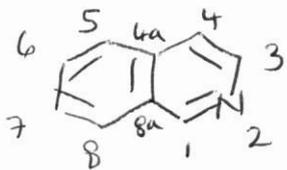


ISOCHINOLINA



NUMERAZIONE:

①

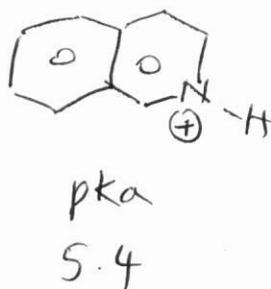
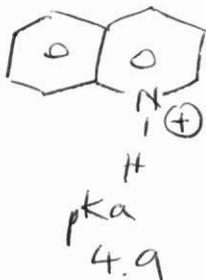
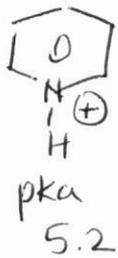
- segue quella del naftalene
- numero piccolo su N
- numeri e lettere ~ chinolina

PROPRIETA' ELETTRONICHE ~ CHINOLINA:

* regola di Hückel con $n=2$ AROMATICA PLANARE

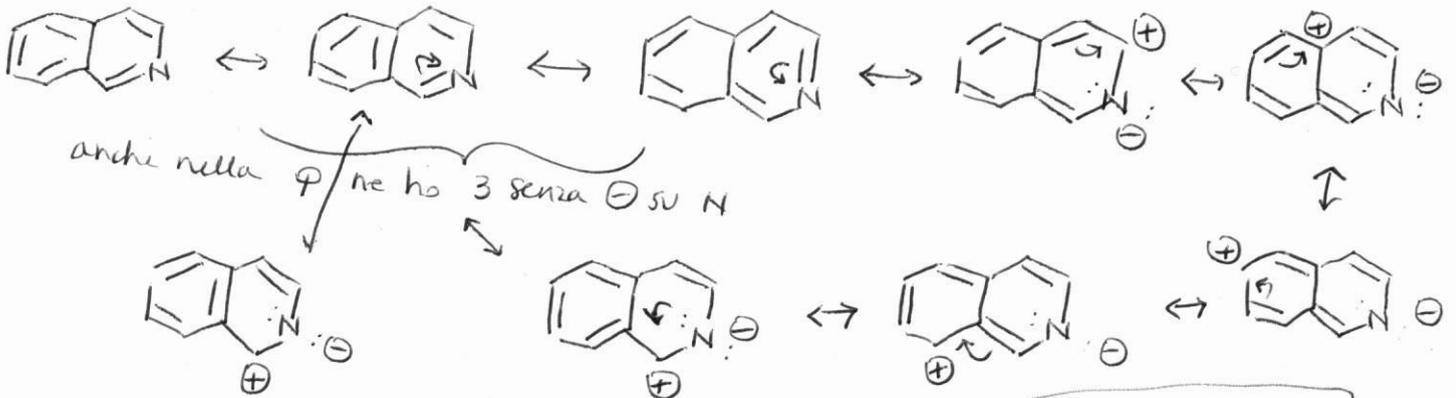
* sp^2

* doppietto N disponibile per basicità

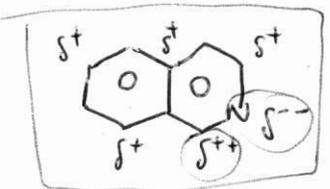


leggermente + BASICA di PYR e di Q perche' doppietto di N e' meno delocalizzato.
(confrontare 10 strutt. ris. Q con 9 strutt. ris. ISO Q.)

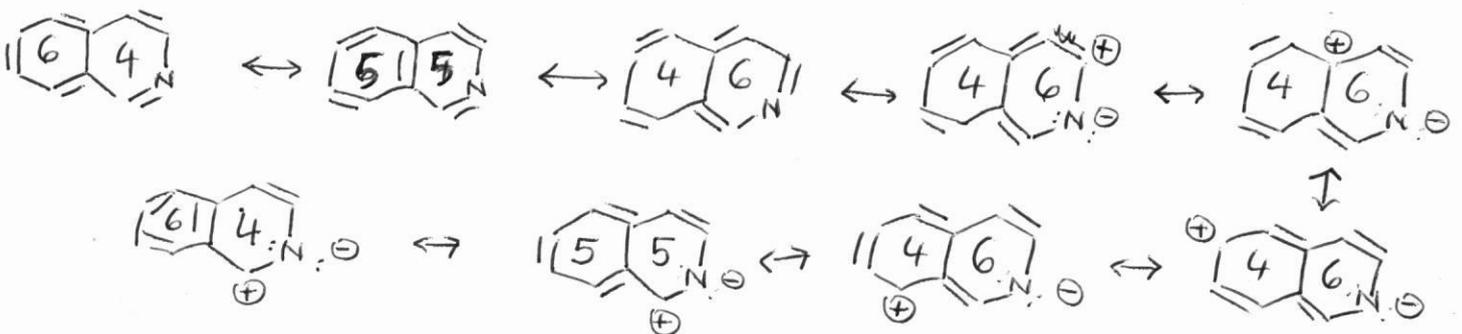
9 STRUTT. RIS.: (nella Q sono 10)



Se confronto gli e π dei 2 ANELLI:



ISOCHINOLINA



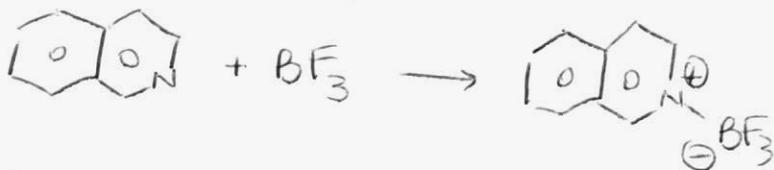
\Rightarrow 2 con 5+5, 2 con 6+4, e ben **(5)** con 4+6 e π su anello AZOTATO
Nella Q: 3 con 5+5, 3 con 6+4 e ^{"solo"} **(4)** con 4+6 e π su anello AZOTATO

REATIVITA' ISOCHINOLINA:

2

① REAZIONI SU N:

(a) con ACIDI di Lewis:

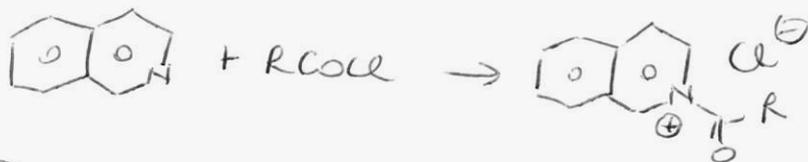


COMPLESSO
ACIDO-BASE di
Lewis

(b) ALCHILAZIONE



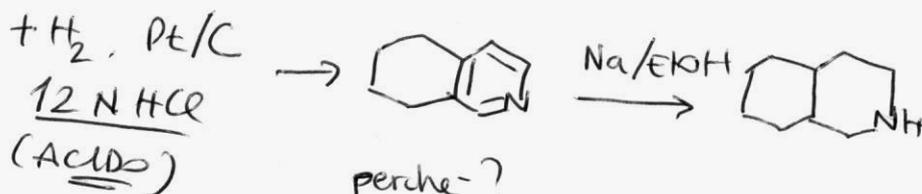
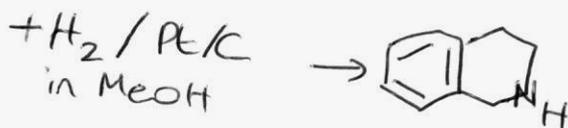
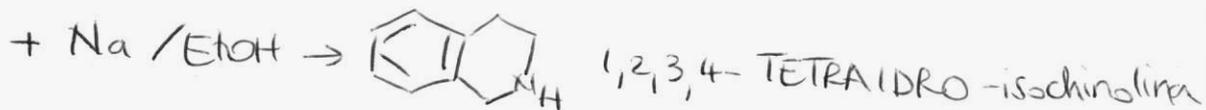
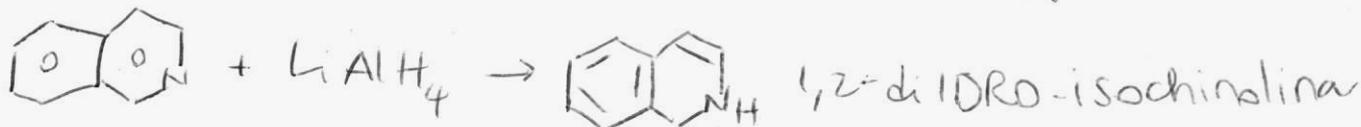
(c) ACILAZIONE



(d) FORMAZ. N-OSSIDO

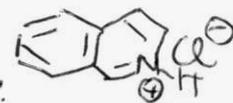


questa è una ossidazione. E la riduzione?



perche'?

POSSIBILE CHE SI FORMI COMPLESSO
CHE RENDE ANELLO AZOTATO
MENO ACCESSIBILE PER RID. CAT



simile a

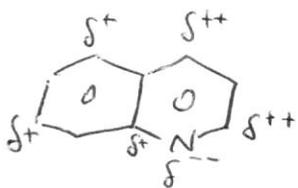
② REAZIONI AL C: S_EA_R

③

Similmente a ρ , S_EA_R avvengono preferenzialmente sull'anello "benzenico" in ⑤ e ⑧ per motivi simili (vedi Brown e appunti su ρ) MA per ISOCHINOLINA

C5 >> C8 perché inoltre:

CHINOLINA

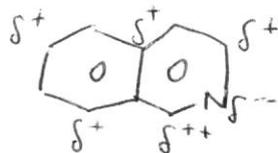


* C5 + povero di e⁻

* C8 disattivato da vicinanza con N

⇒ effetti si compensano a seconda delle condiz. di reazione, posso anche avere sost. C5 + C8 circa 50% ognuna

ISOCHINOLINA

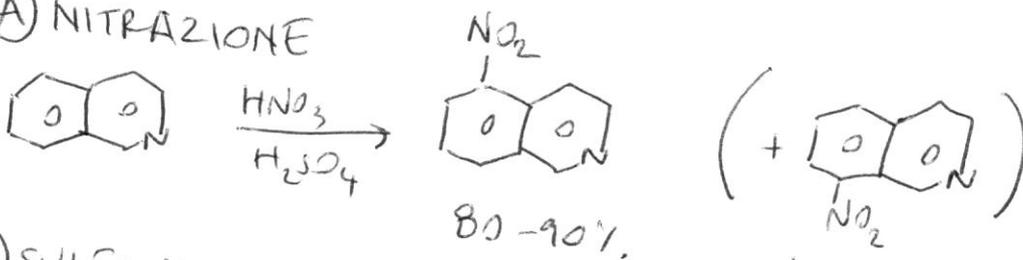


* C8 + povero di e⁻

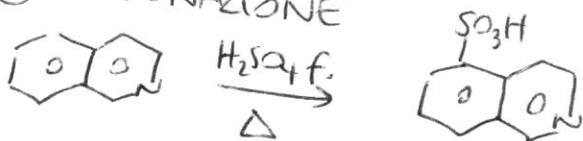
* C8 disattivato da vicinanza N

⇒ C5 + REATTIVO per S_EA_R

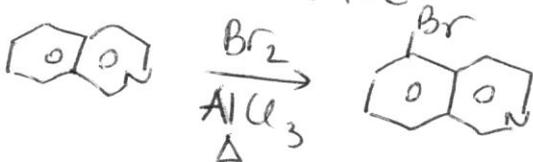
Ⓐ NITRAZIONE



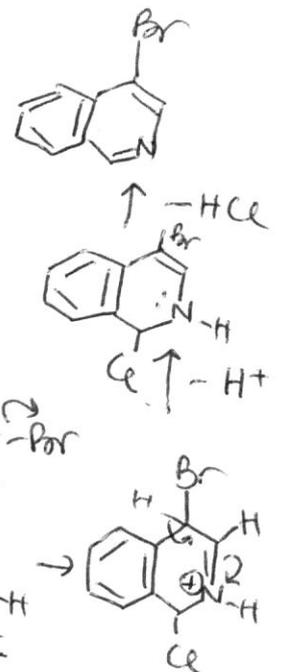
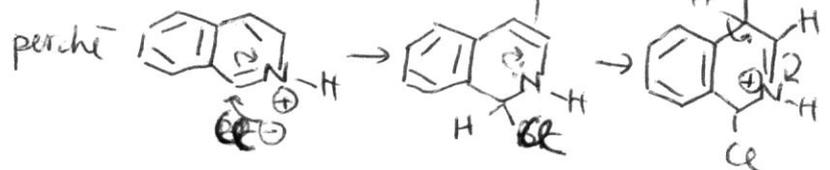
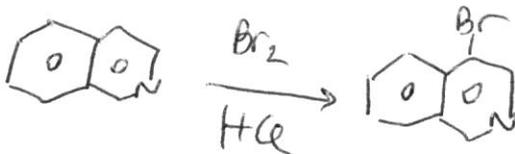
Ⓑ SOLFONAZIONE



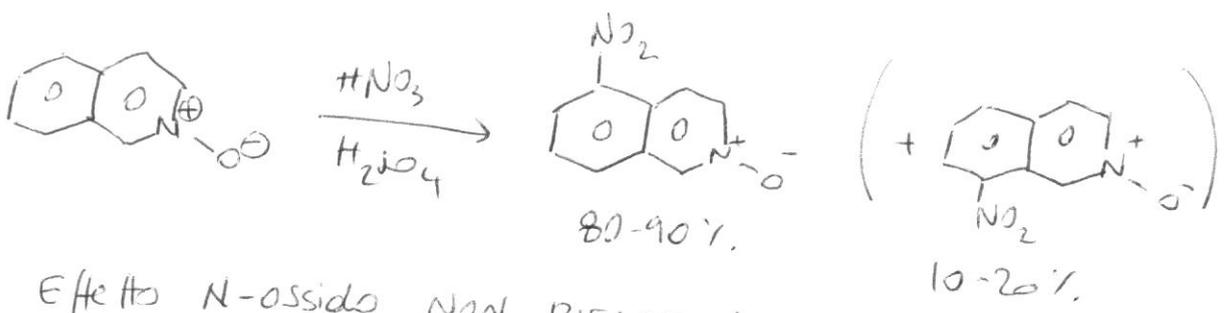
Ⓒ ALOGENAZIONE



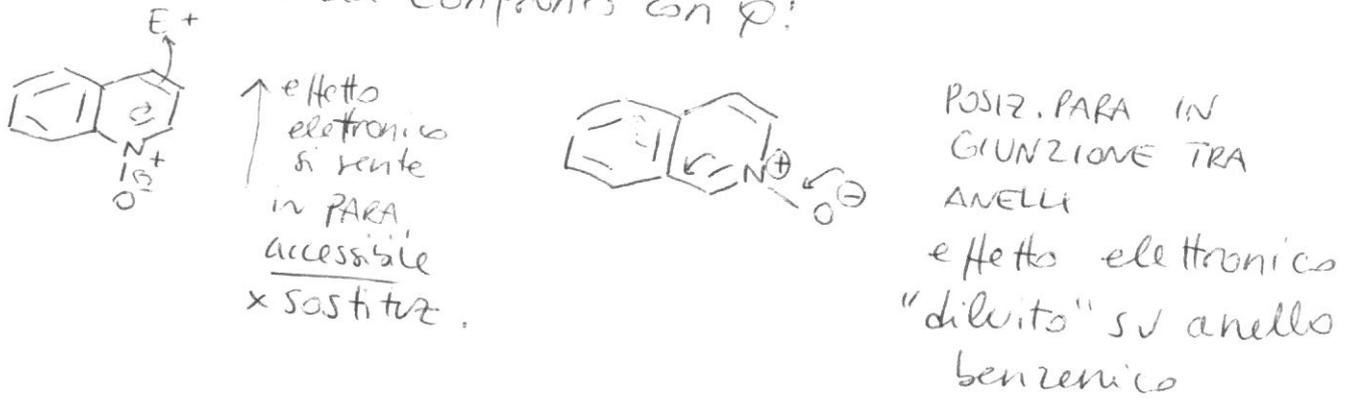
ATTENZIONE PERÒ IN CONDIZ. ACIDE:



S_EAR SU N-OSSIDO

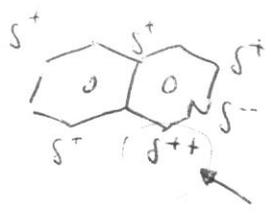


Effetto N-ossido NON RIESCE A PREVALERE SU REATTIVITA' ANELLO "BENZENICO" → reagisce come isochinolina (si vede anche da confronti con p!)

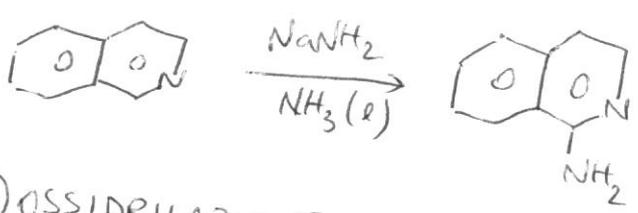


③ S_NAR

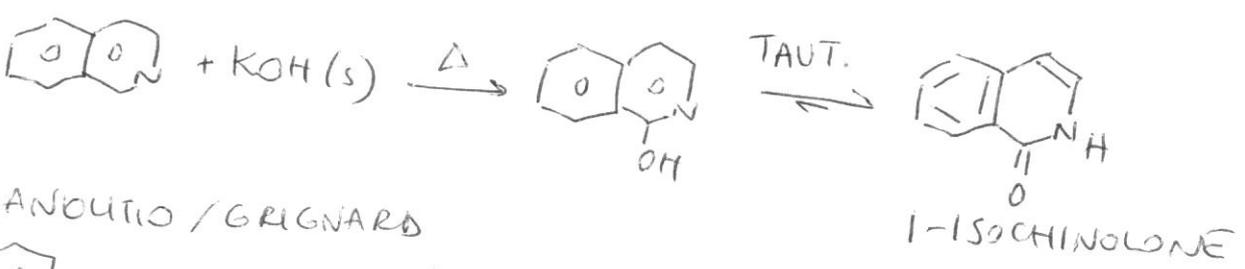
POSIZ. IN α a N PIU' REATTIVE SOPRATTUTTO 1 ⇒ 3
SI VEDE DA STRUTT. RIS.



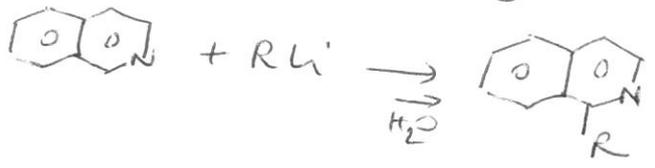
① CHICHIABIN



② OSSIDRILAZIONE



ORGANOLITIO / GRIGNARD

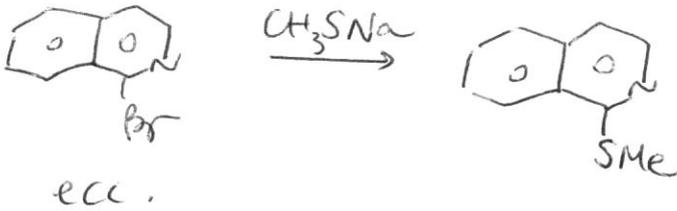


Anche S_NAr su ALOGENODERIVATI:

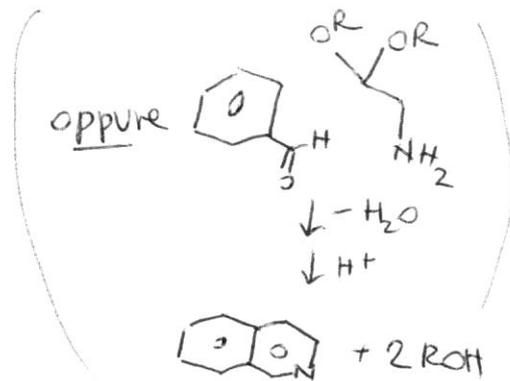
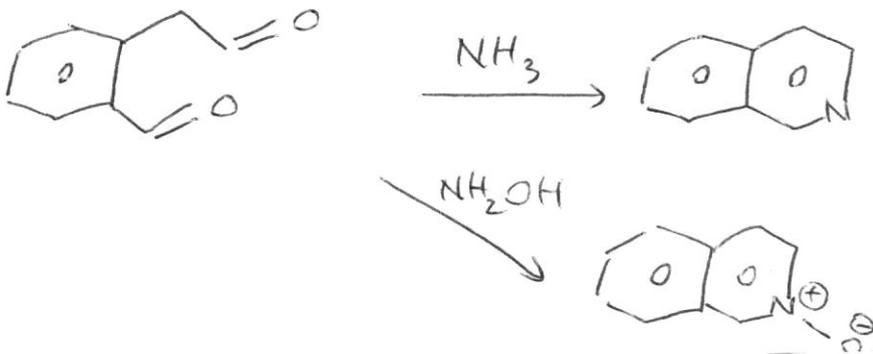
(5)



POSIZ. (7) + REATTIVA
come visto prima

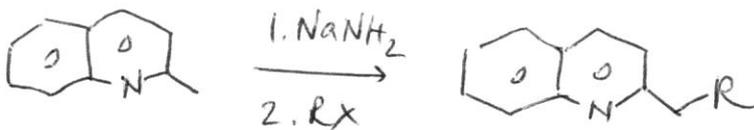
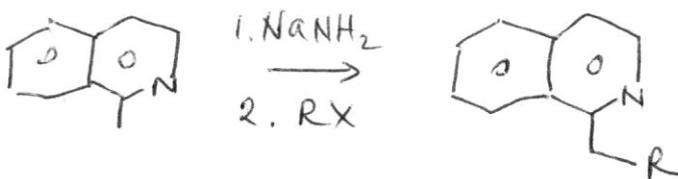


ES. DI SINTESI (CONDENSAZIONI)

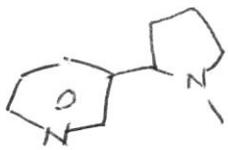


REATTIVITA' CAT. LAT.

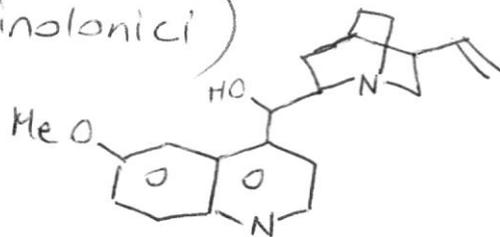
Similmente a pyr e ϕ , CH_3 ACIDI in α a N: 1 >>> 3



COMPOSTI BIOATTIVI CON DERIV. PYR, Q, ISOQ
(oltre ai chinolonici)

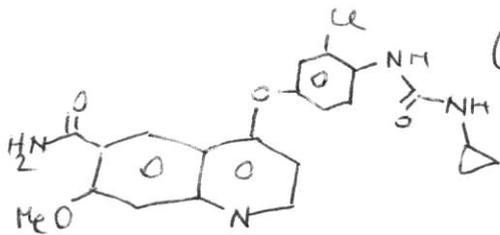


NICOTINA

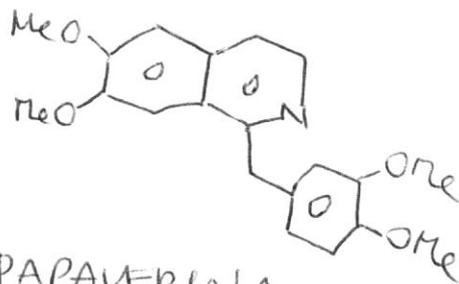


CHININA

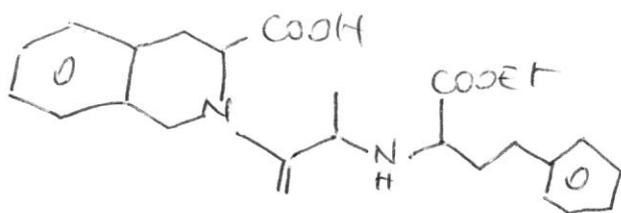
(vedi antimalarici)



lenvatinib
(antitumorale)



PAPAVERINA
(antispasmo)



QUINAPRIL
(anti-iper tensivo...)