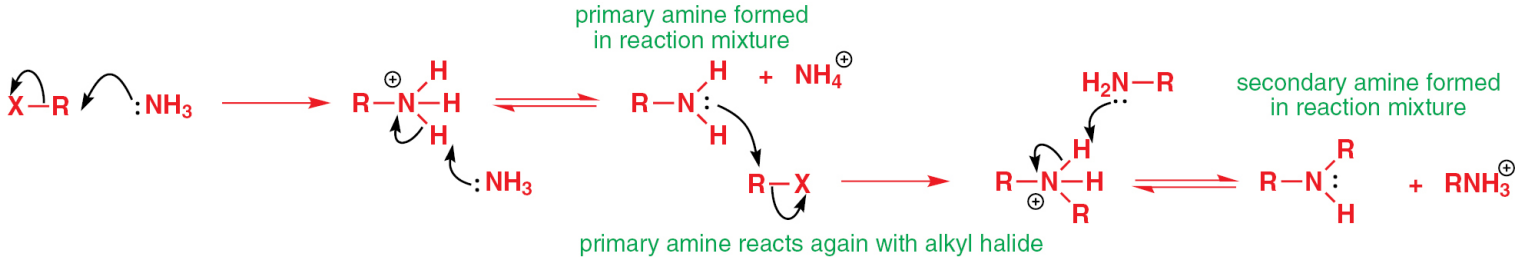
note sui nucleofili a base di azoto, zolfo, fosforo*

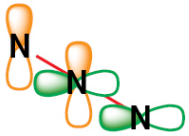
*nelle reazioni S_N2 i nucleofili della porzione inferiore della tavola periodica sono più efficienti di quelli delle prime righe.

Nucleofili a base di azoto

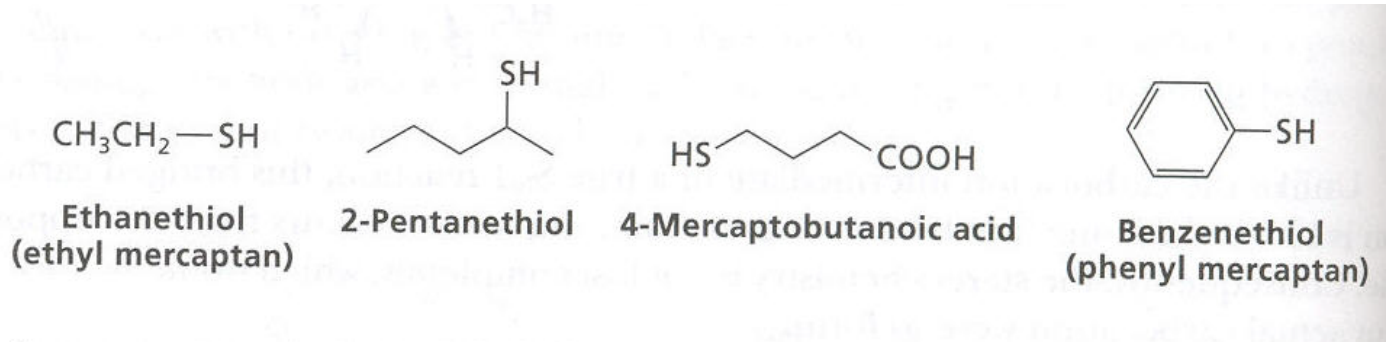


la reazione tra ammoniaca e un alogenuro alchilico si risolve di solito in una miscela di prodotti. Continuando secondo lo schema si arriverebbe all'ammina terziaria e infine al sale di ammonio. Un sistema utile per ottenere ammine primarie e quello che utilizza N_3^- seguito da riduzione con un agente riducente

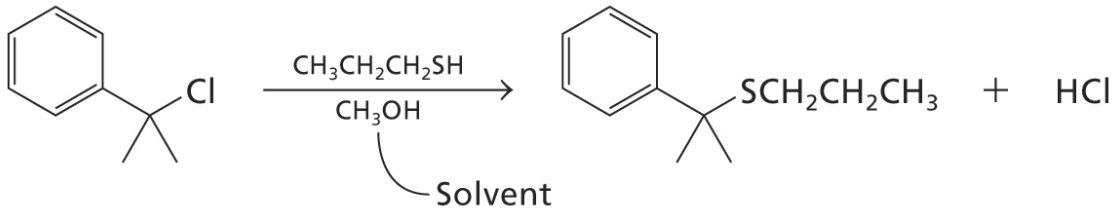
structure of azide ion N_3^-



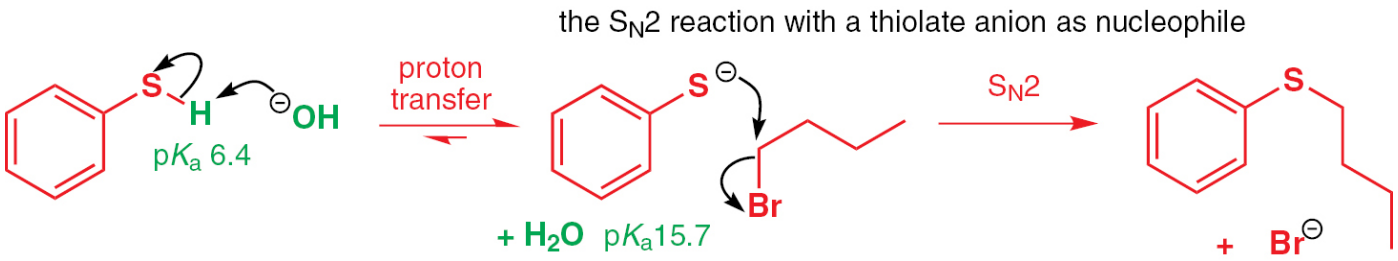
Nucleofili a base di zolfo: tioli

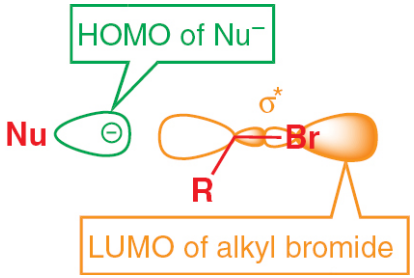


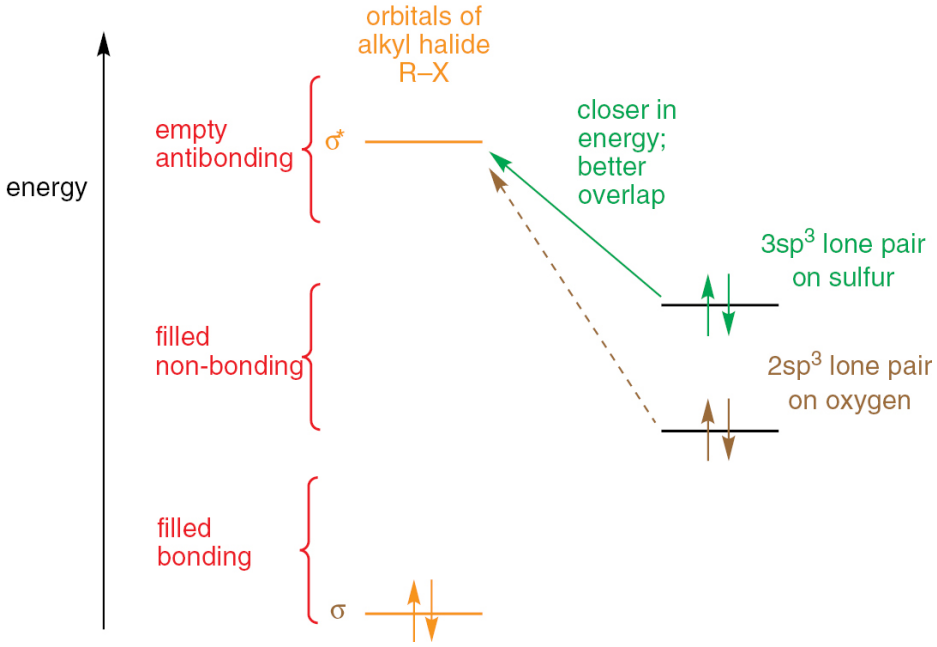
I tioli, meno basici dei corrispondenti alcoli, possono essere usati come nucleofili in reazioni S_N1 per dare solfuri (tioeteri).



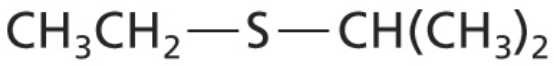
gli anioni tiolato sono eccellenti Nu; migliori di quelli a base di ossigeno (alcossidi) in reazioni S_N2 con alogenuri alchilici. Di solito si combina il tiolo, NaOH e l'alogenuro per ottenere il solfuro in buona resa



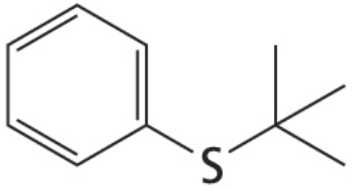




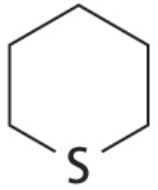
solfuri (tioeteri)



Ethyl isopropyl sulfide

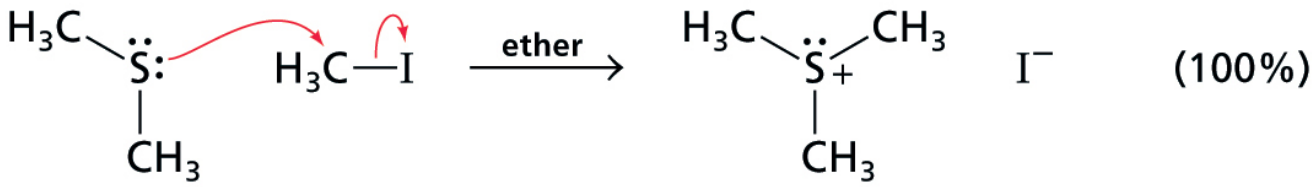


tert-Butyl phenyl sulfide



Thiacyclohexane

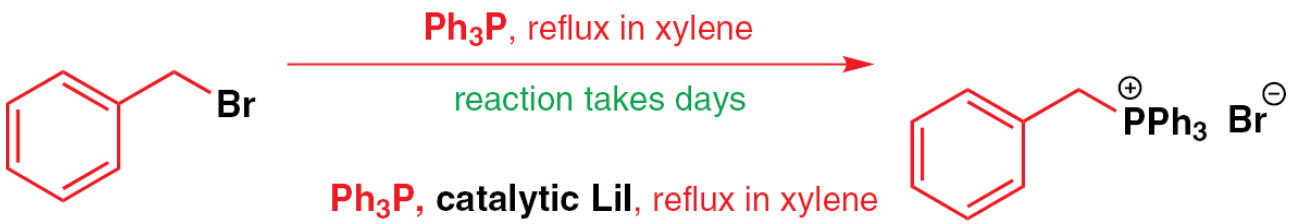
I solfuri sono dei nucleofili. In presenza di metil ioduro si metila lo zolfo formando trimetilsolfonio ioduro.

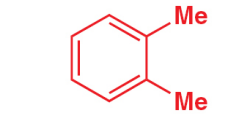


Dimethyl sulfide

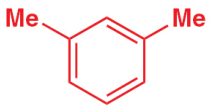
Trimethylsulfonium iodide

un nucleofilo a base di fosforo: la trifenilfosfina

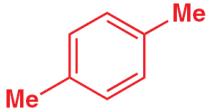




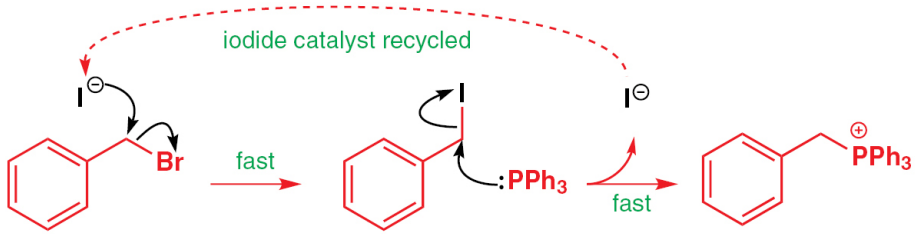
ortho-xylene
1,2-dimethyl benzene



meta-xylene
1,3-dimethyl benzene



para-xylene
1,4-dimethyl benzene



lo xilene commerciale a basso costo è di solito una miscela di isomeri derivata dal petrolio

nucleofili *hard* o *soft*

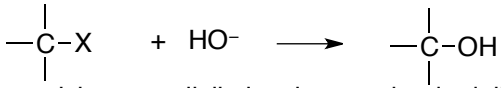
hard (duri) X

- piccoli
- basici (HX debole)
- HOMO a bassa energia
- RO^-, NH_2^-

soft (teneri) Y

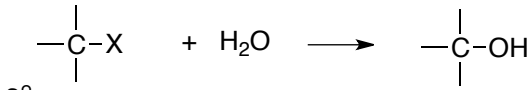
- grandi
- non basici (HY acido forte)
- HOMO ad alta energia
- RS^-, I^-, R_3P

Nu	F^-	H_2O	Et_3N	Br^-	PhO^-	EtO^-	I^-	PhS^-
v relativa	0,0	1.0	1400	5000	$2\cdot10^3$	$6\cdot10^4$	$1{,}2\cdot10^5$	$5{,}0\cdot10^7$



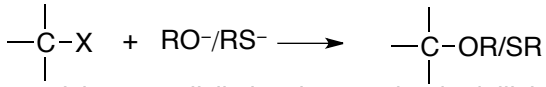
alcoli

competizione con l'eliminazione andando dall'alogenuro primario al terziario



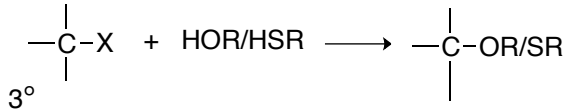
alcoli

3°



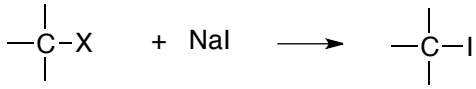
eteri/solfuri

competizione con l'eliminazione andando dall'alogenuro primario al terziario



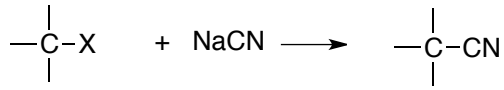
eteri/solfuri

3°

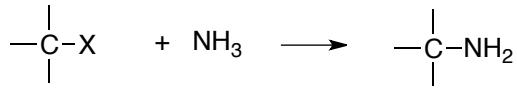


alogenuri

X = Cl, Br; 1° > 2° > 3°

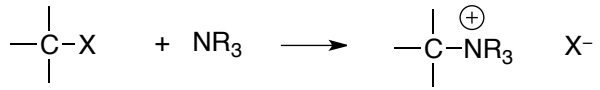


nitrili



ammine

1° > 3°

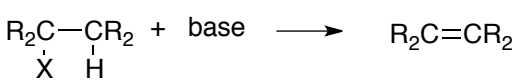


sali di ammonio

1° > 3°

sali di solfonio

1° > 3°

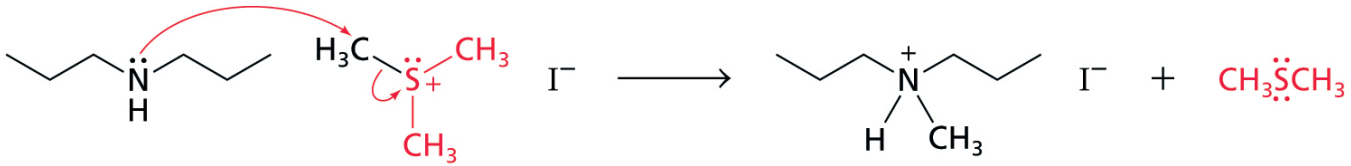


alcheni

3° > 2° > 1°; favorita dalla ramificazione alchilica al C elettrofilo
e a quelli adiacenti

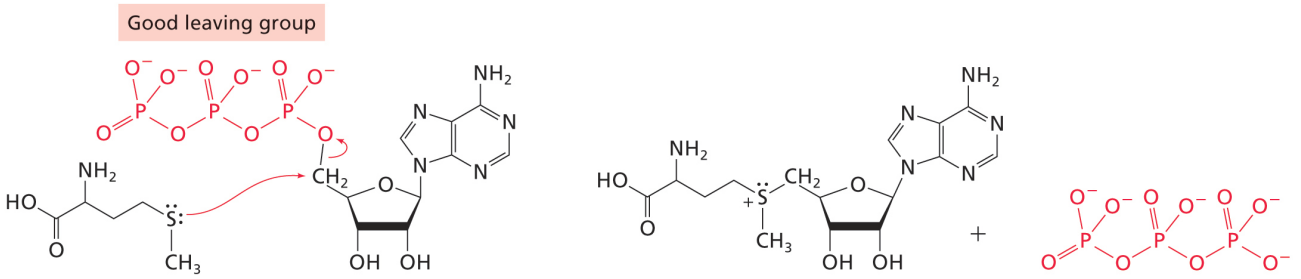
un esempio S_N2 in ambiente biologico

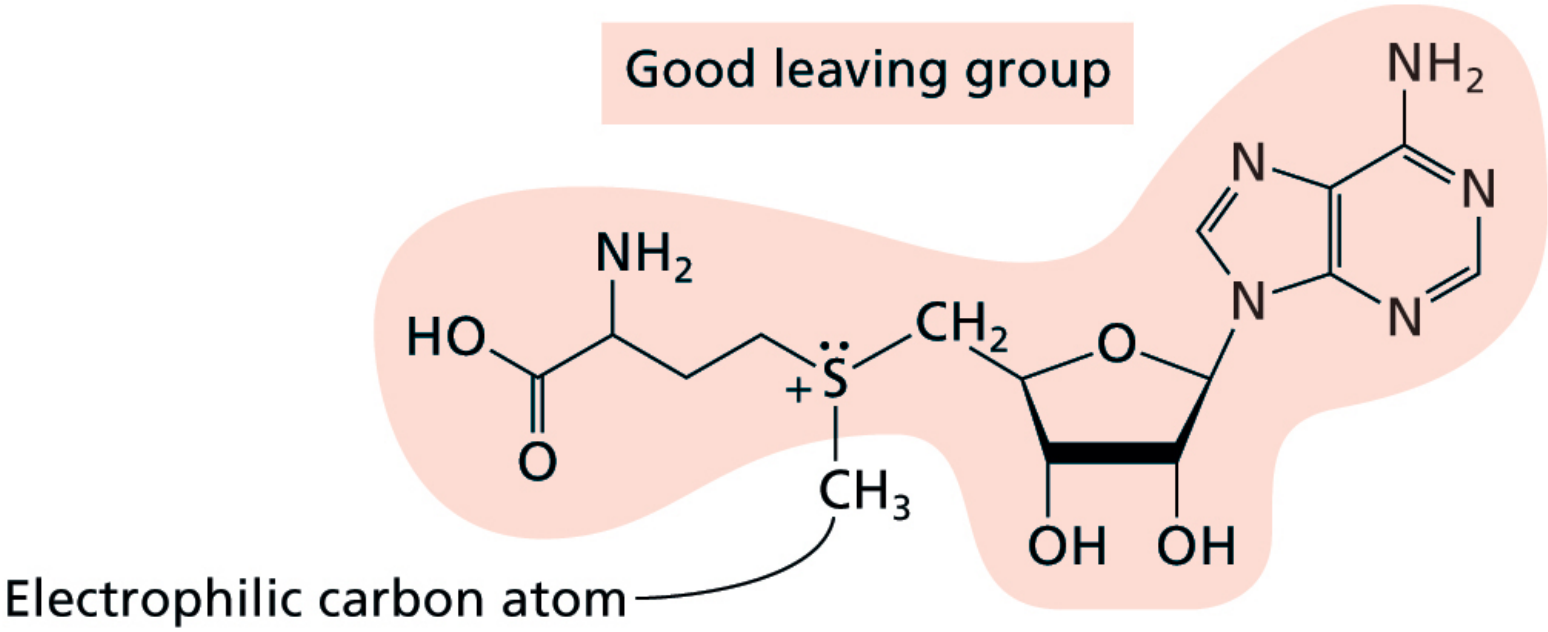
Un sale di solfonio, in presenza di un nucleofilo, reagisce attraverso una una reazione di alchilazione (metilazione) con uscita di dimetilsolfuro (buon gruppo uscente).

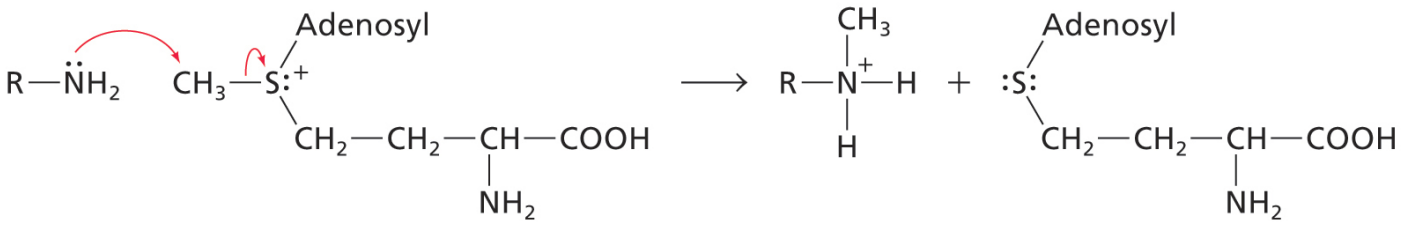


Good leaving group

metilazione delle ammine in ambiente biologico (attraverso un analogo di CH_3-X)

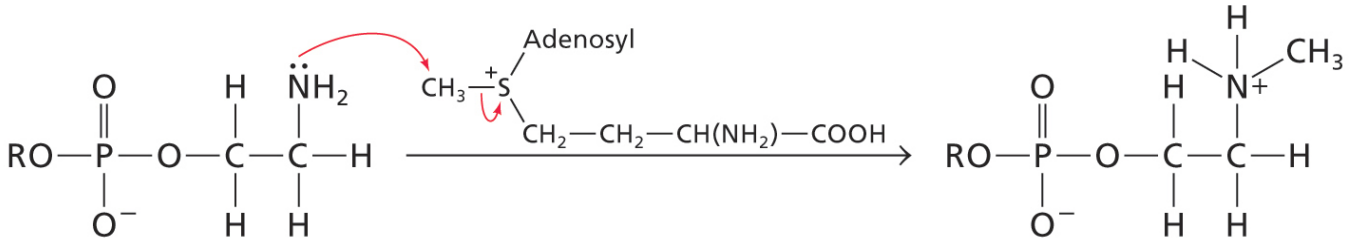




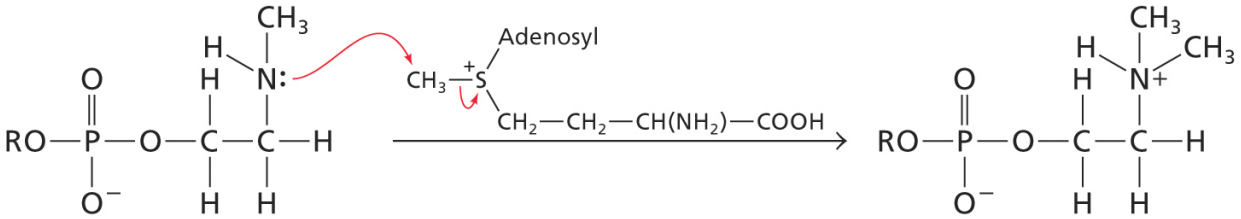


***S*-Adenosylmethionine** **S-Adenosylhomocysteine**

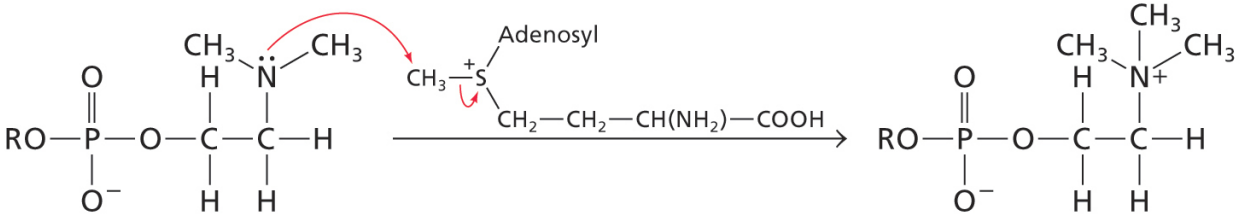
Specific:



Phosphatidylethanolamine → **Phosphatidyl *N*-methylethanolammonium ion**



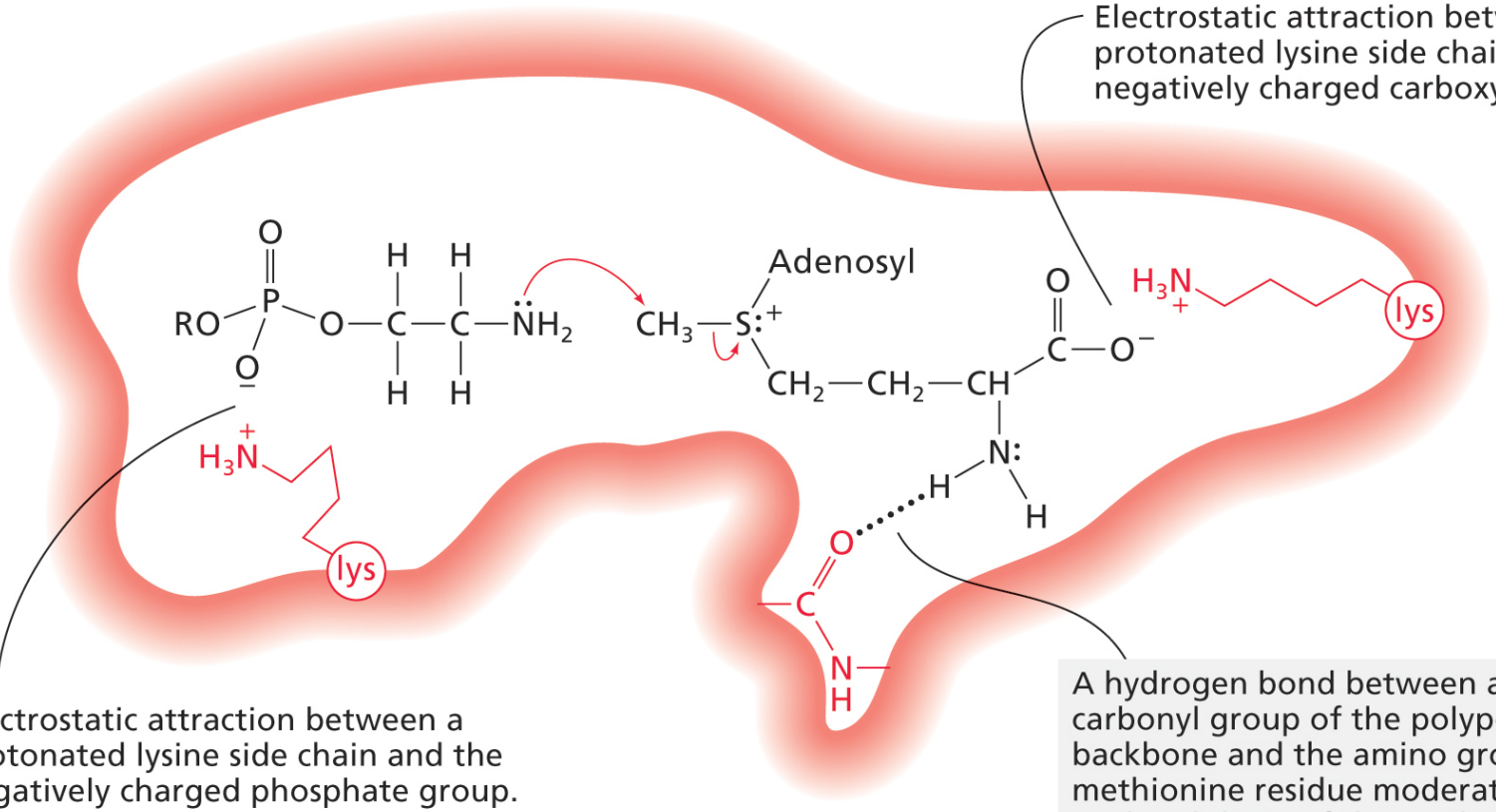
Phosphatidyl *N*-methylethanolamine → **Phosphatidyl *N,N*-dimethylethanolammonium ion**



Phosphatidyl *N,N*-dimethylethanolamine → **Phosphatidylcholine**

costituente delle membrane cellulari

Noncovalent interactions between the substrate molecules and the amino acids that make up the enzyme active site orient the two reactants so that only the desired transformation takes place.



biosintesi dell'adrenalina

Norepinephrine **Epinephrine (adrenaline)**