SUPPLEMENTARY MATERIAL

A new anti-proliferative compound from an endophytic fungus, *Phoma* sp.

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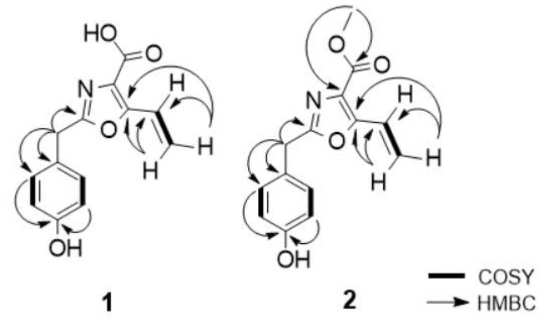
ABSTRACT: A new oxazole-type compound (**1**), named macrooxazole E, and three known macrooxazoles A-C (**2-4**), were isolated from ethyl acetate extracts of cultures of *Phoma* sp. JS0228, an endophytic fungus of *Morus alba*. Structures of the isolated compounds were determined by spectroscopic methods such as 1D-, 2D-NMR, and HRMS. Macrooxazole E (**1**) differed from macrooxazole C only in the presence of a methyl carboxylate instead of the free carboxylic acid. Macrooxazole C showed moderate anti-proliferative activities against MCF-7 and LNCaP cells with IC_{50} values of 0.29 mM and 0.36 mM, respectively. This study presented possibility of the endophytic fungus, *Phoma* sp. JS0228 to produced new natural compounds with bioactivities.

KEYWORDS: *Phoma sp*.; endophyte; macrooxazole; structure elucidation

Content

Figure S1. ^{1}H-^{1}H COSY and key HMBC correlations of compound **1** and **2**



1 **2**

Figure S2. HPLC chromatogram of *Phoma* sp. JS0228 crude extracts (**1**: macrooxazole E, **2**: macrooxazole C).

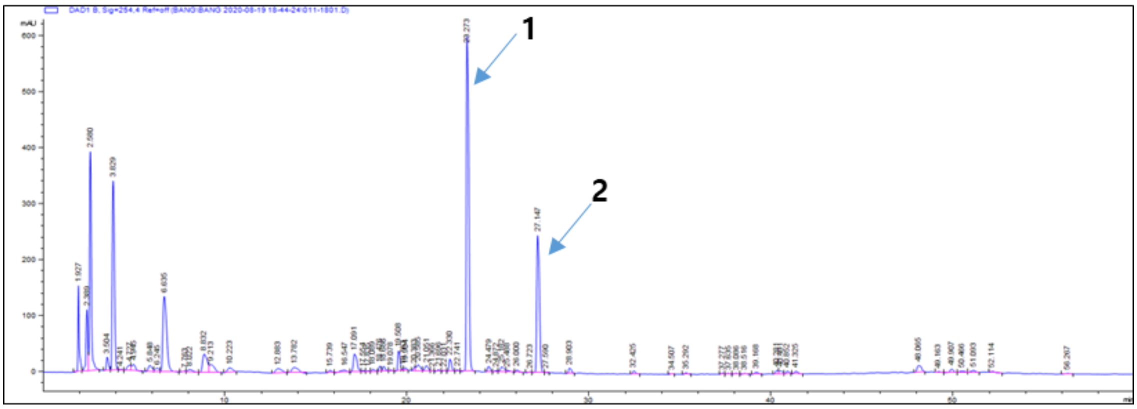


Figure S3. Comparison in inhibitory effects of macrooxazole C on the proliferation of MCF-7 (a) and LNCaP (b) cells. $P < 0.05$ compared to the control value.

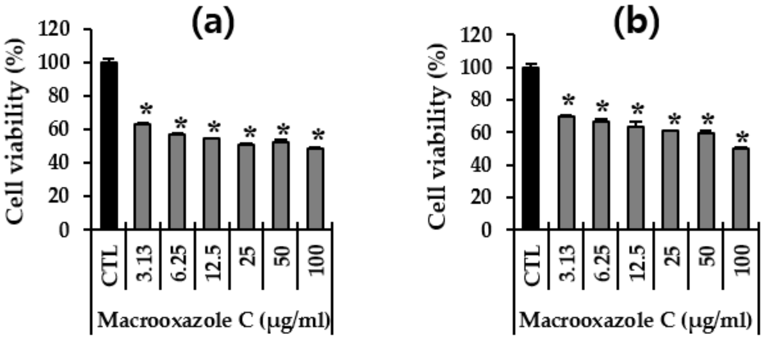


Figure S4. (+)HRESIMS spectrum of macrooxazole E (**1**)

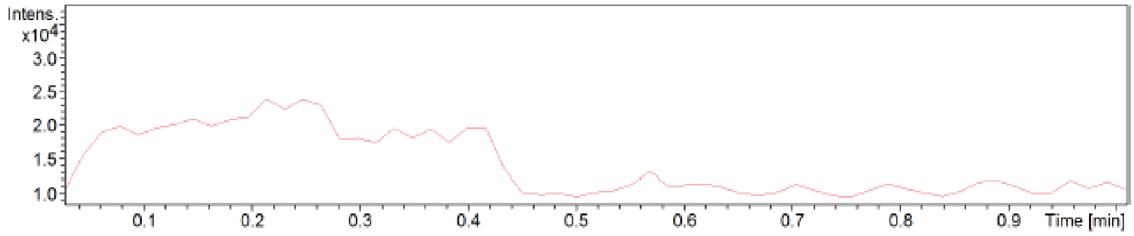
Compound Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Data\2020\DSWU\SSH\KHR\KHR006-1.d	Acquisition Date	12/21/2020 10:39:09 AM
Method	Tune_pos_Standard_50_600_20201008.d.m	Operator	lee
Sample Name	JS228H9-3T	Instrument	compact 8255754.10024
Comment			

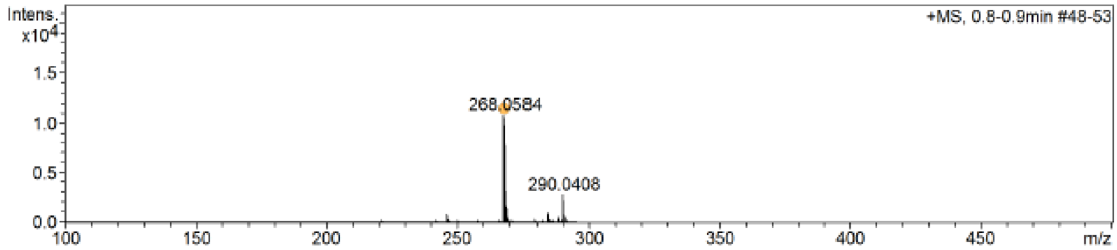
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	290 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
n.a.	0.9	n.a.	Average spectrum	n.a.	n.a.	n.a.	268.0584	n.a.

+MS, 0.8-0.9min #48-53



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule
268.0584	1	C11H6N7O2	268.0577	2.6	5.4	1	100.00	12.5	even	ok
	2	C15H10NO4	268.0604	-7.4	11.2	2	39.83	11.5	even	ok
	3	C10H10N3O6	268.0564	-7.6	15.6	3	35.09	7.5	even	ok
	4	C16H6N5	268.0618	-12.4	24.9	4	9.02	16.5	even	ok
	1	C13H11NNaO4	268.0580	-1.6	3.0	1	100.00	8.5	even	ok
	2	C14H7N5Na	268.0594	-3.4	13.3	2	64.30	13.5	even	ok
	3	C9H7N7NaO2	268.0553	11.6	15.8	3	11.40	9.5	even	ok

Figure S5. ^{1}H NMR spectrum (800 MHz, CD_3OD) of macrooxazole E (**1**)

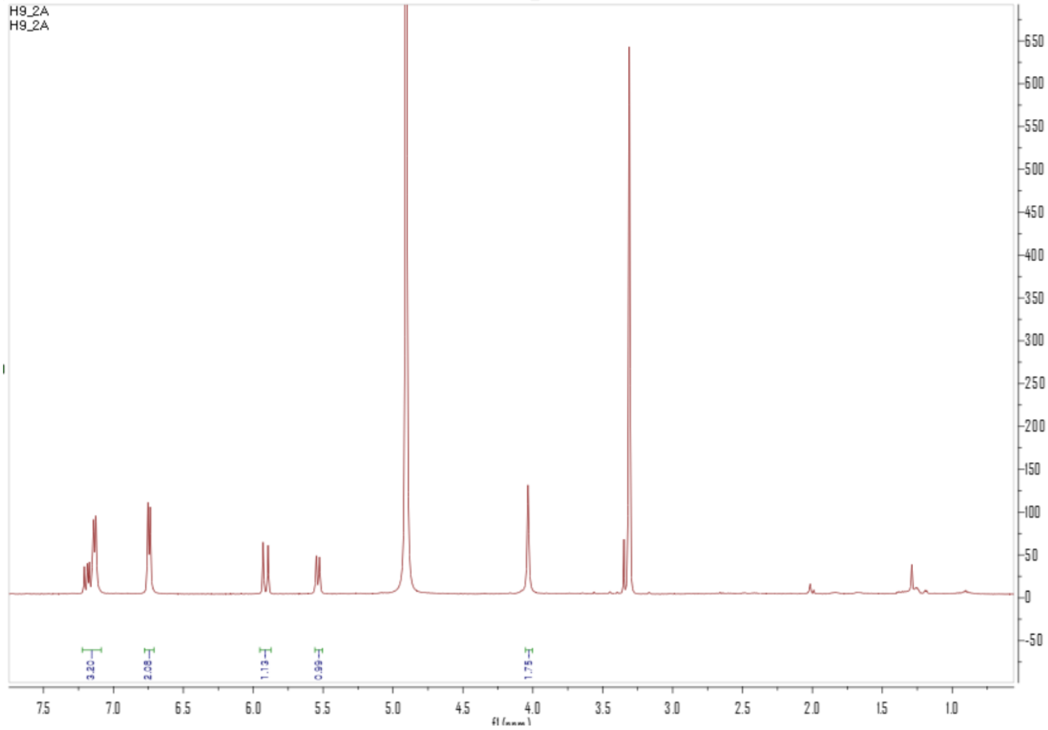


Figure S6. ^{13}C NMR spectrum (200 MHz, CD_3OD) of macrooxazole E (**1**)

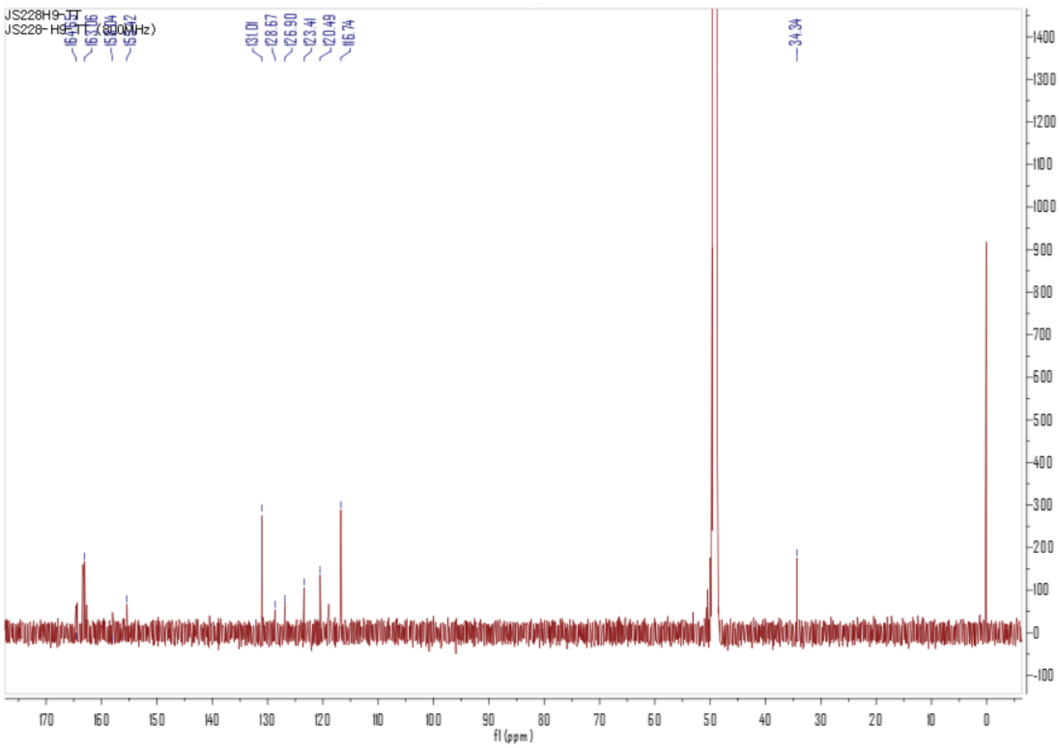


Figure S7. ^{1}H-^{1}H COSY spectrum (800 MHz, CD_3OD) of macrooxazole E (**1**)

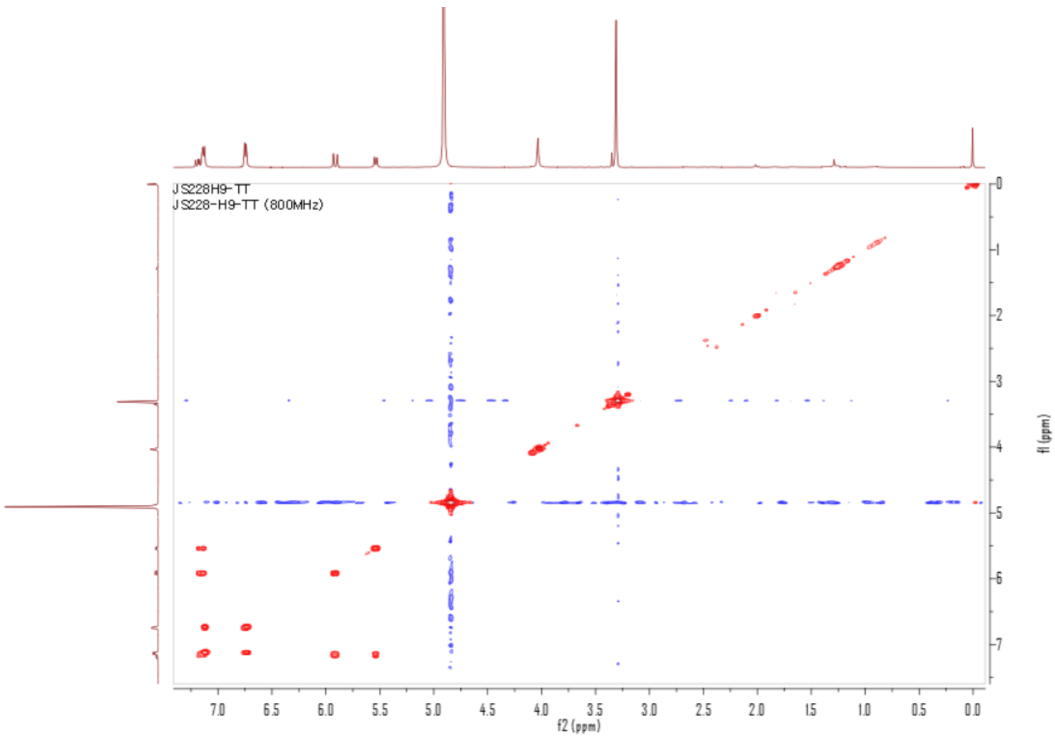


Figure S8. HSQC spectrum (800 MHz, CD_3OD) of macrooxazole E (**1**)

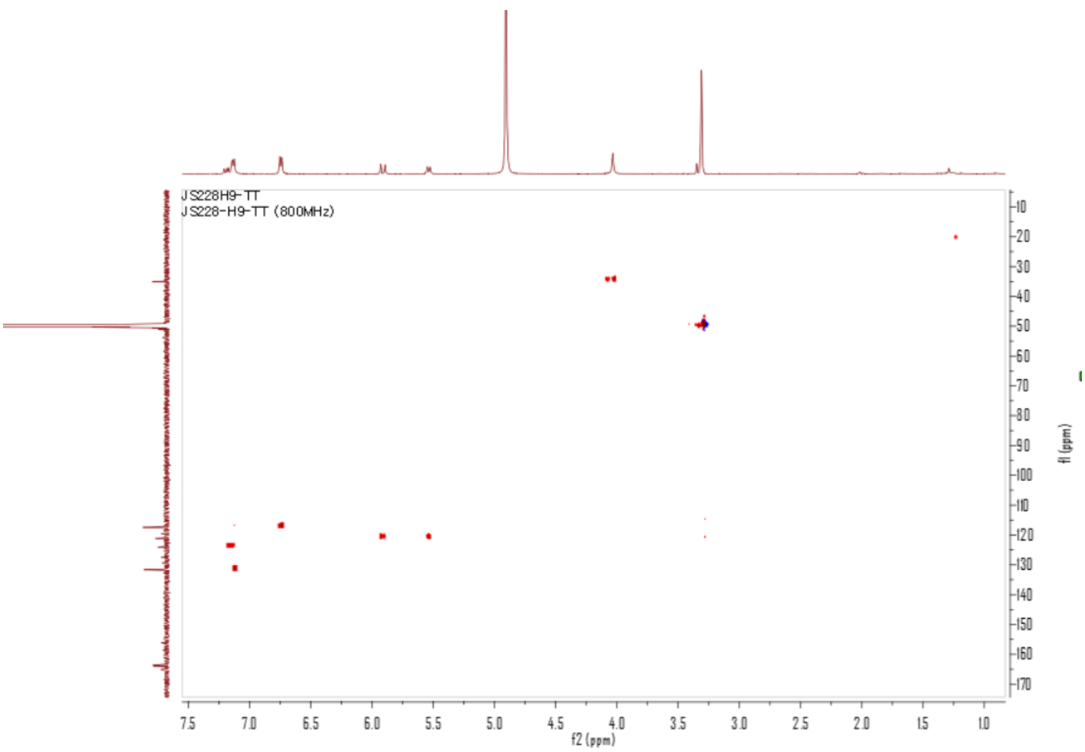


Figure S9. HMBC spectrum (800 MHz, CD_3OD) of macrooxazole E (**1**)

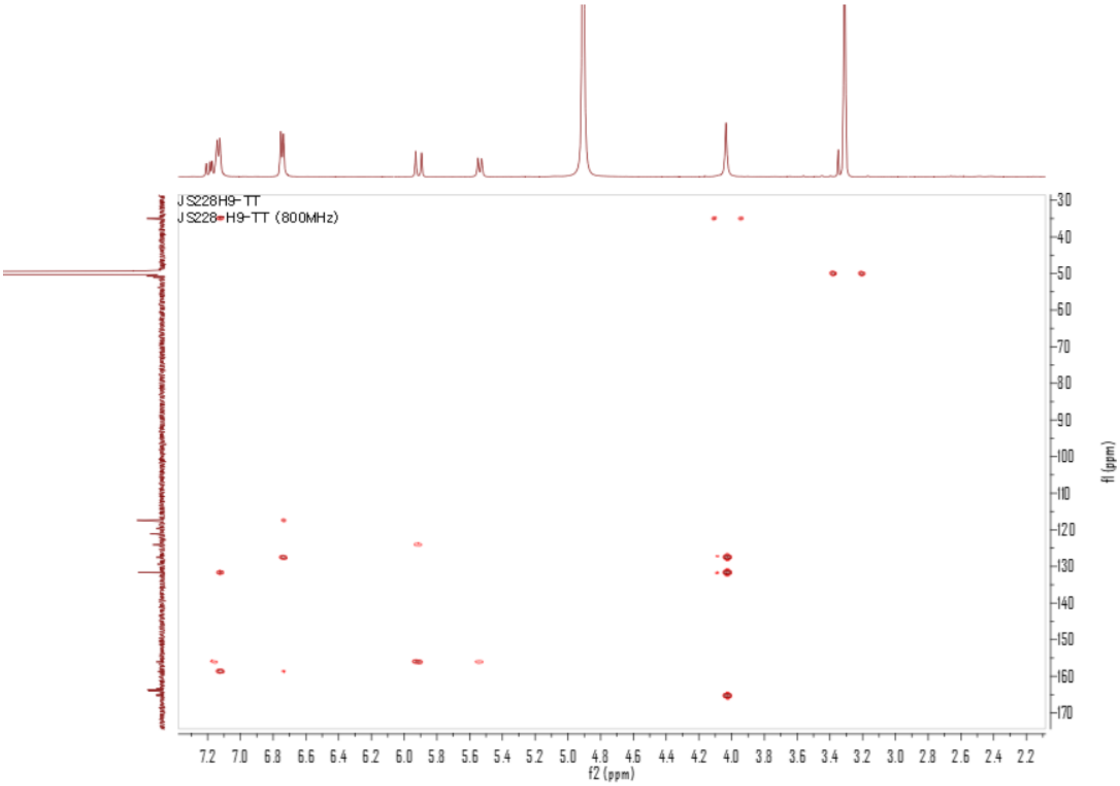


Figure S10. (+)HRESIMS spectrum of macrooxazole C (**2**)

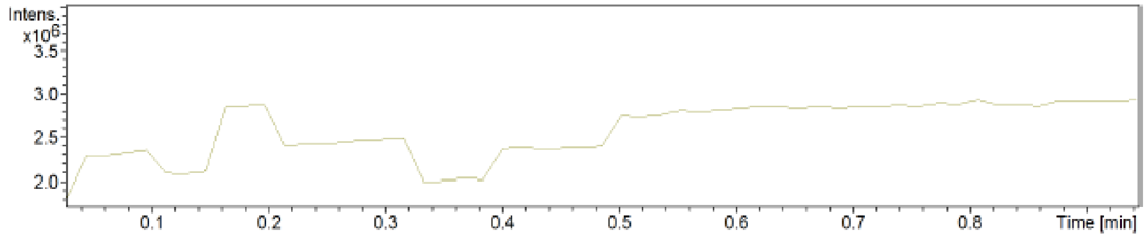
Compound Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Data\2020\DSWU\SSH\KHR\KHR001-1.d	Acquisition Date	12/10/2020 10:36:39 AM	
Method	Tune_pos_Standard_50_600_20201008.d.m	Operator	lee	
Sample Name	KU1_JS228-D1	Instrument	compact	8255754.10024
Comment				

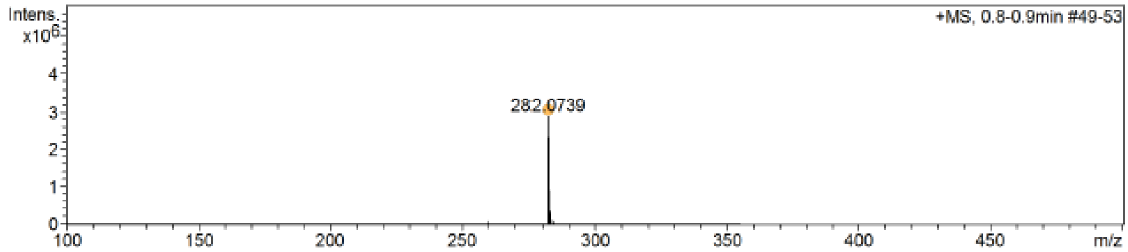
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	350 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
n.a.	0.9	n.a.	Average spectrum	n.a.	n.a.	n.a.	282.0739	n.a.

+MS, 0.8-0.9min #49-53



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule
282.0739	1	C11H12N3O6	282.0721	6.5	1.9	1	53.95	7.5	even	ok
	2	C8H4N13	282.0707	-11.3	5.5	2	15.79	13.5	even	ok
	3	C12H8N7O2	282.0734	1.8	12.5	3	100.00	12.5	even	ok
	4	C16H12NO4	282.0761	-7.8	25.7	4	25.85	11.5	even	ok
	5	C17H8N5	282.0774	12.5	39.0	5	5.27	16.5	even	ok
	1	C10H9N7NaO2	282.0710	10.3	3.0	1	19.26	9.5	even	ok
	2	C14H13NNaO4	282.0737	-0.8	13.1	2	100.00	8.5	even	ok
	3	C15H9N5Na	282.0750	-4.0	26.6	3	47.27	13.5	even	ok

Figure S11. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of macrooxazole C (**2**)

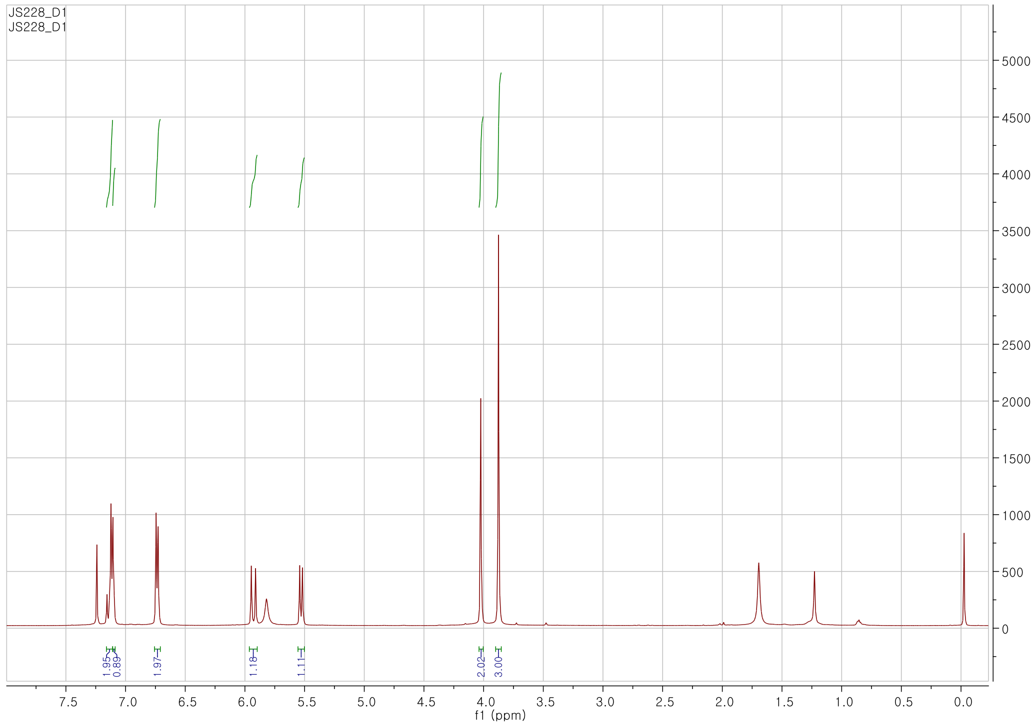


Figure S12. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of macrooxazole C (**2**)

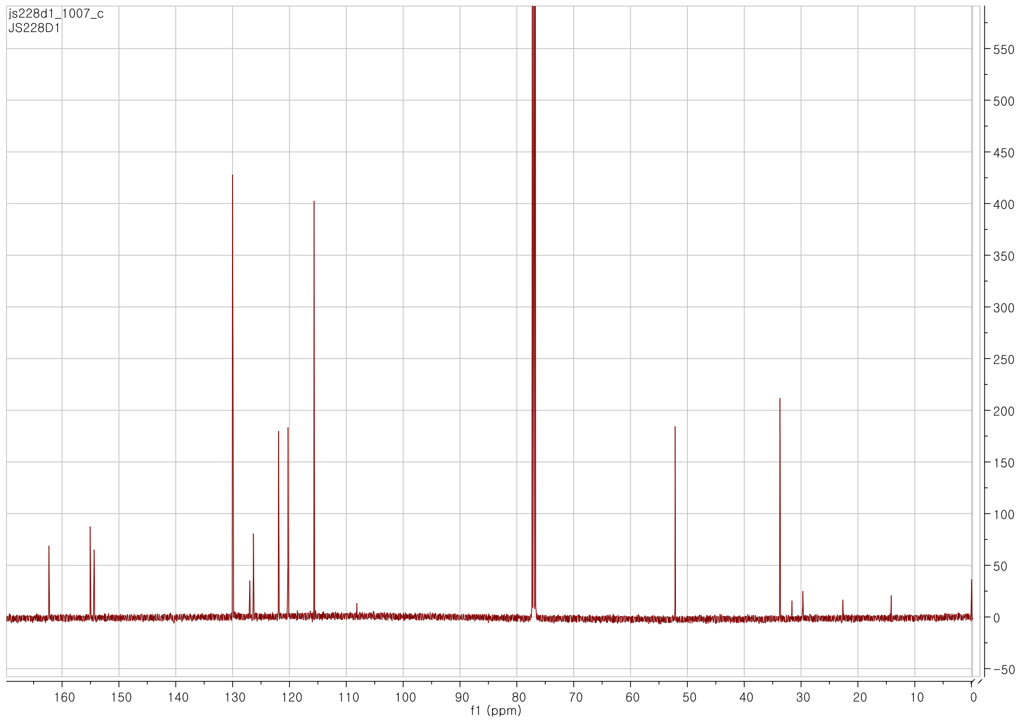


Figure S13. ^{1}H-^{1}H COSY spectrum (500 MHz, $CDCl_3$) of macrooxazole C (**2**)

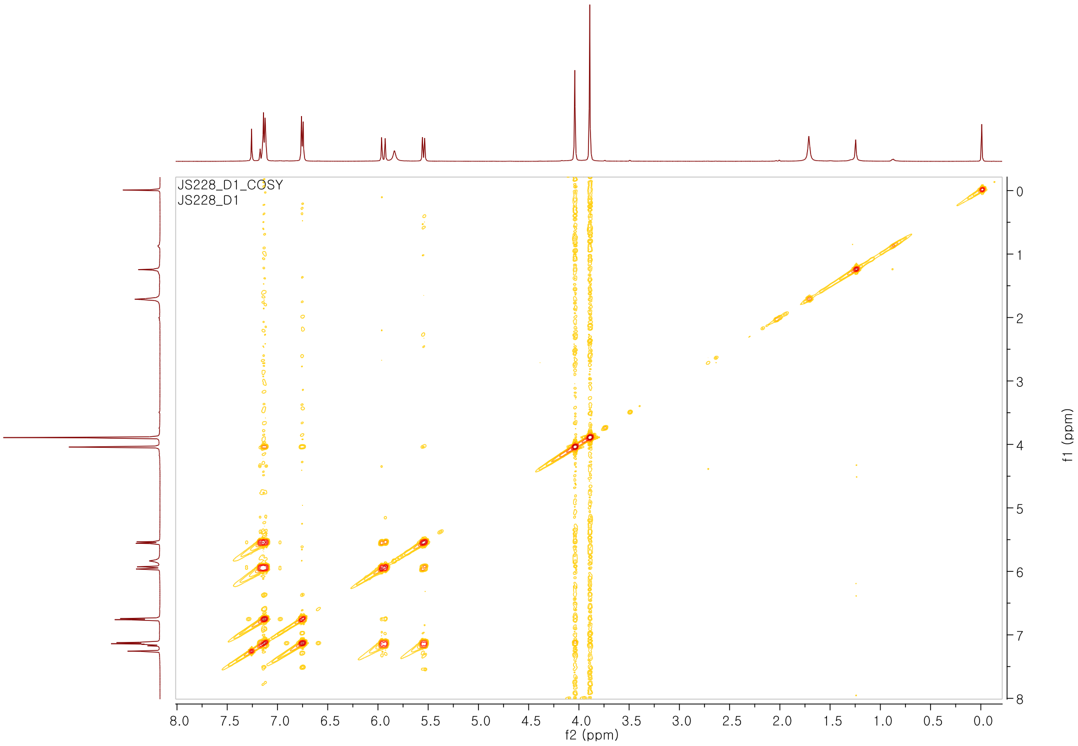


Figure S14. HSQC spectrum (500 MHz, $CDCl_3$) of macrooxazole C (**2**)

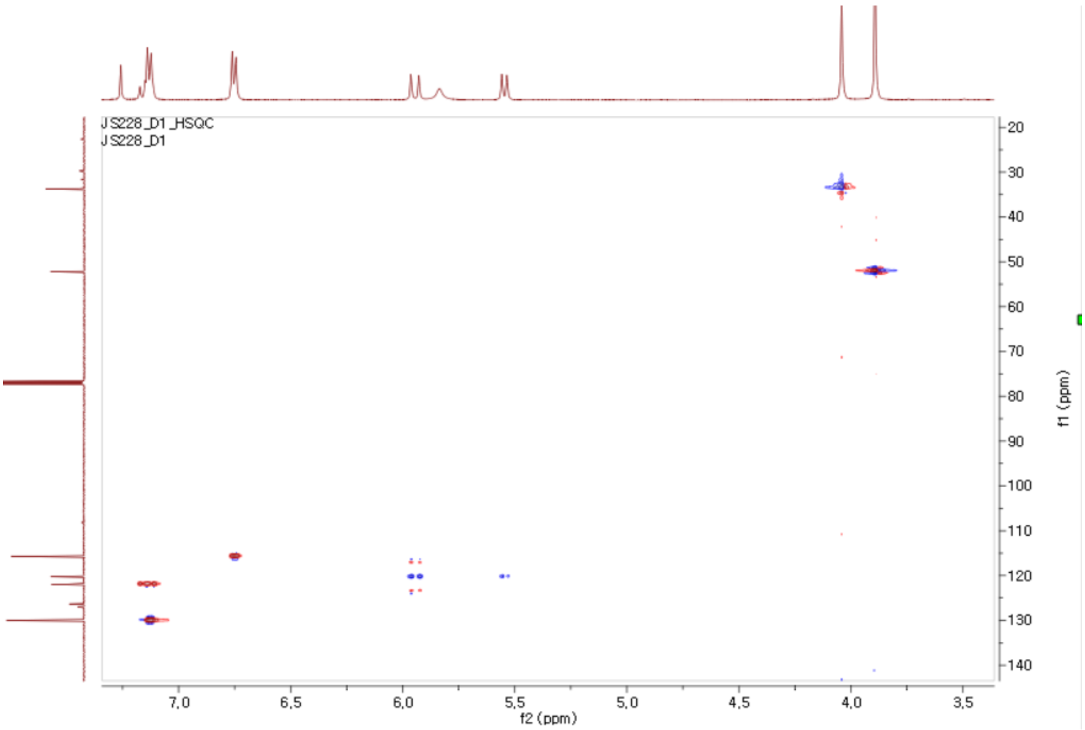


Figure S15. HMBC spectrum (500 MHz, $CDCl_3$) of macrooxazole C (**2**)

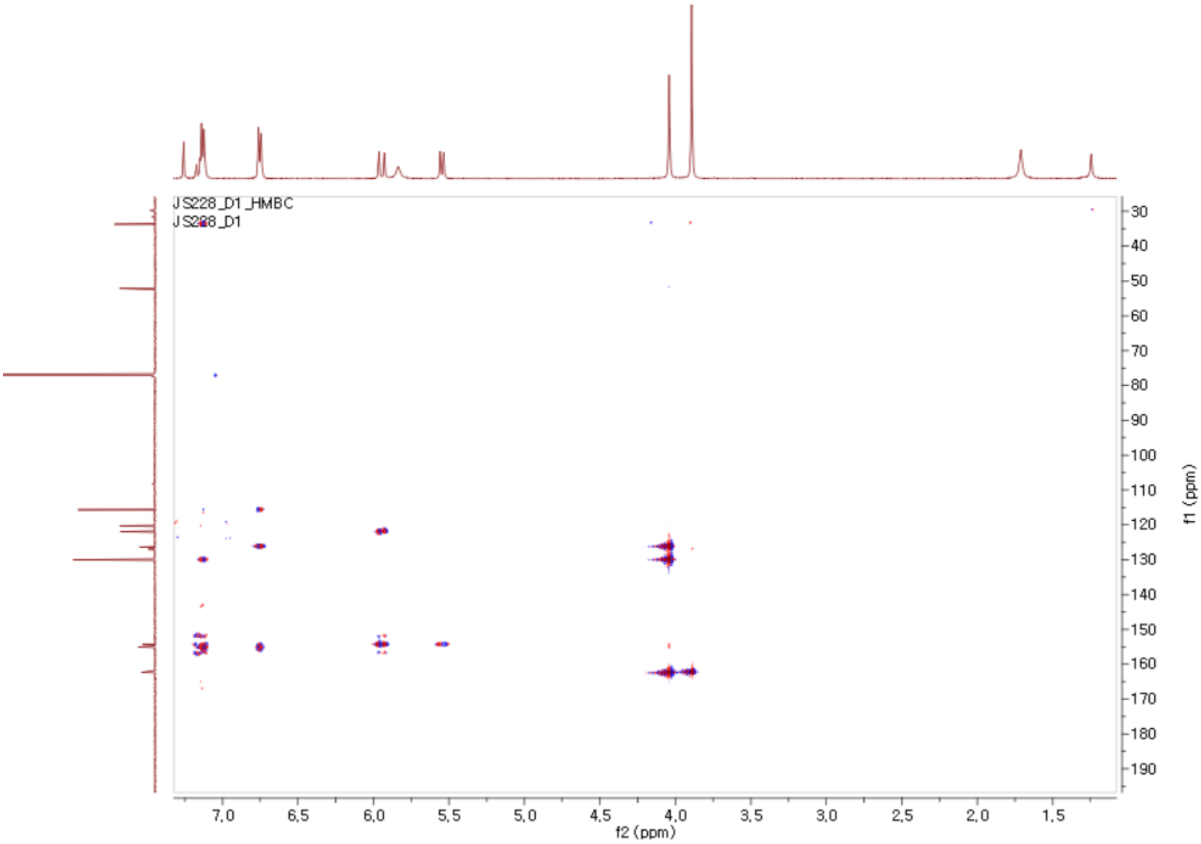


Figure S16. ESIMS Spectrum of macrooxazole E (**1**) and macrooxazole C (**2**)

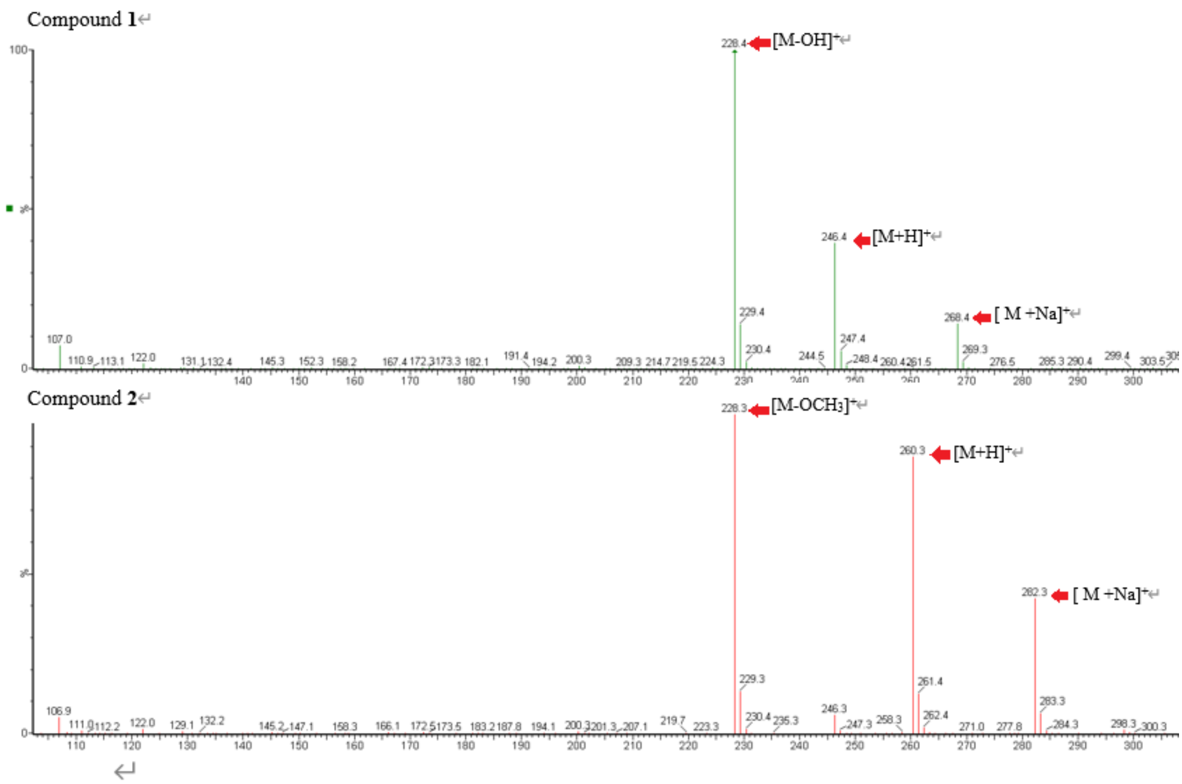


Figure S17. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of macrooxazole A (**3**)

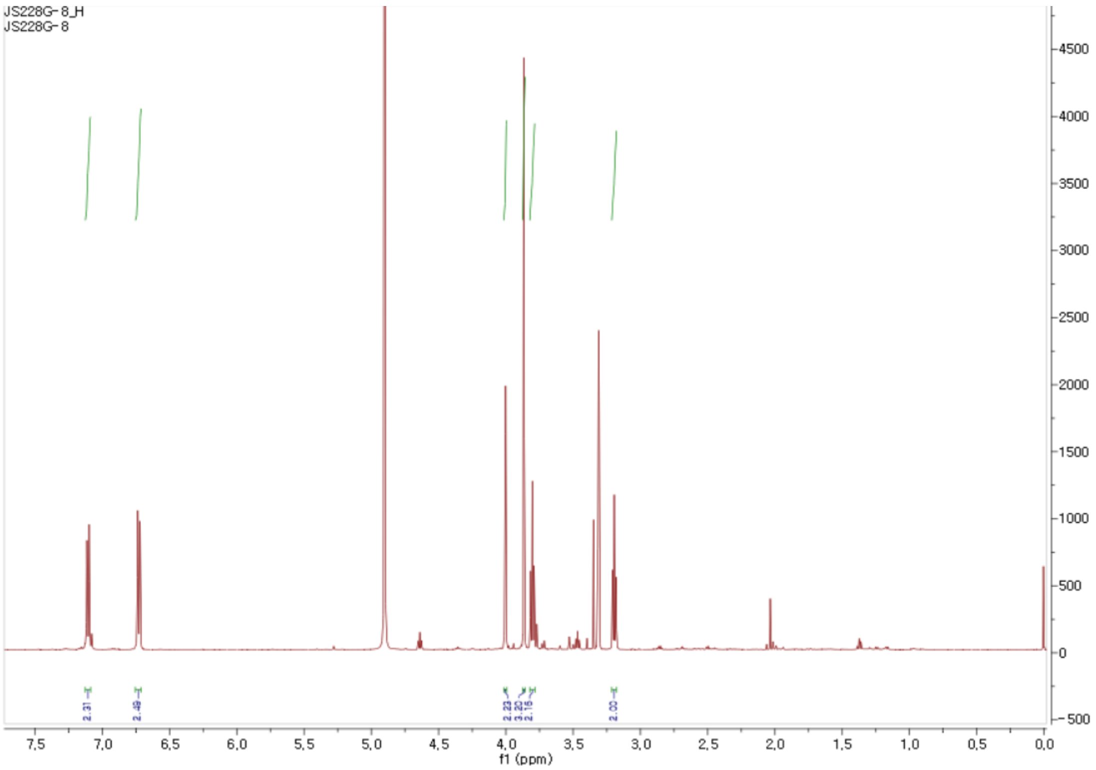


Figure S18. ^{1}H NMR spectrum (500 MHz, CD_3OD) of macrooxazole B (**4**)

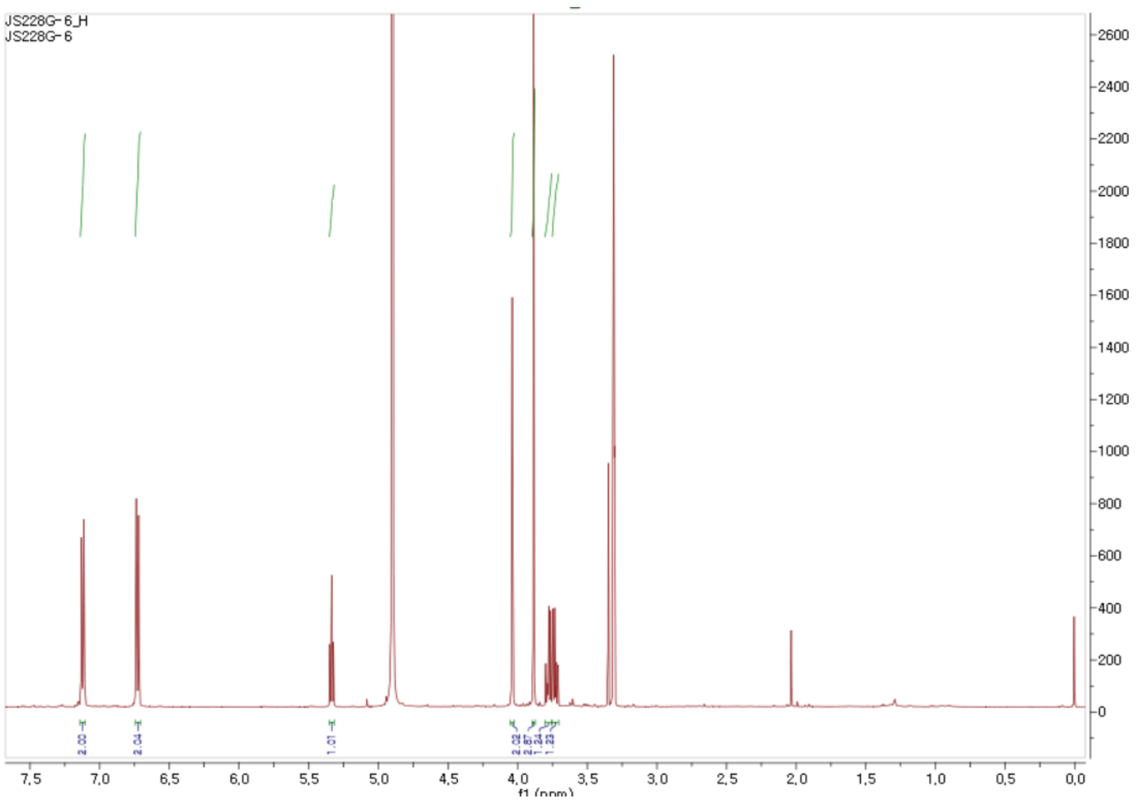


Table S1. NMR spectroscopic data of the isolated compounds **2-5**.

No.	**2**		**3**	**4**	**5**
	*δ*C, Type	*δ*H (*J* in Hz)	*δ*H (*J* in Hz)		
1	-	-	-	-	-
2	162.3, C	-	-	-	-
3	-	-	-	-	7.16, d (3.5)
4	127.0, C	-	-	-	6.47, d (3.5)
5	154.4, C	-	-	-	4.57, s
6	33.8, CH_2	4.05, s	4.00, s	4.04, s	-
7	126.4, C	-	-	-	-
8	130.0, CH	7.13, d (9.0)	7.10, d (8.4)	7.12, d (8.0)	-
9	115.7, CH	6.76, d (9.0)	6.73, d (8.4)	6.73, d (8.0)	-
10	155.1, C	-	-	-	-
11	115.7, CH	6.76, d (9.0)	6.73, d (8.4)	6.73, d (8.0)	-
12	130.0, CH	7.13, d (9.0)	7.10, d (8.4)	7.12, d (8.0)	-
13	162.2, C	-	-	-	-
14	121.9, CH	7.15, dd (18, 12)	3.19, t (6.8)	5.33, t (6.5)	-
15	120.2, CH_2	5.55, dd (12, 1.1) 5.95, dd (18, 1.1)	3.80, t (6.8)	3.73, dd (12, 6.5)	
OCH_3	52.2, CH_3	3.90, s	3.87, s	3.89, s	