Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

SUPPORTING INFORMATION

Computational study of the glycylserine hydrolysis at physiological pH: zwitterionic versus anionic mechanism

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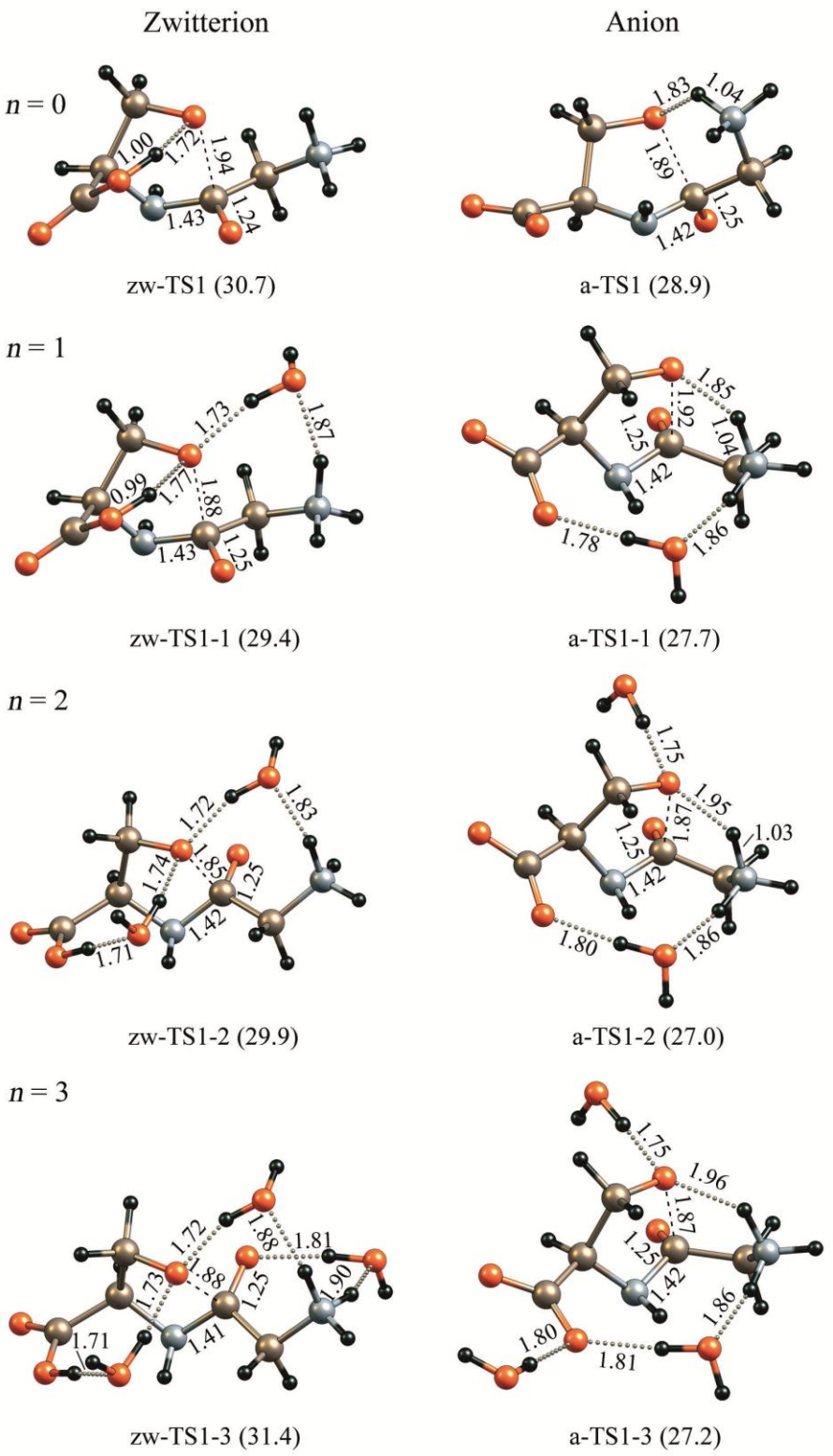

Figure S1. Transition state structures involving different numbers of explicit water molecules (*n*) for the Ser –OH addition on the amide carbon. Relative free energies, given in brackets, are in kcal/mol and the interatomic distances are in Å.

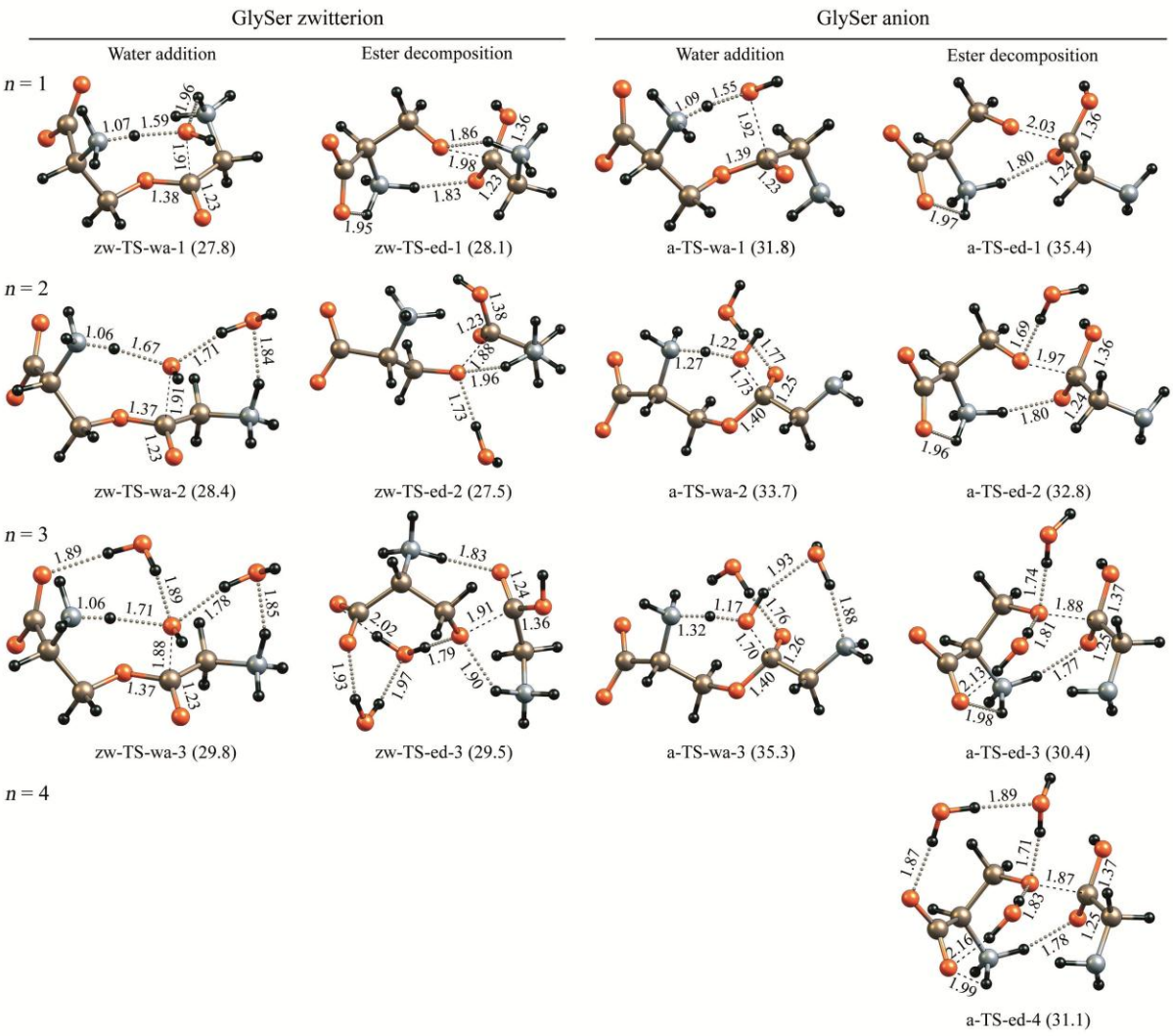

Figure S2. Transition state structures involving different numbers of explicit water molecules (*n*) for the -NH_2 assisted water addition and ester decomposition in GlySer zwitterion and in GlySer anion. Relative free energies, given in brackets, are in kcal/mol and the interatomic distances are in Å.

SMD-M06/6-311+G(2df,2p) optimized molecular geometries

Reactants

GlySer anion (**A**)

N	-3.059073000	1.151741000	0.598934000
C	-3.013131000	-0.131250000	-0.073248000
C	-1.625354000	-0.662366000	-0.313353000
N	-0.613776000	0.141701000	0.018897000
O	-1.473571000	-1.783045000	-0.807520000
C	0.770585000	-0.163775000	-0.240749000
C	1.610576000	1.116528000	-0.265259000
O	1.042145000	2.210858000	-0.092921000
O	2.843637000	0.941156000	-0.442887000
H	-3.960200000	1.586304000	0.448441000
H	-3.563606000	-0.931450000	0.435080000
H	-3.466866000	-0.037705000	-1.062967000
H	0.862793000	-0.642434000	-1.222485000
H	-0.837992000	1.084868000	0.314816000
C	1.325590000	-1.127072000	0.806699000
H	1.348760000	-0.618107000	1.780823000
H	0.657999000	-1.985880000	0.898345000
O	2.604485000	-1.606750000	0.453022000
H	3.083726000	-0.825136000	0.121710000
H	-2.957824000	1.025310000	1.599321000

GlySer zwitterion (**ZW**)

N	-3.971625000	-0.068917000	0.073017000
C	-2.750400000	0.748328000	0.215887000
C	-1.548044000	-0.087199000	-0.141730000
N	-0.377309000	0.456258000	0.188851000
O	-1.682807000	-1.162879000	-0.715421000
C	0.895357000	-0.096582000	-0.215225000
C	1.977187000	0.987407000	-0.154674000
O	3.136178000	0.600408000	-0.445095000
O	1.646188000	2.138888000	0.185353000
H	-4.808998000	0.502924000	0.185167000
H	-3.997076000	-0.815980000	0.769087000
H	-2.822033000	1.596209000	-0.464219000
H	-2.694071000	1.127034000	1.233559000
H	0.829053000	-0.450139000	-1.250150000
H	-0.344630000	1.396257000	0.569422000
C	1.287344000	-1.280407000	0.665105000
H	1.463171000	-0.922274000	1.689153000
H	0.461651000	-1.993414000	0.702658000
O	2.418358000	-1.953594000	0.158636000
H	3.039048000	-1.250042000	-0.104267000
H	-3.995572000	-0.513833000	-0.847441000

H_2O

H	0.000000000	0.759653000	-0.470387000
O	0.000000000	0.000000000	0.117597000
H	0.000000000	-0.759653000	-0.470387000

Ser –OH addition

a-TS1-2

N	0.516355000	2.450458000	-0.764455000
C	1.291090000	2.078772000	0.443563000
C	1.158169000	0.608036000	0.792940000

N	-0.174189000	0.178714000	1.046369000
O	2.104715000	0.096340000	1.431347000
C	-0.446116000	-1.059121000	0.330637000
C	-1.919306000	-1.408923000	0.241066000
O	-2.190846000	-2.610488000	0.030302000
O	-2.758888000	-0.474181000	0.310730000
H	0.792832000	3.366400000	-1.114025000
H	-0.508848000	2.450439000	-0.608281000
H	2.339358000	2.288215000	0.246256000
H	0.961467000	2.692403000	1.282233000
H	0.098191000	-1.879922000	0.803232000
H	-0.851324000	0.869050000	0.737838000
C	0.108216000	-0.819137000	-1.083912000
H	0.278540000	-1.779364000	-1.589815000
H	-0.655004000	-0.273688000	-1.670874000
O	1.274143000	-0.084411000	-0.944129000
H	0.729688000	1.720884000	-1.460654000
O	-2.342043000	2.151135000	-0.477126000
H	-2.566879000	1.236018000	-0.206313000
H	-2.783310000	2.722537000	0.157528000
O	3.045520000	-2.145838000	-0.657769000
H	3.098466000	-2.317164000	0.285801000
H	2.458543000	-1.358232000	-0.728925000

zw-TS1-1

N	-2.809882000	-0.960278000	-0.374765000
C	-1.789564000	-1.101678000	0.682643000
C	-0.424020000	-0.940493000	0.040402000
N	0.637834000	-1.029103000	0.998693000
O	-0.277967000	-1.368866000	-1.120632000
C	1.479233000	0.174794000	0.970645000
C	2.430994000	0.133049000	-0.210531000
O	3.568394000	-0.268579000	-0.123589000
O	1.960260000	0.583050000	-1.365341000
H	-3.658008000	-1.483792000	-0.167645000
H	-2.395199000	-1.312003000	-1.246891000
H	-1.975185000	-0.372625000	1.468457000
H	-1.860281000	-2.106029000	1.101974000
H	2.090397000	0.200982000	1.870878000
H	0.239864000	-1.069370000	1.933733000
C	0.486850000	1.321580000	0.866532000
H	-0.020793000	1.436324000	1.837318000
H	0.983620000	2.273282000	0.638103000
O	-0.377889000	0.932930000	-0.149984000
H	0.996835000	0.795718000	-1.249709000
H	-3.046516000	0.042120000	-0.496761000
O	-2.887716000	1.891532000	-0.306703000
H	-1.927486000	1.697187000	-0.191125000
H	-3.204518000	2.139822000	0.566022000

zw-TS1

N	-3.102637000	-0.270340000	-0.451762000
C	-2.272939000	0.175211000	0.684316000
C	-0.884564000	-0.385727000	0.473887000
N	0.096370000	0.190347000	1.335290000
O	-0.780552000	-1.555139000	0.069755000
C	1.177181000	0.815585000	0.555773000
C	2.098600000	-0.239202000	-0.029262000
O	3.111000000	-0.607250000	0.522267000
O	1.750711000	-0.731318000	-1.208682000
H	-2.975120000	-1.277374000	-0.584950000
H	-2.779391000	0.194222000	-1.303711000
H	-2.290025000	1.260966000	0.728620000
H	-2.699360000	-0.230818000	1.602656000
H	1.778784000	1.432749000	1.221315000
H	-0.331136000	0.949083000	1.860571000
C	0.453579000	1.597569000	-0.531175000

H	-0.034481000	2.468979000	-0.064183000
H	1.157485000	1.983636000	-1.282071000
O	-0.452675000	0.697738000	-1.074459000
H	0.850405000	-0.364318000	-1.442144000
H	-4.092309000	-0.070023000	-0.313085000

GlySer ester forms

a-ester

N	3.957811000	0.756210000	0.295741000
C	2.544673000	0.769665000	0.577499000
C	1.721812000	-0.236813000	-0.176061000
N	-1.889397000	-1.136023000	1.475872000
O	2.155325000	-1.037647000	-0.970551000
C	-1.846525000	-0.787980000	0.066136000
C	-2.276254000	0.647534000	-0.295746000
O	-2.447438000	0.870813000	-1.518860000
O	-2.417037000	1.479574000	0.626059000
H	4.106099000	0.903916000	-0.696454000
H	2.366928000	0.597215000	1.641663000
H	2.121389000	1.754790000	0.368494000
H	-2.521108000	-1.454527000	-0.479046000
H	-1.292380000	-0.491282000	1.984989000
C	-0.474606000	-1.052588000	-0.494072000
H	-0.157164000	-2.074767000	-0.281511000
H	-0.446619000	-0.887082000	-1.571609000
O	0.436778000	-0.138679000	0.143413000
H	-2.825140000	-0.957960000	1.823969000
H	4.333476000	-0.163000000	0.501203000

zw-ester

N	-4.295324000	-0.088876000	-0.012128000
C	-3.038809000	0.564382000	-0.424357000
C	-1.869686000	-0.210684000	0.101834000
N	1.714764000	1.821545000	0.138880000
O	-1.974798000	-1.198370000	0.784929000
C	1.639411000	0.481921000	-0.414069000
C	2.901576000	-0.334765000	-0.107864000
O	3.153281000	-1.279088000	-0.891525000
O	3.552194000	-0.031820000	0.915580000
H	-5.101936000	0.424904000	-0.368847000
H	-4.368046000	-0.135472000	1.006145000
H	-3.000026000	0.611753000	-1.510532000
H	-3.021820000	1.581604000	-0.038045000
H	1.541385000	0.544912000	-1.501038000
H	0.801242000	2.260228000	0.098544000
C	0.478245000	-0.330215000	0.113148000
H	0.473039000	-1.343230000	-0.293738000
H	0.505250000	-0.380262000	1.205535000
O	-0.737698000	0.332222000	-0.290370000
H	1.970693000	1.746726000	1.118462000
H	-4.344126000	-1.047241000	-0.364803000

Water addition

a-TS-wa-1

N	3.444236000	-1.239550000	-0.242226000
C	2.542359000	-0.281287000	-0.866104000
C	1.516021000	0.253893000	0.102281000
N	-1.426468000	1.564150000	0.481346000
O	1.832902000	0.978614000	1.050928000
C	-1.693313000	0.151342000	0.839571000

C	-2.344103000	-0.577796000	-0.344316000
O	-2.545822000	-1.797742000	-0.175966000
O	-2.633424000	0.103871000	-1.348376000
H	2.905365000	-2.019525000	0.119653000
H	3.117969000	0.565059000	-1.240921000
H	2.044794000	-0.749385000	-1.714384000
H	-2.404778000	0.135447000	1.668432000
H	-2.249161000	1.973374000	0.042233000
C	-0.421522000	-0.517049000	1.304658000
H	0.033523000	0.049806000	2.119286000
H	-0.667897000	-1.511048000	1.676379000
O	0.501674000	-0.683365000	0.243207000
H	-1.181229000	2.107137000	1.307449000
H	3.890937000	-0.805254000	0.559079000
O	0.621906000	1.401070000	-1.158007000
H	1.174666000	2.184260000	-1.094616000
H	-0.603108000	1.603728000	-0.227251000

zw-TS-wa-1

N	1.780511000	1.914781000	0.287150000
C	2.504747000	0.776858000	-0.315912000
C	1.627116000	-0.449056000	-0.361310000
N	-1.353392000	-1.301841000	1.220239000
O	2.115049000	-1.562809000	-0.541005000
C	-1.721308000	-0.837908000	-0.140301000
C	-2.104351000	0.647616000	-0.107195000
O	-2.518912000	1.112679000	-1.187970000
O	-1.964974000	1.249932000	0.975769000
H	2.394158000	2.708165000	0.466441000
H	1.384855000	1.551811000	1.167421000
H	2.812637000	1.042106000	-1.326970000
H	3.383006000	0.567140000	0.287510000
H	-2.584282000	-1.413920000	-0.476256000
H	-1.994348000	-0.908551000	1.907271000
C	-0.577583000	-1.072367000	-1.099891000
H	-0.155249000	-2.072085000	-0.975481000
H	-0.948271000	-0.986080000	-2.120786000
O	0.423952000	-0.083007000	-0.920139000
H	-1.382020000	-2.318142000	1.276078000
H	1.007643000	2.222370000	-0.304600000
O	1.110343000	-0.361337000	1.471298000
H	1.757100000	-0.952513000	1.864627000
H	-0.360452000	-0.965390000	1.447052000

Decomposition

a-TS-d-2

N	1.374085000	-0.924548000	2.158347000
C	2.232068000	-0.250836000	1.208810000
C	1.958132000	-0.575785000	-0.238828000
N	-1.094093000	-2.022997000	-0.358251000
O	1.669395000	-1.730303000	-0.614005000
C	-1.588041000	-0.794194000	-1.046358000
C	-2.547907000	-0.050298000	-0.112308000
O	-3.140255000	0.924640000	-0.610492000
O	-2.634111000	-0.460669000	1.069314000
H	0.412805000	-0.659839000	1.964062000
H	2.179772000	0.830183000	1.350067000
H	3.271891000	-0.541131000	1.389664000
H	-2.129194000	-1.090598000	-1.944687000
H	-1.433402000	-1.966773000	0.611431000
C	-0.400598000	0.086275000	-1.420398000
H	0.194049000	-0.453726000	-2.176290000
H	-0.802533000	0.976750000	-1.925512000
O	0.362631000	0.416729000	-0.320647000
H	-1.458815000	-2.872098000	-0.783661000

H	1.424158000	-1.924368000	1.989183000
O	2.758772000	0.184346000	-1.055391000
H	2.748170000	-0.227026000	-1.929874000
H	-0.053832000	-2.054166000	-0.356950000
O	1.133613000	3.009594000	-0.636377000
H	1.964249000	3.020579000	-1.117822000
H	0.909124000	2.055911000	-0.541257000
O	-0.797833000	1.725721000	1.853561000
H	-0.342212000	1.315733000	1.090095000
H	-1.583793000	1.171942000	1.947674000

zw-TS-d-1

N	2.653403000	-0.310243000	-1.443387000
C	2.921980000	-0.358924000	0.012252000
C	1.696154000	-0.780319000	0.779848000
N	-1.321115000	-1.022513000	-1.225111000
O	1.641857000	-0.633691000	2.000778000
C	-1.686753000	0.266052000	-0.576871000
C	-3.078066000	0.152252000	0.042198000
O	-3.605939000	1.228427000	0.384526000
O	-3.539089000	-1.001029000	0.192235000
H	2.522576000	-1.246538000	-1.828005000
H	3.411670000	0.144614000	-1.950949000
H	3.727152000	-1.068195000	0.198789000
H	3.228140000	0.630530000	0.340283000
H	-1.664484000	1.044587000	-1.338117000
H	-1.848977000	-1.759459000	-0.740246000
C	-0.647632000	0.568728000	0.500745000
H	-0.909773000	1.544830000	0.933157000
H	-0.766660000	-0.169991000	1.316281000
O	0.625158000	0.547030000	-0.016612000
H	-1.579835000	-1.045066000	-2.209984000
H	1.777161000	0.214016000	-1.570135000
O	1.134731000	-1.901561000	0.203263000
H	0.544144000	-2.298929000	0.858767000
H	-0.312395000	-1.199452000	-1.130834000
O	1.710794000	3.030137000	-0.175480000
H	2.238591000	3.169841000	0.614400000
H	1.332484000	2.127256000	-0.072639000

Products

Gly anion

C	0.647841000	0.059957000	0.000381000
O	1.700633000	-0.628868000	0.010566000
O	0.599706000	1.310537000	-0.003654000
C	-0.654992000	-0.730763000	-0.015620000
H	-0.625244000	-1.370737000	-0.901532000
N	-1.899979000	0.013584000	0.002330000
H	-1.925076000	0.578315000	0.844839000
H	-0.627330000	-1.415172000	0.835600000
H	-1.882295000	0.683998000	-0.759075000

Gly zwitterion

C	-0.706215000	0.059376000	-0.000598000
O	-0.544899000	1.298972000	-0.010839000
O	-1.780836000	-0.569011000	0.016253000
C	0.555089000	-0.796658000	-0.020795000
H	0.567442000	-1.468553000	0.832982000
N	1.757319000	0.075446000	0.014877000
H	2.280976000	-0.024032000	0.882677000
H	1.397950000	1.041516000	-0.043696000
H	0.574202000	-1.395176000	-0.928137000

H	2.390834000	-0.097868000	-0.762913000

Ser zwitterion

C	0.171223000	0.347511000	-0.662729000
C	-1.111055000	-0.244053000	-0.053207000
C	1.391012000	-0.519991000	-0.478704000
N	0.421516000	1.681575000	-0.050063000
O	-1.818152000	0.530482000	0.623669000
O	-1.329875000	-1.440321000	-0.318031000
O	1.695410000	-0.703037000	0.889163000
H	-0.009483000	0.503507000	-1.727790000
H	2.257850000	-0.036133000	-0.933821000
H	1.231519000	-1.470402000	-0.991401000
H	0.931119000	1.567430000	0.830277000
H	-0.482217000	2.107659000	0.176943000
H	0.962205000	2.291811000	-0.661997000
H	1.072249000	-1.332686000	1.267662000