# **Supporting information**

## Synthesis and Cytotoxicity of 7,9-O-linked Macrocylic C-seco Taxoids

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#### Cell lines and culture [1]

The human breast cancer cell line MCF-7 and its doxorubicin-resistant counterpart MCF-7/ADR were provided by Xiangya Hospital, Central South University. Hela and Hela/βIII cells were a generous gift from Dr. Richard Ludeña at the University of Texas. MCF-7 and MCF-7/ADR were cultured in RPMI 1640 supplemented with 10% fetal bovine serum, 100 units/mL penicillin and 100 µg/mL streptomycin. To maintain the cell drug resistance phenotype, 1 µg/mL doxorubicin was added to the culture of MCF-7/ADR. Hela and Hela/βIII cells were cultured in DMEM supplemented with 10% fetal bovine serum, 100 µg/mL streptomycin, and Hela/βIII cell line was additionally supplemented with 0.5 mg/mL G418 sulfate. All cells were cultured at 37°C in a humidified atmosphere containing 5% CO2.

#### Establishment of model multidrug-resistant breast cancer cell line MCF-7/ADR

The multidrug-resistant breast cancer cell line MCF-7/ADR was established by exposure to doxorubicin (adriamycin) using continuous induction with step-wise increasing drug concentrations. MCF-7 cells from the logarithmic growth period were inoculated in culture medium (10% serum) in the presence of 0.005  $\mu$ g/mL doxorubicin (1/10 of the IC<sub>50</sub> value for cytotoxicity towards MCF-7 cells). After exposure to drug for 48 h, the culture medium was replaced with fresh medium without doxorubicin). When cells returned to normal growth, the procedure was repeated. Depending on the status of cell growth, the inducing concentration of drug was gradually increased step-wise. After culturing for 72 weeks, the MCF-7/ADR cell line model was established, which can grow normally in culture medium containing 1  $\mu$ g/mL doxorubicin.

#### Reference

S1. Cai, P.; Lu, P.; Sharom, F.J.; Fang, W.S.. A semisynthetic taxane Yg-3-46a effectively evades P-glycoprotein and beta-III tubulin mediated tumor drug resistance in vitro. Cancer Lett., 2013, 341, 214-223. [https://doi.org/10.1016/j.canlet.2013.08.010]

### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra for representative compounds

<sup>1</sup>H NMR spectra of compound **14a** 



### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 14b









### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 14c









### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 14d







ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 14e







ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 15b



S12

2.29

3.03

-0.5 -1.0

.04

86

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

9.0 8.5 8.0

0.99



## ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound **15c**







ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 15d





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 15e





## ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound 16a





Sample Name	: P15		
Injection Date	: Fri, 11. Jan. 2	019	Seq. Line : 1
Inj. Volumn	: 3.0 ul		
Acq Operator	:		
Acq Method	: F:\DATA\2019\20	1901\20190111\20190108-	2 2019-01-11 16-33-10\MTH-GEN-
	MS.M		
	HPLC Analysis C	onditions	
1. Column	: XDB C18 4.6*50m	um 1.8um	
2. Mobile Phase	: A:Water+0.05%TF	A B :ACN+0.05%TFA	
	Time	A% E	8
3. Flow Mode	: 0.00	90.0 10	.0
	4.50	0.0 10	0.0
	6.50	0.0 10	0.0
	6.60	90.0 10	.0
4. Flow	: Start Flow :	1.0 ml/min	
5. UV Wavelengt	h: C: 220nm ;		
6. Column Temp.	: Left : 40.0	C Right: 40.0C	
7. Sample Prepa	ration:		

DAD	01 C, Sig=220,4 Ref=off (2019\2	01901\20190111\20190108-	2 2019-01-11 16-33-10	\P15.D)		
mAU			34			
1500			4.0			
1000						
500			937 937 526 526	.700		
0		~	WW 444 4	5 4		-
,	1	2 3	4	5	6	min

#	Meas. Ret	. Time	Height	Height %	Area	Area %
	1	3.847	19.160	0.955	54.417	0.895
	2	3.937	2.686	0.134	6.574	0.108
	3	4.034	1944.258	96.875	5908.744	97.216
	4	4.213	5.175	0.258	11.531	0.190
	5	4.280	1.172	0.058	1.535	0.025
	6	4.336	6.235	0.311	11.735	0.193
	7	4.392	8.282	0.413	17.960	0.295
	8	4.526	11.149	0.556	31.937	0.525
	9	4.700	3.612	0.180	13.318	0.219
	10	5.020	5.247	0.261	20.221	0.333



### ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound 16b





Sample Name	: P11				
Injection Date	: Fri, 30. No	ov. 2018		Seq. Line :	7
Inj. Volumn	: 10.0 ul				
Acq Operator	:				
Acq Method	: F:\DATA\20 MS.M HPLC Analy:	18\201811\201811 sis Conditions	30\20181130-1	2018-11-30 1	5-34-15\MTH-GEN-
1. Column	: XDB C18 4.	6*50mm 1.8um			
2. Mobile Phase	: A:Water+0.0	)5%TFA B :ACN	+0.05%TFA		
	Time	A%	B%		
3. Flow Mode	: 0.00	90.0	10.0	)	
	4.50	0.0	100.	. 0	
	6.50	0.0	100.	. 0	
	6.60	90.0	10.0	)	
4. Flow	: Start Flo	ow: 1.2 ml/mi	n		
5. UV Wavelengt	ch: C: 220nm	;			
6. Column Temp.	.: Left :	40.0C Right	: 40.0C		
<ol><li>Sample Prepa</li></ol>	aration:				
DAD10.0		004044004044000004044	00 4 0040 44 00 45 04	45(044.0)	ī
DADTC, S	sig=220,4 Ref=off (2018	201811/20181130/201811	130-1 2018-11-30 15-34	-15\P11.D)	
mAU -			744		
1500			ŝ		
1000-					
1000					
500			377 549 549 874 990 208		
0			mm 0 0 4		
0,	1	2 3	4	5	6 min

# Meas	. Ret. Time	Height	Height %	Area	Area %
1	3.377	8.992	0.423	24.694	0.369
2	3.453	2.653	0.125	6.044	0.090
3	3.549	5.269	0.248	13.300	0.199
4	3.744	2062.169	96.944	6521.324	97.398
5	3.874	9.349	0.440	26.006	0.388
6	3.990	30.292	1.424	80.850	1.208
7	4.208	8.442	0.397	23.357	0.349



### ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound 16c

 


m/z, Da

 Sample Name : P13 Injection Date : Fri, 7. Dec. 2018 Inj. Volumn : 10.0 ul Seq. Line : 6 Inj. Volumn Acq Operator Acq Method : : F:\DATA\2018\201812\20181205\20181206-3 2018-12-07 17-31-08\MTH-GEN-MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B:ACN+0.05%TFA Time A% 3. Flow Mode : 0.00 90.0 B% 10.0 0.0 100.0 4.50 6.50 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018\201812\20181205\20181206-3 2018-12-07 17-31-08\P13.D) mAU 1 4.094 800-600-400--3.020 3.898 4.235 200-0min # Meas. Ret. Time Height Height % Area Area %

1	3.020	4.379	0.468	14.777	0.595
2	3.212	4.599	0.491	13.769	0.554
3	3.898	3.676	0.393	9.549	0.384
4	4.094	920.609	98.320	2436.865	98.102
5	4.235	3.075	0.328	9.043	0.364



#### ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 16d







#### ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 16e







### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 17a







#### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 17b






### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 17c





#### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 17d





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 17e





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 18a



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### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 18b









ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 18c





# ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound **18d**





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 18e





ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 19a







### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 19b





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 19c





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 19d





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 19e





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 20a



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### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 20b





### ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 20c





# ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 20d









# ESI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound **20e**




## ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 21a



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Sample Name : P1 Injection Date : Thu, 20. Dec. 2018 Seq. Line : 12 Inj. Volumn : 10.0 ul Acq Operator : Acq Method : F:\DATA\2018\201812\20181220\20181220-3 2018-12-20 19-01-52\MTH-GEN-MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% B% 3. Flow Mode : 0.00 90.0 10.0 4.50 0.0 100.0 6.50 0.0 100.0 6.60 90.0 10.0 4. Flow : Start Flow : 1.0 ml/min 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation:

DAD1 C, Sig=2	20,4 Ref=off (2018\201812\20181220\2018	31220-3 2018-12-20 19-01-5	52\P1.D)
mAU		174	1
500-		4.4	
400-			
300-			
200-		55	363
		44	4444 0
	1 2 3	3 4	Ś 6 mi

#	Meas.	Ret. Time	Height	Height %		Area .	Area %
	1	4.056	1.	042	0.173	2.709	0.172
	2	4.155	0.	854	0.142	2.477	0.157
	3	4.474	576.	164	95.863	1506.776	95.760
	4	4.703	0.	702	0.117	2.312	0.147
	5	4.771	1.	199	0.200	3.148	0.200
	6	4.863	1.	095	0.182	2.873	0.183
	7	4.962	1.	040	0.173	2.837	0.180
	8	5.259	18.	929	3.149	50.368	3.201



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## ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 21b





 Sample Name
 : P3

 Injection Date
 : Thu, 6. Dec. 2018
 Seq. Line : 1

 Inj. Volumn
 : 10.0 ul

 Acq Operator
 :

 Acq Method
 : F:\DATA\2018\201812\20181205\20181206-1 2018-12-06 15-00-05\MTH-GEN-MS.M

 HPLC Analysis Conditions

 1. Column
 : XDB C18 4.6\*50mm 1.8um

 2. Mobile Phase :
 A:Water+0.05%TFA
 B%

 3. Flow Mode
 : 0.00
 90.0
 10.0

 4.50
 0.0
 100.0

 6.60
 90.0
 10.0

 4. Flow
 : Start Flow : 1.0 ml/min

 5. UV Wavelength:
 C: 220nm ;

 6. Column Temp. :
 Left : 40.0C
 Right : 40.0C

7. Sample Preparation:

DAD1 C, Sig=	220,4 Ref=off (2018\201812\20181205\2018	81206-1 2018-12-06 15-00-0	5\P3.D)	
mAU -		87	1	
1000		4		
800				
600-				
400-		~	5 0	74
200 -		3.84	1.84	5.7
0			1 1 1	
	1 2	3 4	5	6 min

# Meas. Ret	. Time	Height	Height %	Area	Area %
1	3.847	11.055	0.880	36.969	0.991
2	4.487	1193.638	95.000	3544.731	95.037
3	4.845	4.577	0.364	15.473	0.415
4	5.063	2.493	0.198	6.825	0.183
5	5.774	44.704	3.558	125.850	3.374



ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 21c





Sample Name : P7 : Sat, 15. Dec. 2018 : 10.0 ul Injection Date Seq. Line : 12 Inj. Volumn : F:\DATA\2018\201812\20181215\20181215-2 2018-12-15 15-26-59\MTH-GEN-Acq Operator Acq Method MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% 3. Flow Mode : 0.00 90.0 B% 10.0 0.0 4.50 100.0 6.50 100.0 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 39.5C Right : 39.5C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018/201812/20181215/20181215-2 2018-12-15 15-26-59/P7.D) mAU 4.524 500-400 300 -200--3.851 -3.977 -4.241 -4.463 -4.698 -4.837 5.176 100 0 t Timo Weight Hoight &

# Meas.	. Ret. Time	Height	Height %	Area	Area %
1	3.851	3.420	0.585	10.485	0.665
2	3.977	1.560	0.267	5.856	0.372
3	4.241	2.681	0.458	12.983	0.824
4	4.463	6.693	1.144	21.922	1.391
5	4.524	563.717	96.389	1501.922	95.280
6	4.698	1.048	0.179	2.754	0.175
7	4.837	3.796	0.649	15.872	1.007
8	5.176	1.921	0.328	4.526	0.287



## ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 21d





Sample Name : P5 : Fri, 14. Dec. 2018 : 20.0 ul Seq. Line: 29 Injection Date Inj. Volumn Acq Operator : : F:\DATA\2018\201812\20181214\20181213-2 2018-12-14 08-22-34\MTH-GEN-Acq Method MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% 3. Flow Mode : 0.00 90.0 4.50 0.0 B% 10.0 0.0 6.50 100.0 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018/201812/20181214/20181213-2 2018-12-14 08-22-34\P5.D) mAU -1.696 800 600-400-3.915 4.108 4.483 200-

Ret. Time	Height	Height %	Area	Area %
3.915	7.311	0.765	34.270	0.922
4.108	14.869	1.555	68.751	1.850
4.401	2.866	0.300	8.024	0.216
4.468	5.583	0.584	14.402	0.388
4.696	925.632	96.797	3590.721	96.624
	Ret. Time 3.915 4.108 4.401 4.468 4.696	Ret. Time Height 3.915 7.311 4.108 14.869 4.401 2.866 4.468 5.583 4.696 925.632	Ret. Time         Height         Height %           3.915         7.311         0.765           4.108         14.869         1.555           4.401         2.866         0.300           4.468         5.583         0.584           4.696         925.632         96.797	Ret. Time         Height         Height %         Area           3.915         7.311         0.765         34.270           4.108         14.869         1.555         68.751           4.401         2.866         0.300         8.024           4.468         5.583         0.584         14.402           4.696         925.632         96.797         3590.721

0-



## ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound 21e





Sample Name : P9 Injection Date : Fri, 14. Dec. 2018 Inj. Volumn : 20.0 ul Seq. Line : 39 Acq Operator : . F:\DATA\2018\201812\20181214\20181213-2 2018-12-14 08-22-34\MTH-GEN-MS.M Acq Method HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% 3. Flow Mode : 0.00 90.0 10.0 B% 4.50 0.0 100.0 6.50 0.0 100.0 6.60 90.0 10.0 4. Flow : Start Flow : 1.0 ml/min 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018\201812\20181214\20181213-2 2018-12-14 08-22-34\P9.D) mAU E 4.751 1250 -1000 -750-500-3.598 3.923 4.370 250-0

# Me	as. Ret.	Time	Height	Height %	Area	Area %
T		3.598	17.020	0.987	46.769	0.910
2		3.662	12.113	0.702	37.871	0.737
3		3.923	31.305	1.815	83.825	1.631
4		4.262	8.459	0.490	23.686	0.461
5		4.370	6.397	0.371	14.278	0.278
6		4.458	11.221	0.650	46.630	0.907
7		4.751	1638.653	94.985	4886.958	95.077



## ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound 22a



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Sample Name : P2 Injection Date : Thu, 20. Dec. 2018 Inj. Volumn : 10.0 ul Seq. Line : 13 Inj. Volumn Acq Operator Acq Method : : F:\DATA\2018\201812\20181220\20181220-3 2018-12-20 19-01-52\MTH-GEN-MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% 3. Flow Mode : 0.00 90.0 4.50 0.0 B% 10.0 100.0 6.50 0.0 100.0 6.60 90.0 : Start Flow : 1.0 ml/min 10.0 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018/201812/20181220/20181220-3 2018-12-20 19-01-52/P2.D) mAU 1250 4.504 1000 750-500 4.797 250 -0 7

#	Meas.	Ret.	Time	Height	Height %	Area	Area %
	1		4.395	8.093	0.554	19.549	0.490
	2		4.504	1430.789	97.886	3900.252	97.709
	3		4.698	7.281	0.498	19.407	0.486
	4		4.797	15.528	1.062	52.494	1.315



## ESI-MS, HPLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compound **22b**

286.1

338.3



m/z, Da

756.3

: P4 Sample Name Injection Date : Wed, 26. Dec. 2018 Inj. Volumn : 20.0 ul Seq. Line : 1 Acq Operator : : F:\DATA\2018\201812\20181225\20181225-1 2018-12-26 11-41-49\MTH-GEN-Acq Method MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA Time A% B% 3. Flow Mode : 0.00 90.0 10.0 0.0 4.50 100.0 6.50 0.0 100.0 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018\201812\20181225\20181225-1 2018-12-26 11-41-49\P4.D) mAU \_ 4.524 1500-1000-3.719 3.917 4.172 500-3.027 5.692 119 9 0à # Meas. Ret. Time Height Height % Area Area %

1	3.027	10.339	0.491	46.267	0.420
2	3.719	6.438	0.306	15.240	0.138
3	3.917	25.214	1.197	145.007	1.315
4	4.172	2.467	0.117	12.605	0.114
5	4.524	2047.503	97.211	10768.203	97.647
6	5.692	5.343	0.254	14.518	0.132
7	6.119	8.947	0.425	25.864	0.235



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## ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 22c



Sample Name : P8 : Tue, 11. Dec. 2018 : 20.0 ul Injection Date Seq. Line : 2 Inj. Volumn Acq Operator : Acq Method : F:\DATA\2018\201812\20181210\20181206-3 2018-12-11 13-57-34\MTH-GEN-MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :7 A B :ACN+0.05%TFA A% Time B% 3. Flow Mode : 0.00 90.0 10.0 4.50 0.0 100.0 100.0 6.50 0.0 90.0 10.0 6.60 4. Flow : Start Flow : 1.0 ml/min 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018\201812\20181210\20181206-3 2018-12-11 13-57-34\P8.D) mAU -4.543 1000 -800 600--4.988 5.745 400-4.650 200-0 % Area Area % Meas. Ret. Time Height Height % # -----\_\_\_\_\_ 97.275 4.543 96.297 5409.773 1 1363.175 0.604 27.399 13.001 4.650 0.493 8.546 2 4.929 4.347 3 4.986 9.127 0.645 29.162 0.524 4 5.177 6.224 0.440 16.542 0.297 5 6 5.745 8.868 0.626 23.211 0.417 7 5.869 15.308 1.081 42.210 0.759

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# ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 22d





Sample Name : P6 Injection Date : Fri, 14. Dec. 2018 Seq. Line : 31 Inj. Volumn : 20.0 ul Acq Operator : Acq Method : F:\DATA\2018\201812\20181214\20181213-2 2018-12-14 08-22-34\MTH-GEN-MS.M HPLC Analysis Conditions 1. Column : XDB C18 4.6\*50mm 1.8um 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% B% 3. Flow Mode : 0.00 90.0 10.0 4.50 0.0 100.0 6.50 0.0 100.0 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018\201812\20181214\20181213-2 2018-12-14 08-22-34\P6.D) mAU\_ 4.727 500 -400 300 --5.759 200 4.240 3.722 3.442 100 -0-Height % Area % Meas. Ret. Time Height Area # \_\_\_\_\_ ------1 3.442 1.103 0.181 3.654 0.165 2 3.722 2.003 0.330 9.459 0.426 3 4.240 2.084 0.343 14.781 0.666 4 4.407 6.704 1.103 22.202 1.000 5 4.471 9.064 1.491 31.069 1.399

95.836

0.716

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2128.743

10.987

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95.851

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0.495

6

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4.727

5.759

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582.526

4.352



## ESI-MS, HPLC, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compound 22e





Sample Name : P10 : Fri, 7. Dec. 2018 Injection Date Seq. Line : 20 Inj. Volumn : 15.0 ul Acq Operator : : F:\DATA\2018\201812\20181205\20181206-3 2018-12-07 08-53-22\MTH-GEN-Acq Method MS.M HPLC Analysis Conditions : XDB C18 4.6\*50mm 1.8um 1. Column 2. Mobile Phase : A:Water+0.05%TFA B :ACN+0.05%TFA Time A% Аъ 90.0 B% 3. Flow Mode : 0.00 10.0 4.50 0.0 100.0 6.50 0.0 100.0 6.60 90.0 10.0 : Start Flow : 1.0 ml/min 4. Flow 5. UV Wavelength: C: 220nm ; 6. Column Temp. : Left : 40.0C Right : 40.0C 7. Sample Preparation: DAD1 C, Sig=220,4 Ref=off (2018/201812/20181205/20181206-3 2018-12-07 08-53-22/P10.D) mAU d 4.765 1000 -800 -600 · 400 5.750 5.014 5.334 200 0. mi Area Area % # Meas. Ret. Time Height Height % --------------\_\_\_\_ \_\_\_\_\_ \_\_\_\_ 1 4.765 1246.186 97.861 3744.757 97.945 1.940 5.068 2 5.014 0.152 0.133 3 5.334 3.636 0.286 9.422 0.246 4 5.750 2.668 0.210 6.397 0.167 5 5.957 18.993 1.491 57.681 1.509

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