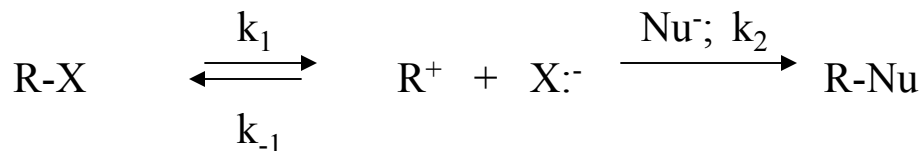


1. Unimolecular Aliphatic Substitution S_N1



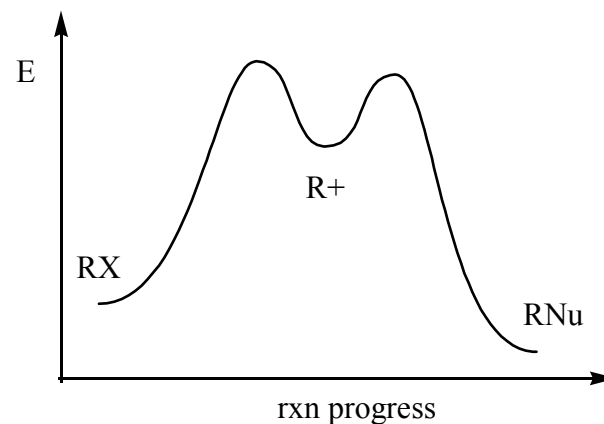
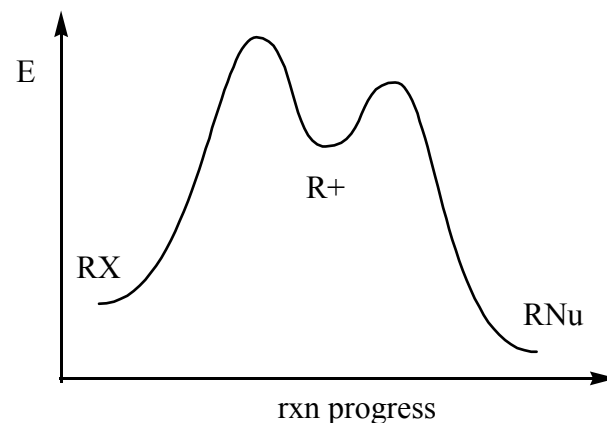
Simple Rate law: $\text{rate} = k_1 [\text{R-X}]$ if $k_2 \gg k_{-1}$

General rate law (if k_2 and k_{-1} comparable):

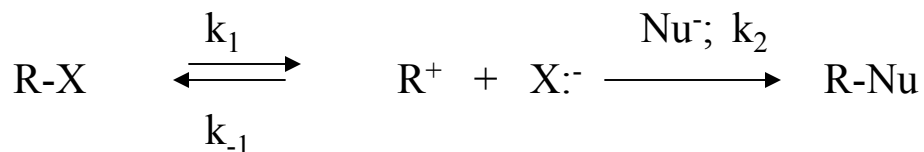
$$\text{Rate} = \frac{d[\text{RNu}]}{dt} = \frac{k_1 k_2 [\text{RX}][\text{Nu}^-]}{k_{-1}[\text{X}^-] + k_2[\text{Nu}^-]}$$

Derived by using steady state approximation for R⁺

- Reduces to simple rate law if $k_2[\text{Nu}^-] \gg k_{-1}[\text{X}^-]$
 - e.g. if $k_2 \gg k_{-1}$ and Nu⁻ & X⁻ are present in equal amounts
 - In solvolysis: Nu = solvent
 - At initial stage of reaction ($[\text{X}^-] \ll [\text{Nu}^-]$)
- Addition of X⁻ will slow down reaction => **Common Ion Effect**



2. General Rate Law for S_N1 reaction:



$$\text{Rate} = \frac{d[\text{RNu}]}{dt} = k_2 [\text{R}^+][\text{Nu}^-] \quad (1)$$

Apply steady state approximation to R⁺, meaning that R⁺ is formed much slower from RX than it decays either to RNu or returns back to RX.

$$\frac{d[\text{R}^+]}{dt} = 0 = [\text{RX}]k_1 - ([\text{R}^+][\text{X}^-]k_{-1} + [\text{R}^+][\text{Nu}^-]k_2) \quad (2)$$

$$\text{Rearrange (2): } [\text{R}^+] = \frac{[\text{RX}]k_1}{[\text{X}^-]k_{-1} + [\text{Nu}^-]k_2} \quad (3)$$

$$\text{Insert (3) into (1) gives general rate law: } \text{Rate} = \frac{d[\text{RNu}]}{dt} = \frac{k_1 k_2 [\text{RX}][\text{Nu}^-]}{k_{-1}[\text{X}^-] + k_2[\text{Nu}^-]}$$

3. Common Ion Effect

-can be used to probe S_N1 mechanism

-requires that R^+ is not too reactive (1st barrier \sim 2nd barrier)

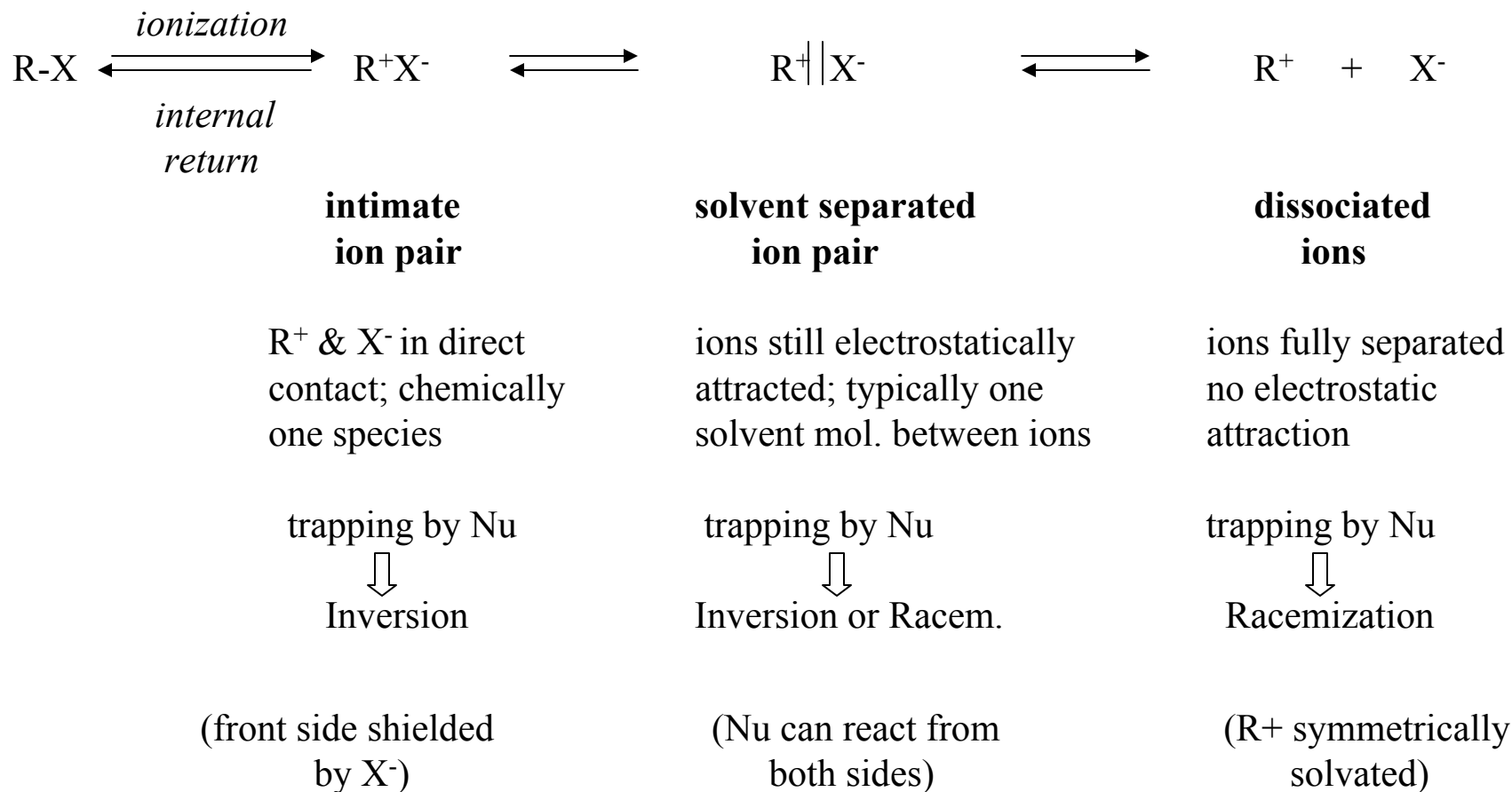
e.g. $(CH_3)_3C^+$ too reactive and no common ion effect observed

-applies only, if R^+ and X^- are fully separated:



each ion fully solvated and separated

4. Winstein Scheme of RX Dissociation

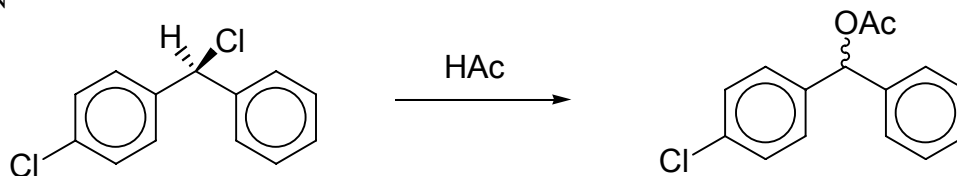


In the formation of R⁺ thru ionization of RX, three different types of ion-pairs have to be considered and are formed consecutively: intimate ion pair, solvent separated ion pair and fully dissociated ion pair. The nucleophile may intercept R⁺ at any stage. Whether Nu reacts with the intimate ion pair, the solvent separated ion pair or the fully dissociated R⁺ depends on the reactivity of the nucleophile, solvent, leaving group and reactivity/stability of R⁺

⇕
nucleophilic assistance

5. Experimental Support for Winstein Scheme

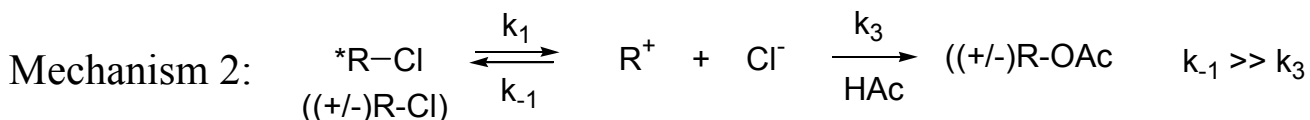
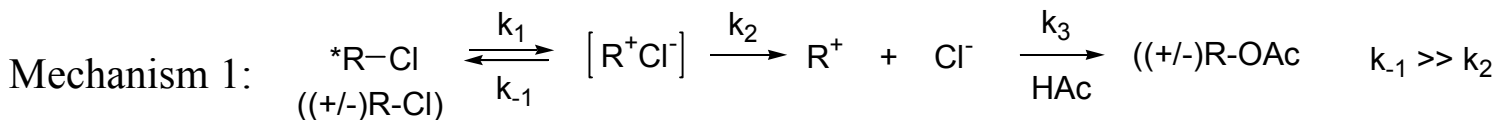
The following experiment (solvolysis of p-chlorobenzhydrylchloride in acetic acid) led Saul Winstein to conclude that at least one ion-pair intermediate must exist between reactant and the dissociated ions in S_N1 reaction:



Experiment 1:

Observation: $k_{\alpha}/k_t \sim 30-70$ k_{α} = rate of loss of overall optical activity of the reaction mixture
 k_t = rate of product formation

Interpretation: $k_a \gg k_t \Rightarrow$ either 'ion-pair' precedes dissociated ions and this 'ion-pair' returns back to reactant (*internal return*) with partial racemization faster than dissociation (mechanism 1) or that dissociated ions ($\text{Cl}^- + \text{R}^+$) recombine faster than R^+ reacts with HAc (mechanism 2)



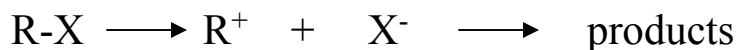
Experiment 2: reaction run with $\text{R}^*-\text{}^{35}\text{Cl}$ in presence of excess ${}^{37}\text{Cl}^-$

Observation: $k_{\text{ex}} \ll k_{\alpha}$ k_{ex} rate of ${}^{35}\text{Cl}/{}^{37}\text{Cl}$ exchange in reactant.

Conclusion: recombination of dissociated ions is slow \Rightarrow mechanism 1 must operate with a minimum of one ion-pair intermediate

6. 'Salt-effects' on rate of solvolysis reactions

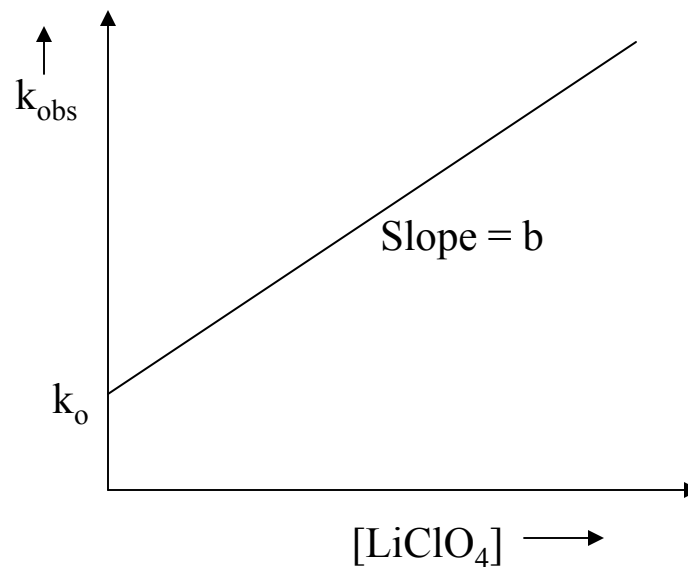
Normal Salt Effect: Rate of S_N1 reaction (or any reaction in which ionic intermediates are formed) increases upon addition of a *non-common salt* that is unreactive, e.g. Li⁺ClO₄⁻ (do not mix up with *common salt effect*)



$$k_{\text{obs}} = k_0 (1 + b [\text{LiClO}_4])$$

k_0 rate of reaction without added salt

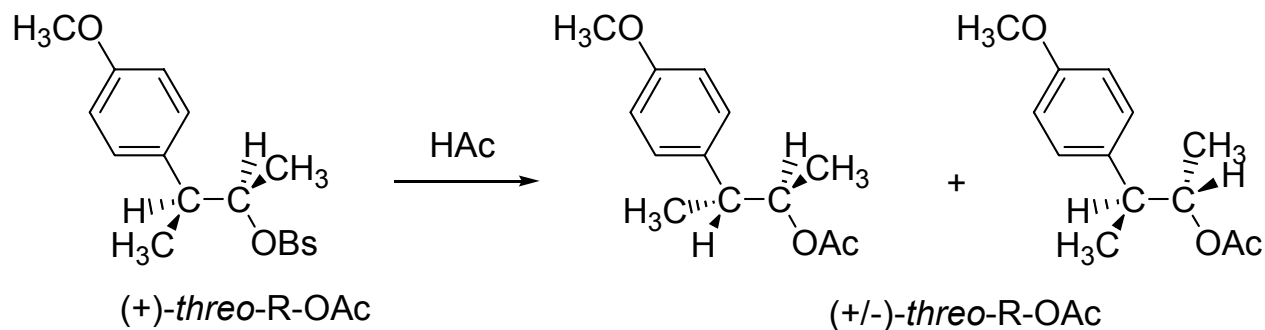
b reaction specific constant



Interpretation: Salt increases dielectric constant of medium \Rightarrow faster ionization of R-X

7. Experimental Support for Full Winstein Scheme

From unusual *Special Salt Effect* observed in solvolysis of (+)-*threo*-1 in HAc

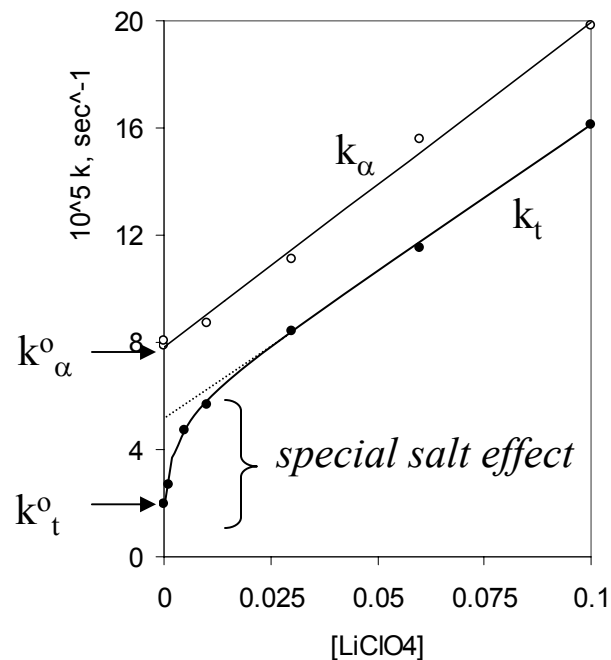


k_t : rate constant of R-OAc formation

k_t^0 : rate constant of R-OAc formation at $[\text{LiClO}_4] = 0$

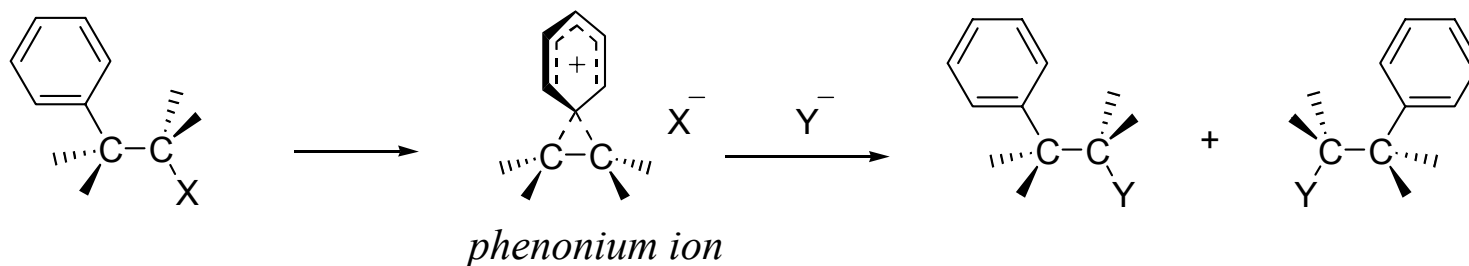
k_α : rate constant of loss of optical activity of reaction mixture

k_α^0 : rate constant of loss of optical activity of reaction mixture at $[\text{LiClO}_4] = 0$



8. Aryl Participation (Phenonium Ion)

π -bond participation \leftrightarrow form of neighboring group participation (*anchimeric assistance*)



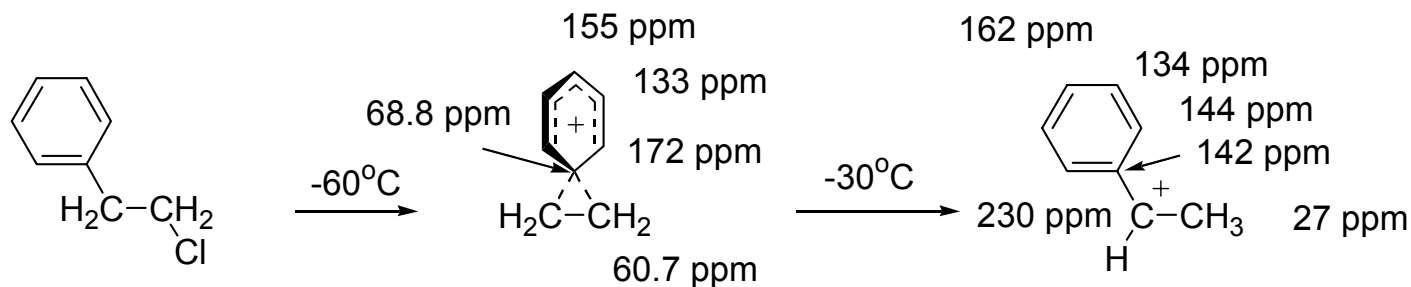
π -bond participation observed, if

- weakly nucleophilic solvent (direct S_N2 slow)
- sufficiently electron-rich aryl ring
- aryl unit at C that is next to C carrying LG
- C carrying LG is primary or secondary (for tert. C $\Rightarrow S_N1$ mechanism)

9. Support for Phenonium ion from ^{13}C NMR in 'Superacidic Medium'

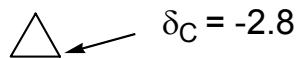
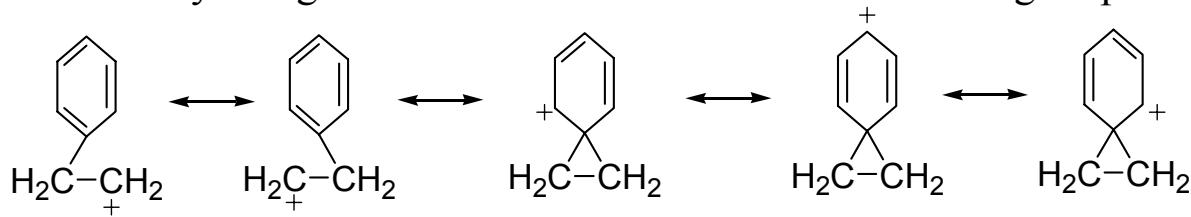
(stable carbocation conditions): Olah, *J. Am. Chem. Soc.* (1976), 98 6284.

δ_c (in $\text{HF-SbF}_5\text{-SO}_2\text{ClF}$)

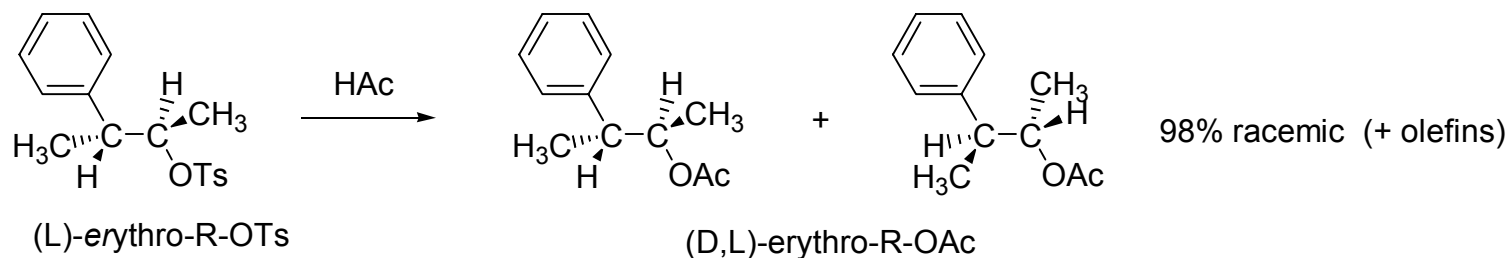
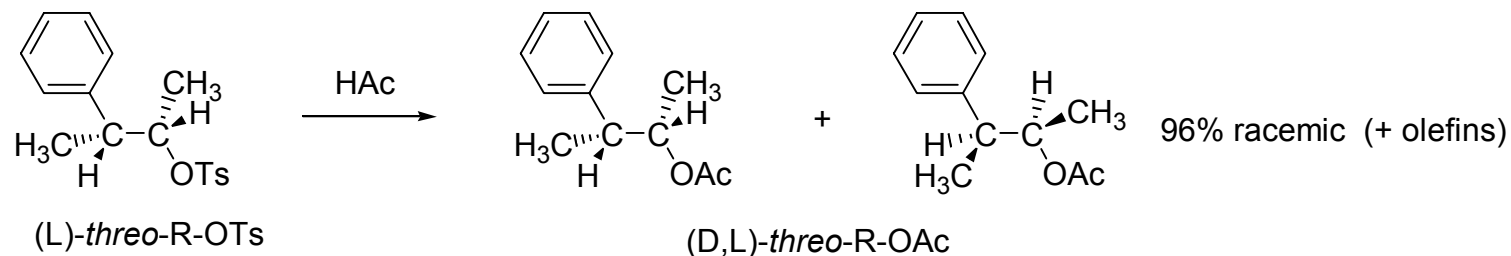


Note:

- 1) Large upfield shift of cyclopropyl CH_2 , which supports that both CH_2 carry partial charge
- 2) δ_c of bridgehead C supports that C is sp^3 hybridized
- 3) All C that carry charge in one of the resonance forms are stronger upfield shifted than others

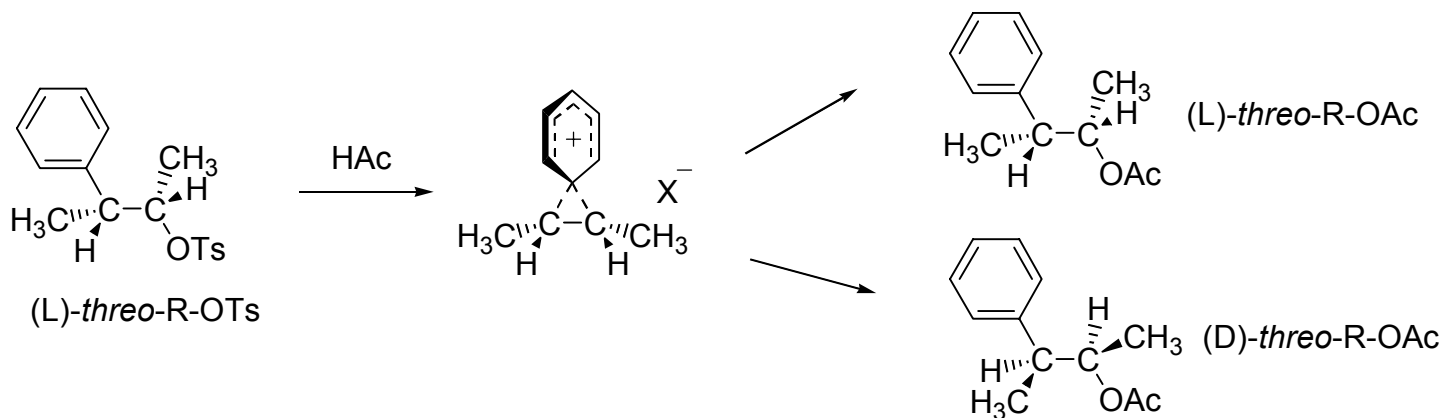


10. Phenonium ion originally proposed by D. J. Cram

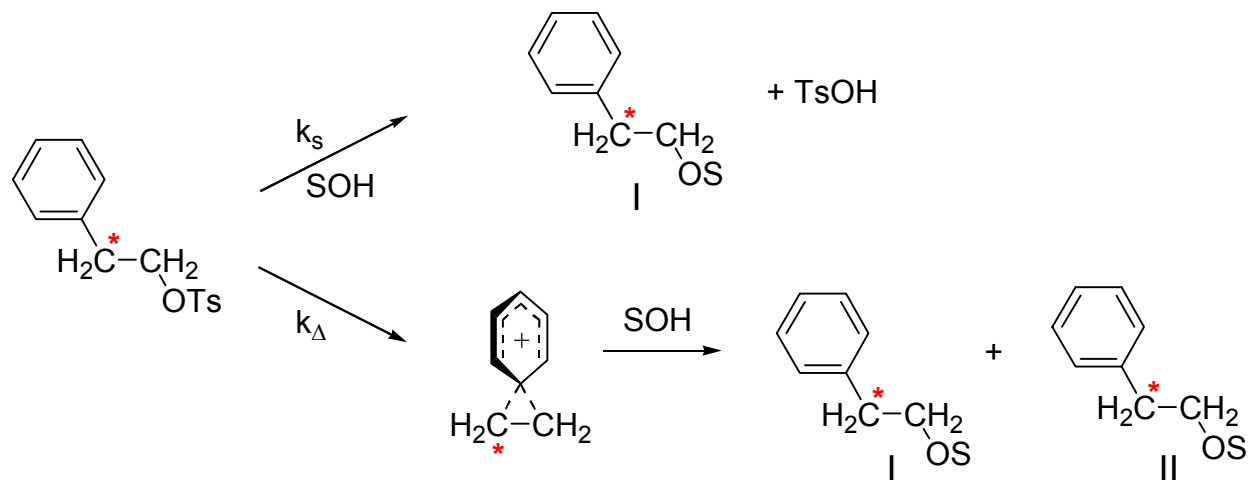


Observations:

- 1) L-threo R-OTs \rightarrow D,L-threo product (racemic); L-erythro expected product of unassisted S_N2
- 2) L-erythro R-OTs \rightarrow D,L-threo product (racemic); L-threo expected product of unassisted S_N2

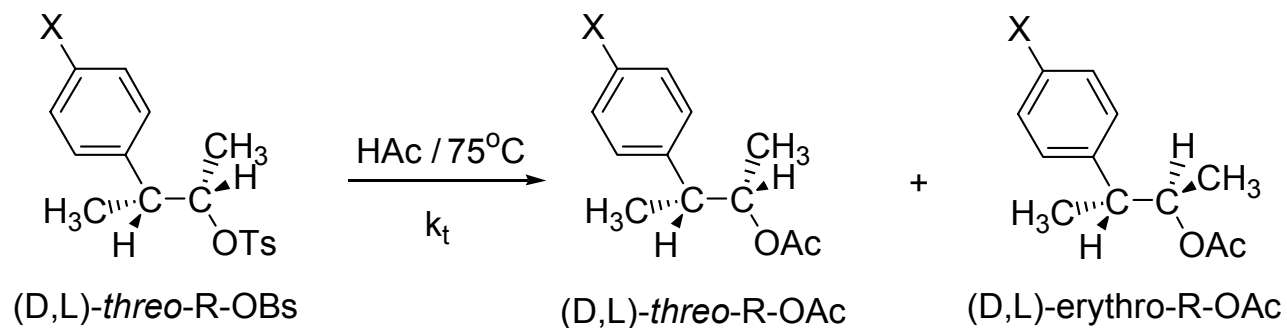


11. Extend of Aryl-participation Depends on Nucleophilicity of Solvent



| Solvent | % rearrangement (100 - (yield(I)-yield(II))) | Comment |
|----------------------|---|--|
| EtOH | 0.3 | $k_s \gg k_\Delta$ |
| CH ₃ COOH | 5.5 | |
| HCOOH | 45 | $k_s \sim k_\Delta$ (I:II = 77.5:22.5) |
| CF ₃ COOH | 100 | $k_s \ll k_\Delta$ (I:II = 1:1) |

12. Substituent Effect on Phenonium Ion Formation



formed via
 phenonium ion
 aryl group assisted
 displacement

formed via solvent
 assisted
 displacement
 S_N2

k_Δ

k_s

Total rate constant of product formation $k_t = k_s + F \times k_\Delta$

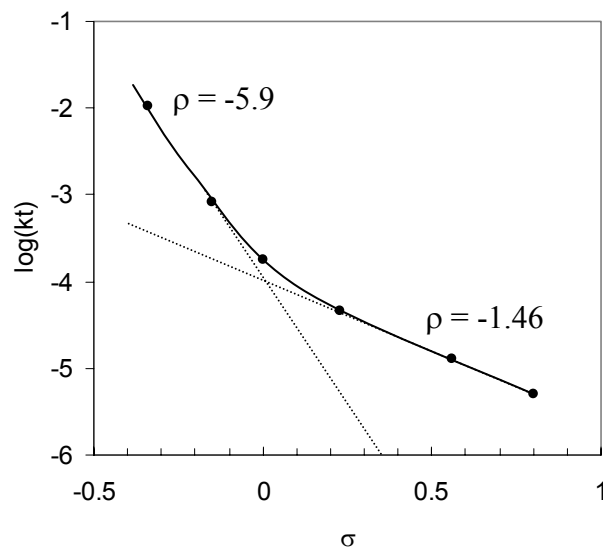
k_Δ = rate constant of D,L-*threo* product formation

k_s = rate constant of D,L-*erythro* product formation

F = fraction of phenonium ion that returns back to D,L-*threo* starting material

12b. Hammett plot $\log k_t$ vers $\sigma = \sigma_R + \sigma_I$

| X | $k_t \times 10^5 \text{ sec}^{-1}$ | % <i>threo</i> -acetate | $\sigma = \sigma_R + \sigma_I$ |
|-----------------|------------------------------------|-------------------------|--------------------------------|
| OMe | 1060 | ~ 100 | -0.34 = -0.61 - 0.27 |
| Me | 81.4 | 88 | -0.15 = -0.11 - 0.04 |
| H | 18 | 59 | 0 |
| Cl | 4.53 | 39 | 0.23 = -0.23 + 0.46 |
| CF ₃ | 1.26 | 11 | 0.56 = 0.08 + 0.48 |
| NO ₂ | 0.495 | 1 | 0.8 = 0.15 + 0.65 |

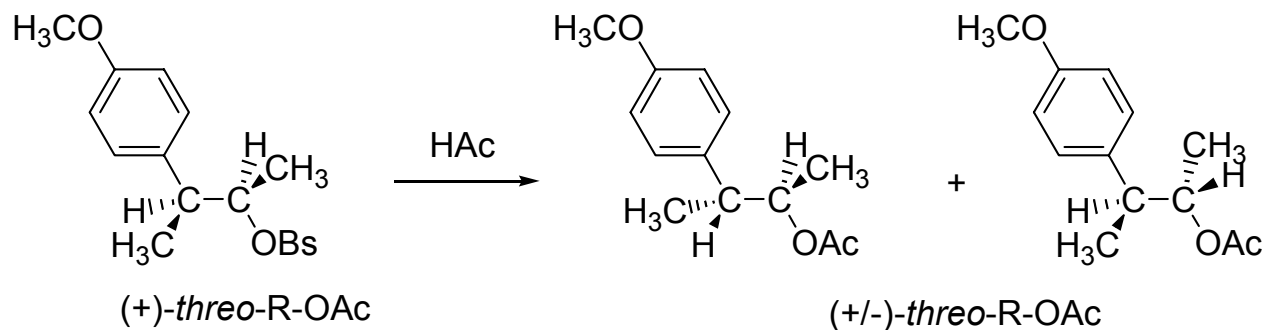


Interpretation:

- 1) non-linear Hammett plot with break point at $\sigma \sim 0$ indicates change in mechanism
- 2) $\sigma < -0.4$: aryl participation; consistently very large negative $\rho = -5.9$, which indicates that for these reactants rate is very sensitive to the electron-density of the aryl group. \Rightarrow large δ^+ in TS
- 3) $\sigma > 0.3$: solvent assisted displacement; small negative $\rho = -1.46 \Rightarrow$ rate little sensitive to electron-density of aryl group. Only small δ^+ at C in TS.

7. Experimental Support for Full Winstein Scheme

From unusual *Special Salt Effect* observed in solvolysis of (+)-*threo*-1 in HAc

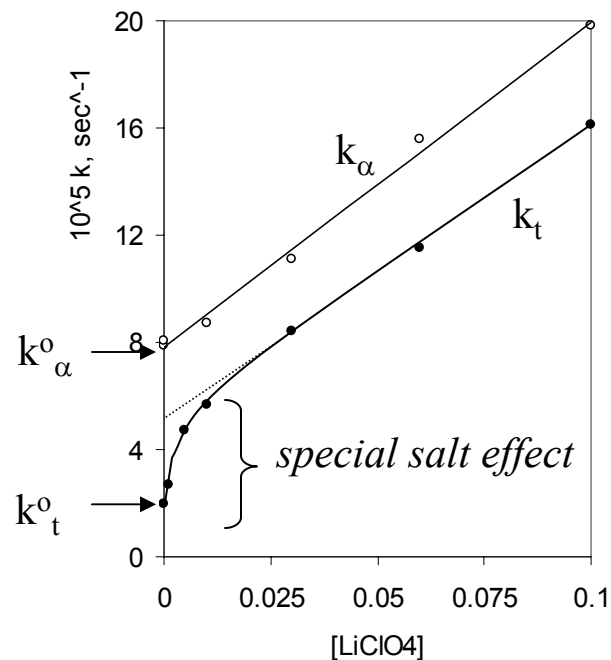


k_t : rate constant of R-OAc formation

k_t^0 : rate constant of R-OAc formation at $[\text{LiClO}_4] = 0$

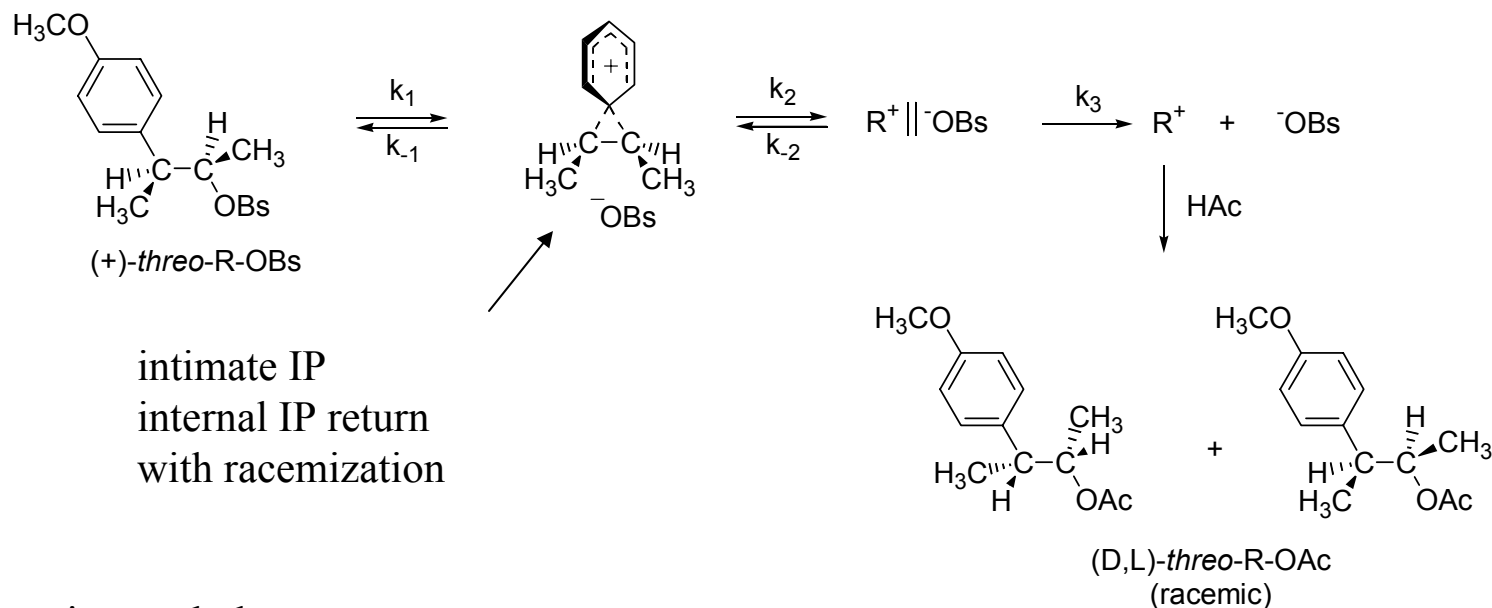
k_α : rate constant of loss of optical activity of reaction mixture

k_α^0 : rate constant of loss of optical activity of reaction mixture at $[\text{LiClO}_4] = 0$



13. Analysis of Unusual *Special Salt Effect* in Solvolysis of *threo*-3-*p*-Anisyl-2-butyl Brosylate (see slight # 7)

Winstein proposed the following mechanism 1:

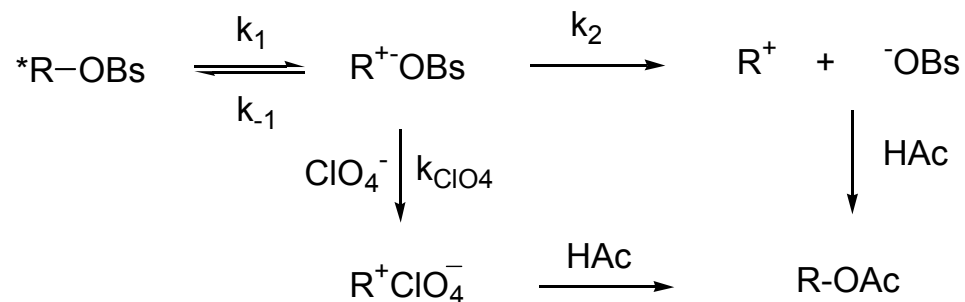


Winstein concludes:

1. $k_\alpha = k_1$: if $\text{R}^*\text{-OBs}$ dissociates, R^+OBs^- will lead to a racemic product no matter if it returns back to R-OBs (internal return) or if it reacts further to R-OAc .
2. A simple mechanism in which $\text{R}^*\text{-OBs}$ dissociates directly to fully dissociated ions (mechanism 2) can be excluded, because then $k_\alpha = k_t$ and normal salt effect should be observed.



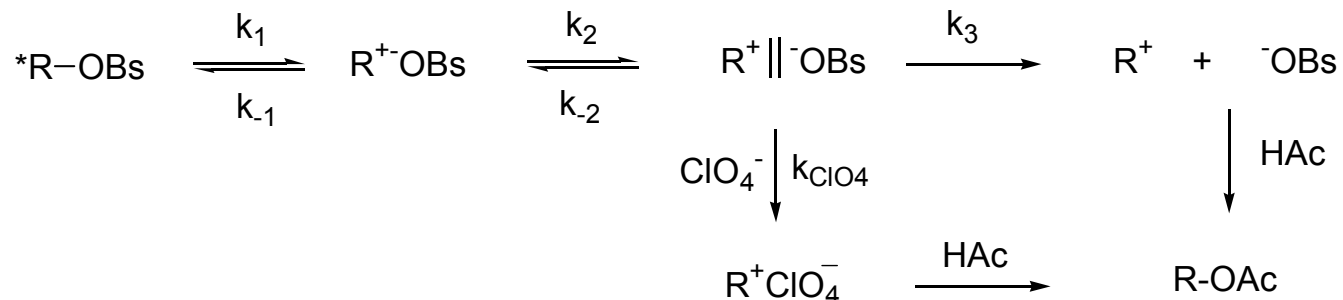
3. If only one ion-pair would precede the fully dissociated ions (mechanism 3), a *special salt effect* is expected.



The ClO_4^- would not only increase ionization of $R^+{}^-OBs$ (k_1) due to the increased dielectric constant of the medium, but it would also intercept the intimate ion pair $R^+{}^-OBs$ leading to $R^+ClO_4^-$, which will not react, but lead to $R-OAc$. Thus, there is a strong increase in the rate k_t at low $[\text{LiClO}_4]$. At higher concentration, all $R^+{}^-OBs$ would be intercepted prior to internal return and the salt effect will go over into a *normal salt effect*.

However, if mechanism 3 would be true, k_t should slowly approach k_α and $k_t = k_\alpha$ at high $[\text{LiClO}_4]$. The fact that k_t is always $< k_\alpha$ rules out mechanism 3.

4. Winstein explains unusual special salt effect with mechanism 1 and proposes that



ClO_4^- only intercepts the solvent separated ion-pair and prevents external ion-pair return at high concentration. However, it does not intercept intimate ion-pair and can't prevent internal ion-pair return.

5. Winstein supports his conclusion further through *induced common ion effect*:

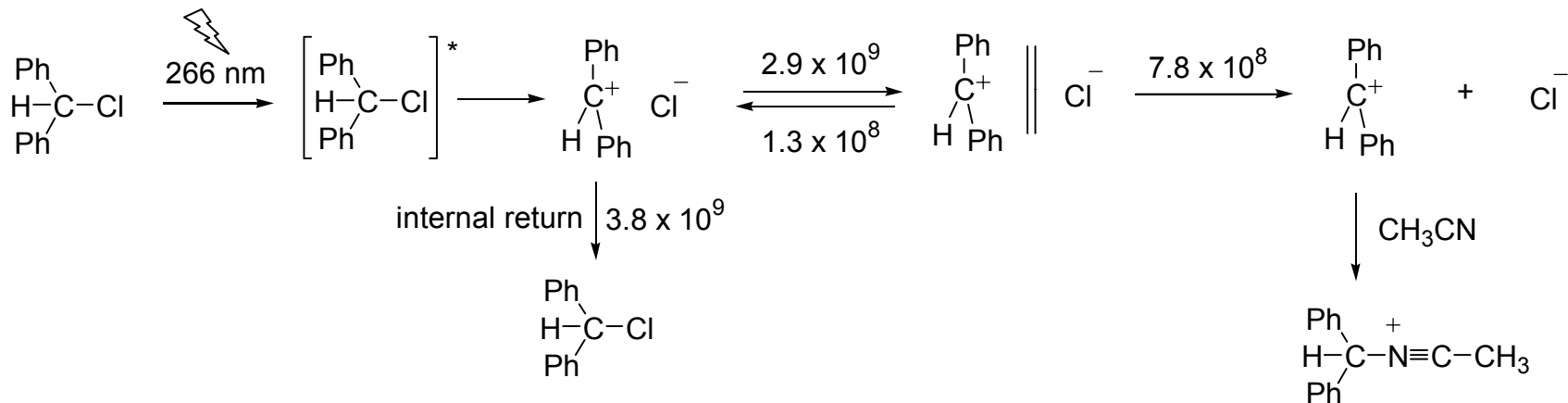
If BsO^- and ClO_4^- are added together, BsO^- competes with ClO_4^- and counteracts special salt effect.

Interpretation:

1. Assumption: internal return is with complete scrambling of ^{18}O label. Thus, k_{ex} is a measure of whether any ion pair returns back to STM.
2. Racemization through internal return or external return requires rotation of R^+ within lifetime of contact ion pair and solvent separated ion pair, respectively
3. Results are consistent with Winstein Scheme and support that added azide intercepts solvent separated ion pair, but not contact ion pair. If it were intercepting the latter, no scrambling of ^{18}O in STM would be observed in presence of azide.
4. The absence of racemization of STM in the presence of azide supports that
 - (a) internal return from contact ion pair is stereospecific (retention)
 - (b) external return from solvent separated ion pair is with partial or complete racemization.
 - (c) no rotation of R^+ within lifetime of contact ion pair.

15. Spectroscopic Observation of Winstein Scheme

(K. S. Peters & B. Li, *J. Phys. Chem.* **1994**, *98*, 401-403)



Laser flash photolysis of benzhydryl chloride at 266 nm produced Ph_2HC^+ , which absorbs at 440 nm (yellow-orange light). Decay of R^+ back to RCl and solvent trapping product was followed spectroscopically on the picosecond time scale ($1 \text{ ps} = 10^{-12} \text{ s}$). Data analysis with simplified solvolysis scheme (left) gives inferior fit. Data analysis with Winstein Scheme (right) gives excellent fit and rate constants k_{1-4} as shown above

