Targeted Dereplication of Microbial Natural Products by High-Resolution MS and Predicted LC-Retention Time

Justine Chervine, [†,#] *Marc Stierhof,* [†,#] *Ming Him Tong,* [†,#] *Doe Peace,* [†] *Kine Østnes Hansen,* [‡] *Dagmar Solveig Urgast,* [†] *Jeanette Hammer Andersen,* [‡] *Yi Yu,* [§] *Rainer Ebel,* [†] *Kwaku Kyeremeh,* [⊥] *Veronica Paget,* [▽] *Gabriela Cimpan* [▽] *Albert Van Wyk,* [▽] *Hai Deng,* [†] *Marcel Jaspars,* [†] *Jioji N. Tabudravu* [†,*]

[†] *The Marine Biodiscovery Centre, Department of Chemistry, University of Aberdeen, AB24 3UE, Scotland, U.K.*

[‡] *Marbio, UiT The Arctic University of Norway, N-9037, Breivika, Tromsø, Norway*

[§] *Key Laboratory of Combinatory Biosynthesis and Drug Discovery (Ministry of Education), School of Pharmaceutical Sciences, Wuhan University, 185 East Lake Road, Wuhan 430071, China*

[⊥] *Marine and Plant Research Laboratory of Ghana, Department of Chemistry, University of Ghana, Accra, P.O. Box LG 56, Ghana*

[▽] *Advanced Chemistry, UK Ltd., Venture House, Arlington Square, Downshire Way, Bracknell, Berks. RG12 1WA, U.K.*

Table of Contents

Table of Mass Chromatograms (Filtered)

Base | ITA | IX | CODA | Compare | MC | Slice

No.	m/z	Area (counts)	Peak Top Mass	tR (min)	Height (counts)	Base Peak Mass	Label	Start tR	End tR	Notation	Class	CHNO	Origin
1	709.300	228633968	709.262	13.558	67227256	711.257	Jasplakinolide	13.512	13.884	[M+H]+	Good	Pass	IX
2	709.576	443109408	709.262	13.512	69244120	711.257	Jasplakinolide	13.463	14.537	[M+H]+	Good	Pass	IX
3	709.300	530313248	709.262	13.224	119033672	711.257	Jasplakinolide	12.882	13.298	[M+H]+	Good	Pass	IX

No.	tR(min)	Mass(Ao)	[M+H]+	M+.	M-.	MF	Structure	Name	MS Match
1	13.224	708.252	709.260	708.252	708.253	$C_{36}H_{45}BrN_4O_6$		Jasplakinolide	Excellent

Figure S1. Jasplakinolide was used to optimise the LCMS data preprocessing settings. The IX algorithm was able to identify jasplakinolide successfully as seen in the Table (IX) and the Table of components.

Base | ITA | IX | CODA | Compare | MC | Slice

No.	m/z	Area (counts)	Peak Top Mass	tR (min)	Base Peak Mass	Label	Start tR	End tR	Notation	Class	Origin
2	524.678	277181408	524.276	19.183	524.276	Antibiotic A-23187	19.131	20.286	[M+H]+	Good	IX
3	524.300	125008472	524.276	19.231	524.276	Antibiotic A-23187	19.183	19.646	[M+H]+	Good	IX
4	560.300	128783	560.271	19.084	524.276		18.886	19.131		Good	IX

Table of Components

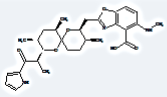
No.	tR(min)	Mass(Ao)	[M+H]+	M+.	M-.	MF	Structure	Name	MS Match
6	19.231	523.268	524.276	523.268	523.269	$C_{29}H_{37}N_3O_6$		Antibiotic A-23187	Excellent

Figure S2. Antibiotic A-23187 was used to optimise the LCMS data preprocessing settings. The IX algorithm was able to identify Antibiotic A-23187 successfully as seen in the Table (IX) and the Table of components.

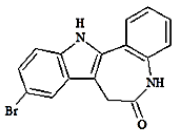
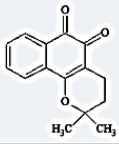
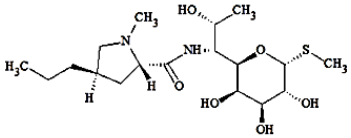
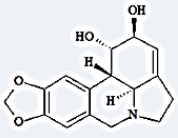
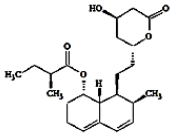
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
79	326.0055	C16H11BrN2O		Kenpaulone	11.4	4.0
80	242.0943	C15H14O3		Beta-Lapachone	11.5	4.0
81	406.2138	C18H34N2O6S		Lincomycin	1.2	4.0
82	287.1158	C16H17NO4		Lycorine	1.2	4.0
83	390.2406	C23H34O5		Mevastatin	14.2	4.0

Figure S3. StrepDB holds 5,102 compounds from *Streptomyces* sp. Compounds No. 79-83 are shown here with names and predicted retention times.

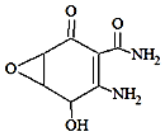
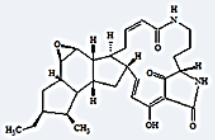
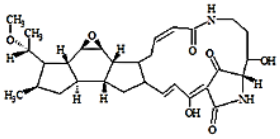
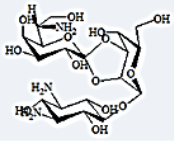
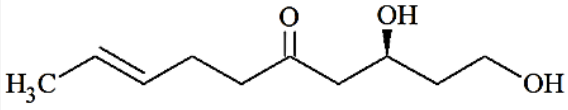
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
1001	184.0484	C7H8N2O4		SS 7313B	2.2	4.0
1002	494.2781	C29H38N2O5		SS 8201B	10.4	4.0
1003	540.2836	C30H40N2O7		SS 8201D	9.4	4.0
1004	529.2119	C19H35N3O14		SS-56-C; SF 1768	0.9	4.0
1005	186.1256	C10H18O3		Streptenol-A	5.1	4.0

Figure S4. Compounds No. 1,001-1,005 in StrepDB.

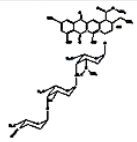
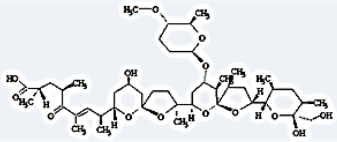
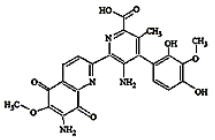
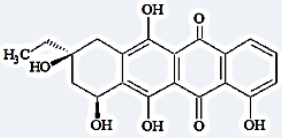
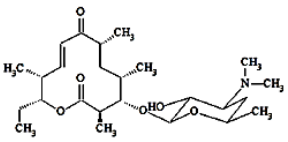
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
2003	827.3364	C42H53NO16		9-Hydroxyaclacinomycin-A	11	4.0
2004	852.5235	C46H76O14		10-Demethyldianemycin	16.8	4.0
2005	492.1281	C24H20N4O8		10'-Demethylstreptonigrin	9.0	4.0
2006	370.1053	C20H18O7		10-Deoxy-beta-rhodomycinone	13.8	4.0
2007	453.309	C25H43NO6		10-Deoxymethymycin	8.9	4.0

Figure S5. Compounds No. 2,003-2,007 in StrepDB.

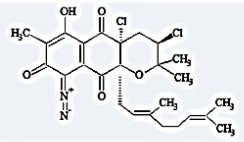
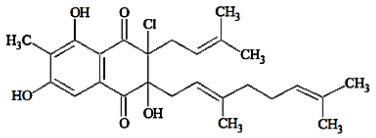
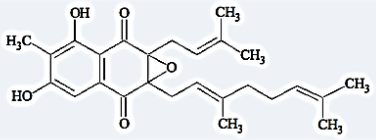
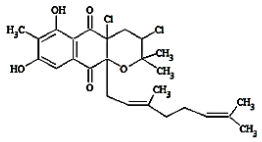
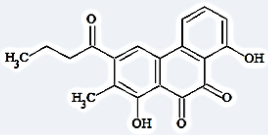
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
3074	520.1532	C26H30Cl2N2O5		SF2415 A3	13.2	4.0
3075	460.2017	C26H33ClO5		SF2415 B1	17.5	4.0
3076	424.225	C26H32O5		SF2415 B2	17.3	4.0
3077	494.1627	C26H32Cl2O5		SF2415 B3	17.5	4.0
3078	324.0998	C19H16O5		SF-2418	14.8	4.0

Figure S6. Compounds No. 3,074-3,078 in StrepDB.

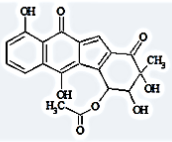
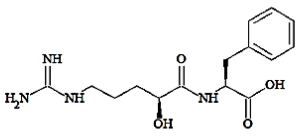
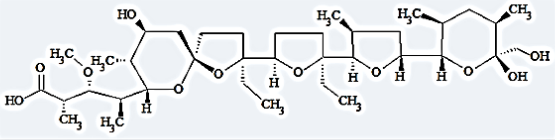
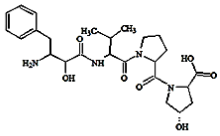
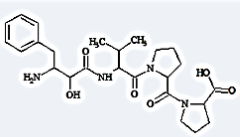
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
4126	384.0845	C20H16O8		Momofulvenone-B	9.6	4.0
4127	322.1641	C15H22N4O4		Monamidocin	1.6	4.0
4128	684.4449	C37H64O11		Monensin-D	14.7	4.0
4129	504.2584	C25H36N4O7		MR-387-A	5.7	4.0
4130	488.2635	C25H36N4O6		MR-387-B	6.2	4.0

Figure S7. Compounds No. 4,126-4,130 in StrepDB.

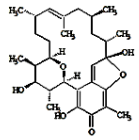
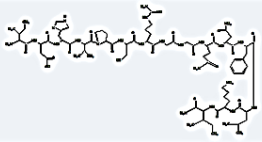
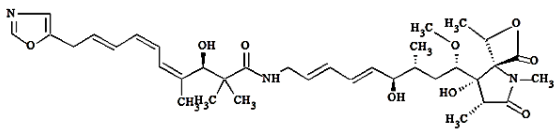
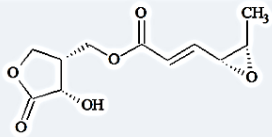
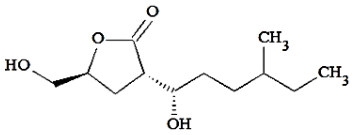
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
4999	486.2981	C29H42O6		Kendomycin	12.2	4.0
5000	1694.9039	C75H122N24O19S		Killer toxin-like protein	68.3	4.0
5001	669.3625	C36H51N3O9		KSM-2690 B	12.2	4.0
5002	242.079	C11H14O6		Lactone II	1.3	4.0
5003	230.1518	C12H22O4		Lactone R4	4.9	4.0

Figure S8. Compounds No. 4,999-5,003 in StrepDB.

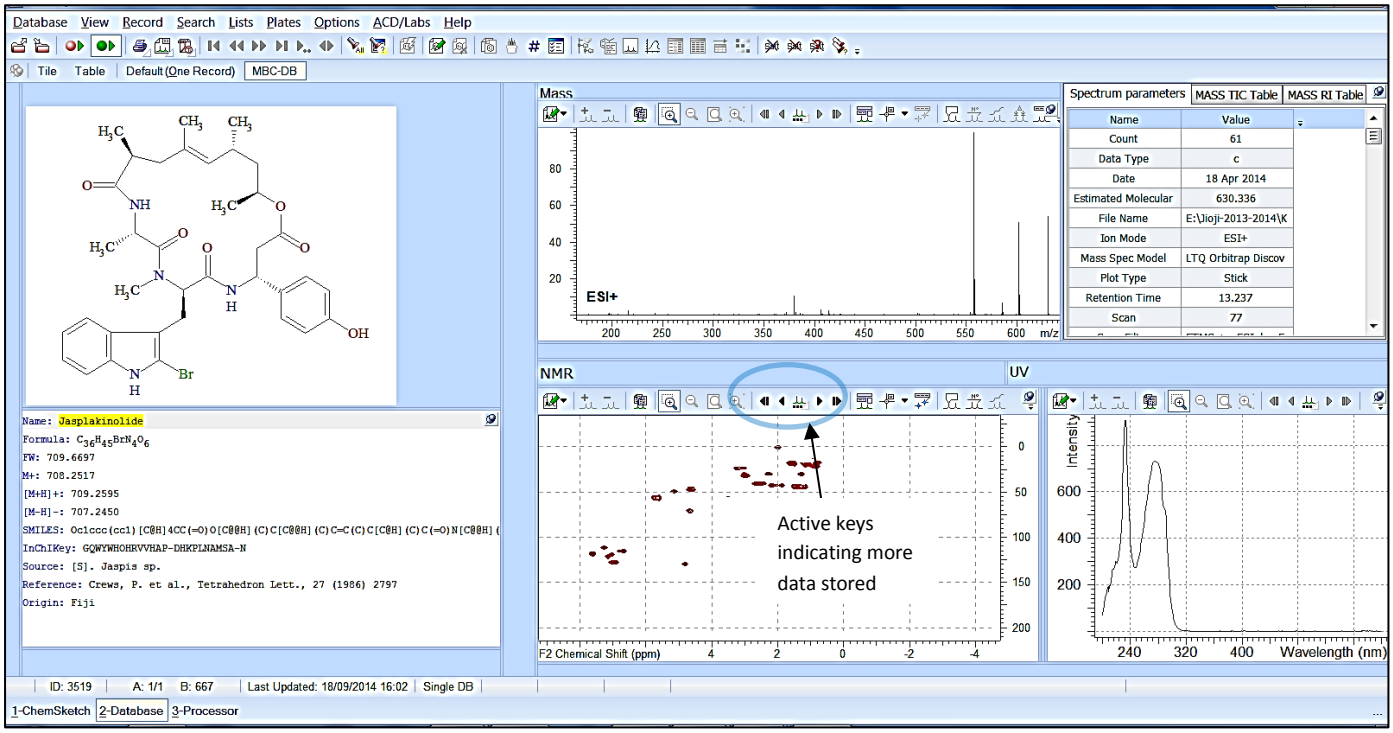


Figure S9. MbcDB holds spectral data such as HRESIMS, MS/MS, UV and NMR for 665 natural products, shown here the data for jasplakinolide; active keys (blue circle) indicate more NMR data is available.

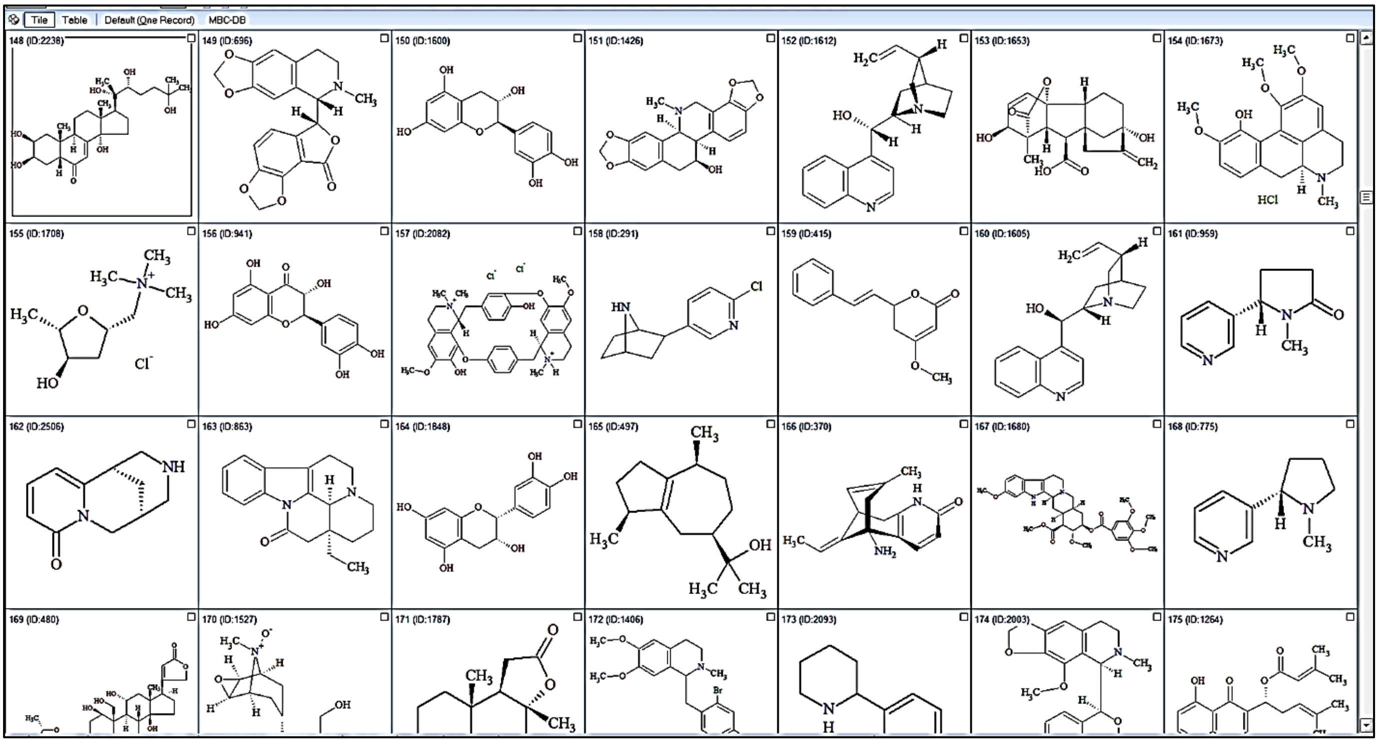
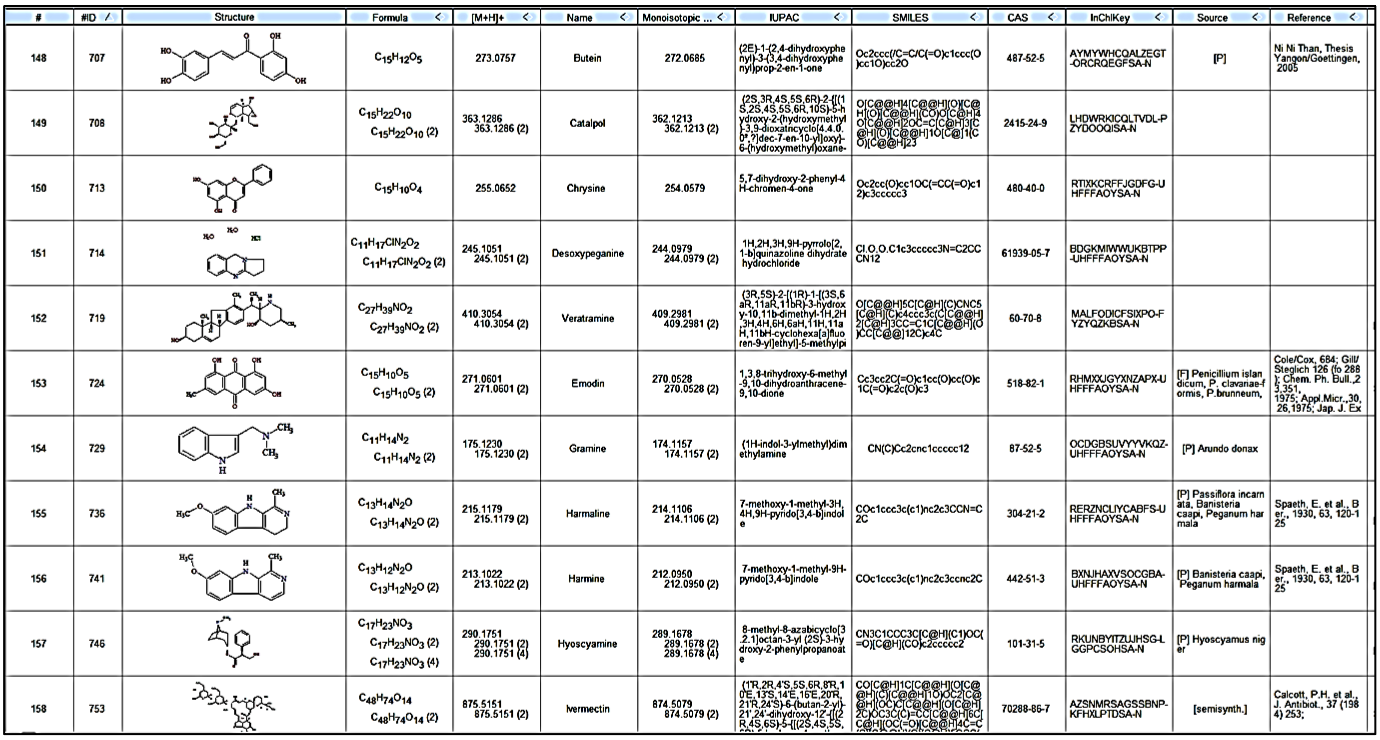


Figure S10. Some compound structures in MbcDB (No. 148-175, Tile view)



#	#ID	Structure	Formula	[M+H]+	Name	Monoisotopic ...	IUPAC	SMILES	CAS	InChIKey	Source	Reference
148	707		$C_{15}H_{12}O_5$	273.0757	Butein	272.0685	(2E)-1-(2,4-dihydroxyphenyl)-3-(3,4-dihydroxyphenyl)prop-2-en-1-one	Oc2ccc(/C=C/C(=O)c1ccc(O)cc1O)cc2O	487-52-5	AYMYWHCQALZEGT-ORCRQEGFSA-N	[P]	Ni Ni Than, Thesis Yangon/Goettingen, 2005
149	708		$C_{15}H_{22}O_{10}$ $C_{15}H_{22}O_{10}$ (2)	363.1286 363.1286 (2)	Catalpol	362.1213 362.1213 (2)	(2S,3R,4S,5S,6R)-2-{[(1S,2S,4S,5S,6R,10S)-5-hydroxy-2-(hydroxymethyl)-3,9-dioxatricyclo[4.4.0.0²,?]dec-7-en-10-yl]oxy}-6-(hydroxymethyl)oxane-	O[C@@H]4[C@@H](O)[C@H](O)[C@@H](CO)O[C@H]4O[C@@H]2OC=C[C@H]3[C@H](O)[C@@H]1O[C@]1(CO)[C@@H]23	2415-24-9	LHDWRKICQLTVDL-PZYDOOQISA-N		
150	713		$C_{15}H_{10}O_4$	255.0652	Chrysine	254.0579	5,7-dihydroxy-2-phenyl-4H-chromen-4-one	Oc2cc(O)cc1OC(=CC(=O)c12)c3ccccc3	480-40-0	RTIXKCRFFJGDFG-UHFFFAOYSA-N		
151	714		$C_{11}H_{17}ClN_2O_2$ $C_{11}H_{17}ClN_2O_2$ (2)	245.1051 245.1051 (2)	Desoxypeganine	244.0979 244.0979 (2)	1H,2H,3H,9H-pyrrolo[2,1-b]quinazoline dihydrate hydrochloride	Cl.O.O.C1c3ccccc3N=C2CCCN12	61939-05-7	BDGKMIWWUKBTPP-UHFFFAOYSA-N		
152	719		$C_{27}H_{39}NO_2$ $C_{27}H_{39}NO_2$ (2)	410.3054 410.3054 (2)	Veratramine	409.2981 409.2981 (2)	(3R,5S)-2-[(1R)-1-[(3S,6aR,11aR,11bR)-3-hydroxy-10,11b-dimethyl-1H,2H,3H,4H,6H,6aH,11H,11aH,11bH-cyclohexa[a]fluoren-9-yl]ethyl]-5-methylpi	O[C@@H]5C[C@H](C)CNC5[C@H](C)c4ccc3c(C[C@@H]2[C@H]3CC=C1C[C@@H](O)CC[C@@]12C)c4C	60-70-8	MALFODICFSIXPO-FYZYQZKBSA-N		
153	724		$C_{15}H_{10}O_5$ $C_{15}H_{10}O_5$ (2)	271.0601 271.0601 (2)	Emodin	270.0528 270.0528 (2)	1,3,8-trihydroxy-6-methyl-9,10-dihydroanthracene-9,10-dione	Cc3cc2C(=O)c1cc(O)cc(O)c1C(=O)c2c(O)c3	518-82-1	RHMXXJGYXNZAPX-UHFFFAOYSA-N	[F] Penicillium islandicum, P. clavariae-formis, P.brunneum,	Cole/Cox, 684; Gill/Steglich 126 (fo 288); Chem. Ph. Bull.,23,351, 1975; Appl.Micr.,30, 26,1975; Jap. J. Ex
154	729		$C_{11}H_{14}N_2$ $C_{11}H_{14}N_2$ (2)	175.1230 175.1230 (2)	Gramine	174.1157 174.1157 (2)	(1H-indol-3-ylmethyl)dimethylamine	CN(C)Cc2cnc1ccccc12	87-52-5	OCDGBSUVYYVKQZ-UHFFFAOYSA-N	[P] Arundo donax	
155	736		$C_{13}H_{14}N_2O$ $C_{13}H_{14}N_2O$ (2)	215.1179 215.1179 (2)	Harmaline	214.1106 214.1106 (2)	7-methoxy-1-methyl-3H,4H,9H-pyrido[3,4-b]indole	COc1ccc3c(c1)nc2c3CCN=C2C	304-21-2	RERZNCLIYCABFS-UHFFFAOYSA-N	[P] Passiflora incarnata, Banisteria caapi, Peganum harmala	Spaeth, E. et al., Ber., 1930, 63, 120-125
156	741		$C_{13}H_{12}N_2O$ $C_{13}H_{12}N_2O$ (2)	213.1022 213.1022 (2)	Harmine	212.0950 212.0950 (2)	7-methoxy-1-methyl-9H-pyrido[3,4-b]indole	COc1ccc3c(c1)nc2c3ccnc2C	442-51-3	BXNJHAXVSOCGBA-UHFFFAOYSA-N	[P] Banisteria caapi, Peganum harmala	Spaeth, E. et al., Ber., 1930, 63, 120-125
157	746		$C_{17}H_{23}NO_3$ $C_{17}H_{23}NO_3$ (2) $C_{17}H_{23}NO_3$ (4)	290.1751 290.1751 (2) 290.1751 (4)	Hyoscyamine	289.1678 289.1678 (2) 289.1678 (4)	8-methyl-8-azabicyclo[3.2.1]octan-3-yl (2S)-3-hydroxy-2-phenylpropanoate	CN3C1CCC3C[C@H](C1)OC(=O)[C@H](CO)c2ccccc2	101-31-5	RKUNBYITZUJHSG-LGGPCSOHSA-N	[P] Hyoscyamus niger	
158	753		$C_{48}H_{74}O_{14}$ $C_{48}H_{74}O_{14}$ (2)	875.5151 875.5151 (2)	Ivermectin	874.5079 874.5079 (2)	(1'R,2R,4'S,5S,6R,8'R,10'E,13'S,14'E,16'E,20'R,21'R,24'S)-6-(butan-2-yl)-21',24'-dihydroxy-12'-{[(2R,4S,6S)-5-{[(2S,4S,5S,	CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)OC2[C@@H](OC)C[C@@H](O[C@H]2C)OC3C(C)=CC[C@@H]6C[C@H](OC(=O)[C@@H]4C=C	70288-86-7	AZSNMRSAGSSBNP-KFHXLPTDSA-N	[semisynth.]	Calcott, P.H. et al., J. Antibiot., 37 (1984) 253;

Figure S11. Names and other associated information for compounds No. 148-158 in MbcDB (Table view).

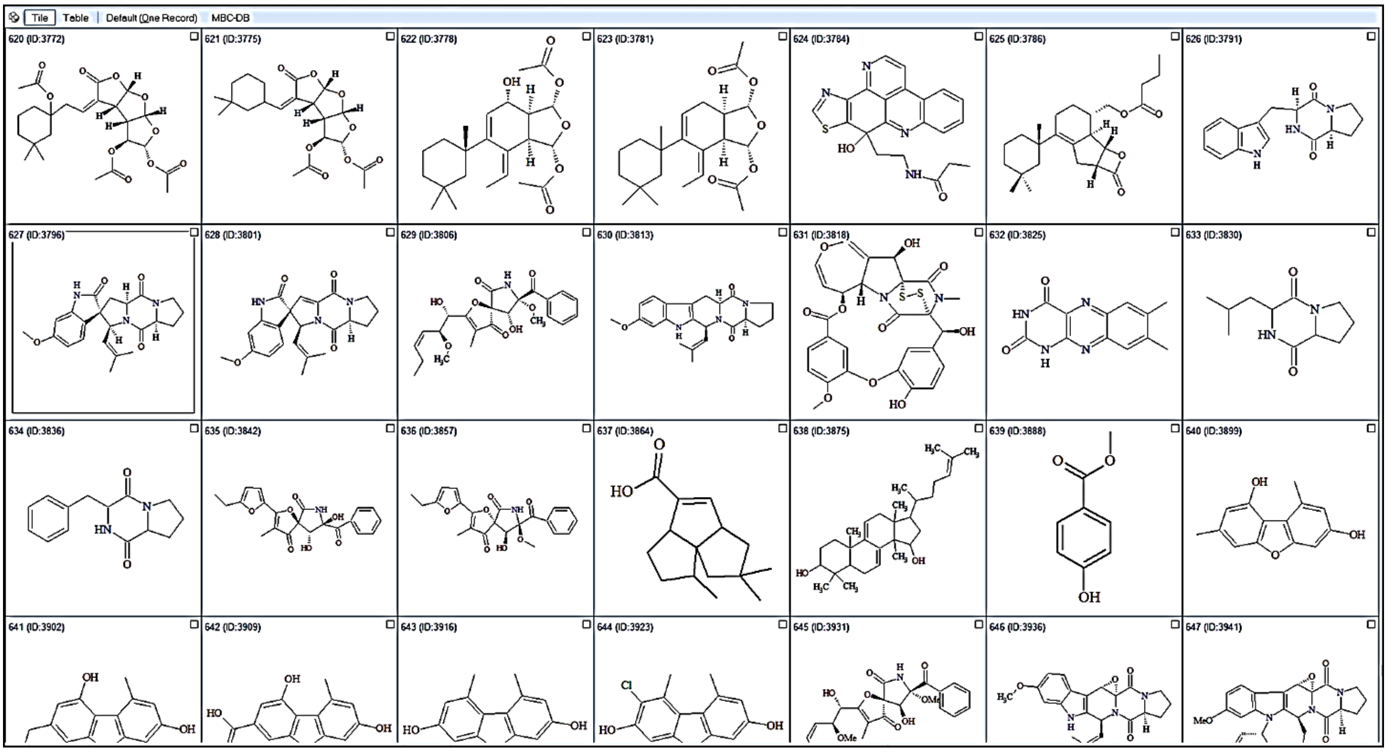


Figure S12. Structures of compounds No. 620-647 in MbcDB (Tile view)

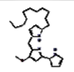
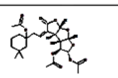
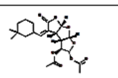
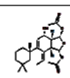
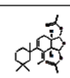
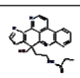
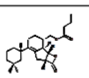
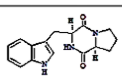
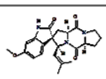
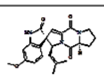
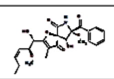
#	#ID	Structure	[M+H]+	Name	Monoisotopic ...	SMILES	CAS	InChIKey	Source	Reference
619	3767		394.2853 394.2853 (4)	Undecylprodigiosin	393.2780 393.2780 (4)	COC2=CC(=N/C2=C\c1ccc(CCCCCCCCCCC)n1)c3cccn3		HIYSWASSDOXZLC-MOHJPFBDSA-N	[S]. Porifera Mycale plumosa, [B]. Actinobacteria	Liu R Cui CB Duan L Gu QQ* Zhu WM* Arch. Pharm. Res. 2005 28(12) 1341-1344
620	3772		481.2068	Gracilin J	480.1995	CC(=O)OC1(CC(C)(C)CCC1)C\C=C3/C(=O)O[C@@H]4O[C@@H]2O[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]2[C@H]34		NMUUJHGEYJKFAT-CARDQYAASA-N	[S]. Porifera Spongionella sp	Rateb ME Houssen WE Schumacher M Harrison WTA Diederich M Ebel R Jaspars M* J. Nat. Prod. 2009 72(8) 14
621	3775		409.1857	Gracilin K	408.1784	CC1(C)CCCC(C1)\C=C3/C(=O)O[C@@H]4O[C@@H]2O[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]2[C@H]34		GOSUIVNRFQNSRC-QBTHFRSLSA-N	[S]. Porifera Spongionella sp	Rateb ME Houssen WE Schumacher M Harrison WTA Diederich M Ebel R Jaspars M* J. Nat. Prod. 2009 72(8) 14
622	3778		407.2428	Gracilin L	406.2355	CC(=O)O[C@H]1O[C@@H](OC(C)=O)[C@@H]2[C@@H](O)C=C(/C(=C\C)[C@H]12)[C@@]3(C)CCCC(C)(C)C3		MHDUGZBUXWJHKW-JEBUWBOWSA-N	[S]. Porifera Spongionella sp	Rateb ME Houssen WE Schumacher M Harrison WTA Diederich M Ebel R Jaspars M* J. Nat. Prod. 2009 72(8) 14
623	3781		391.2479	Gracilin A	390.2406	CC1(C)CCCC(C)(C1)C\2=CC[C@H]3[C@H](OC(C)=O)O[C@H](OC(C)=O)[C@H]3C/2=C\C		APJJQRQXHYHMQ-VOGOUGRGSA-N	[S]. Porifera Spongionella gracilis	Mayol L Piccialli V Sica D Tetrahedron Lett. 1985 26 1357-1360
624	3784		391.1223	Sagitol	390.1150	CCC(=O)NCCC3(O)c4nc1ccccc1c5ccnc(c2ncsc23)c45		KUCCLEBOZAZSDY-UHFFFAOYSA-N	[S]. Porifera Oceanapia sagittaria	Salomon CE Faulkner DJ Tetrahedron Lett. 1996 37 9147-9148
625	3786		389.2686	3'-norspongiolactone	388.2614	CC1(C)CCC[C@@](C)(C1)C=4CC[C@H](COC(=O)CCC)[C@@H]2C=4C[C@H]3C(=O)O[C@@H]23		YPAWZAVNLSHCSY-MFSWYNMTSA-N	[S]. Porifera Spongionella sp	Rateb ME Houssen WE Schumacher M Harrison WTA Diederich M Ebel R Jaspars M* J. Nat. Prod. 2009 72(8) 14
626	3791		284.1394 284.1394 (4)	Brevianamide F	283.1321 283.1321 (4)	O=C3N4CCC[C@H]4C(=O)N[C@H]3Cc2cnc1ccccc12		RYFZBPVMVYTEKZ-KBPBESRZSA-N	[F] Penicillium brevi-compactum; Aspergillus ochraceus; [B] marine Streptomyces sp. Sch15, S. sp. L028; S. sp. TN	Birch, A. J. et al., Tetrahedron 28, 2999, 1972; Kozlovskii, A.G. et al., Mikrobiologiya 1990, 59,
627	3796		396.1918 396.1918 (4)	Spirotryprostatin A	395.1845 395.1845 (4)	C\C(C)=C/[C@@H]3N4C(=O)[C@@H]5CCCN5C(=O)[C@@H]4C[C@@]13c2ccc(OC)cc2NC1=O		MQJKGSIAJNXSCM-ORGXJRBJSA-N	[F]. marine Aspergillus fumigatus	C. B. Cui et al., Tetrahedron 52 (1996) 12651-12666
628	3801		394.1761 394.1761 (4)	6-methyoxyspirotryprostatin B	393.1689 393.1689 (4)	C/C(C)=C\[C@@H]1N4C(=O)[C@@H]5CCCN5C(=O)C4=C[C@]12c3ccc(OC)cc3NC2=O		UHQKDPCPFNXIDU-ZJBJCVSYSA-N	[F]. Ascomycota Aspergillus sydowii	Zhang M Wang WL Fang YC Zhu TJ Gu QQ* Zhu WM* J. Nat. Prod. 2008 71(6) 985-989
629	3806		446.1809 446.1809 (4)	11-O-Methylpseurotin A	445.1737 445.1737 (4)	CC\C=C/[C@H](O)[C@H](O)C=1O[C@@]2(C(=O)C=1C)C(=O)N[C@](OC)(C2O)C(=O)c3ccccc3		SLYDIPAXCVVRNY-BBJHAQHQSA-N	[F]. marine-derived Aspergillus fumigatus	Boot, Claudia M. et al., J. Nat. Prod. 70 (2007) 1672-1675

Figure S13. Names and other associated information for compounds No. 619-629 in MbcDB (Table view).

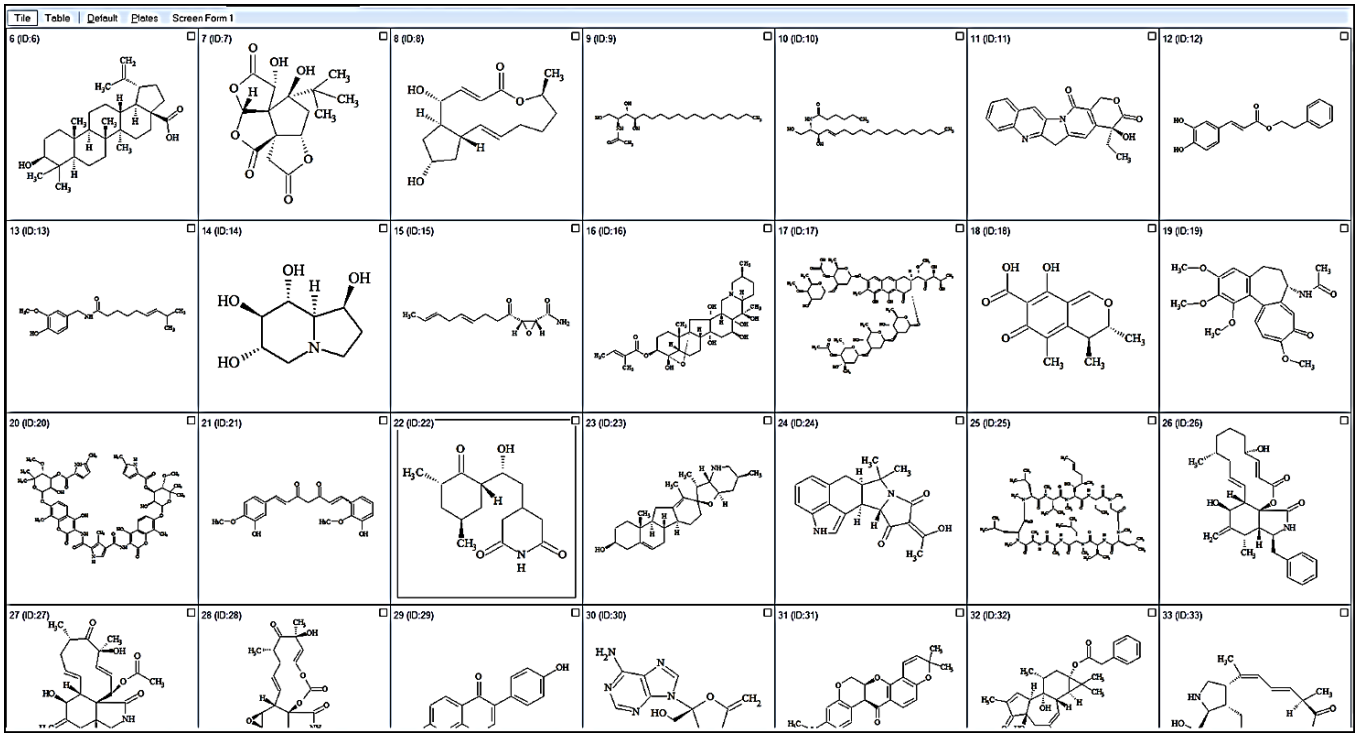
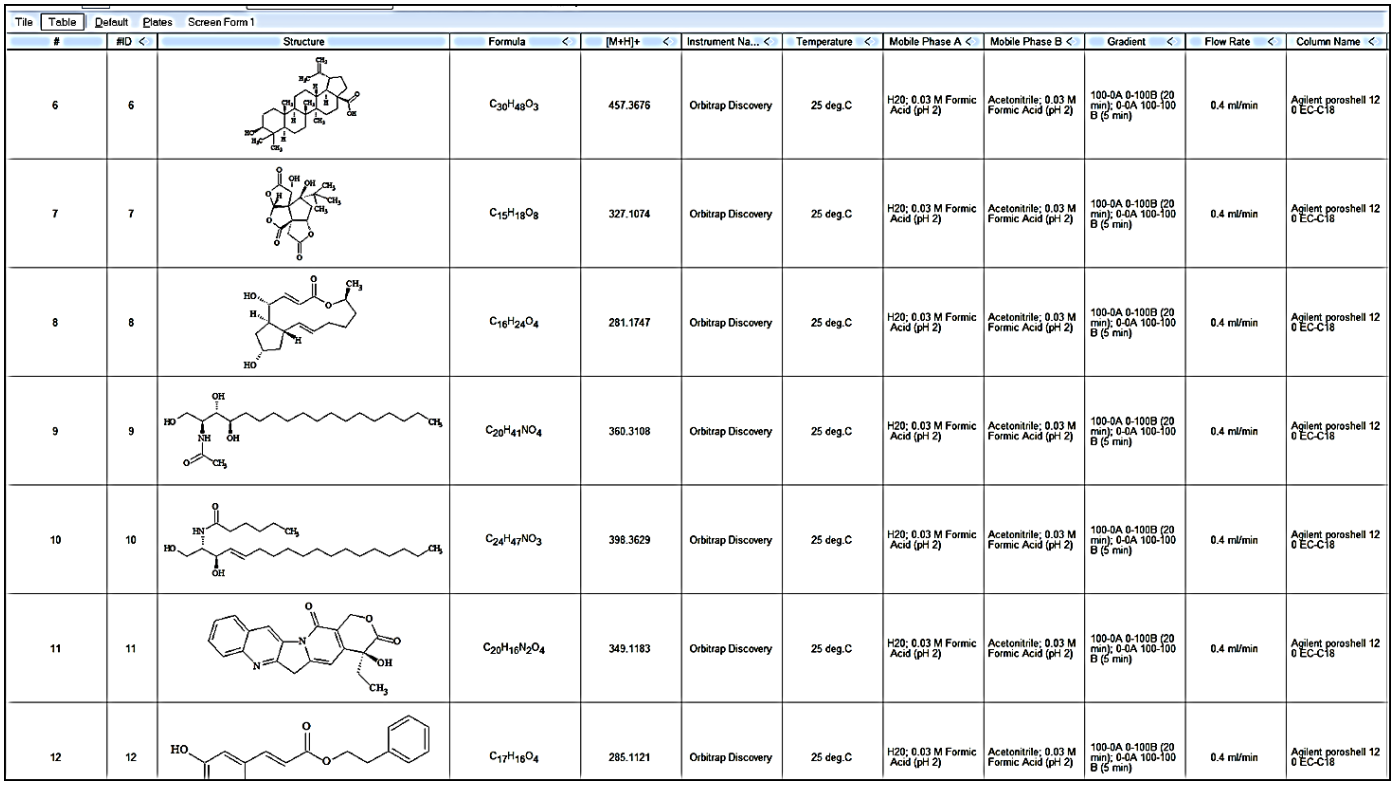


Figure S14. Some of the compounds (No. 6-33) used in the calculation (ChromGenius) of LC retention times are shown here (Tile view).



#	#ID	Structure	Formula	[M+H]+	Instrument Na...	Temperature	Mobile Phase A	Mobile Phase B	Gradient	Flow Rate	Column Name
6	6		$C_{30}H_{48}O_3$	457.3676	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
7	7		$C_{15}H_{18}O_8$	327.1074	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
8	8		$C_{16}H_{24}O_4$	281.1747	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
9	9		$C_{20}H_{41}NO_4$	360.3108	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
10	10		$C_{24}H_{47}NO_3$	398.3629	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
11	11		$C_{20}H_{16}N_2O_4$	349.1183	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18
12	12		$C_{17}H_{16}O_4$	285.1121	Orbitrap Discovery	25 deg.C	H20; 0.03 M Formic Acid (pH 2)	Acetonitrile; 0.03 M Formic Acid (pH 2)	100-0A 0-100B (20 min); 0-0A 100-100 B (5 min)	0.4 ml/min	Agilent poroshell 120 EC-C18

Figure S15. The creation of the 'knowledge base' was performed by analysing known natural products (some are shown here) using a defined LC-method. Some of the experimental parameters used are shown here (Table view).

No	$t_{R/min}$	Mass/ Da $(M+H)^+$	MF	UV (λ_{max})	StrepDB hits
1	15.01	265.15	$C_{14}H_{21}O_3N_2$	200, 320	yes
2	16.61	297.18	$C_{15}H_{25}O_4N_2$	216, 320	None
3	16.73	277.15	$C_{15}H_{21}O_3N_2$	216, 320	None
4	16.83	279.17	$C_{15}H_{23}O_3N_2$	216, 322	None
5	18.82	293.19	$C_{16}H_{25}O_3N_2$	216, 324	None
6	17.02	297.18	$C_{15}H_{25}O_4N_2$	216, 320	None
7	21.87	297.14	$C_{14}H_{21}O_5N_2$	245, 344	None
8	19.16	311.20	$C_{16}H_{27}O_4N_2$	216, 320	None
9	24.46	311.16	$C_{15}H_{23}O_5N_2$	220, 320	None
10	26.43	325.18	$C_{16}H_{25}O_5N_2$	224, 326	None
11	22.27	327.19	$C_{16}H_{27}O_5N_2$	240, 336	None

Table S16. Compounds of interest in the water-butanol fraction based on UV spectra (200-245, 320-344 nm).

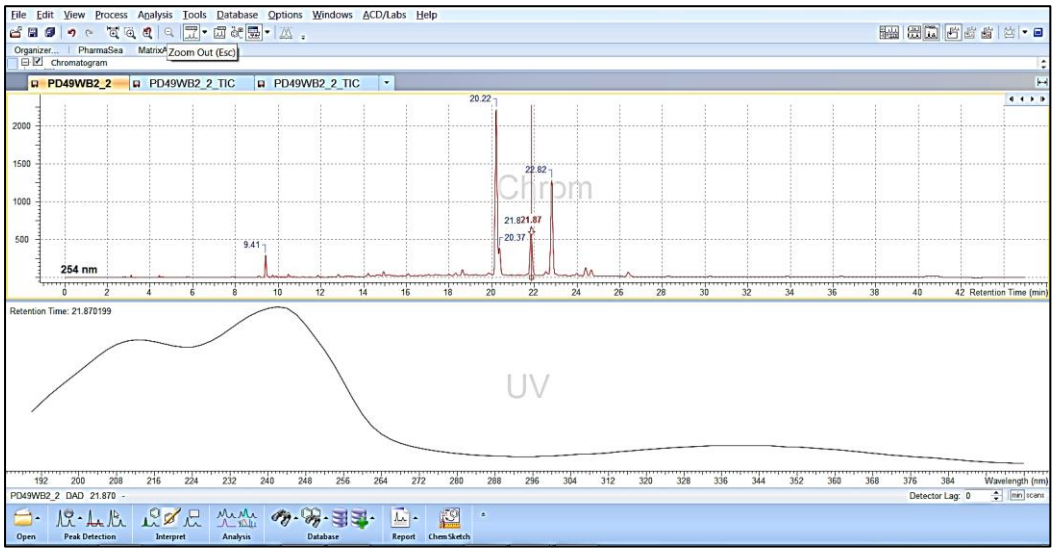
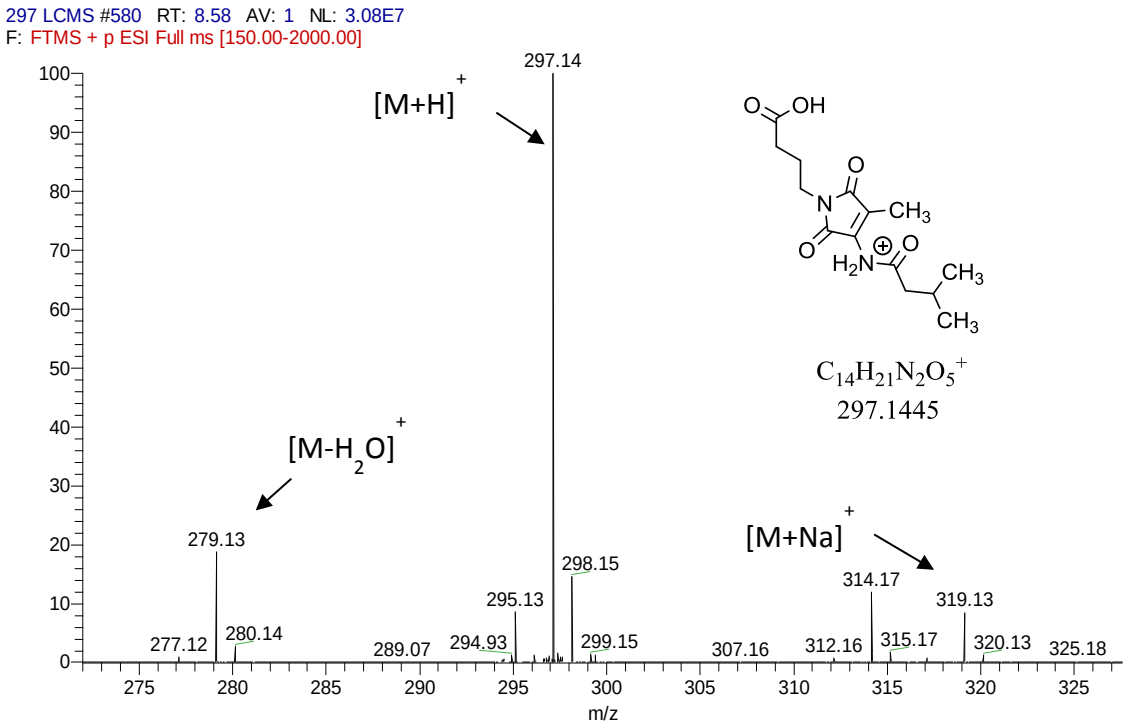


Figure S17. UV spectrum of one of the targeted new compounds, t_R = 21.87 min.



m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
	297.14	0.03	5.5	$C_{14}H_{21}O_5N_2$
	297.15	-1.31	10.5	$C_{15}H_{17}ON_6$

Figure S18. HRESIMS spectrum of of legonmaleimide A (**1**)

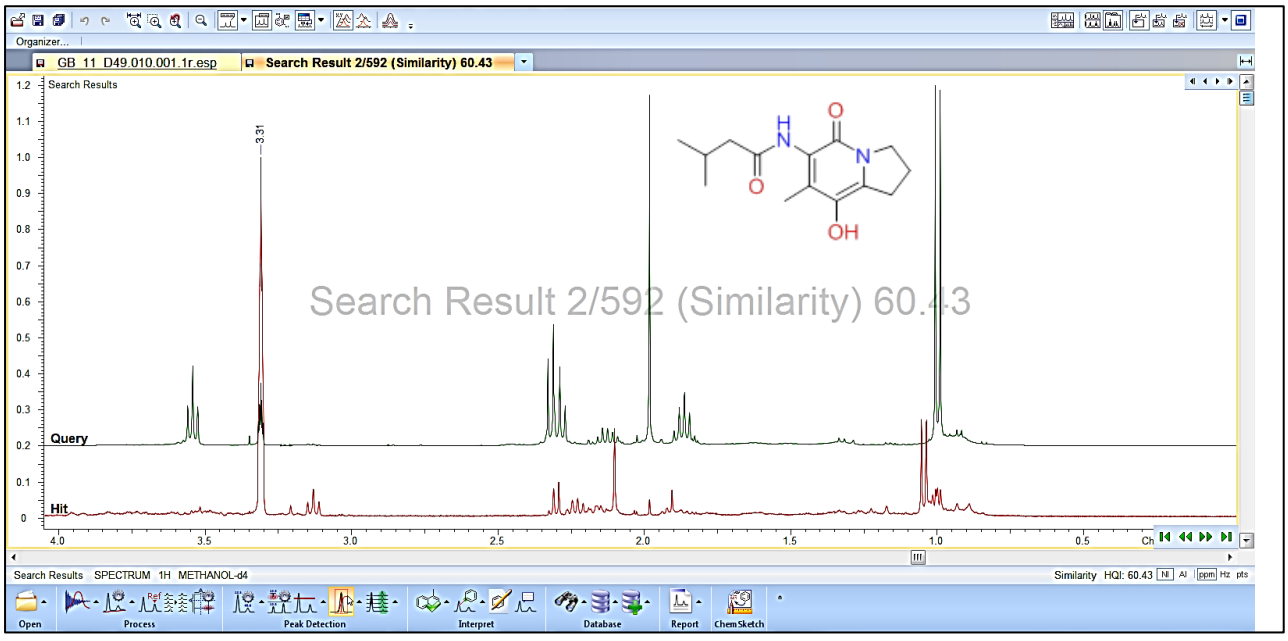


Figure S19. ^{1}H NMR spectrum search of compound **1** (Query)in MbcDB indicate that the query proton spectrum is related to legonindolizidine A (Hit), structure is shown.

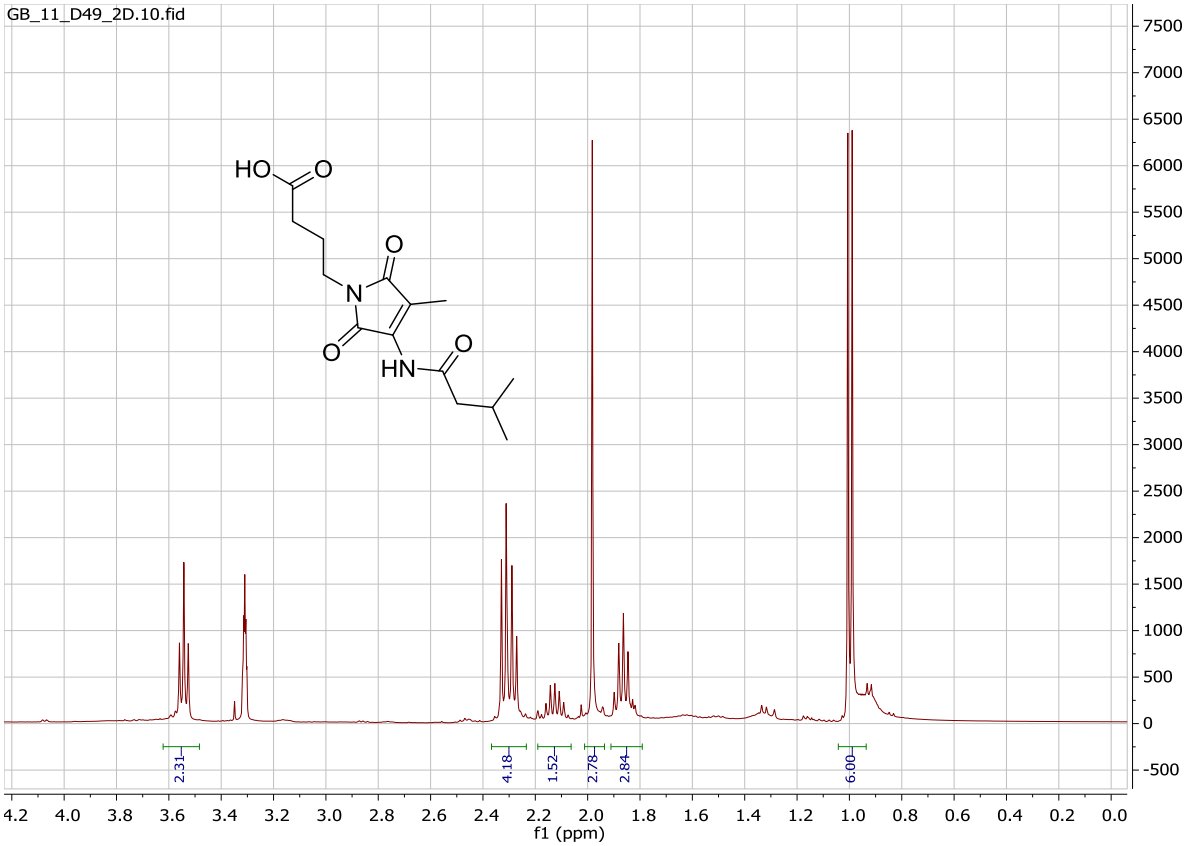


Figure S20. ^{1}H NMR (600 MHz, CD_3OD) spectrum of of legonmaleimide A (**1**)

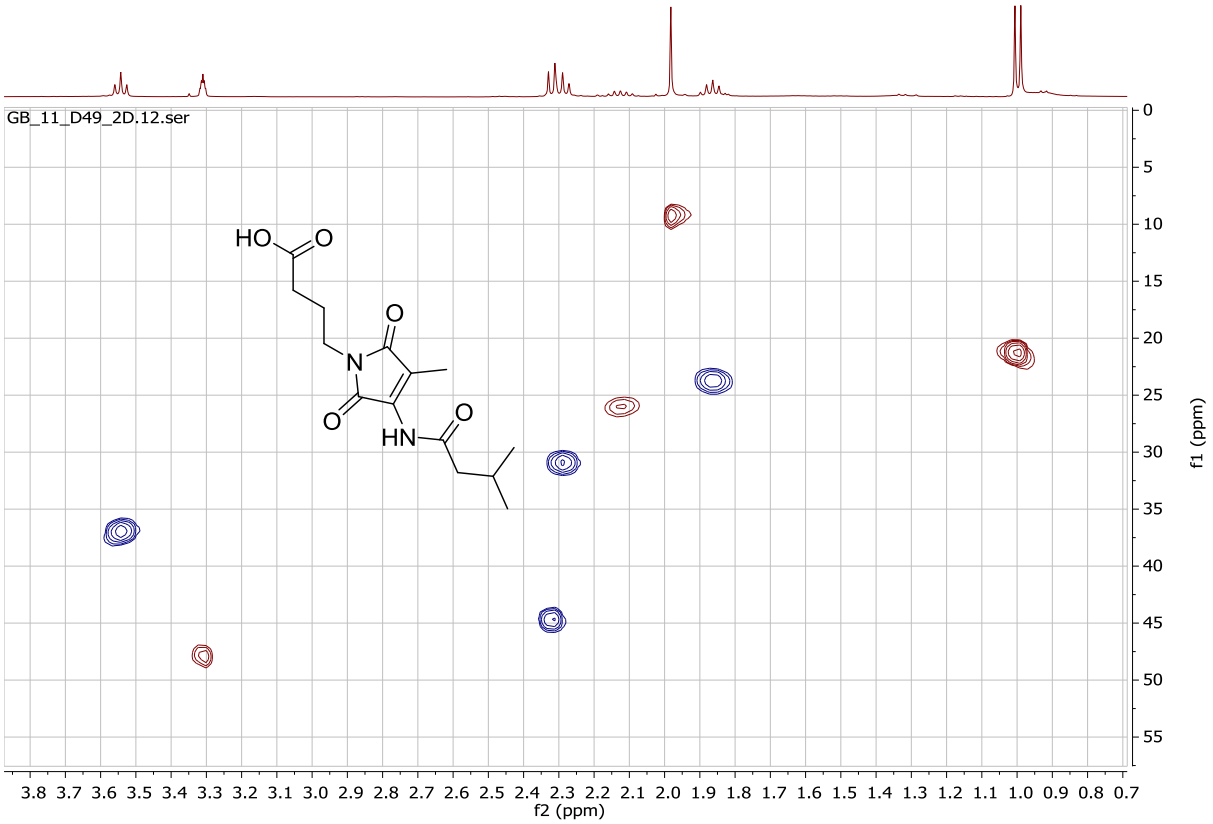


Figure S21. Edited HSQC (600 MHz, CD_3OD) spectrum of of legonmaleimide A (**1**)

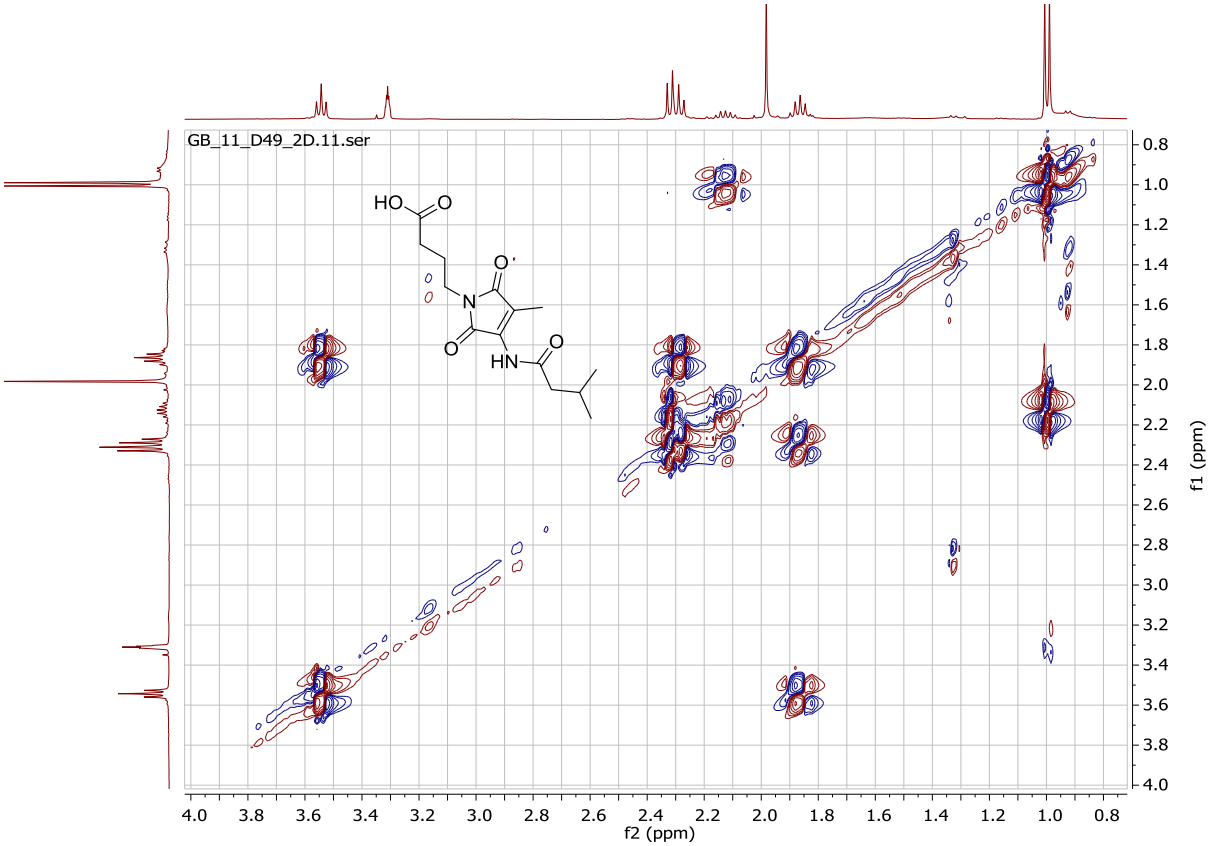


Figure S22. COSY (600MHz, CD_3OD) spectrum of of legonmaleimide A (**1**)

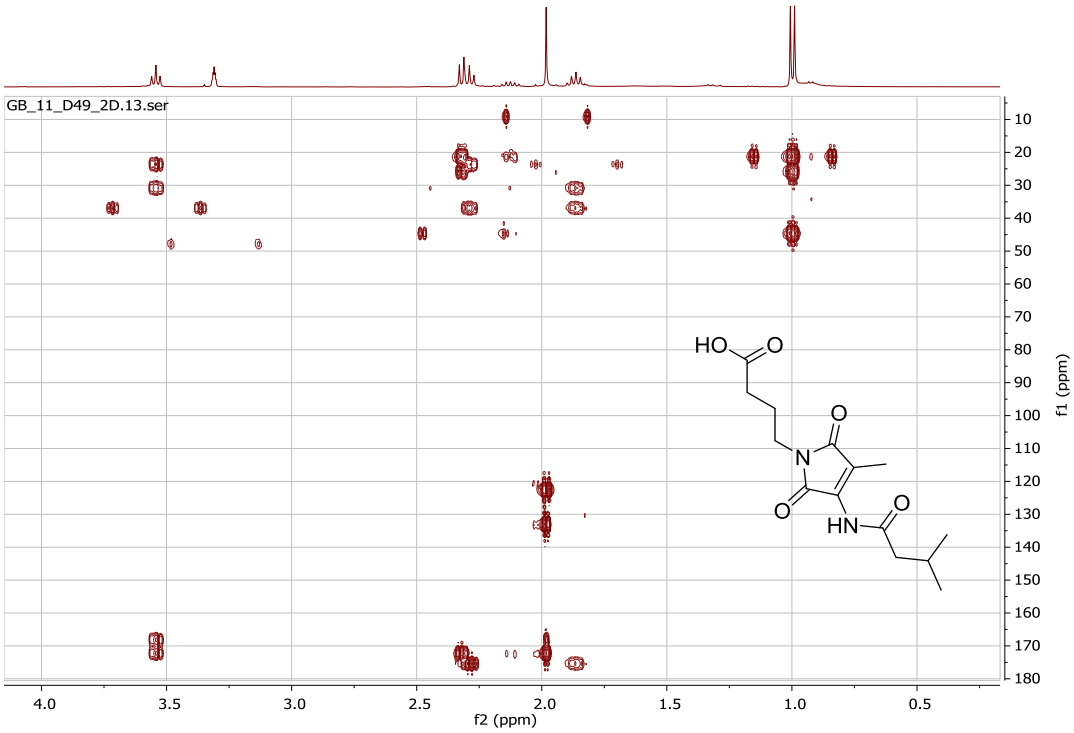


Figure S23. HMBC (600MHz, CD_3OD) spectrum of of legonmaleimide A (**1**)

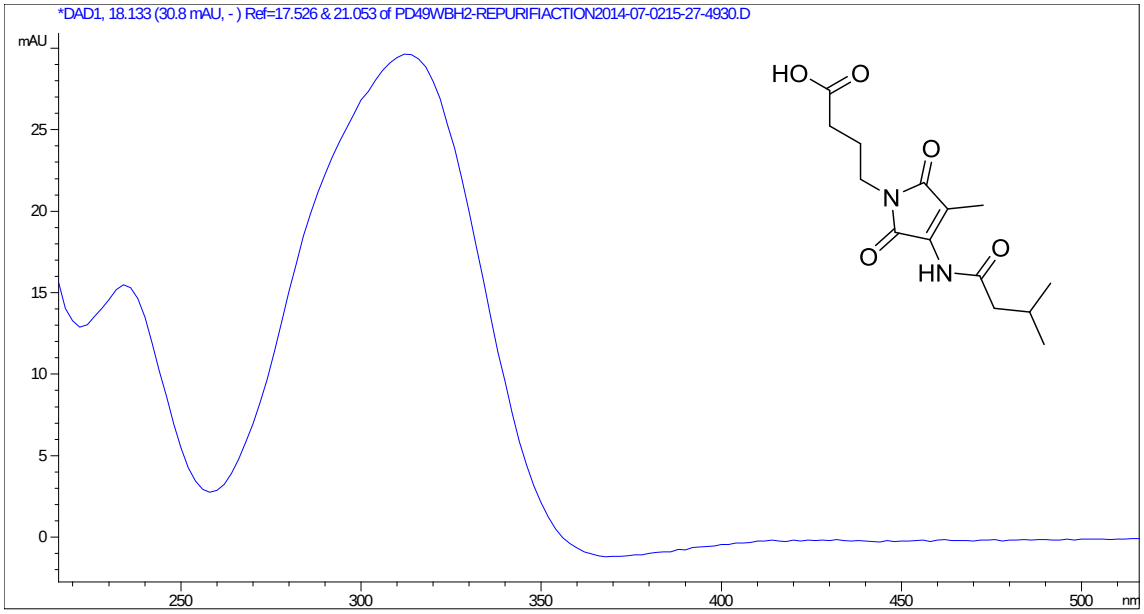


Figure S24. UV spectrum of legonmaleimide A (**1**)

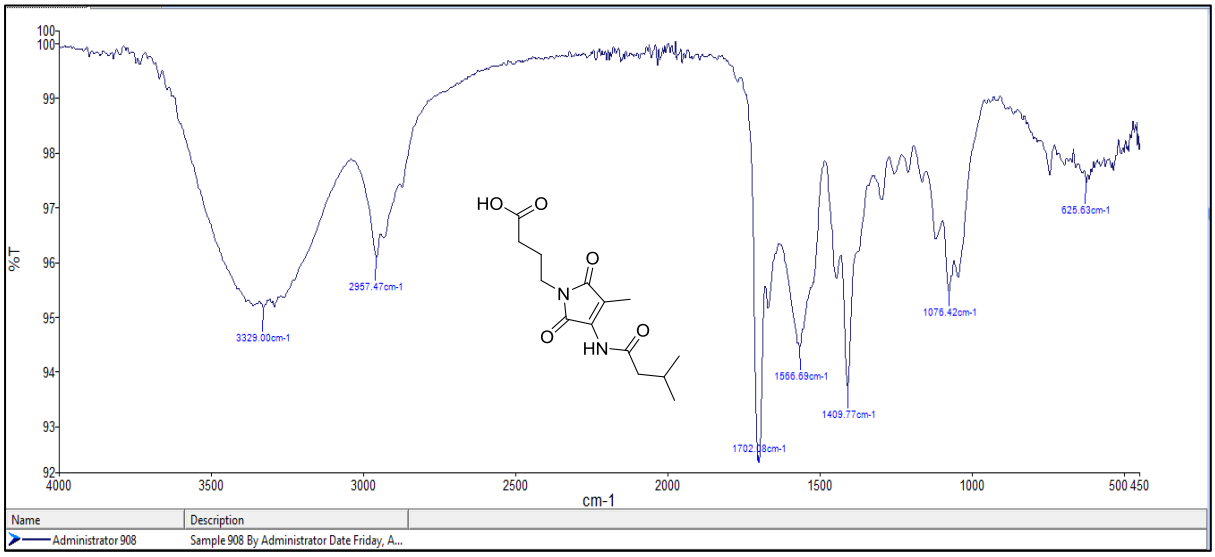


Figure S25. IR spectrum of legonmaleimide A (**1**)

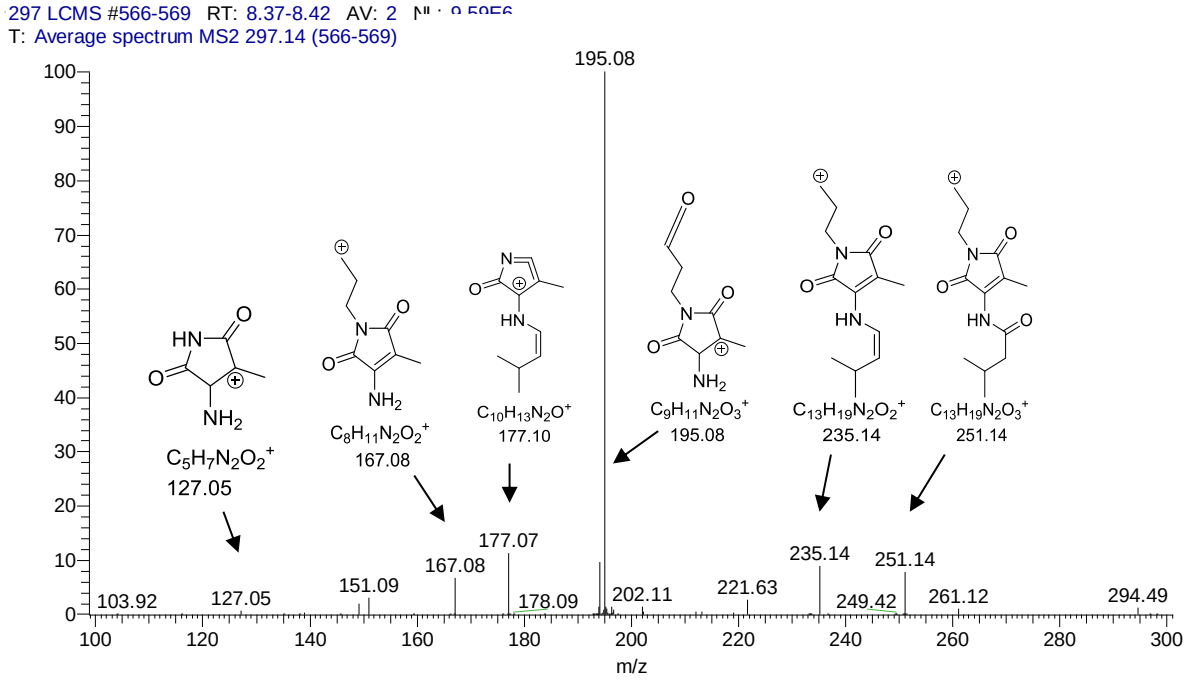
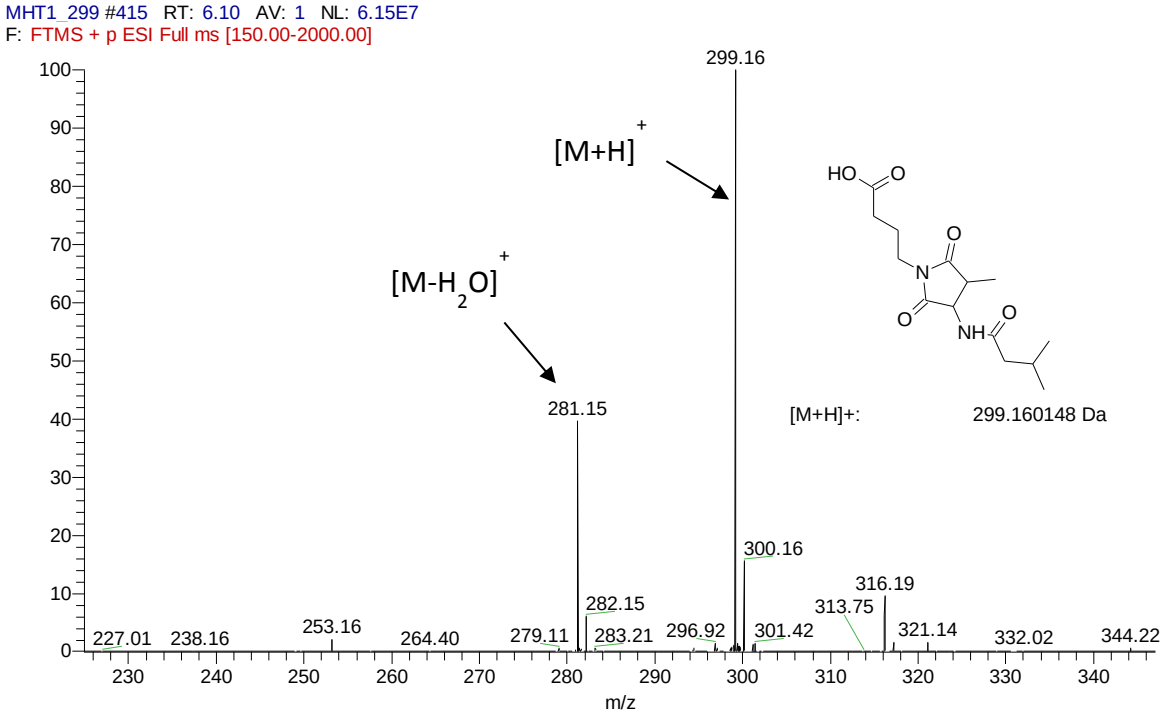


Figure S26. ES$^+$ fragmentation data for legonmaleimide A (**1**)



m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
	299.16	0.22	4.5	$C_{14}H_{23}O_5N_2$
	299.16	-1.12	9.5	$C_{15}H_{19}ON_6$

Figure S27. HRESIMS spectrum of of legonmaleimide B (**2**).

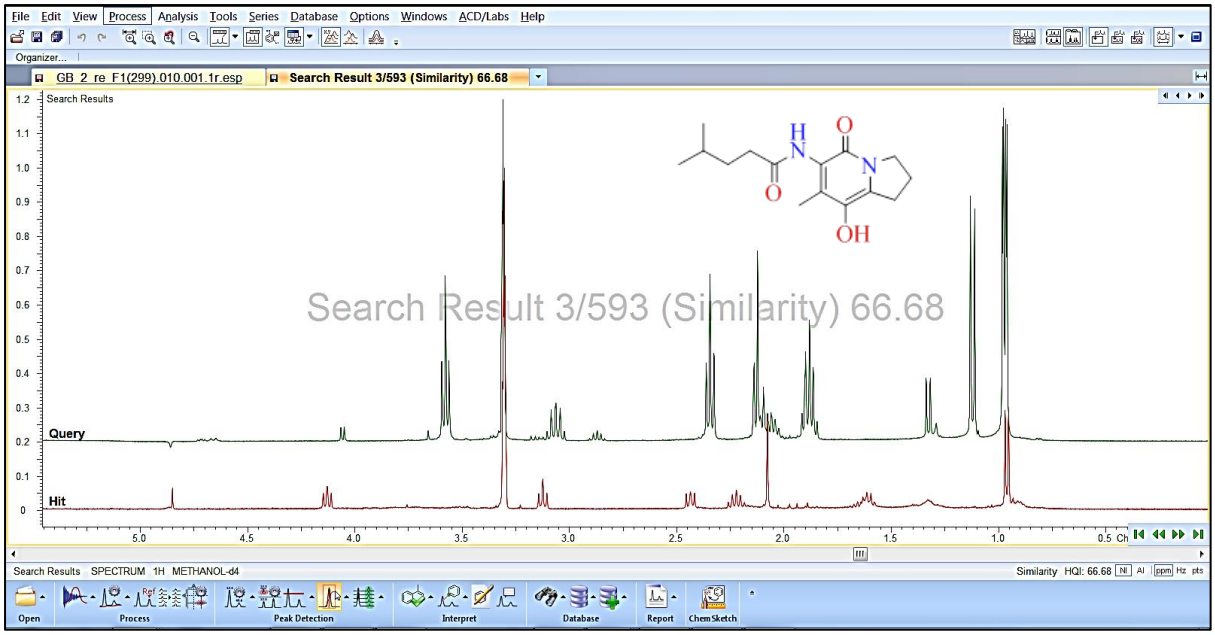


Figure S28. ^{1}H NMR spectrum search of compound **2** (Query) in MbcDB showed some similarity to the proton spectrum of legonindolizidine B (Hit), structure is shown.

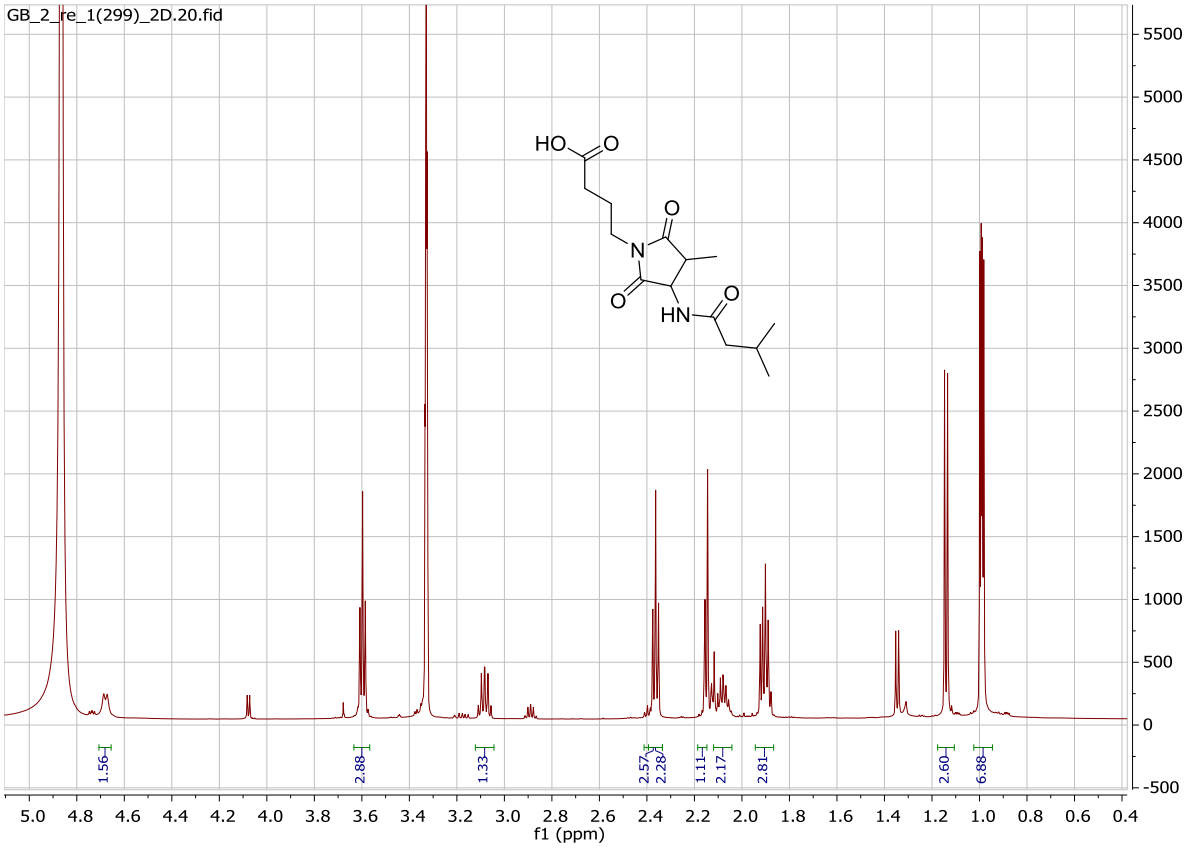


Figure S29. ^{1}H (600 MHz, CD_3OD) spectrum of of legonmaleimide B (**2**)

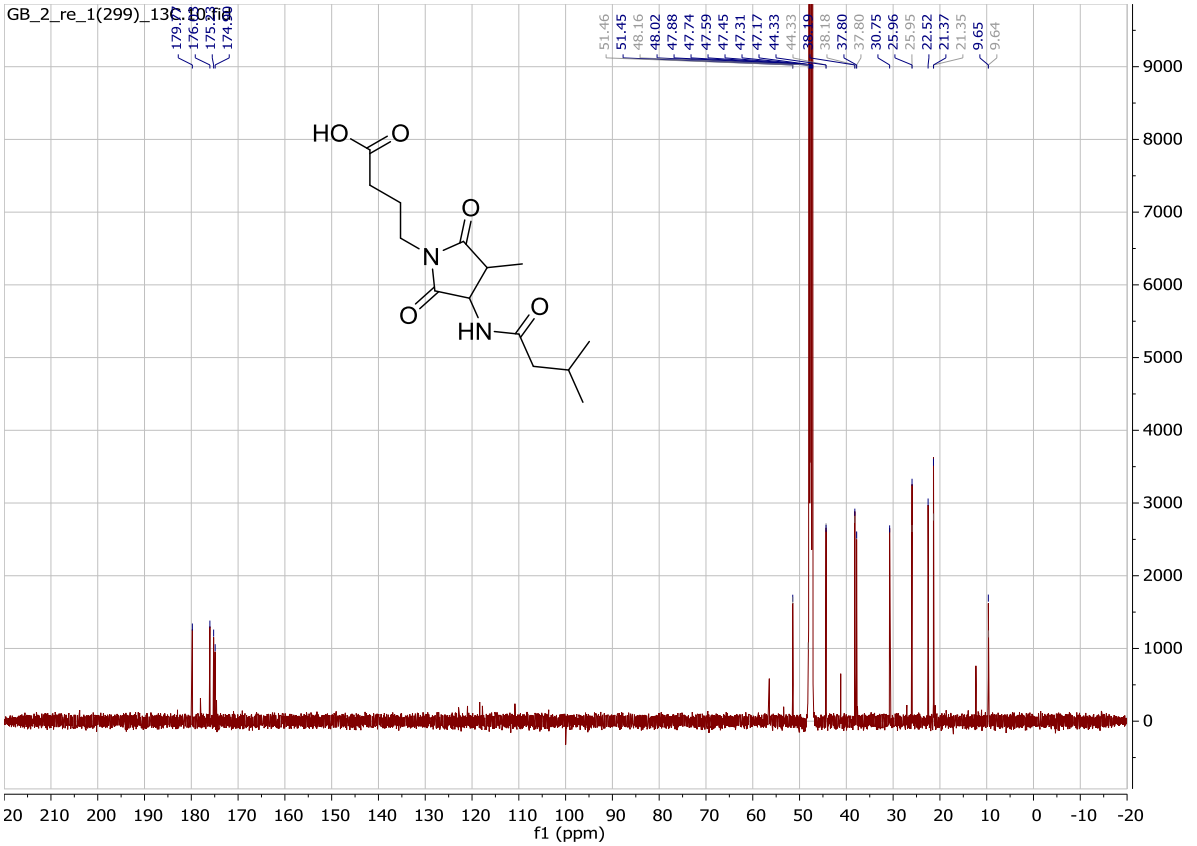


Figure S30. ^{13}C (250 MHz, CD_3OD) spectrum of of legonmaleimide B (**2**).

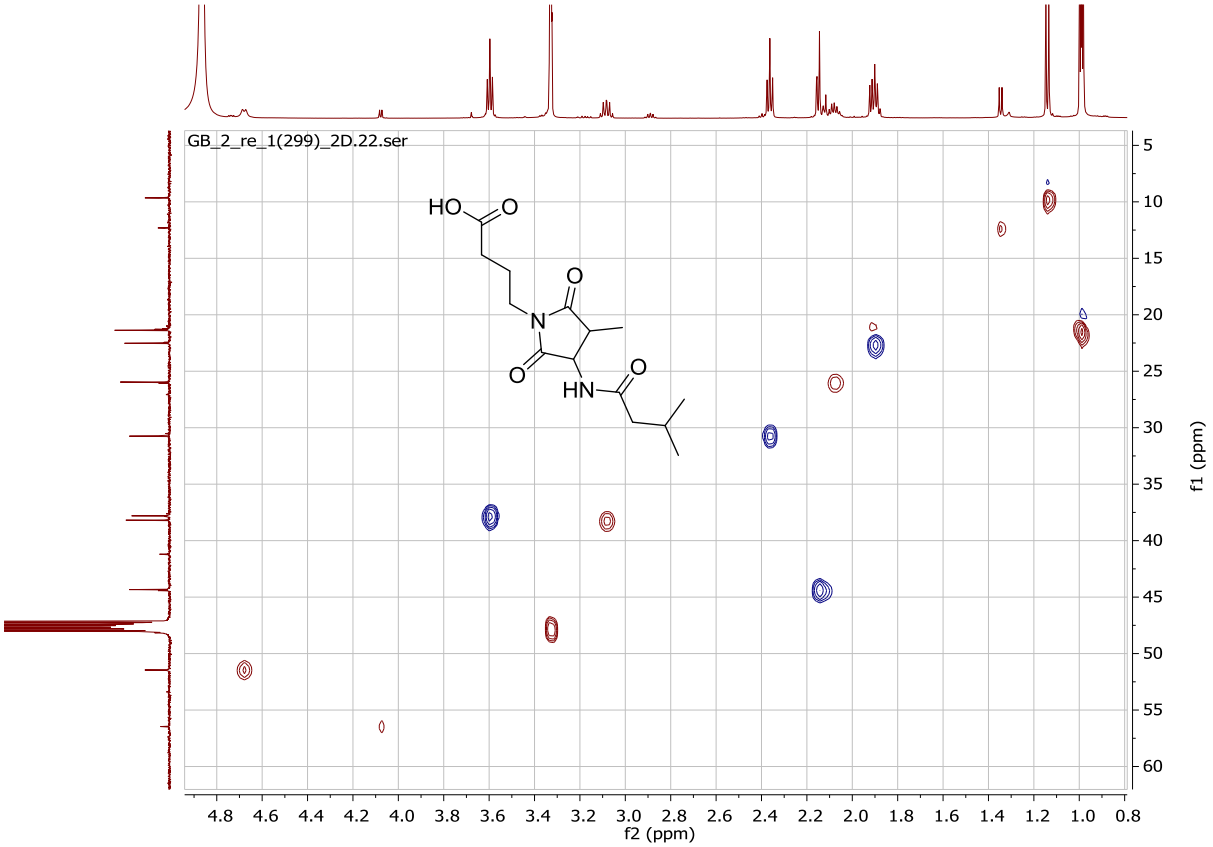


Figure S31. EDITED-HSQC (600 MHz, CD_3OD) spectrum of of legonmaleimide B (**2**)

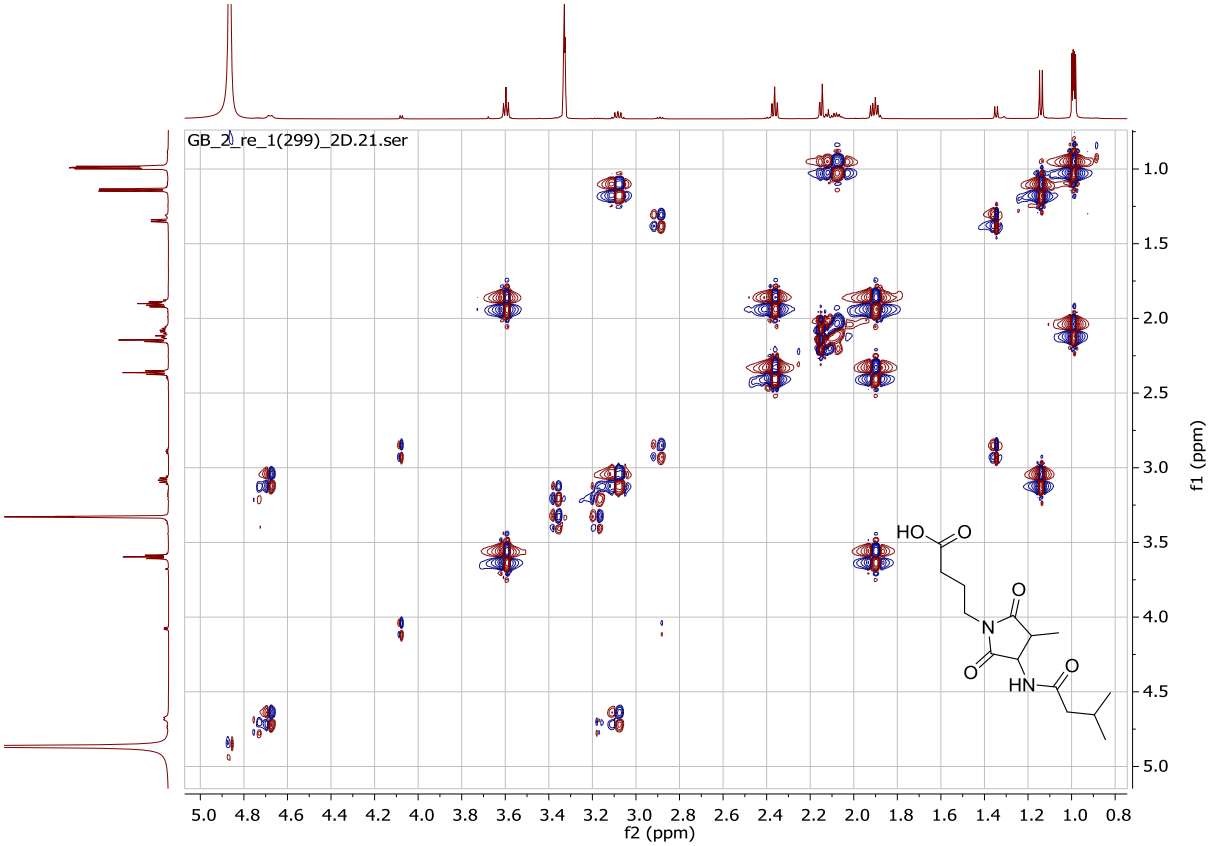


Figure S32. COSY (600 MHz, CD_3OD) spectrum of of legonmaleimide B (**2**)

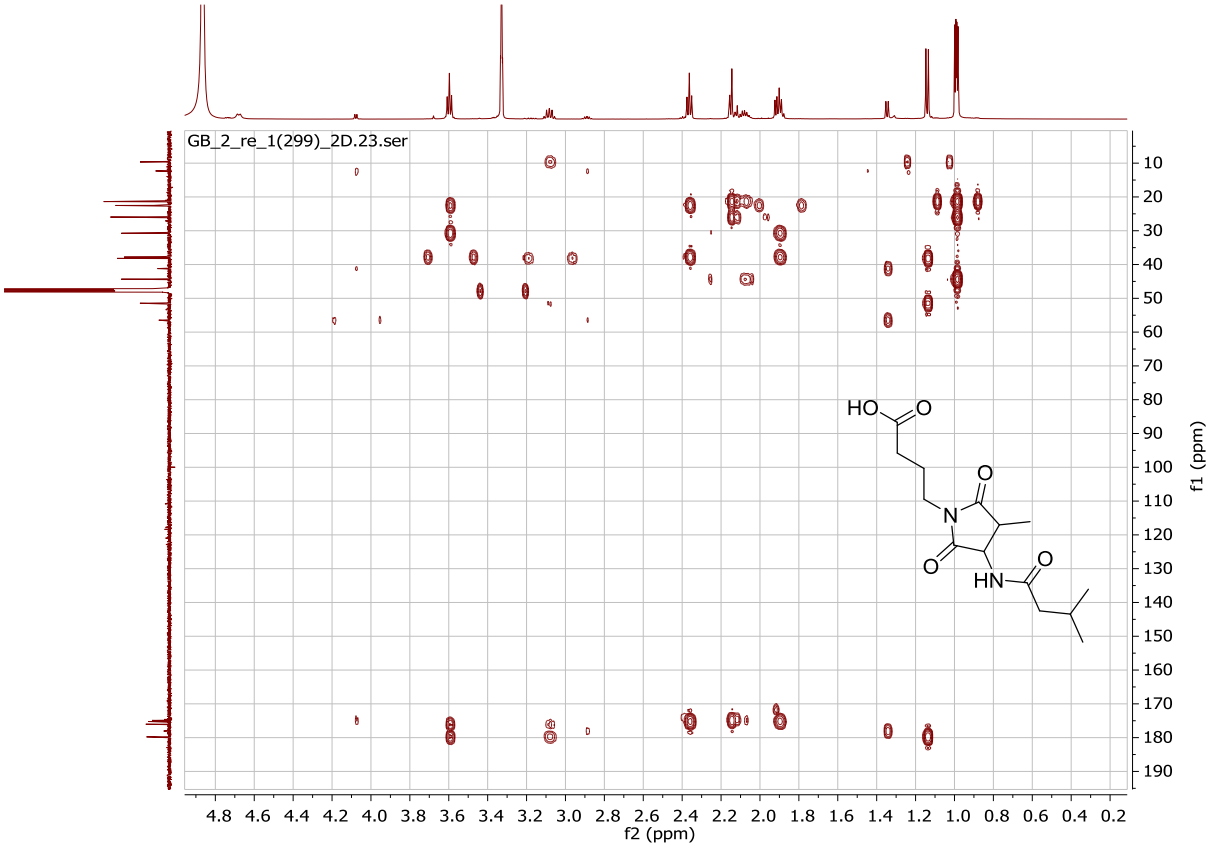


Figure S33. HMBC (600 MHz, CD_3OD) spectrum of of legonmaleimide B (**2**)

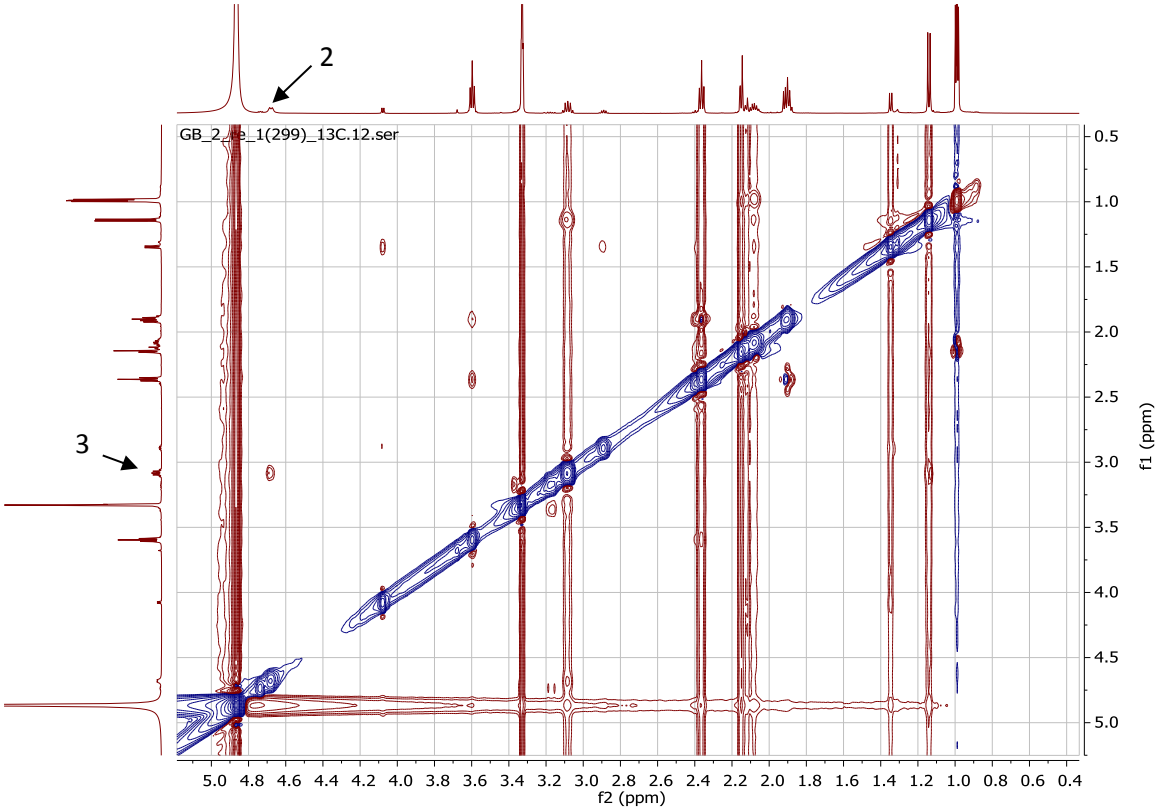


Figure S34. ROESY (600 MHz, 300 ms, CD_3OD) spectrum of of legonmaleimide B (**2**)

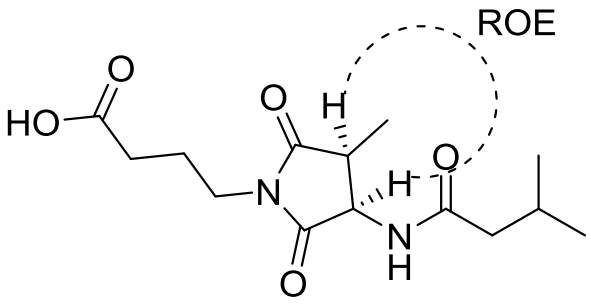


Figure S35. Observed ROE with relative stereochemistry of legonmaleimide B (**2**).

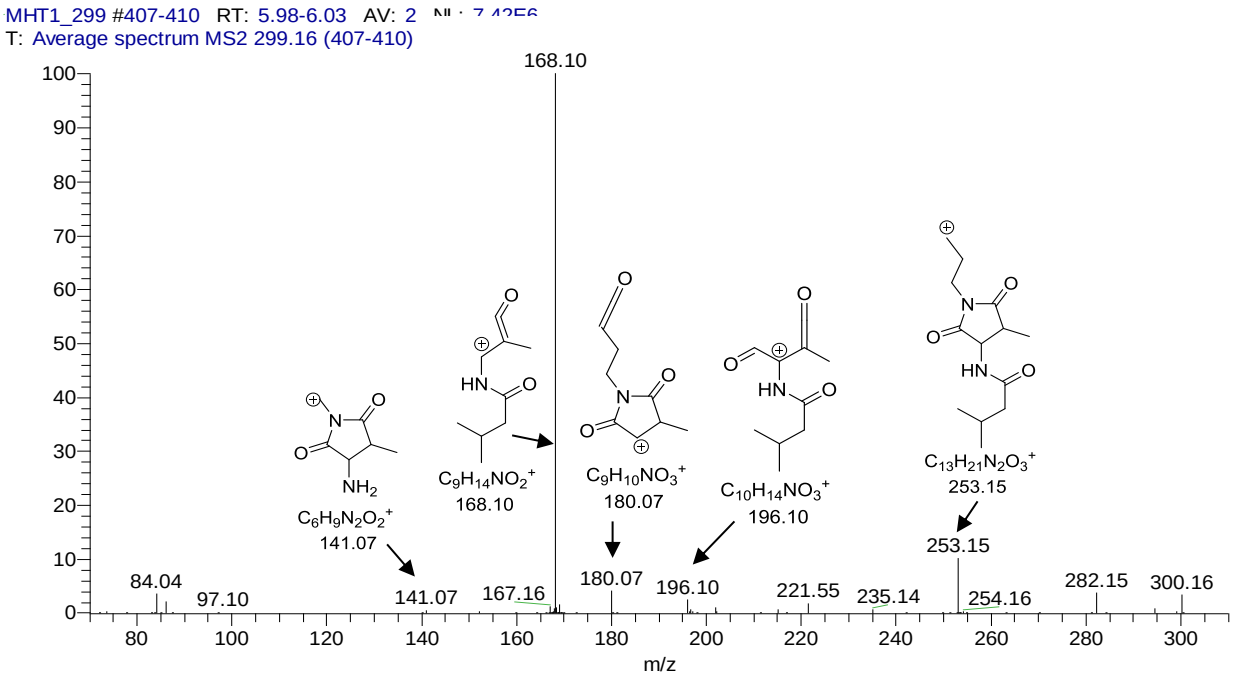


Figure S36. ES$^+$ Fragmentation data for legonmaleimide B (**2**).

Structure Elucidation Report for "PD49_WB_H1C_11July2014"

Initial Data

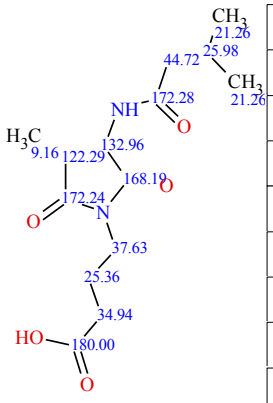
Composition Restrictions:
Molecular Weight = 0.000-1000.000
Double Bonds Equivalent = 0.00-100.00
Allowed Composition = C(0-100) H(0-100) O(0-20) N(0-10)
Molecular Formula = C14H20O5N2

Spectral Data:
standard 1H - 9 peaks
standard 1H (merged) - 10 peaks
standard 13C (merged) - 13 peaks
COSY 1H-1H - 4 peaks
HSQC 13C-1H - 7 peaks
HMBC 13C-1H - 19 peaks

Most Probable Structure

Following structure has been placed to the first position after spectra calculation

Carbon Assignment



#	ID	N	Shift (ppm)	Conf. Limit (ppm)	Difference (ppm)	Atoms	XHn
1	1	1	9.162	0.000		1	CH3(q)
2	2	2,3	21.256	0.000		2	CH3(q)
3	3	5	25.357	0.000		1	CH2(t)
4	4	8	25.982	0.000		1	CH(d)
5	5	4	34.936	0.000		1	CH2(t)
6	6	6	37.632	0.000		1	CH2(t)
7	7	7	44.718	0.000		1	CH2(t)
8	8	10	122.294	0.000		1	C(s)
9	9	11	132.964	0.000		1	C(s)
10	10	12	168.186	0.000		1	C(s)

Figure S37. Elucidation protocol for Legonmaleimide A (1)

Start: Search Molecules by 13C NMR 07/11/2014 17:18:35

Search by CNMR options:

Clear Generated Molecules List = Yes

Maximum Average Deviation = 5.0000 ppm

Keep Molecules with Number of CNMR Shifts Less than in Query = No

Minimum Possible Tolerance for All Atoms (no less than) = 20.00

Maximum Possible Tolerance for All Atoms (no more than) = 20.00

Process subspectra search in C:\ACD12\FULLSTR.CFR

0 structure(s) have been found by NMR spectra and added to Generated Molecules

Process subspectra search in C:\USERS\CHE632\DESKTOP\PUBCHEM FILES\PUBCHEM_2007_01_02.SED

0 structure(s) have been found by NMR spectra and added to Generated Molecules

Finish: Search Molecules by 13C NMR 07/11/2014 17:18:40

Start: Create MCDs for Correlation Spectroscopy Based Generator 07/10/2014 13:50:35

Options:

Clear Existing MCDs = Yes

Minimum CNMR Assignment Error = 1.50

Set Atom Properties From CNMR Data = Yes

Set Atom Properties From HNMR Data = Yes

Allow SPQ Carbons = Yes

1 MCD has been created from MF: C14H20O5N2

Finish: Create MCDs for Correlation Spectroscopy Based Generator 07/10/2014 13:50:35

Start: Check MCDs 07/11/2014 17:15:04

Check MCDs options:

Delete "Bad" MCDs from List A = Yes

Automatically Resolve Contradictions = Yes

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Structure Elucidation Report for "PD49_WB_H1C_11July2014" (Page 12)

Allow Bonds between Heteroatoms = Yes

Allow Bonds between Heteroatoms of the Same Atom Type = Yes

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

Check MCD #1 (ID = 0)

Stage 1

Visible non-standard connectivities were not detected.

Stage 2

Atoms with non-standard connectivities were not detected.

Stage 3

Contradictions in 2D NMR data were not detected.

Evident bonds were not detected during analysis of existing correlations.

Check MCD #1 (ID = 0) passed all tests

Finish: Check MCDs 07/11/2014 17:15:04

Start: Structure Generation 07/11/2014 17:18:41

Correlation Spectroscopy Based Structure Generator options:

Keep Generated Molecules = Yes

Clear Generated Molecules List Before Generation = Yes

Add Structures Already Existing in Generated Molecules List = No

Transfer Spectra to Generated Structures = Yes

Use Assignment when Removing Duplicates = Yes

Allow Filter during Generation = Yes

Use Only 1000 First MCD(s)

Allow "Fuzzy" Generation = Yes

"Fuzzy" Generation Options were Determined Automatically

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Allow Bonds between Heteroatoms = No

Allow Bonds between Heteroatoms of the Same Atom Type = No

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

MCD #1 (ID = 0): (25/0) structures have been generated.

674 molecule(s) have been generated by Correlation Spectroscopy Based Generator and 25 molecule(s) have been stored.

Generation time: 1 s

No (from No) correlation(s) have been extended during generation

Finish: Structure Generation 07/11/2014 17:19:20

Start: Structure Generation 07/11/2014 17:19:53

Structure Elucidation Report for "PD49_WB_H1C_11July2014" (Page 13)

Correlation Spectroscopy Based Structure Generator options:

Keep Generated Molecules = Yes

Clear Generated Molecules List Before Generation = No

Add Structures Already Existing in Generated Molecules List = No

Transfer Spectra to Generated Structures = Yes

Use Assignment when Removing Duplicates = Yes

Allow Filter during Generation = Yes

Use Only 1000 First MCD(s)

Allow "Fuzzy" Generation = Yes

"Fuzzy" Generation Options were Determined Automatically

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Allow Bonds between Heteroatoms = Yes

Allow Bonds between Heteroatoms of the Same Atom Type = Yes

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

MCD #1 (ID = 1): (192/0) structures have been generated.

1337286 molecule(s) have been generated by Correlation Spectroscopy Based Generator and 192 molecule(s) have been stored.

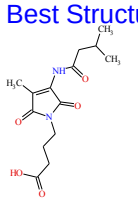
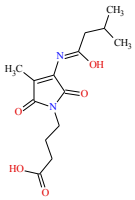
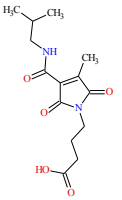
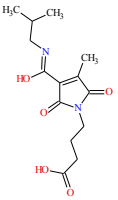
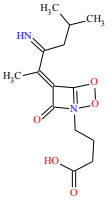
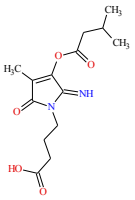
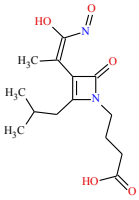
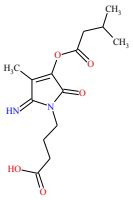
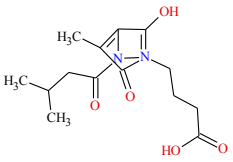
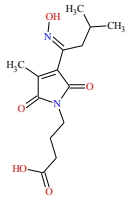
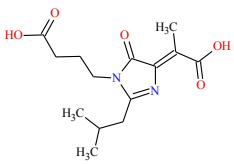
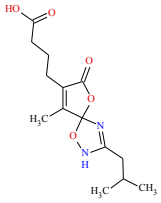
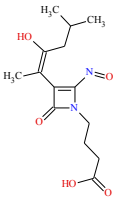
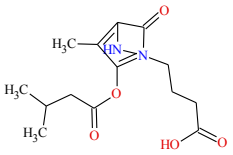
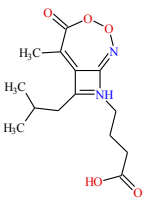
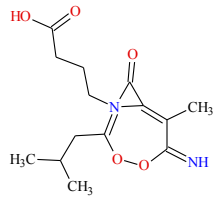
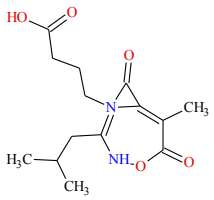
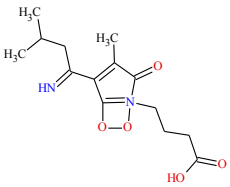
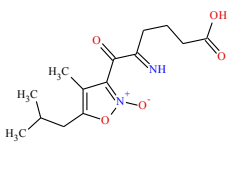
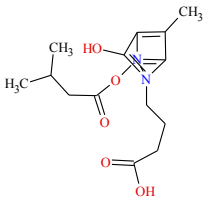
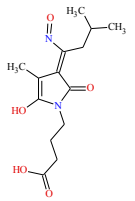
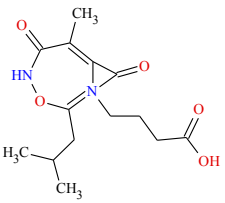
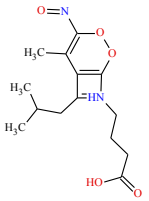
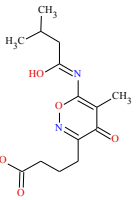
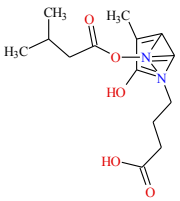
1 (ID:4) The Best Structure 	2 (ID:3) 	3 (ID:33) 	4 (ID:27) 	5 (ID:80) 
$d_A(^{13}C)$: 1.918 (v.12.01) $d_N(^{13}C)$: 2.076 $d_I(^{13}C)$: 2.235	$d_A(^{13}C)$: 3.102 (v.12.01) $d_N(^{13}C)$: 2.890 $d_I(^{13}C)$: 2.227	$d_A(^{13}C)$: 3.004 (v.12.01) $d_N(^{13}C)$: 3.207 $d_I(^{13}C)$: 2.709	$d_A(^{13}C)$: 3.663 (v.12.01) $d_N(^{13}C)$: 3.241 $d_I(^{13}C)$: 2.629	$d_A(^{13}C)$: 9.165 (v.12.01) $d_N(^{13}C)$: 3.345 $d_I(^{13}C)$: 4.390
6 (ID:16) 	7 (ID:21) 	8 (ID:6) 	9 (ID:67) 	10 (ID:1) 
$d_A(^{13}C)$: 4.800 (v.12.01) $d_N(^{13}C)$: 3.377 $d_I(^{13}C)$: 4.121	$d_A(^{13}C)$: 4.545 (v.12.01) $d_N(^{13}C)$: 3.470 $d_I(^{13}C)$: 3.879	$d_A(^{13}C)$: 2.951 (v.12.01) $d_N(^{13}C)$: 3.598 $d_I(^{13}C)$: 3.736	$d_A(^{13}C)$: 7.917 (v.12.01) $d_N(^{13}C)$: 3.702 $d_I(^{13}C)$: 3.913	$d_A(^{13}C)$: 5.039 (v.12.01) $d_N(^{13}C)$: 3.792 $d_I(^{13}C)$: 3.844
11 (ID:5) 	12 (ID:43) 	13 (ID:22) 	14 (ID:51) 	15 (ID:47) 
$d_A(^{13}C)$: 3.907 (v.12.01) $d_N(^{13}C)$: 3.915 $d_I(^{13}C)$: 3.028	$d_A(^{13}C)$: 3.896 (v.12.01) $d_N(^{13}C)$: 4.106 $d_I(^{13}C)$: 3.988	$d_A(^{13}C)$: 7.371 (v.12.01) $d_N(^{13}C)$: 4.148 $d_I(^{13}C)$: 3.578	$d_A(^{13}C)$: 7.903 (v.12.01) $d_N(^{13}C)$: 4.200 $d_I(^{13}C)$: 4.311	$d_A(^{13}C)$: $d_N(^{13}C)$: 4.302 $d_I(^{13}C)$: 3.460
16 (ID:70) 	17 (ID:57) 	18 (ID:61) 	19 (ID:76) 	20 (ID:166) 
$d_A(^{13}C)$: 7.166 (v.12.01) $d_N(^{13}C)$: 4.426 $d_I(^{13}C)$: 2.800	$d_A(^{13}C)$: 6.186 (v.12.01) $d_N(^{13}C)$: 4.434 $d_I(^{13}C)$: 3.158	$d_A(^{13}C)$: 7.515 (v.12.01) $d_N(^{13}C)$: 4.453 $d_I(^{13}C)$: 3.881	$d_A(^{13}C)$: 5.085 (v.12.01) $d_N(^{13}C)$: 4.645 $d_I(^{13}C)$: 3.684	$d_A(^{13}C)$: 4.733 (v.12.01) $d_N(^{13}C)$: 4.685 $d_I(^{13}C)$: 4.119
21 (ID:23) 	22 (ID:92) 	23 (ID:117) 	24 (ID:17) 	25 (ID:135) 
$d_A(^{13}C)$: 5.150 (v.12.01) $d_N(^{13}C)$: 4.715 $d_I(^{13}C)$: 3.280	$d_A(^{13}C)$: 5.284 (v.12.01) $d_N(^{13}C)$: 4.846 $d_I(^{13}C)$: 2.929	$d_A(^{13}C)$: $d_N(^{13}C)$: 4.905 $d_I(^{13}C)$: 3.870	$d_A(^{13}C)$: 4.605 (v.12.01) $d_N(^{13}C)$: 4.981 $d_I(^{13}C)$: 3.569	$d_A(^{13}C)$: 4.720 (v.12.01) $d_N(^{13}C)$: 4.983 $d_I(^{13}C)$: 3.866

Figure S38. The top 25 calculated structures for legonmaleimide A (**1**); the correct structure is placed at the number 1 position.

25/Oct/2016 09:36:26 GB_2_re_1(299)_2D.gnr - Generated Molecules Page: 1(4)

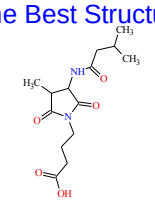
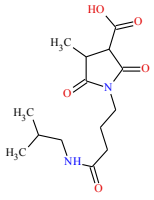
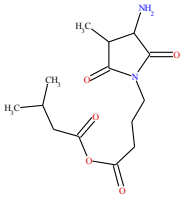
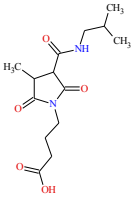
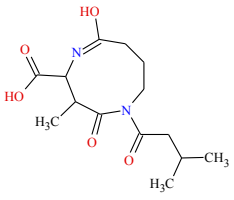
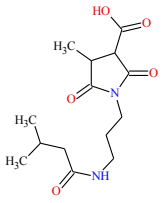
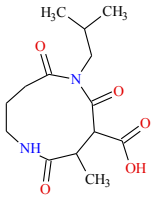
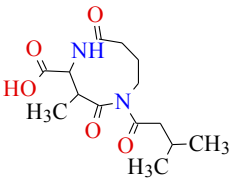
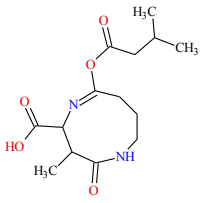
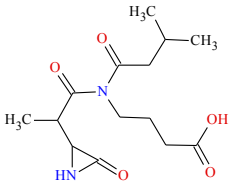
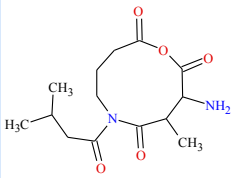
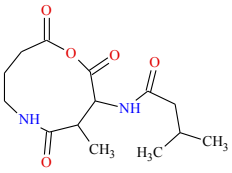
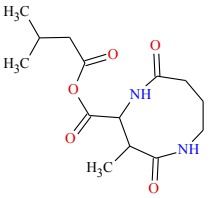
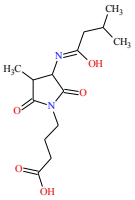
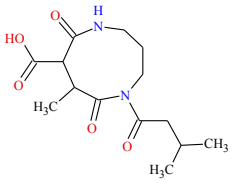
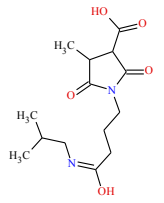
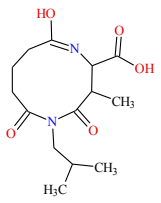
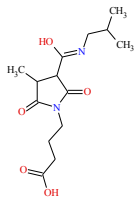
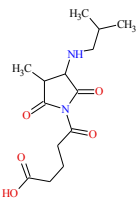
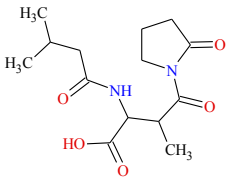
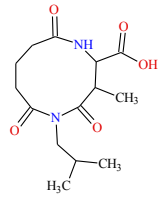
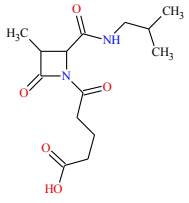
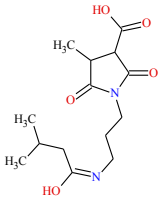
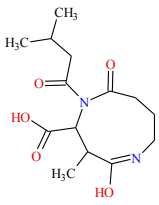
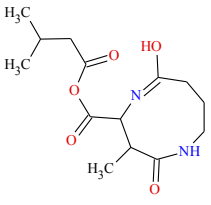
1 (ID:52) The Best Structure 	2 (ID:244) 	3 (ID:94) 	4 (ID:246) 	5 (ID:35) 
$d_A(^{13}C)$: 1.651 (v.14.00) $d_N(^{13}C)$: 1.742 $d_I(^{13}C)$: 1.394	$d_A(^{13}C)$: 2.066 (v.14.00) $d_N(^{13}C)$: 2.446 $d_I(^{13}C)$: 2.120	$d_A(^{13}C)$: 2.141 (v.14.00) $d_N(^{13}C)$: 2.414 $d_I(^{13}C)$: 2.437	$d_A(^{13}C)$: 2.210 (v.14.00) $d_N(^{13}C)$: 2.291 $d_I(^{13}C)$: 2.261	$d_A(^{13}C)$: 2.454 (v.14.00) $d_N(^{13}C)$: 2.925 $d_I(^{13}C)$: 2.834
6 (ID:33) 	7 (ID:232) 	8 (ID:36) 	9 (ID:92) 	10 (ID:40) 
$d_A(^{13}C)$: 2.489 (v.14.00) $d_N(^{13}C)$: 2.640 $d_I(^{13}C)$: 2.489	$d_A(^{13}C)$: 2.536 (v.14.00) $d_N(^{13}C)$: 2.455 $d_I(^{13}C)$: 3.013	$d_A(^{13}C)$: 2.582 (v.14.00) $d_N(^{13}C)$: 1.996 $d_I(^{13}C)$: 2.647	$d_A(^{13}C)$: 2.759 (v.14.00) $d_N(^{13}C)$: 3.863 $d_I(^{13}C)$: 3.278	$d_A(^{13}C)$: 2.764 (v.14.00) $d_N(^{13}C)$: 3.407 $d_I(^{13}C)$: 3.885
11 (ID:37) 	12 (ID:58) 	13 (ID:97) 	14 (ID:8) 	15 (ID:137) 
$d_A(^{13}C)$: 2.852 (v.14.00) $d_N(^{13}C)$: 2.889 $d_I(^{13}C)$: 3.313	$d_A(^{13}C)$: 2.859 (v.14.00) $d_N(^{13}C)$: 2.940 $d_I(^{13}C)$: 3.234	$d_A(^{13}C)$: 2.885 (v.14.00) $d_N(^{13}C)$: 3.047 $d_I(^{13}C)$: 3.350	$d_A(^{13}C)$: 2.919 (v.14.00) $d_N(^{13}C)$: 2.295 $d_I(^{13}C)$: 2.481	$d_A(^{13}C)$: 2.930 (v.14.00) $d_N(^{13}C)$: 2.723 $d_I(^{13}C)$: 3.705
16 (ID:218) 	17 (ID:274) 	18 (ID:225) 	19 (ID:214) 	20 (ID:60) 
$d_A(^{13}C)$: 2.955 (v.14.00) $d_N(^{13}C)$: 3.543 $d_I(^{13}C)$: 2.656	$d_A(^{13}C)$: 2.981 (v.14.00) $d_N(^{13}C)$: 2.712 $d_I(^{13}C)$: 3.063	$d_A(^{13}C)$: 2.990 (v.14.00) $d_N(^{13}C)$: 2.875 $d_I(^{13}C)$: 2.639	$d_A(^{13}C)$: 3.035 (v.14.00) $d_N(^{13}C)$: 3.318 $d_I(^{13}C)$: 3.458	$d_A(^{13}C)$: 3.044 (v.14.00) $d_N(^{13}C)$: 2.613 $d_I(^{13}C)$: 2.886
21 (ID:275) 	22 (ID:254) 	23 (ID:2) 	24 (ID:47) 	25 (ID:96) 
$d_A(^{13}C)$: 3.064 (v.14.00) $d_N(^{13}C)$: 2.422 $d_I(^{13}C)$: 3.015	$d_A(^{13}C)$: 3.093 (v.14.00) $d_N(^{13}C)$: 4.014 $d_I(^{13}C)$: 3.774	$d_A(^{13}C)$: 3.150 (v.14.00) $d_N(^{13}C)$: 3.813 $d_I(^{13}C)$: 3.292	$d_A(^{13}C)$: 3.198 (v.14.00) $d_N(^{13}C)$: 3.218 $d_I(^{13}C)$: 3.298	$d_A(^{13}C)$: 3.220 (v.14.00) $d_N(^{13}C)$: 4.052 $d_I(^{13}C)$: 3.821

Figure S39. The top 25 calculated structures for legonmaleimide B (**2**); the correct structure is placed at the number 1 position.

Structure Elucidation Report for "GB_2_re_1(299)_2D"

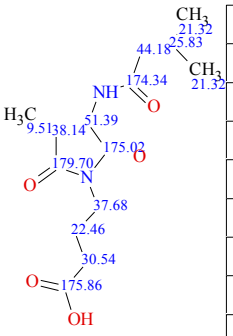
Initial Data

Composition Restrictions:
Molecular Weight = 0.000-1000.000
Double Bonds Equivalent = 0.00-100.00
Allowed Composition = C(0-100) H(0-100) O(0-20) N(0-10)
Molecular Formula = C14H22O5N2

Spectral Data:
standard 1H - 11 peaks
standard 1H (merged) - 11 peaks
standard 13C (merged) - 13 peaks
COSY 1H-1H - 5 peaks
HSQC-DEPT 13C-1H - 9 peaks
HMBC 13C-1H - 21 peaks

Most Probable Structure

Following structure has been placed to the first position after spectra calculation



Carbon Assignment

#	ID	N	Shift (ppm)	Conf. Limit (ppm)	Difference (ppm)	Atoms	XHn
1	1	1	9.515	0.000		1	CH3(q)
2	2	2,3	21.320	0.000		2	CH3(q)
3	3	4	22.457	0.000		1	CH2(t)
4	4	8	25.828	0.000		1	CH(d)
5	5	5	30.537	0.000		1	CH2(t)
6	6	6	37.685	0.000		1	CH2(t)
7	7	9	38.143	0.000		1	CH(d)
8	8	7	44.177	0.000		1	CH2(t)
9	9	10	51.392	0.000		1	CH(d)
10	10	11	174.337	0.000		1	C(s)
11	11	12	175.021	0.000		1	C(s)
12	12	13	175.856	0.000		1	C(s)

S40. Elucidation protocol for legonmaleimide B (2)

Start: Structure Generation 10/09/2016 20:48:48

Correlation Spectroscopy Based Structure Generator options:

Keep Generated Molecules = Yes

Structure Elucidation Report for "GB_2_re_1(299)_2D" (Page 10)

Clear Generated Molecules List Before Generation = No

Add Structures Already Existing in Generated Molecules List = No

Transfer Spectra to Generated Structures = Yes

Use Assignment when Removing Duplicates = Yes

Allow Filter during Generation = Yes

Use Only 1000 First MCD(s)

Allow "Fuzzy" Generation = Yes

"Fuzzy" Generation Options were Determined Automatically

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Allow Bonds between Heteroatoms = No

Allow Bonds between Heteroatoms of the Same Atom Type = No

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

MCD #1 (ID = 0): (0/0) structures have been generated.

1969 molecule(s) have been generated by Correlation Spectroscopy Based Generator and No molecule(s) have been stored.

Generation time: 6 m 17 s (Check: 0 s, Generation: 6 m 17 s 377 ms)

No (from No) connectivities have been extended during generation

1 (from 1 possible) connectivity combination(s) have been used during generation

Generation has been interrupted by the user (stop button pressed)

Finish: Structure Generation 10/09/2016 20:55:06

Start: Structure Generation 10/09/2016 21:02:04

Correlation Spectroscopy Based Structure Generator options:

Keep Generated Molecules = Yes

Clear Generated Molecules List Before Generation = No

Add Structures Already Existing in Generated Molecules List = No

Transfer Spectra to Generated Structures = Yes

Use Assignment when Removing Duplicates = Yes

Allow Filter during Generation = Yes

Use Only 1000 First MCD(s)

Allow "Fuzzy" Generation = Yes

"Fuzzy" Generation Options were Determined Automatically

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Allow Bonds between Heteroatoms = No

Allow Bonds between Heteroatoms of the Same Atom Type = No

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

MCD #1 (ID = 0): data not valid: unable to connect one or more atoms correctly.

46189 molecule(s) have been generated by Correlation Spectroscopy Based Generator and 350 molecule(s) have been stored.

Generation time: 44 s (Check: 0 s, Generation: 43 s 941 ms)

No (from No) connectivities have been extended during generation

1 (from 1 possible) connectivity combination(s) have been used during generation

Finish: Structure Generation 10/09/2016 21:02:48

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	321.3	3728981	0.954	321.142	17.859		[M+Na]+
2	445.3	4202917	0.968	445.204	18.125		[M+Na]+
3	338.3	32340330	0.994	338.196	18.582		[M+H]+
4	460.3	64137156	0.993	460.139	22.564		[M+H]+
5	271.3	462376128	0.993	271.06	22.85		[M+H]+
6	426.3	13229663	0.992	426.262	27.685		[M+H]+
7	486.3	27654190	0.992	486.187	19.304		[M+H]+
8	390.3	13408041	0.992	390.227	21.372		[M+H]+
9	217.3	27887876	0.991	217.097	14.469		[M+H]+
10	257.3	6830104	0.907	257.081	20.884		[M+H]+
11	411.3	949052	0.815	411.237	25.867		[M+H]+
12	277.3	13402048	0.922	277.155	16.729		[M+H]+
13	230.3	2202308	0.924	230.103	15.186		[M+H]+
14	269.3	1806551	0.927	269.087	3.133	1-Methoxy-4-methyl-9-carboxyphenazine, 6-Methoxy-1-phenazinecarboxylic acid, Coaristeromycin, Formycin B, Mansouramycin F, Saphenic acid	[M+H]+
15	325.3	17990222	0.989	325.113	2.813		[M+H]+
16	387.3	17453862	0.987	387.201	14.272		[M+H]+
17	372.3	15235486	0.987	372.144	15.48		[M+H]+
18	265.3	666870336	0.986	265.155	15.01	Legonindolizidine A	[M+H]+
19	442.3	8372159	0.985	442.257	24.947		[M+H]+
20	251.3	23249162	0.985	251.139	13.417		[M+H]+
21	454.3	52479824	0.994	454.292	31.988		[M+H]+
22	459.3	5819877	0.985	459.26	22.273		[M+H]+
23	466.3	2164481	0.952	466.292	30.523		[M+H]+
24	314.3	31123488	0.985	314.172	21.887		[M+H]+
25	295.3	38707048	0.954	295.129	21.961		[M+H]+
26	457.3	9983812	0.984	457.182	15.284		[M+H]+
27	252.3	13525779	0.984	252.159	16.707		[M+H]+
28	285.3	289782912	0.984	285.076	20.4		[M+H]+
29	323.3	5143267	0.965	323.161	25.817		[M+H]+
30	327.3	52088928	0.966	327.192	22.297		[M+H]+
31	313.3	36953640	0.967	313.176	20.616		[M+H]+
32	336.3	2705643	0.967	336.254	19.255		[M+H]+
33	317.3	6763599	0.982	317.15	16.561		[M+H]+
34	268.3	50435632	0.92	268.105	9.458	Adenine 9-beta-D-arabinofuranoside, Thiotetronic acid Tue 3010	[M+H]+
35	468.3	7786411	0.982	468.307	34.335		[M+H]+
36	469.3	6593327	0.969	469.244	25.242		[M+H]+
37	472.3	3502347	0.971	472.142	15.75		[M+H]+
38	423.3	3255521	0.973	423.223	18.125		[M+H]+
39	307.3	13140904	0.981	307.165	26.457		[M+H]+

40	474.3	3226835	0.974	474.154	20.566		[M+H]+
41	356.3	10026267	0.98	356.218	19.496		[M+H]+
42	279.3	319631552	0.975	279.171	17.094		[M+H]+
43	471.3	9176723	0.979	471.258	26.85		[M+H]+
44	371.3	6670929	0.977	371.207	16.443		[M+H]+
45	261.3	10195519	0.907	261.145	13.005		[M+H]+
46	225.3	18144454	0.931	225.149	24.849		[M+H]+
47	297.3	43435116	0.936	297.181	17.452	MF-EA-705beta	[M+H]+
48	205.3	9562740	0.887	205.097	12.98		[M+H]+
49	364.3	17682340	0.883	364.212	19.791		[M+H]+
50	299.3	60761380	0.976	299.16	17.859		[M+H]+
51	400.3	2489691	0.941	400.117	27.319		[M+H]+
52	333.3	5771471	0.944	333.145	19.594		[M+H]+
53	448.3	986932	0.872	448.139	18.484		[M+H]+
54	209.3	12040259	0.975	209.154	13.862		[M+H]+
55	352.3	4798501	0.948	352.162	12.855		[M+H]+
56	255.3	769025216	0.973	255.065	20.253		[M+H]+
57	456.3	26498896	0.984	456.271	26.334		[M+H]+
58	348.3	3194837	0.956	348.217	23.276		[M+H]+
59	263.3	23047560	0.841	263.139	19.914		[M+H]+
60	463.3	720182	0.793	463.228	15.43		[M+H]+
61	303.3	2563504	0.961	303.134	13.515		[M+H]+
62	296.3	23376990	0.969	296.135	11.91		[M+H]+
63	267.3	3600139	0.815	267.134	17.547		[M+H]+
64	470.3	5656044	0.982	470.288	28.324		[M+H]+
65	377.3	3029205	0.967	377.146	14.149		[M+H]+
66	494.3	1608874	0.947	494.261	12.365		[M+H]+
67	424.3	1947217	0.949	424.248	21.689		[M+H]+
68	311.3	170800032	0.961	311.16	24.463		[M+H]+
69	484.3	626532	0.825	484.304	30.146		[M+H]+
70	289.3	2209353	0.937	289.119	13.319		[M+H]+
71	440.3	44614300	0.989	440.249	18.125		[M+H+NH3]+

Table S41. Compound masses in water-butanol fraction of *Streptomyces albus, ΔlgnC* after data processing and dereplication using StrepDB. The known compounds are nos.: 14, 18, 34, and 47. All masses with 'no labels' indicate that they were not found in StrepDB and are potentially new.

Table of Components

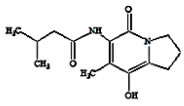
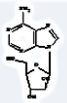
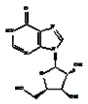
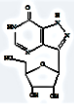
No.	tR(min)	Mass(Ao)	[M+H]+	M+.	MF	Structure	Name	MS Match
1	15.010	264.147	265.155	264.147	$C_{14}H_{20}N_2O_3$		Legonindolizidine A	Excellent
2	9.458	267.097	268.104	267.096	$C_{10}H_{13}N_5O_4$		Adenine 9-beta-D-arabinofuranoside	Excellent
3	3.133	268.081	269.088	268.080	$C_{10}H_{12}N_4O_5$		Coaristeromycin	Good
4	3.133	268.081	269.088	268.080	$C_{10}H_{12}N_4O_5$		Formycin B	Good

Table S42. Some structures of annotated compounds in Table S41 (Water-butanol fraction of *Streptomyces albus, ΔlgnC.* Legonindolizidine A is a known compound having being isolated and characterised previously from this strain.

S43. Optimised IntelliXtract algorithm preprocessing settings used for LCMS data processing.

[12C/13C Error (%)]

Value=10

[Ionization]

Type=Auto

[Polarity]

Auto=True

Positive=True

[Mass Accuracy]

Units=Da

Value=0.5

MC Display (Da)=0.5

MC Calculation (Da)=1

m/z Values=Averaged

Mass Unity Range Shift=0.3

[CODA]

Apply=True

Peak Minimum FWHM=Scans

Value=2

Peak Minimum Height (% of max)=0

Peak S/N Threshold=50

Peak Area Threshold (counts)=100

Pick the Number of Most Abundant Peaks=False

Number of Peaks=1

Apply Smoothing=False

Method=Savitsky-Golay

Shape of FFT=Fix

Fix V1(%)=5

Fix V2(%)=50

Polynomial=1

Points=3

Enhancement=True

Baseline Correction=False

Box Half Width (Scans)=5

Noise Factor=5

MCQ Value=1

Abundance Value (% of TIC)=0

[Components Analysis]

Apply=True

Default Peak Width=0.05

Default Peak Function=Gauss

Lorentz Fraction=1

Vary position within=0.1

Max width limit=10

Min width limit=0.001

Tolerance=3

Max number of iteration=150

Lock Width=True

Lock Height=True

Fixed Width=False

Parameter=0.05

Max Number of Peaks per MC=15

Max Number of Co-eluted Peaks per Region=15

[Missing Isotopes Search]

Apply=True

Good=True

Poor=True

Review=True

Depth of Analysis=3

[Area Threshold Analysis]

Apply=True

Tangent Slope=0.05

[FWHM Threshold Analysis]

Apply=False

Tangent Slope=0.05

[Height Threshold Analysis]

Apply=False

Tangent Slope=0.05

[Search for Adducts]

Proton=1

Ammonia=1

Sodium=1

Potassium=1

Acetonitrile=0

Methanol=0

H2O=0

Lithium=0

Acetate=0

Formate=0

TFA=0

[Search for Multimers]

Proton=2

Ammonia=0

Sodium=1

Potassium=0

Acetonitrile=0

Methanol=0

H2O=0

Lithium=0

Acetate=2

Formate=2

TFA=2

[A + 2]

Percent=30

Abundance Ratio Error (%)=50

Sulfur=True

Sulfur Min=0

Sulfur Max=3

Chlorine=True

Chlorine Min=0

Chlorine Max=3

Bromine=True

Bromine Min=0

Bromine Max=3

[M Ion Error (%)]

Value=20

[Additional M Ion Correction (%)]

Value=5

[Compare Options]

tR Window (min)=0

Abundance=Area

Abundance Ratio=5:1

Isotope Cluster Tolerance=True

Centre of Gravity (%)=50

Cluster Dispersion (%)=50

Boolean Comparison=False

[Keep the following Peaks only]

Notated as Molecular Ions=True

Peaks with other textual descriptors=True

Classified as Good=True

Classified as Review=True

Classified as Poor=True

[Apply Ion Presence Detection for]

Apply=True

Molecular Ions=True

Adduct Ions=True

Primary Fragment Ions=True

Multimer Ions=False

Unconfirmed 12C Ions=True

Unconfirmed 13C Ions=False

Unassigned Ions=True

Label Parent Ion Modifications=False

[Apply Ion Presence Detection Threshold]

Apply=True

Abundance Type=Height

Abundance Units=%

Value=1

[Apply Ion Presence Detection 12C/13C Filter]

Apply=False

12C/13C (Pass)=True

12C/13C (Fail)=False

12C/13C (None)=False

[Label Possible Metabolites]

Apply=False

[Peak Quality Analysis]

W (Area)=20

W (Height)=20

W (Asymmetry)=10

W (S/N)=0

W (Carbon)=20

W (12C/13C)=20

W (Class)=10

W (Uniqueness)=0

[Calculate the Following Mass Values]

Peak Top=True

Peak Top Window Type=% of Peak FWHM

Peak Top Window Value=100

Left Shoulder=False

Exclude the First Scan=True

Right Shoulder=False

Exclude the Last Scan=True

Entire Peak=False

Exclude the First and Last Scans=True

Apply Intensity Based Weighting=True

[Data Analysis Region]

Full=False

Start tR=2

End tR=30

[Structure Search]

Apply=False

Mass Values=Accurate

Mass Accuracy=0.0005

Type of Mass=Peak Top

Molecular Ions=True

12C Ions=False

Unassigned Ions=False

Directory=

Label (User Data field)=

12C/13C (Pass)=True

12C/13C (Fail)=True

12C/13C (None)=True

[Auto Neutral Loss Determination]

Apply=False

Display Accuracy (Decimal Places)=2

[Convert Profile to Centroid]

Apply=True

Mass Values to Center=Top

Abundance to Center=Area

Peak Picking Minimum FWHM (Points)=3

Abundance Threshold (%)=1

Centroid %=80

Apply Smoothing=True

Polynomial=1

Window Width (Points)=3

[Component MC Summing]

Apply=False

[S/N Calculation]

Parameter=Scans

Scans=50

tR=0.1

[Mass Accuracy for Peak Labeling]

Type of Mass=Peak Top

Mass Accuracy=0.005

[HRMS Data Processing Approach]

Apply=False

Type of Mass=Peak Top

Mass Value Window (Da, +/-)=0.005

[Extract Pure Component Spectra]

Apply=True

Extract Selected Components Only=True

Directory=

File Name=

Action if File Name Exists=AutoName

[Peak Quality Threshold]

Apply=False

Value=1

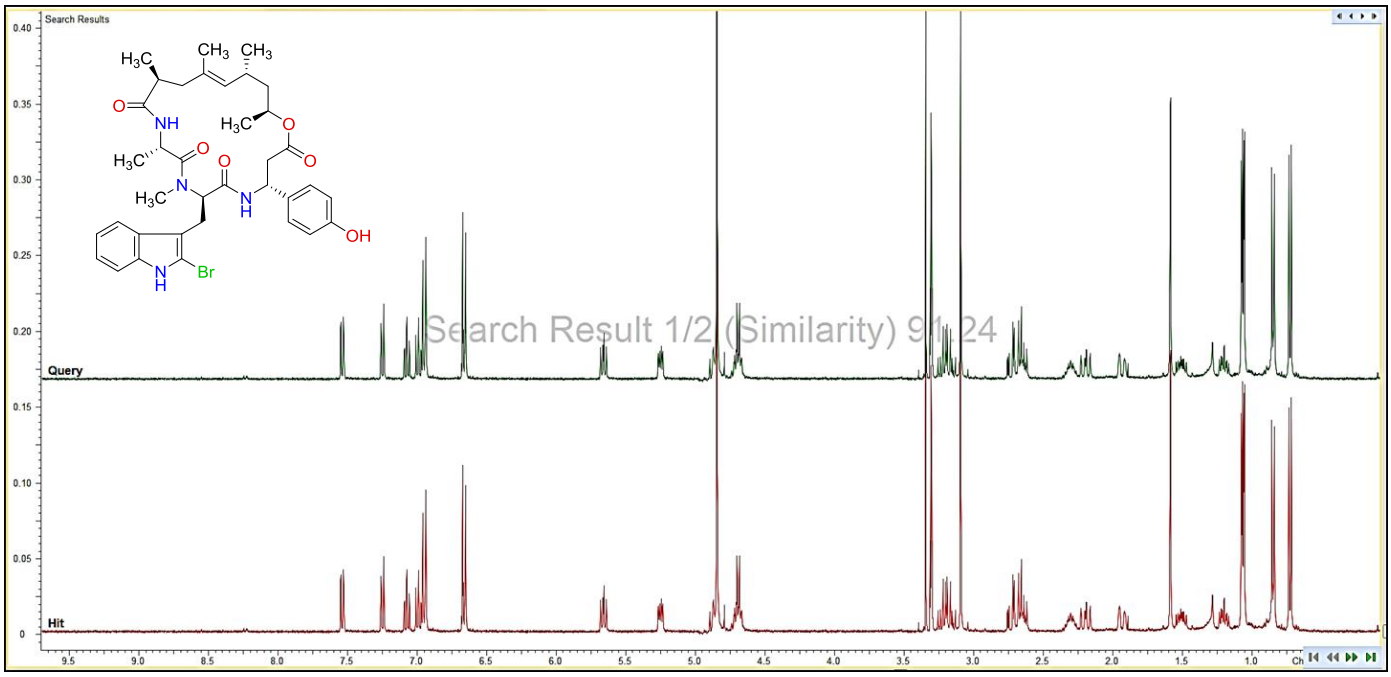


Figure S44. MbcDB dereplication using ^{1}H NMR spectrum. The query and hit compound is shown (jasplakinolide).

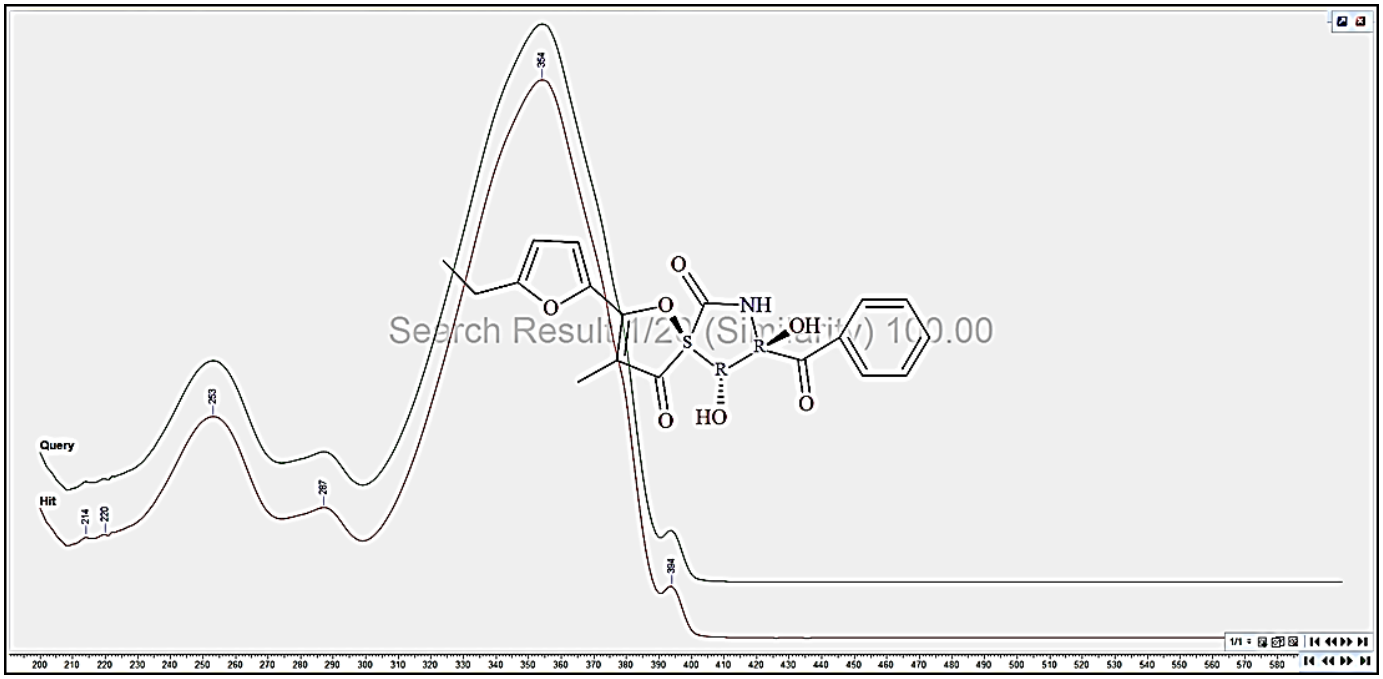


Figure S45. MbcDB dereplication using UV/Vis spectrum. The query and hit compound is shown (azaspirofuran B).

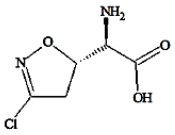
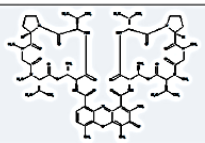
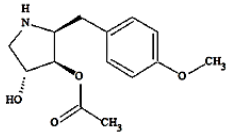
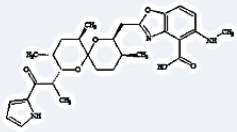
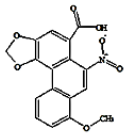
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
1	178.0145	C5H7ClN2O3		Acivicin	-	-
2	1254.6285	C62H86N12O16		Actinomycin D	-	-
3	265.1314	C14H19NO4		Anisomycin	-	-
4	523.2682	C29H37N3O6		Antibiotic A-23187	-	-
5	341.0536	C17H11NO7		Aristolochic acid A	-	-

Figure S46. Both t_R and t_R window (t_R range) are not used. During screening of StrepDB neither t_R nor t_R window is used. It means that screening of StrepDB is performed via HRMS data only.

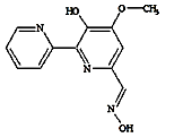
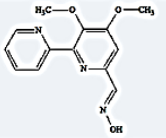
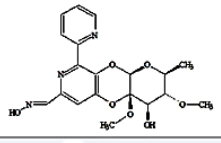
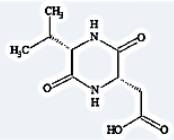
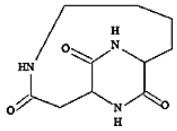
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
823	245.08	C12H11N3O3		Caerulomycin-B	6.38	-
824	259.0957	C13H13N3O3		Caerulomycin-C	11.3	-
825	403.138	C19H21N3O7		Caerulomycin-D	5.33	-
826	214.0954	C9H14N2O4		Cairomycin A	1.69	-
827	225.1113	C10H15N3O3		Cairomycin B	1.87	-

Figure S47. StrepDB with t_R, t_R window (t_R range) not used.

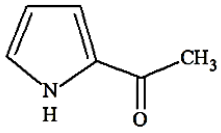
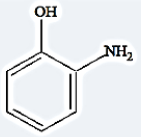
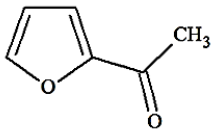
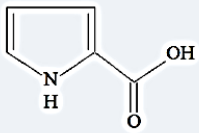
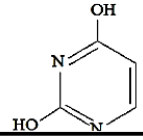
Referenc...	Formula	Structure	Label	tR (Min)	tR Window
109.0528	C6H7NO		2-Acetyl pyrrole	2.4	1.5
109.0528	C6H7NO		Questiomycin B	1.6	1.5
110.0368	C6H6O2		2-Acetylfurane	5.8	1.5
111.032	C5H5NO2		Pyrrole-2-carboxylic acid	1.7	1.5
112.0273	C4H4N2O2		Ozemycin-B	1.1	1.5

Figure S48. StrepDB with t_R window (t_R range) set at 1.5 min.

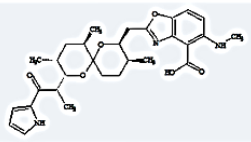
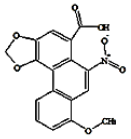
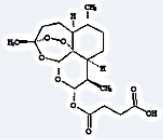
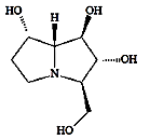
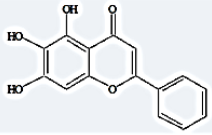
No.	Reference M...	Formula	Structure	Label	tR (Min)	tR Window
4	523.2682	C29H37N3O6		Antibiotic A-23187	18.8	2.0
5	341.0536	C17H11NO7		Aristolochic acid A	13.2	2.0
6	384.1784	C19H28O8		Artesunate	12.3	2.0
7	189.1001	C8H15NO4		Australine-HCl	1.1	2.0
8	270.0528	C15H10O5		Baicalein	9.7	2.0

Figure S49. StrepDB with t_R window (t_R range) set to 2.0 min.

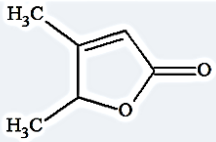
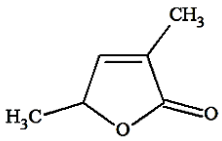
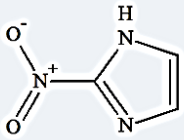
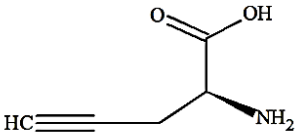
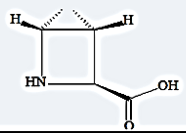
Referenc...	Formula	Structure	Label	tR (Min)	tR Window
112.0524	C6H8O2		Dihydro-dimethylfuranone, struct. b	6.4	2.5
112.0524	C6H8O2		3,5-Dimethyl-3-oxol-2-on	5.1	2.5
113.0225	C3H3N3O2		Dihydrotanshinone	15.0	2.5
113.0477	C5H7NO2		Propargylglycine	2.1	2.5
113.0477	C5H7NO2		SF-1836	1.1	2.5

Figure S50. StrepDB with t_R window (t_R range) set to 2.5 min.

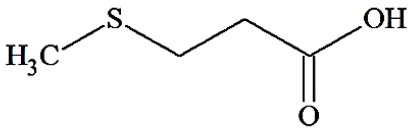
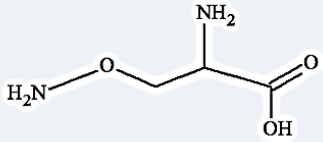
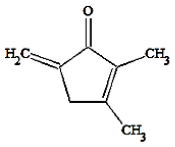
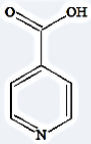
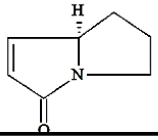
Referenc...	Formula	Structure	Label	tR (Min)	tR Window
120.0245	C4H8O2S		beta-Methylthiopropionic acid	5.56	3.0
120.0535	C3H8N2O3		beta-Aminoxy-D-alanine	1.48	3.0
122.0732	C8H10O		Methylenomycin-B	6.69	3.0
123.032	C6H5NO2		4-Pyridincarboxylic acid	1.08	3.0
123.0684	C7H9NO		Pyrrolam A	1.66	3.0

Figure S51. StrepDB with t_R window (t_R range) set to 3.0 min.

Retention time window(min)	% compounds annotated	% annotated compounds removed (false hits)
Not used	100	0
0	0	100
1.5	10.1	89.9
2.0	13.3	86.7
2.5	17.8	82.2
3.0	26.4	73.6
4.0	31.2	68.8

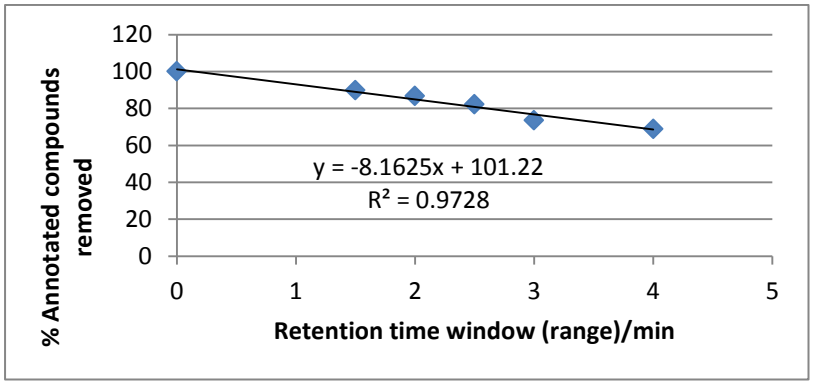


Table S52, Figure S52. Relationship between compounds annotated by StrepDB as a function of retention time, and retention time window (range) used. When retention time and retention time range are not used, it means that StrepDB uses only the HRMS data as a source of compound annotation giving rise to the high number of hits.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label
1	261.3	35488172	0.973	261.124	6.91	cis-Cyclo(tyrosylprolyl), cyclo-(N-Me-Tyr,dehydroAbu), trans-Cyclo(3S-Tyr,8aR-Pro)
2	167.091	37078652	0.968	167.082	9.874	beta-(2-Pyridyl)-L-a-alanine
3	167.3	8620099	0.968	167.082	11.806	beta-(2-Pyridyl)-L-a-alanine
4	213.092	879180	0.893	213.113	12.042	Xanthocidin
5	175.07	5152774	0.964	175.087	8.335	WAP-5044-C
6	507.3	20270028	0.981	507.329	19.947	WA-3854-C
7	879.3	2.02E+08	0.949	879.456	16.863	Viridogrisein I
8	513.3	4206690	0.939	513.177	18.612	Virenomycin M
9	779.3	2284288	0.966	779.406	11.854	Vinorelbine
10	336.202	98463864	0.979	336.161	13.925	Validoxylamine-A
11	336.3	1.02E+08	0.979	336.161	13.967	Validoxylamine-A
12	409.3	4.28E+08	0.978	409.161	15.728	Urauchimycin C
13	485.3	1.69E+08	0.981	485.188	12.918	UK-3A
14	845.3	4935550	0.879	845.442	18.658	Tunicamycin VII, Tunicamycin VIII
15	284.107	9560217	0.967	284.14	10.151	Tryptophan-dehydrobutyrine diketopiperazine; TDD, cis-Cyclo(Pro, Trp)
16	563.3	61565880	0.955	563.298	17.695	TAN-420-C
17	627.3	17212808	0.927	627.363	16.554	T-23-IX
18	840.3	1595652	0.933	840.342	16.817	Sulfurmycin A
19	178.3	4308333	0.893	178.084	8	Streptazone A, USF-142-A
20	208.3	6502358	0.96	208.096	9.652	Streptazolin
21	313.197	1.07E+08	0.981	313.145	12.369	Spatozoate
22	313.3	8.51E+08	0.981	313.144	12.918	Spatozoate
23	322.3	47889532	0.973	322.145	15.822	Salbostatin
24	325.3	19820390	0.985	325.163	16.817	SS-56A
25	134.3	10155379	0.914	134.06	8.619	SS 8215A
26	156.3	1.18E+08	0.979	156.066	12.886	SF-1836-C
27	275.3	1.48E+08	0.988	275.137	10.192	SEN-215
28	460.078	1531760	0.981	460.077	18.885	SE-212305
29	490.3	11216160	0.975	490.195	15.822	SB-203207
30	294.3	2.8E+09	0.975	294.17	12.886	S-632-A1
31	517.3	3240308	0.913	517.187	9.874	Rottlerin
32	280.3	8702635	0.946	280.133	15.178	Remerine-HCl
33	617.3	36323992	0.961	617.326	17.695	Racemomycin-O
34	769.403	748169	0.923	769.41	14.914	RPI-856-C
35	637.3	19827708	0.987	637.393	10.371	RK-397
36	138.3	69460784	0.972	138.055	12.918	Pyrrole-3-yl-2-propenoic acid, Trigonelline-HCl, p-Hydroxybenzamide
37	124.3	4.4E+08	0.98	124.076	11.083	Pyrrolam A
38	810.3	13113622	0.963	810.427	11.71	Protoveratrine B
39	547.3	3589204	0.93	547.347	7.476	Proferrioxamine-A1
40	773.3	8874215	0.971	773.361	13.783	Pluramycin-A
41	209.3	18260110	0.931	209.129	6.863	Pilocarpine

42	209.088	2886396	0.931	209.129	9.741	Pilocarpine
43	377.3	5386373	0.963	377.092	10.419	Phosmidosine C
44	269.3	28698344	0.965	269.128	10.739	Pentostatin
45	226.3	22885360	0.976	226.084	10.787	Pentopyranone
46	228.3	1.75E+08	0.981	228.099	11.176	Pentopyranine-C
47	244.3	33529344	0.971	244.092	12.992	Pentopyranin E
48	340.3	4.86E+08	0.973	340.154	14.04	Papaverine-HCl
49	131.3	35865080	0.962	131.068	10.946	Pantolactone
50	474.181	180255	0.99	474.186	4.991	OA 6129B1, OA 6129B2
51	426.193	87462568	0.977	426.189	12.334	Nisamycin
52	426.3	1.22E+08	0.977	426.188	12.66	Nisamycin
53	388.3	1.17E+08	0.966	388.173	13.59	Naphthoquinone 1
54	771.3	1685872	0.975	771.485	19.896	NK-154183A
55	263.3	20781116	0.943	263.137	9.186	N2-(2-Carboxyethyl)-3-hydroxyarginine
56	212.3	4.45E+08	0.984	212.092	12.918	N-Salicyloyl-2-aminopropan-1,3-diol
57	481.3	9351200	0.77	481.19	12.771	N-Methyl-3'-amino-3'-deoxy K-252A, Panosialin A
58	170.097	42212984	0.96	170.082	12.886	N-(5-Hydroxy-cyclohex-1-ene-2-on)-acetamide
59	170.3	33772288	0.96	170.081	12.334	N-(5-Hydroxy-cyclohex-1-ene-2-on)-acetamide
60	193.3	43969312	0.977	193.086	9.918	Myristicin
61	321.3	1.34E+08	0.979	321.13	12.771	Mycophenolic acid, Reductiline
62	797.414	15676641	0.979	797.417	11.758	Mocimycin
63	123.3	88036704	0.967	123.081	12.886	Methylenomycin-B
64	183.081	17551974	0.974	183.065	13.717	Methylenomycin-A
65	304.3	2685780	0.945	304.106	10.009	Mansouramycin D
66	249.3	13354630	0.934	249.113	14.132	Malioxamycin
67	295.3	4.7E+08	0.969	295.173	12.886	MF-EA-705a
68	573.108	1309181	0.985	573.307	19.801	Lysophosphatidyl inositol 1
69	926.3	18635972	0.985	926.42	17.93	Liposidomycin-Y-(III)
70	513.21	358732	0.939	513.356	19.522	Leptofuranin A, Reductoleptomycin-A
71	175.3	46796244	0.964	175.112	12.918	L-Theanine
72	413.3	2070989	0.912	413.101	15.091	Kinamycin B, PY1, PY3; Kinamycin E
73	318.3	7.57E+08	0.981	318.167	13.812	Kikumycin-B
74	214.3	5395557	0.922	214.107	14.515	Kainic acid, Omuralide
75	727.618	2339189	0.979	727.462	19.846	Kaimonolide A
76	727.3	1584136	0.979	727.462	19.997	Kaimonolide A
77	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin
78	222.112	1525799	0.982	222.113	8.619	Hydrocotarnine-HBr
79	164.3	14088013	0.831	164.065	8.477	Homoalanosine, L-beta-(3-Hydroxyureido)-alanine
80	276.3	3.33E+09	0.985	276.159	12.886	Homatropine-HBr
81	276.137	1.43E+08	0.985	276.159	12.261	Homatropine-HBr
82	454.3	8742493	0.968	454.156	16.817	Herbicidin-B
83	213.3	26356674	0.893	213.103	12.886	Harmine, Pimprinethine
84	183.008	375180	0.974	183.087	7.813	Harmane

85	201.3	59608896	0.959	201.099	6.91	Harmalol-HCl-2H2O
86	553.3	4747773	0.977	553.321	12.042	Habekacin HBK
87	216.3	8918029	0.941	216.09	17.006	Glycerinopyrin, Kinetin
88	216.076	1631653	0.941	216.088	9.83	Glycerinopyrin, Kinetin
89	326.3	22757776	0.951	326.141	15.269	Glucosyldeoxynojirimycin
90	911.3	21452022	0.96	911.477	16.375	GB-6 toxin
91	639.3	7344812	0.916	639.407	19.947	Filipin-II, Kaimonolide B, SI-4155B
92	394.3	28812154	0.97	394.096	12.196	Fibrostatin A, Fuchurmycin D
93	287.3	10565359	0.964	287.173	14.515	FL-657C
94	532.3	6772379	0.964	532.148	9.874	Ezomycin B2
95	180.3	4.38E+08	0.985	180.066	12.886	Erbstatin, p-(Acetylamino)benzoic acid
96	423.3	15037335	0.956	423.199	15.364	Enkastine IV
97	298.3	7632510	0.934	298.144	15.178	Diolmycin-A2
98	337.3	5855232	0.956	337.162	13.783	Dihydrotetrodecamycin, Streptonolid A
99	114.3	1624721	0.882	114.031	5.836	Dihydrotanshinone
100	143.3	1600499	0.939	143.073	5.786	Dihydrosarkomycin
101	143.029	240115	0.939	143.073	6.481	Dihydrosarkomycin
102	221.3	11898333	0.947	221.081	10.371	Differolide, Eugenitin
103	283.3	25475678	0.881	283.107	7.617	Deoxynybomycin, Saphenic acid methyl ester
104	828.3	3727403	0.951	828.44	11.662	Deltamycin A3
105	814.3	26932262	0.956	814.425	11.176	Deltamycin A2
106	800.433	1059960	0.969	800.409	12.042	Deltamycin A1
107	800.3	13061849	0.969	800.405	10.419	Deltamycin A1
108	196.3	5547727	0.946	196.065	9.279	Dehydrodioxolide A
109	191.3	50163508	0.975	191.07	9.652	Dealanylalahopcin
110	510.3	16933912	0.973	510.212	15.459	Deacetylravidomycin M
111	756.3	4678207	0.956	756.42	17.554	DOP; Desisovalerylplatenomycin-W1
112	380.3	3376033	0.94	380.123	13.263	DC-59-H, Maremycin-C1, Maremycin-C2
113	949.3	42443184	0.97	949.498	16.554	Cycloheptamycin
114	171.097	17644056	0.961	171.117	12.334	Cyclo(L-Leu-Gly)
115	171.3	61108080	0.961	171.117	12.886	Cyclo(L-Leu-Gly)
116	285.3	9390015	0.86	285.123	5.786	Coformycin
117	411.161	12008449	0.962	411.17	15.681	Clindamycin B, N-Demethyl-clindamycin
118	316.3	5.13E+09	0.975	316.152	12.918	Clavamycin D
119	316.139	42343772	0.975	316.151	13.925	Clavamycin D
120	473.3	2542606	0.935	473.209	15.269	Citromycin
121	598.358	5709448	0.946	598.363	17.365	Cirramycin-A1
122	598.3	10802550	0.946	598.364	16.772	Cirramycin-A1
123	190.3	3345565	0.952	190.05	8.619	Cinropeptin, Quisqualic acid
124	594.3	26114984	0.983	594.302	11.948	Chymostatin B
125	191.05	2364839	0.975	191.082	8.764	Chrysogine
126	263.163	1886106	0.943	263.107	9.83	Chicamycin B, Neothramycin-A, Neothramycin-B
127	373.3	2232579	0.928	373.044	5.537	Celastramycin B
128	842.3	1880879	0.928	842.45	11.948	Carbomycin
129	197.076	6576451	0.984	197.084	15.178	Cantharidin
130	152.3	2.13E+08	0.973	152.071	12.918	Cammunocin, Methyl 2-aminobenzoate, N-

						Methylanthranilic acid, SIPI-96-1041
131	354.19	25883726	0.956	354.171	15.269	CS-79B
132	354.3	27050244	0.956	354.171	12.404	CS-79B
133	328.3	7764389	0.935	328.155	13.626	Boldine
134	328.179	3139950	0.935	328.154	15.178	Boldine
135	487.12	3785567	0.972	487.138	14.263	Bequinostatin-C
136	487.3	5797510	0.972	487.138	14.177	Bequinostatin-C
137	505.3	924400	0.965	505.149	18.612	Bequinostatin-A
138	674.3	5880812	0.884	674.283	13.497	Baumycin A1, CG-21-B; Betaclamycin S, Cytorhodin M
139	256.118	270308	0.944	256.097	11.995	Bagremycin A
140	256.3	12060516	0.944	256.098	16.817	Bagremycin A
141	536.3	52278832	0.985	536.112	18.795	BE-19412A
142	268.3	1.16E+08	0.963	268.097	14.086	B-15645, Thiotetronic acid Tue 3010, U 68204
143	268.171	9224102	0.963	268.097	12.404	B-15645, Thiotetronic acid Tue 3010, U 68204
144	912.3	10906147	0.972	912.476	16.285	Arylomycin B7
145	385.3	1.87E+08	0.986	385.189	13.967	Artesunate
146	381.3	1.1E+08	0.977	381.261	14.783	Aphidicolin 17-acetate, Aphidicolin-3,18-orthoacetate
147	200.036	445244	0.955	200.092	7.951	Anticapsin
148	200.3	13746728	0.955	200.092	13.717	Anticapsin
149	516.3	875288	0.911	516.154	10.009	Antibiotic F 6
150	619.3	1830343	0.918	619.31	18.841	Amicetin; Allomycin; Amicetin A; Sacromycin; 4009A; NSC-5340;
151	391.082	1070374	0.966	391.107	19.249	Akkamycin B
152	150.3	13688232	0.89	150.091	11.471	A28, Benzylacetamide
153	159.008	650020	0.965	159.041	4.89	A-31475-A, Tricholomic acid
154	341.3	93867280	0.951	341.159	14.04	8-Acetyl-T-2-tetrol, LL-BM434g
155	887.3	7634639	0.975	887.533	17.052	6016
156	207.3	1474023	0.92	207.088	9.652	6-O-Acetyl-2-deoxyglucose
157	293.3	5552911	0.893	293.126	11.567	6-(3-Methyl-2-butenyl)-1-phenazinecarboxylic acid, Endophenazine A
158	247.3	18791462	0.949	247.144	11.995	5-(2-Oxo-1-azabicyclo[3,3,0]octan-5-yl)-1-azabicyclo[3,3,0]oct-3-en-2-, N2-(2-Carboxyethyl)arginine
159	327.3	31118330	0.959	327.111	19.295	5,10,11,11-Tetrahydro-9,11-dihydroxy-8-methyl-5-oxo-1H-pyrrolo-[e,2,1][1,4]-benzodiazepin-2-acrylamide, Azetomycin III, Bilobalide
160	223.3	74709112	0.973	223.095	13.925	4beta,8-Dihydroxy-3alpha-hydroxymetyl-4alpha-methyl-1,2,3,4-, CV-1, Diethyl phthalate, N-Carbamoyl-D-glucosamine
161	427.3	29645048	0.972	427.193	12.573	49A, Cyanonaphthyridinomycin
162	395.3	4970449	0.882	395.111	12.129	4-O-Acetyl-rubiginone D2
163	308.3	24311446	0.973	308.185	13.497	4-O-(6-Amino-6-deoxyglucopyranosyl)-2,5-dideoxystreptamine, Nebramycin-9, S-632-A2, S-632-C
164	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone
165	145.3	3628503	0.964	145.051	8.096	4-Epipentenomycin I, Pentenomycin I

166	139.3	24831520	0.986	139.076	7.57	4,5-Dimethyl-1,3-benzenediol, p-Hydroxyphenylethyl alcohol
167	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein
168	273.126	1031348	0.947	273.044	10.515	3-epi-Sulphostin, Sulphostin
169	187.989	5607526	0.899	188.071	5.786	3-beta-Indoleacrylic acid, Enteromycin carboxamide
170	255.3	5956688	0.936	255.089	15.135	3-O-Methylcyclopolic acid
171	187.3	25236668	0.966	187.087	19.295	3-Indoleacrylamide
172	305.3	25201318	0.931	305.128	19.295	3-Hydroxypiromidic acid
173	192.05	812277	0.966	192.102	8.764	3-Ethyl-1,3-dihydro-3-methoxy-2H-indol-2-one, Louisianin-B, Ulupyrinone
174	302.3	47012196	0.974	302.155	16.817	3-Acetylamino-3-deoxy-1,2,5,6-di-O-isopropylidene- a-D-glucofuranose
175	176.3	41401020	0.97	176.074	13.152	3-(Hydroxyacetyl)-indole, 3-Indolyl carboxylic acid methyl ester
176	176.128	782955	0.97	176.071	11.995	3-(Hydroxyacetyl)-indole, 3-Indolyl carboxylic acid methyl ester
177	176.07	5137654	0.97	176.071	8.241	3-(Hydroxyacetyl)-indole, 3-Indolyl carboxylic acid methyl ester
178	307.3	18974764	0.964	307.144	17.006	3-(3,3-Di-indolyl)propane-1,2-diol
179	127.3	3058745	0.976	127.039	3.81	3- Carboxy-2-4-pentadienal lactol, Maltol, Methyl 2-furancarboxylate
180	159.3	6977116	0.965	159.065	5.537	3,4,6-Trihydroxy-2-methyl-2-cyclohexen-1-one, Butyrolactone Tue 1718 E, Gabosine L, Gabosine N, Streptopyrone
181	683.3	4242486	0.983	683.436	19.947	26-Deoxylaidlomycin
182	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile
183	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile
184	161.3	10166765	0.93	161.071	7.525	2-Methyl-3H-quinazolin-4-one
185	113.3	10099304	0.988	113.06	5.537	2-Hydroxy-3-methylcyclopentenone, 3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b
186	136.3	79092208	0.961	136.076	11.083	2-Amino-acetophenone, 2-Phenylacetamide
187	136.06	6486755	0.961	136.076	9.373	2-Amino-acetophenone, 2-Phenylacetamide
188	116.031	68337	0.977	116.07	5.887	2-Amino-4-hydroxypentanoic acid lactone, 5590, AH 2589-I
189	198.3	6.97E+08	0.984	198.076	12.886	2,5-Dihydroxyphenylalanine, Dioxolide A
190	198.055	2292381	0.984	198.076	8.715	2,5-Dihydroxyphenylalanine, Dioxolide A
191	129.3	9645245	0.877	129.055	5.836	2,5-Bis(hydroxymethyl)furan
192	169.3	23893100	0.983	169.096	13.672	2,4,6,8-Tridecatetrayne
193	169.029	2837344	0.983	169.097	8.431	2,4,6,8-Tridecatetrayne
194	169.122	3.28E+08	0.983	169.097	10.192	2,4,6,8-Tridecatetrayne
195	364.3	42085564	0.983	364.151	15.221	1a-N-Methylmitomycin A, 9a-O-Methylmitomycin B, Mitomycin J, d-(L-a-Aminoadipyl)-L-cysteinyl-D-valine
196	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin
197	407.198	20403190	0.972	407.171	13.967	14,20-Dideoxy-thaxtomin A
198	407.3	27664736	0.972	407.171	14.04	14,20-Dideoxy-thaxtomin A
199	468.3	31487500	0.951	468.213	12.918	1-Nordistamycin A

200	468.712	64509816	0.951	468.213	12.84	1-Nordistamycin A
201	317.3	9.09E+08	0.973	317.157	12.95	1-Isobutyroxymethyl cyclohex-1(6)-ene-2,3,4,5-tetrol-2-isobutyrate
202	135.3	6511666	0.914	135.068	11.471	1-Deoxy-D-threo-pentulose, 1-Deoxy-D-threo-pentulose, see open-chain form
203	332.3	78996256	0.96	332.126	12.886	0231-B, Mitiromycin A
204	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone, Rheosmin, Thymoquinone
205	225.071	79801888	0.985	225.078	15.178	(S)-a-Benzylmalic acid, 5-Hydroxy-4-(hydroxymethyl)-7-methoxy-6-methyl-1(3H)-isobenzofuranone, Reticulol; 6-Demethylkigelin
206	225.3	16425538	0.985	225.078	13.626	(S)-a-Benzylmalic acid, 5-Hydroxy-4-(hydroxymethyl)-7-methoxy-6-methyl-1(3H)-isobenzofuranone, Reticulol; 6-Demethylkigelin
207	141.3	23522992	0.965	141.055	9.232	(R)-2-Methylene-3-oxocyclopentanecarboxylic acid, Butyrolactone Tue 1718 G1, Epiepoformin
208	231.3	40281504	0.946	231.138	12.886	(3S,6S)-Terramide C, 6-Acetamido-6-deoxy-castanospermine, Dehydrobotrydienal, Dehydrocostus lactone
209	197.3	40889116	0.984	197.129	7.289	(3R,7aS)-Cyclo(prolylvalyl), Maculosin-5, cis-(3S,7aS)-Cyclo(prolylvalyl), L,L-form
210	211.3	1.54E+08	0.987	211.145	9.047	(3R,7aR)-Cyclo(leucylprolyl), (3R,7aS)-Cyclo(leucylprolyl), Gancidin-W
211	156.075	1447740	0.979	156.042	7.149	(1R,2R)-(-)-(2-Amino-1-hydroxypropyl)phosphonic acid, (1S,2S)-(+)-(1-Amino-2-hydroxypropyl)phosphonic acid
212	335.3	19622690	0.962	335.146	15.178	(-)-Tetrodecamycin
213	335.134	38089204	0.962	335.146	15.135	(-)-Tetrodecamycin
214	320.173	1846136	0.885	320.149	8.715	(-)-Scopolamine-N-oxide
215	243.3	72625128	0.982	243.149	15.459	(-)-Huperazine, HT-13B, metabolite 2
216	366.3	92880944	0.978	366.178	6.91	(-)-Brevianamide B, Brevianamide D, KF 77AG6, (S,S)-form
217	597.055	450215	0.949	597.357	18.885	(+)-Trienomycin B, (+)-Trienomycin C
218	611.3	66995168	0.949	611.336	16.241	(+)-Ansatrienin A3, Ansatrienin A2, UCF-116-C

Table S53. 218 masses in *Streptomyces* sp. MA37 annotated by StrepDB when t_R and t_R window are not used. Annotation solely based on HRMS data.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	293.126	5515350	0.893	293.126	11.614		[M+Na]+
2	316.151	1.94E+09	0.975	316.151	12.806		[M+Na]+
3	316.152	1.71E+09	0.975	316.152	12.334		[M+Na]+

4	802.4	7319905	0.98	802.4	15.364		[M+Na]+
5	802.4	9794311	0.98	802.4	15.459		[M+Na]+
6	374.175	10075230	0.972	374.175	16.772		[M+Na]+
7	332.125	72979464	0.96	332.125	12.369		[M+K]+
8	425.137	20034810	0.946	425.137	15.633		[M+K]+
9	618.263	3380540	0.941	618.263	4.015		[M+H]+
10	314.139	97988448	0.97	314.139	13.925		[M+H]+
11	174.078	4014152	0.959	174.079	8.335		[M+H]+
12	780.418	21203886	0.971	780.418	15.459		[M+H]+
13	242.284	18634786	0.978	242.284	9.186		[M+H]+
14	425.193	5741643	0.946	425.193	8.814		[M+H]+
15	331.224	1539023	0.967	331.224	19.801		[M+H]+
16	519.103	6021205	0.946	519.103	18.795		[M+H]+
17	366.178	50673692	0.978	366.178	6.816		[M+H]+
18	408.178	2.28E+08	0.987	408.178	14.222		[M+H]+
19	318.168	4.73E+08	0.981	318.168	13.847		[M+H]+
20	309.203	6472254	0.9	309.203	19.157		[M+H]+
21	226.084	22885360	0.976	226.084	10.787		[M+H]+
22	761.381	9505538	0.99	761.381	16.772		[M+H]+
23	503.125	2119604	0.982	503.126	12.163		[M+H]+
24	113.964	665983	0.882	113.964	3.234		[M+H]+
25	478.206	23457526	0.988	478.206	11.662		[M+H]+
26	247.144	17168400	0.949	247.144	11.948		[M+H]+
27	344.071	2202204	0.885	344.071	18.658		[M+H]+
28	206.974	945212	0.92	206.974	4.89		[M+H]+
29	163.086	68975360	0.97	163.086	10.323		[M+H]+
30	352.191	1.23E+08	0.979	352.191	16.817		[M+H]+
31	250.037	1004456	0.835	250.037	9.605		[M+H]+
32	861.443	48970284	0.982	861.443	17.507		[M+H]+
33	126.031	15169197	0.987	126.031	6.332		[M+H]+
34	271.144	90010608	0.98	271.144	11.614		[M+H]+
35	438.198	14075611	0.978	438.198	3.81		[M+H]+
36	863.452	1.34E+08	0.974	863.452	18.212		[M+H]+

Table S54. When calculated t_R is used, without values for t_R window (t_R range). The 'lable' column is blank, indicating 'no' hits generated in StrepDB. The table show only 36 of the 1099 masses.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	485.3	1.69E+08	0.981	485.188	12.918	UK-3A	
2	268.3	1.16E+08	0.963	268.097	14.086	U 68204	[M+H]+
3	268.171	9224102	0.963	268.097	12.404	Thiotetronic acid Tue 3010, U 68204	Review
4	308.3	24311446	0.973	308.185	13.497	S-632-A2	
5	304.3	2685780	0.945	304.106	10.009	Mansouramycin D	Review

6	127.3	3058745	0.976	127.039	3.81	Maltol	
7	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin	Review
8	828.3	3727403	0.951	828.44	11.662	Deltamycin A3	Review
9	231.3	40281504	0.946	231.138	12.886	Dehydrocostus lactone	Review
10	842.3	1880879	0.928	842.45	11.948	Carbomycin	Review
11	354.19	25883726	0.956	354.171	15.269	CS-79B	
12	674.3	5880812	0.884	674.283	13.497	Baumycin A1	[M+H]+
13	912.3	10906147	0.972	912.476	16.285	Arylomycin B7	Good
14	887.3	7634639	0.975	887.533	17.052	6016	
15	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone	Review
16	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein	Good
17	113.3	10099304	0.988	113.06	5.537	3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b	PFI
18	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile	Review
19	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile	Review
20	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin	Good
21	332.3	78996256	0.96	332.126	12.886	0231-B	[M+K]+
22	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone, Thymoquinone	[M+H]+

Table S55. 22 masses in in crude extract of *Streptomyces* sp. MA37 annotated when calculated t_R is used, with t_R window (t_R range) set to 1.5 minutes.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	485.3	1.69E+08	0.981	485.188	12.918	UK-3A	
2	268.3	1.16E+08	0.963	268.097	14.086	U 68204	[M+H]+
3	268.171	9224102	0.963	268.097	12.404	Thiotetronic acid Tue 3010, U 68204	Review
4	308.3	24311446	0.973	308.185	13.497	S-632-A2	
5	304.3	2685780	0.945	304.106	10.009	Mansouramycin D	Review
6	127.3	3058745	0.976	127.039	3.81	Maltol	
7	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin	Review
8	911.3	21452022	0.96	911.477	16.375	GB-6 toxin	Good
9	221.3	11898333	0.947	221.081	10.371	Eugenitin	
10	828.3	3727403	0.951	828.44	11.662	Deltamycin A3	Review
11	814.3	26932262	0.956	814.425	11.176	Deltamycin A2	Review
12	800.3	13061849	0.969	800.405	10.419	Deltamycin A1	[M+H]+
13	231.3	40281504	0.946	231.138	12.886	Dehydrocostus lactone	Review
14	842.3	1880879	0.928	842.45	11.948	Carbomycin	Review
15	354.19	25883726	0.956	354.171	15.269	CS-79B	
16	505.3	924400	0.965	505.149	18.612	Bequinostatin-A	Review
17	674.3	5880812	0.884	674.283	13.497	Baumycin A1	[M+H]+
18	912.3	10906147	0.972	912.476	16.285	Arylomycin B7	Good

19	385.3	1.87E+08	0.986	385.189	13.967	Artesunate	Good
20	887.3	7634639	0.975	887.533	17.052	6016	
21	395.3	4970449	0.882	395.111	12.129	4-O-Acetyl-rubiginone D2	Review
22	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone	Review
23	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein	Good
24	113.3	10099304	0.988	113.06	5.537	3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b	PFI
25	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile	Review
26	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile	Review
27	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin	Good
28	332.3	78996256	0.96	332.126	12.886	0231-B	[M+K]+
29	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone, Thymoquinone	[M+H]+

Table S56. 29 masses in crude extract of *Streptomyces* sp. MA37 annotated when t_R is used, with t_R window (t_R range) set to 2.0 minutes.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	485.3	1.69E+08	0.981	485.188	12.918	UK-3A	
2	611.3	66995168	0.949	611.336	16.241	UCF-116-C	Good
3	268.171	9224102	0.963	268.097	12.404	Thiotetronic acid Tue 3010, U 68204	Review
4	268.3	1.16E+08	0.963	268.097	14.086	Thiotetronic acid Tue 3010, U 68204	[M+H]+
5	627.3	17212808	0.927	627.363	16.554	T-23-IX	
6	283.3	25475678	0.881	283.107	7.617	Saphenic acid methyl ester	[M+H]+
7	308.3	24311446	0.973	308.185	13.497	S-632-A2	
8	637.3	19827708	0.987	637.393	10.371	RK-397	
9	321.3	1.34E+08	0.979	321.13	12.771	Mycophenolic acid	Review
10	304.3	2685780	0.945	304.106	10.009	Mansouramycin D	Review
11	127.3	3058745	0.976	127.039	3.81	Maltol	
12	926.3	18635972	0.985	926.42	17.93	Liposidomycin-Y-(III)	Good
13	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin	Review
14	183.008	375180	0.974	183.087	7.813	Harmane	
15	911.3	21452022	0.96	911.477	16.375	GB-6 toxin	Good
16	221.3	11898333	0.947	221.081	10.371	Eugenitin	
17	828.3	3727403	0.951	828.44	11.662	Deltamycin A3	Review
18	814.3	26932262	0.956	814.425	11.176	Deltamycin A2	Review
19	800.3	13061849	0.969	800.405	10.419	Deltamycin A1	[M+H]+
20	231.3	40281504	0.946	231.138	12.886	Dehydrocostus lactone	Review
21	842.3	1880879	0.928	842.45	11.948	Carbomycin	Review

22	354.19	25883726	0.956	354.171	15.269	CS-79B	
23	354.3	27050244	0.956	354.171	12.404	CS-79B	
24	505.3	924400	0.965	505.149	18.612	Bequinostatin-A	Review
25	674.3	5880812	0.884	674.283	13.497	Baumycin A1	[M+H]+
26	256.118	270308	0.944	256.097	11.995	Bagremycin A	Good
27	912.3	10906147	0.972	912.476	16.285	Arylomycin B7	Good
28	385.3	1.87E+08	0.986	385.189	13.967	Artesunate	Good
29	887.3	7634639	0.975	887.533	17.052	6016	
30	395.3	4970449	0.882	395.111	12.129	4-O-Acetyl-rubiginone D2	Review
31	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone	Review
32	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein	Good
33	187.989	5607526	0.899	188.071	5.786	3-beta-Indoleacrylic acid	Review
34	113.3	10099304	0.988	113.06	5.537	3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b	PFI
35	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile	Review
36	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile	Review
37	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin	Good
38	332.3	78996256	0.96	332.126	12.886	0231-B	[M+K]+
39	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone, Thymoquinone	[M+H]+

Table S57. 39 compounds in crude extract of *Streptomyces* sp. MA37 annotated when t_R is used, with t_R window (t_R range) set to 2.5 minutes.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	261.3	35488172	0.973	261.124	6.91	cyclo-(N-Me-Tyr,dehydroAbu)	PFI
2	178.3	4308333	0.893	178.084	8	USF-142-A	Review
3	485.3	1.69E+08	0.981	485.188	12.918	UK-3A	
4	268.3	1.16E+08	0.963	268.097	14.086	Thiotetronic acid Tue 3010, U 68204	[M+H]+
5	268.171	9224102	0.963	268.097	12.404	Thiotetronic acid Tue 3010, U 68204	Review
6	627.3	17212808	0.927	627.363	16.554	T-23-IX	
7	134.3	10155379	0.914	134.06	8.619	SS 8215A	[M+H]+
8	308.3	24311446	0.973	308.185	13.497	S-632-A2	
9	637.3	19827708	0.987	637.393	10.371	RK-397	
10	426.193	87462568	0.977	426.189	12.334	Nisamycin	Good
11	426.3	1.22E+08	0.977	426.188	12.66	Nisamycin	[M+H]+

12	321.3	1.34E+08	0.979	321.13	12.771	Mycophenolic acid	Review
13	304.3	2685780	0.945	304.106	10.009	Mansouramycin D	Review
14	295.3	4.7E+08	0.969	295.173	12.886	MF-EA-705a	Good
15	926.3	18635972	0.985	926.42	17.93	Liposidomycin-Y-(III)	Good
16	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin	Review
17	183.008	375180	0.974	183.087	7.813	Harmane	
18	911.3	21452022	0.96	911.477	16.375	GB-6 toxin	Good
19	221.3	11898333	0.947	221.081	10.371	Eugenitin	
20	283.3	25475678	0.881	283.107	7.617	Deoxynybomycin, Saphenic acid methyl ester	[M+H]+
21	828.3	3727403	0.951	828.44	11.662	Deltamycin A3	Review
22	814.3	26932262	0.956	814.425	11.176	Deltamycin A2	Review
23	800.3	13061849	0.969	800.405	10.419	Deltamycin A1	[M+H]+
24	231.3	40281504	0.946	231.138	12.886	Dehydrobotrydienal, Dehydrocostus lactone	Review
25	949.3	42443184	0.97	949.498	16.554	Cycloheptamycin	Good
26	190.3	3345565	0.952	190.05	8.619	Cinropeptin	Poor
27	842.3	1880879	0.928	842.45	11.948	Carbomycin	Review
28	354.19	25883726	0.956	354.171	15.269	CS-79B	
29	354.3	27050244	0.956	354.171	12.404	CS-79B	
30	159.3	6977116	0.965	159.065	5.537	Butyrolactone Tue 1718 E, Streptopyrone	Review
31	487.12	3785567	0.972	487.138	14.263	Bequinostatin-C	Good
32	505.3	924400	0.965	505.149	18.612	Bequinostatin-A	Review
33	674.3	5880812	0.884	674.283	13.497	Baumycin A1	[M+H]+
34	256.118	270308	0.944	256.097	11.995	Bagremycin A	Good
35	912.3	10906147	0.972	912.476	16.285	Arylomycin B7	Good
36	385.3	1.87E+08	0.986	385.189	13.967	Artesunate	Good
37	159.008	650020	0.965	159.041	4.89	A-31475-A, Tricholomic acid	Review
38	887.3	7634639	0.975	887.533	17.052	6016	
39	395.3	4970449	0.882	395.111	12.129	4-O-Acetyl-rubiginone D2	Review
40	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone	Review
41	139.3	24831520	0.986	139.076	7.57	4,5-Dimethyl-1,3-benzenediol	[M+H]+
42	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein	Good
43	187.989	5607526	0.899	188.071	5.786	3-beta-Indoleacrylic acid	Review
44	127.3	3058745	0.976	127.039	3.81	3- Carboxy-2-4-pentadienal lactol, Maltol, Methyl 2-furancarboxylate	Poor
45	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile	Review
46	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile	Review
47	113.3	10099304	0.988	113.06	5.537	2-Hydroxy-3-methylcyclopentenone, 3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b	PFI
48	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin	Good
49	332.3	78996256	0.96	332.126	12.886	0231-B	[M+K]+
50	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone,	[M+H]+

						Thymoquinone	
51	611.3	66995168	0.949	611.336	16.241	(+)-Ansatrienin A3, Ansatrienin A2, UCF-116-C	Good

Table S58. 51 masses annotated when calculated t_R is used, with t_R window (t_R range) set to 3.0 minutes.

No.	m/z	Area (counts)	MCQ	Peak Top Mass	tR (min)	Label	Notation
1	261.3	35488172	0.973	261.124	6.91	cyclo-(N-Me-Tyr,dehydroAbu)	PFI
2	779.3	2284288	0.966	779.406	11.854	Vinorelbine	
3	178.3	4308333	0.893	178.084	8	USF-142-A	
4	485.3	1.69E+08	0.981	485.188	12.918	UK-3A	
5	268.171	9224102	0.963	268.097	12.404	Thiotetronic acid Tue 3010, U 68204	
6	268.3	1.16E+08	0.963	268.097	14.086	Thiotetronic acid Tue 3010, U 68204	[M+H]+
7	627.3	17212808	0.927	627.363	16.554	T-23-IX	
8	134.3	10155379	0.914	134.06	8.619	SS 8215A	[M+H]+
9	308.3	24311446	0.973	308.185	13.497	S-632-A2	
10	513.21	358732	0.939	513.356	19.522	Reductoleptomycin-A	
11	637.3	19827708	0.987	637.393	10.371	RK-397	
12	810.3	13113622	0.963	810.427	11.71	Protoveratrine B	
13	481.3	9351200	0.77	481.19	12.771	Panosialin A	
14	474.181	180255	0.99	474.186	4.991	OA 6129B1, OA 6129B2	
15	426.3	1.22E+08	0.977	426.188	12.66	Nisamycin	[M+H]+
16	426.193	87462568	0.977	426.189	12.334	Nisamycin	
17	321.3	1.34E+08	0.979	321.13	12.771	Mycophenolic acid	
18	797.414	15676641	0.979	797.417	11.758	Mocimycin	
19	304.3	2685780	0.945	304.106	10.009	Mansouramycin D	
20	295.3	4.7E+08	0.969	295.173	12.886	MF-EA-705a	
21	573.108	1309181	0.985	573.307	19.801	Lysophosphatidyl inositol 1	
22	926.3	18635972	0.985	926.42	17.93	Liposidomycin-Y-(III)	
23	193.011	1259285	0.977	193.047	7.1	Isoscopoletine, Scopoletin	
24	183.008	375180	0.974	183.087	7.813	Harmane	
25	911.3	21452022	0.96	911.477	16.375	GB-6 toxin	
26	532.3	6772379	0.964	532.148	9.874	Ezomycin B2	
27	221.3	11898333	0.947	221.081	10.371	Eugenitin	
28	143.029	240115	0.939	143.073	6.481	Dihydrosarkomycin	
29	143.3	1600499	0.939	143.073	5.786	Dihydrosarkomycin	PFI
30	223.3	74709112	0.973	223.095	13.925	Diethyl phthalate	
31	283.3	25475678	0.881	283.107	7.617	Deoxynybomycin, Saphenic acid methyl ester	[M+H]+
32	828.3	3727403	0.951	828.44	11.662	Deltamycin A3	
33	814.3	26932262	0.956	814.425	11.176	Deltamycin A2	
34	800.3	13061849	0.969	800.405	10.419	Deltamycin A1	[M+H]+
35	800.433	1059960	0.969	800.409	12.042	Deltamycin A1	

36	231.3	40281504	0.946	231.138	12.886	Dehydrobotrydienal, Dehydrocostus lactone	
37	949.3	42443184	0.97	949.498	16.554	Cycloheptamycin	
38	190.3	3345565	0.952	190.05	8.619	Cinropeptin	
39	842.3	1880879	0.928	842.45	11.948	Carbomycin	
40	354.3	27050244	0.956	354.171	12.404	CS-79B	
41	354.19	25883726	0.956	354.171	15.269	CS-79B	
42	487.12	3785567	0.972	487.138	14.263	Bequinostatin-C	
43	487.3	5797510	0.972	487.138	14.177	Bequinostatin-C	
44	505.3	924400	0.965	505.149	18.612	Bequinostatin-A	
45	674.3	5880812	0.884	674.283	13.497	Baumycin A1	[M+H]+
46	256.118	270308	0.944	256.097	11.995	Bagremycin A	
47	912.3	10906147	0.972	912.476	16.285	Arylomycin B7	
48	385.3	1.87E+08	0.986	385.189	13.967	Artesunate	
49	381.3	1.1E+08	0.977	381.261	14.783	Aphidicolin-3,18-orthoacetate	[M+H]+
50	116.031	68337	0.977	116.07	5.887	AH 2589-I	
51	159.008	650020	0.965	159.041	4.89	A-31475-A, Tricholomic acid	
52	887.3	7634639	0.975	887.533	17.052	6016	
53	395.3	4970449	0.882	395.111	12.129	4-O-Acetyl-rubiginone D2	
54	177.3	10254938	0.954	177.055	7.858	4-Methylumbelliferone	
55	139.3	24831520	0.986	139.076	7.57	4,5-Dimethyl-1,3-benzenediol	[M+H]+
56	559.3	9913180	0.962	559.219	10.231	4',7-Bis-(beta-cymaropyranosyl)-genistein	
57	187.989	5607526	0.899	188.071	5.786	3-beta-Indoleacrylic acid	
58	176.07	5137654	0.97	176.071	8.241	3-Indolyl carboxylic acid methyl ester	
59	127.3	3058745	0.976	127.039	3.81	3- Carboxy-2-4-pentadienal lactol, Maltol, Methyl 2-furancarboxylate	
60	159.3	6977116	0.965	159.065	5.537	3,4,6-Trihydroxy-2-methyl-2-cyclohexen-1-one, Butyrolactone Tue 1718 E, Gabosine L, Streptopyrone	
61	118.3	5944870	0.949	118.065	7.904	2-Phenylacetonitrile	
62	118.049	1544187	0.949	118.065	7.476	2-Phenylacetonitrile	
63	113.3	10099304	0.988	113.06	5.537	2-Hydroxy-3-methylcyclopentenone, 3,5-Dimethyl-3-oxol-2-on, Dihydro-dimethylfuranone, struct. a, Dihydro-dimethylfuranone, struct. b	PFI
64	129.3	9645245	0.877	129.055	5.836	2,5-Bis(hydroxymethyl)furan	[M+H]+
65	886.3	24903178	0.958	886.535	17.095	16,39-Bisdemethyl-rapamycin	
66	332.3	78996256	0.96	332.126	12.886	0231-B	[M+K]+
67	165.3	75294768	0.972	165.091	9.874	(Z)-4-(4-Methyl-1,3-pentadienyl)-2(5H)-furanone, Thymoquinone	[M+H]+
68	611.3	66995168	0.949	611.336	16.241	(+)-Ansatrienin A3, Ansatrienin A2, UCF-116-C	

Table S59. 68 compounds in crude extract of *Streptomyces* sp. MA37 annotated when calculated t_R is used, with t_R window (t_R range) set to 4.0 minutes.

Table of Components

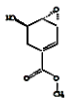
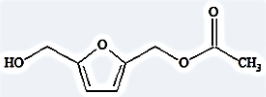
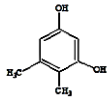
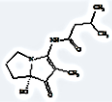
No.	tR(min)	Mass(Ao)	[M+H]+	M+.	MF	Structure	Name	MS Match
1	7.100	170.058	171.065	170.057	$C_8H_{10}O_4$		(+)-3,4-Anhydroshikimic acid methyl	Excellent
2	7.100	170.058	171.065	170.057	$C_8H_{10}O_4$		2,5-Bis(methanol)-furane monoaceta	Excellent
3	7.570	138.068	139.075	138.068	$C_8H_{10}O_2$		4,5-Dimethyl-1,3-benzenediol	Excellent
4	10.151	252.147	253.155	252.147	$C_{13}H_{20}N_2O_3$		Legonmycin A	Excellent

Figure S60. Analysis of *Streptomyces* sp. MA37 showing the presence of legonmycin A with other known compounds identified by StrepDB.

No.	$t_R$exp	t_{Cal}	t_{Rexp}-t_{Rcal}	Mass		No.	$t_R$exp	t_{Cal}	t_{Rexp}-t_{Rcal}	Mass
1	7.6	7.6	0	293.102		40	9.5	9.3	0.2	317.0656
2	9	9.01	0.01	271.0601		41	1.2	1.4	0.2	190.0458
3	7.1	7.11	0.01	479.1184		42	11.4	11.2	0.2	325.1071
4	10.58	10.6	0.02	427.1024		43	6.3	6.51	0.21	465.1028
5	11.7	11.68	0.02	285.1121		44	7	6.79	0.21	233.1285
6	10.3	10.28	0.02	414.3367		45	10.77	10.55	0.22	253.0859
7	10.74	10.77	0.03	283.0965		46	1.2	1.42	0.22	653.359
8	10.9	10.93	0.03	329.102		47	11	10.78	0.22	791.5304
9	1.2	1.23	0.03	163.123		48	8.5	8.28	0.22	457.2333
10	15.3	15.27	0.03	309.2788		49	9.31	9.54	0.23	255.0652
11	17.8	17.76	0.04	747.4654		50	6.1	5.87	0.23	611.1607
12	10.8	10.84	0.04	508.2694		51	7.9	7.67	0.23	333.099
13	5.6	5.56	0.04	292.1543		52	11.26	11.49	0.23	285.1121
14	11.52	11.47	0.05	373.1282		53	10.36	10.6	0.24	281.0808
15	7.2	7.15	0.05	437.1442		54	14.6	14.34	0.26	359.2217
16	8.1	8.15	0.05	623.3116		55	8	7.72	0.28	289.0707
17	6.5	6.44	0.06	451.1235		56	6.1	6.38	0.28	193.0495
18	1.2	1.26	0.06	163.123		57	9.2	9.48	0.28	301.0707
19	13.7	13.76	0.06	395.1489		58	9.63	9.92	0.29	283.0965
20	11	11.06	0.06	283.0965		59	7.3	7.6	0.3	653.3221
21	10.33	10.26	0.07	253.0859		60	1.2	1.5	0.3	174.1125
22	13.9	13.81	0.09	345.1121		61	10.7	11	0.3	387.253
23	13.4	13.3	0.1	395.1489		62	15.7	16	0.3	359.2217
24	13.8	13.9	0.1	335.2217		63	9.2	9.51	0.31	247.1329
25	6.5	6.6	0.1	311.1125		64	1.2	1.52	0.32	231.1339

26	10	10.1	0.1	269.0808		65	9.5	9.83	0.33	415.1387
27	11.8	11.9	0.1	309.1121		66	11.15	11.49	0.34	343.1176
28	9.1	9.22	0.12	204.1019		67	6.3	6.66	0.36	449.1078
29	14	14.14	0.14	427.2115		68	7.2	7.57	0.37	319.0448
30	1.2	1.35	0.15	190.1074		69	1.2	1.57	0.37	189.1022
31	9.2	9.04	0.16	592.348		70	5.6	5.98	0.38	450.285
32	11.4	11.24	0.16	259.0965		71	10.8	11.19	0.39	426.3003
33	1.2	1.37	0.17	189.1022		72	1.1	1.49	0.39	191.1179
34	10.43	10.25	0.18	253.0859		73	7.06	7.45	0.39	433.1129
35	10.43	10.25	0.18	253.0859		74	9.2	8.8	0.4	217.0495
36	9.8	9.62	0.18	609.2807		75	10.9	10.5	0.4	667.2861
37	10.3	10.12	0.18	275.0914		76	10	9.6	0.4	609.2807
38	10.79	10.6	0.19	315.0863		77	9.92	9.52	0.4	255.0652
39	11	10.8	0.2	387.1802		78	9.2	9.6	0.4	351.2067

Table S61. 78 out of the 417 standard compounds used for calculating retention times. The table shows experimental, predicted, differences, and HRMS of the corresponding compound.