* Diazines + Alkyl Halides ⟶ N-alkyl quaternary salts

Note: electrophilic additions take place at one nitrogen only

* Diazines + Peracids ($R-CO_3H$) ⟶ N-oxides

* Diazines + Nucleophile $\xrightarrow[\text{[if there's not leaving Halide]}]{\text{oxidation}}$ Nucleophilic substitution Products

addition ⇒ Reagent

Note: Diazines more easily attacked by nucleophiles than pyridine.

* Halo-diazines + Nucleophile $\xrightarrow[\text{[at } \alpha/\gamma\text{]}]{\text{Halogen}}$ substiuted Diazines

Note: easy nucleophilic displacements, the intermediates being particularly well stabilised

* Diazines + Nucleophilic Redicals $\xrightarrow{\text{Acid sol.}}$ Radical substitution products

Protonation Diazine + H^+ ⟶ mono-protonated cation

Di protonation Diazine + $2H^+$ ⟶ N-N'-Di protonated cation

Note: Only in very strongly acidic media

Alkylation Diazine + Alkyl Halide ⟶ MONO-quaternary Salt

Di alkylation Diazine + tri alkyl oxonium – tetra fluoro borate ⟶ Di-quaternary salt

oxidation Diazine + Peracid ⟶ N-oxide

Note: All three systems react with peracids

pyrazine + Peracid ⟶ N,N'-Dioxide

Note: Pyrazines form N,N'-dioxides the most easily

pyridazine + Peracid ⟶ N,N'-Dioxide

Note: pyridazine requires forcing conditions

electrophilic substitution

No nitration
No sulforation

Diazines + Electrophile ⟶ No reaction

Note: strongly electron-poor nature

Halogenation 2-Methyl pyrazine + cL_2 ⟶ 2 chlorinated Product

Note: mild conditions addition/elimination

Reactions with oxidising agent

Diazine + Alkaline oxidising agent ⟶ nucleophilic addition ⟶ intermediate ⟶ degradation

Alkyl substituent rings

aromatic fused rings

oxidised ⟶ Carboxylic acid residues

Note: leaving the heterocyclic ring untouched

pyrimidine + Bacteria ⟶ O- introduced pyrimidine
[c-2 / c-4]

N, N- Di alkylated uracil + Di methyl dioxirane ⟶ 5,6 epoxides ⟶ 5,6 DiOL

Reaction with Nucleophilic Reagent

pyrimidine + Hot Alkali aq. ⟶ hydroxide addition $\xrightarrow{\text{Heat}}$ Decomposition

pyrimidine + Hot Hydrazine ⟶ pyrazole

Nucleophilic substitution

Diazine + Organolithium ⟶ Di-hydro adduct

Note: Arylation

pyrimidines react at C - 4, and pyridazines at C - 3

Diazine + Grignad ⟶ Di-hydro adduct Note: Grignard reagents add to pyridazines at C - 4

Di-hydro adduct + KMnO4 or DDQ ⟶ Aromatic product Note: Oxidation

Halo-Diazine + Amine
or Thiolate
or Malonate
→ Substitution of the halide → Substituted Diazine

Note:
Nucleophilic Substitution with Displacement of Good Leaving Groups

All the halo - diazines, apart from 5 - halo - pyrimidines, react readily with ' soft ' nucleophiles,

Reaction with Reducing Agents

Pyrazine
or Pyridazine + Na in Hot Ethanol [EtOH] → Hexa-hydro Derivative

Quaternary salt + Borohydride → Di-hydro Compounds

Note: Partial reduction

Diazine + Carbamate on nitrogen → tetra-hydro Derivative

Note: aids in stabilisation and thus allows isolation

2-Amino-Pyrimidine + triethyl silane in trifluoro acetic acid → 3,4,5,6 Tetra-hydro derivatives

Synthesis of Diazines

Pyridazine 1,4 di carbonyl + Hydrazine ⟶ oxidation ⟶ aromatic pyridazine

if [4 carbon compound is unsaturated]

Pyrimidine 1,3 di carbonyl + N-C-N fragment ⟶ Pyrimidine

↳ - urea
- amidine
- guanidne

Pyrazine ⟶ cyclodehydrogenation ⟶ N -hydroxyethylethane - 1,2 - diamine

not easily made

2- amino - Ketone
2- amino - aldehyde ⟶ Self - condensation ⟶ oxidation ⟶ 2 - Amino - Ketone Symmetrical pyrazine

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