

OL-10-18-4_220331162940 #1 RT: 0.00 AV: 1 NL: 1.54E6
T: + c EI Full ms [32.50-500.50]

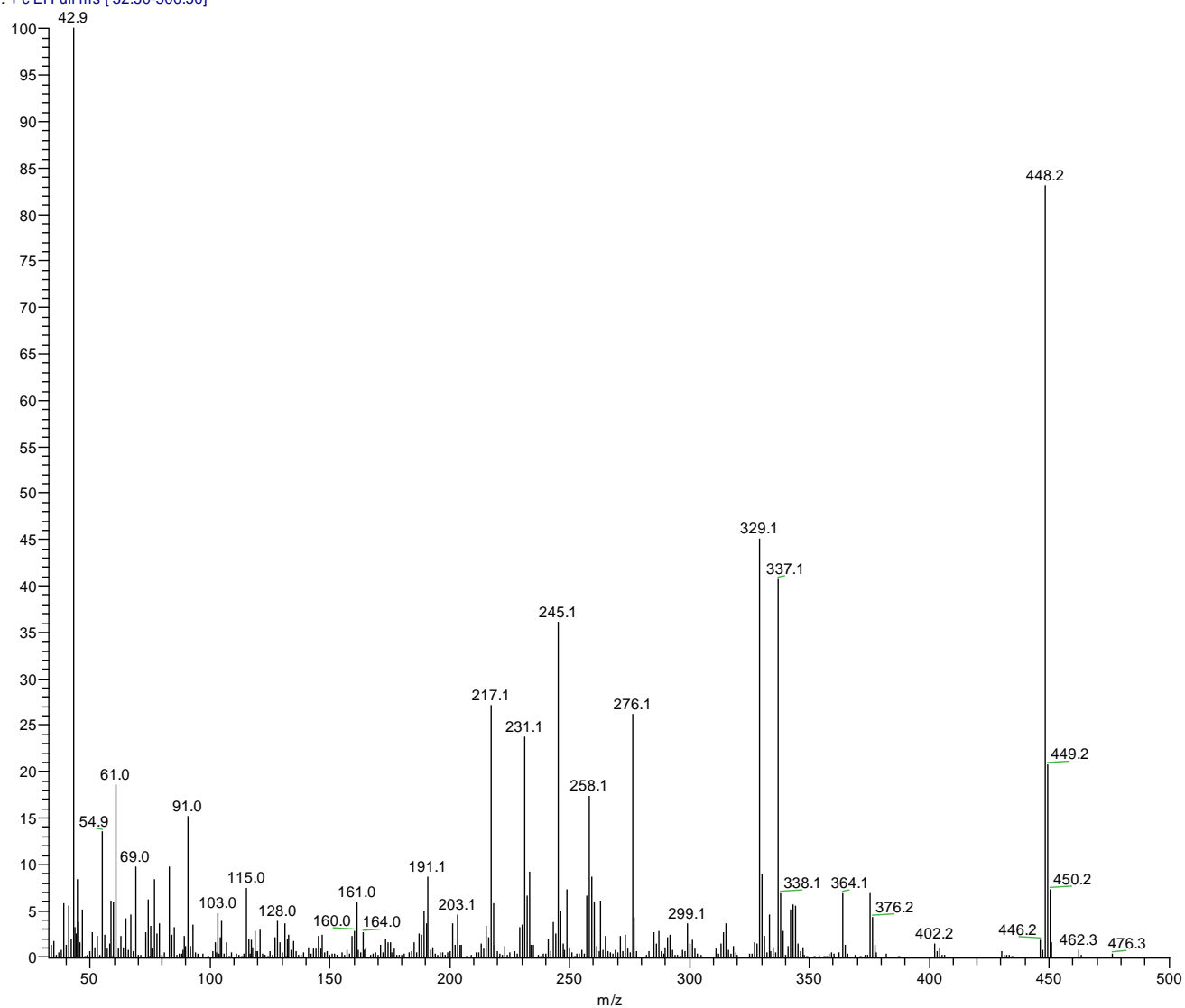


Figure S3. DFS spectrum of 5b.

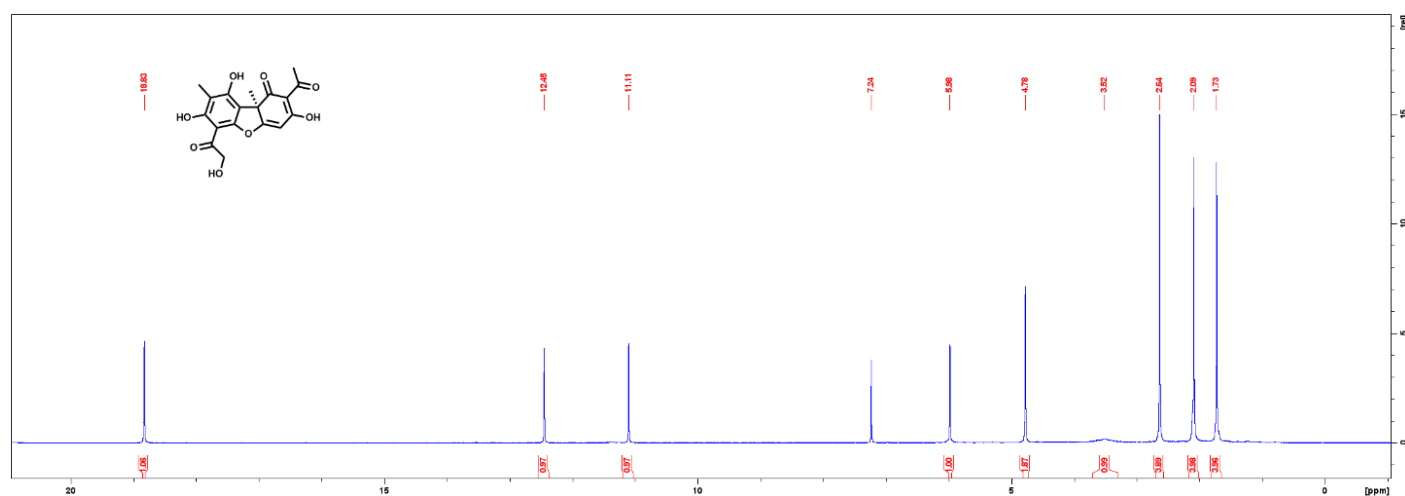
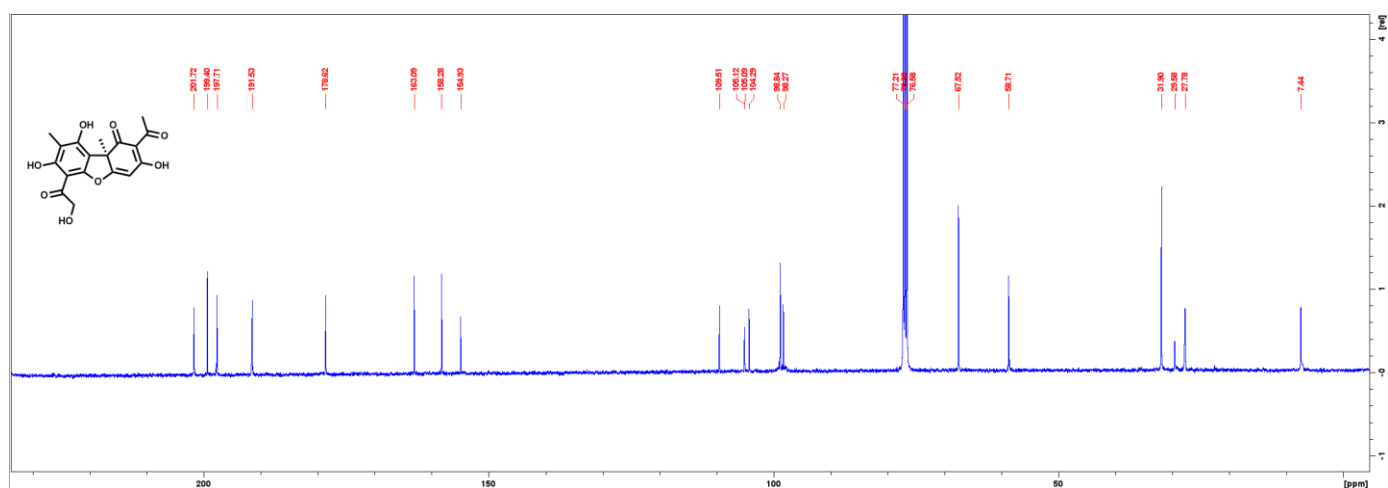


Figure S4. NMR ¹H spectrum of 10.

Figure S5. NMR ^{13}C spectrum of 10.

O18-31 #24 RT: 1.35 AV: 1 NL: 3.63E5
T: + c EI Full ms [32.50-400.50]

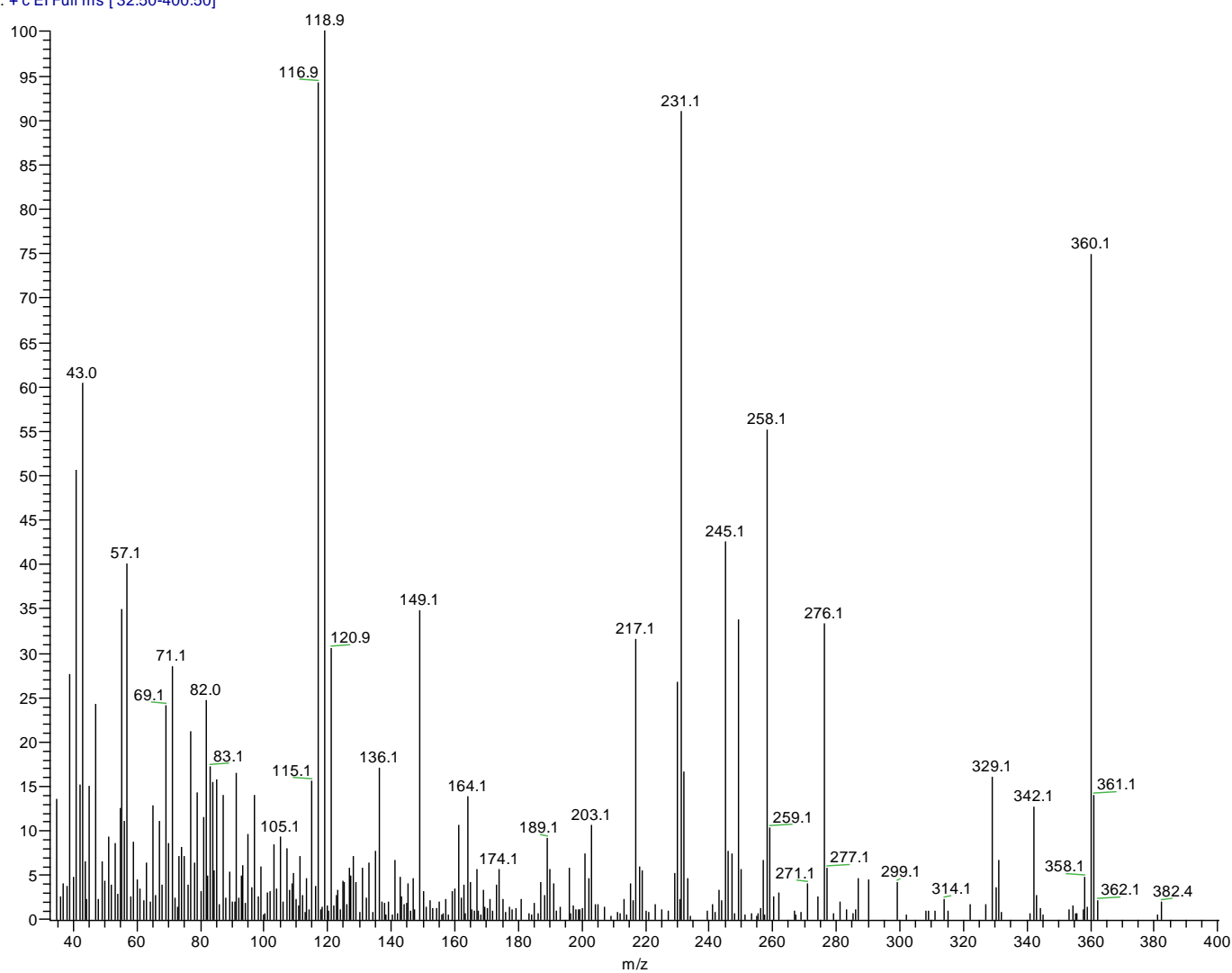
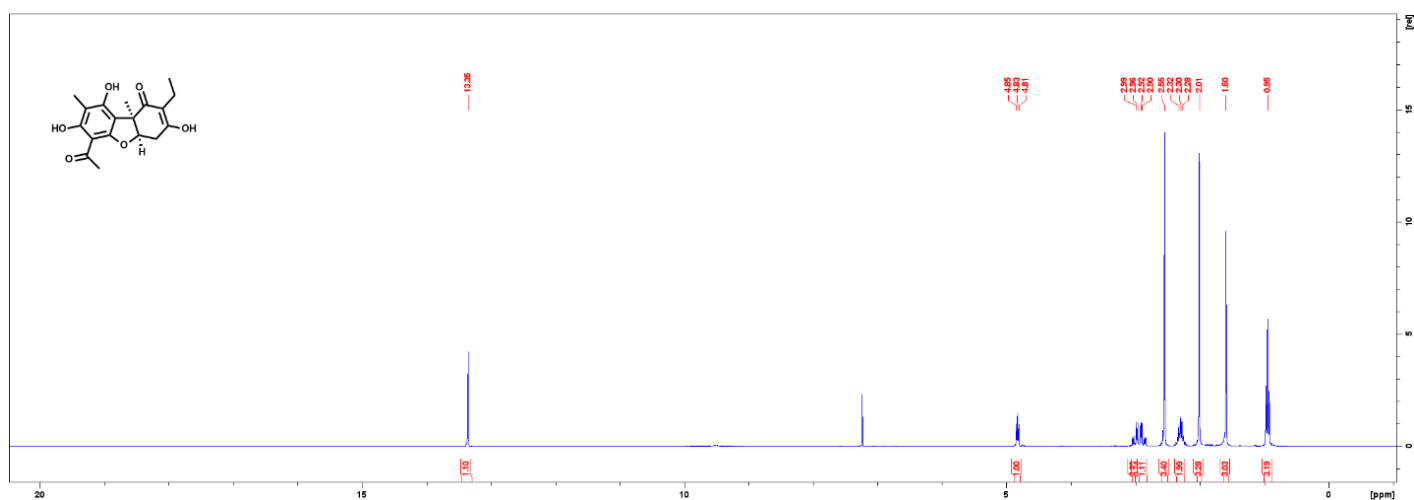
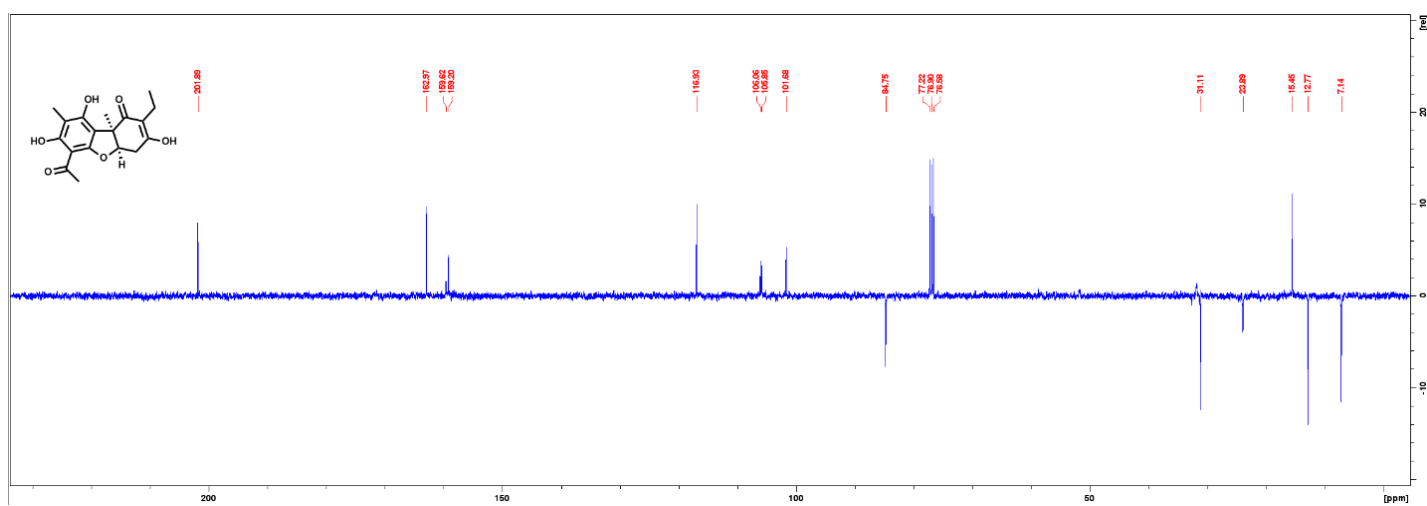


Figure S6. DFS spectrum of 10.

Figure S7. NMR ¹H spectrum of 12.Figure S8. NMR ¹³C spectrum of 12.

OL11-104-6 #19 RT: 1.06 AV: 1 NL: 4.25E5
T: + c EI Full ms [14.50-380.50]

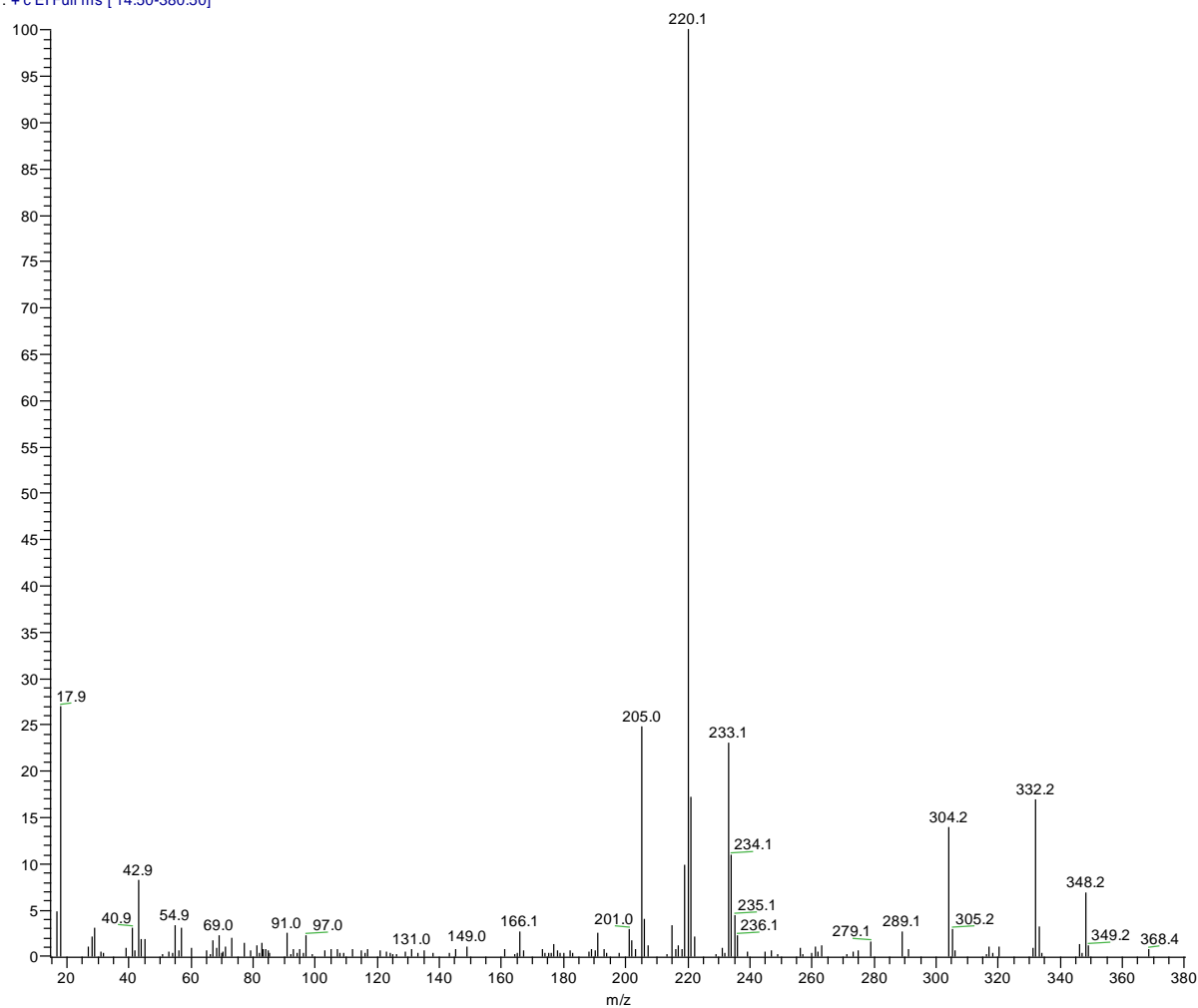


Figure S9. DFS spectrum of 12.

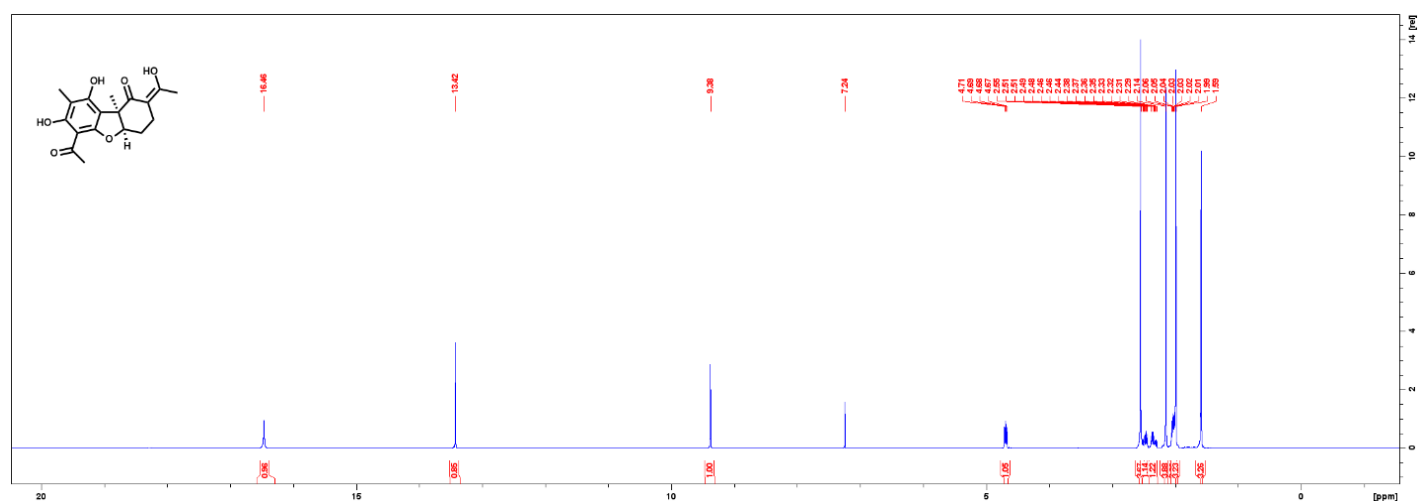
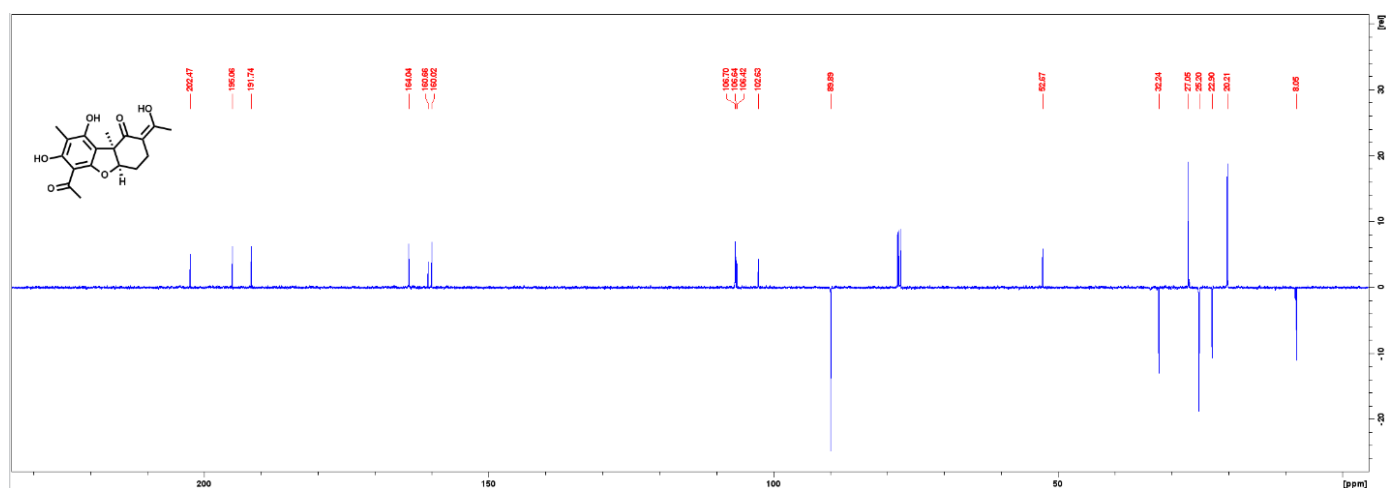


Figure S10. NMR ¹H spectrum of 13.

Figure S11. NMR ^{13}C spectrum of 13.

OL11-104-1 #4 RT: 0.18 AV: 1 NL: 2.36E6
T: + c EI Full ms [32.50-380.50]

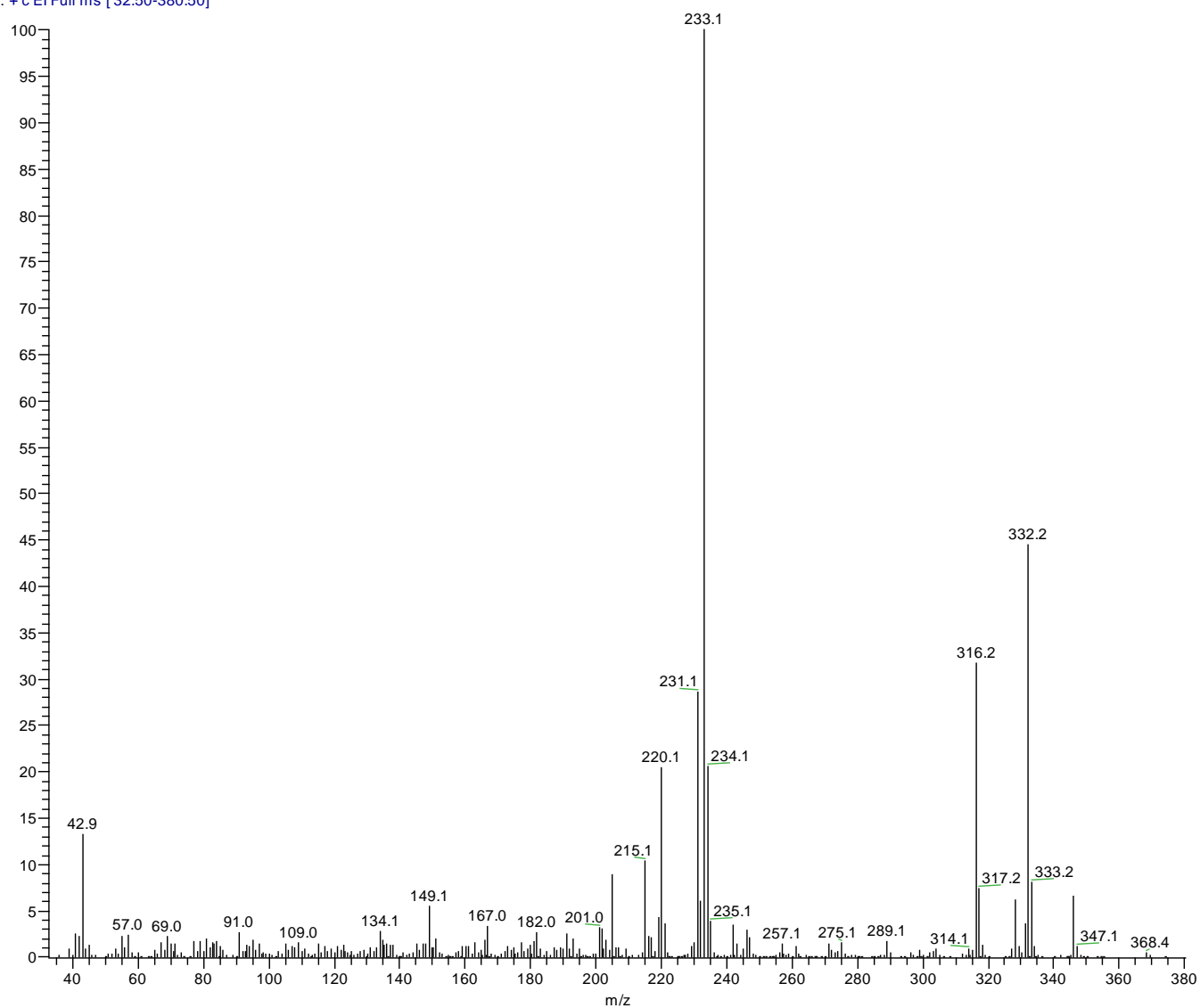
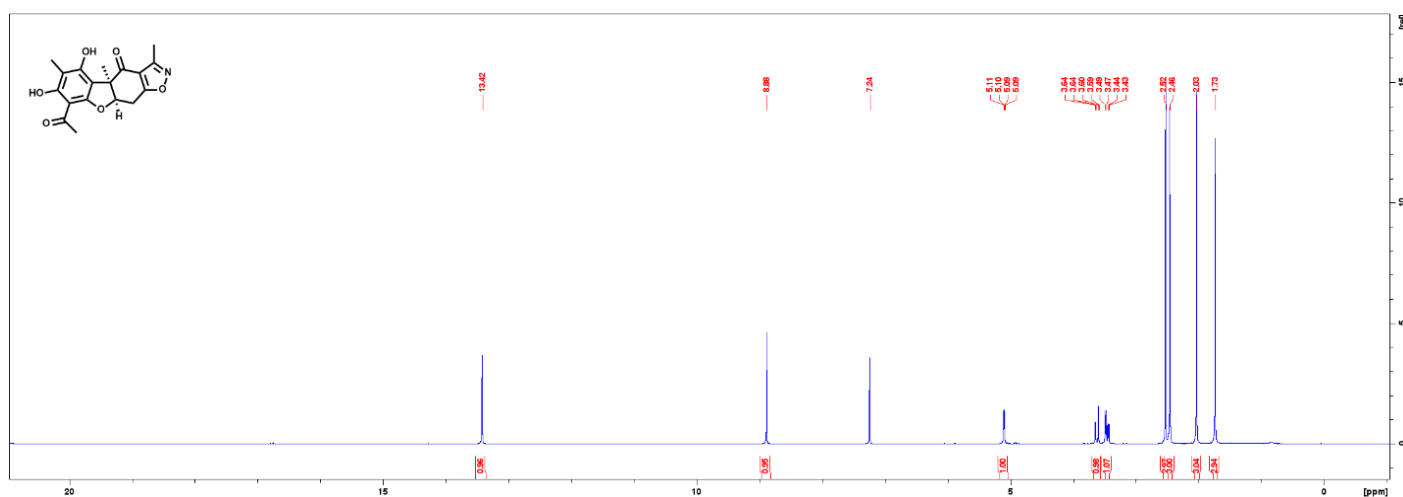
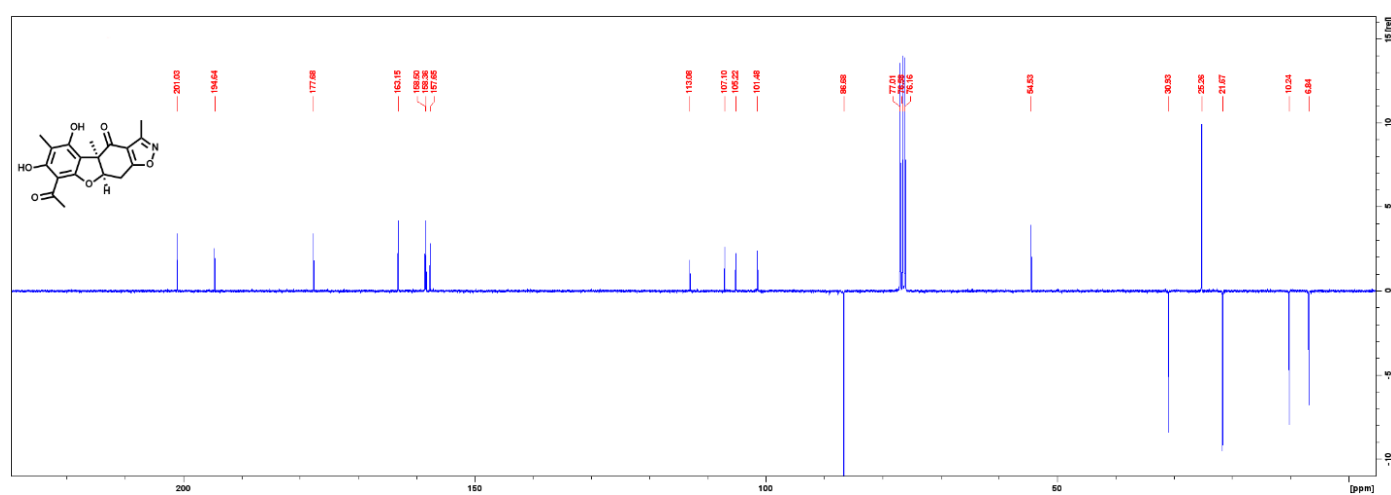


Figure S12. DFS spectrum of 13.

Figure S13. NMR ¹H spectrum of 14.Figure S14. NMR ¹³C spectrum of 14.

OL-12-120-10 #12 RT: 0.82 AV: 1 NL: 1.03E5
T: + c EI Full ms [14.50-370.50]

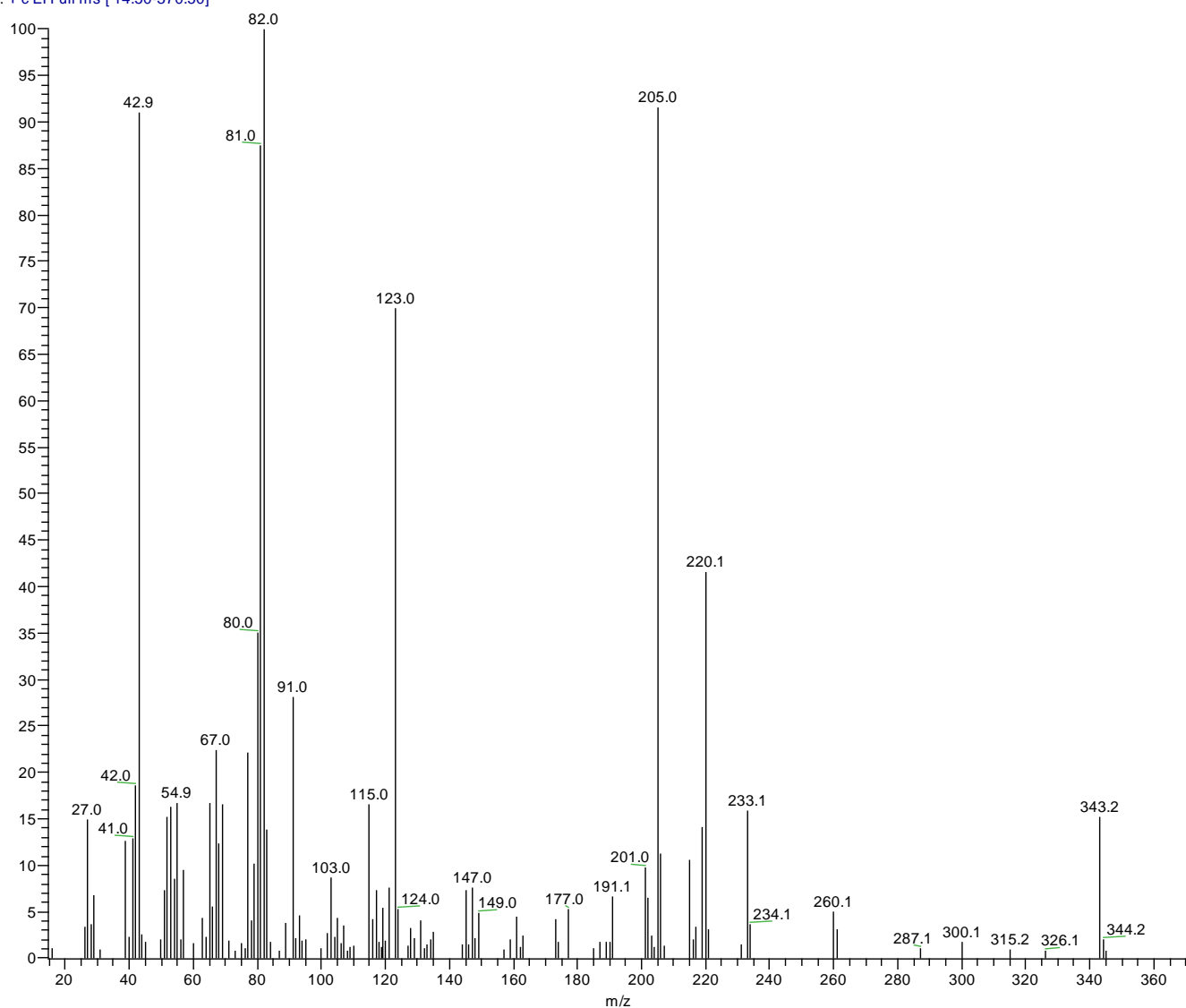
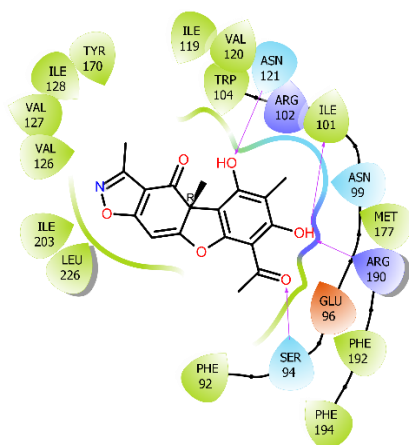
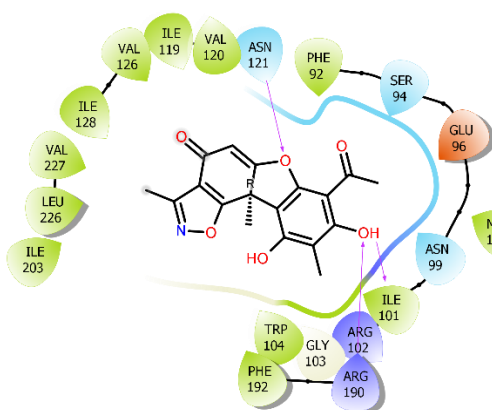


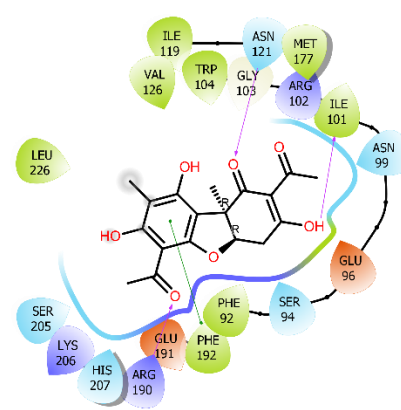
Figure S15. DFS spectrum of 14.



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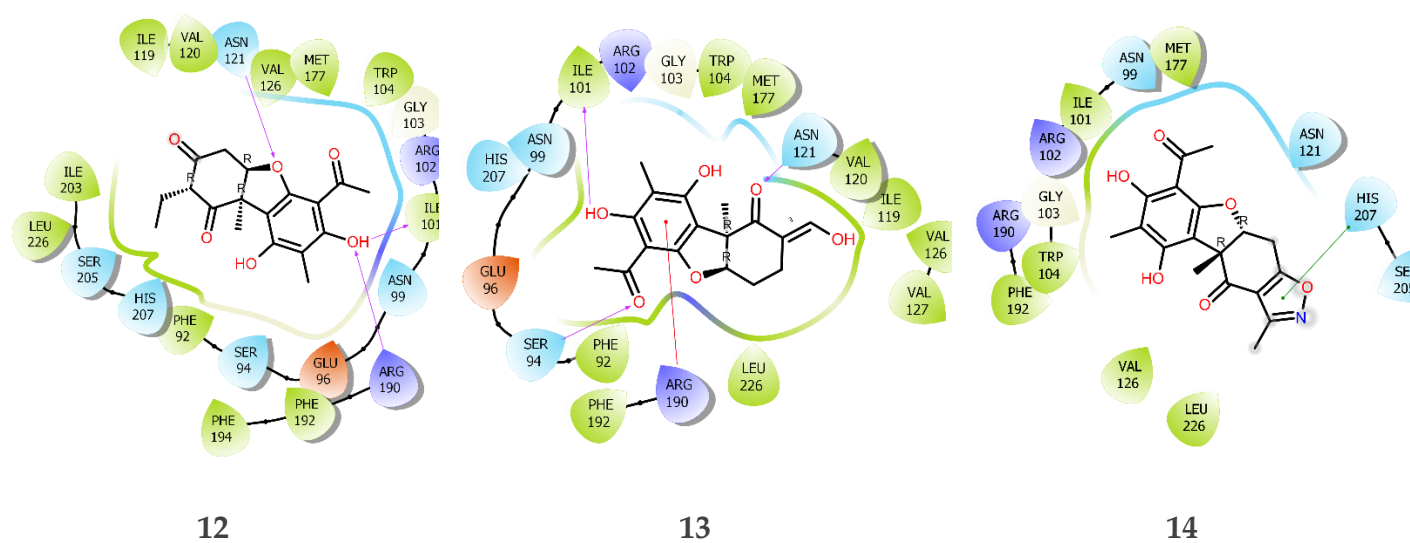


Figure S16. Location ligands in the biliverdin binding site.

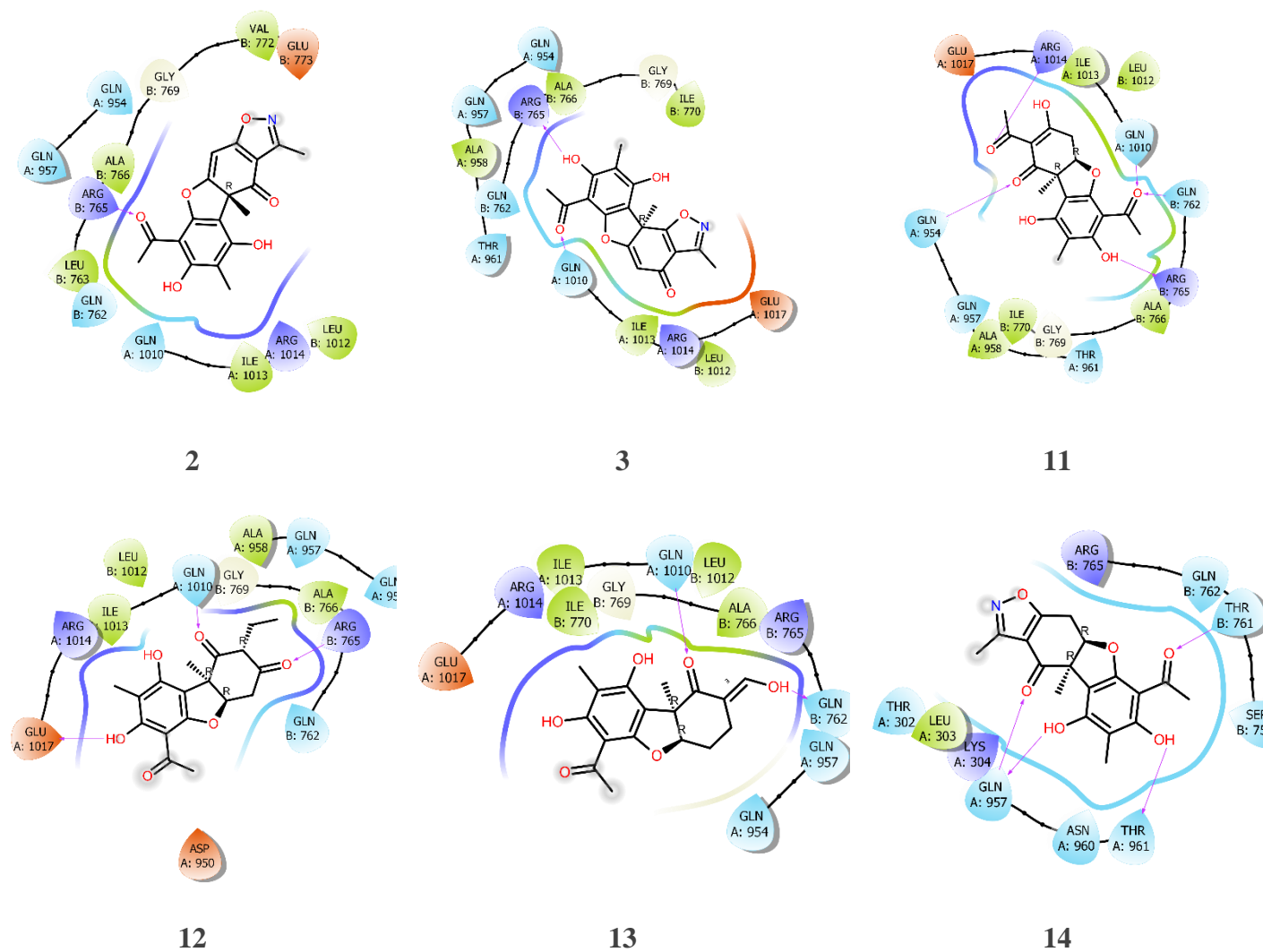


Figure S17. Location ligands in the UA-30 and nelfinavir binding site.

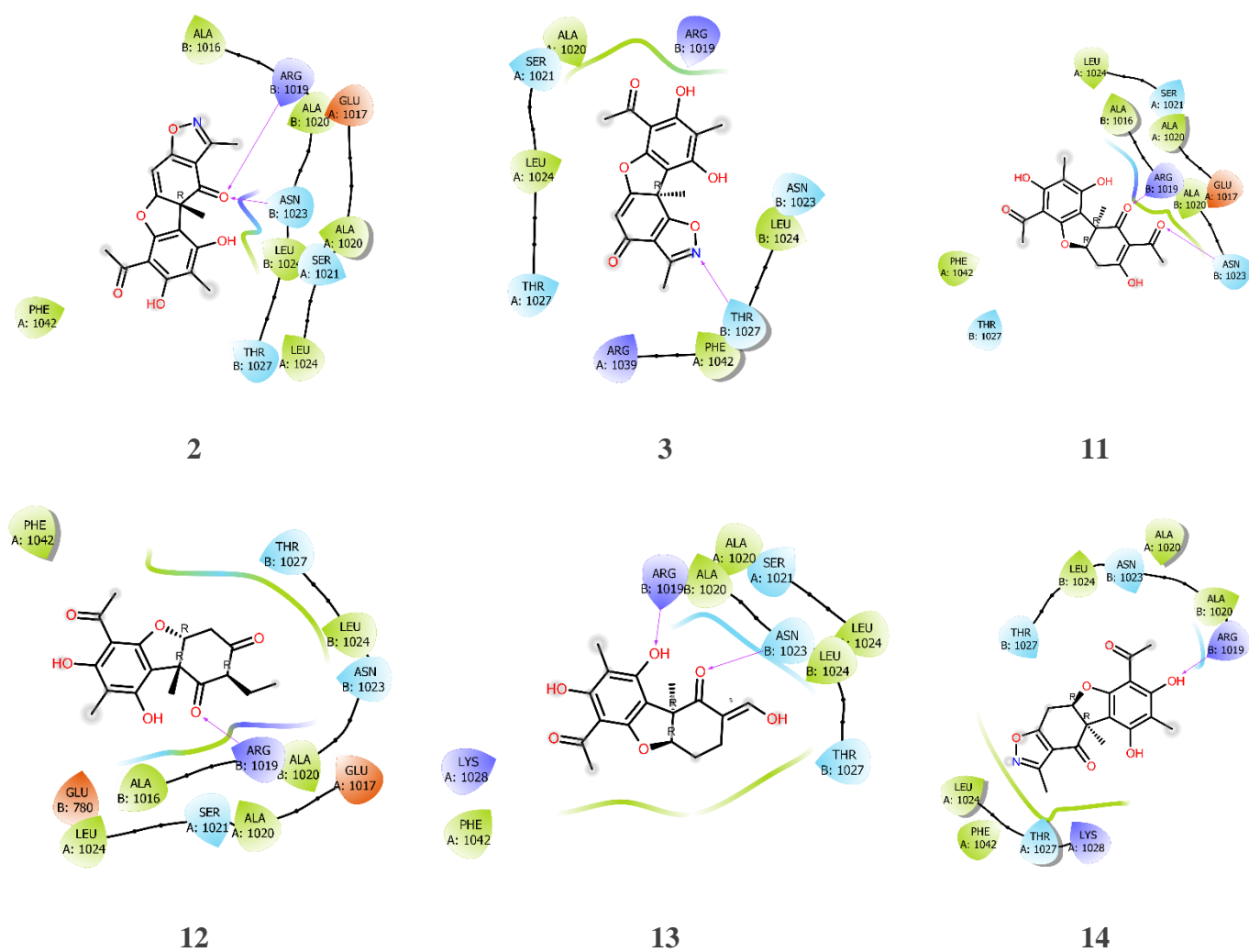
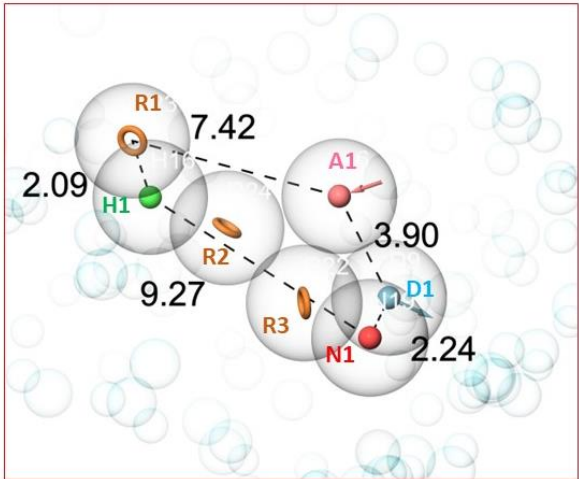
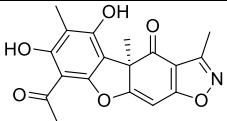
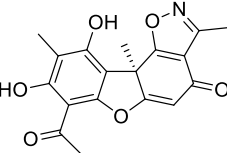
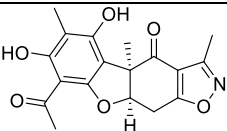
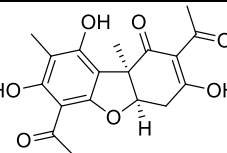
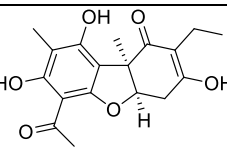
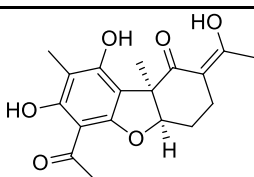



Figure S18. Location ligands in the umifenovir binding site.

Table S1. Molecular modeling results.

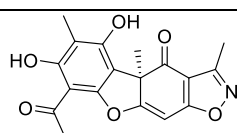
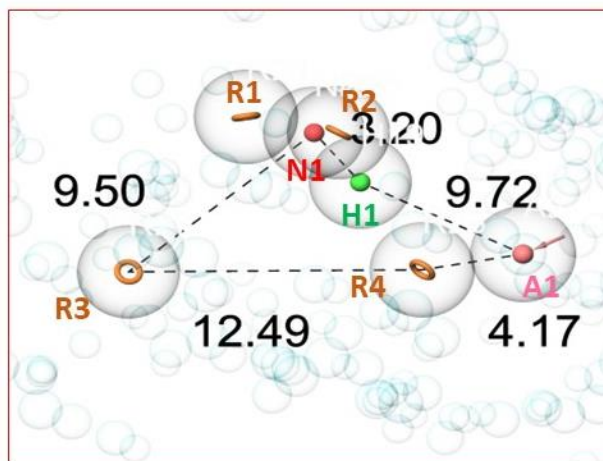
#	Structure	In Vivo (IC ₅₀)	In Vitro (Pseudo- type-Based Assay)	Matched Ligand Site	Glide Score	Emodel	IFD Score	H-Bond	Other Interaction	Clash
	BILIVERDIN BINDING SITE									
										
2	 Chemical Formula: C ₁₈ H ₁₅ NO ₆ Molecular Weight: 341,31	n/a	yes	R1; H1; R2; A1	−6.118	−43.497	−614.43	Asn121, Ser94 Arg120, Ile101,	Leu226, Ile203, Trp104 hydro- phobic	Asn121
3	 Chemical Formula: C ₁₈ H ₁₅ NO ₆ Molecular Weight: 341,31	9.2	> 25	R1; H1; R2; A1	−8.124	−57.934	−613.90	Asn121, Arg120, Ile101,	Trp104 hydro- phobic	
14	 Chemical Formula: C ₁₈ H ₁₇ NO ₆ Molecular Weight: 343,33	n/a	n/a	H1; R2; A1	−5.406	−43.406	−615.87	none	His207 pi-pi stacking; Ile101, Trp104 hydro- phobic	Ile101
11	 Chemical Formula: C ₁₈ H ₁₈ O ₇ Molecular Weight: 346,33	21.0	22	R1; H1; D1; R3	−7.465	−63.583	−617.77	Asn121, Ile101, Arg190	Phe190 pi-pi stacking	
12	 Chemical Formula: C ₁₈ H ₂₀ O ₆ Molecular Weight: 332,35	91.0	>25 (5)	H1; R2; A1	−8.116	−55.76	−616.79	Asn121, Ile101, Arg190	Ile203, Phe92, Trp104 hydro- phobic	




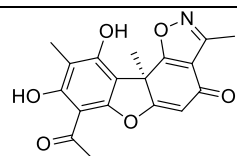
13		6.7	5	H1; R2; A1	-8.908	-70.987	-615.62	Asn121; Ile101; Se94	Arg190 – pi-cation;
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Chemical Formula: C₁₈H₂₀O₆
Molecular Weight: 332,35

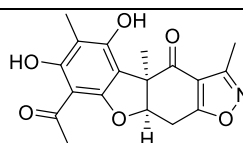
UA-30 AND NELFINAVIR BINDING SITE




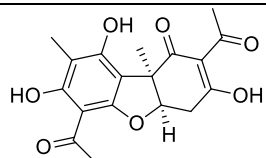
2		n/a	yes	A1; H1; R4	-6.923	-53.724	-6010.48	B: Arg765	B: Ala766 hydrophobic
<p>Chemical Formula: C₁₈H₁₅NO₆</p> <p>Molecular Weight: 341.31</p>									




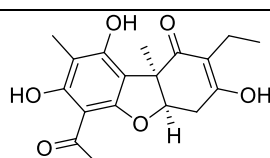
3		9.2	> 25	A1; H1; R2; R4	-7.513	-63.046	-6011.35	B: Arg765 A: Gln1010	A: Leu1013; B: Leu1012. A: Gln954;	B: Arg765
Chemical Formula: C ₁₈ H ₁₅ NO ₆ Molecular Weight: 341,31										




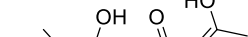
14		n/a	n/a	R1	-6.192	-48.886	-6011.77	A: Gln957 A: Thr961 B: Thr761	B: Arg765 B: Ser768.	A: Thr302
<p>Chemical Formula: C₁₈H₁₇NO₆</p> <p>Molecular Weight: 343.33</p>										



11	 <p>Chemical Formula: C₁₈H₁₈O₇ Molecular Weight: 346.33</p>	21.0	22	R2	-8.806	-66.965	-6014.29	A: Arg765; B: Gln762; A: Gln1010; A: Arg1014; A: Gln954	B: Leu1012 hy- dropobic	A: Gln954
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12		91.0	>25 (5)	R2	-6.180	-54.713	-6009.85	A: Gln1010; B: Arg765; A: Glu1017	B: Ala766; B: Leu1012 hy- drophobic
Chemical Formula: C ₁₈ H ₂₀ O ₆ Molecular Weight: 332,35									

13	 <p>Chemical Formula: C₁₈H₂₀O₆ Molecular Weight: 332,35</p>	6.7	5	D3; R3	-4.288	-35.676	-6081.82	B: Arg1019 B: Asn1023	B: Leu 1024; B: Ala1020 hydrophobic
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