Supporting Information

trans-Selective and Switchable Arene Hydrogenation of Phenol Derivatives

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1. Materials and Methods

Unless otherwise noted, all reactions were carried out under an atmosphere of argon in oven-dried glassware. Reaction temperatures are reported as the temperature of the bath / metal block surrounding the vessel unless otherwise stated. The solvents used were purified by distillation over the drying agents indicated in parentheses: *n*-hexane (CaH_2), dichloromethane (CaH_2), diethylether (Na-benzophenone), THF (Na-benzophenone). Dichloroethane (4Å), 1,4-dioxane (4Å), ethyl acetate (4Å), methanol (3Å) and ethanol (4Å) were purchased as dry solvents from commercial suppliers and stored over molecular sieves. *n*-Heptane (Acros Organics, 99+%) and *iso*-propanol (Fisher Scientific, 99.8%) were used as received from supplier.

All hydrogenation reactions were carried out in Berghof High Pressure Reactors using hydrogen gas. Commercially available chemicals were obtained from Acros Organics, Aldrich Chemical Co., Strem Chemicals, Alfa Aesar, ABCR, Combi-Blocks, Chempur and TCI Europe and used as received unless otherwise stated. Palladium/Al_2O_3 was obtained from Johnson Matthey 5 wt% Palladium on alumina A302099-5; CODE: S4020; 10 g on dry basis; Lot: C-15059; JM Order: 7248; %water: 2.01. Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short wave UV light, and/or $KMnO_4$ and ninhydrin staining solutions followed by heating. Flash chromatography was performed on Merck silica gel (40–63 mesh) by standard technique eluting with solvents as indicated.

GC-MS spectra were recorded on an Agilent Technologies 7890A GC-system with an Agilent 5975C VL MSD or an Agilent 5975 inert Mass Selective Detector (EI) and a HP-5MS column (0.25 mm x 30 m, film: 0.25 µm). The major signals are quoted in m/z with the relative intensity in parentheses. The method indicated as '50_40' starts with the injection temperature T_0 (50 °C); after holding this temperature for 3 min, the column is heated by 40 °C/min to temperature T1 (290 °C or 320 °C). GC-FID analysis was undertaken on an Agilent Technologies 6890A equipped with an HP-5 quartz column (0.32 mm x 30 m, film: 0.25 µm) using flame ionization detection. Method: Initial temperature 50 °C, hold 3 min, increment 40 °C/min, final temperature 280 °C, hold 3 min. High resolution mass spectra (HRMS) were obtained by the MS service of the OrganischChemisches Institut, Westfälische Wilhelms-Universität Münster, using electrospray ionisation (ESI) on a Bruker Daltonics MicroTof spectrometer. Infrared spectra were recorded on a Shimadzu FTIR 8400S spectrometer as neat compound. The wave numbers ($\tilde{\nu}$) of recorded IR-signals are quoted in cm^{-1}.

^{1}H and ^{13}C, ^{19}F and ^{11}B NMR spectra were recorded on a Bruker AV 300 or AV 400, Varian 500 MHz INOVA or Varian Unity plus 600 in the indicated solvents. Chemical shifts (δ) are given in ppm relative to TMS. The residual solvent signals were used as references and the

chemical shifts converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; methanol-d_4: δ_H = 3.31 ppm, δ_C = 49.00 ppm; acetone-d_6: δ_H = 2.05 ppm, δ_C = 29.84 ppm; CD_3CN: δ_H = 1.94 ppm, δ_C = 1.32 ppm; toluene-d_8: δ_H = 7.09, 7.01, 6.97 and 2.08 ppm, δ_C = 137.48, 128.87, 127.96, 125.13 and 20.43 ppm; DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.52 ppm). ^{19}F and ^{11}B NMR spectra are not calibrated by an internal reference. The multiplicities of the signals are reported as s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), hept (heptet) and m (multiplet). Coupling constants (*J*) are quoted in Hz.

Data sets for compounds **2f**, **2q**, **2m** and **2o** were collected with a Bruker D8 Venture CMOS diffractometer. Programs used: data collection: APEX3 V2016.1-0[1] (Bruker AXS Inc., **2016**); cell refinement: SAINT V8.37A (Bruker AXS Inc., **2015**); data reduction: SAINT V8.37A (Bruker AXS Inc., **2015**); absorption correction, SADABS V2014/7 (Bruker AXS Inc., **2014**); structure solution *SHELXT-2015*[2] (Sheldrick, G. M. *Acta Cryst.*, **2015**, *A71*, 3-8); structure refinement *SHELXL-2015*[3] (Sheldrick, G. M. *Acta Cryst.*, **2015**, *C71* (1), 3-8) and graphics, *XP*[4] (Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, **1998**). *R*-values are given for observed reflections, and wR^2 values are given for all reflections.

[1] *APEX3* (**2016**), *SAINT* (**2015**) and *SADABS* (**2015**), Bruker AXS Inc., Madison, Wisconsin, USA.

[2] Sheldrick, G. M., *SHELXT – Integrated space-group and crystal-structure determination*, *Acta Cryst.*, **2015**, *A71*, 3-8.

[3] Sheldrick, G.M., *Crystal structure refinement with SHELXL*, *Acta Cryst.*, **2015**, *C71 (1)*, 3-8.

[4] *XP – Interactive molecular graphics, Version 5.1,* Bruker AXS Inc., Madison, Wisconsin, USA, **1998**.

2. Preparation of Starting Materials

All used starting materials are commercially available and were used without further purification.

3. Optimization of Reaction Conditions

General Procedure

A 4 mL screw-cap glass vial, equipped with a magnetic stirring bar, was charged with catalyst, *p*-cresol (0.1 mmol, 1.0 equiv.) and solvent (as indicated, 1.0 mL). The prepared glass vial was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the indicated pressure was set. The reaction mixture was stirred at the indicated temperature overnight. After the autoclave was carefully depressurized, DMAP (0.01 mmol, 0.1 equiv.), imidazole (0.45 mmol, 4.5 equiv.), TBSCl (0.3 mmol, 3.0 equiv.) and dichloromethane (1.0 mL, 0.1 M) were added and the mixture was stirred at 40 °C overnight. After full conversion of the cyclohexanol to the corresponding silylether (indicated by GC-MS analysis), mesitylene (14 µL, 0.101 mmol) was added as internal standard and the mixture was stirred vigorously for 5 min. After filtration over Whatman® filter, conversion, yield and diastereomeric ratio (d.r.) were determined by GC-FID analysis.

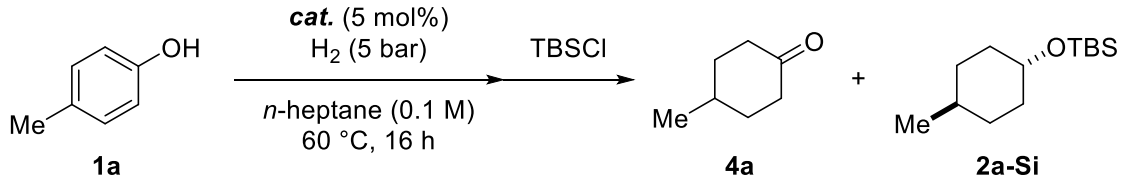


Table S1. Screening of palladium catalysts.

entry	catalyst	conversion [%]	yield **4a** [%]	yield **2a-Si** [%] (d.r.)
1	5 wt% Pd/C	100	31	69 (69:31)
2	5 wt% Pd/$C_{ox.}$	100	traces	98 (50:50)
3	5 wt% Pd/Al_2O_3	100	0	99 (79:21)
4	0.5 wt% Pd/Al_2O_3	100	traces	96 (81:19)
5	5 wt% Pd/SiO_2	77	77	0
6	5 wt% Pd/$CaCO_3$	70	60	10 (61:39)
7	20 wt% Pd$(OH)_2$/C	100	48	52(40:60)

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), *n*-heptane (1.0 mL, 0.1 M). TBS-protection after hydrogenation. Conversion of *p*-cresol. Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard.

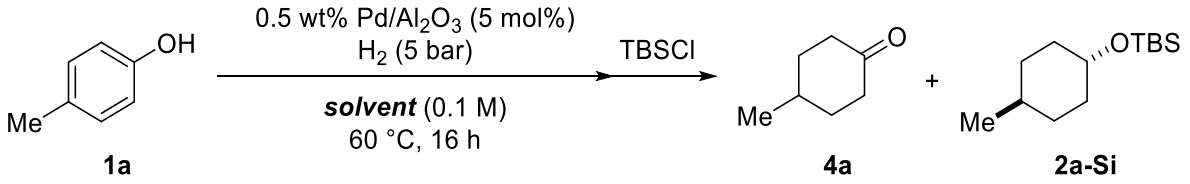


Table S2. Screening of solvents

entry	solvent	conversion [%]	yield **4a** [%]	yield **2a-Si** [%] (d.r.)
1	1,4-dioxane	90	30	60 (77:23)
2	DCE	100	85	15 (50:50)
3	toluene	60	51	traces
4	$CHCl_3$	traces	traces	0
5	MTBE	100	0	99 (81:19)
6	THF	86	32	traces
7	$PhCF_3$	99	87	12 (68:32)
8	cyclohexane	100	traces	98 (83:17)
9	*n*-heptane	100	traces	96 (81:19)
10[a]	EtOH	32	traces	24 (75:25)
11[a]	TFE	100	traces	95 (77:23)
12	AcOH	100	0	99 (n.d.)
13	NEt_3	no conv.	0	0

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). TBS-protection after hydrogenation. Conversion of *p*-cresol. Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard. [a] 2 mol% catalyst loading.

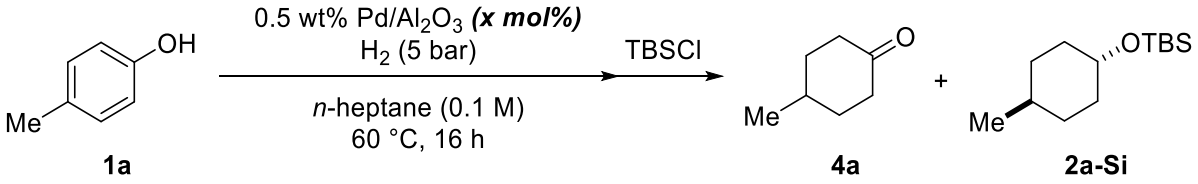


Table S3. Screening of catalyst loading.

entry	catalyst loading	conversion [%]	yield **4a** [%]	yield **2a-Si** [%] (d.r.)
1	10 mol%	100	0	99 (81:19)
2	2 mol%	100	0	99 (81:19)
3	1 mol%	100	50	50 (75:25)

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). TBS-protection after hydrogenation. Conversion of *p*-cresol. Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard.

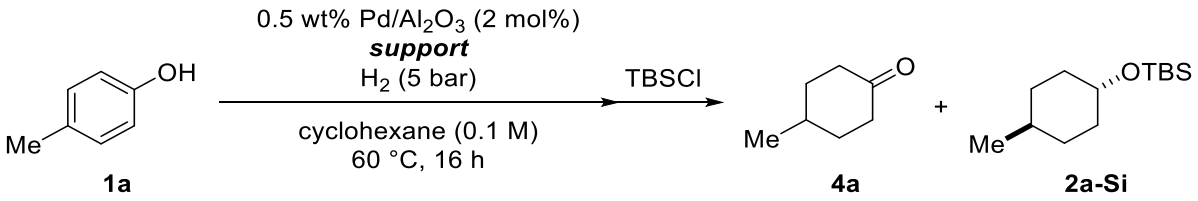


Table S4. Screening of additional catalyst supports.

entry	support	conversion [%]	yield **4a** [%]	yield **2a-Si** [%] (d.r.)
1	SiO_2 (50 mg)	100	traces	97 (84:16)
2	neutral Al_2O_3 (50 mg)	100	traces	98 (81:19)
3	basic Al_2O_3 (50 mg)	100	0	99 (80:20)
4	acidic Al_2O_3 (50 mg)	100	0	99 (80:20)
5	crushed 4Å MS (50 mg)	100	0	99 (79:21)
6	4Å MS (50 mg)	99	traces	98 (74:26)
7	TiO_2 (25 mg)	100	traces	97 (79:21)
8	SiO_2 (25 mg)	100	traces	98 (80:20)
9	SiO_2 (100 mg)	100	11	89 (80:20)
10[a]	AcOH	100	66	34 (68:32)

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). TBS-protection after hydrogenation. Conversion of *p*-cresol. Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard. [a]AcOH (1 Vol%) was added.

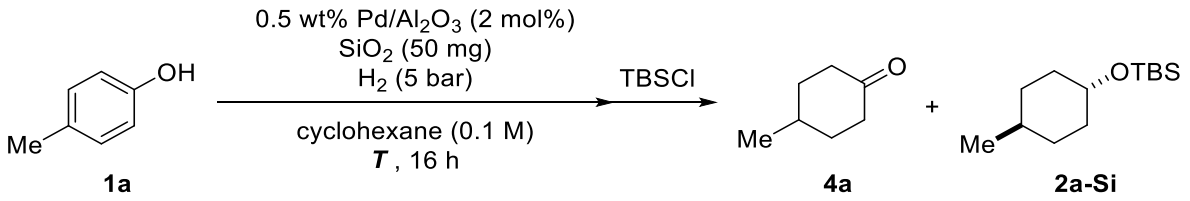


Table S5. Screening of temperature.

entry	temperature	conversion [%]	yield **4a** [%]	yield **2a-Si** [%] (d.r.)
1	40 °C	99	38	61 (80:20)
2	50 °C	100	0	99 (77:23)
3	80 °C	100	0	99 (77:23)

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). TBS-protection after hydrogenation. Conversion of *p*-cresol. Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard.

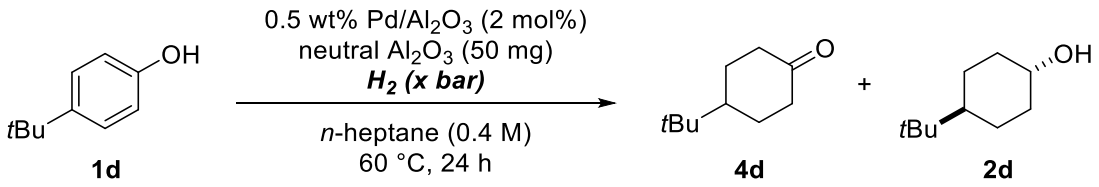
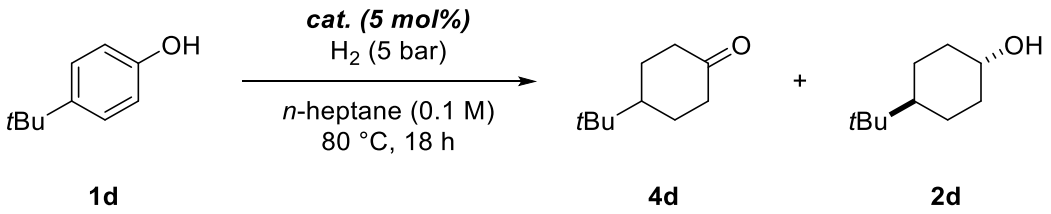


Table S6. Screening of hydrogen pressure.

entry	H_2 (bar)	conversion [%]	yield **4d** [%]	yield **2d** [%] (d.r.)
1	5	100	traces	98 (88:12)
2	3	100	16	84 (86:14)
3[a]	5	100	traces	99 (88:12)

Reaction conditions: **1d** (0.4 mmol, 1.0 equiv.), solvent (1.0 mL, 0.4 M). Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard. [a] 5 wt% Pd/Al_2O_3 without additional neutral Al_2O_3 at 80 °C.

Due to significant amounts of insoluble solids in the process of up-scaling (0.4 mmol) when employing 0.5 wt% Pd/Al_2O_3 (2 mol%) and additional neutral alumina (>200 mg in 1.0 mL solvent), the reproducibility of the reaction was low. Therefore, we decided to reduce the quantities of solids, which restored reproducibility and diastereoselectivity.

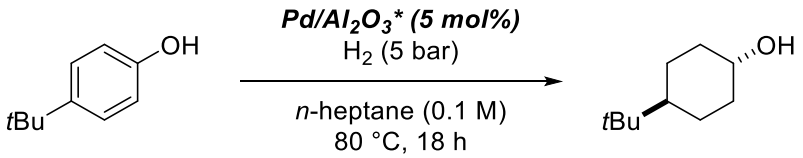


1d **4d** **2d**

Table S7. Screening of other metal-supported heterogeneous catalysts.

entry	catalyst (5 mol%)	conv. of SM [%]	yield **4d** [%]	yield **2d** [%] (d.r.)
1	5 wt% Ru/Al_2O_3	100	-	87 (60:40)
2	5 wt% Ru/AC	100	-	89 (65:35)
3	5 wt% Pt/Al_2O_3	100	-	78 (80:20)
4	5 wt% Rh/AC	100	-	92 (10:90)

Reaction conditions: **1d** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard. AC = activated carbon.



1d **2d**

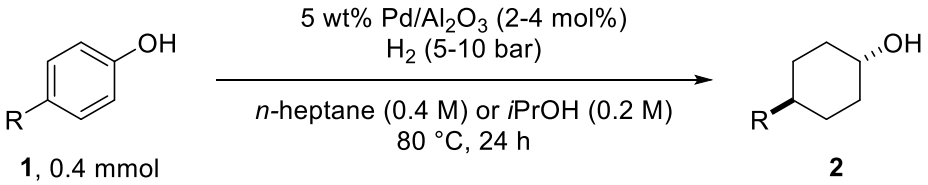
Table S8. Reproducibility of the reaction with Pd/Al_2O_3 from different suppliers.

entry	catalyst	supplier	conv. of SM [%]	yield **2d** [%] (d.r.)
1[a]	5 wt% Pd/Al_2O_3	Johnson Matthey	100	92 (88:12)
2	5 wt% Pd/Al_2O_3 powder, dry	Acros Organics	100	87 (88:12)
3	5 wt% Pd/Al_2O_3 reduced, dry powder	ABCR	4[b]	-
4	5 wt% Pd/Al_2O_3 reduced, dry (Escat 1241) lot 1386628	ABCR	100	98 (88:12)
5	5 wt% Pd/Al_2O_3 reduced, dry (Escat 1241) lot 1349664	ABCR	100	98 (86:14)
6	0.5 wt% Pd/Al_2O_3 reduced, pellets	ABCR	100	70 (84:16)

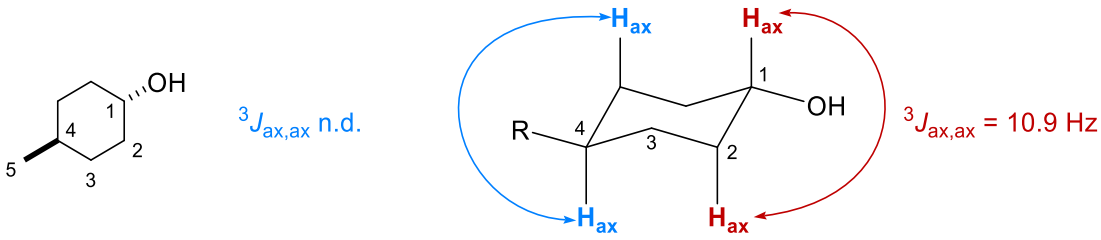
Reaction conditions: **1d** (0.1 mmol, 1.0 equiv.), solvent (1.0 mL, 0.1 M). Yields and d.r. values (*trans*/*cis*) determined by GC-FID analysis using mesitylene as internal standard. [a] Standard catalyst, see "Materials and Methods" section for more details. [b] 4-*t*Bu-cyclohexanone was observed.

4. Synthesis of *trans*-configurated Cyclohexanols

General procedure A for the trans-selective hydrogenation of phenols



A 4 mL screw-cap glass vial, equipped with a magnetic stirring bar, was charged with 5 wt% Pd/Al_2O_3 (2-4 mol%) and solid substrates (0.4 mmol, 1.0 equiv.) as indicated. Solvent (1.0 mL, 0.4 M) and liquid substrates were added. The prepared glass vial was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the indicated pressure was set. The reaction mixture was stirred at 80 °C for 24 h. After the autoclave was carefully depressurized, the crude mixture was purified by column chromatography on silica gel.



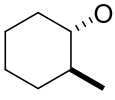
2a, colorless oil, procedure **A**: 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 20% to 30% Et_2O in pentane. 90% total yield, 80:20 d.r. (determined by ^1H NMR) The major diastereomer was isolated and characterized (74% yield). The hydroxy group occupies the equatorial position based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2. The *J* coupling between H_{ax}C4 & H_{ax}C3 could not be determined due to overlapping multiplets.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (tt, $^3J_{ax,ax}$ = 10.9 Hz, $^3J_{ax,eq}$ = 4.3 Hz, 1H, H_{ax}C1), 1.99 – 1.87 (m, 2H), 1.76 – 1.65 (m, 2H), 1.59 (bs, 1H, *H*O), 1.43 – 1.17 (m, 3H), 1.05 – 0.91 (m, 2H), 0.88 (d, $^3J_{HH}$ = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 67.1, 32.4, 31.3, 29.1, 21.8;

ESI-MS calculated $[C_7H_{14}O+Na]^+$ 137.0937, found: 137.0921.

Analytical data are in good accordance with those previously reported for this compound.[1]



2ac, colorless oil, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% to 20% Et_2O in pentane. 82% total

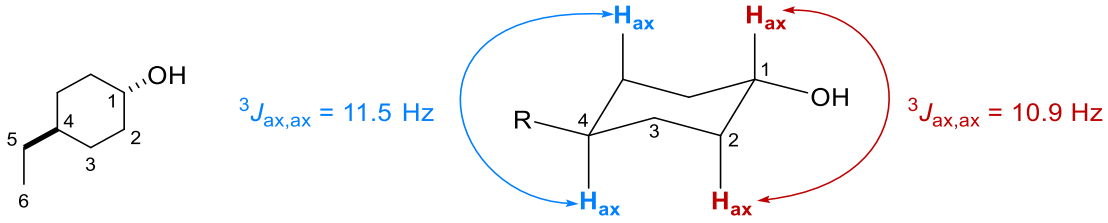
yield, 55:45 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (44% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (m, 1H, *H*C1), 1.99 – 1.89 (m, 1H), 1.82 – 1.66 (m, 4H), 1.65 – 1.54 (m, 1H), 1.34 – 1.12 (m, 4H), 1.00 (d, $^{3}J_{HH}$ = 6.5 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 76.7, 40.4, 35.6, 33.8, 25.8, 25.3, 18.7;

ESI-MS calculated $[C_7H_{14}O+Na]^+$ 137.093, found: 137.0923.

Analytical data are in good accordance with those previously reported for this compound.[1]



2b, colorless oil, procedure **A**: 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 5% to 10% Et2O in pentane. 87% total yield, 80:20 d.r. determined by GC-FID. The major diastereomer was isolated and characterized (59% yield). The *trans*-configuration was determined based on the $^{3}J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. Determination of $^{3}J_{ax,ax}$ coupling between H_{ax}C4 & H_{ax}C3 was possible with homonuclear decoupling experiments by irradiation at H_2C5.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.54 (tt, $^{3}J_{ax,ax}$ = 10.9 Hz, $^{3}J_{ax,eq}$ = 4.3 Hz, 1H, H_{ax}C1), 2.00 – 1.92 (m, 2H, *H*C2), 1.77 (dm, $^{2}J_{HH}$ = 13.0 Hz, 2H, H_{eq}C3), 1.50 (bs, 1H, *H*O), 1.28 – 1.19 (m, 2H, *H*C2), 1.19 (q, $^{3}J_{HH}$ = 7.1 Hz, 2H, H_2C5), 1.09 (tm, $^{3}J_{ax,ax}$ = 11.5 Hz, 1H, H_{ax}C4), 0.94 (ddd, $^{2}J_{HH}$ = 13.4 Hz, $^{3}J_{ax,ax}$ = 11.0 Hz, $^{3}J_{ax,eq}$ = 2.6 Hz, 2H, H_{ax}C3), 0.87 (t, $^{3}J_{HH}$ = 7.5 Hz, 3H, H_3C6);

^{13}C NMR (151 MHz, $CDCl_3$) δ 71.4 (C1), 38.6 (C4), 35.8 (C2), 31.0 (C3), 29.4 (C5), 11.8 (C6);

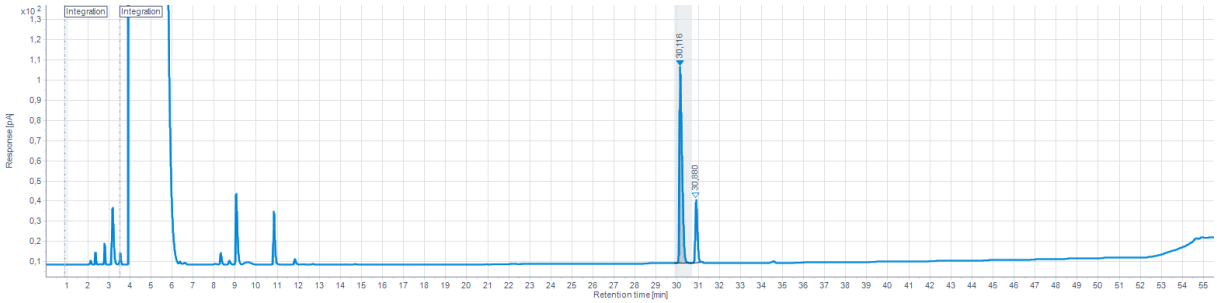
ESI-MS calculated $[C_8H_{16}O+Na]^+$: 151.1093, found: 151.1093;

IR $\tilde{\nu}$ = 3317, 2925, 2854, 1463, 1449, 1369, 1091, 1052, 1009, 964, 897, 862;

Analytical data are in good accordance with those previously reported for this compound.[1]

GC-FID (prior to purification):

Pd-catalyzed (*trans*)

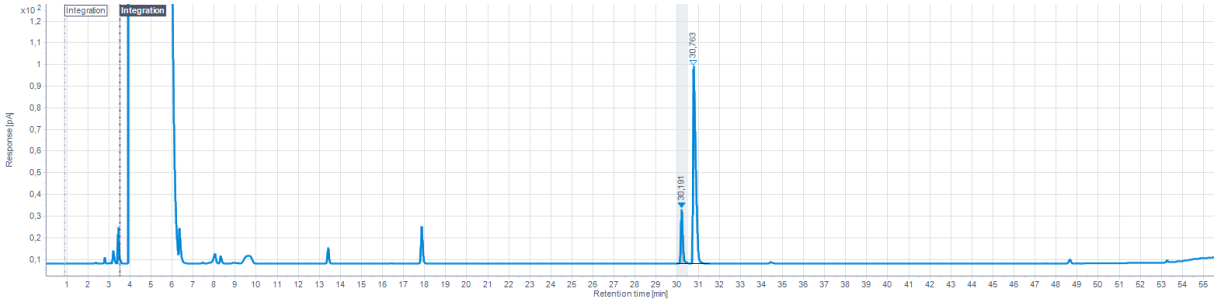


Injection Results

Peaks | Summary

#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	30,116	807,799	79,970	96,912	75,59			29,862	30,714
2		FID1A	30,880	202,331	20,030	31,293	24,41			30,743	31,075

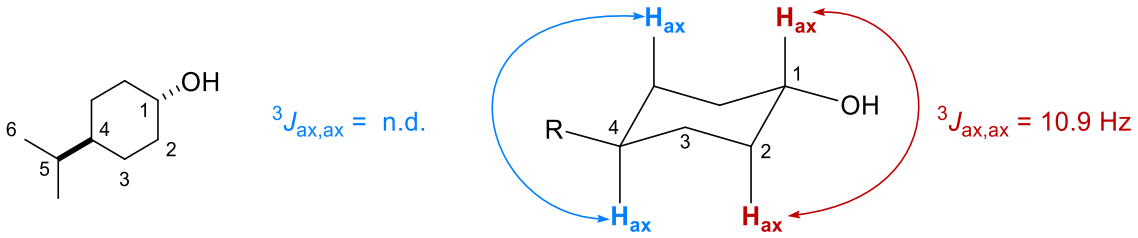
Rh-catalyzed (*cis*)



Injection Results

Peaks | Summary

#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	30,191	155,383	16,668	25,119	21,62			29,978	30,547
2		FID1A	30,763	776,863	83,332	91,049	78,38			30,564	31,538



2c, colorless oil, 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% to 20% EtOAc in pentane. 88% total yield, 87:13 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (73% yield). The hydroxy group occupies the equatorial position based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2. The *J* coupling between H_{ax}C4 & H_{ax}C3 could not be determined due to overlapping multiplets in several solvents ($CDCl_3$, C_6D_6, CD_3OD). Based on the confirmed *trans*-configuration for similar substrates with ethyl or *tert*-butyl groups and the bulkiness of *iso*-propyl compared to a hydroxy group, it seems very likely that the *iso*-propyl group occupies the equatorial position and the reported product is indeed the *trans*-diastereomer.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.51 (tt, $^3J_{ax,ax}$ = 10.9 Hz, $^3J_{ax,eq}$ = 4.4 Hz, 1H, H_{ax}C1), 2.02 – 1.93 (m, 2H, H_{eq}C2), 1.75 – 1.68 (m, 2H, H_2C3), 1.59 (bs, 1H, *H*O), 1.41 (m, 1H, *H*C5), 1.21

(ddm, $^{2}J_{HH}$ = 12.0 Hz, $^{3}J_{ax,ax}$ = 10.7 Hz, 2H, H_{ax}C2), 1.05 – 0.97 (m, 3H, *H*C4, H_2C3), 0.84 (d, $^{3}J_{HH}$ = 6.8 Hz, 6H, H_3C6);

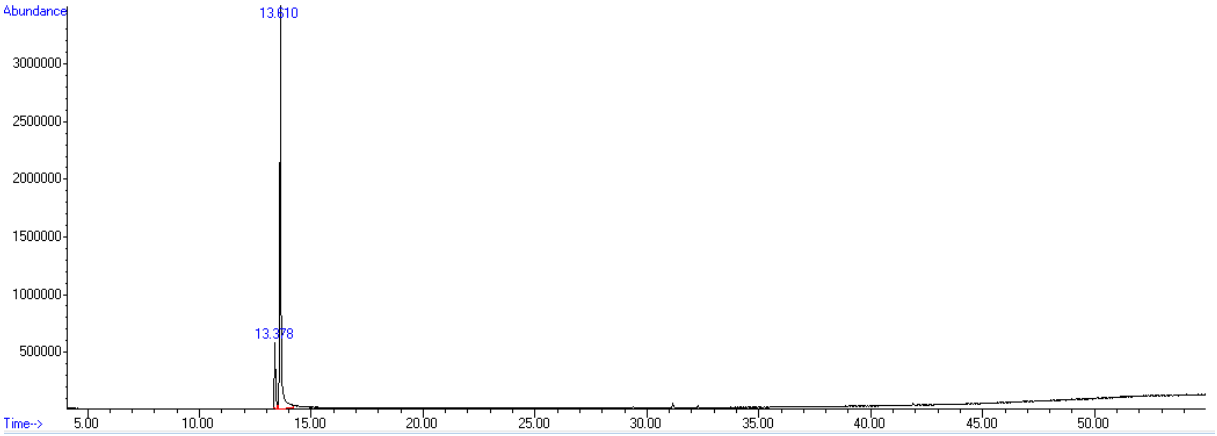
^{13}C NMR (151 MHz, $CDCl_3$) δ 71.4 (C1), 43.2 (C4), 35.9 (C2), 32.5 (C5), 28.0 (C3), 20.1 (C6);

ESI-MS calculated $[C_9H_{18}O+Na]^+$: 165.1250, found: 165.1251;

IR $\tilde{\nu}$ = 3333, 2928, 2857, 1464, 1450, 1385, 1368, 1086, 1053, 991, 941, 897;

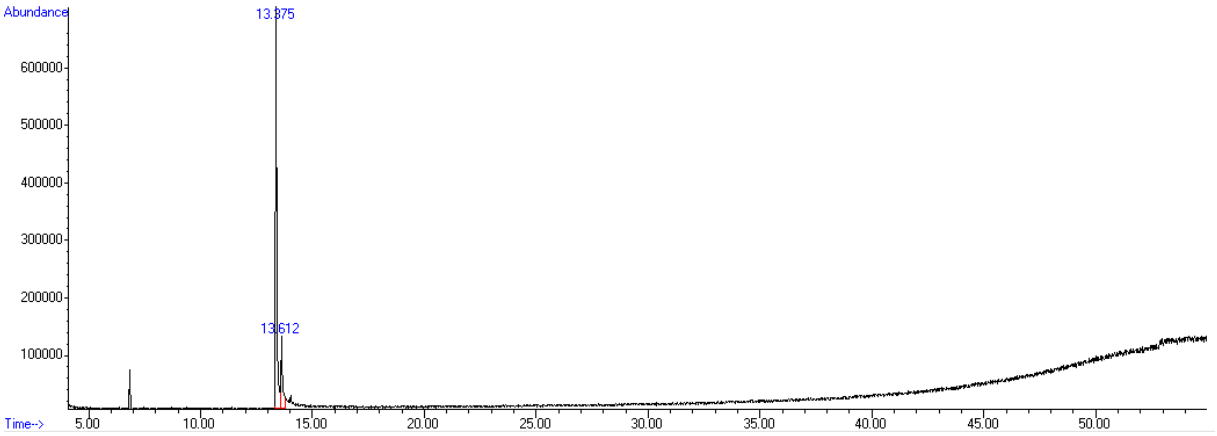
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

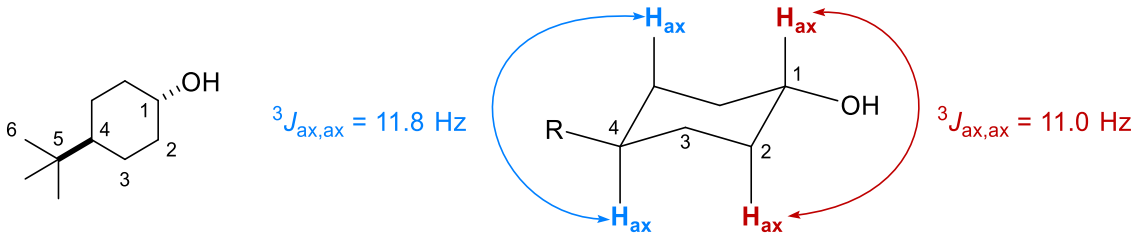


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	13.378	1576	1585	1600	M	578101	17248177	14.50%	12.660%
2	13.610	1614	1625	1728	M	3499425	118990683	100.00%	87.340%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	13.375	1575	1585	1617	M2	698734	23717419	100.00%	79.264%
2	13.612	1617	1625	1654	M4	123510	6204587	26.16%	20.736%



2d, white solid, procedure **A**: 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% to 20% EtOAc in pentane. 90% total yield, 87:13 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (75% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.51 (tt, $^3J_{ax,ax}$ = 11.0 Hz, $^3J_{ax,eq}$ = 4.4 Hz, 1H, H_{ax}C1), 2.04 – 1.97 (m, 2H, H_{2eq}C2), 1.81 – 1.74 (m, 2H, H_{2eq}C3), 1.46 (bs, 1H, O*H*), 1.26 – 1.17 (m, 2H, H_{2ax}C2), 1.09 – 1.00 (m, 2H, H_{2ax}C3), 0.96 (tt, $^3J_{ax,ax}$ = 11.8 Hz, $^3J_{ax,eq}$ = 3.1 Hz, 1H, H_{ax}C4), 0.84 (s, 9H, H_3C6);

^{13}C NMR (151 MHz, $CDCl_3$) δ 71.4 (C1), 47.3 (C4), 36.2 (C2), 32.4 (C5), 27.8 (C6), 25.8 (C3);

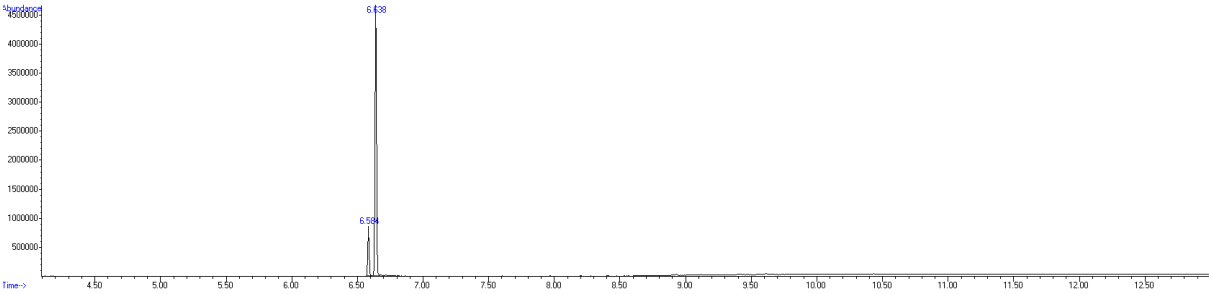
ESI-MS calculated $[C_{10}H_{20}O+Na]^+$ 179.1406, found: 179.1403;

IR $\tilde{\nu}$ = 3323, 2928, 2858, 1465, 1448, 1363, 1066, 1054, 1037, 981, 900;

Analytical data are in good accordance with those previously reported for this compound.[1]

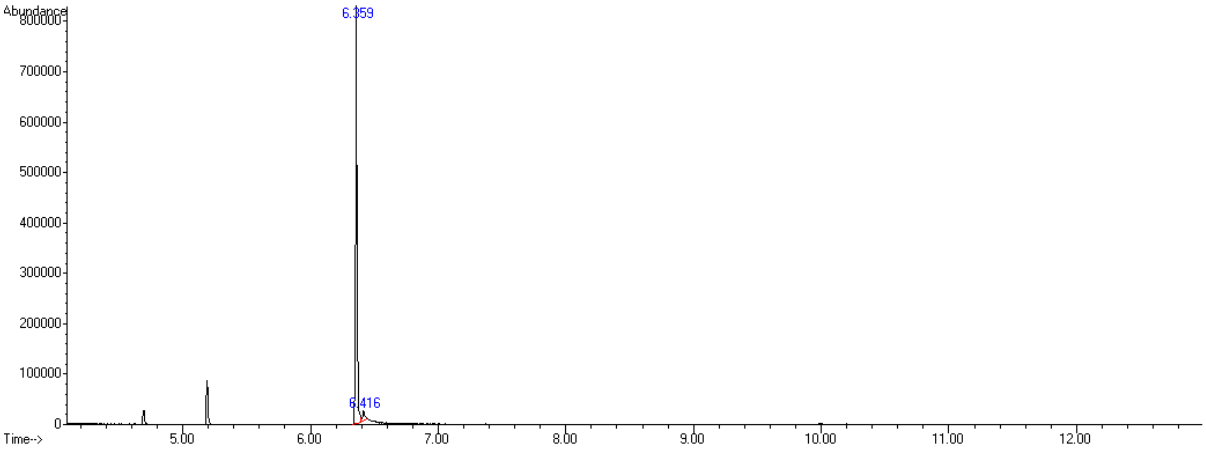
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

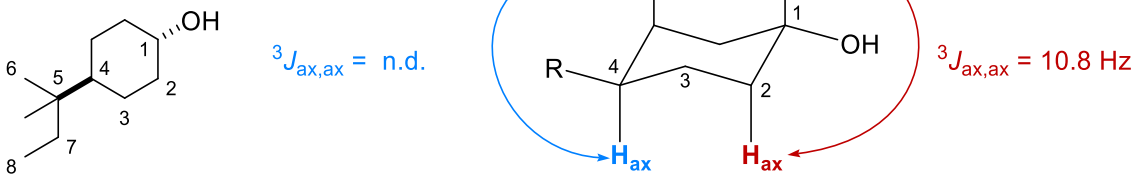


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.584	424	426	429	M	839634	5832138	14.89%	12.963%
2	6.638	432	435	441	M	4813697	39158240	100.00%	87.037%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.359	383	388	394	M	855497	6529607	100.00%	93.283%
2	6.416	394	397	404	M4	20459	470131	7.20%	6.717%



2e, white solid, 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% to 20% EtOAc in pentane. 99% total yield, 91:9 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (91% yield). The hydroxy group occupies the equatorial position based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2. The *J* coupling between H_{ax}C4 & H_{ax}C3 could not be determined due to overlapping multiplets in several solvents ($CDCl_3$, C_6D_6, CD_3OD). Based on the confirmed *trans*-configuration for similar substrates with ethyl or *tert*-butyl groups and the bulkiness of *tert*-amyl compared to a hydroxy group, it seems very likely that the *tert*-amyl group occupies the equatorial position and the reported product is indeed the *trans*-diastereomer.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.49 (tt, $^3J_{ax,ax}$ = 11.0 Hz, $^3J_{ax,eq}$ = 4.4 Hz, 1H, H_{ax}C1), 2.02 – 1.95 (m, 2H, H_2C2), 1.74 (bs, 1H, *H*O), 1.73 – 1.66 (m, 2H, H_2C3), 1.23 (q, $^3J_{HH}$ = 7.5 Hz, 2H, H_2C7), 1.19 (m, 2H, H_2C2), 1.09 – 0.98 (m, 3H, H_{ax}C3, *H*C4), 0.77 (t, $^3J_{HH}$ = 7.6 Hz, 3H, H_3C8), 0.76 (s, 6H, H_3C6);

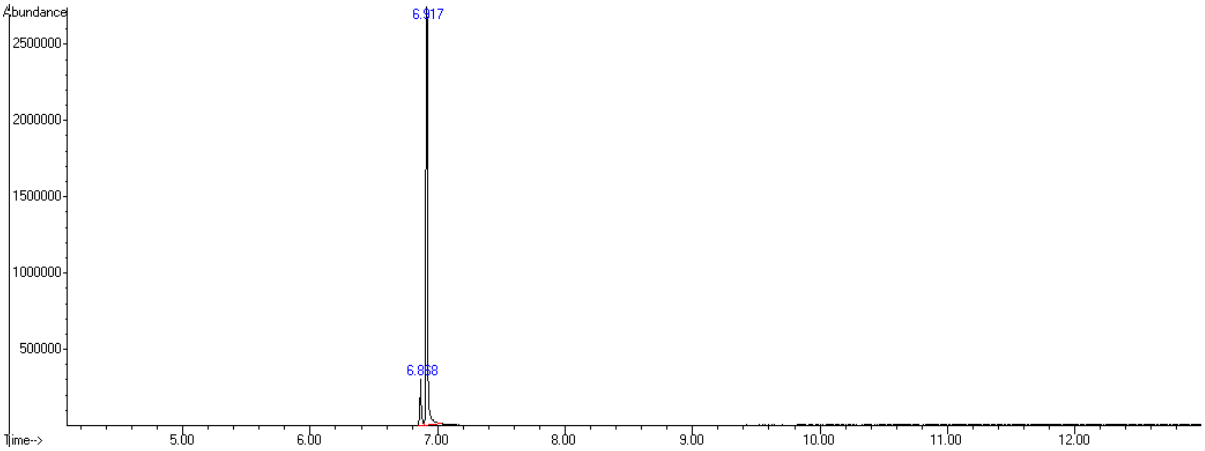
^{13}C NMR (151 MHz, $CDCl_3$) δ 71.3 (C1), 44.5 (C4), 36.3 (C2), 34.7 (C5), 32.9 (C7), 25.3 (C3), 24.4 (C6), 8.2 (C8);

ESI-MS calculated $[C_{11}H_{22}O+Na]^+$: 193.1563, found: 193.1570;

IR $\tilde{\nu}$ = 3300, 2930, 2861, 1451, 1379, 1364, 1121, 1069, 980, 899;

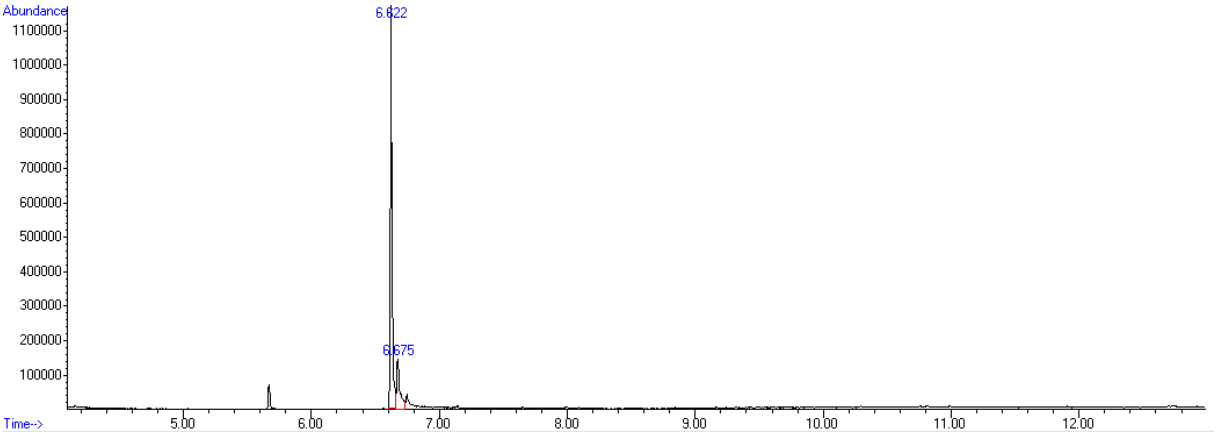
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

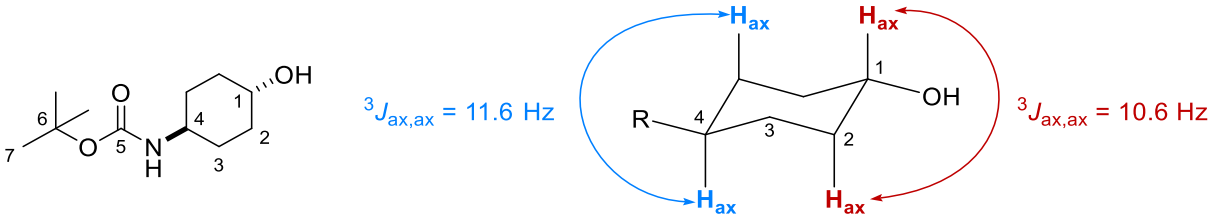


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.868	471	475	479	BV	276506	2327469	9.44%	8.626%
2	6.917	479	483	503	VB	2793858	24653473	100.00%	91.374%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.622	430	433	439	M	1234362	10737152	100.00%	81.792%
2	6.675	439	442	451	M	150402	2390224	22.26%	18.208%



2f, white solid, 4 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), 48 h. Purification with 50% EtOAc in pentane. 84% total yield, 80:20 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (47% yield). The *trans*-configuration

was determined based on the $^{3}J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. The *trans*-configuration was confirmed by a crystal structure.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.37 (bs, 1H, *H*N), 3.59 (tt, $^{3}J_{ax,ax}$ = 10.5 Hz, $^{3}J_{ax,eq}$ = 4.0 Hz, 1H, H_{ax}C1), 3.39 (tm, $^{3}J_{ax,ax}$ = 11.6 Hz, 1H, H_{ax}C4), 2.12 – 1.88 (m, 4H, H_2C2, H_2C3), 1.63 (bs, 1H, *H*O), 1.43 (s, 9H, H_3C7), 1.41 – 1.28 (m, 2H, H_2C2), 1.26 – 1.05 (m, 2H, H_2C3);

^{1}H NMR (599 MHz, $CDCl_3$) δ 4.35 (bs, 1H, *H*N), 3.57 (tt, $^{3}J_{ax,ax}$ = 10.6 Hz, $^{3}J_{ax,eq}$ = 4.2 Hz, 1H, H_{ax}C1), 3.40 (bs, 1H, H_{ax}C4), 2.04 – 1.91 (m, 4H, H_2C2, H_{eq}C3), 1.54 (s, 1H, *H*O), 1.42 (s, 9H, H_3C7), 1.35 (dm, $^{2}J_{HH}$ = 13.2 Hz, 2H, H_2C2), 1.14 (ddm, $^{2}J_{HH}$ = 12.5 Hz, $^{3}J_{ax,ax}$ = 11.1 Hz, 2H, H_{ax}C3);

^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4 (C5), 79.4 (C6), 69.9 (C1), 49.0 (C4), 34.1 (C2), 31.3 (C3), 28.5 (C7);

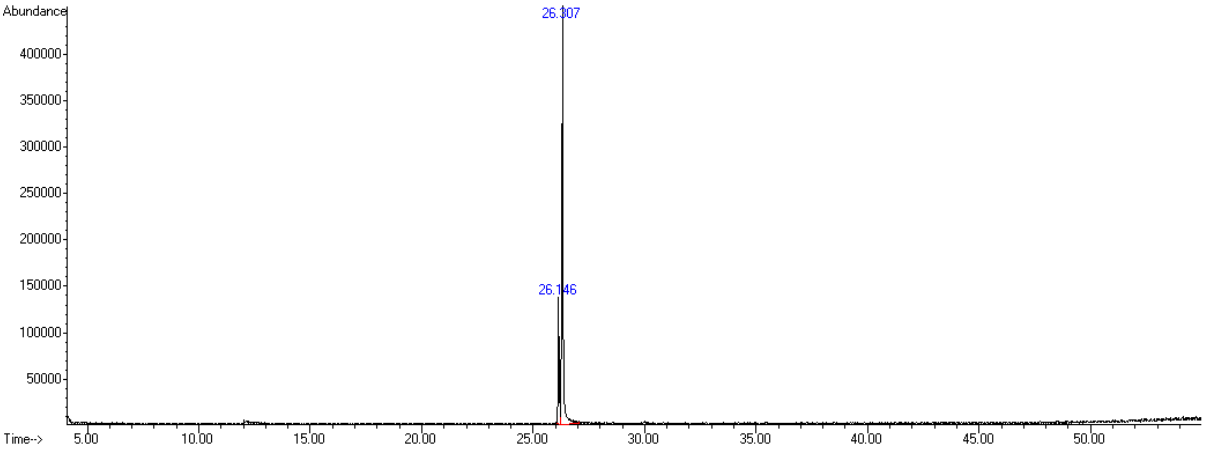
ESI-MS calculated $[C_{11}H_{21}NO_3+Na]^+$: 238.1414, found: 238.1429;

IR $\tilde{\nu}$ = 3342, 2935, 2856, 1680, 1653, 1559, 1533, 1363, 1314, 1230, 1171, 1069, 951, 891;

Analytical data are in good accordance with those previously reported for this compound.[2]

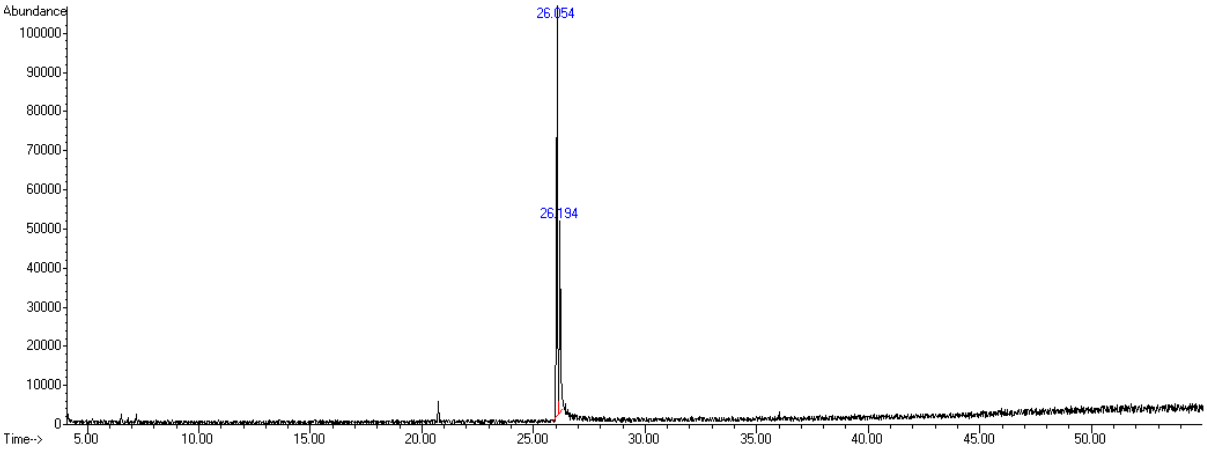
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

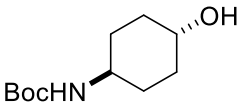


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.146	3753	3764	3777	M2	136145	3885491	24.46%	19.655%
2	26.307	3778	3791	3919	M	455635	15882568	100.00%	80.345%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.054	3713	3748	3762	BV	103342	2837564	100.00%	62.600%
2	26.194	3762	3772	3799	VV 3	48674	1695297	59.74%	37.400%

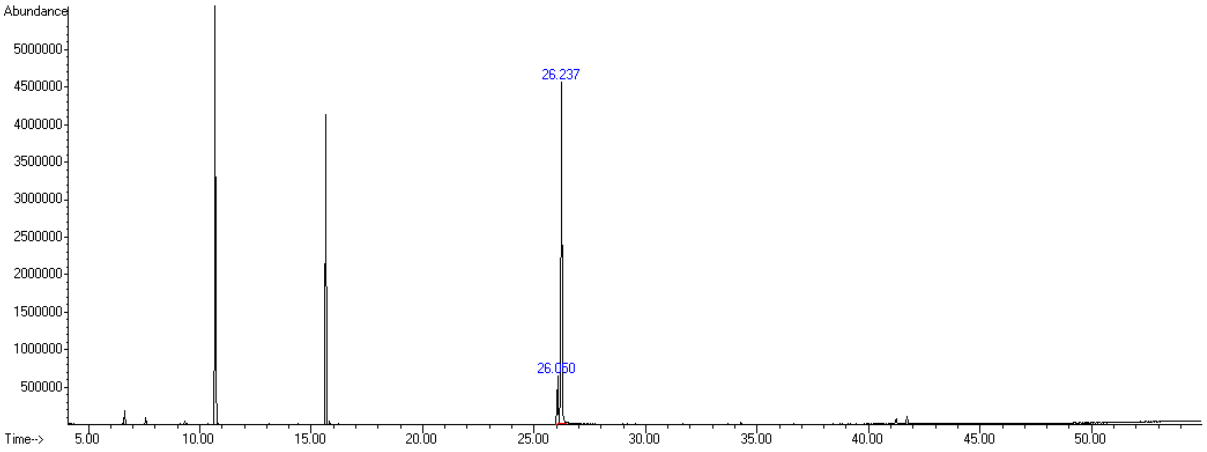


2f, white solid, procedure **A**: starting from 4-aminophenol, 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL), additive: K_2CO_3 (0.2 equiv.) Addition of K_2CO_3 increased the reactivity. Boc-protection prior to isolation by addition of NEt_3 (3.0 equiv.) and Boc_2O (3.0 equiv.). Purification with 40% to 50% EtOAc in pentane. 78% total yield, 88:12 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (54% yield).

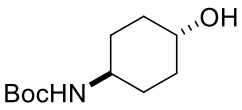
Analytical data are in accordance with compound **2f**.

GC-MS (prior to purification):

Pd-catalyzed (*trans*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.050	3736	3748	3761	VV 2	633849	19502582	13.43%	11.839%
2	26.237	3761	3779	3823	VB	4478967	145231780	100.00%	88.161%

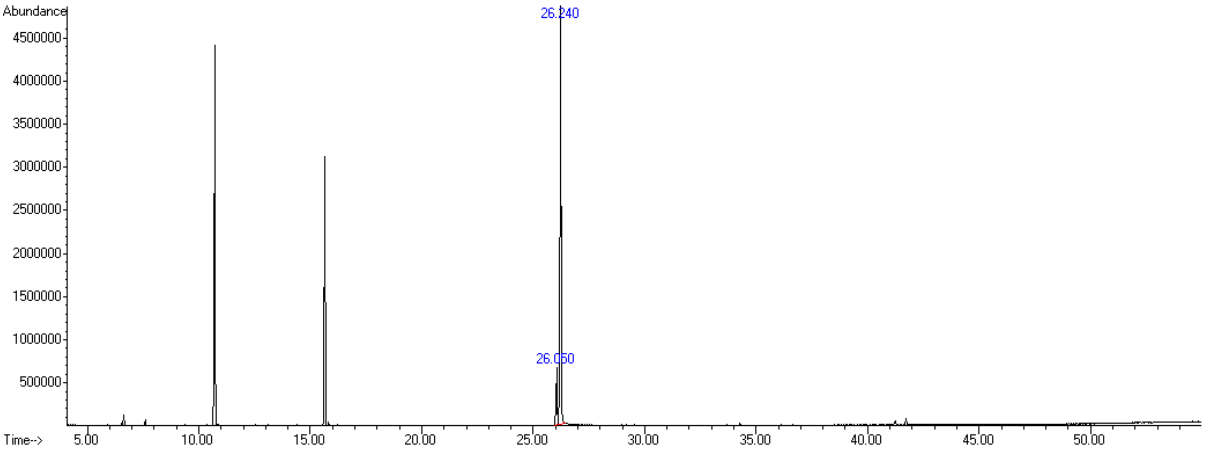


2f, white solid, procedure **A**: starting from 4-nitrophenol, 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL), additive: K_2CO_3 (0.2 equiv.) Addition of K_2CO_3 increased the reactivity. Boc-protection prior to isolation by addition of NEt_3 (3.0 equiv.) and Boc_2O (3.0 equiv.). Purification with 40% to 50% EtOAc in pentane. 80% total yield, 89:11 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (51% yield).

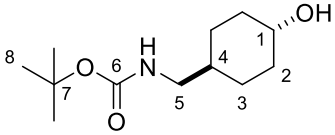
Analytical data are in accordance with compound **2f**.

GC-MS (prior to purification):

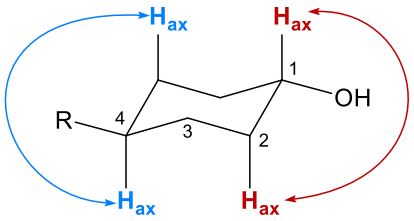
Pd-catalyzed (*trans*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.050	3734	3748	3761	BV	662545	19948342	12.99%	11.497%
2	26.240	3761	3780	3822	VV	4850292	153553588	100.00%	88.503%



$^3J_{ax,ax}$ = 11.6 Hz



$^3J_{ax,ax}$ = 10.9 Hz

2g, off-white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), 48 h. Purification with 40% to 50% EtOAc in pentane. 93% total yield, 77:23 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (43% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. Determination of $^3J_{ax,ax}$ coupling between H_{ax}C4 & H_{ax}C3 and *J* couplings assigned to H_{ax}C2 and H_{ax}C3 were possible with homonuclear decoupling experiments by irradiation at H_2C5.

^{1}H NMR (599 MHz, $CDCl_3$) δ 4.58 (bs, 1H, *H*N), 3.54 (tt, $^3J_{ax,ax}$ = 10.9 Hz, $^3J_{ax,eq}$ = 4.3 Hz, 1H, H_{ax}C1), 2.96 (t, $^3J_{HH}$ = 6.5 Hz, 2H, H_2C5), 2.02 – 1.91 (m, 2H, H_{eq}C2), 1.77 (ddm, $^2J_{HH}$ = 13.4 Hz, $^3J_{eq,ax}$ = 4.3 Hz, 2H, H_{eq}C3), 1.54 (bs, 1H, *H*O), 1.43 (s, 9H, H_3C8), 1.41 – 1.33 (tm, $^3J_{ax,ax}$ = 11.6 Hz, 1H, H_{ax}C4), 1.24 (tdd, $^2J_{HH}$ = 12.5 Hz, $^3J_{ax,ax}$ =10.8 Hz, $^3J_{ax,eq}$ = 3.5 Hz, 2H, H_{ax}C2), 1.03 – 0.93 (tdd, $^2J_{HH}$ = 13.7 Hz, $^3J_{ax,ax}$ = 11.5 Hz, $^3J_{ax,eq}$ = 3.4 Hz, 2H, H_{ax}C3);

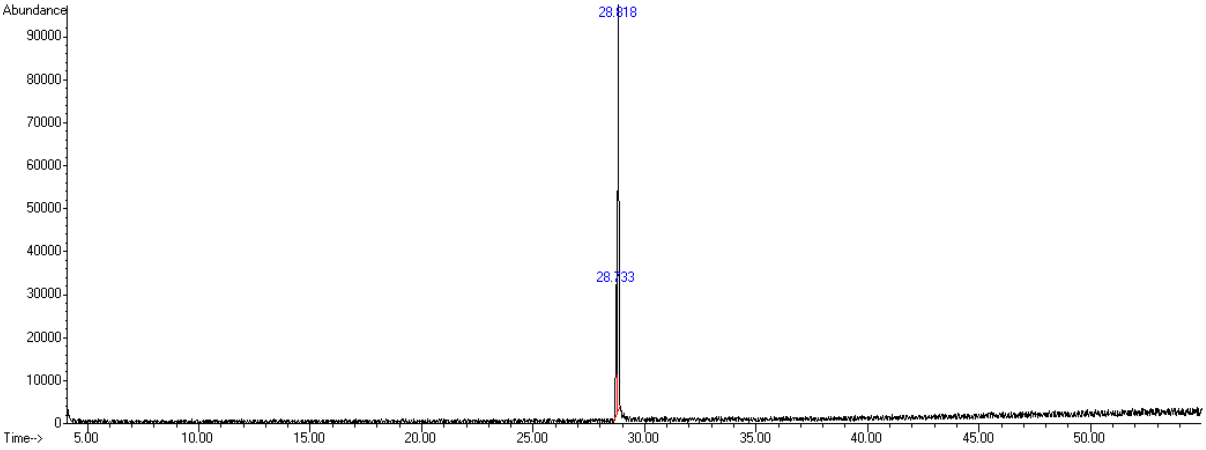
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.0 (C6), 78.9 (C7), 70.2 (C1), 47.8 (C5), 37.6 (C4), 33.9 (C2), 29.4 (C3), 28.0 (C8);

ESI-MS calculated $[C_{12}H_{23}NO_3+Na]^+$: 252.1570, found: 252.1574;

IR $\tilde{\nu}$ = 3335, 2978, 2928, 2857, 1686, 1522, 1452, 1366, 1273, 1248, 1169, 1045, 1013, 731;

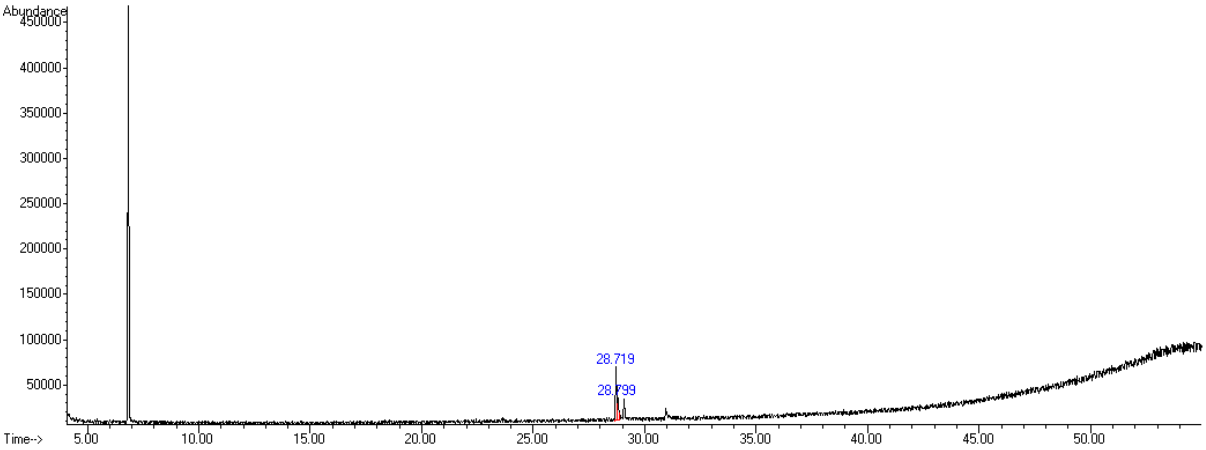
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

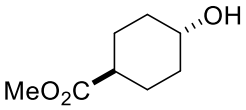


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	28.733	4186	4205	4211	BV 2	29907	801701	30.15%	23.163%
2	28.818	4211	4220	4232	VV 3	94623	2659371	100.00%	76.837%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	28.719	4192	4203	4212	M3	59367	1825977	100.00%	69.781%
2	28.799	4212	4217	4226	M5	24465	790762	43.31%	30.219%



2h, colorless oil, 3 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 30% EtOAc in pentane. 99% total yield, 56:44 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (38% yield). The hydroxy group occupies the equatorial position based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2.

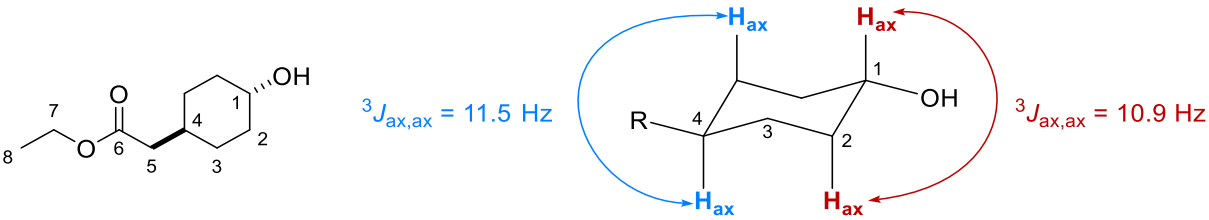
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.63 – 3.52 (m, 1H), 2.24 (tt, $^3J_{ax,ax}$ = 11.9 Hz, $^3J_{ax,eq}$ = 3.5 Hz, 1H, H_{ax}C1), 2.07 – 1.93 (m, 4H), 1.81 (s, 1H), 1.57 – 1.39 (m, 2H), 1.36 – 1.16 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 69.9, 51.8, 42.2, 34.6, 27.3;

ESI-MS calculated $[C_8H_{14}O_3+Na]^+$: 181.0835, found: 181.0842;

IR $\tilde{\nu}$ = 3366, 2935, 1734, 1718, 1457, 1436, 1236, 1198, 1170, 1137, 1067, 1033, 961, 894;

Analytical data are in good accordance with those previously reported for this compound.[3]



2i, colorless oil, 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 20% to 30% EtOAc in pentane. 89% total yield, 76:24 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (67% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. Determination of $^3J_{ax,ax}$ coupling between H_{ax}C4 & H_{ax}C3 and was possible with homonuclear decoupling experiments by irradiation at H_2C5.

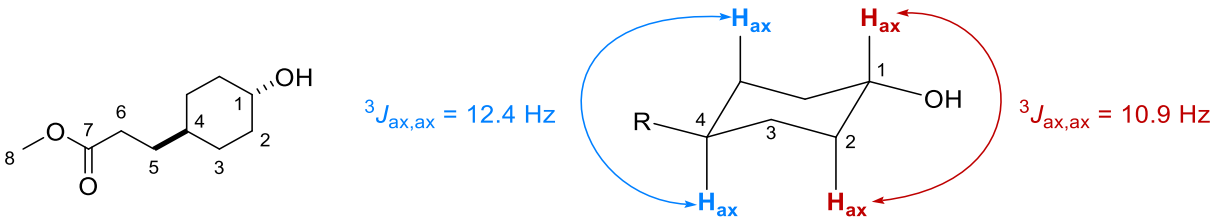
^{1}H NMR (599 MHz, $CDCl_3$) δ 4.08 (q, $^3J_{HH}$= 7.2 Hz, 2H, H_2C7), 3.60 – 3.46 (tm, $^3J_{ax,ax}$ = 10.9 Hz, 1H, H_{ax}C1), 2.14 (d, $^3J_{HH}$ = 7.0, 2H, H_2C5), 2.04 (bs, 1H, *H*O), 2.01 – 1.89 (m, 2H, H_2C2), 1.80 – 1.71 (m, 2H, H_2C3), 1.73 – 1.65 (tm, $^3J_{ax,ax}$ = 11.5 Hz, 1H, H_{ax}C4), 1.29 – 1.23 (m, 2H, H_2C2), 1.21 (t, $^3J_{HH}$ = 7.1 Hz, 3H, H_3C8), 1.06 – 0.95 (m, 2H, H_2C3);

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.0 (C6), 71.4 (C1), 59.5 (C7), 41.4 (C5), 35.2 (C2), 34.0 (C4), 31.0 (C3), 13.9 (C8);

ESI-MS calculated $[C_{10}H_{18}O_3+Na]^+$: 209.1148, found: 209.1161;

IR $\tilde{\nu}$ = 3361, 2926, 1734, 1717, 1457, 1370, 1285, 1221, 1156, 1107, 1030, 971, 932;

Analytical data are in good accordance with those previously reported for this compound.[4]



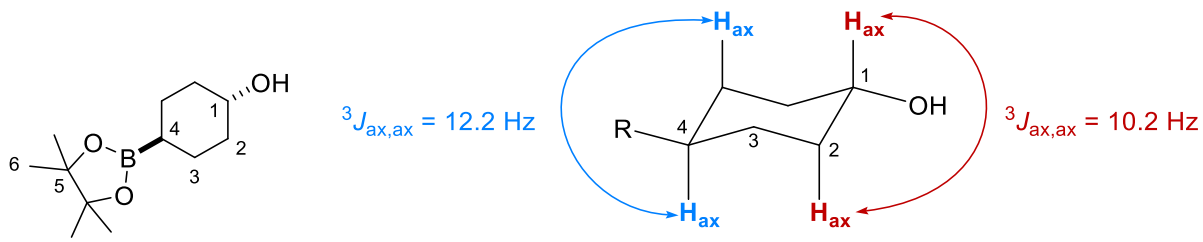
2j, colorless oil, 3 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 20% to 30% EtOAc in pentane. 91% total yield, 78:22 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (68% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. Determination of $^3J_{ax,ax}$ coupling between H_{ax}C4 & H_{ax}C3 and was possible with homonuclear decoupling experiments by irradiation at H_2C5.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.64 (s, 3H, H_3C8), 3.51 (tt, $^3J_{ax,ax}$ = 10.9 Hz, $^3J_{ax,eq}$ = 4.3 Hz, 1H, H_{ax}C1), 2.32 – 2.26 (m, 2H, H_2C6), 1.98 – 1.90 (m, 2H, H_2C2), 1.78 (bs, 1H, *H*O), 1.77 – 1.71 (m, 2H, H_2C3), 1.51 (dt, $^3J_{HH}$ = 8.2, 7.0 Hz, 2H, H_2C5), 1.21 (m, 2H, H_2C2), 1.18 (tm, $^3J_{ax,ax}$ = 12.4 Hz, 1H, H_{ax}C4), 0.99 – 0.89 (m, 2H, H_2C3);

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.5 (C7), 71.0 (C1), 51.6 (C8), 36.3 (C4), 35.4 (C2), 32.0 (C6), 31.6 (C5), 31.0 (C3);

ESI-MS calculated $[C_{10}H_{18}O_3+Na]^+$: 209.1148, found: 209.1162;

IR $\tilde{\nu}$ = 3383, 2928, 2857, 1728, 1452, 1437, 1265, 1169, 1047, 1015, 909, 729, 646.



2k, white solid, 3 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% EtOAc in CH_2Cl_2. 65% total yield, 78:22 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (33% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.53 (tt, $^3J_{ax,ax}$ = 10.2 Hz, $^3J_{ax,eq}$ = 4.2 Hz, 1H, H_{ax}C1), 2.00 – 1.93 (m, 2H, H_2C2), 1.85 – 1.78 (m, 2H, H_2C3), 1.49 (bs, 1H, *H*O), 1.31 – 1.14 (m, 4H, H_2C2, H_2C3), 1.21 (s, 12H, H_3C6), 0.79 (tt, $^3J_{ax,ax}$ = 12.2 Hz, $^3J_{ax,eq}$ = 3.5 Hz, 1H, H_{ax}C4);

^{13}C NMR (151 MHz, $CDCl_3$) δ 83.1 (C5), 70.9 (C1), 36.2 (C2), 26.9 (C3), 24.4 (C6);

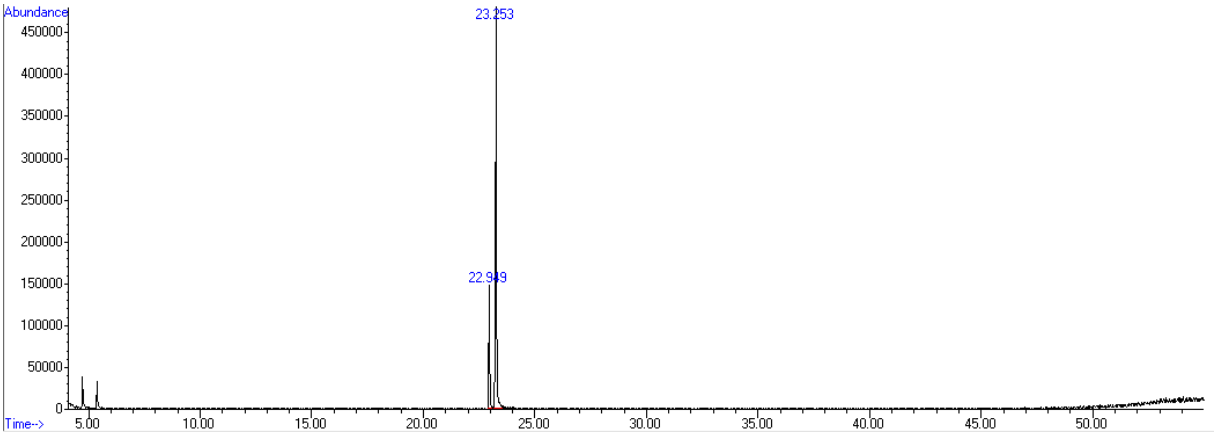
^{11}B NMR (128 MHz, $CDCl_3$) δ 34.4 (bs);

ESI-MS calculated $[C_{12}H_{23}BO_3+Na]^+$: 249.1632, found: 249.1640;

IR $\tilde{\nu}$ = 3306, 2976, 2926, 2852, 1381, 1363, 1319, 1146, 1092, 1059, 961, 862, 848;

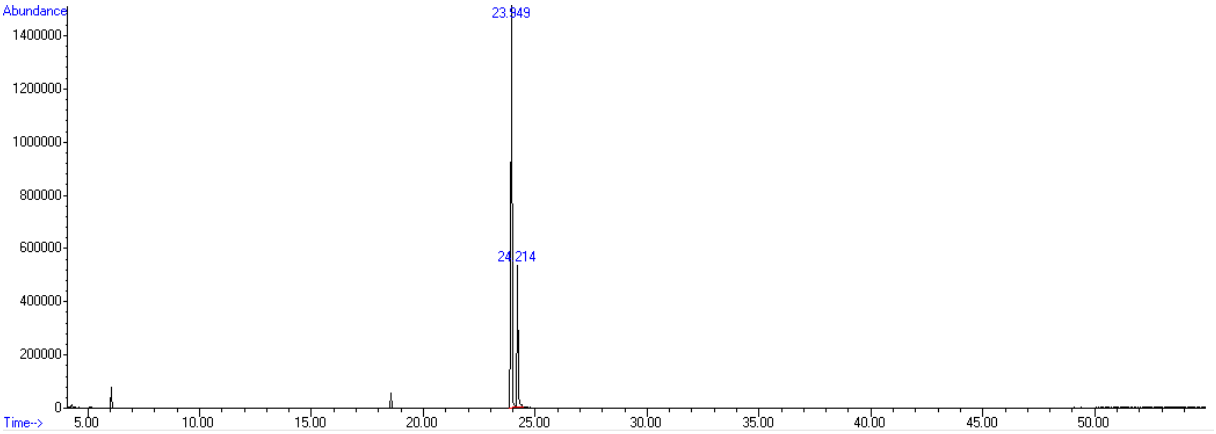
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

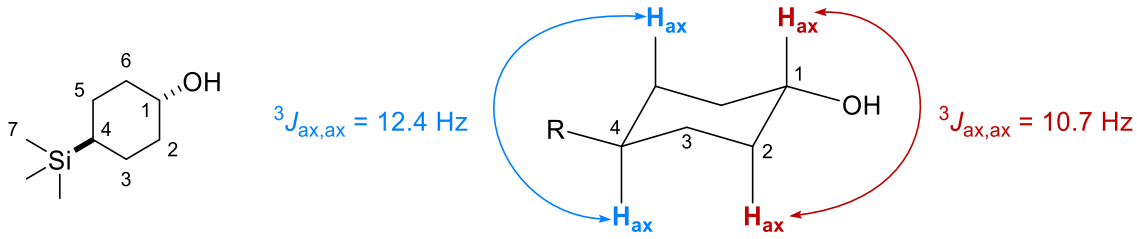


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	22.949	3210	3218	3235	M2	148996	3608228	27.76%	21.725%
2	23.253	3258	3270	3322	M2	483486	13000058	100.00%	78.275%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	23.949	3371	3389	3420	M2	1511071	48586427	100.00%	76.595%
2	24.214	3422	3434	3473	M2	536769	14846548	30.56%	23.405%



2l, white solid, 2 mol% catalyst loading, 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 15% EtOAc in pentane. 86% total yield, 85:15 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (65% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.50 (tt, $^3J_{ax,ax}$ = 10.7 Hz, $^3J_{ax,eq}$ = 4.3 Hz, 1H, H_{ax}C1), 2.06 – 1.99 (m, 2H, H_2C2), 1.79 – 1.72 (m, 2H, H_2C3), 1.43 (bs, 1H, *H*O), 1.22 – 1.06 (m, 4H, H_2C2, H_2C3), 0.44 – 0.38 (tm, $^3J_{ax,ax}$ = 12.4 Hz, 1H, H_{ax}C4), –0.06 (s, 9H, H_3C5);

^{13}C NMR (151 MHz, $CDCl_3$) δ 71.4 (C1), 38.0 (C2), 26.6 (C3), 24.2 (C4), –3.3 (C5);

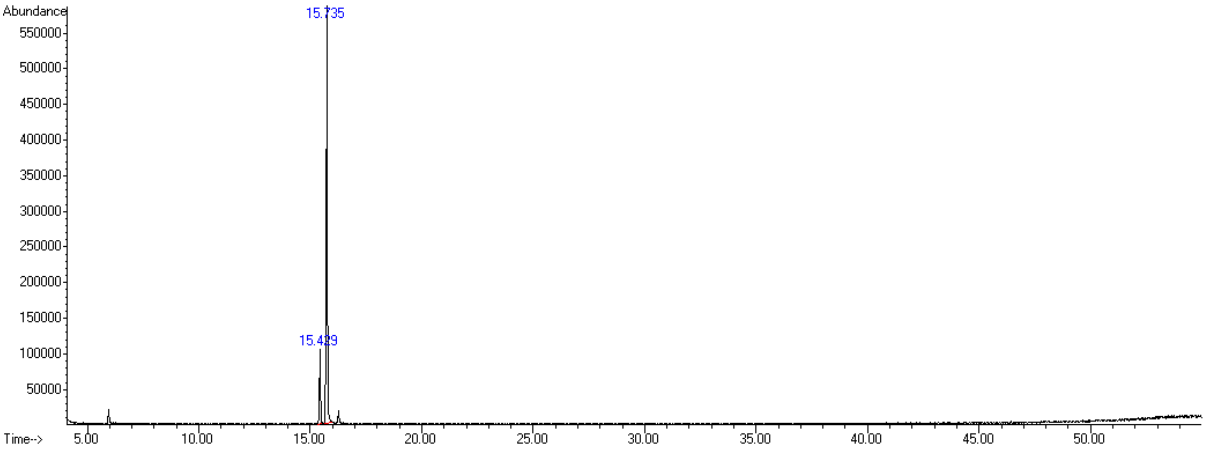
^{29}Si NMR (119 MHz, $CDCl_3$) δ 2.9;

ESI-MS calculated $[C_9H_{20}OSi+Na]^+$: 195.1176, found: 195.1184;

IR $\tilde{\nu}$ = 3271, 2924, 2847, 1445, 1248, 1053, 966, 891, 854, 831, 734, 702, 689;

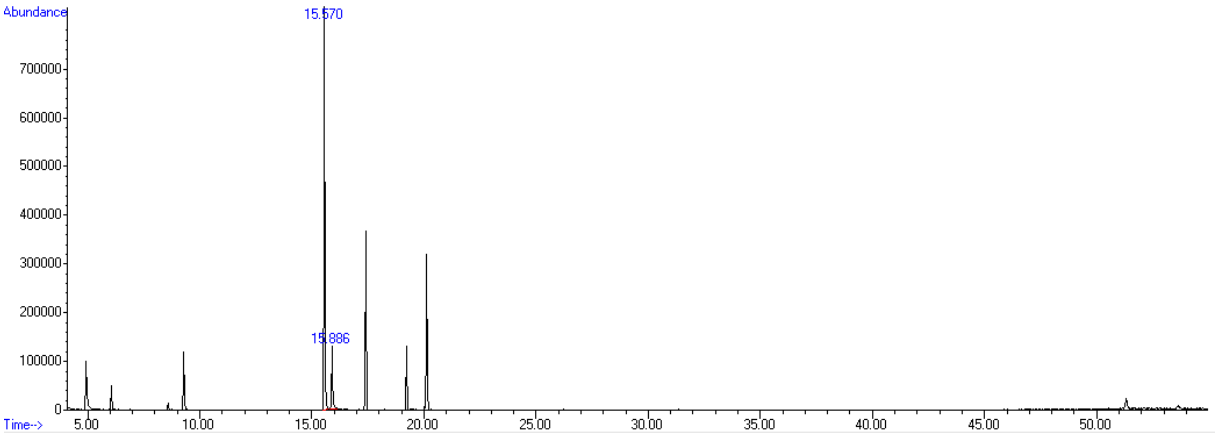
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

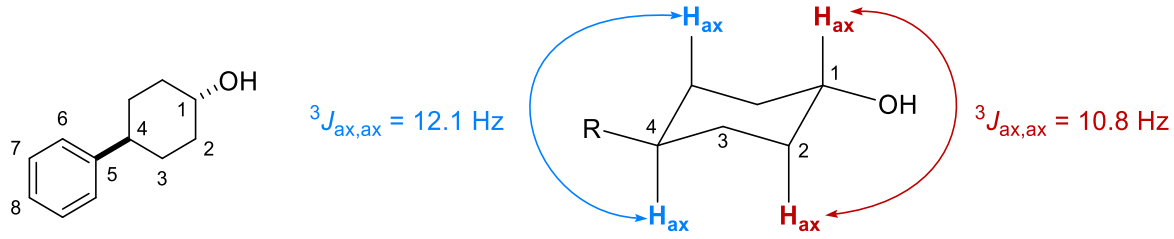


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	15.429	1919	1935	1956	BB 4	102553	2798938	17.62%	14.982%
2	15.735	1971	1988	2037	BB	580288	15882491	100.00%	85.018%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	15.570	1948	1959	1992	M	832402	20639012	100.00%	82.408%
2	15.886	2003	2013	2059	M2	129488	4406029	21.35%	17.592%



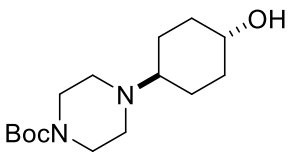
2m, white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL), additive: K_2CO_3 (0.1 equiv.). Addition of K_2CO_3 increased the reactivity and selectivity. Purification with 10% to 20% EtOAc in pentane. 76% total yield, 90:10 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (44% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. The *trans*-configuration was confirmed by a crystal structure.

^{1}H NMR (599 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H, H_{Ar}), 7.22 – 7.18 (m, 3H, H_{Ar}), 3.69 (tt, $^3J_{ax,ax}$ = 10.8 Hz, $^3J_{ax,eq}$ = 4.4 Hz, 1H, H_{ax}C1), 2.50 (tt, $^3J_{ax,ax}$ = 12.1, $^3J_{ax,eq}$ = 3.5 Hz, 1H, H_{ax}C4), 2.15 – 2.05 (m, 2H, H_2C2), 1.98 – 1.91 (m, 2H, H_{eq}C3), 1.60 (bs, 1H, *H*O), 1.55 (dddd, $^2J_{HH}$ = 13.2 Hz, $^3J_{ax,ax}$ = 11.9 Hz, $^3J_{ax,eq}$ = 3.1 Hz, $^3J_{ax,eq}$ = 3.1 Hz, 2H, H_{ax}C3), 1.49 – 1.39 (m, 2H, H_2C2);

^{13}C NMR (151 MHz, $CDCl_3$) δ 146.7 (C5), 128.5 (C_{Ar}), 126.9 (C_{Ar}), 126.2 (C_{Ar}), 70.8 (C1), 43.6 (C4), 36.1 (C2), 32.6 (C3).

ESI-MS calculated $[C_{12}H_{16}O+Na]^+$: 199.1093, found: 199.1103.

Analytical data are in good accordance with those previously reported for this compound.[5]



2n, off-white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL), additive: K_2CO_3 (0.2 equiv.). Addition of K_2CO_3 increased the reactivity. Purification with 2% to 5% to 10% MeOH in CH_2Cl_2. 79% total yield, 87:13 d.r. determined by GC-MS. Both diastereomers were isolated and characterized together and the major signals are reported. The hydroxy group occupies the equatorial position based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.57 (dt, $^3J_{ax,ax}$ = 9.7 Hz, $^3J_{ax,eq}$ = 5.3 Hz, 1H, H_{ax}C1), 3.50 – 3.35 (m, 4H), 2.63 – 2.41 (m, 4H), 2.30 (bs, 1H), 2.09 – 1.96 (m, 2H), 1.94 – 1.80 (m, 2H), 1.76 – 1.50 (m, 2H), 1.45 (s, 9H), 1.37 – 1.20 (m, 3H);

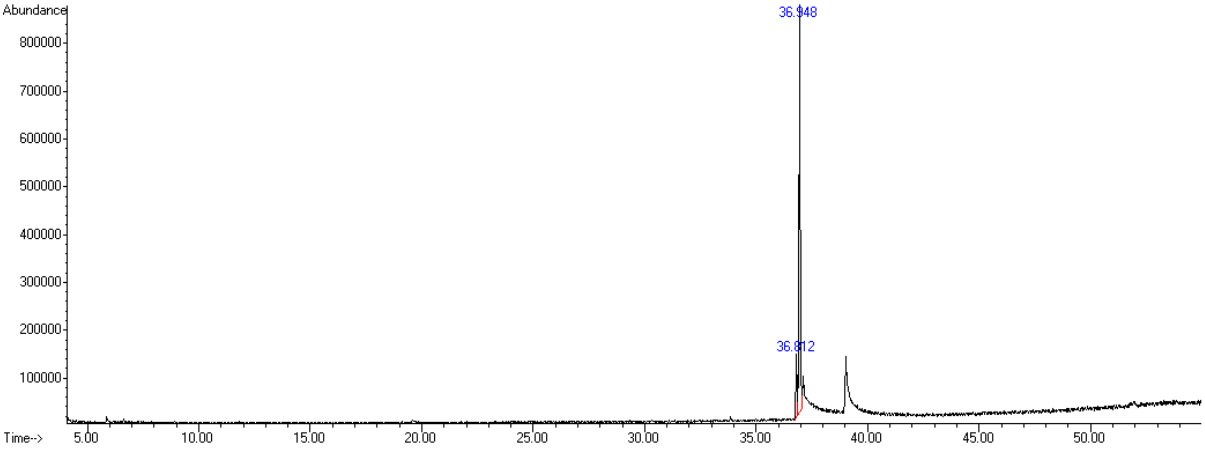
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 79.8, 70.6, 62.9, 49.2, 49.0, 34.7, 32.0, 28.6, 26.5;

ESI-MS calculated $[C_{15}H_{28}N_2O_3+H]^+$: 285.2173, found: 285.2189;

IR $\tilde{\nu}$ = 2930, 2853, 1686, 1404, 1252, 1175, 1119, 1074, 955, 868, 775;

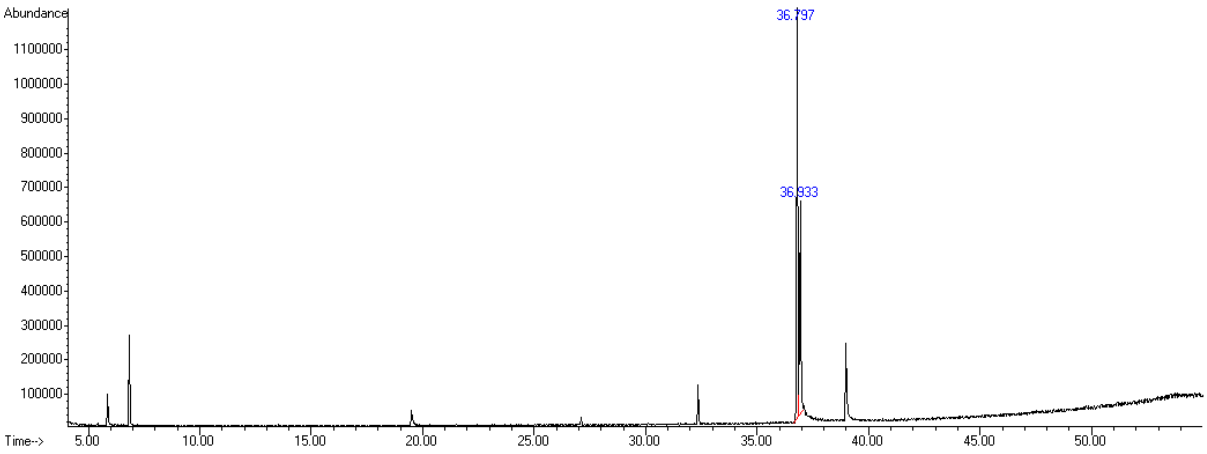
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

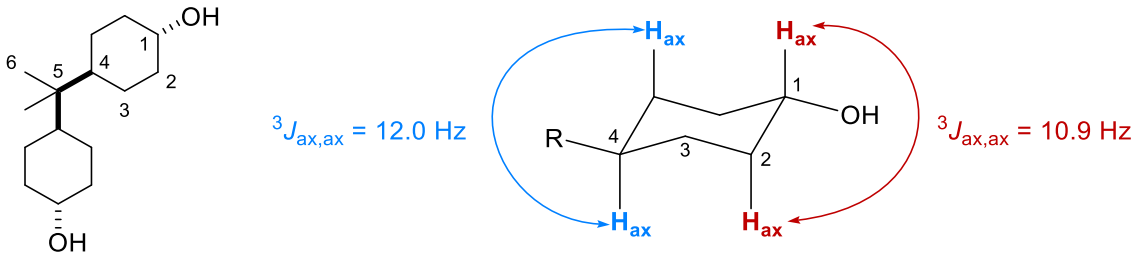


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	36.812	5572	5584	5594	BV 2	131393	4540244	15.48%	13.402%
2	36.948	5594	5607	5628	VV	854052	29338186	100.00%	86.598%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	36.797	5558	5581	5594	PU	1179685	37303856	100.00%	62.908%
2	36.933	5594	5605	5631	VV	615909	21994866	58.96%	37.092%



2o, white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL). Purification with 40% to 50% EtOAc in pentane. 87% total yield, 67:31:2 d.r. (*trans*/*trans*:*trans*/*cis*:*cis*/*cis*) determined by GC-MS. The major diastereomer was isolated and characterized (54% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C4 & H_{ax}C3. The multiplets of H_{ax}C4 and H_{ax}C2 are overlapping. The *trans*-configuration was confirmed by a crystal structure.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.52 (tt, $^3J_{ax,ax}$ = 10.9 Hz, $^3J_{ax,eq}$ = 4.4 Hz, 2H, H_{ax}C1), 2.06 – 1.98 (m, 4H, H_2C2), 1.74 – 1.67 (m, 4H, H_{eq}C3), 1.52 (bs, 2H, *H*O), 1.28 – 1.22 (tm, $^3J_{ax,ax}$ = 12.0 Hz, 2H, H_{ax}C4), 1.24 – 1.16 (m, 4H, H_2C2), 1.05 (dddd, $^2J_{HH}$ = 13.1 Hz, $^3J_{ax,ax}$ = 11.6 Hz, $^3J_{ax,eq}$ = 3.1 Hz, $^3J_{ax,eq}$ = 3.1 Hz, 4H, H_{ax}C3), 0.72 (s, 6H, H_3C6);

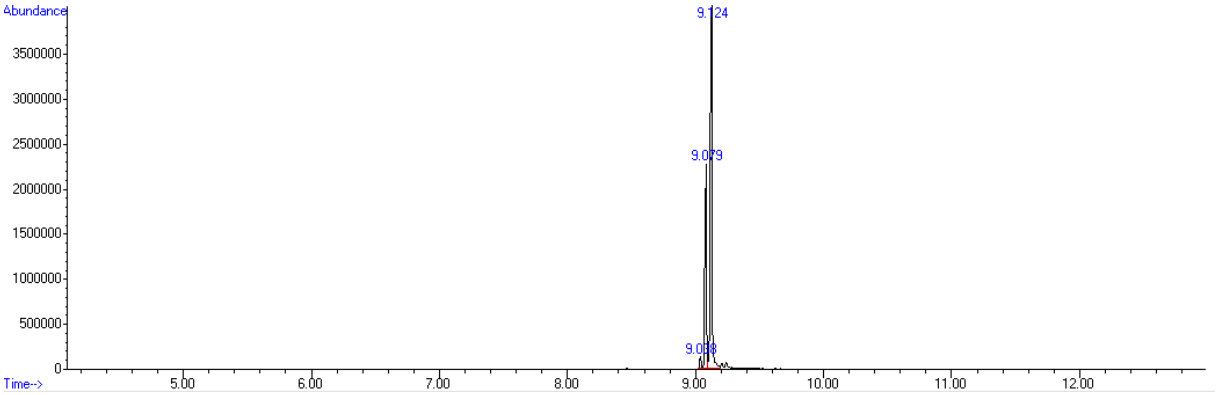
^{13}C NMR (151 MHz, $CDCl_3$) δ 71.5 (C1), 43.3 (C4), 36.8 (C5), 36.4 (C2), 25.1 (C3), 20.8 (C6);

ESI-MS calculated $[C_{15}H_{28}O_2+Na]^+$: 263.1982, found: 263.1978;

IR $\tilde{\nu}$ = 3342, 2982, 1734, 1373, 1238, 1045, 914, 731, 648, 633, 608.

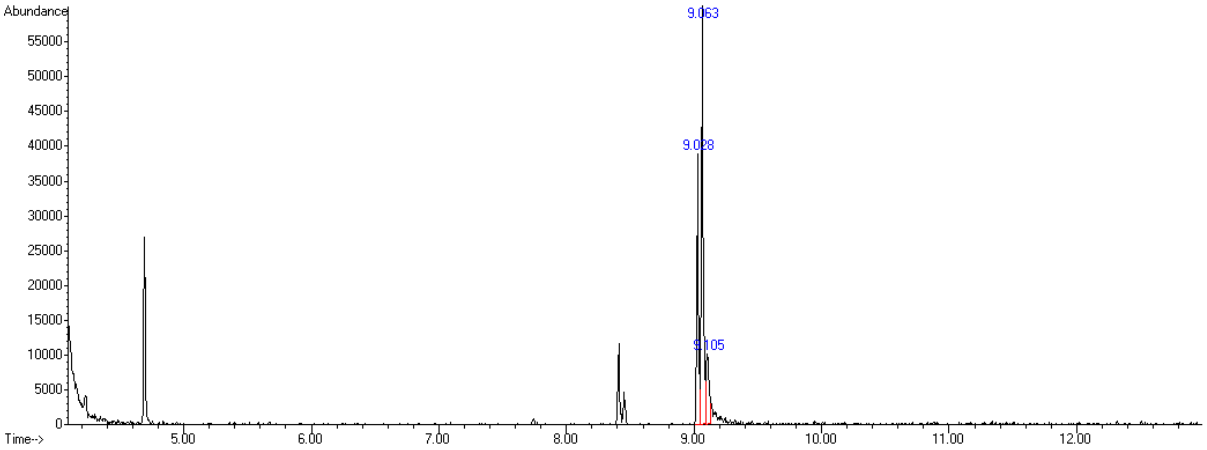
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

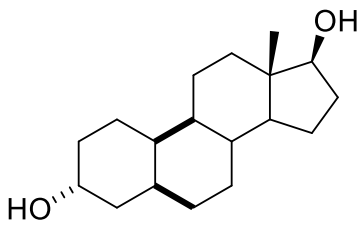


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	9.038	842	845	848	M	126147	990231	2.47%	1.668%
2	9.079	848	852	855	M	2333135	18331466	45.76%	30.870%
3	9.124	855	860	871	M	4378875	40060255	100.00%	67.462%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total	
1	9.028	840	843	847	M	39038	321015	53.82%	29.786%	ketone
2	9.063	847	849	854	M	60445	596446	100.00%	55.343%	
3	9.105	854	856	860	M3	10218	160264	26.87%	14.871%	



2p, white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL). Purification with 40% to 50% EtOAc in pentane. 72% total yield, 90:10 d.r. determined by GC-MS. Both diastereomers were isolated and characterized together. The signals of the major diastereomer are reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (m, 1H), 3.63 (m, 1H), 2.08 – 1.95 (m, 2H), 1.86 – 1.36 (m, 15H), 1.24 (m, 4H), 1.16 – 0.97 (m, 2H), 0.95 – 0.80 (m, 2H), 0.72 (s, 3H);

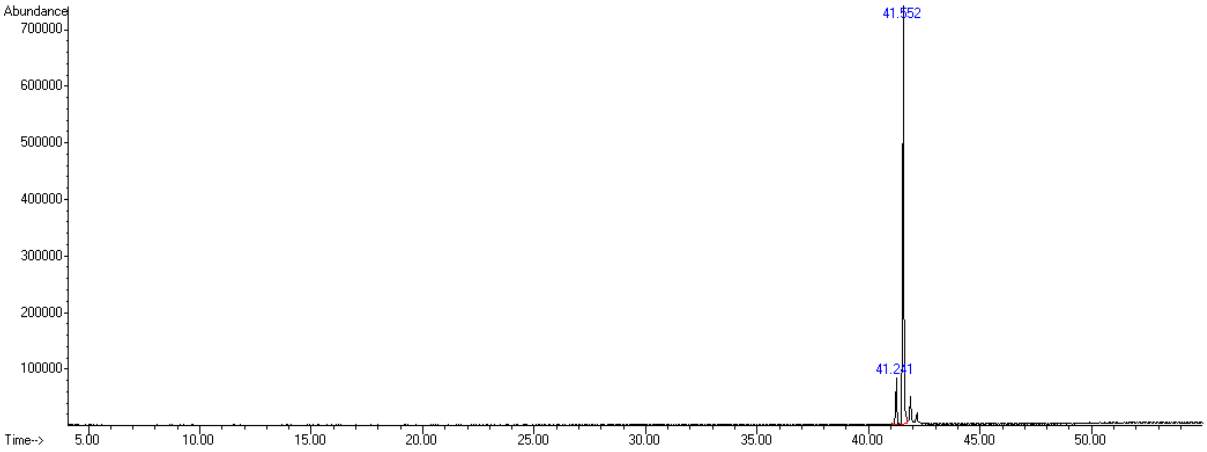
^{13}C NMR (101 MHz, $CDCl_3$) δ 82.1, 67.4, 51.1, 48.0, 43.6, 41.5, 38.7, 37.2, 37.0, 34.9, 33.7, 32.3, 30.7, 28.9, 25.9, 23.4, 15.8, 11.2;

ESI-MS calculated $[C_{18}H_{30}O_2+Na]^+$: 301.2138, found: 301.2149;

IR $\tilde{\nu}$ = 3376, 2915, 2847, 1717, 1653, 1449, 1373, 1265, 1063, 1051, 1026, 955, 582;

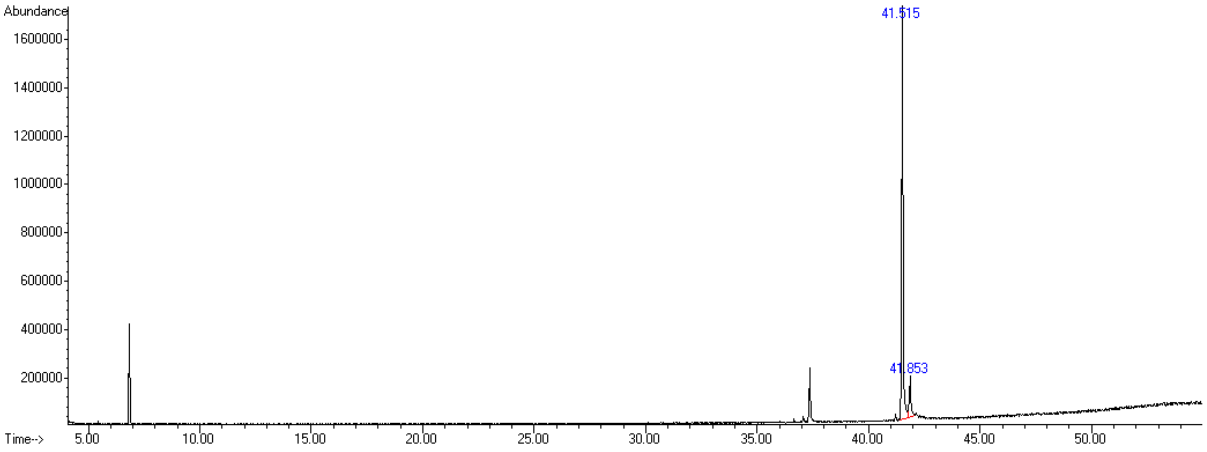
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

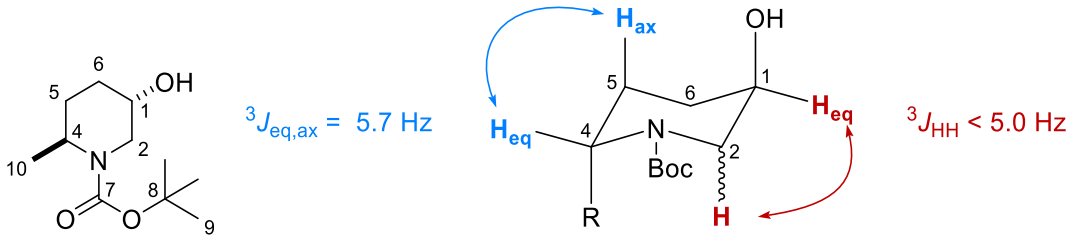


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	41.241	6305	6340	6359	BV 7	82382	2701245	11.38%	10.214%
2	41.552	6376	6393	6421	BV 2	735745	23744400	100.00%	89.786%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	41.515	6370	6386	6434	PV 2	1698318	66695306	100.00%	89.540%
2	41.853	6434	6444	6480	VV 8	166707	7791058	11.68%	10.460%



2q, white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.4 M, 1.0 mL). Boc-protection prior to isolation by addition of NEt_3 (3.0 equiv.) and Boc_2O (3.0 equiv.). Purification with 20% to 30% EtOAc in pentane. 95% total yield, 87:13 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (72% yield). The *trans*-configuration was determined based on the $^3J_{eq,ax}$ couplings between H_{eq}C1 & H_{ax}C2, and H_{eq}C4 & H_{ax}C3. Determination of $^3J_{eq,ax}$ coupling between H_{eq}C4 & H_{ax}C5 was possible with homonuclear decoupling experiments by irradiation at H_3C10. Hydroxy and methyl group occupy the corresponding axial position. The *trans*-configuration was confirmed by a crystal structure.

^{1}H NMR (599 MHz, $CDCl_3$) δ 4.41 – 4.35 (dm, $^3J_{eq,ax}$ = 5.7 Hz, 1H, H_{eq}C4), 3.96 (ddm, $^2J_{HH}$ = 14.3 Hz, $^3J_{eq,eq}$ = 2.6 Hz, 1H, H_{eq}C2), 3.90 (m, 1H, H_{eq}C1), 3.04 – 2.98 (m, 1H, H_{ax}C2), 2.06 (dm, $^2J_{HH}$ = 13.8 Hz, 1H, H_2C5), 1.79 – 1.70 (m, 1H, H_2C6), 1.70 – 1.63 (m, 1H, H_2C6), 1.45 (s, 9H, H_3C9), 1.27 (dm, $^2J_{HH}$ = 13.8 Hz, 1H, H_2C5), 1.24 (s, 1H, *H*O), 1.12 (d, $^3J_{HH}$ = 6.9 Hz, 3H, H_3C10);

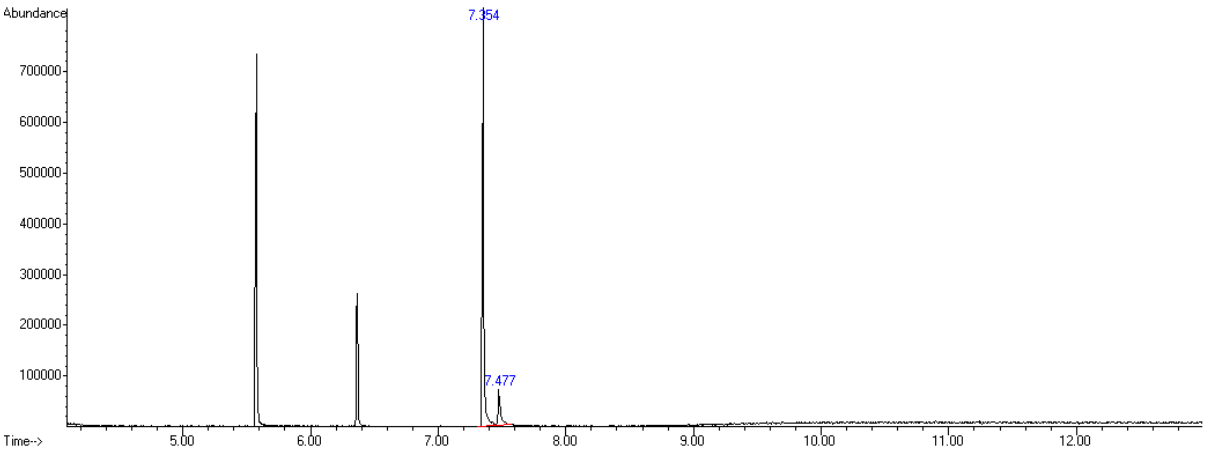
^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1 (C7), 79.7 (C8), 64.8 (C1), 46.2 (C4), 44.7 (C2), 28.6 (C9), 25.4 (C6), 23.9 (C5), 15.4 (C10);

ESI-MS calculated $[C_{11}H_{21}NO_3+Na]^+$ 238.1414, found: 238.1435;

IR $\tilde{\nu}$ = 3449, 2967, 2895, 1651, 1422, 1362, 1335, 1248, 1153, 1090, 1034, 1018, 874, 831, 766, 638;

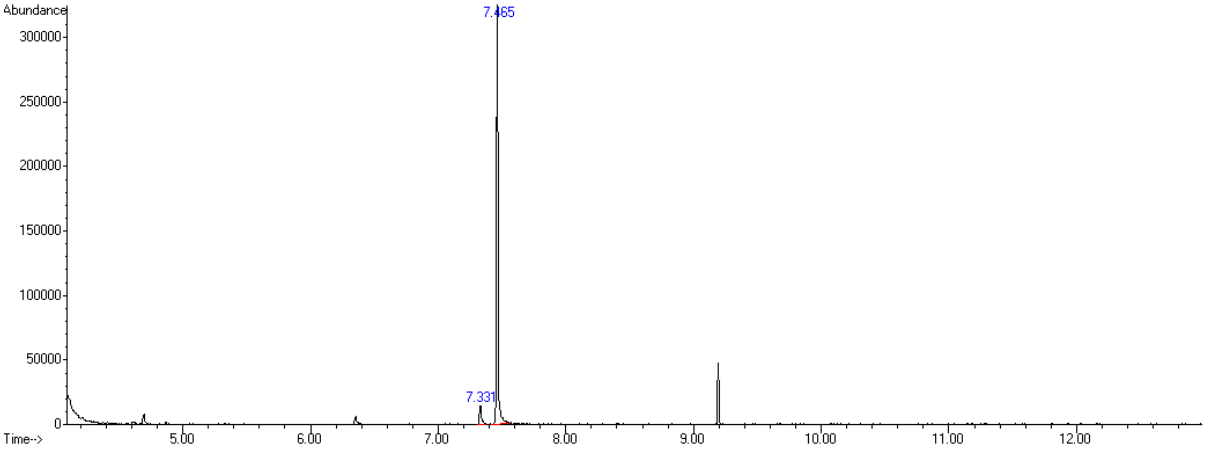
GC-MS (prior to purification):

Pd-catalyzed (*trans*)

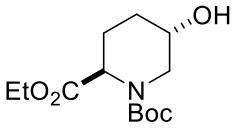


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.354	550	557	573	BV	728975	6378940	100.00%	86.534%
2	7.477	573	579	597	VB 2	66732	992664	15.56%	13.466%

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.331	550	554	562	M	15564	167464	6.80%	6.365%
2	7.465	568	576	593	BB	274324	2463534	100.00%	93.635%



2r, colorless oil, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.4 M, 1.0 mL). Boc-protection prior to isolation by addition of NEt_3 (3.0 equiv.) and Boc_2O (3.0 equiv.). Purification with 10% to 30% EtOAc in pentane. 62% total yield, 73:27 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (47% yield).

The title compound exists as a mixture of multiple rotamers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (m, 1H), 4.28 – 3.93 (m, 3H), 3.61 (s, 1H), 2.69 (dt, *J* = 41.8, 11.4 Hz, 1H), 2.42 – 2.14 (m, 2H), 2.02 – 1.89 (m, 1H), 1.79 – 1.60 (m, 1H), 1.51 – 1.35 (m, 9H), 1.32 – 1.12 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 171.5, 155.6, 155.3, 80.6, 66.8, 66.6, 61.4, 54.1, 52.9, 48.6, 47.7, 30.6, 30.0, 29.8, 28.6, 28.4, 25.1, 24.9, 23.8, 21.9, 21.9, 14.4;

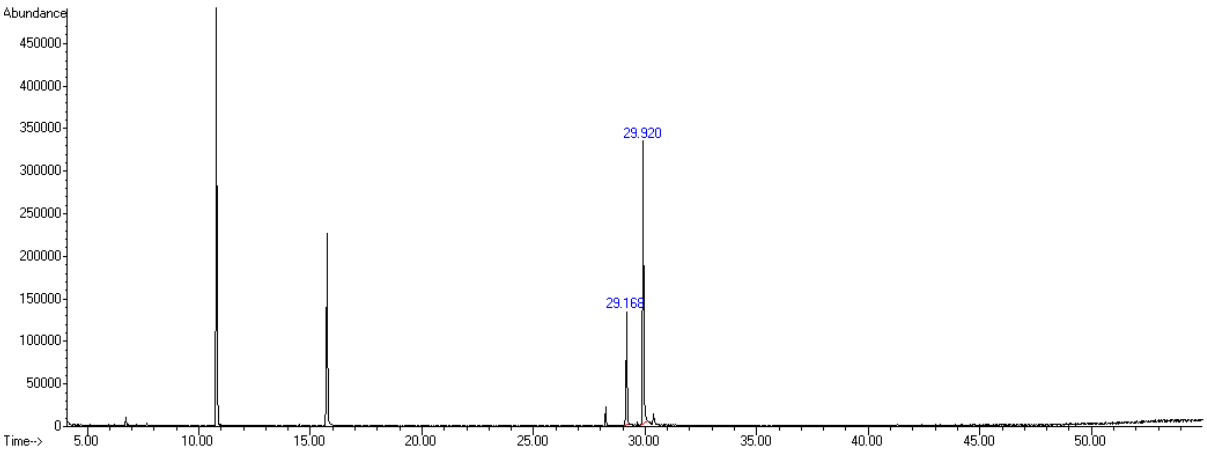
ESI-MS calculated $[C_{13}H_{23}NO_5+Na]^+$ 296.1468, found: 296.1479;

IR $\tilde{\nu}$ = 2978, 2362, 1734, 1696, 1684, 1395, 1368, 1340, 1240, 1146, 1072, 1022, 978, 874;

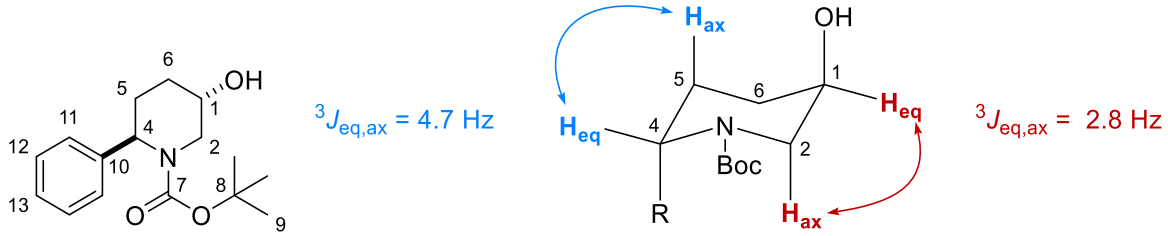
Analytical data are in good accordance with those previously reported for this compound.[6]

GC-MS (prior to purification):

Pd-catalyzed (*trans*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	29.168	4263	4280	4302	BV 2	132773	3857614	36.71%	26.851%
2	29.920	4386	4408	4441	BV 3	333071	10509051	100.00%	73.149%



2s, white solid, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.2 M, 2.0 mL). Boc-protection prior to isolation by addition of NEt_3 (1.5 equiv.) and Boc_2O (1.5 equiv.). Purification with 20% to 30% EtOAc in pentane. 75% total yield, 67:33 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (40% yield). The *trans*-configuration was determined based on the $^3J_{eq,ax}$ couplings between H_{eq}C1 & H_{ax}C2, and H_{eq}C4 & H_{ax}C5. Hydroxy and phenyl group occupy the corresponding axial positions.

^{1}H NMR (599 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 2H, H_{Ar}C12), 7.27 – 7.20 (m, 3H, H_{Ar}C11, H_{Ar}C13), 5.44 (d, $^3J_{eq,ax}$ = 4.7 Hz, 1H, H_{eq}C4), 4.09 (dd, $^2J_{HH}$ = 14.6 Hz, $^3J_{ax,eq}$ = 2.7 Hz, 1H, H_{ax}C2), 3.87 (dm, $^3J_{eq,ax}$ = 2.8 Hz, 1H, H_{eq}C1), 2.91 (dd, $^2J_{HH}$ = 14.4 Hz, $^3J_{eq,eq}$ = 1.9 Hz, 1H, H_{eq}C2), 2.34 (dm, $^2J_{HH}$ = 13.9 Hz, 1H, H_2C5), 2.12 (dm, $^2J_{HH}$ = 14.4 Hz, 1H, H_2C5), 2.00 (bs, 1H, *H*O), 1.75 – 1.68 (m, 1H, H_2C6), 1.63 (dm, $^2J_{HH}$ = 13.9 Hz, 1H, H_2C6), 1.48 (s, 9H, H_3C9);

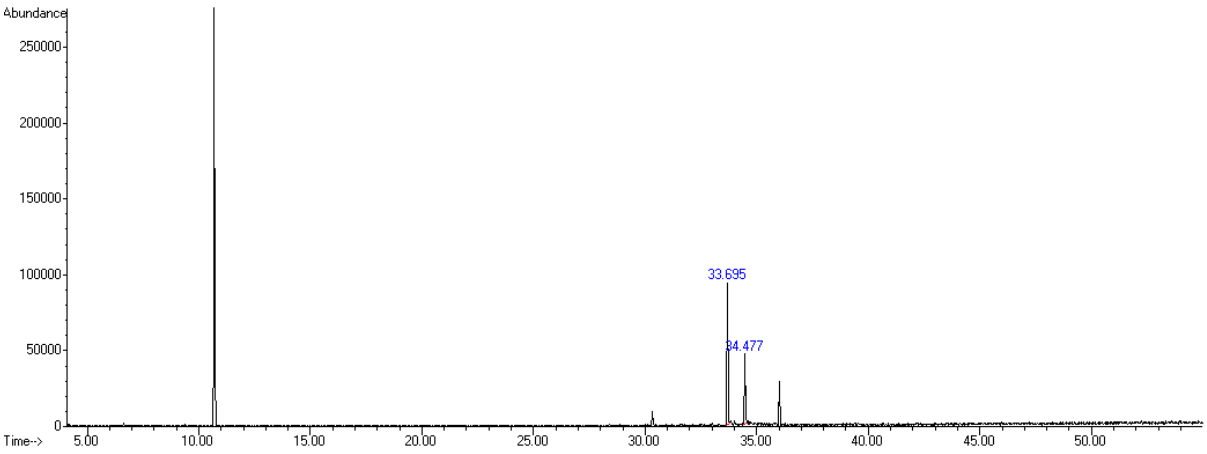
^{13}C NMR (151 MHz, $CDCl_3$) δ 156.8 (C8), 139.5 (C10), 128.8, 126.8, 126.5, 80.3 (C8), 65.0 (C1), 53.4 (C4), 46.0 (C2), 28.6 (C9), 26.4 (C6), 21.7 (C5);

ESI-MS calculated $[(C_{16}H_{23}NO_3)_2+Na]^+$ 577.3248, found: 577.3262;

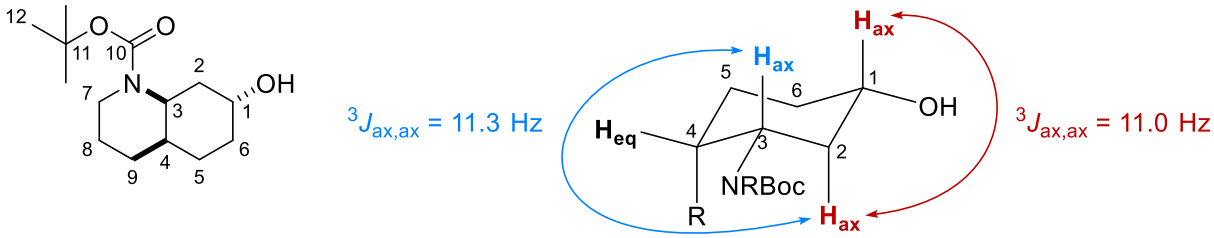
Analytical data are in good accordance with those previously reported for this compound.[7]

GC-MS (prior to purification):

Pd-catalyzed (*trans*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	33.695	5040	5052	5074	BB 2	92784	2634537	100.00%	66.696%
2	34.477	5175	5185	5210	BB 3	44940	1315527	49.93%	33.304%



2t, yellow oil, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *iso*-propanol (0.4 M, 1.0 mL). Boc-protection prior to isolation by addition of NEt_3 (3.0 equiv.) and Boc_2O (3.0 equiv.). Purification with 10% to 30% EtOAc in pentane. 91% total yield, 93:7 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (78% yield). The *trans*-configuration was determined based on the $^3J_{ax,ax}$ couplings between H_{ax}C1 & H_{ax}C2, and H_{ax}C3 & H_{ax}C2.

^{1}H NMR (599 MHz, $CDCl_3$) δ 3.63 (tt, $^2J_{HH}$ = 11.0 Hz, $^3J_{eq,ax}$ = 4.4 Hz, 1H, H_{ax}C1), 3.52 (ddd, $^2J_{HH}$ = 13.7 Hz, $^3J_{eq,ax}$ = 6.1 Hz, $^3J_{eq,eq}$ = 3.8 Hz, 1H, H_{eq}C7), 3.20 (ddd, $^2J_{HH}$ = 13.7 Hz, $^3J_{ax,ax}$ = 10.0 Hz, $^3J_{ax,eq}$ = 5.1 Hz, 1H, H_{ax}C7), 2.98 (td, $^3J_{ax,ax}$ = 11.3 Hz, $^3J_{ax,eq}$ = 3.2 Hz, 1H, H_{ax}C3), 2.45 – 2.38 (m, 1H, H_2C2), 2.12 (bs, 1H, *H*O), 2.00 – 1.92 (m, 1H, H_2C6), 1.75 – 1.62 (m, 3H, H_2C8, H_2C5, H_{eq}C9), 1.60 – 1.50 (m, 1H, H_2C8), 1.50 – 1.40 (m, 2H, H_2C2, *H*C4), 1.43 (s, 9H, H_3C12), 1.33 – 1.20 (m, 1H, H_2C6), 1.07 (ddd, $^2J_{HH}$ = 12.9 Hz, $^3J_{ax,ax}$ = 9.0 Hz, $^3J_{ax,eq}$ = 4.0 Hz, 1H, H_{ax}C9), 1.05 – 0.95 (m, 1H, H_2C5);

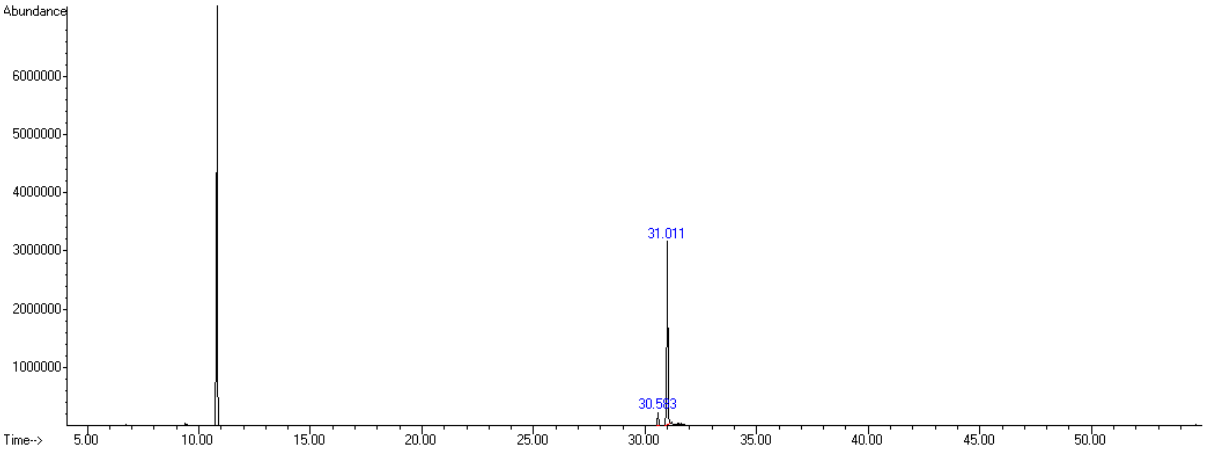
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4 (C10), 79.4 (C11), 69.7 (C1), 59.2 (C3), 40.7 (C2), 39.8 (C7), 37.4 (C4), 35.2 (C6), 29.9 (C5), 28.6 (C12), 27.0 (C9), 22.9 (C8);

ESI-MS calculated $[C_{14}H_{25}NO_3+Na]^+$ 278.1727, found: 278.1739;

IR $\tilde{\nu}$ = 3428, 2972, 2928, 2861, 1686, 1668, 1408, 1364, 1250, 1165, 1146, 1059, 957, 772;

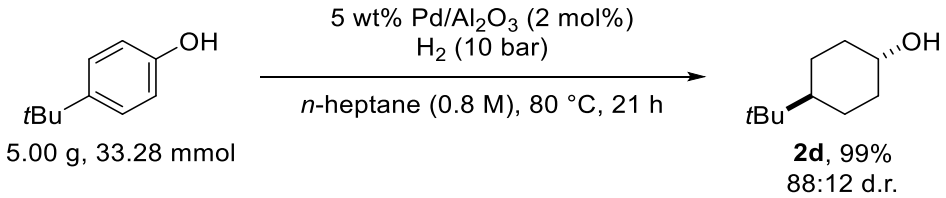
GC-MS (prior to purification):

Pd-catalyzed (*trans*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	30.583	4508	4521	4537	BB 2	222719	6821613	6.97%	6.513%
2	31.011	4573	4594	4619	BV	3116749	97922847	100.00%	93.487%

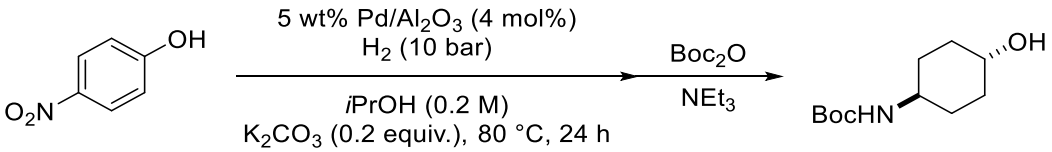
4.1 Scale-up Hydrogenation



5.00 g, 33.28 mmol

2d, 99%
88:12 d.r.

A 100 mL glass cylinder, equipped with a magnetic stirring bar, was charged with 5 wt% Pd/Al_2O_3 (1.42 g, 0.66 mmol, 2 mol%), *p-tert*-butylphenol (5.00 g, 33.28 mmol, 1.0 equiv.) and *n*-heptane (42.0 mL, 0.8 M). The prepared glass cylinder was placed in a 400 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the hydrogen pressure was set to 10 bar. The reaction mixture was stirred at 80 °C for 21 h. After the autoclave was carefully depressurized, the crude mixture was filtered over a pad of silica gel (eluent: 100% EtOAc) and both diastereomers were isolated together. White solid, 99% total yield (5.18 g, 33.15 mmol), 88:12 d.r. (determined by ^{1}H NMR). Characterization data was in accordance with **2d**.

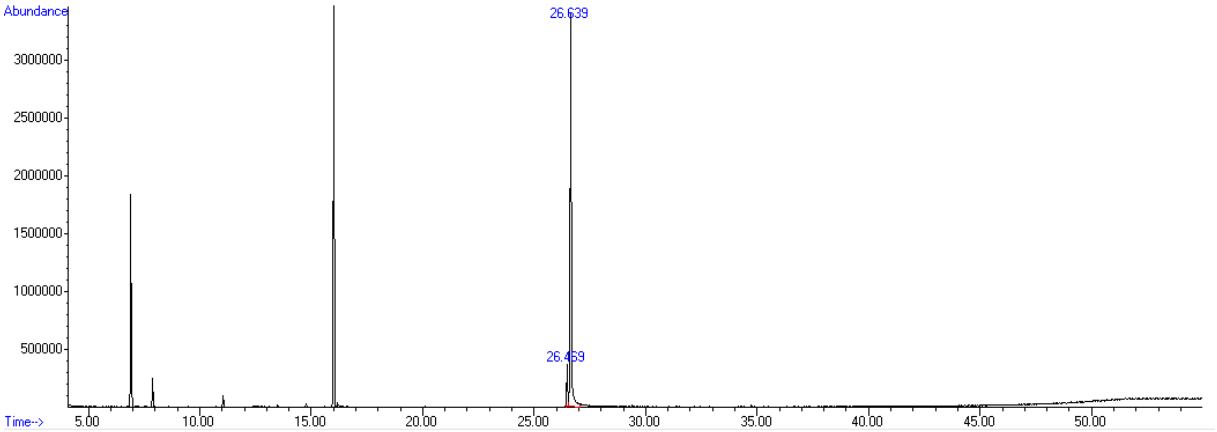


3.0 mmol

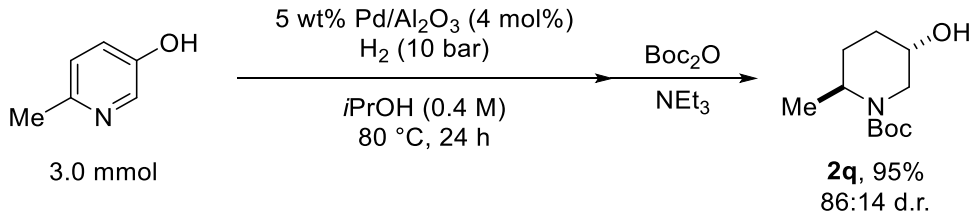
2f, 87%, 90:10 d.r.

A 50 mL glass cylinder, equipped with a magnetic stirring bar, was charged with 5 wt% Pd/Al_2O_3 (255 mg, 0.12 mmol, 4 mol%), *p*-nitrophenol (417 mg, 3.0 mmol, 1.0 equiv.), K_2CO_3 (83 mg, 0.6 mmol, 0.2 equiv.) and *iso*-propanol (15.0 mL, 0.2 M). The prepared glass cylinder was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the hydrogen pressure was set to 10 bar. The reaction mixture was stirred at 80 °C for 24 h. After the autoclave was carefully depressurized, the crude mixture was purified by column chromatography on silica gel (40% to 50% EtOAc in pentane). White solid, 87% total yield (559 mg, 2.60 mmol), 90:10 d.r. The major isomer was isolated in 40% yield (257 mg, 1.19 mmol). Characterization data was in accordance with **2f**.

Pd-catalyzed (*trans*)



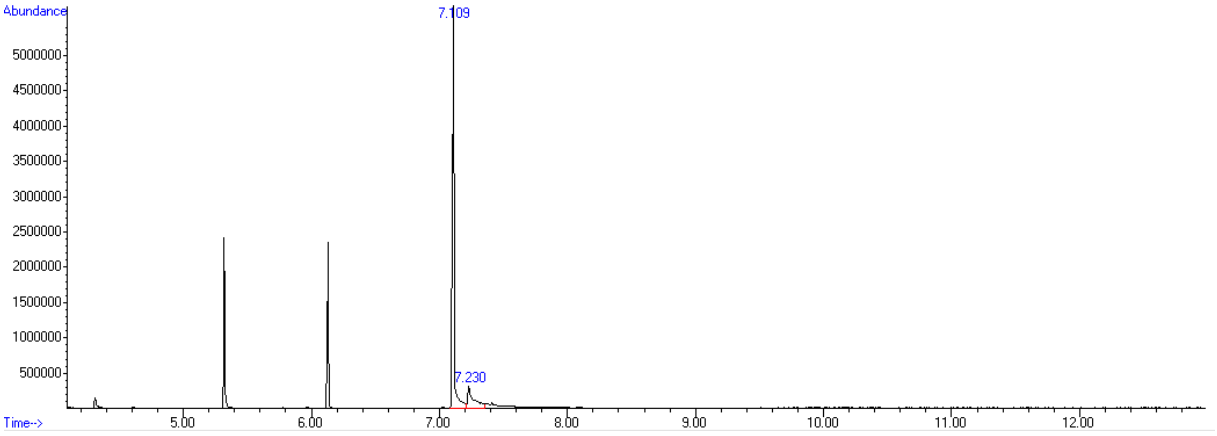
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.469	3809	3819	3836	rM	365062	11688422	10.55%	9.542%
2	26.639	3837	3848	3894	rM	3398491	110811935	100.00%	90.458%



A 50 mL glass cylinder, equipped with a magnetic stirring bar, was charged with 5 wt% Pd/Al_2O_3 (255 mg, 0.12 mmol, 4 mol%), 5-hydroxy-2-methylpyridine (327 mg, 3.0 mmol, 1.0 equiv.) and *iso*-propanol (7.5 mL, 0.4 M). The prepared glass cylinder was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the hydrogen pressure was set to 10 bar. The reaction mixture was stirred at 80 °C for 24 h. After the autoclave was carefully depressurized, the crude mixture was purified by column chromatography on silica gel (20% to 40% EtOAc in pentane). White solid, 95% total yield (613 mg, 2.85 mmol), 86:14 d.r. The major isomer was isolated in 60% yield (390 mg, 1.81 mmol). Characterization data was in accordance with **2q**.

GC-MS (prior to purification):

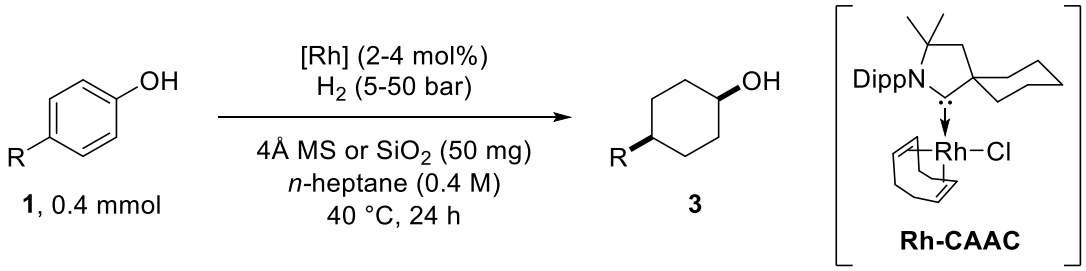
Pd-catalyzed (*trans*)



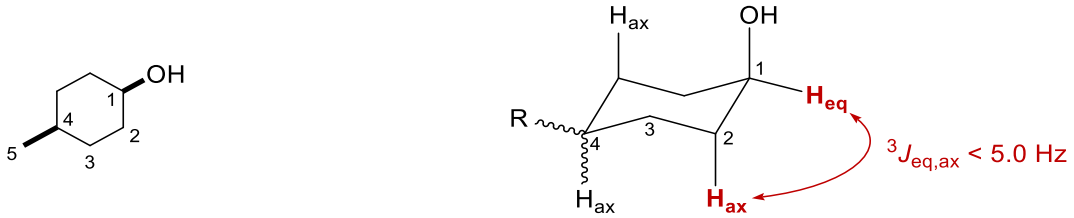
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.109	511	516	533	M	6086368	59570902	100.00%	86.162%
2	7.230	533	536	557	M	315088	9567170	16.06%	13.838%

5. Synthesis of *cis*-configurated Cyclohexanols

General procedure B for the cis-selective hydrogenation of phenols



A 4 mL screw-cap glass vial, equipped with a magnetic stirring bar, was charged with $[Rh(COD)Cl]_2$ or [Rh–CAAC][8] (2-4 mol%), catalyst support (50 mg) and solid substrates (0.4 mmol, 1.0 equiv.) as indicated. Solvent (1.0 mL, 0.4 M) and liquid substrates were added. The prepared glass vial was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the indicated pressure was set. The reaction mixture was stirred at 40 °C for 24 h. After the autoclave was carefully depressurized, the crude mixture was purified by column chromatography on silica gel.



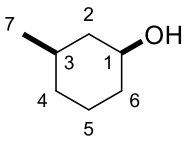
3a, colorless oil, procedure **B**: $[Rh(COD)Cl]_2$ 2 mol% catalyst loading, support: 4Å MS (50 mg), 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 10% to 20% Et_2O in pentane. 77% total yield, 91:9 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized. The hydroxy group occupies the axial position based on the $^3J_{eq,ax}$ coupling of H_{eq}C1. The *J* coupling of *H*C4 could not be determined due to overlapping multiplets.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (tt, $^3J_{HH}$ = 4.8 Hz, $^3J_{HH}$ = 3.1 Hz, 1H, H_{eq}C1), 1.79 – 1.65 (m, 2H), 1.62 – 1.39 (m, 6H), 1.39 – 1.23 (m, 2H), 0.91 (d, $^3J_{HH}$ = 6.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 67.1, 32.4, 31.3, 29.1, 21.8;

ESI-MS calculated $[C_7H_{14}O+Na]^+$ 137.0937, found: 137.0903.

Analytical data are in good accordance with those previously reported for this compound.[1]



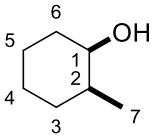
3ab, colorless oil, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 10% Et_2O in CH_2Cl_2. 86% total yield, 83:17 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (77% yield). Procedure **B**: $[Rh(COD)Cl]_2$ 4 mol% catalyst loading, support: 4Å MS (50 mg), 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. 74% total yield, 73:27 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (48% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (m, 1H, *H*C1), 2.00 – 1.88 (m, 2H), 1.80 – 1.70 (m, 1H), 1.69 (bs, 1H, *H*O), 1.59 (dm, $^2J_{HH}$ = 12.9 Hz, 1H), 1.51 – 1.35 (m, 1H), 1.35 – 1.18 (m, 1H), 1.17 – 1.01 (m, 1H), 0.92 (d, $^3J_{HH}$ = 6.6 Hz, 3H), 0.87 – 0.68 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 71.0, 44.8, 35.6, 34.2, 31.6, 24.3, 22.5;

ESI-MS calculated $[C_7H_{14}O+Na]^+$ 137.0937, found: 137.0904.

Analytical data are in good accordance with those previously reported for this compound.[1]

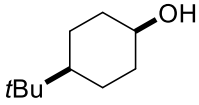


3ac, colorless oil, procedure **B**: $[Rh(COD)Cl]_2$ 2 mol% catalyst loading, support: 4Å MS (50 mg), 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 5% to 30% Et_2O in pentane. 70% total yield, >95:5 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (m, 1H, *H*C1), 1.79 – 1.69 (m, 1H), 1.67 – 1.57 (m, 2H), 1.56 – 1.47 (m, 2H), 1.44 – 1.31 (m, 4H), 1.30 – 1.19 (m, 1H), 0.93 (d, $^3J_{HH}$ = 6.9 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 71.3, 36.0, 32.7, 28.9, 24.7, 20.8, 17.1;

Analytical data are in good accordance with those previously reported for this compound.[1]



3b, white solid, procedure **B**: $[Rh(COD)Cl]_2$ 2 mol% catalyst loading, support: SiO_2 (50 mg), 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 5% to 20% EtOAc in pentane. 90% total yield, 93:7 d.r. determined by GC-MS. Both diastereomers were isolated and characterized together.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.03 (m, 1H, *H*C1), 1.87 – 1.79 (m, 2H), 1.58 – 1.42 (m, 4H), 1.37 (m, 2H), 1.24 (s, 1H), 0.99 (m, 1H), 0.86 (s, 9H);

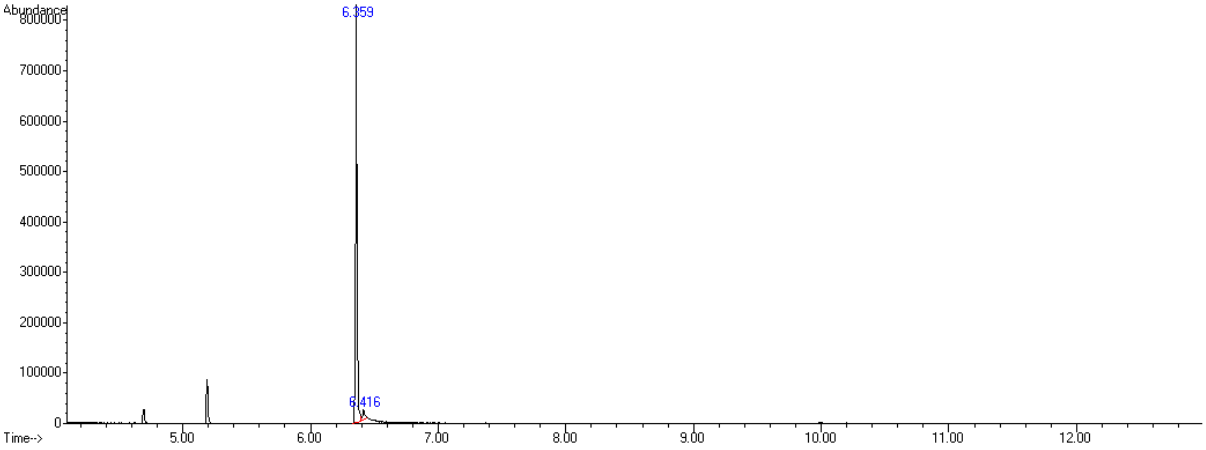
^{13}C NMR (101 MHz, $CDCl_3$) δ 66.1, 48.2, 33.6, 32.7, 27.6, 21.1;

IR $\tilde{\nu}$ = 3395, 2938, 2864, 1558, 1363, 1276, 1180, 1147, 1029, 1007, 958, 928, 904;

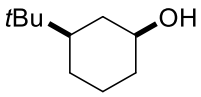
Analytical data are in good accordance with those previously reported for this compound.[1]

GC-MS (prior to purification):

Rh-catalyzed (*cis*)



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.359	383	388	394	M	855497	6529607	100.00%	93.283%
2	6.416	394	397	404	M4	20459	470131	7.20%	6.717%



3c, colorless oil, procedure **A**: 4 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 30% Et_2O in pentane. 80% total yield, 91:9 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (73% yield). Procedure **B**: 2 mol% catalyst loading, 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 30% Et_2O in pentane. 85% total yield, 66:34 d.r. determined by ^{1}H NMR.

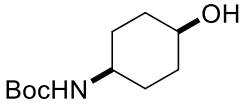
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 (dm, $^3J_{ax,ax}$ = 10.7 Hz, 1H, H_{ax}C1), 2.11 – 1.89 (m, 3H), 1.80 (dm, $^2J_{HH}$ = 12.6 Hz, 1H), 1.67 (dm, $^2J_{HH}$ = 12.3 Hz, 1H), 1.29 – 1.00 (m, 3H), 0.99 – 0.88 (m, 2H), 0.85 (s, 9H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 72.0, 46.8, 37.3, 35.9, 32.5, 27.7, 26.4, 24.5;

ESI-MS calculated $[C_{10}H_{20}O+Na]^+$ 179.1406, found: 179.1401;

IR $\tilde{\nu}$ = 3320, 2935, 2859, 1559, 1457, 1395, 1365, 1240, 1060, 1015, 976, 842;

Analytical data are in good accordance with those previously reported for this compound.[1]



3d, white solid, procedure **B**: [Rh–CAAC] 2 mol% catalyst loading, support: SiO_2 (50 mg), 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 20% to 50% EtOAc in pentane. 98% total yield, 63:37 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (47% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (s, 1H), 3.88 (t, $^3J_{HH}$ = 3.9 Hz, 1H, *H*C1), 3.52 (s, 1H), 1.73 – 1.55 (m, 8H), 1.44 (s, 10H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.4, 79.3, 66.5, 47.9, 31.4, 28.6, 27.8;

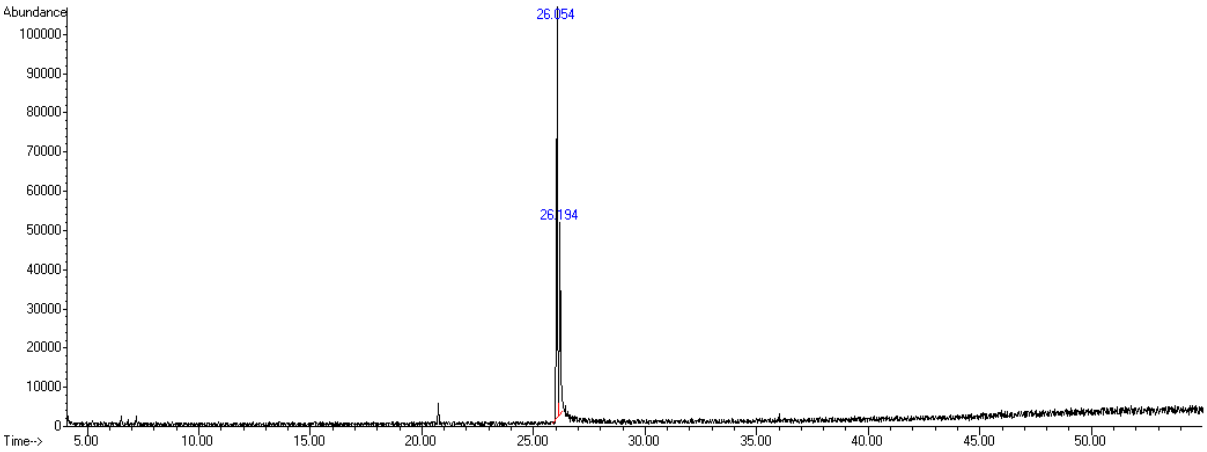
ESI-MS calculated $[C_{11}H_{21}NO_3+Na]^+$ 238.1414, found: 238.1421;

IR $\tilde{\nu}$ = 3355, 2980, 1696, 1684, 1558, 1521, 1507, 1173, 1070, 1026, 973, 954;

Analytical data are in good accordance with those previously reported for this compound.[9]

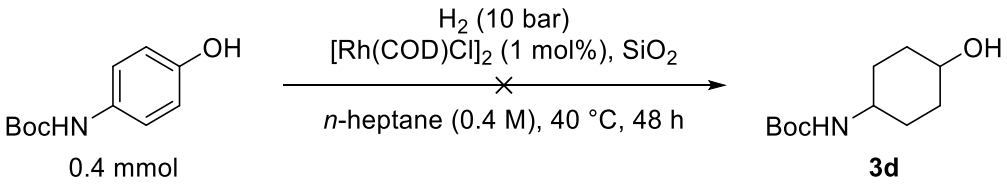
GC-MS (prior to purification):

Rh-catalyzed (*cis*)

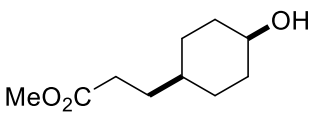


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	26.054	3713	3748	3762	BV	103342	2837564	100.00%	62.600%
2	26.194	3762	3772	3799	VV 3	48674	1695297	59.74%	37.400%

$[Rh(COD)Cl]_2$-catalyzed hydrogenation:



Product **3d** could not be observed by GC-MS or TLC. A possible pathway of decomposition is cleavage of the Boc-group and formation of the highly polar 4-aminocyclohexanol.



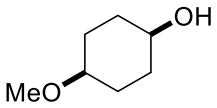
3e, colorless oil, 2 mol% $[Rh(COD)Cl]_2$, support: 4Å MS (50 mg), 10 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL). Purification with 30% to 40% EtOAc in pentane. 90% total yield, 73:27 d.r. determined by ^{1}H NMR. The major diastereomer was isolated and characterized (64% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 (pseudo-p, $^3J_{HH}$ = 4.7 Hz, 1H, *H*C1), 3.65 (s, 3H), 2.38 – 2.26 (m, 2H), 1.76 – 1.64 (m, 2H), 1.62 – 1.46 (m, 6H), 1.45 – 1.22 (m, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 66.9, 51.6, 36.0, 32.3, 31.9, 31.2, 26.7;

ESI-MS calculated $[C_{10}H_{18}O_3+Na]^+$: 209.1148, found: 209.1147;

IR $\tilde{\nu}$ = 3372, 2924, 2855, 1736, 1437, 1258, 1202, 1159, 1072, 1034, 986, 877, 682, 644.



3f, yellow oil, procedure **B**: [Rh–CAAC] 2 mol% catalyst loading, support: SiO_2 (50 mg), 5 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 5% to 50% EtOAc in pentane. 76% total yield, 80:20 d.r. determined by GC-MS. Both diastereomers were isolated and characterized together.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (m, 1H, *HC*1), 3.32 (m, 3H), 3.30 – 3.11 (m, 1H), 2.06 – 1.92 (m, 1H), 1.89 – 1.77 (m, 2H), 1.70 – 1.61 (m, 4H), 1.59 – 1.49 (m, 2H), 1.42 (s, 1H), 1.37 – 1.26 (m, 1H);

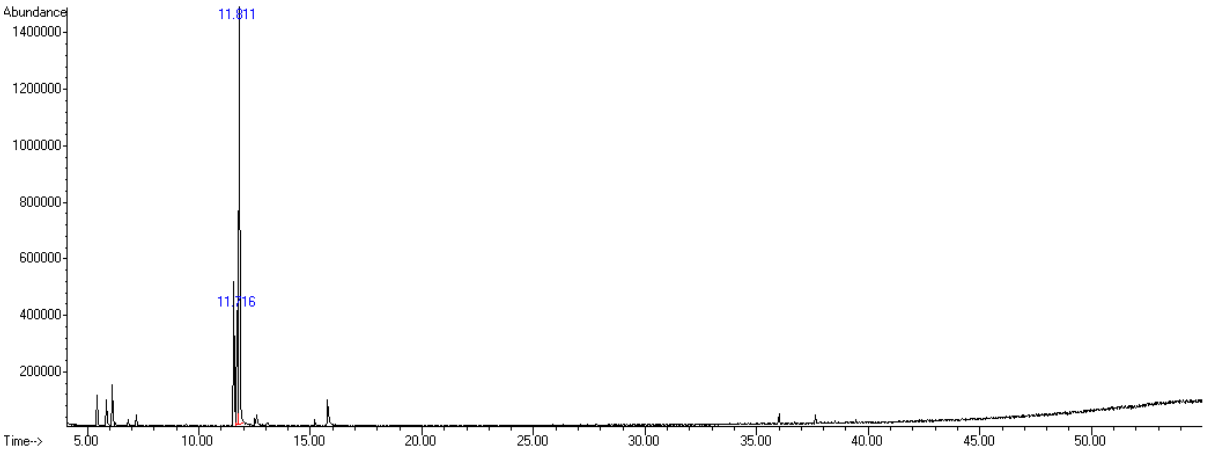
^{13}C NMR (101 MHz, $CDCl_3$) δ 78.2, 75.7, 69.8, 68.6, 56.1, 55.7, 32.7, 30.6, 29.0, 27.2;

ESI-MS calculated $[C_7H_{14}O_2+Na]^+$ 153.0886, found: 153.0883;

Analytical data are in good accordance with those previously reported for this compound.[10]

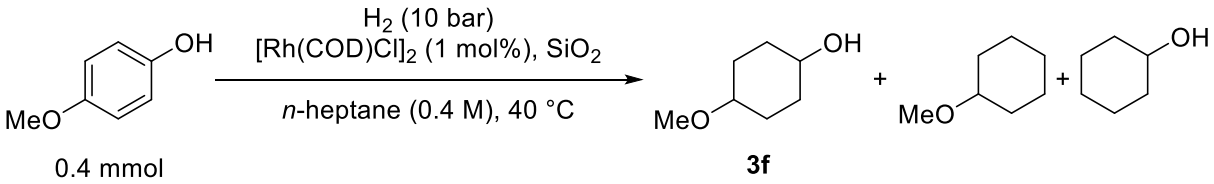
GC-MS (prior to purification):

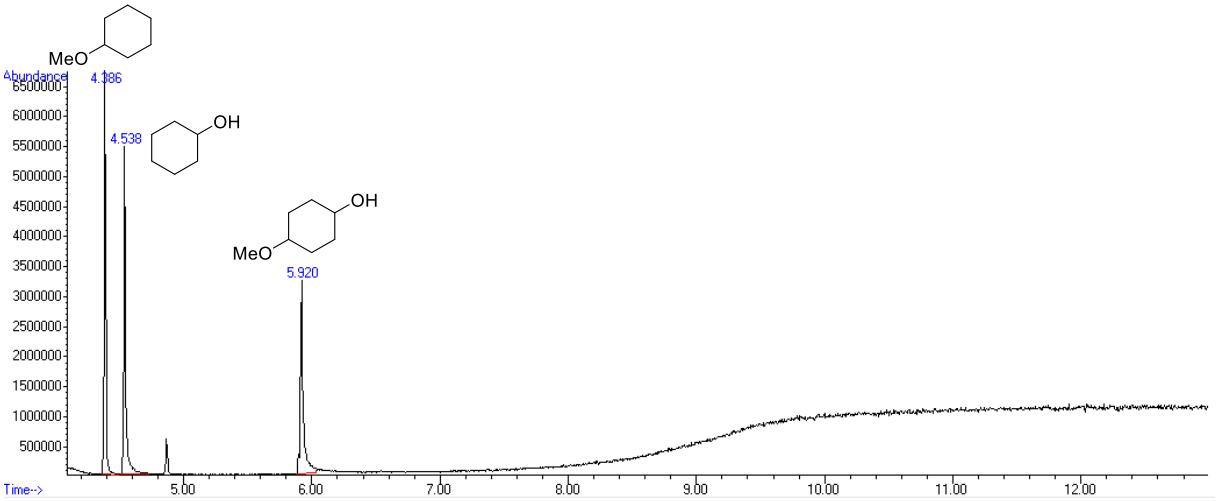
Rh-catalyzed (*cis*)



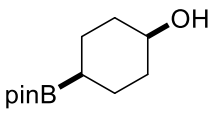
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	11.716	1294	1302	1310	VV 2	401414	9929160	24.31%	19.557%
2	11.811	1310	1318	1357	VB	1479182	40842072	100.00%	80.443%

[Rh(COD)Cl]$_2$-catalyzed hydrogenation:





peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	4.386	47	51	69	M	6754259	56801634	94.62%	34.498%
2	4.538	73	77	112	M	5469018	60030337	100.00%	36.459%
3	5.920	306	313	332	M	3248350	47821214	79.66%	29.044%



3g, white solid, procedure **B**: [Rh–CAAC] 2 mol% catalyst loading, support: 4Å MS (50 mg), 50 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 10% to 20% EtOAc in CH_2Cl_2. 94% total yield, 76:24 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (m, 1H, *H*C1), 1.78 (m, 4H), 1.54 – 1.38 (m, 4H), 1.36 (bs, 1H), 1.24 (s, 12H), 1.11 (m, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 83.2, 69.6, 34.6, 25.0, 24.3;

^{11}B NMR (128 MHz, $CDCl_3$) δ 34.4 (bs);

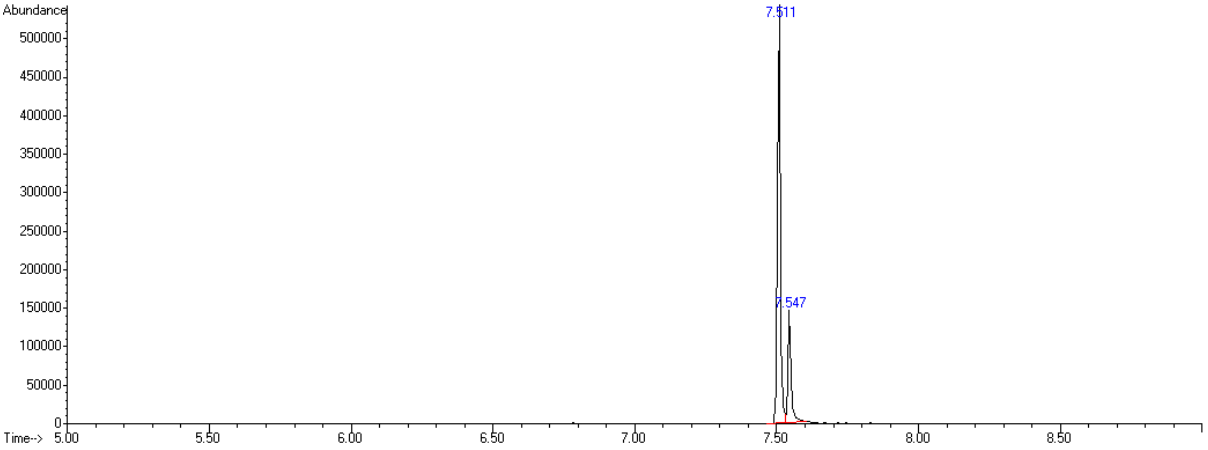
ESI-MS calculated $[C_{12}H_{23}BO_3Si+Na]^+$: 249.1632, found: 249.1648;

IR $\tilde{\nu}$ = 3309, 2987, 2926, 2852, 1370, 1307, 1224, 1143, 1062, 1052, 972, 859;

Analytical data are in good accordance with those previously reported for this compound.[11]

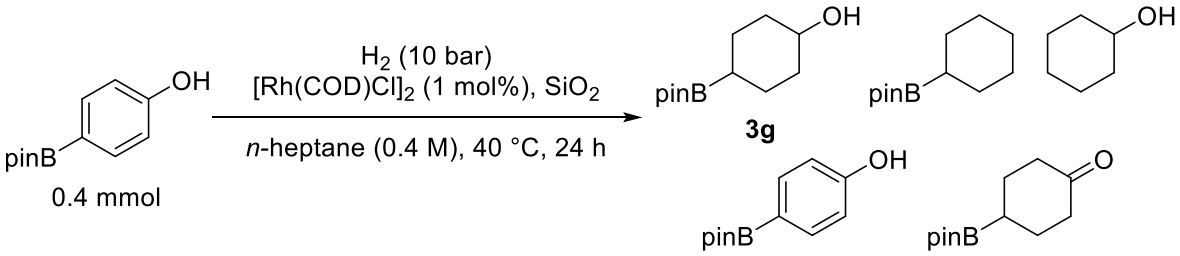
GC-MS (prior to purification):

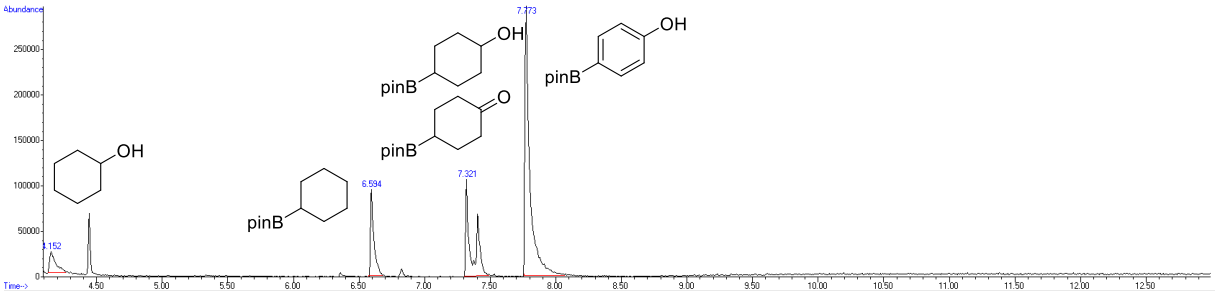
Rh-catalyzed (*cis*)



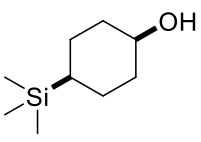
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.511	577	584	588	BV	496633	3652472	100.00%	76.189%
2	7.547	588	590	601	VB	123847	1141484	31.25%	23.811%

$[Rh(COD)Cl]_2$-catalyzed hydrogenation:





peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	4.152	8	11	30	M5	23721	750886	10.29%	5.946%
2	6.594	425	428	443	M2	96255	1750484	23.98%	13.861%
3	7.321	549	552	580	M3	107078	2827739	38.74%	22.391%
4	7.773	626	629	679	M	296555	7299931	100.00%	57.803%



3h, white solid, procedure **B**: [Rh–CAAC] 2 mol% catalyst loading, support: 4Å MS (50 mg), 20 bar H_2, solvent: *n*-heptane (0.4 M, 1.0 mL), temperature: 40 °C. Purification with 10% to 30% Et_2O in pentane. 92% total yield, 78:22 d.r. determined by GC-MS. The (volatile) major diastereomer was isolated and characterized (71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (m, *H*C1), 1.82 – 1.71 (m, 2H), 1.60 – 1.40 (m, 6H), 1.31 (s, 1H, *H*O), 0.56 (m, 1H, *H*C4), –0.05 (s, 9H, H_3C7);

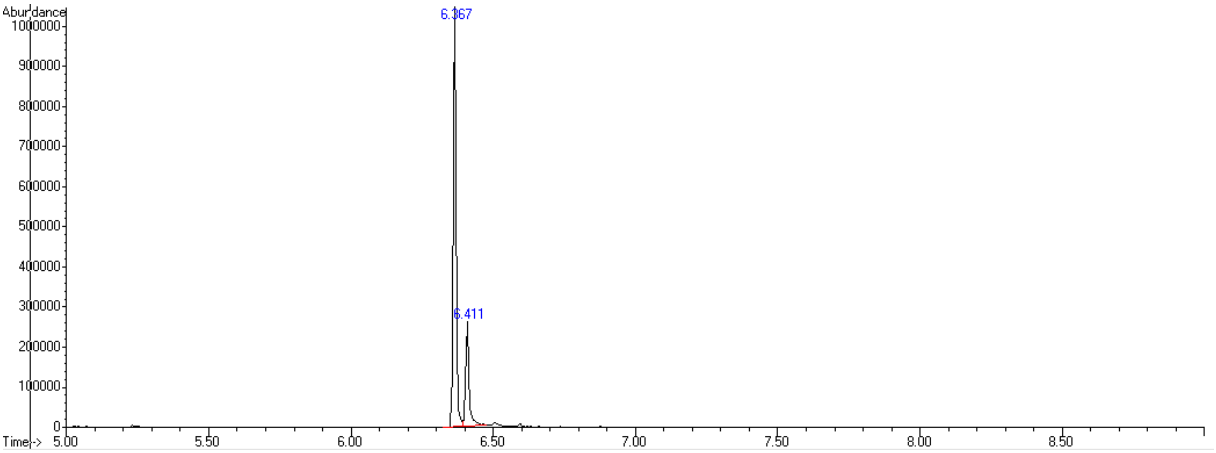
^{13}C NMR (101 MHz, $CDCl_3$) δ 66.9 (C1), 34.2, 25.6, 21.1, –3.3 (C7);

ESI-MS calculated $[C_9H_{20}O_3Si+Na]^+$: 195.1176, found: 195.1180;

IR $\tilde{\nu}$ = 3308, 2918, 1453, 1273, 1244, 1086, 999, 872, 829, 766, 745, 702, 687, 610;

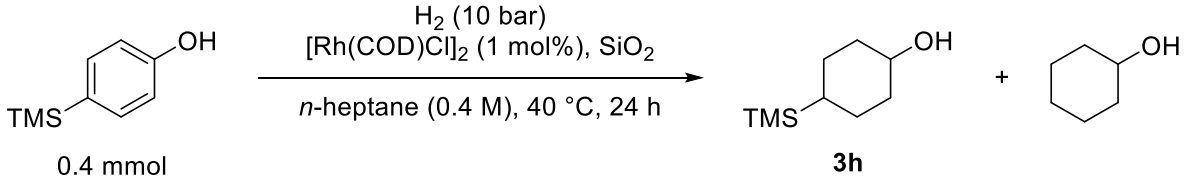
GC-MS (prior to purification):

Rh-catalyzed (*cis*)

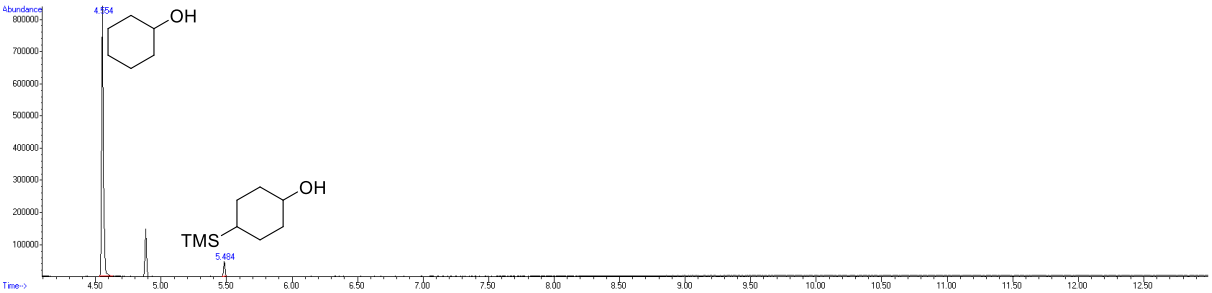


peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	6.367	382	389	393	BV	999551	7863922	100.00%	77.509%
2	6.411	393	397	408	VB	224652	2281920	29.02%	22.491%

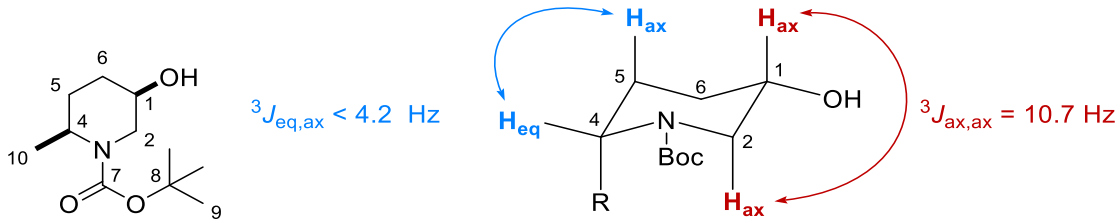
$[Rh(COD)Cl]_2$-catalyzed hydrogenation:



0.4 mmol **3h**



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	4.554	76	80	94	M	856880	7430607	100.00%	95.223%
2	5.484	236	238	242	M	47633	372763	5.02%	4.777%



3i, off-white solid, procedure **B**: [Rh–CAAC] 2 mol% catalyst loading, support: 4Å MS (50 mg), 10 bar H_2, solvent: *iso*-propanol (0.4 M, 1.0 mL), temperature: 40 °C. Boc-protection prior to isolation by addition of NEt_3 (1.5 equiv.) and Boc_2O (1.5 equiv.). Purification with 10% to 20% EtOAc in pentane. 98% total yield, 94:6 d.r. determined by GC-MS. The major diastereomer was isolated and characterized (88% yield). The *cis*-configuration was determined based on the $^3J_{ax,ax}$ coupling between H_{ax}C1 & H_{ax}C2 and $^3J_{eq,ax}$ coupling between H_{eq}C4 & H_{ax}C5. Determination of $^3J_{eq,ax}$ coupling between H_{eq}C4 & H_{ax}C5 was possible with homonuclear decoupling experiments by irradiation at H_3C10. The hydroxy group occupies the equatorial position, whereas the methyl group is in the axial position.

^{1}H NMR (599 MHz, $CDCl_3$) δ 4.32 (dm, $^3J_{eq,ax}$ < 4.2 Hz, 1H, H_{eq}C4), 4.12 – 4.05 (m, 1H, H_{eq}C2), 3.56 (dm, $^3J_{ax,ax}$ = 10.7 Hz, 1H, H_{ax}C1), 2.60 (dd, $^2J_{HH}$ = 12.8 Hz, $^3J_{ax,ax}$ = 10.7 Hz, 1H, H_{ax}C2), 2.18 (bs, 1H, *H*O), 1.86 (dm, $^2J_{HH}$ = 14.0 Hz, 1H, H_2C6), 1.73 – 1.64 (m, 1H, H_2C5), 1.58 – 1.50 (m, 2H, H_2C5, H_2C6), 1.44 (s, 9H, H_3C9), 1.12 (d, $^3J_{HH}$ = 6.9 Hz, 3H, H_3C10);

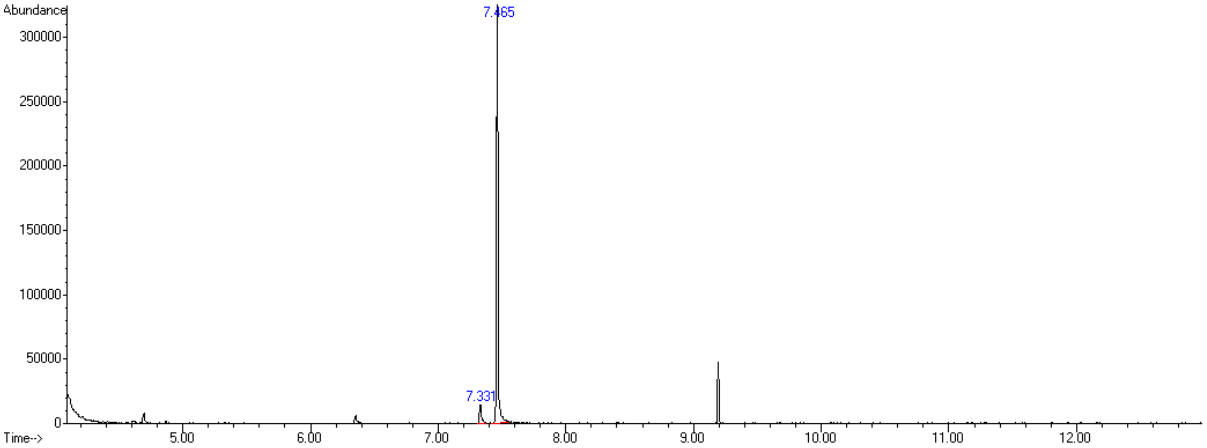
^{13}C NMR (151 MHz, $CDCl_3$) δ 154.9 (C7), 79.7 (C8), 67.6 (C1), 45.3 (C2), 45.1 (C4, overlapped), 28.6 (C9), 28.5 (C5), 28.4 (C6), 15.6 (C10);

ESI-MS calculated $[C_{11}H_{21}NO_3+Na]^+$: 238.1414, found: 238.1424;

IR $\tilde{\nu}$ = 3470, 2945, 1668, 1418, 1368, 1344, 1256, 1240, 1157, 1144, 1071, 1028, 999, 871, 768;

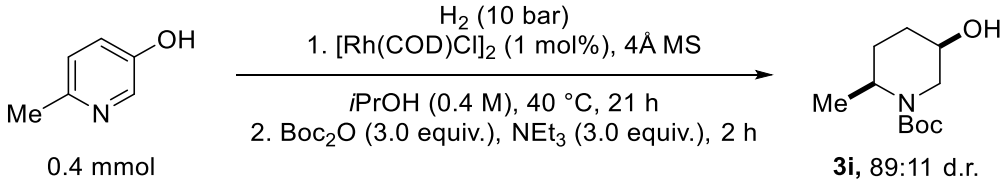
GC-MS (prior to purification):

Rh-catalyzed (*cis*)



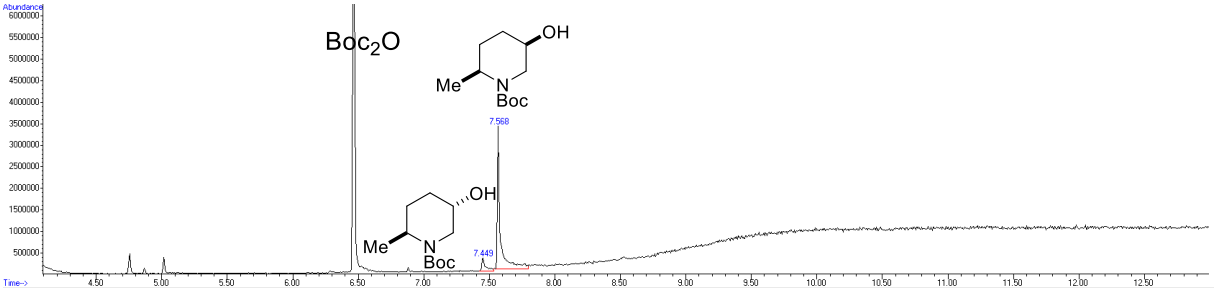
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.331	550	554	562	M	15564	167464	6.80%	6.365%
2	7.465	568	576	593	BB	274324	2463534	100.00%	93.635%

[Rh(COD)Cl]$_2$-catalyzed hydrogenation:



0.4 mmol

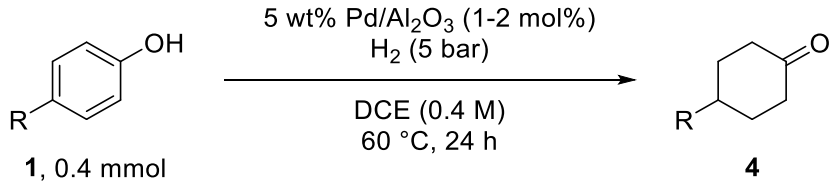
3i, 89:11 d.r.



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.449	569	574	588	M3	301624	6506353	12.81%	11.352%
2	7.568	591	594	633	M	3292835	50810545	100.00%	88.648%

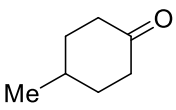
6. Synthesis of Cyclohexanones

General procedure C for the reduction of phenols to ketones



1, 0.4 mmol **4**

A 4 mL screw-cap glass vial, equipped with a magnetic stirring bar, was charged with 5 wt% Pd/Al_2O_3 (1-2 mol%) and solid substrates (0.4 mmol, 1.0 equiv.) as indicated. 1,2-dichloroethane (1.0 mL, 0.4 M) and liquid substrates were added. The prepared glass vial was placed in a 150 mL stainless steel autoclave under air. The autoclave was pressurized and depressurized with hydrogen gas three times before the indicated pressure was set. The reaction mixture was stirred at 60 °C for 24 h. After the autoclave was carefully depressurized, the crude mixture was purified by column chromatography on silica gel.



4a, colorless oil, procedure **C**: 1 mol% catalyst loading, 5 bar H_2. Purification with 50% CH_2Cl_2 in pentane. 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 – 2.28 (m, 4H), 2.06 – 1.95 (m, 2H), 1.94 – 1.81 (m, 1H), 1.48 – 1.35 (m, 2H), 1.02 (d, ^3J = 6.5 Hz, 3H);

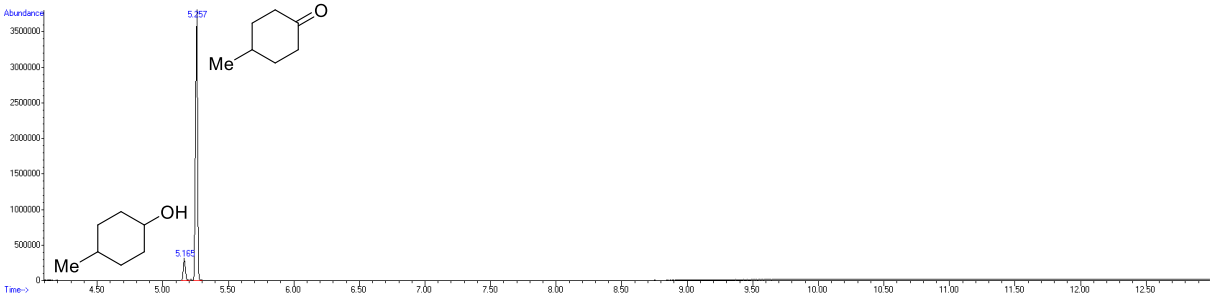
^{13}C NMR (101 MHz, $CDCl_3$) δ 211.3, 41.0, 34.9, 31.3, 21.2;

GC-MS (EI) 111.9 $[M]^+$ (100);

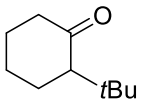
IR $\tilde{\nu}$ = 2955, 2929, 1754, 1714, 1459, 1288, 1244, 1185, 1124, 1047, 1004, 895, 806, 737;

Analytical data are in good accordance with those previously reported for this compound.[1]

GC-MS spectrum of the crude reaction mixture for product **4a**:



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	5.165	180	184	191	M	313258	2747767	7.83%	7.264%
2	5.257	196	200	207	M	3978476	35078935	100.00%	92.736%



4b, colorless oil, procedure **C**: 2 mol% catalyst loading, 5 bar H_2. Purification with 5% EtOAc in pentane. 85% yield.

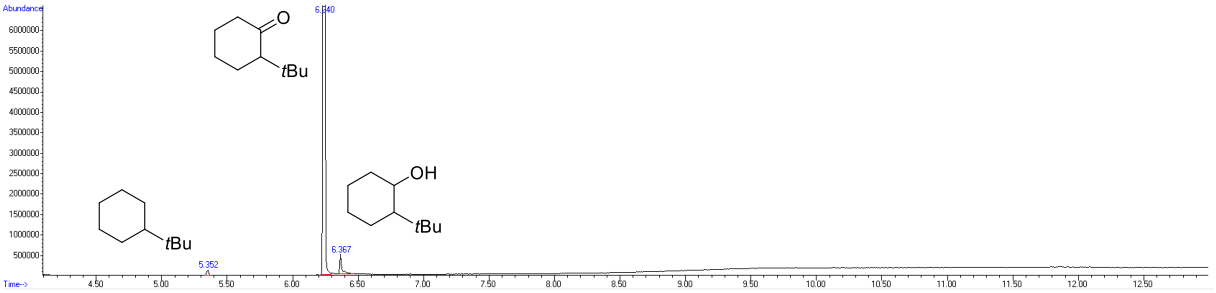
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 – 2.22 (m, 2H), 2.20 – 2.08 (m, 2H), 2.08 – 1.98 (m, 1H), 1.91 – 1.82 (m, 1H), 1.73 – 1.56 (m, 2H), 1.53 – 1.38 (m, 1H), 0.97 (s, 9H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 213.0, 60.4, 44.4, 32.0, 30.0, 28.8, 27.8, 26.2;

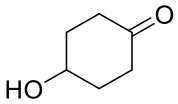
ESI-MS calculated $[C_{10}H_{18}O+Na]^+$: 177.1250, found: 177.1250.

Analytical data are in good accordance with those previously reported for this compound.[12]

GC-MS spectrum of the crude reaction mixture for product **4b**:



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	5.352	213	216	220	M	121294	1007573	0.27%	0.262%
2	6.240	363	367	377	M	39310063	376127903	100.00%	97.963%
3	6.367	385	389	422	M	483594	6812769	1.81%	1.774%



4c, yellow oil, procedure **C**: 2 mol% catalyst loading, 5 bar H_2. Purification with 30% to 50% EtOAc in pentane. 50% yield.

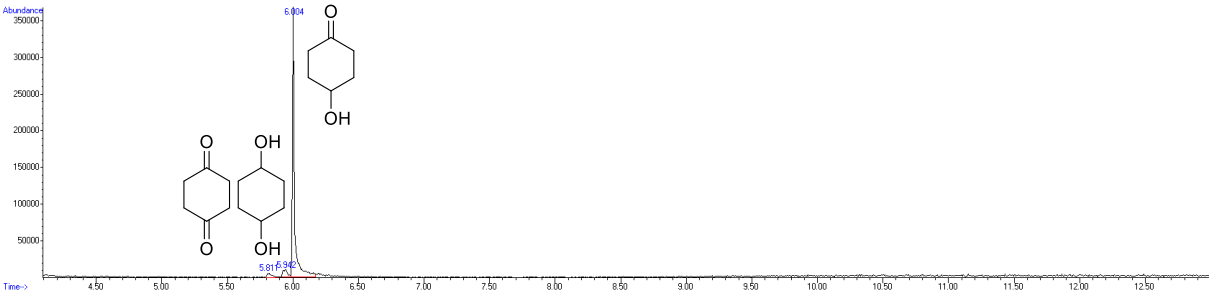
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 (tt, *J* = 6.6, 3.3 Hz, 1H), 2.68 – 2.52 (m, 2H), 2.36 – 2.23 (m, 2H), 2.10 – 1.91 (m, 4H), 1.86 (bs, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 211.1, 77.2, 66.4, 37.3, 33.9;

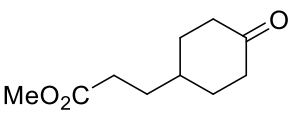
ESI-MS calculated $[C_6H_{10}O_2+Na]^+$ 137.0573, found: 137.0556.

Analytical data are in good accordance with those previously reported for this compound.[13]

GC-MS spectrum of the crude reaction mixture for product **4c**:



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	5.811	291	294	307	M4	5948	141506	3.52%	3.220%
2	5.942	312	317	324	M8	10037	227677	5.66%	5.181%
3	6.004	324	327	356	M	367808	4025598	100.00%	91.600%



4d, white solid, procedure **C**: 2 mol% catalyst loading, 5 bar H_2. Purification with 20% to 30% EtOAc in pentane. 70% yield.

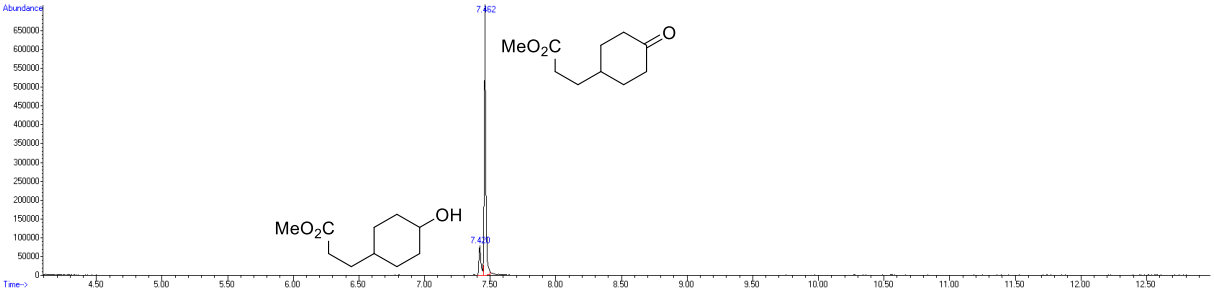
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3H), 2.41 – 2.26 (m, 6H), 2.08 – 2.01 (m, 2H), 1.79 – 1.69 (m, 1H), 1.69 – 1.63 (m, 2H), 1.46 – 1.34 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.9, 174.1, 51.8, 40.7, 35.6, 32.4, 32.0, 30.6;

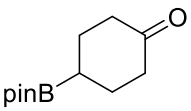
ESI-MS calculated $[C_{10}H_{16}O_3+Na]^+$: 207.0992, found: 207.1009;

IR $\tilde{\nu}$ = 2953, 2930, 1734, 1713, 1437, 1381, 1319, 1267, 1198, 1167, 1144, 980, 852, 733, 702.

GC-MS spectrum of the crude reaction mixture for product **4d**:



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.420	566	569	573	M	79393	856369	16.76%	14.354%
2	7.462	573	576	582	M	718200	5109867	100.00%	85.646%



4e, yellow oil, procedure **C**: 2 mol% catalyst loading, 5 bar H_2. Purification with 5% to 10% EtOAc in pentane. 73% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 – 2.20 (m, 4H), 2.11 – 1.98 (m, 2H), 1.79 (m, 2H), 1.32 (tt, $^3J_{HH}$ = 10.2, 3.9 Hz, 1H), 1.24 (s, 12H);

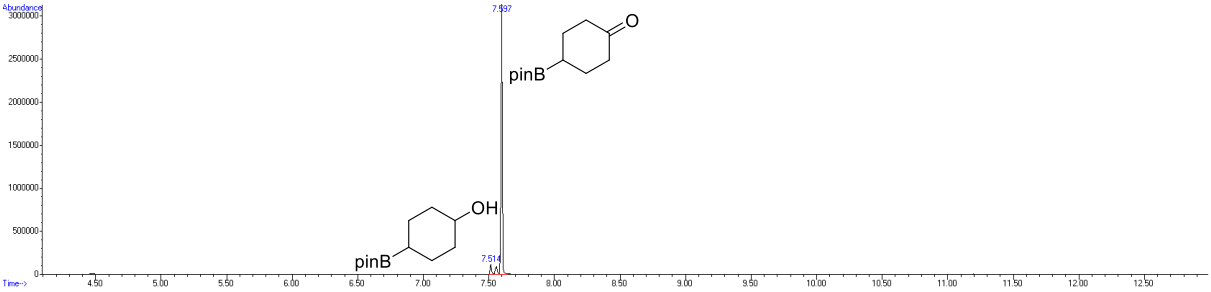
^{13}C NMR (75 MHz, $CDCl_3$) δ 212.7, 83.5, 42.4, 28.7, 24.9;

^{11}B NMR (96 MHz, $CDCl_3$) δ 33.5 (bs);

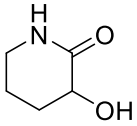
ESI-MS calculated $[C_{12}H_{21}BO_3+Na]^+$: 247.1478, found: 247.1494;

IR $\tilde{\nu}$ = 2976, 2931, 1713, 1379, 1339, 1316, 1225, 1142, 980, 966, 853, 772, 669.

GC-MS spectrum of the crude reaction mixture for product **4e**:



peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	7.514	582	585	596	M2	122039	1709327	7.86%	7.289%
2	7.597	596	599	606	M	3135609	21742202	100.00%	92.711%



4f, yellow oil, procedure **C**: 2 mol% catalyst loading, 5 bar H_2. Purification with 1% to 5% MeOH in CH_2Cl_2. 69% yield.

^{1}H NMR (500 MHz, Methanol-d_4) δ 4.05 (dd, J = 9.5, 5.8 Hz, 1H), 3.33 – 3.24 (m, 2H), 2.21 – 2.13 (m, 1H), 2.00 – 1.92 (m, 1H), 1.90 – 1.80 (m, 1H), 1.80 – 1.71 (m, 1H);

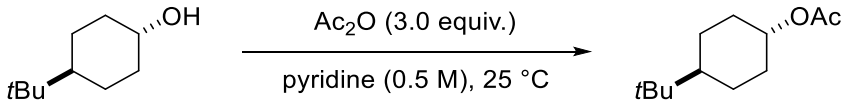
^{13}C NMR (126 MHz, Methanol-d_4) δ 175.6, 68.7, 42.9, 30.5, 21.1;

ESI-MS calculated $[C_5H_9NO_2+Na]^+$: 138.1212, found: 138.0511;

IR $\tilde{\nu}$ = 3251, 2955, 1653, 1559, 1457, 1374, 1288, 1091, 901, 827, 750;

Analytical data are in good accordance with those previously reported for this compound.[14]

7. Application



2d, >99:1 d.r. — **5**, 94%, >99:1 d.r. *trans-woody acetate*

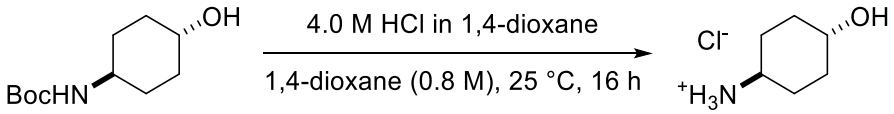
Acetic anhydride (85 µL, 0.9 mmol, 3.0 equiv.) was added to a solution of *trans*-4-*tert*-butylcyclohexanol (47 mg, 0.3 mmol, 1.0 equiv.) in pyridine (0.6 mL, 0.5 M) and stirred for 16 h at room temperature. After addition of water, the mixture was extracted with Et_2O (3 x 5 mL) and dried over magnesium sulfate. The crude product was purified by column chromatography on silica gel (5% Et_2O in *n*-pentane) to provide **5** as a colorless oil (56 mg, 0.28 mmol, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75 – 4.48 (m, 1H), 2.08 – 1.95 (m, 4H), 1.87 – 1.73 (m, 2H), 1.37 – 1.21 (m, 3H), 1.18 – 0.96 (m, 3H), 0.84 (s, 9H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 73.9, 47.2, 32.5, 32.2, 27.7, 25.6, 21.6;

ESI-MS calculated $[C_{12}H_{22}O_2+Na]^+$: 221.1512, found: 221.1511;

IR $\tilde{\nu}$ = 2946, 2864, 1735, 1468, 1452, 1367, 1240, 1046, 1027, 971, 904, 894.



2f, >99:1 d.r. — 99%

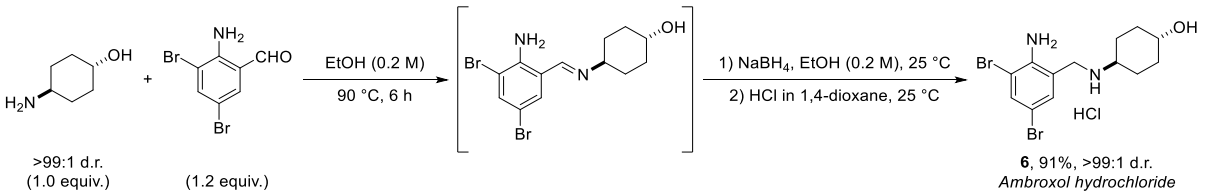
4.0 M HCl in 1,4-dioxane (2.6 mL, 10.5 mmol, 10.0 equiv.) was added to a solution of *trans*-4-Boc-aminocyclohexanol (226 mg, 1.05 mmol, 1.0 equiv.) in 1,4-dioxane (1.3 mL, 0.8 M). The mixture was stirred for 16 h at room temperature and the solvent was evaporated. The product was obtained as a white solid (160 mg, 1.05 mmol, 99%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 3.62 – 3.49 (m, 1H), 3.07 (t, J = 11.2 Hz, 1H), 2.03 (t, J = 10.5 Hz, 4H), 1.56 – 1.25 (m, 4H);

^{13}C NMR (101 MHz, Methanol-d_4) δ 69.5, 50.7, 33.8, 29.9;

ESI-MS calculated $[C_6H_{14}NO+H]^+$: 116.1070, found: 116.1068;

IR $\tilde{\nu}$ = 3250, 2932, 2898, 2854, 1683, 1630, 1613, 1537, 1460, 1391, 1365, 1162, 1071, 1050, 947, 899.



The synthesis was conducted according to a modified literature procedure.[15] A mixture of *trans*-4-aminocyclohexanol (115 mg, 1.0 mmol, 1.0 equiv.) and 2-amino-3,5-dibromobenzaldehyde (335 mg, 1.2 mmol, 1.0 equiv.) in ethanol (5.0 mL, 0.2 M) was heated to 90 °C for 6 h. After cooling to room temperature, $NaBH_4$ (91 mg, 2.4 mmol, 2.4 equiv.) was added and the mixture was stirred at room temperature for 17 h. Saturated, aqueous NH_4Cl solution was added to quench the reaction. The mixture was basified with saturated, aqueous K_2CO_3 solution and extracted with EtOAc (3 x 30 mL). The combined extracts were dried over magnesium sulfate and the crude product was purified by silica gel chromatography (5% MeOH in CH_2Cl_2). The product was dissolved in methanol and treated with 4M HCl in 1,4-dioxane. After evaporation of the solvent, Ambroxol hydrochloride **6** was obtained as a white solid (379 mg, 0.91 mmol, 91%).

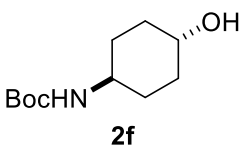
^{1}H NMR (400 MHz, Methanol-d_4) δ 7.64 (d, J = 2.2 Hz, 1H), 7.46 (d, J = 2.2 Hz, 1H), 4.24 (s, 2H), 3.63 – 3.52 (m, 1H), 3.22 (tt, J = 11.7, 3.8 Hz, 1H), 2.24 (d, J = 12.4 Hz, 2H), 2.07 (d, J = 11.0 Hz, 2H), 1.62 – 1.47 (m, 2H), 1.43 – 1.27 (m, 2H);

^{13}C NMR (101 MHz, Methanol-d_4) δ 144.8, 136.8, 134.4, 120.0, 112.0, 109.5, 69.6, 58.4, 46.2, 33.9, 28.2;

ESI-MS calculated $[C_{13}H_{19}Br_2N_2O+H]^+$: 376.9859, found: 378.9835;

IR $\tilde{\nu}$ = 3192, 2919, 2914, 2853, 2699, 2685, 1630, 1584, 1458, 1413, 1286, 1062, 896, 865.

8. X-ray Diffraction Data



2f

X-ray crystal structure analysis of **2f**: A colorless plate-like specimen of $C_{11}H_{21}NO_3$, approximate dimensions 0.052 mm x 0.069 mm x 0.120 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. A total of 2140 frames were collected. The total exposure time was 24.99 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 33803 reflections to a maximum θ angle of 69.27° (0.82 Å resolution), of which 4551 were independent (average redundancy 7.428, completeness = 99.7%, R_{int} = 7.66%, R_{sig} = 4.69%) and 4145 (91.08%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.8601(3) Å, b = 5.6544(2) Å, c = 44.1243(15) Å, volume = 2460.06(14) $Å^3$, are based upon the refinement of the XYZ-centroids of 9942 reflections above 20 σ(I) with 8.015° < 2θ < 138.3°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.792. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9230 and 0.9660. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group *Pca*2_1, with Z = 8 for the formula unit, $C_{11}H_{21}NO_3$. The final anisotropic full-matrix least-squares refinement on F^2 with 290 variables converged at R1 = 5.72%, for the observed data and wR2 = 13.08% for all data. The goodness-of-fit was 1.094. The largest peak in the final difference electron density synthesis was 0.226 $e^-/Å^3$ and the largest hole was -0.215 $e^-/Å^3$ with an RMS deviation of 0.053 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.163 g/cm^3 and F(000), 944 e^-. The hydrogens at O1A, O1B, N1A and N1B atoms were refined freely, but with distance restraints (SADI, DFIX, U-fixed value). CCDC Nr.: 2004851.

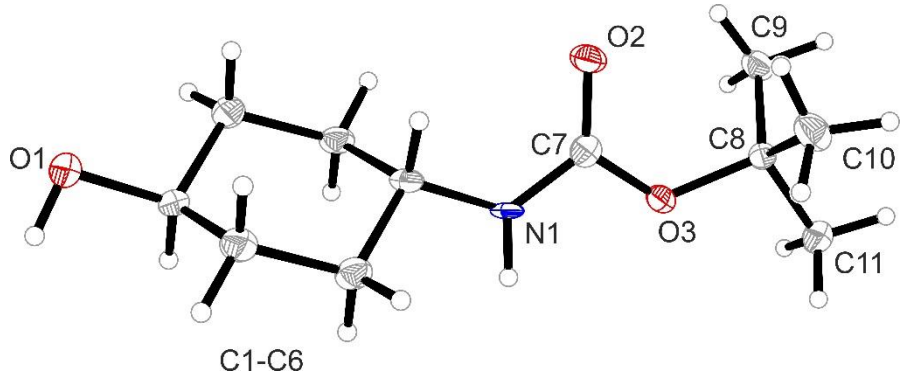
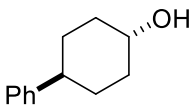


Figure S1. Crystal structure of compound **2f**. Thermal ellipsoids are shown at 30% probability.



2m

X-ray crystal structure analysis of **2m**: A colorless plate-like specimen of $C_{12}H_{16}O$, approximate dimensions 0.035 mm x 0.136 mm x 0.164 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. A total of 1243 frames were collected. The total exposure time was 22.04 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 10527 reflections to a maximum θ angle of 68.73° (0.83 Å resolution), of which 1794 were independent (average redundancy 5.868, completeness = 99.6%, R_{int} = 3.26%, R_{sig} = 2.44%) and 1589 (88.57%) were greater than $2\sigma(F^2)$. The final cell constants of a = 14.6389(3) Å, b = 5.30300(10) Å, c = 13.1361(3) Å, β = 106.9940(10)°, volume = 975.23(4) $Å^3$, are based upon the refinement of the XYZ-centroids of 5882 reflections above 20 σ(I) with 6.313° < 2θ < 137.4°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.895. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9120 and 0.9800. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_1/c$, with Z = 4 for the formula unit, $C_{12}H_{16}O$. The final anisotropic full-matrix least-squares refinement on F^2 with 122 variables converged at R1 = 3.41%, for the observed data and wR2 = 8.67% for all data. The goodness-of-fit was 1.049. The largest peak in the final difference electron density synthesis was 0.197 $e^-/Å^3$ and the largest hole was -0.197 $e^-/Å^3$ with an RMS deviation of 0.032 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.200 g/cm^3 and F(000), 384 e^-. The hydrogen at O1 atom was refined freely. CCDC Nr.: 2004853.

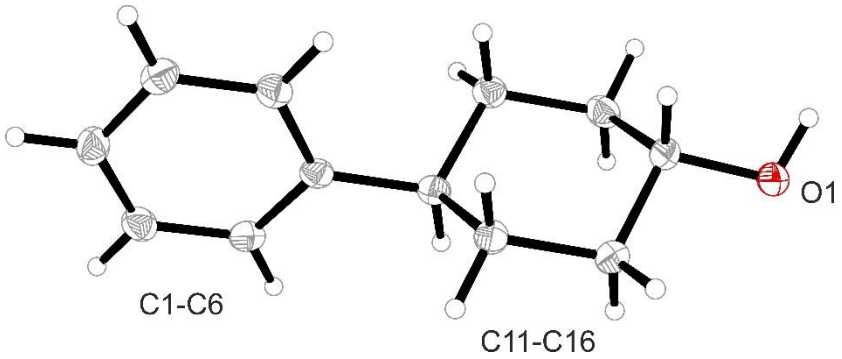
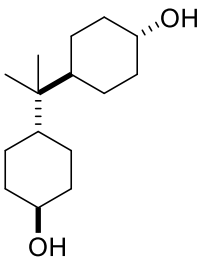


Figure S2. Crystal structure of compound **2m**. Thermal ellipsoids are shown at 50% probability.



2o

X-ray crystal structure analysis of **2o**: A colorless plate-like specimen of $C_{15}H_{28}O_2$, approximate dimensions 0.056 mm x 0.148 mm x 0.152 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. A total of 601 frames were collected. The total exposure time was 8.35 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 15292 reflections to a maximum θ angle of 66.87° (0.84 Å resolution), of which 2523 were independent (average redundancy 6.061, completeness = 99.1%, R_{int} = 6.24%, R_{sig} = 4.68%) and 2197 (87.08%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.1475(2) Å, b = 19.6782(5) Å, c = 7.9541(2) Å, β = 92.1100(10)°, volume = 1430.82(6) $Å^3$, are based upon the refinement of the XYZ-centroids of 8274 reflections above 20 σ(I) with 8.987° < 2θ < 133.6°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.776. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9210 and 0.9700. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_1/c$, with Z = 4 for the formula unit, $C_{15}H_{28}O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 165 variables converged at R1 = 7.29%, for the observed data and wR2 = 20.31% for all data. The goodness-of-fit was 1.122. The largest peak in the final difference electron density synthesis was 0.391 $e^-/Å^3$ and the largest hole was -0.403 $e^-/Å^3$ with an RMS deviation of 0.112 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.116 g/cm^3 and F(000), 536 e^-. The hydrogens at O1 and O2 atoms were refined freely. CCDC Nr.: 2004854.

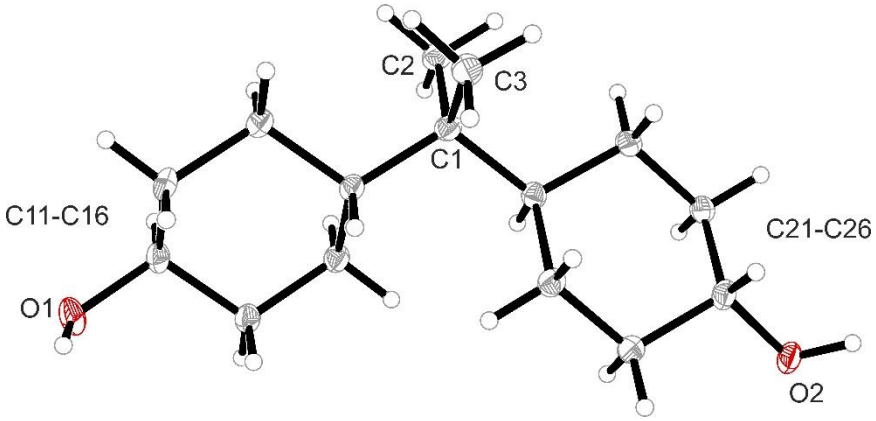
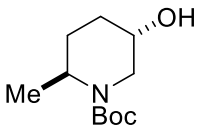


Figure S3. Crystal structure of compound **2o**. Thermal ellipsoids are shown at 50% probability.



2q

X-ray crystal structure analysis of **2q**: A colorless plate-like specimen of $C_{11}H_{21}NO_3$, approximate dimensions 0.075 mm x 0.079 mm x 0.158 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. A total of 2380 frames were collected. The total exposure time was 48.50 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 65017 reflections to a maximum θ angle of 66.59° (0.84 Å resolution), of which 2113 were independent (average redundancy 30.770, completeness = 99.8%, R_{int} = 10.21%, R_{sig} = 2.93%) and 1684 (79.70%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.2362(3) Å, b = 10.9879(3) Å, c = 23.7378(7) Å, volume = 2409.06(12) $Å^3$, are based upon the refinement of the XYZ-centroids of 9865 reflections above 20 σ(I) with 7.448° < 2θ < 134.4°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.856. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.8980 and 0.9500. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group *Pbca*, with Z = 8 for the formula unit, $C_{11}H_{21}NO_3$. The final anisotropic full-matrix least-squares refinement on F^2 with 141 variables converged at R1 = 5.90%, for the observed data and wR2 = 15.49% for all data. The goodness-of-fit was 1.071. The largest peak in the final difference electron density synthesis was 0.317 $e^-/Å^3$ and the largest hole was -0.219 $e^-/Å^3$ with an RMS deviation of 0.045 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.187 g/cm^3 and F(000), 944 e^-. CCDC Nr.: 2004852.

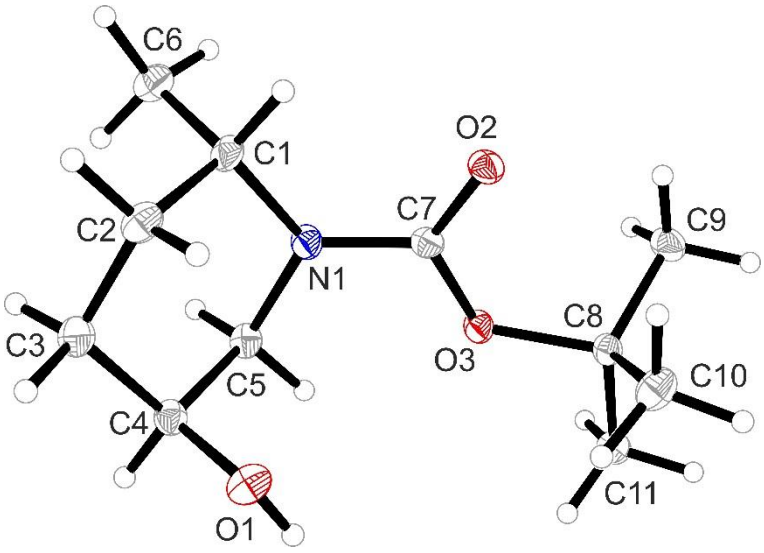
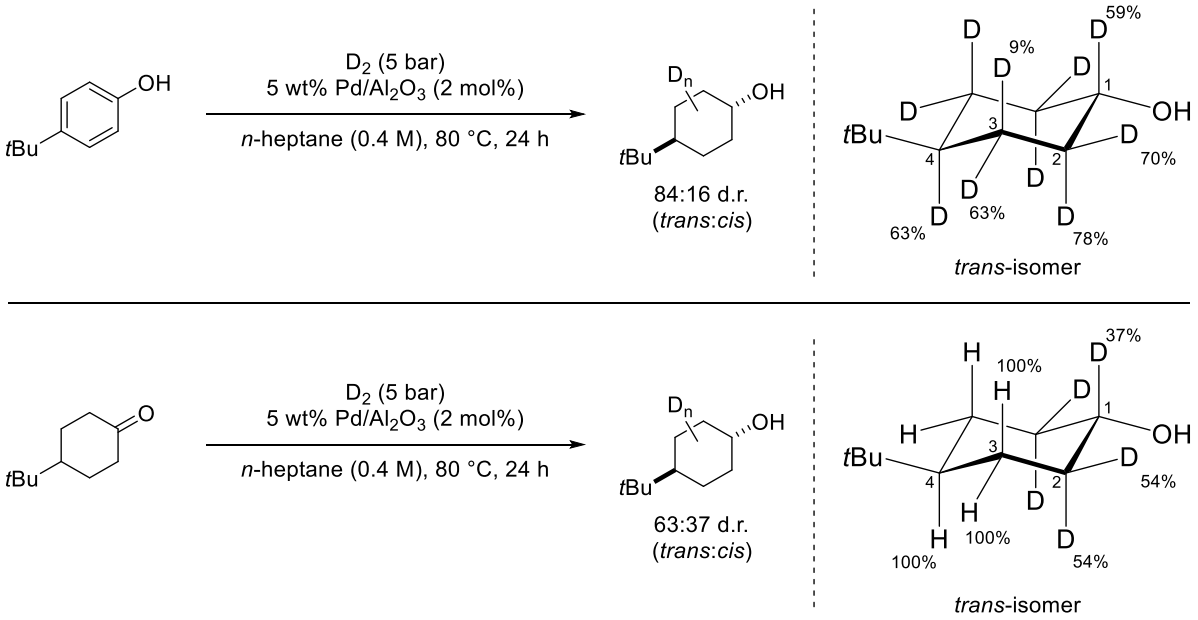


Figure S4. Crystal structure of compound **2q**. Thermal ellipsoids are shown at 15% probability.

9. Mechanistic Studies

9.1 Deuteration Experiments

The deuteration was conducted according to general procedure A for the *trans*-selective hydrogenation of phenols using deuterium gas instead of hydrogen gas. The major *trans*-isomer was isolated by column chromatography on silica gel and analyzed by ^{1}H and ^{2}H NMR spectroscopy.



Scheme S1. Deuteration of *p*-*t*Bu-phenol and 4-*t*Bu-cyclohexanone under standard conditions for the *trans*-selective hydrogenation of phenols. d.r. values determined by GC-MS analysis. All experiments conducted on 0.4 mmol scale.

Deuteration of *p*-*t*Bu-phenol revealed a *syn*-addition of D_2 at the 3- and 4-position (low deuterium incorporation at the axial position at carbon 3). Additionally, deuterium scrambling at the 2-position was observed, which can be rationalized due to the formation of keto-enol intermediates.

To test this hypothesis, we conducted the deuteration of 4-*t*Bu-cyclohexanone under identical conditions. Scrambling of deuterium at the 2-position supports the formation of enol intermediates in the deuteration of ketones and phenols.

9.2 Reaction Profile

The hydrogenation was conducted on a 0.4 mmol scale according to general procedure A for the *trans*-selective hydrogenation of phenols using 1 mol% catalyst loading (8.5 mg, 0.004 mmol, 1 mol%). The stirring was stopped after the indicated time and the hydrogen gas was released after a 30 min cool-down period of the autoclave to avoid boiling of the solvent.

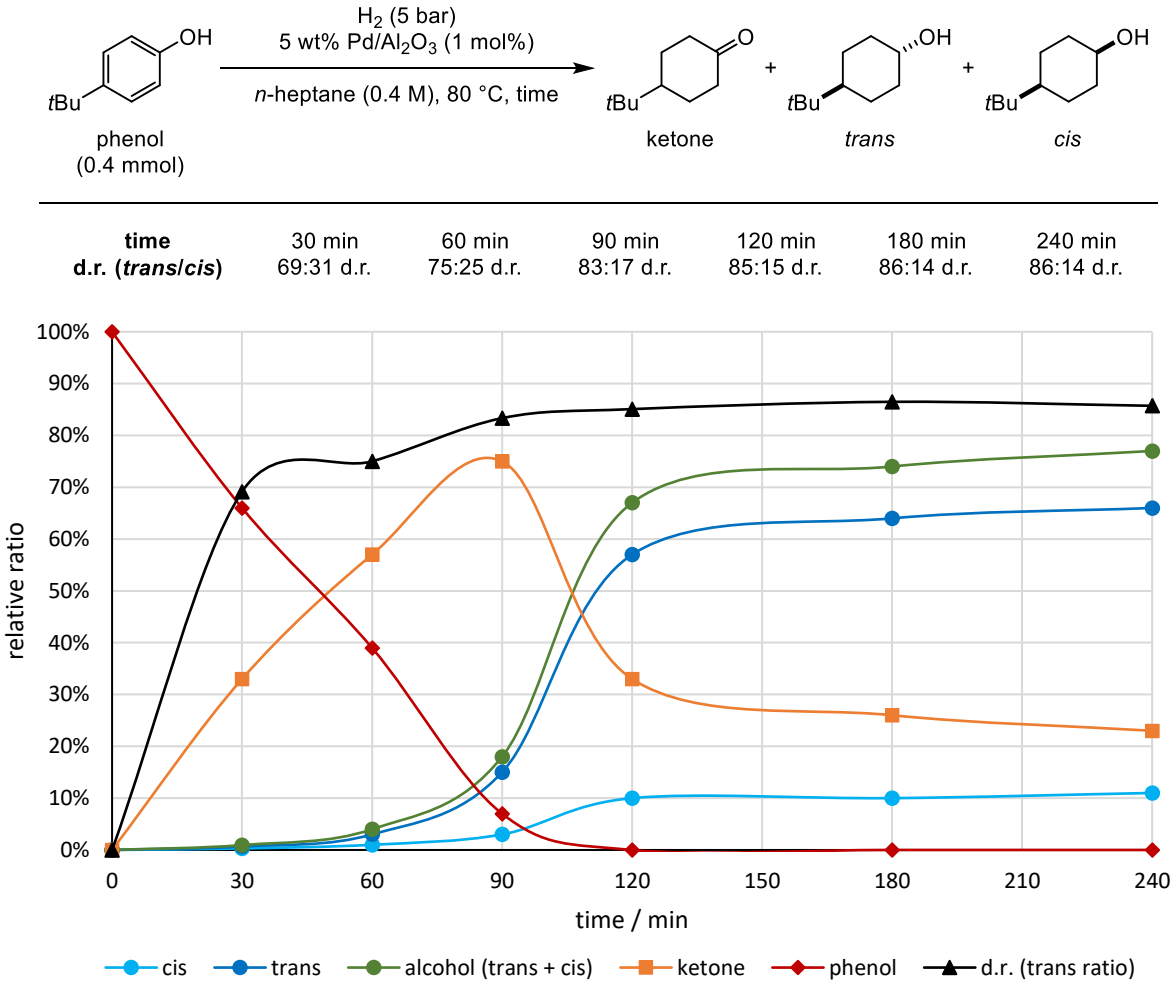
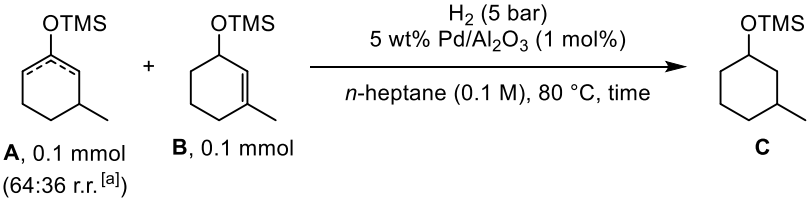


Figure S5. Reaction profile for the first 4 h of the hydrogenation of *p*-*t*Bu-phenol. Relative ratios and d.r. values determined by GC-MS analysis.

The starting material (*p*-*t*Bu-phenol) is quickly converted into the corresponding cyclohexanone and completely consumed after 120 min. With the consumption of the phenol the corresponding cyclohexanone reaches a maximum after around 90 min and is slowly consumed after 120 min (the effective concentration of cyclohexanone might be lower, since the corresponding enol form (unstable and short-lived) could not be detected by GC-MS and ^{1}H NMR analysis). The formation of the cyclohexanols is slow within the first 60 min of the reaction. With increasing concentration of the cyclohexanone, the formation of the alcohols increases. In the beginning of the reaction, the *cis*-isomer is formed faster compared to the later course of the reaction (30 min/69:31 d.r. and 60 min/75:25 d.r.). This can be rationalized with

a fast, continuous all-*syn*-addition of hydrogen to the aromatic phenol until the phenol is consumed. After consumption of the phenol, the *trans*-isomer can be formed *via* keto-enol formation (see deuteration experiments), combined with desorption and re-adsorption to the catalyst surface. The rate of hydrogenation for cyclohexanone to cyclohexanols is relatively low.

To test which double bond (enol or olefin) is hydrogenated faster, a competition experiment was conducted. To mimic the steric influence as good as possible, a trisubstituted alkene double bond, since enols are inherently trisubstituted, within a disubstituted cyclohexane derivative, was chosen as the model substrate (Scheme S2).



time	rel. ratio	rel. ratio	rel. ratio
30 min	43%	3%	54%
60 min	43%	3%	54%
90 min	32%	0%	68%
120 min	31%	0%	69%
180 min	30%	0%	70%

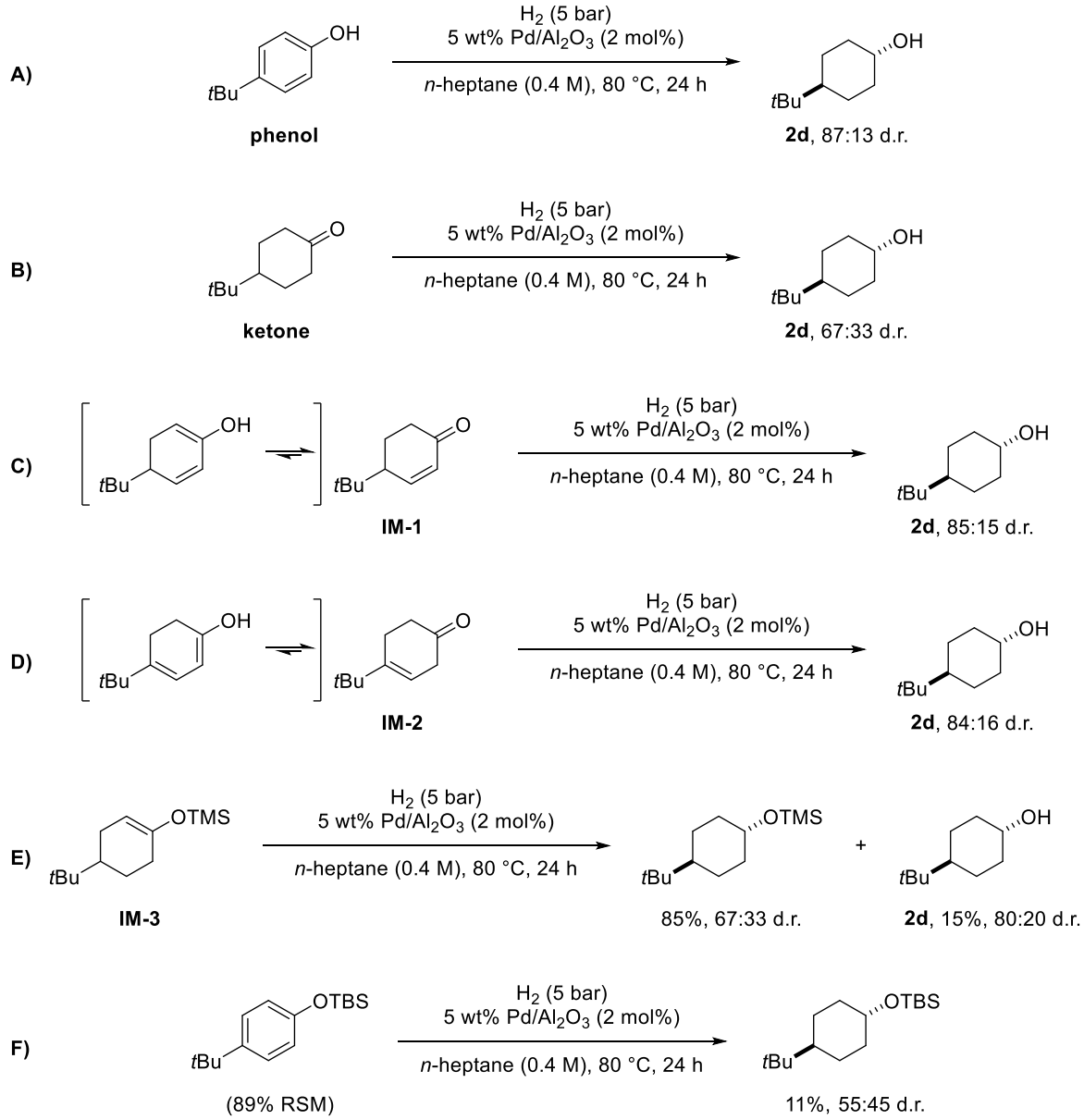
Scheme S2. Competitive hydrogenation of enol and alkene double bonds. The relative ratios were determined by ^{1}H NMR analysis of the crude reaction mixture. [a]Regiomeric ratio of the silyl enol ether was determined by ^{1}H NMR analysis.

A 1:1 ratio of substrates **A** and **B** was submitted to hydrogenation conditions and the crude reaction mixture was analyzed by ^{1}H NMR. Substrate **B**, bearing an alkene double bond, was almost completely hydrogenated after 30 min, whereas silyl enol ether **A** was hydrogenated with a significantly lower rate. Although the introduction of a TMS group to form a stable enol species is a manipulation of the substrate, it demonstrates, that the alkene double bond is hydrogenated at a significant higher rate.

The absence of olefins and enones as intermediates in the *trans*-selective hydrogenation of phenols can be explained by the fast hydrogenation of alkene double bonds under the employed conditions.

9.3 Hydrogenation of Intermediates

Enone intermediates **IM-1** and **IM-4** were synthesized by palladium-catalyzed dehydrogenative oxidation of 4-*t*Bu-cyclohexanone following a literature procedure.[16] **IM-2** was synthesized by a modified Birch reduction,[17] starting from *p*-*t*Bu-anisole, and subsequent acid-catalyzed hydrolysis of the corresponding methyl enol ether.[18] Silyl enol ether **IM-3** was synthesized according to a literature procedure.[19]



Scheme S3. Mechanistic experiments for the *trans*-selective hydrogenation of *p*-*t*Bu-phenol derivatives. Relative ratios and d.r. values determined by GC-MS analysis. All experiments conducted on 0.4 mmol scale.

A) *trans*-Selective hydrogenation under standard conditions (general procedure A).

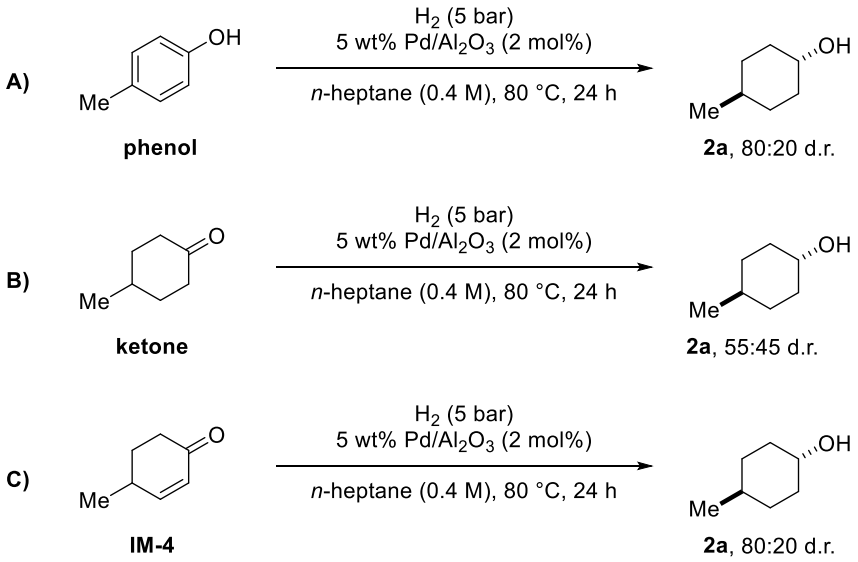
B) Hydrogenation of 4-*t*Bu-cyclohexanone under standard conditions: decrease in *trans*-selectivity → cyclohexanone not key intermediate for high *trans*-selectivity.

C) Hydrogenation of 4-*t*Bu-cyclohexenone **IM-1** under standard conditions: very low decrease in *trans*-selectivity → enone **IM-1** ("diene") possibly reaction intermediate in the *trans*-selective hydrogenation of phenols.

D) Hydrogenation of 4-*t*Bu-cyclohex-3-en-1-one **IM-2** under standard conditions: very low decrease in *trans*-selectivity → **IM-2** ("diene") possibly reaction intermediate in the *trans*-selective hydrogenation of phenols.

E) Hydrogenation of silyl enol ether **IM-3** under standard conditions: decrease in *trans*-selectivity → **IM-3** ("enol") provides *trans*-isomer as the major product, however the effect of the TMS group ("locked enol") is not negligible. Unprotected hydroxy group necessary for high *trans*-selectivity. Additionally, cleavage of the silyl ether was observed.

F) Hydrogenation of TBS-protected *p*-*t*Bu-phenol: low reactivity of non-phenolic arenes under palladium-catalyzed standard conditions (89% remaining starting material).



Scheme S4. Mechanistic experiments for the *trans*-selective hydrogenation of *p*-cresol derivatives. d.r. values determined by ^{1}H NMR analysis. All experiments conducted on 0.4 mmol scale.

A) *trans*-Selective hydrogenation under standard conditions (general procedure A).

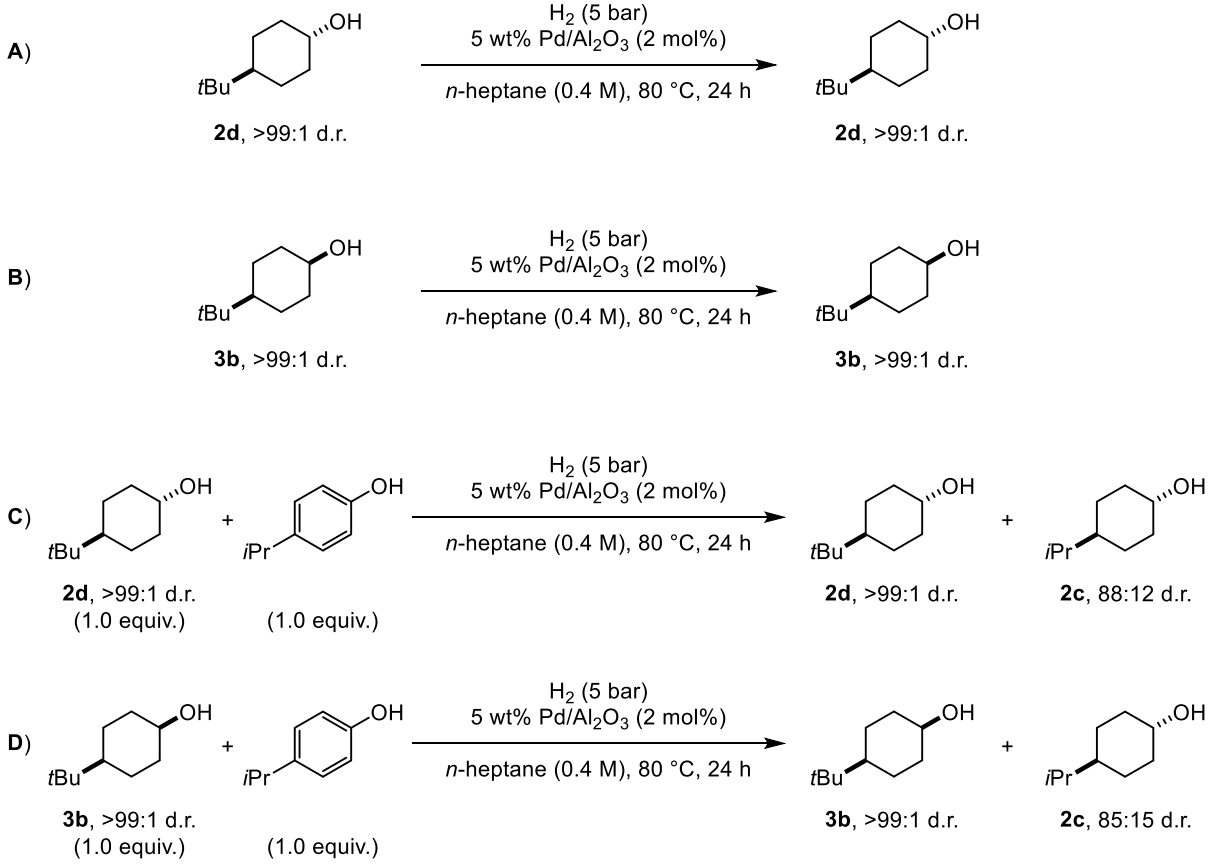
B) Hydrogenation of 4-Me-cyclohexanone under standard conditions: significant decrease in *trans*-selectivity → cyclohexanone not key intermediate for high *trans*-selectivity.

C) Hydrogenation of 4- Me-cyclohexenone **IM-4** under standard conditions: retention of *trans*-selectivity → enone **IM-4** ("diene") possibly reaction intermediate in the *trans*-selective hydrogenation of phenols.

Comparison of the diastereoselectivity in the direct hydrogenation of 4-*t*Bu-cyclohexanone (67:33 d.r., Scheme S3, B) and 4-Me-cyclohexanone (55:45 d.r., Scheme S4, B) reveals, that the existing stereocenter has an influence on the desorption and re-adsorption on the surface. Sterically more demanding substituents in the 4-position favor the process of desorption and have a beneficial influence on the *trans*-selectivity.

This trend can also be seen by comparison of the diastereoselectivity in the *trans*-selective hydrogenation of phenols (manuscript Scheme 2, substrates **2a-e**). With increasing steric bulk in *para*-position, the diastereomeric ratio increases.

9.4 Isomerization Experiments



Scheme S5. Isomerization experiments with *trans*- and *cis*-4-*t*Bu-cyclohexanol. d.r. values determined by GC-MS analysis. All experiments conducted on 0.4 mmol scale.

A) Hydrogenation of diastereomerically pure *trans*-4-*t*Bu-cyclohexanol under standard conditions: no isomerization under reaction conditions → d.r. not driven by equilibrium.

B) Hydrogenation of diastereomerically pure *cis*-4-*t*Bu-cyclohexanol under standard conditions: no isomerization under reaction conditions → d.r. not driven by equilibrium.

C) Hydrogenation of diastereomerically pure *trans*-4-*t*Bu-cyclohexanol in the presence of *p*-*i*Pr-phenol under standard conditions: no isomerization under reaction conditions for successful *trans*-selective phenol hydrogenation.

D) Hydrogenation of diastereomerically pure *cis*-4-*t*Bu-cyclohexanol in the presence of *p*-*i*Pr-phenol under standard conditions: no isomerization under reaction conditions for successful *trans*-selective phenol hydrogenation.

9.5 Mechanistic Summary

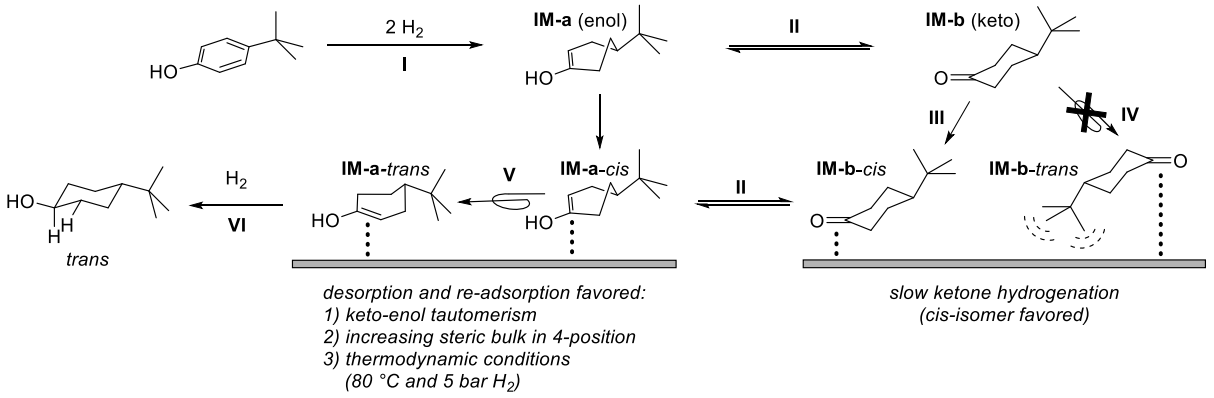


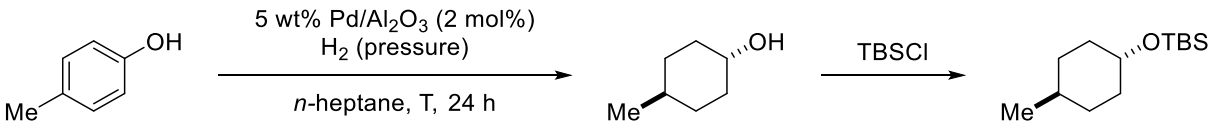
Figure S6. Tentative schematic representation of the mechanism for the *trans*-selective hydrogenation of *p*-*t*Bu-phenol catalyzed by Pd/Al_2O_3.

p-*t*Bu-phenol is quickly converted into the corresponding cyclohexanone (**I**). With consumption of the phenol the cyclohexanone concentration increases. The cyclohexanone is in equilibrium with the corresponding enol intermediate (**II**, shown by deuterium scrambling, chapter 9.1). With increasing concentration of the cyclohexanone, the formation of cyclohexanols starts. The direct hydrogenation of the ketone intermediate **IM-b** is relatively slow (chapter 9.2). The *cis*-cyclohexanol could be formed by slow, direct ketone hydrogenation of **IM-b**-*cis* (**III**) or fast, continuous phenol hydrogenation (all-*syn* H_2-addition). The direct formation of the *trans*-cyclohexanol, starting from the ketone, is disfavored because of steric interactions (**IV**).

Therefore, the favored reaction pathway for the formation of the *trans*-isomer is the hydrogenation of diene and enol intermediate **IM-a**, which can be formed by keto-enol tautomerism on the catalyst surface (**II**). **IM-a**-*trans* is formed by the desorption of **IM-a**-*cis* and re-adsorption as **IM-a**-*trans* (**V**). The process of desorption and re-adsorption could be facilitated *via* the formation of the more stable ketone intermediate **IM-b** (**II**). In addition, the process is favored with increasing steric bulk in the 4-position and by the high reaction temperatures. Finally, *syn*-addition of hydrogen to **IM-a**-*trans* provides the desired *trans*-cyclohexanol (**VI**).

Key to the high *trans*-selectivity in the hydrogenation of *p*-*t*Bu-phenol (87:13 d.r.) compared to the direct hydrogenation of 4-*t*Bu-cyclohexanone (67:33 d.r.) could be the low concentration of the cyclohexanone intermediate. The effective concentration of cyclohexanone might be even lower, since the unstable and short-lived diene and enol intermediates could not be detected with our analytical tools. The low cyclohexanone concentration disfavors the direct ketone hydrogenation, which would lead to the *cis*-isomer, and favors the tautomerization, as well as desorption and re-adsorption, leading to an increased *trans* ratio.

10. Reaction-Condition Based Sensitivity Assessment



The sensitivity assessment of general procedure A was conducted by following a modified procedure from Glorius and coworkers.[20] A description of the experiments included in the assessment is given in Table S9. Each reaction was prepared separately. Volume changes due to solvation of starting materials were neglected. All reactions were run in a suitable autoclave and stopped after 24 h. After the autoclave was carefully depressurized, the crude mixture was diluted with CH_2Cl_2 (1.0 mL) and imidazole (2.5 equiv.), DMPA (0.2 equiv.) and TBSCl (2.0 equiv.) were added. The mixture was stirred at 40 °C for 16 h. Mesitylene was added as an internal standard and yield and diastereomeric ratio were determined by GC-FID analysis. The deviation from the yield of the 'standard' experiment was calculated for each experiment (Table S10). The deviation values are plotted in a radar diagram.

Standard conditions: n = 0.1 mmol, c = 0.1 M, V = 1.0 mL, T = 80 °C, $p(H_2)$ = 5 bar.

Table S9. Preparation of sensitivity assessment of general procedure **A**.

Number	Experiment	Preparation[a]
0	Standard	Standard
1	high *c*	From 0.1 M (1.0 mL) to 0.2 M (0.5 mL)
2	low *c*	From 0.1 M (1.0 mL) to 0.05 M (2.0 mL)
3	H_2O	Add water (10 µL)
4	low $p(H_2)$	From 5 bar to 3 bar
5	high $p(H_2)$	From 5 bar to 7 bar
6	low *T*	From 80 °C to 60 °C
7	high *T*	From 80 °C to 100 °C
8	high O_2	No H_2 fill-and-release cycle for the autoclave
9	low O_2	Setup under argon atmosphere
10	big scale	Big scale (2.0 mmol, 0.2 M, V = 10.0 mL, 2 mol%)

[a]Pd/Al_2O_3 (4.3 mg, 0.002 mmol, 2 mol%) was added to each reaction vessel.

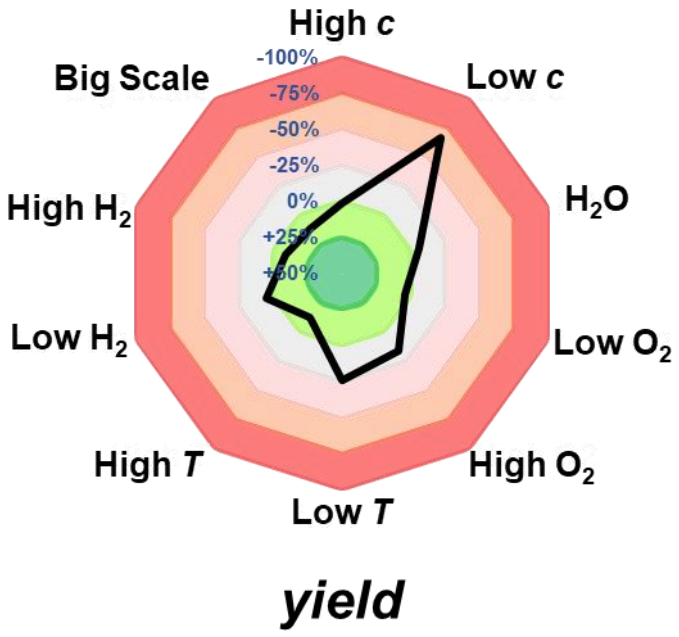
Results:

TableS10. Results of sensitivity assessment of general procedure **A**.

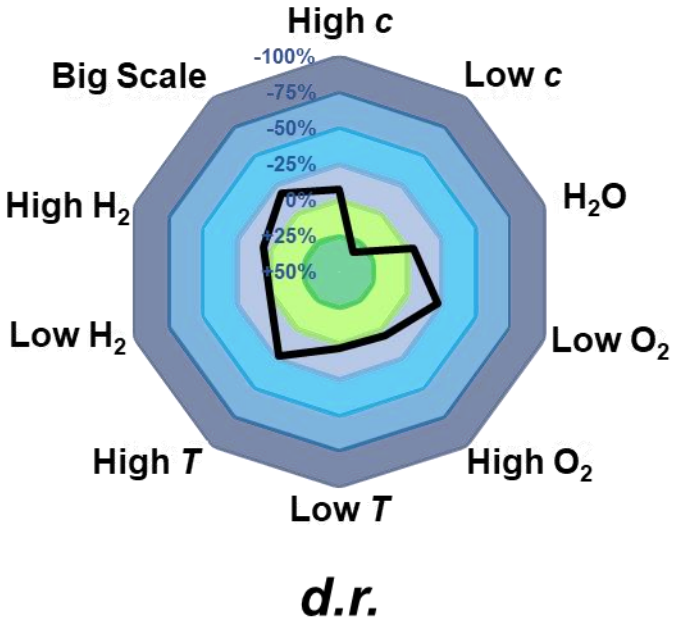
Number	Experiment	Yield / %	Deviation / %	d.r.[a]	Deviation / %
0	Standard	90	-	80:20	-
1	high *c*	90	1	79:21	-7
2	low *c*	31	-66	84:16	33
3	H_2O	84	-6	79:21	-4
4	low *p*(H_2)	84	-5	80:20	-1
5	high *p*(H_2)	96	9	79:21	-6
6	low *T*	68	-24	80:20	-3
7	high *T*	99	12	76:24	-22
8	high O_2	75	-16	79:21	-5
9	low O_2	93	4	76:24	-22
10	big scale	99	12	77:23	-18

[a]Diastereomeric ratio given as *trans*/*cis* ratio.

Sensitivity: yield



Sensitivity: d.r.



The influence on yield and diastereoselectivity was investigated by systematic variation of key reaction parameters. Notably, the yield of the reaction was found to be sensitive towards low concentration but tolerable of a range of hydrogen pressures, the presence of water, and variable oxygen levels. In general, the diastereoselectivity was insensitive towards any variation in the reaction conditions. However, there was a slight increase in diastereoselectivity connected with a drastic loss of yield when lowering the concentration.

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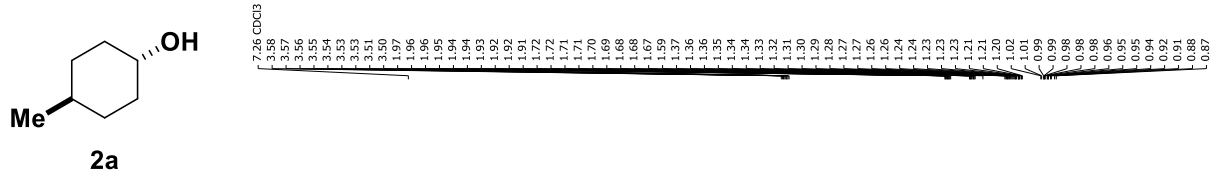
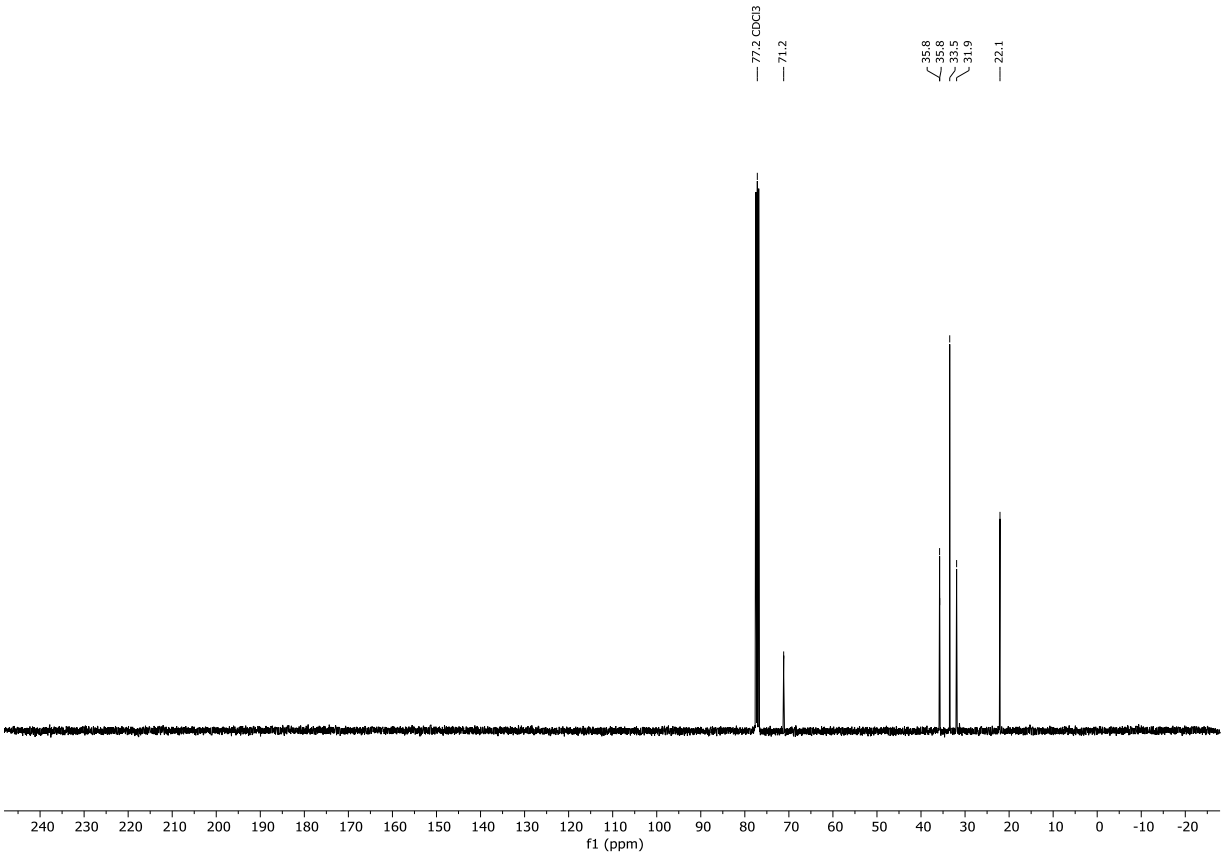
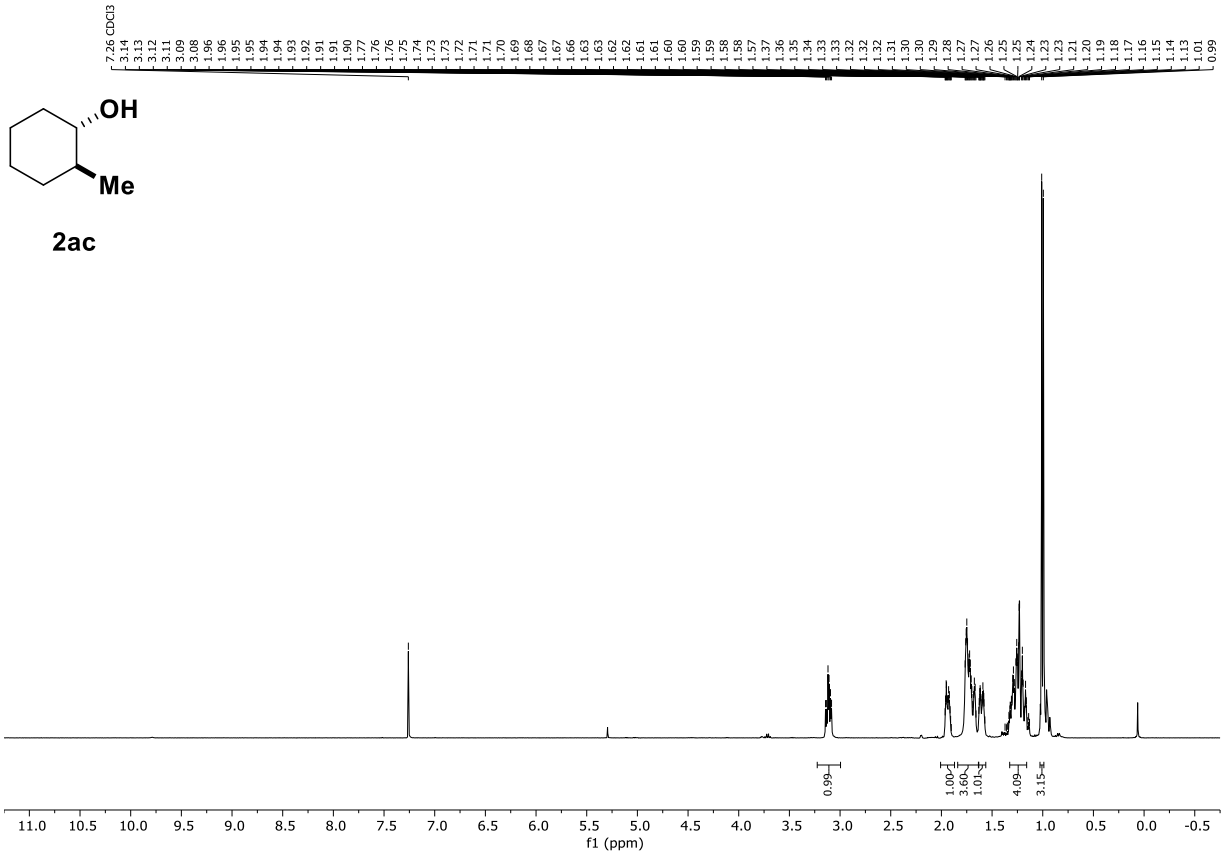
12. NMR Spectra

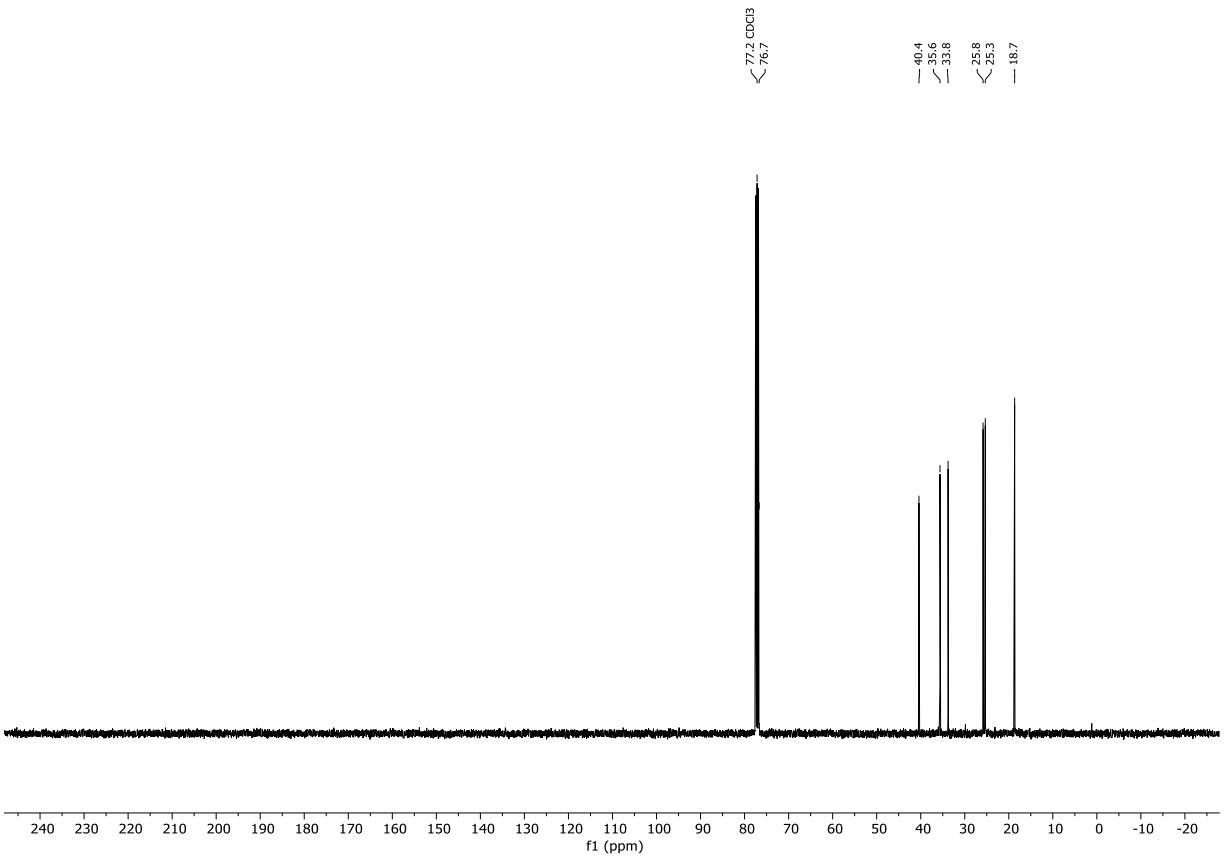
11.1 *trans*-Cyclohexanols

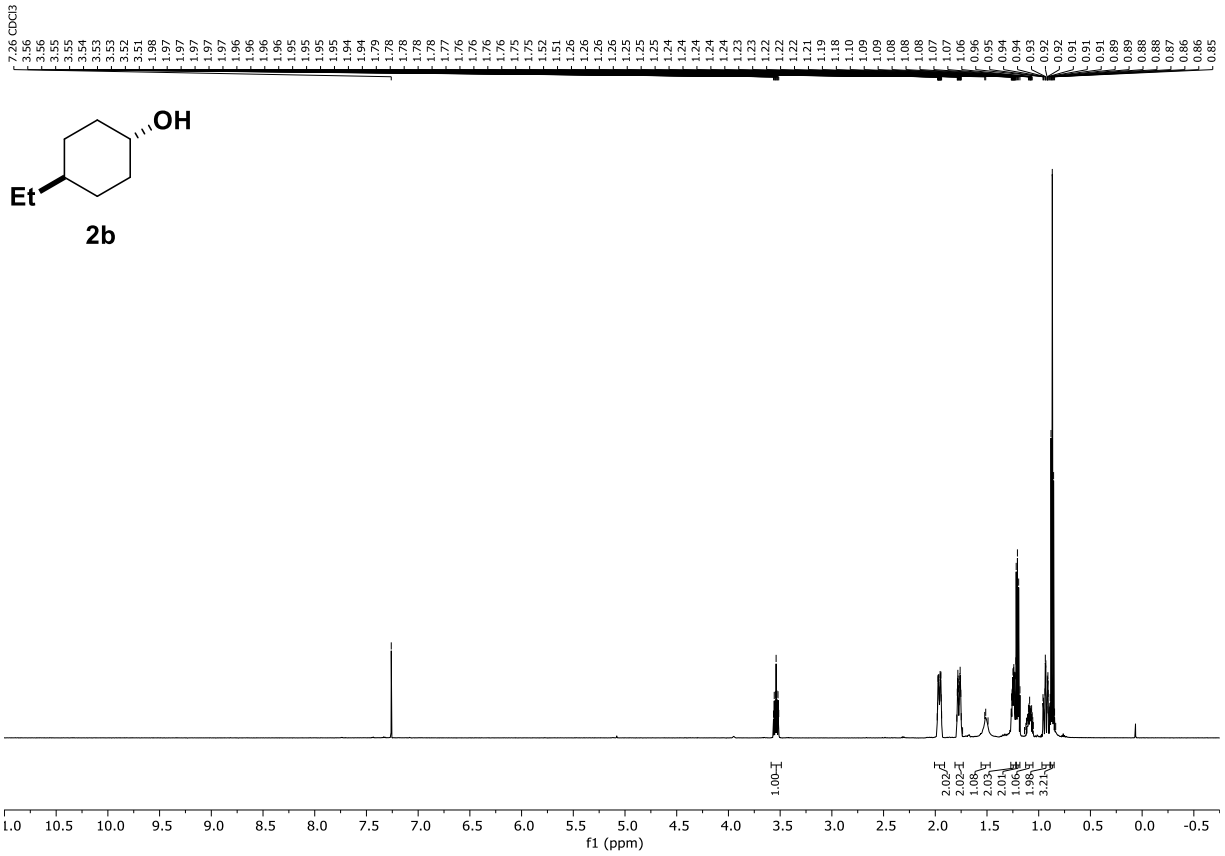


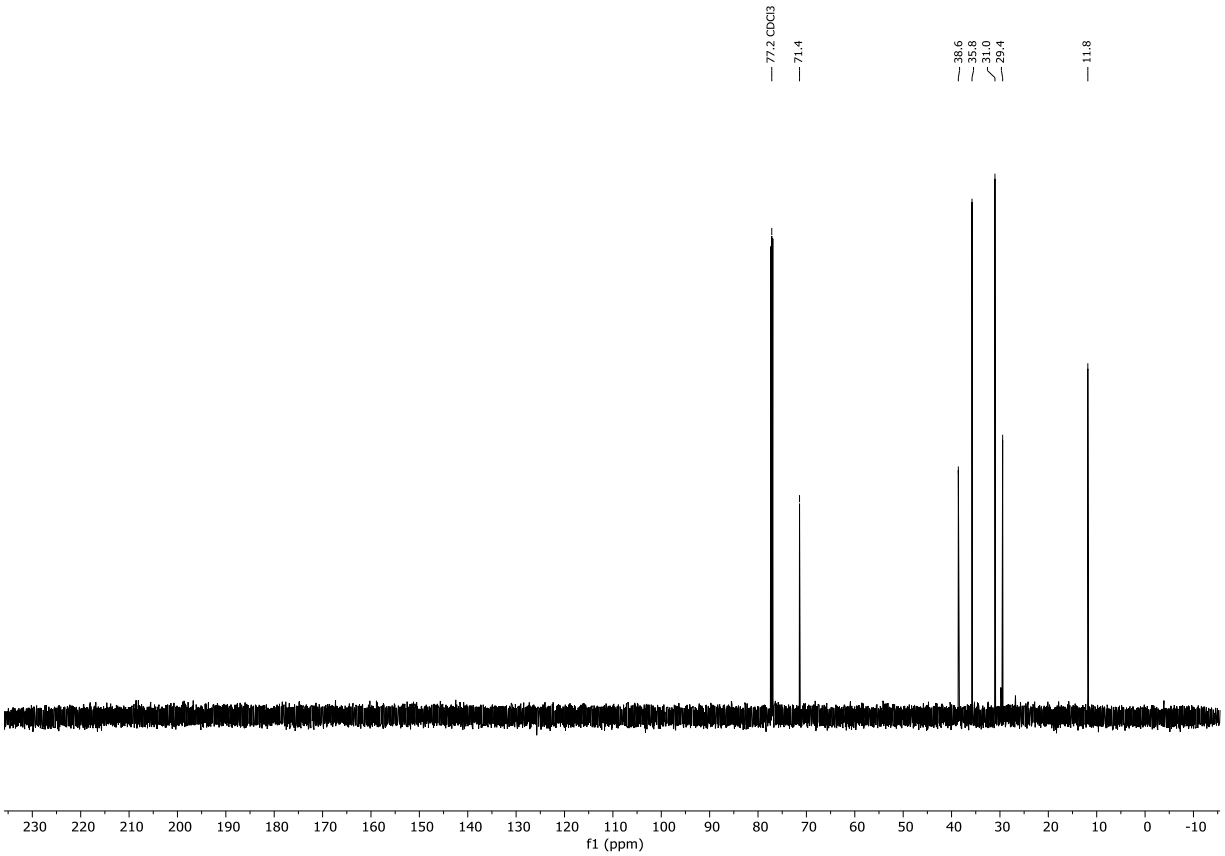
2a

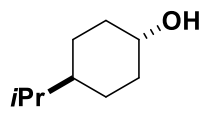



7.26 CDCl3
OH
Me
2ac
0.99
1.00
3.60
1.01
4.09
3.15
f1 (ppm)


77.2 CDCl3
76.7
40.4
35.6
33.8
25.8
25.3
18.7
f1 (ppm)

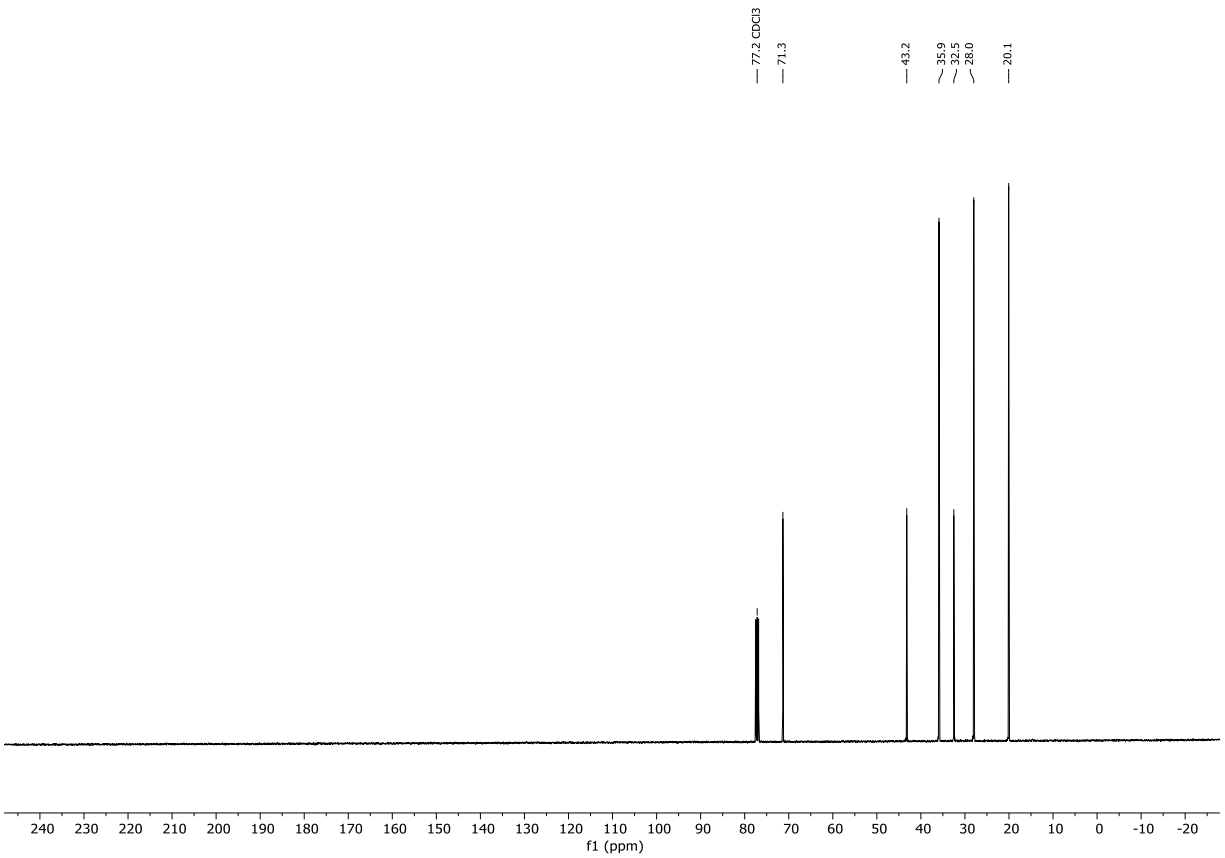

7.26 CDCl3
OH
Et
2b
1.00
2.02
2.02
1.08
2.03
2.01
1.06
1.98
3.21
f1 (ppm)

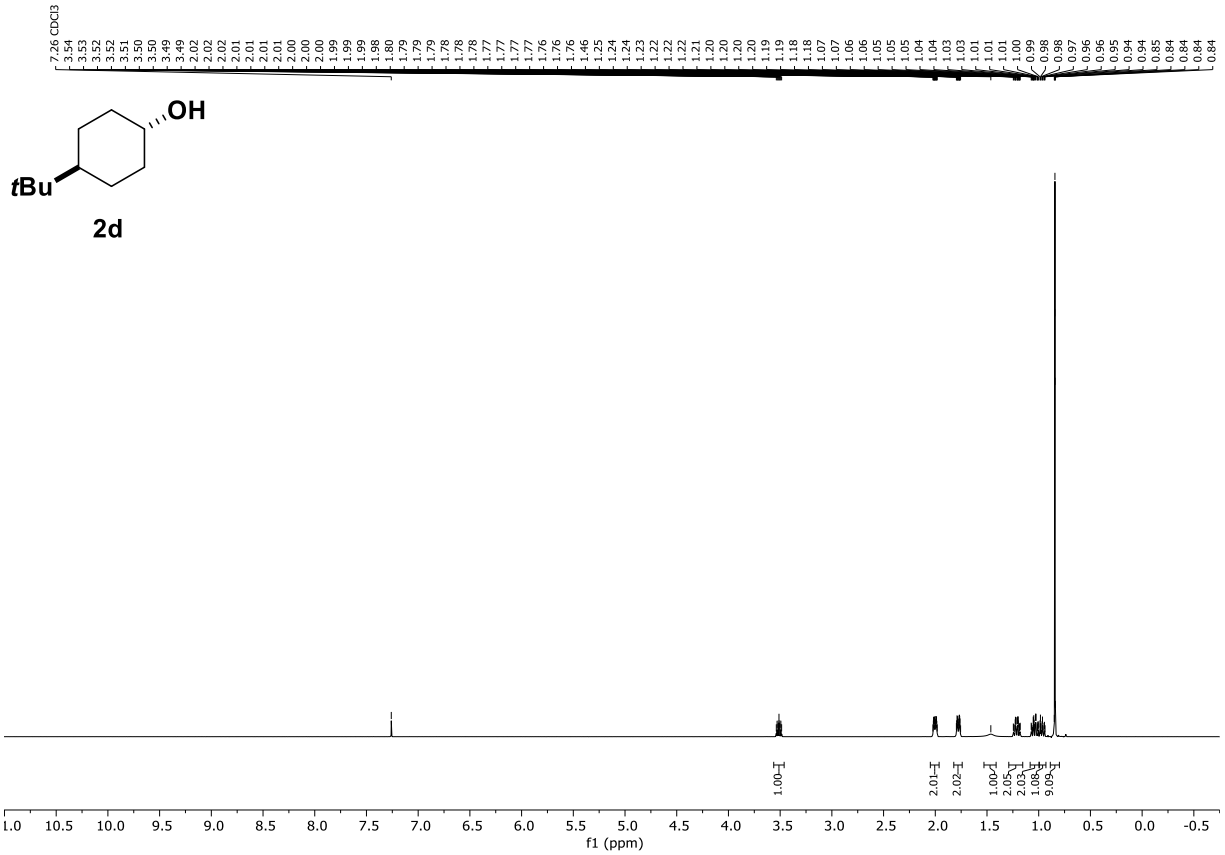

77.2 CDCl3
71.4
38.6
35.8
31.0
29.4
11.8
f1 (ppm)

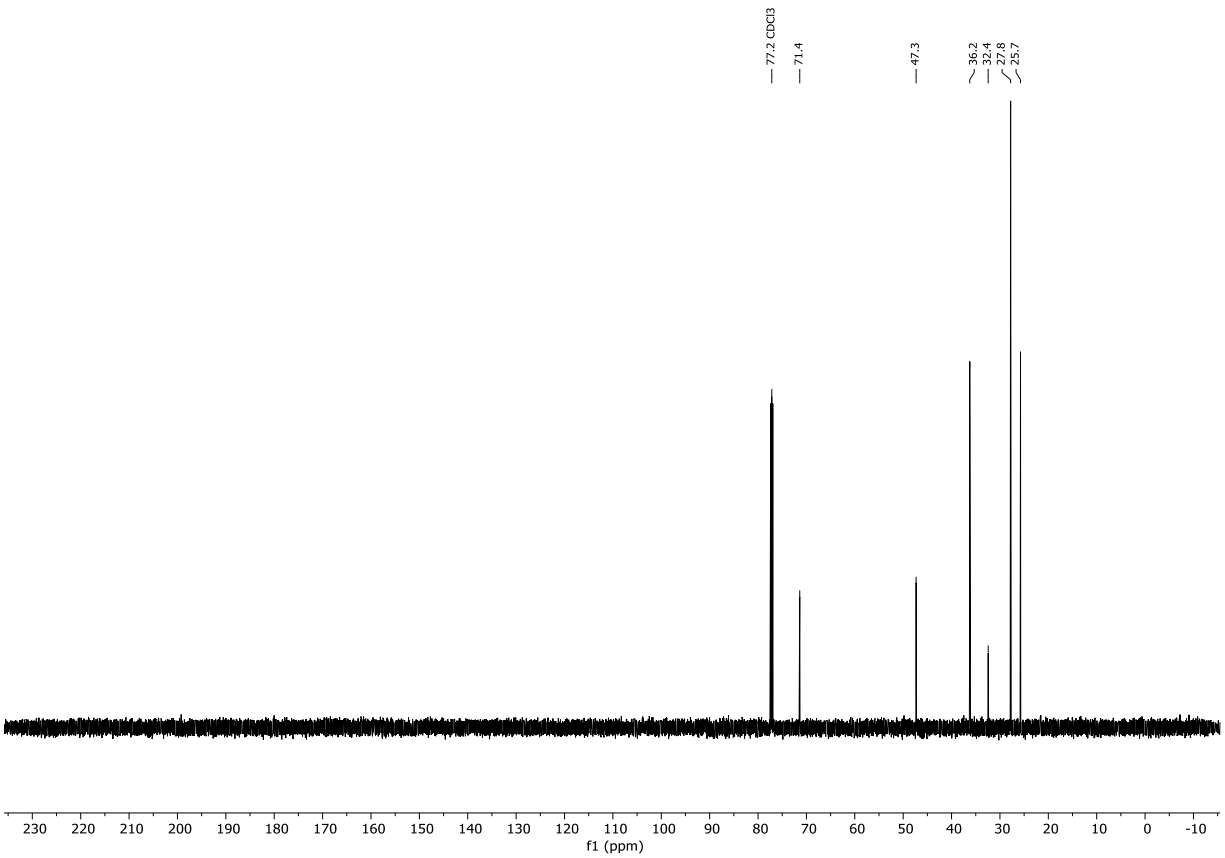

OH
iPr

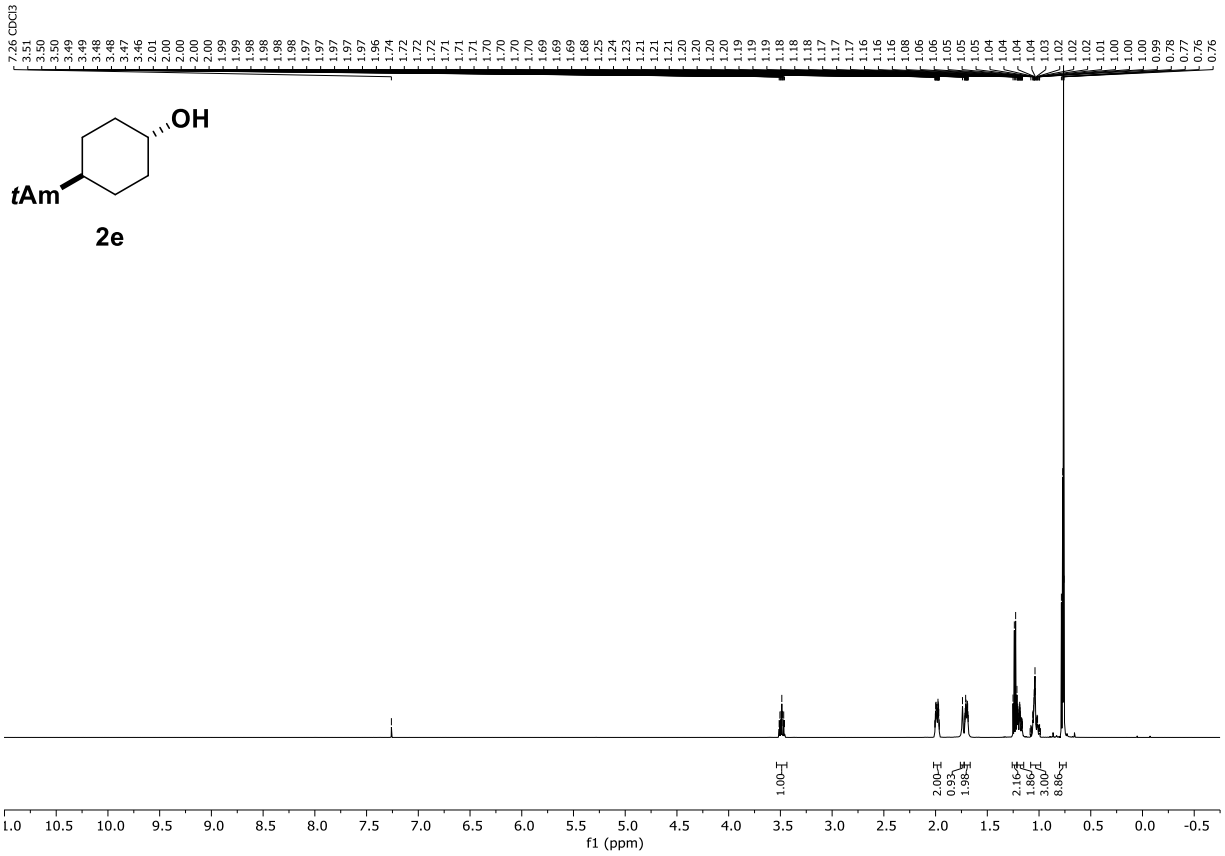
2c

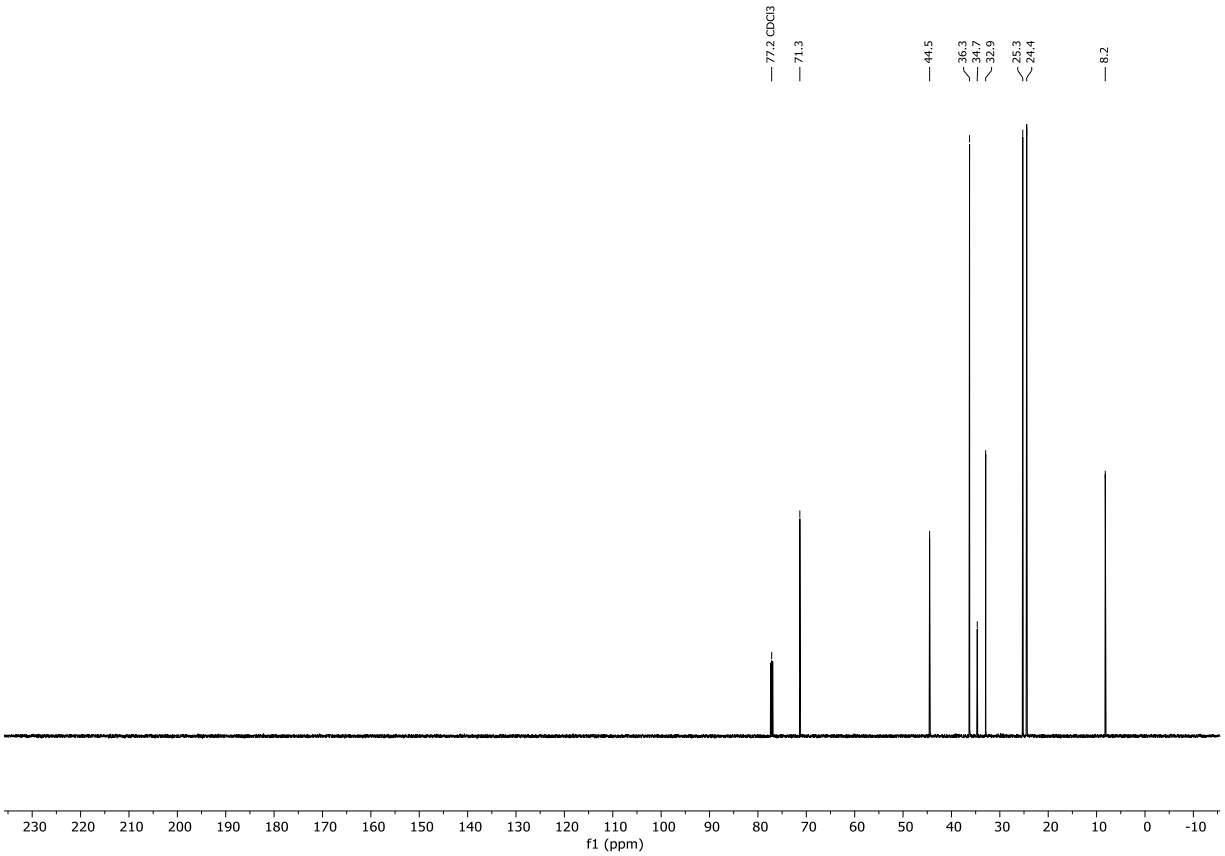
7.26 CDCl3
3.54
3.53
3.52
3.51
3.50
3.49
3.48
3.47
3.46
1.98
1.98
1.95
1.95
1.76
1.72
1.71
1.70
1.42
1.41
1.41
1.40
1.39
1.38
1.22
1.21
1.19
1.18
1.16
1.02
1.02
1.00
0.98
0.97
0.84
1.00
2.17
3.03
1.02
2.09
3.07
6.06
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

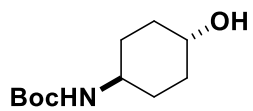

77.2 CDCl3
71.3
43.2
35.9
32.5
28.0
20.1
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


7.26 CDCl3
OH
tBu
2d
1.00
2.01
2.02
1.00
2.05
2.03
1.08
9.09
f1 (ppm)


77.2 CDCl3
71.4
47.3
36.2
32.4
27.8
25.7
f1 (ppm)

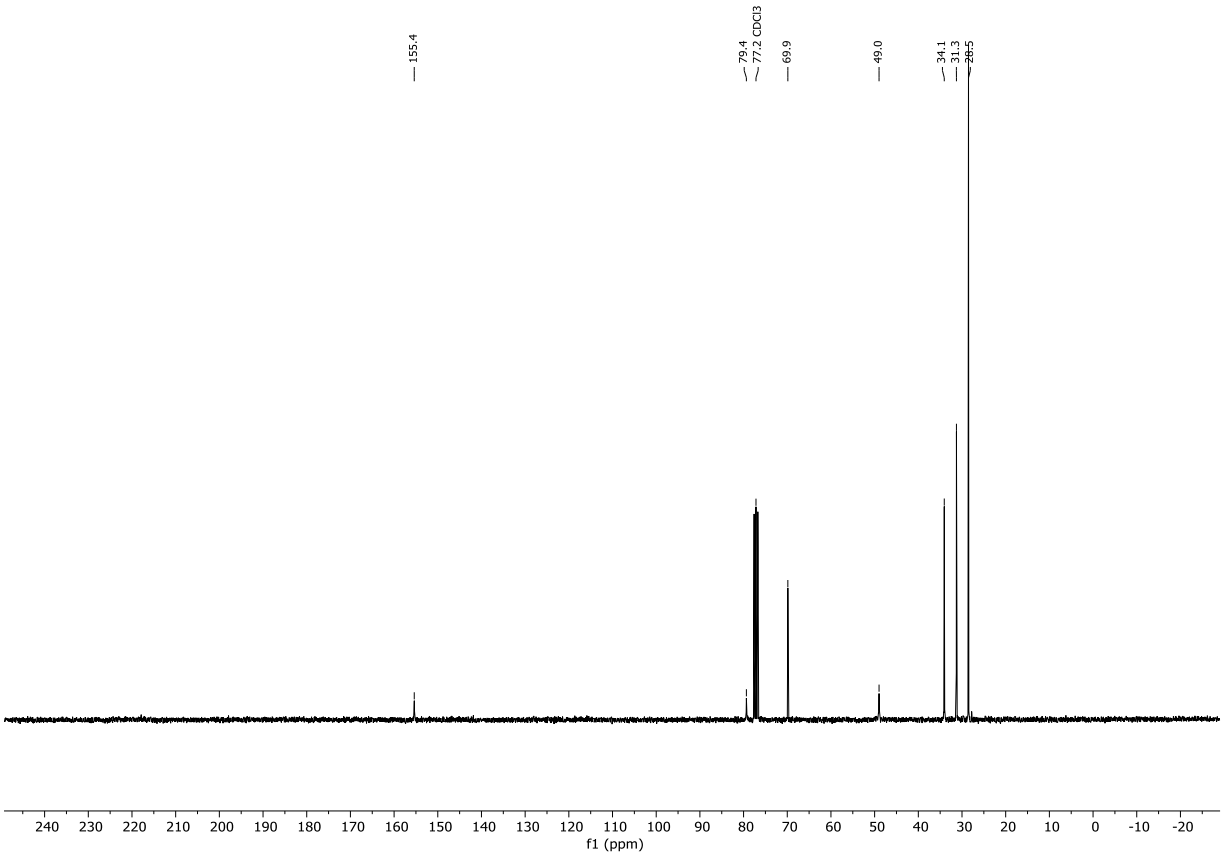

7.26 CDCl3
OH
tAm
2e
1.00
2.00
0.93
1.98
2.16
1.86
3.00
8.86
f1 (ppm)

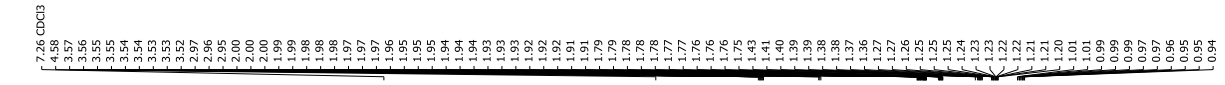

77.2 CDCl3
71.3
44.5
36.3
34.7
32.9
25.3
24.4
8.2
f1 (ppm)


OH
BocHN

2f

7.26 cdcl3
4.36
3.61
3.60
3.60
3.59
3.58
3.58
3.57
3.57
3.56
3.42
2.03
2.02
2.01
2.00
1.99
1.99
1.99
1.98
1.97
1.97
1.97
1.96
1.96
1.96
1.96
1.95
1.95
1.95
1.94
1.94
1.94
1.93
1.55
1.43
1.40
1.39
1.38
1.38
1.37
1.36
1.35
1.35
1.34
1.33
1.32
1.19
1.18
1.17
1.17
1.16
1.16
1.15
1.15
1.14
1.14
1.13
1.12
0.81
1.00
0.94
4.03
1.00
9.00
2.10
1.97
f1 (ppm)


155.4
79.4
77.2 CDCl3
69.9
49.0
34.1
31.3
28.5
f1 (ppm)


7.26 CDCl3
4.58
3.57
3.56
3.55
3.55
3.54
3.54
3.53
3.53
3.52
2.97
2.96
2.95
2.00
2.00
2.00
1.99
1.99
1.98
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1.40
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1.38
1.38
1.37
1.36
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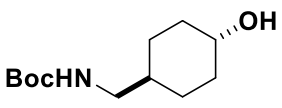
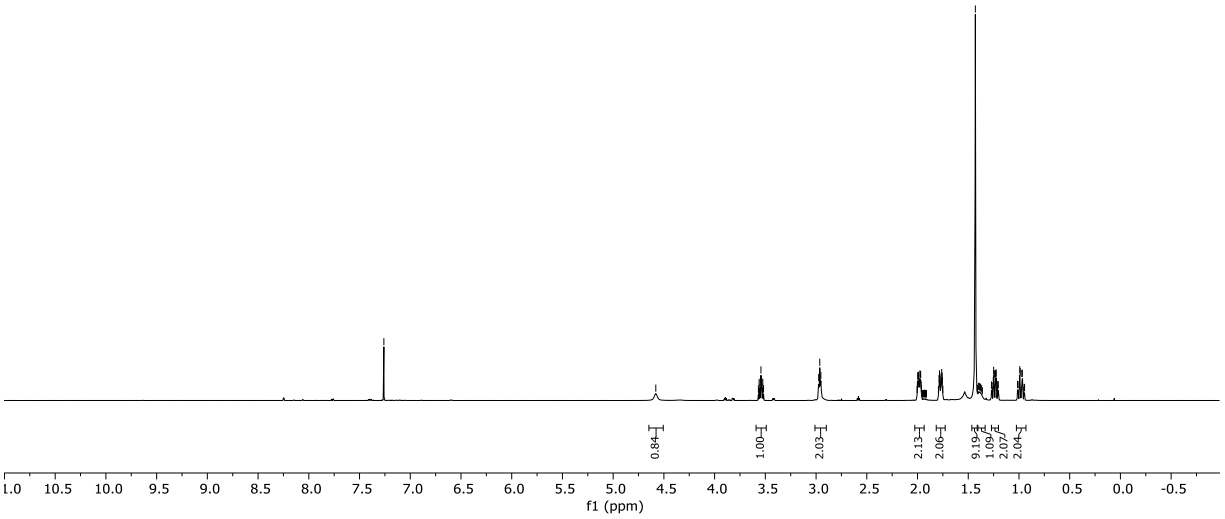
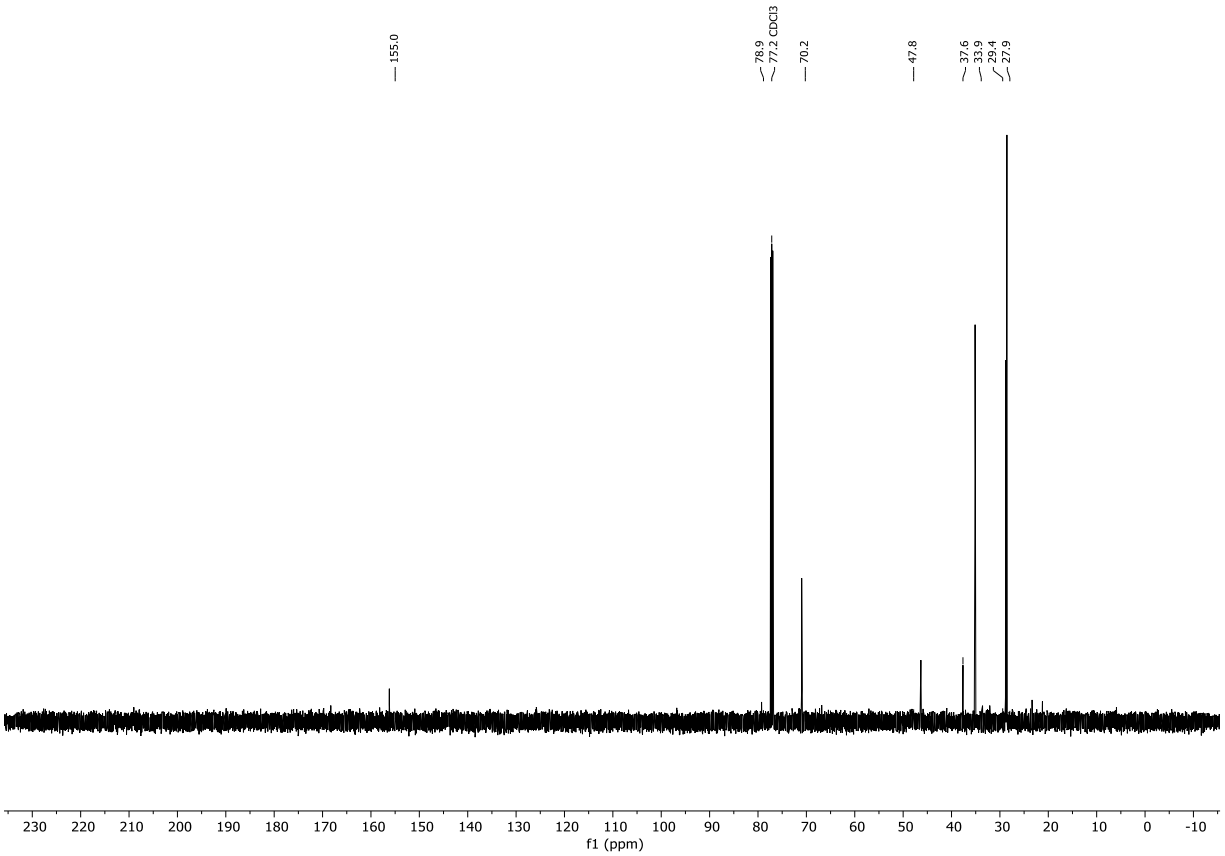
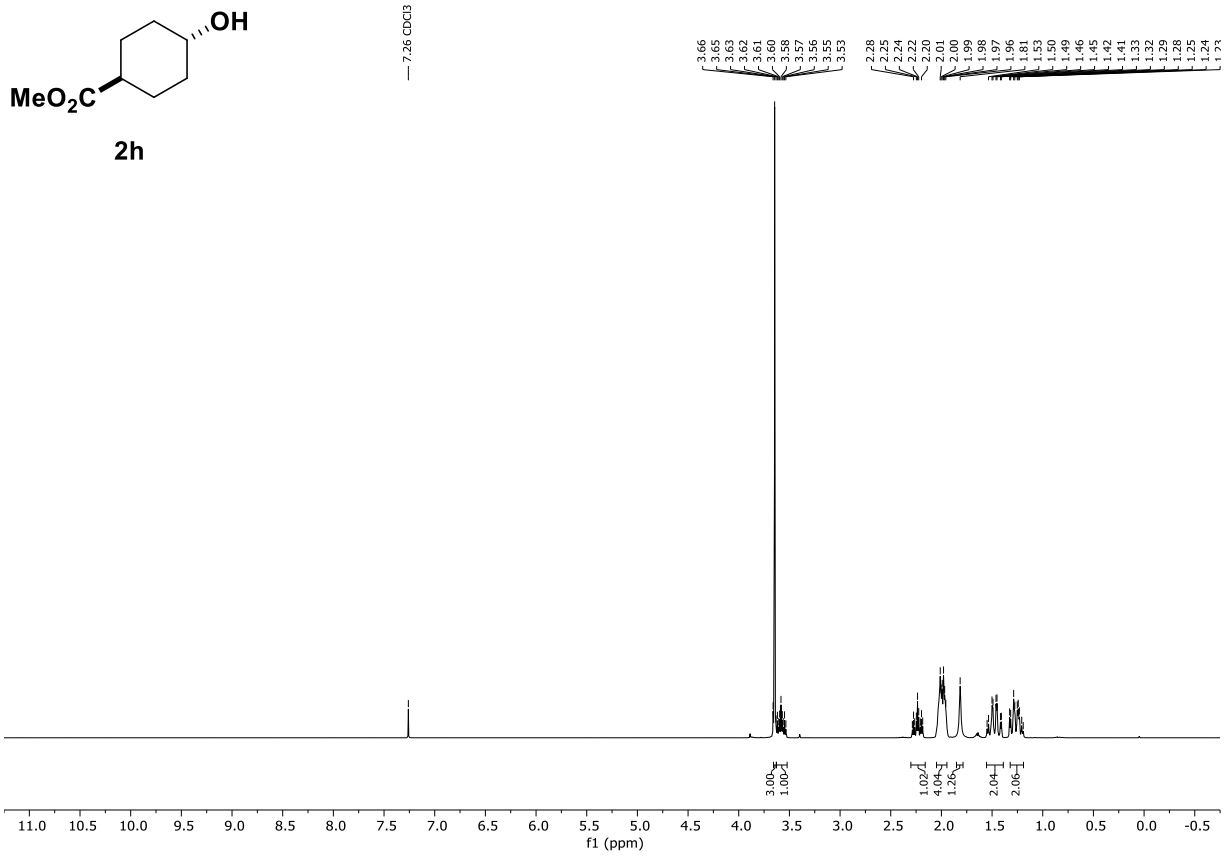
1.27
1.26
1.25
1.25
1.25
1.24
1.23
1.23
1.22
1.22
1.22
1.21
1.21
1.20
1.01
1.01
0.99
0.99
0.99
0.97
0.97
0.96
0.95
0.95
0.94

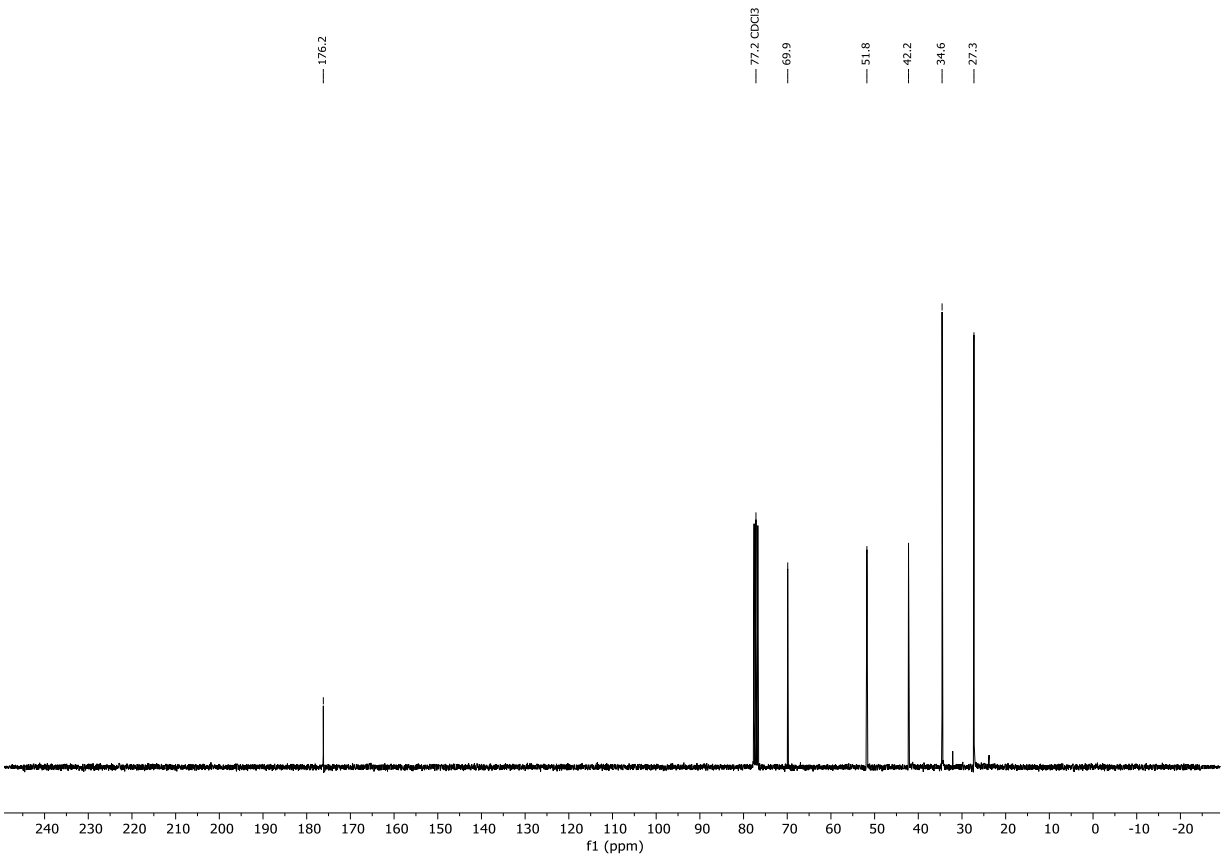

OH
BocHN

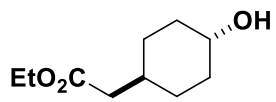
2g


0.84
1.00
2.03
2.13
2.06
9.19
1.09
2.07
2.04
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


155.0
78.9
77.2 CDCl3
70.2
47.8
37.6
33.9
29.4
27.9
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
MeO2C
2h
7.26 CDCl3
3.66
3.65
3.63
3.62
3.61
3.60
3.58
3.57
3.56
3.55
3.53
2.28
2.25
2.24
2.22
2.20
2.01
2.00
1.99
1.98
1.97
1.96
1.81
1.53
1.50
1.49
1.46
1.45
1.42
1.41
1.33
1.32
1.29
1.28
1.25
1.24
3.00
1.00
1.02
4.04
1.26
2.04
2.06
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


176.2
77.2 CDCl3
69.9
51.8
42.2
34.6
27.3
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


OH
EtO2C

2i

7.26 CDCl3
4.15
4.13
4.10
4.08
3.59
3.58
3.56
3.56
3.54
3.53
3.52
3.51
3.49
2.18
2.16
1.99
1.98
1.95
1.94
1.81
1.77
1.75
1.74
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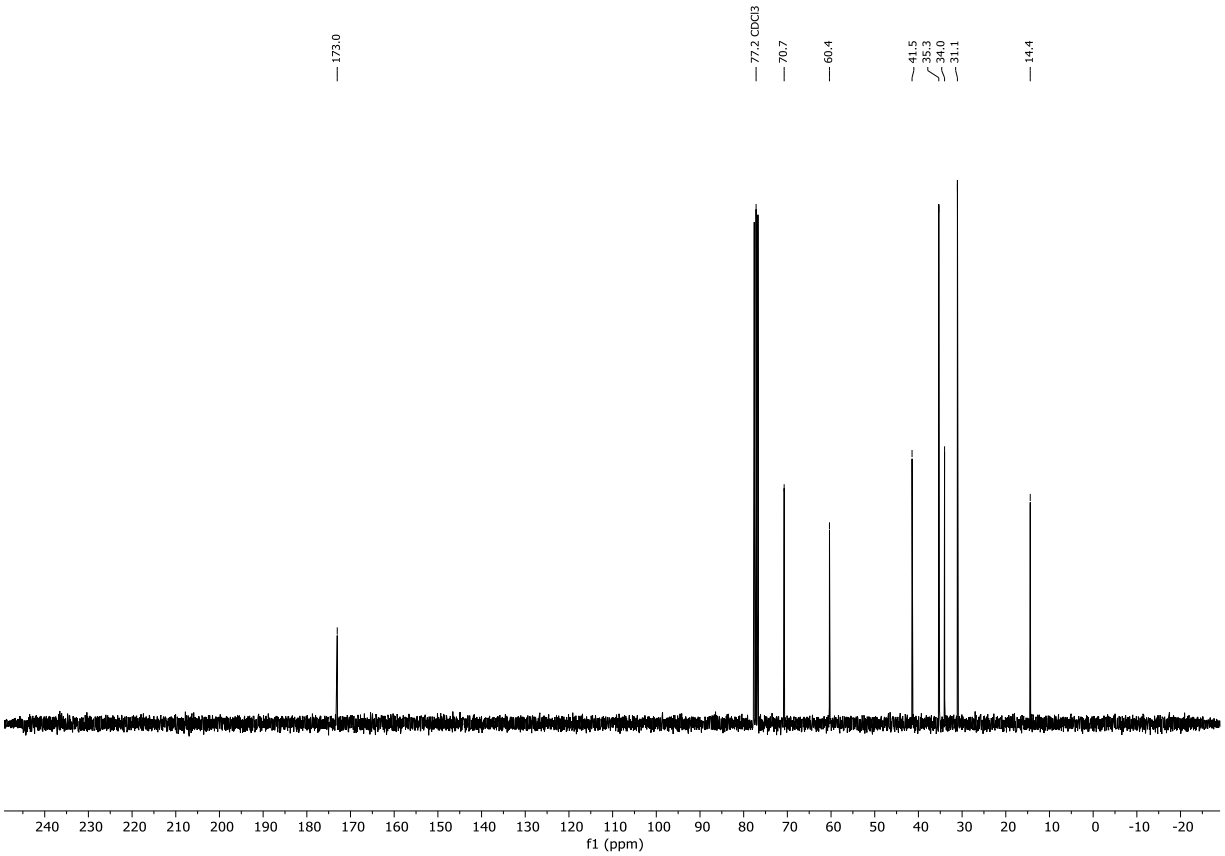
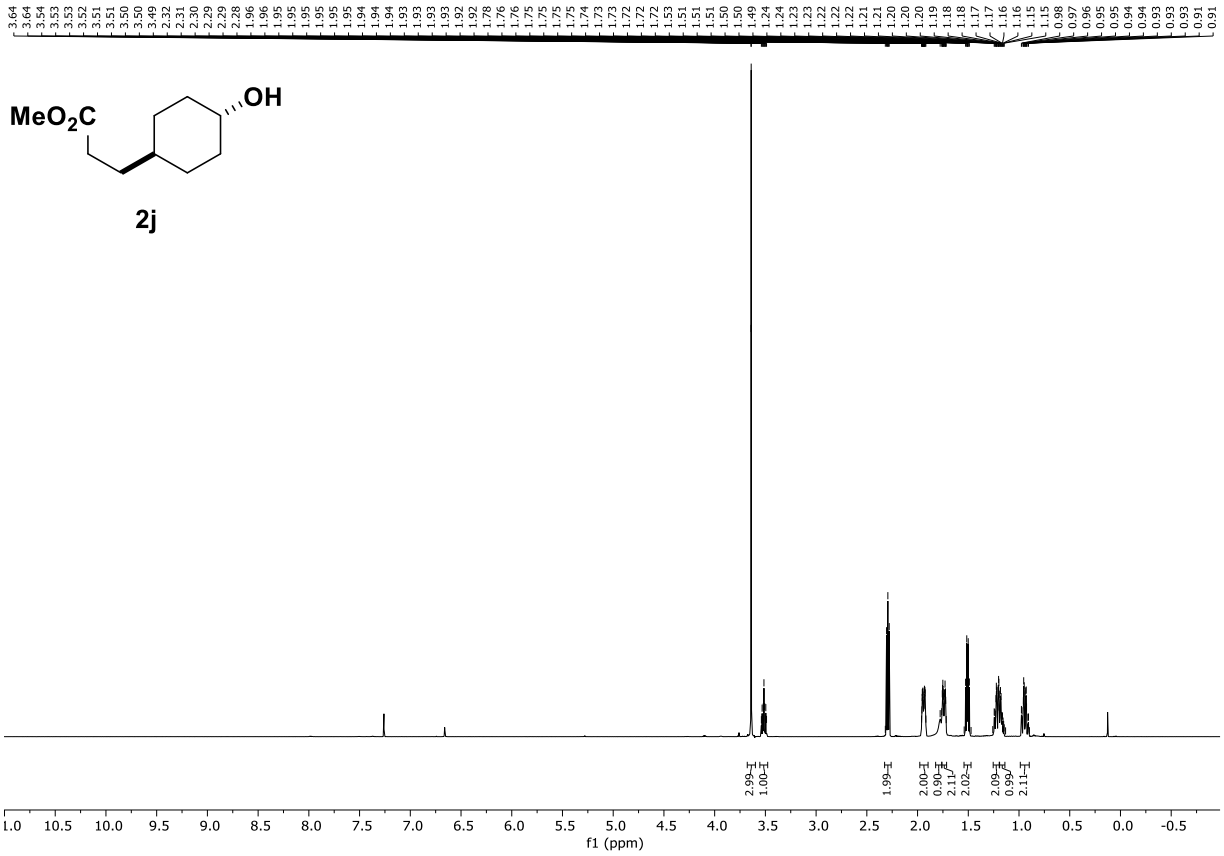
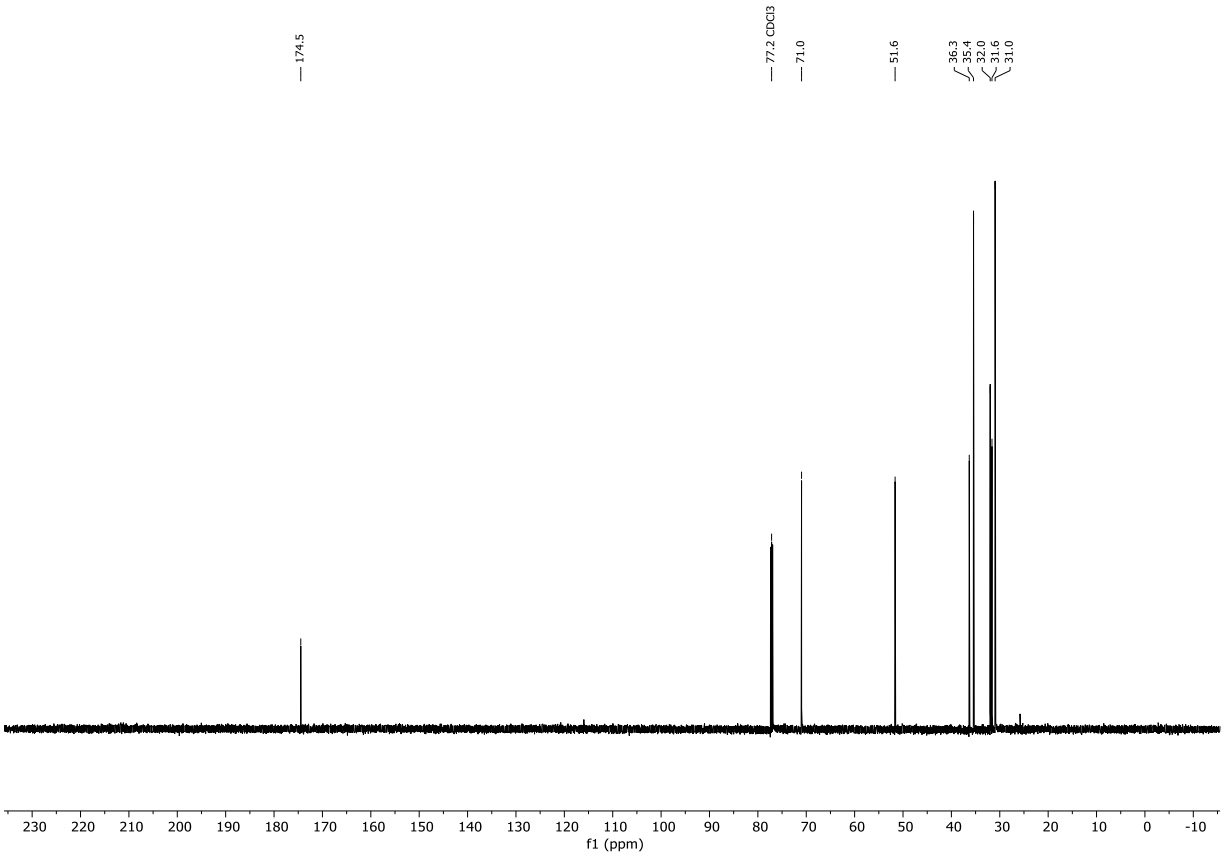
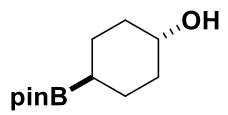
1.53
1.35
1.34
1.31
1.27
1.25
1.23
1.22
1.10
1.09
1.06
1.02
0.97
2.02
1.00
2.01
2.04
3.08
1.12
5.19
2.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


173.0
77.2 CDCl3
70.7
60.4
41.5
35.3
34.0
31.1
14.4
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

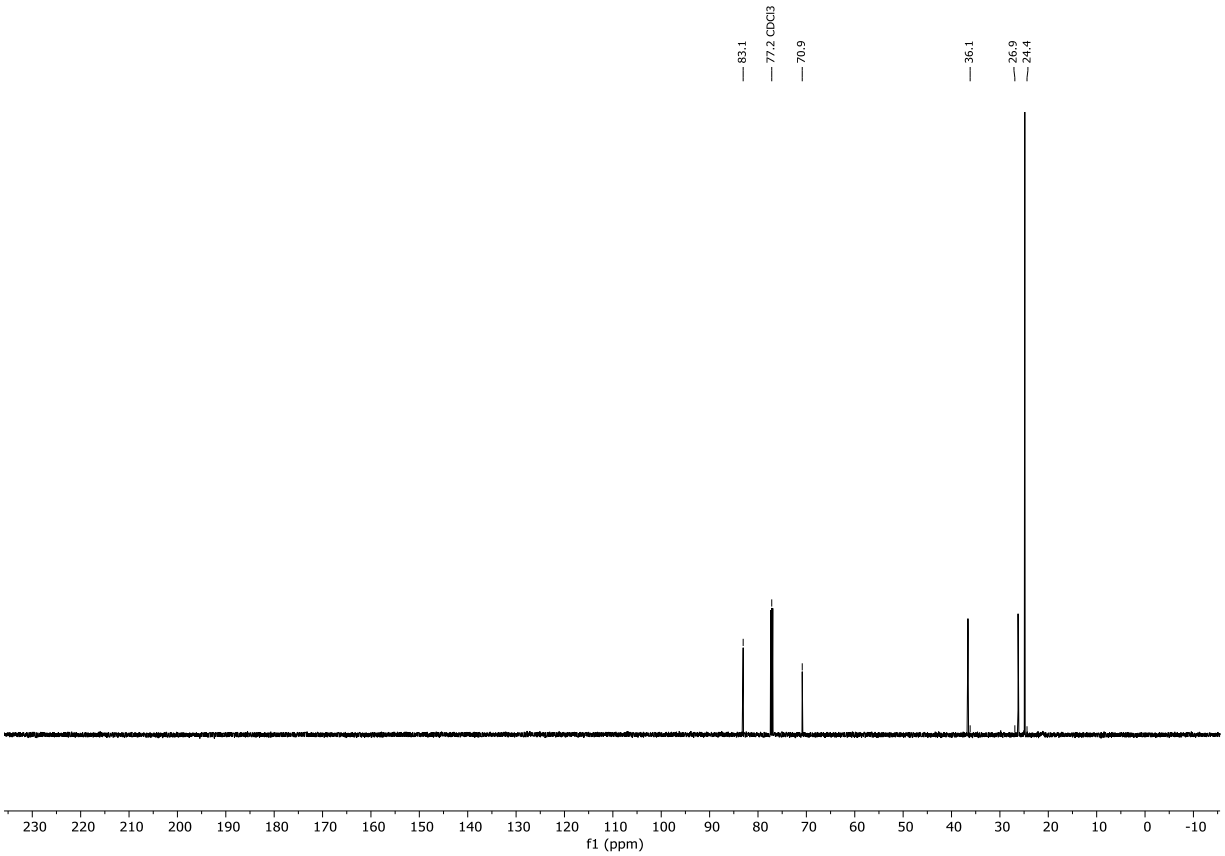

MeO2C
OH
2j
f1 (ppm)

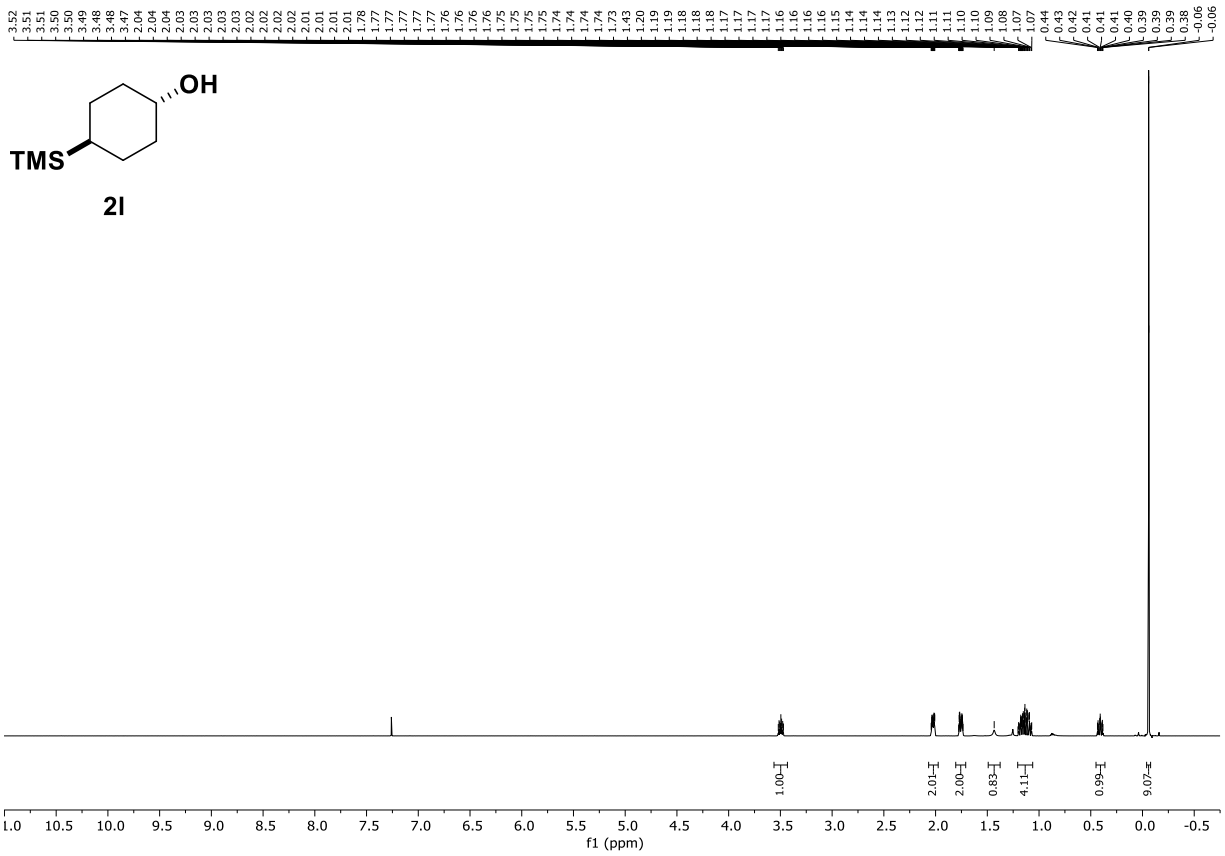

174.5
77.2 CDCl3
71.0
51.6
36.3
35.4
32.0
31.6
31.0
f1 (ppm)


OH
pinB

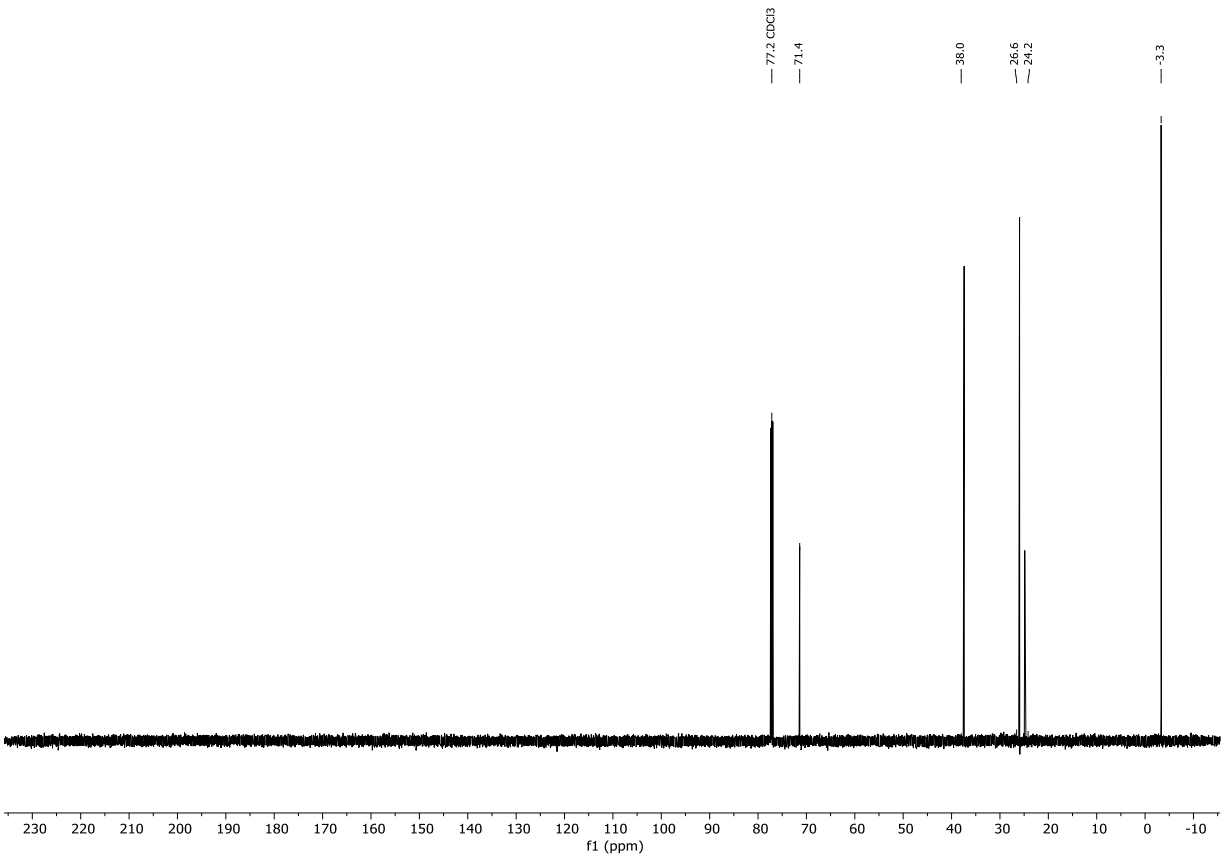
2k

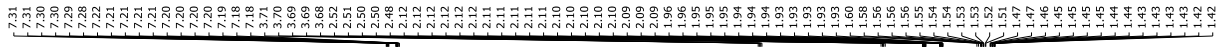
7.26 CDCl3
1.00
2.02
2.07
0.97
2.00
11.98
1.94
1.04

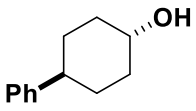

83.1
77.2 CDCl3
70.9
36.1
26.9
24.4
f1 (ppm)


OH
TMS
1.00
2.01
2.00
0.83
4.11
0.99
9.07
f1 (ppm)

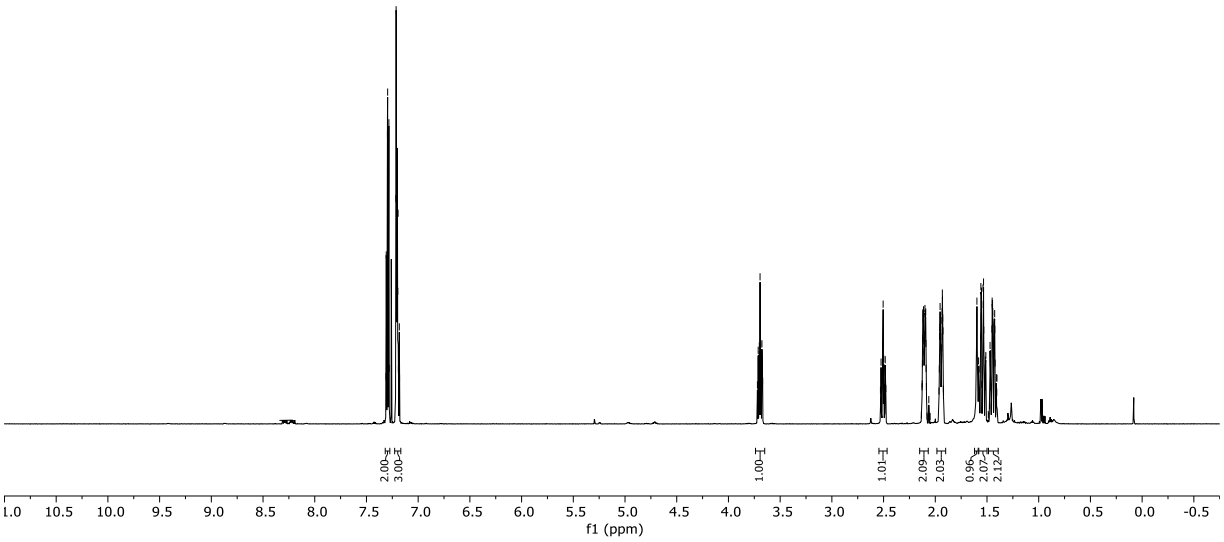
2l

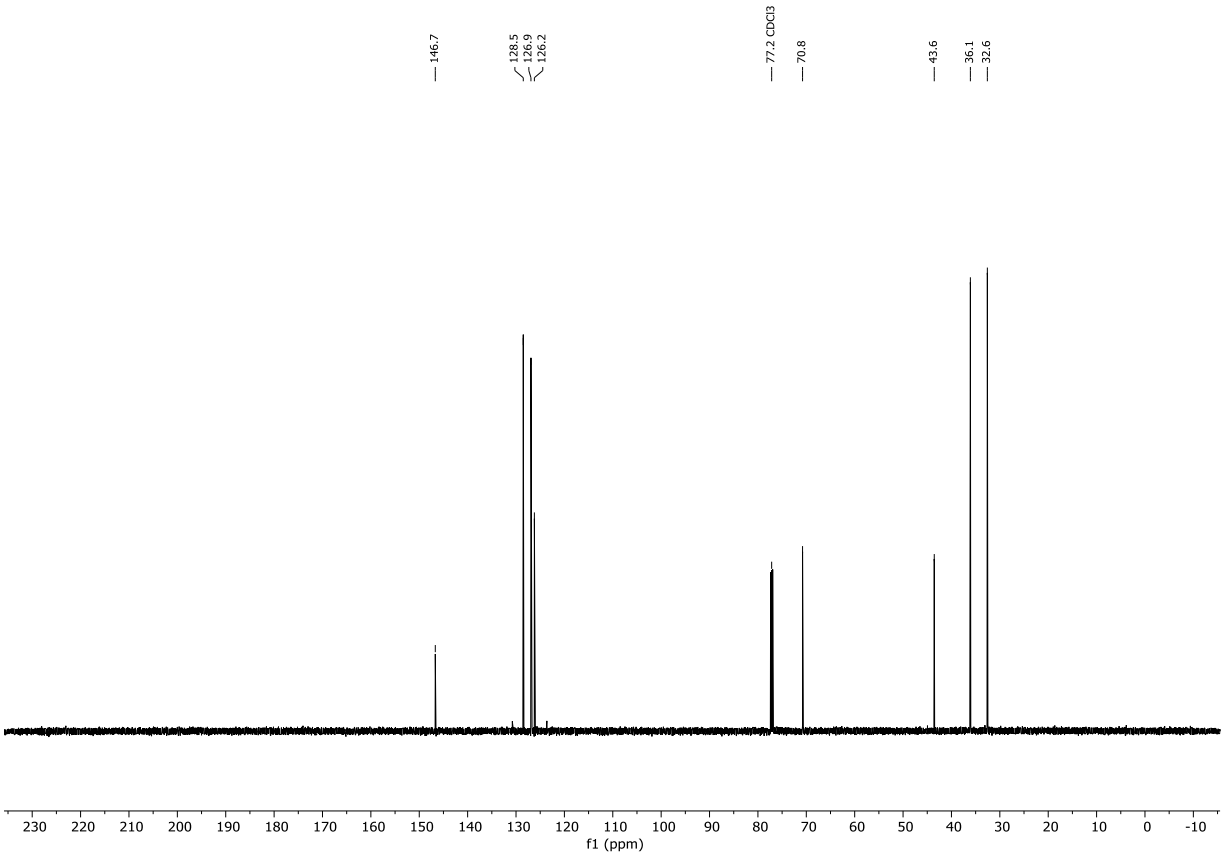

77.2 CDCl3
71.4
38.0
26.6
24.2
-3.3
f1 (ppm)

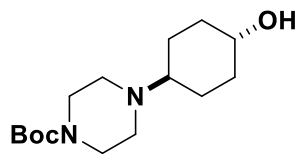



OH
Ph

2m

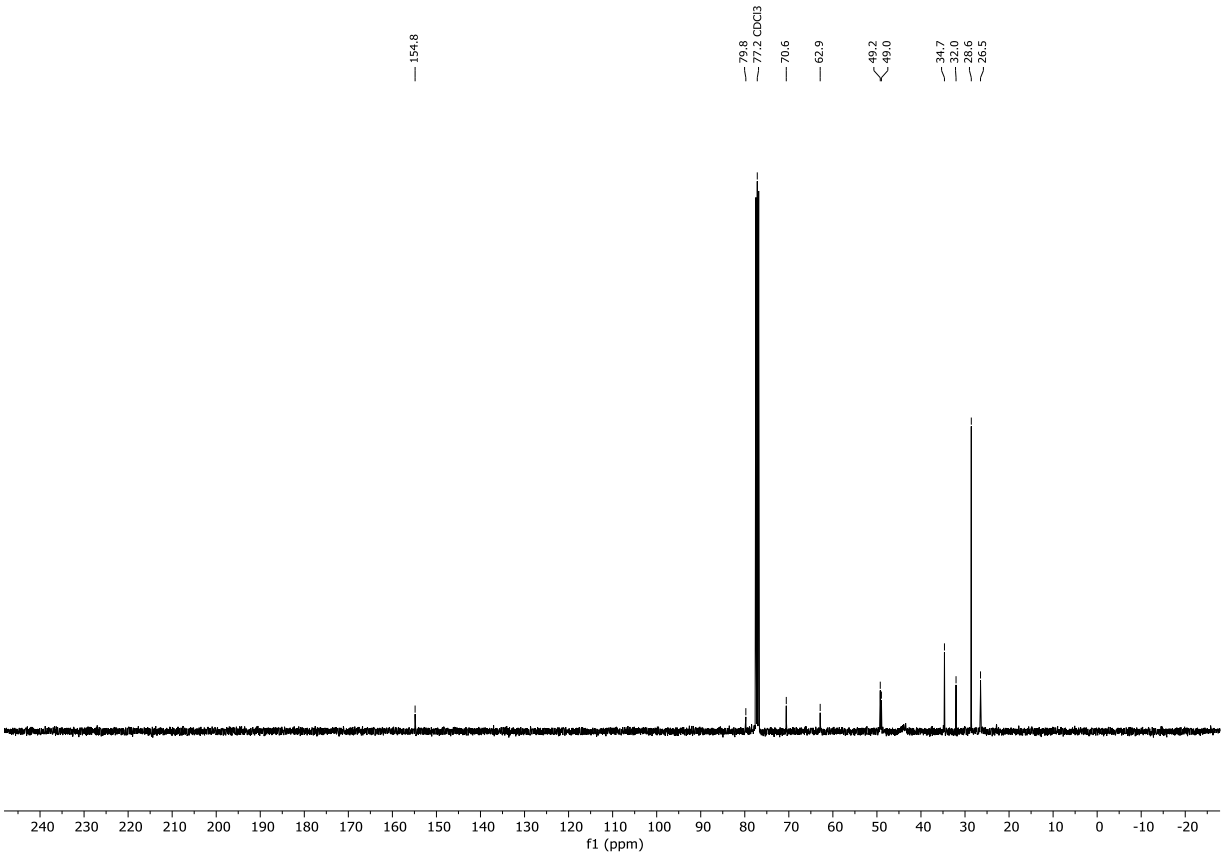

2.00
3.00
1.00
1.01
2.09
2.03
0.96
2.07
2.12
f1 (ppm)

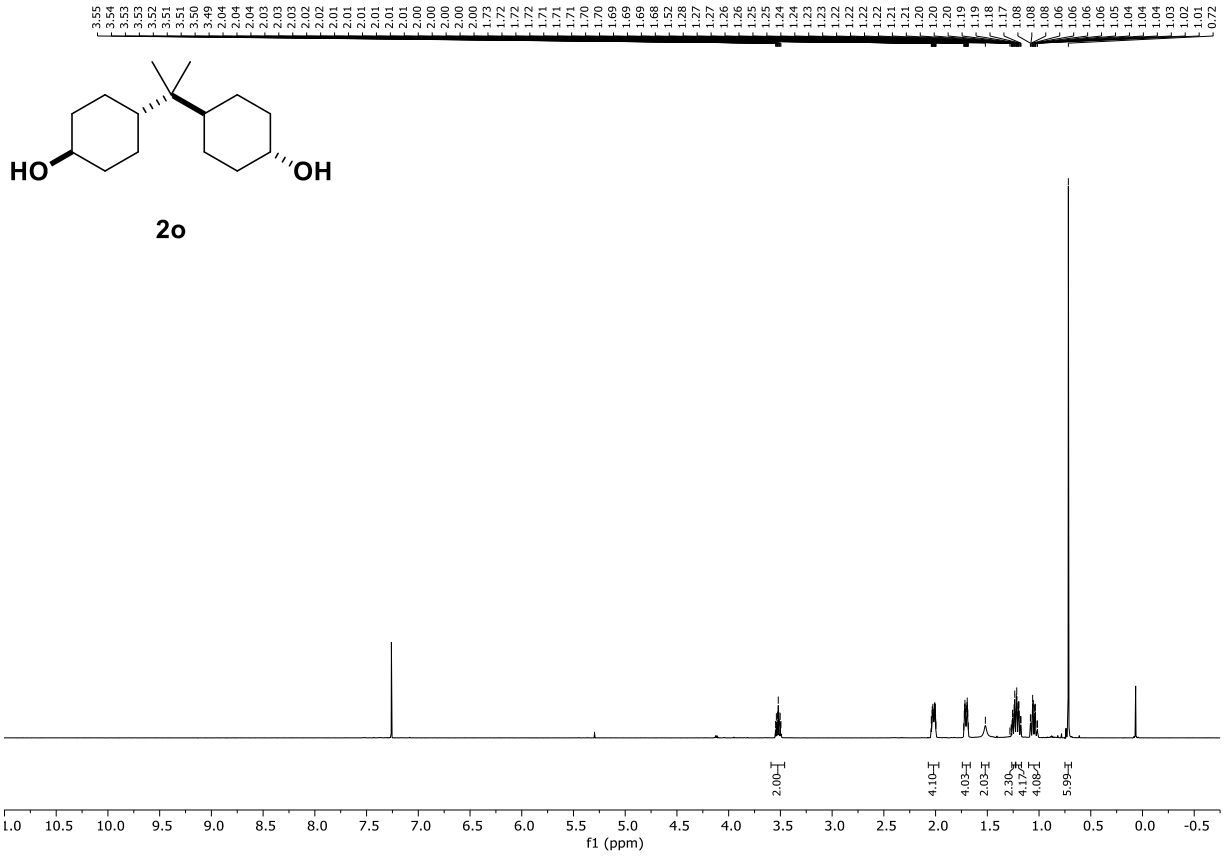

146.7
128.5
126.9
126.2
77.2 CDCl3
70.8
43.6
36.1
32.6
f1 (ppm)

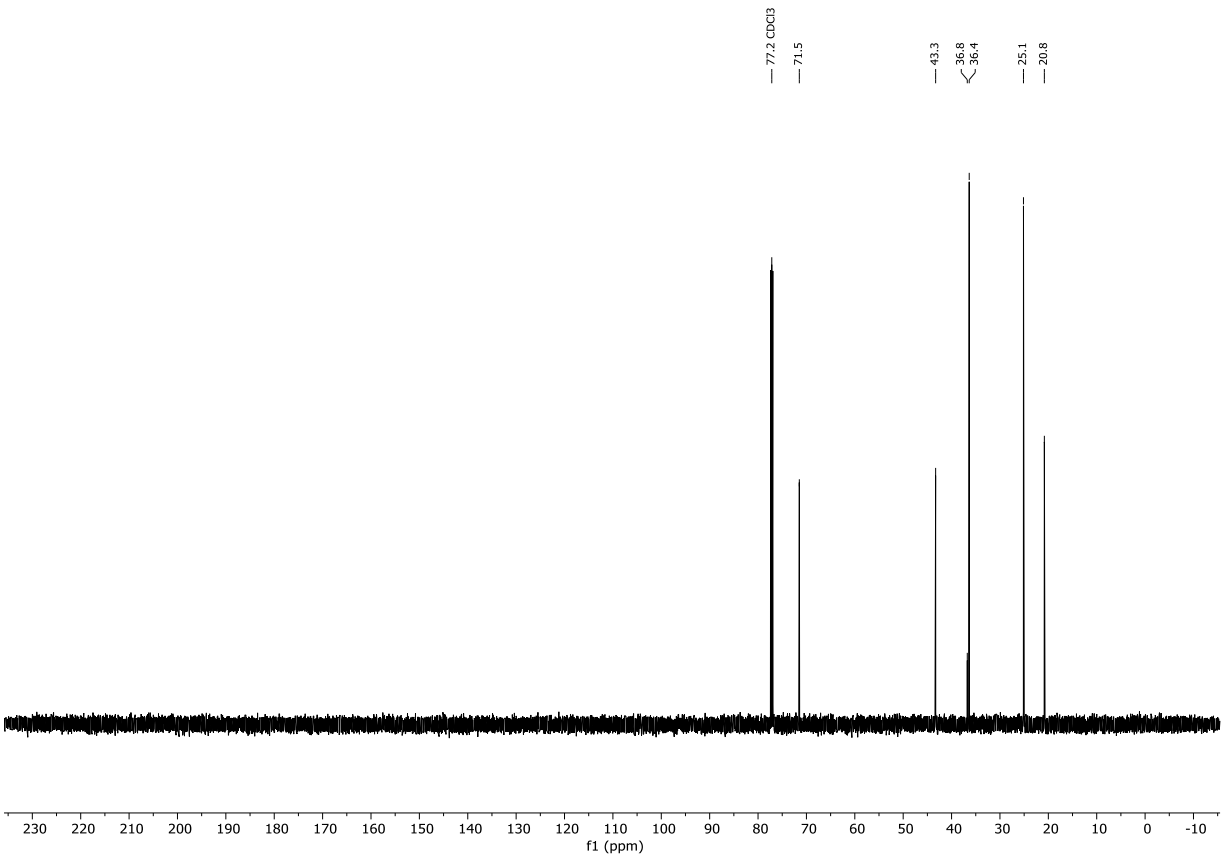

OH
N
BocN

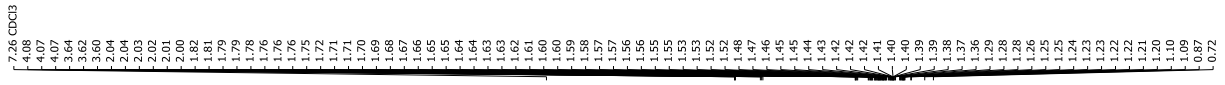
2n

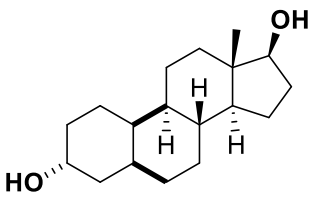
7.26 CDCl3
3.60
3.59
3.58
3.57
3.56
3.54
3.53
3.45
3.42
2.55
2.50
2.30
2.03
2.03
2.02
1.88
1.86
1.85
1.83
1.82
1.82
1.74
1.71
1.64
1.61
1.57
1.57
1.56
1.54
1.50
1.45
1.32
1.31
1.30
1.27
1.00
4.19
4.22
1.00
1.72
2.11
2.22
9.38
3.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


154.8
79.8
77.2 CDCl3
70.6
62.9
49.2
49.0
34.7
32.0
28.6
26.5
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


HO
OH
2o
2.00
4.10
4.03
2.03
2.30
4.17
4.08
5.99
f1 (ppm)

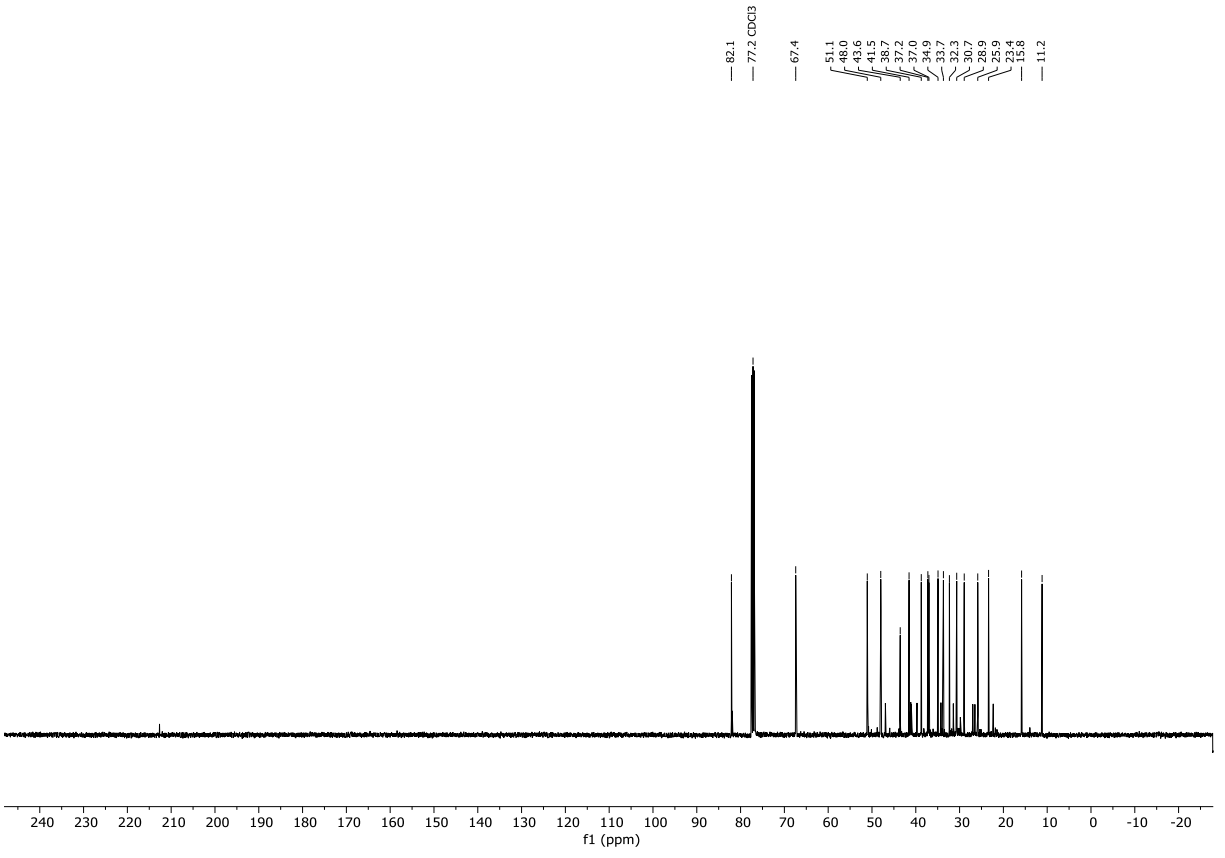

77.2 CDCl3
71.5
43.3
36.8
36.4
25.1
20.8
f1 (ppm)

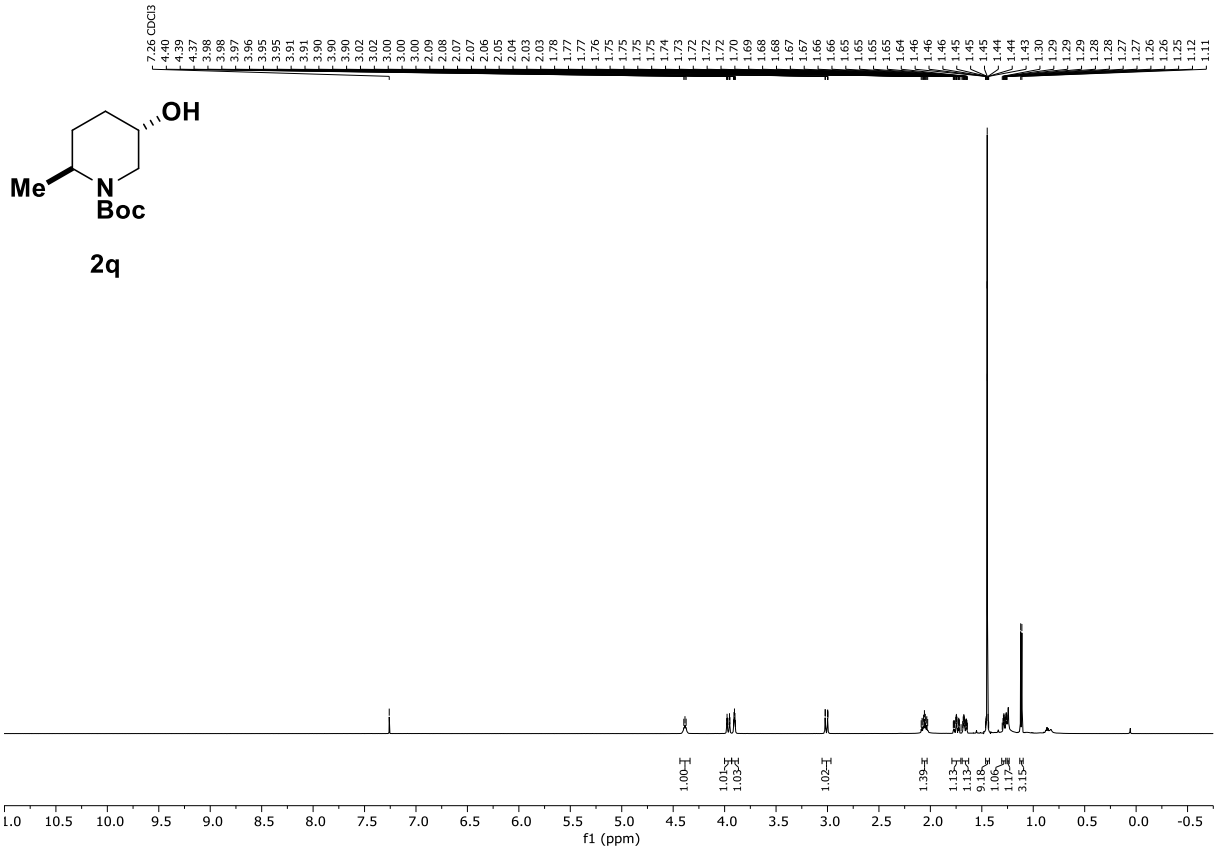

7.26 CDCl3
4.08
4.07
4.07
3.64
3.62
3.60
2.04
2.04
2.03
2.02
2.01
2.00
1.82
1.81
1.79
1.79
1.78
1.76
1.76
1.76
1.75
1.72
1.71
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.65
1.64
1.64
1.63
1.63
1.62
1.61
1.60
1.60
1.59
1.58
1.57
1.57
1.56
1.56
1.55
1.55
1.53
1.53
1.52
1.52
1.48
1.47
1.46
1.45
1.45
1.44
1.43
1.42
1.42
1.41
1.40
1.40
1.39
1.39
1.38
1.37
1.36
1.29
1.28
1.28
1.26
1.25
1.25
1.24
1.23
1.23
1.22
1.22
1.21
1.20
1.10
1.09
0.87
0.72


OH
H
H
H
HO

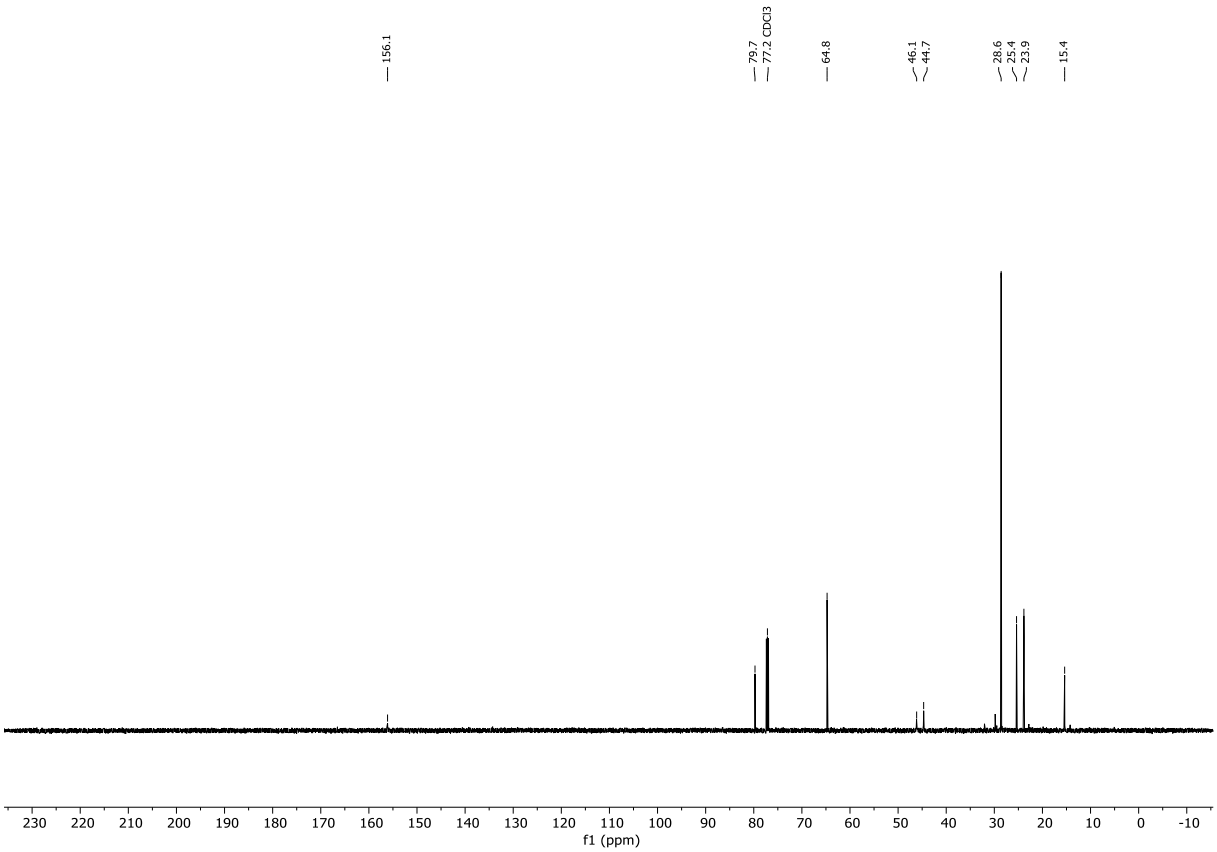
2p

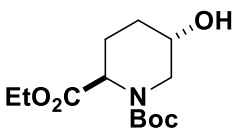
1.00
1.19
2.10
15.32
4.04
2.19
2.08
3.35
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


82.1
77.2 CDCl3
67.4
51.1
48.0
43.6
41.5
38.7
37.2
37.0
34.9
33.7
32.3
30.7
28.9
25.9
23.4
15.8
11.2
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)



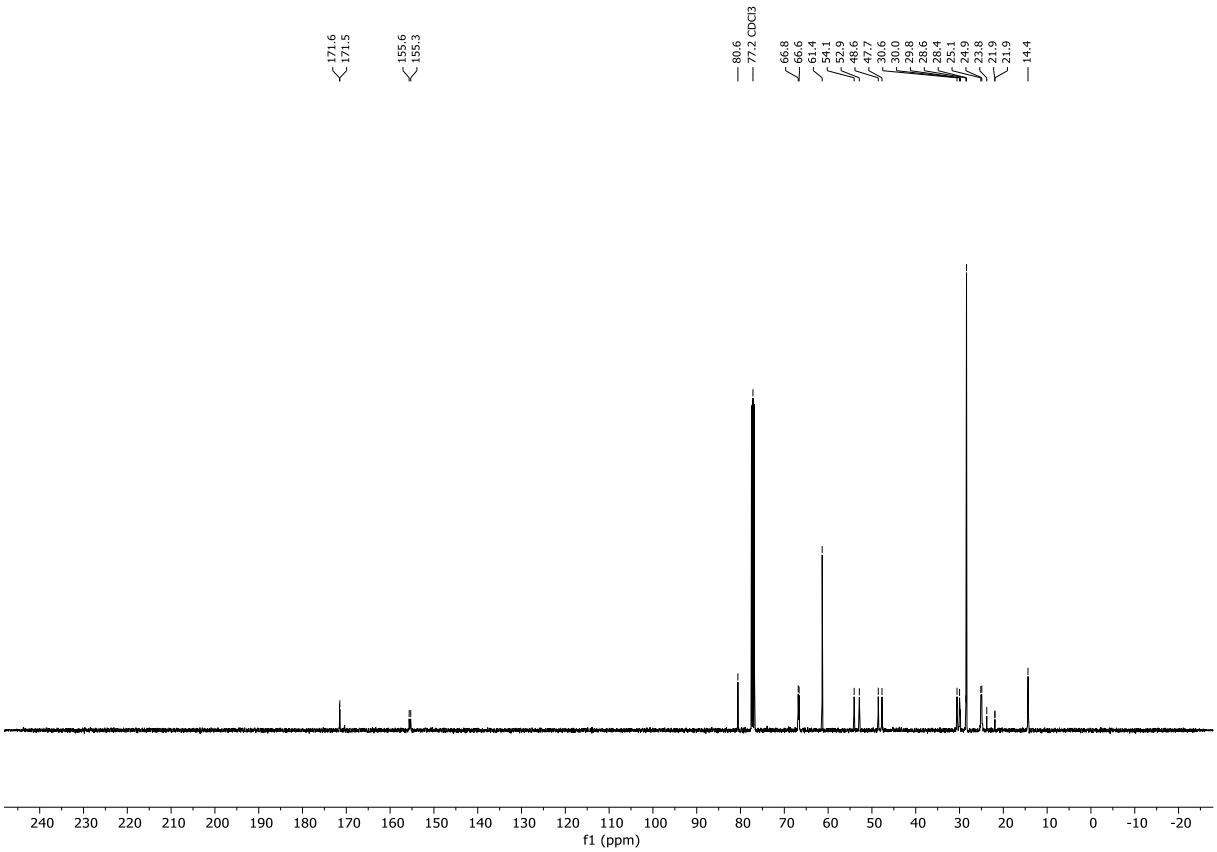
2q

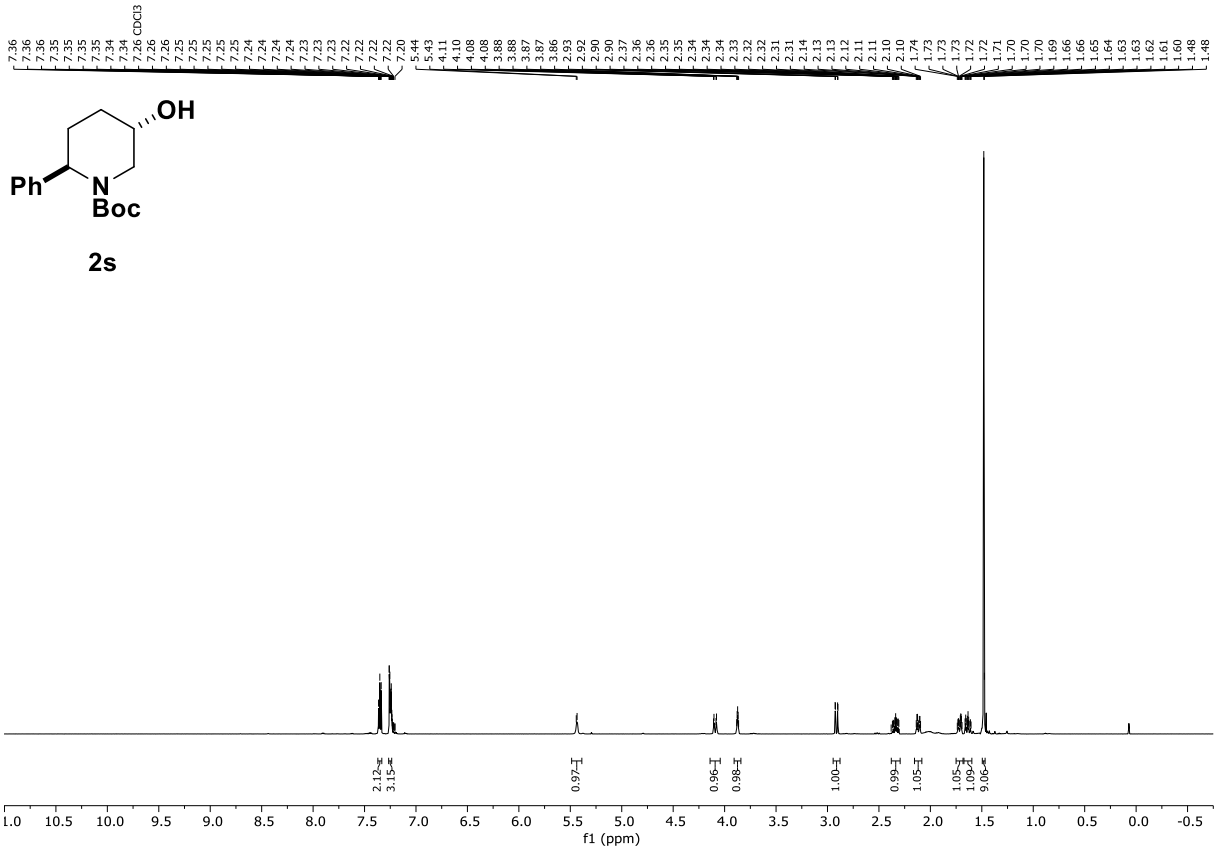


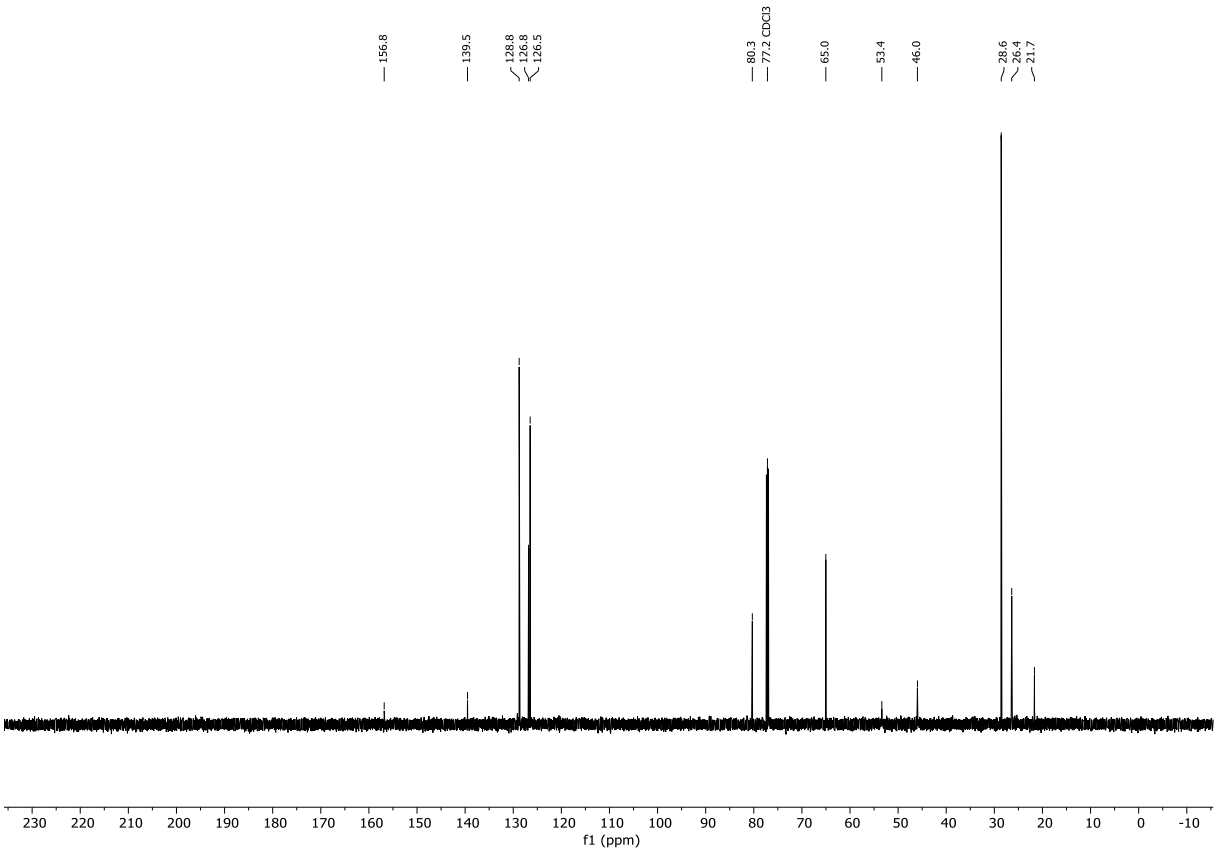

OH
EtO2C
N
Boc

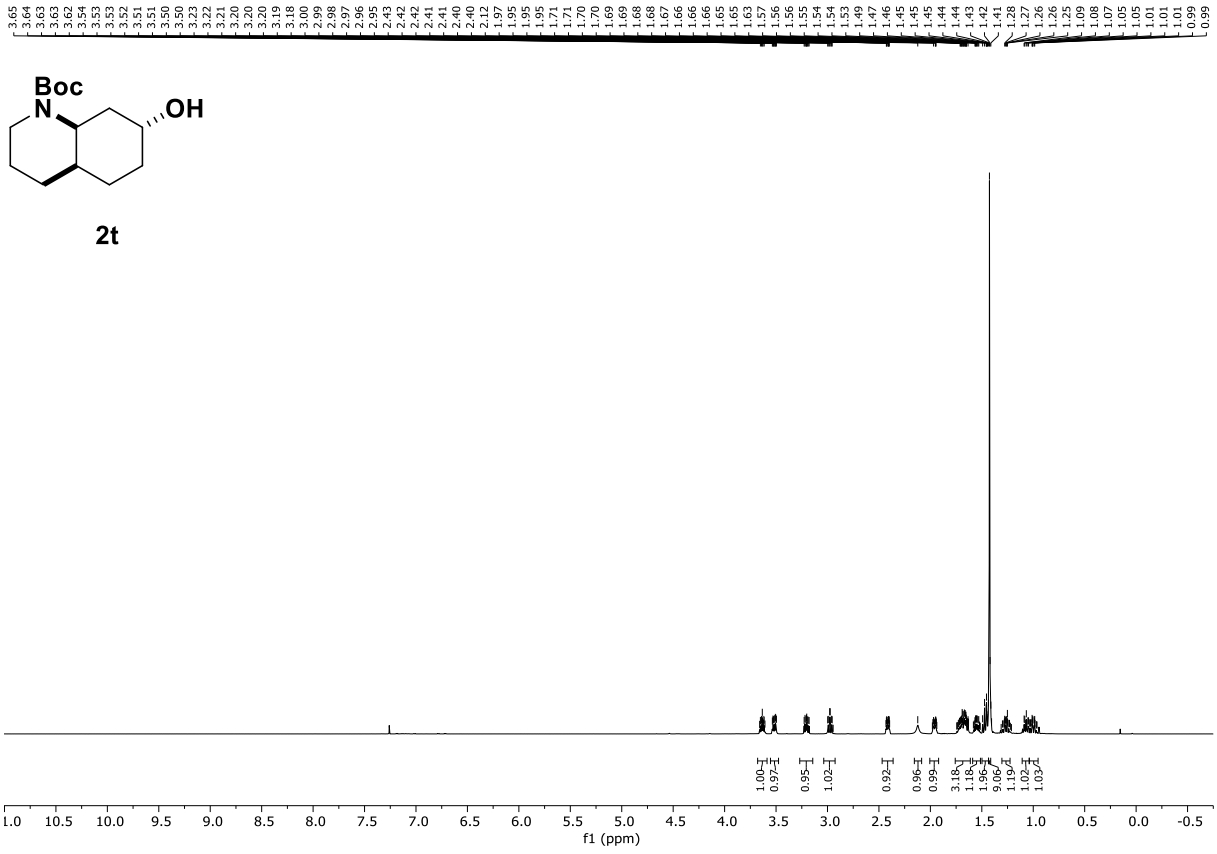
2r

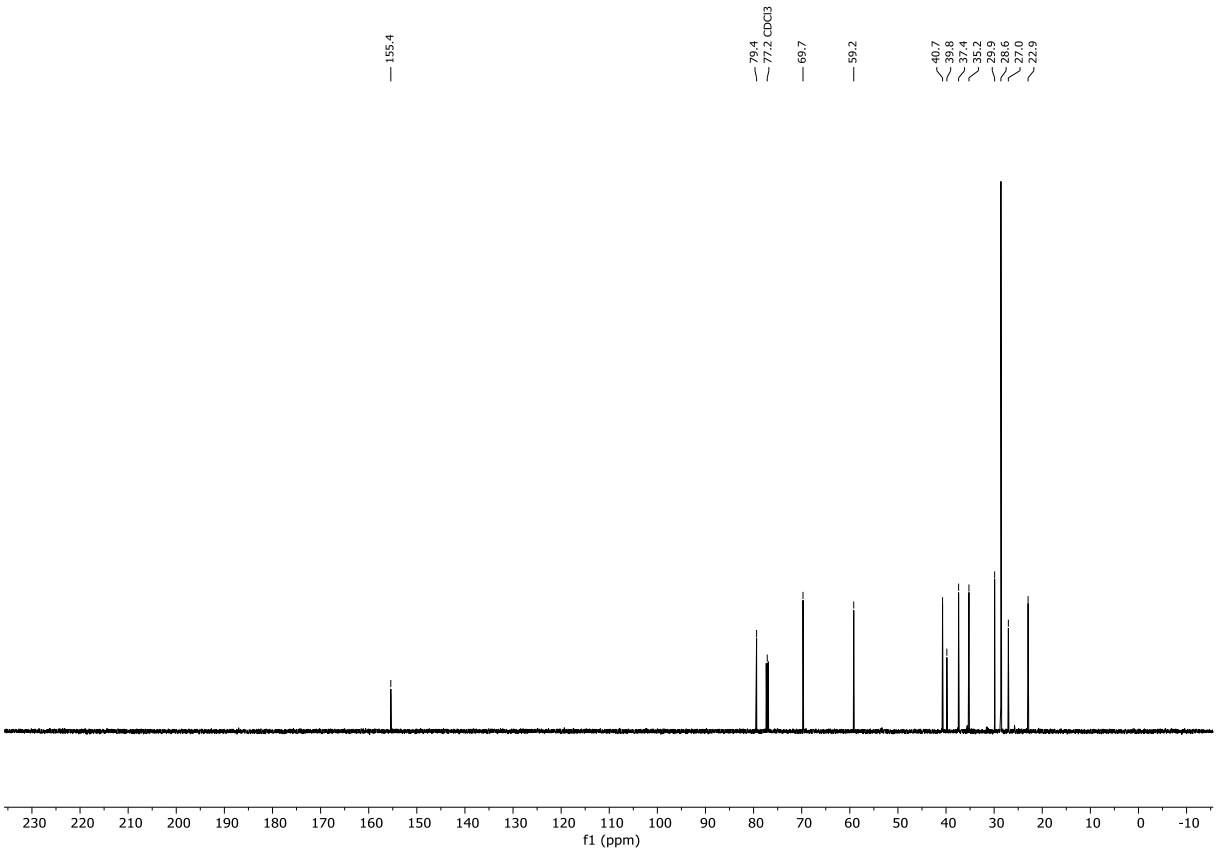
7.26 CDCl3
4.78
4.61
4.17
4.08
4.08
4.05
3.61
2.77
2.74
2.71
2.66
2.63
2.61
2.28
2.25
1.96
1.93
1.74
1.73
1.71
1.68
1.66
1.65
1.45
1.41
1.27
1.25
1.23
1.18
1.15
1.00
2.75
0.98
1.00
1.66
0.99
1.02
9.00
4.24
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


171.6
171.5
155.6
155.3
80.6
77.2 CDCl3
66.8
66.6
61.4
54.1
52.9
48.6
47.7
30.6
30.0
29.8
28.6
28.4
25.1
24.9
23.8
21.9
21.9
14.4
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

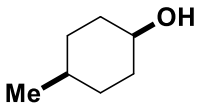

OH
Ph
N
Boc
2s
f1 (ppm)


156.8
139.5
128.8
126.8
126.5
80.3
77.2 CDCl3
65.0
53.4
46.0
28.6
26.4
21.7
f1 (ppm)

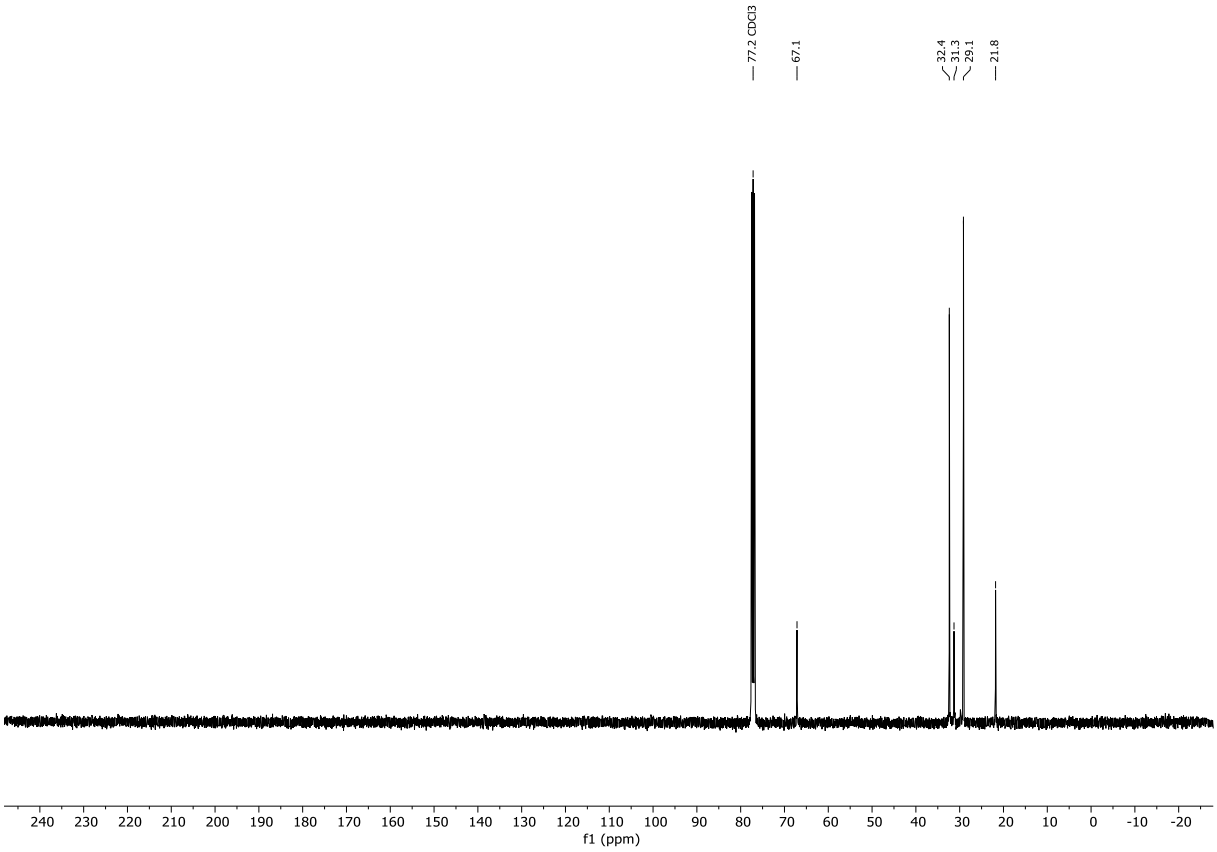

Boc
N
OH
2t
f1 (ppm)

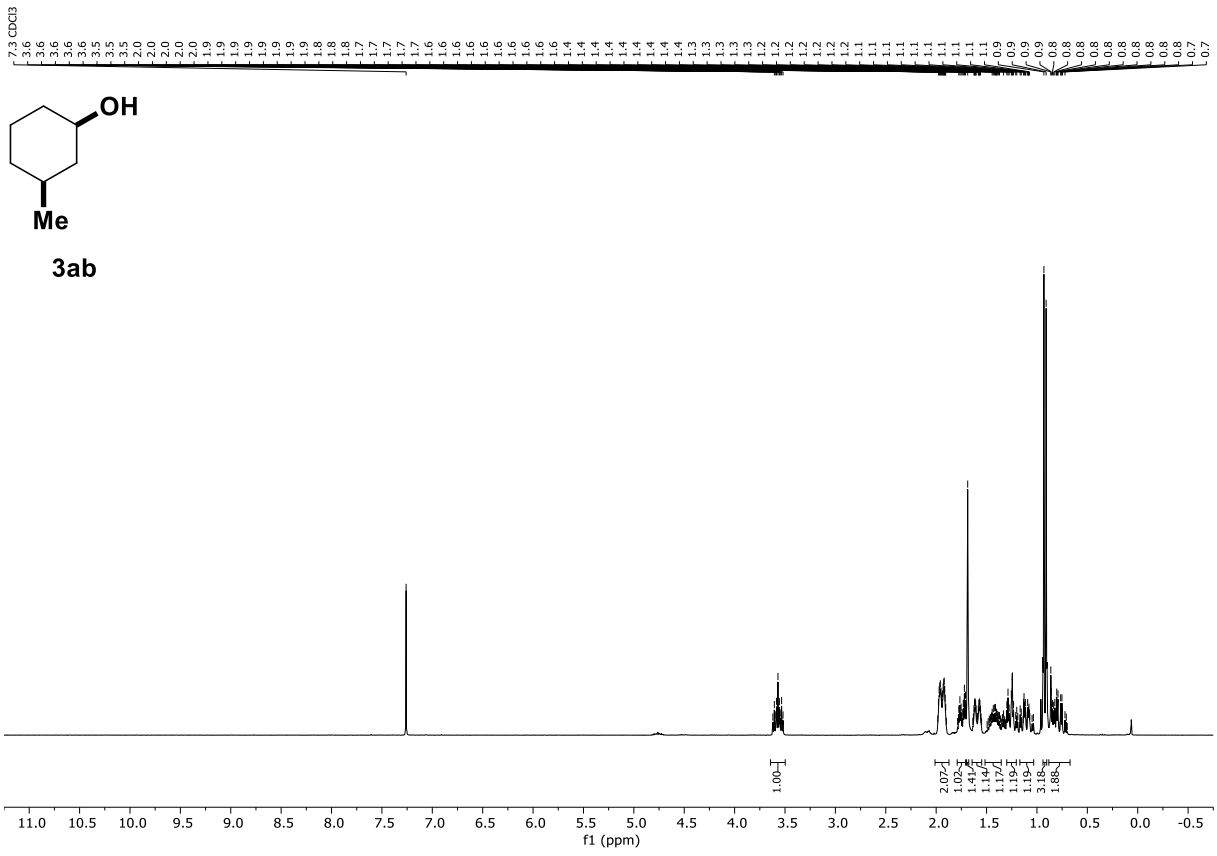

155.4
79.4
77.2 CDCl3
69.7
59.2
40.7
39.8
37.4
35.2
29.9
28.6
27.0
22.9
f1 (ppm)

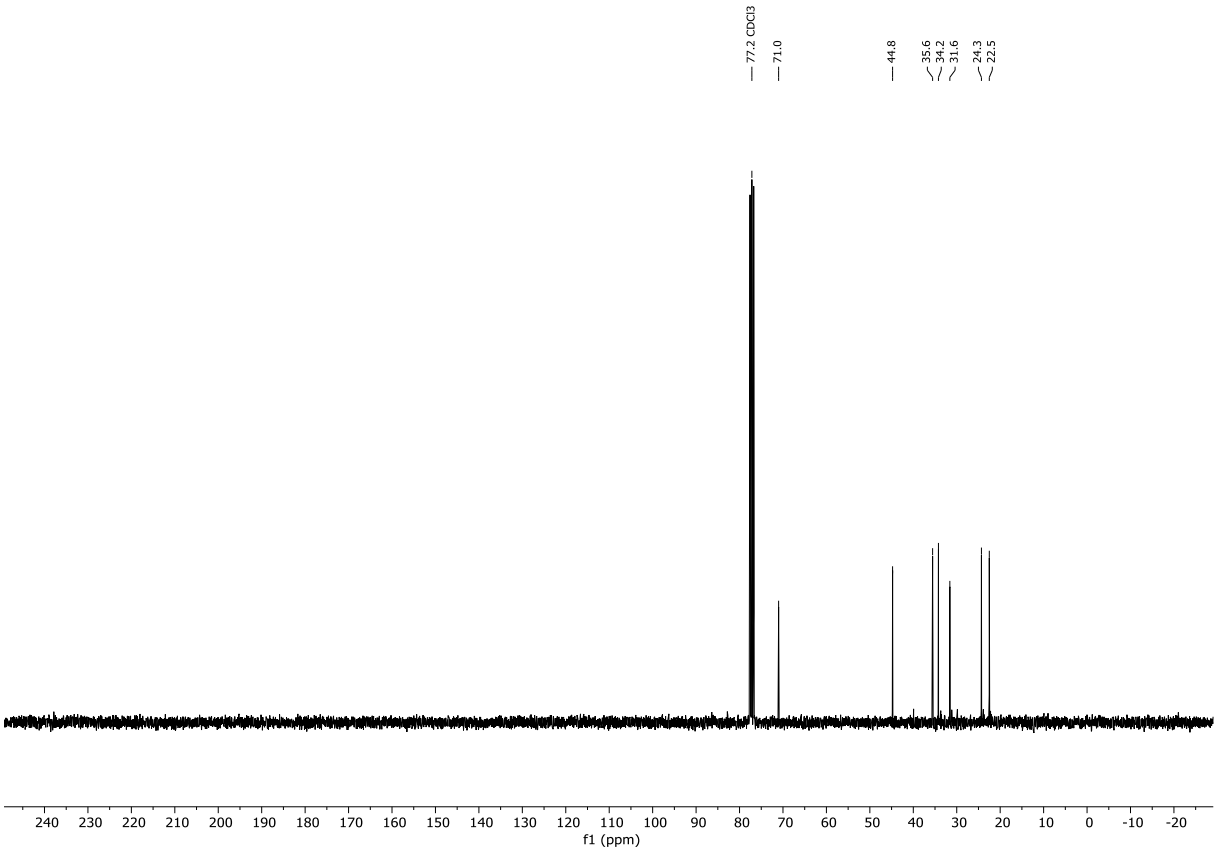
11.2 *cis*-Cyclohexanols

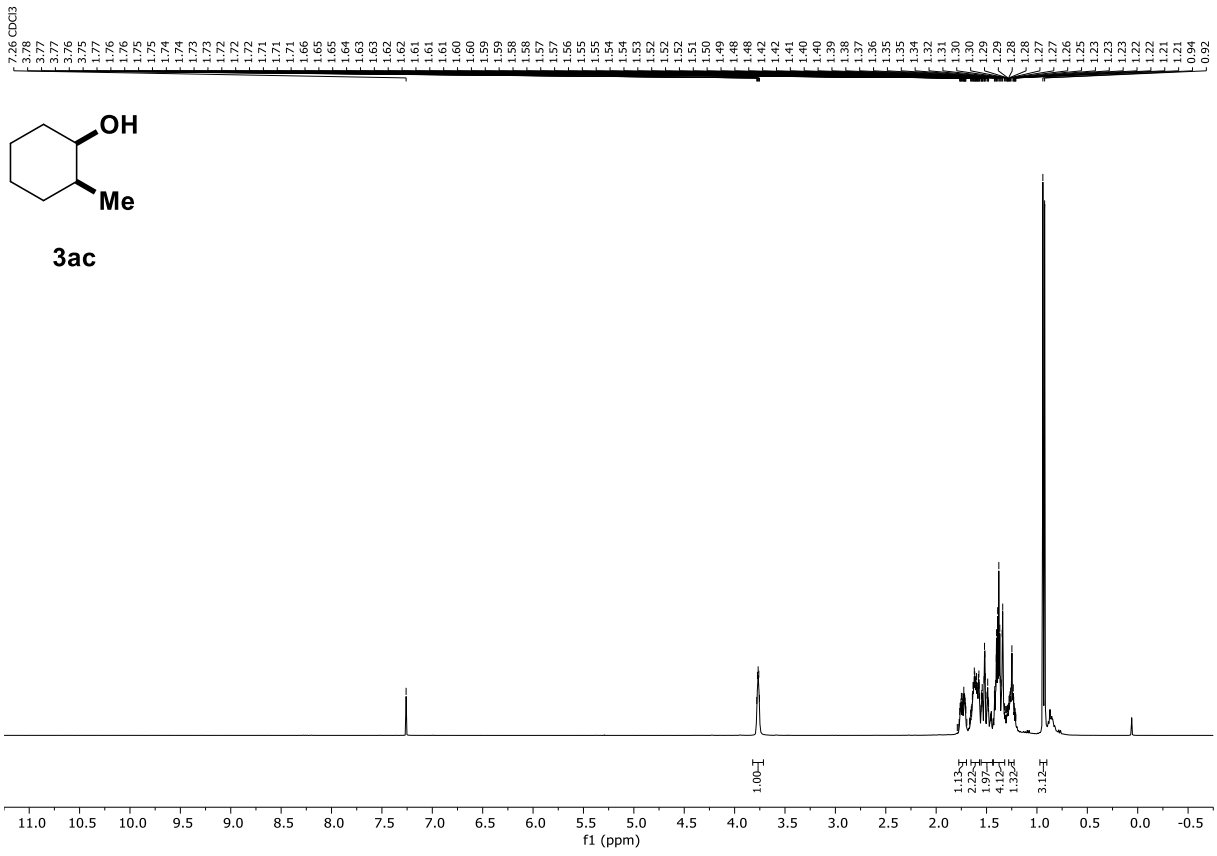


3a

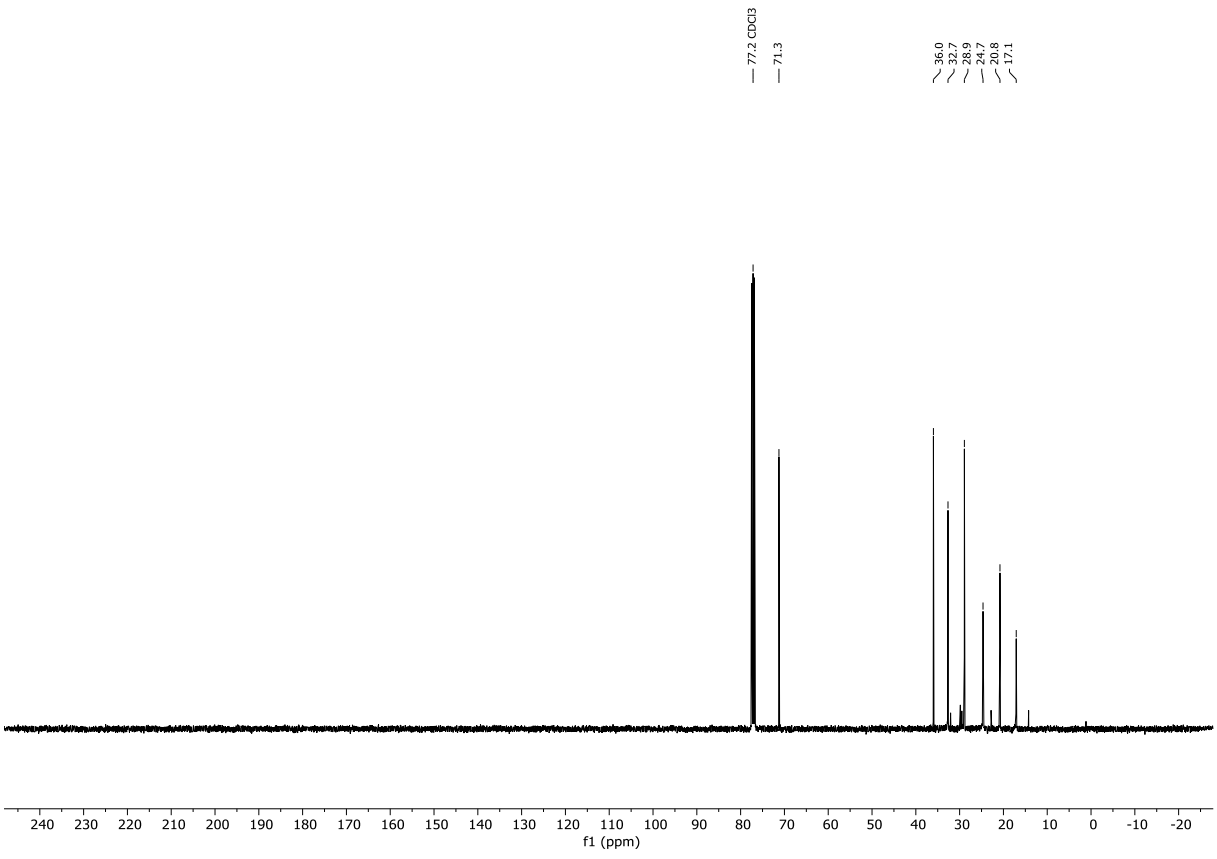


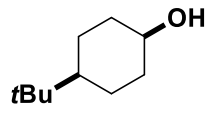

OH
Me
3ab
f1 (ppm)


77.2 CDCl3
71.0
44.8
35.6
34.2
31.6
24.3
22.5
f1 (ppm)


7.26 CDCl3
OH
Me
1.00
1.13
2.22
1.97
4.12
1.32
3.12
f1 (ppm)

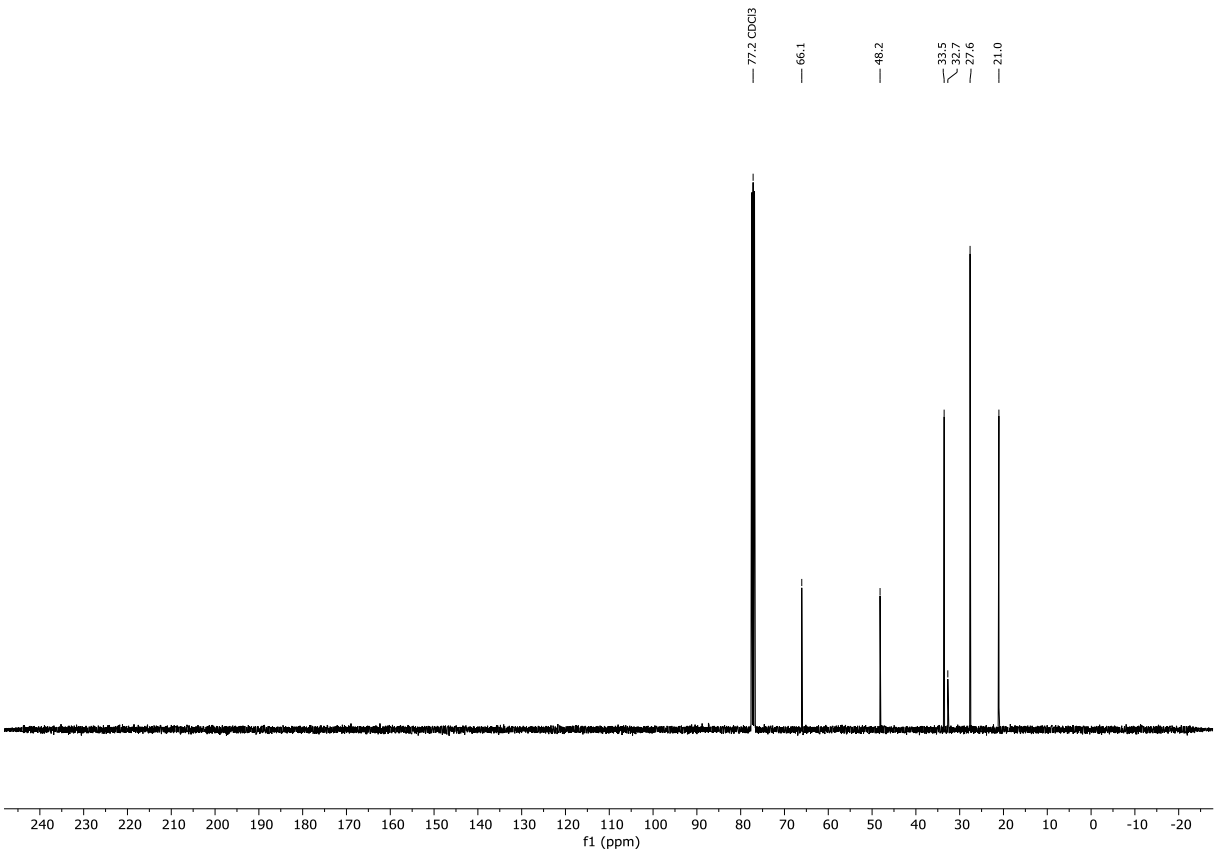
3ac

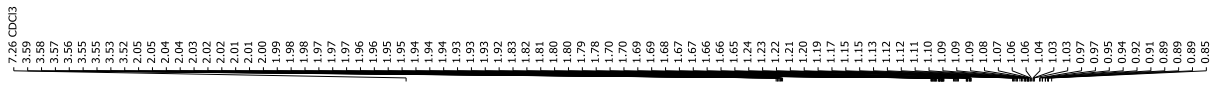

77.2 CDCl3
71.3
36.0
32.7
28.9
24.7
20.8
17.1
f1 (ppm)

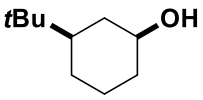

OH
tBu

3b

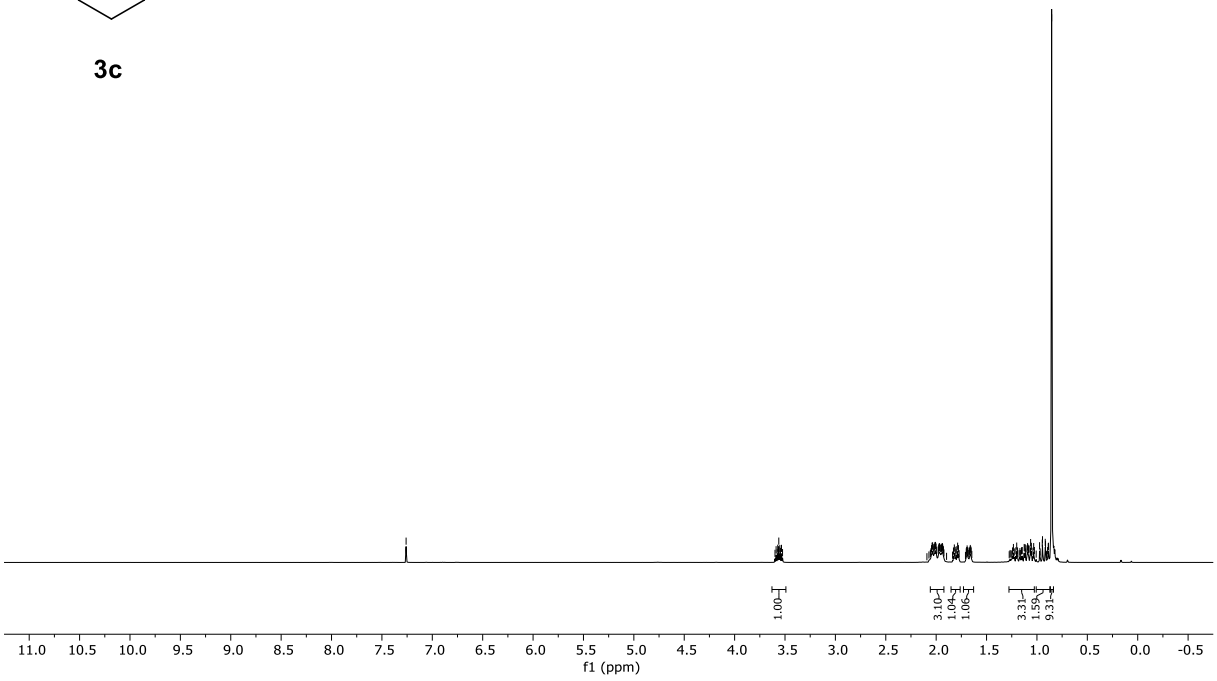
7.26 CDCl3
4.05
4.04
4.03
4.02
1.86
1.85
1.85
1.85
1.84
1.84
1.83
1.83
1.83
1.82
1.82
1.81
1.81
1.80
1.80
1.56
1.56
1.55
1.54
1.53
1.53
1.52
1.52
1.49
1.49
1.48
1.48
1.46
1.45
1.45
1.44
1.40
1.39
1.37
1.36
1.34
1.34
1.33
1.31
1.30
1.29
1.24
1.03
1.02
1.01
1.00
0.99
0.98
0.97
0.96
0.95
0.86
1.00
2.04
4.21
2.15
0.90
1.04
9.24
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

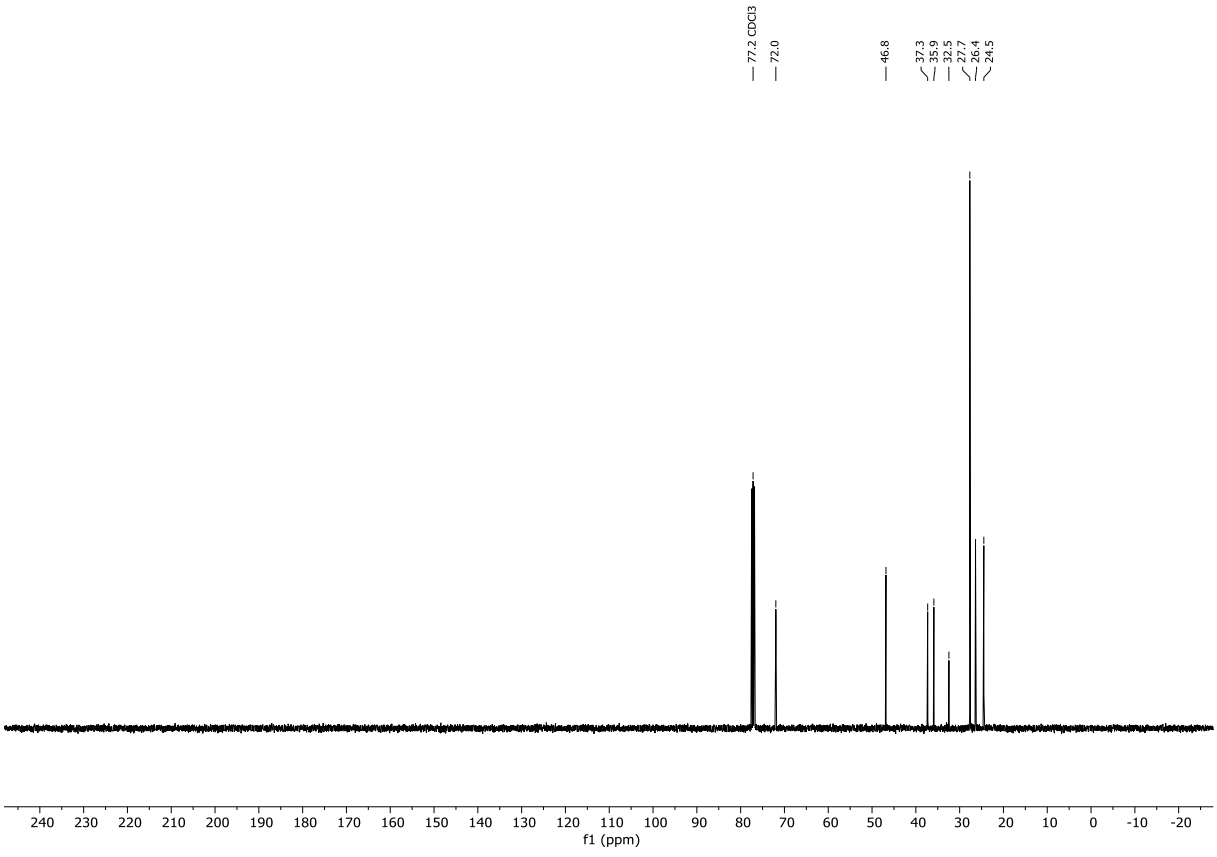

77.2 CDCl3
66.1
48.2
33.5
32.7
27.6
21.0
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

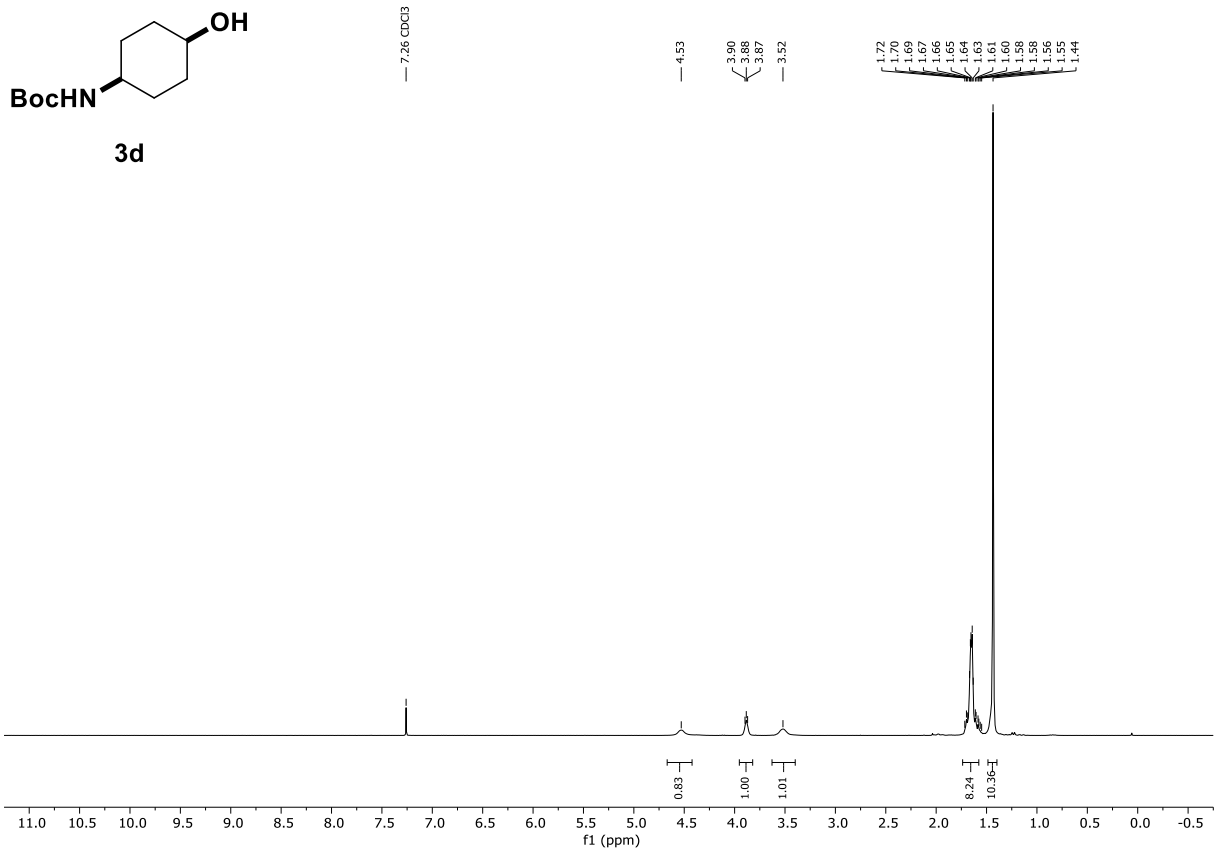

7.26 CDCl3
3.59
3.58
3.57
3.56
3.55
3.55
3.53
3.52
2.05
2.04
2.04
2.03
2.02
2.02
2.01
2.01
2.00
1.99
1.98
1.98
1.97
1.97
1.97
1.96
1.96
1.95
1.95
1.94
1.94
1.94
1.93
1.93
1.93
1.92
1.83
1.82
1.81
1.80
1.80
1.79
1.78
1.70
1.70
1.69
1.69
1.68
1.67
1.67
1.66
1.66
1.65
1.24
1.23
1.22
1.21
1.20
1.19
1.17
1.15
1.15
1.13
1.12
1.12
1.11
1.10
1.09
1.09
1.09
1.08
1.07
1.06
1.06
1.04
1.03
1.03
0.97
0.97
0.95
0.94
0.92
0.91
0.89
0.89
0.89
0.85

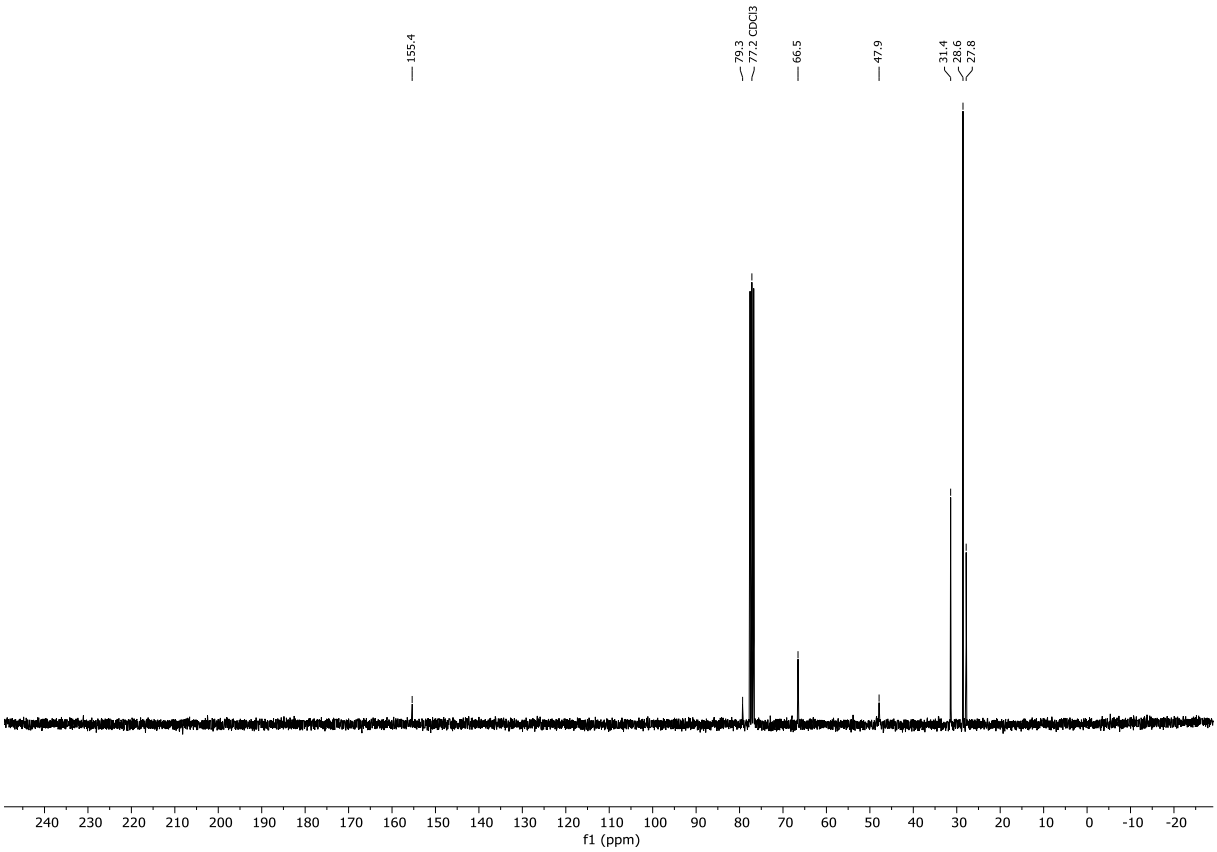

tBu
OH

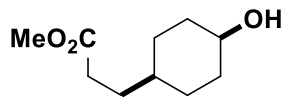
3c


1.00
3.10
1.04
1.06
3.31
1.59
9.31
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


77.2 CDCl3
72.0
46.8
37.3
35.9
32.5
27.7
26.4
24.5
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

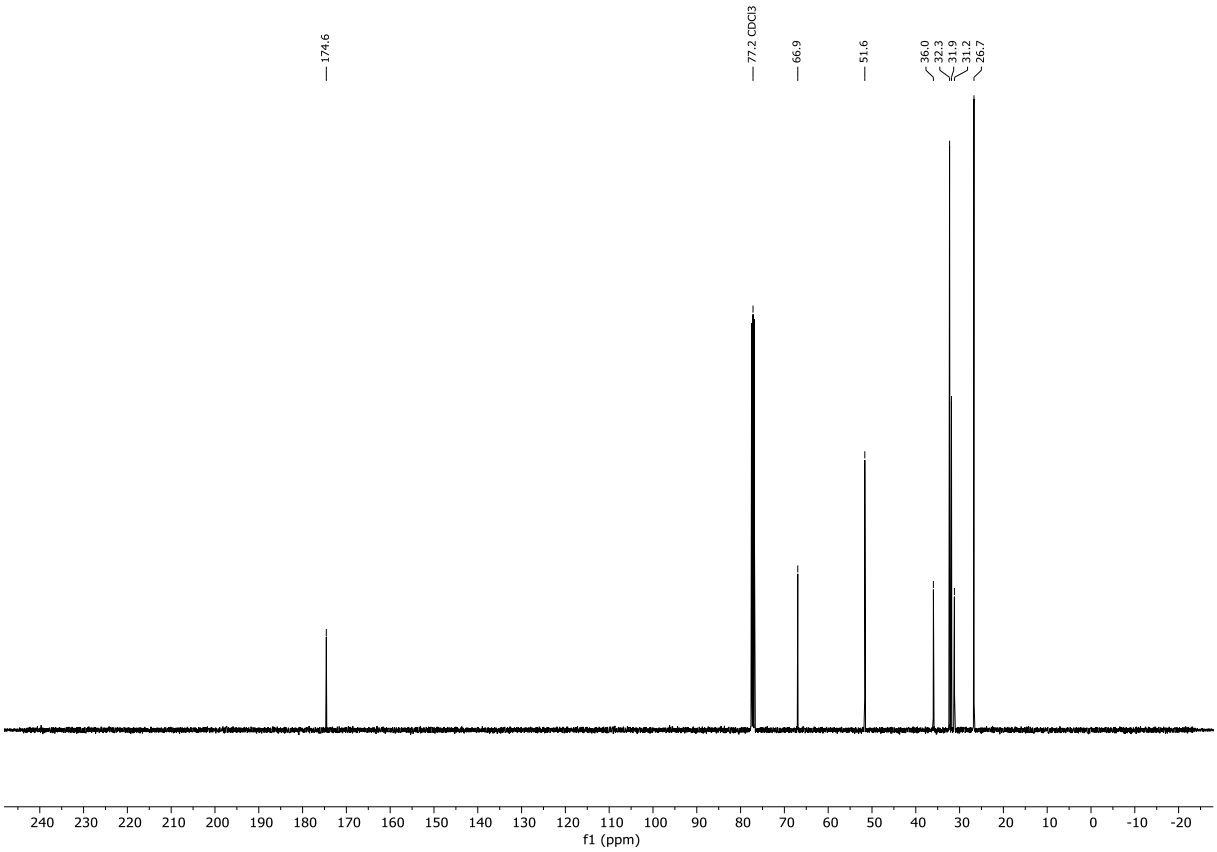

OH
BocHN
3d
7.26 CDCl3
4.53
3.90
3.88
3.87
3.52
1.72
1.70
1.69
1.67
1.66
1.65
1.64
1.63
1.61
1.60
1.58
1.58
1.56
1.55
1.44
0.83
1.00
1.01
8.24
10.36
f1 (ppm)

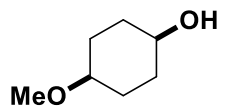

155.4
79.3
77.2 CDCl3
66.5
47.9
31.4
28.6
27.8
f1 (ppm)


MeO2C
OH

3e

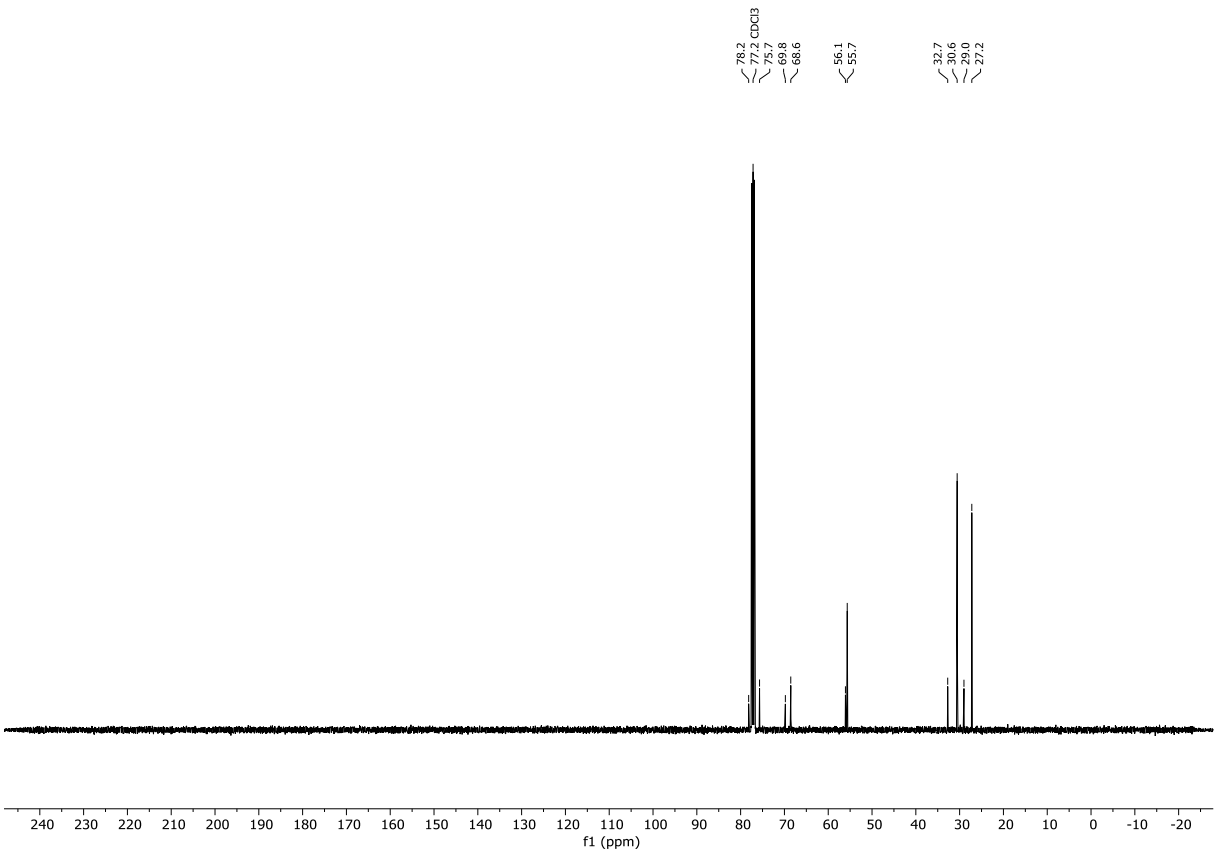
7.26 CDCl3
3.97
3.96
3.95
3.95
3.94
3.65
2.34
2.32
2.30
1.72
1.69
1.67
1.61
1.59
1.57
1.55
1.52
1.50
1.49
1.48
1.41
1.40
1.38
1.37
1.34
1.32
1.00
3.04
2.08
2.13
6.09
4.07
f1 (ppm)

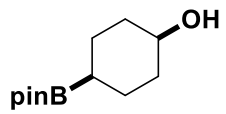

174.6
77.2 CDCl3
66.9
51.6
36.0
32.3
31.9
31.2
26.7
f1 (ppm)


OH
MeO

3f

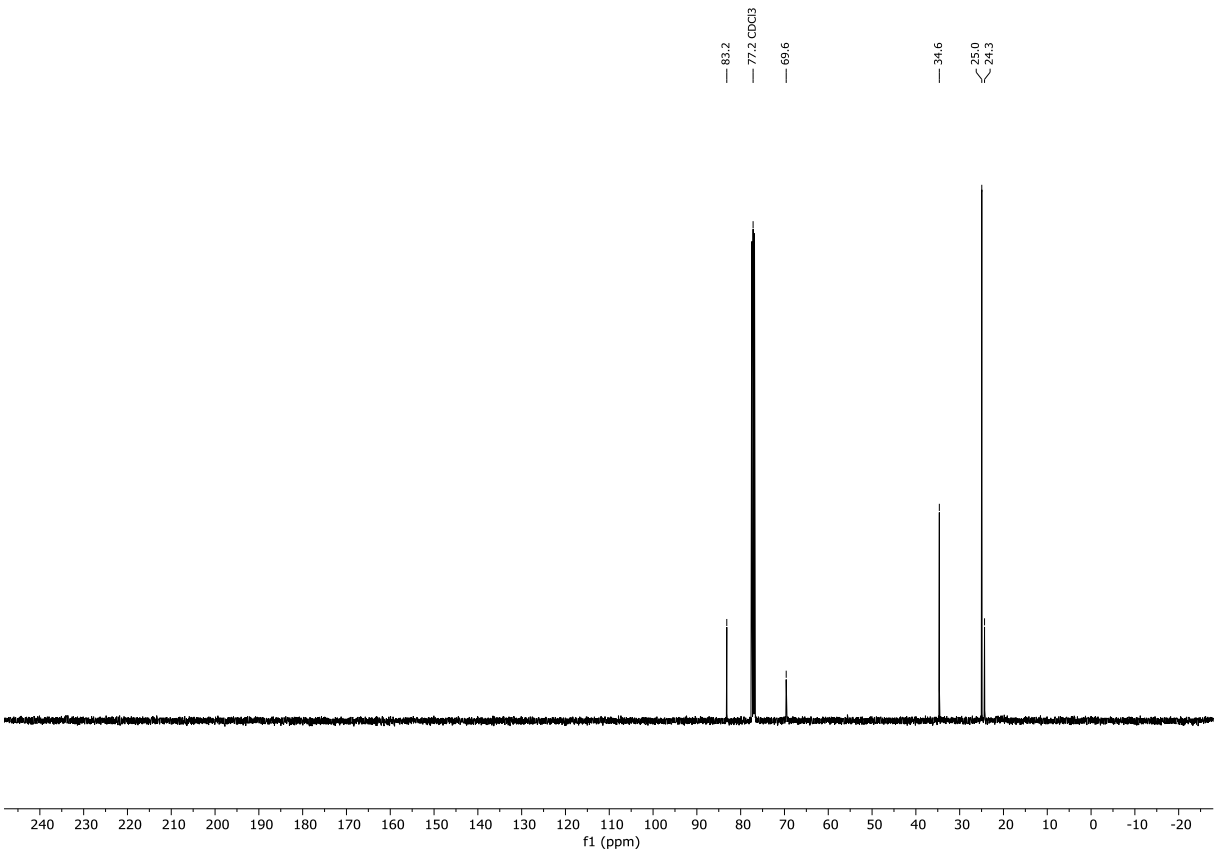
7.26 CDCl3
3.76
3.74
3.73
3.71
3.70
3.33
3.31
3.29
3.28
3.28
3.27
3.26
1.85
1.83
1.82
1.80
1.79
1.68
1.67
1.67
1.64
1.62
1.58
1.57
1.56
1.54
1.54
1.52
1.51
1.50
1.42
1.32
1.31
1.30
1.00
3.00
0.92
0.97
1.72
3.85
1.95
0.80
1.31
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

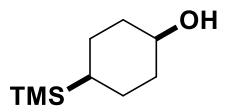

78.2
77.2 CDCl3
75.7
69.8
68.6
56.1
55.7
32.7
30.6
29.0
27.2
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


OH
pinB

3g

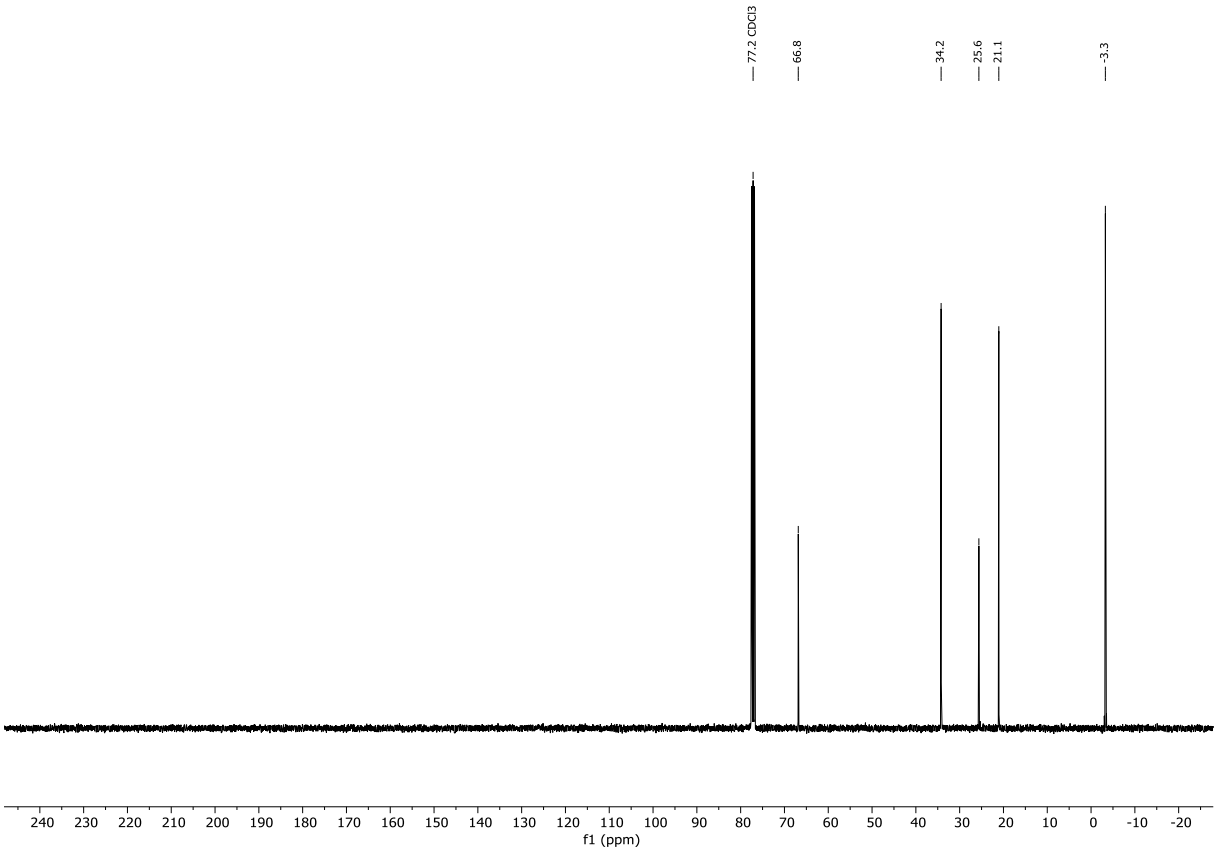
7.26 CDCl3
3.73
3.72
3.71
3.70
3.69
1.84
1.83
1.82
1.81
1.80
1.79
1.78
1.77
1.76
1.74
1.73
1.72
1.50
1.49
1.48
1.47
1.45
1.43
1.41
1.40
1.39
1.38
1.36
1.24
1.11
1.00
4.09
4.07
0.88
12.13
1.04
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

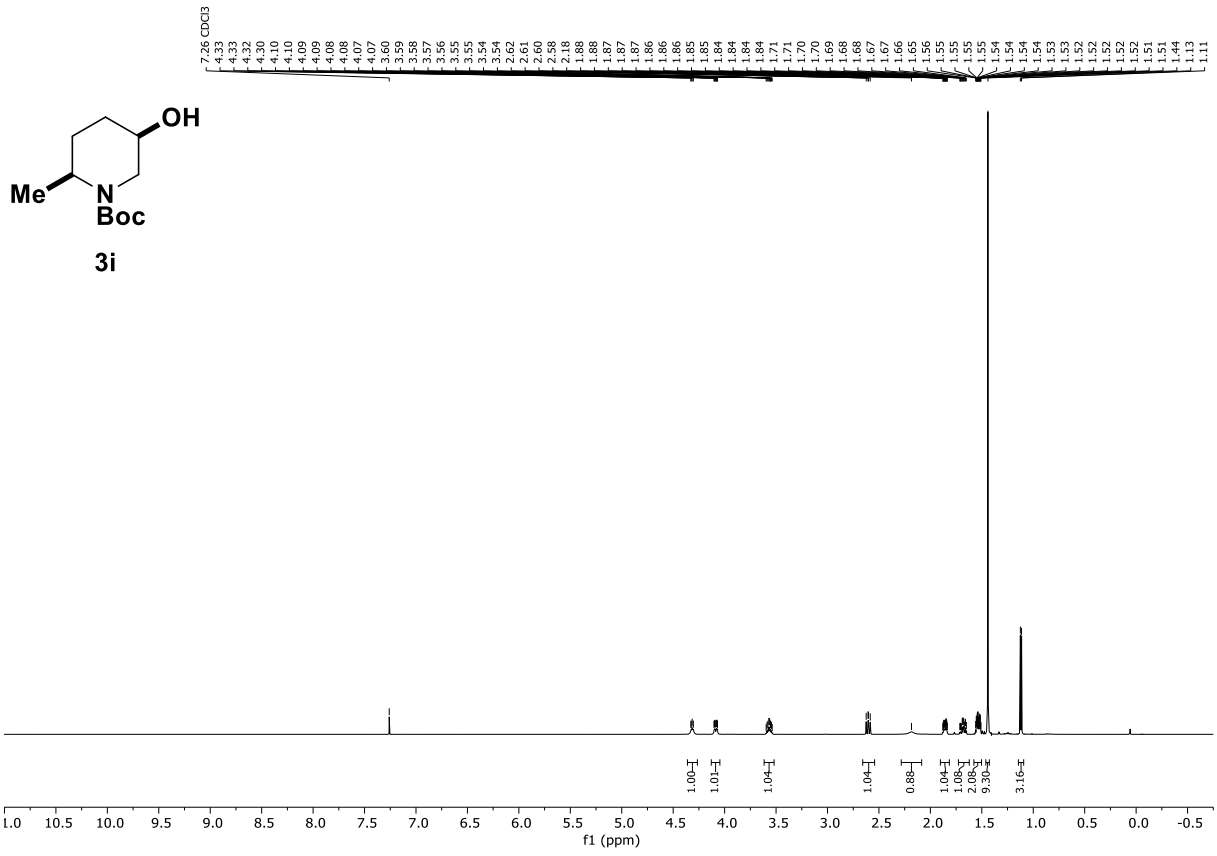

83.2
77.2 CDCl3
69.6
34.6
25.0
24.3
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

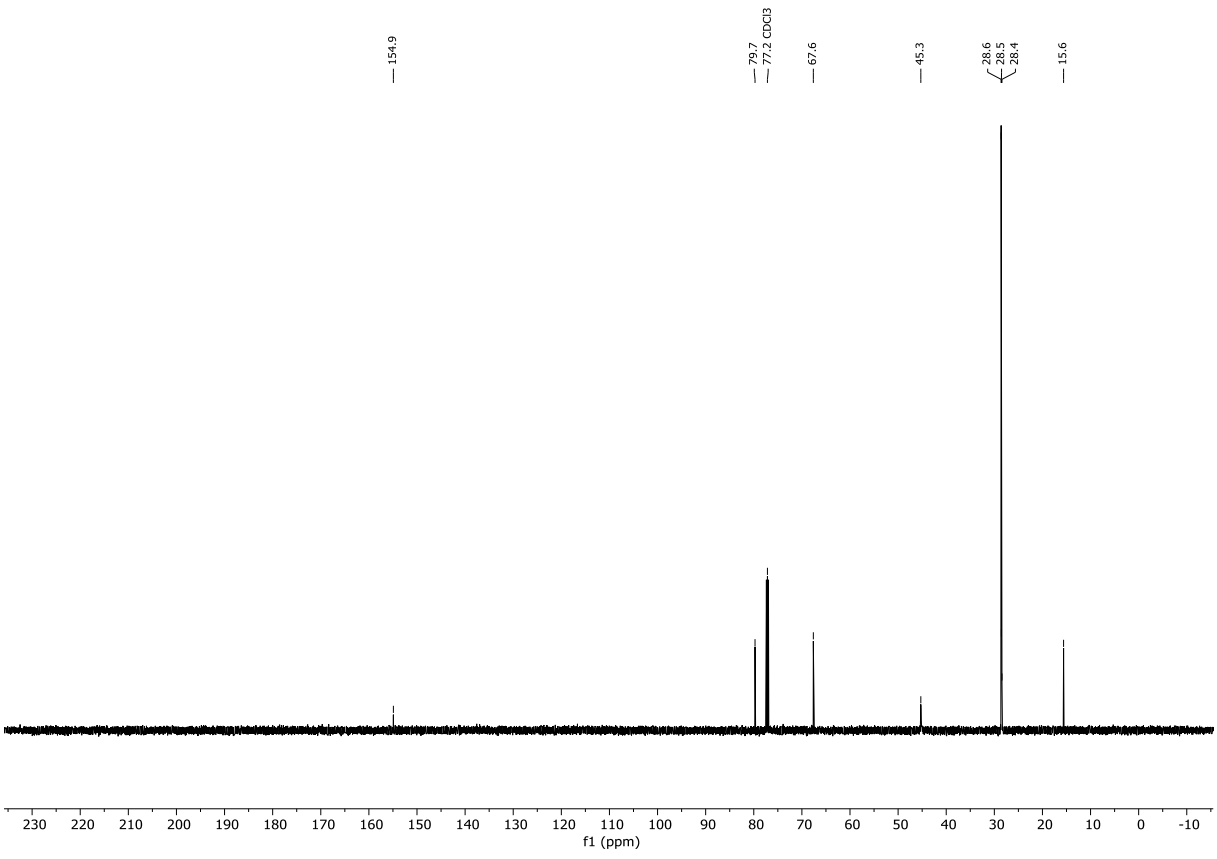

OH
TMS

3h

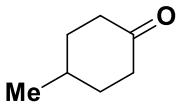
7.26 CDCl3
1.00
2.05
6.19
1.00
0.99
9.11
f1 (ppm)


77.2 CDCl3
66.8
34.2
25.6
21.1
-3.3
f1 (ppm)

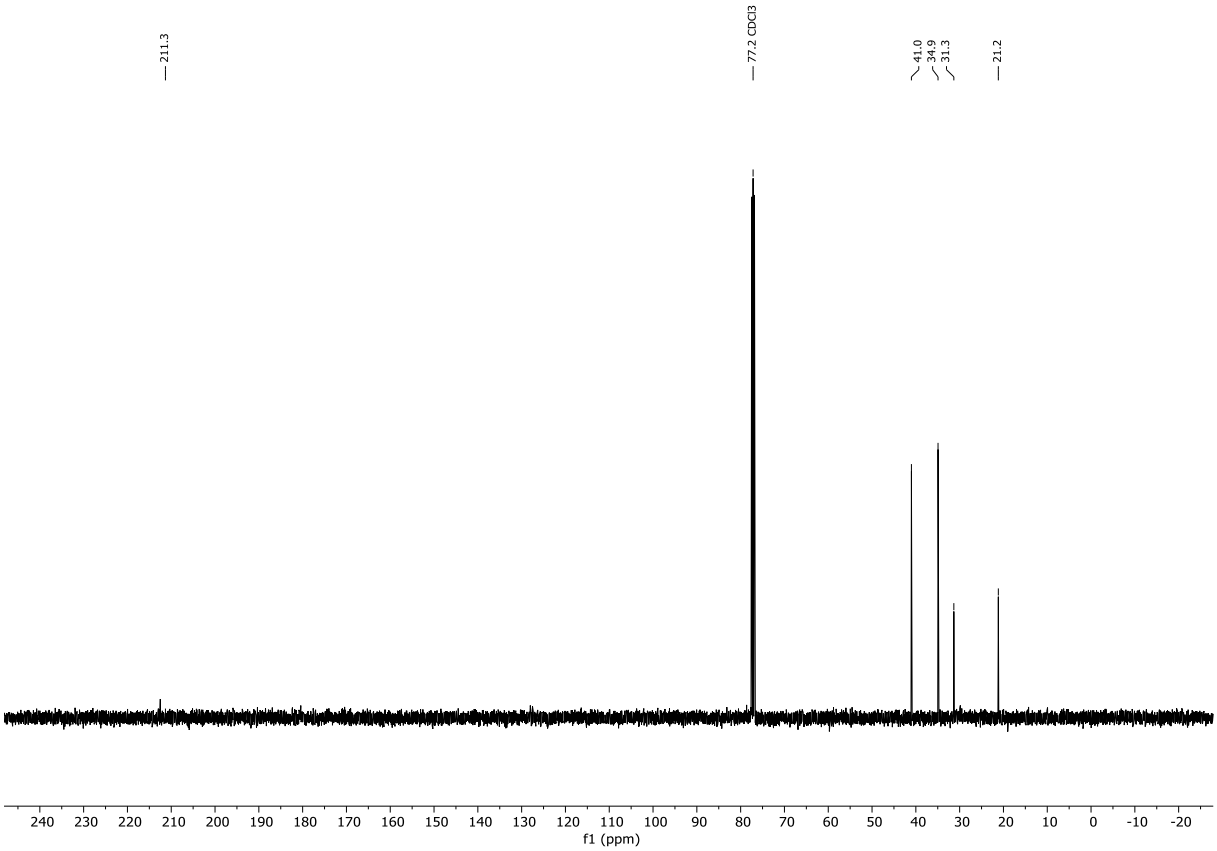

OH
Me
N
Boc
3i
f1 (ppm)

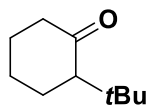

154.9
79.7
77.2 CDCl3
67.6
45.3
28.6
28.5
28.4
15.6
f1 (ppm)

11.3 Cyclohexanones



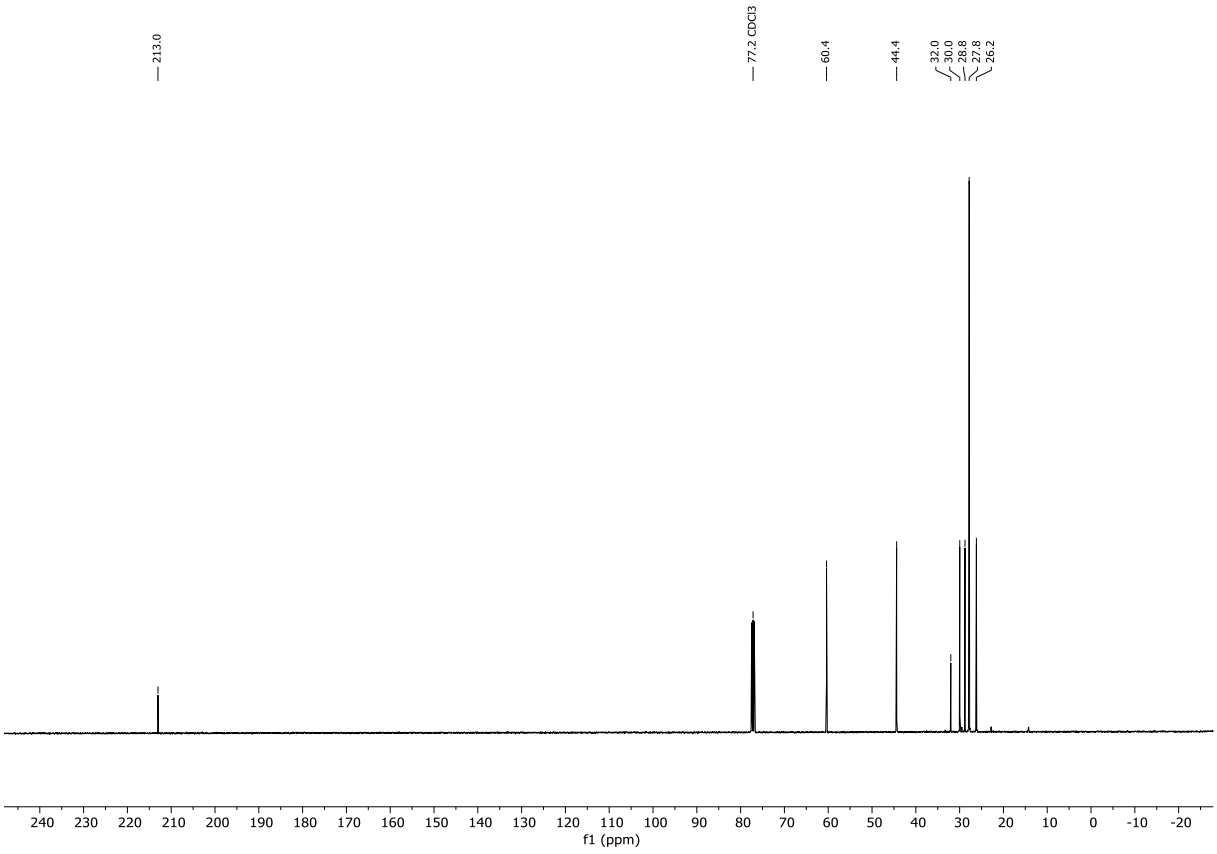
4a

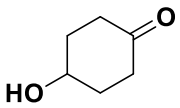



O
tBu

4b

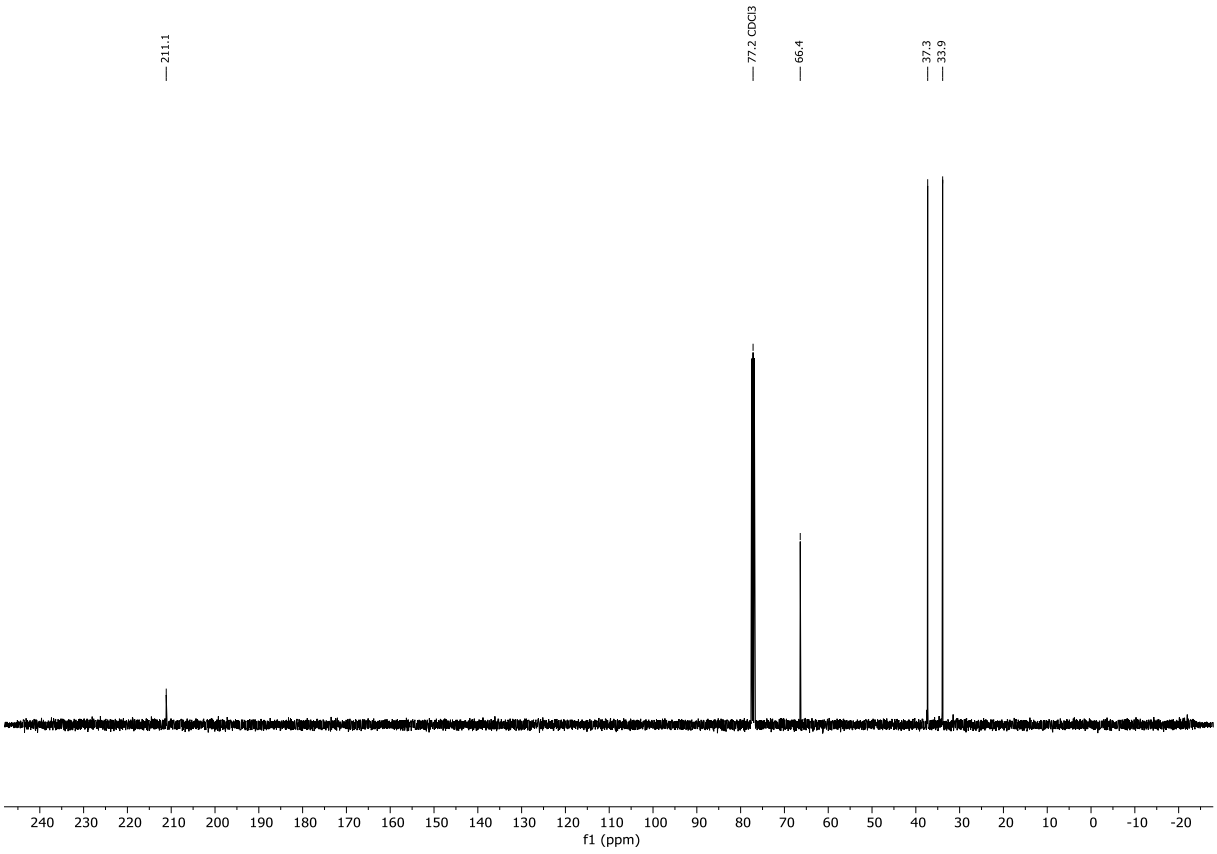
7.26 CDCl3
0.97
1.98
2.00
1.02
1.00
2.00
1.06
9.08
f1 (ppm)

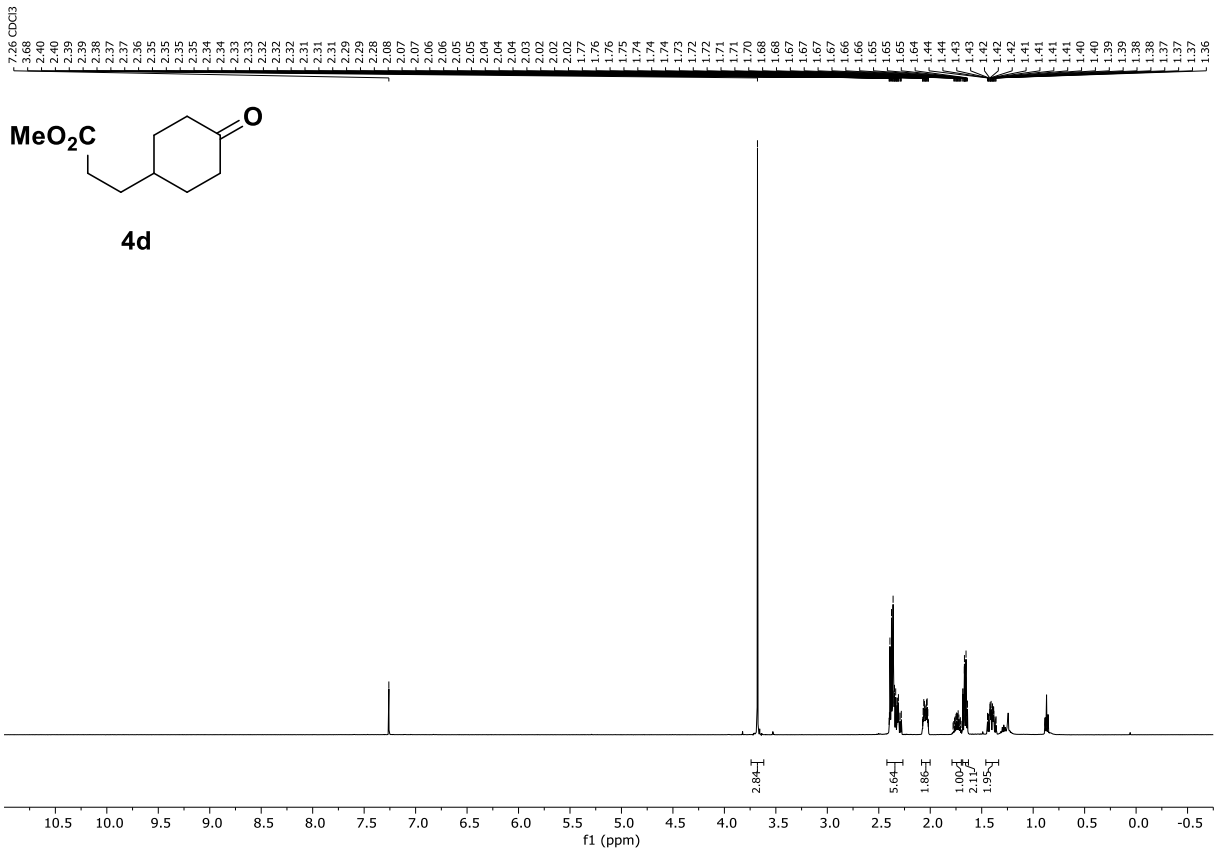

213.0
77.2 CDCl3
60.4
44.4
32.0
30.0
28.8
27.8
26.2
f1 (ppm)

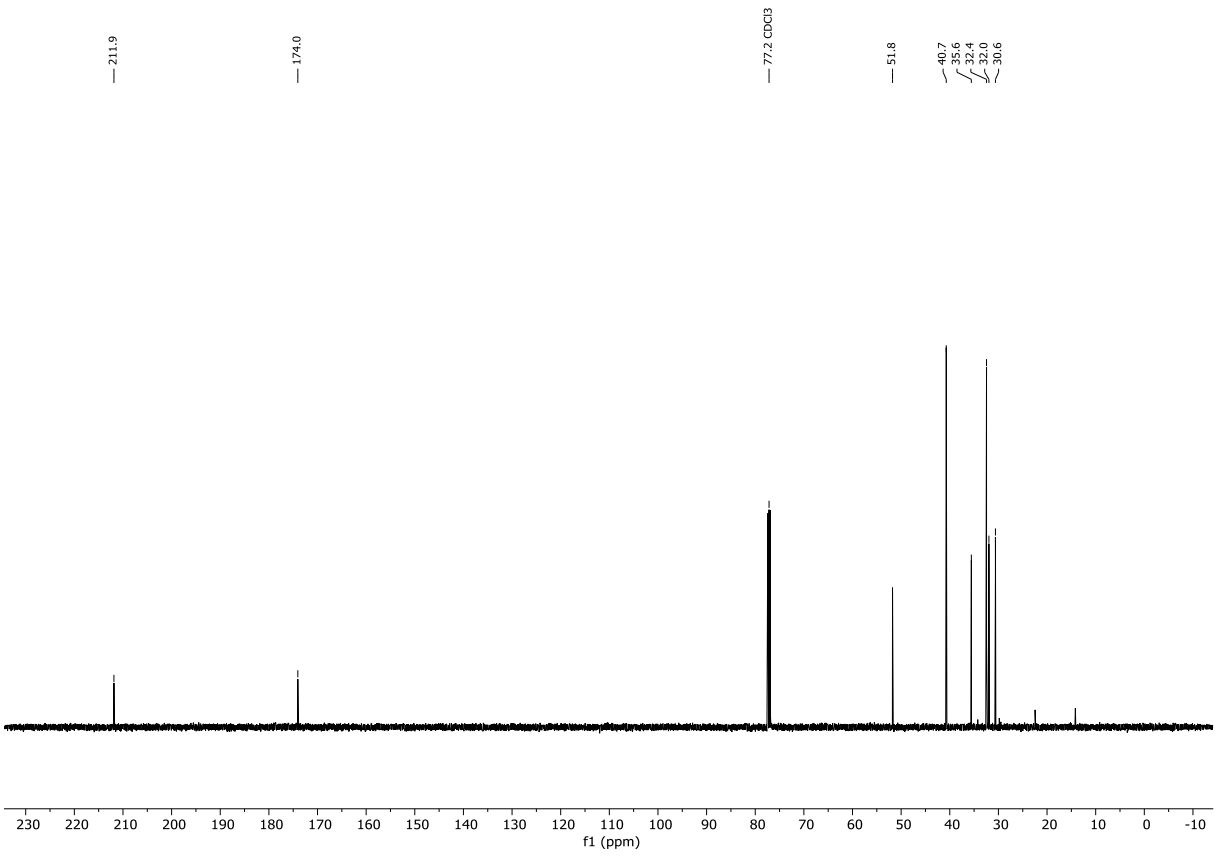

O
HO

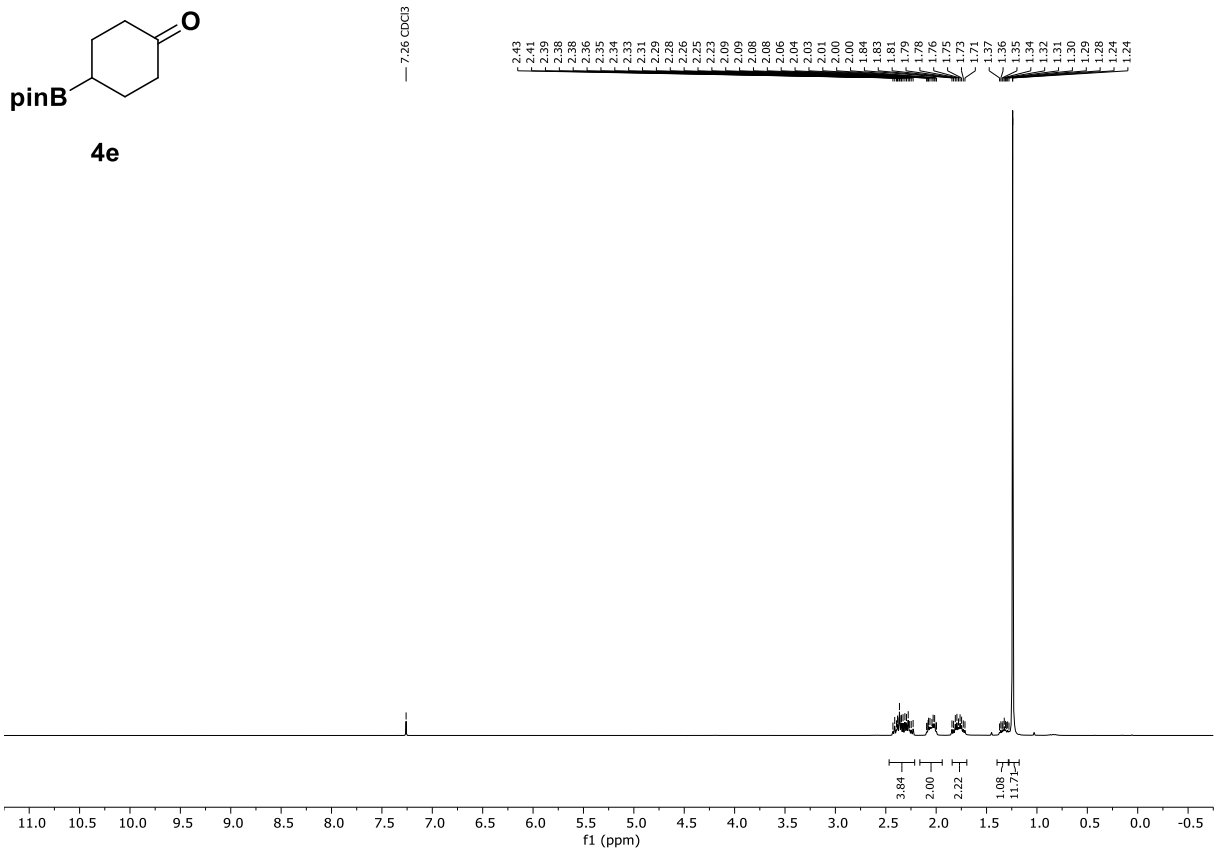
4c

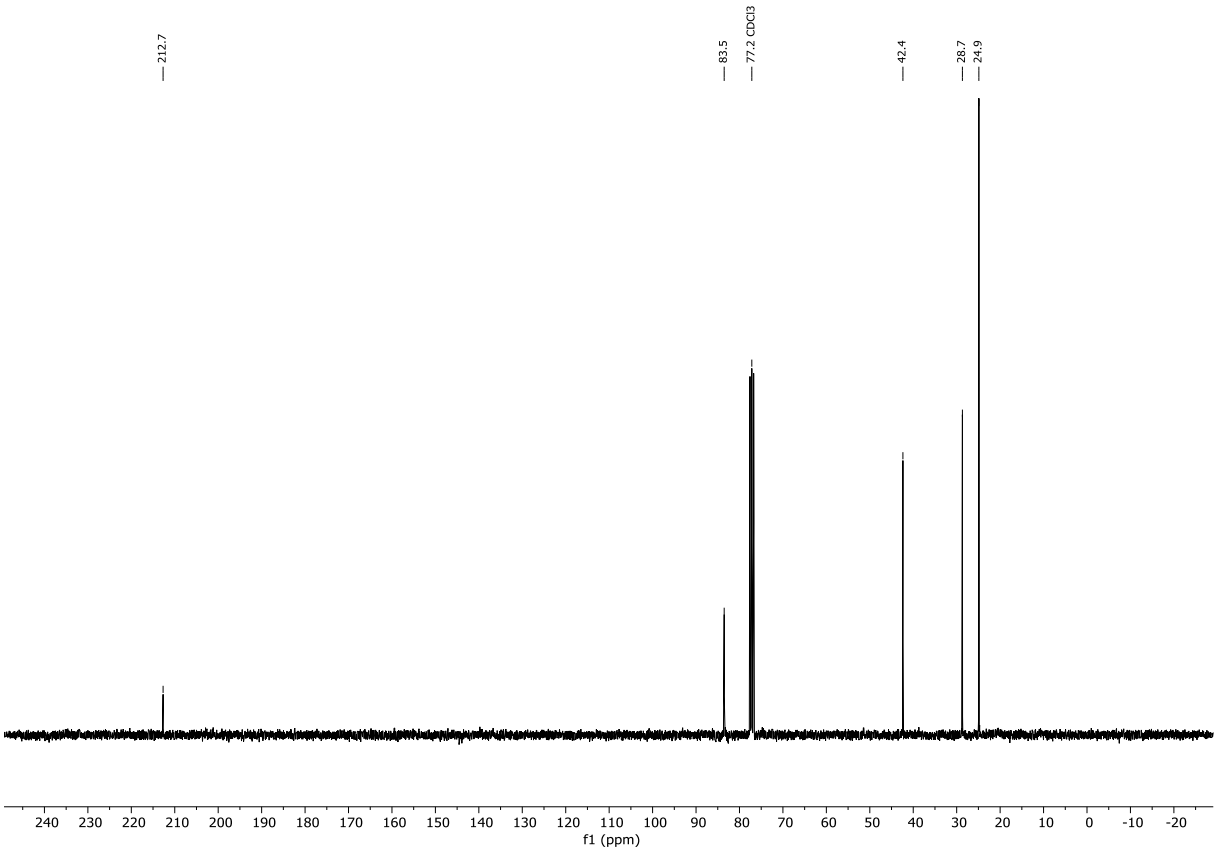
7.26 CDCl3
4.21
4.20
4.19
4.18
4.18
4.17
4.16
2.63
2.62
2.61
2.60
2.58
2.57
2.56
2.33
2.32
2.30
2.28
2.26
2.09
2.08
2.07
2.06
2.04
2.03
2.02
2.01
2.00
1.98
1.97
1.95
1.93
1.92
1.86
1.00
2.06
2.08
4.16
1.38
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

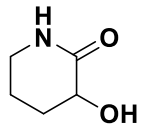

211.1
77.2 CDCl3
66.4
37.3
33.9
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


7.26 CDCl3
MeO2C
O
4d
2.84
5.64
1.86
1.00
2.11
1.95
f1 (ppm)

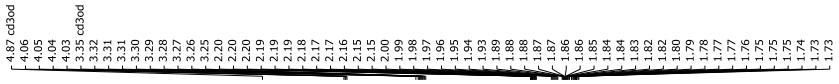

211.9
174.0
77.2 CDCl3
51.8
40.7
35.6
32.4
32.0
30.6
f1 (ppm)

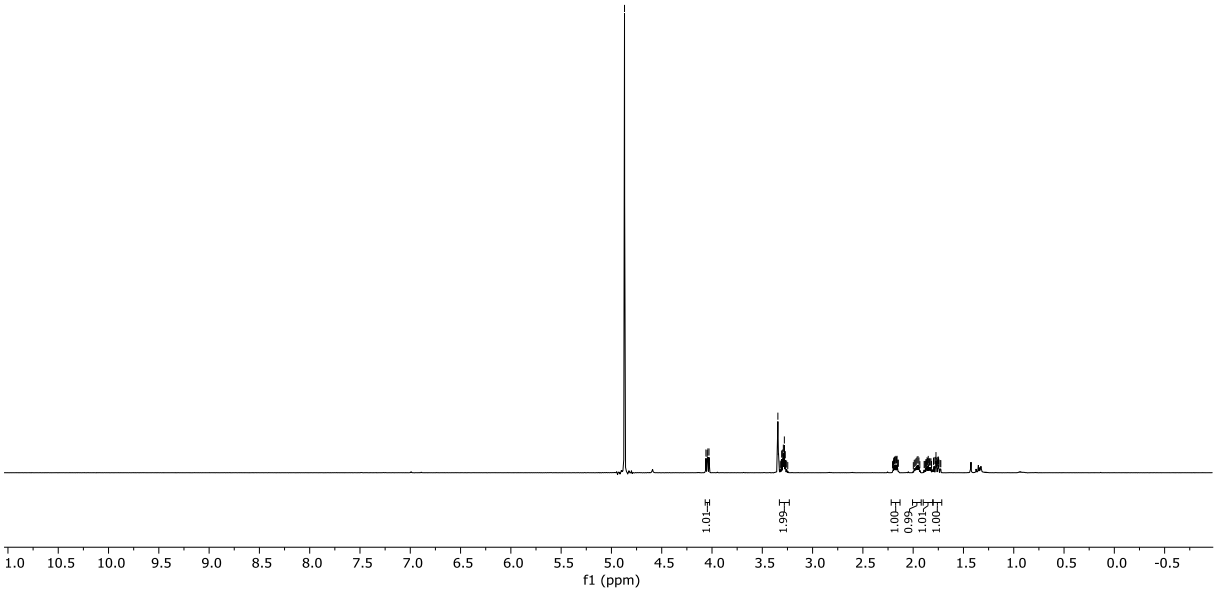

pinB
O
4e
7.26 CDCl3
2.43
2.41
2.39
2.38
2.38
2.36
2.35
2.34
2.33
2.31
2.29
2.28
2.26
2.25
2.23
2.09
2.09
2.08
2.08
2.06
2.04
2.03
2.01
2.00
2.00
1.84
1.83
1.81
1.79
1.78
1.76
1.75
1.73
1.71
1.37
1.36
1.35
1.34
1.32
1.31
1.30
1.29
1.28
1.24
1.24
3.84
2.00
2.22
1.08
11.71
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

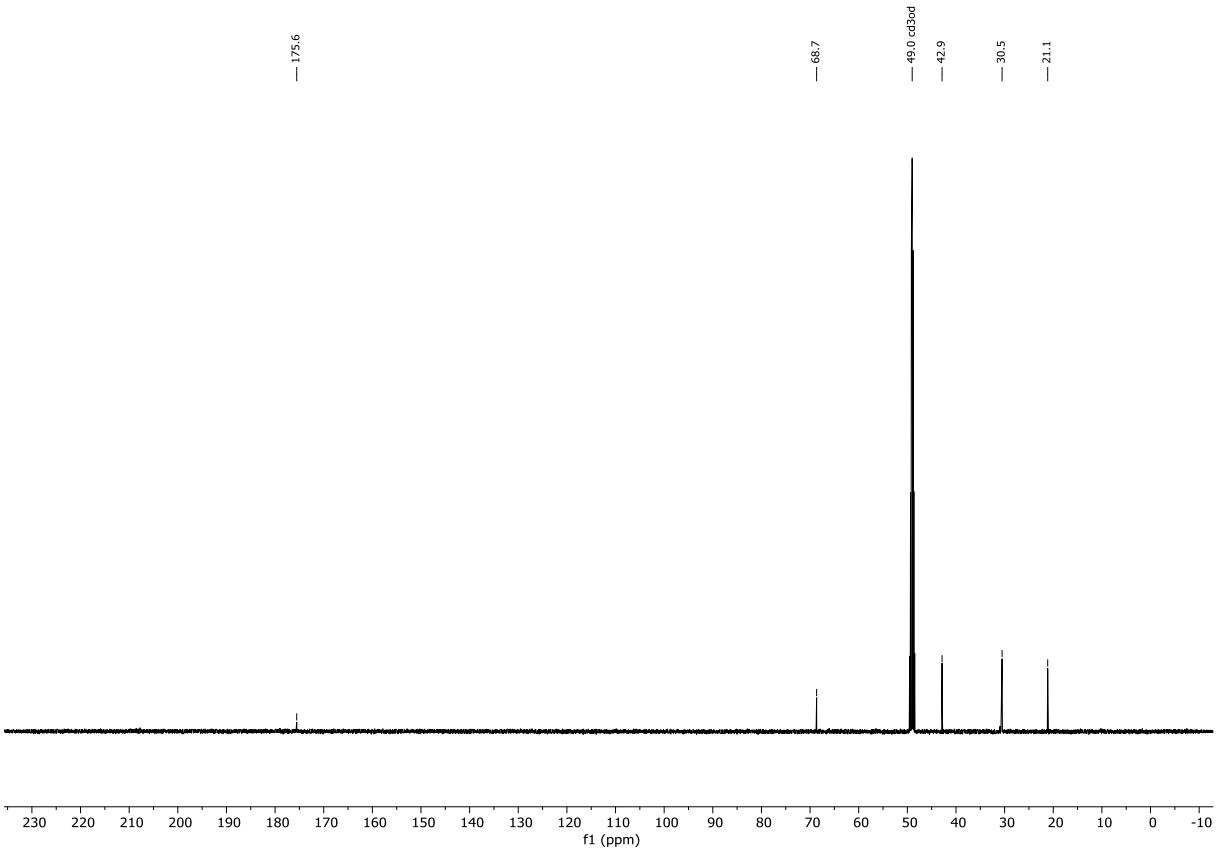

212.7
83.5
77.2 CDCl3
42.4
28.7
24.9
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


H
N
O
OH

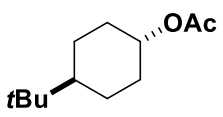
4f


4.87 cd3od
4.06
4.05
4.04
4.03
3.35 cd3od
3.32
3.31
3.31
3.30
3.29
3.28
3.27
3.26
3.25
2.20
2.20
2.20
2.19
2.19
2.19
2.18
2.17
2.17
2.16
2.15
2.15
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.93
1.89
1.88
1.88
1.87
1.87
1.86
1.86
1.85
1.84
1.84
1.83
1.82
1.82
1.80
1.79
1.78
1.77
1.77
1.77
1.76
1.75
1.75
1.75
1.74
1.73
1.73

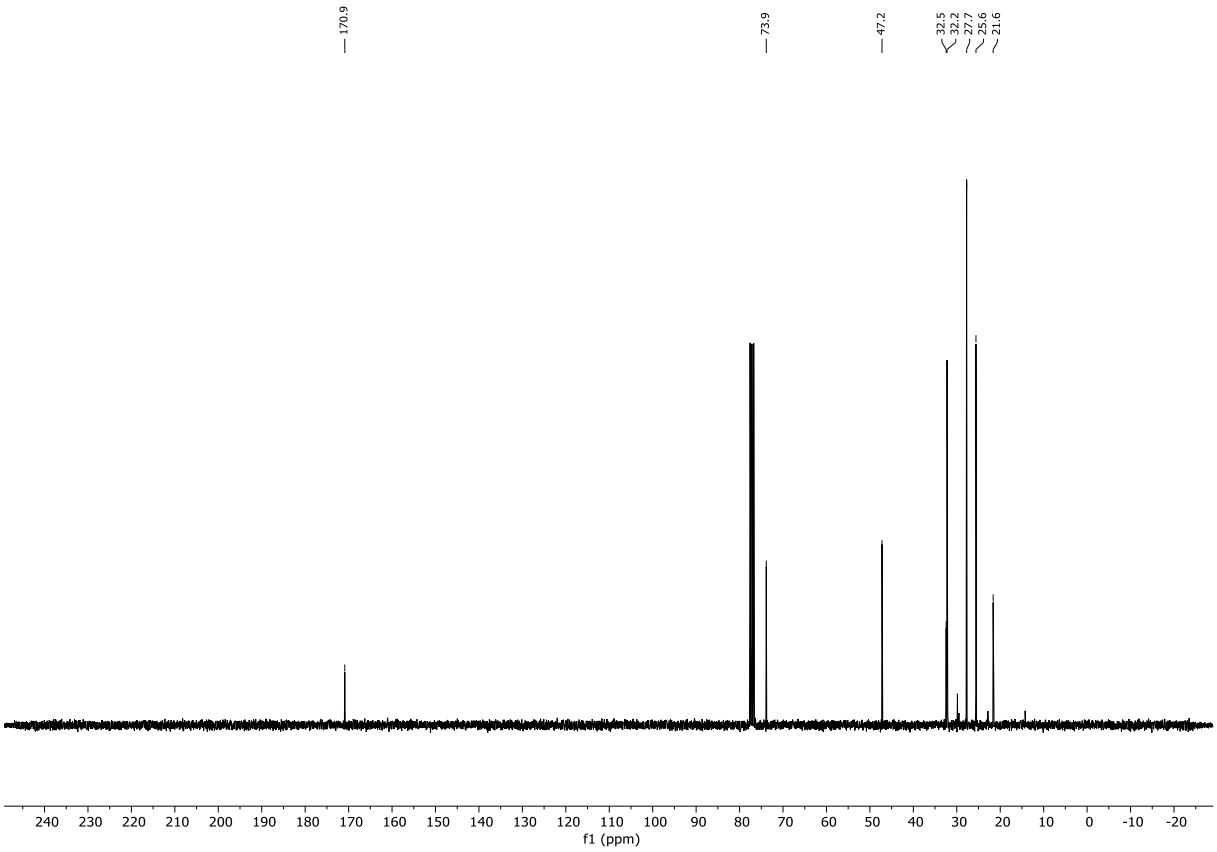

1.01
1.99
1.00
0.99
1.01
1.00
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

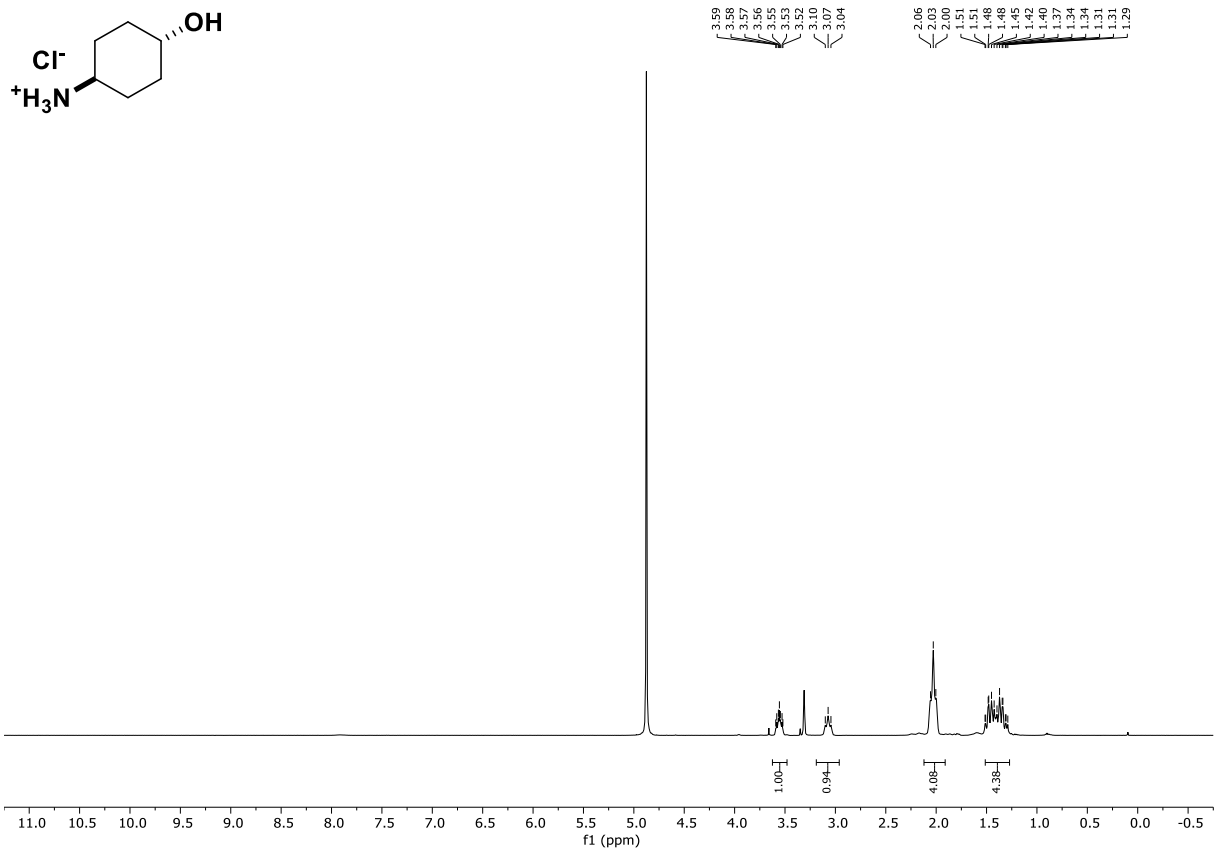

175.6
68.7
49.0 cd3od
42.9
30.5
21.1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

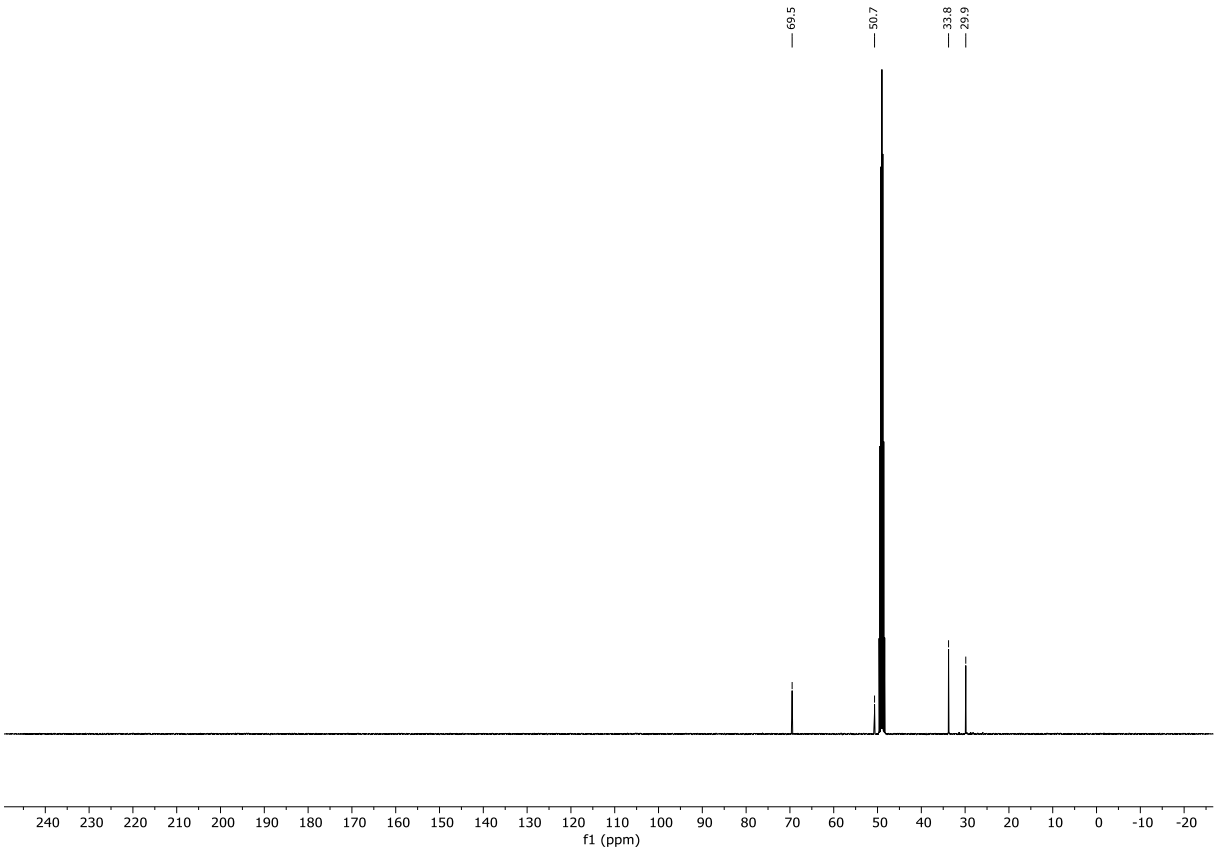
11.4 Application

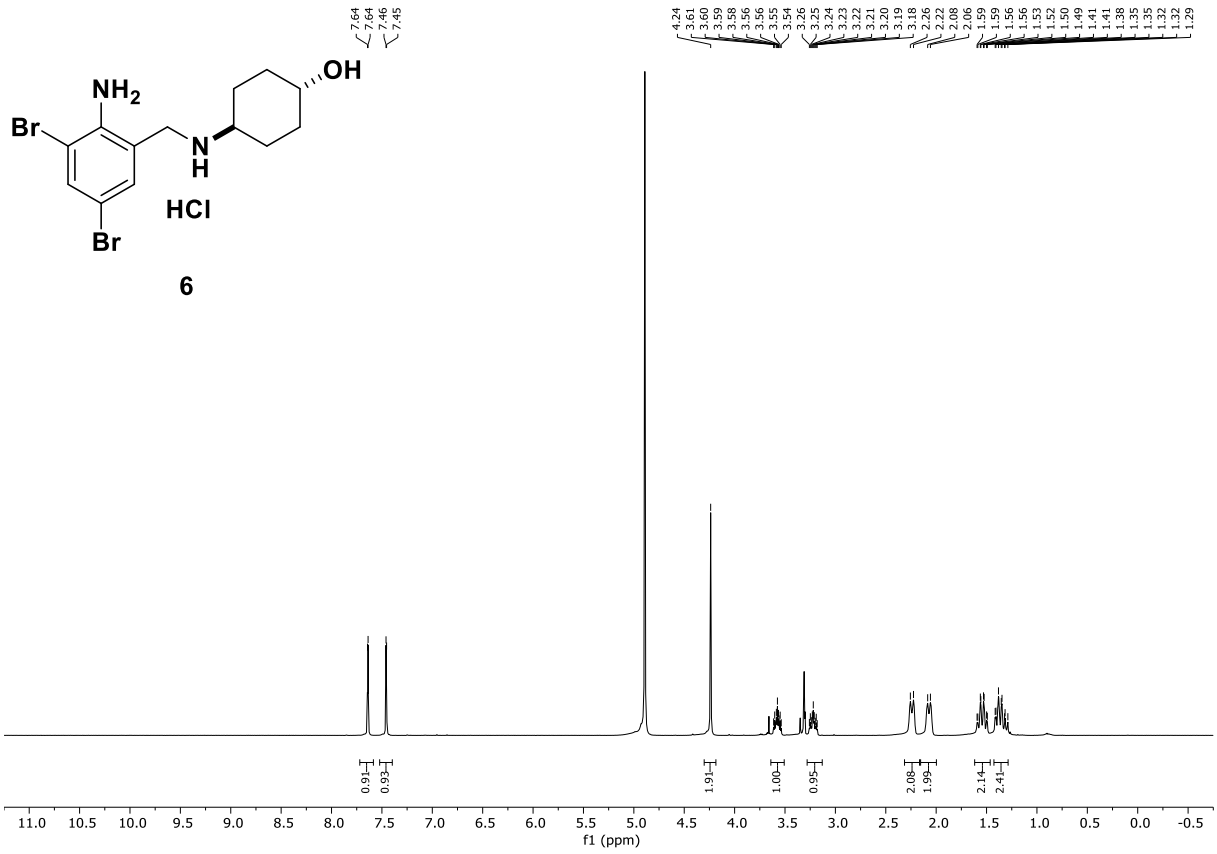


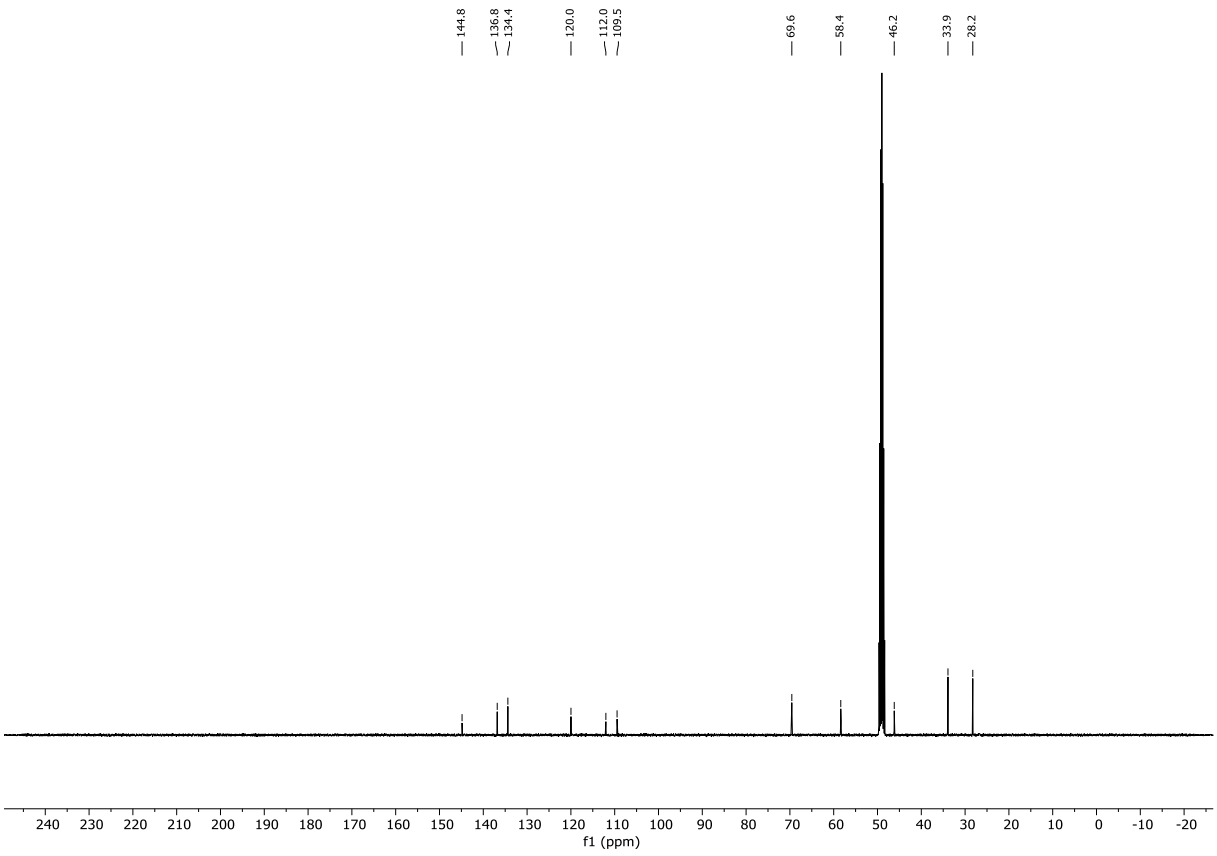
5




OH
Cl-
+H3N
3.59
3.58
3.57
3.56
3.55
3.53
3.52
3.10
3.07
3.04
2.06
2.03
2.00
1.51
1.51
1.48
1.48
1.45
1.42
1.40
1.37
1.34
1.34
1.31
1.31
1.29
1.00
0.94
4.08
4.38
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


69.5
50.7
33.8
29.9
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


NH2
Br
N
H
OH
HCl
Br
6
f1 (ppm)


f1 (ppm)