





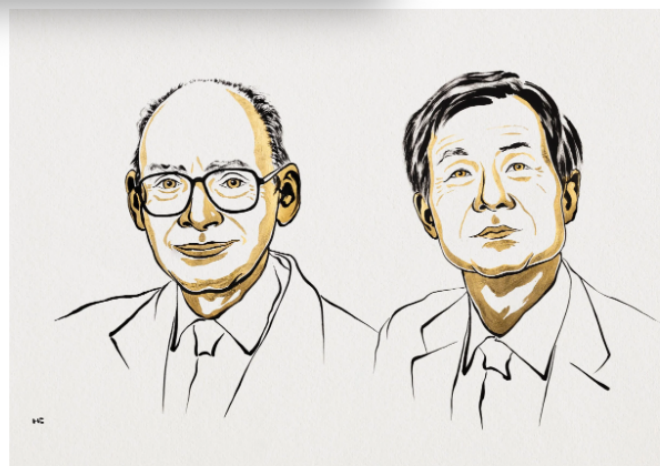
Hey, it is Chemistry  
Nobel Prize Day!

## The 2026 chemistry laureates

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry 2026 to [Henri B. Kagan](#) and [Kenso Soai](#) “for the discovery of non-linear effects and autocatalysis in asymmetric organic synthesis.”

Henri Kagan discovered a new way of manipulating chemical reactions, allowing a greater excess of one of the mirror images to be created than was previously assumed possible. His discovery has been revolutionary for chemists who develop reactions for the manufacture of pharmaceuticals, flavours, scents and new materials.

Kenso Soai designed the first chemical reaction in which only one of the potential mirror images was formed. Other than life itself, no one had ever achieved this feat. The *Soai reaction* is one of the most spectacular chemical experiments ever conducted.



Ill. Niklas Elmehed © Nobel Prize Outreach

## Nobel Prize in Chemistry 2026

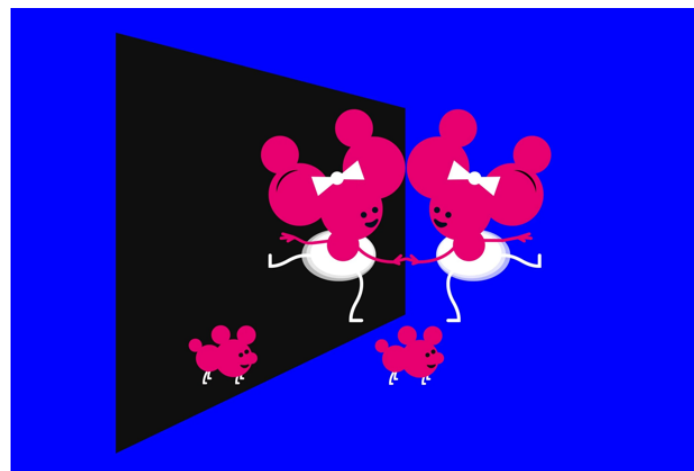
### They made chemistry choose a mirror image

Some molecules, such as amino acids, exist as two variants that are each other's mirror image. However, living organisms only contain one of these mirror images. How chemical asymmetry such as this could have emerged was long a mystery to chemists. Henri B. Kagan and Kenso Soai have been awarded the Nobel Prize in Chemistry 2026 for discovering a solution to this puzzle.

[Press release](#)

[Popular information: They solved chemistry's asymmetric mystery](#)

[Scientific background: Non-linear effects and auto catalysis in asymmetric organic catalysis](#)



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## Nonlinear Effects in Asymmetric Synthesis. Examples in Asymmetric Oxidations and Aldolization Reactions

C. Puchot,<sup>†</sup> O. Samuel,<sup>‡</sup> E. Duñach,<sup>‡</sup> S. Zhao,<sup>‡</sup> C. Agami,<sup>†</sup> and H. B. Kagan<sup>\*‡</sup>

Contribution from U.A. CNRS N°255, Laboratoire de Synthèse Asymétrique, Université Paris-Sud, 91405 Orsay, France, and U.A. CNRS N°408, Laboratoire de Chimie Organique, Université Paris VI, 75005 Paris, France. Received August 1, 1985

**Abstract:** It has been shown in three experiments that there is a strong departure from the linear relationship usually assumed between the enantiomeric excess of a chiral auxiliary and the extent of the asymmetric synthesis. This gives useful information on the reaction mechanisms. Asymmetric oxidation of methyl *p*-tolyl sulfide or asymmetric epoxidation of geraniol in the presence of various chiral titanium complexes, as well as the proline-catalyzed Hajos-Parrish reaction, is investigated in detail.

Horeau and Guetté<sup>1</sup> discussed the importance of diastereomeric interactions of a mixture of enantiomers in the liquid phase. These interactions are responsible for some *unusual physical properties*

of mixtures of enantiomers such as the nonequivalence of the enantiomeric excess and the optical purity<sup>2</sup> or the different NMR spectra for a racemic mixture or a pure enantiomer.<sup>3-6</sup> The

<sup>\*</sup> Université Paris VI.

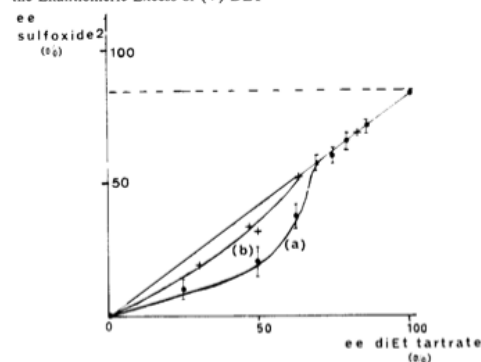
<sup>‡</sup> Université Paris-Sud.

(1) Horeau, A.; Guetté, J. P. *Tetrahedron* 1974, 30, 1923-1931.  
(2) Horeau, A. *Tetrahedron Lett.* 1969, 3121-3124.

0002-7863/86/1508-2353\$01.50/0 © 1986 American Chemical Society

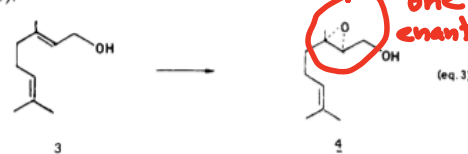
### Nonlinear Effects in Asymmetric Synthesis

**Scheme II.** Nonlinear Effect in the Asymmetric Oxidation of Sulfide 1 (Equation 2) and Enantiomeric Excess of (*R*)-2 as a Function of the Enantiomeric Excess of (+)-DET<sup>a</sup>



<sup>a</sup> (a) Stoichiometric conditions:  $\text{Ti}(\text{O}-i\text{-Pr})_4/\text{DET}/\text{H}_2\text{O}/i\text{-BuOOH}/1, 1:2:1:0.5$  or  $1:1:1:1.1$ . (b) Catalytic conditions:  $\text{Ti}(\text{O}-i\text{-Pr})_4/\text{DET}/\text{H}_2\text{O}/i\text{-BuOOH}/1, 0.5:1:0.5:1:1$ .

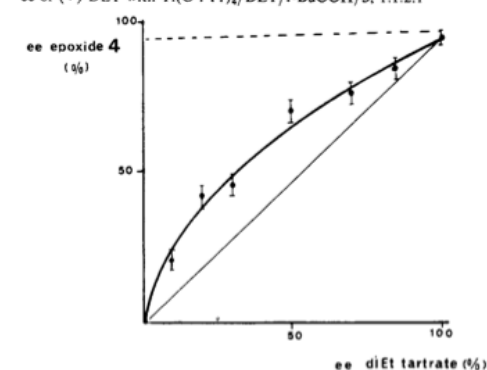
was also investigated in the specific case of (*E*)-geraniol (3) (eq 3).



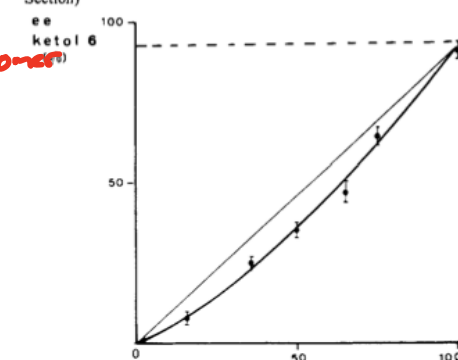
Finally, we studied a catalytic system dealing with an asymmetric Robinson annulation. The Hajos-Parrish reaction is a useful asymmetric synthesis which allows, for example, to transform the triketone 5 into *cis*-ketol 6 (ee 92%) in DMF under the influence of a catalytic amount of pure (*S*)-proline<sup>24,25</sup> (eq 4). Two of us are currently investigating extensively the mechanism of this reaction.<sup>26,27</sup>

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**Scheme III.** Nonlinear Effect in the Epoxidation of Geraniol 3 (Equation 3) and Enantiomeric Excess of (-)-4 as a Function of the ee of (+)-DET with  $\text{Ti}(\text{O}-i\text{-Pr})_4/\text{DET}/i\text{-BuOOH}/3, 1:1:2:1$



**Scheme IV.** Nonlinear Effect in the Hajos-Parrish Reaction (Equation 4) and Enantiomeric Excess of Ketol 6 as a Function of the ee of (*S*)-Proline under Catalytic Conditions (See Experimental Section)



# Asymmetric Self-catalytic Reaction. Self-production of Chiral 1-(3-Pyridyl)alkanols as Chiral Self-catalysts in the Enantioselective Addition of Dialkylzinc Reagents to Pyridine-3-carbaldehyde

Kenso Soai,\* Seiji Niwa, and Hiroshi Hori

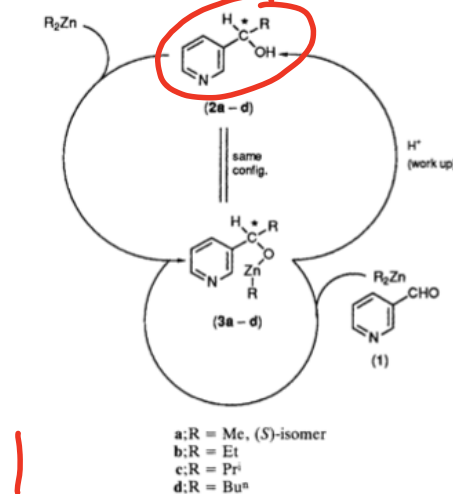
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Shinjuku, Tokyo, 162 Japan

Optically active 1-(3-pyridyl)alkanols, chiral self-catalysts, produced themselves of the same configuration in the enantioselective addition of dialkylzinc reagents to pyridine-3-carbaldehyde.

Increasing interest has been centred on catalytic carbon-carbon bond forming reactions.<sup>1</sup> However in nearly all cases reported, the structures of the chiral catalysts and the products are *different*. If the structures of the product and the chiral catalysts were the *same* (chiral self-catalyst), the reaction

system would become an interesting real self-production of chiral molecules. Although the implication of asymmetric self-catalysis has been described,<sup>2</sup> no apparent example is known.<sup>3</sup>

We are continuing to study the enantioselective synthesis of



Scheme 1

amino-alcohols by asymmetric reduction of ketones<sup>4</sup> and by asymmetric alkylation of aldehydes,<sup>5</sup> and we now report an example of an asymmetric self-catalytic reaction in which a chiral molecule plays the role of a chiral catalyst to afford the same chiral molecule of the same configuration. When pyridine-3-carbaldehyde (**1**) (1 mmol) was treated with di-isopropylzinc (2 mmol) using (–)-2-methyl-1-(3-pyridyl)propan-1-ol (**2c**) (0.030 g, 20 mol%), [ $\alpha$ ]<sub>D</sub><sup>22</sup> –35.7° (c 2.3, MeOH) (86% enantiomeric excess, e.e.)<sup>†</sup> as a chiral catalyst, (–)-(**2c**) (0.132 g, 47% e.e., determined by HPLC using a chiral column) was obtained.<sup>‡</sup> This result shows that (–)-(**2c**)

<sup>†</sup> Prepared from the reaction of pyridine-3-carbaldehyde and diisopropylzinc using (1*S*,2*R*)-(–)-*N,N*-dibutylnorephedrine<sup>5,6</sup> as a chiral catalyst.

<sup>‡</sup>  $\text{Pr}_2\text{Zn}$  (2 ml of 1 M hexane solution) was added to a toluene solution (2 ml) of (–)-(**2c**) (0.2 mmol) at room temperature. After 20 min, (**1**) (1.0 mmol) was added, then the mixture was stirred at room temperature for 2 h. The mixture was cooled to 0 °C, and quenched by the addition of HCl (1 M; 5 ml). The mixture was adjusted to pH 8–9 by the addition of satd. aq.  $\text{NaHCO}_3$ , and the precipitate was filtered off. The filtrate was extracted with  $\text{AcOEt}$  (4 × 20 ml), dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated under reduced pressure. The residue was purified by TLC (silica gel, eluant  $\text{AcOEt-MeOH}$ , 20:1), followed by bulb-to-bulb distillation (140 °C at 2 mmHg). HPLC analysis was performed with Daicel Chiralcel OD, eluant 10% propan-2-ol in hexane, flow rate 0.2 ml/min, UV detector (254 nm), retention time 62.7 min for major isomer (–)-(**2c**), 70.3 min for minor isomer (+)-(**2c**).

acts as a chiral self-catalyst to produce itself with retention of configuration [(–)-(**2c**), 0.102 g, 67% yield, 35% e.e.].<sup>§</sup> In a similar manner, (–)-1-(3-pyridyl)propan-1-ol (**2b**) (20 mol%, 56% e.e.) produced itself [(–)-(**2b**) (66%, 14% e.e.)] in the enantioselective addition of  $\text{Et}_2\text{Zn}$  to (**1**). Asymmetric self-catalytic reaction was also observed in methylation [(*S*)-(–)-(**2a**) of 42% e.e. afforded (*S*)-(–)-(**2a**) of 7% e.e.] and in butylation [(–)-(**2d**) of 47% e.e. afforded (–)-(**2d**) of 6% e.e.].

The mechanism of this reaction may be as follows (Scheme 1). Chiral compounds (**2a–d**) are considered to form the chiral zinc monoalkoxides (**3a–d**), which catalyse the enantioselective addition of  $\text{R}_2\text{Zn}$  to (**1**) and the amount of (**3a–d**) increases. The configuration of the asymmetric carbon atom bonded to the hydroxy group in the chiral ligand is one factor which determines the sense of the asymmetric induction.<sup>7</sup> Acidic hydrolysis of (**3a–d**) during work-up afforded increased amounts of chiral (**2a–d**).<sup>8</sup>

Received, 12th March 1990; Com. 001091J

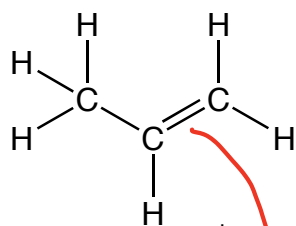
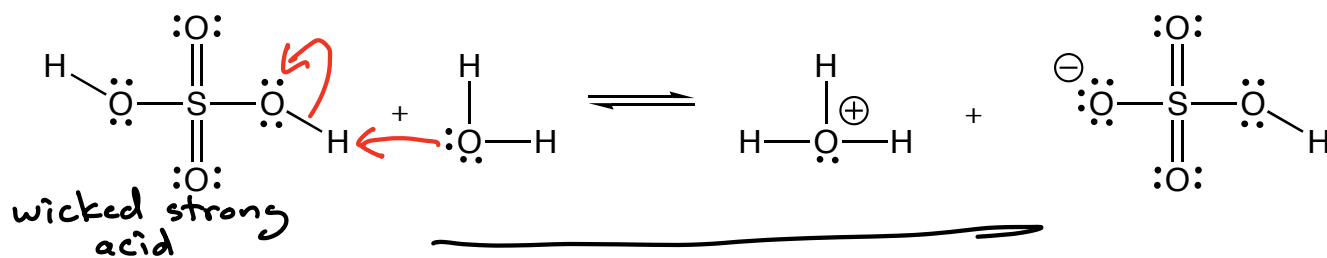
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- The metal alkoxide of an aminoalcohol catalyses the addition of  $\text{Et}_2\text{Zn}$  to benzaldehyde: see T. Mukaiyama, K. Soai, T. Sato, H. Shimizu, and K. Suzuki, *J. Am. Chem. Soc.*, 1979, **101**, 1455. For the non-self-catalytic asymmetric induction, see refs. 6 and 7; P. A. Chaloner and S. A. R. Perera, *Tetrahedron Lett.*, 1987, **28**, 6163; K. Soai and M. Watanabe, *J. Chem. Soc., Chem. Commun.*, 1990, 43; K. Soai, M. Watanabe, and M. Koyano, *ibid.*, 1989, 534, and references cited therein.

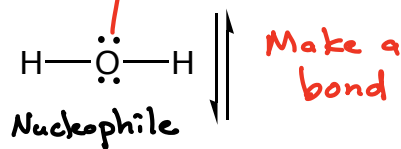
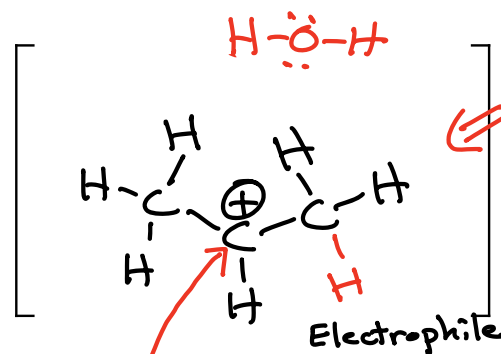
<sup>§</sup> The same (–)-(**2c**) (86% e.e.; 20 mol%) catalyses the enantioselective addition of  $\text{Et}_2\text{Zn}$  to benzaldehyde in hexane at room temperature to afford (*S*)-(–)-1-phenylpropanol of 16% e.e. in 87% yield.



## Acid-catalyzed Hydration of an Alkene

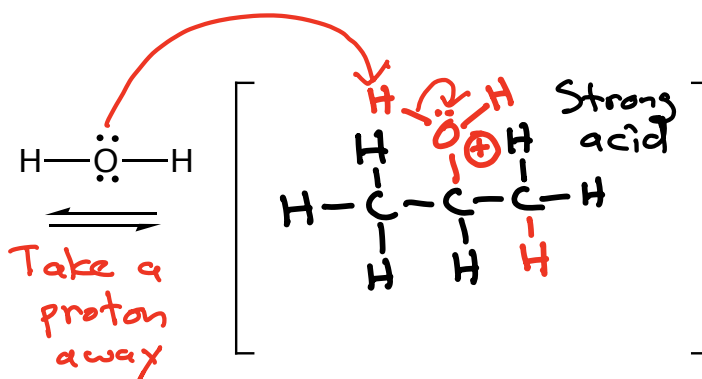
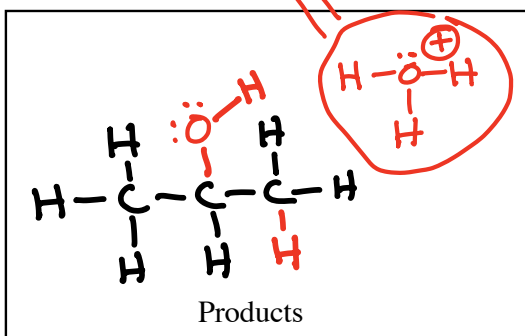


Add a proton



Catalytic in Acid!  
 $\Rightarrow$  The  $[\text{H}_3\text{O}^+]$  does not change during the reaction

strong acid

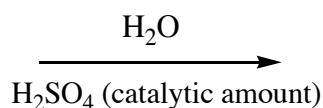
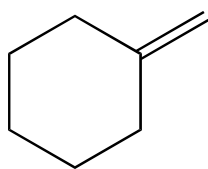


Summary: Proton adds to make a carbocation intermediate, water attacks to make a new bond, take a proton away to make the product alcohol. Catalytic in  $\text{H}_3\text{O}^+$

Regiochemistry: Markovnikov's Rule

Stereochemistry: Mixed (time capsule)

Example:

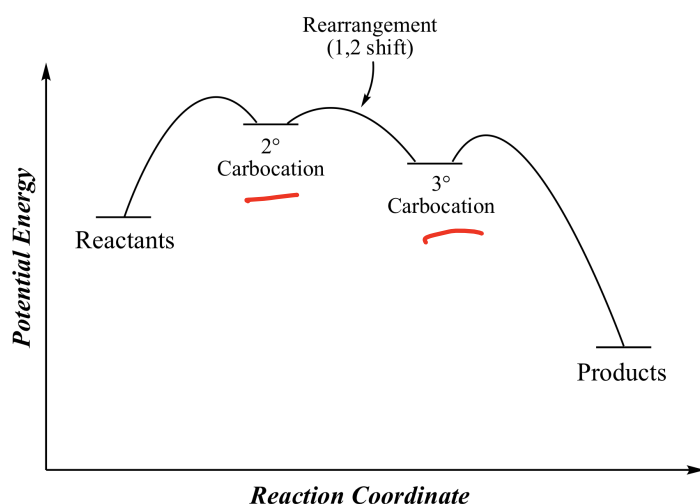


(Not chiral)

-OH on more substituted C atom  $\Rightarrow$  Markovnikov's Rule



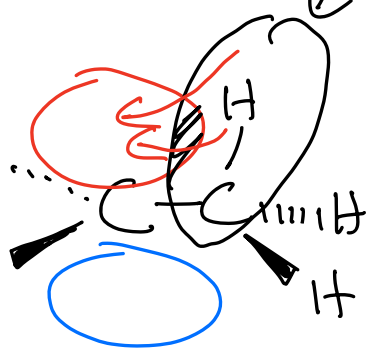
Carbocation intermediates can sometimes rearrange (Called 1,2 Shift) If a carbocation intermediate of equal or greater stability can be produced by shifting an adjacent H atom (or rarely an alkyl group), **rearrangement** will compete with product formation to give a mixture of products.



**Motive** → A 3° (tertiary) carbocation is more stable than a 2° (secondary) carbocation

Opportunity  $\rightarrow$  The mechanism is really just hyperconjugation "taken to the extreme"

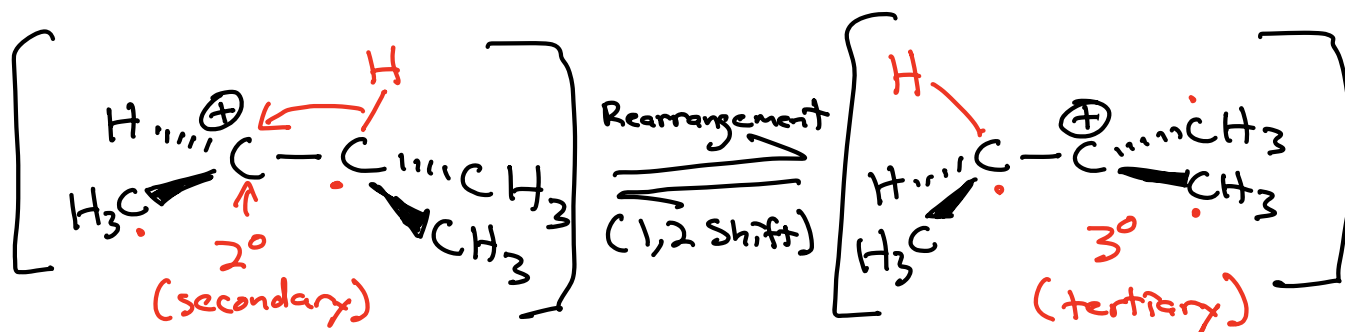
1) Hyperconjugation  $\rightarrow$  overlap of adjacent  $\sigma$  bonding electron density with the empty 2p orbital of a carbocation



delocalizes the  $\oplus$  charge

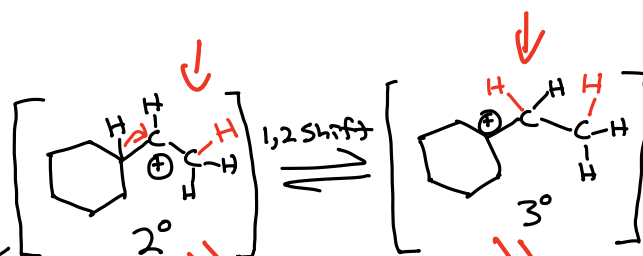
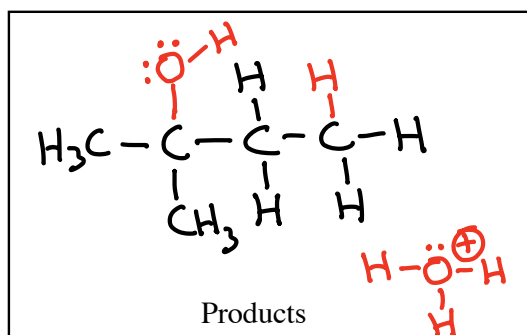
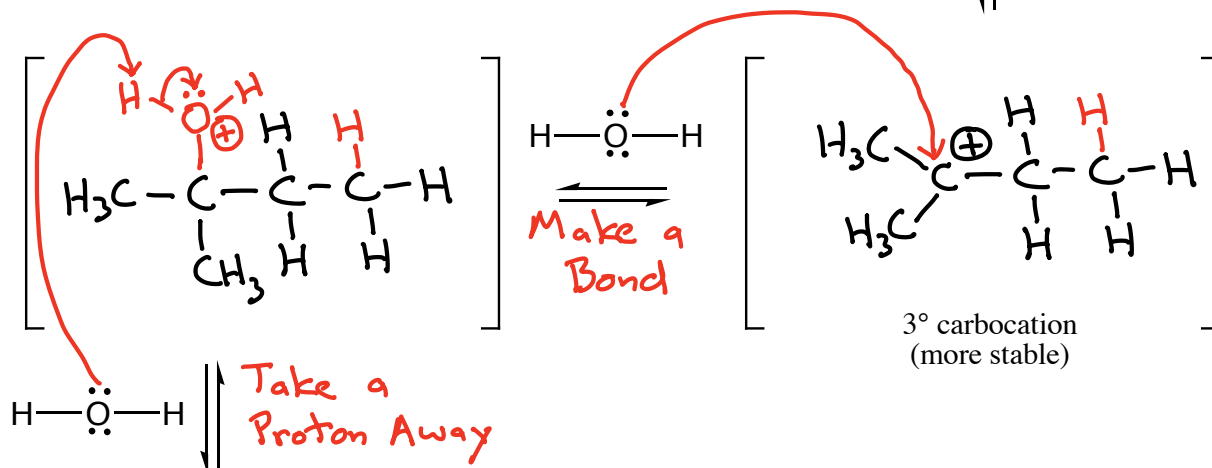
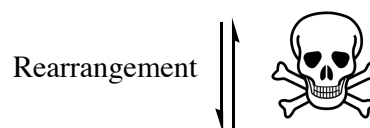
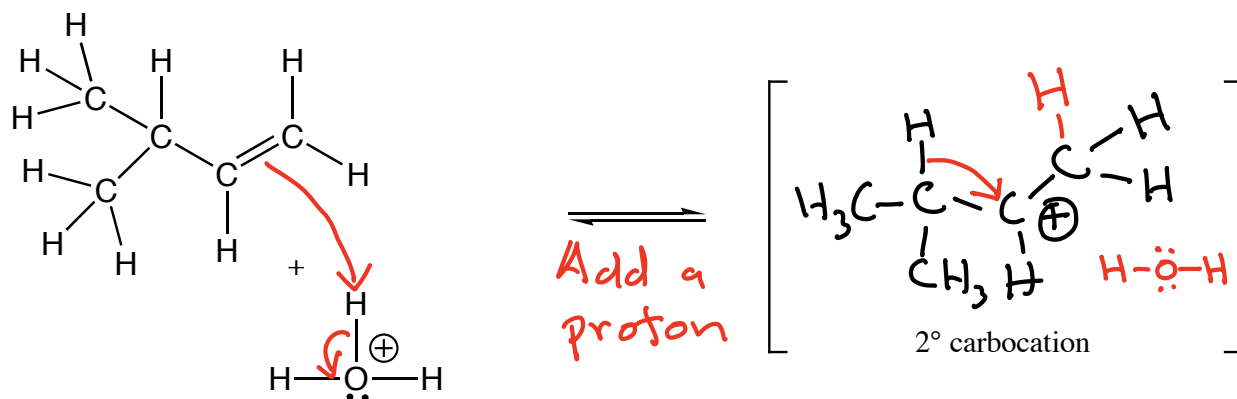
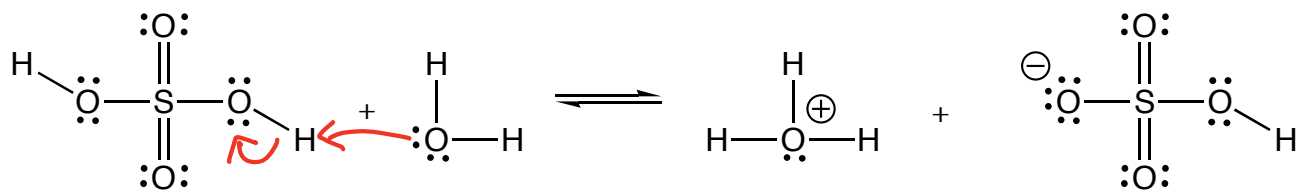
Some electron density of the C-H  $\sigma$  bond is pulled into the empty 2p orbital

(red arrows in the figure)

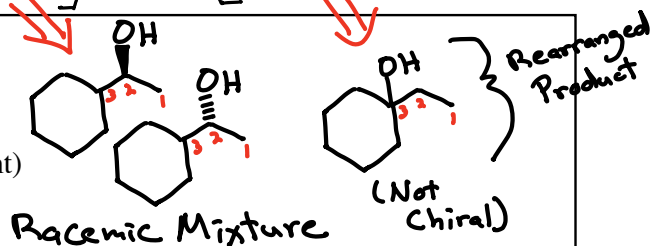
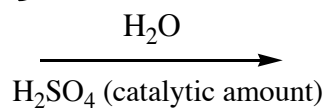
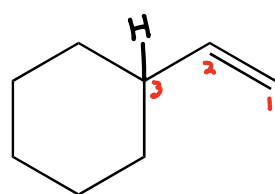


More Stable Carbocation

## Cation Rearrangement

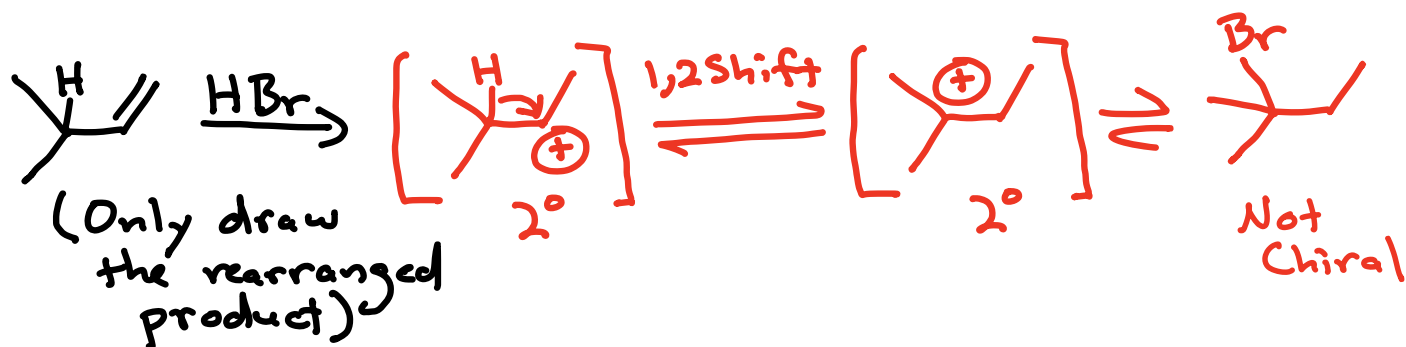
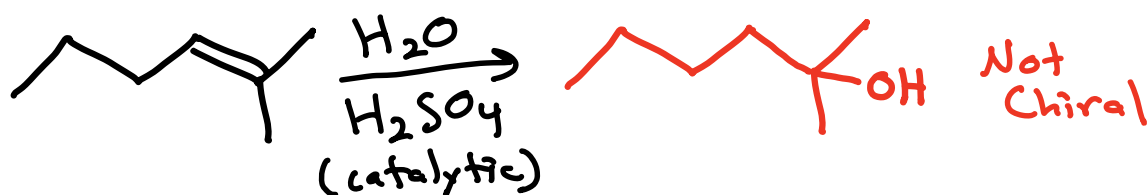
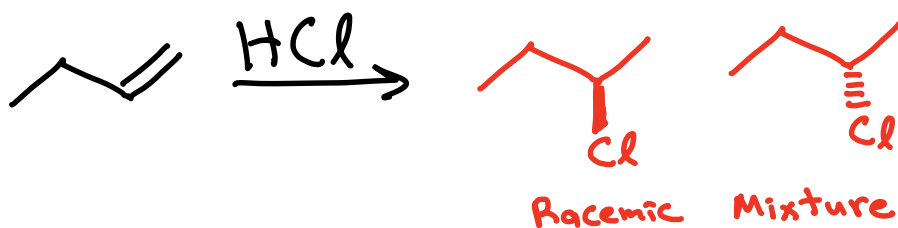
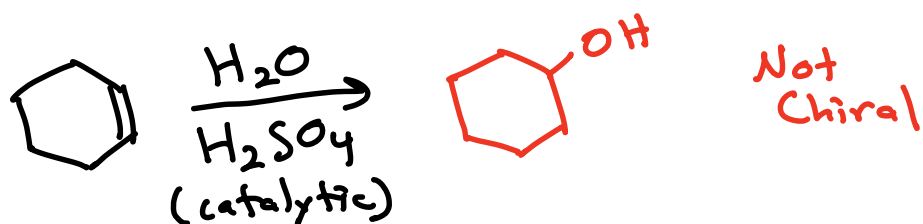


Example:

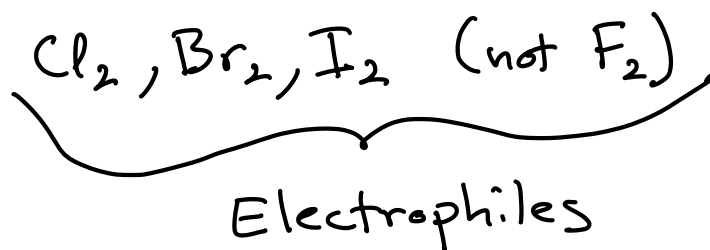
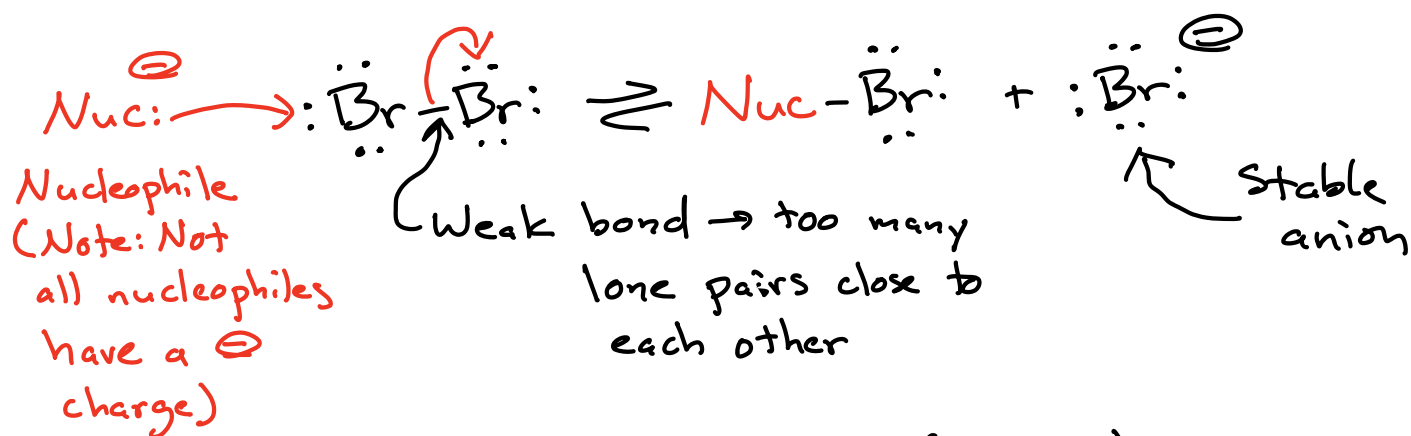




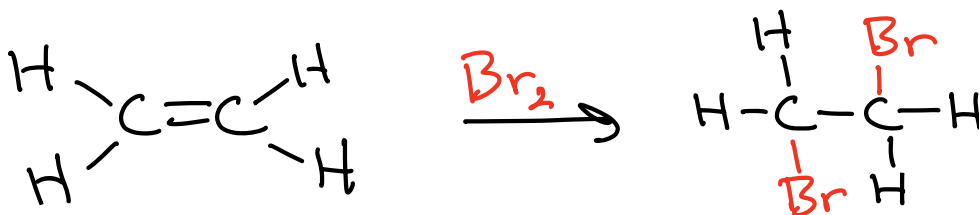
## Examples



New definition of an electrophile →  
 a relatively weak bond that can  
 break to create a stable anion

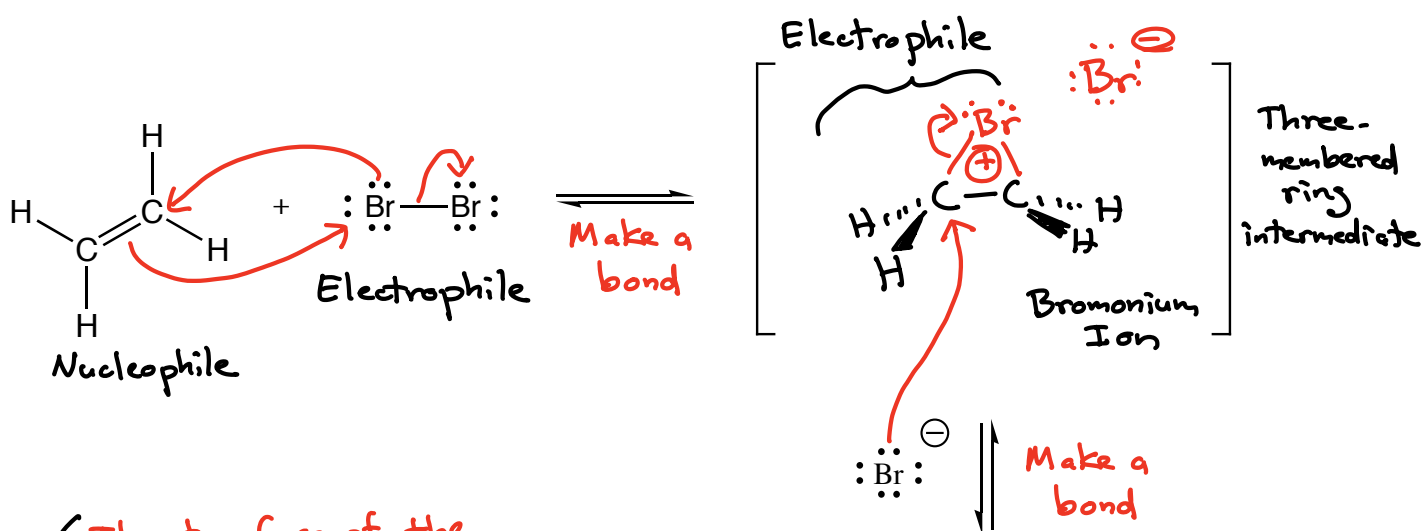


Overall New Reaction



"adjacent" → Vicinal  
 Dihalide

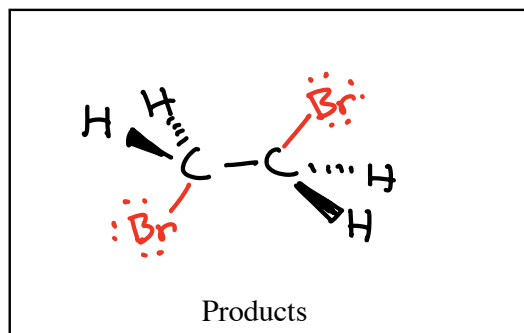
## Alkene Halogenation



Called "anti" addition stereochemistry

The top face of the intermediate is "blocked" by the Br atom, so the  $\text{Br}^-$  nucleophile must react from the opposite face

⇓  
Gives only a "trans" product—never "cis"

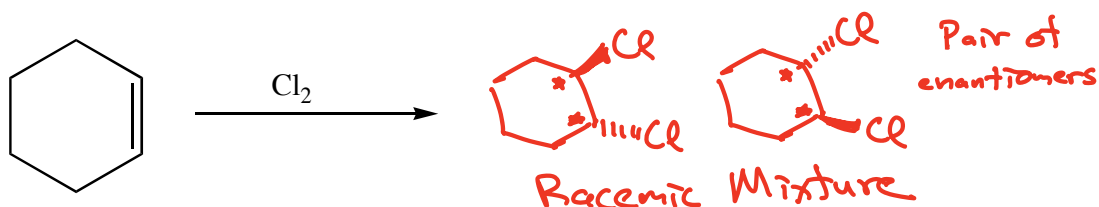


Summary: Alkenes react with  $\text{X}_2$  to give a three-membered ring intermediate, then a new bond is made by  $\text{X}^-$  reacting from behind the C-X bond of the intermediate.

Regiochemistry: Not applicable  $\rightarrow$  Br is on both atoms

Stereochemistry: Anti addition geometry  $\rightarrow$  trans products

Example:



# Alkene Reaction Stereochemistry Possibilities

Anti → groups add to opposite faces of the original double bond

Syn → groups add to the same face of the original double bond

Mixed → groups add both anti and syn in the reaction

# How to think about unsymmetrical halonium ions

