## Dr. Elaheh Mosaddegh

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## Nucleophilic substitution

## **Dr. Elaheh Mosaddegh**













$$Cl(CH_2)_4CH \xrightarrow{H_2O} \sqrt{O} + HCl$$

## 

Solvolysis Rates of ω–Chloro Alcohols

ω-Chloro alcohol	Approximate relative rate
Cl(CH <sub>2</sub> ) <sub>2</sub> OH	2000
Cl(CH <sub>2</sub> ) <sub>3</sub> OH	1
Cl(CH <sub>2</sub> ) <sub>4</sub> OH	5700
Cl(CH <sub>2</sub> ) <sub>5</sub> OH	20



#### Relative Solvolysis Rates of Some ω-Methoxyalkyl *p*-Bromobenzenesulfonates in Acetic Acid

CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> OSO <sub>2</sub> Ar	1.00
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> OSO <sub>2</sub> Ar	0.28
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>3</sub> OSO <sub>2</sub> Ar	0.67
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>4</sub> OSO <sub>2</sub> Ar	657
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>5</sub> OSO <sub>2</sub> Ar	123
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>6</sub> OSO <sub>2</sub> Ar	1.16

#### **Relative Rates of Cyclization as a Function of Ring Size**

Ring size	Lactonization of ω- bromo carboxylates <sup>a</sup>	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)	Cyclization of ω- bromoalkylmalonates <sup>b</sup>
3	$8.2 \times 10^{-4}$	22.0	-2.5	
4	0.92	17.7	-5.0	0.58
5	108	15.9	-5.5	833
6	1.00	17.2	-4.1	1.00
7	$3.7 \times 10^{-3}$	17.4	-13.5	$8.7 \times 10^{-3}$
8	$3.8 \times 10^{-5}$	21.7	-9.2	$1.5 \times 10^{-4}$
9	$4.3 \times 10^{-5}$	20.3	-14.0	$1.7 \times 10^{-5}$
10	$1.3 \times 10^{-4}$	17.3	-20.7	$1.4 \times 10^{-6}$
11	$3.3 \times 10^{-4}$	16.4	-22.3	$2.9 \times 10^{-6}$
12	$4.1 \times 10^{-4}$	17.6	-18.0	$4.0 \times 10^{-4}$
13	$1.2 \times 10^{-3}$	15.3	-23.0	$7.4 \times 10^{-4}$
17				$2.9 \times 10^{-3}$
18	$2.0 \times 10^{-3}$	15.2	-21.8	
21				$4.3 \times 10^{-3}$
23	$2.3 \times 10^{-3}$	14.5	-22.3	











#### **Extent of Aryl Rearrangement in 2-Phenylethyl Tosylate Solvolysis**

	Solvent		
Substituent	80% Ethanol	Acetic acid	Formic acid
NO <sub>2</sub>	0	_	_
CF <sub>3</sub>	0	_	_
Cl	7	_	_
Н	21	38	78
CH <sub>3</sub>	63	71	94
CH <sub>3</sub> O	93	94	99





**Structure and Reactions of Carbocation Intermediates** 

**Structure and Stability of Carbocations** 

## $(CH_3)_3C-CI \longrightarrow (CH_3)_3C^+ + CI^-$

## $ROH + H^{+} \longrightarrow R^{+} + H_{2}O$



#### Values of pK<sub>R+</sub> for Some Carbocations

Carbocation	pK <sub>R</sub> +	Carbocation	pK <sub>R</sub> +
A. Triarylmethyl			
Triphenyl	-6.63	4, 4', 4"-Tri(dimethylamino)phenyl	+9.36
4, 4', 4"-Trimethyltriphenyl	-3.56	4, 4', 4"-Trichlorotriphenyl	-7.74
4-Methoxytriphenyl	-3.40	4-Nitrotriphenyl	-9.15
4, 4'-Dimethoxytriphenyl	-1.24	4, 4', 4"-Trinitrotriphenyl	-16.27
4, 4', 4"-Trimethoxytriphenyl	+0.82		
B. Diarylmethyl			
Diphenyl	-13.3	2, 2', 4, 4', 6, 6'-Hexamethyldiphenyl	-6.6
4, 4'-Dimethyldiphenyl	-10.4	4, 4'-Dichlorodiphenyl	-13.96
4, 4'-Dimethoxydiphenyl	-5.71	· · ·	
C. Other Carbocations			
Benzyl <sup>b</sup>	$\leq -20$	Triphenylcyclopropenyl <sup>e</sup>	+3.1
t-Butyl <sup>c</sup>	-15.5	2,4,6-trimethylbenzyl	-17.4
2-Phenyl-2-propylb	-12.3	Trimethylcyclopropenyl <sup>f</sup>	+7.8
Tropylium (Cycloheptatrienyl)	+4.7	Tricyclopropylcyclopropenyl <sup>g</sup>	+9.7
Tricyclopropylmethyld	-2.3		-



bisected conformation



perpendicular conformation



bisected conformation



perpendicular conformation



### R<sup>+</sup> + H<sup>-</sup> → R-H

 $R-H \longrightarrow R^+ + H^-$ 

 $R' + H' \longrightarrow R-H$ 

∆**G**hom

∆G<sub>H</sub>Γ

 $R^{+} + H^{-} \rightarrow R^{+} + H^{-} - F \Delta E^{\circ} [(H^{+}/H^{-}) - (R^{+}/R^{-})]$ 

### $\Delta G_{H^-} = \Delta G_{hom} - F \Delta E^{\circ} [(H^{\circ} / H^{-}) - (R^{+} / R^{\circ})]$

#### **Solution Hydride Affinity of Some Carbocations**

Carbocation	ΔH (kcal/mol)	ΔH <sub>gas</sub> (kcal/mol)
Tropylium ion	83	200
Ph <sub>3</sub> C <sup>+</sup>	96	215
Ph₂C⁺H	105	222
PhCH <sup>+</sup> <sub>2</sub>	118	238
p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sup>+</sup> <sub>2</sub>	106	227
p-NCC <sub>6</sub> H <sub>4</sub> CH <sup>+</sup> <sub>2</sub>	122	247

#### **ΔH for Ionization of Chlorides and Alcohols in SO<sub>2</sub>CIF**

	ΔH (kcal/mol)		
Reactant	X=CI	X=OH	
(CH <sub>3</sub> ) <sub>2</sub> CH–X	-15		
Ph <sub>2</sub> C(CH <sub>3</sub> )–X	-16		
(CH <sub>3</sub> ) <sub>3</sub> C–X	-25	-35	
PhC(CH <sub>3</sub> ) <sub>2</sub> –X	-30	-40	
Ph <sub>2</sub> C(CH <sub>3</sub> )–X		-37.5	
Ph <sub>3</sub> C–X		-49	
( <mark>)}₃C−X</mark>		-59	



MP2/6-31G<sup>\*\*</sup> optimized structure of t-butyl cation with three hydrogens aligned with the *p* orbital





Distribution of LUMO orbitals of isomeric 1-methylcyclohexyl cations showing dominant C–C (C) and C–H (D) hyperconjugation.



 $\theta$  = Deviation of – CH<sub>3</sub> from the plane of C(1) –C(2) –C(6) of the cyclohexane ring







bridged ethylium carbocation

1-propyl cation rearranges to2-propyl cation by hydride shift



neopentyl cation rearranges to t-pentyl cation by methyl shift



#### **Proton removal leads to alkene formation**









#### $H_3CCH^+-F \longrightarrow H_3CCH=F^+$ $H_3CCH^+-CI \longrightarrow H_3CCH=CI^+$





#### Destabilization of 2-Substituted i-Propyl Cation by EWG Substituents

Z	Solvolysis rate relative to Z = H	Destabilization HF/4-31G (kcal/mol)
CN	~ 10 <sup>-3</sup>	9.9
CF <sub>3</sub>	~ 10 <sup>-3</sup>	37.3
CH=O	_	6.1





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**10**<sup>-3</sup>

**10**<sup>-10</sup>



#### **Direct Observation of Carbocations**

#### Protonation, Ionization, and Rearrangement in Superacid

A. Alcohols in  $FSO_3H$ —SbF<sub>5</sub>—SO<sub>2</sub>

ALLER

## $1^a$ ROH $\xrightarrow{-60^\circ C}$ RO+H<sub>2</sub>

R = methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *s*-butyl, *n*-amyl, *i*-amyl, neopentyl, *n*-hexyl, neohexyl

- $2^{b}$  (CH<sub>3</sub>)<sub>2</sub>CHCH<sub>2</sub>OH  $\xrightarrow{-60^{\circ}\text{C}}$  (CH<sub>3</sub>)<sub>2</sub>CHCH<sub>2</sub>O<sup>+</sup>H<sub>2</sub>  $\xrightarrow{-30^{\circ}\text{C}}$  (CH<sub>3</sub>)<sub>3</sub>C<sup>+</sup>
- $3^{\circ}$  (CH<sub>3</sub>)<sub>3</sub>COH  $\xrightarrow{-60^{\circ}C}$  (CH<sub>3</sub>)<sub>3</sub>C<sup>+</sup>



#### D. Bicyclooctyl systems in $SbF_5 - SO_2CIF$ , -78°C



#### **Competing Reactions of Carbocations**



Reaction energy profile illustrating competition between elimination and substitution by solvent for a *tert*-cation.



## $(H_3C)_3C - C^+(CH_3)_2 \longrightarrow (H_3C)_2C^+ - C(CH_3)_3$

![](_page_40_Figure_1.jpeg)

![](_page_40_Figure_2.jpeg)

#### **Mechanisms of Rearrangement of Carbocations**

![](_page_41_Figure_0.jpeg)

![](_page_42_Figure_0.jpeg)

![](_page_42_Picture_1.jpeg)

![](_page_43_Figure_0.jpeg)

![](_page_43_Picture_1.jpeg)

![](_page_44_Figure_0.jpeg)

![](_page_45_Figure_0.jpeg)

![](_page_45_Figure_1.jpeg)

![](_page_46_Picture_0.jpeg)

![](_page_47_Figure_0.jpeg)

![](_page_47_Figure_1.jpeg)

![](_page_48_Picture_0.jpeg)

![](_page_48_Picture_1.jpeg)

![](_page_49_Figure_0.jpeg)

Energy surface for the rearrangement of the 3-methyl-2-butyl cation to the 2-methyl-2butyl cation.

![](_page_50_Figure_0.jpeg)

![](_page_51_Picture_0.jpeg)

![](_page_52_Picture_0.jpeg)

#### **Bridged (Nonclassical) Carbocations**

![](_page_52_Figure_2.jpeg)

![](_page_52_Picture_3.jpeg)

![](_page_53_Figure_0.jpeg)

![](_page_53_Figure_1.jpeg)

![](_page_54_Figure_0.jpeg)

![](_page_55_Figure_0.jpeg)

Contrasting energy profiles for stable and unstable bridged norbornyl cation. (A) Bridged ion is a transition structure for rearrangement between classical structures. (B) Bridged ion is an intermediate in rearrangement of one classical structure to the other. (C) Bridged ion is the most stable structure.

![](_page_56_Picture_0.jpeg)

![](_page_56_Picture_1.jpeg)

![](_page_56_Picture_2.jpeg)

## $\pi$ complex

corner-protonated cyclopropane

![](_page_57_Figure_0.jpeg)

Computational energy diagram (B3LYP)/6-311+G\*) for intermediates and transition states in ionization and rearrangement of protonated 2-norbornanol.

![](_page_58_Figure_0.jpeg)

![](_page_59_Picture_0.jpeg)

#### The Role Carbocations and Carbonium Ions in Petroleum Processing

#### **Octane Numbers for Some Hydrocarbons**

Heptanes	RON	Octanes	RON
n-Heptane	0.0	n-Octane	-19.0
2-Methylhexane	42.4	2-Methylheptane	21.7
3-Methylhexane	52.0	3-Methylheptane	36.8
3-Ethylpentane	65.0	4-Methylheptane	26.7
2,2-Dimethylpentane	92.8	3-Ethylhexane	33.5
2,3-Dimethylpentane	91.1	2,2-Dimethylhexane	72.5
2,4-Dimethylpentane	83.1	2,3-Dimethylhexane	71.5
3,3-Dimethylpentane	80.8	2,4-Dimethylhexane	65.2
2,2,3-Trimethylpentane	112.1	2,5-Dimethylhexane	55.5
•		3,3-Dimethylhexane	75.5
		3,4-Dimethylhexane	76.3
		2-Methyl-3-ethylpentane	87.3
		3-Methyl-3-ethylpentane	80.8
		2,2,3-Trimethylpentane	109.6
		2,2,4-Trimethylpentane	100.0
		2,3,3-Trimethylpentane	106.1
		2,3,4-Trimethylpentane	102.7

$$\begin{array}{c} H_{8}C \\ C = CH_{2} \xrightarrow{H^{+}} (CH_{8})_{3}C^{+} \\ H_{3}C \\ (CH_{3})_{3}C^{+} \cdots H_{2}C = C \xrightarrow{CH_{8}} (CH_{8})_{3}CCH_{2}C^{+}(CH_{8})_{2} \end{array}$$

$$(CH_{3})_{3}CCH_{2}CH_{1}(CH_{3})_{2} \xrightarrow{H_{2}} (CH_{3})_{3}CCH_{2}C=CH_{2} + (CH_{3})_{3}CCH=C(CH_{3})_{2} \\ CH_{3} \end{array}$$

 $(CH_3)_3CCH_2C^+(CH_3)_2 + H^-C(CH_3)_3 \longrightarrow (CH_3)_3CCH_2CH(CH_3)_2 + {}^+C(CH_3)_3$ 

$$(CH_3)_3C^{+} \cdots H_2C^{+}C^{+}CH_3 \longrightarrow (CH_3)_3CCH_2C^{+}(CH_3)_2$$

# $H \xrightarrow{CH_3C+HCH_3 + H_2}$ $CH_3CH_2CH_3 \longrightarrow CH_3CH_2 \xrightarrow{H} H \xrightarrow{H} H$ $CH_3CH_2^+ + CH_4$

#### $(CH_3)_2CH^+ + H_2C=CHCH_2CH_3 \longrightarrow (CH_3)_2CHCH_2C^+HCH_2CH_3$

## $CH_3CH=CHCH_2CH_2CH_2^+ \longrightarrow H_3C \longrightarrow H_2C^+ ($

# $\begin{array}{rcl} CH_3CH_3 &+ H^{\pm} &\longrightarrow & CH_3^{\pm} &+ CH_4 \\ CH_3CH_2CH_3 &+ H^{\pm} &\longrightarrow & CH_3CH_2^{\pm} &+ CH_4 \\ \hline & (CH_3)_3CCH_2CH_3 &+ H^{\pm} &\longrightarrow & (CH_3)C^{\pm} &+ CH_3CH_3 \end{array}$

![](_page_63_Figure_1.jpeg)

![](_page_63_Figure_2.jpeg)

## <mark>СӉСӉ<sup>+</sup> + СӉСӉ</mark>СӉСӉ — → СӉСӉСӉСӉ + Ҥ СӉ

![](_page_64_Figure_1.jpeg)

and  $CH_3CH_2^+ + CH_3CH_2CH_3 \longrightarrow CH_3CH_3 + CH_3C^+HCH_3$  $CH_3C^+HCH_3 + :C = O^+ \longrightarrow (CH_3)_2CHC = O^+$ 

 $CH_3CH_2^+ + :C = O^+ \longrightarrow CH_3CH_2C = O^+$ 

 $CH_3CH_2CH_3 + H^+ \longrightarrow CH_3CH_2^+ + CH_4$ 

![](_page_65_Figure_0.jpeg)

![](_page_65_Figure_1.jpeg)

![](_page_65_Picture_2.jpeg)

![](_page_66_Picture_0.jpeg)

![](_page_67_Figure_0.jpeg)

Representation of C(2)-C(3) and C(1)-C(2) protonation and fragmentation to an alkane and alkene.

![](_page_68_Picture_0.jpeg)