Alkyl Halides
Substitution & Elimination

Chapter 7 · 8 hand-style mechanism cards

1. SN2: one step, backside attack
2. SN1: carbocation and racemization
3. E2: anti-periplanar, Zaitsev vs Hofmann
4. E2 in cyclohexanes: axial leaving group
5. E1 and carbocation rearrangements
6. Which pathway? Secondary substrates
7. Solvent effects
8. Alcohols to halides and alkenes; Williamson retrosynthesis

- blue arrow: electrons of the nucleophile or base
- red arrow: electrons of a bond that shifts or becomes a new bond
- green arrow: electrons leaving with the leaving group

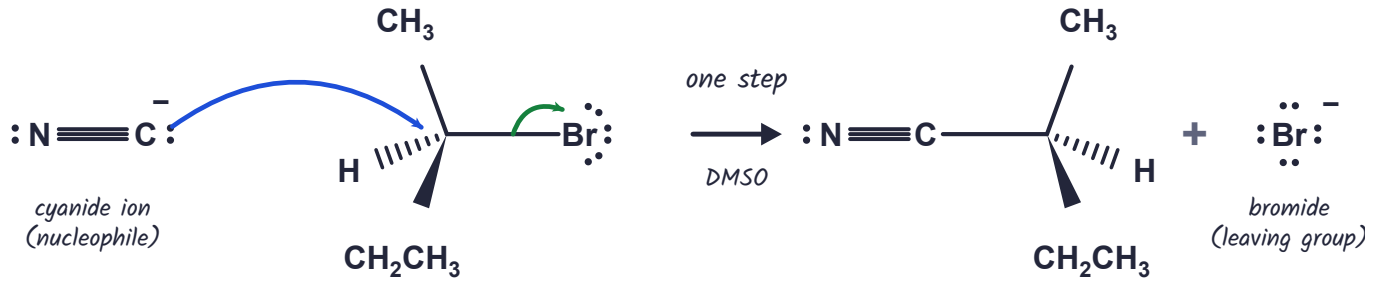
Wedge = toward you, dashed wedge = away from you, plain line = in the plane. Dots are lone pairs. Curved arrows start at electrons and end at an atom or bond.

SN2: one step, backside attack

hand-style mechanism card · bimolecular substitution with inversion

blue = nucleophile or base electrons · red = bond electrons moving · green = electrons leaving with the leaving group

1 Concerted: bond forms as bond breaks



cyanide ion (nucleophile)

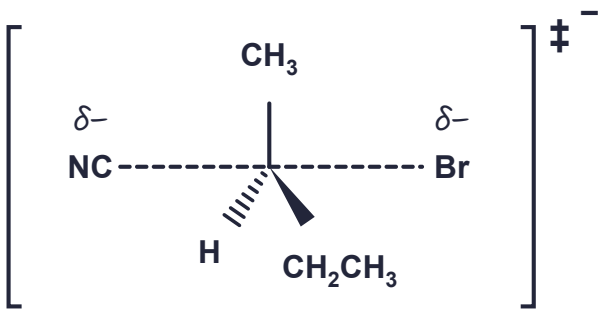
(R)-2-bromobutane

(S)-2-methylbutanenitrile

bromide (leaving group)

Cyanide uses its lone pair on **carbon** to attack the back side of C–Br (**blue**); the C–Br electrons leave as bromide (**green**). The three other groups flip like an umbrella in a gale: the stereocenter is inverted.

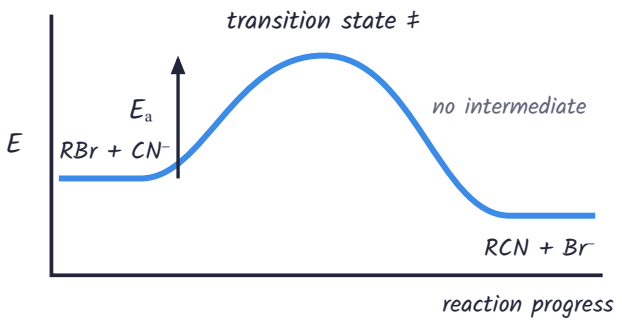
2 Transition state



Nu and LG on one line; C is flat (sp^2-like) in between

Five groups on one carbon for an instant: Nu···C···LG is a straight line, the other three lie in a plane.

3 One barrier, no intermediate



Only one step, so only one hump. The nucleophile is in the transition state, which is why [Nu] matters.

4 Rate law

$$\text{rate} = k[\text{R–Br}][\text{Nu}^-]$$

Second order overall (first order in each reactant): doubling $[Nu^-]$ or [RBr] doubles the rate; doubling both gives 4×. Switching to a better nucleophile changes k, not the order.

5 Substrate: sterics decide

CH_3–X fastest > **1°** > **2° slow** >> **3° none**

The back side of a 3° carbon is blocked by three alkyl groups. A 1° halide with a bulky neighbor (neopentyl, $(CH_3)_3CCH_2$–Br) is also nearly inert to SN2.

6 Who attacks fast? Nucleophile quick guide

strong / good: I^-, HS^-, RS^-, CN^-, N_3^-, RNH_2 · **basic too:** HO^-, RO^- · **moderate:** Br^-, Cl^-, RCO_2^- · **poor:** H_2O, ROH

Why the back side? The nucleophile donates into the empty σ^* orbital of C–LG, whose big lobe points away from the leaving group (180°).

Good leaving group = weak base. $I^- > Br^- > Cl^- >> F^-$. HO^- and RO^- do not leave from an alkyl group.

Best conditions: good nucleophile that is not too basic, in a polar aprotic solvent (DMSO, DMF, acetone, CH_3CN). See card 7.

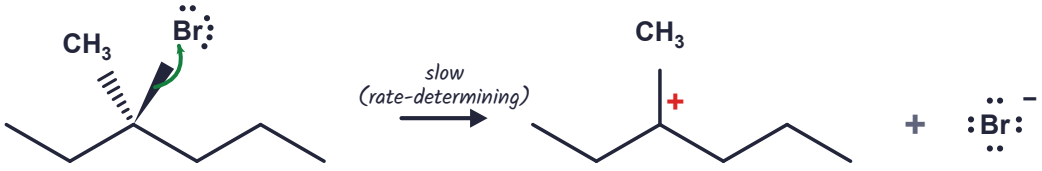
Exam trap SN2 always inverts the 3-D arrangement, but the label R/S flips only if the new group ranks where the old one did. Reassign CIP priorities every time. And an SN2 at a stereocenter never gives a racemic mixture.

SN1: cation first, Nu second

hand-style mechanism card · unimolecular substitution, solvolysis, racemization

blue = nucleophile or base electrons *red = bond electrons moving* *green = electrons leaving with the leaving group*

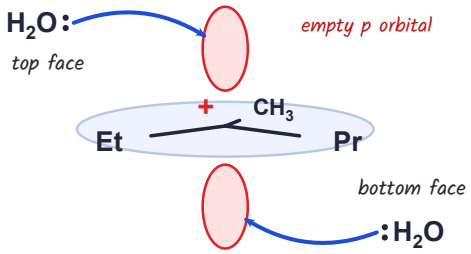
1 Step 1: the leaving group departs first



(R)-3-bromo-3-methylhexane — planar carbocation (sp^2, empty p orbital)

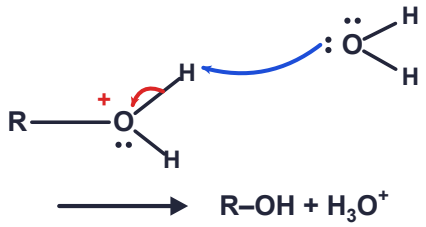
C–Br electrons leave with bromide (**green**), leaving a planar sp^2 carbocation. Slow step; only the substrate is involved.

2 Step 2: attack on either face



Solvent water donates a lone pair to the empty p orbital (**blue**); both faces are open.

3 Step 3: lose a proton



water (solvent) is also the base

A second water takes H^+ (**blue**); the O–H electrons stay on oxygen (**red**).

4 Stereochemical result



(R)-3-methylhexan-3-ol
OH where Br was: "retention"

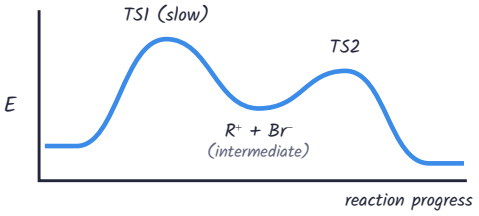
(S)-3-methylhexan-3-ol
OH on the far side: "inversion"

Both faces attack, so the product is nearly racemic. A small excess of **inversion** is typical: bromide, still close as an ion pair, partly shields the face it left.

5 Rate law and energy profile

$$\text{rate} = k[\text{R–Br}]$$

First order: Nu acts after the slow step, so it is not in the rate law.



Helps SN1: 3° or allylic/benzylic C, weak Nu (H_2O, ROH), polar protic solvent, good LG. 2° is slow; 1°/methyl: none.

Solvolysis: the solvent is the nucleophile. Cations: 3° > 2° >> 1°; they may rearrange (card 5).

E1 competes (same cation); heat favors the alkene (card 5).

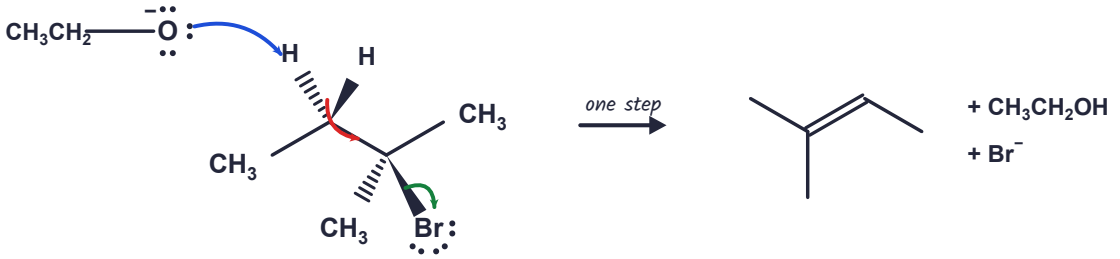
Exam trap "Racemic" assumes a free, flat cation. If a problem says slight excess of inversion, the inverted product is the major one. A stronger or more concentrated nucleophile never speeds up an SN1.

E2: anti-periplanar, Zaitsev vs Hofmann

hand-style mechanism card · bimolecular elimination

blue = nucleophile or base electrons *red = bond electrons moving* *green = electrons leaving with the leaving group*

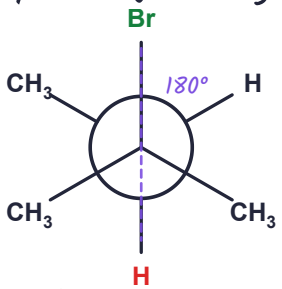
1 One step: the H, the C–C and the leaving group all move together



2-bromo-2-methylbutane — 2-methylbut-2-ene (Zaitsev)

Ethoxide takes the H (**blue**); the C–H pair becomes the new π bond (**red**); the C–Br pair leaves with bromide (**green**). H (dash) and Br (wedge) sit on opposite faces, anti.

2 Anti-periplanar geometry



front C (C2): bonds meet at the center
back C (C3): bonds start at the circle

C–H and C–Br must lie in one plane, 180° apart (staggered). Rotate about C2–C3 until an H is anti to Br; syn (0°, eclipsed) is a poor alternative.

3 Rate law and requirements

$$\text{rate} = k[\text{R–Br}][\text{B}^-]$$

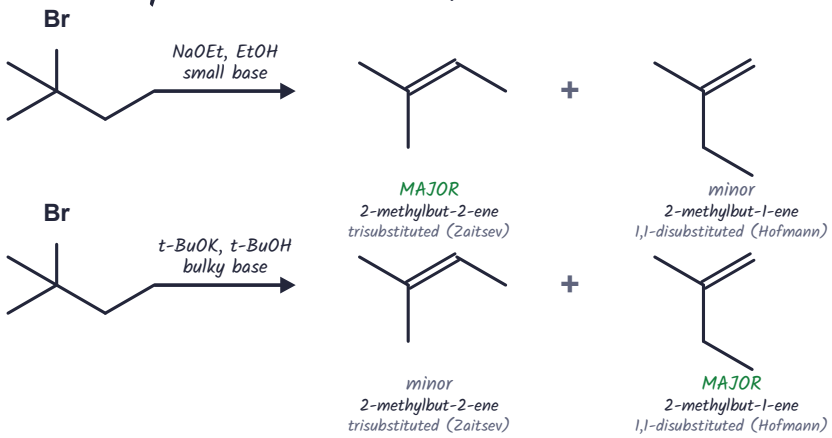
strong base needed: HO^-, RO^-, NH_2^-

works for 2° and 3° halides **at least one β-H**

Second order: the base is in the single transition state. Heat favors elimination over substitution.

- an H on the carbon next to C–LG
- that H and LG can become anti (180°)
- a good leaving group (Br, I, Cl, OTs)

4 Which alkene? It depends on the size of the base



Same anti requirement, but the **base** picks the β-H: a small base takes the interior CH_2 hydrogen; a bulky base removes a more accessible methyl H.

Why more substituted? Alkyl groups stabilize C=C (hyperconjugation); that lowers the transition state.

Bulky bases: t-BuOK (also LDA). **Small bases:** HO^-, CH_3O^-, $CH_3CH_2O^-$.

Stereospecific: a given diastereomer gives one alkene geometry (E or Z).

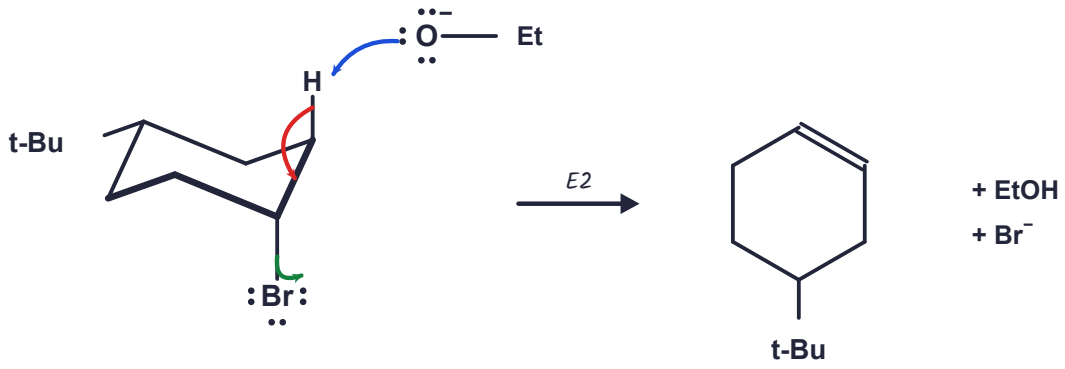
Exam trap "Zaitsev always wins" is false. With a bulky base the less substituted (Hofmann) alkene is the major product. Also, a 3° or 2° halide with a strong base gives mainly E2 (3°: never SN2; 2°: SN2 is minor).

E2 in cyclohexanes: axial leaving group

hand-style mechanism card · chair conformations and trans-diaxial elimination

blue = nucleophile or base electrons · red = bond electrons moving · green = electrons leaving with the leaving group

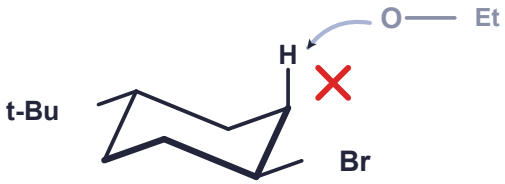
1 E2 needs a trans-diaxial H and leaving group



cis-1-bromo-4-tert-butylcyclohexane — *4-tert-butylcyclohexene*

*tert-Butyl locks the ring (it stays equatorial). In the cis isomer Br is axial, so each neighboring carbon has an axial H on the opposite face (H up, Br down): anti to Br. Ethoxide removes it (**blue**), the C–H pair makes the π bond (**red**), Br leaves (**green**).*

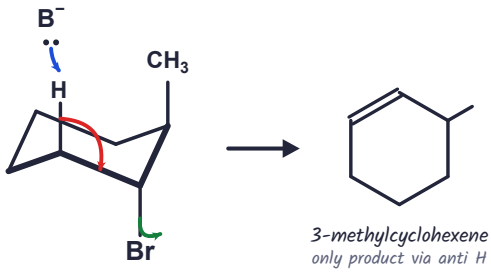
2 No axial Br: no E2



trans-1-bromo-4-tert-butylcyclohexane
(Br and t-Bu both equatorial)

In the trans isomer Br is equatorial. The neighboring axial H is gauche (about 60°), not anti, to it. Elimination is extremely slow; SN2 or other paths may take over.

3 Product follows the axial H



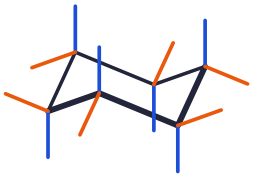
trans-1-bromo-2-methyl-cyclohexane (diaxial chair)

3-methylcyclohexene
only product via anti H

Diaxial Br and CH_3: the carbon bearing CH_3 has an equatorial H, which cannot be removed. Only the axial H on the other neighbor works, giving the less substituted alkene.

4 Reading a chair

axial: straight up / down, alternating
equatorial: roughly along the ring edge



Recipe

1. Put the leaving group axial (ring flip if needed).
2. Look at each neighbor: is its axial H on the opposite face? Axial positions alternate up/down, so adjacent axial bonds always point opposite ways.
3. Only those H atoms can leave; the alkene forms toward them.
4. If the flip puts a big group axial, that chair is less populated and E2 is slower.

Axial = anti. Axial bonds on neighboring carbons point in opposite directions (up/down): exactly the 180° geometry E2 needs.

Ring flip swaps axial and equatorial. A substituent that is equatorial can still react if the ring can flip to the diaxial chair.

Zaitsev is not automatic: if the more substituted carbon has no anti H, the other alkene forms.

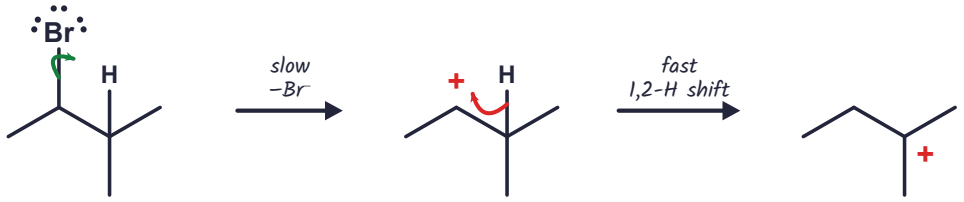
Exam trap Do not apply Zaitsev blindly to a ring. First draw the chair with the leaving group axial, then list which neighbors carry an axial H. A substituent on a neighbor that occupies the axial position blocks that carbon from E2.

E1: cation, shift, then lose H+

hand-style mechanism card · unimolecular elimination and 1,2-shifts

blue = nucleophile or base electrons *red = bond electrons moving* *green = electrons leaving with the leaving group*

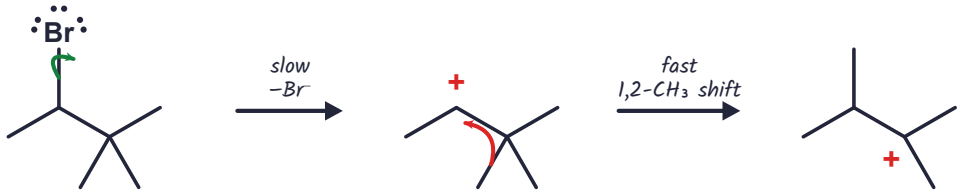
1 Hydride shift: 2° cation becomes 3°



2-bromo-3-methylbutane — 2° carbocation — 3° carbocation (more stable)

After slow ionization (**green**), the neighboring C–H bond electrons slide to the cationic carbon (**red**): the H moves with its pair and the + lands on the more substituted carbon.

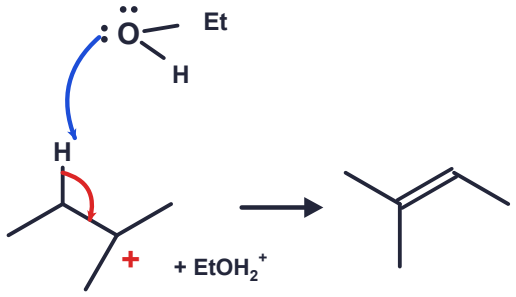
2 Methyl shift: same idea



2-bromo-3,3-dimethylbutane — 2° carbocation — 3° carbocation (more stable)

The neighbor is quaternary, so a C–CH_3 bond shifts (**red**) to give a 3° cation. Both are 1,2-shifts.

3 Last step: lose H^+ next to C^+



EtOH is the base — 2-methylbut-2-ene *major (Zaitsev)*

The weak base (solvent) removes an H from the carbon next to C^+ (**blue**); the C–H pair becomes the π bond (**red**). The 3° cation from panel 1 gives mostly the trisubstituted alkene.

4 E1 at a glance

$$rate = k[R\text{–}Br]$$

weak base, ionizing solvent **heat favors E1 over SN1**

more stable cation = faster E1

CH_3^+ < 1° < 2° < 3°

allylic / benzylic: comparable to 3° or better

carbocation stability ladder

Same slow step as SN1, so the two compete. A strong base would instead trigger E2 (card 3). Minor products also form without a shift, e.g. 3-methylbut-1-ene from the 2° cation.

When does a cation shift? When the shift gives a more stable cation: next to a 3° C–H, or next to a quaternary carbon (methyl shift).

No 1° cations. If the leaving group is on a 1° carbon, ionization does not happen alone; it goes SN2/E2 unless the shift is simultaneous.

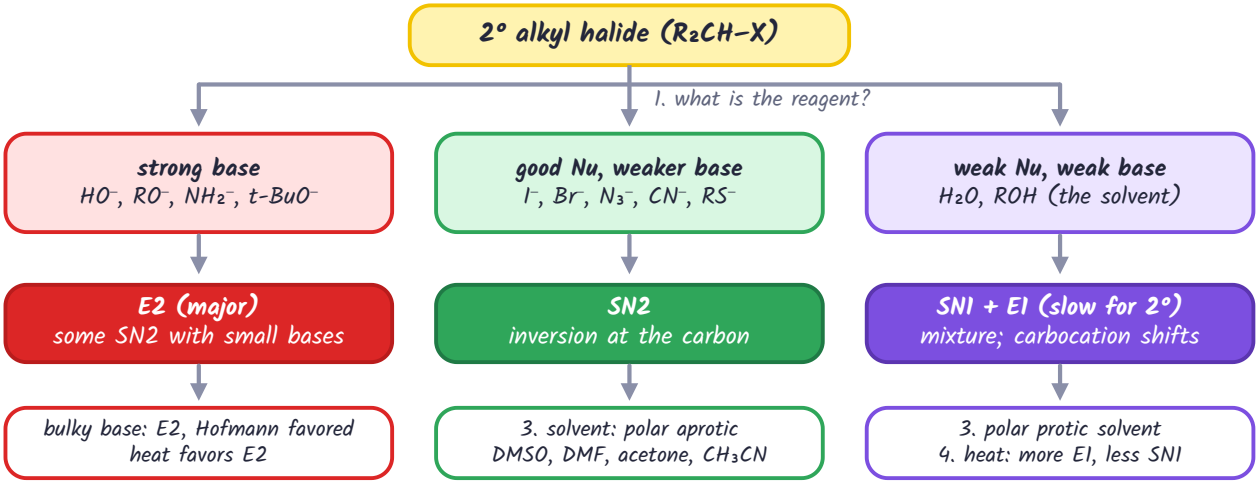
Count carbons: a shift moves a group by one position; the carbon skeleton of the alkene may differ from the starting halide.

Exam trap Predict E1 (and SN1) products from the *most stable cation*, not from where the halogen was. If a 2° cation sits next to a 3° C–H or a quaternary carbon, expect a hydride or methyl shift before the proton leaves.

Which pathway? Secondary halides

hand-style decision card · reagent, then substrate, solvent, heat

1 Decision flow: reagent, substrate, solvent, heat



For a **2°** halide the reagent decides first, then the solvent; heat tilts the mixture toward elimination.

2 Eight secondary-halide cases

Reagent, solvent (2-bromobutane)	Pathway	What you get
NaN_3, DMSO	SN2	2-azidobutane, inverted
NaCN, DMF	SN2	2-methylbutanenitrile, inverted
NaI, acetone	SN2	2-iodobutane (NaBr precipitates)
$NaSCH_3$, EtOH	SN2	sec-butyl methyl sulfide, inverted
NaOEt, EtOH, 55 °C	E2	but-2-ene (Zaitsev) major; some ether (SN2)
NaOH, EtOH/H_2O, heat	E2	alkenes mainly; minor butan-2-ol
t-BuOK, t-BuOH	E2	more but-1-ene (Hofmann) than with EtO^-
H_2O or EtOH, heat	SN1 + E1	slow; alcohol/ether plus alkenes partly racemic (racemization plus some inversion)

Same 2° substrate, only the conditions change. A charged reagent means a bimolecular path (SN2 or E2); a neutral solvent as the reagent means a unimolecular path (SN1 or E1).

3 Substrate shortcut, then heat

CH_3, 1° SN2 (E2 if the base is bulky) **2°** reagent decides

3° never SN2: strong base → E2; weak base, protic solvent → SN1 + E1

allylic, benzylic all four paths possible

$$\Delta G = \Delta H - T\Delta S$$

Elimination makes more molecules (ΔS more positive): heat favors E over S.

Nucleophile vs base: a nucleophile attacks carbon (rate); a base takes H^+. HO^- and RO^- are both, and on 2° carbons the base role wins.

Weak-base nucleophiles (I^-, N_3^-, CN^-, RS^-) are large or polarizable and attack carbon much faster than they take H^+.

Mixtures are normal. Questions ask for the *major* product; name the pathway first, then draw.

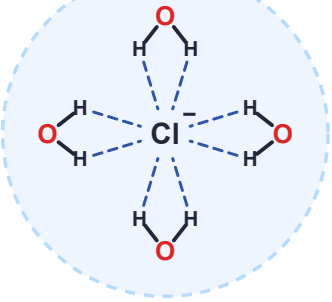
Exam trap A 2° halide with HO^- or RO^- gives mainly E2, not SN2. For SN2 on a 2° carbon pick a good nucleophile that is a weak base, in a polar aprotic solvent, at low temperature.

Solvent effects

hand-style concept card · protic vs aprotic, nucleophile strength, SN1/SN2 rates

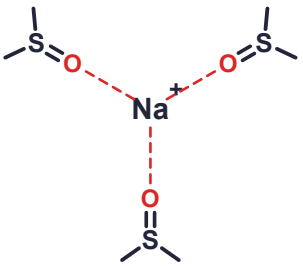
1 What the solvent does to the nucleophile

in water, methanol, ethanol



protic: O–H bonds cage the anion

in DMSO, DMF, acetone, acetonitrile



aprotic (DMSO shown): S=O binds the cation, anion stays bare



"naked" anion

A protic solvent donates hydrogen bonds to anions and ties them up. An aprotic polar solvent dissolves the salt by wrapping the cation but leaves the anion unsolvated and very reactive.

2 Halide nucleophilicity flips with the solvent

Protic (water, ROH): I^- > Br^- > Cl^- > F^- *large, polarizable ions shed their solvent shell easily*

Aprotic (DMSO, DMF): F^- > Cl^- > Br^- > I^- *no cage: nucleophilicity follows basicity*

3 Rate effects

Pathway	Protic	Aprotic	Reason
SN2, anionic Nu	slower	much faster	caged Nu^- loses reactivity; naked Nu^- is strong
SN1 (rate-limiting ionization)	faster	slower	H-bonds and ion–dipole forces stabilize the leaving group and the cation
E2, anionic base	moderate	faster	same reason as SN2: freer base
E1	faster	slower	same slow step as SN1

Two different jobs: SN2/E2 need a strong, free anion (aprotic helps); SN1/E1 need the solvent to pull the leaving group off (protic helps).

4 Common solvents (dielectric constant ε approx.)

Polar protic (O–H or N–H): H_2O ε≈80 · CH_3OH 33 · CH_3CH_2OH 25 · CH_3CO_2H 6

Polar aprotic (no O–H, N–H): DMSO 47 · DMF 37 · CH_3CN ≈37 · acetone 21

Nonpolar: hexane ≈2 *does not dissolve ionic nucleophiles, so it is rarely used for SN2 with salts.*

Solvolysis *uses a protic solvent as the nucleophile: water (hydrolysis), alcohols (alcoholysis).*

Fast SN2 recipe: *primary or secondary halide, N_3^- or CN^- or I^-, in DMSO, DMF or acetone.*

Add water *to an SN1 reaction and the rate rises: more ionizing power.*

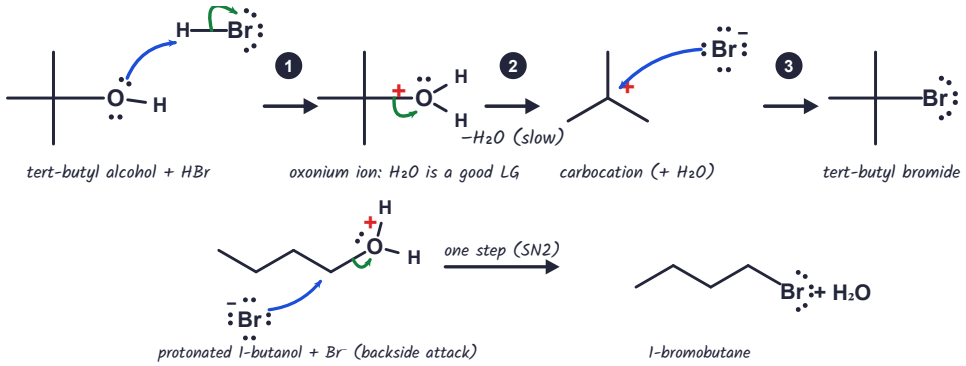
Exam trap

"Protic" means an O–H or N–H hydrogen-bond donor, not "contains hydrogen." Acetone, DMSO and DMF are full of H atoms but are aprotic. And never quote one fixed halide order: it reverses between protic and aprotic solvents.

Alcohols to halides and alkenes

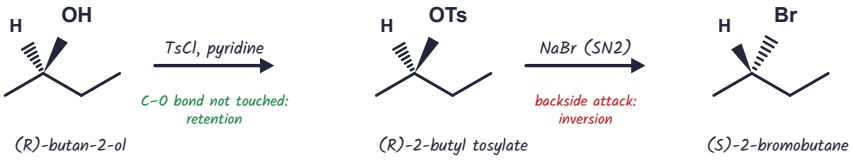
hand-style mechanism card · HBr, TsCl, H_2SO_4 and Williamson retrosynthesis

1 HBr: SN1 for 3° alcohols, SN2 for 1°



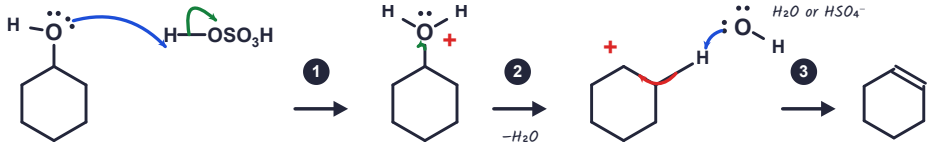
Acid turns HO^- into a good leaving group, H_2O. 3°: cation first, then Br^- attacks (**blue**). 1°: no stable cation, so Br^- displaces H_2O directly (conc. HBr, heat). A 2° alcohol is borderline.

2 TsCl, then a nucleophile: two clean steps



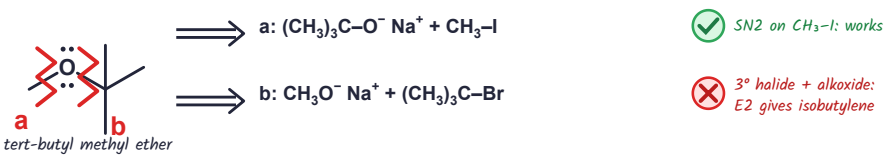
Making the tosylate breaks only the O–H bond: configuration kept. OTs leaves slightly better than Br^-, so step 2 is a normal SN2 (inversion). No cation, no rearrangement. Ts = p-toluenesulfonyl.

3 Conc. H_2SO_4, heat: dehydration (E1)



Steps 1–2 as above; then a weak base removes a β-H (**blue**) and the C–H pair becomes C=C (**red**). Cation shifts are possible; the most substituted alkene usually wins.

4 Williamson ether synthesis: retrosynthesis



Cut the C–O bond so the **alkyl halide is methyl or 1°**; put the bulky group on the alkoxide (ROH + NaH). Likewise ethyl isopropyl ether: $(CH_3)_2CHO^-$ + CH_3CH_2Br, not the reverse.

$SOCl_2$/pyridine: 1°/2° ROH to RCl by SN2, no rearrangement.

Temperature steers: ethanol + H_2SO_4 gives ether near 140 °C, ethylene near 170 °C.

Exam trap

HBr on a 2° alcohol can rearrange (3-methylbutan-2-ol gives 2-bromo-2-methylbutane by a hydride shift); TsCl or $SOCl_2$/pyridine keeps the skeleton. In a Williamson synthesis a 3° halide gives alkene, not ether.