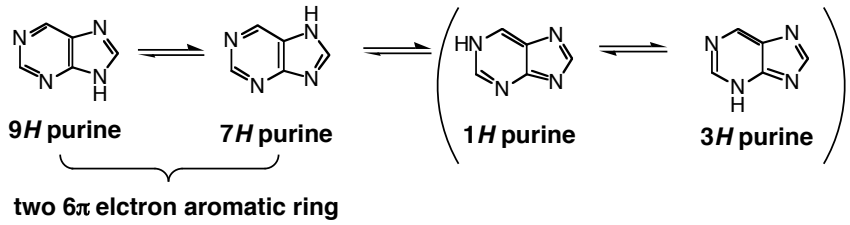
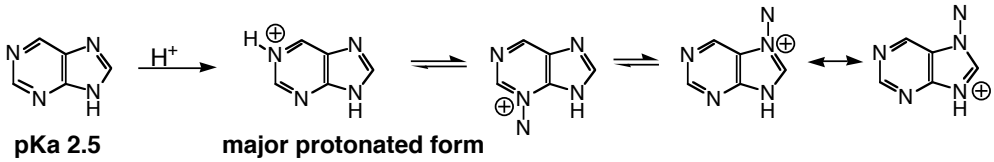
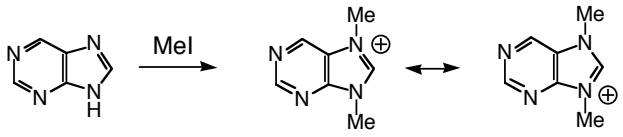
PURINES - kap 24



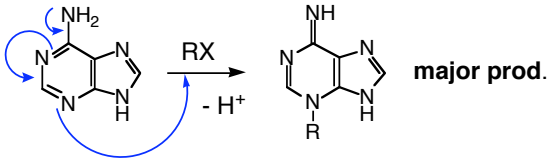
Reaction with electrophiles at N - Protonation



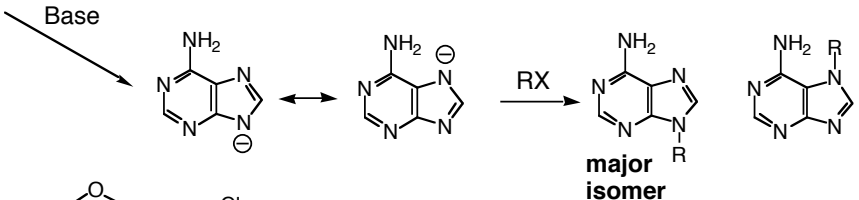
Reaction with electrophiles at N - Alkylation

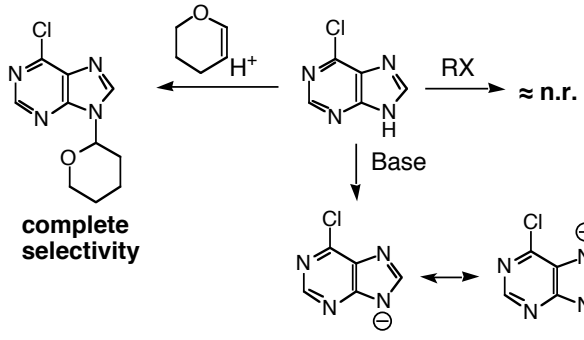


Selectivity depends on substituents and conditions



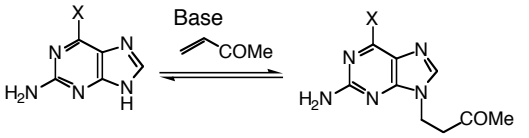
major prod.



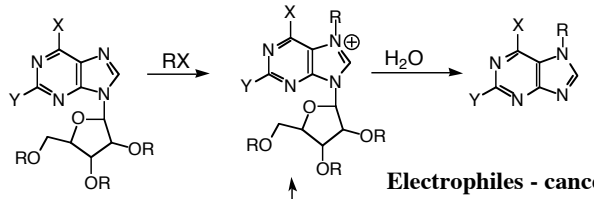


N7/N9: - Sterical factors (Large 6-subst)

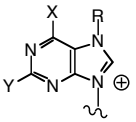
Termodyn. control (reversible react.)

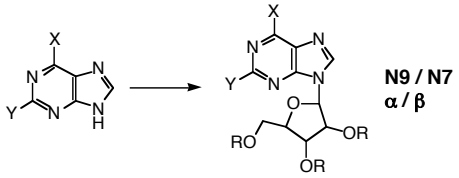


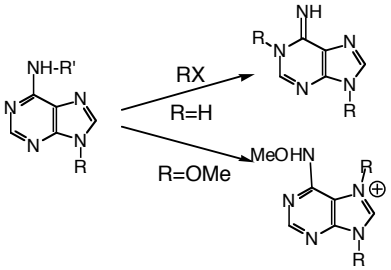
X	Time	N9 / N7
Cl	1h	4.3 : 1
Cl	24h	19 : 1
Cl	24h	200 : 1
OMe	1h	1 : 1
OMe	14 days	Still mixt.

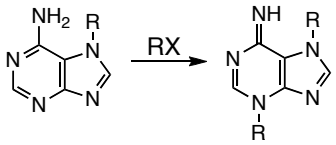


Electrophiles - cancer





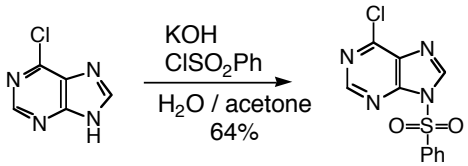




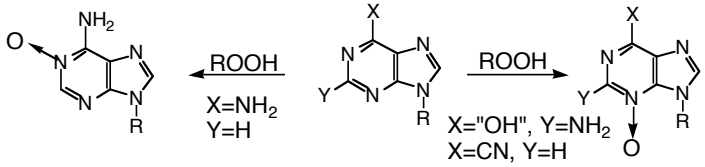
Reaction with electrophiles at N - Acylation / Sulfonation

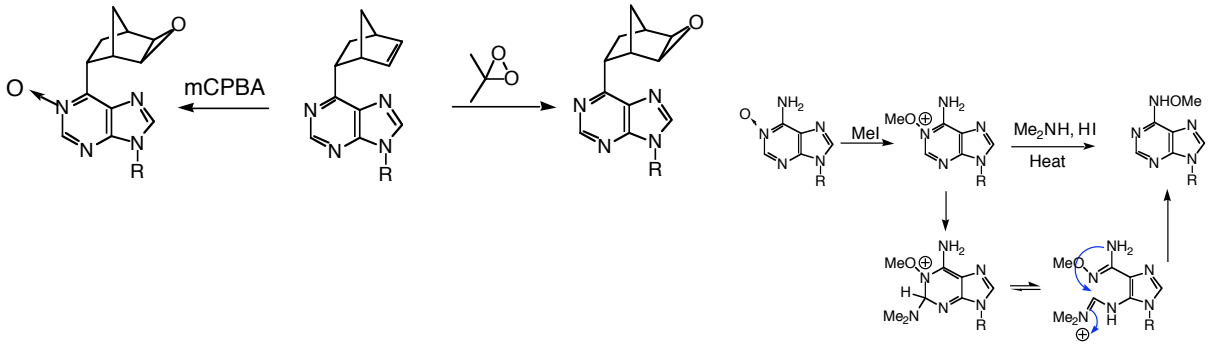
Acylation products generally unstable

Sulfonation - Stable prod., selective N9

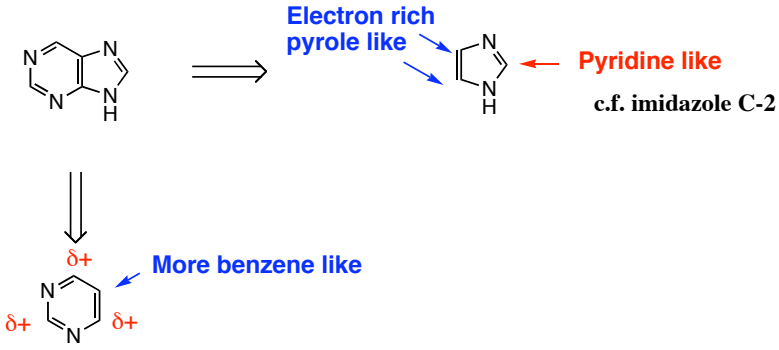


Reaction with electrophiles at N - oxidation





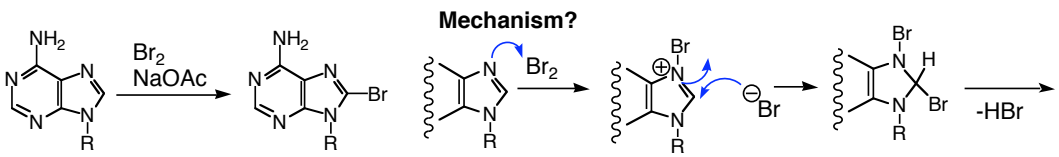
Reaction with electrophiles at C

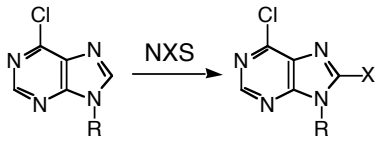


No good position for E-fil Ar subst

Reaction with electrophiles at C

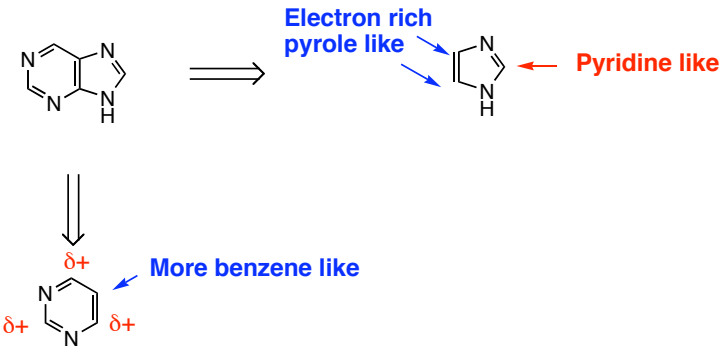
E-fil Ar subst, generally not working



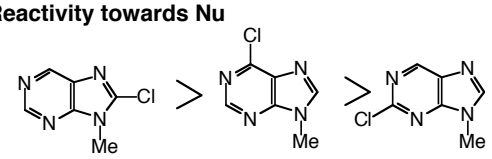


Radical mech.?

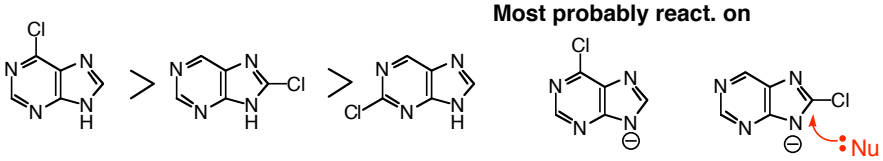
Reaction with nucleophiles

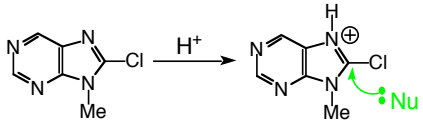


Reactivity towards Nu

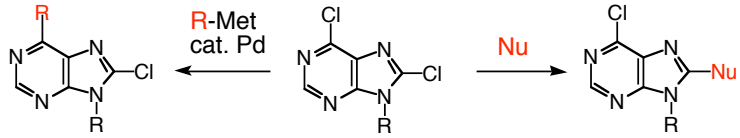


Most probably react. on



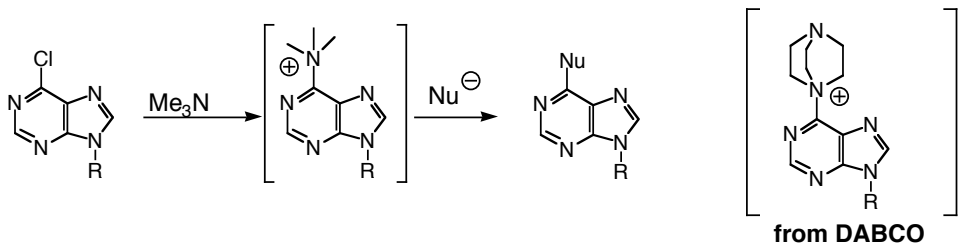


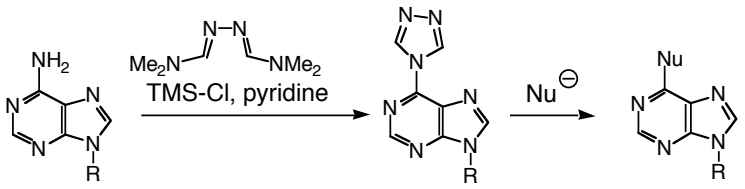
activated for Nu attack



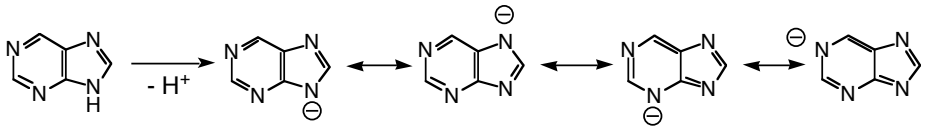
Nu.Ar.Subst: Reactivity F>Cl>Br>I

Other leaving groups

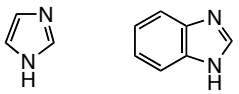




Deprotonation at N

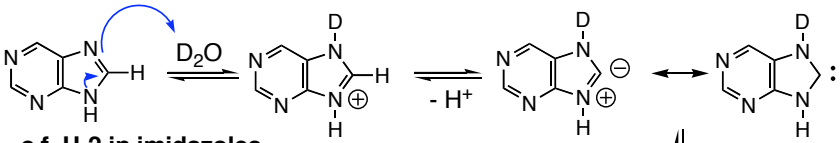


pKa 8.9

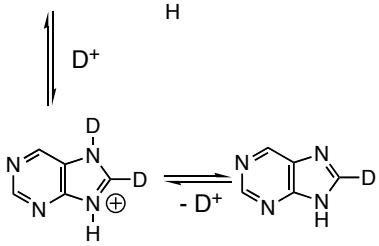


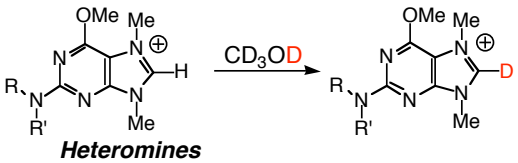
pKa 14.2 pKa 12.3

Deprotonation at C / C-metallation

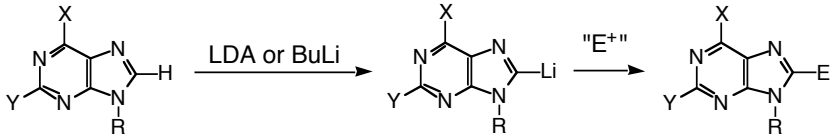


c.f. H-2 in imidazoles



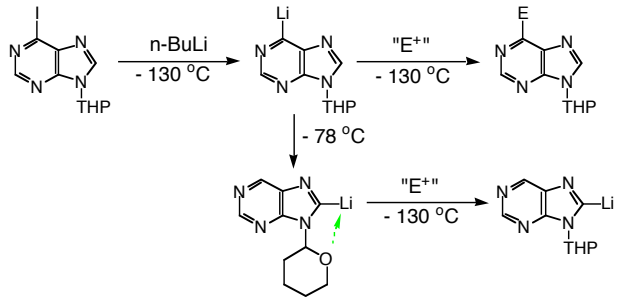


Heteromines

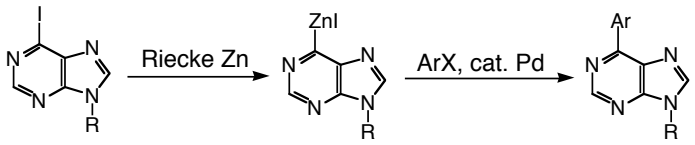


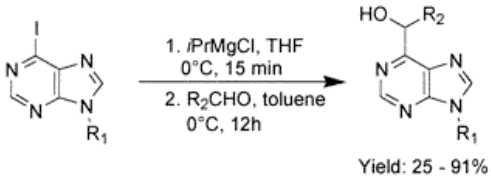
X, Y: NH_2, "OH" ; Excess base

Identity of R is important

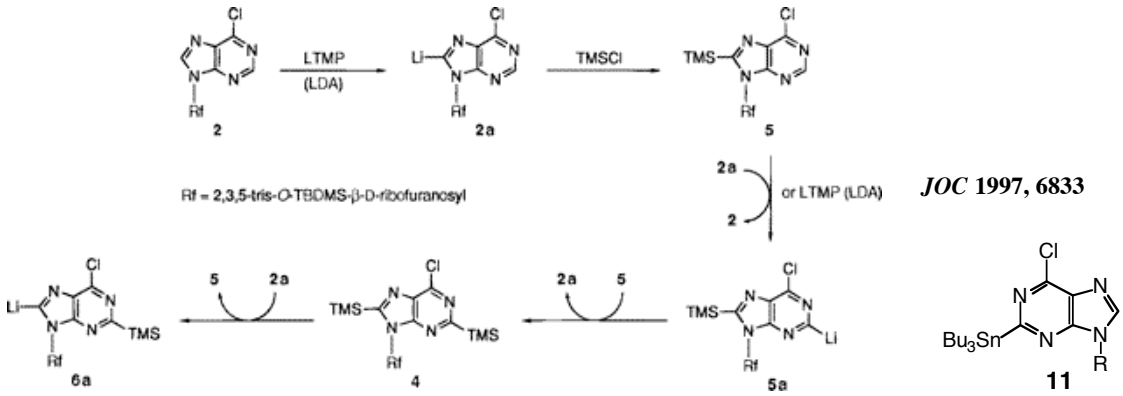


Other metallated species more stable

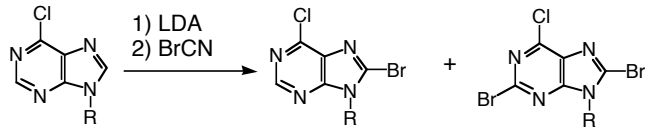




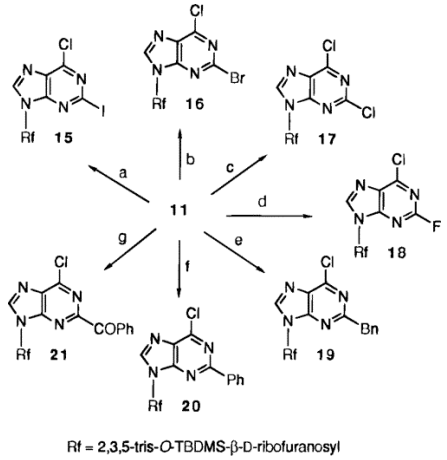
***Org. Lett*, 2003, 4289**



***JOC* 1997, 6833**

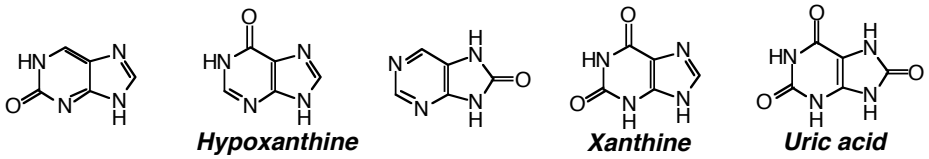


Nolsøe *et al., Synth Commun* 1998, 4303

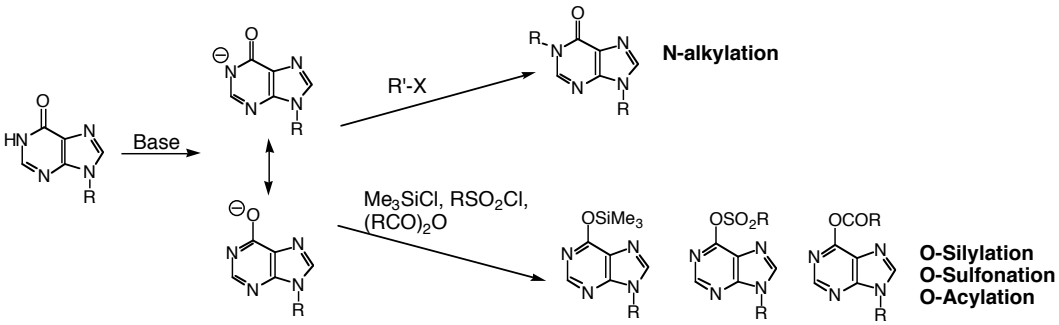


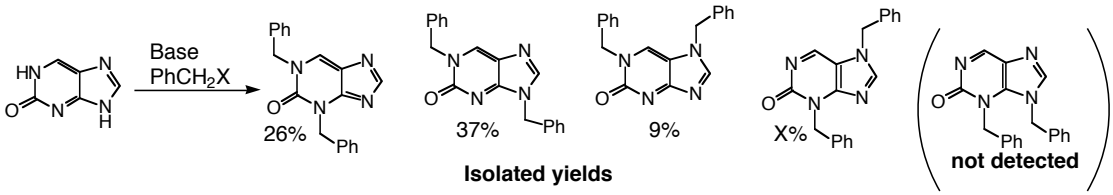
Oxy purines

-Oxo forms

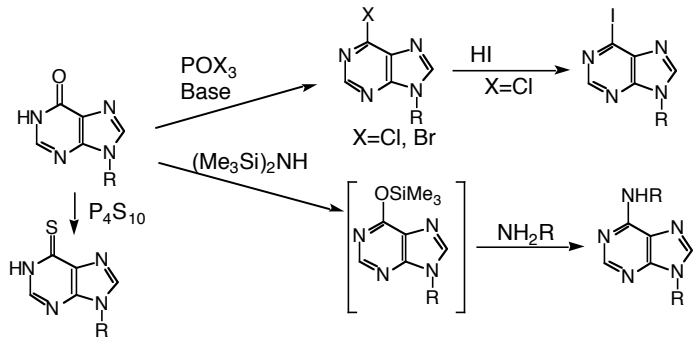


Alkylation, acylation etc



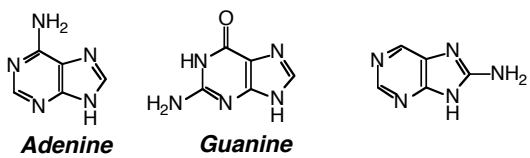


Replacement of O with other hetero atoms

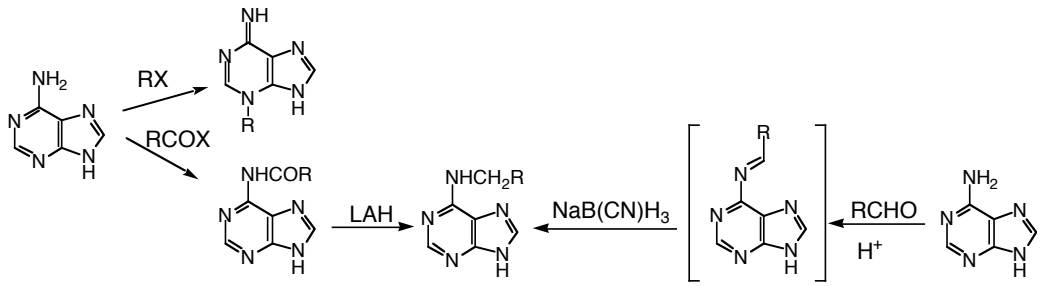


Amino purines

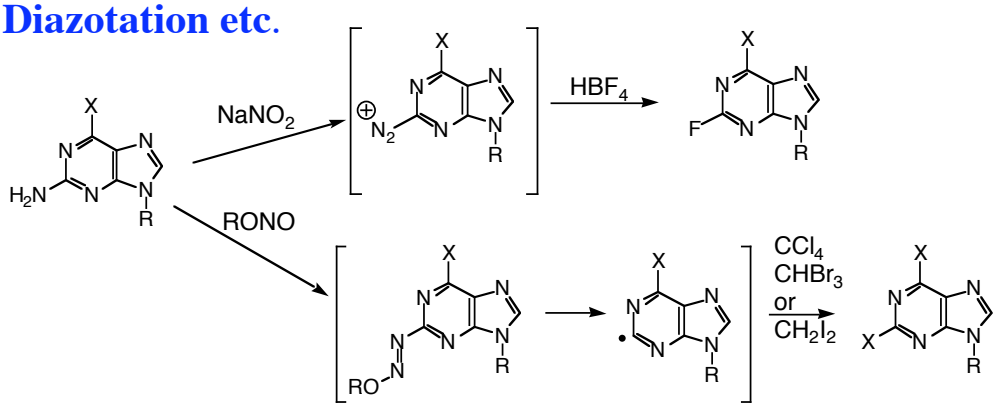
Amino form



Alkylation, acylation etc



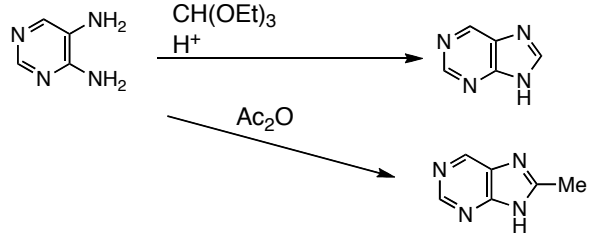
Diazotation etc.

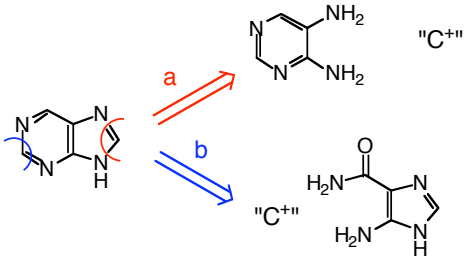


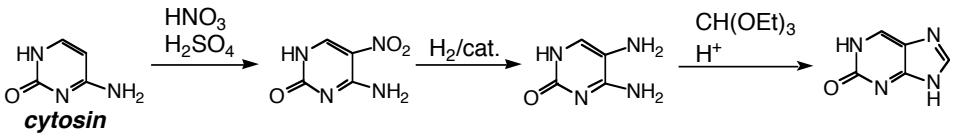
Synthesis of Purines

Carbonyl condensations

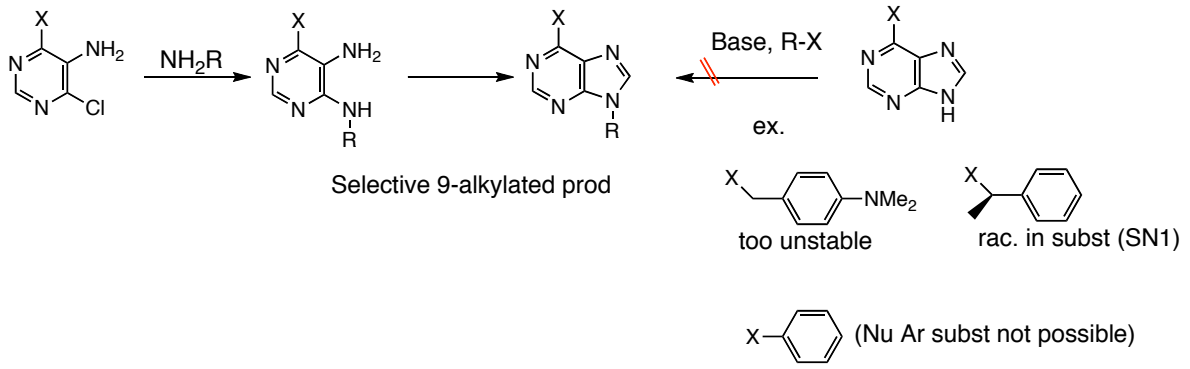
Strategy A - Traube synth. etc

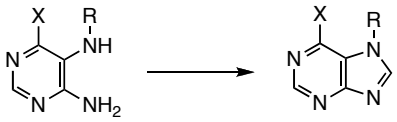






cytosin

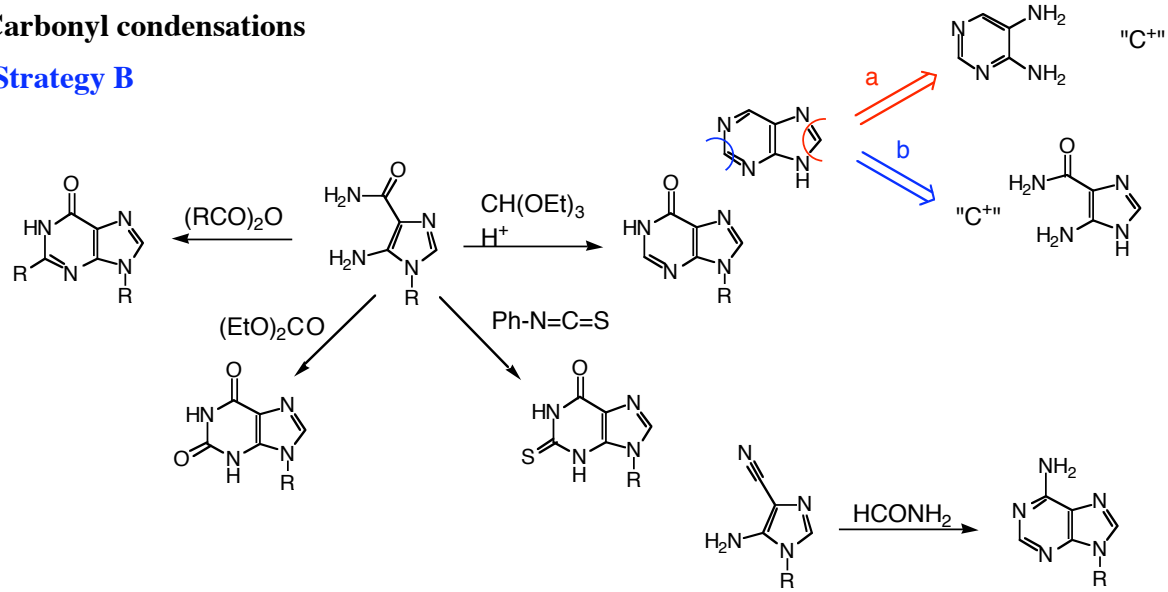




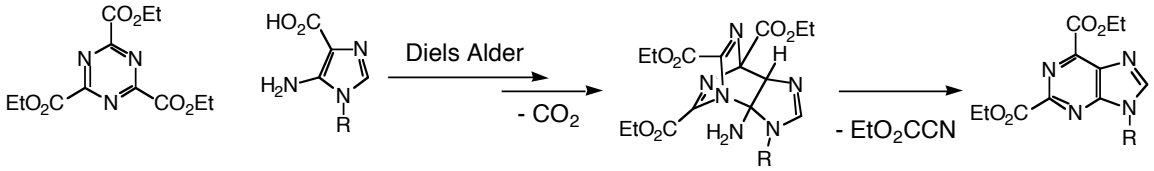
Selective 7-alkylated prod

Carbonyl condensations

Strategy B

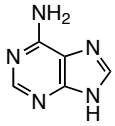


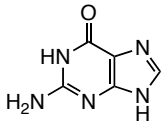
Cycloadditions



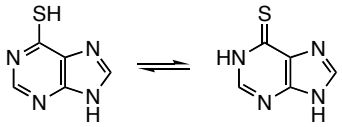
Bioactive Purines

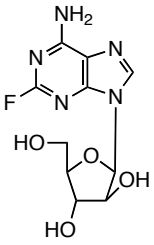
DNA / RNA bases

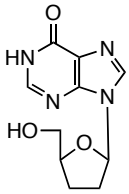

Adenine

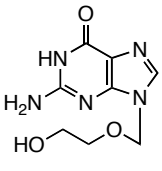

Guanine

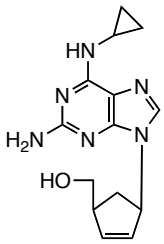
Anticancer / antiviral drugs


6-MP

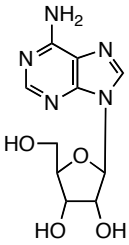

Fludarabine

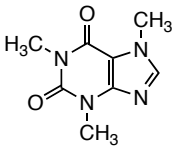

ddI


Acyclovir


Abacavir

Adenosine and adenosine reseptor ligands

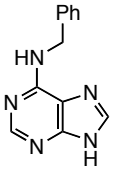


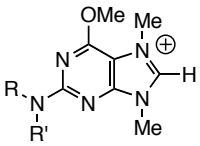

Coffein

Antag. A_1 & A_{2A}

At least 4 sub-types. A_1, A_{2A}, A_{2B}, A_3
No drugs (yet)...
Parkinston and selective A_{2A} antag. ??

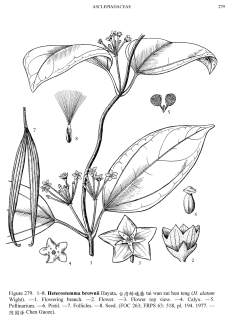
Cytokinins - Plant growth hormones




Heteromines

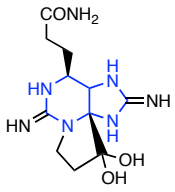
Heteromines

- Isolated from *Heterostemma brownii*
- Treatment of tumors in Taiwanese folk medicine



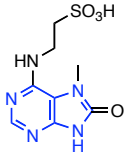
Purine-Containing Marine Natural Products

From marine algae, sponges, gorgonians (sea fans), ascidians (tunicates) etc., etc.

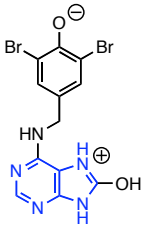


Saxitoxin

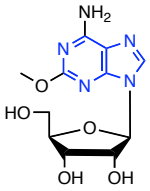
(red tide)



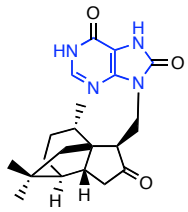
Microxine



Aplidiamine



Spongosine



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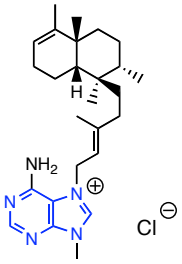
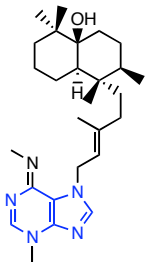
Agelasines



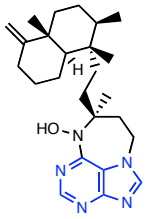
Agelasine A

Agelasimines



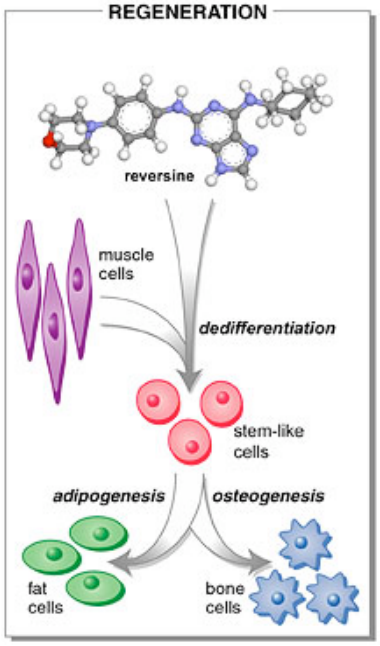
Agelasimine A

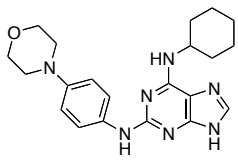
Asmarines



Asmarine A

Reversine





http://www.scripps.edu/news/press/122203.html