Supporting Information

Modeling Differential Enthalpy of Absorption of CO₂ with Piperazine as a Function of Temperature

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Table S1: Gaseous Phase Gibbs free energy of piperazine species, using G3MP2B3, G3MP2, G4MP2, CBS-QB3 and DFT level of theories, at 298 K. (All values are in Hartrees)

| Amine                        | G3MP2B3   | G3MP2    | G4MP2    | CBS-QB3   | DFT(B3LYP/6-311++G(d,p)) |
|------------------------------|-----------|----------|----------|-----------|--------------------------|
| Piperazine (PZ)              | -267.5044 | -267.4909 | -267.5300 | -267.4474 | -267.8927                |
| Protonated Piperazine (PZH⁺) | -267.8644 | -267.8512 | -267.8900 | -267.8064 | -268.2527                |
| Diprotonated Piperazine (PZH₂⁺) | -268.0543 | -268.0413 | -268.0798 | -267.9951 | -267.9951                |
| Piperazine Carbamate (PZCOO⁻) | -455.3540 | -455.3337 | -455.4021 | -455.2877 | -455.9889                |
| Protonated Piperazine Carbamate (H⁺ PZCOO⁻) | -455.8307 | -455.8103 | -455.8858 | -455.7632 | -456.4658                |
| Piperazine Dicarbamate PZ(COO)₂⁻ | -643.1179 | -643.0911 | -643.1886 | -643.0422 | -644.0004                |

Table S2: Gaseous Phase enthalpy of piperazine species, using G3MP2B3, G3MP2, G4MP2, CBS-QB3, DFT and HF level of theories, at 298 K. (All values are in Hartrees)

| Amine                        | G3MP2B3   | G3MP2    | G4MP2    | CBS-QB3   | DFT(B3LYP/6-311++G(d,p)) |
|------------------------------|-----------|----------|----------|-----------|--------------------------|
| Piperazine (PZ)              | -267.4692 | -267.4557 | -267.4949 | -267.4123 | -267.8580                |
| Protonated Piperazine (PZH⁺) | -267.8290 | -267.8157 | -267.8547 | -267.7712 | -268.2170                |
| Diprotonated Piperazine (PZH₂⁺) | -268.0192 | -268.0063 | -268.0449 | -267.9603 | -267.9951                |
| Piperazine Carbamate (PZCOO⁻) | -455.3119 | -455.2917 | -455.3601 | -455.2549 | -455.9470                |
| Protonated Piperazine Carbamate (H⁺ PZCOO⁻) | -455.7878 | -455.7676 | -455.8443 | -455.7208 | -456.4234                |
| Piperazine Dicarbamate PZ(COO)₂⁻ | -643.0691 | -643.0424 | -643.1401 | -642.9940 | -643.9521                |
### Table S3: Gaseous Phase Gibbs free energy and enthalpy of bicarbonate (HCO$_3$), water (H$_2$O), CO$_2$ and H$_3$O$^+$ using G3MP2B3, G3MP2, G4MP2, CBS-QB3, DFT and HF level of theories, at 298 K. (All values are in Hartrees)

| Species        | G3MP2B3    | G3MP2     | G4MP2     | CBS-QB3    | DFT(B3LYP/6-311++G(d,p)) |
|----------------|------------|-----------|-----------|------------|--------------------------|
| Bicarbonate    | -264.2052  | -264.1949 | -264.2390 | -264.1876  | -264.5509                |
| Water          | -76.3633   | -76.3600  | -76.3735  | -76.3551   | -76.4549                 |
| CO$_2$         | -76.6214   | -76.6184  | -76.6325  | -76.6129   | -76.7142                 |
| H$_3$O$^+$     | -188.4072  | -188.3995 | -188.4301 | -188.3934  | -188.6566                |

### Gaseous phase Enthalpy

| Species        | G3MP2B3    | G3MP2     | G4MP2     | CBS-QB3    | DFT(B3LYP/6-311++G(d,p)) |
|----------------|------------|-----------|-----------|------------|--------------------------|
| Bicarbonate    | -264.1749  | -264.1647 | -264.2087 | -264.1573  | -264.5210                |
| Water          | -76.3419   | -76.3386  | -76.3521  | -76.3337   | -76.4335                 |
| CO$_2$         | -76.6002   | -76.5973  | -76.6113  | -76.5918   | -76.6930                 |
| H$_3$O$^+$     | -188.3822  | -188.3753 | -188.4052 | -188.3685  | -188.6317                |

### Table S4: Underlying data for Table 2 for Piperazine species: energy of solute and cluster in gas phase, thermal corrections to the energy and entropy of solute and cluster.

| Amine                              | $E^a(A)$ [a.u.] | $E^a(A(S)_5)$ [a.u.] | $E_{corr}^a(A)$ [a.u.] | $E_{corr}^a(A(S)_5)$ [a.u.] | $S_{total}^c(A)$ [cal/mol] | $S_{total}^c(A(S)_5)$ [cal/mol] |
|------------------------------------|-----------------|-----------------------|------------------------|-----------------------------|--------------------------|-------------------------------|
| Piperazine (PZ)                    | -266.17         | -646.32               | 0.16                   | 0.31                        | 72.37                    | 158.61                        |
| Protonated Piperazine (PZH$^+$)    | -266.56         | -646.73               | 0.18                   | 0.33                        | 72.87                    | 161.63                        |
| Diprotonated Piperazine (PZH$_2^{2+}$) | -266.77         | -647.01               | 0.20                   | 0.34                        | 73.38                    | 154.31                        |
| Piperazine Carbamate (PZCOO$^-$)   | -453.25         | -833.45               | 0.17                   | 0.32                        | 85.90                    | 164.29                        |
| Protonated Piperazine Carbamate (H$^+$ PZCOO$^-$) | -453.75         | -833.93               | 0.18                   | 0.33                        | 87.12                    | 158.29                        |
| Piperazine Dicarbamate PZ (COO)$_2^{2-}$ | -640.25         | -1020.48              | 0.17                   | 0.32                        | 98.89                    | 175.98                        |

a: Energy of solute and solute-solvent cluster, standard state of 1 atmosphere. b: Thermal correction to the energy and zero-point energy for solute and solute-solvent cluster, standard state of 1 atmosphere. c: Total entropy of solute and solute-solvent cluster, standard state of 1 atmosphere.
Table S5: Quantitative details of optimized structures of the first solvation shell from molecular simulations for a set of 100 initial geometries of Piperazine.

| Energy  | Total Entropy | Trans Ent | Rot Ent | Vib Ent | dGsolv | Area   |
|---------|---------------|-----------|---------|---------|---------|--------|
| -646.305 | 163.72        | 41.405    | 32.617  | 89.697  | -22.37  | 245.31 |
|         |Ignoring Geometry|          |         |         |         |        |
| -646.319 | 159.891       | 41.405    | 32.678  | 85.807  | -18.91  | 243.3268|
| -646.294 | 148.909       | 41.405    | 32.527  | 74.976  | -22.72  | 237.7864|
|         |Ignoring Geometry|          |         |         |         |        |
| -646.317 | 169.288       | 41.405    | 32.647  | 95.235  | -18.83  | 241.1956|
| -646.295 | 157.396       | 41.405    | 32.604  | 83.387  | -24.67  | 245.8227|
| -646.298 | 172.153       | 41.405    | 32.663  | 98.084  | -23.99  | 247.86 |
|         |Ignoring Geometry|          |         |         |         |        |
| -646.322 | 158.088       | 41.405    | 32.198  | 84.484  | -16.29  | 230.4662|
| -646.325 | 158.613       | 41.405    | 32.216  | 84.992  | -15.62  | 228.4892|
| -646.319 | 165.669       | 41.405    | 32.651  | 91.612  | -19.19  | 243.2776|
| -646.324 | 153.053       | 41.405    | 32.397  | 79.25   | -16.4   | 236.1716|
| -646.325 | 155.324       | 41.405    | 32.357  | 81.562  | -15.82  | 235.5874|
| -646.325 | 160.946       | 41.405    | 32.338  | 87.203  | -15.8   | 237.753|
| -646.325 | 161.02        | 41.405    | 32.334  | 87.28   | -15.65  | 235.8431|
| -646.306 | 157.32        | 41.405    | 32.435  | 83.48   | -20.68  | 235.0066|
|         |Ignoring Geometry|          |         |         |         |        |
| -646.304 | 155.833       | 41.405    | 32.947  | 81.48   | -22.83  | 250.3674|
| -646.325 | 157.494       | 41.405    | 32.572  | 83.517  | -16.61  | 242.7598|
| -646.315 | 157.256       | 41.405    | 32.428  | 83.423  | -17.76  | 229.2114|
|         |Ignoring Geometry|          |         |         |         |        |
| -646.325 | 158.564       | 41.405    | 32.489  | 84.67   | -16.37  | 239.0556|
| -646.319 | 156.669       | 41.405    | 32.442  | 82.822  | -15.5   | 237.5191|
| -646.306 | 167.729       | 41.405    | 33.111  | 93.212  | -23.13  | 258.3611|
|        |       |       |       |       |       |
|--------|-------|-------|-------|-------|-------|
| -646.325 | 160.62 | 41.405 | 32.357 | 86.858 | -15.8 |
| -646.316 | 170.457 | 41.405 | 32.72 | 96.331 | -18.58 |
| -646.316 | 169.643 | 41.405 | 32.788 | 95.45 | -18.76 |
| -646.314 | 166.851 | 41.405 | 32.739 | 92.706 | -19.68 |
| -646.323 | 163.496 | 41.405 | 32.248 | 89.843 | -15.77 |
| -646.321 | 158.884 | 41.405 | 32.572 | 84.906 | -16.67 |
| -646.314 | 171.654 | 41.405 | 32.556 | 97.693 | -17.73 |
| -646.324 | 159.213 | 41.405 | 32.356 | 85.451 | -16.28 |
| -646.323 | 159.862 | 41.405 | 32.441 | 88.112 | -15.89 |
| -646.325 | 161.878 | 41.405 | 32.361 | 92.706 | -19.68 |
| -646.305 | 167.522 | 41.405 | 32.532 | 93.585 | -21.88 |
|         |         |       |       |       |       |
| -646.303 | 170.672 | 41.405 | 32.952 | 96.315 | -23.19 |
|         |         |       |       |       |       |
|         |         |       |       |       |       |
| -646.311 | 161.21 | 41.405 | 32.45 | 87.354 | -18.71 |
| -646.318 | 156.708 | 41.405 | 32.641 | 82.662 | -18.02 |
| -646.315 | 141.846 | 41.405 | 32.499 | 67.942 | -17.49 |
| -646.307 | 146.326 | 41.405 | 32.52 | 72.401 | -21.06 |
| -646.32 | 150.774 | 41.405 | 32.118 | 77.251 | -15.32 |
| -646.324 | 155.405 | 41.405 | 32.261 | 81.739 | -16.31 |
| -646.319 | 166.572 | 41.405 | 32.653 | 92.513 | -19.1 |
| -646.321 | 160.461 | 41.405 | 32.273 | 86.783 | -17.65 |
| -646.305 | 145.376 | 41.405 | 32.519 | 71.452 | -21.12 |
| -646.323 | 155.253 | 41.405 | 32.238 | 81.61 | -16.11 |
| -646.318 | 160.085 | 41.405 | 33.036 | 85.644 | -19.07 |
|         |         |       |       |       |       |
|         |         |       |       |       |       |
| -646.323 | 147.587 | 41.405 | 32.438 | 73.743 | -17.26 |
| -646.309 | 147.564 | 41.405 | 32.389 | 73.769 | -20.33 |
| -646.326 | 157.726 | 41.405 | 32.538 | 83.782 | -16.39 |
| -646.32 | 156.62 | 41.405 | 32.428 | 82.786 | -15.96 |
| -646.325 | 150.803 | 41.405 | 32.539 | 76.858 | -16.75 |
| -646.316 | 132.908 | 41.405 | 32.678 | 58.824 | -18.91 |
| -646.325 | 161.305 | 41.405 | 32.334 | 87.566 | -15.74 |
| -646.321 | 159.668 | 41.405 | 32.609 | 85.654 | -17.17 |

Ignoring Geometry

|        |       |       |       |       |       |
|--------|-------|-------|-------|-------|-------|
| -646.311 | 161.21 | 41.405 | 32.45 | 87.354 | -18.71 |
| -646.318 | 156.708 | 41.405 | 32.641 | 82.662 | -18.02 |
| -646.315 | 141.846 | 41.405 | 32.499 | 67.942 | -17.49 |
| -646.307 | 146.326 | 41.405 | 32.52 | 72.401 | -21.06 |
| -646.32 | 150.774 | 41.405 | 32.118 | 77.251 | -15.32 |
| -646.324 | 155.405 | 41.405 | 32.261 | 81.739 | -16.31 |
| -646.319 | 166.572 | 41.405 | 32.653 | 92.513 | -19.1 |
| -646.321 | 160.461 | 41.405 | 32.273 | 86.783 | -17.65 |
| -646.305 | 145.376 | 41.405 | 32.519 | 71.452 | -21.12 |
| -646.323 | 155.253 | 41.405 | 32.238 | 81.61 | -16.11 |
| -646.318 | 160.085 | 41.405 | 33.036 | 85.644 | -19.07 |

Ignoring Geometry

|        |       |       |       |       |       |
|--------|-------|-------|-------|-------|-------|
| -646.323 | 147.587 | 41.405 | 32.438 | 73.743 | -17.26 |
| -646.309 | 147.564 | 41.405 | 32.389 | 73.769 | -20.33 |
| -646.326 | 157.726 | 41.405 | 32.538 | 83.782 | -16.39 |
| -646.32 | 156.62 | 41.405 | 32.428 | 82.786 | -15.96 |
| -646.325 | 150.803 | 41.405 | 32.539 | 76.858 | -16.75 |
| -646.316 | 132.908 | 41.405 | 32.678 | 58.824 | -18.91 |
| -646.325 | 161.305 | 41.405 | 32.334 | 87.566 | -15.74 |
| -646.321 | 159.668 | 41.405 | 32.609 | 85.654 | -17.17 |
|       |       |       |       |       |       |
|-------|-------|-------|-------|-------|-------|
| -646.318 | 149.127 | 41.405 | 32.364 | 75.357 | -17.9 |
| -646.314 | 159.774 | 41.405 | 32.449 | 85.92  | -19.38 |
| -646.317 | 162.344 | 41.405 | 32.257 | 88.682 | -18.06 |
| -646.324 | 163.612 | 41.405 | 32.333 | 89.874 | -16.05 |
| -646.312 | 145.752 | 41.405 | 32.442 | 71.905 | -19.88 |
| -646.325 | 153.77 | 41.405 | 32.269 | 80.095 | -15.41 |
|Ignoring Geometry|       |       |       |       |       |
| -646.316 | 161.571 | 41.405 | 32.725 | 87.441 | -18.59 |
| -646.319 | 140.073 | 41.405 | 32.331 | 66.336 | -16.94 |
| -646.317 | 168.667 | 41.405 | 32.733 | 94.529 | -18.09 |
|Ignoring Geometry|       |       |       |       |       |
| -646.316 | 163.947 | 41.405 | 32.718 | 89.823 | -18.55 |
| -646.318 | 168.933 | 41.405 | 32.544 | 94.983 | -17.82 |
|Ignoring Geometry|       |       |       |       |       |
| -646.323 | 161.505 | 41.405 | 32.337 | 87.763 | -15.99 |
| -646.308 | 152.546 | 41.405 | 32.145 | 78.996 | -17.57 |
| -646.315 | 166.811 | 41.405 | 33.002 | 92.404 | -18.46 |
|Ignoring Geometry|       |       |       |       |       |
| -646.323 | 160.65 | 41.405 | 32.306 | 86.938 | -15.69 |
| -646.314 | 157.047 | 41.405 | 32.645 | 82.997 | -18.14 |
| -646.312 | 163.127 | 41.405 | 32.915 | 88.807 | -19.72 |
| -646.318 | 148.439 | 41.405 | 32.854 | 74.179 | -17.92 |
| -646.317 | 148.034 | 41.405 | 32.605 | 74.024 | -17.34 |
| -646.318 | 161.229 | 41.405 | 32.63 | 87.193 | -19.19 |
| -646.319 | 169.929 | 41.405 | 32.554 | 95.969 | -18.53 |
| -646.317 | 158.319 | 41.405 | 32.248 | 84.665 | -19.46 |
| -646.308 | 164.258 | 41.405 | 32.287 | 90.566 | -20.3 |
| -646.319 | 163.935 | 41.405 | 32.653 | 89.877 | -19.06 |
| -646.321 | 156.593 | 41.405 | 32.571 | 82.616 | -16.66 |
| -646.3 | 154.608 | 41.405 | 32.858 | 80.345 | -22.89 |
|Ignoring Geometry|       |       |       |       |       |
| -646.294 | 149.73 | 41.405 | 32.454 | 75.871 | -23.48 |
| -646.297 | 158.089 | 41.405 | 32.8 | 83.884 | -23.92 |
| -646.317 | 166.152 | 41.405 | 32.502 | 92.245 | -18.61 |
| -644.932 | 138.712 | 41.405 | 34.194 | 63.112 | -83.85 |
| -646.324 | 157.924 | 41.405 | 32.369 | 84.15 | -15.93 |

Summary

| Valid Geometries | 82 |

S7
Minimum Energy Value  -646.326

*The rows designated by 'ignoring geometries' refers to the geometries of first solvation shell from molecular simulations which are not able to converge due to poor representation of solvation shell surrounding the molecule. In case of PZ, a total of 82 geometries converged, with a minimum energy of -646.326 hartrees.

Molecular Geometries of ESS clusters for various Piperazine species (x,y,z Cartesian Coordinates in Å).

Piperazine (PZ)

|  | x         | y         | z         |
|---|-----------|-----------|-----------|
| 1 | 14.436801000 | 12.445319000 | 11.200365000 |
| 6 | 13.701667000 | 12.402752000 | 11.996441000 |
| 6 | 13.451001000 | 11.844386000 | 14.342504000 |
| 6 | 12.345521000 | 10.858112000 | 13.980855000 |
| 6 | 12.593730000 | 11.413792000 | 11.651703000 |
| 1 | 13.010262000 | 12.798860000 | 14.612159000 |
| 1 | 12.776373000 | 9.860958000  | 13.848817000 |
| 1 | 13.035020000 | 10.443174000 | 11.407581000 |
| 1 | 13.281732000 | 13.398630000 | 12.098855000 |
| 1 | 14.009096000 | 11.492490000 | 15.203248000 |
| 1 | 11.621961000 | 10.796846000 | 14.786658000 |
| 1 | 12.048470000 | 11.750938000 | 10.776946000 |
| 7 | 14.386986000 | 12.075983000 | 13.244801000 |
| 1 | 14.955720000 | 11.260439000 | 13.110878000 |
| 7 | 11.668737000 | 11.308433000 | 12.772225000 |
| 1 | 10.930926000 | 10.668766000 | 12.537294000 |
| 8 | 7.264649000  | 13.360265000 | 12.674861000 |
| 1 | 8.190963000  | 13.525580000 | 12.861638000 |
| 1 | 6.798000000  | 13.508984000 | 13.485987000 |
| 8 | 10.010451000 | 13.674910000 | 13.306176000 |
| 1 | 10.585967000 | 12.922305000 | 13.124981000 |
| 1 | 10.543258000 | 14.455821000 | 13.240880000 |
| 8 | 9.393287000  | 9.381990000  | 11.866322000 |
| 1 | 8.597279000  | 9.869406000  | 11.649289000 |
| 1 | 9.109502000  | 8.517478000  | 12.129576000 |
| 8 | 7.020737000  | 10.881018000 | 11.320049000 |
| 1 | 6.729606000  | 11.075799000 | 10.439715000 |
| 1 | 7.045247000  | 11.717690000 | 11.789076000 |
| 8 | 15.458372000 | 14.787857000 | 13.906454000 |
| 1 | 15.265810000 | 13.870233000 | 13.714703000 |
| 1 | 16.381856000 | 14.837876000 | 14.108961000 |
### Protonated Piperazine

|   | 1  | 14.107271000 | 14.741269000 | 12.645002000 |
|---|----|--------------|--------------|--------------|
| 6 | 13.617029000 | 13.778370000 | 12.588084000 |
| 6 | 13.514367000 | 11.739589000 | 11.313397000 |
| 6 | 12.016099000 | 11.889871000 | 11.107369000 |
| 6 | 12.122765000 | 14.007245000 | 12.434482000 |
| 1 | 13.699129000 | 14.610280000 | 11.561745000 |
| 1 | 13.810870000 | 13.252921000 | 13.526743000 |
| 1 | 13.931132000 | 11.231738000 | 10.453678000 |
| 1 | 11.504808000 | 10.937745000 | 11.093840000 |
| 1 | 11.685804000 | 14.644377000 | 13.309442000 |
| 7 | 14.101642000 | 13.056715000 | 11.430426000 |
| 1 | 15.100716000 | 13.017794000 | 11.411320000 |
| 7 | 11.436414000 | 12.691619000 | 12.229751000 |
| 1 | 11.478657000 | 12.145621000 | 13.084150000 |
| 1 | 10.448649000 | 12.149020000 | 12.052230000 |
| 8 | 8.536733000 | 13.107876000 | 11.900526000 |
| 1 | 8.314474000 | 13.708279000 | 12.620407000 |
| 8 | 8.499890000 | 13.395174000 | 11.371750000 |
| 8 | 8.367960000 | 10.398411000 | 12.915509000 |
| 1 | 8.367389000 | 11.201121000 | 12.553359000 |
| 1 | 8.065730000 | 9.728774000 | 12.873758000 |
| 8 | 8.363718000 | 14.698841000 | 14.155606000 |
| 1 | 9.001059000 | 14.440877000 | 14.820748000 |
| 1 | 7.733165000 | 15.278300000 | 14.563300000 |
| 8 | 10.911780000 | 10.944826000 | 14.587597000 |
| 1 | 10.107345000 | 10.595814000 | 14.193396000 |
| 1 | 11.350021000 | 10.221168000 | 15.018088000 |
| 8 | 10.552780000 | 13.623306000 | 15.662040000 |
| 1 | 10.825141000 | 13.860363000 | 16.539704000 |
| 1 | 10.618081000 | 12.673338000 | 15.592331000 |

### Diprotonated Piperazine

|   | 6  | 11.838698000 | 11.396256000 | 13.732897000 |
|---|----|--------------|--------------|--------------|
| 6 | 11.940618000 | 11.619427000 | 11.265783000 |
| 6 | 13.296244000 | 12.292444000 | 11.373875000 |
| 6 | 13.190472000 | 12.060859000 | 13.864128000 |
| 6 | 11.910759000 | 10.319348000 | 13.662688000 |
| 1 | 12.024124000 | 10.545246000 | 11.147804000 |
| 1 | 13.220115000 | 13.367826000 | 11.422993000 |
| 1 | 13.096314000 | 13.129821000 | 13.997019000 |
| 1 | 11.227579000 | 11.647989000 | 14.587959000 |
| 1 | 11.403390000 | 12.003620000 | 10.407430000 |
| 1 | 13.921052000 | 12.051648000 | 10.528437000 |
| 1 | 13.731724000 | 11.652276000 | 14.707170000 |
| 7 | 14.001254000 | 11.843753000 | 12.625577000 |
|   | 14.264825000 | 10.869561000 | 12.540969000 |
|---|--------------|--------------|--------------|
| 1 | 14.874640000 | 12.341864000 | 12.729184000 |
| 7 | 11.147514000 | 11.883815000 | 12.499549000 |
| 1 | 10.243590000 | 11.459594000 | 12.455766000 |
| 1 | 10.913744000 | 12.884058000 | 12.614556000 |
| 8 | 7.604342000  | 12.423375000 | 12.923902000 |
| 1 | 7.464042000  | 11.831961000 | 12.186229000 |
| 6 | 6.715093000  | 12.748108000 | 13.081631000 |
| 8 | 5.134490000  | 13.631470000 | 10.120894000 |
| 1 | 8.625477000  | 13.553828000 | 9.179687000  |
| 1 | 9.163734000  | 13.094481000 | 10.549871000 |
| 8 | 16.786918000 | 13.940653000 | 13.023203000 |
| 1 | 16.724441000 | 14.880772000 | 13.168229000 |
| 1 | 17.654977000 | 13.678755000 | 13.314339000 |
| 8 | 15.668377000 | 13.752466000 | 10.359648000 |
| 1 | 16.121546000 | 14.287507000 | 9.719341000  |
| 1 | 16.238061000 | 13.673386000 | 11.118320000 |
| 8 | 9.850512000  | 14.134335000 | 13.294483000 |
| 1 | 9.051367000  | 13.591180000 | 13.383213000 |
| 1 | 9.582010000  | 14.985319000 | 12.957315000 |

**Piperazine Carbamate**

|   | 14.971896000 | 14.087384000 | 11.424184000 |
|---|--------------|--------------|--------------|
| 6 | 13.667213000 | 14.030760000 | 12.214344000 |
| 1 | 14.743788000 | 14.146989000 | 10.363782000 |
| 1 | 15.529508000 | 14.981666000 | 11.688830000 |
| 7 | 15.827936000 | 12.927060000 | 11.630178000 |
| 6 | 15.093565000 | 11.689627000 | 11.401432000 |
| 1 | 13.888249000 | 14.133017000 | 13.282859000 |
| 1 | 13.015900000 | 14.844163000 | 11.938313000 |
| 7 | 12.985130000 | 12.779826000 | 11.958272000 |
| 1 | 16.177194000 | 12.935897000 | 12.570951000 |
| 6 | 13.790818000 | 11.599767000 | 12.191843000 |
| 1 | 14.870793000 | 11.625969000 | 10.340616000 |
| 1 | 15.738588000 | 10.851707000 | 11.650187000 |
| 6 | 11.599177000 | 12.717606000 | 12.072041000 |
| 1 | 14.022513000 | 11.502100000 | 13.258565000 |
| 1 | 13.231508000 | 10.725984000 | 11.900792000 |
| 8 | 10.981586000 | 13.792323000 | 12.141409000 |
| 8 | 11.078746000 | 11.578957000 | 12.082403000 |
| 8 | 10.678004000 | 9.386416000  | 10.159848000 |
| 1 | 11.009916000 | 10.025258000 | 10.787424000 |
| 1 | 9.776856000  | 9.652950000  | 10.021905000 |
| 8 | 8.394432000  | 11.440297000 | 11.041375000 |
| 1 | 8.060665000  | 12.326587000 | 10.931501000 |
| 1 | 9.299195000  | 11.569541000 | 11.330595000 |
| 8 | 8.263192000  | 14.412607000 | 11.299633000 |
| 1 | 9.212616000  | 14.297095000 | 11.346213000 |
|    | Z   | X1   | Y1   | Z2   |
|----|-----|------|------|------|
| 1  | 8.014148000 | 14.463167000 | 12.216959000 |
| 8  | 8.928462000  | 11.032473000 | 13.582823000 |
| 1  | 9.778607000  | 11.106697000 | 13.283498000 |
| 1  | 8.326307000  | 10.946313000 | 14.250289000 |
| 8  | 8.934802000  | 14.028464000 | 13.693052000 |
| 1  | 9.711219000  | 14.060880000 | 14.384811000 |
| 1  | 8.788471000  | 13.095509000 | 14.384811000 |

### Protonated Piperazine Carbamate

|    | Z   | X1   | Y1   | Z2   |
|----|-----|------|------|------|
| 1  | 14.830499000 | 13.256320000 | 10.771892000 |
| 6  | 14.083107000 | 13.503385000 | 11.507227000 |
| 6  | 13.693750000 | 13.718377000 | 13.865429000 |
| 6  | 12.490706000 | 12.784533000 | 13.819353000 |
| 6  | 12.882581000 | 12.578519000 | 11.327605000 |
| 1  | 13.374399000 | 14.749742000 | 13.724144000 |
| 1  | 12.788216000 | 11.765846000 | 14.013436000 |
| 1  | 13.175927000 | 11.543518000 | 11.385972000 |
| 1  | 13.783883000 | 14.538297000 | 11.349610000 |
| 1  | 14.165630000 | 13.639425000 | 14.830056000 |
| 1  | 11.703808000 | 13.064597000 | 14.507886000 |
| 1  | 12.355179000 | 12.744194000 | 10.397147000 |
| 7  | 14.638094000 | 13.372061000 | 12.831656000 |
| 7  | 11.890749000 | 12.803136000 | 12.438559000 |
| 1  | 11.428410000 | 13.686173000 | 12.293732000 |
| 1  | 11.180559000 | 12.074950000 | 12.390452000 |
| 6  | 15.062750000 | 12.277375000 | 13.092381000 |
| 8  | 16.038436000 | 11.757449000 | 12.094119000 |
| 8  | 15.628328000 | 11.946767000 | 14.269717000 |
| 8  | 14.918072000 | 9.634928000  | 10.565049000 |
| 1  | 15.335271000 | 10.386270000 | 10.991002000 |
| 1  | 15.581112000 | 8.955220000  | 10.584960000 |
| 8  | 12.978775000 | 9.161905000  | 12.658444000 |
| 1  | 13.587306000 | 9.062626000  | 13.396094000 |
| 1  | 13.537018000 | 9.163533000  | 11.881161000 |
| 8  | 17.341864000 | 9.298867000  | 12.536515000 |
| 1  | 17.053699000 | 10.215385000 | 12.477716000 |
| 1  | 18.251350000 | 9.316060000  | 12.800220000 |
| 8  | 15.122489000 | 9.143571000  | 14.531875000 |
| 1  | 15.315595000 | 10.076045000 | 14.642435000 |
| 1  | 15.839770000 | 8.828473000  | 14.008388000 |
| 8  | 10.519287000 | 10.364820000 | 12.486572000 |
| 1  | 9.745355000  | 9.818375000  | 12.500978000 |
| 1  | 11.289294000 | 9.789258000  | 12.578180000 |

### Piperazine dicarbamate

|    | Z   | X1   | Y1   | Z2   |
|----|-----|------|------|------|
| 6  | 12.689179000 | 12.162924000 | 11.966989000 |
| 6  | 13.204979000 | 12.514889000 | 14.293909000 |
| 6  | 14.653191000 | 12.115719000 | 14.036985000 |
|   |       |               |               |               |
|---|-------|---------------|---------------|---------------|
| 6 | 14.133500000 | 11.751536000  | 11.700441000  |
| 1 | 12.594728000 | 13.231478000  | 12.744701000  |
| 1 | 13.125915000 | 13.605187000  | 14.235738000  |
| 1 | 14.772529000 | 11.054180000  | 14.276494000  |
| 1 | 14.208581000 | 10.661266000  | 11.751969000  |
| 1 | 12.022685000 | 11.625351000  | 11.310963000  |
| 1 | 12.907512000 | 12.216823000  | 15.286960000  |
| 1 | 15.314767000 | 12.777170000  | 14.677302000  |
| 1 | 14.426620000 | 12.058737000  | 10.708615000  |
| 7 | 15.028312000 | 12.364522000  | 12.661289000  |
| 7 | 12.314185000 | 11.894758000  | 13.336597000  |
| 6 | 16.365288000 | 12.619828000  | 12.345183000  |
| 6 | 10.955809000 | 11.709724000  | 13.667155000  |
| 8 | 16.670995000 | 12.523517000  | 11.123954000  |
| 8 | 10.179724000 | 11.497891000  | 12.719279000  |
| 8 | 17.128145000 | 12.967131000  | 13.245550000  |
| 8 | 10.660197000 | 11.750859000  | 14.873465000  |
| 8 | 10.394474000 | 9.869981000   | 16.949193000  |
| 1 | 10.294928000 | 10.549791000  | 16.273307000  |
| 8 | 11.173629000 | 9.408336000   | 16.672376000  |
| 8 | 18.402165000 | 14.429287000  | 10.173640000  |
| 1 | 17.789737000 | 13.755151000  | 10.509761000  |
| 1 | 18.849744000 | 14.728101000  | 10.953618000  |
| 8 | 7.510047000  | 11.576915000  | 12.002095000  |
| 1 | 7.798407000  | 11.823985000  | 11.135142000  |
| 1 | 8.343480000  | 11.504270000  | 12.486189000  |
| 8 | 17.604673000 | 10.744022000  | 9.239010000   |
| 1 | 17.339030000 | 11.262286000  | 10.009523000  |
| 1 | 16.896421000 | 10.874872000  | 8.626610000   |
| 8 | 19.612089000 | 12.683913000  | 8.160224000   |
| 1 | 19.348359000 | 13.397471000  | 8.735425000   |
| 1 | 19.120977000 | 11.935583000  | 8.491351000   |
Simulation Details

The molecular dynamics (MD) simulations were isothermal-isobaric simulations (nPT) with periodic boundary conditions at 298K and 1 bar. The particle-mesh Ewald procedure was used to handle long-range electrostatic interactions. Temperature was controlled by Langevin dynamics, while pressure was controlled by weak coupling to an external bath. The time-step in the simulations was set to 0.002 ps. Solute molecule geometries were fully constrained during simulations. Solute coordinates were restrained with a harmonic potential. The restraining weight was set at 5 kcal/mol Å². The nonbonded cutoff was set to 8 Å for all simulations. Bonds length involving hydrogen atoms were maintained by use of a SHAKE algorithm. The systems were equilibrated in nPT simulations for 800 ps before geometries were extracted. Cluster geometries were extracted from the MD trajectory every 2 ps. These clusters consisted of the solute and the 5 closest solvent molecules.

Water solvent was represented with the TIP3P force field1. The number of solvent molecules in simulations for a given solute was taken to be 100. The solutes geometries were obtained from HF/6-31+G (d) calculations in vacuum. Solute charges were calculated with the CM2 model2.

The force field Lennard-Jones parameters were drawn from force fields reported in the scientific literature. We selected the force fields that appeared to have the most detailed parameterization for a given solute. For many ionic species no special force field have been developed, and in these cases we drew on atomic parameters for neutral species. For atoms where no force field stood out in terms of parameterization we drew on the GAFF force field3. GAFF would be our recommended default when no solute specific force field is available. Below are given the Lennard-Jones parameters utilized in the present work.

Table S2: Force Field Parameters

| Atoms       | Sigma [Å] | Epsilon [Kcal/mol] | Reference            |
|-------------|-----------|--------------------|----------------------|
| O (OH, H₂O⁺) | 3.104     | 0.152              | TIP3P water¹        |
| N           | 3.202     | 0.17               | GAFF³               |
| C           | 3.349     | 0.1094             | GAFF³               |
| C (Aromatic) | 3.349     | 0.086              | GAFF³               |
| S           | 3.73      | 0.4945             | Kristof and Lizli⁴   |
| H           | 2.435     | 0.0157             | GAFF³               |
|                |          |        |          |
|----------------|----------|--------|----------|
| H (N)          | 2.435    | 0.0157 | GAFF³    |
| H (Aromatic)   | 2.561    | 0.015  | GAFF³    |

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**QM/PB Continuum Solvent Model**

In the PB models, the solution is characterized as a charge distribution of the solute in a cavity mimicking the molecular shape which surrounded by a continuous dielectric representing the solvent. The solvent is polarized by the solute and the solvent polarization generates an electrostatic field called the reaction field. The electrostatic potential of the reaction field can be described by the Poisson-Boltzmann equation:

\[ ((r) (r)) - (r)^2 \sinh((r)) = -4 (r) \]

The (r) is the charge distribution of the solute calculated via semi empirical QM methods. The (r) is the electrostatic potential that is to be obtained. The (r) is the dielectric function describing the dielectric discontinuity and it usually only has two values: \( \text{out} \) for the region outside of the cavity and \( \text{in} \) for the space within the (molecular) cavity. The (r) is a modified Debye-Huckel parameter that reflects the salt concentration and temperature. When the charge density on the solute is low and the ionic strength is low, the term can be approximated via a linear term yielding the so-called linear Poisson-Boltzmann equation:

\[ [(r) (r)] - (r)^2 = -4 (r) \]

Even for the linearized PB equation, analytical solutions can only be obtained for systems defined by a simple dielectric boundary, e.g., a sphere. For a boundary as complex as that of a protein or DNA molecule, the finite difference approach (among others) substitutes for the analytical differential equation solution yielding a numerical solution of the PB equation.

The electrostatic potential of the reaction field generated by a fixed set of (r) will, in turn, polarize the solute charge distribution and generate a new 'r' (i.e. distort the gas phase wave function). Thus the gas phase solute Hamiltonian, \( H^0 \) is perturbed by a potential energy operator coming from the interaction between the solute and the reaction field:

\[ H = H^0 + V_{\text{int}} \]
\[ V_{\text{int}} = \int ds \frac{\sigma(r')}{|r - r'|} \] (4)

The equation 4 is an integral over all the virtual surface charges, and \( r' \) is the coordinates of the surface charges. The virtual surface charges (\( \sigma \)) are calculated from the converged electrostatic potential of the reaction field. And the full set of virtual surface charges should generate an electrostatic field which is identical to the reaction field. Thus, the perturbation (\( V_{\text{int}} \)) due to the reaction field could be accurately calculated by equation 4, where \( r \) is the coordinates of each solute atom and \( r' \) loops through all the virtual surface charges. After the QM SCF converges with the perturbed \( H' \), the perturbed wave function is used to obtain a new solute charge distribution \( 'r(\sigma) \) using CM1 or CM2 methods. A new PB equation constructed with the updated \( 'r(\sigma) \) which then needs to be solved self-consistently again. This iterative calculation of QM and PB defines the so-called self-consistent reaction field (SCRF) calculation. The solvation free energy of the solute is obtained via equation 5 after the SCRF converges.

\[ \Delta G_{\text{soln}} = \frac{1}{2} \sum_i Z_i V_{\text{int}} + \langle \psi' | H_M + V_{\text{int}} | \psi' \rangle - \langle \psi_0 | H_M | \psi_0 \rangle + G_{\text{np}} = \frac{1}{2} \sum_i Z_i V_{\text{int}} + \langle \psi' | V_{\text{int}} | \psi' \rangle \\
+ \left[ \langle \psi' | H_M | \psi' \rangle - \langle \psi_0 | H_M | \psi_0 \rangle \right] + G_{\text{np}} = G_{rf} + G_{wf} + G_{np} \] (5)

The \( G_{rf} \) is the electrostatic interaction of the solute charge distribution (including core and electrons) with the electrostatic potential generated by the reaction field. It is more efficient and accurate to calculate the \( G_{rf} \) using the virtual surface charge, (see equation 6), instead of using the electrostatic potential directly.

\[ G_{rf} = \frac{1}{2} \int \rho(r) \int ds \frac{\sigma(r')}{|r - r'|} \] (6)

\( G_{wf} \), the wave function distortion energy is generated by the change of the gas phase wave function by the presence of solvent. It is the difference of the heat of formation calculated from polarized Fock matrix itself (without the interaction with the surface charges) and the heat of formation obtained in vacuum. \( G_{np} \), the non-polar energy, contains contributions from cavity formation and solvent-solute dispersion-repulsion interactions. It is generally made proportional to the molecular surface area, using two surface tension parameters \( a \) & \( b \) (equation 7).

\[ G_{np} = a * S + b \] (7)
Figure 1 summarizes the origin of these three energy components of the solvation free energy.

The components of the solvation free energy in the QM/PB model. \( G_{\text{wfd}} \) is the penalty originating from the polarization of the solute’s wave function in vacuum relative to the wave function in solution. \( G_{\text{np}} \) models non-polar effects, including the entropy to make the molecular cavity in the solvent. \( G_{\text{rf}} \) is the electrostatic interaction between the polarized solute and the surrounding solvent.

**Constant terms utilized in calculations**

Dielectric constant of water: 78.39

The free energy of proton: -265.9 Kcal/mol.

\( \Delta G_s(5H_2O) \) Poisson Boltzmann model: -15.7 kcal/mol

Energy for pure water clusters\((5H_2O)\): -380.133 [au]

Thermal energy correction and ZPE for pure water clusters\((5H_2O)\): 0.1435 [au]

Entropy for pure water clusters\((5H_2O)\): 114.8 [cal/mol]

Standard state correction utilized \( (RT\ln[R^T]) - RT\ln(55.34/5) = -3.32 \text{ kcal/mol} \)

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