

**How Microsolvation Affects the Balance of Atomic Level Mechanism in
Substitution and Elimination Reactions: Insight into the Role Solvent Molecules
Plays in Inducing Mechanistic Transitions**

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Table S1. Energy decomposition analysis (EDA) of the anti-E2 and inv-S_N2 transition states of the HO⁻(H₂O)_{n=0-3} + CH₃CH₂Br reactions, Energy unit, kcal mol⁻¹.

Species	ΔE_1	ΔE_2	ΔE_{strain}	ΔE_{int}	ΔE_{TS}
0H ₂ O _w -aE	0.01	3.81	3.82	-23.62	-19.8
1H ₂ O _w -aE	1.37	17.40	18.77	-30.47	-11.7
2H ₂ O _w -aE	2.30	26.07	28.37	-33.08	-4.71
3H ₂ O _w -aE	4.97	34.77	39.74	-35.49	4.25
0H ₂ O _w -iS	0.00	4.71	4.71	-25.13	-20.42
1H ₂ O _w -iS	0.75	12.23	12.98	-26.22	-13.24
2H ₂ O _w -iS	0.77	17.26	18.03	-26.15	-8.12
3H ₂ O _w -iS	2.66	22.66	25.32	-26.19	-0.87

Note: Here ΔE_1 is the strain energy change of the HO⁻(H₂O)_{n=0-3} from the reactant to the transition state, ΔE_2 is the strain energy change of CH₃CH₂Br from the reactant to the transition state, $\Delta E_{\text{strain}} = \Delta E_1 + \Delta E_2$ and $\Delta E_{\text{TS}} = \Delta E_{\text{strain}} + \Delta E_{\text{int}}$, Energy unit, kcal mol⁻¹.

Table S2. Energy decomposition analysis (EDA) of the interaction energies of the anti-E2 and inv-S_N2 transition states of the HO⁻(H₂O)_{n=0-3} + CH₃CH₂Br reactions, Energy unit, kcal mol⁻¹.

Species	E_{els}	E_{orb}	E_{x}	E_{rep}	E_{DFTc}	E_{dc}	E_{xrep}	E_{c}	E_{int}
0H ₂ O _w -aE	-30.73	-26.61	-21.83	62.10	-5.43	-1.12	40.27	-6.55	-23.62
1H ₂ O _w -aE	-51.86	-56.63	-42.74	129.35	-7.16	-1.43	86.61	-8.59	-30.47
2H ₂ O _w -aE	-60.04	-70.34	-50.61	157.81	-7.90	-2.00	107.20	-9.90	-33.08
3H ₂ O _w -aE	-66.04	-79.91	-55.55	176.49	-8.26	-2.22	120.94	-10.48	-35.49
0H ₂ O _w -iS	-30.80	-22.50	-19.29	55.03	-6.13	-1.44	35.74	-7.57	-25.13
1H ₂ O _w -iS	-37.02	-28.54	-24.13	72.77	-7.04	-2.26	48.64	-9.30	-26.22
2H ₂ O _w -iS	-39.98	-32.07	-26.95	84.07	-7.85	-3.37	57.12	-11.22	-26.15
3H ₂ O _w -iS	-42.97	-35.94	-29.92	95.29	-8.60	-4.05	65.37	-12.65	-26.19

Note: $\Delta E_{\text{int}} = \Delta E_{\text{els}} + \Delta E_{\text{xrep}} + \Delta E_{\text{orb}} + \Delta E_{\text{c}}$, $\Delta E_{\text{xrep}} = \Delta E_{\text{x}} + \Delta E_{\text{rep}}$, $\Delta E_{\text{c}} = \Delta E_{\text{DFTc}} + \Delta E_{\text{dc}}$. where ΔE_{int} : interaction energy, ΔE_{els} : electrostatic energy, ΔE_{x} : exchange energy, ΔE_{rep} : Pauli repulsion, ΔE_{orb} : orbital interaction, ΔE_{DFTc} : correlation energy, ΔE_{dc} : dispersion correction.

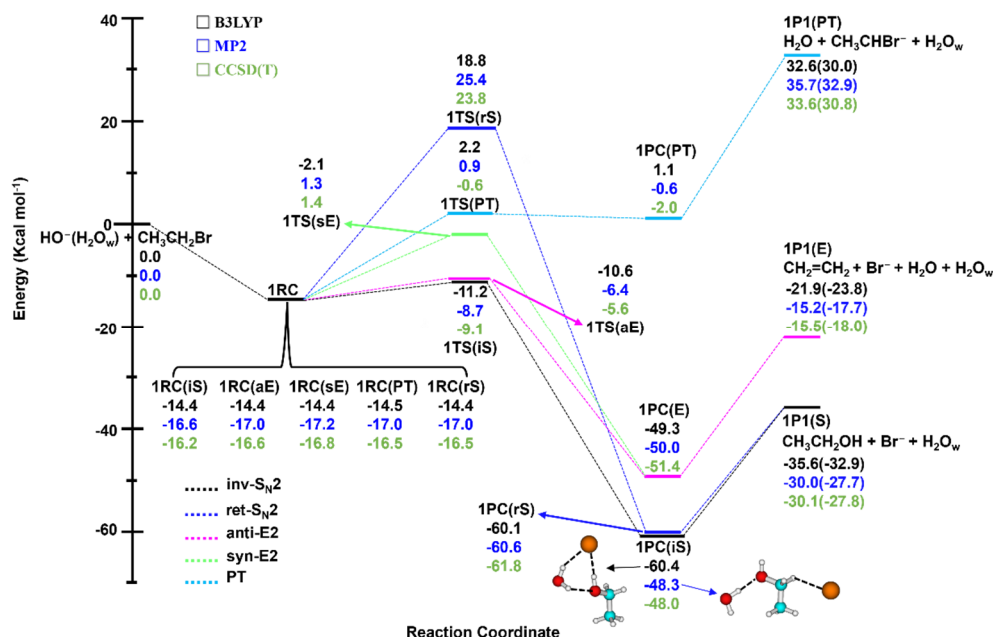


Figure S1. The classical relative energies of $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br}$ reactions under B3LYP/ECP/d, MP2/ECP/d and CCSD(T)/PP/t/MP2/ECP/d methods. The reported energies in kcal mol⁻¹ are relative to the isolated molecules and ions without zero-point energy (ZPE). Numbers in parentheses include ZPE.

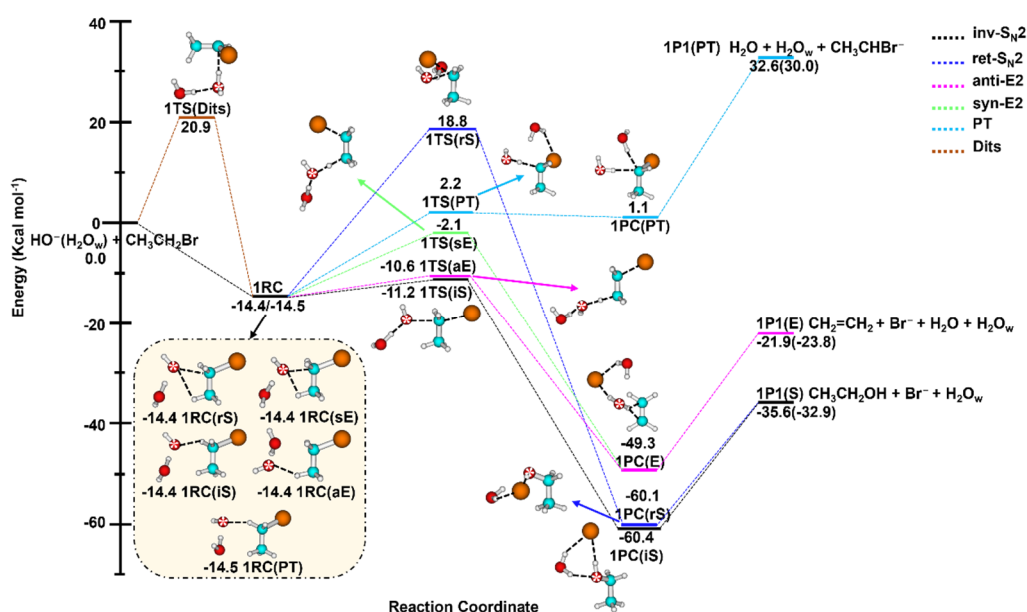


Figure S2. Potential energy profile and stationary points for S_N2, E2, and PT pathways in reaction $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br}$ at the B3LYP/ECP/d level of theory. Energies in kcal mol⁻¹ are relative to reactants without zero-point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included. Note that here oxygen atoms with asterisks represent O and oxygen atoms without asterisks represent O_w.

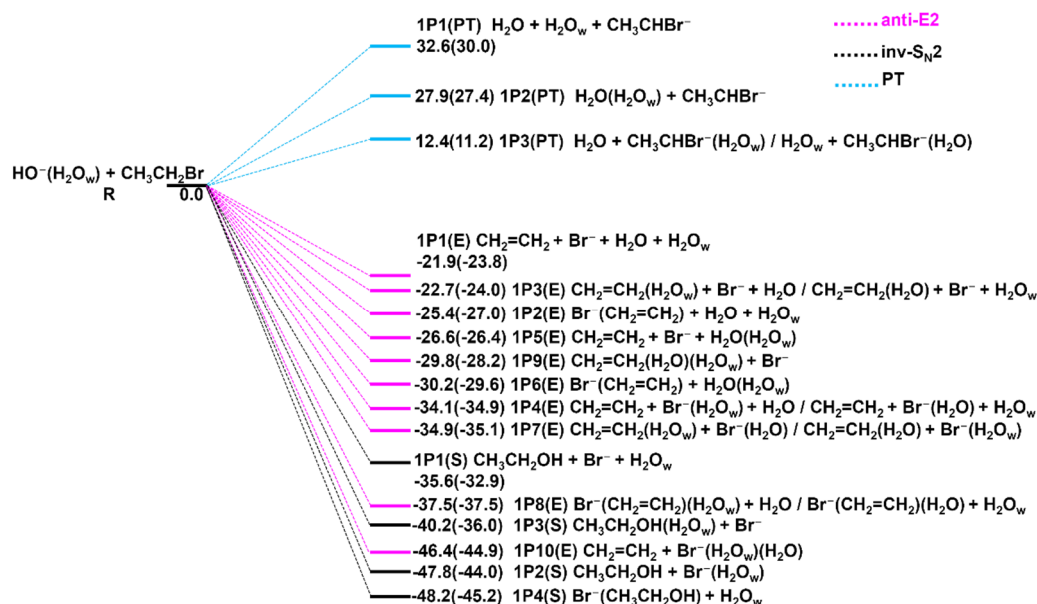


Figure S3. Classical relative energies of the isolated and complexed products of the S_N2, E2, and PT pathways in the HO[−](H₂O_w) + CH₃CH₂Br reaction at the B3LYP/ECP/d level. Energies in kcal mol^{−1} are relative to reactants without zero point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included.

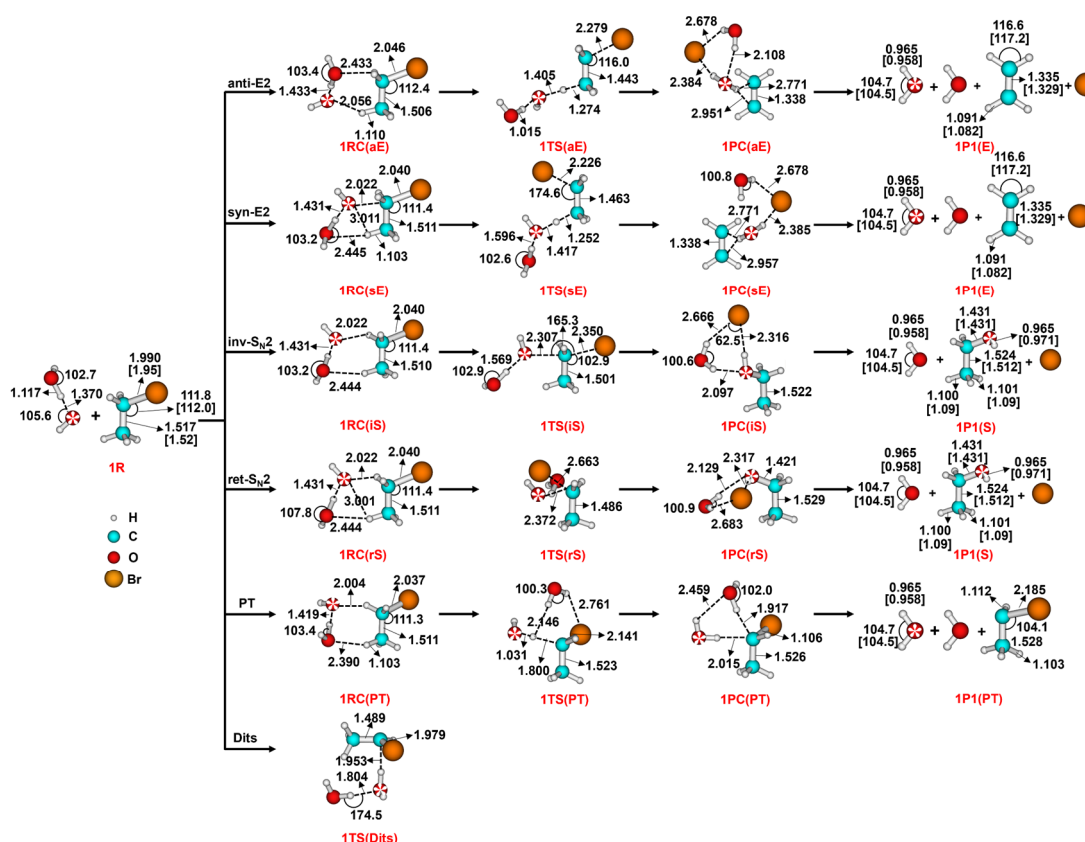


Figure S4. Stationary point structures of S_N2, E2 and PT channels in the HO[−](H₂O_w) + CH₃CH₂Br reaction optimized at the B3LYP/ECP/d level of theory. Bond distances (in

Å) and angles (in degree) are shown for each reaction pathway and the available experimental data ^{a,b} are given in parentheses. ^a Lide, D. R. CRC Handbook of Chemistry and Physics; CRC Press: Boca Raton, FL, 2005. ^b Chase, M. W., Jr.; Davies, C. A.; Downey, J. R., Jr.; Frurip, D. J.; McDonald, R. A.; Syverud, A. N. JANAF Thermochemical Tables; National Bureau of Standards: Washington, D.C., 1985; Vol. 14.

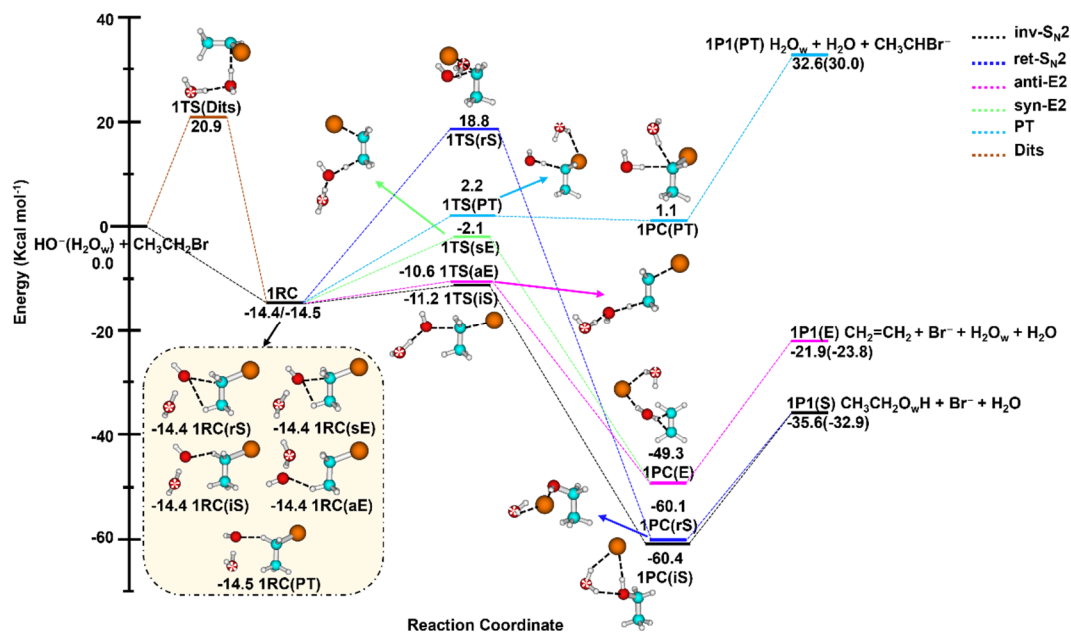


Figure S5. Potential energy profile and stationary points for O_w -induced S_N2 , E2 and PT pathways in reaction $HO^-(H_2O_w) + CH_3CH_2Br$ at the B3LYP/ECP/d level of theory. Energies in kcal mol^{-1} are relative to reactants without zero-point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included. Note that here oxygen atoms with asterisks represents O and oxygen atoms without asterisks represent O_w .

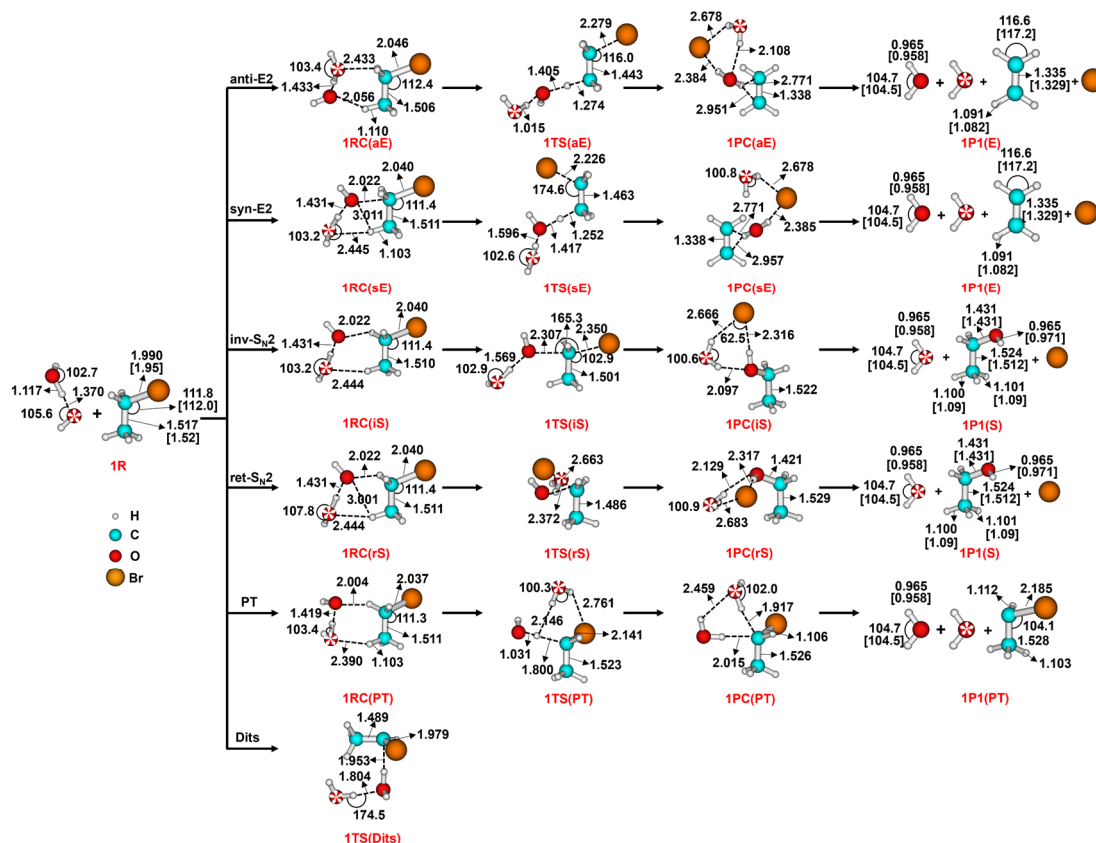


Figure S6. Stationary point structures of O_w-induced S_N2, E2, and PT channels in the HO[−](H₂O_w) + CH₃CH₂Br reaction optimized at the B3LYP/ECP/d level of theory. Bond distances (in Å) and angles (in degree) are shown for each reaction pathway and the available experimental data (refs a and b as in Figure. S4) are given in parentheses.

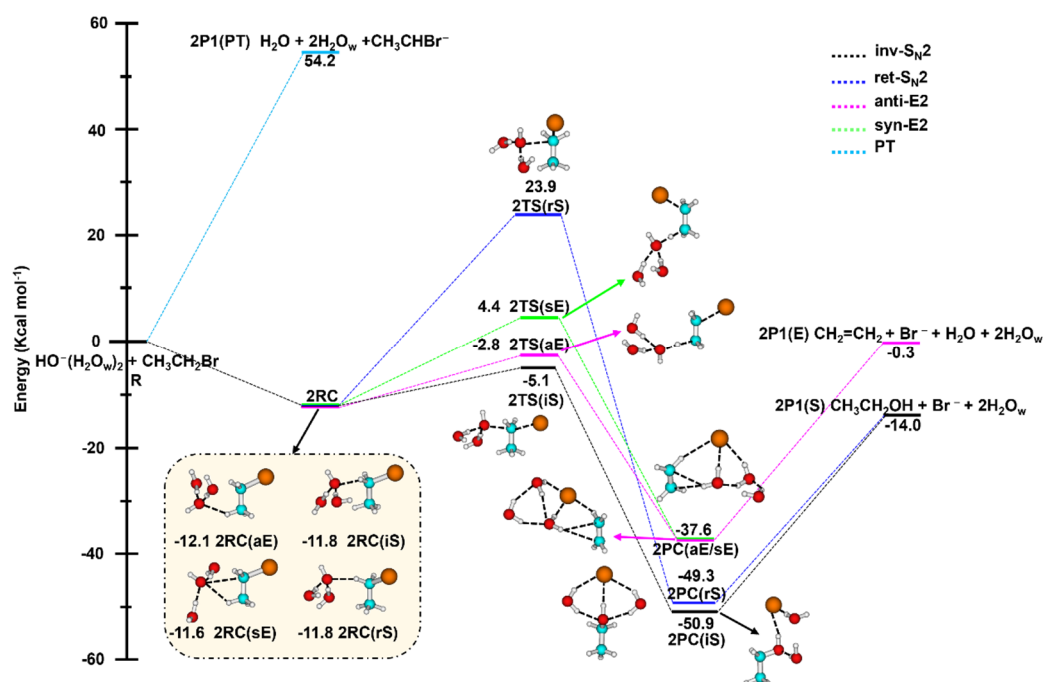


Figure S7. Potential energy profile and stationary points for S_N2 , E2, and PT pathways in reaction $HO^-(H_2O)_2 + CH_3CH_2Br$ at the B3LYP/ECP/d level of theory. Energies in kcal mol^{-1} are relative to reactants without zero-point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included.

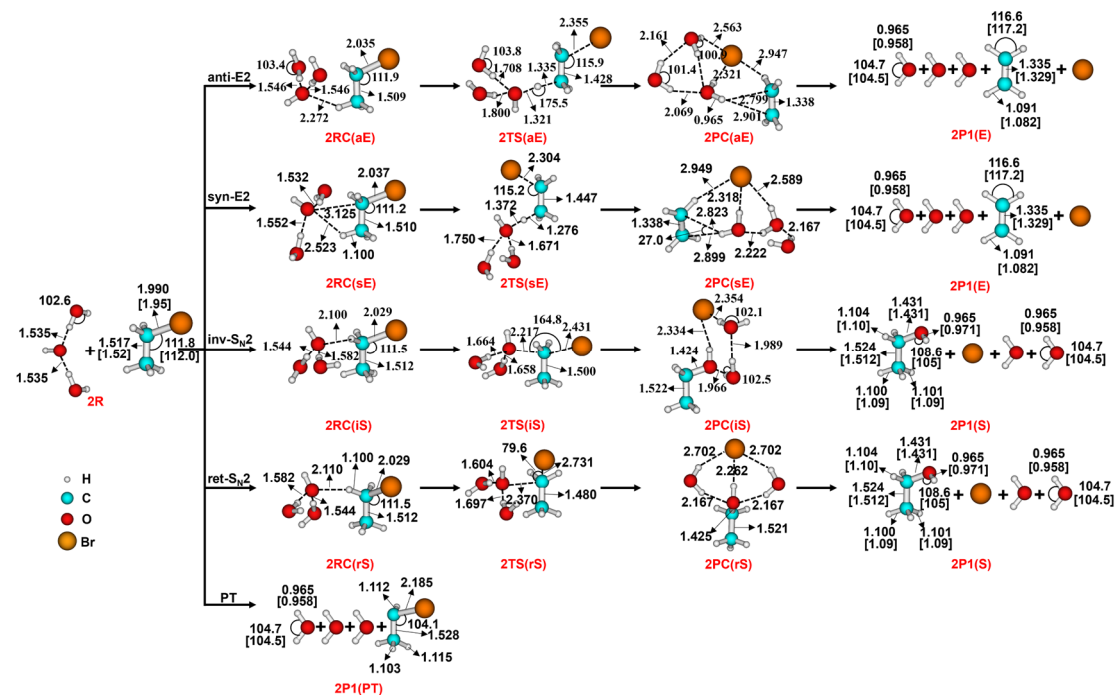


Figure S8. Stationary point structures of S_N2 , E2, and PT channels in the $HO^-(H_2O)_2 + CH_3CH_2Br$ reaction optimized at the B3LYP/ECP/d level of theory. Bond distances (in Å) and angles (in degree) are shown for each reaction pathway and the available experimental data (refs a and b as in Figure S4) are given in parentheses.

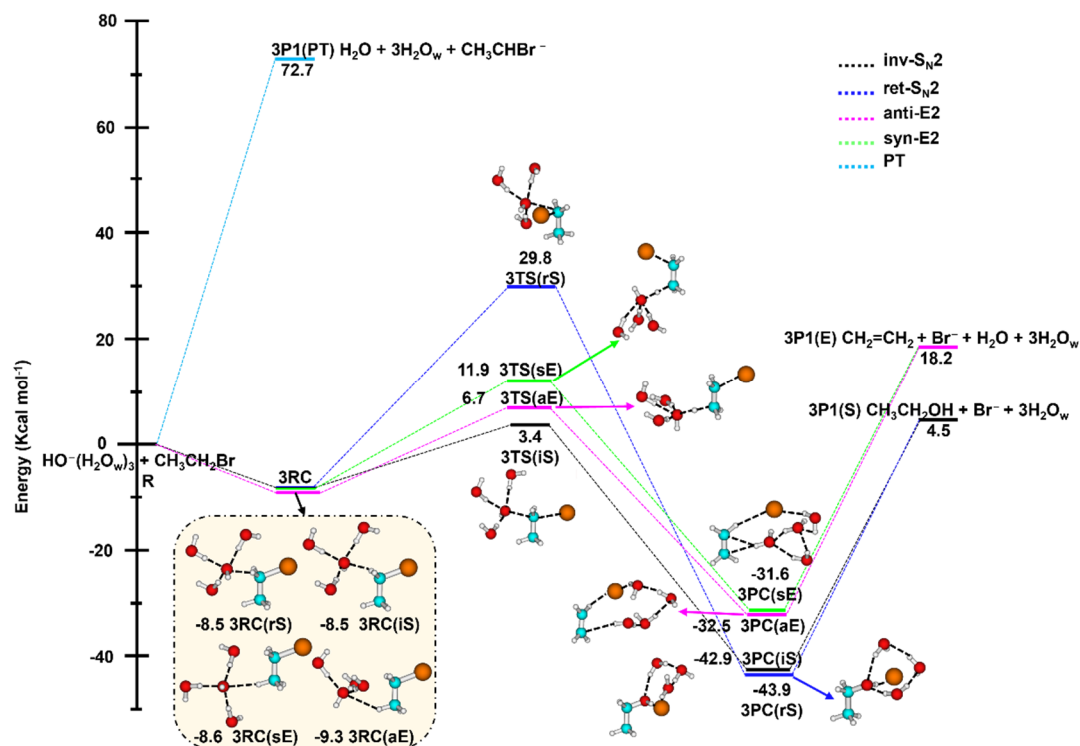


Figure S9. Potential energy profile and stationary points for S_N2 , E2, and PT pathways in reaction $HO^-(H_2O)_3 + CH_3CH_2Br$ at the B3LYP/ECP/d level of theory. Energies in $kcal\ mol^{-1}$ are relative to reactants without zero-point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included.

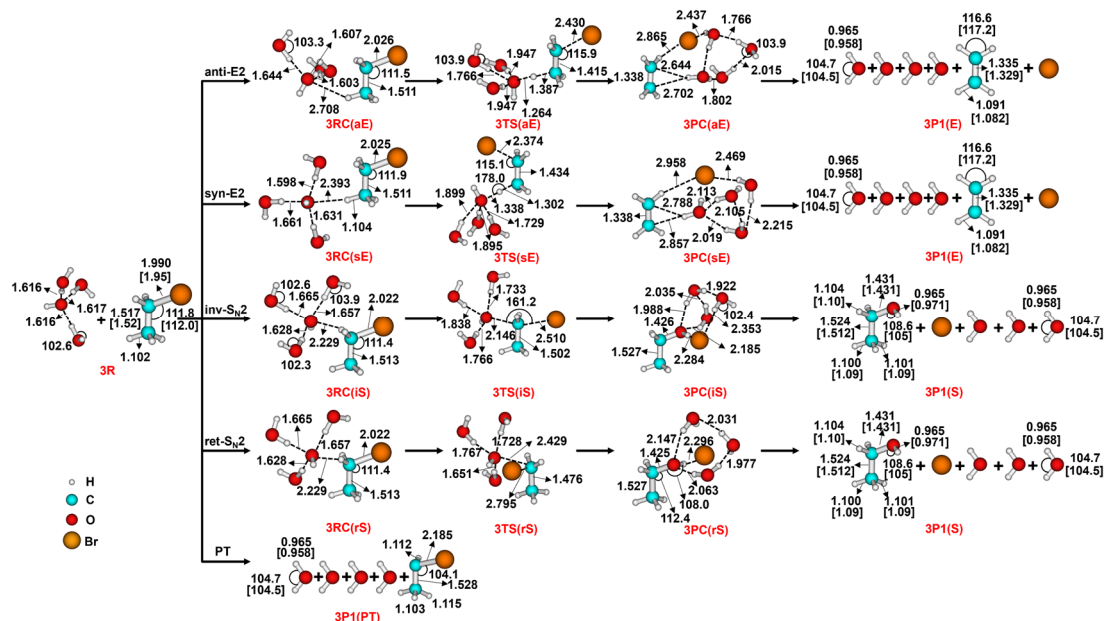


Figure S10. Stationary point structures of S_N2 , E2, and PT channels in the $HO^-(H_2O)_3$

+ CH₃CH₂Br reaction optimized at the B3LYP/ECP/d level of theory. Bond distances (in Å) and angles (in degree) are shown for each reaction pathway and the available experimental data (refs a and b as in Figure S4) are given in parentheses.

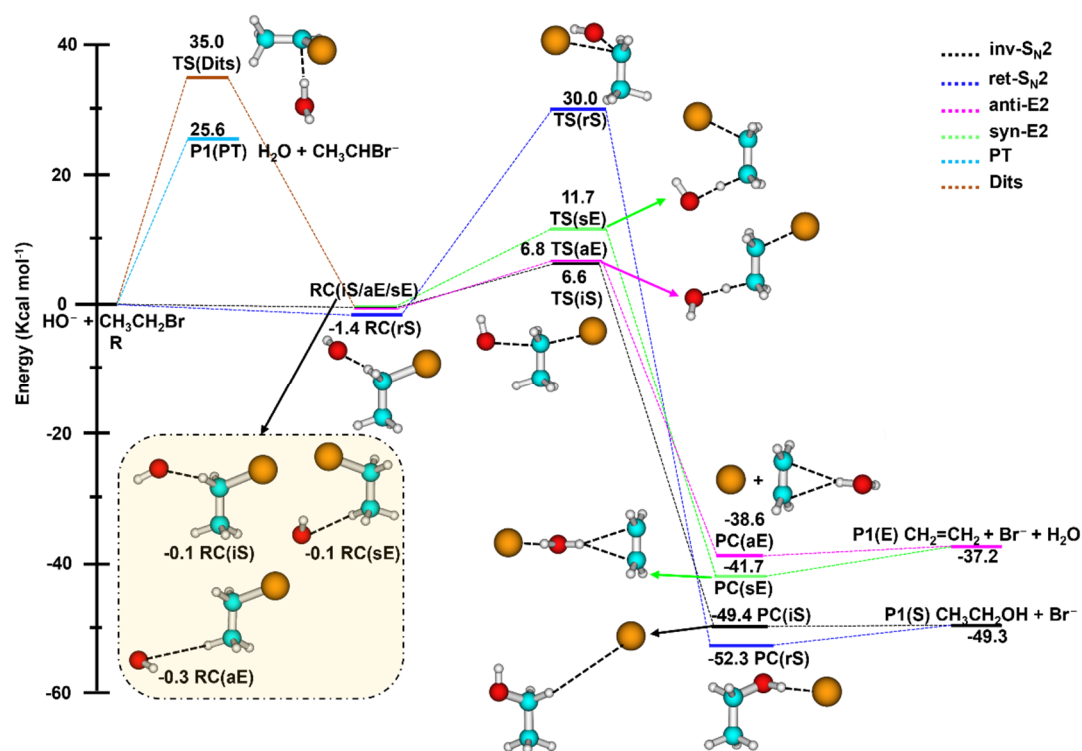


Figure S11. Potential energy profile and stationary points for S_N2, E2, and PT pathways in reaction HO⁻(PCM, water) + CH₃CH₂Br at the B3LYP/ECP/d level of theory. Energies in kcal mol⁻¹ are relative to reactants without zero-point energy (ZPE). The numbers in parentheses denote calculated reaction energies with ZPE included.

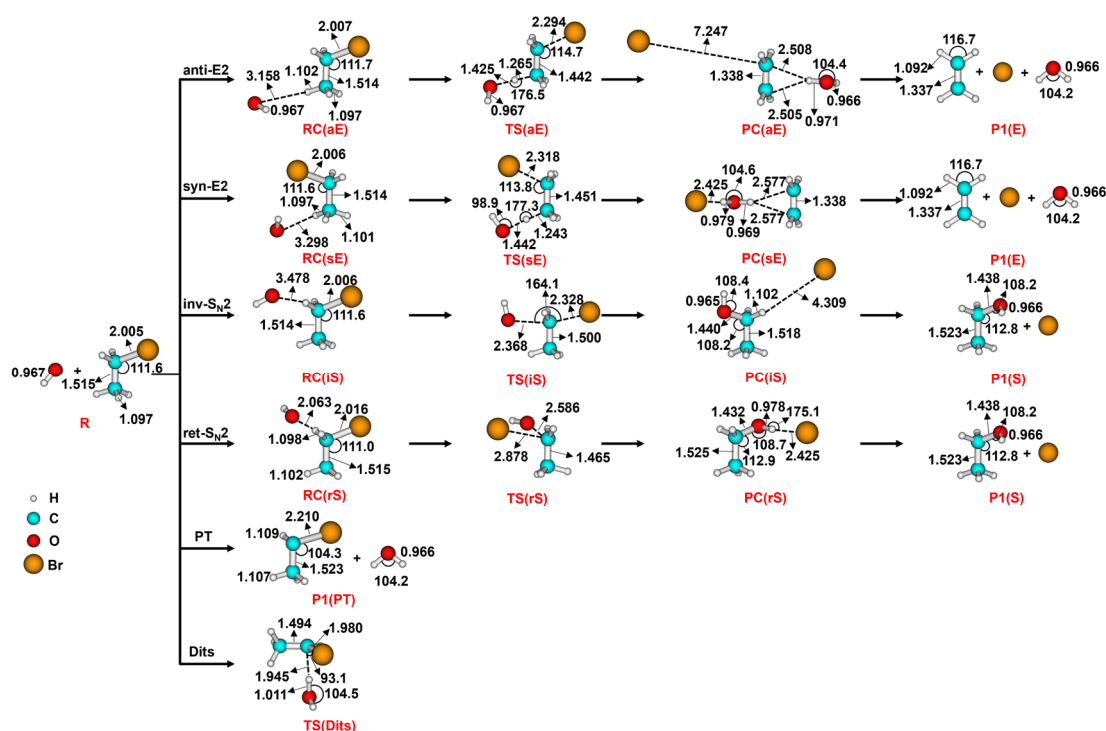


Figure S12. Stationary point structures of $\text{S}_{\text{N}}2$, E2, and PT channels in the HO^- (PCM, water) + $\text{CH}_3\text{CH}_2\text{Br}$ reaction optimized at the B3LYP/ECP/d level of theory. Bond distances (in Å) and angles (in degree) are shown for each reaction pathway and the available experimental data (refs a and b as in Figure. S4) are given in parentheses.

Species	$0\text{H}_2\text{O}_{\text{w}}$	$1\text{H}_2\text{O}_{\text{w}}$	$2\text{H}_2\text{O}_{\text{w}}$	$3\text{H}_2\text{O}_{\text{w}}$
aE	 0.07	 0.13	 0.16	 0.19
iS	 0.05	 0.11	 0.14	 0.17

Figure S13. Root mean square deviation (RMSD) of $\text{CH}_3\text{CH}_2\text{Br}$ fragment from initial reactant $\text{CH}_3\text{CH}_2\text{Br}$ in the transition state structure of inv-SN_2 and anti-E2 in HO^- $(\text{H}_2\text{O}_{\text{w}})_{n=0-3}$ + $\text{CH}_3\text{CH}_2\text{Br}$ reaction. Red and blue represent the $\text{CH}_3\text{CH}_2\text{Br}$ segments in the reactants and transition states, respectively. RMSD is defined as follows:

$$\text{RMSD} = \sqrt{\frac{1}{N} \sum_i^{\text{natom}} [(x_i^{\text{TS}} - x_i^{\text{R}})^2 + (y_i^{\text{TS}} - y_i^{\text{R}})^2 + (z_i^{\text{TS}} - z_i^{\text{R}})^2]}$$

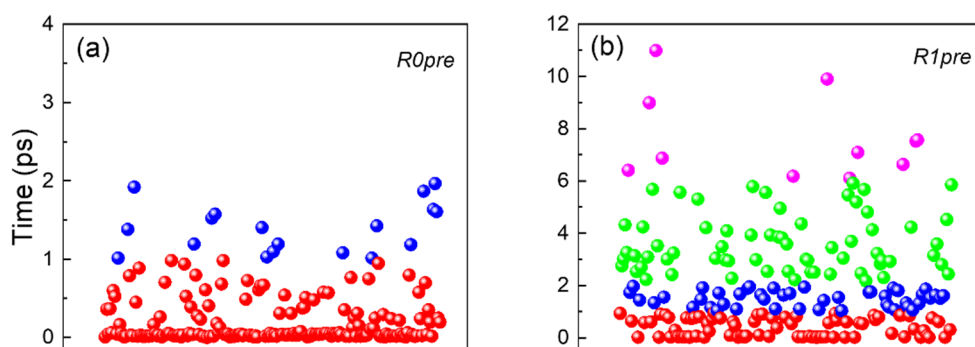


Figure S14. Interaction time, defined as the time between the first point of collision and the onset of the transition state. (a) Interaction time for the pre mechanism in $\text{HO}^- + \text{CH}_3\text{CH}_2\text{Br}$ (b) Interaction time for the pre-mechanism in $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br}$.

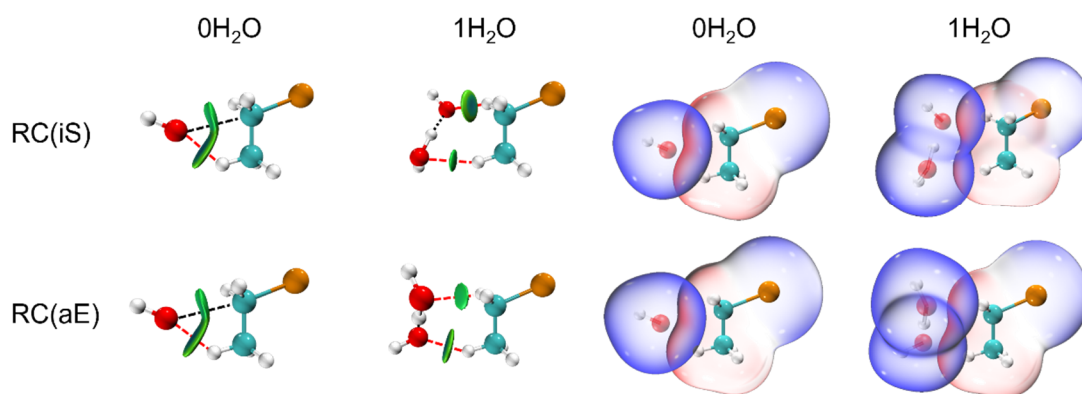


Figure S15. IGMH (left), ESP (right) analysis of $\text{HO}^-(\text{H}_2\text{O}_w)_{n=0-1} + \text{CH}_3\text{CH}_2\text{Br}$ reaction entrance channel complexes

Animations S1 – S8

Animation S1. A trajectory showing the indirect mechanism that proceeds via 1RC complexes in the entrance channel (see Figure. S2) for the solvated O-anti-E2 reaction $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{HO}-\text{H} + \text{CH}_2=\text{CH}_2 + \text{Br}^- + \text{H}_2\text{O}_w$.

Animation S2. A trajectory showing the indirect mechanism that proceeds via 1RC complexes in the entrance channel (see Figure. S5) for the solvated O_w -anti-E2 reaction $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{HO}_w-\text{H} + \text{CH}_2=\text{CH}_2 + \text{Br}^- + \text{H}_2\text{O}$.

Animation S3. An indirect trajectory occurs by the formation of 1RC complexes for solvated O-inv- $\text{S}_{\text{N}}2$ reaction $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{CH}_2\text{OH} + \text{Br}^- + \text{H}_2\text{O}_w$.

Animation S4. An indirect trajectory occurs by the formation of 1RC complexes for solvated O_w -inv- $\text{S}_{\text{N}}2$ reaction $\text{HO}^-(\text{H}_2\text{O}_w) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{CH}_2\text{O}_w\text{H} + \text{Br}^- + \text{H}_2\text{O}$.

Animation S5. A direct rebound trajectory occurring for solvated anti-E2 reaction $\text{HO}^-(\text{H}_2\text{O}) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_2=\text{CH}_2 + \text{Br}^- + 2\text{H}_2\text{O}$.

Animation S6. A direct stripping trajectory occurring for solvated anti-E2 reaction $\text{HO}^-(\text{H}_2\text{O}) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_2=\text{CH}_2 + \text{Br}^- + 2\text{H}_2\text{O}$.

Animation S7. A direct rebound trajectory occurs for solvated inv- $\text{S}_{\text{N}}2$ reaction $\text{HO}^-(\text{H}_2\text{O}) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{CH}_2\text{OH} + \text{Br}^- + \text{H}_2\text{O}$.

Animation S8. A direct stripping trajectory occurs for solvated inv- $\text{S}_{\text{N}}2$ reaction $\text{HO}^-(\text{H}_2\text{O}) + \text{CH}_3\text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{CH}_2\text{OH} + \text{Br}^- + \text{H}_2\text{O}$.

Notes: In the animation, the color coding for atoms is as follows: C_α , C_β , H, H in hydroxide ion, O in hydroxide ion, O in water molecules, and Br for blue, cyan, white, silver, magenta, red and pink, respectively.