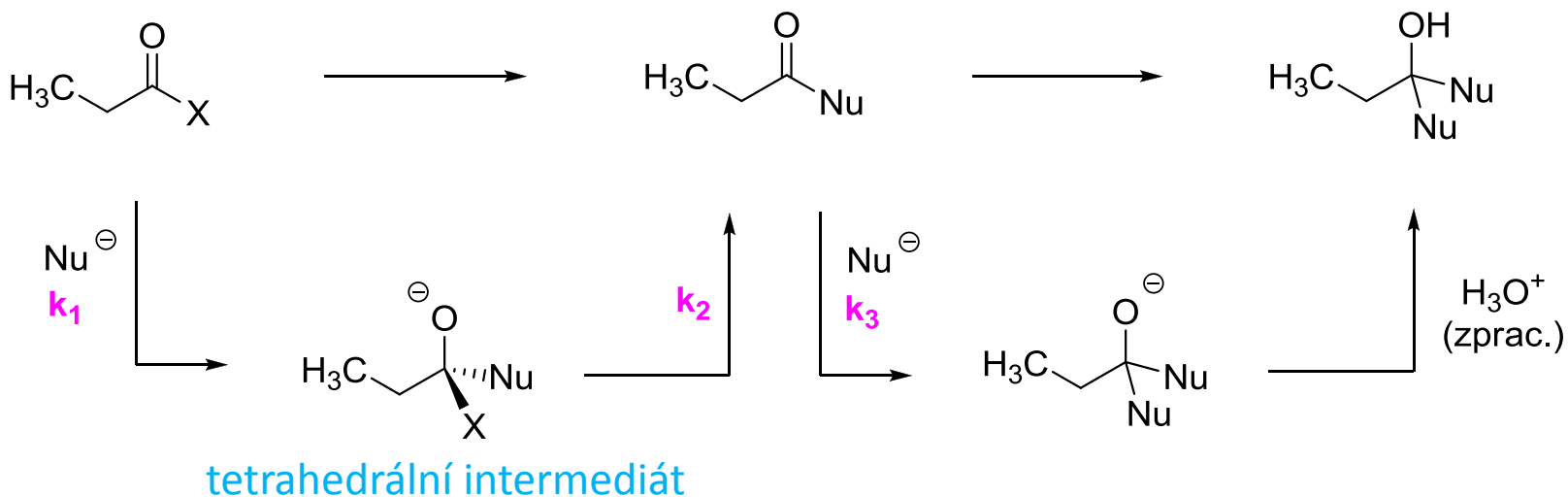




Q: jak se zastavit na oxidačním stupni ketonu nebo aldehydu?



Varianta A:

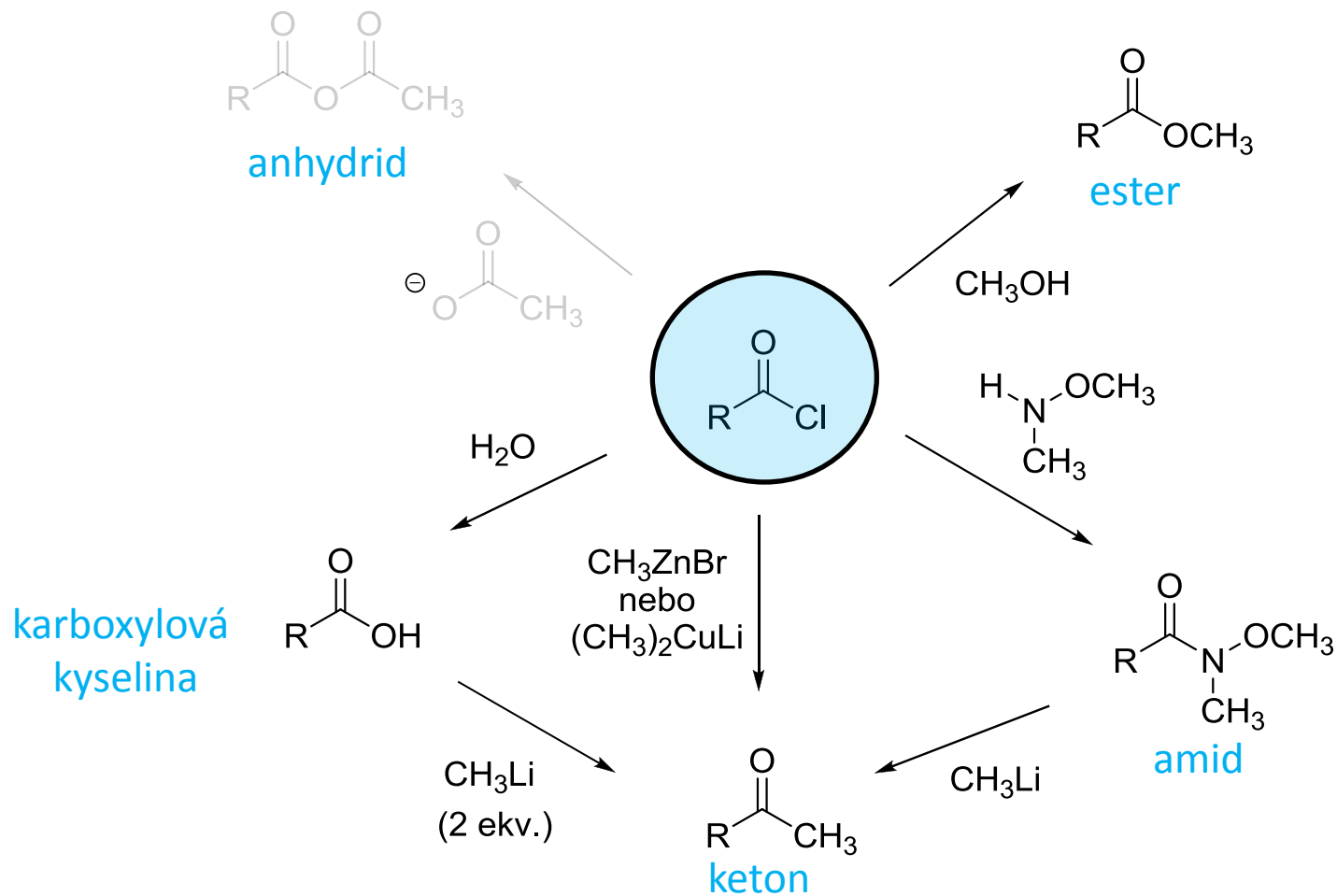
nukleofil reaguje mnohem pomaleji s aldehydem/ketonem než s výchozí látkou: $k_3 \ll k_1, k_2$

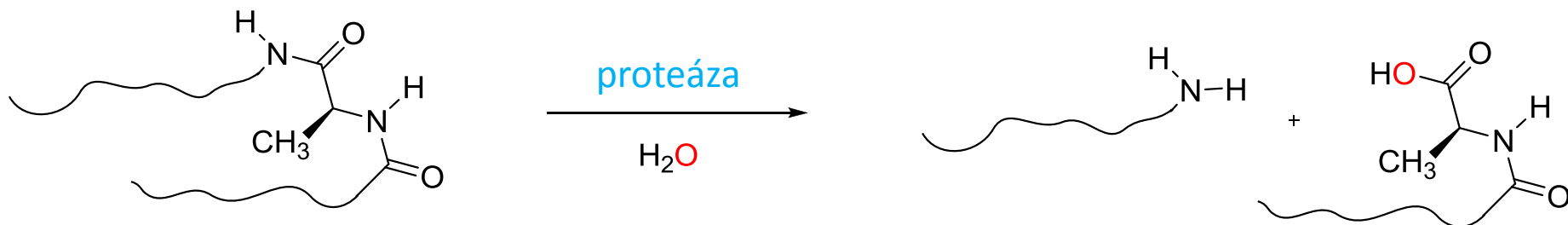
Varianta B:

vzniklý tetraedrání intermediát (k_1) se rozkládá až po zpracování reakce (např. X je velmi špatně odstupující skupina): $k_1 \gg k_2$



- Chloridy jsou velmi důležité intermediáty v organické syntéze





Proteasom

- multiproteinový komplex s proteolytickými vlastnostmi
- selektivní degradace nepotřebných (poškozených) proteinů
- vzniklé peptidy jsou pak využity k syntéze nových proteinů

Struktura a funkce proteasomu

Nobelova cena za chemii 2004 & 2009

Aaron Ciechanover

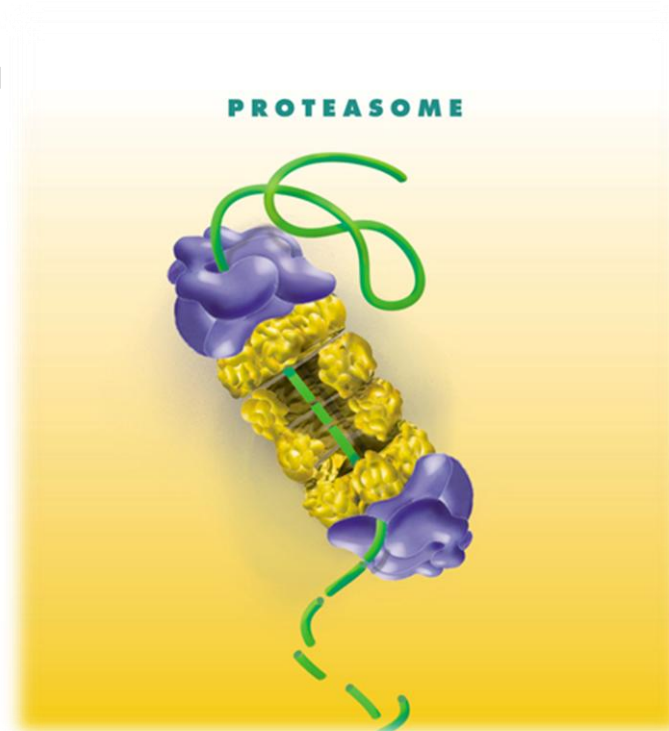
Avram Hershko

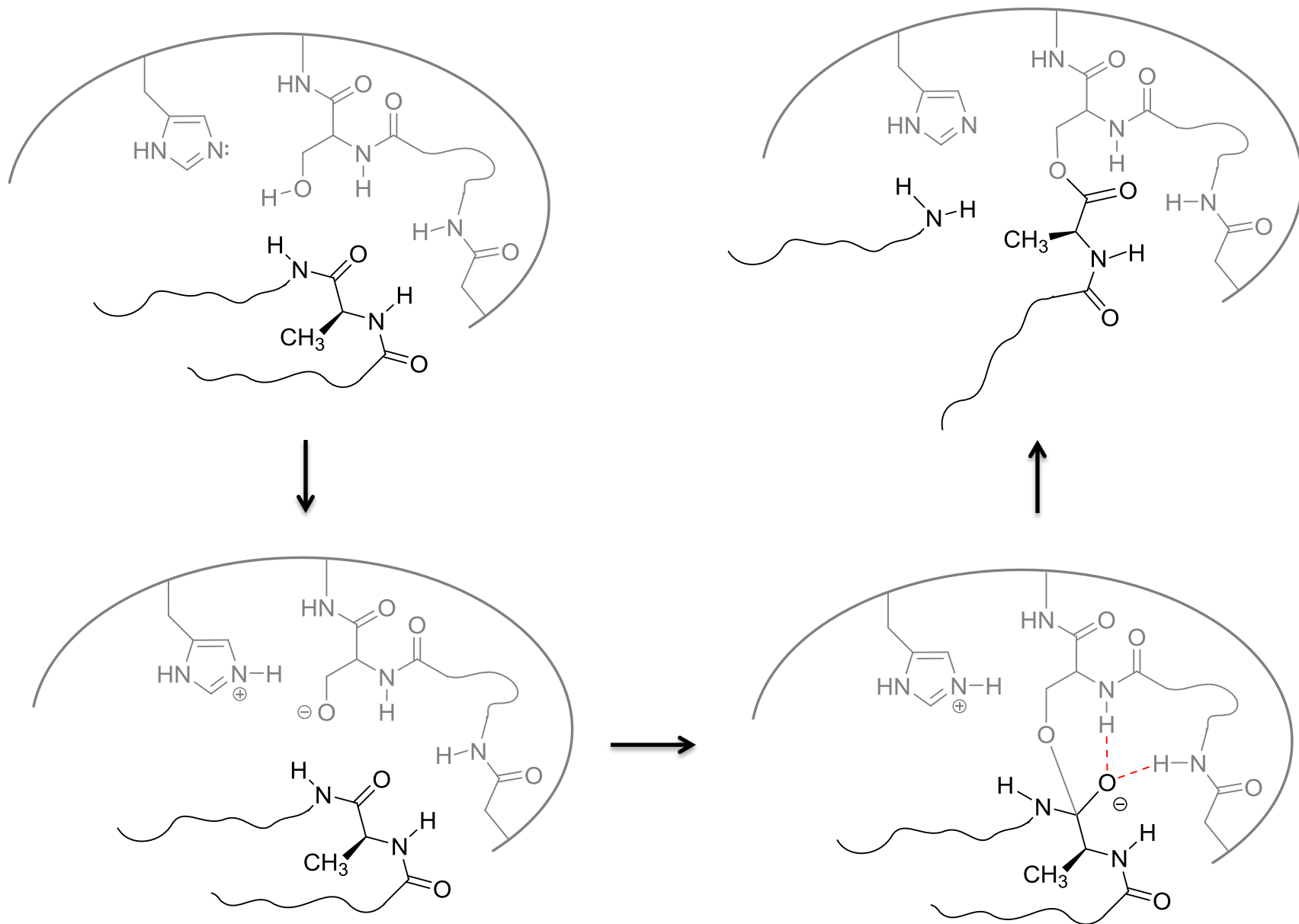
Irwin Rose

Venkatraman Ramakrishnan

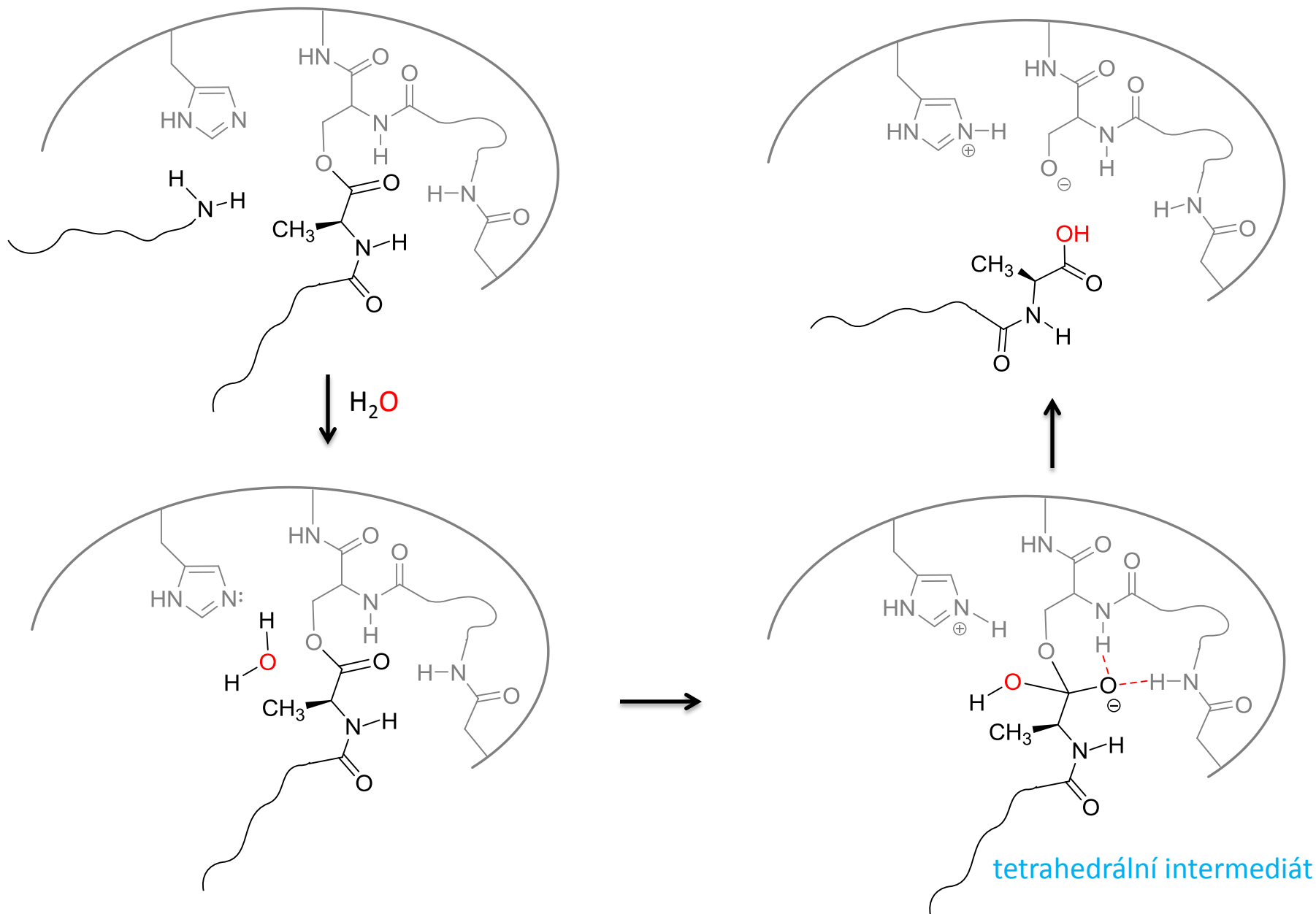
Thomas A. Steitz

Ada E. Yonath





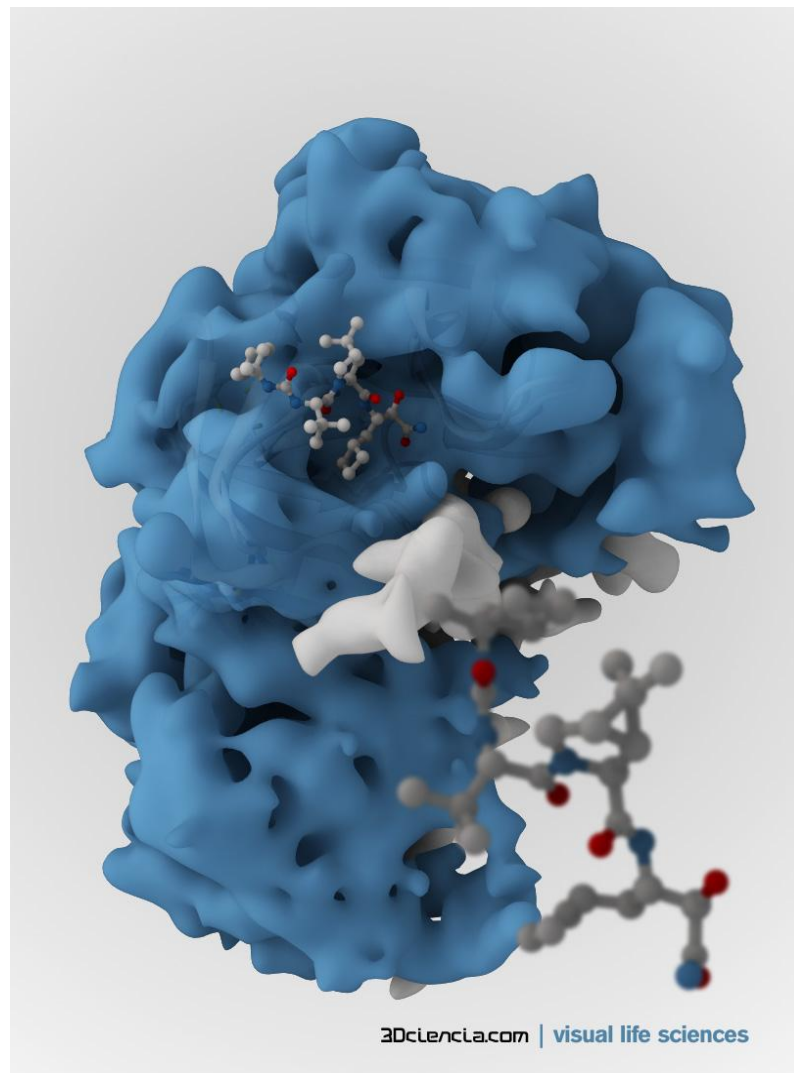
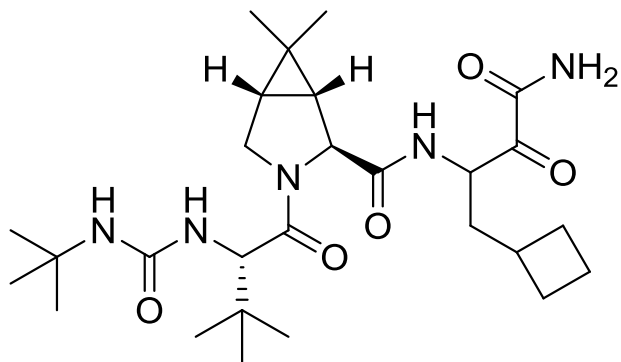
tetrahedrání intermediát

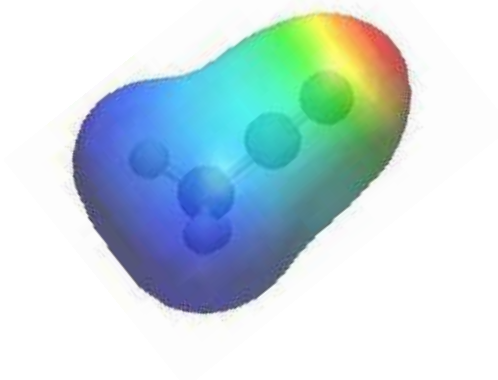
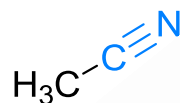
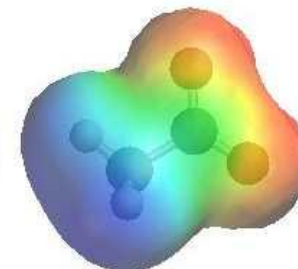
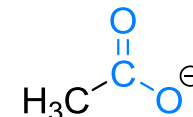
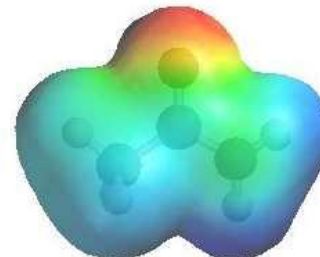
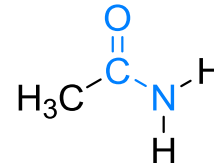
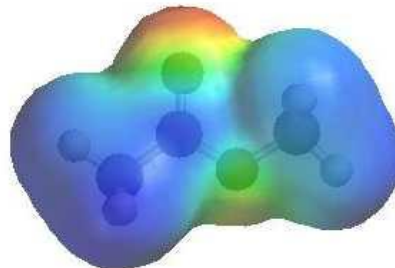
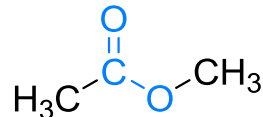
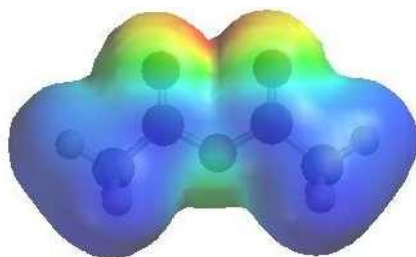
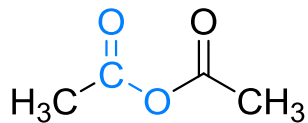
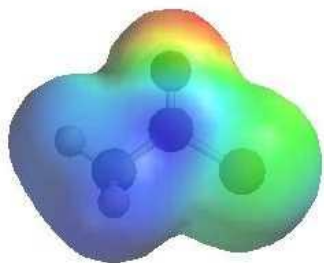
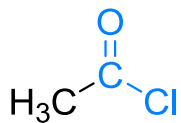




proteáza NS3 virusu hepatitidy C: důležitá pro replikaci viru

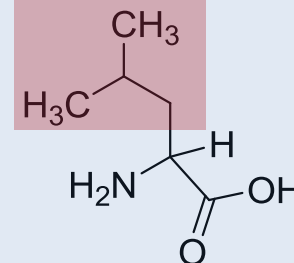
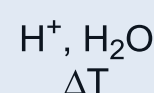
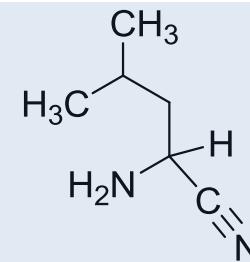
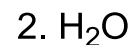
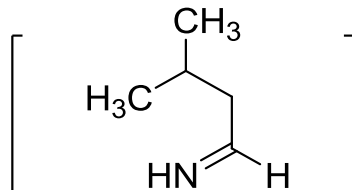
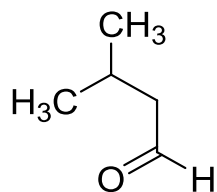
boceprevir: inhibitor proteázy NS3 virusu hepatitidy C
váže se do aktivního místa NS3





*nitril je v oxidačním stupni
karboxylové kyseliny*

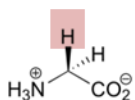
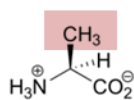
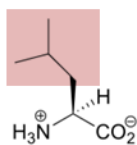
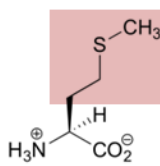
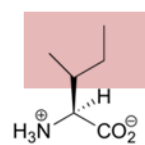




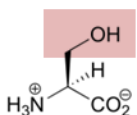
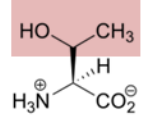
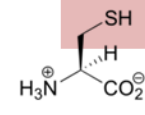
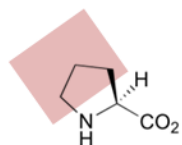
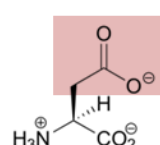
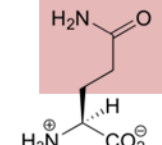
Leucin

hydrolyza nitrilu na
karboxylovou kyselinu

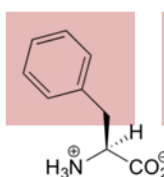
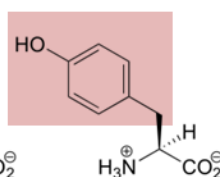
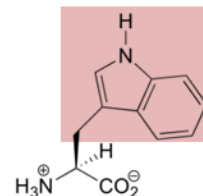
Nonpolar, aliphatic side groups

Glycine
Gly, GAlanine
Ala, AValine
Val, VLeucine
Leu, LMethionine
Met, MIsoleucine
Ile, I

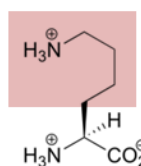
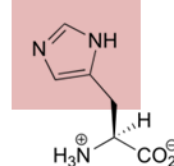
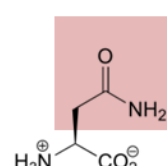
Polar, uncharged side groups

Serine
Ser, SThreonine
Thr, TCysteine
Cys, CProline
Pro, PAspartate
Asp, DGlutamine
Gln, Q

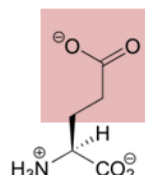
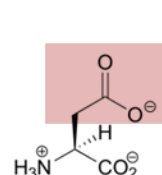
Aromatic side groups

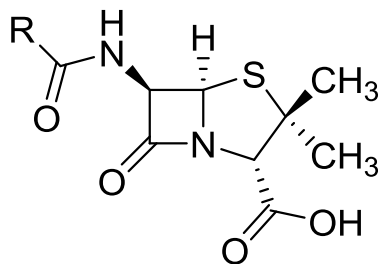
Phenylalanine
Phe, FTyrosine
Tyr, YTryptophan
Trp, W

Positively charged side groups

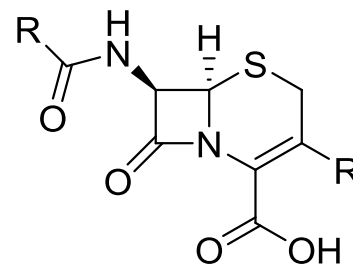
Lysine
Lys, KHistidine
His, HAsparagine
Asn, N

Negatively charged side groups

Glutamate
Glu, EAspartate
Asp, D



Penicilin



Cephalosporin

Inhibice bakteriální transpeptidázy – klíčový enzym pro tvorbu buněčné stěny

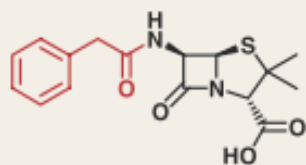
Resistance bakterií vůči běžně používaným antibiotikům (např. beta-laktamáza) vyžaduje přípravu nových strukturálních analogů (organická syntéza).

Generation 1

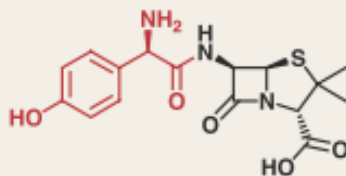
Generation 2

Generation 3

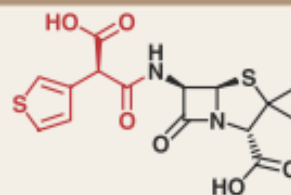
Generation 4



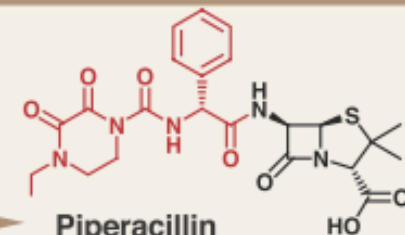
Penicillin G



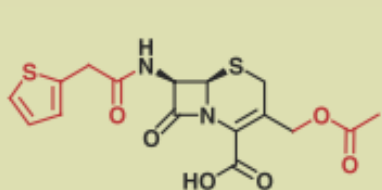
Amoxicillin



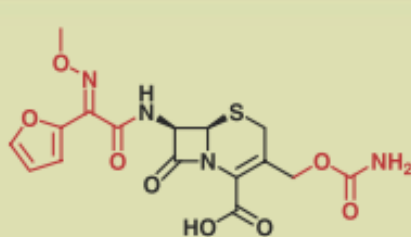
Ticarcillin



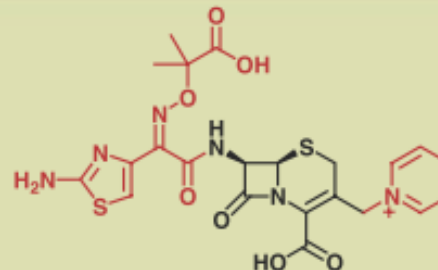
Piperacillin



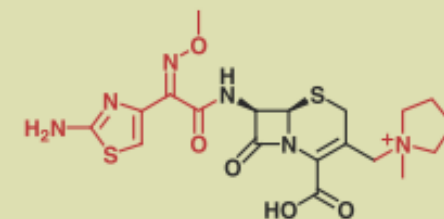
Cefalotin



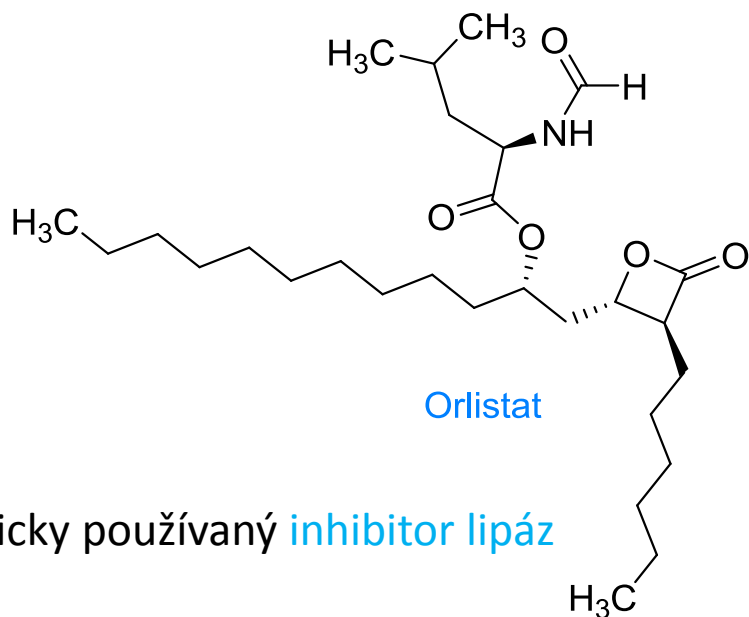
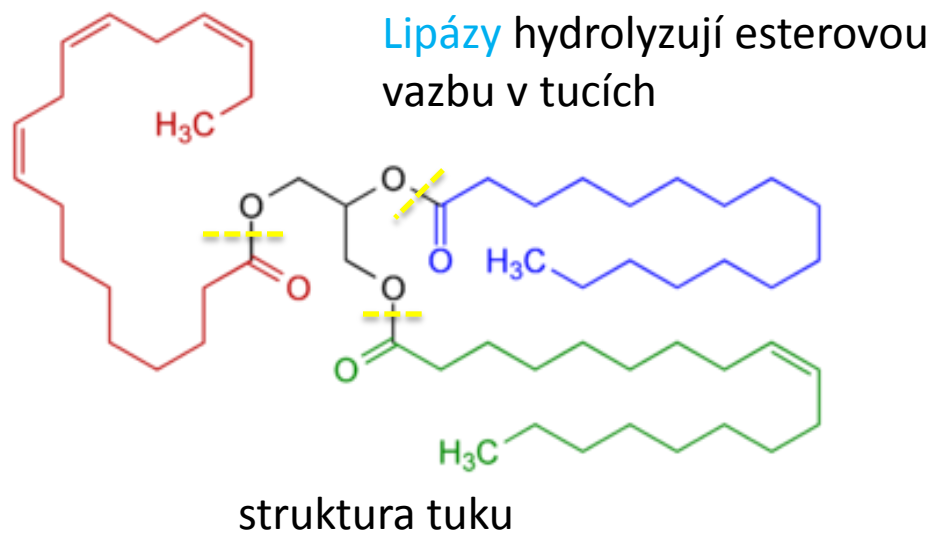
Cefuroxime



Ceftazidime



Cefepime



- klinicky používaný **inhibitor lipáz**

komplex lipázy a orlistatu

