

Supplementary Information

Ireland-Claisen Rearrangement Strategy towards the Synthesis of Schizophrenia Drug, (+) Asenapine

Raghunath Reddy Anugu,^{a,c} Prathama S. Mainkar,^a Balasubramanian Sridhar^b and
Srivari Chandrasekhar^{*a,c}

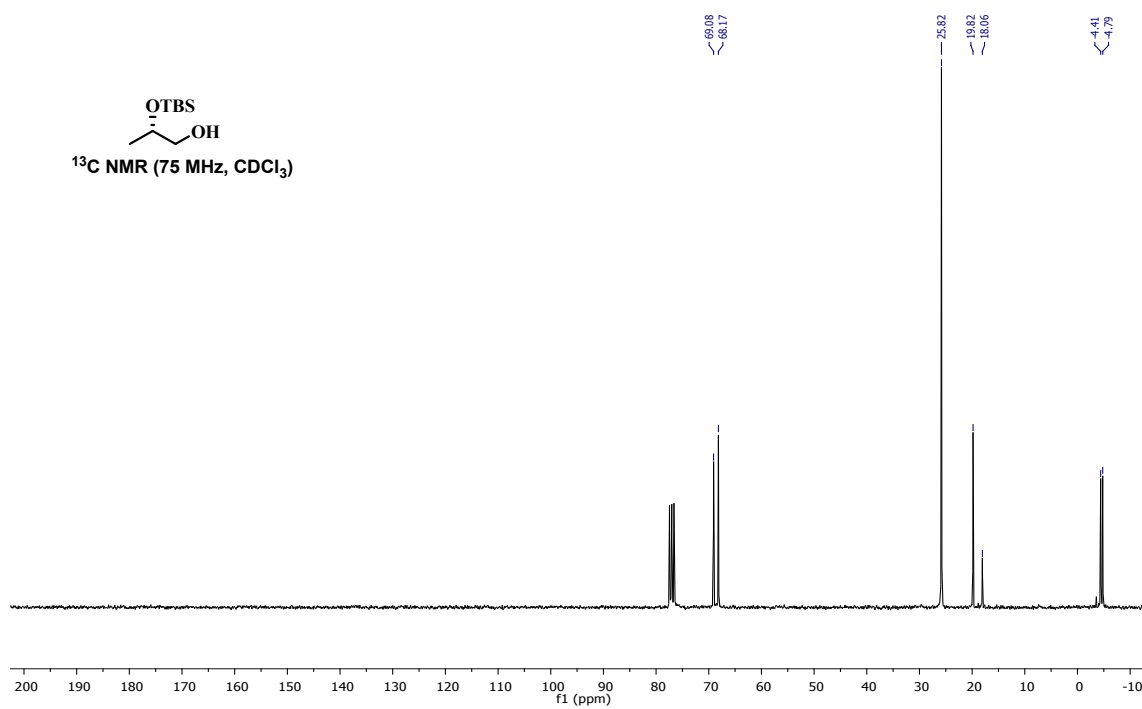
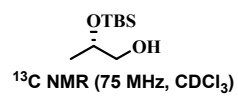
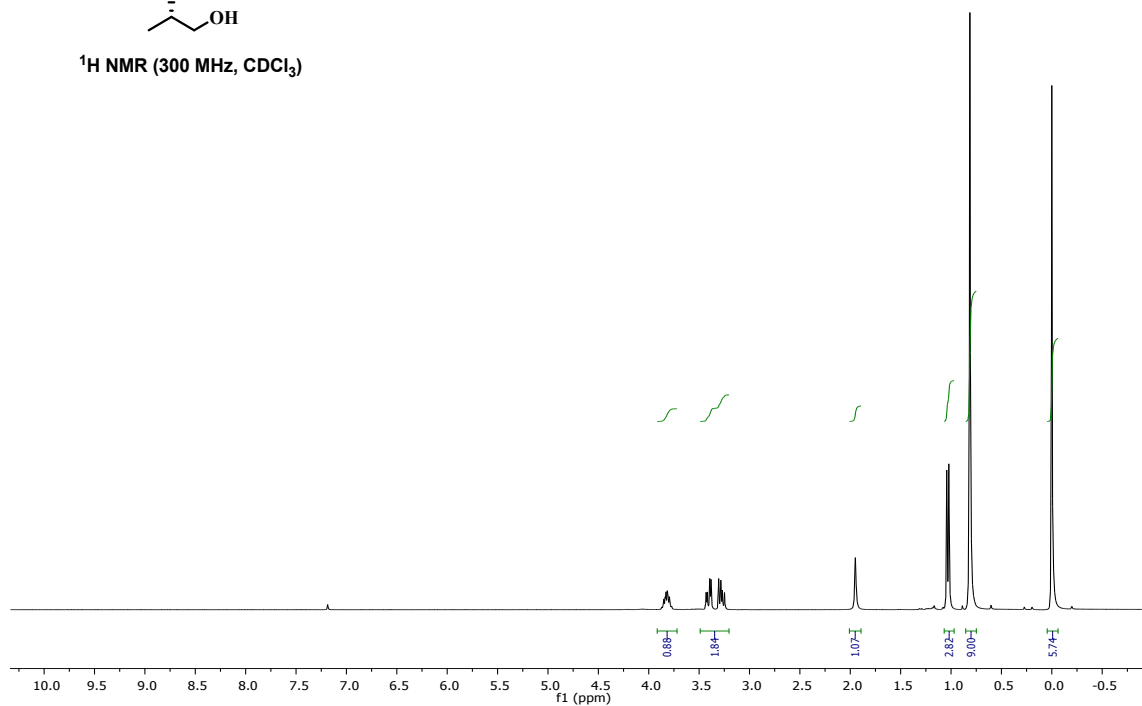
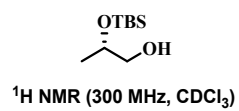
^aDivision of Natural Products Chemistry, ^bLaboratory of X-ray Crystallography,
CSIR-Indian Institute of Chemical Technology, Hyderabad, India 500 007

^cAcademy of Scientific and Innovative Research, New Delhi-110025, India

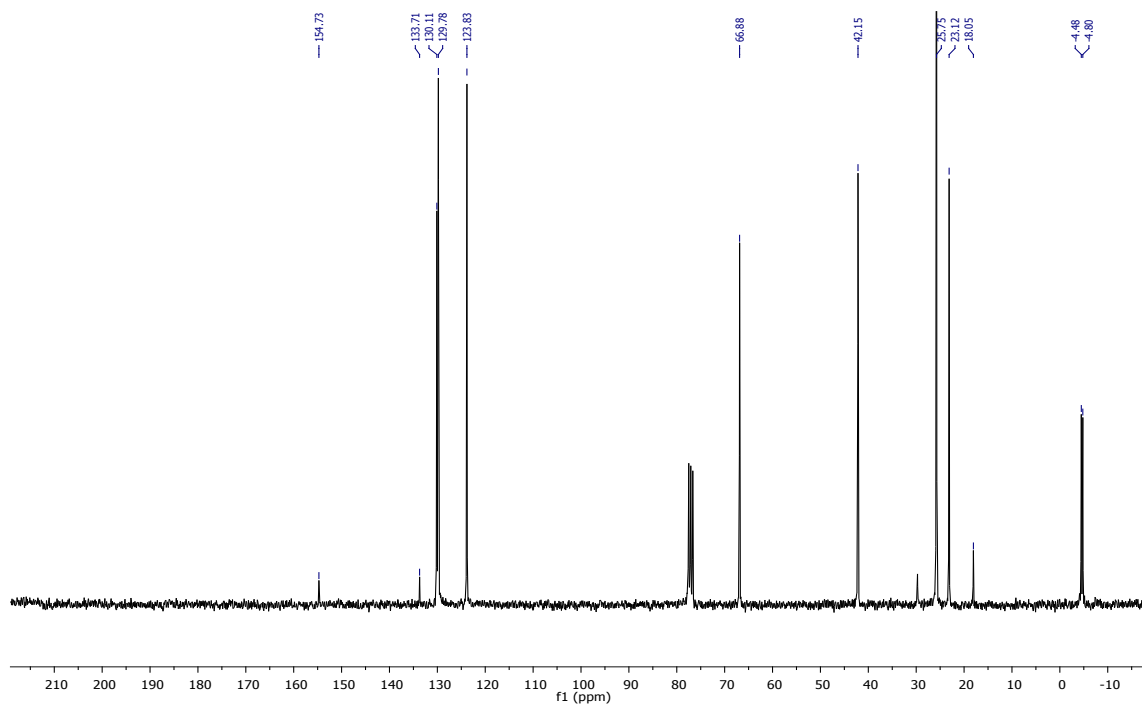
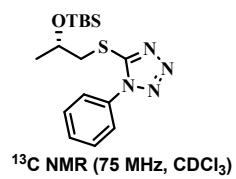
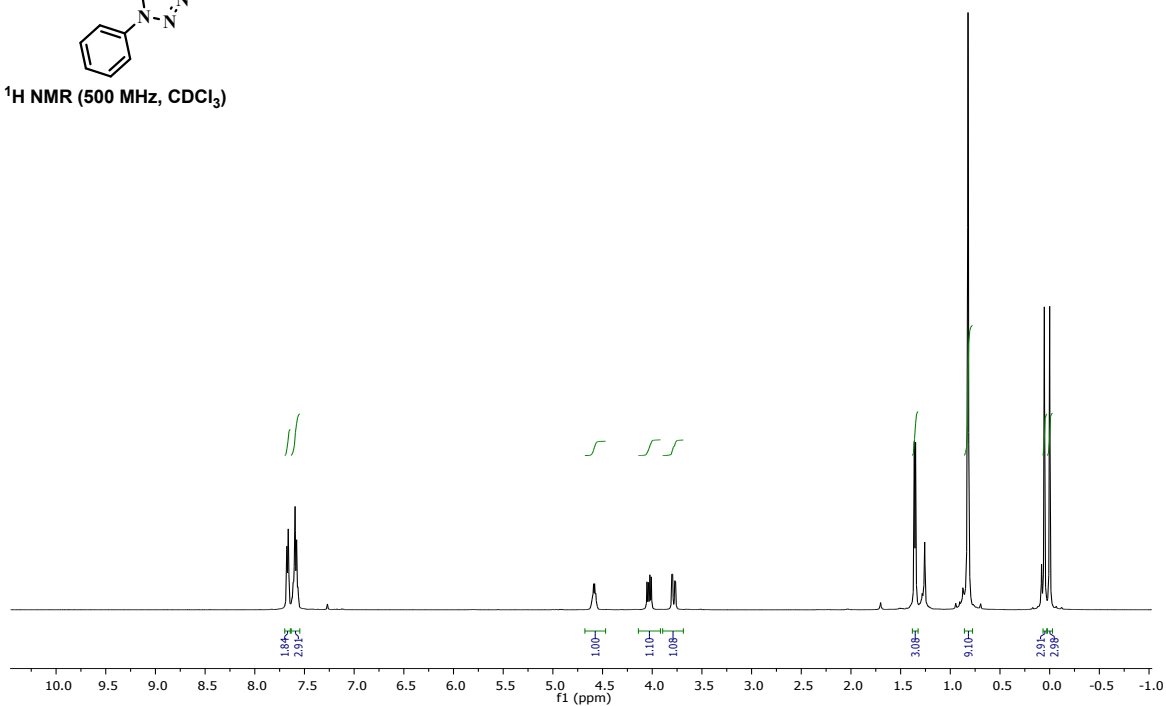
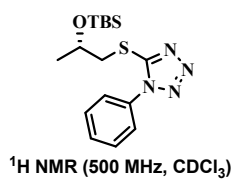
E-mail: srivari@iict.res.in

	Page
1. ¹ H NMR, ¹³ C NMR spectra	S-2 to S-17

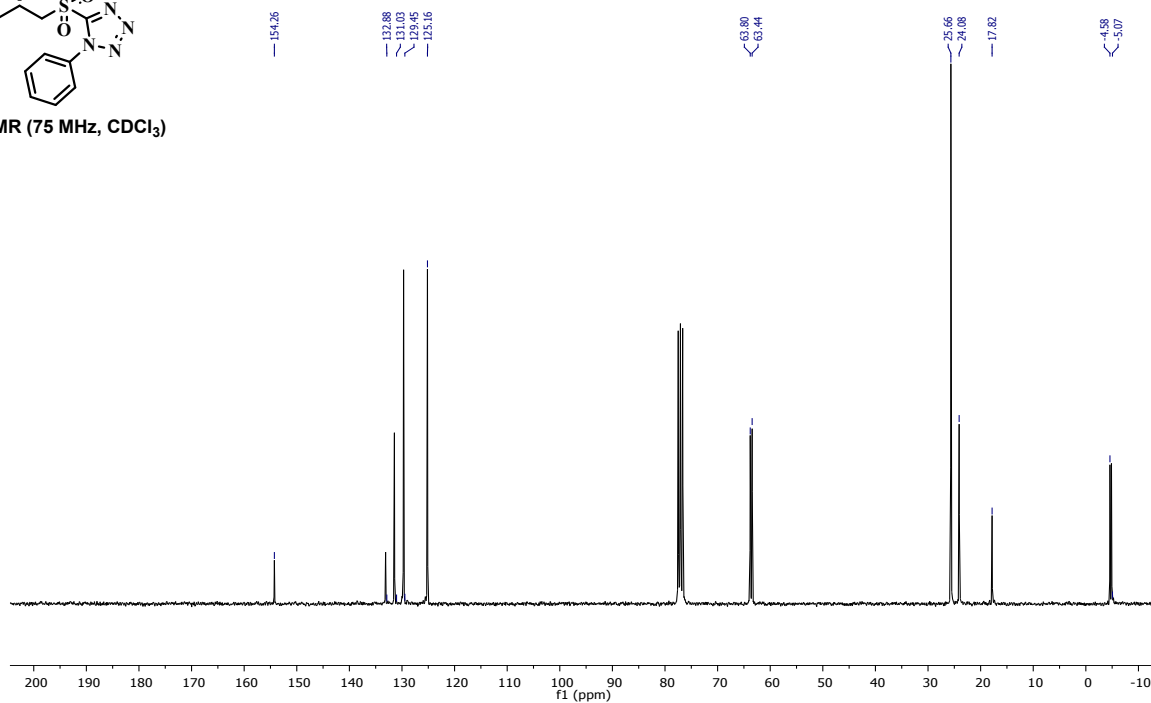
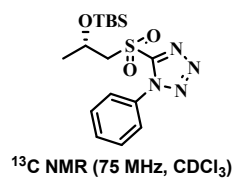
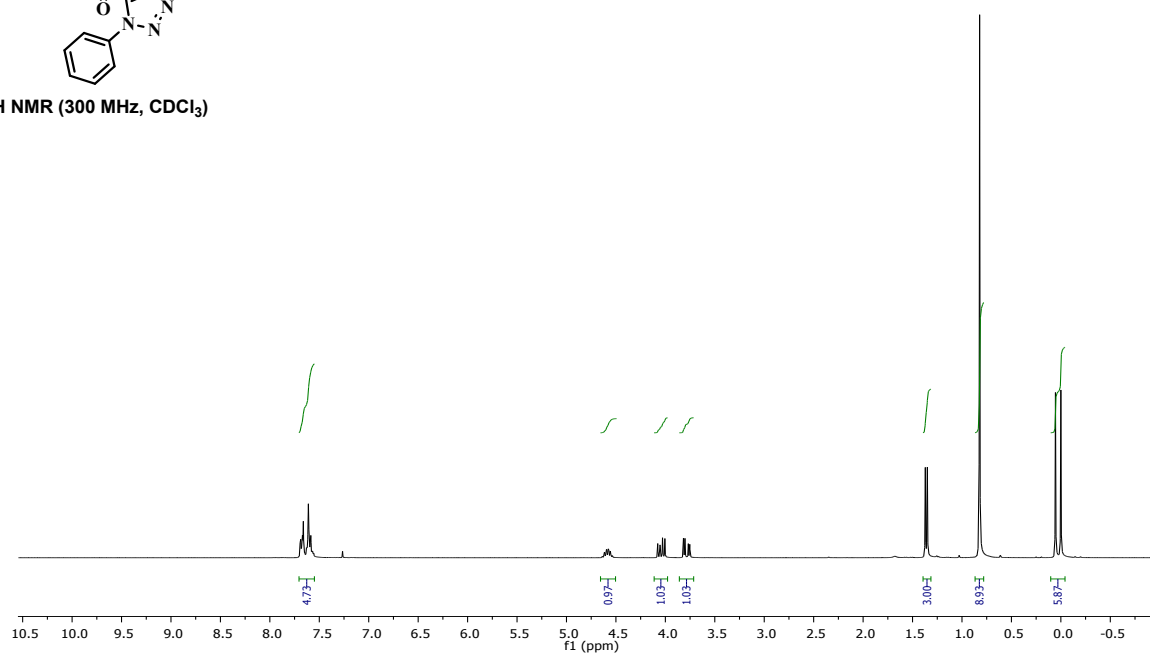
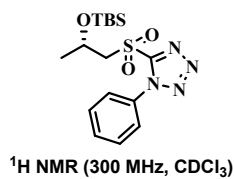
(S)-2-(*tert*-Butyldimethylsilyloxy)propan-1-ol (8):



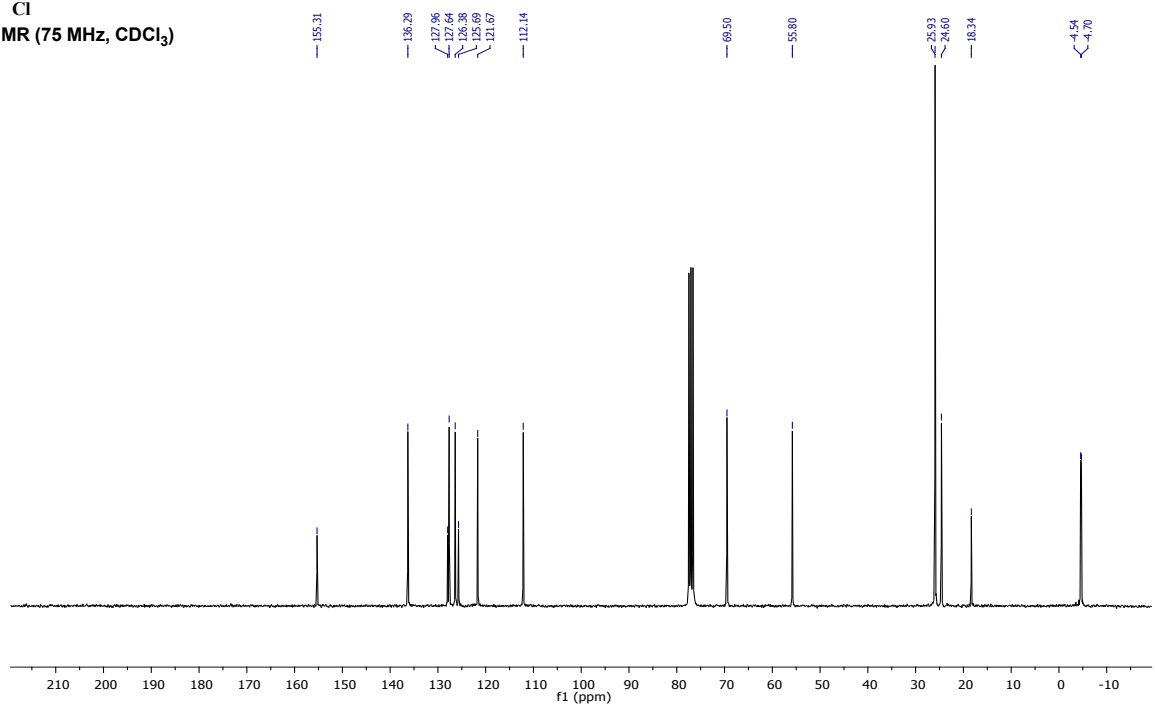
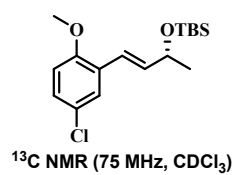
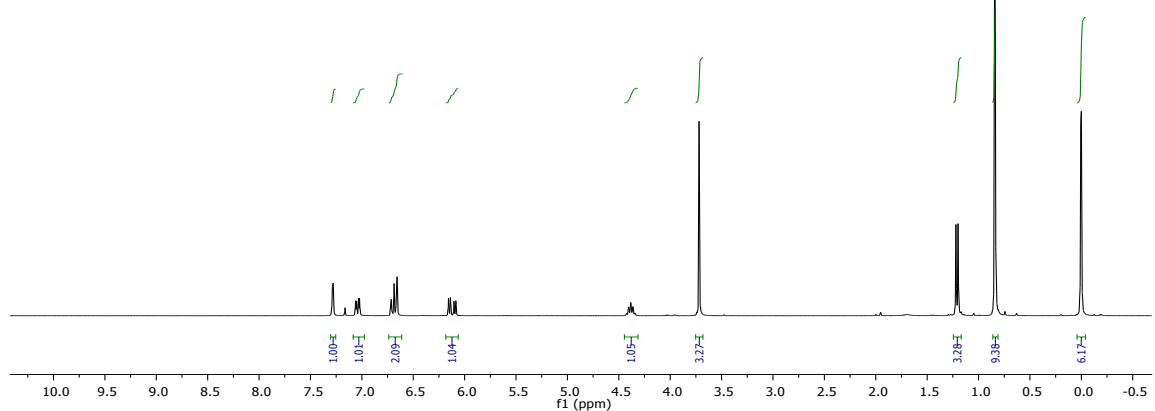
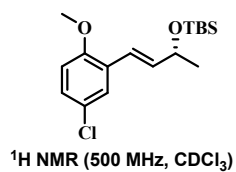
(S)-5-(2-(*tert*-Butyldimethylsilyloxy)propylthio)-2-phenyl-2*H*-tetrazole (9):



(S)-5-(2-(*tert*-Butyldimethylsilyloxy)propylsulfonyl)-2-phenyl-2*H*-tetrazole (10):



(*R,E*)-*tert*-Butyl(4-(5-chloro-2-methoxyphenyl)but-3-en-2-yloxy)dimethylsilane (12):



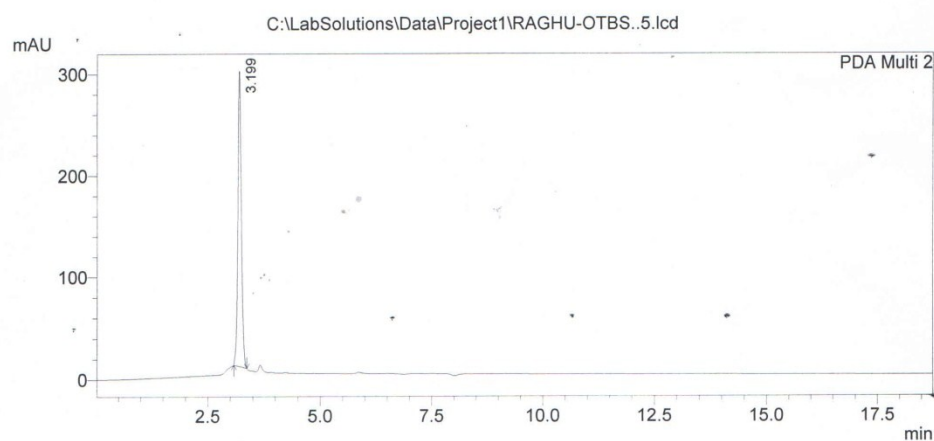
Compound 12 HPLC report:

11/17/2015 16:25:45 1 / 1

IICT NPL

Acquired by : Admin
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Sample ID : RAGHU-OTBS
Vial # : 70
Injection Volume : 20 uL
Data File Name : RAGHU-OTBS..5.lcd
Method File Name : RAGHU.lcm
Batch File Name :
Report File Name : Report Format.lcr
Data Acquired : 11/16/2015 4:42:32 PM
Data Processed : 11/16/2015 5:01:22 PM
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Column:: CHIRAL PAK IA 250mm X 4.6 mm, 5u
FLOWRATE:1 ml/min
DECTION:210nm

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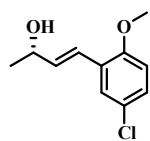


PeakTable

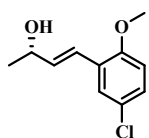
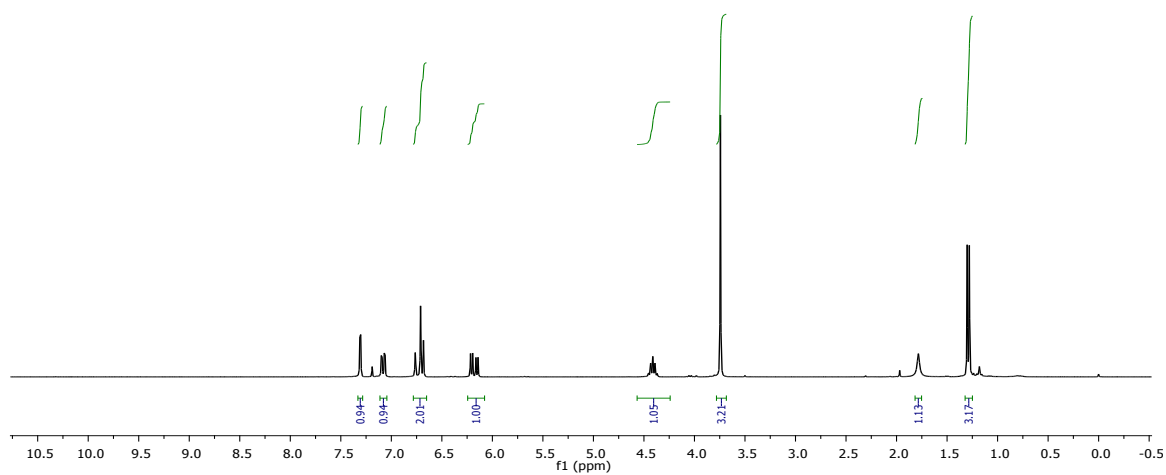
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C:\LabSolutions\Data\Project1\RAGHU-OTBS..5.lcd

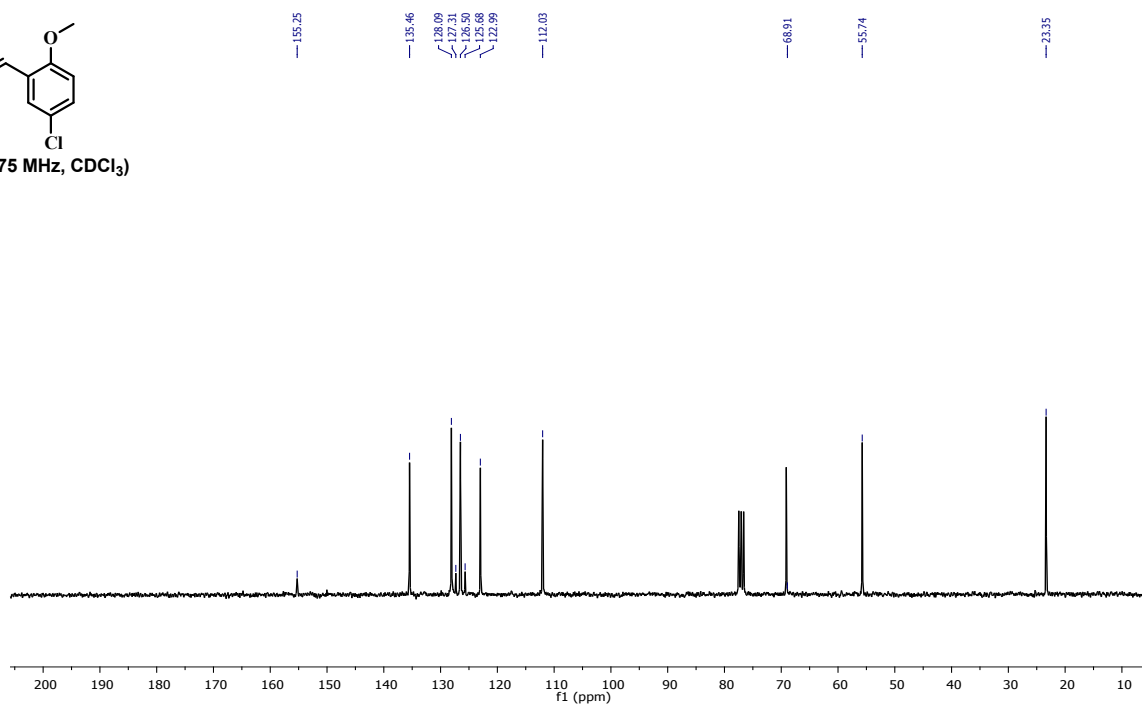
(*S,E*)-4-(5-Chloro-2-methoxyphenyl)but-3-en-2-ol (5):



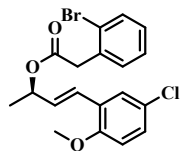
¹H NMR (300 MHz, CDCl₃)



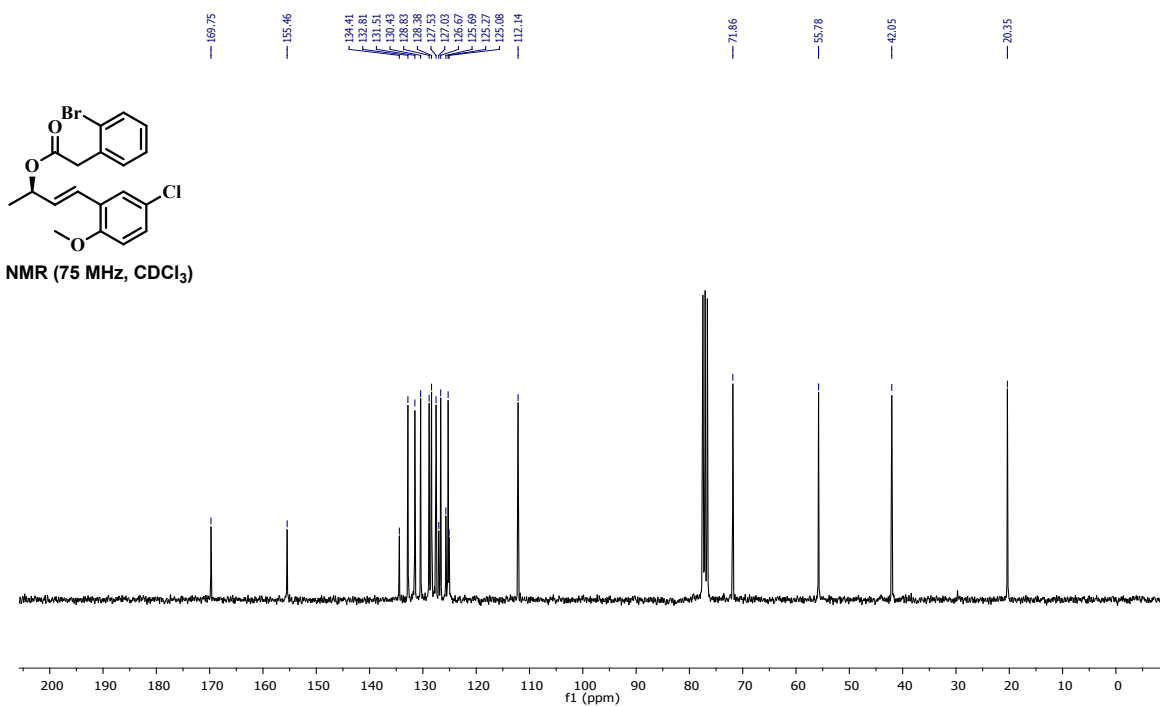
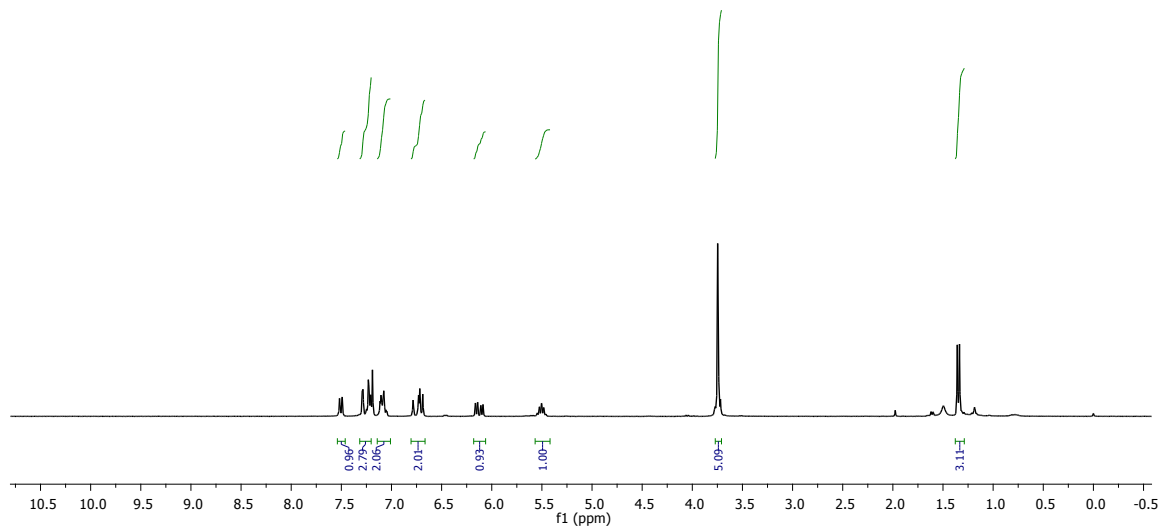
¹³C NMR (75 MHz, CDCl₃)



(*R,E*)-4-(5-Chloro-2-methoxyphenyl)but-3-en-2-yl 2-(2-bromophenyl)acetate (4):



¹H NMR (300 MHz, CDCl₃)



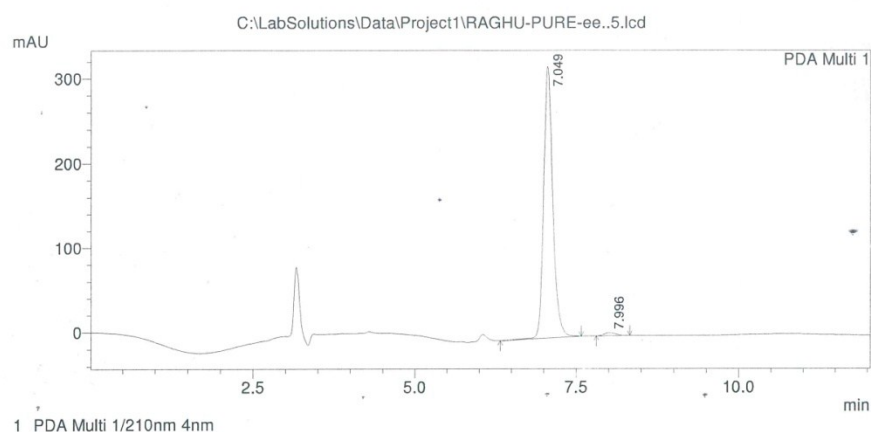
Compound 4 HPLC report:

11/13/2015 10:31:52 1 / 1

IICT NPL

Acquired by : Admin
Sample Name : RAGHU-PURE-ee
Sample ID : RAGHU-PURE-ee
Vial # : 66
Injection Volume : 20uL
Data File Name : RAGHU-PURE-ee..5.lcd
Method File Name : RAGHU.lcm
Batch File Name :
Report File Name : Report Format.lcr
Data Acquired : 11/12/2015 5:18:34 PM
Data Processed : 11/13/2015 10:29:51 AM
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Column:: CHIRAL PAK IA 250mm X 4.6 mm, 5u)
Flowrate: 1mL/min
DETECTION : 210nm

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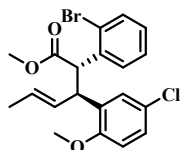


PeakTable

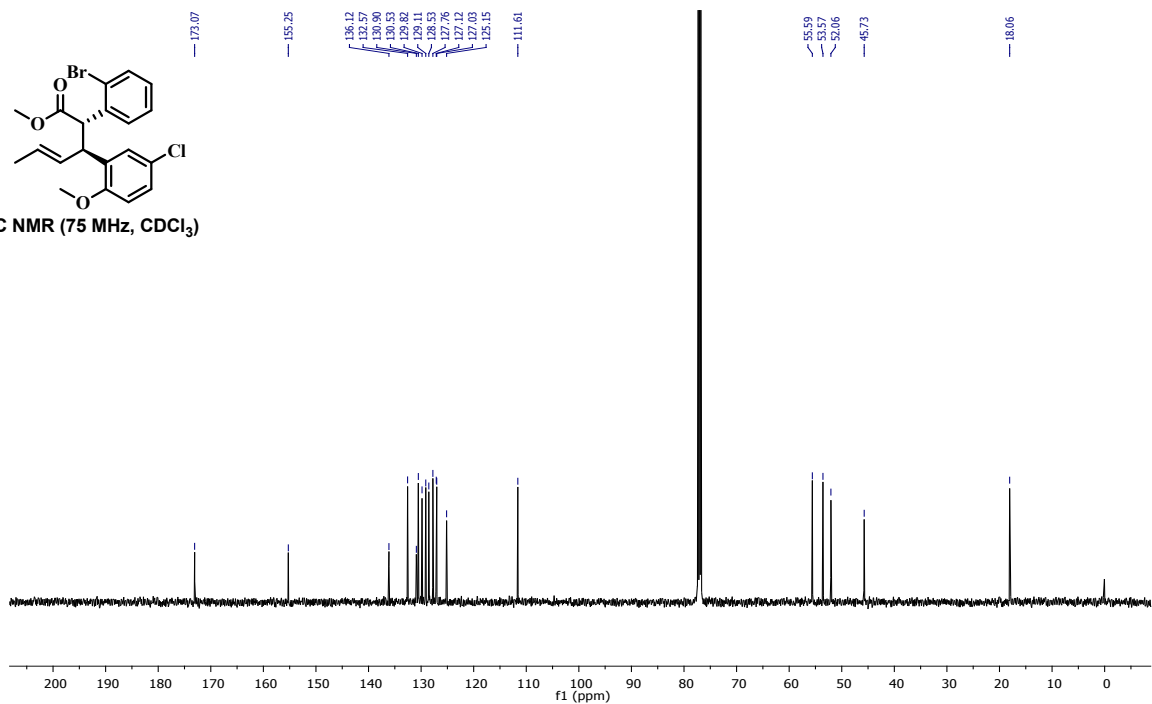
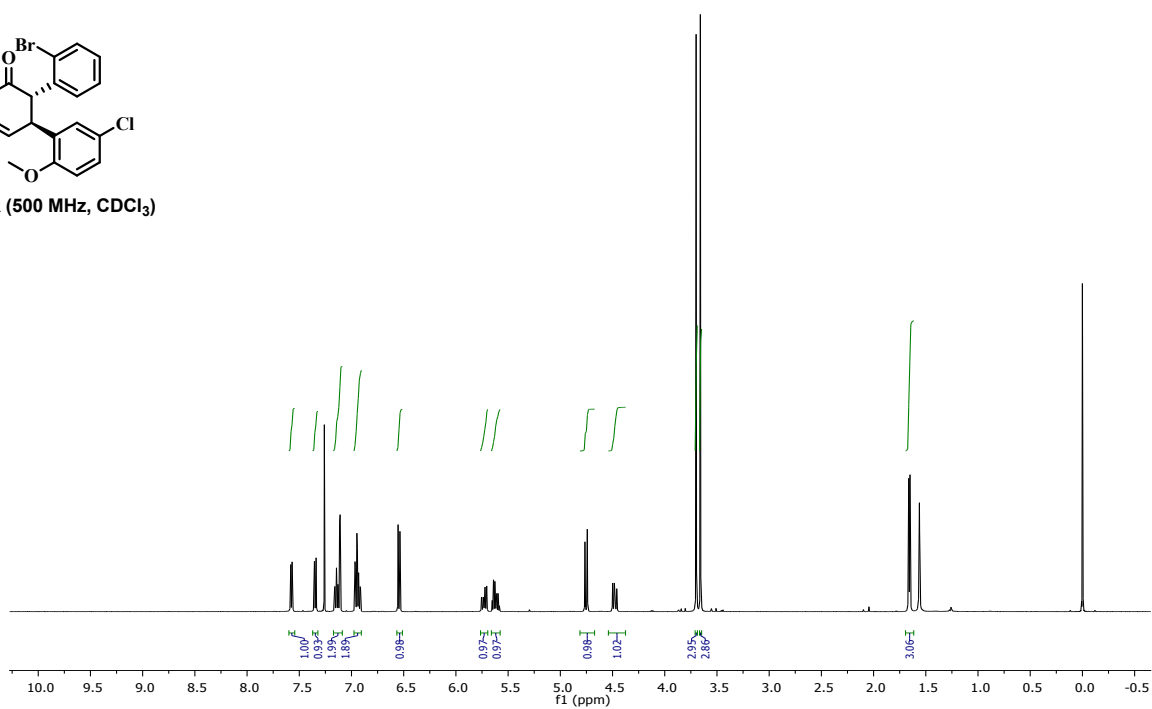
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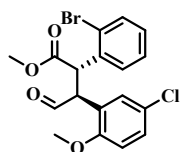
(2*S*,3*S*,*E*)-Methyl 2-(2-bromophenyl)-3-(5-chloro-2-methoxyphenyl)hex-4-enoate (3):



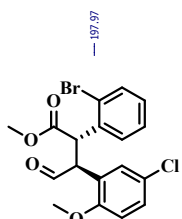
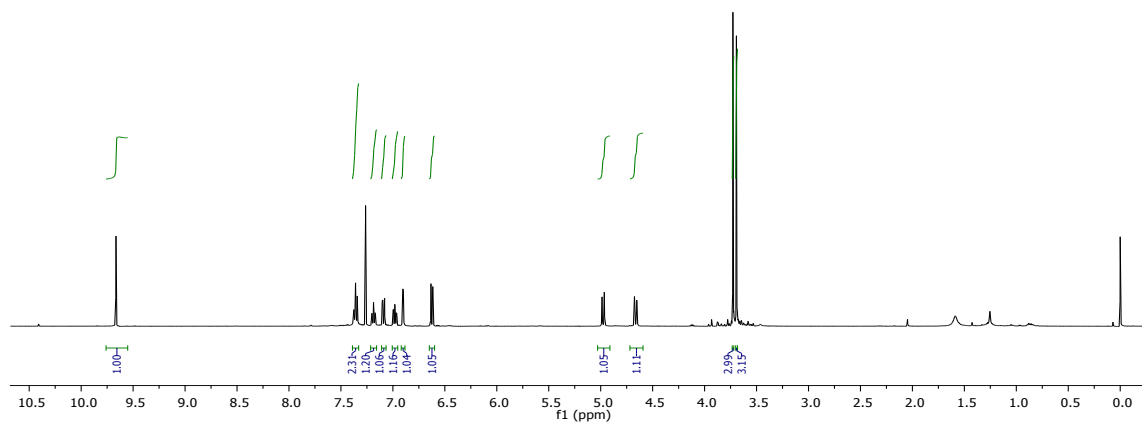
¹H NMR (500 MHz, CDCl₃)



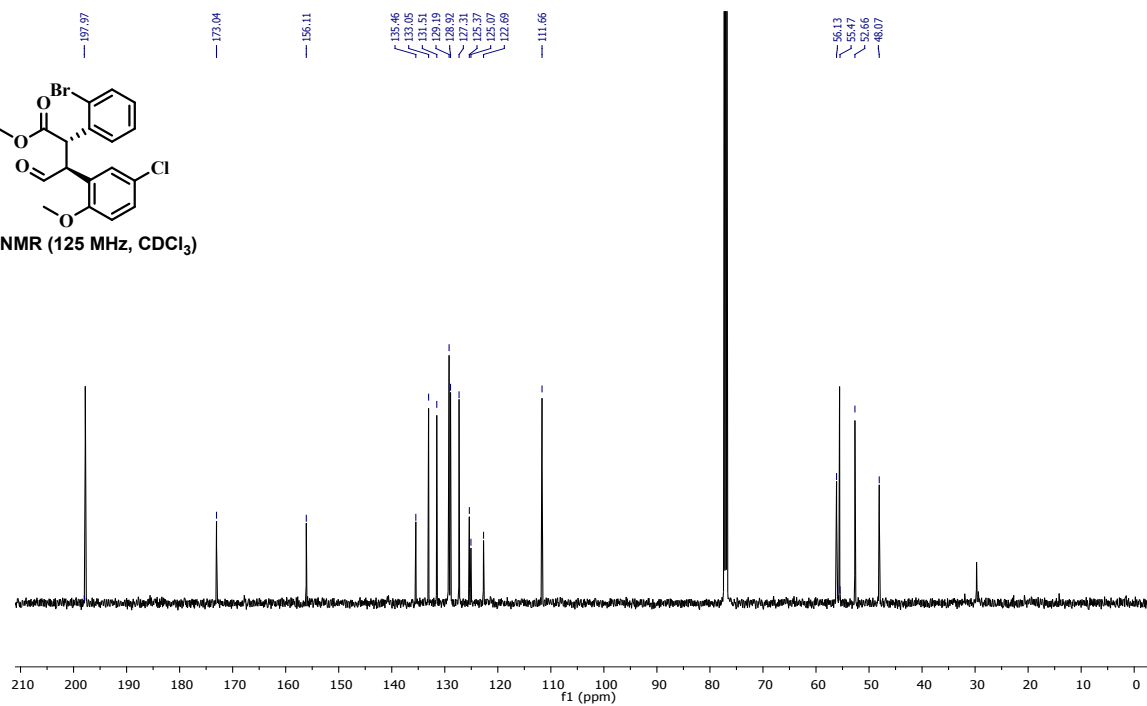
(2*S*,3*S*)-Methyl 2-(2-bromophenyl)-3-(5-chloro-2-methoxyphenyl)-4-oxobutanoate (13):



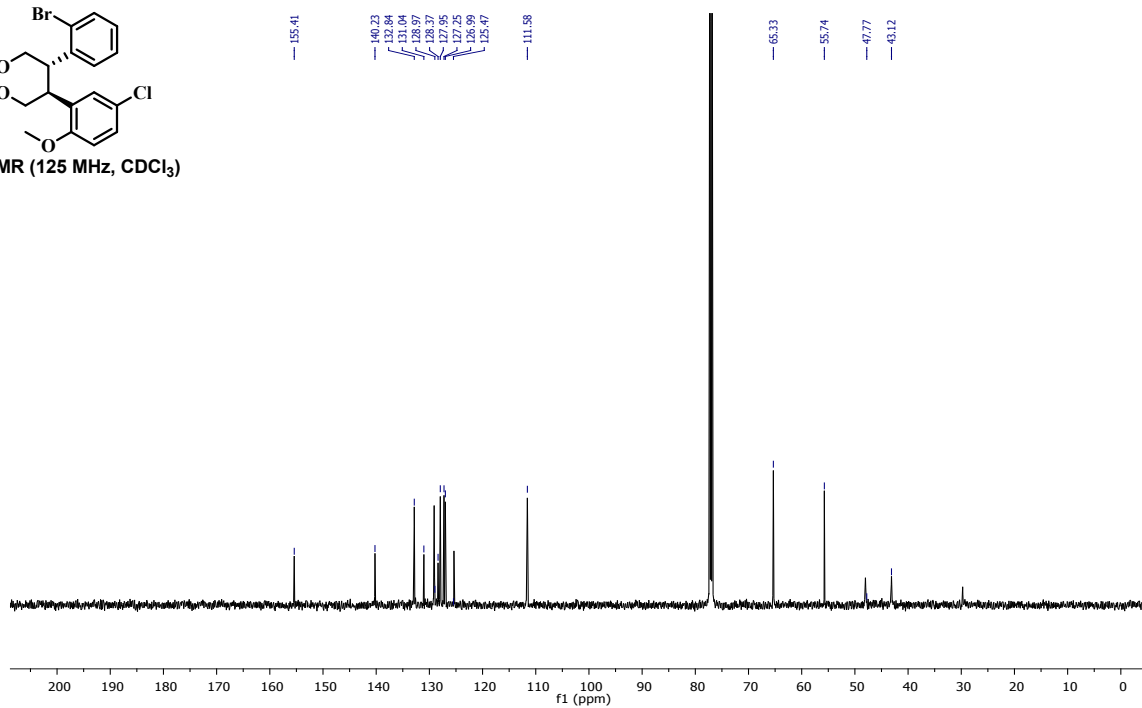
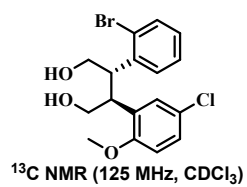
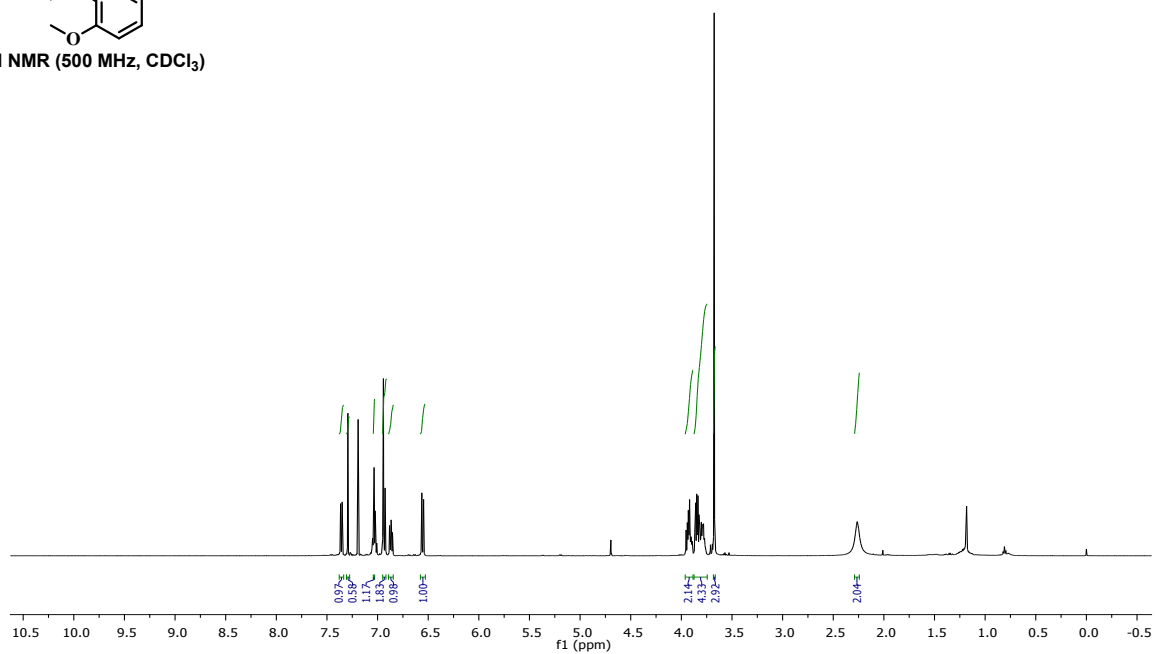
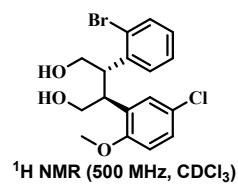
¹H NMR (500 MHz, CDCl₃)



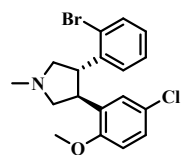
¹³C NMR (125 MHz, CDCl₃)



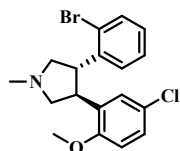
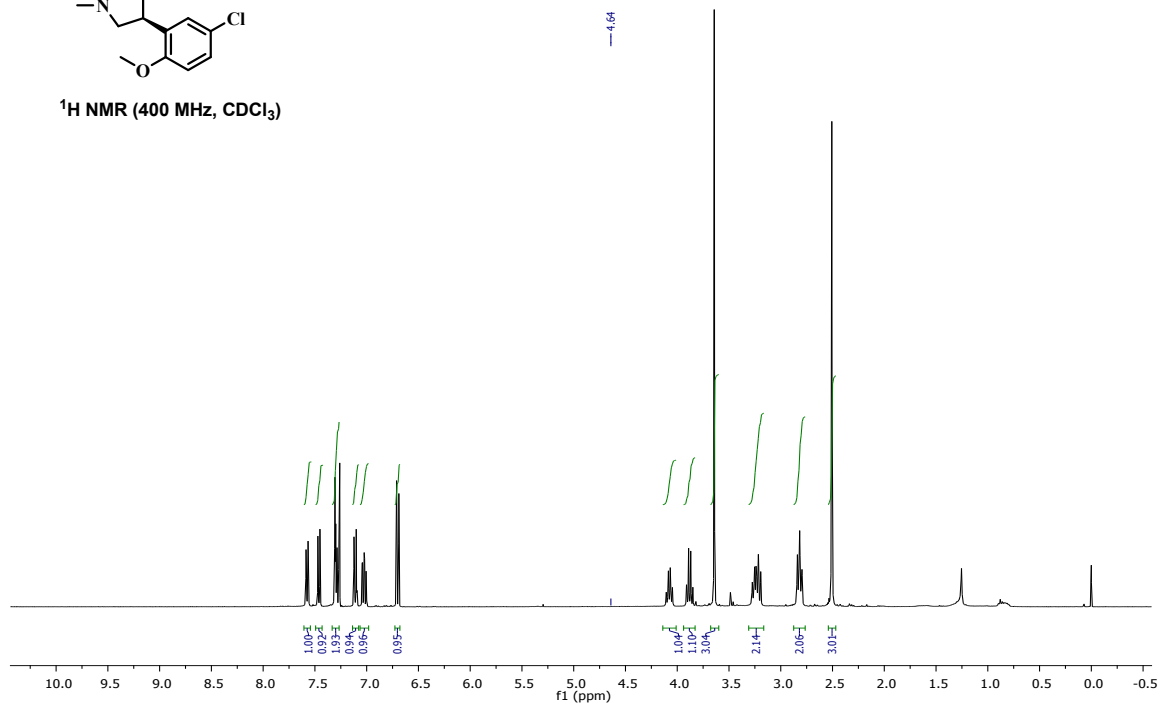
(2*S*,3*S*)-2-(2-Bromophenyl)-3-(5-chloro-2-methoxyphenyl)butane-1,4-diol (14):



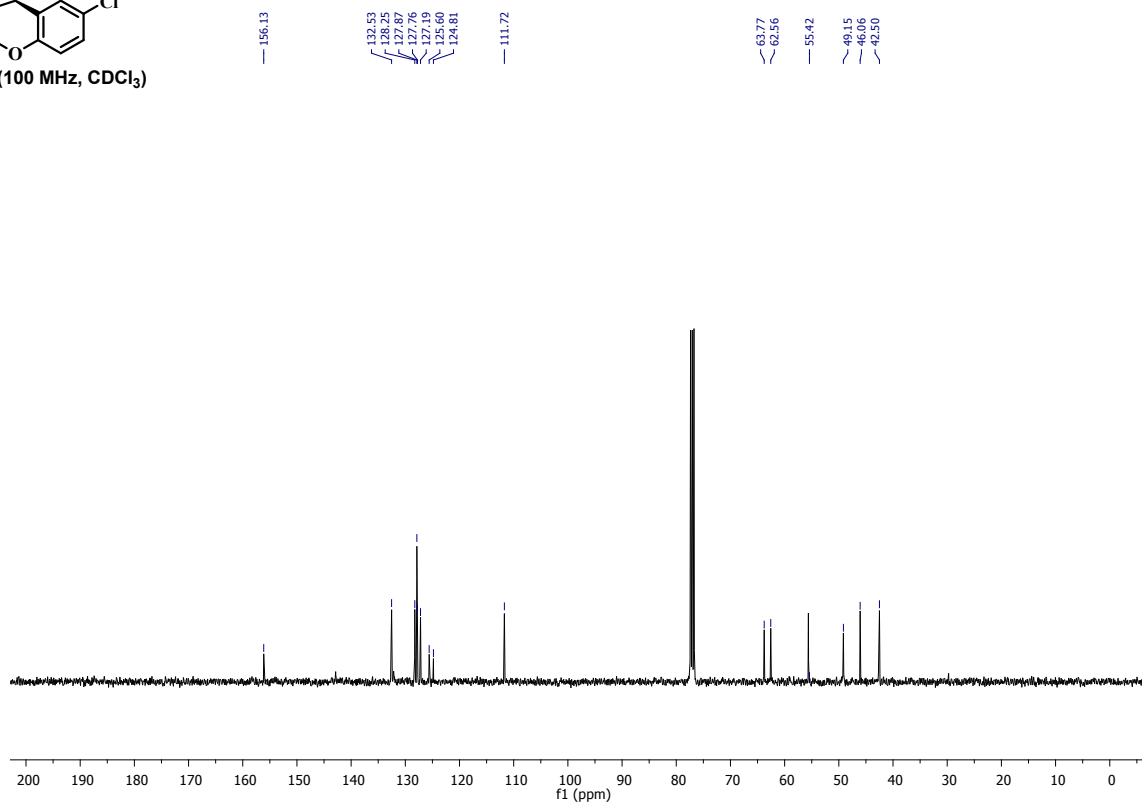
(3*S*,4*S*)-3-(2-Bromophenyl)-4-(5-chloro-2-methoxyphenyl)-1-methylpyrrolidine (2):



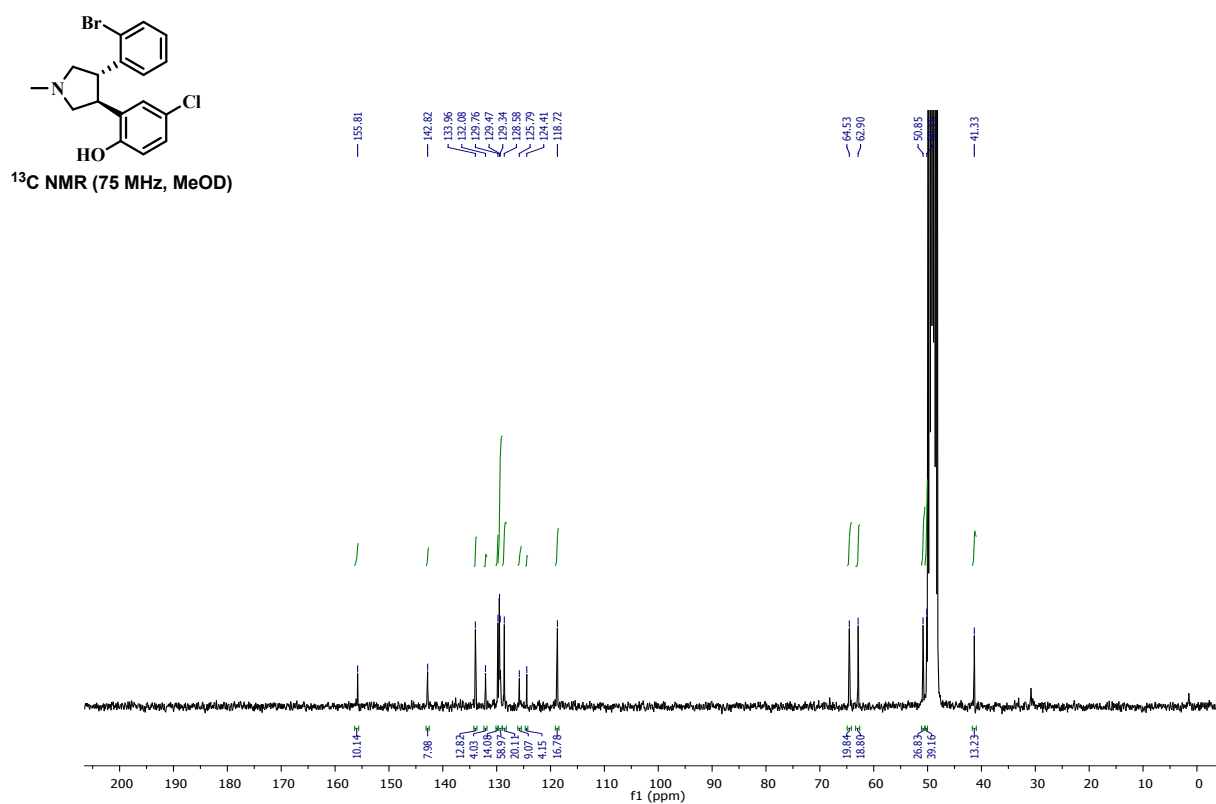
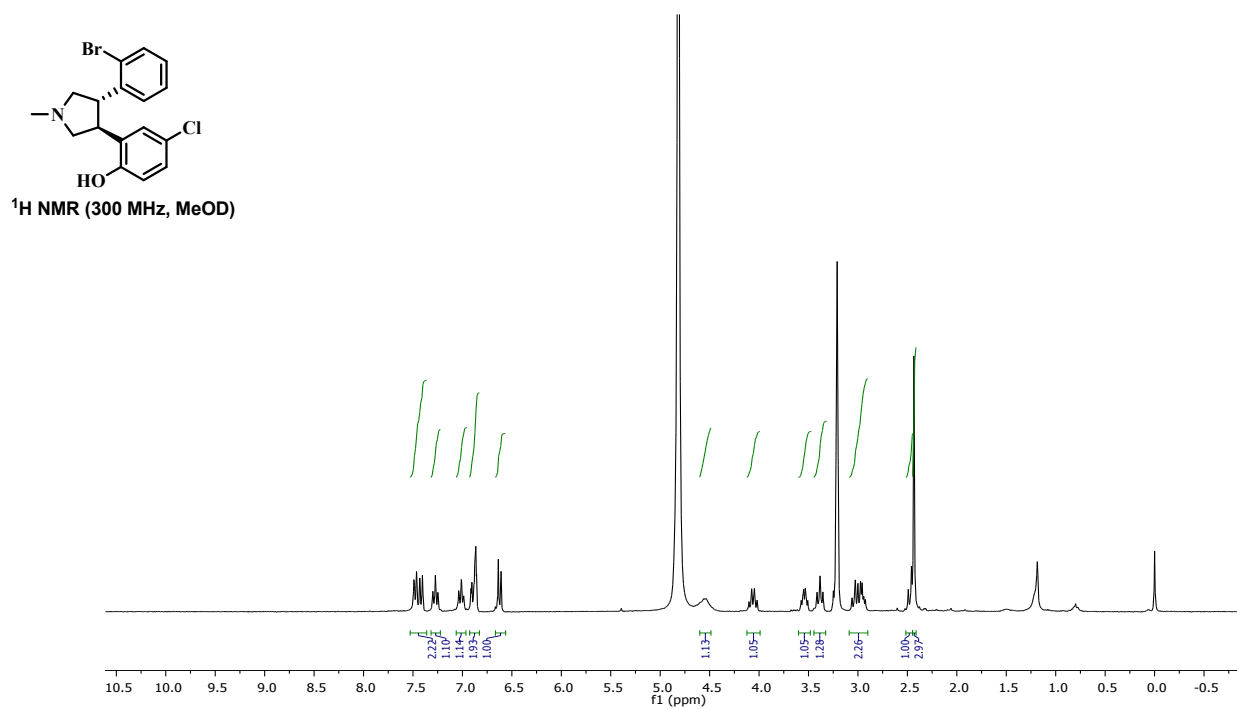
¹H NMR (400 MHz, CDCl₃)



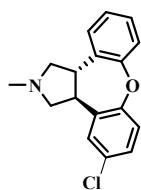
¹³C NMR (100 MHz, CDCl₃)



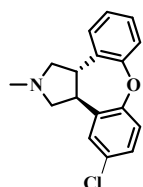
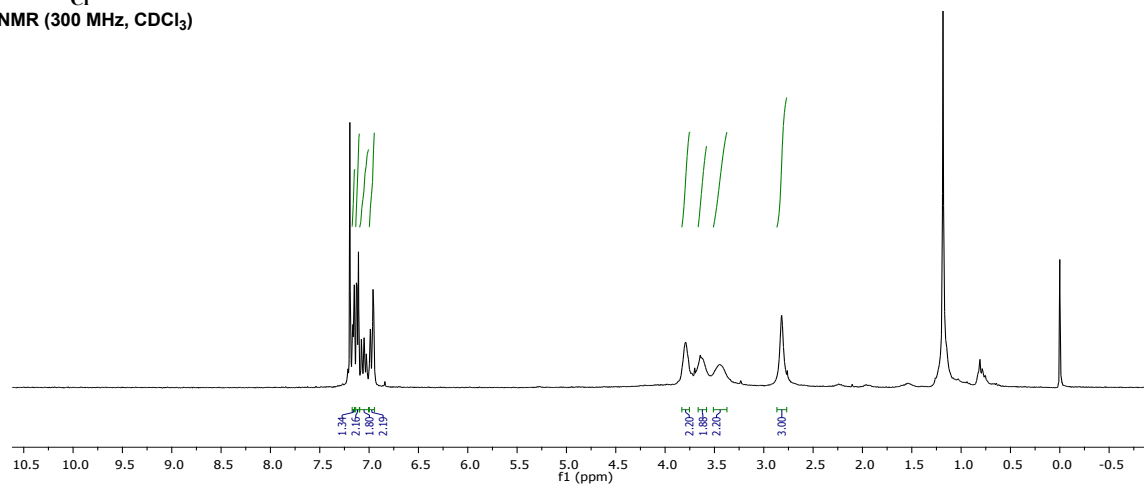
2-((3*S*,4*S*)-4-(2-Bromophenyl)-1-methylpyrrolidin-3-yl)-4-chlorophenol (15):



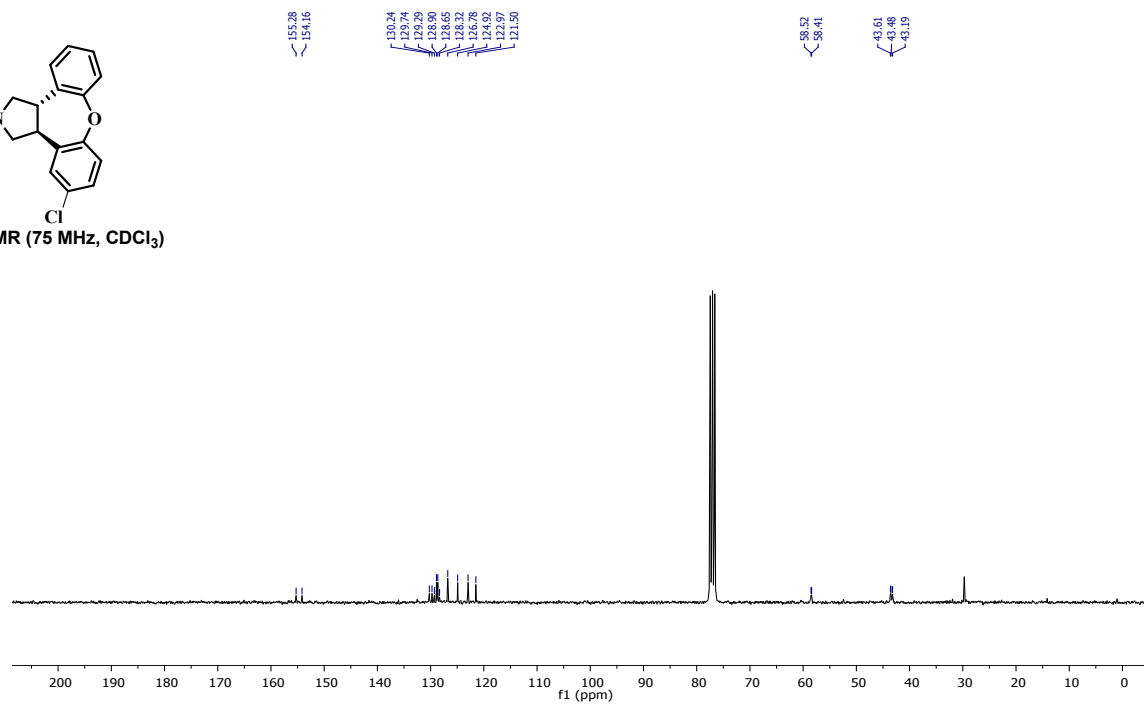
***trans*-(5-Chloro-2-methyl-2,3,3a,12b-tetrahydro-1H-dibenz[2,3:6,7]oxepine-[4,5-c]pyrrole (1):**



¹H NMR (300 MHz, CDCl₃)



¹³C NMR (75 MHz, CDCl₃)



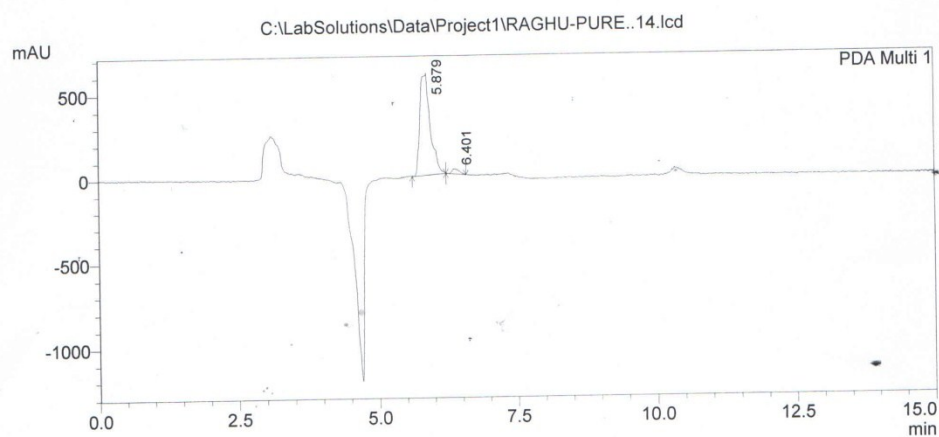
(+)-Asenapine HPLC report:

11/24/2015 12:22:14 1 / 1

IICT NPL

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Sample ID : RAGHU-PURE
Vial # : 27
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Method File Name : RAGHU.lcm
Batch File Name :
Report File Name : Report Format.lcr
Data Acquired : 11/24/2015 11:13:24 AM
Data Processed : 11/24/2015 12:21:18 PM
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FLOWRATE:1 ml/min
DECTION:210nm

<Chromatogram>



PeakTable

PDA Ch1 210nm 4nm

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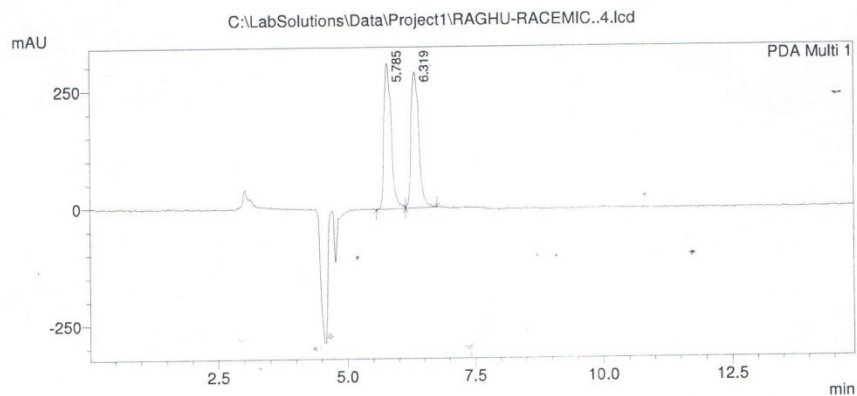
Recemic Asenapine HPLC report:

11/23/2015 11:49:43 1 / 1

IICT NPL

Acquired by : Admin
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 Sample ID : RAGHU-RACEMIC
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 Method File Name : RAGHU.lcm
 Batch File Name :
 Report File Name : Report Format.lcr
 Data Acquired : 11/23/2015 11:27:04 AM
 Data Processed : 11/23/2015 11:42:02 AM
 MOBILE PHASE: 10% IPA IN HEXANE
 Column: CHIRAL PAK IA 250mm X 4.6 mm, 5u (0.1% DEA)
 FLOWRATE: 1 ml/min
 DETECTION: 210nm

<Chromatogram>



PeakTable

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