

Legame Co-C

1958

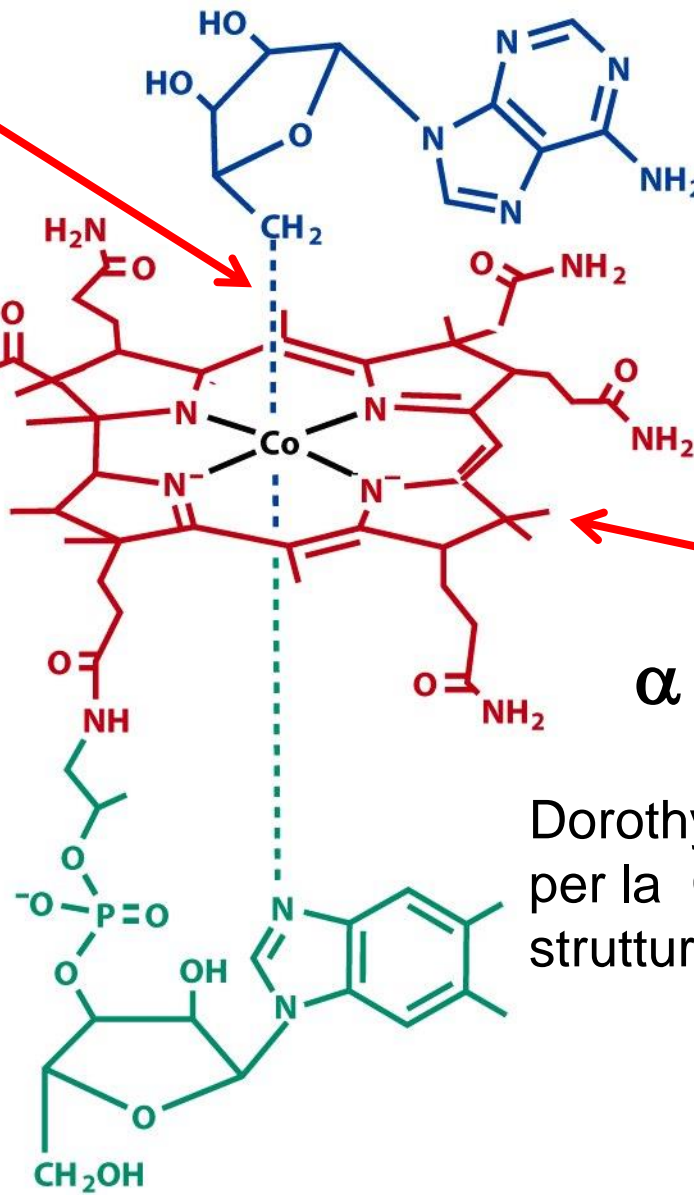
$\beta$

catena amidica

Anello corrinico

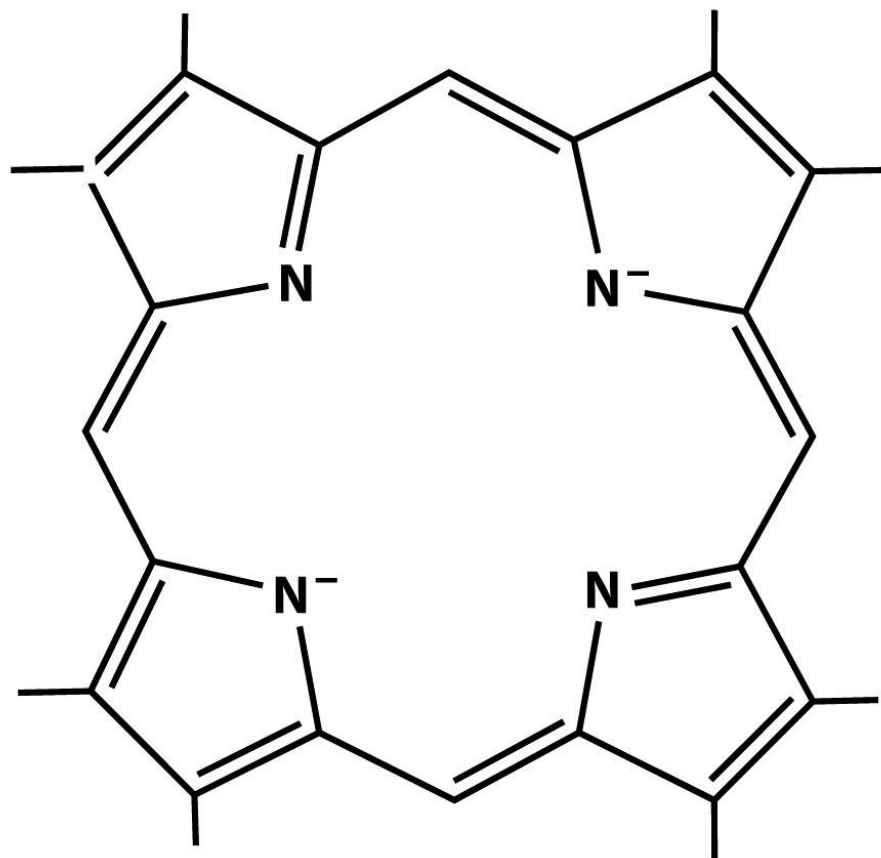
$\alpha$

Dorothy Hodgkin, premio Nobel per la Chimica nel 1964 per la struttura ai raggi X

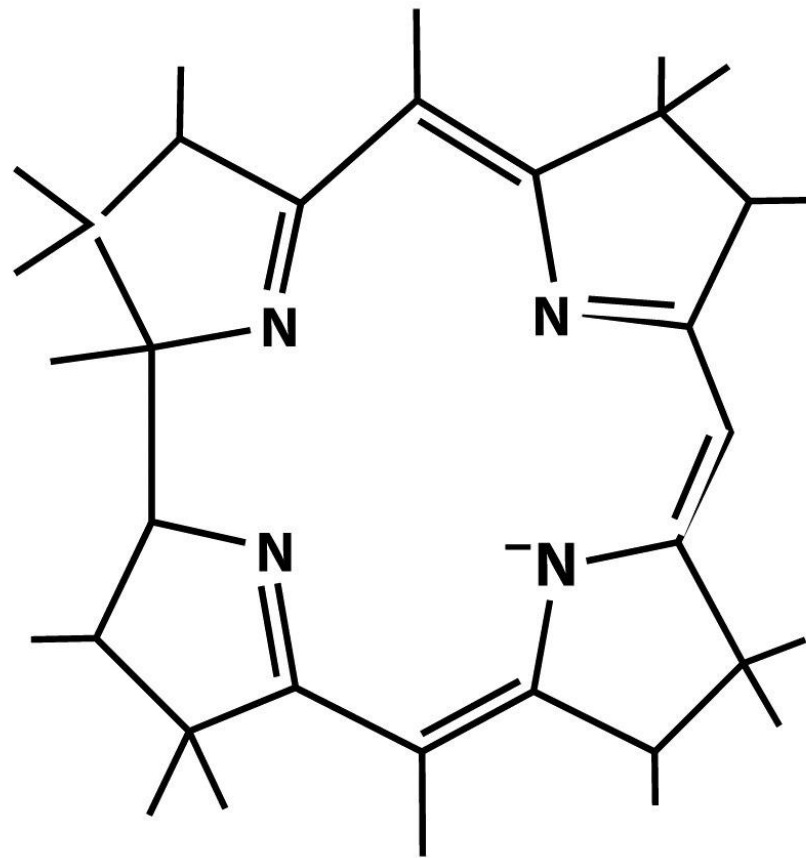


Coenzyme B<sub>12</sub>

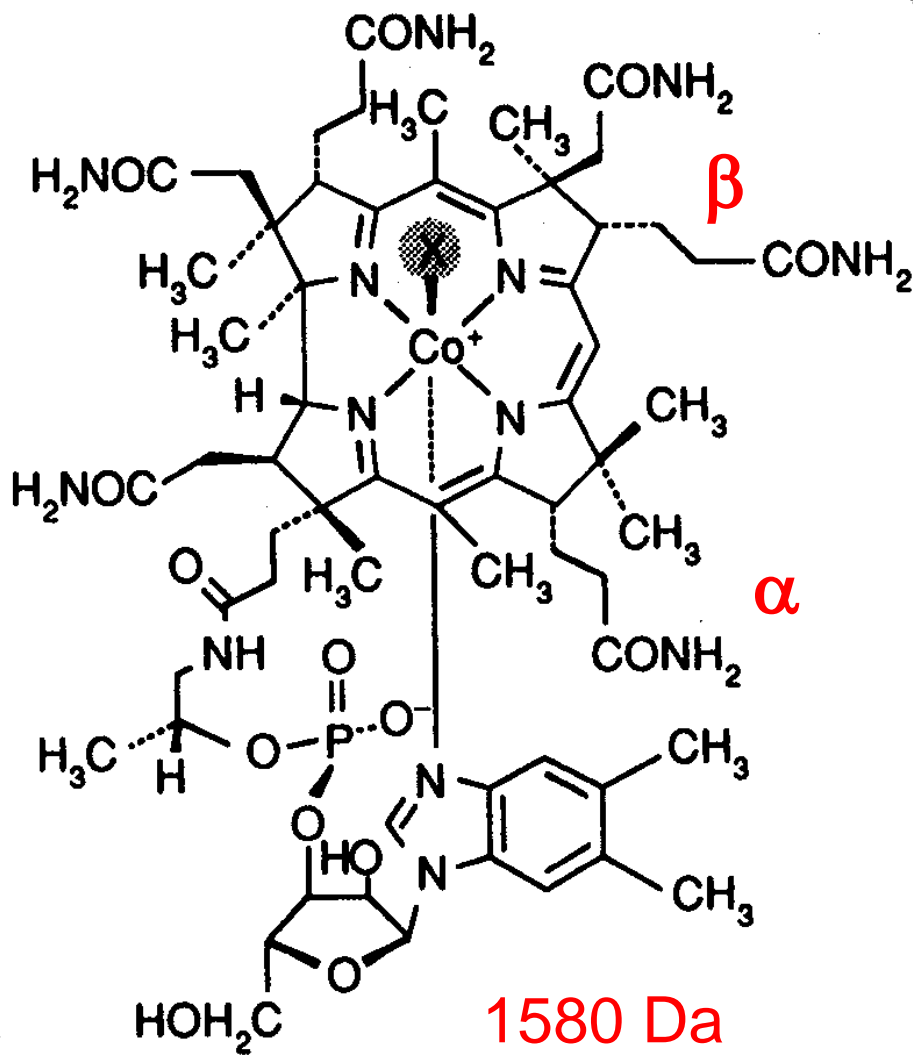
5'-desossiadenosilcobalamina




**Porphyrin<sup>2-</sup>**

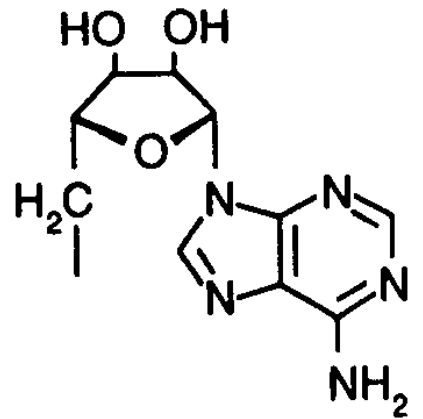


**Corrin<sup>-</sup>**



-  = CH<sub>3</sub> : methylcobalamin (MeCbl or MeB<sub>12</sub>)
- CN : cyanocobalamin (vitamin B<sub>12</sub>)
- OH : hydroxycobalamin
- H<sub>2</sub>O : aquacobalamin
- R : 5'-deoxyadenosylcobalamin (coenzyme B<sub>12</sub>, AdoCbl or AdoB<sub>12</sub>)

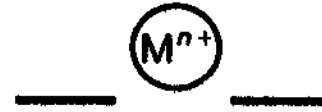
R = 5'-deoxyadenosyl



7 catene amidiche laterali,  
9 centri chirali



*in-plane* coordination  
(side view)



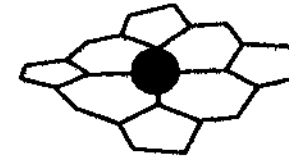
*out-of-plane* coordination  
(side view)



'doming' of the  
macrocycle



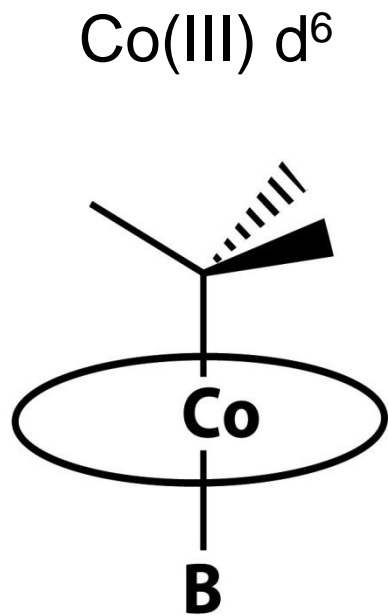
saddle-shaped  
macrocycle



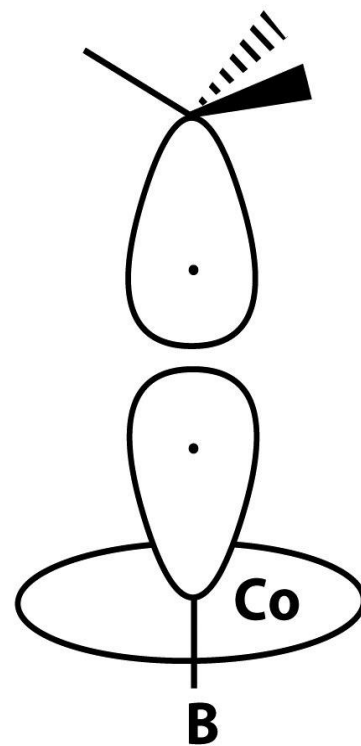
'ruffling' of the  
macrocycle

Distorsione nelle cobalamine

*Co sempre basso spin*



C. N. = 6

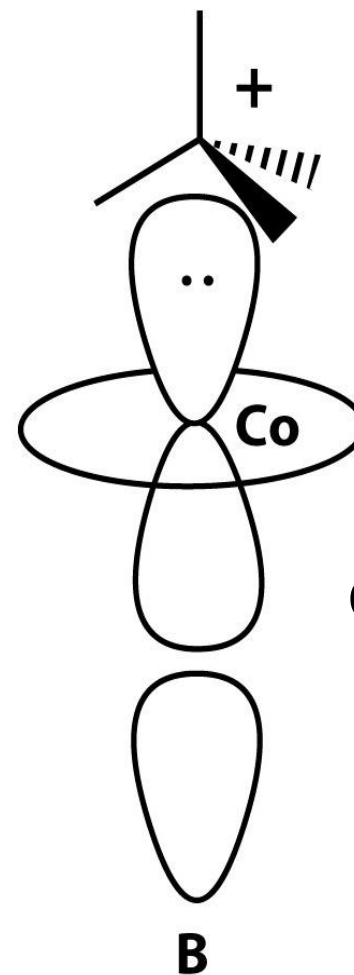


Co(II)  $d^7$

C. N. = 5

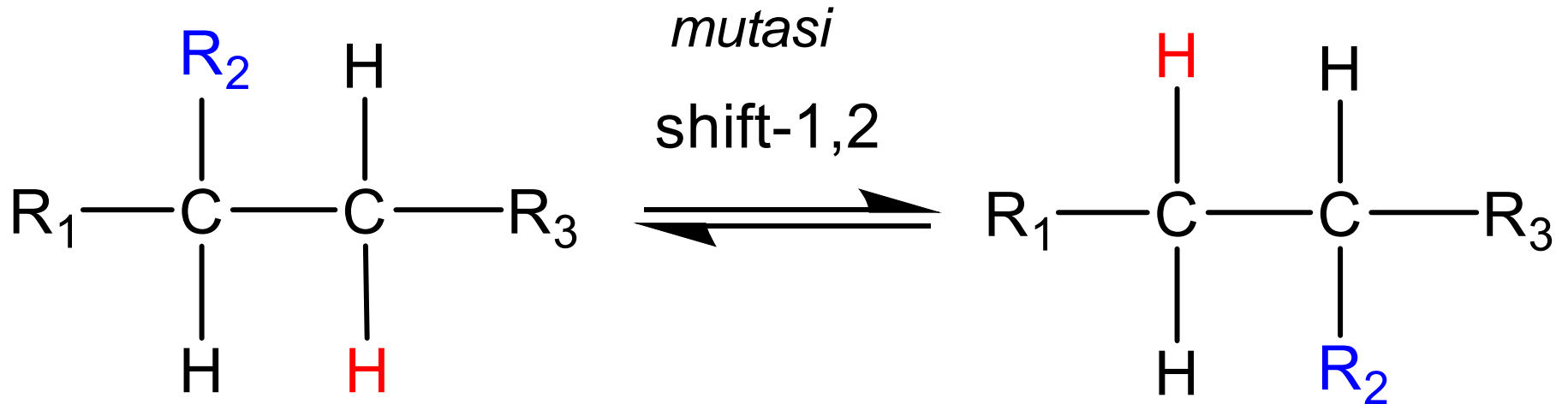
supernucleofilo

Co(I)  $d^8$



C. N. = 4

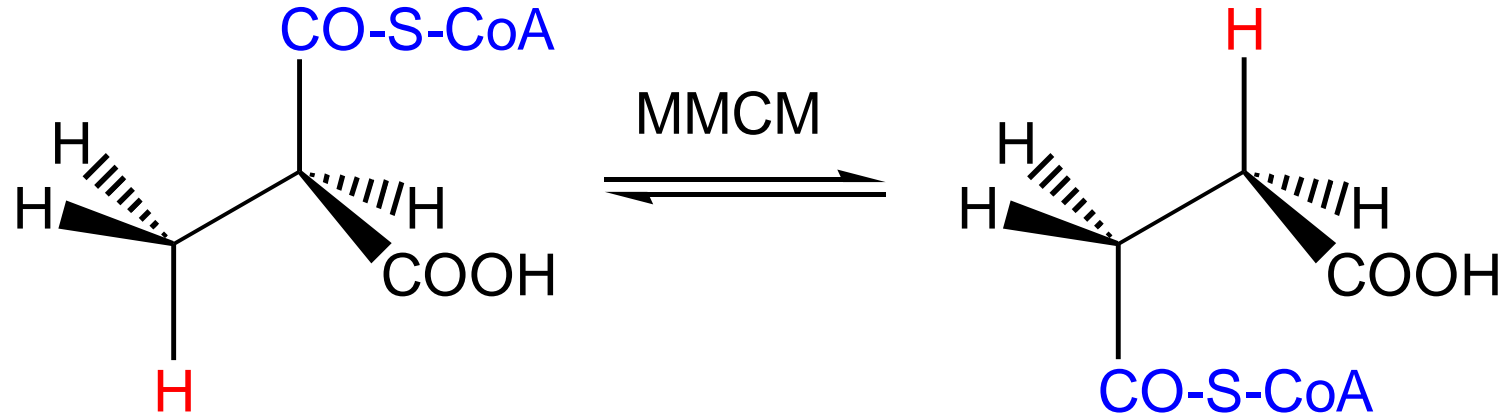
# Reazioni catalizzate dal coenzima B<sub>12</sub>



Enzima	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
Diolo deidratasi	CH <sub>3</sub>	OH	OH
Etanolamina deaminasi	H	NH <sub>2</sub>	OH
Glutammato mutasi	H	CH(NH <sub>2</sub> )COO H	COOH
Glicerolo deidratasi	CH <sub>2</sub> OH	OH	OH

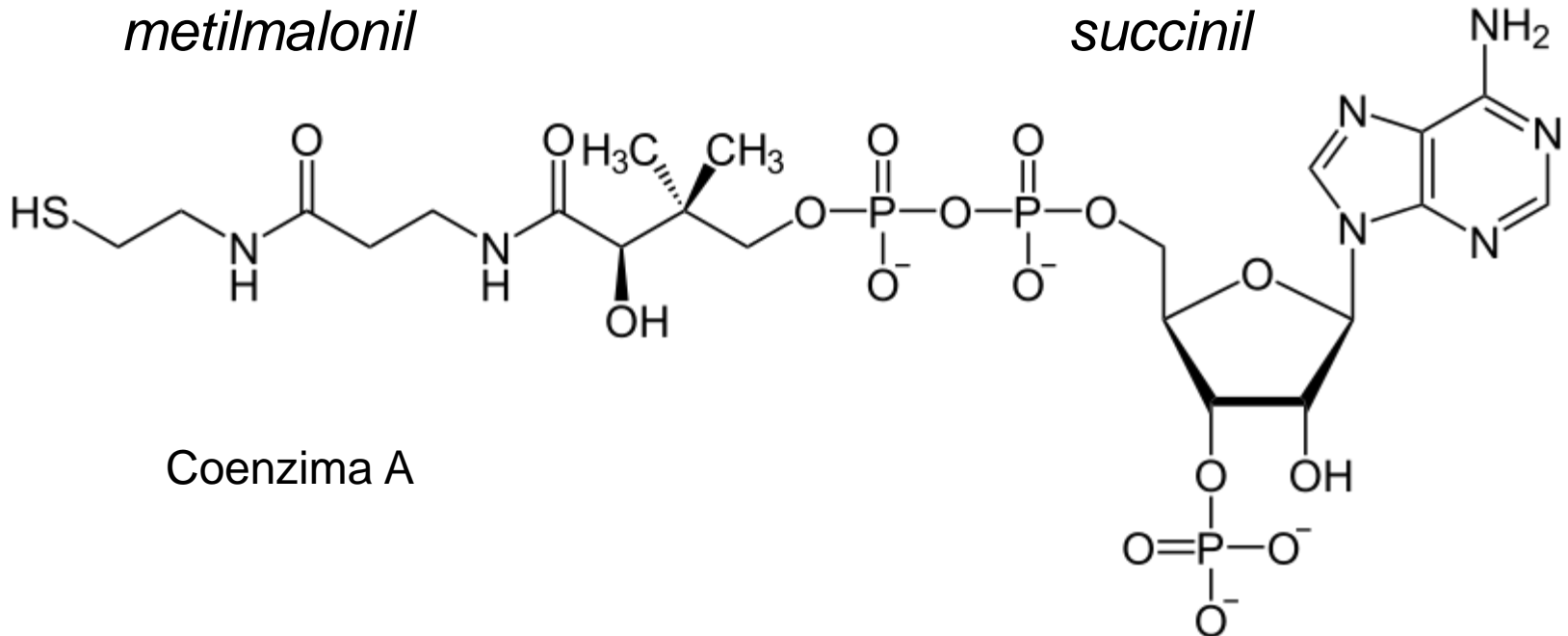
# MetilMalonil-Coenzima A-Mutasi

(succinil-CoA necessario nel ciclo di Krebs)

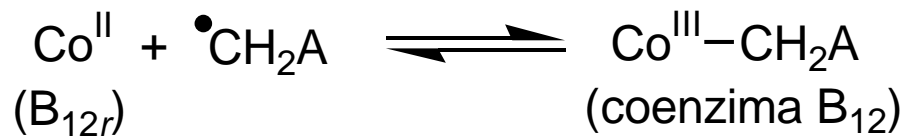
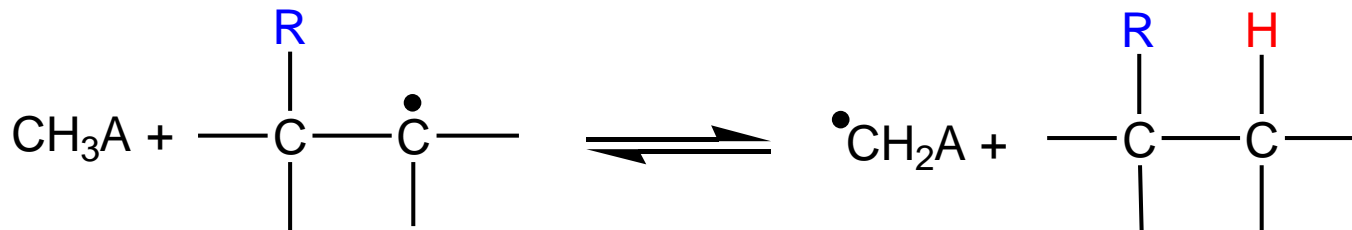
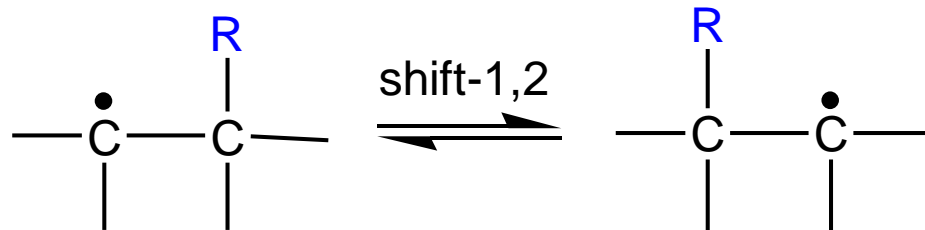
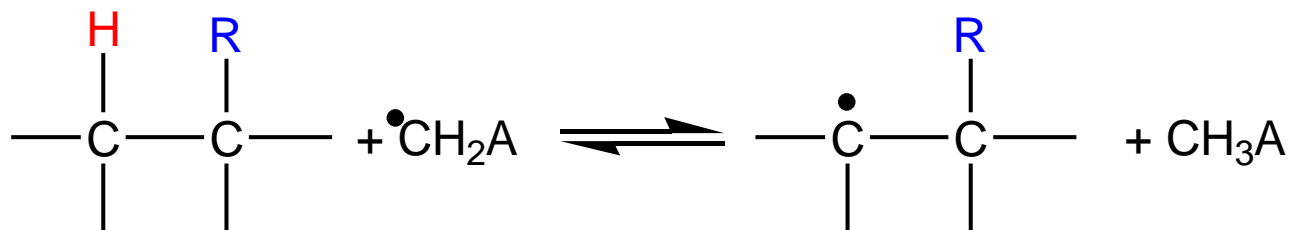
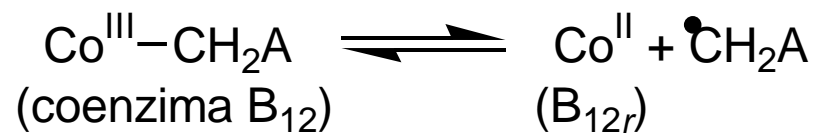


*metilmalonil*

*succinil*

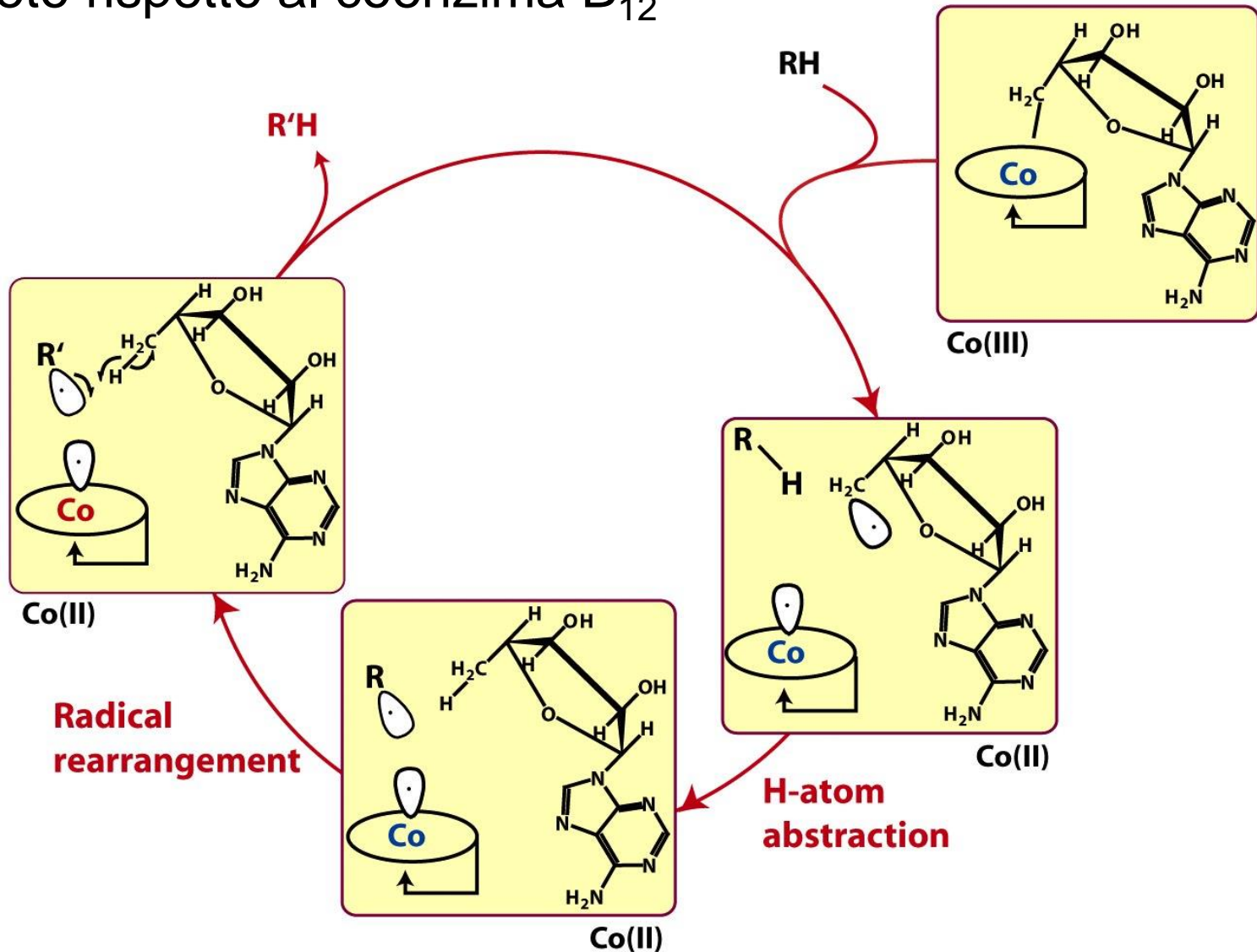


Coenzima A

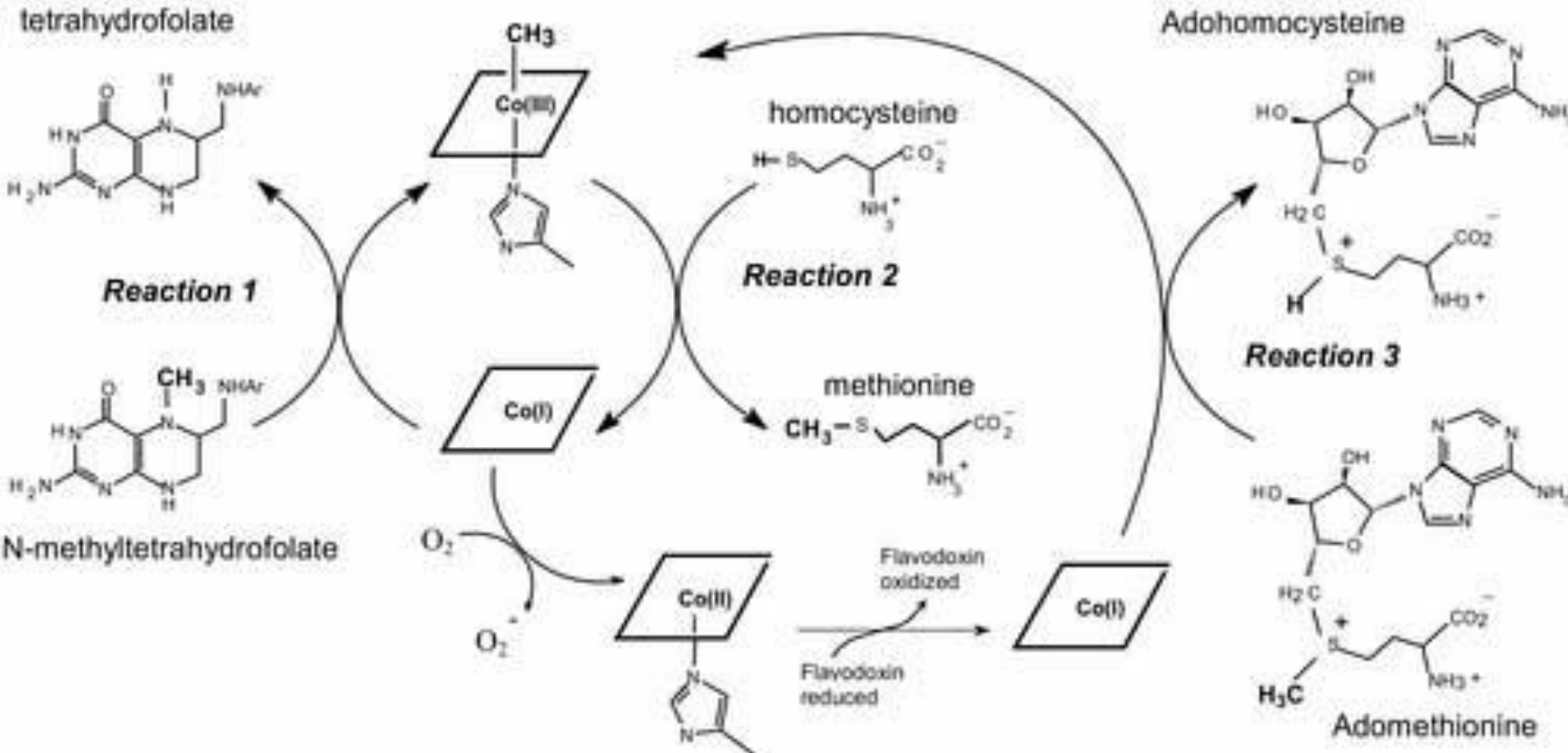




La rottura del legame Co–C è  $10^{12}$  volte più veloce nell'enzima completo rispetto al coenzima B<sub>12</sub>

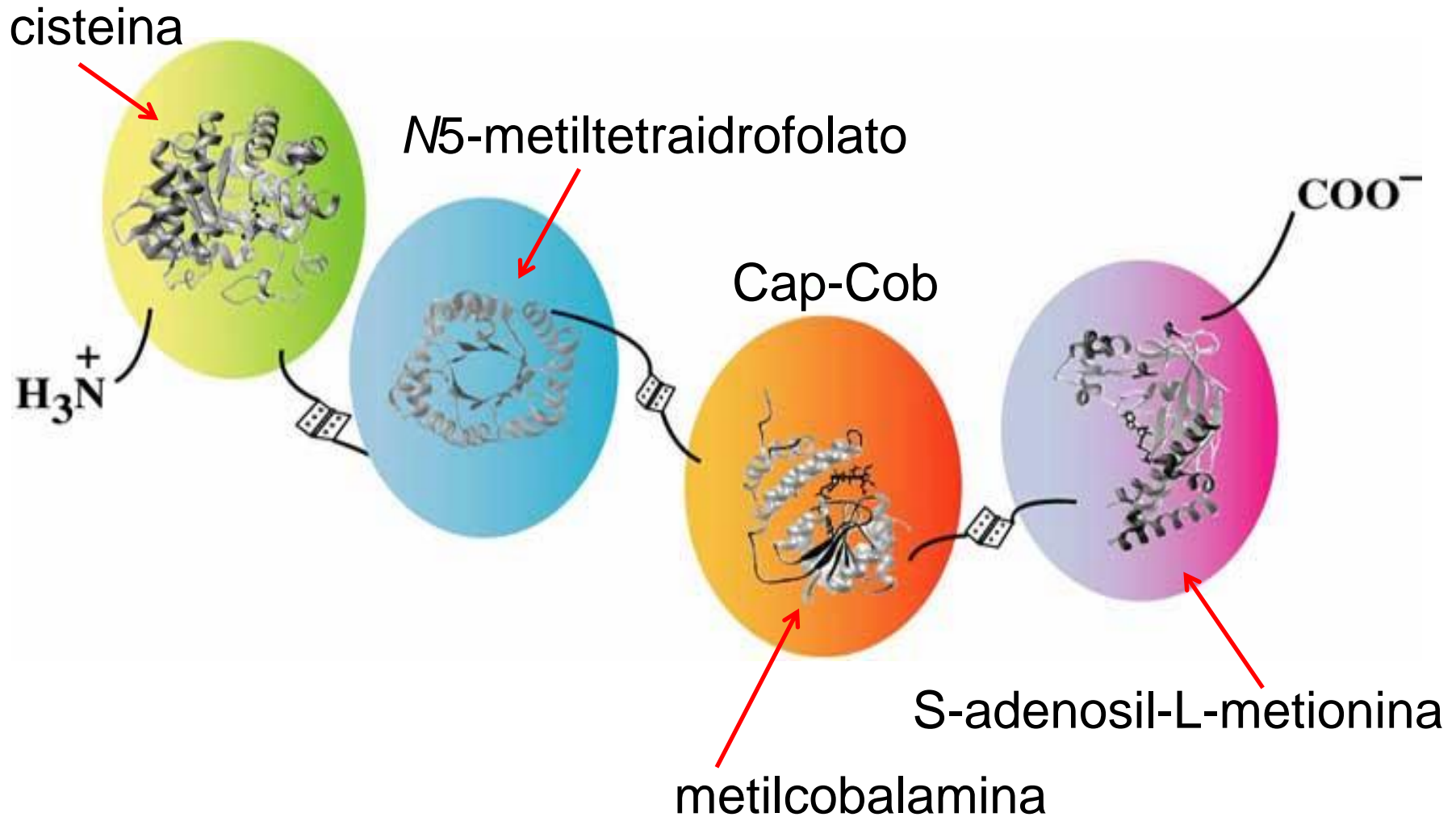


# Metilcobalamina: cofattore della Metionina Sintasi

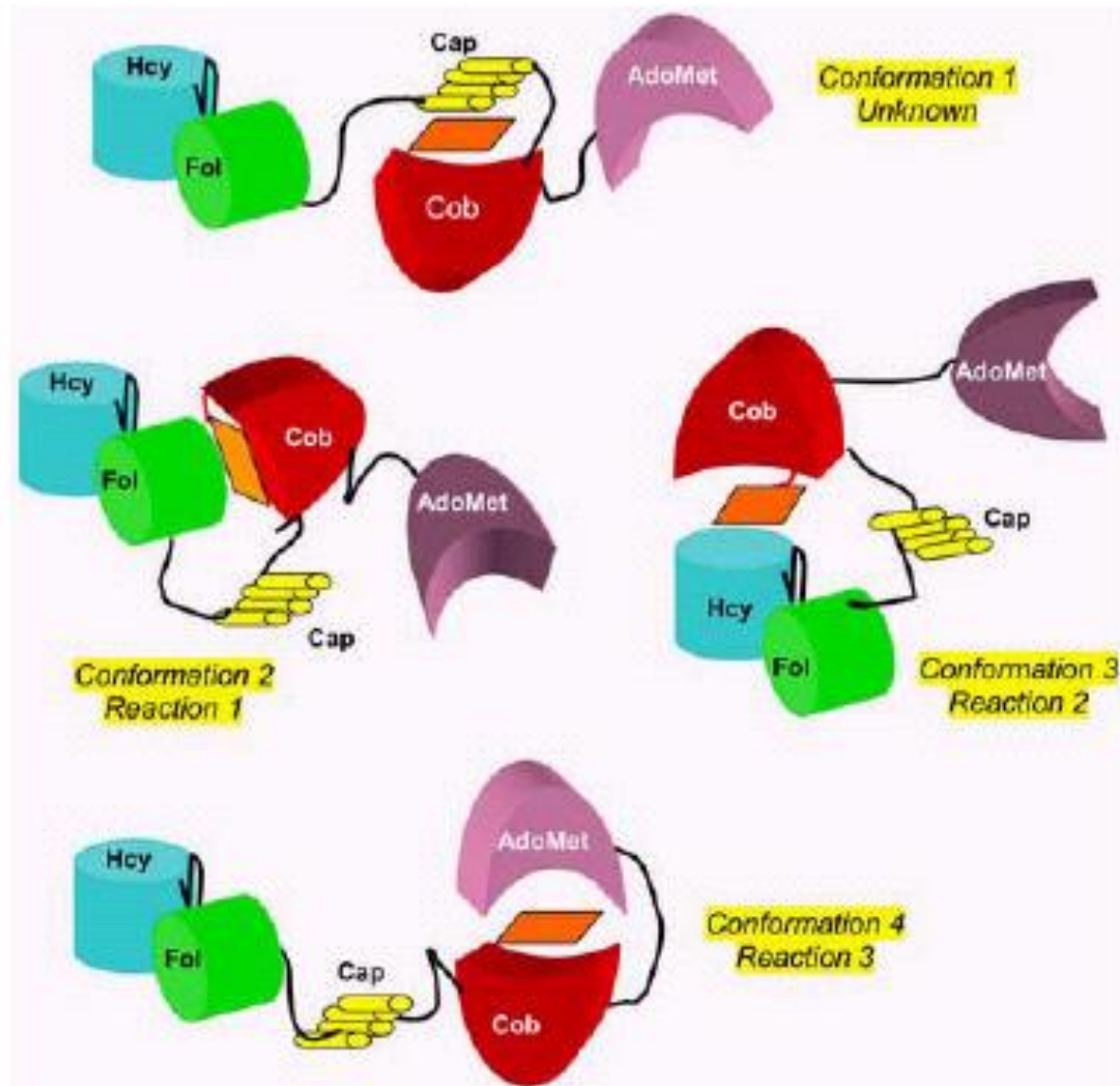


S-adenosil-L-metionina

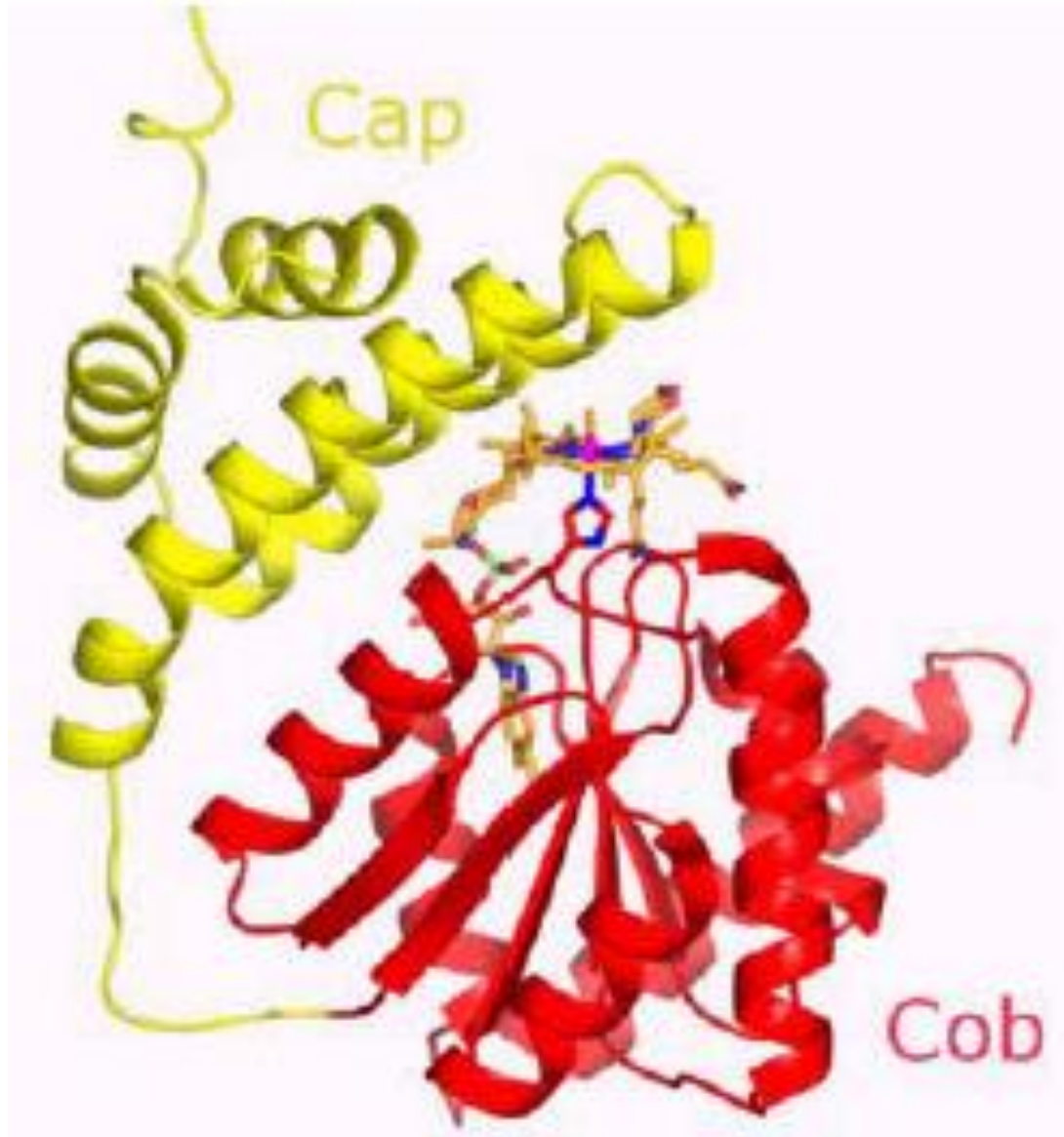
# Metionina Sintasi



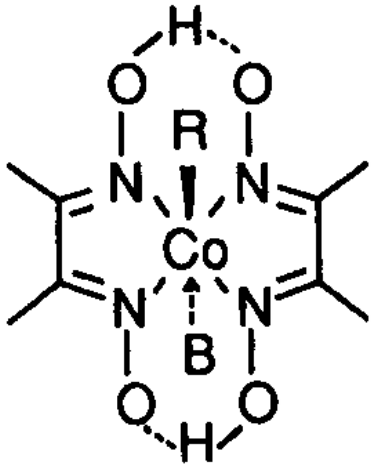
# Variazioni conformazionali della metionina sintasi



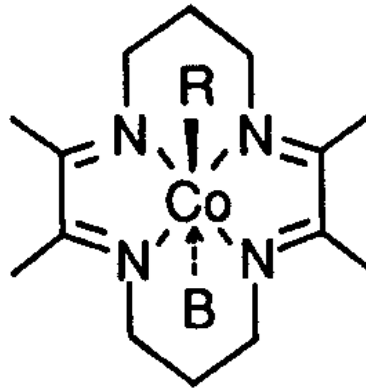
# Metilcobalamina in Cap-Cob: *base-off/His-on*



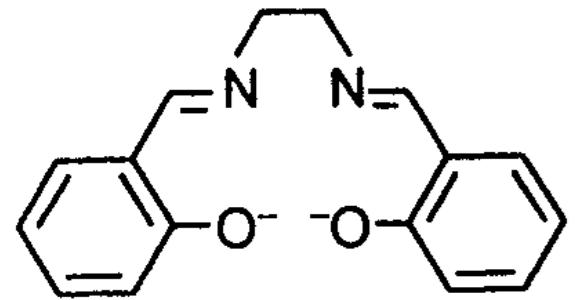
# Modelli



cobaloxime  
complex

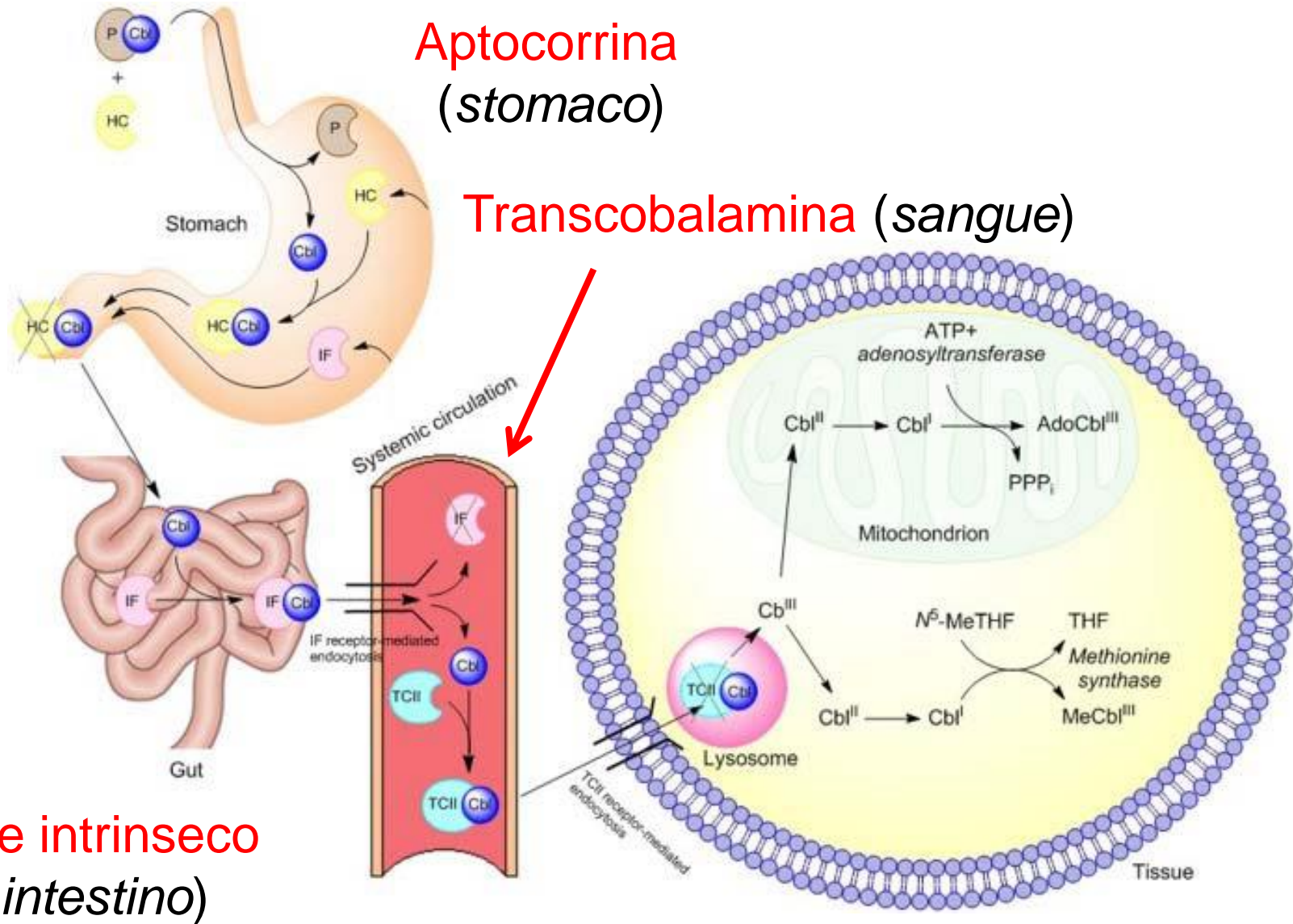


a Costa complex

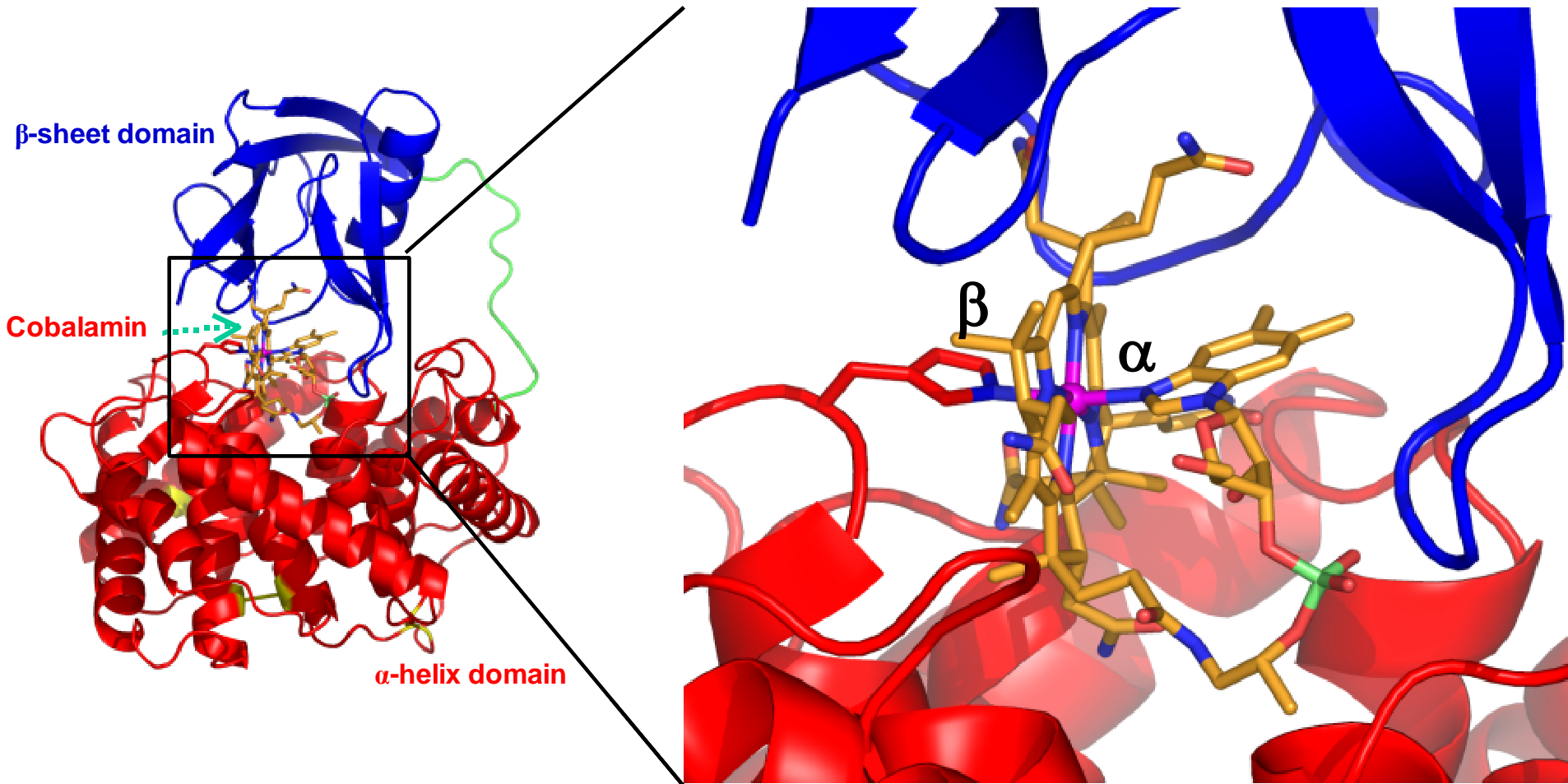


*salen* ligand

# Uptake e Trasporto della Cobalamina



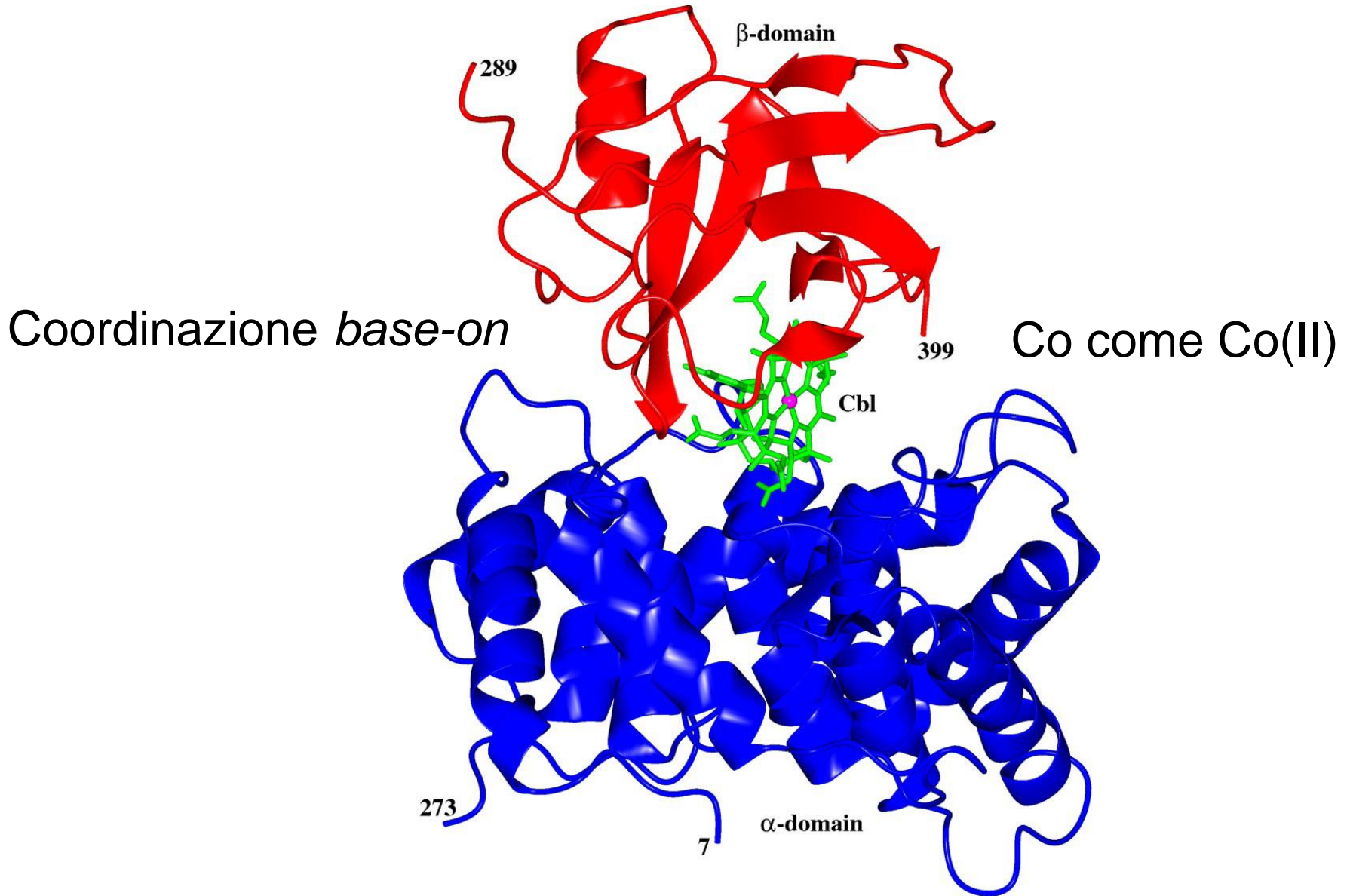
# Struttura TC+Cobalamina (2006)



Coordinazione *base-on/His-on* (su  $\beta$ )



# Complesso IF-Cbl (2007)



# Addotto IF-Cbl con CUB<sub>5-8</sub> recettori della cubilina

