

## Supporting Information

# Potent Anticancer Activity with High Selectivity of a chiral Palladium N-heterocyclic Carbene Complex

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Howard University,  
Washington DC, USA 20059

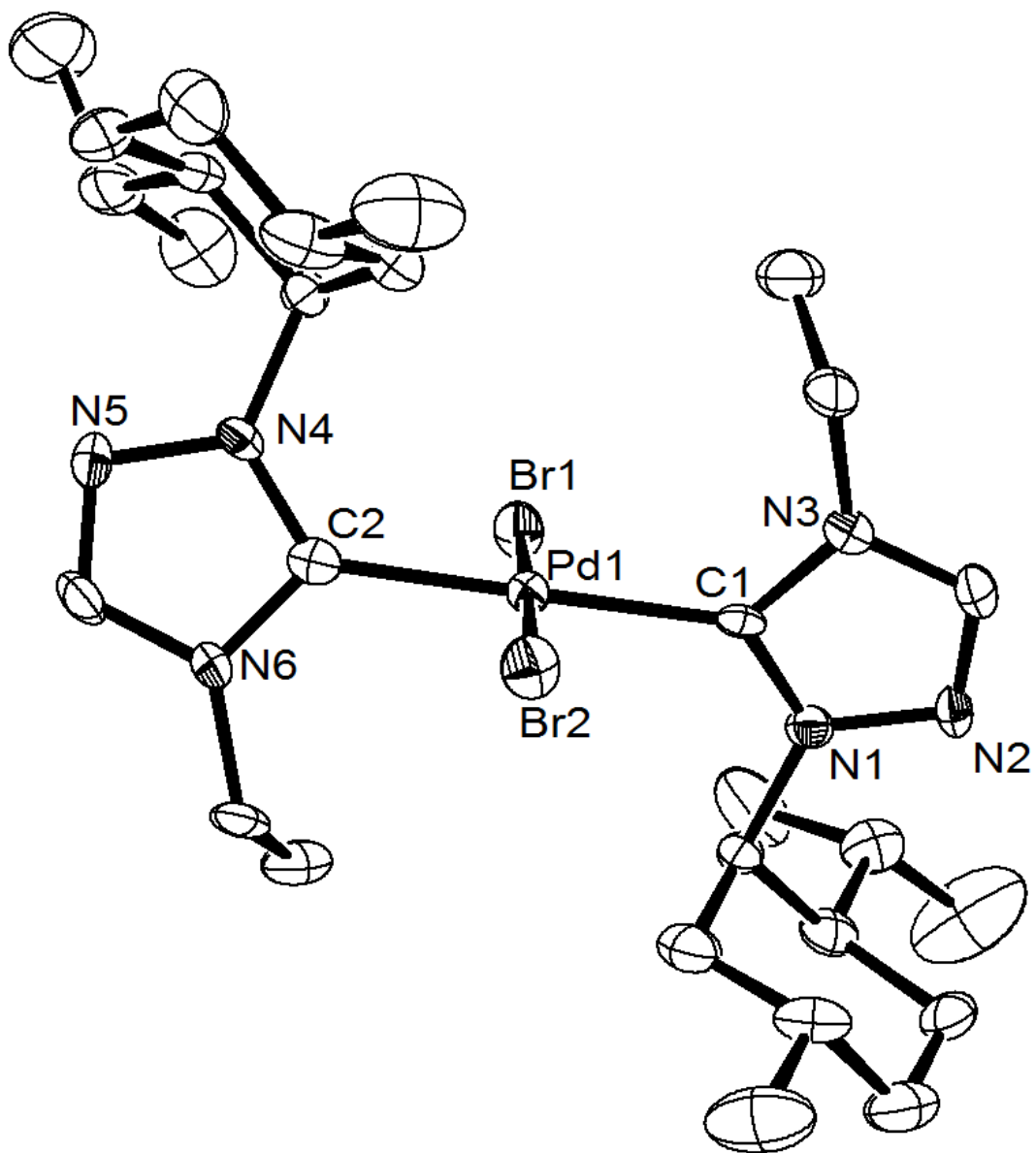
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Email: [pghosh@chem.iitb.ac.in](mailto:pghosh@chem.iitb.ac.in), [panda@iitb.ac.in](mailto:panda@iitb.ac.in)

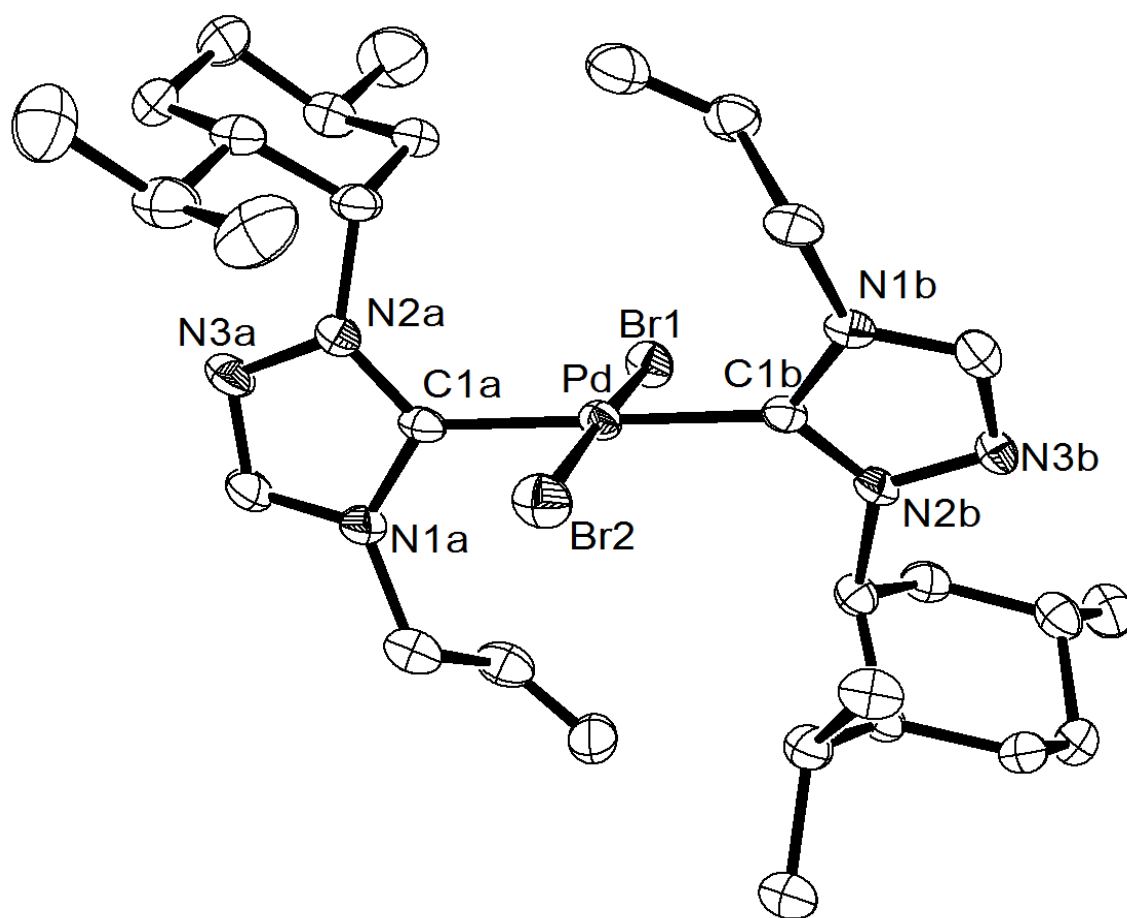
Fax: +91 22 2572 3480

Current Affiliation: AK: Department of Chemistry, University of Delhi, Delhi, 110007, India.

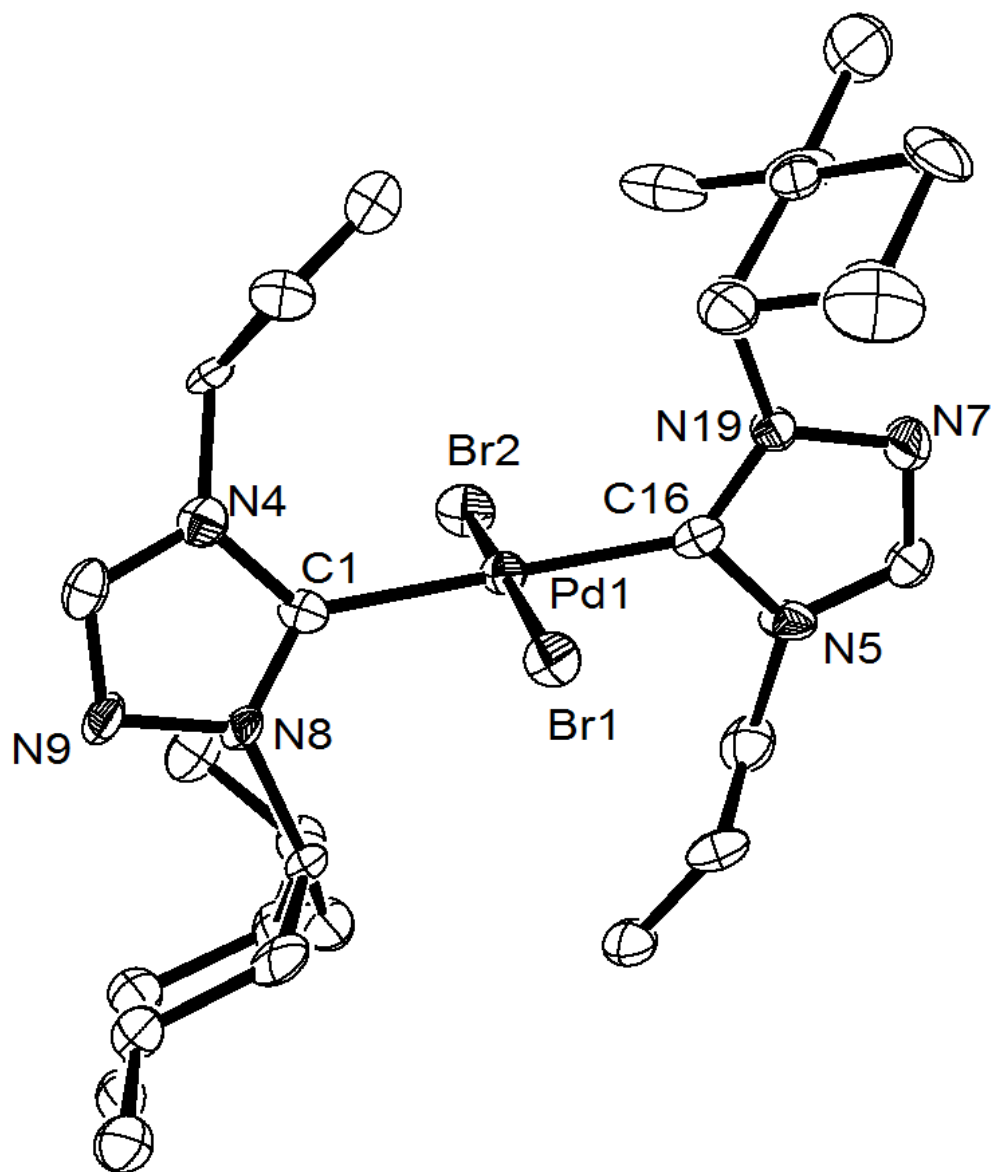
MKG: Department of Chemistry, IIT Kanpur, Kanpur, 208016, India.



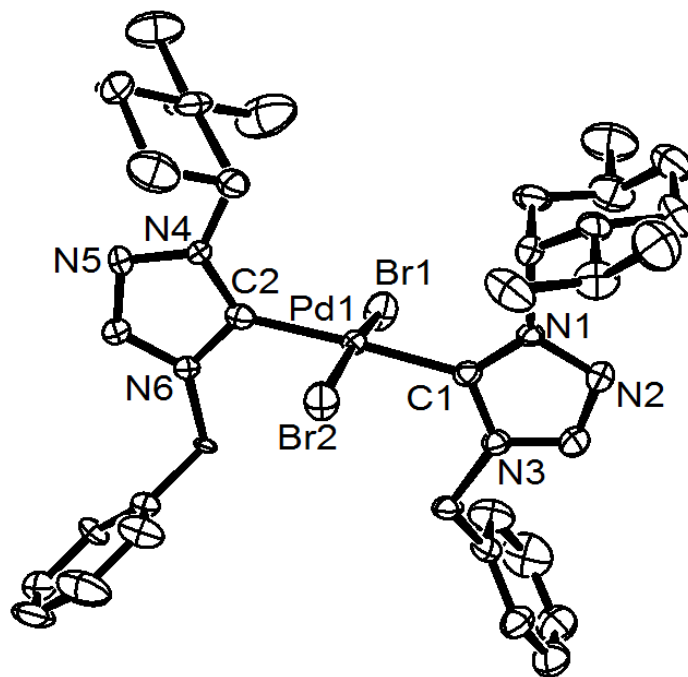
**Figure S1.** ORTEP of *1R,2R,5S-1b* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 2.025(3), Pd(1)–C(2) 2.020(3), Pd(1)–Br(1) 2.4352(7), Pd(1)–Br(2) 2.4551(7), C(1)–Pd(1)–C(2) 179.41(15), Br(1)–Pd(1)–Br(2) 177.984(17), C(1)–Pd(1)–Br(2) 91.57(10), C(1)–Pd(1)–Br(1) 90.02(10).



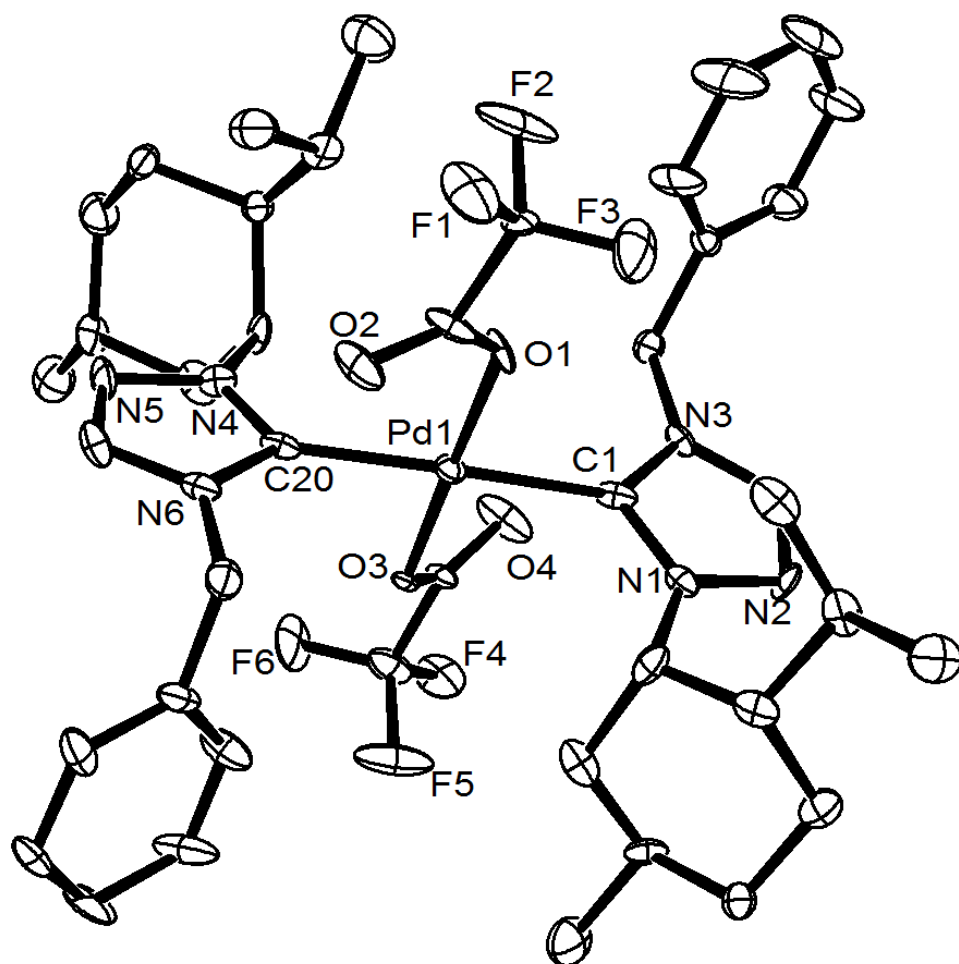
**Figure S2.** ORTEP of *1S,2S,5R-2b* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd–C(1a) 2.008(6), Pd–C(1b) 2.028(5), Pd–Br(1) 2.4479(9), Pd–Br(2) 2.4319(10), C(1a)–Pd–C(1b) 179.2(2), Br(1)–Pd–Br(2) 175.32(5), C(1a)–Pd–Br(2) 89.72(15), C(1b)–Pd–Br(1) 90.24(15).



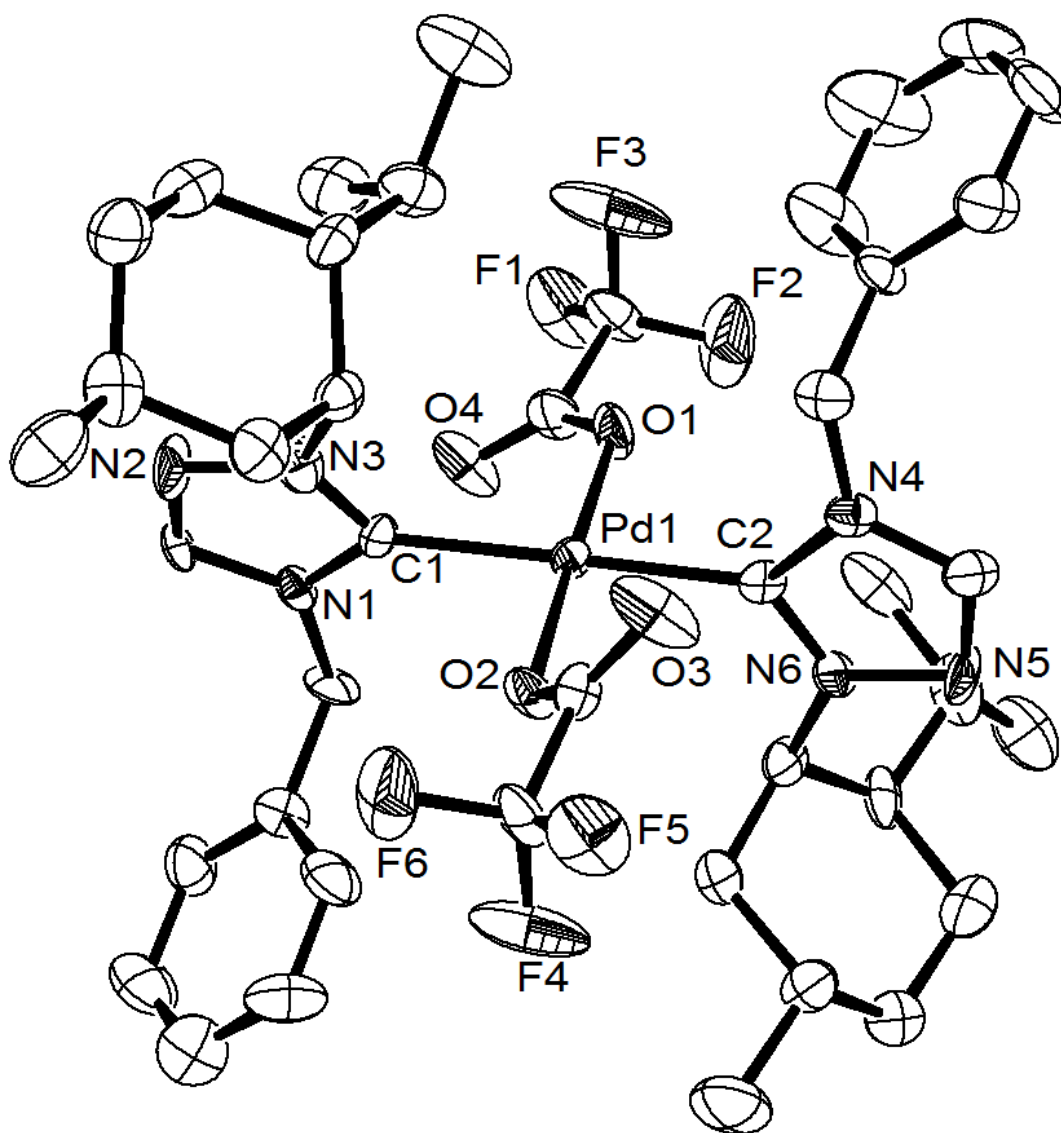
**Figure S3.** ORTEP of *1R,2R,5S-2b* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 2.049(11), Pd(1)–C(16) 2.012(12), Pd(1)–Br(1) 2.4369(15), Pd(1)–Br(2) 2.4446(15), C(1)–Pd(1)–C(16) 178.8(5), Br(1)–Pd(1)–Br(2) 175.39(7), C(1)–Pd(1)–Br(2) 90.9(3), C(1)–Pd(1)–Br(1) 90.1(3).



**Figure S4.** ORTEP of *1R,2R,5S-3b* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 2.018(9), Pd(1)–C(2) 2.022(9), Pd(1)–Br(1) 2.4354(12), Pd(1)–Br(2) 2.4370(12), C(1)–Pd(1)–C(2) 177.5(5), Br(1)–Pd(1)–Br(2) 169.51(5), C(1)–Pd(1)–Br(2) 91.3(3), C(1)–Pd(1)–Br(1) 87.8(3).



**Figure S5.** ORTEP of *1S,2S,5R-3c* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 2.022(10), Pd(1)–C(20) 2.028(10), Pd(1)–O(1) 2.006(6), Pd(1)–O(3) 2.017(6), C(1)–Pd(1)–C(20) 176.8(5), O(1)–Pd(1)–O(3) 179.1(4), C(1)–Pd(1)–O(1) 87.0(4), C(20)–Pd(1)–O(3) 85.0(3).



**Figure S6.** ORTEP of *1R,2R,5S-3c* with thermal ellipsoids are shown at the 50 % probability level. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 2.033(8), Pd(1)–C(2) 2.020(8), Pd(1)–O(1) 2.022(5), Pd(1)–O(2) 2.021(5), C(1)–Pd(1)–C(2) 176.7(3), O(1)–Pd(1)–O(2) 178.7(3), C(1)–Pd(1)–O(1) 95.3(3), C(2)–Pd(1)–O(2) 91.3(3).

PG-AK-11-216-1-1H

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EXPNO 11  
PROCNO 1  
Date\_ 20151007  
Time 17.18  
INSTRUM spect  
PROBHD 5 mm PABBO BB-  
PULPROG zg30  
TD 54274  
SOLVENT CDCl3  
NS 8  
DS 0  
SWH 8223.685 Hz  
FIDRES 0.151522 Hz  
AQ 3.2999091 sec  
RG 71.8  
DW 60.800 usec  
DE 6.50 usec  
TE 297.8 K  
D1 1.0000000 sec  
TD0 1

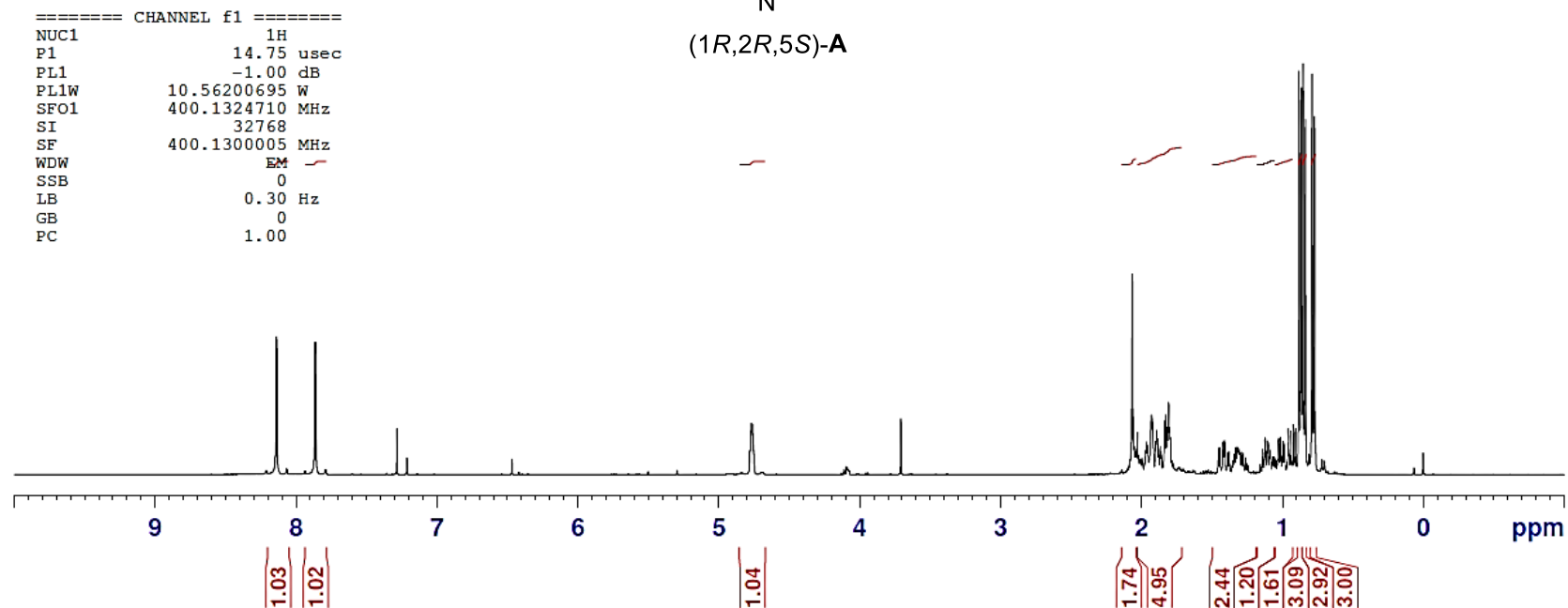
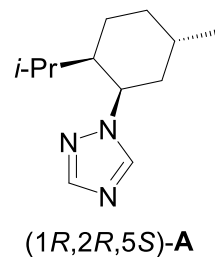


Figure S7. <sup>1</sup>H NMR spectrum of 1R,2R,5S-A in CDCl<sub>3</sub>.



PG-AK-11-216-1-13C

Current Data Parameters  
NAME PG-AK-11-216-1-13C  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20160301  
Time\_ 22.47  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDC13  
NS 100  
DS 4  
SWH 29761.904 Hz  
FIDRES 0.454131 Hz  
AQ 1.1010048 sec  
RG 197.27  
DW 16.800 usec  
DE 6.50 usec  
TE 296.4 K  
D1 1.00000000 sec  
D11 0.03000000 sec  
TD0 1

=====  
CHANNEL f1  
SFO1 125.7703637 MHz  
NUC1 13C  
P1 8.90 usec  
PLW1 103.00000000 W

=====  
CHANNEL f2  
SFO2 500.1320005 MHz  
NUC2 1H  
PCPD2 waltz16  
PCPD2 80.00 usec  
PLW2 13.00000000 W  
PLW12 0.34327999 W  
PLW13 0.21969999 W

F2 - Processing parameters  
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SF 125.7577707 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

151.06  
143.63

77.46  
77.20  
76.95

58.12

46.78

41.13

34.87

29.24

26.62

25.11

22.42

21.21

20.61

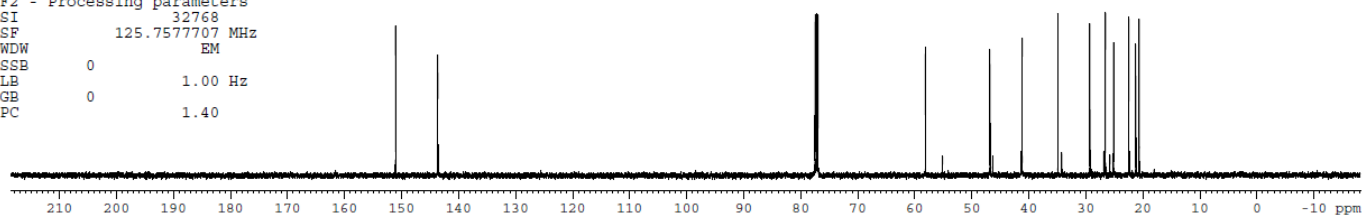
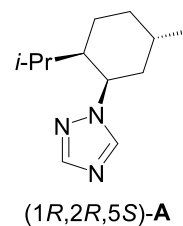
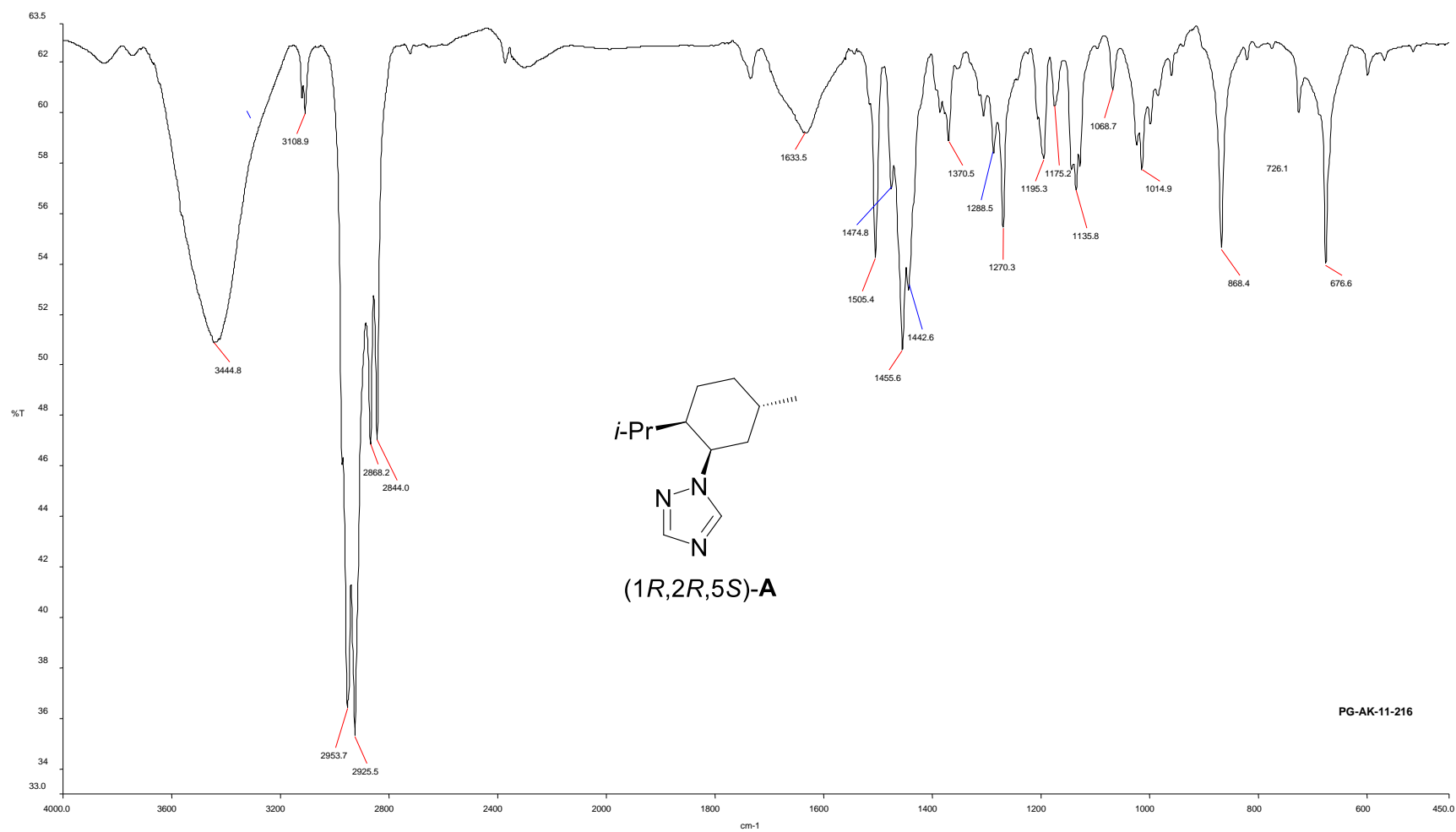


Figure S8.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1*R*,2*R*,5*S*-A in  $\text{CDCl}_3$ .



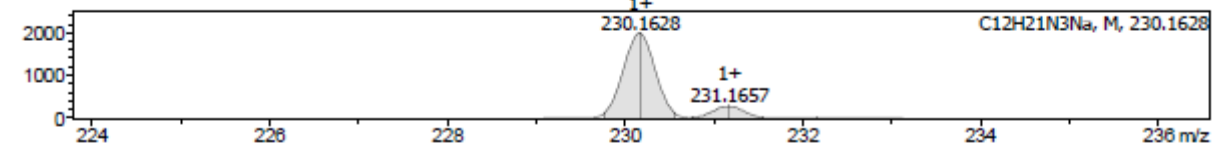
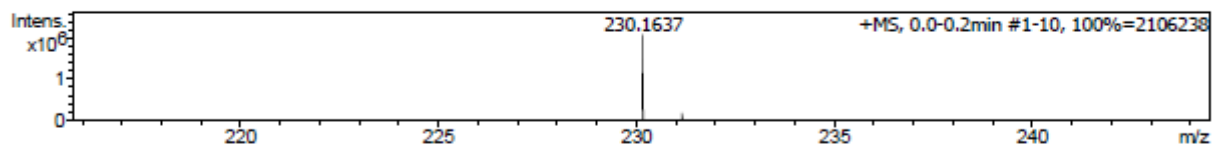
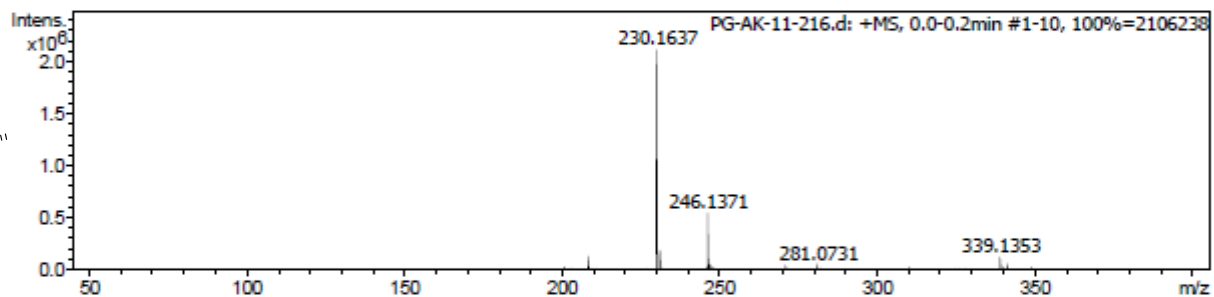
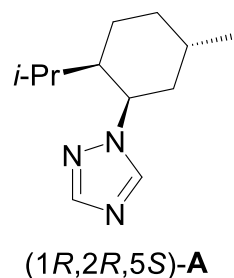
**Figure S9.** Infrared spectrum of 1R,2R,5S-A in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

<b>Analysis Info</b>		Acquisition Date 2/29/2016 8:22:45 PM	
Analysis Name	D:\Data\FEB-2016\PG-AK-11-216.d	Operator	PFG APP IN
Method	Tune_pos_NAICSI-1000a.m	Instrument	maXis impact 282001.00081
Sample Name	PG-AK-11-216		
Comment	C12H21N3		

**Acquisition Parameter**

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	400 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source

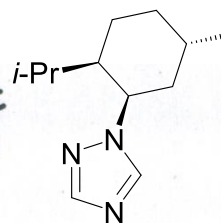


Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
230.1637	1	C12H21N3Na	230.1628	3.9	31.2	2	100.00	3.5	even	ok

**Figure S10.** High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-A.

# Eager 300 Report

Page: 1 Sample: PG-AK-11-216-1 (PG-AK-11-216-1)



Method Name : PGCP13102015  
Method File : D:\CHNS-2015\PGCP13102015.mth  
Chromatogram : PG-AK-11-216-1  
Operator ID : CHANDNI  
Analysed : 10/13/2015 15:28  
Sample ID : PG-AK-11-216-1 (# 22)  
Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
Printed : 10/13/2015 18:36  
Instrument N. : Instrument #1  
Sample weight : .881

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret. Time	Area	BC	Area ratio	K factor
Nitrogen	19.3771	40	184872	FU	8.597494	.108295E+07
Carbon	69.0840	63	1589435	FU	1.000000	.260680E+07
Hydrogen	9.9775	178	599593	RS	2.650857	.665180E+07
Totals	98.4386		2373900			

Figure S11. Elemental analysis data of (1R,2R,5S)-A.

**CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI**

Monday, 30-NOV-2015

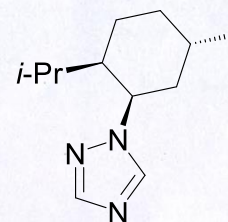
This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0

Time Delay : Disabled

Temperature Correction : OFF



**(1R,2R,5S)-A**

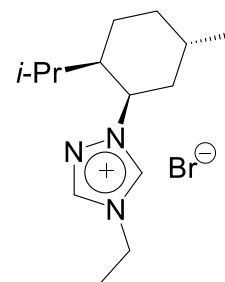
<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>
5	-40.941	0.0822	-40.851	-41.001

<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
1	pg-ak-11-216-a2	16:53:19	-41.001	SR	-0.205	589	50	1	24.8
2	pg-ak-11-216-a2	16:53:26	-41.001	SR	-0.205	589	50	1	24.8
3	pg-ak-11-216-a2	16:53:33	-41.001	SR	-0.205	589	50	1	24.8
4	pg-ak-11-216-a2	16:53:42	-40.851	SR	-0.204	589	50	1	24.8
5	pg-ak-11-216-a2	16:53:49	-40.851	SR	-0.204	589	50	1	24.9

**Figure S12.** Specific rotation of (1R,2R,5S)-A in CHCl<sub>3</sub>.

PG-AK-11-219-1-1H

NAME PG-AK-11-219-1-1H  
EXPNO 1  
PROCNO 1  
Date\_ 20151008  
Time 22.40  
INSTRUM spect  
PROBHD 5 mm PABBO BB-  
PULPROG zg30  
TD 54274  
SOLVENT CDCl3  
NS 9  
DS 0  
SWH 8223.685 Hz  
FIDRES 0.151522 Hz  
AQ 3.2999091 sec  
RG 144  
DW 60.800 usec  
DE 6.50 usec  
TE 297.4 K  
D1 1.00000000 sec  
TD0 1



(1R,2R,5S)-1a

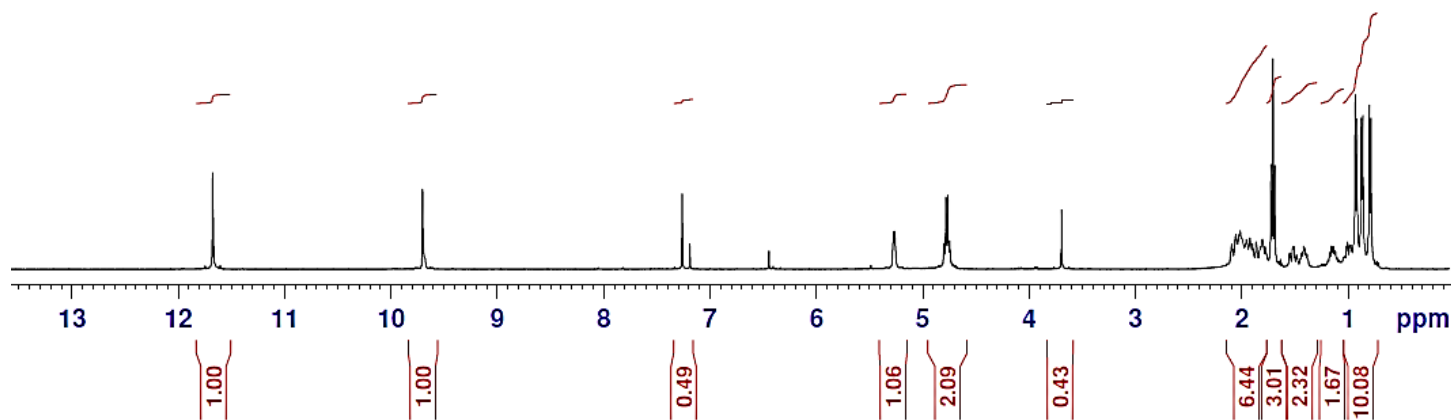


Figure S13.  $^1\text{H}$  NMR spectrum of (1R,2R,5S)-1a in  $\text{CDCl}_3$ .

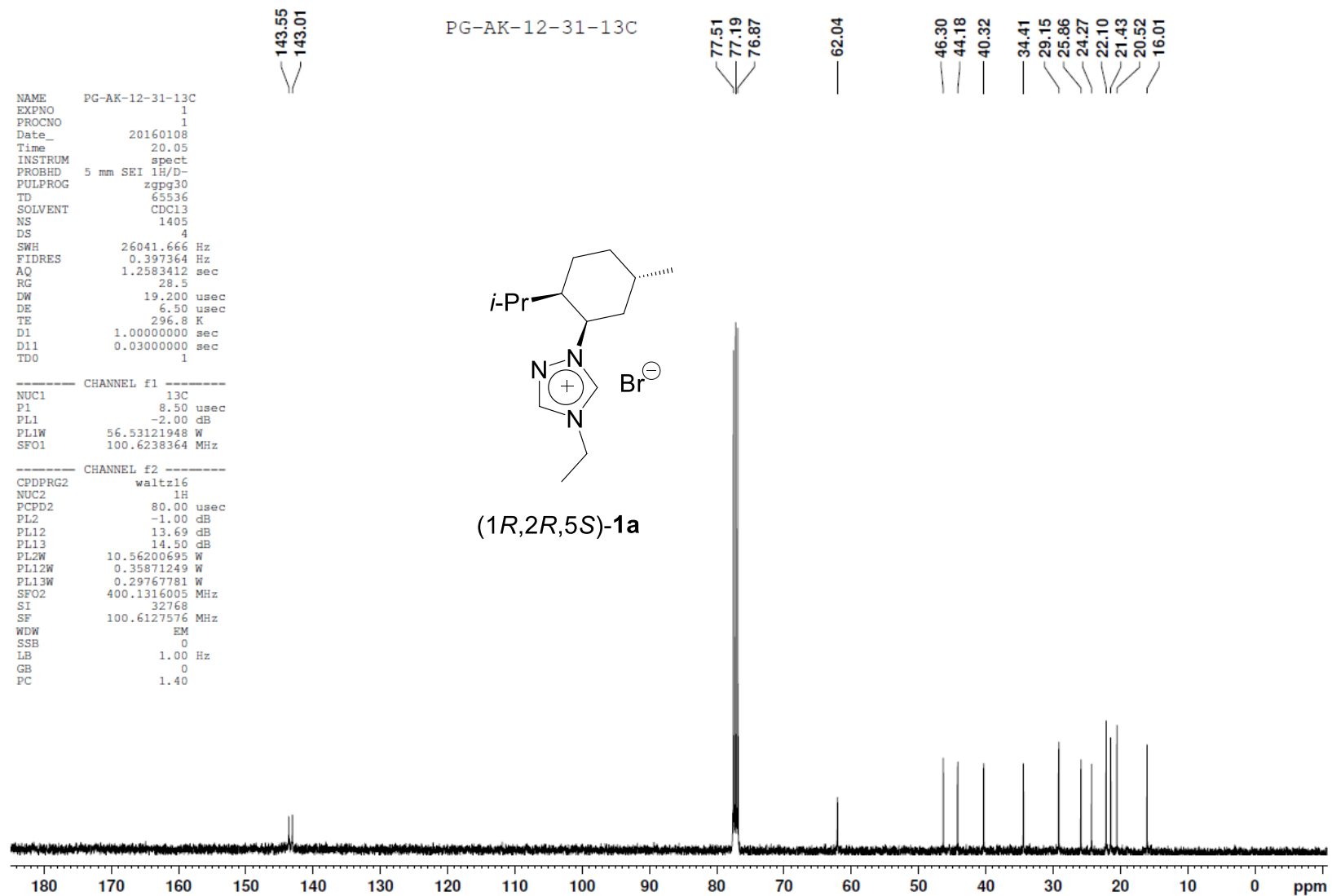
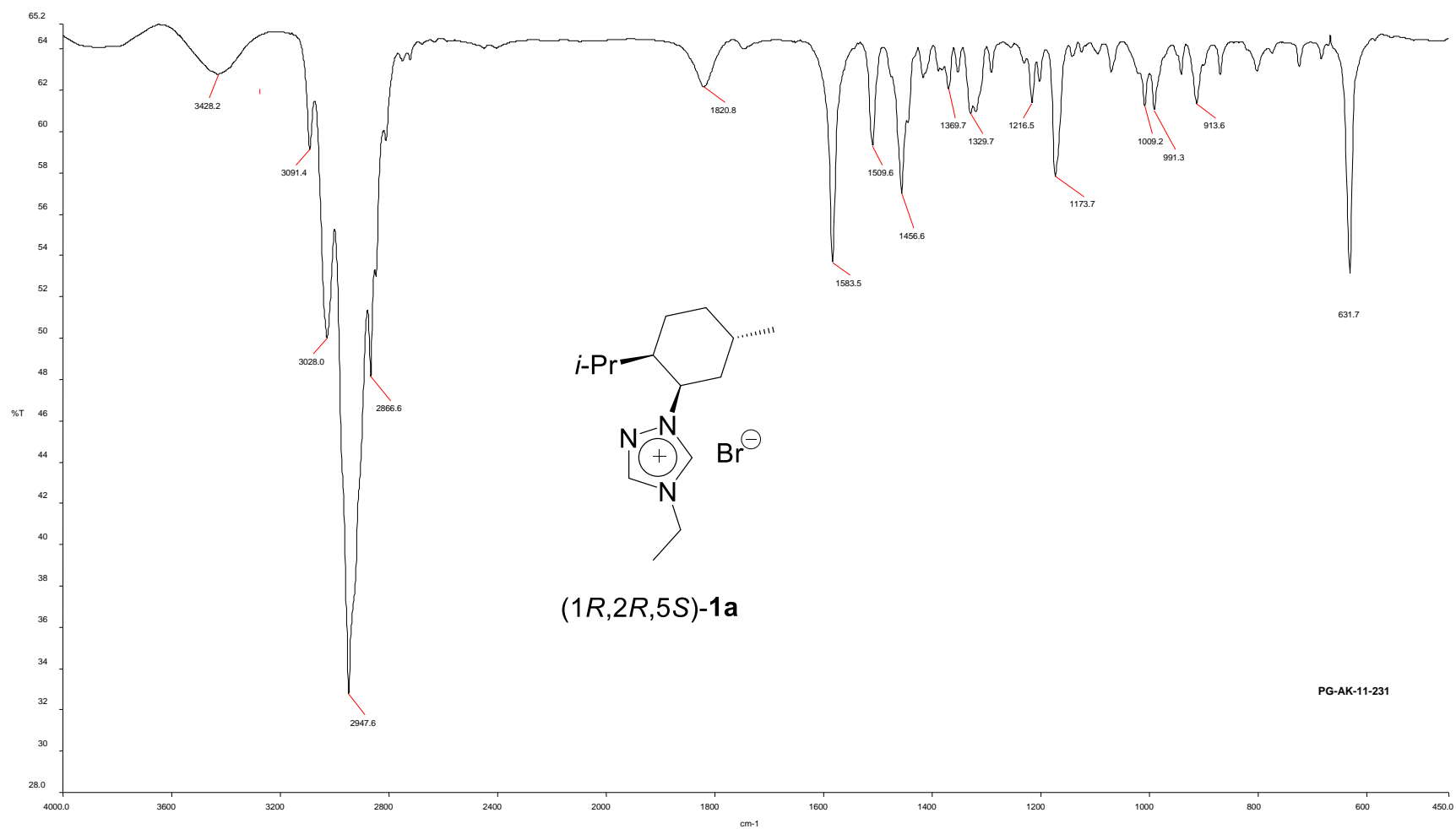


Figure S14.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1*R*,2*R*,5*S*-1a in  $\text{CDCl}_3$ .



**Figure S15.** Infrared spectrum of 1R,2R,5S-1a in KBr.



DEPARTMENT OF CHEMISTRY, I.I.T.(B)

Analysis Info

Analysis Name D:\Data\FEB-2016\PG-AK-11-231.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-AK-11-231  
 Comment C14H26N3Br

Acquisition Date 2/29/2016 8:32:51 PM

Operator PFG APP IN  
 Instrument maXis impact 282001.00081

Acquisition Parameter

Source Type ESI Ion Polarity Positive Set Nebulizer 0.3 Bar  
 Focus Active Set Capillary 3700 V Set Dry Heater 180 °C  
 Scan Begin 50 m/z Set End Plate Offset -500 V Set Dry Gas 4.0 l/min  
 Scan End 500 m/z Set Collision Cell RF 1200.0 Vpp Set Divert Valve Source

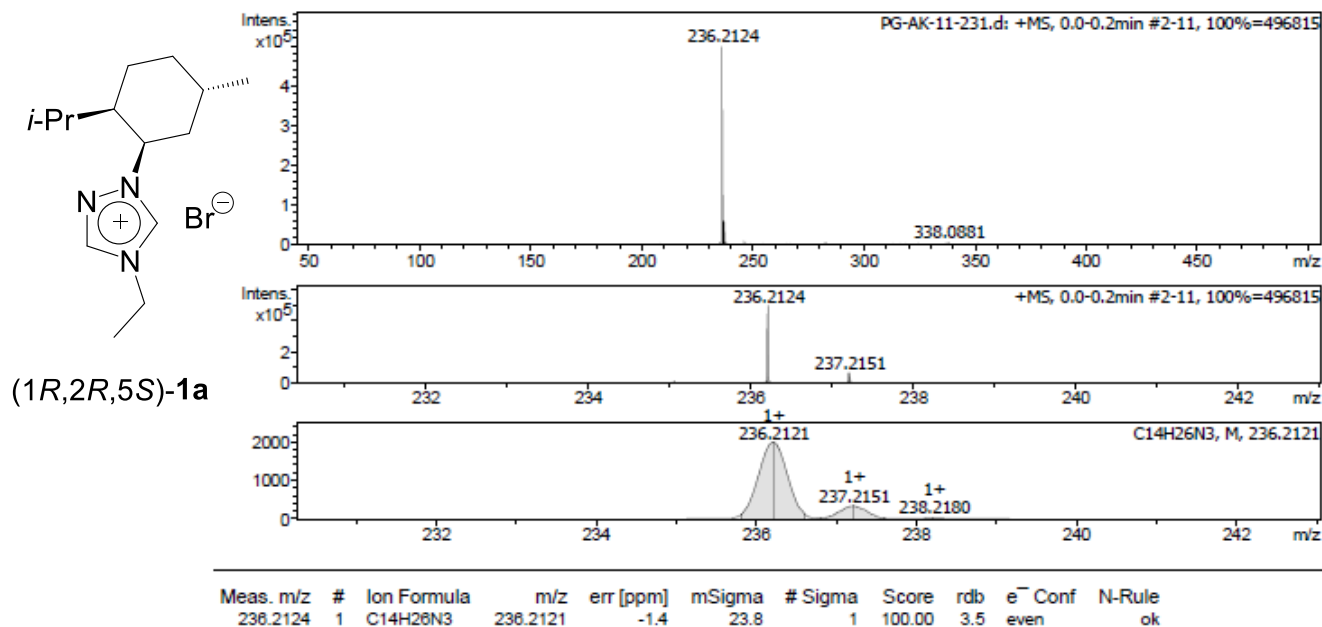
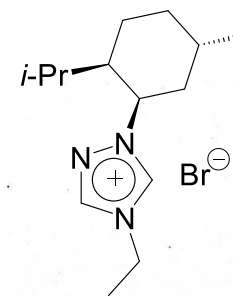


Figure S16. High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-1a.

# Eager 300 Report

Page: 1    Sample: PG-AK-11-231-2 (PG-AK-11-231-2)



Method Name : PGCP26102015	Company Name : C.E. Instruments
Method File : D:\CHNS-2015\PGCP26102015.mth	Printed : 10/30/2015 09:57
Chromatogram : PG-AK-11-231-2	Instrument N. : Instrument #1
Operator ID : CHANDNI	Sample weight : .788
Analysed : 10/26/2015 12:13	
Sample ID : PG-AK-11-231-2 (# 7)	
Analysis Type : UnkNown (Area)	

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret. Time	Area	BC	Area ratio	K factor
Nitrogen	13.2688	41	121875	RS	9.069481	.116562E+07
Carbon	53.9449	65	1105343	RS	1.000000	.260028E+07
Hydrogen	8.3895	178	446363	RS	2.476332	.655078E+07
Totals	75.6032		1673581			

Figure S17. Elemental analysis data of (1R,2R,5S)-1a.

**CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI**

Tuesday, 27-OCT-2015

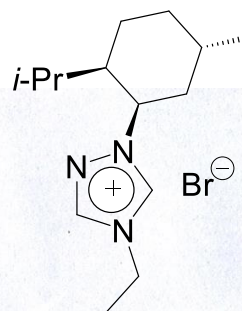
This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0

Time Delay : Disabled

Temperature Correction : OFF



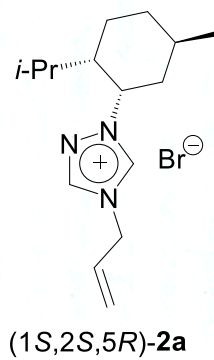
**(1R,2R,5S)-1a**

<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>					
5	-21.972	0.1866	-21.820	-22.277					
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
1	pg-ak-11-231-1	17:28:17	-21.972	SR	-0.110	589	50.00	1.000	24.9
2	pg-ak-11-231-1	17:28:24	-21.820	SR	-0.109	589	50.00	1.000	24.9
3	pg-ak-11-231-1	17:28:31	-21.820	SR	-0.109	589	50.00	1.000	24.9
4	pg-ak-11-231-1	17:28:37	-21.972	SR	-0.110	589	50.00	1.000	24.9
5	pg-ak-11-231-1	17:28:44	-22.277	SR	-0.111	589	50.00	1.000	24.9

**Figure S18.** Specific rotation of (1R,2R,5S)-1a in CHCl<sub>3</sub>.

PG-AK-4-124-1-1H

NAME PG-AK-4-124-1-1H  
EXPNO 1  
PROCNO 1  
Date\_ 20111118  
Time 14.32  
INSTRUM spect  
PROBHD 5 mm PABBO BB-  
PULPROG zg30  
TD 22386  
SOLVENT CDC13  
NS 53  
DS 0  
SWH 8012.820 Hz  
FIDRES 0.357939 Hz  
AQ 1.3969364 sec  
RG 71.8  
DW 62.400 usec  
DE 6.50 usec  
TE 293.8 K  
D1 1.0000000 sec  
TDO 1



===== CHANNEL f1 =====  
NUC1 1H  
P1 13.50 usec  
PL1 -1.00 dB  
PL1W 10.56200695 W  
SF01 400.1324008 MHz  
SI 32768  
SF 400.1299905 MHz  
WDW EM  
SSB 0  
LB 0.00 Hz  
GB 0  
PC 1.00

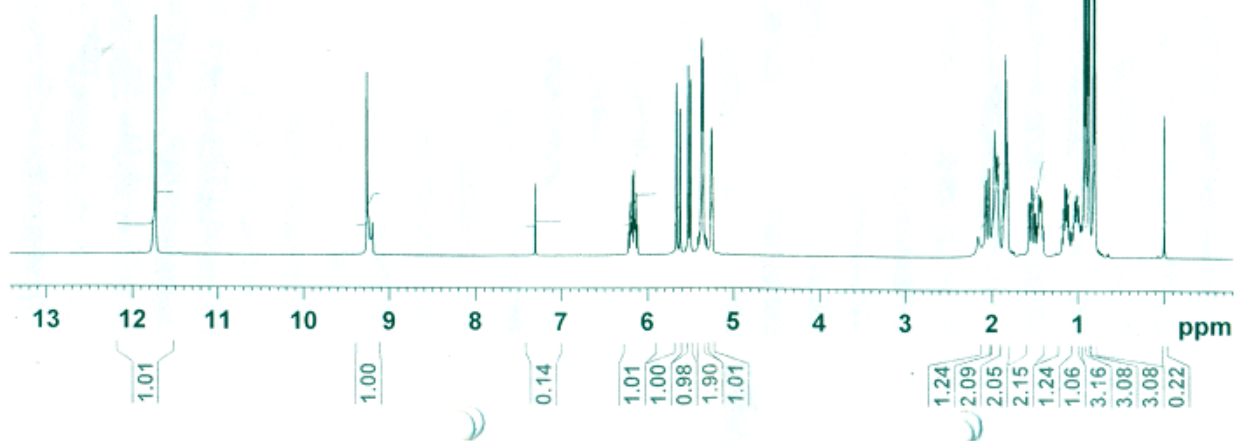


Figure S19. <sup>1</sup>H NMR spectrum of 1S,2S,5R-2a in CDCl<sub>3</sub>.

PG-AK-4-124-13C

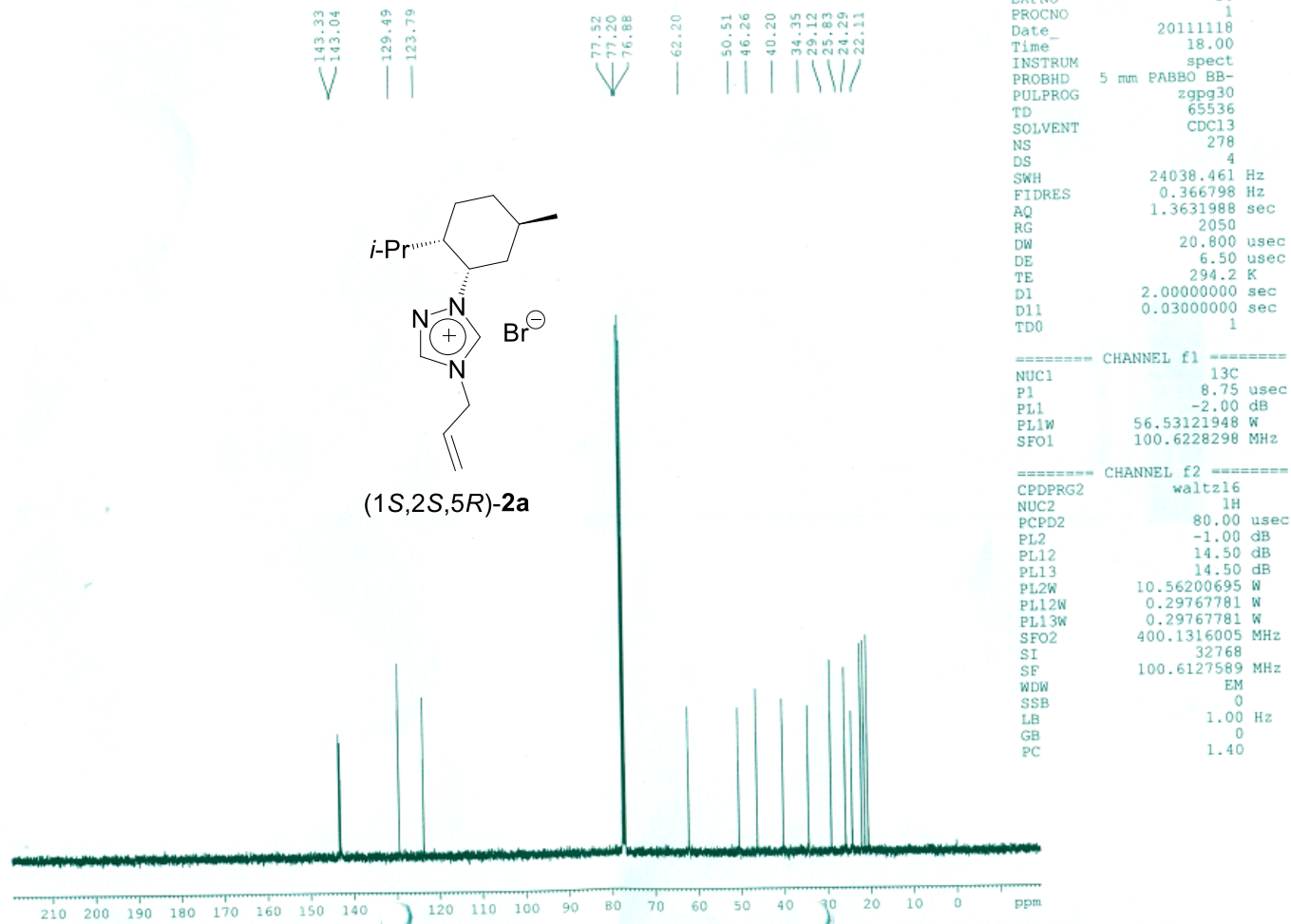
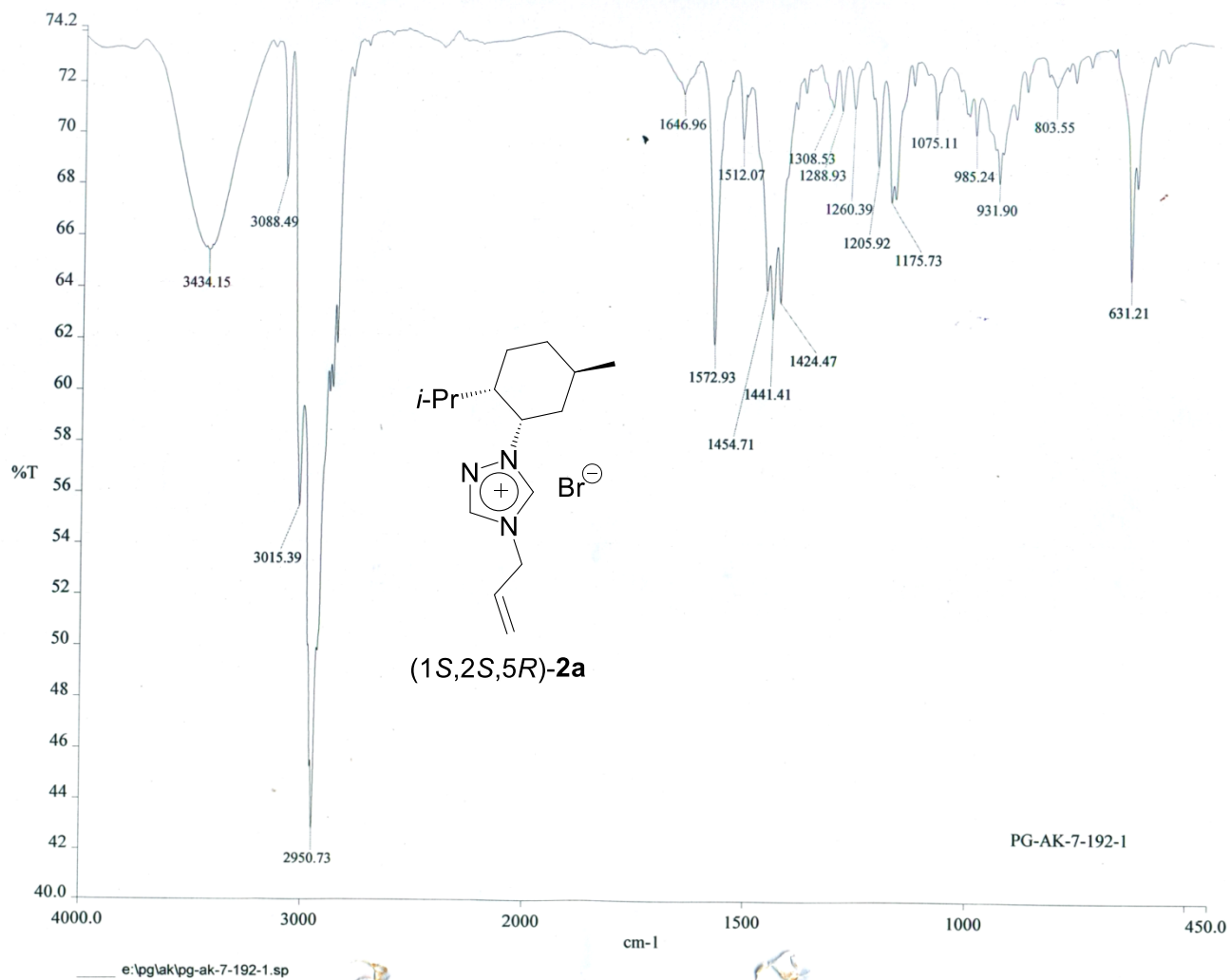


Figure S20.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1S,2S,5R-2a in  $\text{CDCl}_3$ .



**Figure S21.** Infrared spectrum of 1*S*,2*S*,5*R*-2a in KBr.

## Elemental Composition Report

Page 1

### Single Mass Analysis (displaying only valid results)

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 100.0

Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions

3 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Micromass : Q-ToF micro (YA-105)

Dept. Of Chemistry I.I.T.(B)

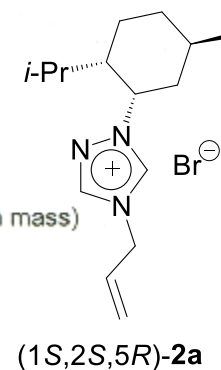
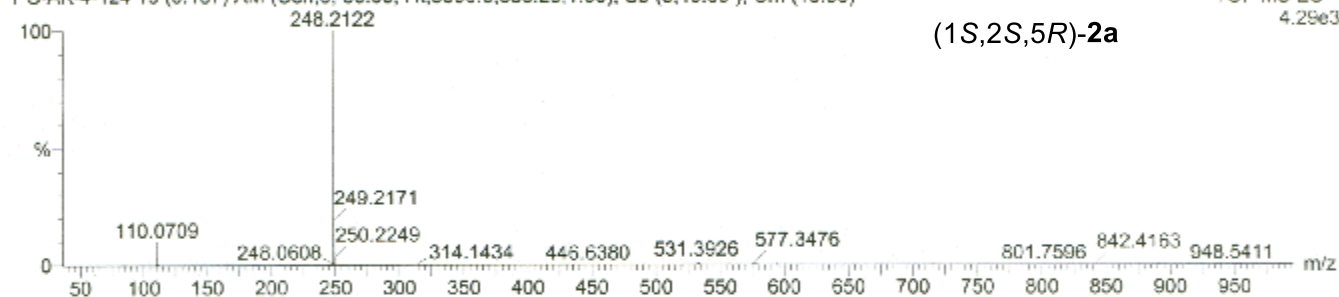
01-Dec-201110:00:59

C<sub>15</sub>H<sub>26</sub>N<sub>3</sub>Br

PG-AK-4-124 19 (0.187) AM (Cen,5, 80.00, HI,5000.0,556.28,1.00); Sb (5,40.00 ); Cm (13:33)

TOF MS ES+

4.29e3



Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
248.2122	248.2127	-0.5	-2.1	4.5	1	C <sub>15</sub> H <sub>26</sub> N <sub>3</sub>

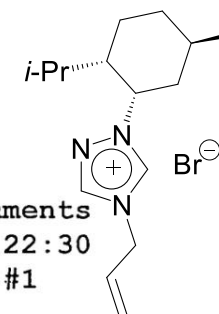
Figure S22. High Resolution Mass Spectrometry (HRMS) data of 1S,2S,5R-2a.

## Eager 300 Report

Page: 1    Sample: PG-AK-7-192 (PG-AK-7-192)

Method Name : SP-19-08-13  
 Method File : D:\CHNS2012-13\SP-190813.mth  
 Chromatogram : PG-AK-7-192  
 Operator ID : MNRAO  
 Analysed : 08/19/2013 14:14  
 Sample ID : PG-AK-7-192 (# 18)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 8/19/2013 22:30  
 Instrument N. : Instrument #1  
 Sample weight : .671



(1S,2S,5R)-2a

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
1	0.0000	18	3652	RS		0.0000
Nitrogen	12.6831	43	112844	FU	8.757821	.132596E+07
Carbon	54.9056	66	988271	FU	1.000000	.267626E+07
Hydrogen	7.3224	178	306922	RS	3.219941	.604146E+07
Totals	74.9112		1411689			

Figure S23. Elemental analysis data of 1S,2S,5R-2a.



PG-AK-7-192.p1d

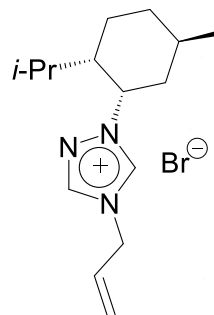
[Comment]  
Sample name  
Comment  
User  
Division  
Company IITB

[Data Information]  
Creation Date 8/1/2013 1 08 PM

[Measurement Information]  
Instrument Name JASCO POLARIMETER  
Model Name P-2000  
Serial No A043361232  
Polarizer Dichrom  
Faraday Cell Flint Glass

Accessory PTC-203  
Accessory S/N A017861234  
Path Length 100 mm

Light Source Na  
Monitor wavelength 589 nm  
D I T 5 sec  
No of cycle 5  
Cycle interval 5 sec  
Temp Monitor Cell  
Temp Corr Factor None  
Aperture(S) 3.0mm  
Aperture(L) Auto  
Mode Specific O R  
Path Length 100 mm  
Concentration 1 w/v  
Factor 1



(1S,2S,5R)-2a

No	Sample Name	Measurement Date	Temperature[C]	Optical Rotation Monitor	Specific O R	S D	C V	Comment
1	PG-AK-7-192			0.22	21.7280	0.0901	0.4147	CHCl3
2	PG-AK-7-192-1	8/1/2013 1 07 PM	25.00	0.22	21.6800			
3	PG-AK-7-192-2	8/1/2013 1 07 PM	25.00	0.22	21.8400			
4	PG-AK-7-192-3	8/1/2013 1 07 PM	25.00	0.22	21.7000			
5	PG-AK-7-192-4	8/1/2013 1 07 PM	25.00	0.22	21.8000			
6	PG-AK-7-192-5	8/1/2013 1 08 PM	24.99	0.22	21.6200			

Figure S24. Specific rotation of 1S,2S,5R-2a in CHCl<sub>3</sub>.

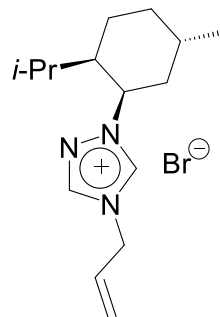
Current Data Parameters  
NAME PG-AK-11-217-1-1H  
EXPNO 5  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20151019  
Time\_ 23.05  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.152588 Hz  
AQ 3.2767999 sec  
RG 80.35  
DW 50.000 usec  
DE 6.50 usec  
TE 297.5 K  
D1 1.00000000 sec  
TDO 1

==== CHANNEL f1 =====  
SFO1 500.1330885 MHz  
NUC1 1H  
P1 13.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300126 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

PG-AK-11-217-1-1H



(1R,2R,5S)-2a

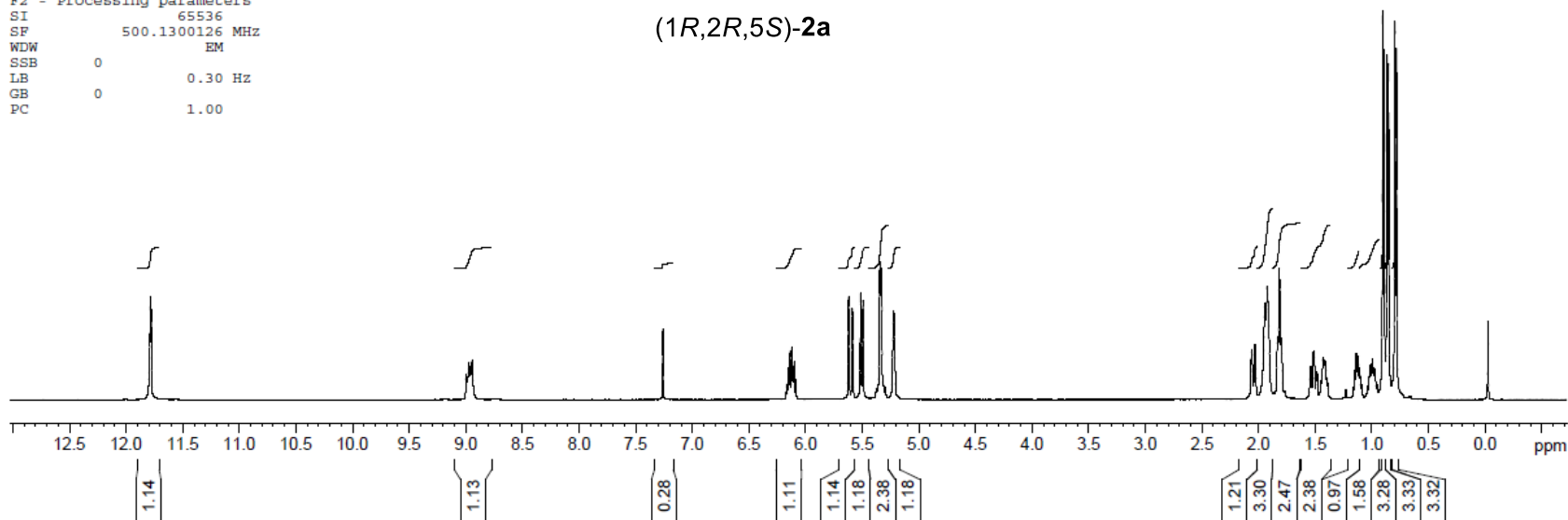


Figure S25.  $^1\text{H}$  NMR spectrum of (1R,2R,5S)-2a in  $\text{CDCl}_3$ .

PG-APP-AK-11-217-2-13C

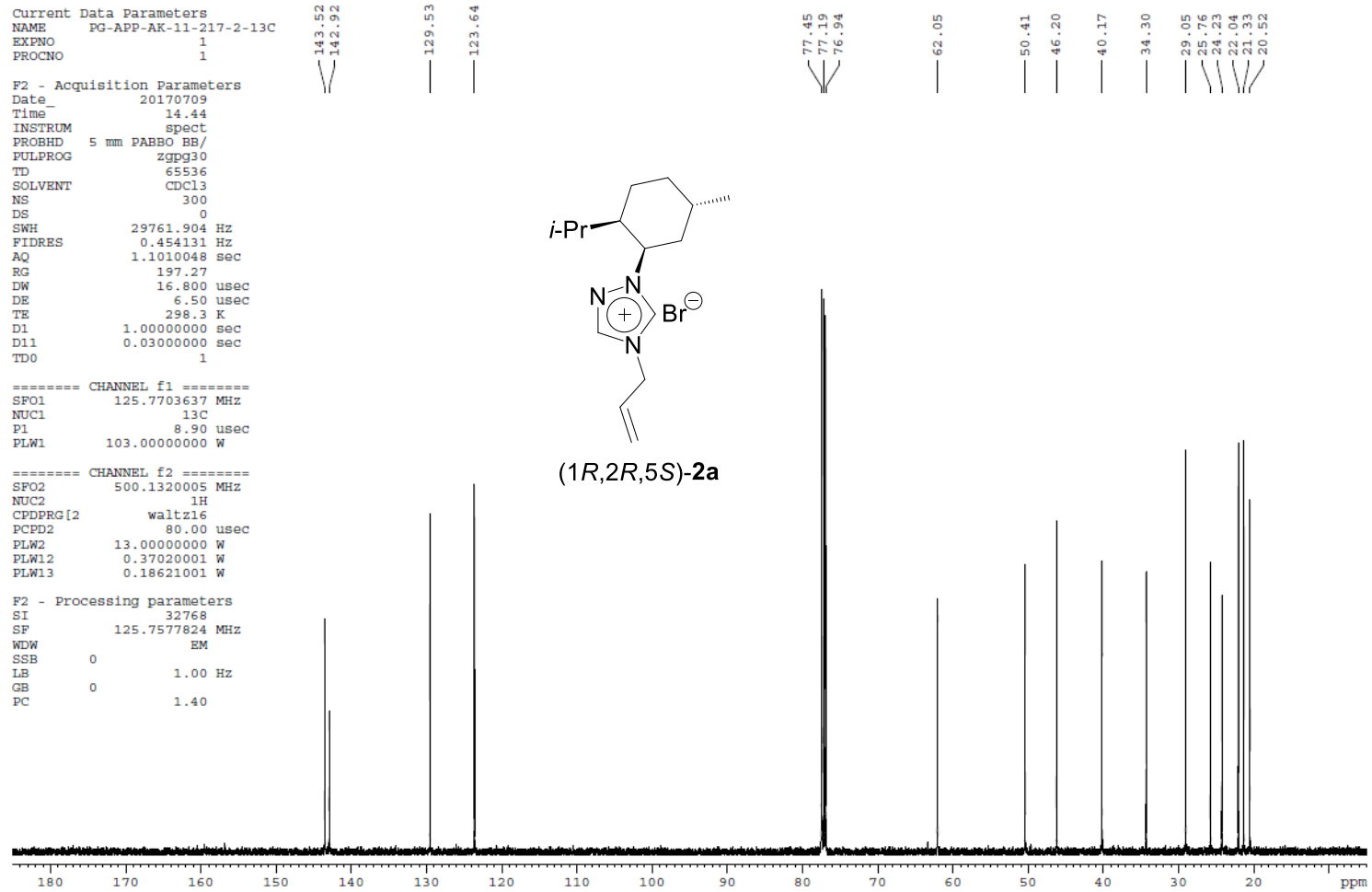
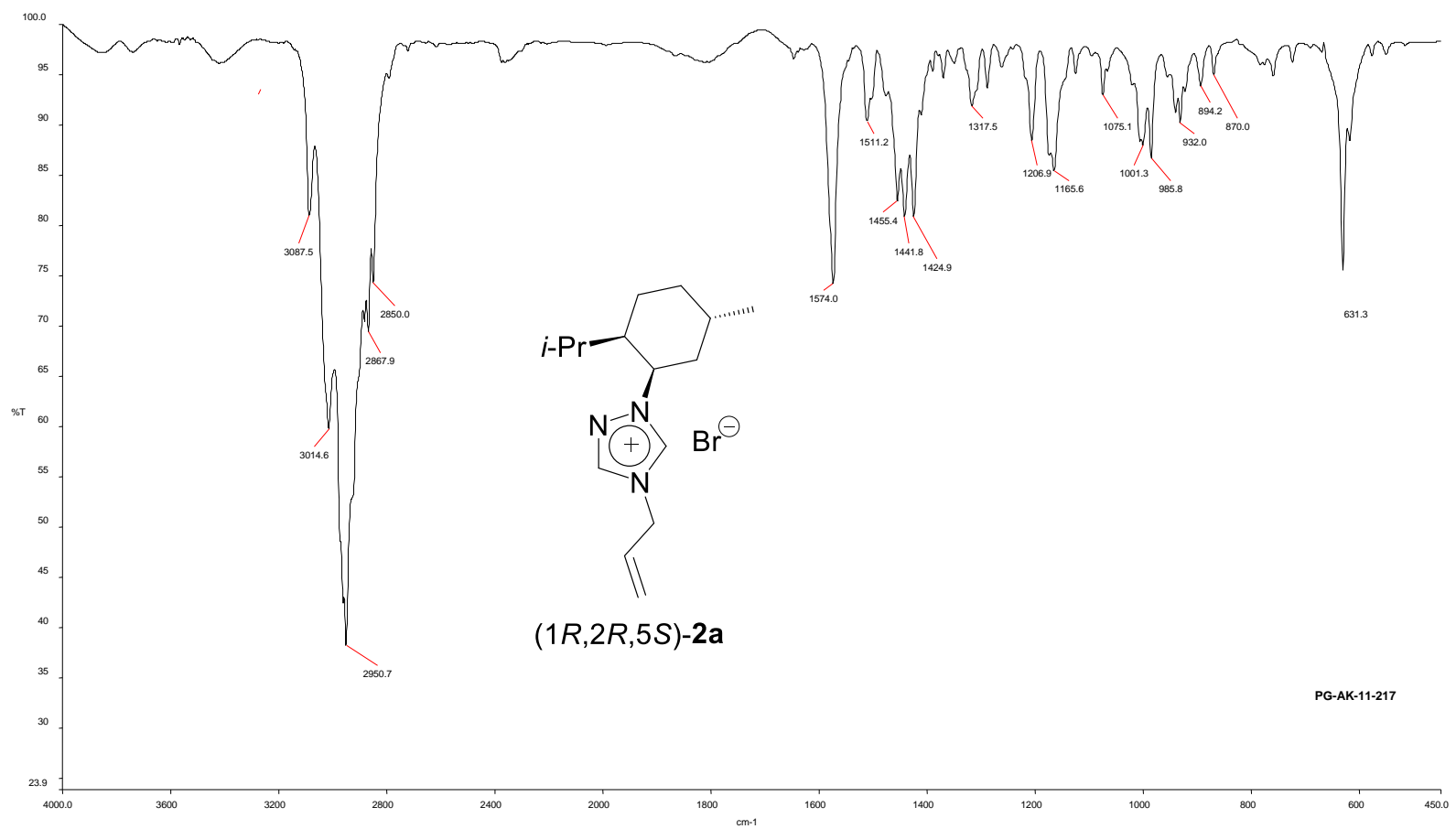


Figure S26.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1R,2R,5S-2a in  $\text{CDCl}_3$ .

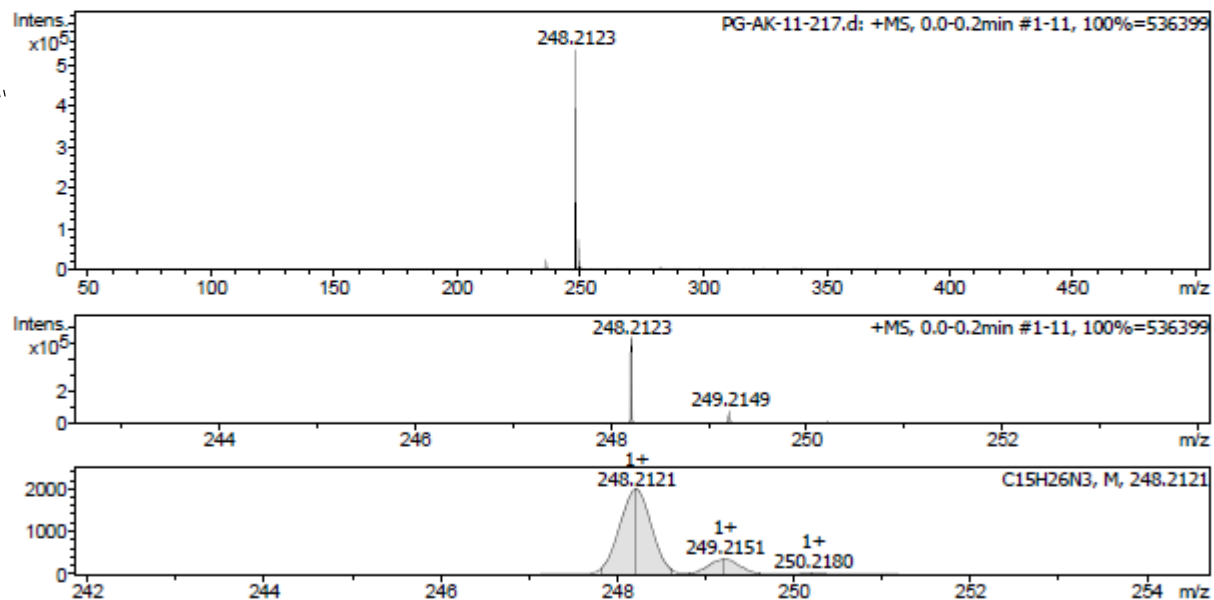
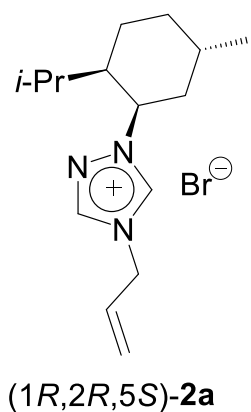


**Figure S27.** Infrared spectrum of 1R,2R,5S-2a in KBr.

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**Analysis Info**  
 Analysis Name D:\Data\FEB-2016\PG-AK-11-217.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-AK-11-217  
 Comment C15H26N3Br  
 Acquisition Date 2/29/2016 8:40:26 PM  
 Operator PG APP IN  
 Instrument maXis impact 282001.00081

**Acquisition Parameter**  
 Source Type ESI Ion Polarity Positive Set Nebulizer 0.3 Bar  
 Focus Active Set Capillary 3700 V Set Dry Heater 180 °C  
 Scan Begin 50 m/z Set End Plate Offset -500 V Set Dry Gas 4.0 l/min  
 Scan End 500 m/z Set Collision Cell RF 1200.0 Vpp Set Divert Valve Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
248.2123	1	C15H26N3	248.2121	-0.8	21.1	1	100.00	4.5	even	ok

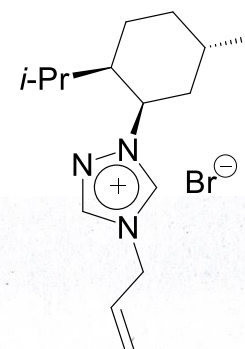
Figure S28. High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-2a.

## Eager 300 Report

Page: 1    Sample: PG-AK-11-217-1 (PG-AK-11-217-1)

Method Name : PGCP13102015  
 Method File : D:\CHNS-2015\PGCP13102015.mth  
 Chromatogram : PG-AK-11-217-1  
 Operator ID : CHANDNI  
 Analysed : 10/13/2015 14:19  
 Sample ID : PG-AK-11-217-1 (# 19)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 10/13/2015 18:36  
 Instrument N. : Instrument #1  
 Sample weight : .566



(1R,2R,5S)-2a

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	13.0268	41	79848	RS	10.189700	.108295E+07
Carbon	54.9502	64	813622	RS	1.000000	.260680E+07
Hydrogen	7.3945	175	293284	RS	2.774178	.665180E+07
Totals	75.3715		1186754			

Figure S29. Elemental analysis data of (1R,2R,5S)-2a.

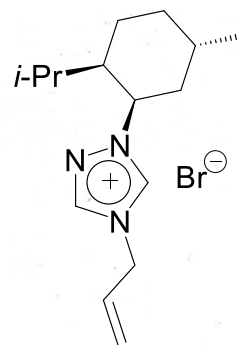
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 12-OCT-2015

This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
Time Delay : Disabled  
Temperature Correction : OFF



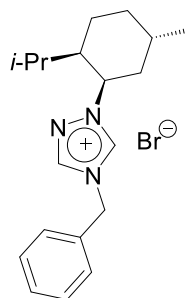
(1R,2R,5S)-2a

<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>						
5	-21.599	0.0000	-21.599	-21.599						
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>	
1	pg-ak-11-217-1	12:51:46	-21.599	SR	-0.108	589	50	1	24.9	
2	pg-ak-11-217-1	12:51:53	-21.599	SR	-0.108	589	50	1	24.9	
3	pg-ak-11-217-1	12:52:00	-21.599	SR	-0.108	589	50	1	24.9	
4	pg-ak-11-217-1	12:52:07	-21.599	SR	-0.108	589	50	1	24.9	
5	pg-ak-11-217-1	12:52:13	-21.599	SR	-0.108	589	50	1	24.9	

Figure S30. Specific rotation of (1R,2R,5S)-2a in CHCl<sub>3</sub>.

NAME PG-AK-11-218-1-1H  
 EXPNO 1  
 PROCNO 1  
 Date\_ 20151029  
 Time\_ 22.39  
 INSTRUM spect  
 PROBHD 5 mm SEI 1H/D-  
 PULPROG zg30  
 TD 54274  
 SOLVENT CDCl3  
 NS 16  
 DS 0  
 SWH 8223.685 Hz  
 FIDRES 0.151522 Hz  
 AQ 3.2999091 sec  
 RG 32  
 DW 60.800 usec  
 DE 6.50 usec  
 TE 294.1 K  
 D1 1.0000000 sec  
 TD0 1

PG-AK-11-218-1-1H



(1*R*,2*R*,5*S*)-**3a**

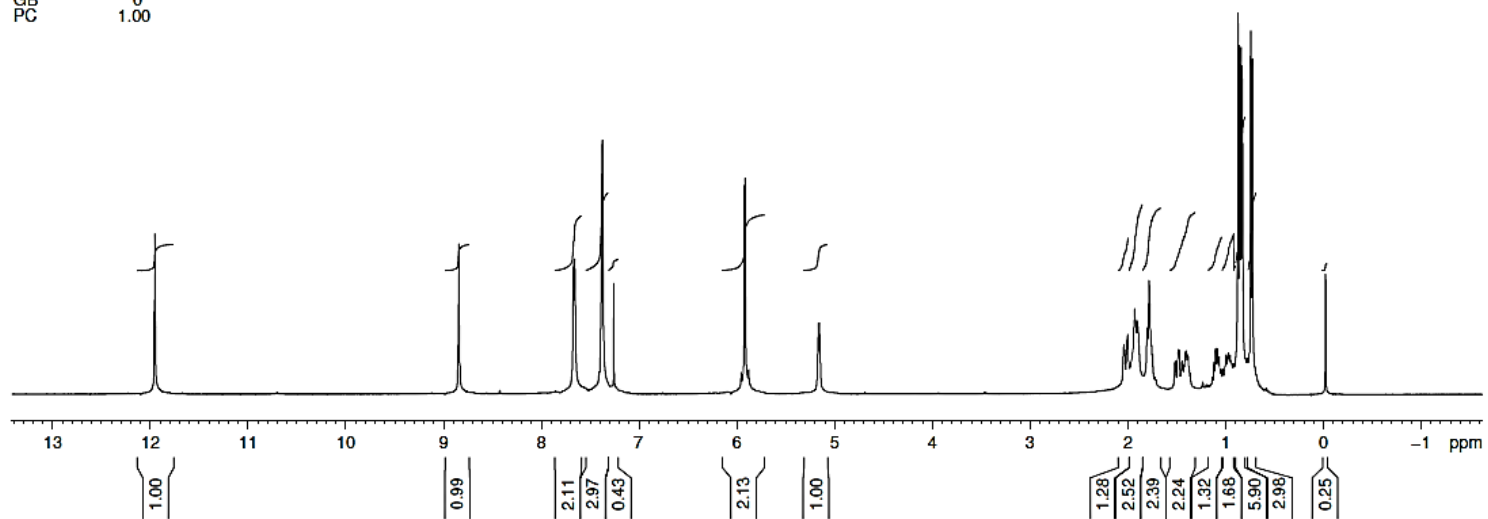


Figure S31. <sup>1</sup>H NMR spectrum of (1*R*,2*R*,5*S*)-**3a** in CDCl<sub>3</sub>.



PG-APP-AK-11-218-2-13C

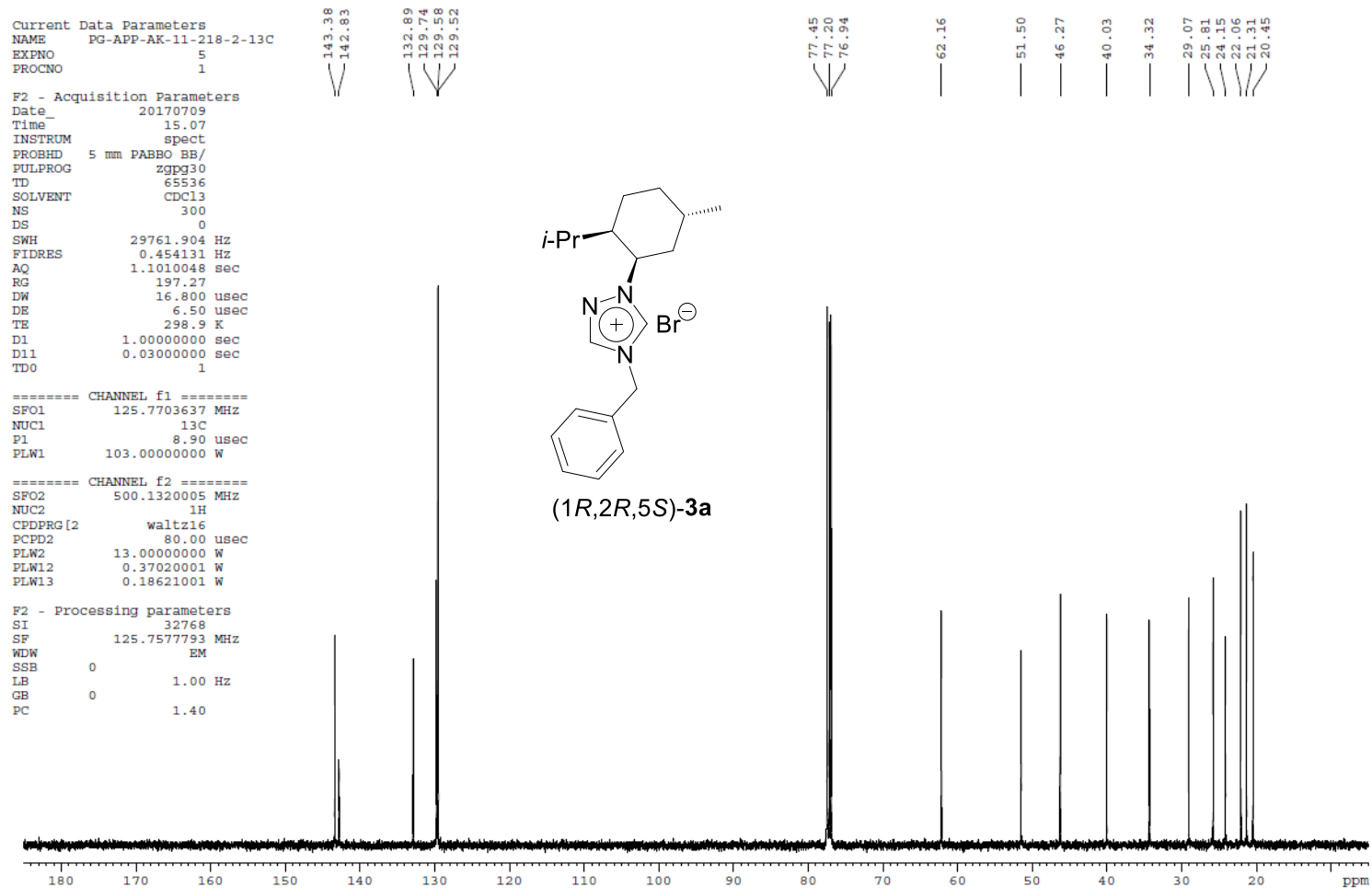
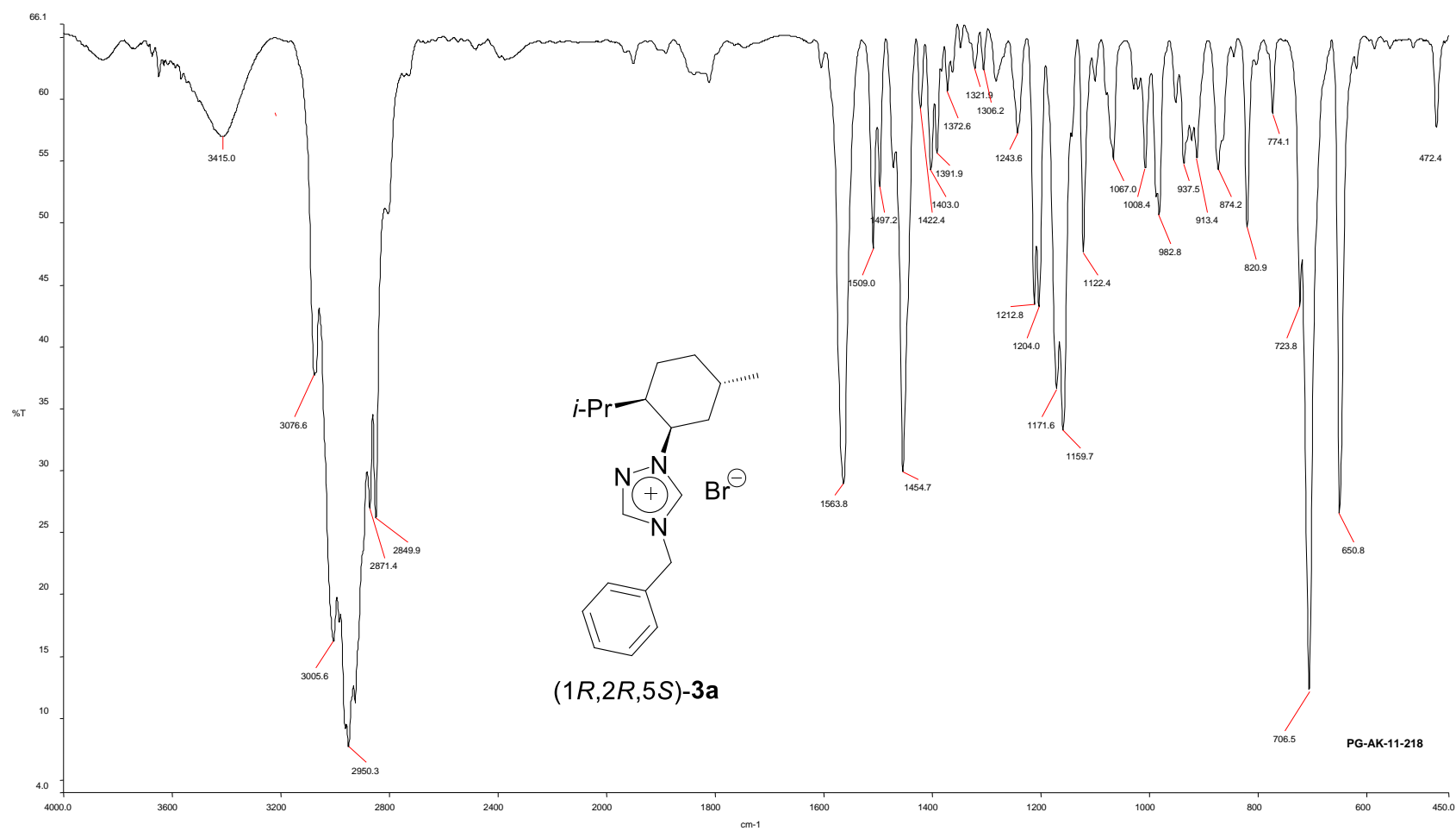


Figure S32.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1*R*,2*R*,5*S*)-**3a** in  $\text{CDCl}_3$ .

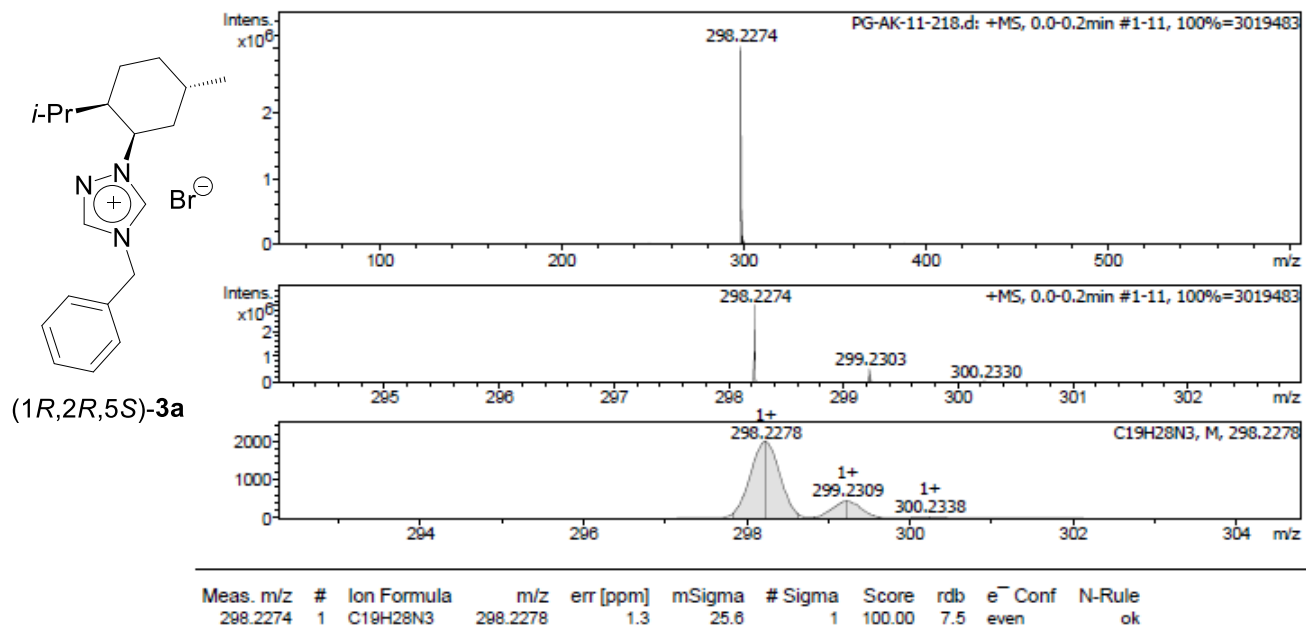


**Figure S33.** Infrared spectrum of 1R,2R,5S-3a in KBr.

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<b>Analysis Info</b>		Acquisition Date 2/29/2016 8:47:34 PM	
Analysis Name	D:\Data\FEB-2016\PG-AK-11-218.d	Operator	PG APP IN
Method	Tune_pos_NAICSI-1000a.m	Instrument	maXis impact 282001.00081
Sample Name	PG-AK-11-218		
Comment	C19H28N3Br		

<b>Acquisition Parameter</b>					
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	600 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source

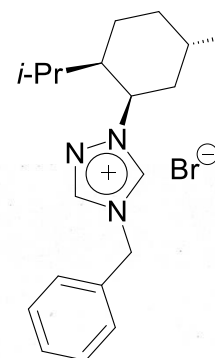


**Figure S34.** High Resolution Mass Spectrometry (HRMS) data of **1R,2R,5S-3a**.

## Eager 300 Report

Page: 1    Sample: PG-AK-11-218-1 (PG-AK-11-218-1)

Method Name : PGCP13102015	
Method File : D:\CHNS-2015\PGCP13102015.mth	
Chromatogram : PG-AK-11-218-1	
Operator ID : CHANDNI	Company Name : C.E. Instruments
Analysed : 10/13/2015 15:18	Printed : 10/13/2015 18:36
Sample ID : PG-AK-11-218-1 (# 21)	Instrument N. : Instrument #1
Analysis Type : UnkNown (Area)	Sample weight : .815



(1R,2R,5S)-3a

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	11.2482	41	99276	FU	12.849350	.108295E+07
Carbon	59.9083	64	1275636	FU	1.000000	.260680E+07
Hydrogen	6.6576	178	375811	RS	3.394355	.665180E+07
Totals	77.8141		1750723			

Figure S35. Elemental analysis data of (1R,2R,5S)-3a.

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Monday, 12-OCT-2015

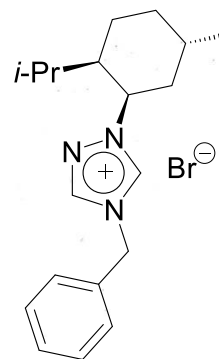
This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0

Time Delay : Disabled

Temperature Correction : OFF



(1R,2R,5S)-3a

<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>						
5	-16.174	0.0827	-16.083	-16.234						
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>	
1	pg-ak-11-218-1	12:57:21	-16.083	SR	-0.080	589	50	1	24.8	
2	pg-ak-11-218-1	12:57:28	-16.083	SR	-0.080	589	50	1	24.8	
3	pg-ak-11-218-1	12:57:35	-16.234	SR	-0.081	589	50	1	24.8	
4	pg-ak-11-218-1	12:57:41	-16.234	SR	-0.081	589	50	1	24.8	
5	pg-ak-11-218-1	12:57:48	-16.234	SR	-0.081	589	50	1	24.9	

Figure S36. Specific rotation of (1R,2R,5S)-3a in CHCl<sub>3</sub>.

NAME PG-AK-11-224-1-1  
 EXPNO 19  
 PROCNO 1  
 Date\_ 20151016  
 Time 19.23  
 INSTRUM spect  
 PROBHD 5 mm PABBO BB-  
 PULPROG zg30  
 TD 54274  
 SOLVENT CDCl3  
 NS 7  
 DS 0  
 SWH 8223.685 Hz  
 FIDRES 0.151522 Hz  
 AQ 3.2999091 sec  
 RG 144  
 DW 60.800 usec  
 DE 6.50 usec  
 TE 295.5 K  
 D1 1.0000000 sec  
 TD0 1

PG-AK-11-224-1-1H

===== CHANNEL f1 =====  
 NUC1 1H  
 P1 14.75 usec  
 PL1 -1.00 dB  
 PL1W 10.56200695 W  
 SFO1 400.1324710 MHz  
 SI 32768  
 SF 400.1300099 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

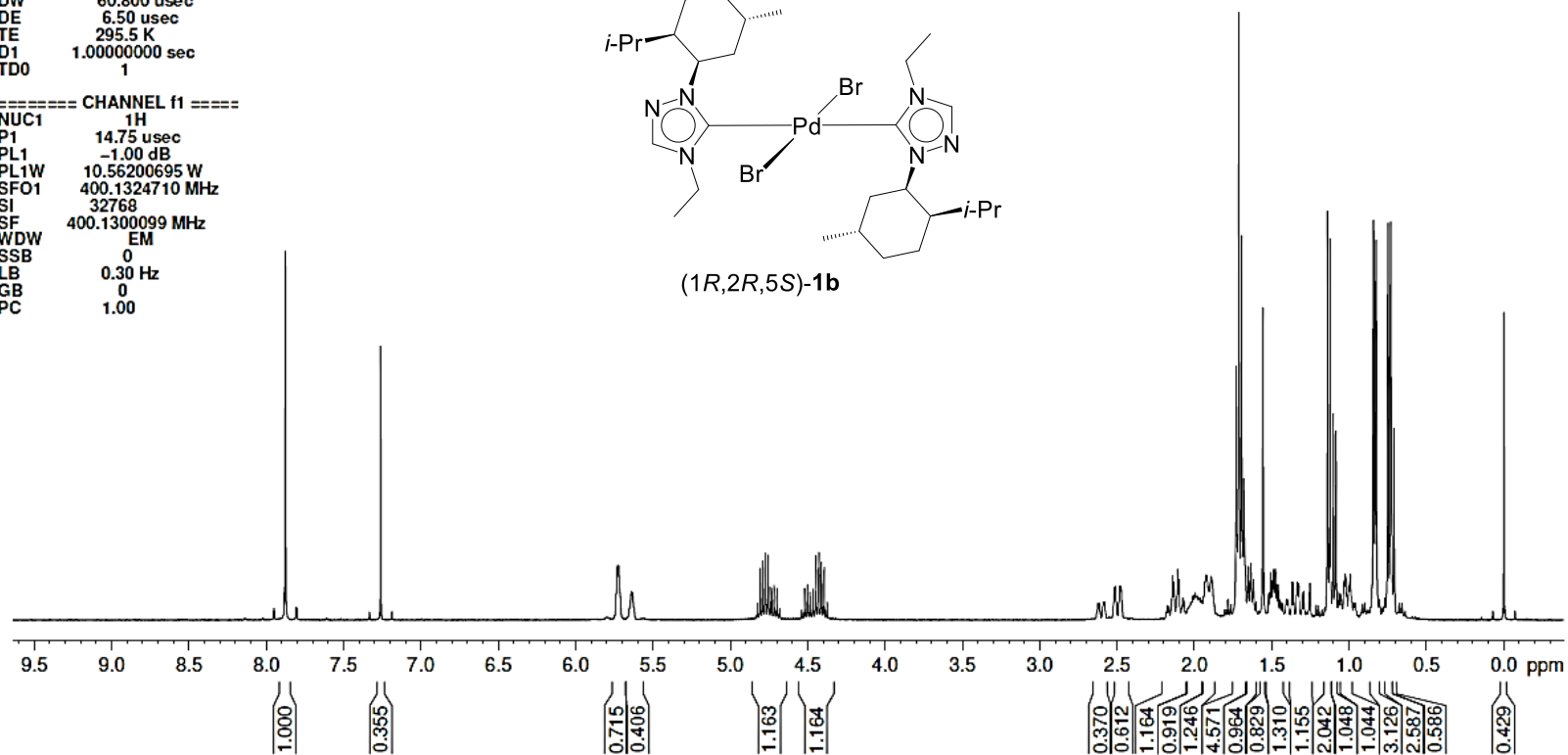
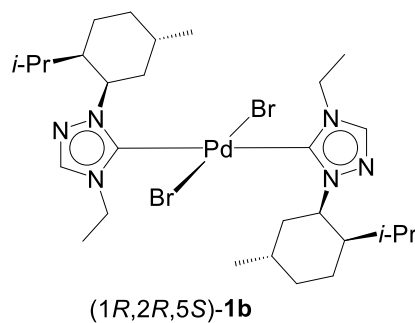


Figure S37. <sup>1</sup>H NMR spectrum of (1R,2R,5S)-1b in CDCl<sub>3</sub>.

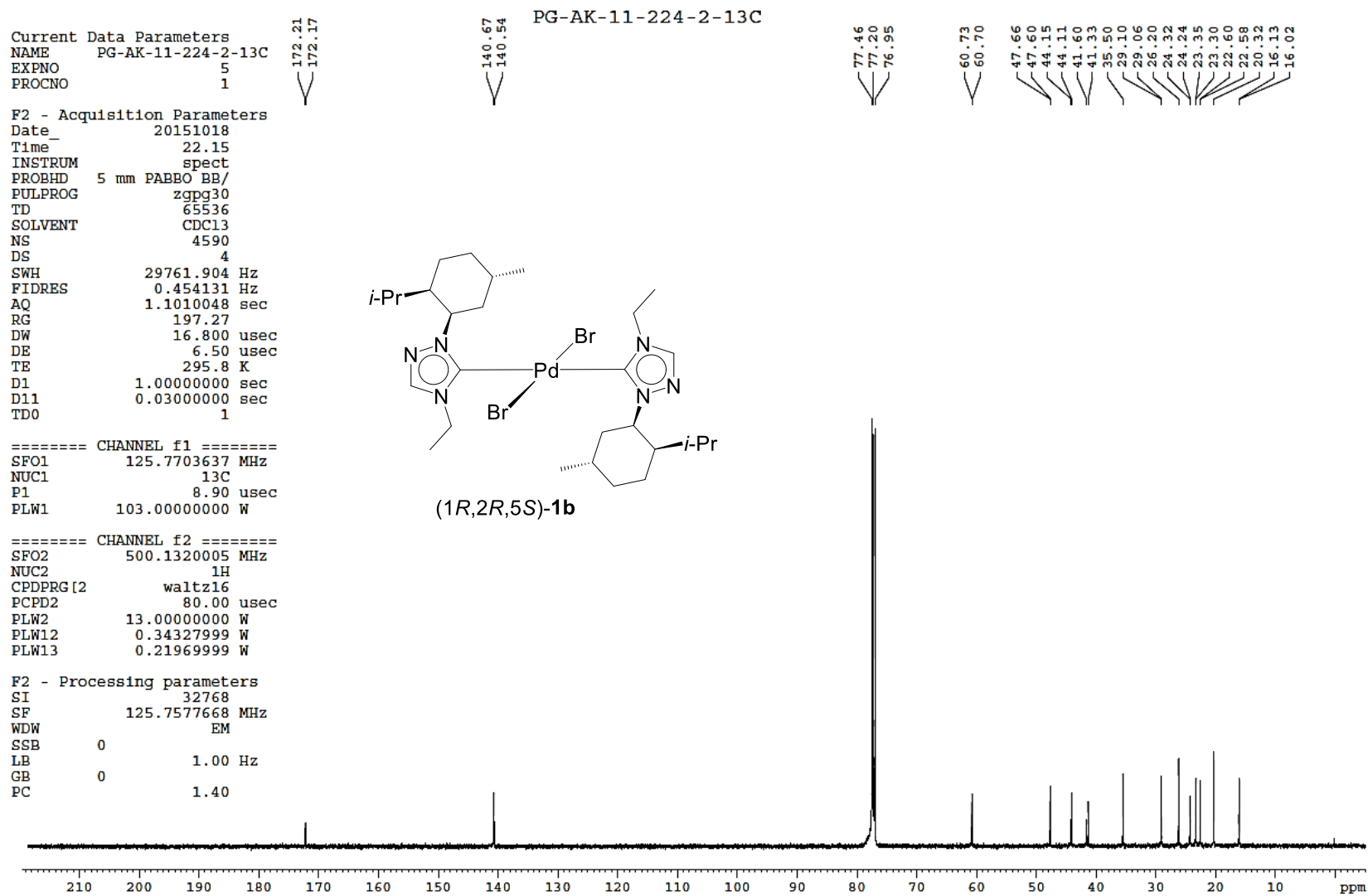
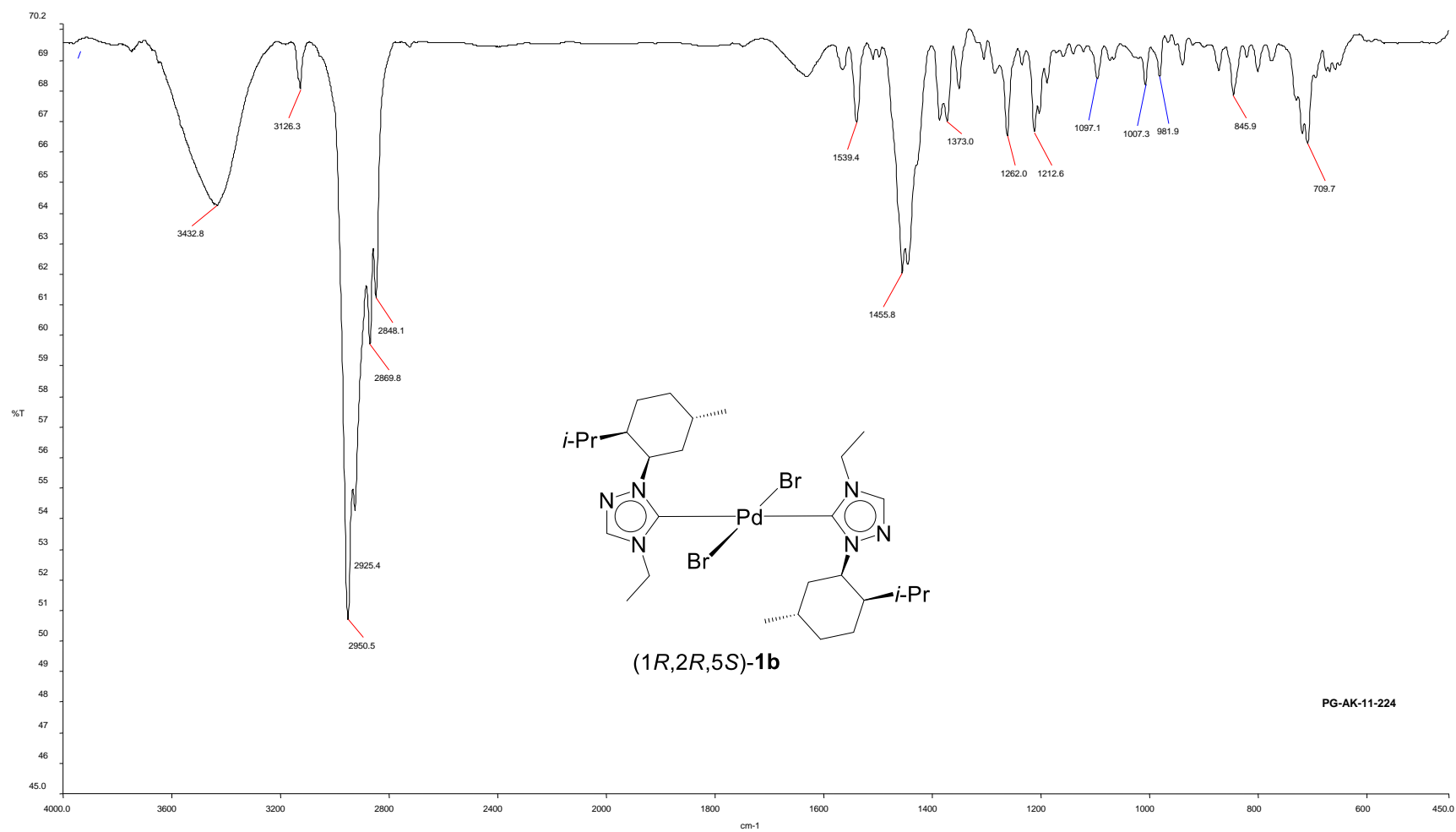


Figure S38.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1*R*,2*R*,5*S*)-**1b** in  $\text{CDCl}_3$ .



**Figure S39.** Infrared spectrum of **1R,2R,5S-1b** in KBr.



DEPARTMENT OF CHEMISTRY, I.I.T.(B)

Analysis Info

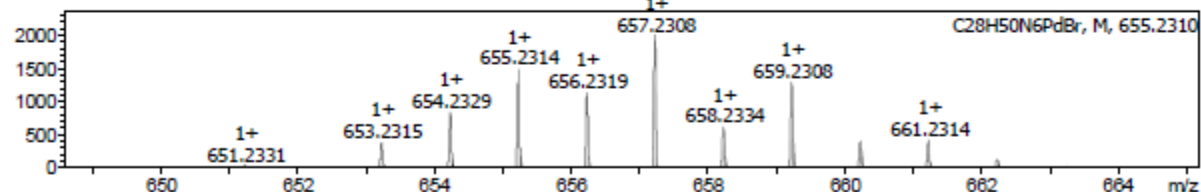
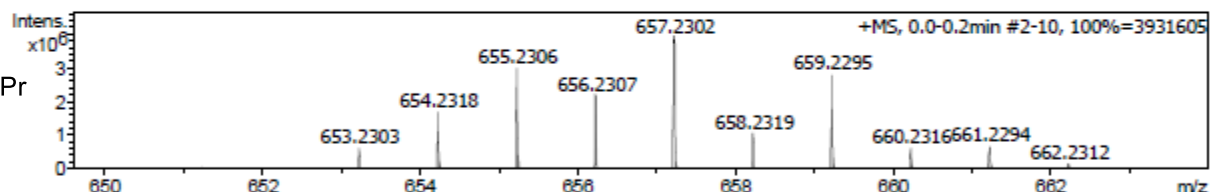
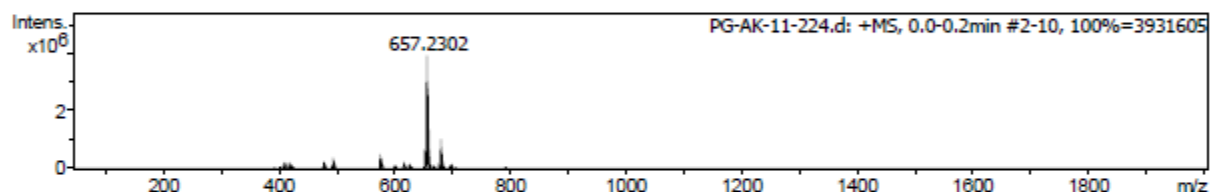
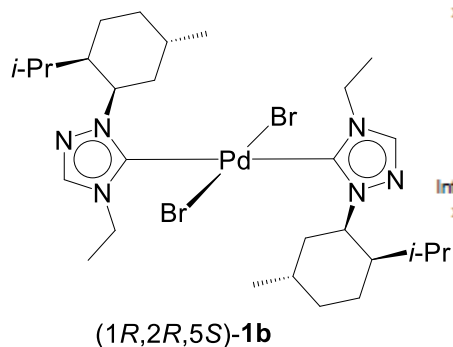
Analysis Name D:\Data\FEB-2016\PG-AK-11-224.d  
 Method Tune\_pos\_NAICSI-2000.m  
 Sample Name PG-AK-11-224  
 Comment C28H50N6PdBr2

Acquisition Date 2/22/2016 9:33:35 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3800 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2000 m/z	Set Collision Cell RF	2100.0 Vpp	Set Divert Valve	Source



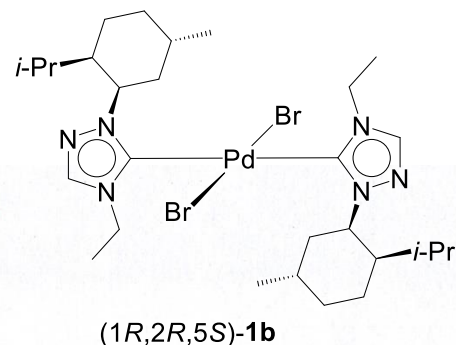
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdB	e <sup>-</sup> Conf	N-Rule
657.2302	1	C28H50BrN6Pd	655.2314	-0.9	30.0	1	100.00	8.5	even	ok

Figure S40. High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-1b.

## Eager 300 Report

Page: 1    Sample: PG-AK-11-224-1 (PG-AK-11-224-1)

Method Name : PGCP13102015	Company Name : C.E. Instruments
Method File : D:\CHNS-2015\PGCP13102015.mth	Printed : 10/13/2015 18:36
Chromatogram : PG-AK-11-224-1	Instrument N. : Instrument #1
Operator ID : CHANDNI	Sample weight : .677
Analysed : 10/13/2015 12:46	
Sample ID : PG-AK-11-224-1 (# 10)	
Analysis Type : UnkNown (Area)	



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	11.6158	41	85162	RS	9.577969	.108295E+07
Carbon	46.0572	65	815679	RS	1.000000	.260680E+07
Hydrogen	6.4525	175	305461	RS	2.670321	.665180E+07
Totals	64.1256		1206302			

**Figure S41.** Elemental analysis data of (1R,2R,5S)-1b.

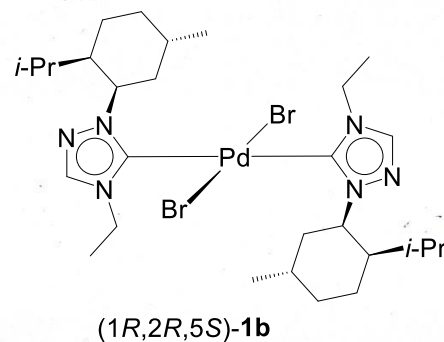
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 12-OCT-2015

This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
Time Delay : Disabled  
Temperature Correction : OFF



<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>
5	29.857	0.0680	29.887	29.735

<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
1	pg-ak-11-224-2	12:03:38	29.735	SR	0.149	589	50	1	24.9
2	pg-ak-11-224-2	12:03:44	29.887	SR	0.149	589	50	1	24.9
3	pg-ak-11-224-2	12:03:51	29.887	SR	0.149	589	50	1	25.0
4	pg-ak-11-224-2	12:03:58	29.887	SR	0.149	589	50	1	25.0
5	pg-ak-11-224-2	12:04:05	29.887	SR	0.149	589	50	1	25.0

Figure S42. Specific rotation of (1R,2R,5S)-1b in CHCl<sub>3</sub>.

NAME PG-AK-4-133-1-1H  
 EXPRO 2  
 PROCNO 1  
 Date 20111123  
 Time 14.57  
 INSTRUM spect  
 PROBHD 5 mm PABBO BB-  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 0  
 SWH 8223.685 Hz  
 FIDRES 0.125483 Hz  
 AQ 3.9846387 sec  
 RG 64  
 DW 60.800 usec  
 DE 6.50 usec  
 TE 293.4 K  
 D1 2.00000000 sec  
 TDO 1

PG-AK-4-133-1-1H

----- CHANNEL f1 -----  
 NUCL1 1H  
 P1 13.50 usec  
 PL1 -1.00 dB  
 PL1W 10.56200695 W  
 SFO1 400.1324710 MHz  
 SI 32768  
 SF 400.1300073 MHz  
 WTM EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 FC 1.00

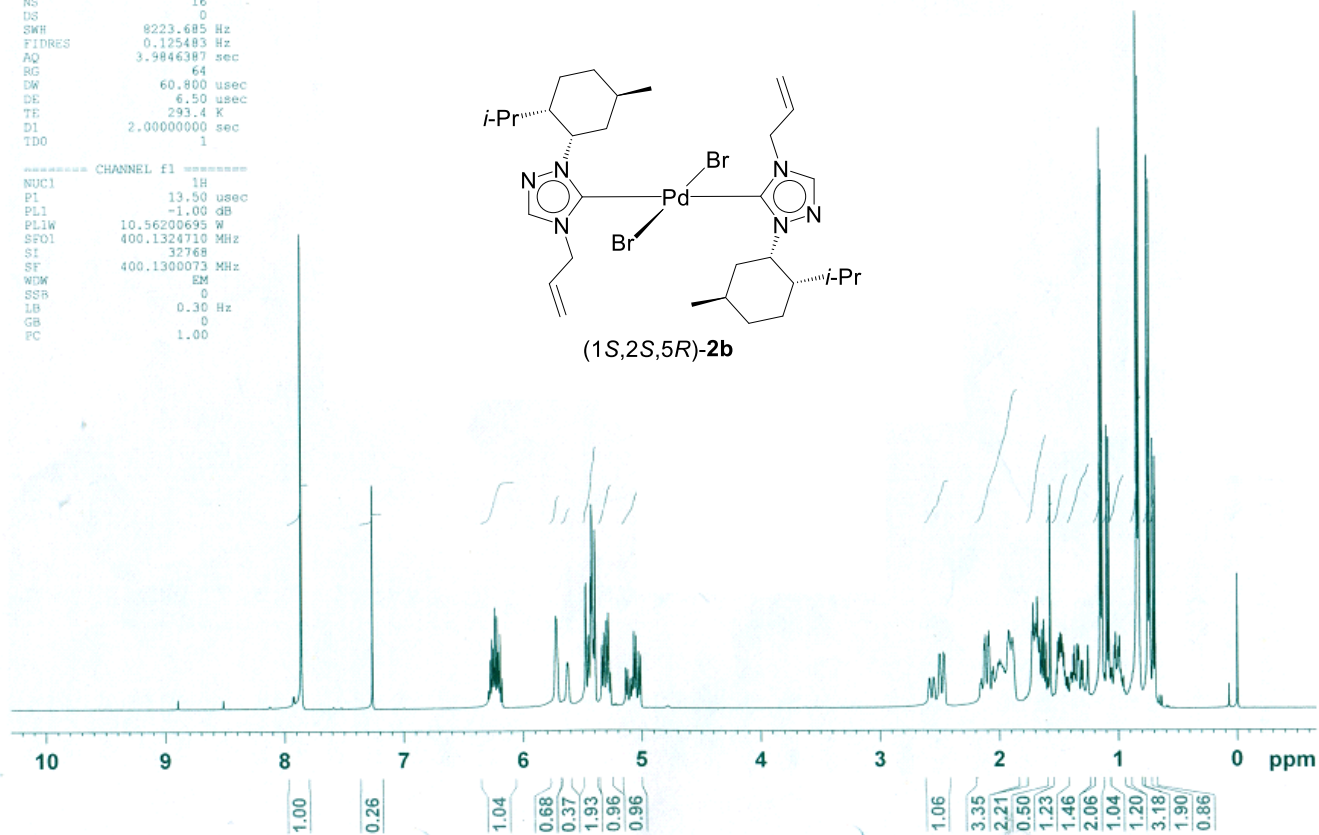
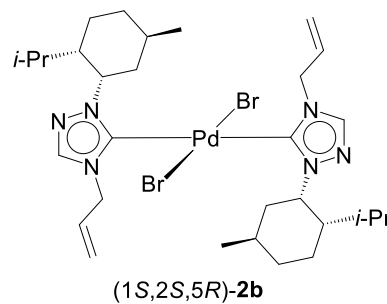
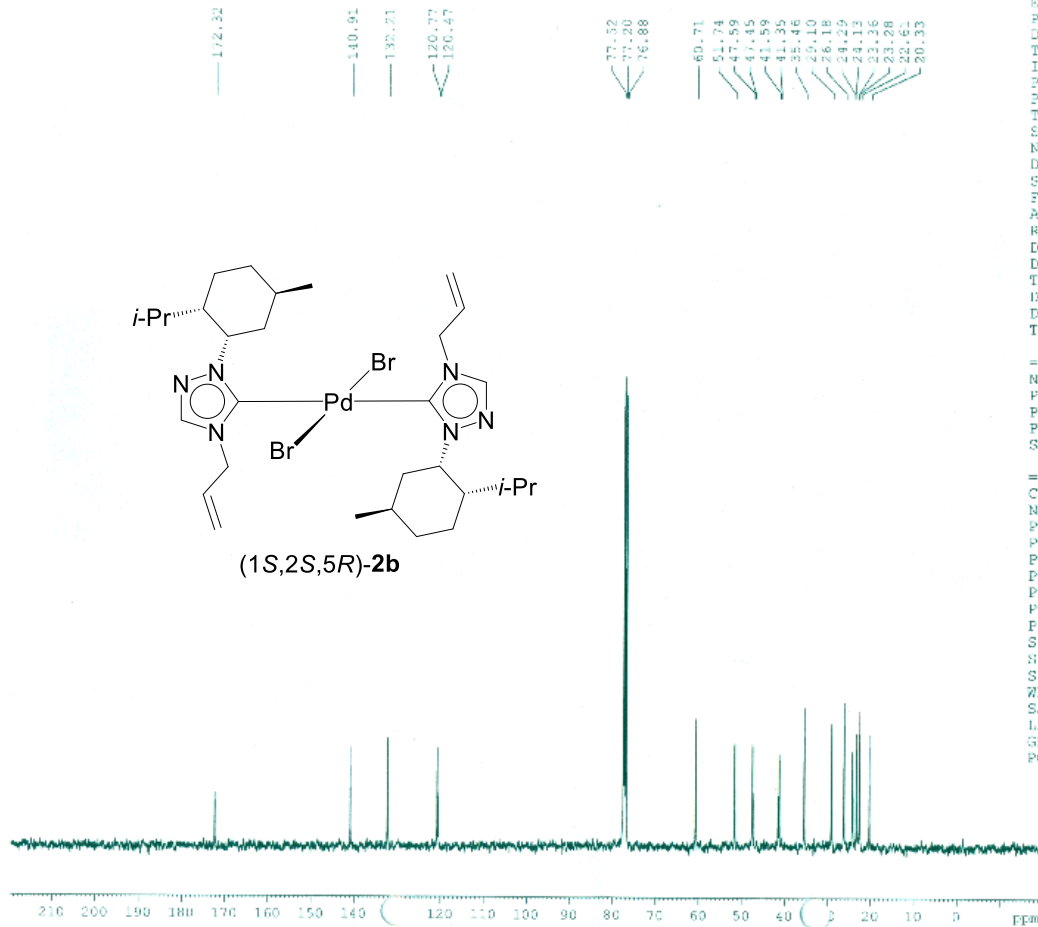


Figure S43.  $^1\text{H}$  NMR spectrum of 1S,2S,5R-2b in  $\text{CDCl}_3$ .

PG-AK-4-133-1-13C



```

NAME PG-AK-4-133-1-13C
EXPNO 3
PROCNO 1
Date_ 20111123
Time 15.07
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 388
DS 6
SWE 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 294.3 K
D1 1.0000000 sec
D11 0.0300000 sec
TD0 1

```

```

===== CHANNEL f1 =====
NUC1 13C
P1 8.75 usec
PL1 -2.00 dB
PLW 56.53121948 W
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -1.00 dB
PL12 14.50 dB
PL13 14.50 dB
PLW 10.56200695 W
PL12X 0.29767781 W
PL13X 0.29767781 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127527 MHz
WDW EM
SSE 0
LB 5.00 Hz
GB 0
PC 1.40

```

Figure S44.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1S,2S,5R-2b in  $\text{CDCl}_3$ .

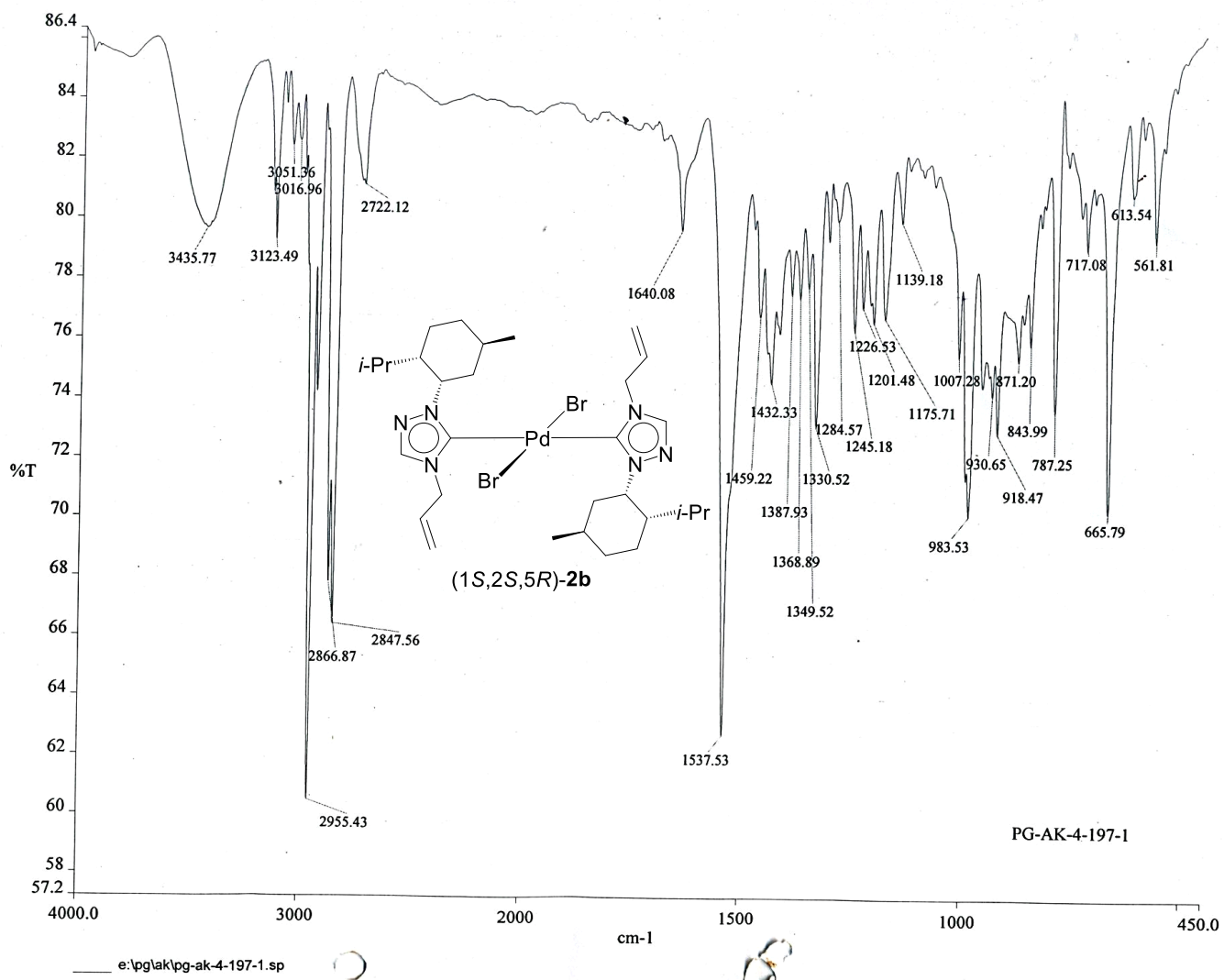


Figure S45. Infrared spectrum of 1S,2S,5R-2b in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

Analysis Info

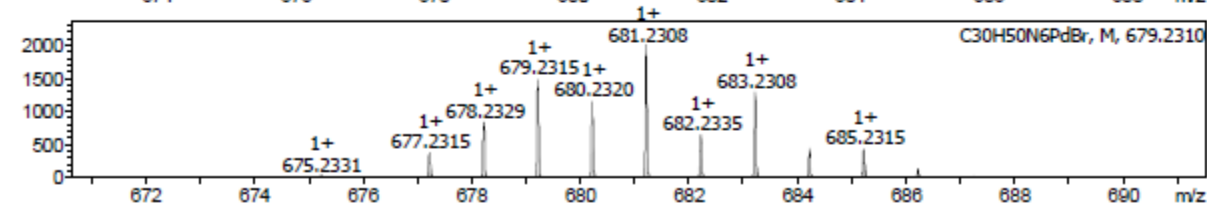
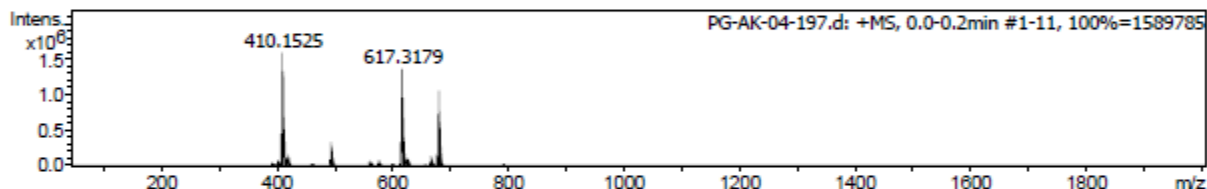
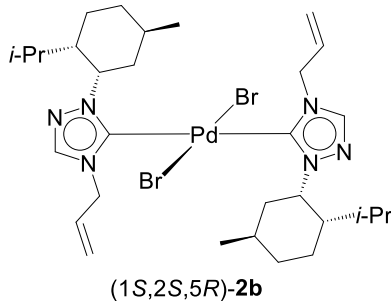
Analysis Name D:\Data\FEB-2016\PG-AK-04-197.d  
 Method Tune\_pos\_NAICSI-2000.m  
 Sample Name PG-AK-04-197  
 Comment C30H50N6PdBr2

Acquisition Date 2/22/2016 9:18:40 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3800 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2000 m/z	Set Collision Cell RF	2100.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
681.2299	1	C30H50BrN6Pd	679.2315	-1.3	50.7	1	100.00	8.5	even	ok

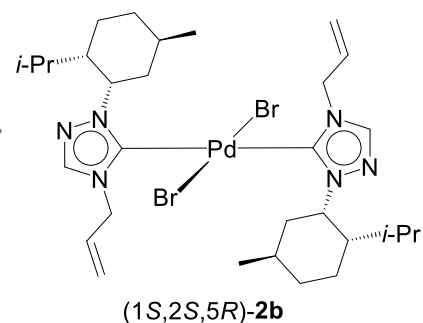
Figure S46. High Resolution Mass Spectrometry (HRMS) data of 1S,2S,5R-2b.

# Eager 300 Report

Page: 1 Sample: PG-AK-4-197-2 (PG-AK-4-197-2)

Method Name : SP-050312  
 Method File : D:\CHNS2012\SP-050312.mth  
 Chromatogram : PG-AK-4-197-2  
 Operator ID : MNRAO  
 Analysed : 03/05/2012 18:24  
 Sample ID : PG-AK-4-197-2 (# 23)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 3/5/2012 19:58  
 Instrument N. : Instrument #1  
 Sample weight : .755



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	11.1258	44	113335	FU	8.001876	.134923E+07
Carbon	47.7199	68	906896	FU	1.000000	.251716E+07
Hydrogen	6.5555	178	283533	RS	3.198556	.572859E+07
Totals	65.4013		1303765			

Figure S47. Elemental analysis data of 1S,2S,5R-2b.



[Comment]  
 Sample name  
 Comment  
 User  
 Division  
 Company IITB

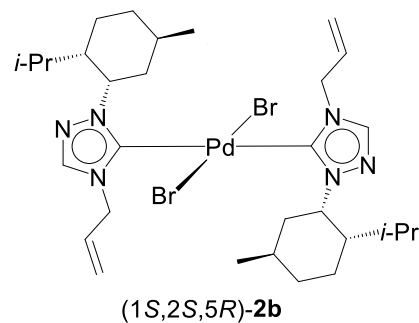
[Data Information]  
 Creation Date 6/10/2013 3 53 PM

[Measurement Information]  
 Instrument Name JASCO POLARIMETER  
 Model Name P-2000  
 Serial No A043361232  
 Polarizer Dichrom  
 Faraday Cell Flint Glass

Accessory PTC-203  
 Accessory S/N A017861234  
 Path Length 100 mm

Light Source Na  
 Monitor wavelength 589 nm  
 D I T 5 sec  
 No of cycle 5  
 Cycle interval 5 sec  
 Temp Monitor Cell  
 Temp Corr Factor None  
 Aperture(S) 3.0mm  
 Aperture(L) Auto  
 Mode Specific O R  
 Path Length 100 mm  
 Concentration 1 w/v  
 Factor 1

[Comment]  
 Sample name  
 Comment  
 User  
 Division  
 Company IITB



No	Sample No	Mode	Calc Data	Meas Data	Temperature(C)	Comment	
1	1	PG-AK-6-150-1	Specific O R	-41.6360	-0.4164	24.99	CHCl <sub>3</sub>
2	2	PG-AK-6-150-2	Specific O R	-41.7160	-0.4172	24.99	CHCl <sub>3</sub>
3	3	PG-AK-6-150-3	Specific O R	-41.7260	-0.4173	24.99	CHCl <sub>3</sub>
4	4	PG-AK-6-150-4	Specific O R	-41.4760	-0.4148	24.99	CHCl <sub>3</sub>
5	5	PG-AK-6-150-5	Specific O R	-41.8560	-0.4186	24.99	CHCl <sub>3</sub>
6	6	Avg		-41.6820			
7	7	S D		0.1396			
8	8	C V		0.3348			

**Figure S48.** Specific rotation of 1S,2S,5R-2b in CHCl<sub>3</sub>.

NAME PG-AK-11-222-1-1  
 EXPNO 4  
 PROCNO 1  
 Date\_ 20151017  
 Time 0.46  
 INSTRUM spect  
 PROBHD 5 mm PABBO BB-  
 PULPROG zg30  
 TD 54274  
 SOLVENT CDCl3  
 NS 16  
 DS 0  
 SWH 8223.685 Hz  
 FIDRES 0.151522 Hz  
 AQ 3.2999091 sec  
 RG 101  
 DW 60.800 usec  
 DE 6.50 usec  
 TE 295.4 K  
 D1 1.0000000 sec  
 TD0 1

PG-AK-11-222-1-1H

===== CHANNEL f1 =====  
 NUC1 1H  
 P1 14.75 usec  
 PL1 -1.00 dB  
 PL1W 10.56200695 W  
 SFO1 400.1324710 MHz  
 SI 32768  
 SF 400.1300098 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

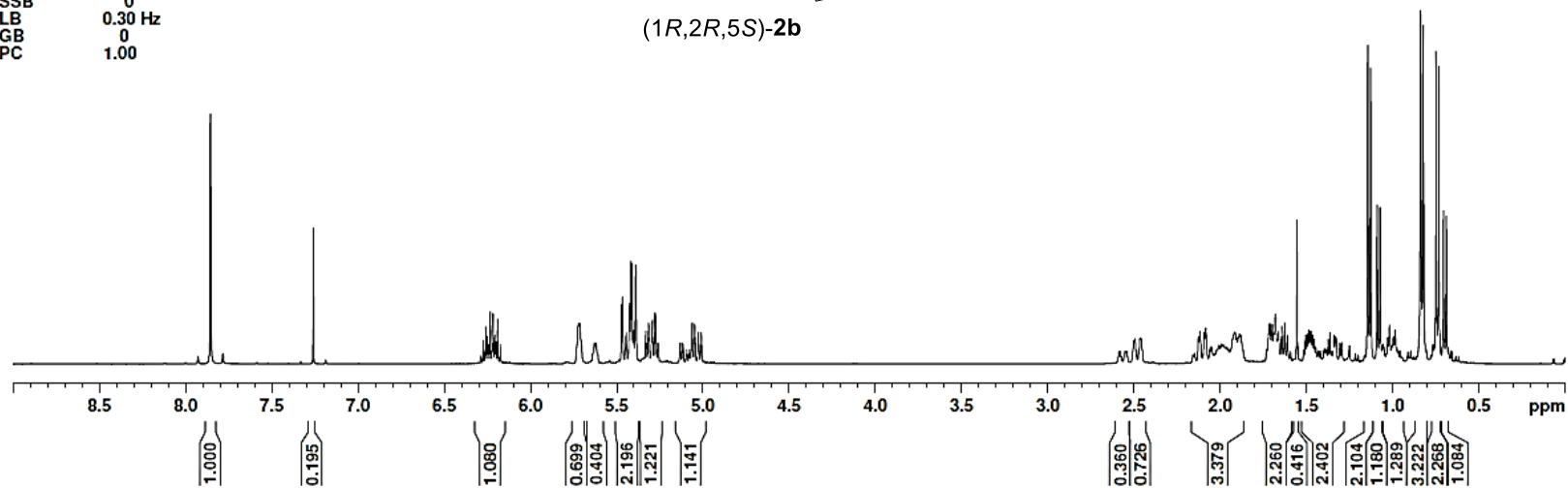
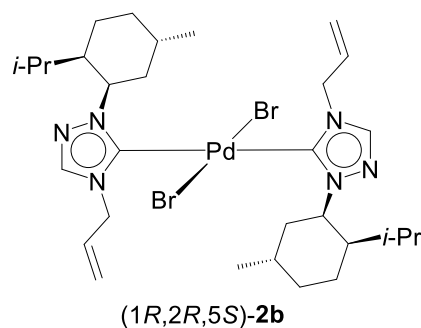


Figure S49. <sup>1</sup>H NMR spectrum of (1*R*,2*R*,5*S*)-**2b** in CDCl<sub>3</sub>.

PG-AK-11-222-1-13C

```

NAME      PG-AK-11-222-1-13C
EXPNO     5
PROCNO    1
Date_     20151017
Time      0.51
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD        65536
SOLVENT   CDCl3
NS        421
DS        4
SWH       26041.666 Hz
FIDRES    0.397364 Hz
AQ        1.2583412 sec
RG        2050
DW        19.200 usec
DE        6.50 usec
TE        296.3 K
D1        1.00000000 sec
D11       0.03000000 sec
TD0       1
  
```

```

===== CHANNEL f1 =====
NUC1      13C
P1        8.50 usec
PL1       -2.00 dB
PL1W      56.53121948 W
SFO1      100.6238364 MHz
  
```

```

===== CHANNEL f2 =====
CPDPRG2   waltz16
NUC2      1H
PCPD2     80.00 usec
PL2       -1.00 dB
PL12      13.69 dB
PL13      14.50 dB
PL2W      10.56200695 W
PL12W     0.35871249 W
PL13W     0.29767781 W
SFO2      400.1316005 MHz
SI        32768
SF        100.6127516 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
  
```

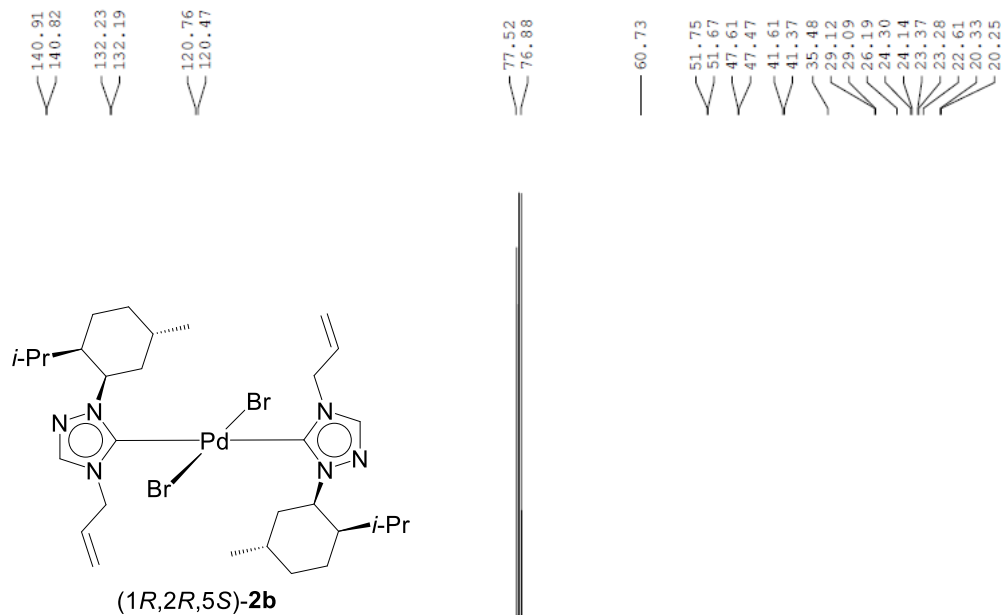
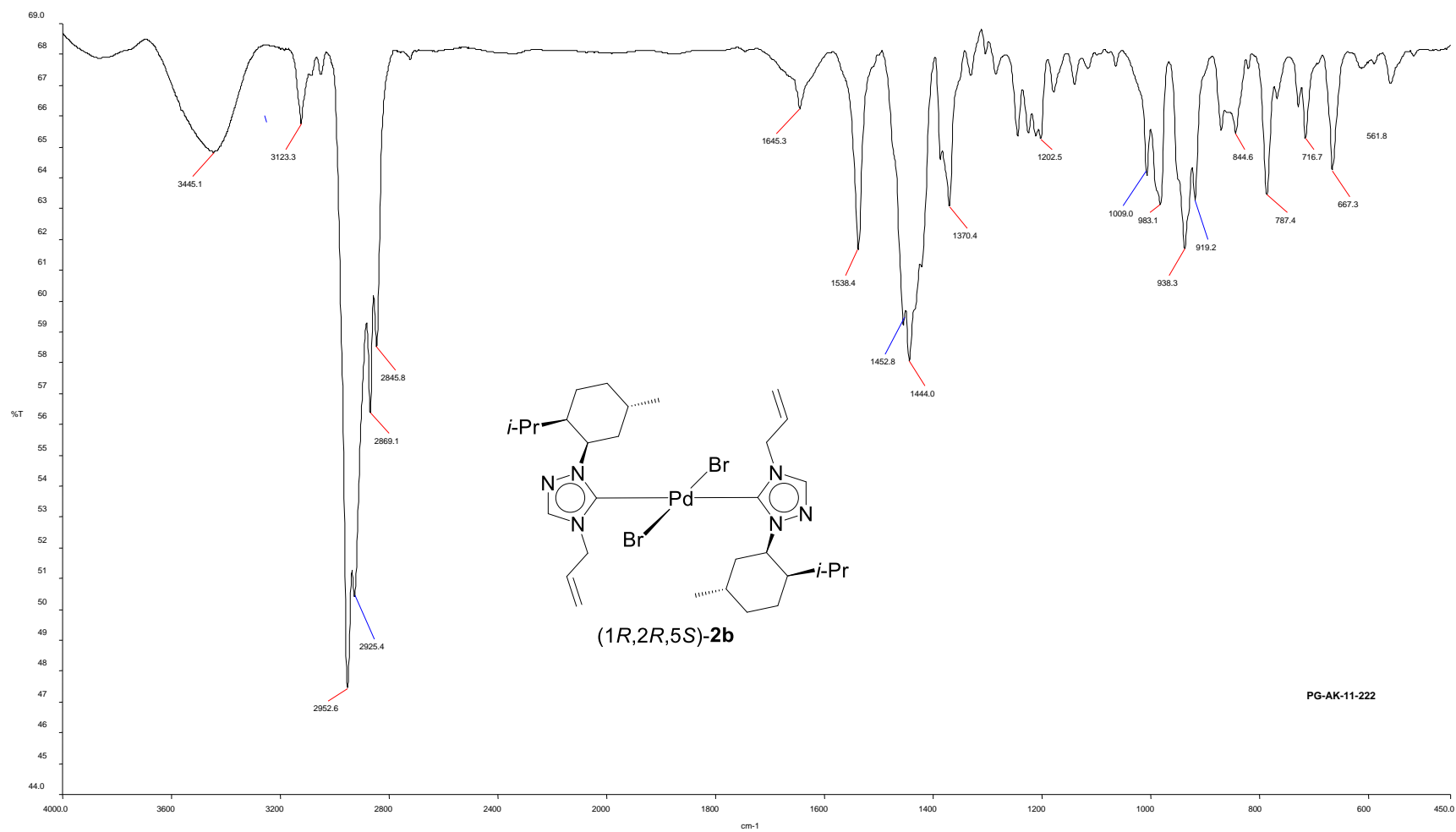


Figure S50.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1R,2R,5S)-2b in  $\text{CDCl}_3$ .



PG-AK-11-222

**Figure S51.** Infrared spectrum of 1R,2R,5S-2b in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

**Analysis Info**

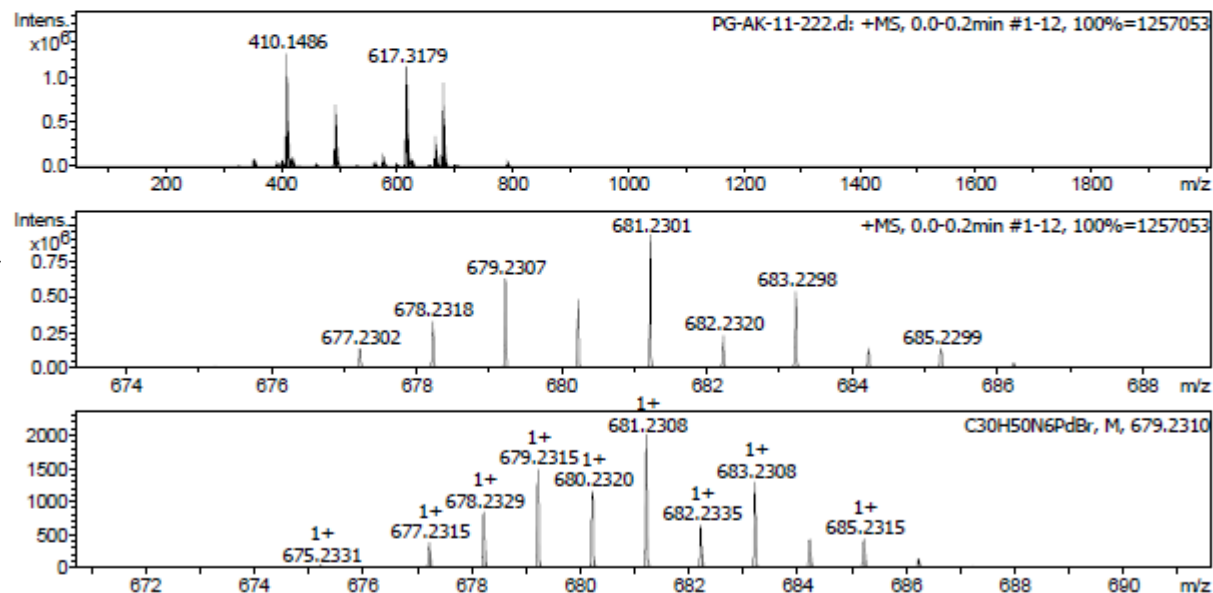
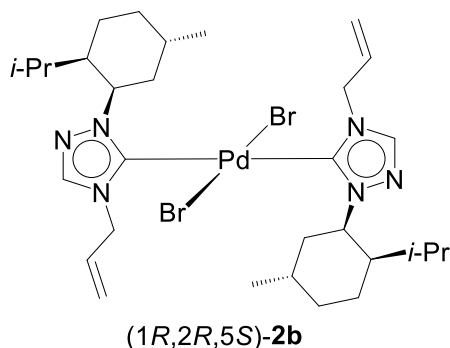
Analysis Name D:\Data\FEB-2016\PG-AK-11-222.d  
 Method Tune\_pos\_NAICSI-2000.m  
 Sample Name PG-AK-11-222  
 Comment C30H50N6PdBr2

Acquisition Date 2/22/2016 9:17:19 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

**Acquisition Parameter**

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3800 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2000 m/z	Set Collision Cell RF	2100.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdB	e <sup>-</sup> Conf	N-Rule
681.2301	1	C30H50BrN6Pd	679.2315	-1.0	52.8	1	100.00	8.5	even	ok

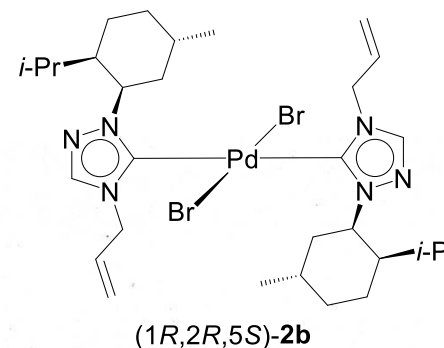
**Figure S52.** High Resolution Mass Spectrometry (HRMS) data of **1R,2R,5S-2b**.

# Eager 300 Report

Page: 1 Sample: PG-AK-11-222-2 (PG-AK-11-222-2)

Method Name : PGCP13102015  
Method File : D:\CHNS-2015\PGCP13102015.mth  
Chromatogram : PG-AK-11-222-2  
Operator ID : CHANDNI  
Analysed : 10/13/2015 13:17  
Sample ID : PG-AK-11-222-2 (# 13)  
Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
Printed : 10/13/2015 18:36  
Instrument N. : Instrument #1  
Sample weight : .784



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	11.1318	41	94512	RS	10.356680	.108295E+07
Carbon	47.7544	64	978831	RS	1.000000	.260680E+07
Hydrogen	6.3743	175	347305	RS	2.818360	.665180E+07
Totals	65.2604		1420648			

Figure S53. Elemental analysis data of (1R,2R,5S)-2b.

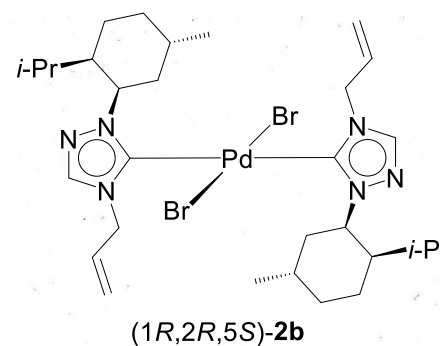
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 12-OCT-2015

This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
Time Delay : Disabled  
Temperature Correction : OFF



<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>					
5	39.430	0.1341	39.639	39.340					
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
1	pg-ak-11-222-1	12:20:47	39.340	SR	0.197	589	50	1	25.1
2	pg-ak-11-222-1	12:20:54	39.340	SR	0.197	589	50	1	25.1
3	pg-ak-11-222-1	12:21:00	39.340	SR	0.197	589	50	1	25.1
4	pg-ak-11-222-1	12:21:07	39.493	SR	0.197	589	50	1	25.1
5	pg-ak-11-222-1	12:21:19	39.639	SR	0.198	589	50	1	25.1

Figure S54. Specific rotation of (1R,2R,5S)-2b in CHCl<sub>3</sub>.

NAME PG-AK-11-223-1-1  
EXPNO 1  
PROCNO 1  
Date\_ 20151017  
Time 0.08  
INSTRUM spect  
PROBHD 5 mm PABBO BB-  
PULPROG zg30  
TD 54274  
SOLVENT CDCl3  
NS 10  
DS 0  
SWH 8223.685 Hz  
FIDRES 0.151522 Hz  
AQ 3.2999091 sec  
RG 114  
DW 60.800 usec  
DE 6.50 usec  
TE 295.3 K  
D1 1.0000000 sec  
TD0 1

PG-AK-11-223-1-1H

==== CHANNEL f1 =====  
NUC1 1H  
P1 14.75 usec  
PL1 -1.00 dB  
PL1W 10.56200695 W  
SFO1 400.1324710 MHz  
SI 32768  
SF 400.1300095 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

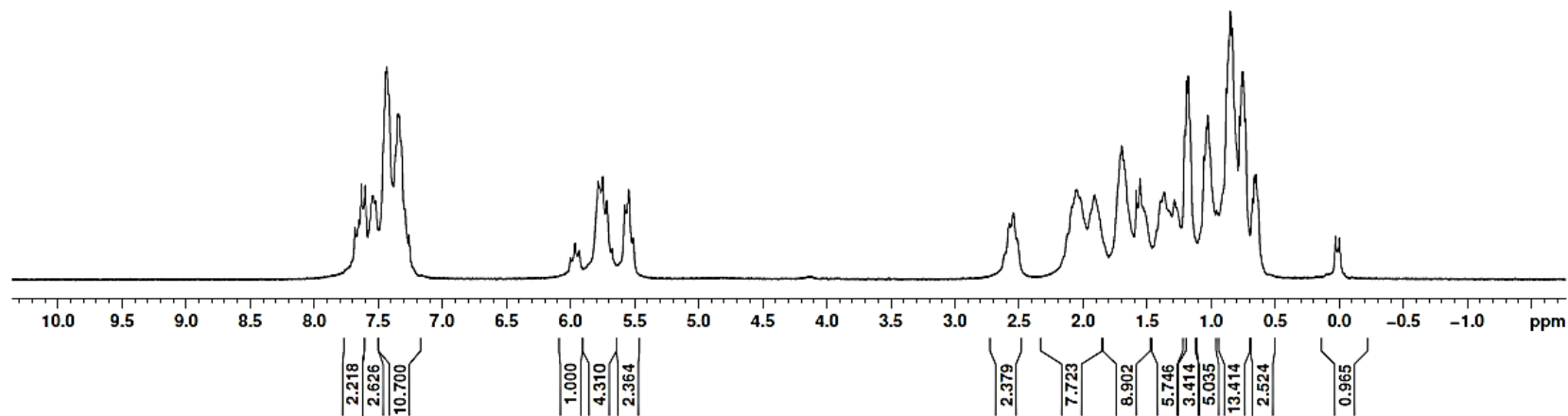
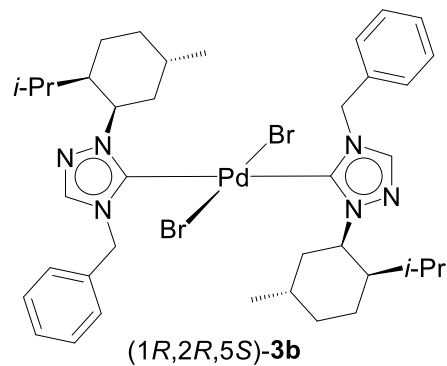


Figure S55.  $^1\text{H}$  NMR spectrum of (1R,2R,5S)-3b in  $\text{CDCl}_3$ .



PG-AK-11-223-13C

```

NAME      PG-AK-11-223-13C
EXPNO     1
PROCNO    1
Date_     20151018
Time      20.46
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD        65536
SOLVENT   CDCl3
NS        1209
DS        4
SWH       26041.666 Hz
FIDRES    0.397364 Hz
AQ        1.2583412 sec
RG        2050
DW        19.200 usec
DE        6.50 usec
TE        295.6 K
D1        1.00000000 sec
D11       0.03000000 sec
TD0       1
  
```

```

===== CHANNEL f1 =====
NUC1      13C
P1        8.50 usec
PL1       -2.00 dB
PL1W      56.53121948 W
SFO1     100.6238364 MHz
  
```

```

===== CHANNEL f2 =====
CPDPRG2   waltz16
NUC2      1H
PCPD2     80.00 usec
PL2       -1.00 dB
PL12     13.69 dB
PL13     14.50 dB
PL2W     10.56200695 W
PL12W    0.35871249 W
PL13W    0.29767781 W
SFO2     400.1316005 MHz
SI        32768
SF        100.6127528 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
  
```

172.50  
172.46

140.99  
140.86  
134.75  
134.63  
129.30  
129.23  
129.20  
129.00  
128.85  
128.80

77.51  
77.19  
76.88

60.78  
52.80  
52.76  
47.64  
47.35  
41.47  
41.36  
35.49  
35.44  
29.16  
29.07  
26.22  
26.18  
24.18  
23.93  
23.33  
22.63  
22.59  
20.27  
20.13

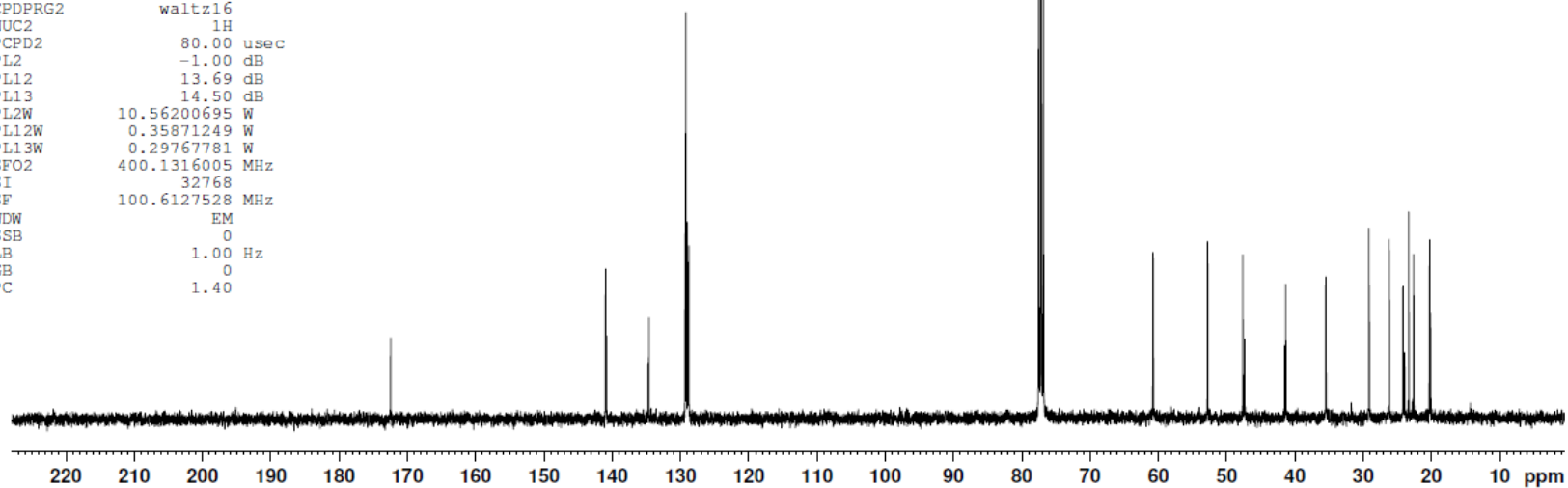
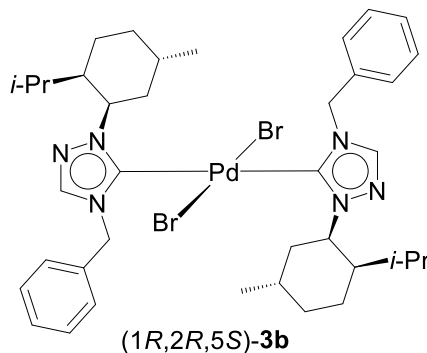
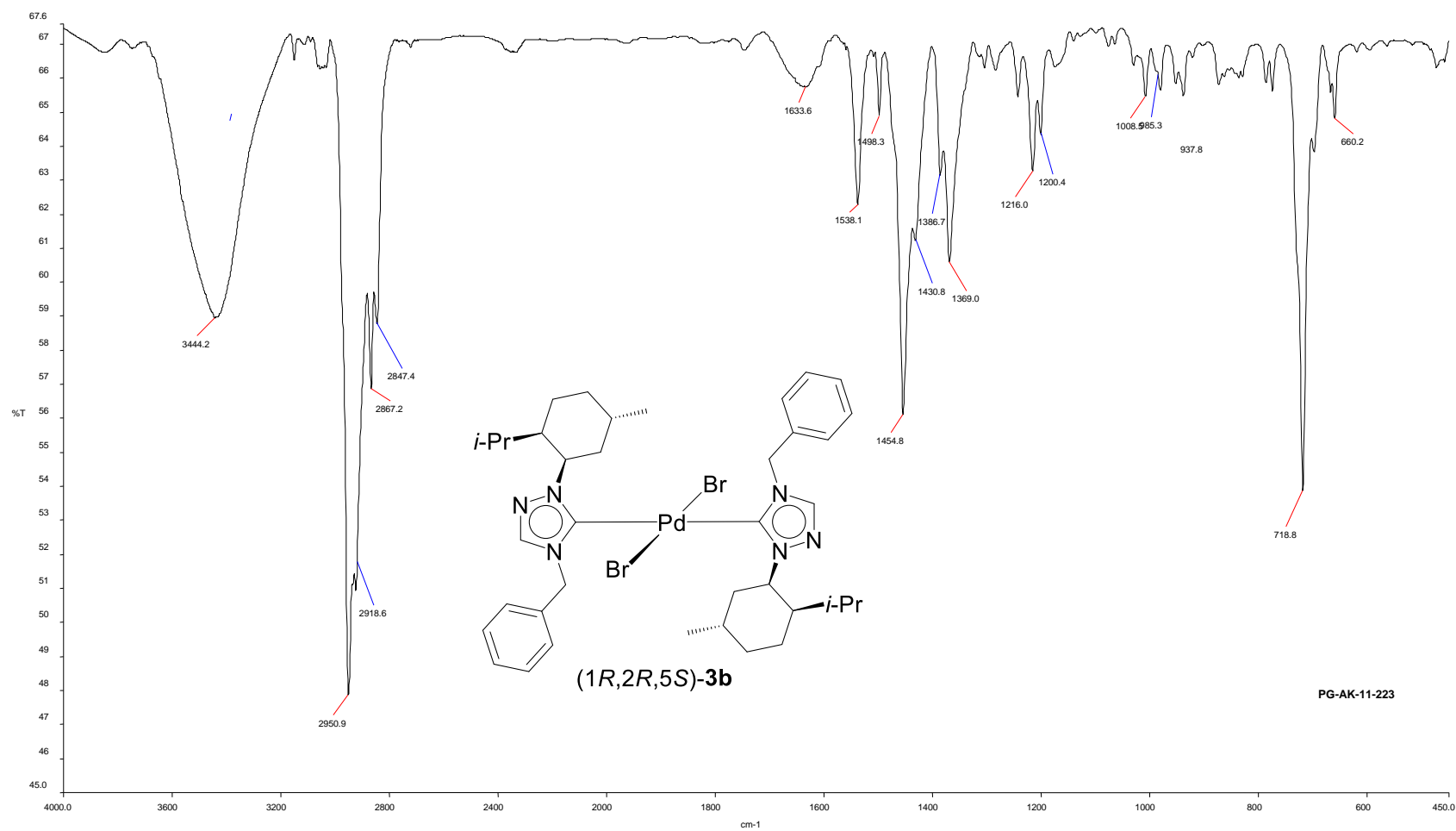


Figure S56.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1R,2R,5S)-3b in  $\text{CDCl}_3$ .



PG-AK-11-223

Figure S57. Infrared spectrum of 1R,2R,5S-3b in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

Analysis Info

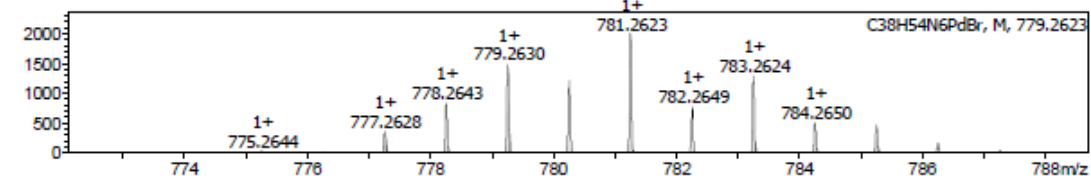
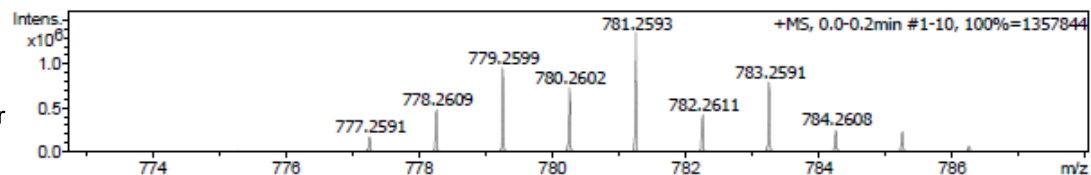
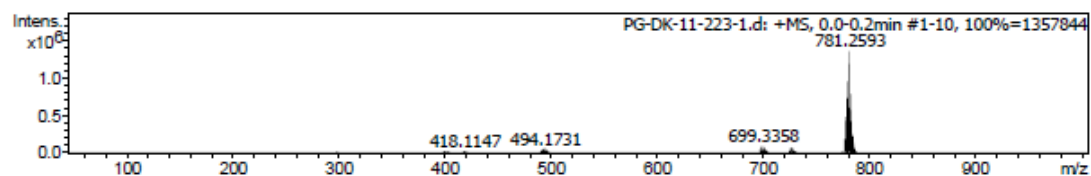
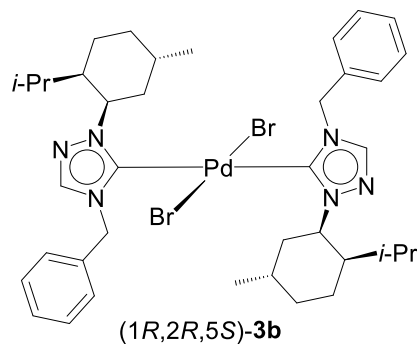
Analysis Name D:\Data\FEB-2016\PG-DK-11-223-1.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-DK-11-223-1  
 Comment C38H54N6PdBr2

Acquisition Date 2/22/2016 11:36:27 AM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
781.2593	1	C38H54N6Pd	779.2630	-3.9	50.7	1	100.00	14.5	even	ok

Figure S58. High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-3b.

## Eager 300 Report

Page: 1    Sample: PG-AK-11-223-2 (PG-AK-11-223-2)

Method Name : PGCP13102015

Method File : D:\CHNS-2015\PGCP13102015.mth

Chromatogram : PG-AK-11-223-2

Operator ID : CHANDNI

Analysed : 10/13/2015 13:37

Sample ID : PG-AK-11-223-2 (# 15)

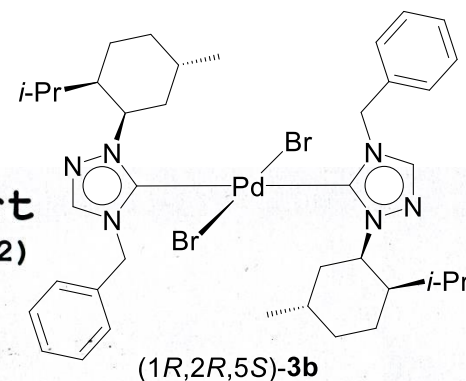
Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments

Printed : 10/13/2015 18:36

Instrument N. : Instrument #1

Sample weight : 1.004



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	9.5675	41	104025	RS	13.525010	.108295E+07
Carbon	53.6476	63	1406939	RS	1.000000	.260680E+07
Hydrogen	6.2084	178	429505	RS	3.275722	.665180E+07
Totals	69.4235		1940469			

Figure S59. Elemental analysis data of (1R,2R,5S)-3b.

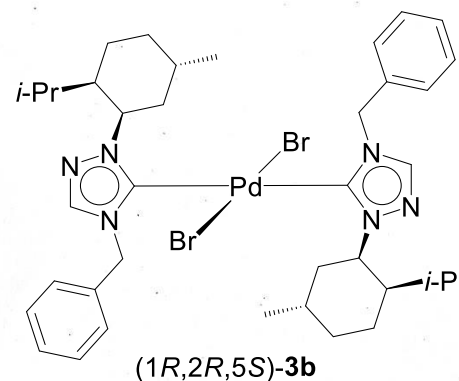
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 12-OCT-2015

This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
Time Delay : Disabled  
Temperature Correction : OFF



<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>					
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
5	44.991	0.0000	44.991	44.991					
1	pg-ak-11-223-1	12:13:09	44.991	SR	0.225	589	50	1	24.9
2	pg-ak-11-223-1	12:13:16	44.991	SR	0.225	589	50	1	24.9
3	pg-ak-11-223-1	12:13:23	44.991	SR	0.225	589	50	1	24.9
4	pg-ak-11-223-1	12:13:29	44.991	SR	0.225	589	50	1	24.9
5	pg-ak-11-223-1	12:13:36	44.991	SR	0.225	589	50	1	24.9

Figure S60. Specific rotation of (1R,2R,5S)-3b in CHCl<sub>3</sub>.

Current Data Parameters  
NAME PG-AK-9-97-1-1H  
EXPNO 8  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20140327  
Time 21.46  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 12  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.152588 Hz  
AQ 3.2767999 sec  
RG 134.65  
DW 50.000 usec  
DE 6.50 usec  
TE 297.8 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 500.1330885 MHz  
NUC1 1H  
P1 13.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300000 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

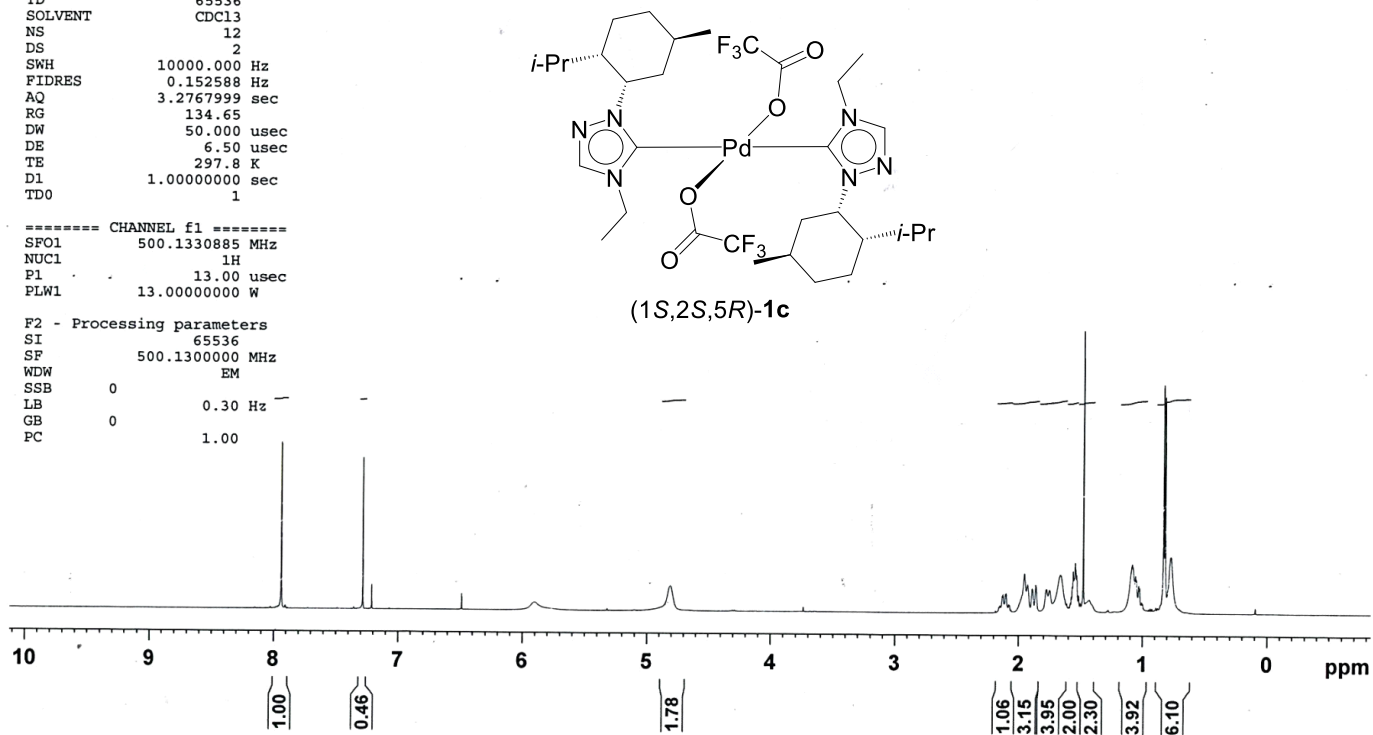


Figure S61. <sup>1</sup>H NMR spectrum of 1S,2S,5R-1c in CDCl<sub>3</sub>.

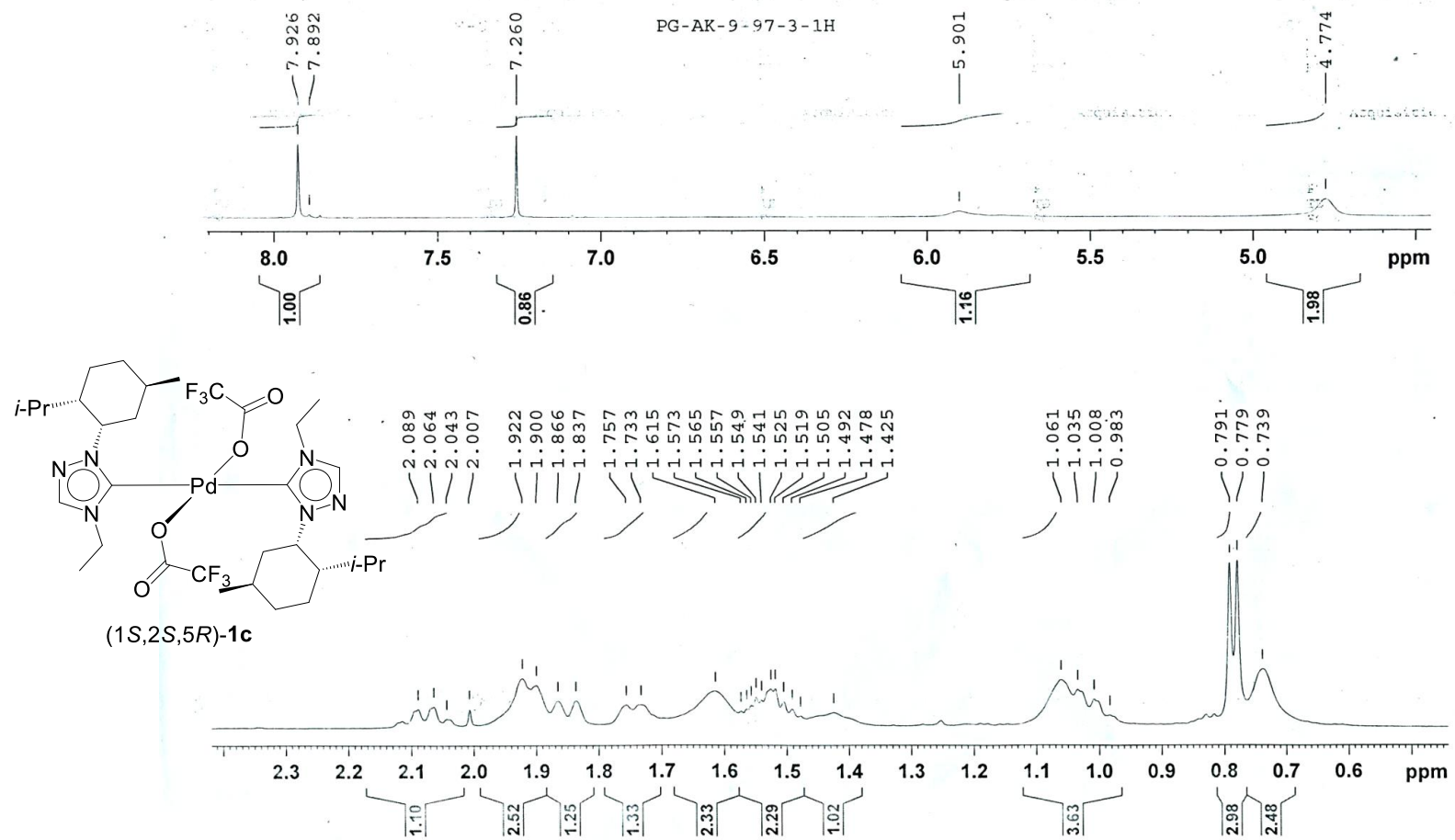


Figure S62. Expanded  $^1\text{H}$  NMR spectrum of 1S,2S,5R-1c in  $\text{CDCl}_3$ .

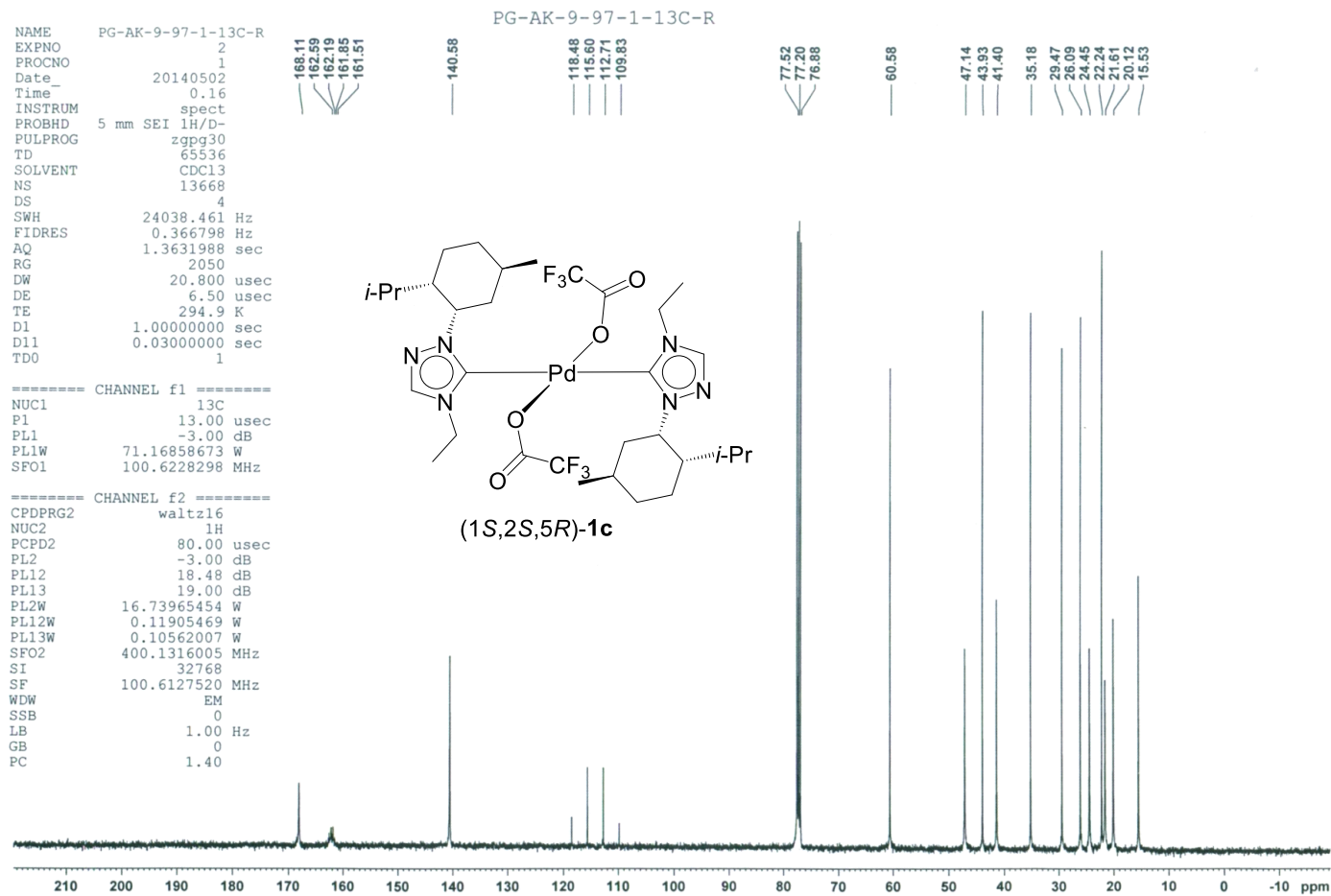


Figure S63.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1S,2S,5R-1c in  $\text{CDCl}_3$ .



Current Data Parameters  
NAME PG-AK-9-97-1-19F  
EXPNO 9  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20140327  
Time 21.49  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgflqn  
TD 131072  
SOLVENT CDCl3  
NS 16  
DS 4  
SWH 187500.000 Hz  
FIDRES 1.430511 Hz  
AQ 0.3495253 sec  
RG 197.27  
DW 2.667 usec  
DE 6.50 usec  
TE 297.7 K  
D1 1.00000000 sec  
TD0 1

----- CHANNEL f1 -----  
SFO1 470.5453180 MHz  
NUC1 19F  
P1 13.50 usec  
PLW1 40.00000000 W

F2 - Processing parameters  
SI 65536  
SF 470.5923770 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

PG-AK-9-97-1-19F

---73.79

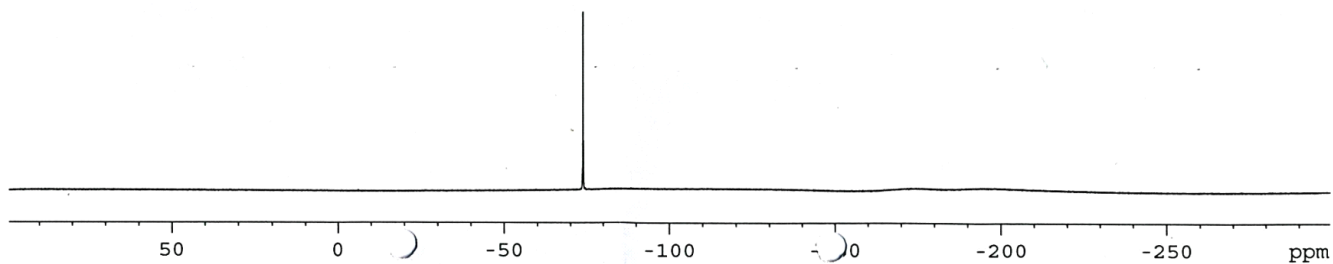
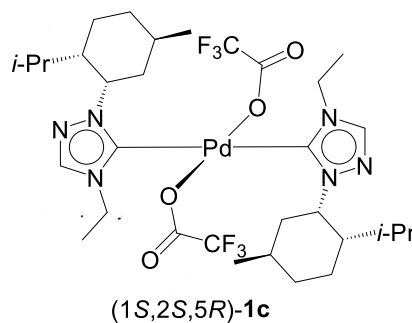


Figure S64. <sup>19</sup>F{<sup>1</sup>H} NMR spectrum of 1S,2S,5R-1c in CDCl<sub>3</sub>.

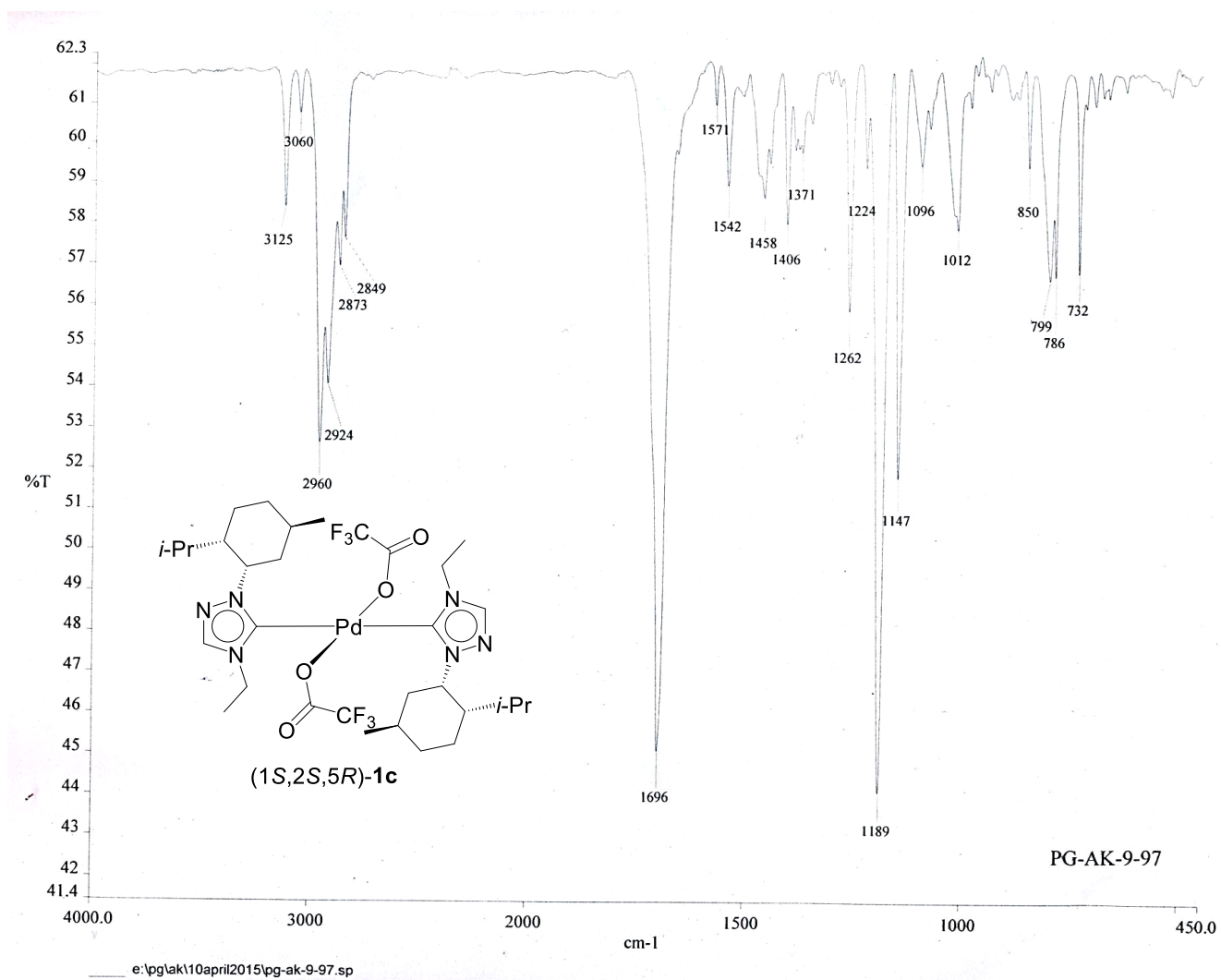


Figure S65. Infrared spectrum of 1S,2S,5R-1c in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

Analysis Info

Analysis Name D:\Data\FEB-2016\PG-AK-09-97.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-AK-09-97  
 Comment C32H50N6O4PdF6

Acquisition Date 2/29/2016 9:01:53 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source

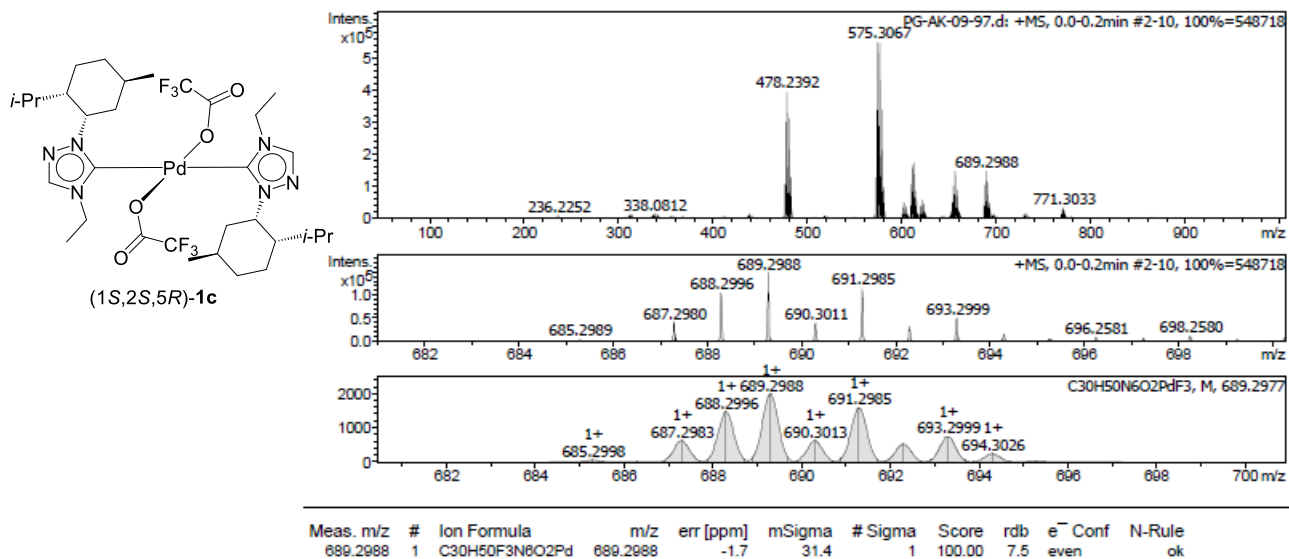


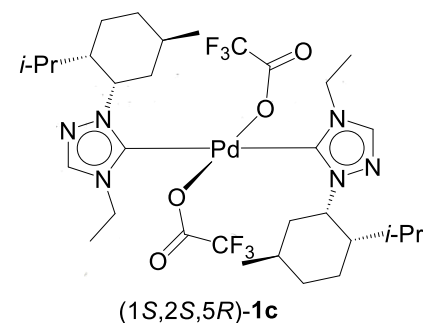
Figure S66. High Resolution Mass Spectrometry (HRMS) data of 1S,2S,5R-1c.

## Eager 300 Report

Page: 1    Sample: PG-AK-9-97-1 (PG-AK-9-97-1)

Method Name : PGCP11052015  
 Method File : D:\CHNS-2015\PGCP11052015.mth  
 Chromatogram : PG-AK-9-97-1  
 Operator ID : CHANDNI  
 Analysed : 05/11/2015 11:48  
 Sample ID : PG-AK-9-97-1 (# 6)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 5/13/2015 19:41  
 Instrument N. : Instrument #1  
 Sample weight : .815



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	10.7128	42	103089	RS	10.013580	.118073E+07
Carbon	48.3356	65	1032285	RS	1.000000	.262045E+07
Hydrogen	5.9624	175	340944	RS	3.027726	.667788E+07
Totals	65.0108		1476318			

Figure S67. Elemental analysis data of 1S,2S,5R-1c.

CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 01-DEC-2014

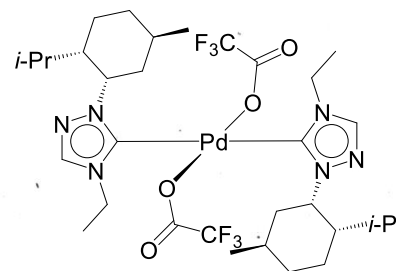
This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0

Time Delay : Disabled

Temperature Correction : OFF



(1S,2S,5R)-1c

<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>						
5	47.857	0.0671	47.902	47.752						
<u>S.No</u>	<u>Sample ID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>	
1	pg-ak-9-111	11:54:32	47.752	SR	0.478	589	100	1	25.1	
2	pg-ak-9-111	11:54:39	47.827	SR	0.478	589	100	1	25.1	
3	pg-ak-9-111	11:54:46	47.902	SR	0.479	589	100	1	25.0	
4	pg-ak-9-111	11:54:53	47.902	SR	0.479	589	100	1	25.0	
5	pg-ak-9-111	11:54:59	47.902	SR	0.479	589	100	1	25.0	

**Figure S68.** Specific rotation of 1S,2S,5R-1c in CHCl<sub>3</sub>.

Current Data Parameters  
NAME PG-AK-11-225-1-1H  
EXPNO 4  
PROCNO 1

PG-AK-11-225-1-1H

F2 - Acquisition Parameters  
Date\_ 20151026  
Time\_ 0.14  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 50  
DS 0  
SWH 10000.000 Hz  
FIDRES 0.152588 Hz  
AQ 3.2767999 sec  
RG 80.35  
DW 50.000 usec  
DE 6.50 usec  
TE 295.5 K  
DL 1.00000000 sec  
TDO 1

==== CHANNEL f1 =====  
SFO1 500.1330885 MHz  
NUC1 1H  
P1 13.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300127 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

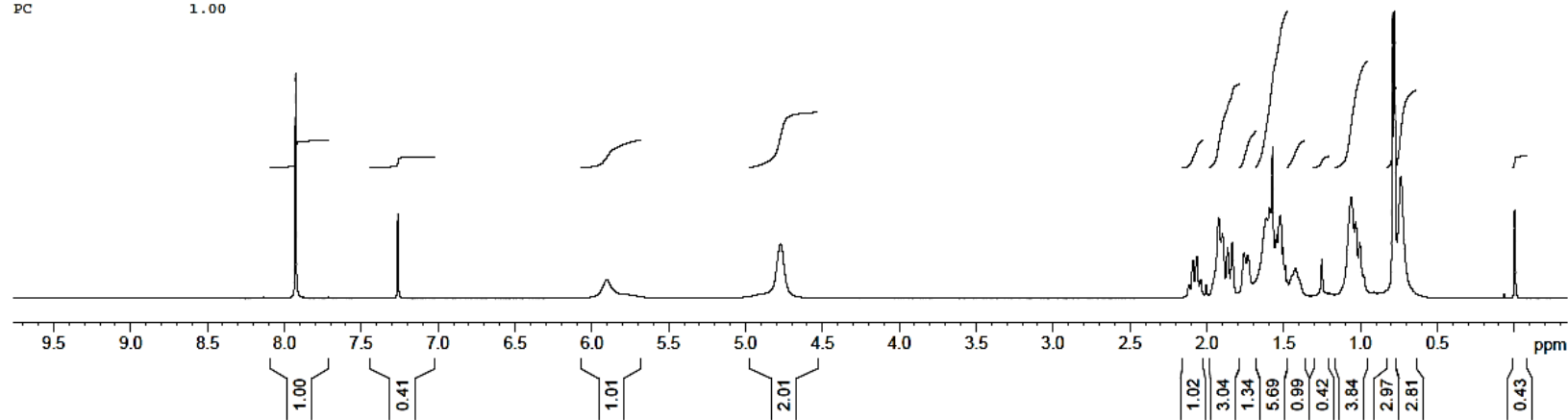
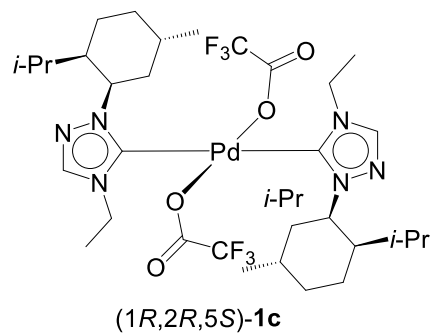


Figure S69. <sup>1</sup>H NMR spectrum of (1R,2R,5S)-1c in CDCl<sub>3</sub>.

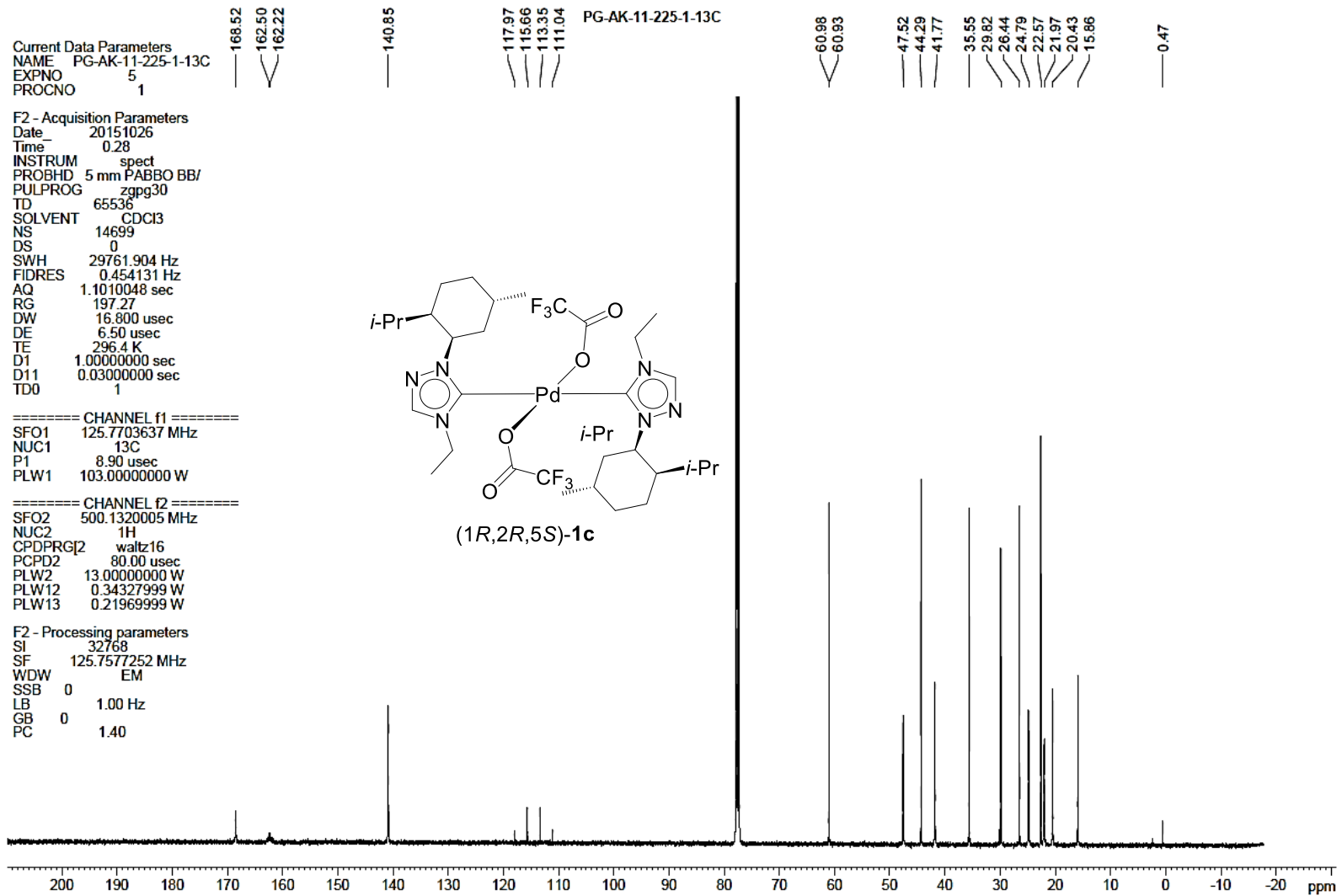
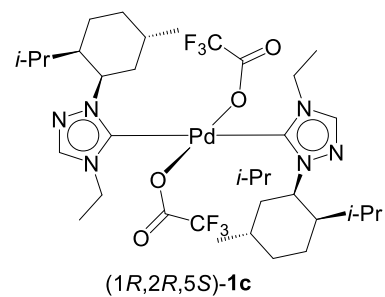


Figure S70.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1*R*,2*R*,5*S*)-**1c** in  $\text{CDCl}_3$ .

PG-AK-11-225-1-19F

-73.88



Current Data Parameters  
NAME PG-AK-11-225-1-19F  
EXPNO 4  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20151026  
Time\_ 21.37  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgfglqn  
TD 131072  
SOLVENT CDCl3  
NS 48  
DS 4  
SWH 113636.367 Hz  
FIDRES 0.866977 Hz  
AQ 0.5767168 sec  
RG 197.27  
DW 4.400 usec  
DE 6.50 usec  
TE 295.5 K  
D1 1.00000000 sec  
TD0 1

==== CHANNEL f1 =====  
SFO1 470.5453180 MHz  
NUC1 19F  
P1 13.50 usec  
PLW1 40.00000000 W

F2 - Processing parameters  
SI 65536  
SF 470.5923770 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

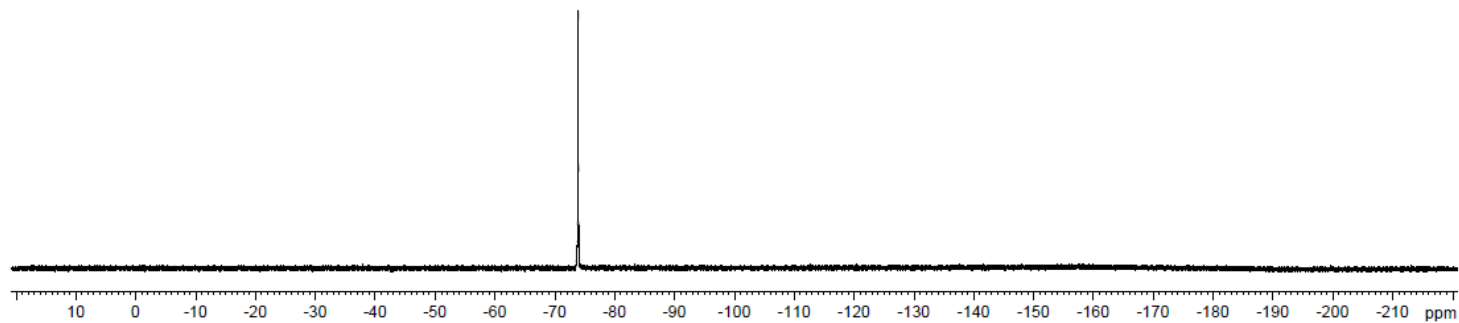
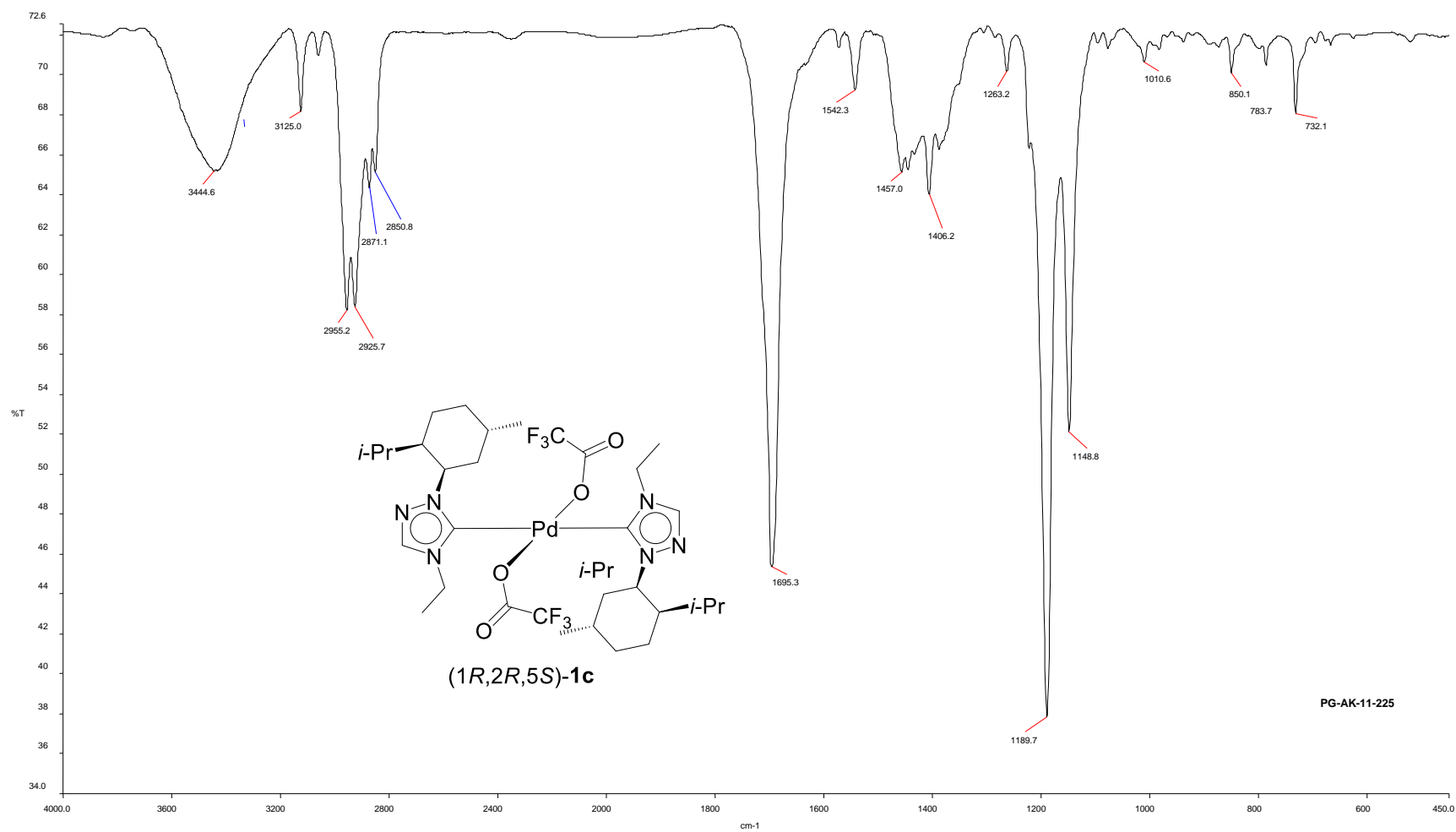


Figure S71. <sup>19</sup>F{<sup>1</sup>H} NMR spectrum of (1R,2R,5S)-1c in CDCl<sub>3</sub>.





**Figure S72.** Infrared spectrum of 1*R*,2*R*,5*S*-1c in KBr.

DEPARTMENT OF CHEMISTRY, I.I.T.(B)

**Analysis Info**

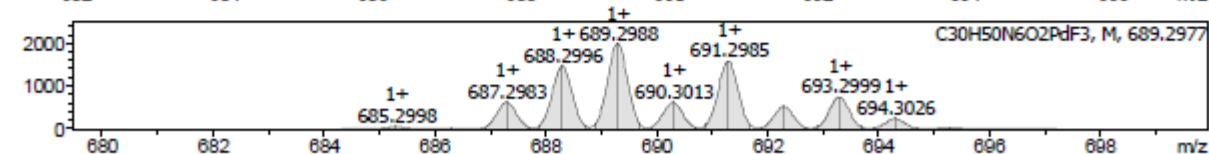
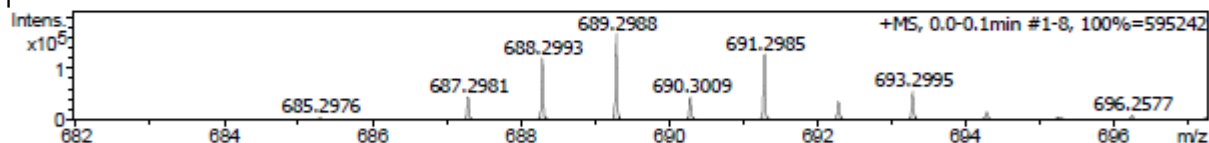
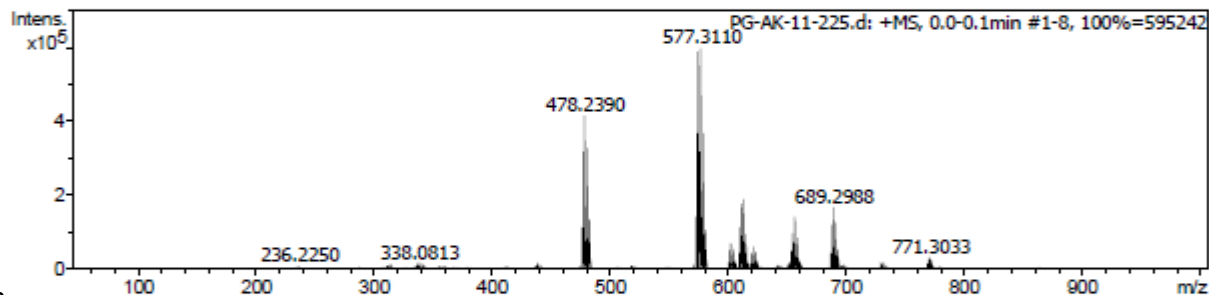
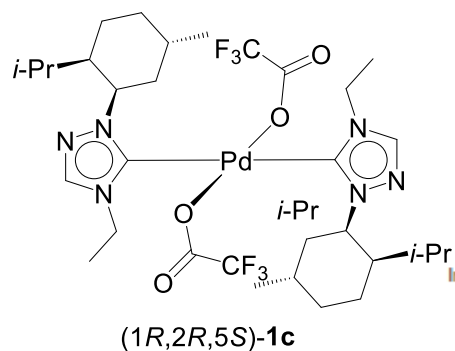
Analysis Name D:\Data\FEB-2016\PG-AK-11-225.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-AK-11-225  
 Comment C32H50N6O4PdF6

Acquisition Date 2/29/2016 9:03:39 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

**Acquisition Parameter**

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
689.2988	1	C30H50F3N6O2Pd	689.2988	-1.6	34.6	1	100.00	7.5	even	ok

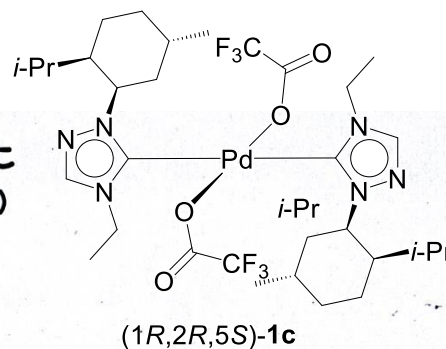
**Figure S73.** High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-1c.

# Eager 300 Report

Page: 1 Sample: PG-AK-11-225-1 (PG-AK-11-225-1)

Method Name : PGCP13102015  
 Method File : D:\CHNS-2015\PGCP13102015.mth  
 Chromatogram : PG-AK-11-225-1  
 Operator ID : CHANDNI  
 Analysed : 10/13/2015 14:08  
 Sample ID : PG-AK-11-225-1 (# 18)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 10/13/2015 18:36  
 Instrument N. : Instrument #1  
 Sample weight : .644



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	10.6417	41	74217	RS	10.955020	.108295E+07
Carbon	48.2606	64	813049	RS	1.000000	.260680E+07
Hydrogen	5.7098	178	259480	RS	3.133376	.665180E+07
Totals	64.6121		1146746			

Figure S74. Elemental analysis data of (1R,2R,5S)-1c.

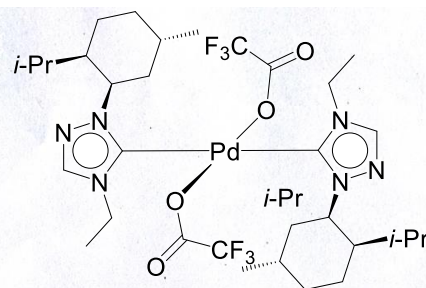
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Tuesday, 27-OCT-2015

This sample was measured on an Autopol IV, Serial #82083  
 Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
 Time Delay : Disabled  
 Temperature Correction : OFF



(1R,2R,5S)-1c  
 Maximum

n	Average	Std.Dev.	Maximum	Minimum
5	-47.974	0.1665	-47.792	-48.096

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Conc.	Temp.
1	pg-ak-11-225-1	17:20:17	-47.792	SR	-0.239	589	50.00	1.000	25.1
2	pg-ak-11-225-1	17:20:24	-47.792	SR	-0.239	589	50.00	1.000	25.1
3	pg-ak-11-225-1	17:20:31	-48.096	SR	-0.240	589	50.00	1.000	25.1
4	pg-ak-11-225-1	17:20:38	-48.096	SR	-0.240	589	50.00	1.000	25.1
5	pg-ak-11-225-1	17:20:45	-48.096	SR	-0.240	589	50.00	1.000	25.1

Figure S75. Specific rotation of (1R,2R,5S)-1c in CHCl<sub>3</sub>.

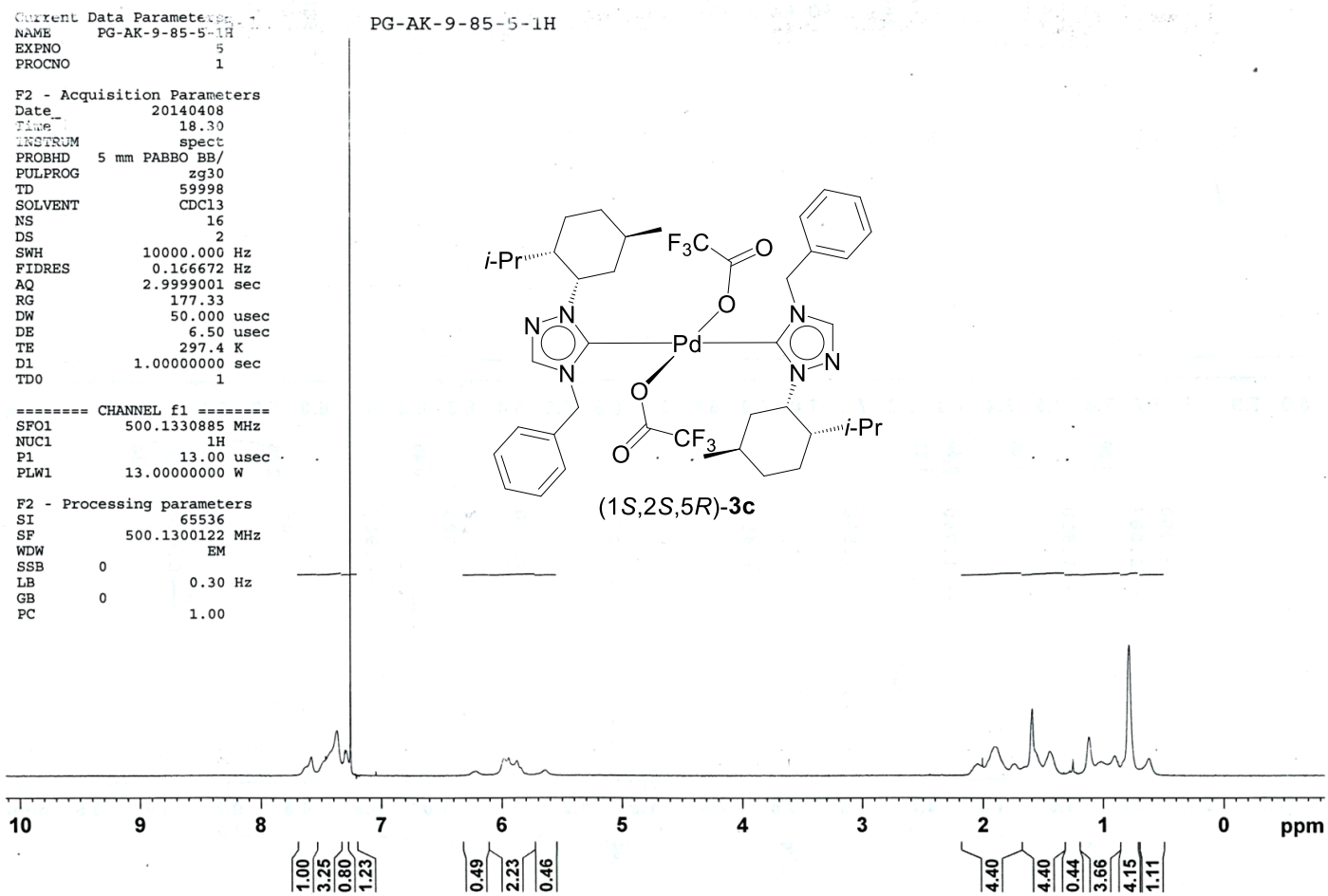


Figure S76.  $^1\text{H}$  NMR spectrum of 1*S*,2*S*,5*R*-**3c** in  $\text{CDCl}_3$ .

PG-AK-9-85-3-13C

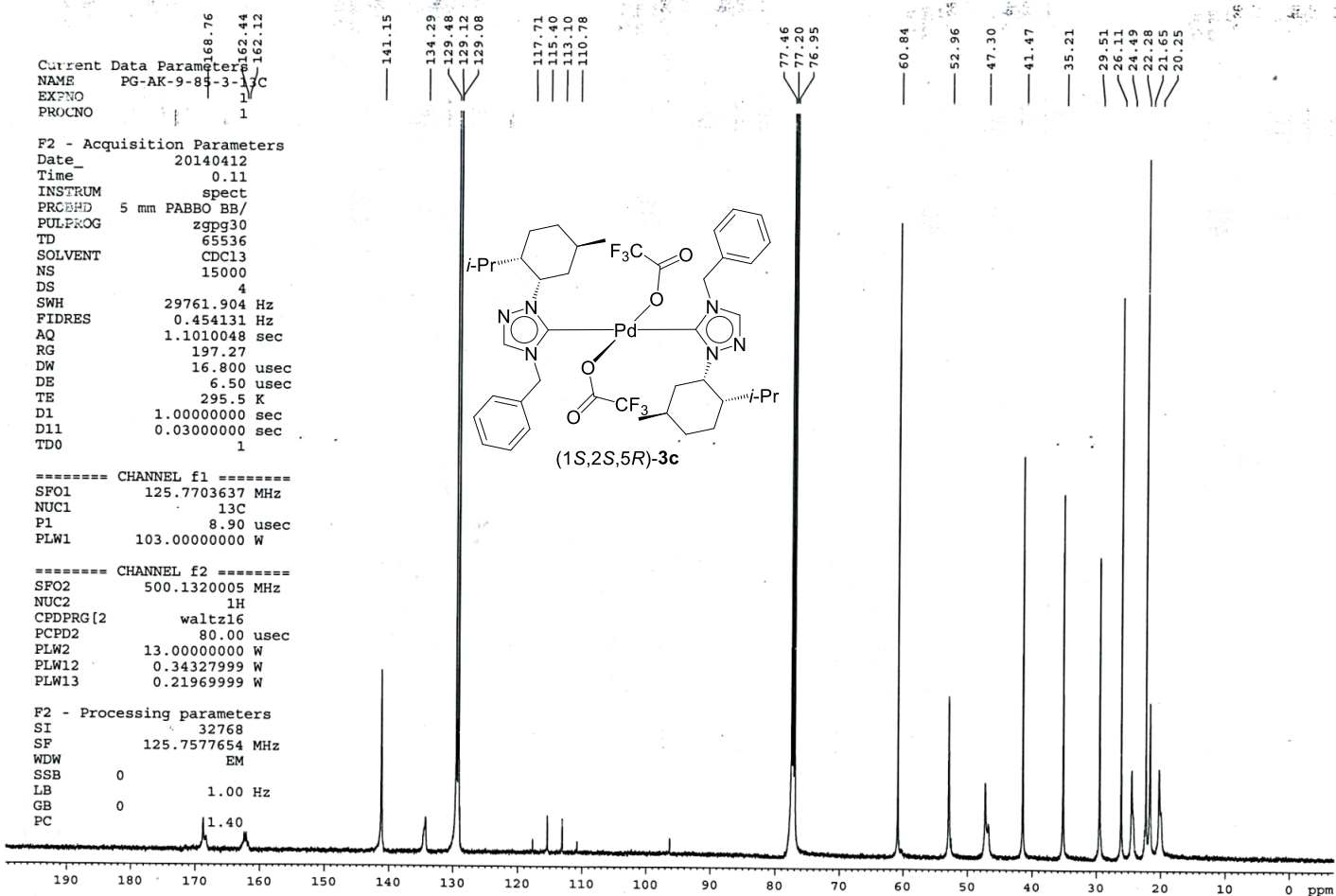


Figure S77.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of 1S,2S,5R-3c in  $\text{CDCl}_3$ .

PG-AK-9-85-5-19F

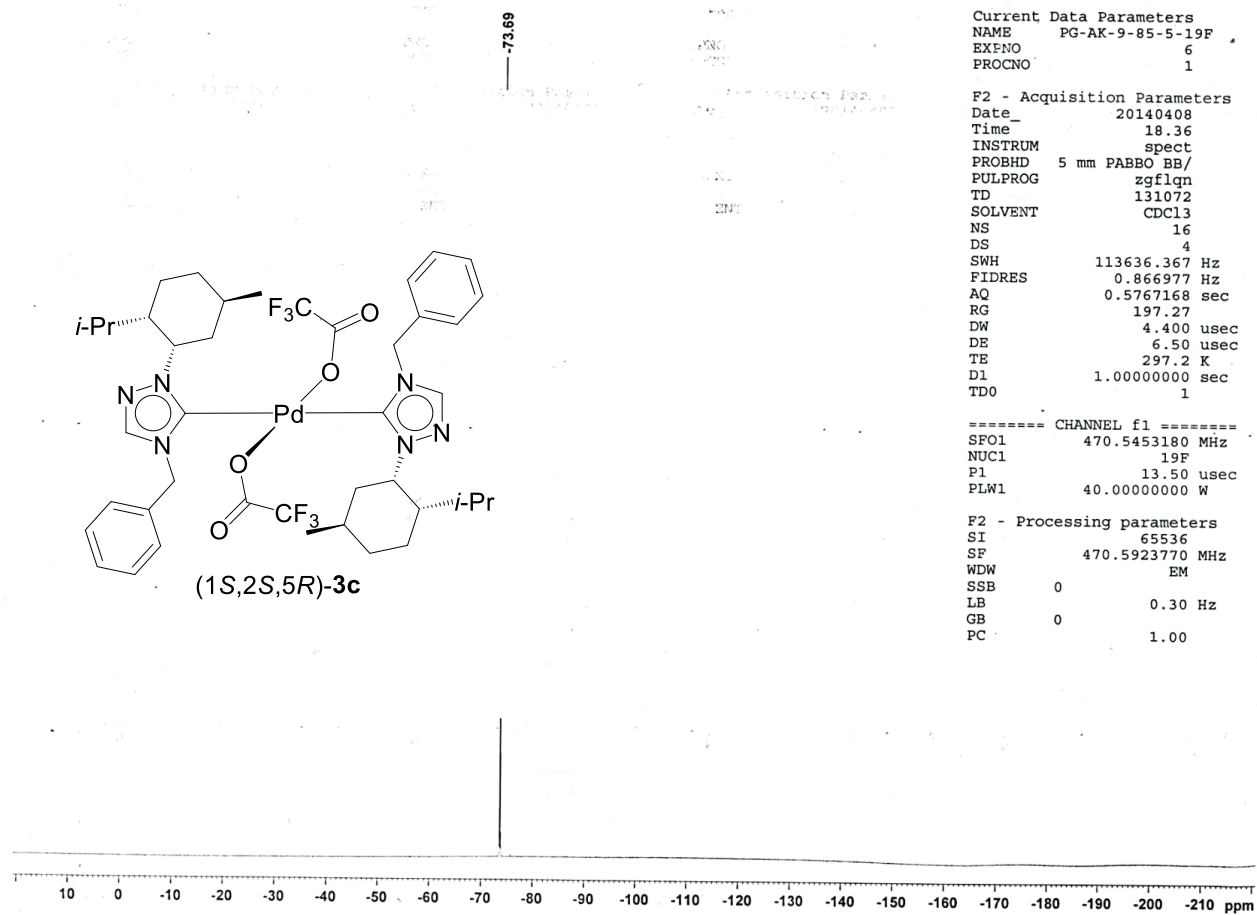
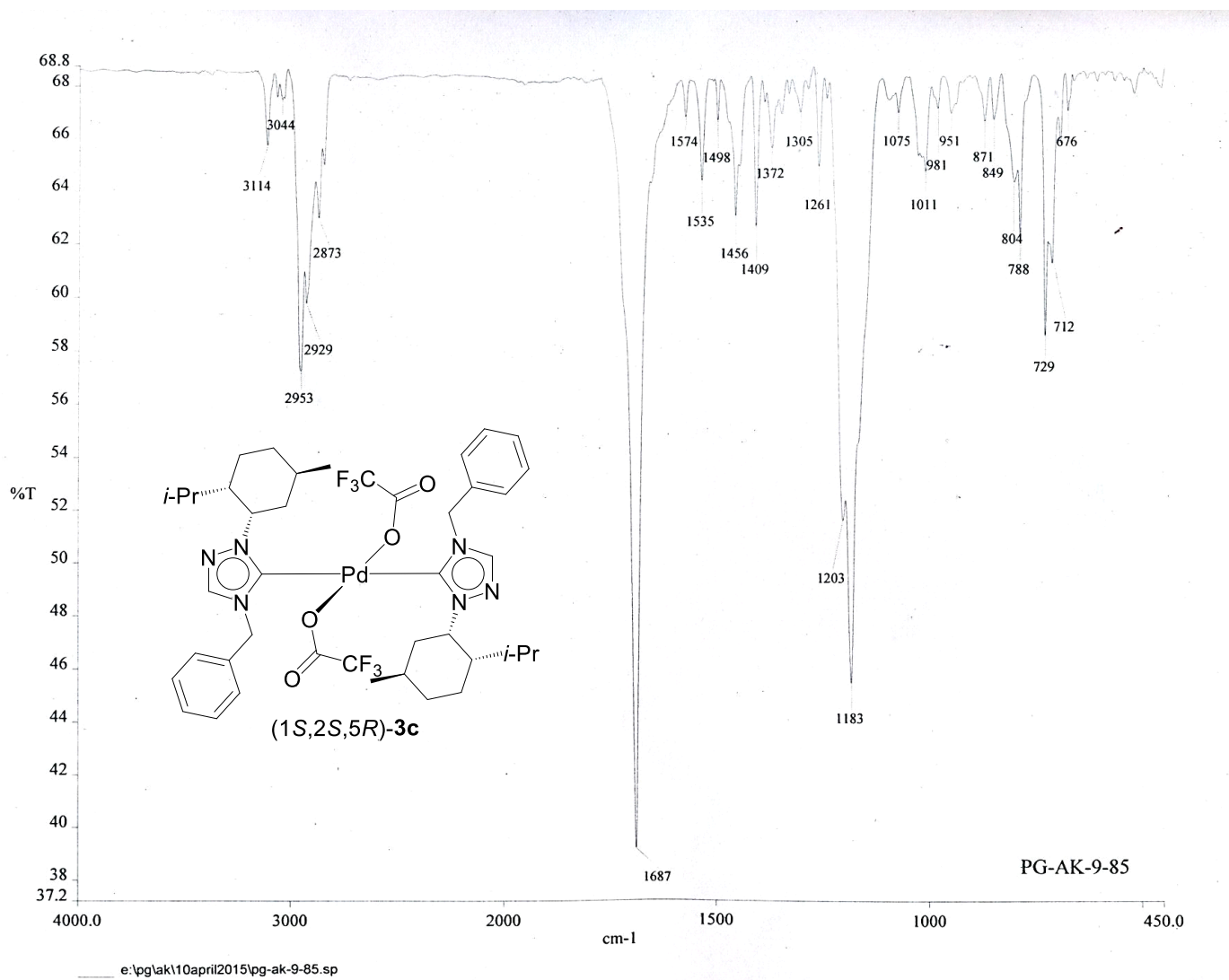


Figure S78.  $^{19}\text{F}\{^1\text{H}\}$  NMR spectrum of 1S,2S,5R-3c in  $\text{CDCl}_3$ .



**Figure S79.** Infrared spectrum of 1*S*,2*S*,5*R*-3c in KBr.



DEPARTMENT OF CHEMISTRY, I.I.T.(B)

**Analysis Info** Acquisition Date 2/29/2016 9:17:02 PM  
 Analysis Name D:\Data\FEB-2016\PG-AK-09-85.d  
 Method Tune\_pos\_NAICSI-1000a.m Operator PG APP IN  
 Sample Name PG-AK-09-85 Instrument maXis impact 282001.00081  
 Comment C42H54N6O4PdF6

**Acquisition Parameter**  
 Source Type ESI Ion Polarity Positive Set Nebulizer 0.3 Bar  
 Focus Active Set Capillary 3700 V Set Dry Heater 180 °C  
 Scan Begin 50 m/z Set End Plate Offset -500 V Set Dry Gas 4.0 l/min  
 Scan End 1000 m/z Set Collision Cell RF 1200.0 Vpp Set Divert Valve Source

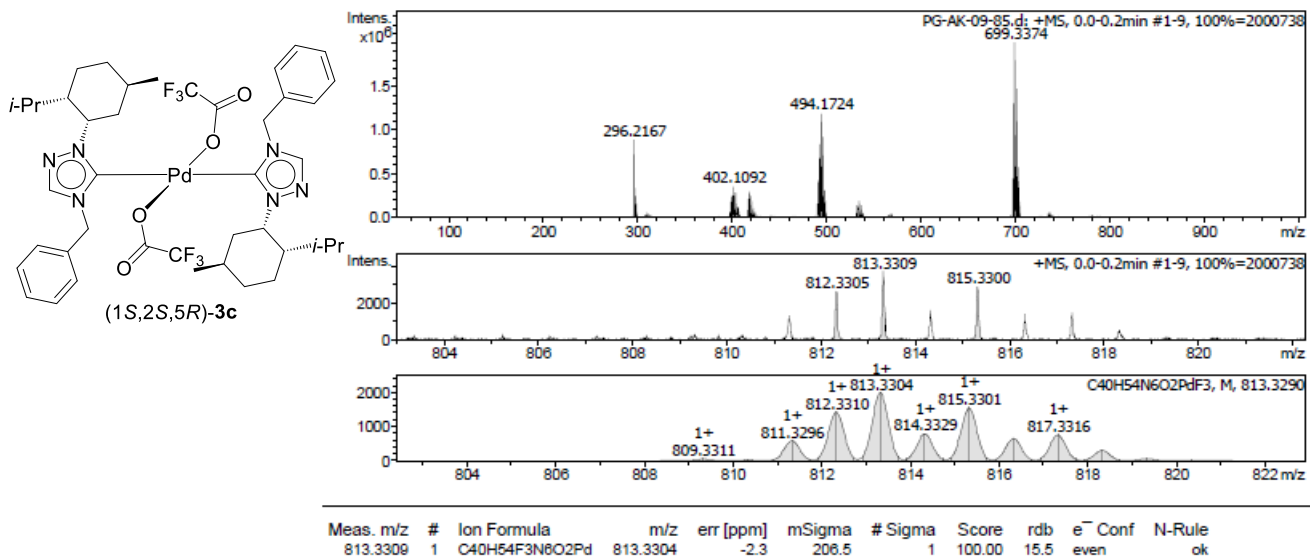
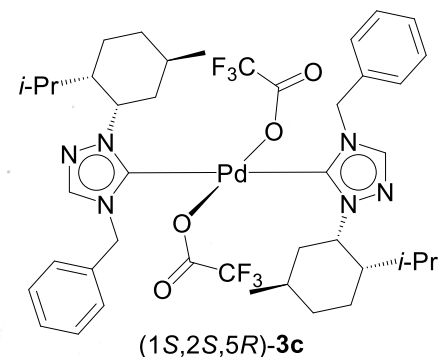


Figure S80. High Resolution Mass Spectrometry (HRMS) data of 1*S*,2*S*,5*R*-3*c*.

## Eager 300 Report

Page: 1    Sample: PG-AK-9-85 (PG-AK-9-85)

Method Name : SP-070414	Company Name : C.E. Instruments
Method File : D:\CHNS-2014\SP-070414.mth	Printed : 4/8/2014 01:06
Chromatogram : PG-AK-9-85	Instrument N. : Instrument #1
Operator ID : MNRAO	Sample weight : .568
Analysed : 04/07/2014 17:54	
Sample ID : PG-AK-9-85 (# 10)	
Analysis Type : UnkNown (Area)	



Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	8.6513	40	76436	FU	10.880470	.155549E+07
Carbon	54.3093	64	831657	FU	1.000000	.269601E+07
Hydrogen	5.5081	175	251404	RS	3.308051	.686517E+07
Totals	68.4687		1159497			

**Figure S81.** Elemental analysis data of 1S,2S,5R-3c.

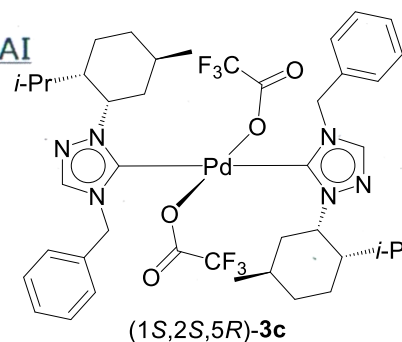
CENTRAL FACILITY LAB CHEMISTRY DEPT. IIT MUMBAI

Monday, 01-DEC-2014

This sample was measured on an Autopol IV, Serial #82083  
 Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0  
 Time Delay : Disabled  
 Temperature Correction : OFF



n	Average	Std.Dev.	Maximum	Minimum
5	40.237	1.2469	40.945	38.017

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Conc.	Temp.
1	pg-ak-9-85	12:04:50	38.017	SR	0.380	589	100.00	1.000	25.1
2	pg-ak-9-85	12:05:08	40.871	SR	0.409	589	100.00	1.000	25.0
3	pg-ak-9-85	12:05:15	40.718	SR	0.407	589	100.00	1.000	25.0
4	pg-ak-9-85	12:05:22	40.945	SR	0.409	589	100.00	1.000	25.0
5	pg-ak-9-85	12:05:29	40.632	SR	0.406	589	100.00	1.000	25.0

Figure S82. Specific rotation of 1S,2S,5R-3c in CHCl<sub>3</sub>.

NAME PG-AK-11-226-1-1  
 EXPNO 6  
 PROCNO 1  
 Date\_ 20151030  
 Time 1.09  
 INSTRUM spect  
 PROBHD 5 mm SEI 1H/D-  
 PULPROG zg30  
 TD 54274  
 SOLVENT CDCl3  
 NS 16  
 DS 0  
 SWH 8223.685 Hz  
 FIDRES 0.151522 Hz  
 AQ 3.2999091 sec  
 RG 71.8  
 DW 60.800 usec  
 DE 6.50 usec  
 TE 294.0 K  
 D1 1.0000000 sec  
 TD0 1

PG-AK-11-226-1-1H

===== CHANNEL f1 =====  
 NUC1 1H  
 P1 14.75 usec  
 PL1 -1.00 dB  
 PL1W 10.56200695 W  
 SFO1 400.1324710 MHz  
 SI 32768  
 SF 400.1300095 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

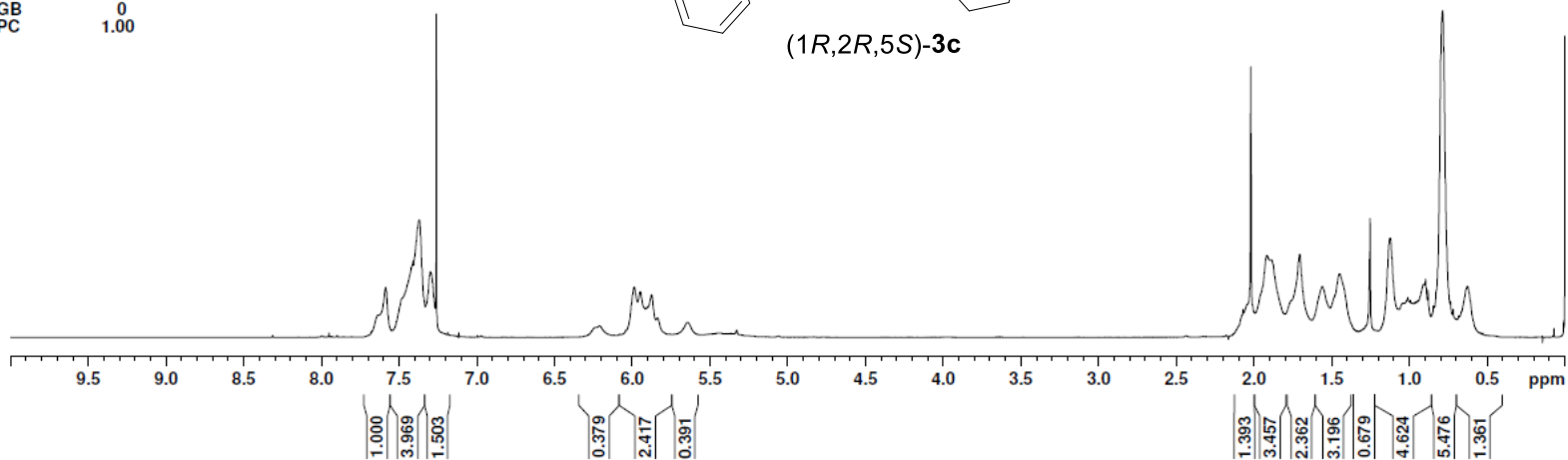
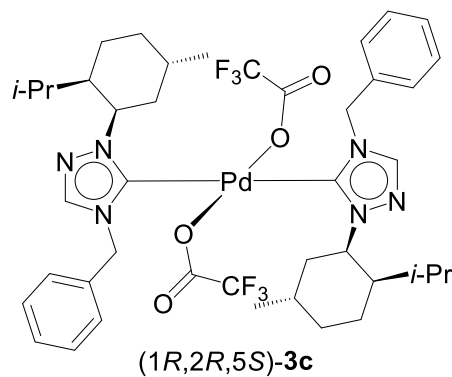


Figure S83.  $^1\text{H}$  NMR spectrum of (1R,2R,5S)-3c in  $\text{CDCl}_3$ .

NAME PG-AK-11-226-1-13C  
 EXPNO 7  
 PROCNO 1  
 Date\_ 20151030  
 Time 1.20  
 INSTRUM spect  
 PROBHD 5 mm SEI 1H/D-  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 12765  
 DS 4  
 SWH 26041.666 Hz  
 FIDRES 0.397364 Hz  
 AQ 1.2583412 sec  
 RG 32  
 DW 19.200 usec  
 DE 6.50 usec  
 TE 295.2 K  
 D1 1.00000000 sec  
 D11 0.03000000 sec  
 TDO 1

PG-AK-11-226-1-13C

----- CHANNEL f1 -----  
 NUC1 13C  
 P1 8.50 usec  
 PL1 -2.00 dB  
 PL1W 56.53121948 W  
 SFO1 100.6238364 MHz  
 ----- CHANNEL f2 -----  
 CPDPRG2 waltz16  
 NUC2 1H  
 PCPD2 80.00 usec  
 PL2 -1.00 dB  
 PL12 13.69 dB  
 PL13 14.50 dB  
 PL2W 10.56200695 W  
 PL12W 0.35871249 W  
 PL13W 0.29767781 W  
 SFO2 400.1316005 MHz  
 SI 32768  
 SF 100.6127495 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

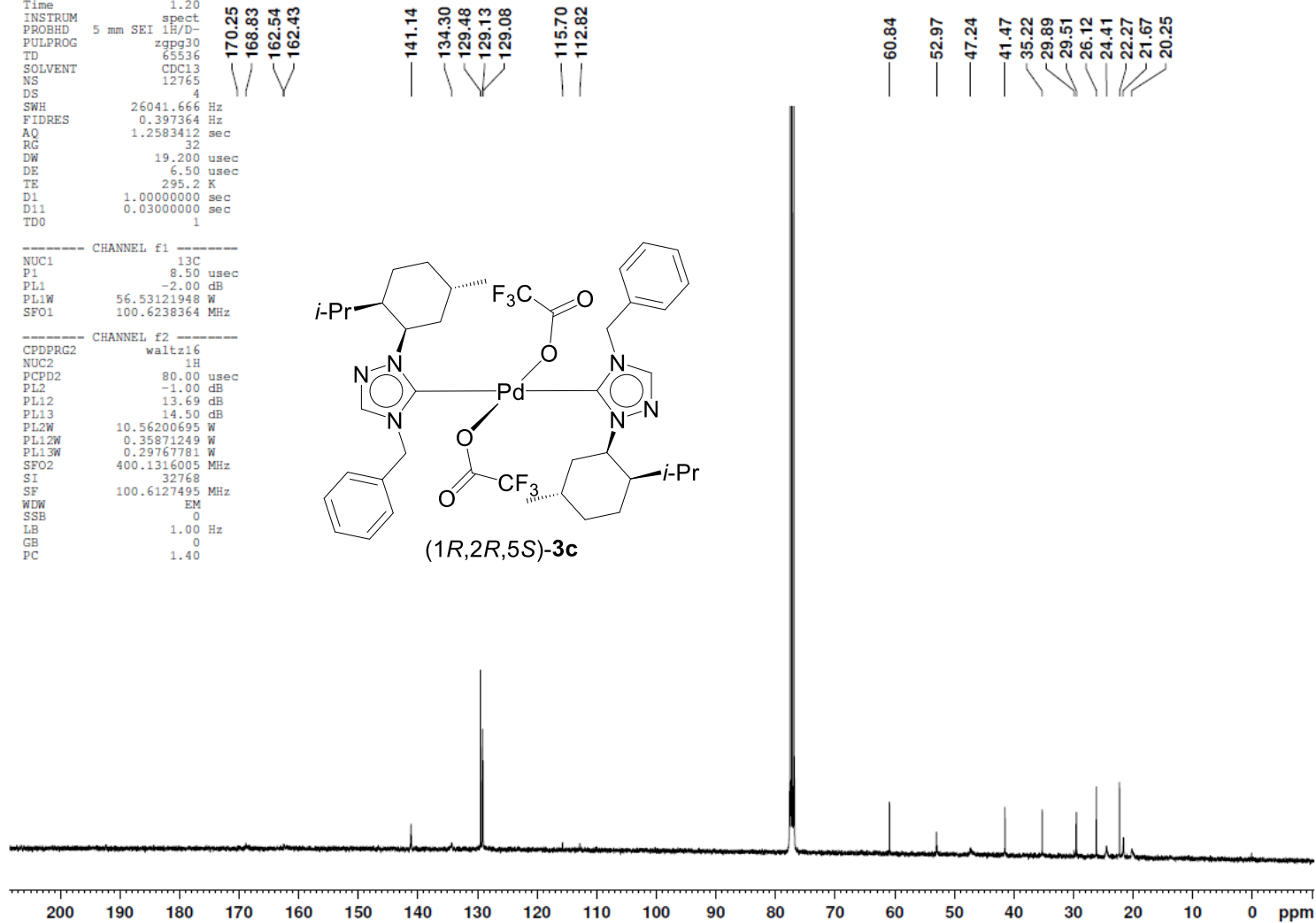
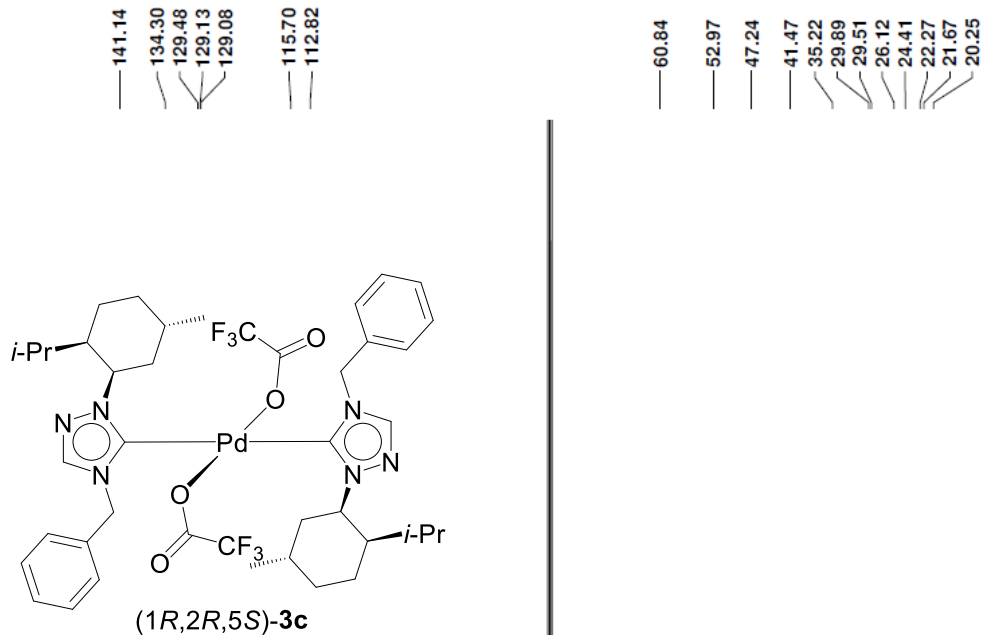


Figure S84.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (1R,2R,5S)-3c in  $\text{CDCl}_3$ .

PG-AK-11-226-1-19F

Current Data Parameters  
NAME PG-AK-11-226-1-19F  
EXPNO 15  
PROCNO 1

F2 - Acquisition Parameters  
Date 20151101  
Time 0.04  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgfg1qn  
TD 131072  
SOLVENT CDCl3  
NS 102  
DS 4  
SWH 113636.367 Hz  
FIDRES 0.866977 Hz  
AQ 0.5767168 sec  
RG 197.27  
DW 4.400 usec  
DE 6.50 usec  
TE 297.6 K  
D1 1.00000000 sec  
TD0 1

----- CHANNEL f1 -----  
SFO1 470.5453180 MHz  
NUC1 19F  
P1 13.50 usec  
PLW1 40.00000000 W

F2 - Processing parameters  
SI 65536  
SF 470.5923770 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

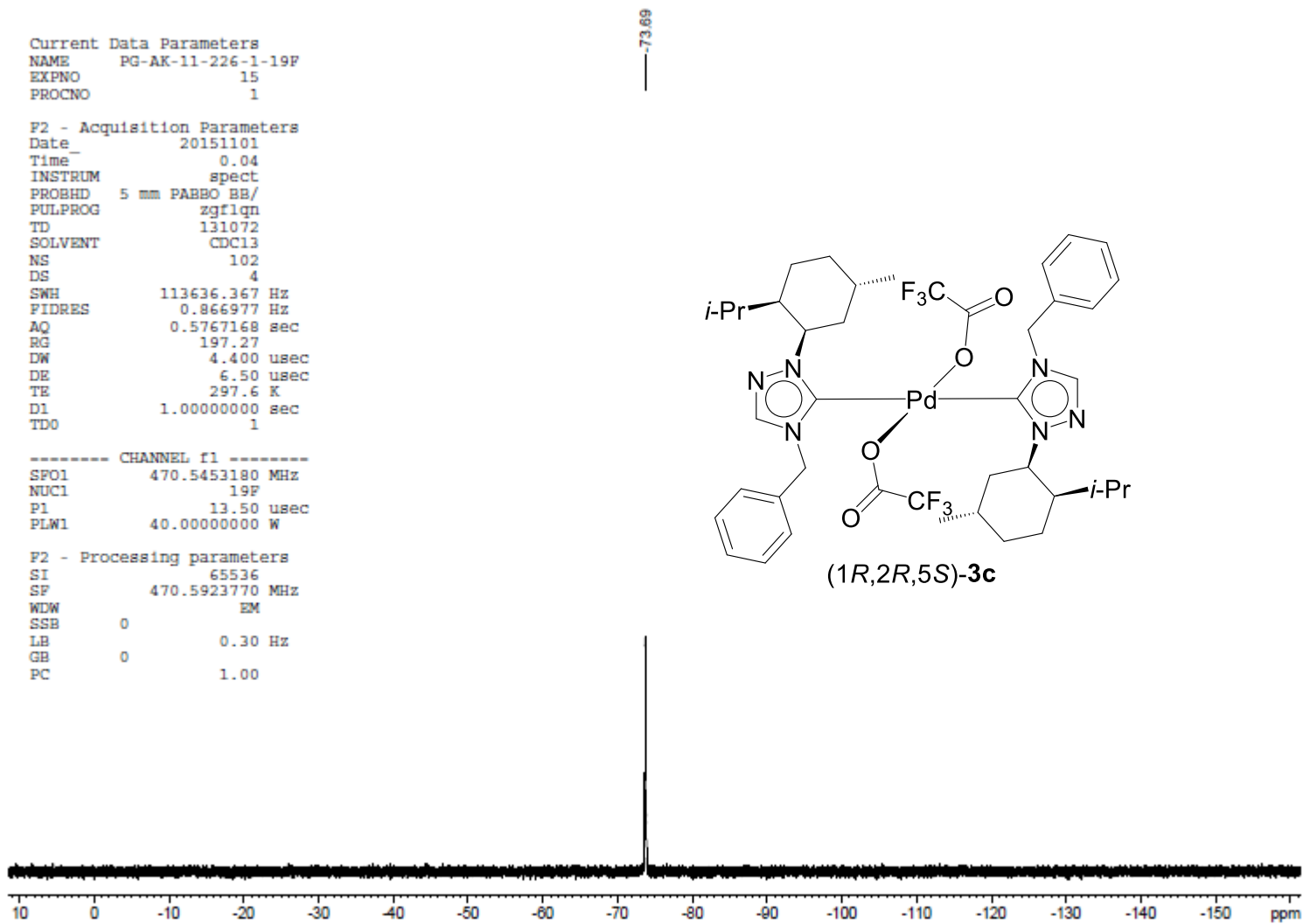
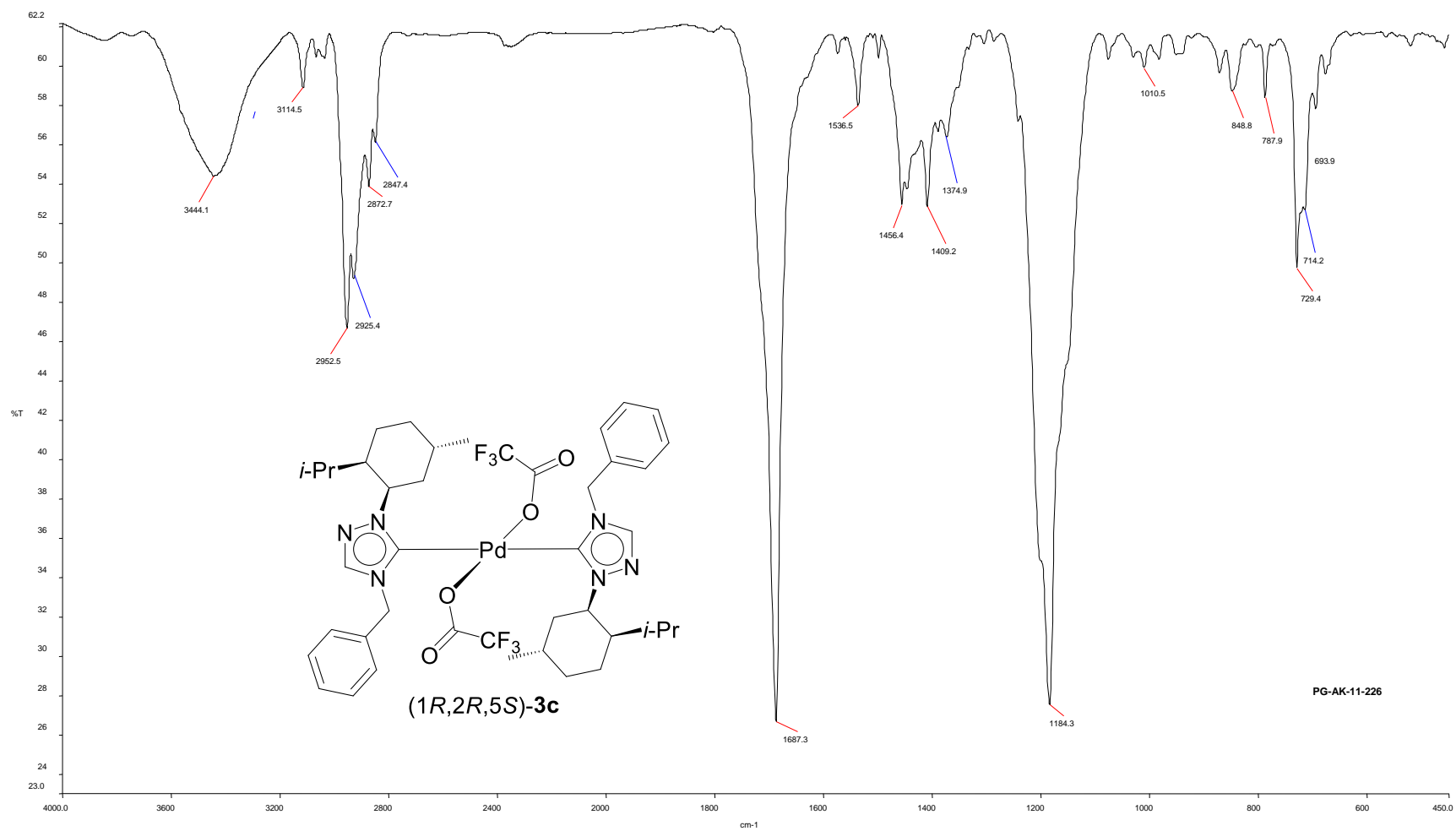


Figure S85.  $^{19}\text{F}\{^1\text{H}\}$  NMR spectrum of (1R,2R,5S)-3c in  $\text{CDCl}_3$ .



**Figure S86.** Infrared spectrum of 1*R*,2*R*,5*S*-3c in KBr.

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**Analysis Info**

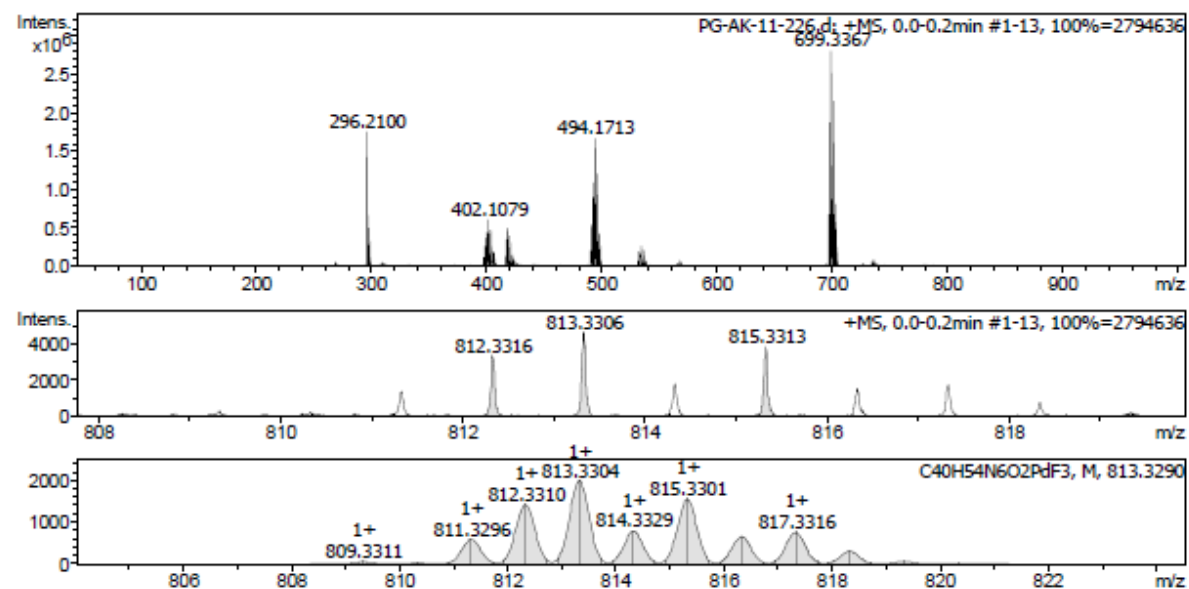
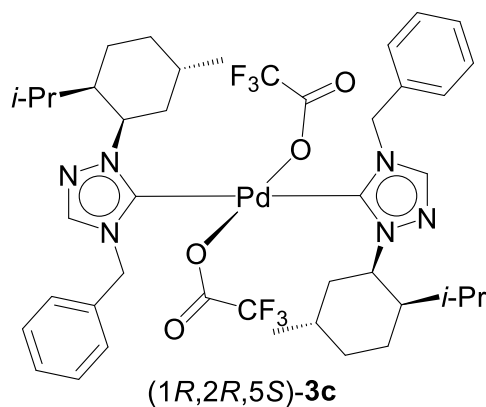
Analysis Name D:\Data\FEB-2016\PG-AK-11-226.d  
 Method Tune\_pos\_NAICSI-1000a.m  
 Sample Name PG-AK-11-226  
 Comment C42H54N6O4PdF6

Acquisition Date 2/29/2016 9:20:17 PM

Operator PG APP IN  
 Instrument maXis impact 282001.00081

**Acquisition Parameter**

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3700 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
813.3306	1	C40H54F3N6O2Pd	813.3304	-2.0	207.4	1	100.00	15.5	even	ok

**Figure S87.** High Resolution Mass Spectrometry (HRMS) data of 1R,2R,5S-3c.



## Eager 300 Report

Page: 1    Sample: PG-AK-11-226-1 (PG-AK-11-226-1)

Method Name : PGCP13102015  
 Method File : D:\CHNS-2015\PGCP13102015.mth  
 Chromatogram : PG-AK-11-226-1  
 Operator ID : CHANDNI  
 Analysed : 10/13/2015 14:29  
 Sample ID : PG-AK-11-226-1 (# 20)  
 Analysis Type : UnkNown (Area)

Company Name : C.E. Instruments  
 Printed : 10/13/2015 18:36  
 Instrument N. : Instrument #1  
 Sample weight : 1.044

Calib. method : using 'K Factors'

!!! Warning missing one or more peaks.

Element Name	%	Ret.Time	Area	BC	Area ratio	K factor
Nitrogen	8.7208	41	98597	RS	14.867610	.108295E+07
Carbon	53.7587	63	1465902	RS	1.000000	.260680E+07
Hydrogen	5.5882	178	402959	RS	3.637844	.665180E+07
Totals	68.0677		1967458			

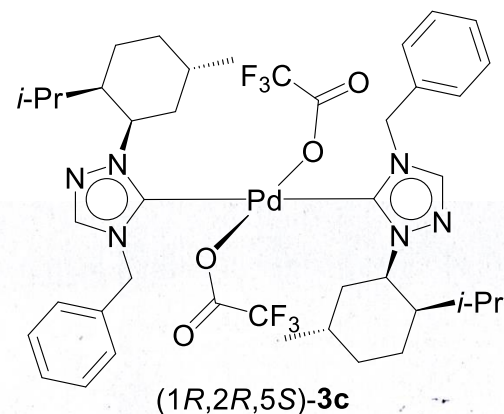


Figure S88. Elemental analysis data of (1R,2R,5S)-3c.

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Tuesday, 27-OCT-2015

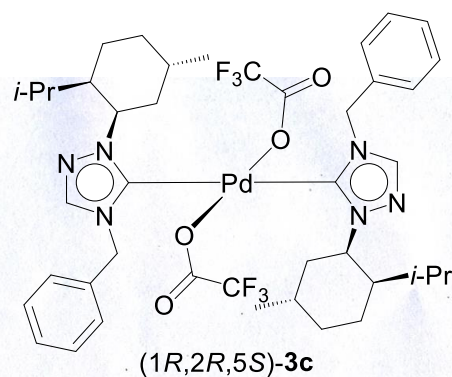
This sample was measured on an Autopol IV, Serial #82083  
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Lot ID : pg

Set Temperature : 25.0

Time Delay : Disabled

Temperature Correction : OFF

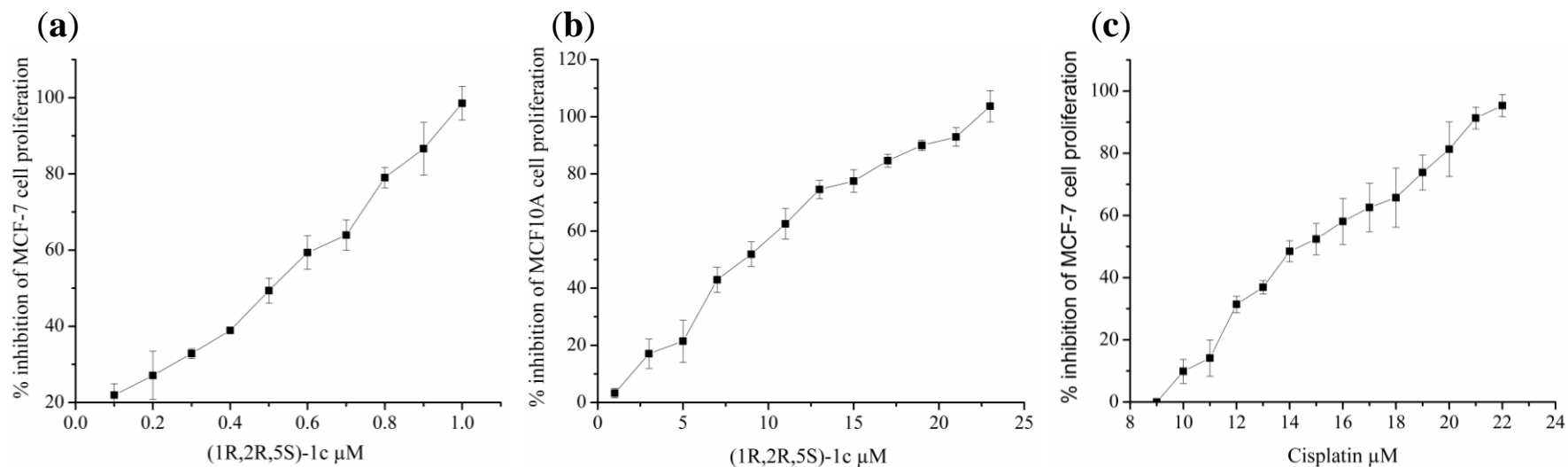


<u>n</u>	<u>Average</u>	<u>Std.Dev.</u>	<u>Maximum</u>	<u>Minimum</u>
5	-44.424	0.0675	-44.303	-44.454

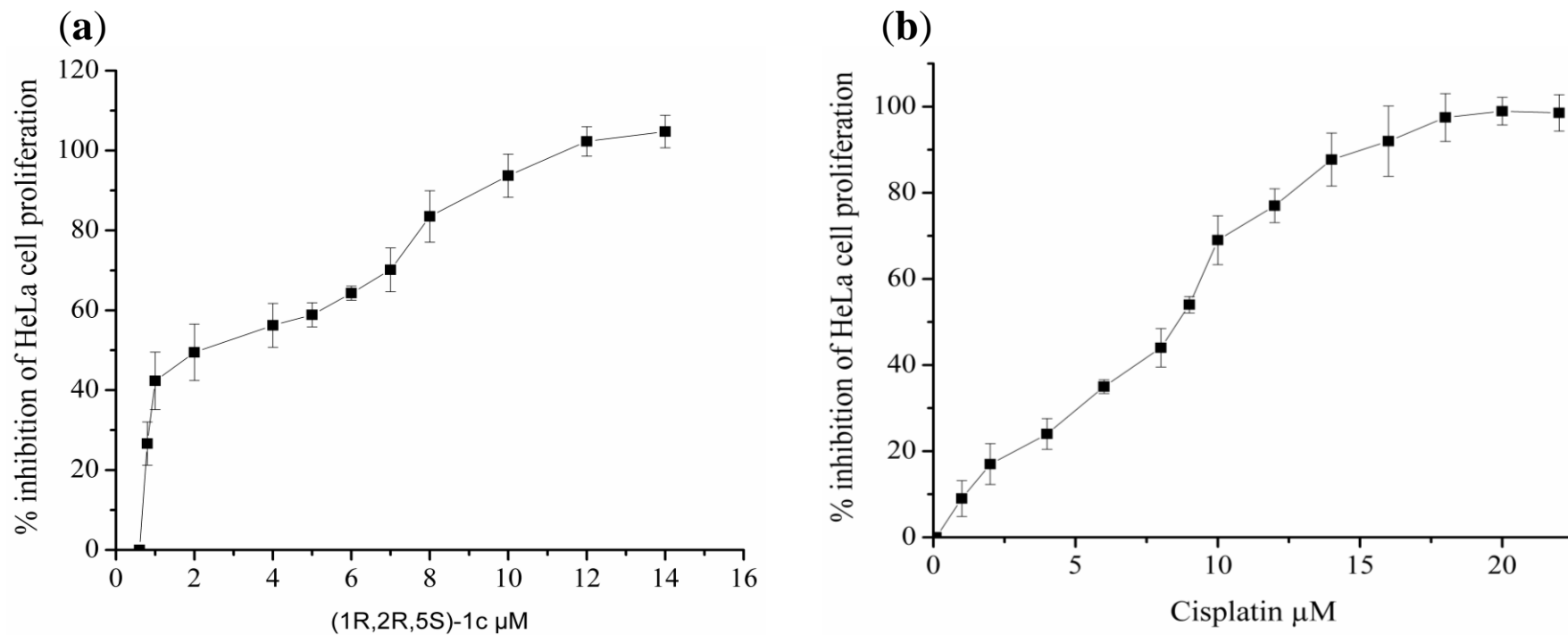
  

<u>S.No</u>	<u>SampleID</u>	<u>Time</u>	<u>Result</u>	<u>Scale</u>	<u>OR °Arc</u>	<u>WLG</u>	<u>Lg.mm</u>	<u>Conc.</u>	<u>Temp.</u>
1	pg-ak-11-226-1	17:12:09	-44.454	SR	-0.222	589	50.00	1.000	24.9
2	pg-ak-11-226-1	17:12:16	-44.454	SR	-0.222	589	50.00	1.000	24.9
3	pg-ak-11-226-1	17:12:23	-44.454	SR	-0.222	589	50.00	1.000	24.9
4	pg-ak-11-226-1	17:12:29	-44.454	SR	-0.222	589	50.00	1.000	24.9
5	pg-ak-11-226-1	17:12:36	-44.303	SR	-0.222	589	50.00	1.000	24.9

Figure S89. Specific rotation of (1R,2R,5S)-3c in CHCl<sub>3</sub>.

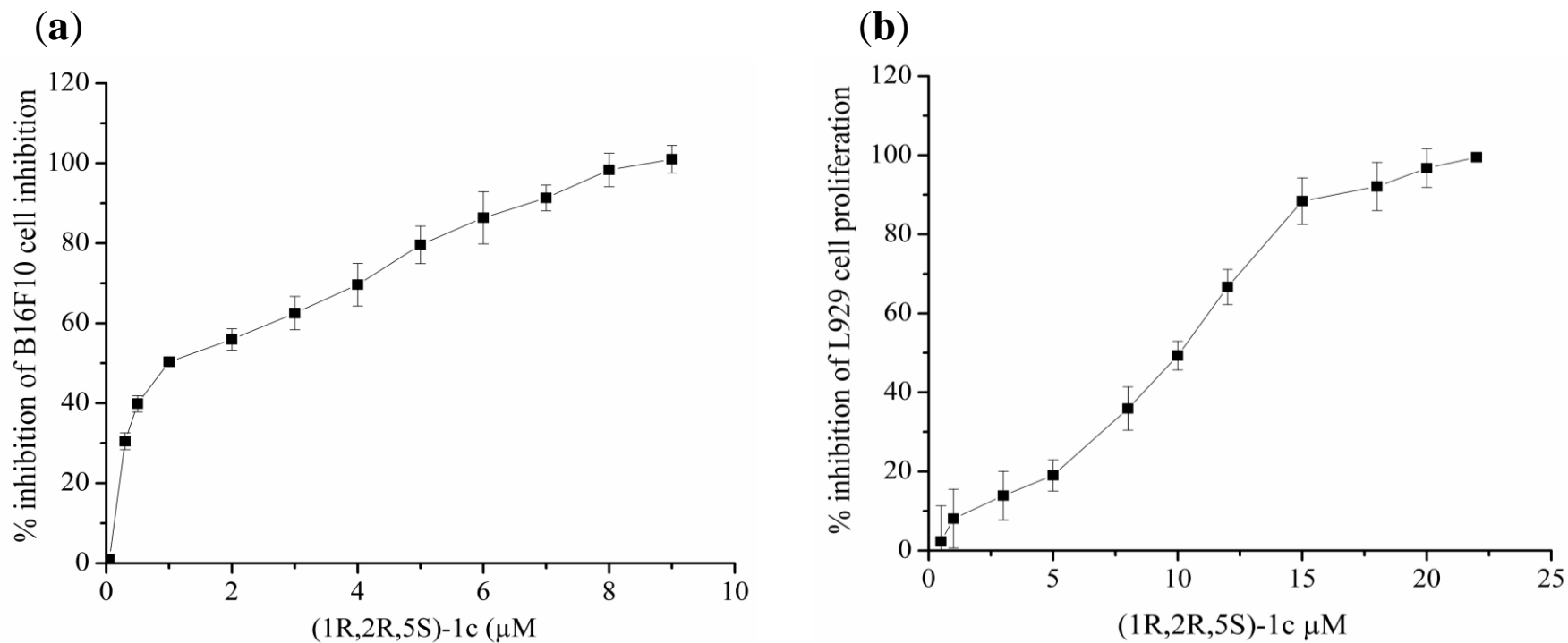


**Figure S90.** Antiproliferative activity of (1R,2R,5S)-1c against (a) MCF-7 and (b) MCF10A. (c) Antiproliferative activity of cisplatin against MCF7 measured using sulforhodamine B assay. The experiment was performed three times and average data was plotted. Error bars indicate standard deviation.



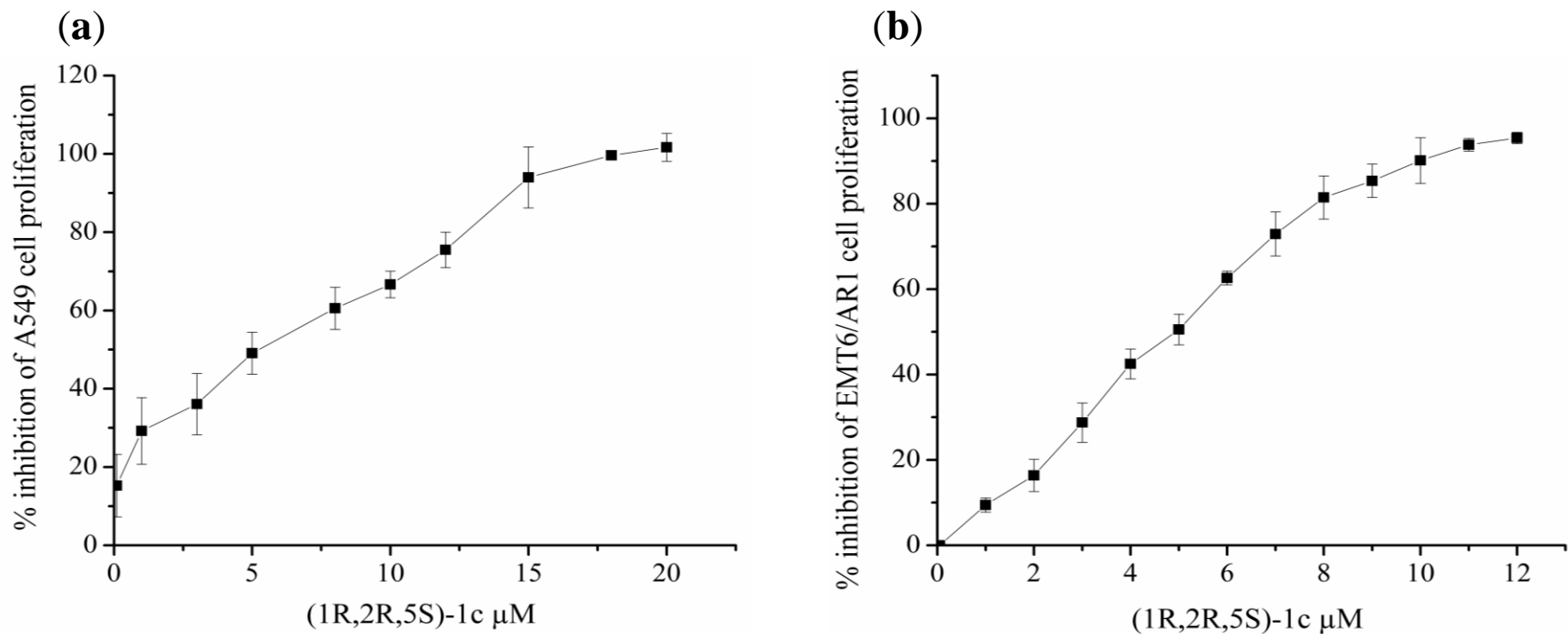
**Figure S91.** Antiproliferative activity of **(a)** (1R,2R,5S)-1c and **(b)** cisplatin against HeLa measured using sulforhodamine B assay.

The experiment was performed three times and average data was plotted. Error bars indicate standard deviation.



**Figure S92.** Antiproliferative activity of (1R,2R,5S)-1c against (a) B16F10 and (b) L929 measured using sulforhodamine B assay.

The experiment was performed three times and average data was plotted. Error bars indicate standard deviation.

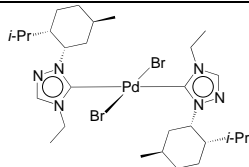
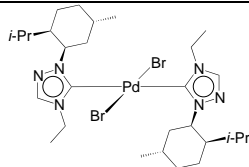
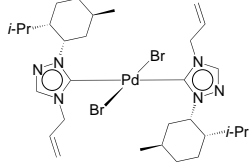
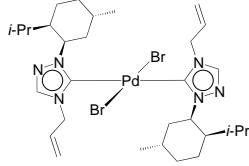
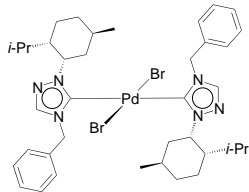
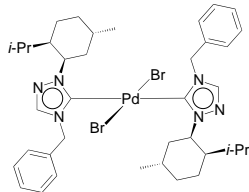
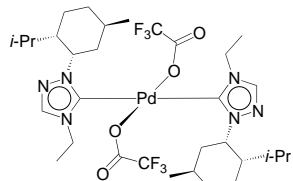
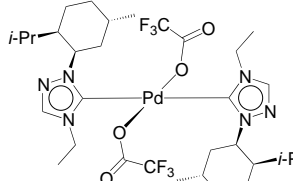
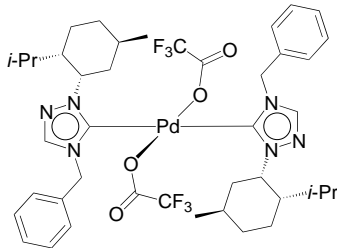
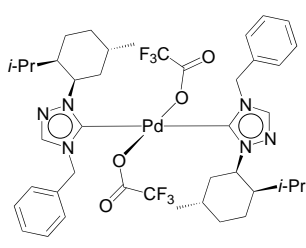


**Figure S93.** Antiproliferative activity of (1R,2R,5S)-1c against (a) A549 and (b) EMT6/AR1 cells measured using sulforhodamine B assay. The experiment was performed three times and average data was plotted. Error bars indicate standard deviation.

**Table S1.** X-ray crystallographic data for (1*R*,2*R*,5*S*)-(1-3)**b**, (1*S*,2*S*,5*R*)-2**b**, (1*S*,2*S*,5*R*)-1**c**, (1*R*,2*R*,5*S*)-1**c**, (1*S*,2*S*,5*R*)-3**c** and (1*R*,2*R*,5*S*)-3**c**.

Compound	(1 <i>R</i> ,2 <i>R</i> ,5 <i>S</i> )-1 <b>b</b>	(1 <i>S</i> ,2 <i>S</i> ,5 <i>R</i> )-2 <b>b</b>	(1 <i>R</i> ,2 <i>R</i> ,5 <i>S</i> )-2 <b>b</b>	(1 <i>R</i> ,2 <i>R</i> ,5 <i>S</i> )-3 <b>b</b>	(1 <i>S</i> ,2 <i>S</i> ,5 <i>R</i> )-1 <b>c</b>	(1 <i>R</i> ,2 <i>R</i> ,5 <i>S</i> )-1 <b>c</b>	(1 <i>S</i> ,2 <i>S</i> ,5 <i>R</i> )-3 <b>c</b>	(1 <i>R</i> ,2 <i>R</i> ,5 <i>S</i> )-3 <b>c</b>
Lattice	Triclinic	Triclinic	Triclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Formula	C <sub>28</sub> H <sub>50</sub> N <sub>6</sub> PdBr <sub>2</sub>	C <sub>30</sub> H <sub>50</sub> N <sub>6</sub> PdBr <sub>2</sub>	C <sub>30</sub> H <sub>50</sub> N <sub>6</sub> PdBr <sub>2</sub>	C <sub>76</sub> H <sub>108</sub> N <sub>12</sub> Pd <sub>2</sub> Br <sub>4</sub>	C <sub>32</sub> H <sub>50</sub> N <sub>6</sub> F <sub>6</sub> PdO <sub>4</sub>	C <sub>96</sub> H <sub>150</sub> N <sub>18</sub> F <sub>18</sub> Pd <sub>3</sub> O <sub>12</sub>	C <sub>42</sub> H <sub>54</sub> N <sub>6</sub> F <sub>6</sub> PdO <sub>4</sub>	C <sub>42</sub> H <sub>54</sub> N <sub>6</sub> F <sub>6</sub> PdO <sub>4</sub>
Formula weight	736.96	760.98	760.97	1722.18	803.18	2409.53	927.31	927.31
Space group	<i>P</i> 1	<i>P</i> 1	<i>P</i> 1	<i>P</i> 1	<i>P</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub>
<i>a</i> /Å	8.095(2)	7.7060(15)	7.715(4)	11.565(3)	10.561(2)	18.899(5)	9.702(3)	9.734(6)
<i>b</i> /Å	14.812(4)	7.8581(16)	7.865(4)	13.039(3)	11.169(2)	11.212(3)	20.111(6)	20.3275(10)
<i>c</i> /Å	15.641(4)	14.256(3)	14.299(7)	13.719(3)	16.133(3)	27.511(7)	11.874(4)	11.937(7)
$\alpha$ /°	66.874(12)	101.44(3)	101.479(8)	98.396(4)	90.00	90.00	90.00	90.00
$\beta$ /°	76.588(14)	95.42(3)	95.384(5)	95.925(4)	92.303(3)	95.294(4)	109.578(3)	109.531(8)
$\gamma$ /°	77.346(14)	90.11(3)	90.079(7)	101.192(3)	90.00	90.00	90.00	90.00
<i>V</i> /Å <sup>3</sup>	1660.4(7)	842.1(3)	846.3(7)	1989.1(8)	1901.4(6)	5805(3)	2182.9(12)	2226.0(19)
<i>Z</i>	2	1	1	1	2	2	2	2
Temperature (K)	150(2)	150(2)	273	150(2)	100(2)	150(2)	100(2)	150(2)
Radiation ( $\lambda$ , Å)	0.71075	0.71073	0.71070	0.71075	0.7107	0.71075	0.7107	0.71070
$\rho$ (calcd.), g cm <sup>-3</sup>	1.474	1.501	1.493	1.438	1.403	1.379	1.411	1.383
$\theta$ max, deg.	25.00	32.4597	29.13	25.00	29.20	25.00	29.14	25.00
No. of data	11225	7372	5340	13098	6953	18768	5437	7729
No. of parameters	683	358	352	859	450	1348	538	538
<i>R</i> <sub>1</sub>	0.0258	0.0373	0.0553	0.0369	0.0397	0.0719	0.0571	0.0763
<i>wR</i> <sub>2</sub>	0.0529	0.0670	0.1204	0.0823	0.0793	0.1488	0.0925	0.1545
GOF	0.892	0.929	1.151	1.086	1.030	1.057	0.857	1.044
Flack	0.007(5)	0.009(6)	0.941(17)	0.015(6)	-0.035(14)	-0.02(2)	-0.03(4)	0.05(4)

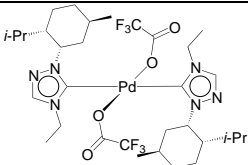
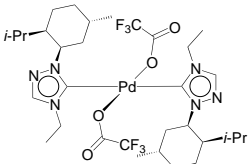
**Table S2.** Anticancer activity of chiral Pd–NHC complexes, *(1S,2S,5R)*-(**1–3**)**b** and *(1R,2R,5S)*-(**1–3**)**b**, *(1S,2S,5R)*-(**1, 3**)**c** and *(1R,2R,5S)*-(**1,3**)**c**, against MCF-7 cells.

S. No.	compound	$[\alpha]_D^{25}$	IC <sub>50</sub> (μM)	compound	$[\alpha]_D^{25}$	IC <sub>50</sub> (μM)
1	 <b>(1S,2S,5R)-1b</b>	– 29.4	2.2 ± 0.1	 <b>(1R,2R,5S)-1b</b>	+ 29.8	2.3 ± 1
2	 <b>(1S,2S,5R)-2b</b>	– 41.7	≈ 10	 <b>(1R,2R,5S)-2b</b>	+ 39.4	≈ 10
3	 <b>(1S,2S,5R)-3b</b>	– 45.2	> 10	 <b>(1R,2R,5S)-3b</b>	+ 45.0	> 10
4	 <b>(1S,2S,5R)-1c</b>	+ 47.8	0.7 ± 0.005	 <b>(1R,2R,5S)-1c</b>	– 48.0	0.55 ± 0.02
5	 <b>(1S,2S,5R)-3c</b>	+ 40.2	>10	 <b>(1R,2R,5S)-3c</b>	– 44.4	> 10

Data are average IC<sub>50</sub> values from three independent set of experiments and ± indicates S.D.

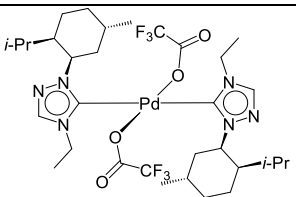


**Table S3.** Anticancer activity of chiral Pd–NHC complexes (*1S,2S,5R*)-**1c** and (*1R,2R,5S*)-**1c**, against MCF-7 and HeLa cells in comparison to cisplatin.

S. No.	compound	MCF-7 IC <sub>50</sub> (μM)	Hela IC <sub>50</sub> (μM)
1	 <b>(1<i>S</i>,2<i>S</i>,5<i>R</i>)-1c</b>	0.7 ± 0.005	2.6 ± 1.6
2	 <b>(1<i>R</i>,2<i>R</i>,5<i>S</i>)-1c</b>	0.55 ± 0.02	2.3 ± 1
3	cisplatin	14.9 ± 0.4	8.5 ± 0.7

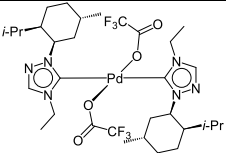
Data are average IC<sub>50</sub> values from three independent set of experiments and ± indicates S.D.

**Table S4.** Anticancer activity of the most potent complex (*1R,2R,5S*)-**1c** against various cancer cell lines.

compound	IC <sub>50</sub> (μM) values				
	MCF-7 (breast cancer)	HeLa (cervical cancer)	A549 (lung cancer)	B16F10 (skin cancer)	EMT6/AR1 (multidrug resistant mammary cancer)
 ( <i>1R,2R,5S</i> )- <b>1c</b>	0.55 ± 0.02	2.3 ± 1	5.7 ± 1.6	1.3 ± 0.4	4.8 ± 0.3

Data are average IC<sub>50</sub> values from three independent set of experiments and ± indicates S.D.

**Table S5.** IC<sub>50</sub> values of complex (*1R,2R,5S*)-**1c** against MCF-7 and B16F10 in comparison to their respective noncancerous counterparts MCF10A and L929.

compound	MCF-7	MCF10A	B16F10	L929
	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)
 <p>(<i>1R,2R,5S</i>)-<b>1c</b></p>	0.55 ± 0.02	8.6 ± 0.9	1.3 ± 0.4	10.5 ± 0.2

Data are average IC<sub>50</sub> values from three independent set of experiments and ± indicates S.D.

