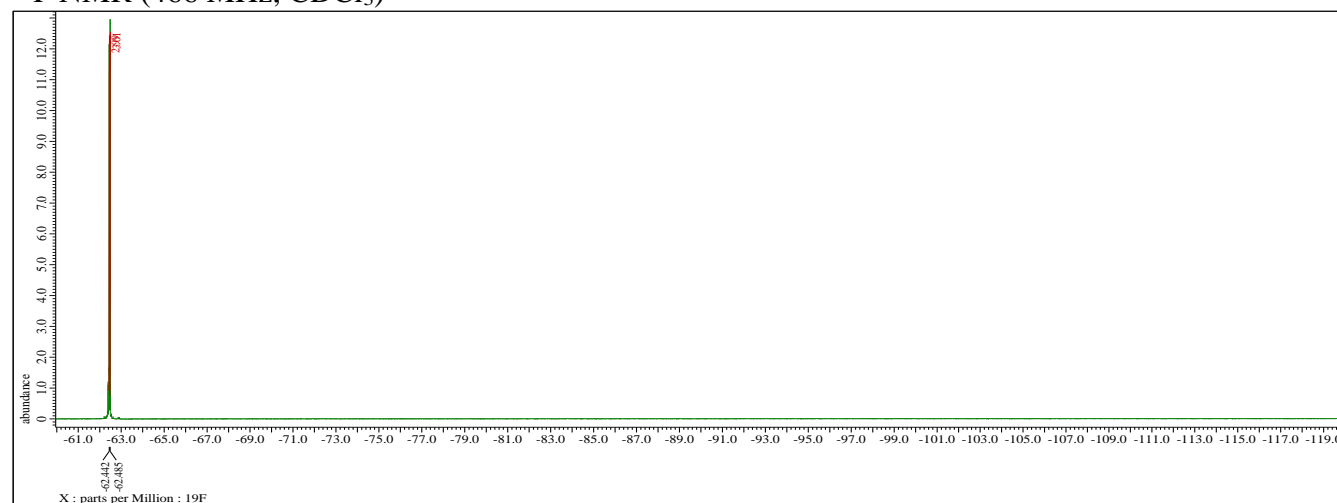
(E)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(2-phenylethylidene)piperidin-2-one (2l)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

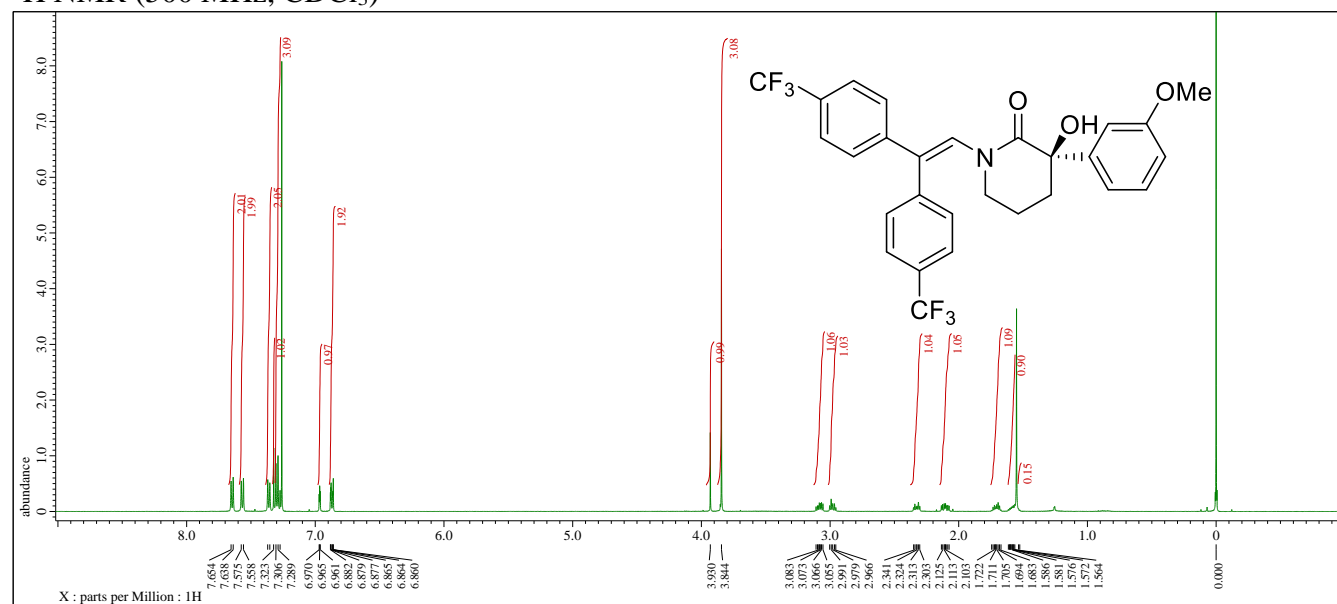
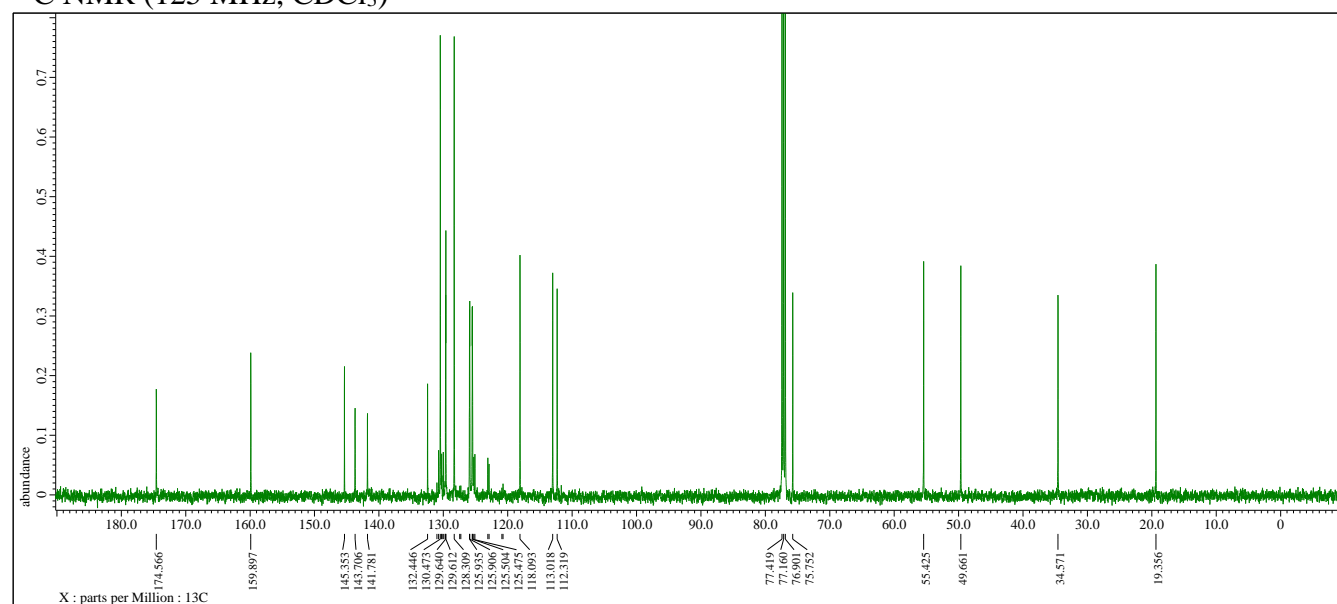
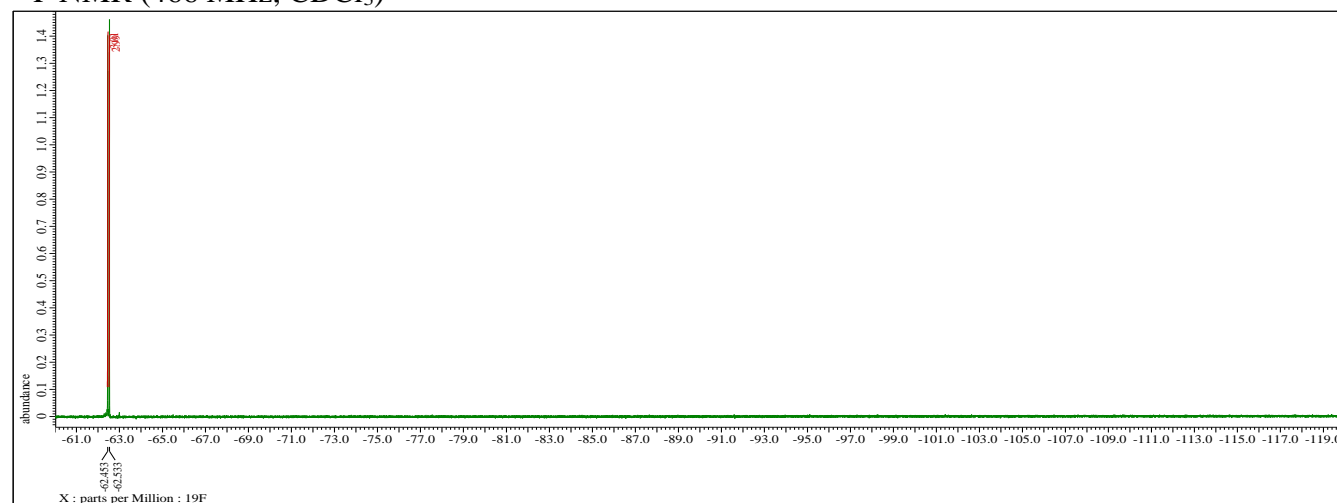
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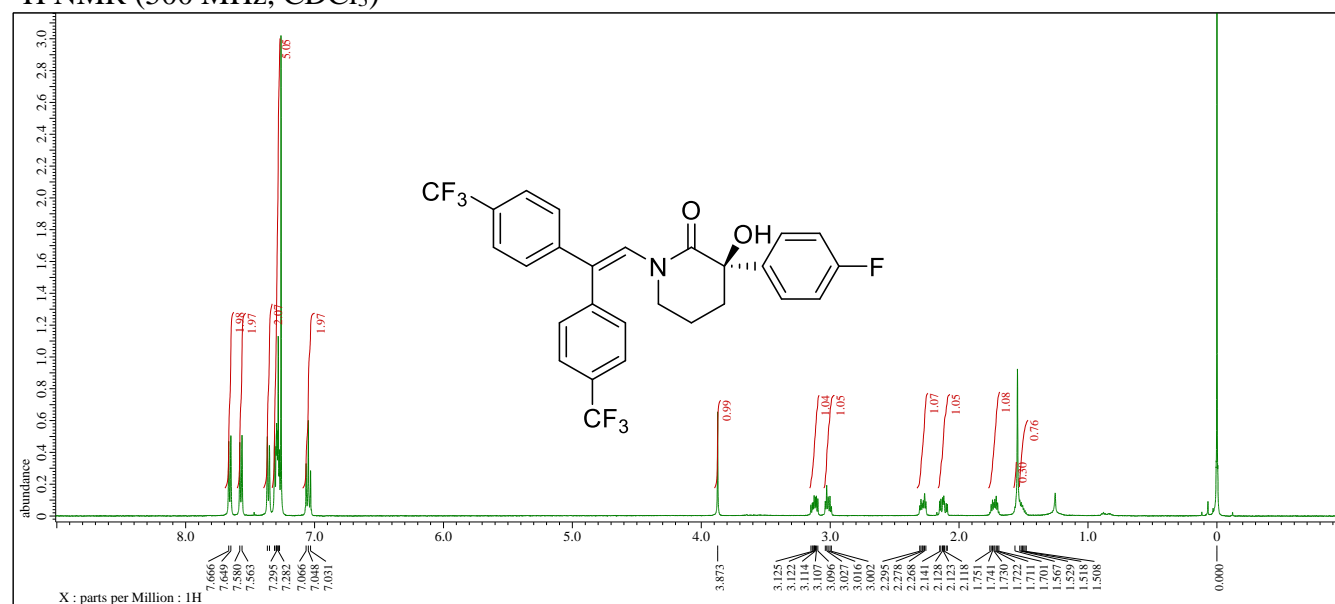
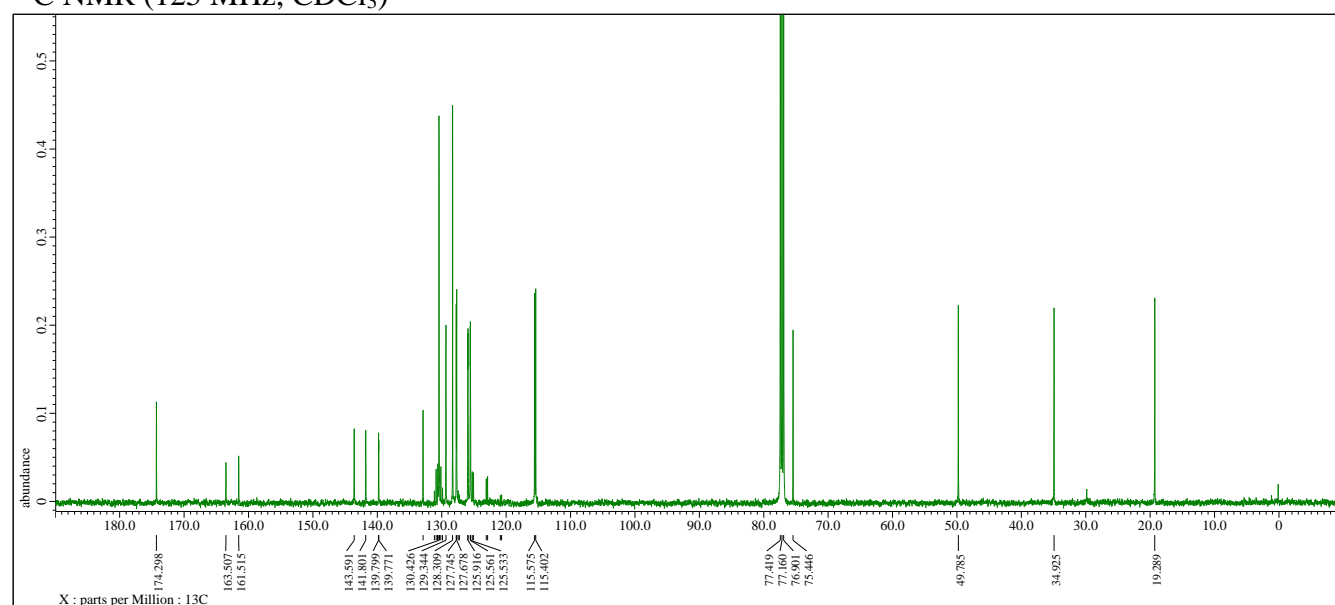
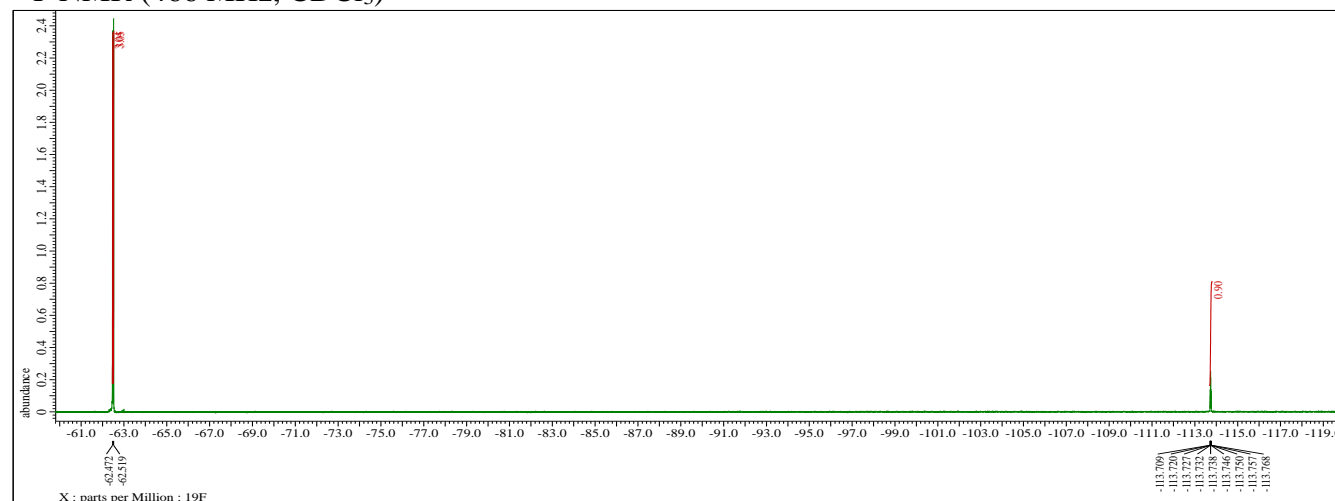
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpiperidin-2-one (3a)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

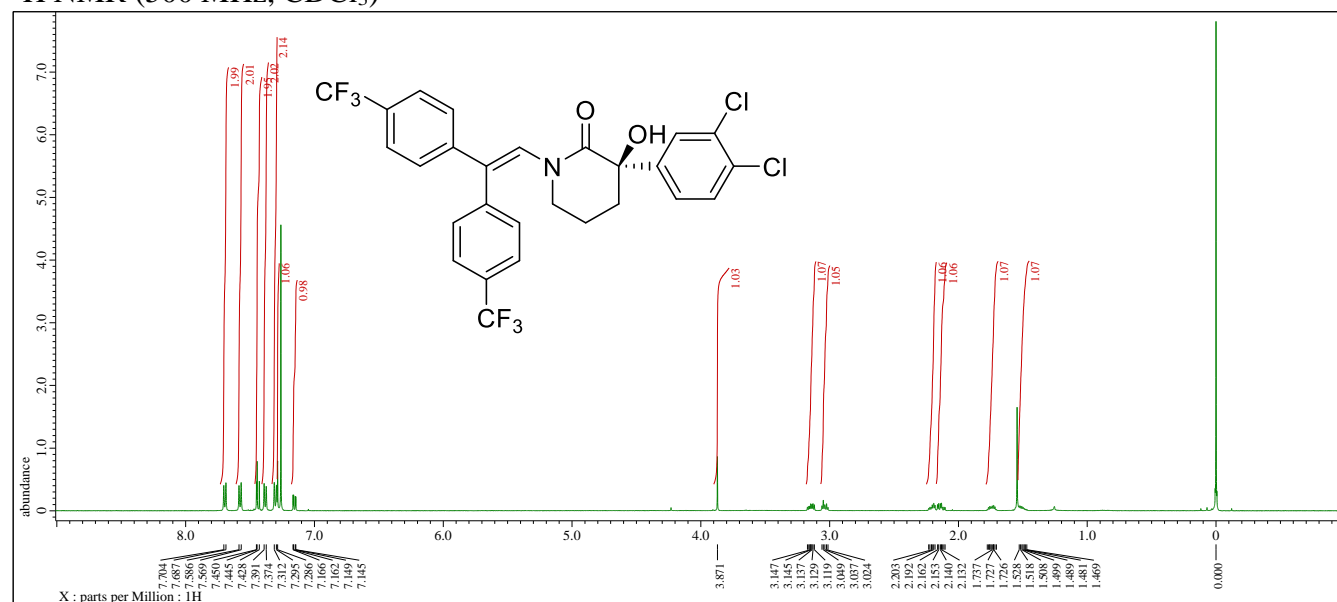
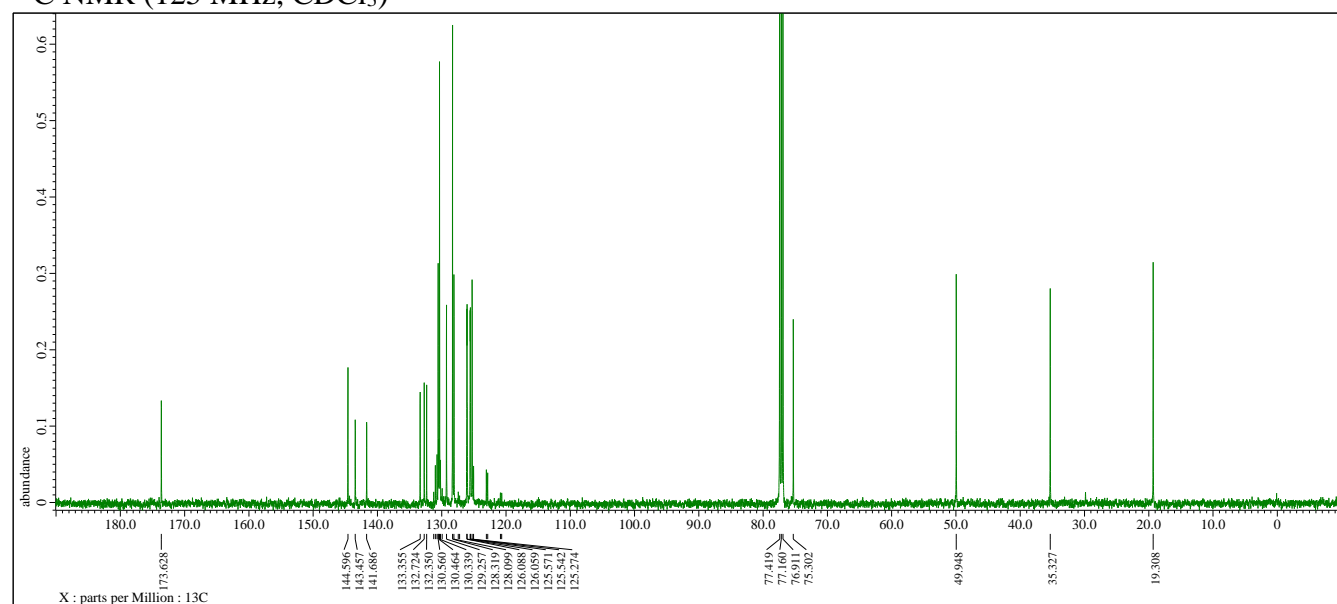
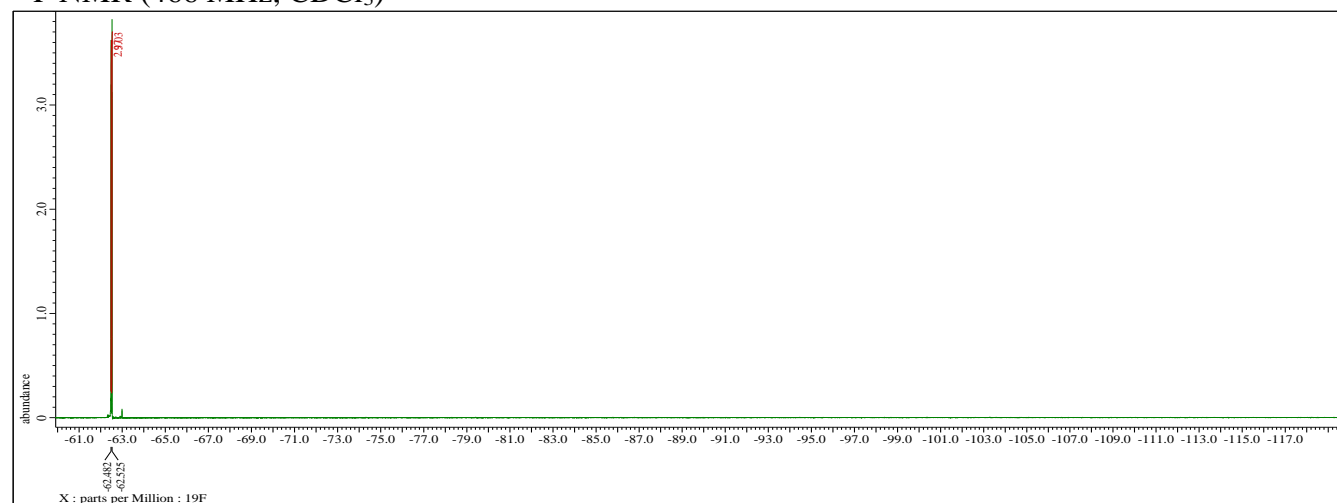
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroperoxy-3-phenylpiperidin-2-one (3a')¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

(R)-1-(2,2-Diphenylvinyl)-3-hydroxy-3-phenylpiperidin-2-one**¹H NMR (500 MHz, CDCl₃)****¹³C NMR (125 MHz, CDCl₃)**

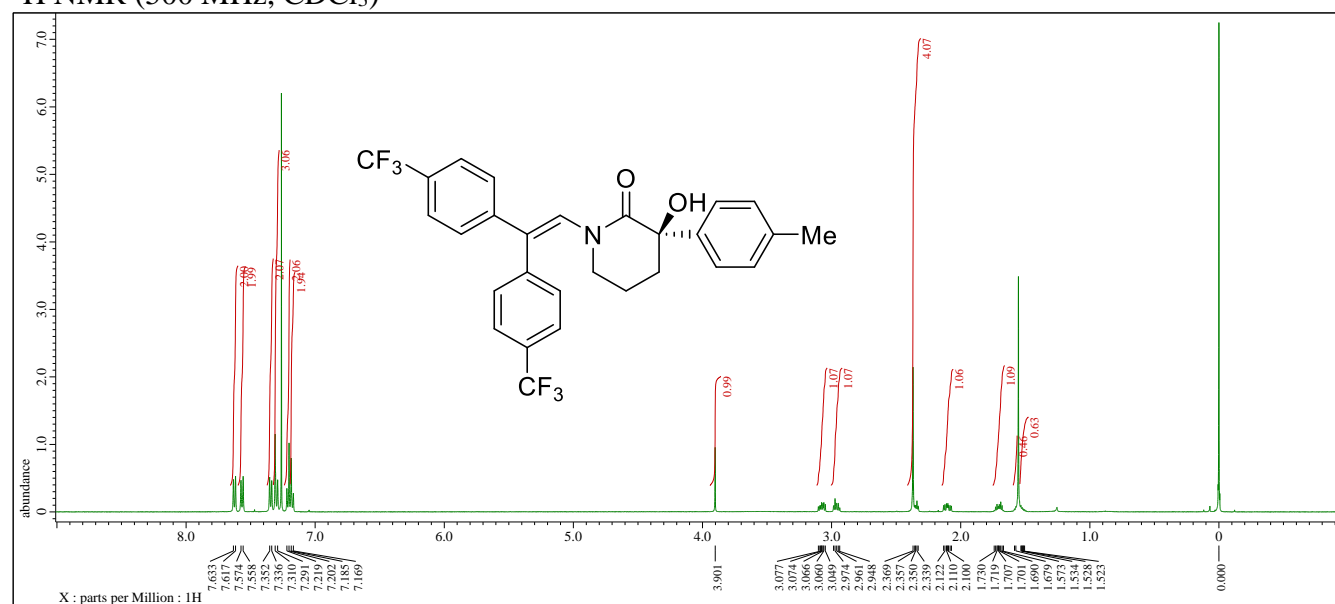
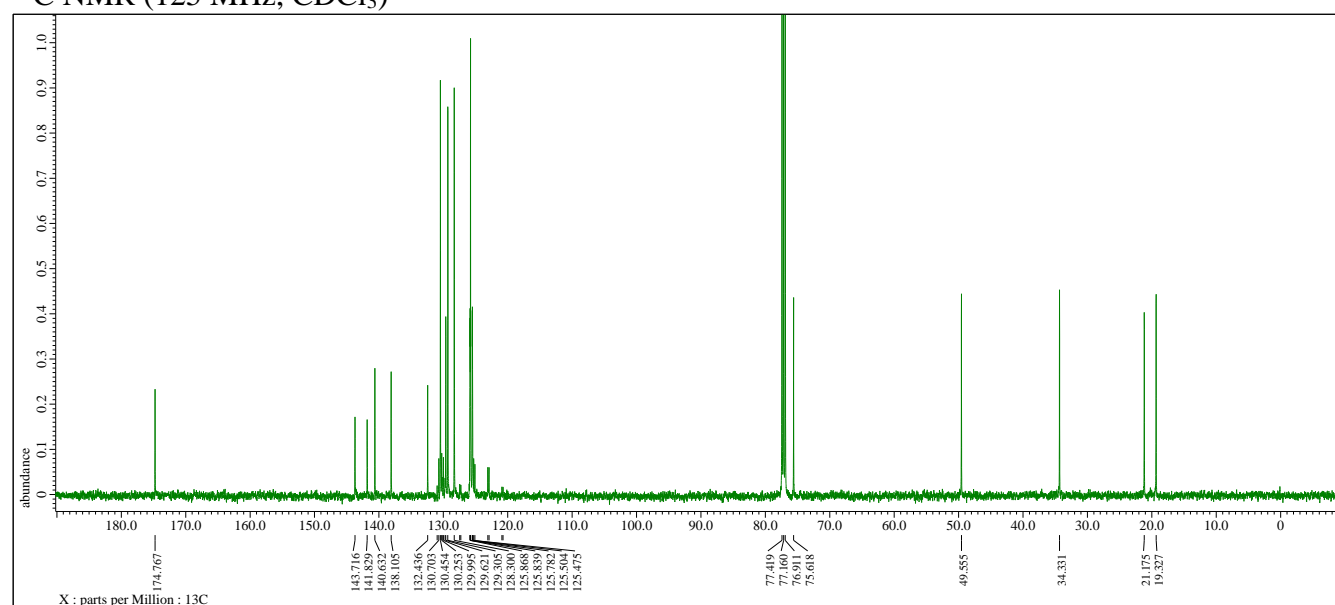
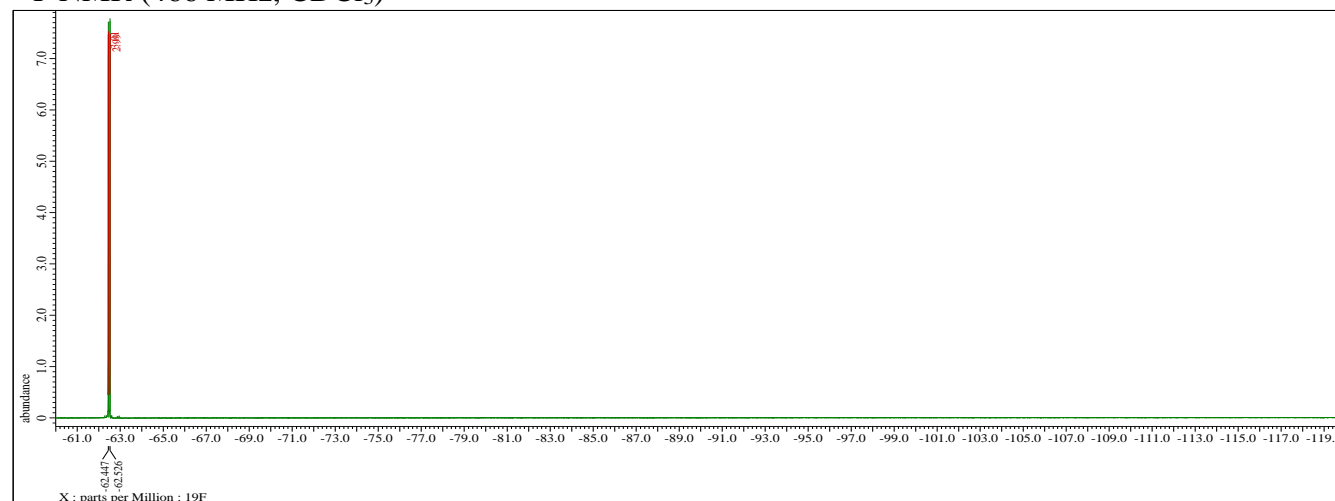
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(4-methoxyphenyl)piperidin-2-one (3b)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-methoxyphenyl)piperidin-2-one (3c)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

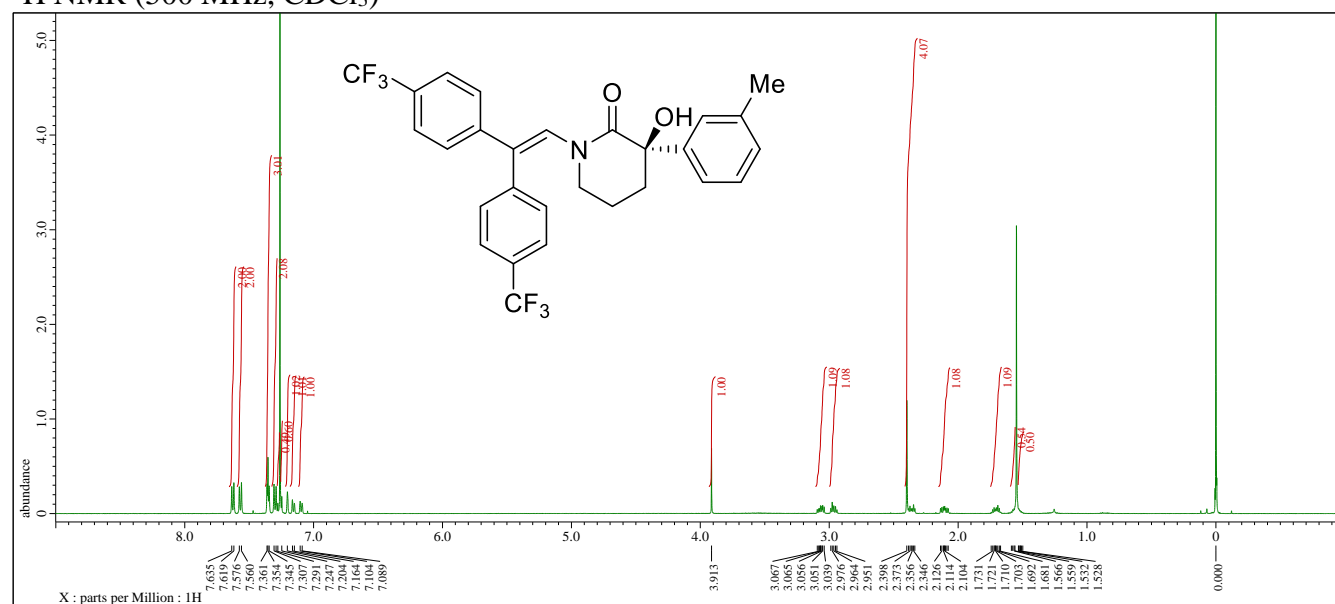
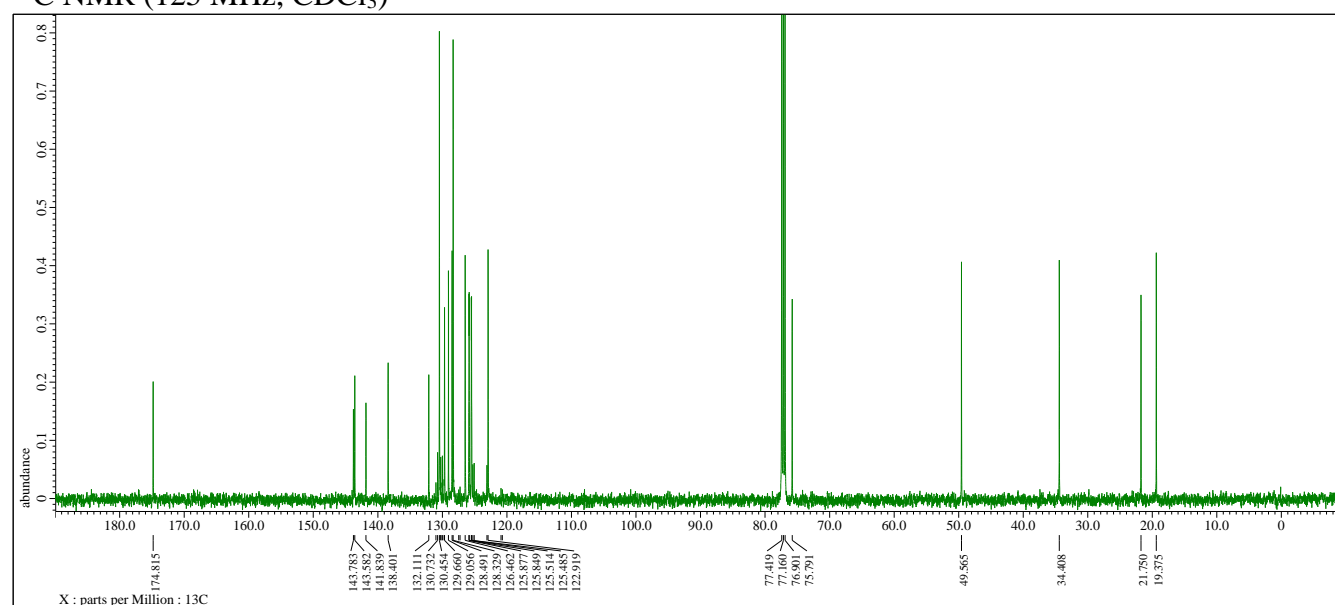
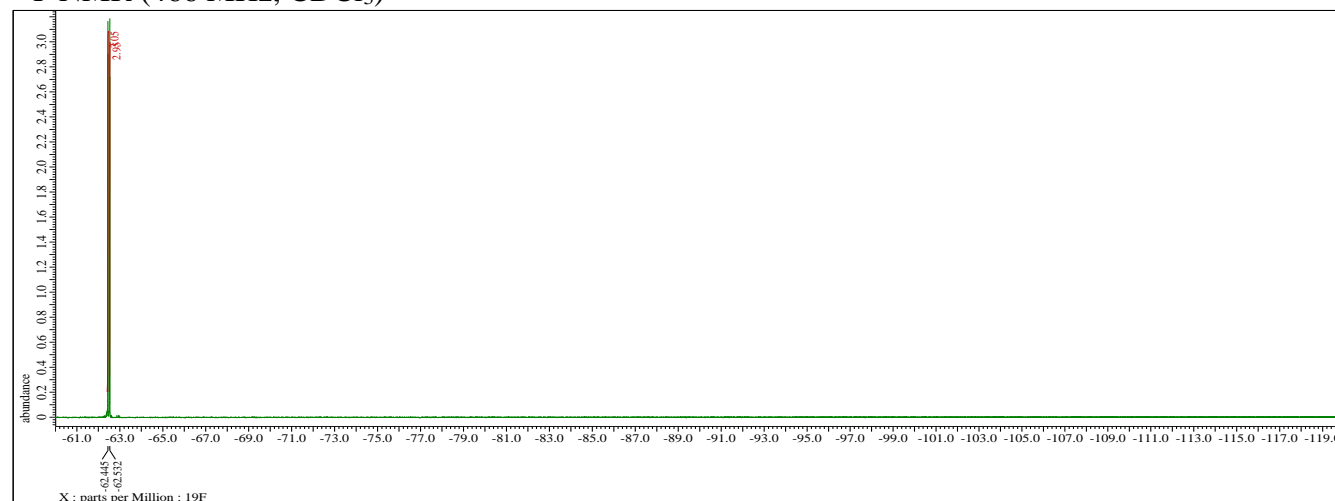
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-fluorophenyl)-3-hydroxypiperidin-2-one (3d)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(3,4-dichlorophenyl)-3-hydroxypiperidin-2-one (3e)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

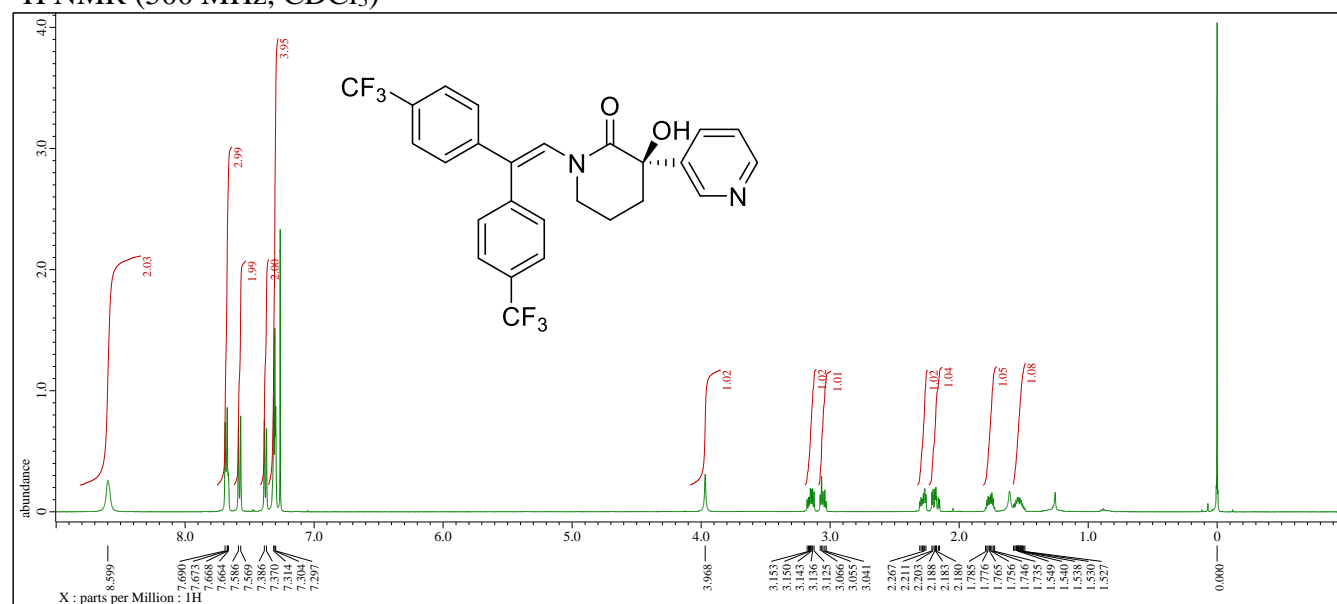
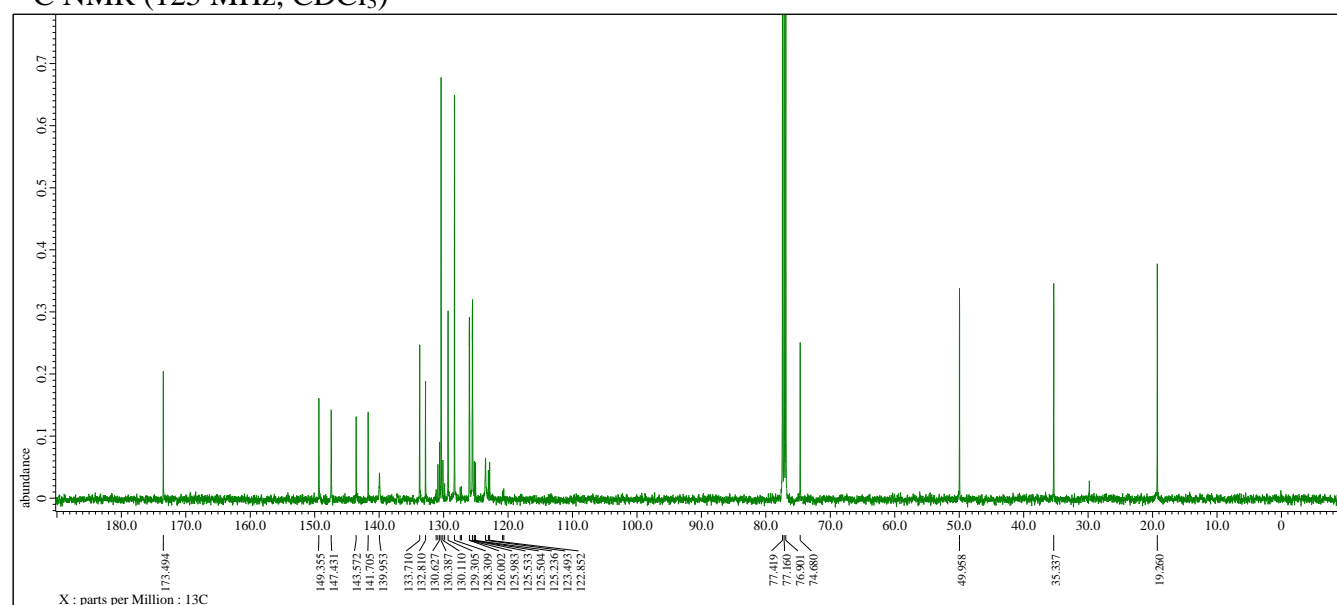
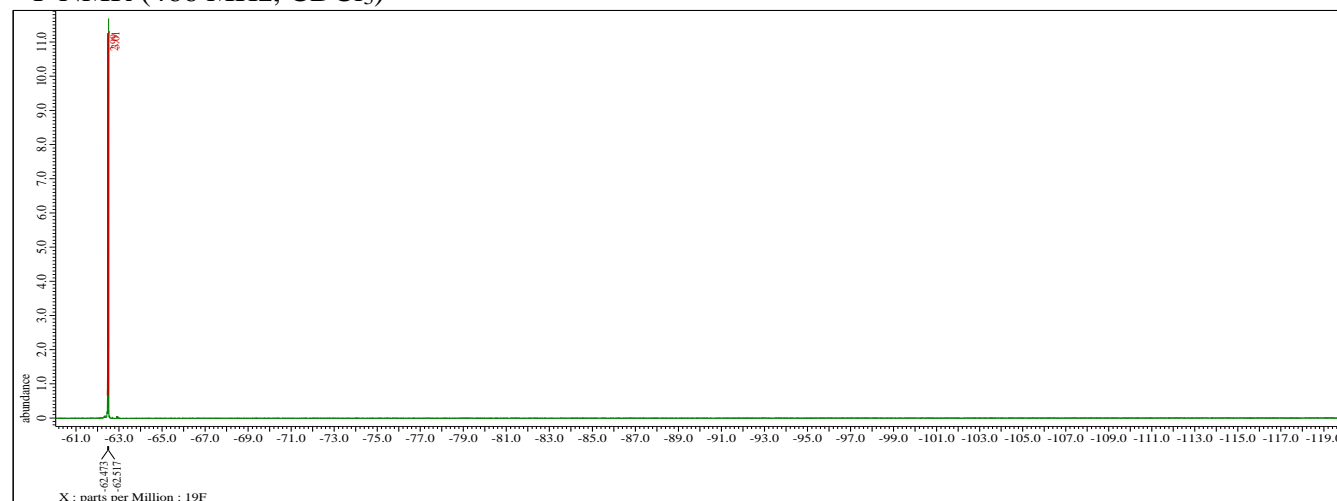
SUPPORTING INFORMATION

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(p-tolyl)piperidin-2-one (3g)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

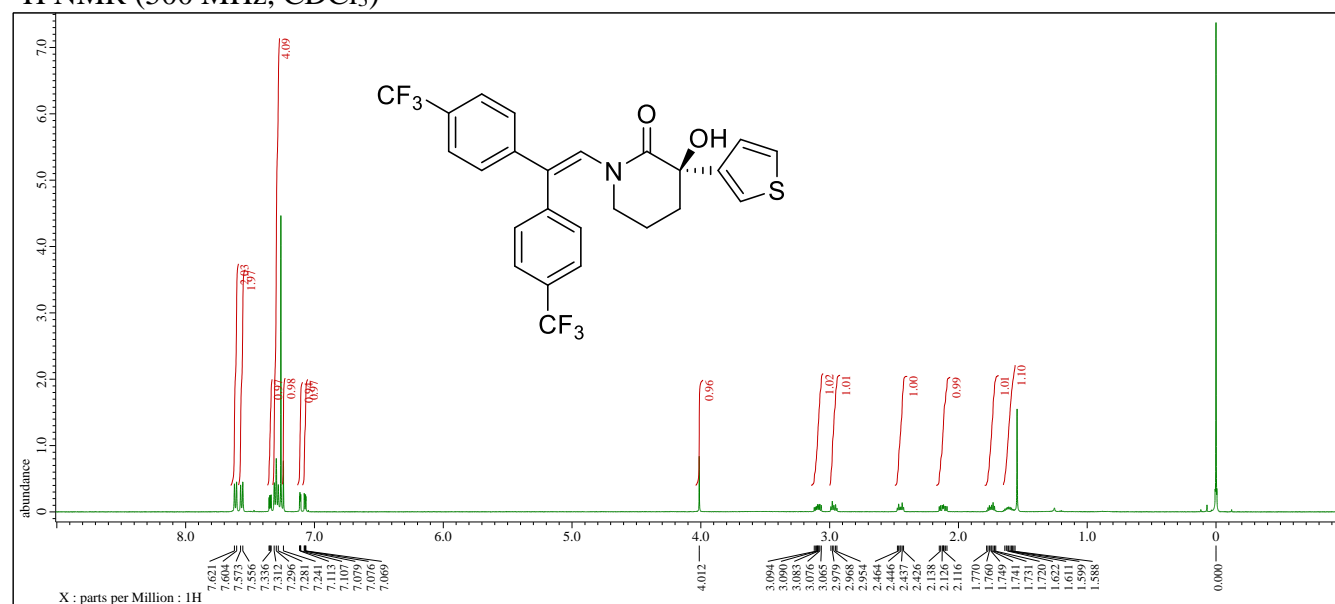
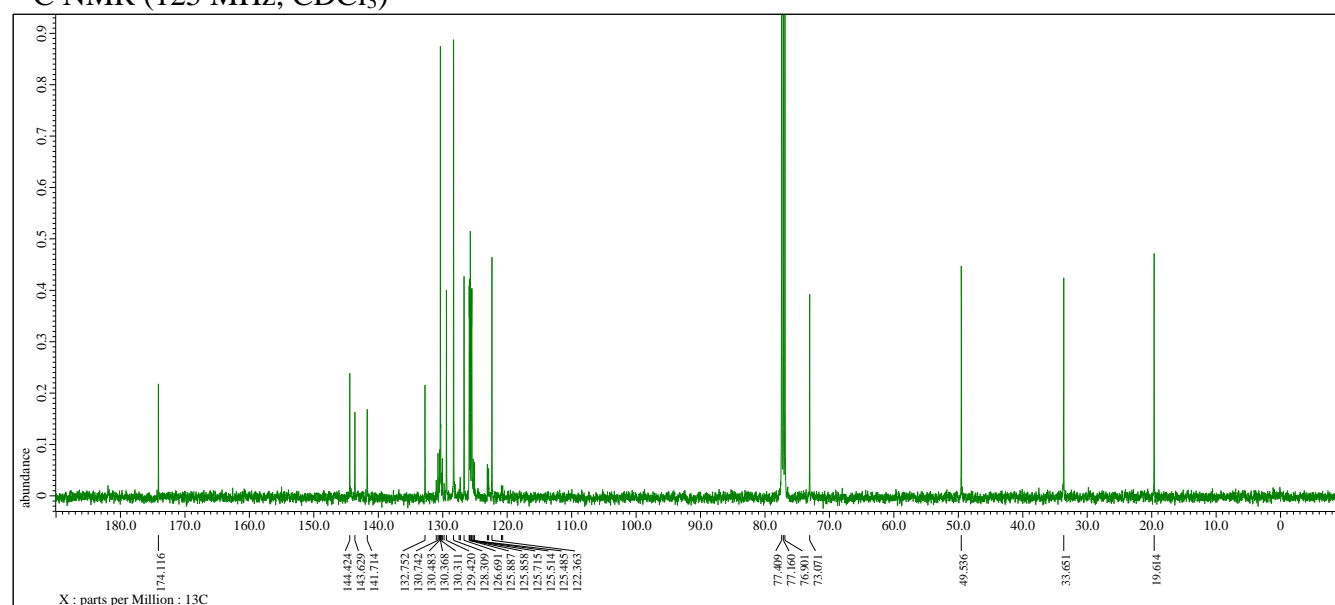
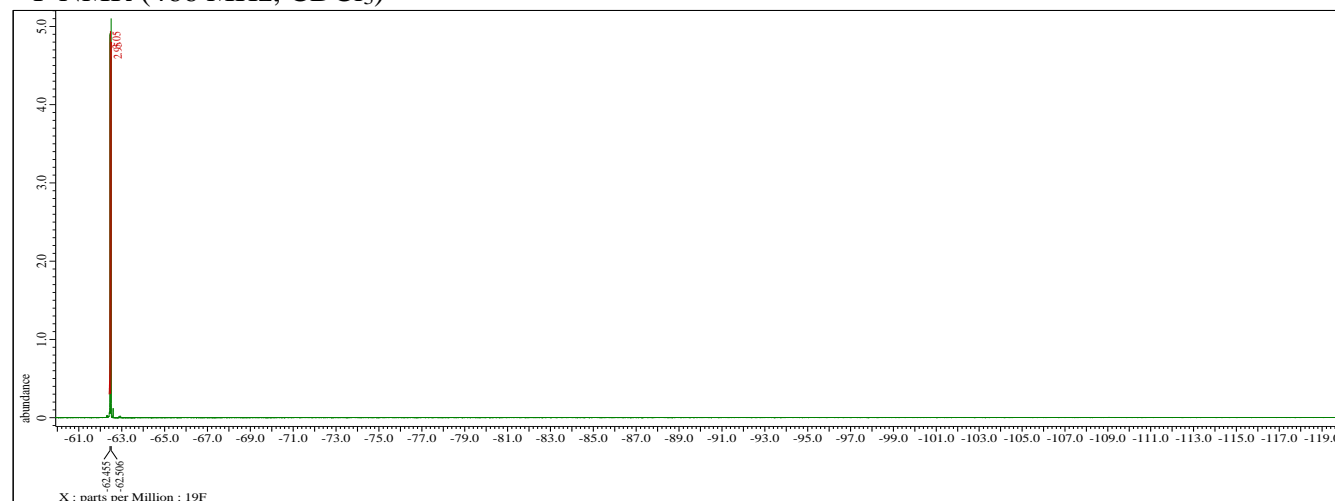
SUPPORTING INFORMATION

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(*m*-tolyl)piperidin-2-one (3h)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

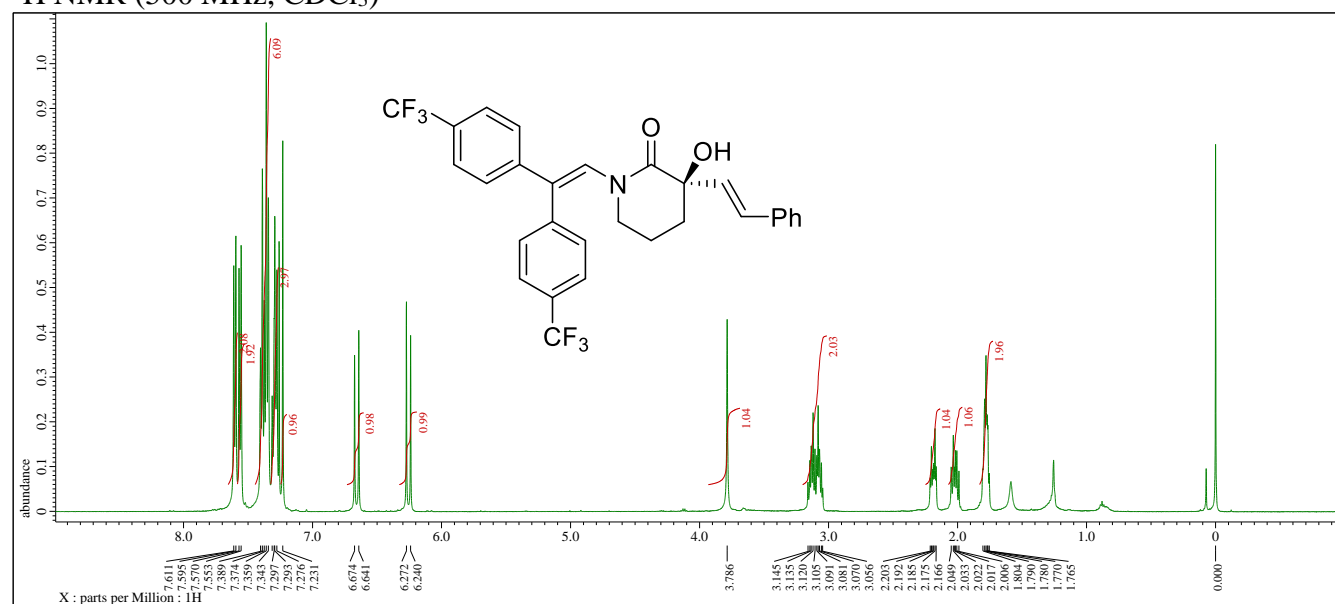
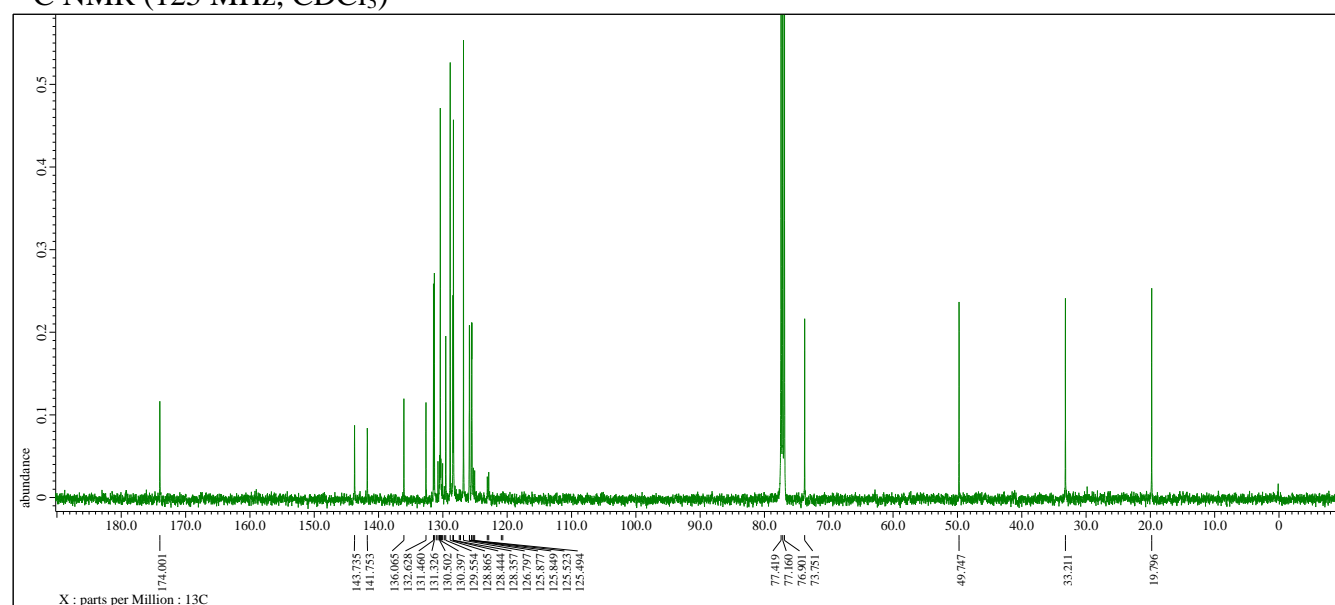
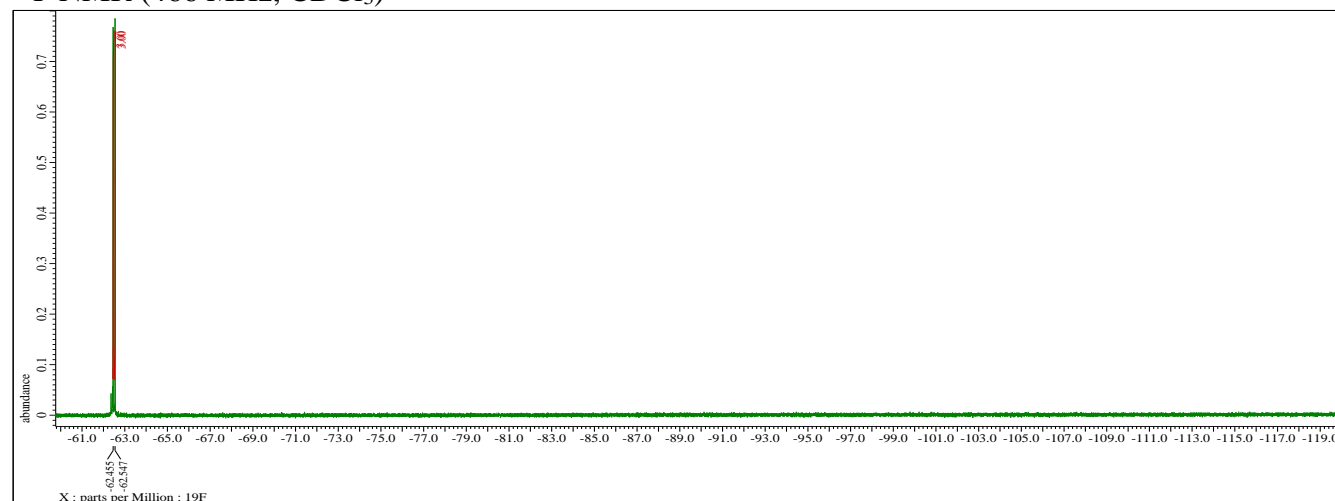
SUPPORTING INFORMATION

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(pyridin-3-yl)piperidin-2-one (3j)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

SUPPORTING INFORMATION

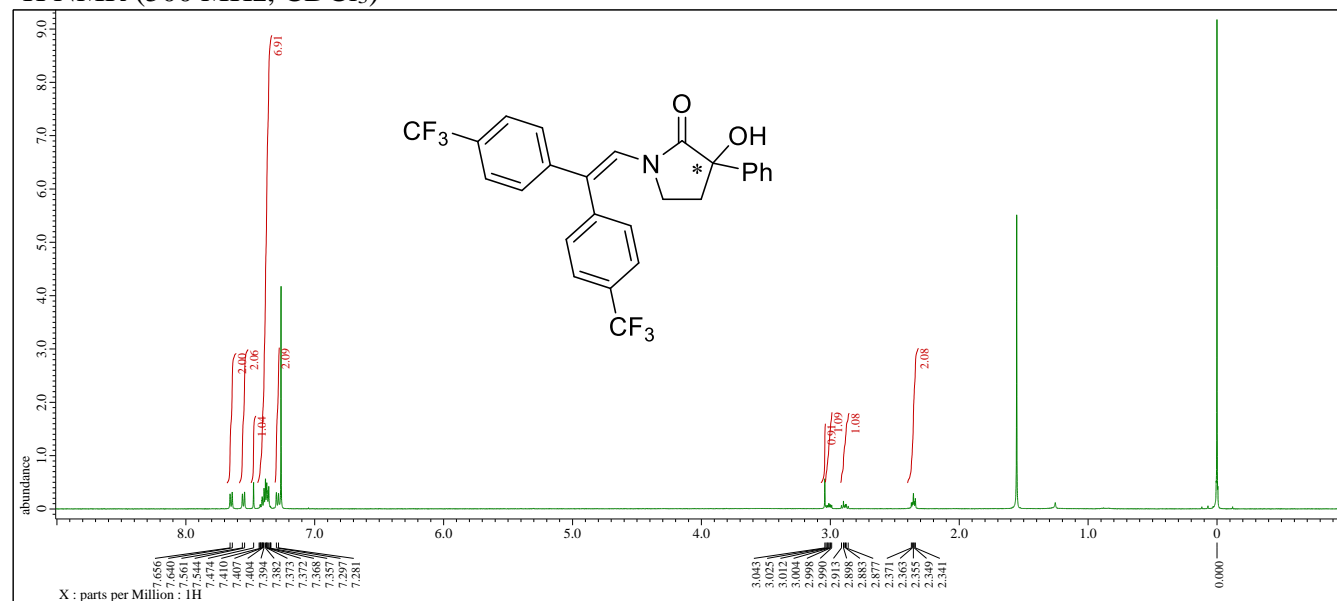
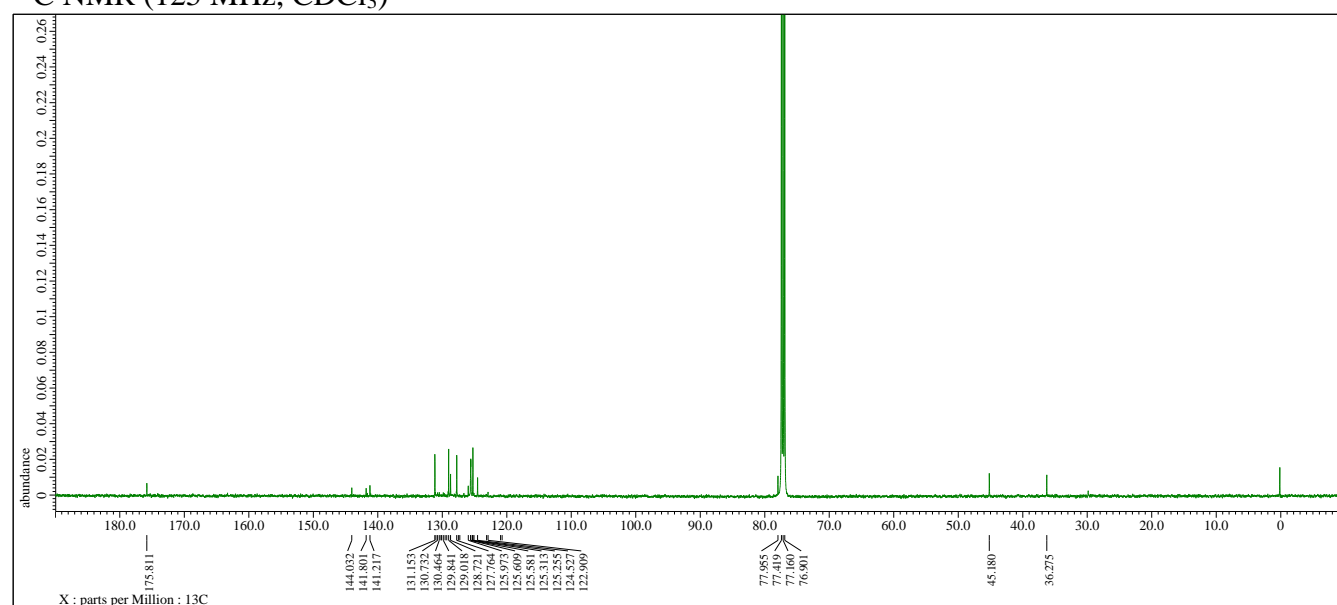
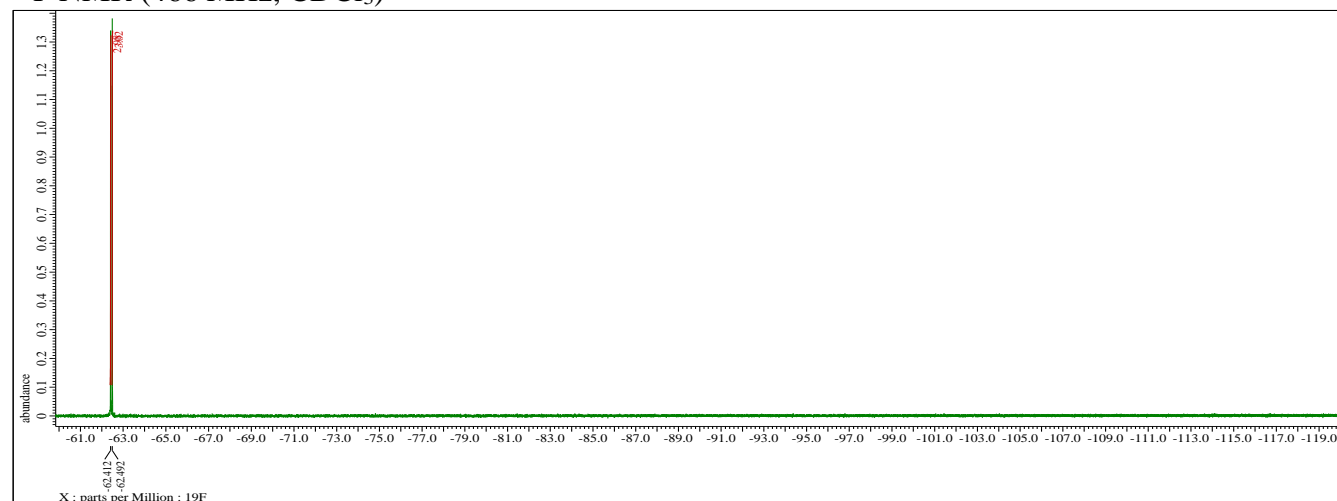
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-thienyl)piperidin-2-one (3k)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

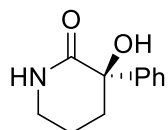
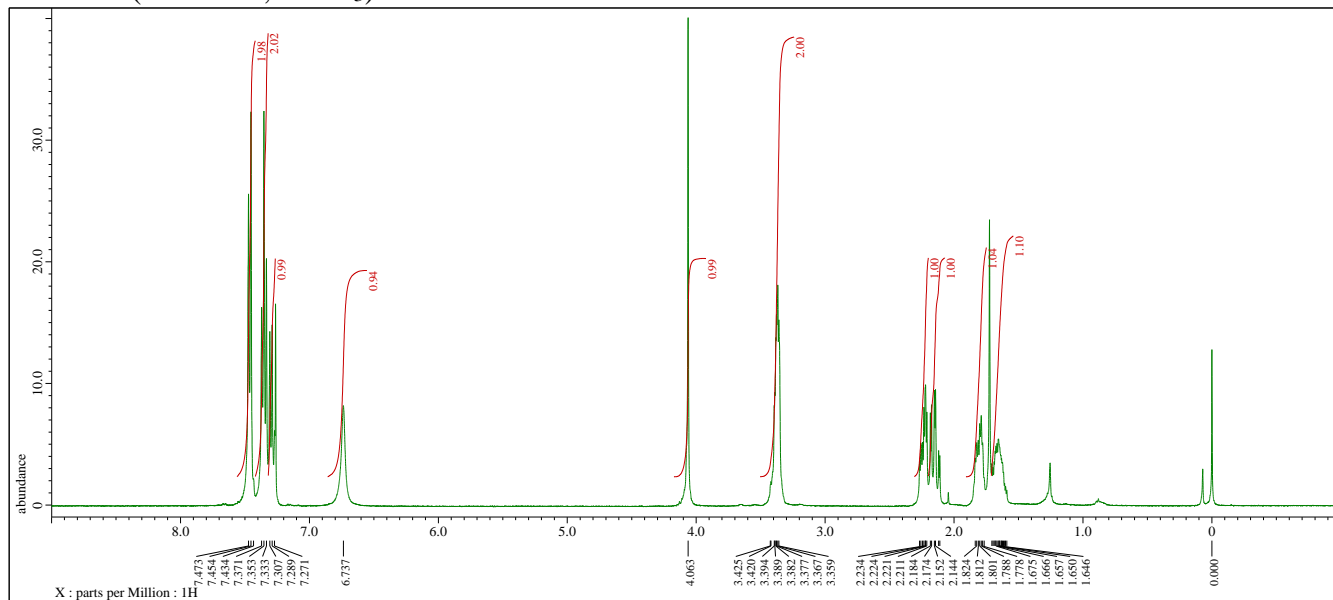
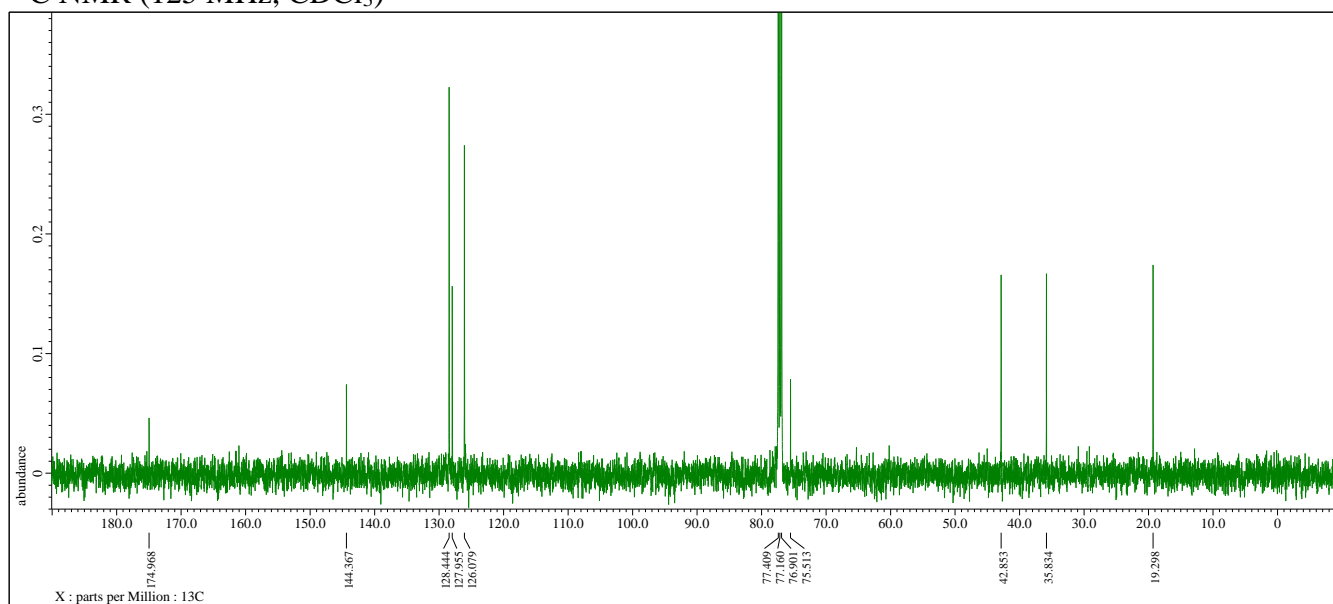
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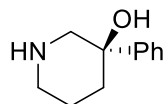
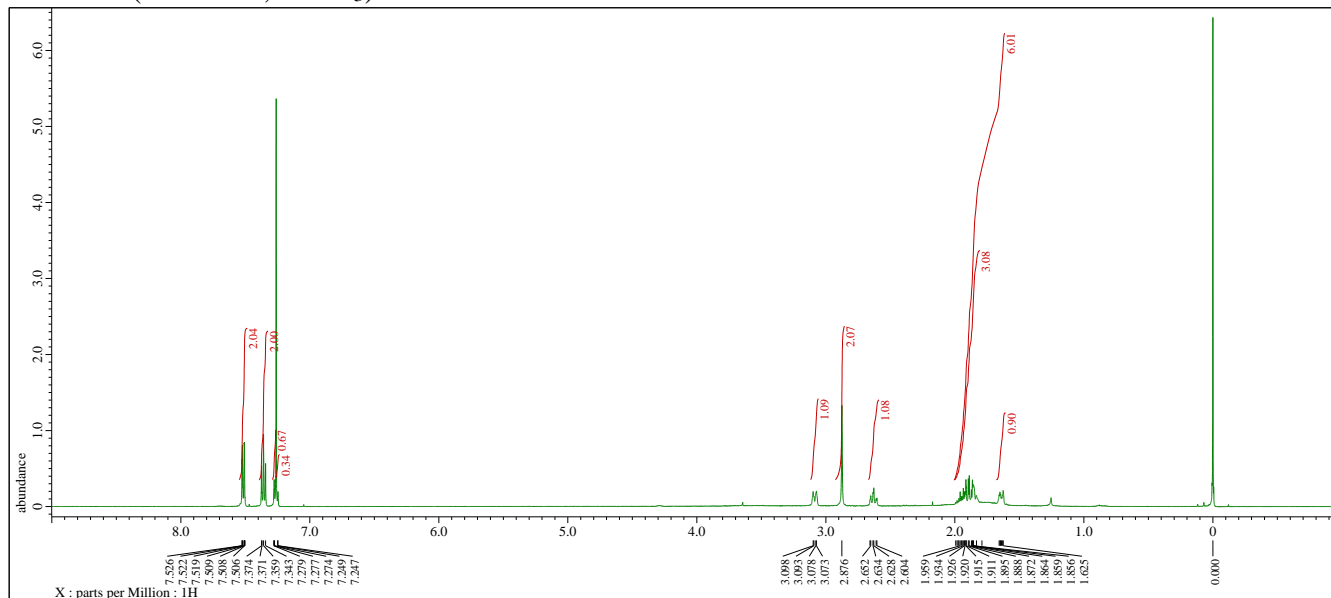
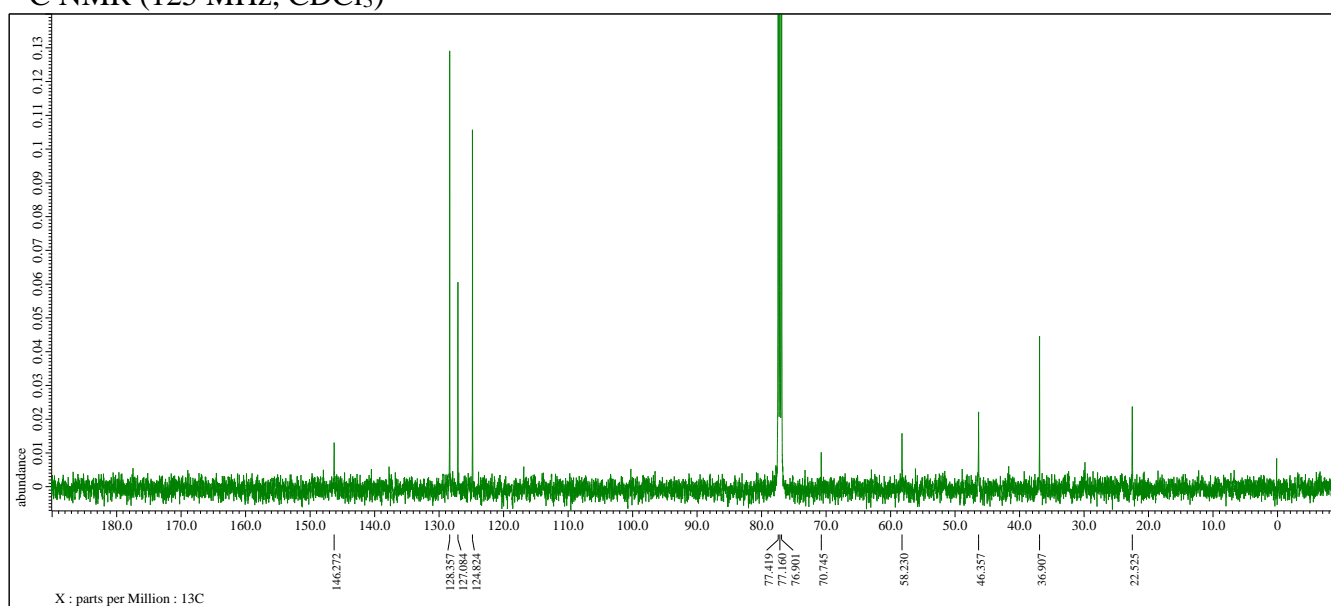
(*R,E*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-styrylpiperidin-2-one (31)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

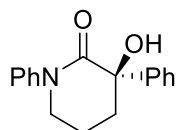
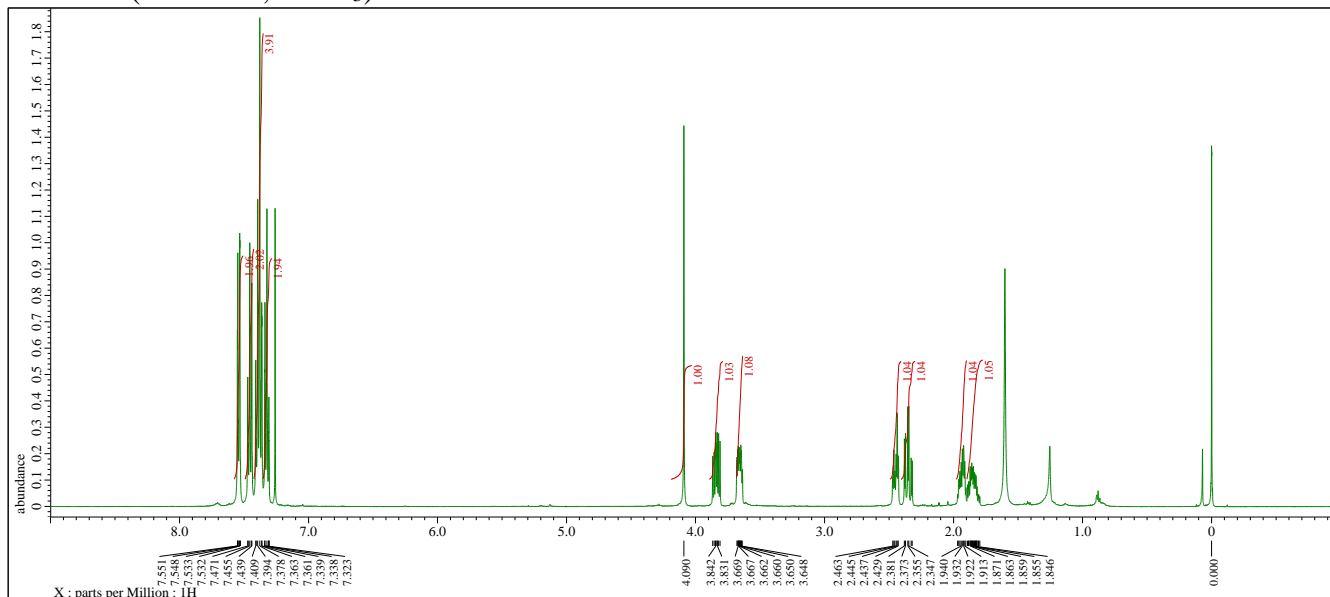
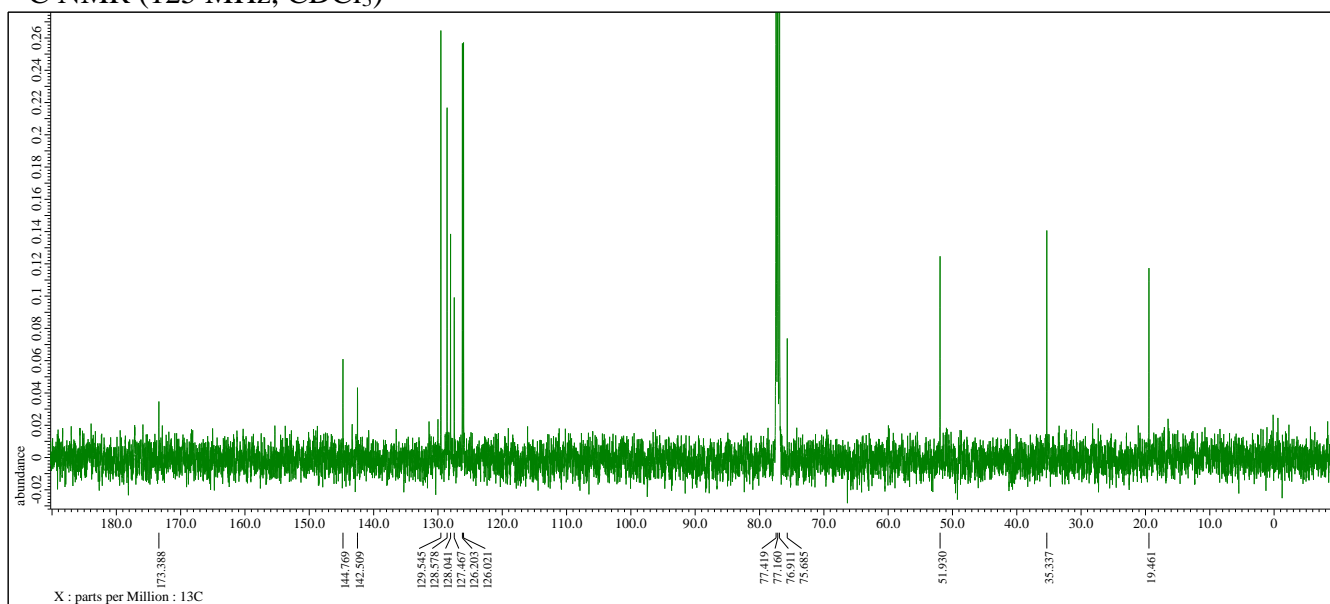
SUPPORTING INFORMATION

1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpyrrolidin-2-one (3m)

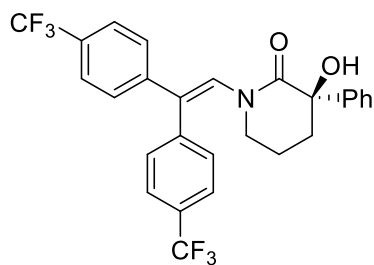
¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)¹⁹F NMR (466 MHz, CDCl₃)

(R)-3-Hydroxy-3-phenylpiperidin-2-one (4a)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)

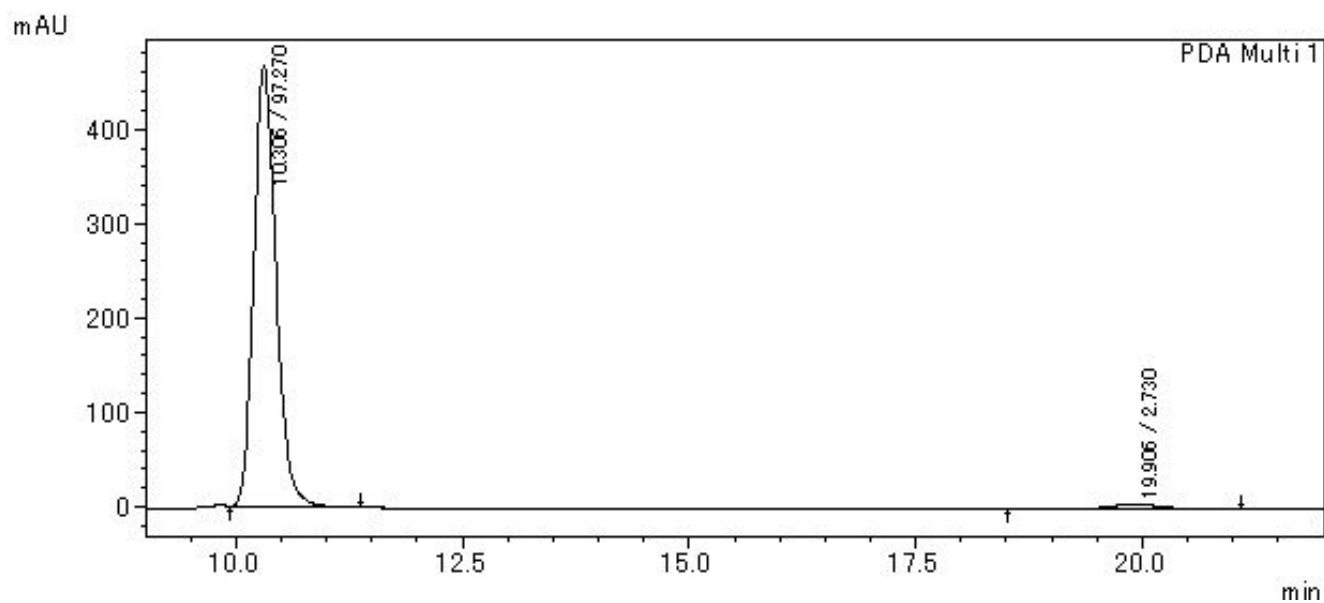
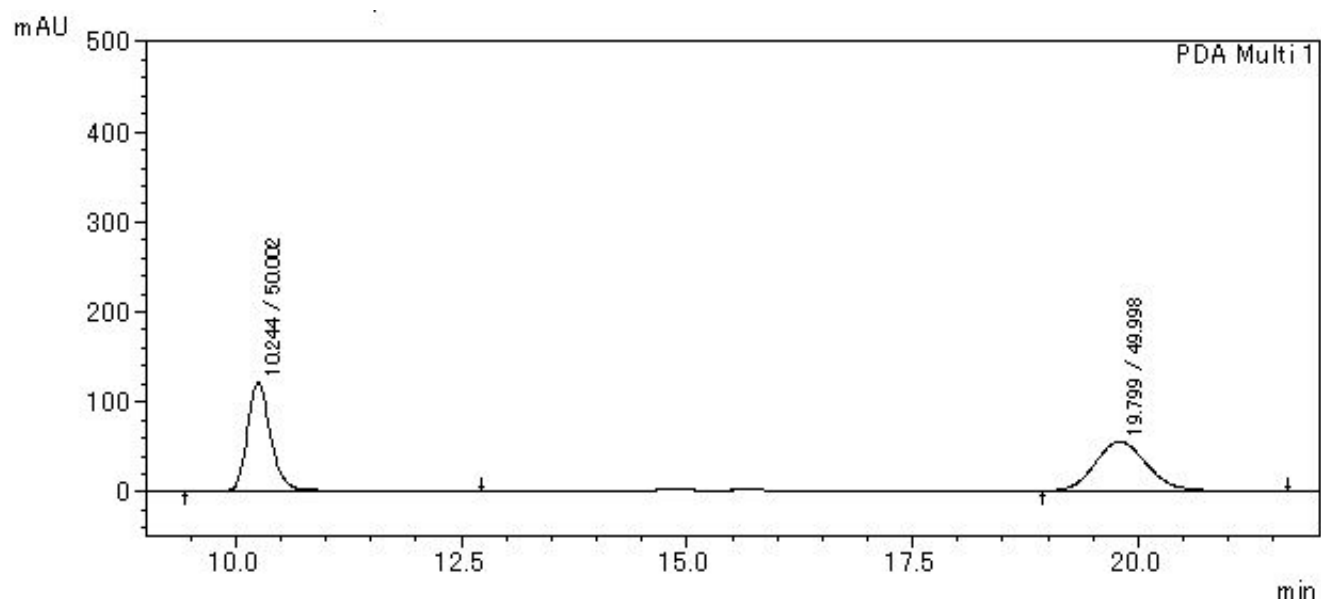
(R)-3-Phenylpiperidin-3-ol (5a)¹H NMR (500 MHz, CDCl₃)¹³C NMR (125 MHz, CDCl₃)

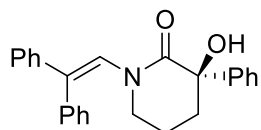
(R)-3-Hydroxy-1,3-diphenylpiperidin-2-one (6a)**¹H NMR (500 MHz, CDCl₃)****¹³C NMR (125 MHz, CDCl₃)**

HPLC analysis

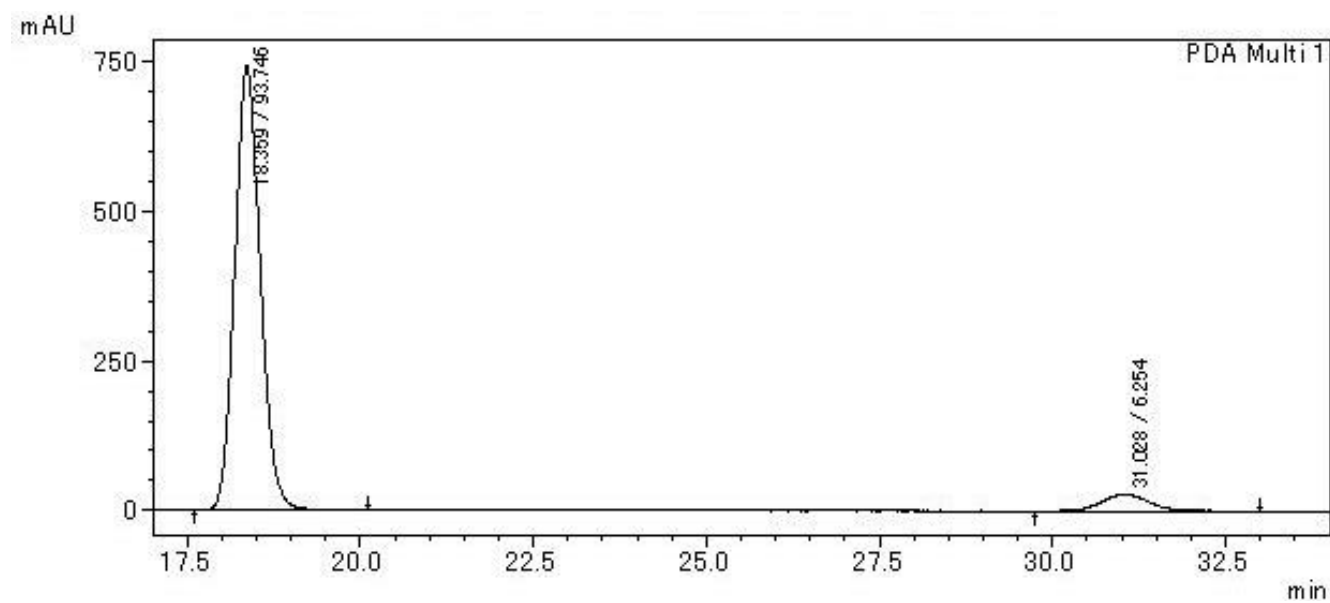
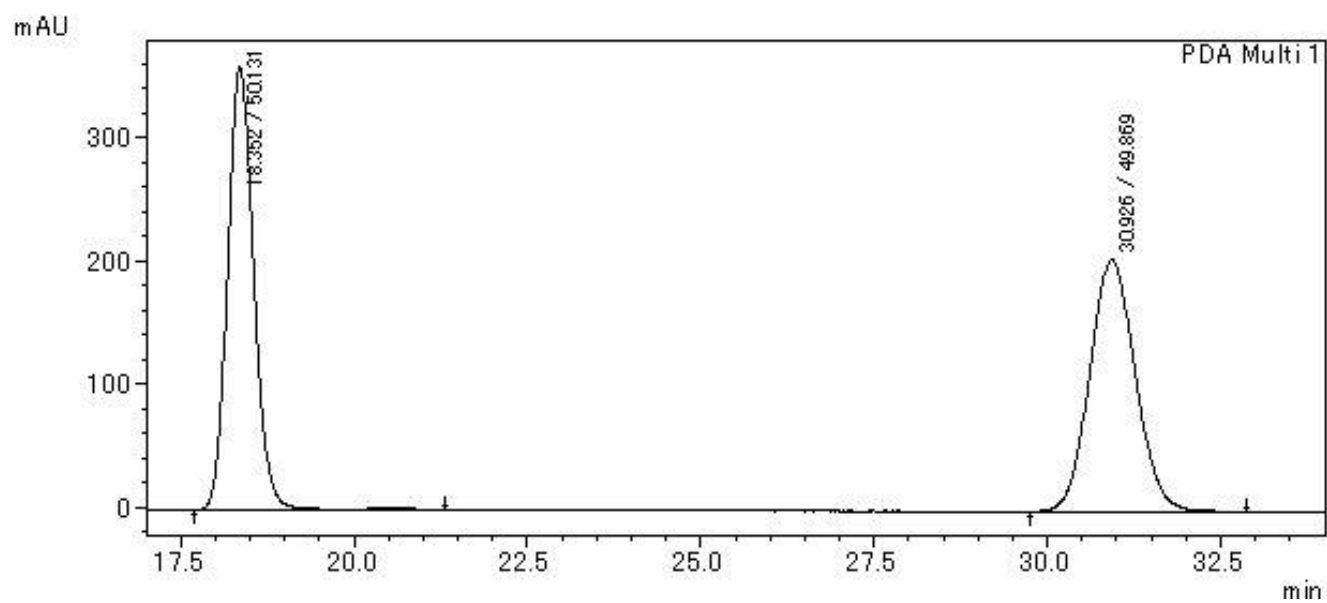
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpiperidin-2-one (3a)

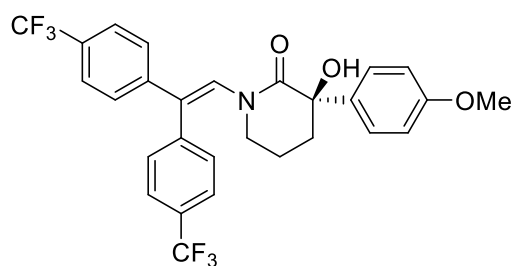
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 10.3 min (major) and 19.9 min (minor).



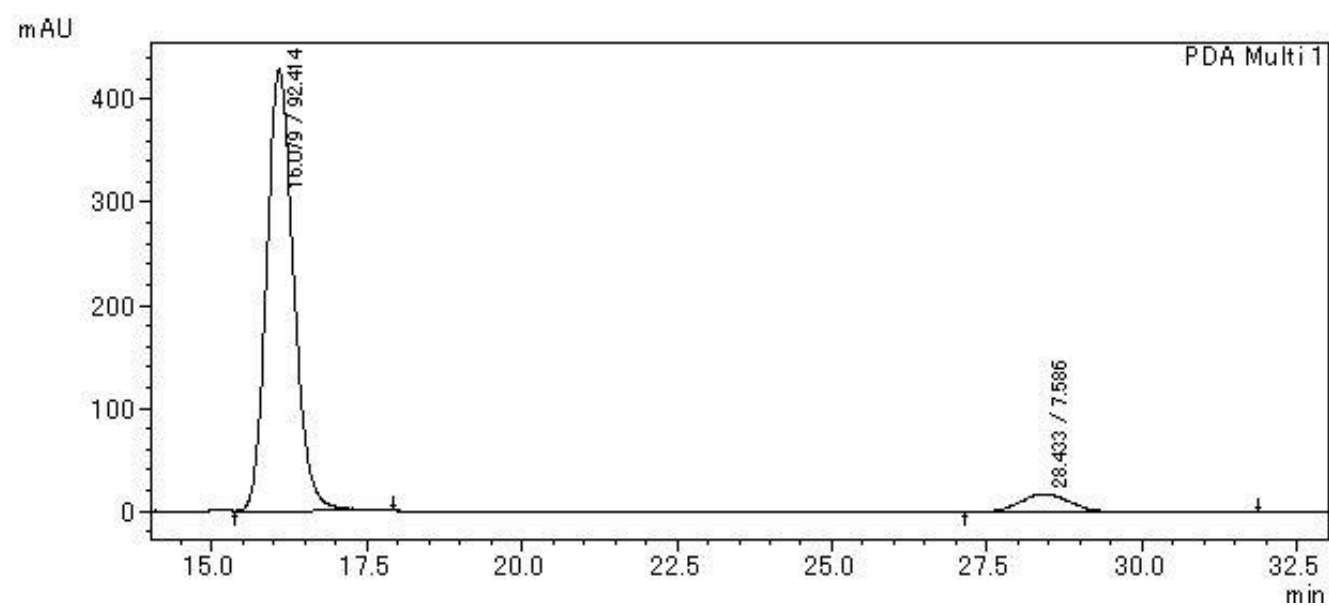
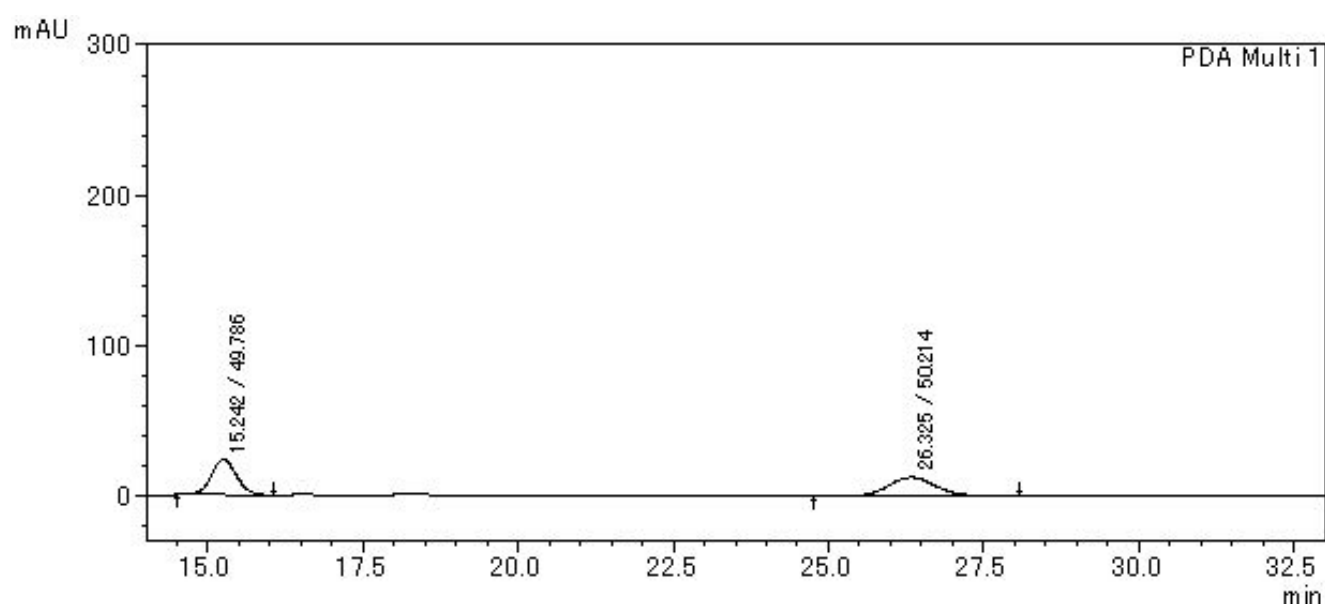
(R)-1-(2,2-Diphenylvinyl)-3-hydroxy-3-phenylpiperidin-2-one

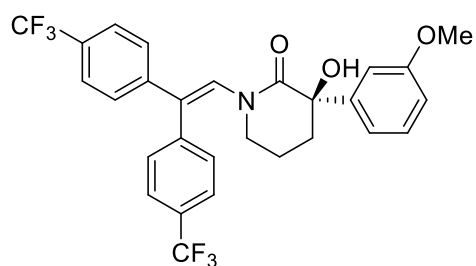
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 18.4 min (major) and 31.0 min (minor).



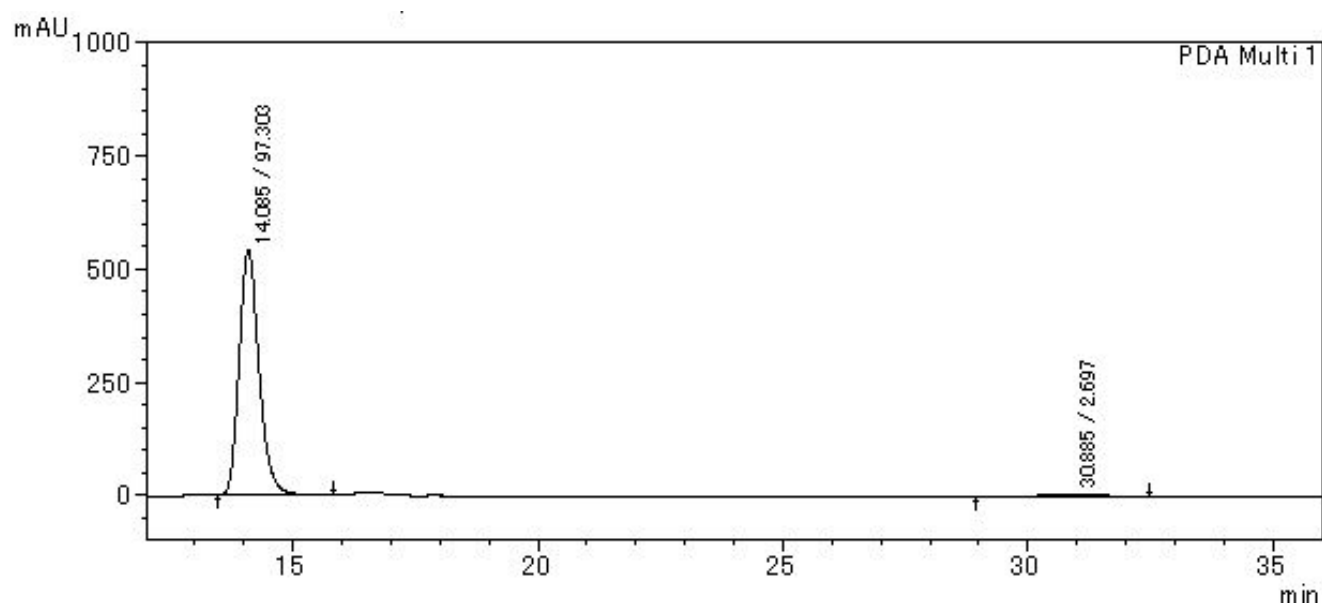
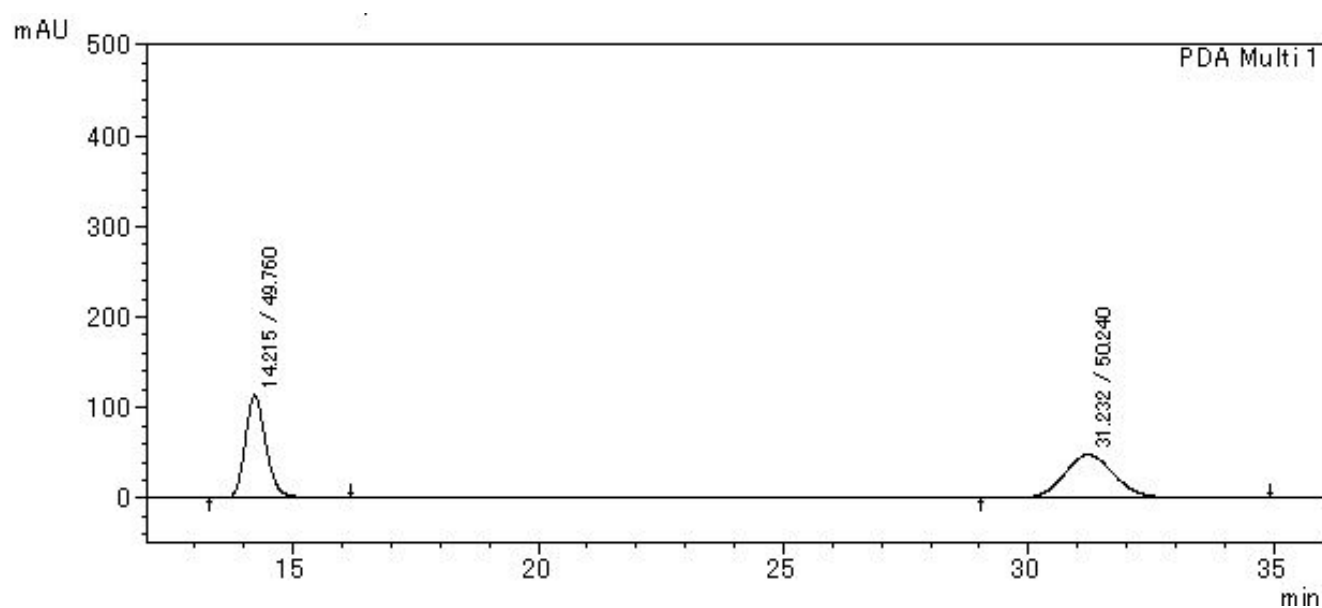
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(4-methoxyphenyl)piperidin-2-one (3b)

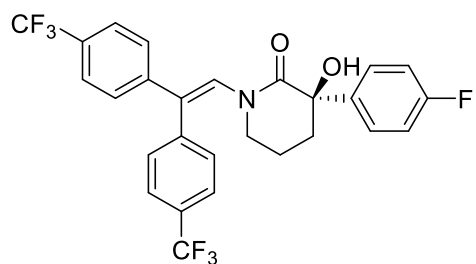
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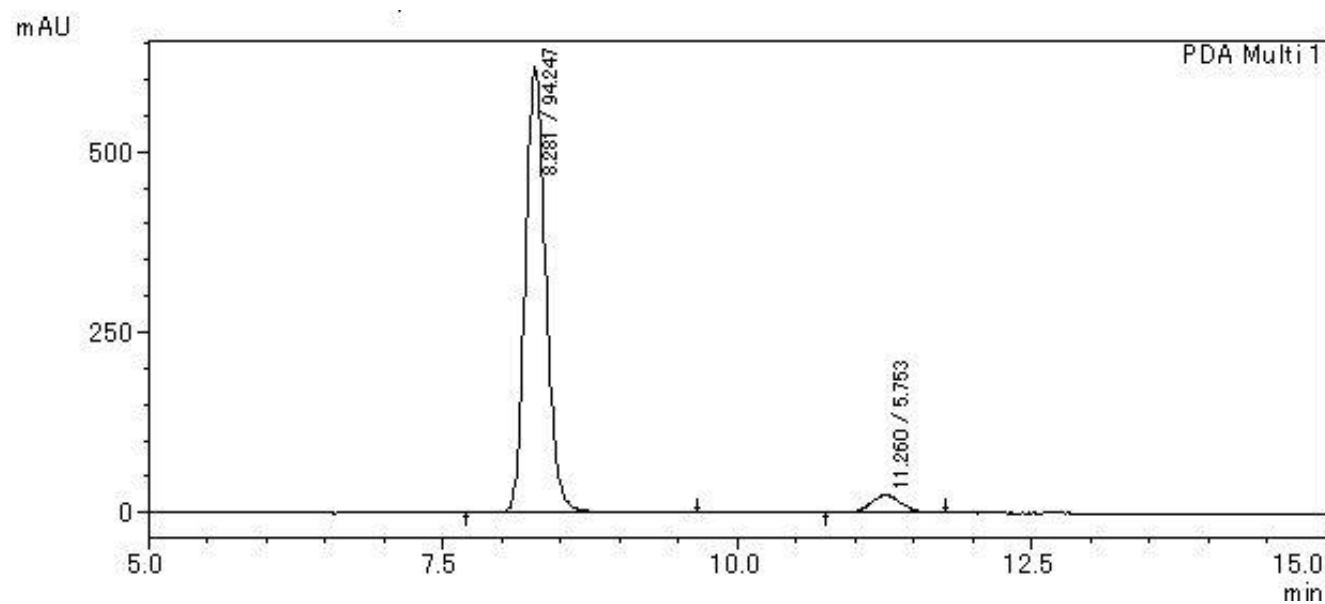
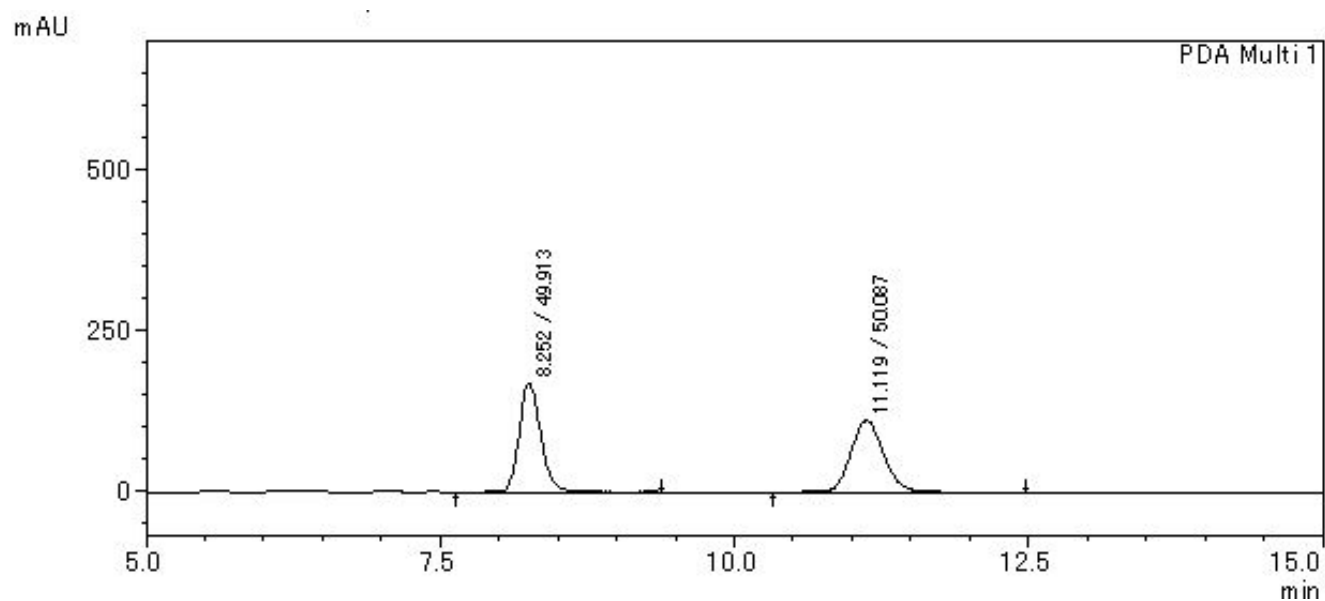
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-methoxyphenyl)piperidin-2-one (3c)

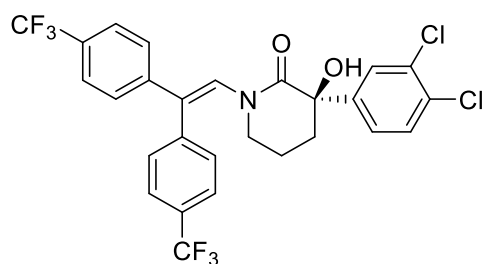
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 14.1 min (major) and 30.9 min (minor).



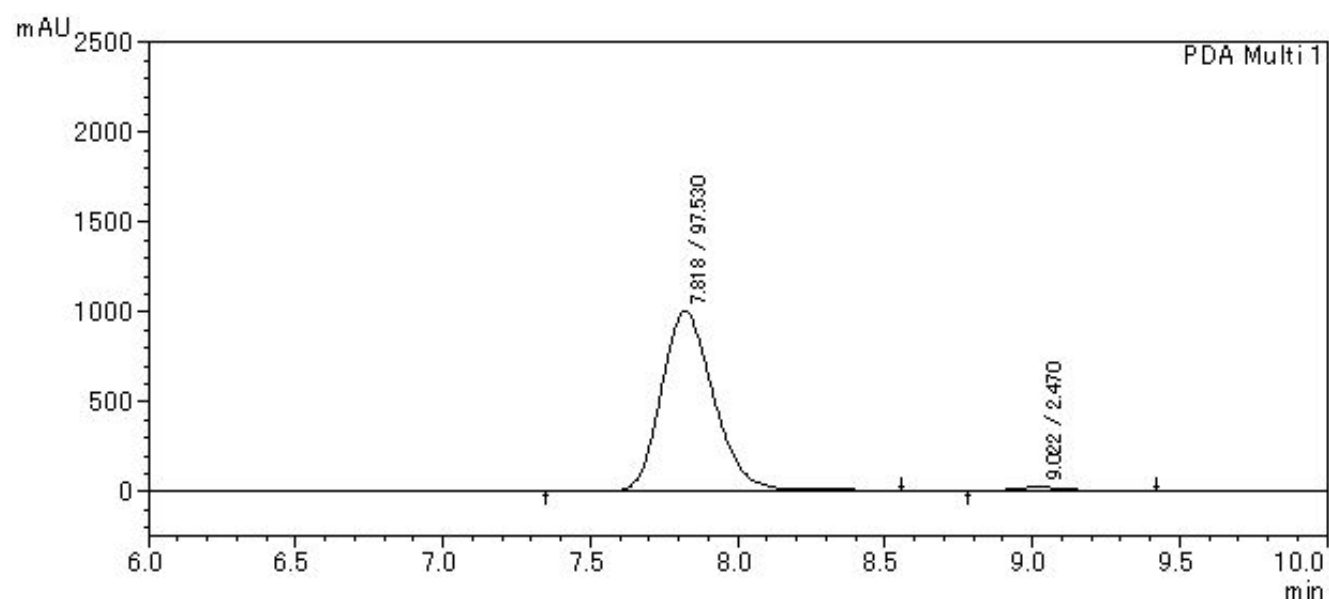
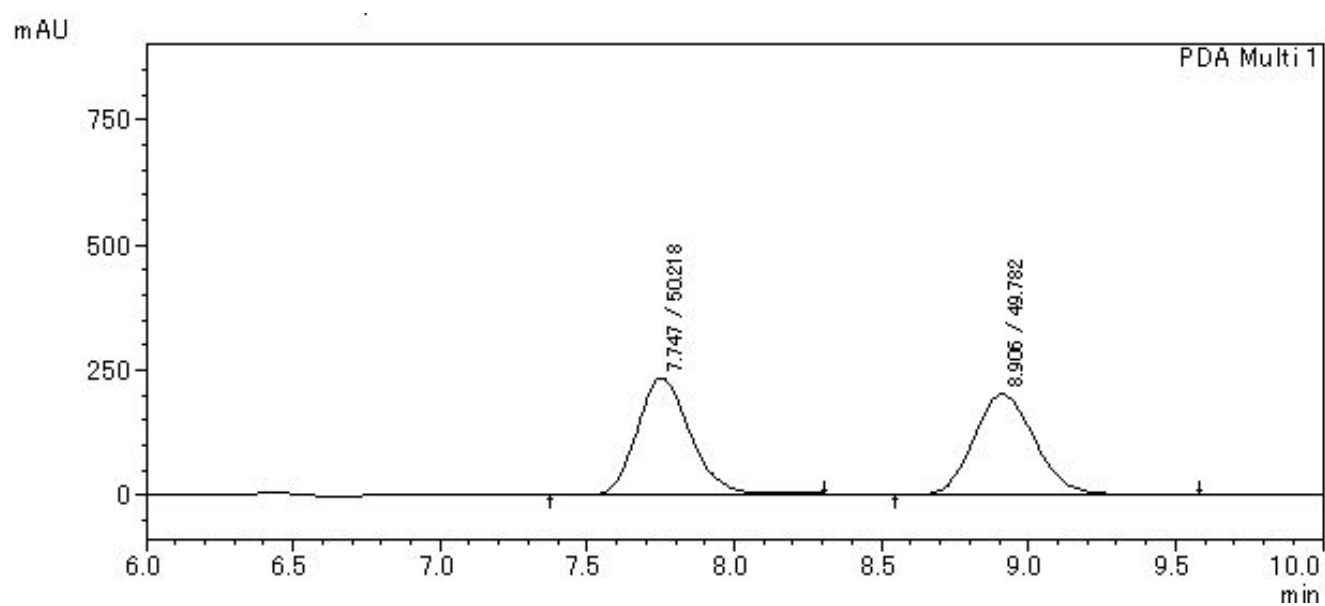
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-fluorophenyl)-3-hydroxypiperidin-2-one (3d)

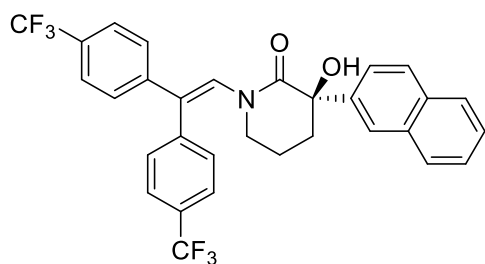
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 207$ nm, retention time: 8.3 min (major) and 11.3 min (minor).



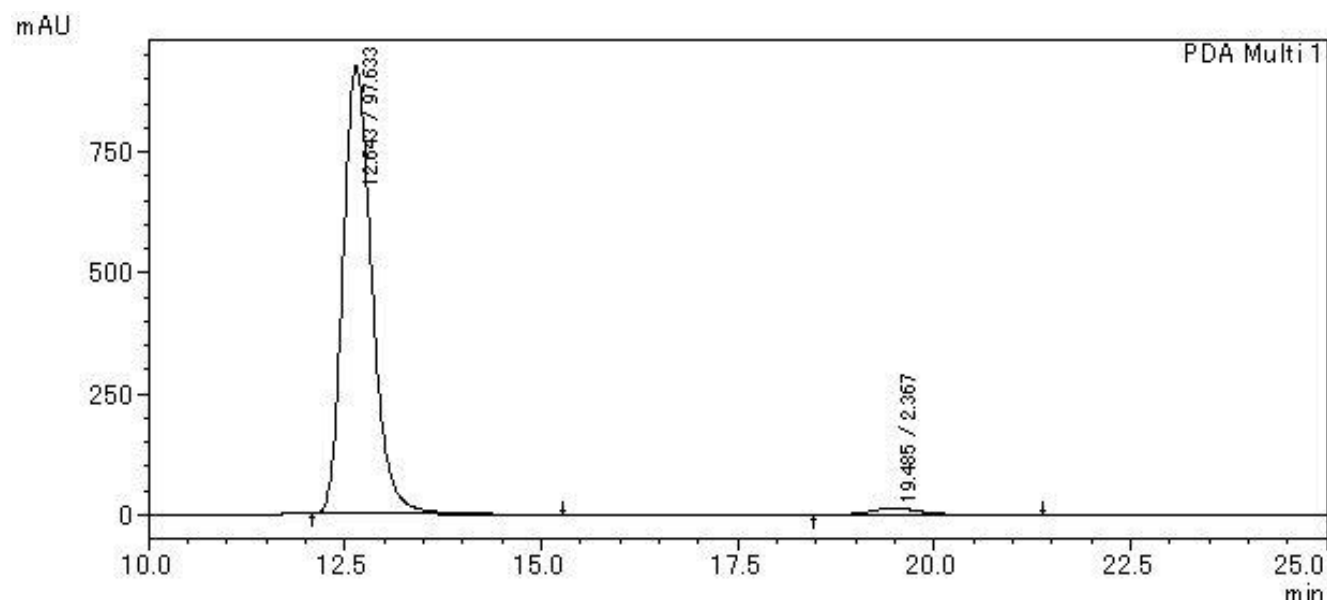
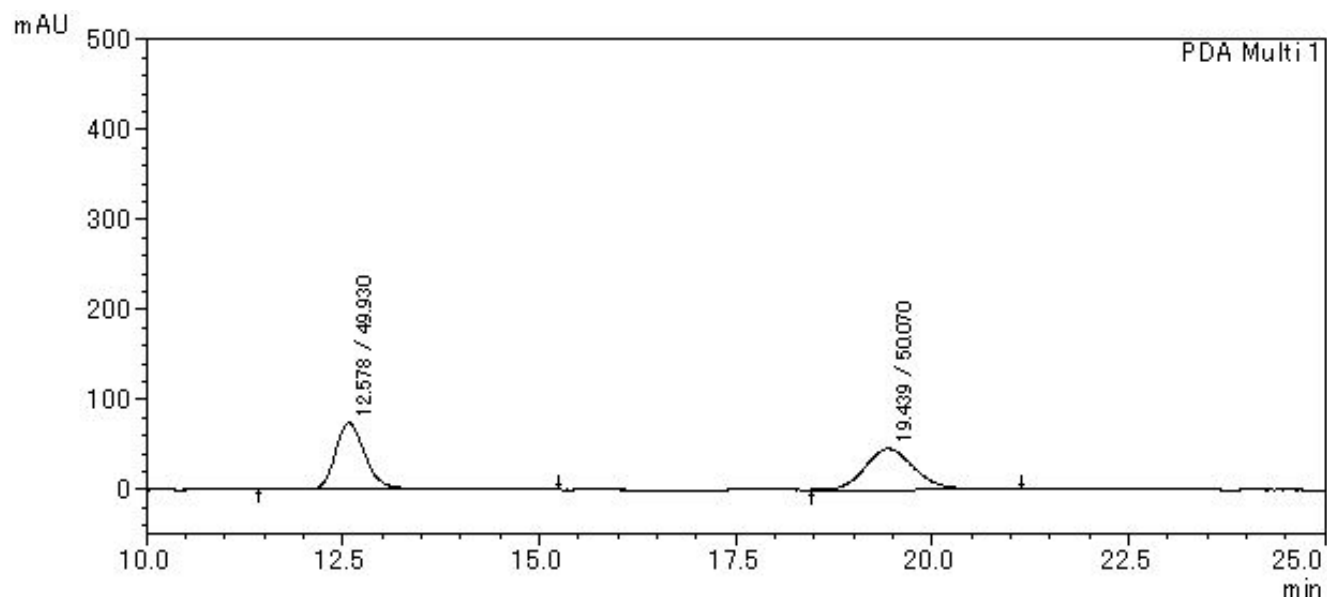
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(3,4-dichlorophenyl)-3-hydroxypiperidin-2-one (3e)

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 220$ nm, retention time: 7.8 min (major) and 9.0 min (minor).



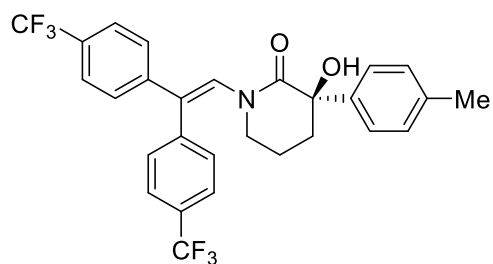
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(naphthalen-2-yl)piperidin-2-one (3f)

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 225$ nm, retention time: 12.6 min (major) and 19.5 min (minor).

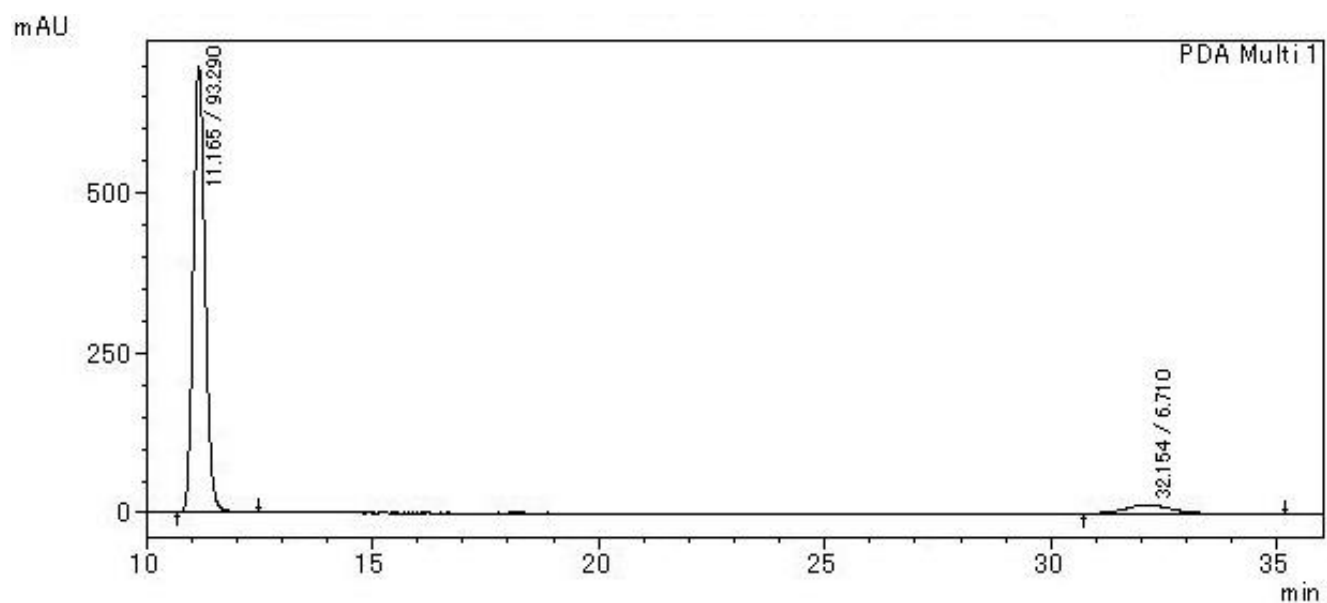
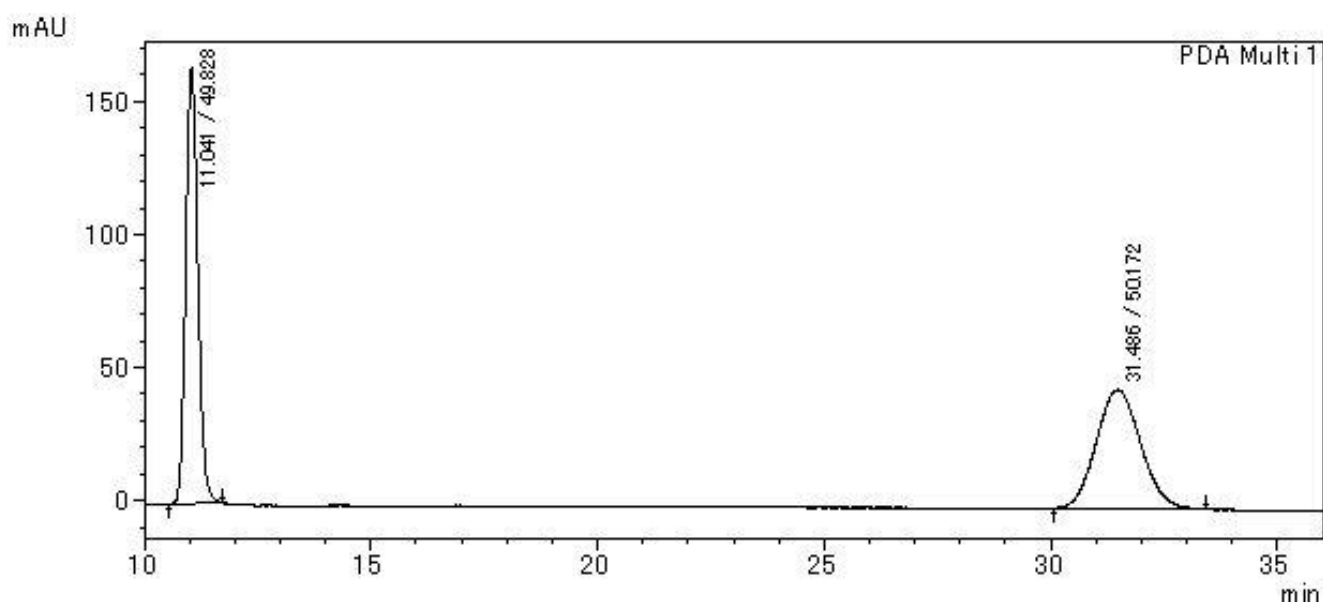


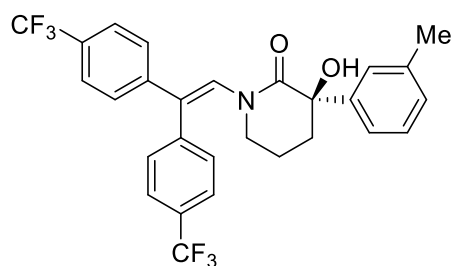
SUPPORTING INFORMATION

(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(p-tolyl)piperidin-2-one (3g)

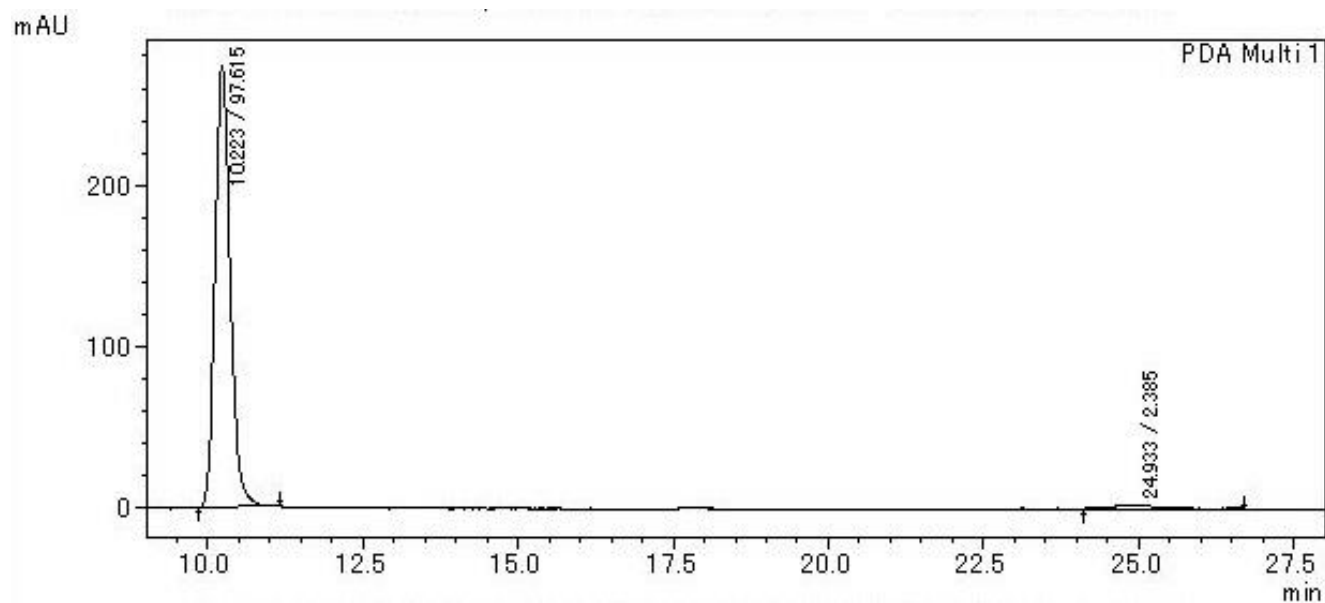
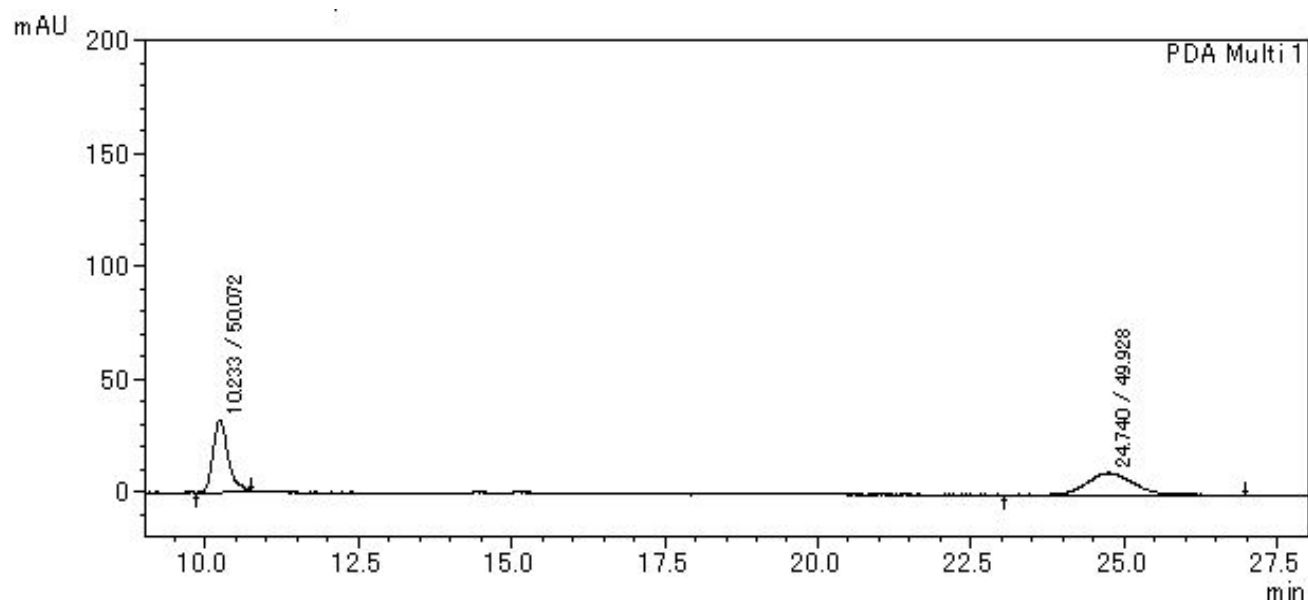


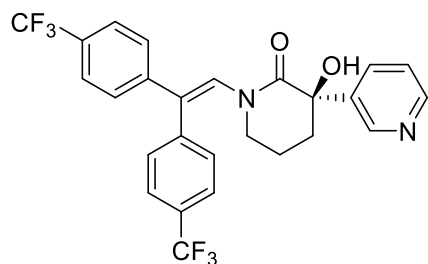
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 11.2 min (major) and 32.2 min (minor).



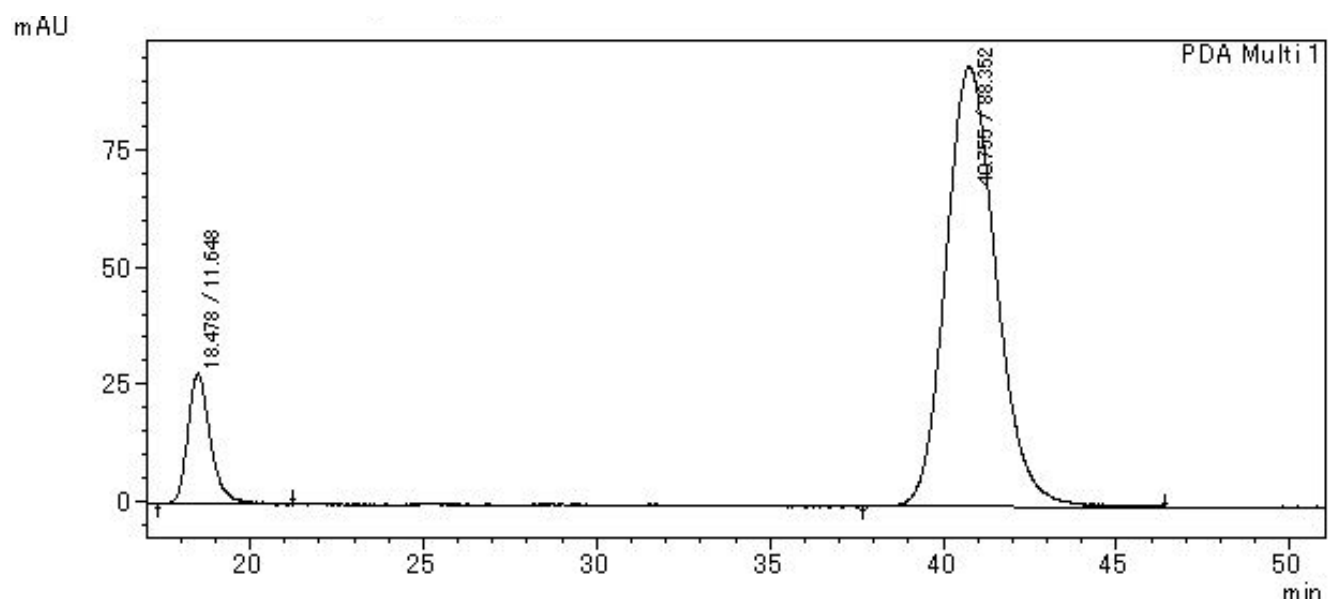
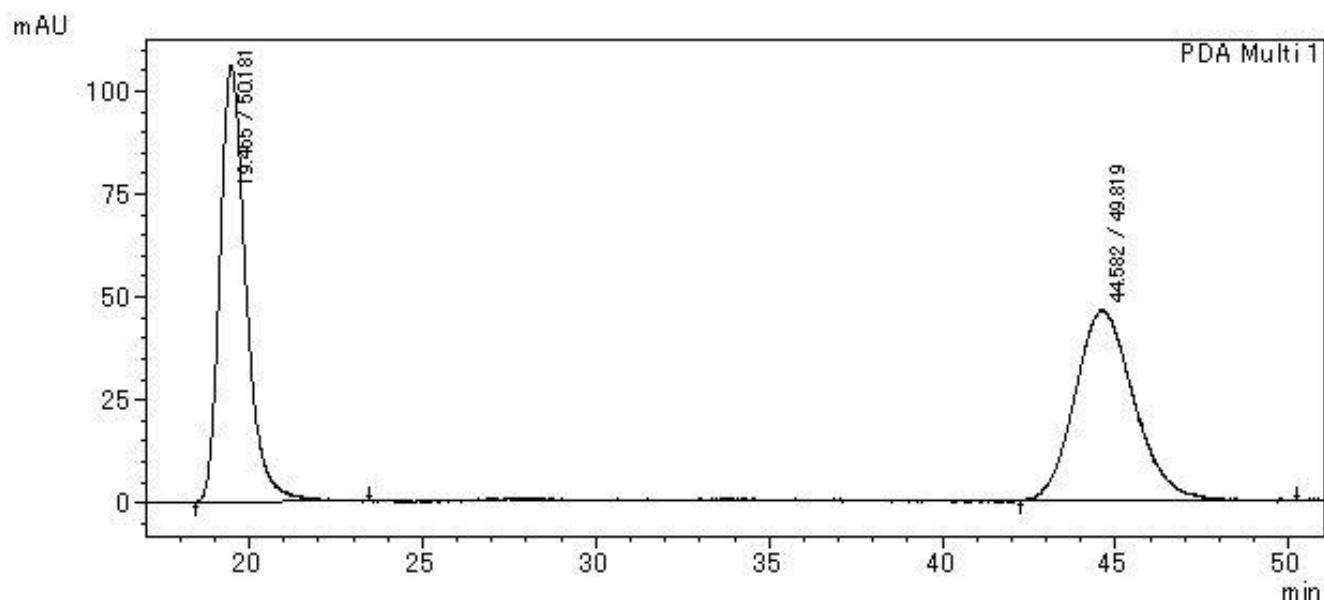
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(*m*-tolyl)piperidin-2-one (3h)

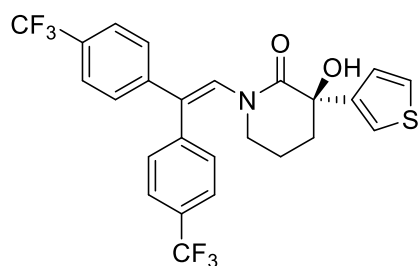
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 10.2 min (major) and 24.9 min (minor).



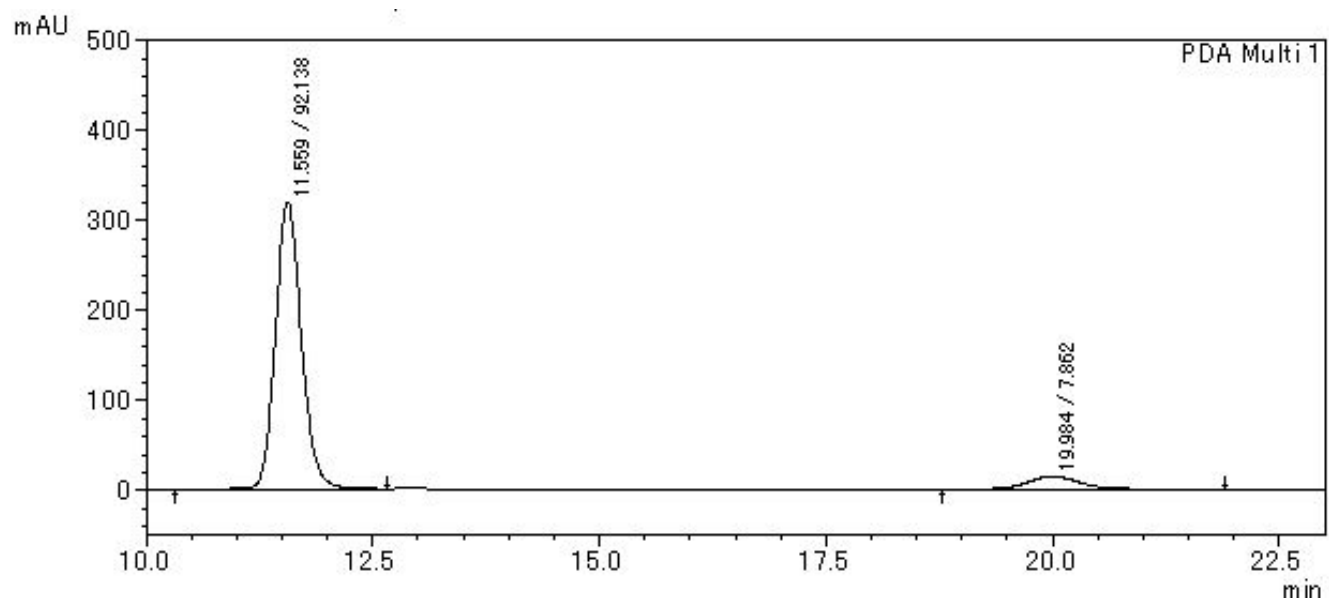
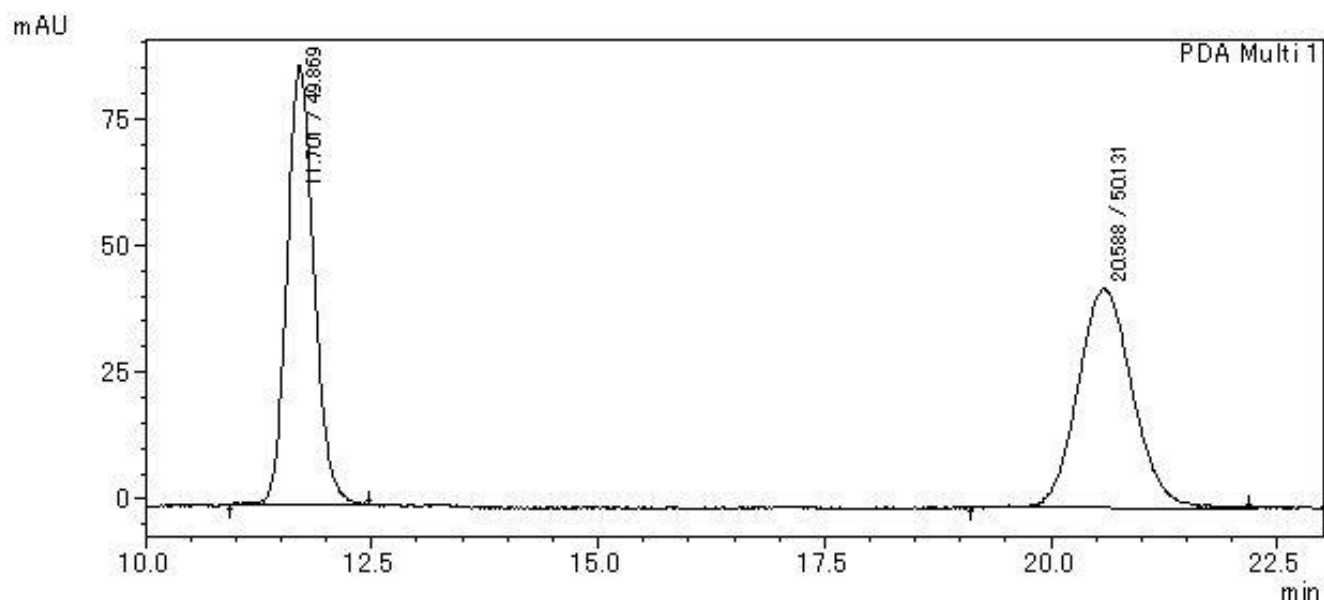
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(pyridin-3-yl)piperidin-2-one (3j)

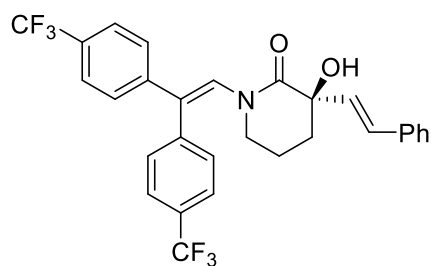
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 18.5 min (minor) and 40.8 min (major).



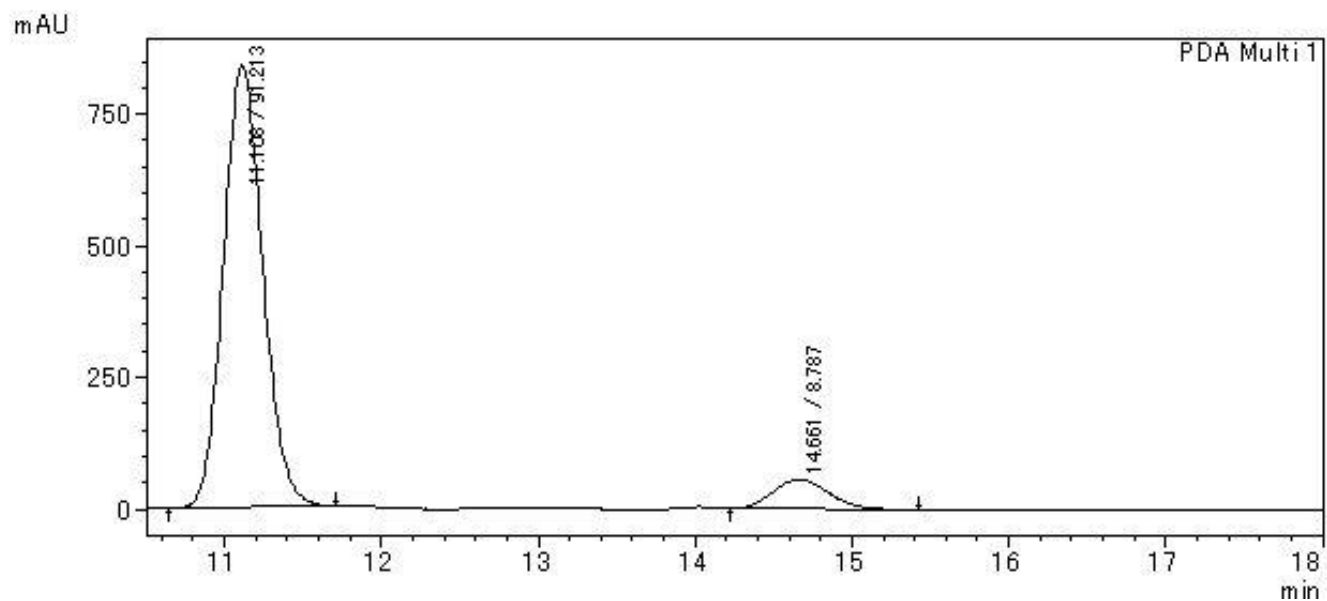
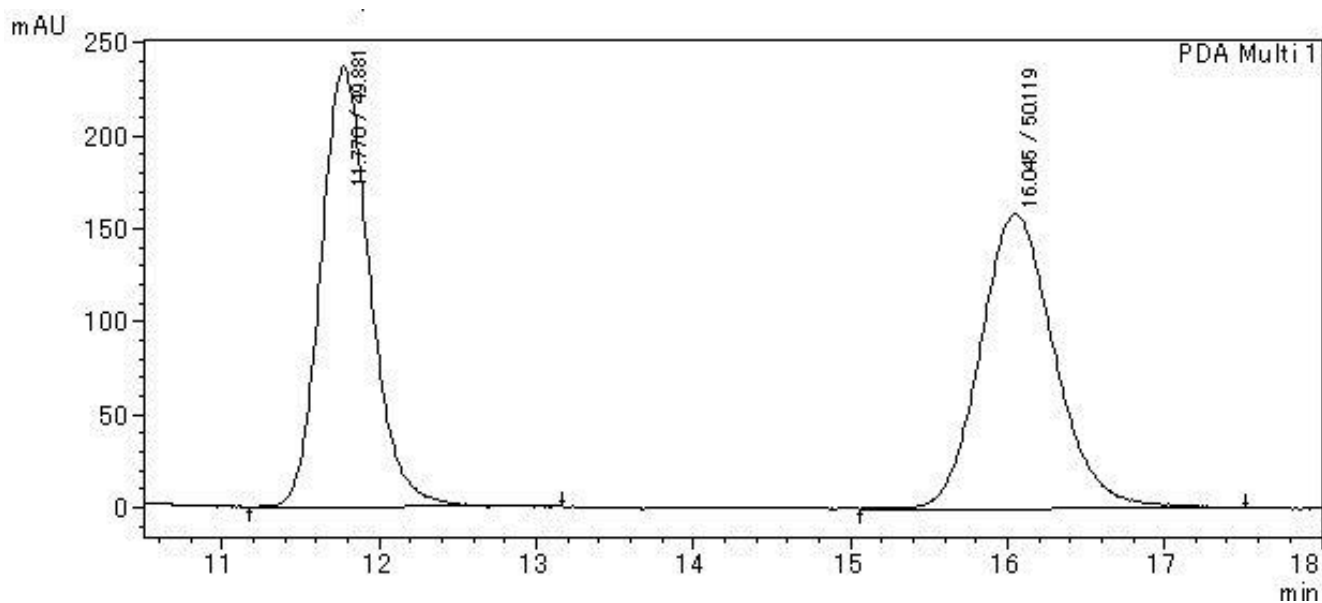
(R)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-(3-thienyl)piperidin-2-one (3k)

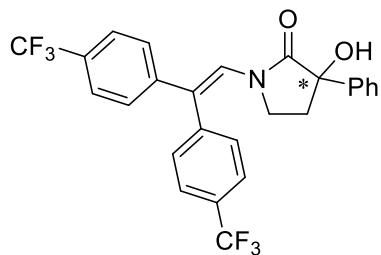
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 11.6 min (major) and 20.0 min (minor).



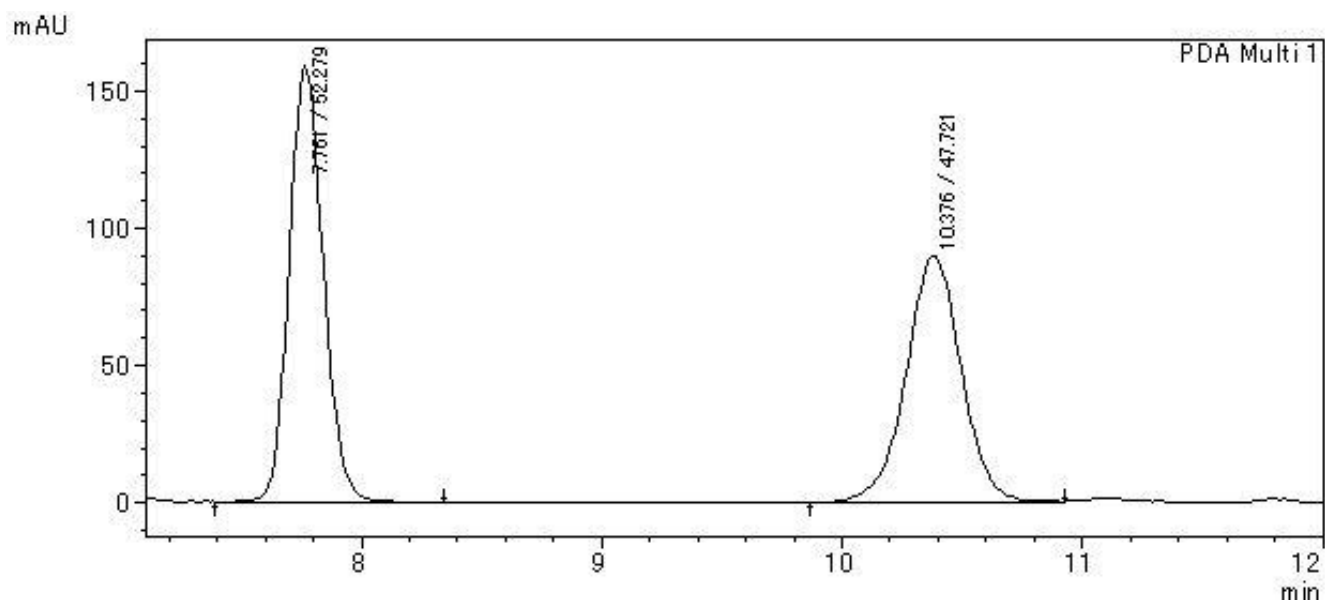
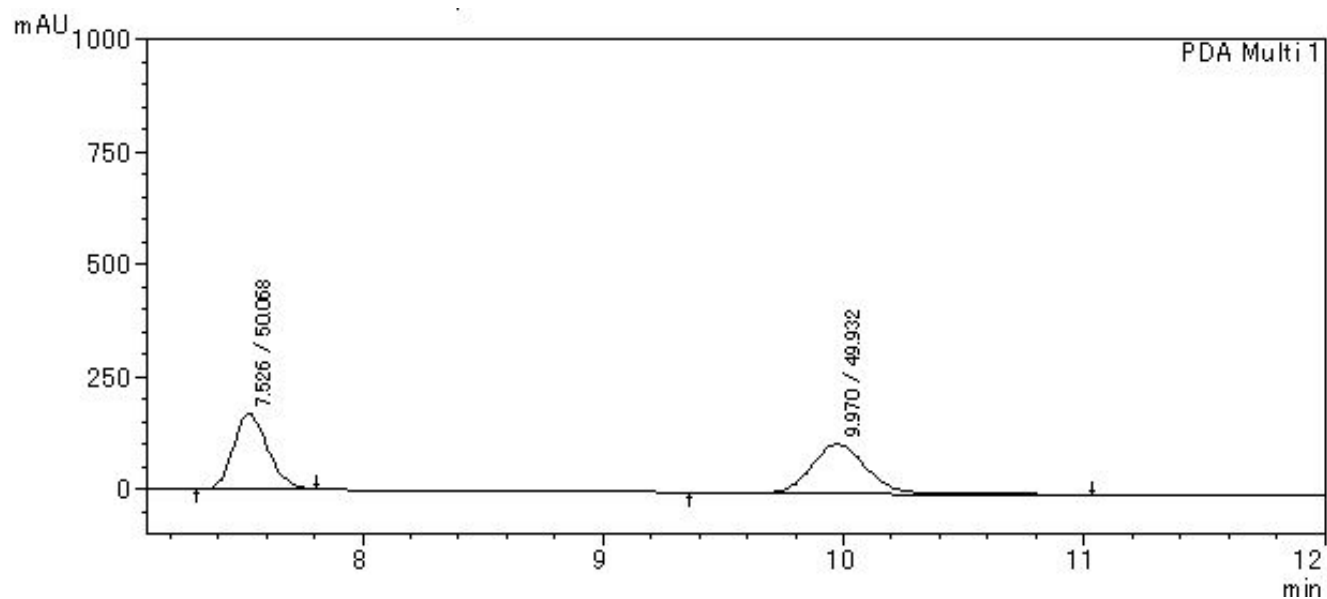
(*R,E*)-1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-styrylpiperidin-2-one (3l)

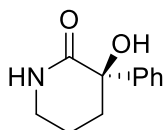
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, λ = 206 nm, retention time: 11.1 min (major) and 14.7 min (minor).



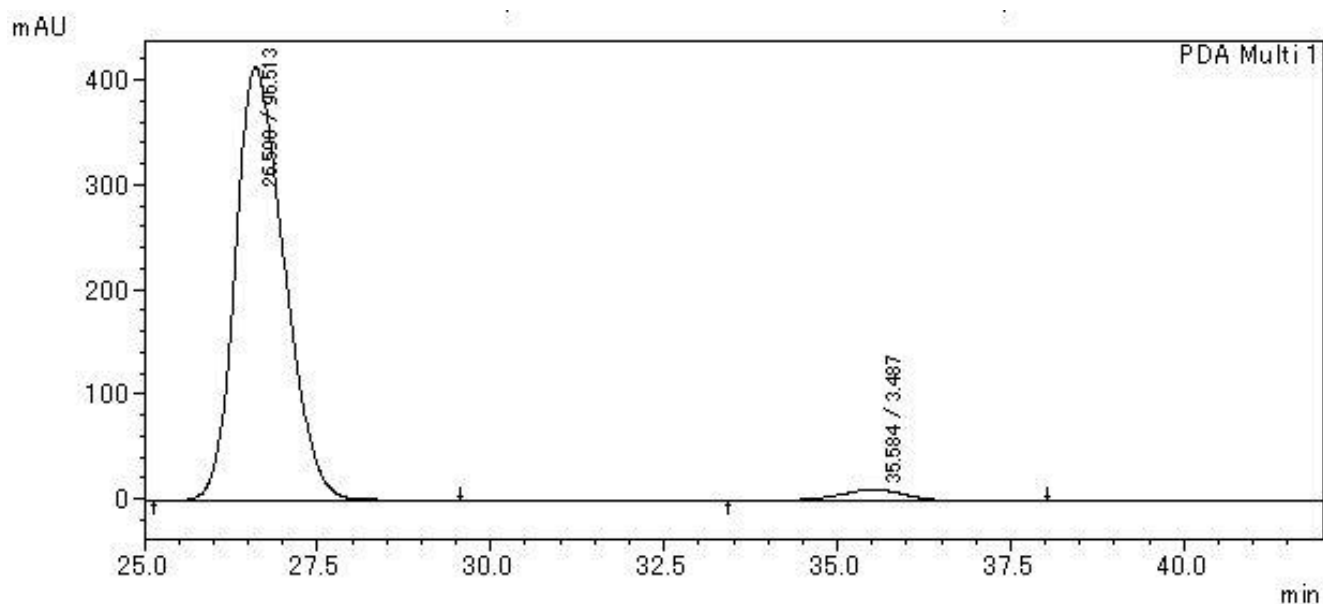
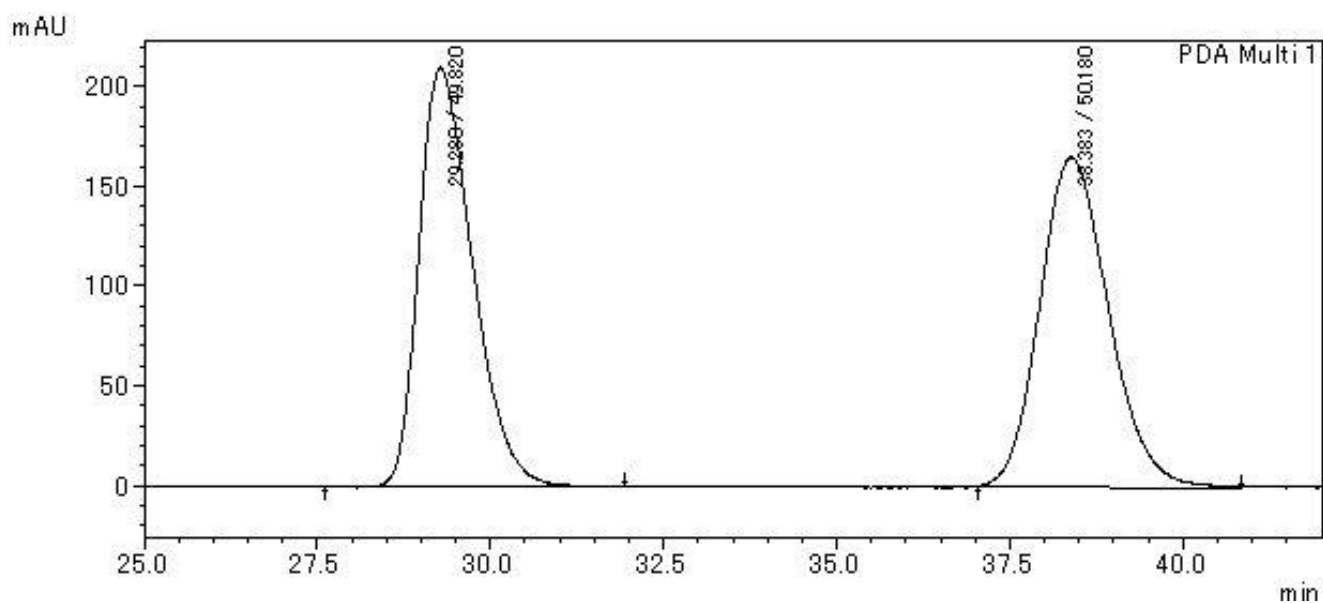
1-(2,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-hydroxy-3-phenylpyrrolidin-2-one (3m)

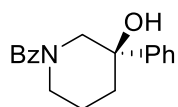
Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 7.8 min (major) and 10.4 min (minor).



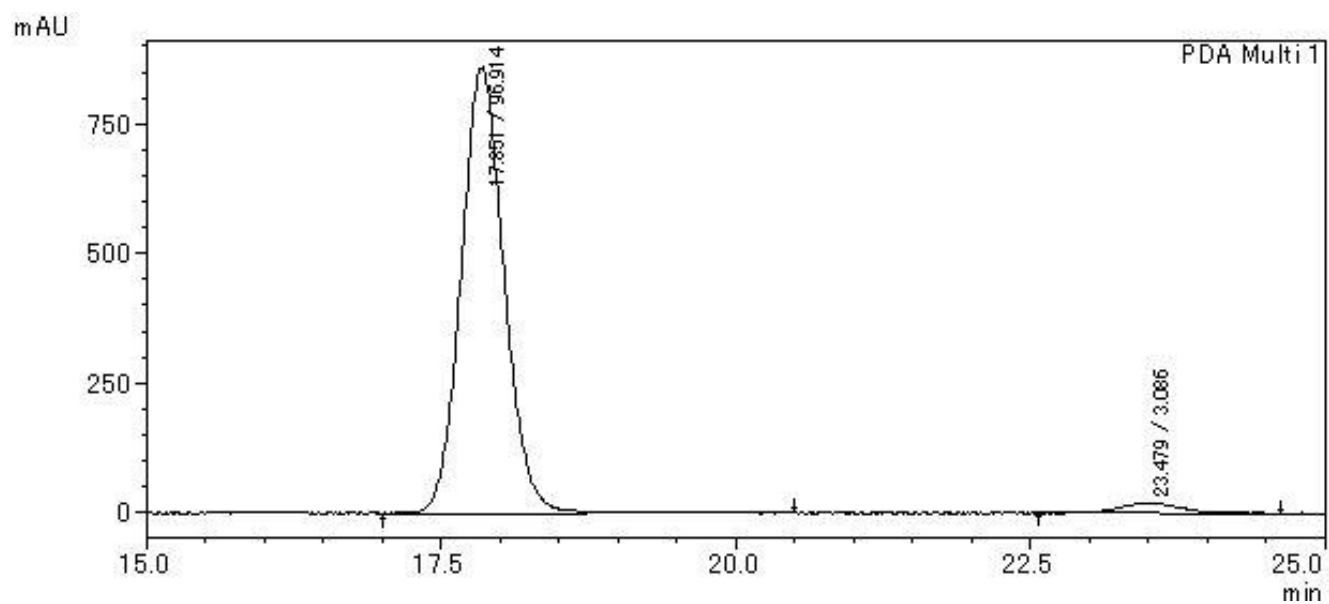
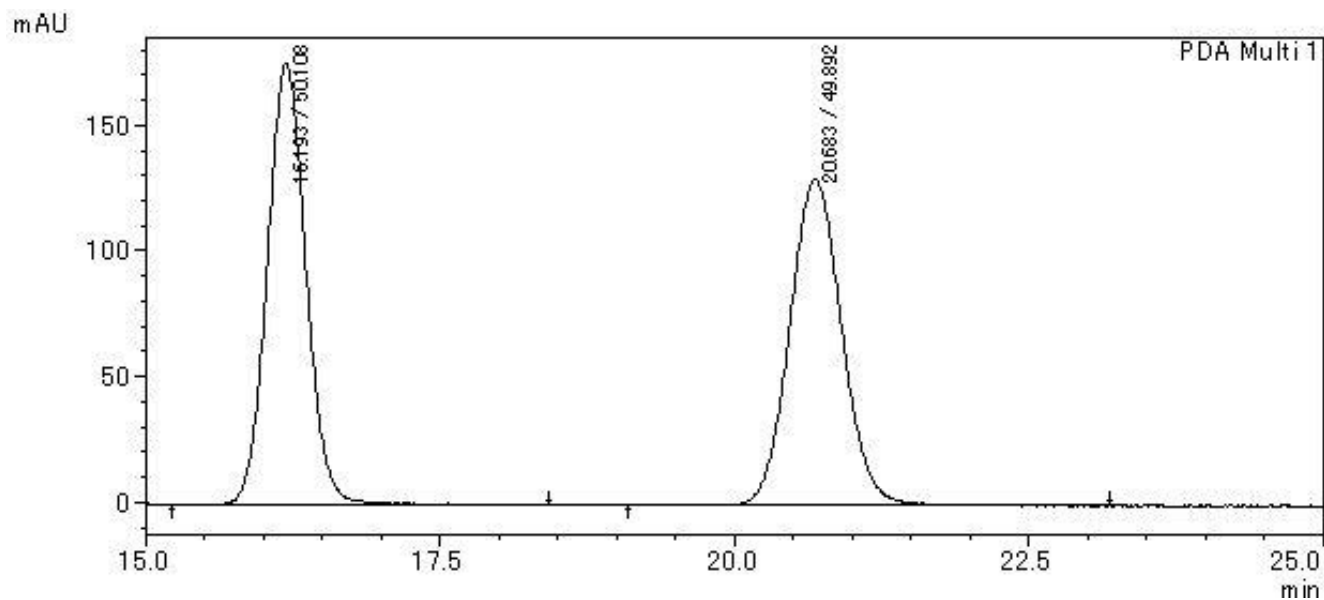
(R)-3-Hydroxy-3-phenylpiperidin-2-one (4a)

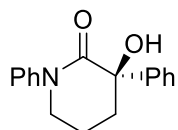
Daicel Chiralpak IC, 2-propanol, flow rate 0.4 mL/min, $\lambda = 206$ nm, retention time: 26.6 min (major) and 35.6 min (minor).



(R)-1-Benzoyl-3-phenylpiperidin-3-ol (7a)

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 17.9 min (major) and 23.5 min (minor).



(R)-3-Hydroxy-1,3-diphenylpiperidin-2-one (6a)

Daicel Chiralpak IC-3, hexane/2-propanol = 1/1, flow rate 0.5 mL/min, $\lambda = 206$ nm, retention time: 27.8 min (major) and 48.1 min (minor).

