Electronic Supplementary information (ESI)

Diastereoselective addition to *N*-acyliminium ions with aryl- and alkenyl boronic acids *via* a Petasis-type reaction

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1. General Methods.

All manipulations of oxygen- and moisture-sensitive materials were conducted with a test tube under a nitrogen atmosphere. All melting points are measured by MICRO MELTING POINT APPARATUS (Yanaco) and these are not corrected. ^{1}H, ^{13}C and ^{19}F NMR spectra were taken at 400, 100 and 376 MHz, with on JEOL AL 400 respectively using tetramethylsilane (^{1}H and ^{13}C) and trichlorofluoromethane (^{19}F) as an internal standard. Since the presence of rotamers for each compounds (**2**–**4**, **7d**, **7h**, **7i**, **7o**, **7q**, **7r**, **8**, **9a**, and **9b**) were confirmed by NMR analysis at ambient temperature, variable-temperature NMR spectroscopy at about 50 ˚C were performed. Infrared spectra were recorded on a Shimadzu IRAffinity-1 spectrometer and expressed in cm^{-1}. Mass spectra (MS) and high resolution mass spectra were recorded with JEOL JMS-700N instrument using electron ionization (EI) mass spectrometry. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Nacalai tesque) with the indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates (Merck).

Materials.

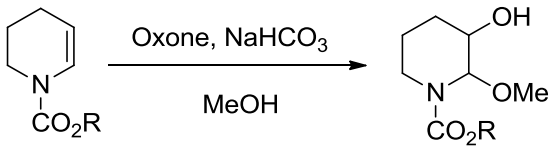
Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers and were used without further purification. All chemicals were purchased from Aldrich, Nacalai tesque, Tokyo Chemical Industry and Wako Pure Chemical Industries and used as received. Dry dichloromethane was purchased from Wako Pure Chemical Industries. The preparation of **1**[1], **2**[2], **4**[3], and **9c**[4] has been reported. The synthesis of the *cis*-isomers (**7a**, **7b**, **7d**, and **7j**) has been reported[5] and the ^{1}H NMR datas of compounds prepared by us is consistent with literature examples. The coupling constant $J_{2,3}$ values for *cis*-isomers were 5.6–5.8 Hz, compared with <1.0 Hz for the corresponding *trans*-isomers.[8, 13] The stereochemistry of **7c**, **7e**, **7f**–**i**, **7k**, **7m**–**r** and **8** was readily

determined from the examination of the coupling constant $J_{2,3}$, which was 5.2–6.1 Hz, consistent with $J_{2,3}$ values for *cis*-isomers.

. On the other hand, the major isomer were expected to be the *trans*-isomer **10a**–**c** by the examination of their coupling constant $J_{2,3}$= <1.0 Hz, consistent with examples for *trans*-2-aryl-3-hydroxypiperidines.

2. Experimental Procedures and Characterization data

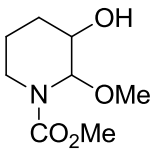
Preparation of N-Protected-3-hydroxy-2-methoxypiperidine 2–4



2 : R=Me
3 : R=Ph
4 : R=Bn

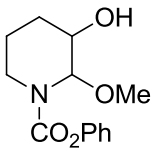
General Procedure

A solution of *N*-carbomethoxy-1,2,3,4-tetrahydropyridine[6] (10.1 mmol) in MeOH (20 mL) was added to a suspension of Oxone (7.38 g, 12.0 mmol) and $NaHCO_3$ (1.01 g, 12.0 mmol) in MeOH (20 mL) at room temperature. After stirring for 2 h, further Oxone (7.38 g, 12.0 mmol) and $NaHCO_3$ (1.01 g, 12.0 mmol) was added. The mixture was stirred for 12 h, after which solids were removed by filtration. The filtrate was diluted with EtOAc (50 mL) and saturated aqueous $NaHCO_3$ (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Product was obtained as a colorless oil which was purified by silica gel column chromatography (EtOAc/*n*-hexane=1/1).



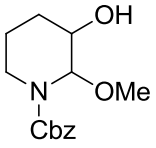
2

***N*-Methoxycarbonyl-3-hydroxy-2-methoxypiperidine** (**2**): inseparable mixture of diastereomers (dr = 1/1), colorless oil, 22% yield; IR (neat) 3431, 2947, 1682, 1443, 1408, 1373, 1348, 1263, 1192, 1155, 1132, 1076, 1040, 995, 962, 770, 733, 664 cm^{-1}; ^1H NMR ($CDCl_3$, 50 ˚C) δ 1.40–2.07 (m, 5H), 2.82 (t, *J*=13.0 Hz, 1/2H), 2.95 (dt, *J*=3.0, 13.0 Hz, 1/2H), 3.28 (s, 3/2H), 3.33 (s, 3/2H), 3.48–3.58 (m, 1/2H), 3.73 (s, 3/2H), 3.79 (s, 3/2H), 3.89–4.00 (m, 3/2H), 5.13–5.52 (m , 1H); ^{13}C NMR ($CDCl_3$, 50 ˚C) δ 18.6, 23.9, 25.6, 27.8, 37.7, 38.4, 52.6, 54.6, 55.1, 66.0, 69.1, 84.5, 85.4, 156.2, 157.3; HRMS (EI) m/z Anal. Calcd for $C_8H_{15}NO_4$ 189.1001, found $[M]^+$ 189.0995.



3

***N*-Phenoxycarbonyl-3-hydroxy-2-methoxypiperidine** (**3**): inseparable mixture of diastereomers (dr = 1/1), colorless oil, 66% yield; IR (neat) 3437, 2938, 1697, 1412, 1373, 1350, 1263, 1200, 1153, 1069, 1024, 997, 966, 864, 800, 748, 689, 667, 601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C), rotamers, δ 1.45–2.16 (m, 5 H), 2.86–3.17 (m, 1H), 3.39 (s, 3/2H), 3.44 (s, 3/2H), 3.59–3.71 (m, 1/2H), 3.90–4.13 (m, 3/2H), 5.34 (s, 1/2H), 5.49 (s, 1/2H), 7.11 (t, *J*=7.1 Hz, 2H), 7.17–7.21 (m, 1H), 7.33–7.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 ˚C), rotamers, δ 18.4, 23.4–23.8, 25.2, 27.4, 37.6, 38.2–39.0, 54.5, 54.8–55.5, 65.5, 68.7–68.9, 84.0–84.9, 85.7, 121.1, 121.3, 124.9, 125.1, 128.8, 128.9, 150.9, 151.1, 153.4–153.9, 154.8; HRMS (EI) m/z Anal. Calcd for $C_{13}H_{17}NO_4$ 251.1158, found $[M]^+$ 251.1144.

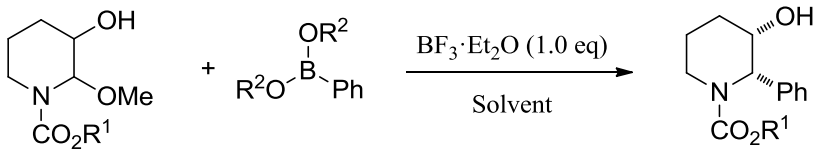


4

***N*-Benxyloxycarbonyl-3-hydroxy-2-methoxypiperidine** (**4**)**:** inseparable mixture of diastereomers (dr = 1/1), colorless oil, 68% yield; IR (neat) 3421, 2940, 1678, 1418, 1344, 1304, 1260, 1192, 1153, 1130, 1074, 1028, 961, 874, 766, 735, 696, 664, 604 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C), δ 1.35–2.06 (m, 5 H), 2.83 (t, *J*=12.7 Hz, 1/2H), 2.97 (t, *J*=12.7 Hz, 1/2H), 3.24 (s, 3/2H), 3.28–3.39 (m, 3/2H), 3.50–3.59 (m, 1/2H), 3.81–4.02 (m, 3/2H), 5.07–5.48 (m, 3H), 7.32 (br. s, 5H); ^{13}C NMR ($CDCl_3$, 50 ˚C) δ 18.7, 23.9, 25.6, 28.0, 37.8, 38.5, 54.8, 55.1–55.8, 66.2, 67.3, 67.4, 69.1, 84.5, 85.5, 127.8, 128.0, 128.1, 128.47, 128.51, 136.4, 136.6, 155.6, 156.7; HRMS (EI) m/z Anal. Calcd for $C_{14}H_{19}NO_4$ 265.1314, found $[M]^+$ 265.1317.

Optimization for the diastereoselective nucleophilic substitution of N,O-acetals with phenylboronic acid

Table 1. Diastereoselective nucleophilic substitution of N-acyliminium ions with phenyl boronic acid.



2–4 **5a–7a**

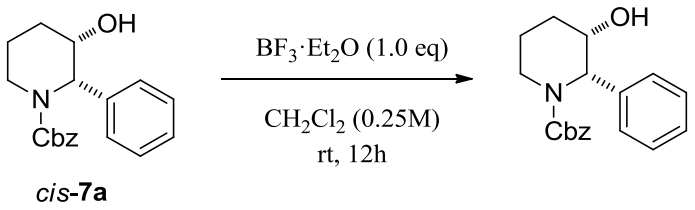
Entry	R^1 (Substrate)	OR^2, OR^2	Solvent	Temp	Time (h)	Product	dr (*cis* : *trans*)[a]	Yield (%)[b]
1	Me (**2**)	OH, OH	CH_2Cl_2	–30 °C to rt	6	**5a**	–	trace
2	Ph (**3**)	OH, OH	CH_2Cl_2	–30 °C to rt	18	**6a**	7.2:1	14
3	Ph (**3**)	$O(CH_2)_2O$	CH_2Cl_2	–30 °C to rt	18	**6a**	–	trace
4	Ph (**3**)	OH, OH	CH_2Cl_2	–78 °C to rt	18	**6a**	–	0
5	Bn (**4**)	OH, OH	CH_2Cl_2	–30 °C to rt	24	**7a**	8.3:1	69
6[c]	Bn (**4**)	OH, OH	CH_2Cl_2	–30 °C to rt	24	**7a**	–	0
7	Bn (**4**)	OH, OH	MeCN	–30 °C to rt	24	**7a**	–	0

[a] The diastereomer ratio was determined by ^{1}H-NMR spectroscopy of the crude mixture. [b] Yield of isolated product after purification by column chromatography. [c] The reaction performed with 1.0 equivalent of $TiCl_4$ instead of $BF_3{\cdot}Et_2O$.

As shown in Table 1, we examined the optimization conditions for Lewis acid-mediated arylation reactions with phenylboronic acid and *N*-acyliminium ion precursors **2–4**. An initial survey using substrate **2** indicated that the reaction in the presence of $BF_3{\cdot}Et_2O$ did not proceed. The *N*,*O*-acetal **3** possessing a *N*-phenoxycarbonyl group reacted slightly with phenyboronic acid, providing the desired product **6a**. The use of the corresponding ethylene glycol boronate did not obtained practically the desired product **6a**. In contrast, the reaction of *N*-Cbz piperidine **4** proceeded with good diastereoselectivity (*cis*:*trans*=8.2:1 by ^{1}H NMR), and gave the *cis*-adduct **7a** in 69% yield as a single isomer after purification by column chromatography. Otherwise, $TiCl_4$ was found to be a poor mediator. In addition, this process at low temperature –78 °C was ineffective. The reaction in MeCN was carried out, however the desired product **7a** did not obtained.

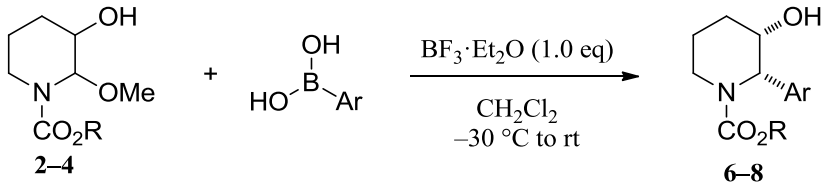
Examination of the presence and absence of the isomerization for 7a

We performed examinations on dependence of diastereoselectivity on the presence or absence of epimerization for *cis*-**7a** caused by $BF_3{\cdot}Et_2O$ to elucidate an origin of the lower diastereoselectivitiy of **7a**. A solution of *cis*-**7a** in dichloromethane was added $BF_3{\cdot}Et_2O$ at room temperature. After stirring for 12 h, the diastereomer ratio was detected by ^{1}H NMR analysis, however the conversion from *cis*- to *trans*-isomers did not been observed.



cis-**7a**

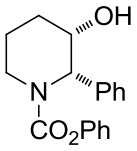
Preparation of N-Alkoxycarbonyl-2-arylpiperidin-3-ol (6–8)



2–4 **6–8**

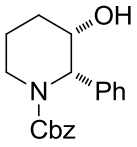
General Procedure

To stirred suspension of substrate (0.50 mmol) and organoboronic acid (0.50 mmol) in CH_2Cl_2 (2.0 mL) were added $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) at –30 °C under N_2 atmosphere. The reaction mixture was warmed to rt over 4 h and stirred for a time specified in Table 1 and 2 of a letter, quenched with saturated aqueous NH_4Cl (10 mL) and the aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography (EtOAc/*n*-hexane=1/1) afforded a desired product. The diastereomer ratio was determined by ^{1}H NMR analysis of the crude mixtures. The spectral data of the arylation products (**6**–**8**) are as follows.



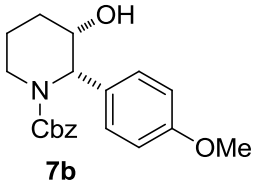
6a

***N*-Phenoxycarbonyl-*cis*-2-phenylpiperidine-3-ol** (**6a**): The title compound was prepared according to the general procedure. From **3** (125.8 mg, 0.50 mmol) and phenylboronic acid (61.0 mg, 0.50 mmol) , $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 18 h. The diastereomer ratio (*cis*/*trans* = 7.2/1) was determined by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **6a** (20.0 mg, 14%) as a colorless paste as a single isomer. IR (neat) 3441, 2945, 1692, 1494, 1416, 1366, 1263, 1200, 1163, 1146, 1078, 1024, 962, 862, 731, 698, 548 cm^{-1}; ^{1}H NMR ($CDCl_3$), δ 1.51–1.95(m, 5H), 3.19 (dt, *J*=4.2, 13.0 Hz, 1H), 4.17–4.19 (m, 2H), 5.54 (d, *J*=5.9 Hz, 1H), 7.01 (d, *J*=7.6 Hz, 2H), 7.17 (t, *J*=7.6 Hz, 1H), 7.31–7.39 (m, 5H), 7.54 (d, *J*=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.1, 27.6, 40.1, 59.6, 69.9, 121.6, 125.3, 127.5, 128.4, 128.6, 129.2, 137.5, 151.3, 154.5; HRMS (EI) m/z Anal. Calcd for $C_{18}H_{19}NO_3$ 297.1365, found $[M]^+$ 297.1361.



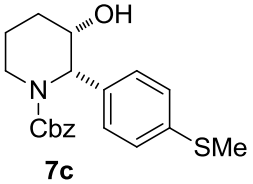
7a

***N*-Benzyloxycarbonyl-*cis*-2-phenylpiperidin-3-ol** (**7a**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and phenylboronic acid (61.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The diastereomer ratio (*cis*/*trans* = 8.3/1) was determined by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7a** (108 mg, 69%) as a colorless paste as a single isomer. IR (neat) 3441, 2945, 1670, 1421, 1252, 1148, 1082, 1063, 962, 735, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.65–2.10 (m, 5H), 3.05 (t, *J*=12.7 Hz, 1H), 4.05–4.10 (m, 2H), 5.08 (d, *J*=12.5 Hz, 1H), 5.13 (d, *J*=12.5 Hz, 1H), 5.44 (d, *J*=5.6 Hz, 1H), 7.23–7.35 (m, 8H), 7.46 (d, *J*=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.2, 27.5, 39.7, 59.1, 67.3, 67.0, 127.3, 127.6, 127.9, 128.4, 128.41, 128.44, 136.5, 137.7, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{19}H_{21}NO_3$ 311.1521, found $[M]^+$ 311.1502.



7b

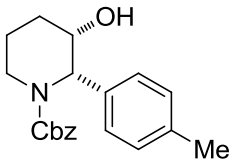
***N*-Benzyloxycarbonyl-*cis*-2-(4-methoxyphenyl)piperidin-3-ol** (**7b**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 4-methoxyphenylboronic acid (76.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 5 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7b** (146.9 mg, 86%) as a colorless paste as a single isomer. IR (neat) 3443, 2940, 1670, 1611, 1510, 1422, 1342, 1246, 1179, 1148, 1080, 1028, 962, 831, 760, 734, 696, 606 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59–1.98 (m, 5H), 3.02 (dt, *J*=3.7, 13.2 Hz, 1H), 3.79 (s, 3H), 4.01–4.08 (m, 2H), 5.08 (d, *J*=12.2 Hz, 1H), 5.13 (d, *J*=12.2 Hz, 1H), 5.42 (d, *J*=5.6 Hz, 1H), 6.85 (d, *J*=8.5 Hz, 2H), 7.25–7.34 (m, 5H), 7.39 (d, *J*=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.4, 27.7, 39.6, 55.2, 58.5, 67.2, 70.0, 113.8, 127.7, 127.9, 128.4, 129.5, 129.8, 136.6, 155.9, 158.7; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{23}NO_4$ 341.1627, found $[M]^+$ 341.1628.



7c

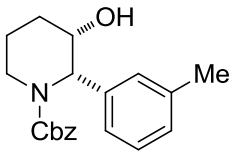
***N*-Benzyloxycarbonyl-*cis*-2-[4-(methylthio)phenyl]piperidin-3-ol** (**7c**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and

4-(methylthio)phenylboronic acid (84.0 mg, 0.50 mmol), $BF_3 \cdot OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 5 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7c** (126.0 mg, 71%) as a colorless paste as a single isomer. IR (neat) 3429, 2945, 1670, 1495, 1422, 1344, 1248, 1148, 1080, 1028, 961, 824, 733, 693, 606, 557 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.56–1.86 (m, 5H), 2.96 (dt, *J*=3.2, 13.2 Hz, 1H), 3.79 (s, 3H), 4.01–4.06 (m, 2H), 5.08 (d, *J*=12.4 Hz, 1H), 5.14 (d, *J*=12.4 Hz, 1H), 5.44 (d, *J*=5.4 Hz, 1H), 7.18 (d, *J*=8.3 Hz, 2H), 7.26–7.36 (m, 5H), 7.41 (d, *J*=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.6, 23.4, 27.5, 39.6, 58.4, 67.2, 70.0, 126.3, 127.6, 127.9, 128.3, 129.0, 134.4, 136.4, 137.2, 155.8; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{23}NO_3S$ 357.1399, found $[M]^+$ 357.1387.



7d

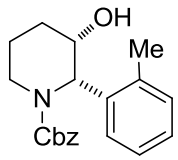
***N*-Benzyloxycarbonyl-*cis*-2-(4-methylphenyl)piperidin-3-ol** (**7d**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 4-methylphenylboronic acid (68.0 mg, 0.50 mmol), $BF_3 \cdot OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 19 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7d** (108.3 mg, 67%) as a colorless paste as a single isomer. IR (neat) 3424, 2943, 1670, 1514, 1421, 1342, 1250, 1182, 1148, 1080, 1063, 1028, 962, 816, 735, 696, 608, 569 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C) δ 1.66–1.86 (m, 4H), 2.33 (s, 3H), 3.10 (dt, *J*=3.6, 13.4 Hz, 1H), 4.05–4.10 (m, 2H), 5.08 (d, *J*=12.4 Hz, 1H), 5.13 (d, *J*=12.4 Hz, 1H), 5.39 (d, *J*=5.8 Hz, 1H), 7.12 (d, *J*=8.0 Hz, 2H), 7.21–7.34 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 20.9, 23.3, 27.5, 39.6, 58.7, 67.2, 69.9, 127.6, 127.8, 128.3, 128.4, 129.0, 134.5, 136.5, 136.7, 155.8; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{23}NO_3$ 325.1678, found $[M]^+$ 325.1667.



7e

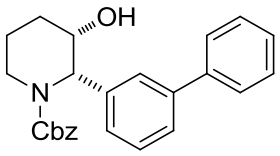
***N*-Benzyloxycarbonyl-*cis*-2-(3-methyphenyl)piperidin-3-ol** (**7e**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 3-methylphenylboronic acid (68.0 mg, 0.50 mmol), $BF_3 \cdot OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7e** (107.3 mg, 66%) as a colorless paste as a single isomer. IR (neat) 3431, 2943, 1670, 1420, 1342, 1250, 1146, 1080, 1063, 1028, 966, 908, 887, 870, 793, 733, 696, 608 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59–1.89 (m, 4H), 2.15 (br.

s, OH), 2.31 (s, 3H), 3.06 (dt, *J*=3.7, 13.2 Hz, 1H), 4.00–4.10 (m, 2H), 5.06 (d, *J*=12.4 Hz, 1H), 5.13 (d, *J*=12.4 Hz, 1H), 5.39 (d, *J*=5.4 Hz, 1H), 7.07 (d, *J*=7.3 Hz, 1H), 7.18–7.28 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 21.5, 23.1, 27.4, 39.7, 59.1, 67.2, 69.8, 125.3, 127.6, 127.8, 128.0, 128.2, 128.3, 129.2, 136.5, 137.6, 138.0, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{23}NO_3$ 325.1678, found $[M]^+$ 325.1679.



7f

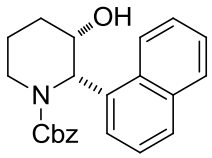
***N*-Benzyloxycarbonyl-*cis*-2-(2-methyphenyl)piperidin-3-ol** (**7f**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 2-methylphenylboronic acid (68.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7f** (79.0 mg, 49%) as a colorless paste as a single isomer. IR (neat) 3443, 2945, 1672, 1416, 1342, 1260, 1150, 1126, 1078, 1055, 1016, 959, 770, 729, 696, 608 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.43 (br. s, OH), 1.78–1.97 (m, 4H), 2.03 (s, 3H), 3.46 (dt, *J*=4.9, 13.2 Hz, 1H), 4.05–4.11 (m, 1H), 4.15 (dd, *J*=5.1, 14.2 Hz, 1H), 4.95 (d, *J*=12.4 Hz, 1H), 5.04 (d, *J*=12.4 Hz, 1H), 5.36 (d, *J*=5.4 Hz, 1H), 7.05 (br. s, 2H), 7.13–7.19 (m, 3H), 7.24–7.28 (m, 3H), 7.35–7.37 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 19.7, 21.2, 26.4, 40.0, 56.8, 67.2, 67.6, 126.0, 127.2, 127.4, 127.6, 127.8, 128.3, 130.9, 136.4, 137.1, 137.2, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{23}NO_3$ 325.1678, found $[M]^+$ 325.1683.



7g

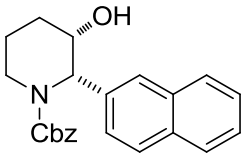
***N*-Benzyloxycarbonyl-*cis*-2-(3-biphenyl)piperidin-3-ol** (**7g**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 3-biphenylboronic acid (99.2 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7g** (83.3 mg, 43%) as a colorless paste as a single isomer. IR (neat) 3410, 2924, 1670, 1420, 1250, 1179, 1148, 1078, 1026, 962, 908, 864, 760, 733, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57–1.96 (m, 5H), 3.46 (dt, *J*=3.7, 13.4 Hz, 1H), 4.06–4.15 (m, 2H), 5.08 (d, *J*=12.4 Hz, 1H), 5.15 (d, *J*=12.4 Hz, 1H), 5.50 (d, *J*=5.2 Hz, 1H), 7.23–7.53 (m, 13H), 7.67 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 23.1, 27.6, 39.8, 59.3, 67.3, 70.0, 126.2, 127.18, 127.23, 127.3, 127.4, 127.7, 127.9, 128.1, 128.4, 128.7, 128.8, 136.5, 138.4, 141.0, 141.4, 155.9; HRMS (EI) m/z

Anal. Calcd for $C_{25}H_{25}NO_3$ 387.1834, found $[M]^+$ 387.1828.



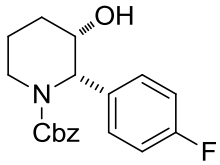
7h

***N*-Benzyloxycarbonyl-*cis*-2-(1-naphthyl)piperidin-3-ol** (**7h**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 1-naphthaleneboronic acid (86.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7h** (128.9 mg, 71%) as a colorless paste as a single isomer. IR (neat) 3421, 2949, 2359, 1682, 1418, 1254, 1150, 1126, 1007, 949, 781, 733, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C) δ 1.62 (br. s, OH), 1.80–1.98 (m, 3H), 2.05–2.18 (m, 1H), 3.42–3.50 (m, 1H), 4.17 (br. d, *J*=12.2 Hz, 1H), 4.36(br. s, 1H), 4.98 (d, *J*=12.4 Hz, 1H), 5.04 (d, *J*=12.4 Hz, 1H), 6.00 (d, *J*=5.4 Hz, 1H), 6.96 (br. s, 2H), 7.14–7.21 (m, 3H), 7.42–7.52 (m, 3H), 7.61 (d, *J*=7.1 Hz, 1H), 7.79 (d, *J*=8.3 Hz, 1H), 7.86–7.89 (m, 1H), 8.13 (d, *J*=8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.2, 26.4, 39.7, 57.0, 67.1, 68.0, 123.1, 125.0, 125.7, 126.3, 127.3, 127.6, 128.2, 128.2, 128.3, 128.9, 131.5, 133.9, 134.4, 136.3, 155.8; HRMS (EI) m/z Anal. Calcd for $C_{23}H_{23}NO_3$ 361.1678, found $[M]^+$ 361.1687.



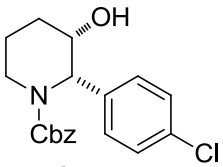
7i

***N*-Benzyloxycarbonyl-*cis*-2-(2-naphthyl)piperidin-3-ol** (**7i**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 2-naphthaleneboronic acid (86.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7i** (128.1 mg, 71%) as a colorless paste as a single isomer. IR (neat) 3418, 2943, 1665, 1420, 1256, 1148, 1167, 1078, 970, 945, 818, 731, 696, 604 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C) δ 1.68–1.98 (m, 5H), 3.16 (dt, *J*=3.1, 13.0 Hz, 1H), 4.11–4.20 (m, 2H), 5.09 (d, *J*=12.4 Hz, 1H), 5.15 (d, *J*=12.4 Hz, 1H), 5.58 (d, *J*=5.4 Hz, 1H), 7.17–7.27 (m, 5H), 7.43–7.48 (m, 2H), 7.52–7.55 (m, 1H), 7.75–7.83 (m, 3H), 7.93 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 23.7, 27.5, 39.8, 59.1, 67.3, 70.1, 125.9, 126.0, 126.4, 127.37, 127.39, 127.6, 127.9, 128.0, 128.0, 128.3, 132.5, 133.1, 135.2, 136.4, 156.0; HRMS (EI) m/z Anal. Calcd for $C_{23}H_{23}NO_3$ 361.1678, found $[M]^+$ 361.1669.



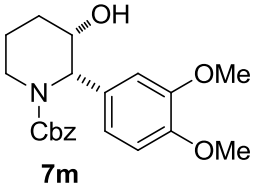
7j

***N*-Benzyloxycarbonyl-*cis*-2-(4-fluorophenyl)piperidin-3-ol** (**7j**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 4-fluorophenylboronic acid (70.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7j** (62.3 mg, 38%) as a colorless paste as a single isomer. IR (neat) 3421, 2943, 1670, 1508, 1422, 1342, 1251, 1223, 1148, 1080, 1028, 962, 833, 735, 696, 606 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60–1.87 (m, 4H), 2.04 (br. s, OH), 2.96 (dt, *J*=3.2, 13.0 Hz, 1H), 4.02–4.10 (m, 2H), 5.09 (d, *J*=12.4 Hz, 1H), 5.15 (d, *J*=12.4 Hz, 1H), 5.45 (d, *J*=5.6 Hz, 1H), 6.99 (t, *J*=8.8 Hz, 2H), 7.24–7.35 (m, 5H), 7.45 (dd, *J*=5.6, 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.4, 27.6, 39.6, 58.3, 67.4, 70.1, 115.2 (d, *J*=20.6 Hz), 127.7, 128.0, 128.4, 130.2 (d, *J*=8.2 Hz), 133.4 (d, *J*=3.3 Hz), 136.4, 155.9, 161.9 (d, *J*=244.5 Hz); ^{19}F NMR ($CDCl_3$) δ –115.9 (s, 1F); HRMS (EI) m/z Anal. Calcd for $C_{19}H_{20}FNO_3$ 329.1427, found $[M]^+$ 329.1426.



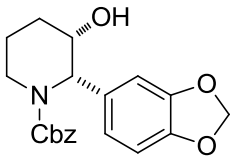
7k

***N*-Benzyloxycarbonyl-*cis*-2-(4-chlorophenyl)piperidin-3-ol** (**7k**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 4-fluorophenylboronic acid (78.2 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7k** (57.5 mg, 33%) as a colorless paste as a single isomer. IR (neat) 3428, 2943, 1670, 1491, 1420, 1342, 1294, 1248, 1182, 1148, 1082, 1012, 962, 829, 765, 731, 696, 608, 580, 567 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.58–1.89 (m, 4H), 2.02 (br. s, OH), 2.95 (dt, *J*=3.4, 13.4 Hz, 1H), 4.00–4.12 (m, 2H), 5.09 (d, *J*=12.4 Hz, 1H), 5.15 (d, *J*=12.4 Hz, 1H), 5.45 (d, *J*=5.4 Hz, 1H), 7.24–7.36 (m, 7H), 7.42 (d, *J*=8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.4, 27.6, 39.6, 58.4, 67.4, 70.1, 127.8, 128.0, 128.45, 128.49, 129.9, 133.1, 136.3, 136.4, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{19}H_{20}35ClNO_3$ 345.1132, found $[M]^+$ 345.1128.



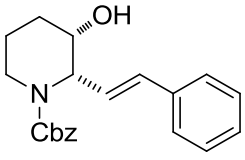
7m

***N*-Benzyloxycarbonyl-*cis*-2-(3,4-dimethoxyphenyl)piperidin-3-ol** (**7m**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 3,4-dimethoxyphenylboronic acid (91.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 5 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane= 1/1) of the crude residue afforded **7m** (119.4 mg, 64%) as a colorless paste as a single isomer. IR (neat) 3443, 2938, 1670, 1514, 1420, 1344, 1250, 1244, 1082, 1026, 970, 766, 735, 698, 605 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.64–1.88 (m, 5H), 3.06 (dt, *J*=3.6, 13.2 Hz, 1H), 3.77 (s, 3H), 3.87 (s, 3H), 4.06–4.10 (m, 2H), 5.08 (d, *J*=12.4 Hz, 1H), 5.15 (d, *J*=12.4 Hz, 1H), 5.39 (d, *J*=5.8 Hz, 1H), 6.82 (d, *J*=8.6 Hz, 1H), 6.96 (d, *J*=2.2 Hz, 1H), 7.03 (dd, *J*=2.2, 8.6 Hz, 1H), 7.25–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.3, 27.7, 39.6, 55.75, 55.81, 58.8, 67.3, 70.0, 110.9, 112.1, 125.7, 127.8, 127.9, 128.4, 130.0, 136.6, 148.2, 148.8, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{25}NO_5$ 371.1733, found $[M]^+$ 371.1736.



7n

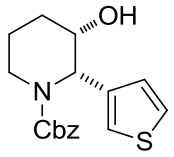
***N*-Benzyloxycarbonyl-*cis*-2-[3,4-(methylenedioxy)phenyl]piperidin-3-ol** (**7n**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 3,4-(methylenedioxy)phenylboronic acid (83.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 14 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7n** (110.3 mg, 62%) as a pale yellow paste as a single isomer. IR (neat) 3431, 2945, 1670, 1503, 1489, 1420, 1344, 1234, 1120, 1072, 1038, 964, 935, 810, 733, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.58–1.87 (m, 5H), 3.05 (dt, *J*=3.9, 13.9 Hz, 1H), 4.00–4.10 (m, 2H), 5.08 (d, *J*=12.4 Hz, 1H), 5.16 (d, *J*=12.4 Hz, 1H), 5.35 (d, *J*=5.6 Hz, 1H), 5.94 (s, 2H), 6.76 (d, *J*=8.0 Hz, 1H), 6.92 (d, *J*=8.0 Hz, 1H), 6.99 (s, 1H), 7.23–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.2, 27.5, 39.6, 58.8, 67.3, 69.9, 101.0, 108.1, 109.0, 121.8, 127.8, 127.9, 128.4, 131.4, 136.5, 146.6, 147.7, 155.9; HRMS (EI) m/z Anal. Calcd for $C_{20}H_{21}NO_5$ 335.1421, found $[M]^+$ 335.1417.



7o

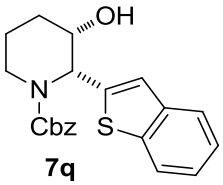
***N*-Benzyloxycarbonyl-*cis*-2-(*E*)-styrylpiperidin-3-ol** (**7o**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and (*E*)-styrylboronic acid (71.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 14 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography

(EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7o** (136.5 mg, 81%) as a colorless paste as a single isomer. IR (neat) 3414, 2941, 1670, 1420, 1342, 1296, 1248, 1159, 1120, 1064, 1010, 964, 876, 784, 733, 694 cm^{-1}; ^1H NMR ($CDCl_3$, 50 ˚C) δ 1.49–1.59 (m, 3H), 1.72–1.79 (m, 1H), 1.83–1.93 (m, 1H), 3.05 (br. t, *J*=12.6 Hz, 1H), 3.83 (br. s, 1H), 4.04 (br. d, *J*=13.4 Hz, 1H), 5.09 (br. t, *J*=6.4 Hz, 1H), 5.14 (d, *J*=12.2 Hz, 1H), 5.19 (d, *J*=12.2 Hz, 1H), 6.34 (dd, *J*=6.4, 16.2 Hz, 1H), 6.57 (d, *J*=16.2 Hz, 1H), 7.21–7.37 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 24.1, 28.6, 38.9, 57.6, 67.3, 68.9, 121.8, 126.3, 127.6, 127.7, 127.9, 128.39, 128.41, 133.9, 136.4, 136.5, 155.7; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{23}NO_3$ 337.1678, found $[M]^+$ 337.1680.



7p

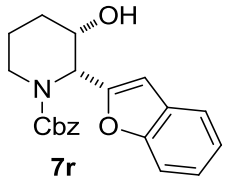
***N*-Benzyloxycarbonyl-*cis*-2-(3-thienyl)piperidin-3-ol** (**7p**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 3-thiopheneboronic acid (83.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 5 h. The only *cis*-isomer was observed by ^1H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane= 1/2 to 1/1) of the crude residue afforded **7p** (90.0 mg, 57%) as a colorless paste as a single isomer. IR (neat) 3443, 2943, 1667, 1422, 1256, 1078, 1062, 1028, 970, 789, 766, 735, 694, 600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50–1.90 (m, 4H), 2.31 (br. s, OH), 2.82 (dt, *J*=3.2, 13.2 Hz, 1H), 3.94–4.06 (m, 2H), 5.12 (d, *J*=12.4 Hz, 1H), 5.16 (d, *J*=12.4 Hz, 1H), 5.61 (d, *J*=5.4 Hz, 1H), 7.10 (d, *J*=5.2 Hz, 1H), 7.25–7.39 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 24.1, 28.1, 39.3, 55.9, 67.4, 70.1, 123.2, 125.3, 127.8, 128.0, 128.2, 128.5, 136.5, 137.4, 155.6; HRMS (EI) m/z Anal. Calcd for $C_{17}H_{19}NO_3S$ 317.1086, found $[M]^+$ 317.1076.



7q

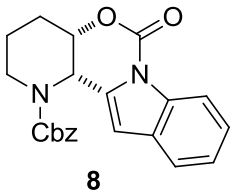
***N*-Benzyloxycarbonyl-*cis*-2-(benzo[*b*]thiophen-2yl)piperidin-3-ol** (**7q**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and benzo[b]thiophene-2-boronic acid (89.1 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^1H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7q** (110.4 mg, 60%) as a white solid from dichloromethane/*n*-hexane as a single isomer. mp:148–149 ˚C; IR (neat) 3410, 2943, 1670, 1418, 1248, 1155, 1069, 1026, 949, 745, 766, 727, 696, 607, 559 cm^{-1}; ^1H NMR ($CDCl_3$, 50 ˚C) δ 1.55–1.68 (m, 1H), 1.74–1.96 (m, 4H), 3.07 (dt, *J*=3.4, 13.2 Hz, 1H), 4.03–4.12 (m, 2H), 5.16 (d, *J*=12.4 Hz, 1H), 5.19 (d, *J*=12.4 Hz, 1H), 5.87 (d, *J*=5.4 Hz, 1H), 7.26–7.34 (m, 8H),

7.68 (d, *J*=6.8 Hz, 1H), 7.77 (d, *J*=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.9, 28.0, 39.5, 56.7, 67.6, 69.8, 121.8, 123.2, 123.8, 124.0, 124.1, 127.8, 128.0, 128.4, 136.2, 139.0, 139.7, 139.9, 155.6; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{21}NO_3S$ 367.1242, found $[M]^+$ 367.1256.



7r

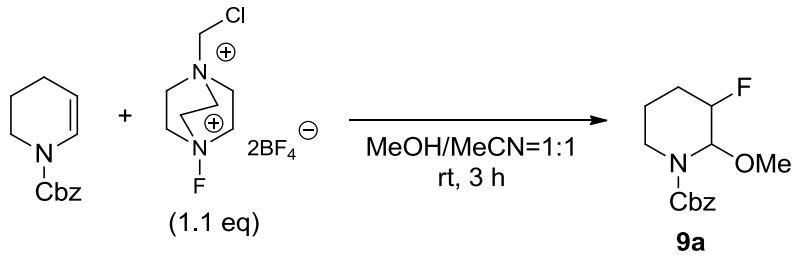
***N*-Benzyloxycarbonyl-*cis*-2-(benzofuran-2yl)piperidin-3-ol** (**7r**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 2-benzofuranboronic acid (89.1 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **7r** (158.4 mg, 90%) as a pale yellow paste as a single isomer. IR (neat) 3421, 2943, 1670, 1454, 1420, 1252, 1157, 1080, 968, 739, 696, 607 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C) δ 1.56–1.71 (m, 1H), 1.80–2.04 (m, 4H), 3.09 (dt, *J*=2.7, 13.2 Hz, 1H), 3.93–4.03 (m, 1H), 4.09 (dd, *J*=3.6, 13.7 Hz, 1H), 5.13 (d, *J*=12.4 Hz, 1H), 5.19 (d, *J*=12.4 Hz, 1H), 5.72 (d, *J*=5.8 Hz, 1H), 6.71 (s, 1H), 7.18–7.33 (m, 7H), 7.43 (d, *J*=8.1 Hz, 1H), 7.51 (d, *J*=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.9, 29.0, 40.1, 54.3, 67.5, 69.1, 106.9, 111.2, 120.9, 122.8, 124.1, 127.8, 128.0, 128.4, 136.3, 154.0, 154.6, 155.5; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{21}NO_4$ 351.1471, found $[M]^+$ 361.1471.



8

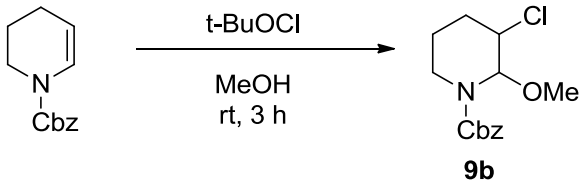
1-Benxyloxycabonyl-6-oxo-2,3,4,4a,6,12b-hexahydropyrido[2',3',5,6][1,3]oxazino[3,4-a]indole (**8**): The title compound was prepared according to the general procedure. From **4** (132.7 mg, 0.50 mmol) and 1-(*N*-methoxycarbonyl)indole-2-boronic acid[7] (109.5 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/2 to 1/1) of the crude residue afforded **8** (114.7 mg, 61%) as a colorless paste as a single isomer. IR (neat) 2924, 1746, 1697, 1454, 1421, 1393, 1358, 1342, 1254, 1198, 1152, 1109, 1067, 1036, 964, 814, 745, 733, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$, 50 ˚C) δ 1.53–1.61 (m, 2H), 1.68–1.77 (m, 1H), 2.17–2.19 (m, 1H), 2.93 (dt, *J*=2.2, 13.0 Hz, 1H), 4.10 (br. d, *J*=11.8 Hz, 1H), 4.59 (quin, *J*=6.1 Hz, 1H), 5.23 (d, *J*=12.2 Hz, 1H), 5.27 (d, *J*=12.2 Hz, 1H), 6.01 (d, *J*=6.1 Hz, 1H), 6.32 (s, 1H), 7.27–7.37 (m, 7H), 7.49 (d, *J*=7.6 Hz, 1H), 8.27 (d, *J*=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.4, 26.4, 38.9, 48.3, 68.0, 75.4, 105.7, 115.2, 120.6, 124.0, 124.8, 128.1, 128.3, 128.6, 129.0, 131.1, 135.6, 135.9, 145.8, 155.4; HRMS (EI) m/z Anal. Calcd for $C_{22}H_{20}N_2O_4$ 376.1423, found $[M]^+$ 376.1411.

***Preparation of N*-benxyloxycarbonyl-3-fluoro-2-methoxypiperidine (9a)**



To a solution of *N*-benzyloxycarbonyl-1,2,3,4-tetrahydropyridine[6] (10.1 mmol) in MeOH (10 mL) and acetonitrile (10 mL) was added Selectfluor® (11.1 mmol) at room temperature. The mixture was stirred for 3 h. The filtrate was diluted with EtOAc (50 mL) and distillated water (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Product was obtained as a colorless oil which was purified by silica gel column chromatography (EtOAc/*n*-hexane=1/10). inseparable mixture of diastereomers (dr = 1/3), 68% yield; IR (neat) 2951, 1697, 1420, 1242, 1161, 1123, 1038, 768, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 50 ˚C), δ 1.38–1.58 (m, 1 H), 1.68–2.00 (m, 3H), 2.67–3.02 (m, 1H), 3.23 (br. s, 3H), 3.77–4.09 (m, 1H), 4.32–4.64 (m, 1H), 5.10–5.26 (m, 2H), 5.39 (br. s, 1H), 7.22–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 50 ˚C) rotamers, δ 18.8, 23.4, 24.2 (d, *J*=20.6 H), 24.4 (d), 37.4, 38.0, 54.7, 55.3, 67.2–67.3(m), 67.4–67.5 (m), 82.3, 82.6, 85.8 (d, *J*=171 Hz), 85.9 (d, *J*=171 Hz), 88.7 (d, *J*=187 Hz), 127.8, 128.0, 128.2, 128.4, 128.5, 136.3, 136.6, 156.1; ^{19}F NMR ($CDCl_3$) δ –183.8 (br. s, 1/4F), –191.4 (br. s, 3/4F); HRMS (EI) m/z Anal. Calcd for $C_{14}H_{18}FNO_3$ 267.1271, found $[M]^+$ 267.1251.

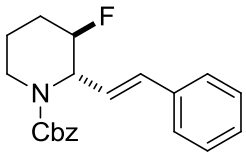
***Preparation of N*-benxyloxycarbonyl-3-chloro-2-methoxypiperidine (9b)**



The chlorination of *N*-benzyloxycarbonyl-1,2,3,4-tetrahydropyridine[6] was carried out under the condition reported by Shono[8] as follows. To a solution of *N*-benzyloxycarbonyl-1,2,3,4-tetrahydropyridine[6] (10.1 mmol) in MeOH (20 mL) was added *tert*-butyl hypochlorite (10.1 mmol) at room temperature. The mixture was stirred for 6 h. The filtrate was diluted with EtOAc (50 mL) and distillated water (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Product was obtained as a colorless oil which was purified by silica gel column chromatography (EtOAc/*n*-hexane=1/10). inseparable mixture of diastereomers, 70% yield; IR (neat) 2949, 1701, 1418, 1342, 1304, 1265, 1229, 1153, 1145, 1074, 878, 766, 735, 696, 638, 604 cm^{-1}; ^1H NMR ($CDCl_3$, 50 ˚C) δ 1.41–1.59 (m,

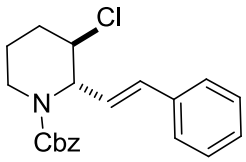
1H), 1.70–1.86 (m, 1H), 1.95–2.26 (m, 2H), 2.97 (br. t, *J*=11.7 Hz, 1H), 3.25 (br. s, 3H), 3.85–4.17 (m, 2H), 5.19 (s, 2H), 5.40 (br. s, 1H), 7.30–7.41 (m, 5H); HRMS (EI) m/z Anal. Calcd for $C_{14}H_{18}ClNO_3$ 283.0975, found $[M]^+$ 283.0975.

Preparation of N*-Benzyloxycarbonyl-3-halo-2-(*E*)-styrylpiperidine *(10a–c)



10a

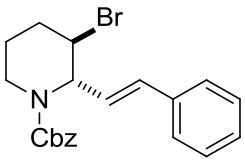
***N*-Benzyloxycarbonyl-*trans*-3-fluoro-2-(*E*)-styrylpiperidine** (**10a**): The title compound was prepared according to the general procedure for N-Alkoxycarbonyl-2-arylpiperidin-3-ol. From **9a** (133.6 mg, 0.50 mmol) and (*E*)-styrylboronic acid (71.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The diastereomer ratio (major/minor=12/1) was determined by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/10) of the crude residue afforded **10a** (105.1 mg, 62%) as a colorless paste as a single isomer. IR (neat) 2949, 1694, 1422, 1295, 1250, 1197, 1150, 1120, 964, 874, 748, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.61–1.71 (m, 1H), 1.74–1.82 (m, 1H), 1.87–1.95 (m, 1H), 1.98–2.06 (m, 1H), 3.03 (br. t, *J*=13.2 Hz, 1H), 4.19 (d, *J*=12.4 Hz, 1H), 4.80 (d, *J*=46.2 Hz, 1H), 5.14 (d, *J*=12.4 Hz, 1H), 5.21 (d, *J*=12.4 Hz, 1H), 5.26 (br. s, 1H), 6.04 (dd, *J*=5.6, 16.1 Hz, 1H), 6.49 (d, *J*=16.1 Hz, 1H), 7.24–7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 18.9, 25.4 (d, *J*=12.4 Hz), 39.5, 57.0 (d, *J*=23.1 Hz), 67.2, 88.6 (d, *J*=176.4 Hz), 122.6 (d, *J*=11.5 Hz), 126.5, 127.8, 128.0, 128.1, 128.5, 128.7, 133.1, 136.5 (d, *J*=59.4 Hz), 156.2; ^{19}F NMR ($CDCl_3$) δ –179.1 (s, 1F); HRMS (EI) m/z Anal. Calcd for $C_{21}H_{22}FNO_2$ 339.1635, found $[M]^+$ 339.1635.



10b

***N*-Benzyloxycarbonyl-*trans*-3-chloro-2-(*E*)-styrylpiperidine** (**10b**): The title compound was prepared according to the general procedure. From **9b** (141.9 mg, 0.50 mmol)[4] and (*E*)-styrylboronic acid (71.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The single isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/10) of the crude residue afforded **10b** (110.3 mg, 62%) as a colorless paste as a single isomer. IR (neat) 2951, 1692, 1420, 1344, 1248, 1213, 1120, 1186, 1144, 1115, 1028, 964, 908, 878, 750, 733, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.49 (d, *J*=12.2 Hz, 1H), 1.93–2.17 (m, 3H), 3.03(br. t, *J*=13.0 Hz, 1H), 4.21 (br. d, *J*=12.9 Hz, 1H), 4.38 (br. s, 1H), 5.19 (s. 2H), 5.23 (br. s, 1H), 6.14 (dd,

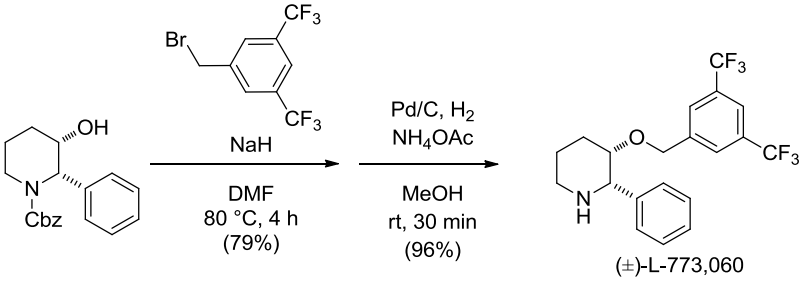
J=5.5, 16.0 Hz, 1H), 7.24–7.37 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 18.8, 27.5, 39.4, 59.1, 59.5, 67.3, 124.3, 126.5, 127.7, 127.9, 128.1, 128.5, 128.7, 133.3, 136.1, 136.8, 156.1; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{22}ClNO_2$ 355.1339, found $[M]^+$ 355.1345.



10c

***N*-Benzyloxycarbonyl-*trans*-3-bromo-2-(*E*)-styrylpiperidin-3-ol** (**10c**): The title compound was prepared according to the general procedure. From **9c** (164.1 mg, 0.50 mmol)[4] and (*E*)-styrylboronic acid (71.0 mg, 0.50 mmol), $BF_3{\cdot}OEt_2$ (61.7 μL, 0.50 mmol) with stirring for 24 h. The only *cis*-isomer was observed by ^{1}H NMR analysis of the crude mixtures. Column chromatography (EtOAc/*n*-hexane=1/10) of the crude residue afforded **10c** (144.1 mg, 72%) as a colorless paste as a single isomer. IR (neat) 2949, 1692, 1441, 1420, 1344, 1250, 1204, 1173, 1064, 1142, 1111, 1026, 964, 908, 876 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52–1.59 (m, 1H), 2.01–2.21 (m, 3H), 3.04 (br. t, *J*=13.0 Hz, 1H), 4.23 (br. d, *J*=13.4 Hz, 1H), 4.54 (br. s, 1H), 5.20 (s, 2H), 5.29 (br. s, 1H), 6.18 (dd, *J*=5.6, 16.1 Hz, 1H), 6.50 (d, *J*=16.1 Hz, 1H), 7.26–7.39 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 19.8, 28.1, 39.4, 52.3, 60.0, 67.3, 124.5, 126.5, 127.8, 128.0, 128.2, 128.5, 128.7, 133.3, 136.1, 136.7, 156.0; HRMS (EI) m/z Anal. Calcd for $C_{21}H_{22}BrNO_2$ 399.0834, found $[M]^+$ 399.0874.

Preparation of (±)-L773,060 (1) from 7a



(±)-L-773,060

To a stirred solution of sodium hydride (30.7 mg, 60% dispersion in mineral oil, 0.77 mmol) and dry DMF (2 mL) at 0 °C, was added a solution of **7a** (200.0 mg, 0.64 mmol) and 3,5-bis(trifluoromethyl)benzyl bromide (129.0 μL, 0.70 mmol) in 2 mL of dry DMF. The reaction mixture was heated to 80 °C and stirred for 4 h. The mixture was quenched with water (3 mL) and extracted with EtOAc (10 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude so obtained was purified by flash chromatography (EtOAc/*n*-hexane=1/5) affording *O*-benzyl ether product as a pale yellow paste (272.8 mg, 79%). IR (neat) 2947, 1694, 1422, 1350, 1275, 1171, 1126, 1096, 955, 885, 737, 700, 683 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.58–1.76 (m, 2H), 1.95–2.06 (m, 2H), 2.85 (br. t, *J*=13.0 Hz, 1H), 3.87–3.94 (m, 1H), 4.05 (br. d, *J*=12.7 Hz, 1H), 4.68 (d, *J*=12.7 Hz, 1H), 4.72 (d, *J*=12.7 Hz, 1H), 5.16 (d,

J=12.4 Hz, 1H), 5.22 (d, *J*=12.4 Hz, 1H), 5.80 (br. s, 1H), 7.24–7.38 (m, 8H), 7.55 (br. s, 2H), 7.69 (br. s, 2H), 7.77 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 24.0, 25.7, 39.5, 55.7, 67.4, 69.1, 78.5, 121.3 (sep, *J*=4.1 Hz), 123.2 (q, *J*=270.9 Hz), 127.0–127.1 (m), 127.2, 127.7, 128.0, 128.28, 128.34, 128.4, 131.5 (q, *J*=32.9 Hz), 136.6, 137.4, 140.9, 155.8; ^{19}F NMR ($CDCl_3$) δ –63.4 (s, 6F); HRMS (EI) m/z Anal. Calcd for $C_{28}H_{25}F_6NO_3$ 537.1739, found $[M]^+$ 537.1729.

The hydrogenolysis of *N*-Cbz was carried out under the condition reported by Sajiki[9] as follows. A mixture of *O*-benzyl ether compound (200 mg, 0.37 mmol) and 10% Pd/C (10 mg), ammonium acetate (14.3 mg, 0.19 mmol) in MeOH (3 mL) was stirred for 30 min after H_2 substitution from air into the reaction flask by using two vacuum/ H_2 balloon cycles. The reaction mixture was filtered through a Celite pad, and washed with MeOH (5 mL). The filtrate was concentrated and the residue was diluted with water (5mL) and extracted with EtOAc (10 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude was recrystallized from dichloromethane/*n*-hexane to obtain (±)-L773,060 (**1**)[1] as a white solid (123.7 mg, 96%). IR (neat) 2935, 1450, 1373, 1275, 1167, 1123, 889, 843, 756, 700, 681 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57–1.76 (m, 2H), 1.95 (br. s, NH), 2.00–2.11 (m, 1H), 2.22 (br. d, *J*=14.2 Hz, 1H), 2.91 (dt, *J*=3.0, 12.7 Hz, 1H), 3.41 (br. d, *J*=12.5 Hz, 1H), 3.73 (br. s, 1H), 4.00 (br. s, 1H) 4.19 (d, *J*=12.7 Hz, 1H), 4.54 (d, *J*=12.7 Hz, 1H), 7.30–7.35 (m, 3H), 7.43–7.45 (m, 2H), 7.48 (br. s, 2H), 7.69 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.3, 27.1, 45.7, 63.0, 69.7, 75.7, 121.2 (sep, *J*=4.1 Hz), 123.1 (q, *J*=271.7 Hz), 127.0, 127.2–127.3 (m), 127.9, 128.3, 131.2 (q, *J*=32.9 Hz), 138.0, 140.5; ^{19}F NMR ($CDCl_3$) δ –63.6 (s, 6F); HRMS (EI) m/z Anal. Calcd for $C_{20}H_{19}F_6NO$ 403.1371, found $[M]^+$ 403.1376.

3. References

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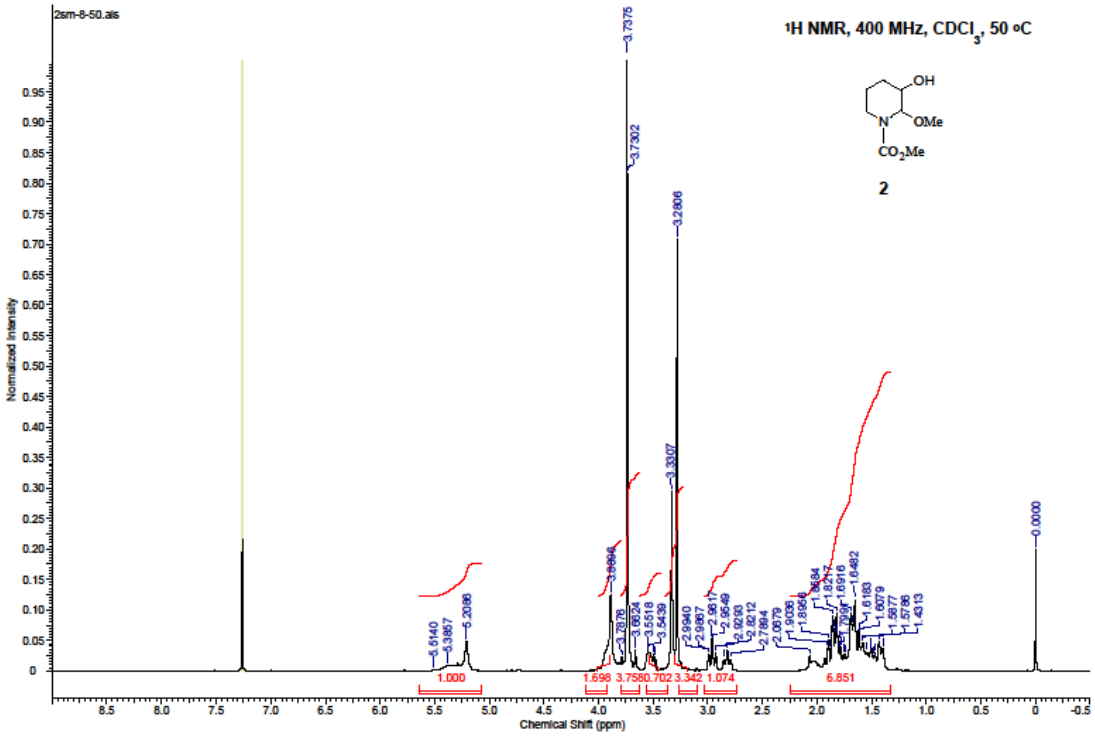
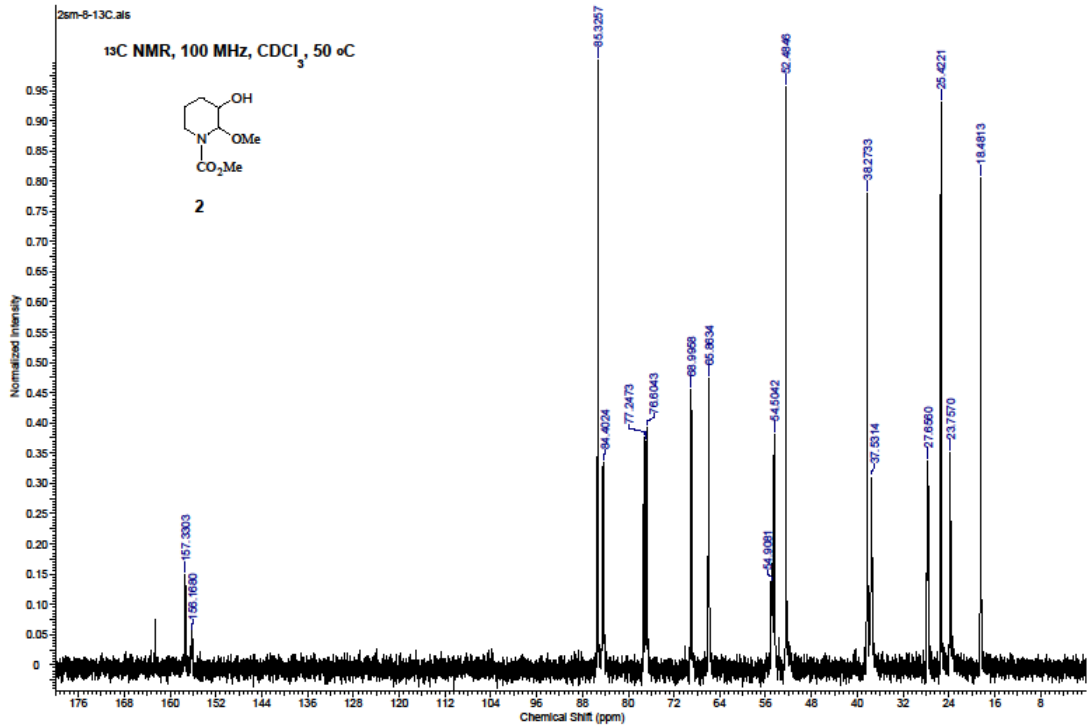
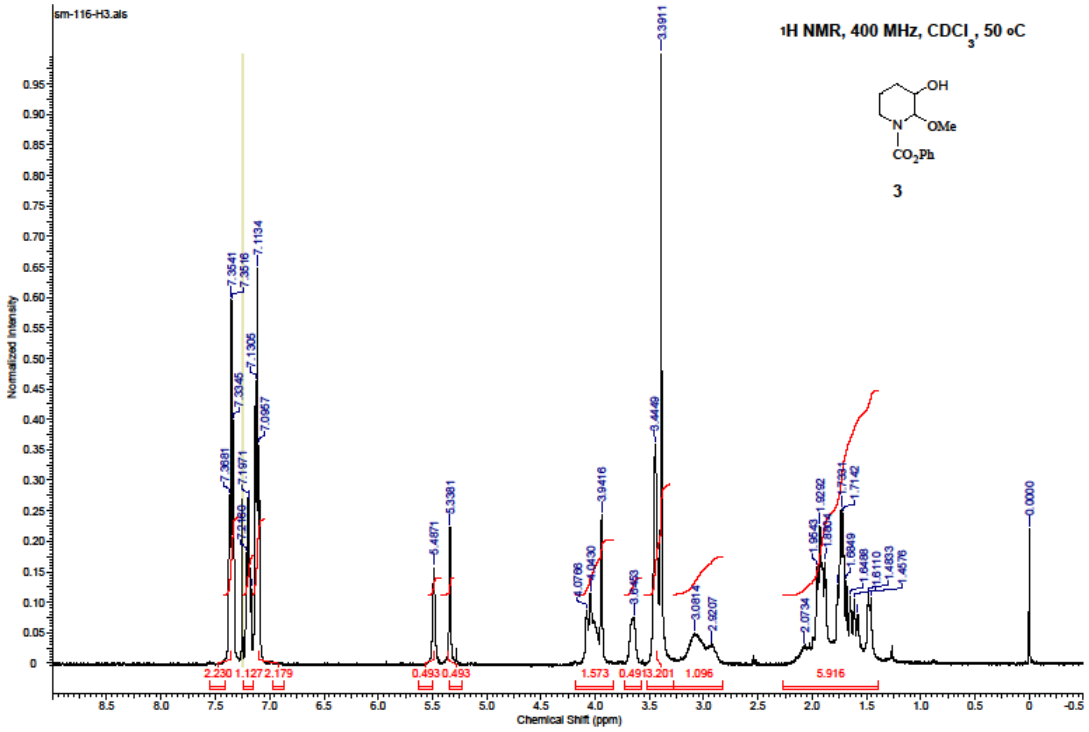
4. ^{1}H , ^{13}C and ^{19}F NMR spectra



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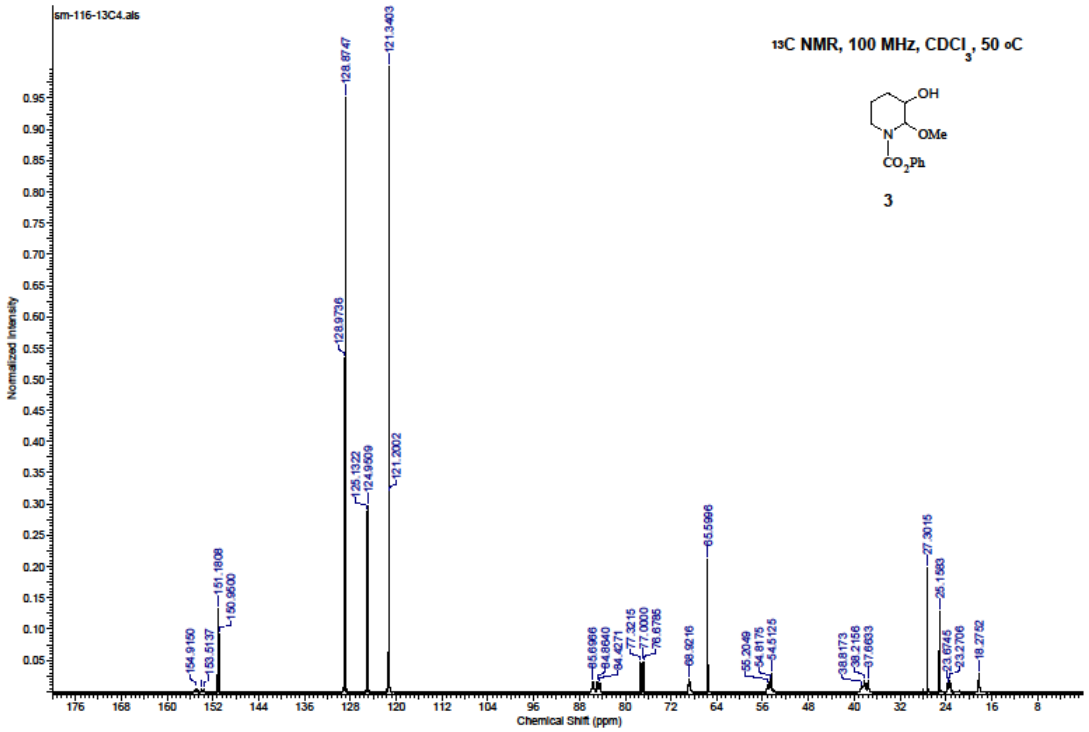
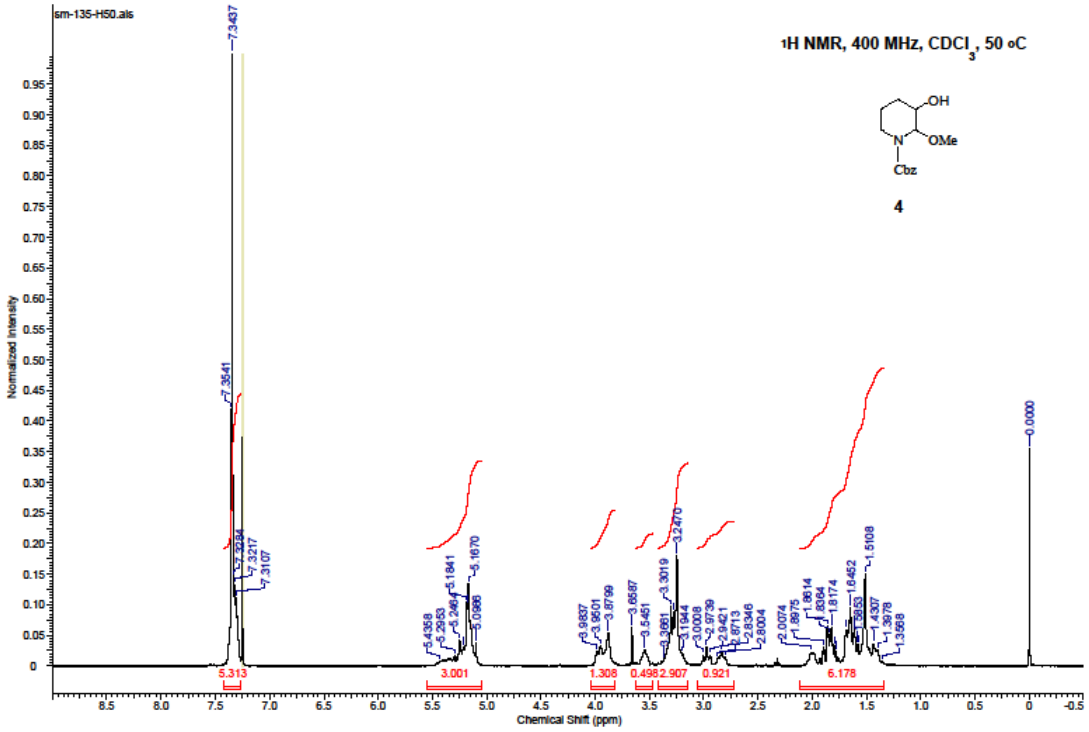
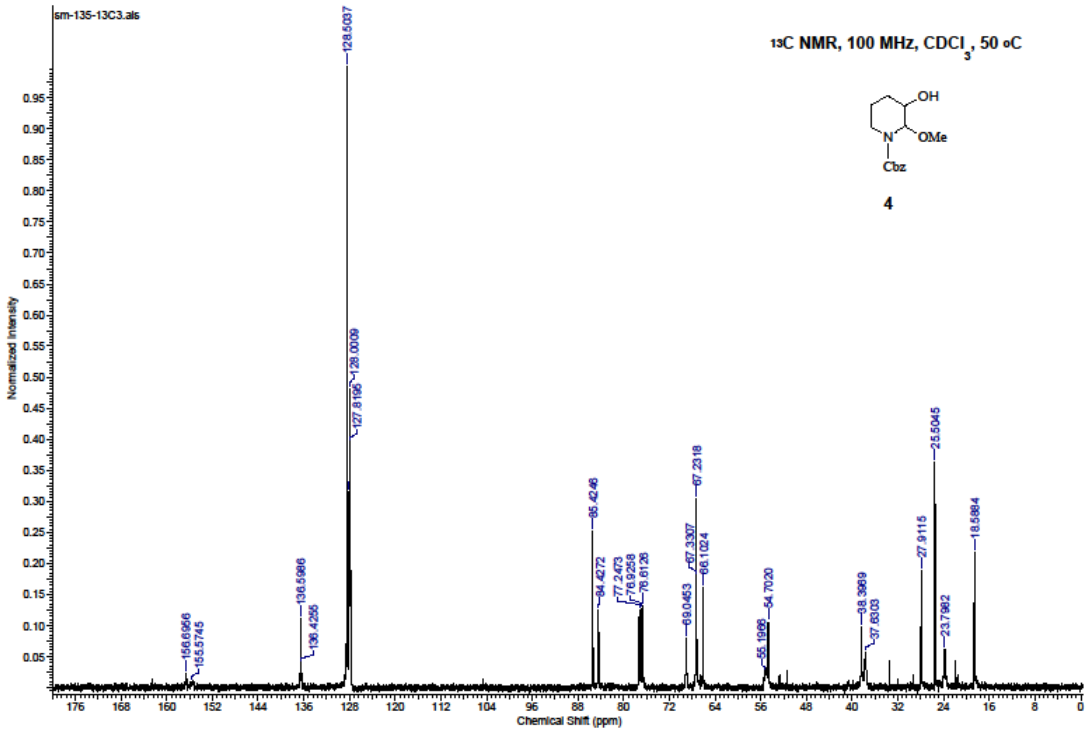
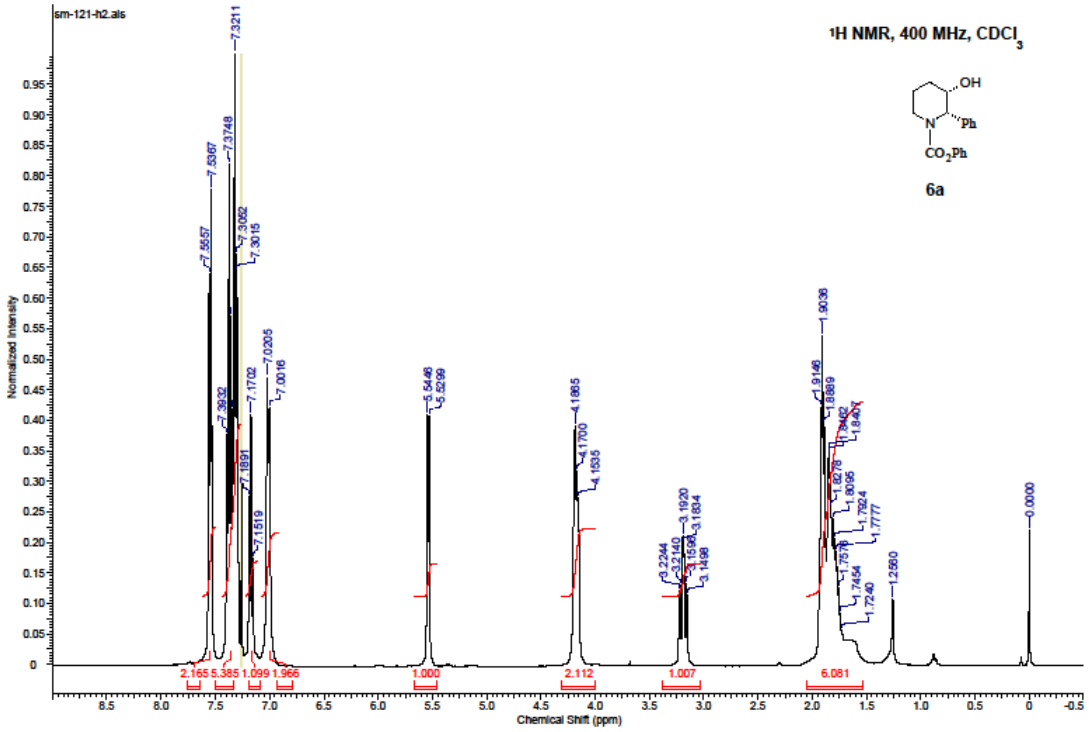
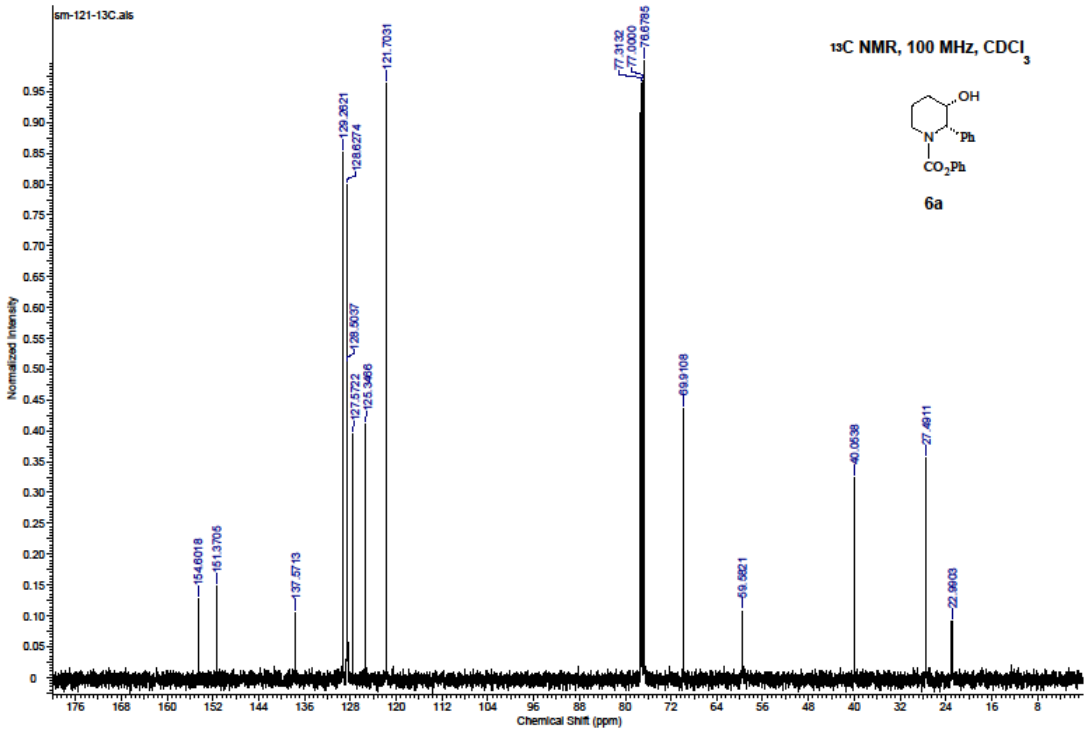
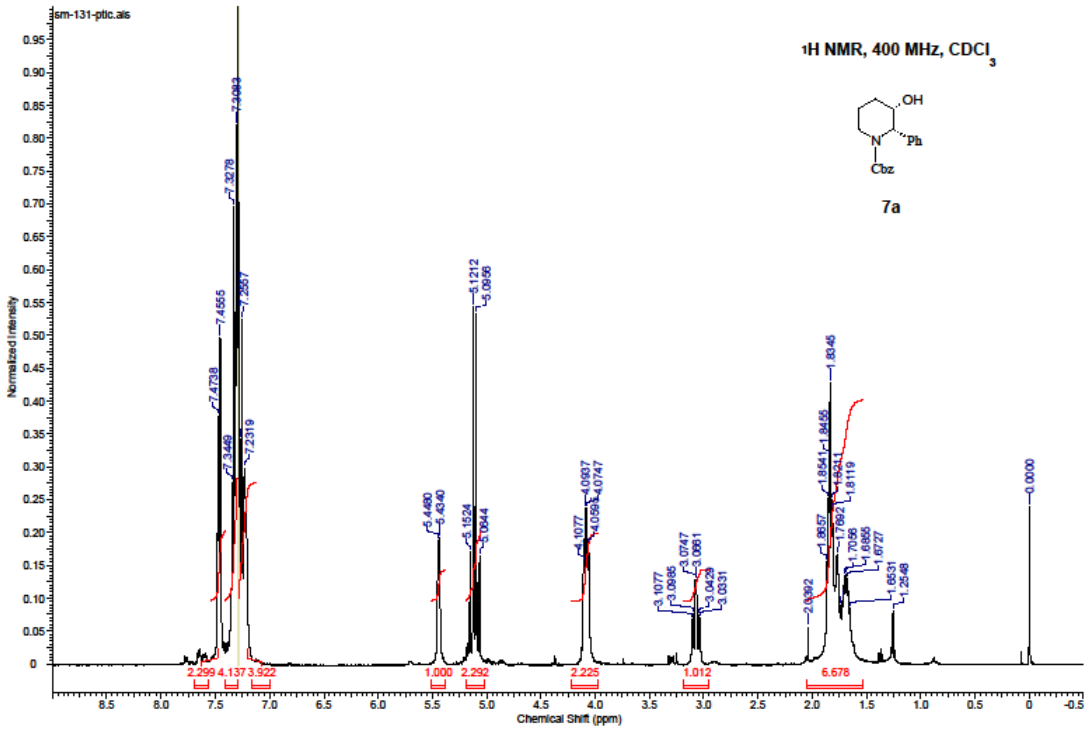

sm-116-13C4.als
13C NMR, 100 MHz, CDCl3, 50 oC
OH
OMe
N
CO2Ph
3
Normalized Intensity
Chemical Shift (ppm)
128.8747
121.3403
128.9736
125.1322
124.9509
121.2002
151.1808
150.9600
154.9150
153.5137
65.5996
27.3015
25.1583
23.6745
23.2706
18.2752

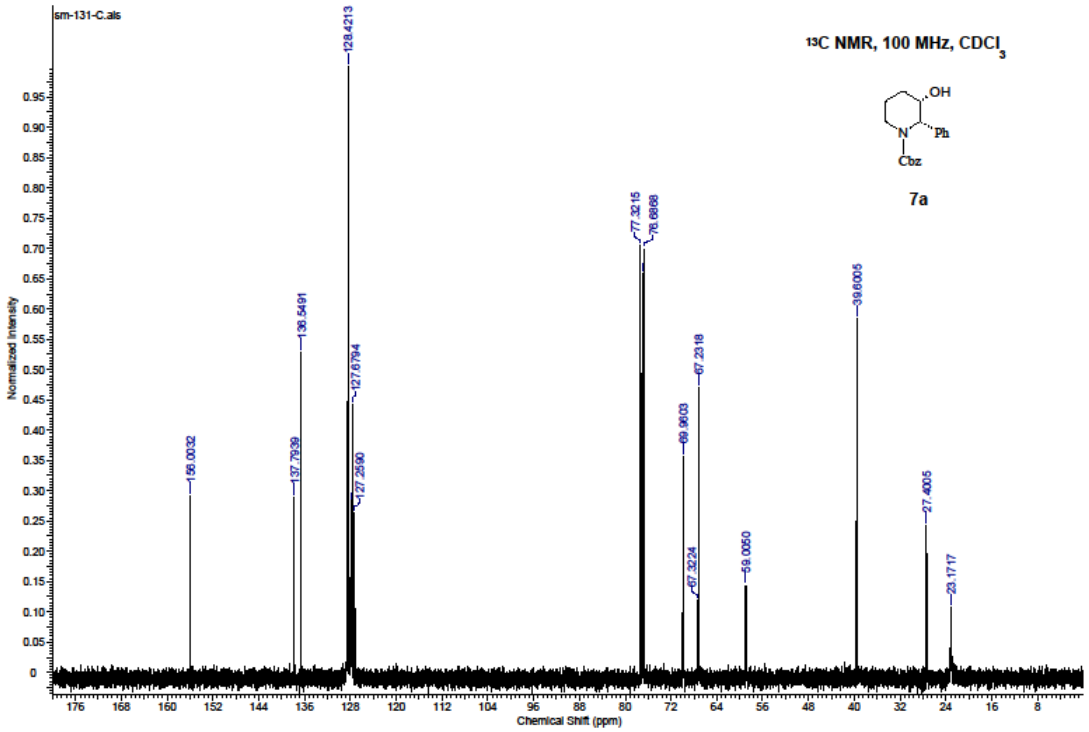

sm-135-H50.als
1H NMR, 400 MHz, CDCl3, 50 oC
OH
OMe
N
Cbz
4
Normalized Intensity
Chemical Shift (ppm)
5.313
3.001
1.308
0.498
2.907
0.921
6.178

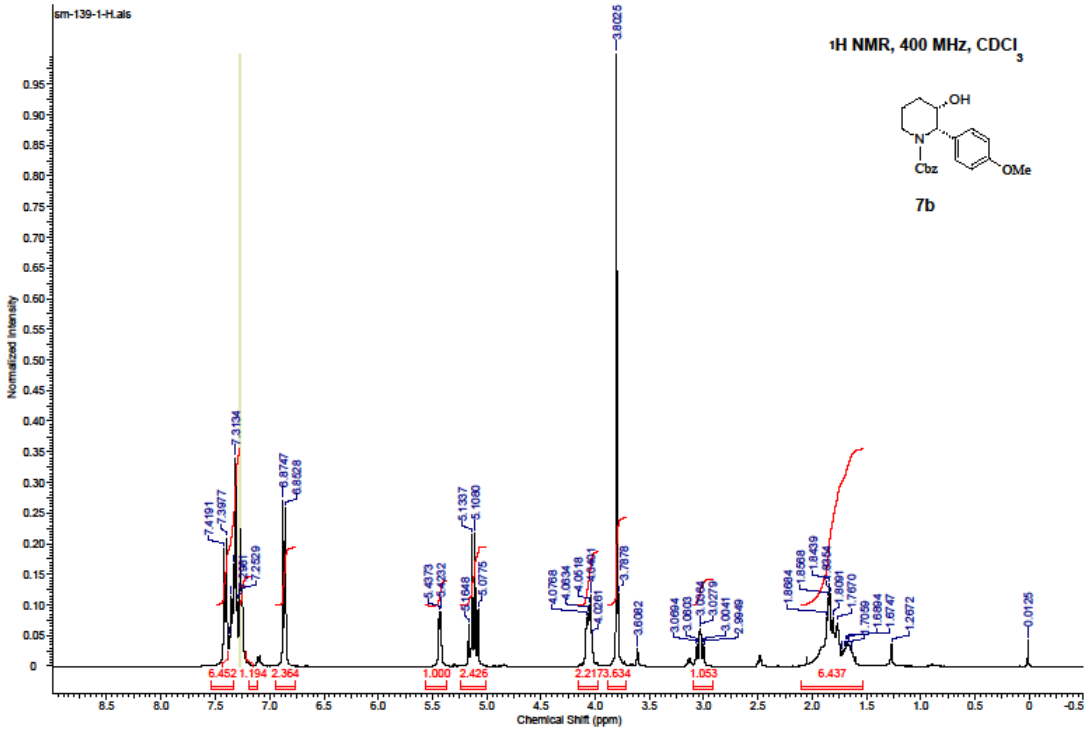

sm-135-13C3.als
13C NMR, 100 MHz, CDCl3, 50 oC
OH
OMe
N
Cbz
4
Normalized Intensity
Chemical Shift (ppm)

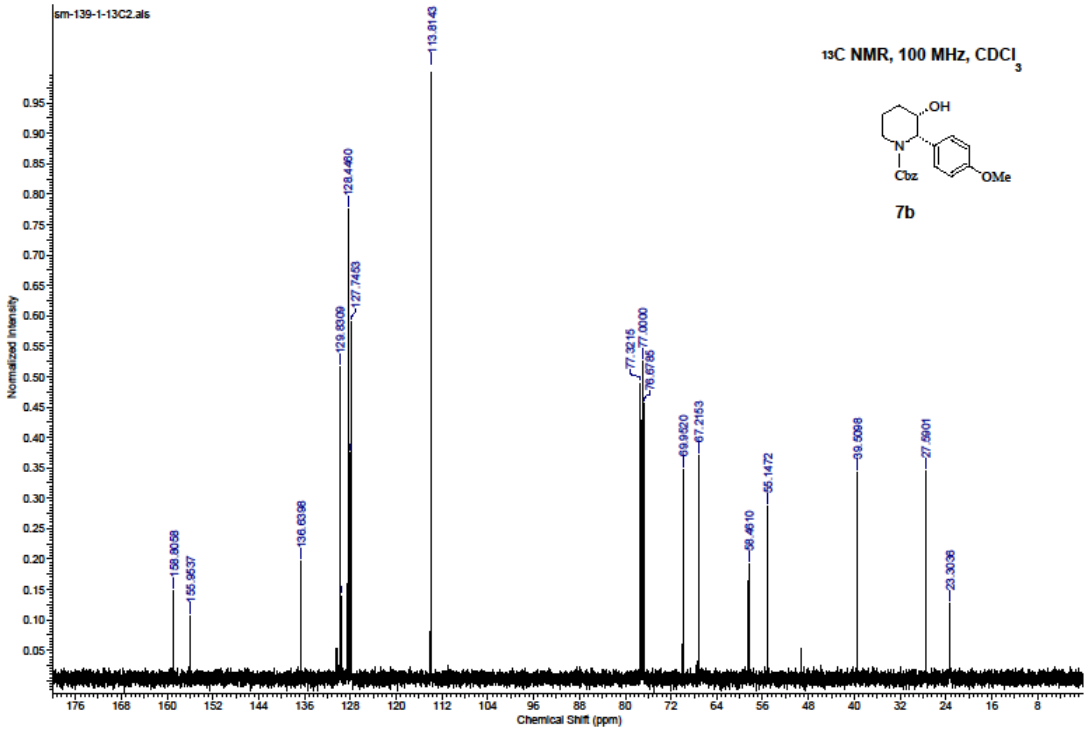

sm-121-h2.als
¹H NMR, 400 MHz, CDCl3
OH
Ph
N
CO2Ph
6a
Normalized Intensity
Chemical Shift (ppm)
2.165
5.385
1.099
1.966
1.000
2.112
1.007
6.081

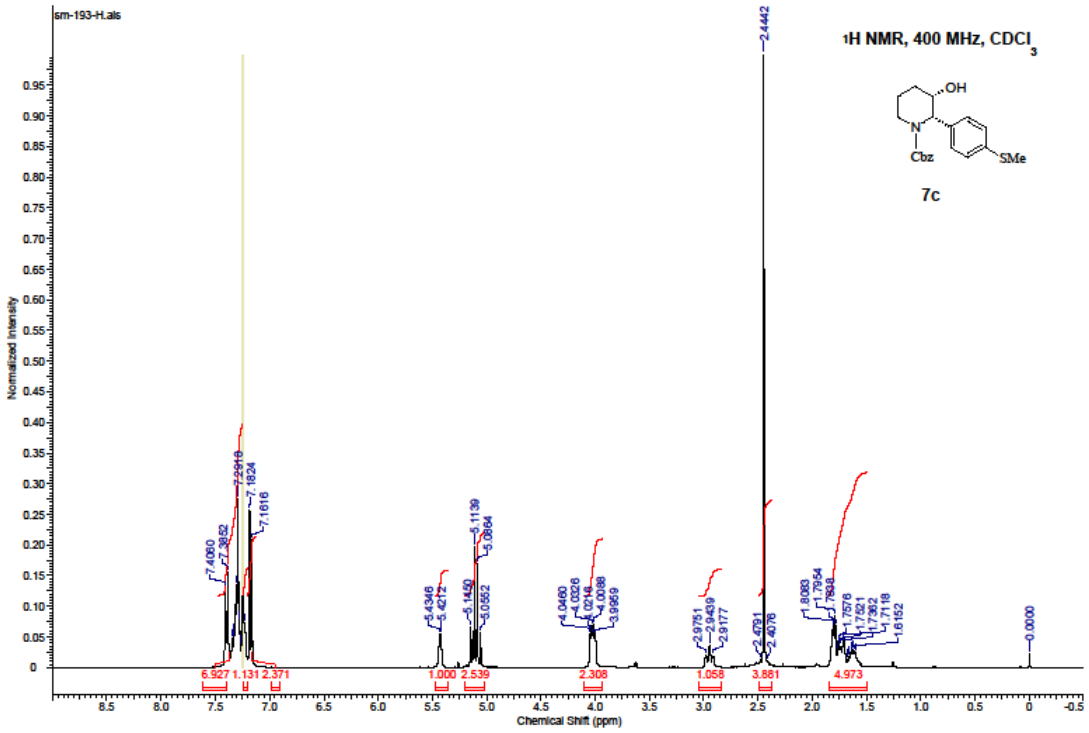

sm-121-13C.als
¹³C NMR, 100 MHz, CDCl3
OH
Ph
N
CO2Ph
6a
Normalized Intensity
Chemical Shift (ppm)

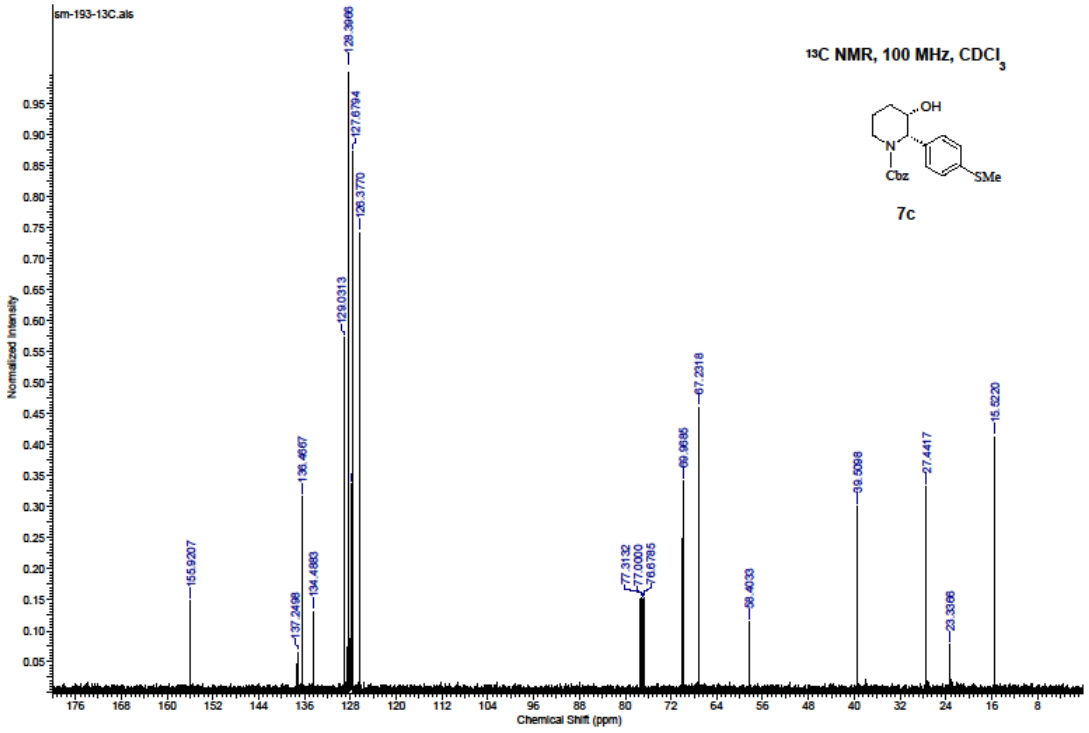

sm-131-ptlc.als
¹H NMR, 400 MHz, CDCl3
OH
Ph
N
Cbz
7a
Normalized Intensity
Chemical Shift (ppm)
2.299
4.137
3.922
1.000
2.292
2.225
1.012
6.678

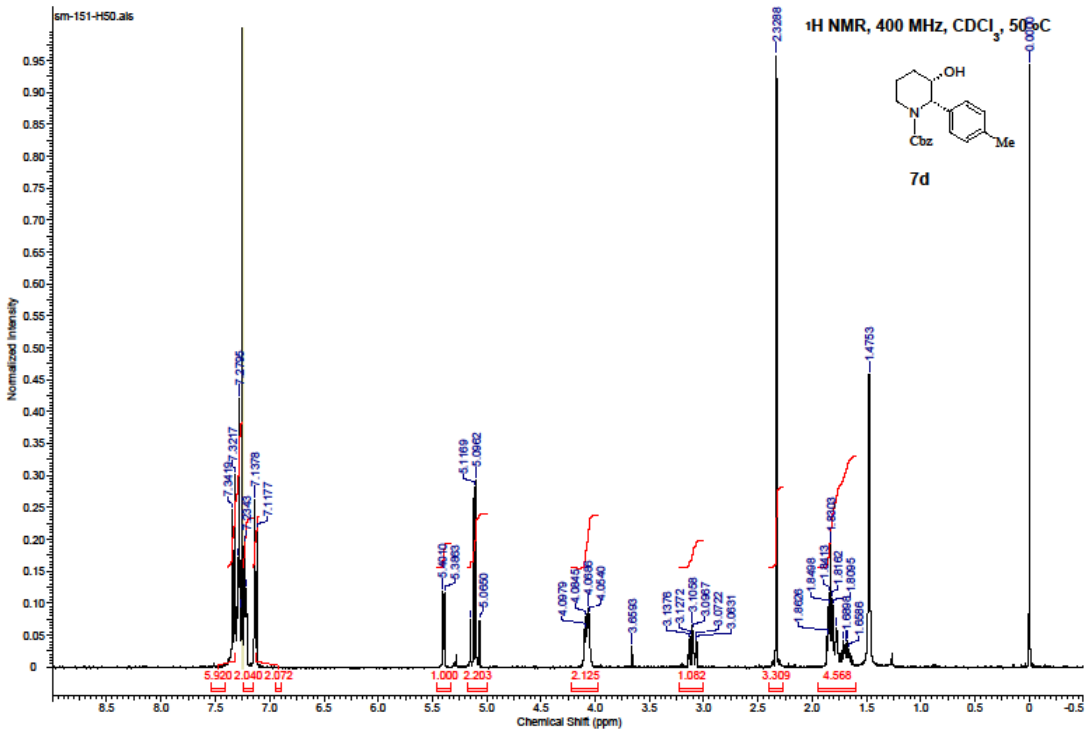

sm-131-C.als
¹³C NMR, 100 MHz, CDCl3
OH
Ph
N
Cbz
7a
Normalized Intensity
Chemical Shift (ppm)
166.0032
137.7939
136.5491
128.4213
127.6794
127.2590
77.3215
76.6868
69.9603
67.2318
67.3224
59.0050
39.6005
27.4005
23.1717

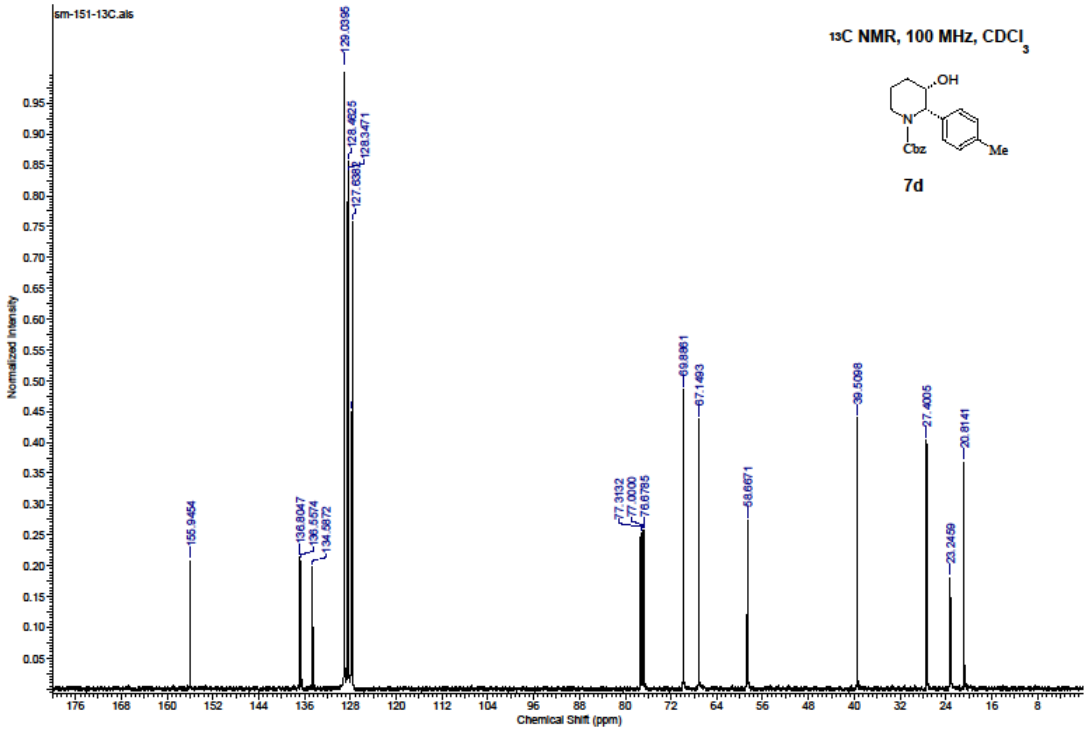

sm-139-1-H.als
1H NMR, 400 MHz, CDCl3
OH
N
Cbz
OMe
7b
Normalized Intensity
Chemical Shift (ppm)
7.4191
7.3977
7.3134
7.2529
6.8747
6.8528
5.4373
5.4232
5.1337
5.1060
5.1048
5.0775
4.0768
4.0634
4.0516
4.0441
4.0261
3.7876
3.6892
3.0694
3.0563
3.0364
3.0279
3.0041
2.9949
1.8884
1.8698
1.8439
1.8354
1.8091
1.7670
1.7059
1.6884
1.6747
1.2672
0.0125
6.452
1.194
2.364
1.000
2.426
2.217
3.634
1.053
6.437

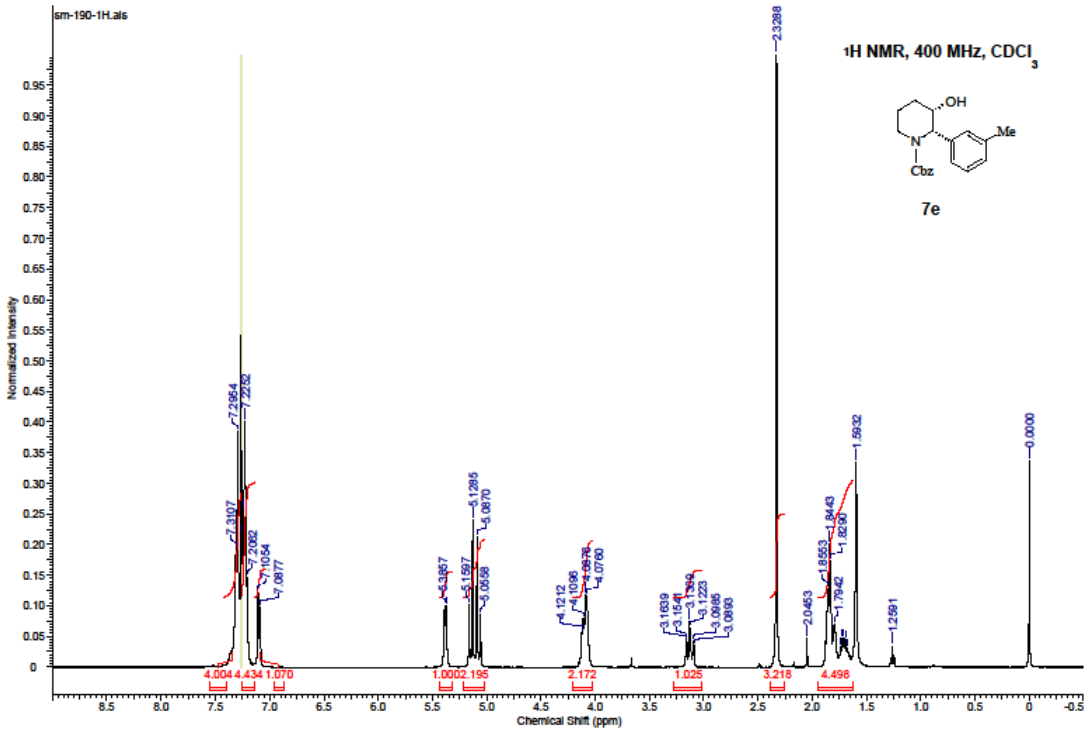

sm-139-1-13C2.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
OMe
7b
Normalized Intensity
Chemical Shift (ppm)
158.8058
155.9637
136.6396
129.8309
128.4490
127.7453
113.8143
77.3215
77.0000
76.6785
69.9520
67.2153
55.1472
39.5098
27.5901
23.3036

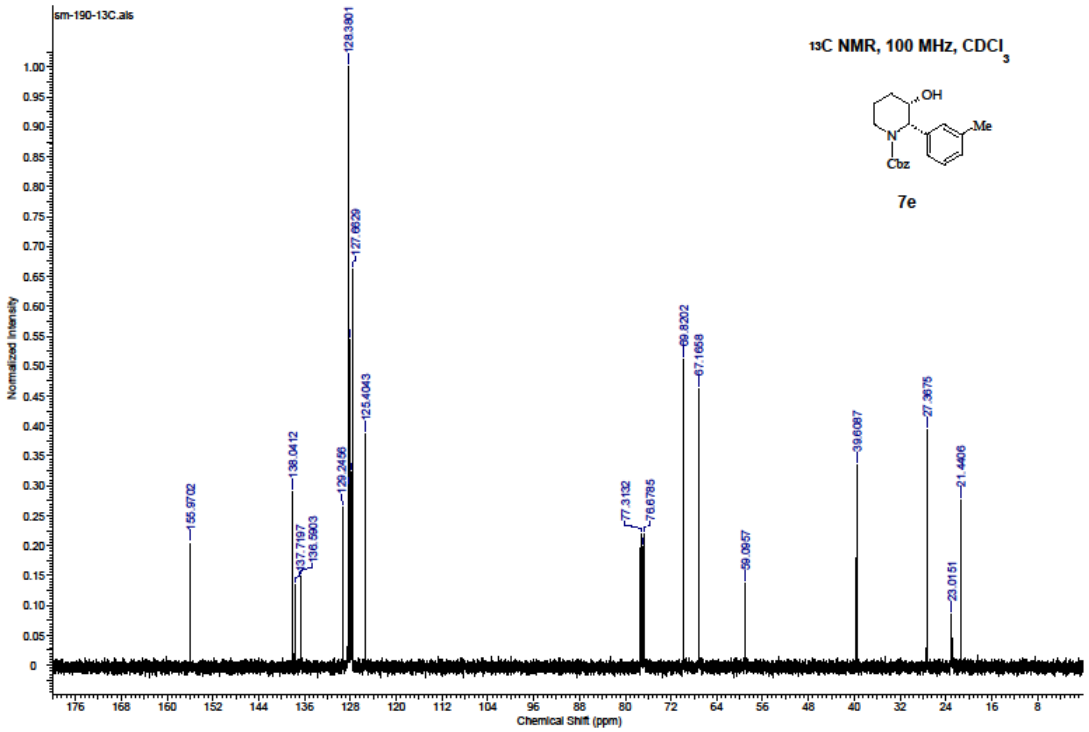

sm-193-H.als
¹H NMR, 400 MHz, CDCl3
OH
N
Cbz
SMe
7c
Normalized Intensity
Chemical Shift (ppm)
2.4442
7.4060
7.3952
7.2919
7.1824
7.1616
5.4346
5.4212
5.1139
5.0864
5.0552
4.0460
4.0226
4.0214
4.0098
3.9959
2.9751
2.9439
2.9177
2.4761
2.4076
1.8083
1.7954
1.7838
1.7576
1.7521
1.7362
1.7178
1.6152
0.0000
6.927
1.131
2.371
1.000
2.539
2.308
1.058
3.881
4.973

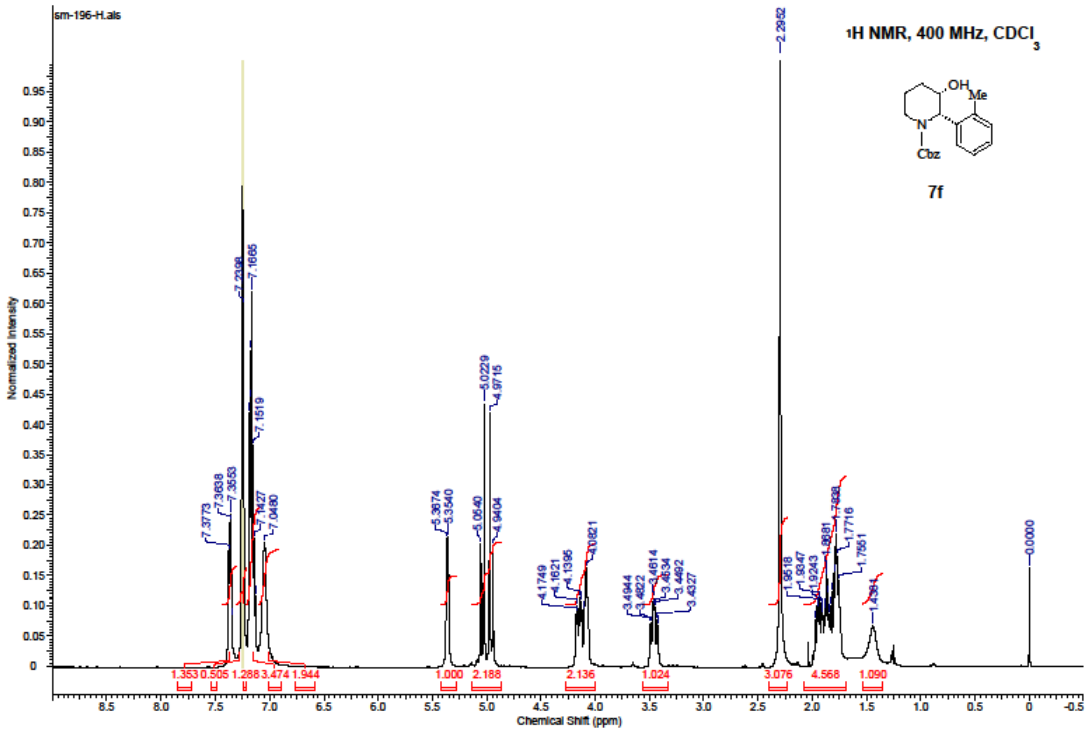

sm-193-13C.als
¹³C NMR, 100 MHz, CDCl3
OH
N
Cbz
SMe
7c
Normalized Intensity
Chemical Shift (ppm)
155.9207
137.2498
136.4967
134.4883
129.0313
128.3966
127.6794
126.3770
77.3132
77.0000
76.6785
69.9695
67.2318
58.4033
39.5098
27.4417
23.3366
15.5220

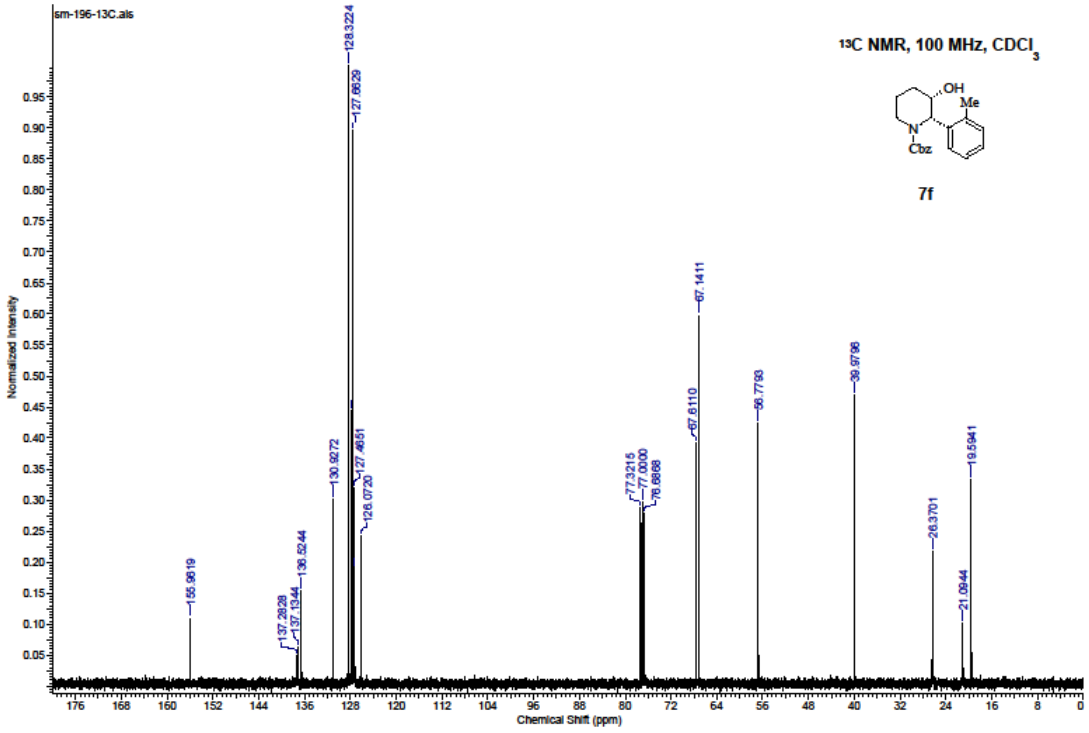

sm-151-H50.als
1H NMR, 400 MHz, CDCl3, 50°C
OH
N
Cbz
Me
7d
Normalized Intensity
Chemical Shift (ppm)
7.2736
7.3419
7.3217
7.2943
7.1378
7.1177
5.1169
5.0962
5.0650
3.6593
2.3288
1.4753
1.8803
5.920
2.040
2.072
1.000
2.203
2.125
1.082
3.309
4.568

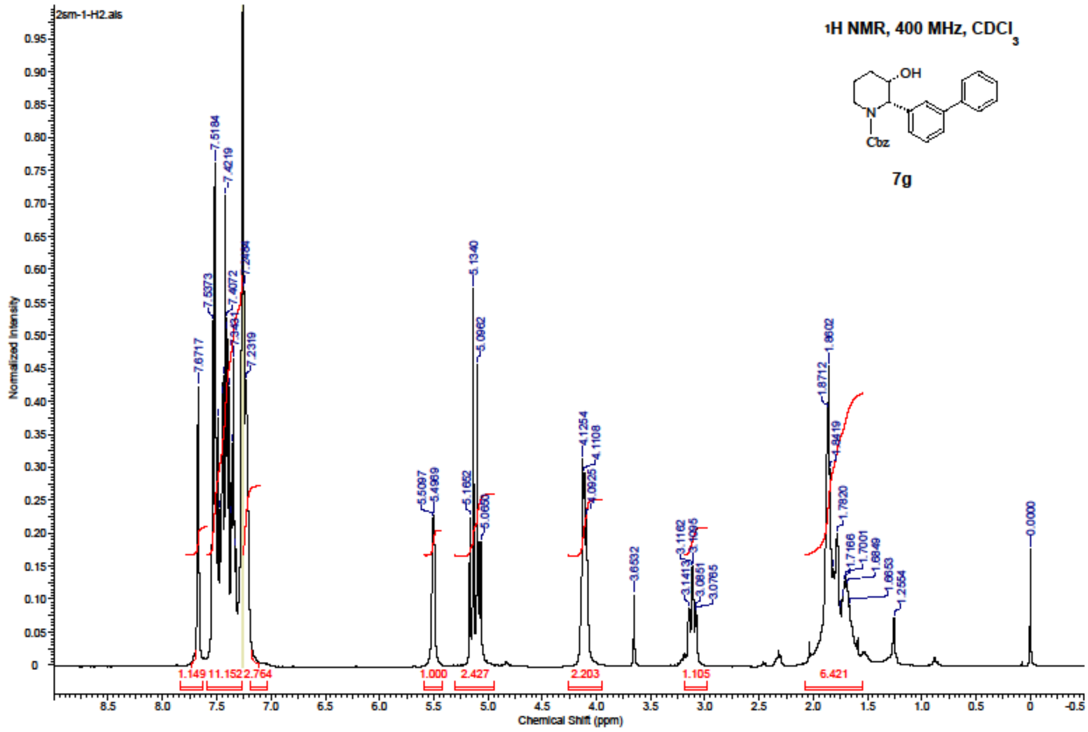

sm-151-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
Me
7d
Normalized Intensity
Chemical Shift (ppm)
129.0395
128.4625
128.0471
127.6385
155.9454
136.8047
136.5574
134.3872
77.3132
77.0000
76.6765
69.8861
67.1493
58.6671
39.5098
27.4005
23.2459
20.8141

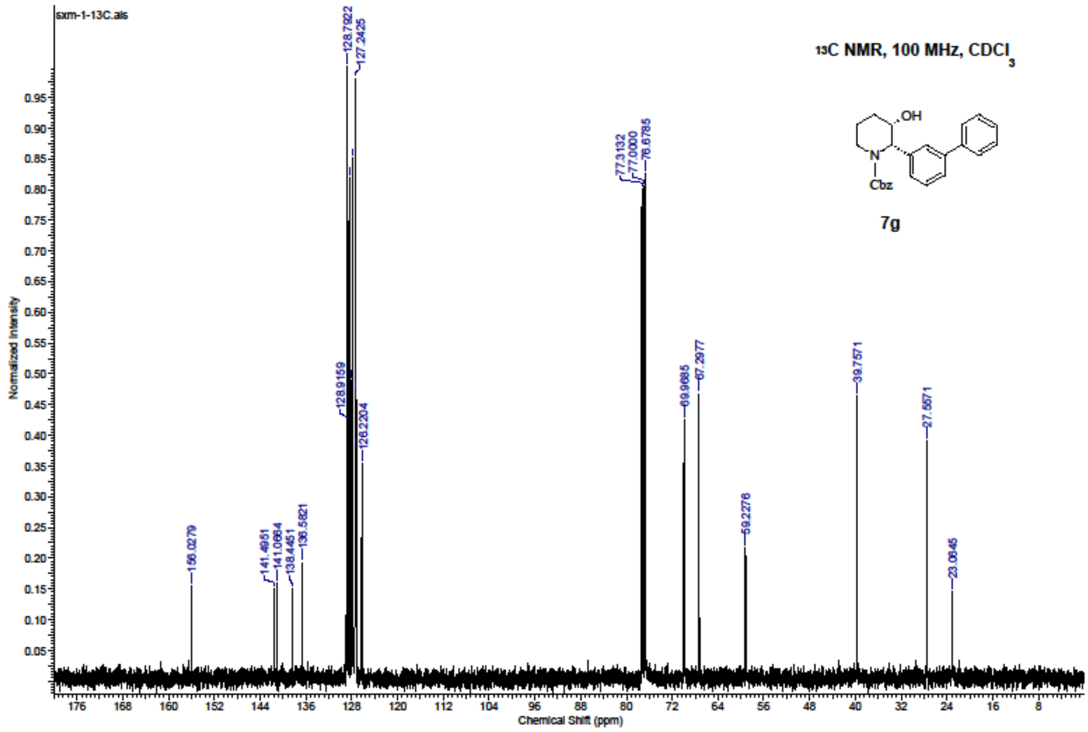

sm-190-1H.als
1H NMR, 400 MHz, CDCl3
OH
Me
N
Cbz
7e
Normalized Intensity
Chemical Shift (ppm)
2.3288
1.5932
0.0000
7.2964
7.2252
7.3107
7.2082
7.1054
7.0877
5.1285
5.0870
5.3357
5.1597
5.0556
4.1212
4.1096
4.0878
4.0760
3.1639
3.1541
3.1223
3.0988
3.0693
2.0453
1.8553
1.8443
1.8290
1.7942
1.2591
4.004
4.434
1.070
1.000
2.195
2.172
1.025
3.218
4.498

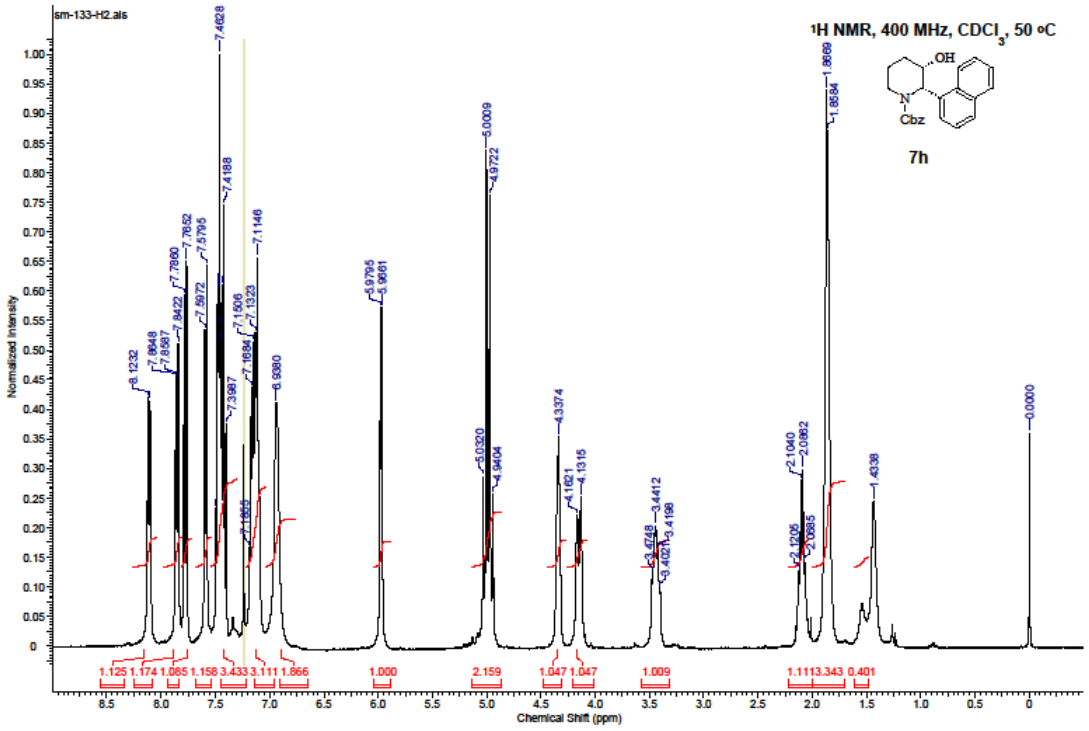

sm-190-13C.als
13C NMR, 100 MHz, CDCl3
OH
Me
N
Cbz
7e
Normalized Intensity
Chemical Shift (ppm)
128.3801
127.6629
125.4043
155.9702
138.0412
137.7197
136.5903
129.2466
77.3132
76.6785
69.8202
67.1658
59.0957
39.6087
27.3075
23.0151
21.4406

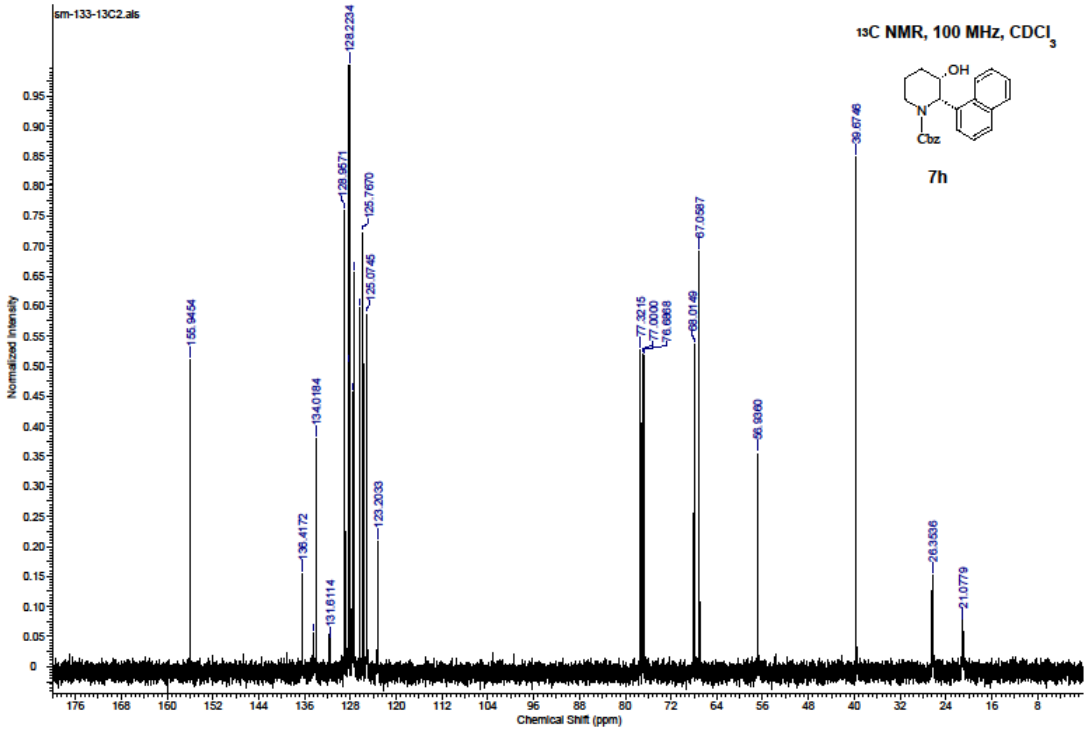

sm-196-H.als
¹H NMR, 400 MHz, CDCl3
OH
Me
N
Cbz
7f
Normalized Intensity
Chemical Shift (ppm)

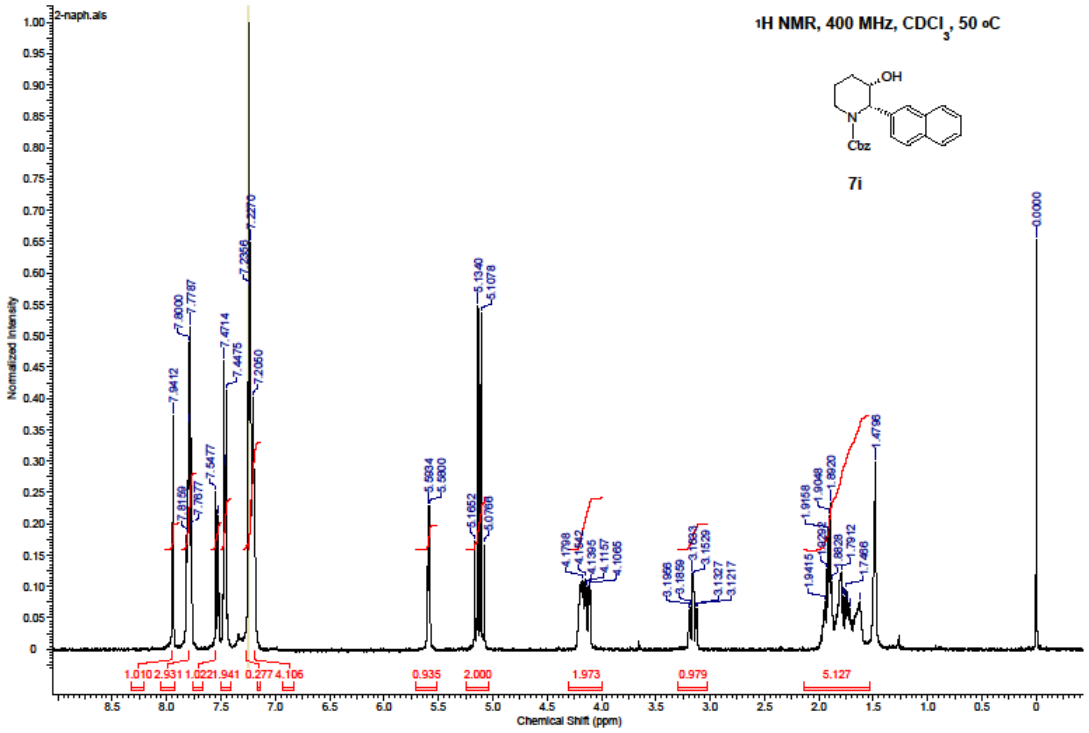

sm-196-13C.als
¹³C NMR, 100 MHz, CDCl3
OH
Me
N
Cbz
7f
Normalized Intensity
Chemical Shift (ppm)

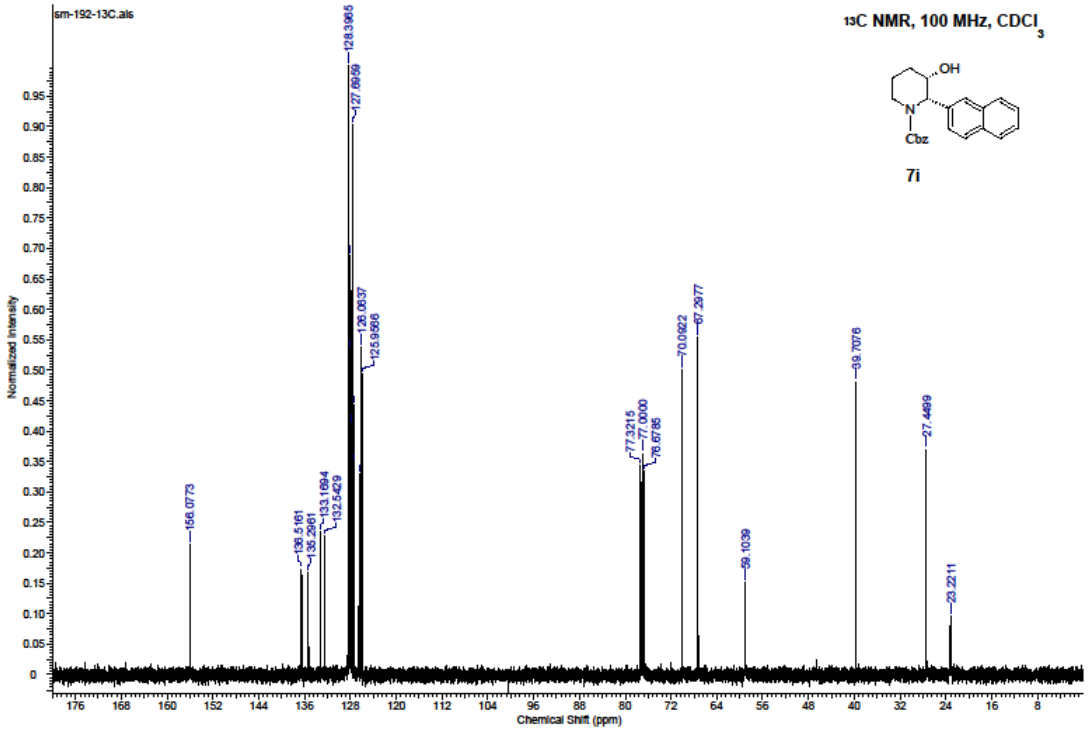


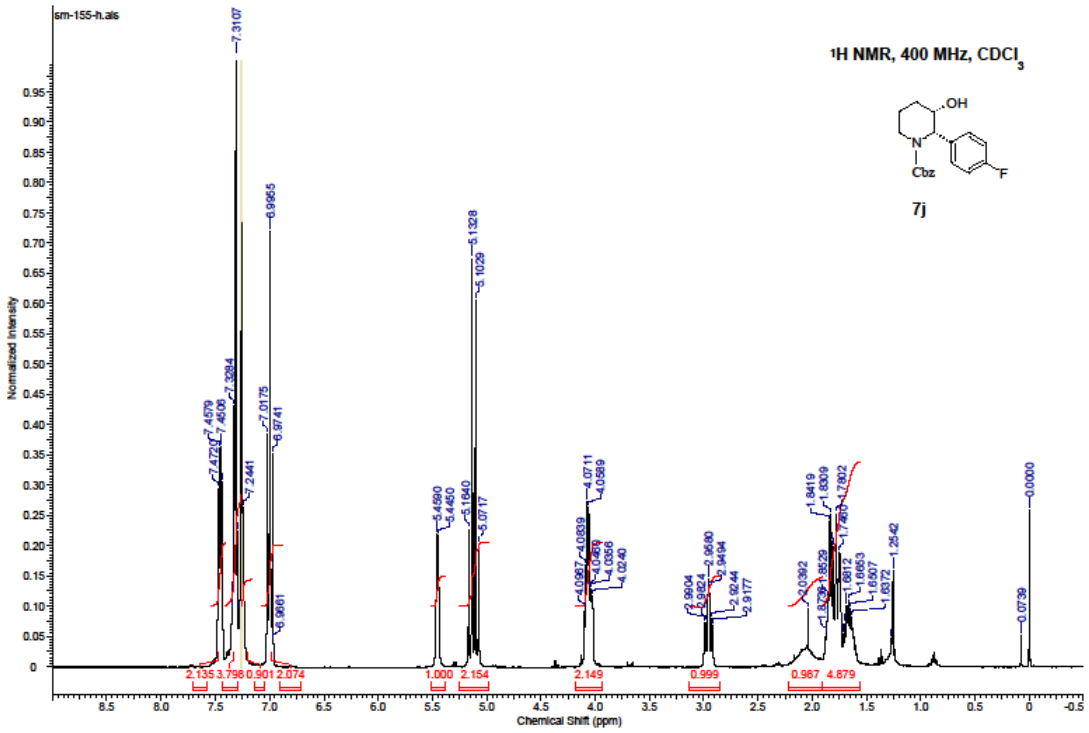


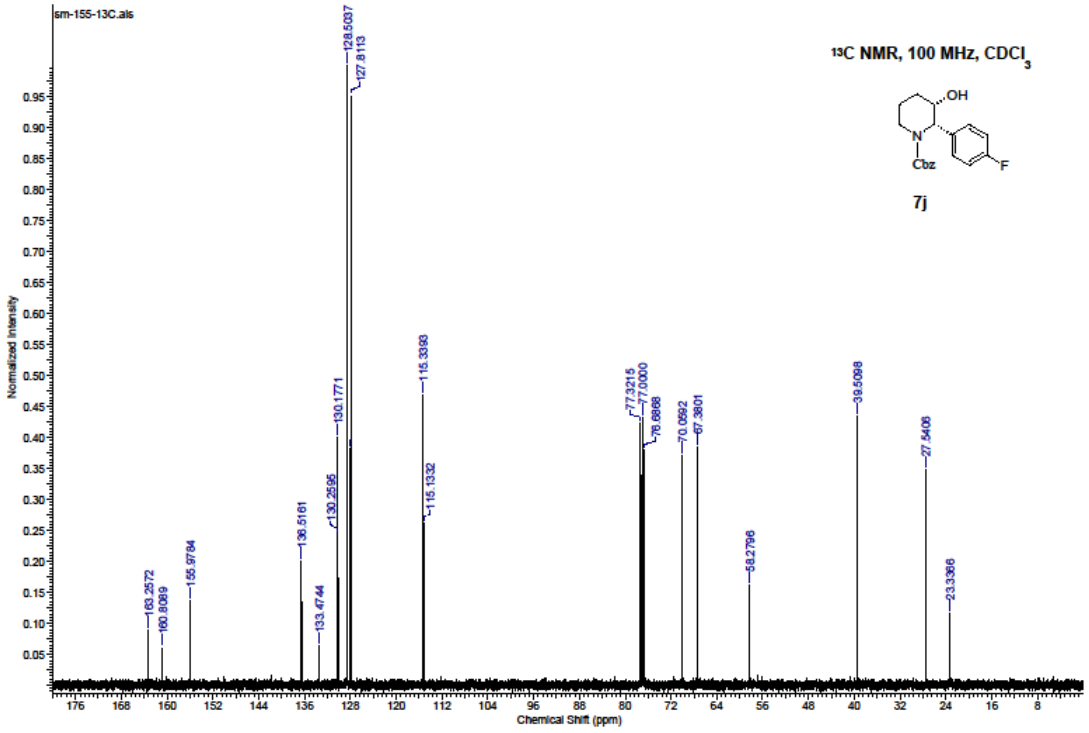

sm-133-H2.als
^{1}H NMR, 400 MHz, CDCl$_3$, 50 °C
OH
N
Cbz
7h
Normalized Intensity
Chemical Shift (ppm)

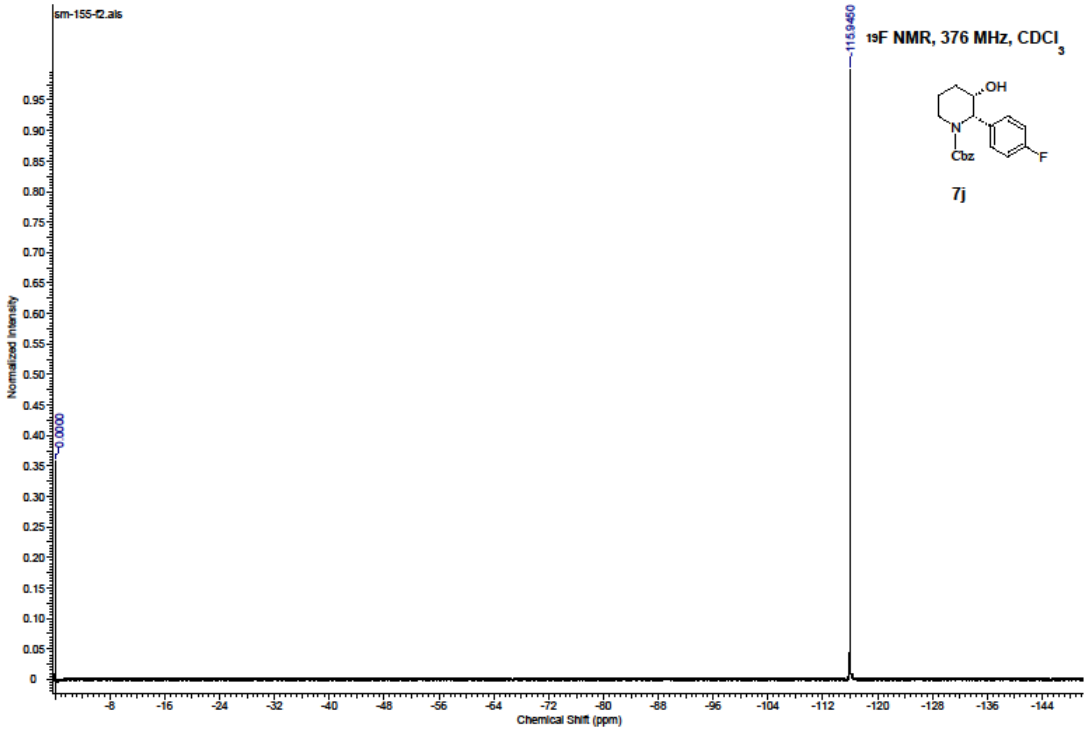

sm-133-13C2.als
^{13}C NMR, 100 MHz, CDCl$_3$
OH
N
Cbz
7h
Normalized Intensity
Chemical Shift (ppm)

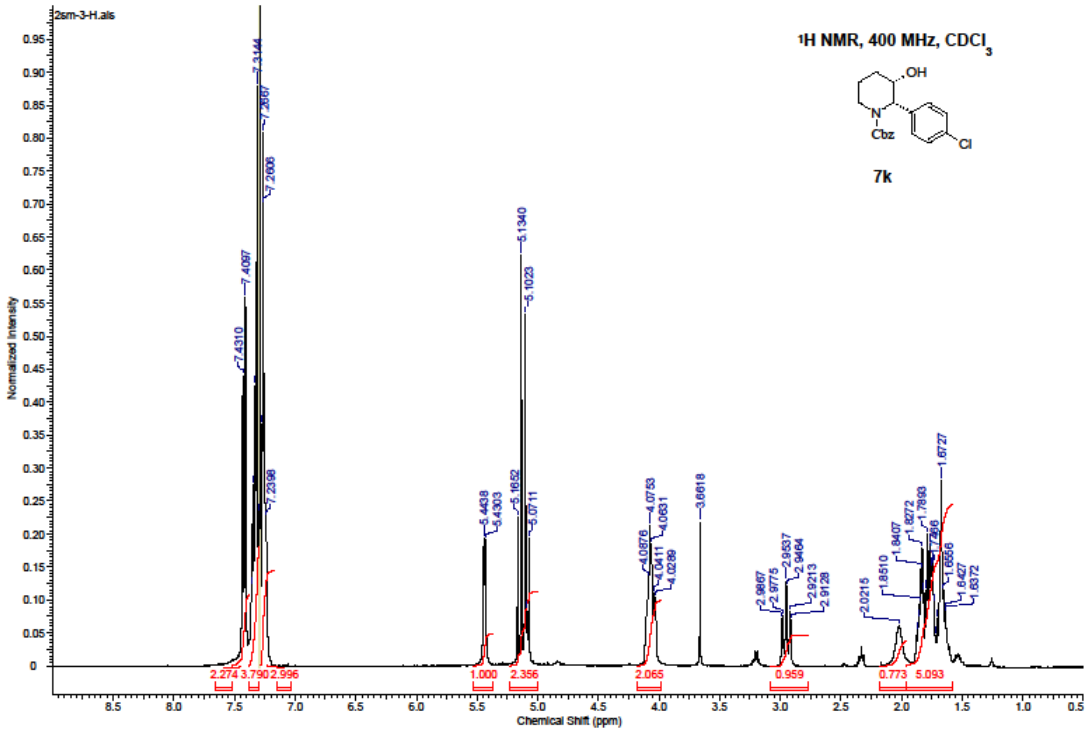

2-naph.als
1H NMR, 400 MHz, CDCl3, 50 oC
OH
N
Cbz
7i
Normalized Intensity
Chemical Shift (ppm)

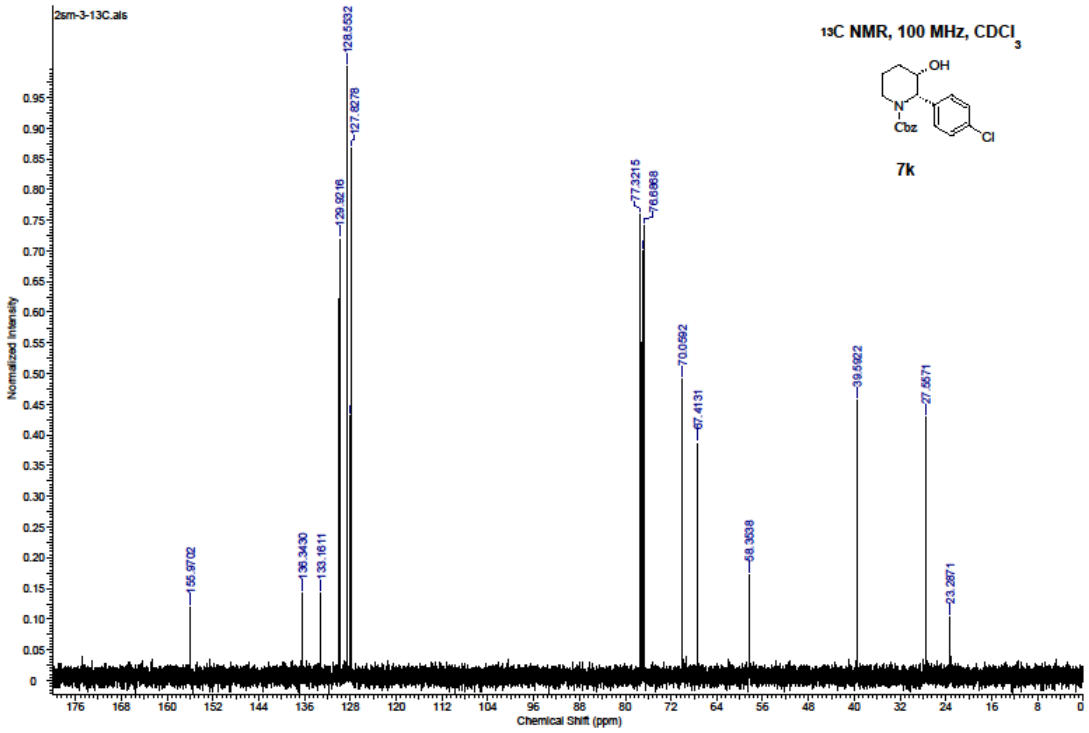

sm-192-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
7i
Normalized Intensity
Chemical Shift (ppm)

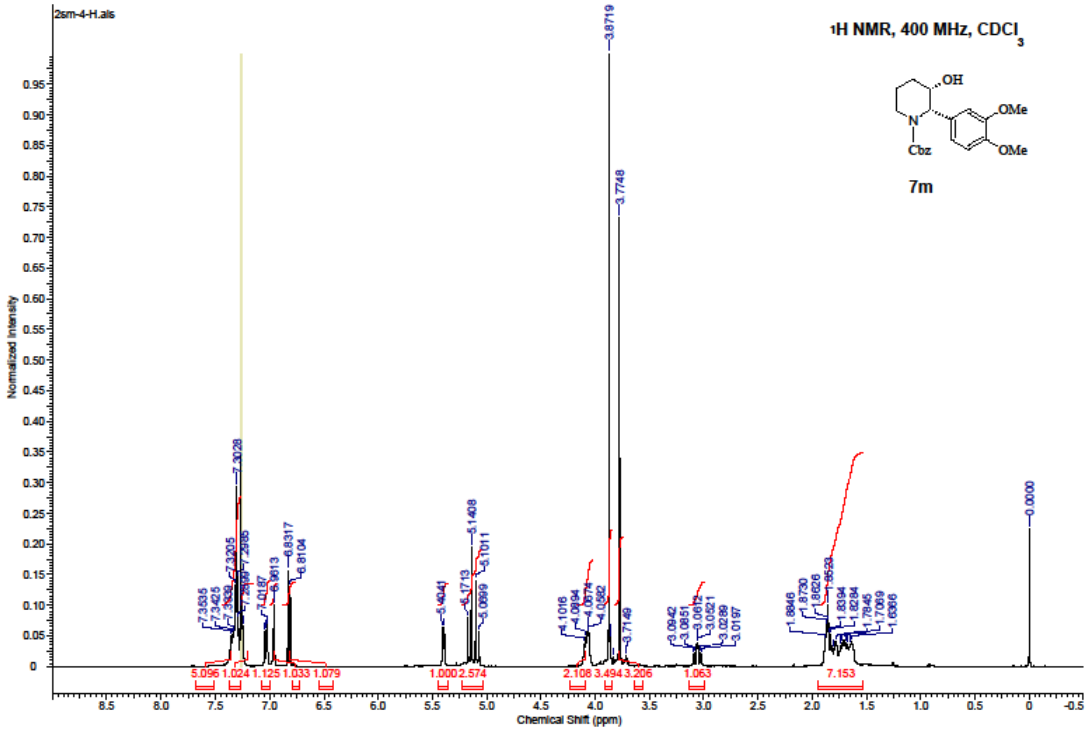

sm-155-h.als
¹H NMR, 400 MHz, CDCl3
OH
N
Cbz
F
7j
Normalized Intensity
Chemical Shift (ppm)

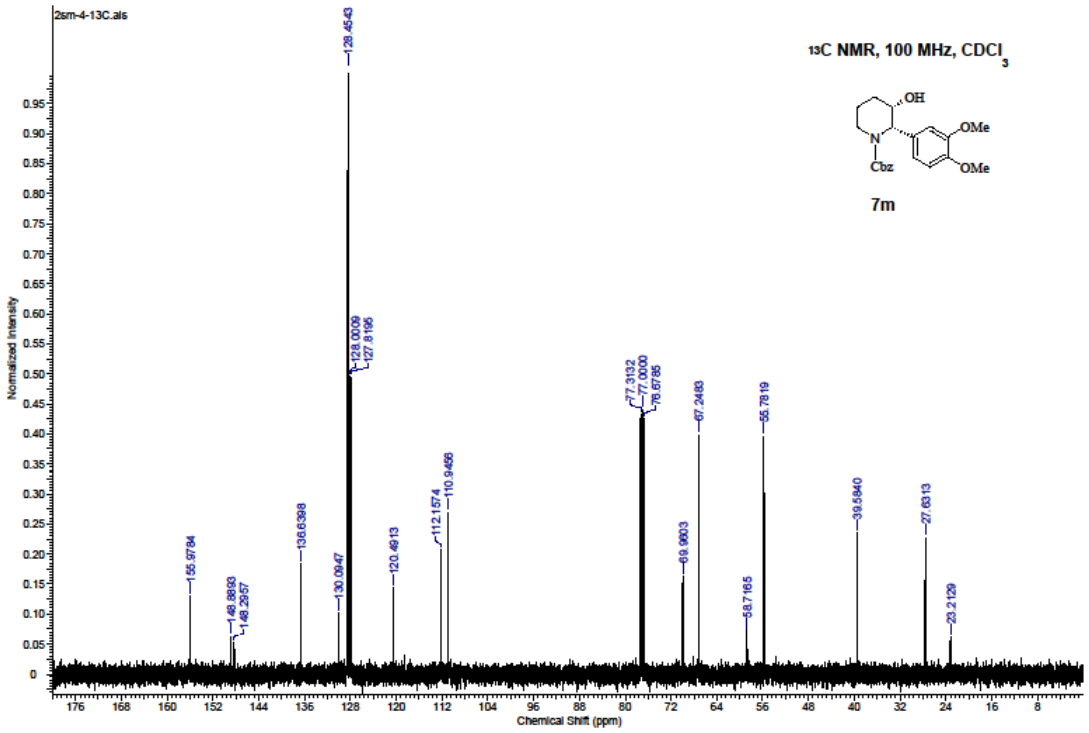

sm-155-13C.als
¹³C NMR, 100 MHz, CDCl3
OH
N
Cbz
F
7j
Normalized Intensity
Chemical Shift (ppm)

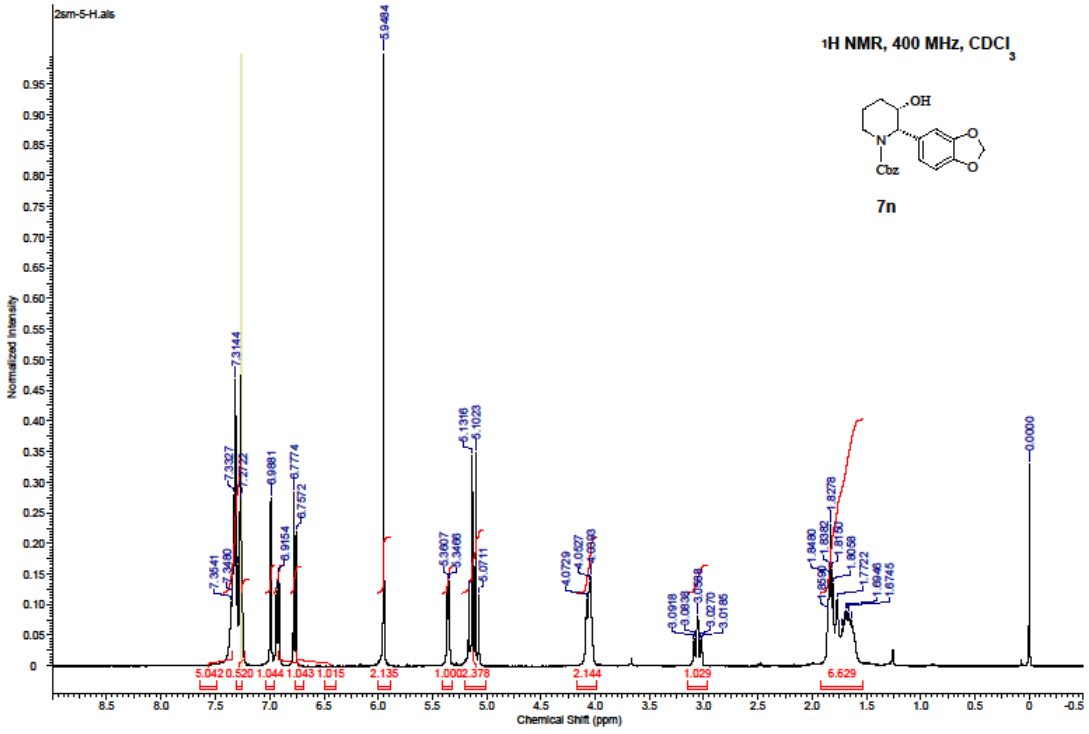

sm-155-f2.als
19F NMR, 376 MHz, CDCl3
-115.9450
-0.000
OH
N
Cbz
F
7j
Normalized Intensity
Chemical Shift (ppm)

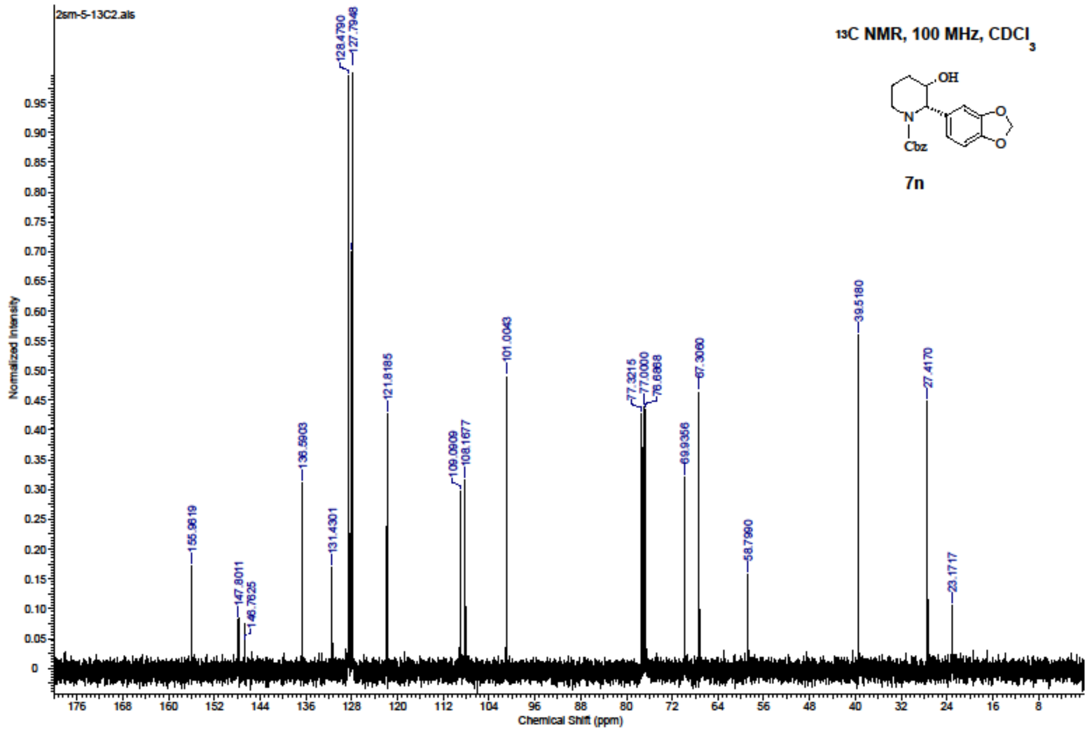

2sm-3-H.als
1H NMR, 400 MHz, CDCl3
OH
N
Cbz
Cl
7k
7.4310
7.4097
7.3144
7.2667
7.2606
7.2396
5.1340
5.1023
5.4438
5.4303
5.1652
5.0711
4.0753
4.0631
4.0411
4.0289
4.0876
3.6618
2.9867
2.9775
2.9637
2.9464
2.9213
2.9129
2.0215
1.8510
1.8407
1.8272
1.7893
1.7727
1.7566
1.6556
1.6427
1.6372
2.274
3.790
2.996
1.000
2.356
2.065
0.959
0.773
5.093
Normalized Intensity
Chemical Shift (ppm)

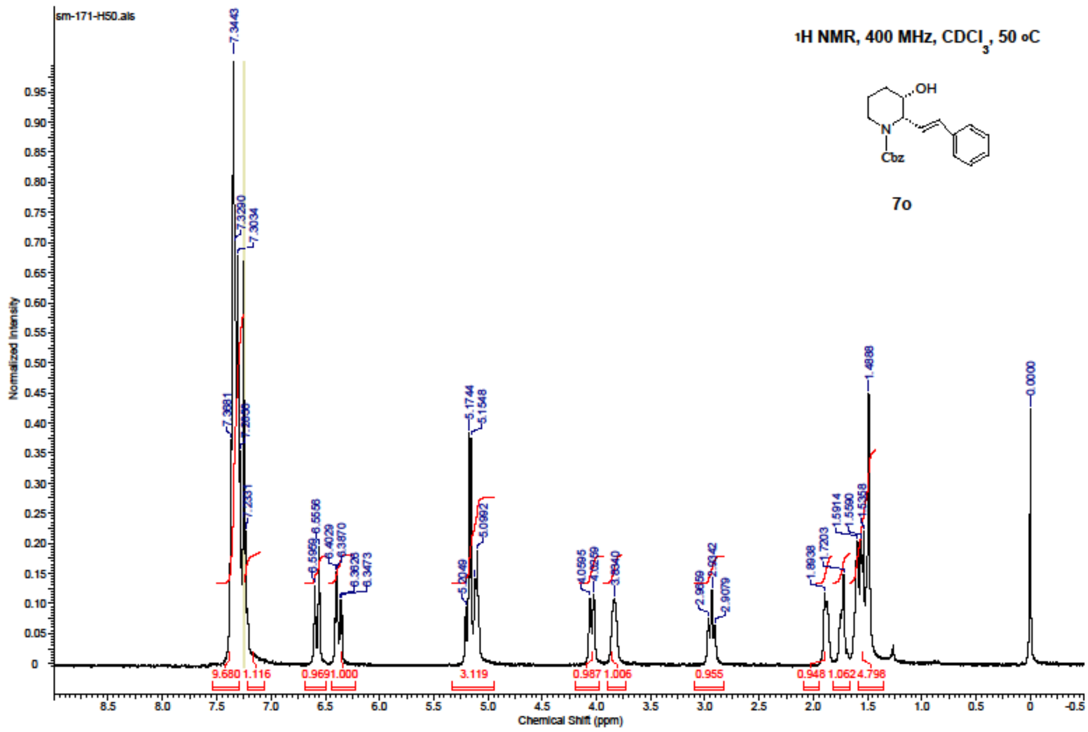

2sm-3-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
Cl
7k
128.5532
127.8278
129.8216
77.3215
76.6868
70.0592
67.4131
39.5922
27.5571
58.3038
23.2871
136.3430
133.1611
155.9702
Normalized Intensity
Chemical Shift (ppm)

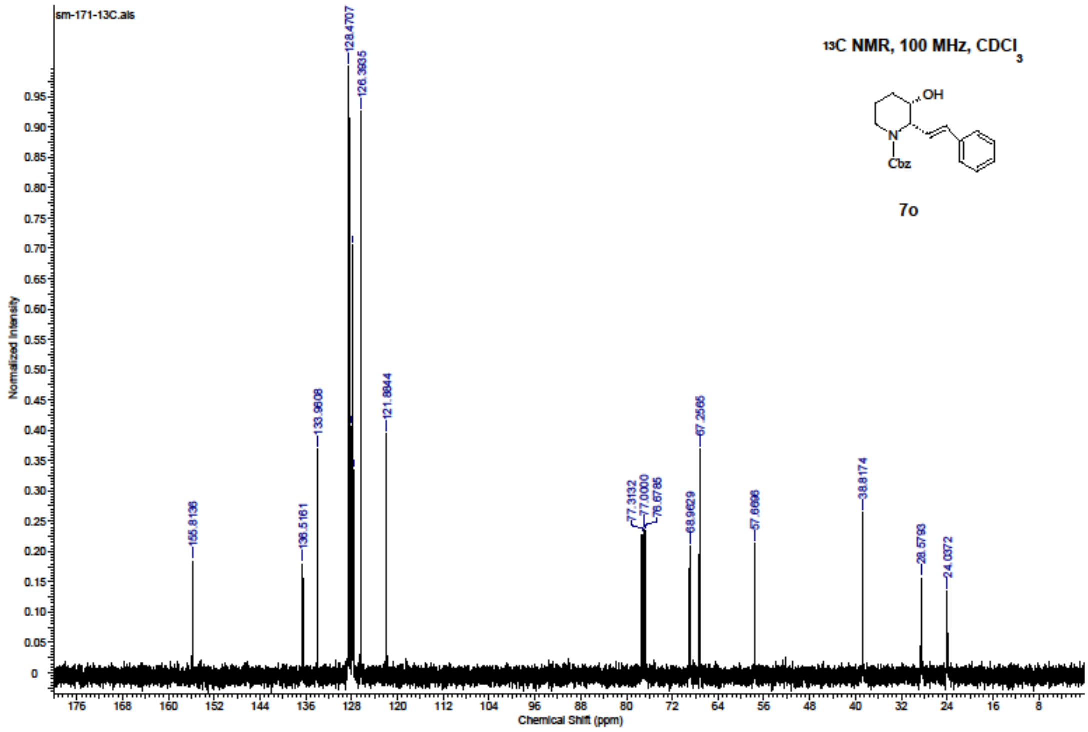

2sm-4-H.als
1H NMR, 400 MHz, CDCl3
OH
N
Cbz
OMe
OMe
7m
3.8719
3.7748
7.3028
5.1408
5.1011
6.8317
6.8104
0.0000
5.096 1.024 1.125 1.033 1.079
1.000 2.574
2.108 3.494 3.206
1.063
7.153
Normalized Intensity
Chemical Shift (ppm)

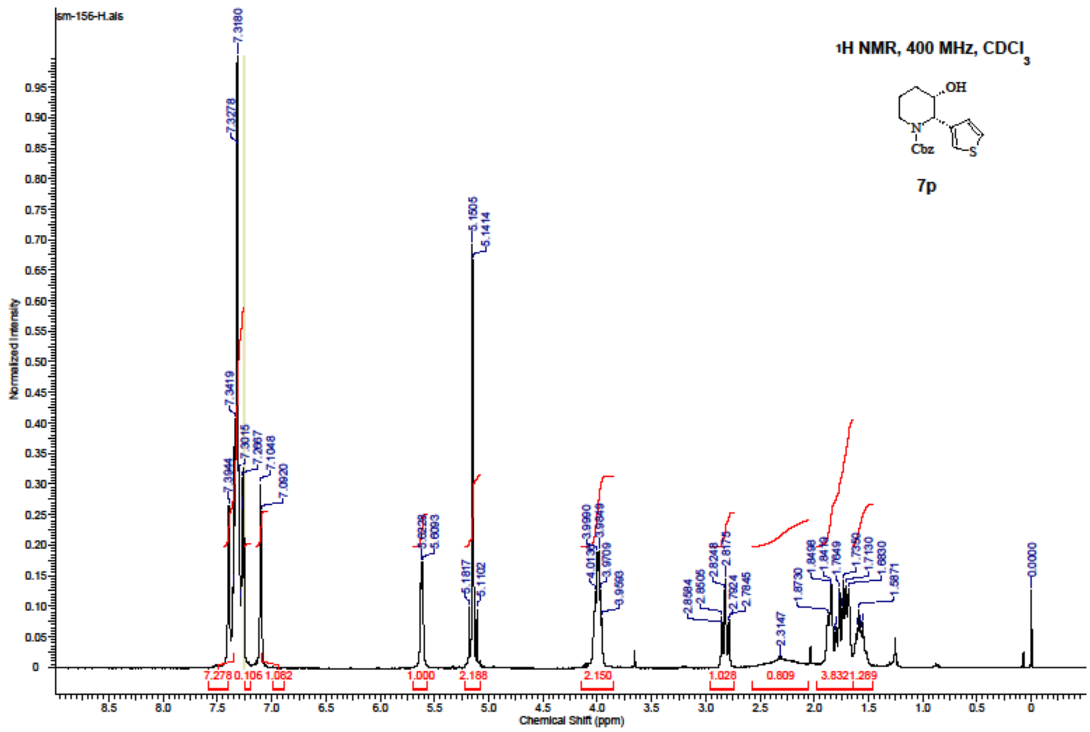

2sm-4-13C.als
13C NMR, 100 MHz, CDCl3
OH
OMe
N
Cbz
OMe
7m
Normalized Intensity
Chemical Shift (ppm)
128.4543
128.0009
127.8196
77.3132
77.0000
76.6785
67.2483
55.7819
155.9784
148.8893
148.2957
136.6388
130.0947
120.4913
112.1574
110.9456
69.9903
58.7165
39.5840
27.6313
23.2129

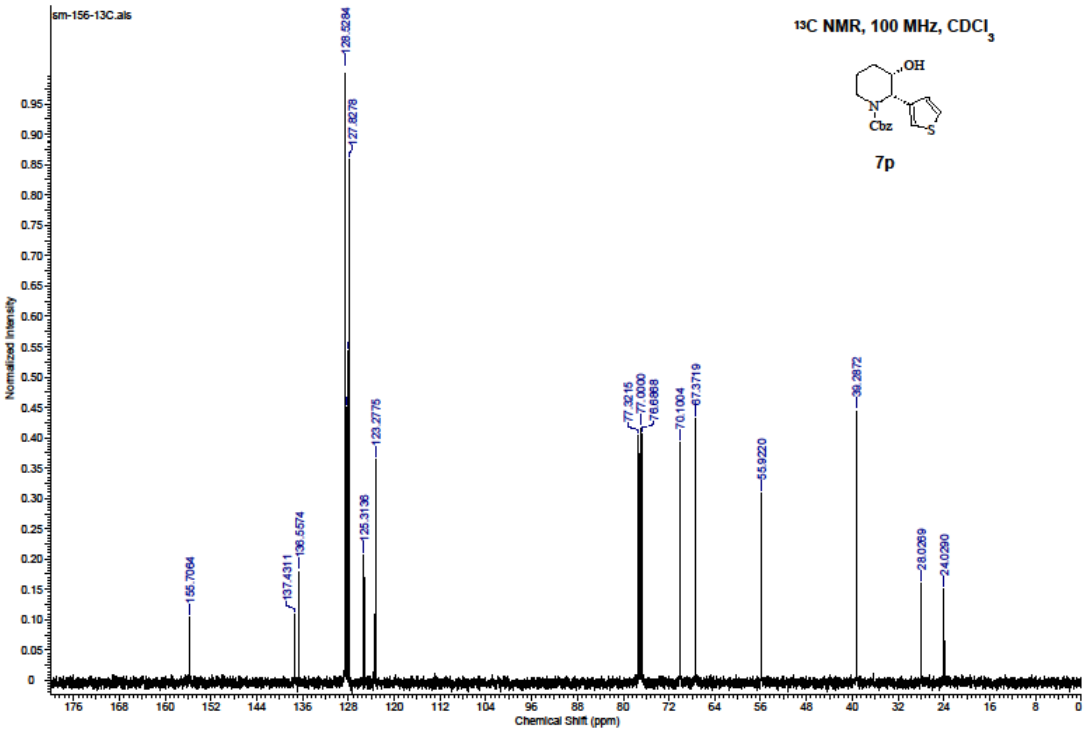

2sm-5-H.als
1H NMR, 400 MHz, CDCl3
OH
N
Cbz
O
O
7n
Normalized Intensity
Chemical Shift (ppm)
5.9484
7.3144
7.3327
7.2722
6.9881
6.9154
6.7774
6.7572
5.1316
5.1023
5.3607
5.3466
5.0711
4.0729
4.0327
4.0040
3.0918
3.0838
3.0594
3.0270
3.0185
1.8480
1.8352
1.8278
1.8176
1.8058
1.7722
1.6946
1.6745
0.0000
5.042
0.520
1.044
1.043
1.015
2.135
1.000
2.378
2.144
1.029
6.629

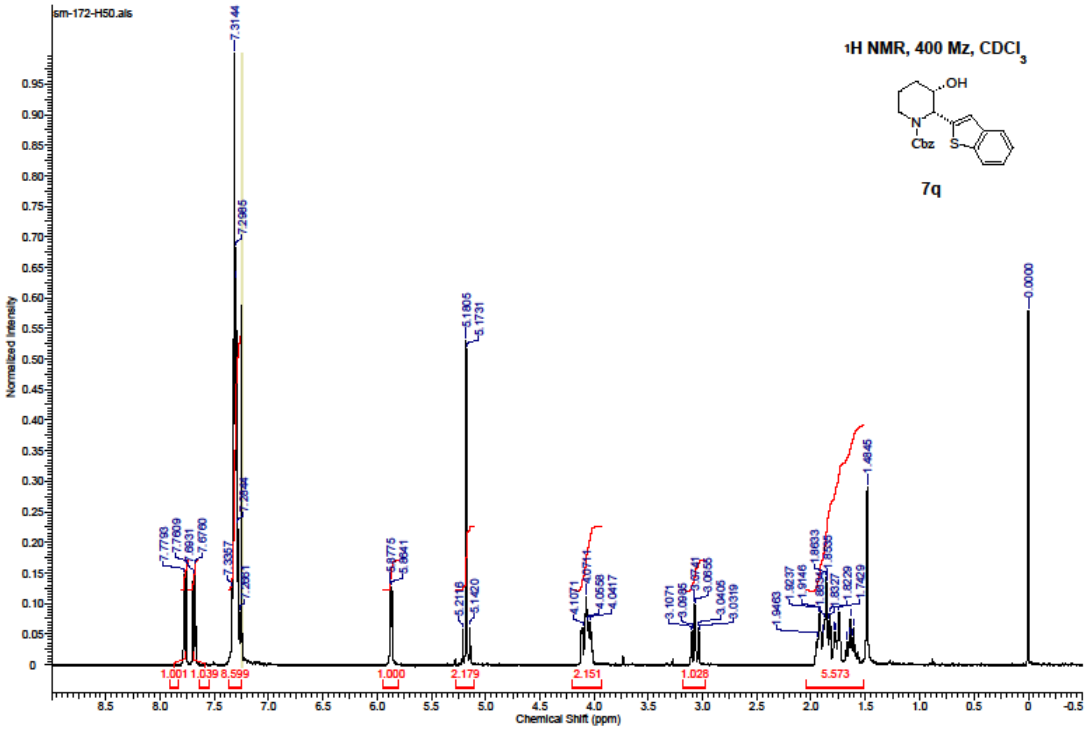

2sm-5-13C2.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
O
O
7n
Normalized Intensity
Chemical Shift (ppm)
155.9619
147.8011
146.7825
136.5903
131.4301
128.4790
127.7948
121.8185
109.0909
108.1677
101.0043
77.3215
77.0000
76.6868
69.9356
67.3060
58.7990
39.5180
27.4170
23.1717

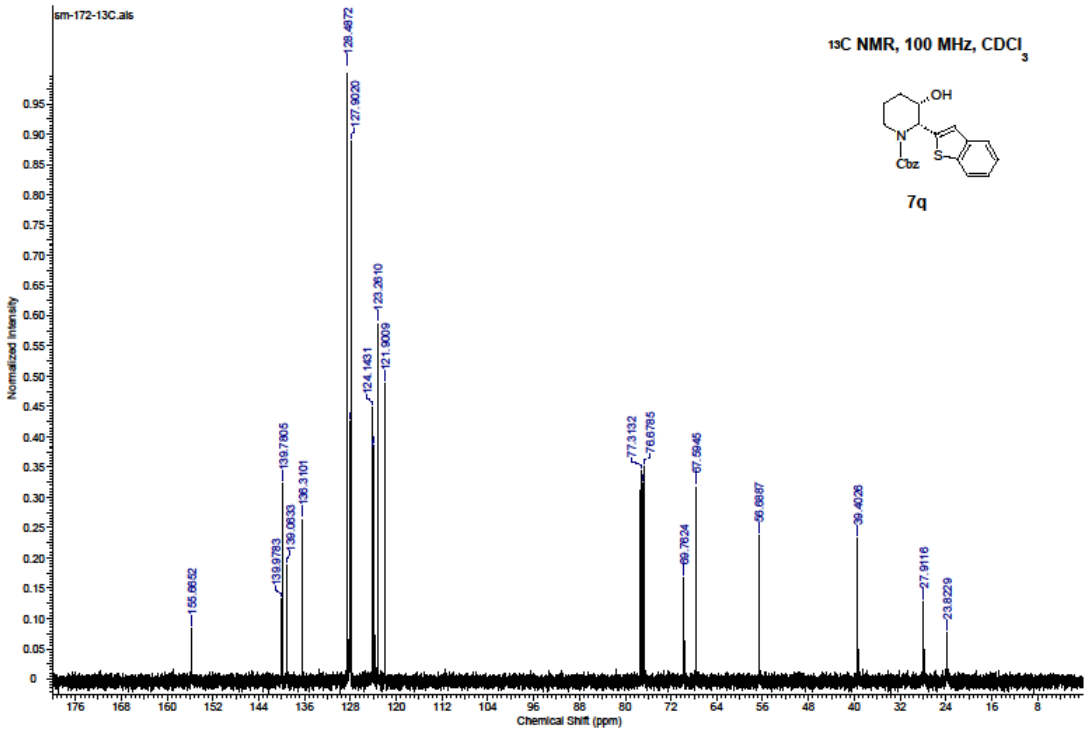

sm-171-H50.als
1H NMR, 400 MHz, CDCl3, 50 oC
OH
N
Cbz
7o
Normalized Intensity
Chemical Shift (ppm)
7.3443
7.3290
7.3034
7.3681
7.2331
6.5556
6.4029
6.3870
6.3628
6.3473
5.1744
5.1548
5.0992
4.0595
3.8840
2.9242
2.9079
1.8938
1.7203
1.5914
1.5590
1.5358
1.4888
0.0000
9.680
1.116
0.969
1.000
3.119
0.987
1.006
0.955
0.948
1.062
4.798

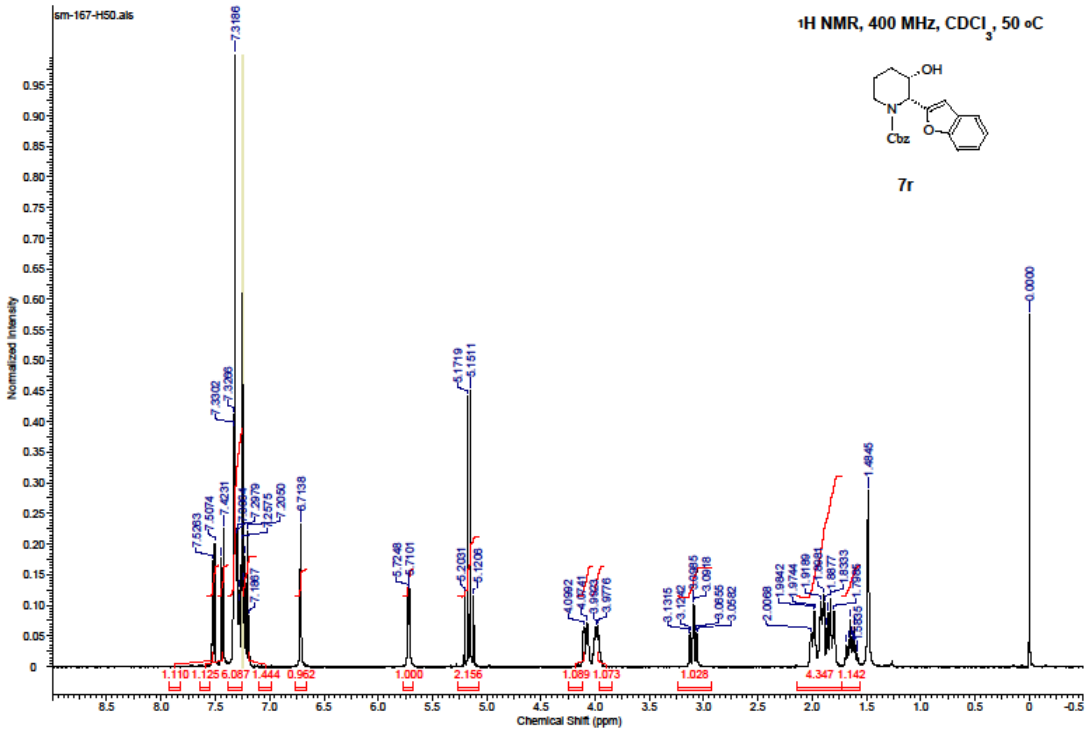

sm-171-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
7o
Normalized Intensity
Chemical Shift (ppm)
155.8136
136.5161
133.9608
128.4707
126.3935
121.8844
77.3132
77.0000
76.6785
68.9629
67.2565
57.6696
38.8174
28.5793
24.0372

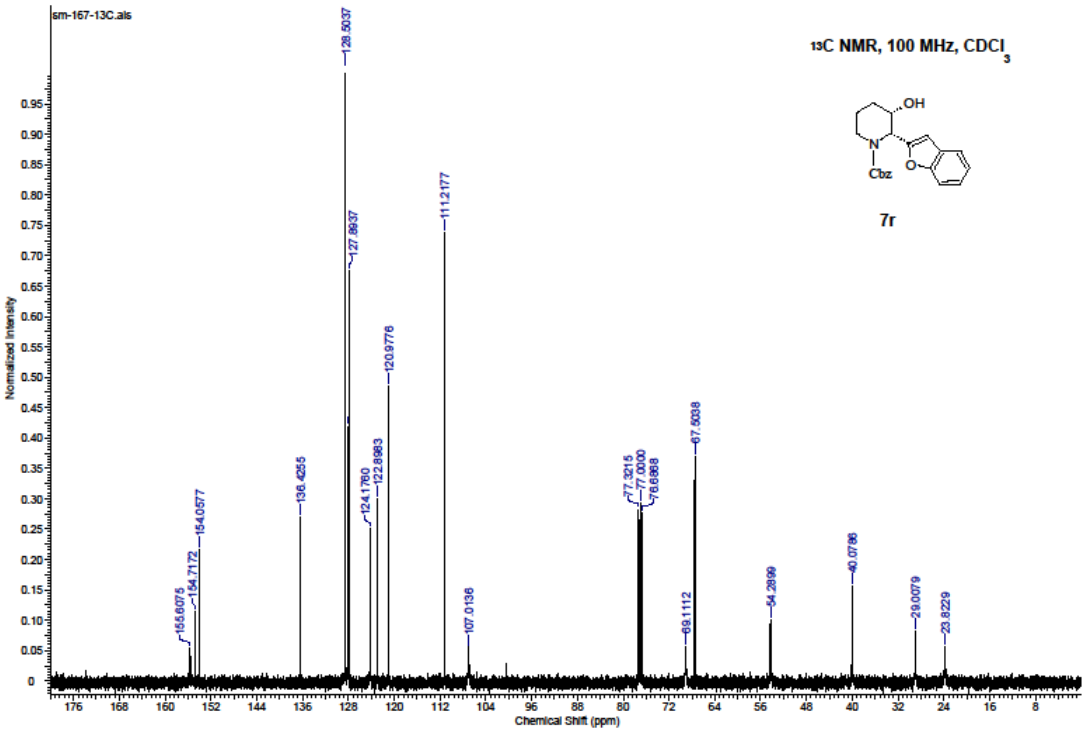

sm-156-H.als
1H NMR, 400 MHz, CDCl3
OH
N
Cbz
S
7p
Normalized Intensity
Chemical Shift (ppm)
7.3180
7.3278
7.3419
7.3944
5.1505
5.1414
0.0000
7.278 0.106 1.082
1.000
2.188
2.150
1.028
0.809
3.832 1.269

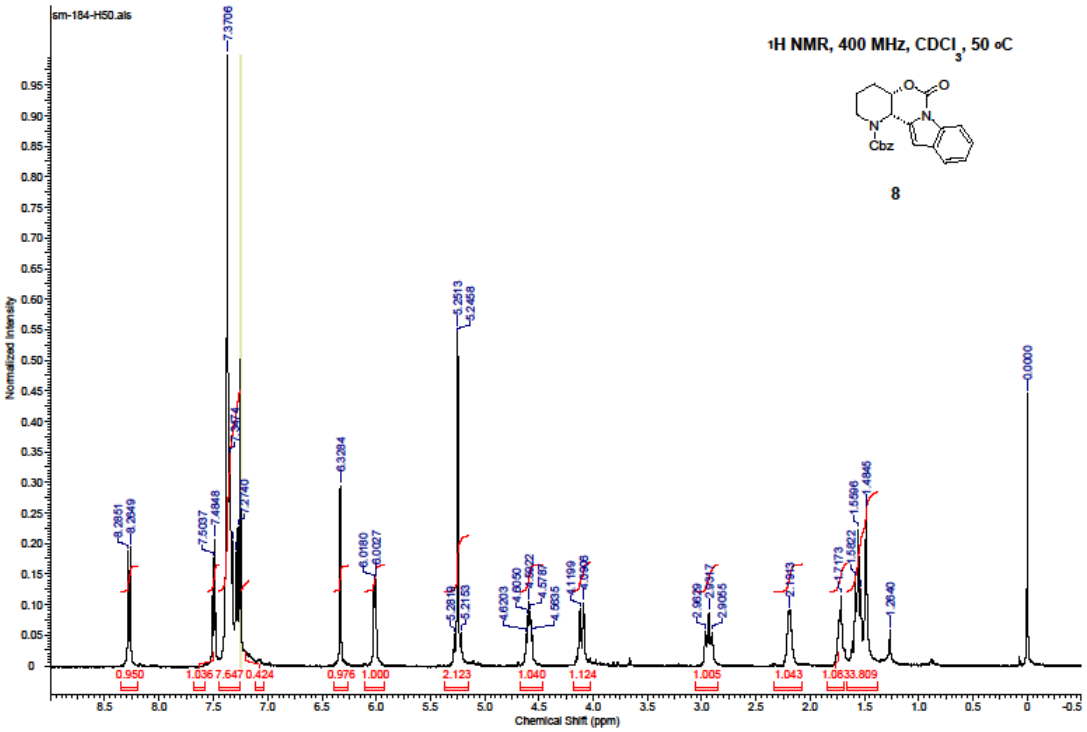

sm-156-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
S
7p
Normalized Intensity
Chemical Shift (ppm)
128.5284
127.8278
123.2775
125.3136
155.7064
137.4311
136.5574
77.3215
77.0000
76.6868
70.1004
67.3719
55.9220
38.2872
28.0289
24.0290

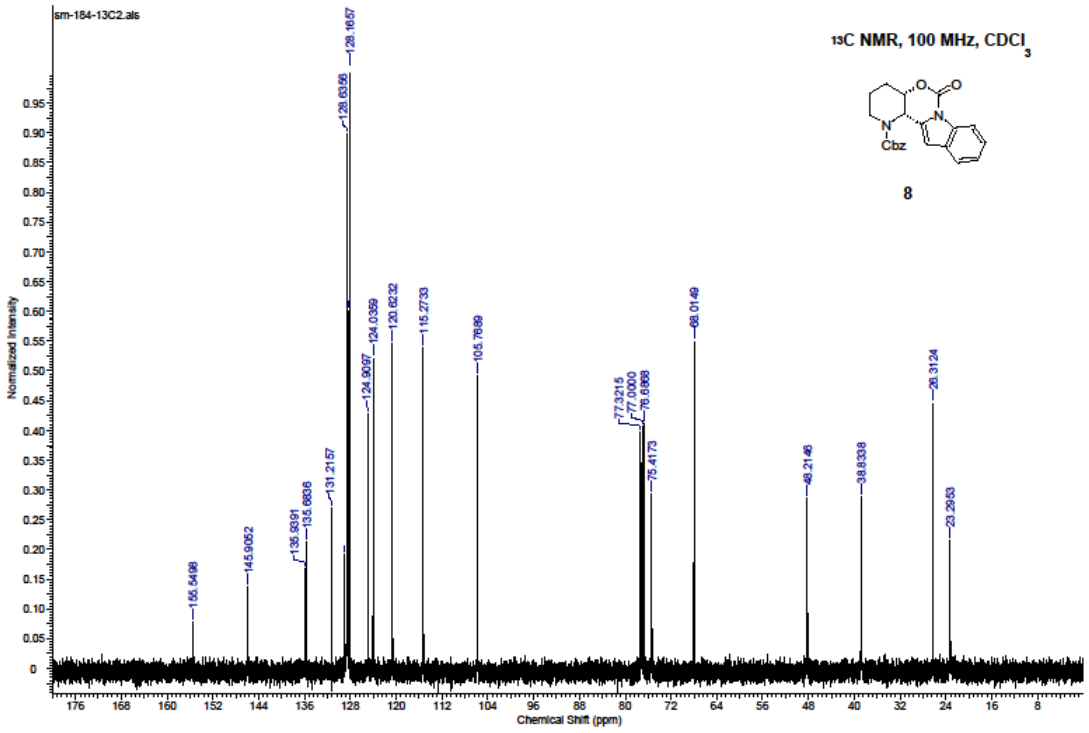

sm-172-H50.als
1H NMR, 400 Mz, CDCl3
OH
N
Cbz
S
7q
Normalized Intensity
Chemical Shift (ppm)
7.3144
7.2985
5.1805
5.1731
0.0000
1.001
1.039
8.599
1.000
2.179
2.151
1.028
5.573

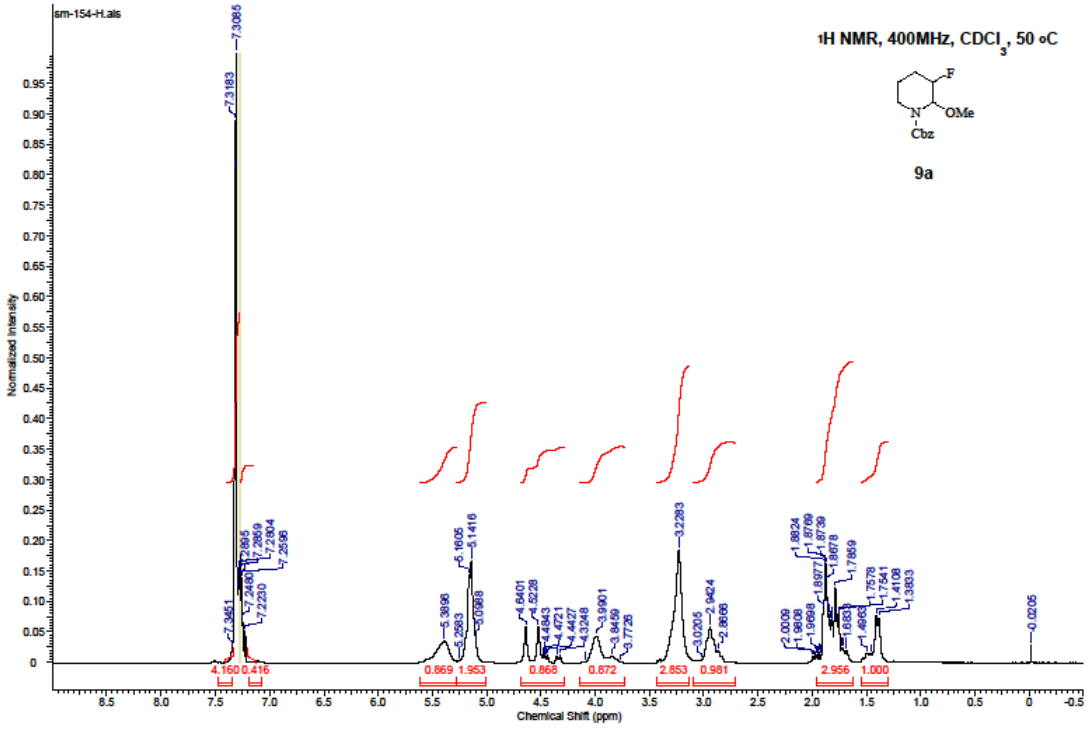

sm-172-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
Cbz
S
7q
Normalized Intensity
Chemical Shift (ppm)
155.6652
139.9783
139.7805
139.0833
136.3101
128.4672
127.9020
124.1431
123.2610
121.9009
77.3132
76.6785
69.7624
67.5945
56.6887
39.4026
27.9116
23.8229

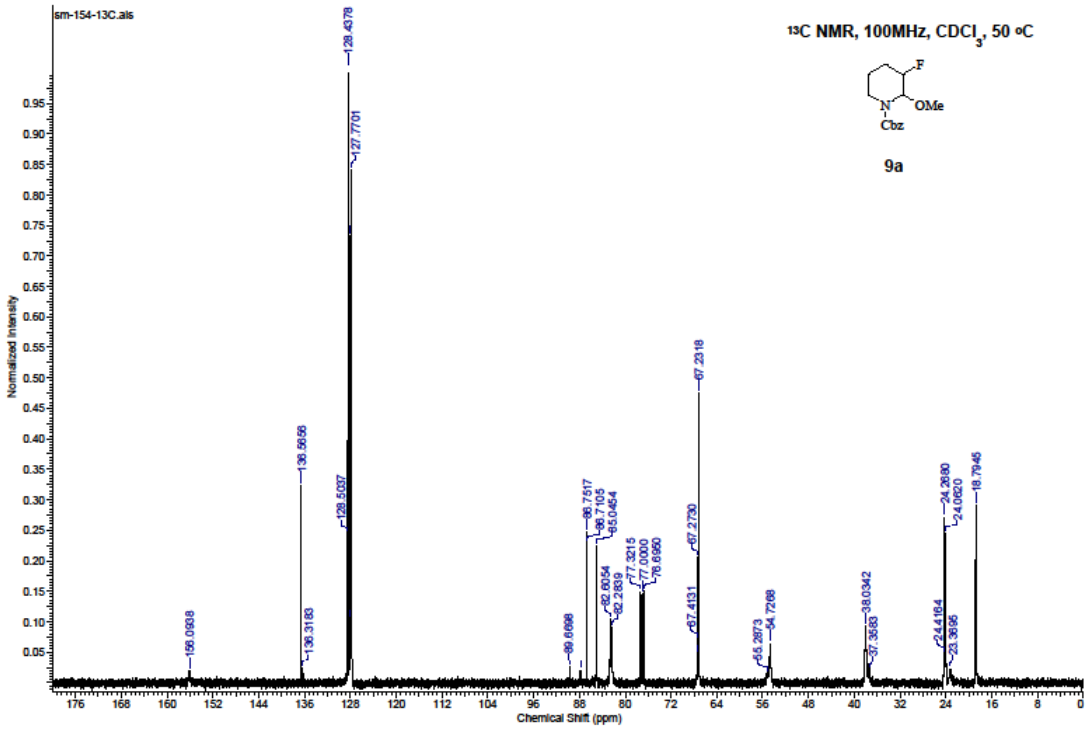

sm-167-H50.als
1H NMR, 400 MHz, CDCl3, 50 oC
OH
N
Cbz
O
7r
Normalized Intensity
Chemical Shift (ppm)
7.3186
7.3302
7.3266
7.5263
7.5074
7.4231
7.2379
7.2275
7.2050
7.1887
6.7138
6.7248
6.7101
6.1719
6.1511
5.2091
5.1208
4.0992
4.0741
3.9923
3.9776
3.1315
3.1242
3.0985
3.0918
3.0656
3.0582
2.0068
1.9842
1.9744
1.9189
1.8481
1.8333
1.8077
1.7996
1.5835
1.4945
0.0000
1.110 1.125 6.087 1.444 0.962 1.000 2.156 1.089 1.073 1.028 4.347 1.142

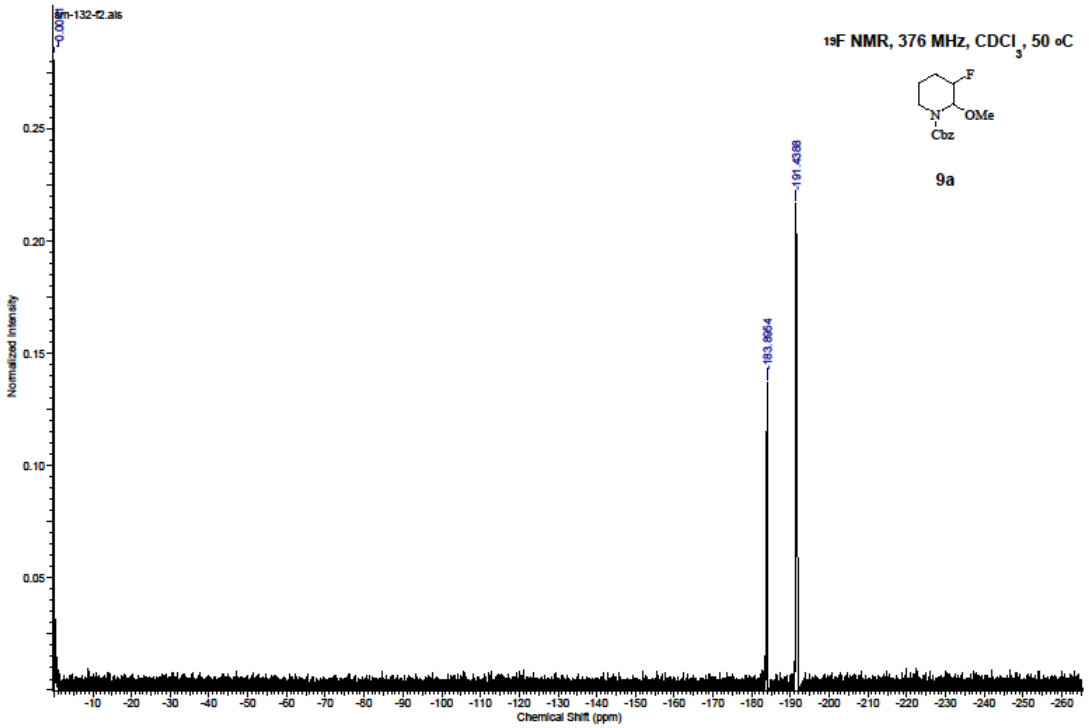

sm-167-13C.als
13C NMR, 100 MHz, CDCl3
OH
N
O
Cbz
7r
Normalized Intensity
Chemical Shift (ppm)
128.5037
127.8937
120.9776
111.2177
136.4255
124.1760
122.8983
154.7172
154.0577
155.6075
107.0136
77.3215
77.0000
76.6888
67.5038
69.1112
54.2899
40.0786
29.0079
23.8229

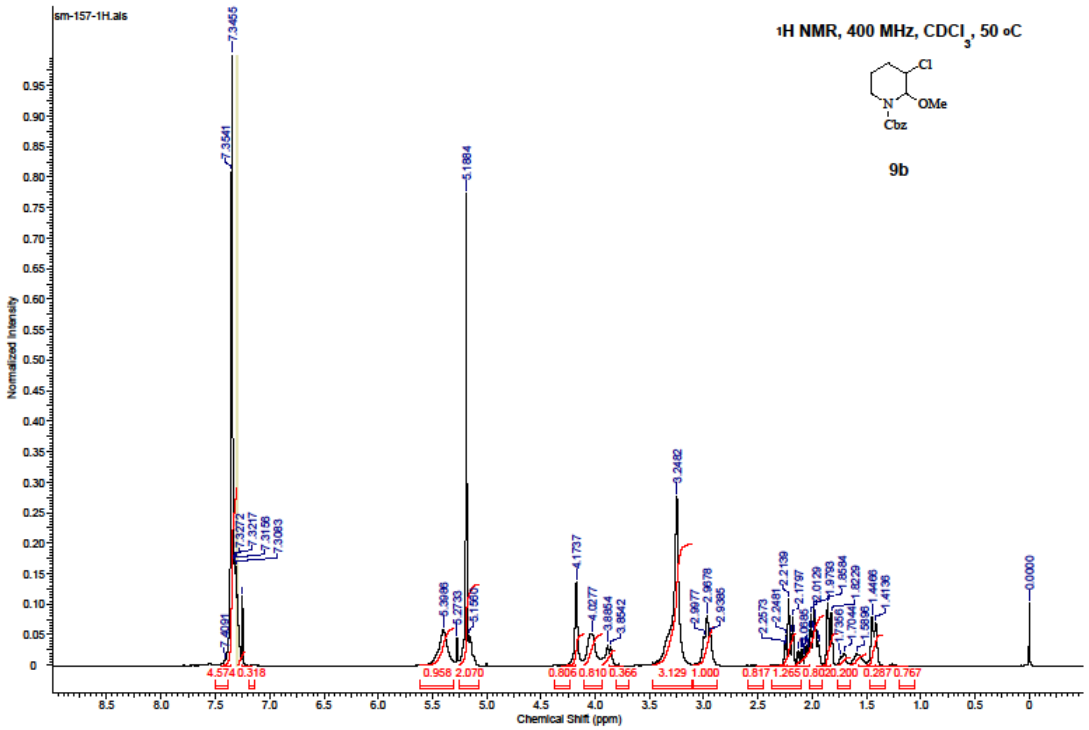

sm-184-H50.als
1H NMR, 400 MHz, CDCl3, 50 oC
O
O
N
N
Cbz
8
Normalized Intensity
Chemical Shift (ppm)
7.3706
7.3654
7.2740
7.5037
7.4848
8.2851
8.2649
6.3284
6.0180
6.0027
5.2513
5.2458
5.2819
5.2153
4.6203
4.6050
4.5922
4.5787
4.5635
4.1199
4.0905
2.9629
2.9347
2.9055
2.1943
1.7173
1.5822
1.5696
1.4845
1.2640
0.0000
0.950
1.036
7.547
0.424
0.975
1.000
2.123
1.040
1.124
1.005
1.043
1.083
3.809

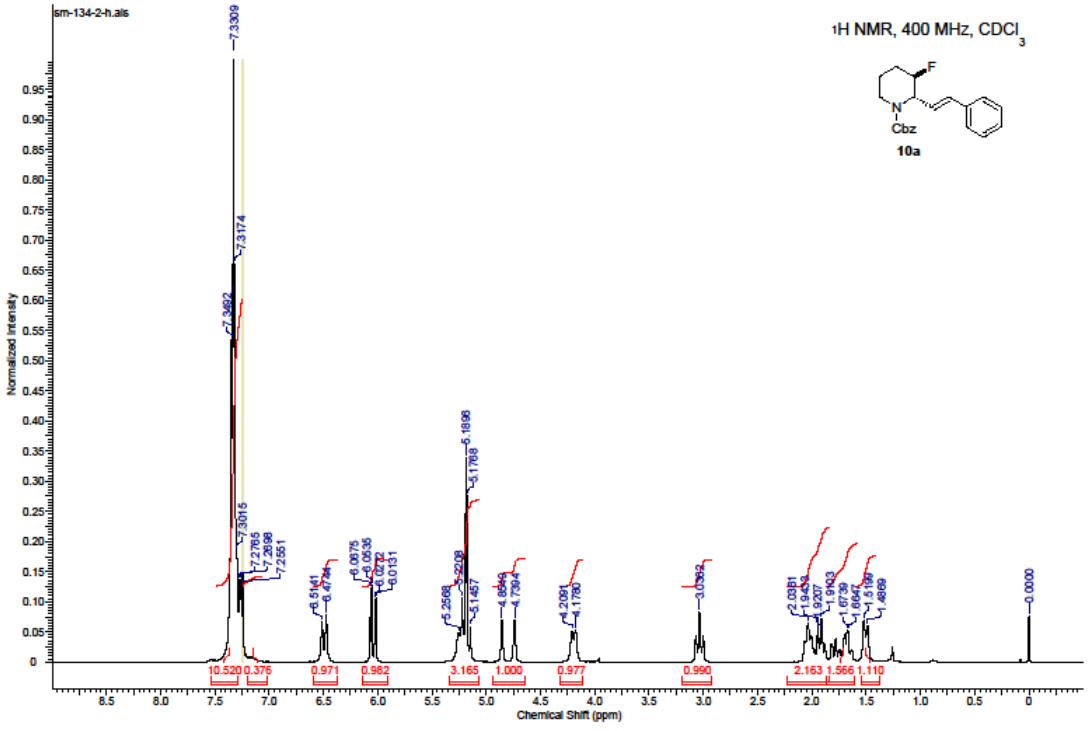

sm-184-13C2.als
13C NMR, 100 MHz, CDCl3
Cbz
8
Normalized Intensity
Chemical Shift (ppm)

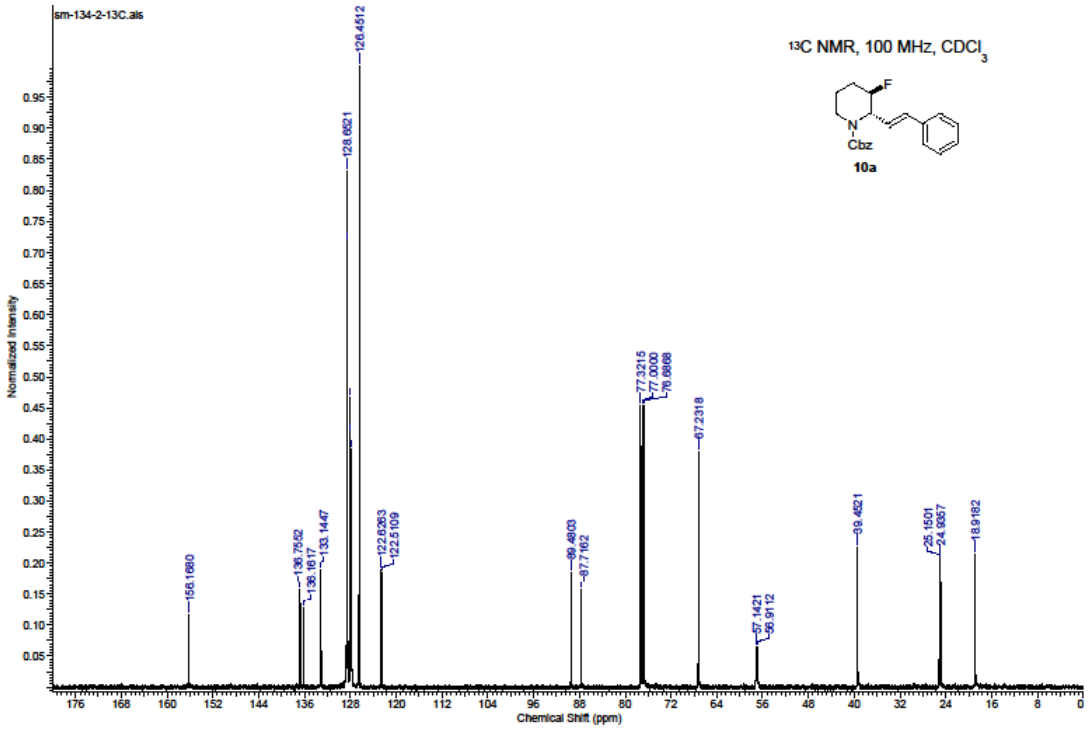

sm-154-H.als
1H NMR, 400MHz, CDCl3, 50 oC
F
OMe
Cbz
9a
Normalized Intensity
Chemical Shift (ppm)

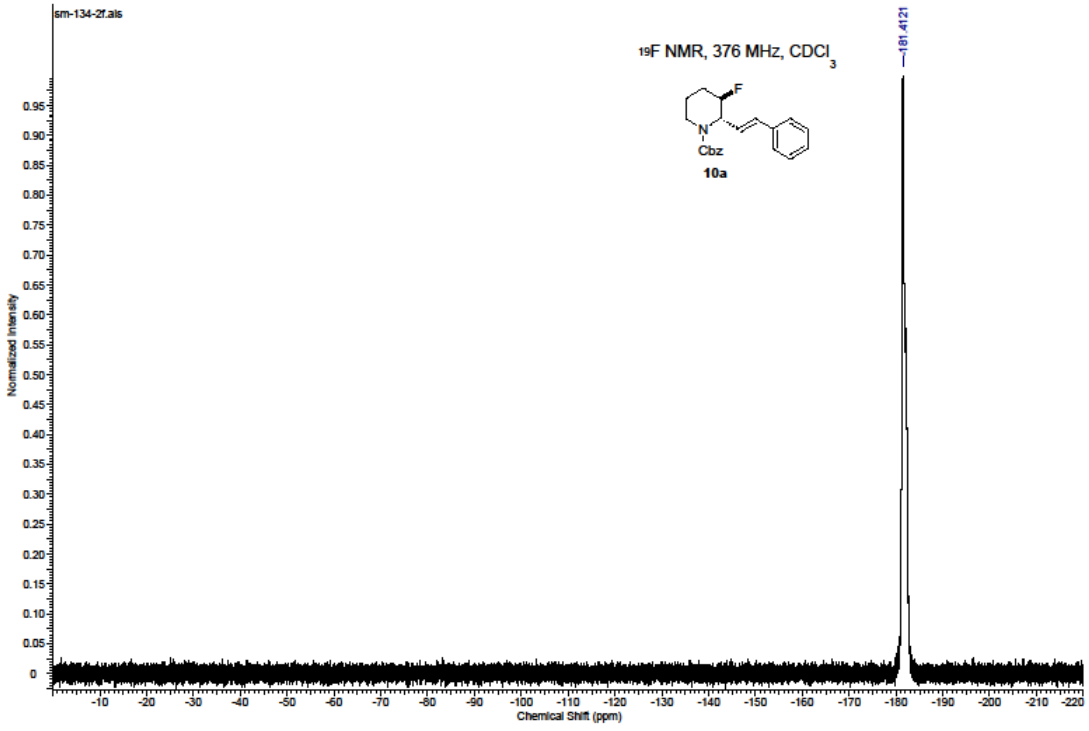

sm-154-13C.als
13C NMR, 100MHz, CDCl3, 50 oC
F
OMe
N
Cbz
9a
Normalized Intensity
Chemical Shift (ppm)
128.4378
127.7701
136.5656
136.3183
129.0057
166.0938
99.8666
86.7517
86.7105
85.0454
82.6054
82.2883
77.3215
77.0000
76.6960
67.2318
67.2730
67.4131
55.2673
54.7268
38.0342
37.3583
24.2680
24.0620
24.4164
23.9895
18.7945

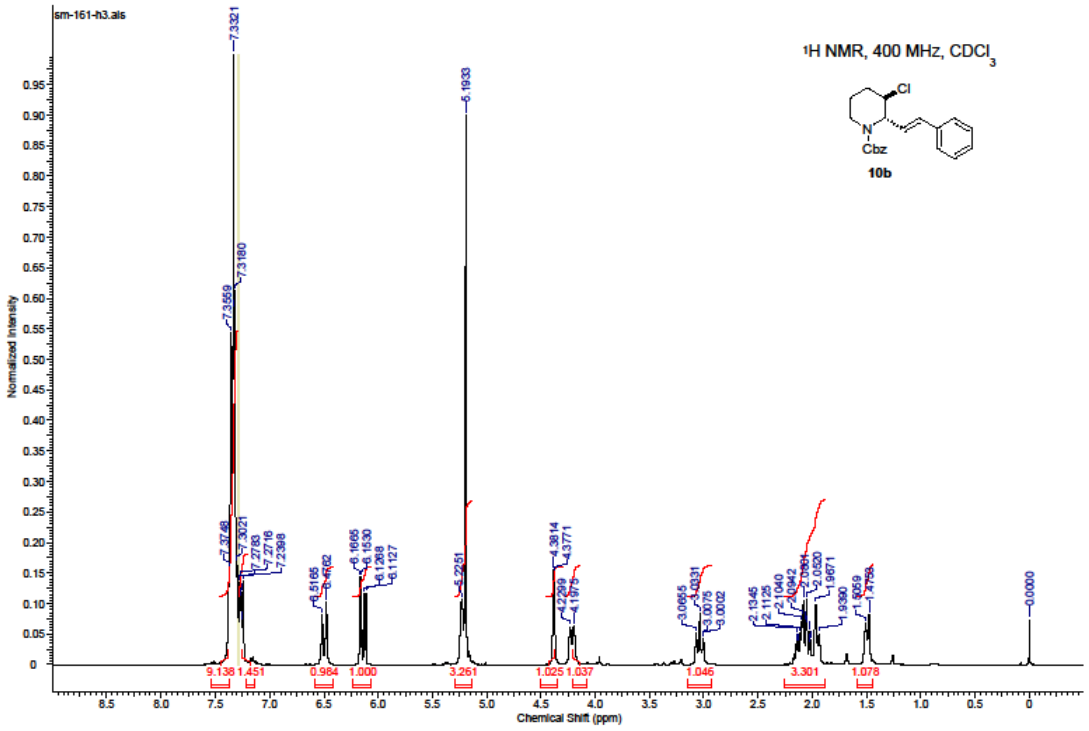

sm-132-f2.als
19F NMR, 376 MHz, CDCl3, 50 oC
F
OMe
N
Cbz
9a
Normalized Intensity
Chemical Shift (ppm)
191.4388
183.8654

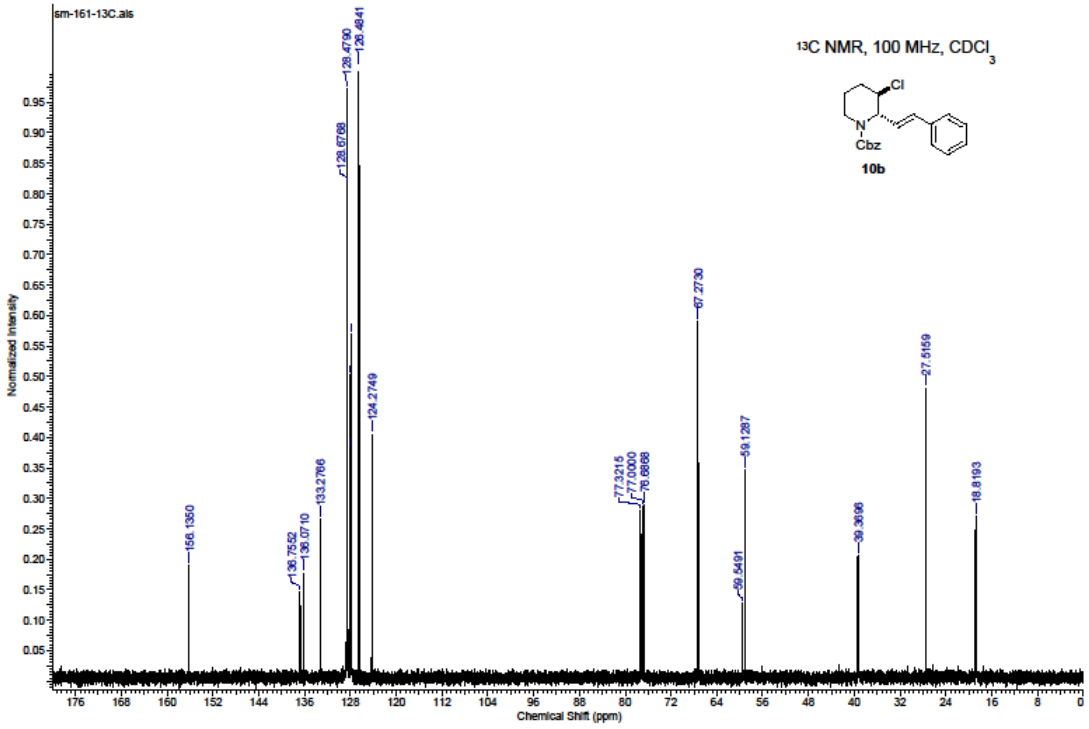

sm-157-1H.als
1H NMR, 400 MHz, CDCl3, 50 oC
Cl
OMe
N
Cbz
9b
Normalized Intensity
Chemical Shift (ppm)

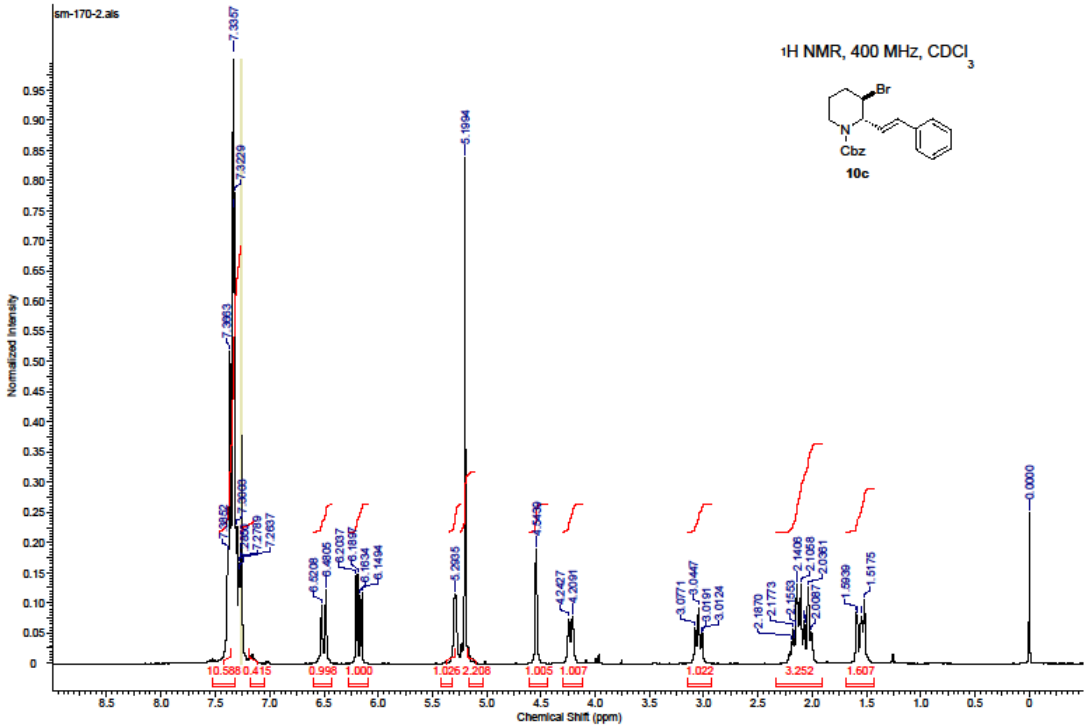

sm-134-2-h.als
1H NMR, 400 MHz, CDCl3
F
N
Cbz
10a
Normalized Intensity
Chemical Shift (ppm)

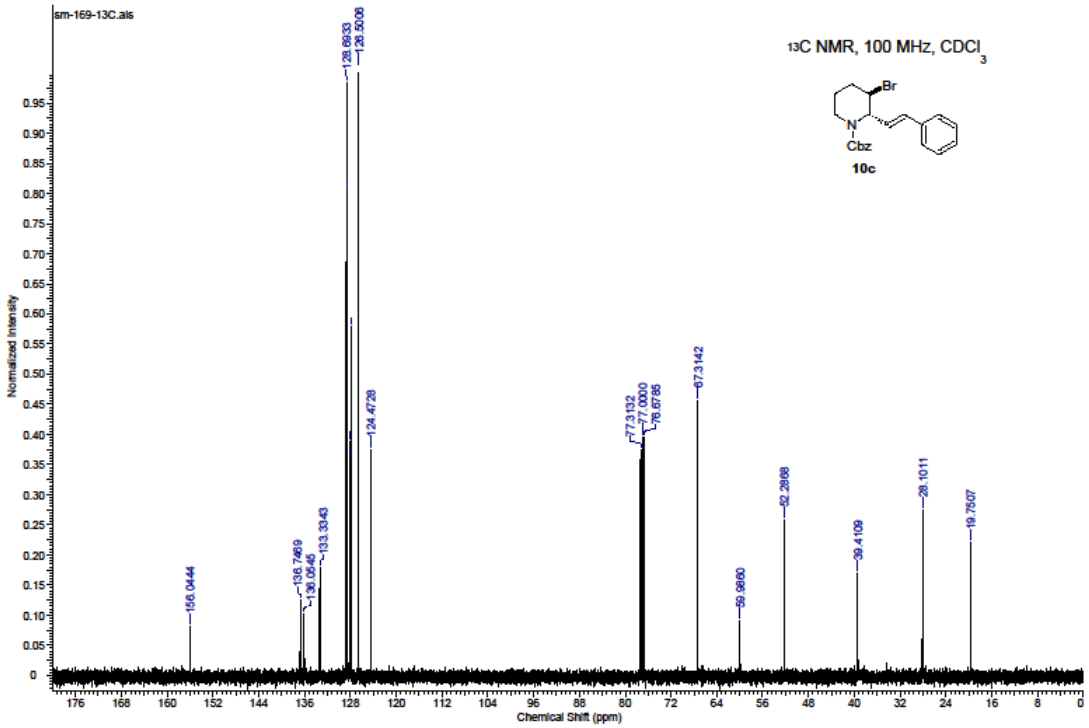

sm-134-2-13C.als
^{13}C NMR, 100 MHz, CDCl$_3$
F
N
Cbz
10a
126.4512
128.6821
156.1680
136.7552
136.1617
133.1447
122.6283
122.5109
89.4803
87.7162
77.3215
77.0000
76.6868
67.2318
57.1421
56.9112
39.4521
25.1501
24.9557
18.9182
Normalized Intensity
Chemical Shift (ppm)

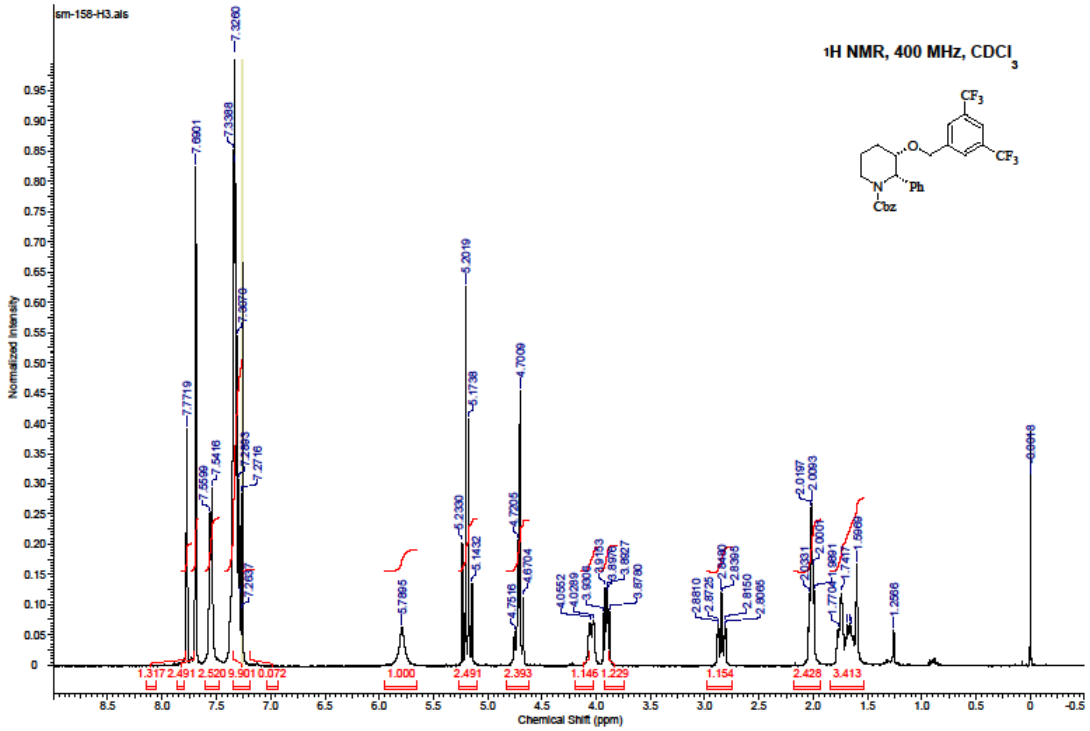

sm-134-2f.als
^{19}F NMR, 376 MHz, CDCl$_3$
F
N
Cbz
10a
-181.4121
Normalized Intensity
Chemical Shift (ppm)

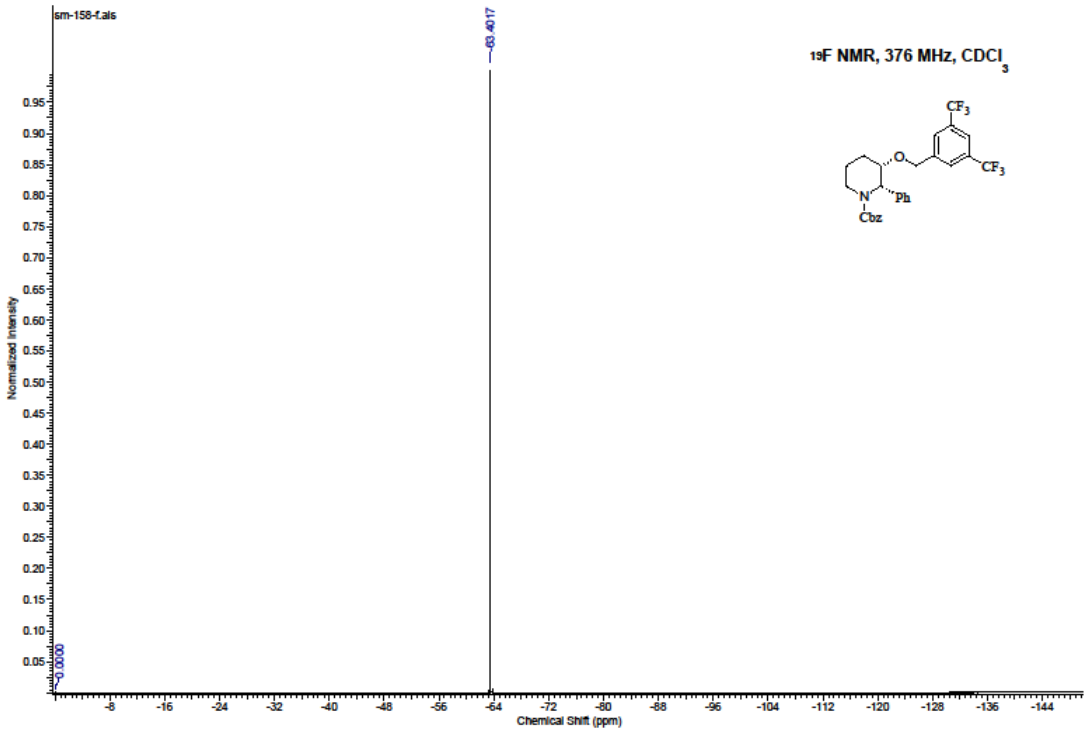

sm-161-h3.als
^{1}H NMR, 400 MHz, CDCl$_3$
Cl
N
Cbz
10b
Normalized Intensity
Chemical Shift (ppm)
7.3321
7.3459
7.3180
5.1933
9.138
1.451
0.984
1.000
3.261
1.025
1.037
1.046
3.301
1.078

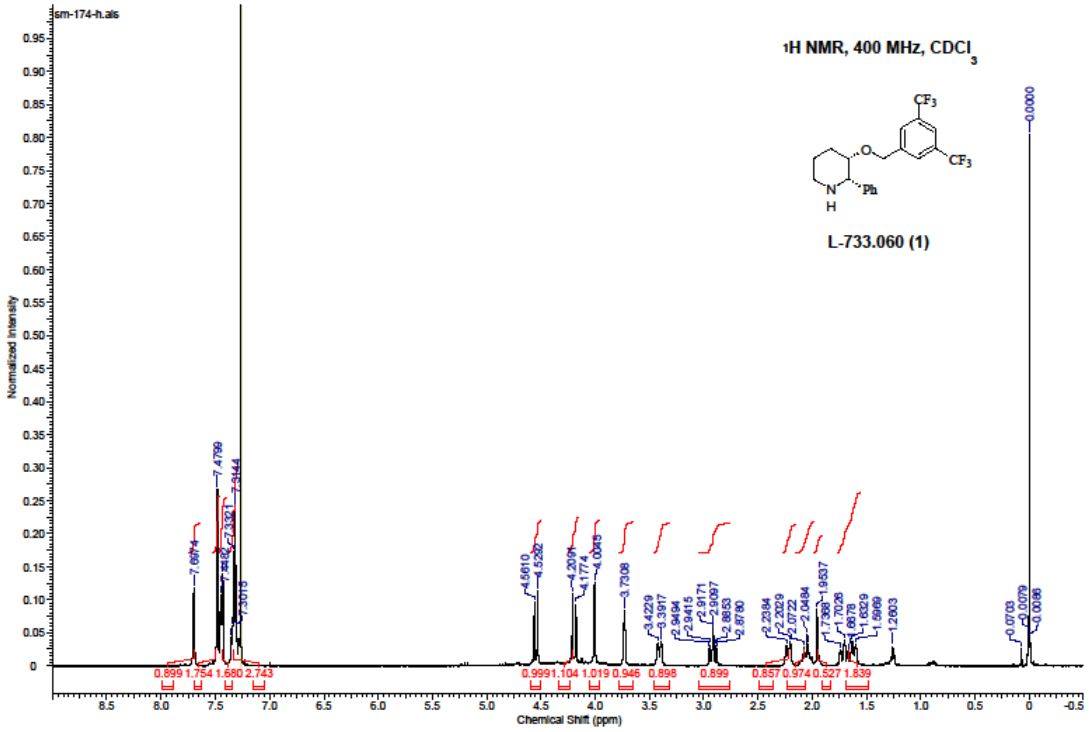

sm-161-13C.als
^{13}C NMR, 100 MHz, CDCl$_3$
Cl
N
Cbz
10b
Normalized Intensity
Chemical Shift (ppm)
128.4841
128.4790
128.6768
124.2749
133.2766
156.1350
136.7552
136.0710
67.2730
59.1287
59.5491
39.3696
27.5159
18.8193

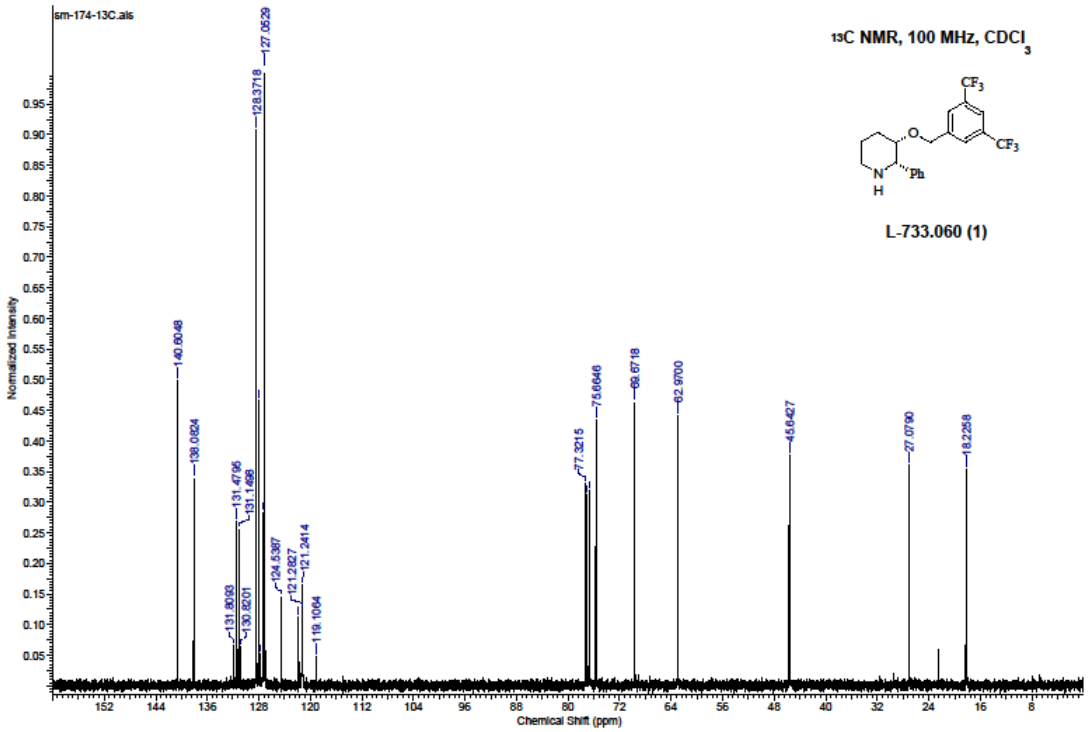

sm-170-2.als
1H NMR, 400 MHz, CDCl3
Br
N
Cbz
10c
Normalized Intensity
Chemical Shift (ppm)
7.3357
7.3229
7.3063
5.1994
0.0000
10.588
0.415
0.998
1.000
1.026
2.208
1.005
1.007
1.022
3.252
1.607

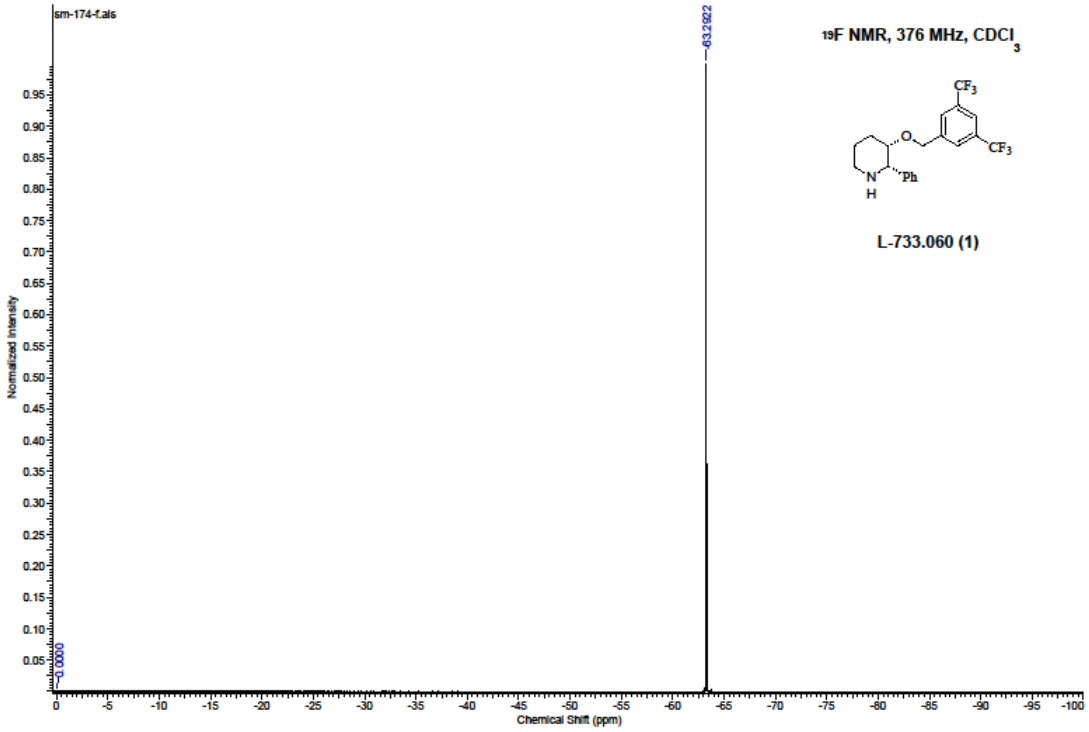

sm-169-13C.als
13C NMR, 100 MHz, CDCl3
Br
N
Cbz
10c
Normalized Intensity
Chemical Shift (ppm)
128.6933
128.5006
124.4728
77.3132
77.0000
76.6785
67.3142
59.9680
52.2868
39.4109
28.1011
19.7507
156.0444
136.7469
136.0545
133.3343


sm-158-H3.als
^{1}H NMR, 400 MHz, CDCl$_3$
Normalized Intensity
Chemical Shift (ppm)
1.317 2.491 2.520 9.901 0.072 1.000 2.491 2.393 1.146 1.229 1.154 2.428 3.413


sm-158-f.als
^{19}F NMR, 376 MHz, CDCl$_3$
Normalized Intensity
Chemical Shift (ppm)


sm-174-h.als
¹H NMR, 400 MHz, CDCl3
L-733.060 (1)
Normalized Intensity
Chemical Shift (ppm)


sm-174-13C.als
¹³C NMR, 100 MHz, CDCl3
L-733.060 (1)
Normalized Intensity
Chemical Shift (ppm)


sm-174-f.als
-63.2922
19F NMR, 376 MHz, CDCl3
CF3
O
CF3
N
H
Ph
L-733.060 (1)
Normalized Intensity
Chemical Shift (ppm)