

The S_N2 reaction

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1 At a glance

S_N2 = Substitution, Nucleophilic, bimolecular

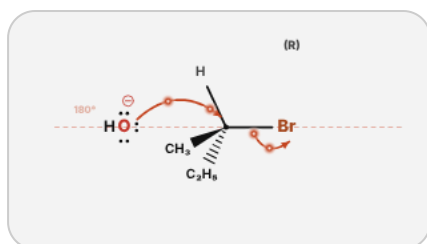
- A nucleophile replaces a leaving group on an sp³ carbon **in one step**, with no intermediate.
- The new bond forms **at the same time** as the old bond breaks (a concerted reaction).
- Rate = $k[\text{substrate}][\text{nucleophile}]$: **second order** overall.
- The nucleophile attacks from the **back side**, 180° from the leaving group, so the carbon's configuration is **inverted**.
- Fastest with methyl and 1° substrates, strong nucleophiles, good leaving groups and polar aprotic solvents.



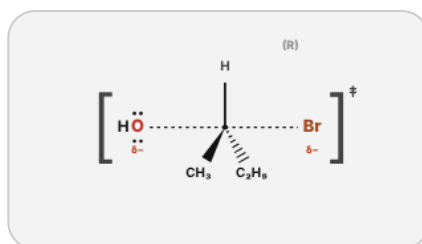
The name was given by Hughes and Ingold in the 1930s: "2" means two species, the substrate and the nucleophile, take part in the single, rate-determining step.

2 The mechanism

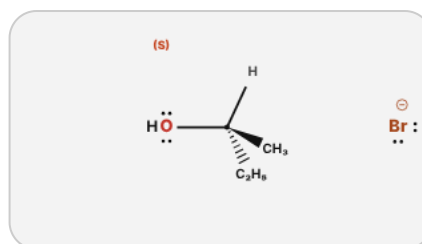
Take (*R*)-2-bromobutane reacting with hydroxide ion. Everything happens in one smooth step, but it is easiest to understand in three snapshots:



a. Two curved arrows. A lone pair on O attacks C; the C–Br bonding pair moves onto Br.



b. Transition state (‡). O and Br are both partly bonded to C, each carrying δ^- .



c. Product. (S)-Butan-2-ol and bromide ion. The three groups have flipped.

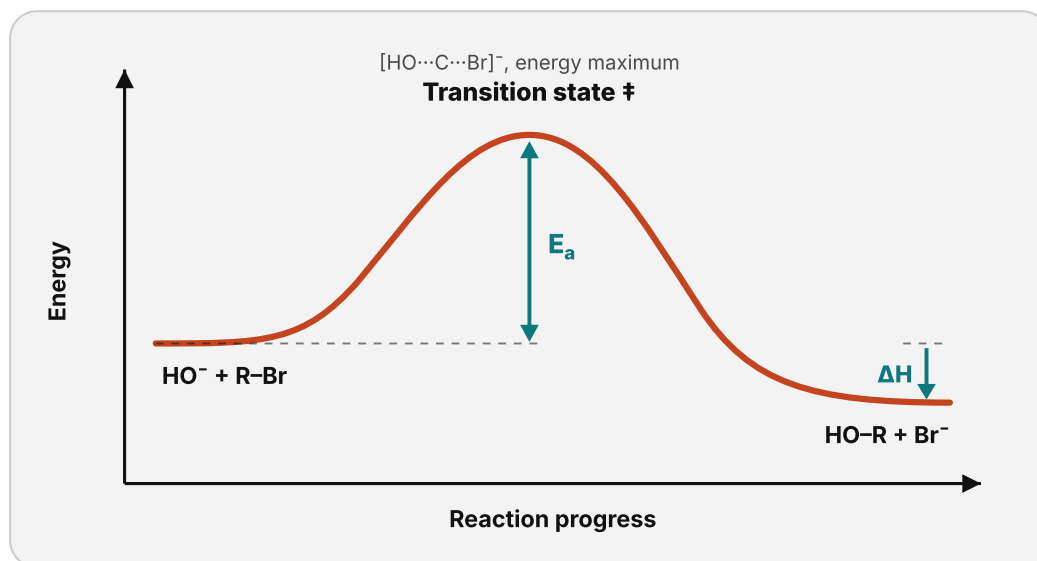
Why must the attack come from the back?

The nucleophile pushes its electrons into the empty σ^* (antibonding) orbital of the C–Br bond. The large lobe of σ^* points *away* from Br, behind the carbon. Attack from that side gives the best overlap; attack from the front would run into the electron-rich bromine.

Curved arrows, the exam way: arrow 1 starts at a lone pair on O and ends at the carbon; arrow 2 starts in the middle of the C–Br bond and ends on Br. Both arrows are drawn in the same diagram, because both happen in the same step.

3 Transition state and energy profile

At the top of the energy hill, the carbon has five groups around it: Nu and LG on a straight axis, partly bonded, and the three other groups lying flat in one plane at 120° , like a trigonal bipyramid. The negative charge is shared between Nu and LG (δ^- on each).



Transition state $\neq$ intermediate.

A transition state is the highest-energy arrangement on the path; it lasts for a single molecular vibration and cannot be isolated. An intermediate sits in an energy valley between two humps. The S_N2 profile has **one hump and no valley**; the S_N1 profile has two humps with a carbocation in the valley.

4 Kinetics: the rate law

$$\text{Rate} = k [\text{R-Br}] [\text{HO}^-]$$

Both species are in the only step, so the rate depends on both: first order in each, **second order overall**. The units of k are $\text{L mol}^{-1} \text{s}^{-1}$ ($\text{M}^{-1} \text{s}^{-1}$).

Experiment	[R-Br]	[HO ⁻]	Relative rate
1	0.1 M	0.1 M	1
2 (double R-Br)	0.2 M	0.1 M	2
3 (double HO ⁻)	0.1 M	0.2 M	2
4 (double both)	0.2 M	0.2 M	4

Exam shortcut

New rate = (factor for substrate) $\times$ (factor for nucleophile). Double one and triple the other: $2 \times 3 = 6$ times faster.

5 Stereochemistry: Walden inversion

Because the nucleophile enters from the back, the three other groups are pushed through a flat arrangement to the other side, like an umbrella turned inside out by wind. The carbon's 3D arrangement is **inverted**. This is called **Walden inversion**, after Paul Walden, who first observed that one enantiomer could be converted into the other (1896).



- Every molecule reacts with inversion, so an enantiomerically pure substrate gives an enantiomerically pure product. The product is **optically active**, not racemic.
- **Proof that every step inverts (1935):** Hughes and co-workers treated optically active 2-iodooctane with radioactive iodide. The optical activity was lost exactly twice as fast as

radioactive iodine was taken up: each exchange inverts one molecule, which cancels the rotation of one unreacted molecule.

Careful: inversion is about shape, R/S is a label.

The geometry always inverts in S_N2 . The descriptor usually changes from *R* to *S* (or *S* to *R*) when the nucleophile takes the same priority rank as the leaving group, as with Br replaced by OH here. If the priorities change rank, the letter can stay the same even though the molecule has inverted. Always re-assign R/S from the CIP rules.

6 Four factors that control the rate

a. The substrate: steric hindrance decides

The nucleophile must reach the back of the carbon. Every extra alkyl group around that carbon blocks the path and crowds the five-groups transition state.



- **Branching next door matters too:** neopentyl bromide, $(\text{CH}_3)_3\text{C-CH}_2\text{Br}$, is primary, yet its S_N2 is extremely slow because the bulky tert-butyl group shields the back of the CH_2 carbon.
- **Allylic and benzylic** halides ($\text{CH}_2=\text{CH-CH}_2\text{-X}$, $\text{C}_6\text{H}_5\text{-CH}_2\text{-X}$) react fast: the π system overlaps with and stabilises the transition state.
- **Vinyl and aryl** halides do not undergo S_N2 : the back side is blocked by the molecule itself, and the C-X bond is stronger.

b. The nucleophile: stronger reacts faster

- An anion is a better nucleophile than its neutral conjugate acid: $\text{HO}^- > \text{H}_2\text{O}$, $\text{CH}_3\text{O}^- > \text{CH}_3\text{OH}$, $\text{NH}_2^- > \text{NH}_3$.
- In polar protic solvents, nucleophilicity increases down a group: $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ and $\text{HS}^- > \text{HO}^-$. Larger ions are more polarisable and less tightly held by hydrogen bonds.

Nucleophile (with CH_3Br)	Relative rate	
H_2O	1	
CH_3COO^-	500	
NH_3	700	
Cl^-	1,000	

Nucleophile (with CH ₃ Br)	Relative rate	
HO ⁻	10,000	
CH ₃ O ⁻	25,000	
I ⁻	100,000	
CN ⁻	125,000	
HS ⁻	125,000	

Data: OpenStax *Organic Chemistry*, section 11.3 (via LibreTexts). The bar is on a log scale.

c. The leaving group: weak bases leave best

A good leaving group is stable on its own after it takes the bonding pair, which means it is a weak base (the conjugate base of a strong acid).



HO⁻, RO⁻ and NH₂⁻ are strong bases and do **not** leave. To substitute an alcohol, first turn OH into a good leaving group: protonate it with HBr (water leaves) or convert it to a tosylate (TsO⁻ leaves).

d. The solvent: polar aprotic is best

- **Polar aprotic solvents** such as DMSO, DMF, acetone, acetonitrile and HMPA dissolve the salt but cannot hydrogen-bond to the anion. The nucleophile is left "naked" and very reactive.
- **Polar protic solvents** such as water and methanol wrap the anion in a cage of hydrogen bonds, which must be broken before it can attack. The reaction is slower.
- Example: azide ion with 1-bromobutane is about **200,000 times faster** in HMPA than in methanol (OpenStax, section 11.3).

7 S_N2 versus S_N1

Feature	S _N 2	S _N 1
Steps	One (concerted)	Two
Intermediate	None; one transition state	Carbocation

Feature	S _N 2	S _N 1
Rate law	$k[\text{RX}][\text{Nu}]$: second order	$k[\text{RX}]$: first order
Best substrates	$\text{CH}_3 > 1^\circ > 2^\circ$	$3^\circ > 2^\circ$, allylic, benzylic
Stereochemistry	Complete inversion	Mainly racemisation (often slight excess of inversion)
Nucleophile	Strong, usually anionic	Weak is fine (often the solvent)
Solvent	Polar aprotic	Polar protic
Rearrangement	Never	Possible (carbocation shifts)

8 One-minute revision

1. One step, no intermediate; bond making and breaking happen together.
2. Rate = $k[\text{RX}][\text{Nu}^-]$; second order.
3. Back-side attack at 180° into $\sigma^*(\text{C-X})$: Walden inversion; enantiopure in, enantiopure out.
4. $\text{CH}_3 > 1^\circ > 2^\circ \gg 3^\circ$; neopentyl is very slow; vinyl and aryl do not react.
5. Strong anionic nucleophile, weak-base leaving group, polar aprotic solvent.

Organic Pulse · free notes by Dr. Sandeep G. Sontakke. Main sources: Clayden *et al.*, *Organic Chemistry* (2nd ed.), ch. 15; OpenStax *Organic Chemistry*, sections 11.2–11.3.

Watch the shorts: [youtube.com/@OrganicPulse-y9q](https://www.youtube.com/@OrganicPulse-y9q)