Supporting information

Jejucarbazoles A-C, Carbazole Glycosides with Indoleamine 2,3-dioxygenase 1 Inhibitory Activity from *Streptomyces* sp. KCB15JA151

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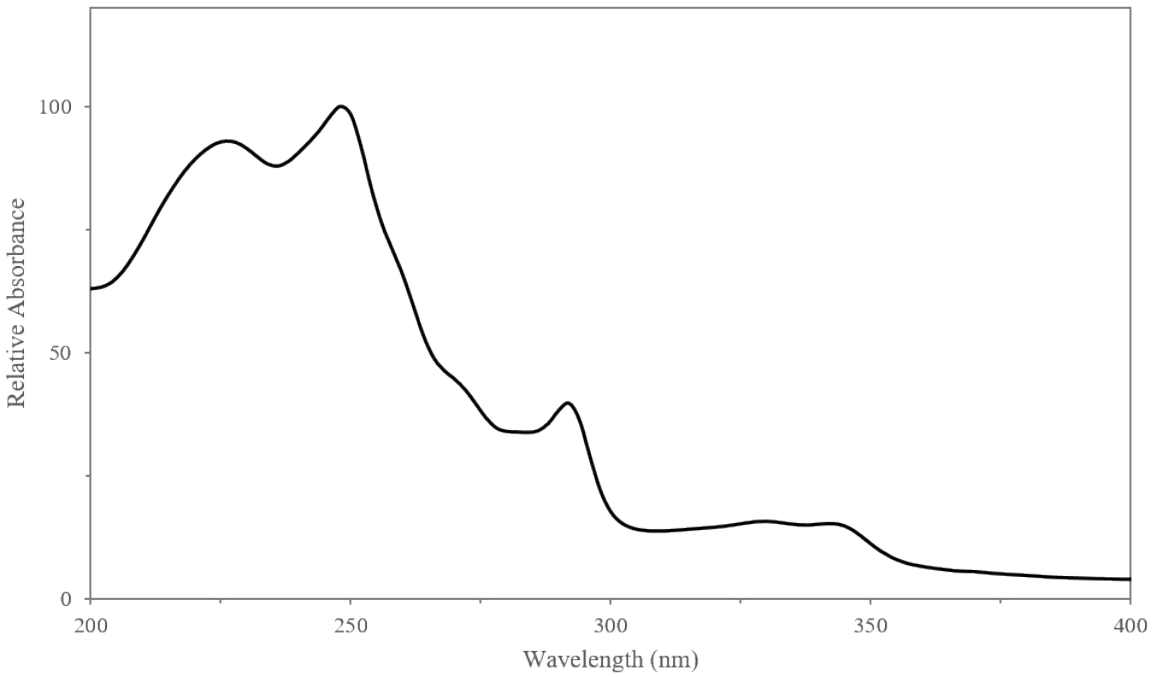


Fig. S1. UPLC-UV spectrum of compound **1** in MeCN-H2O containing 0.05% Formic acid

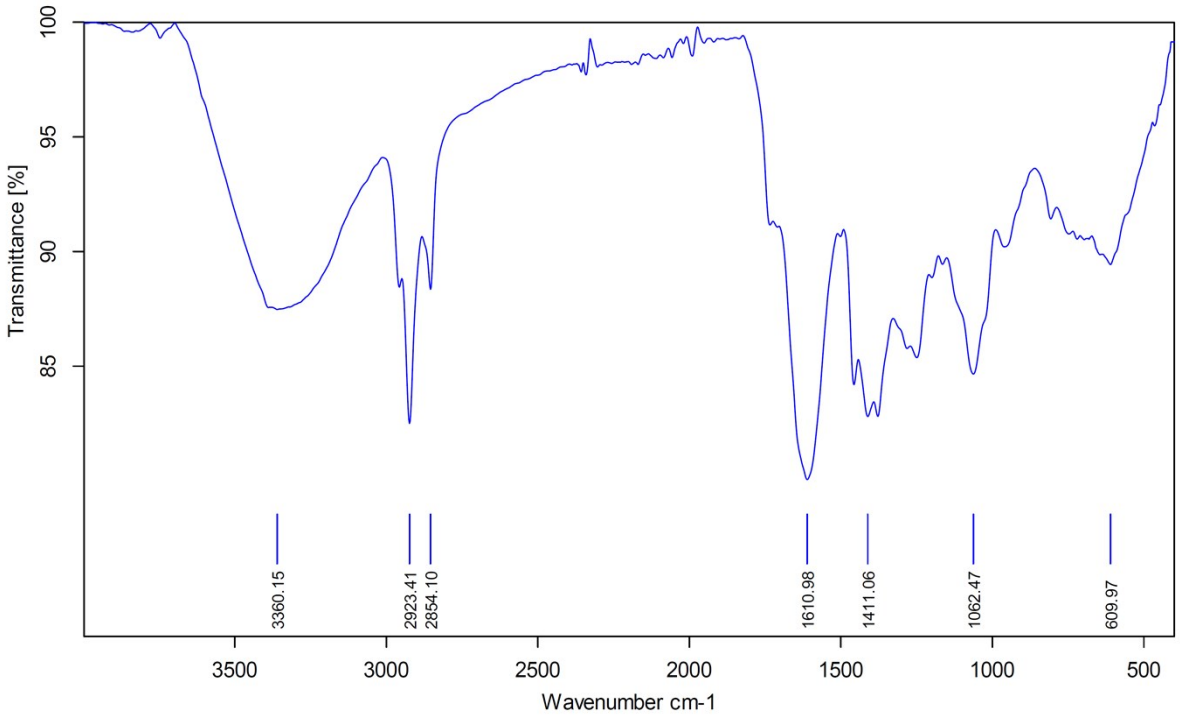


Fig. S2. IR spectrum of compound **1**

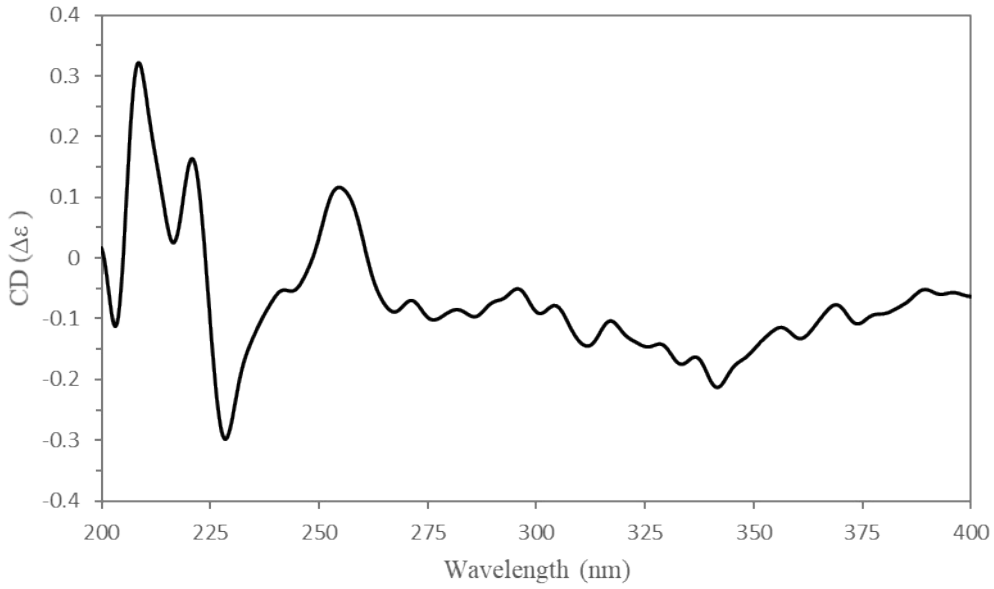


Fig. S3. CD spectrum of compound **1**

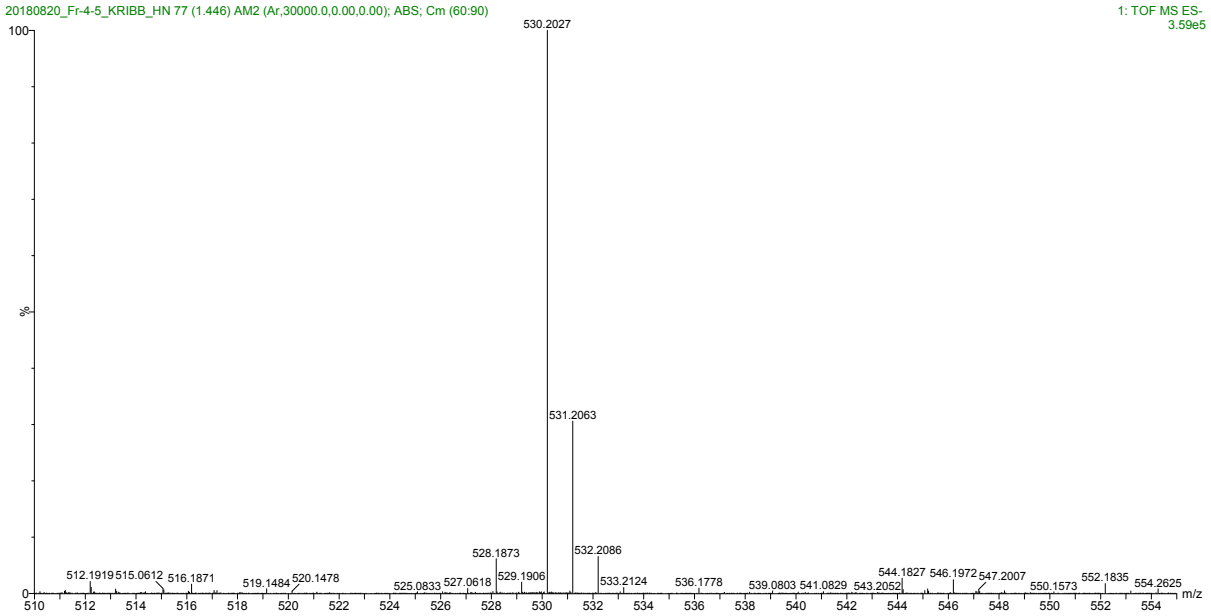


Fig. S4. HR-ESI-TOF-MS negative spectrum in compound **1**

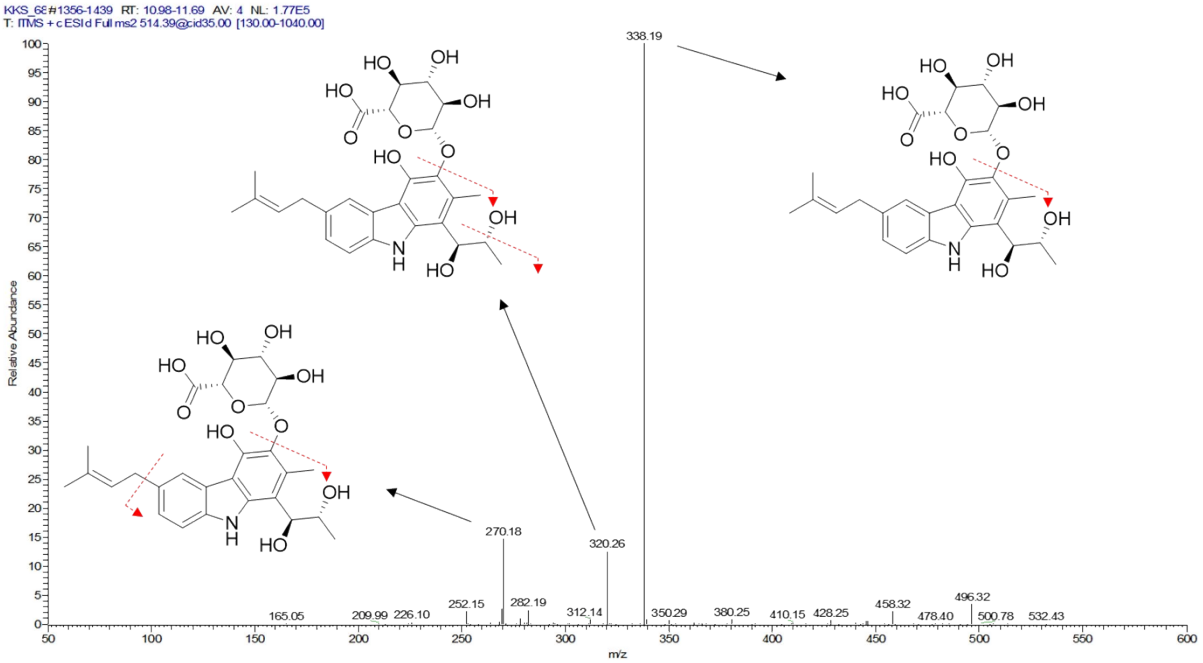


Fig. S5. MS/MS fragmentation spectrum of compound **1** (parent ion, 514.39 $[M + H - H_2O]^+$)

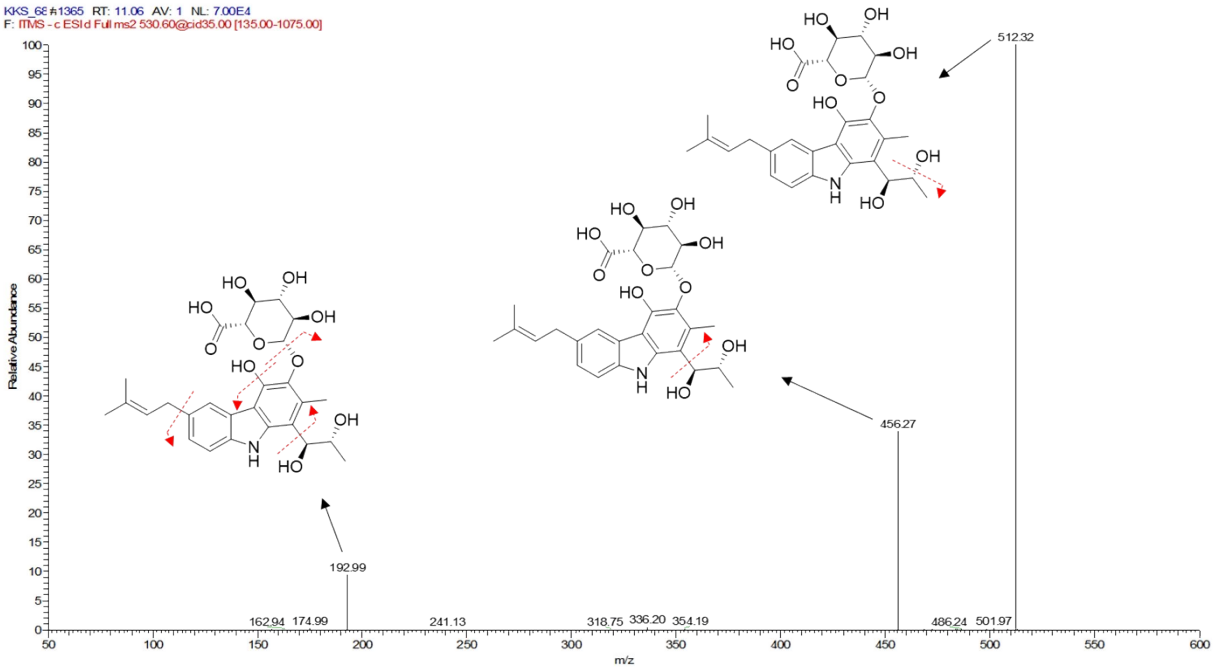
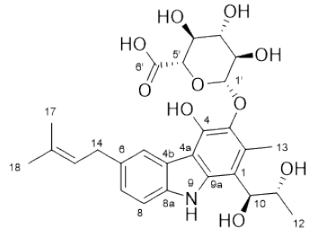


Fig. S6. MS/MS fragmentation spectrum of compound **1** (parent ion, 530.60 $[M - H]^-$)



Jejucarbazole A (**1**)

Fig. S7. ^{1}H NMR spectrum of compound **1** in Acetone-d_6

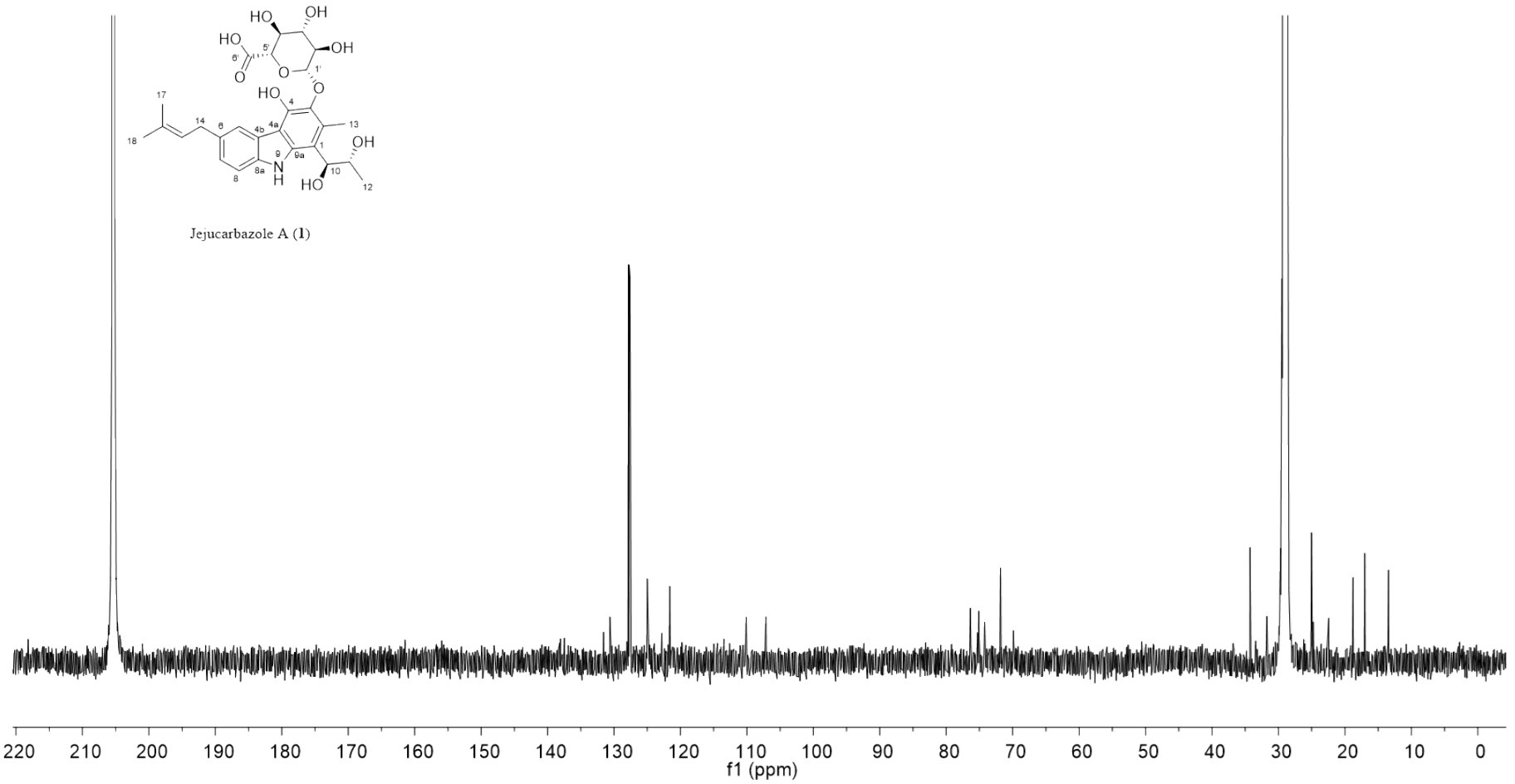


Fig. S8. ^{13}C NMR spectrum of compound **1** in Acetone-d_6

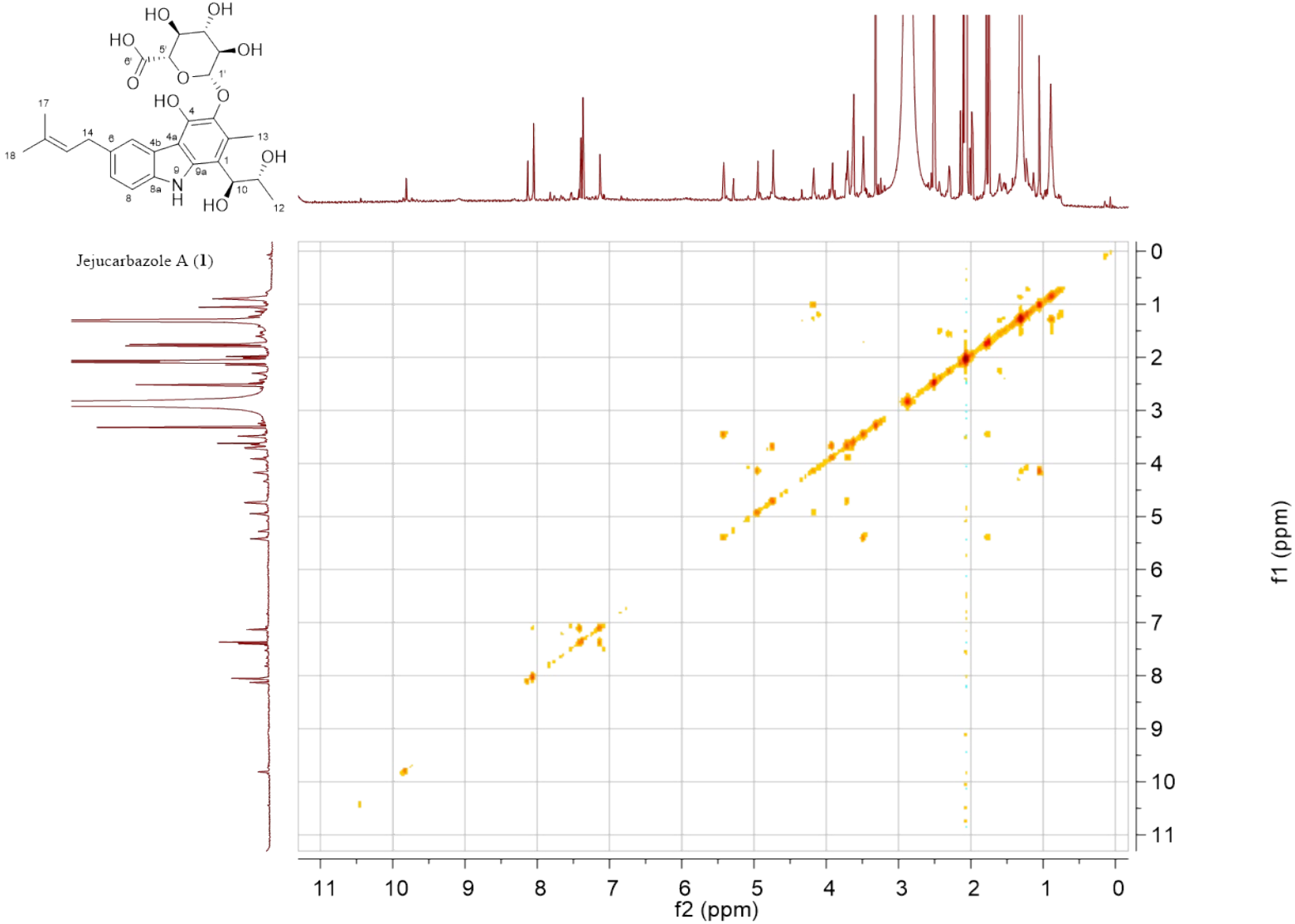


Fig. S9. COSY NMR spectrum of compound **1** in Acetone-d_6

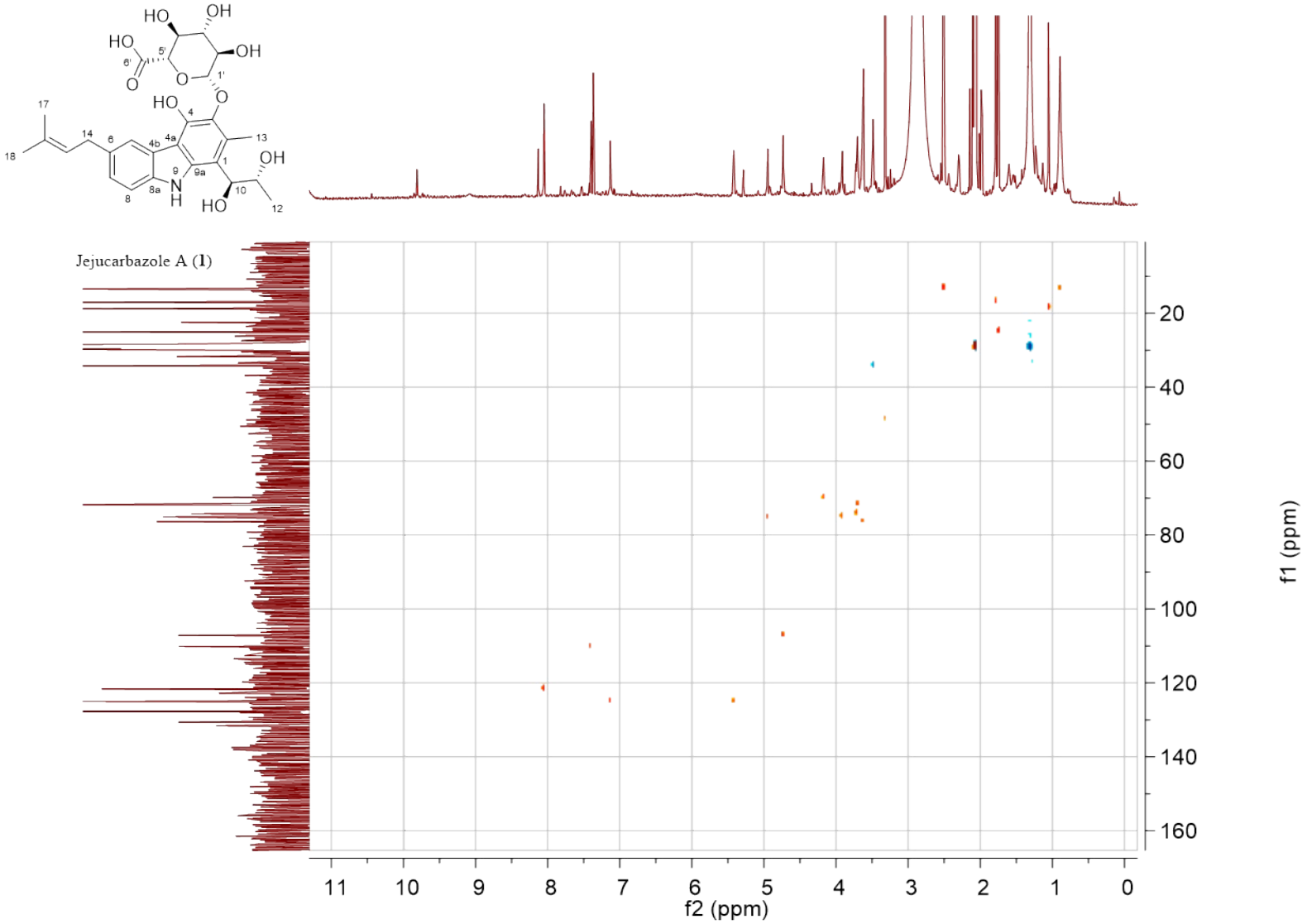


Fig. S10. HSQC-DEPT NMR spectrum of compound **1** in Acetone-d_6

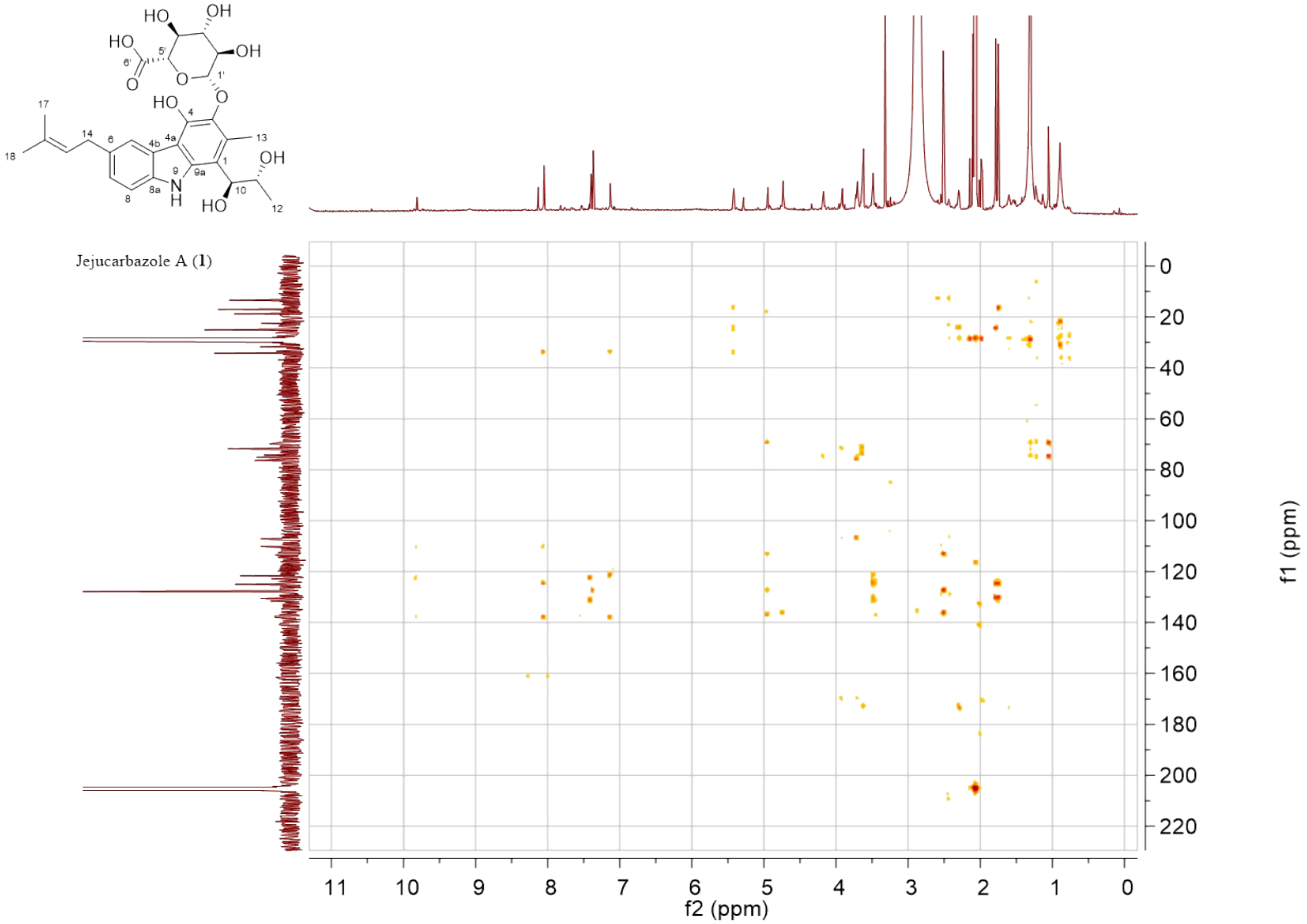


Fig. S11. HMBC NMR spectrum of compound **1** in Acetone-d_6

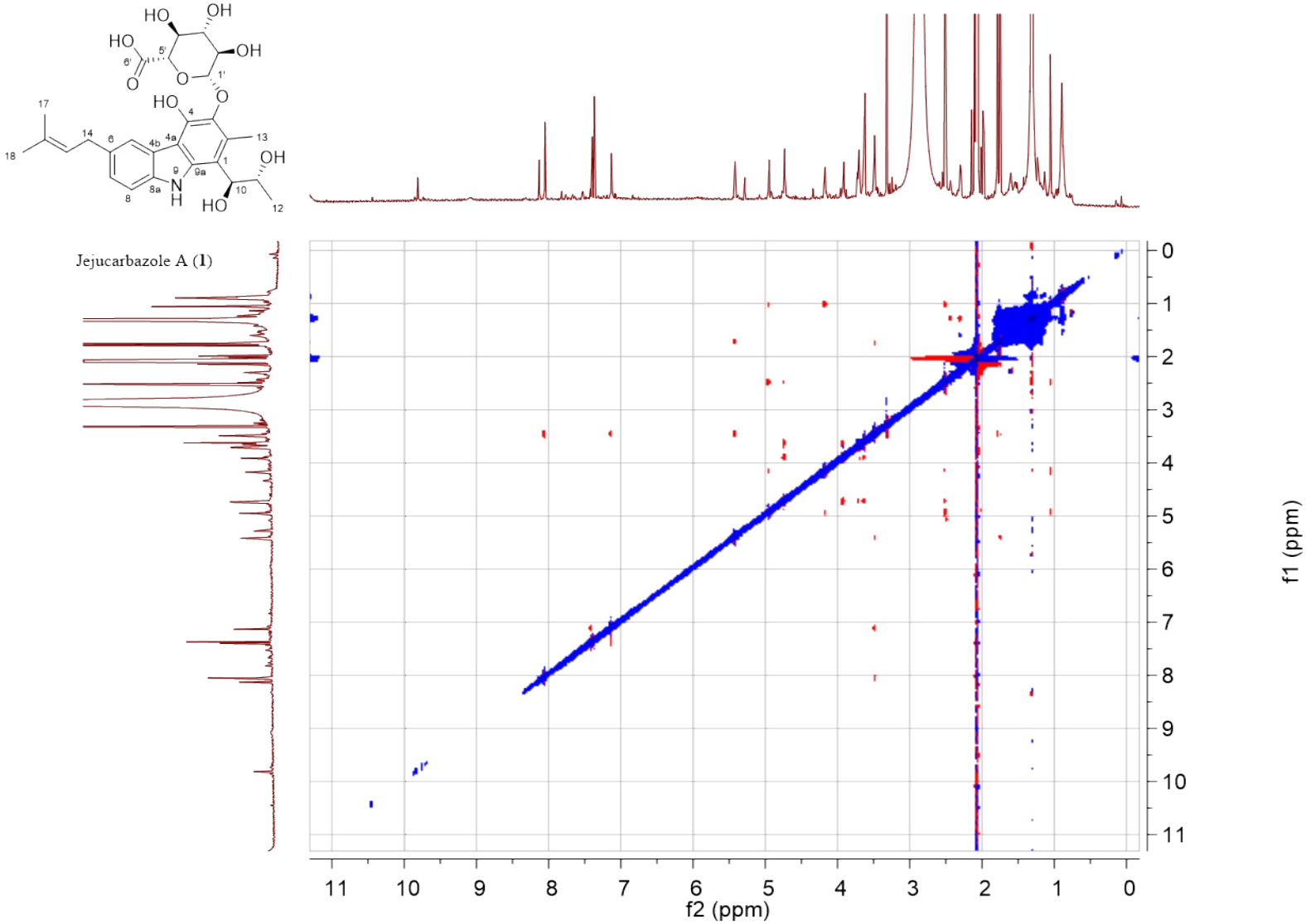


Fig. S12. ROESY NMR spectrum of compound **1** in Acetone-d_6

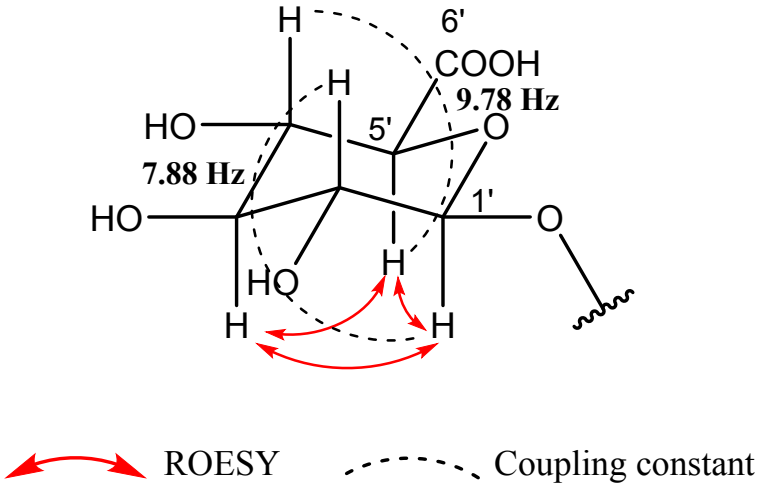


Fig. S13. The relative configuration of the sugar unit in compound **1**

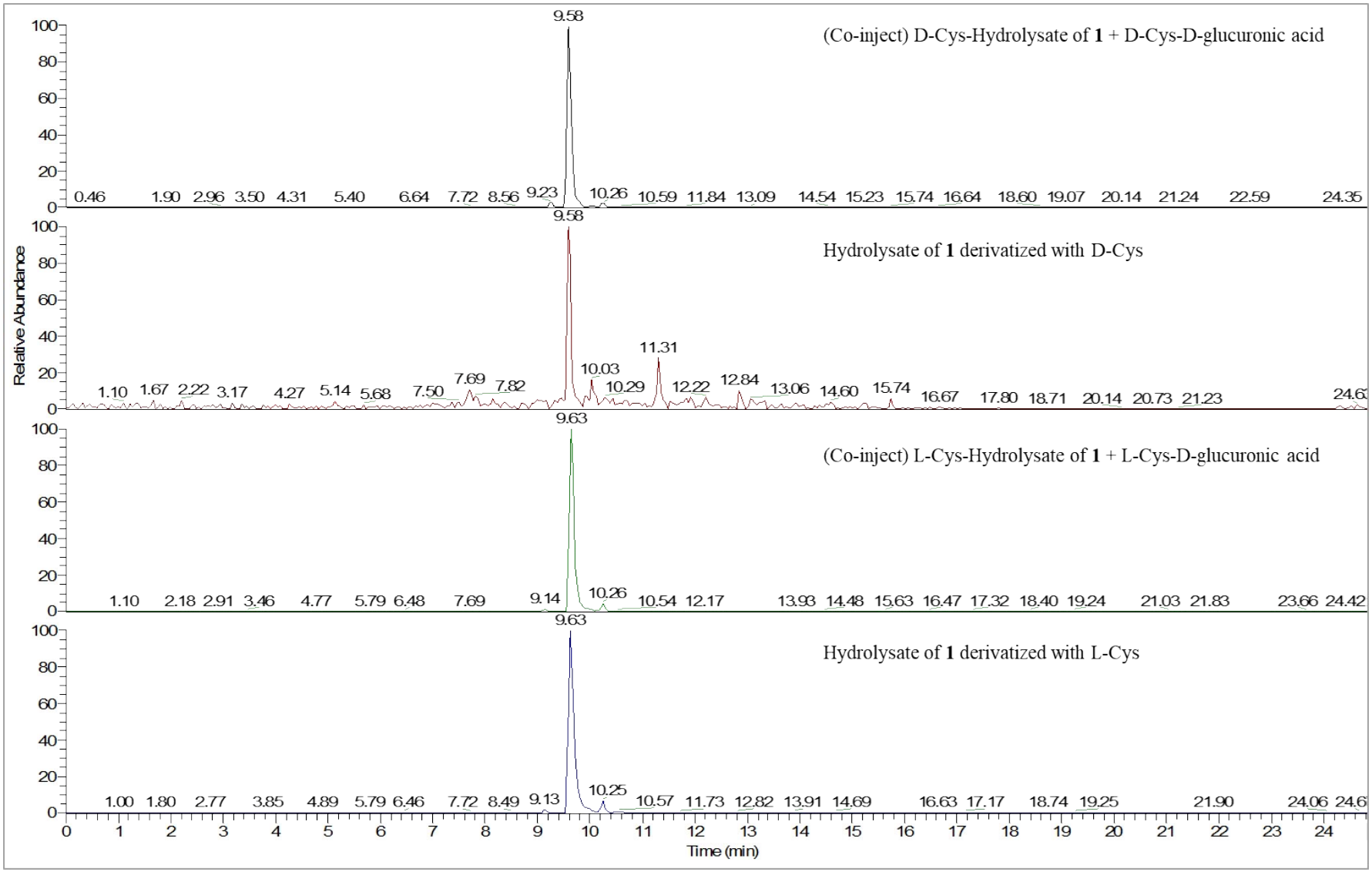


Fig. S14. LC-MS analysis for thiocarbamate derivatives of the sugar unit in **1** (Selected ion at m/z 461.0-461.99 $[M+H]^+$)

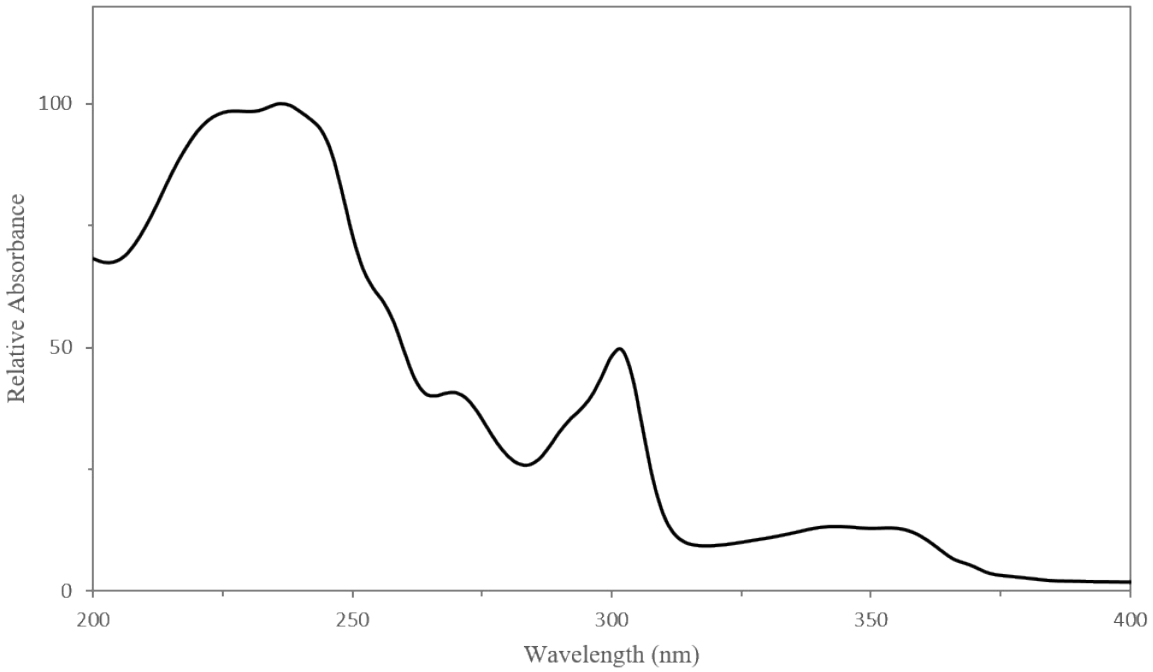


Fig. S15. UPLC-UV spectrum of compound **2** in MeCN-H2O containing 0.05% Formic acid

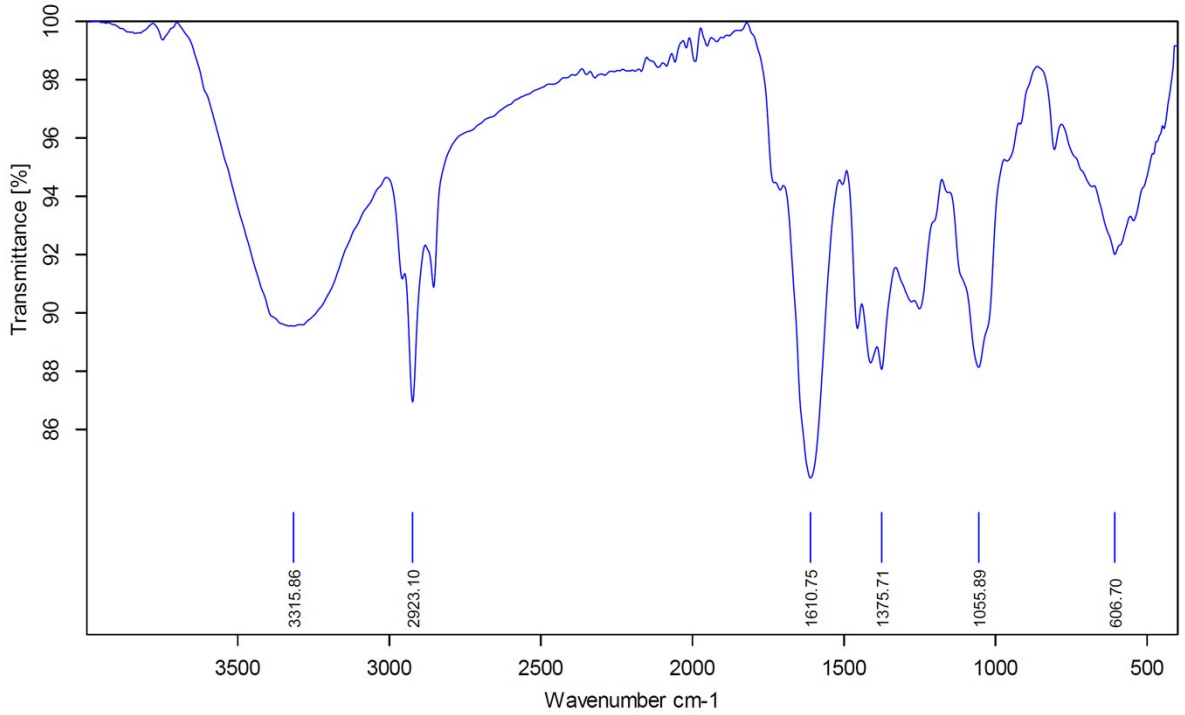


Fig. S16. IR spectrum of compound **2**

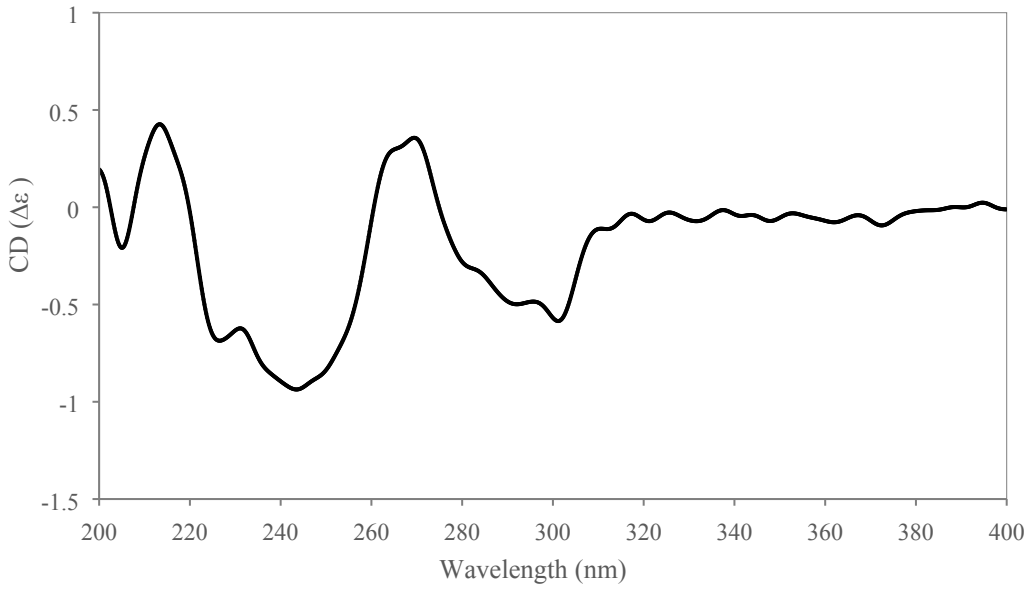


Fig. S17. CD spectrum of compound **2**

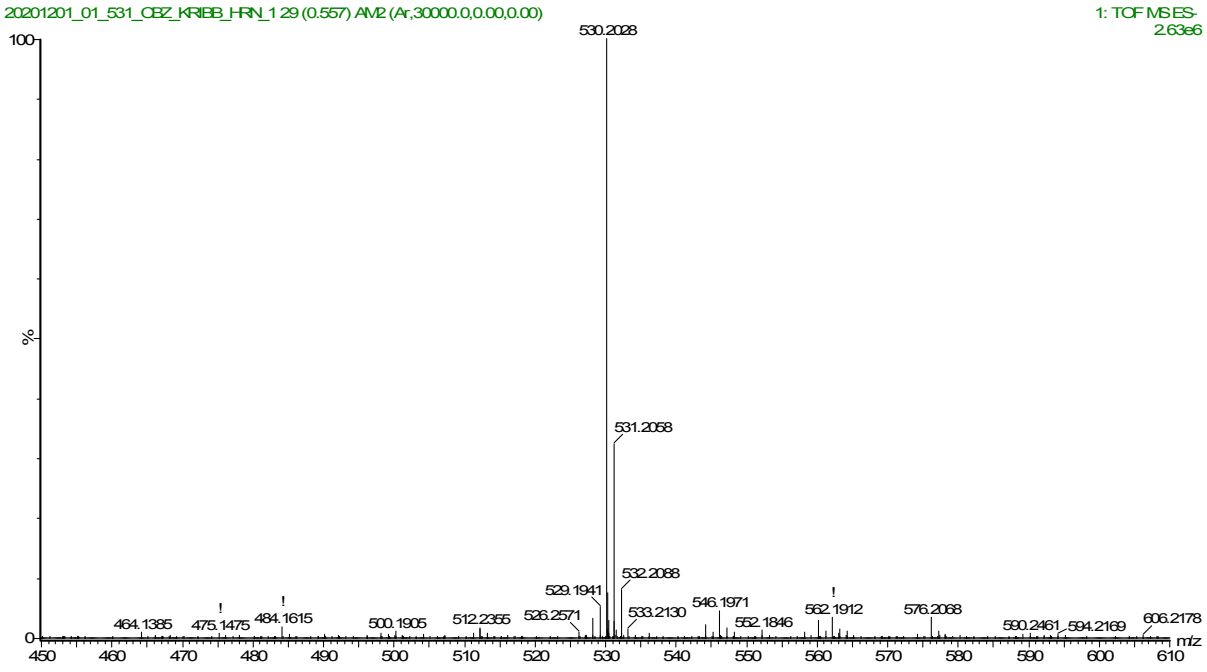


Fig. S18. HR-ESI-TOF-MS negative spectrum in compound **2**

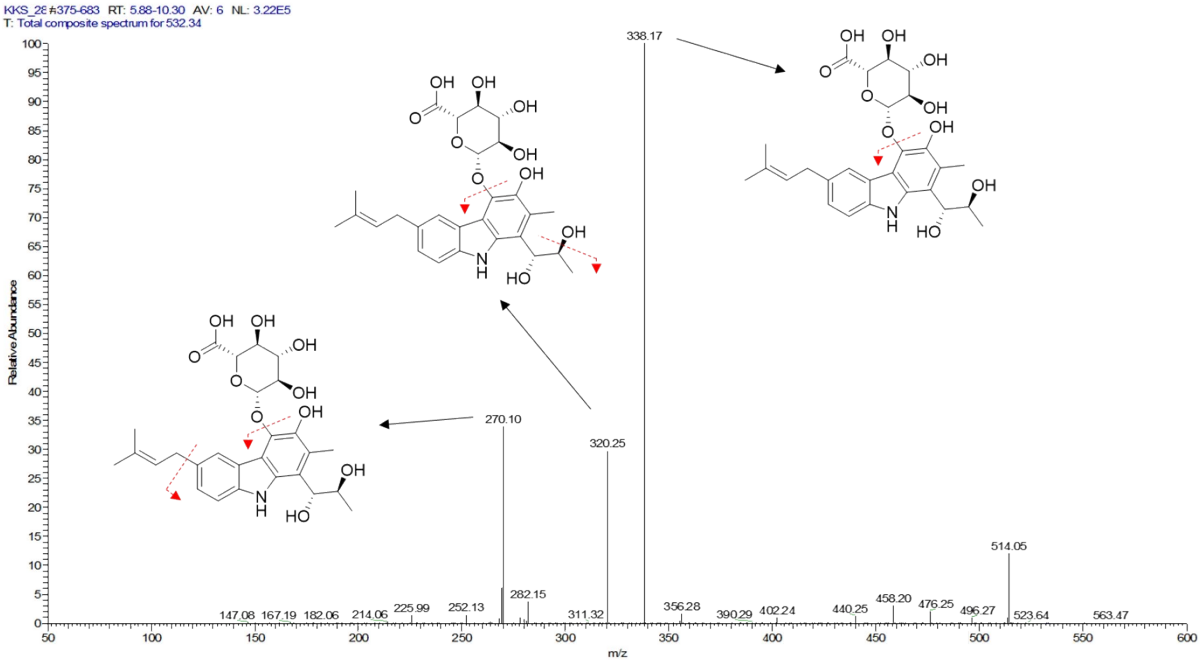


Fig. S19. MS/MS fragmentation spectrum of compound **2** (parent ion, 532.34 $[M + H]^+$)

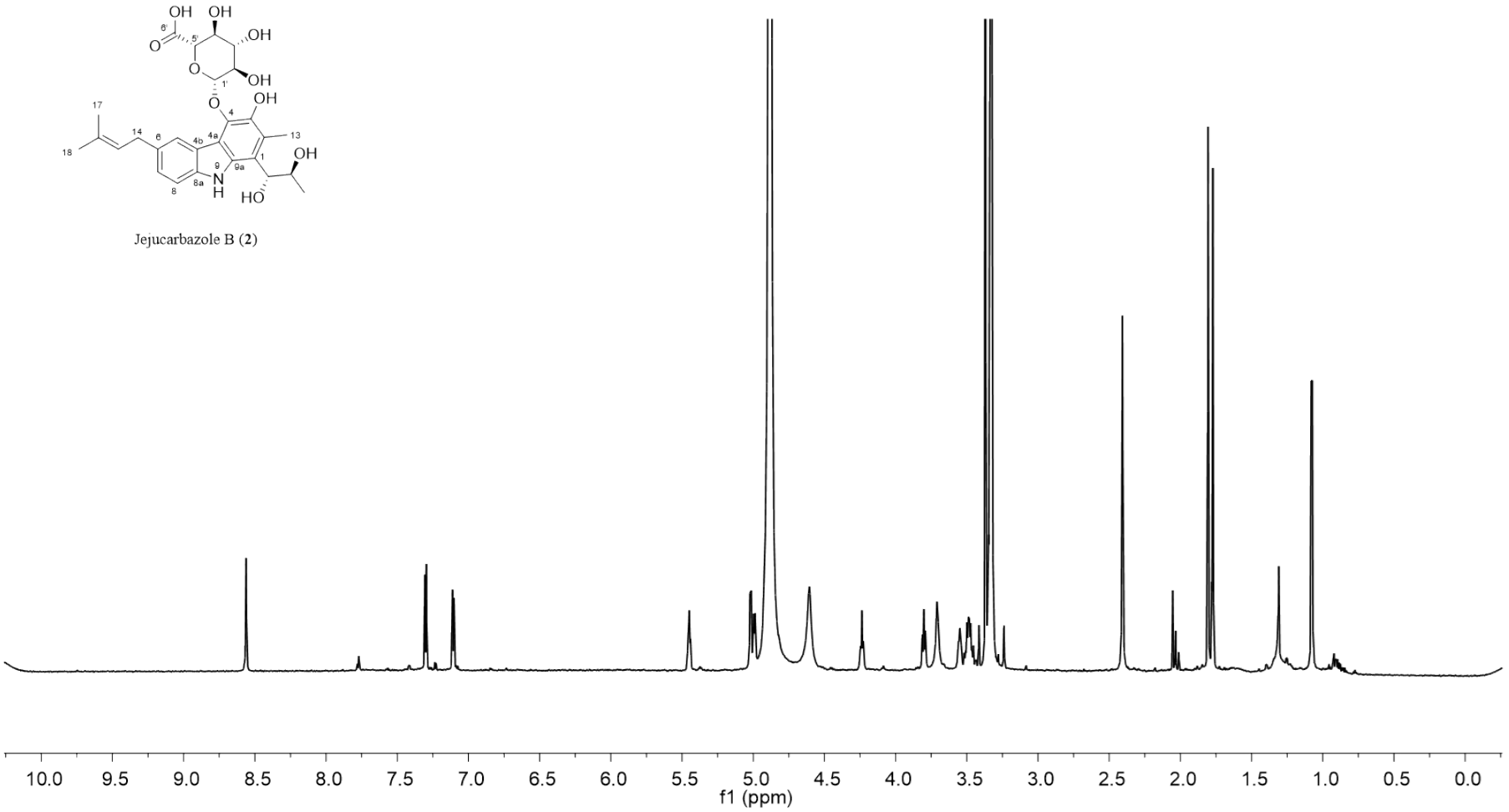
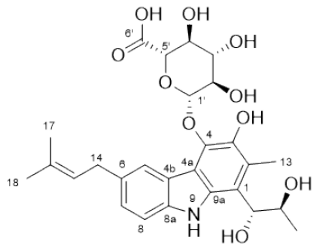


Fig. S20. ^{1}H NMR spectrum of compound **2** in CD_3OD



Jejucarbazole B (**2**)

Fig. S21. ^{13}C NMR spectrum of compound **2** in CD_3OD

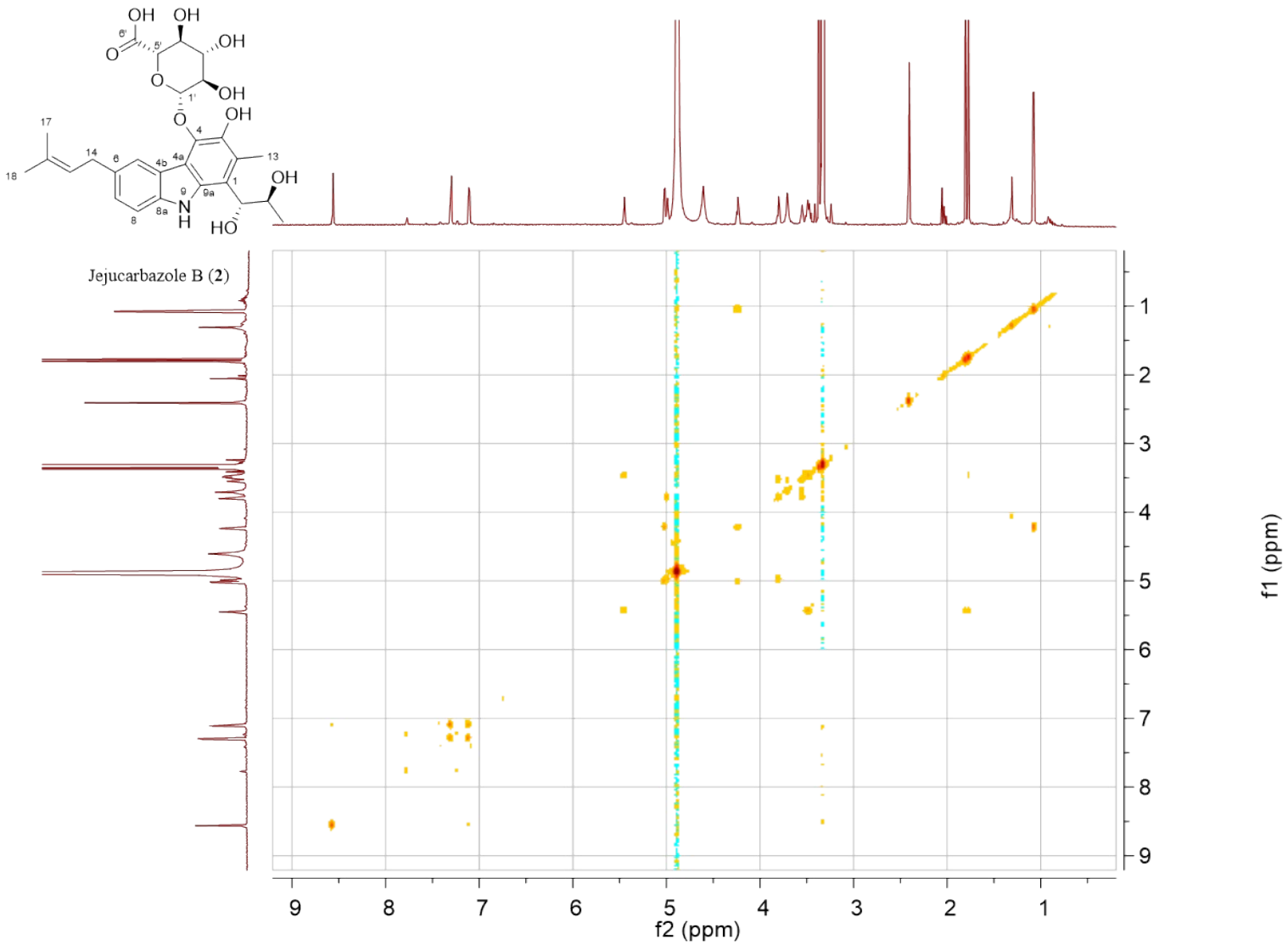


Fig. S22. COSY NMR spectrum of compound **2** in CD_3OD

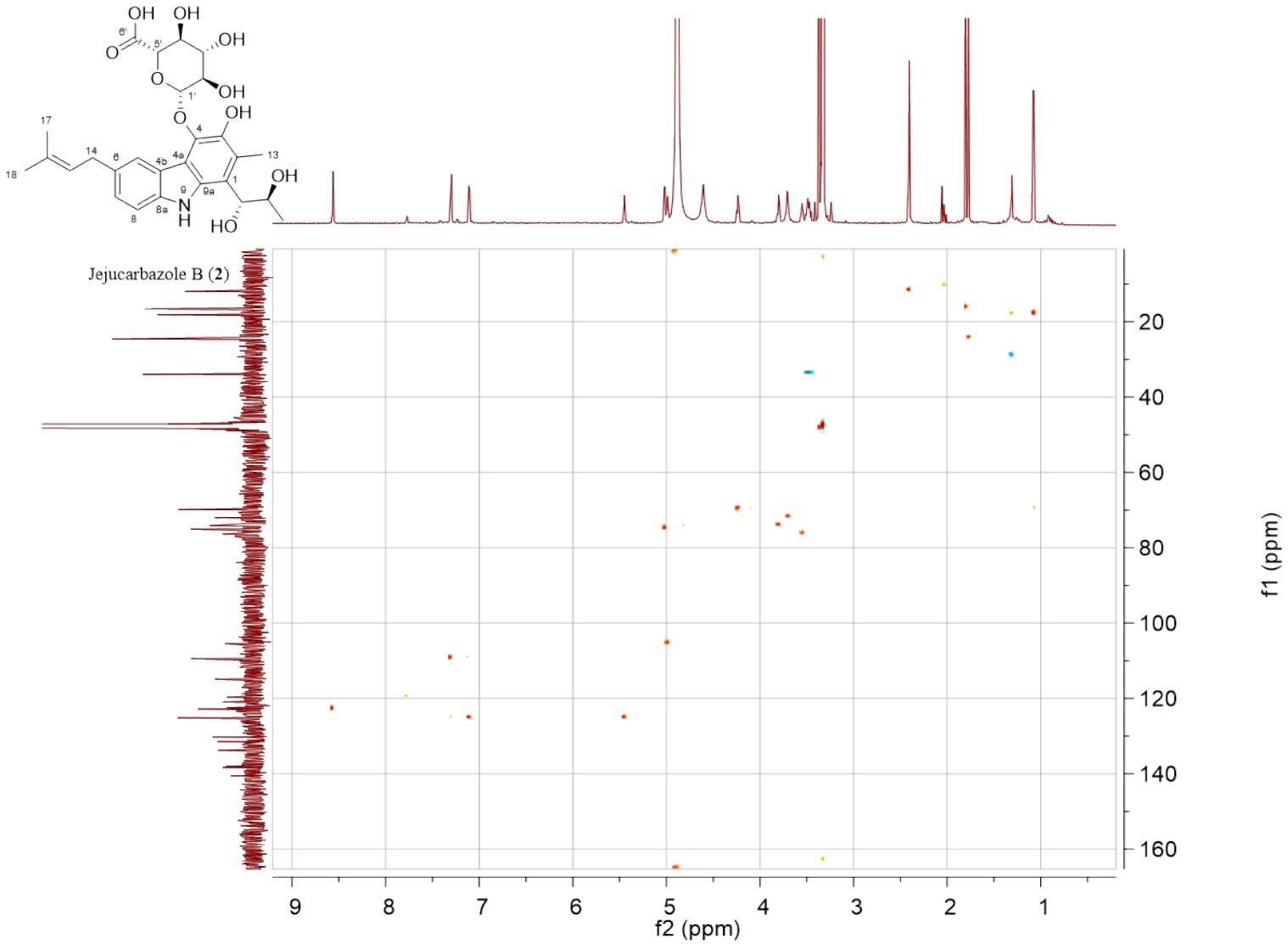


Fig. S23. HSQC-DEPT NMR spectrum of compound **2** in CD_3OD

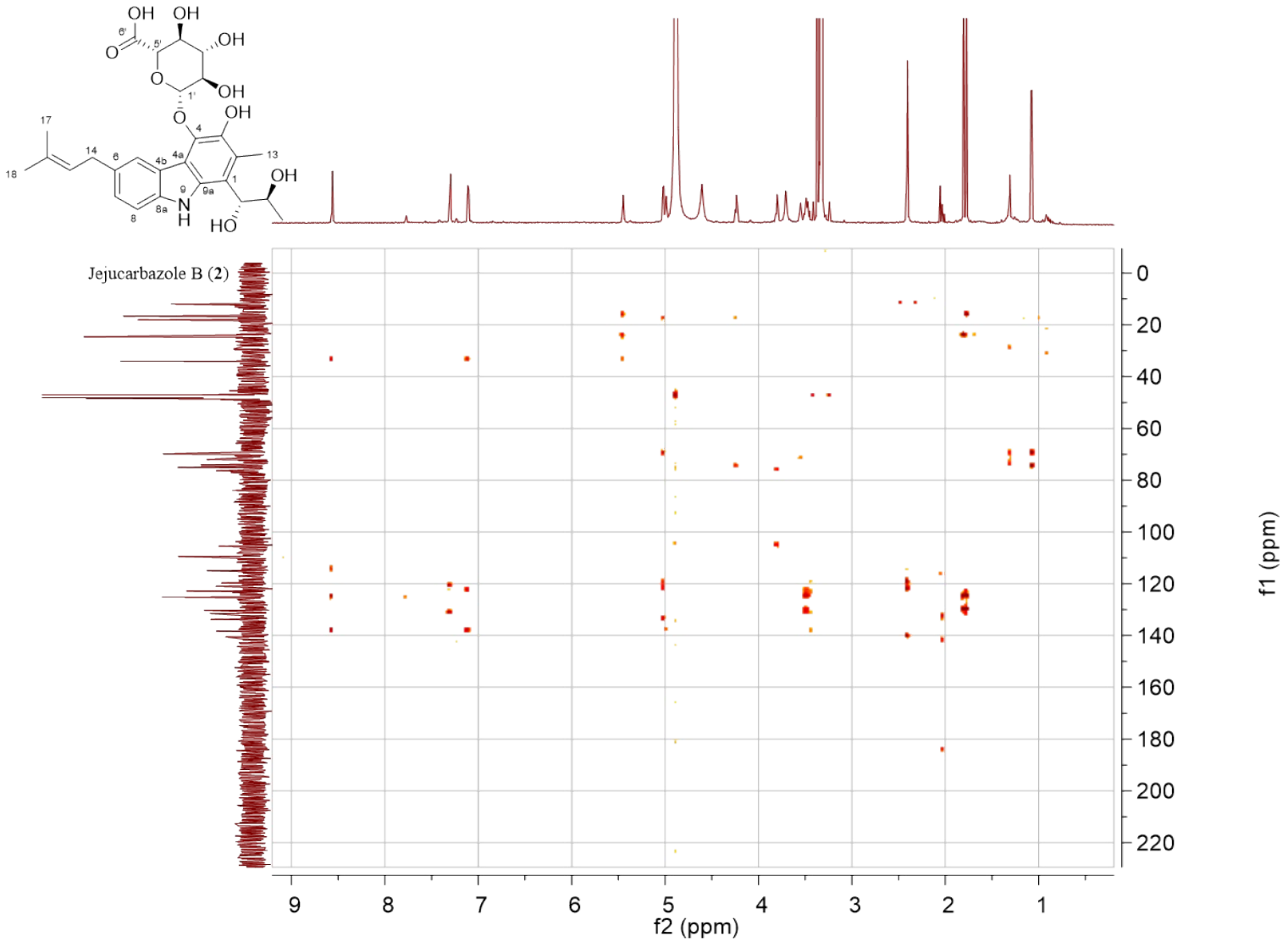


Fig. S24. HMBC NMR spectrum of compound **2** in CD_3OD

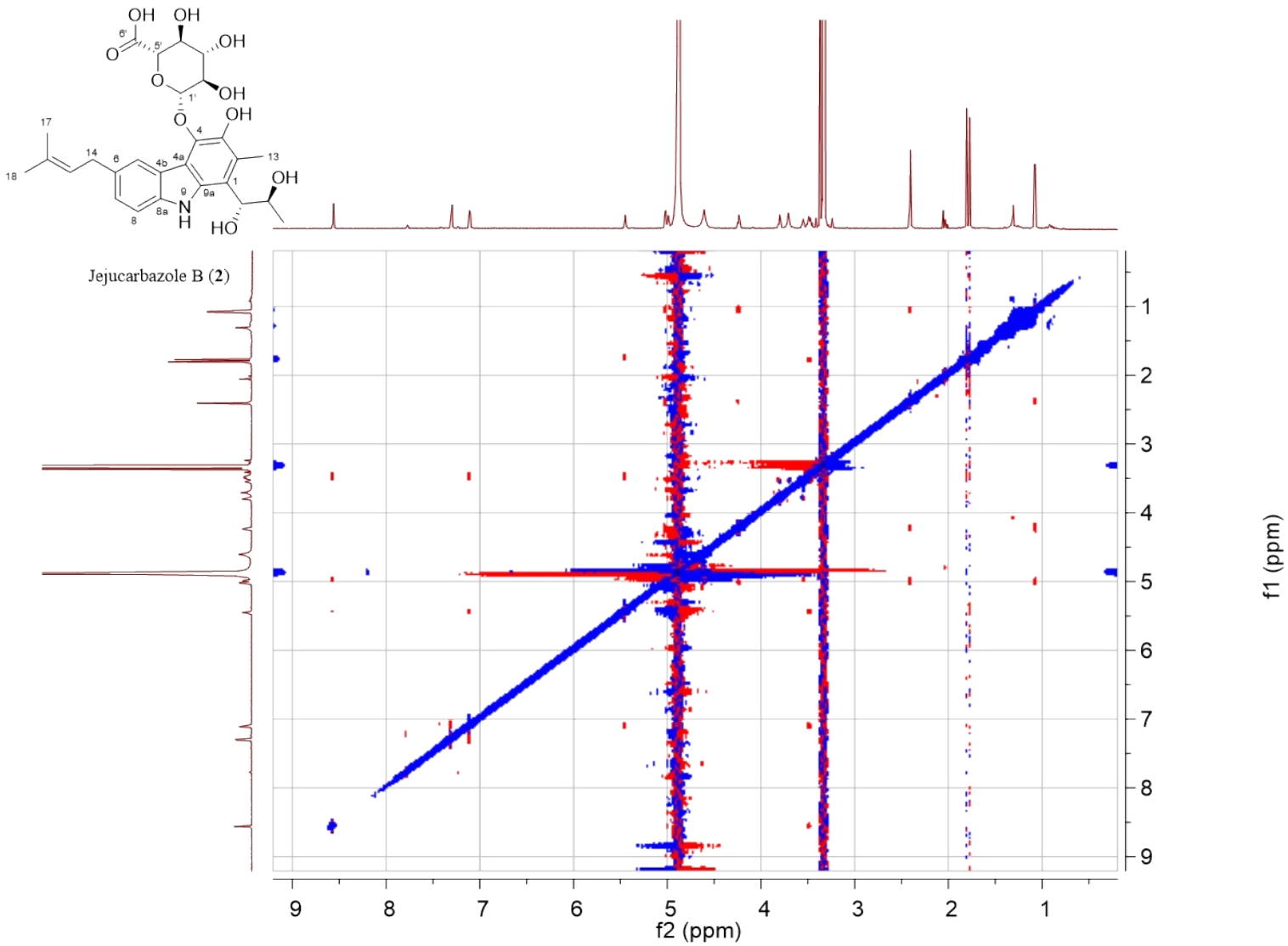


Fig. S25. ROESY NMR spectrum of compound **2** in CD_3OD

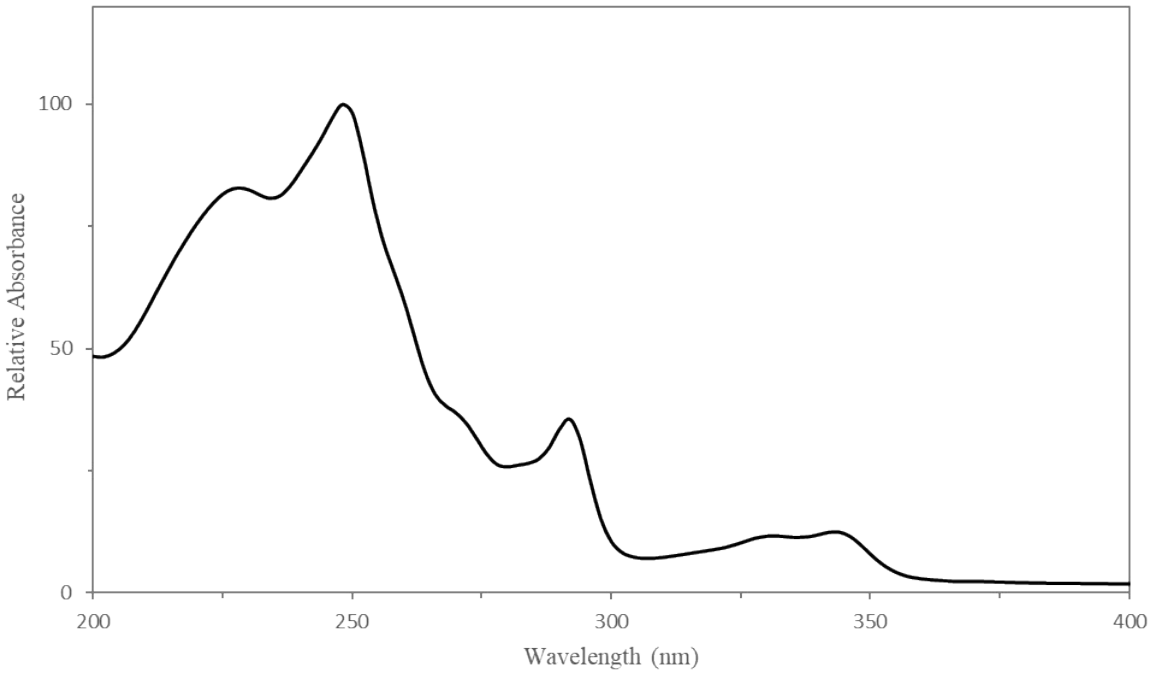


Fig. S26. UPLC-UV spectrum of compound **3** in MeCN-H2O containing 0.05% Formic acid

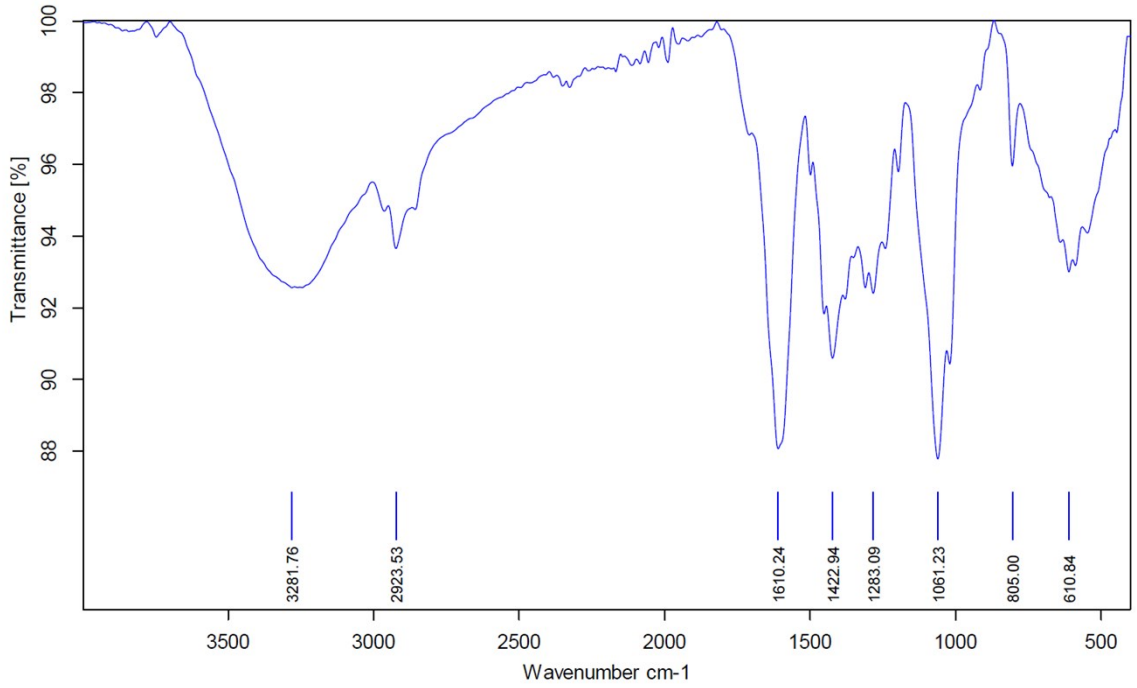


Fig. S27. IR spectrum of compound **3**

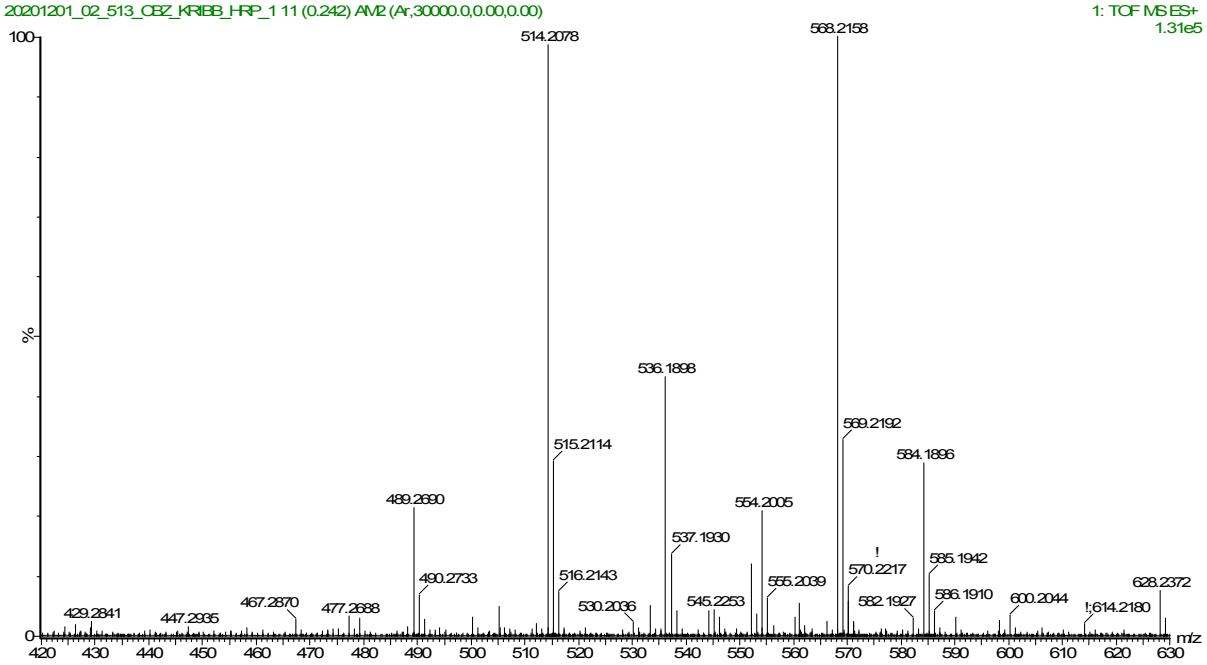


Fig. S28. HR-ESI-TOF-MS positive spectrum in compound **3**

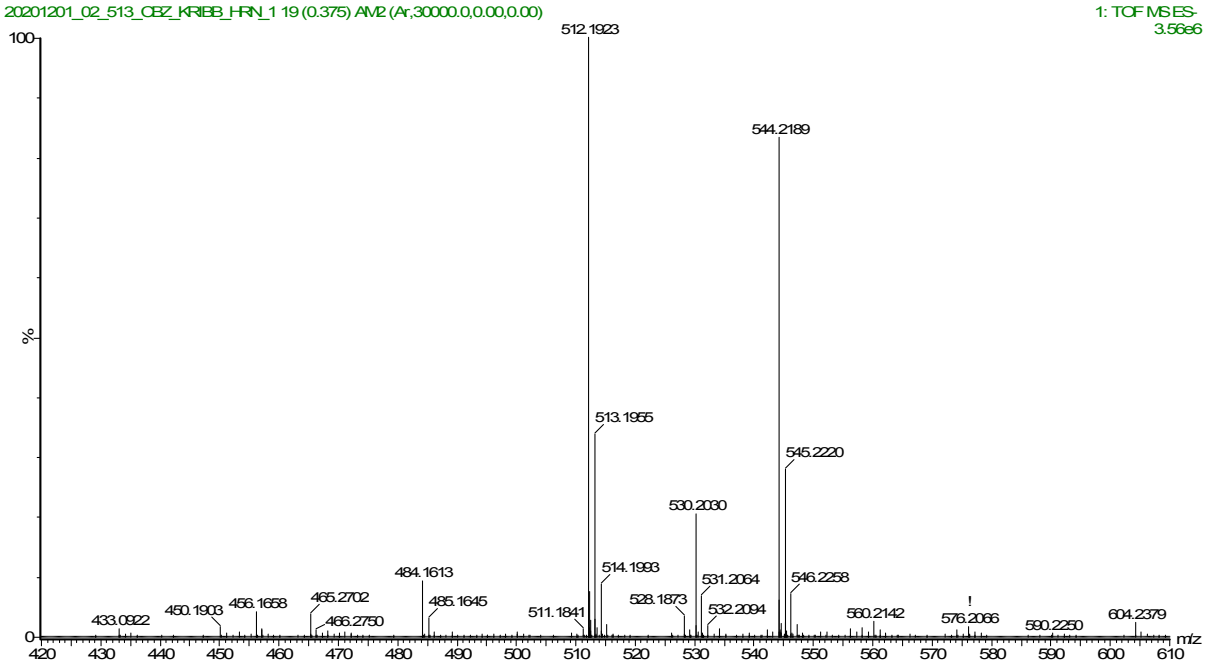


Fig. S29. HR-ESI-TOF-MS negative spectrum in compound **3**

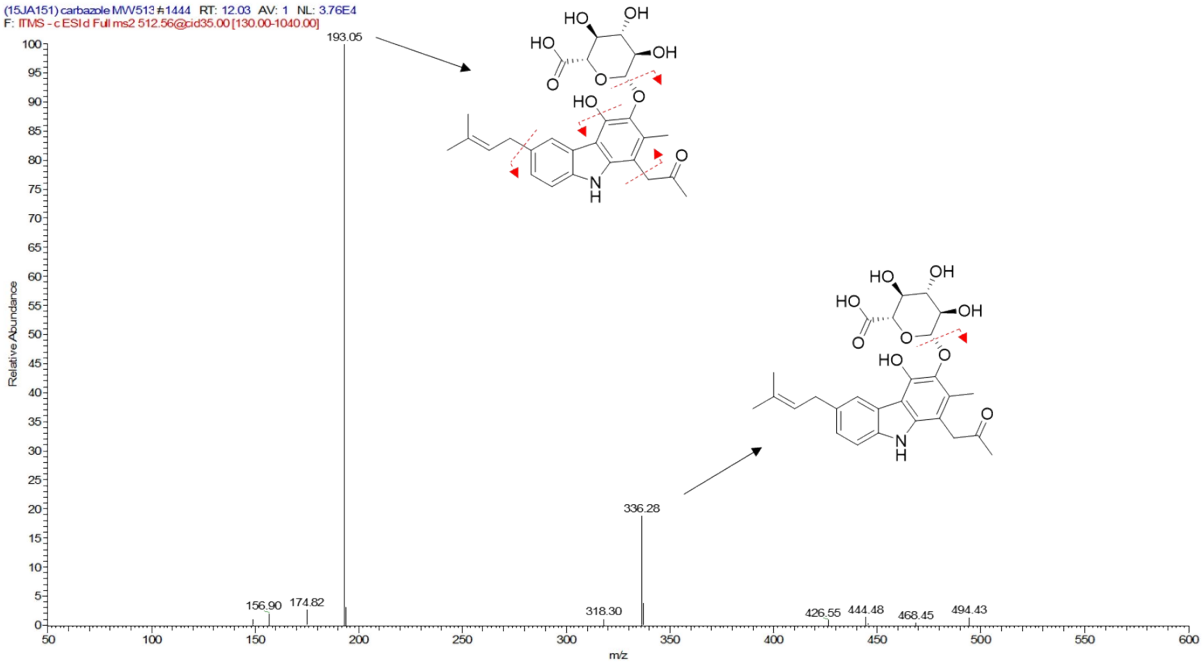


Fig. S30. MS/MS fragmentation spectrum of compound **3** (parent ion, 512.56 $[M - H]^-$)

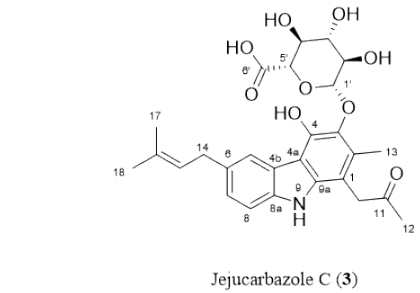
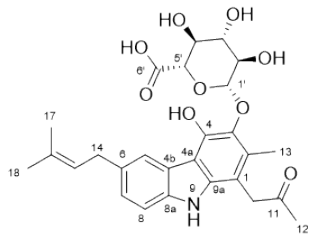


Fig. S31. ^{1}H NMR spectrum of compound **3** in CD_3OD



Jejucarbazole C (**3**)

Fig. S32. ^{13}C NMR spectrum of compound **3** in CD_3OD

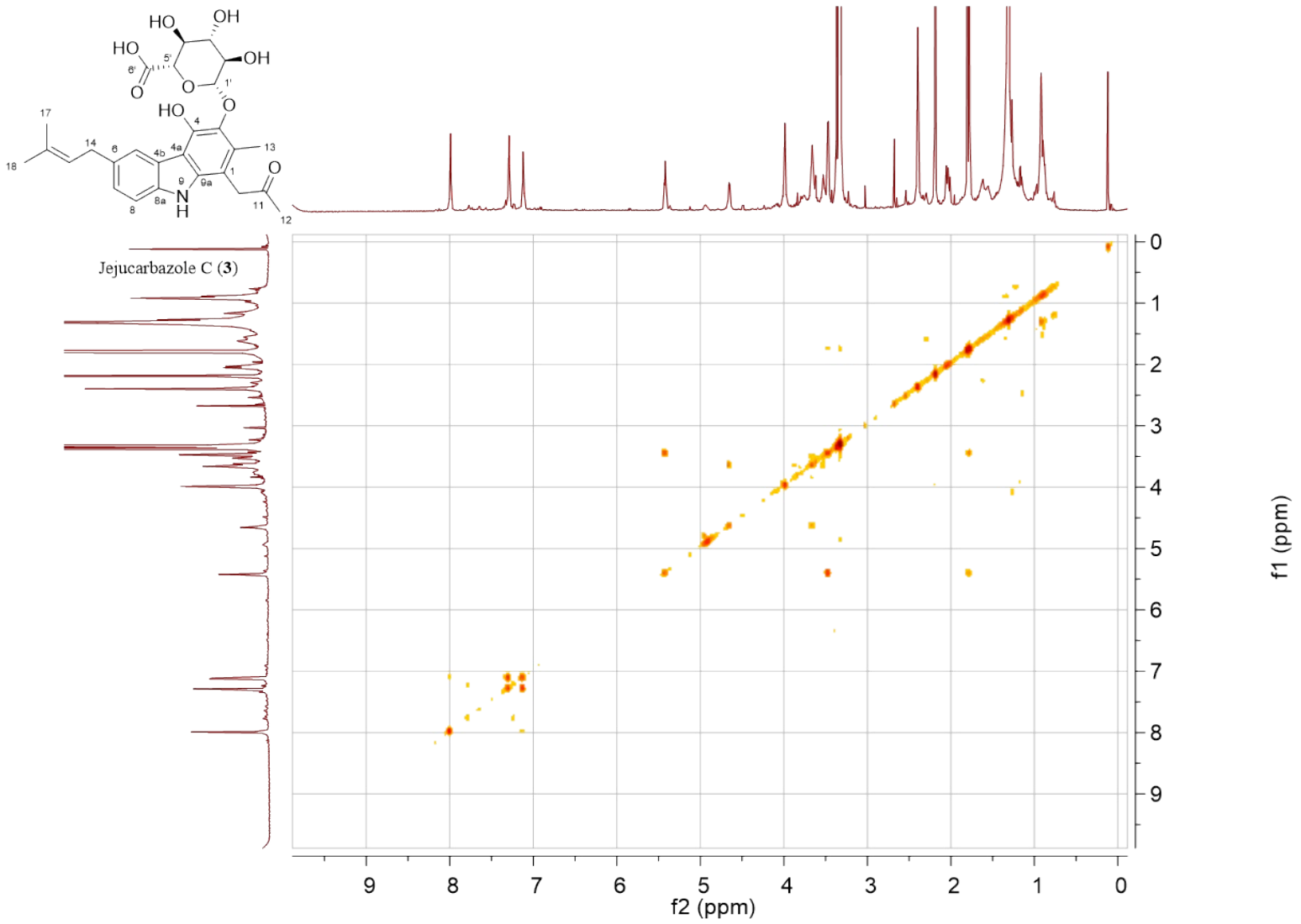


Fig. S33. COSY NMR spectrum of compound **3** in CD_3OD

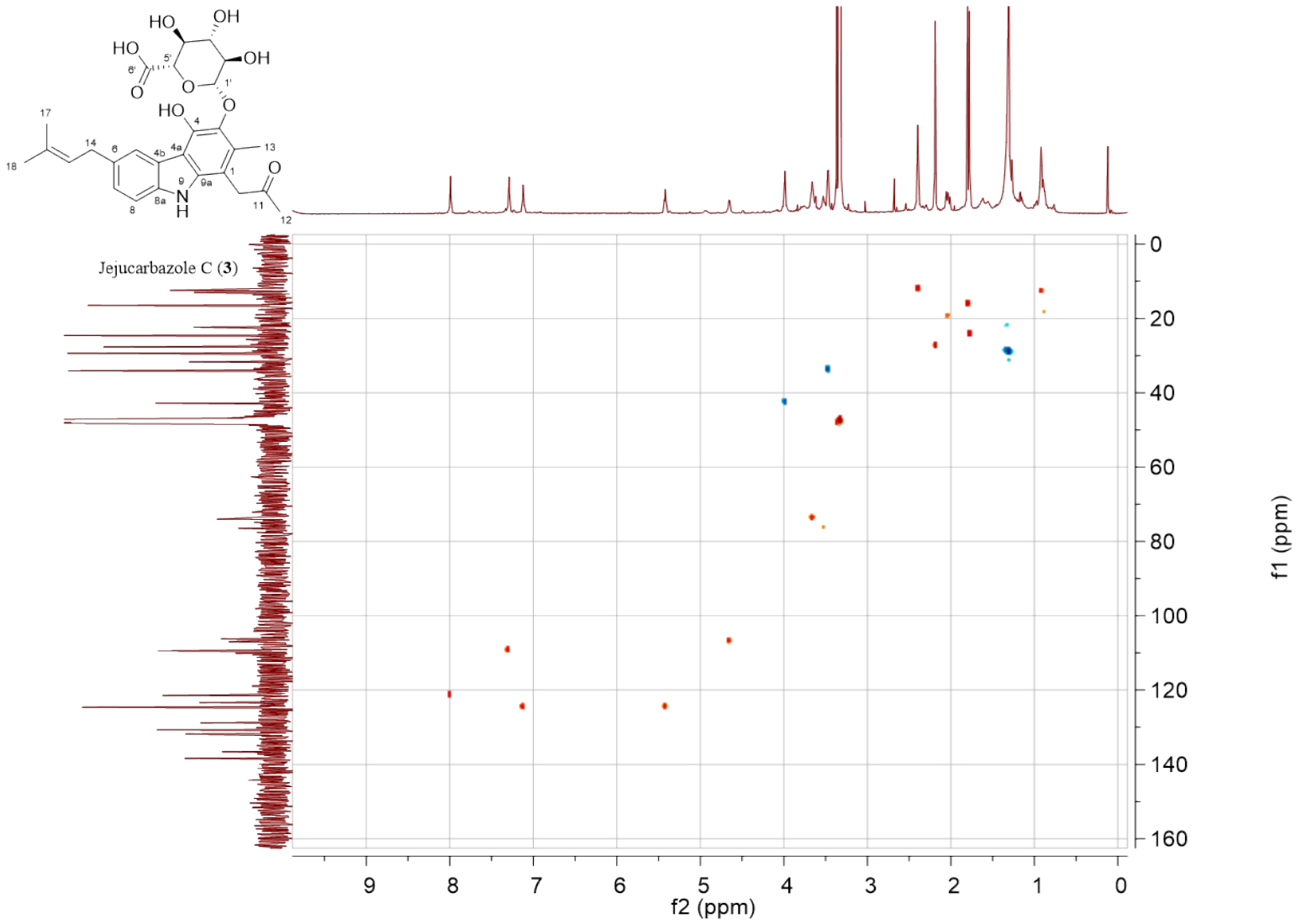


Fig. S34. HSQC-DEPT NMR spectrum of compound **3** in CD_3OD

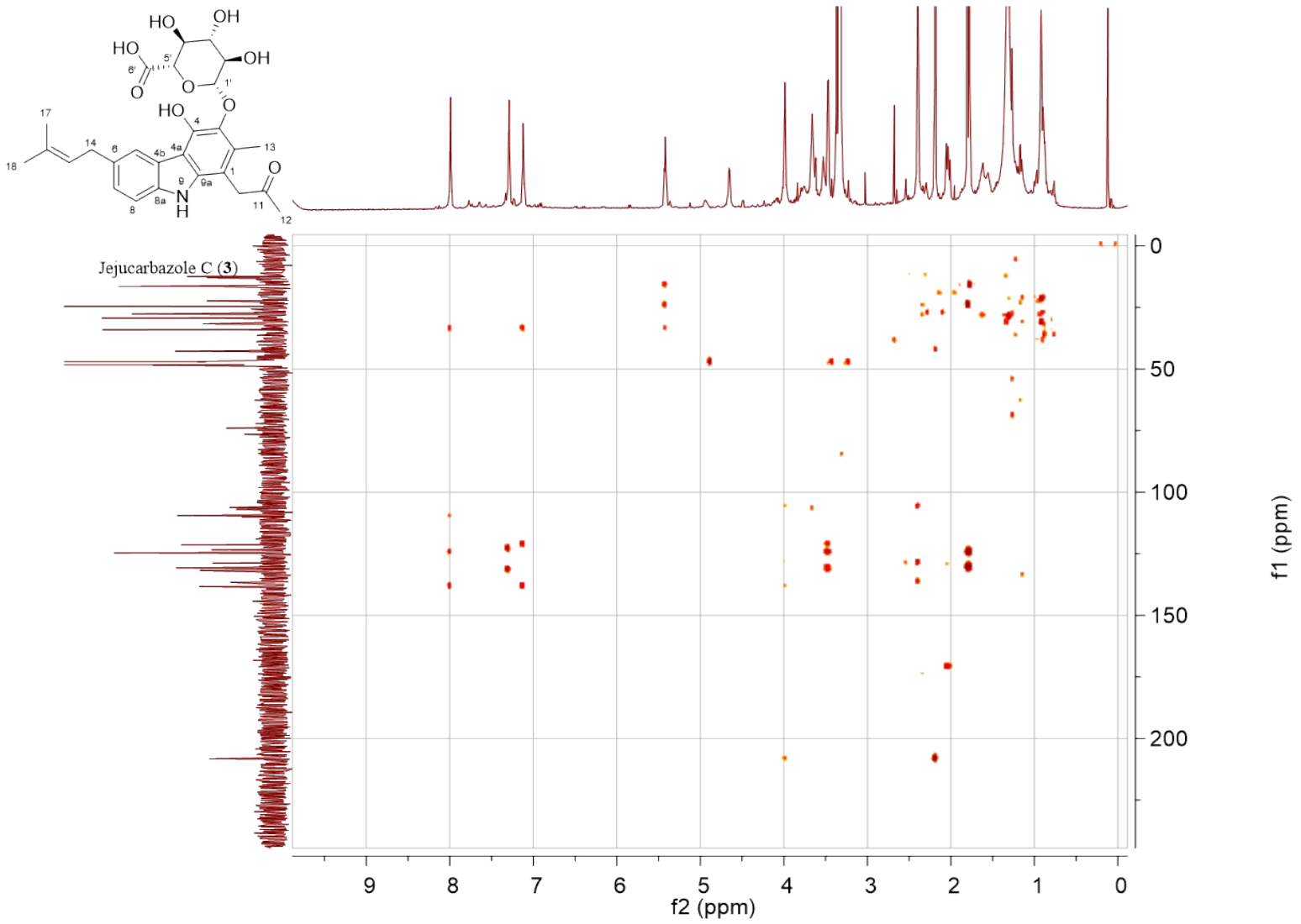


Fig. S35. HMBC NMR spectrum of compound **3** in CD_3OD

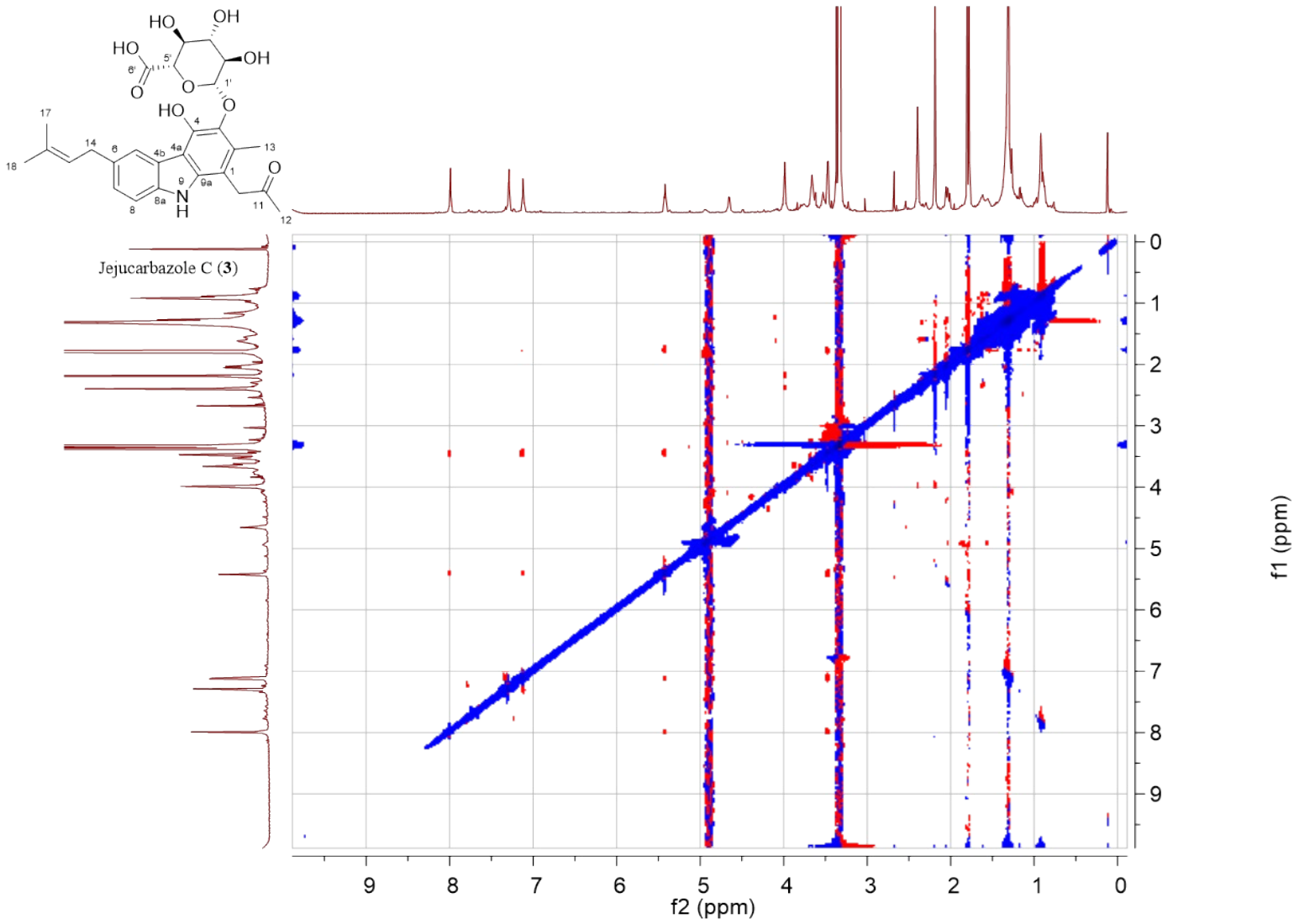
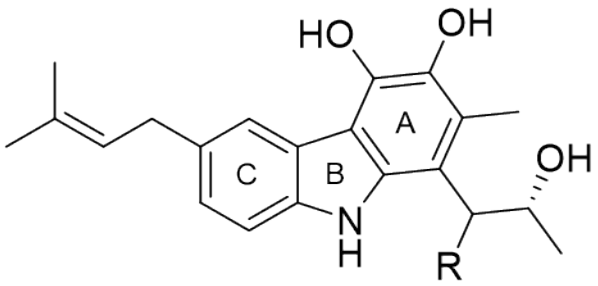
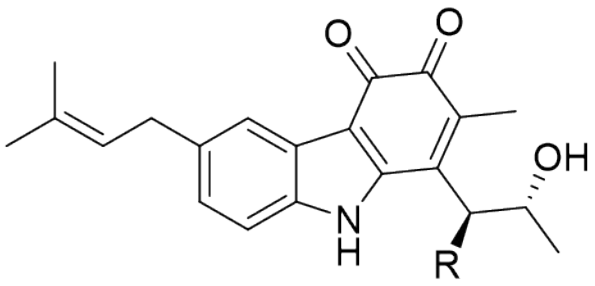


Fig. S36. ROESY NMR spectrum of compound **3** in CD_3OD



Neocarazostatin A: R = OH
Neocarazostatin B: R = H
Neocarazostatin C: R = OMe

Dihydroxyl type CA



Carquinostatin A: R = H
Carquinostatin B: R = OH

ortho-Quinone type CA

Fig. S37. Chemical structures of neocarazostains and carquinostatins

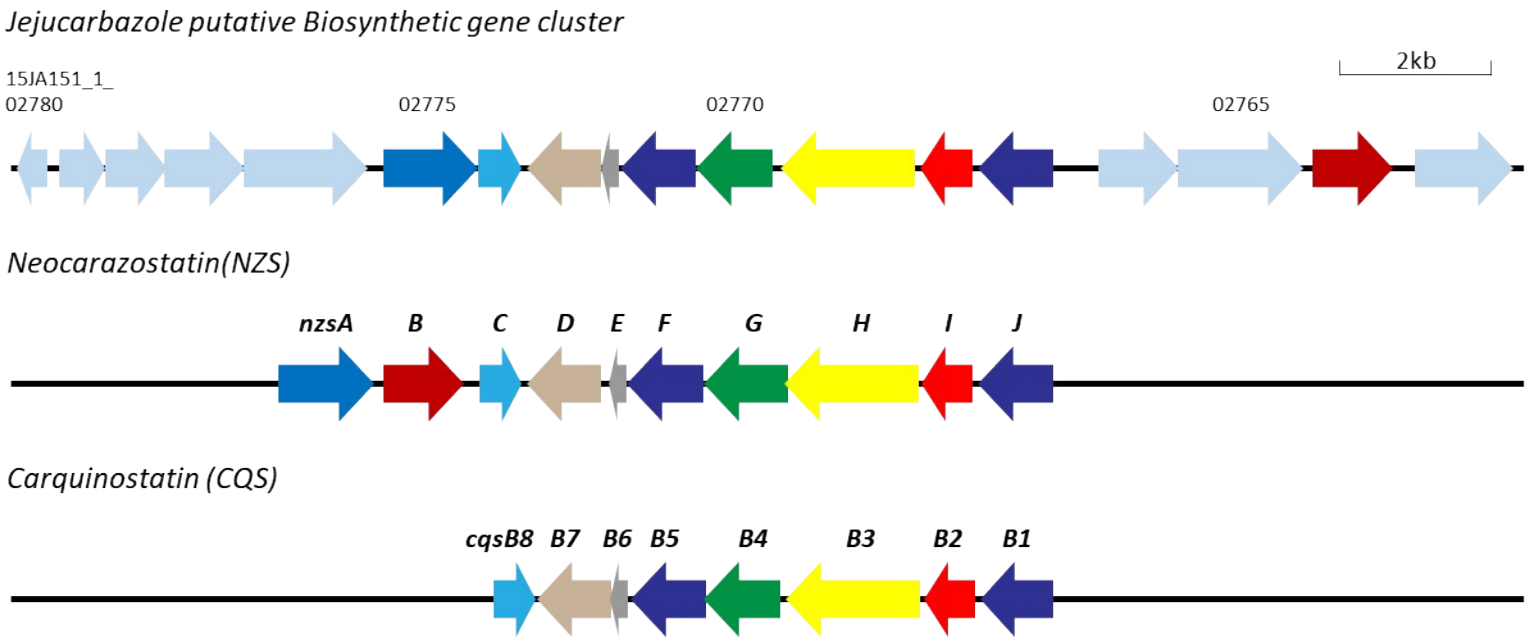


Fig. S38. Comparison of the putative jejucarbazole biosynthetic gene cluster in Streptomyces sp. KCB15JA151 with neocarazostatin (GenBank: LC406090.1) and carquinostatin (GenBank: KP657980.1) gene clusters.

Table S1. Predicted functions and homologues in the putative jejucarbazole biosyntehtic gene cluster

Protein	Size (aa)	Predicted Function	Homologue in Neocarazostatin		Best match	
			Protein / GeneBank (residue)	Identity/Similarity	Organism / GeneBank (residue)	Identity/Similarity
15JA151_1_02780	133	Putative response regulatory protein			*Streptomyces sp.* WELS2 / WP_181792968.1 (133)	99 / 99
15JA151_1_02779	206	Heme-copper oxidase subunit III			*Streptomyces*/ WP_030783240.1 (206)	100 / 100
15JA151_1_02778	270	C-type cytochrome			*Streptomyces eurythermus* / WP_189752509.1 (270)	100 / 100
15JA151_1_02777	352	Rieske 2Fe-2S domain-containing protein			*Streptomyces sp.* WELS2 / WP_181792970.1 (352)	99 / 100
15JA151_1_02776	545	Ubiquinol-cytochrome c reductase cytochrome b subunit			*Streptomyces achromogenes* / WP_030621189.1 (545)	97 / 96
15JA151_1_02775	417	Cytochrome P450	nzsA / ALL53314.1 (418)	65 / 79	*Streptomyces eurythermus* / WP_189752507.1 (417)	99 / 99
15JA151_1_02774	190	IPP isomerase	nzsC / ALL53316.1 (185)	75 / 81	*Streptomyces* / WP_030783251.1 (189)	99 / 98
15JA151_1_02773	325	aminotransferase	nzsD / ALL53317.1 (325)	64 / 74	*Streptomyces*/ WP_051815689.1 (325)	97 / 98
15JA151_1_02772	79	ACP	nzsE / ALL53318.1 (80)	65 / 77	*Streptomyces* / WP_030783257.1 (79)	100 / 100

15JA151_1_02771	336	β-ketosynthase III	nzsF / ALL53319.1 (337)	78 / 83	*Streptomyces achromogenes* / WP_189996525.1 (336)	98 / 98
15JA151_1_02770	337	Isoprenyl transferase	nzsG / ALL53320.1 (371)	64 / 81	*Streptomyces* / WP_030783263.1 (337)	98 / 98
15JA151_1_02769	592	Acetolactate synthase	nzsH / ALL53321.1 (593)	76 / 82	*Streptomyces achromogenes* / WP_189996527.1 (592)	97 / 98
15JA151_1_02768	226	Cyclase/aromatase	nzsI / ALL53322.1 (227)	80 / 89	*Streptomyces* / WP_030783270.1 (230)	99 / 100
15JA151_1_02767	331	β-ketosynthase III	nzsJ / ALL53323.1 (331)	73 / 83	*Streptomyces sp.* WELS2 / WP_181792983.1 (349)	97 / 99
15JA151_1_02766	355	Rieske 2Fe-2S domain-containing protein			*Streptomyces sp.* DSM 40868 / WP_167512969.1 (355)	98 / 98
15JA151_1_02765	551	Cytochrome b N-terminal domain-containing protein			*Streptomyces eurythermus* / WP_189752499.1 (551)	97 / 99
15JA151_1_02764	354	Tryptophan biosynthesis	nzsB / ALL53315.1 (355)	76 / 87	*Streptomyces* / WP_030783280.1 (354)	99 / 99
15JA151_1_02763	453	Aminotransferase class V-fold PLP-dependent enzyme			*Streptomyces achromogenes* / WP_189996532.1 (453)	99 / 99

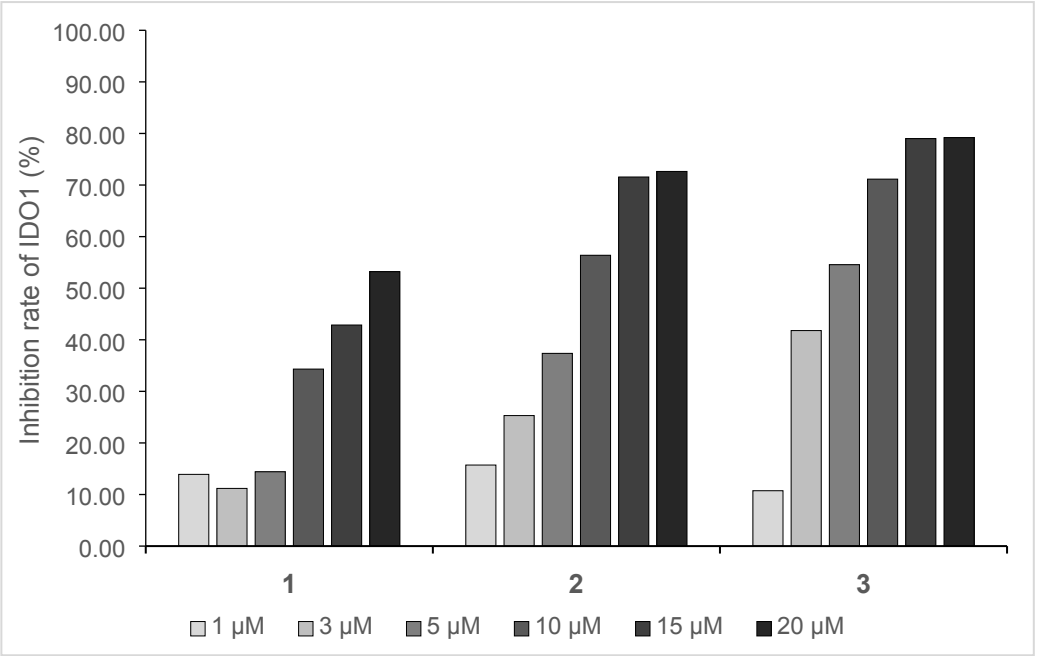


Fig. S39. IDO1 inhibition rate of jejucarbazoles A-C

Table S2. Docking scores of compounds **1**-**3** against holo-IDO1 enzyme (PDB id: 6AZU) with/without heme and apo-IDO1 enzyme (PDB id: 6AZV)

	Docking Score (Kcal/mol)		
	6AZU(holo-IDO1) with heme	6AZU(holo-IDO1) without heme	6AZV(apo-IDO1)
Compound **1**	-8.2	-8.4	-8.1
Compound **2**	-7.3	-7.7	-8.3
Compound **3**	-7.9	-8.3	-9.1

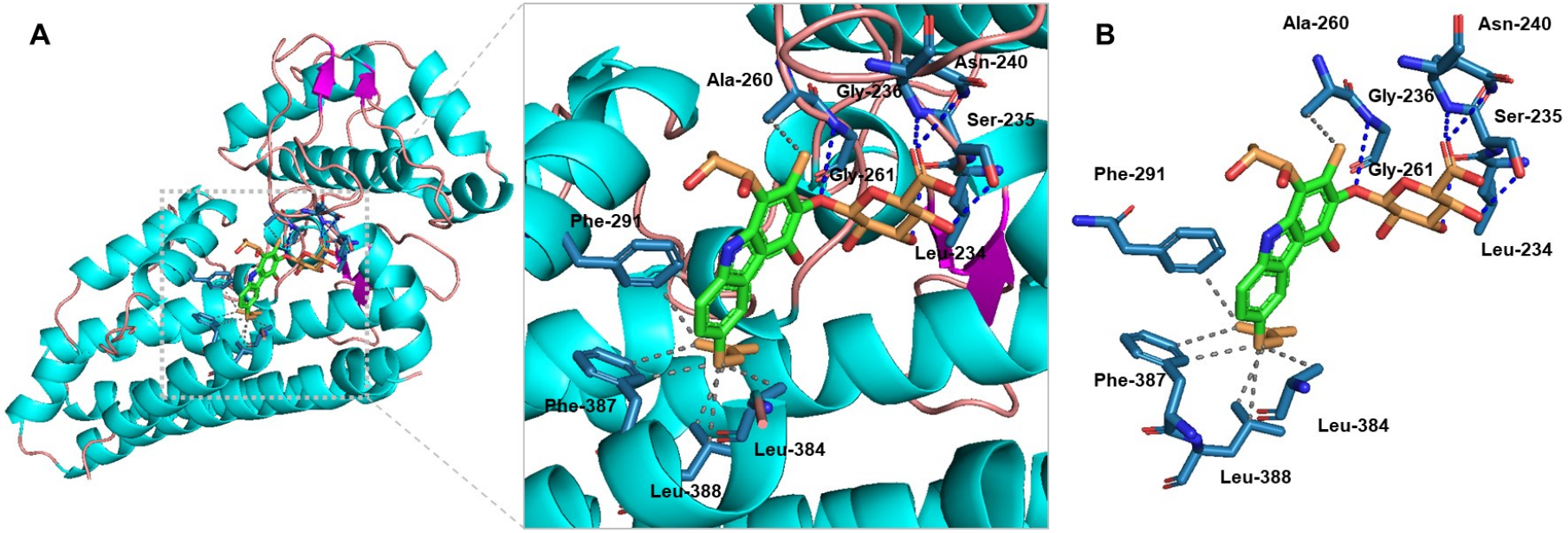


Fig. S40. Molecular-docking analysis of compound **1** with the apo-IDO1 enzyme (PDB id: 6AZV). (A) Putative binding mode for compound **1** with apo-IDO1. (B) Protein-ligand interaction profile between compound **1** with apo-IDO1. The gray dashed lines represent hydrophobic interactions; the blue dashed lines represent hydrogen bonds.

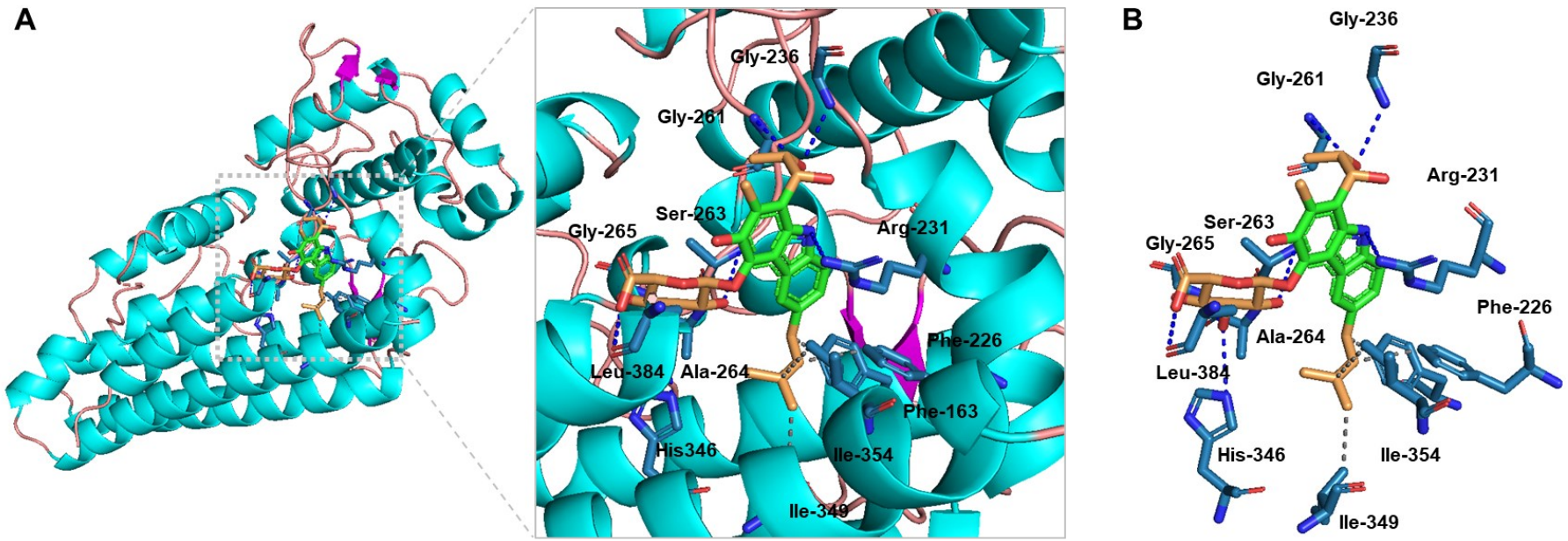


Fig. S41. Molecular-docking analysis of compound **2** with the apo-IDO1 enzyme (PDB id: 6AZV). (A) Putative binding mode for compound **2** with apo-IDO1. (B) Protein-ligand interaction profile between compound **2** with apo-IDO1. The gray dashed lines represent hydrophobic interactions; the blue dashed lines represent hydrogen bonds.