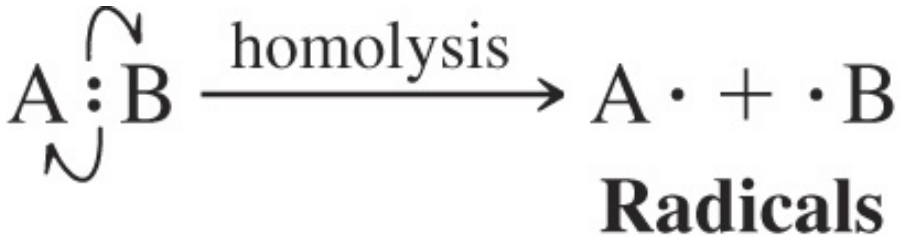
第10章 部分自由基反應 (Radical Reactions)

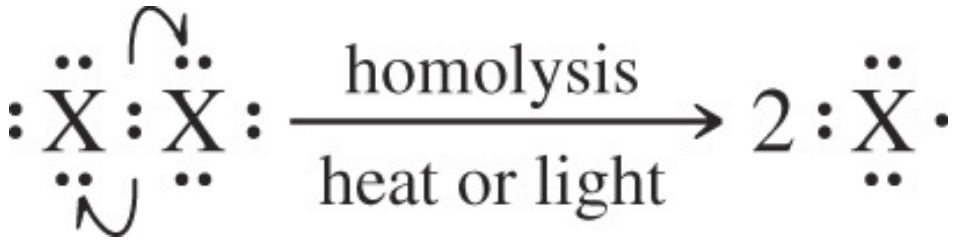
1) 自由基之介紹

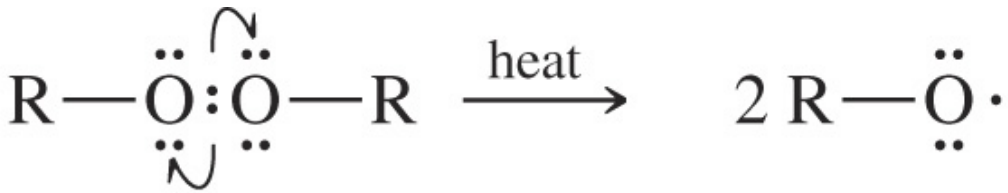
a)

化學鍵通過homolysis型的斷裂即可產生高活性的自由基：



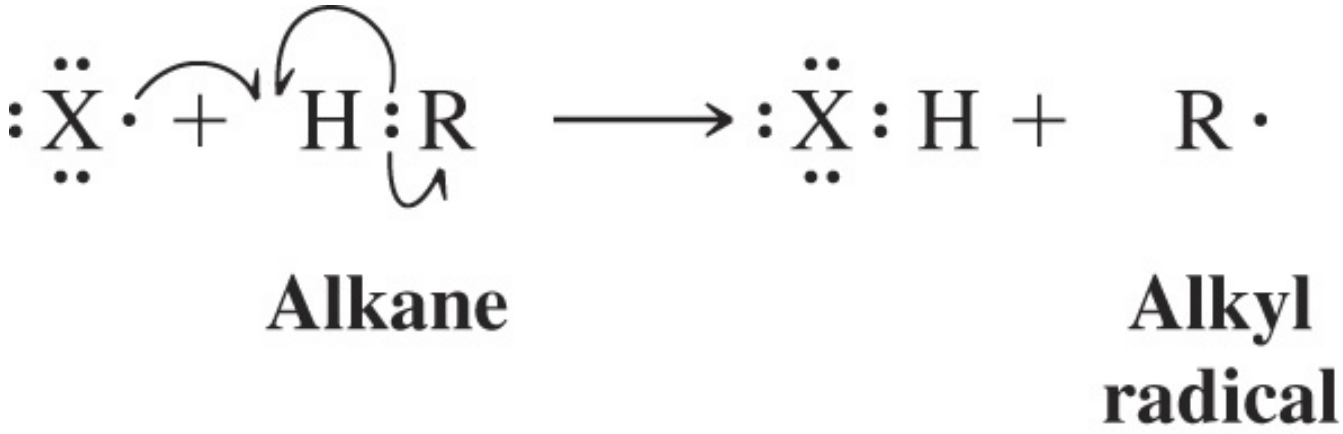
而要產生這種方式的裂解必須外加以能量:





Dialkyl peroxide **Alkoxyl radicals**

自由基有極高的反應活性， 可以產生一系列如hydrogen abstraction 的反應:



b) homolytic bond dissociation energy

自由基之間發生結合而產生更穩定的共價鍵：釋放能量（exothermic）：

$$H\cdot + H\cdot \longrightarrow H{-}H \qquad \Delta H = -436\ kJmol^{-1}$$

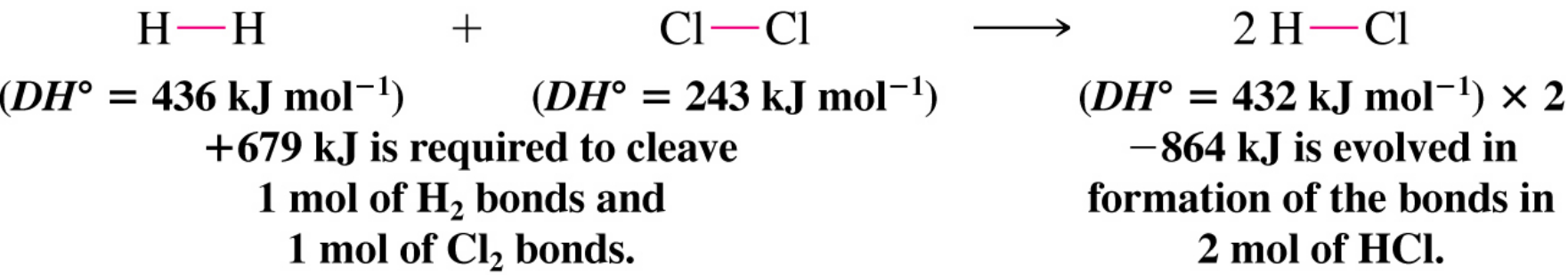
$$Cl\cdot + Cl\cdot \longrightarrow Cl{-}Cl \qquad \Delta H = -243\ kJmol^{-1}$$

反之，斷裂共價鍵而產生自由基則需要提供能量，我們把這種能量稱為homolytic bond dissociation energy (DHº)

$$H{-}H \longrightarrow H\cdot + H\cdot \qquad \Delta H^\circ = +436\ kJ\ mol^{-1}$$

$$Cl{-}Cl \longrightarrow Cl\cdot + Cl\cdot \qquad \Delta H^\circ = +243\ kJ\ mol^{-1}$$

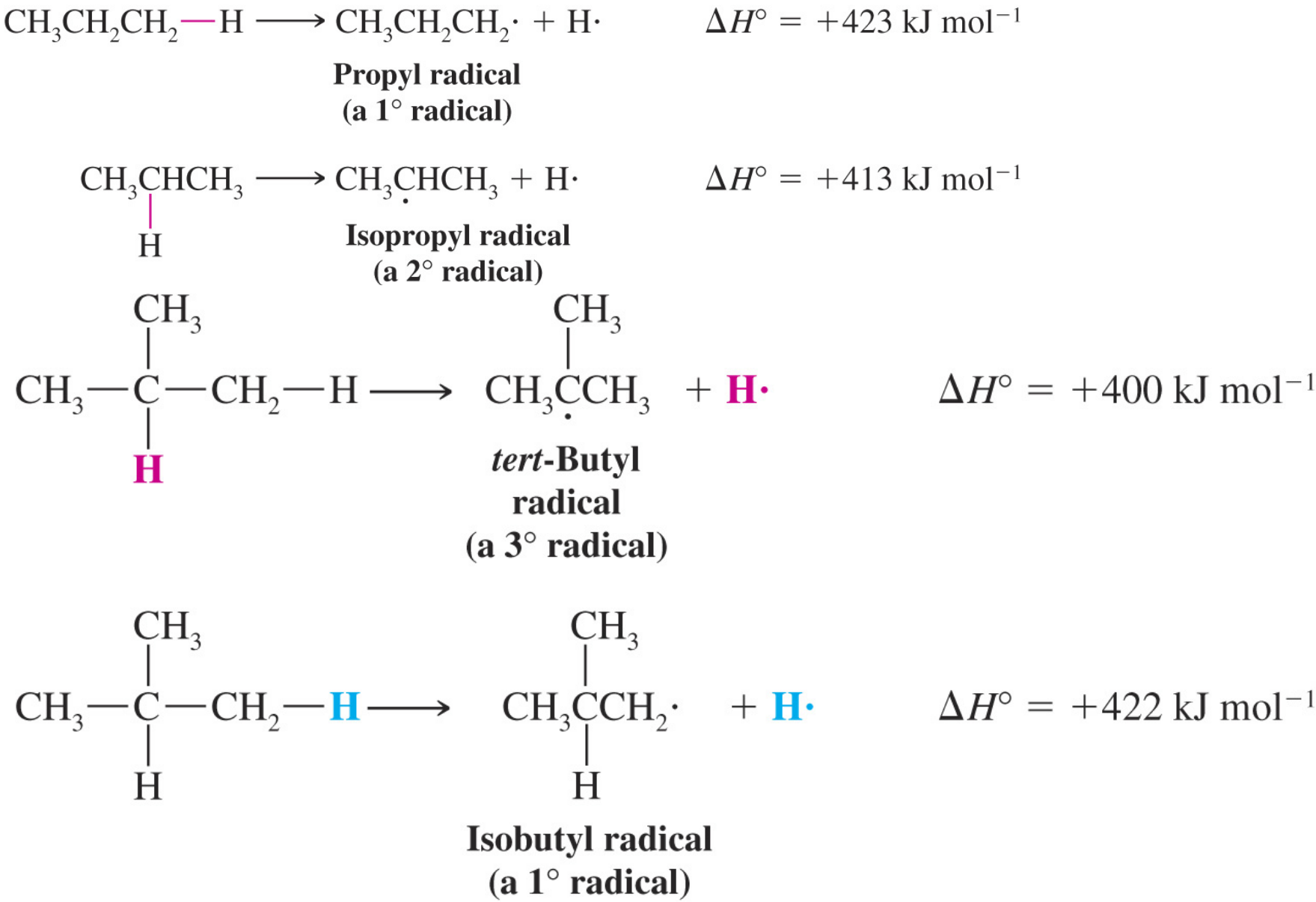
利用DH°可以計算自由基反應的整體能量變化:

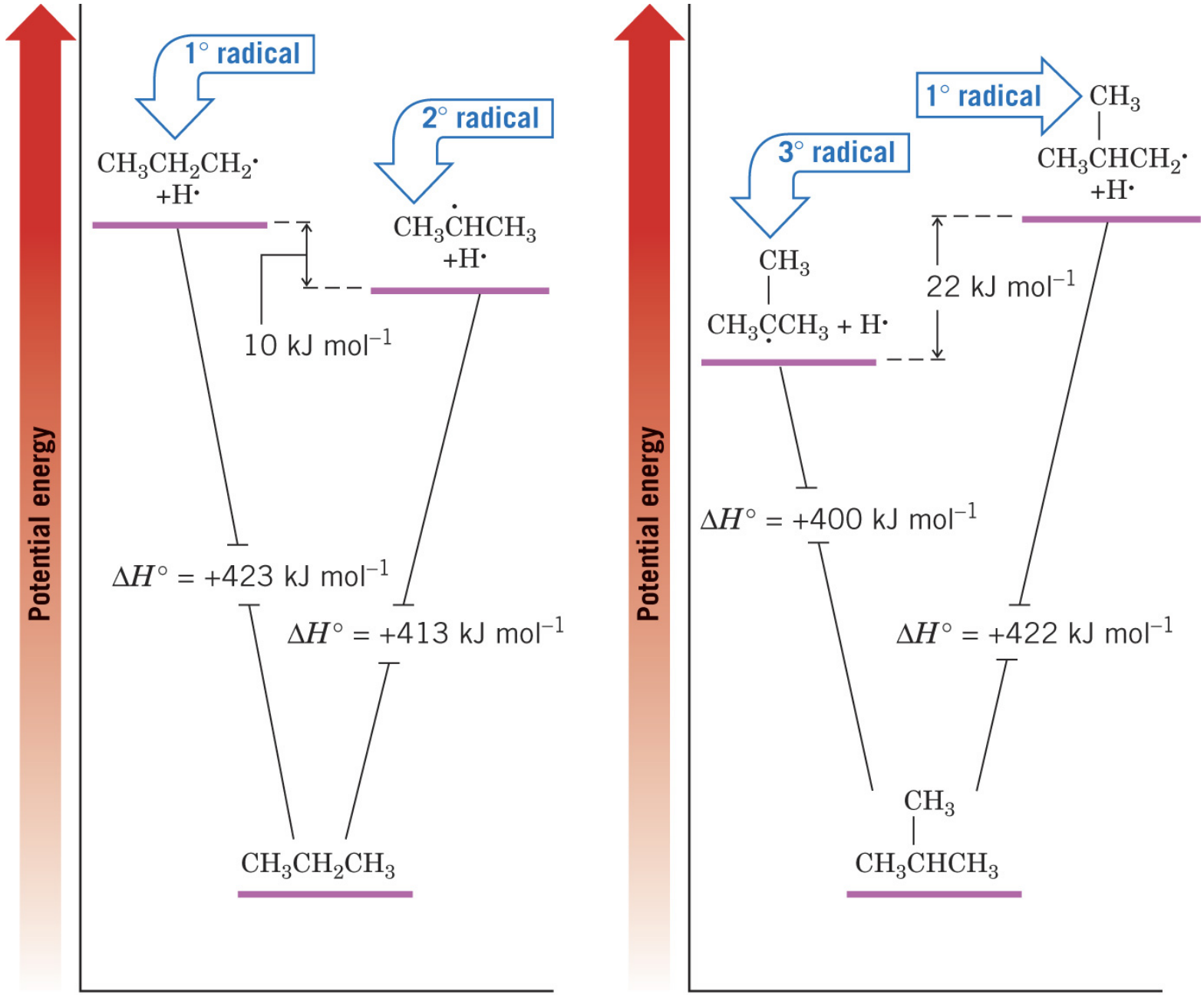


$$\Delta H^\circ = (-864\ \text{kJ} + 679\ \text{kJ}) = -185\ \text{kJ} \quad \text{for 2 mol HCl produced}$$

課堂練習(page 452)：　利用DH°可以計算下列反應的能量：

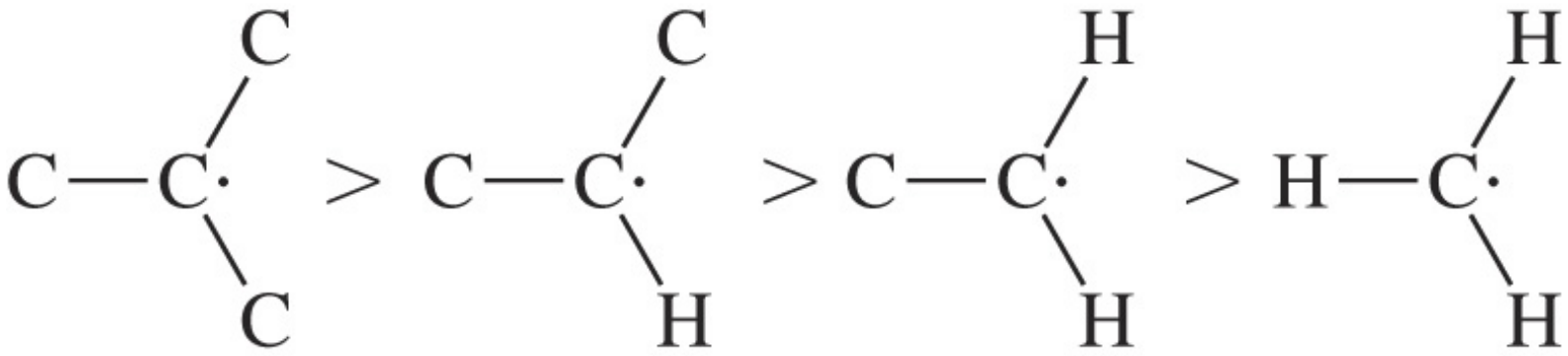
c）烷基自由基能量大小之比較

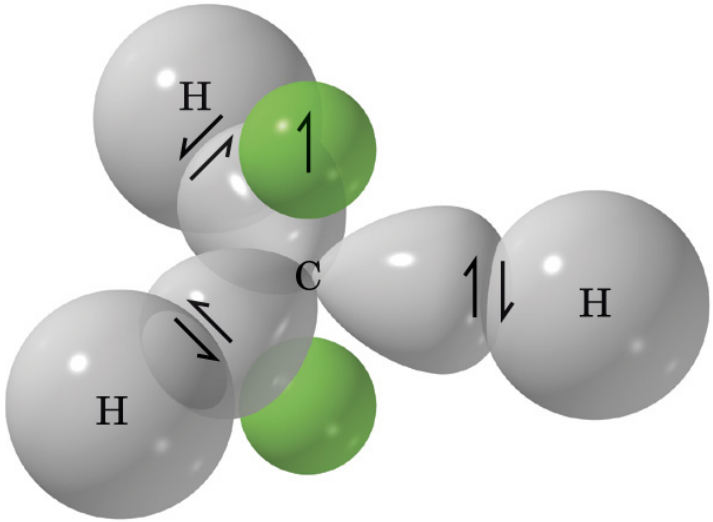



Potential energy
1° radical
$CH_3CH_2CH_2\cdot$
+H·
2° radical
$CH_3\dot{C}HCH_3$
+H·
10 kJ mol^{-1}
ΔH° = +423 kJ mol^{-1}
ΔH° = +413 kJ mol^{-1}
$CH_3CH_2CH_3$
(a)
Potential energy
1° radical
CH_3
$CH_3CHCH_2\cdot$
+H·
3° radical
CH_3
$CH_3\dot{C}CH_3$ + H·
22 kJ mol^{-1}
ΔH° = +400 kJ mol^{-1}
ΔH° = +422 kJ mol^{-1}
CH_3
CH_3CHCH_3
(b)

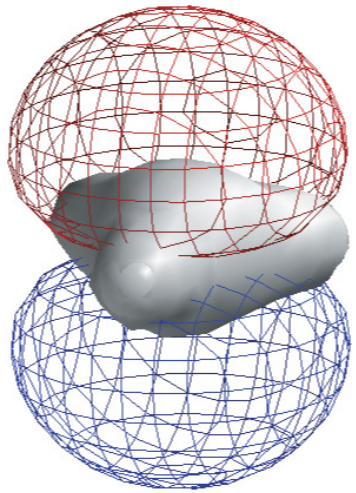
故自由基穩定性大小的順序為 （即能量由小到大的順序）：

Tertiary > Secondary > Primary > Methyl





(a)



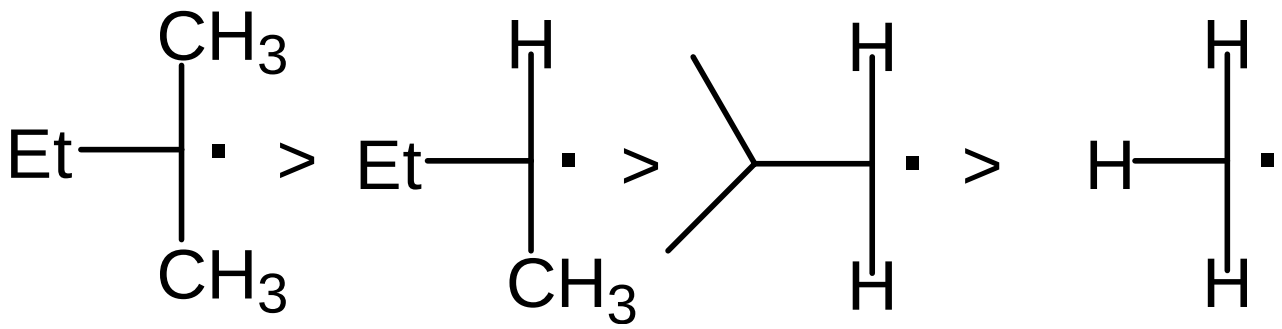
(b)

hyperconjugation

The most substituted radical is most stable

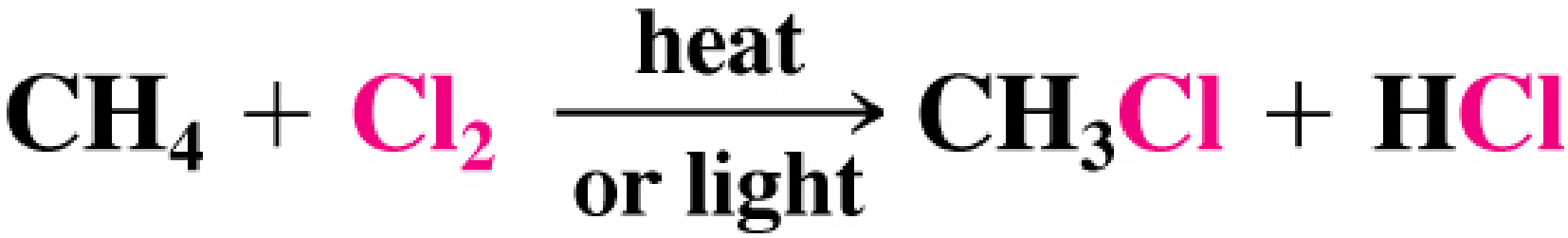
Radicals are electron deficient, as are carbocations, and are therefore also stabilized by hyperconjugation

課堂練習(page 454):比較自由基的穩定性:



2) 自由基的化學反應

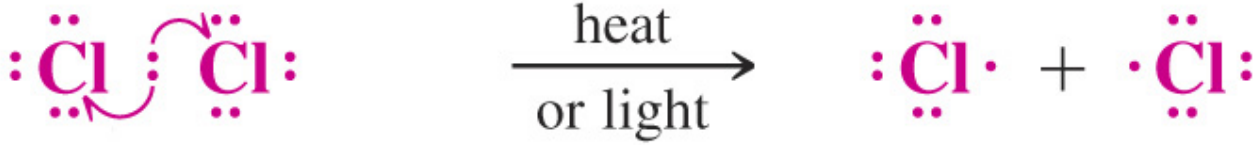
A)甲烷的氯化反應



反應機制： a)幾乎所有的自由基反應都經過以下三個階段，1) chain initiation, 2)chain propagation, 3) chain termination

chain initiation:

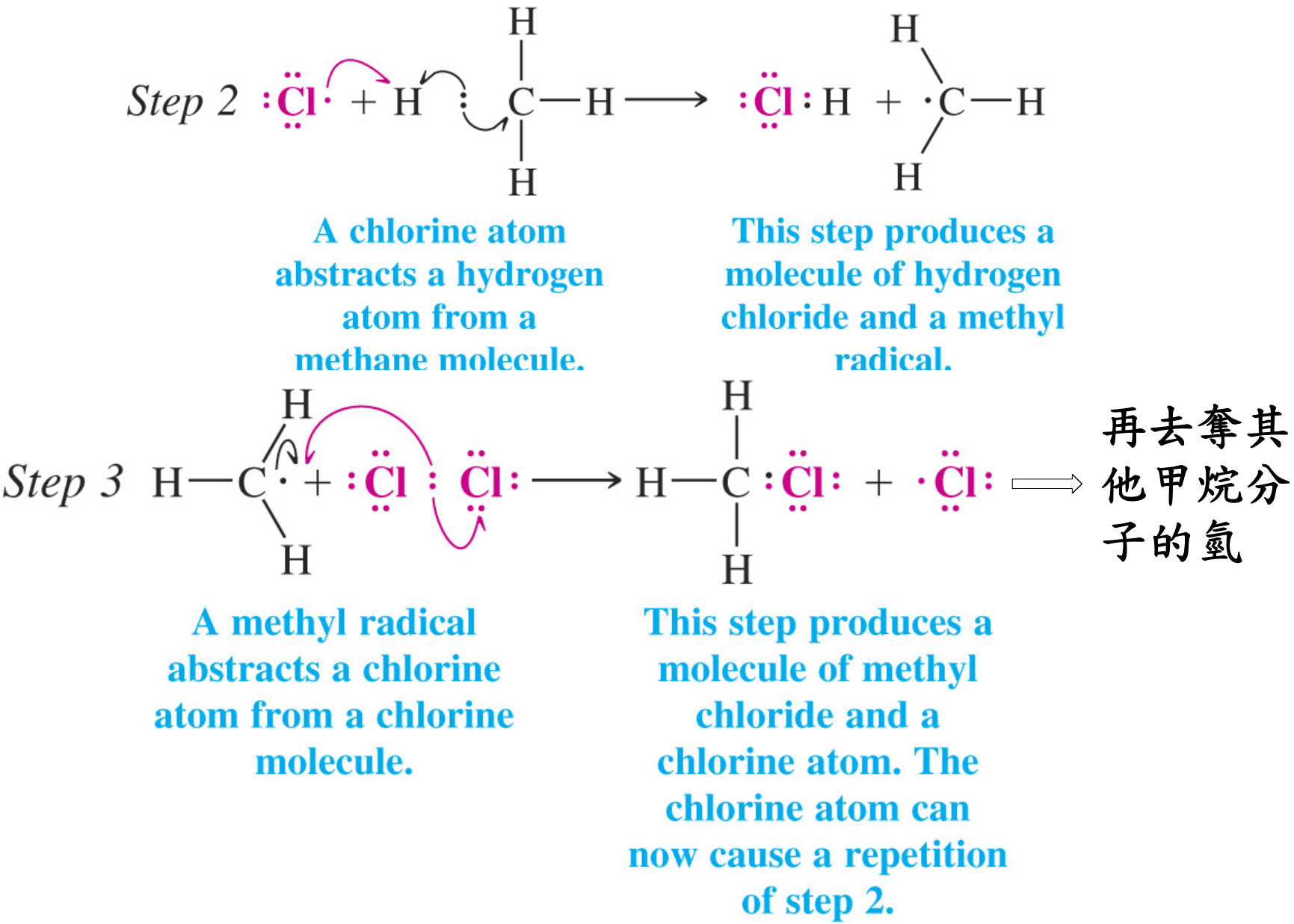
Step 1



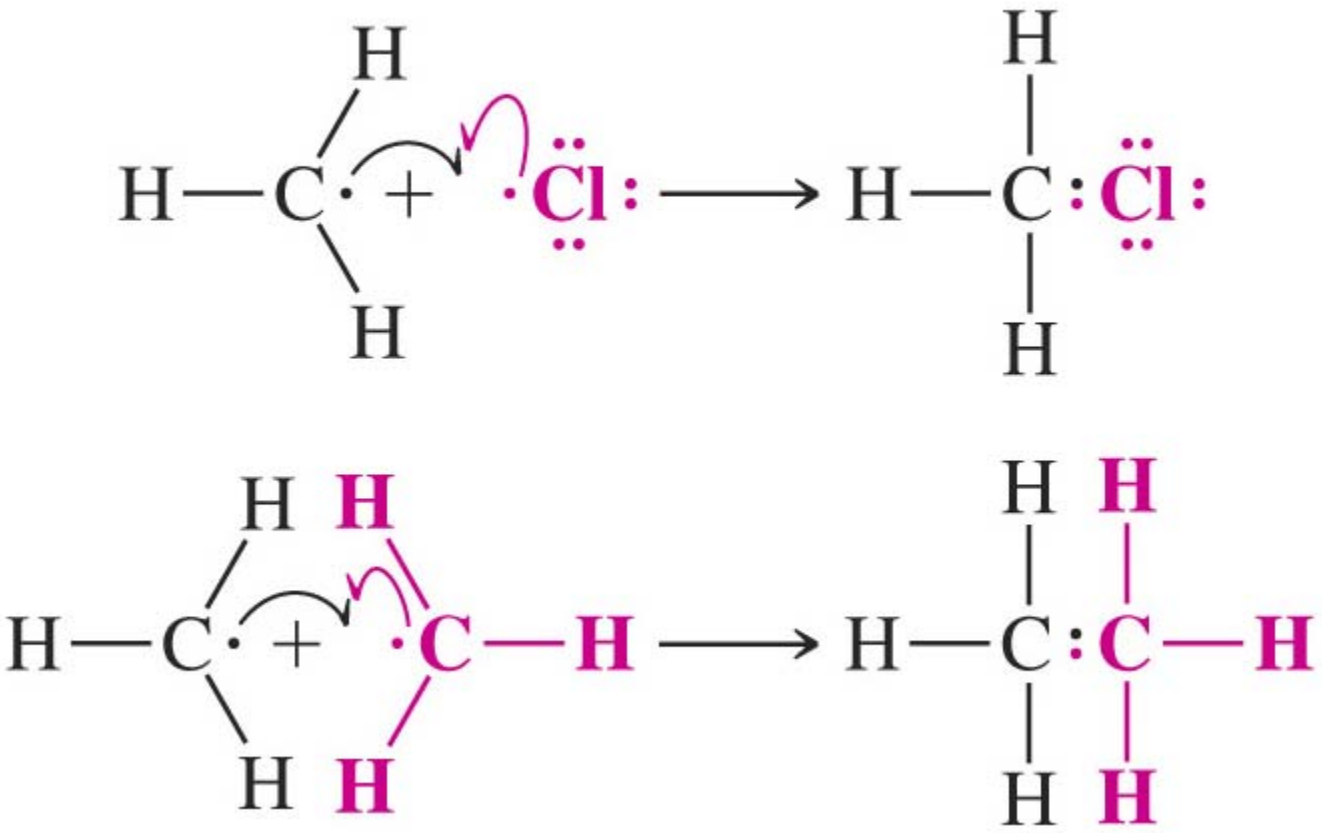
Under the influence of heat or light a molecule of chlorine dissociates; each atom takes one of the bonding electrons.

This step produces two highly reactive chlorine atoms.

chain propagation:



chain termination



從能量角度討論反應機制：

Chain Initiation

Step 1 $\mathrm{Cl{-}Cl \longrightarrow 2\ Cl\cdot}$ $\Delta H^\circ = +243\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 243)

Chain Propagation

Step 2 $\mathrm{CH_3{-}H + Cl\cdot \longrightarrow CH_3\cdot + H{-}Cl}$ $\Delta H^\circ = +8\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 440) **(*DH*° = 432)**

Step 3 $\mathrm{CH_3\cdot + Cl{-}Cl \longrightarrow CH_3{-}Cl + Cl\cdot}$ $\Delta H^\circ = -109\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 243) **(*DH*° = 352)**

Chain Termination

$\mathrm{CH_3\cdot + Cl\cdot \longrightarrow CH_3{-}Cl}$ $\Delta H^\circ = -352\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 352)

$\mathrm{CH_3\cdot + \cdot CH_3 \longrightarrow CH_3{-}CH_3}$ $\Delta H^\circ = -378\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 378)

$\mathrm{Cl\cdot + Cl\cdot \longrightarrow Cl{-}Cl}$ $\Delta H^\circ = -243\ \mathrm{kJ\ mol^{-1}}$

(*DH*° = 243)

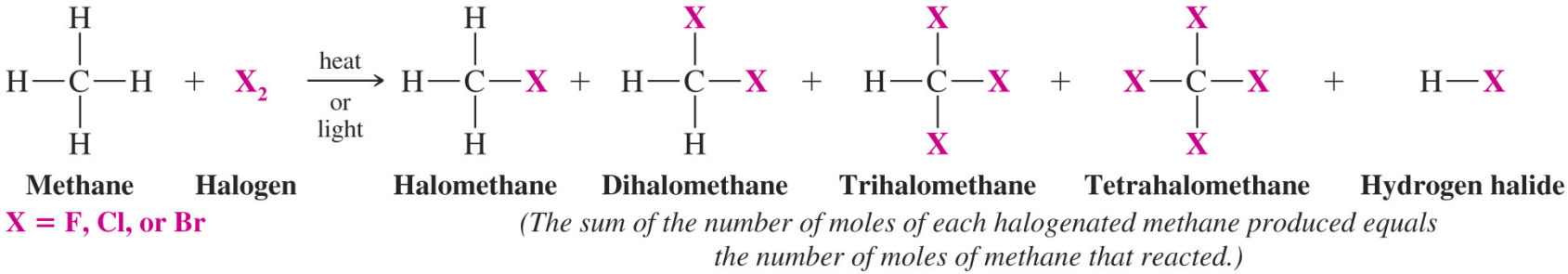
The chain propagation steps have overall D_rH° = -101 kJ mol^{-1} and are highly exothermic

$$Cl\cdot + CH_3{-}H \longrightarrow CH_3\cdot + H{-}Cl \qquad \Delta H^\circ = +8 \text{ kJ mol}^{-1}$$

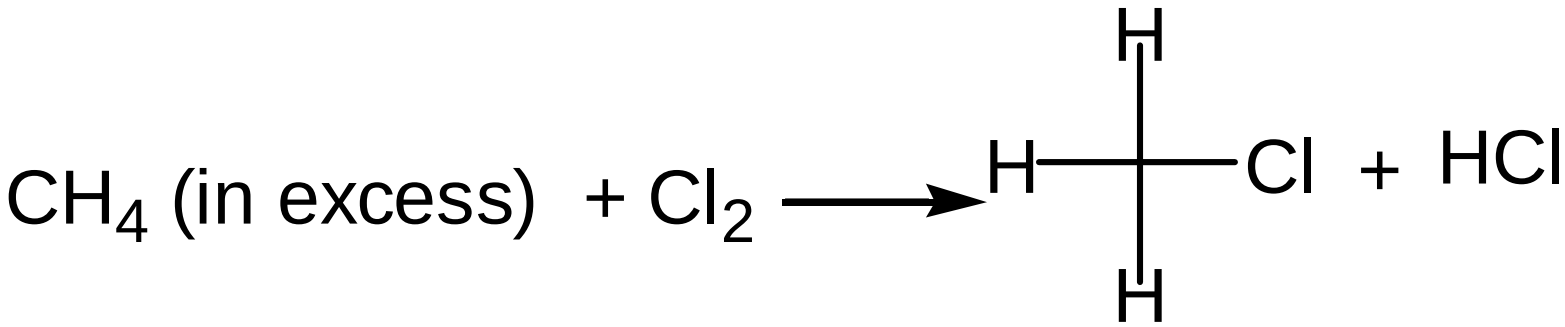
$$CH_3\cdot + Cl{-}Cl \longrightarrow CH_3{-}Cl + Cl\cdot \qquad \Delta H^\circ = -109 \text{ kJ mol}^{-1}$$

$$CH_3{-}H + Cl{-}Cl \longrightarrow CH_3{-}Cl + H{-}Cl \qquad \Delta H^\circ = -101 \text{ kJ mol}^{-1}$$

當CH_3Cl形成後，它會與氯分子發生繼續作用：



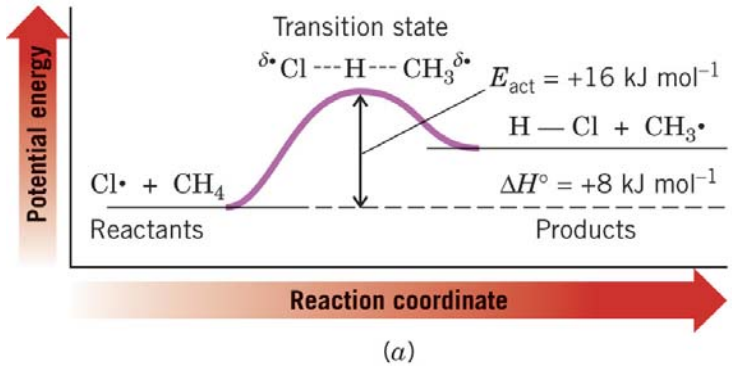
為了產生單一的CH_3Cl，可用過量的CH_4

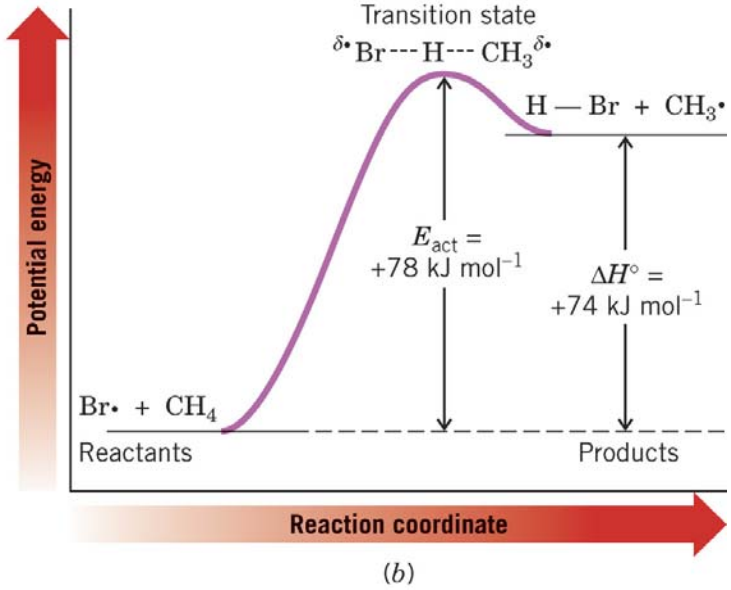


B)甲烷與F_2, Br_2 發生的自由基反應

反應性的順序：F2>C12>Br2　I2幾乎不反應

其原因是因為propagation 第一步的活化能不同





FLUORINATION

	$\Delta H°$ (kJ mol^{-1})	E_{act} (kJ mol^{-1})
Chain Initiation		
$F_2 \longrightarrow 2\ F\cdot$	+159	+159
Chain Propagation		
$F\cdot + CH_4 \longrightarrow HF + CH_3\cdot$	−130	+5.0
$CH_3\cdot + F_2 \longrightarrow CH_3F + F\cdot$	−302	Small
Overall $\Delta H°$ =	−432	

CHLORINATION

	$\Delta H°$ (kJ mol^{-1})	E_{act} (kJ mol^{-1})
Chain Initiation		
$Cl_2 \longrightarrow 2\ Cl\cdot$	+243	+243
Chain Propagation		
$Cl\cdot + CH_4 \longrightarrow HCl + CH_3\cdot$	+8	+16
$CH_3\cdot + Cl_2 \longrightarrow CH_3Cl + Cl\cdot$	−109	Small
Overall $\Delta H°$ =	−101	

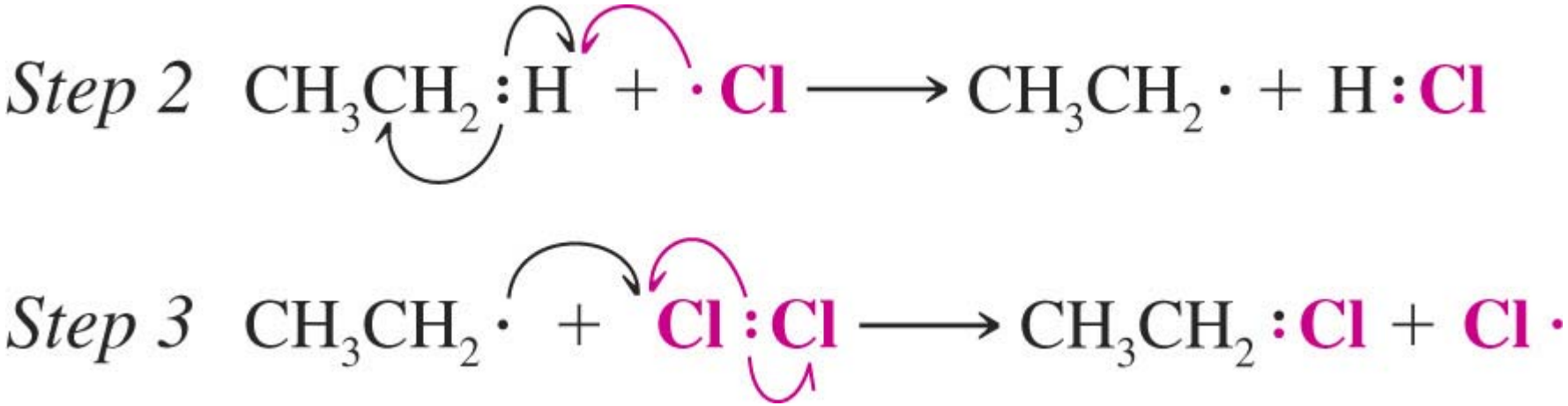
BROMINATION

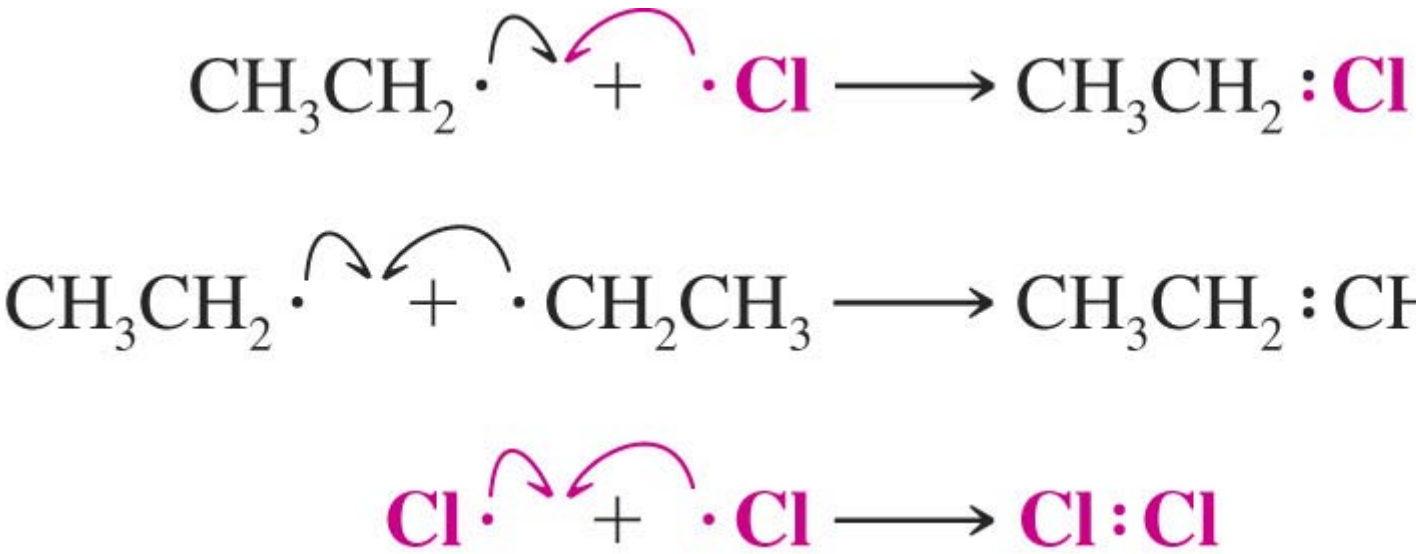
	$\Delta H°$ (kJ mol^{-1})	E_{act} (kJ mol^{-1})
Chain Initiation		
$Br_2 \longrightarrow 2\ Br\cdot$	+193	+193
Chain Propagation		
$Br\cdot + CH_4 \longrightarrow HBr + CH_3\cdot$	+74	+78
$CH_3\cdot + Br_2 \longrightarrow CH_3Br + Br\cdot$	−100	Small
Overall $\Delta H° = -26$		

IODINATION

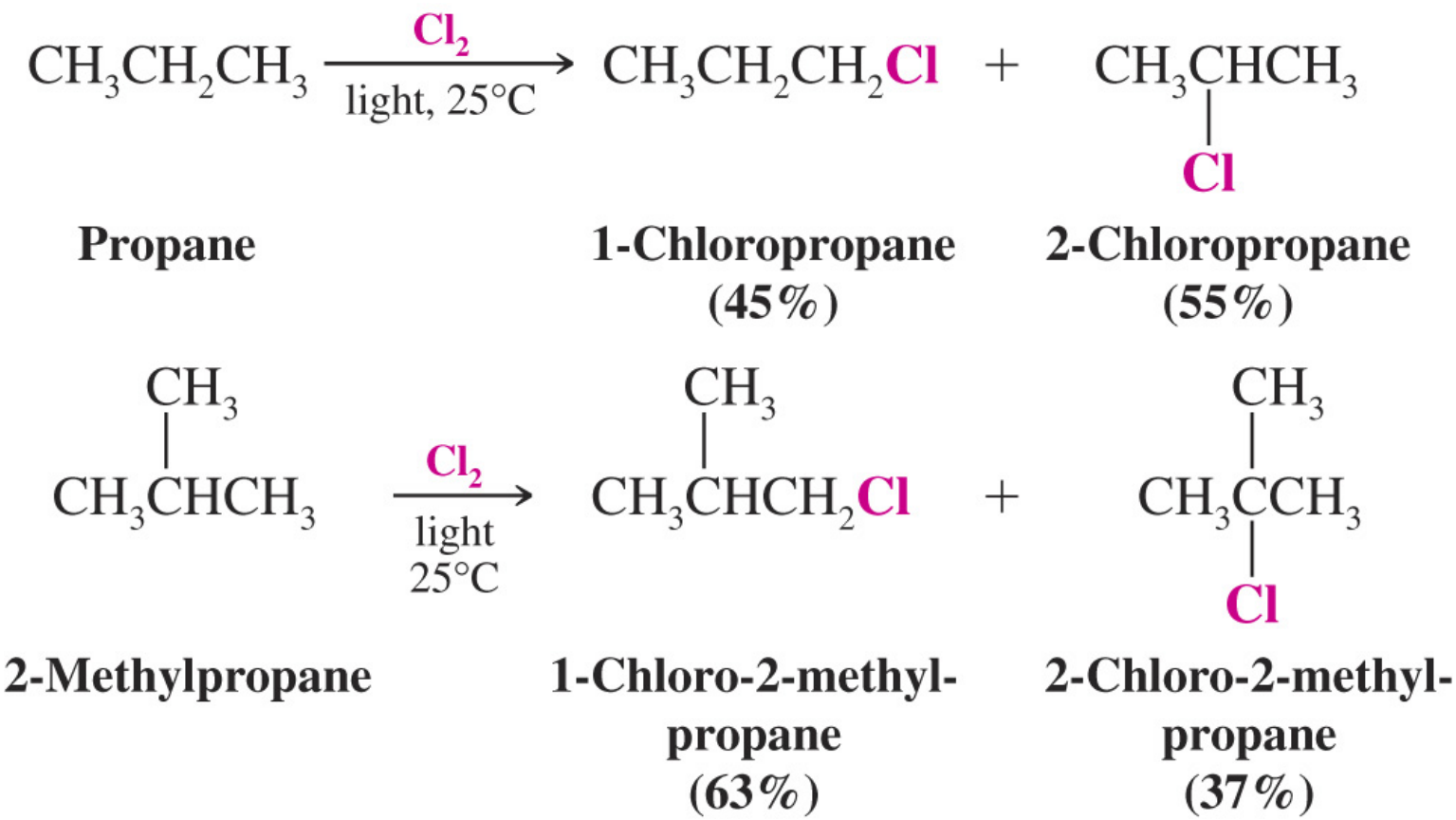
	$\Delta H°$ (kJ mol^{-1})	E_{act} (kJ mol^{-1})
Chain Initiation		
$I_2 \longrightarrow 2\ I\cdot$	+151	+151
Chain Propagation		
$I\cdot + CH_4 \longrightarrow HI + CH_3\cdot$	+142	+140
$CH_3\cdot + I_2 \longrightarrow CH_3I + I\cdot$	−89	Small
	Overall $\Delta H° = +53$	

C)Cl_2與其他烷烴的反應



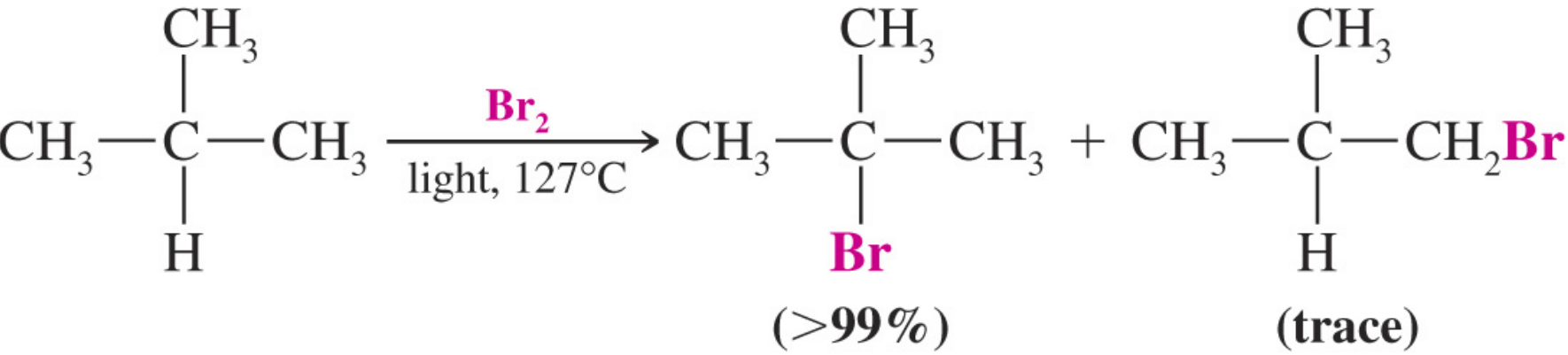

CH3CH2 · + · Cl ⟶ CH3CH2 : Cl
CH3CH2 · + · CH2CH3 ⟶ CH3CH2 : CH2CH3
Cl · + · Cl ⟶ Cl : Cl

當烷烴裏有不同的氫原子時，與Cl2的反應通常得到單取代的混合物 （即反應的regioselectivity較低），及多取代的產物。

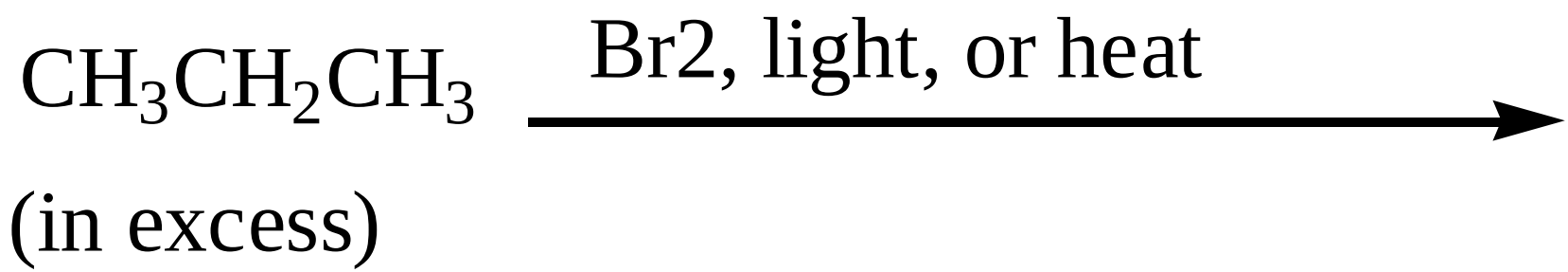


但反應活性還是:3°H>2°H>1°H (explain)

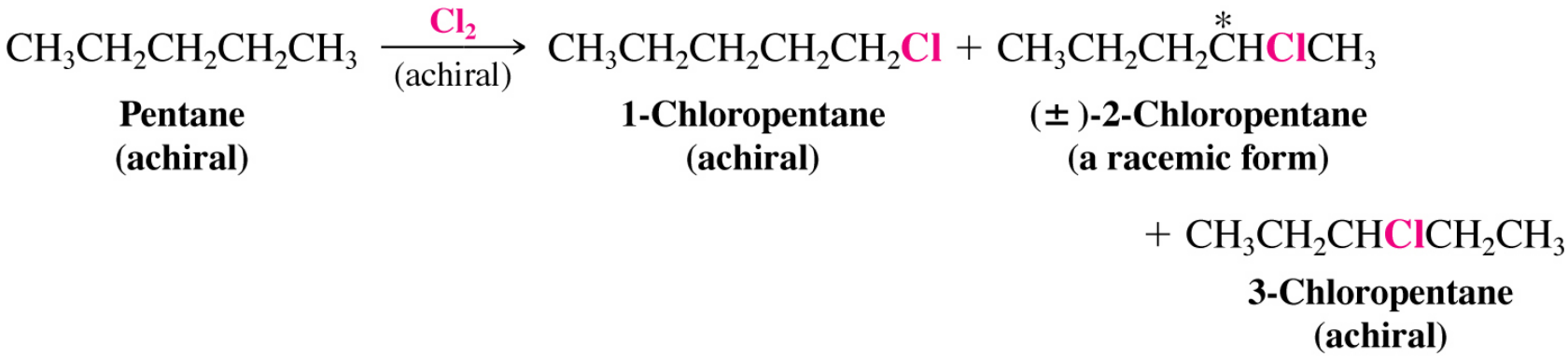
D)Br_2與其他烷烴的反應:高regioselectivity

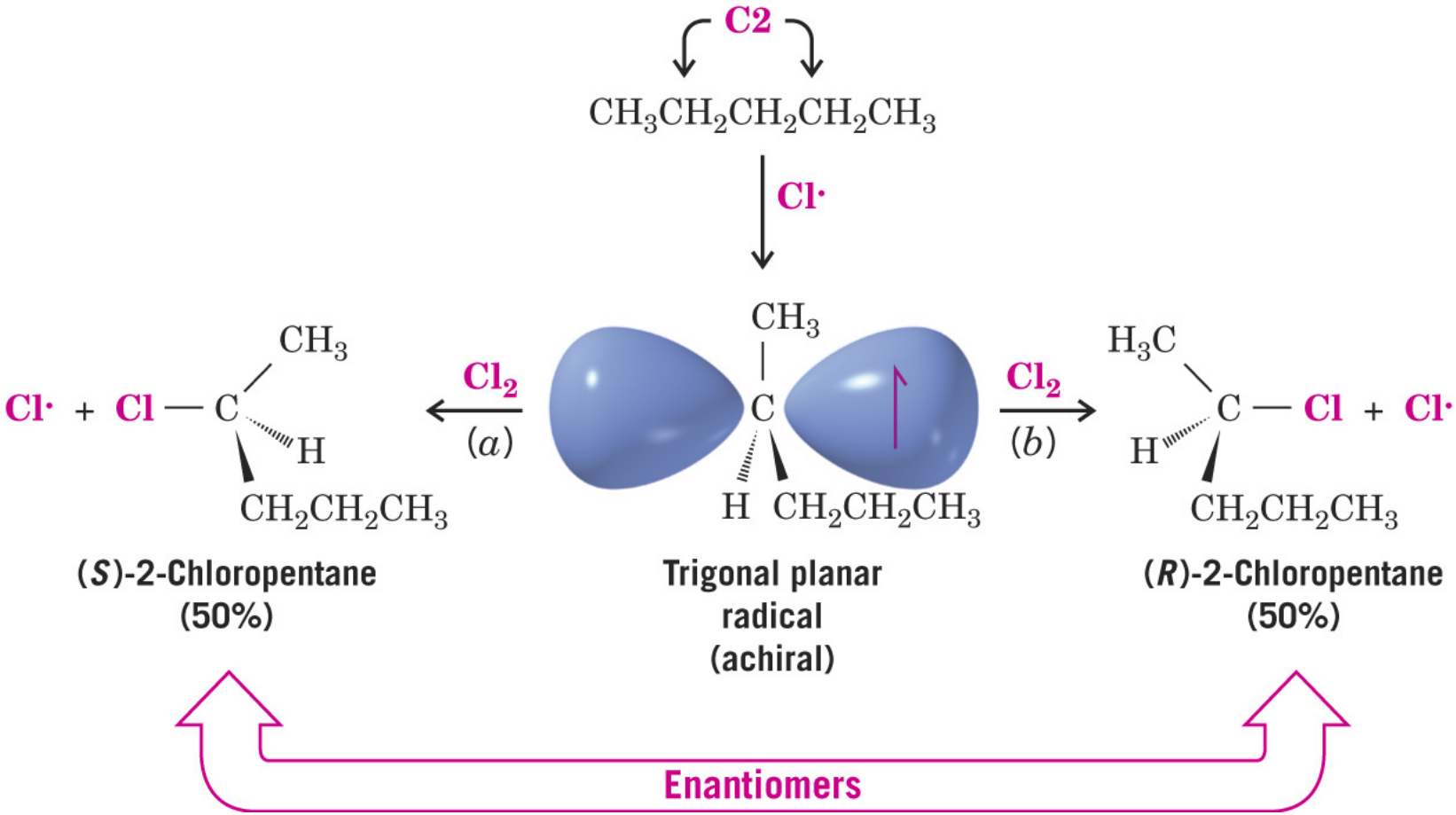


課堂練習：

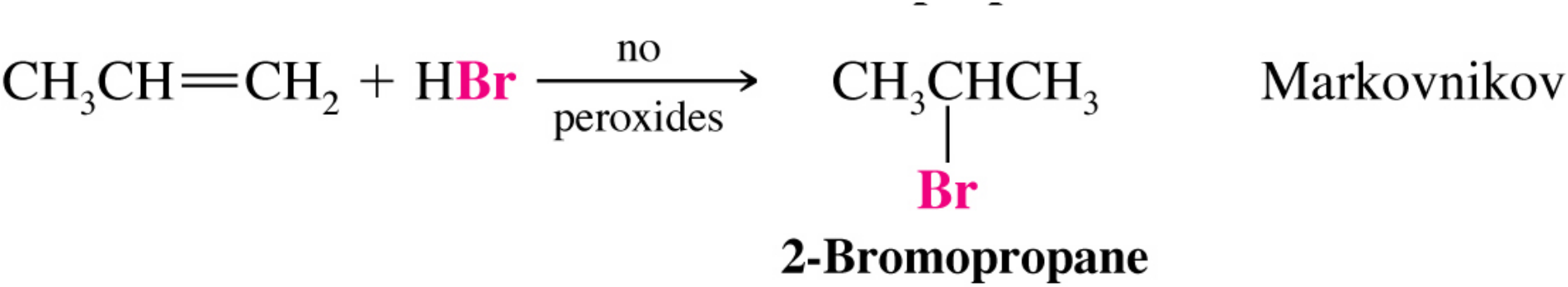


E)反應中的立體化學


CH3CH2CH2CH2CH3
Cl2
(achiral)
CH3CH2CH2CH2CH2Cl
+ CH3CH2CH2*CHClCH3
+ CH3CH2CHClCH2CH3
Pentane
(achiral)
1-Chloropentane
(achiral)
(±)-2-Chloropentane
(a racemic form)
3-Chloropentane
(achiral)


C2
CH3CH2CH2CH2CH3
Cl·
CH3
Cl· + Cl — C — H
CH2CH2CH3
Cl2
(a)
CH3
C
H CH2CH2CH3
Cl2
(b)
H3C
C — Cl + Cl·
H
CH2CH2CH3
(S)-2-Chloropentane
(50%)
Trigonal planar
radical
(achiral)
(R)-2-Chloropentane
(50%)
Enantiomers

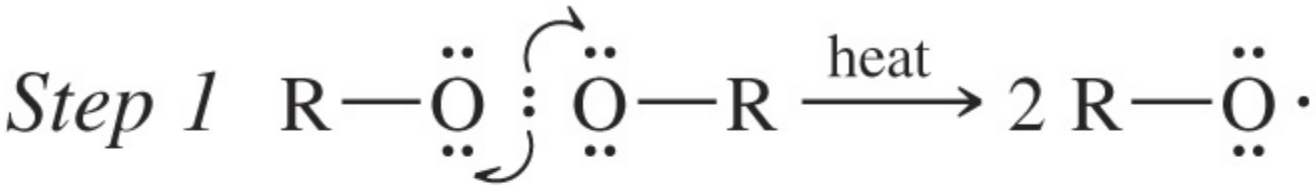
F) HBr在過氧化物的存在下與烯烴的加成反應——Anti Markkovnikov (Radical Addition to Alkenes: The anti-Markovnikov Addition of Hydrogen Bromide)



Anti-Markovnikov

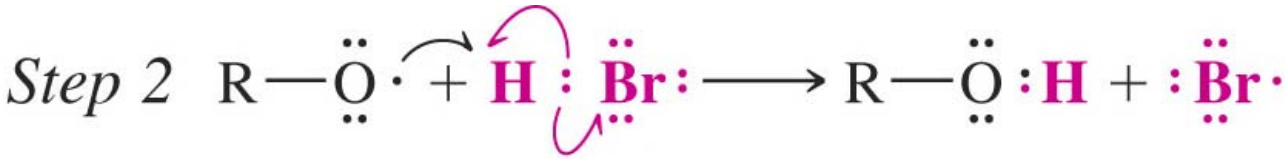
反應機制:

chain initiation:

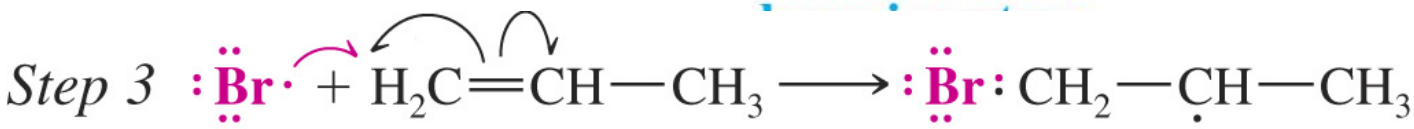


Heat brings about homolytic cleavage of the weak oxygen–oxygen bond.

chain propagation:



The alkoxyl radical abstracts a hydrogen atom from HBr, producing a



2° Radical

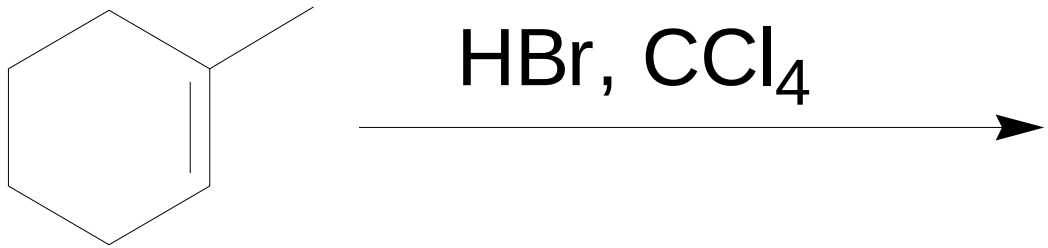
A bromine atom adds to the double bond to produce the more stable 2° radical.

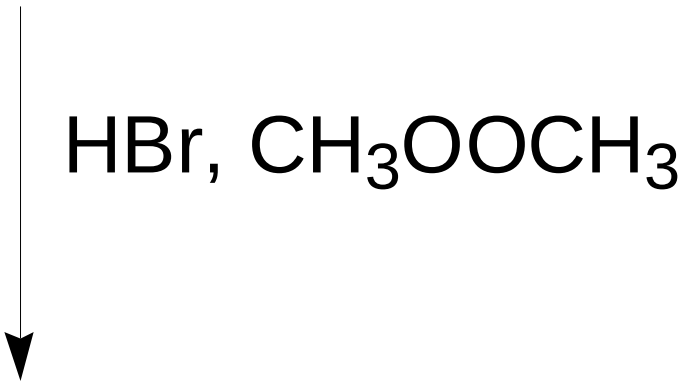
1-Bromopropane

The 2° radical abstracts a hydrogen atom from HBr. This leads to the product and regenerates a bromine atom. Then repetitions of steps 3 and 4 lead to a chain reaction.

chain termination:

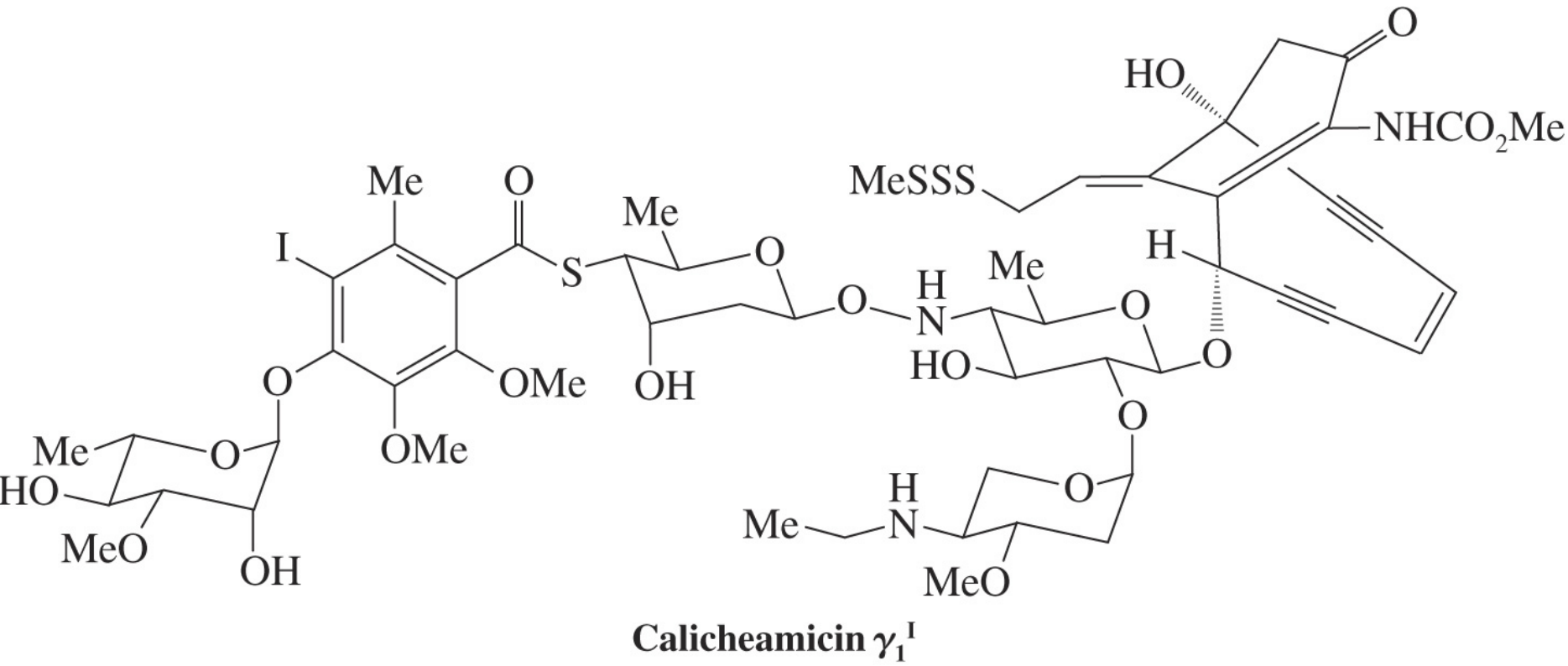
課堂練習:





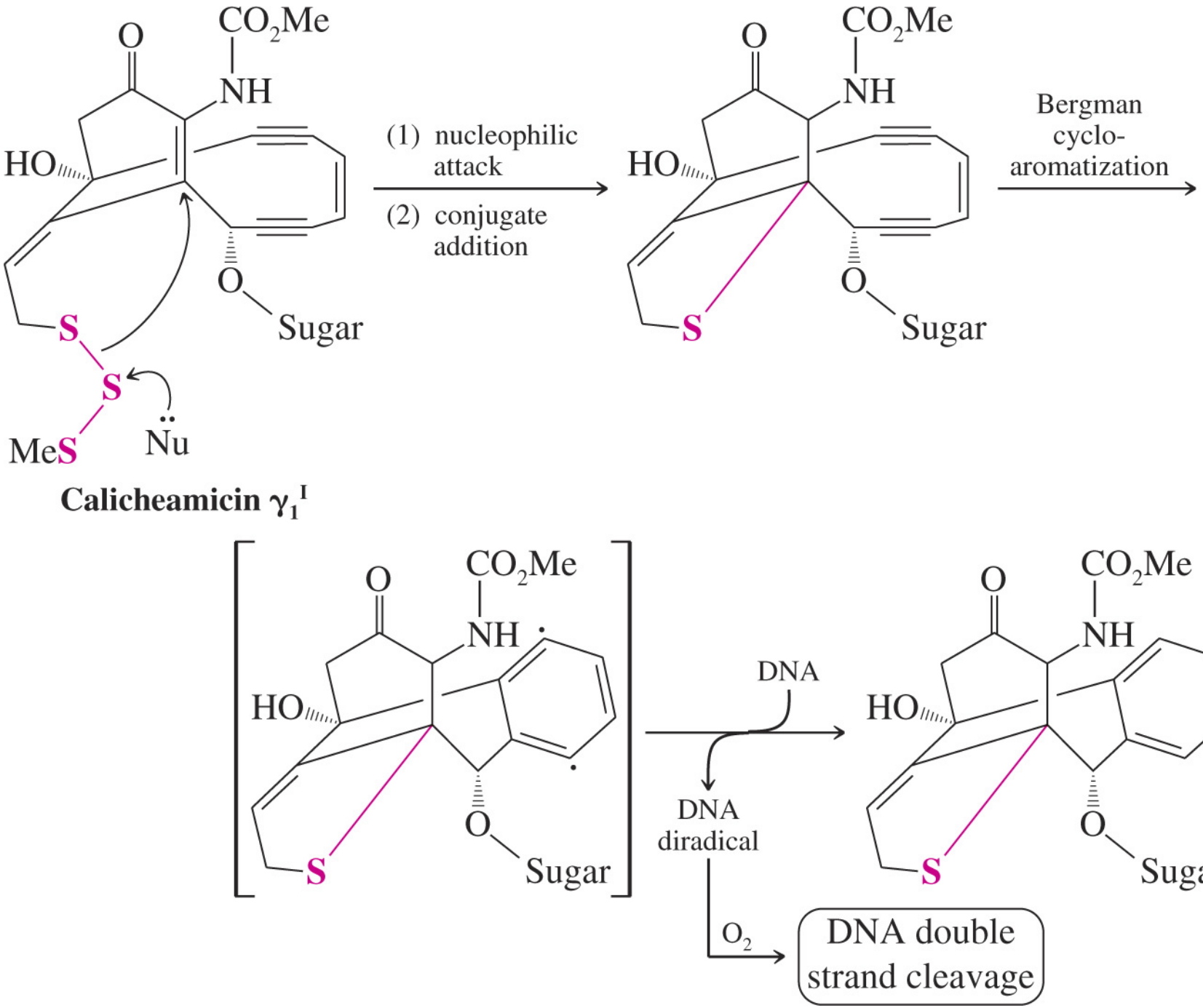
3）其它自由基反應

A）Calicheamicinγ[1] 引起癌細胞apoptosis



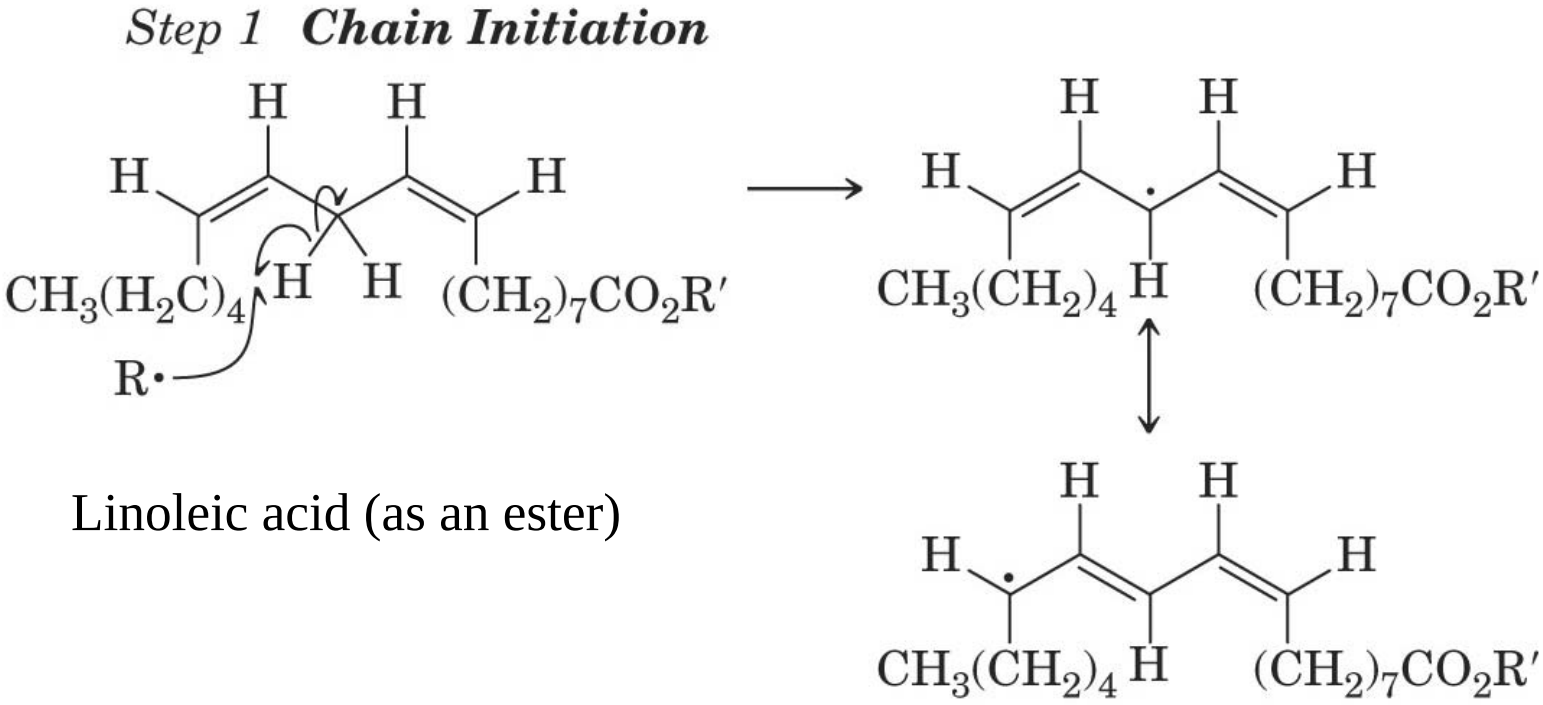
Calicheamicin γ_1^I

Isolated from *Micromonospora echinospora*



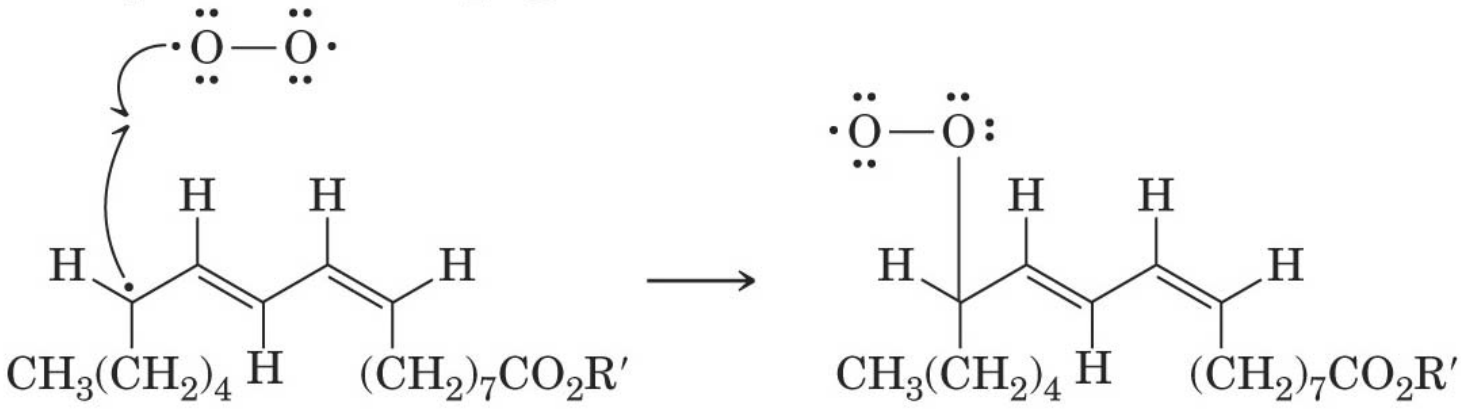
Calicheamicin γ_1^I

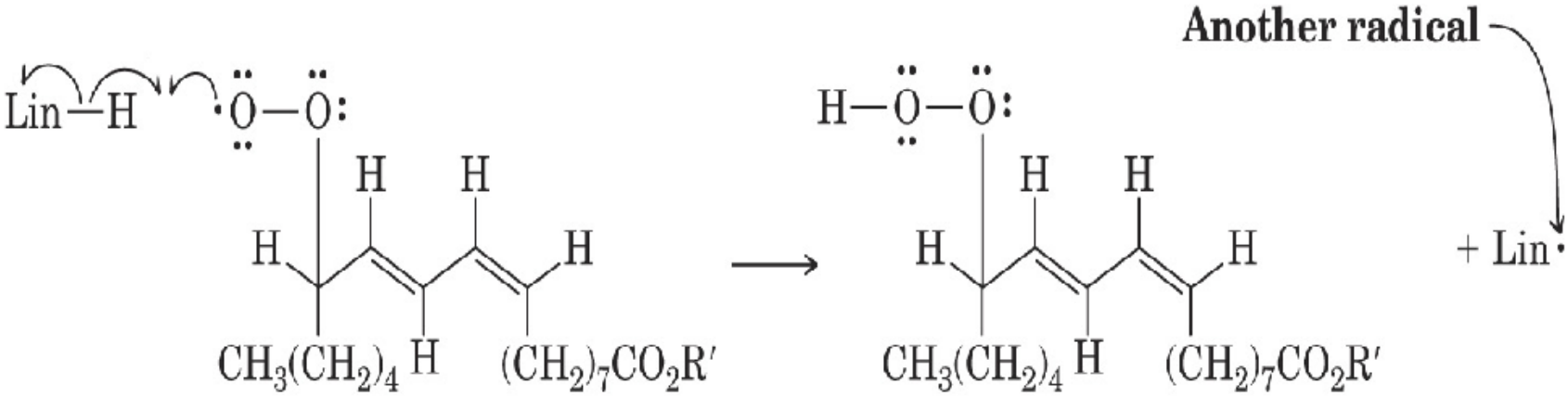
B）不飽和脂肪酸的氧化



Linoleic acid (as an ester)

Step 2 ***Chain Propagation***





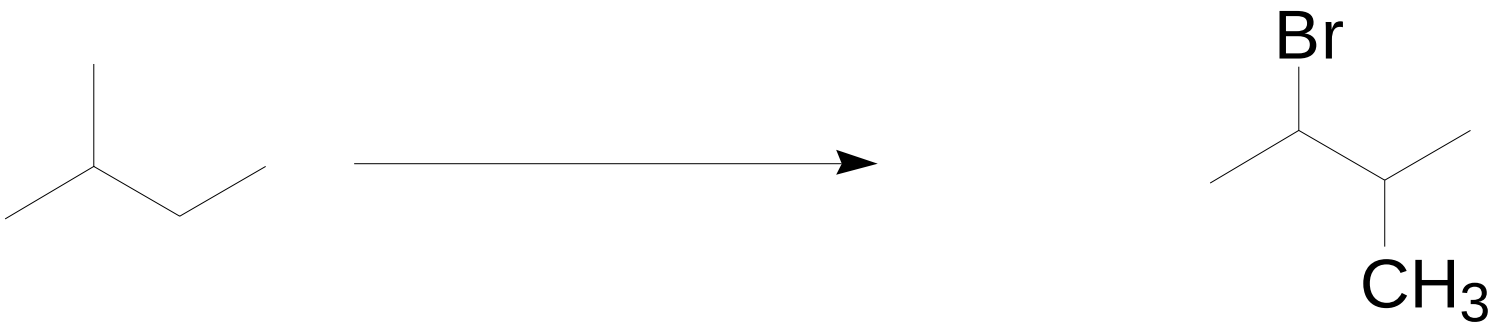
Hydrogen abstraction from another molecule of the linoleic ester

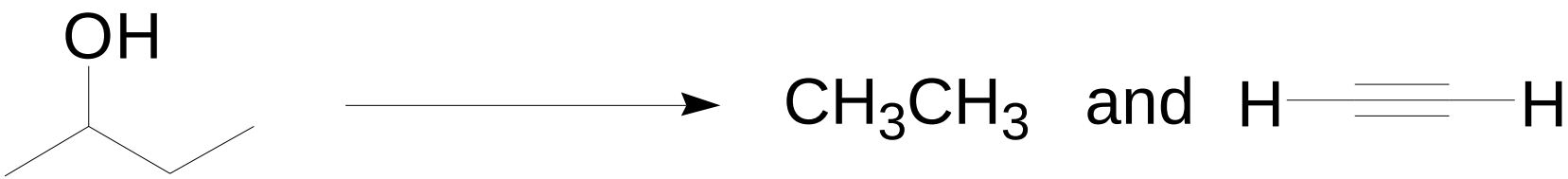
A hydroperoxide

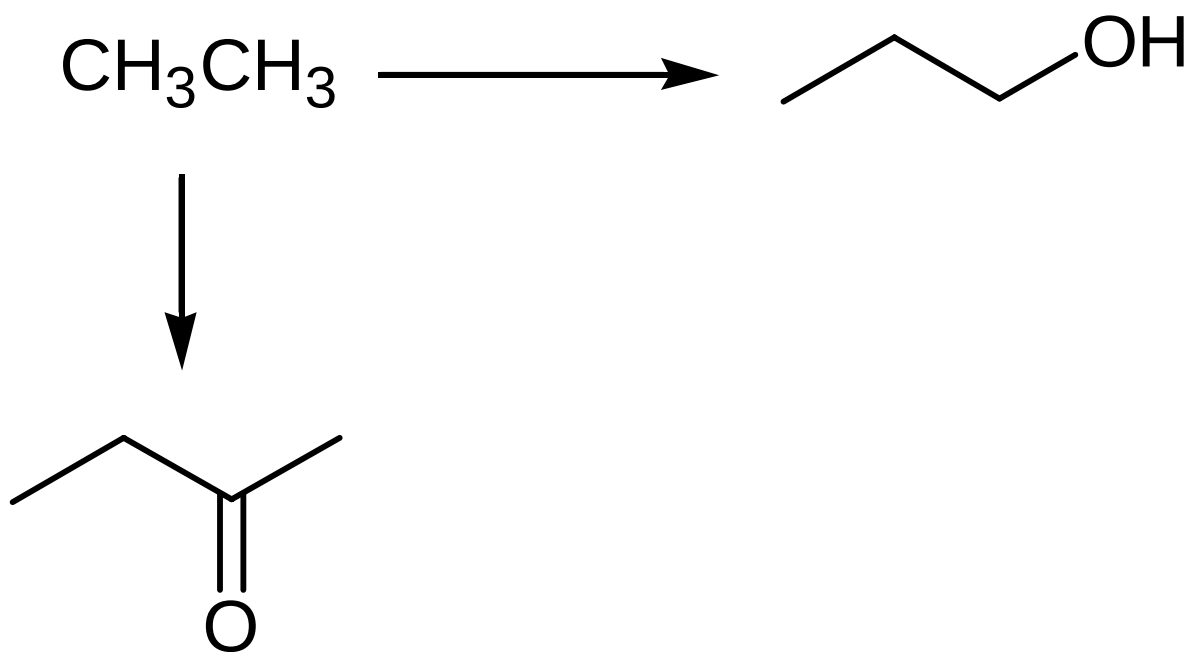
課堂練習:由給出的起始物設計合成產物

$CH_3CH_3 \longrightarrow CH_3CH_2I$

$CH_3CH_3 \longrightarrow CH_3CH_2OCH_2CH_3$






CH3CH3
OH
O