

Supporting Information

for

A novel and practical asymmetric synthesis of dapoxetine hydrochloride

Yijun Zhu^{1,2}, Zhenren Liu¹, Hongyan Li¹, Deyong Ye^{2,*} and Weicheng Zhou^{1,*}

Address: ¹State Key Lab of New Drug & Pharmaceutical Process, Shanghai Key Lab of Anti-Infectives, State Institute of Pharmaceutical Industry, No.285, Gebaini Rd, Shanghai 201203, China and ²School of Pharmacy, Fudan University, No.826, Zhangheng Rd., Shanghai 201203, China

Email: Deyong Ye - dyye@shmu.edu.cn;

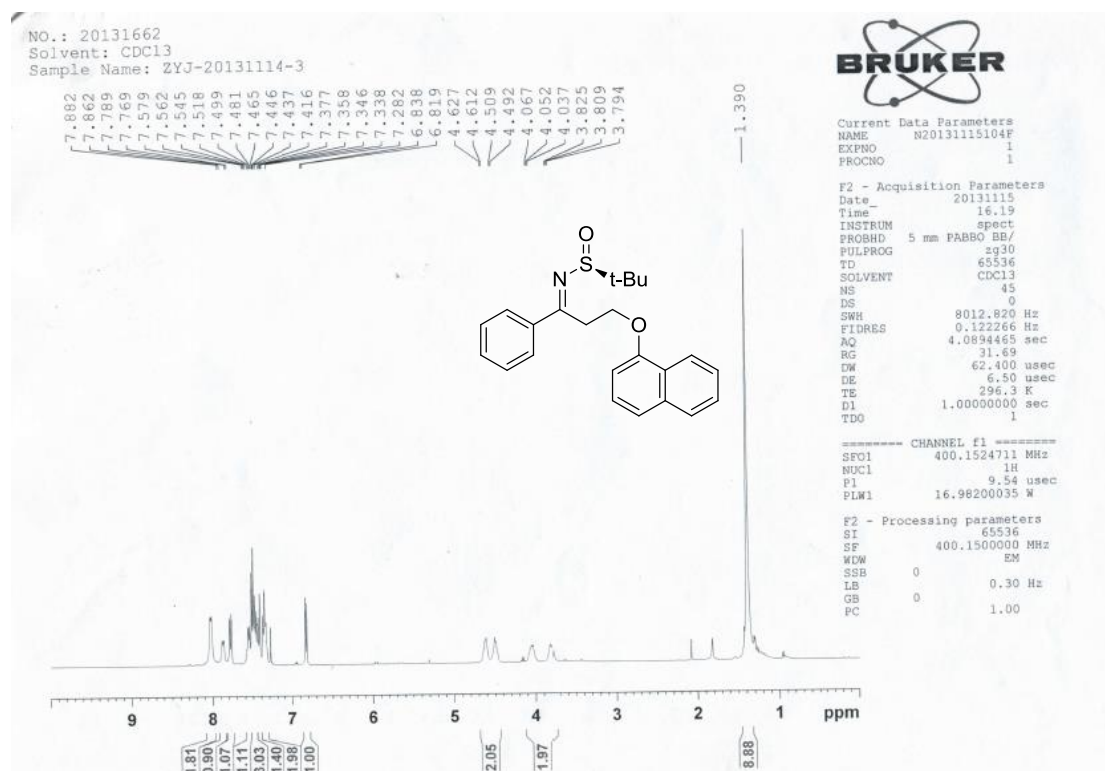
Weicheng Zhou - zhouweicheng58@163.com

* Corresponding author

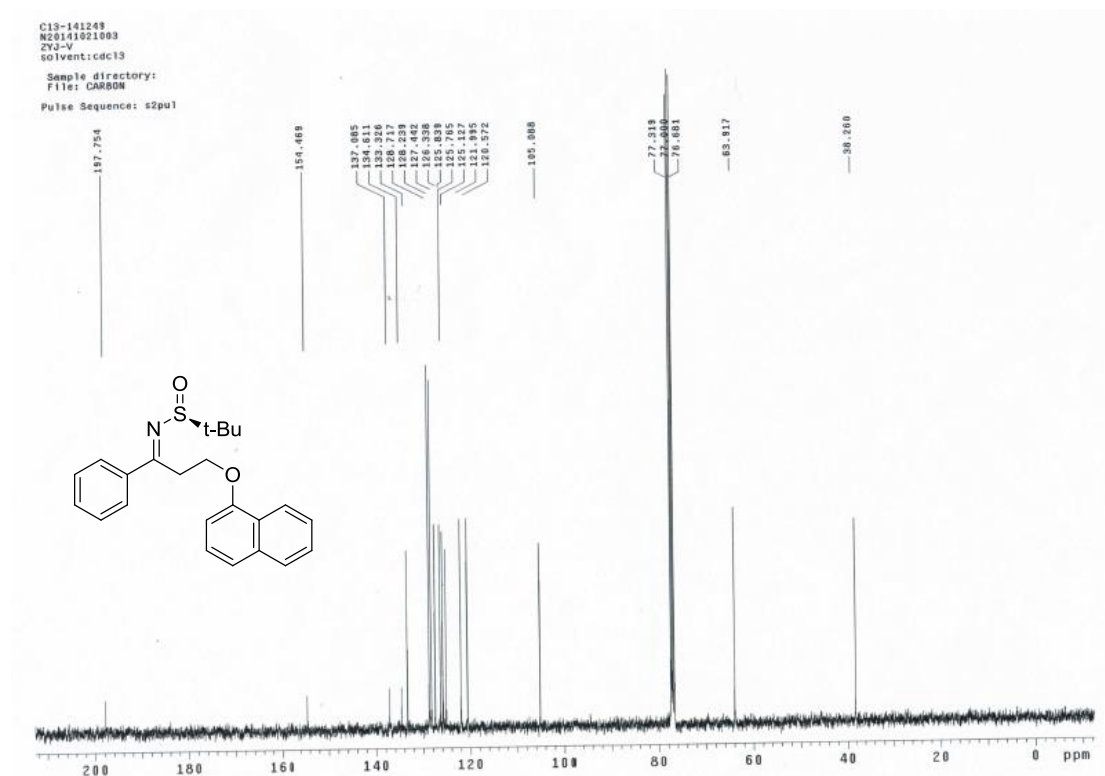
¹H NMR, ¹³C NMR and ESIMS spectra of compounds 1, 4, 5, 5", 6 and 7 and chiral HPLC diagrams of 1 and 7

Table of contents

^1H NMR and ^{13}C NMR spectra of compound 4	S3
HRMS of 4 and ^1H NMR spectrum of 5	S4
^{13}C NMR and HRMS spectra of 5	S5
^1H NMR and ESIMS spectra of compound 5	S6
^1H NMR and ^{13}C NMR spectra of compound 6	S7
ESIMS of 6 and ^1H NMR spectrum of 7	S8
^{13}C NMR and ESIMS spectra of 7	S9
^1H NMR and ^{13}C NMR spectra of compound 1	S10
ESI-MS spectra of compound 1	S11
Chiral HPLC of 7	S12
Chiral HPLC of 1	S13



¹H NMR spectrum of compound 4



¹³C NMR spectrum of compound 4

Elemental Composition Report

Single Mass Analysis

Tolerance = 30.0 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

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

Elements Used:

C: 10-40 H: 10-40 N: 0-1 O: 0-2 Na: 1-1 S: 1-1

SIPI

Q-ToF micro

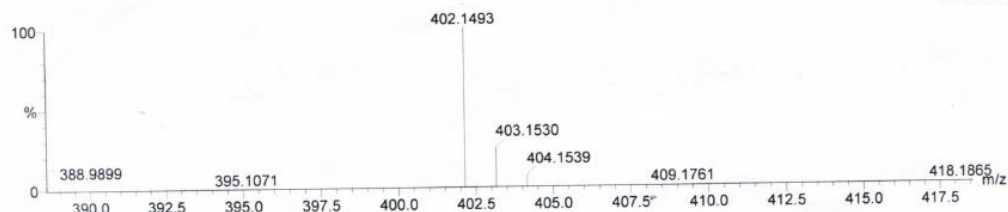
14:10:51,13-Nov-2015

ZYJ-V

YA019

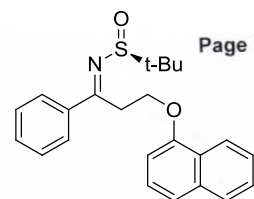
TOF MS ES+
3.42e+003

Q15-1893HR 22 (0.407) AM (Cen.2, 80.00, Ar,5000.0,360.29,1.00); Sm (Mn, 2x3.00); Sb (1,40.00); Cm (9.22)

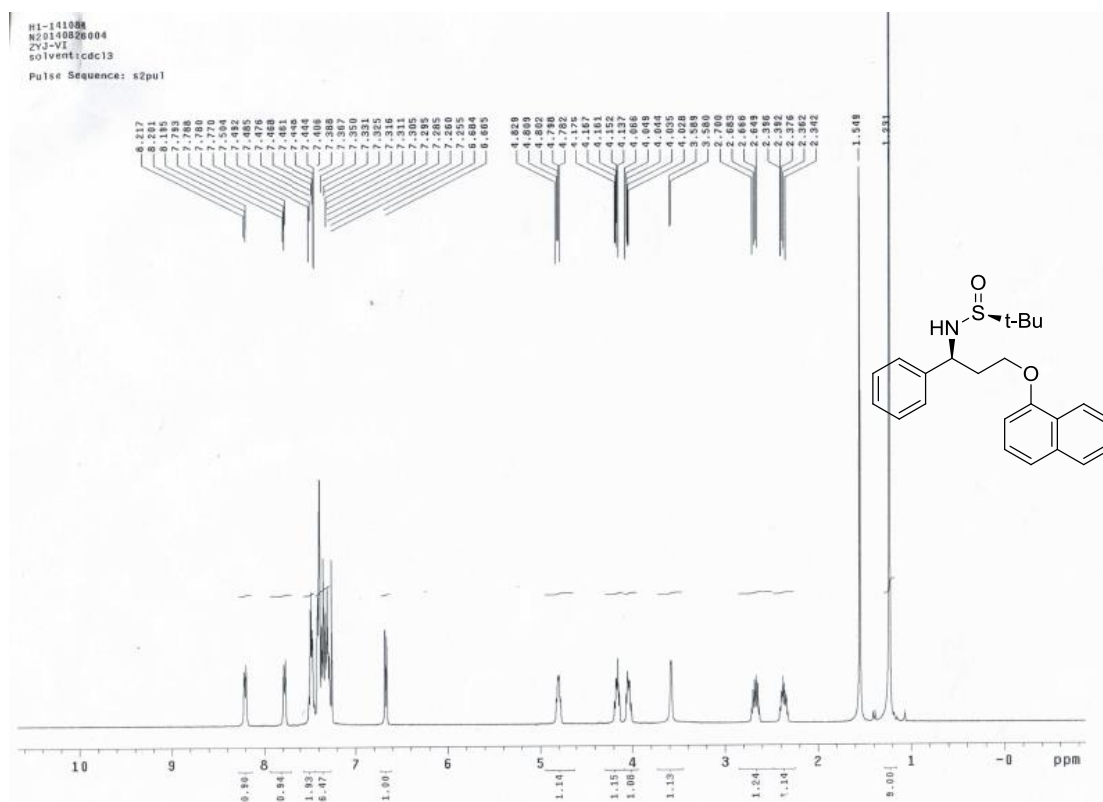


Minimum: -1.5
Maximum: 5.0 30.0 50.0

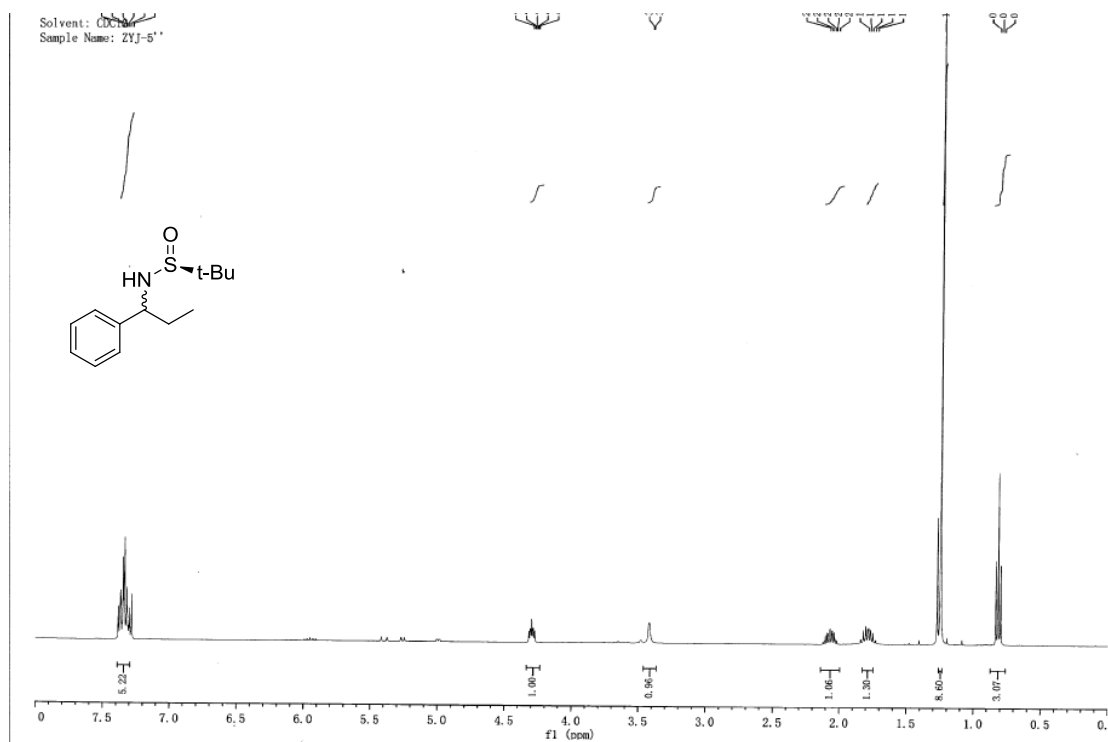
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
402.1493	402.1504	-1.1	-2.7	11.5	9.4	C23 H25 N O2 Na S



HRMS spectrum of compound 4

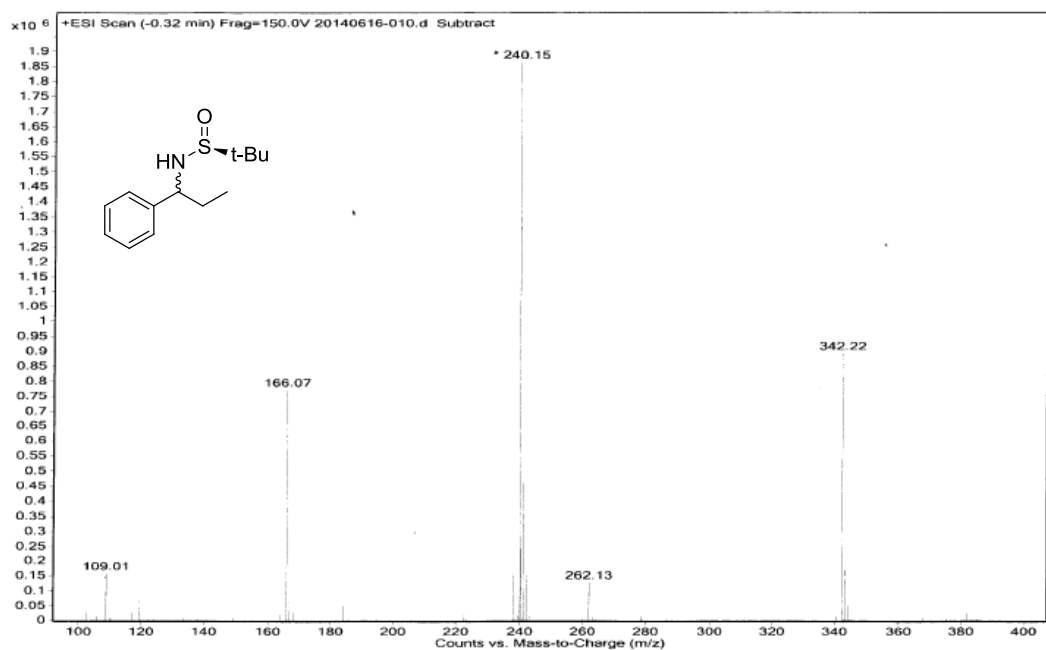


¹H NMR spectrum of compound 5

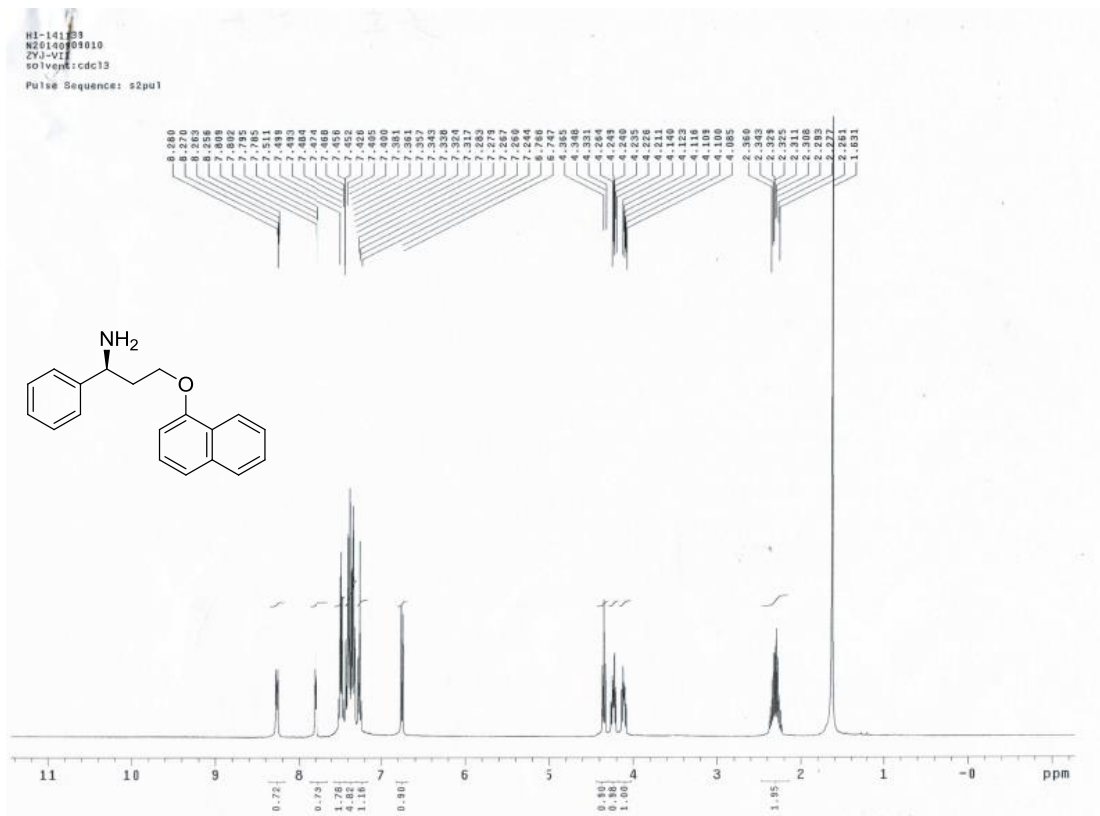


¹H NMR spectrum of compound 5

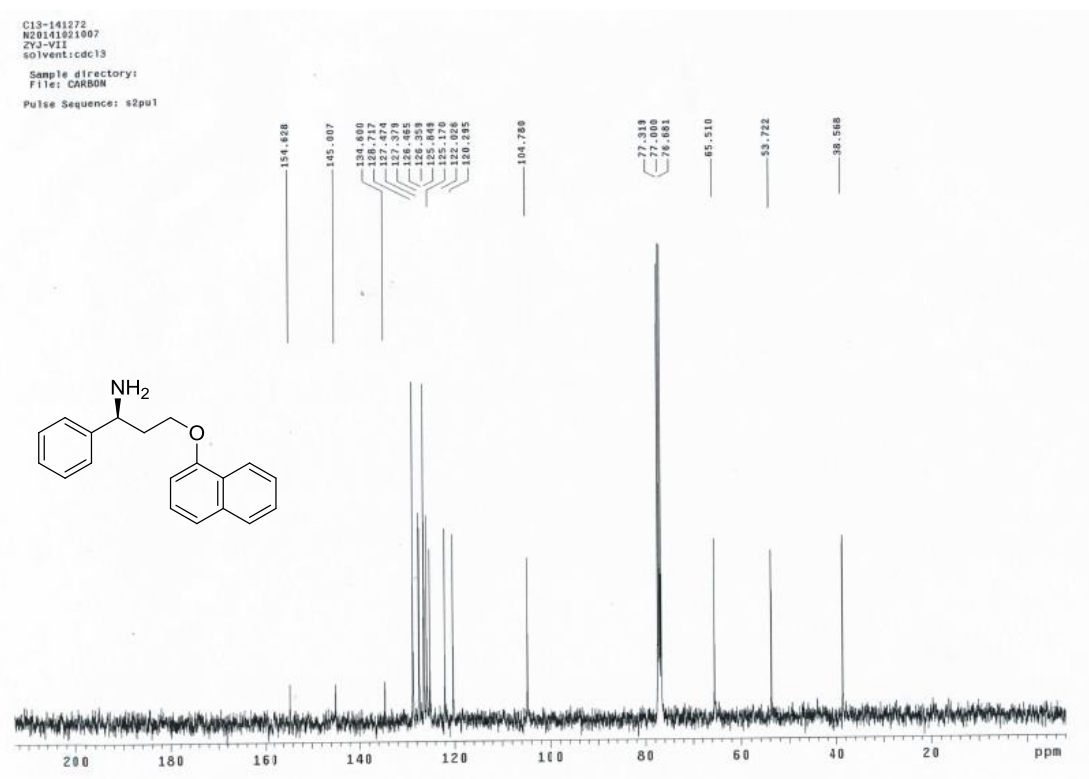
Sample Name	Position	Vial 70	Instrument Name	Instrument 1	User Name
Inj Vol	InjPosition		SampleType	Sample	IRM Calibration Status
Data Filename	20140616-010.d	ACQ Method	Comment	N20140616012F	Acquired Time
					Success
					6/16/2014 3:45:43 PM



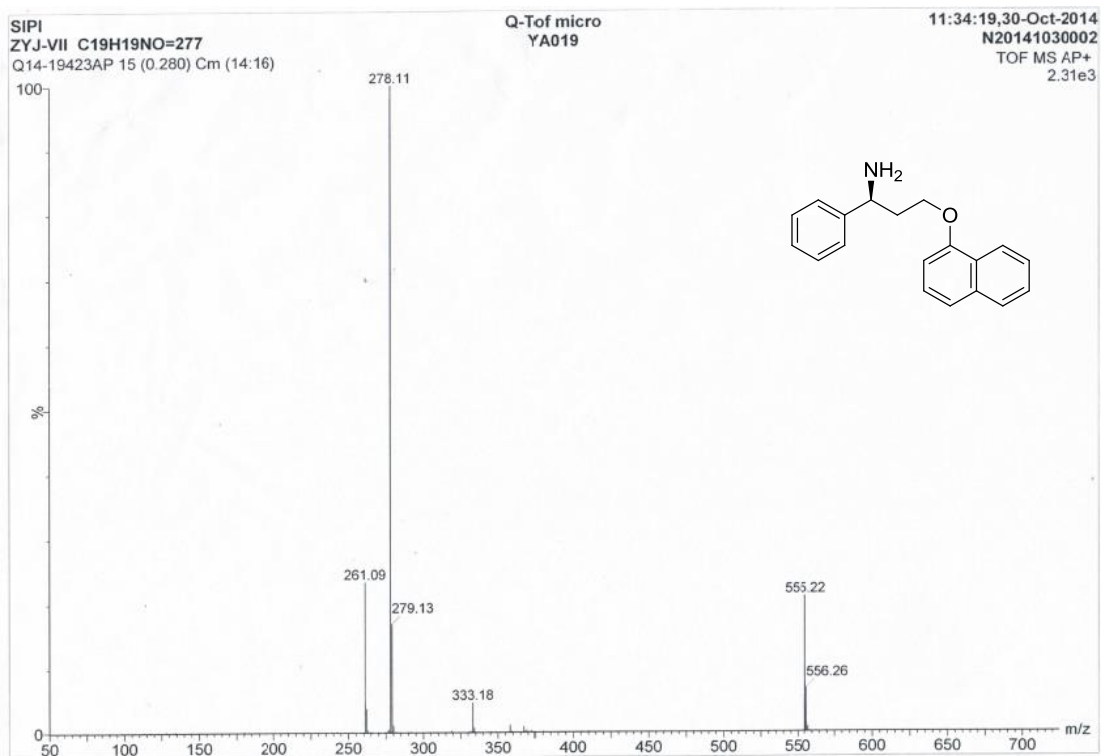
ESIMS spectrum of compound 5



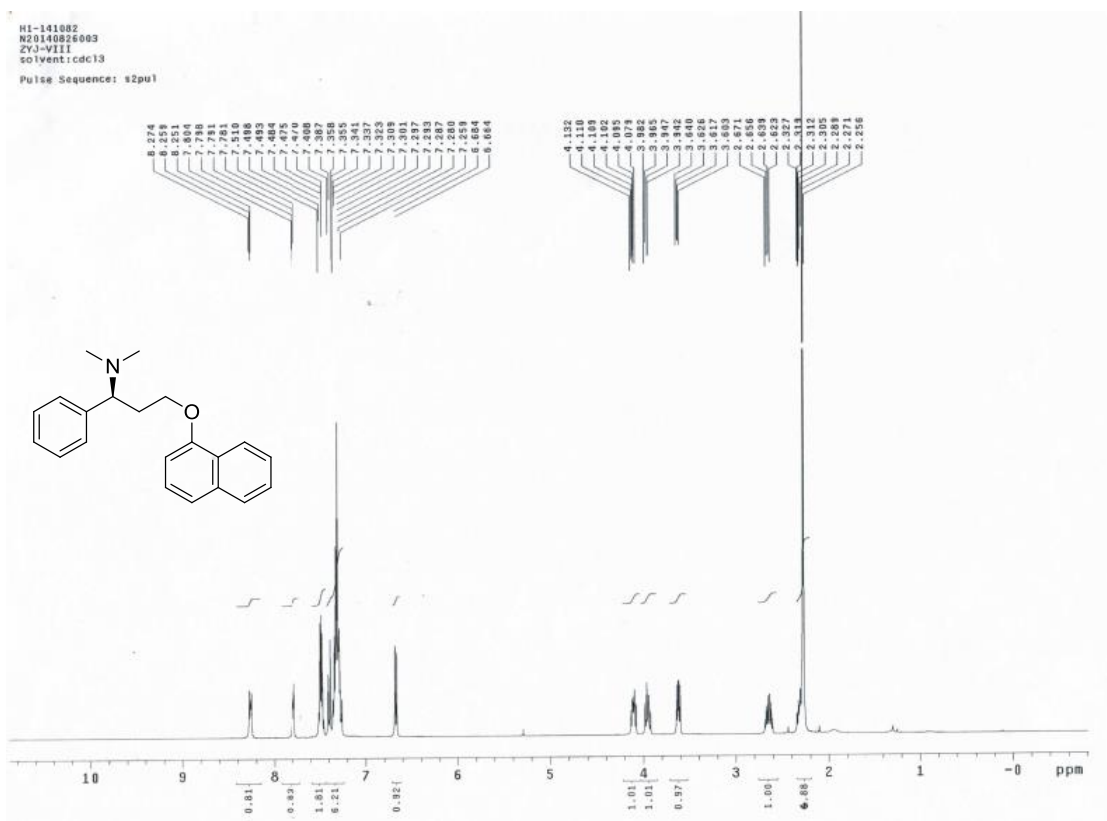
^1H NMR spectrum of compound 6



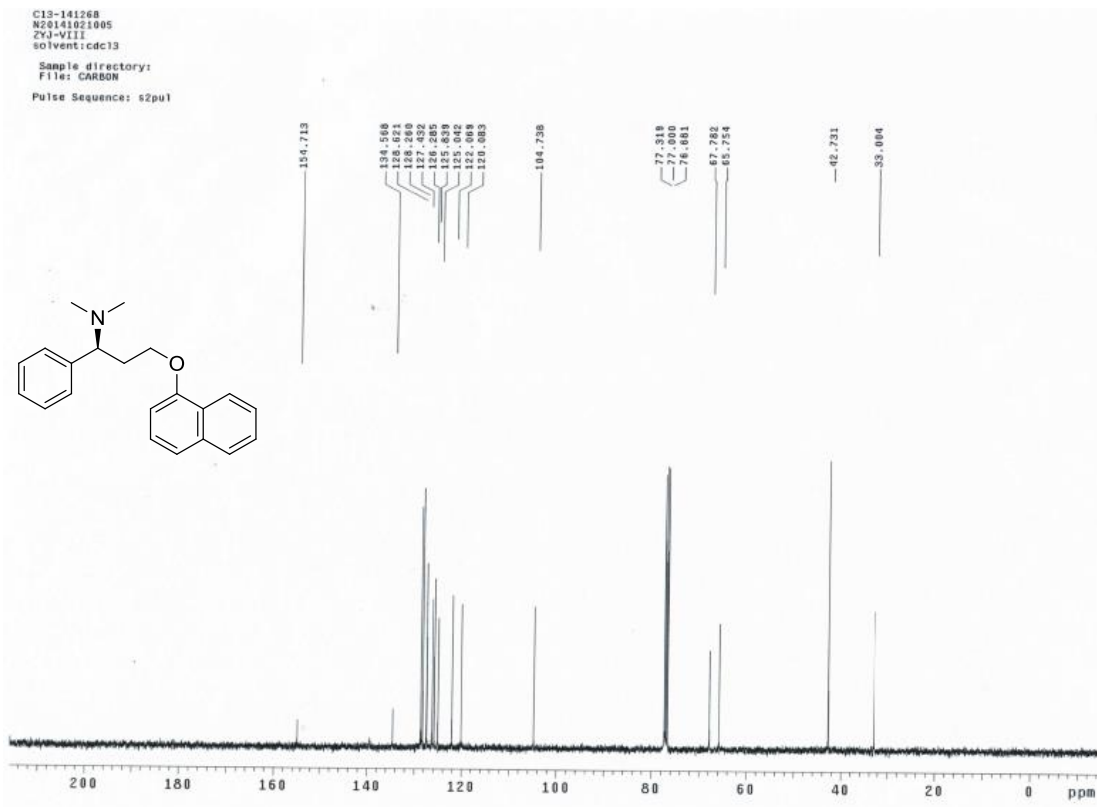
^{13}C NMR spectrum of compound 6



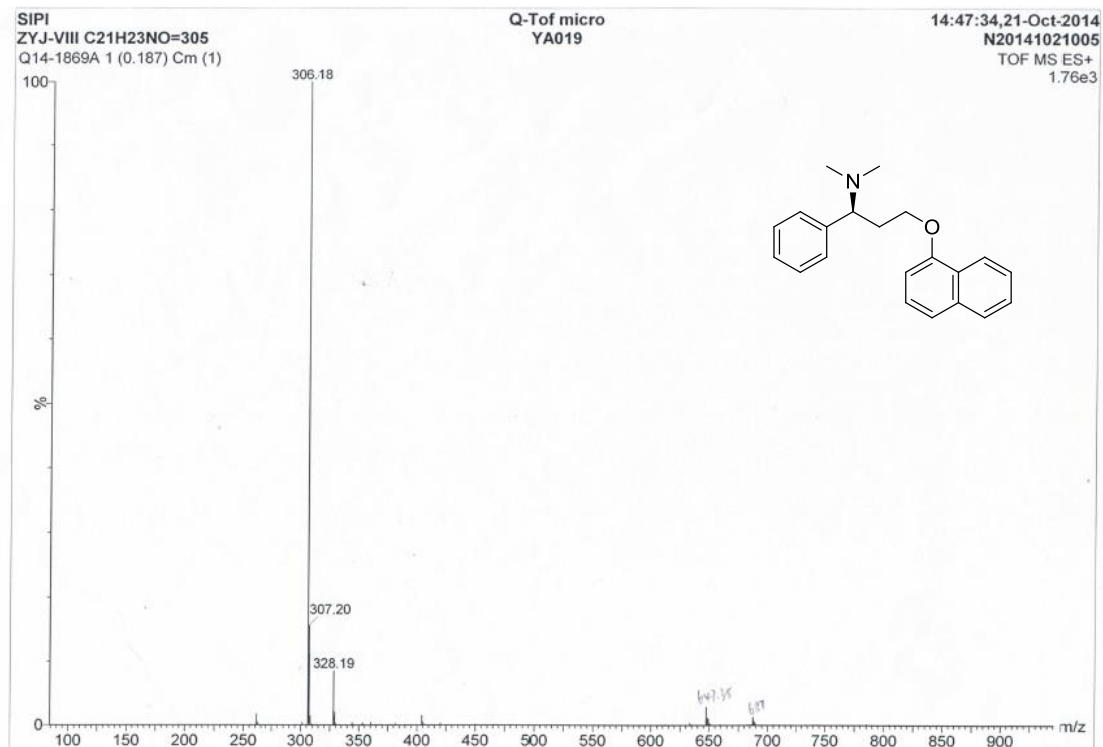
ESIMS spectrum of compound 6



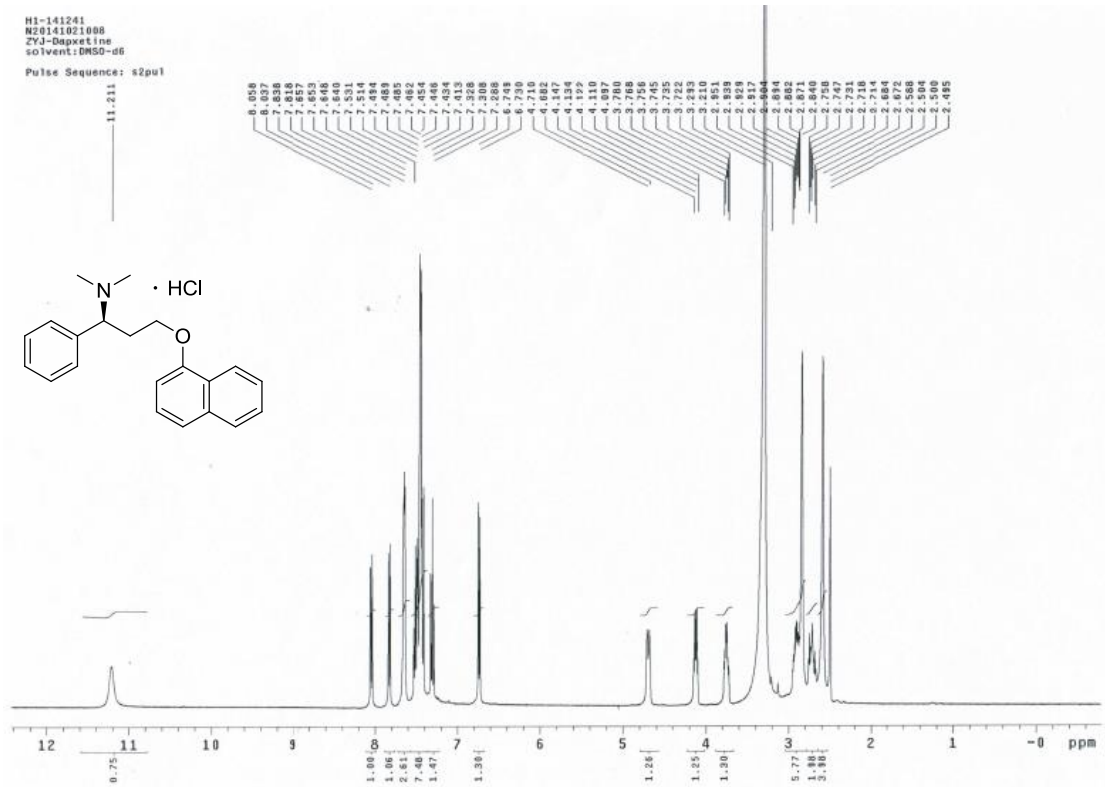
¹H NMR spectrum of compound 7



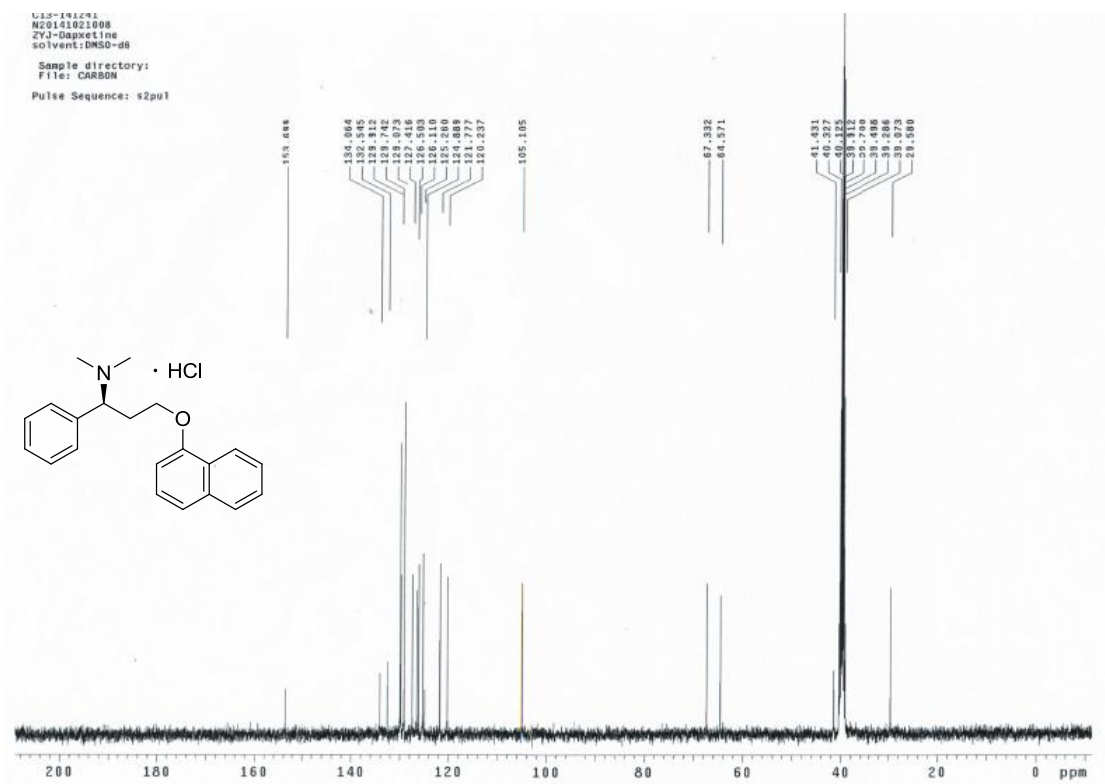
^{13}C NMR spectrum of compound 7



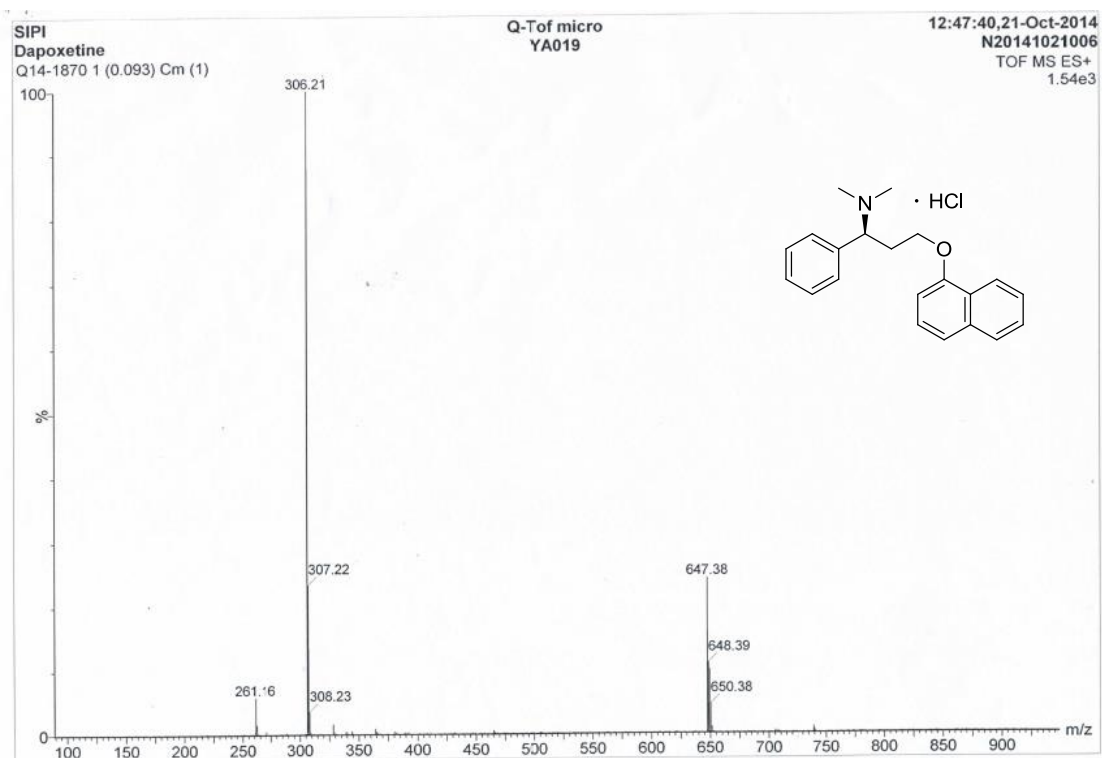
ESIMS spectrum of compound 7



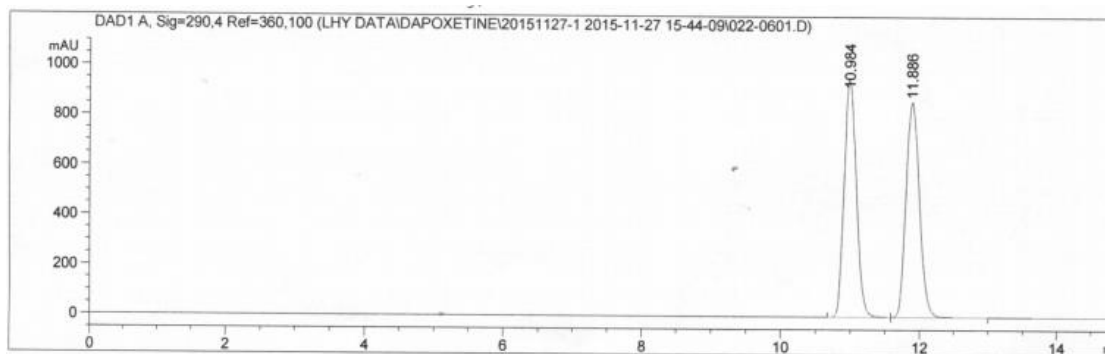
¹H NMR spectrum of compound 1



¹³C NMR spectrum of compound 1



ESIMS spectrum of compound **1**



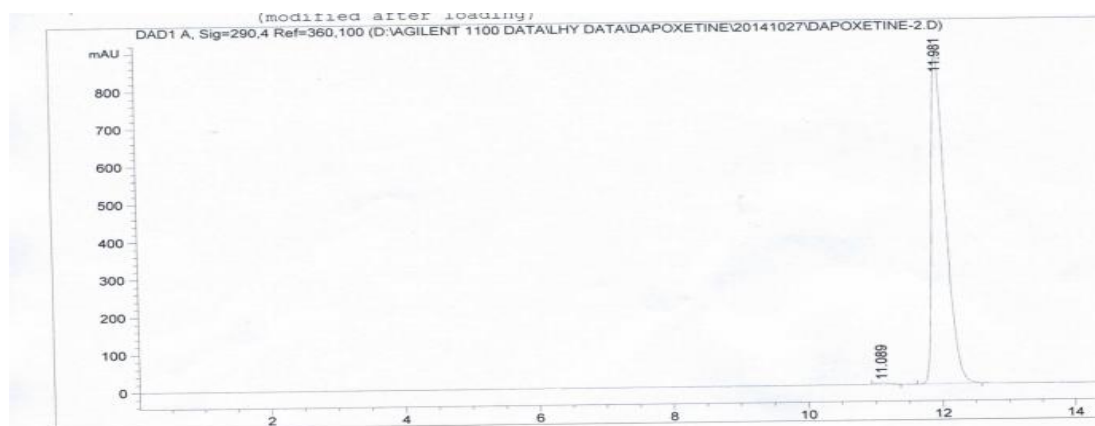
=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=290,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.984	BB	0.1886	1.14817e4	952.94586	49.9049
2	11.886	BB	0.2081	1.15254e4	861.45459	50.0951

Chiral HPLC of Racemic-7



=====
 Area Percent Report
 =====

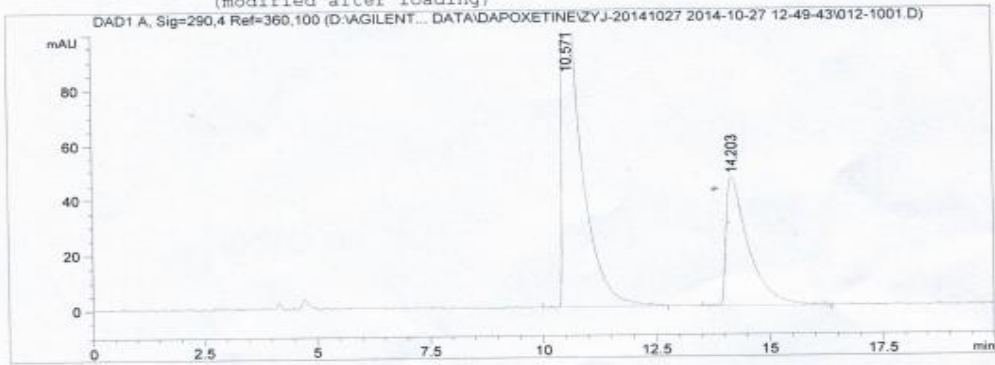
Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=290,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.089	BB	0.1448	47.24658	4.21311	0.3667
2	11.981	BB	0.2249	1.28360e4	876.36298	99.6333

Chiral HPLC of 7

Last changed : 10/27/2014 12:48:24 PM by LHY
 Analysis Method : D:\AGILENT 1100 DATA\METHODS\P_TADALAFIL_对映体和非对映体.M
 Last changed : 12/3/2014 8:54:22 AM by lxr
 (modified after loading)



Area Percent Report

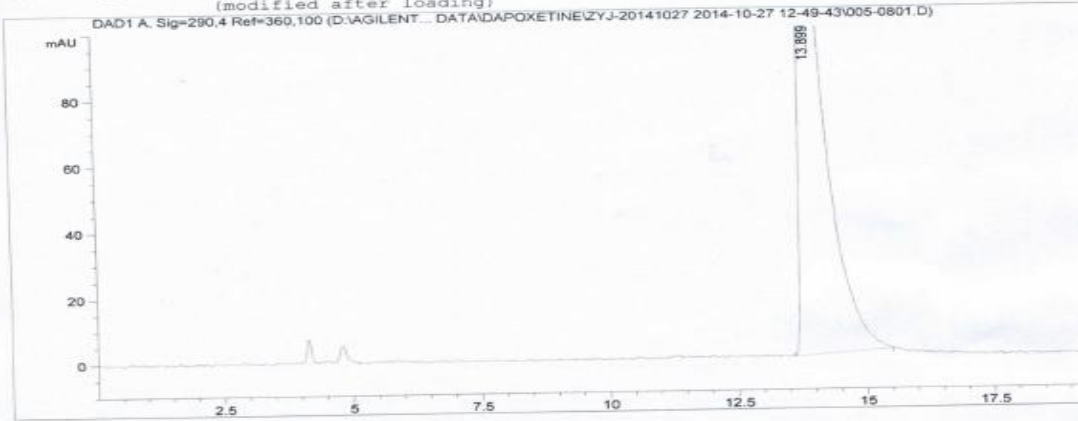
Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=290,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.571	BB	0.3648	3743.35107	145.16963	70.0842
2	14.203	BB	0.4891	1597.87012	46.47349	29.9158

Mixed Sample of (R)-1 and (S)-1

Last changed : 10/27/2014 12:48:24 PM by LHY
 Analysis Method : D:\AGILENT 1100 DATA\LHY DATA\DAPOXETINE\ZYJ-20141027 2014-10-27 12-49-43
 \005-0801.D\DA.M (DAPOXETINE_TEST_8.M, From Data File)
 Last changed : 12/3/2014 8:49:13 AM by lxr
 (modified after loading)



Area Percent Report

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=290,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.899	BB	0.4288	5424.02246	177.34618	100.0000

Chiral HPLC of 1