Transition State Analogs

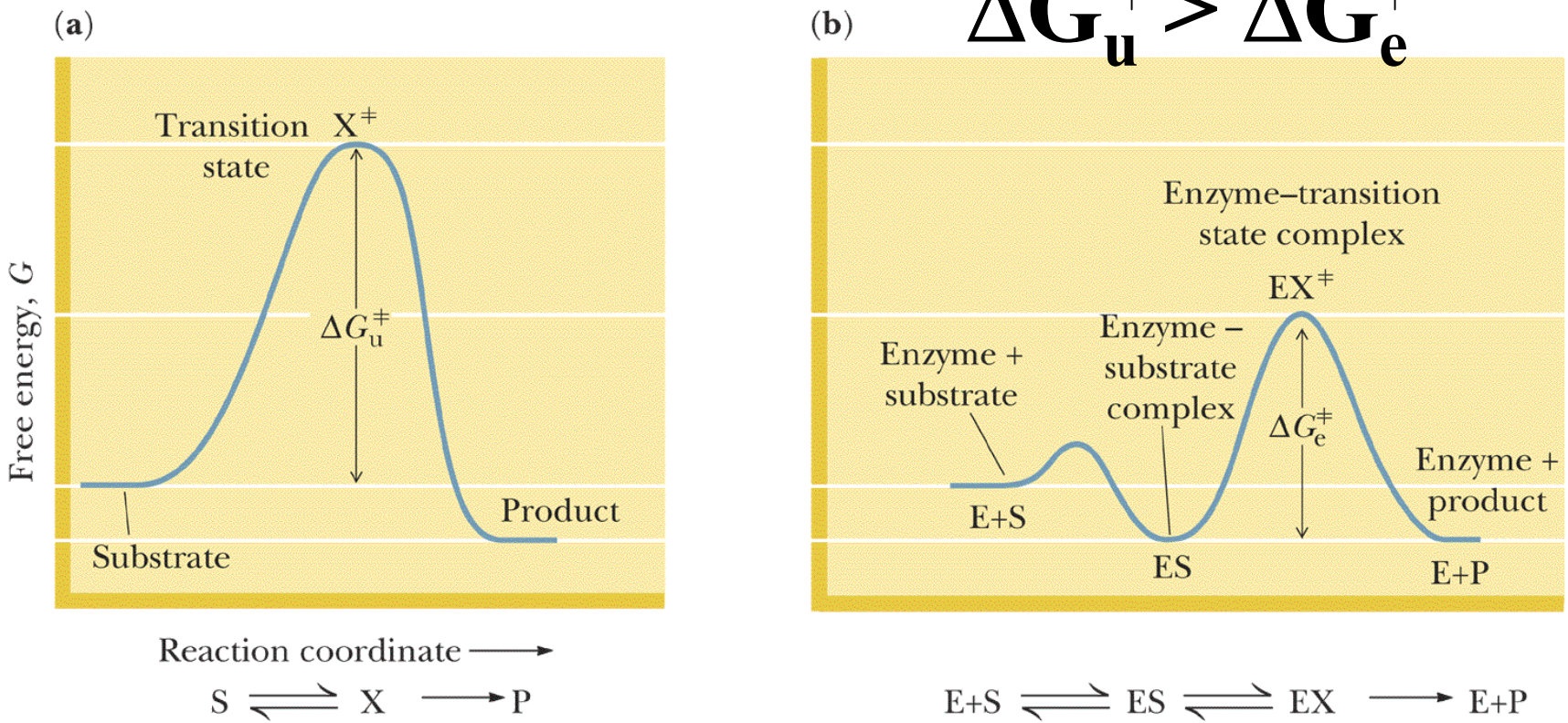
(catalytic antibodies and TSA examples)

Transition State Stabilization

Garrett/Grisham, Biochemistry with a Human Focus
Figure 11.1

Transition state is MORE stable than ES!

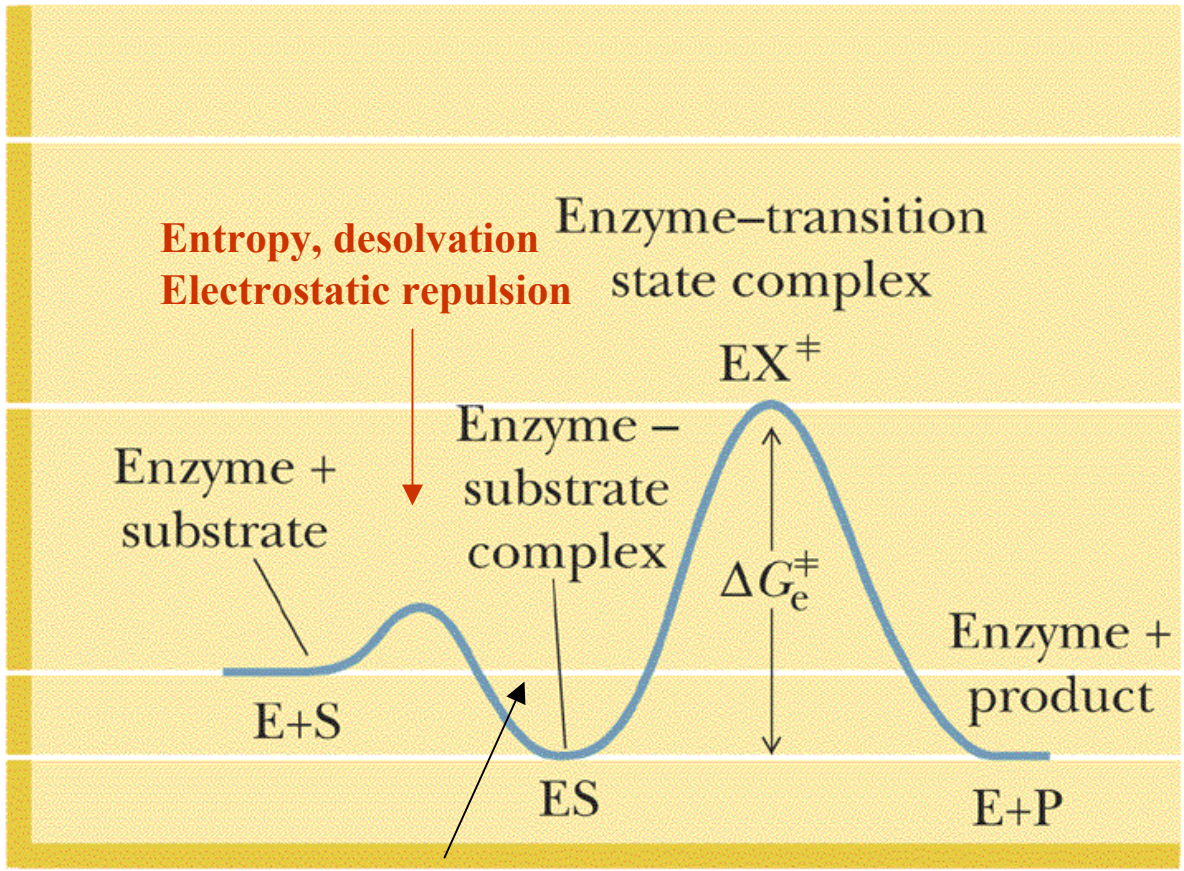
$$\Delta G_u^{\ddagger} > \Delta G_e^{\ddagger}$$



Transition state is MORE stable than ES!

$$\Delta G_u^{\ddagger} > \Delta G_e^{\ddagger}$$

(b)



$$E+S \rightleftharpoons ES \rightleftharpoons EX \longrightarrow E+P$$

Entropy loss in Formation of ES

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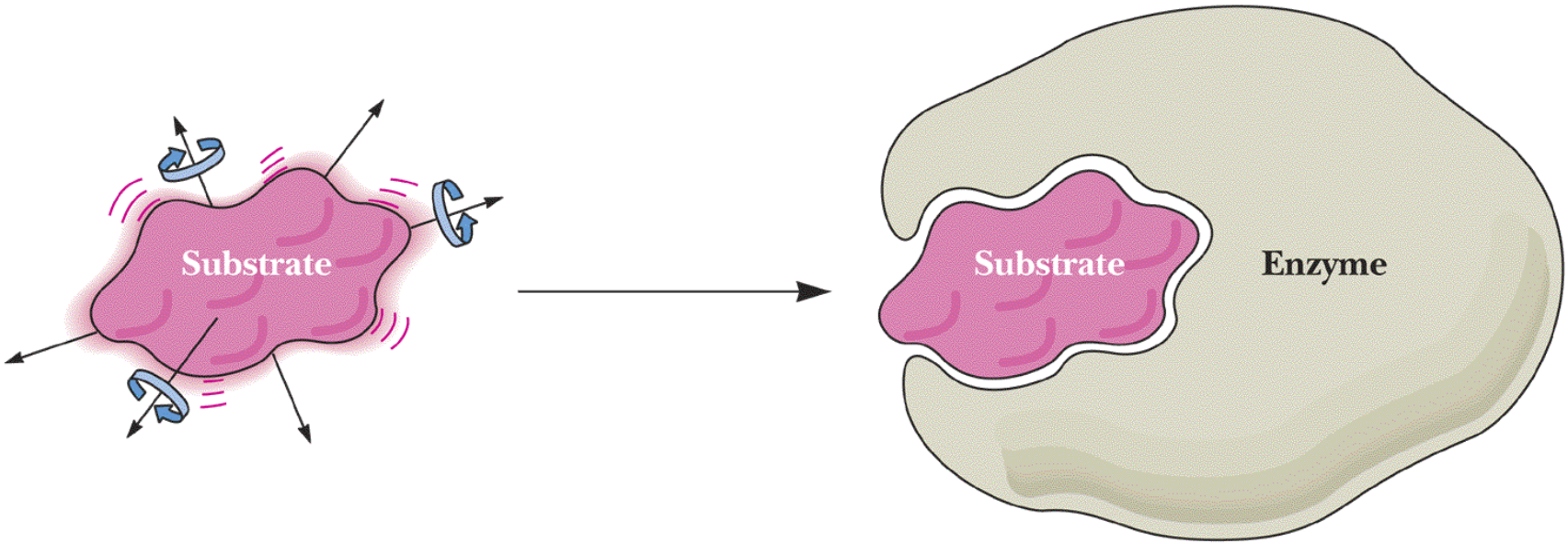
Figure 11.2



Substrate (and enzyme) are free to undergo translational motion. A disordered, high-entropy situation

The highly ordered, low-entropy complex

ES Destabilization by Desolvation of S

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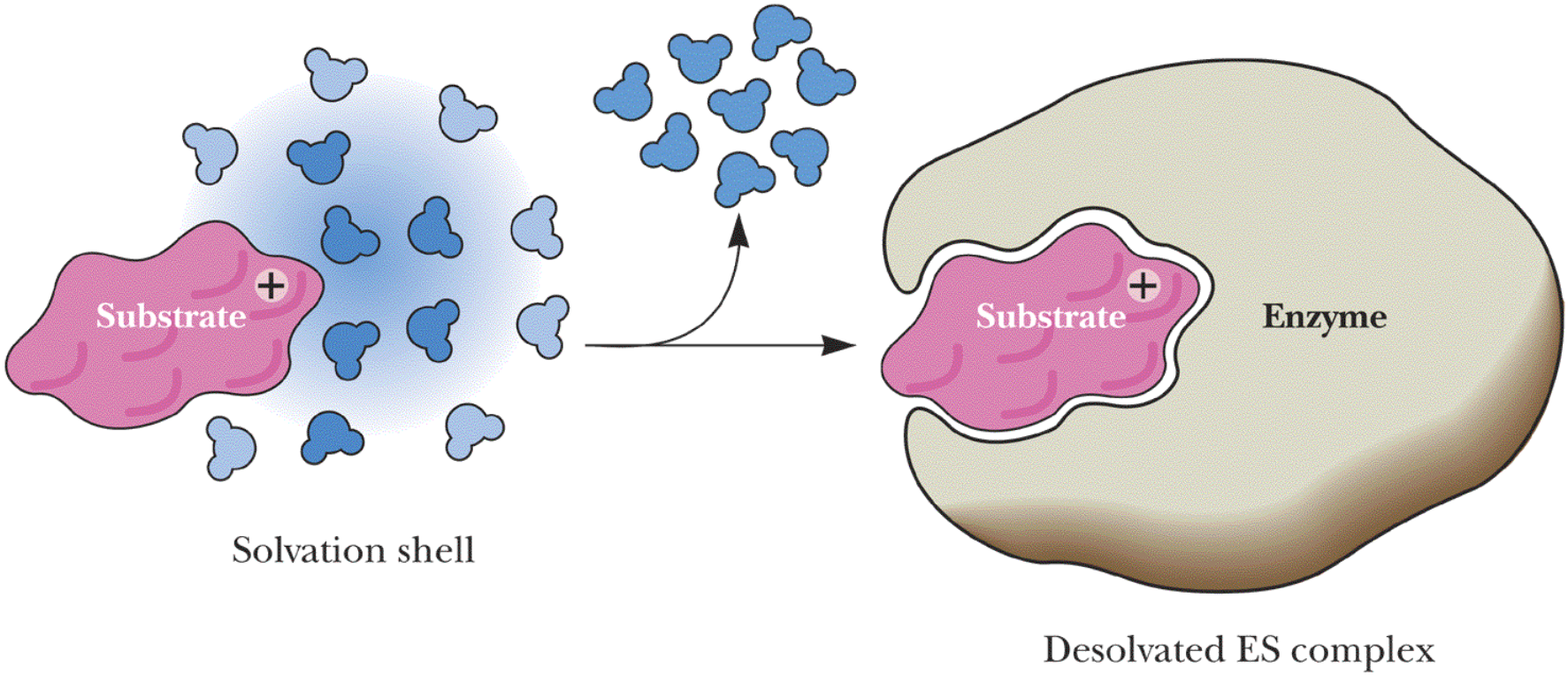
Figure 11.3



Electrostatic Destabilization in ES

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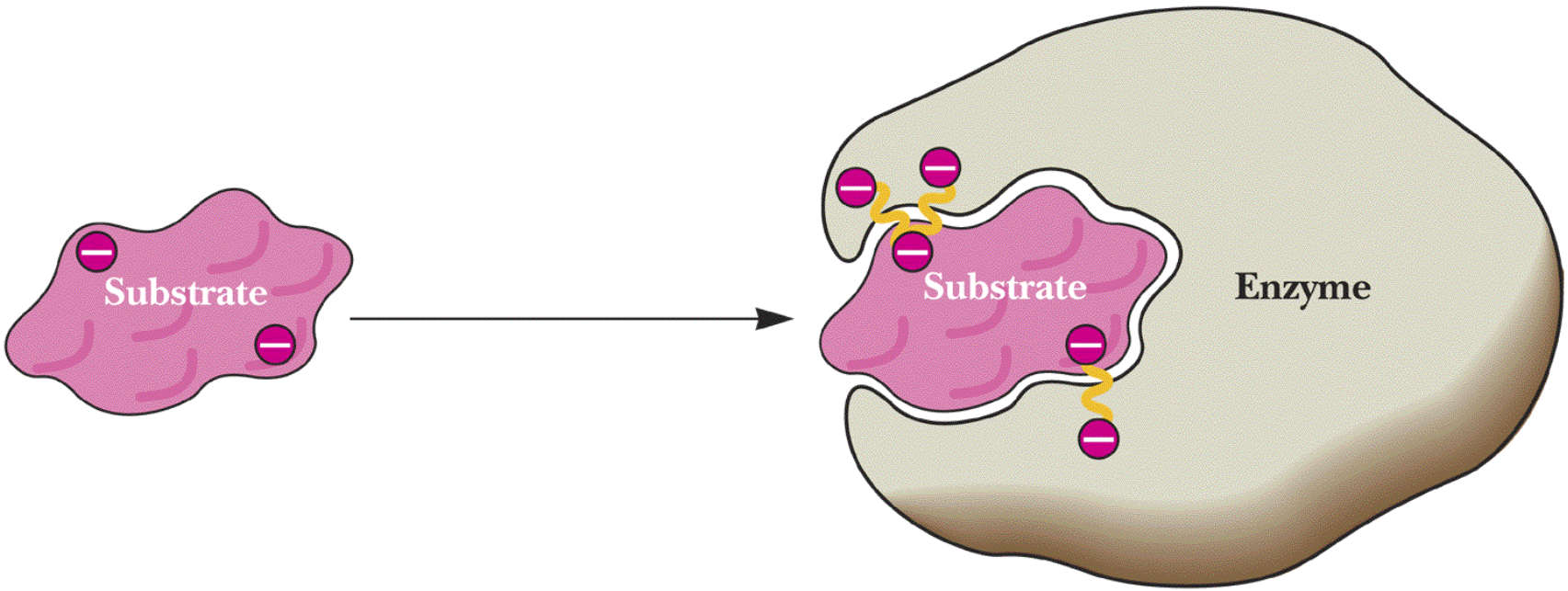
Figure 11.4



Electrostatic destabilization in ES complex

TSA Example #1

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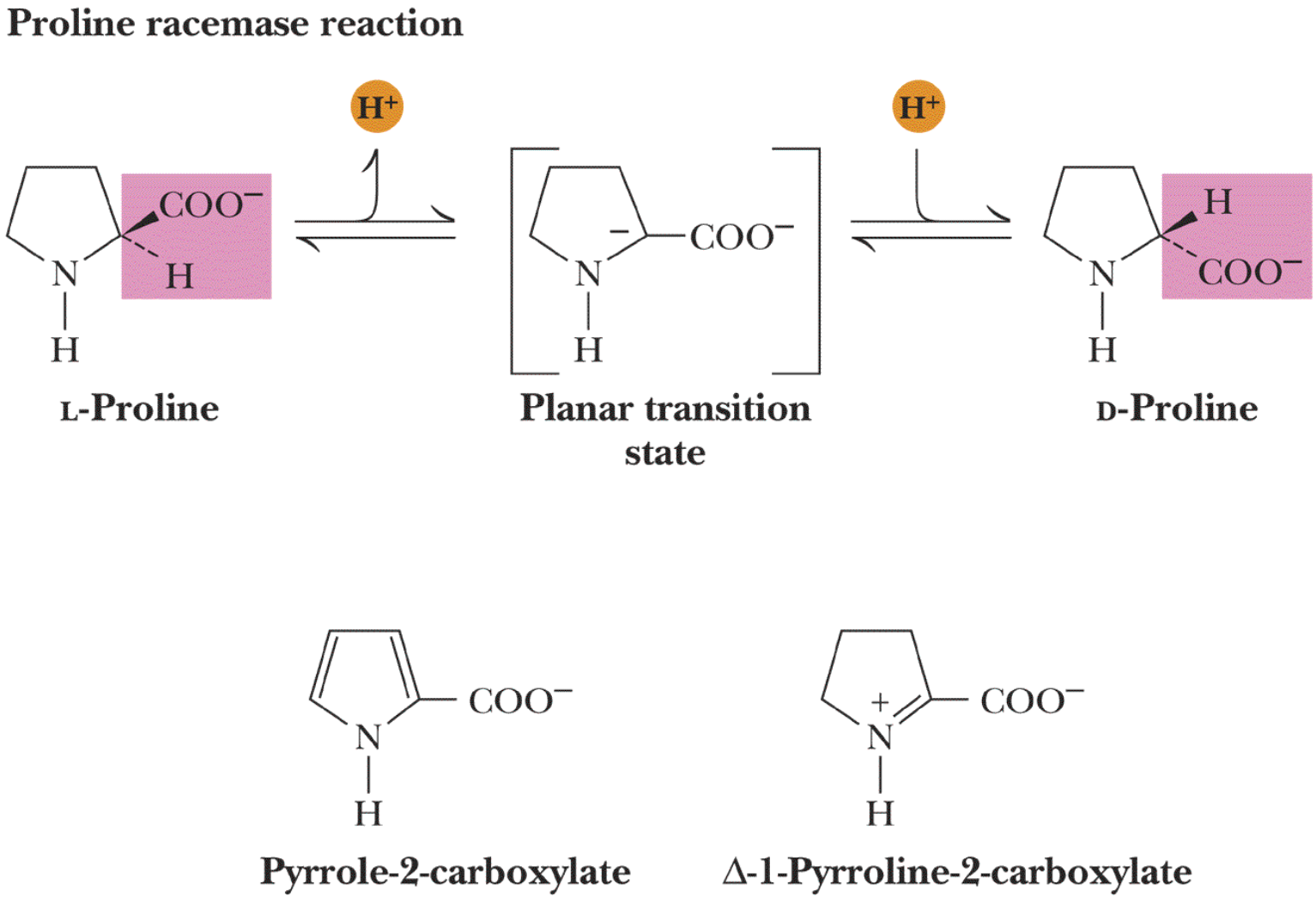
Figure 11.5



TSA Example #2

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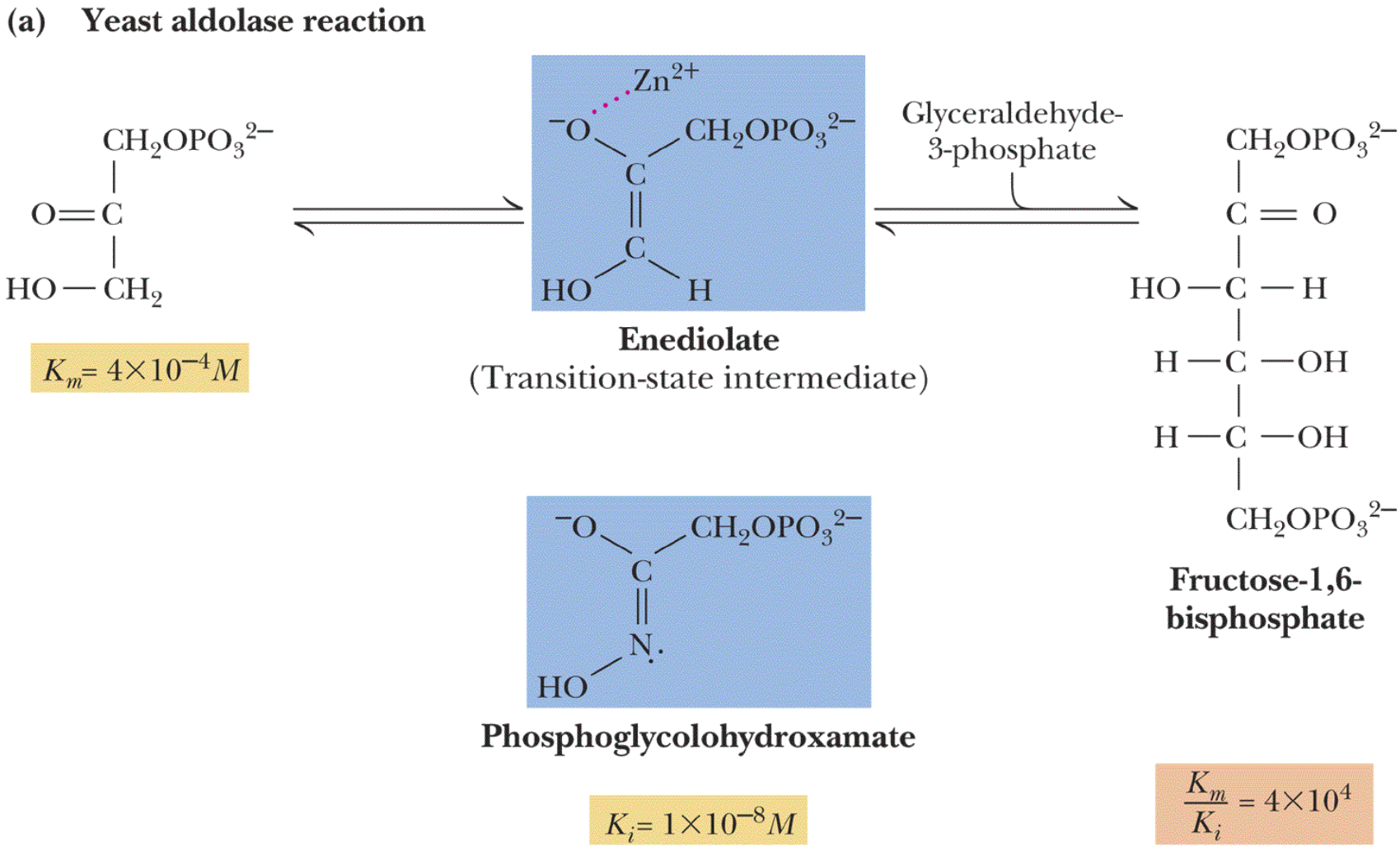
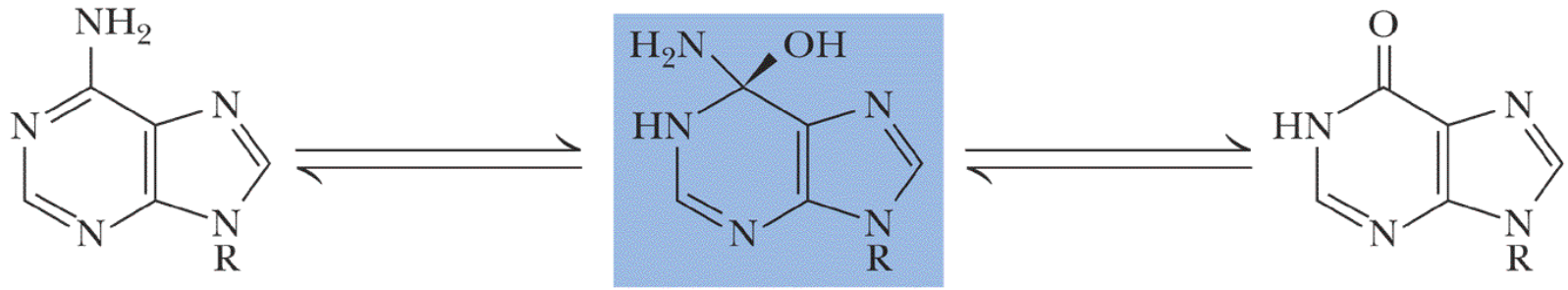
Figure 11.6a



TSA Example #3

Garrett/Grisham, Biochemistry with a Human Focus
Figure 11.6b

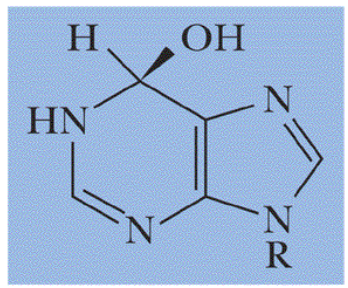
(b) Calf intestinal adenosine deaminase reaction



Adenosine
$K_m = 3 \times 10^{-5} M$

Transition-state intermediate

Inosine



Hydrated form of purine ribonucleoside
$K_i = 3 \times 10^{-13} M$

$$\frac{K_m}{K_i} = 1 \times 10^8$$

Antibody Structure

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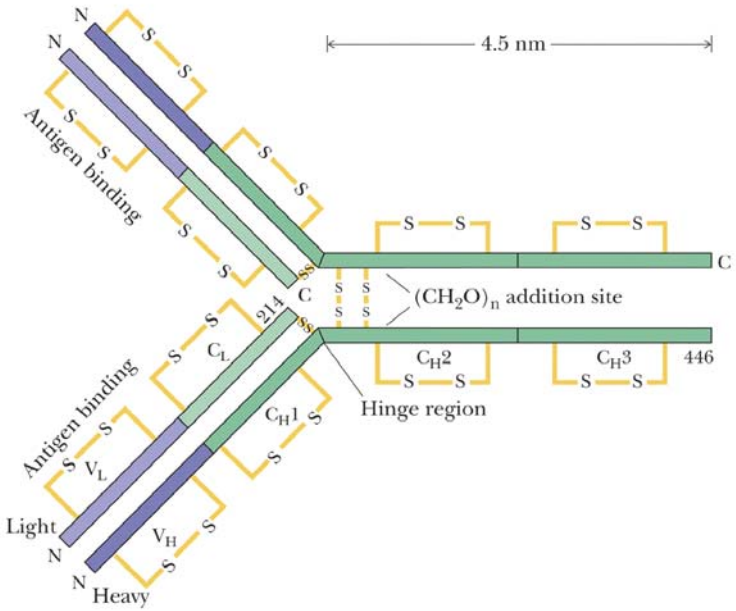
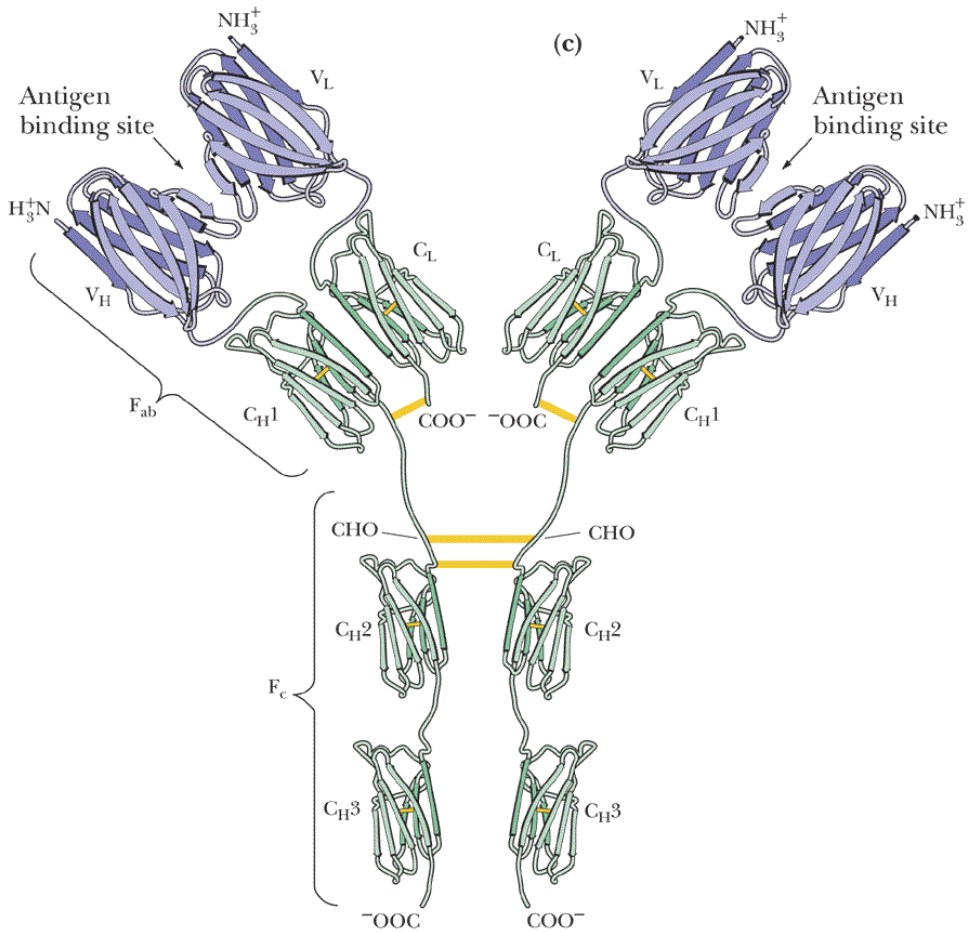
Figure 12.6





Catalytic Antibody Example

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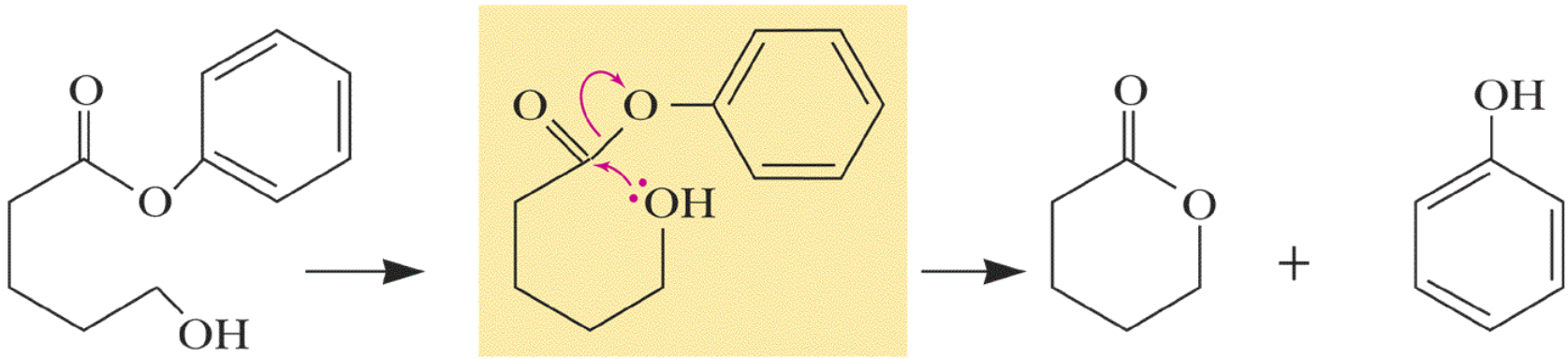
Figure 10.20

(a)



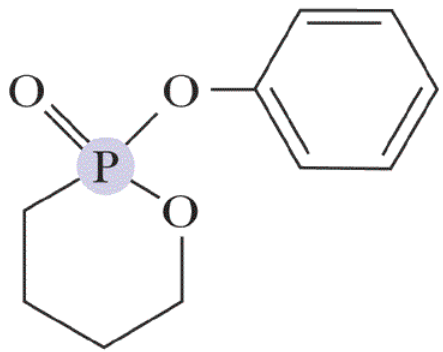
Hydroxy ester

Cyclic transition state

δ-Lactone

(b)

Antibodies are raised to a transition state analog.



Cyclic phosphonate ester