

Supplementary Material

Induction of Antibacterial Metabolites by Co-Cultivation of Two Red-Sea-Sponge-Associated Actinomycetes *Micromonospora* sp. UR56 and *Actinokinespora* sp. EG49

Mohamed S. Hifnawy^{1§}, Hossam M. Hassan^{2§}, Rabab Mohammed², Mohamed M. Fouda³, Ahmed M. Sayed³, Ahmed A. Hamed⁴, Sameh F. AbouZid², Mostafa E. Rateb⁵, Hani A. Alhadrami^{6,7,*} and Usama Ramadan Abdelmohsen^{8,9*}.

¹*Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Cairo, Egypt 11787,*

²*Department of Pharmacognosy, Faculty of Pharmacy, Beni-Suef University, Beni-Suef, Egypt 62514,*

³*Department of Pharmacognosy, Faculty of Pharmacy, Nahda University, Beni-Suef, Egypt 62513,*

⁴*Microbial Chemistry Department, National Research Center, 33 El-Buhouth Street, 12622, Giza, Egypt,*

⁵*School of Computing, Engineering & Physical Sciences, University of the West of Scotland, Paisley PA1 2BE, UK,*

⁶*Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, 21589, Saudi Arabia,*

⁷*King Fahd Medical Research Centre, King Abdulaziz University, Jeddah, 21589, Saudi Arabia*

⁸*Department of Pharmacognosy, Faculty of Pharmacy, Minia University, 61519 Minia, Egypt,*

⁹*Department of Pharmacognosy, Faculty of Pharmacy, Deraya University, Universities Zone, P.O. Box 61111 New Minia City, 61519 Minia.*

*Correspondence: usama.ramadan@mu.edu.eg (URA) and hani.alhadrami@kau.edu.sa (HAA).

§Equal contributions: Mohamed S. Hifnawy and Hossam M. Hassan as first authors

Table S1. The dereplication results of the ethyl acetate fraction of micromonospora UR 56.

Table S2. The dereplication results of the ethyl acetate fraction of Actinokinospora EG49.

Table S3. The dereplication results of the ethyl acetate fraction of co-culture.

Figure S1: $^1\text{H-NMR}$ Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate)(CDCl_3).

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Figure S12: HMBC Spectrum of compound 2 (phencomycin)(CDCl_3).

Figure S13: HRESIMS of compound 2 (phencomycin).

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Figure S16: $^{13}\text{C-NMR}$ spectrum of compound 3 (Phenazine -1-carboxylic acid) (CDCl_3).

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Figure S23: $^{13}\text{C-NMR}$ spectrum of compound 11 (N-(2-hydroxyphenyl)-acetamide)(MeOD).

Figure S24: ^1H - ^1H COSY Spectrum of compound **11** (N-(2-hydroxyphenyl)-acetamide)(MeOD).

Figure S25: HSQC Spectrum of compound **11**(N-(2-hydroxyphenyl)-acetamide)(MeOD).

Figure S26: HMBC Spectrum of compound **11**(N-(2-hydroxyphenyl)-acetamide)(MeOD).

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Figure S28: ^1H -NMR Spectrum of compound **12** (P-anisamide)(CDCl_3).

Figure S29: DEPTQ spectrum of compound **12**(p-anisamide)(CDCl_3) .

Figure S30: Dereplicated metabolites from metabolomic analysis of *Micromonospora* sp UR 56.

Figure S31: Dereplicated metabolites from metabolomic analysis of *Actinokineospora* sp. *EG49*.

Figure S32. Dereplicated metabolites from metabolomic analysis of **co-culture** *Micromonospora* sp. UR 56 and *Actinokineospora* sp. *EG49*.

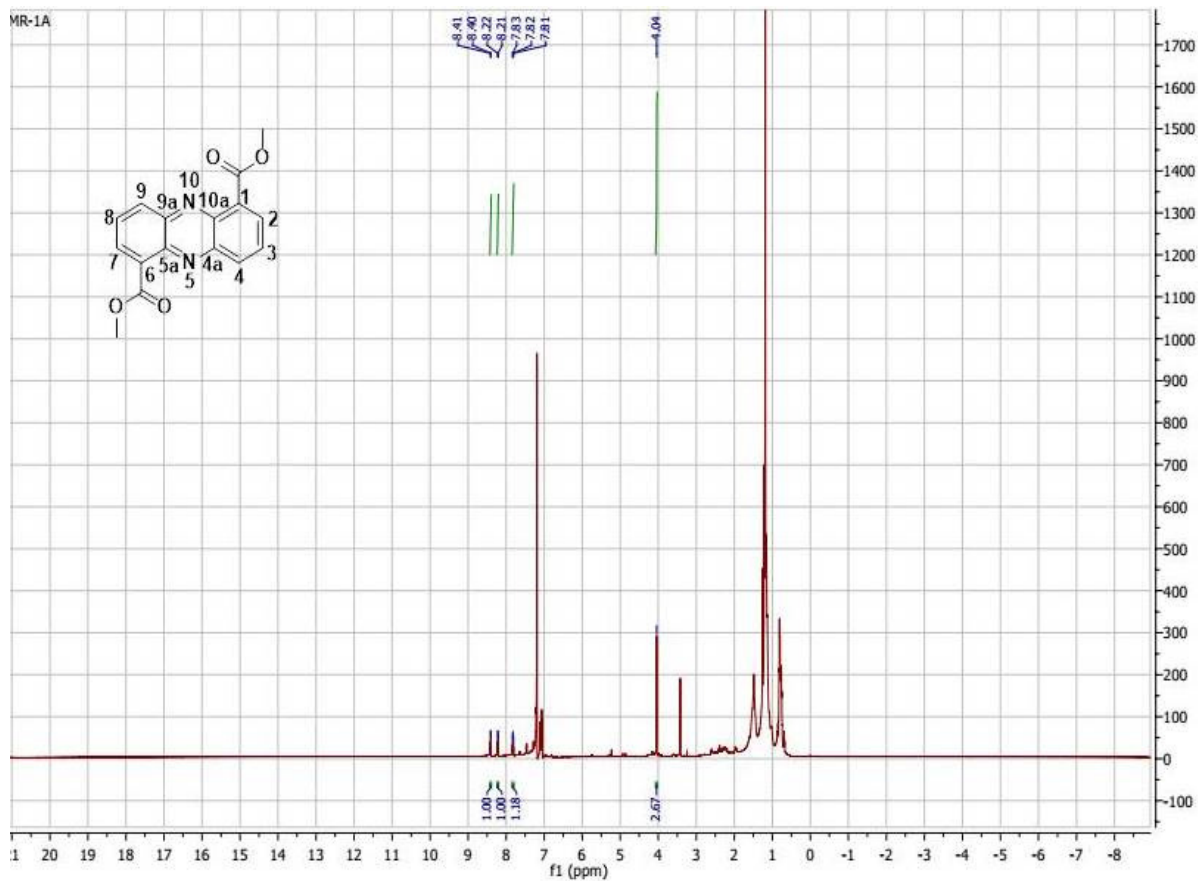


Figure S1: $^1\text{H-NMR}$ Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate)(CDCl₃).

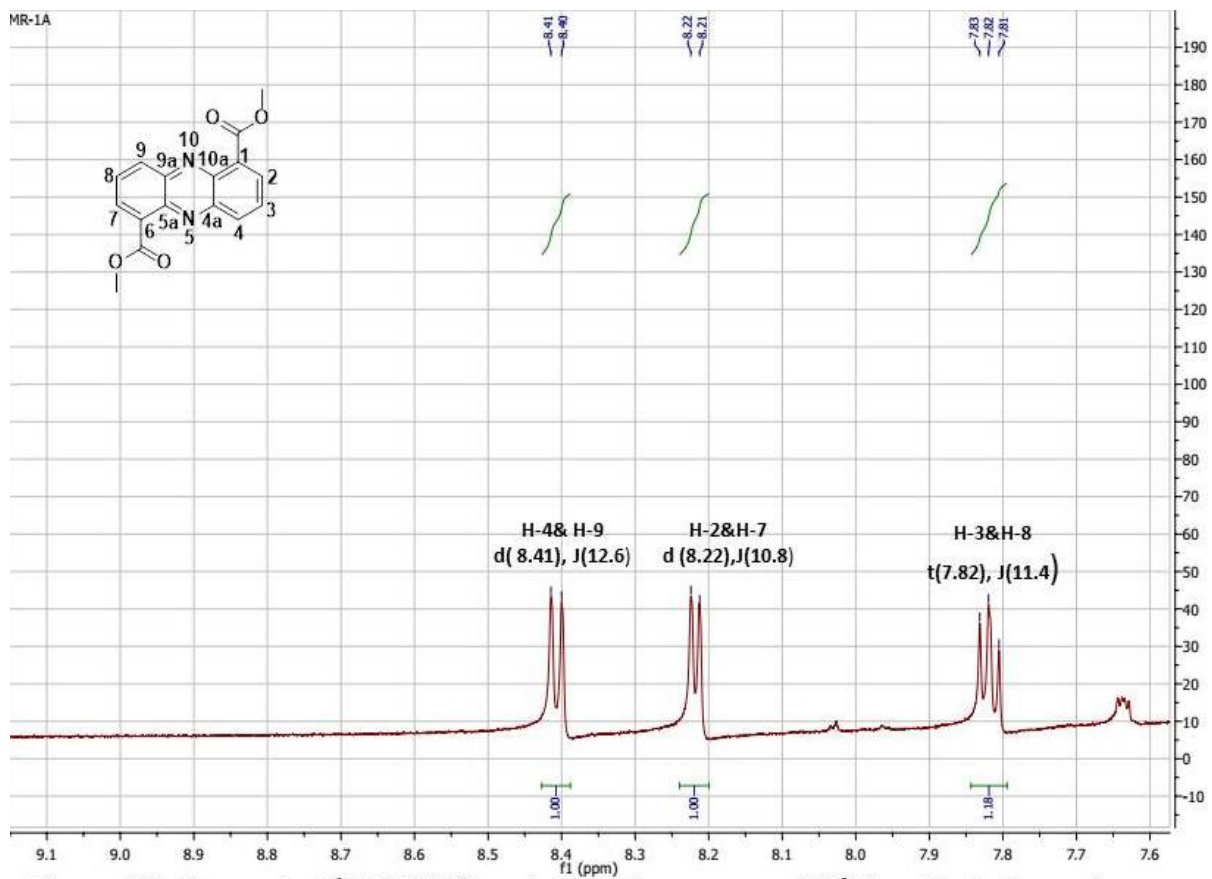


Figure S2: Expanded ^1H -NMR Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate)(CDCl_3).

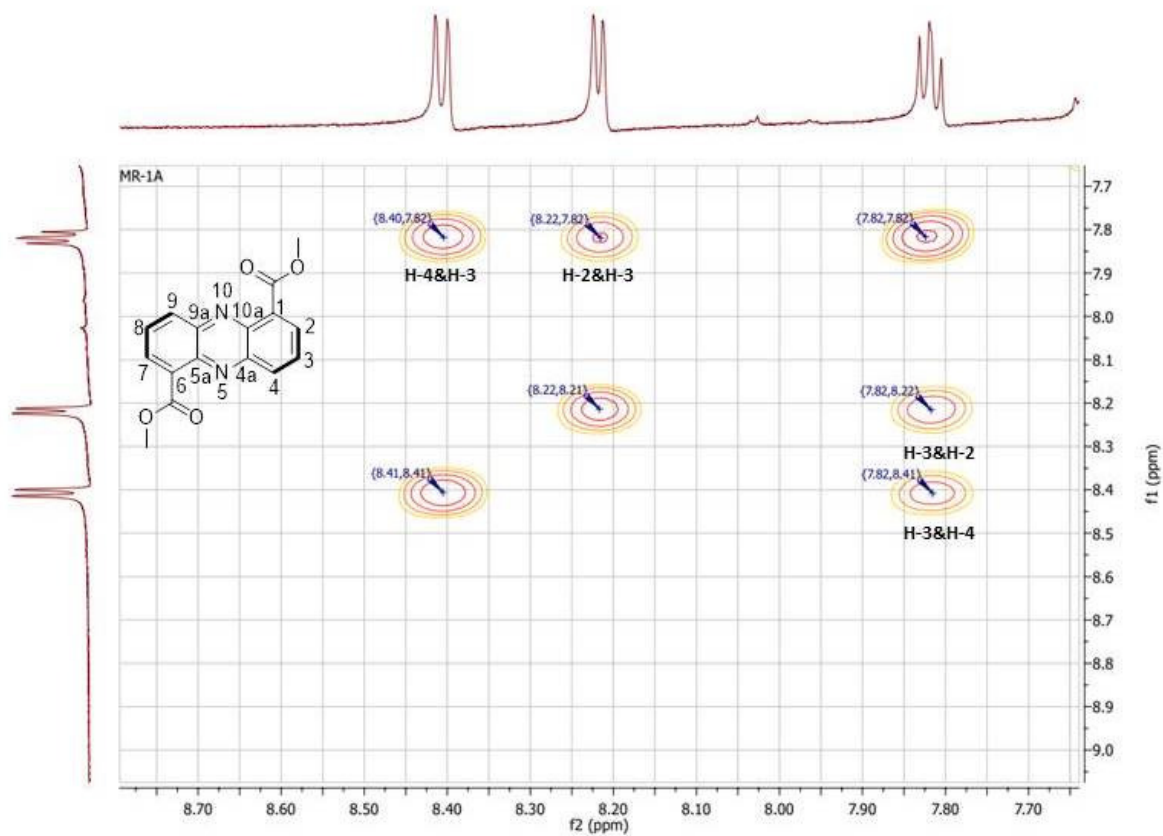


Figure S3: ^1H - ^1H COSY Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate)(CDCl_3).

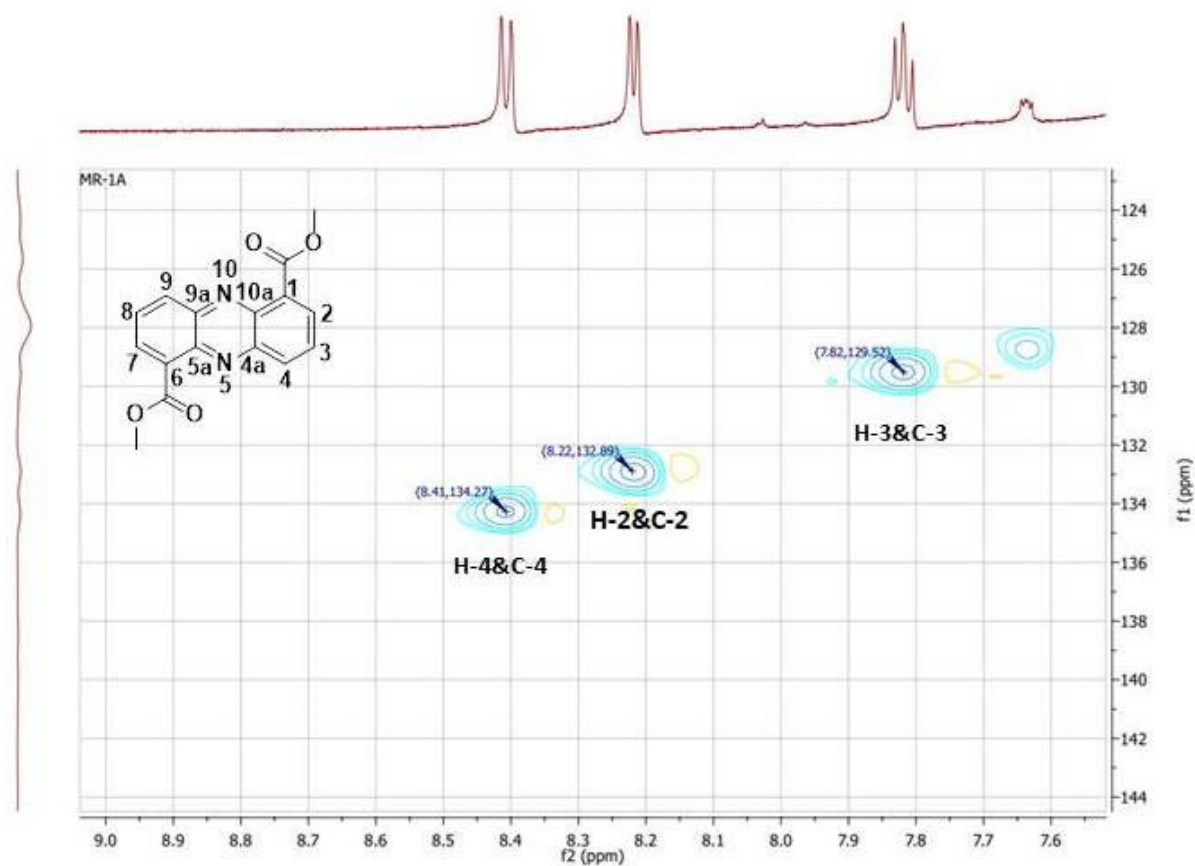


Figure S4: HSQC Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate)(CDCl₃).

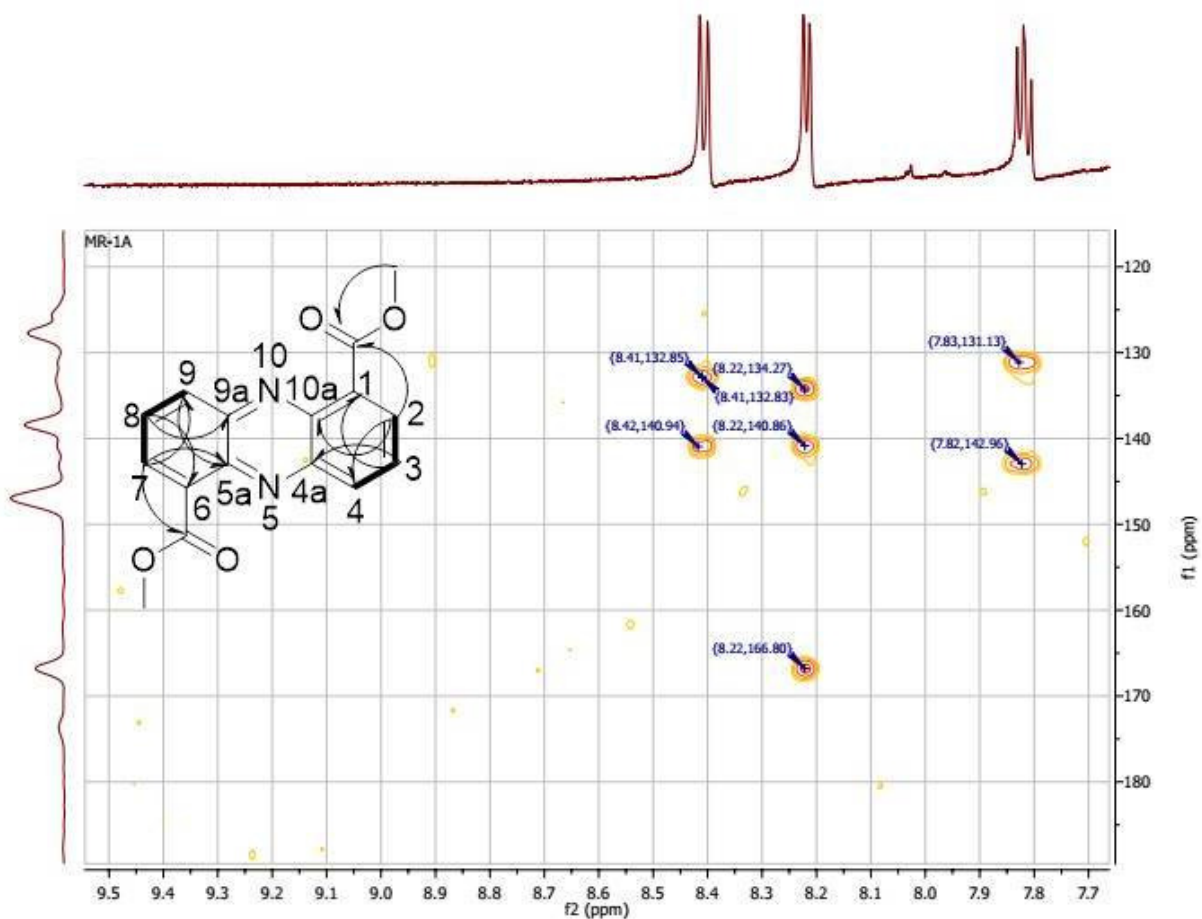
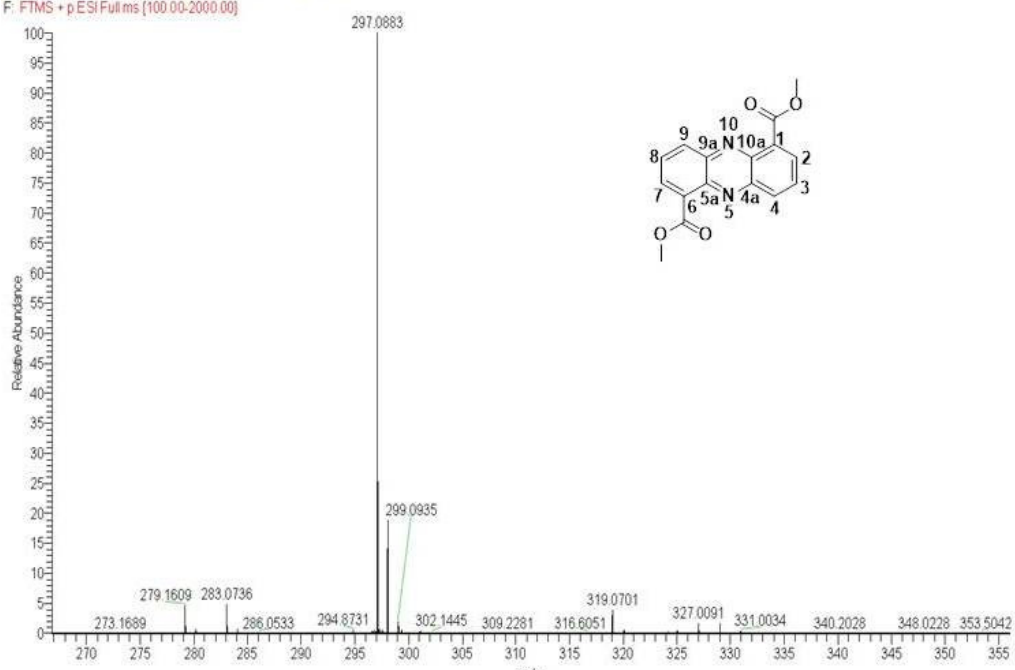
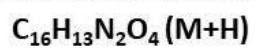


Figure S5: HMBC Spectrum of compound 1 (dimethyl phenazine-1,6-dicarboxylate (CDCl₃))

MR758_1A#232-253 RT: 9.64-10.29 AV: 11 NL: 8.50E6
F: FTMS + p.ESI Fullms [100.00-2000.00]



FigureS6: HRESIMS of compound 1 (dimethyl phenazine-1,6-dicarboxylate).



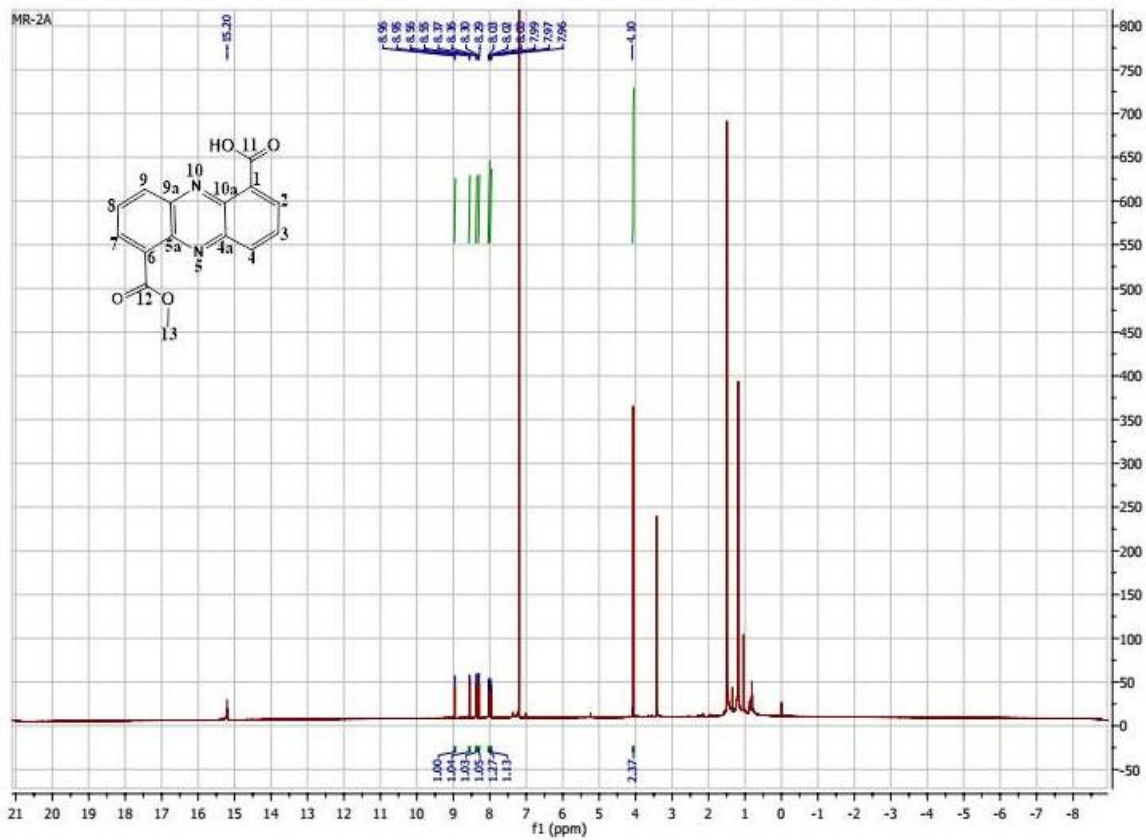


Figure S7: ¹H-NMR Spectrum of compound 2 (phencomycin)(CDCl₃).

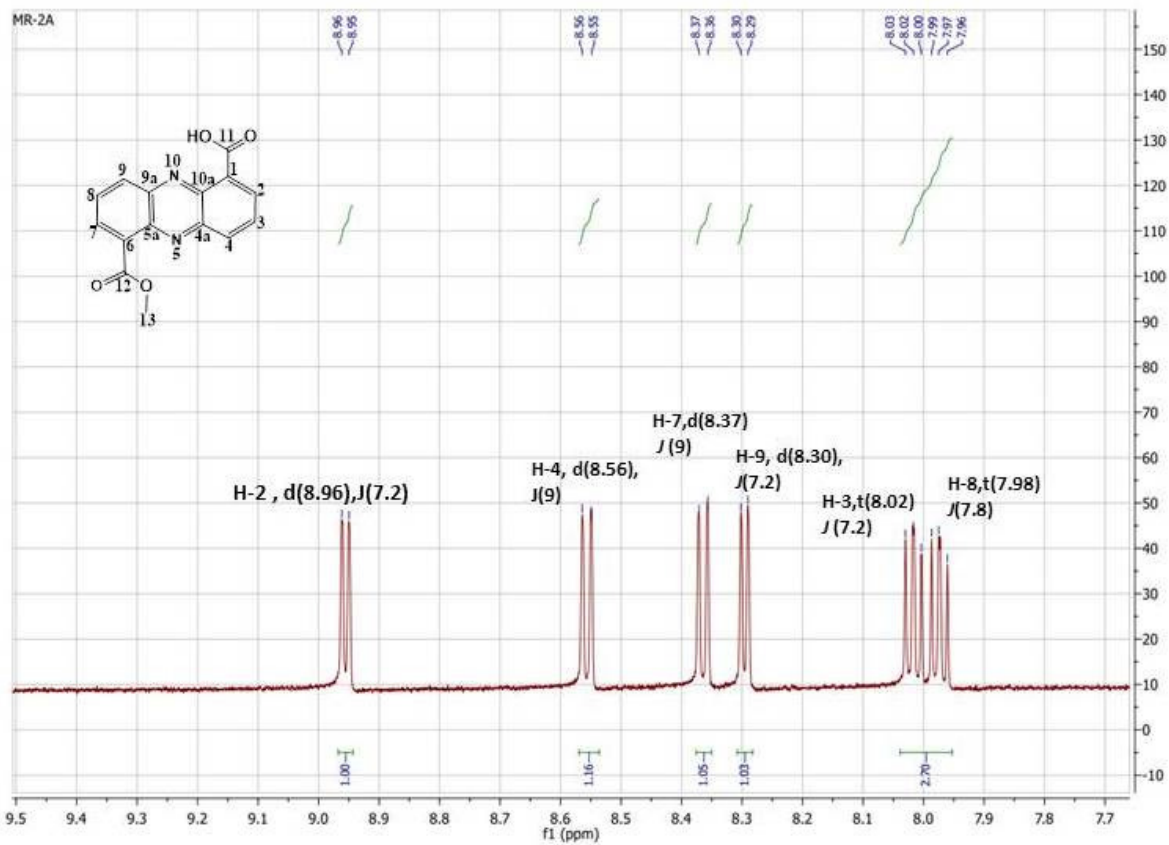


Figure S8: Expanded ^1H -NMR Spectrum of compound 2 (phencomycin)(CDCl_3).

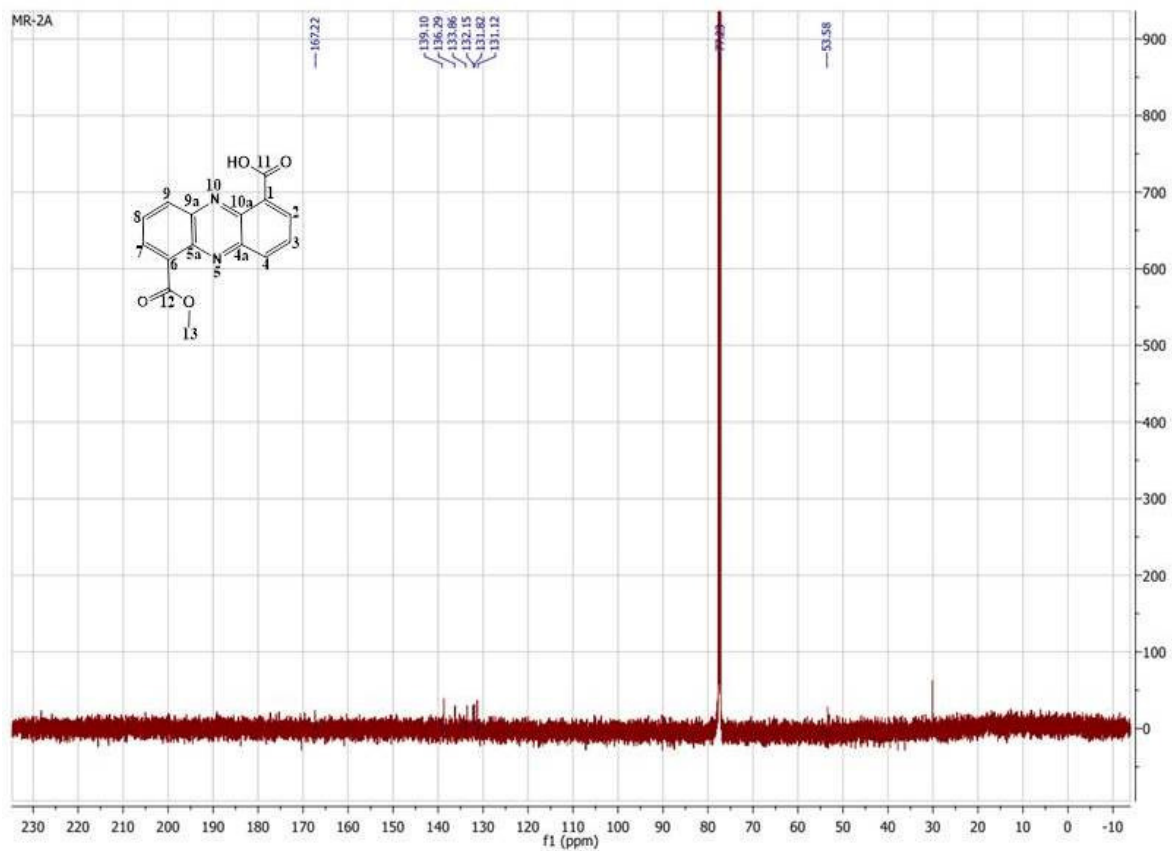


Figure S9: ^{13}C -NMR spectrum of compound 2 (phencomycin)(CDCl_3).

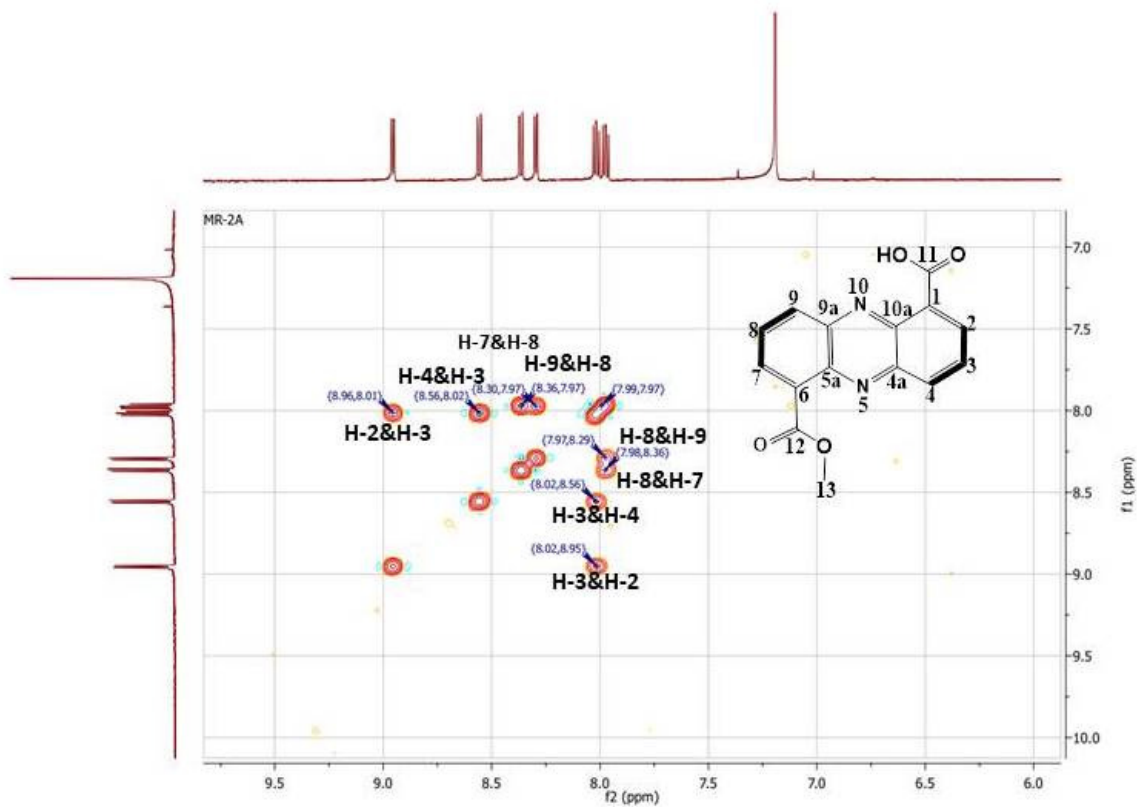


Figure S10: ^1H - ^1H COSY Spectrum of compound 2 (phencomycin)(CDCl_3).

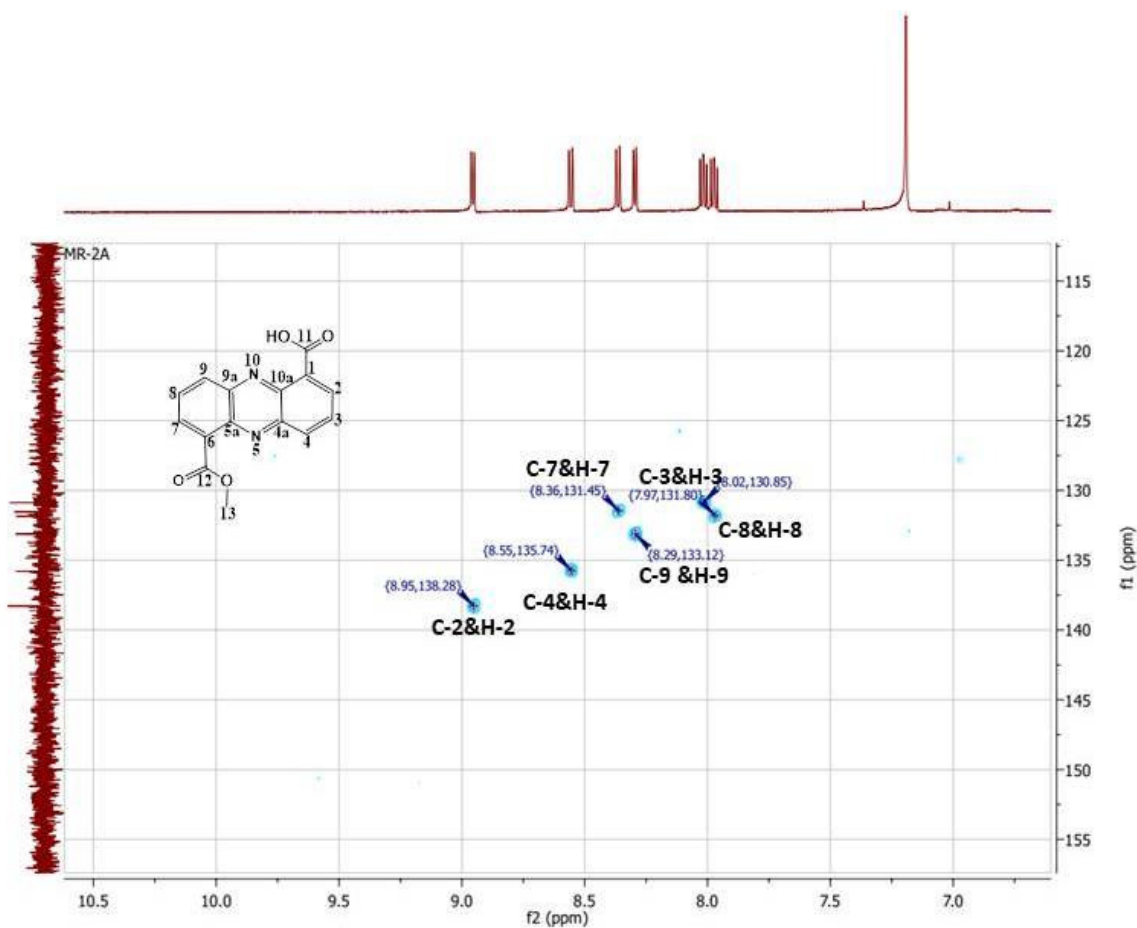
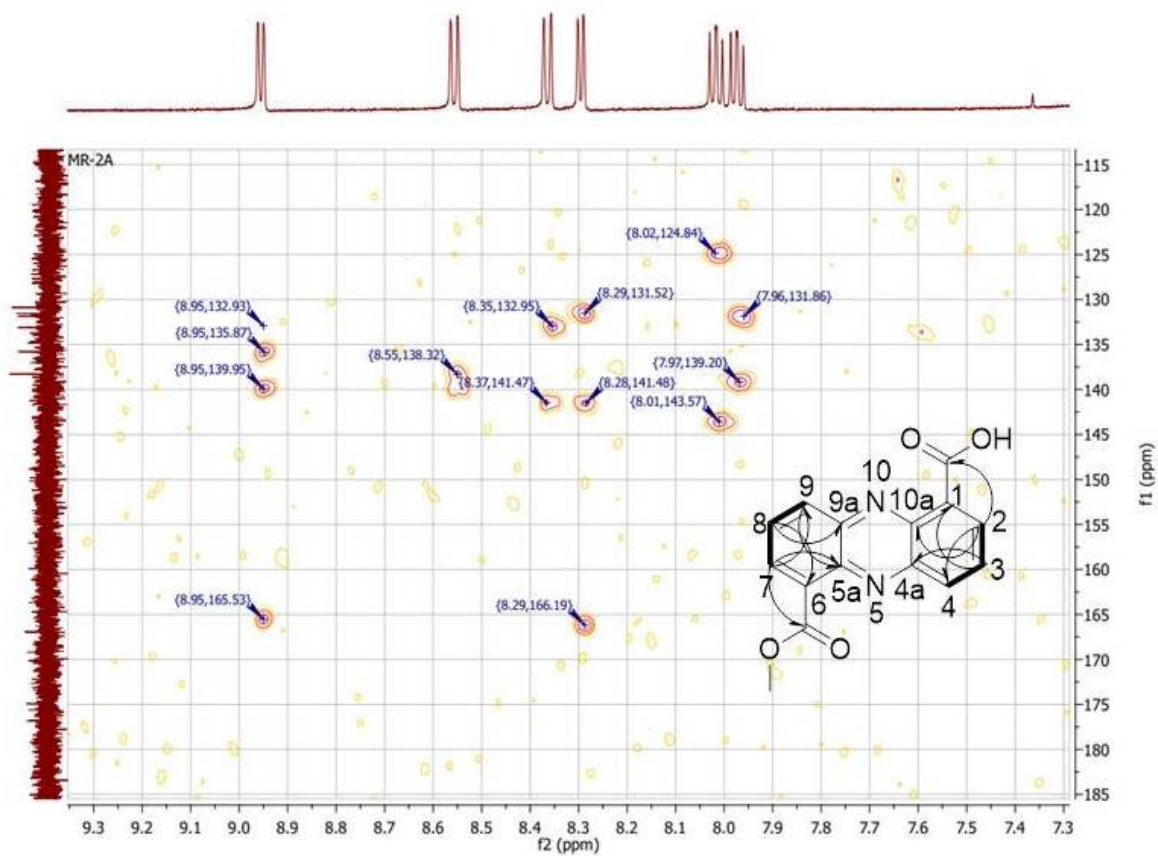
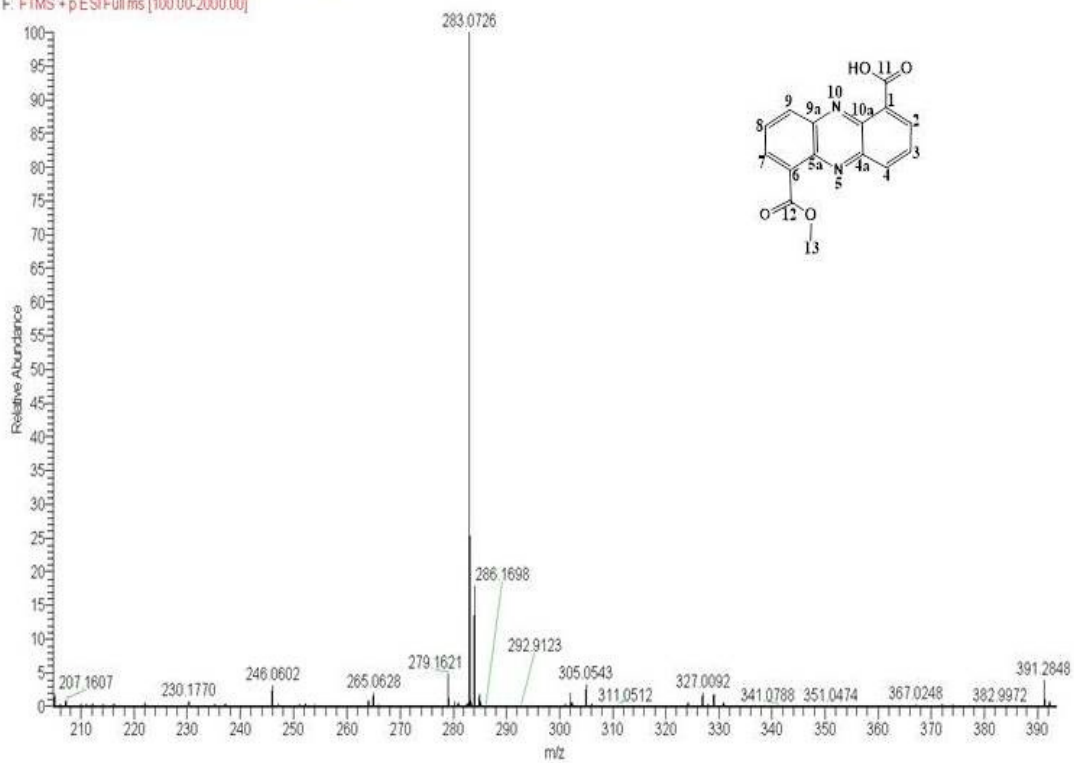


Figure S11: HSQC Spectrum of compound 2 (phencomycin)(CDCl_3).

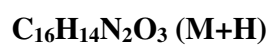


FigureS12: HMBC Spectrum of compound 2 (phencomycin)

MR759_2A#214-232 RT: 8.94-9.50 AV: 10 NL: 7.80E6
F: FTMS + pESI Fullms [100.00-2000.00]



FigureS13: HRESIMS of compound 2 (phencomycin)



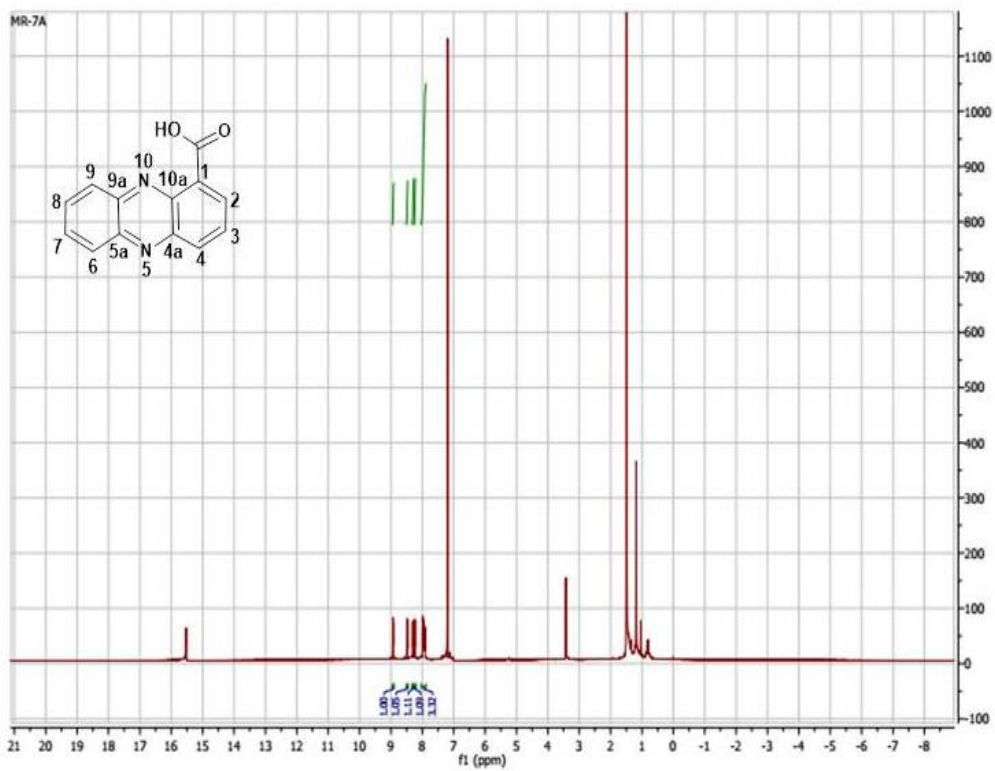


Figure S14: ^1H -NMR Spectrum of compound 3 (Phenazine -1-carboxylic acid) (CDCl_3).

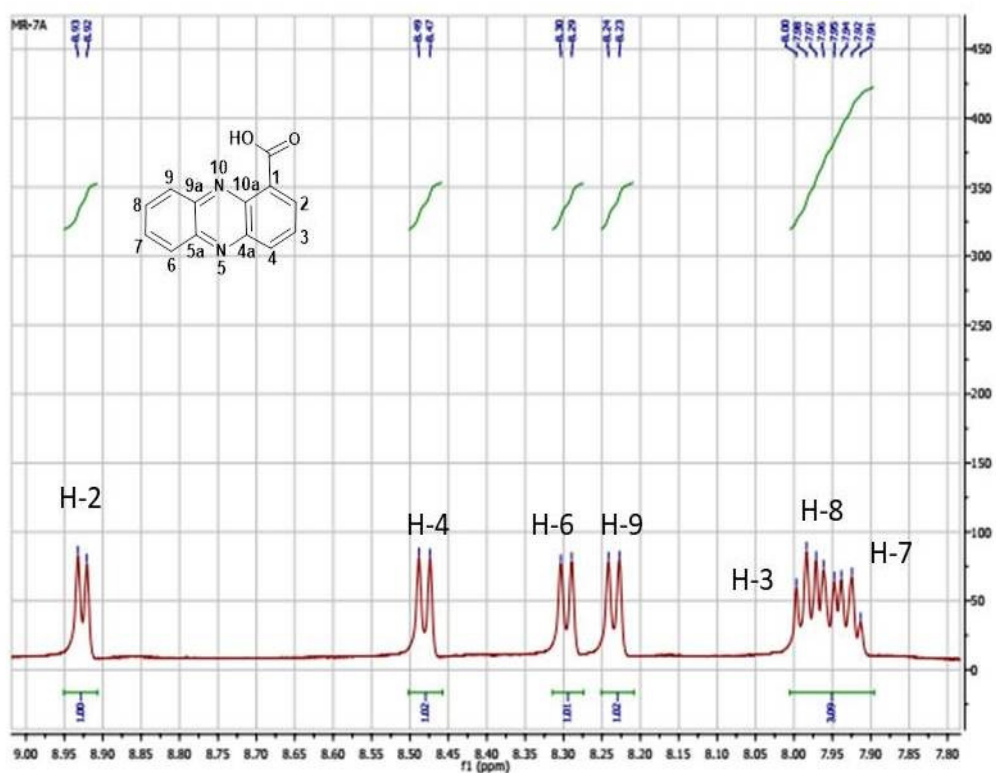


Figure S15: Expanded ¹H-NMR Spectrum of compound 3 (Phenazine-1-carboxylic acid) (CDCl₃).

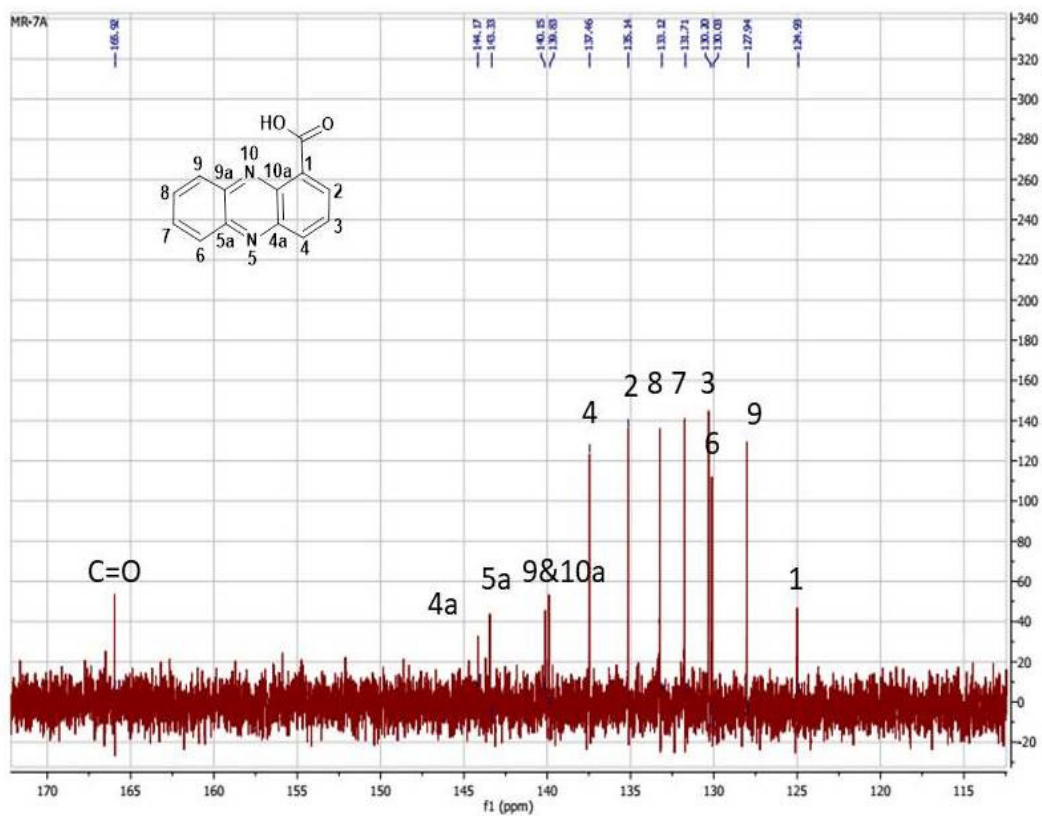


Figure S16: ¹³C-NMR spectrum of compound 3 (Phenazine-1-carboxylic acid) (CDCl₃).

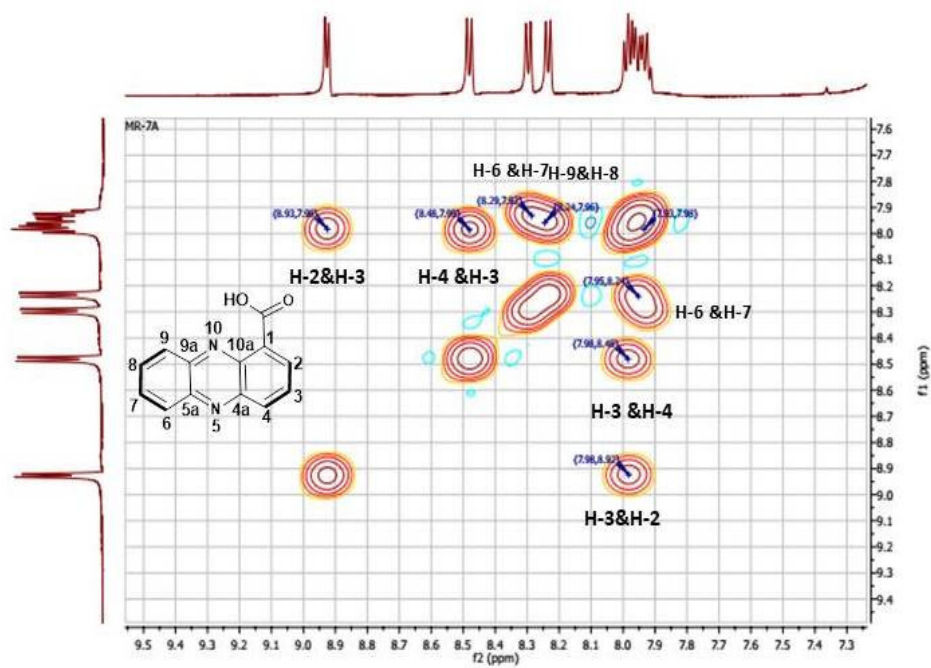


Figure S17: ^1H - ^1H COSY Spectrum of compound 3 (Phenazine -1-carboxylic acid) (CDCl_3).

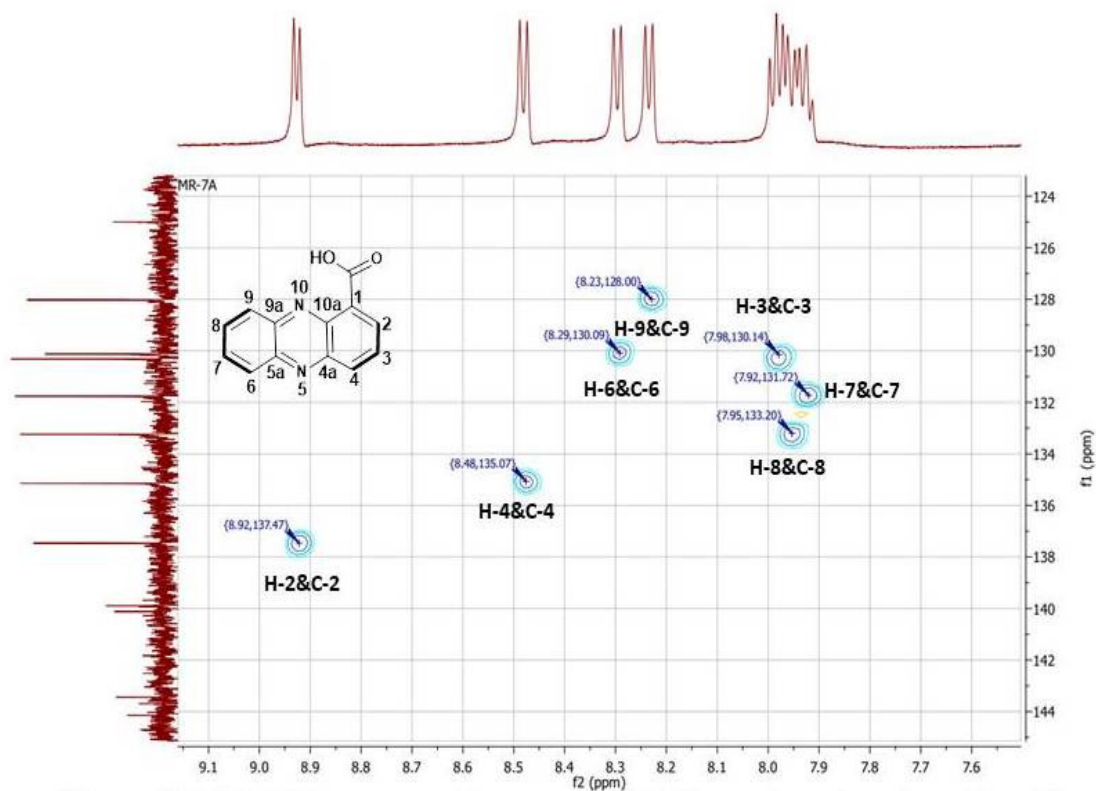
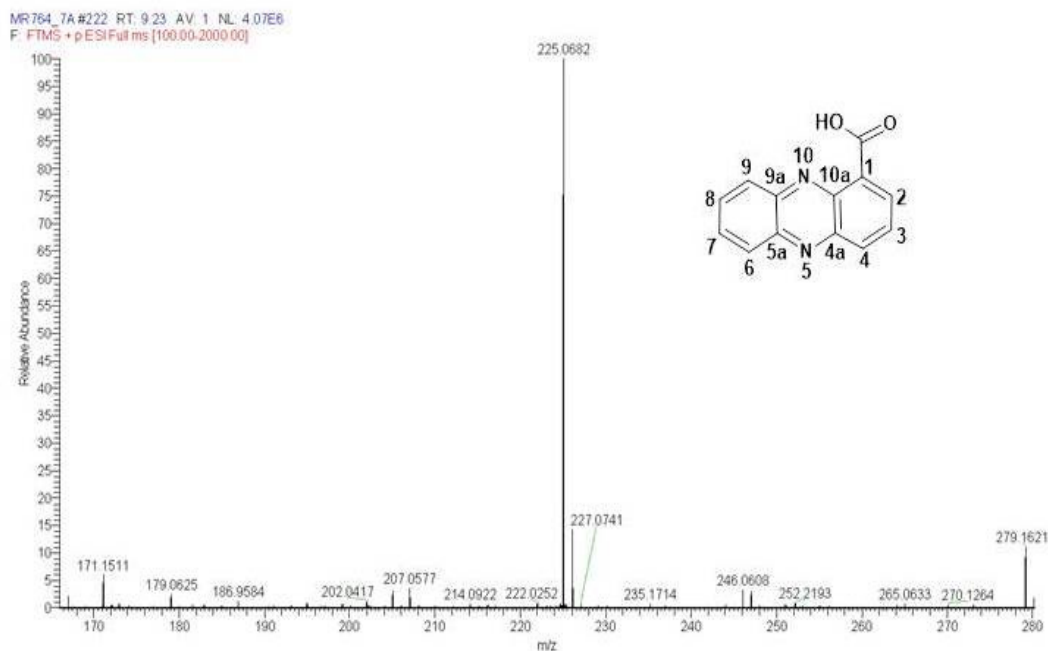
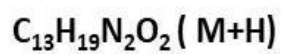


Figure S18: HSQC Spectrum of compound 3 (Phenazine -1-carboxylic acid) (CDCl₃).



FigureS19: HRESIMS of compound 3(Phenazine -1-carboxylic acid).



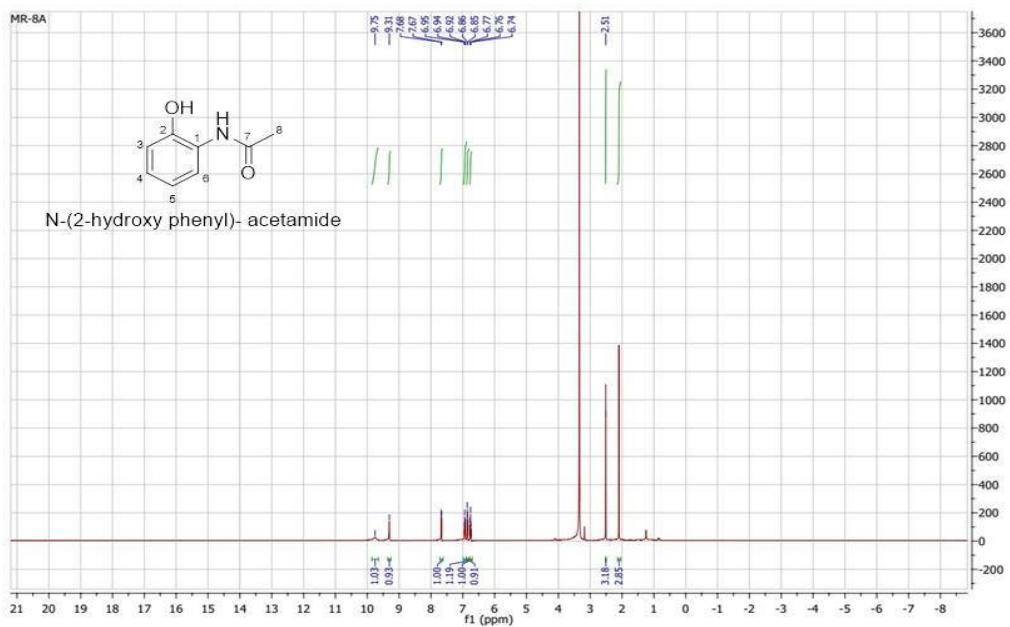


Figure S20: $^1\text{H-NMR}$ Spectrum of compound **1 1** (N-(2-hydroxyphenyl)-acetamide) (MeOD).

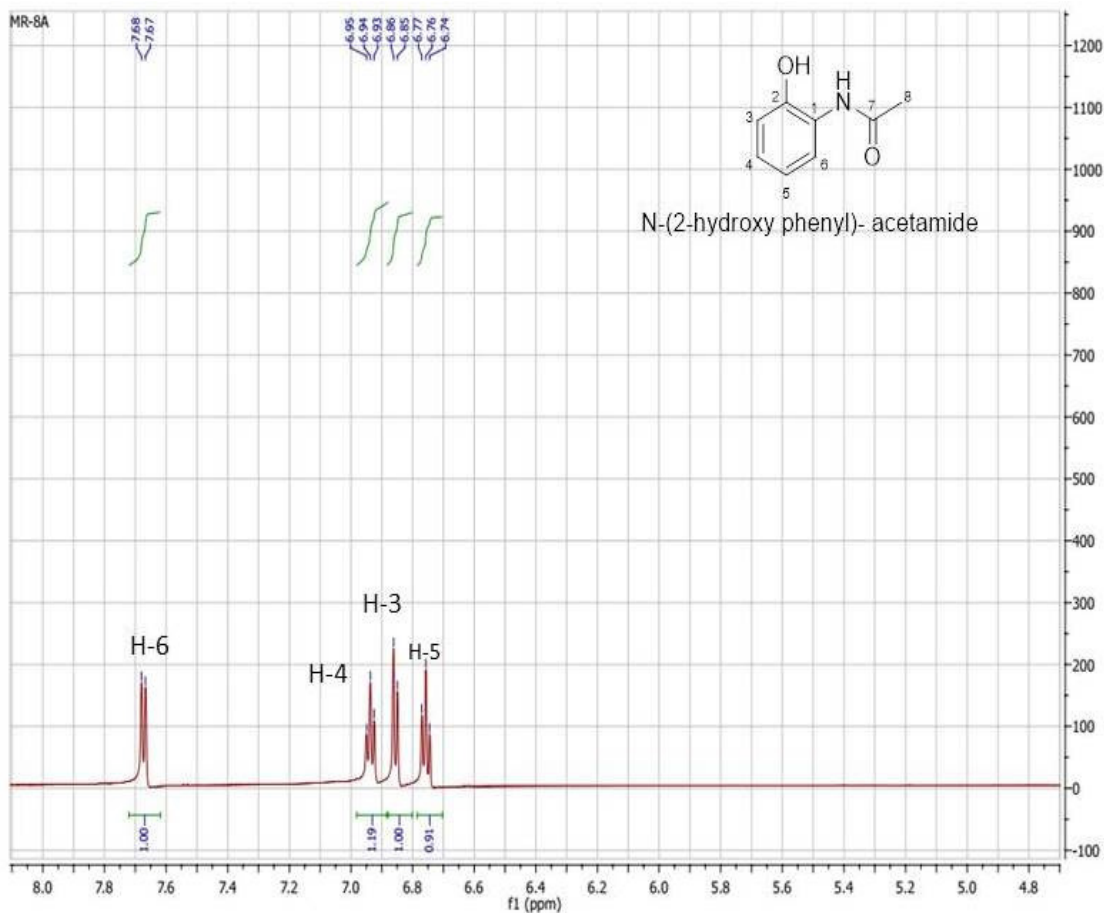


Figure S21: Expanded ^1H -NMR Spectrum of compound 11 (N-(2-hydroxyphenyl)-acetamide)(MeOD).

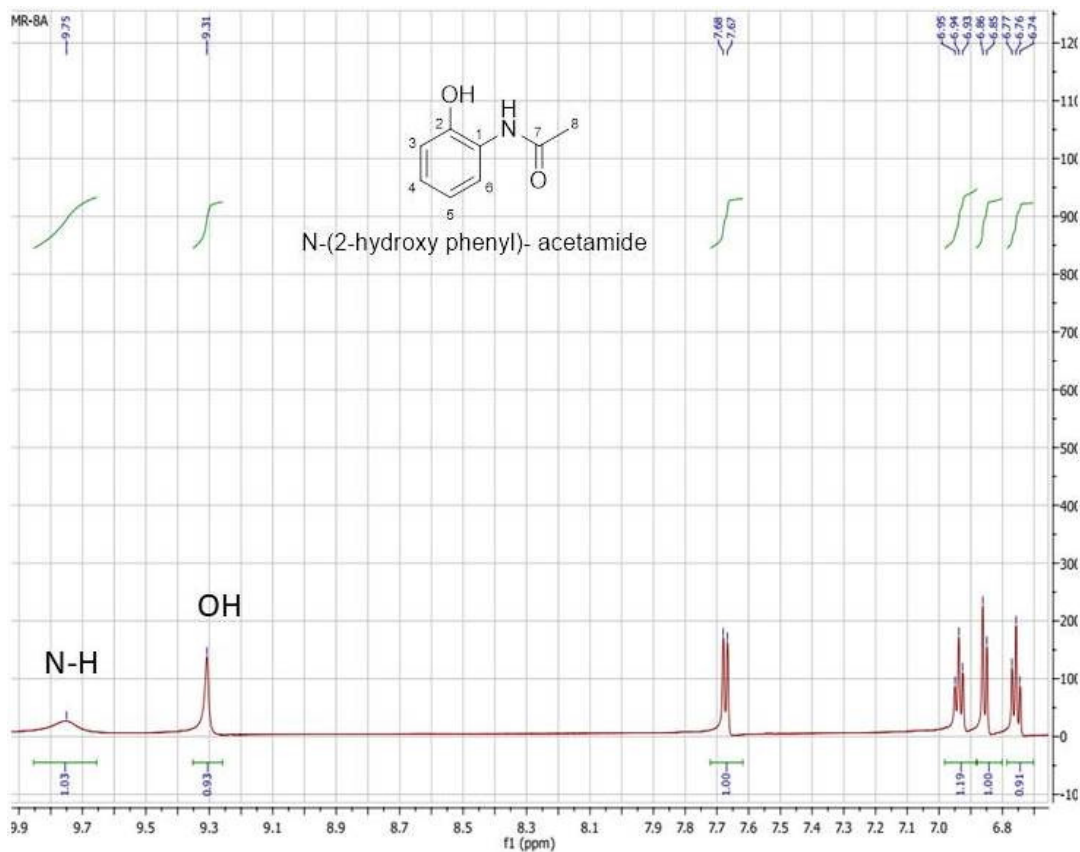


Figure S22: Expanded ^1H -NMR Spectrum of compound 11 (N-(2-hydroxyphenyl)-acetamide) (MeOD).

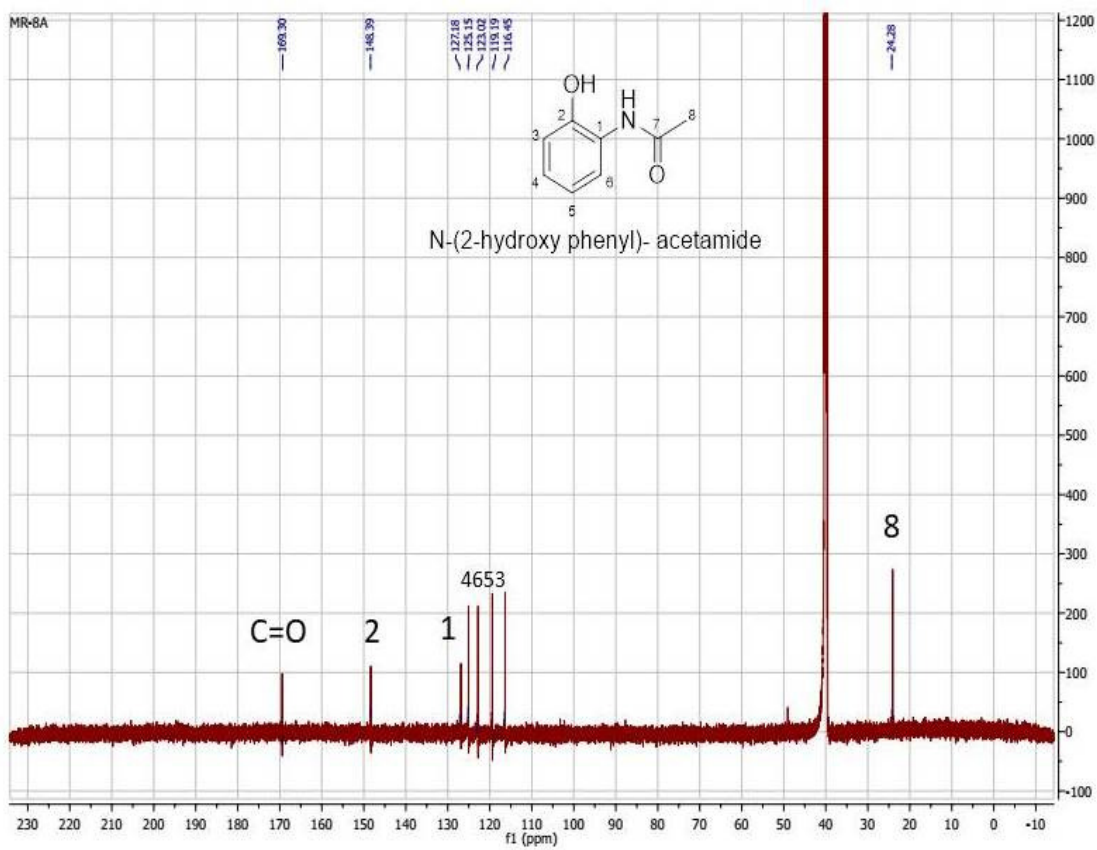


Figure S23: ^{13}C -NMR spectrum of compound 11 (N-(2-hydroxyphenyl)-acetamide)(MeOD).

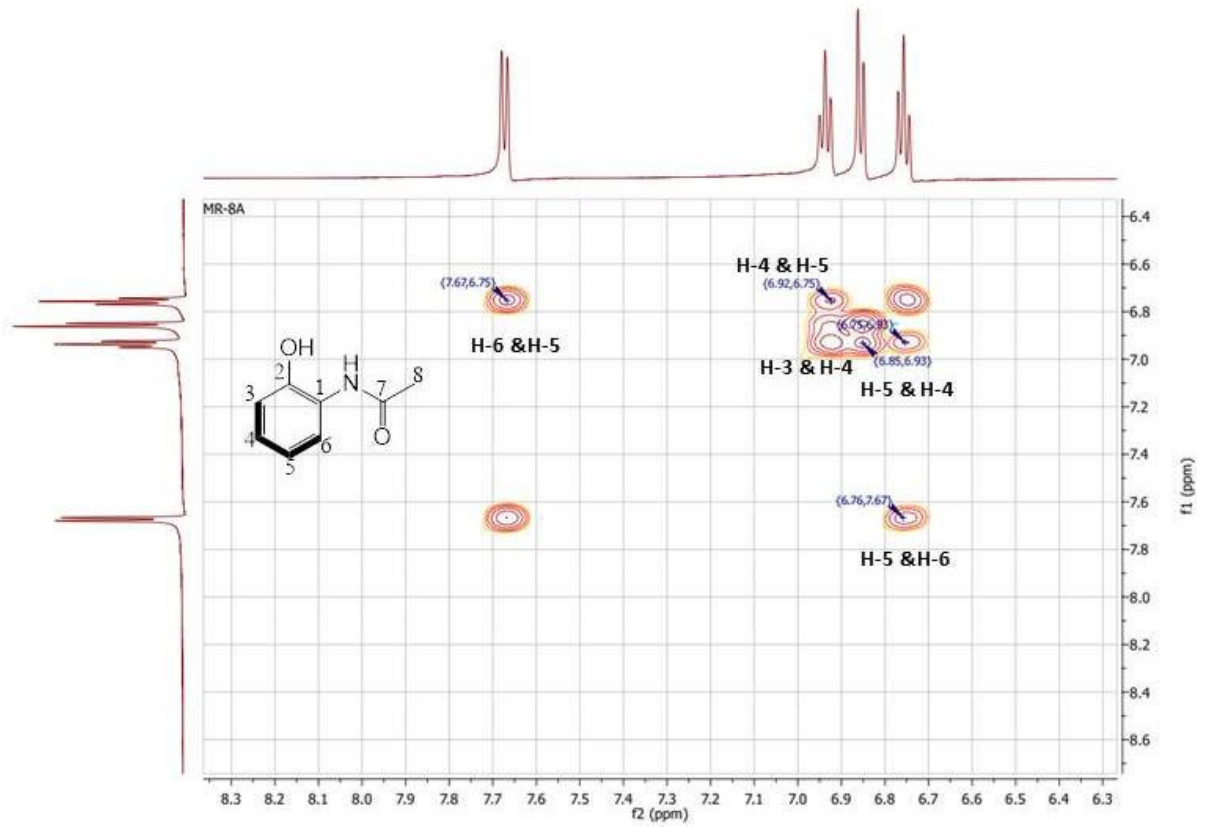


Figure S24: ^1H - ^1H COSY Spectrum of compound 11 (N-(2-hydroxyphenyl)-acetamide)(MeOD).

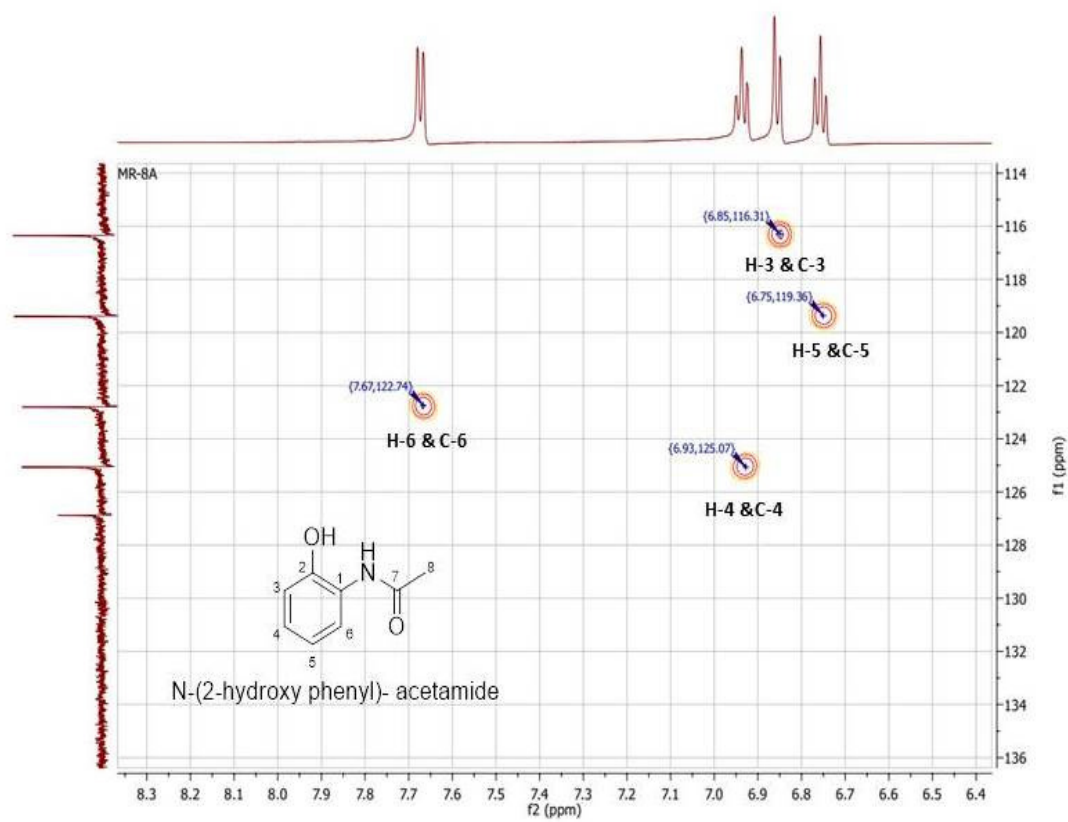


Figure S25: HSQC Spectrum of compound 11(N-(2 hydroxyphenyl)-acetamide)(MeOD).

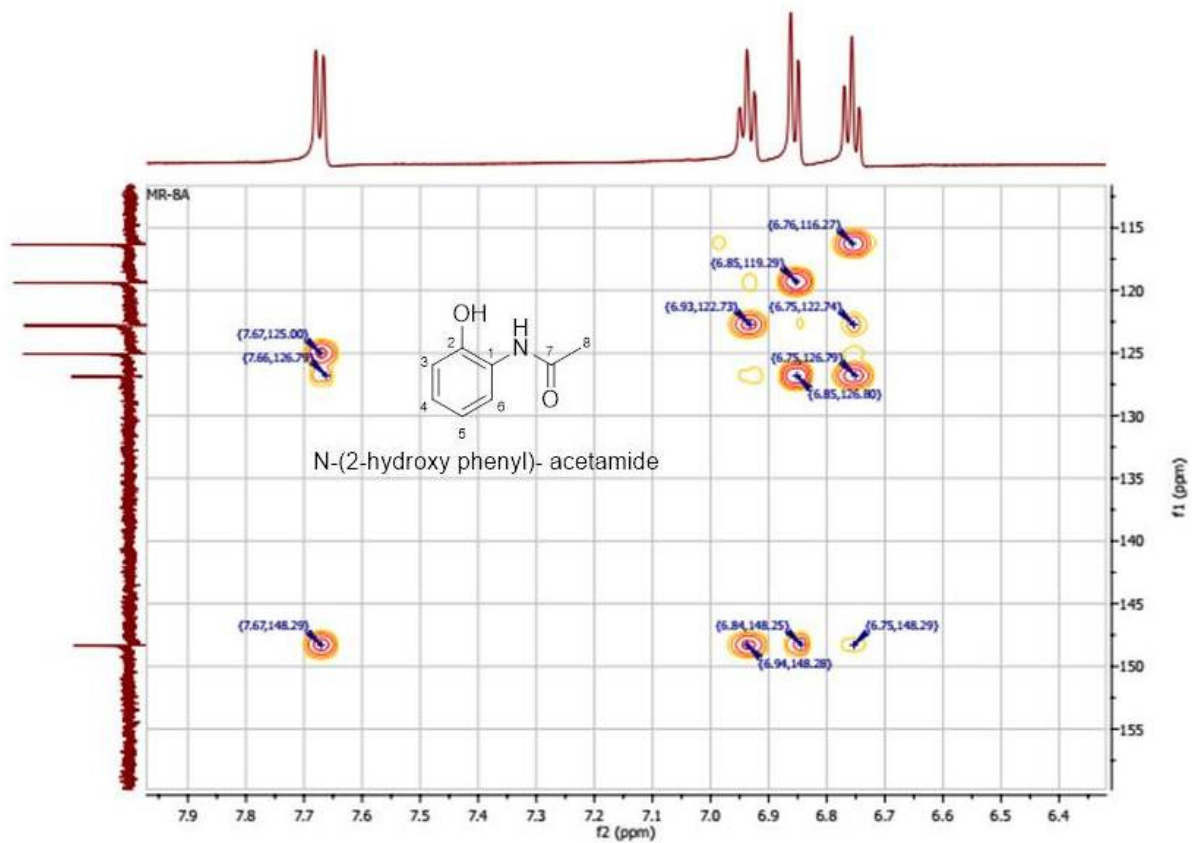
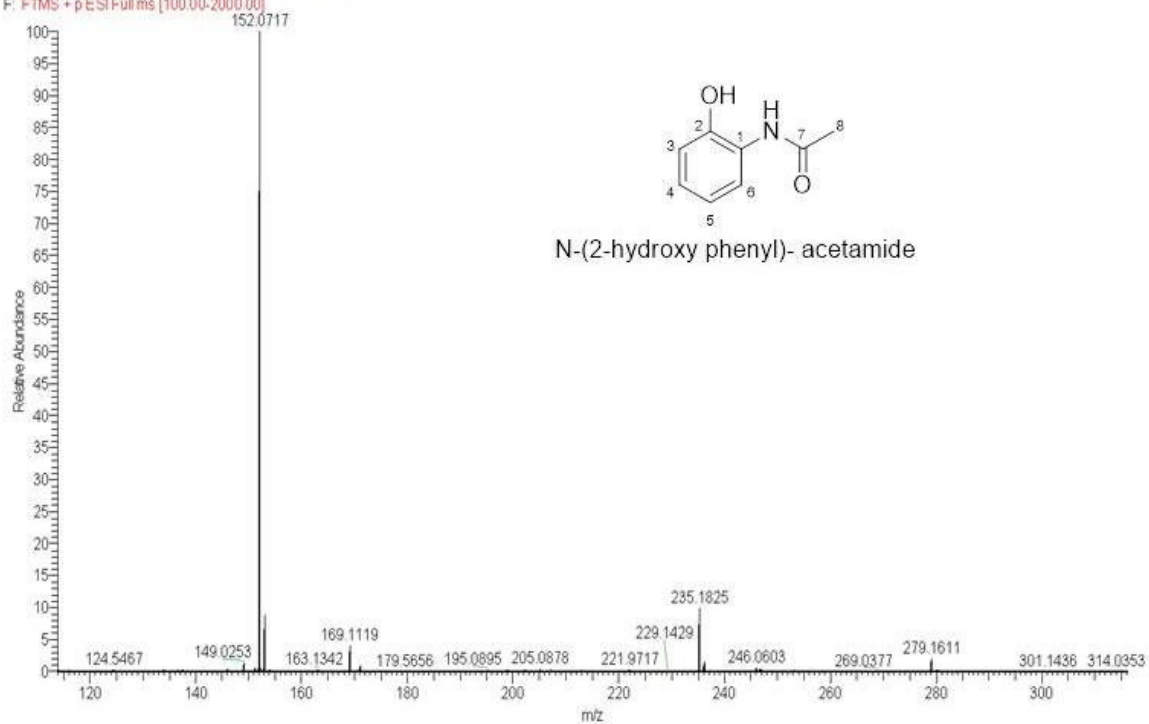


Figure S26: HMBC Spectrum of compound 11(N-(2-hydroxyphenyl)-acetamide)(MeOD).

MR765_8A #68-133 RT: 3.32-5.43 AV: 33 NL: 1.18E7
F: FTMS + pESI Full ms (100.00-2000.00)



FigureS27: HRESIMS of compound 11 (N-(2-hydroxyphenyl)-acetamide)(MeOD). $C_8H_{10}O_2N(M+H)$

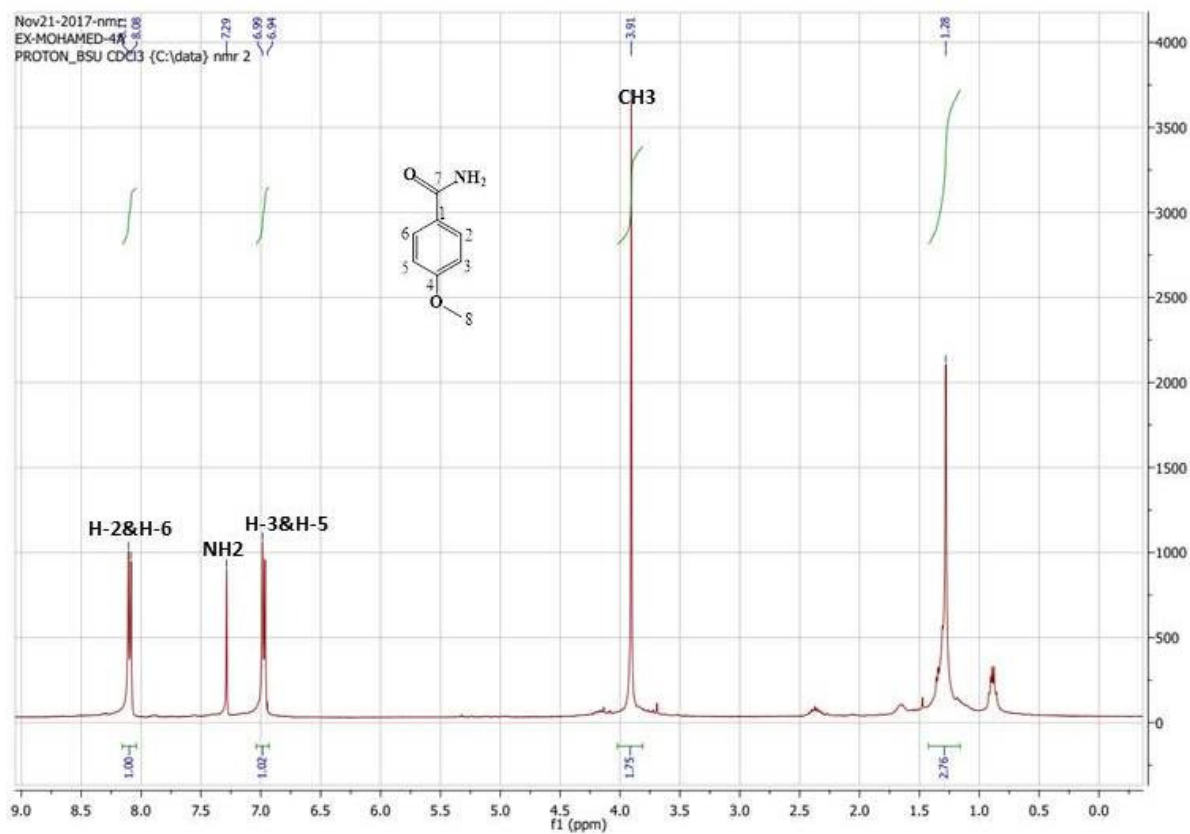


Figure S28: ¹H-NMR Spectrum of compound 12 (P-anisamide)(CDCl₃).

EX-MOHAMEDFOUDA-4A
DEPTQ-BSU CDC13 (C:\data) nmr 14

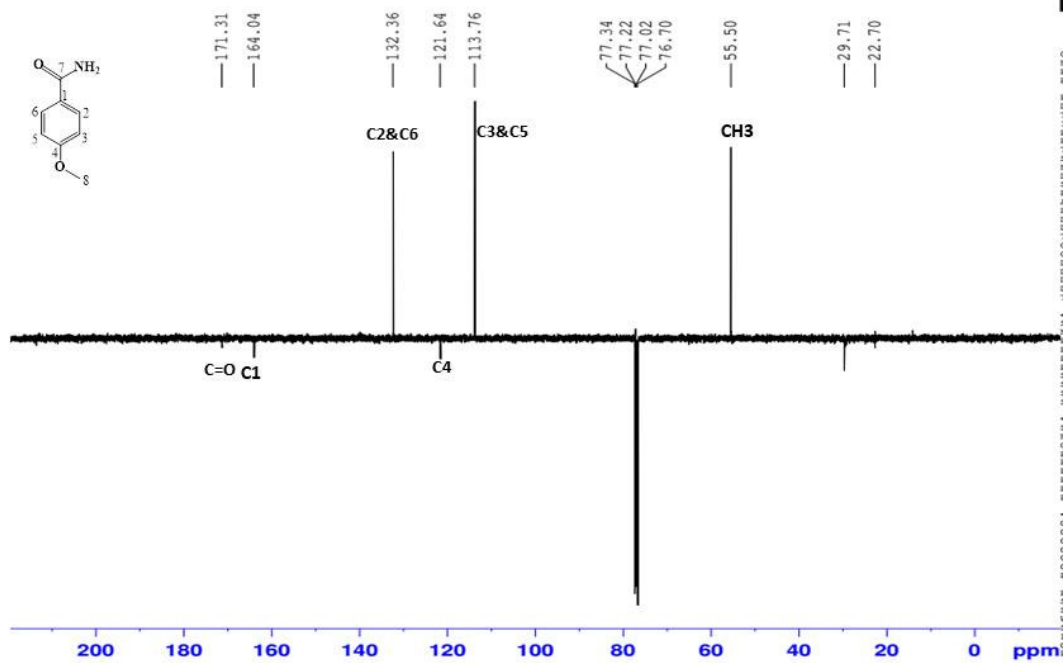
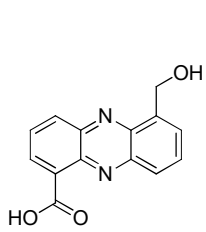


Figure S29: DEPTQ spectrum of compound 12(p-anisamide)(CDCl₃) .

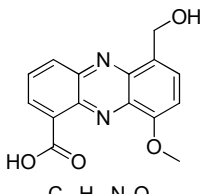
Table (S1). The dereplication results of the ethyl acetate fraction of micromonospora UR 56.

Polarity	Rt(min)	m/z	Formula	Name	Source	Class	Activity	Reference
[M-H] ⁻	4.48	253.0607	C ₁₄ H ₁₀ N ₂ O ₃	9-Methoxy-1-phenazinecarboxylic acid. (1)	-----	Phenazine	-----	[1]
[M-H] ⁻	4.38	281.0557	C ₁₅ H ₁₀ N ₂ O ₄	Griseoluteic acid (2)	Streptomyces y-9031725	Phenazine	Active against HeLa cells and Ehrlich carcinoma	[2]
[M-H] ⁻	4.44	341.0769	C ₁₇ H ₁₄ N ₂ O ₆	Griseolutein A (3)	Streptomyces griseoluteus	Phenazine	Antibacterial activity against gram +ve and gram -ve bacteria	[3]
[M-H] ⁻	7.44	507.2489	C ₂₉ H ₃₆ N ₂ O ₆	Aestivophoenin C (4)	Streptomyces purpeofuscus	Phenazine	Neuronal cell protecting agent, antioxidant	[4]
[M+H] ⁺	3.16	211.1447	C ₁₁ H ₁₈ N ₂ O ₂	cyclo(D)-Pro-(D)-Leu (5)	Actinobacteria	diketopiperazine	Antifungal and antitumor	[5]
[M-H] ⁻	3.53	223.0600	C ₁₁ H ₁₂ O ₅	Reticulol (6)	Streptomyces mobaraensis	benzopyrane	Inhibitor of cyclic nucleotide phosphodiesterase. Calmodulin antagonist	[6]
[M-H] ⁻	4.44	297.0506	C ₁₅ H ₁₀ N ₂ O ₅	SE-212021 Umycin-A; SM-35 Carboxyexfoliazone (7)	Streptomyces sp. Streptomyces sp. DSM 3813	phenoxazine	Anthelmintic	[7]

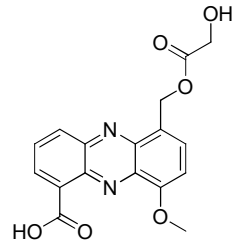
[M-H] ⁻	7.29	511.2799	C ₂₉ H ₄₀ N ₂ O ₆	Dihydromaltophilin (8)	Streptomyces sp	Lactam	antifungal, angiogenesis inhibitor and antiulcer	[8]
[M+H] ⁺	11.56	629.4235	C ₃₄ H ₆₀ O ₁₀	X-14889-B; Ferensimycin-A; 5057-A (9)	Streptomyces sp. x-14889 (ATCC31679)	Poly ether	Active against Gram-positive bacteria. Effective in the treatment of coccidiosis of fowl	[9]
[M-H] ⁻	5.82	670.3025	C ₃₉ H ₄₅ NO ₉	Naphthomycin C (10)	Streptomyces collinus Tue 2357	Ansamycin	Antibacterial and antifungal	[10]
[M-H] ⁻	12.91	1042.6429	C ₅₃ H ₉₃ N ₃ O ₁₇	Neocopiamycin A (12)	Streptomyces hygroscopicus var. crystallogenes ifm 1136 (ATCC 19040)	Lactone	Antifungal	[11]
[M+H] ⁺	11.62	598.1100	C ₃₂ H ₂₂ O ₁₂	Crisamicin A (13)	Micromonospo ra m. purpureochro mogenes celinoensis	Quinone	Active against Gram-positive bacteria. Immunomodula tor	[12]



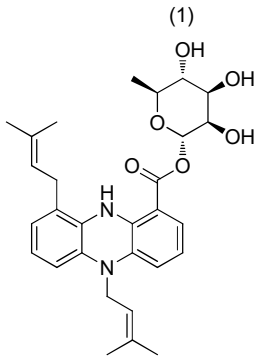
$C_{14}H_{10}N_2O_3$
Exact mass:254.0691
1-hydroxymethyl-6-carboxy phenazine
(1)



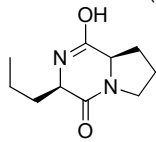
$C_{15}H_{12}N_2O_4$
Exact mass:284.0797
Griseoluteic acid
(2)



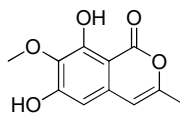
$C_{17}H_{14}N_2O_6$
Exact mass:342.0852
Griseolutein A
(3)



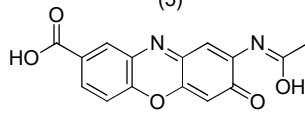
$C_{29}H_{36}N_2O_6$
Exact mass:508.2573
Aestivophoenin C
(4)



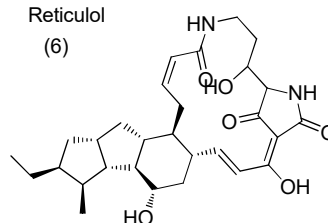
$C_{11}H_{18}N_2O_2$
Exact mass:210.1368
cyclo(D)-Pro-(D)-Leu
(5)



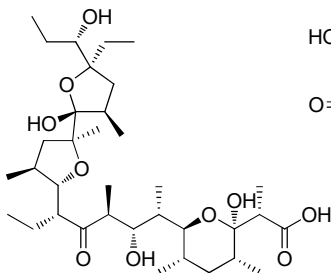
$C_{11}H_{10}O_5$
Exact mass:222.0528
Reticulol
(6)



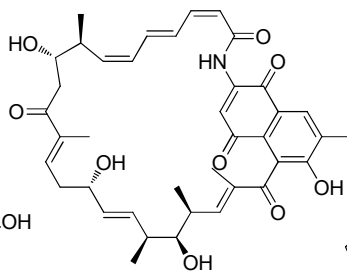
$C_{15}H_{10}N_2O_5$
Exact mass:298.0590
Umycin-A
(7)



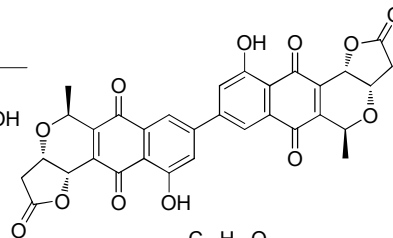
$C_{29}H_{40}N_2O_6$
Exact mass:512.2886
Dihydromaltophilin
(8)



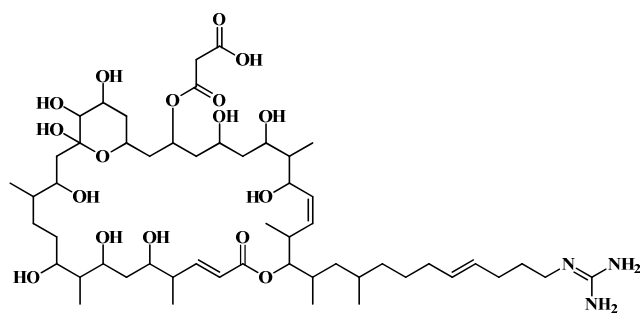
$C_{34}H_{60}O_{10}$
Exact mass:628.4186
Ferensimycin-A
(9)



$C_{39}H_{45}NO_9$
Exact mass:671.3094
Naphthomycin C
(10)



$C_{32}H_{22}O_{12}$
Exact mass:598.1111
Crisamicin A
(11)



$C_{53}H_{93}N_3O_{17}$

Exact mass:1043.6505

Neocopiamycin A

12

Fig S30. Dereplicated metabolites from metabolomic analysis of *Micromonospora* sp UR 56

Table (S2). The dereplication results of the ethyl acetate fraction of *Actinokinospora* EG49.

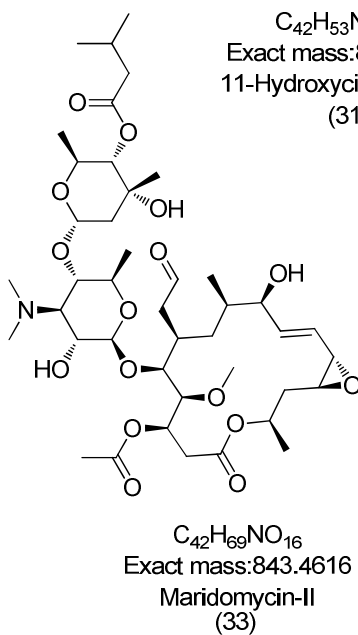
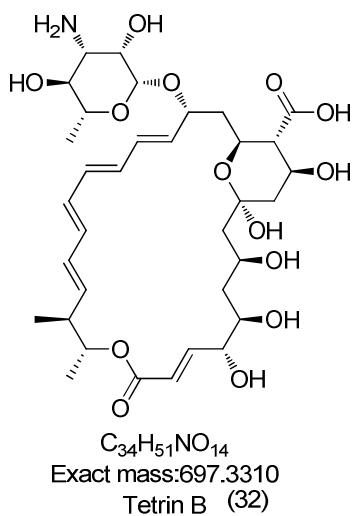
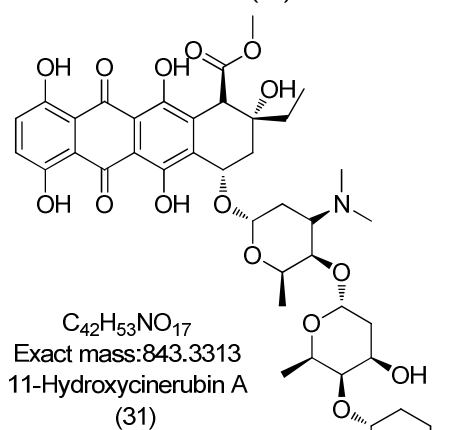
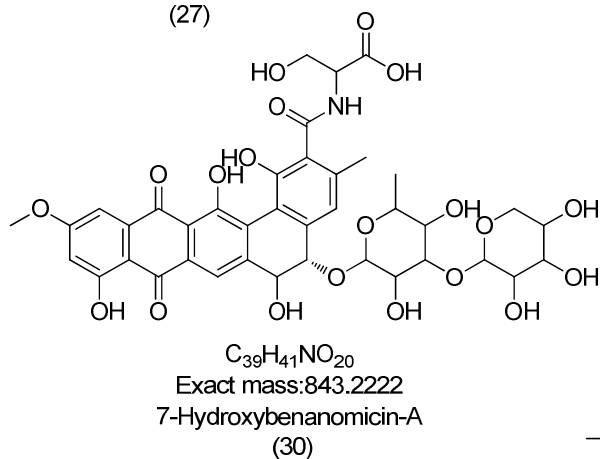
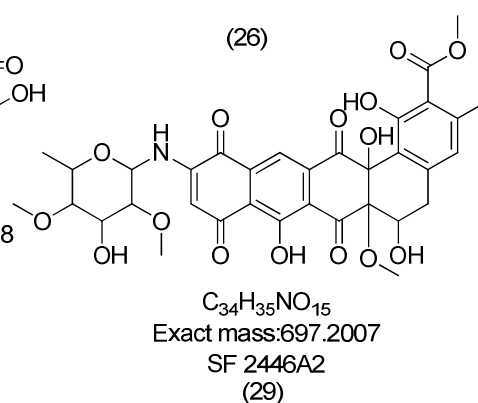
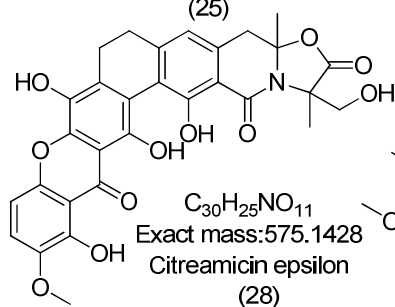
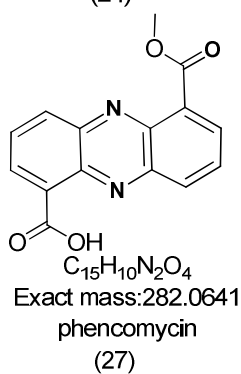
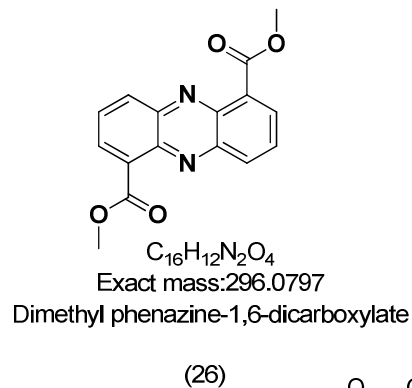
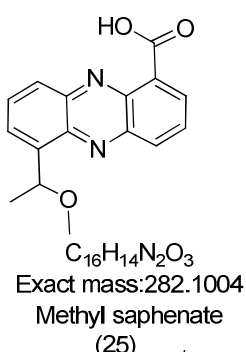
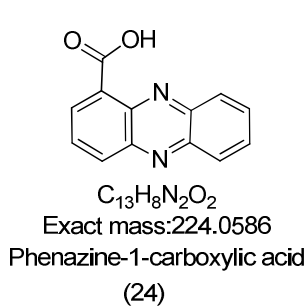
Polarity	Rt(min)	m/z	Formula	Name	Source	Activity	Class	Reference
[M+H] ⁺	11.98	611.2127	C ₃₂ H ₃₄ O ₁₂	Actinosporin A (13)	Actinokinospora EG 49	Anti-trypanosomal	Anthraquinone	[13]
[M+H] ⁺	10.60	519.1444	C ₂₅ H ₂₆ O ₁₂	Actinosporin B (14)	Actinokinospora EG 49	-----	Anthraquinone	[13]
[M-H] ⁻	4.80	467.1350	C ₂₅ H ₂₄ O ₉	Atramycin A (15)	Streptomyces atratus	Antitumor	Anthraquinone	[14]
[M-H] ⁻	4.35	451.1386	C ₂₅ H ₂₄ O ₈	Atramycin B (16)	Streptomyces atratus	Antitumor	Anthraquinone	[14]
[M+H] ⁺	3.14	152.0709	C ₈ H ₉ NO ₂	Streptokordin (17)	Actinobacteria Streptomyces sp	Cytotoxic	Methyl pyridine	[15]
[M+H] ⁺	2.43	197.1289	C ₁₀ H ₁₆ N ₂ O ₂	Cyclo-(proly-valyl)(18)	Actinobacteria	-----	diketopiperazine	
[M-H] ⁻	2.31	463.1708	C ₂₂ H ₂₈ N ₂ O ₉	Antibiotic 19A(19)	USF Streptomyces sp. USF19	Lipoxygenase inhibitor	Quinone	[16]
[M+H] ⁺	12.65	701.481	C ₃₈ H ₆₈ O ₁₁	Inostamycin (20)	Streptomyces sp.	Antibacterial and antimetastic	polyether	[17]

[M-H] ⁻	6.87	253.049	C ₁₅ H ₁₀ O ₄	Daidzein(21)	Micromonospora halophytica	Antioxidant with anticancer and bone-protectant	isoflavones	[18]
[M-H] ⁻	4.90	341.0657	C ₁₈ H ₁₄ O ₇	Momofulvenone- A(22)	Streptomyces diastatochromogenes (strain Tue 2895)	-----	Quinone	[19]
[M+H] ⁺	12.03	523.3602	C ₂₆ H ₄₆ N ₆ O ₅	Lucentamycin C (23)	Actinobacteria Nocardiopsis lucentensis	cytotoxic	Peptide	[20]

Table (S3).The dereplication results of the ethyl acetate fraction of co-culture.

Name	Formula	m/z	Source	Class	Activity	Reference
Phenazine-1-carboxylic acid (24) Tubermycin B	C ₁₃ H ₈ N ₂ O ₂	224.0580	Streptomyces antibioticus strain Tue 2706	Phenazine	Antibacterial	[21]
Saphenic acid methyl ether (methyl saphenate)(25)	C ₁₆ H ₁₄ N ₂ O ₃	282.0999	Streptomyces antibioticus strain Tue 2706	Phenazine	----- -	[22]
dimethyl Phenazine 1,6-dicarboxylate (26)	C ₁₆ H ₁₂ N ₂ O ₄	296.0781	Prod. by a Streptomyces sp	phenazine	----- -	[23]
Phenazine -1,6-carboxylic acid mono methyl ester (phencomycin)(27)	C ₁₅ H ₁₀ N ₂ O ₄	282.0648	Prod. by a Streptomyces sp	Phenazine	Antibacterial and antitumor	[23]
Citreamicin ε (28)	C ₃₀ H ₂₅ NO ₁₁	575.14275	Actinobacteria Streptomyces caelestis	Quinone	Antibacterial including MRSA	[24]
Antibiotic SF 2446A2(29)	C ₃₄ H ₃₅ NO ₁₅	697.2001	Streptomyces sp. sf2446	Quinone	Active against Gram-positive bacteria and mycoplasmas	[25]
7 - Hydroxybenanomicin-A (30)	C ₃₉ H ₄₁ NO ₂₀	843.2216	Actinomadura sp. mh193-16f4	Quinone	-----	[26]
11-Hydroxycinerubin A (31)	C ₄₂ H ₅₃ NO ₁₇	843.3308	Streptomyces galilaeus	Quinone	----- -	[27]
Tetrin B (32)	C ₃₄ H ₅₁ NO ₁₄	697.3304	Streptomyces sp.	Macrolide	Antifungal	[28]
Maridomycin-II (33)	C ₄₂ H ₆₉ NO ₁₆	843.4610	Streptomyces platensis-malvinus	Macrolide	Antibacterial	[29]
Dactylocycline-A(34)	C ₃₁ H ₄₀ ClN ₃ O ₁₃	697.2244	Dactylosporangium sp.	Tetracyclin	Antibacterial	[30]

			(ATCC 53693)			
pulicatin A (35)	C ₁₁ H ₁₃ NO ₂ S	223.0667	Actinobacteria Streptomyces sp	Thiazole	-----	[31]
Antibiotic MSD 92 (36)	C ₈ H ₉ N ₅ O ₃	223.0699	Streptomyces sp. IM2096 Streptomyces sp. GW7/2495	pyrimidotriazine	Antibacterial	[32]
MKN-003A (37)	C ₁₃ H ₂₀ O ₃	224.1412	Actinobacteria Streptomyces sp	butenolide	Antifouling	[33]
Cairomycin B (38)	C ₁₀ H ₁₅ N ₃ O ₃	225.1108	Streptomyces AS-C-19	Cyclic peptide	Antibacterial	[34]
(E)-4-Phenyl-3-(pyridine-2-yl)but-2-en-1-ol (39)	C ₁₅ H ₁₅ NO	225.1148	Streptomyces sp.	Pyridine	Antiproliferative agent	[35]
Lemonomycin (40)	C ₂₇ H ₄₁ N ₃ O ₉	551.2837	Streptomyces candidus	isoquinoline	Antibacterial and antitumor	[36]
Sinefungin VA (41)	C ₂₃ H ₃₇ N ₉ O ₇	551.2810	Streptomyces sp. K05-0178	nucleoside	antitrypanosomal	[37]
Deacetylanisomycin (42)	C ₁₂ H ₁₇ NO ₃	223.1203	marine Streptomyces sp. SA3097	Pyrrolidine	----- ---	[38]
1-Hydroxyanthraquinone (43)	C ₁₄ H ₈ O ₃	224.0468	Synthetic	Quinone	----- ---	[39]
Pyramidamycin D (44)	C ₁₀ H ₁₂ N ₂ O ₄	224.0791	Streptoverticillium morookaense	Amide	----- ----	[40]
5-Chloro-6-methoxy-1-methylisatin (45)	C ₁₀ H ₈ ClNO ₃	225.0187	Micromonospora carbonacea	Indole	----- ----	[41]



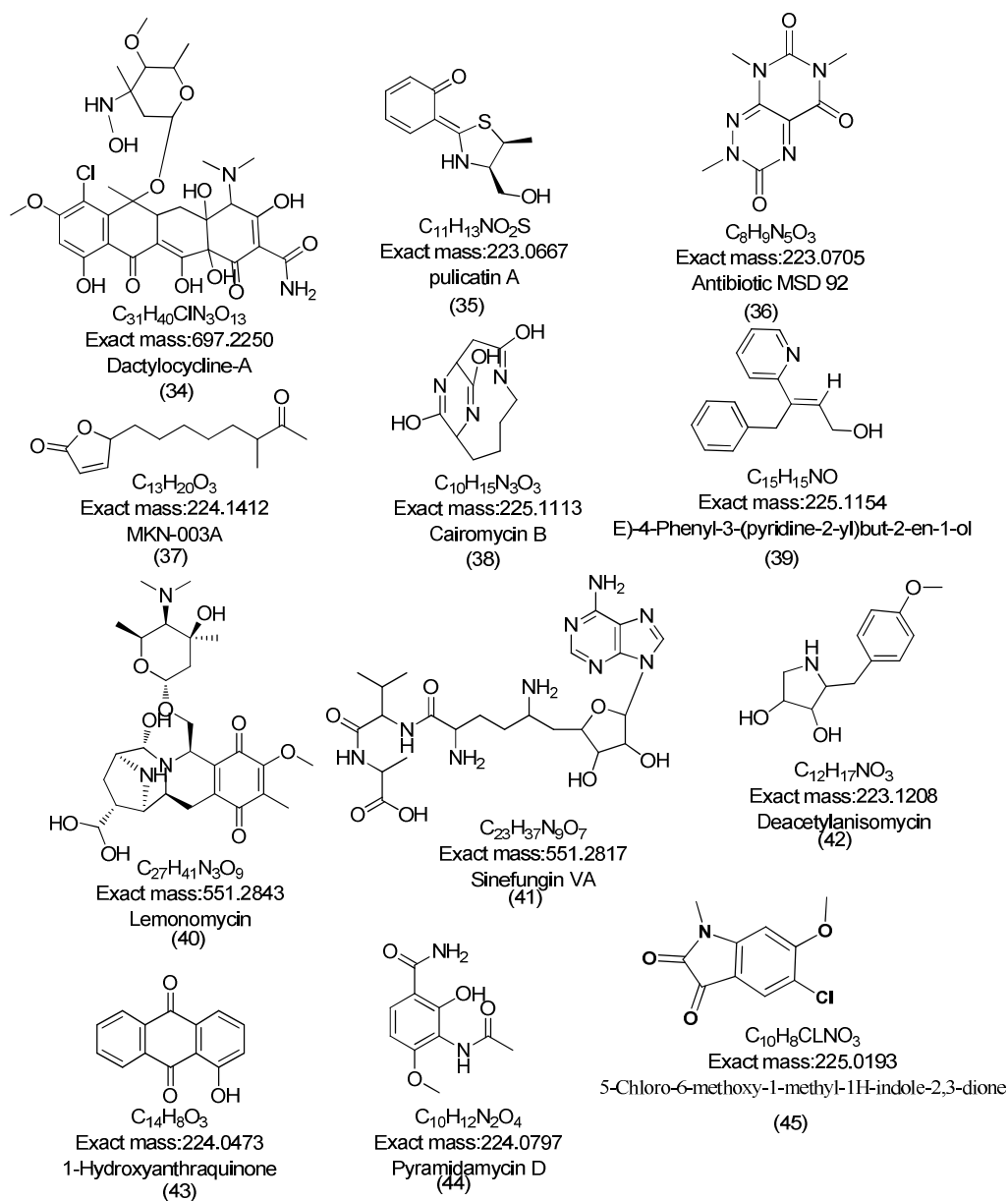


Fig S32. Dereplicated metabolites from metabolomic analysis of *co-culture Micromonospora sp. UR 56* and *Actinokineospora sp. EG49*.

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