Supporting Information

α-Glucosidase and α-Amylase Inhibitors from *Arcytophyllum thymifolium*

Luigi Milella,[†] Stella Milazzo,[‡] Marinella De Leo,[‡] Mariela Beatriz Vera Saltos,[⊥] Immacolata Faraone,[†] Tiziano Tuccinardi,[‡,§] Margherita Lapillo,[‡] Nunziatina De Tommasi,*[,‖] and Alessandra Braca[‡,§]

[†]Dipartimento di Scienze, Università degli Studi della Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, Italy

[‡]Dipartimento di Farmacia, Università di Pisa, via Bonanno 6 and 33, 56126 Pisa, Italy

[§]Centro Interdipartimentale di Ricerca "Nutraceutica e Alimentazione per la Salute", Università di Pisa, via del Borghetto 80, 56124 Pisa, Italy

[⊥]Departamento de Ciencias de la Vida, Universidad de las Fuerzas Armadas, ESPE, Av. General Rumiñahui s/n, Sangolqui, Ecuador

[‖]Dipartimento di Farmacia, Università degli Studi di Salerno, via Giovanni Paolo II 132, 84084 Fisciano (SA), Italy

Figure S1. ^{1}H NMR spectrum of compound **1** (CD_3OD, 600 MHz)

Figure S2. HSQC spectrum of compound **1** (CD_3OD, 600 MHz)

Figure S3. HMBC spectrum of compound **1** (CD_3OD, 600 MHz)

Figure S4. HRESIMS of compound **1**

Figure S5. ^{1}H NMR spectrum of compound **2** (CD_3OD, 600 MHz)

Figure S6. HSQC spectrum of compound **2** (CD_3OD, 600 MHz)

Figure S7. HRESIMS spectrum of compound **2**

Figure S8. ^{1}H NMR spectrum of compound **3** (CD_3OD, 600 MHz)

Figure S9. HSQC spectrum of compound **3** (CD_3OD, 600 MHz)

Figure S10. HMBC spectrum of compound **3** (CD_3OD, 600 MHz)

Figure S11. HRESIMS spectrum of compound **3**

Figure S12. ^{1}H NMR spectrum of compound **4** (CD_3OD, 600 MHz)

Figure S13. HSQC spectrum of compound **4** (CD_3OD, 600 MHz)

Figure S14. HMBC spectrum of compound **4** (CD_3OD, 600 MHz)

Figure S15. HRESIMS spectrum of compound **4**

Figure S16. ^{1}H NMR spectrum of compound **5** (CD_3OD, 600 MHz)

Figure S17. 1D TOCSY spectrum of compound **5** (aglycone moiety) (CD_3OD, 600 MHz)

Figure S18. 1D TOCSY spectrum of compound **5** (sugar moiety) (CD_3OD, 600 MHz)

Figure S19. HSQC spectrum of compound **5** (CD_3OD, 600 MHz)

Figure S20. HRESIMS spectrum of compound **5**

Figure S21. ^{1}H NMR spectrum of compound **6** (CD_3OD, 250 MHz)

Figure S22. HSQC spectrum of compound **6** (CD_3OD, 250 MHz)

Figure S23. ^{1}H NMR spectrum of compound **7** (CD_3OD, 600 MHz)

Figure S24. HSQC spectrum of compound **7** (CD_3OD, 600 MHz)

Figure S25. HMBC spectrum of compound **7** (CD_3OD, 600 MHz)

Figure S26. Sequence alignment of α-1,4-glucosidase (P53341) and oligo-1,6-glucosidase (3A4A PDB code, P53051) from *Saccharomyces cerevisiae*

Figure S27. Ramachandran plot of the *α*-1,4-glucosidase model. The most favoured regions are coloured in red, additional allowed regions are indicated in yellow, while generously allowed and disallowed zones are pointed out by light yellow and white fields, respectively

(To insert Ramachandran Plot)

Figure S28. Residue analysis of the binding site of the *α*-1,4-glucosidase homology model (grey) and oligo-1,6-glucosidase X-ray crystal structure complexed with maltose (magenta). The three conserved catalytic residues are coloured yellow

Figure S29. Analysis of the MD simulation of the reference complex (PDB code 3A4A). In the first plot (A), the total energy trend of the system *vs* the time is reported; the second plot (B) shows the RMSD of the position of the heavy atoms of maltose from its crystallographic coordinates during the simulation

Figure S30. Analysis of the MD simulations of the *α*-1,4-glucosidase model complexed with compound **4** (pose 4). The plot shows the RMSD of the position of the ligand with respect to its initial docking pose

Figure S1. ^{1}H NMR spectrum of compound **1** (CD_3OD, 600 MHz)

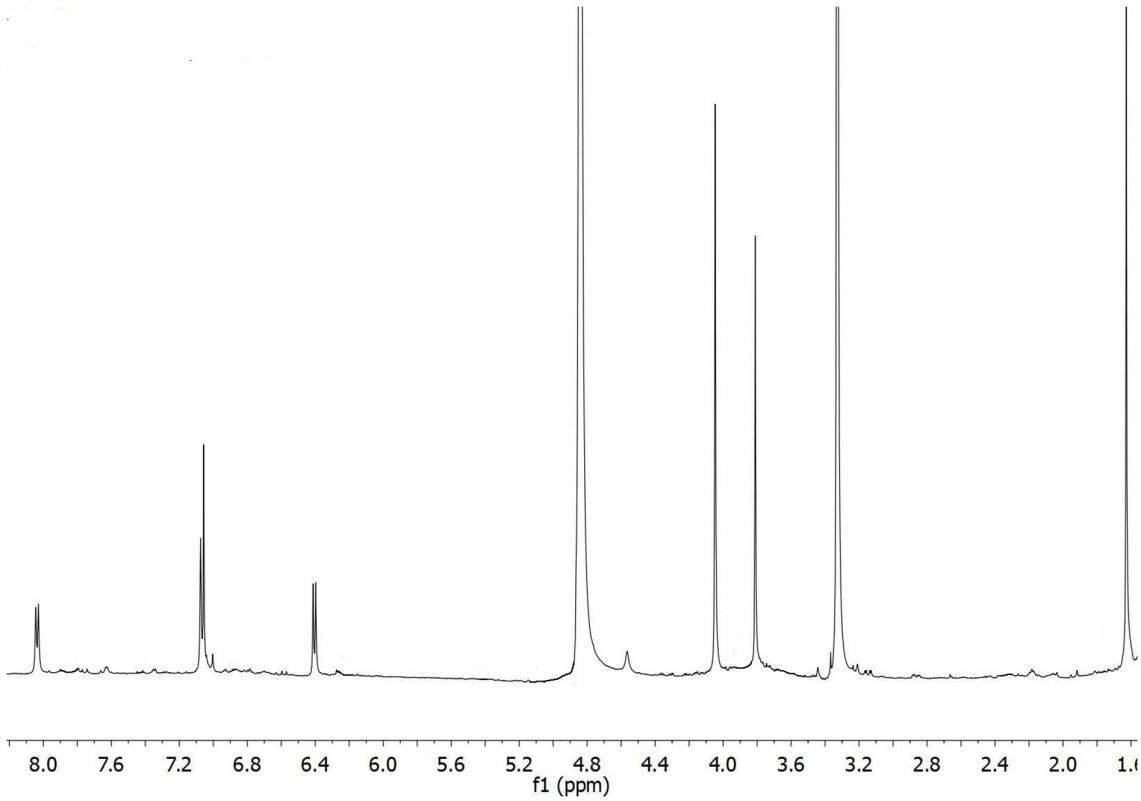


Figure S2. HSQC spectrum of compound **1** (CD_3OD, 600 MHz)

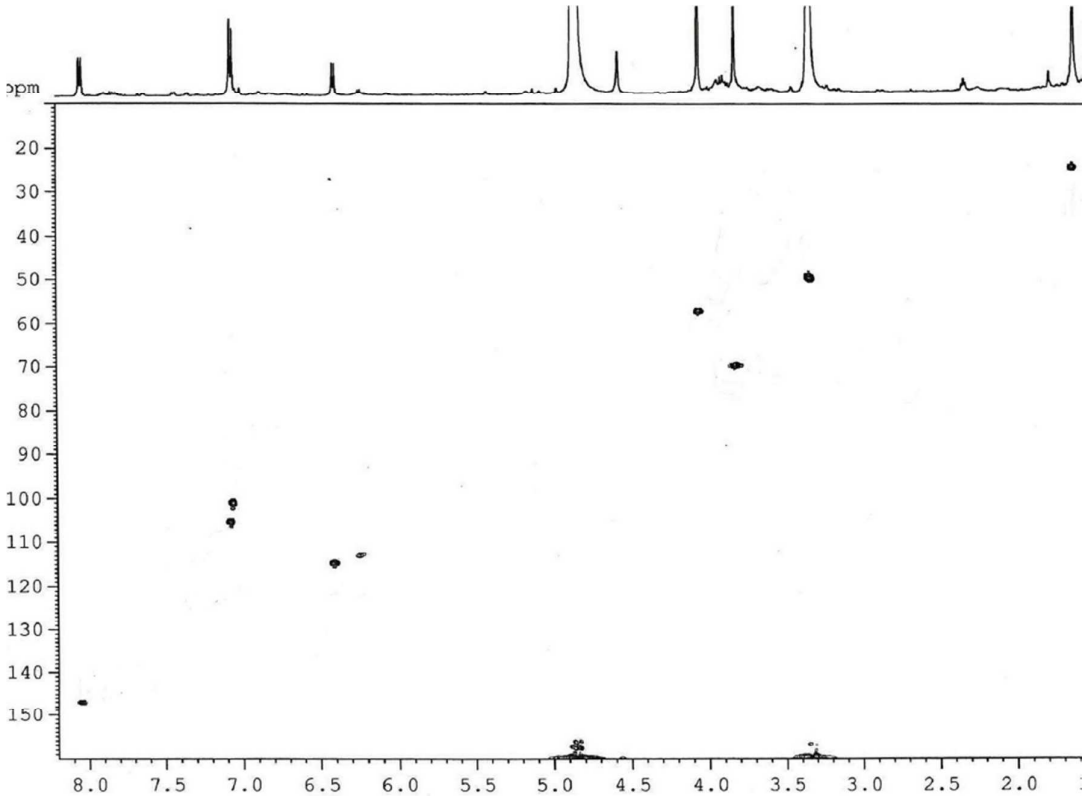


Figure S3. HMBC spectrum of compound **1** (CD_3OD, 600 MHz)

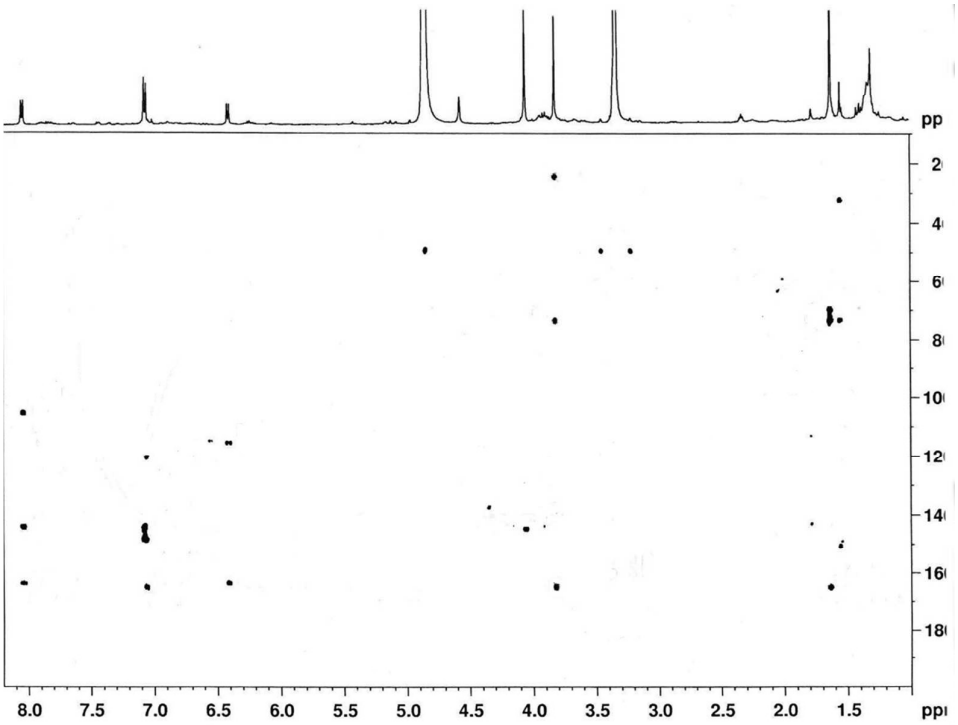
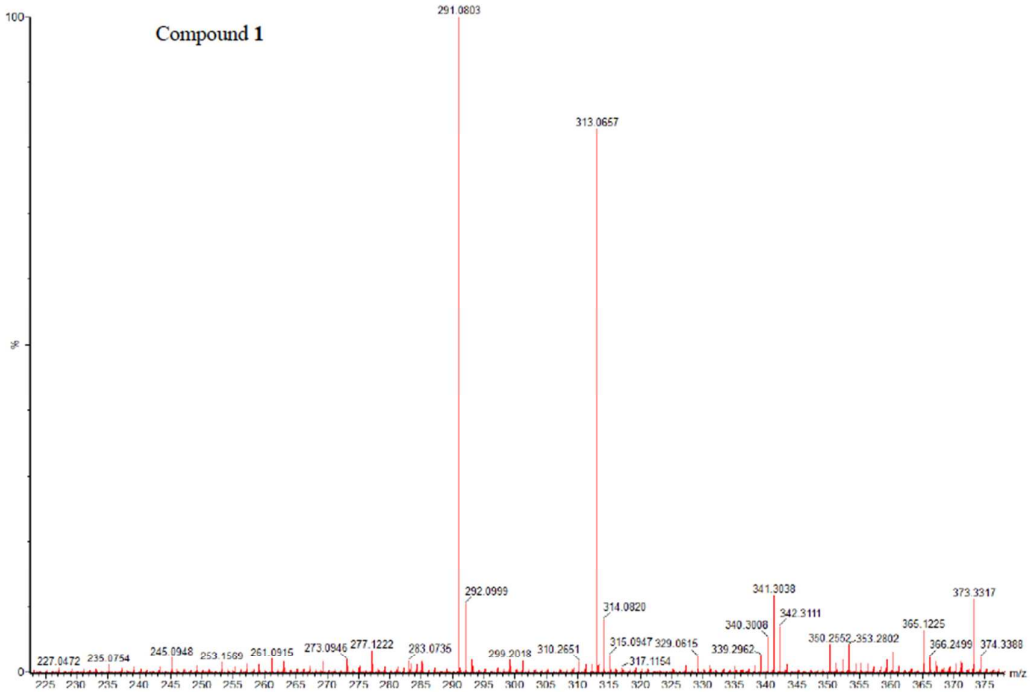


Figure S4. HRESIMS spectrum of compound **1**



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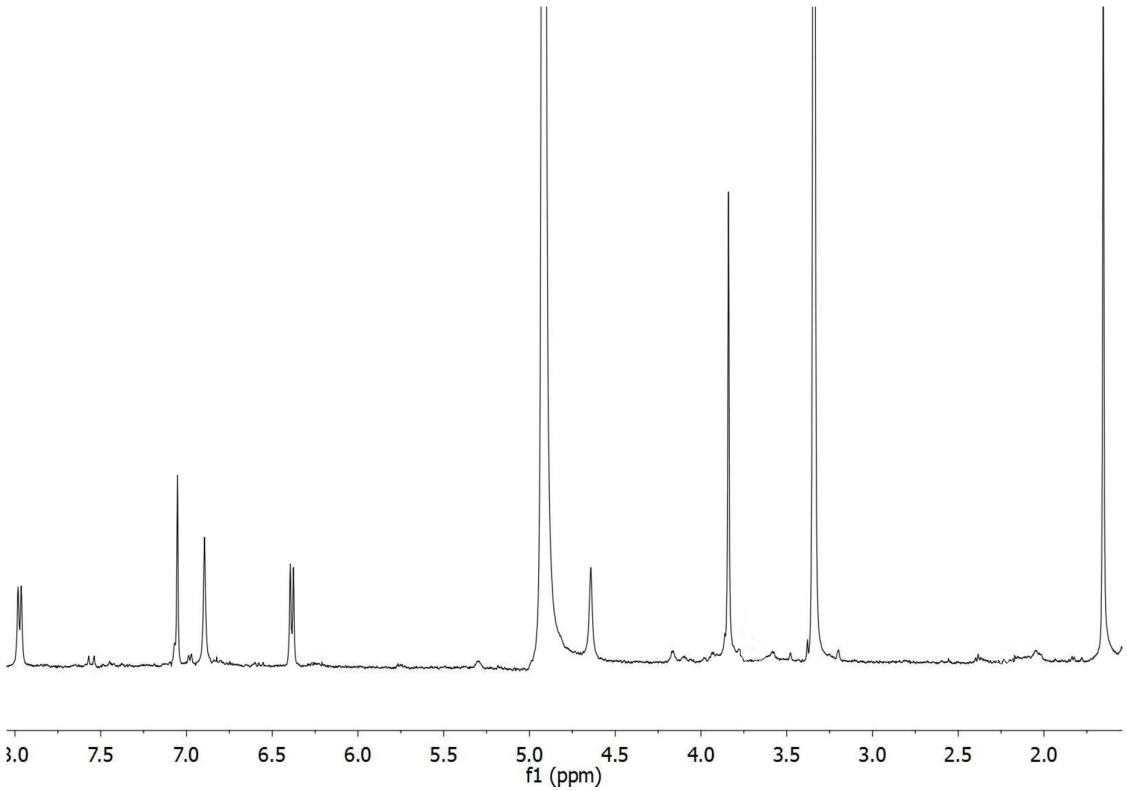

Figure S6. HSQC spectrum of compound **2** (CD_3OD, 600 MHz)

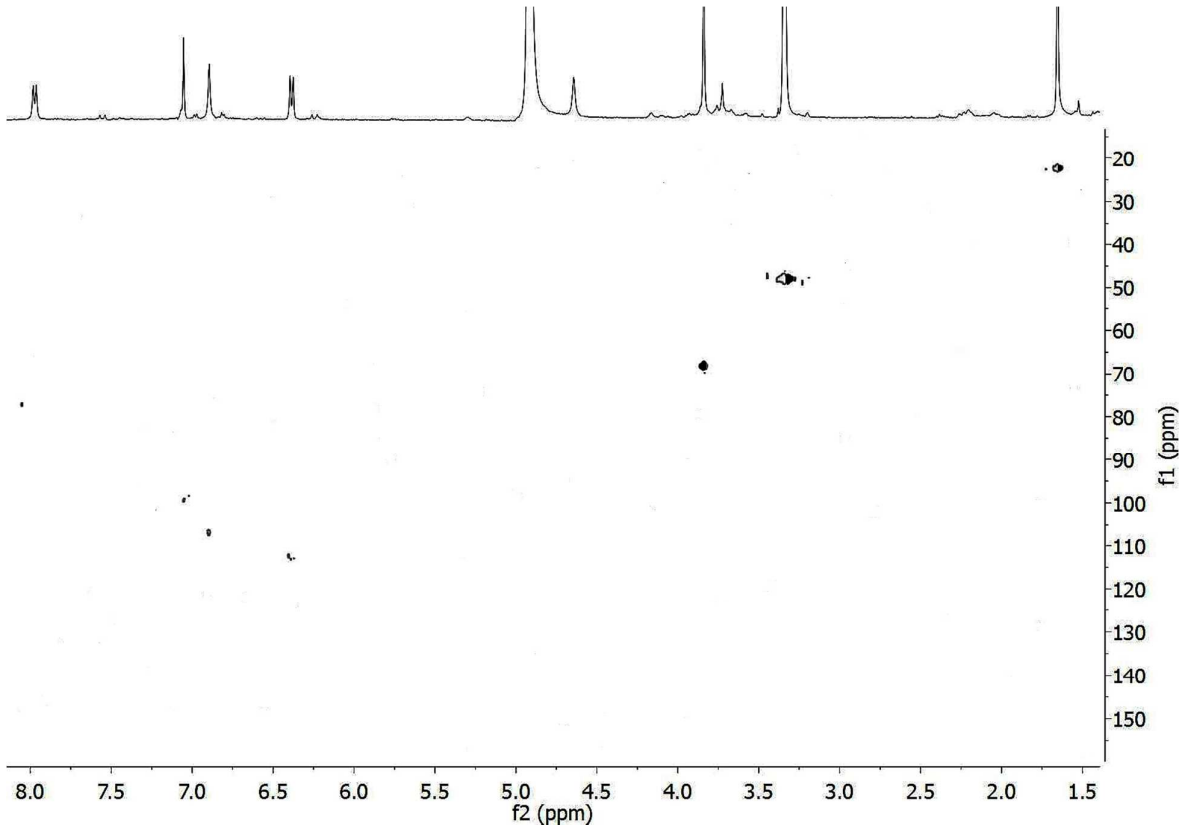

Figure S7. HRESIMS spectrum of compound **2**

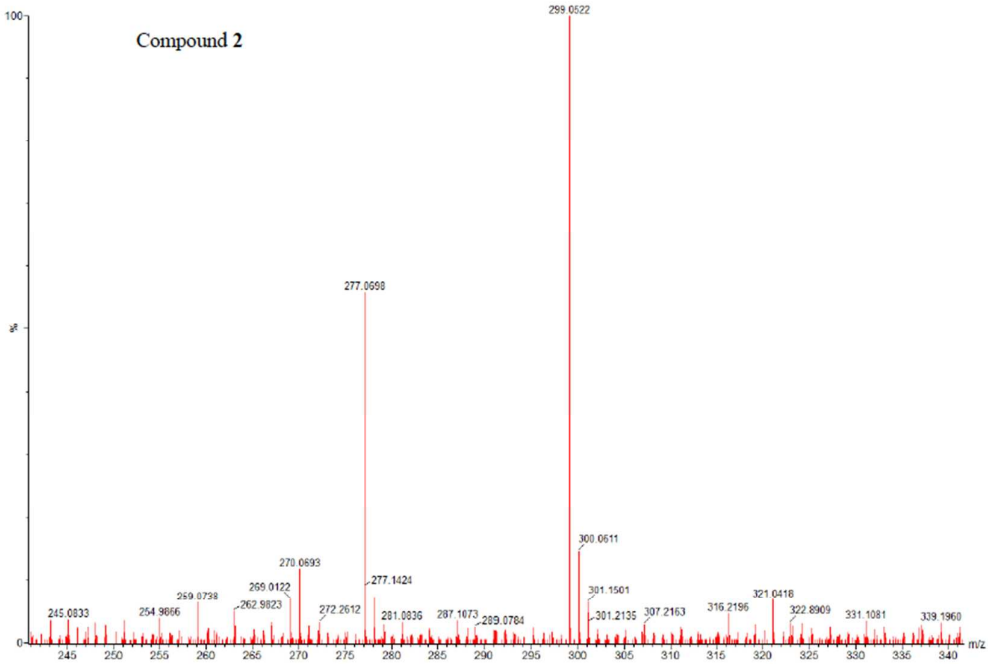

Figure S8. ^{1}H NMR spectrum of compound **3** (CD_3OD, 600 MHz)

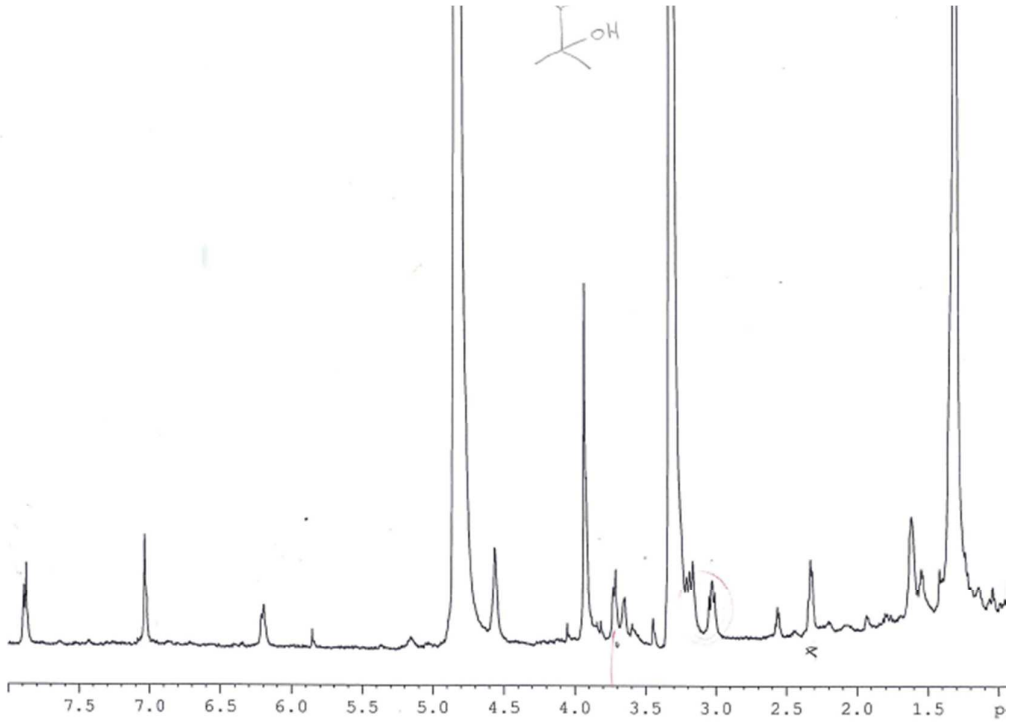

Figure S9. HSQC spectrum of compound **3** (CD_3OD, 600 MHz)

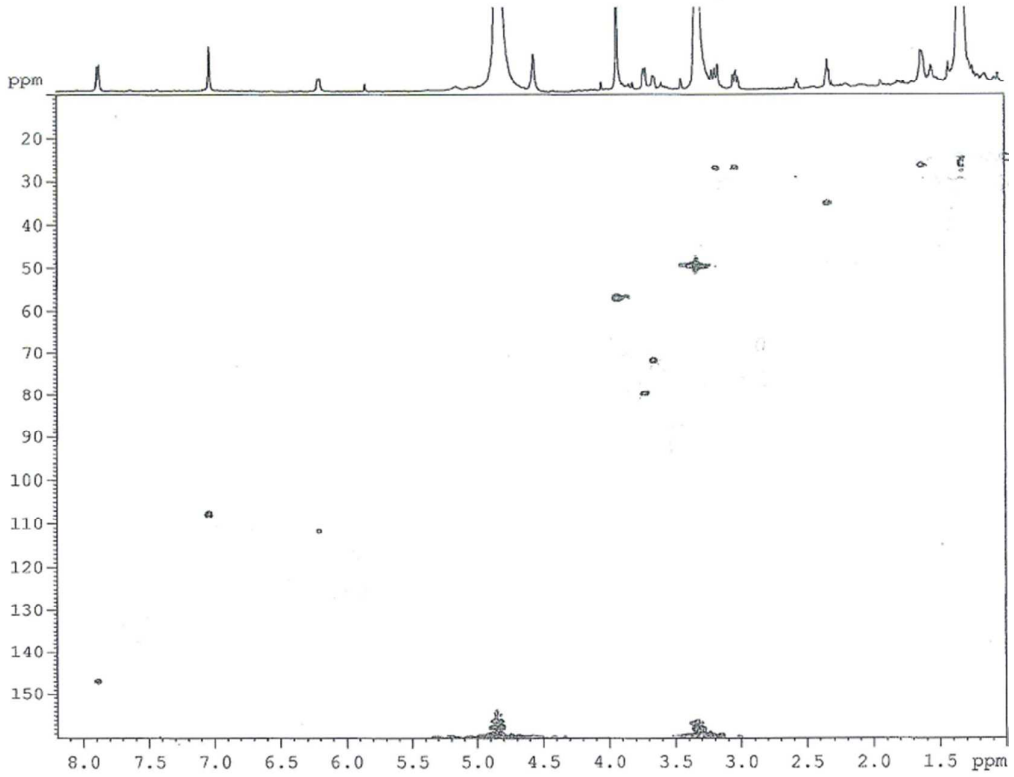

Figure S10. HMBC spectrum of compound **3** (CD_3OD, 600 MHz)

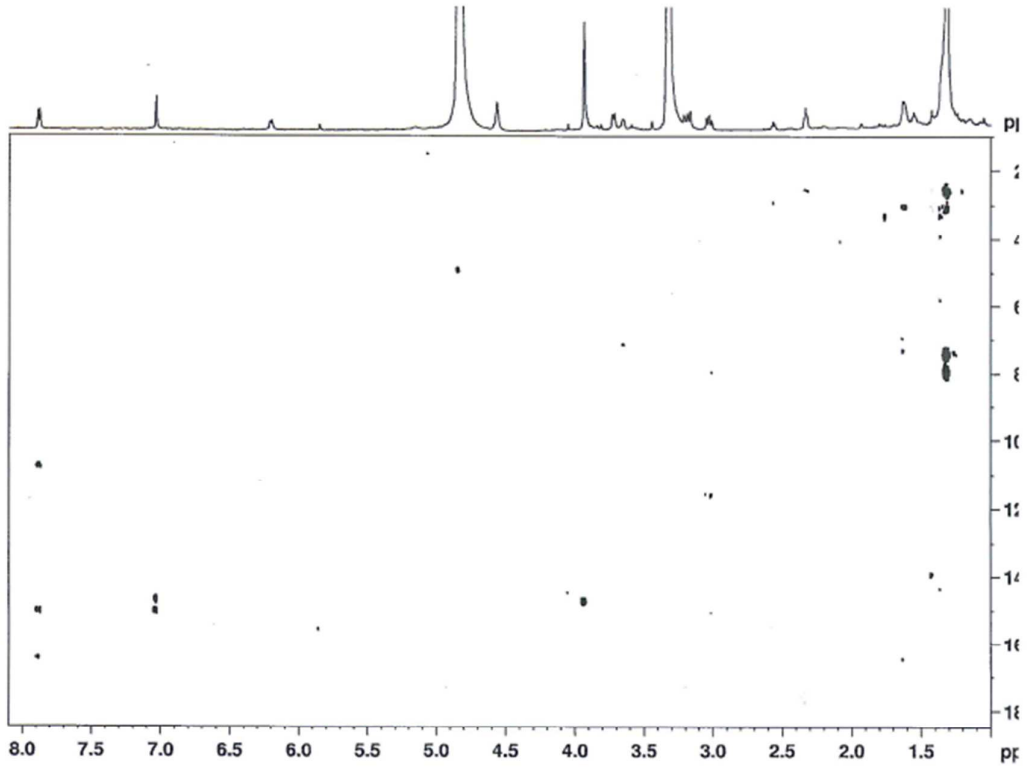

Figure S11. HRESIMS spectrum of compound **3**

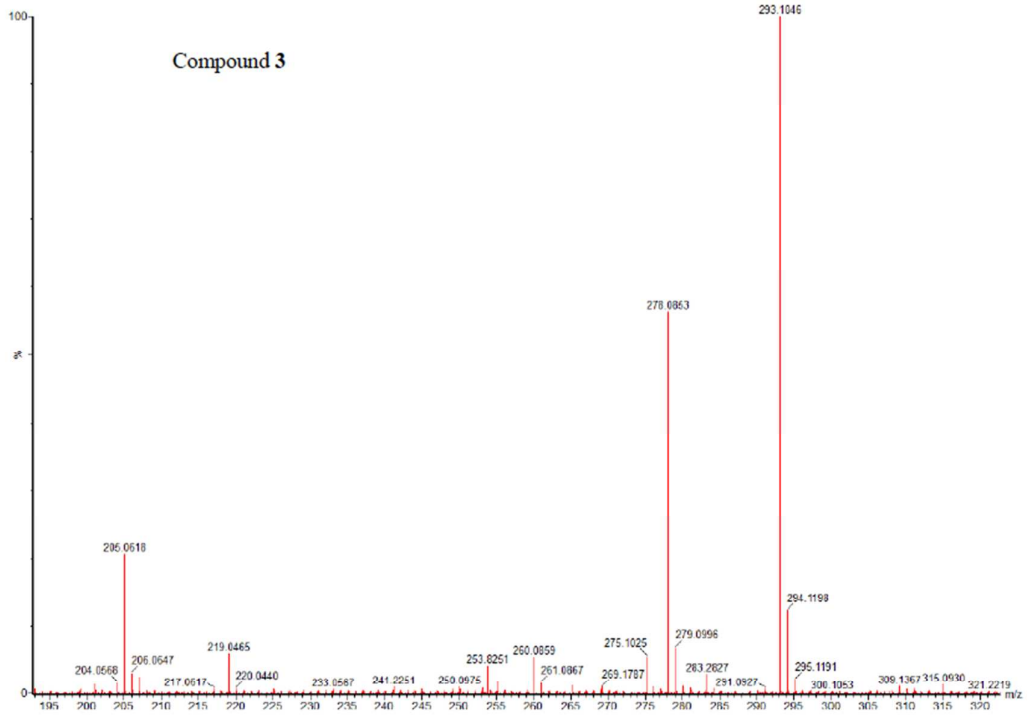

Figure S12. ^{1}H NMR spectrum of compound **4** (CD_3OD, 600 MHz)

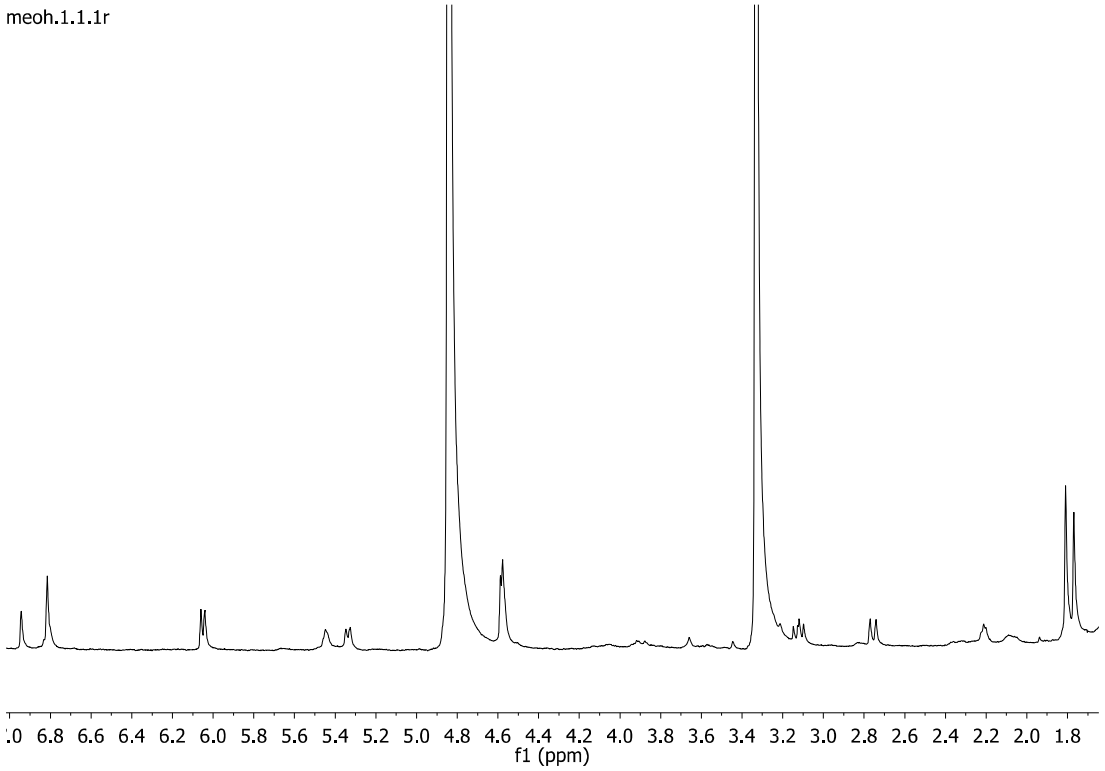

Figure S13. HSQC spectrum of compound **4** (CD_3OD, 600 MHz)

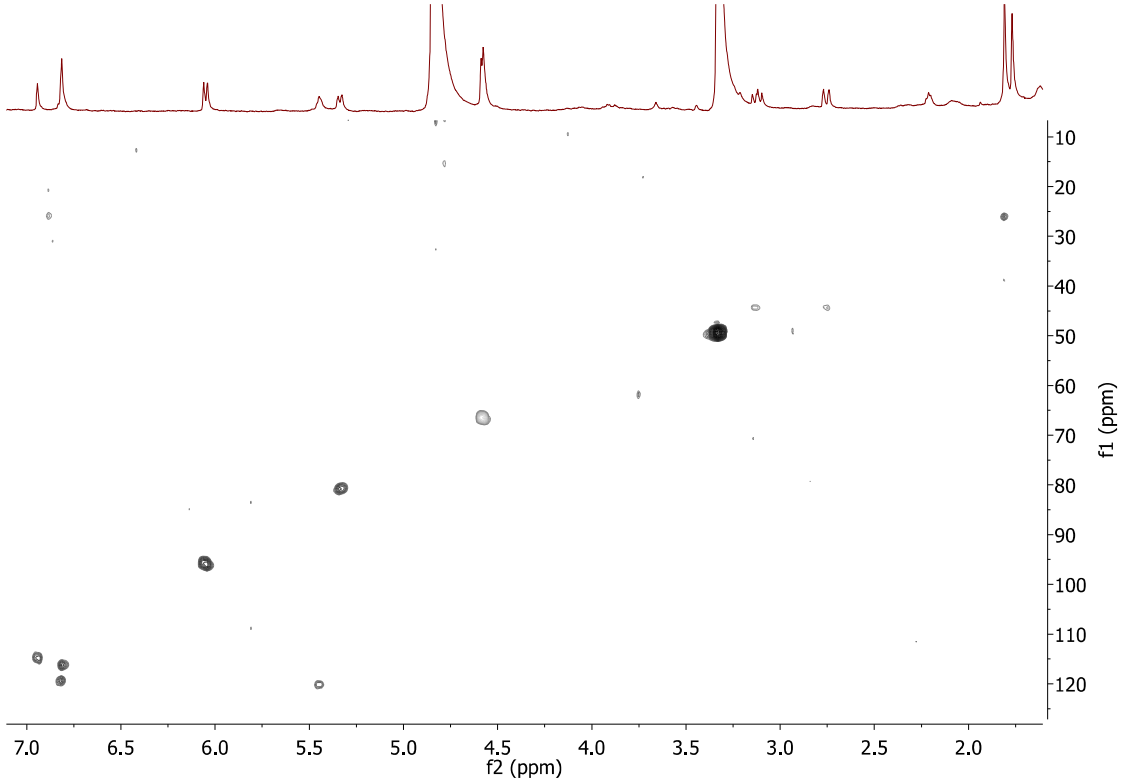

Figure S14. HMBC spectrum of compound **4** (CD_3OD, 600 MHz)

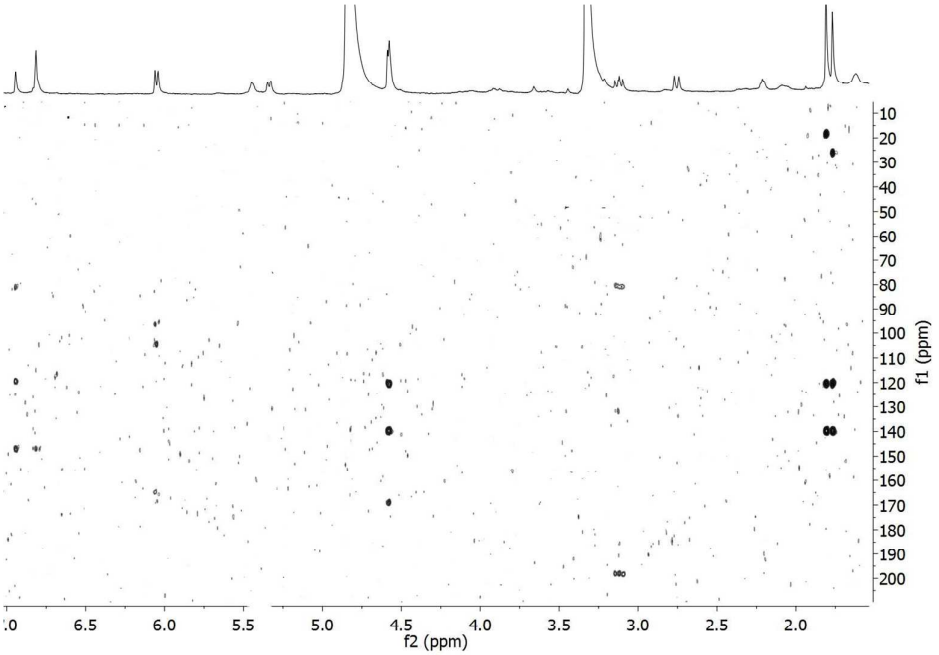

Figure S15. HRESIMS spectrum of compound **4**

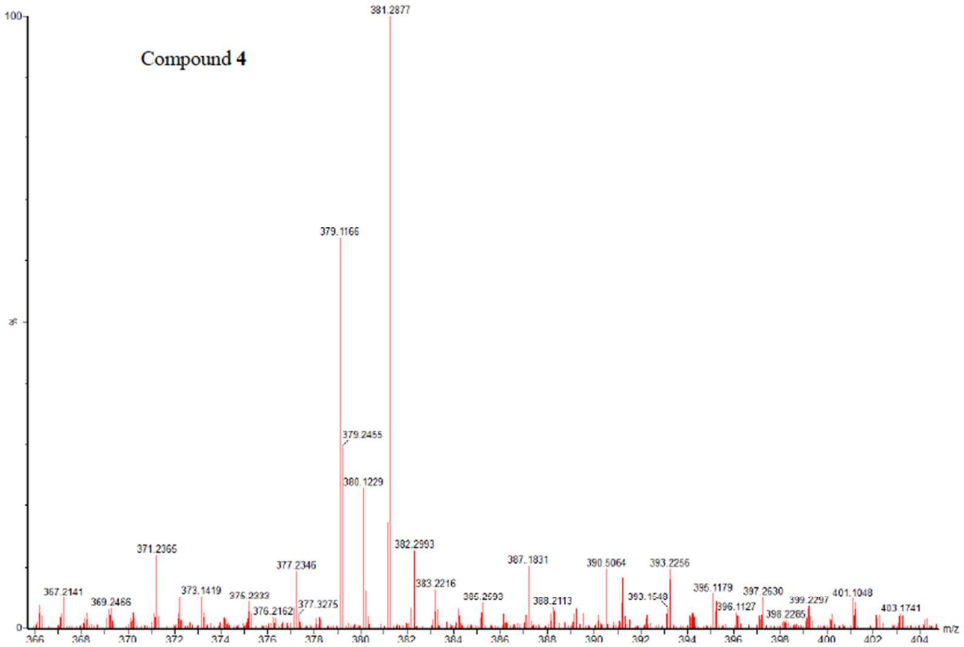

Figure S16. ^{1}H NMR spectrum of compound **5** (CD_3OD, 600 MHz)

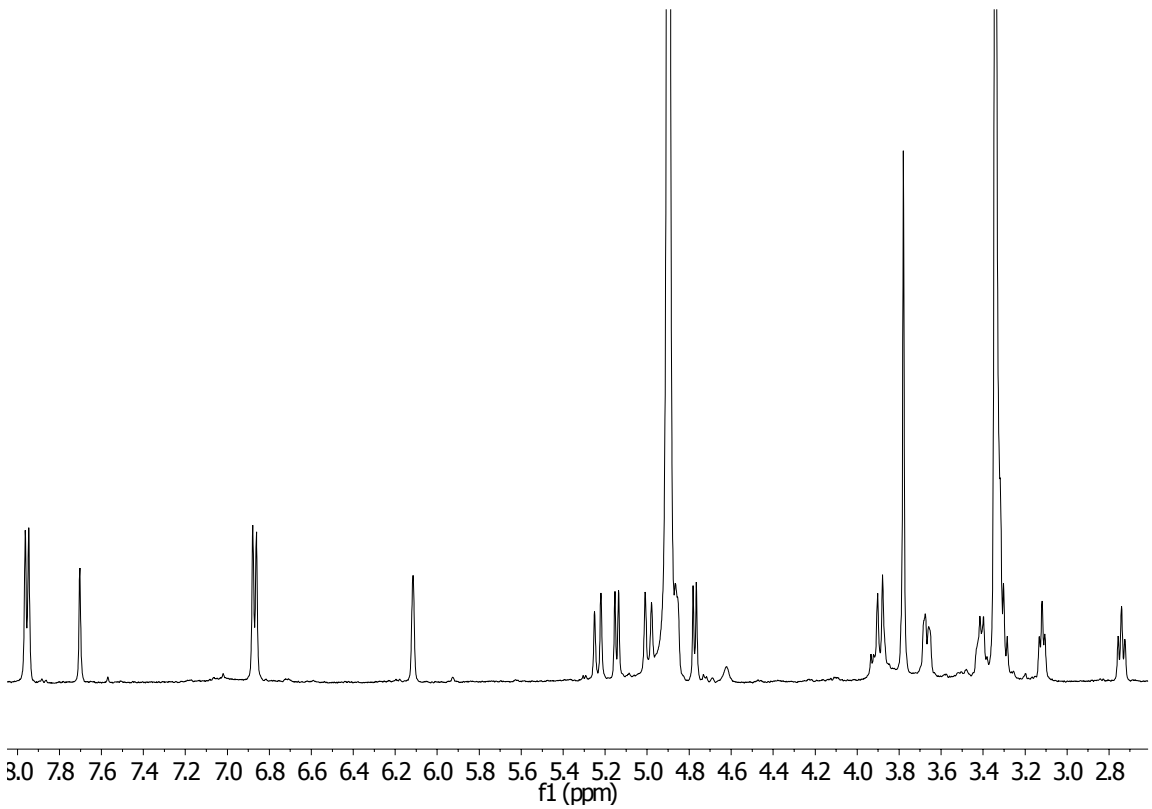

Figure S17. 1D TOCSY spectrum of compound **5** (aglycone moiety) (CD_3OD, 600 MHz)

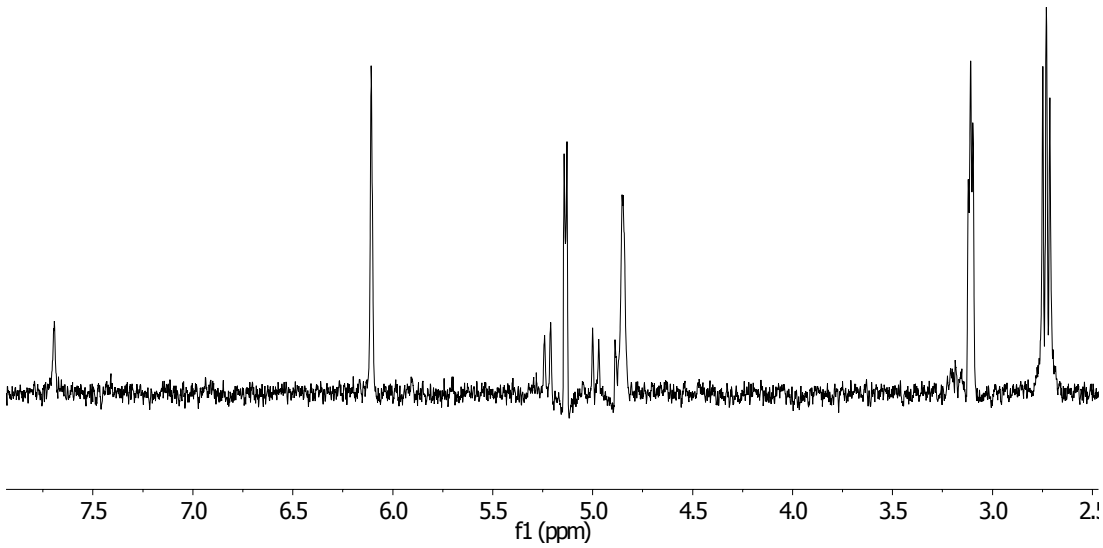

Figure S18. 1D TOCSY spectrum of compound **5** (sugar moiety) (CD_3OD, 600 MHz)

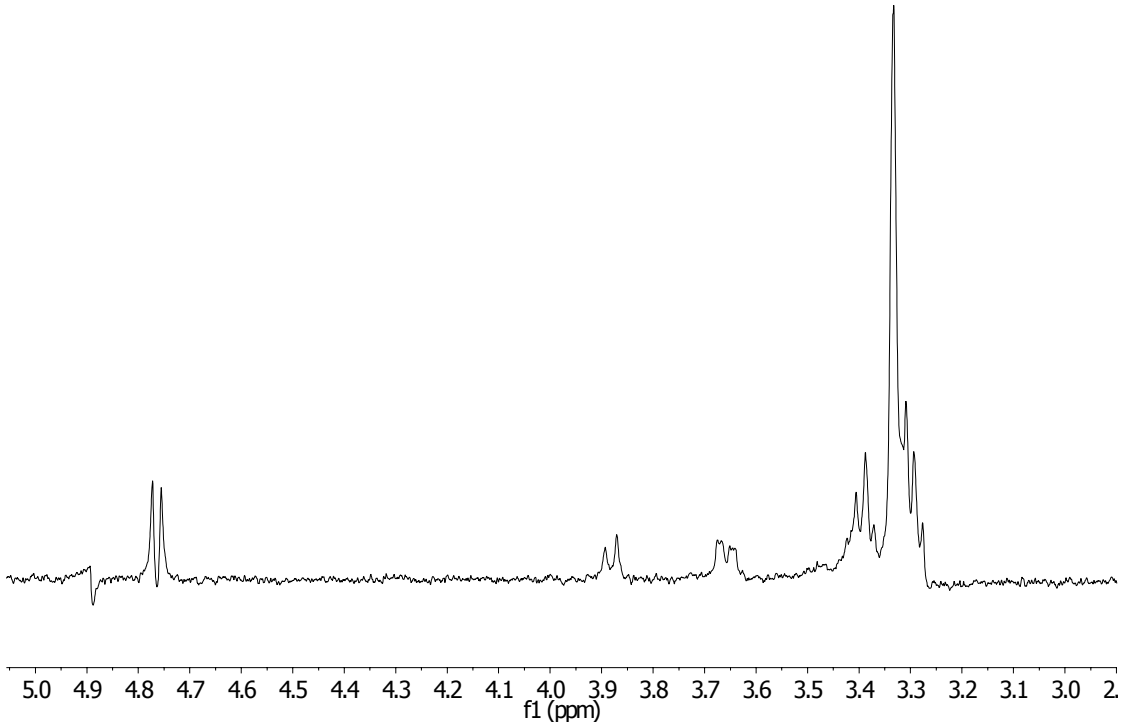

Figure S19. HSQC spectrum of compound **5** (CD_3OD, 600 MHz)

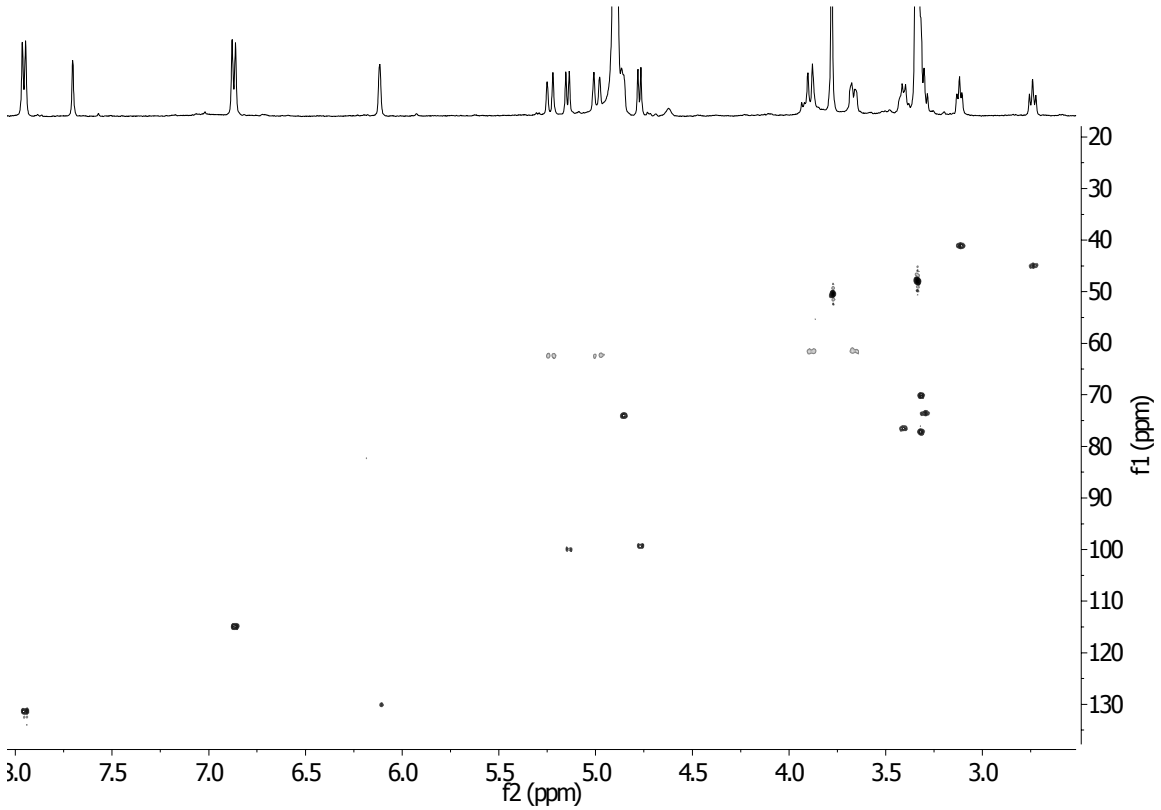

Figure S20. HRESIMS spectrum of compound **5**

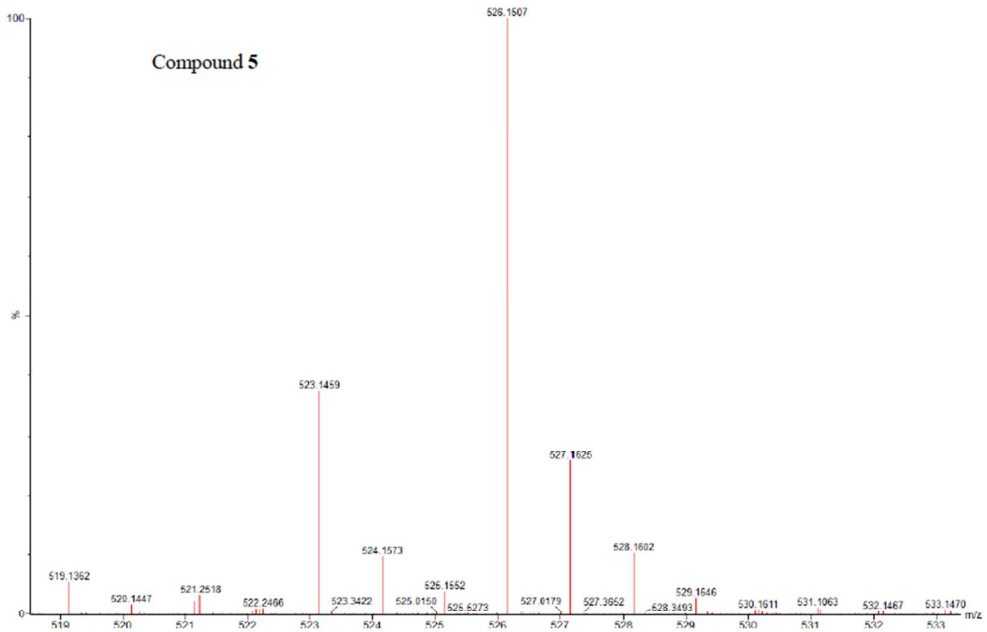

Figure S21. ^{1}H NMR spectrum of compound **6** (CD_3OD, 250 MHz)

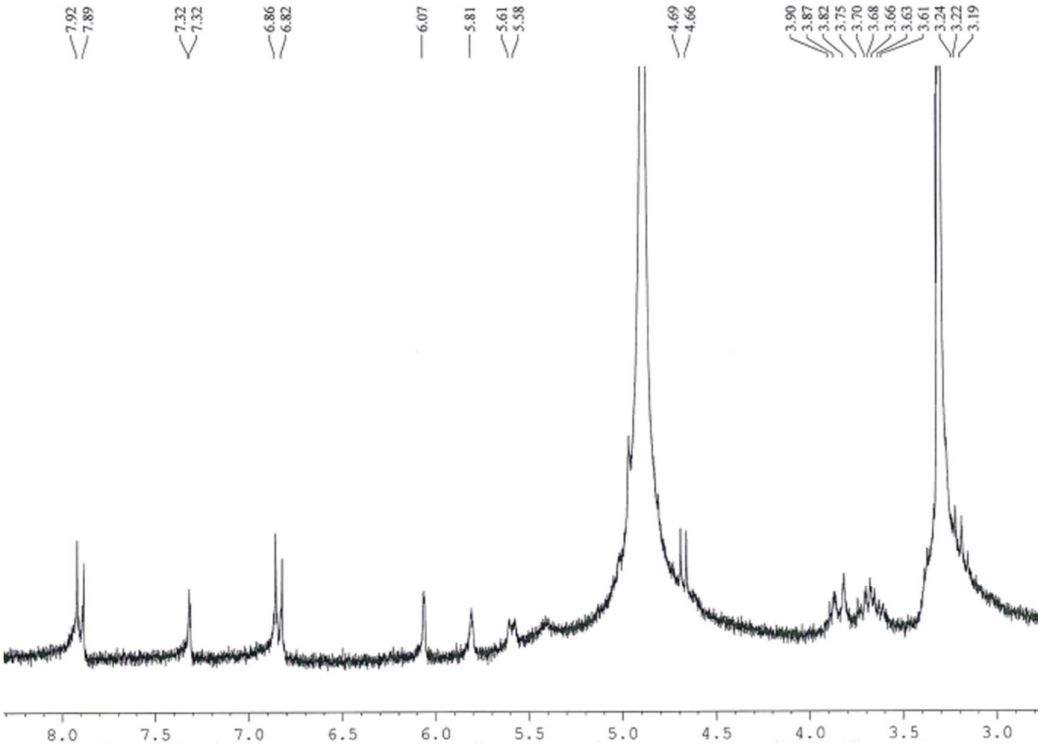

Figure S22. HSQC spectrum of compound **6** (CD_3OD, 250 MHz)

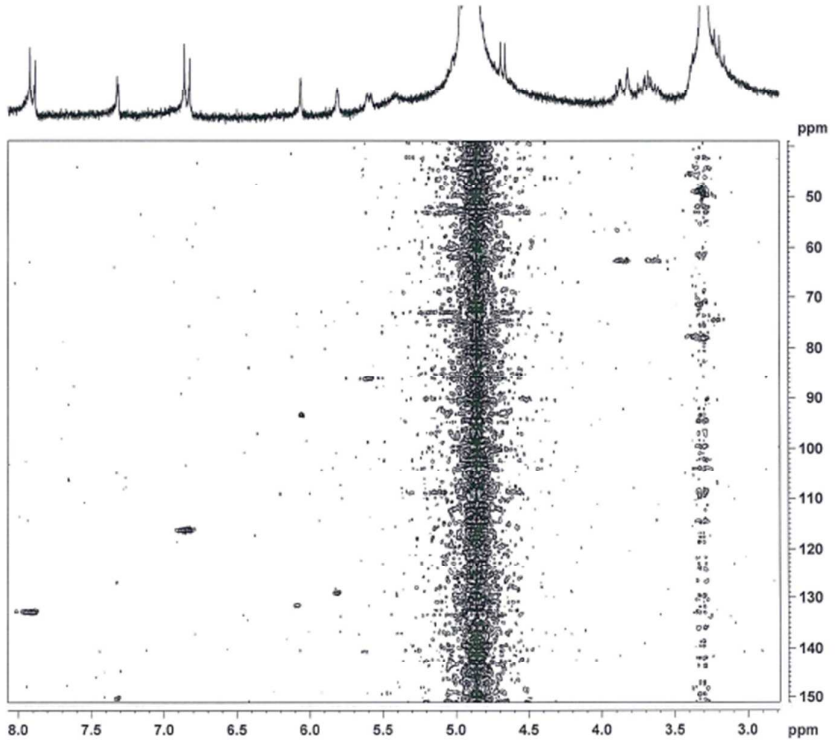

Figure S23. ^{1}H NMR spectrum of compound **7** (CD_3OD, 600 MHz)

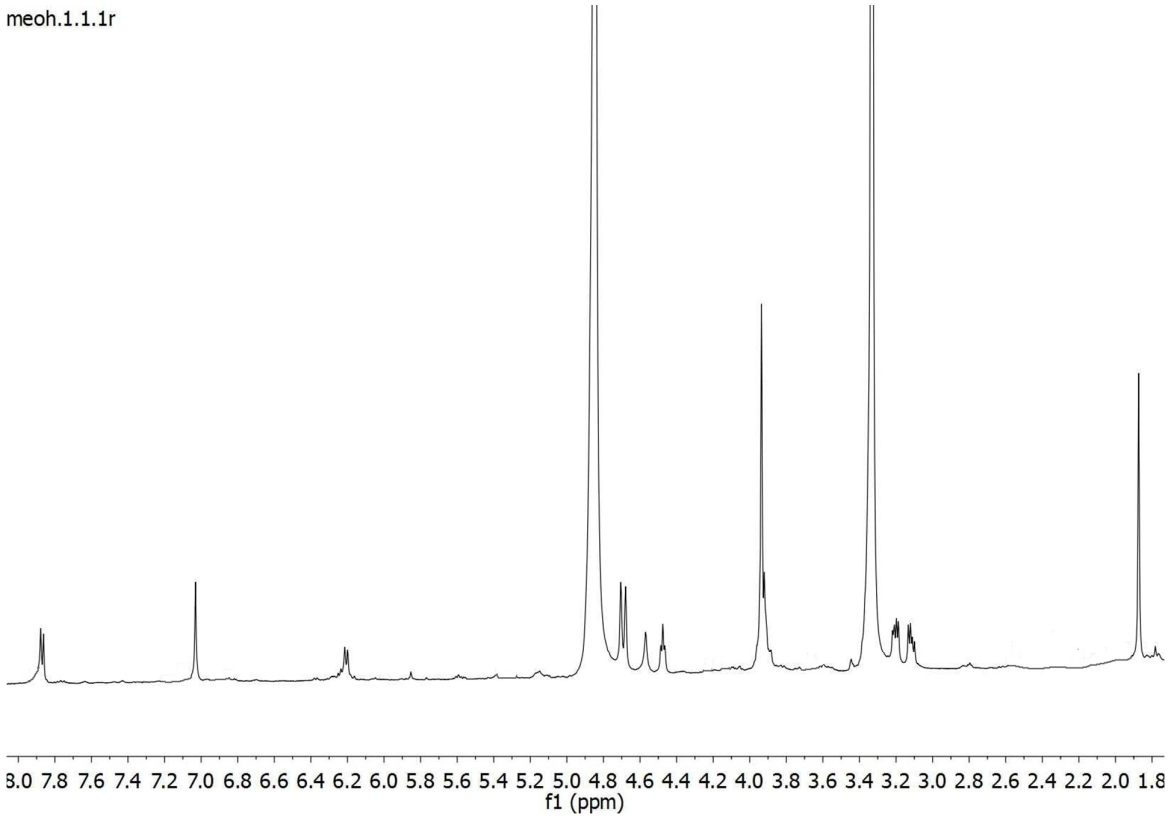

Figure S24. HSQC spectrum of compound **7** (CD_3OD, 600 MHz)

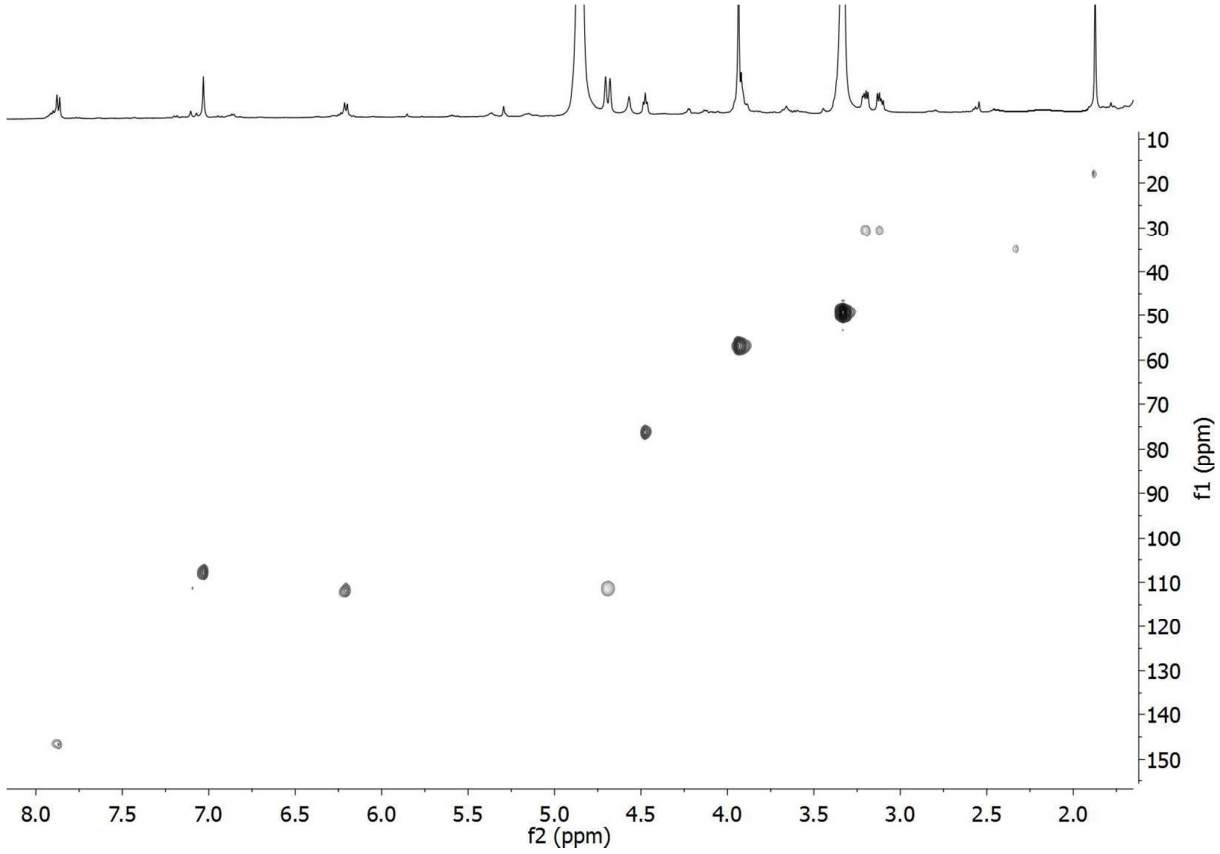

Figure S25. HMBC spectrum of compound **7** (CD_3OD, 600 MHz)

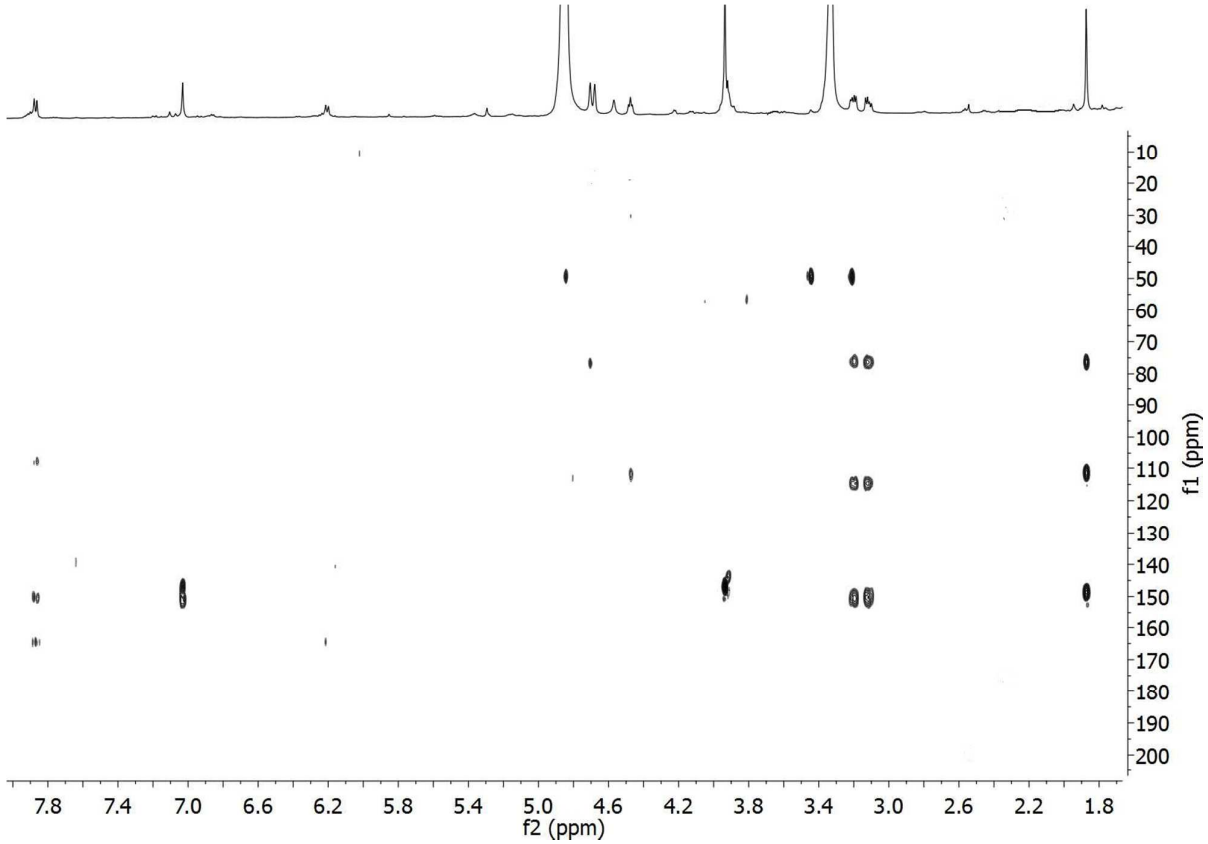

Figure S26. Sequence alignment of α-1,4-glucosidase (P53341) and oligo-1,6-glucosidase (3A4A PDB code, P53051) from *Saccharomyces cerevisiae*

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P53341|α-Glucosidase         -MTISDHPETEPKWWKEATIYQIYPASFKDSNNDGWGDLKGITSKLQYIK
P53051|oligo-Glucosidase     MTISSAHPETEPKWWKEATFYQIYPASFKDSNDDGWGDMKGIASKLEYIK
                                 * *************:************:*****:***:***:***

P53341|α-Glucosidase         DLGVDAIWVCPFYDSPQQDMGYDISNYEKVWPTYGTNEDCFELIDKTHKL
P53051|oligo-Glucosidase     ELGADAIWISPFYDSPQDDMGYDIANYEKVWPTYGTNEDCFALIEKTHKL
                             :**.****:.*******:******:*************** **:*****

P53341|α-Glucosidase         GMKFITDLVINHCSTEHEWFKESRSSKTNPKRDWFFWRPPKGYDAEGKPI
P53051|oligo-Glucosidase     GMKFITDLVINHCSSEHEWFKESRSSKTNPKRDWFFWRPPKGYDAEGKPI
                             **************:**********************************

P53341|α-Glucosidase         PPNNWKSFFGGSAWTFDETTNEFYLRLFASRQVDLNWENEDCRRAIFESA
P53051|oligo-Glucosidase     PPNNWKSYFGGSAWTFDEKTQEFYLRLFCSTQPDLNWENEDCRKAIYESA
                             *******:**********.*:*******.* * **********:**:***

P53341|α-Glucosidase         VGFWLDHGVDGFRIDTAGLYSKRPGLPDSPIFDKTSKLQHPNWGSHNGPR
P53051|oligo-Glucosidase     VGYWLDHGVDGFRIDVGSLYSKVVGLPDAPVVDKNSTWQSSDPYTLNGPR
                             **:************...****  ****:*:.**.*. * .:  : ****

P53341|α-Glucosidase         IHEYHQELHRFMKNRVKDGREIMTVGEVAHGSDN--ALYTSAARYEVSEV
P53051|oligo-Glucosidase     IHEFHQEMNQFIRNRVKDGREIMTVGEMQHASDETKRLYTSASRHELSEL
                             ***:***:::*::**************: *.**:   *****:*:*:**:

P53341|α-Glucosidase         FSFTHVEVGTSPFFRYNIVPFTLKQWKEAIASNFLFINGTDSWATTYIEN
P53051|oligo-Glucosidase     FNFSHTDVGTSPLFRYNLVPFELKDWKIALAELFRYINGTDCWSTIYLEN
                             *.*:*.:*****:****:*** **:** *:*. * :*****.*:* *:**

P53341|α-Glucosidase         HDQARSITRFADDSPKYRKISGKLLTLLECSLTGTLYVYQGQEIGQINFK
P53051|oligo-Glucosidase     HDQPRSITRFGDDSPKNRVISGKLLSVLLSALTGTLYVYQGQELGQINFK
                             ***.******.***** * ******::* .:************:******

P53341|α-Glucosidase         EWPIEKYEDVDVKNNYEIIKKSFGKNSKEMKDFFKGIALLSRDHSRTPMP
P53051|oligo-Glucosidase     NWPVEKYEDVEIRNNYNAIKEEHGENSEEMKKFLEAIALISRDHARTPMQ
                             :**:******:::***: **:..*:**:***.*::.***:****:****

P53341|α-Glucosidase         WTKDKPNAGFTGPDVKPWFLLNESFEQGINVEQESRDDDSVLNFWKRALQ
P53051|oligo-Glucosidase     WSREEPNAGFSGPSAKPWFYLNDSFREGINVEDEIKDPNSVLNFWKEALK
                             *::::*****:**..**** **:**.:*****:* :* :*******.**:

P53341|α-Glucosidase         ARKKYKELMIYGYDFQFIDLDSDQIFSFTKEYEDKTLFAALNFSGEEIEF
P53051|oligo-Glucosidase     FRKAHKDITVYGYDFEFIDLDNKKLFSFTKKYNNKTLFAALNFSSDATDF
                             ** :*:: :*****:*****..::*****:*::**********.:  :*

P53341|α-Glucosidase         SLPREGASLSFILGNYD--DTDVSSRVLKPWEGRIYLVK
P53051|oligo-Glucosidase     KIPNDDSSFKLEFGNYPKKEVDASSRTLKPWEGRIYISE
                             .:*.:.:*:.: :***   :.*.***.*********: :
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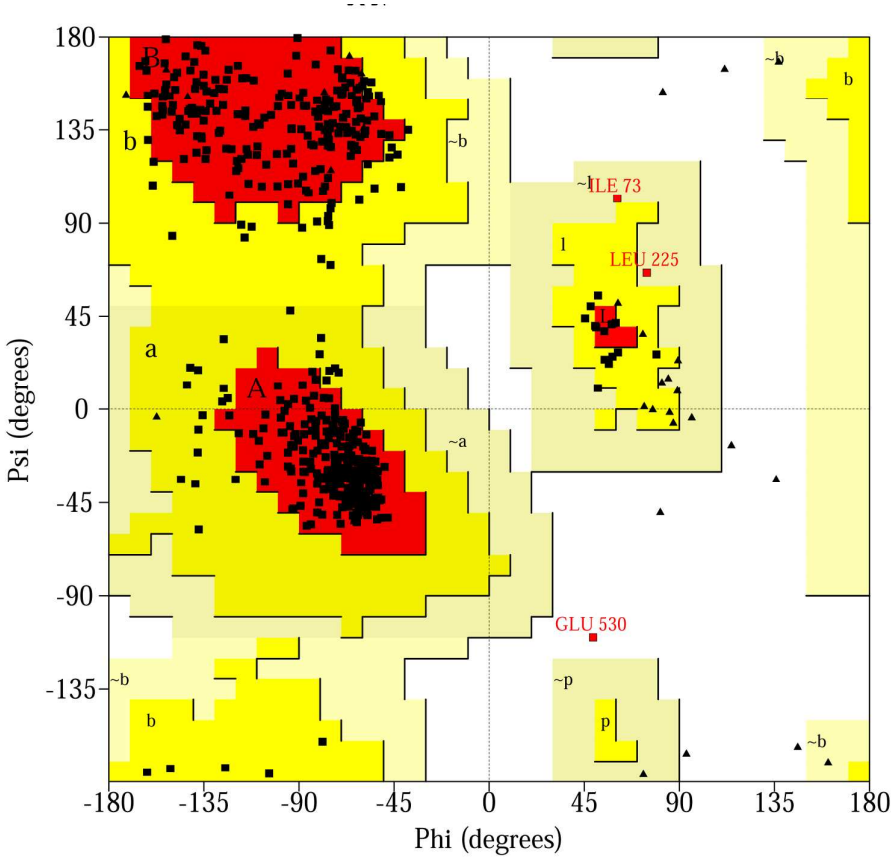
Figure S27. Ramachandran plot of the α-1,4-glucosidase model. The most favoured regions are coloured in red, additional allowed regions are indicated in yellow, while generously allowed and disallowed zones are pointed out by light yellow and white fields, respectively.

(To insert Ramachandran Plot).



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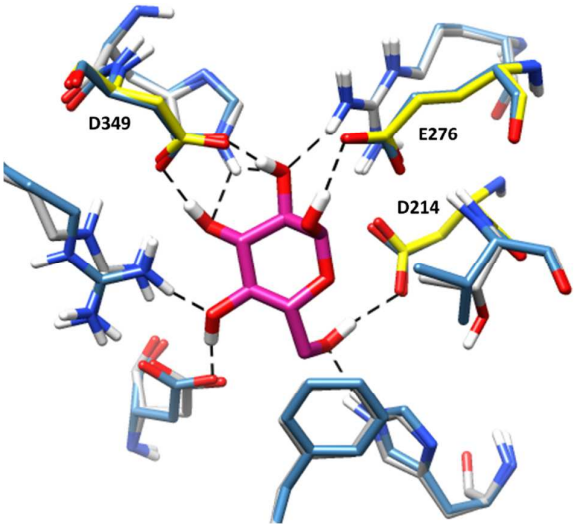

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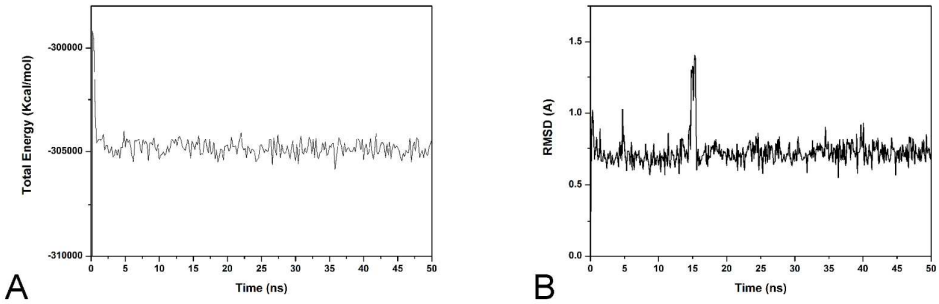

Figure S30. Analysis of the MD simulations of the α-1,4-glucosidase model complexed with compound **4** (pose 4). The plot shows the RMSD of the position of the ligand with respect to its initial docking pose.