

Supporting Information for

**Highly Enantioselective Synthesis of
2,3-Dihydro-1*H*-imidazo[2,1-*a*]isoindol-5(9*bH*)-ones via Catalytic
Asymmetric Intramolecular Cascade Imidization- Nucleophilic
Addition-Lactamization**

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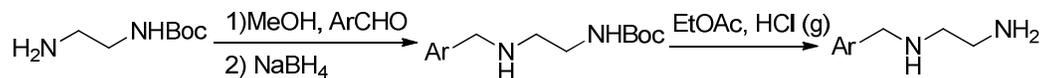
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General Considerations: All reactions were carried out with magnetic stirring and in screw-cap test tubes in argon atmosphere. The test tubes were dried in advance with a high temperature hot gun or in oven. Molecular sieves (4Å, both powder and ball) were dried at high temperature under high vacuum before use. Anhydrous toluene, benzene, dichloromethane, chloroform, and acetonitrile were refluxed and distilled from CaH₂. Anhydrous THF and ether were freshly distilled from sodium and benzophenone before use. Substituted BINOL phosphoric acids were prepared from chiral BINOL according to the known literature procedures.^[1] Phthalide was purchased from commercial source and substituted phthalides were synthesized according to known literature.^[2] Flash column chromatography was performed with silica gel (200-300 mesh). HPLC analysis was performed on an Agilent 1200 series system using a Daicel Chiralcel OD-H, OJ-H or Chiralpak AS-H column. ¹H NMR and ¹³C NMR were recorded on a Varian Mercury-Plus 300 MHz instrument or a Bruker Avance III 400 MHz instrument with chemical shifts reported relative to Tetramethylsilane (TMS). The HRMS data were measured on a Bruker Daltonics ESI-Q-TOF maXis 4G mass spectrometer (ESI). The optical rotation data were recorded on a Bellingham Stanley ADP440+BS Polarimeter. Compounds described in the literature were characterized by comparing their ¹H NMR and ¹³C NMR with the reported values.

Experimental Section:

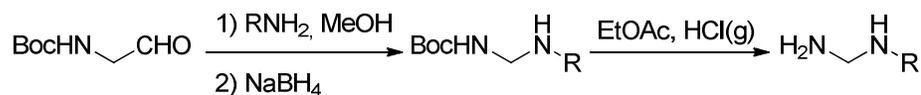
General Procedure for Preparation of N¹-Substituted Ethane-1,2-diamine

Procedure A

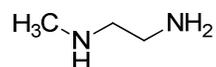


Tert-butyl (2-(arylmethylamino)ethyl)carbamate was synthesized according to a known literature.^[3] To a saturated solution of hydrogen chloride in EtOAc, tert-butyl (2-(alkylamino)ethyl)carbamate was added and the resultant mixture was further stirred overnight. The solvent was evaporated in vacuo and the residue was basified with saturated NaHCO₃ solution, extracted with DCM, dried with MgSO₄ and concentrated in vacuo to yield the final product.

Procedure B

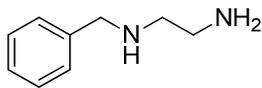


To a solution of tert-butyl (2-oxoethyl)carbamate (4.0 mmol) in THF, amine (4.0 mmol) was added and the mixture was heated to reflux for 1 h. After cooled to room temperature, sodium borohydride was added and the mixture was stirred at room temperature until the starting materials were consumed, determined by TLC analysis. Then the solvent was removed in vacuo and the residue was purified by flash chromatography (eluent: EtOAc) to yield tert-butyl (2-(alkylamino)ethyl)carbamate. Then tert-butyl (2-(alkylamino)ethyl)carbamate was added to the saturated solution of hydrogen chloride in EtOAc and the resultant mixture was further stirred overnight. The solvent was evaporated in vacuo and the residue was basified with saturated NaHCO₃ solution, extracted with DCM, dried with MgSO₄ and concentrated in vacuo to yield the final product.

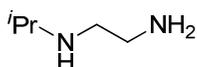


N¹-methylethane-1,2-diamine (2b) This compound was synthesized according to a known literature.^[4] ¹H NMR (300 MHz, CDCl₃) δ:

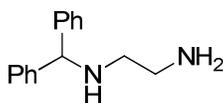
2.80-2.76 (m, 2H), 2.63-2.59 (m, 2H), 2.42 (s, 3H), 1.44 (br s, 3H).



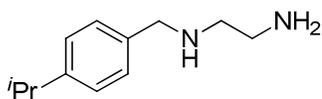
N¹-benzylethane-1,2-diamine (2a) This compound was prepared as a colorless oil according to general procedure A; ¹H NMR (300 MHz, CDCl₃) δ: 7.28-7.20 (m, 5H), 3.76 (s, 2H), 2.79-2.72 (m, 2H), 2.67-2.63(m, 2H), 1.49 (br s, 3H); The ¹H NMR data are identical to the data in the literature.^[5]



N¹-isopropylbenzylethane-1,2-diamine (2c) This compound was prepared as a colorless oil according to general procedure B; ¹H NMR (300 MHz, CDCl₃) δ: 2.75-2.70 (m, 3H), 2.60-2.56 (m, 2H), 1.40 (br s, 3H), 1.99 (d, *J* = 6.3 Hz, 1H). The ¹H NMR data are identical to the data in the literature.^[6]

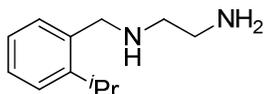


N¹-benzhydrylethane-1,2-diamine (2d) This compound was prepared as colorless oil according to general procedure B; ¹H NMR (300 MHz, CDCl₃) δ: 7.42-7.18 (m, 10H), 4.84 (s, 1H), 2.84-2.80 (m, 2H), 2.67-2.64 (m, 2H), 1.65 (br s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ: 144.3, 128.7, 127.5, 127.2, 67.7, 51.2, 42.4; HRMS(ESI) *m/z* calcd for C₁₅H₁₉N₂ [M+H]⁺ 227.1543, found 227.1548.

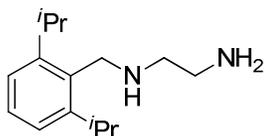


N¹-(4-isopropylbenzyl)ethane-1,2-diamine (2e) This compound was prepared as a colorless oil according to general procedure A; ¹H NMR (300 MHz, CDCl₃) δ: 7.24-7.15 (m, 4H), 3.76 (s, 2H), 2.91-2.84 (m, 1H), 2.81 (dd, *J* = 11.1, 5.7 Hz, 2H), 2.69 (t, *J* = 5.4 Hz, 2H), 1.49 (br s, 3H), 1.24 (d, *J* = 6.9 Hz, 6H); ¹³C NMR(75 MHz, CDCl₃) δ: 147.7, 138.0, 128.3, 126.6, 53.9, 52.3, 42.1, 34.1, 24.4; HRMS(ESI) *m/z*

calcd for C₁₂H₂₁N₂ [M+H]⁺ 193.1699, found 193.1696



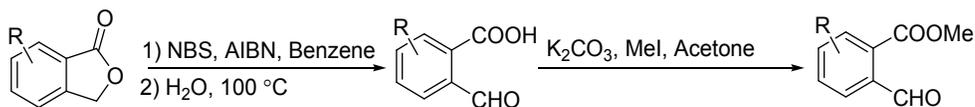
N¹-(2-isopropylbenzyl)ethane-1,2-diamine (2f) This compound was prepared as a colorless oil according to general procedure A; ¹H NMR (300 MHz, CDCl₃) δ: 7.30-7.10 (m, 4H), 3.82 (s, 2H), 3.31-3.22 (m, 1H), 2.81 (t, *J* = 5.4 Hz, 2H), 2.75-2.72 (m, 2H), 1.62 (br s, 3H), 1.25 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ: 147.4, 137.0, 129.3, 127.6, 125.8, 125.5, 52.7, 51.6, 42.1, 28.9, 24.5; HRMS(ESI) *m/z* calcd for C₁₂H₂₁N₂ [M+H]⁺ 193.1699, found 193.1702



N¹-(2,6-diisopropylbenzyl)ethane-1,2-diamine (2g) This compound was prepared as a colorless oil according to general procedure A; ¹H NMR (300 MHz, CDCl₃) δ: 7.25-7.13 (m, 3H), 3.81 (s, 2H), 3.38-3.26 (m, 2H), 2.82 (m, 4H), 1.38 (br s, 3H), 1.28 (d, *J* = 6.6 Hz, 12H); ¹³C NMR (75 MHz, CDCl₃) δ: 147.8, 134.1, 127.8, 123.1, 53.3, 46.2, 42.2, 29.6, 25.0; HRMS(ESI) *m/z* calcd for C₁₅H₂₇N₂ [M+H]⁺ 235.2169, found 235.2166

General Procedure for Preparation of Methyl 2-formylbenzoates:

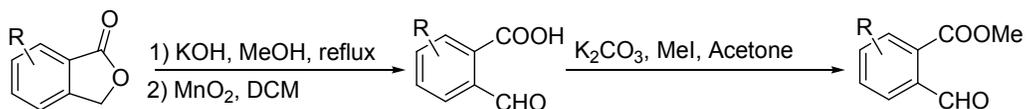
Procedure A



To a solution of phthalides (2.0 mmol) in 10 mL dry benzene was added NBS (0.41g, 2.2 mmol) and AIBN (16.4 mg, 0.1 mmol) was added at room temperature. Then the mixture was refluxed at 85 °C overnight. It was cooled to room temperature and purified by flash chromatograph (silica gel, petroleum ether and ethyl acetate as eluent). The product was then suspended in 20 mL of H₂O and heated to 100 °C. After

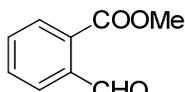
1 h, the mixture was cooled to room temperature and then extracted with EtOAc (3×30 mL). The combined extracts were dried over MgSO₄, filtered and concentrated under reduced pressure to give a corresponding 2-formylbenzoic acid as a solid. To a solution of the corresponding 2-formylbenzoic acid in acetone were added Me₂SO₄ (0.126 g, 1 mmol) and K₂CO₃ (0.276 g, 2 mmol). After stirring for 2 h at room temperature, the mixture was refluxed for 1 h and cooled to ambient temperature, filtered and washed with acetone (3×15 mL). The combined filtrates were concentrated in vacuo and the residue was purified by flash chromatography (silica gel, eluent: petroleum/ethyl acetate = 20:1) to give methyl 2-formylbenzoate.

Procedure B

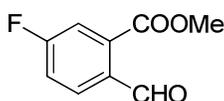


To a solution of phthalides (5 mmol) in an aqueous solution of MeOH (85%, 20 mL) was added powdered KOH (0.42 g, 7.5 mmol), the mixture was refluxed for 1.5 h. After cooling to room temperature, the MeOH was removed in vacuo, and the residue was diluted with H₂O (10 mL). The mixture was then neutralized to pH 4-5 by addition of a solution of KHSO₄ (1 M). The formed solid was filtrated, and washed with water (3×5 mL) to give an intermediate. To a solution of the intermediate in dry CH₂Cl₂ (150 mL) was added active MnO₂ (1.0 g) at room temperature, and the mixture was stirred at room temperature for 5 h. The reaction was worked by filtrating off MnO₂, and the filtrate was concentrated. The residue was purified by flash chromatography (n-hexane/ethyl acetate = 1/2) to give corresponding 2-formylbenzoic acid. To a solution of the corresponding 2-formylbenzoic acid in acetone were then added methyl iodide (0.630 g, 5 mmol) and K₂CO₃ (1.38 g, 10 mmol). After stirring for 2 h at room temperature, the mixture was refluxed for 1 h and cooled to ambient temperature, filtered and washed with acetone (3×15 mL). The combined filtrates were concentrated in vacuo and the residue was purified by flash chromatography (silica gel, eluent: petroleum/ethyl acetate = 20:1) to give

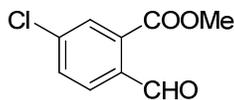
corresponding methyl 2-formylbenzoate.



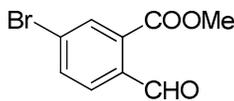
methyl 2-formylbenzoate (1a) This compound was prepared according to procedure A. It was obtained as a colorless oil in 72% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.56 (s, 1H), 7.94-7.87 (m, 2H), 7.62-7.59 (m, 2H), 3.95 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[7]



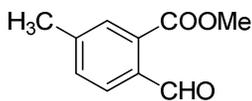
methyl 5-fluoro-2-formylbenzoate (1b) This compound was prepared according to procedure A. It was obtained as a white solid in 60% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.52 (s, 1H), 8.00-7.95 (m, 1H), 7.64-7.60 (m, 1H), 7.34-7.28 (m, 1H), 3.98 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[8]



methyl 5-chloro-2-formylbenzoate (1c) This compound was prepared according to procedure A. It was obtained as a white solid in 65% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.55 (s, 1H), 7.94-7.87 (m, 2H), 7.62-7.58 (m, 1H), 3.98 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[8]

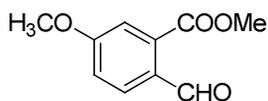


methyl 5-bromo-2-formylbenzoate (1d) This compound was prepared according to procedure A. It was obtained as a white solid in 70% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.56 (s, 1H), 8.12-8.10 (m, 1H), 7.81-7.78 (m, 2H), 3.99 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[7]

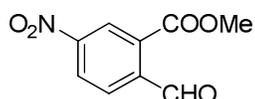


methyl 2-formyl-5-methylbenzoate (1e) This compound was

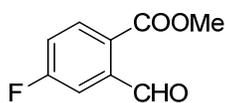
prepared according to procedure A. It was obtained as a colorless oil in 56% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.51 (s, 1H), 7.82 (d, $J = 7.8$ Hz, 1H), 7.72 (s, 1H), 7.41 (d, $J = 7.8$ Hz, 1H), 3.95 (s, 3H), 2.44 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[9]



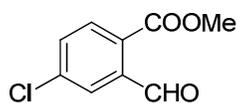
methyl 2-formyl-5-methoxybenzoate (1f) This compound was prepared according to procedure A. It was obtained as a white solid in 75% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.41 (s, 1H), 7.92 (d, $J = 8.7$ Hz, 1H), 7.35 (s, 1H), 7.10-7.06 (m, 1H), 3.95 (s, 3H), 3.89 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[7]



methyl 2-formyl-5-nitrobenzoate (1g) This compound was prepared according to procedure A. It was obtained as a yellow solid in 73% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.65 (s, 1H), 8.80-8.79 (m, 1H), 8.46-8.43 (m, 1H), 8.07-8.04 (m, 1H), 4.04 (s, 3H).^[7]

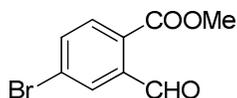


methyl 4-fluoro-2-formylbenzoate (1h) This compound was prepared according to procedure A. It was obtained as a white solid in 60% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.61 (d, $J = 2.7$ Hz, 1H), 8.05-8.00 (m, 1H), 7.60-7.56 (m, 1H), 7.32-7.26 (m, 1H), 3.96 (s, 3H); ^{13}C NMR(100 MHz, CDCl_3) δ : 190.7, 165.9 (d, $J = 60.7$ Hz), 163.6, 140.0 (d, $J = 6.9$ Hz), 133.4 (d, $J = 8.5$ Hz), 127.8 (d, $J = 3.2$ Hz), 119.7 (d, $J = 21.9$ Hz), 115.1 (d, $J = 23.1$ Hz), 52.8; HRMS(ESI) m/z calcd for $\text{C}_9\text{H}_7\text{FO}_3\text{Na}$ ($[\text{M}+\text{Na}]^+$) 205.0271, found. 205.0276.

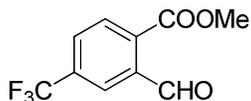


methyl 4-chloro-2-formylbenzoate (1i) This compound was

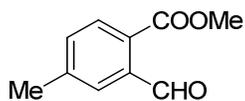
prepared according to procedure A. It was obtained as a white solid in 66% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.59 (s, 1H), 7.95-7.86 (m, 2H), 7.60-7.56 (m, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 190.7, 165.7, 139.3, 138.5, 132.7, 132.0, 129.8, 128.3, 52.8; HRMS(ESI) m/z calcd for $\text{C}_9\text{H}_7\text{ClO}_3\text{Na}([\text{M}+\text{Na}]^+)$ 220.9976, found 220.9978.



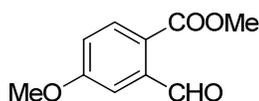
methyl 4-bromo-2-formylbenzoate (1j) This compound was prepared according to procedure A. It was obtained as a white solid in 68% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.57 (s, 1H), 8.02 (d, $J = 2.1$ Hz, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.74 (dd, $J = 8.4, 2.1$ Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 190.7, 165.9, 138.4, 135.8, 132.1, 131.4, 130.3, 127.7, 52.9; HRMS(ESI) m/z calcd for $\text{C}_9\text{H}_7\text{BrO}_3\text{Na}([\text{M}+\text{Na}]^+)$ 264.9470, found 264.9474.



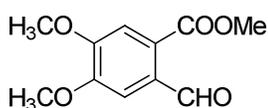
methyl 2-formyl-4-(trifluoromethyl)benzoate (1k) This compound was prepared according to procedure A. It was obtained as a colorless oil in 65% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.59 (s, 1H), 8.17 (d, $J = 0.6$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 7.87 (dd, $J = 8.1, 1.2$ Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 190.4, 165.6, 137.4, 134.8, 134.3 (q, $J = 33.3$ Hz), 131.1, 129.4 (q, $J = 3.4$ Hz), 125.5 (d, $J = 3.4$ Hz), 123.0 (q, $J = 271.3$ Hz); HRMS(ESI) m/z calcd for $\text{C}_{10}\text{H}_7\text{F}_3\text{O}_3\text{Na}([\text{M}+\text{Na}]^+)$ 255.0239, found 255.0240.



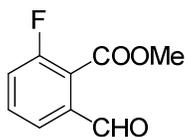
methyl 2-formyl-4-methylbenzoate (1l) This compound was prepared according to procedure B. It was obtained as a colorless oil in 50% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.59 (s, 1H), 7.85 (d, $J = 8.1$ Hz, 2H), 7.69 (s, 1H), 7.40 (dd, $J = 8.1, 0.9$ Hz, 1H), 3.93 (s, 3H), 2.43 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[10]



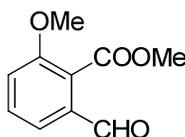
methyl 2-formyl-4-methoxybenzoate (1m) This compound was prepared according to procedure A. It was obtained as a white solid in 75% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.67 (s, 1H), 7.85 (d, $J = 8.7$ Hz, 2H), 7.37 (d, $J = 2.7$ Hz, 1H), 7.08 (dd, $J = 8.7, 2.7$ Hz, 1H), 3.93 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 192.3, 166.2, 162.7, 139.4, 132.7, 123.9, 118.8, 111.9, 55.7; 52.4; HRMS(ESI) m/z calcd for $\text{C}_{10}\text{H}_{10}\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$) 217.0471, found 217.0473.



methyl-2-formyl-4,5-dimethylbenzoate (1n) This compound was prepared according to procedure A. It was obtained as a white solid in 76% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.58 (s, 1H), 7.45 (s, 1H), 7.41 (s, 1H), 3.96 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[10]

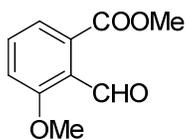


methyl 2-fluoro-6-formylbenzoate (1o) This compound was prepared according to procedure A. It was obtained as a white solid in 68% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.04 (s, 1H), 7.70-7.67 (m, 1H), 7.62-7.55 (m, 1H), 7.40-7.34 (dd, $J = 8.4, 2.1$ Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 189.4, 164.5, 160.8, 158.3, 135.7, 132.0(d, $J = 8.3$ Hz), 126.3, 127.6(d, $J = 22.1$ Hz), 53.1; HRMS(ESI) m/z calcd for $\text{C}_9\text{H}_7\text{FO}_3\text{Na}$ ($[\text{M}+\text{Na}]^+$) 205.0271, found. 205.0275.



methyl 2-formyl-6-methoxybenzoate (1p) This compound was prepared according to procedure A. It was obtained as a white solid in 75% overall

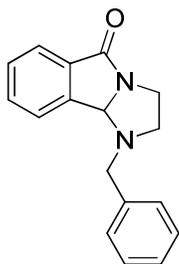
yield. ^1H NMR (300 MHz, CDCl_3) δ : 9.92 (s, 1H), 7.54-7.40 (m, 2H), 7.20-7.17 (m, 1H), 3.95 (s, 3H), 3.86 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[10]



methyl 2-formyl-3-methoxybenzoate (1q) This compound was prepared according to procedure A. It was obtained as a white solid in 70% overall yield. ^1H NMR (300 MHz, CDCl_3) δ : 10.42 (s, 1H), 7.52-7.47 (m, 1H), 7.15-7.06 (m, 2H), 3.89 (s, 3H), 3.88 (s, 3H). The ^1H NMR data are identical to the data in the literature.^[11]

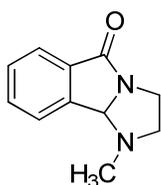
Typical Procedure for Asymmetric Intramolecular Amidation:

To a flame-dried reaction tube charged with 4 Å molecular sieves (50 mg, pre-activated with a high temperature hot gun) was added catalyst (*R*)-**4i** (7.5 mg, 0.01 mmol), toluene (0.5 mL) and methyl 2-formylbenzoate (**1a**) (0.1 mmol, 16.4 mg) successively at room temperature. The mixture was cooled to 0 °C and stirred for 5 min. Then N^1 -(2,6-diisopropylbenzyl)ethane-1,2-diamine (**2g**) (0.1 mmol, 23.4 mg) which dissolved in 0.5 mL anhydrous toluene was added via a syringe. The reaction mixture was stirred at 0 °C until the starting materials were consumed, determined by TLC analysis. The crude product was purified directly by column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the desired product **3g**.



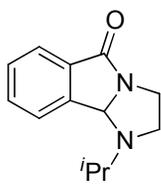
1-benzyl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3a) 23.9 mg, white solid: m.p. 103.2-104.4 °C; $[\alpha]_{\text{D}}^{25} = -21.5$ (c = 0.9, CHCl_3); 91% yield, 59% ee; HPLC Analysis: Daicel Chiralcel OD-H column: *n*-hexane/*i*-PrOH =

90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 15.94$ min, $t_{\text{minor}} = 17.54$ min. ^1H NMR (300 MHz, CDCl_3) δ : 7.82-7.79 (m, 1H), 7.50-7.47 (m, 2H), 7.38-7.35 (m, 1H), 7.27-7.23 (m, 5H), 4.89 (s, 1H), 4.16 (d, $J = 12.9$ Hz, 1H), 3.80-3.70 (m, 1H), 3.53 (d, $J = 12.6$ Hz, 1H), 3.45-3.35 (m, 2H), 2.92-2.82 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 173.0, 143.9, 137.6, 134.3, 132.2, 129.8, 129.0, 128.7, 127.7, 124.5, 123.7, 81.8, 56.8, 56.2, 41.8; HRMS(ESI) m/z calcd for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$) 265.1335, found 265.1336.



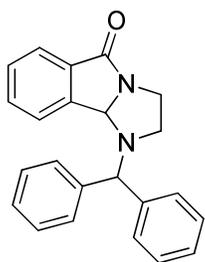
1-methyl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3b)

17.7 mg, white solid: m.p. 87.9-89.0 °C; $[\alpha]_{\text{D}}^{25} = -5.8$ ($c = 1.0$, CHCl_3); 94% yield, 19% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 10.43$ min, $t_{\text{minor}} = 12.16$ min. ^1H NMR (300 MHz, CDCl_3): δ 7.78 (d, $J = 6.6$ Hz, 1H), 7.58-7.47 (m, 3H), 4.63 (s, 1H), 3.83-3.73 (m, 1H), 3.58-3.41 (m, 2H), 3.01-2.92 (m, 1H), 2.51 (s, 3H); The ^1H NMR data are identical to the data in the literature.^[12]

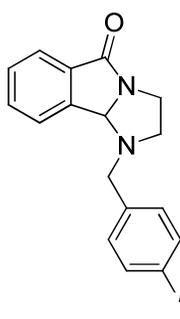


1-isopropyl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3c)

8.9 mg, white solid: m.p. 91.2-92.8 °C; $[\alpha]_{\text{D}}^{25} = -16.4$ ($c = 0.9$, CHCl_3); 40% yield, 29% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 8.02$ min, $t_{\text{minor}} = 9.12$ min. ^1H NMR (300 MHz, CDCl_3): δ 7.80-7.77 (m, 1H), 7.53-7.44 (m, 3H), 5.03 (s, 1H), 3.84-3.76 (m, 1H), 3.51-3.31 (m, 3H), 3.16-3.08 (m, 1H), 2.20 (d, $J = 6.3$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR(75 MHz, CDCl_3): δ 173.2, 144.7, 134.2, 132.1, 129.60, 124.7, 123.6, 77.7, 48.0, 47.6, 42.1, 22.3, 14.7; HRMS(ESI) m/z calcd for $\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$) 217.1335, found 217.1340.

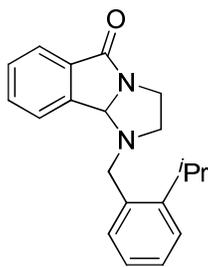


1-benzhydryl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3d) 18.7 mg, white solid: m.p. 211.4-212.5 °C; $[\alpha]_D^{25} = -32.4$ (c = 1.1, CHCl₃); 55 % yield, 77 % ee; HPLC Analysis: Daicel Chiralcel OD-H column: *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 27.71$ min, $t_{\text{minor}} = 25.38$ min. ¹H NMR (300 MHz, CDCl₃) δ : 7.73 (d, $J = 7.5$ Hz, 1H), 7.72-7.13 (m, 12H), 6.17 (d, $J = 7.5$ Hz, 1H), 5.04 (s, 1H), 4.90 (s, 1H), 3.89-3.80 (m, 1H), 3.38-3.82 (m, 2H), 2.94-2.85 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ : 172.9, 143.9, 142.3, 141.6, 133.7, 131.2, 129.0, 128.6, 128.5, 128.1, 127.6, 127.4, 125.1, 123.4, 81.4, 71.6, 54.7, 41.0; HRMS(ESI) m/z calcd for C₂₃H₂₁N₂O ($[M+H]^+$) 341.1648, found 341.1650.

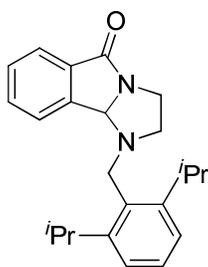


1-(4-isopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3e) 26.9 mg, white solid: m.p. 101.1-102.0 °C; $[\alpha]_D^{25} = -13.2$ (c = 1.5, CHCl₃); 88% yield, 64% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 13.36$ min, $t_{\text{minor}} = 20.51$ min. ¹H NMR (300 MHz, CDCl₃) δ : 7.82-7.80 (m, 1H), 7.50-7.487 (m, 2H), 7.34-7.33 (m, 1H), 7.20-7.13 (m, 5H), 4.89 (s, 1H), 4.12 (d, $J = 12.6$ Hz, 1H), 3.81-3.72 (m, 1H), 3.54 (d, $J = 12.6$ Hz, 1H), 3.46-3.40 (m, 2H), 2.94-2.85 (m, 1H), 1.24 (d, $J = 6.9$ Hz); ¹³C NMR (75 MHz, CDCl₃) δ : 172.8, 148.2, 143.7, 134.5, 134.0, 131.8, 129.5, 128.7, 126.4, 124.2, 123.4, 81.4, 56.2, 55.8, 41.4, 33.7, 23.9;

HRMS(ESI) m/z calcd for $C_{20}H_{23}N_2O$ ($[M+H]^+$) 307.1805, found 307.1800.

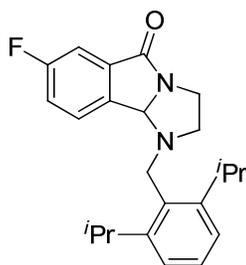


1-(2-isopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3f) 26.3 mg, white solid: m.p. 95.0-97.2 °C; $[\alpha]_D^{25} = +18.0$ ($c = 1.2$, $CHCl_3$); 86 % yield, 72% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: n -hexane/ i -PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{major} = 8.98$ min, $t_{minor} = 17.01$ min. 1H NMR (300 MHz, $CDCl_3$) δ : 7.83-7.81 (m, 1H), 7.52-7.49 (m, 2H), 7.34-7.21 (m, 4H), 7.13-7.08 (m, 1H), 4.90 (s, 1H), 4.25 (d, $J = 12.3$ Hz, 1H), 3.84-3.69 (m, 1H), 3.55 (d, $J = 12.3$ Hz, 1H), 3.47-3.34 (m, 2H), 3.15-3.06 (m, 1H), 2.94-2.84 (m, 1H), 1.07 (d, $J = 6.9$ Hz), 1.02 (d, $J = 6.9$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ : 173.1, 148.1, 143.7, 133.9, 131.8, 129.9, 129.7, 128.0, 125.5, 125.4, 124.2, 123.2, 81.8, 55.8, 54.3, 41.5, 28.1, 23.6; HRMS(ESI) m/z calcd for $C_{20}H_{23}N_2O$ ($[M+H]^+$) 307.1805, found 307.1806.

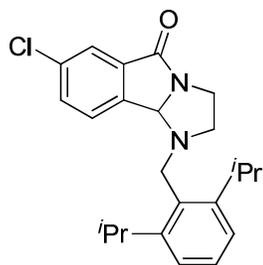


1-(2,6-diisopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3g) 31.3 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 119.0-120.1 °C; $[\alpha]_D^{25} = +51.6$ ($c = 1.5$, $CHCl_3$); 90% yield, 96% ee; HPLC Analysis: Daicel Chiralcel OD-H column: n -hexane/ i -PrOH = 95:5, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{major} = 9.74$ min, $t_{minor} = 10.75$ min; 1H NMR (300 MHz, $CDCl_3$) δ : 7.84-7.82 (m, 1 Hz, H), 7.54-7.51 (m, 5H), 4.90 (s, 1H), 4.13 (d, $J = 12.3$ Hz, 1H), 3.87 (d, $J = 12.3$ Hz, 1H), 3.69-3.63 (m, 1H), 3.47-3.21 (m, 4H), 3.06-2.91 (m, 1H), 1.11 (d, $J = 6.9$ Hz, 6H), 1.05 (d, $J = 6.9$

Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 173.4, 148.7, 143.6, 133.8, 131.7, 130.5, 129.5, 127.9, 124.4, 123.6, 123.0, 81.20, 54.8, 46.9, 41.9, 28.7, 24.5, 23.7; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 349.2274, found 349.2280.

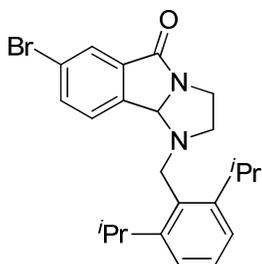


1-(2,6-diisopropylbenzyl)-7-fluoro-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3h) 34.0 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 121.3-122.1 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = +50.0$ ($c = 1.7$, CHCl_3); 93% yield, 95% ee; HPLC Analysis: Daicel Chiralcel OD-H column: *n*-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 16.12$ min, $t_{\text{minor}} = 14.76$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.47 (d, $J = 7.2$ Hz, 1H), 7.28-7.10 (m, 5H), 4.90 (s, 1H), 4.13 (d, $J = 12.3$ Hz, 1H), 3.87 (d, $J = 12.3$ Hz, 1H), 3.69-3.64 (m, 1H), 3.46-3.21 (m, 4H), 3.05-2.97 (m, 1H), 1.11 (d, $J = 6.9$ Hz, 6H), 1.07(d, $J = 6.6$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 172.0 (d, $J = 3.0$ Hz), 163.5 (d, $J = 247.6$ Hz), 148.5, 139.3 (d, $J = 2.5$ Hz), 136.1 (d, $J = 8.4$ Hz), 130.4, 128.1, 124.9 (d, $J = 8.3$ Hz), 123.1, 119.0 (d, $J = 23.3$ Hz), 111.1 (d, $J = 23.1$ Hz), 80.7, 54.9, 47.2, 41.8, 28.8, 24.5, 23.7; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OF}$ $[\text{M}+\text{H}]^+$ 367.2180, found 367.2188.

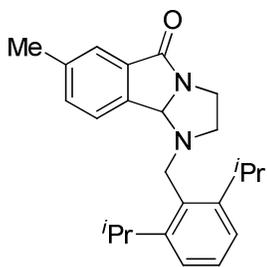


7-chloro-1-(2,6-diisopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3i) 35.1 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 93.7-94.2 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = +47.4$ ($c = 1.8$, CHCl_3); 92% yield, 92% ee; HPLC Analysis: Daicel Chiralcel OD-H column:

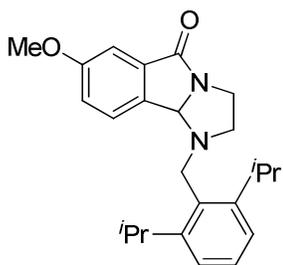
n-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 15.94$ min, $t_{\text{minor}} = 14.26$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.78 (d, $J = 1.8$ Hz, 1H), 7.47-7.43 (m, 1H), 7.28-7.23 (m, 1H), 7.11 (d, $J = 7.8$ Hz, 3H), 4.90 (s, 1H), 4.12 (d, $J = 12.6$ Hz, 1H), 3.87 (d, $J = 12.6$ Hz, 1H), 3.66 (d, $J = 9.9, 8.1$ Hz, 1H), 3.46-3.20 (m, 4H), 3.06-3.02 (m, 1H), 1.11 (d, $J = 6.9$ Hz, 6H), 1.08 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 171.8, 148.5, 141.9, 135.8, 135.7, 131.8, 130.4, 128.1, 124.6, 124.5, 123.1, 80.9, 55.0, 47.3, 41.9, 28.8, 24.5, 23.8; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OCl}$ $[\text{M}+\text{H}]^+$ 383.1885, found 383.1889.



7-bromo-1-(2,6-diisopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3j) 39.6 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 97.9-98.8 °C; $[\alpha]_{\text{D}}^{25} = +45.2$ ($c = 2.0$, CHCl_3); 93% yield, 92% ee; HPLC Analysis: Daicel Chiralcel OD-H column: *n*-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 17.36$ min, $t_{\text{minor}} = 15.11$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.94 (s, 1H), 7.60 (d, $J = 8.1$ Hz, 1H), 7.26-7.23 (m, 1H), 7.12-7.03 (m, 3H), 4.89 (s, 1H), 4.12 (d, $J = 12.3$ Hz, 1H), 3.87 (d, $J = 12.3$ Hz, 1H), 3.72-3.63 (m, 1H), 3.46-3.21 (m, 4H), 3.02 (dd, $J = 17.7, 9.9$ Hz, 1H), 1.11 (d, $J = 6.6$ Hz, 6H), 1.08 (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 171.5, 148.4, 142.3, 135.8, 134.5, 130.3, 128.1, 127.4, 124.9, 123.5, 123.1, 80.9, 54.9, 47.3, 41.7, 28.8, 24.5, 23.7; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OBr}$ $[\text{M}+\text{H}]^+$ 427.1379, found 427.1386.

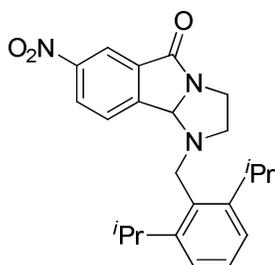


1-(2,6-diisopropylbenzyl)-7-methyl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3k) 32.9 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 148.5-149.8 °C; $[\alpha]_D^{25} = +128.6$ ($c = 2.0$, CHCl_3); 91% yield, 91% ee; HPLC Analysis: Daicel Chiralpak AS-H column: *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 11.61$ min, $t_{\text{minor}} = 8.00$ min; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.63 (s, 1H), 7.35-7.22 (m, 3H), 7.11 (d, $J = 7.8$ Hz, 3H), 4.90 (s, 1H), 4.15 (d, $J = 12.3$ Hz, 1H), 3.83 (d, $J = 12.3$ Hz, 1H), 3.65 (dd, $J = 18.0, 9.9$ Hz, 1H), 3.45-3.39 (m, 1H), 3.32-3.23 (m, 3H), 3.00 (dd, $J = 17.7, 9.3$ Hz, 1H), 2.47 (s, 3H), 1.13 (d, $J = 6.6$ Hz, 6H), 1.06 (d, $J = 6.6$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 173.6, 148.5, 140.9, 139.6, 134.0, 132.6, 130.6, 128.0, 124.6, 123.0, 81.1, 54.8, 46.9, 41.8, 28.7, 24.6, 23.8, 21.4; HRMS(ESI) m/z calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$) 363.2436, found 363.2438.

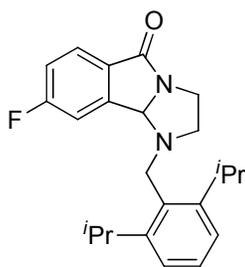


1-(2,6-diisopropylbenzyl)-7-methoxy-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3l) 34.0 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 5:1), white solid: m.p. 154.5-155.8 °C; $[\alpha]_D^{25} = +62.0$ ($c = 1.7$, CHCl_3); 90% yield, 94% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 21.28$ min, $t_{\text{minor}} = 15.45$ min; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.30-7.04 (m, 6H), 4.87 (s, 1H), 4.12 (d, $J = 12.6$ Hz, 1H), 3.87-3.80 (m, 4H), 3.63 (dd, $J = 18.0, 9.0$ Hz, 1H), 3.45-3.39 (m, 1H), 3.29-3.23 (m, 3H), 3.03-2.95 (m, 1H), 1.12 (d, $J = 6.6$ Hz, 6H), 1.06 (d, $J = 6.6$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 173.3, 160.9, 148.5, 136.0, 135.4, 130.6,

127.9, 124.1, 123.0, 119.7, 107.1, 80.9, 55.6, 54.8, 46.9, 41.8, 28.7, 24.5, 23.7;
HRMS(ESI) m/z calcd for $C_{24}H_{31}N_2O_2$ $[M+H]^+$ 379.2380, found 379.2391.

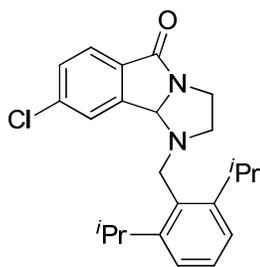


1-(2,6-diisopropylbenzyl)-7-nitro-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3m) 35.4 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 5:1), white solid: m.p. 165.8-166.5 °C; $[\alpha]_D^{25} = +20.4$ ($c = 1.8$, $CHCl_3$); 90% yield, 91% ee; HPLC Analysis: Daicel Chiralpak AS-H column: n -hexane/ i -PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{major} = 17.81$ min, $t_{minor} = 13.78$ min; 1H NMR (300 MHz, $CDCl_3$) δ : 8.59 (s, 1H), 8.29 (dd, $J = 8.4$, 1.8 Hz, 1H), 7.31-7.26 (m, 1H), 7.14-7.07 (m, 3H), 5.02 (s, 1H), 4.18 (d, $J = 12.6$ Hz, 1H), 3.98 (d, $J = 12.6$ Hz, 1H), 3.81-3.72 (m, 1H), 3.53-3.39 (m, 2H), 3.31-3.22 (m, 2H), 3.13-3.04 (m, 1H), 1.11 (d, $J = 6.6$ Hz, 6H), 1.08 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 170.4, 149.3, 149.0, 148.5, 135.5, 130.1, 128.4, 126.5, 124.7, 123.3, 119.6, 80.8, 55.4, 47.9, 41.9, 28.9, 24.4, 23.8; HRMS(ESI) m/z calcd for $C_{23}H_{28}N_3O_3$ $[M+H]^+$ 394.2125, found 394.2132.

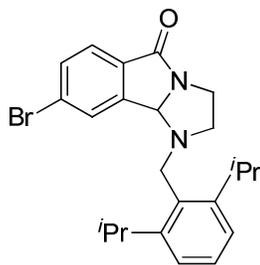


1-(2,6-diisopropylbenzyl)-8-fluoro-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3n) 34.4 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 127.8-128.7 °C; $[\alpha]_D^{25} = +50.0$ ($c = 1.7$, $CHCl_3$); 94% yield, 96% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: n -hexane/ i -PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{major} = 12.99$ min, $t_{minor} = 17.17$ min; 1H NMR (300 MHz, $CDCl_3$) δ : 7.78 (dd, $J = 8.4$, 5.1 Hz, 1H),

7.30-7.11 (m, 4H), 6.79 (dd, $J = 8.4, 1.8$ Hz, 1H), 4.90 (s, 1H), 4.13 (d, $J = 12.3$ Hz, 1H), 3.89 (d, $J = 12.3$ Hz, 1H), 3.70-3.64 (m, 1H), 3.46-3.23 (m, 4H), 3.02 (dd, $J = 14.7, 9.3$ Hz, 1H), 1.11 (d, $J = 6.9$ Hz, 6H), 1.08 (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 172.3, 165.1 (d, $J = 251.0$ Hz), 148.5, 146.2 (d, $J = 9.3$ Hz), 130.4, 129.7 (d, $J = 2.1$ Hz), 128.2, 126.2 (d, $J = 9.6$ Hz), 123.1, 117.0 (d, $J = 23.2$ Hz), 111.1 (d, $J = 24.4$ Hz), 80.7, 55.2, 47.4, 41.9, 28.9, 24.5, 23.8; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OF}$ $[\text{M}+\text{H}]^+$ 367.2180, found 367.2183

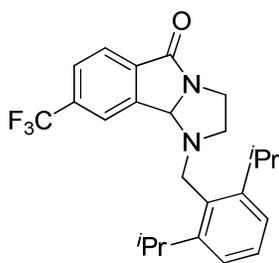


8-chloro-1-(2,6-diisopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3o) 35.1 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 175.2-175.8 °C; $[\alpha]_{\text{D}}^{25} = +111.2$ ($c = 1.76$, CHCl_3); 92% yield, 96% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 10.12$ min, $t_{\text{minor}} = 15.72$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.72 (d, $J = 8.1$ Hz, 1H), 7.47 (d, $J = 8.1$ Hz, 1H), 7.30-7.25 (m, 1H), 7.14-7.06 (m, 3H), 4.91 (s, 1H), 4.14 (d, $J = 12.6$ Hz, 1H), 3.89 (d, $J = 12.6$ Hz, 1H), 3.74-3.65(m, 1H), 3.46-3.20 (m, 4H), 3.47-3.22 (m, 4H), 3.07-2.98 (m, 1H), 1.12 (d, $J = 6.9$ Hz, 6H), 1.09 (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 172.3, 148.5, 145.3, 138.2, 132.1, 130.3, 129.9, 128.3, 125.4, 124.1, 123.1, 80.6, 55.3, 47.5, 41.9, 28.8, 24.4, 23.8; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OCl}$ $[\text{M}+\text{H}]^+$ 383.1885, found 383.1889.

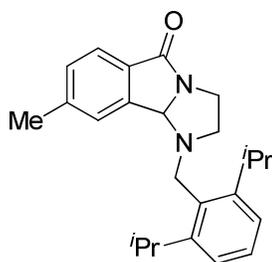


8-bromo-1-(2,6-diisopropylbenzyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one

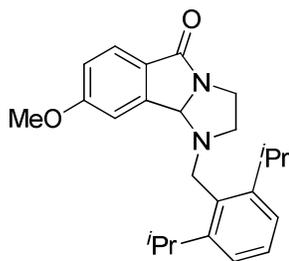
2,1-a[isoindol-5(9bH)-one (3p) 39.2 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 179.6-180.8 °C; $[\alpha]_{\text{D}}^{25} = +128.6$ (c = 2.0, CHCl₃); 92% yield, 96% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 10.30$ min, $t_{\text{minor}} = 16.90$ min; ¹H NMR (300 MHz, CDCl₃) δ : 7.67-7.61 (m, 2H), 7.28-7.12 (m, 4H), 4.91 (s, 1H), 4.14 (d, $J = 12.6$ Hz, 1H), 3.89 (d, $J = 12.6$ Hz, 1H), 3.74-3.65 (m, 1H), 3.47-3.22 (m, 4H), 3.08-2.99 (m, 1H), 1.12 (d, $J = 7.2$ Hz, 6H), 1.09 (d, $J = 6.9$ Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ : 172.4, 148.5, 145.5, 132.8, 132.5, 130.3, 128.3, 127.1, 126.5, 125.6, 123.1, 80.6, 55.3, 47.5, 41.9, 28.8, 24.4, 23.8; HRMS(ESI) m/z calcd for C₂₃H₂₈N₂OBr ([M+H]⁺) 427.1379, found 427.1386.



1-(2,6-diisopropylbenzyl)-8-(trifluoromethyl)-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3q) 37.8 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 165.5-166.4 °C; $[\alpha]_{\text{D}}^{25} = +36.3$ (c = 1.9, CHCl₃); 91% yield, 92% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 7.81$ min, $t_{\text{minor}} = 11.83$ min; ¹H NMR (300 MHz, CDCl₃) δ : 7.90 (d, $J = 8.1$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.30-2.25 (m, 2H), 7.12 (d, $J = 7.8$ Hz, 2H), 5.00 (s, 1H), 4.18 (d, $J = 12.3$ Hz, 1H), 3.94 (d, $J = 12.3$ Hz, 1H), 3.80-3.71 (m, 1H), 3.53-3.41 (m, 2H), 3.30-3.21 (m, 2H), 3.13-3.04 (m, 1H), 1.08 (d, $J = 6.6$ Hz, 12H); ¹³C NMR (100 MHz, CDCl₃) δ : 171.6, 148.4, 144.3, 137.0, 133.6 (q, $J = 32.3$ Hz), 130.2, 128.4, 126.7 (d, $J = 3.7$ Hz), 124.7, 123.6 (q, $J = 271.2$ Hz), 123.2, 120.92 (q, $J = 3.8$ Hz), 89.9, 50.5, 47.8, 41.9, 28.9, 24.4, 23.7; HRMS(ESI) m/z calcd for C₂₄H₂₈N₂O₃F₃ ([M+H]⁺) 417.2148, found 417.2150.

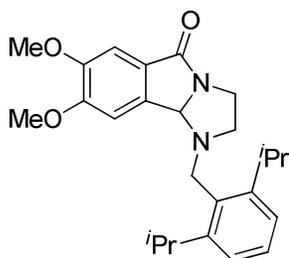


1-(2,6-diisopropylbenzyl)-8-methyl-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3r) 33.3 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 195.6-196.8 °C; $[\alpha]_{\text{D}}^{25} = +86.25$ ($c = 1.6$, CHCl_3); 92% yield, 92% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 10.68$ min, $t_{\text{minor}} = 14.46$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.69 (d, $J = 7.5$ Hz, 1H), 7.32-7.22 (m, 2H), 7.12-7.08 (m, 3H), 4.89 (s, 1H), 4.16 (d, $J = 12.6$ Hz, 1H), 3.84 (d, $J = 12.6$ Hz, 1H), 3.71-3.62 (m, 1H), 3.45-3.23 (m, 4H), 3.05-2.96 (m, 1H), 2.42 (s, 3H), 1.11 (d, $J = 6.6$ Hz, 6H), 1.06 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 173.7, 148.5, 144.1, 142.4, 131.1, 130.7, 130.3, 127.9, 124.0, 123.9, 123.0, 81.1, 55.1, 47.1, 41.9, 28.7, 24.5, 23.7, 21.8; HRMS(ESI) m/z calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$) 363.2436, found 363.2431.

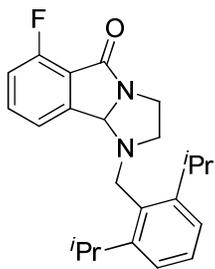


1-(2,6-diisopropylbenzyl)-8-methoxy-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3s) 34.4 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 5:1), white solid: m.p. 180.5-181.3 °C; $[\alpha]_{\text{D}}^{25} = +138.6$ ($c = 1.7$, CHCl_3); 91% yield, 90% ee; HPLC Analysis: Daicel Chiralpak AS-H column: *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 23.81$ min, $t_{\text{minor}} = 10.80$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.72 (d, $J = 8.4$ Hz, 1H), 7.27-7.22 (m, 1H), 7.13 (d, $J = 7.5$ Hz, 2H), 7.02 (dd, $J = 8.4, 2.1$ Hz, 1H), 6.79 (d, $J = 2.1$ Hz, 1H), 4.89 (s, 1H), 4.16 (d, $J = 12.3$ Hz, 1H), 3.87-3.82 (m, 4H), 3.71-3.61 (m, 1H), 3.43-3.26 (m, 4H), 3.05-2.96 (m, 1H), 1.13 (d, $J = 6.9$ Hz, 6H), 1.08 (d, $J =$

6.6 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 173.5, 162.9, 148.5, 146.1, 130.6, 128.0, 126.1, 125.6, 123.0, 116.0, 108.3, 81.0, 55.7, 55.0, 47.2, 41.9, 28.7, 24.5, 23.8; HRMS(ESI) m/z calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$) 379.2380, found 379.2376.

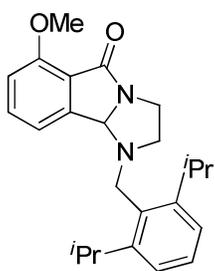


1-(2,6-diisopropylbenzyl)-7,8-dimethoxy-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3t) 36.3 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 5:1), white solid: m.p. 202.1-203.6 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = +96.6$ ($c = 1.7$, CHCl_3); 89% yield, 87% ee; HPLC Analysis: Daicel Chiralpak AS-H column: n -hexane/ i -PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 18.70$ min, $t_{\text{minor}} = 13.16$ min; ^1H NMR (300 MHz, CDCl_3) δ : 7.24-7.21 (m, 2H), 7.12-7.10 (m, 2H), 6.59 (s, 1H), 4.88 (s, 1H), 4.12 (d, $J = 12.6$ Hz, 1H), 3.92 (s, 3H), 3.86-3.81 (m, 4H), 3.65-6.60 (m, 1H), 3.43-3.28 (m, 4H), 3.07-2.99 (m, 1H), 1.12-1.09 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ : 173.9, 152.6, 150.4, 148.6, 137.9, 130.9, 128.2, 126.2, 123.1, 105.8, 105.6, 81.3, 56.3, 56.1, 55.6, 47.8, 41.8, 28.8, 24.5, 24.0; HRMS(ESI) m/z calcd for $\text{C}_{25}\text{H}_{33}\text{N}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$) 409.2485, found 409.2493.



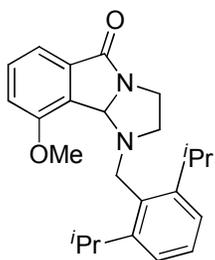
1-(2,6-diisopropylbenzyl)-6-fluoro-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3u) 34.0 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 10:1), white solid: m.p. 134.5-136.3 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = +62.7$ ($c = 1.7$, CHCl_3); 93% yield, 91% ee; HPLC Analysis: Daicel Chiralpak AS-H column: n -hexane/ i -PrOH = 95:5, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 23.78$

min, $t_{\text{minor}} = 12.60$ min; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.54-7.48 (m, 1H), 7.27-7.09 (m, 5H), 4.91 (s, 1H), 4.17 (d, $J = 12.6$ Hz, 1H), 3.86 (d, $J = 12.6$ Hz, 1H), 3.68 (dd, $J = 18.0, 9.9$ Hz, 1H), 3.43-3.19 (m, 4H), 3.04-2.95 (m, 1H), 1.12 (d, $J = 6.6$ Hz, 6H), 1.07 (d, $J = 6.9$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 170.2, 158.7 (d, $J = 259.7$ Hz), 148.4, 146.2, 133.9 (d, $J = 7.5$ Hz), 130.3, 128.0, 123.0, 120.7 (d, $J = 13$ Hz), 119.4 (d, $J = 4.0$ Hz), 117.0 (d, $J = 19.4$ Hz), 80.8, 76.7, 54.7, 46.9, 42.0, 28.7, 24.5, 23.7; HRMS(ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{OF}$ $[\text{M}+\text{H}]^+$ 367.2180, found 367.2175



1-(2,6-diisopropylbenzyl)-6-methoxy-2,3-dihydro-1H-imidazo[2,

1-a]isoindol-5(9bH)-one (3v) 35.2 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 3:1), white solid: m.p. 127.0-127.8 °C; $[\alpha]_{\text{D}}^{25} = +31.7$ ($c = 1.7$, CHCl_3); 93% yield, 92% ee; HPLC Analysis: Daicel Chiralpak AS-H column: n -hexane/ i -PrOH = 90:10, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 11.05$ min, $t_{\text{minor}} = 9.54$ min; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ : 7.53-7.47 (m, 1H), 7.25-7.20 (m, 1H), 7.10-6.97 (m, 4H), 4.86 (s, 1H), 4.16 (d, $J = 12.3$ Hz, 1H), 3.98 (s, 3H), 3.79 (d, $J = 12.3$ Hz, 1H), 3.67-3.58 (m, 1H), 3.40-3.20 (m, 4H), 3.01-2.92 (m, 1H), 1.13 (d, $J = 6.9$ Hz, 6H), 1.05 (d, $J = 6.9$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 172.6, 157.6, 148.5, 146.2, 133.6, 130.5, 127.7, 122.9, 120.5, 115.4, 111.7, 80.6, 55.9, 54.5, 46.7, 42.3, 28.7, 24.6, 23.8; HRMS(ESI) m/z calcd for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 379.2380, found 379.2372.



1-(2,6-diisopropylbenzyl)-9-methoxy-2,3-dihydro-1H-imidazo[2,1-a]isoindol-5(9bH)-one (3w) 34.8 mg, (Flash column chromatography, eluent: petroleum ether/ethyl acetate = 3:1), white solid: m.p. 108.3-109.5 °C; $[\alpha]_D^{25} = +45.6$ (c = 1.7, CHCl₃); 92% yield, 30% ee; HPLC Analysis: Daicel Chiralcel OJ-H column: *n*-hexane/*i*-PrOH = 95: 5, flow rate: 1.0 mL/min, $\lambda = 225$ nm: $t_{\text{major}} = 8.72$ min, $t_{\text{minor}} = 10.94$ min; ¹H NMR (300 MHz, CDCl₃) δ : 7.48-7.42 (m, 1H), 7.21-7.15 (m, 1H), 7.09-6.92 (m, 4H), 4.81 (s, 1H), 4.11 (d, $J = 12.4$ Hz, 1H), 3.93 (s, 3H), 3.74 (d, $J = 12.4$ Hz, 1H), 3.63-3.53 (m, 1H), 3.36-3.16 (m, 4H), 3.00-2.90 (m, 1H), 1.08 (d, $J = 6.9$ Hz, 6H), 1.00 (d, $J = 6.9$ Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ : 173.2, 155.3, 148.4, 135.8, 131.3, 131.3, 131.1, 127.5, 122.8, 116.4, 113.6, 80.1, 55.4, 54.7, 46.6, 41.8, 29.6, 28.6, 24.7, 23.7; HRMS(ESI) m/z calcd for C₂₄H₃₀N₂O₂ ([M+H]⁺) 379.2380, found 379.2375.

Reference

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X-ray data for 3p

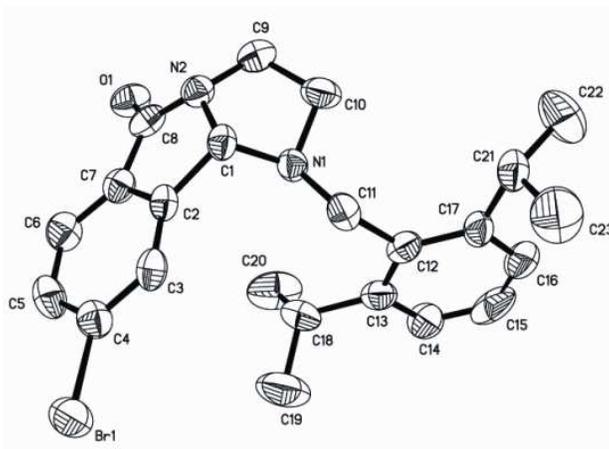


Table 1. Crystal data and structure refinement for s.

Identification code	s
Empirical formula	C ₂₃ H ₂₇ Br N ₂ O
Formula weight	427.37
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 6.2860(7) Å alpha = 90 deg. b = 10.3353(11) Å beta = 90 deg. c = 34.353(4) Å gamma = 90 deg.
Volume	2231.8(4) Å ³
Z, Calculated density	4, 1.272 Mg/m ³
Absorption coefficient	1.856 mm ⁻¹
F(000)	888
Crystal size	0.30 x 0.10 x 0.10 mm
Theta range for data collection	3.08 to 26.00 deg.
Limiting indices	-6 ≤ h ≤ 7, -11 ≤ k ≤ 12, -42 ≤ l ≤ 39
Reflections collected / unique	8804 / 4266 [R(int) = 0.0559]
Completeness to theta = 26.00	99.6 %

Absorption correction	None
Max. and min. transmission	0.8362 and 0.6060
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4266 / 0 / 248
Goodness-of-fit on F ²	1.038
Final R indices [I > 2σ(I)]	R1 = 0.0631, wR2 = 0.1689
R indices (all data)	R1 = 0.1463, wR2 = 0.2179
Absolute structure parameter	0.02(2)
Largest diff. peak and hole	0.333 and -0.446 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for s.

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br(1)	7514(2)	-3719(1)	-6767(1)	93(1)
O(1)	-310(9)	-8251(6)	-7293(2)	83(2)
N(1)	4361(9)	-9196(5)	-6533(2)	61(2)
N(2)	2903(10)	-9175(6)	-7129(2)	63(2)
C(1)	4807(11)	-8741(7)	-6927(2)	60(2)
C(2)	4748(12)	-7301(7)	-6965(2)	59(2)
C(3)	6185(12)	-6352(7)	-6856(2)	65(2)
C(4)	5629(13)	-5051(7)	-6903(2)	71(2)
C(5)	3665(15)	-4703(8)	-7086(3)	83(3)
C(6)	2249(16)	-5674(8)	-7199(2)	79(2)
C(7)	2722(15)	-6967(7)	-7136(2)	65(2)
C(8)	1565(14)	-8175(9)	-7200(2)	71(2)
C(9)	2082(15)	-10357(8)	-6968(2)	80(2)
C(10)	3574(15)	-10531(8)	-6622(2)	87(3)
C(11)	6126(12)	-9115(7)	-6252(2)	68(2)
C(12)	5405(12)	-9295(8)	-5819(2)	67(2)
C(13)	4074(14)	-8322(7)	-5664(2)	72(2)
C(14)	3399(16)	-8473(9)	-5295(3)	91(3)
C(15)	4080(20)	-9499(13)	-5085(2)	117(4)
C(16)	5356(16)	-10452(10)	-5234(3)	90(3)
C(17)	6011(14)	-10359(8)	-5599(2)	70(2)

C(18)	3302(15)	-7118(8)	-5897(3)	86(3)
C(19)	4040(20)	-5862(10)	-5751(4)	150(5)
C(20)	951(15)	-7080(13)	-5969(4)	135(5)
C(21)	7320(17)	-11451(7)	-5753(2)	84(2)
C(22)	6604(19)	-12759(9)	-5674(4)	139(5)
C(23)	9719(17)	-11198(12)	-5615(4)	140(4)

Table 3. Bond lengths [Å] and angles [deg] for s.

Br(1)-C(4)	1.876(8)
O(1)-C(8)	1.224(9)
N(1)-C(1)	1.460(8)
N(1)-C(11)	1.473(9)
N(1)-C(10)	1.496(9)
N(2)-C(8)	1.355(10)
N(2)-C(9)	1.437(9)
N(2)-C(1)	1.455(9)
C(1)-C(2)	1.495(9)
C(1)-H(1A)	0.9800
C(2)-C(3)	1.384(10)
C(2)-C(7)	1.445(11)
C(3)-C(4)	1.398(10)
C(3)-H(3A)	0.9300
C(4)-C(5)	1.431(11)
C(5)-C(6)	1.396(12)
C(5)-H(5A)	0.9300
C(6)-C(7)	1.386(11)
C(6)-H(6A)	0.9300

C(7)-C(8)	1.462(11)
C(9)-C(10)	1.526(12)
C(9)-H(9A)	0.9700
C(9)-H(9B)	0.9700
C(10)-H(10A)	0.9700
C(10)-H(10B)	0.9700
C(11)-C(12)	1.565(10)
C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700
C(12)-C(17)	1.389(11)
C(12)-C(13)	1.413(11)
C(13)-C(14)	1.345(11)
C(13)-C(18)	1.557(11)
C(14)-C(15)	1.352(14)
C(14)-H(14A)	0.9300
C(15)-C(16)	1.369(15)
C(15)-H(15A)	0.9300
C(16)-C(17)	1.322(11)
C(16)-H(16A)	0.9300
C(17)-C(21)	1.495(11)
C(18)-C(19)	1.465(12)
C(18)-C(20)	1.499(12)
C(18)-H(18A)	0.9800
C(19)-H(19A)	0.9600
C(19)-H(19B)	0.9600
C(19)-H(19C)	0.9600
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600

C(21)-C(22)	1.450(12)
C(21)-C(23)	1.602(13)
C(21)-H(21A)	0.9800
C(22)-H(22A)	0.9600
C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600
C(23)-H(23A)	0.9600
C(23)-H(23B)	0.9600
C(23)-H(23C)	0.9600
C(1)-N(1)-C(11)	116.4(5)
C(1)-N(1)-C(10)	99.9(6)
C(11)-N(1)-C(10)	115.8(6)
C(8)-N(2)-C(9)	119.7(7)
C(8)-N(2)-C(1)	111.2(6)
C(9)-N(2)-C(1)	112.0(6)
N(2)-C(1)-N(1)	100.6(5)
N(2)-C(1)-C(2)	104.2(6)
N(1)-C(1)-C(2)	113.4(6)
N(2)-C(1)-H(1A)	112.6
N(1)-C(1)-H(1A)	112.6
C(2)-C(1)-H(1A)	112.6
C(3)-C(2)-C(7)	121.0(6)
C(3)-C(2)-C(1)	131.7(7)
C(7)-C(2)-C(1)	107.2(7)
C(2)-C(3)-C(4)	119.1(7)
C(2)-C(3)-H(3A)	120.4
C(4)-C(3)-H(3A)	120.4
C(3)-C(4)-C(5)	120.5(8)
C(3)-C(4)-Br(1)	121.3(6)

C(5)-C(4)-Br(1)	118.0(6)
C(6)-C(5)-C(4)	119.4(7)
C(6)-C(5)-H(5A)	120.3
C(4)-C(5)-H(5A)	120.3
C(7)-C(6)-C(5)	120.8(9)
C(7)-C(6)-H(6A)	119.6
C(5)-C(6)-H(6A)	119.6
C(6)-C(7)-C(2)	118.9(8)
C(6)-C(7)-C(8)	133.9(9)
C(2)-C(7)-C(8)	107.2(7)
O(1)-C(8)-N(2)	126.6(8)
O(1)-C(8)-C(7)	125.0(8)
N(2)-C(8)-C(7)	108.4(7)
N(2)-C(9)-C(10)	100.3(6)
N(2)-C(9)-H(9A)	111.7
C(10)-C(9)-H(9A)	111.7
N(2)-C(9)-H(9B)	111.7
C(10)-C(9)-H(9B)	111.7
H(9A)-C(9)-H(9B)	109.5
N(1)-C(10)-C(9)	104.7(6)
N(1)-C(10)-H(10A)	110.8
C(9)-C(10)-H(10A)	110.8
N(1)-C(10)-H(10B)	110.8
C(9)-C(10)-H(10B)	110.8
H(10A)-C(10)-H(10B)	108.9
N(1)-C(11)-C(12)	113.4(6)
N(1)-C(11)-H(11A)	108.9
C(12)-C(11)-H(11A)	108.9
N(1)-C(11)-H(11B)	108.9

C(12)-C(11)-H(11B)	108.9
H(11A)-C(11)-H(11B)	107.7
C(17)-C(12)-C(13)	121.3(7)
C(17)-C(12)-C(11)	122.2(7)
C(13)-C(12)-C(11)	116.5(7)
C(14)-C(13)-C(12)	117.4(8)
C(14)-C(13)-C(18)	118.6(8)
C(12)-C(13)-C(18)	124.0(7)
C(13)-C(14)-C(15)	119.5(9)
C(13)-C(14)-H(14A)	120.2
C(15)-C(14)-H(14A)	120.2
C(14)-C(15)-C(16)	123.4(8)
C(14)-C(15)-H(15A)	118.3
C(16)-C(15)-H(15A)	118.3
C(17)-C(16)-C(15)	118.9(9)
C(17)-C(16)-H(16A)	120.5
C(15)-C(16)-H(16A)	120.5
C(16)-C(17)-C(12)	119.3(8)
C(16)-C(17)-C(21)	116.9(8)
C(12)-C(17)-C(21)	123.8(7)
C(19)-C(18)-C(20)	110.1(9)
C(19)-C(18)-C(13)	115.7(8)
C(20)-C(18)-C(13)	114.4(9)
C(19)-C(18)-H(18A)	105.1
C(20)-C(18)-H(18A)	105.1
C(13)-C(18)-H(18A)	105.1
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5

C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(18)-C(20)-H(20A)	109.5
C(18)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(18)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(22)-C(21)-C(17)	117.8(9)
C(22)-C(21)-C(23)	112.9(9)
C(17)-C(21)-C(23)	106.8(8)
C(22)-C(21)-H(21A)	106.2
C(17)-C(21)-H(21A)	106.2
C(23)-C(21)-H(21A)	106.2
C(21)-C(22)-H(22A)	109.5
C(21)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(21)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(21)-C(23)-H(23A)	109.5
C(21)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(21)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for s.

The anisotropic displacement factor exponent takes the form:

$$-2 \pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$$

	U11	U22	U33	U23	U13	U12
Br(1)	105(1)	73(1)	102(1)	-4(1)	4(1)	-11(1)
O(1)	62(3)	101(4)	85(4)	-19(3)	-14(3)	5(3)
N(1)	61(4)	56(3)	65(4)	5(3)	-10(3)	-2(3)
N(2)	64(4)	67(4)	59(4)	-5(3)	0(3)	4(3)
C(1)	63(4)	65(4)	52(4)	11(4)	6(4)	7(4)
C(2)	61(5)	65(5)	51(4)	14(3)	5(4)	4(4)
C(3)	52(4)	82(6)	60(4)	19(4)	2(3)	10(4)
C(4)	74(6)	66(5)	73(5)	3(4)	11(4)	9(4)
C(5)	82(6)	68(5)	97(6)	21(5)	15(5)	17(5)
C(6)	65(5)	86(5)	86(5)	5(4)	-7(5)	19(5)
C(7)	61(5)	75(5)	59(4)	2(3)	2(5)	6(5)
C(8)	64(5)	98(6)	50(4)	-13(4)	5(4)	0(5)
C(9)	79(7)	89(6)	72(5)	-16(4)	-7(5)	-6(5)
C(10)	108(7)	62(5)	91(6)	-16(5)	2(5)	-11(5)
C(11)	57(4)	61(4)	86(5)	12(4)	-8(4)	-3(4)
C(12)	68(5)	77(5)	54(5)	-2(4)	-2(4)	-16(4)
C(13)	80(6)	69(5)	67(5)	-10(4)	1(4)	-15(4)
C(14)	123(8)	91(6)	58(5)	-3(5)	21(5)	-4(5)
C(15)	150(10)	163(11)	38(5)	-1(6)	5(6)	-67(9)
C(16)	121(8)	102(7)	48(5)	5(5)	-2(5)	-5(6)
C(17)	84(6)	67(5)	60(5)	17(4)	-8(4)	-12(4)
C(18)	93(7)	61(5)	104(7)	-14(5)	5(5)	-14(4)

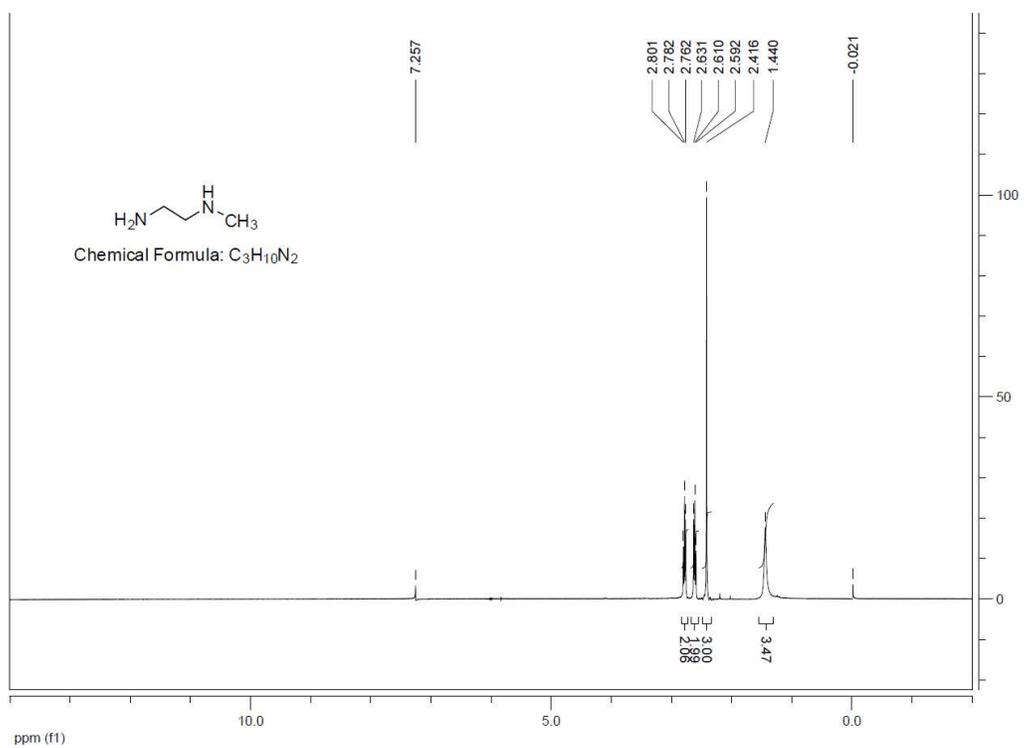
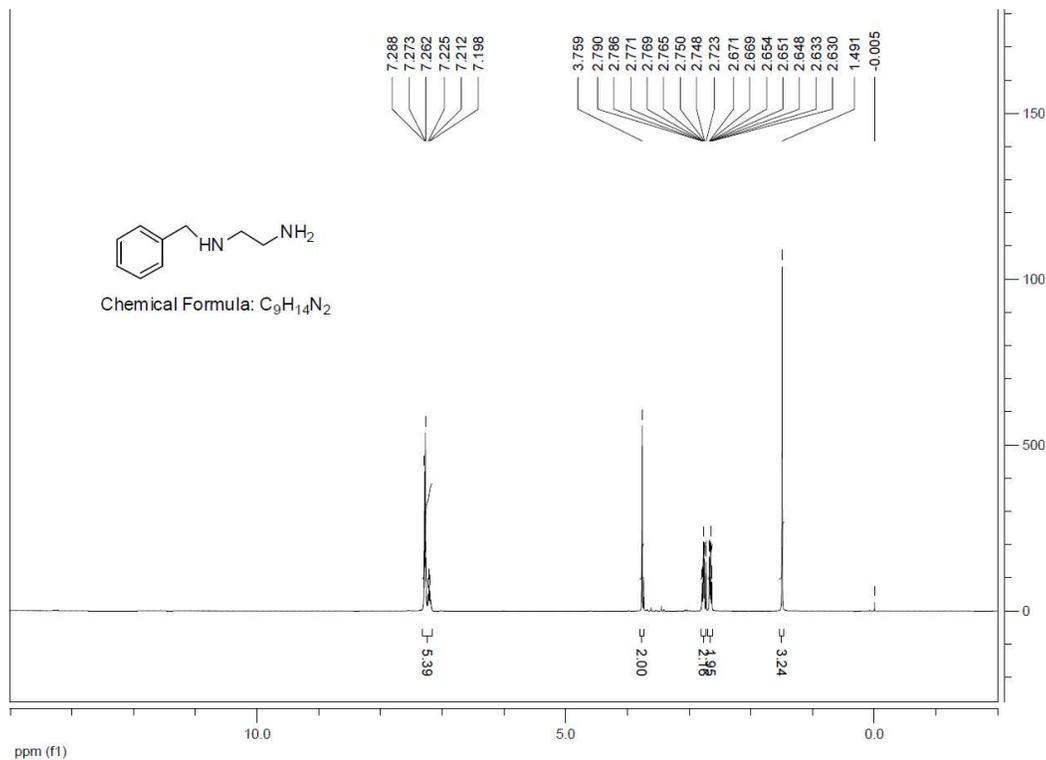
C(19)	155(11)	93(8)	204(13)	-37(8)	-38(10)	-29(8)
C(20)	64(7)	156(11)	185(12)	-59(10)	-24(7)	7(7)
C(21)	103(6)	80(5)	70(5)	21(4)	-11(5)	1(7)
C(22)	149(11)	80(7)	187(12)	36(7)	14(9)	-20(6)
C(23)	115(10)	141(10)	163(11)	18(10)	-15(9)	-21(9)

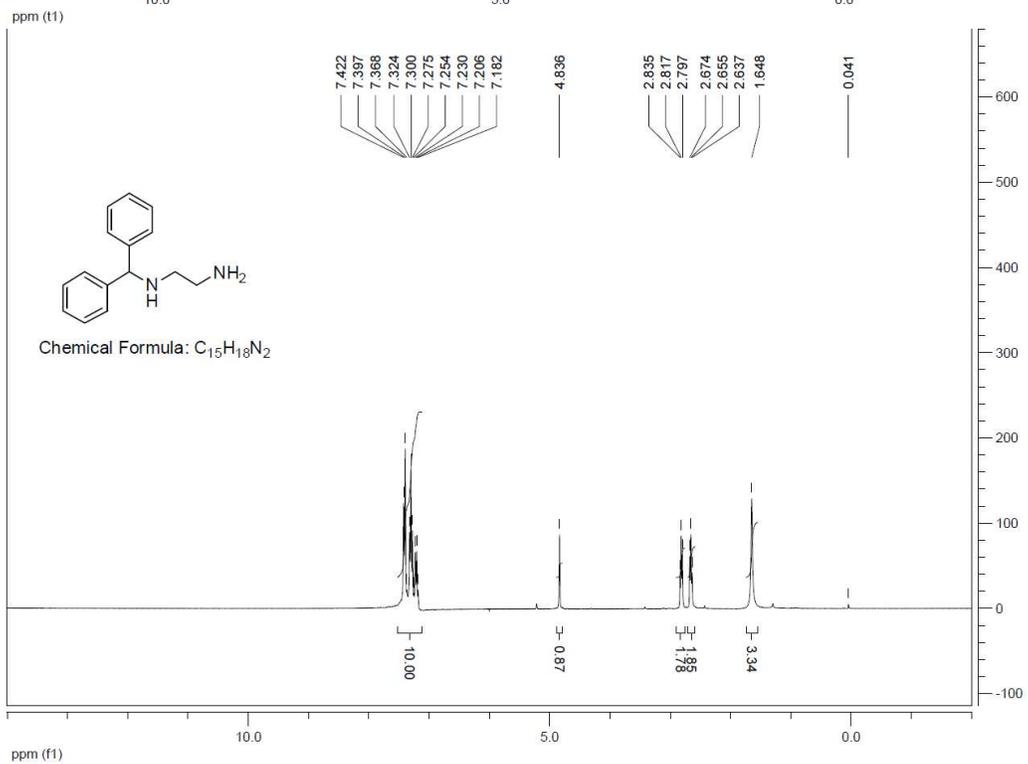
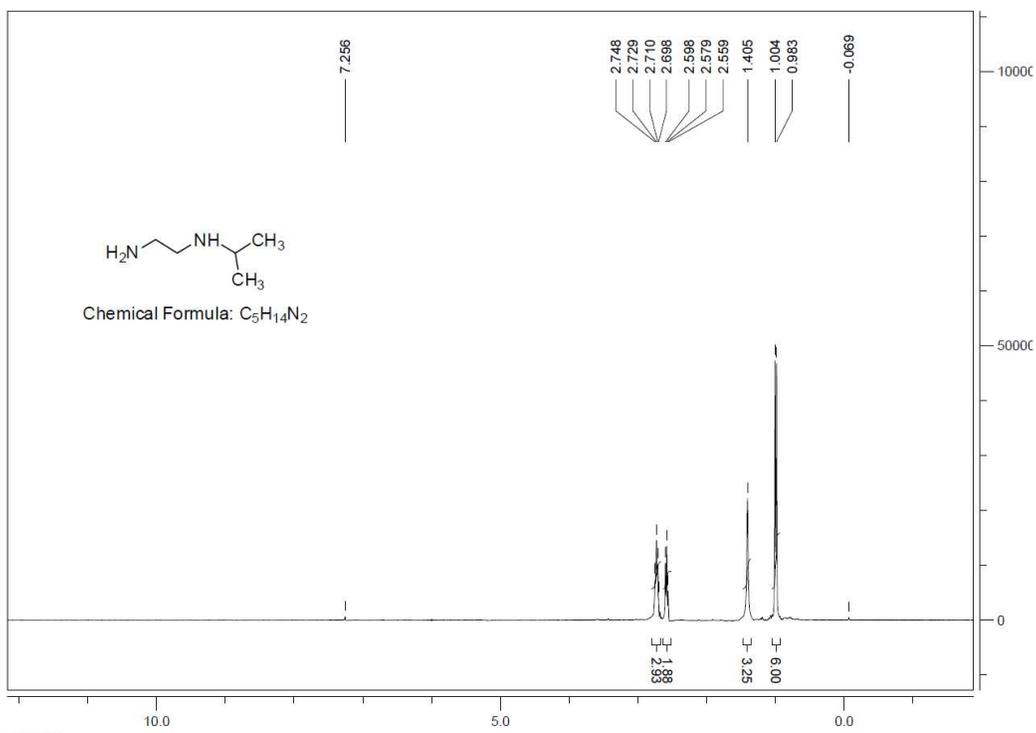
Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for s.

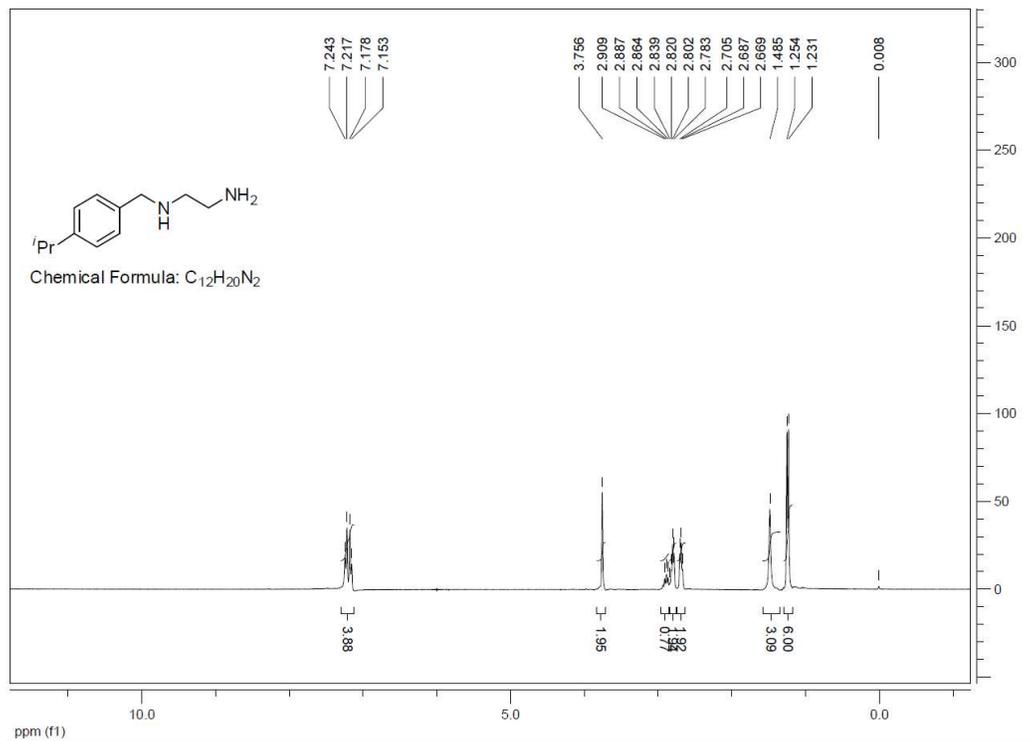
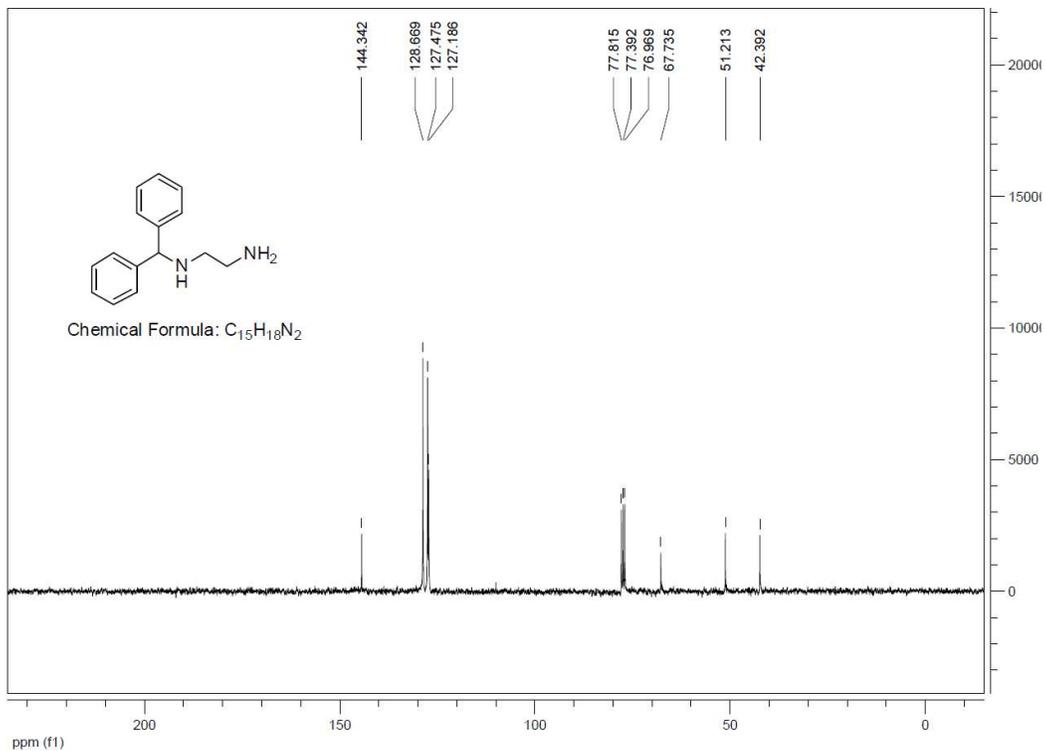
	x	y	z	U(eq)
H(1A)	6110	-9118	-7035	72
H(3A)	7503	-6577	-6754	78
H(5A)	3335	-3838	-7129	99
H(6A)	974	-5450	-7319	95
H(9A)	2197	-11070	-7151	96
H(9B)	613	-10265	-6886	96
H(10A)	2818	-10890	-6400	104
H(10B)	4746	-11100	-6688	104
H(11A)	6811	-8278	-6278	82
H(11B)	7170	-9774	-6315	82
H(14A)	2470	-7876	-5185	109
H(15A)	3662	-9561	-4826	140
H(16A)	5756	-11153	-5081	108
H(18A)	3950	-7207	-6155	103
H(19A)	3550	-5189	-5922	226
H(19B)	5561	-5855	-5741	226
H(19C)	3474	-5720	-5495	226

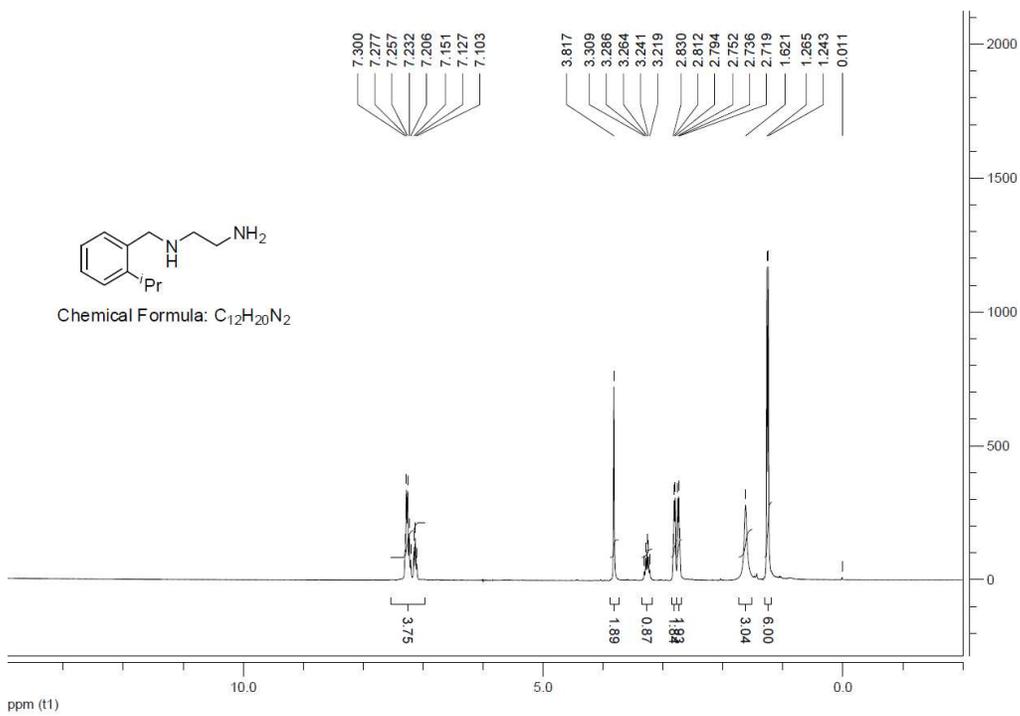
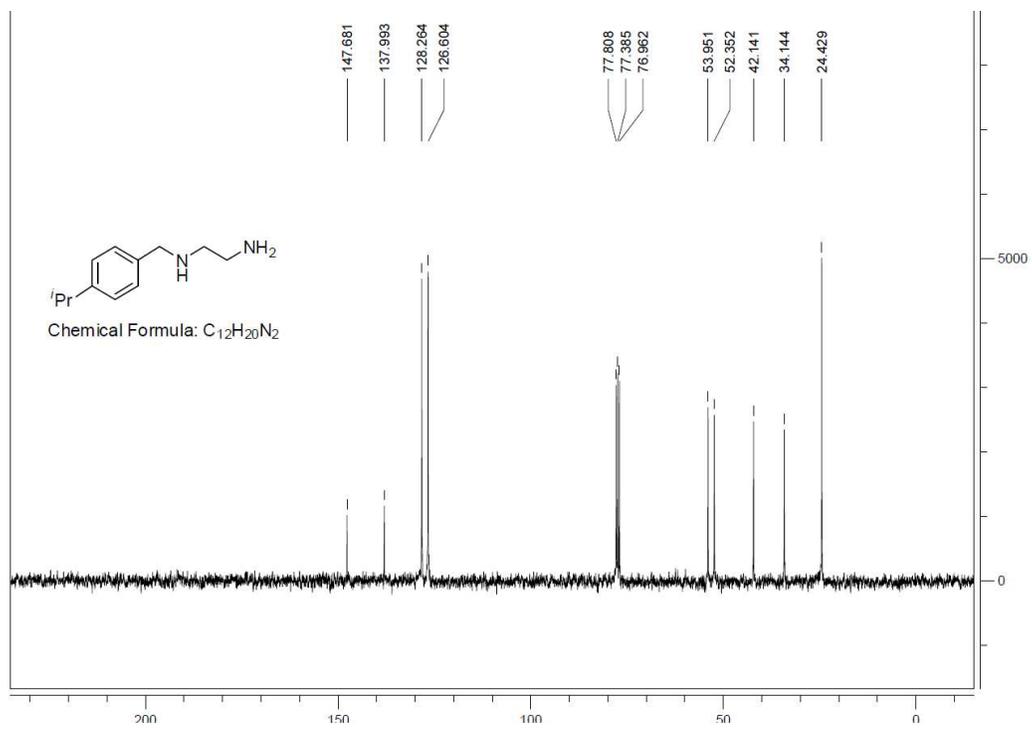
H(20A)	548	-6227	-6051	202
H(20B)	208	-7297	-5734	202
H(20C)	593	-7692	-6169	202
H(21A)	7321	-11358	-6037	101
H(22A)	5193	-12873	-5775	208
H(22B)	6594	-12905	-5398	208
H(22C)	7550	-13364	-5796	208
H(23A)	10654	-11789	-5746	209
H(23B)	9821	-11327	-5338	209
H(23C)	10117	-10325	-5677	209

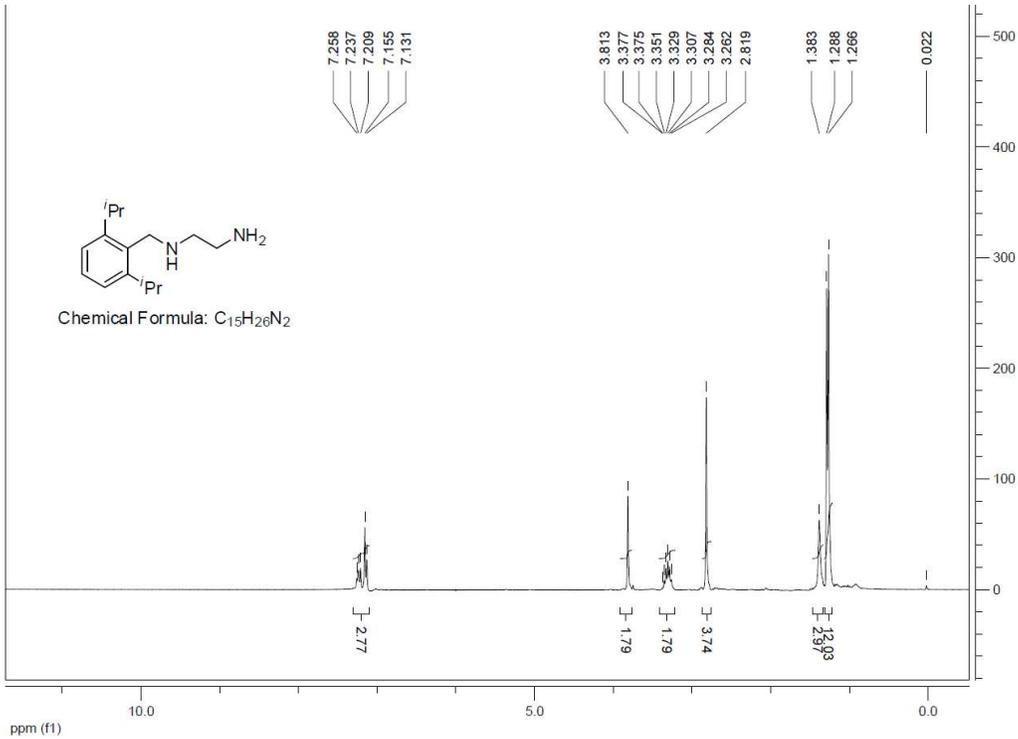
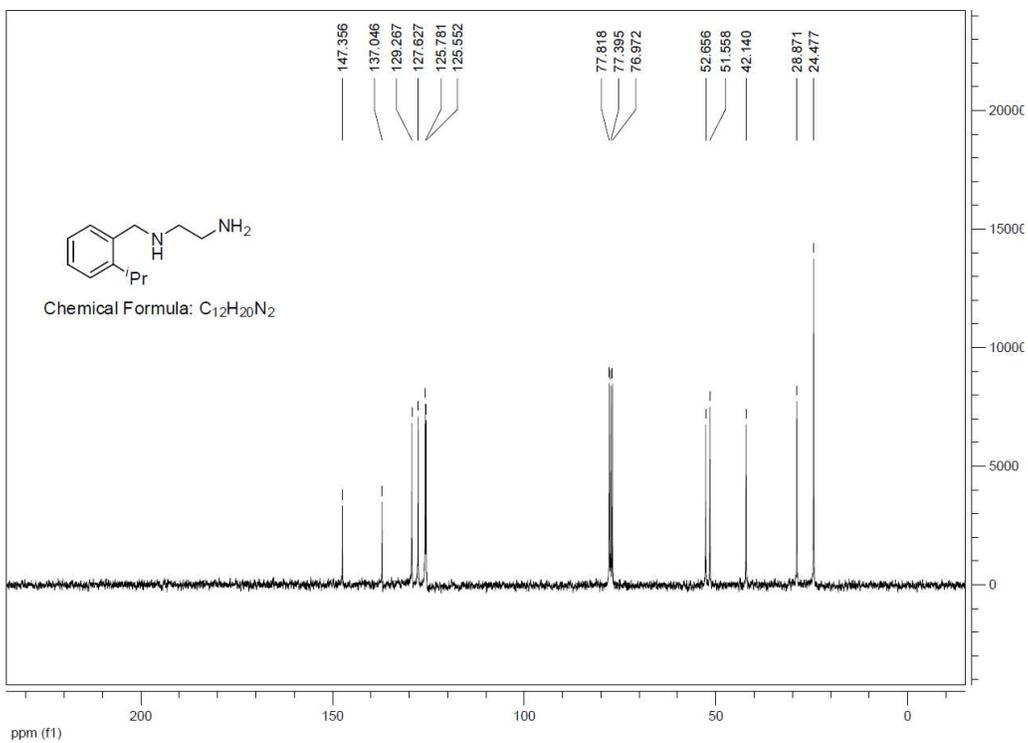
Copies of ^1H NMR, ^{13}C NMR and chiral HPLC Spectra for all products

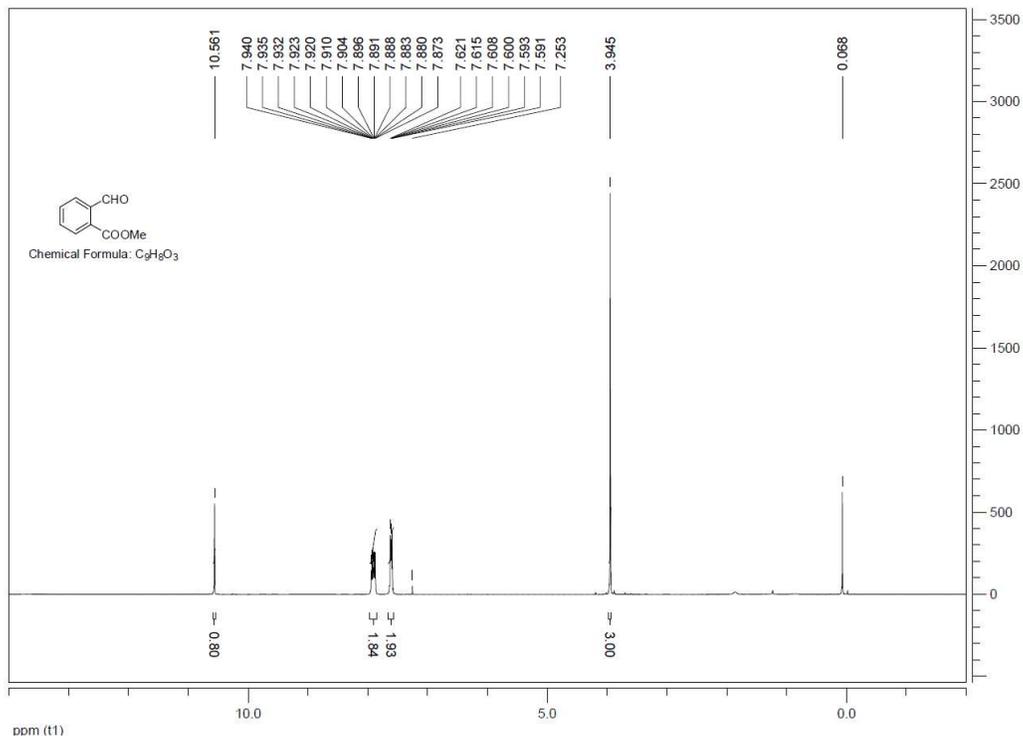
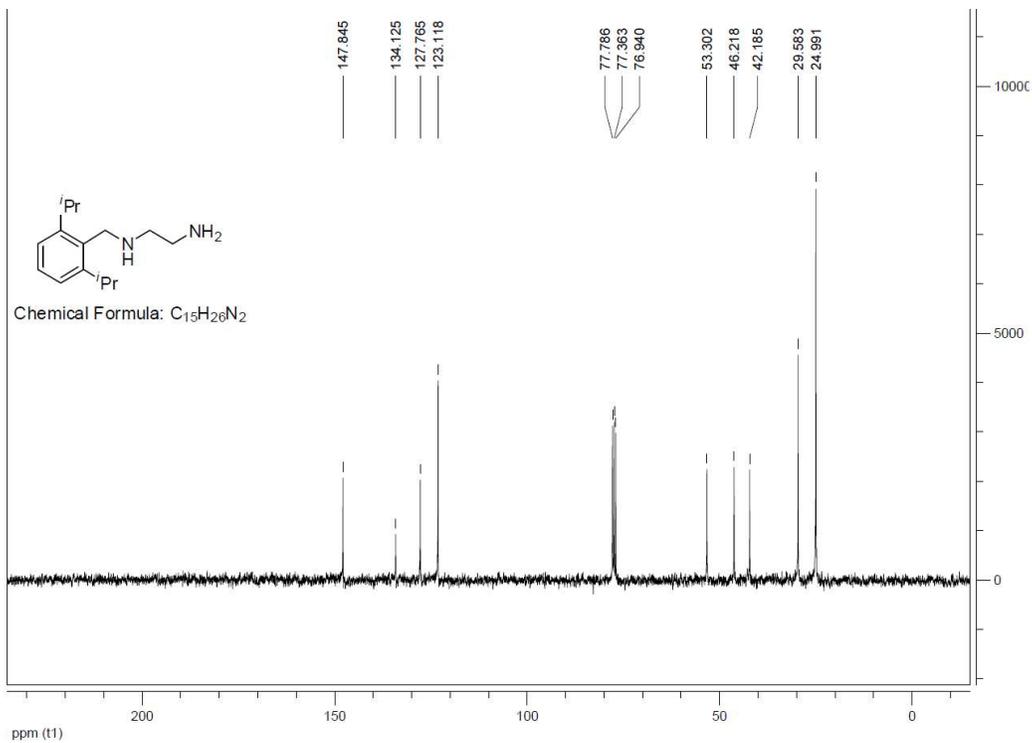


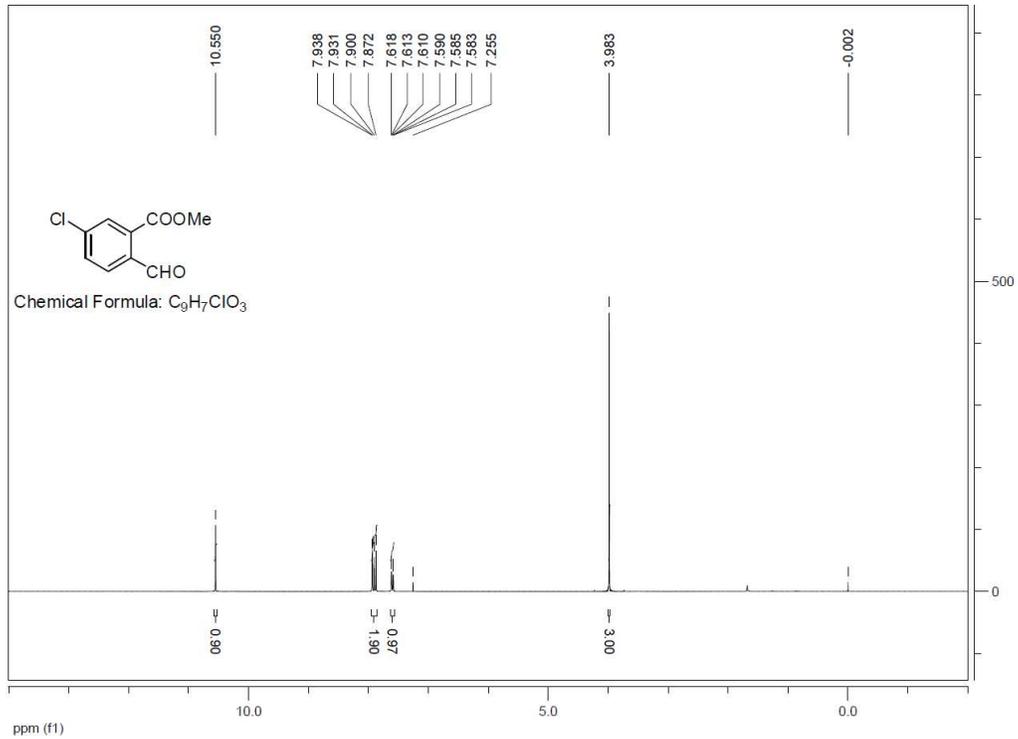
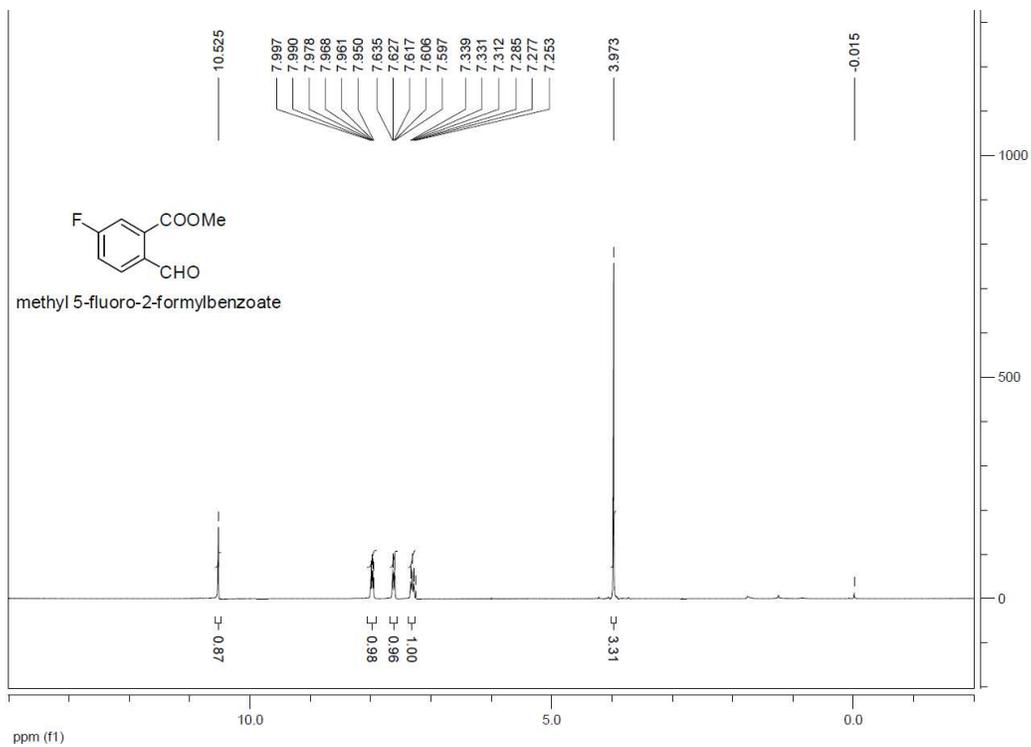


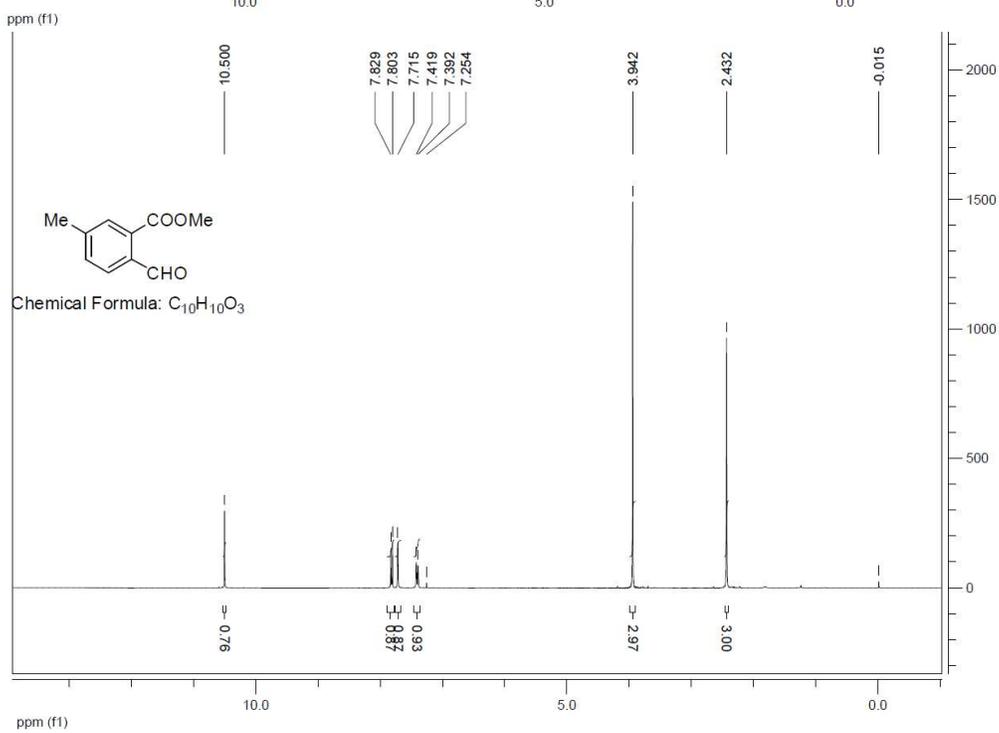
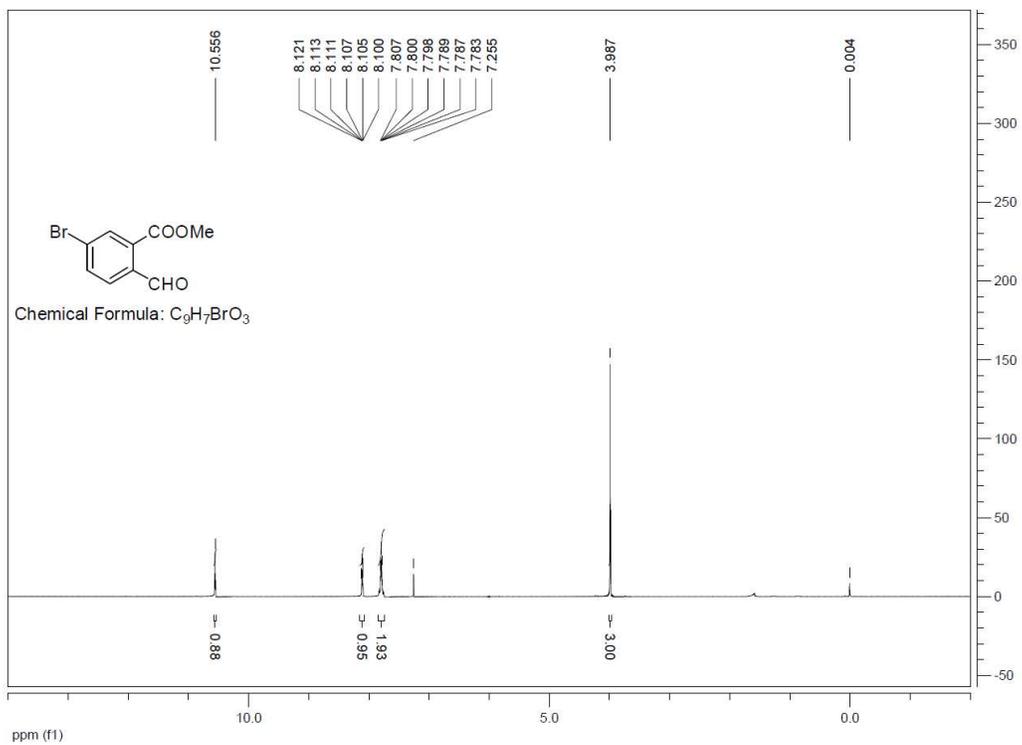


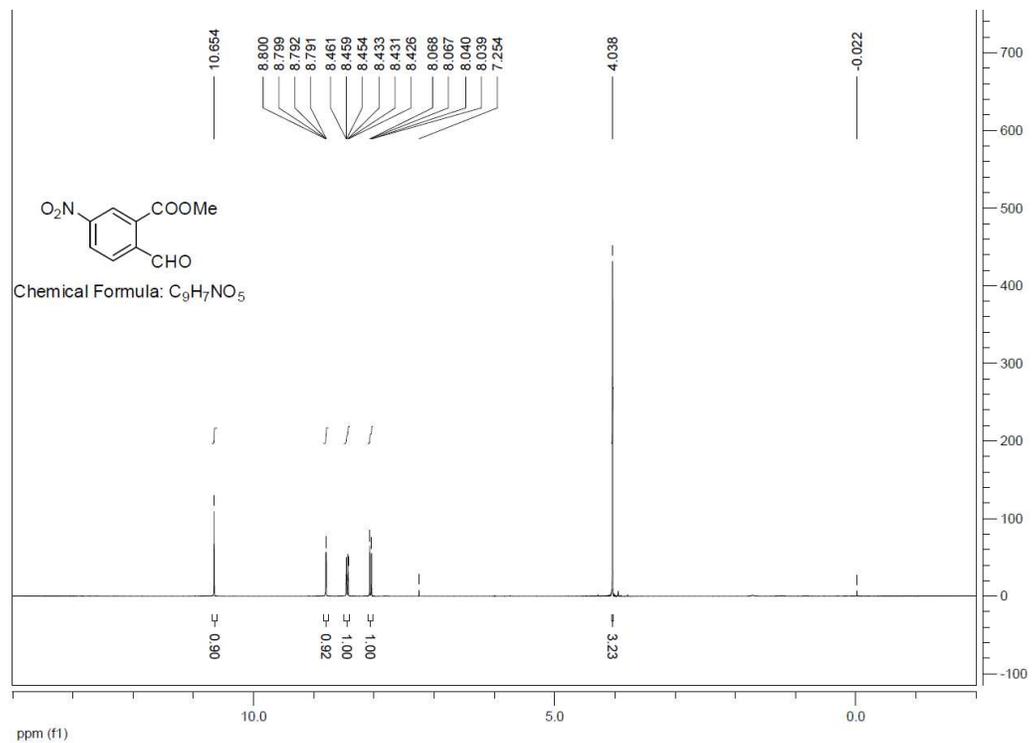
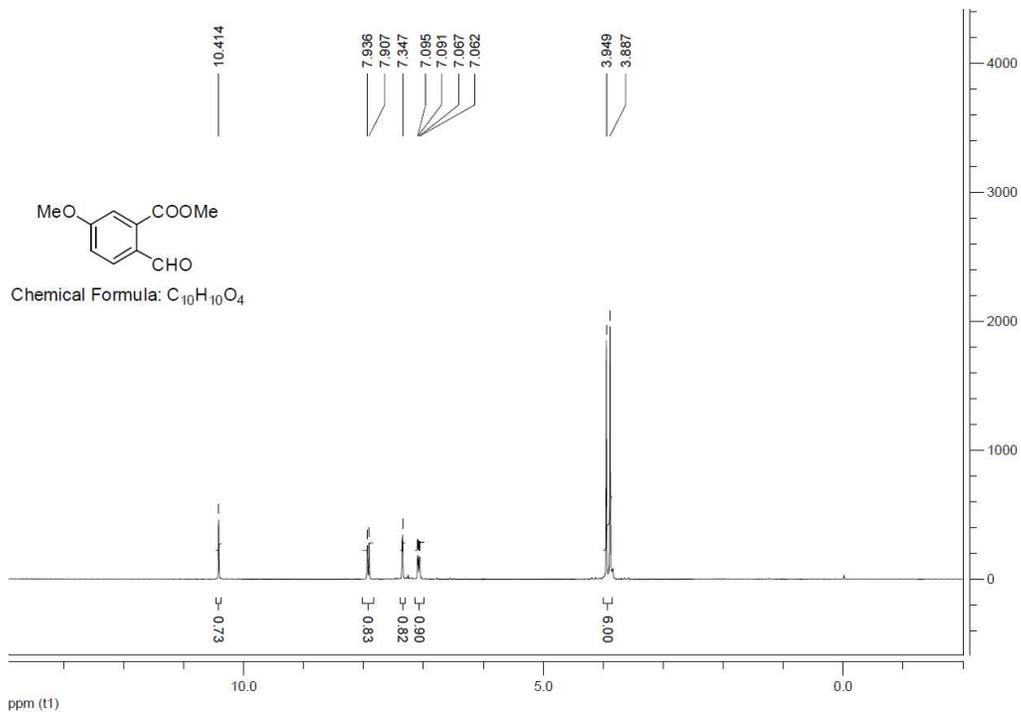


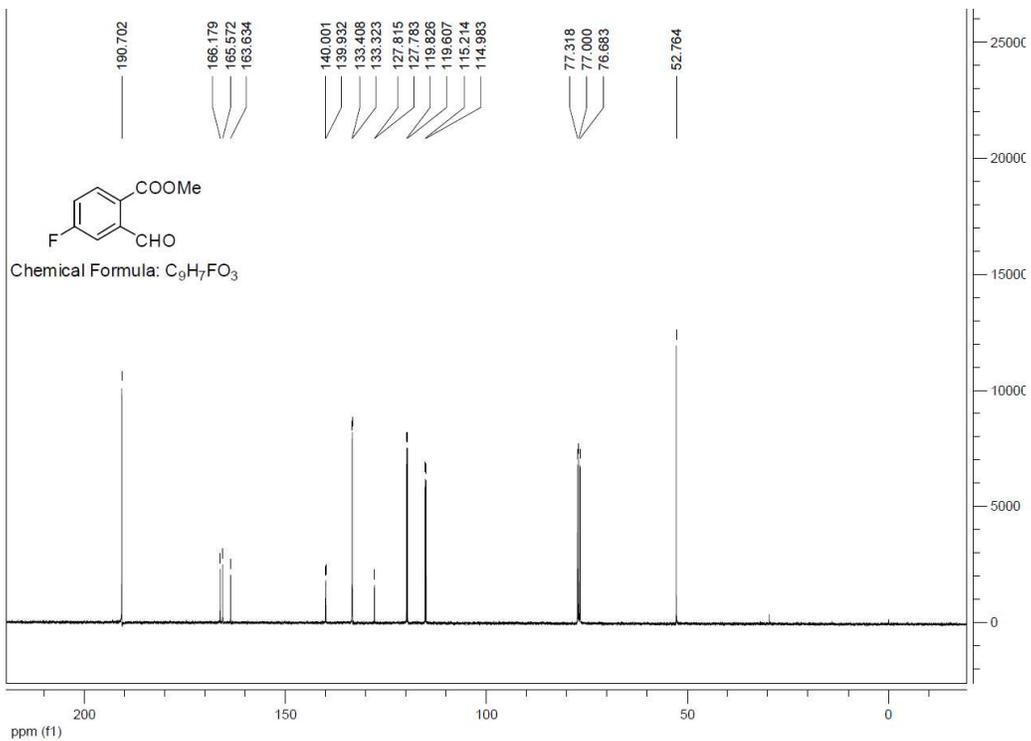
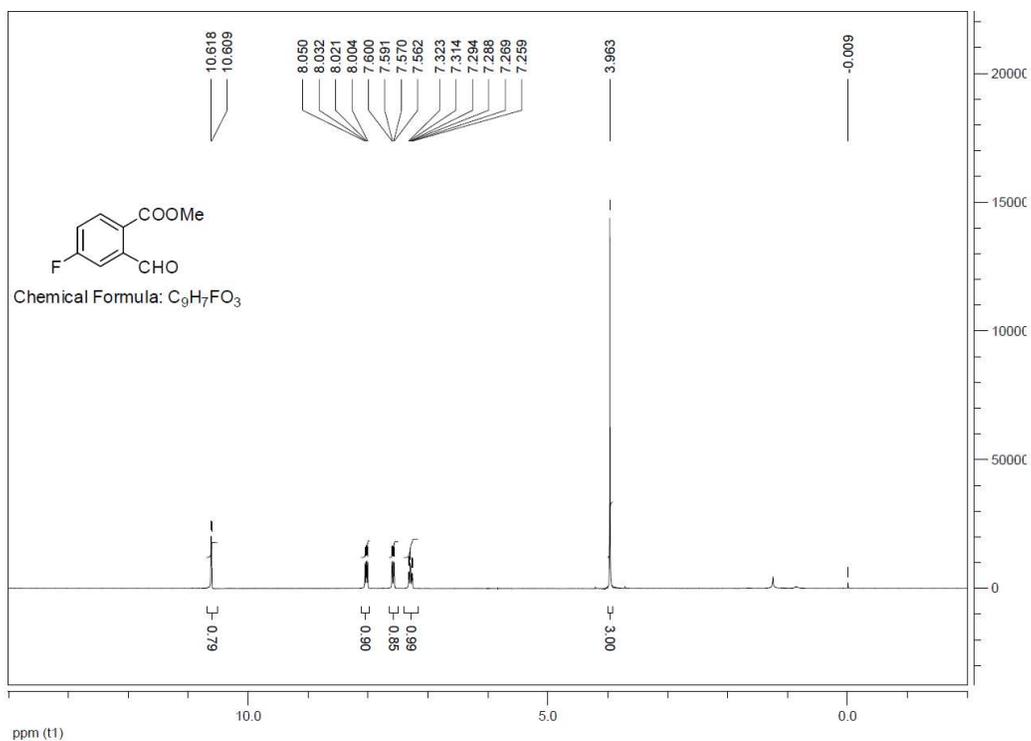


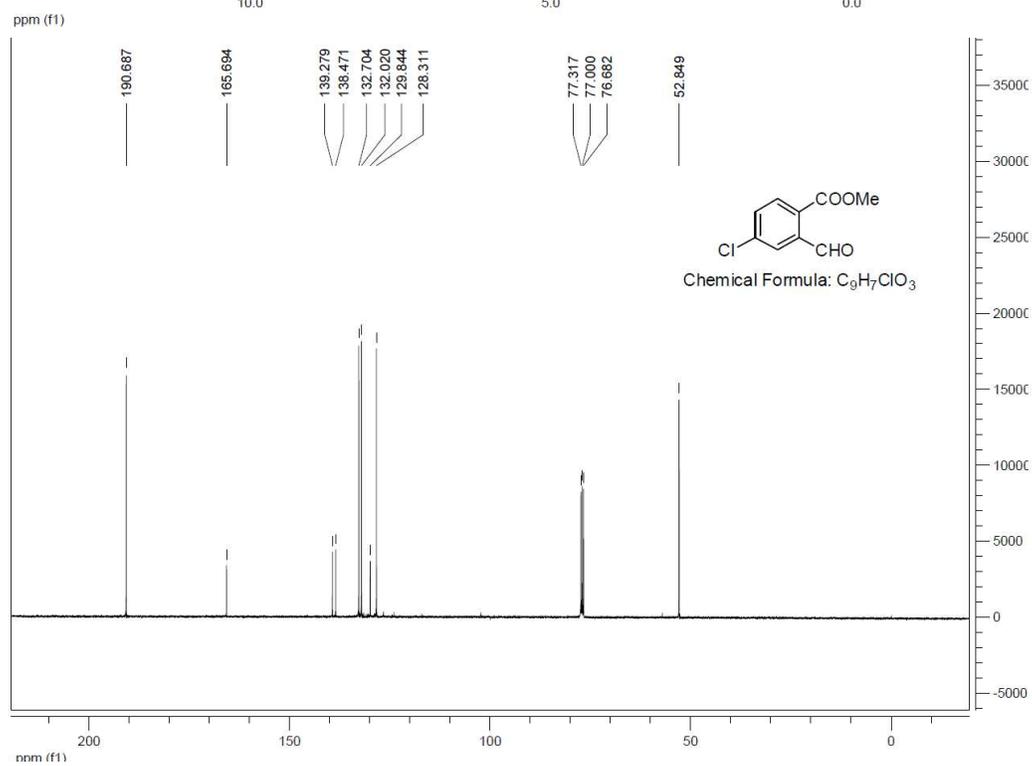
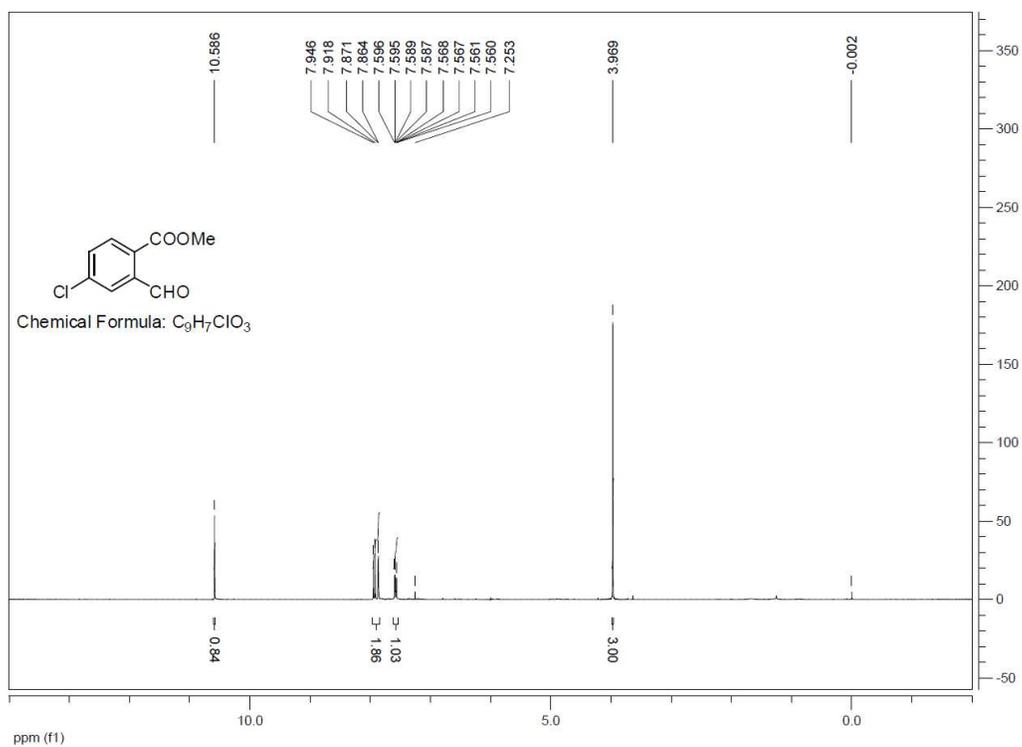


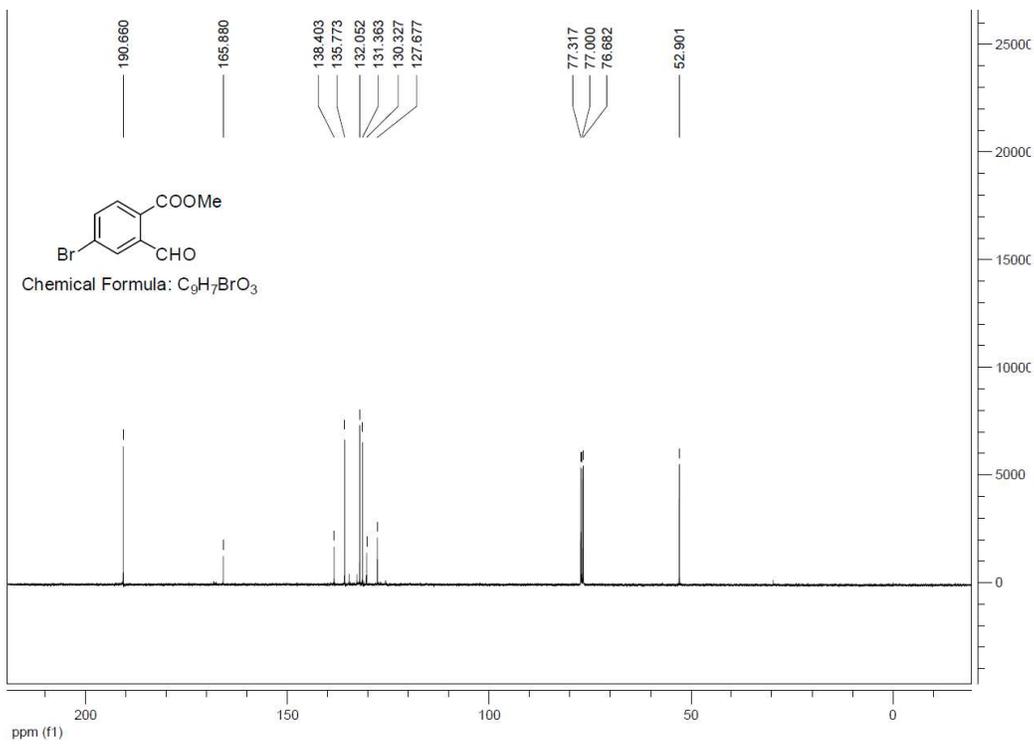
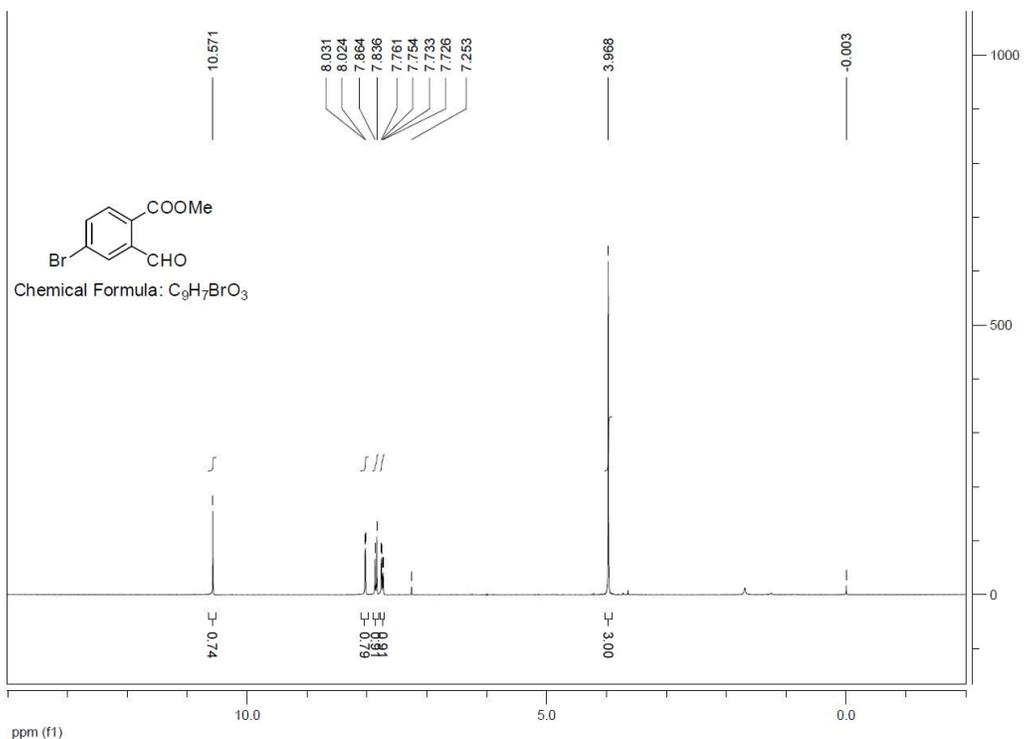


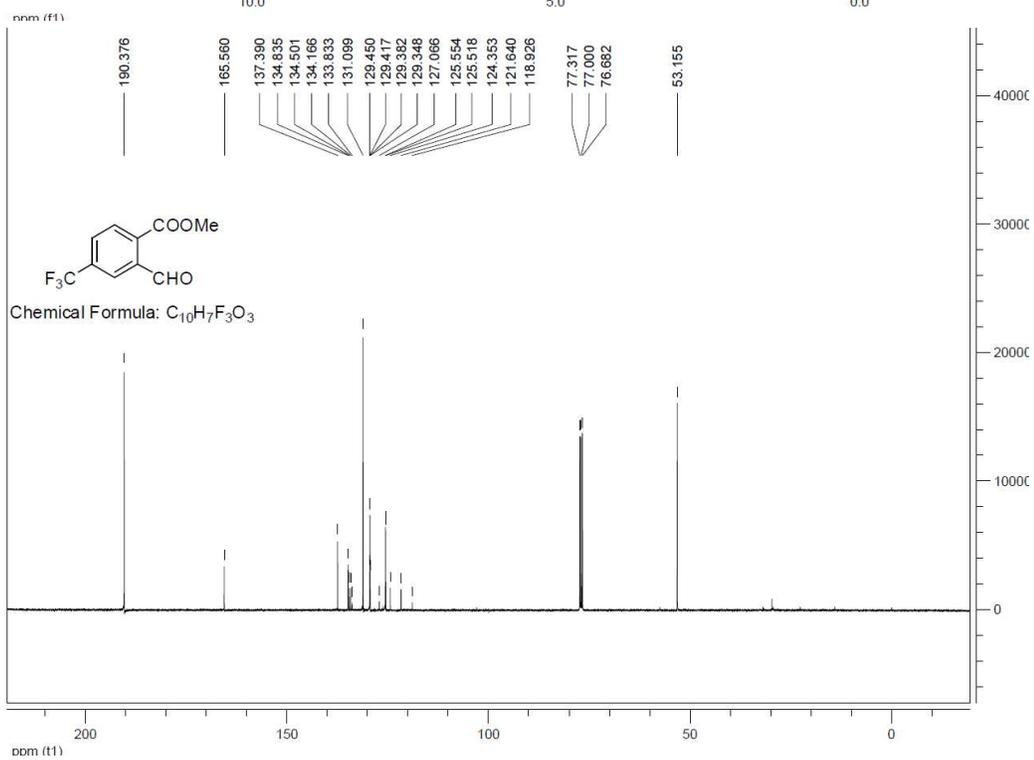
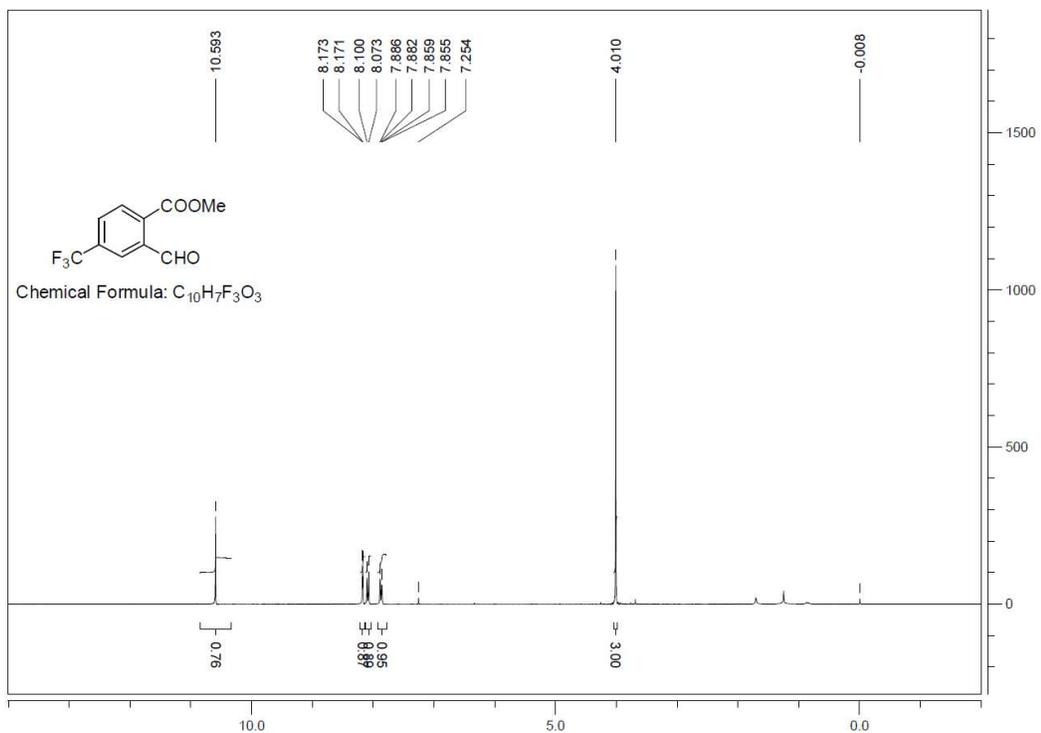


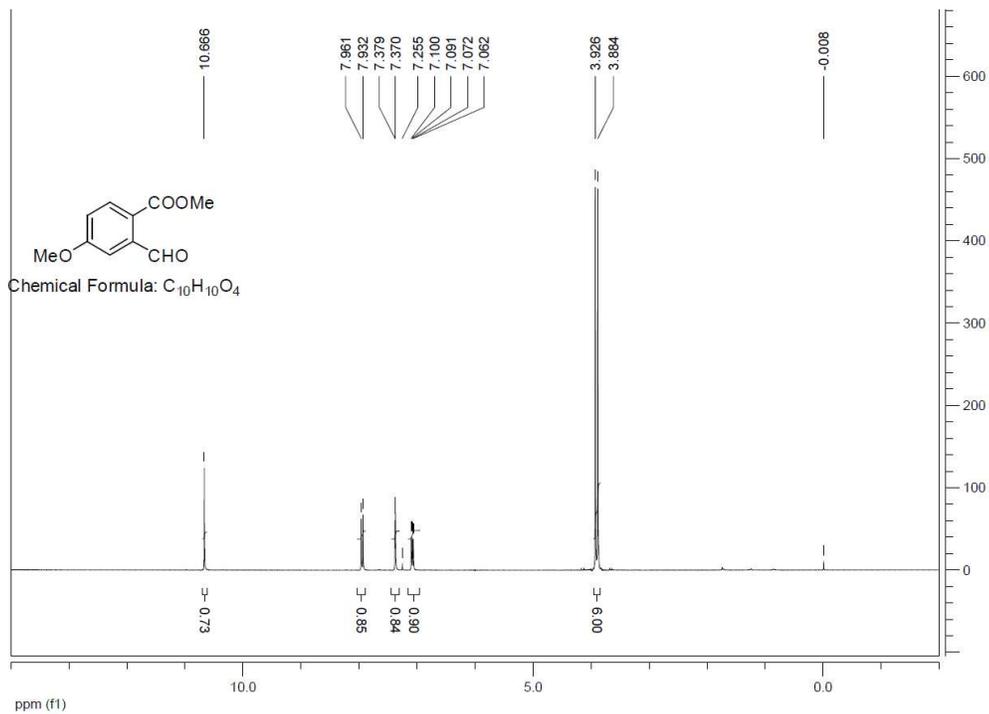
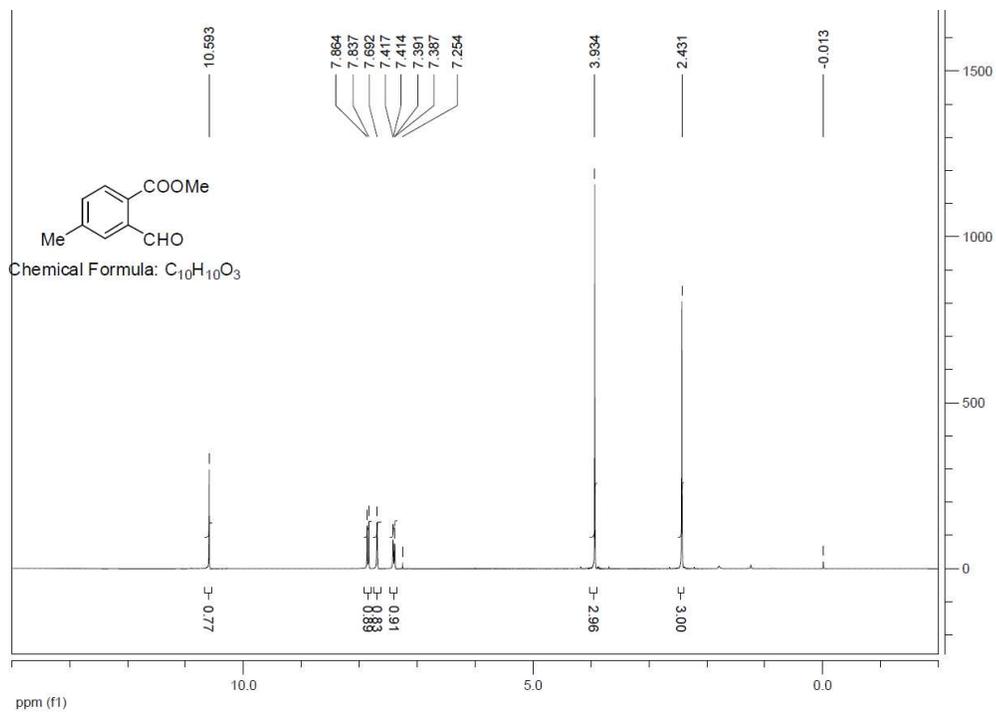


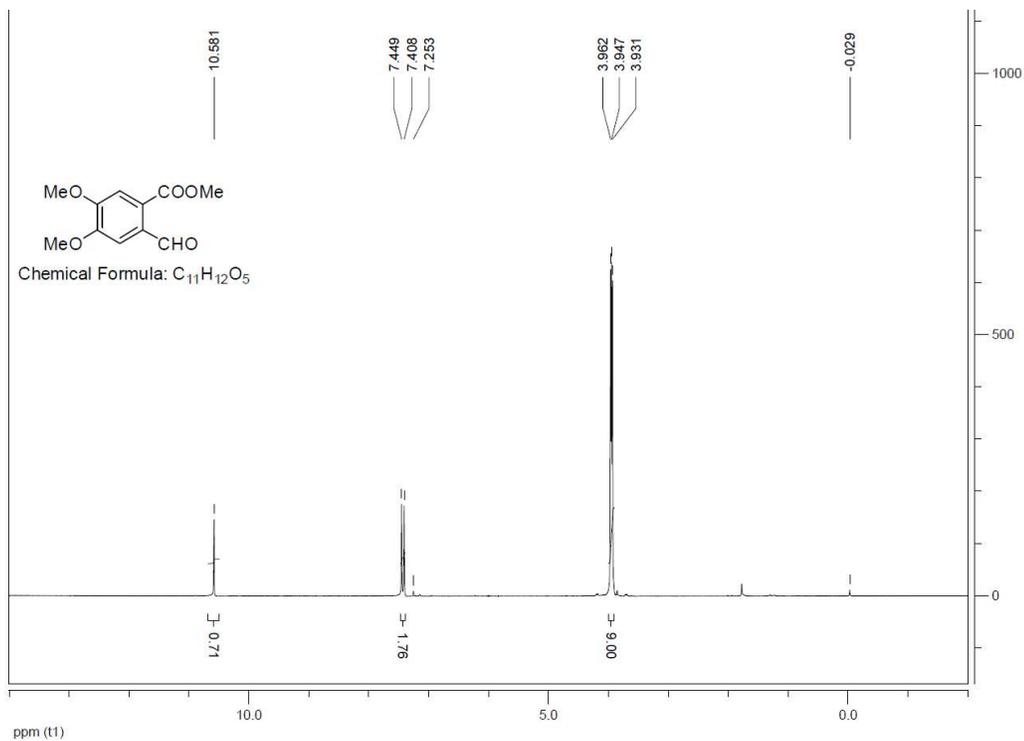
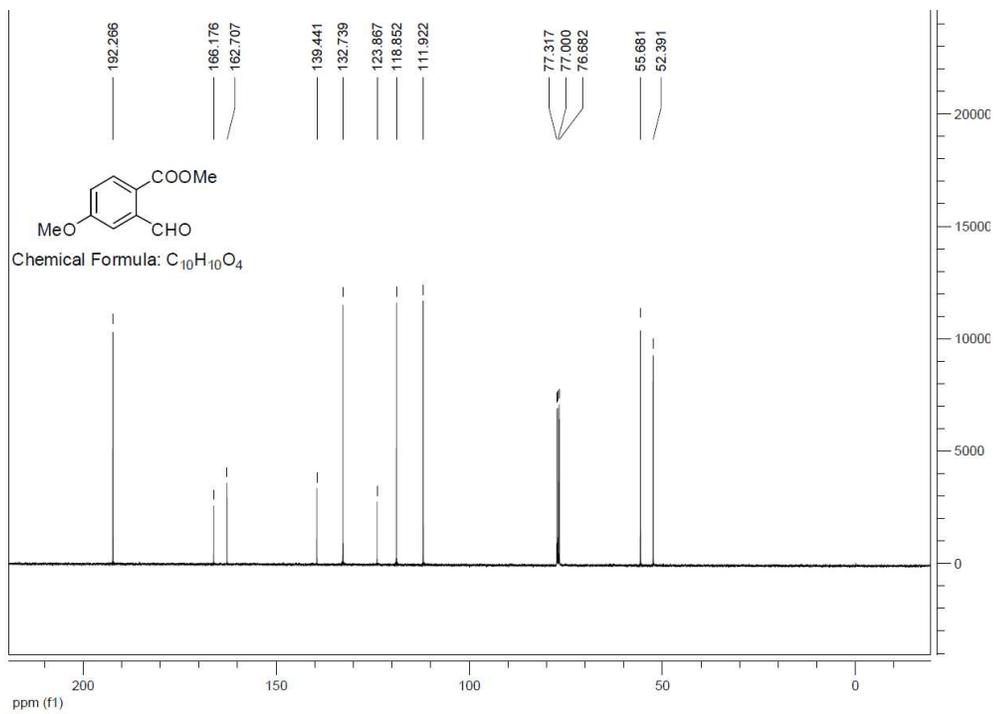


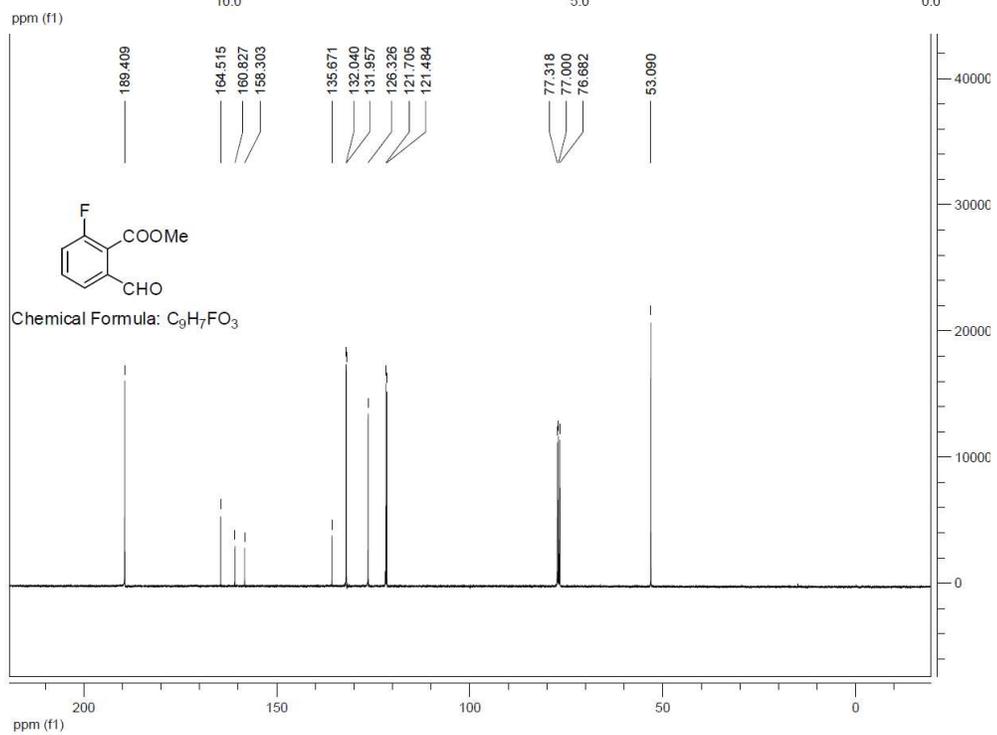
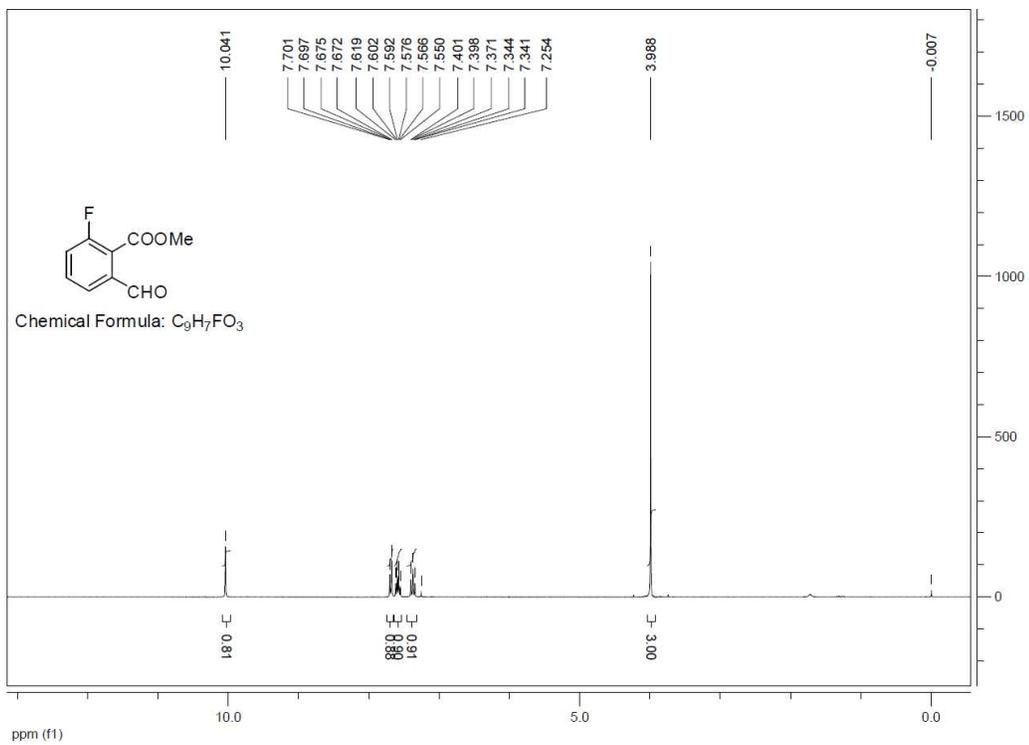


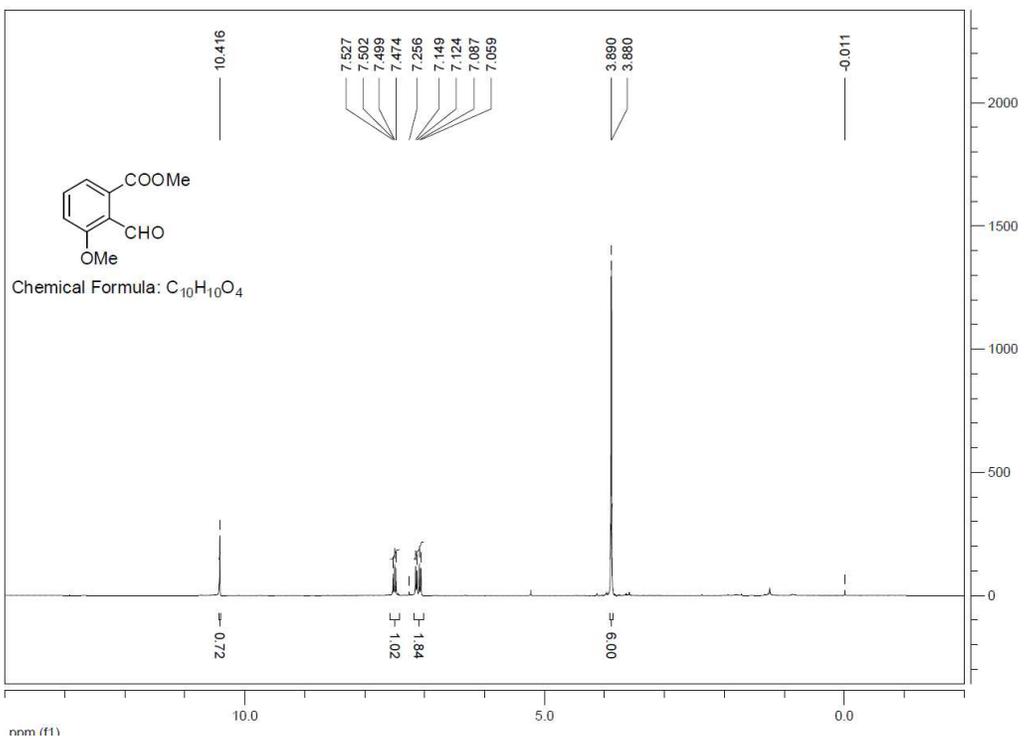
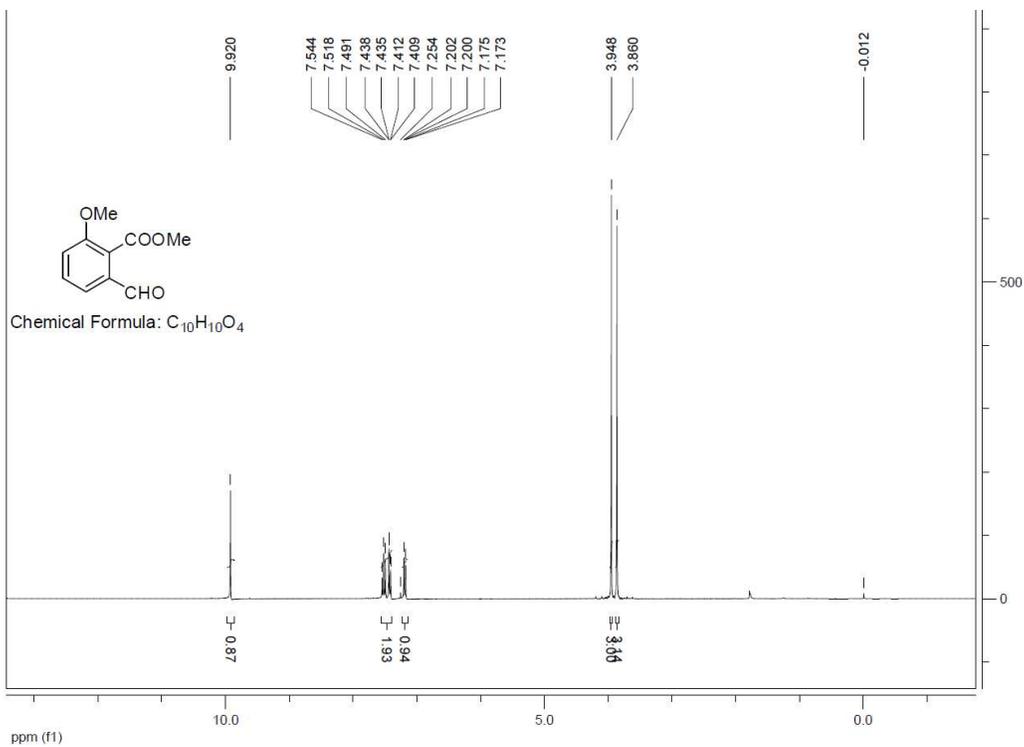




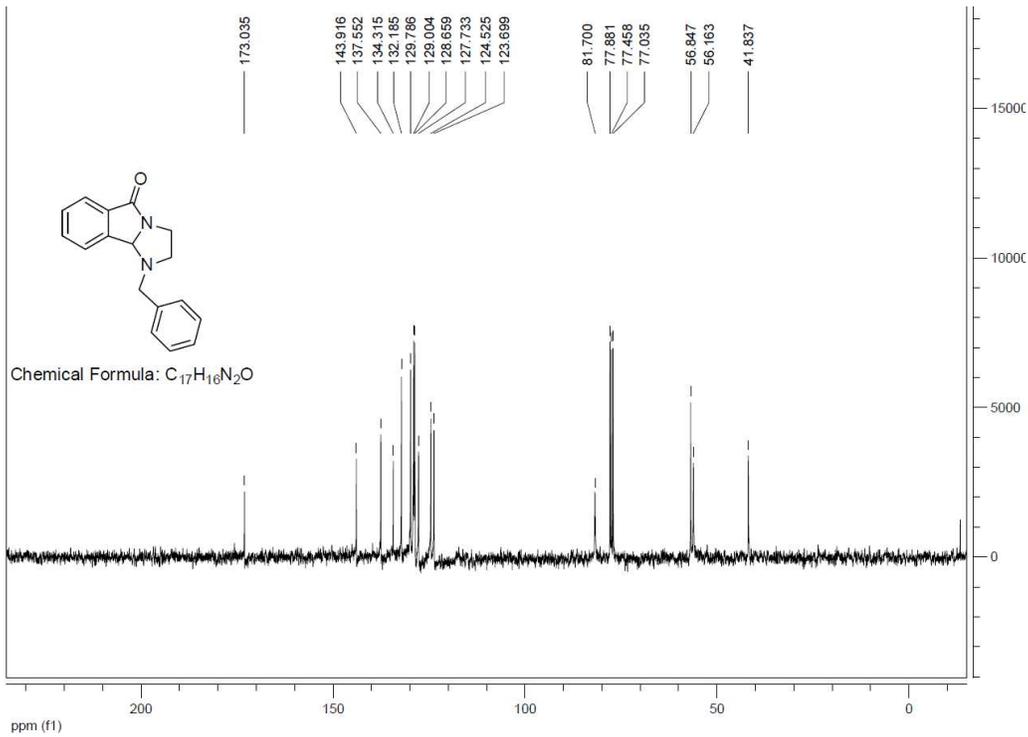
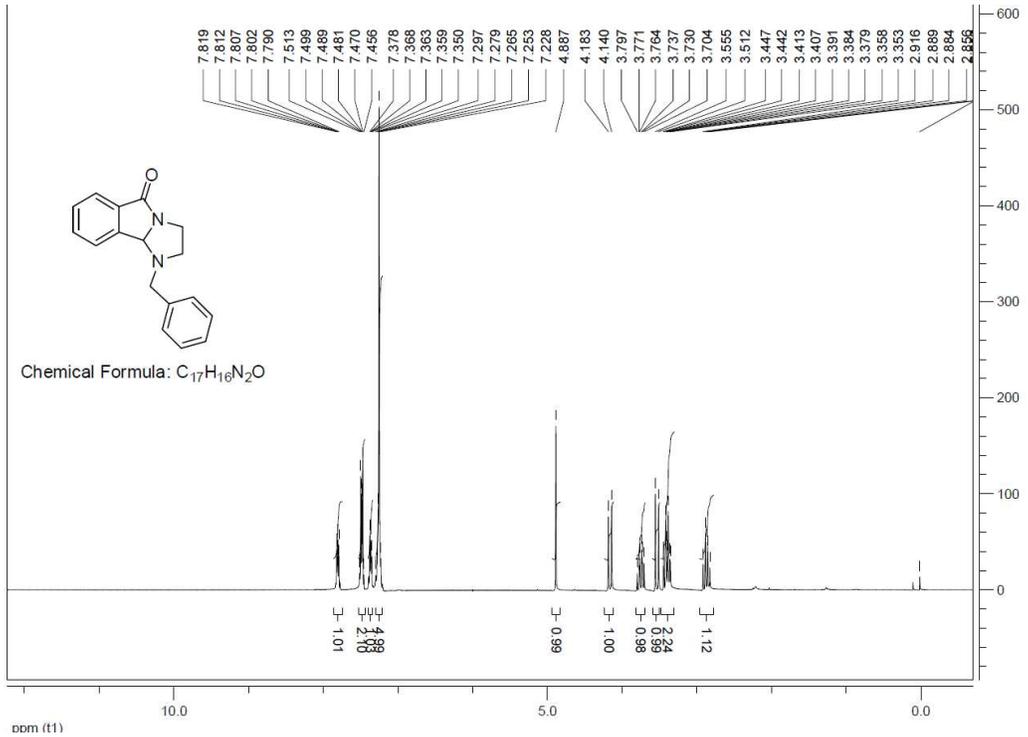




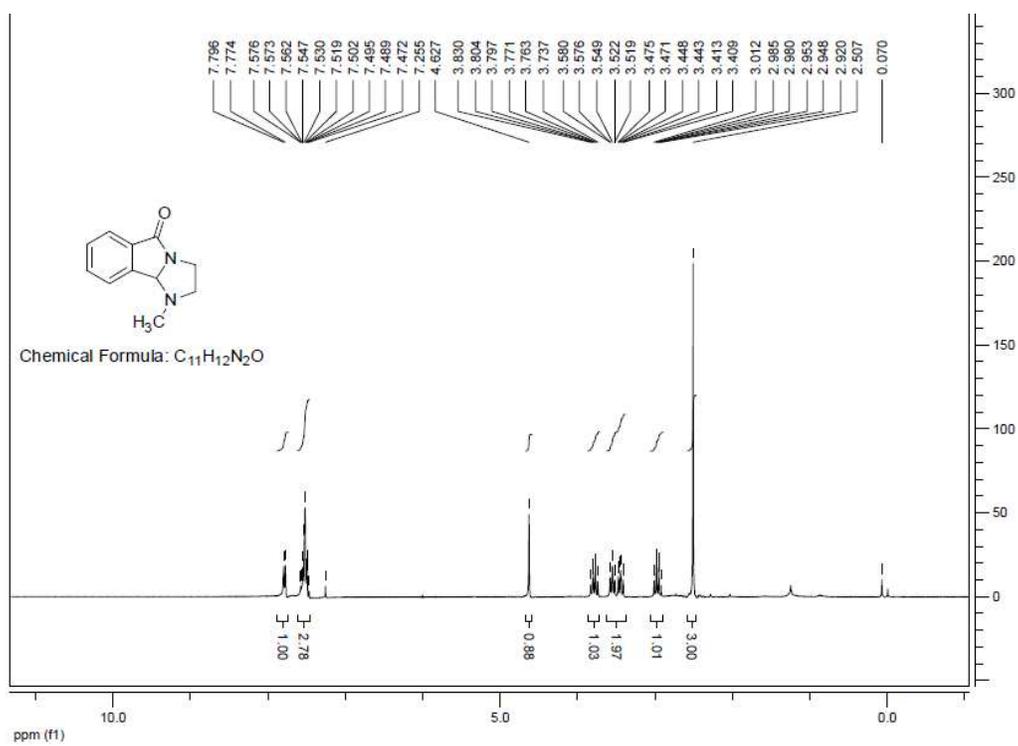




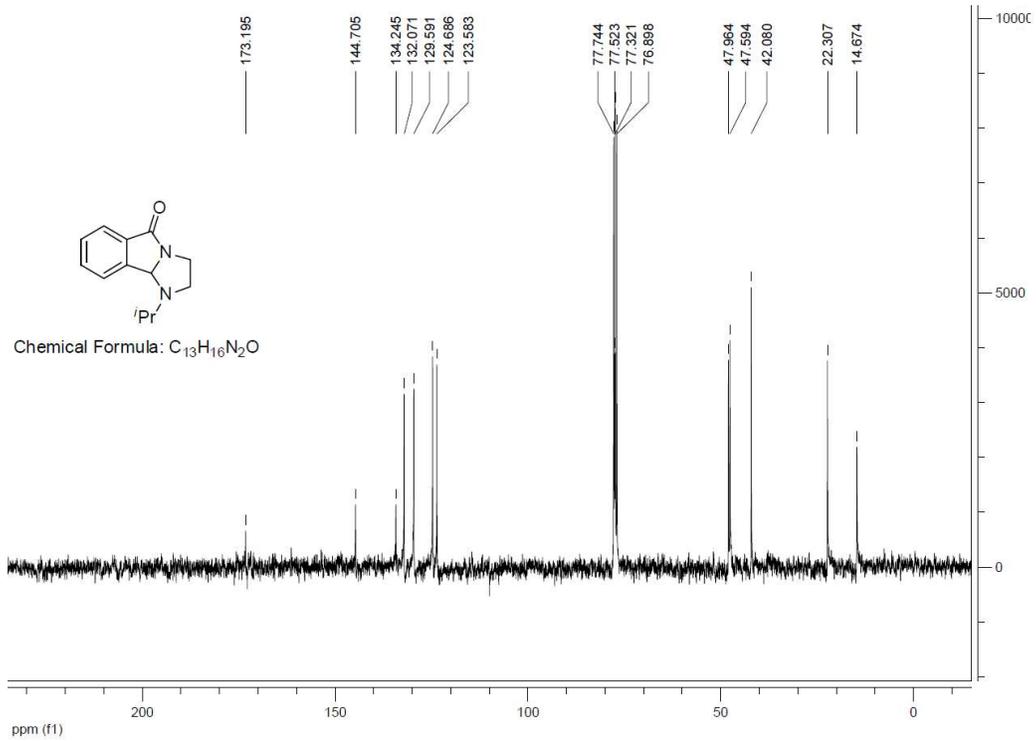
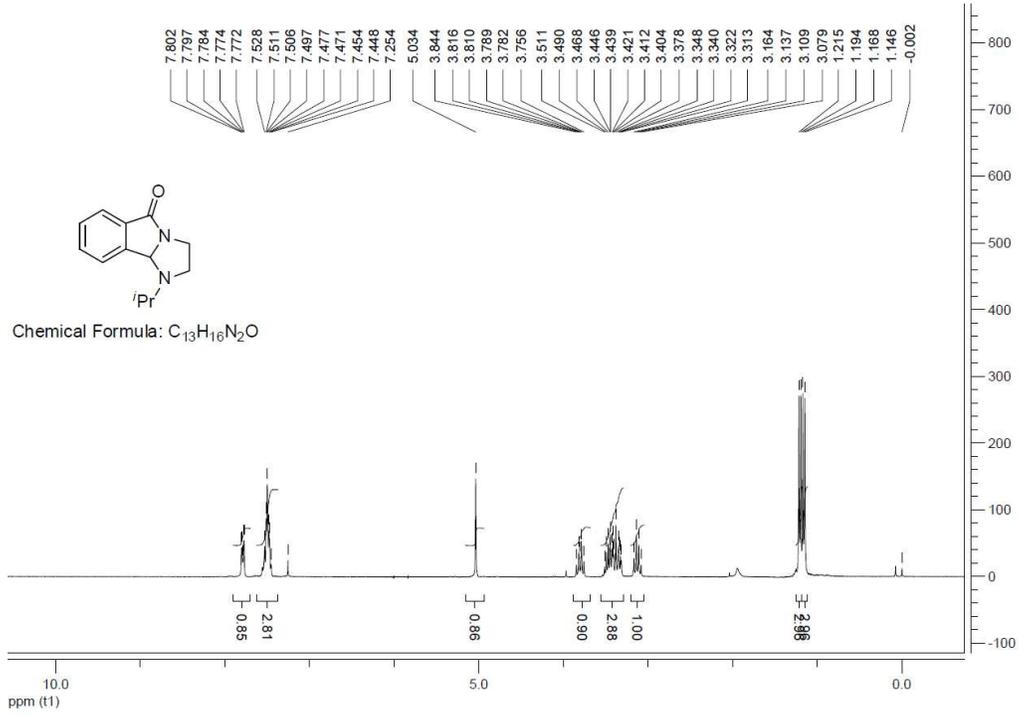
Product 3a



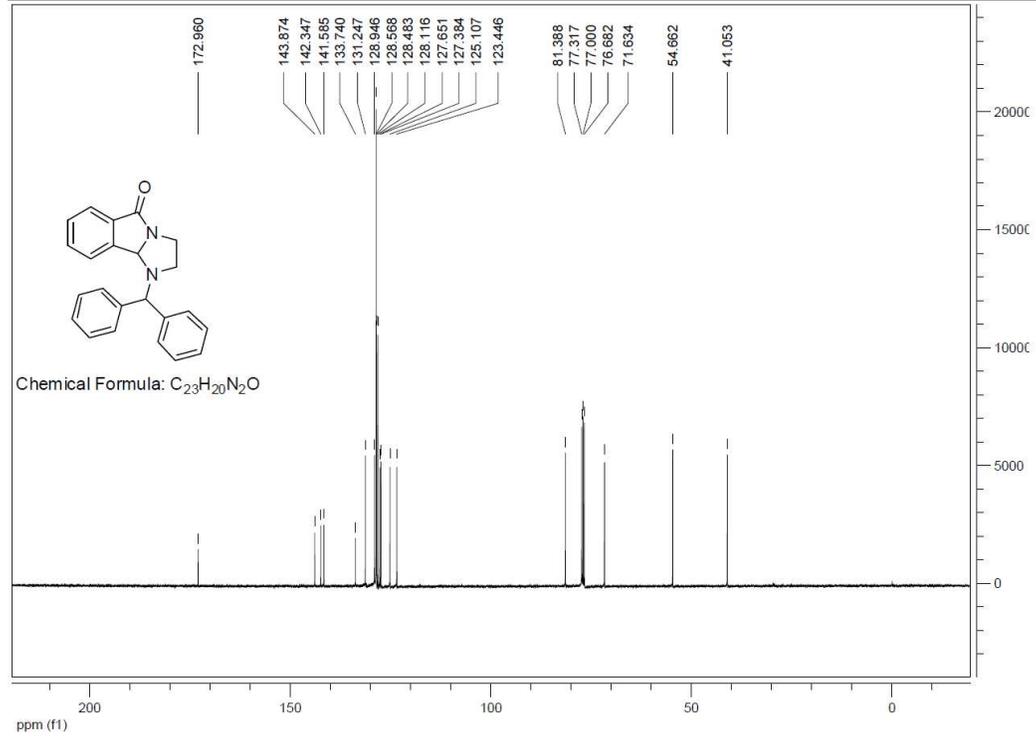
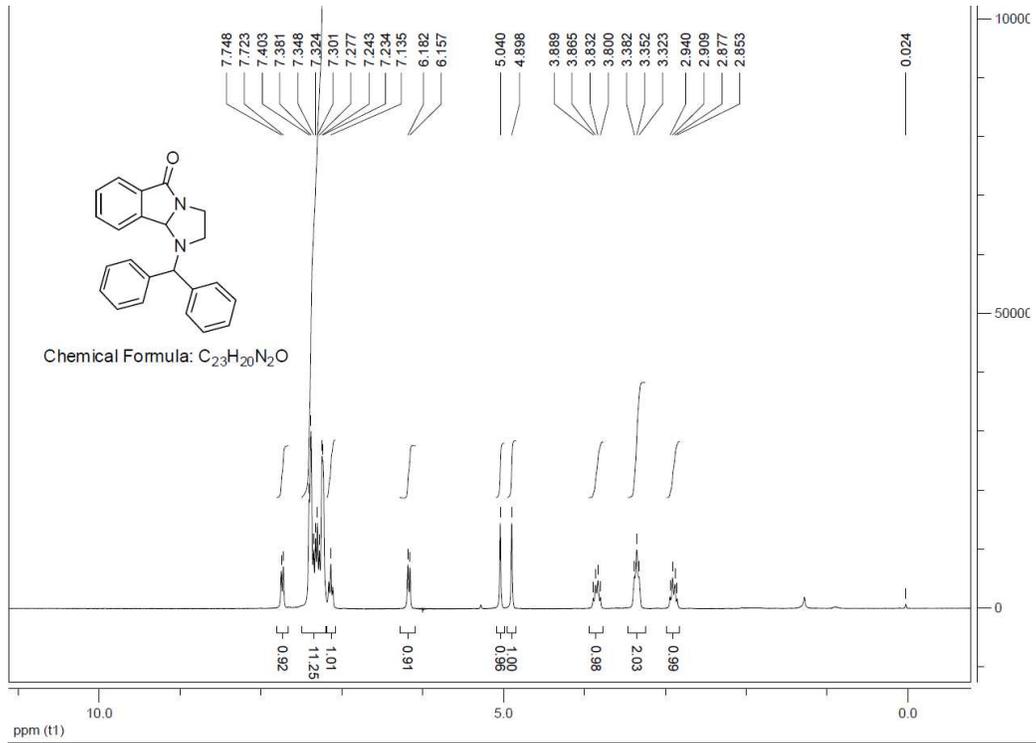
Product 3b



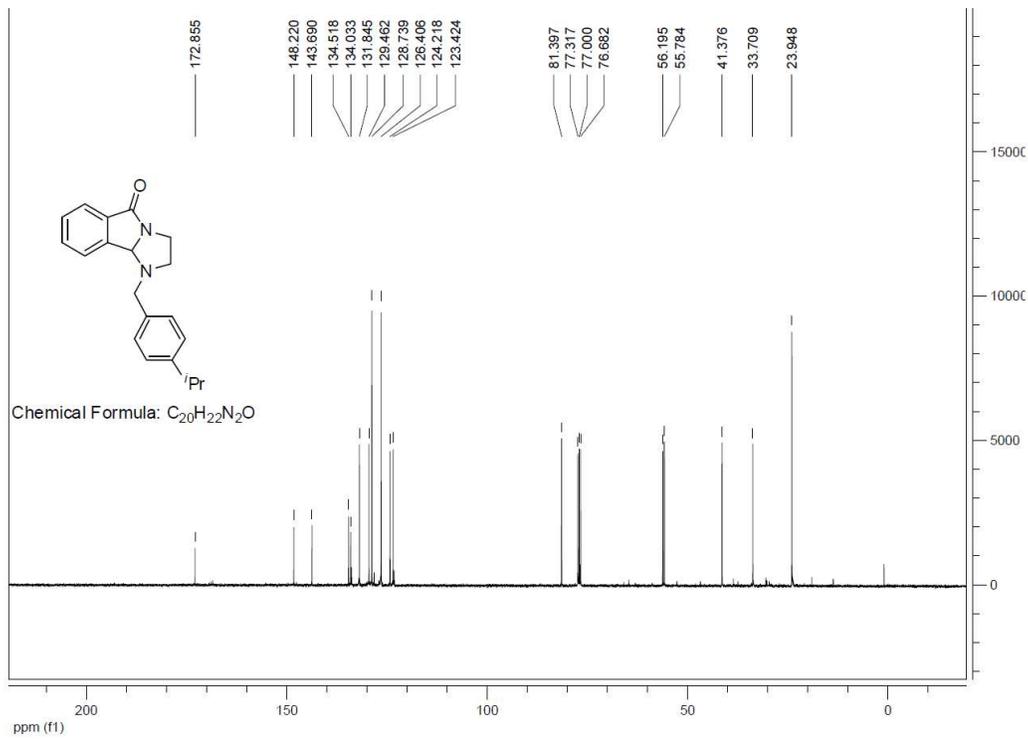
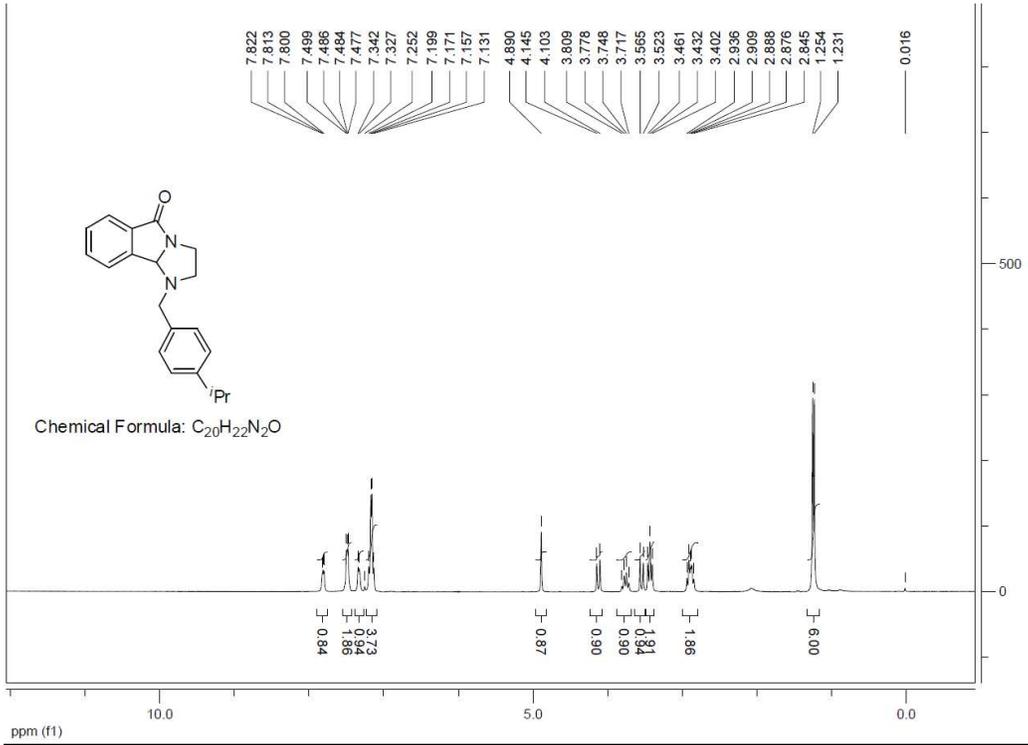
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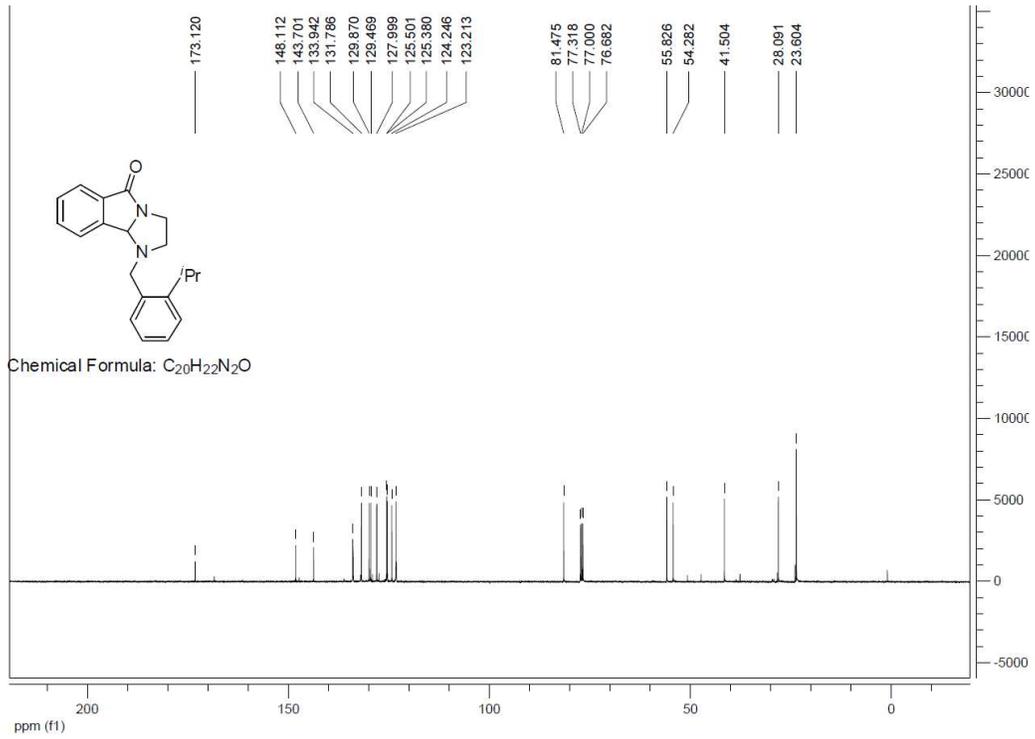
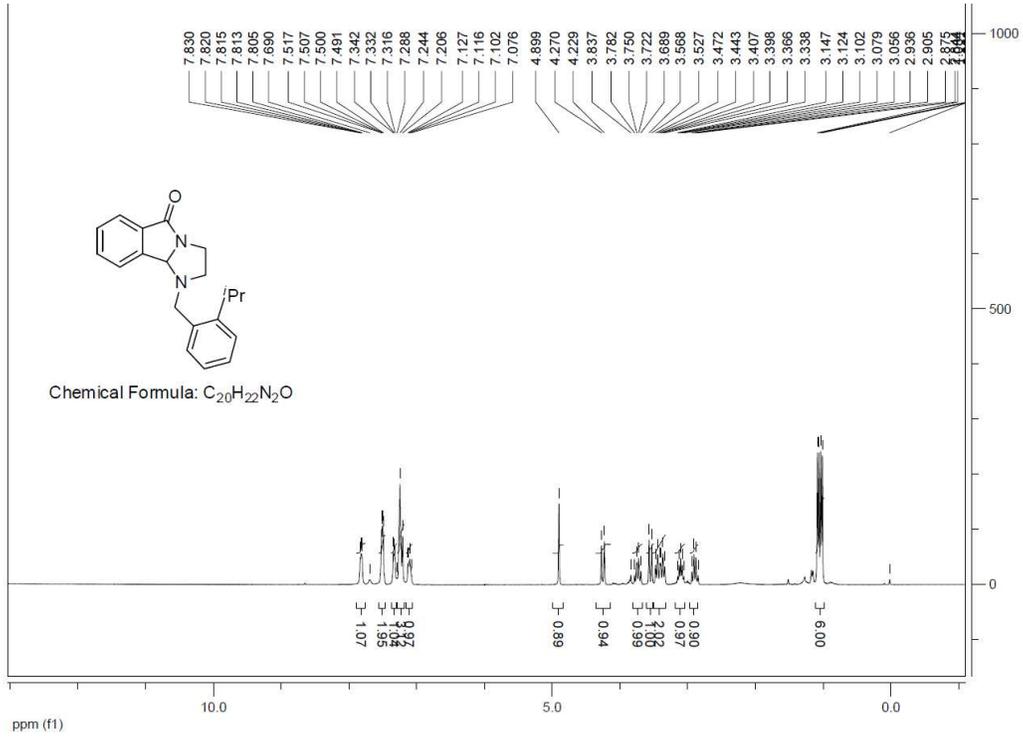
Product 3d



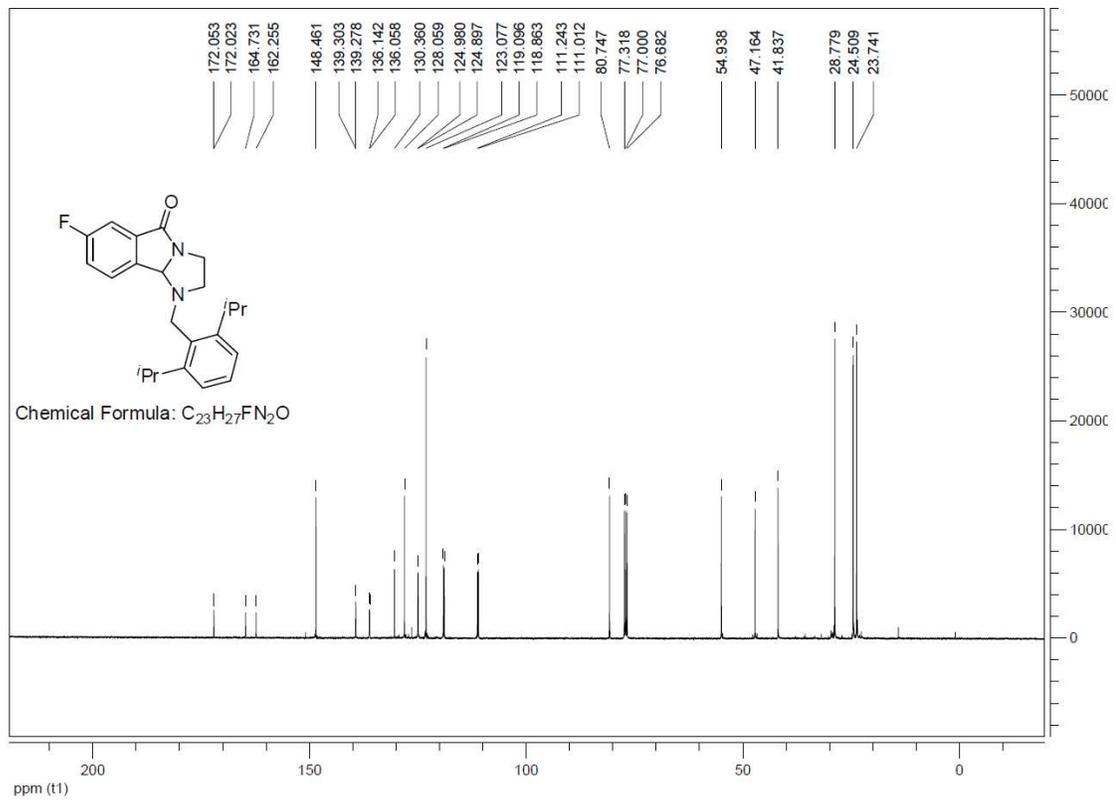
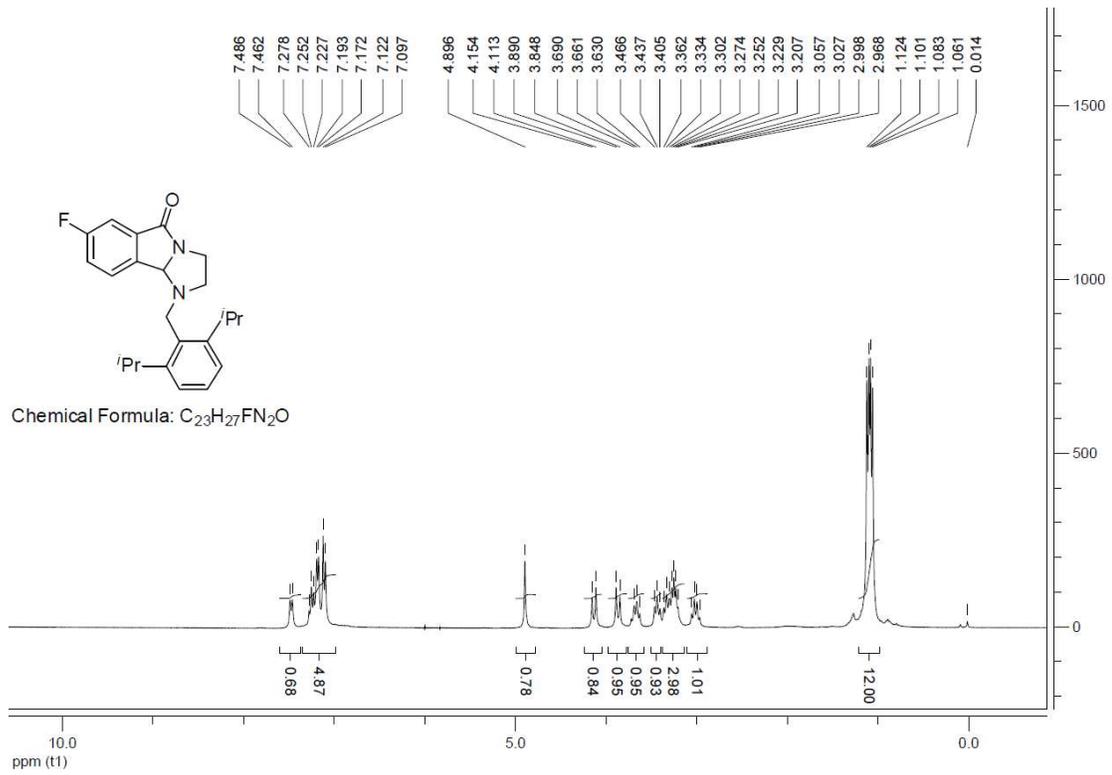
Product 3e



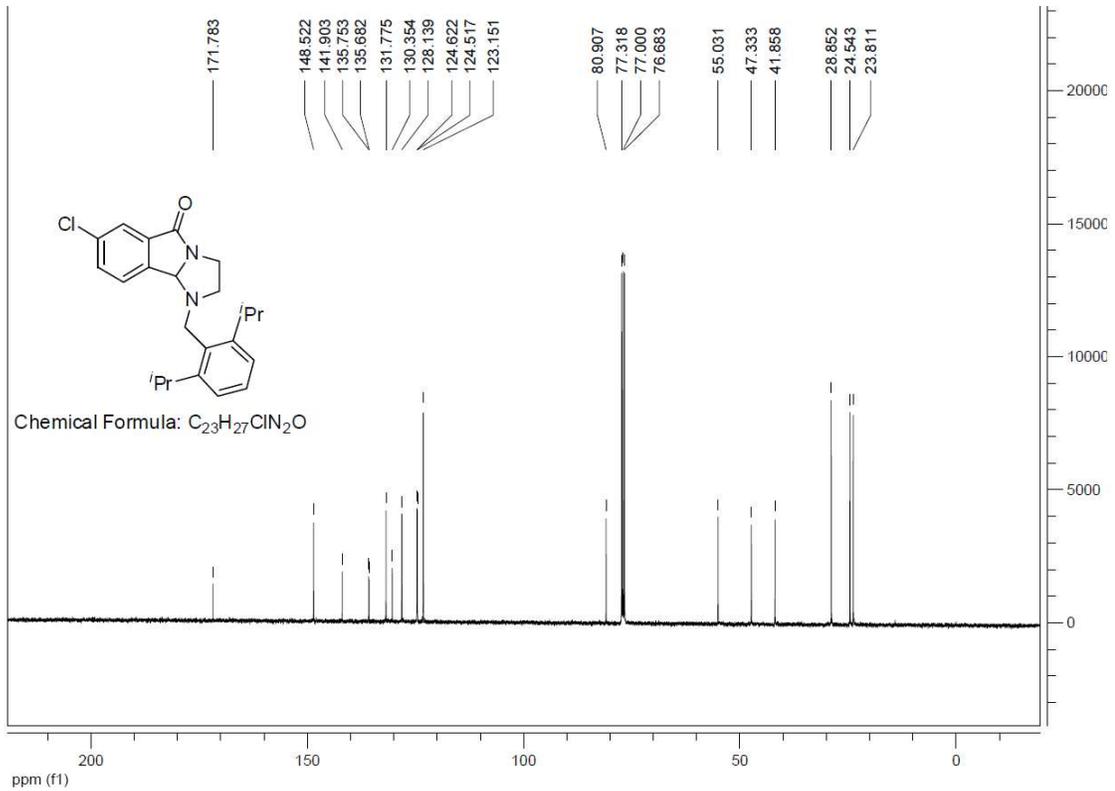
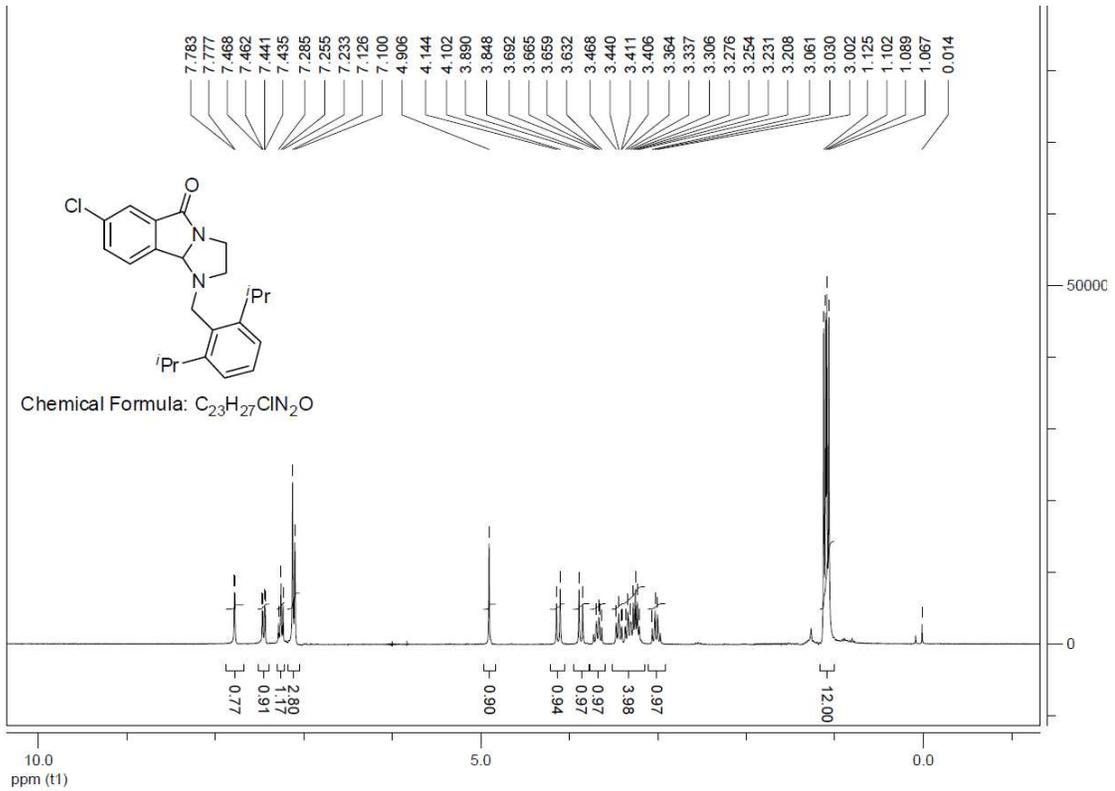
Product 3f



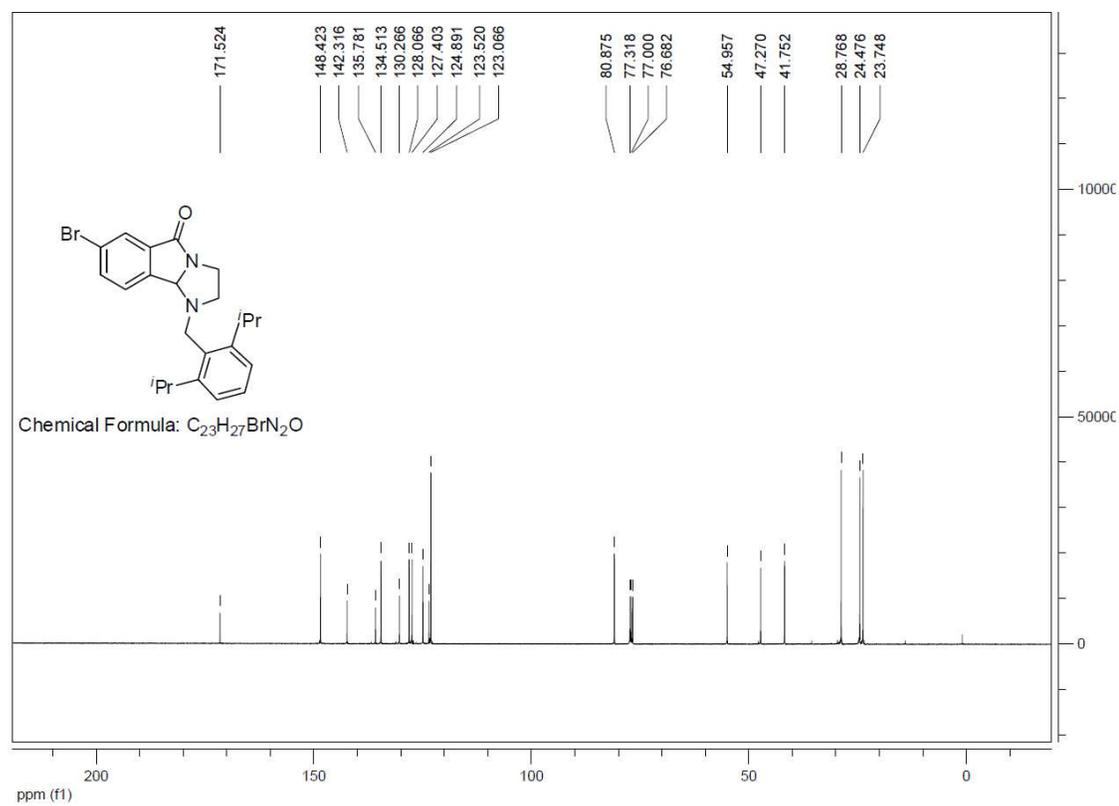
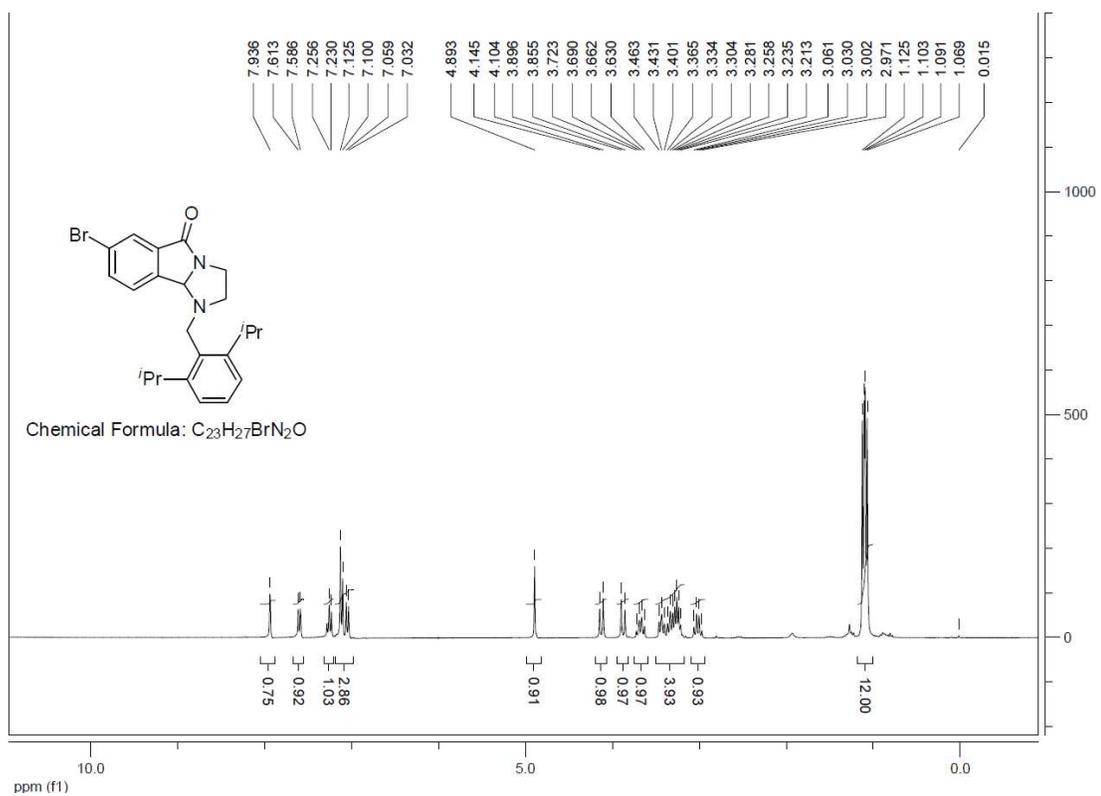
Product 3h



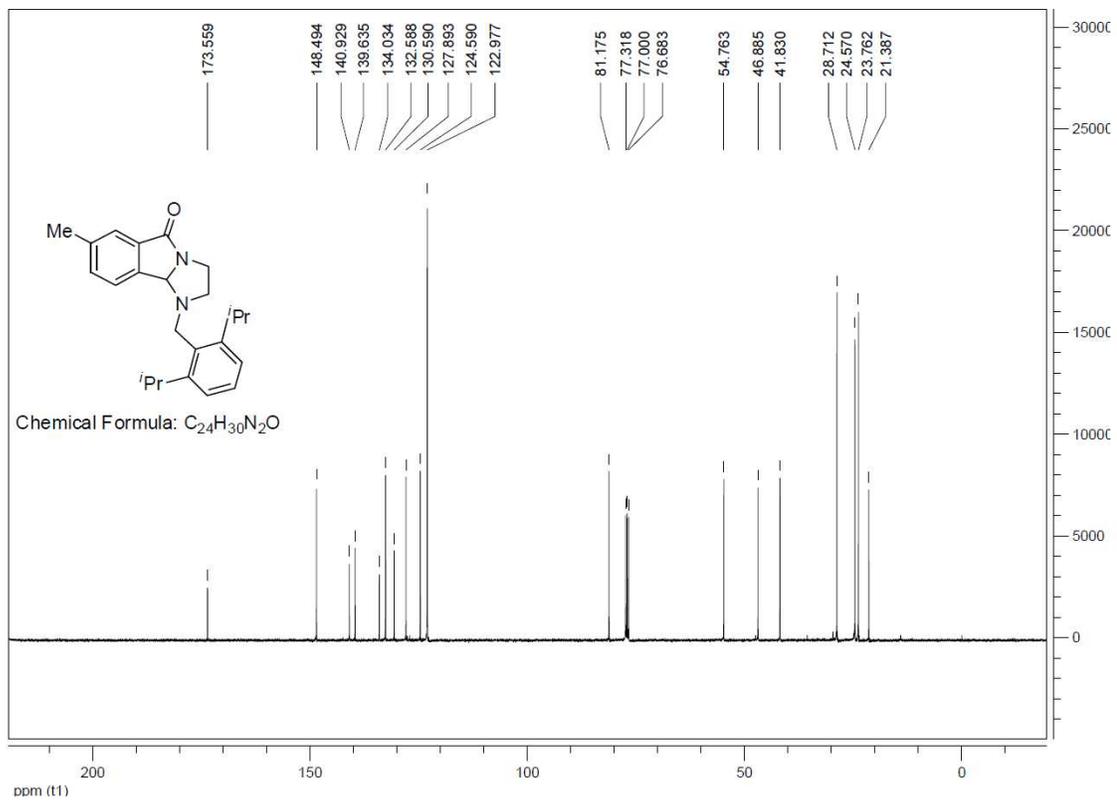
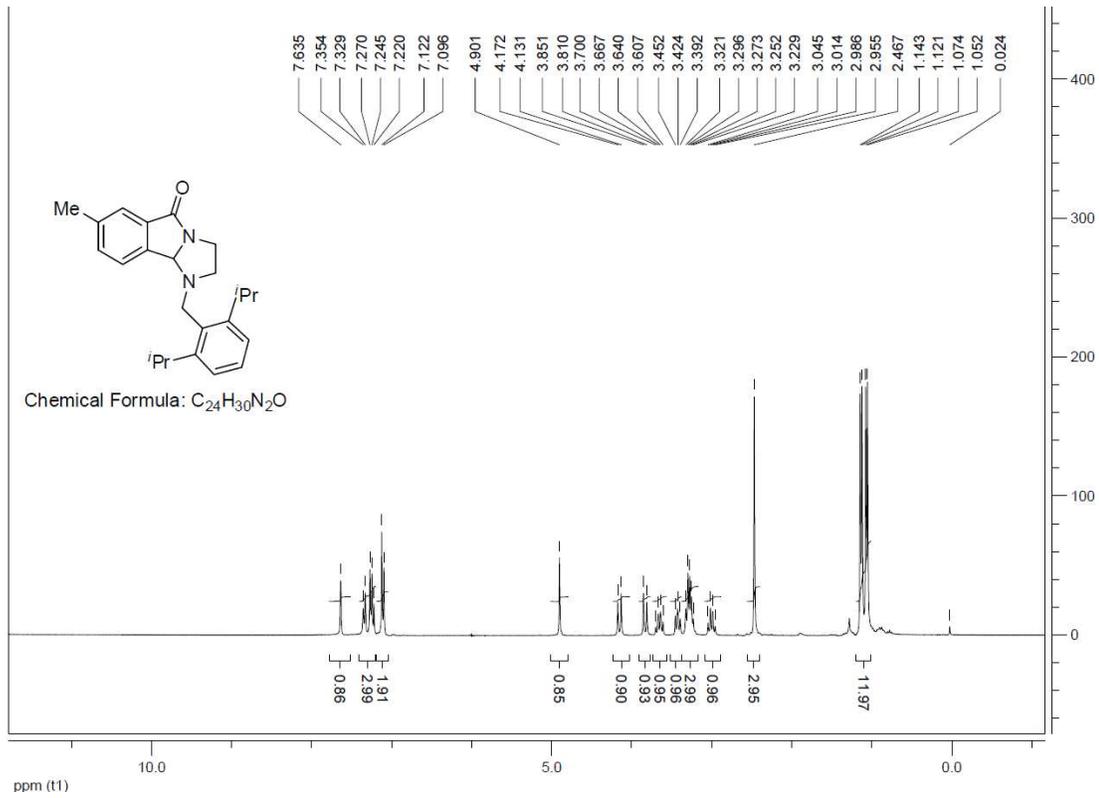
Product 3i



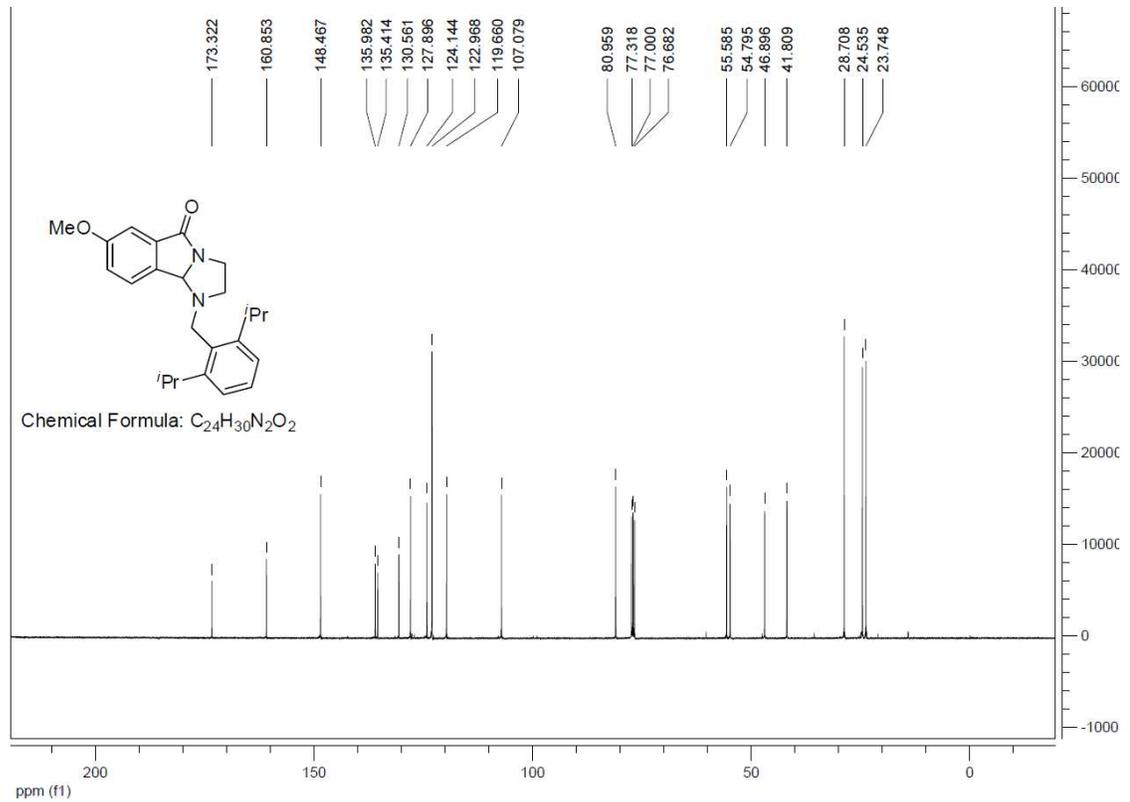
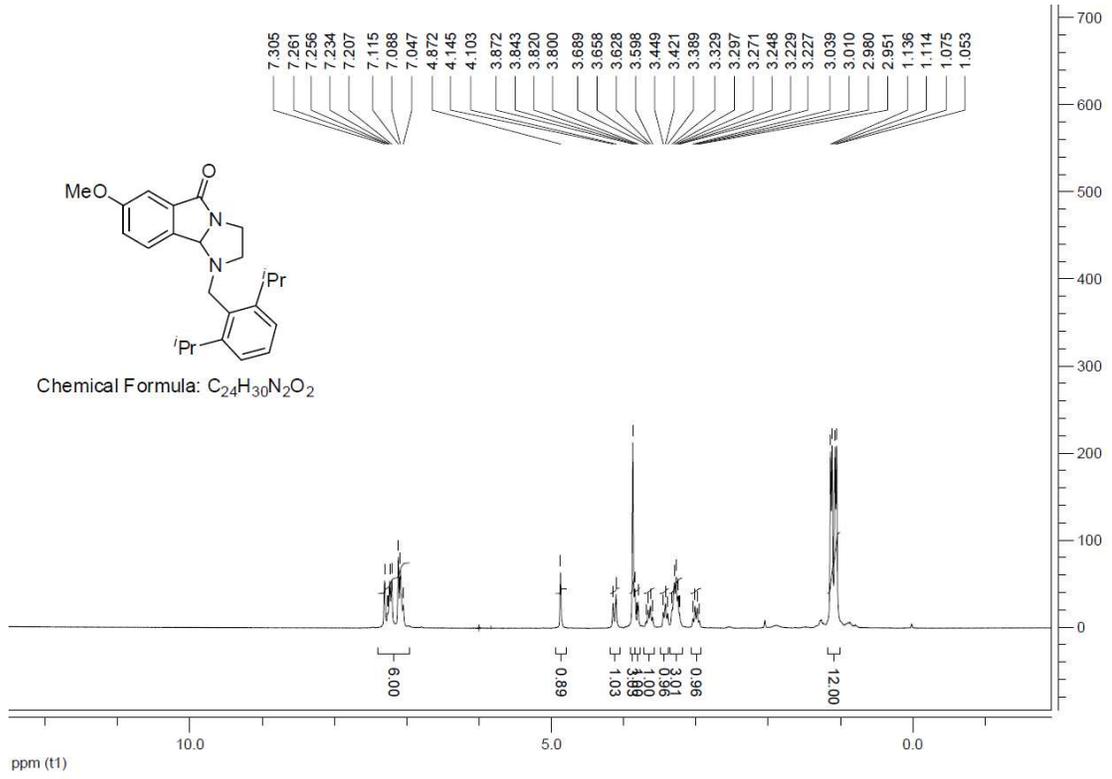
Product 3j



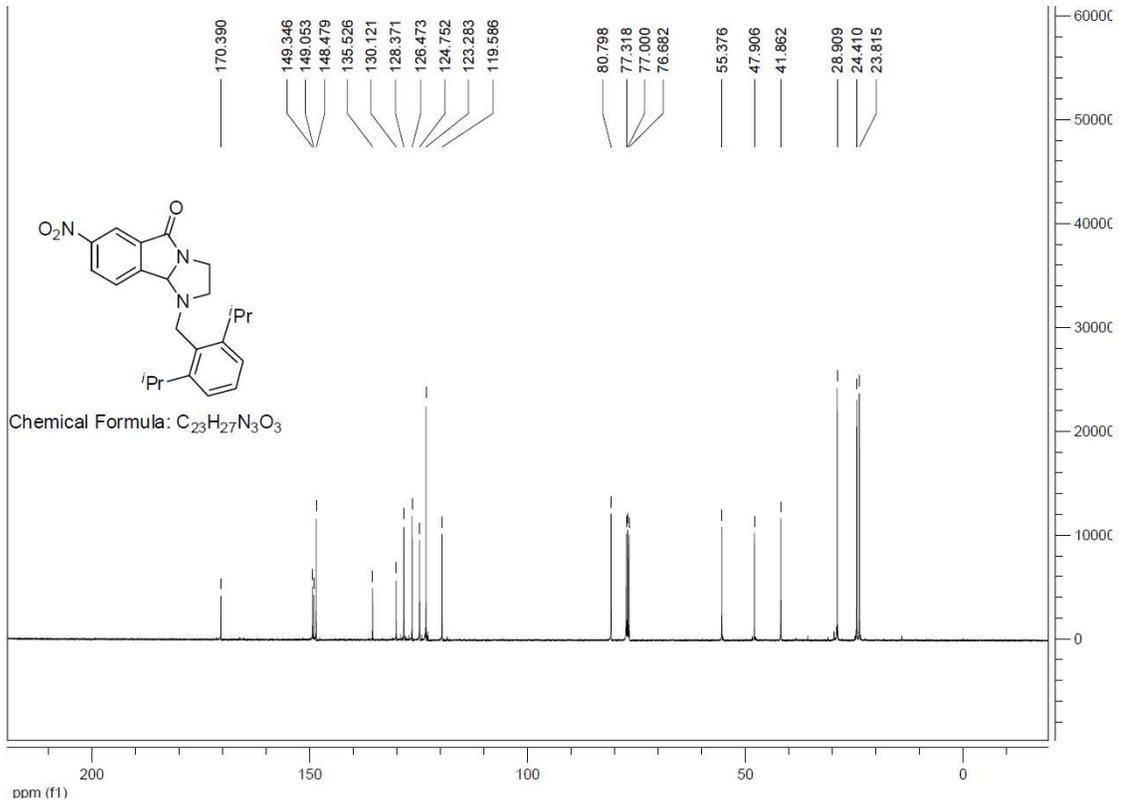
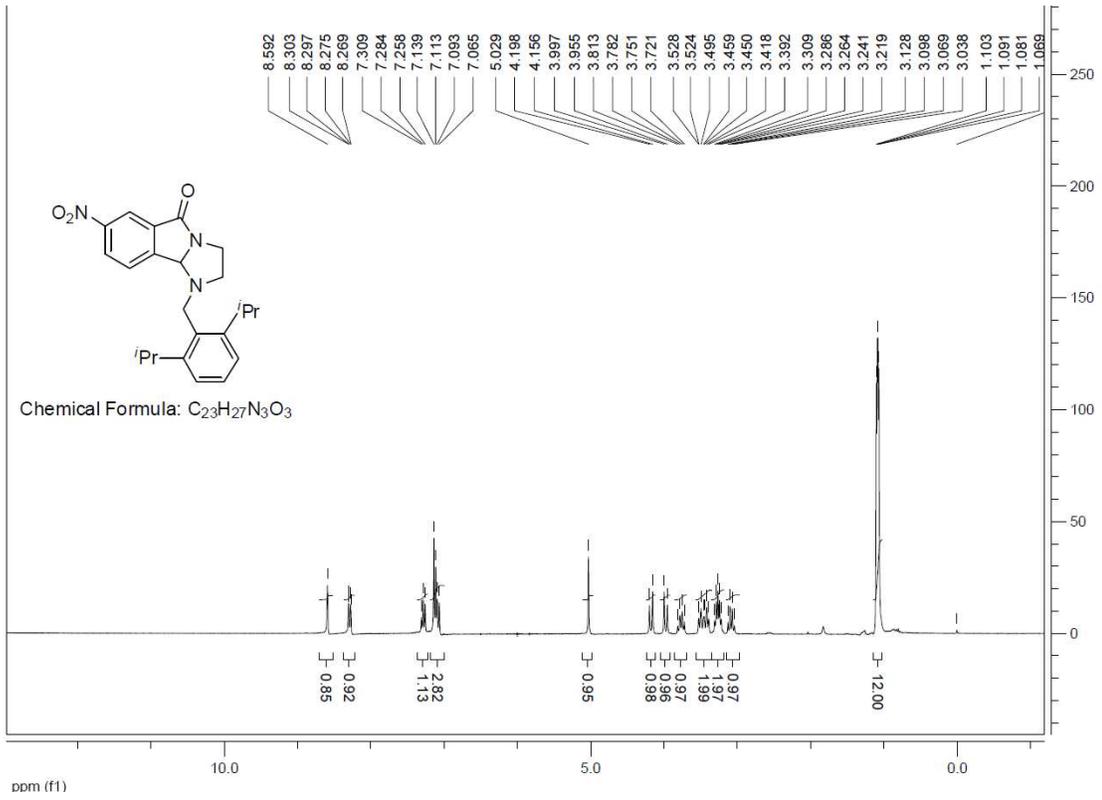
Product 3k



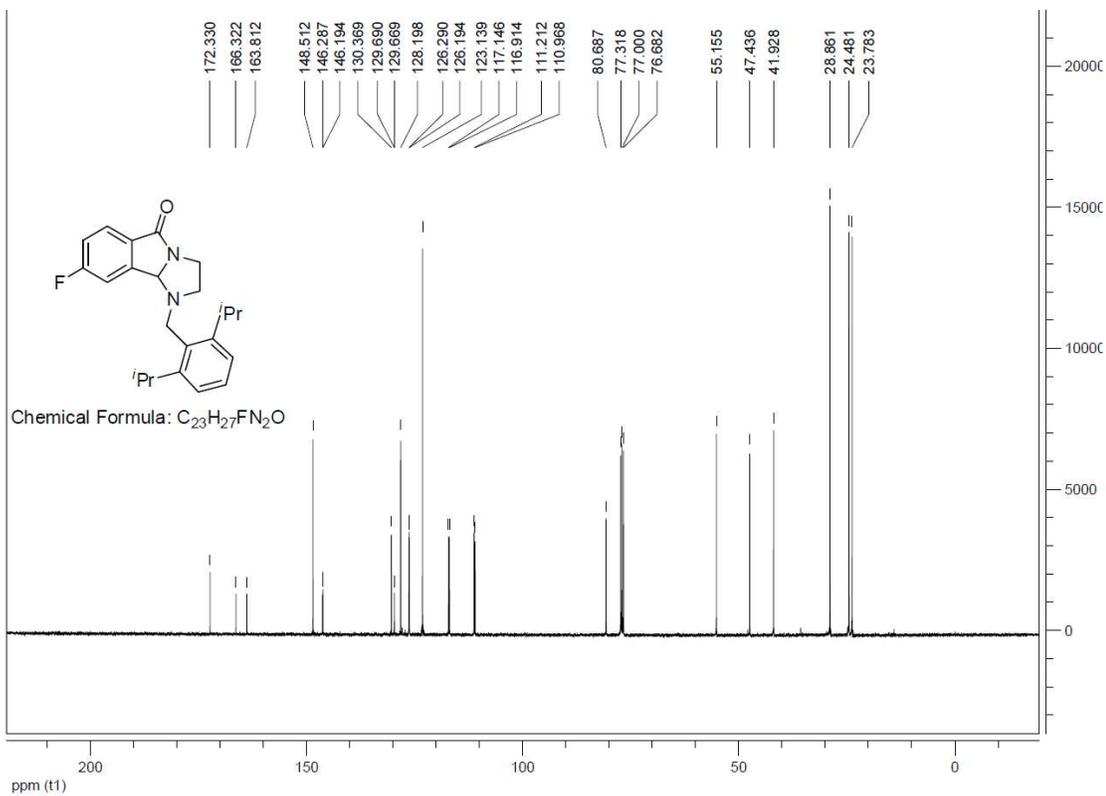
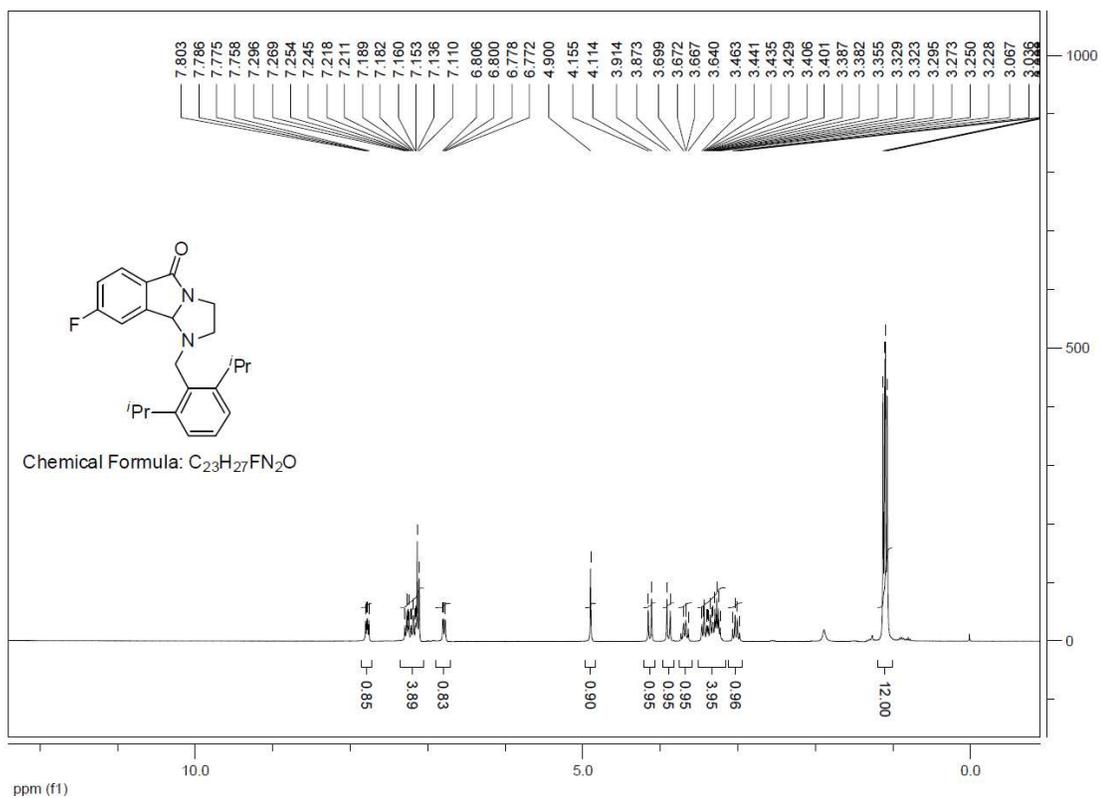
Product 31



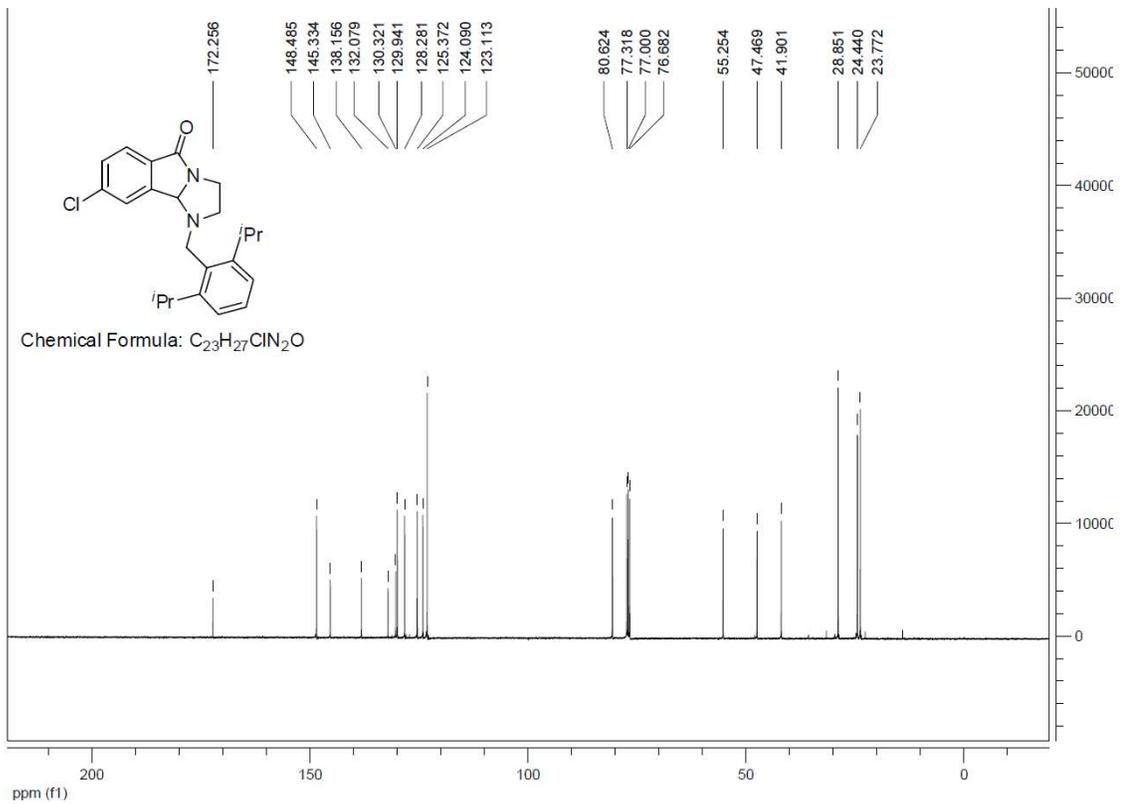
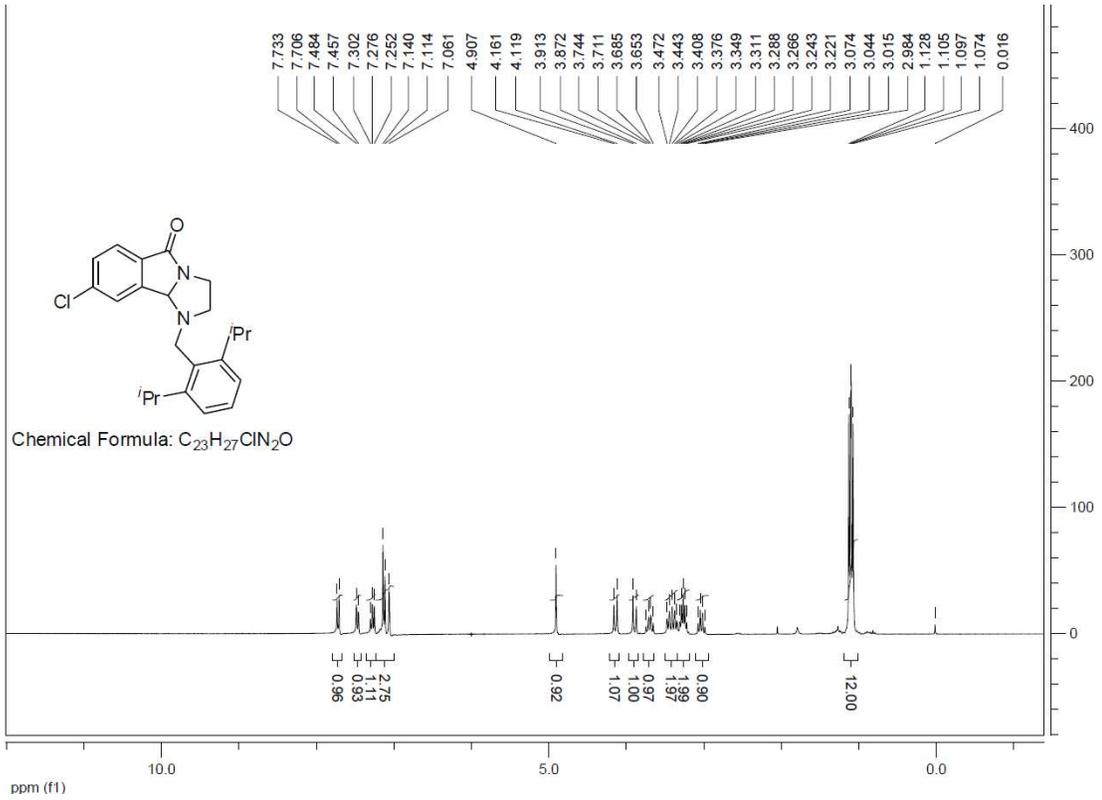
Product 3m



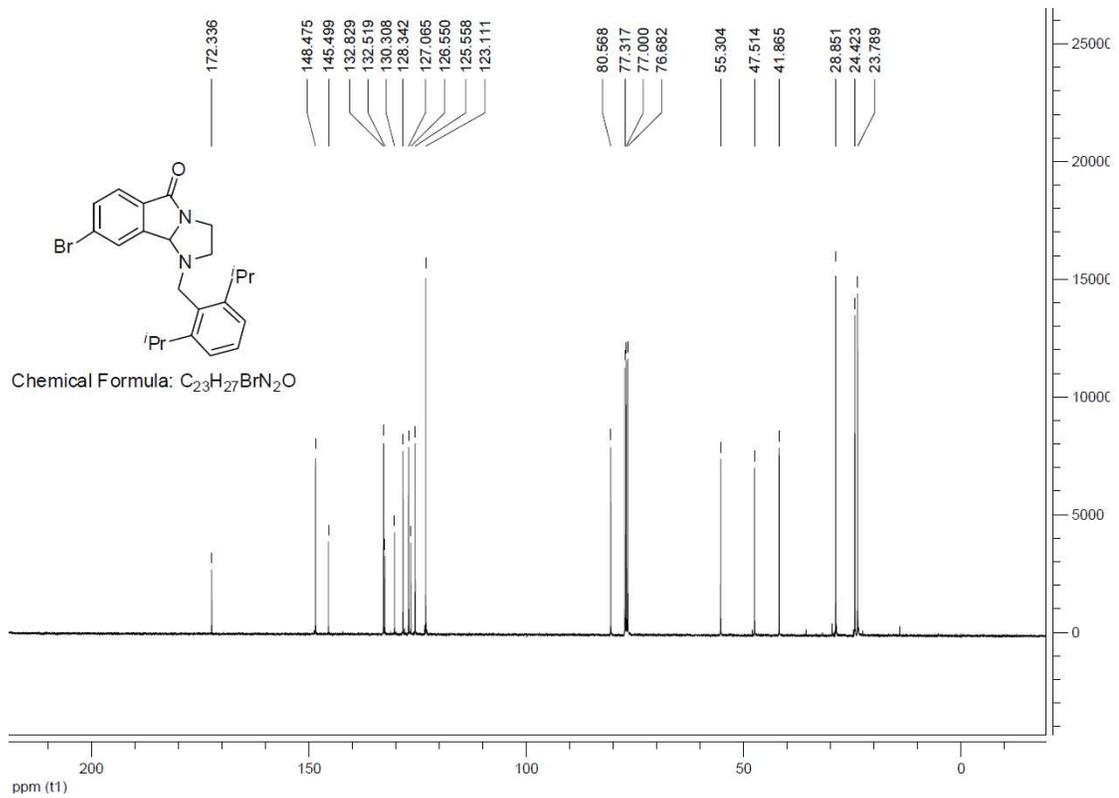
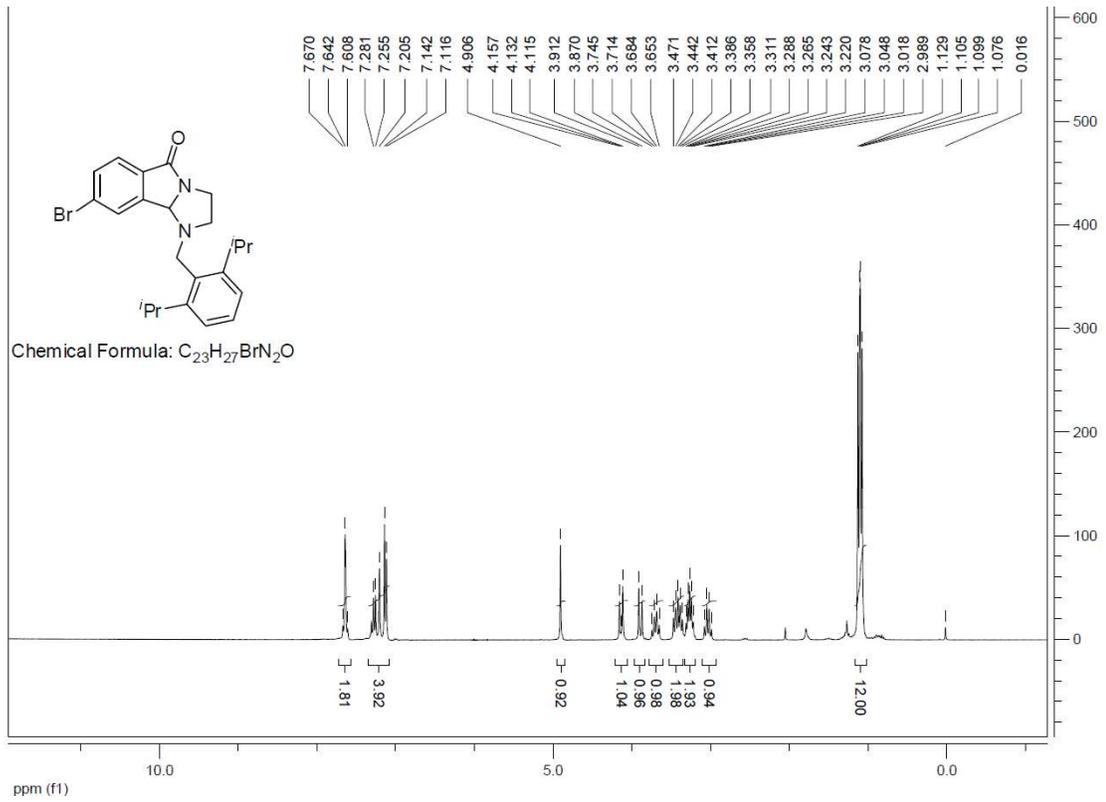
Product 3n



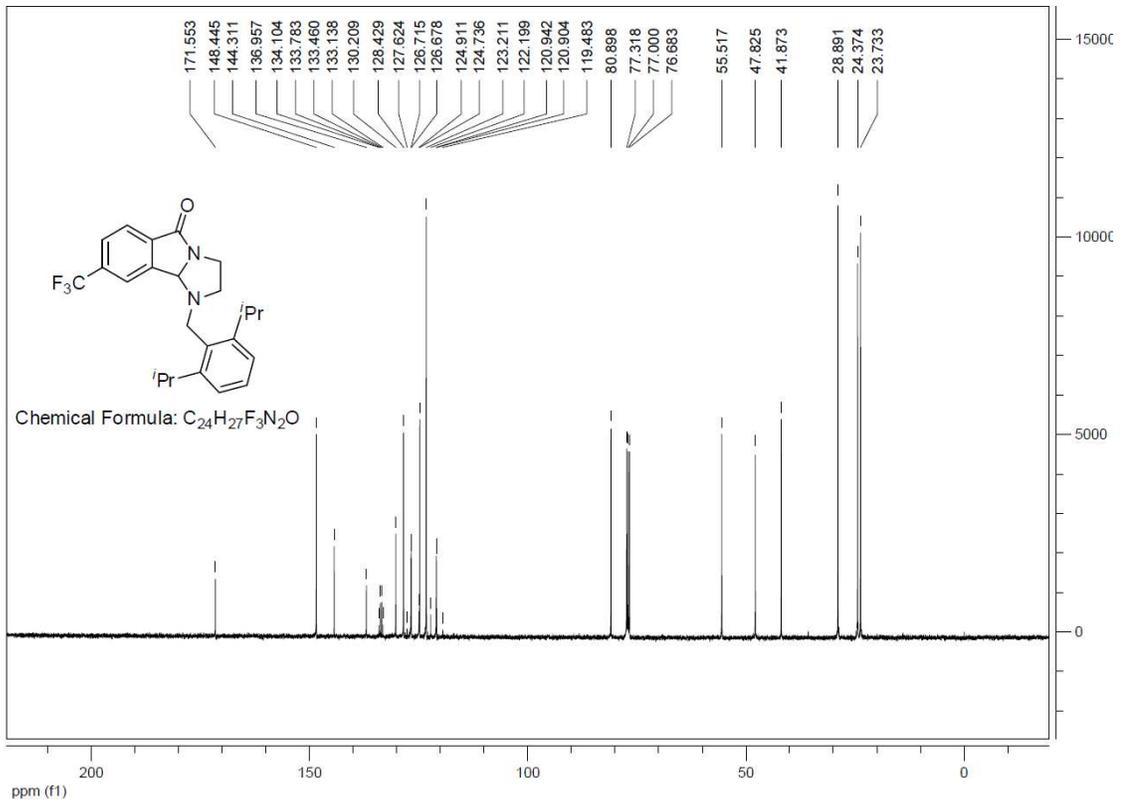
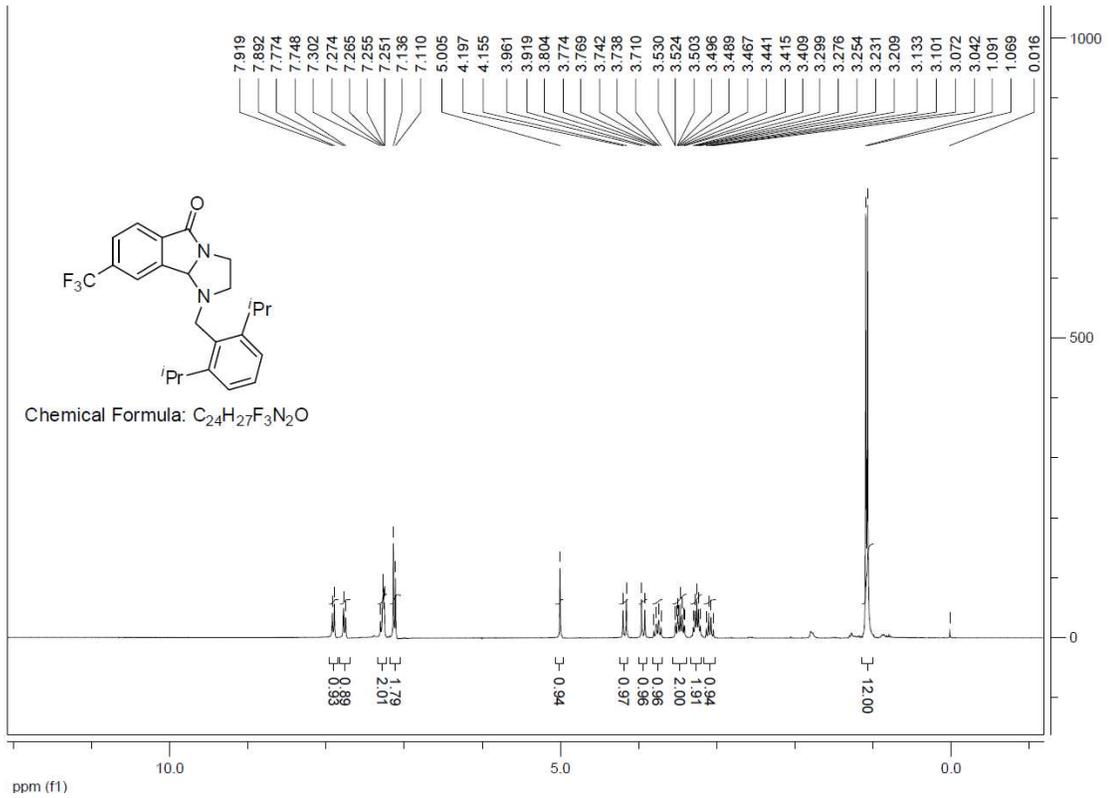
Product 3o



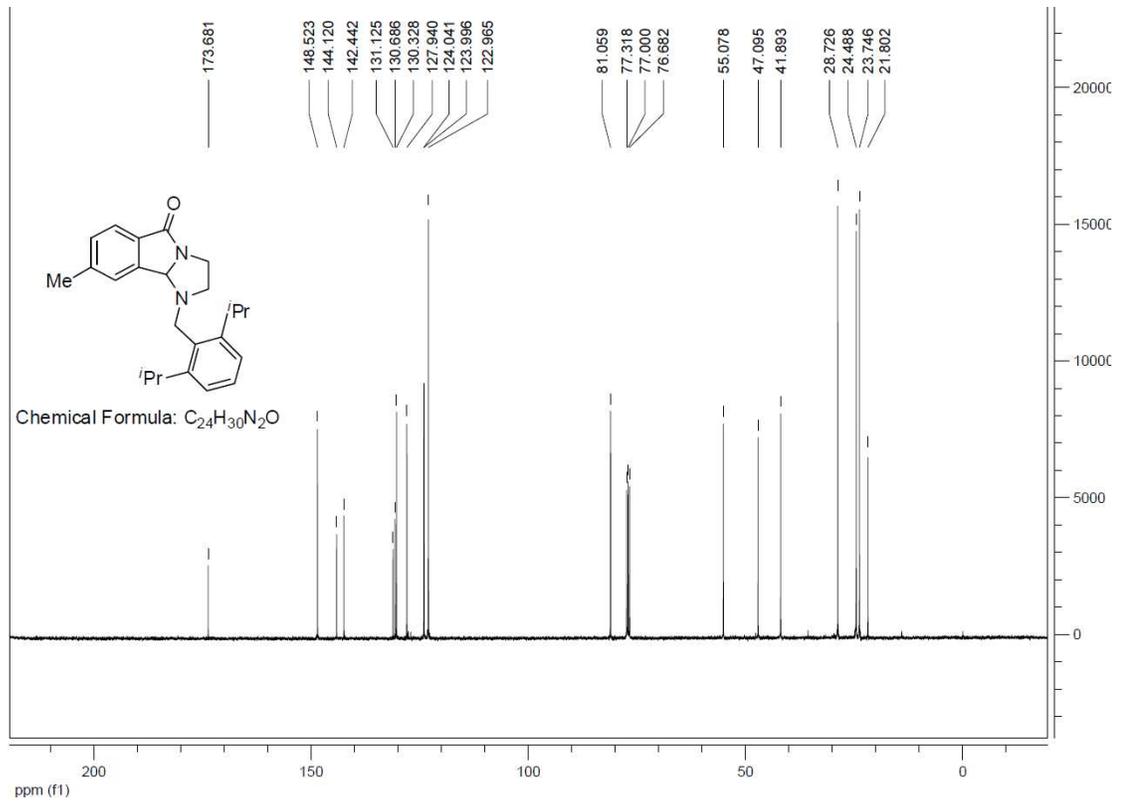
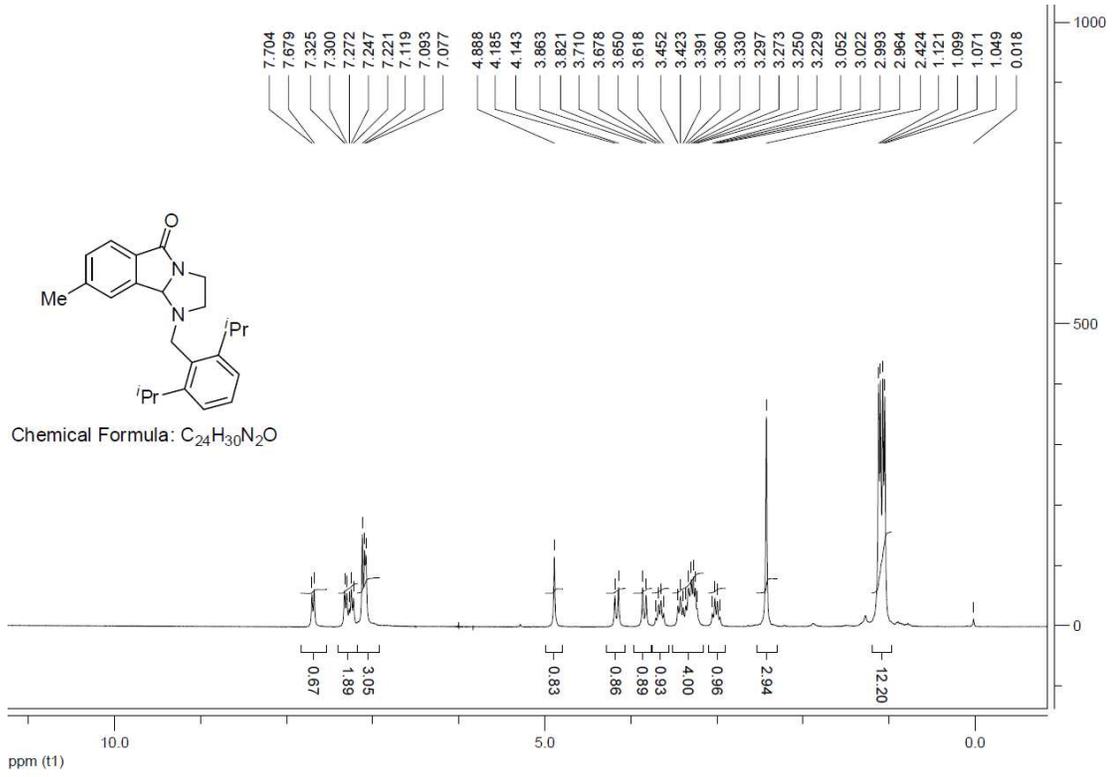
Product 3p



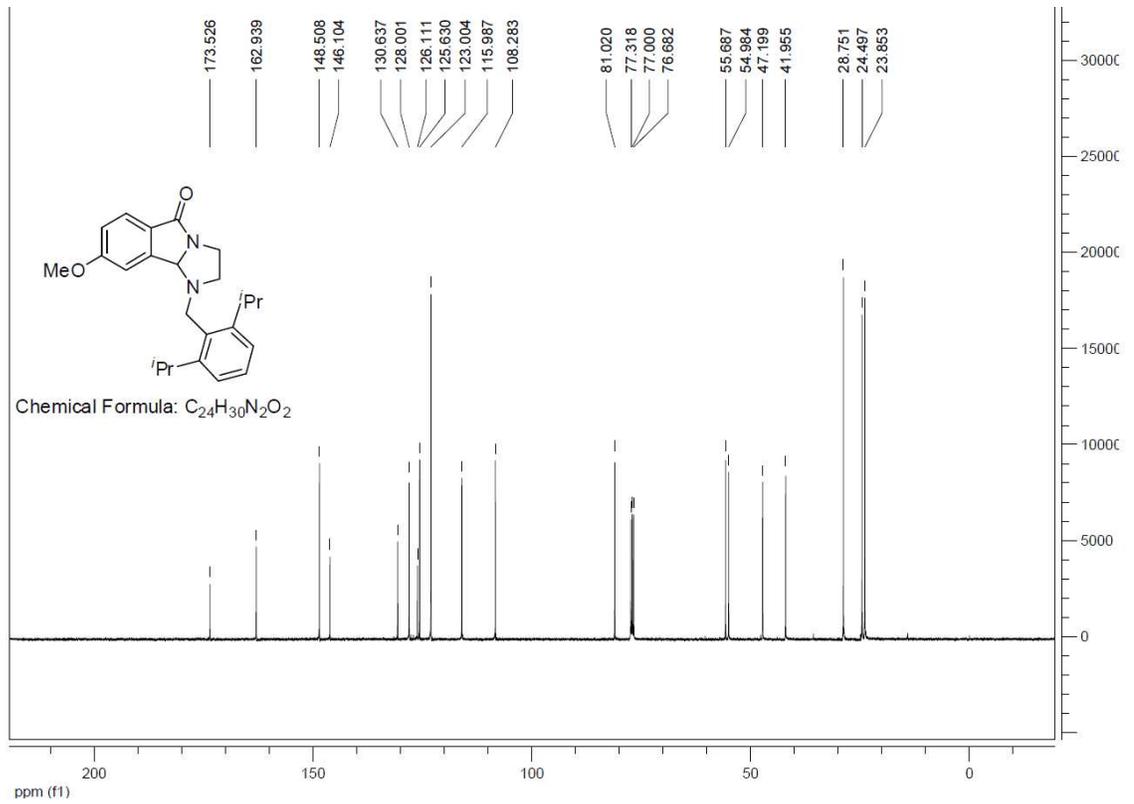
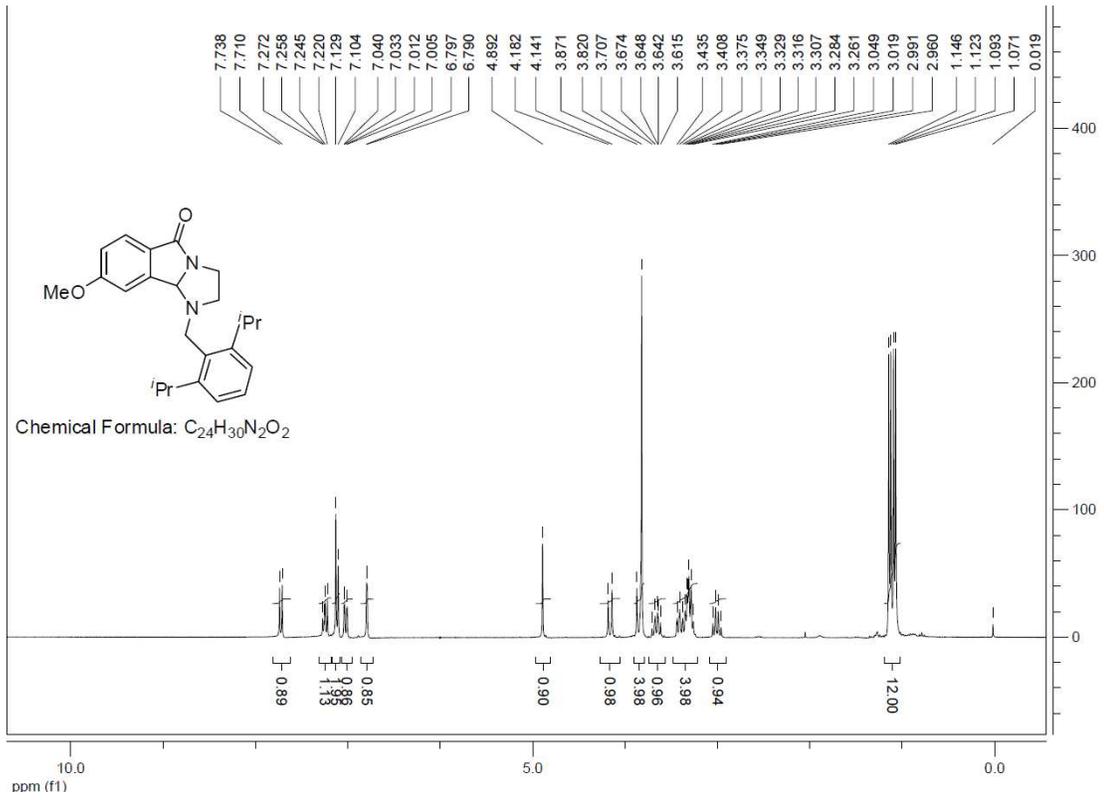
Product 3q



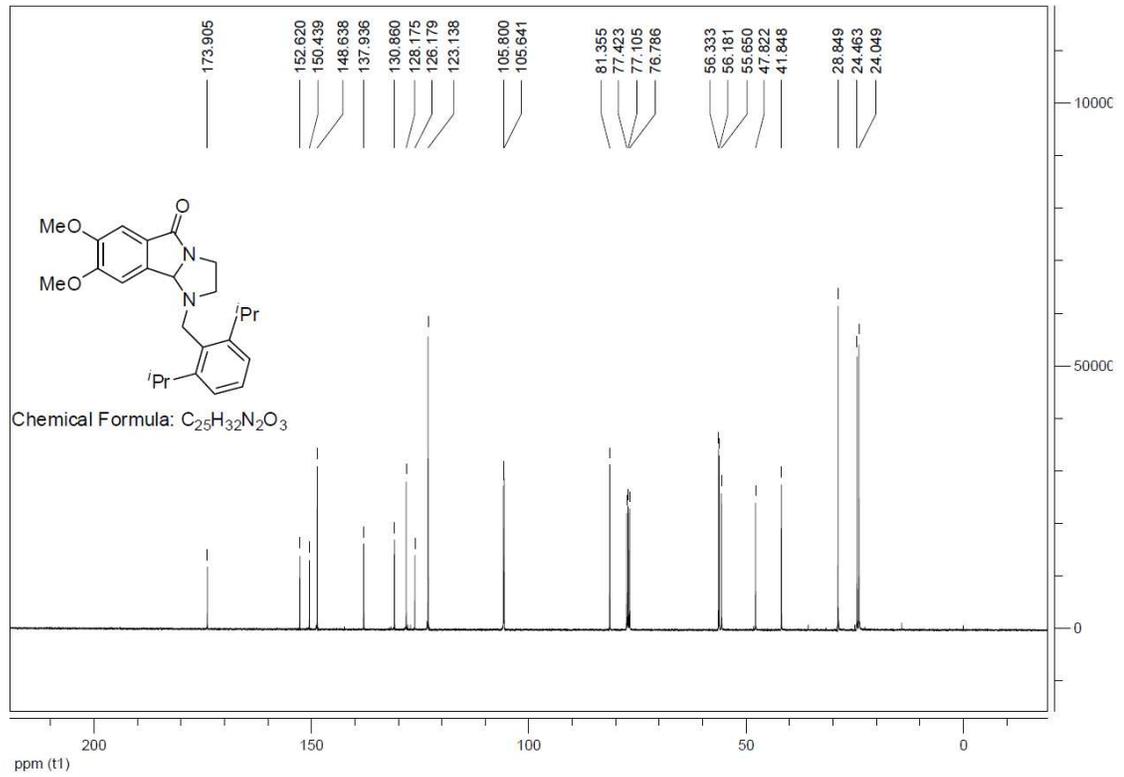
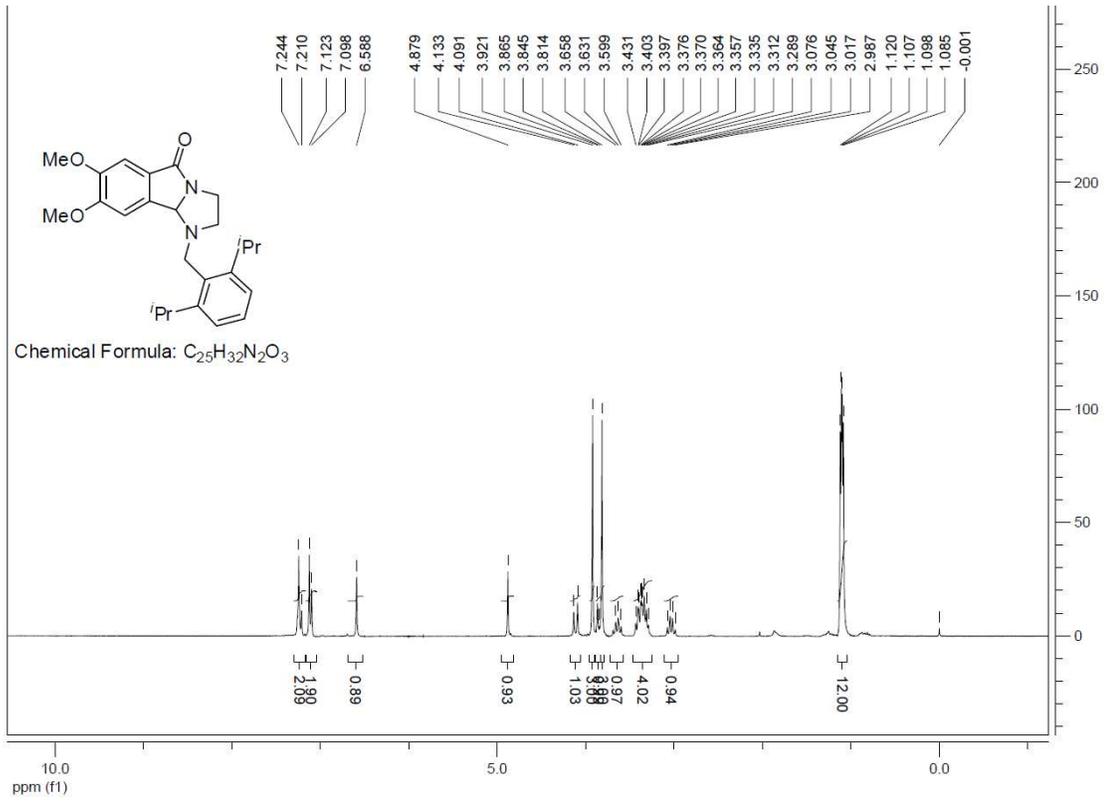
Product 3r



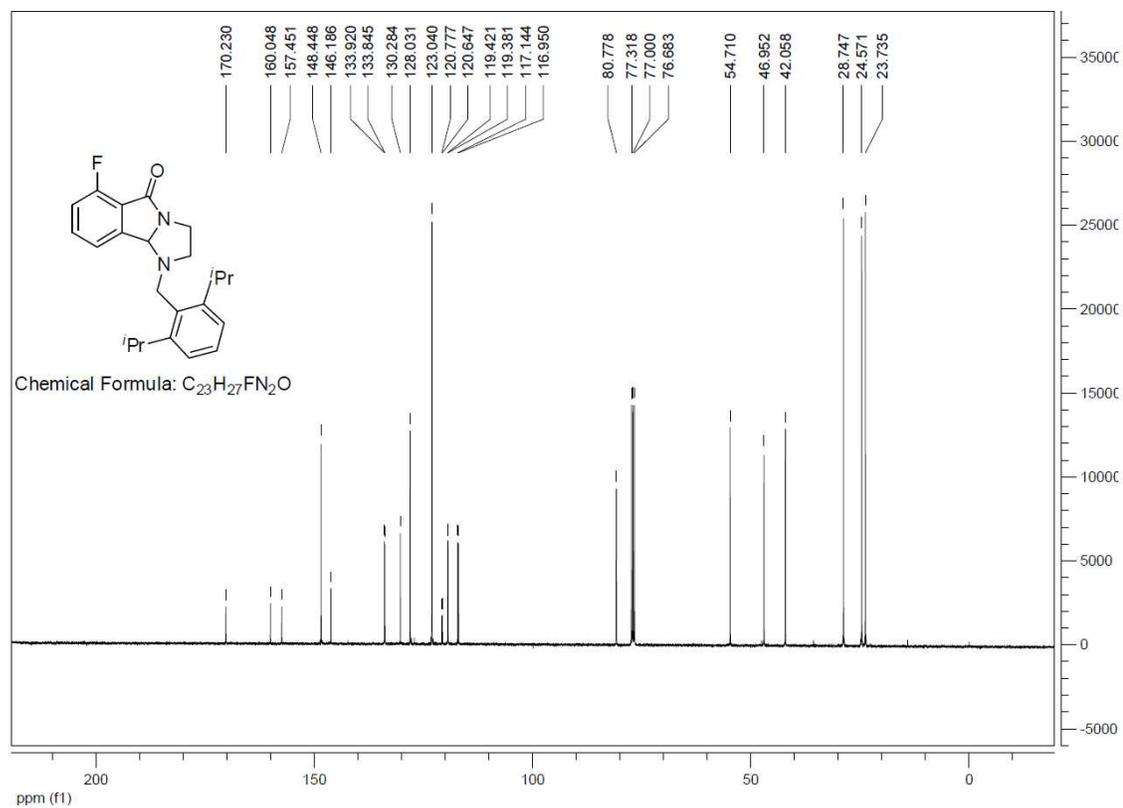
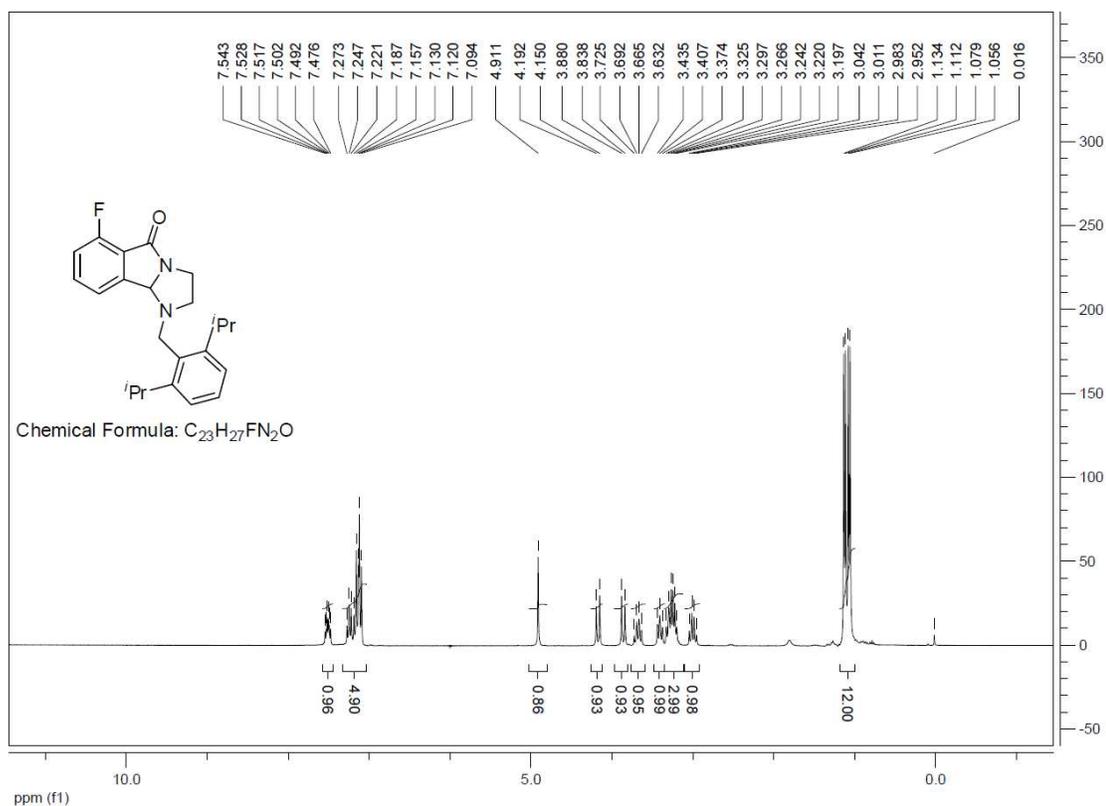
Product 3s



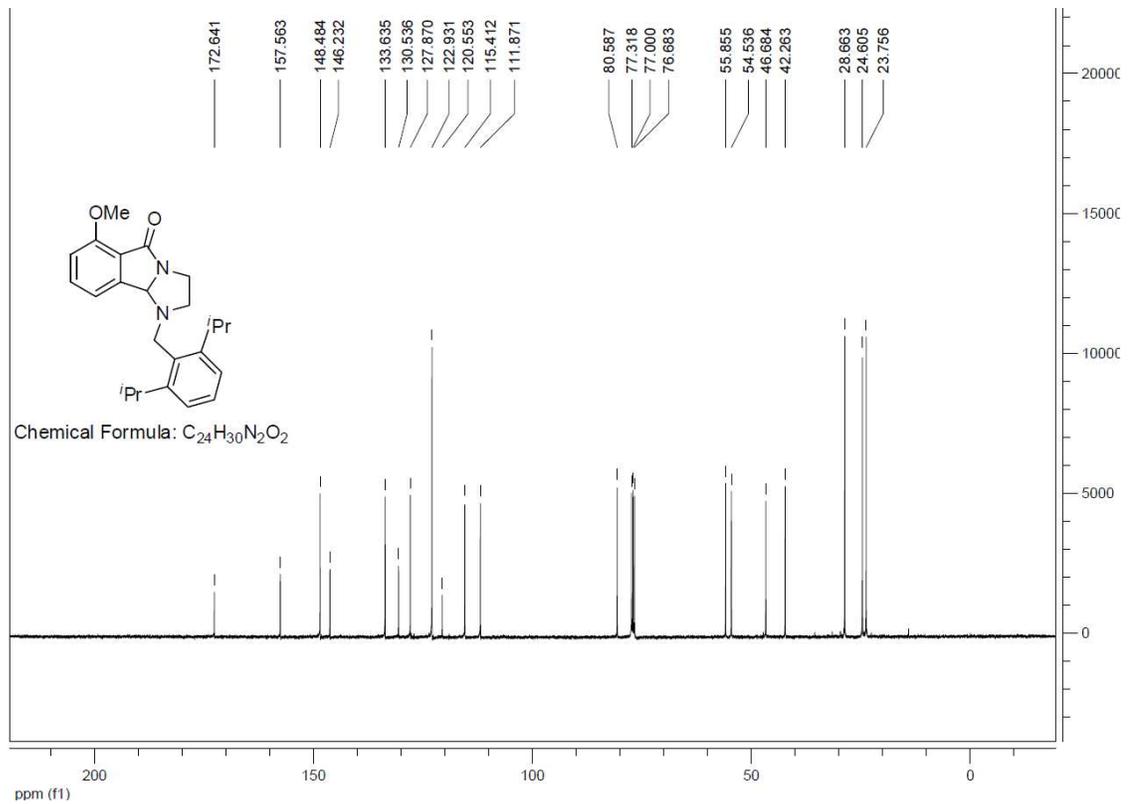
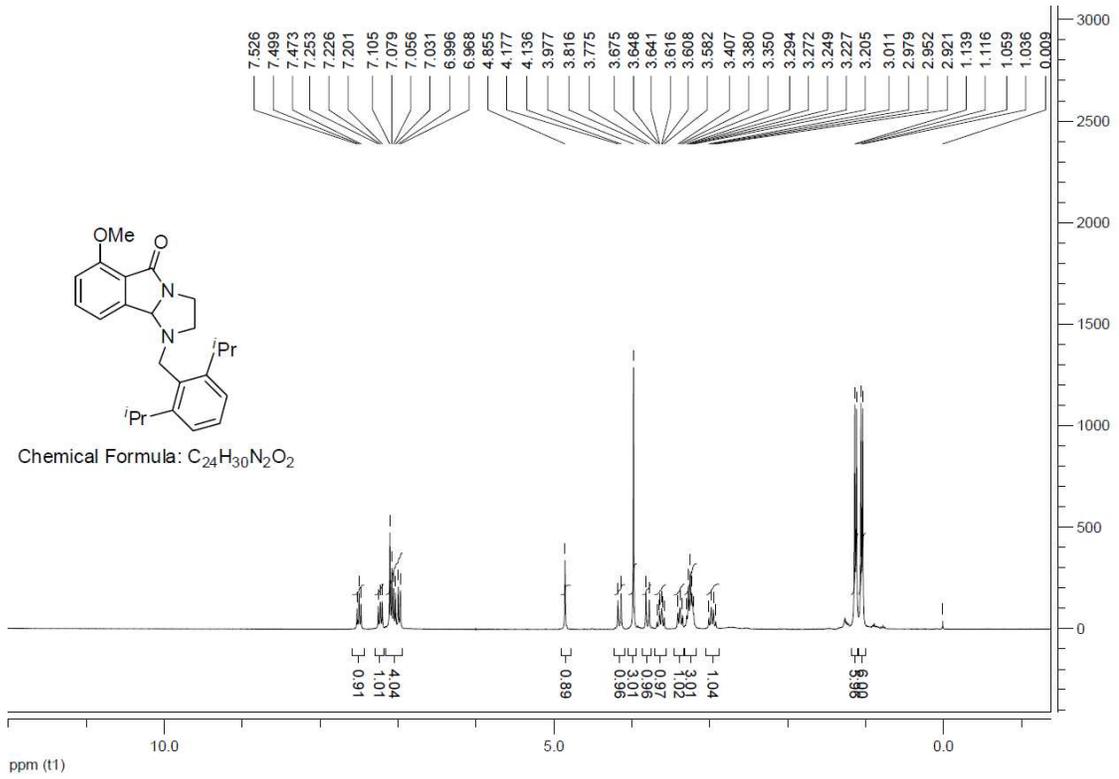
Product 3t



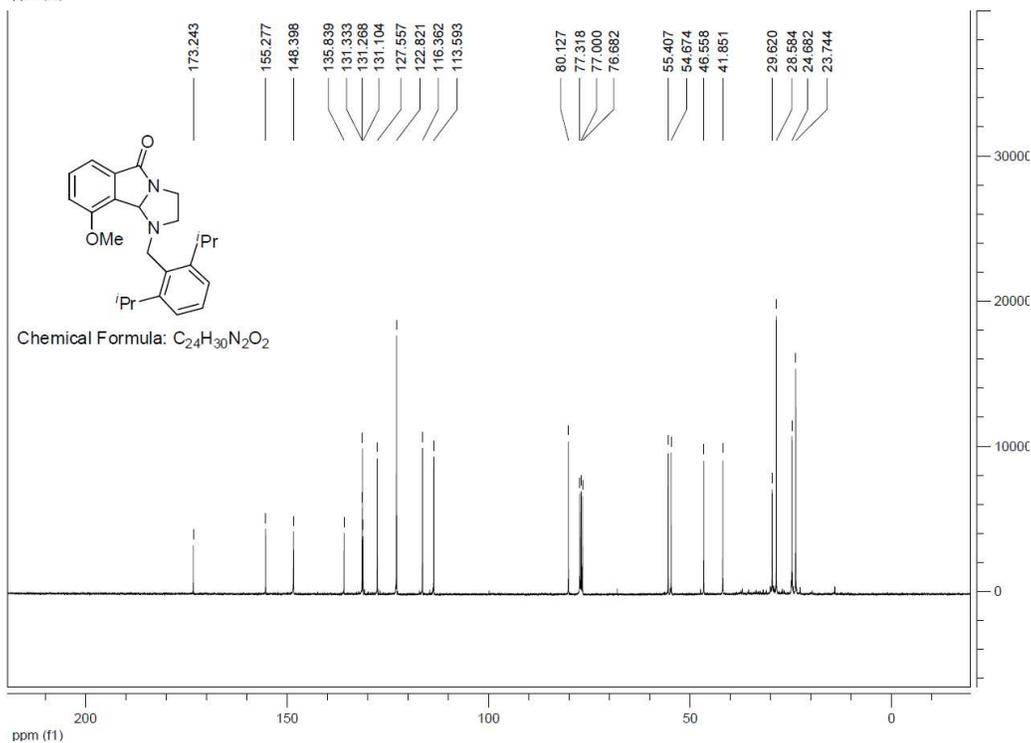
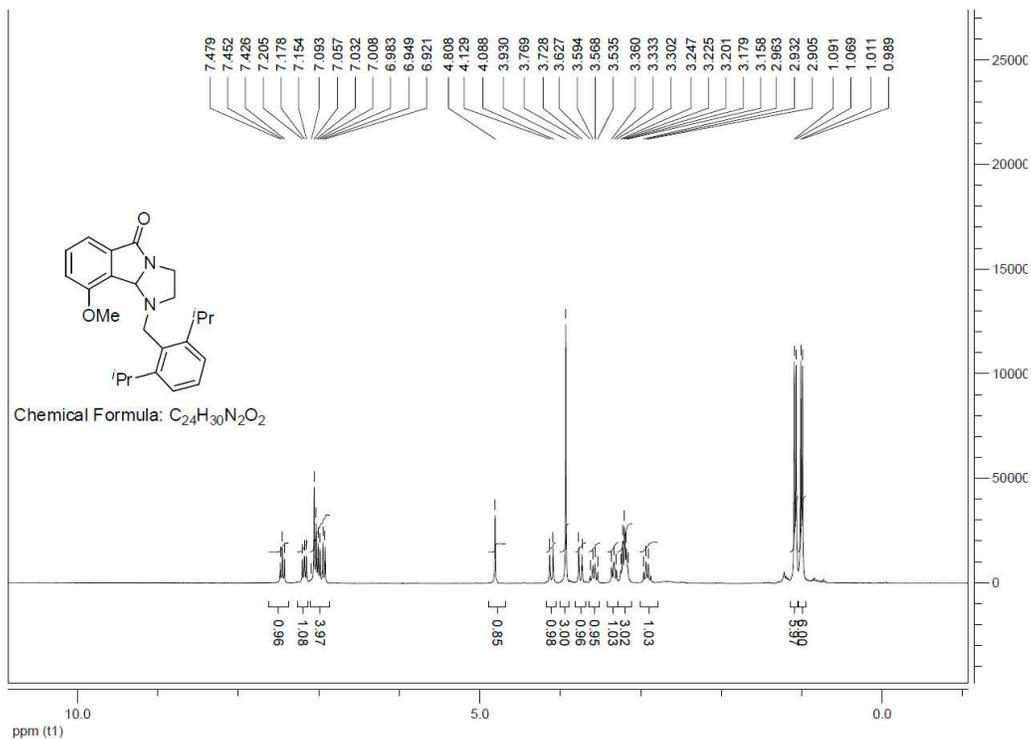
Product 3u

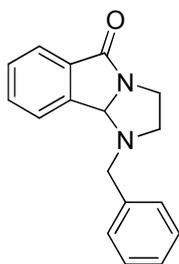


Product 3v

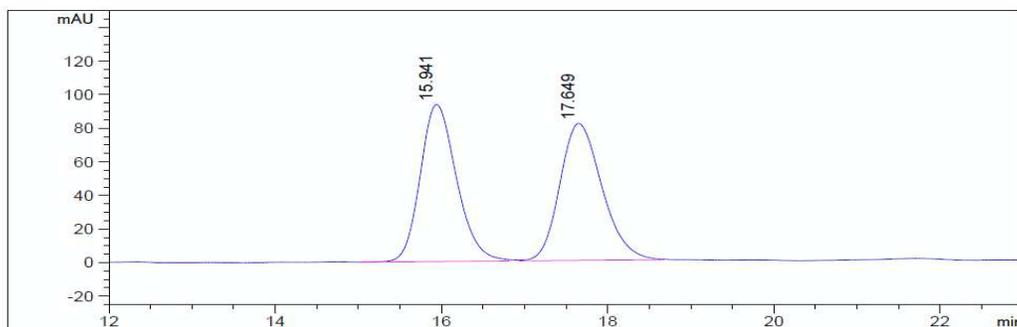


Product 3w

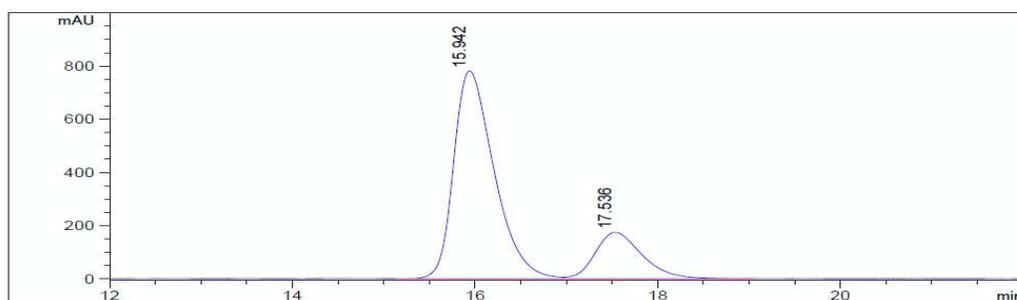




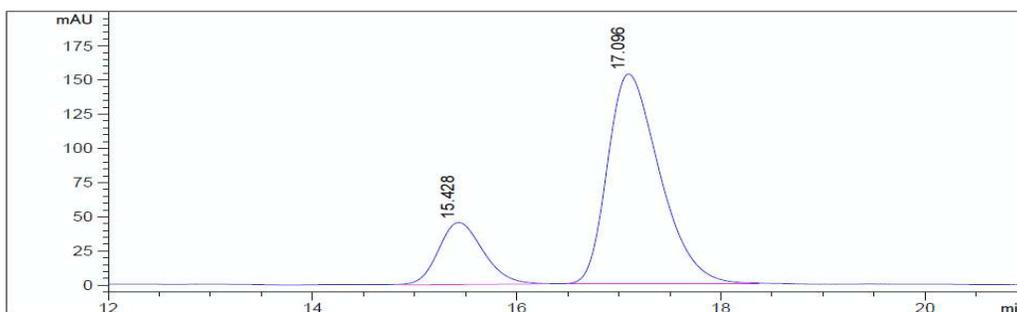
3a (The top one is racemic, the middle one is catalyzed by (*R*)-4*i*, the bottom one is catalyzed by (*S*)-4*i*)



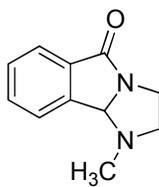
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.94	2833.314	93.415	0.453	49.69
2	17.65	2868.135	81.428	0.468	50.30



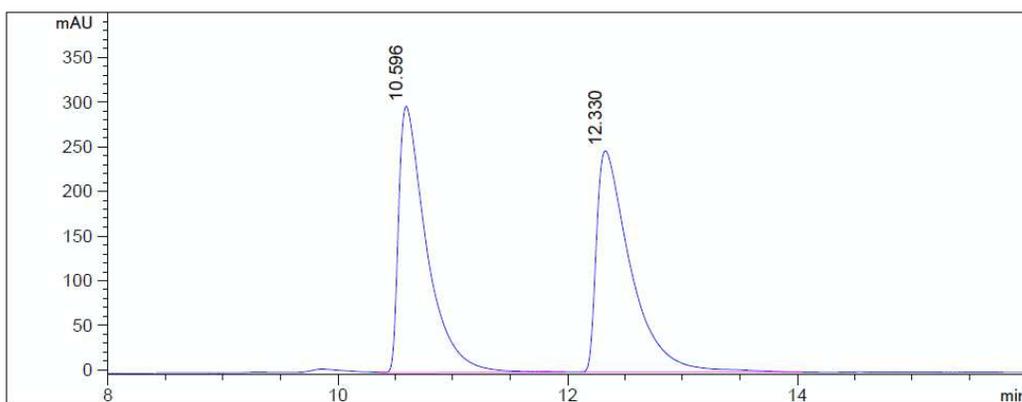
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.94	23950.652	780.380	0.470	79.54
2	17.54	6157.234	173.373	0.546	20.45



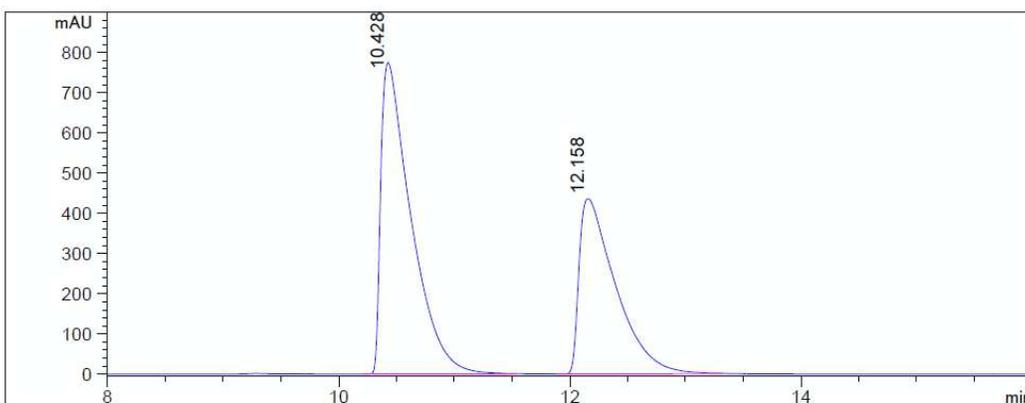
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.43	1384.922	45.364	0.509	20.30
2	17.10	5436.361	153.199	0.591	79.69



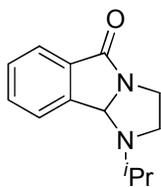
3b (The top one is racemic and bottom one is chiral)



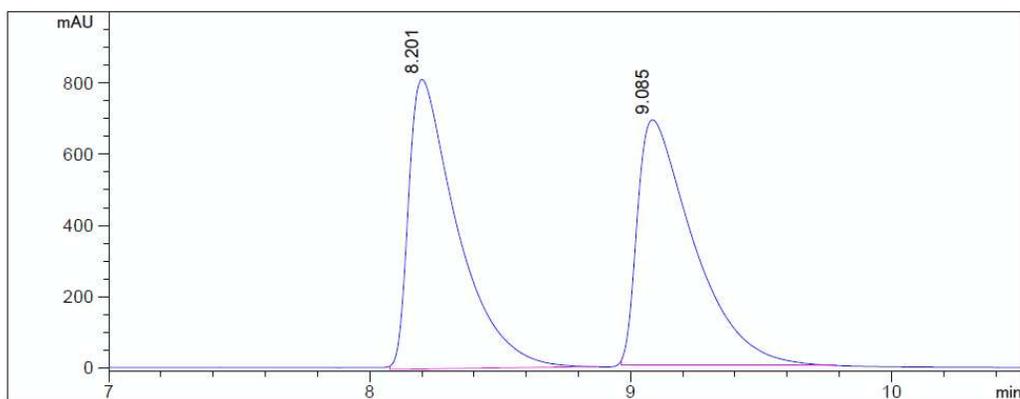
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.60	5055.986	298.275	0.283	49.65
2	12.33	5127.184	247.643	0.345	50.35



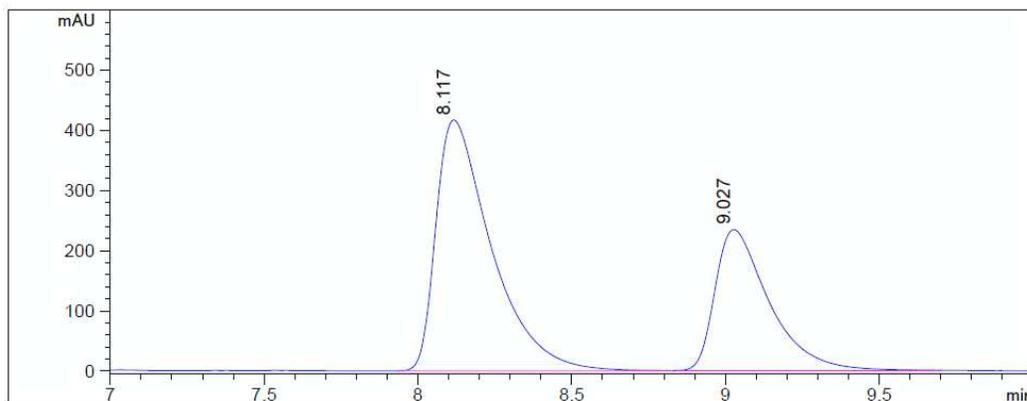
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.43	14089.854	773.981	0.263	59.54
2	12.16	9574.643	435.842	0.313	40.46



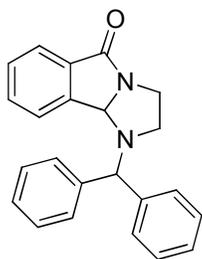
3c (The top one is racemic and bottom one is chiral)



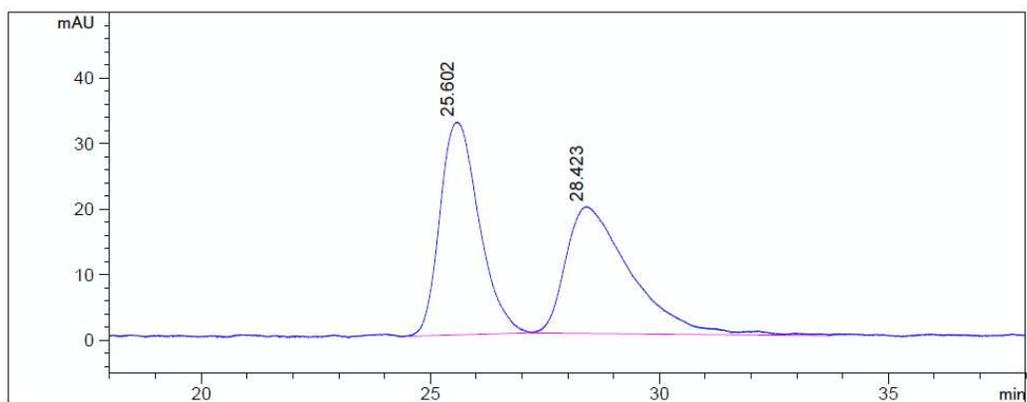
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.20	10538.622	815.330	0.215	50.5
2	9.08	10301.804	689.820	0.249	49.4



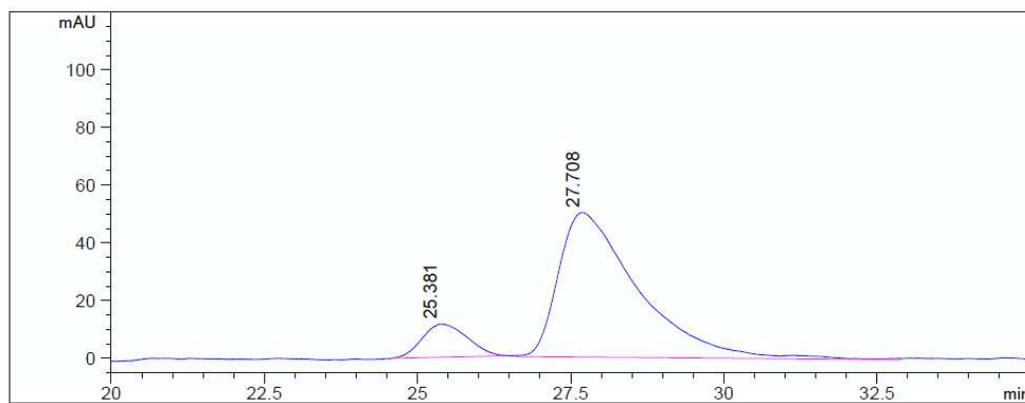
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.12	5232.319	416.834	0.189	64.48
2	9.03	2881.705	234.563	0.183	35.51



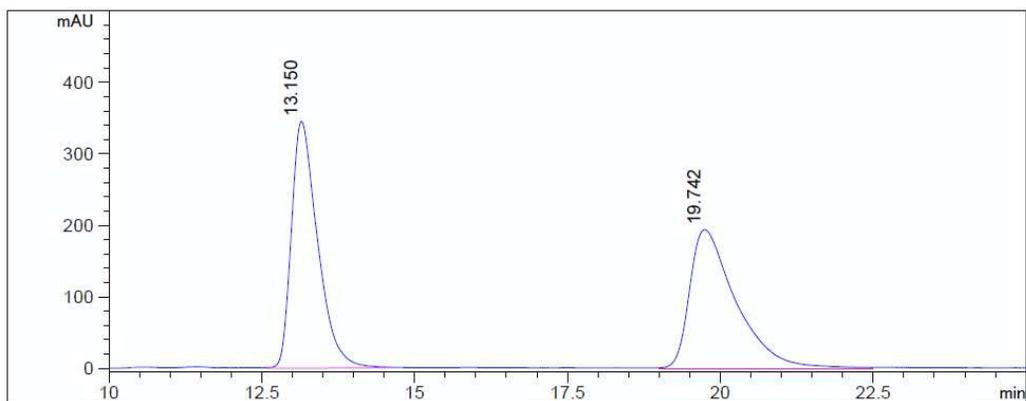
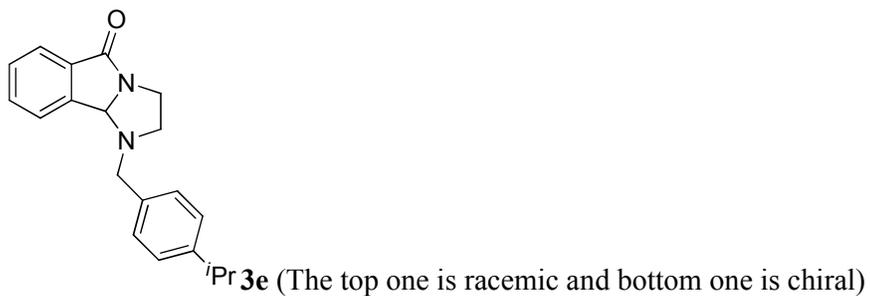
3d (The top one is racemic and bottom one is chiral)



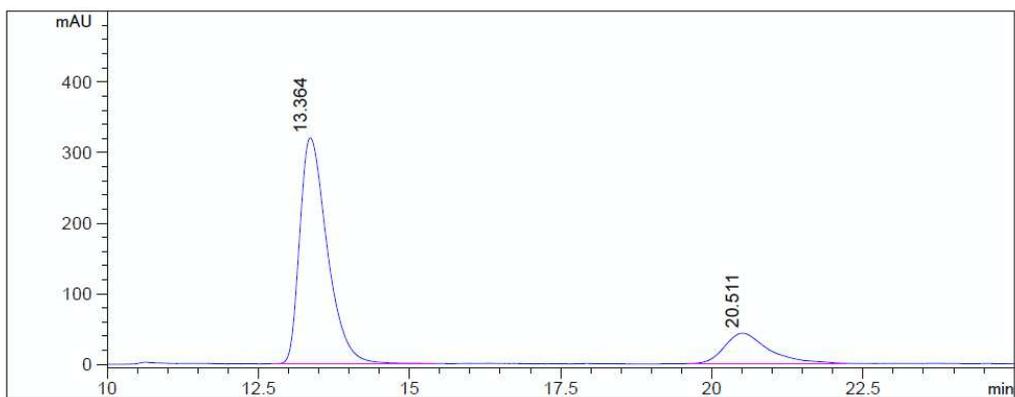
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	25.60	1929.456	32.490	0.990	50.28
2	28.42	1907.423	19.371	1.641	49.71



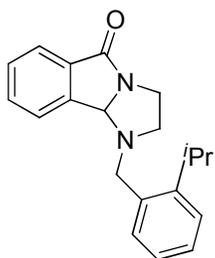
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	25.38	586.113	11.539	0.847	11.47
2	27.71	4521.019	50.105	1.504	88.52



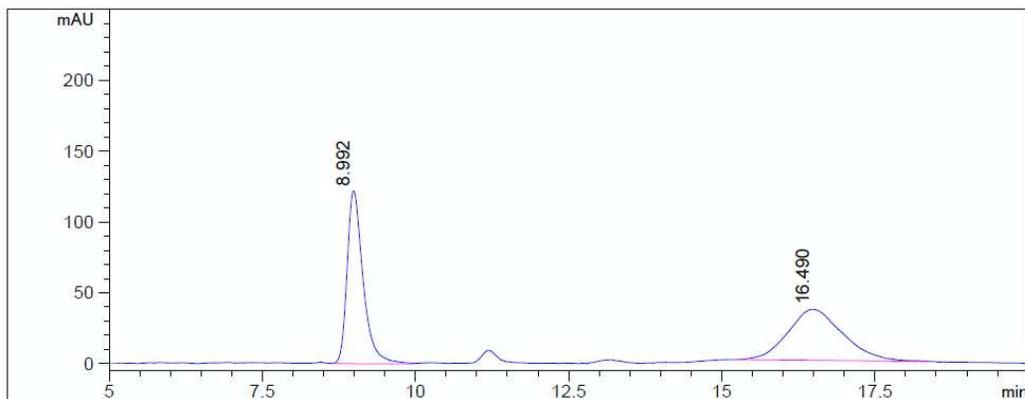
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.15	10318.264	345.224	0.498	50.31
2	19.74	10188.377	193.688	0.877	49.68



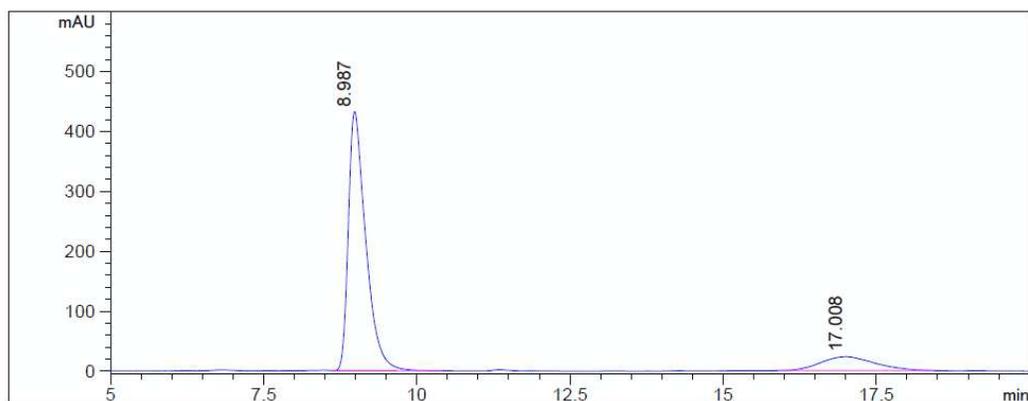
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.36	10161.636	319.972	0.529	81.98
2	20.51	2233.096	43.302	0.860	18.01



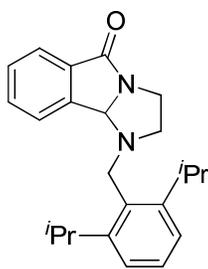
3f (The top one is racemic and bottom one is chiral)



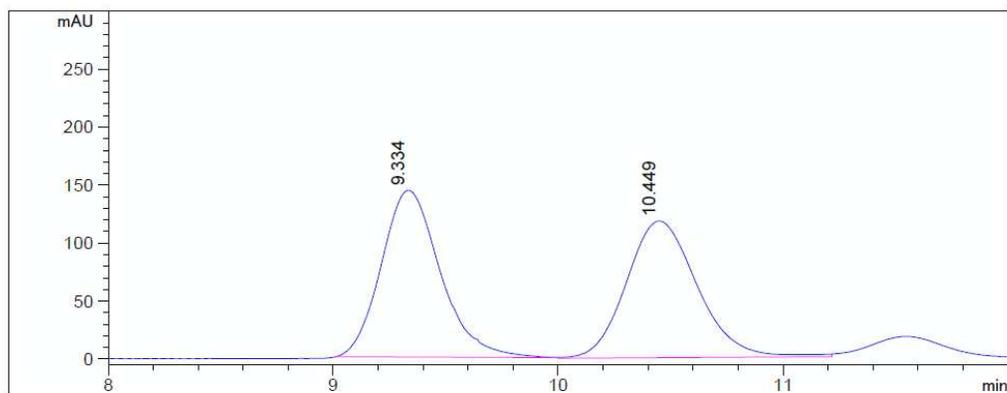
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.99	2214.992	121.880	0.303	49.70
2	16.49	2241.279	35.922	1.040	50.29



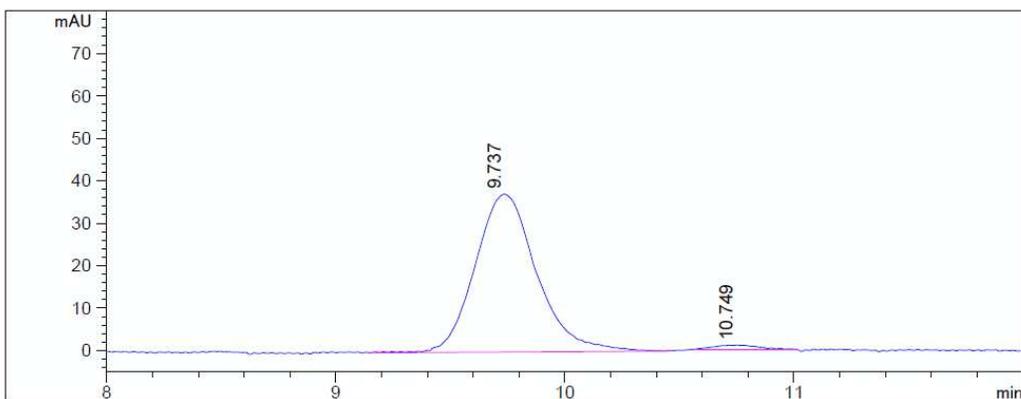
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.99	8580.044	432.604	0.331	85.94
2	17.01	1403.736	23.130	1.011	14.06



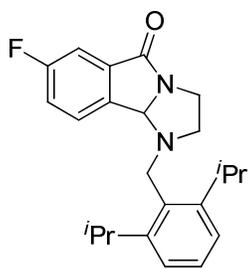
3g (The top one is racemic and bottom one is chiral)



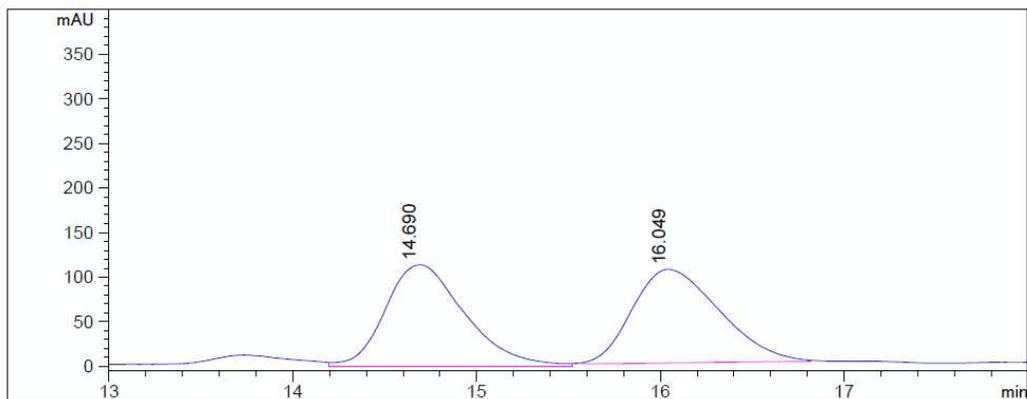
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	9.33	2620.637	143.640	0.304	50.35
2	10.45	2583.329	117.879	0.365	49.64



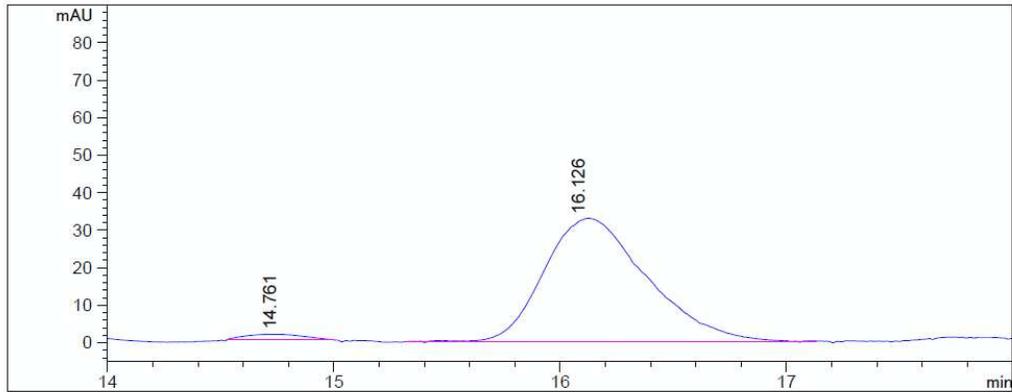
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	9.74	694.910	37.263	0.311	98.14
2	10.75	13.164	1.021	0.215	1.85



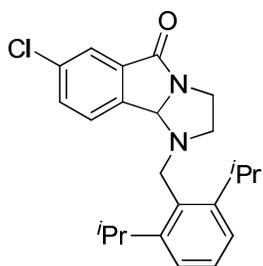
3h (The top one is racemic and bottom one is chiral)



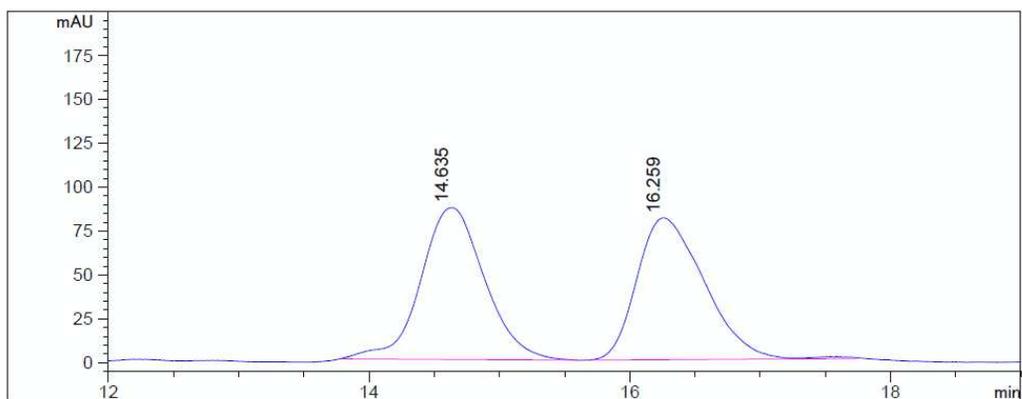
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.69	3445.922	114.050	0.406	49.96
2	16.05	3450.380	104.902	0.548	50.03



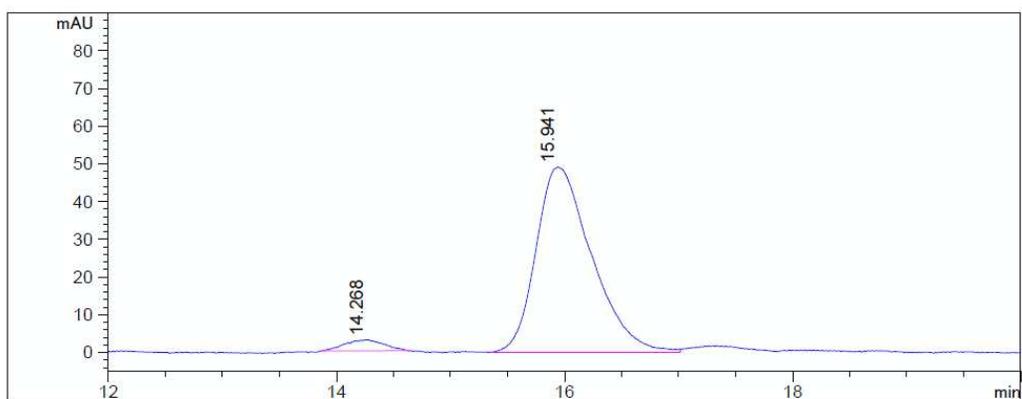
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.76	26.874	1.490	0.301	2.49
2	16.13	1050.823	32.968	0.531	97.50



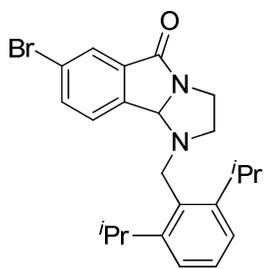
3i (The top one is racemic and bottom one is chiral)



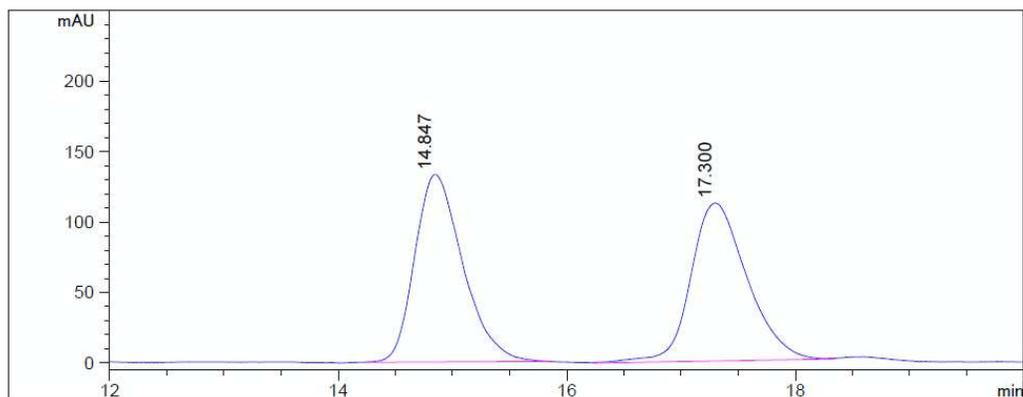
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.64	2946.067	86.505	0.568	50.33
2	16.26	2906.910	80.871	0.599	49.66



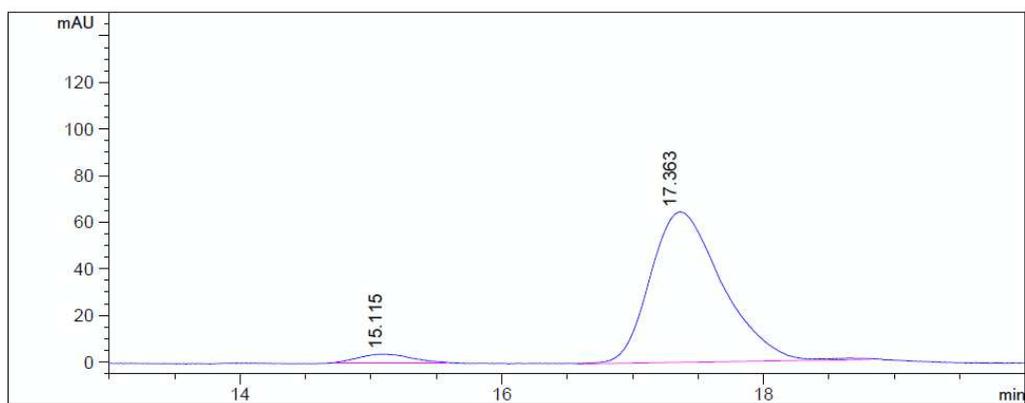
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.27	69.954	2.900	0.402	4.01
2	15.94	1671.099	49.169	0.566	95.98



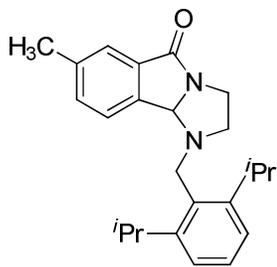
3j (The top one is racemic and bottom one is chiral)



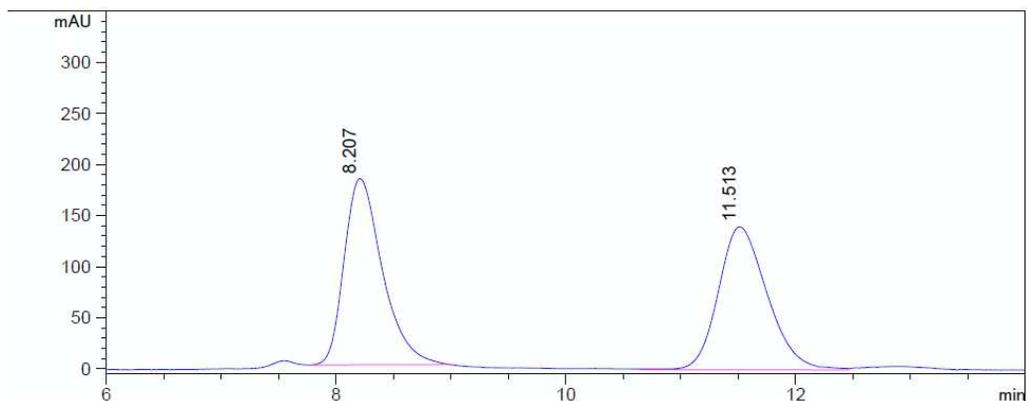
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.85	3885.610	132.966	0.487	50.38
2	17.30	3826.064	112.052	0.569	49.61



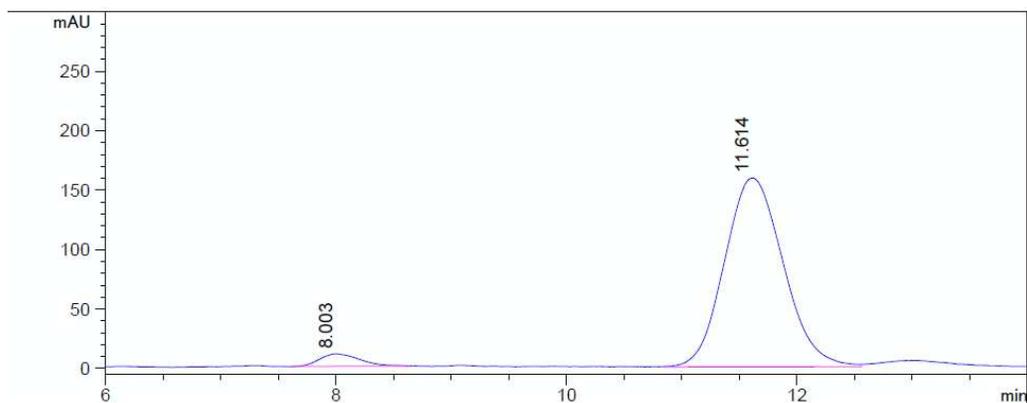
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.11	98.270	3.655	0.448	3.83
2	17.36	2463.525	64.602	0.636	96.16



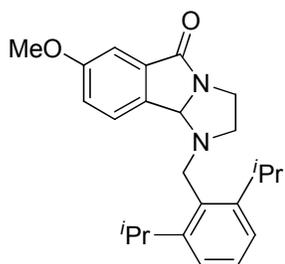
3k (The top one is racemic and bottom one is chiral)



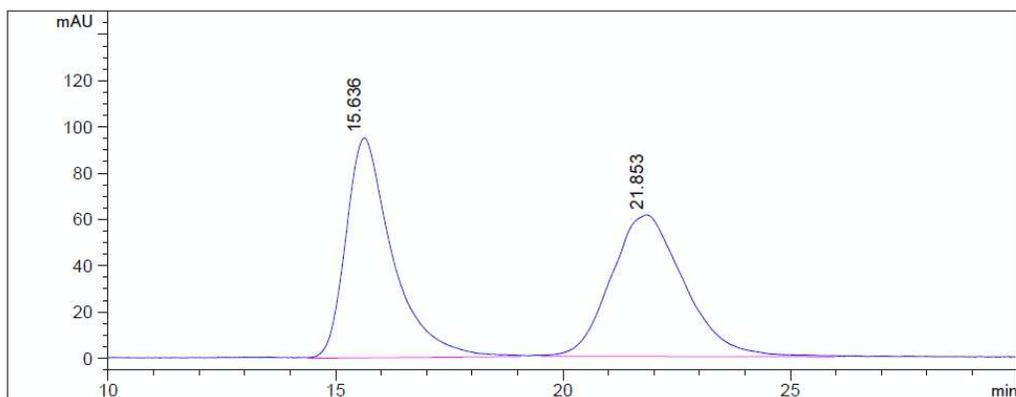
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.21	4220.843	182.256	0.386	50.48
2	11.51	4140.083	139.955	0.493	49.51



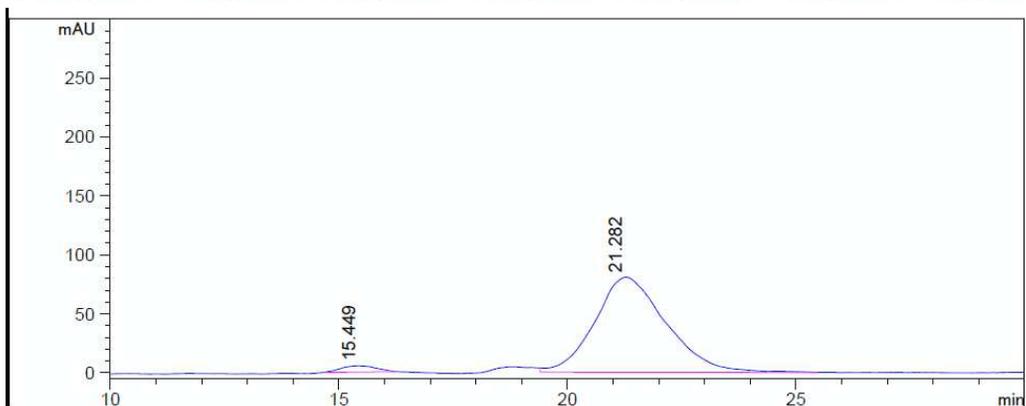
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.00	252.231	10.471	0.309	4.28
2	11.61	5632.769	158.856	0.591	95.71



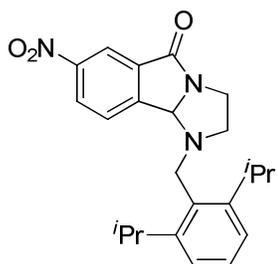
31 (The top one is racemic and bottom one is chiral)



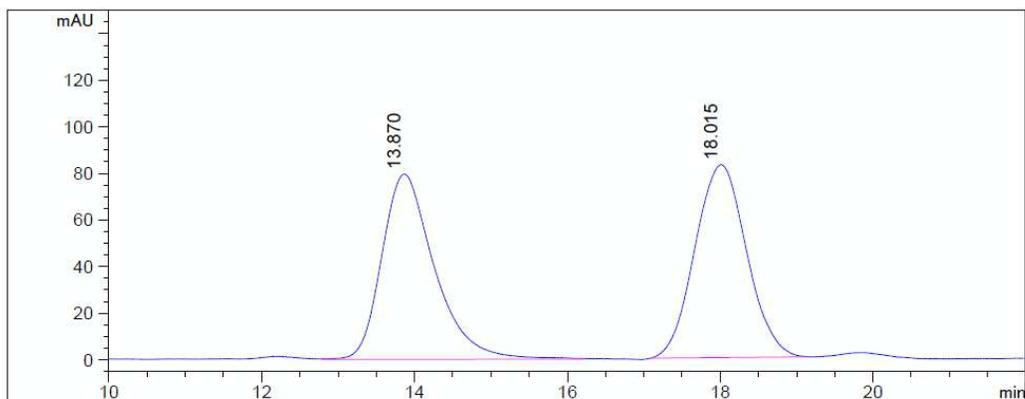
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.64	6771.506	95.081	1.187	49.70
2	21.85	6853.087	61.311	1.863	50.29



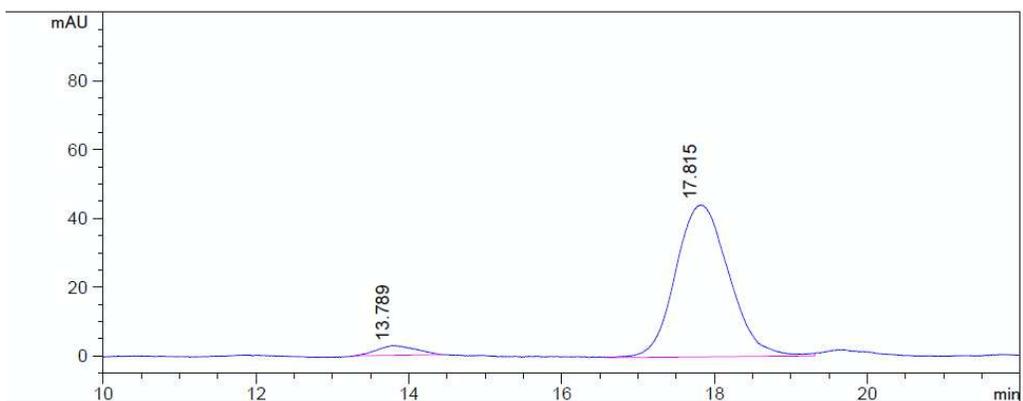
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	15.45	288.635	5.409	0.889	3.18
2	21.28	8778.656	80.755	1.812	96.81



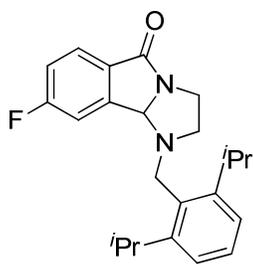
3m (The top one is racemic and bottom one is chiral)



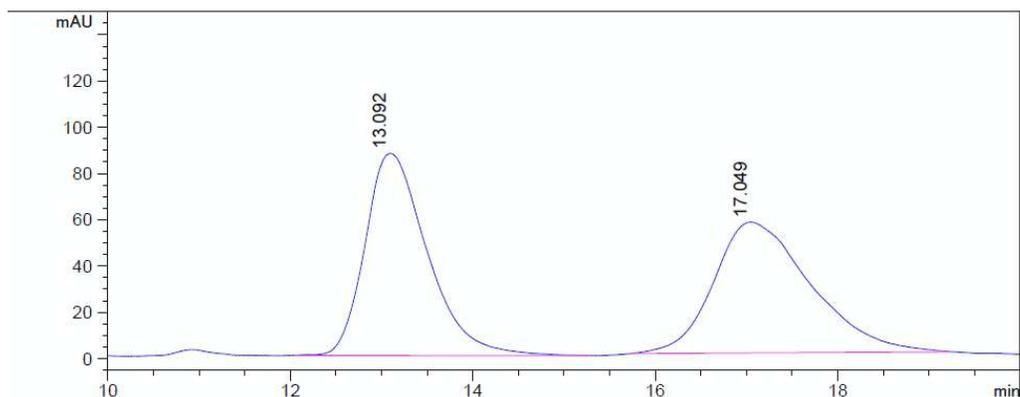
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.87	3822.335	79.634	0.800	49.59
2	18.01	3885.181	82.862	0.781	50.40



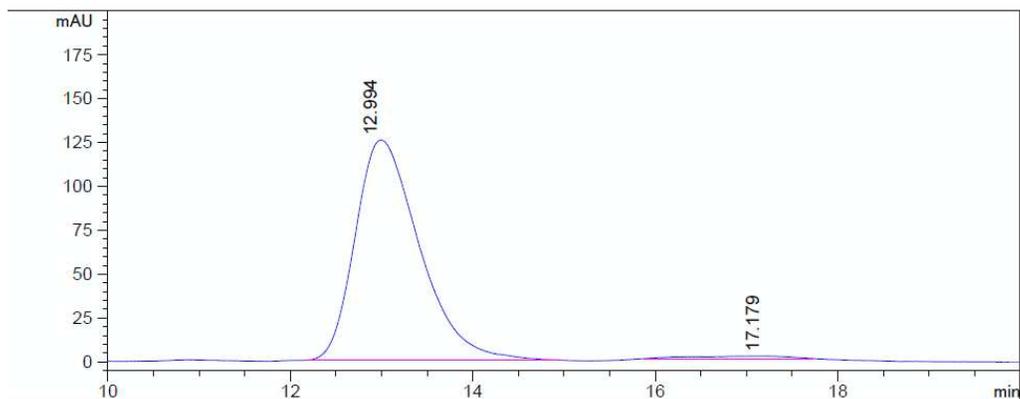
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.79	97.694	2.809	0.580	4.36
2	17.81	2141.564	44.186	0.808	95.63



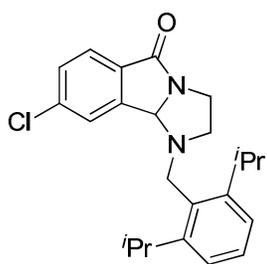
3n (The top one is racemic and bottom one is chiral)



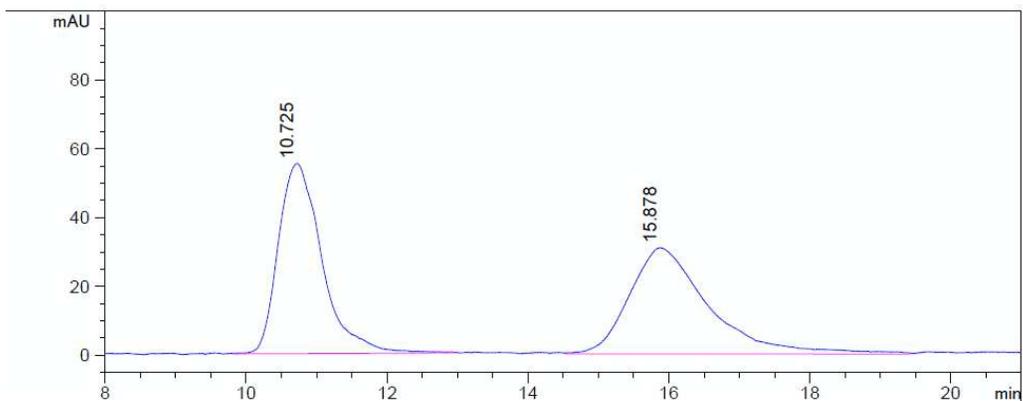
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.09	4148.410	87.341	0.792	49.79
2	17.05	4183.424	56.568	1.233	50.21



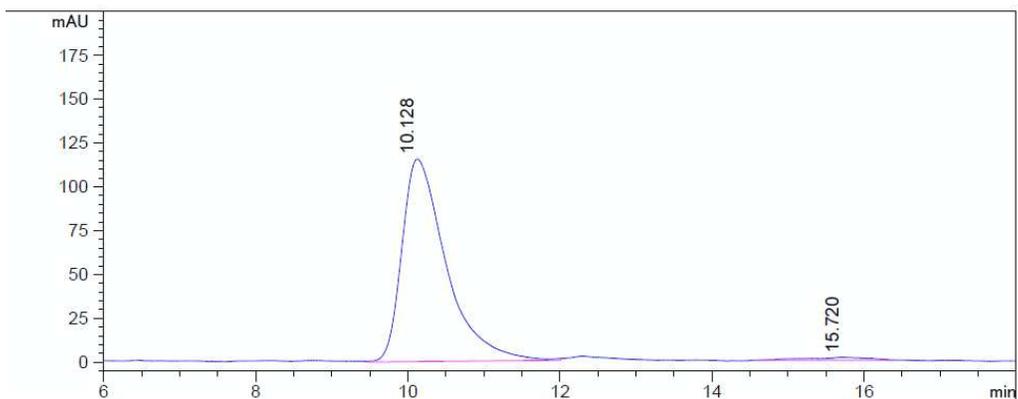
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	12.99	6157.674	125.573	0.817	97.79
2	17.18	139.058	1.742	1.331	2.20



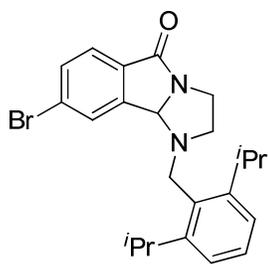
30 (The top one is racemic and bottom one is chiral)



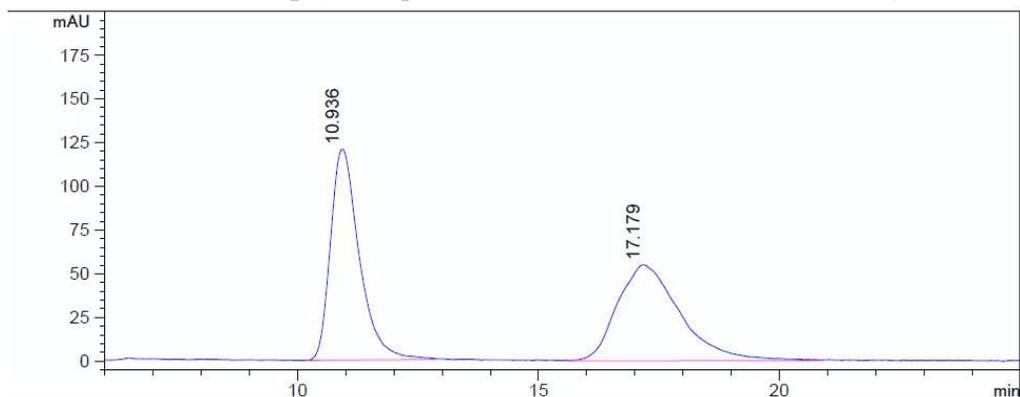
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.72	2377.715	55.210	0.718	49.72
2	15.88	2403.826	30.894	1.297	50.27



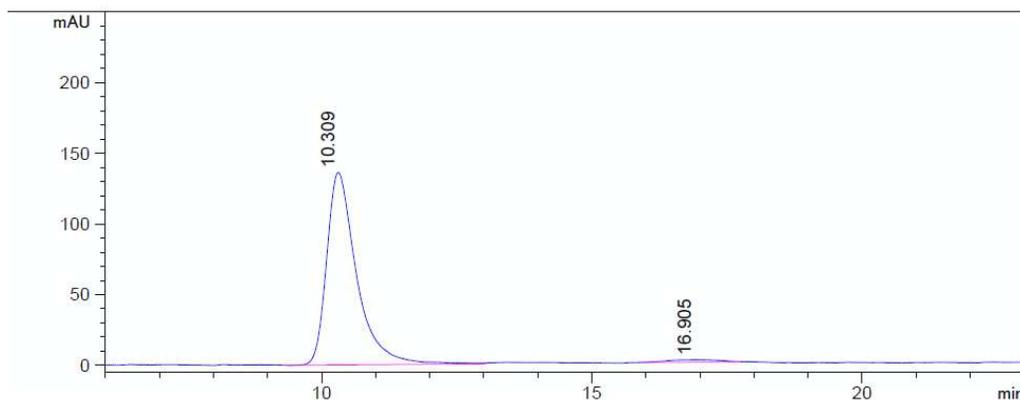
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.13	4656.105	115.377	0.673	98.11
2	15.72	89.688	1.705	0.877	1.89



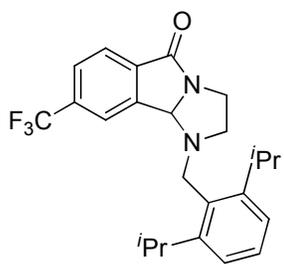
3p (The top one is racemic and bottom one is chiral)



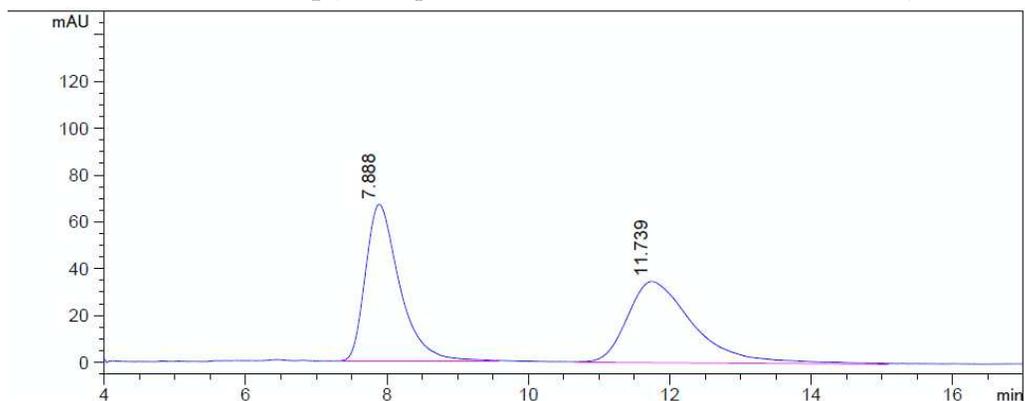
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.94	5022.980	120.648	0.694	50.26
2	17.18	4970.052	54.880	1.509	49.73



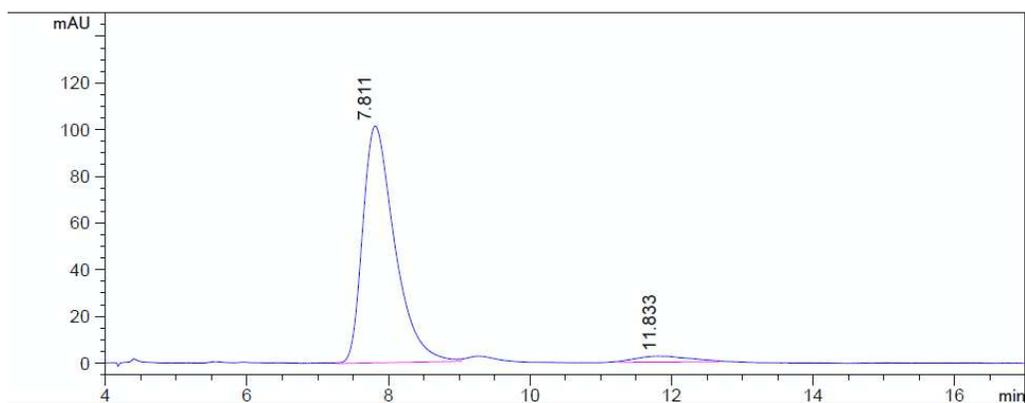
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.31	5258.182	136.183	0.644	97.88
2	16.90	113.424	1.773	1.066	2.11



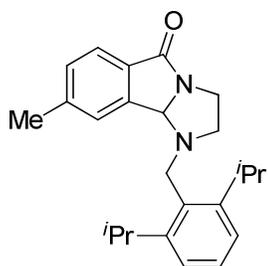
3q (The top one is racemic and bottom one is chiral)



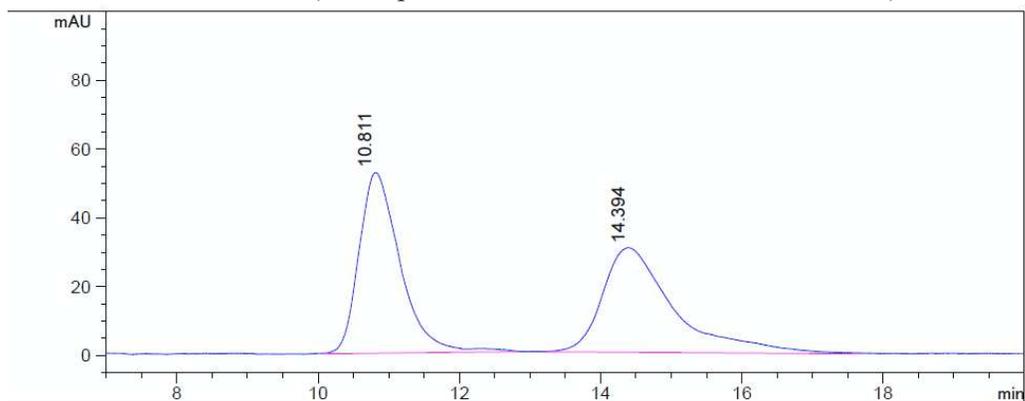
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	7.89	2262.175	67.138	0.562	50.10
2	11.74	2252.497	34.670	1.083	49.89



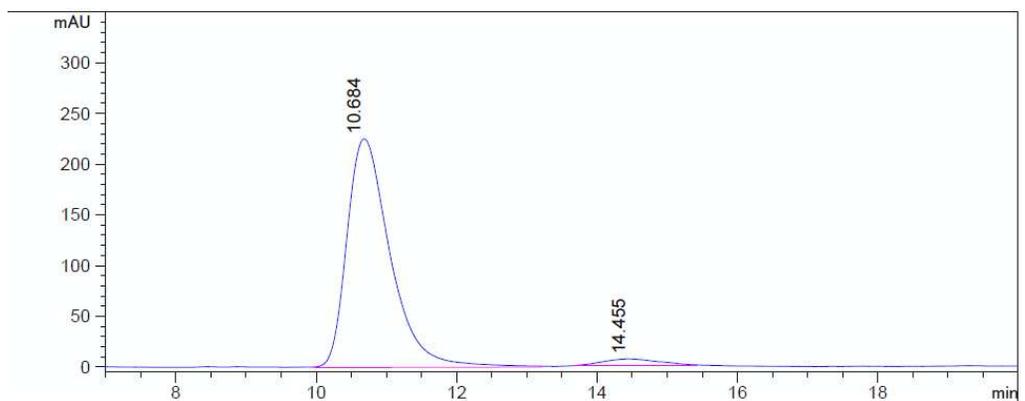
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	7.81	3184.684	101.426	0.523	96.02
2	11.83	131.874	2.543	0.864	3.97



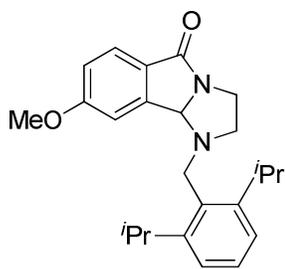
3r (The top one is racemic and bottom one is chiral)



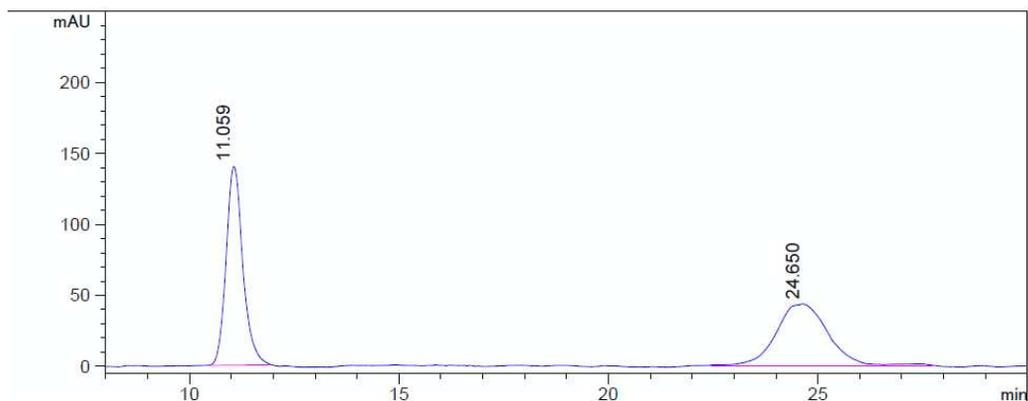
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.81	2129.569	52.539	0.676	50.07
2	14.39	2123.147	30.439	1.163	49.92



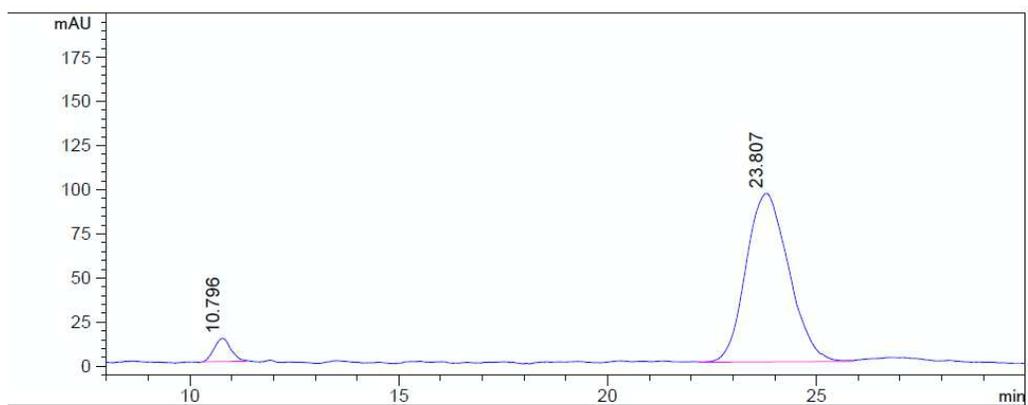
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.68	9685.061	225.626	0.715	95.97
2	14.46	406.614	6.891	0.984	4.02



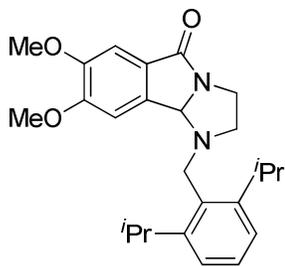
3s (The top one is racemic and bottom one is chiral)



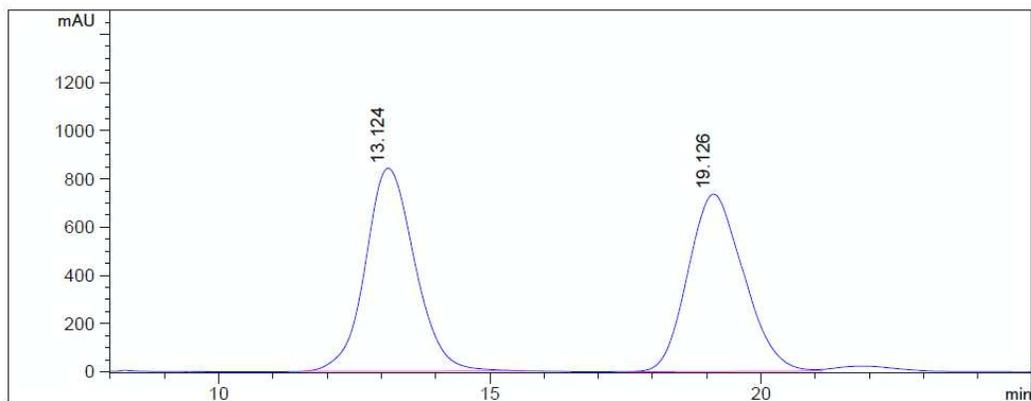
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	11.06	3887.985	139.907	0.463	50.46
2	24.65	3816.908	43.656	1.457	49.53



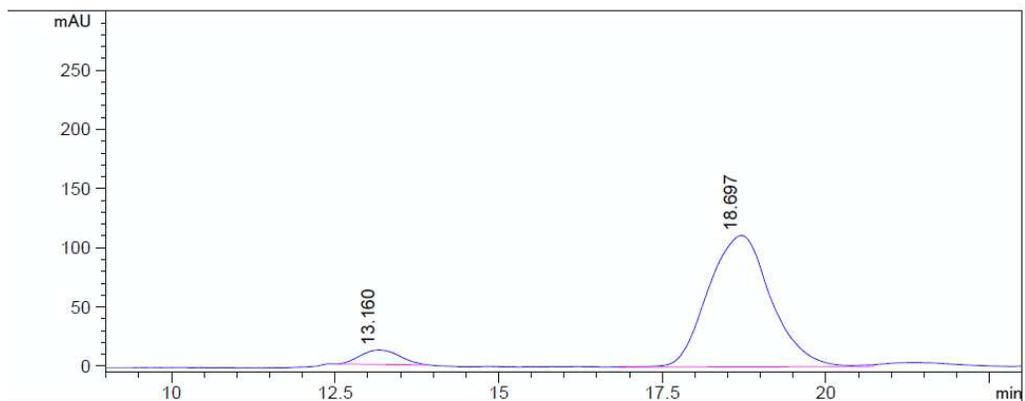
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	10.80	364.030	13.110	0.463	5.08
2	23.81	6794.064	95.496	1.186	94.91



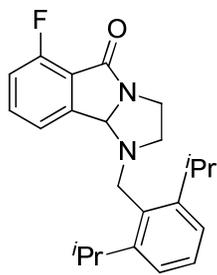
3t (The top one is racemic and bottom one is chiral)



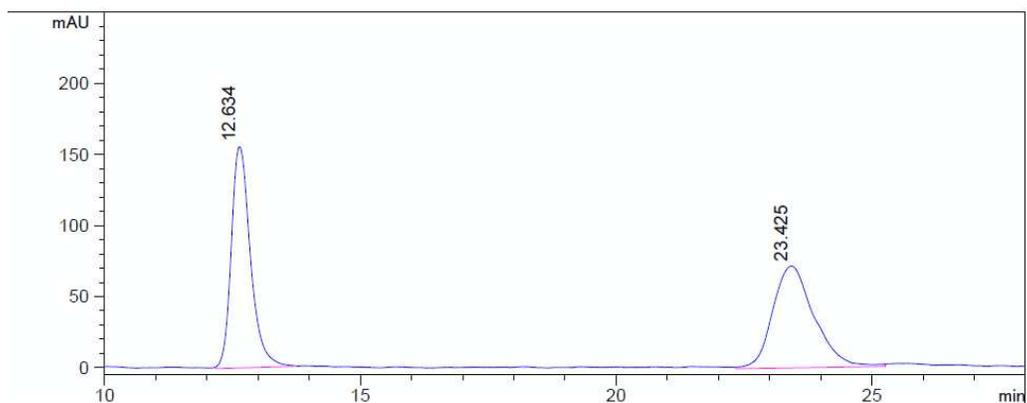
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.12	53557.621	841.874	1.060	50.46
2	19.13	52576.793	736.039	1.191	49.53



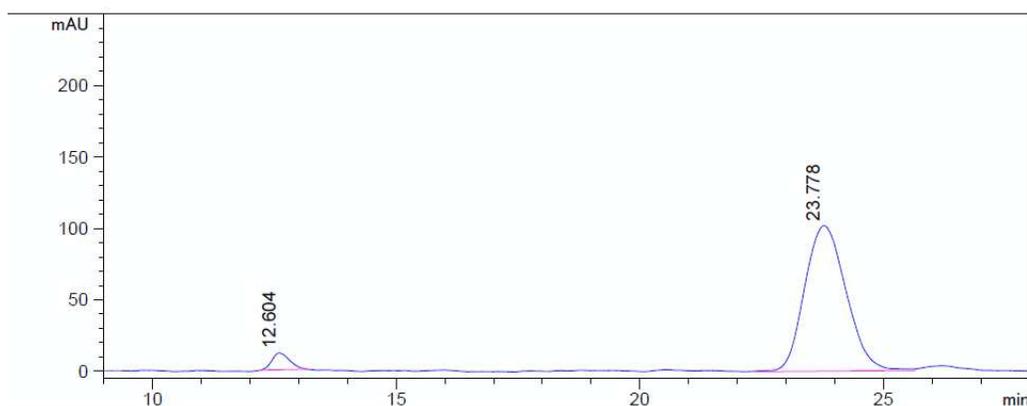
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	13.16	510.667	12.310	0.691	6.46
2	18.70	7392.637	110.827	1.112	93.53



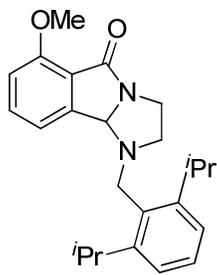
3u (The top one is racemic and bottom one is chiral)



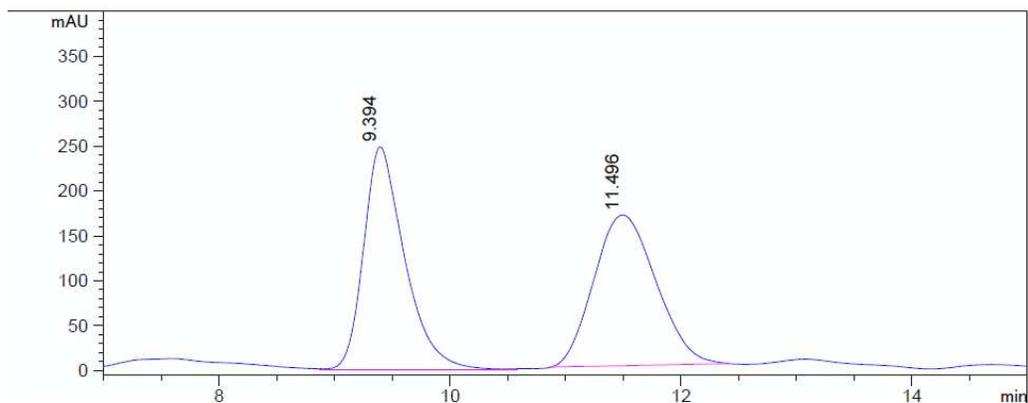
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	12.63	4058.760	155.568	0.435	50.15
2	23.42	4034.307	71.691	0.938	49.84



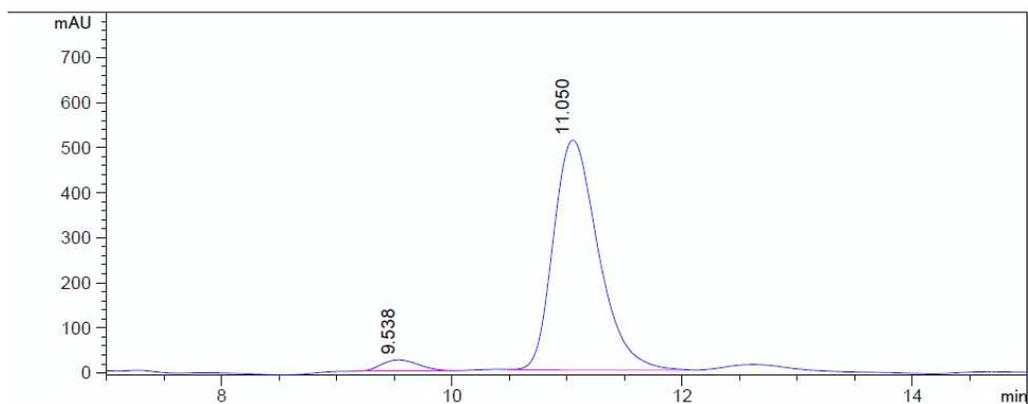
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	12.60	295.358	11.794	0.417	4.67
2	23.78	6025.324	101.888	0.986	95.32



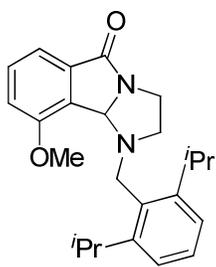
3v (The top one is racemic and bottom one is chiral)



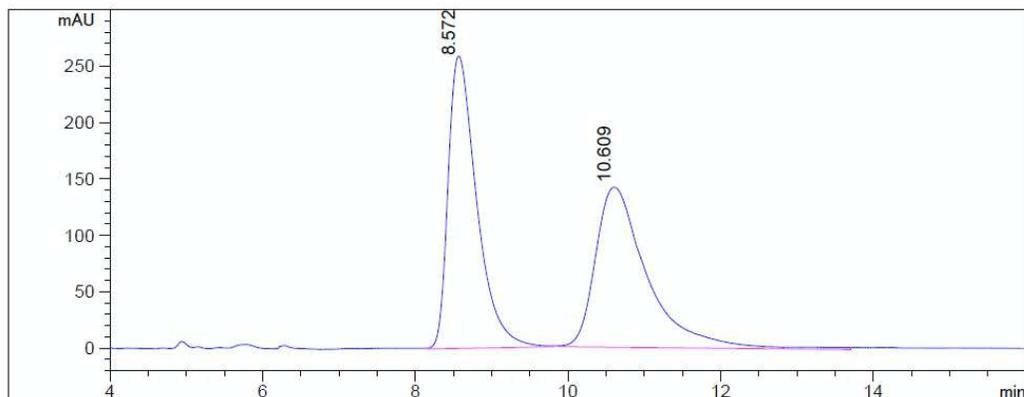
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	9.39	6108.188	247.686	0.411	49.34
2	11.50	6269.668	167.618	0.623	50.65



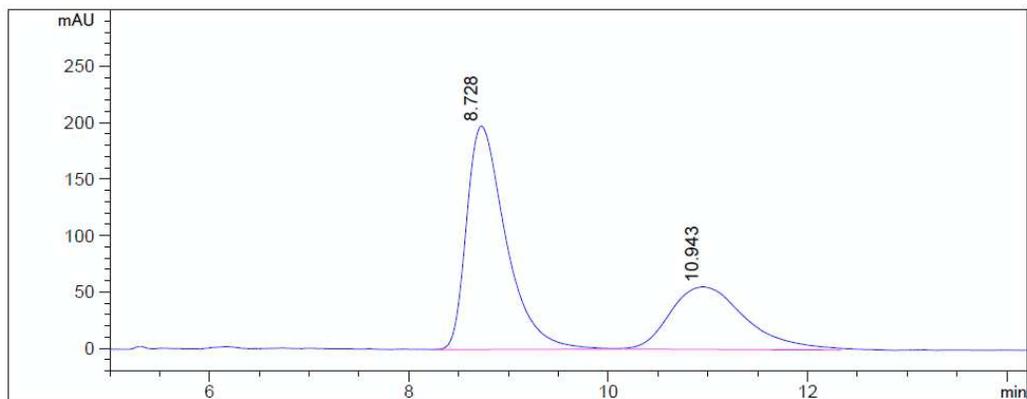
Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	9.54	589.769	25.110	0.391	4.08
2	11.05	13835.564	509.933	0.452	95.91



3w (The top one is racemic and bottom one is chiral)



Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.57	6756.421	259.142	0.435	50.22
2	10.61	6695.519	141.869	0.787	49.77



Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	8.73	5436.260	197.800	0.458	65.17
2	10.94	2904.221	55.287	0.875	34.82