David Van Vranken and Gregory Weiss

Introduction to Bioorganic Chemistry and Chemical Biology

Chapter 2
The Chemical Origins of Biology

Complex living organisms are beholden to elementary scientific principles

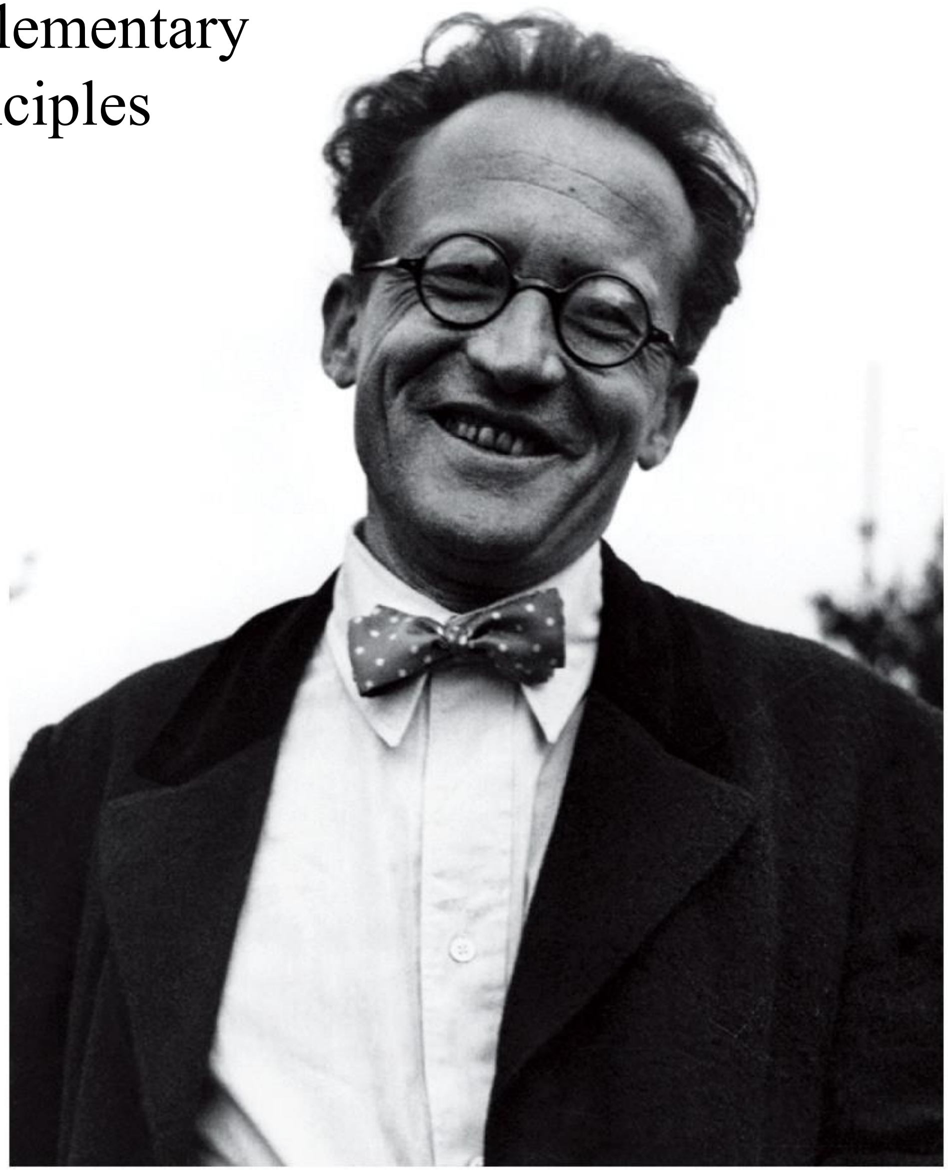


Figure 2.1 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Figure 2.2 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

The first application of curved arrows was used to represent resonance. Curved arrows were introduced to mechanistic organic chemistry before line depictions of were widely adopted.

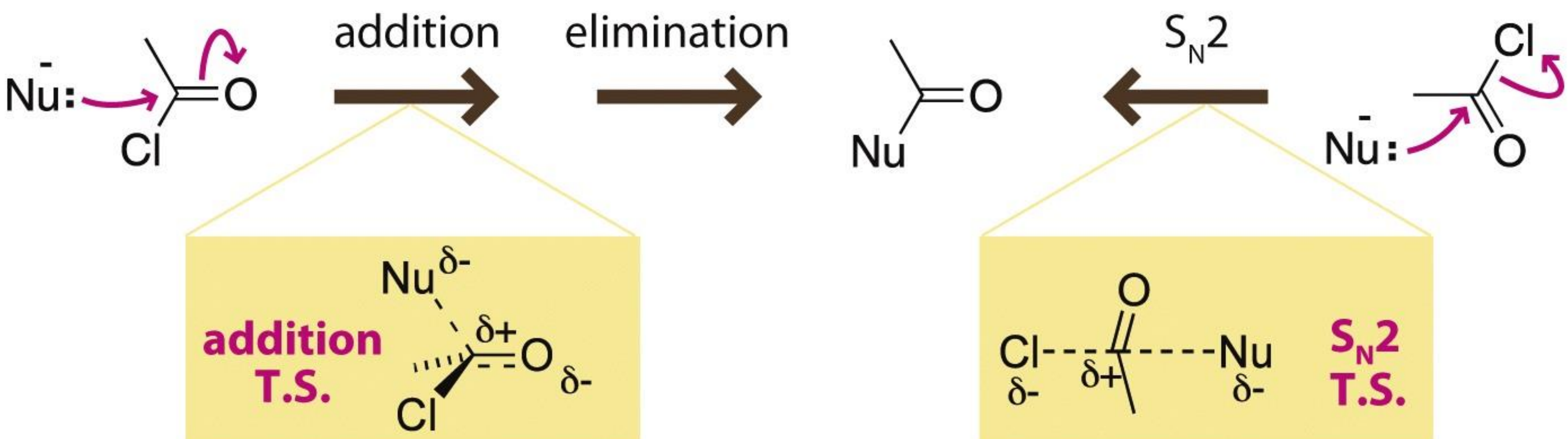


Figure 2.3 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

charge

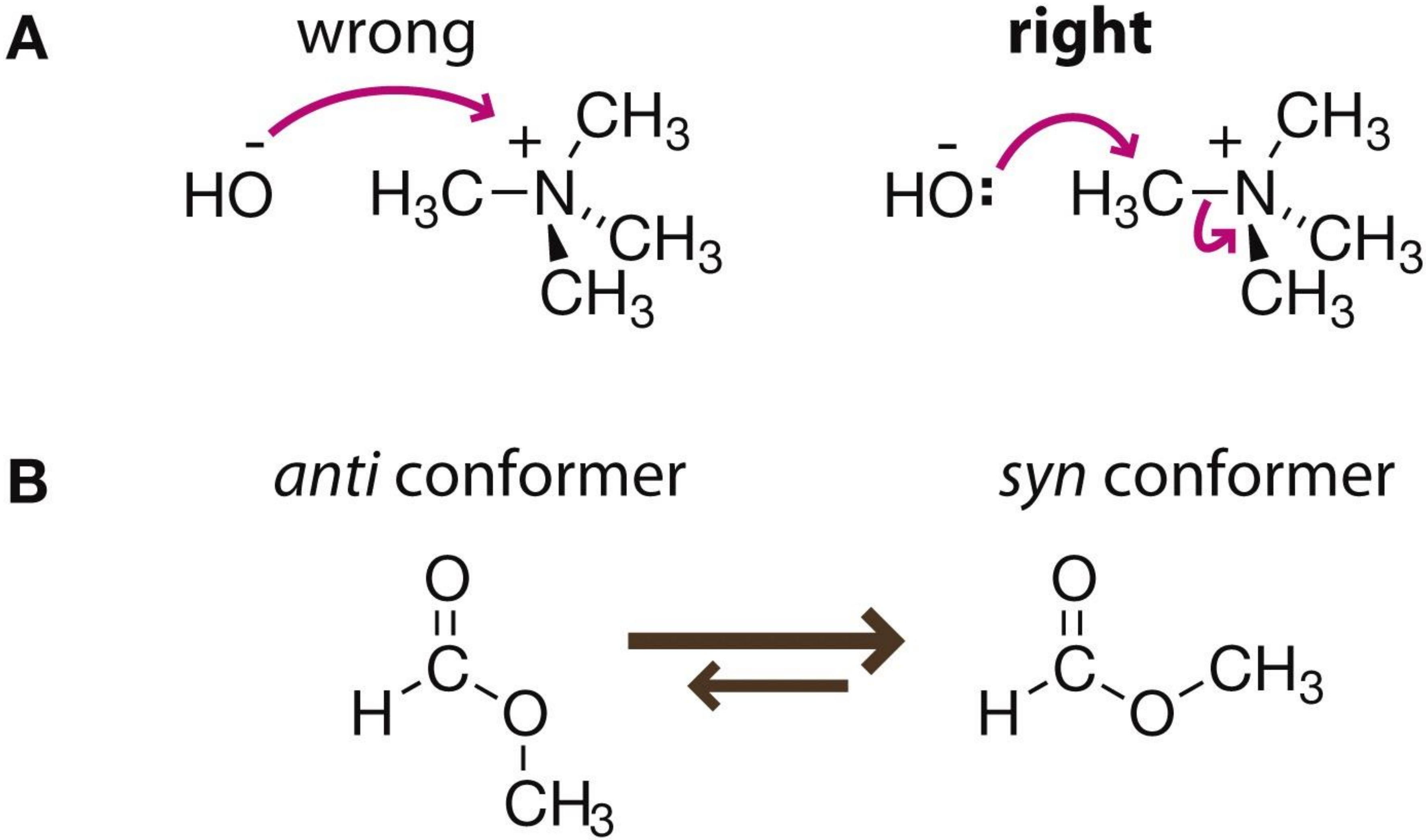


Figure 2.4 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Sterics cannot explain the syn conformer formation

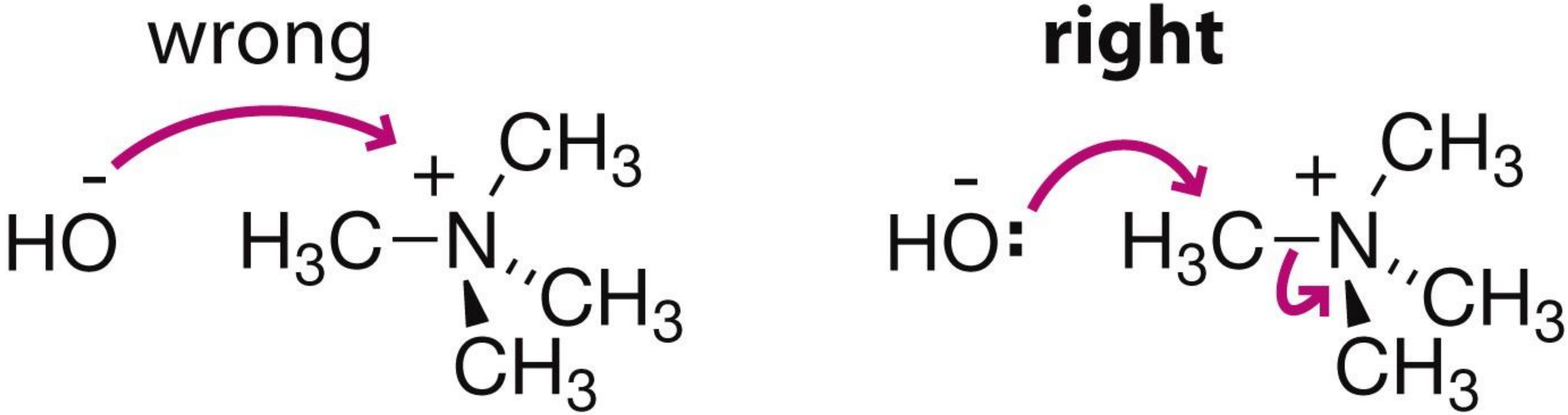
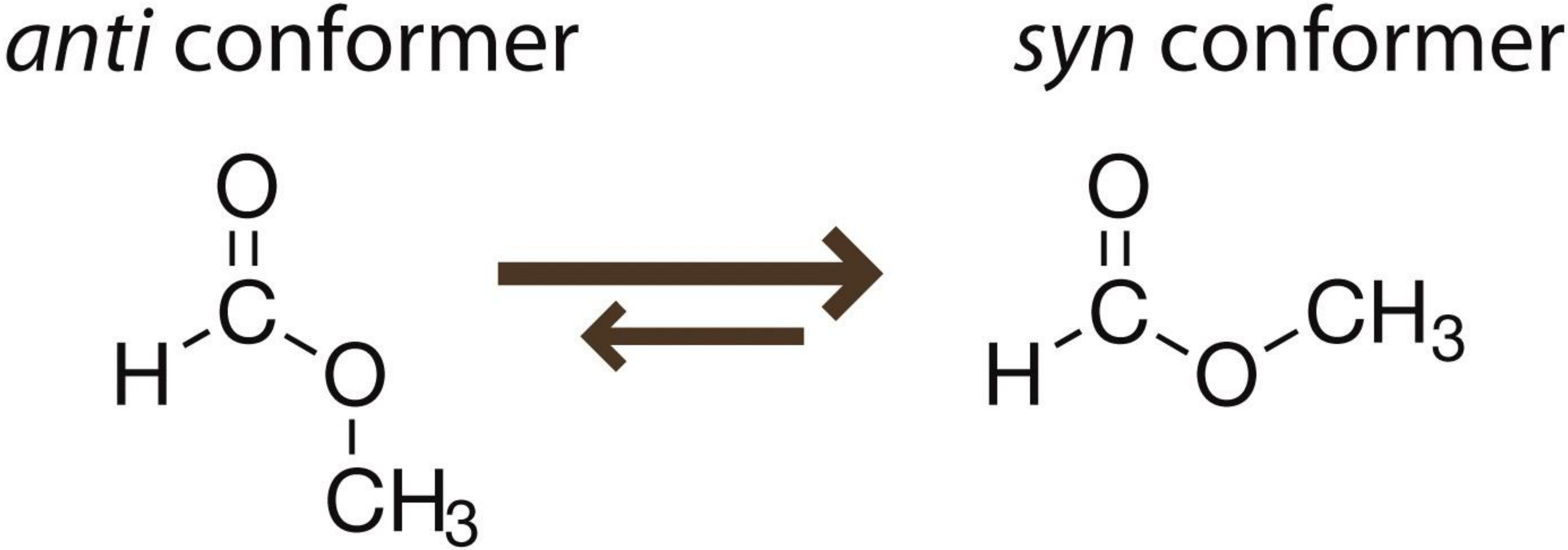


Figure 2.4a Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Violation of the octet rule for N



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Orbital interactions

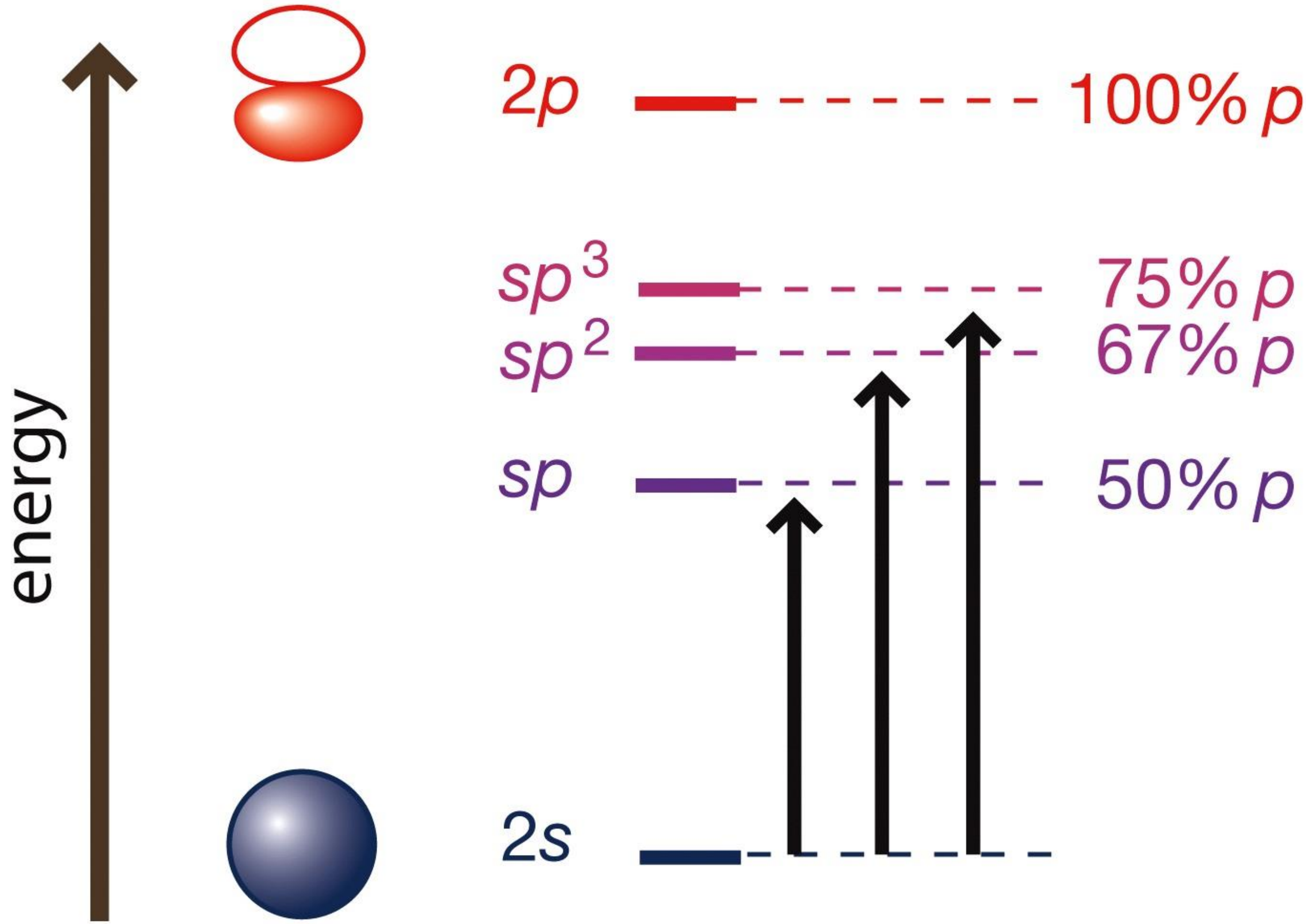
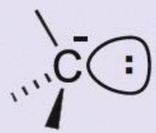
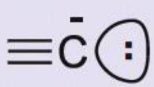


Figure 2.5 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Electrons in orbitals with higher p character are more reactive than electrons in orbitals with lower p character

Table 2.1 *p* Character and basicity.

pK_a'	lone pair	%*p*
50	 sp^3	75
41	 sp^2	67
24	 sp	50

lone pair reactivity

Table 2.1 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

S character confers stability. P character confers nucleophilicity and basicity

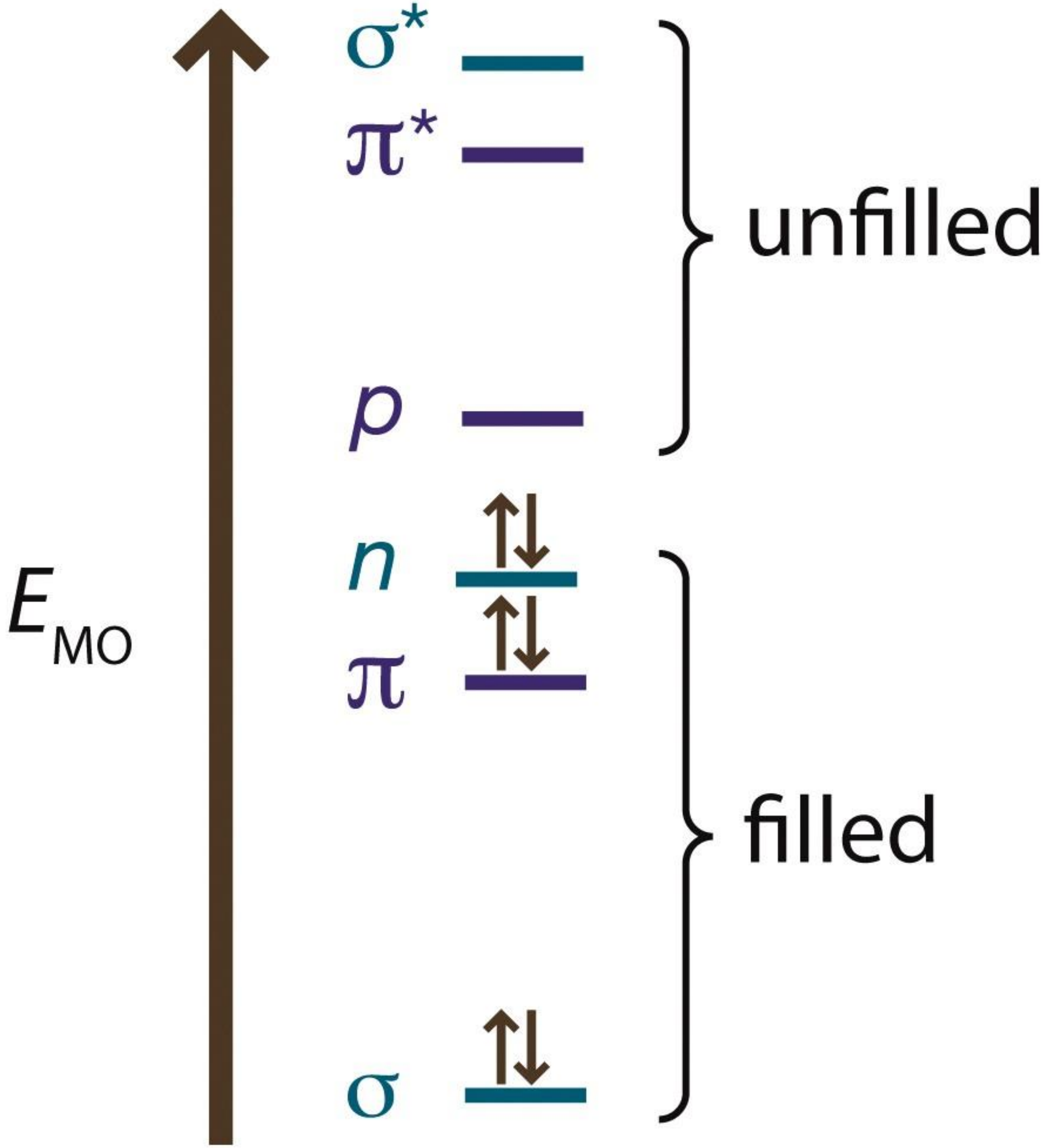


Figure 2.6 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

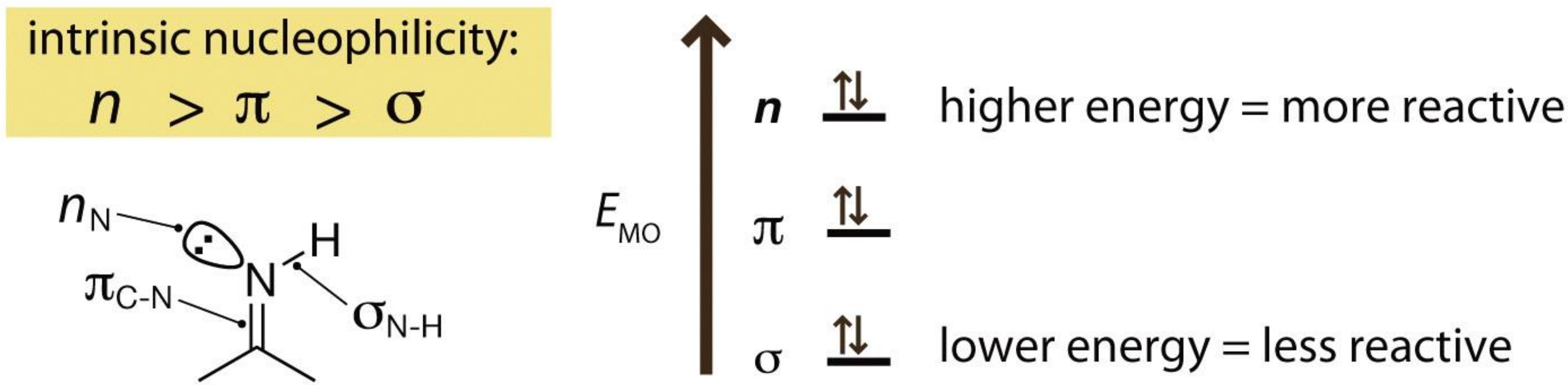


Figure 2.7 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

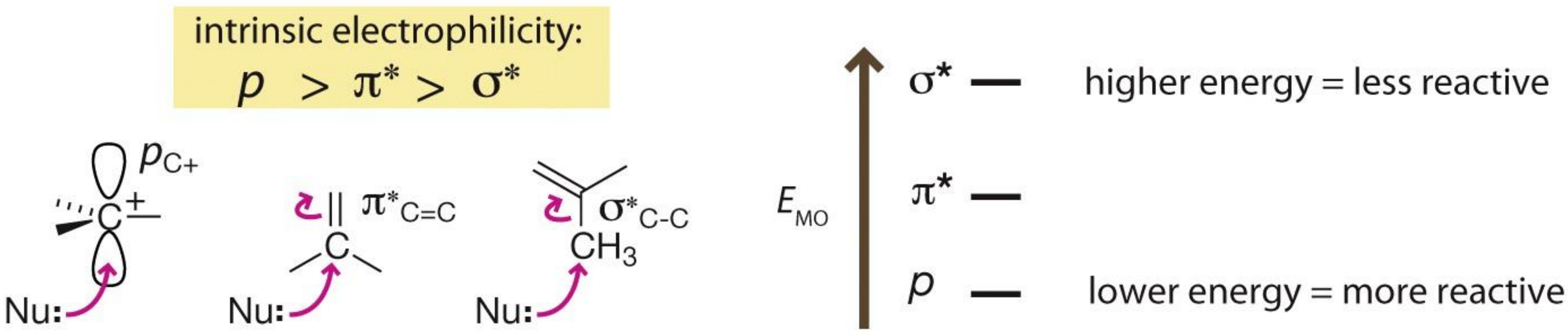


Figure 2.8 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

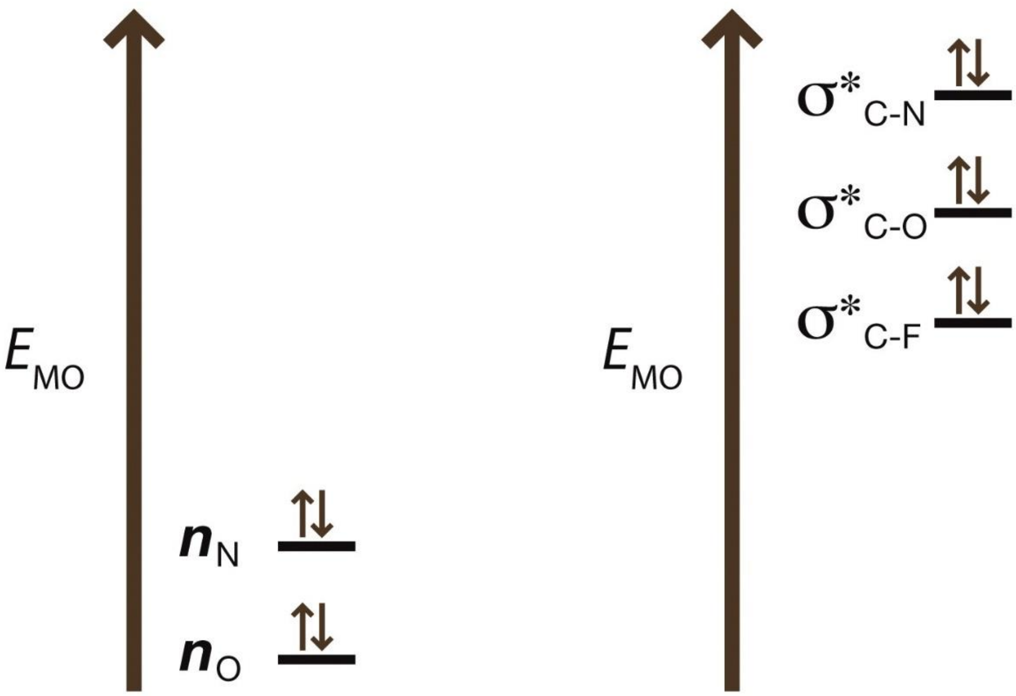


Figure 2.9 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Η ηλεκτραρνητικότητα επηρεάζει τα μετωπικά τροχιακά και τις αλληλεπιδράσεις Coulomb

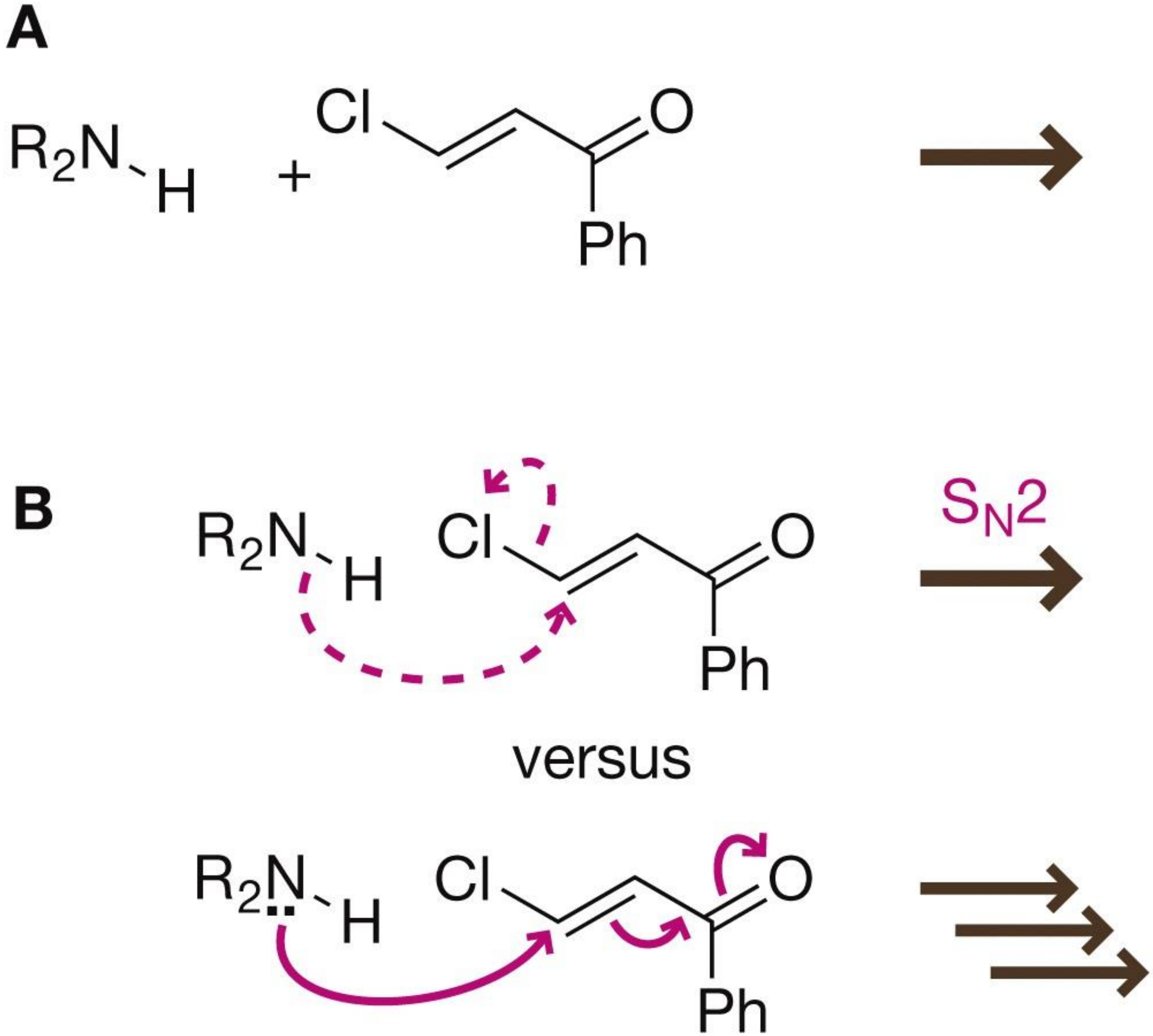


Figure 2.10 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Figure 2.10a Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

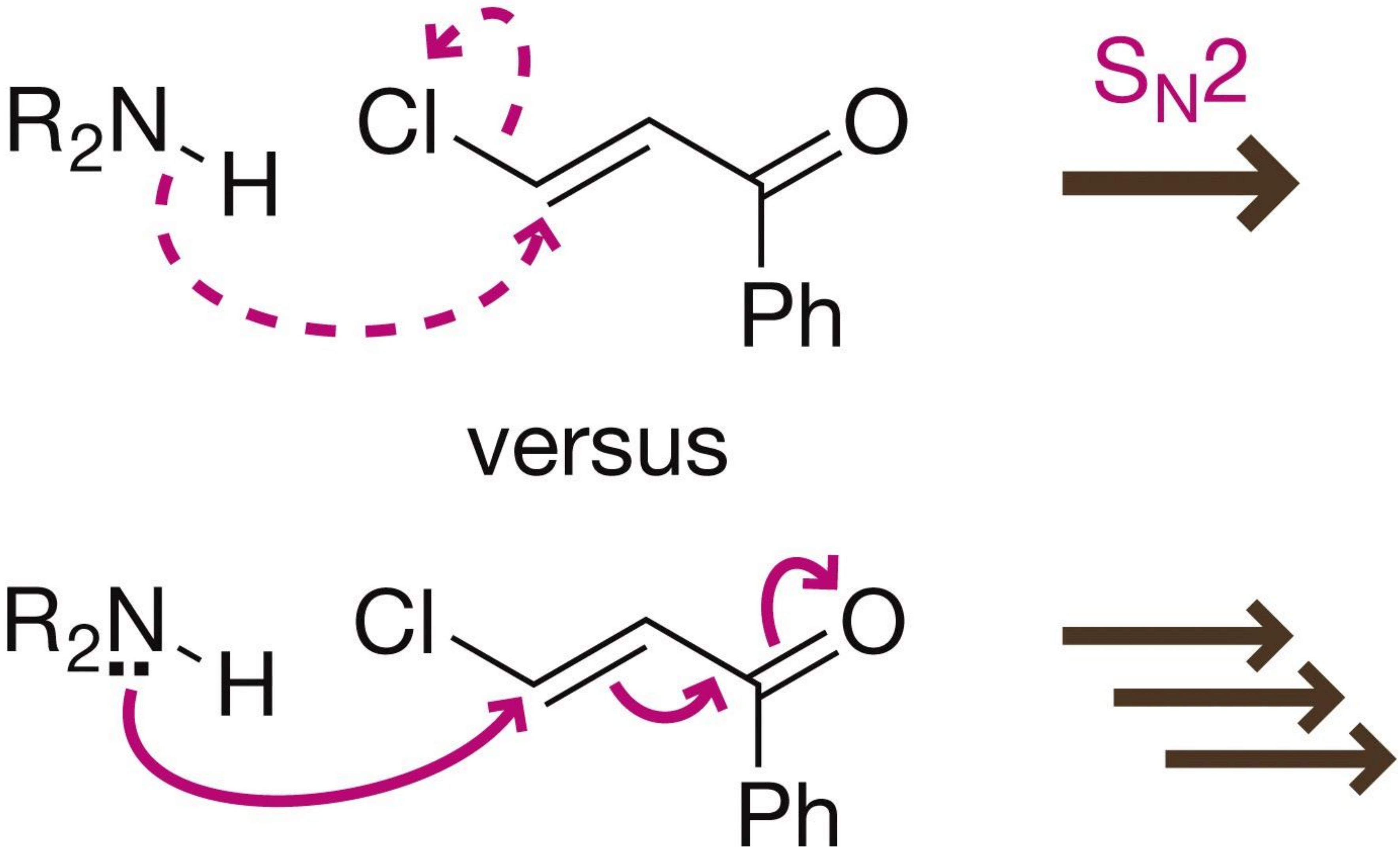


Figure 2.10b Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

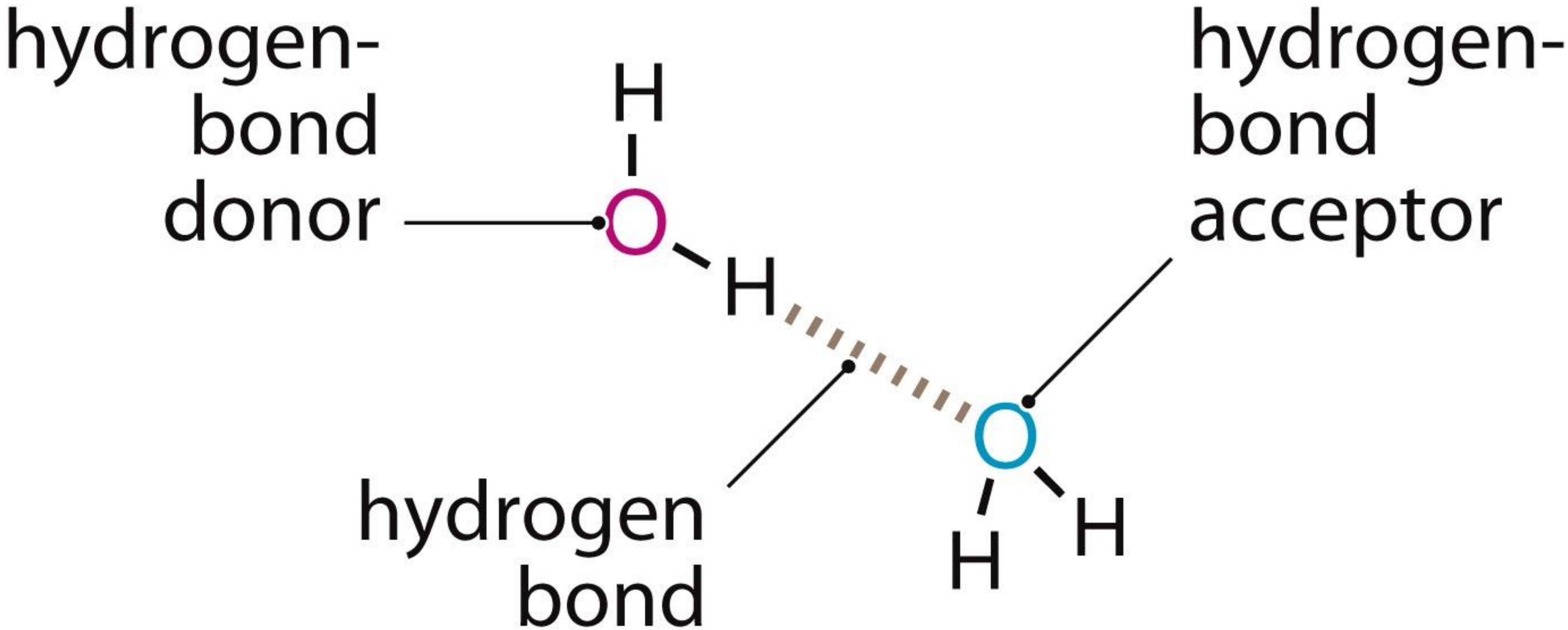


Figure 2.11 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Η ζωή θα ήταν διαφορετική χωρίς τους δεσμούς υδρογόνου

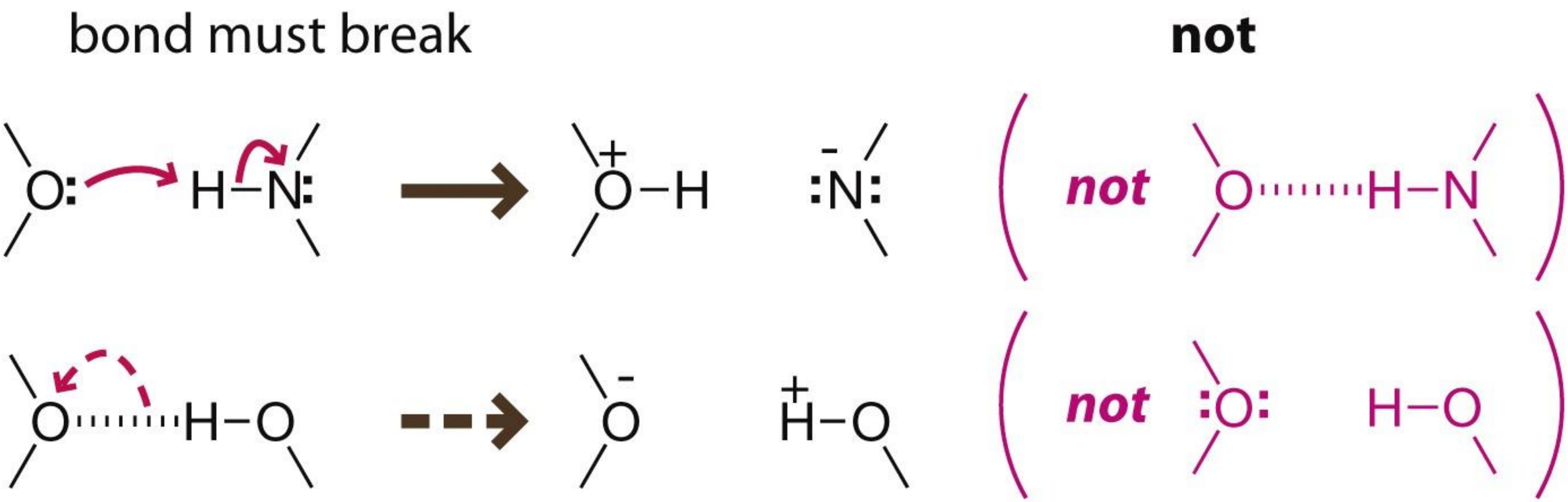


Figure 2.12 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

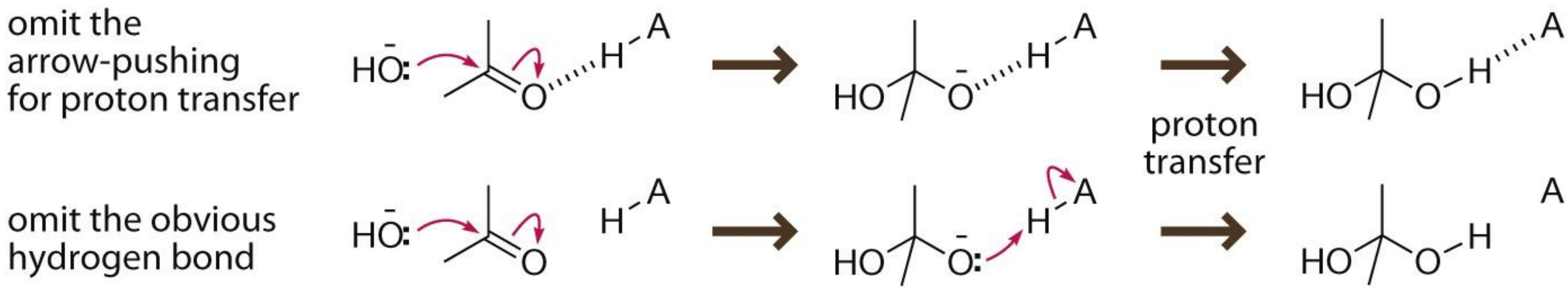


Figure 2.13 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Proton transfer form heteroatoms are usually fast

$$H_2O \quad + \quad H{-}A \quad \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \quad H_2\overset{+}{O}{-}H \quad + \quad A^-$$

Figure 2.14 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Υδατικά οξέα

Table 2.2 Rate constants for proton transfers to water (see Figure 2.14).

HA	pK_a	k_1 ($M^{-1}s^{-1}$)	k_{-1} ($M^{-1}s^{-1}$)
HF	3.2	10^8	10^{11}
AcOH	4.7	10^6	10^{11}
H_2S	7.2	10^4	10^{11}
$MeCOCH_2CO_2Et$	9.0	10^{-3}	6×10^7
NH_4^+	9.3	25	$\sim 10^{11}$
CH_3NO_2	10.2	10^{-8}	6×10^2

Table 2.2 Introduction to Bioorganic Chemistry and Chemical Biology

$$K_{eq} = \frac{k_{forward}}{k_{reverse}}$$

Figure 2.15 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

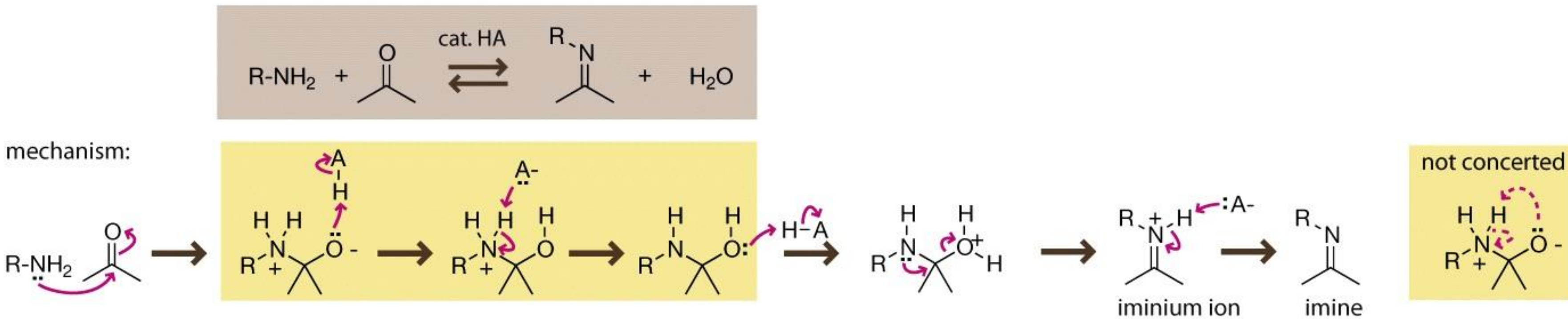


Figure 2.16 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

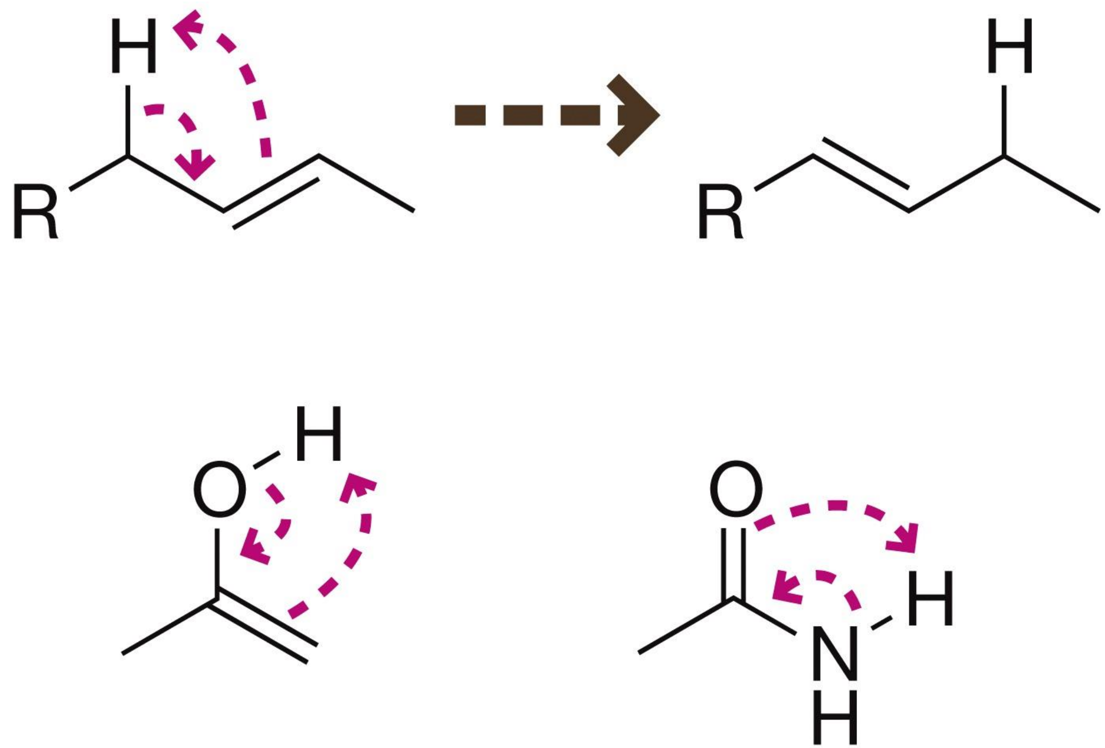


Figure 2.17 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

1,3-sigmatropic implausible
Tautomerization occurs with acid base catalysis

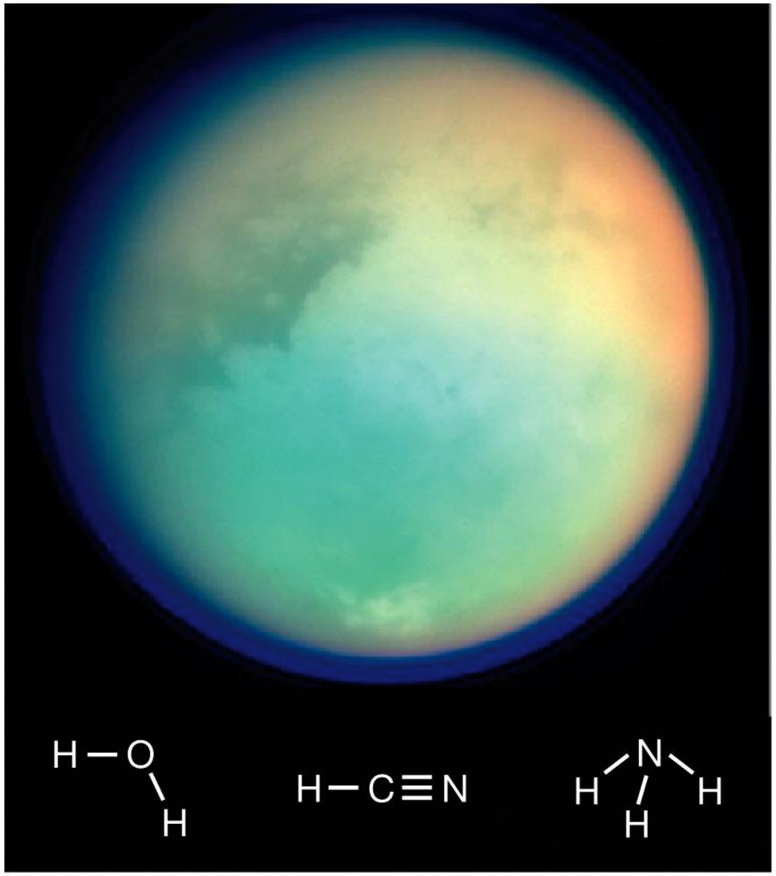


Figure 2.18 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Prebiotic chemistry

Celestial building blocks can be found in Titan (Saturn)

100,000 years homo sapiens neaderthalensis
Oldest fossils 3,6 billion years
Water, ammonia, hydrogen cyanide, acetonitrile, acrylonitrile, cyanogen, cyanoacetylene
The oxygen is not an obligate component
Earth was oxygen free until the evolution of photosynthetic bacteria -2,7 billion years ago

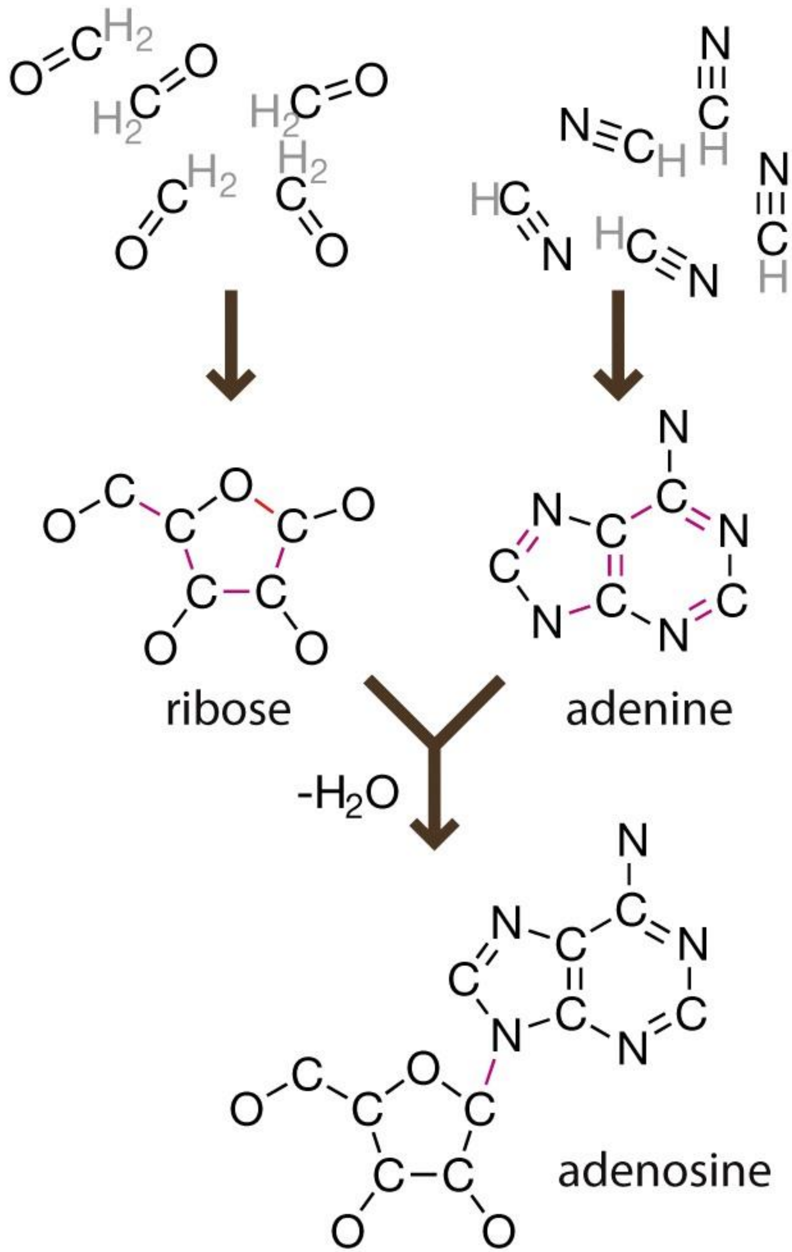


Figure 2.19 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

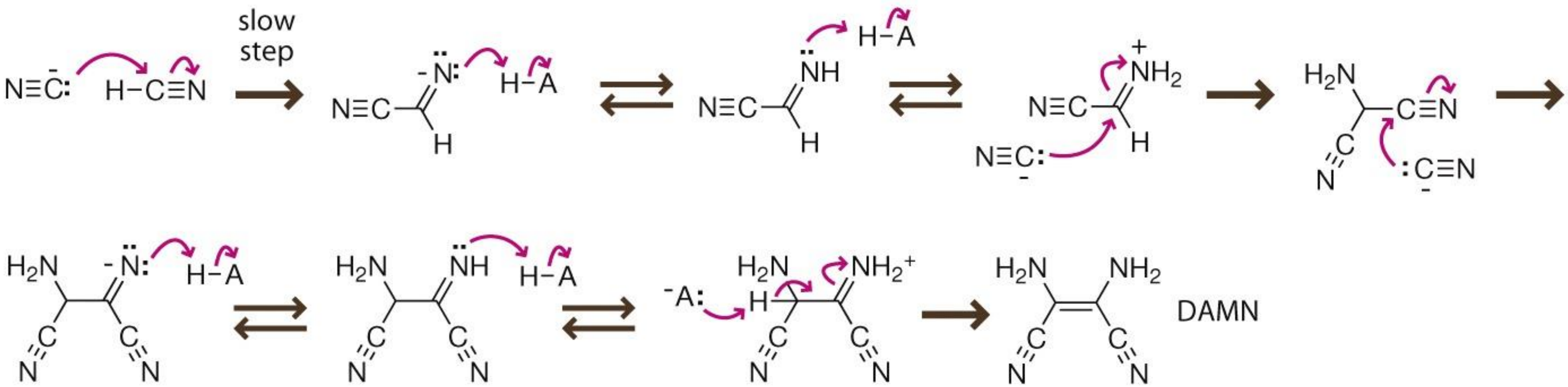


Figure 2.20 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Prebiotic carbon-carbon bond formation. Under basic conditions cyanide can serve both as a nucleophile and a electrophile, ultimately leading to DNA building blocks like DAMN

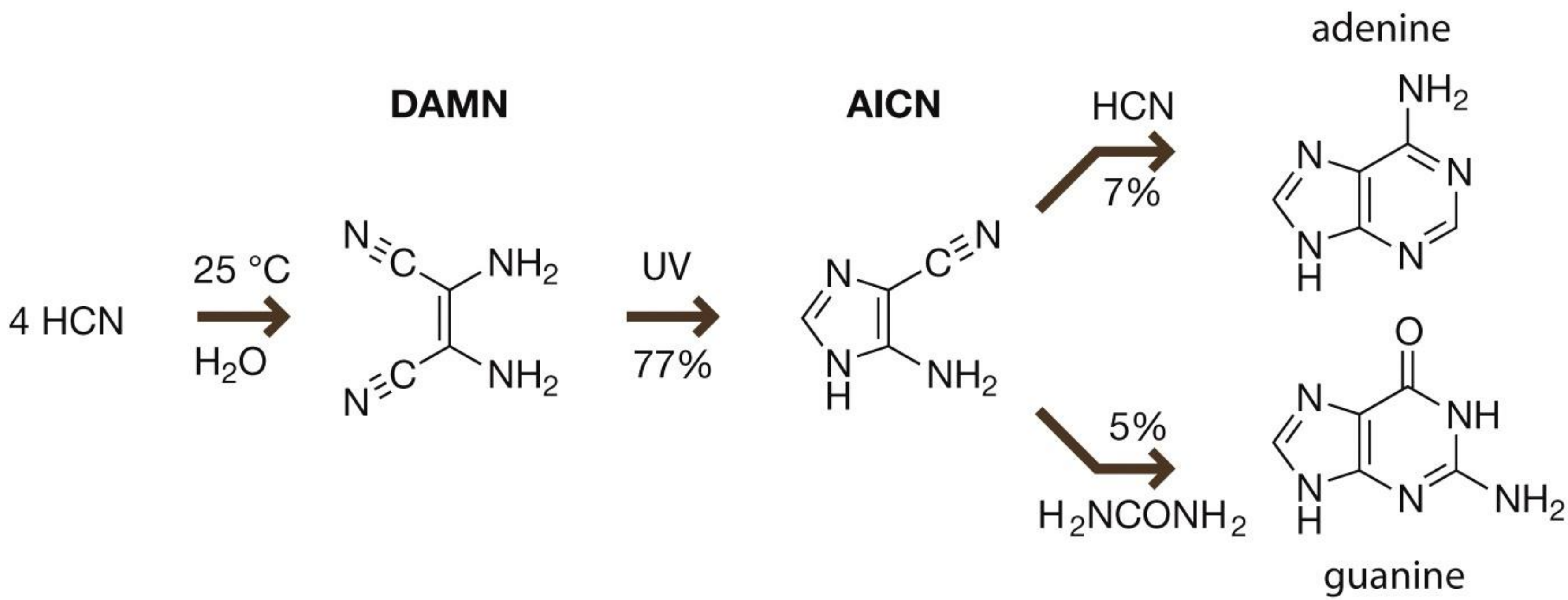
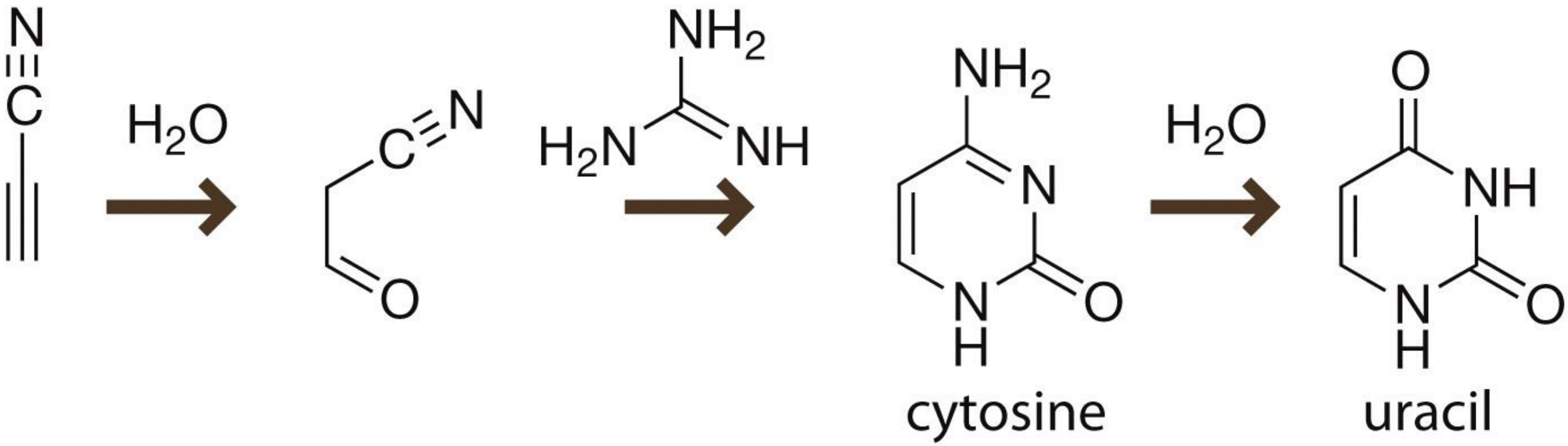


Figure 2.21 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

DAMN (diaaminomaleonitrile) is a key intermediate for the formation of adenine and guanine under prebiotic conditions



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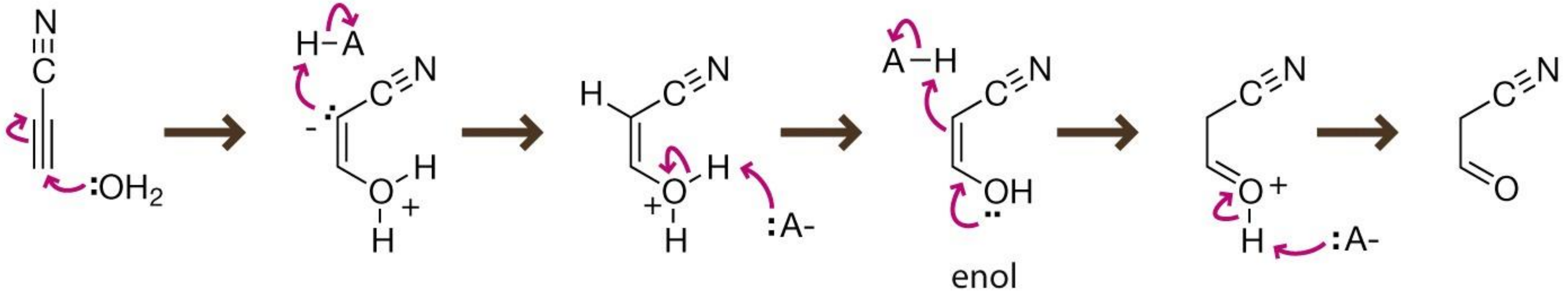
Cyanoacetylene is a precursor in the formation of pyrimidine bases



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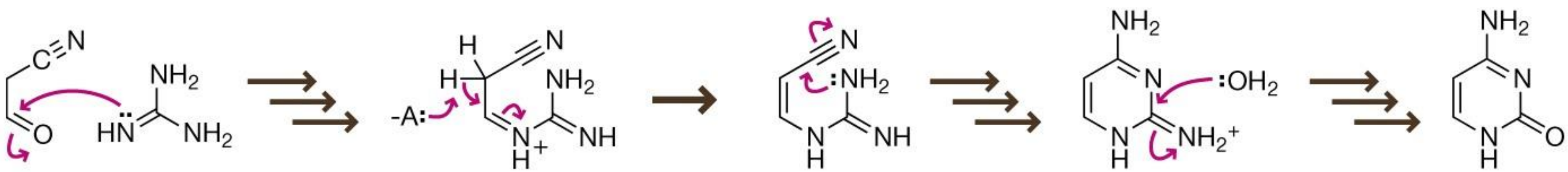

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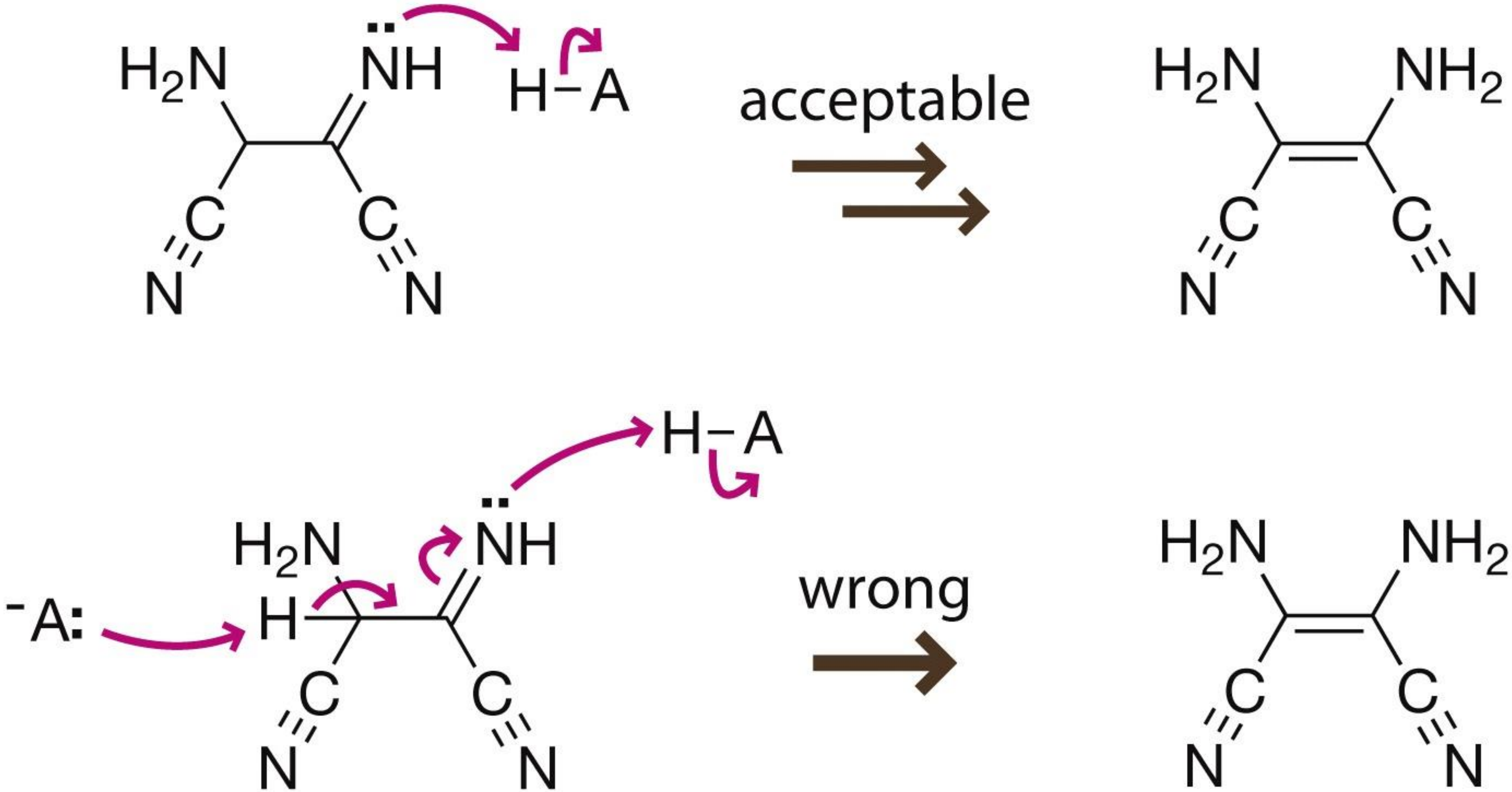
Mechanism for the formation of cytosine



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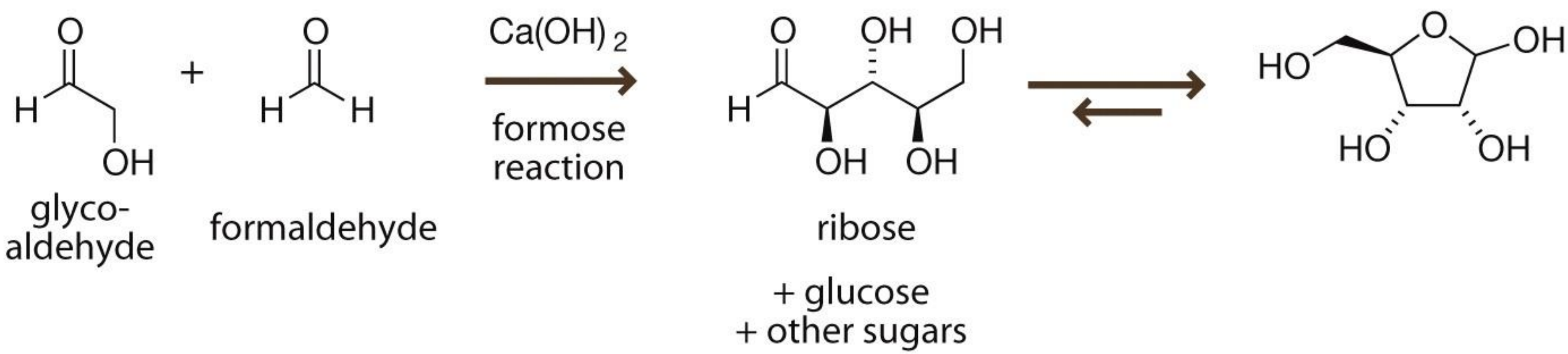

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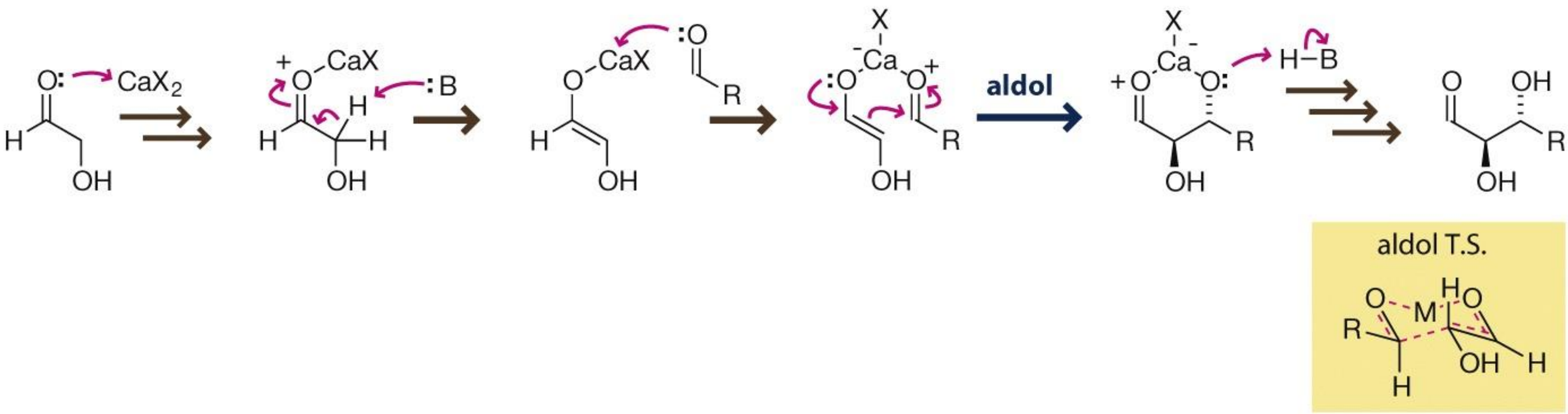
Prebiotic formation of carbohydrates



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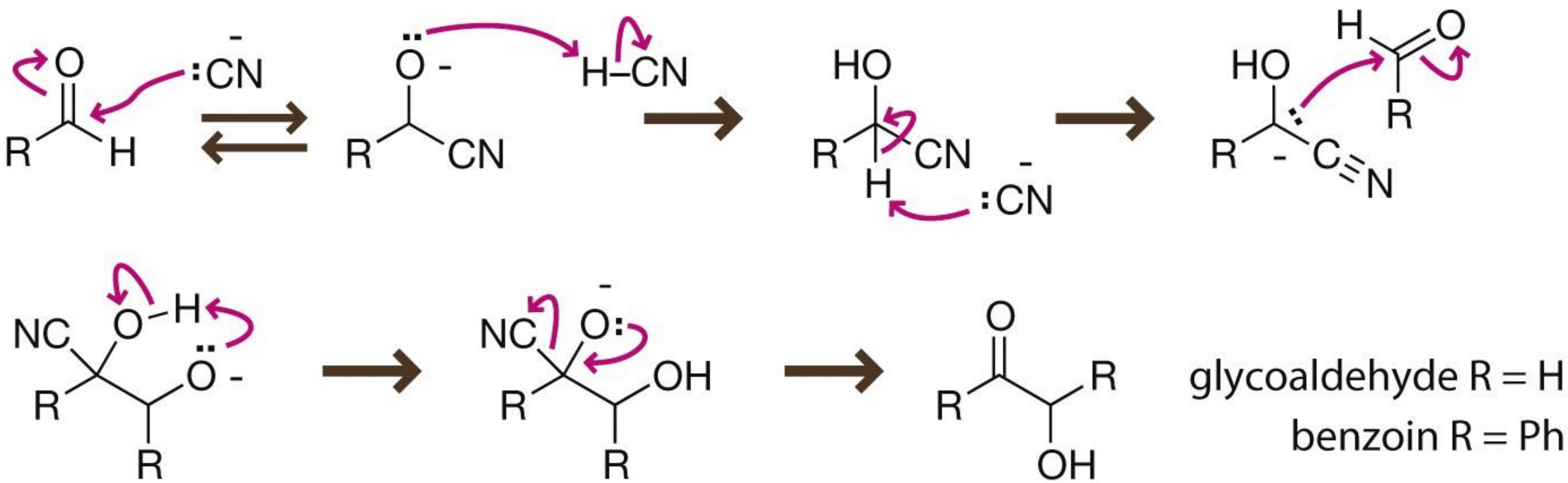

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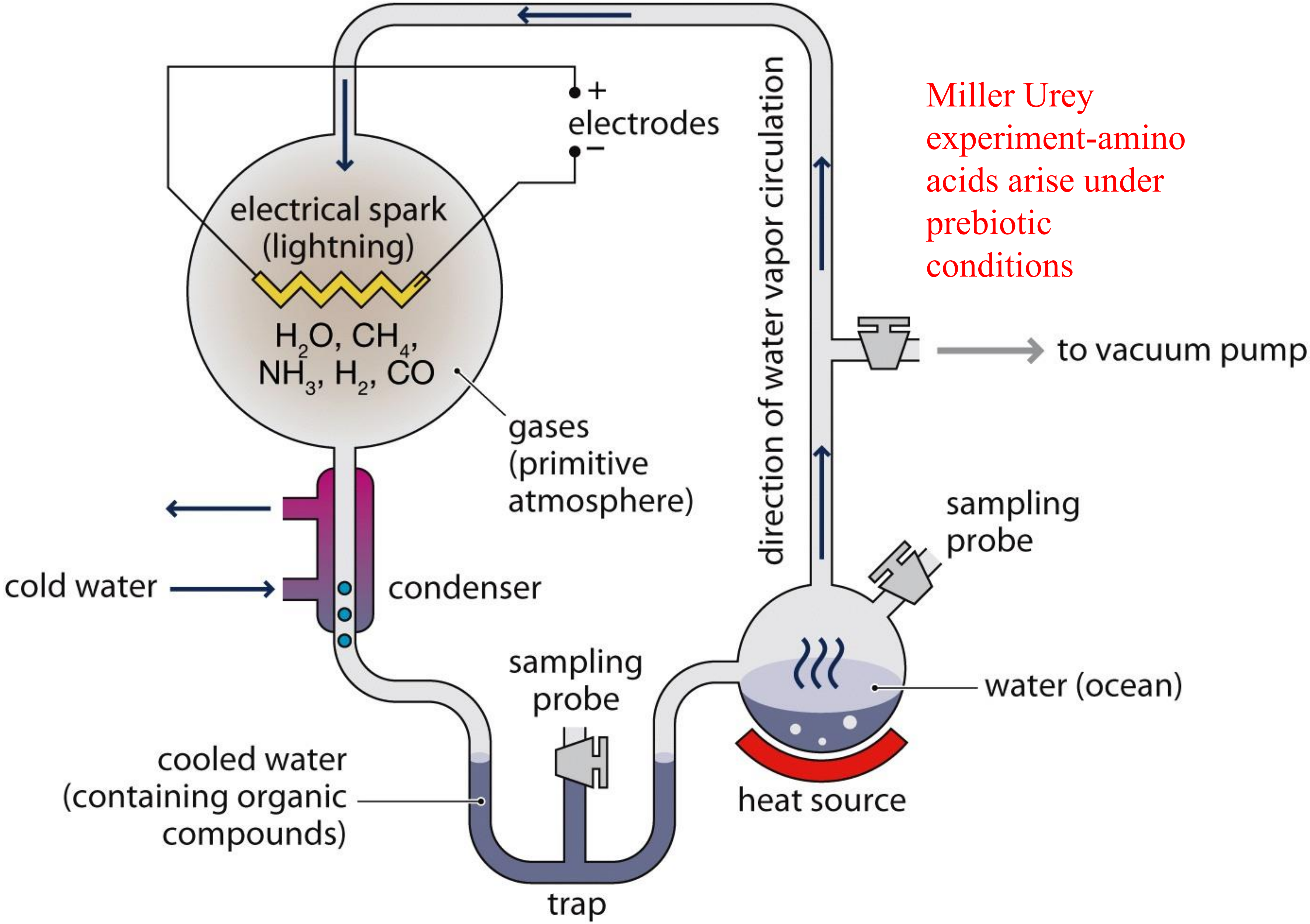
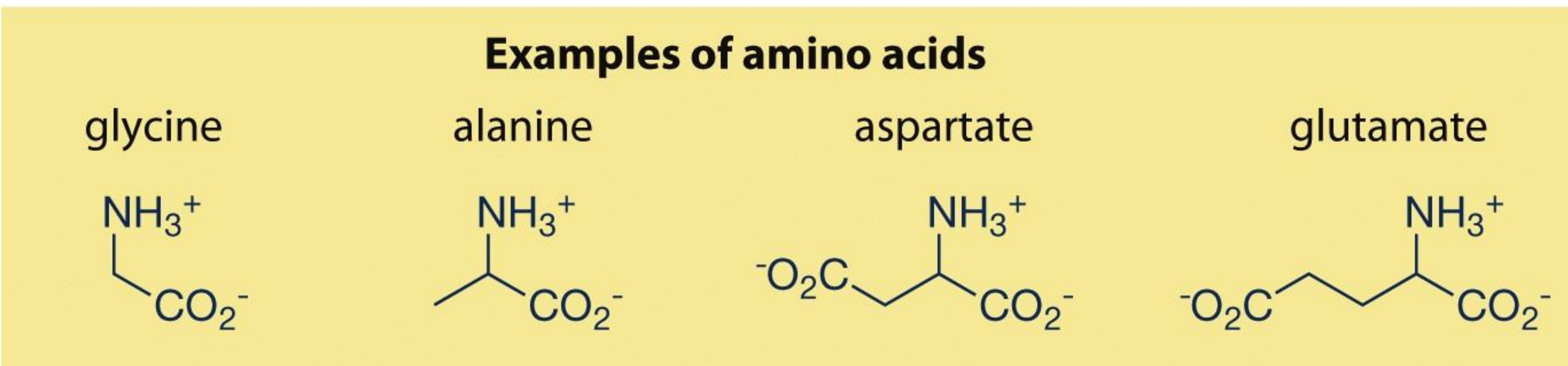
The prebiotic reactions explain the formation of RNA, not DNA
Reverse transcriptase catalyses the formation of DNA from RNA



Miller Urey experiment-amino acids arise under prebiotic conditions

Figure 2.29 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

$$CH_4 + NH_3 + H_2 \xrightarrow[\text{(ii) } H_2O]{\text{(i) electrical discharge}} \textbf{amino acids} + \text{other products}$$



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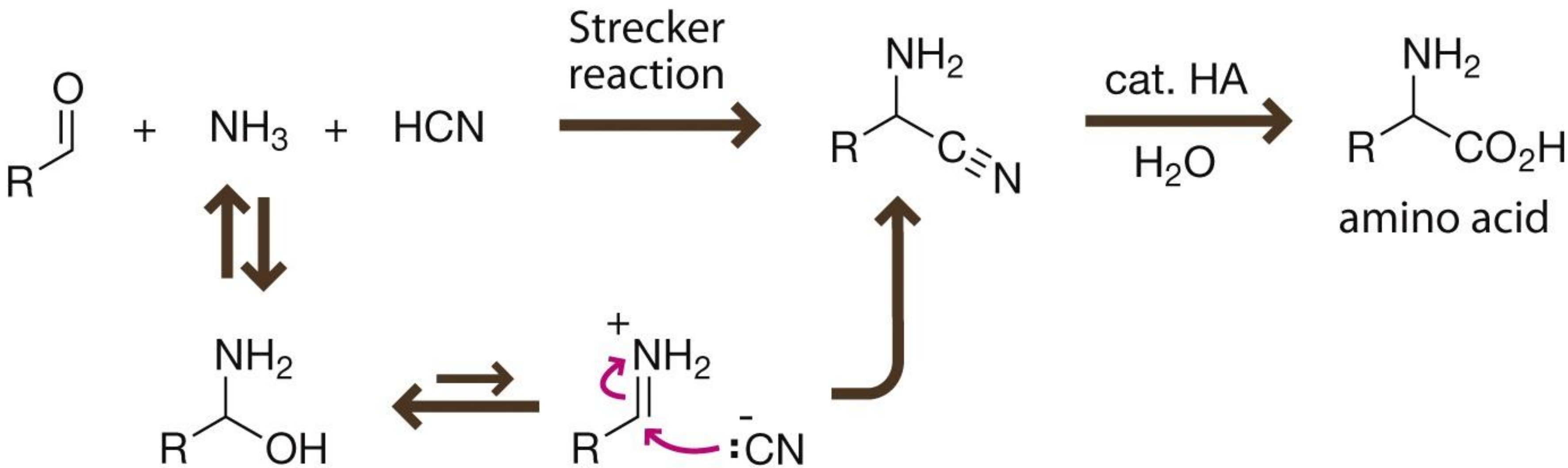

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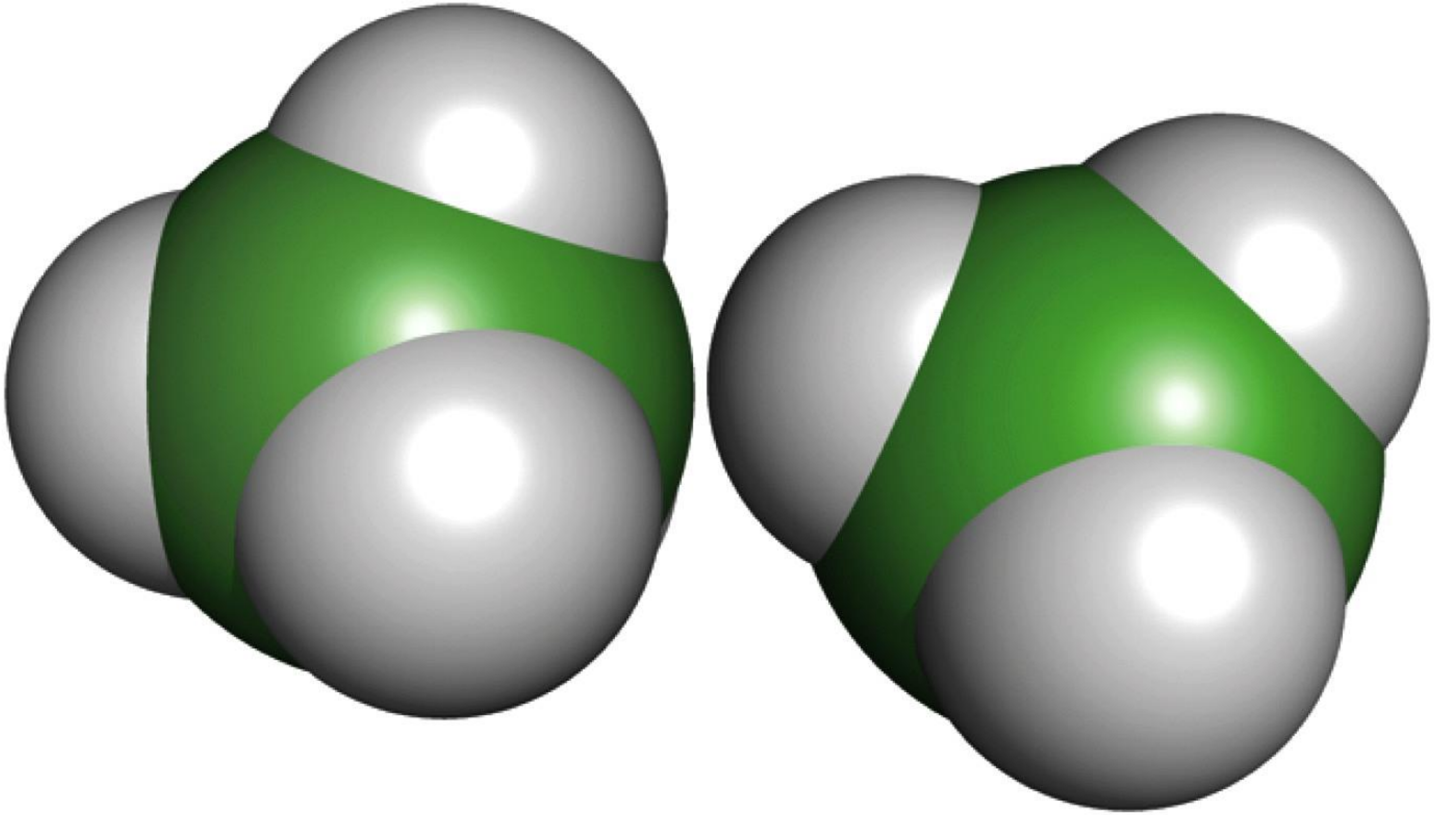


Figure 2.32 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

The weak attraction between two methane molecules is not easily quantified by pertubational molecular orbital theory that we used to think about bonding interactions

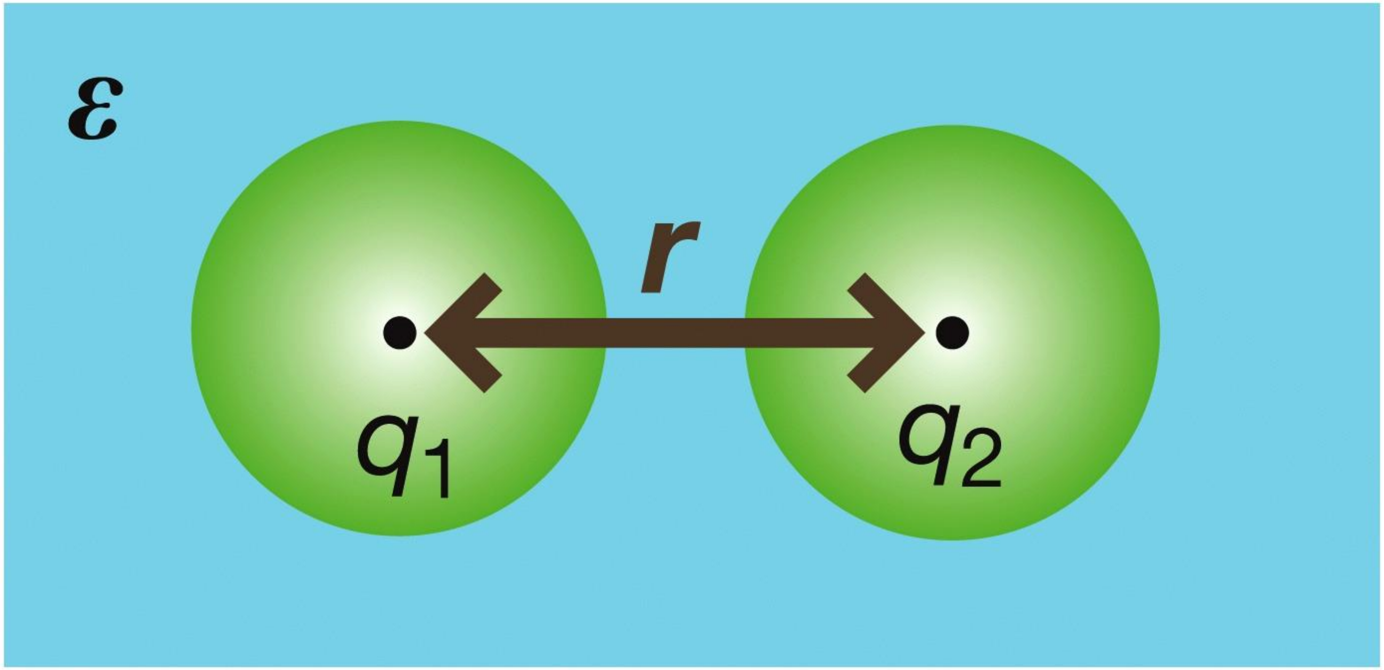
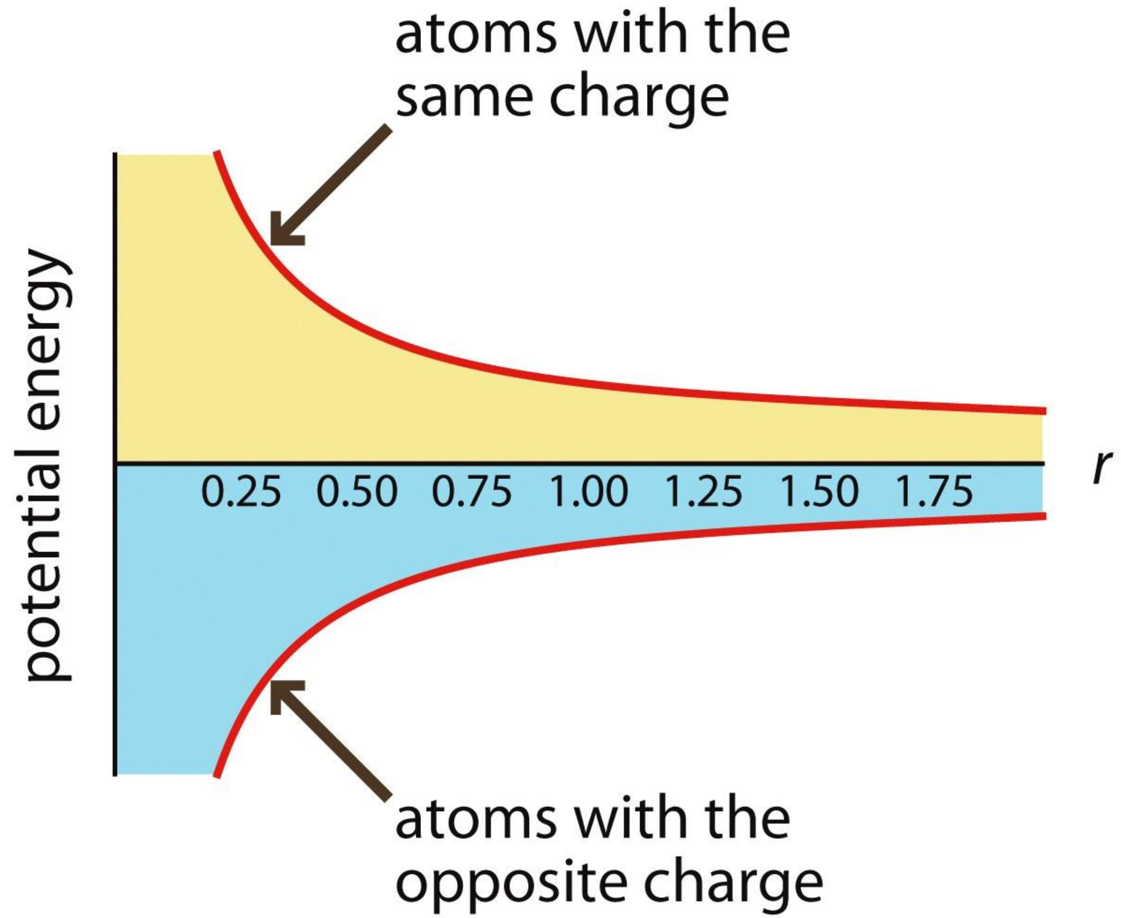


Figure 2.33 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Nonbonding interactions can be quantified by an equation involving electrostatic interactions and both attractive and repulsive van der Waals interactions



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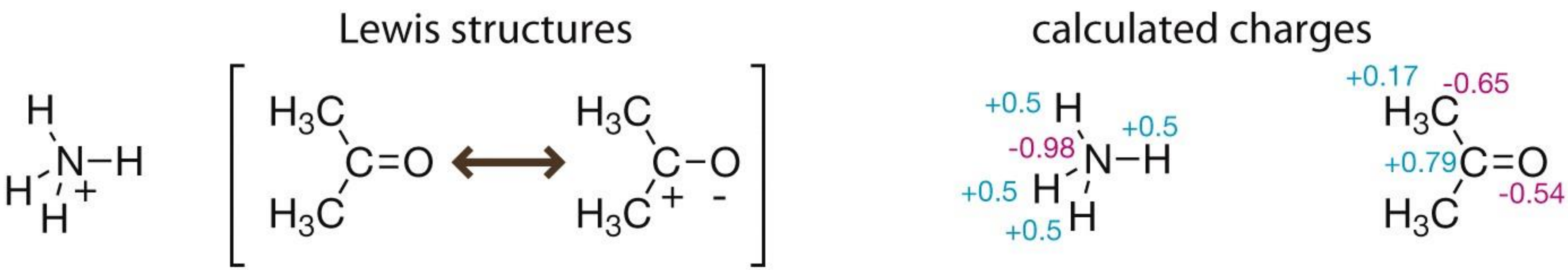
The Coulombic potential. As distance between the atoms increases the potential energy for the interaction approaches zero



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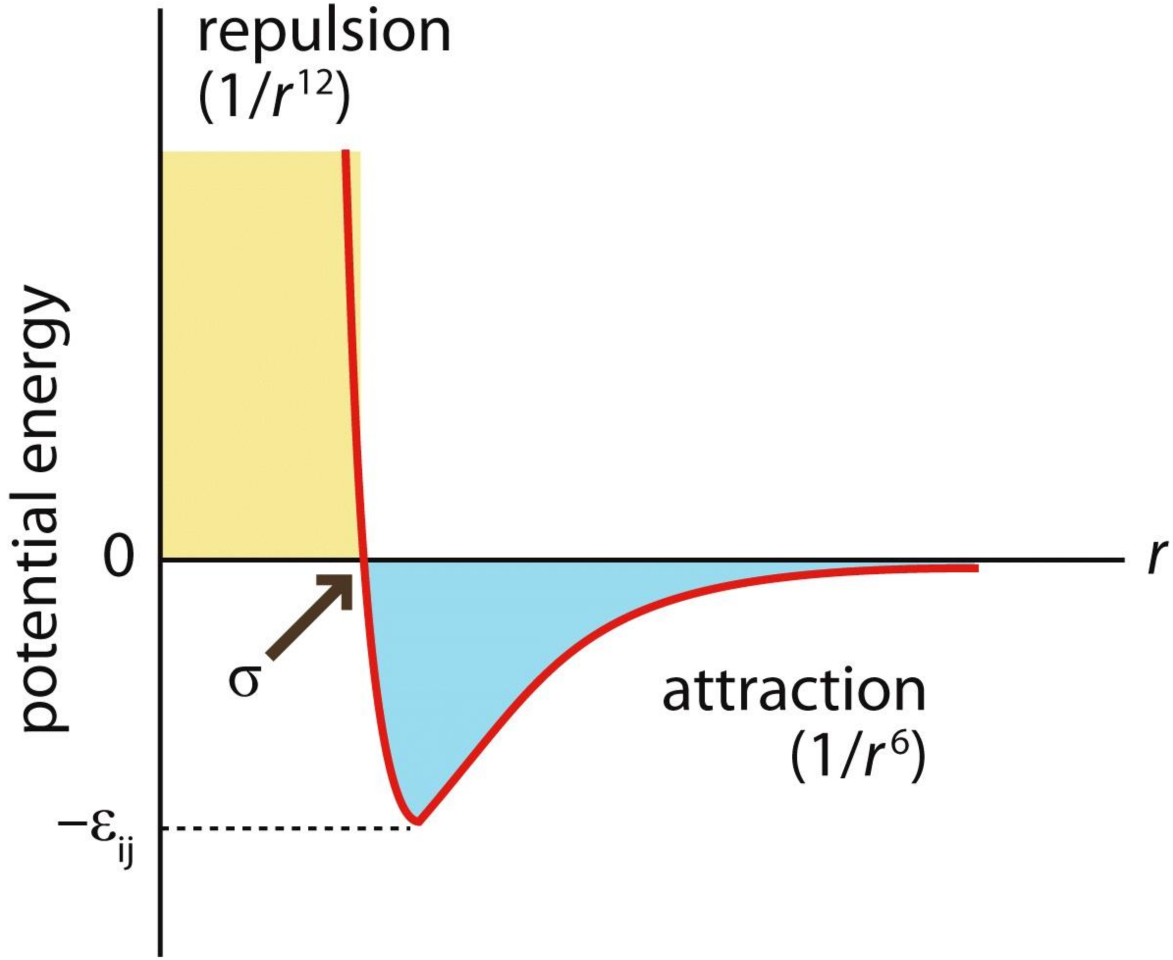
The formal charge in Lewis structures offer misleading picture of the partial charges on atoms



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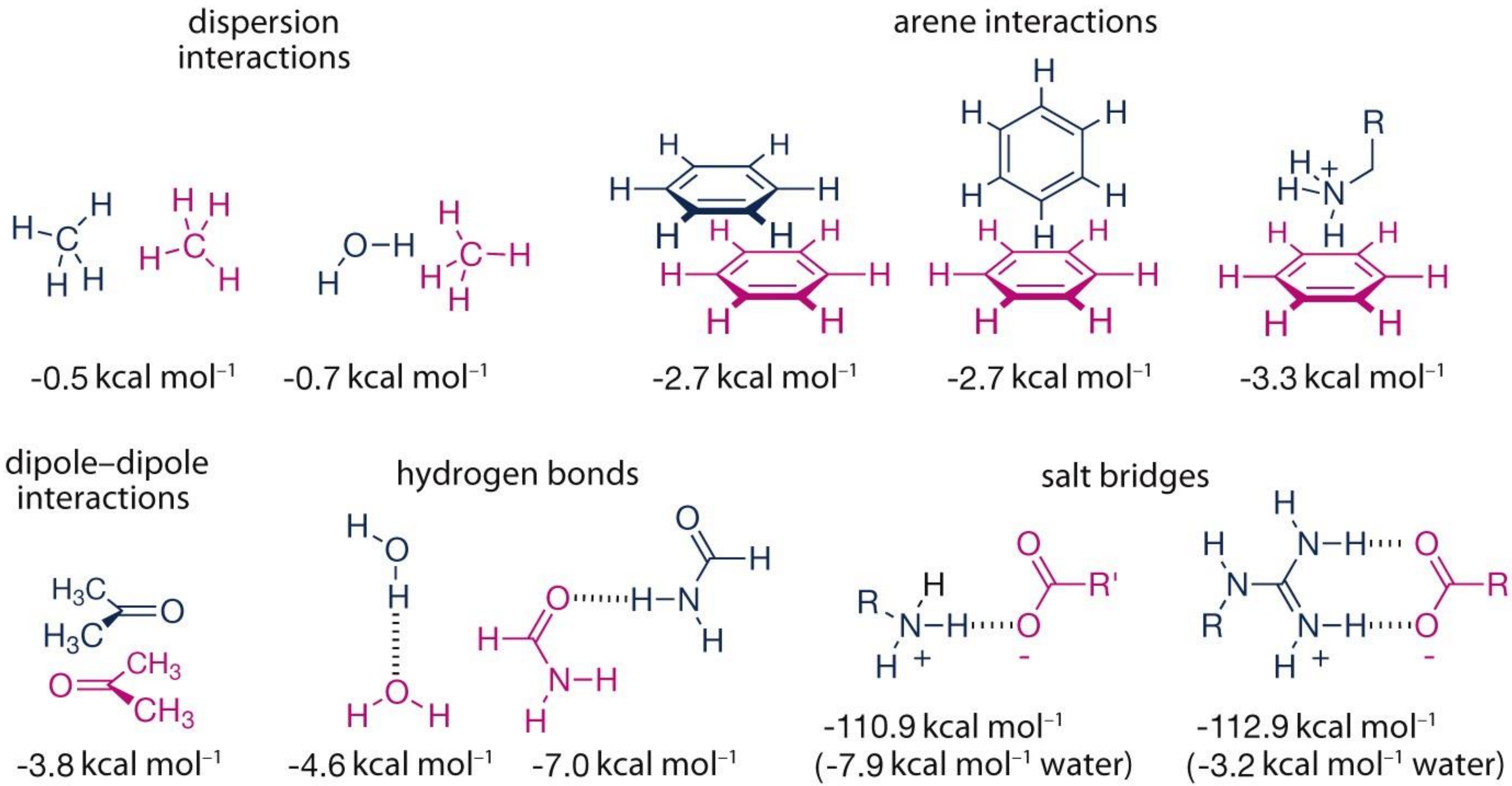
The Lennard Jones potential. As the distance r between the atoms increases the attraction between the atoms (blue) approaches zero. Strong repulsion (yellow) results when the twoatoms are too close.



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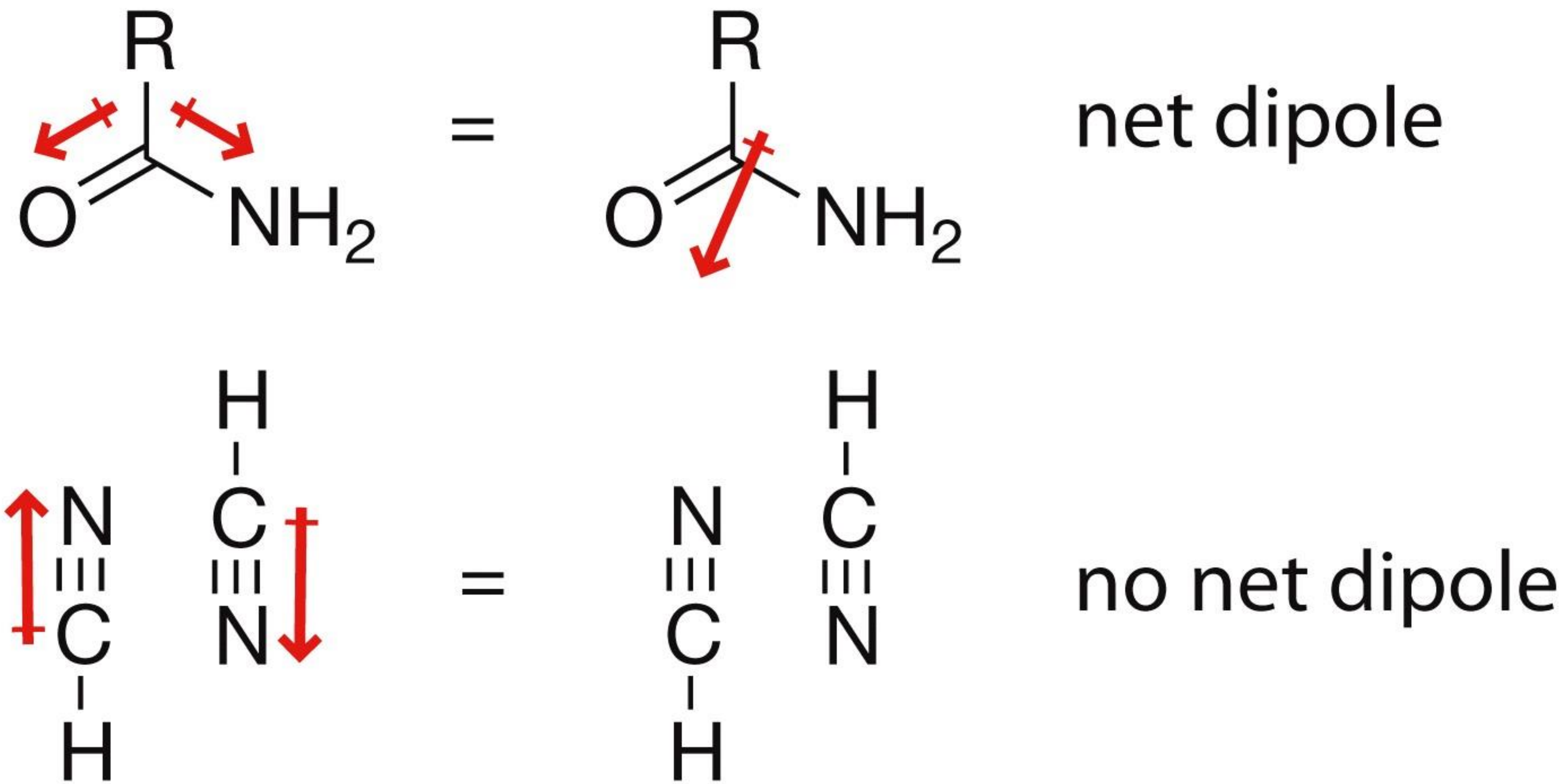

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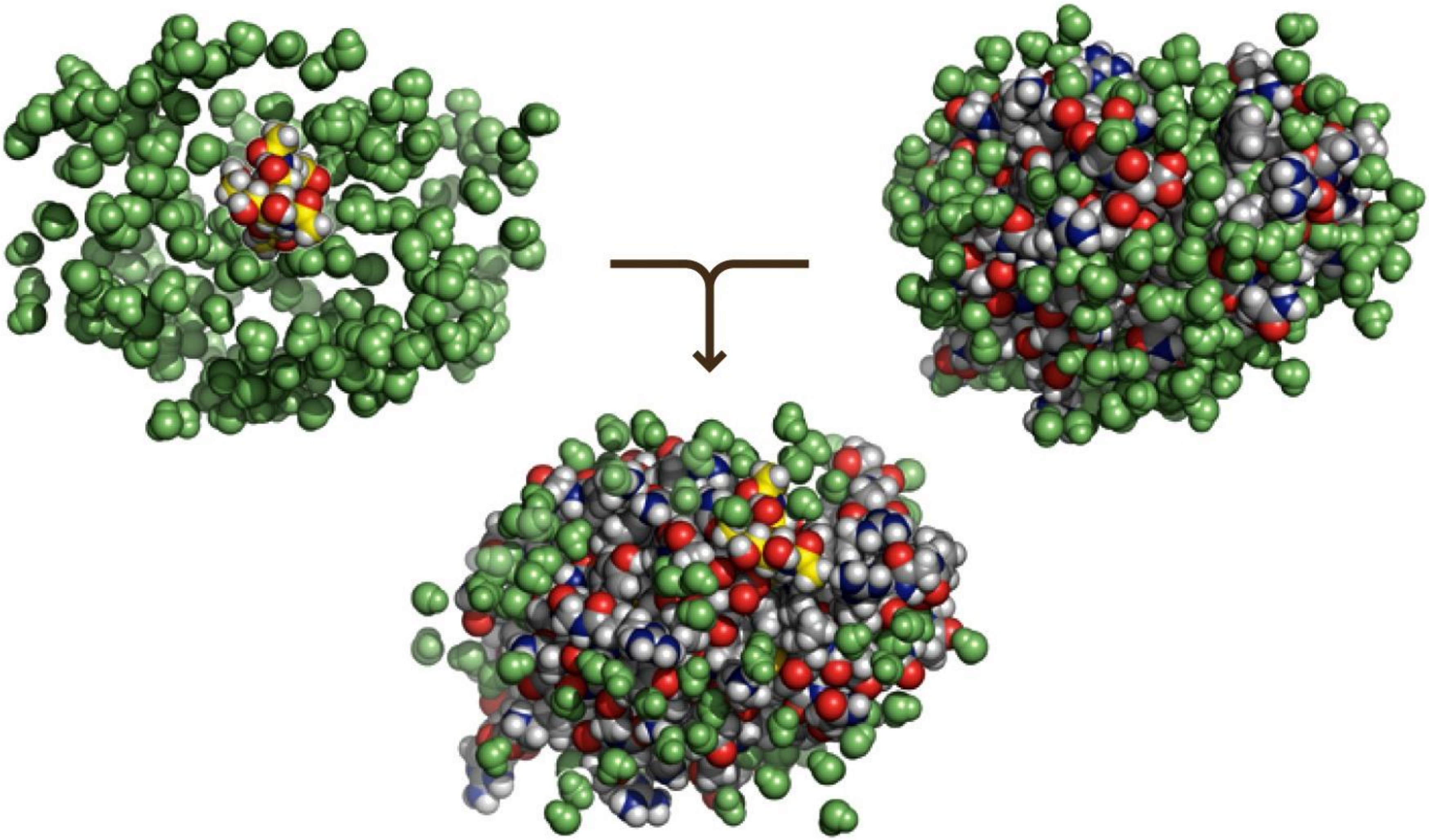

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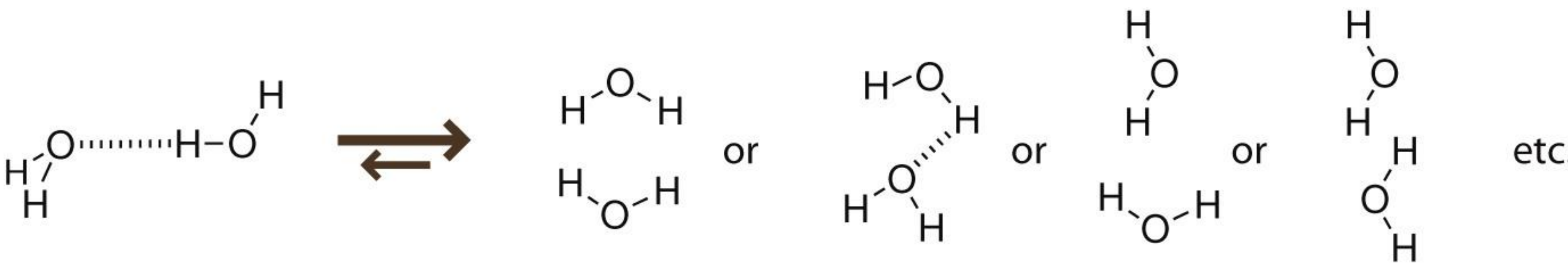
Both a ligand and a protein must give up many favorable interactions with water to form a protein ligand complex



ΔH_{298} **-4.6** kcal mol^{-1}

$-T\Delta S_{298}$ +6.3 kcal mol^{-1}

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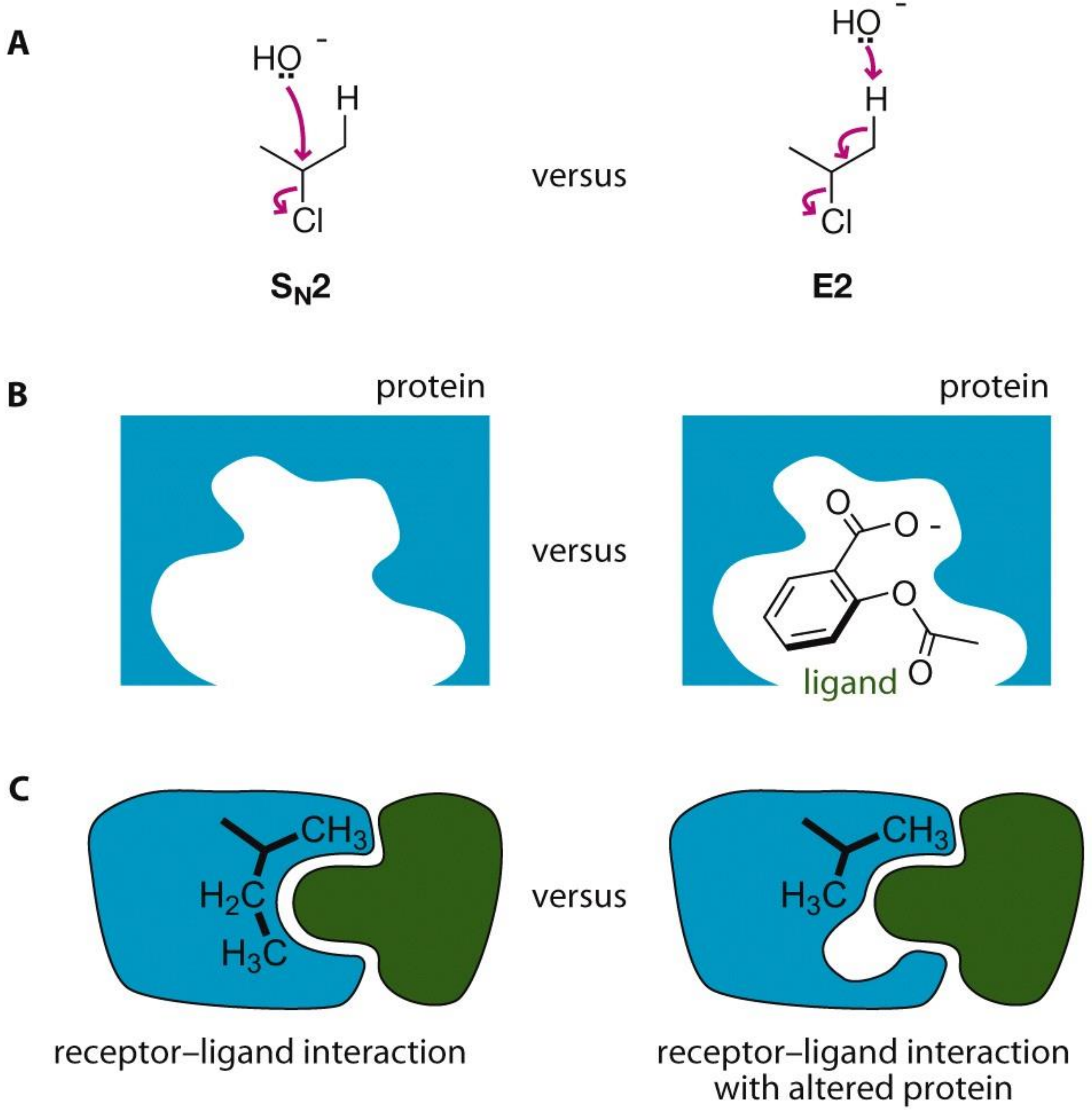
Entropy complicates hydrogen-bonding.
An ideal hydrogen bond between water molecule is thermodynamically unfavorable relative to the multitude of other possibilities



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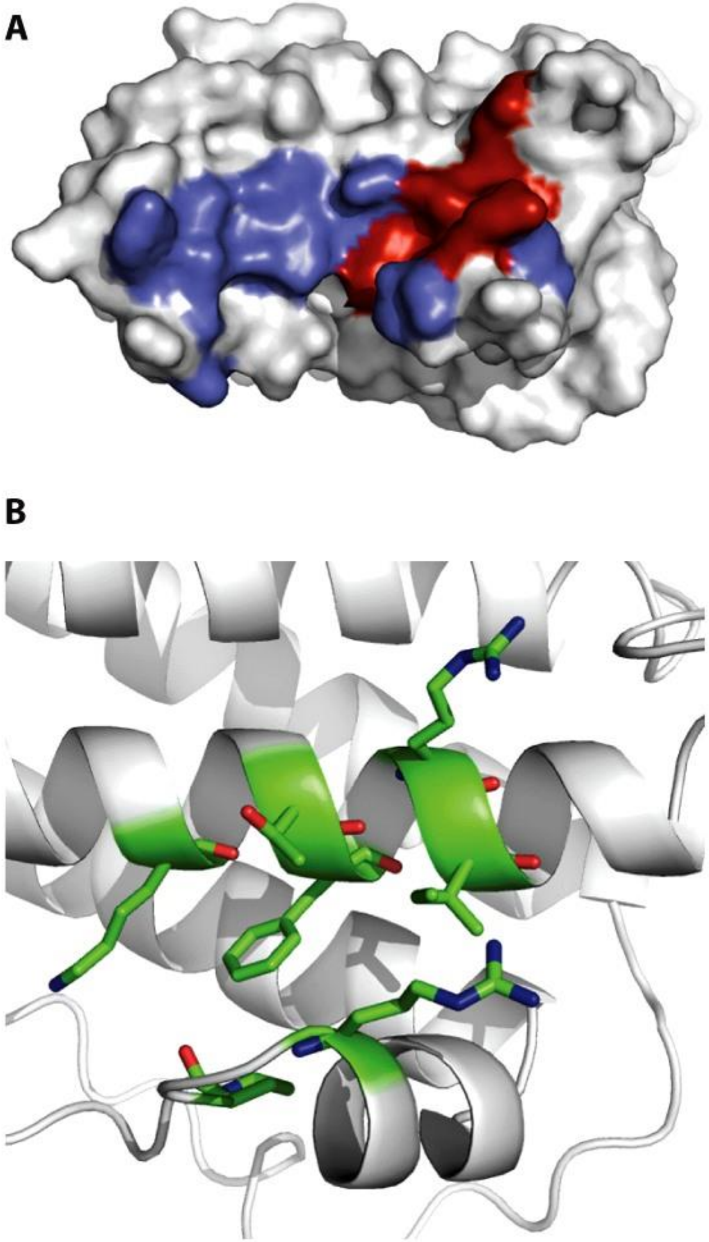
A

B



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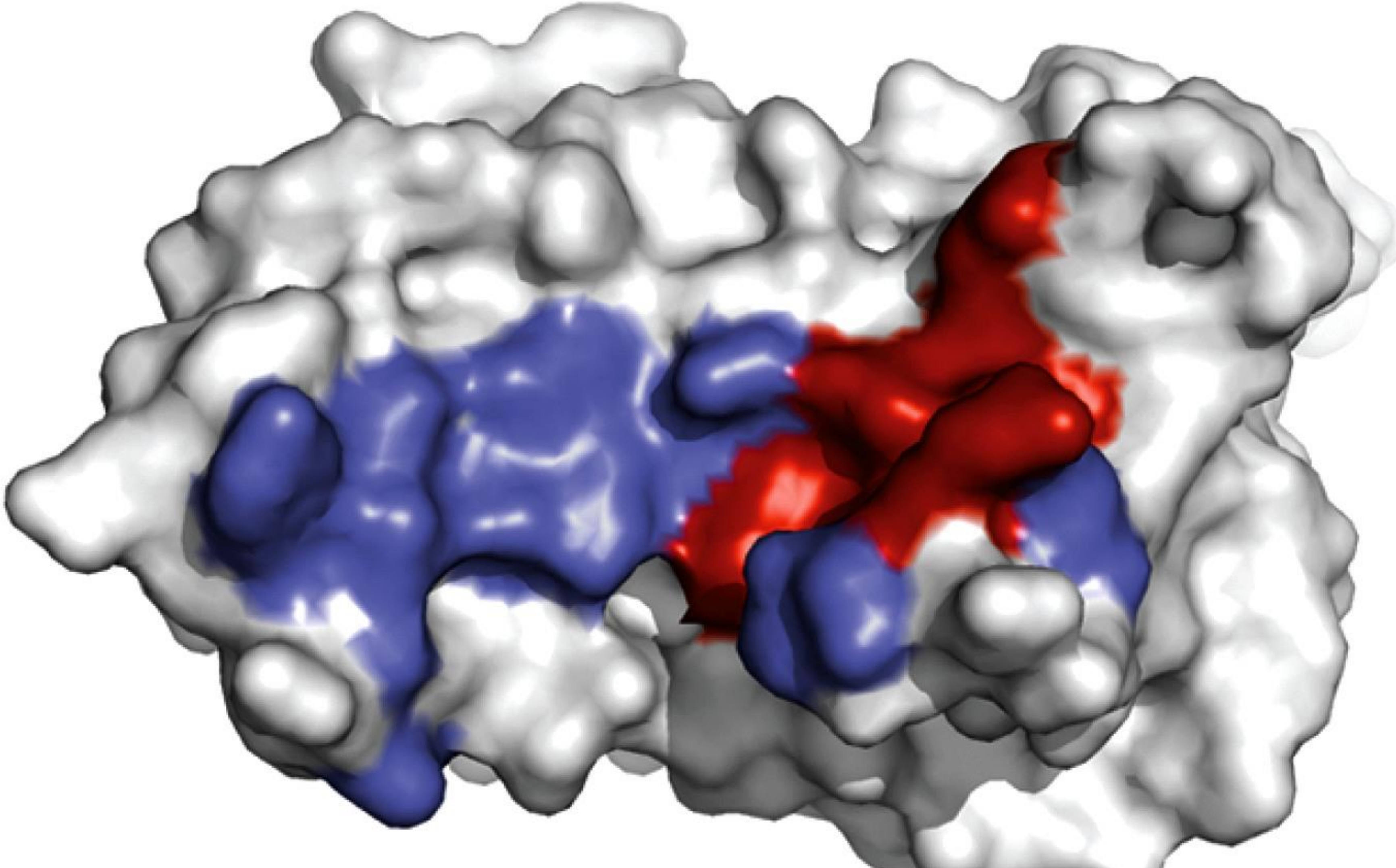

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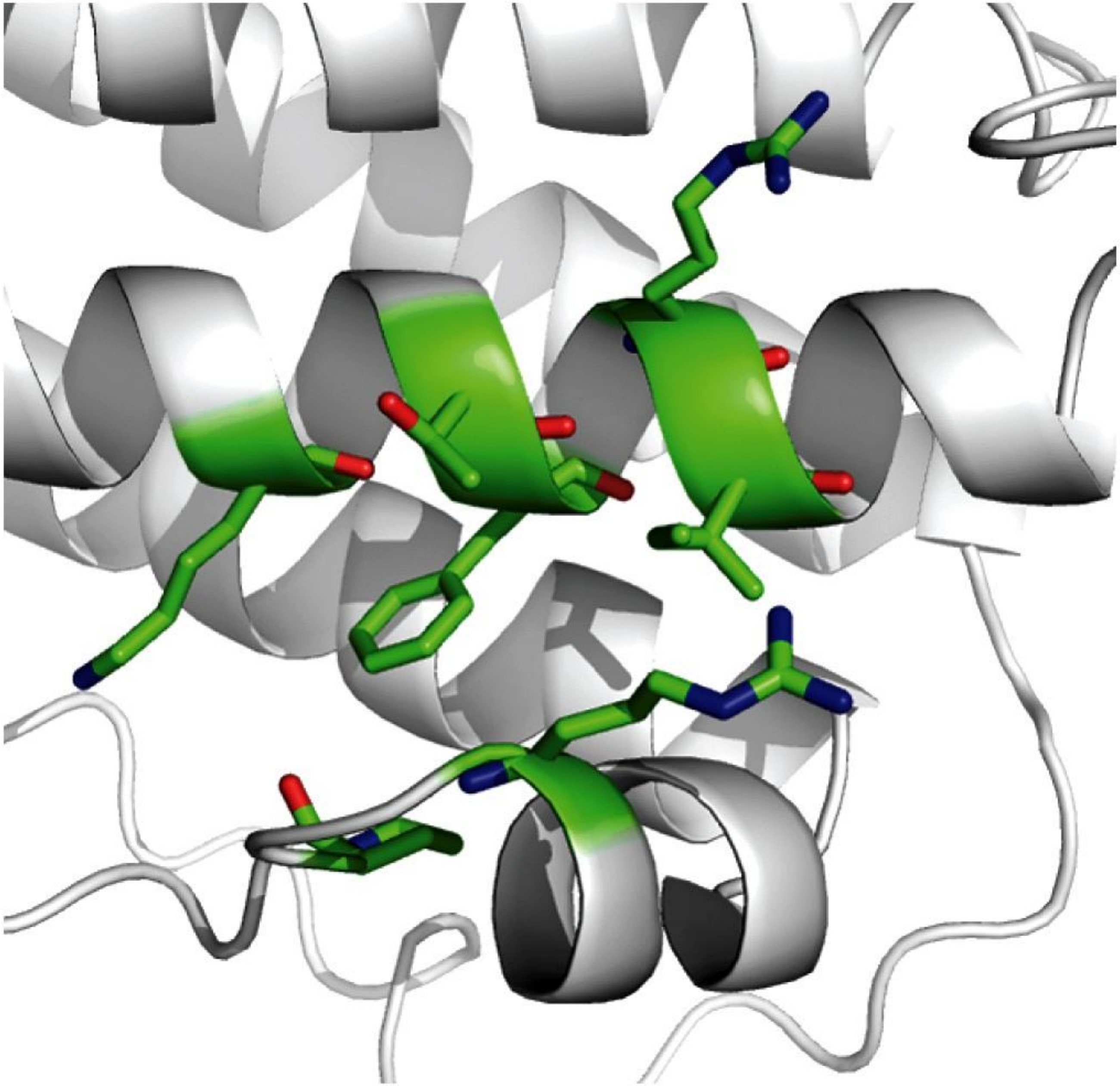

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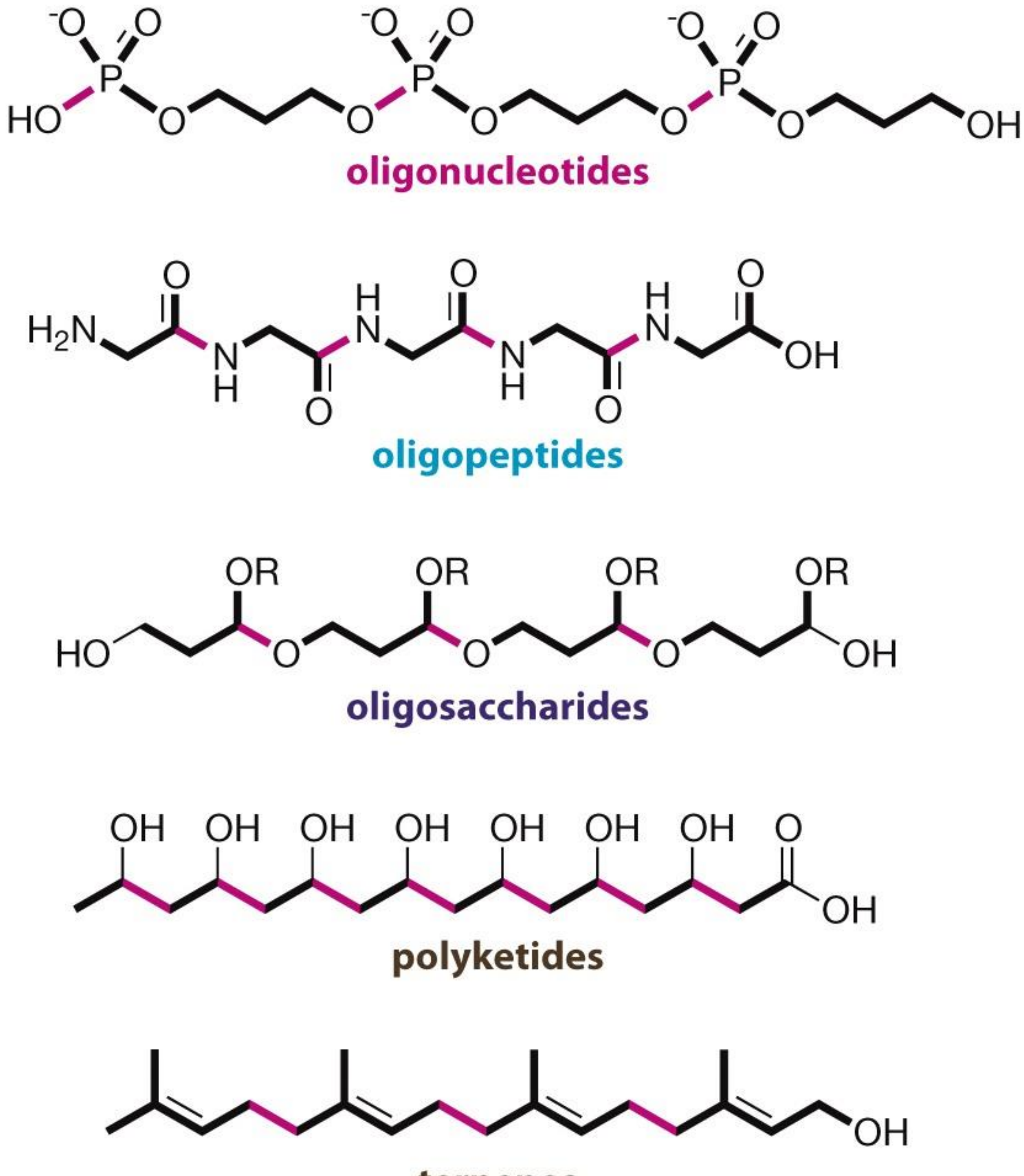

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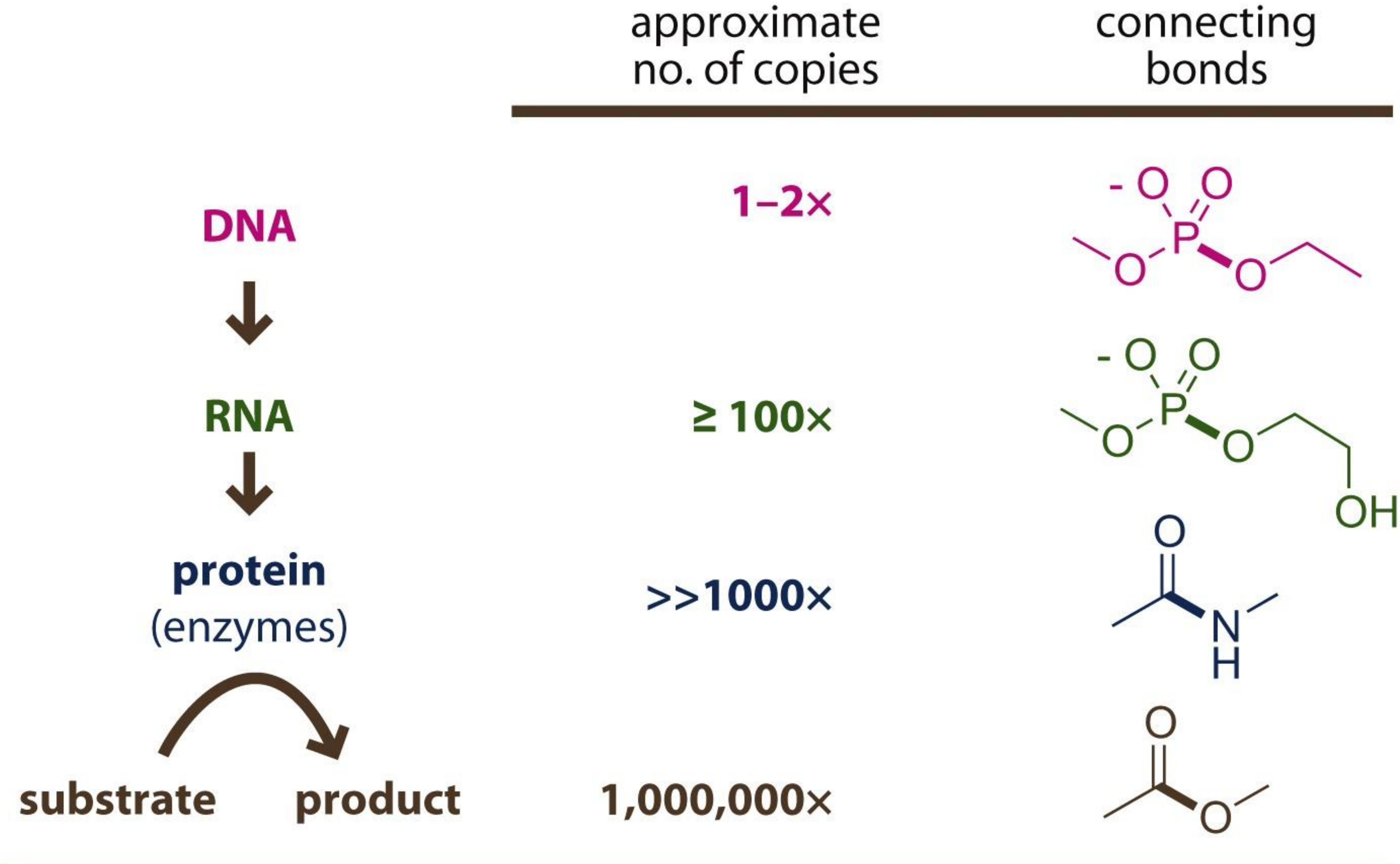

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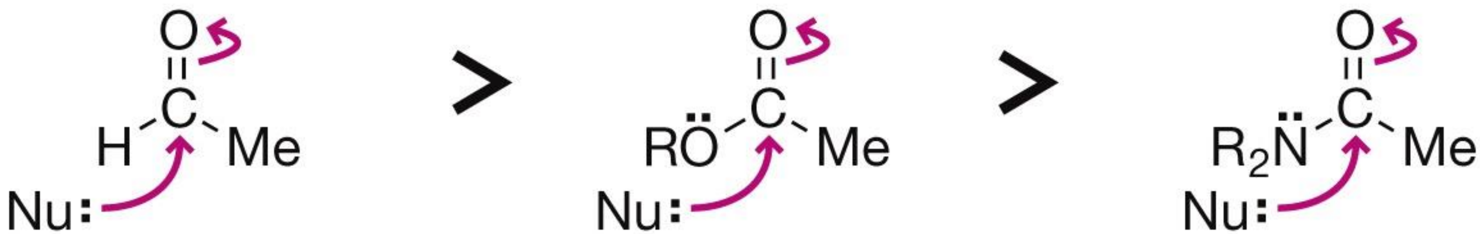
Table 2.3 Half-lives for hydroxide-dependent hydrolysis of various functional groups in neutral water.

Functionality	Relevance	Half-life at pH 7 (years)
carboxylic ester	lipids	<1
carboxylic amide	peptides	300
ribose phosphate diester	RNA	2200
phosphate diester	DNA	220,000
β-glucofuranoside	RNA/DNA	22,000,000

relative rates



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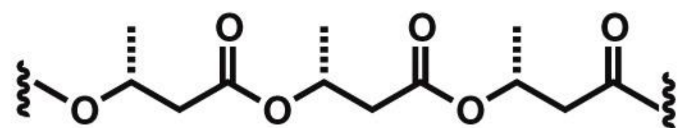

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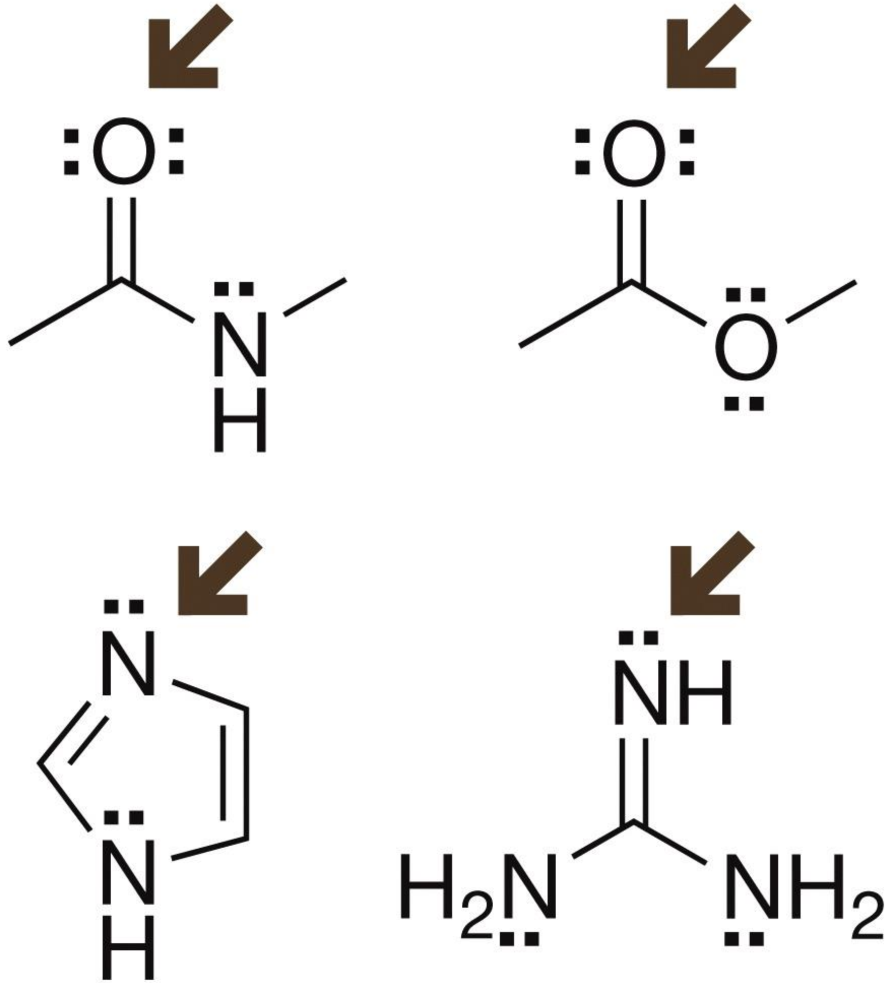
Polyesters-biodegradable



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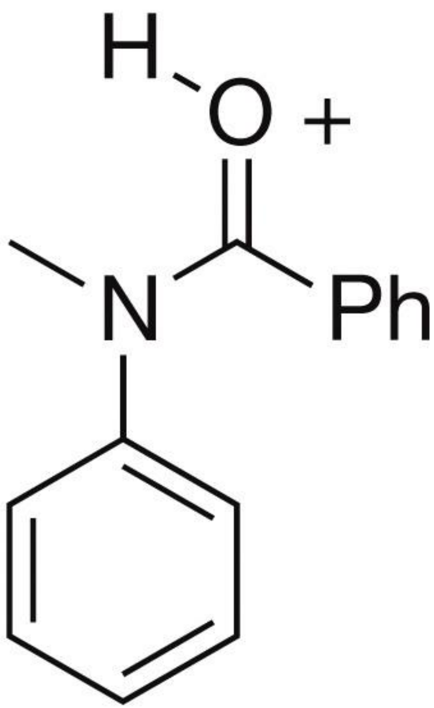
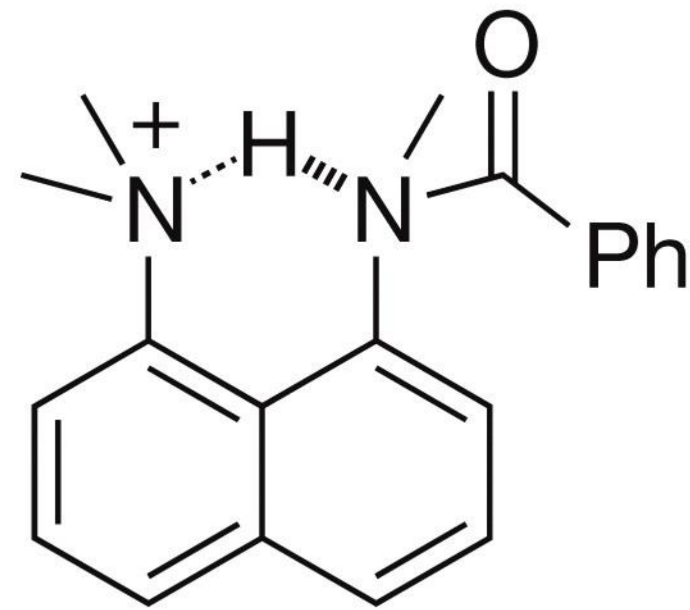
Preferred cites of protonation



normal case



special case

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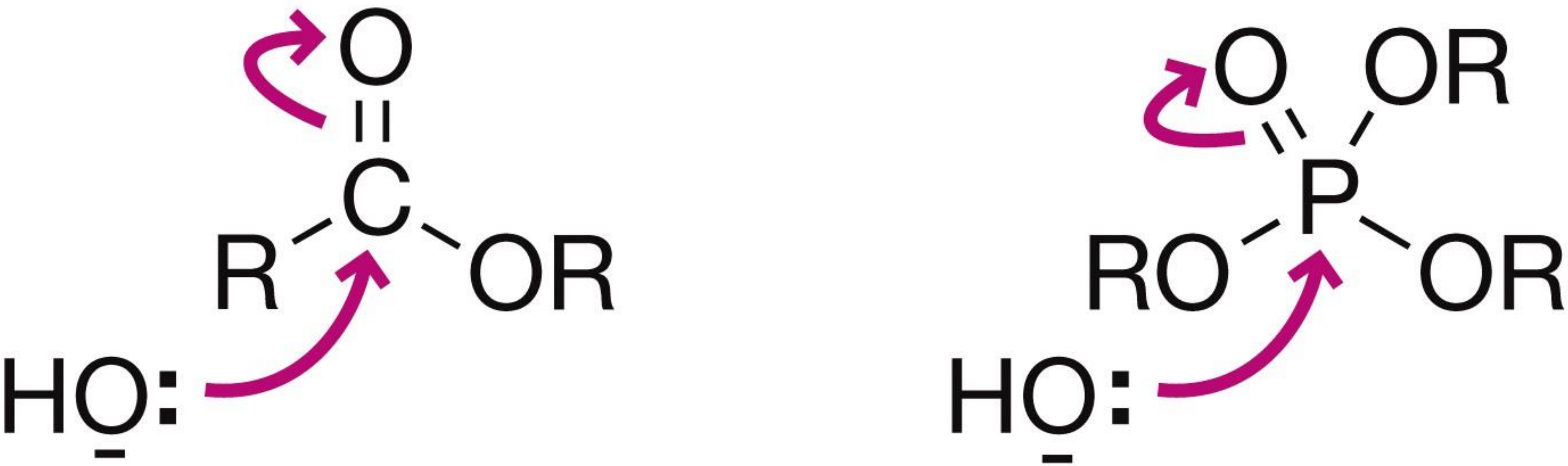


Figure 2.50 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)

Nucleophilic attack on a carboxylic ester is faster than attack on a phosphate ester

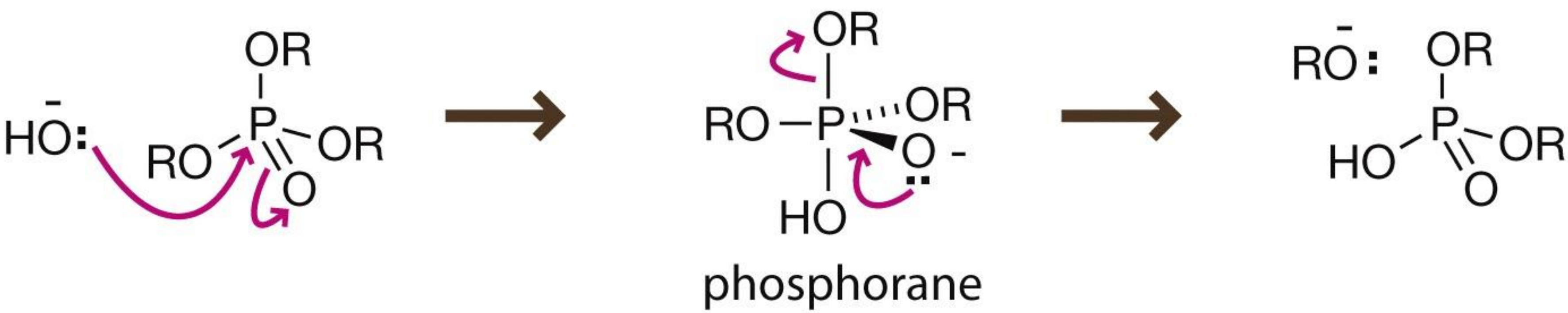
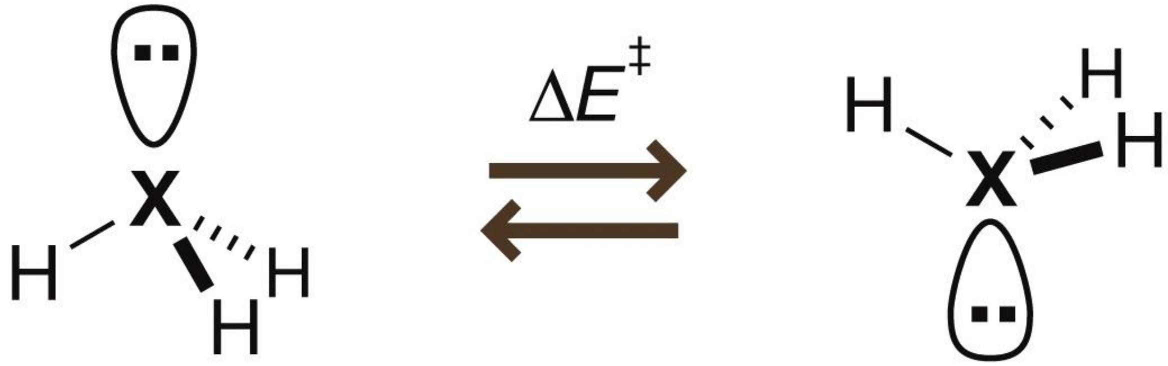


Figure 2.51 Introduction to Bioorganic Chemistry and Chemical Biology (© Garland Science 2013)



$:XH_3$ inversion barrier in kcal mol^{-1}

C^- 13.0	N 16.5	O^+ 1.7
Si^- 34.7	P 37.8	S^+ 32.4

Slower inversion

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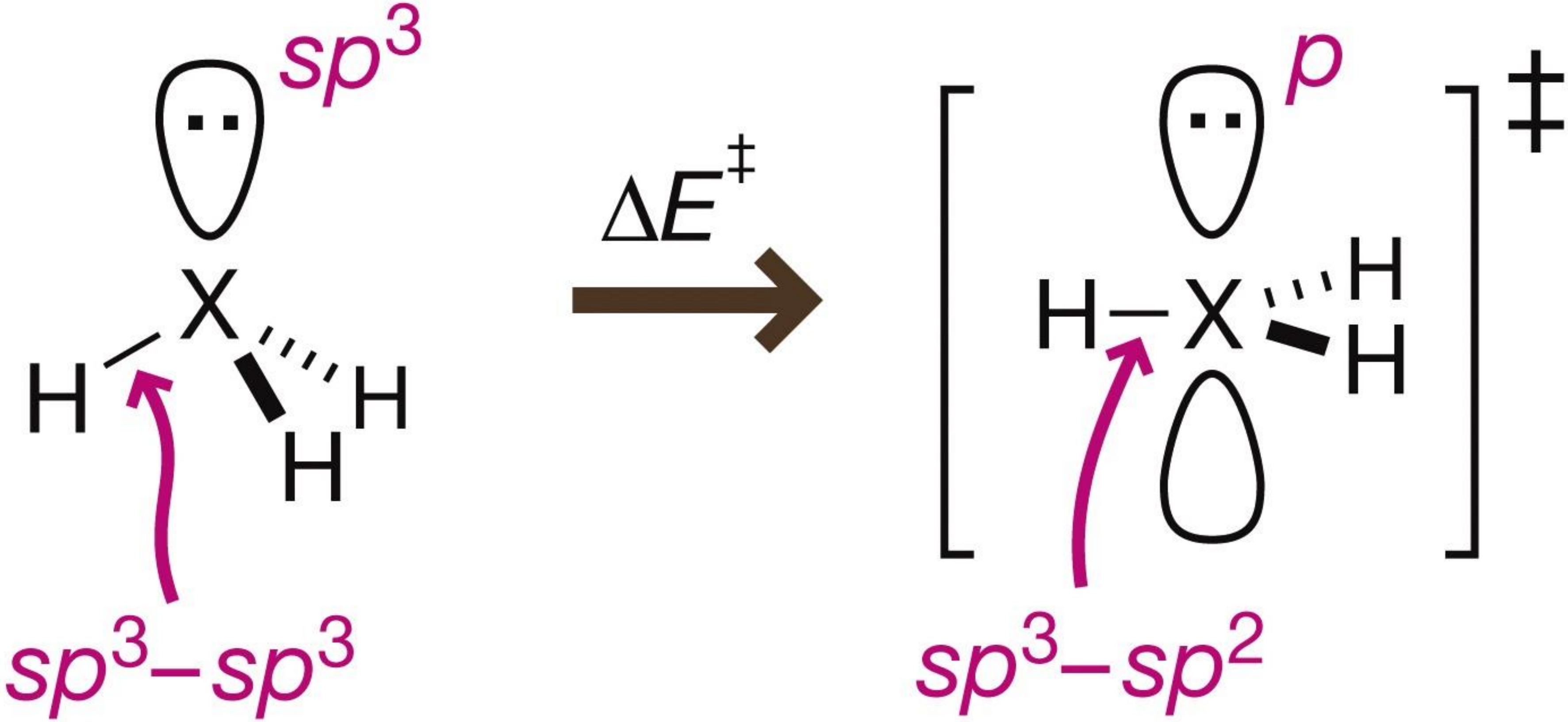

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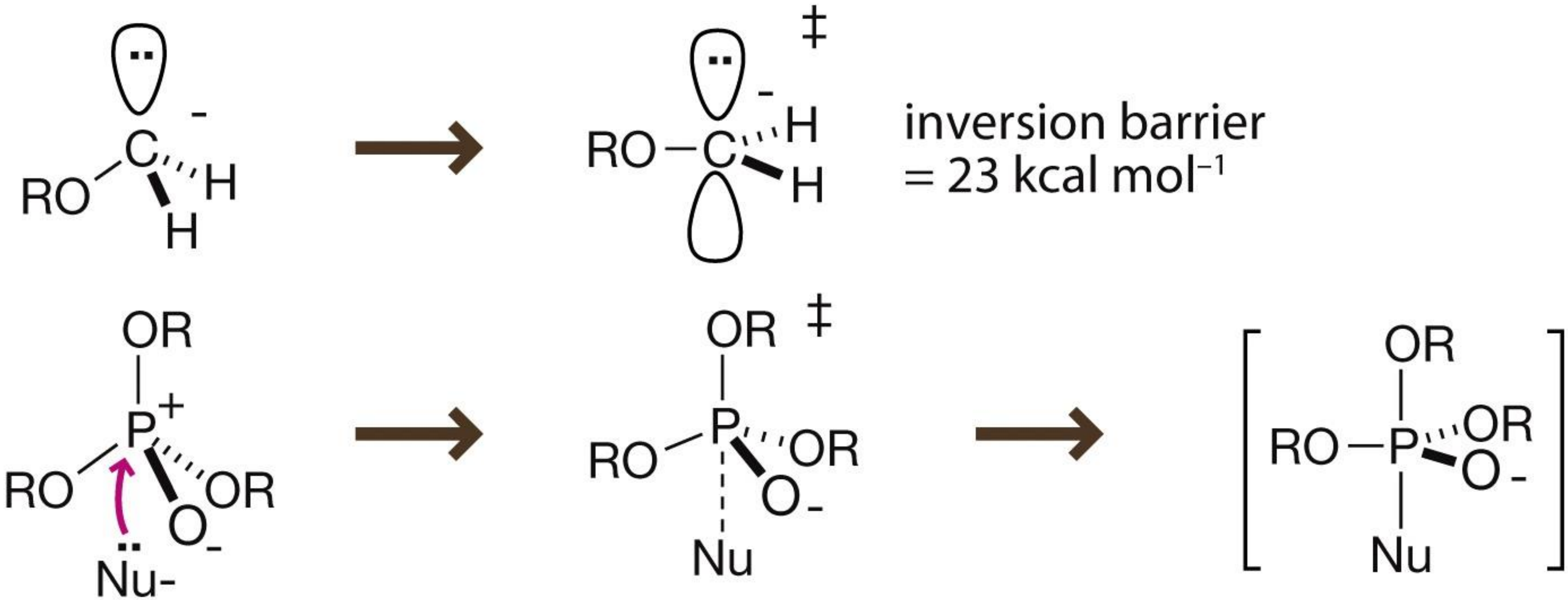

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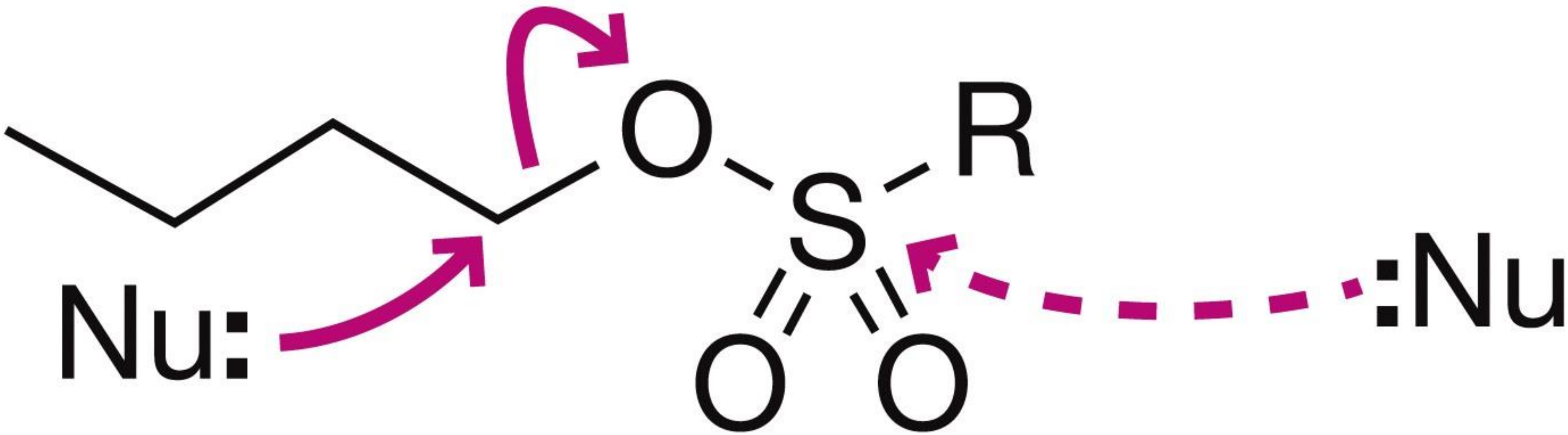

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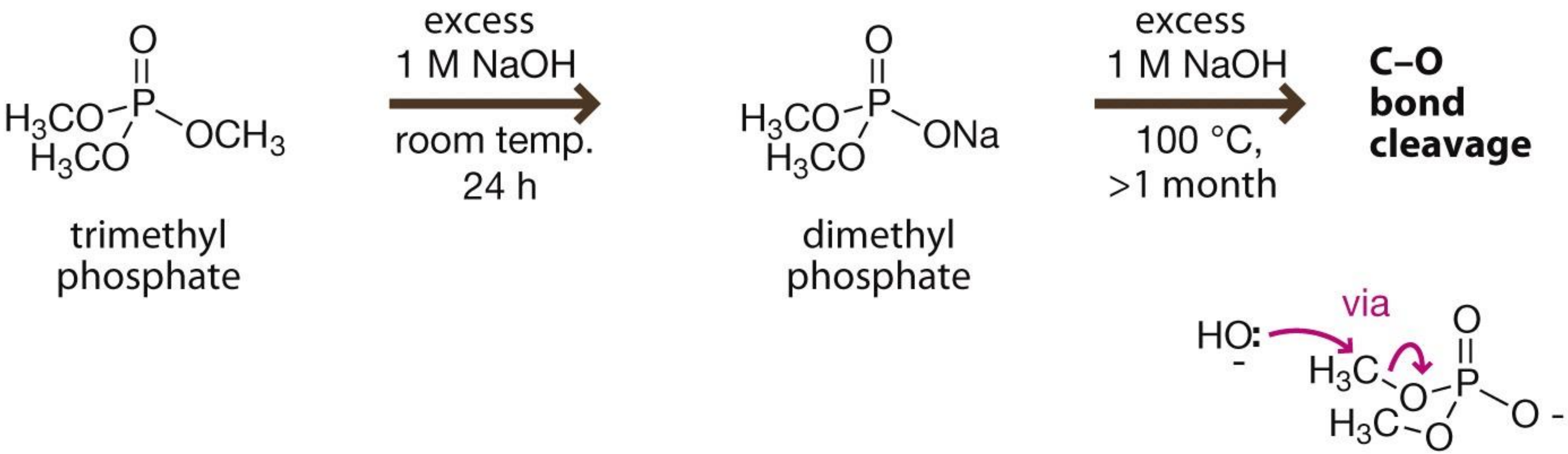

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