

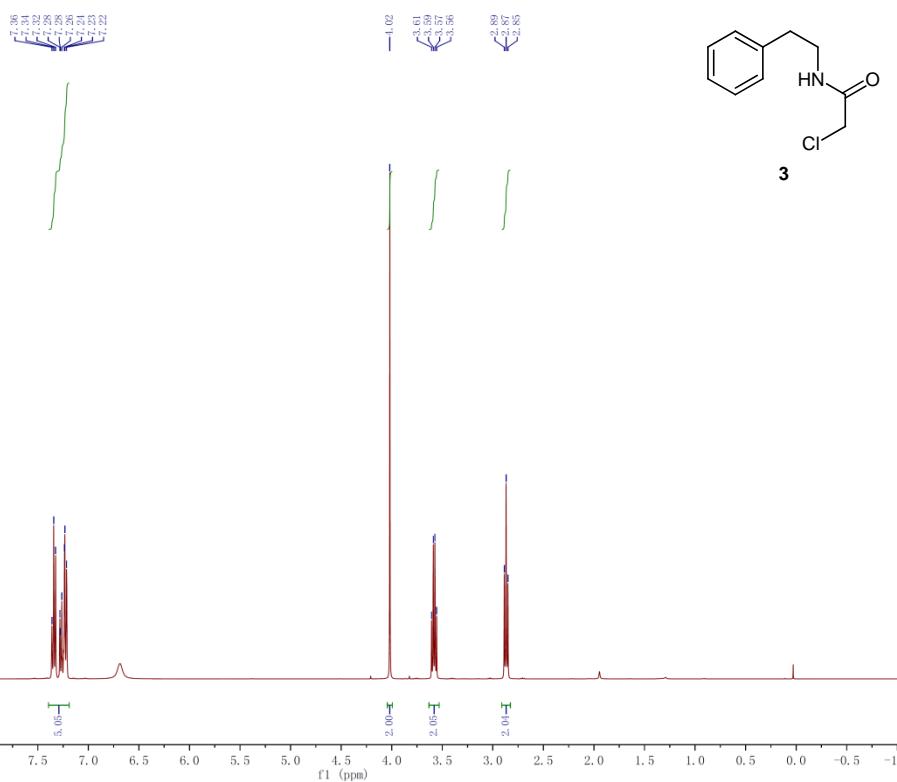
Supporting Information

A CONCISE AND HIGHLY EFFICIENT SYNTHESIS OF PRAZIQUANTEL AS AN ANTHELMINTIC DRUG

Zhezhou Yang, Lin Zhang, Huirong Jiao, Rusheng Bao, Weiwei Xu, and Fuli Zhang*

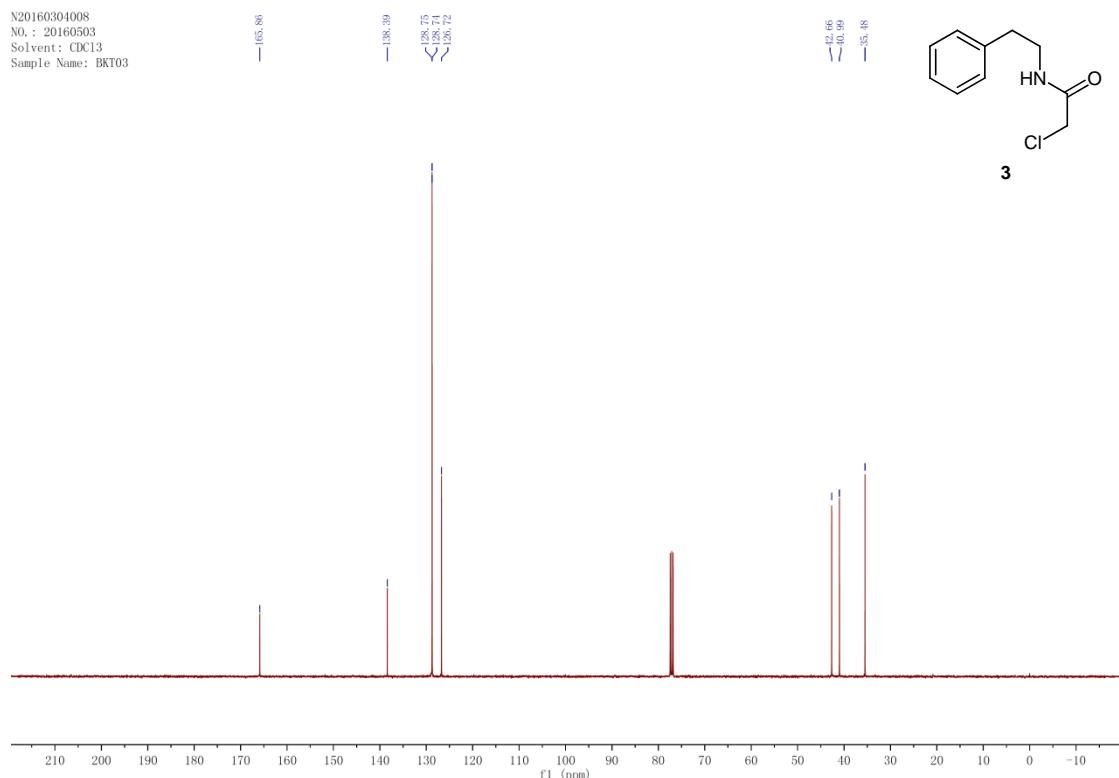
*Shanghai Institute of Pharmaceutical Industry, China State Institute of Pharmaceutical Industry,
285 Gebaini Road, Shanghai 201203, China; zhangfuli1@sinopharm.com

N20160304008
No.: 20160503
Solvent: CDCl₃
Sample Name: BKT03

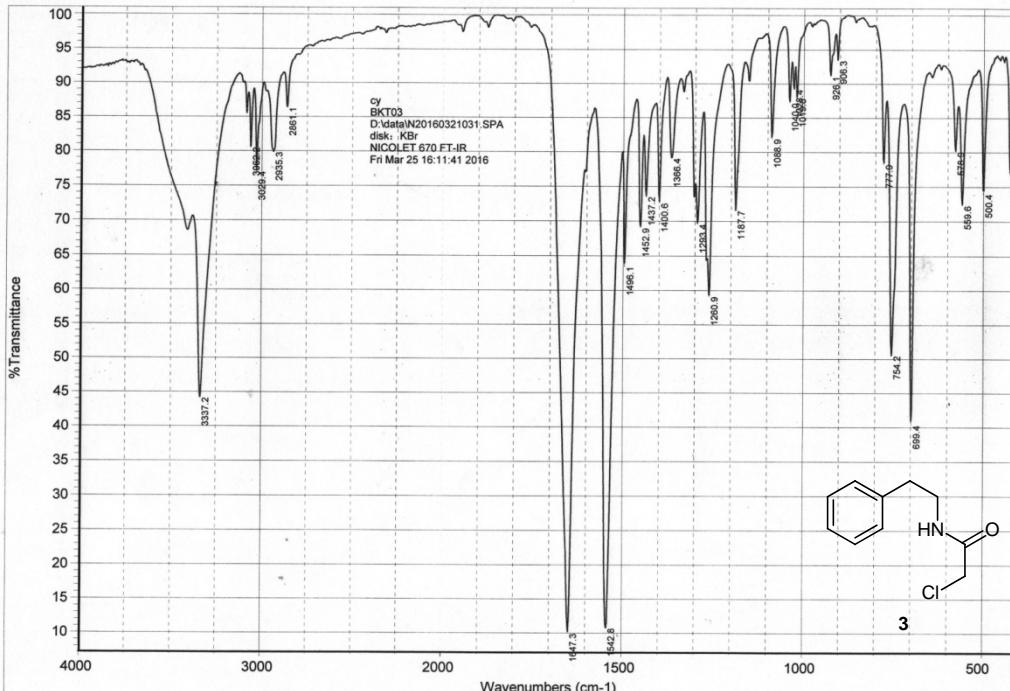


¹H NMR spectrum of 2-chloro-N-phenethylacetamide (3) (400 MHz, CDCl₃)

N20160304008
No.: 20160503
Solvent: CDCl₃
Sample Name: BKT03



¹³C NMR spectrum of 2-chloro-N-phenethylacetamide (3) (100 MHz, CDCl₃)



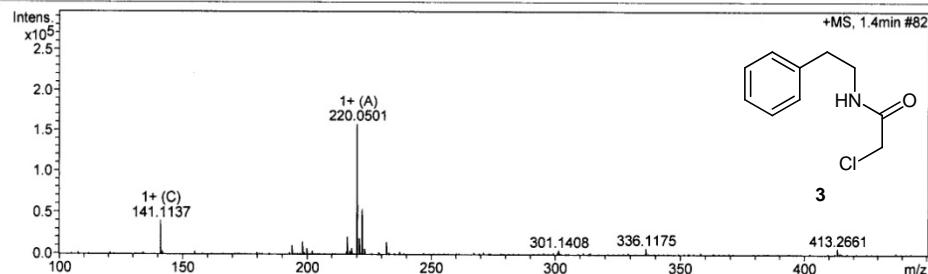
FT-IR spectrum of 2-chloro-N-phenethylacetamide (3)

Mass Spectrum SmartFormula Report

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Analysis Name	D:\Data\SHUJVFENXI\ZHANGFL-group\BKT-03_RE1_01_4720.d		
Method	20150915.m	Operator	BDAL@DE
Sample Name	BKT-03	Instrument / Ser#	maXis 4G 21240
Comment			

Acquisition Parameter

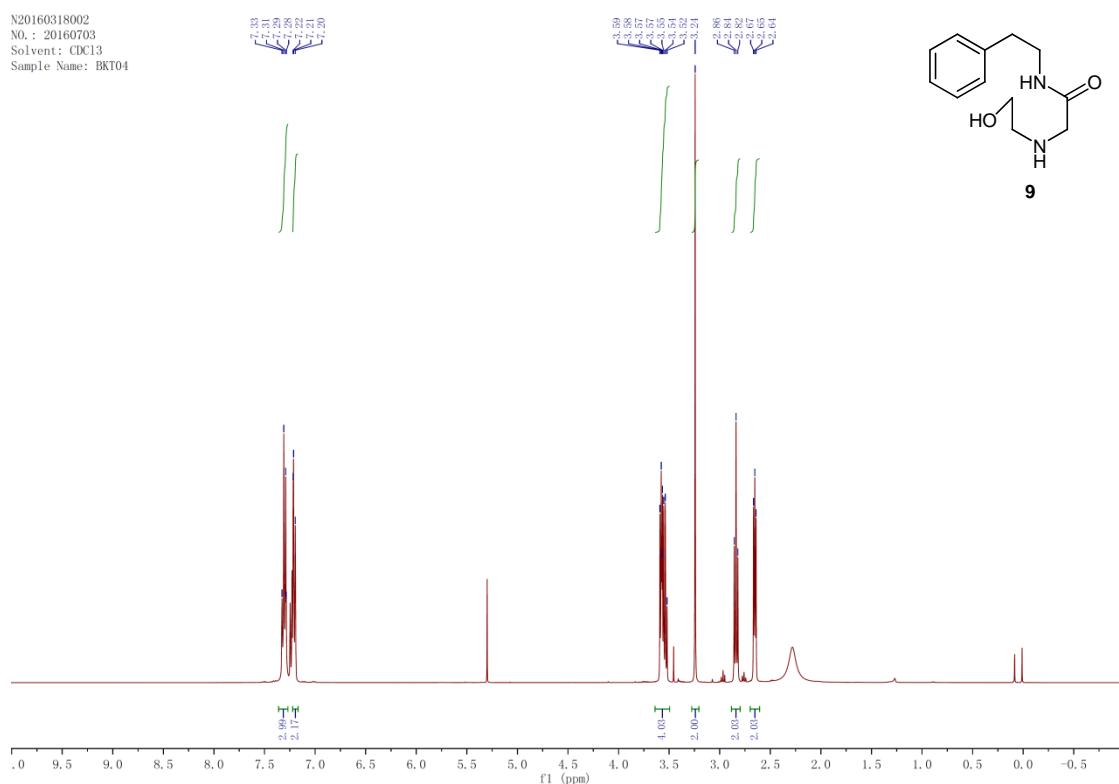
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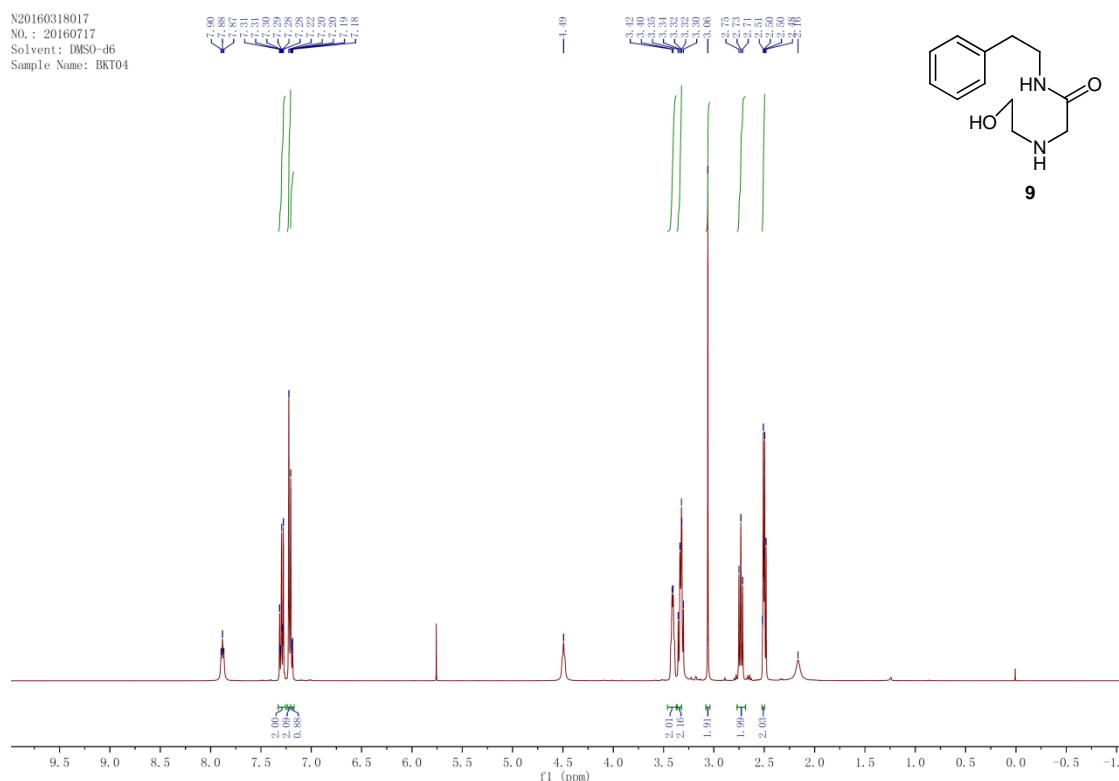
HRMS spectrum of 2-chloro-N-phenethylacetamide (3)

N20160318002
NO. : 20160703
Solvent: CDCl₃
Sample Name: BKT04



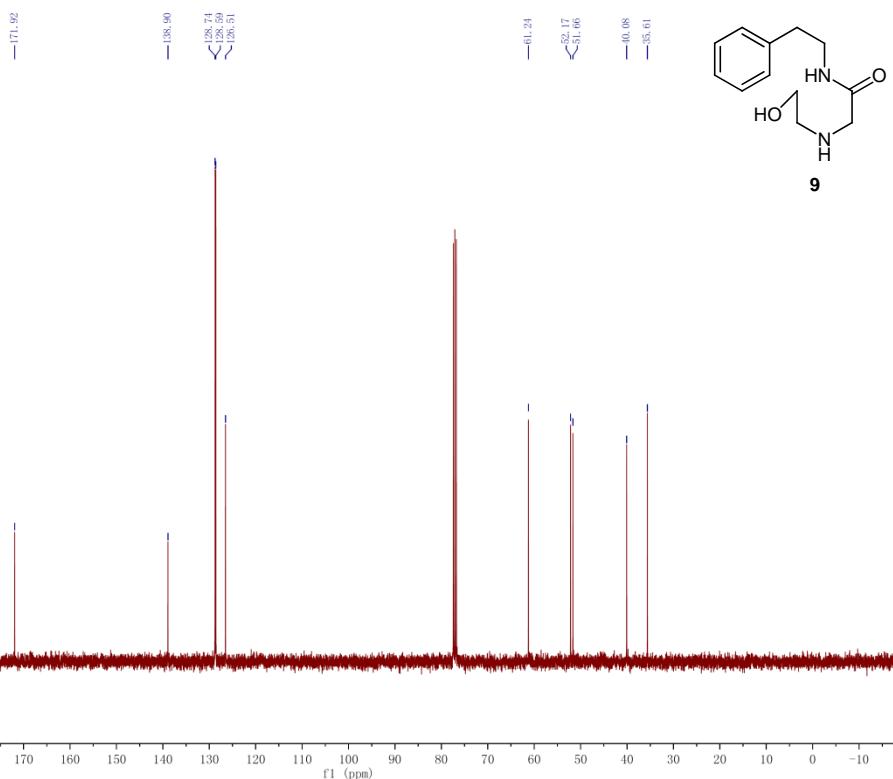
¹H NMR spectrum of 2-(2-hydroxyethylamino)-N-phenethylacetamide (9) (400 MHz, CDCl₃)

N20160318017
NO. : 20160717
Solvent: DMSO-d6
Sample Name: BKT04

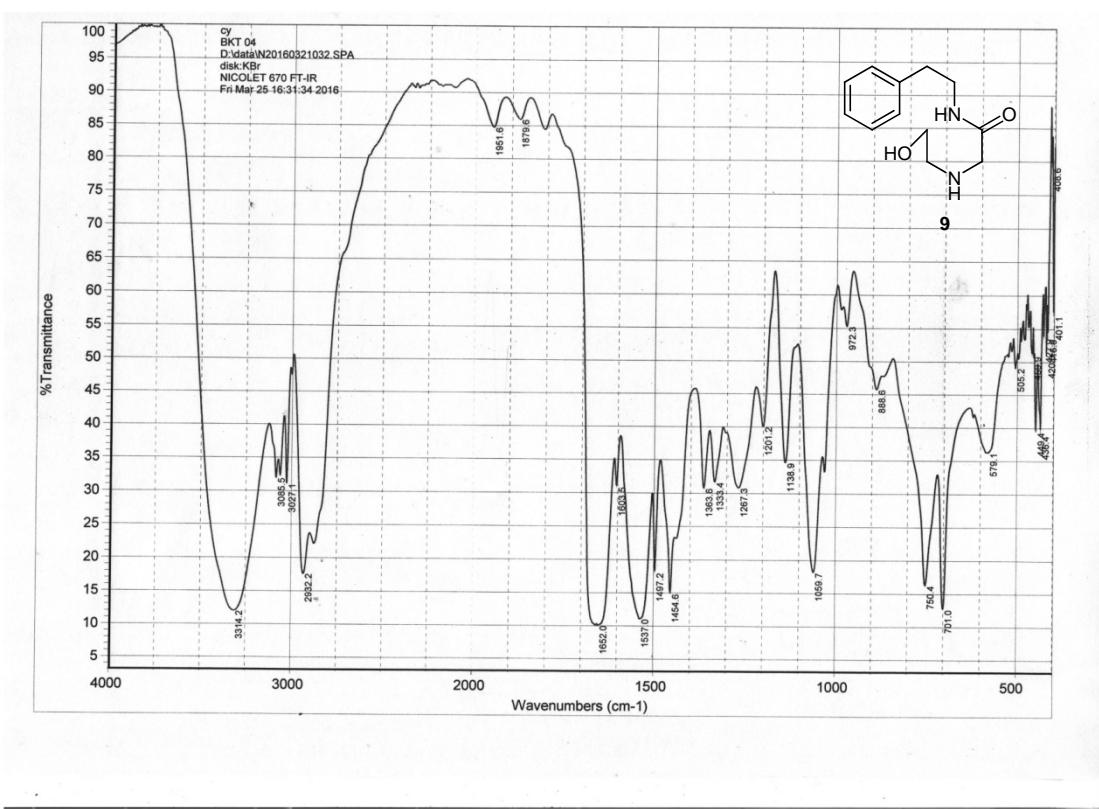


¹H NMR spectrum of 2-(2-hydroxyethylamino)-N-phenethylacetamide (9) (400 MHz, DMSO-d₆)

N20160318002
No. : 20160703
Solvent: CDCl₃
Sample Name: BKT04



¹³C NMR spectrum of 2-(2-hydroxyethylamino)-N-phenethylacetamide (9) (100 MHz, CDCl₃)



FT-IR spectrum of 2-(2-hydroxyethylamino)-N-phenethylacetamide (9)

Mass Spectrum SmartFormula Report

Analysis Info

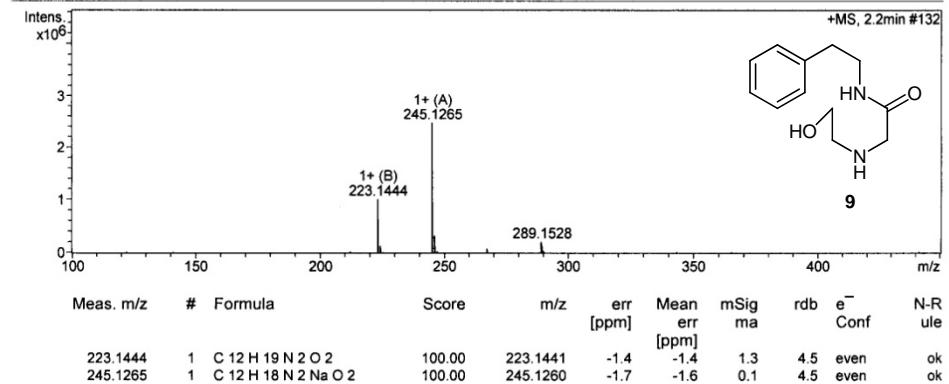
Analysis Name D:\Data\SHUJVFENXI\ZHANGFL-group\BKT-04_RA2_01_4954.d
 Method 20150915.m
 Sample Name BKT-04
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Acquisition Date 3/28/2016 2:19:57 PM

 Operator BDAL@DE
 Instrument / Ser# maXis 4G 21240

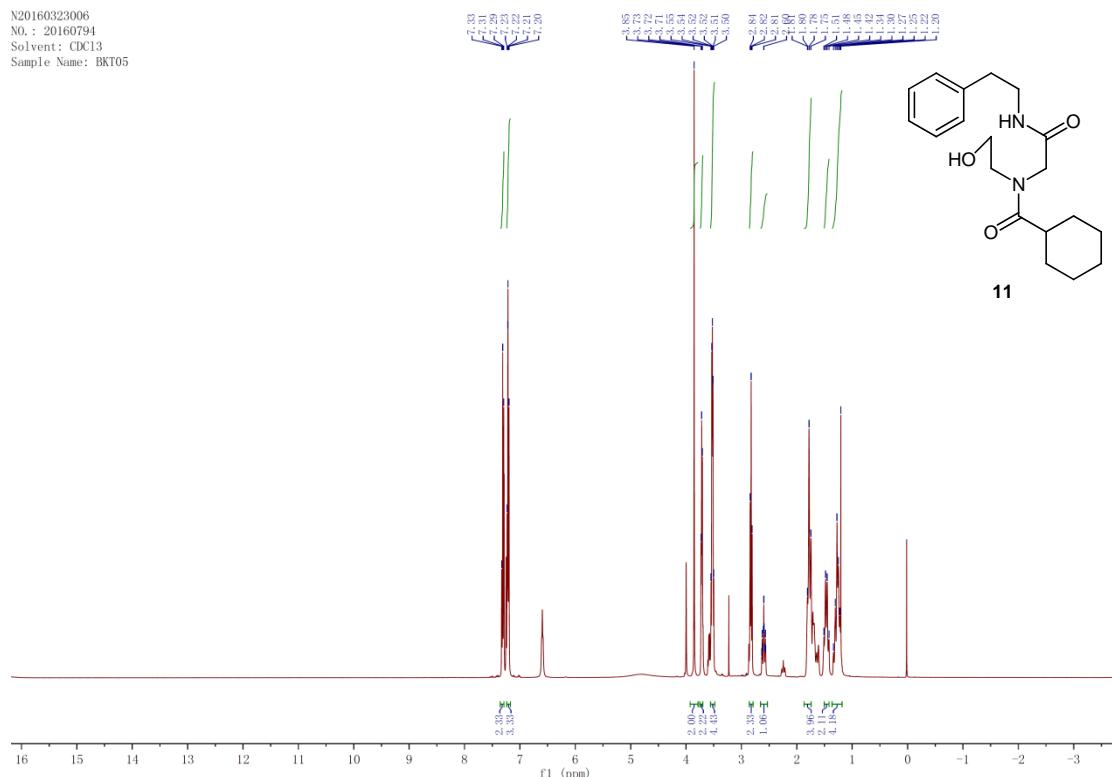
Acquisition Parameter

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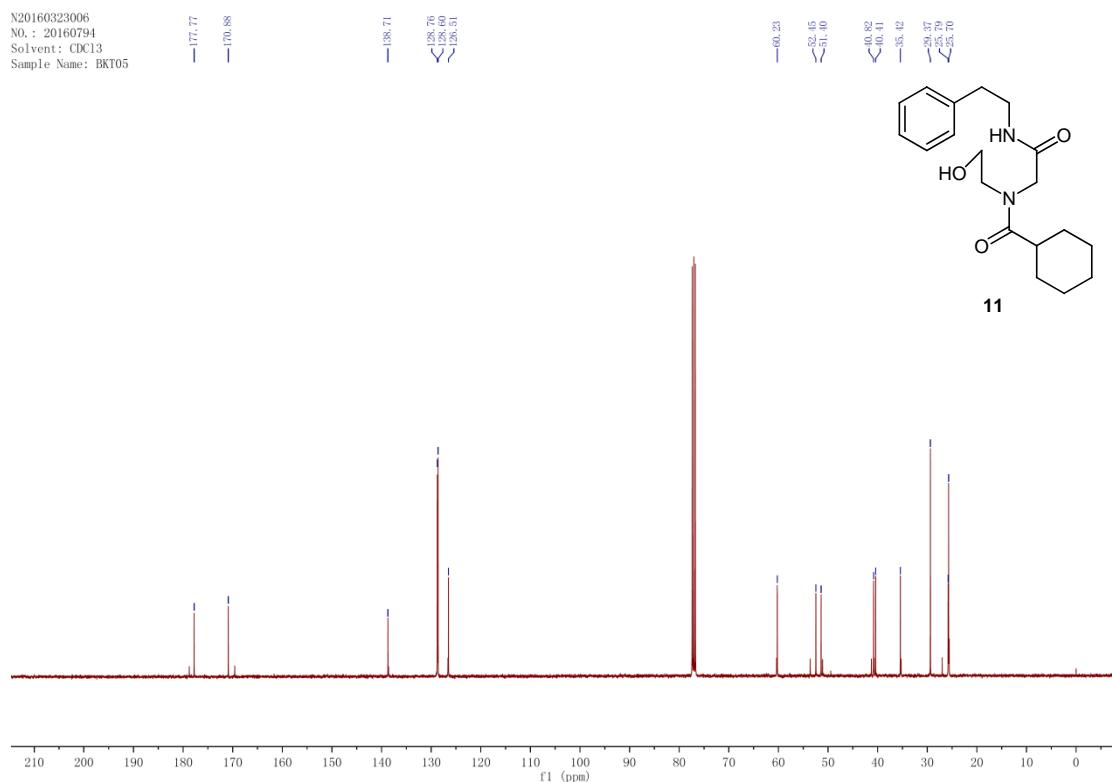
HRMS spectrum of 2-(2-hydroxyethylamino)-N-phenethylacetamide (9)

N20160323006
 NO. : 20160794
 Solvent: CDCl₃
 Sample Name: BKT05

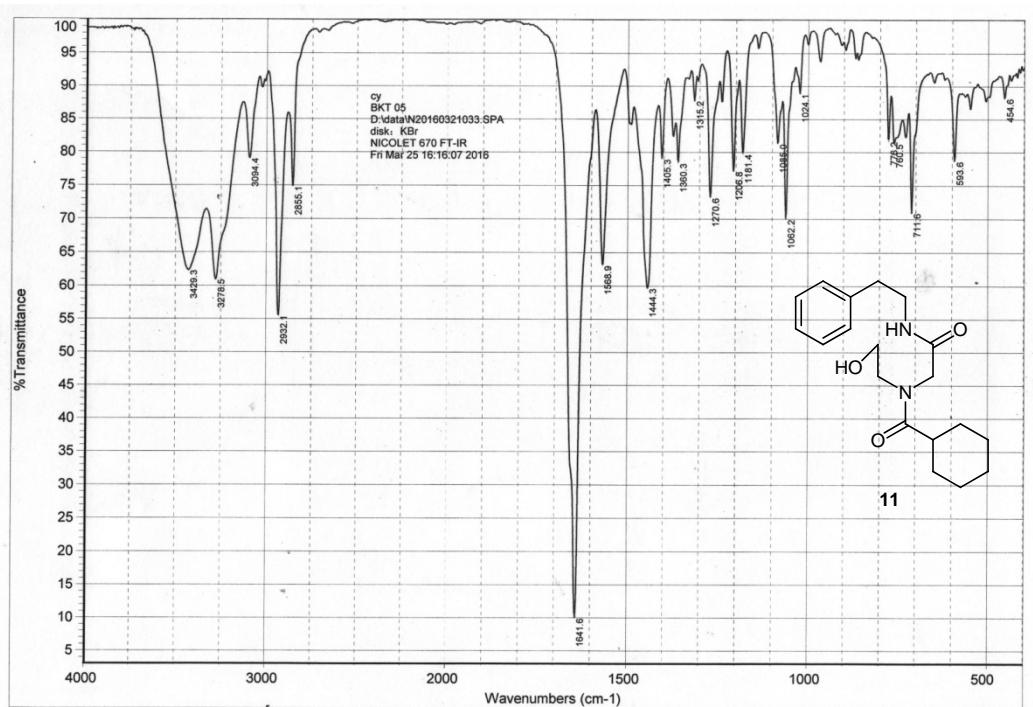


¹H NMR spectrum of N-(2-hydroxyethyl)-N-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamide (11) (400 MHz, CDCl₃)

N20160323006
No. : 20160794
Solvent: CDCl₃
Sample Name: BKT05



¹³C NMR spectrum of *N*-(2-hydroxyethyl)-*N*-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamide (11) (100 MHz, CDCl₃)



FT-IR spectrum of *N*-(2-hydroxyethyl)-*N*-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamide (11)

Mass Spectrum SmartFormula Report

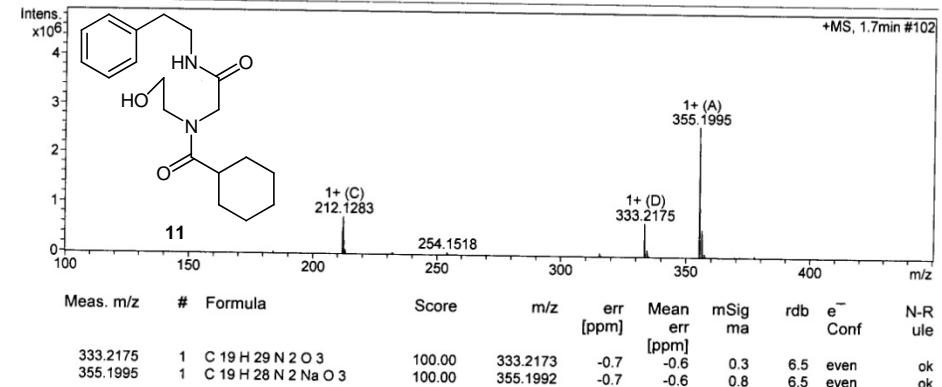
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 Sample Name BKT-05
 Comment

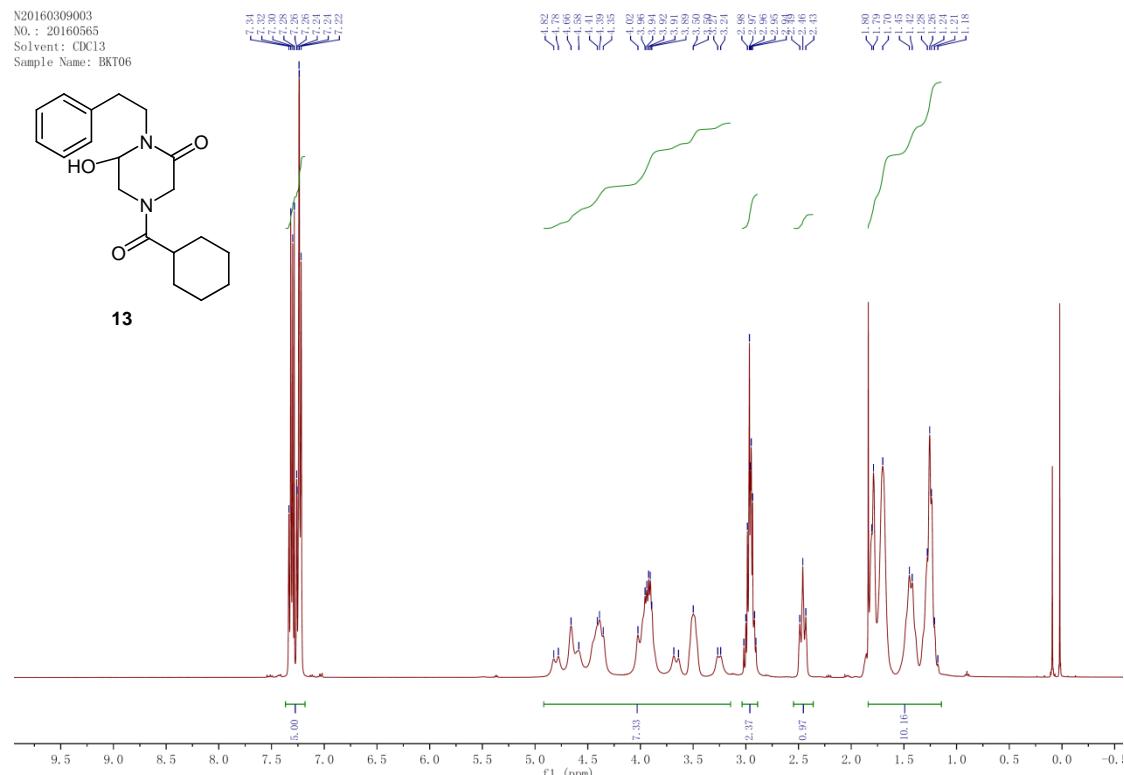
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 Instrument / Ser# maXis 4G 21240

Acquisition Parameter

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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste

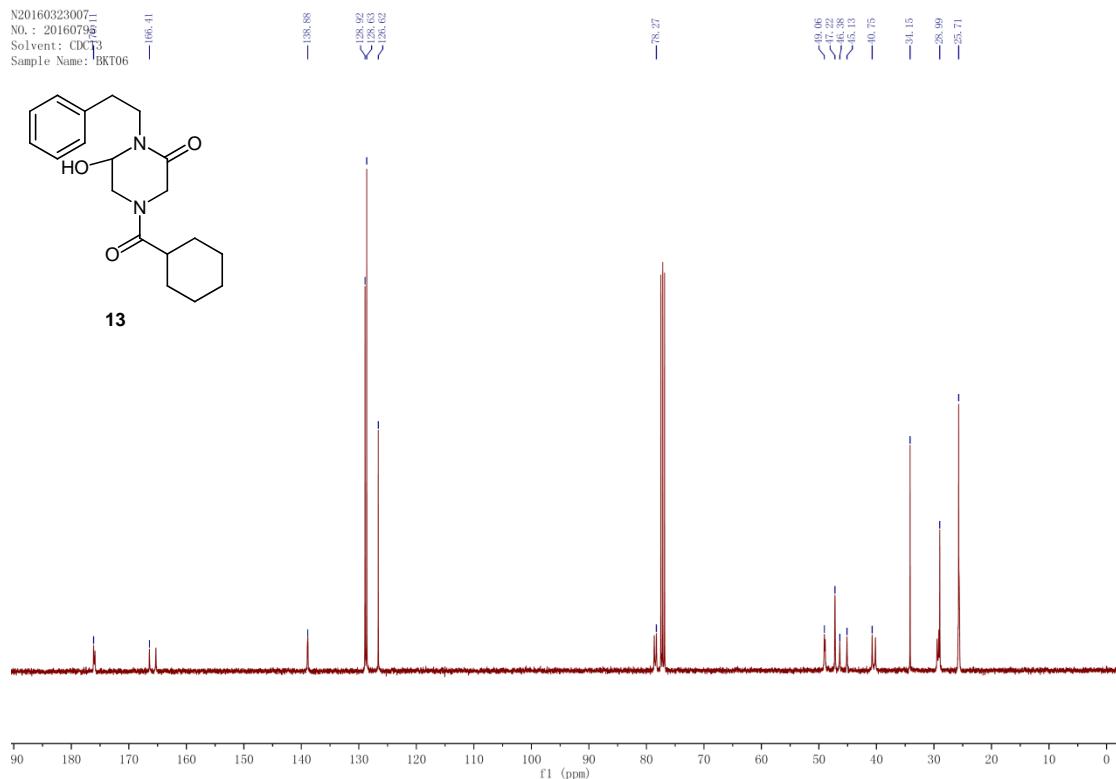
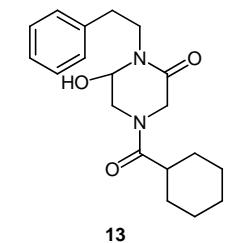


HRMS spectrum of *N*-(2-hydroxyethyl)-*N*-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarbamate (11)



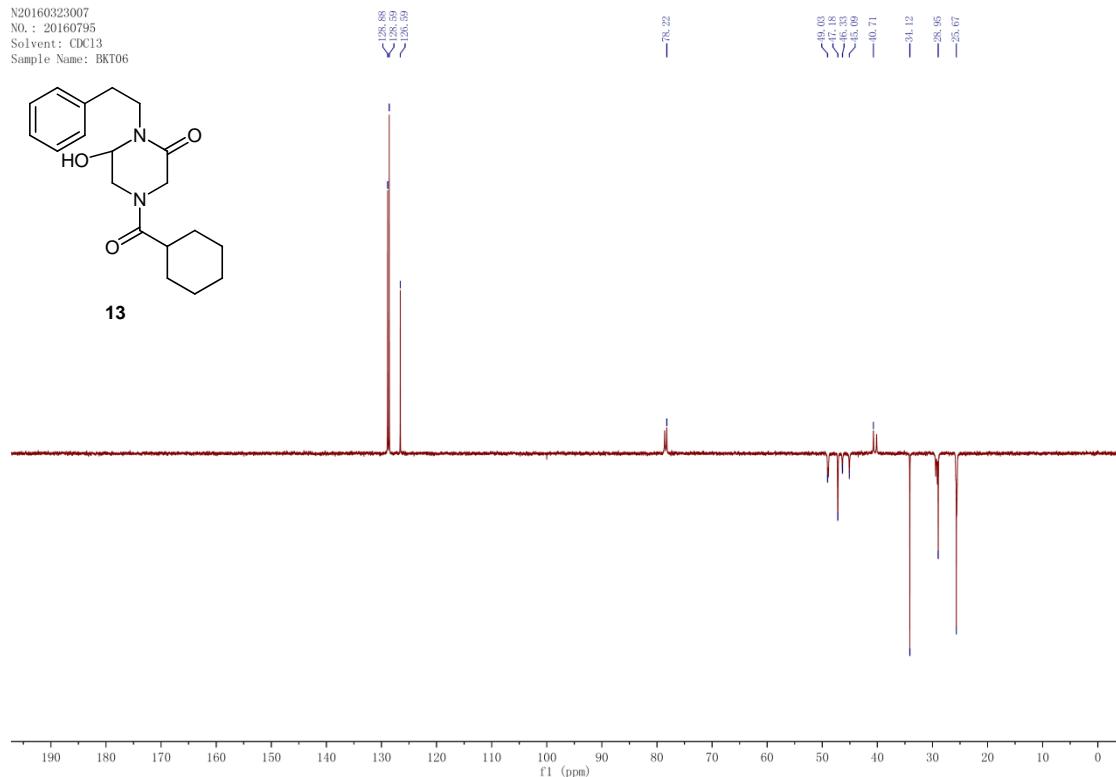
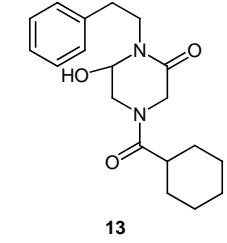
¹H NMR spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13) (400 MHz, CDCl₃)

N20160323007
No.: 20160795
Solvent: CDCl₃
Sample Name: BKT06



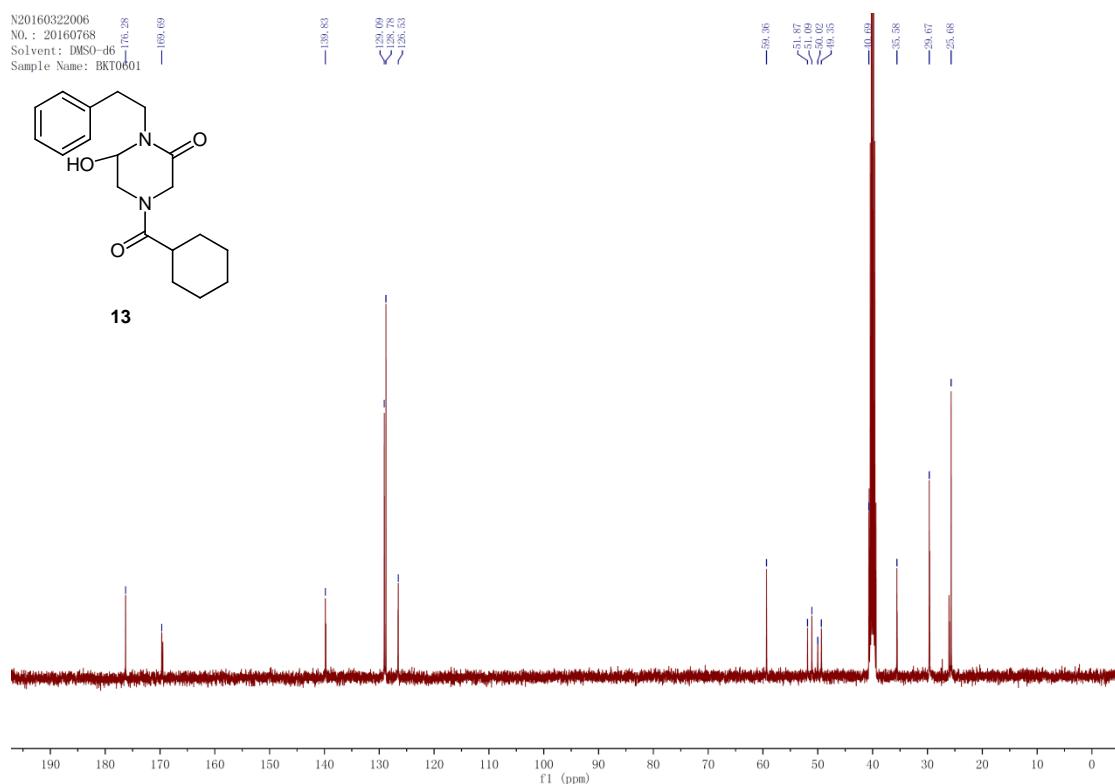
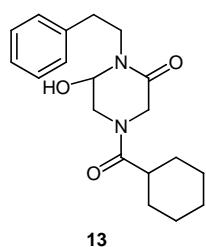
¹³C NMR spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13) (100 MHz, CDCl₃)

N20160323007
No.: 20160795
Solvent: CDCl₃
Sample Name: BKT06

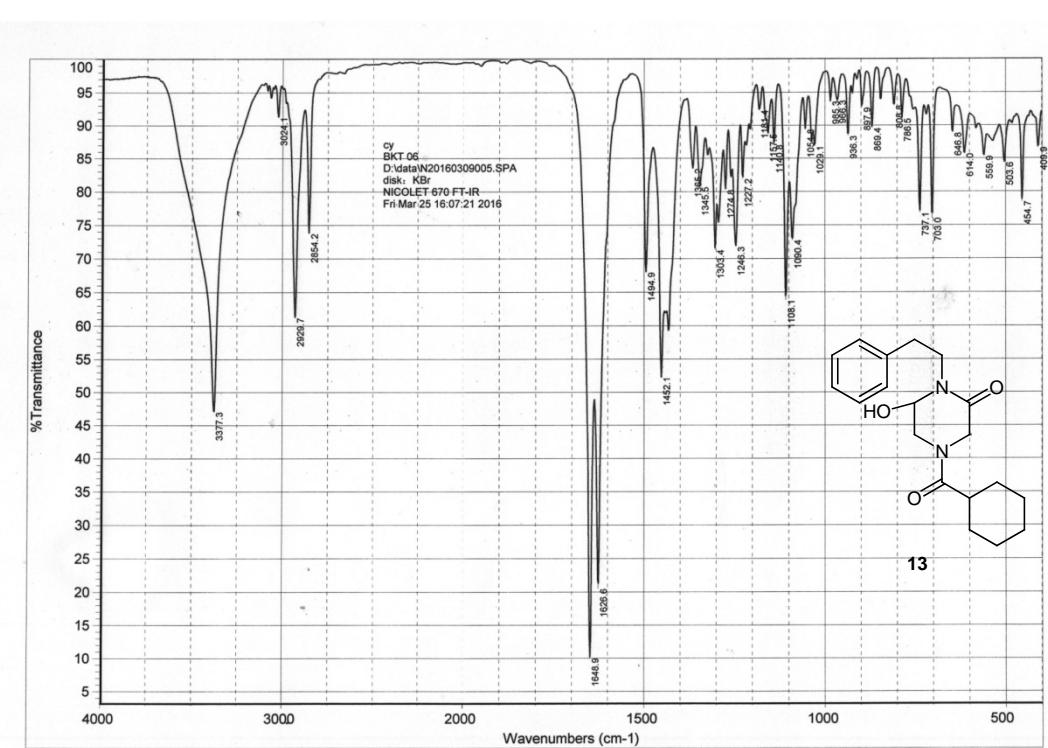


DEPT spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13) (100 MHz, CDCl₃)

N201603222006
 No. : 20160768
 Solvent: DMSO-d6 — (76.28)
 Sample Name: BKT0601 — (89.69)



¹³C NMR spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13) (100 MHz, DMSO-d6)



FT-IR spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13)

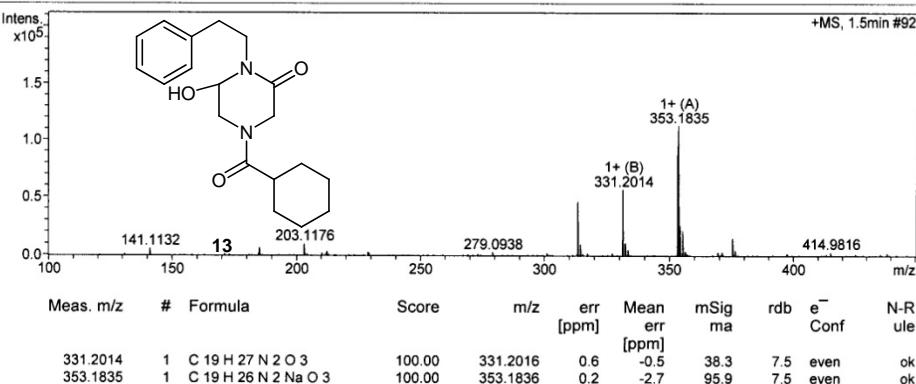
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\SHUJVFENXI\ZHANGFL-group\BKT-06_RE3_01_4722.d	Acquisition Date	3/15/2016 10:39:33 AM
Method	20150915.m	Operator	BDAL@DE
Sample Name	BKT-06	Instrument / Ser#	maXis 4G 21240
Comment			

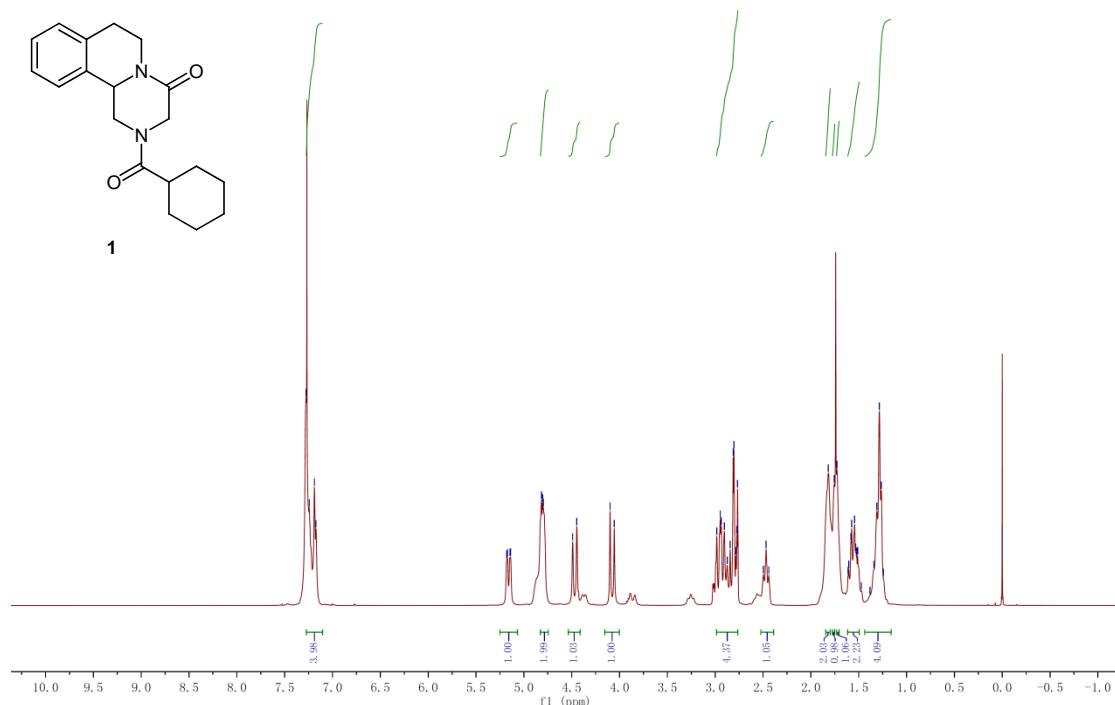
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste

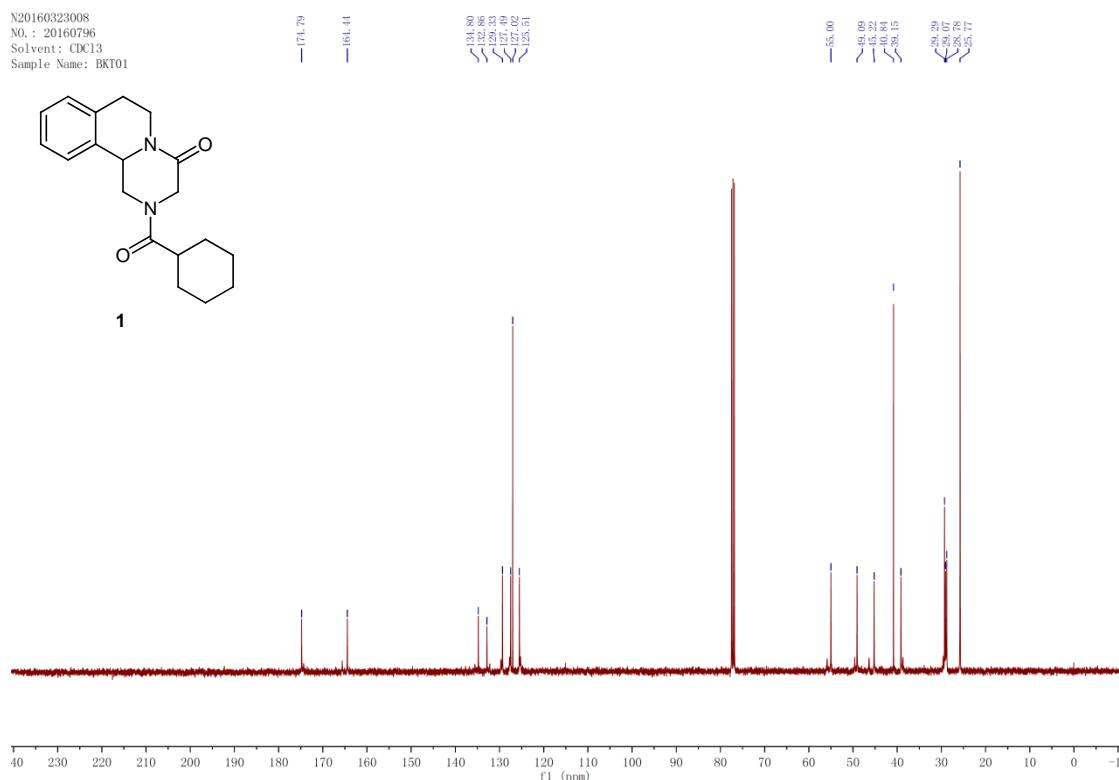
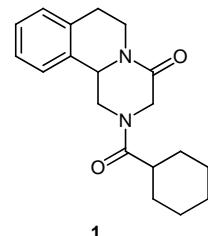


HRMS spectrum of 4-(cyclohexanecarbonyl)-6-hydroxy-1-phenethylpiperazin-2-one (13)

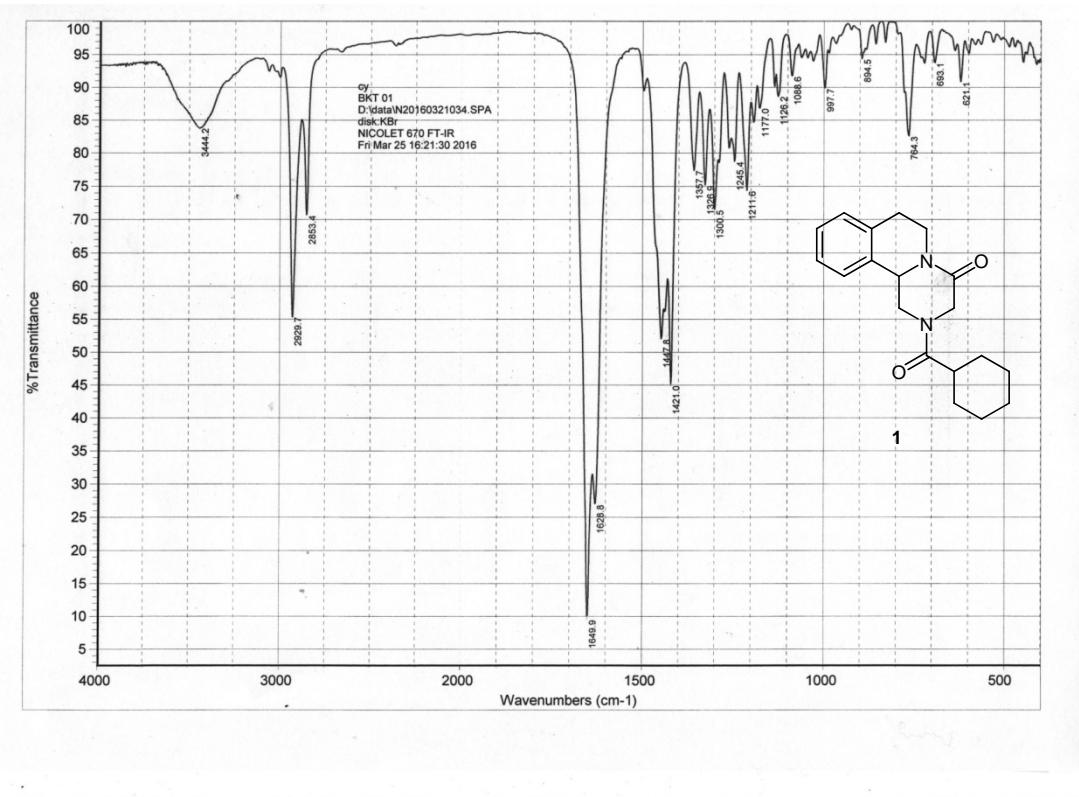
N20160323008
No. : 20160796
Solvent: CDCl₃
Sample Name: BKT01



N20160323008
NO. : 20160796
Solvent: CDCl₃
Sample Name: BKT01



¹³C NMR spectrum of 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one (**1**) (100 MHz, CDCl₃)



FT-IR spectrum of 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one (**1**)

Mass Spectrum SmartFormula Report

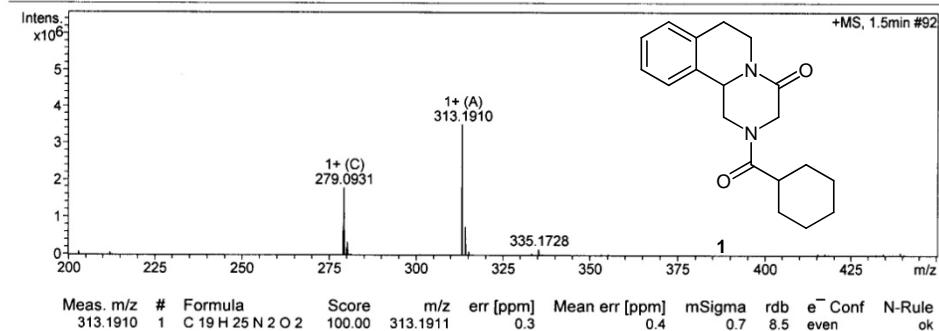
Analysis Info

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 Method 20150915.m
 Sample Name BKT-01
 Comment

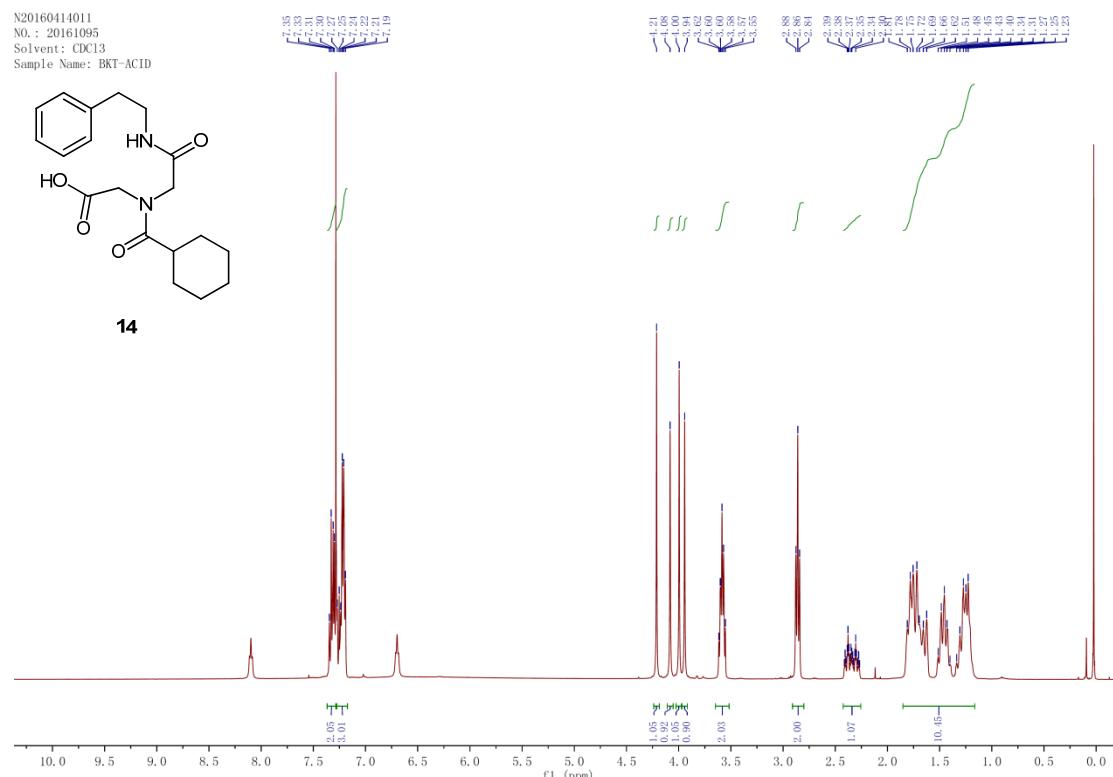
Acquisition Date 3/15/2016 11:59:24 AM
 Operator BDAL@DE
 Instrument / Ser# maxis 4G 21240

Acquisition Parameter

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 Set Divert Valve Waste

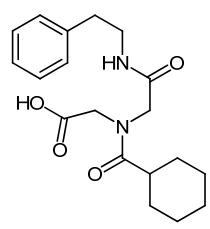


HRMS spectrum of 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one (1)

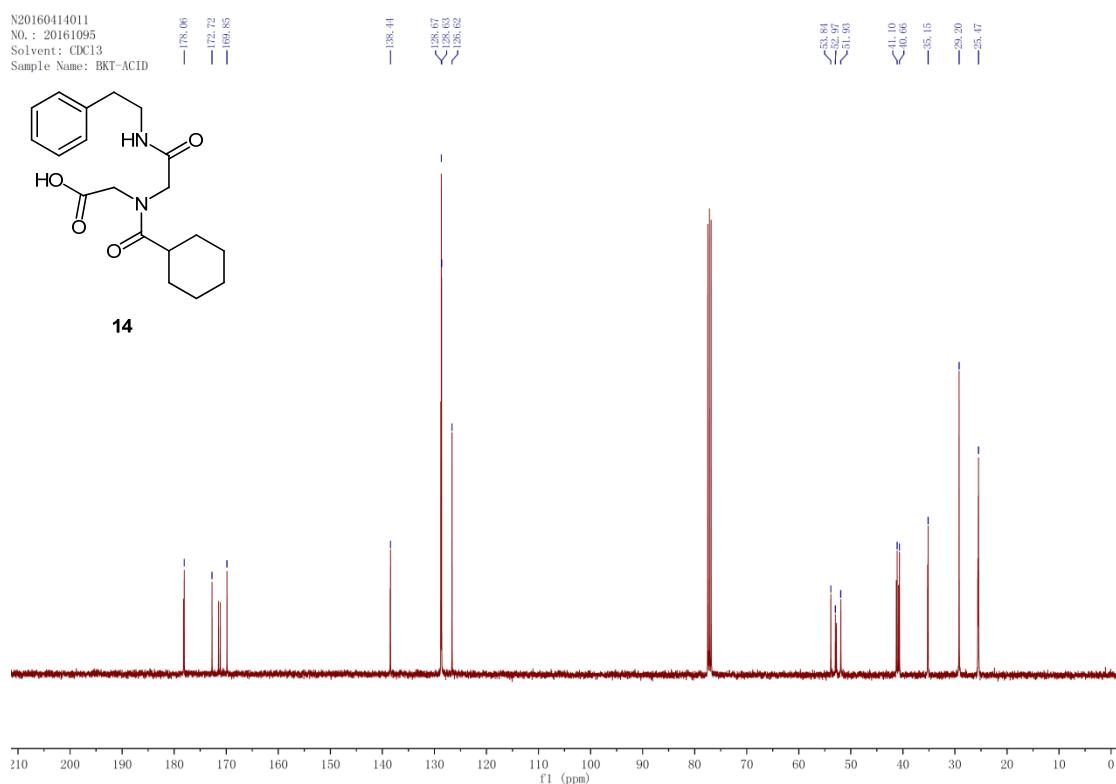


¹H NMR spectrum of 2-(*N*-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamido)acetic acid (14) (400 MHz, CDCl₃)

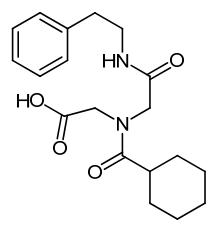
N20160414011
No. : 20161095
Solvent: CDCl₃
Sample Name: BKT-ACID



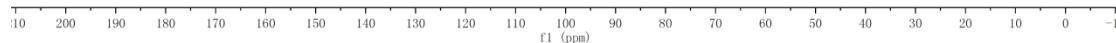
14

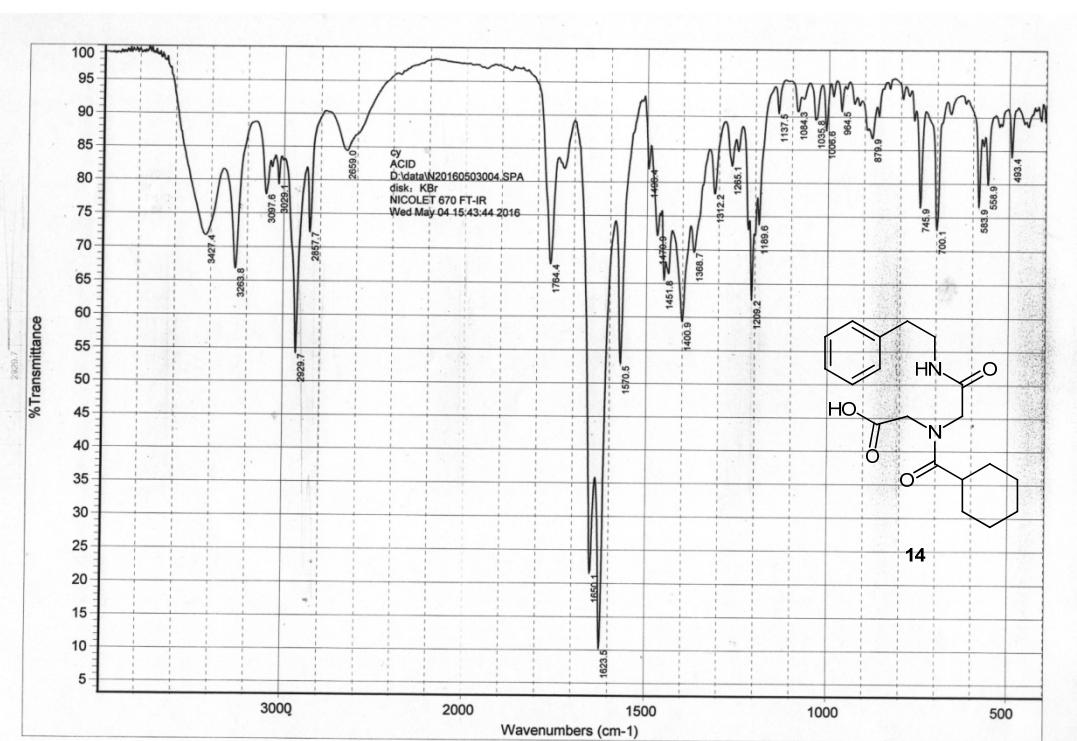


N20160414011
No. : 20161095
Solvent: CDCl₃
Sample Name: BKT-ACID

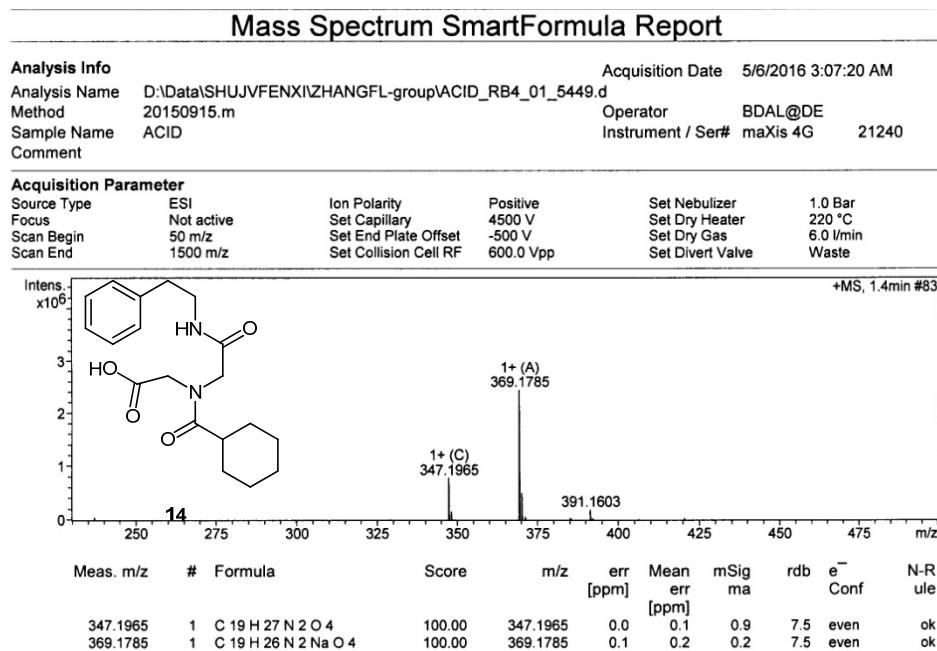


14



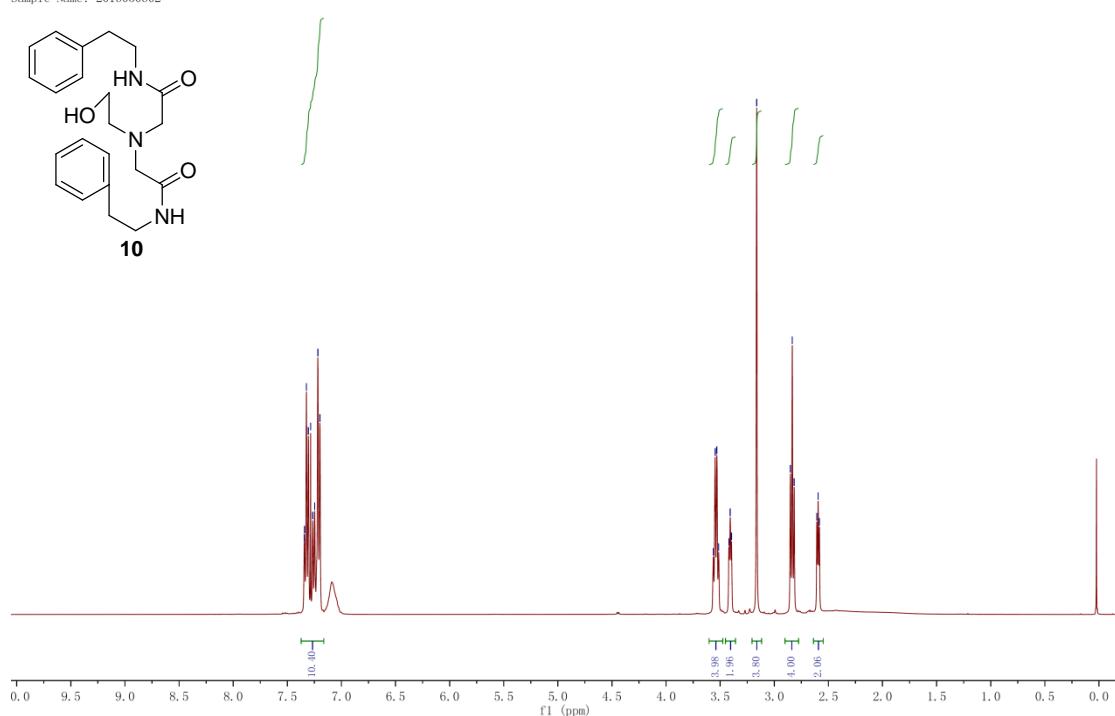


FT-IR spectrum of 2-(N-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamido)acetic acid (14)



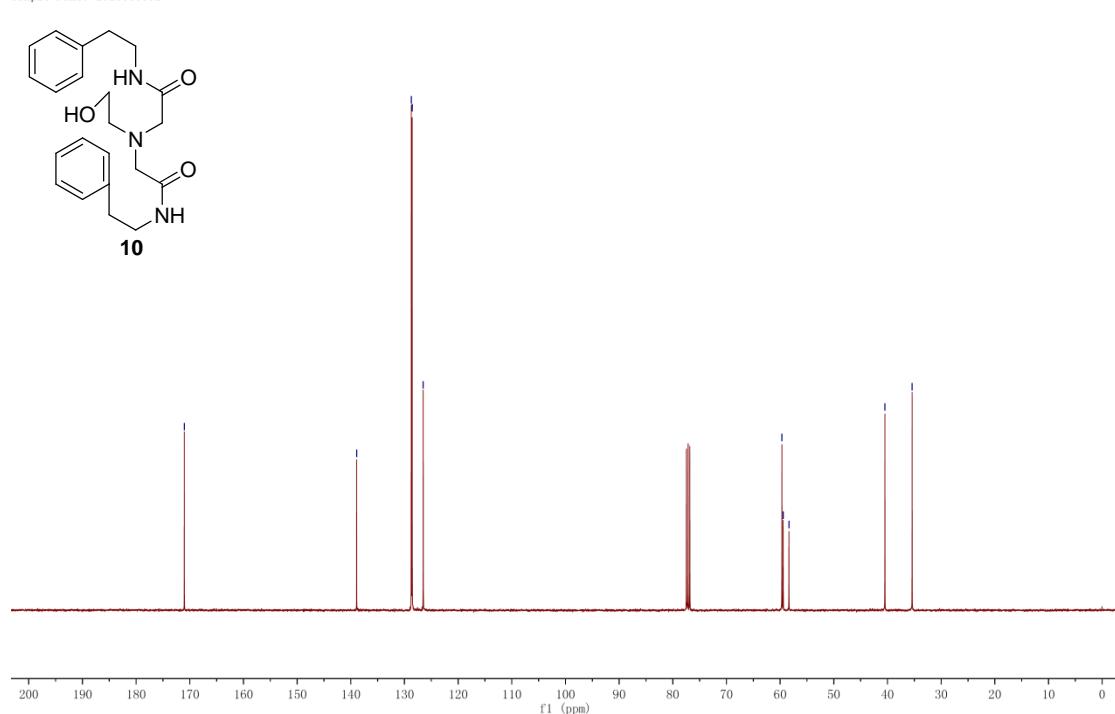
HRMS spectrum of 2-(N-(2-oxo-2-(phenethylamino)ethyl)cyclohexanecarboxamido)acetic acid (14)

N20160506007
No.: 20161376
Solvent: CDCl₃
Sample Name: 2016050602

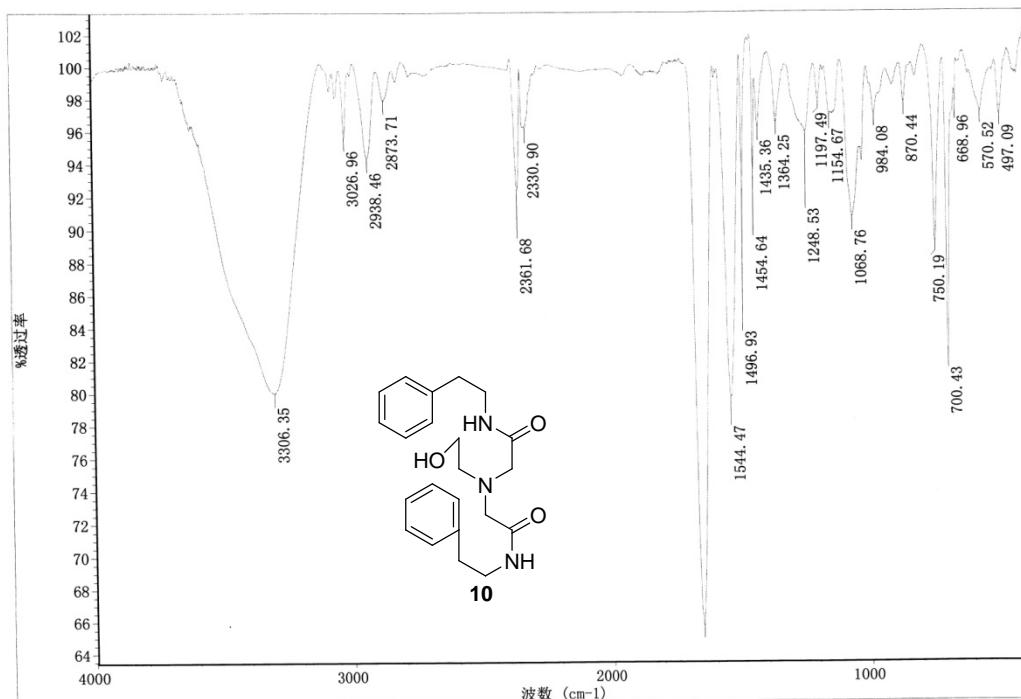


¹H NMR spectrum of 2,2'-(2-hydroxyethylazanediyi)bis(N-phenethylacetamide) (10) (400 MHz, CDCl₃)

N20160506007
No.: 20161376
Solvent: CDCl₃
Sample Name: 2016050602



¹³C NMR spectrum of 2,2'-(2-hydroxyethylazanediyi)bis(N-phenethylacetamide) (10) (100 MHz, CDCl₃)



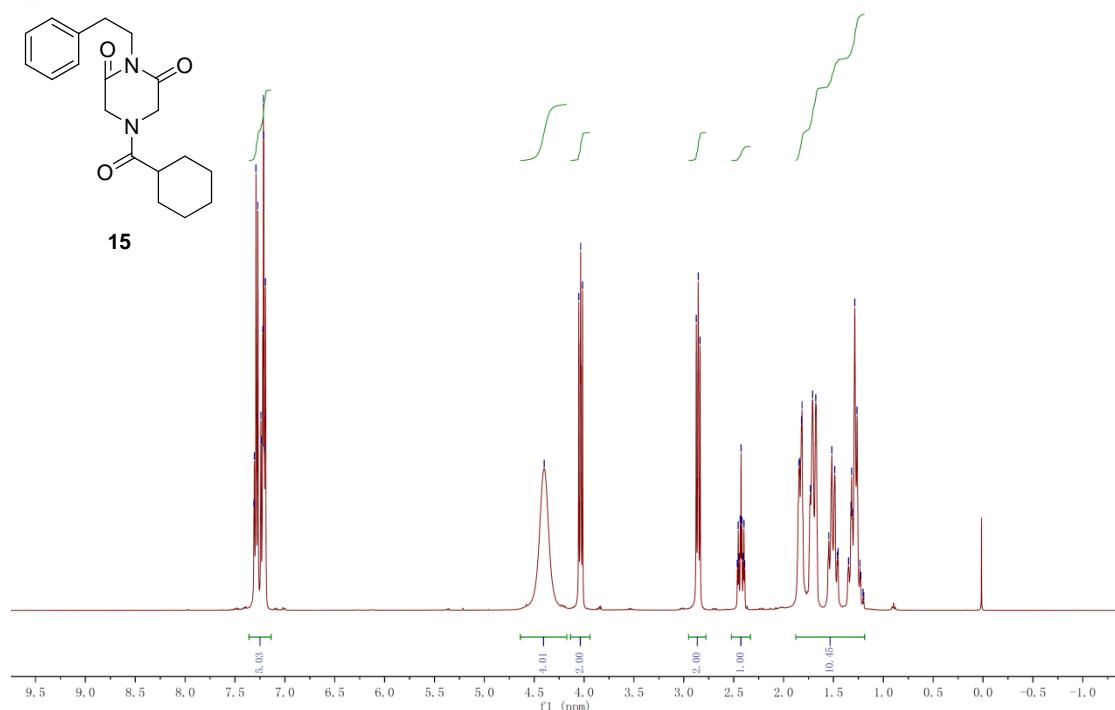
FT-IR spectrum of 2,2'-(2-hydroxyethylazanediyl)bis(N-phenethylacetamide) (**10**)

Mass Spectrum SmartFormula Report

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Comment			
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Set Nebulizer 1.0 Bar Set Dry Heater 220 °C Set Dry Gas 6.0 l/min Set Divert Valve Waste			
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406.2105	1	C 22 H 29 N 3 Na O 3	100.00
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			406.2101 -1.0
			Mean err [ppm]
			1.3 -0.5
			mSig ma
			7.4 2.3
			rdb e⁻ Conf
			9.5 even 9.5 even
			N-R rule
			ok ok

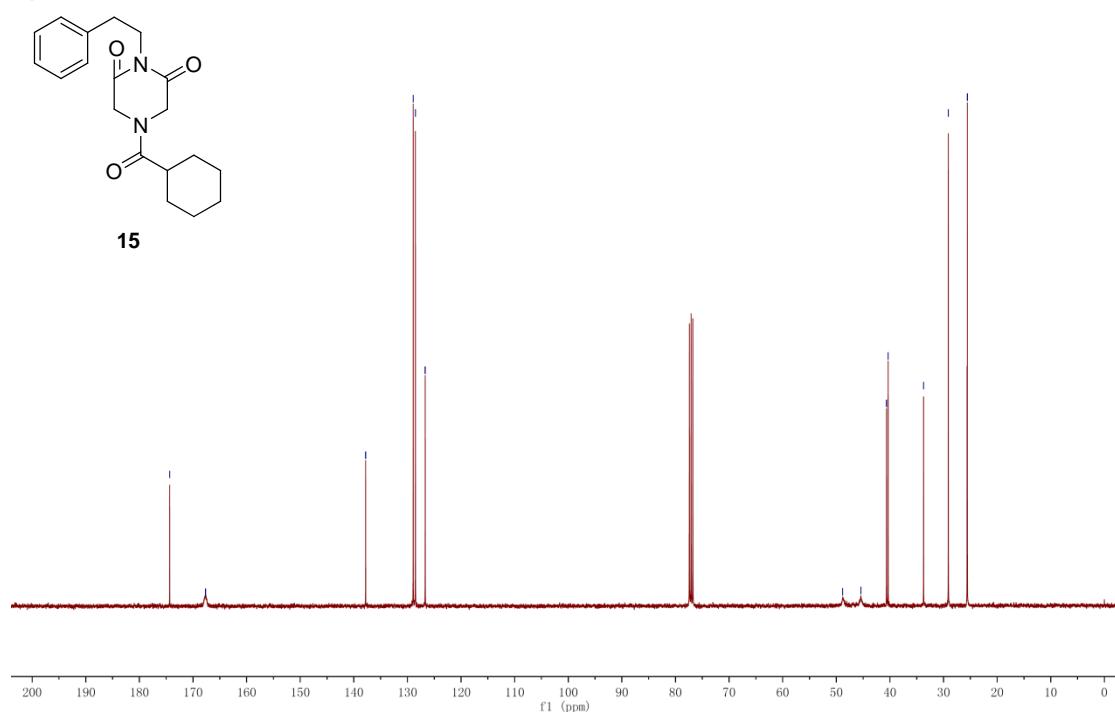
HRMS spectrum of 2,2'-(2-hydroxyethylazanediyl)bis(N-phenethylacetamide) (**10**)

N20160830011
No.: 201612362
Solvent: CDCl₃
Sample Name: 2016083002

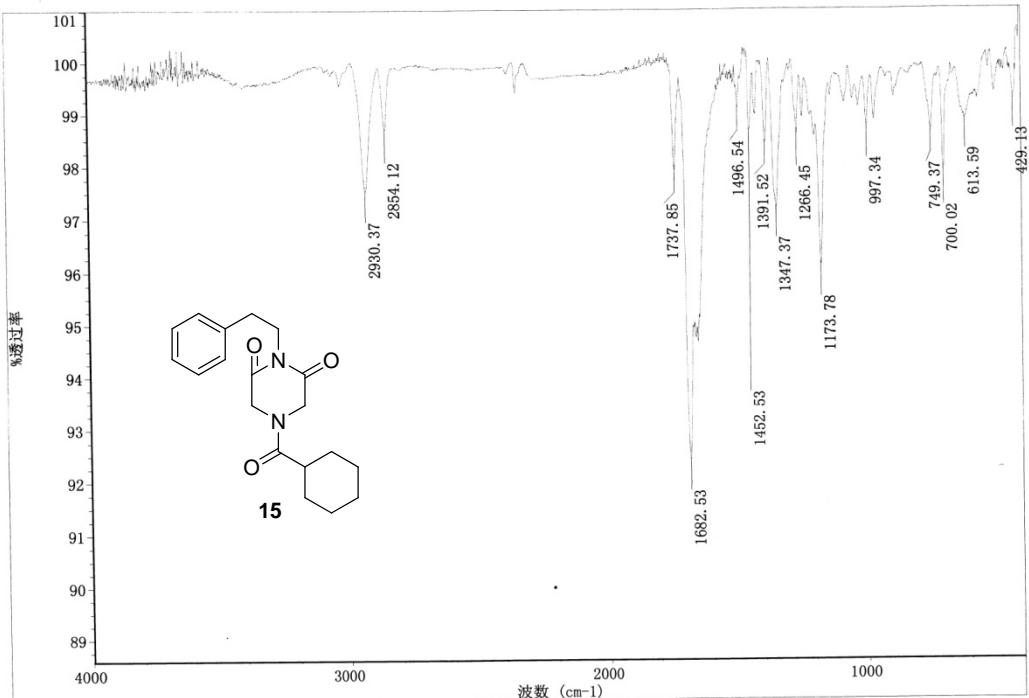


¹H NMR spectrum of 4-(cyclohexanecarbonyl)-1-phenethylpiperazine-2,6-dione (15) (400 MHz, CDCl₃)

N20160830011
No.: 201612362
Solvent: CDCl₃
Sample Name: 2016083002



¹³C NMR spectrum of 4-(cyclohexanecarbonyl)-1-phenethylpiperazine-2,6-dione (15) (100 MHz, CDCl₃)



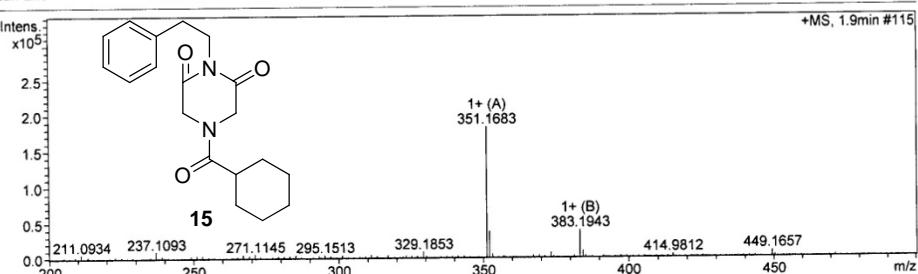
FT-IR spectrum of 4-(cyclohexanecarbonyl)-1-phenethylpiperazine-2,6-dione (**15**)

Mass Spectrum SmartFormula Report

Analysis Info		Acquisition Date
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Sample Name	20160830014	Instrument / Ser# maXis 4G 21240
Comment		

Acquisition Parameter

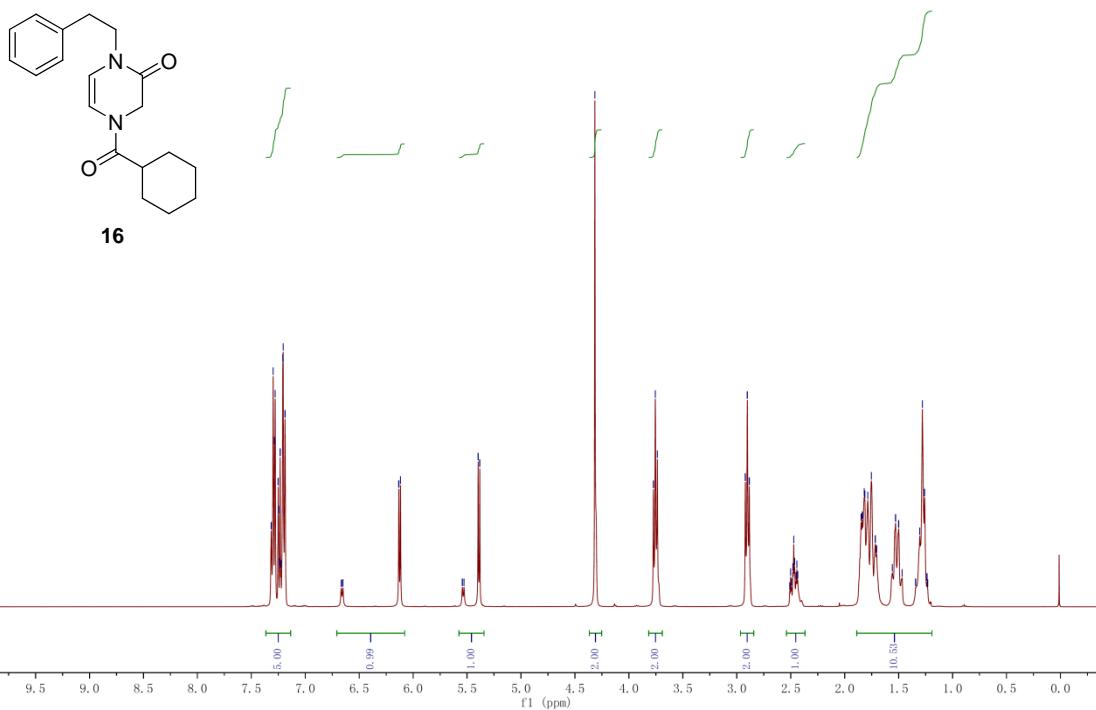
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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste



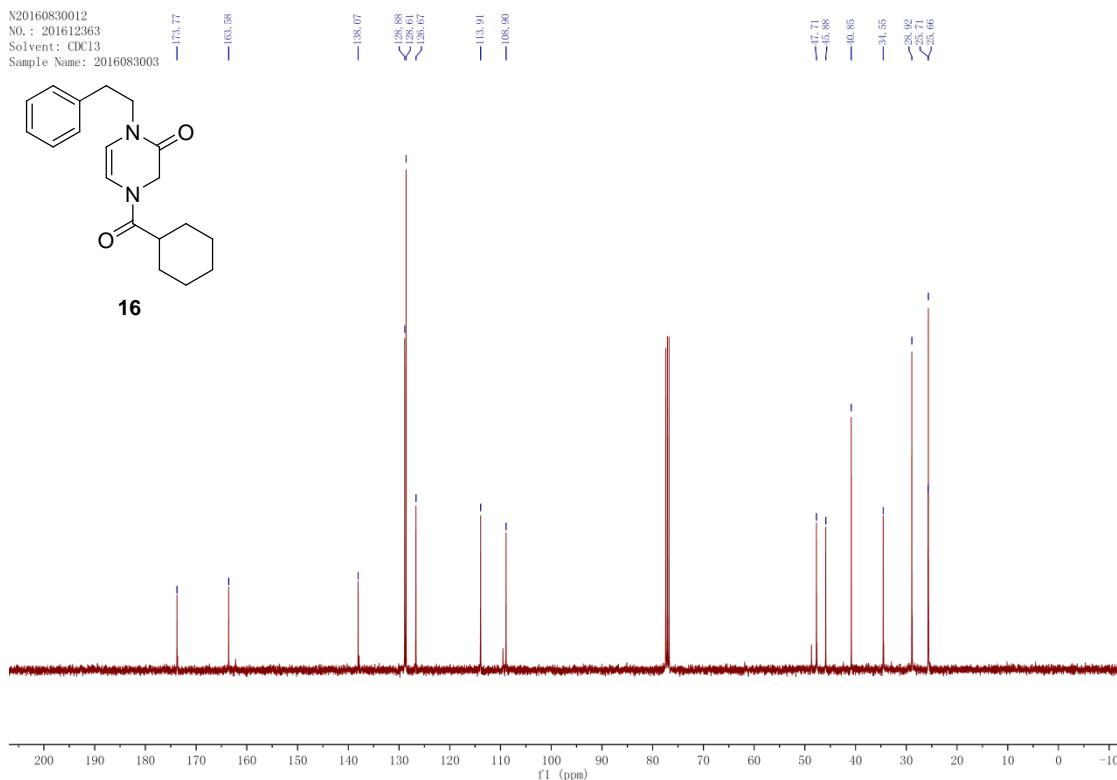
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HRMS spectrum of 4-(cyclohexanecarbonyl)-1-phenethylpiperazine-2,6-dione (**15**)

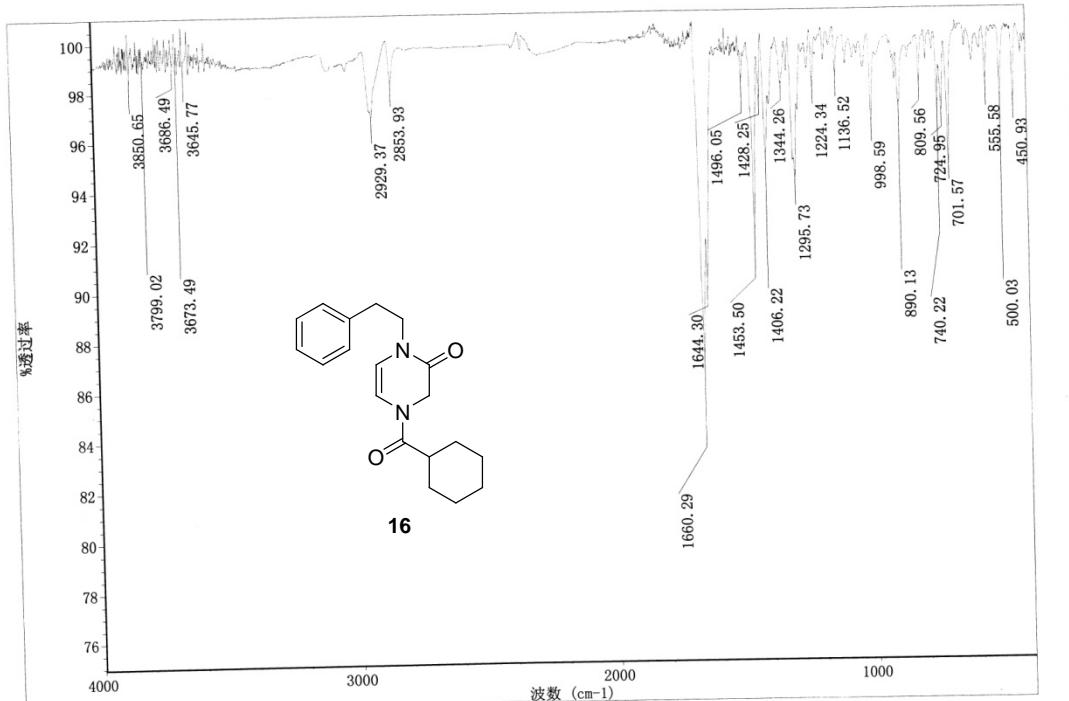
N20160830012
No.: 201612363
Solvent: CDCl₃
Sample Name: 2016083003



¹H NMR spectrum of 4-(cyclohexanecarbonyl)-1-phenethyl-3,4-dihydropyrazin-2-one (16) (400 MHz, CDCl₃)



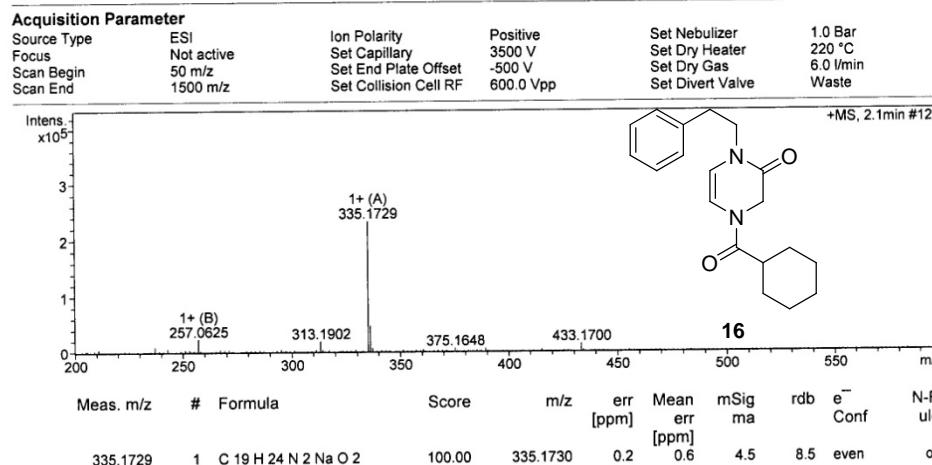
¹³C NMR spectrum of 4-(cyclohexanecarbonyl)-1-phenethyl-3,4-dihydropyrazin-2-one (16) (100 MHz, CDCl₃)



FT-IR spectrum of 4-(cyclohexanecarbonyl)-1-phenethyl-3,4-dihydropyrazin-2-one (16)

Mass Spectrum SmartFormula Report

Analysis Info		Acquisition Date
Analysis Name	D:\Data\SHUJV\FENXI\ZHANGFL-group\20160830015_RA3_01_6462.d	9/6/2016 3:48:14 AM
Method	20150915.m	Operator BDAL@DE
Sample Name	20160830015	Instrument / Ser# maXis 4G 21240
Comment		



HRMS spectrum of 4-(cyclohexanecarbonyl)-1-phenethyl-3,4-dihydropyrazin-2-one (16)