

Introduction:

- Planar, five membered heteroaromatic molecule with pyrrole type and pyridine type annular nitrogens.
- Named first as gluoxaline (first synthesis with glyoxal and ammonia).
- Aphotic nature, susceptible to electrophilic and nucleophilic attack.
- High stability to thermal, acid, base, oxidation and reduction conditions.
- Extensive intramolecular hydrogen bonding.

Biological Properties:

- Against fungal infections.
- Treatment of hypoxic tumor cells.
- Anticancer agents.
- Anti-HIV agents

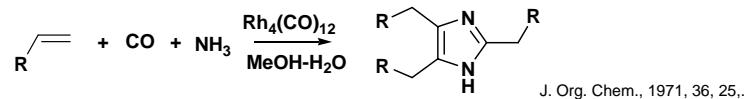
Synthesis of Imidazoles:

"There are no really general ways of synthesizing imidazoles and it is invariably necessary to consider a number of divergent methods whenever a synthesis is contemplated"

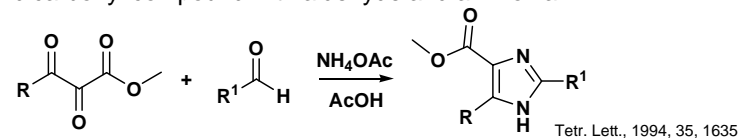
Ring Formation:

-Fragments C-C, N, C and N:

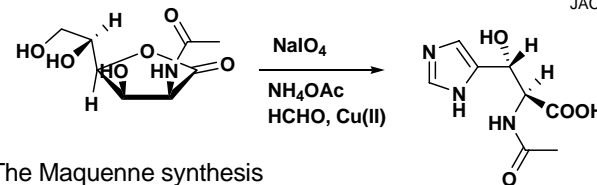
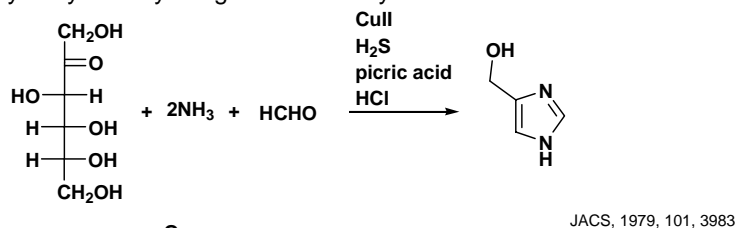
1. Combination of an alkene, carbon monoxide and ammonia



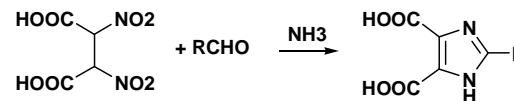
2. A dicarbonyl compound with aldehyde and ammonia



3. Hydroxycarbonyl reagent with aldehyde and ammonia



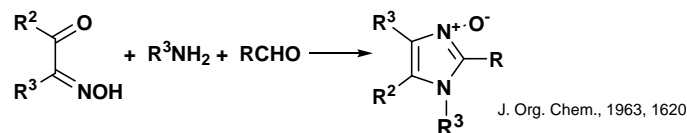
4. The Maquenne synthesis



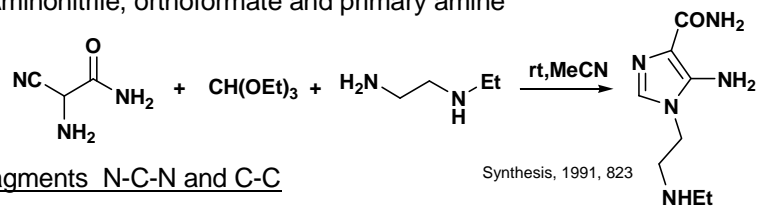
Ring Formation:

-Fragments a C-C-N, C and N:

1. Hydroxyimino ketone, aldehyde and ammonia

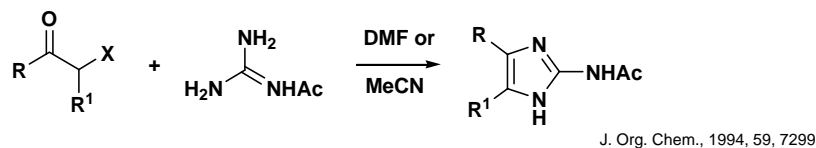


2. Aminonitrile, orthoformate and primary amine

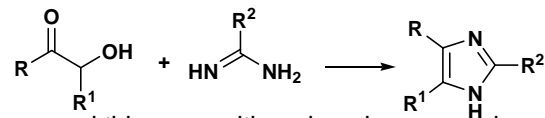


-Fragments N-C-N and C-C

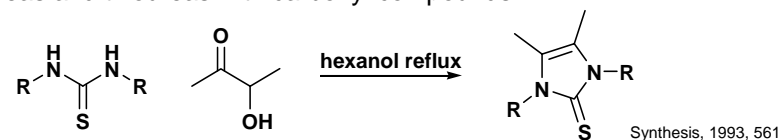
1. Halocarbonyl or dicarbonyl compounds with guanidines



2. Amidines and hydroxy or halocarbonyl compounds

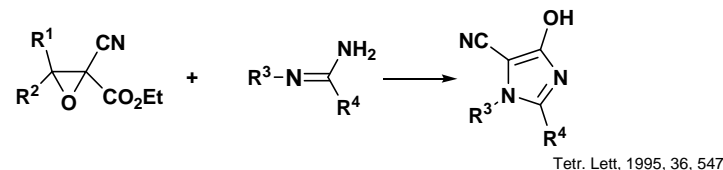


3. Ureas and thioureas with carbonyl compounds



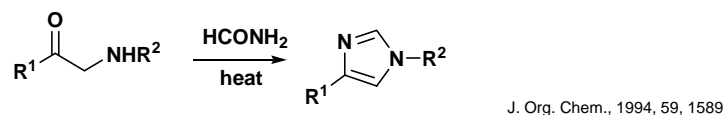
-Fragments N-C-N and C-C

4. Cyanoepoxides and amidines or guanidines

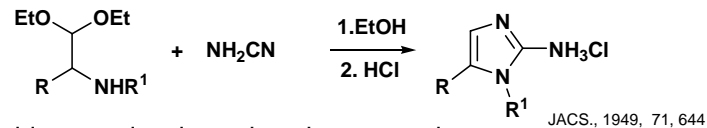
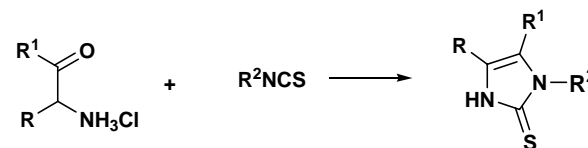


-Fragments C-C-N and C-N

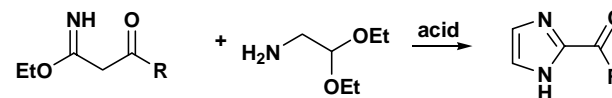
1. Aminocarbonyl compounds with N-C reagents



2. Marckwald Synthesis. Aminocarbonyl compounds with cyanates or cyanamide



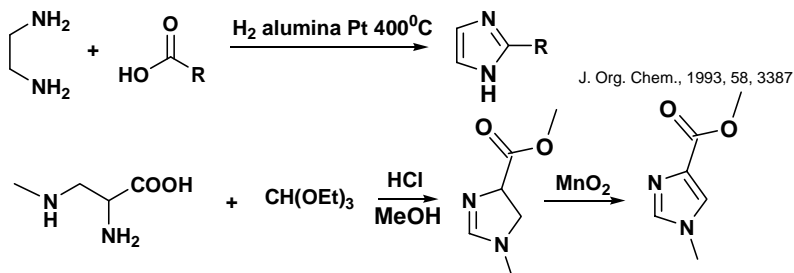
3. Amidates and aminocarbonyl compounds



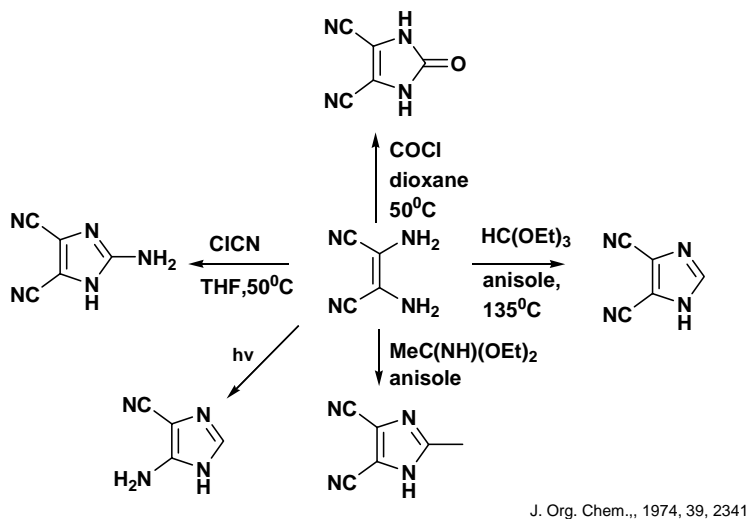
Ring Formation:

-Fragments N-C-C-N and C:

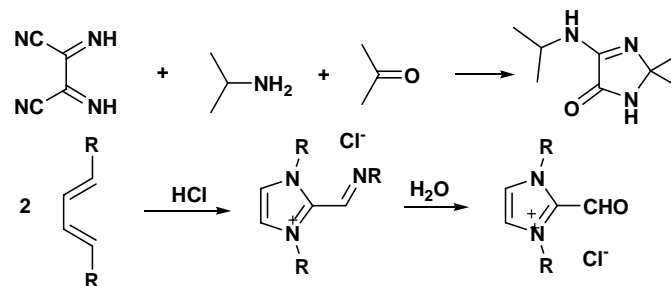
1. 1,2-Diaminoalkanes and carbon reagents



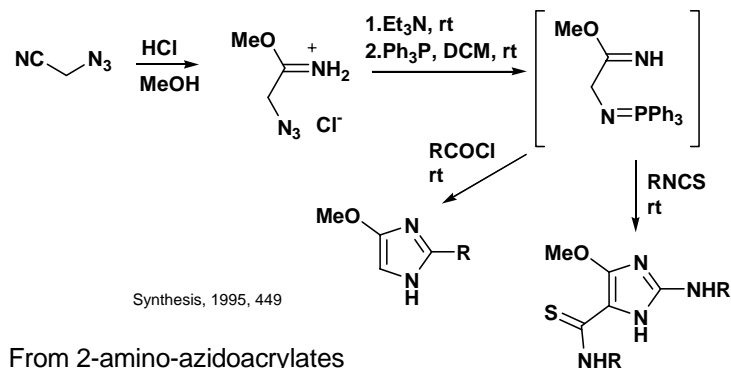
2. Use of diaminomaleonitrile (DAMN)



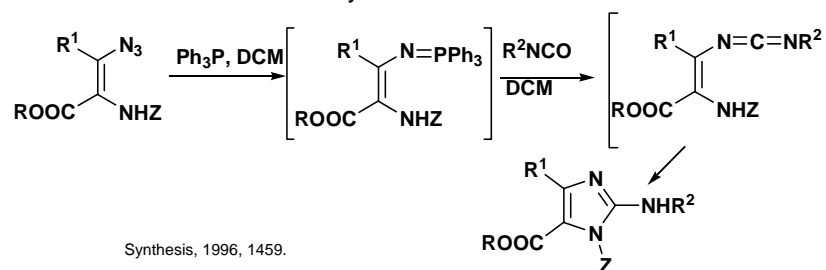
3. Involving cyclization of diiminocompounds.



4. Pinner salt method



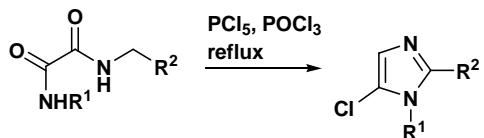
5. From 2-amino-azidoacrylates



Ring Formation:

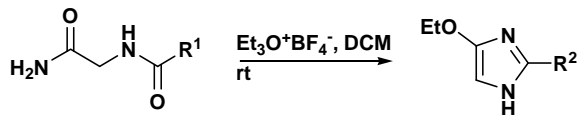
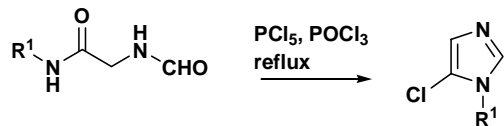
-Fragment C-N-C-C-N:

1. Wallach Synthesis



JACS, 1967, 1259

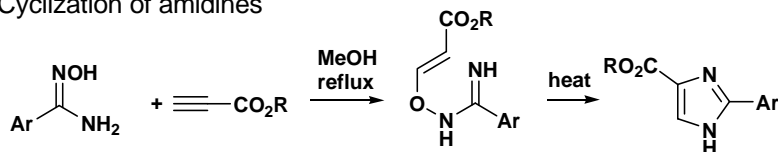
2. From acylated glycines and formamido acetamides



J. Med. Chem., 1975, 18, 90

-Fragment N-C-N-C-C:

1. Cyclization of amidines



Tetr. Lett., 1971, 18, 1459.

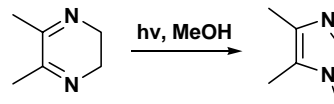
Ring Transformation

-Ring enlargement of azirines by reaction with nitriles



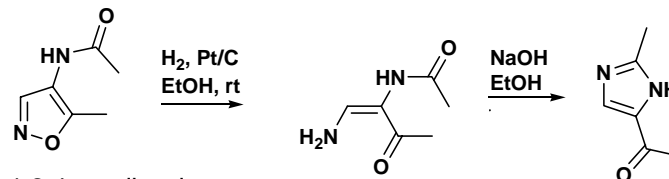
JACS, 1967, 89, 4457.

-From Dihydropyrazines



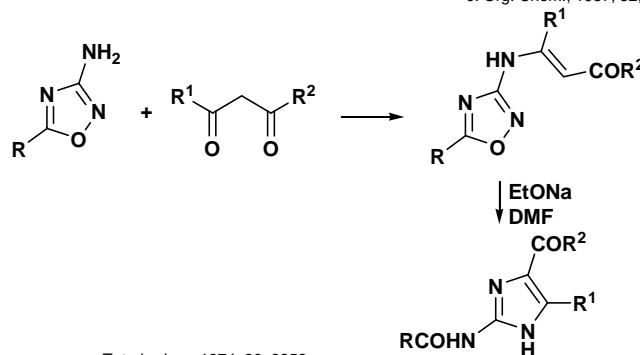
JACS, 1967, 89, 2375.

-From Aminoisoxazoles



J. Org. Chem., 1987, 52, 2714

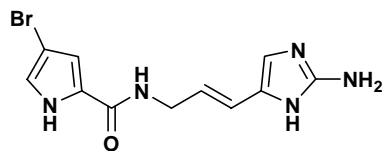
-From 1,2,4-oxadiazoles



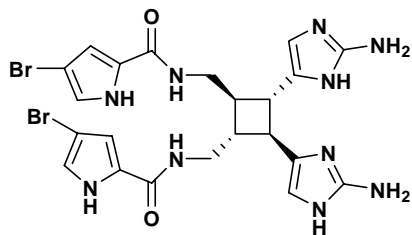
Tetrahedron, 1974, 30, 3859

Natural Products:

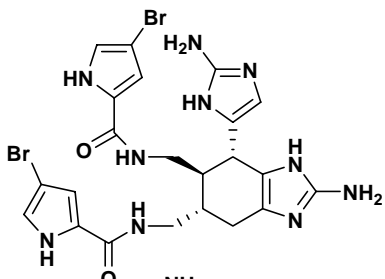
Oroidin



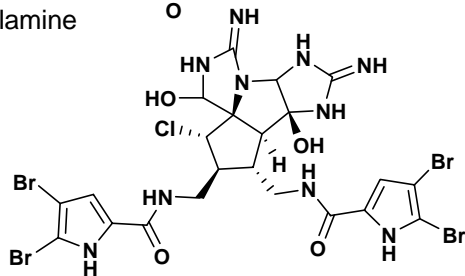
Sceptrin



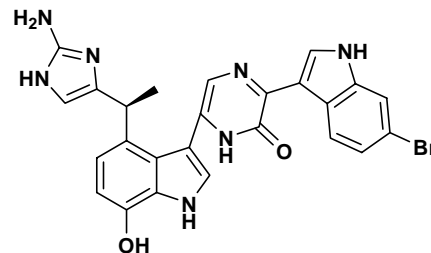
Ageliferin



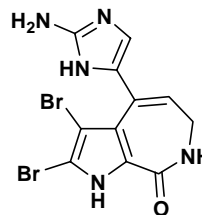
Axinellamine



Dragmacydin D



Stevensine



Temozolomide

