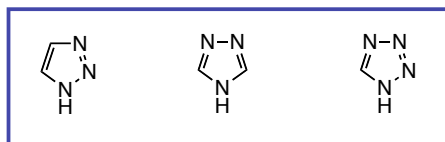


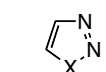
Heterocycles cont. more than 2 heteroatoms in one ring Chapt. 26

5-membered rings

Triazoles and tetrazoles



X=O, S



unstable X=O



Only X=S

6-membered rings

Triazines and tetrazines



unknown

5-membered rings

Triazoles and tetrazoles (pentazoles highly unstable)

More acidic - less basic comp to diazoles



pKa (base): ca 0 (NB aromaticity)
pKa (Acid): 17.5



pKa (base): 7.1
pKa (Acid): 14.2



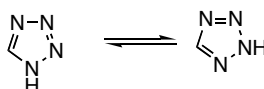
pKa (base): 2.5
pKa (Acid): ca 12



pKa (base): 2.2
pKa (Acid): 10.3



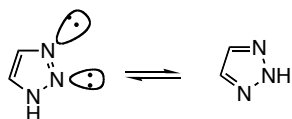
pKa (base): 1.2
pKa (Acid): 9.4



pKa (base): ?
pKa (Acid): 4.9

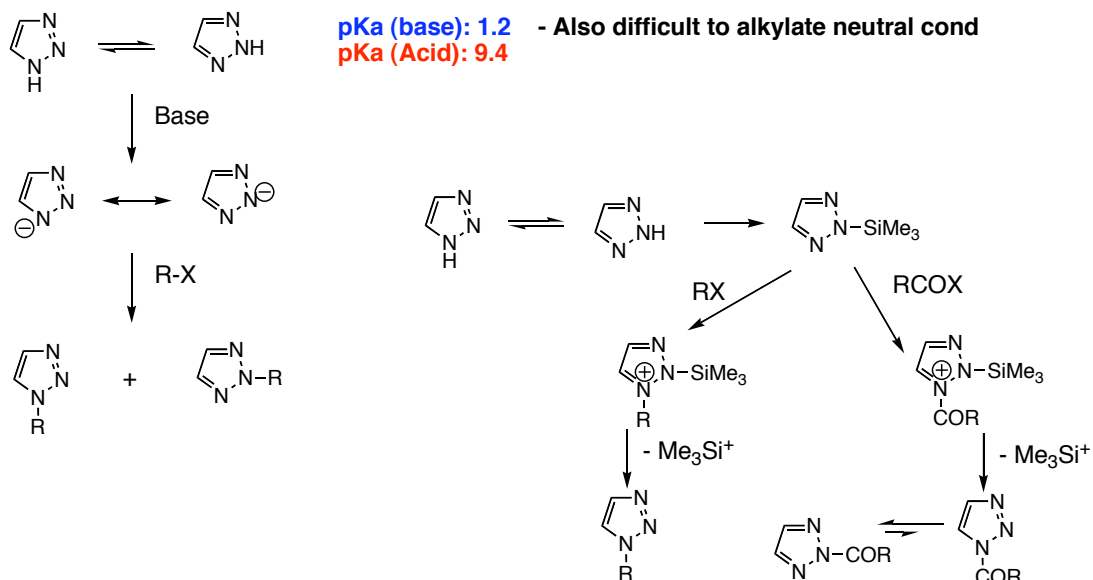
Bioisostere - CO₂H

1,2,3-Triazole



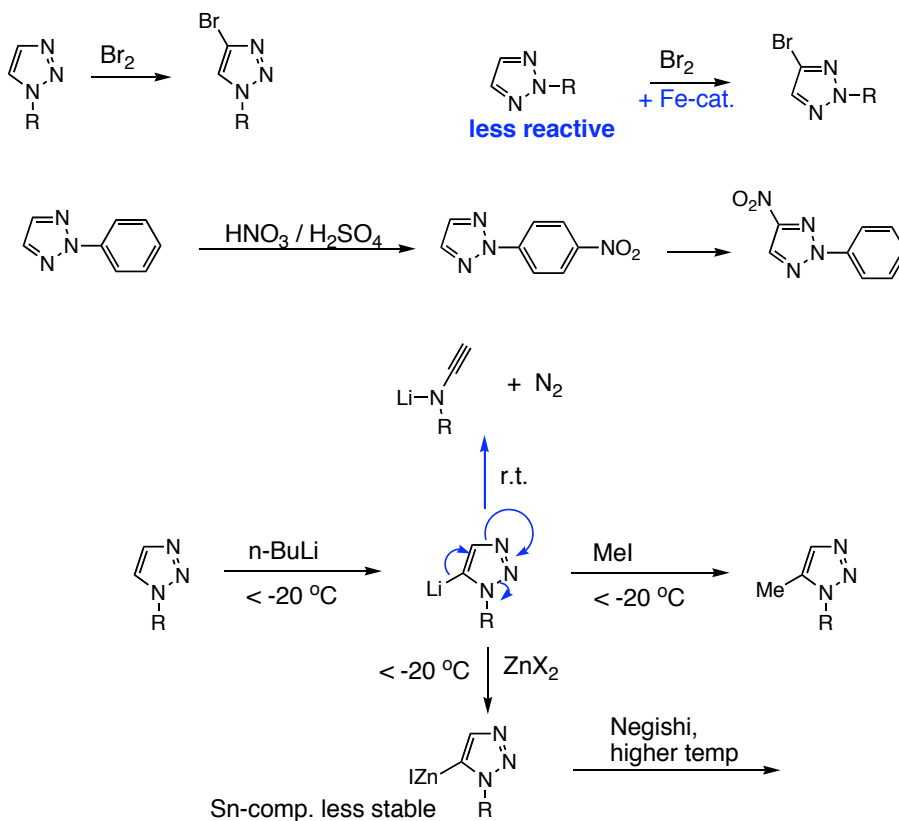
More aromatic
(calculations)

React. at N

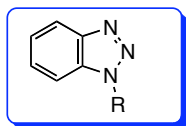


React. at C

1,2,3-Triazole

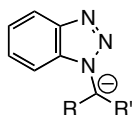


Benzo-1,2,3-Triazole

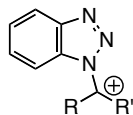


usefull synthetic intermediates

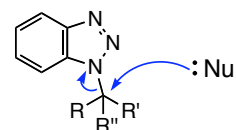
Reviews, see for instance:
Tetrahedron 2005, 2555



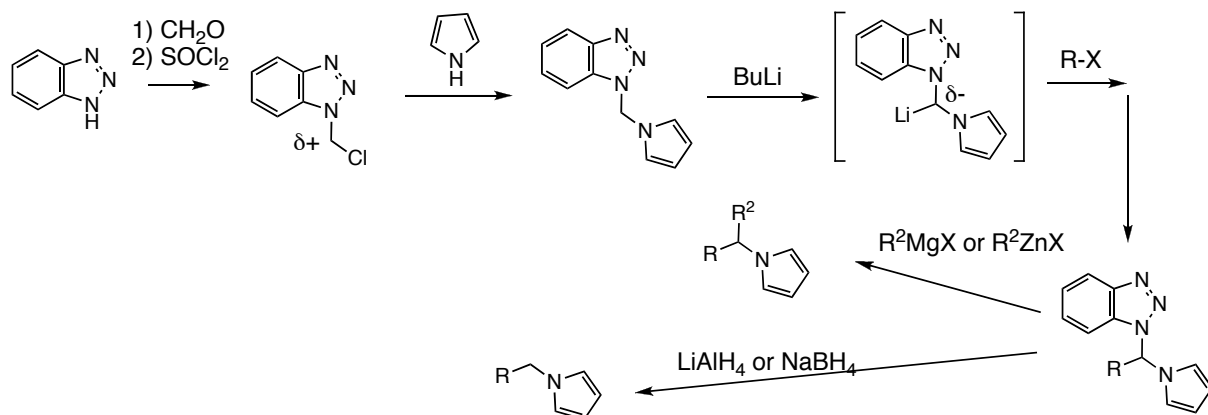
Stabilized anion



Stabilized cation

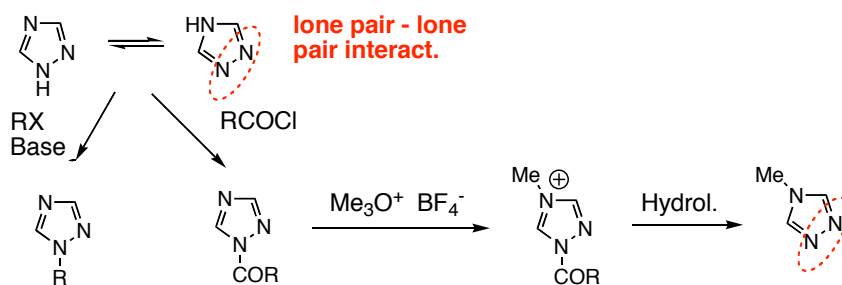


Good leaving group

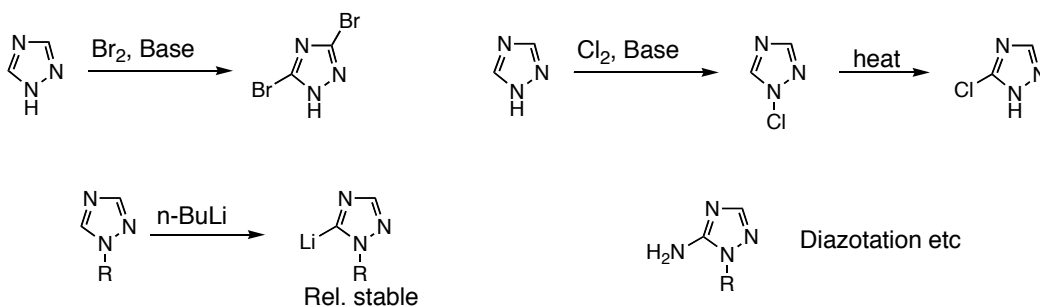


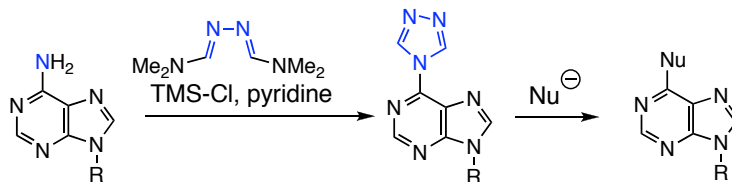
1,2,4-Triazole

React. at N



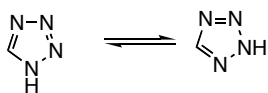
React. at C





Small diff. stab. taut.

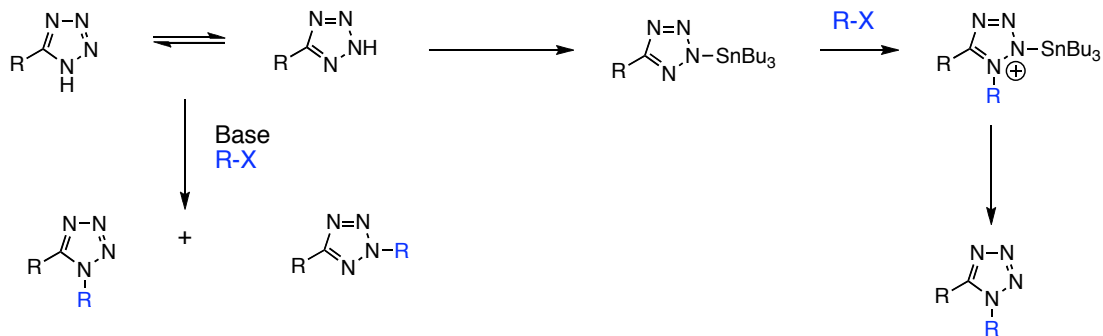
Tetrazole



Bioisostere - CO_2H

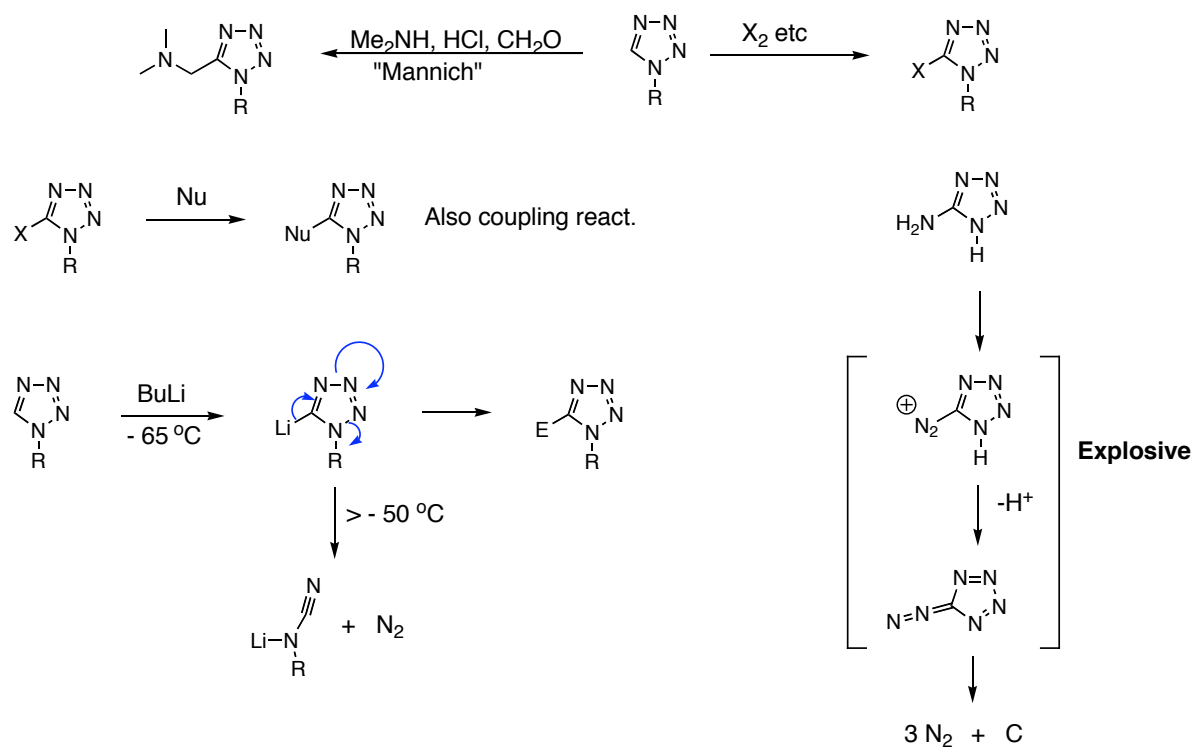
pKa (base): ?
pKa (Acid): 4.9

React. at N



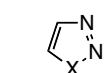
R / Selectivity
Ca same selectivity in acylations

React. at C



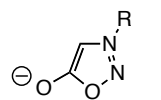
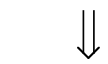
Oxadiazoles and thiadiazoles

X=O, S



unstable X=O

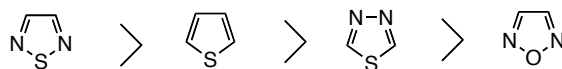
Only X=S
(thiadiazole)



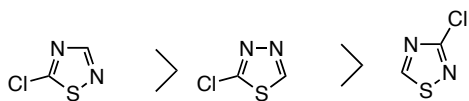
Sydnone
Mesoionic

- No acidic NH
- Generally low basicity (cf triazoles)
- Some examples N-quat.
- Few ex. Introd of E-fils on C
- Prone to Nu attack

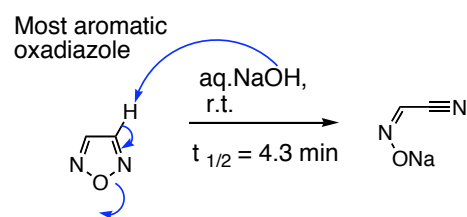
Aromaticity (NMR shifts, bond lengths)



Reactiv. towards Nu (piperidine)

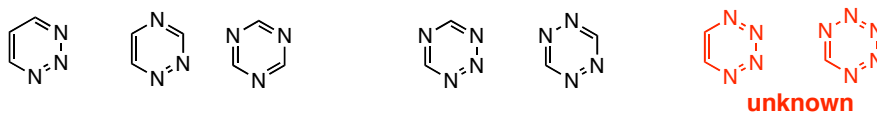


Ring opening (esp. O-cont. rings)

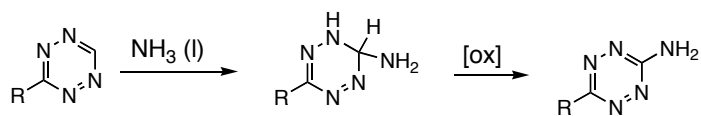


C-lithiation easy, but often low stab of lithiated prod

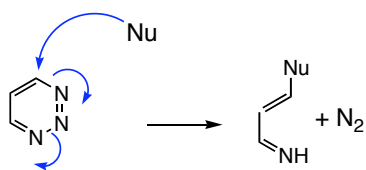
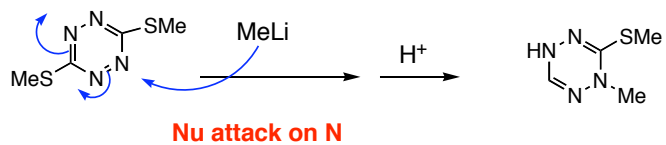
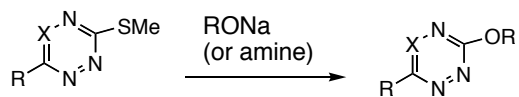
6-membered rings Triazines and tetrazines



Highly activated for Nu attack
No simple react with electrophiles



NaNH₂ in react with pyridine and diazines



**Diels Alder react. Leading to azines with fewer N
(see synth of pyridines, diazines)**