Supplementary Material for

How the disulfide conformation determines the disulfide/thiol redox potential

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Table S1: Dihedral angles and relative energies ΔE_{rel} (calculated at the MP2/6-311++G(d,p) level in gas phase and aqueous solution) of the neutral disulfide and disulfide anion. F: optimized with fixed dihedral angles; R: optimized with relaxed dihedral angles; TS: optimized to a transition state for rotation around SS bond.

Dihedral angles of starting structures χ_2, χ_3, χ_2'	Dihedral angles after optimization of neutral disulfide: χ_2, χ_3, χ_2'	ΔE_{rel} kcal/mol neutral, gasphase	ΔE_{rel} kcal/mol neutral, solvent	Dihedral angles after optimization of disulfide anion: χ_2, χ_3, χ_2'	ΔE_{rel} kcal/mol anion, solvent
60,90,60	F	0.46	0.48	F	2.08
	R: 68,87,68	0.00	0.00	R: 80,86,80	0.00
60,90,-60	F	0.83	0.76	F*	1.95
	R: 68,97,-65	0.35	0.32	R: 76,109,-75	0.37
60,90,-5	F*	4.09	4.00	F*	4.92
	R (TS) 66,91,-4	3.97	3.87	ND	ND
-60,90,-60	F*	5.73	5.33	F*	4.53
	R: -71, <i>III</i> ,-71	2.05	1.86	R: -80,130,-80	1.06
-25,90,-60	F*	6.98	6.69	ND	ND
	R: -71, <i>III</i> ,-71	2.05	1.86	ND	ND
180,90,180	F	1.22	1.07	F	1.22
	R: 179,85,179	1.13	0.97	R: -175,86,-175	1.05
180,90,75	F	0.67	0.58	F	0.73
	R: 180,86,68	0.53	0.44	R: -175,86,81	0.51
180,90,-65	F	1.09	0.94	F*	1.77
	R: 178,96,-64	0.86	0.74	R: 179,109,-74	ND
180,90,-120	F*	2.92	2.73	F*	2.10
	R(TS): 176,85,-125	2.83	2.61	R: 76,109,-75	ND
180,90,120	F*	2.82	2.70	F*	2.01
	R(TS): 178,86,121	2.75	2.62	R: -174,86,81	ND
180,90,0	F*	4.39	4.22	F*	4.78
	R(TS): 175,90,-4	4.41	4.17	R: 179,109,-74	ND
-60,-90,60	F	0.83	0.76	F*	1.95
	R: -68,-97,65	0.35	0.32	R: -76,-109,76	0.37
60,90,-120	F*	2.45	2.34	F**	ND
	R(TS): 67,86,-125	2.27	2.13	R: 76,109,-75	ND
-130,-90,120	F*	4.49	4.35	F**	2.79
	R: -178,-96,64	ND	ND	ND	ND
90,-90,90	F**	4.12	3.86	F**	2.31
	R: -178,-96,64	ND	ND	R: 80,-130,80	ND
60,-140,60	F*	5.40	5.23	F**	3.36
	R: 71,- <i>III</i> ,71	2.05	1.86	ND	ND
-60,90,-120	F*	3.45	3.24	F*	2.50
	R: -64,96,178	ND	ND	ND	ND
-40,-90,120	F*	3.84	3.65	F**	3.99
	R(TS): -67,-86,125	2.27	2.12	R: -76,-109,75	ND

* Structures having one imaginary frequency. ** Structures having two imaginary frequencies.

Table S2: Disulfide/thiol reduction potential.

	E° (V)	$\Delta E^\circ_{\text{rel}}$ (V)	ΔE_{rel} (kcal/mol) neutral, gas phase
68,87,68 (R)	3.88373	0	0
68,97,-65 (R)	3.90822	0.024489	0.35
-68,-97,65 (R)	3.90811	0.02438	0.35
60,90,60 (F)	3.89429	0.010561	0.46
179,86,68 (R)	3.88568	0.001948	0.53
180,90,75 (F)	3.8885	0.004777	0.67
60,90,-60 (F)	3.91711	0.033386	0.83
-60,-90,60 (F)	3.9173	0.033576	0.83
178,96,-64 (R)	3.90777	0.024047	0.86
180,90,-65 (F)	3.90945	0.025721	1.09
179,85,179 (R)	3.88673	0.003004	1.13
180,90,180 (F)	3.88723	0.003499	1.22
-71,111,-71 (R)	3.95749	0.073764	2.05
71,-111,71 (R)	3.95749	0.073764	2.05
67,86,-125 (R,TS)	3.9954	0.111669	2.27
-67,- 86,125(R,TS)	3.99537	0.111641	2.27
60,90,-120 (F)*	4.00061	0.116886	2.45
178,86,121 (R, TS)	3.99021	0.106485	2.75
180,90,120 (F)*	3.9923	0.108576	2.82
176,85,-125 (R,TS)	3.99193	0.108201	2.83
180,90,-120 (F)*	3.99762	0.113892	2.92
-60,90,-120(F)*	4.01966	0.135934	3.45
-40,-90,120(F)*	4.03744	0.153717	3.84
66,91,-4 (R, TS)	4.07636	0.19263	3.97
60,90,-5* (F)	4.07816	0.194429	4.09

90,-90,90 (F) **	4.0938	0.210076	4.12
180,90,0 (F) *	4.07416	0.190437	4.39
175,90,-4 (R, TS)	4.0749	0.191173	4.41
-130,-90,120 (F) *	4.09741	0.213683	4.49
60,-140,60 (F) *	4.14071	0.256983	5.4
-60,90,-60 * (F)	4.10919	0.225463	5.73
-25,90,-60 * (F)	4.17268	0.288954	6.98

* Structures having one imaginary frequency. ** Structures having two imaginary frequencies.

Table S3: ΔE_{adiab} , ΔE_{EA} , ΔE_{reorg} and their relative values calculated at the MP2/6-311++G(d,p)level in aqueous solution (see Scheme S1 for the definition of ΔE_{adiab} , ΔE_{EA} , ΔE_{reorg}).

Dihedral angles χ_2, χ_3, χ_2' (R/F)	E_{rel} Gas phase	ΔE_{adiab} (3)	ΔE_{EA} (4)	ΔE_{reorg} (5)	$\Delta E_{adiab,rel}$	$\Delta E_{EA,rel}$	$\Delta E_{reorg,rel}$
68,87,68 (R)	0.00	-52.26	-18.29	-33.97	0.00	0.00	0.00
68,97,-65 (R)	0.35	-52.58	-18.57	-34.01	-0.32	-0.28	-0.04
60,90,60 (F)	0.46	-52.75	-17.85	-34.89	-0.48	0.44	-0.92
60,90,-60 (F)	0.83	-53.02	-17.70	-35.32	-0.76	0.58	-1.34
-71,111,-71 (R)	2.05	-54.12	-19.03	-35.09	-1.86	-0.73	-1.12
66,91,-4 [*] (R, TS)	3.97	-56.14	-12.17	-43.97	-3.87	6.12	-9.99
60,90,-5 [*] (F)	4.09	-56.26	-18.91	-37.34	-4.00	-0.63	-3.37
-60,90,-60 [*] (F)	5.73	-57.60	-15.65	-41.95	-5.33	2.64	-7.97
-25,90,-60 [*] (F)	6.98	-58.96	-11.98	-46.98	-6.69	6.31	-13.00
180,86,68 (R)	0.53	-52.70	-12.04	-40.67	-0.44	6.25	-6.69
180,90,75 (F)	0.67	-52.84	-12.03	-40.80	-0.58	6.25	-6.83
178,96,-64 (R)	0.86	-53.00	-12.03	-40.97	-0.74	6.26	-6.99
180,90,-65 (F)	1.09	-53.20	-12.43	-40.77	-0.94	5.86	-6.80
179,85,179 (R)	1.13	-53.24	-16.76	-36.47	-0.97	1.52	-2.50
180,90,180 (F)	1.22	-53.33	-19.79	-36.54	-1.07	1.50	-2.57
178,86,121 (R, TS)	2.75	-54.89	-11.58	-43.30	-2.62	6.70	-9.33
180,90,120 (F) [*]	2.82	-54.96	-11.53	-43.42	-2.70	6.75	-9.45
176,85,-125 (R, TS)	2.83	-54.88	-11.63	-43.25	-2.61	6.66	-9.27
180,90,-120 (F) [*]	2.92	-54.99	-11.50	-43.49	-2.72	6.79	-9.51
180,90,0 (F) [*]	4.39	-56.43	-12.17	-44.27	-4.17	6.12	-10.29
175,90,-4 (R, TS)	4.41	-56.48	20.46	-36.02	16.25	38.75	-22.50
-68,-97,65 (R)	0.35	-52.58	-18.57	-34.01	-0.32	-0.28	-0.03
-60,-90,60 (F)	0.83	-53.02	-17.73	-45.29	-0.76	0.55	-1.31
71,-III,71 (R)	2.05	-54.12	-19.03	-35.08	-1.86	-0.75	-1.11
67,86,-125 (R, TS)	2.27	-54.39	-19.30	-35.09	-2.13	-1.01	-1.11
60,90,-120 (F) [*]	2.45	-54.50	-11.85	-42.75	-2.34	6.44	-8.78
90,-90,90 (F) ^{**}	4.12	-56.12	-19.38	-36.74	-3.86	-1.10	-2.77
-130,-90,120 (F) [*]	4.49	-56.61	-20.97	-35.65	-4.35	-2.68	-1.67
60,-140,60 (F) [*]	5.40	-57.49	-22.92	-34.57	-5.23	-4.64	-0.59
-60,90,-120(F) [*]	3.45	-5.50	-11.46	-44.04	-3.24	6.82	-10.07
-40,-90,120(F) [*]	3.84	-55.91	-12.06	-43.85	-3.65	6.22	-9.87
-67,-86,125 (R, TS)	2.27	-54.39	-19.30	-35.09	-2.13	-1.01	-1.12

* Structures having one imaginary frequency. ** Structures having two imaginary frequencies.

Table S4: Overview of the different structure-groups and determinants of ΔE_{rel} (*Structures having one imaginary frequency; **: Structures having two imaginary frequencies). The colored circles corresponds to the colors used in Figure 3 and 4 of the main text.

1. χ_2 (or χ_2') $\sim 120^\circ$ or -120° (green circles)

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
(-40,-90,120) -67,-86,125 R(TS)	2.27	2.058	4.90 3.76	4.34 4.59	3.48 4.18
-40,-90,120 (F) *	3.84	2.053	4.49 3.89	3.34 4.40	3.29 4.14
(60,90,-120) 67,86,-125 R(TS)	2.27	2.058	4.90 3.76	4.59 4.34	3.48 4.48
60,90,-120 (F) *	2.45	2.057	4.83 3.84	4.34 4.58	3.42 4.14
-60,90,-120 (F) *	3.45	2.058	3.78 3.92	4.47 3.67	4.19 3.51

2. $\chi_3 < -120^\circ$ (purple circles)

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
60,-140,60 (F) *	5.40	2.090	4.31	4.50 4.50	3.38 3.38
(60,-140,60) 71,-111,71 (R)	2.05	2.068	3.58 4.12	4.13 4.13	3.59 3.59

3A. $70^\circ < \chi_3 < 120^\circ$ and χ_2 (or χ_2') = 180° (orange circles):

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
180,90,180 (F)	1.22	2.058	6.46 3.78	5.07 5.07	4.41 4.41
(180,90,180) 179,85,179 (R)	1.13	2.058	6.43 3.70	5.02 5.02	4.41 4.41
180,90,75 (F)	0.67	2.060	5.82 3.77	4.74 5.07	3.57 4.41
(180,90,75) 180,86,68 (R)	0.53	2.059	5.65 3.72	5.04 4.59	4.41 3.49
180,90,-65 (F)	1.09	2.058	4.80 3.84	3.60 5.13	3.51 4.43
(180,90,-65) 178,96,-64 (R)	0.86	2.059	4.87 3.89	5.12 3.67	4.42 3.47
180,90,-120* (F)	2.92	2.057	5.66 3.82	4.32 5.12	4.14 4.42

180,90,120* (F)	2.82	2.056	6.47 3.81	5.22 5.12	4.13 4.42
(180,90,120) 178,86,121(R,TS)	2.75	2.056	6.45 3.76	5.09 5.18	4.41 4.14
(180,90,-120) 176,85,-125(R,TS)	2.83	2.056	5.73 3.74	5.09 4.37	4.41 4.18

3B. $70^\circ < \chi_3 < 120^\circ$ and χ_2 and $\chi_2' \neq 180^\circ$:

3B-1) Structures having favourable intra-molecular interactions:

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
60,90,60 (F)	0.46	2.058	5.59 3.82	4.56 4.56	3.41 3.41
(60,90,60) 68,87,68 (R)	0.00	2.060	5.70 3.74	4.61 4.61	3.49 3.49
60,90,-60 (F)	0.83	2.059	4.44 3.86	3.58 4.44	3.44 3.45
(60,90,-60) 68,97,-65 (R)	0.35	2.061	4.44 3.91	3.71 4.78	3.47 3.51
-60,-90,60 (F)	0.83	2.059	4.44 3.89	3.58 4.60	3.45 3.44
(-60,-90,60) -68,-97,65 (R)	0.35	2.061	4.72 3.91	3.71 4.78	3.50 3.48

3B-2) Structures having unfavorable intra-molecular interactions

a. Eclipsed: short S₁-Ca₂ distance (blue circles)

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
60,90,-5 (F)*	4.09	2.053	4.90 3.93	3.80 4.64	3.20 3.43
(60,90,-5) 66,91,-4 (R, TS)	3.97	2.054	4.99 3.92	3.81 4.72	3.19 3.47

b. Staple: Short d(Ca₁-Ca₂) distances (red circles)

Dihedral angles χ_2, χ_3, χ_2'	E_{rel} kcal/mol	d (S ₁ - S ₂)	d (Ca ₁ -Ca ₂) d (Cb ₁ -Cb ₂)	d (Ca ₁ -Cb ₂) d (Cb ₁ -Ca ₂)	d (S ₁ -Ca ₂) d (S ₂ -Ca ₁)
-60,90,-60 (F)*	5.73	2.061	3.30 4.07	3.96 3.97	3.68 3.68
(-60,90,-60) -71, III , -71 (R)	2.05	2.068	3.58 4.11	4.19 4.19	3.59 3.59
-25,90,-60 (F)*	6.98	2.056	3.31 4.05	3.89 3.88	3.42 3.61
(-25,90,-60) -71, III , -71 (R)	2.05	2.068	3.58 4.12	4.12 4.13	3.59 3.59

Table S5: ΔE_{bind} , ΔE_{prep} , ΔE_{int} and their relative values calculated at the MP2/6-311++G(d,p)level in gas phase (see main manuscript for the definition of ΔE_{bind} , ΔE_{prep} , ΔE_{int}).

Dihedral angles χ_2, χ_3, χ_2' (R/F)	E_{rel}	ΔE_{bind} (4)	ΔE_{prep} (5)	ΔE_{int} (6)	$\Delta E_{bind,rel}$	$\Delta E_{prep,rel}$	$\Delta E_{int,rel}$
68,87,68 (R)	0.00	-61.20	0.37	-61.57	0.00	0.00	0.00
68,97,-65 (R)	0.35	-60.84	0.60	-61.44	0.35	0.12	0.23
60,90,60 (F)	0.46	-60.73	0.47	-61.20	0.46	0.10	0.37
60,90,-60 (F)	0.83	-60.36	0.60	-60.96	0.83	0.23	0.60
-71,111,-71 (R)	2.05	-59.15	0.63	-59.78	2.05	0.26	1.79
66,91,-4 (R, TS)	3.97	-57.22	0.98	-58.20	3.97	0.61	3.36
60,90,-5* (F)	4.09	-57.11	1.01	-58.11	4.09	0.64	3.45
-60,90,-60* (F)	5.73	-55.46	2.23	-57.76	5.73	0.68	3.80
-25,90,-60* (F)	6.98	-54.21	2.43	-57.69	6.98	1.86	3.88
180,86,68 (R)	0.53	-60.67	1.18	-61.85	0.53	0.81	-0.29
180,90,75 (F)	0.67	-60.52	0.93	-61.46	0.67	0.57	0.11
178,96,-64 (R)	0.86	-60.34	1.34	-61.68	0.86	0.97	-0.11
180,90,-65 (F)	1.09	-60.10	1.10	-61.20	1.09	0.73	0.36
179,85,179 (R)	1.13	-60.07	1.51	-61.58	1.13	1.14	-0.01
180,90,180 (F)	1.22	-59.98	1.53	-61.50	1.22	1.16	0.06
178,86,121 (R, TS)	2.75	-58.44	1.27	-59.71	2.75	0.90	1.85
180,90,120 (F)*	2.82	-58.38	1.27	-59.65	2.82	0.90	1.92
176,85,-125 (R,TS)	2.83	-58.36	1.25	-59.62	2.83	0.88	1.95
180,90,-120 (F)*	2.92	-58.28	1.42	-59.69	2.92	1.05	1.87
180,90,0 (F)*	4.39	-56.81	1.77	-58.58	4.39	1.40	2.99
175,90,-4 (R, TS)	4.41	-56.79	1.52	-58.31	4.41	1.15	3.26
-68,-97,65 (R)	0.35	-60.84	0.46	-61.30	0.35	0.09	0.27
-60,-90,60 (F)	0.83	-60.36	0.60	-60.96	0.83	0.23	0.60
71,-III,71 (R)	2.05	-59.15	0.63	-59.78	2.05	0.26	1.79
67,86,-125 (R,TS)	2.27	-58.92	0.68	-59.60	2.27	0.31	1.97
60,90,-120 (F)*	2.45	-58.74	0.64	-59.39	2.45	0.27	2.18
90,-90,90 (F)**	4.12	-57.08	0.84	-57.92	4.12	0.47	3.64
-130,-90,120 (F)*	4.49	-56.71	1.05	-57.76	4.49	0.68	3.80
60,-140,60 (F)*	5.40	-55.80	0.48	-56.28	5.40	0.11	5.28
-60,90,-120(F)*	3.45	-57.72	0.75	-58.46	3.45	0.38	3.10
-40,-90,120(F)*	3.84	-57.35	0.85	-58.21	3.84	0.48	3.36
-67,-86,125 (R,TS)	2.27	-58.92	0.68	-59.60	2.27	0.31	1.97

* Structures having one imaginary frequency. ** Structures having two imaginary frequencies.

Table S6: Geometry of CH₃CH₂S[•] fragment.

	Relaxed CH ₃ CH ₂ S [•] fragment	Fragment in 180,90,180 structure	Fragment in 60,90,60 structure
CCS angle	115°	109°	114°
C-S bond length	1.80 Å	1.82 Å	1.82 Å
C-C bond length	1.52 Å	1.52 Å	1.52 Å
conformation	staggered	staggered	staggered

Table S7: $\Delta E_{SS,bind}$, $\Delta E_{non-cov}$ and their relative values calculated at the MP2/6-311++G(d,p) level in gas phase (see main manuscript for the definition of $\Delta E_{SS,bind}$, $\Delta E_{non-cov}$).

Dihedral angles χ_2, χ_3, χ_2 (R/F)	E_{rel}	$\Delta E_{SS,bind}$ (8)	$\Delta E_{non-cov}$ (7)	$\Delta E_{SS,bind, rel}$	$\Delta E_{non-cov, rel}$
68,87,68 (R)	0.00	-123.58	62.01	0.00	0.00
68,97,-65 (R)	0.35	-123.53	62.09	0.05	0.07
60,90,60 (F)	0.46	-123.73	62.53	-0.15	0.51
60,90,-60 (F)	0.83	-123.68	62.72	-0.10	0.70
-71,111,-71 (R)	2.05	-123.13	63.35	0.45	1.33
66,91,-4* (R)	3.97	-123.98	65.78	-0.40	3.76
60,90,-5* (F)	4.09	-124.00	65.89	-0.42	3.87
-60,90,-60* (F)	5.73	-123.53	65.85	0.04	3.84
-25,90,-60* (F)	6.98	-123.86	67.21	-0.28	5.20
180,86,68 (R)	0.53	-123.65	61.80	-0.07	-0.22
180,90,75 (F)	0.67	-123.62	61.88	-0.04	-0.13
178,96,-64 (R)	0.86	-123.63	61.95	-0.05	-0.06
180,90,-65 (F)	1.09	-123.70	62.50	-0.12	0.48
179,85,179 (R)	1.13	-123.74	62.17	-0.16	0.15
180,90,180 (F)	1.22	-123.75	62.25	-0.17	0.23
178,86,121 (R, TS)	2.75	-123.86	64.14	-0.28	2.13
180,90,120 (F)*	2.82	-123.83	64.18	-0.25	2.16
176,85,-125 (R,TS)	2.83	-123.84	64.22	-0.26	2.21
180,90,-120 (F)*	2.92	-123.81	64.11	-0.23	2.10
180,90,0 (F)*	4.39	-124.07	65.45	-0.49	3.48
175,90,-4 (R, TS)	4.41	-124.06	65.75	-0.47	3.73
-68,-97,65 (R)	0.35	-123.53	62.23	0.05	0.22
-60,-90,60 (F)	0.83	-123.66	62.70	-0.08	0.68
71,-III,71 (R)	2.05	-123.12	63.35	0.46	1.33
67,86,-125 (R,TS)	2.27	-123.74	64.15	-0.13	2.13
60,90,-120 (F)*	2.45	-123.79	64.40	-0.21	2.39
90,-90,90 (F)**	4.12	-123.67	65.75	-0.09	3.74
-130,-90,120 (F)*	4.49	-123.96	66.20	-0.38	4.18
60,-140,60 (F)*	5.40	-121.71	65.43	1.87	3.42
-60,90,-120(F)*	3.45	-123.72	65.25	-0.14	3.24
-40,-90,120(F)*	3.84	-124.00	65.79	-0.42	3.78
-67,-86,125 (R,TS)	2.27	-123.74	64.15	-0.16	2.13

* Structures having one imaginary frequency. ** Structures having two imaginary frequencies.

With $\Delta E_{\text{EA}} = E_{\text{opt}}(\text{neutral}) - E_{\text{opt}}(\text{anion with same conformation as neutral})$

Scheme S1: Disulfide/thiol reduction via different steps. Subscript (left/right) refers to (oxidation state/geometry), for example, (red/ox) = reduced form of the species having the geometry of the oxidized form. (LEC= Lowest energy conformation)

Figure S1: ΔE_{rel} (black circles) and ΔE_{reorg2} (white diamond) correlate with E° .

Figure S2 ΔE_{Pauli} , ΔV_{elstat} and ΔE_{oi} between two CH_4 molecules as a function of the C-C distance. The orientation of the CH_4 molecules was taken from a) the (-60,90,-60) (F) conformation and b) the (-60,90,-25) (F) conformation.