Supporting Information

An Enantio selective Synthesis of ((1*R*,2*R*)-Cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate, a Lurasidone Hydrochloride Intermediate.

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^1H , ^{13}C , Mass, and SOR spectrum

^1H NMR of (1*S*,2*S*)-cyclohexane-1,2-dicarboxylic acid and (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**9** & **10**).

HRMS spectrum of (1S,2S)-cyclohexane-1,2-dicarboxylic acid and (1R,2R)-cyclohexane-1,2-dicarboxylic acid (9 & 10).

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

8 formula(s) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-20 H: 0-14 O: 0-5

C677/CYCL2/t05

141211011 21 (0.399) Cm (21-36.38)

9 & 10

Page 1

1: TOF MS ES+
5.10e+002

Minimum:				-1.5		
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
173.0821	173.0814	0.7	4.0	2.5	7.2	C8 H13 O4

ARDA/CB/RNR/192
R. Nagarajan
11/12/2017

HPLC chromatogram of (1*S*,2*S*)-cyclohexane-1,2-dicarboxylic acid and (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**9 & 10**). (Chemical purity)

```
=====
Acq. Operator   : Umesh                      Seq. Line :    5
Acq. Instrument : CPS1/ARD/HPLC/016          Location  : Vial 1
Injection Date  : 10/21/2013 10:48:55 AM      Inj       :    1
                                           Inj Volume: 10 µl

Acq. Method     : C:\CHEM32\1\METHODS\CYCLCNT3.M
Last changed    : 10/18/2013 4:57:41 PM by Umesh
Analysis Method : C:\CHEM32\1\METHODS\CYCLCNT3.M
Last changed    : 10/21/2013 11:52:22 AM by Praveena
                  (modified after loading)
Method Info     : HPLC conditions:
                  Column: Zorbax SB CN (150*4.6mm)*(3.5µ)
                  M.P-A: 0.1% H3PO4 in H2O M.P-B: ACN
=====
```

Area Percent Report

```
=====
Sorted By       : Signal
Calib. Data Modified : 10/21/2013 11:52:21 AM
Multiplier      : 1.0000
Dilution        : 1.0000
Use Multiplier & Dilution Factor with ISTDs
=====
```

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area %	Name
1	5.639	BB	0.1389	1.21536	0.0109	
2	6.270	BV	0.1521	319.44009	2.8669	
3	6.652	VV	0.1521	8.67218	0.0778	
4	6.980	MF T	0.3128	1.05094e4	94.3208	
5	7.579	FM T	0.1314	240.64565	2.1598	
6	9.551	BV	0.1855	5.01024	0.0450	
7	9.903	VB	0.1673	1.86422	0.0167	
8	12.001	BB	0.1852	4.92142	0.0442	
9	15.215	BB	0.2027	10.78146	0.0968	
10	16.663	BB	0.1665	9.39272e-1	8.430e-3	
11	17.453	MF	0.1991	1.24012	0.0111	
12	17.742	FM	0.3236	16.89157	0.1516	
13	18.942	BB	0.1506	9.32567e-1	8.370e-3	
14	21.921	BB	0.1893	1.89417	0.0170	
15	22.990	BB	0.1541	1.20312	0.0108	
16	26.894	VB	0.0662	8.47458	0.0761	
17	27.190	BV	0.0769	1.36953	0.0123	
18	28.350	BB	0.0700	1.75730	0.0158	
19	28.586	BB	0.0438	5.53660	0.0497	

HPLC chromatogram of (1*S*,2*S*)-cyclohexane-1,2-dicarboxylic acid and (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**9 & 10**). (Chiral purity)

SAMPLE INFORMATION

Sample_Name	: C077/CYCL3/008 BEF RC	Acquired By	: System
Sample_Type	: Unknown	Date Acquired	: 10/22/2013 2:21:08 PM
Injection Volume	: 2	Channel Name	: PDA 210.0 nm
Vial no	: 10.00 ul	Acq Method Set	: CYCLT40
Run Time	: 40.00 Minutes	Date Processed	: 10/23/2013 7:03:11 AM
System Name	: HPLC_005_PDA_UV	Project Name	: Alliance_005_OCT_2013
Sample Set Name	: 13102202	Processing Method	: 1
Injection #	: 1		

HPLC CONDITIONS

Column : Chiralpak IC (250*4.6)mm5μ
 Mobile_phase : n-hexane:IPA: TFA (950:50:1)
 Diluent : Methanol:mp(1:1);
 Flow rate : 1.0 mL/min, Column temp: 25 °C, Inj vol:10μl
 Wavelength : 210nm

Auto-Scaled Chromatogram

Peak Results

	Name	RT	Area	% Area	RT Ratio
1		14.934	129846	3.47	
2		16.065	1511146	40.35	
3		20.269	2104224	56.18	

Analysis/Unit/14
 28/10/13

¹HNMR of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

NMR-400MHz
AR.No:ME1013/2602
Analyst: Haribabu
Date:25th Oct.2013

NUCLEUS : H1
FRQ (MHz): 400.22
EXP : s2pul

NMR-400MHz
AR.No:ME1013/2602
Analyst: Haribabu
Date:25th Oct.2013

NUCLEUS : H1
FRQ (MHz): 400.22
EXP : s2pul

^{13}C NMR of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

NAME-400MHz
AN.No: ME1214/1074
Analyst: Narresh B
Date: 10th Dec 2014

NUCLEUS : $\text{C}13$
FREQ (MHz): 100.62
EXP : s2pul

Chemical HPLC chromatogram of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

SAMPLE INFORMATION			
Sample Name:	C077/CYCL4/024	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	13111501
Vial:	69	Acq. Method Set:	CYCL5 RID
Injection #:	1	Processing Method:	1
Injection Volume:	10.00 ul	Channel Name:	410
Run Time:	35.0 Minutes	Proc. Chnl. Descr.:	
Date Acquired:	11/15/2013 2:03:16 PM IST		
Date Processed:	11/18/2013 10:00:31 AM IST		

Column: Zorbax XDB-C8(250*4.6)mm, 3.5.µm
Column temp: 40°C, RID: Sensitivity: 65,
RID temp: 35°C, Run time: 40 min, Flow : 0.8 ml/min

Peak Results

	Name	RT	Area	% Area	RT Ratio
1		3.014	17384	0.17	
2		4.831	10423543	99.83	

Chiral HPLC chromatogram of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

HRMS spectrum of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

Mass spectrum of (1*R*,2*R*)-cyclohexane-1,2-dicarboxylic acid (**10**):

^1H NMR of ((1*R*,2*R*)-cyclohexane-1,2-diyl)dimethanol (**2**):

^{13}C NMR of ((1*R*,2*R*)-cyclohexane-1,2-diyl)dimethanol (**2**):

Chiral HPLC chromatogram of ((1*R*,2*R*)-cyclohexane-1,2-diyl)dimethanol (**2**):

SAMPLE INFORMATION			
Sample Name:	C077/CYCL4/023	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	13111501
Vial:	71	Acq. Method Set:	CYCL5 RID
Injection #:	1	Processing Method:	1
Injection Volume:	10.00 ul	Channel Name:	410
Run Time:	35.0 Minutes	Proc. Chnl. Descr.:	
Date Acquired:	11/15/2013 3:14:55 PM IST		
Date Processed:	11/18/2013 10:01:33 AM IST		

Column: Zorbax XDB-C8(250*4.6)mm, 3.5.µm
Column temp: 40°C, RID: Sensitivity: 65,
RID temp: 35°C, Run time: 40 min, Flow : 0.8 ml/min

Auto-Scaled Chromatogram

Peak Results

	Name	RT	Area	% Area	RT Ratio
1		4.799	26024	0.67	
2		5.182	3877045	99.28	
3		6.884	1188	0.03	
4		7.297	786	0.02	

Am130210m11/26
Umm9

HRMS spectrum of ((1*R*,2*R*)-cyclohexane-1,2-diyl)dimethanol (**2**):

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

5 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-10 H: 0-18 O: 0-3

C077/CYCL4/032

141211014 27 (0.501) Cm (25:27-61:70)

Mass spectrum of ((1*R*,2*R*)-cyclohexane-1,2-diyl)dimethanol (**2**):

141211014 27 (0.501) Cm (25:27-61:70)

¹HNMR of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):

^{13}C NMR of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):

NAME-400MHz
AR. No: ME1214/1207
Analyst: Nareesh B
Date: 11th Dec 2014

NUCLEUS : C13
FRQ (MHz): 100.65
EXP : s2pul

SOR data of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):

[Data Information]

Creation Date 11/14/2013 12:43 PM

[Measurement Information]

Instrument Name Polarimeter
Model Name P-2000
Serial No. A035861232
Polarizer Glan-Taylor Prism
Faraday Cell Flint Glass

Accessory PTC-203
Accessory S/N A014261234
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 Holder
Temp. Corr. Factor None
Aperture(S) 8.0mm
Aperture(L) Auto
Mode Specific O.R.
Path Length 100 mm
Concentration 4.048 w/v
Factor 1

	No.	Sample No.	Calc. Data	Meas. Data	PMT Voltage[V]	Temperature(C)
1	*	1 C077-CYCL5-029-1	-27.4629	-1.1117	239	19.97
2	*	2 C077-CYCL5-029-2	-27.5099	-1.1136	234	19.96
3	*	3 C077-CYCL5-029-3	-27.4926	-1.1129	238	19.97
4	*	4 C077-CYCL5-029-4	-27.5247	-1.1142	238	19.98
5	*	5 C077-CYCL5-029-5	-27.4876	-1.1127	239	19.98
6	*	6 Avg.	-27.4956			
7		7 S.D	0.0234			
8		8 C.V	0.0851			

Chiral HPLC chromatogram of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):

ata file : C:\CHEM32\2\DATA\K1718208\CYCL000011.D
 mple info:

1

Injection Date : 18/ Nov/2013 09:42:23 pm Seq Line : 2
 mple Name : C077/CYCL5/029 Vial No. : 82
 q Operator : Umesh Inj. No. : 1
 Inj. Vol. : 10.000µl

q. Method : C:\CHEM32\1\METHODS\LURACHIRAL.M

alysis Method : HPLC conditions:

Column:Chiral PAK IC (250 X 4.6 mm) 5.0.µm

M.Phase: N-HEXANE:IPA:ETOH:DEA(650:200:150:5)

Column temp : 27°C flow-1.0mL/min , Inj 10µl

Compound Name	RT	RelRT	Area	Area%	Symmetry	Plates	Resolution
1 Undesired	23.005	0.94	4319.037	0.282	1.127	752997.24	
2 desdired	24.566	1.00	1527029.125	99.718	0.000	6199.08	2.302

reference no. :

analysed by/ Date :

Checked by/ Date :

*** End of Report ***

Chemical HPLC chromatogram of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (3):

SAMPLE INFORMATION			
Sample Name:	C077/CYCL5/029	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	13111501
Vial:	66	Acq. Method Set:	CYCL5 RID
Injection #:	1	Processing Method:	1
Injection Volume:	10.00 ul	Channel Name:	410
Run Time:	35.0 Minutes	Proc. Chnl. Descr.:	
Date Acquired:	11/15/2013 12:15:21 PM IST		
Date Processed:	11/18/2013 9:58:27 AM IST		

Column: Zorbax XDB-C8(250*4.6)mm, 3.5.µm
 Column temp: 40°C, RID: Sensitivity: 65,
 RID temp: 35°C, Run time: 40 min, Flow: 0.8 ml/min

Peak Results

	Name	RT	Area	% Area	RT Ratio
1		3.321	11103	0.10	
2		4.527	9600	0.08	
3		6.045	4676	0.04	
4		7.717	14759	0.13	
5		10.697	9587	0.08	
6		16.898	54042	0.47	
7		18.041	11480370	99.10	

ANN 302106/136
CW9
18/11/2013

HRMS spectrum of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

35 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-12 H: 0-23 O: 0-7 S: 0-3

C077/CYCL5/029

141211012 22 (0.413) Cm (22:23-61:64)

Minimum:					-1.5	
Maximum:		5.0	5.0		50.0	
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
301.0778	301.0780	-0.2	-0.7	0.5	16.6	C10 H21 O6 S2

Mass spectrum of ((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(methylene) dimethanesulfonate (**3**):