### **Supporting Information**

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# A Novel Nitrogen-containing Glyceride from Fungal Saprobe Tubeufia rubra reverses MDR of Tumor Cell Lines to Doxorubicin

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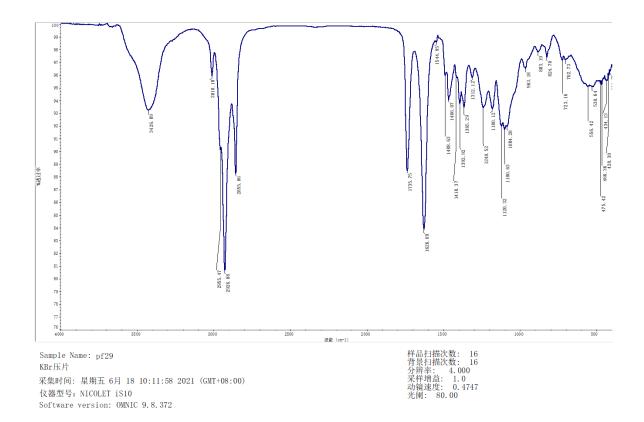


Figure S1: IR spectrum of Rubracin A

### **Qualitative Analysis Report**

Data Filename			20200605ESIA12.d	Sample Name	pf29		
Sample Typ	e	:	Sample	Position			
Instrument Name Acq Method IRM Calibration Status		e i	Agilent G6230 TOF MS	User Name	KIB 6/4/2020 12:20:40 PM ESI.m		
		)	ESI.m	Acquired Time			
		Status	Success	DA Method			
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Figure S2: HR-ESI-MS spectrum of Rubracin A;

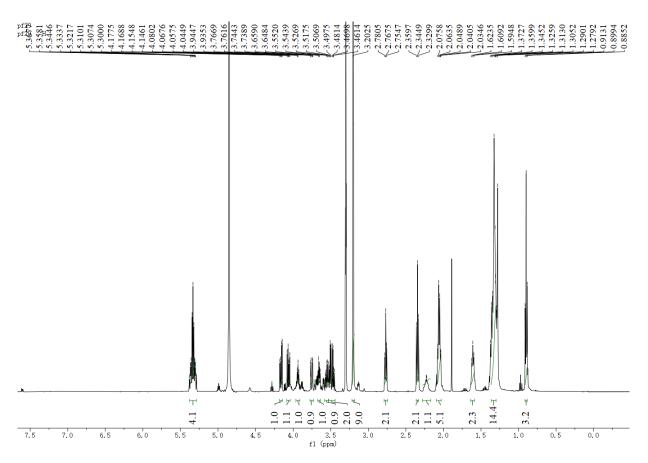


Figure S3: <sup>1</sup>H-NMR spectrum of Rubracin A in methanol-d4

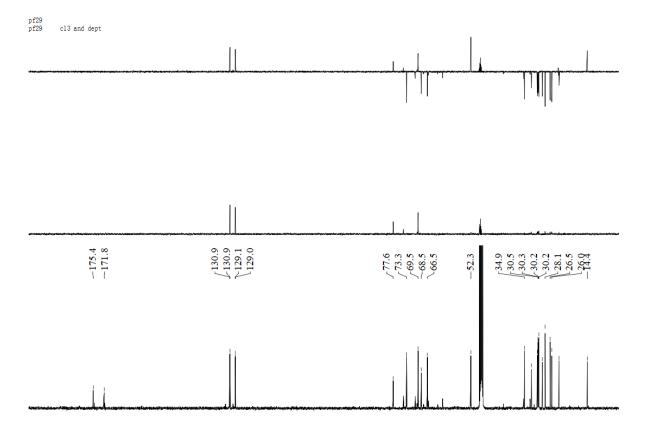


Figure S4: <sup>13</sup>C-NMR and DEPT spectrum of Rubracin A in methanol-d4

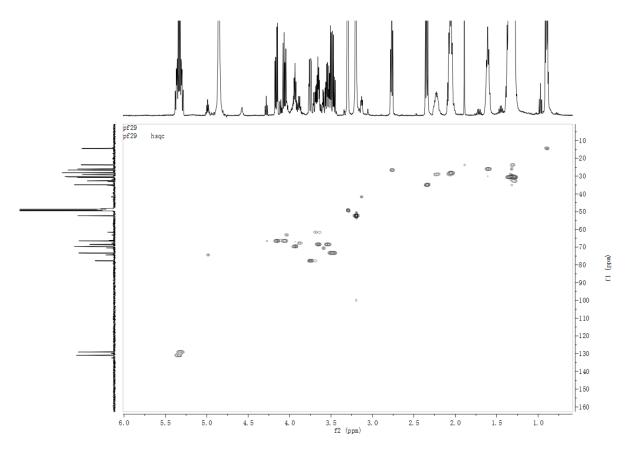


Figure S5: HSQC spectrum of Rubracin A in methanol-d4

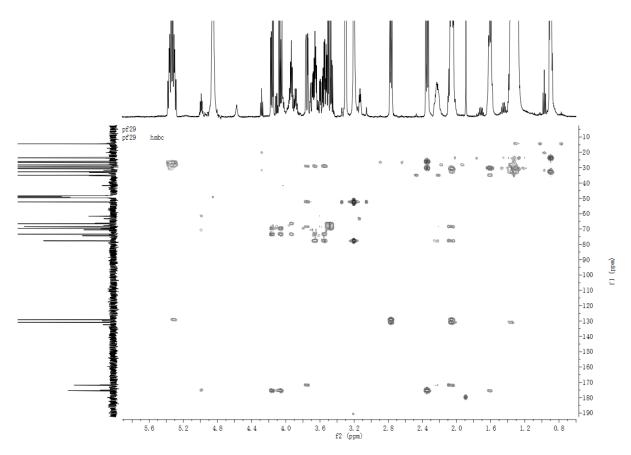


Figure S6: HMBC spectrum of Rubracin A in methanol-d4

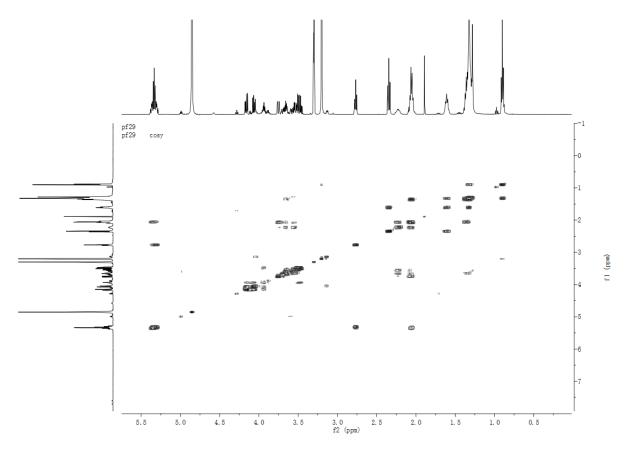


Figure S7: <sup>1</sup>H-<sup>1</sup>H COSY spectrum of Rubracin A in methanol-d4

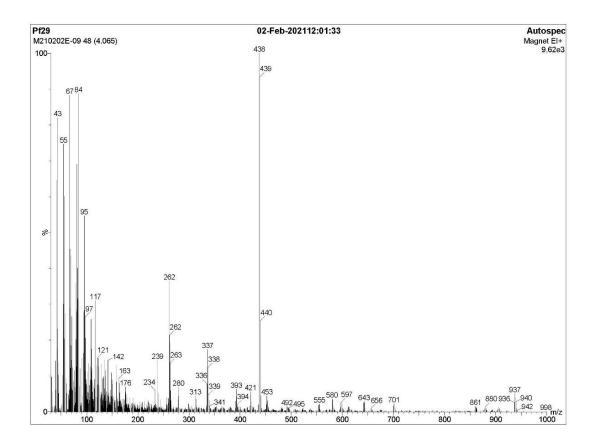


Figure S8 : EI-MS fragment ions of Rubracin A

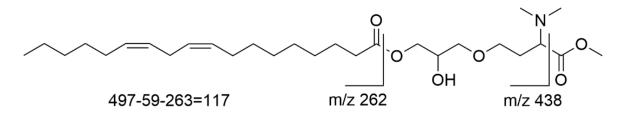


Figure S9: MS Fragmentation of Rubracin A

#### 光谱峰值检测报告

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数据集: PF29 - RawData

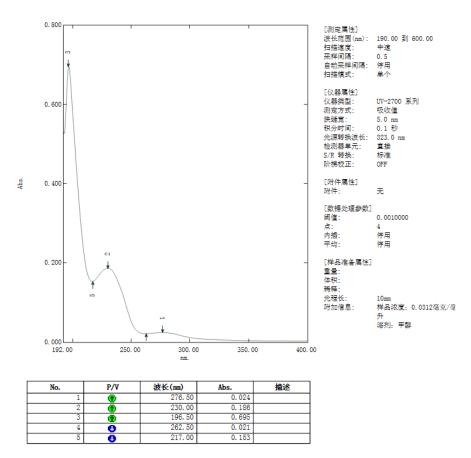


Figure S10: UV (Methanol) spectrum for Rubracin A

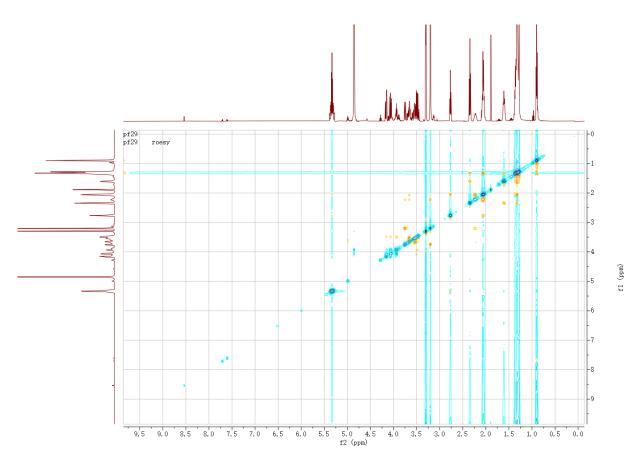
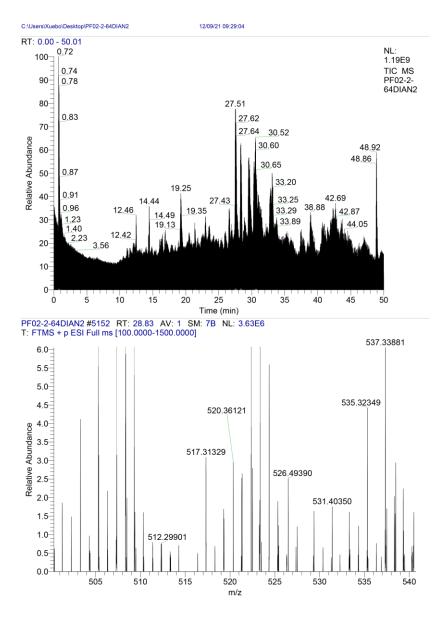


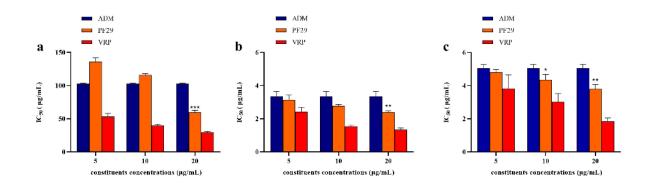
Figure S11: ROESY spectrum of Rubracin A



**Figure S12:** The UHPLC/MS chromatogram of Rubracin A (m/z 520.3611 [M + Na]<sup>+</sup>) was isolated from EtOAc extract (35.77g).

a	1.0 -	PF29		<b>b</b> <sub>1.0</sub>	<b>–</b> PF:	29		с <sub>1.0 г</sub>	PF29	
	0.8-			0.8	-			0.8-		
atio				atio				atio		
inhibition ratio	0.6-			9.0 ratio 9.0 value - 10 value -	-			inhibition ratio 0.4 – 0.4 –		
ibiti	0.4-			ii 19 0.4	-			ii 0.4-		
ihhi				inh			T	hni		_
	0.2 -		т	0.2	-			0.2 -		
	0.0			0.0		بالباب		0.0		
		12.5 25 50	100 200		3.13 6.25	12.5 25 50	100	3.1	13 6.25 12.5 2	5 50 100
	PF 29	concentratio	on (µg/mL)		PF29 cond	entration (µg	/mL)	P	F29 concentrat	ion (µg/mL)
10 17	A549/ADR-PF29	Oug/m1	1.6ug/ml	3.125ug/ml	6.25ug/ml	12.5ug/ml	25ug/m1	50ug/m1	100ug/m1	对照孔
18	重复1	1.873				1. 752	1. 695	1. 459	1. 415	0. 111
9	重复2	1.824			1.766	1.715	1.645	1.456	1.444	0.156
20	重复3	1.884	1.805	1.756	1.756	1.705	1.702	1.503	1.386	0.174
21	OD值	1.860333333	1.804333333	1.784	1.769666667	1.724	1.680666667	1.472666667	1.415	0.147
22										
	抑制率	(	0.032684825	0.044552529	0.052918288	0.079571984		0.226264591		
54	抑制率	(	0.032684825	0.044552529	0.052918288	0.079571984		0. 226264591		
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	抑制率 562/ADR-PF29	( Oug/ml	0.032684825 1.6ug/ml	0.044552529 3.125ug/m1	0.052918288 6.25ug/ml	0.079571984 12.5ug/m1		0.226264591 50ug/m1		对照孔
K 重	562/ADR-PF29 复1	Oug/m1 1.985	1.6ug/ml 1.862			12.5ug/ml 1.812	0. 104863813 25ug/ml 1. 715		0. 259922179	
K 重 重	562/ADR-PF29 复1 复2	0ug/m1 1.985 1.998	1.6ug/ml 1.862 1.867	3.125ug/ml 1.865 1.825	6.25ug/ml 1.812 1.807	12.5ug/ml 1.812 1.785	0.104863813 25ug/ml 1.715 1.762	50ug/ml 1.695 1.655	0.259922179 100ug/m1 1.579 1.559	对照孔 0.123 0.158
K 重 重 重	562/ADR-PF29 复1 复2 复3	Oug/ml 1.985 1.998 1.923	1.6ug/m1 1.862 1.867 1.919	3.125ug/ml 1.865 1.825 1.837	6.25ug/ml 1.812 1.807 1.808	12.5ug/ml 1.812 1.785 1.768	0.104863813 25ug/ml 1.715 1.762 1.733	50ug/ml 1.695 1.655 1.712	0.259922179 100ug/ml 1.579 1.559 1.549	对照孔 0.123 0.158 0.175
K 重 重 ①D	562/ADR-PF29 复1 复2 复3 值	0ug/ml 1.985 1.998 1.923 1.968666667	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12. 5ug/m1 1. 812 1. 785 1. 768 1. 788333333	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 7366666667	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/m1 1.579 1.559 1.549 1.562333333	对照孔 0.123 0.158
K 重 重 のD	562/ADR-PF29 复1 复2 复3	Oug/ml 1.985 1.998 1.923	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12.5ug/ml 1.812 1.785 1.768	0.104863813 25ug/ml 1.715 1.762 1.733	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/ml 1.579 1.559 1.549	对照孔 0.123 0.158 0.175
K 重 重 重	562/ADR-PF29 复1 复2 复3 值	0ug/ml 1.985 1.998 1.923 1.968666667	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12. 5ug/m1 1. 812 1. 785 1. 768 1. 788333333	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 7366666667	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/m1 1.579 1.559 1.549 1.562333333	对照孔 0.123 0.158 0.175
K 重 重 のD	562/ADR-PF29 复1 复2 复3 值	0ug/ml 1.985 1.998 1.923 1.968666667	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12. 5ug/m1 1. 812 1. 785 1. 768 1. 788333333	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 7366666667	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/m1 1.579 1.559 1.549 1.562333333	对照孔 0.123 0.158 0.175
K 重 重 のD	562/ADR-PF29 复1 复2 复3 值	0ug/ml 1.985 1.998 1.923 1.968666667	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12. 5ug/m1 1. 812 1. 785 1. 768 1. 788333333	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 7366666667	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/m1 1.579 1.559 1.549 1.562333333	对照孔 0.123 0.158 0.175
K 重重重 0D 抑	562/ADR-PF29 复1 复2 复3 值	0ug/ml 1.985 1.998 1.923 1.968666667	1.6ug/ml 1.862 1.867 1.919 1.882666667	3.125ug/ml 1.865 1.825 1.837 1.842333333	6.25ug/ml 1.812 1.807 1.808 1.809	12. 5ug/m1 1. 812 1. 785 1. 768 1. 788333333	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 7366666667	50ug/m1 1.695 1.655 1.712 1.687333333	0.259922179 100ug/m1 1.579 1.559 1.549 1.562333333	对照孔 0.123 0.158 0.175
K 重 重 0D 抑	562/ADR-PF29 复1 复2 复3 值 <b>制率</b>	0ug/ml 1.985 1.998 1.923 1.968666667 0	1.6ug/ml 1.862 1.867 1.919 1.882666667 0.04733945	3.125ug/ml 1.865 1.825 1.837 1.84233333 0.069541284	6.25ug/ml 1.812 1.807 1.808 1.809 0.087889908	12.5ug/ml 1.812 1.785 1.768 1.788333333 0.099266055	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 736666667 0. 127706422	50ug/ml 1.695 1.655 1.712 1.687333333 0.154862385	0.259922179 100ug/ml 1.579 1.559 1.549 1.56233333 0.223669725	对照孔 0.123 0.158 0.175 0.152
K 重重重 0D 抑	562/ADR-PF29 复1 复2 复3 值 削率 F7/ADR-PF29	0ug/ml 1.985 1.998 1.923 1.968666667 0 0 0 0 0 0 0 0 0 0 0 0 0	1. 6ug/ml 1. 862 1. 867 1. 919 1. 882666667 0. 04733945 6. 25ug/ml	3.125ug/ml 1.865 1.825 1.837 1.84233333 0.069541284 12.5ug/ml	6.25ug/ml 1.812 1.807 1.808 1.809 0.087889908 25ug/ml	12.5ug/m1 1.812 1.785 1.768 1.78833333 0.099266055 50ug/m1	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 736666667 0. 127706422	50ug/m1 1.695 1.655 1.712 1.68733333 0.154862385 200ug/m1	0. 259922179 100ug/ml 1. 579 1. 559 1. 549 1. 56233333 0. 223669725 400ug/ml	对照孔 0.123 0.158 0.175 0.152 对照孔
K 重 重 0D 抑	562/ADR-PF29 复1 复2 复3 值 前率 F7/ADR-PF29 重复1	0ug/ml 1.985 1.998 1.923 1.968666667 0 0 0 0 0 0 0 0 1.923 1.923 1.968666667 0	1. 6ug/ml 1. 862 1. 867 1. 919 1. 882666667 0. 04733945 6. 25ug/ml 2. 095	3.125ug/ml 1.865 1.825 1.837 1.84233333 0.069541284 12.5ug/ml 1.969	6.25ug/ml 1.812 1.807 1.808 1.809 0.087889908 25ug/ml 1.936	12.5ug/m1 1.812 1.785 1.768 1.78833333 0.099266055 50ug/m1 1.939	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 736666667 0. 127706422 100ug/ml 1. 965	50ug/m1 1.695 1.655 1.712 1.68733333 0.154862385 200ug/m1 1.916	0. 259922179 100ug/ml 1. 579 1. 559 1. 549 1. 56233333 0. 223669725 400ug/ml 1. 939	对照孔 0.123 0.158 0.175 0.152 对照孔 0.102
K 重 重 のD 抑	562/ADR-PF29 复1 复2 复3 值 <b>削率</b> F7/ADR-PF29 重复1 重复2	0ug/ml 1.985 1.998 1.923 1.968666667 0 0 0 0 0 0 0 0 1.968 0 0 0 0 0 0 0 0 0 0 0 0 0	1. 6ug/ml 1. 862 1. 867 1. 919 1. 882666667 0. 04733945 6. 25ug/ml 2. 095 2. 003	3.125ug/ml 1.865 1.825 1.837 1.84233333 0.069541284 12.5ug/ml 1.969 1.989	6.25ug/ml 1.812 1.807 1.808 1.809 0.087889908 25ug/ml 1.936 1.967	12.5ug/ml 1.812 1.785 1.768 1.78833333 0.099266055 50ug/ml 1.939 1.972	0. 104863813 25ug/ml 1. 715 1. 762 1. 733 1. 736666667 0. 127706422 100ug/ml 1. 965 1. 904	50ug/ml 1.695 1.655 1.712 1.687333333 0.154862385 200ug/ml 1.916 1.984 1.817	0. 259922179 100ug/ml 1. 579 1. 559 1. 549 1. 56233333 0. 223669725 400ug/ml 1. 939 1. 874 1. 818	对照孔 0.123 0.158 0.175 0.152 对照孔 0.102 0.104

**Figure S13:** The raw data and Cytotoxic activities of Rubracin A against MCF-7/Dox (a), A549/Dox (b), and K562/Dox (c).



**Figure 14:** IC<sub>50</sub> values of MCF-7/Dox (a), A549/Dox (b), and K562/Dox (c) of Rubracin A combined with doxorubicin

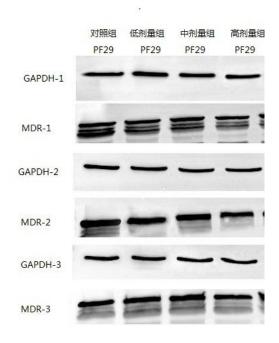


Figure 15: Western Blot results of Rubracin A

Cell lines	IC <sub>50</sub> (µg/mL)	RF <sup>a</sup>
MCF-7	2.661±0.353	
MCF-7//Dox	102.762±0.953	38.6
A549	0.131±0.006	
A549//Dox	3.330±0.327	25.4
K562	0.104±0.031	
K562//Dox	5.053±0.226	48.6

Table S1: The IC<sub>50</sub> of doxorubicin against the sensitive cell lines and MDR tumor cell lines

 $^a$  Reversal fold (RF) = IC\_{50} (Drug-resistant tumor cells)/IC\_{50} (Sensitive cells).

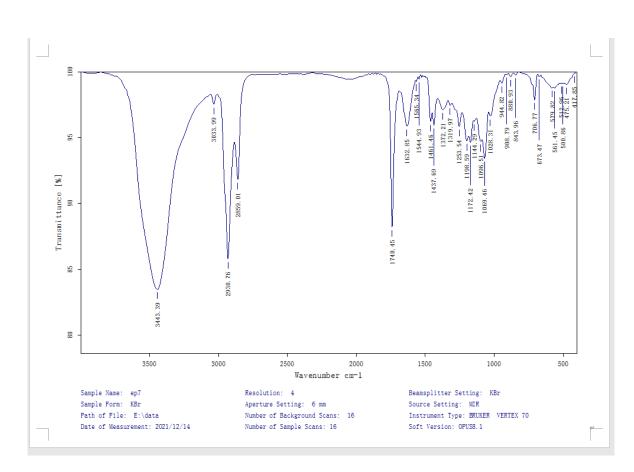


Figure S16: IR spectrum of Rubracin H

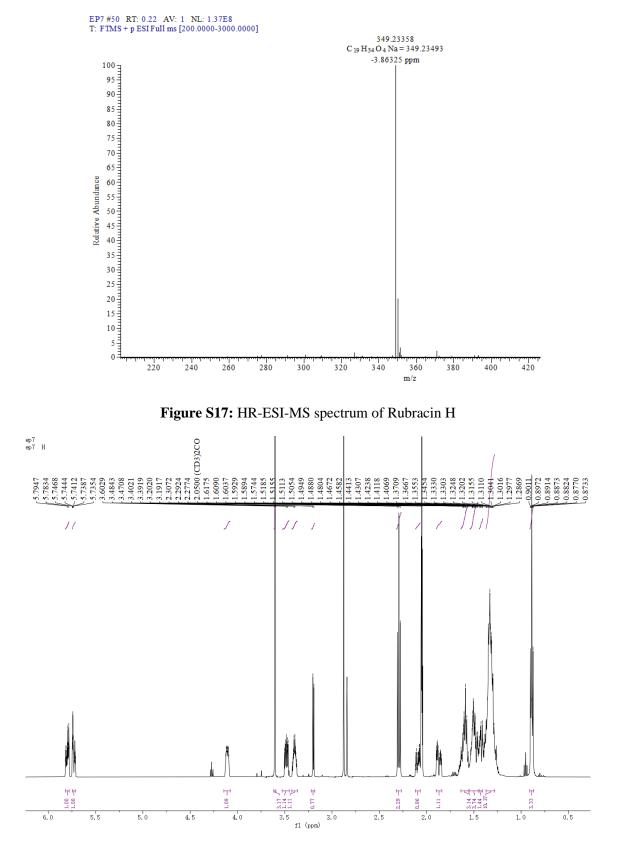


Figure S18: <sup>1</sup>H-NMR spectrum of Rubracin H in Acetone-d6

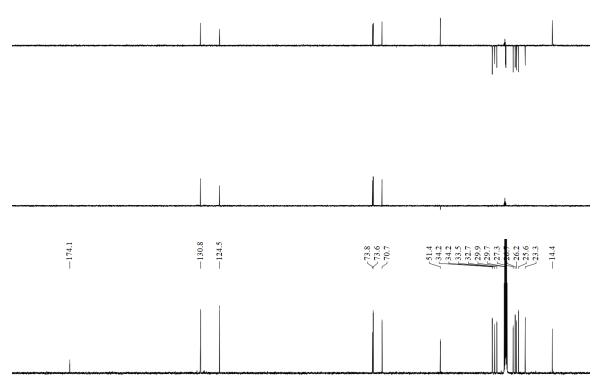


Figure S19: <sup>13</sup>C-NMR and DEPT spectrum of Rubracin H in Acetone-d6

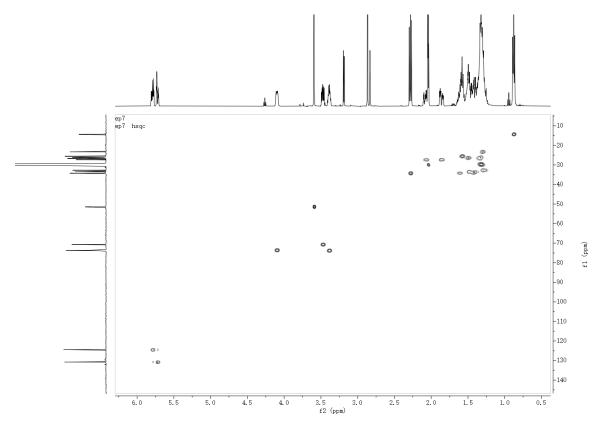


Figure S20: HSQC spectrum of Rubracin H in Acetone-d6

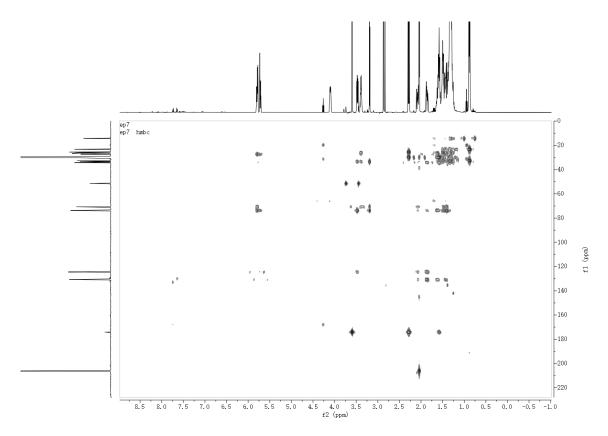


Figure S21: HMBC spectrum of Rubracin H in Acetone-d6

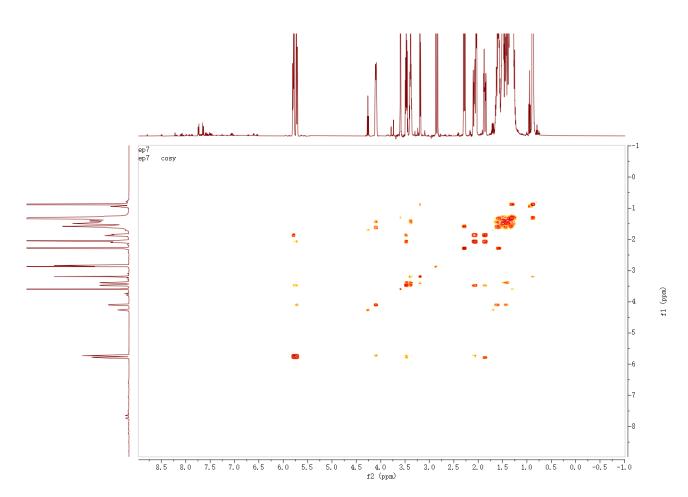


Figure S22: <sup>1</sup>H-<sup>1</sup>H COSY spectrum of Rubracin H in Acetone-d6

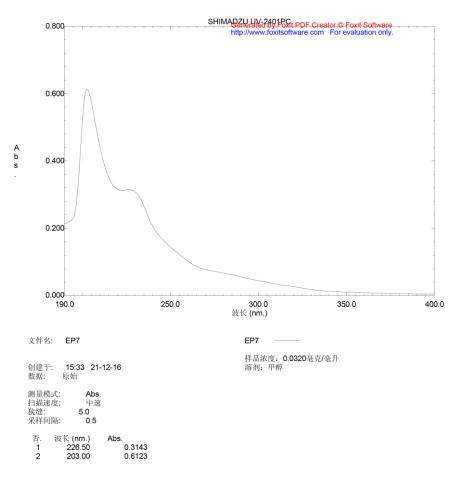


Figure S23: UV (Methanol) spectrum for Rubracin H

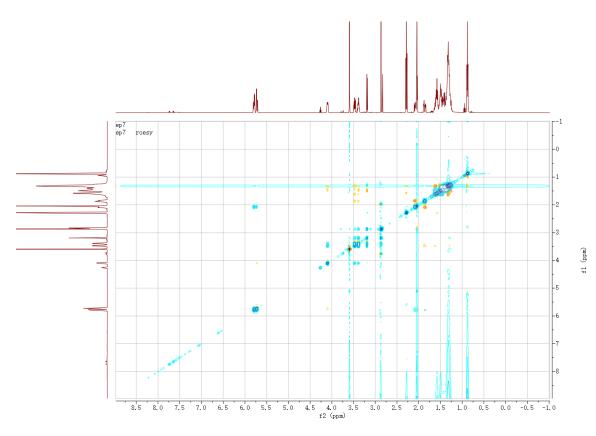


Figure S24: ROESY spectrum of Rubracin H

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