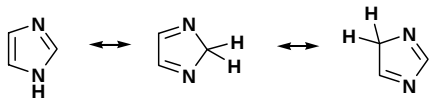
The Baran Group Meeting

Synthesis of Imidazoles

Alexandros Zografos



Indroduction:

-Planar, five membered heteroaromatic molecule with pyrrole type and pyridine type annular nitrogens.

-Named first as gluoxaline (first synthesis with glyoxal and ammonia).

-Aphoteric 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

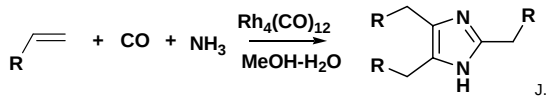
Synthesis of Imidazoles:

"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:

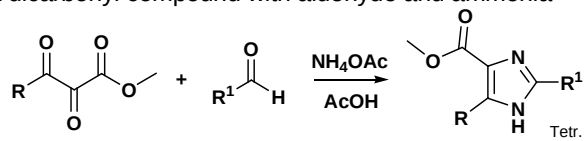
-Fragments C-C, N, C and N:

1. Combination of an alkene, carbon monoxide and ammonia



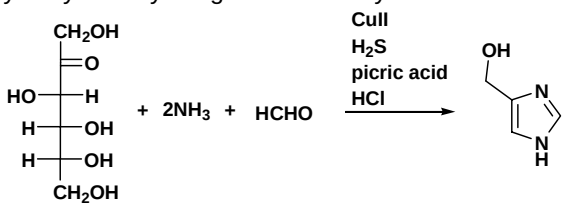
J. Org. Chem., 1971, 36, 25,.

2. A dicarbonyl compound with aldehyde and ammonia

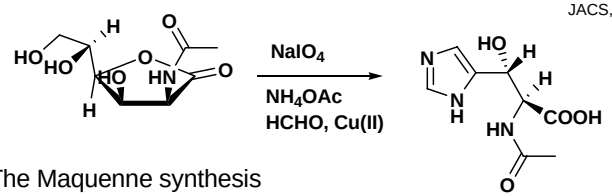


Tetr. Lett., 1994, 35, 1635

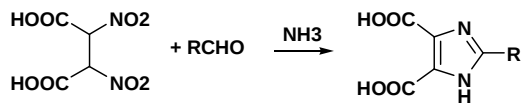
3. Hydroxycarbonyl reagent with aldehyde and ammonia



JACS, 1979, 101, 3983



4. The Maquenne synthesis



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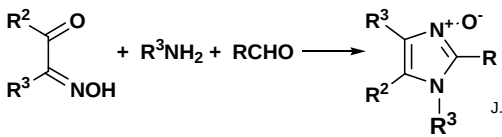
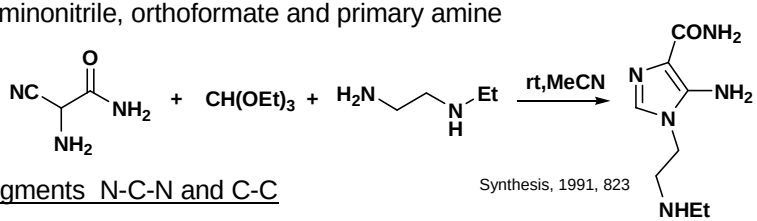
Ring Formation:

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

1. Hydroxyimino ketone, aldehyde and ammonia

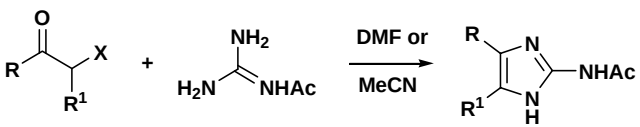


2. Aminonitrile, orthoformate and primary amine

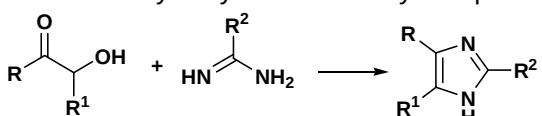


-Fragments N-C-N and C-C

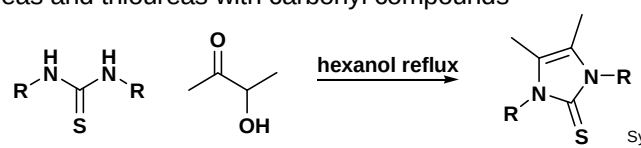
1. Halocarbonyl or dicarbonyl compounds with guanidines



2. Amidines and hydroxy or halocarbonyl compounds

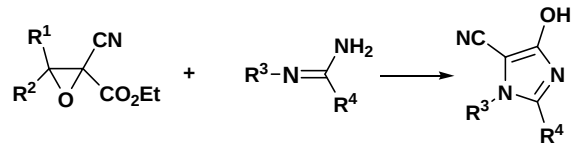


3.Ureas and thioureas with carbonyl compounds



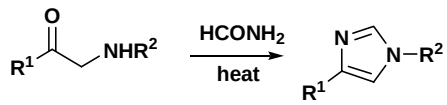
-Fragments N-C-N and C-C

4. Cyanoepoxides and amidines or guanidines

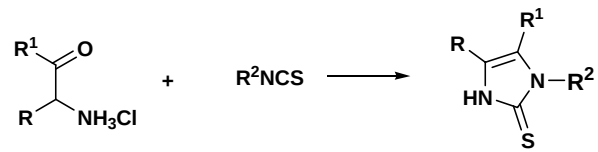


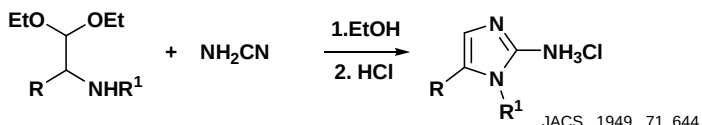
-Fragments C-C-N and C-N

1. Aminocarbonyl compounds with N-C reagents

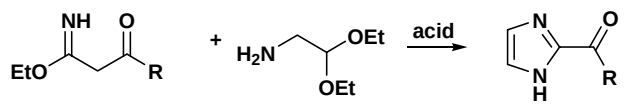


2. Marckwald Synthesis. Aminocarbonyl compounds with cyanates or cyanamide





3. Amidates and aminocarbonyl compounds



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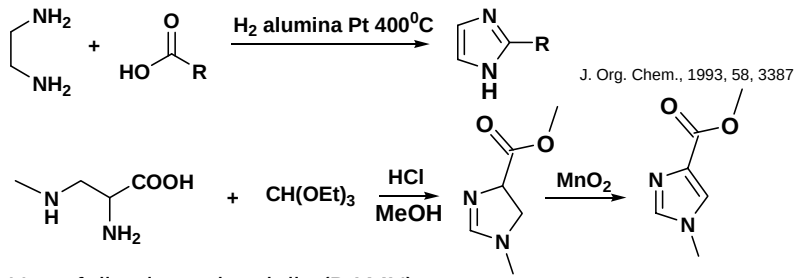
Ring Formation:

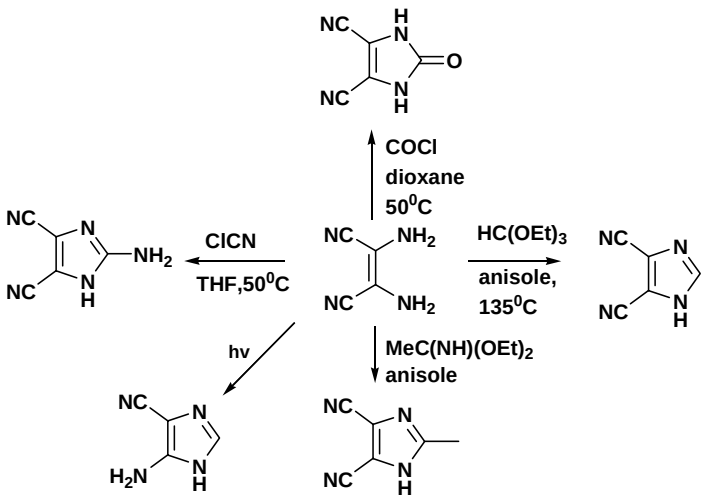
-Fragments N-C-C-N and C:

1. 1,2-Diaminoalkanes and carbon reagents



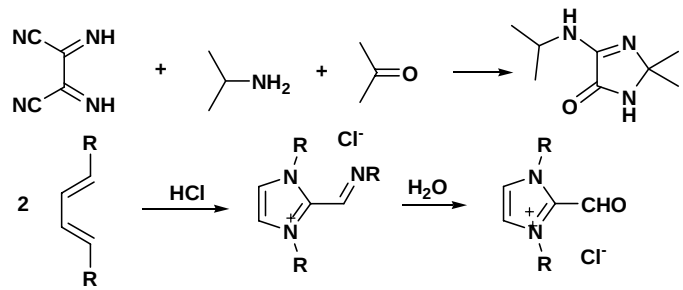
J. Org. Chem., 1993, 58, 3387

2. Use of diaminomaleonitrile (DAMN)

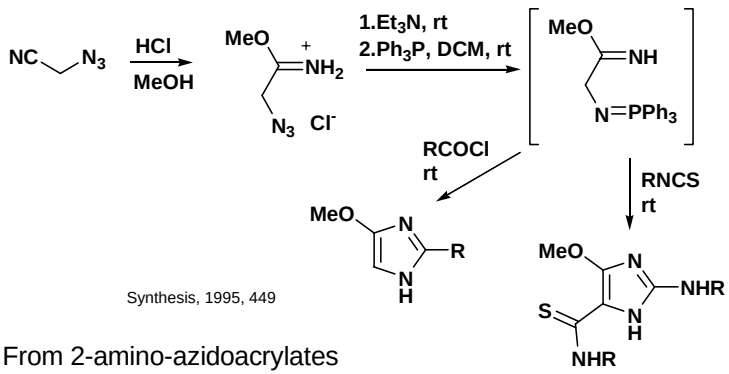


J. Org. Chem.,, 1974, 39, 2341

3. Involving cyclization of diiminocompounds.

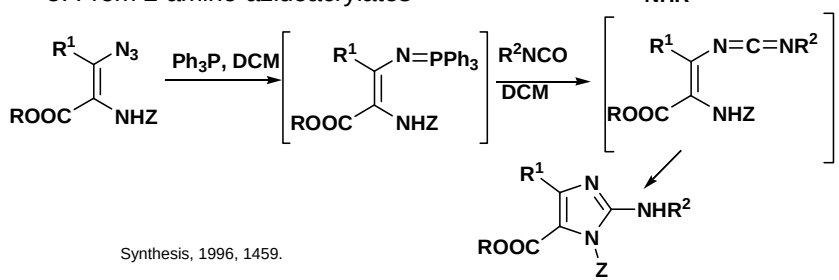


4. Pinner salt method



Synthesis, 1995, 449

5. From 2-amino-azidoacrylates



Synthesis, 1996, 1459.

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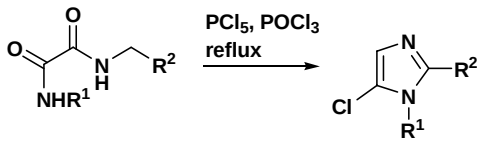
Ring Formation:

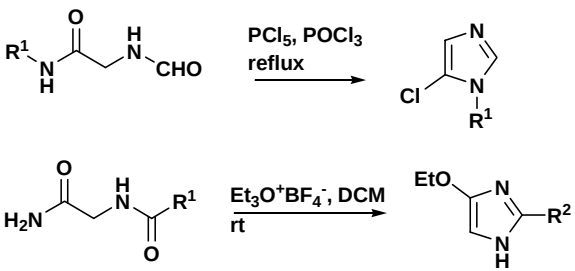
-Fragment C-N-C-C-N:

1. Wallach Synthesis



JACS, 1967, 1259

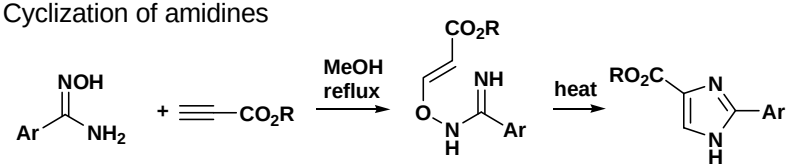
2. From acylated glycines and formamido acetamides



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

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

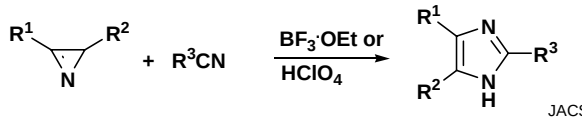
1. Cyclization of amidines



Tetr. Lett., 1971, 18, 1459.

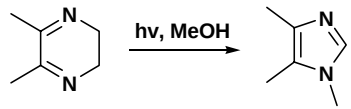
Ring Transformation

-Ring enlargement of azirines by reaction with nitriles



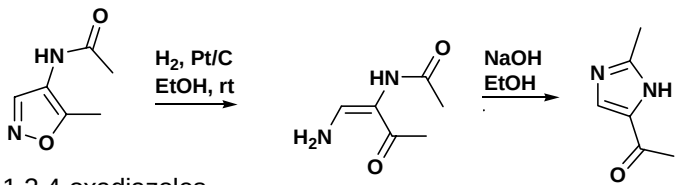
JACS, 1967, 89, 4457.

-From Dihydropyrazines



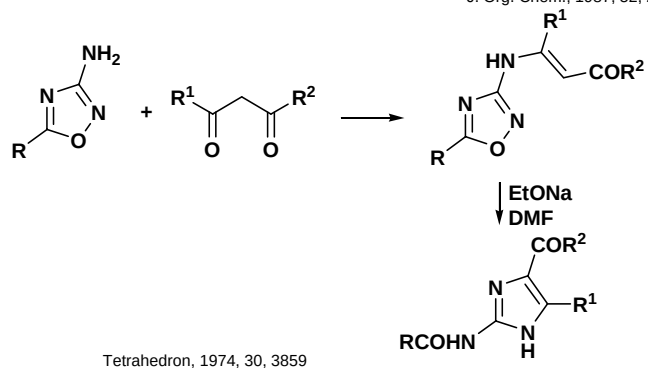
JACS, 1967, 89, 2375.

-From Aminoisoxazoles



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

-From 1,2,4-oxadiazoles



Tetrahedron, 1974, 30, 3859

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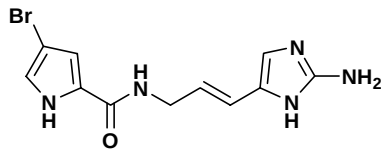
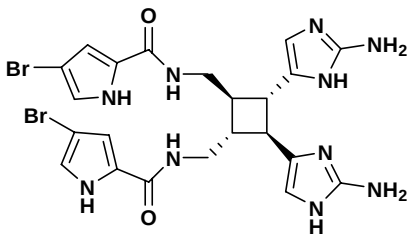
Natural Products:

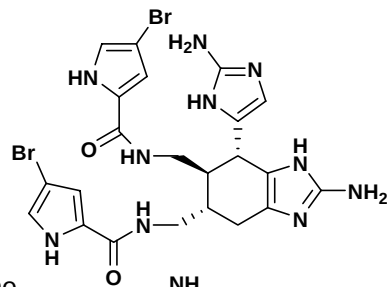
Oroidin



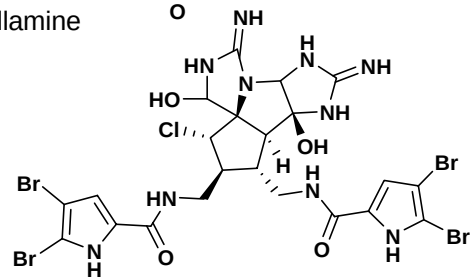
Sceptrin



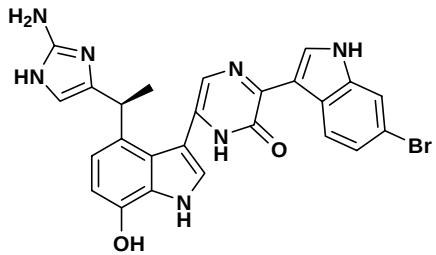
Ageliferin



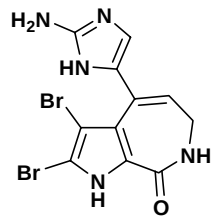
Axinellamine



Dragmacydin D



Stevensine



Temozolomide