Supporting Information

Desymmetrization of Aziridine with Malononitrile using Cinchona Alkaloid Amide/Zinc(II) Catalysts

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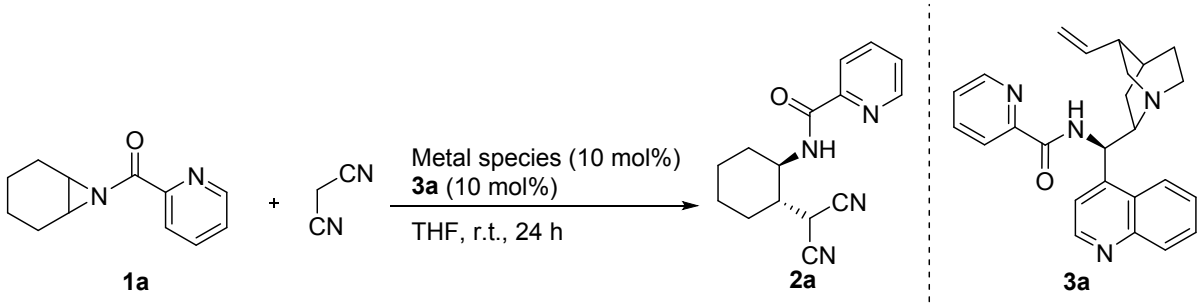
General Methods:

All reactions were performed in oven-dried glassware under a positive pressure of argon. Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or *p*-anisaldehyde in ethanol/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ^{1}H NMR (300 MHz), ^{13}C NMR (75.5 MHz) spectra for solution in $CDCl_3$, were recorded on a Varian Gemini-300. Chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CHCl_3$. HPLC analyses were performed on a JASCO PU-2080 Plus using 4.6 x 250 mm DAICEL CHIRALPAK column. ESI Mass spectra was recorded on a SHIMADZU LCMS-2050EV. Optical rotations were measured on a JASCO P-2200. Infrared spectra were recorded on a JASCO FT/IR-4600 spectrometer.

Optimization of reaction conditions:

Table S1. Screening of Lewis acids.[a]

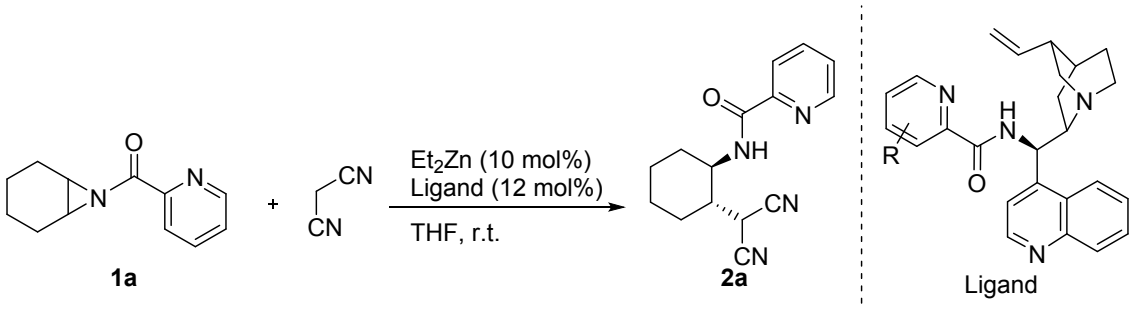


Entry	Metal species	Yield (%)	Ee (%)[b]
1	none	-	-
2 [c]	Et_2Zn	63	90
3	$Zn(OAc)_2$	53	11
4	$Zn(OTf)_2$	41	14
5[d]	$Zn(OTf)_2$	58	81
6 [d]	$Cu(OTf)_2$	10	79
7 [d]	$Ni(OTf)_2$	35	33[e]
8 [d]	$Sc(OTf)_3$	16	0

[a] Reaction condition; aziridine **1** (0.1 mmol), malononitrile (1.5 equiv.), Et_2Zn (10 mol %), **3** (1 mol %) in THF (0.1 M) were used. [b] Ee was determined by HPLC analysis using a chiral column.

[c] Ligand **3** (12 mol%) was used. [d] Et_3N (1.0 equiv.) was added. [e] Opposite enantiomer was obtained.

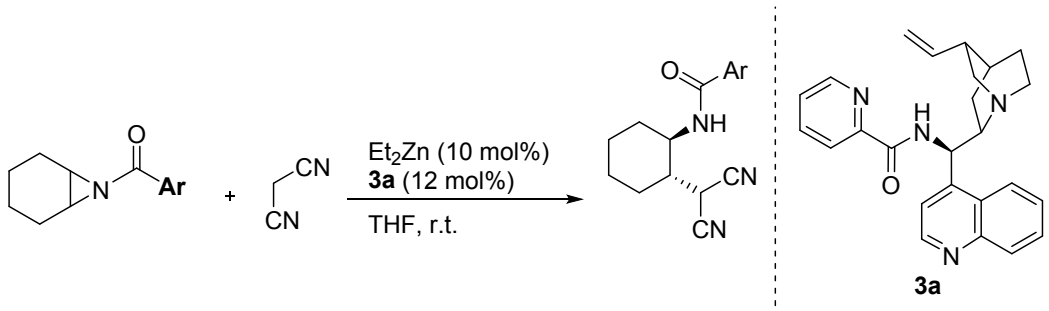
Table S2. Screening of ligands.[a]

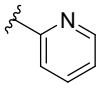
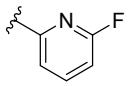
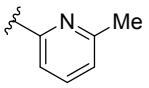
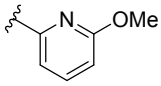
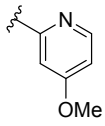
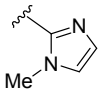
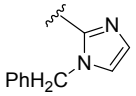
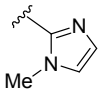


Entry	R (chiral ligand)	Time (h)	Yield (%)	Ee (%)[b]
1	H	6	74	88
2	4-CF_3	20	45	24
3	4-Cl	24	57	61
4	4-OMe	12	71	91
5	6-F	40	60	3[c]
6	6-Me	32	54	30[c]
7	6-OMe	32	60	6[c]

[a] Reaction condition; aziridine **1** (0.1 mmol), malononitrile (5.0 equiv.), Et_2Zn (10 mol %), ligand (12 mol %) in THF (0.2 M) were used. [b] Ee was determined by HPLC analysis using a chiral column. [c] Opposite enantiomer was obtained.

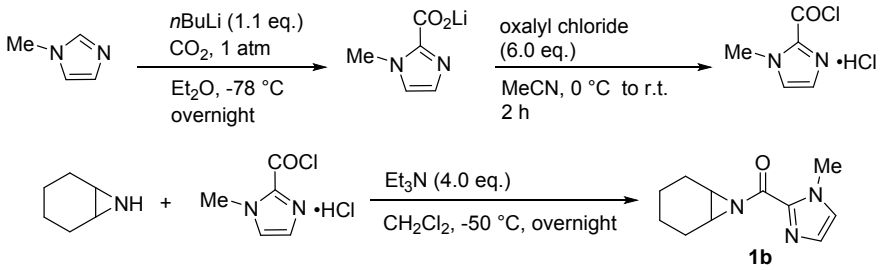
Table S3. Screening of protecting groups.[a]



Entry	Ar	Time (h)	Yield (%)	Ee (%)[b]
1		6	74	88
2		72	-	-
3		66	trace	-
4		66	19	24
5		17	69	81
6		3	84	92
7		6	88	95
8		12	82	96
9[c]		20	89	97

[a] Reaction condition; aziridine **1** (0.1 mmol), malononitrile (5.0 equiv.), Et_2Zn (10 mol %), **3** (12 mol %) in THF (0.2 M) were used. [b] Ee was determined by HPLC analysis using a chiral column.
[c] At 0 °C.

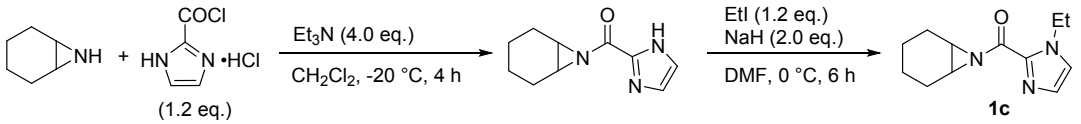
General procedure for synthesis of *N*-(imidazolecarbonyl)aziridines:



A solution of 1-methylimidazole (3.16 mL, 40 mmol) in Et_2O (120 mL) was cooled to −78 °C and added *n*-BuLi (1.6 M solution in Hexane, 44 mmol) dropwise. After stirring for 1 h, CO_2 gas was bubbled to the reaction mixture, and stirred overnight. The reaction mixture was filtrated and washed with Et_2O, and dried in vacuo to afford lithium 1-methyl-1*H*-imidazole-2-carboxylate as a white solid in quantitative yield. This compound was used in the next step without futher purification.

To a solution of lithium 1-methyl-1*H*-imidazole-2-carboxylate (924 mg, 7.0 mmol) in CH_3CN (10.5 mL), oxalyl chloride (3.6 mL, 42 mmol) was added dropwise at 0 °C. After stirring for 30 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 2 h. The volatile compounds were removed under reduced pressure, and the yellow crude compound was used in the next step immediately without futer purification.

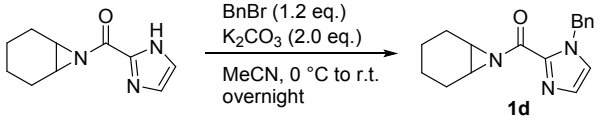
7-Aza-bicyclo[4.1.0]heptane (340 mg, 3.5 mmol) in CH_2Cl_2 (9.1 mL) was added Et_3N (1.9 mL, mmol) and cooled to −50 °C. 1-Methyl-1*H*-imidazole-2-carbonyl chloride hydrochloride (760 mg, 4.2 mmol) was added slowly to the reactin mixture and stirred for overnight. The mixture was added H_2O and warmed to room temperature. The organic layer was separated and water layer was extracted with CH_2Cl_2 twice. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residure was purified by flash column chromatography (Hexane/AcOEt=70/30) to afford **1b** in 58% yield as a white solid.



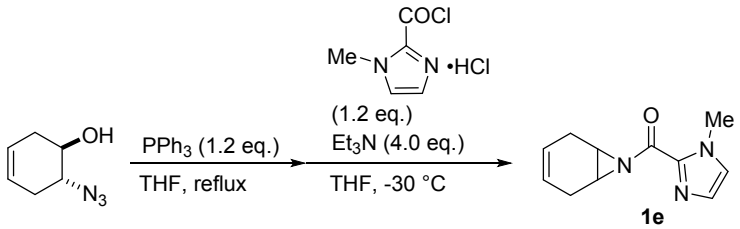
7-Aza-bicyclo[4.1.0]heptane (219 mg, 2.3 mmol) in CH_2Cl_2 (5.6 mL) was cooled to −20 °C and added Et_3N (1.3 mL, 9.0 mmol) followed by imidazole-2-acylchloride hydrochloride salt (453 mg, 2.7 mmol) synthesized by previous report.[1,2] After stirring overnight, the reaction mixture was added H_2O, and warmed to room temperature. The mixture was extracted with CH_2Cl_2 three times and the combined organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography (Hexane/AcOEt=50/50) to afford (7-azabicyclo[4.1.0]heptan-7-yl)(1*H*-imidazol-2-yl)methanone in 85% yield as a white solid.

A solution of (7-azabicyclo[4.1.0]heptan-7-yl)(1*H*-imidazol-2-yl)methanone (279 mg, 1.5 mmol)

in DMF (4.0 mL) was cooled to 0 °C and added NaH (117 mg, 60% mineral oil suspension, 2.9 mmol). After stirring for 30 min, ethyliodide (0.14 mL, 1.8 mmol) was added dropwise. After stirring for 6 h, the reaction mixture was added H_2O and warmed to room temperature. The reaction mixture extracted with AcOEt twice. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residure was purified by flash column chromatography (Hexane/AcOEt=70/30) to afford **1c** in 40% yield as a white solid.

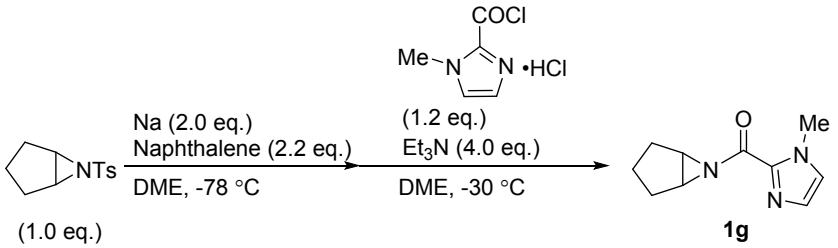


A solution of (7-azabicyclo[4.1.0]heptan-7-yl)(1*H*-imidazol-2-yl)methanone (191 mg, 1.0 mmol) and K_2CO_3 (276 mg, 1.2 mmol) in MeCN (2.5 mL) was cooled to 0 °C and added benzylbromide (0.14 mL, 1.2 mmol) dropwise. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was diluted with MeCN and filtrated through celite, and the volatile compounds were removed under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane/AcOEt=80/20) to afford **1d** in 58% yield as a white solid.



A solution of *trans*-6-azidocyclohex-3-enol (417 mg, 3.0 mmol) in THF (15 mL) was added triphenylphosphine (944 mg, 3.6 mmol) and refluxed for 5 h. The reaction mixture was cooled to −30 °C, and Et_3N (1.67 mL, 12 mmol) was added to the solution followed by 1-methyl-1*H*-imidazole-2-carbonyl chloride hydrochloride (650 mg, 3.6 mmol) in portionwise. After stirring overnight, the reaction mixture was added H_2O and warmed to room temperature. The mixture was extracted with CH_2Cl_2 three times and the combined organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography (Hexane/AcOEt=60/40) to afford **1e** in 51% yield as a white solid.

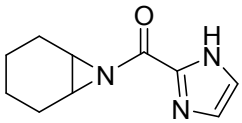
Compound **1f**, **1h** were prepared by similar method for the preparation of **1e**.



Chopped sodium metal (322 mg, 14 mmol) was added to a solution of naphthalene (1.97 g, 15.4

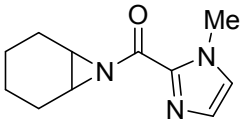
mmol) in 1,2-dimethoxyethane (12 mL) and stirred at room temperature for 1 h. The reaction mixture became a dark green solution, and it was added to a solution of 6-tosyl-6-azabicyclo[3.1.0]hexane (1.66 mg, 7.0 mmol) in 1,2-mimethoxyethane (24 mL) at –78 °C. After stirring for 1 h, the reaction mixture was added H_2O (0.25 mL), and stirred for 30 min at room temperature. Then, $MgSO_4$ was added to the reaction mixture and stirred for 15 min. The precipitate was filtrated off through celite and washed with Et_2O. After removal of Et_2O under reduced pressure, the residure was cooled to −30 °C, and Et_3N (3.9 mL, 28 mmol) was added to the solution followed by 1-methyl-1*H*-imidazole-2-carbonyl chloride hydrochloride (1.52 g, 8.4 mmol) in portionwise. After stirring overnight, the reaction mixture was added H_2O and warmed to room temperature. The mixture was extracted with AcOEt three times and the combined organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography (Hexane/AcOEt=50/50) to afford **1g** in 38% yield as a white solid.
Compound **1i** was prepared by similar method for the preparation of **1g**.

(7-Azabicyclo[4.1.0]heptan-7-yl)(1*H*-imidazol-2-yl)methanone;



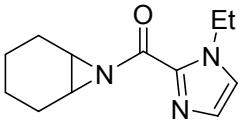
m.p. 111.8-112.4 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.30-1.39 (m, 2H), 1.48-1.59 (m, 2H), 1.91-1.95 (m, 2H), 2.18-2.27 (m, 2H), 2.97-2.98 (m, 2H), 7.21 (d, *J* = 3.0 Hz, 1H), 7.27 (d, *J* = 3.0 Hz, 1H), 11.5 (br, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 20.0, 23.8, 37.7, 119.8, 131.2, 141.3, 170.5; **IR** (ATR) 2945, 2910, 1665, 1389, 1310, 1198, 1092, 947, 799, 697 cm^{-1}; **HRMS** (ESI) calculated for $C_{10}H_{13}N_3NaO^+$ $[M+Na]^+$ 213.0956. found 214.0957.

(7-Azabicyclo[4.1.0]heptan-7-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1b**) ;



m.p. 57.8-58.8 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.29-1.38 (m, 2H), 1.50-1.57 (m, 2H), 1.87-1.95 (m, 2H), 2.15-2.24 (m, 2H), 2.91-2.92 (m, 2H), 4.00 (s, 3H), 6.98 (d, *J* = 0.9 Hz, 1H), 7.12 (d, *J* = 0.9 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 20.2, 23.9, 36.1, 37.7, 125.9, 129.1, 139.7, 171.0; **IR** (ATR) 2931, 1651, 1404, 1273, 1191, 1132, 895, 823, 776, 675 cm^{-1}; **HRMS** (ESI) calculated for $C_{11}H_{15}N_3NaO^+$ $[M+Na]^+$ 228.1113. found 228.1116.

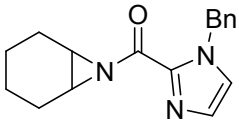
(7-Azabicyclo[4.1.0]heptan-7-yl)(1-Ethyl-1*H*-imidazol-2-yl)methanone (**1c**) ;



m.p. 52.0-53.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.26-1.33 (m, 2H), 1.34-1.44 (m, 3H), 1.48-1.59 (m, 2H), 1.87-1.95 (m, 2H), 2.15-2.25 (m, 2H), 2.91-2.92 (m, 2H), 4.45 (q, *J* = 7.2 Hz , 2H), 7.05 (d, *J* = 0.9 Hz, 1H), 7.13 (d, *J* = 0.9 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 16.7, 20.2, 37.7, 43.6, 124.1, 129.3, 139.0, 170.8; **IR** (ATR) 2922, 1661, 1407, 1268, 1136, 894, 784, 670 cm^{-1}; **HRMS** (ESI) calculated for

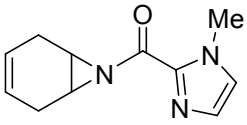
$C_{12}H_{17}N_3NaO^+$ $[M+Na]^+$ 242.1269. found 242.1269.

(1-Benzyl-1*H*-imidazol-2-yl)(7-azabicyclo[4.1.0]heptan-7-yl)methanone (**1d**);



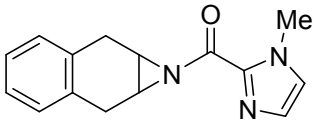
m.p. 52.5-53.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.27-1.36 (m, 2H), 1.47-1.55 (m, 2H), 1.85-1.93 (m, 2H), 2.14-2.88 (m, 2H), 2.88-2.89 (m, 2H), 5.64 (s, 2H), 7.02 (s, 1H), 7.15 (s, 1H), 7.18-7.20 (m, 2H), 7.24-7.34 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 20.1, 23.9, 37.8, 51.6, 124.9, 127.7, 128.0, 128.9, 129.5, 136.9, 139.3, 170.9; **IR** (ATR) 2937, 1739, 1658, 1410, 1272, 1200, 1121, 894, 770, 723 cm^{-1}; **HRMS** (ESI) calculated for $C_{17}H_{19}N_3NaO^+$ $[M+Na]^+$ 304.1426. found 304.1415.

(7-azabicyclo[4.1.0]hept-3-en-7-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1e**);



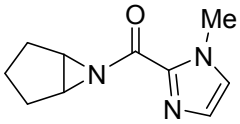
m.p. 96.4-97.2 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.44-2.50 (m, 2H), 2.81-2.87 (m, 2H), 3.07 (s, 2H), 3.99 (s, 3H), 5.51 (s, 2H), 6.98 (d, J = 0.6 Hz, 1H), 7.11 (d, J = 0.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.0, 35.9, 36.8, 122.4, 125.8, 128.9, 139.6, 170.2; **IR** (ATR) 3722, 2306, 1658, 1407, 1281, 1140, 1044, 1002, 900, 876, 779, 684 cm^{-1}; **HRMS** (ESI) calculated for $C_{11}H_{13}N_3NaO^+$ $[M+Na]^+$ 226.0956. found 226.0953.

(1-Methyl-1*H*-imidazol-2-yl)(1a,2,7,7a-tetrahydro-1*H*-naphtho[2,3-b]azirin-1-yl)methanone (**1f**);



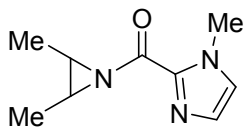
m.p. 154.5-155.5 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.16-3.21 (m, 2H), 3.33 (s, 2H), 3.49-3.55 (m, 2H), 3.70 (s, 3H), 6.89 (s, 1H), 6.98-7.01 (m, 2H), 7.07-7.11 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 29.3, 35.6, 37.6, 125.5, 126.7, 128.7, 129.3, 132.6, 139.6, 169.2; **IR** (ATR) 3022, 2922, 1758, 1657, 1416, 1277, 1140, 887, 761, 666 cm^{-1}; **HRMS** (ESI) calculated for $C_{15}H_{15}N_3NaO^+$ $[M+Na]^+$ 2761113. found 276.1114.

(6-Azabicyclo[3.1.0]hexan-6-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1g**);



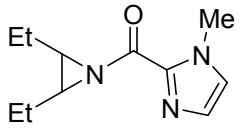
m.p. 61.0-62.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.21-1.29 (m, 1H), 1.60-1.78 (m, 3H), 2.21-2.28 (m, 2H), 3.35 (s, 2H), 4.01 (s, 3H), 6.98 (s, 1H), 7.13 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 19.4, 27.0, 36.1, 44.1, 125.8, 128.9, 139.6, 168.8; **IR** (ATR) 2968, 1739, 1652, 1408, 1269, 1228, 1133, 915, 811, 668 cm^{-1}; **HRMS** (ESI) calculated for $C_{10}H_{13}N_3NaO^+$ $[M+Na]^+$ 214.0956. found 214.0961.

(2,3-Dimethylaziridin-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1h**);



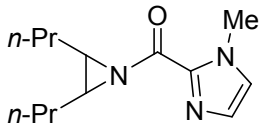
m.p. 80.0-61.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.41 (d, *J* = 5.4 Hz, 6H), 2.75-2.79 (m, 1H), 4.00 (s, 3H), 6.99 (s, 1H), 7.12 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 12.9, 36.0, 38.1, 126.0, 129.1, 139.6, 171.2; **IR** (ATR) 3129, 3114, 2958, 1656, 1453, 1416, 1453, 1416, 1312, 1283, 1164, 903, 788, 670 cm^{-1}; **HRMS** (ESI) calculated for $C_9H_{13}N_3NaO^+$ $[M+Na]^+$ 202.0956. found 202.0961.

(2,3-Diethylaziridin-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone (**1i**);



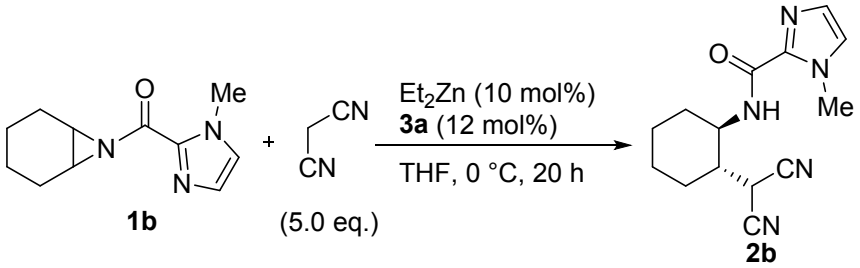
m.p. 71.5-72.5 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.11 (t, *J* = 7.5 Hz, 6H), 1.54-1.63 (m, 2H), 1.90-1.99 (m, 2H), 2.63-2.66 (m, 2H), 4.00 (s, 3H), 6.99 (d, *J* = 0.9 Hz, 1H), 7.11 (d, *J* = 0.9 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 11.6, 21.0, 35.9, 44.3, 125.9, 128.9, 139.5, 171.1; **IR** (ATR) 2961, 1658, 1407, 1284, 1144, 1011, 907, 788, 663 cm^{-1}; **HRMS** (ESI) calculated for $C_{11}H_{17}N_3NaO^+$ $[M+Na]^+$ 230.1269. found 230.1273.

(2,3-Dipropylaziridin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone (**1j**);



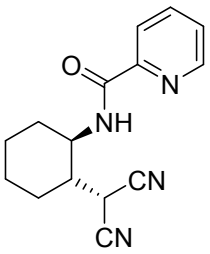
m.p. 80.5-81.5 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.96-1.03 (m, 6H), 1.50-1.62 (m, 6H), 1.83-1.88 (m, 2H), 2.67-2.69 (m, 2H), 3.99 (s, 3H), 6.99 (s, 1H), 7.12 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 14.1, 20.7, 29.9, 36.0, 42.9, 126.0, 129.0, 139.6, 171.3; **IR** (ATR) 2953, 1657, 1410, 1285, 1153, 914, 794, 663 cm^{-1}; **HRMS** (ESI) calculated for $C_{13}H_{21}N_3NaO^+$ $[M+Na]^+$ 258.1582. found 258.1587.

General procedure for the enantioselective desymmetrization of aziridines with malononitrile:



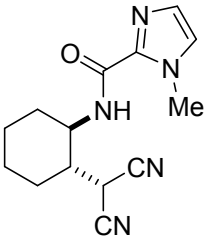
Ligand **3a** (4.8 mg, 0.012 mmol) and Et_2Zn (1.11M solution in toluene, 9.0 μL, 0.01 mmol) was dissolved in THF (0.5 mL) and stirred at room temperature for 30 min. Aziridine **1b** (20.5 mg, 0.1 mmol) was added to a solution and cooled to 0 °C, then malononitrile (33.1 mg, 0.5 mmol) was added. After stirring for 20 h, the reaction mixture was diluted with AcOEt and filtraed through the celite pad, and the volatile compounds were removed under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane/AcOEt=50/50) to give (1*R*,2*S*)-**2b** in 89% yield 97% ee) as a white solid. (1*S*,2*R*)-**2b** can be synthesised by using ligand **3b** instead of **3a** in 74% yield 94% ee).

***N*-((1*R*,2*S*)-2-(Dicyanomethyl)cyclohexyl)picolinamide (2a);**



$[\alpha]_D^{25}$ −33.2 (*c* 0.59, $CHCl_3$, 88% ee); **m.p.** 109.0-111.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.35-1.72 (m, 4H), 1.89-1.97 (m, 2H), 2.06-2.16 (m, 2H), 2.23-2.27 (m, 1H), 3.92-4.04 (m, 1H), 4.09-4.10 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.7, 24.8, 26.6, 28.3, 33.0, 45.9, 50.1, 111.4, 113.0, 122.7, 126.9, 137.8, 148.2, 149.0, 164.9; **IR** (ATR) 3339, 2925, 2362, 1737, 1655, 1520, 1365, 1217, 729 cm^{-1}; **HRMS** (ESI) calculated for $C_{15}H_{16}N_4NaO^+$ $[M+Na]^+$ 291.1222. found 291.1230; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 70:30, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 15.6, $t_{(1R,2S)}$ = 20.2 min.

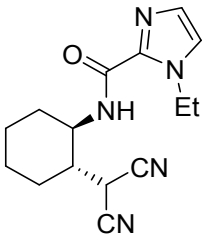
***N*-(2-(Dicyanomethyl)cyclohexyl)-1-methyl-1*H*-imidazole-2-carboxamide (2b);**



(1*S*,2*R*)-**2b**: **$[\alpha]_D^{25}$** −13.6 (*c* 0.72, $CHCl_3$, 97% ee); (1*R*,2*S*)-**2b**: **$[\alpha]_D^{25}$** +34.5 (*c* 0.59, $CHCl_3$, 94% ee); **m.p.** 151.0-152.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.29-1.52 (m, 3H), 1.54-1.68 (m, 1H), 1.87-1.94 (m, 2H), 1.98-2.12 (m, 2H), 2.21-2.25 (m, 1H), 3.84-3.96 (m, 1H), 4.06 (s, 3H), 4.11 (d, *J* = 3.3 Hz, 1H), 7.01 (s, 2H), 7.21 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.6, 24.8, 26.4, 28.1, 33.0, 35.8, 45.5, 49.5, 111.5, 112.9, 126.1, 127.8, 138.4, 159.5; **IR** (ATR) 3288, 2925, 2360, 1650, 1550, 1270, 1155, 825, 748, 658 cm^{-1}; **HRMS** (ESI) calculated for $C_{14}H_{17}N_5NaO^+$ $[M+Na]^+$ 294.1331. found 294.1330; **HPLC** (DAICEL CHIRALPAK ID-3,

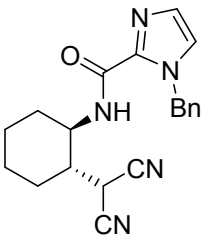
Hexane:*i*PrOH = 80:20, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 12.9, $t_{(1R,2S)}$ = 20.0 min.

***N*-((1*R*,2*S*)-2-(Dicyanomethyl)cyclohexyl)-1-ethyl-1*H*-imidazole-2-carboxamide** (**2c**);



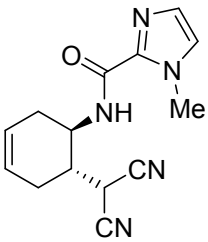
[α]$_D^{25}$ −24.2 (*c* 0.81, $CHCl_3$, 95% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.31-1.54 (m, 6H), 1.57-1.67 (m, 1H), 1.87-1.94 (m, 2H), 1.99-2.11 (m, 2H), 2.20-2.25 (m, 1H), 3.84-3.94 (m, 1H), 4.11 (d, *J* = 3.6 Hz, 1H), 4.44-4.61 (m, 2H), 7.01 (s, 1H), 7.07 (s, 1H), 7.35 (d, *J* = 9.0 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 16.7, 24.7, 24.8, 26.5, 28.2, 33.1, 43.5, 45.7, 49.6, 111.4, 112.9, 124.3, 128.0, 137.7, 159.3; **IR** (ATR) 3366, 2936, 2360, 1662, 1534, 1497, 1263, 1155, 765 cm^{-1}; **HRMS** (ESI) calculated for $C_{15}H_{19}N_5NaO^+$ $[M+Na]^+$ 308.1487. found 308.1493; **HPLC** (DAICEL CHIRALPAK IG, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 17.7, $t_{(1R,2S)}$ = 20.5 min.

1-Benzyl-*N*-((1*R*,2*S*)-2-(dicyanomethyl)cyclohexyl)-1*H*-imidazole-2-carboxamide (**2d**);



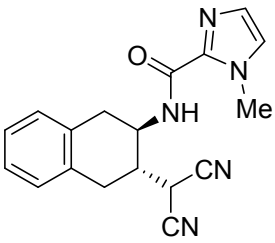
[α]$_D^{25}$ −23.6 (*c* 0.85, $CHCl_3$, 96% ee); **m.p.** 135.0-136.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.26-1.45 (m, 3H), 1.51-1.60 (m, 1H), 1.86-2.02 (m, 3H), 2.05-2.07 (m, 1H), 2.18-2.22 (m, 1H), 3.86-3.91 (m, 2H), 5.64-5.75 (m, 2H), 7.03 (s, 1H), 7.04 (s, 1H), 7.21-7.24 (m, 2H), 7.28-7.39 (m, 4H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.7, 24.8, 26.3, 28.1, 32.9, 45.8, 49.5, 51.6, 111.4, 112.9, 125.1, 127.9, 128.2, 128.3, 129.0, 136.6, 138.1, 159.4; **IR** (ATR) 3726, 3702, 3624, 3603, 2364, 2341, 2309, 1655, 1529, 1496, 1464, 784, 731, 669 cm^{-1}; **HRMS** (ESI) calculated for $C_{20}H_{21}N_5NaO^+$ $[M+Na]^+$ 370.1644. found 370.1653; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 17.4, $t_{(1R,2S)}$ = 20.1 min.

***N*-((1*R*,6*S*)-6-(Dicyanomethyl)cyclohex-3-en-1-yl)-1-methyl-1*H*-imidazole-2-carboxamide** (**2e**);



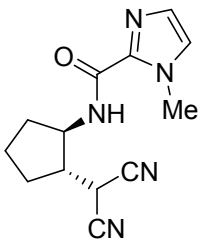
[α]$_D^{25}$ −40.6 (*c* 0.58, $CHCl_3$, 94% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.29-2.67 (m, 5H), 4.06 (s, 3H), 4.14 (d, *J* = 4.5 Hz, 1H), 4.19-4.24 (m, 1H), 5.73 (s, 2H), 7.01 (s, 2H), 7.41 (d, *J* = 8.7 Hz, 1H);**^{13}C NMR** (75 MHz, $CDCl_3$) δ 25.8, 28.1, 31.6, 35.9, 40.7, 46.8, 111.4, 112.5, 124.2, 125.0, 126.3, 127.9, 138.3, 159.5; **IR** (ATR) 3726, 3381, 3033, 2844, 1721, 1659, 1536, 1498, 1473, 1269, 1154, 734, 679 cm^{-1}; **HRMS** (ESI) calculated for $C_{14}H_{15}N_5NaO^+$ $[M+Na]^+$ 292.1174. found 292.1174; **HPLC** (DAICEL CHIRALPAK ID-3, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 209 nm) $t_{(1S,6R)}$ = 17.2, $t_{(1R,6S)}$ = 20.6 min.

***N*-((2*R*,3*S*)-3-(Dicyanomethyl)-1,2,3,4-tetrahydronaphthalen-2-yl)-1-methyl-1*H*-imidazole-2-carboxamide** (**2f**);



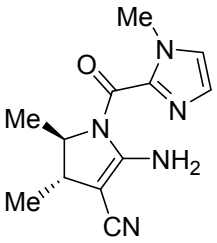
[α]$_D^{25}$ −33.1 (*c* 0.27, $CHCl_3$, 73% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.64-2.71 (m, 1H), 2.98-3.37 (m, 4H), 4.07 (s, 3H), 4.33 (d, *J* = 4.8 Hz, 1H), 4.37-4.40 (m, 1H),7.02 (s, 2H), 7.11-7.12 (m, 1H), 7.20-7.26 (m, 3H), 7.49 (d, *J* = 8.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 26.2, 31.8, 35.3, 35.9, 42.0, 47.8, 111.3, 112.5, 126.3, 127.2, 128.0, 128.8, 132.4, 133.0, 138.3, 159.7; **IR** (ATR) 3362, 2929, 2359, 2254, 1665, 1536, 1496, 1474, 1154, 909, 730 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{17}N_5NaO^+$ $[M+Na]^+$ 342.1331. found 342.1318; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 209 nm) $t_{(2S,3R)}$ = 26.8, $t_{(2R,3S)}$ = 30.0 min.

***N*-((1*R*,2*S*)-2-(Dicyanomethyl)cyclopentyl)-1-methyl-1*H*-imidazole-2-carboxamide** (**2g**);



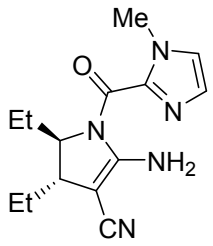
[α]$_D^{25}$ −13.3 (*c* 0.47, $CHCl_3$, 95% ee); **m.p.** 99.0-100.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.69-1.92 (m, 4H), 2.17-2.25 (m, 2H), 2.38-2.42 (m, 1H), 4.02 (s, 3H), 4.15-4.20 (m, 1H), 4.63 (d, *J* = 4.2 Hz, 1H), 6.98 (s, 1H), 6.98 (s, 1H), 7.47 (br, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 22.8, 26.5, 28.5, 32.4, 35.7, 48.2, 54.0, 112.2, 112.9, 126.0, 127.9, 138.3, 160.1; **IR** (ATR) 3390, 2969, 2360, 1735, 1655, 1506, 1281, 1091, 912, 731 cm^{-1}; **HRMS** (ESI) calculated for $C_{13}H_{15}N_5NaO^+$ $[M+Na]^+$ 280.1174. found 280.1173; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 14.5, $t_{(1R,2S)}$ = 16.5 min.

(4*S*,5*R*)-2-amino-4,5-dimethyl-1-(1-methyl-1*H*-imidazole-2-carbonyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (**2h**);



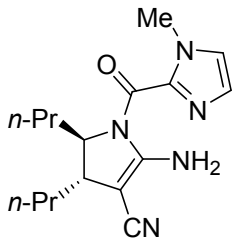
[α]$_D^{25}$ +56.0 (*c* 0.51, $CHCl_3$, 90% ee); **m.p.** 126.5-127.5 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.17-1.22 (m, 6H), 2.48-2.52 (m, 1H), 3.93 (s, 3H), 5.21 (br, 1H), 6.39 (br, 2H), 7.02 (s, 1H), 7.11 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 20.8, 21.7, 36.3, 40.9, 64.4, 66.4, 119.6, 125.9, 128.3, 138.7, 156.3, 160.3; **IR** (ATR) 3400, 2962, 2179, 1644, 1551, 1404, 1167, 987, 780, 658 cm^{-1}; **HRMS** (ESI) calculated for $C_{12}H_{15}N_5NaO^+$ $[M+Na]^+$ 268.1174. found 268.1174; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 215 nm) $t_{(4R,5S)}$ = 17.8, $t_{(4S,5R)}$ = 22.6 min.

(4*S*,5*R*)-2-amino-4,5-diethyl-1-(1-methyl-1*H*-imidazole-2-carbonyl)-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (**2i**);



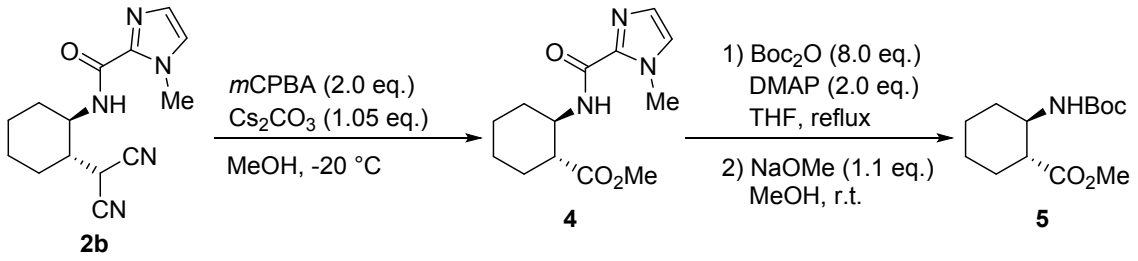
[α]$_D^{25}$ +46.7 (*c* 0.63, $CHCl_3$, 94% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.2 Hz, 3H), 1.00 (t, *J* = 7.2 Hz, 3H), 1.47-1.67 (m, 4H), 2.45-2.49 (m, 1H), 3.92 (s, 3H), 5.25 (br, 1H), 6.41 (br, 2H), 7.00 (s, 1H), 7.10 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 8.9, 10.7, 28.5, 36.2, 44.4, 64.7, 66.8, 120.0, 125.8, 128.3, 138.8, 157.4, 160.3; **IR** (ATR) 3726, 3700, 2970, 2366, 1468, 1434, 1376, 1334, 1158, 806, 754 cm^{-1}; **HRMS** (ESI) calculated for $C_{14}H_{19}N_5NaO^+$ $[M+Na]^+$ 396.1487. found 296.1491; **HPLC** (DAICEL CHIRALPAK ID-3, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 215 nm) $t_{(4S,5R)}$ = 22.2, $t_{(4R,5S)}$ = 25.1 min.

(4*S*,5*R*)-2-amino-1-(1-methyl-1*H*-imidazole-2-carbonyl)-4,5-dipropyl-4,5-dihydro-1*H*-pyrrole-3-carbonitrile (**2j**);



[α]$_D^{25}$ +15.9 (*c* 0.63, $CHCl_3$, 94% ee); **m.p.** 119.0-120.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 0.82 (t, *J* = 6.6 Hz, 3H), 0.90-1.00 (m, 3H), 1.25-1.27 (m, 3H), 1.37-1.62 (m, 5H), 2.49-2.53 (m, 1H), 3.92 (s, 3H), 5.34 (br, 1H), 6.42 (br, 2H), 7.01 (d, *J* = 0.6 Hz, 1H), 7.10 (d, *J* = 0.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 14.0, 14.2, 17.8, 19.6, 36.1, 37.6, 38.1, 43.2, 64.8, 66.1, 120.1, 125.7, 128.2, 138.8, 157.3, 160.4; **IR** (ATR) 3400, 2959, 2178, 1655, 1650, 1557, 1411, 1143, 771 cm^{-1}; **HRMS** (ESI) calculated for $C_{16}H_{23}N_5NaO^+$ $[M+Na]^+$ 324.1800. found 324.1797; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 90:10, 1.0 mL/min, 215 nm) $t_{(4R,5S)}$ = 28.4, $t_{(4S,5R)}$ = 36.1 min.

Transformation of 2b to various optically active compounds:

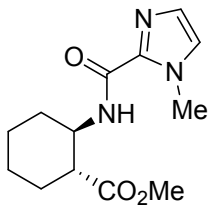


A solution of **2b** (97% ee, 85.7 mg, 0. 32 mmol) in MeOH (6.3 mL) was cooled to −20 °C and *m*-CPBA (141 mg, 0.63 mmol) was added to the solution followed by Cs_2CO_3 (116 mg, 0.33 mmol). After stirring for 30 min, the reaction mixture was diluted with H_2O and warmed to room temperature, and extracted with CH_2Cl_2 three times. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residure was purified by flash column chromatography (Et_2O/Hexane=95/5) to afford **4** in 67% yield (97% ee) as a colorless oil.

To a solution of **4** (97% ee, 21.6 mg, 0.08 mmol) and 4-dimethylaminopyridine (19.5 mg, 0.16 mmol) in THF (0.32 mL), di-*tert*-butyl dicarbonate (150 μL, 0.64 mmol) was added and refluxed for 14 h. The reaction mixture was cooled to room temperature and diluted with H_2O, and extracted with AcOEt three times. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residure was purified by flash column chromatography (Hexane/AcOEt=60/40) to afford *N*-Boc-β-aminoester in 79% yield (96% ee) as a colorless solid.

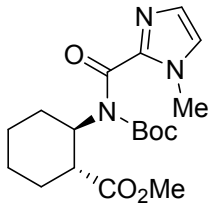
N-Boc-β-aminoester (96% ee, 24.6 mg, 0.067 mmol) was dissolved in MeOH (0.33 mL) and added NaOMe (4.0 mg, 0.074 mmol). After stirring for 24 h at room temperature, the reaction was quenched with HCl aq. (1.0 M, 0.6 mL), and the volatile was removed under reduced pressure. The residure was added H_2O and extracted with AcOEt three times. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/AcOEt=80/20) to afford **5** in 92% yield (96% ee) as a white solid.

Methyl (1*R*,2*R*)-2-(1-methyl-1*H*-imidazole-2-carboxamido)cyclohexane-1-carboxylate (**4**);



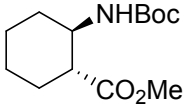
$[\alpha]_D^{25}$ −28.1 (*c* 1.06, $CHCl_3$, 98% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.23-1.46 (m, 3H), 1.62-1.78 (m, 3H), 1.96-2.01 (m, 1H), 2.06-2.11 (m, 1H), 2.43 (dt, *J* = 3.6, 11.1 Hz, 1H), 3.63 (s, 3H), 4.03 (s, 3H), 4.06-4.16 (m, 1H), 6.94 (s, 1H), 6.98 (s, 1H), 7.34 (d, *J* = 8.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.5, 24.6, 28.7, 32.6, 35.7, 49.3, 49.5, 51.9, 125.5, 127.5, 139.0, 158.5, 174.4; **IR** (ATR) 3377, 2933, 1733, 1662, 1540, 1266, 1173, 1020, 733 cm^{-1}; **HRMS** (ESI) calculated for $C_{13}H_{19}N_3NaO_3^+$ $[M+Na]^+$ 288.1324. found 288.1337; **HPLC** (DAICEL CHIRALPAK IC-3, Hexane:*i*PrOH = 70:30, 1.0 mL/min, 215 nm) $t_{(1R,2R)}$ = 10.6, $t_{(1S,2S)}$ = 17.3 min.

Methyl (1*R*,2*R*)-2-(*N*-(*tert*-butoxycarbonyl)-1-methyl-1*H*-imidazole-2-carboxamido) Cyclohexane-1-carboxylate;

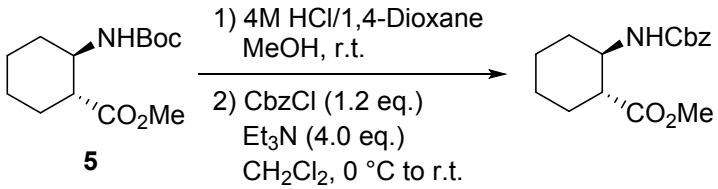


[α]$_D^{25}$ −23.3 (*c* 0.95, $CHCl_3$, 98% ee); **m.p.** 89.5-90.5 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.18-1.57 (m, 3H), 1.24 (s, 9H), 1.73-2.08 (m, 5H), 3.33 (dt, *J* = 3.6, 11.9 Hz, 1H), 3.62 (s, 3H), 3.84 (s, 3H), 4.47 (dt, *J* = 3.6, 11.9 Hz, 1H), 6.94 (s, 1H), 7.03 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.8, 25.7, 27.6, 29.2, 30.2, 34.3, 46.8, 51.8, 57.6, 82.7, 124.2, 128.3, 142.1, 153.2, 163.8, 174.8; **IR** (ATR) 2947, 1731, 1669, 1421, 1315, 1233, 1106, 768, 660 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{27}N_3NaO_5^+$ $[M+Na]^+$ 388.1848. found 388.1848; **HPLC** (DAICEL CHIRALPAK ID-3, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 215 nm) $t_{(1R,2R)}$ = 9.8, $t_{(1S,2S)}$ = 12.7 min.

Methyl (1*R*,2*R*)-2-((*tert*-butoxycarbonyl)amino)cyclohexane-1-carboxylate (5);[3]

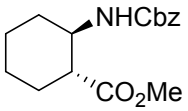


[α]$_D^{25}$ −5.8 (*c* 0.73, $CHCl_3$, 96% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.12-1.26 (m, 2H), 1.31-1.48 (m, 1H), 1.42 (s, 9H), 1.54-1.74 (m, 3H), 1.89-1.93 (m, 1H), 2.01-2.06 (m, 1H), 2.23 (dt, *J* = 3.3 Hz, 11.1 Hz, 1H), 3.62-3.63 (m, 1H), 3.67 (s, 3H), 4.50 (br, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.5, 24.9, 28.5, 28.6, 33.2. 50.4, 51.4, 51.9, 79.3, 155.1, 174.6; **HRMS** (ESI) calculated for $C_{13}H_{23}NnaO_4^+$ $[M+Na]^+$ 280.1525. found 280.1520.

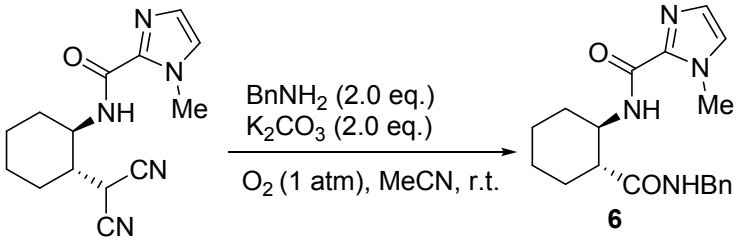


In order to determine the enantiomeric excess, we replaced the Boc group for **5** to Cbz group. **5** (96% ee, 9.0 mg, 0.035 mmol) was dissolved in MeOH (60 μL) and added hydrogen chloride (4 M in 1,4-dioxane, 530 μL). After stirring for 1 h at room temperature, the solution was removed under reduced pressure and the residure was suspended in CH_2Cl_2 (0.85 mL). The solution was cooled to 0 °C and added Et_3N (19.5 μL, 0.14 mmol) followed by benzyl chloroformate (5.9 μL, 0.042 mmol). After stirring overnight at room temperature, sat. $NaHCO_3$ aq. was added to the reaction mixture and extracted with CH_2Cl_2 three times. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Benzene/AcOEt=90/10) to afford *N*-Cbz-β-aminoester in 56% yield (97% ee) as a colorless oil.

Methyl (1*R*,2*R*)-2-(((benzyloxy)carbonyl)amino)cyclohexane-1-carboxylate;[3]

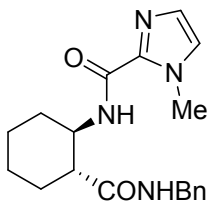


[α]$_D^{25}$ −10.6 (*c* 0.27, $CHCl_3$, 97% ee); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.16-1.25 (m, 2H), 1.32-1.41 (m, 1H), 1.58-1.76 (m, 3H), 1.89-1.96 (m, 1H), 2.05-2.08 (m, 1H), 2.23-2.30 (m, 1H), 3.62 (s, 3H), 3.68-3.76 (m, 1H), 4.71 (m, 1H), 5.07 (s, 2H), 7.29-7.38 (m, 5H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 24.4, 24.6, 28.6, 32.9, 49.8, 51.8, 66.6, 128.0, 128.5, 136.6, 155.4, 174.4; **HRMS** (ESI) calculated for $C_{16}H_{21}NaNO_4^+$ $[M+Na]^+$ 314.1368. found 314.1375.

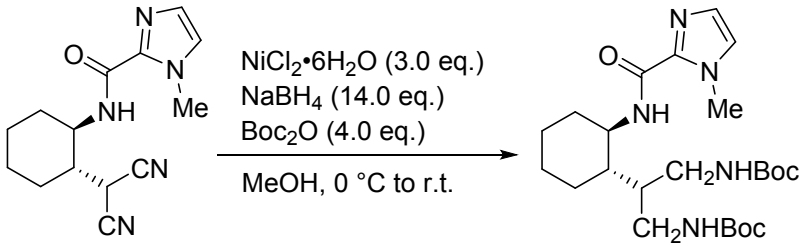


Compound **6** was synthesized by modified previous method.[4] To a solution of **2b** (98% ee, 27.1 mg, 0.1 mmol) and K_2CO_3 (27.6 mg, 0.2 mmol) in CH_3CN (1.0 mL), benzylamine (22.0 μL, 0.2 mmol) was added. The reaction mixture was stirred for 24 h under an oxygen atmosphere (balloon). The reaction mixture was diluted with $CHCl_3$ and filtrated through celite, and the volatile compounds were removed under reduced pressure. The crude product was purified by flash column chromatography (Hexane/AcOEt=20/80) to afford **6** in 91% yield (99% ee) as a colorless solid.

***N*-((1*R*,2*R*)-2-(Benzylcarbonyl)cyclohexyl)-1-methyl-1*H*-imidazole-2-carboxamide** (**6**);

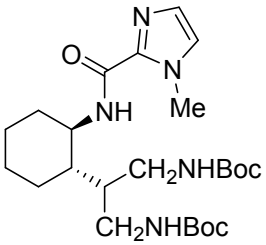


[α]$_D^{25}$ −16.9 (*c* 0.97, $CHCl_3$, 99% ee); **m.p.** 222.0-223.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.26-1.49 (m, 3H), 1.52-1.65 (m, 1H), 1.78-1.81 (m, 2H), 2.00-2.11 (m, 2H), 2.32-2.44 (m, 2H), 3.79 (s, 3H), 4.03-4.10 (m, 1H), 4.31-4.47 (m, 2H), 6.57 (s, 1H), 6.92 (s, 1H), 6.98 (s, 1H), 7.04-7.13 (m, 5H), 7.51 (d, *J* = 9.6 Hz, 1H);**^{13}C NMR** (75 MHz, $CDCl_3$) δ 25.1, 25.2, 30.4, 33.1, 35.6, 43.4, 49.6, 52.0, 125.6, 127.1, 127.3, 127.6, 128.3, 138.5, 138.8, 158.9, 173.7; **IR** (ATR) 3730, 3303, 2933, 2855, 2347, 1640, 1546, 1470, 1270, 743, 656 cm^{-1}; **HRMS** (ESI) calculated for $C_{19}H_{24}N_4NaO_2^+$ $[M+Na]^+$ 363.1797. found 363.1800.; **HPLC** (DAICEL CHIRALPAK ID-3, Hexane:*i*PrOH = 70:30, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 46.8, $t_{(1R,2S)}$ = 53.8 min.



A solution of **2b** (98% ee, 27.1 mg, 0.1 mmol) in MeOH (0.7 mL) was cooled to 0 °C and added di-*tert*-butyl dicarbonate (150 μL, 0.64 mmol) in MeOH (0.3 mL). Nickel chloride hexahydrate (71.3 mg, 0.3 mmol) was added to the reaction mixture, followed by sodium borohydride (53 mg, 1.4 mmol) was added at once. After stirring for 30 min at 0 °C, the reaction mixture was warmed to r.t. and stirred for 24 h. Diethylenetriamine (71 μL, 0.66 mmol) was added to the reaction mixture and stirred for 1 h. The mixture was diluted with AcOEt and washed with sat. $NaHCO_3$ aq., and dried over Na_2SO_4. The volatile compounds were removed under reduced pressure and the residure was purified by flash column chromatography (Hexane/Acetone=80/20) to afford **7** in 59% yield (98% ee) as a colorless solid.

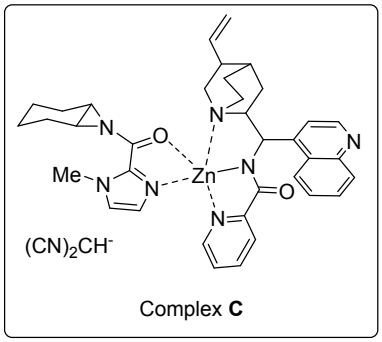
Di-*tert*-Butyl (2-((1*S*,2*R*)-2-(1-methyl-1H-imidazole-2-carboxamido)cyclohexyl)propane -1,3-diyl)dicarbamate (**7**);



$[\alpha]_D^{25}$ +7.1 (*c* 0.86, $CHCl_3$, 98% ee); **m.p.** 159.0-160.0 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.11-1.26 (m, 3H), 1.29-1.42 (m, 20H), 1.75-1.80 (m, 4H), 1.98-2.05 (m, 1H), 3.05-3.25 (m, 4H), 3.88-3.93 (m 1H), 4.06 (s, 3H), 5.29-5.36 (m, 2H), 6.97 (s, 1H), 6.99 (s, 1H), 7.30 (br 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 25.2, 25.4, 26.0, 28.5, 28.6, 33.7, 35.8, 39.5, 40.2, 41.9, 44.4, 49.5, 79.1, 125.7, 127.7, 159.2; **IR** (ATR) 3331, 2933, 1706, 1650, 1514, 1363, 1252, 1157, 720 cm^{-1}; **HRMS** (ESI) calculated for $C_{24}H_{41}N_5NaO_5^+$ $[M+Na]^+$ 502.3005. found 502.2996; **HPLC** (DAICEL CHIRALPAK IG, Hexane:*i*PrOH = 80:20, 1.0 mL/min, 215 nm) $t_{(1S,2R)}$ = 16.8, $t_{(1R,2S)}$ = 25.8 min.

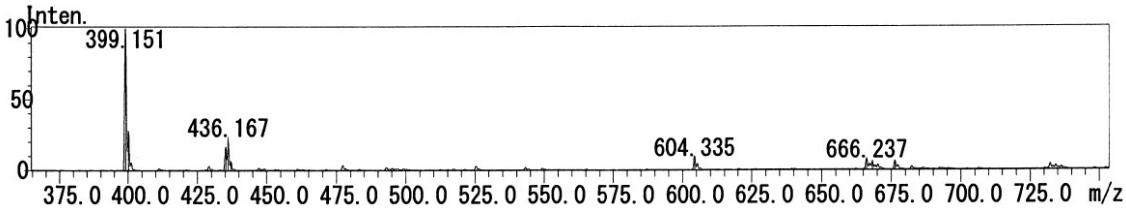
ESI-Mass spectroscopic analysis:

In order to clarify the assumed reaction mechanism, we investigated the ESI-Mass spectroscopic analysis of complex **C** (aziridine **1b** (0.1 mmol), malononitrile (5.0 equiv.), Et_2Zn (10 mol %), **3a** (12 mol %) in THF (0.2 M) , cation mode).

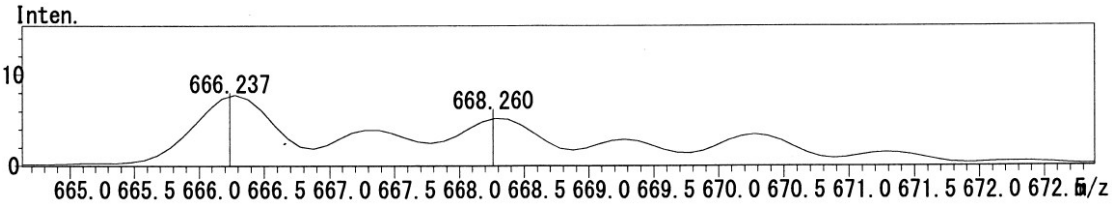


Complex **C**

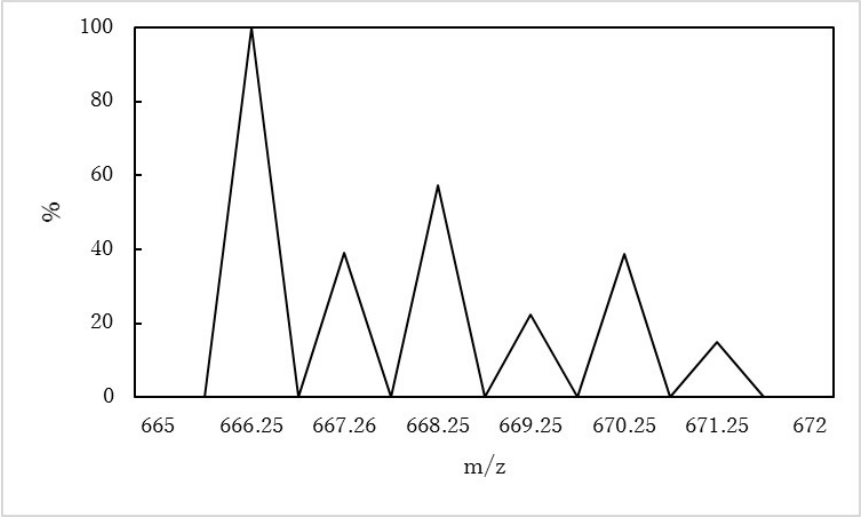
Calculated for [(complex **C**) - $(CN)_2CH^-]^+$ 666.2



Expanding spectra for [(complex **C**) - $(CN)_2CH^-]^+$



Simulated mass spectra



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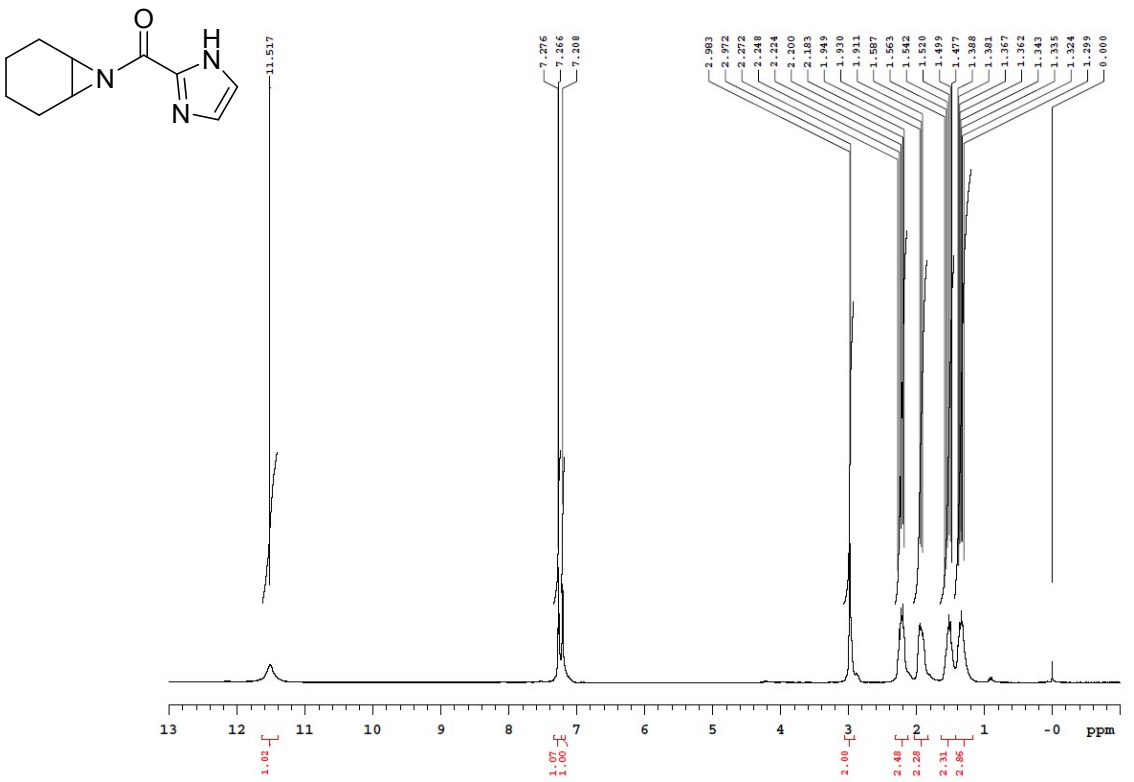
1) E. Galeazzi, A. GuzmBn, J. L. Navaz, *J. Org. Chem.*, 1995, **60**, 1990.

2) B. Lassalle-Kaiser, R. Guillot, J. Sainton, M.-F. Charlot, A. Aukauloo, *Chem. Eur. J.*, 2008, **14**, 4307.

3) D. H. Appella, P. R. LePlae, T. L. Raguse, S. H. Gellman, *J. Org. Chem.*, 2000, **65**, 4766.

4) J. Li, M. J. Lear, Y. Hayashi, *Angew. Chem. Int. Ed.*, 2016, **55**, 9060.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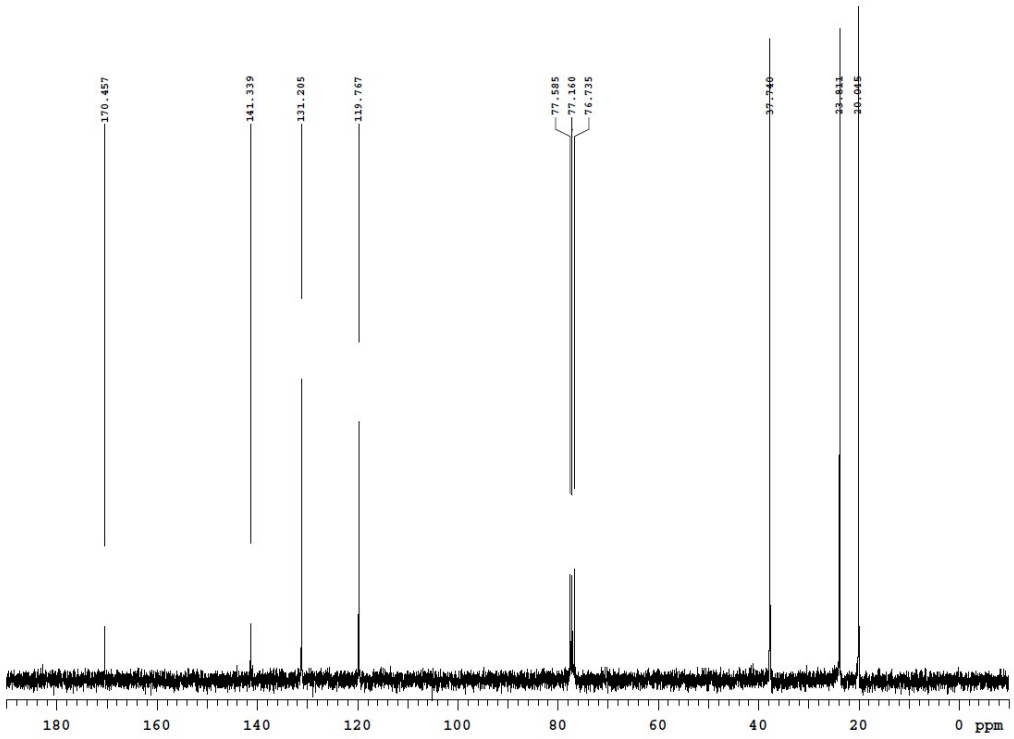
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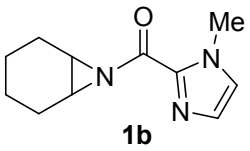
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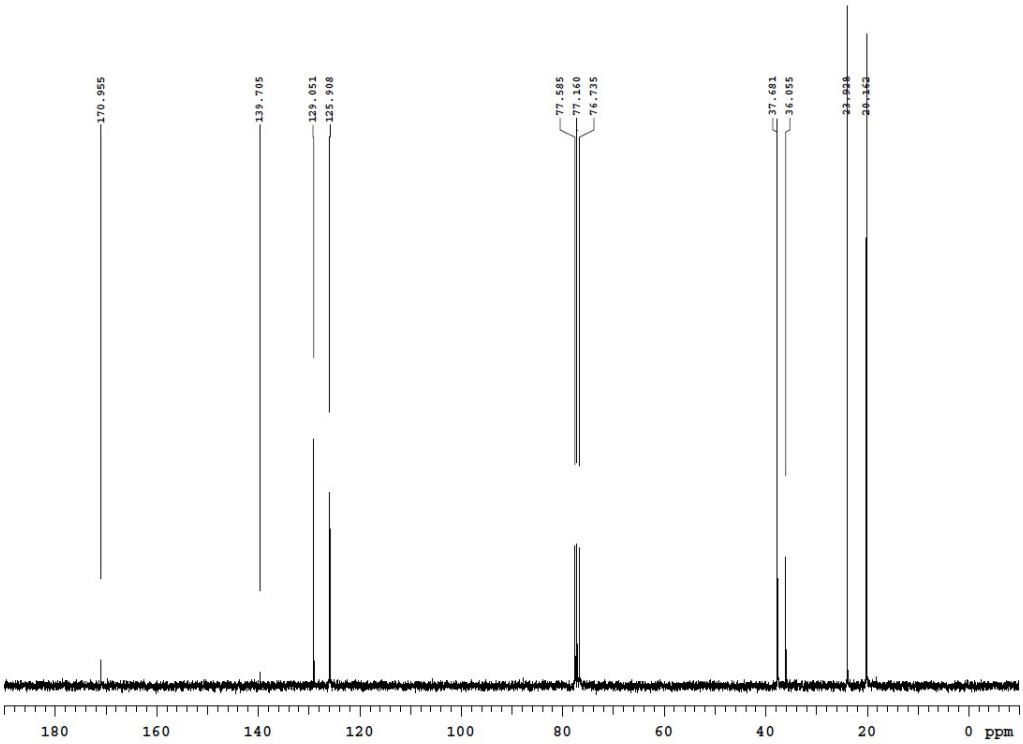
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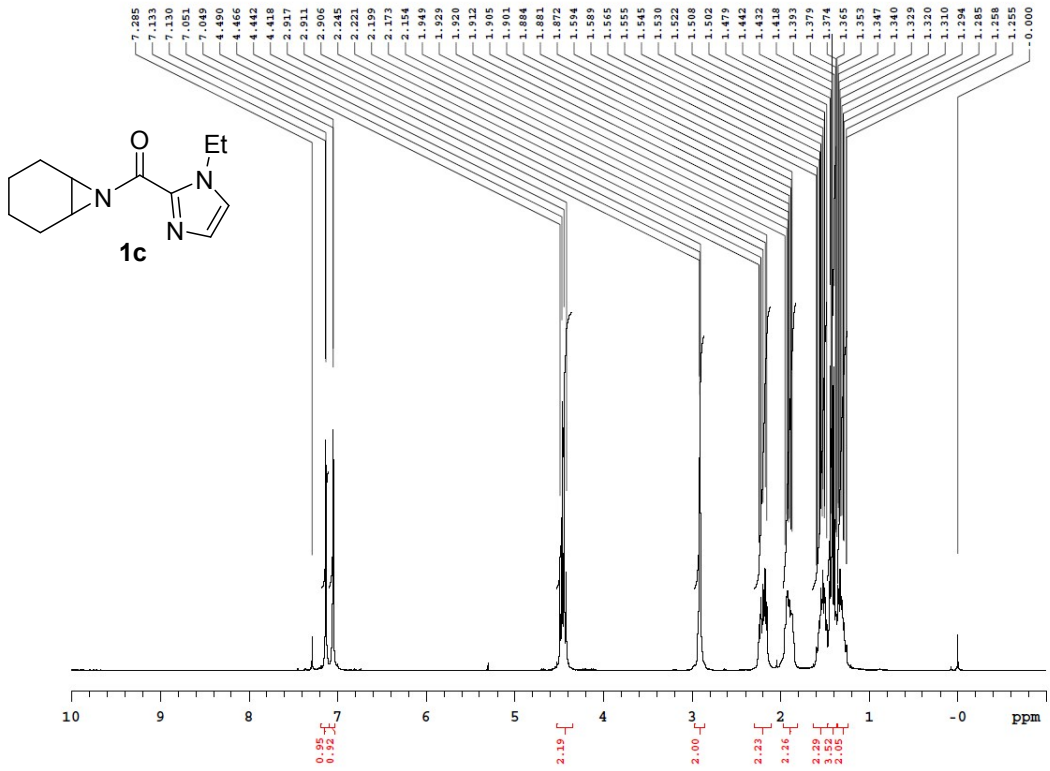
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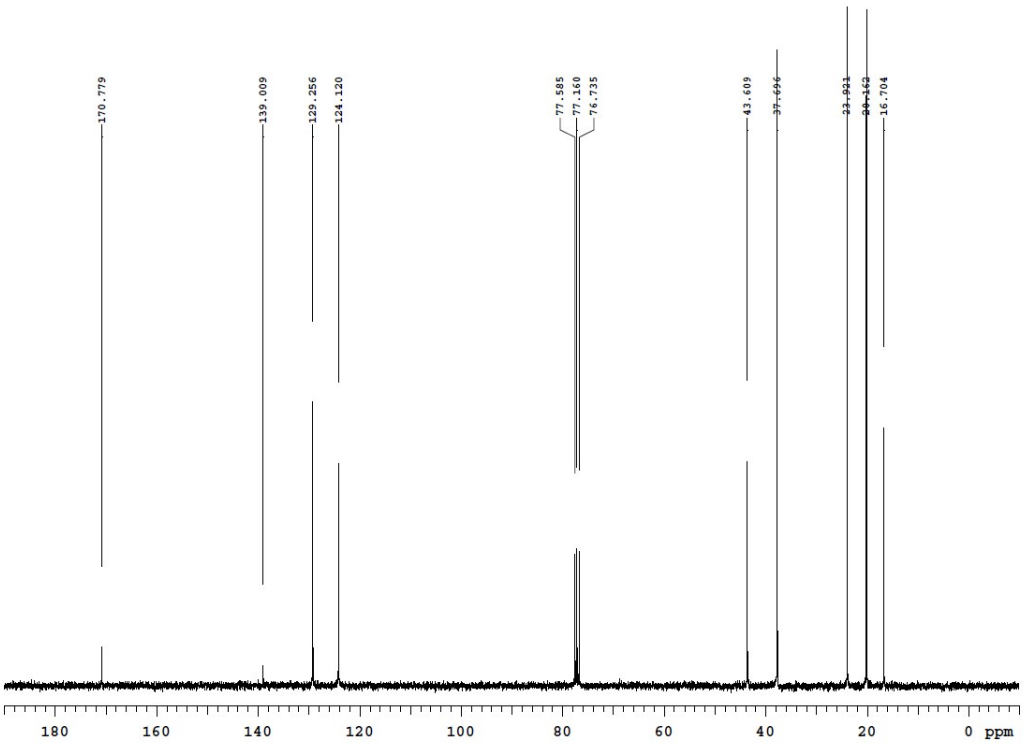
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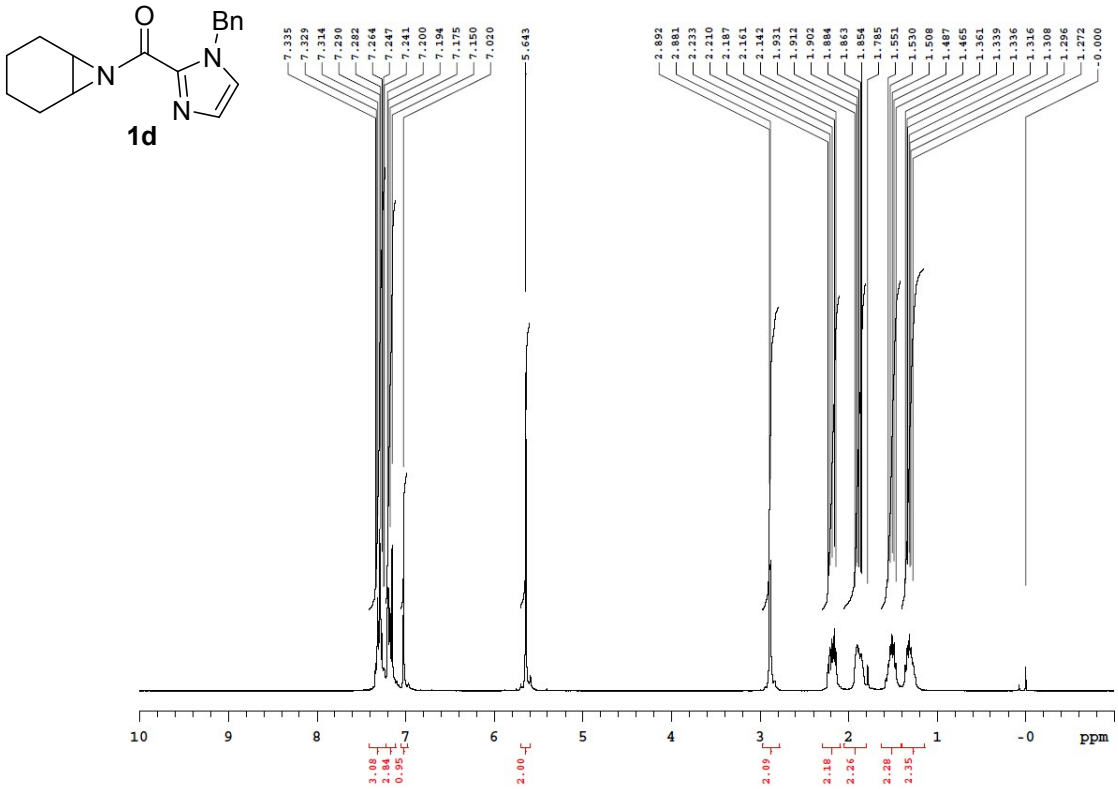
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1.854
1.785
1.551
1.530
1.508
1.487
1.465
1.361
1.339
1.336
1.316
1.308
1.296
1.272
-0.000
10
9
8
7
6
5
4
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2.00
2.09
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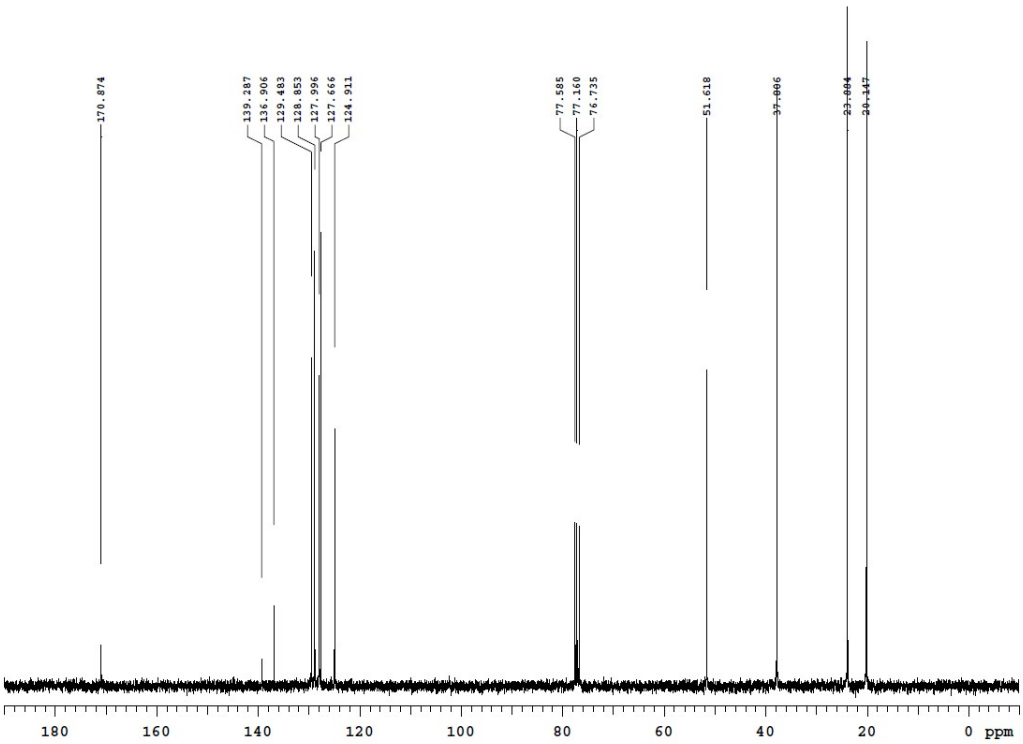
2.26
2.28
2.35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124.911
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20.147
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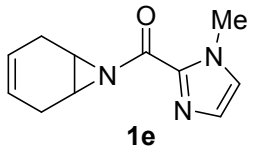
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Me
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N

1e

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2.868
2.807
2.501
2.439
1.713
-0.000
10
9
8
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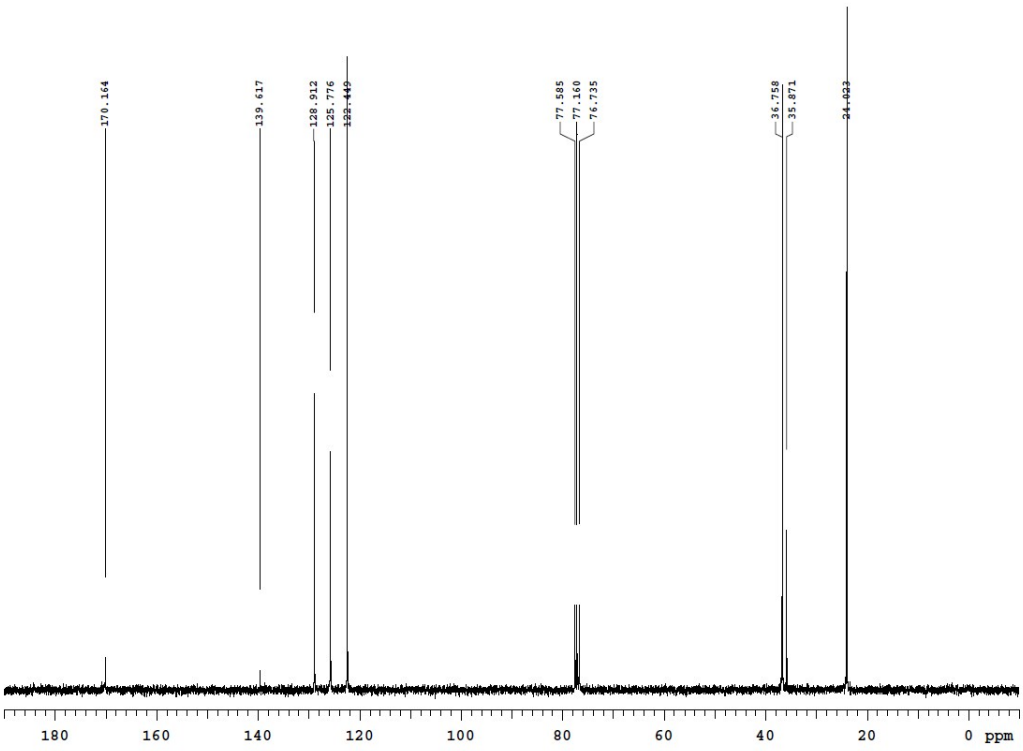
2.31
2.31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24.033
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140
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60
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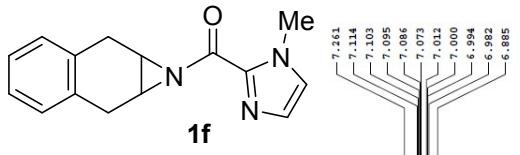
O
Me
N
N
N

1f

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7.073
7.012
7.000
6.994
6.982
6.885
3.703
3.550
3.493
3.334
3.212
3.156
1.690
0.000
10
9
8
7
6
5
4
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2
1
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ppm
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0.95
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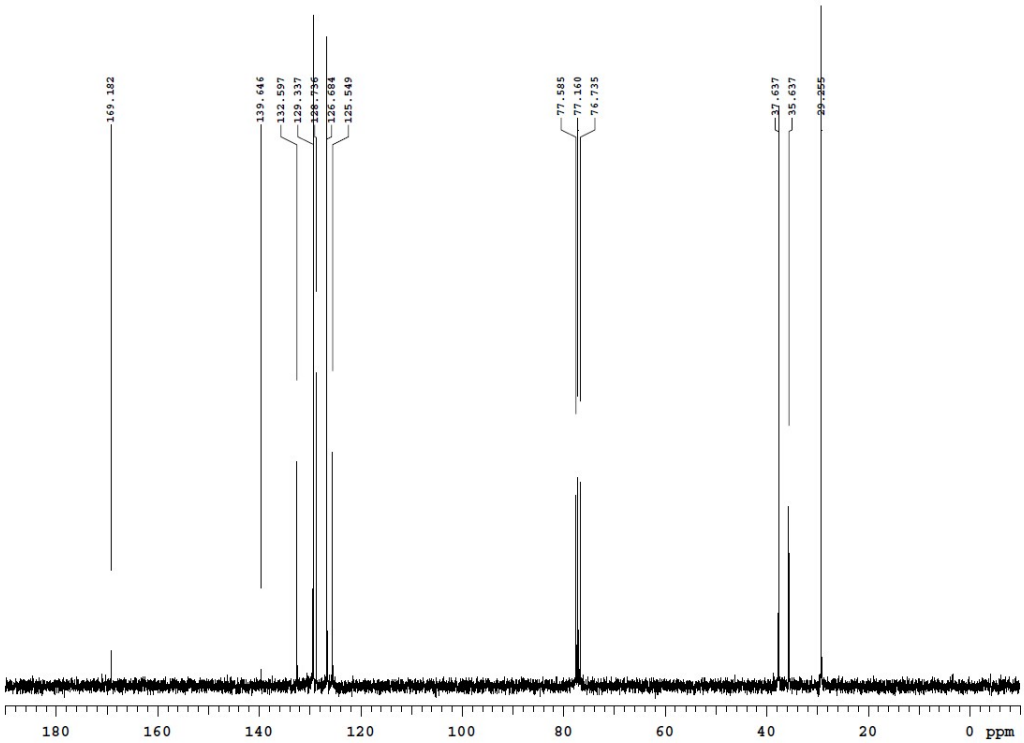
1.99
2.12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125.549
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77.160
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37.637
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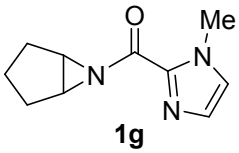
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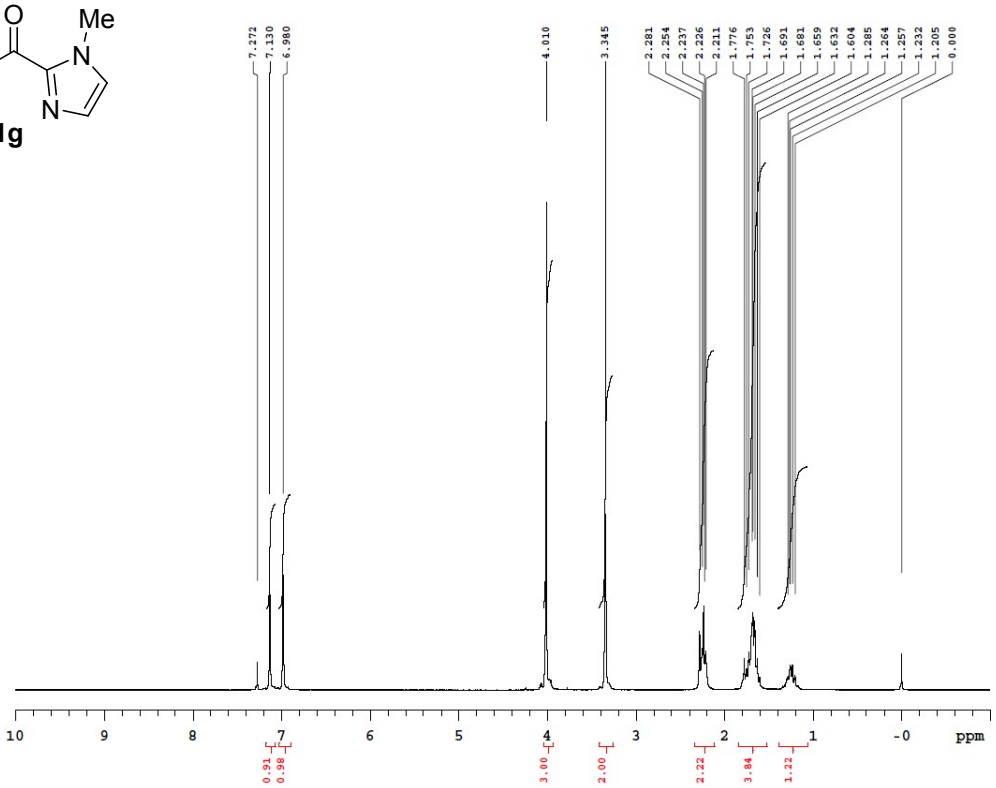
N
N
N

1g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2.237
2.226
2.211
1.776
1.753
1.726
1.691
1.681
1.659
1.632
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1.285
1.264
1.257
1.232
1.205
0.000
10
9
8
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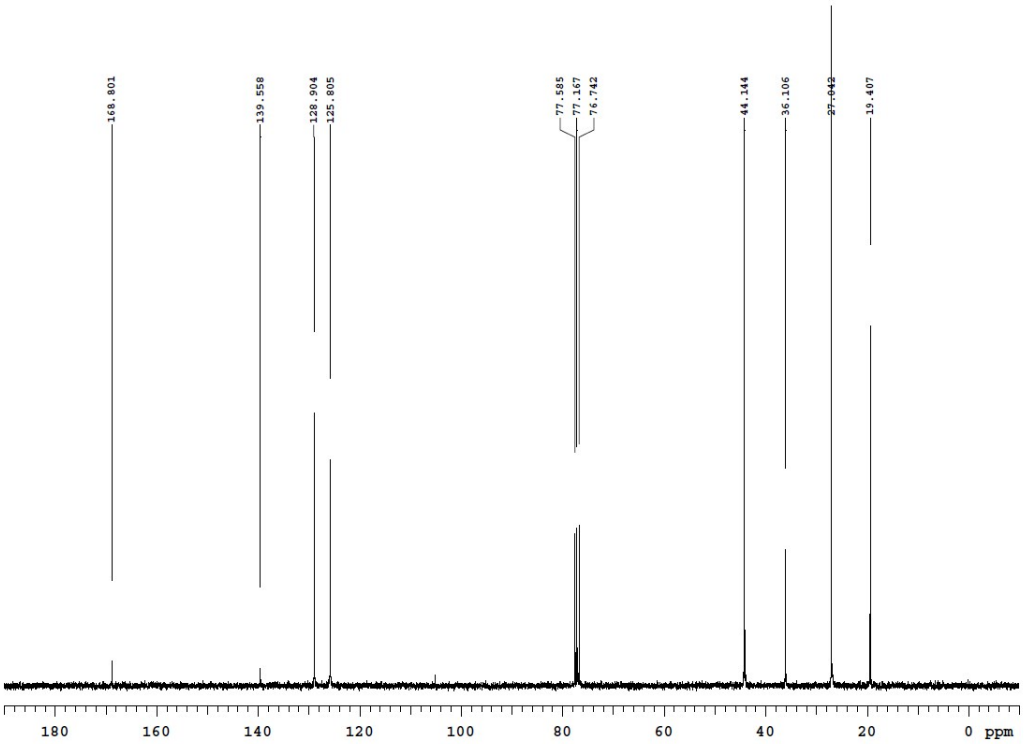
1.22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77.167
76.742
44.144
36.106
27.042
19.407
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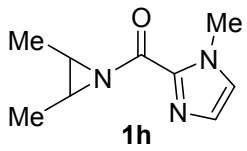
140
120
100
80
60
40
20
0 ppm


Me
O
Me
N
N
Me
N

1h

7.268
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6.987
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2.793
2.780
2.775
2.768
2.762
2.749
1.437
1.421
1.403
1.388
-0.000
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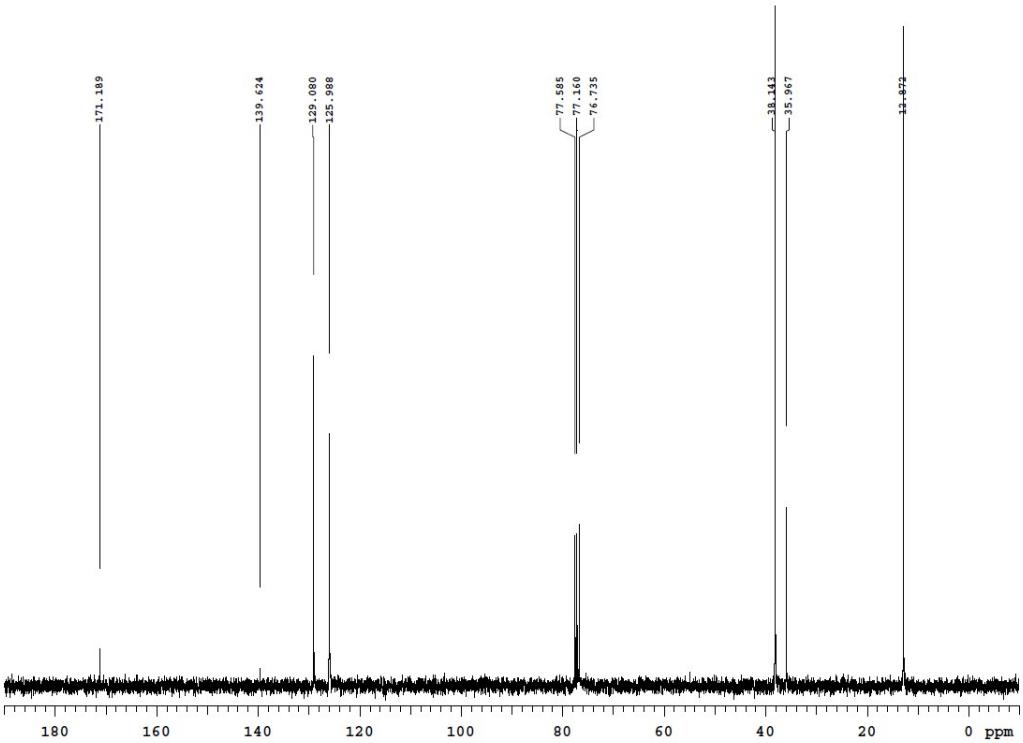
9
8
7
6
5
4
3
2
1
-0
ppm
0.90
0.94
3.05
2.00
6.41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129.080
125.988
77.585
77.160
76.735
38.143
35.967
13.872
180
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140
120
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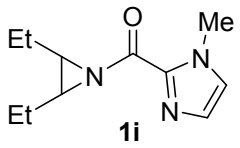
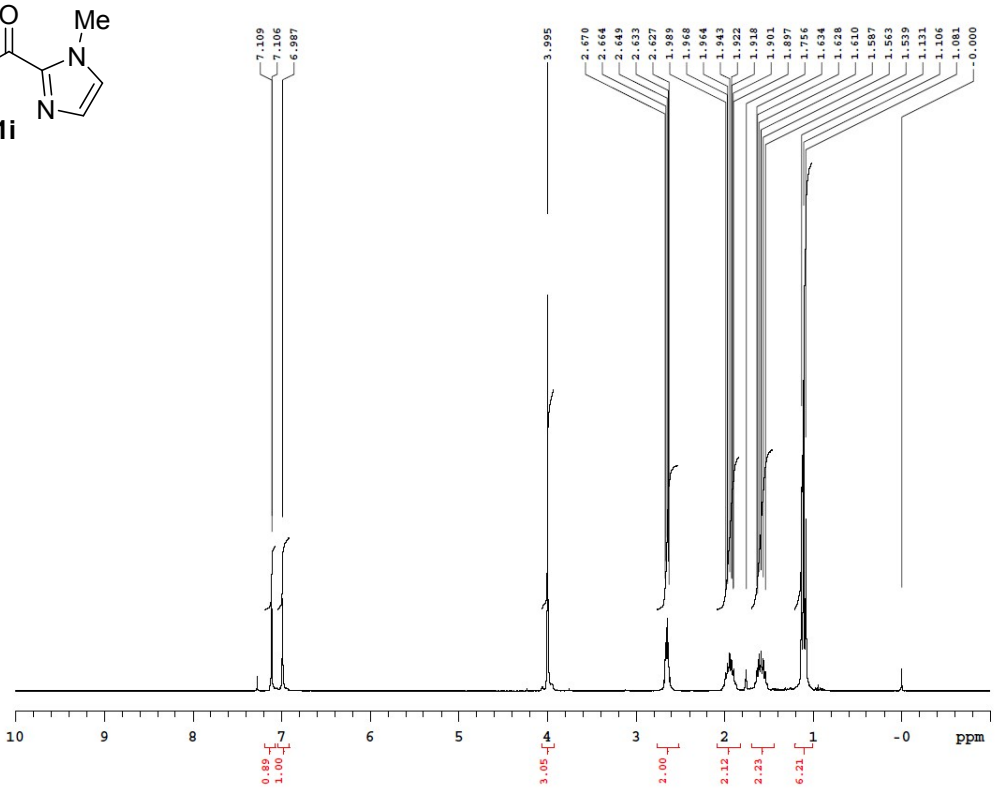
80
60
40
20
0 ppm


Et
O
Me
N
N
Et
N

1i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7.106
6.987
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2.664
2.649
2.633
2.627
1.989
1.968
1.964
1.943
1.922
1.918
1.901
1.897
1.756
1.634
1.628
1.610
1.587
1.563
1.539
1.131
1.106
1.081
-0.000
10
9
8
7
6
5
4
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2
1
-0
ppm
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3.05
2.00
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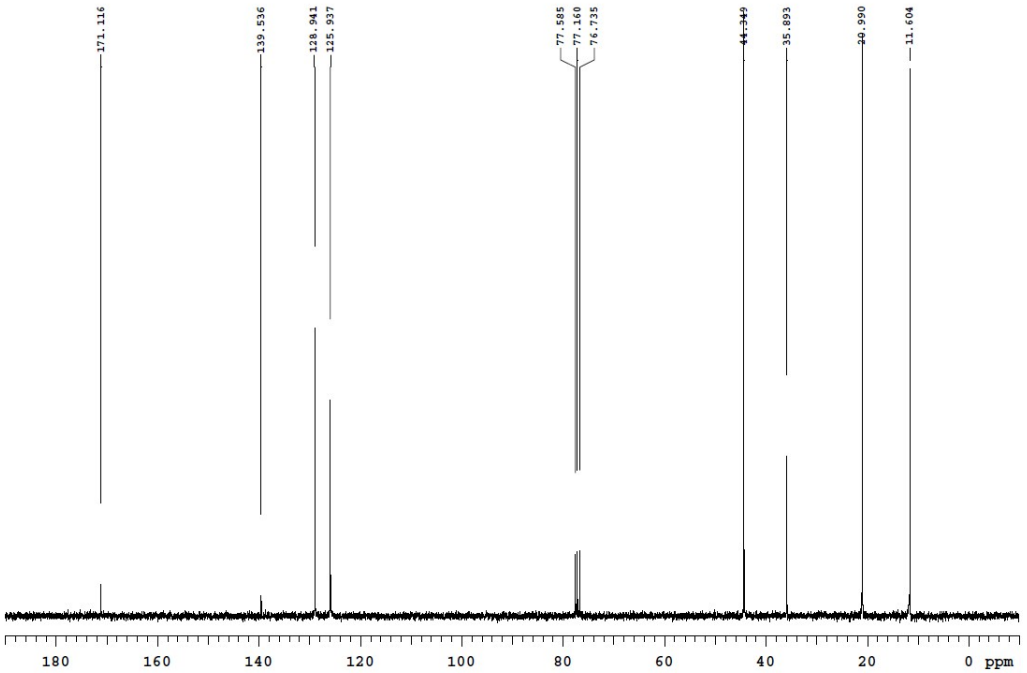
2.23
6.21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128.941
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77.585
77.160
76.735
44.349
35.893
20.990
11.604
180
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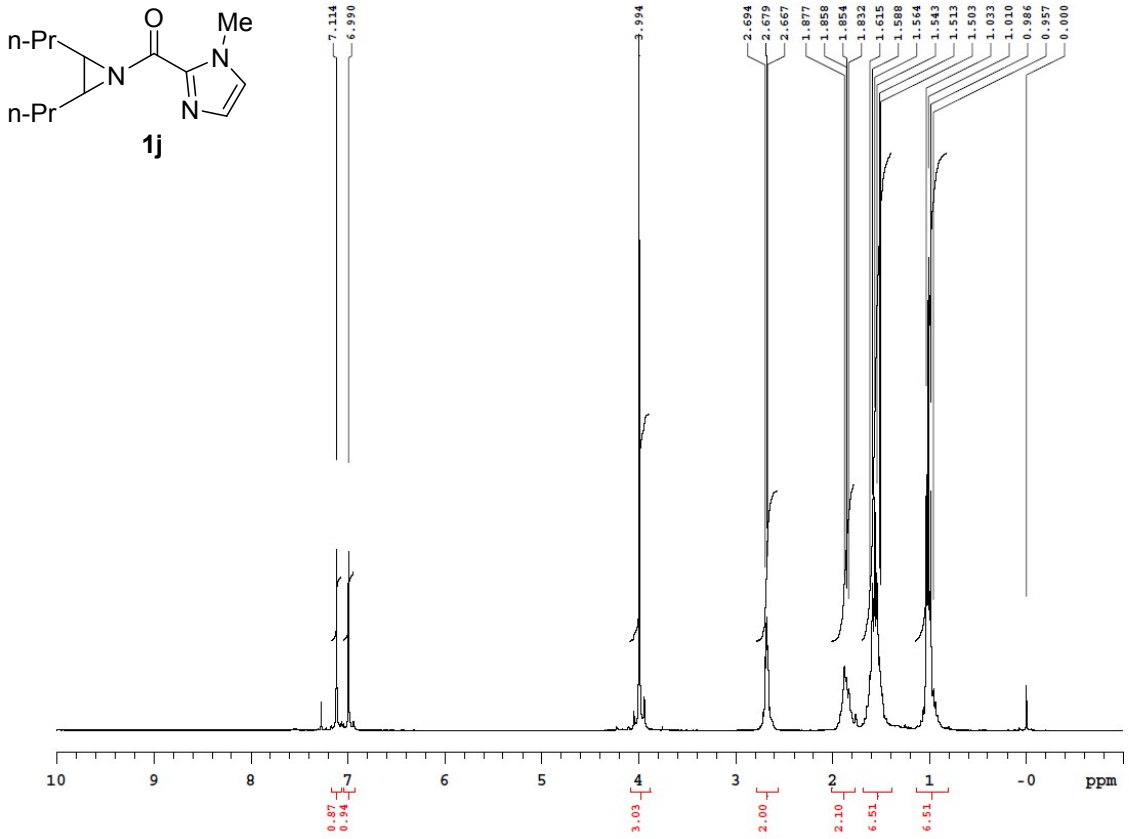
140
120
100
80
60
40
20
0 ppm


n-Pr
n-Pr
O
N
N
Me
N
1j
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2.694
2.679
2.667
1.877
1.858
1.854
1.832
1.615
1.588
1.564
1.543
1.513
1.503
1.033
1.010
0.986
0.957
0.000
10
9
8
7
6
5
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2
1
-0
ppm
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0.94
3.03
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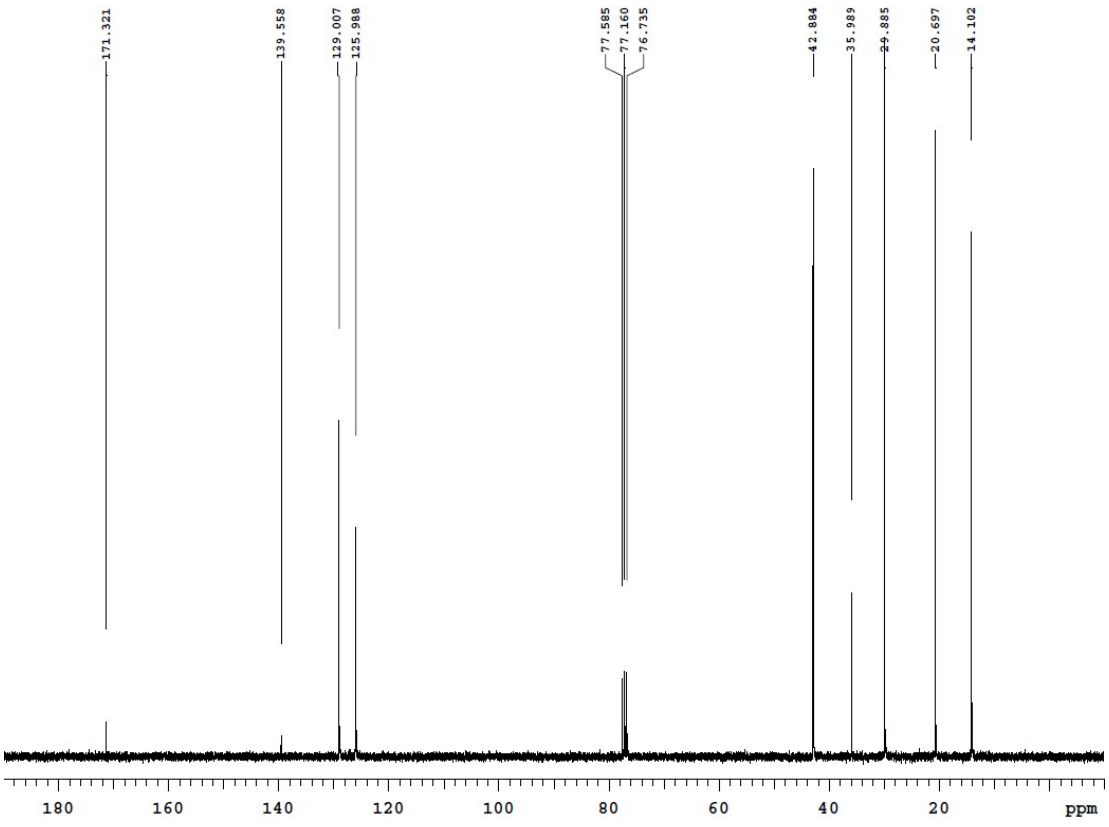
2.10
6.51
6.51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77.160
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29.885
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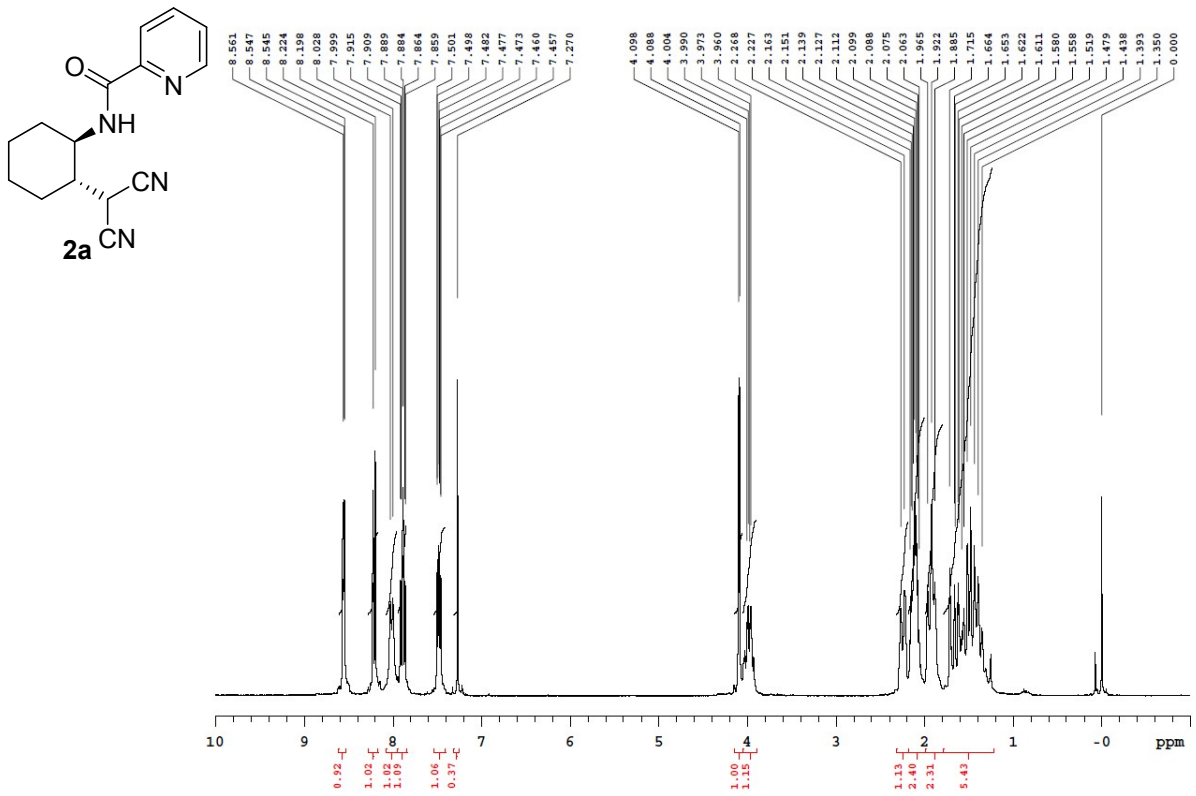
140
120
100
80
60
40
20
ppm


O
N
NH
CN
CN
2a
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8.547
8.545
8.224
8.198
8.028
7.999
7.915
7.909
7.889
7.884
7.864
7.859
7.501
7.498
7.482
7.477
7.473
7.460
7.457
7.270
4.098
4.088
4.004
3.990
3.973
3.960
2.268
2.227
2.163
2.151
2.139
2.127
2.112
2.099
2.088
2.075
2.063
1.965
1.922
1.885
1.715
1.664
1.653
1.622
1.611
1.580
1.558
1.519
1.479
1.438
1.393
1.350
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
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1.02
1.09
1.06
0.37
1.00
1.15
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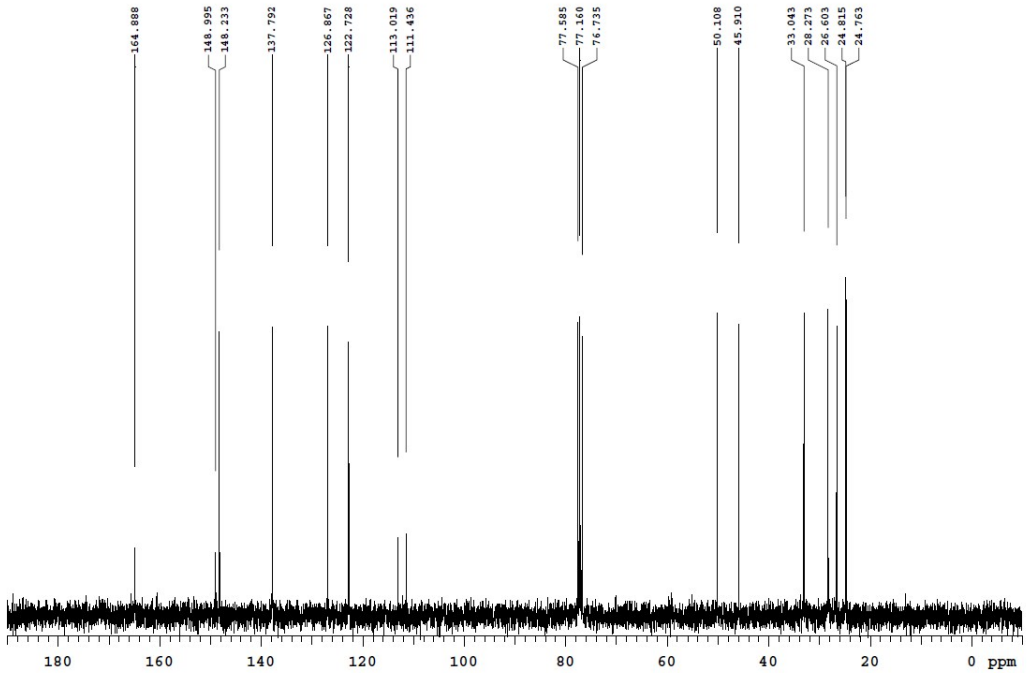
2.31
5.43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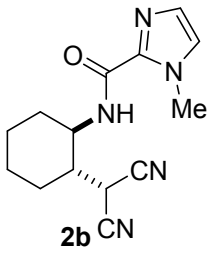
113.019
111.436
77.585
77.160
76.735
50.108
45.910
33.043
28.273
26.603
24.815
24.763
180
160
140
120
100
80
60
40
20
0 ppm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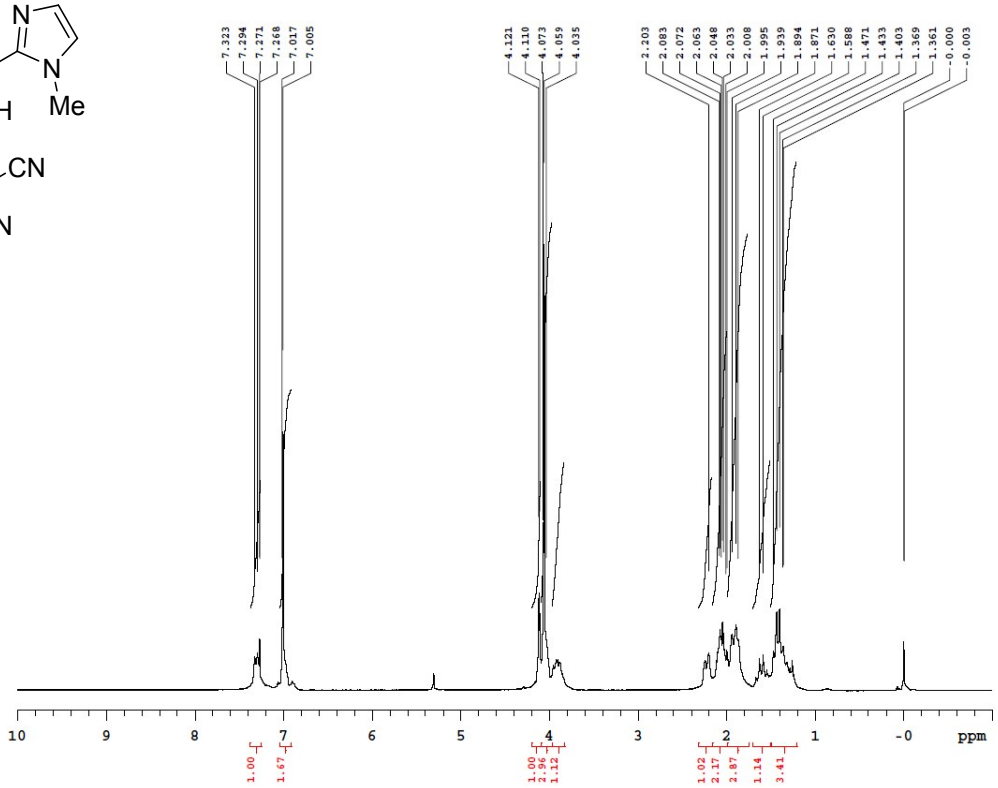
N
N
Me
NH
CN
CN
2b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7.005
4.121
4.110
4.073
4.059
4.035
2.203
2.083
2.072
2.063
2.048
2.033
2.008
1.995
1.939
1.894
1.871
1.630
1.588
1.471
1.433
1.403
1.369
1.361
-0.000
-0.003
10
9
8
7
6
5
4
3
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-0
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1.02
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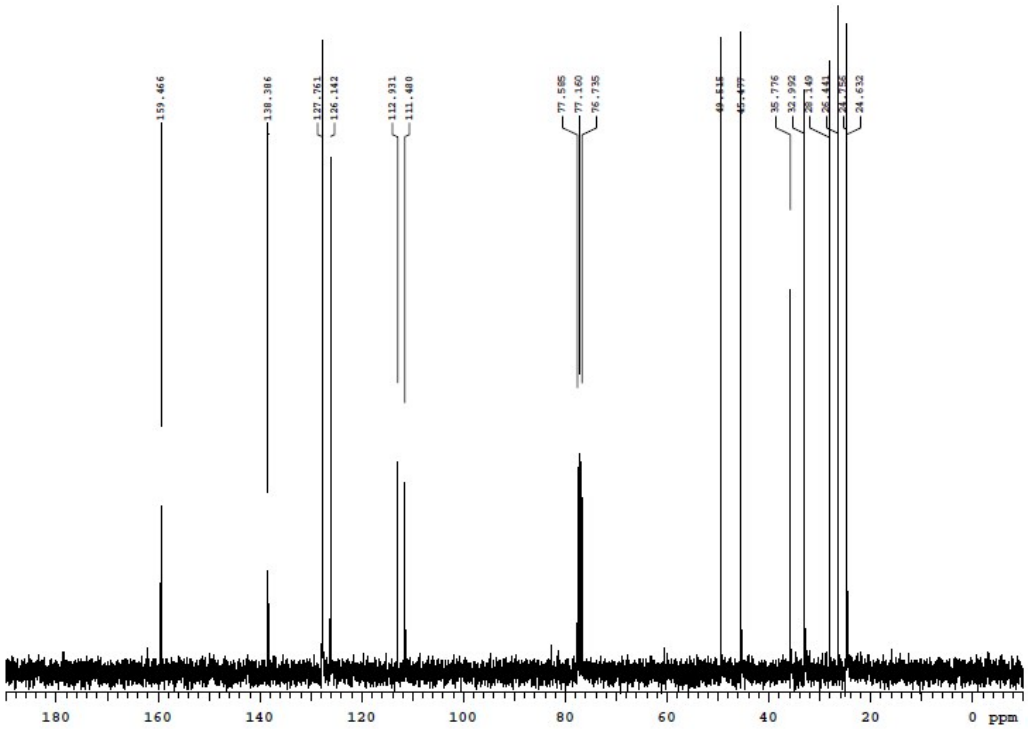
3.41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77.585
77.160
76.735
49.815
49.477
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32.992
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25.441
24.756
24.632
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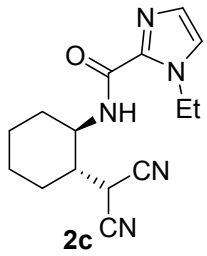
160
140
120
100
80
60
40
20
0 ppm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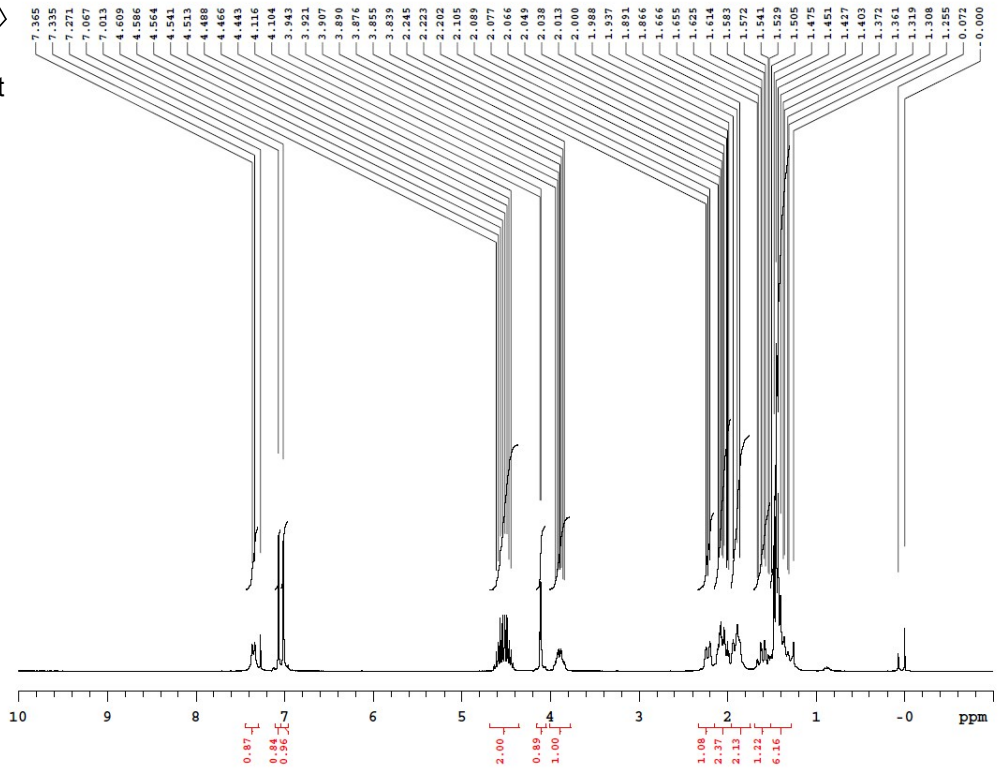
N
N
Et
NH
CN
CN

2c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4.564
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4.513
4.488
4.466
4.443
4.116
4.104
3.943
3.921
3.907
3.890
3.876
3.855
3.839
2.245
2.223
2.202
2.105
2.089
2.077
2.066
2.049
2.038
2.013
2.000
1.988
1.937
1.891
1.866
1.666
1.655
1.625
1.614
1.583
1.572
1.541
1.529
1.505
1.475
1.451
1.427
1.403
1.372
1.361
1.319
1.308
1.255
0.072
-0.000
10
9
8
7
6
5
4
3
2
1
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1.08
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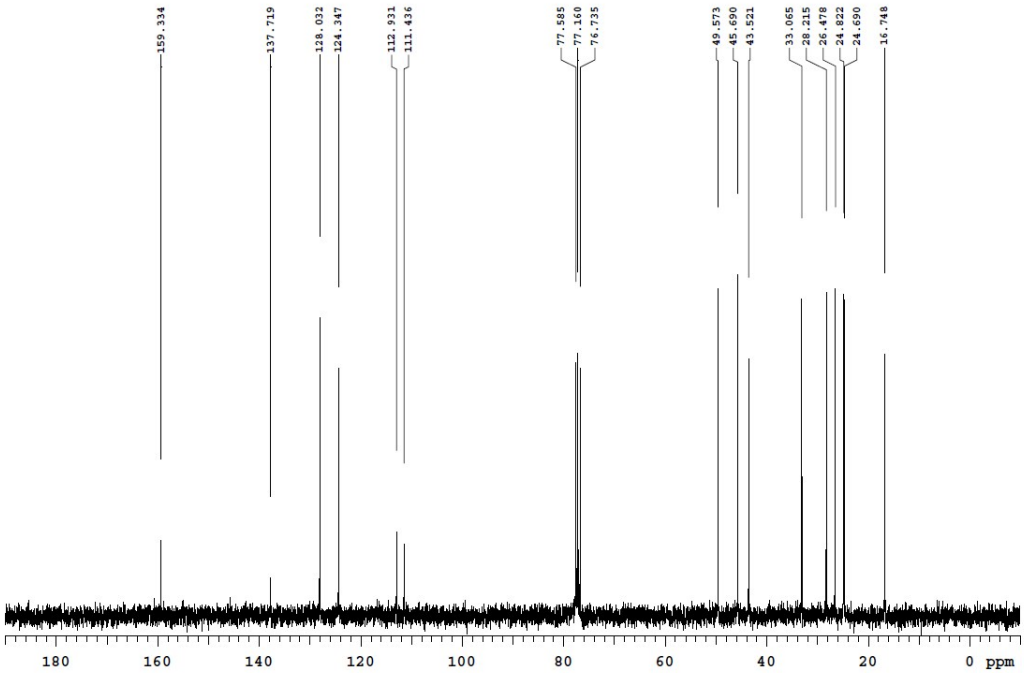
2.13
1.22
6.16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77.160
76.735
49.573
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43.521
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24.822
24.690
16.748
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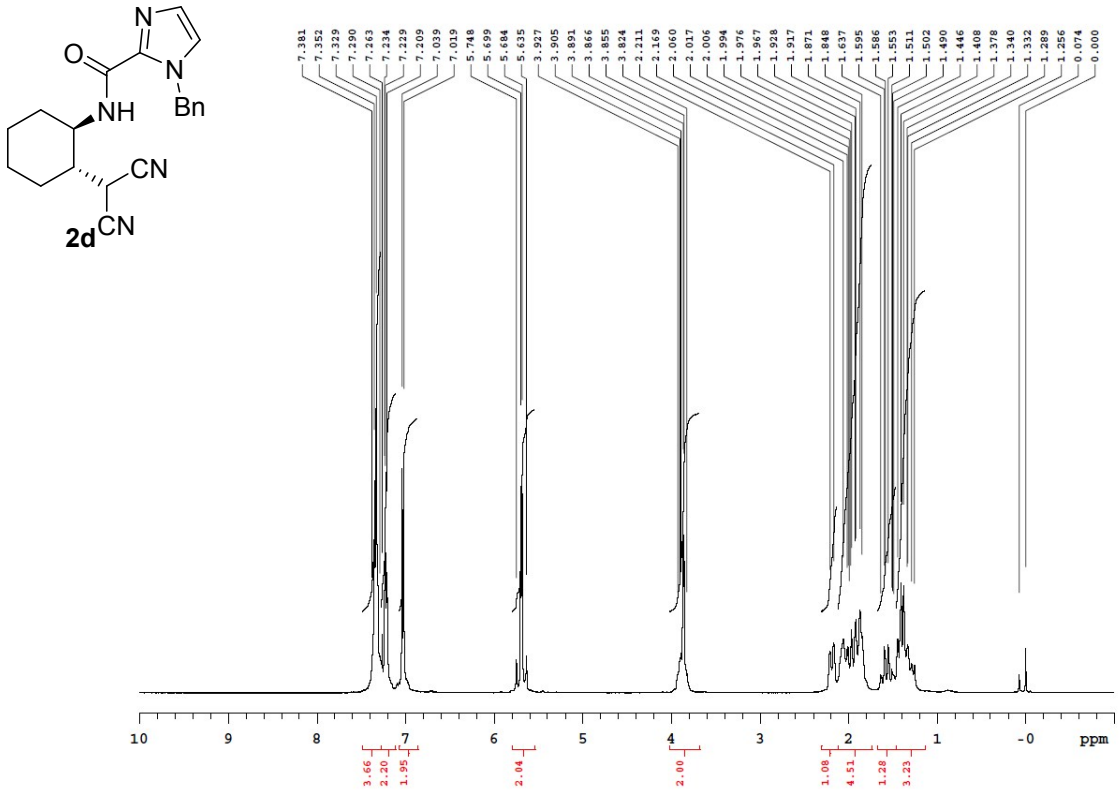
160
140
120
100
80
60
40
20
0 ppm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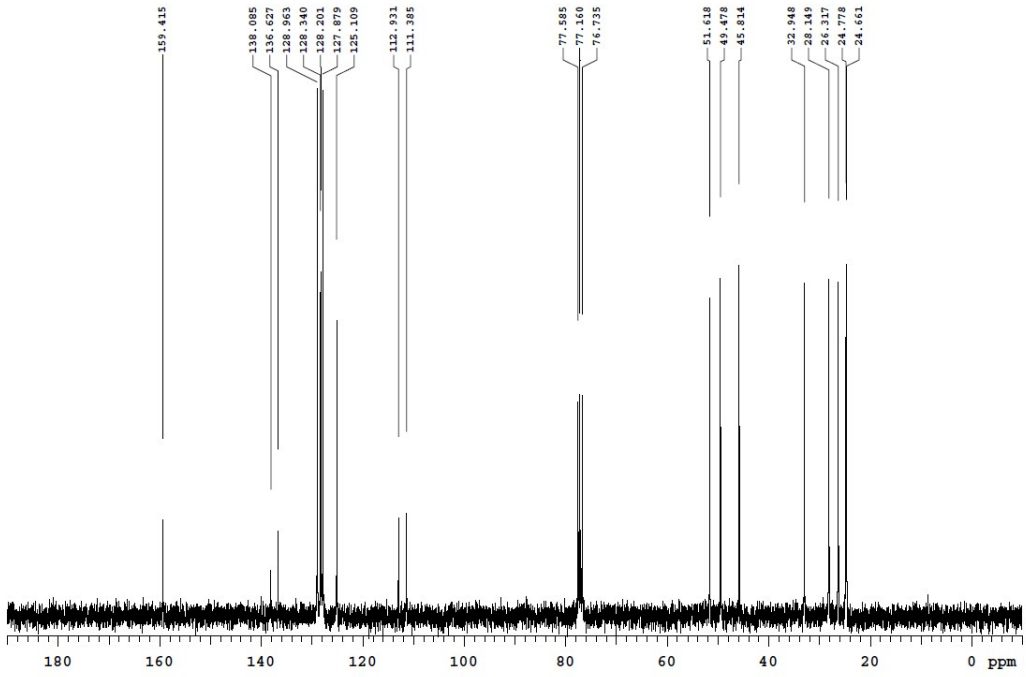

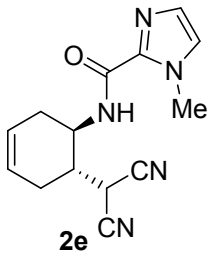
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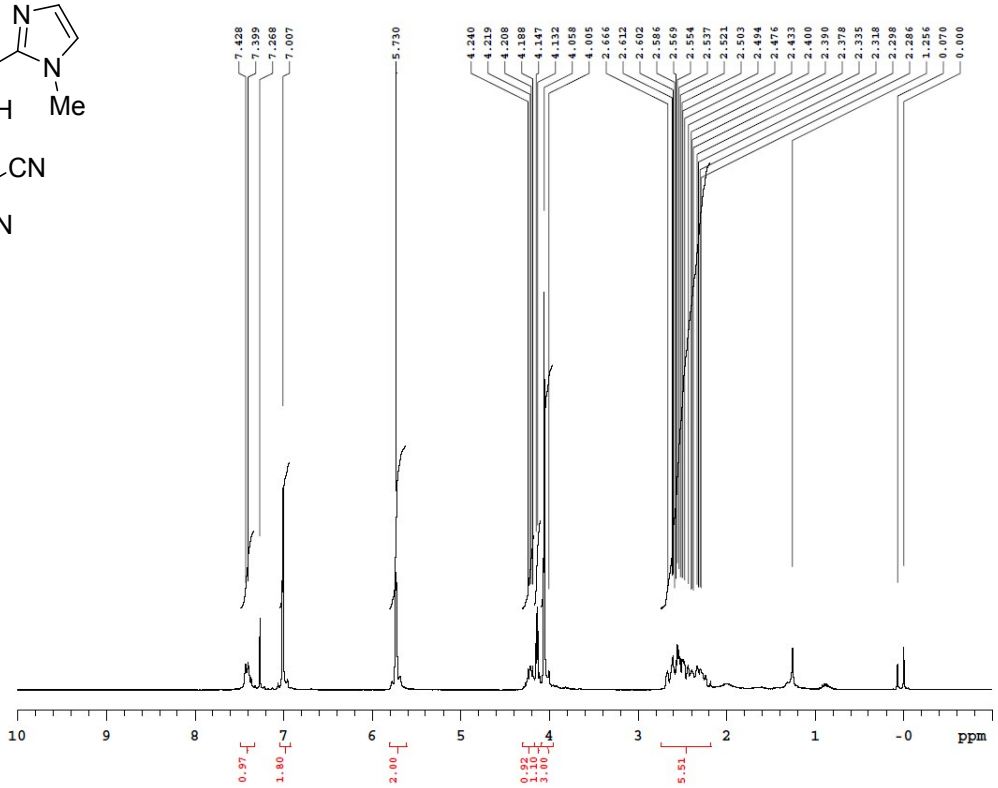
N
Me
NH
CN
CN
2e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4.188
4.147
4.132
4.058
4.005
2.666
2.612
2.602
2.586
2.569
2.554
2.537
2.521
2.503
2.494
2.476
2.433
2.400
2.390
2.378
2.335
2.318
2.298
2.286
1.256
0.070
0.000
10
9
8
7
6
5
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2
1
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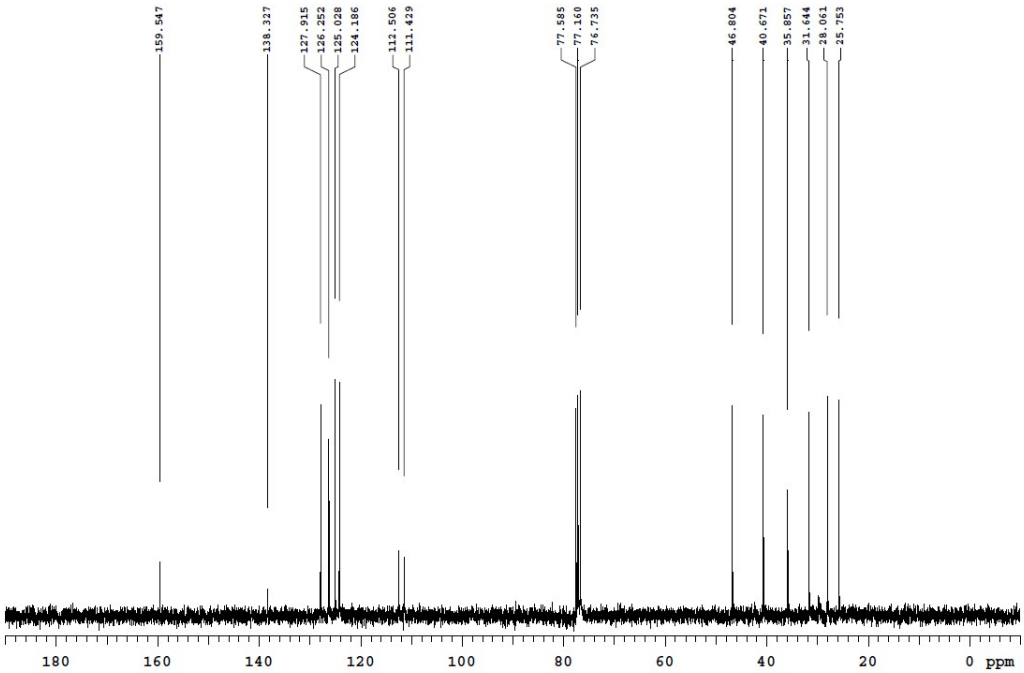
5.51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126.252
125.028
124.186
112.506
111.429
77.585
77.160
76.735
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31.644
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25.753
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140
120
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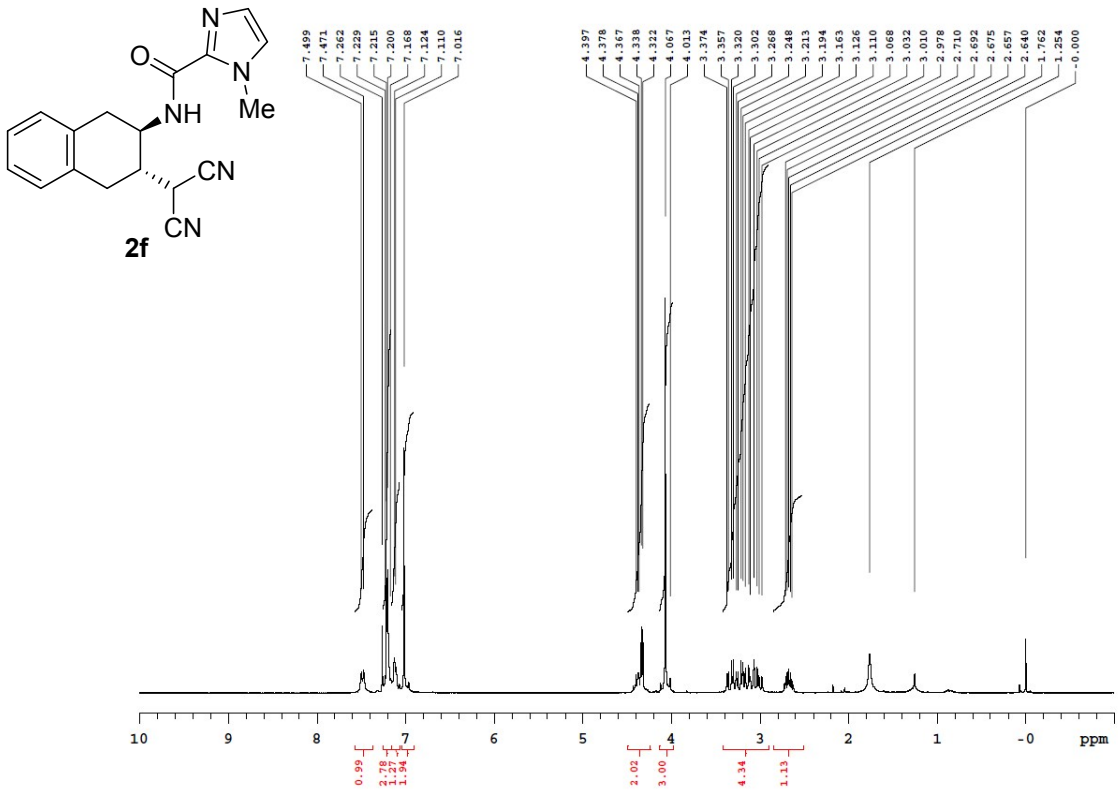
80
60
40
20
0 ppm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O
N
Me
NH
CN
CN
2f
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7.262
7.229
7.215
7.200
7.168
7.124
7.110
7.016
4.397
4.378
4.367
4.338
4.322
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4.013
3.374
3.357
3.320
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3.268
3.248
3.213
3.194
3.163
3.126
3.110
3.068
3.032
3.010
2.978
2.710
2.692
2.675
2.657
2.640
1.762
1.254
-0.000
10
9
8
7
6
5
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2
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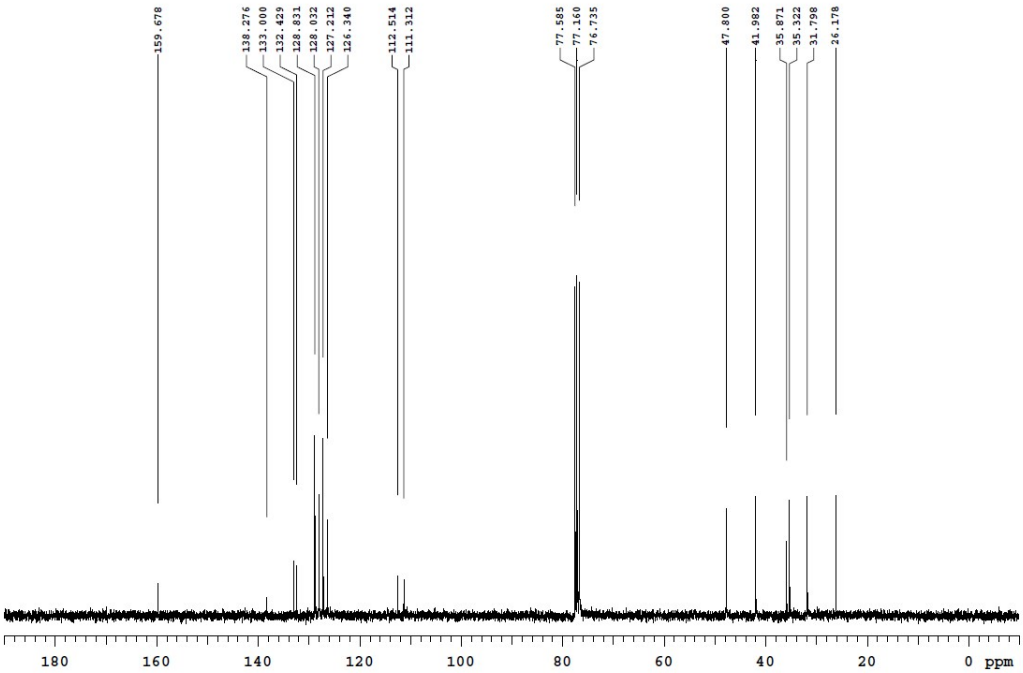
1.13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126.340
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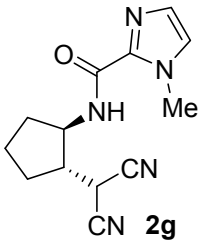
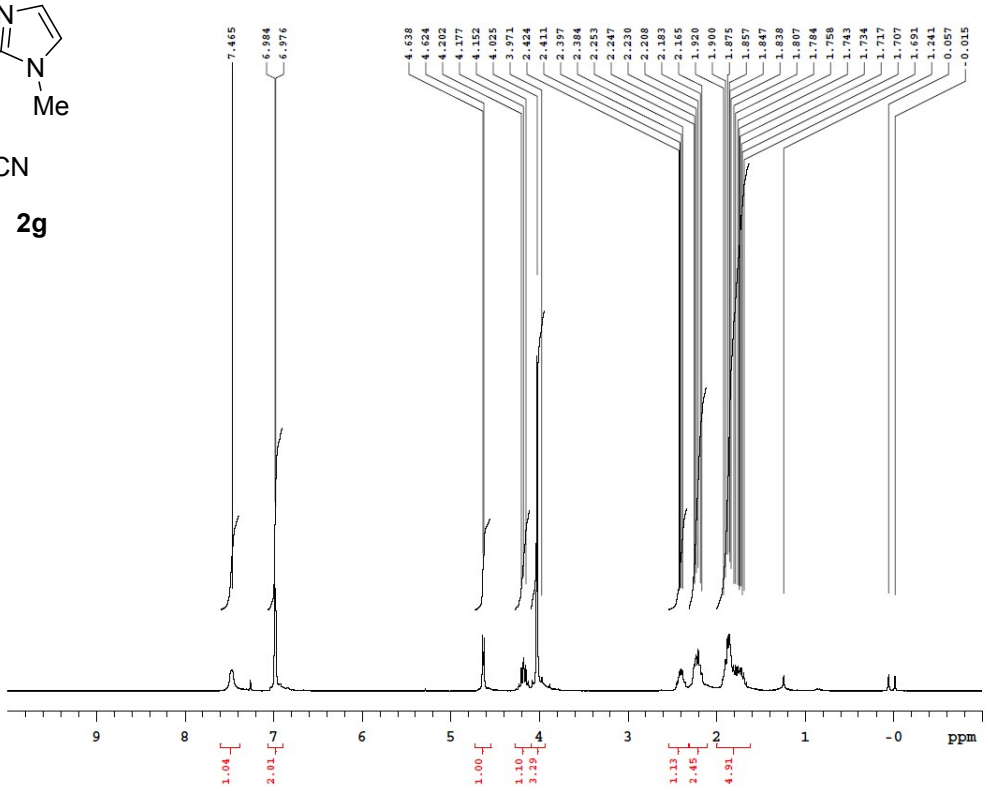
111.312
77.585
77.160
76.735
47.800
41.982
35.871
35.322
31.798
26.178
180
160
140
120
100
80
60
40
20
0
ppm


N
O
N
NH
Me
CN
CN

2g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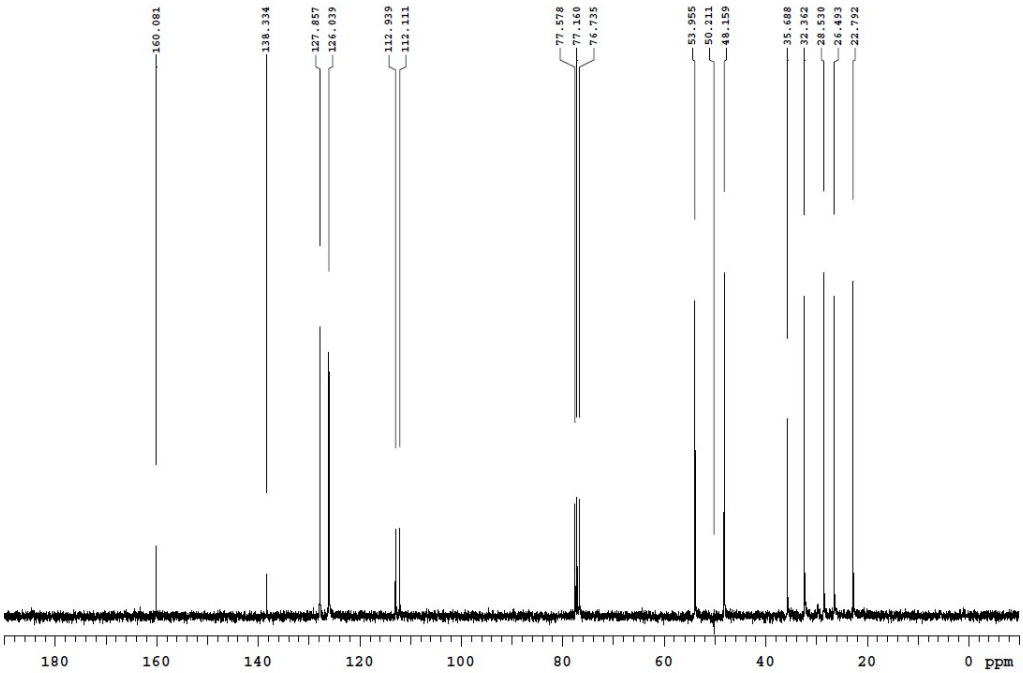
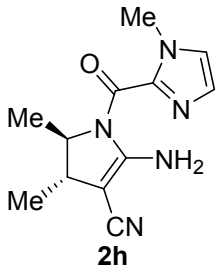
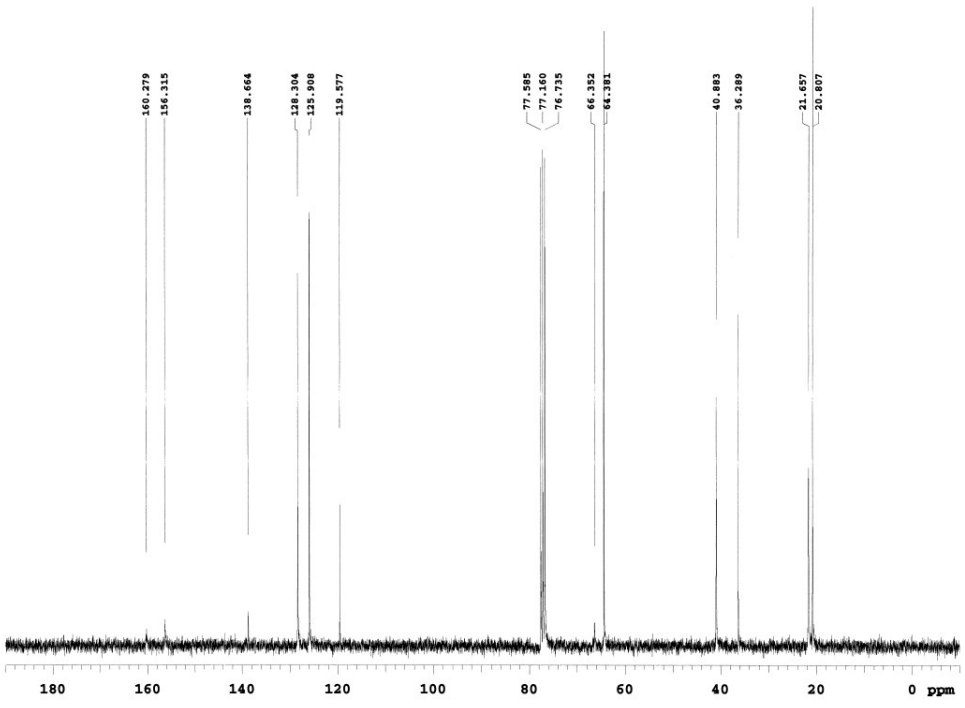
6.984
6.976
4.638
4.624
4.202
4.177
4.152
4.025
3.971
2.424
2.411
2.397
2.384
2.253
2.247
2.230
2.208
2.183
2.165
1.920
1.900
1.875
1.857
1.847
1.838
1.807
1.784
1.758
1.743
1.734
1.717
1.707
1.691
1.241
0.057
-0.015
9
8
7
6
5
4
3
2
1
-0
ppm
1.04
2.01
1.00
1.10
3.29
1.13
2.45
4.91


160.081
138.334
127.857
126.039
112.939
112.111
77.578
77.160
76.735
53.955
50.211
48.159
35.688
32.362
28.530
26.493
22.792
180
160
140
120
100
80
60
40
20
0 ppm


Me
N
O
N
Me
N
NH2
Me
CN

2h

7.267
7.111
7.015
6.385
5.212
3.934
3.881
2.521
2.498
2.477
1.219
1.197
1.171
1.144
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.77
1.00
1.93
0.87
3.00
1.00
6.58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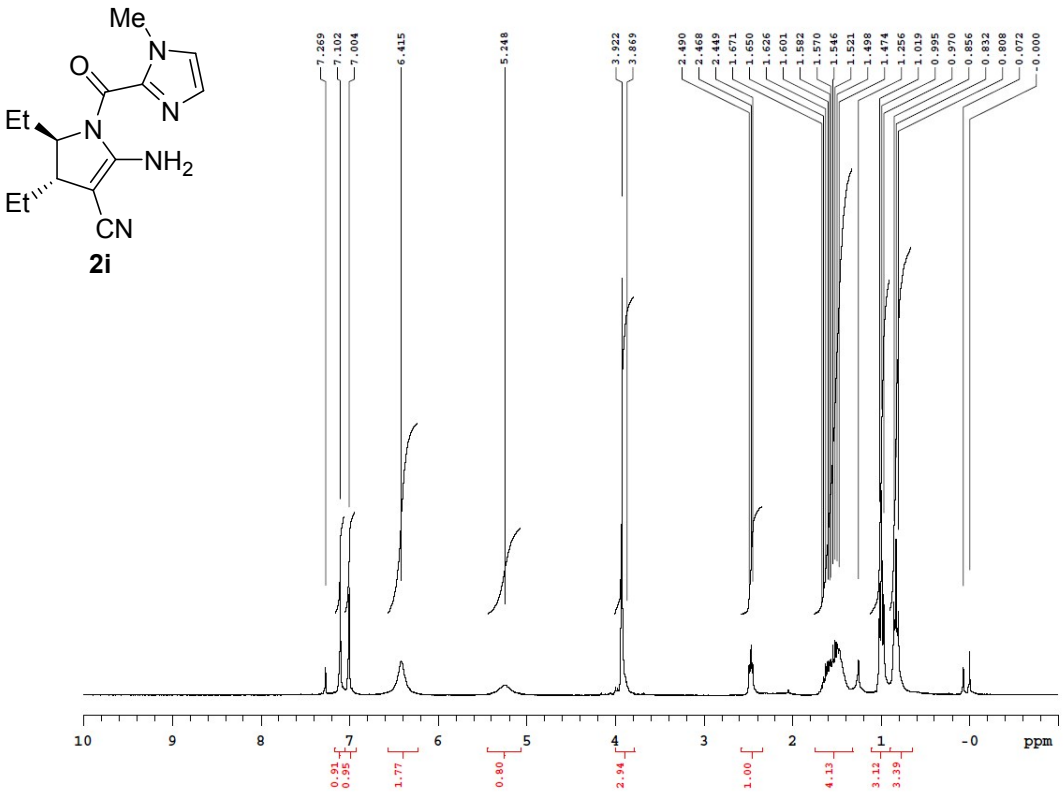
156.315
138.664
128.304
125.908
119.577
77.585
77.160
76.735
66.352
64.381
40.883
36.289
21.657
20.807
180
160
140
120
100
80
60
40
20
0 ppm


Me
N
O
N
Et
N
NH2
Et
CN
7.269
7.102
7.004
6.415
5.248
3.922
3.869
2.490
2.468
2.449
1.671
1.650
1.626
1.601
1.582
1.570
1.546
1.521
1.498
1.474
1.256
1.019
0.995
0.970
0.856
0.832
0.808
0.072
-0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.91
0.95
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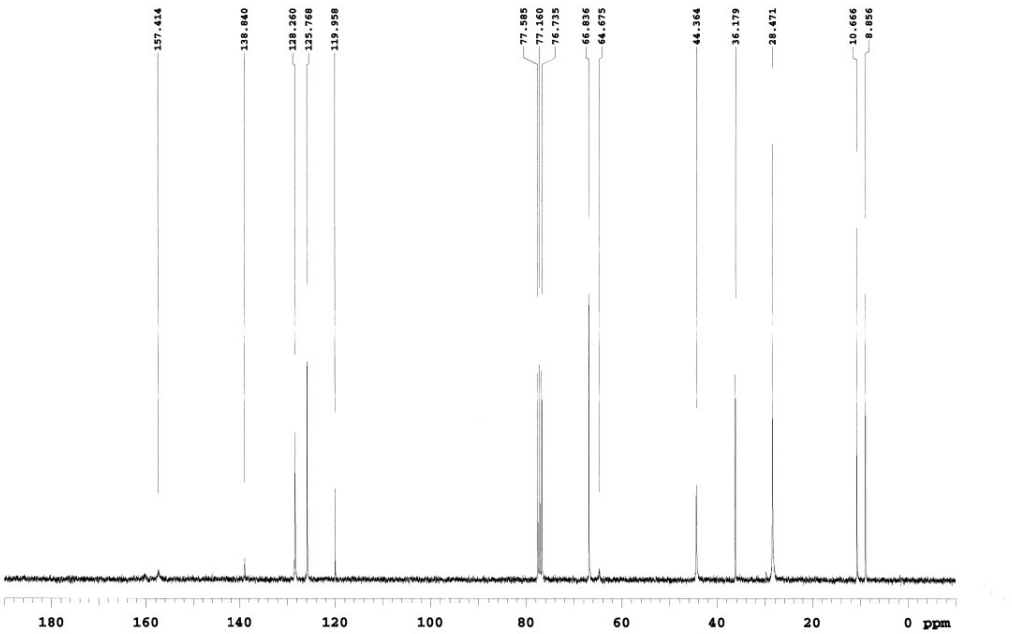
0.80
2.94
1.00
4.13
3.12
3.39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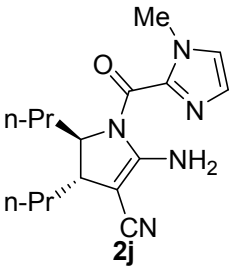
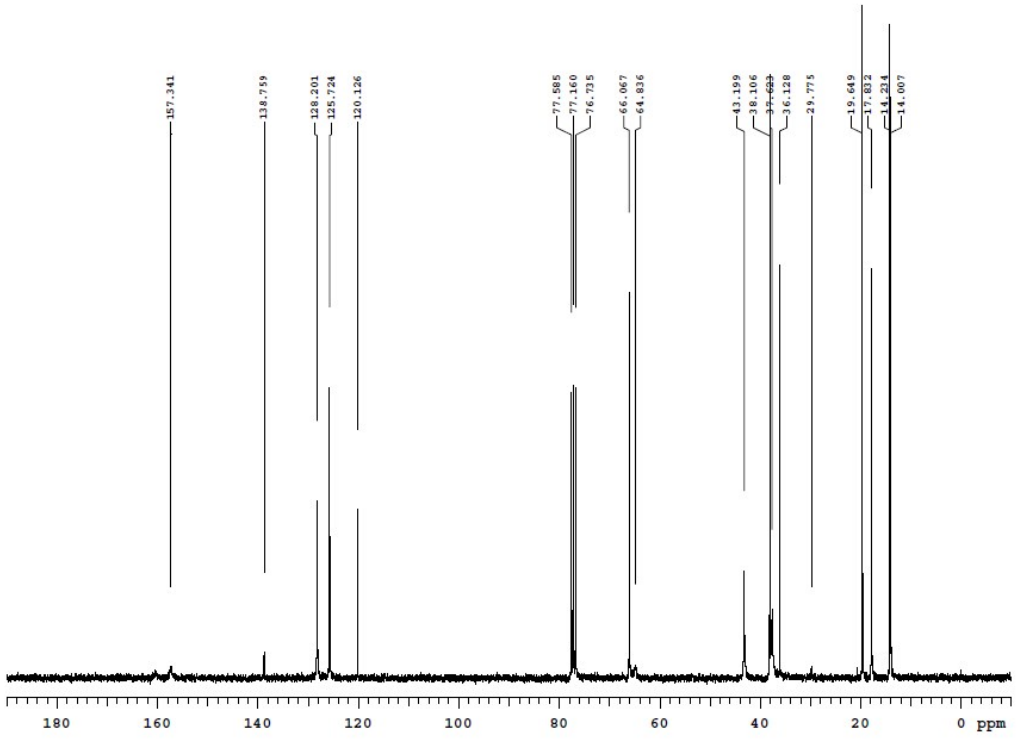
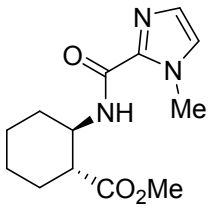
128.260
125.768
119.958
77.585
77.160
76.735
66.836
64.675
44.364
36.179
28.471
10.666
8.856
180
160
140
120
100
80
60
40
20
0 ppm


Me
N
O
N
n-Pr
N
NH2
n-Pr
CN

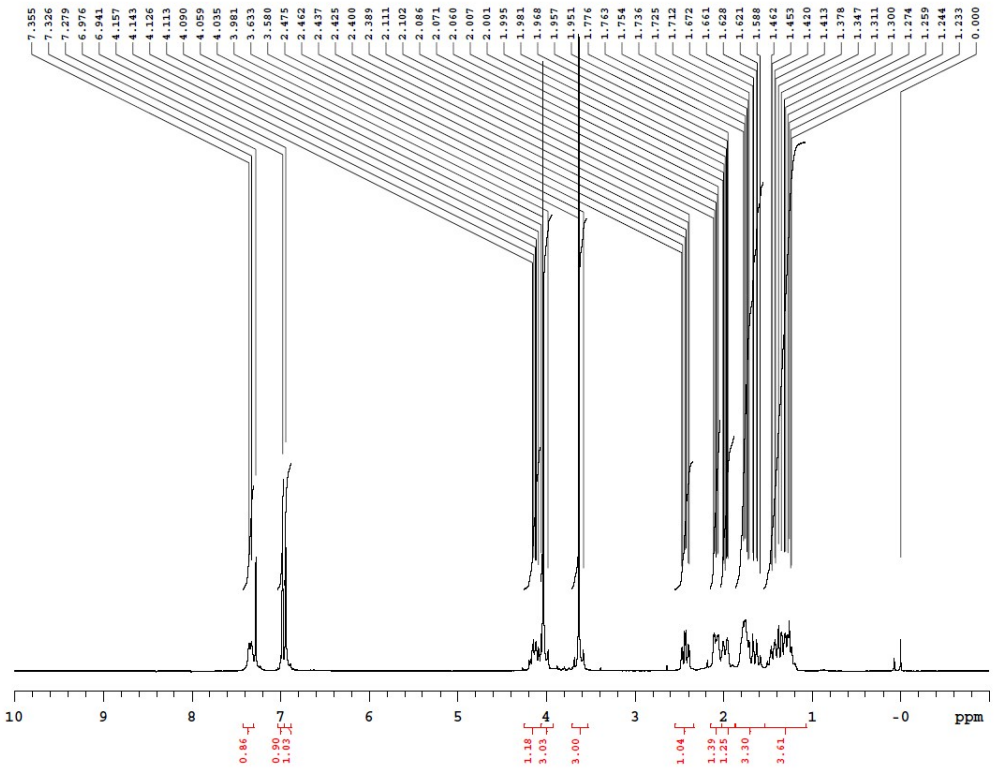
2j

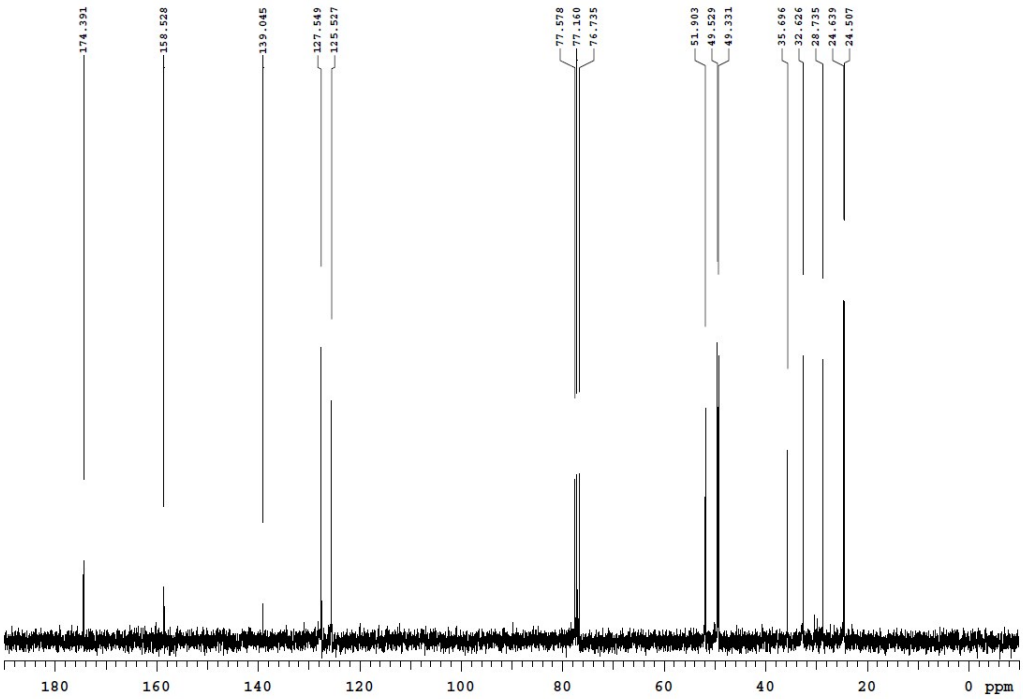
7.273
7.102
7.100
7.012
6.416
5.339
3.977
3.923
3.871
2.529
2.512
2.492
1.722
1.621
1.597
1.579
1.550
1.532
1.507
1.491
1.463
1.443
1.420
1.397
1.368
1.272
1.253
1.001
0.970
0.948
0.924
0.903
0.897
0.845
0.823
0.801
0.071
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.91
0.96
1.82
0.81
3.01
1.00
5.67
3.27
3.39
3.11

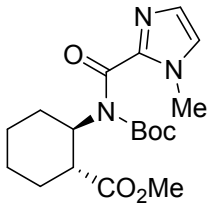

157.341
138.759
128.201
125.724
120.126
77.585
77.160
76.735
66.067
64.836
43.199
38.106
37.623
36.128
29.775
19.649
17.832
14.234
14.007
180
160
140
120
100
80
60
40
20
0 ppm

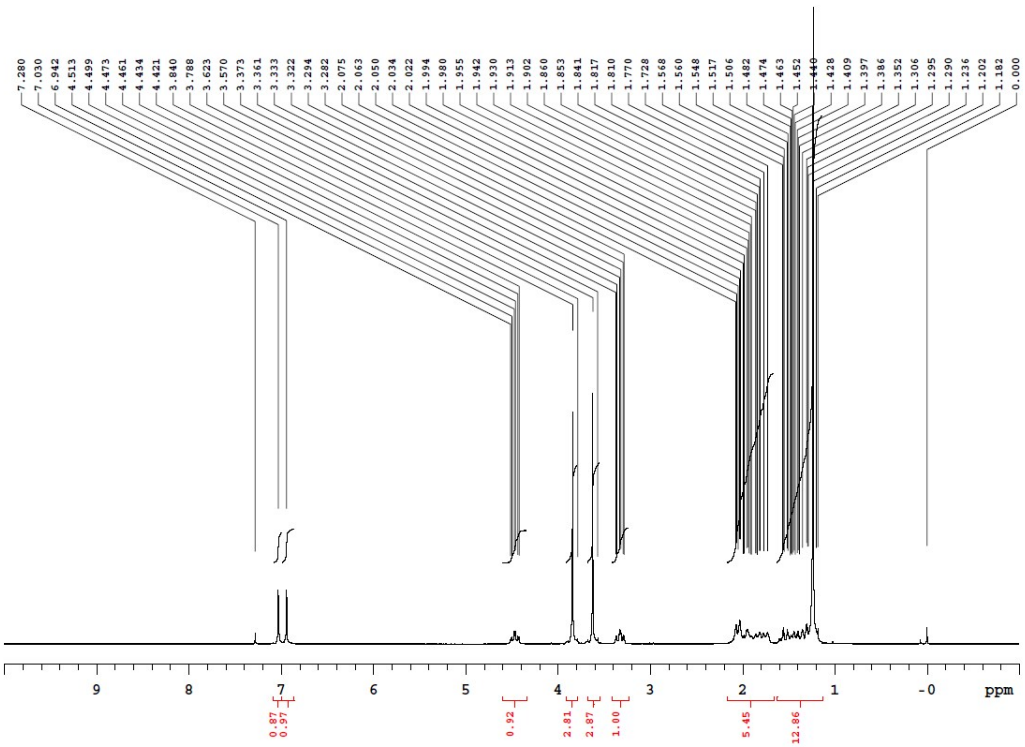

N
O
N
NH
Me
CO2Me

4


7.355
7.326
7.279
6.976
6.941
4.157
4.143
4.126
4.113
4.090
4.059
4.035
3.981
3.633
3.580
2.475
2.462
2.437
2.425
2.400
2.389
2.111
2.102
2.086
2.071
2.060
2.007
2.001
1.995
1.981
1.968
1.957
1.951
1.776
1.763
1.754
1.736
1.725
1.712
1.672
1.661
1.628
1.621
1.588
1.462
1.453
1.420
1.413
1.378
1.347
1.311
1.300
1.274
1.259
1.244
1.233
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.86
0.90
1.03
1.18
3.03
3.00
1.04
1.39
1.25
3.30
3.61


174.391
158.528
139.045
127.549
125.527
77.578
77.160
76.735
51.903
49.529
49.331
35.696
32.626
28.735
24.639
24.507
180
160
140
120
100
80
60
40
20
0 ppm


N
O
N
Me
N
Boc
CO2Me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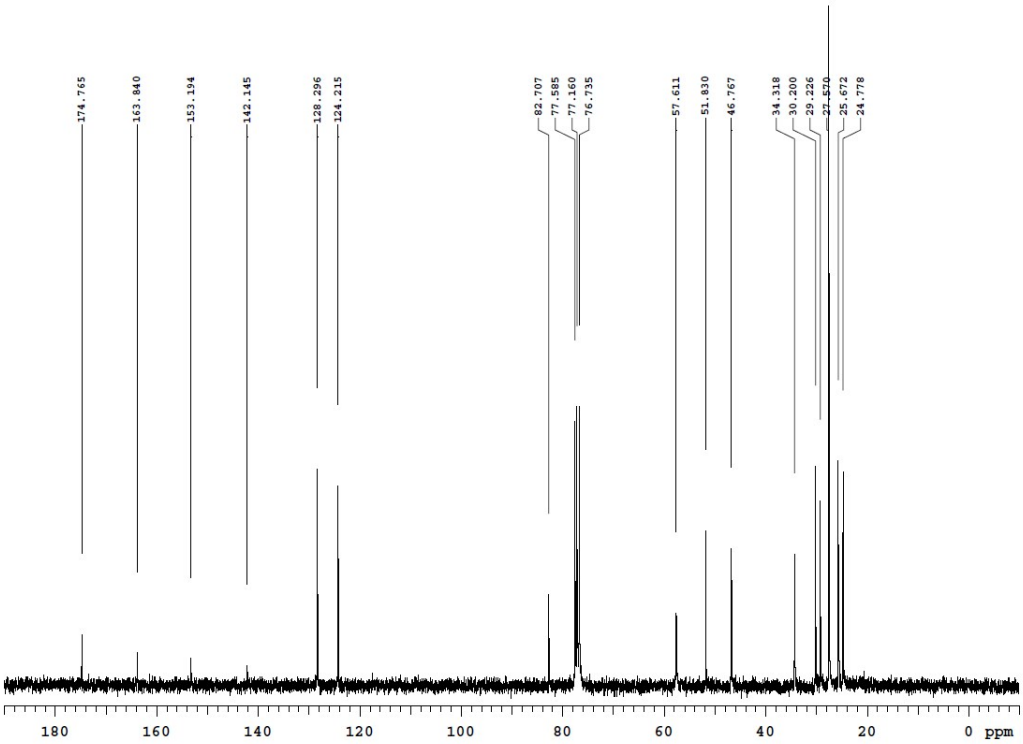
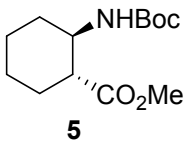
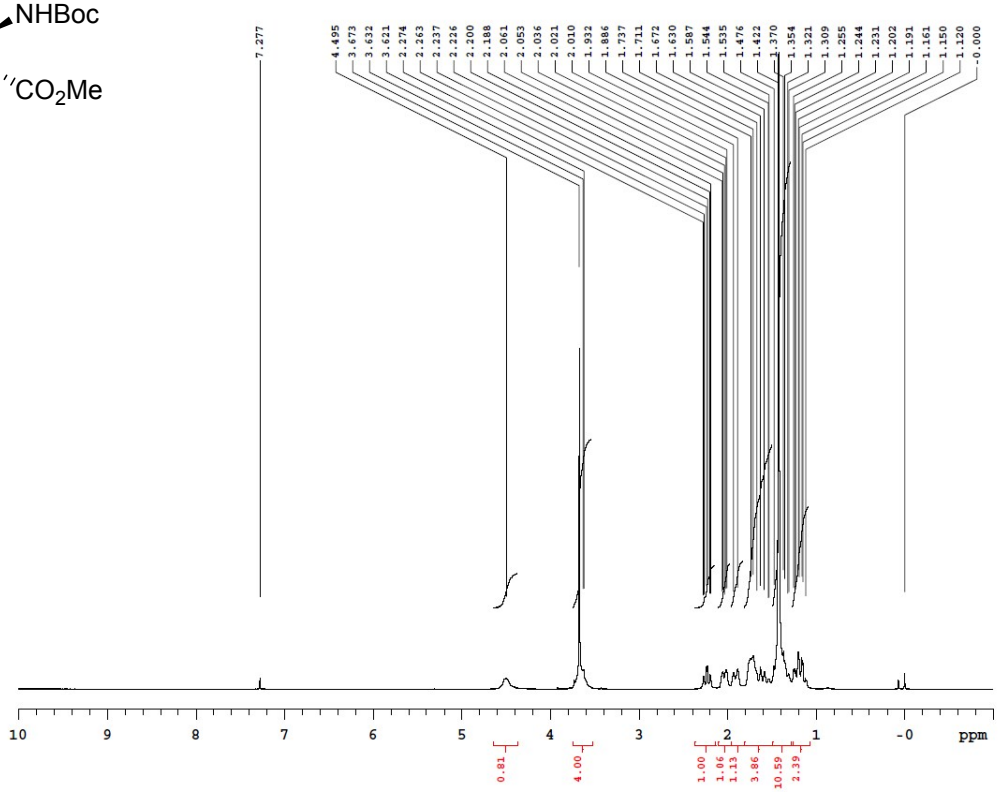
7.030
6.942
4.513
4.499
4.473
4.461
4.434
4.421
3.840
3.788
3.623
3.570
3.373
3.361
3.333
3.322
3.294
3.282
2.075
2.063
2.050
2.034
2.022
1.994
1.980
1.955
1.942
1.930
1.913
1.902
1.860
1.853
1.841
1.817
1.810
1.770
1.728
1.568
1.560
1.548
1.517
1.506
1.482
1.474
1.463
1.452
1.440
1.428
1.409
1.397
1.386
1.352
1.306
1.295
1.290
1.236
1.202
1.182
0.000
9
8
7
6
5
4
3
2
1
-0
ppm
0.87
0.97
0.92
2.81
2.87
1.00
5.45
12.86


174.765
163.840
153.194
142.145
128.296
124.215
82.707
77.585
77.160
76.735
57.611
51.830
46.767
34.318
30.200
29.226
27.570
25.672
24.778
180
160
140
120
100
80
60
40
20
0 ppm


NHBoc
CO2Me

5


7.277
4.495
3.673
3.632
3.621
2.274
2.263
2.237
2.226
2.200
2.188
2.061
2.053
2.036
2.021
2.010
1.932
1.886
1.737
1.711
1.672
1.630
1.587
1.544
1.535
1.476
1.422
1.370
1.354
1.321
1.309
1.255
1.244
1.231
1.202
1.191
1.161
1.150
1.120
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
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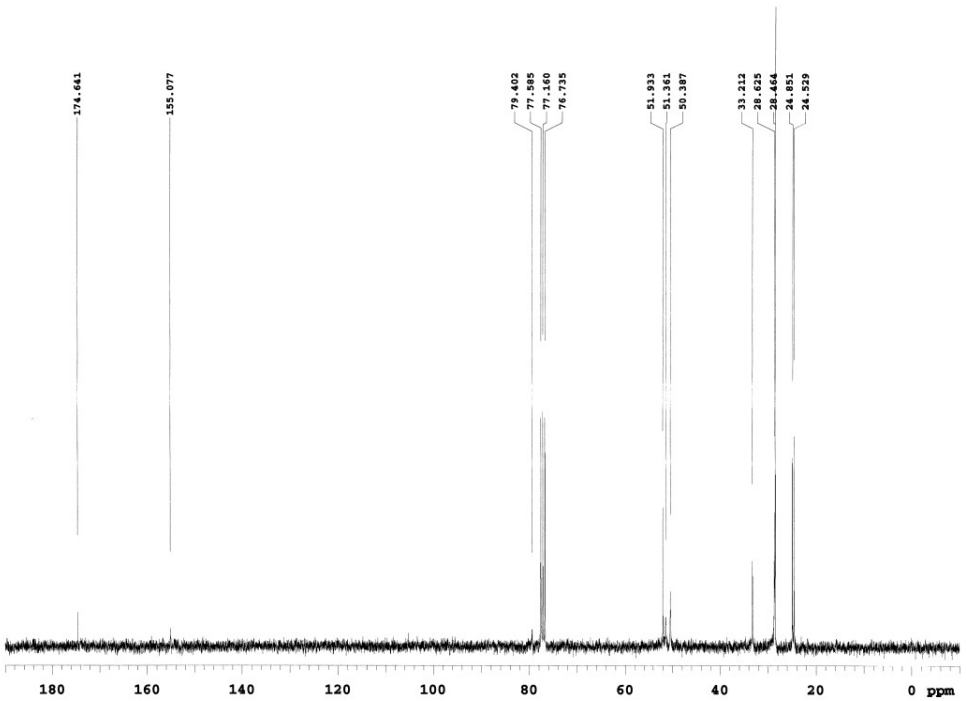
1.00
1.06
1.13
3.86
10.59
2.39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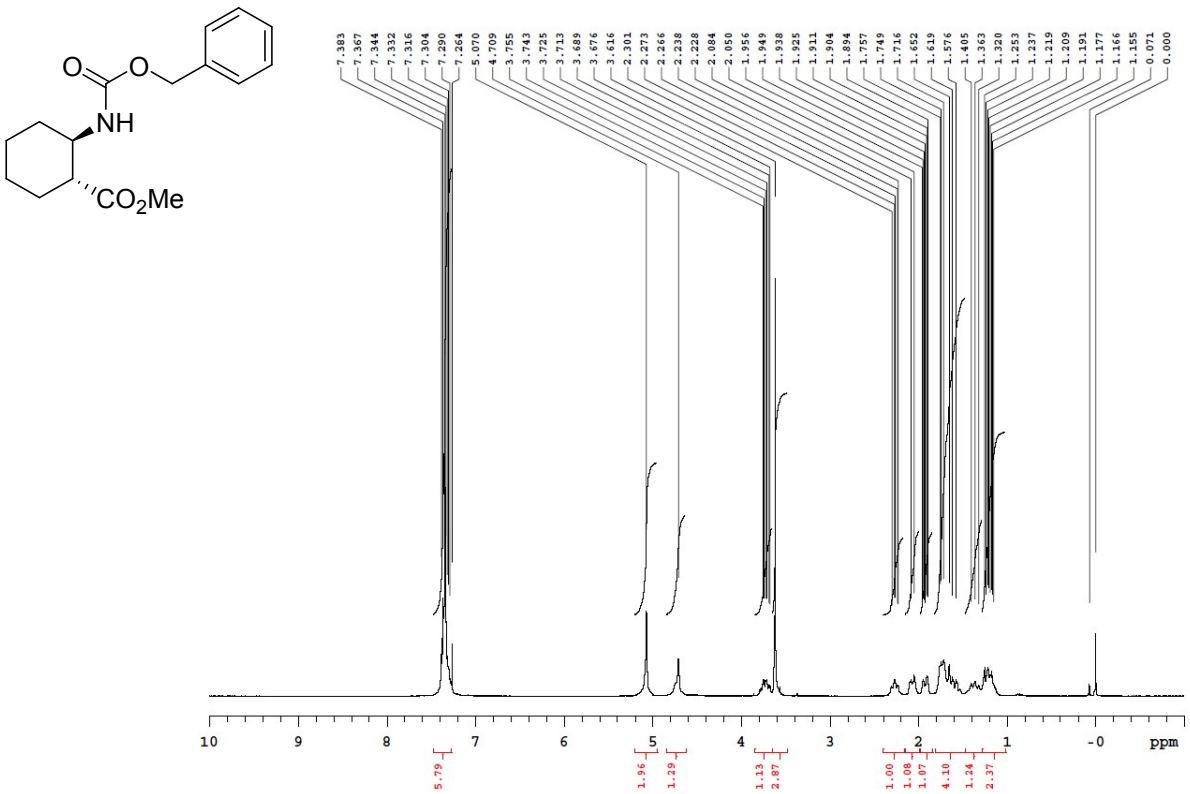
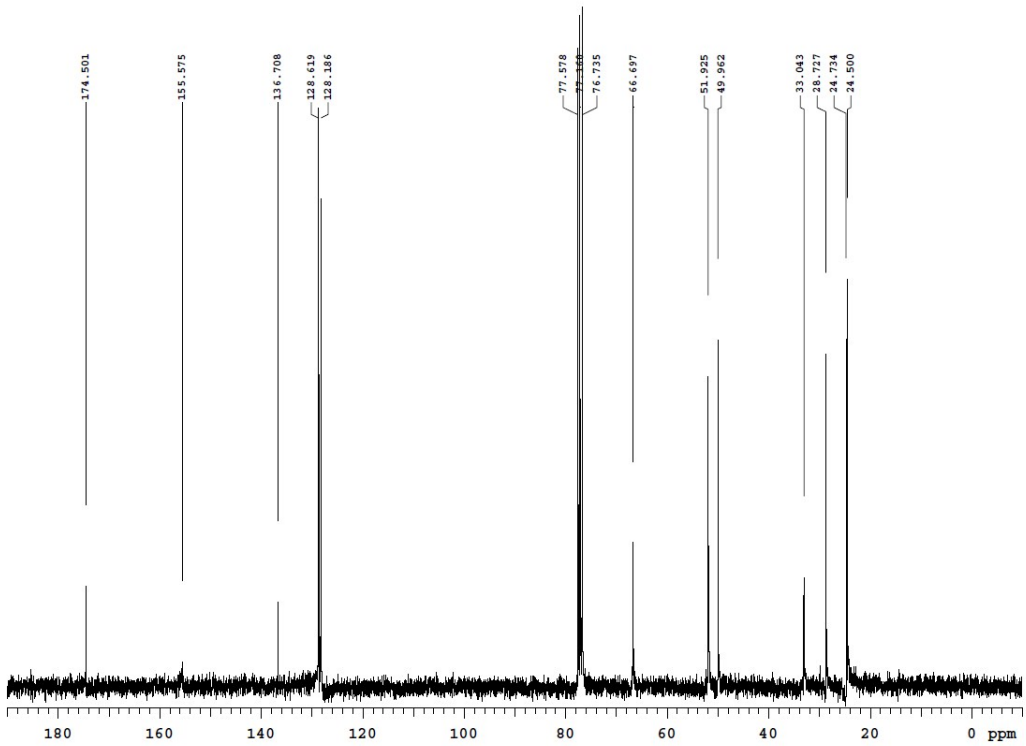
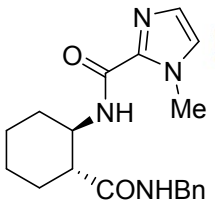
79.402
77.585
77.160
76.735
51.933
51.361
50.387
33.212
28.625
28.464
24.851
24.529
180
160
140
120
100
80
60
40
20
0
ppm


O
O
NH
CO2Me
7.383
7.367
7.344
7.332
7.316
7.304
7.290
7.264
5.070
4.709
3.755
3.743
3.725
3.713
3.689
3.676
3.616
2.301
2.273
2.266
2.238
2.228
2.084
2.050
1.956
1.949
1.938
1.925
1.911
1.904
1.894
1.757
1.749
1.716
1.652
1.619
1.576
1.405
1.363
1.320
1.253
1.237
1.219
1.209
1.191
1.177
1.166
1.155
0.071
0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
5.79
1.96
1.39
1.13
2.87
1.00
1.08
1.97
4.10
1.24
2.37


174.501
155.575
136.708
128.619
128.186
77.578
76.735
66.697
51.925
49.962
33.043
28.727
24.734
24.500
180
160
140
120
100
80
60
40
20
0 ppm


N
O
N
Me
NH
CONHBn

6

7.525
7.493
7.271
7.130
7.121
7.102
7.088
7.069
7.045
7.040
6.979
6.915
6.570
4.467
4.447
4.418
4.398
4.374
4.355
4.325
4.306
4.077
4.066
4.046
4.033
3.823
3.787
2.443
2.432
2.405
2.395
2.366
2.355
2.316
2.113
2.069
2.028
2.013
2.002
1.807
1.780
1.608
1.566
1.523
1.447
1.411
1.382
1.330
1.318
1.273
1.258
-0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
0.79
0.20
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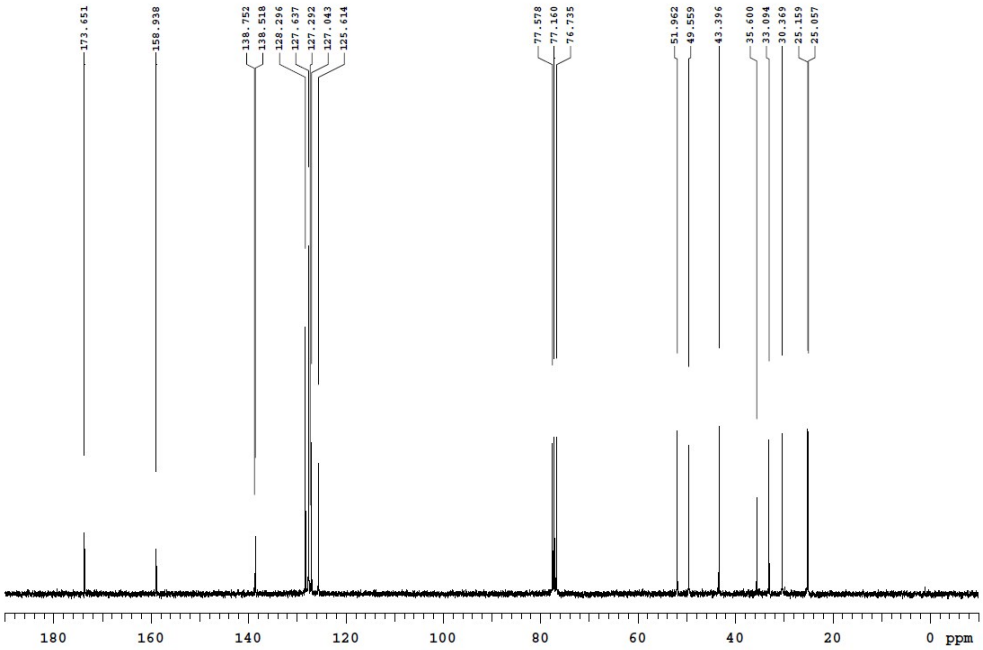
0.98
1.98
0.93
2.01
1.00
2.74
1.36
2.00
2.03
1.15
3.49


173.651
158.938
138.752
138.518
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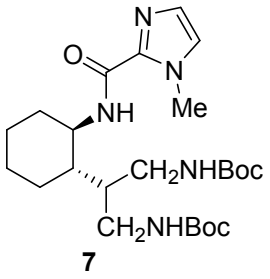
127.637
127.292
127.043
125.614
77.578
77.160
76.735
51.962
49.559
43.396
35.600
33.094
30.369
25.159
25.057
180
160
140
120
100
80
60
40
20
0 ppm


N
O
N
Me
NH
CH2NHBoc
CH2NHBoc

7

7.300
7.267
6.992
6.966
5.356
5.302
5.288
4.111
4.055
4.005
3.934
3.916
3.903
3.884
3.245
3.214
3.199
3.167
3.146
3.125
3.092
3.069
3.046
3.021
2.048
1.982
1.802
1.750
1.615
1.407
1.341
1.309
1.285
1.256
1.237
1.185
1.151
1.110
0.070
0.000
9
8
7
6
5
4
3
2
1
-0
ppm
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0.75
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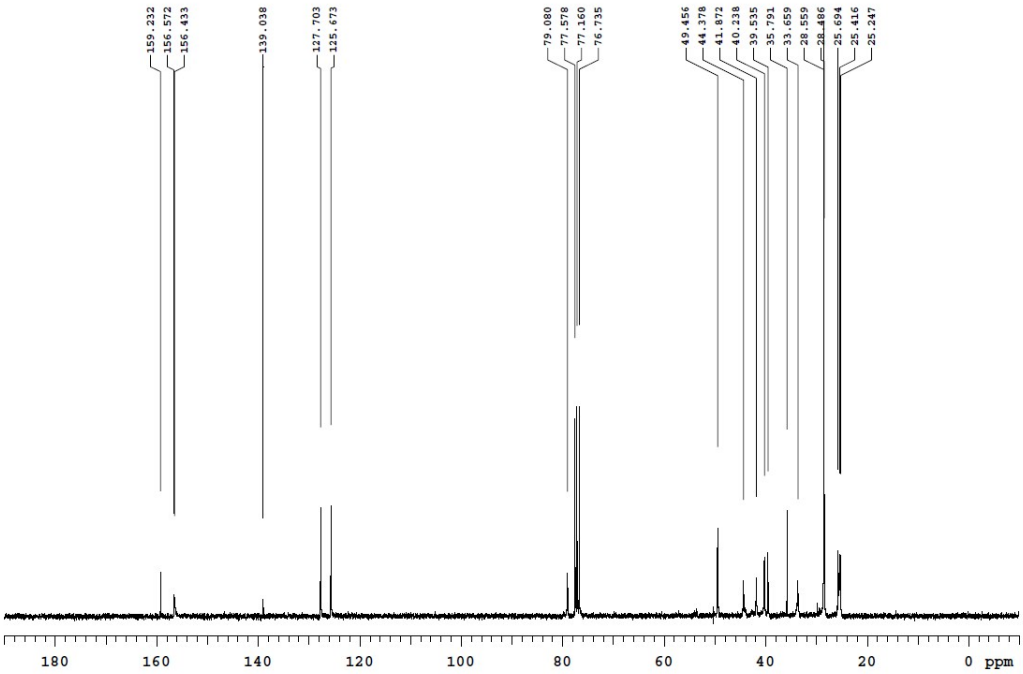
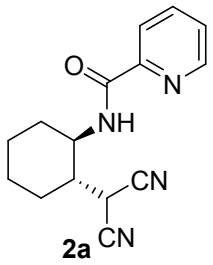
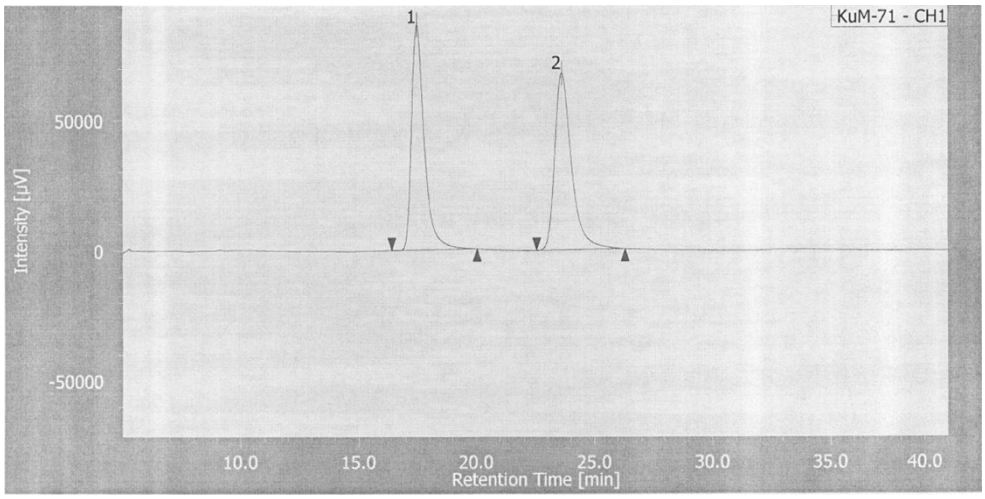
4.38
1.21
6.67
22.71
4.07


159.232
156.572
156.433
139.038
127.703
125.673
79.080
77.578
77.160
76.735
49.456
44.378
41.872
40.238
39.535
35.791
33.659
28.559
28.486
25.694
25.416
25.247
180
160
140
120
100
80
60
40
20
0 ppm

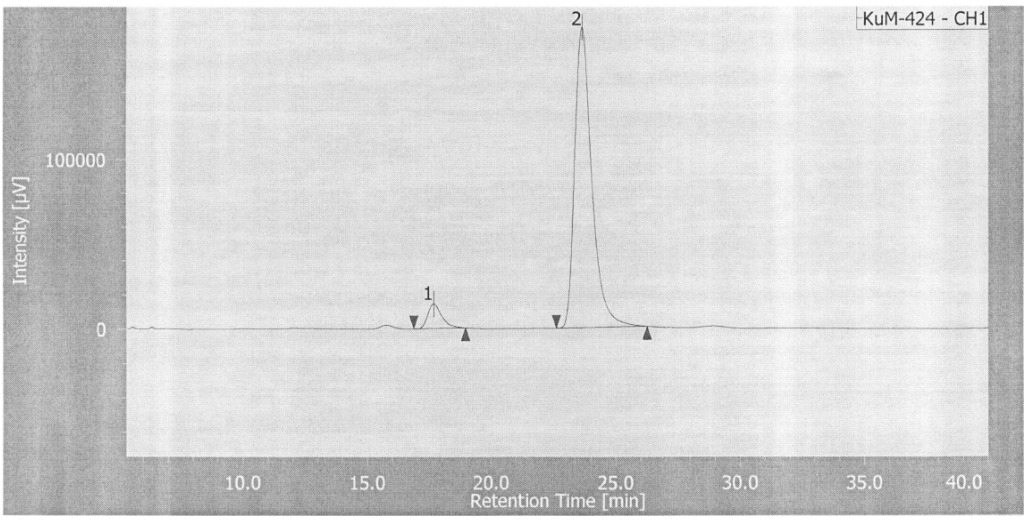


2a

racemic-**2a**



(1*R*,2*S*)-**2a**

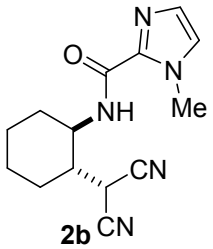


racemic-**2a**

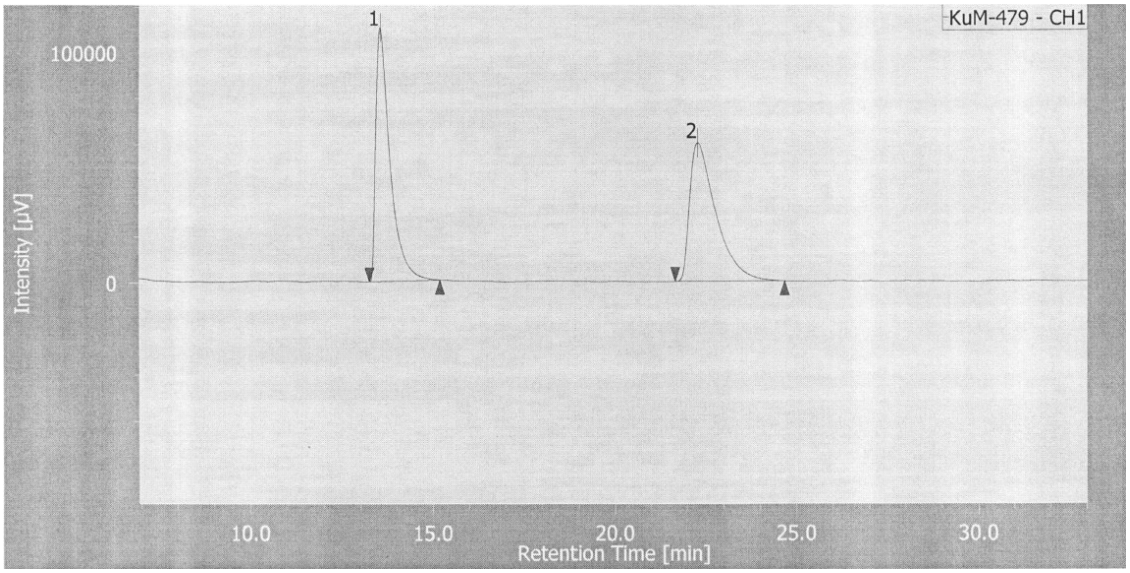
Peak	tR (min)	Area (%)
1	17.5	49.4
2	23.6	50.6

(1*R*,2*S*)-**2a**

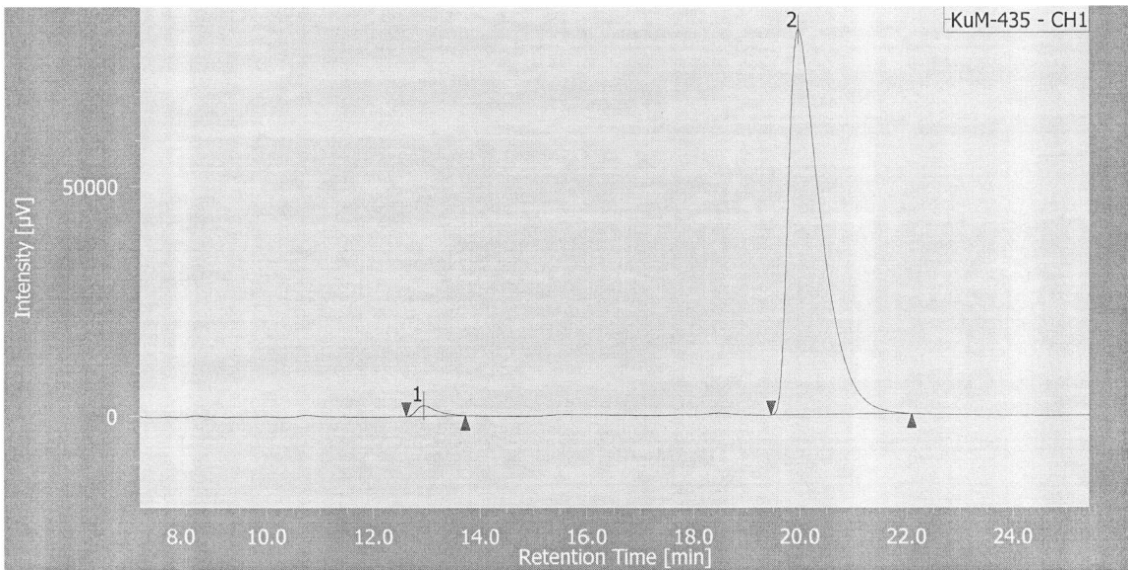
Peak	tR (min)	Area (%)
1	17.7	6.2
2	23.6	93.8



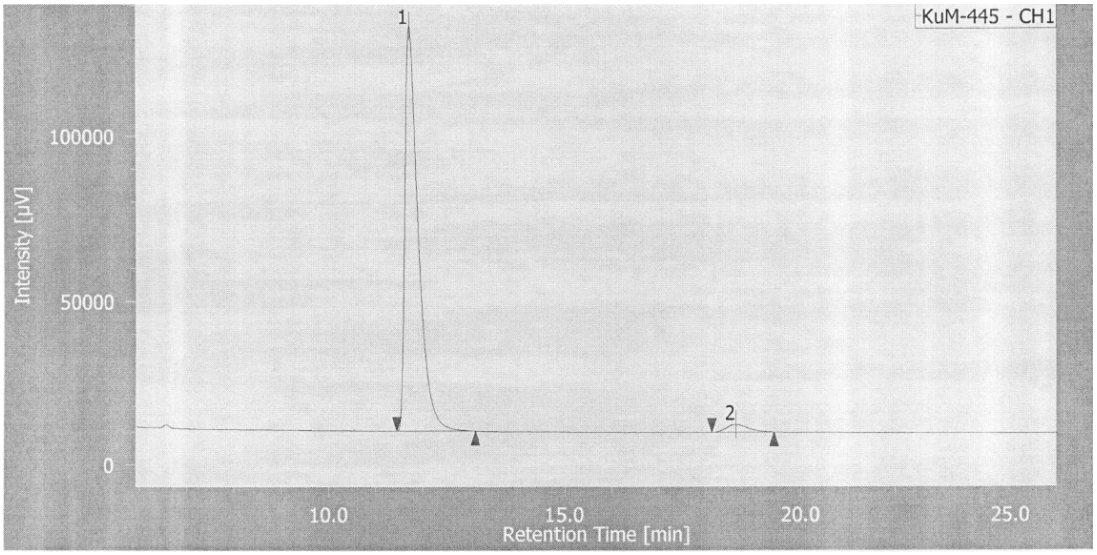
racemic-**2b**



(1*R*,2*S*)-**2b**



(1*S*,2*R*)-**2b**



racemic-**2b**

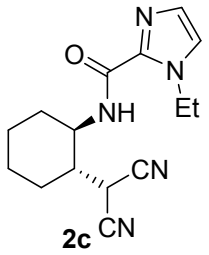
Peak	tR (min)	Area (%)
1	14.0	49.9
2	23.1	50.1

(1*R*,2*S*)-**2b**

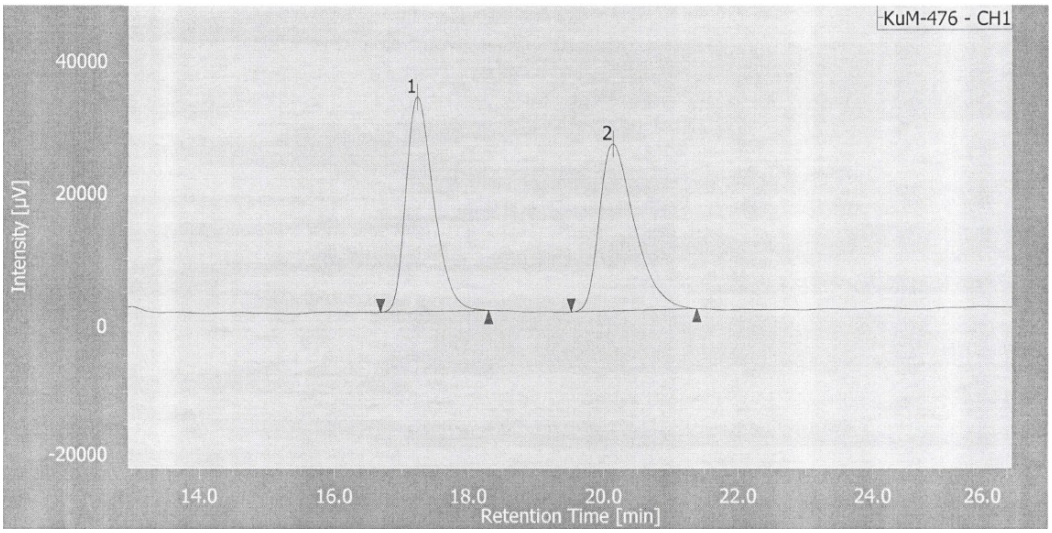
Peak	tR (min)	Area (%)
1	14.0	49.9
2	23.1	50.1

(1*S*,2*R*)-**2b**

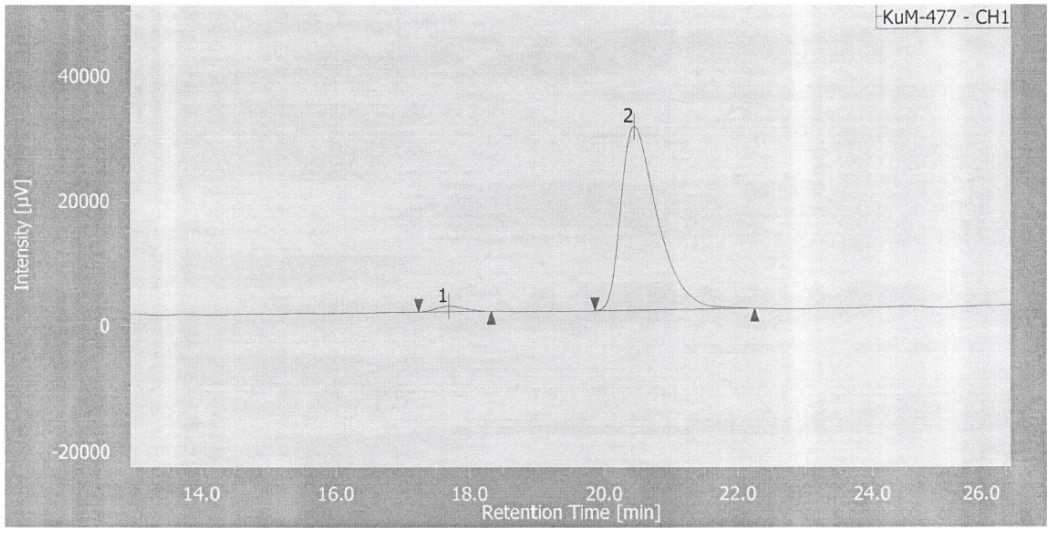
Peak	tR (min)	Area (%)
1	11.7	97.0
2	18.6	3.0



racemic-**2c**



(1*R*,2*S*)-**2c**

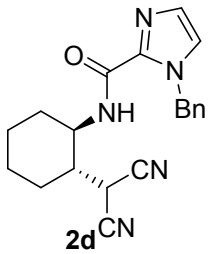


racemic-**2c**

Peak	tR (min)	Area (%)
1	17.2	50.3
2	20.1	49.7

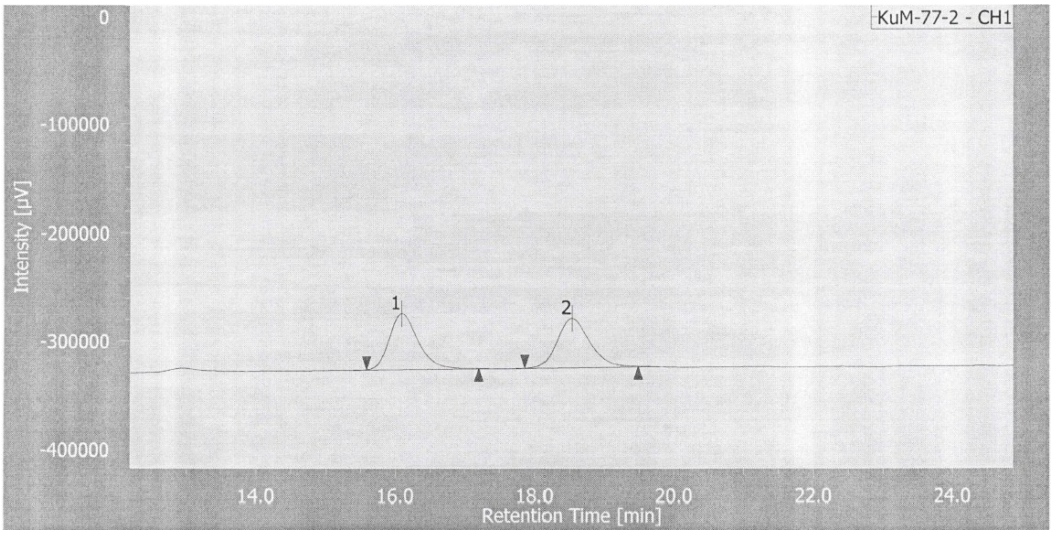
(1*R*,2*S*)-**2c**

Peak	tR (min)	Area (%)
1	17.7	2.3
2	20.5	97.7

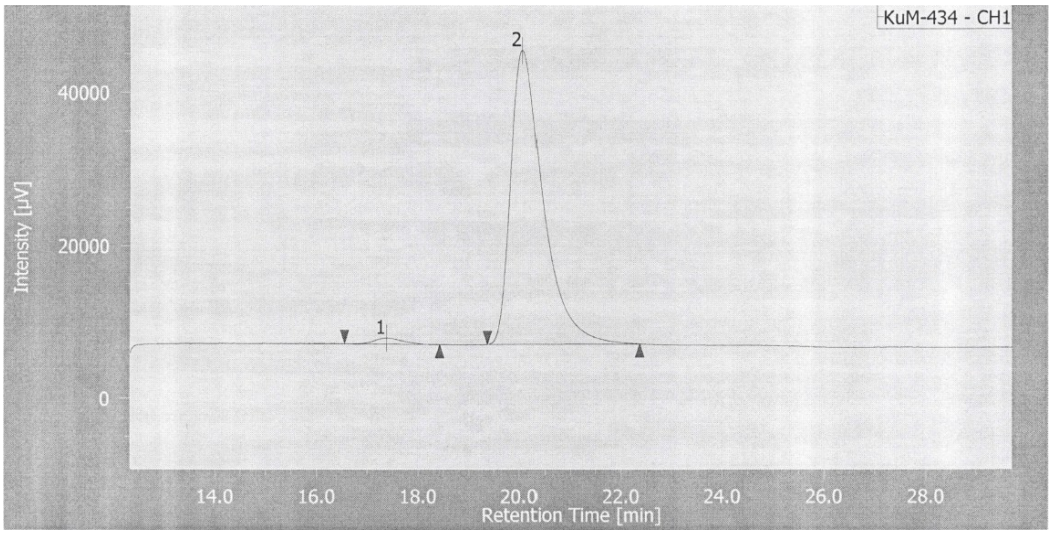


2d

racemic-**2d**



(1*R*,2*S*)-**2d**

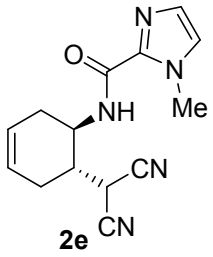


racemic-**2d**

Peak	tR (min)	Area (%)
1	16.1	50.1
2	18.5	49.9

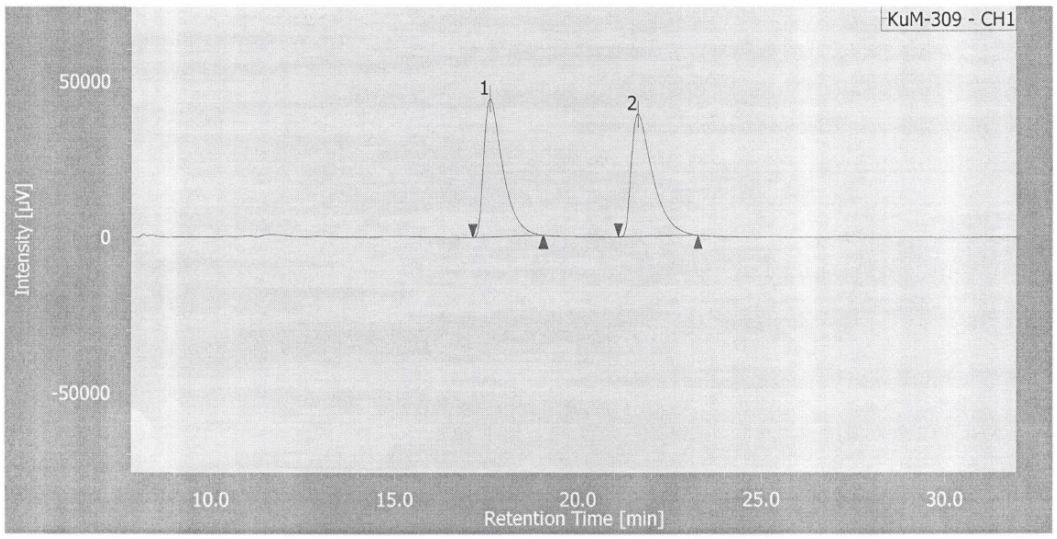
(1*R*,2*S*)-**2d**

Peak	tR (min)	Area (%)
1	17.4	1.8
2	20.1	98.2

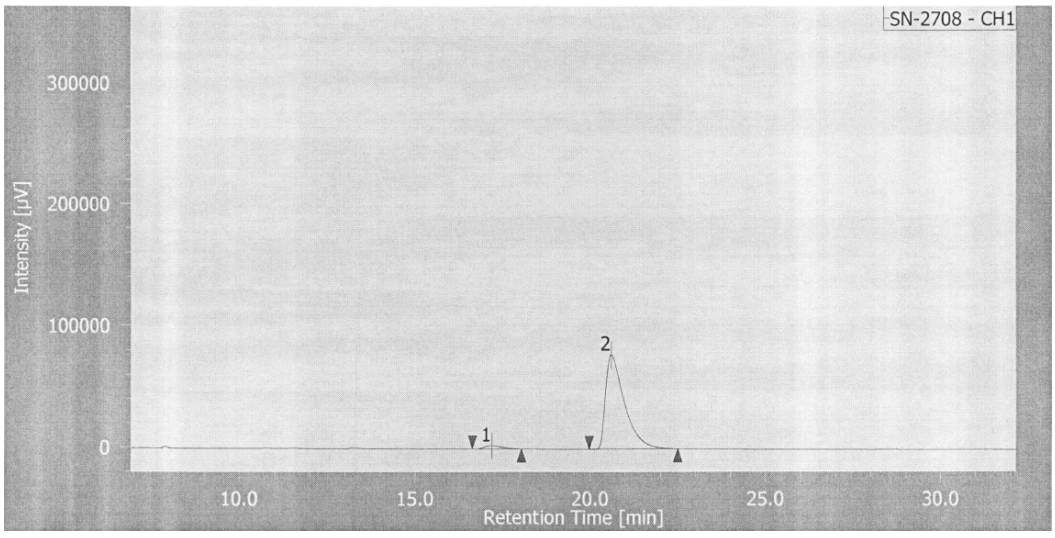


2e

racemic-**2e**



(1*R*,6*S*)-**2e**

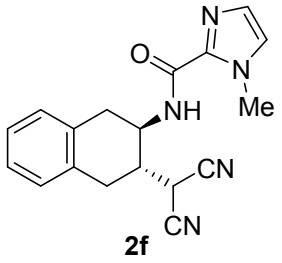


racemic-**2e**

Peak	tR (min)	Area (%)
1	17.6	50.0
2	21.6	50.0

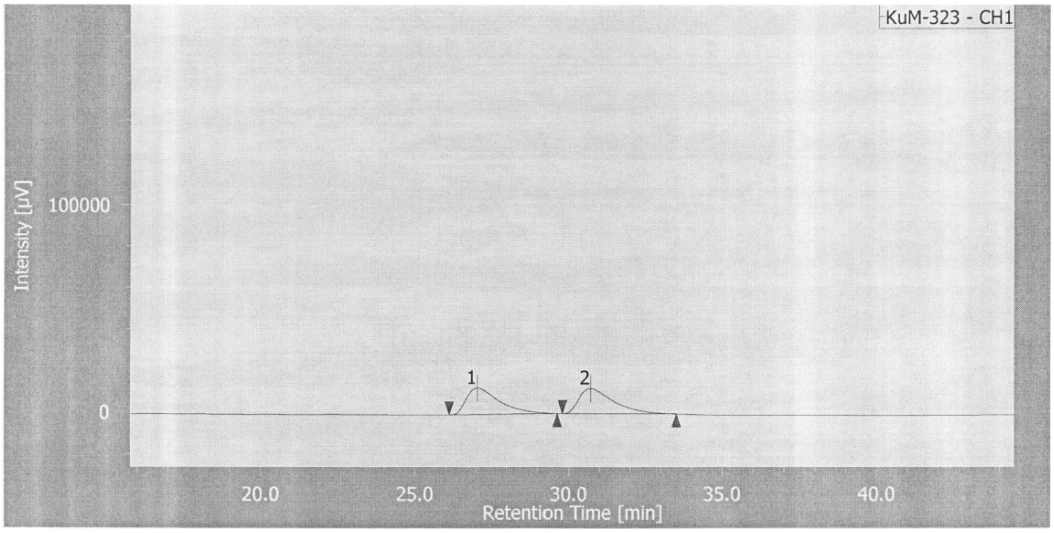
(1*R*,6*S*)-**2e**

Peak	tR (min)	Area (%)
1	17.2	3.1
2	20.6	96.9

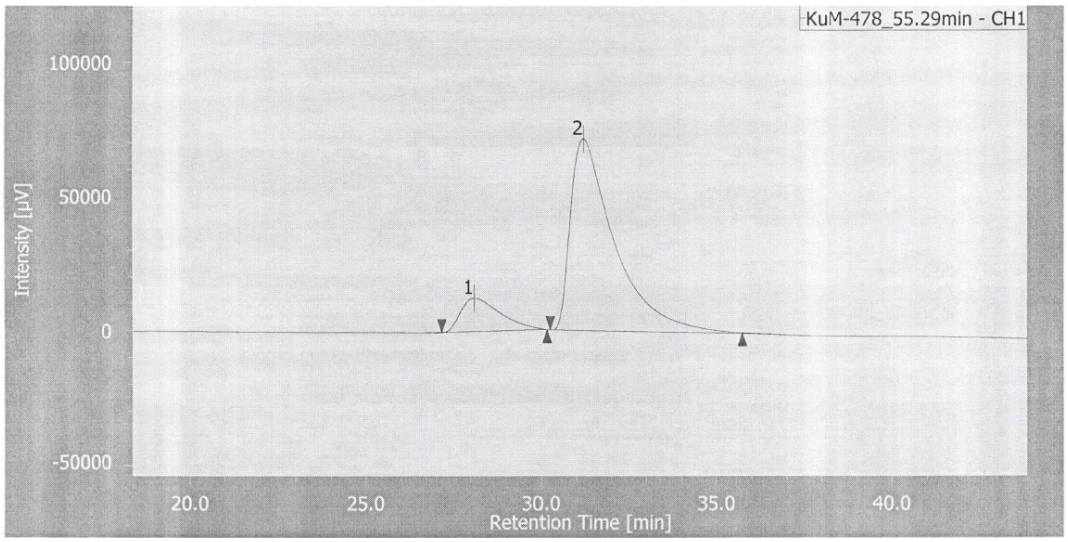


2f

racemic-**2f**



(2*R*,3*S*)-**2f**

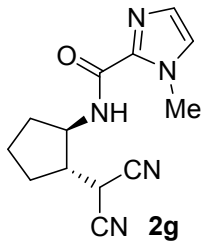


racemic-**2f**

Peak	tR (min)	Area (%)
1	27.0	50.2
2	30.7	49.8

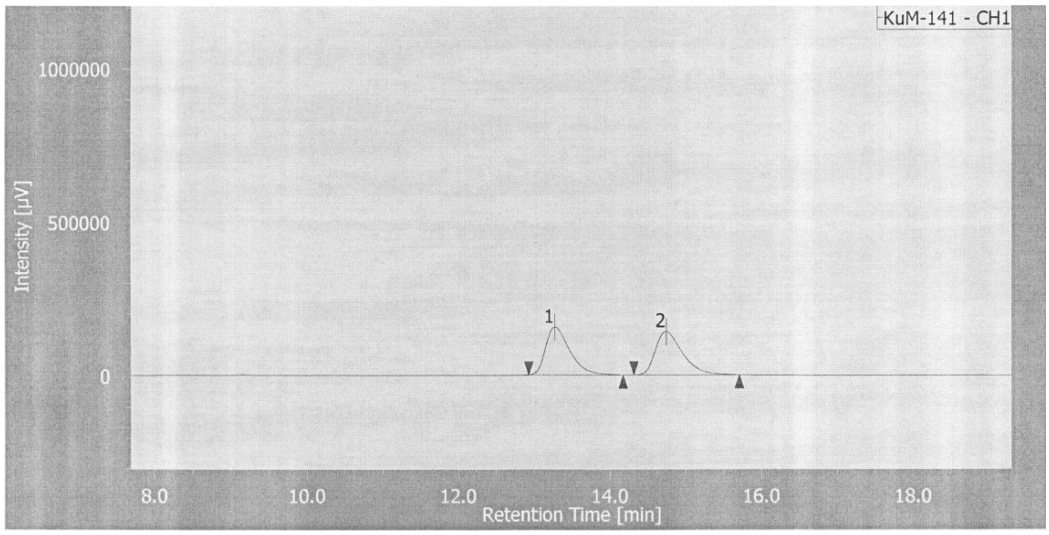
(2*R*,3*S*)-**2f**

Peak	tR (min)	Area (%)
1	28.1	13.6
2	31.2	86.4

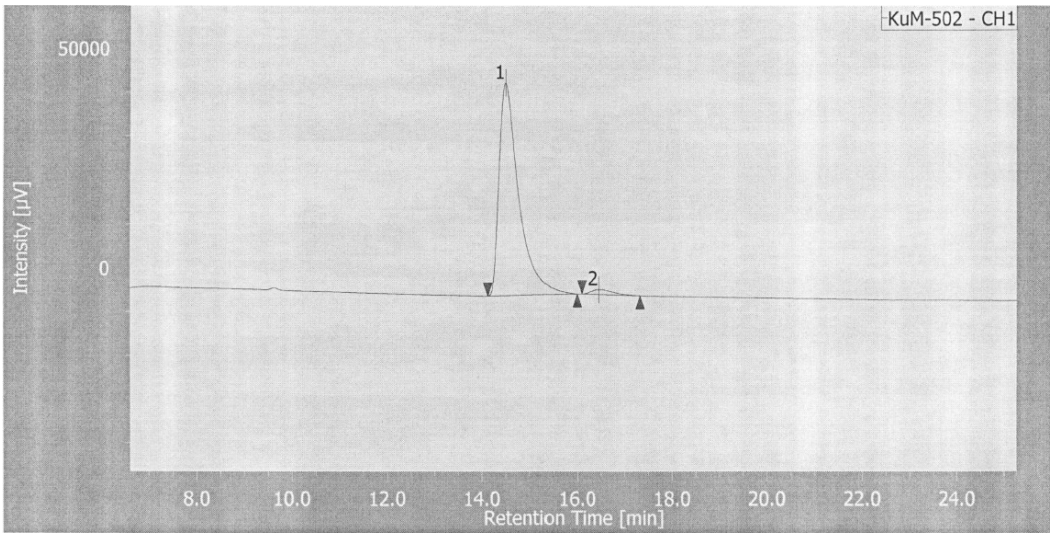


2g

racemic-**2g**



(1*R*,2*S*)-**2g**

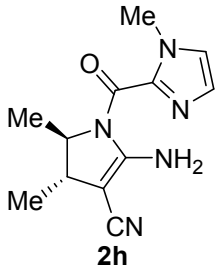


racemic-**2g**

Peak	tR (min)	Area (%)
1	13.3	50.1
2	14.7	49.9

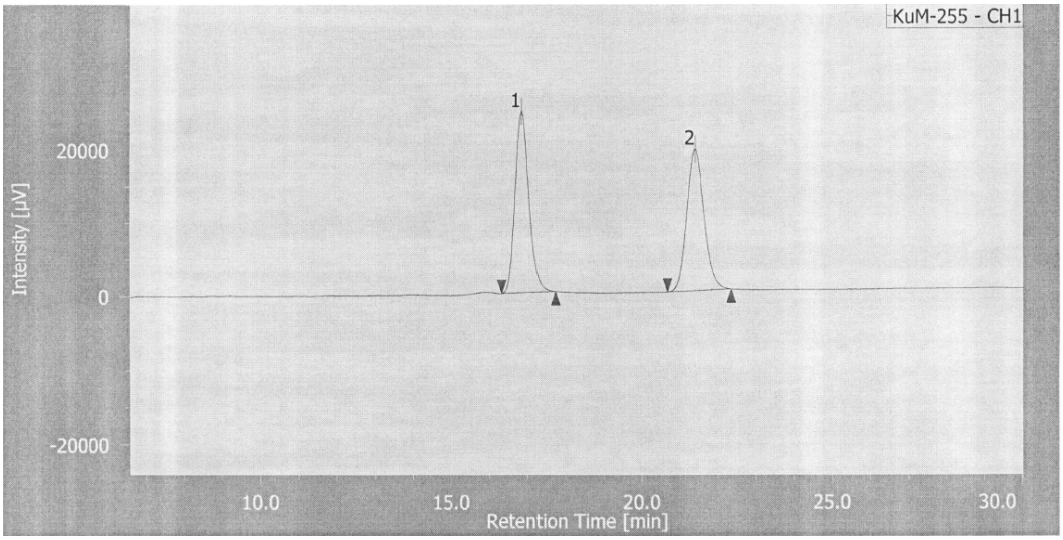
(1*R*,2*S*)-**2g**

Peak	tR (min)	Area (%)
1	14.5	97.4
2	16.5	2.6

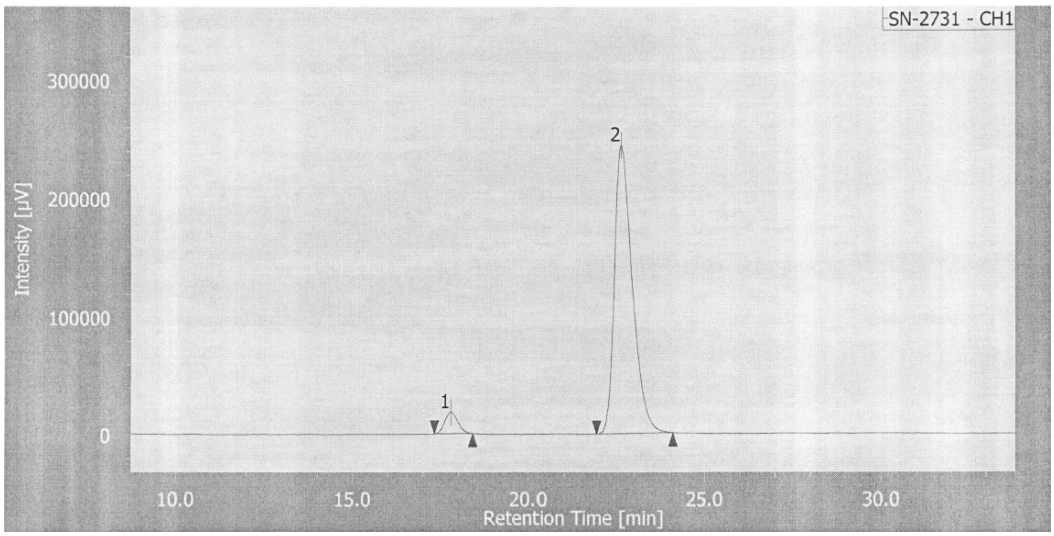


2h

racemic-**2h**



(4*S*,5*R*)-**2h**

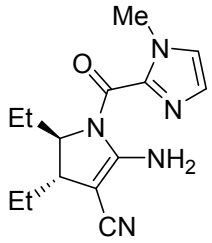


racemic-**2h**

Peak	tR (min)	Area (%)
1	16.9	50.1
2	21.4	49.9

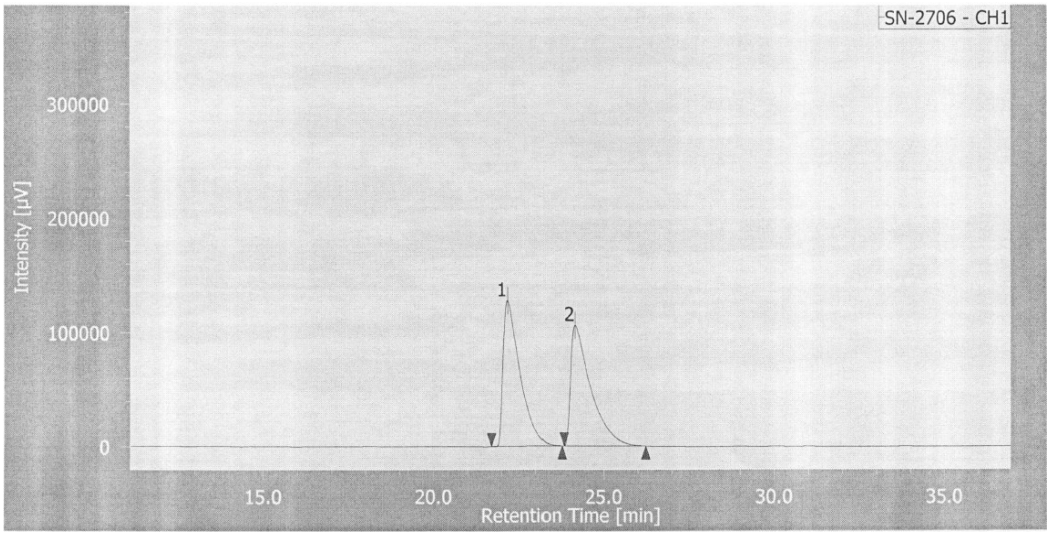
(4*S*,5R)-**2h**

Peak	tR (min)	Area (%)
1	17.8	5.2
2	22.6	94.8

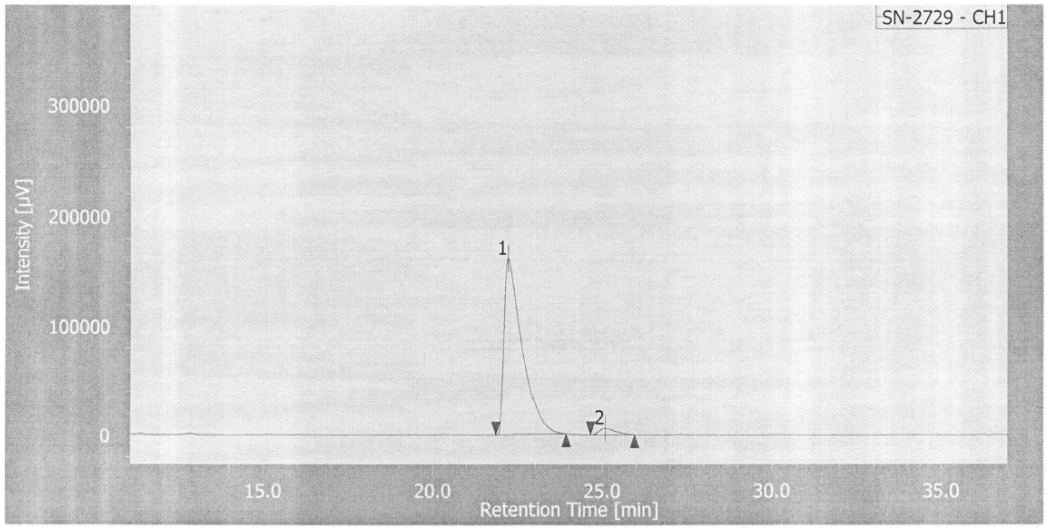


2i

racemic-**2i**



(4*S*,5*R*)-**2i**

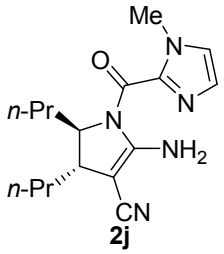


racemic-**2i**

Peak	tR (min)	Area (%)
1	22.2	50.2
2	24.1	49.8

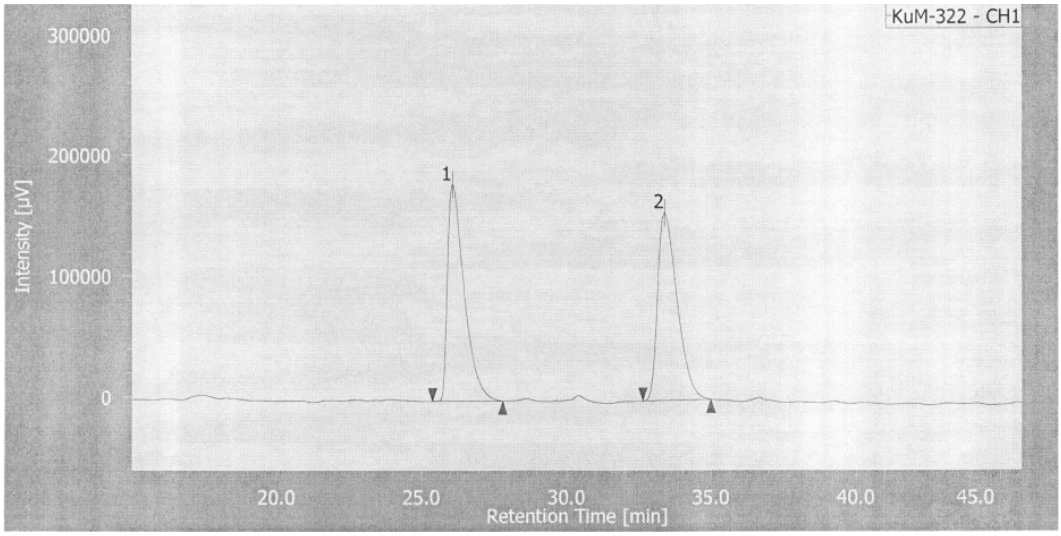
(4*S*,5*R*)-**2i**

Peak	tR (min)	Area (%)
1	22.2	96.9
2	25.1	3.1

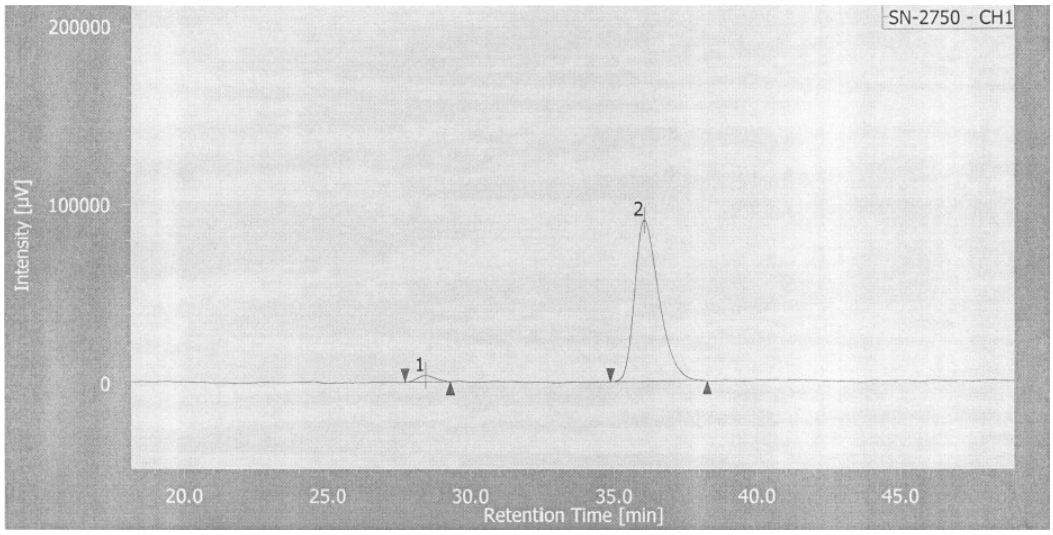


2j

racemic-**2j**



(4*S*,5*R*)-**2j**

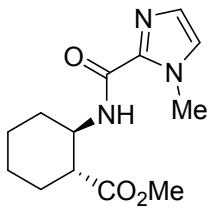


racemic-**2j**

Peak	tR (min)	Area (%)
1	26.1	48.9
2	33.4	50.1

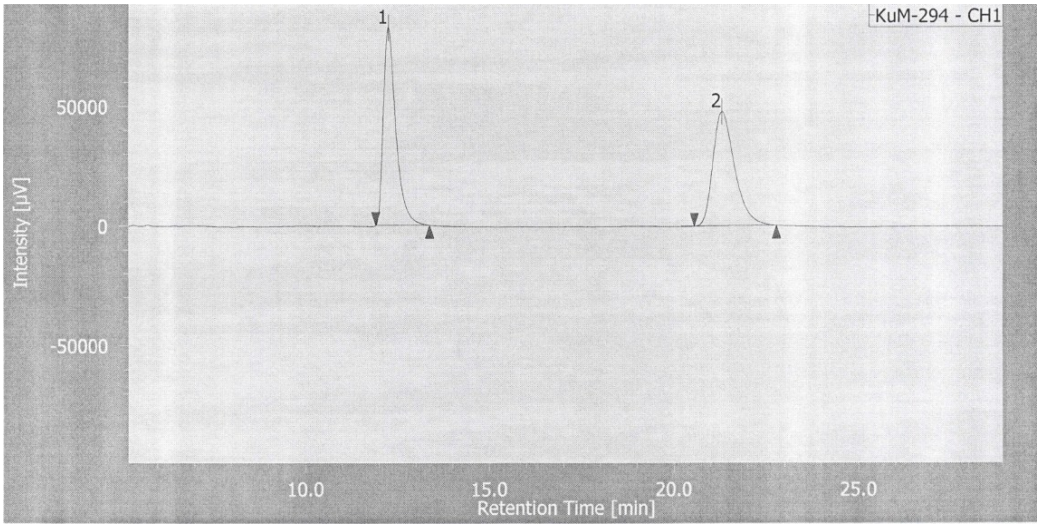
(4*S*,5*R*)-**2j**

Peak	tR (min)	Area (%)
1	28.4	2.8
2	36.1	97.2

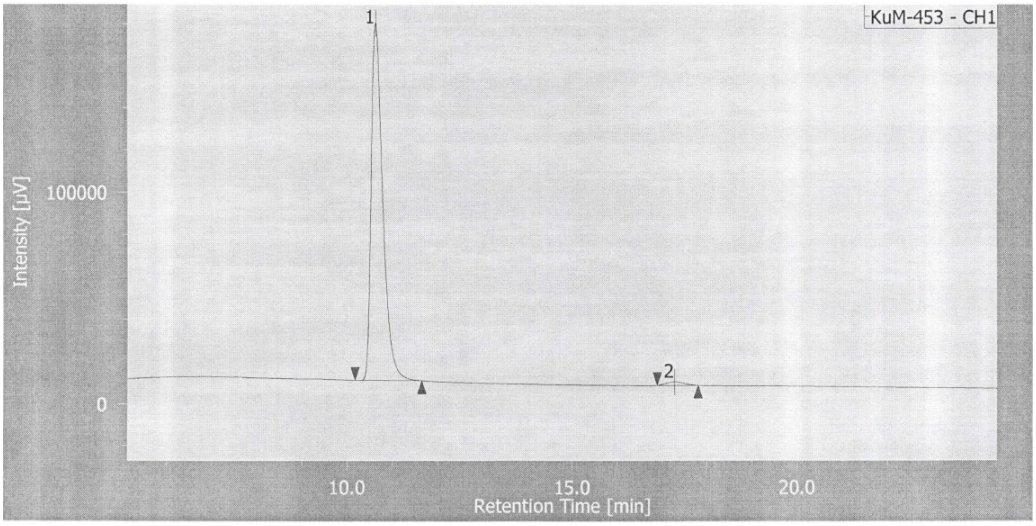


4

racemic-**4**



(1*R*,2*R*)-**4**

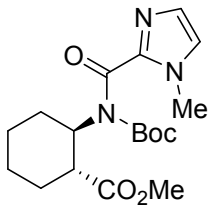


racemic-**4**

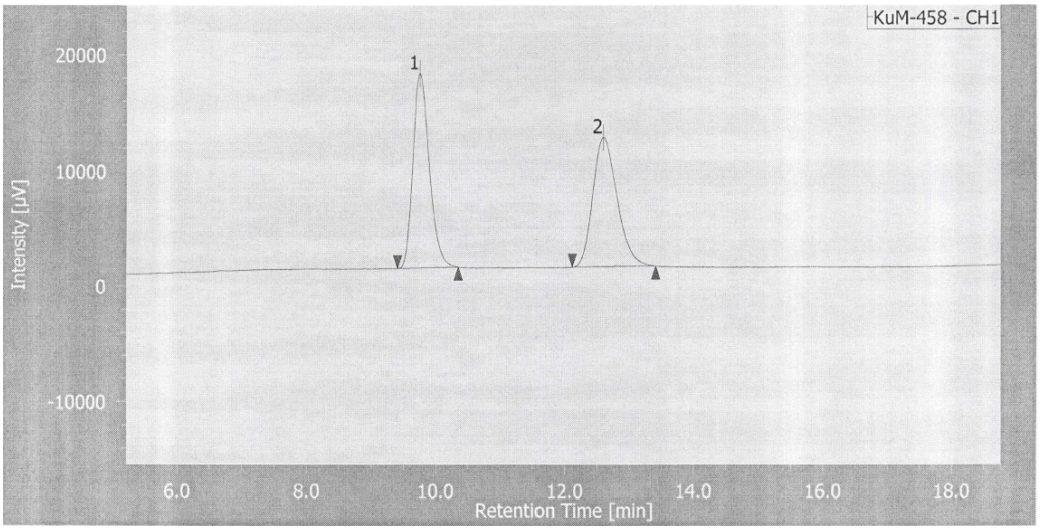
Peak	tR (min)	Area (%)
1	12.3	49.9
2	21.3	50.1

(1*R*,2*R*)-**4**

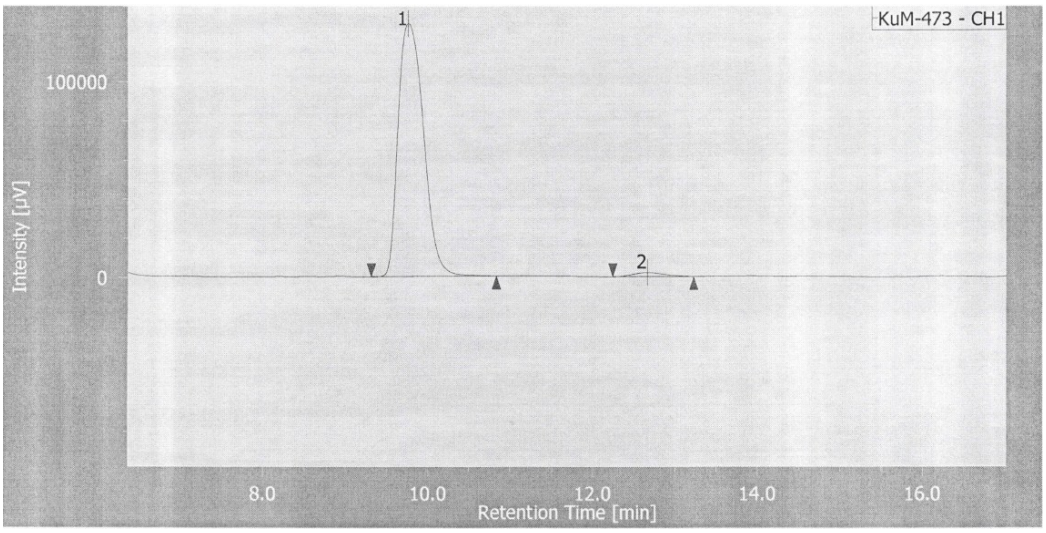
Peak	tR (min)	Area (%)
1	10.6	98.5
2	17.3	1.5



racemic



(1*R*,2*R*)

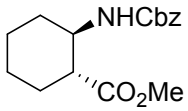


racemic-**4**

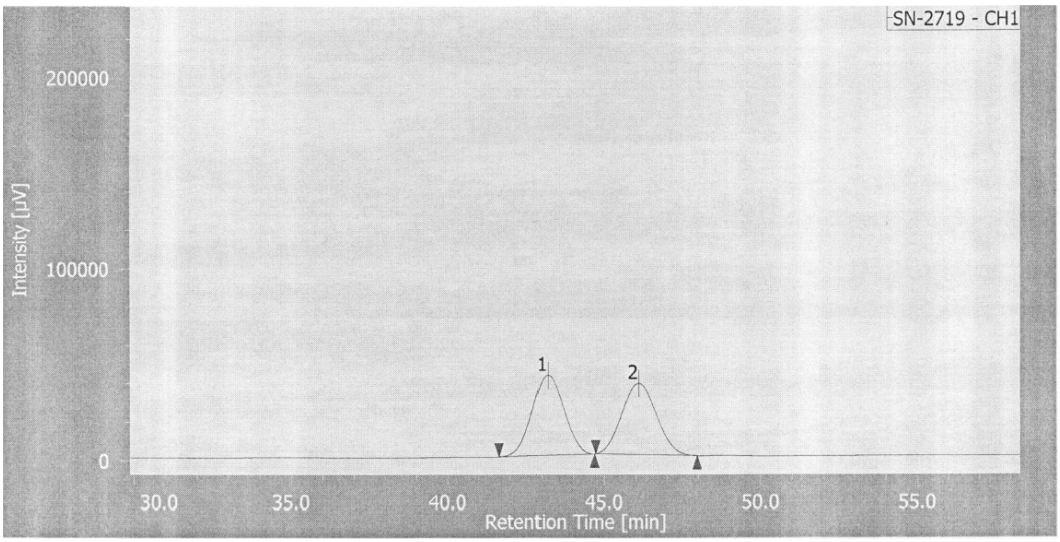
Peak	tR (min)	Area (%)
1	9.8	50.2
2	12.6	49.8

(1*R*,2*R*)-**4**

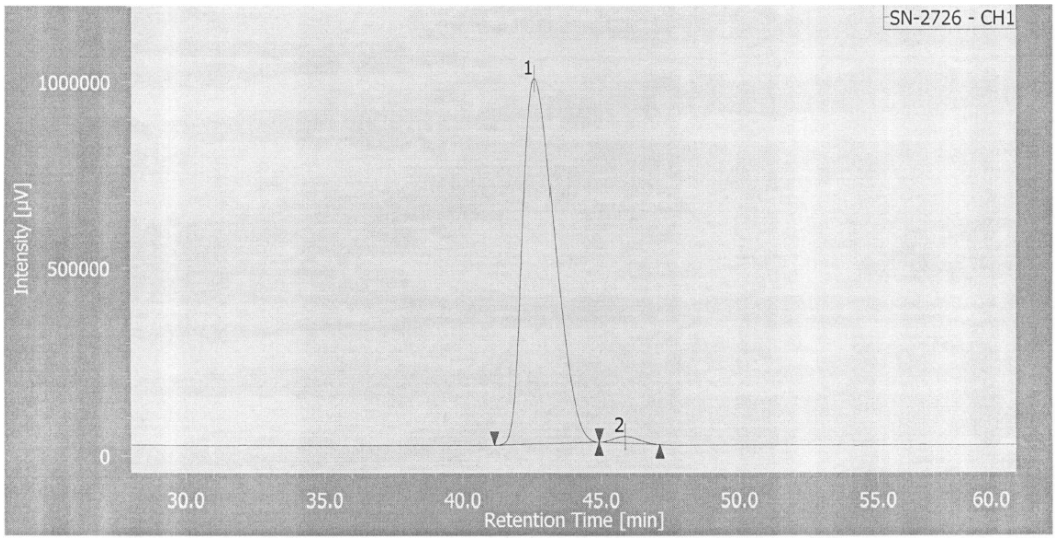
Peak	tR (min)	Area (%)
1	9.8	98.1
2	12.7	1.9



racemic



(1*R*,2*R*)

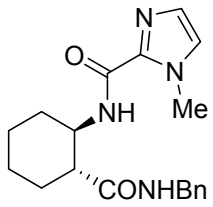


racemic

Peak	tR (min)	Area (%)
1	43.2	50.5
2	46.1	49.5

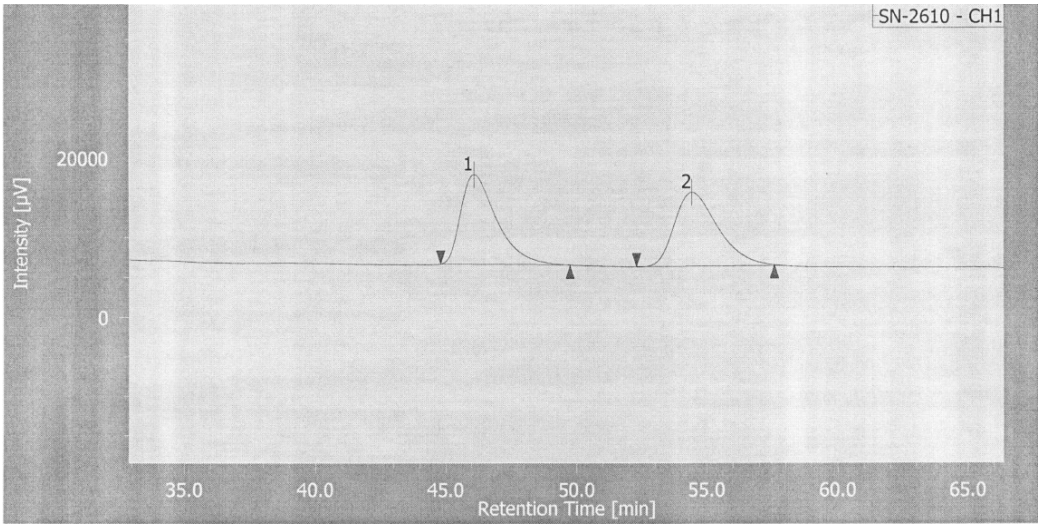
(1*R*,2*R*)

Peak	tR (min)	Area (%)
1	42.6	98.6
2	45.9	1.4

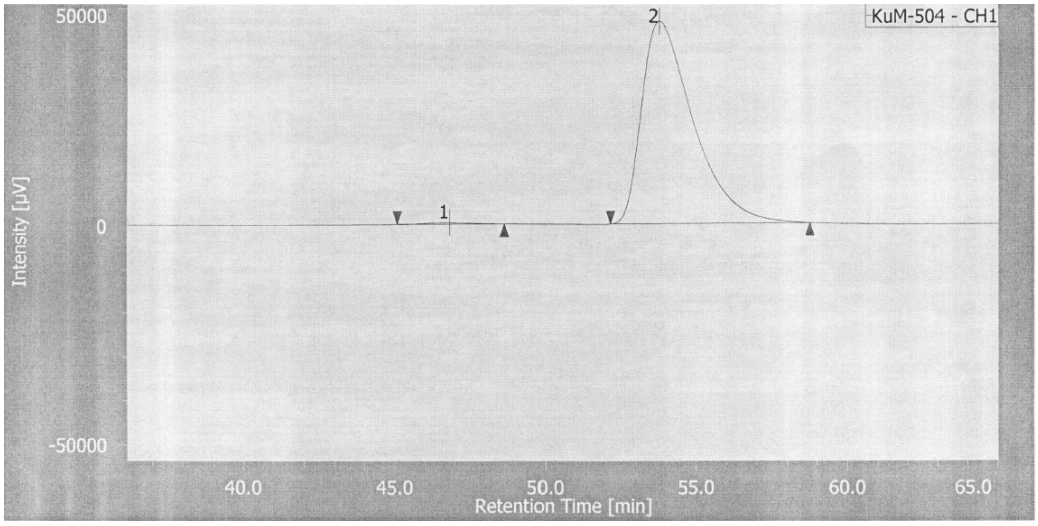


6

racemic-**6**



(1*R*,2*R*)-**6**

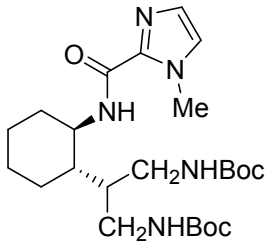


racemic-**6**

Peak	tR (min)	Area (%)
1	46.1	50.0
2	54.4	50.0

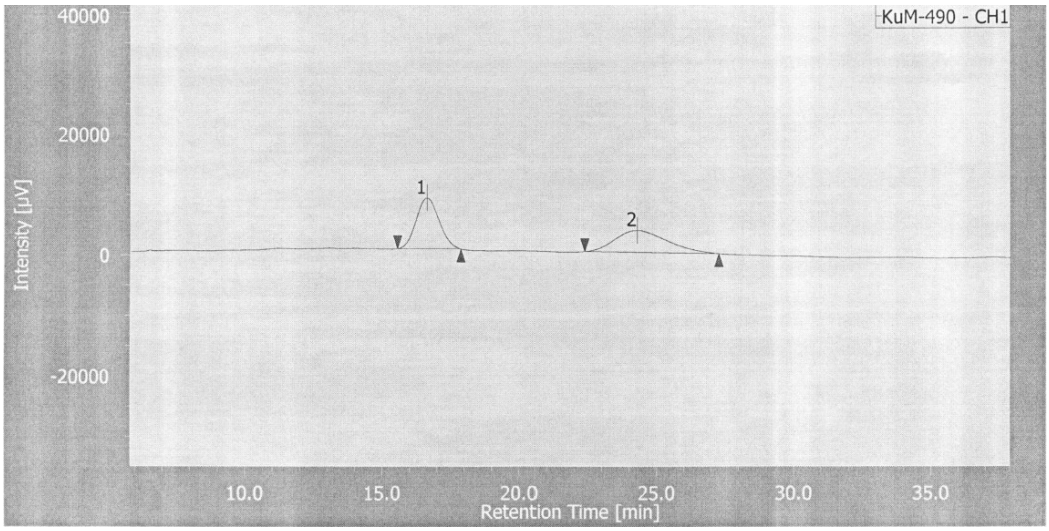
(1*R*,2*R*)-**6**

Peak	tR (min)	Area (%)
1	46.8	0.7
2	53.8	99.3

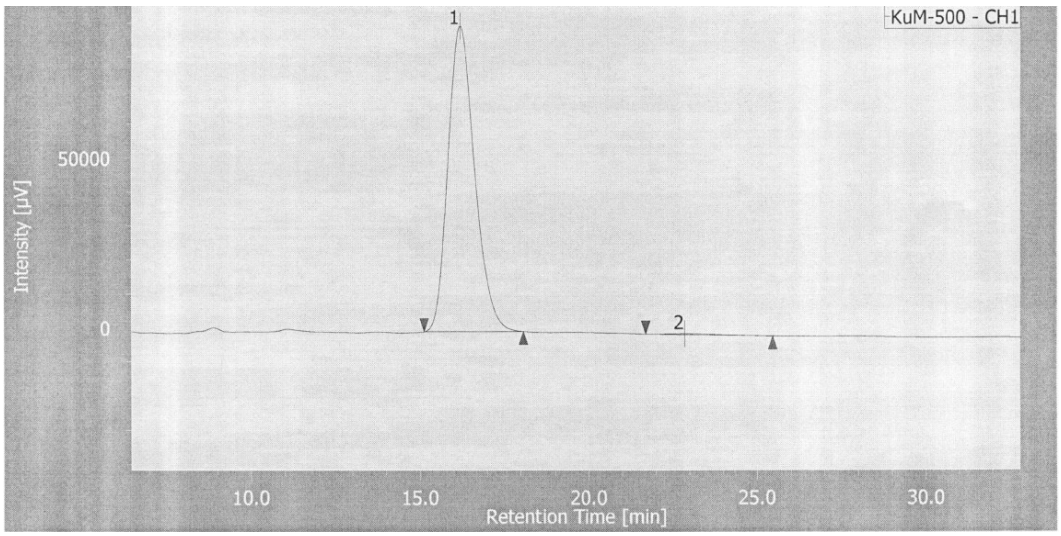


7

racemic-**7**



(1*S*,2*R*)-**7**



racemic-**7**

Peak	tR (min)	Area (%)
1	16.6	50.0
2	24.3	50.0

(1*S*,2*R*)-**7**

Peak	tR (min)	Area (%)
1	16.2	99.3
2	22.9	0.7