Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Catalysis by solvation rather than desolvation effect: Exploring the Catalytic power of Methyltransferases

Edson Silva[1], Anderson H. Lima[2] and Jerônimo Lameira[1*]

[1]*Institute of Biological Sciences, Federal University of Pará, 66075-110, Belém, PA, Brazil.*

[2]*Institute of Exact and Natural Sciences, Federal University of Pará, 66075-110, Belém, PA, Brazil.*

*Corresponding author: Jerônimo Lameira; Phone: +55 91-32018235; email: lameira@ufpa.br

Figure S1. The two EVB states and atom types used to simulate the methyl transfer from SAM to chloride.

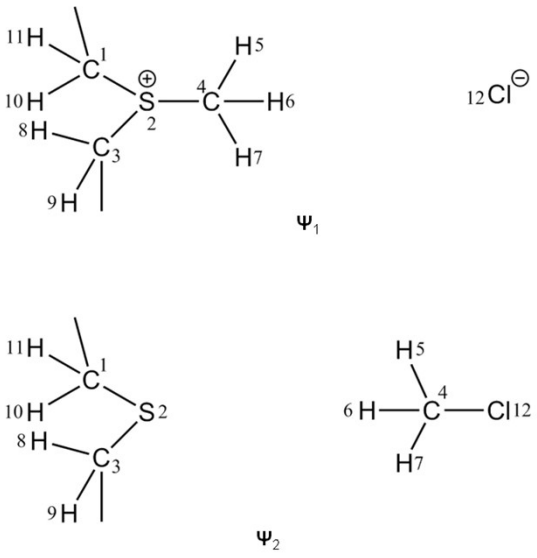

Table S1. Activation and reaction energies (kcal/mol) obtained from HF, M062X and MP2 with set basis 6-31+G(d,p), for reaction involving Cl^- and trimethylsulfonium in gaseous and aqueous environment. The ZPVEs were included in the calculations.

	HF		M062X		MP2	
	Gas	**Solvent**	**Gas**	**Solvent**	**Gas**	**Solvent**
ΔE^{*}(kcal/mol)	5.44	30.29	1.39	10.89	3.76	17.37
ΔE^{0}(kcal/mol)	-35.30	7.94	-34.85	0.80	-36.50	4.27

Table S2. Key distance calculated at HF, M062X and MP2 with set basis 6-31+G(d,p), level of optimization for Reactants State (RS), Transitions State (TS) and Products State (PS).

	HF			M062X			MP2		
	RS	**TS**	**PS**	**RS**	**TS**	**PS**	**RS**	**TS**	**PS**
S-C	1.82	2.18	3.22	1.83	2.05	3.12	1.81	2.08	3.13
C-Cl	3.01	2.52	1.79	2.90	2.52	1.79	2.93	2.47	1.78
Cl-S	4.78	4.70	5.00	4.62	4.58	4.91	4.64	4.55	4.92

Table S3. Key distance calculated at EVB for reaction involving Cl^- and trimethylsulfoniu, for the Reactants State (RS), the Transitions State (TS) and Products State (PS) on Water, Protein and Mutant (Y70T).

	Water			Protein			Mutant		
	RS	**TS**	**PS**	**RS**	**TS**	**PS**	**RS**	**TS**	**PS**
S-C	1.81	1.98	5.58	1.77 (±0.01)	1.93 (±0.02)	4.13 (±0.52)	1.78 (±0.01)	2.00 (±0.03)	3.42 (±0.11)
C-Cl	3.35	2.13	1.73	2.67 (±0.23)	2.75 (±0.05)	1.77 (±0.06)	2.79 (±0.03)	2.22 (±0.04)	1.84 (±0.04)
Cl-S	4.49	4.10	4.81	4.29 (±0.23)	4.18 (±0.04)	4.76 (±0.42)	3.92 (±0.09)	4.19 (±0.03)	4.38 (±0.42)

Table S4. The EVB Parameters for reaction involving Cl^- and trimethylsulfonium in solution.

Charges:

	Reactant State		Product State	
Atom number	**Atom Type**	**Charge**	**Atom Type**	**Charge**
1	C0	-0.354179	C0	-0.184985
2	S+	0.314698	S0	-0.361849
3	C0	-0.354179	C0	-0.184985
4	C0	-0.354179	C0	-0.530236
5	H0	0.238665	H0	0.149500
6	H0	0.238665	H0	0.149500
7	H0	0.238665	H0	0.149500
8	H0	0.238665	H0	0.017991
9	H0	0.238665	H0	0.282833
10	H0	0.238665	H0	0.282833
11	H0	0.238665	H0	0.282833
12	L^-	-0.922816	L0	-0.131068

Bonds: $\Delta M = D\left(1 - e^{\{-a(b-b_0)\}_2}\right)$

Bond Type	D	b_0	a
C0-S+	70.0	1.80	2.0
C0-S0	70.0	1.80	2.0
C0-L-	120.0	1.40	0.8
C0-L0	120.0	1.35	0.8

Bond Angles: $U_0 = \frac{1}{2}K_0\left(\theta - \theta_0\right)^2$

Bond Type	θ	K_θ
X-S+-Y	102.5	100.0
X-S0-Y	103.5	100.0
X-C0-Y	109.5	50.0
X-L- -Y	120.0	50.0
X-L0-Y	109.0	50.0

Nobonded : $U_{nb} = A_i A_j r^{-12} - B_i B_j r^{-6}$

Bond Type	A	B
H0	7.00	0.00
S+	1831.8	23.0
S0	1022.5	23.0

C0	632.0	24.0
L-	1400.0	24.0
L0	774.0	24.0

Nobonded: $U_{nb} = Ae^{\{-ar\}}$

Bond Type	A	a
C0…S+	19999.0	4.0
C0…S0	19999.0	4.0

off-diagonal and shift parameters

A=-21.0
α= -140.0
μ=0.0

Table S5. Contributions to Solvation free Energy (kcal/mol) for the Reactant State (RS) and the Transition State (TS) in the water reference reaction. The energies were obtained through LRA.

	Water		**Water**	
	RS (SAM)	**RS (Cl)**	**TS (SAM)**	**TS (Cl)**
Intra	-99.04	-63.62	-78.9	-44.56
Solvation/p	0.00	0.00	0.00	0.00
Solvation /w	4.82	-24.11	3.21	-14.36
Elect (total)	-94.21	-87.74	-75.69	-56.92
$\langle U_Q - U_0 \rangle_Q$	-125.55	-155.08	-108.83	-120.01
$\langle U_Q - U_0 \rangle_0$	5.57	10.43	29.06	39.6
ΔG_{solv}	-59.99	-72.33	-39.88	-40.21

Table S5. Contributions to Solvation free Energy (kcal/mol) for the Reactant State (RS) and the Transition State (TS) in the protein native.

	Protein		Protein	
	RS (SAM)	**RS (CI)**	**TS (SAM)**	**TS (CI)**
Intra	-96.42 (±0.26)	-61.10 (±0.44)	-78.24 (±2.74)	-46.80 (±1.62)
Solvation/p	30.82 (±0.93)	-60.22 (±1.02)	27.16 (±3.89)	-61.10 (±2.83)
Solvation /w	-16.82 (±0.43)	16.95 (±0.57)	-13.43 (±8.10)	22.85 (±3.43)
Elect (total)	-82.43 (±0.24)	-104.38 (±1.16)	-64.52 (±1.47)	-85.05 (±2.22)
$\langle U_Q - U_0 \rangle_Q$	-109.40 (±1.03)	-130.06 (±0.09)	-96.99 (±7.86)	-109.68 (±2.29)
$\langle U_Q - U_0 \rangle_0$	-3.62 (±1.46)	-43.51 (±2.95)	13.56 (±3.7)	-25.00 (±0.01)
ΔG_{solv}	-56.51 (±1.25)	-86.78 (±1.43)	-41.71 (±2.08)	-67.34 (±1.15)

Table S5. Contributions to Solvation free Energy (kcal/mol) for the Reactant State (RS) and the Transition State (TS) in the Mutant.

	Mutant		Mutant	
	RS (SAM)	**RS (CI)**	**TS (SAM)**	**TS (CI)**
Intra	-133.90 (±37.89)	-68.94 (±0.06)	-82.85 (±0.08)	-46.79 (±0.26)
Solvation/p	30.87 (±1.82)	-56.84 (±0.24)	27.75 (±3.09)	-52.70 (±2.06)
Solvation /w	-8.93 (±1.61)	22.22 (±2.65)	-11.79 (±0.40)	17.05 (±1.33)
Elect (total)	-84.97 (±0.49)	-103.56 (±2.47)	-66.88 (±3.41)	-80.93 (±2.70)
$\langle U_Q - U_0 \rangle_Q$	-133.86 (±0.30)	-136.62 (±1.67)	-91.92 (±0.39)	-112.95 (±3.5)
$\langle U_Q - U_0 \rangle_0$	-8.84 (±0.48)	-40.79 (±2.55)	21.05 (±12.21)	-11.36 (±1.9)
ΔG_{solv}	-61.35 (±0.38)	-88.7 (±2.11)	-35.43 (±5.9)	-62.16 (±3.1)