THEORITICAL ASPECTS OF VARIOUS METHODS FOR SYNTHESIS OF BENZIMIDAZOLES

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Abstract

In this article we Investigates demonstrate various techniques synthesis of benzimidazole derivatives, a portion of these strategies is basic and inexpensive which can do in research center conditions. On the opposite side there are staggering expenses strategies, which need costly crude materials, high temperature, and long time. Be that as it may, present audit indicates techniques synthesis of benzimidazole derivatives including the contrast between them. A standout amongst the most significant procedures in the arrangement of benzimidazole derivatives known as the Van Leusen strategy, which respond aldimines with tosylmethylisocynide (TosMIC).Reaction expanded in two stage and named as the Van Leusen three-segment reaction (VL-3CR).

1. INTRODUCTION

Imidazole was first arranged by the reaction of glyozal with smelling salts; Debus detached another sort of compound and named it glyoxaline. This name is as yet utilized in the advanced literature especially by English specialists. The name imidazole is expected to.

Fe characterized the five membered polyheteroatomic ring frameworks containing atleast one tertiary nitrogen as azoles the term imidazole suggests a five membered heterocyclic ring framework containing notwithstanding tertiary nitrogen, an imino gathering.

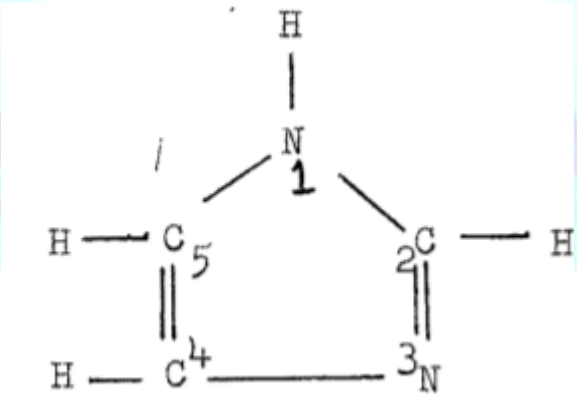


Figure 1: Imidazole

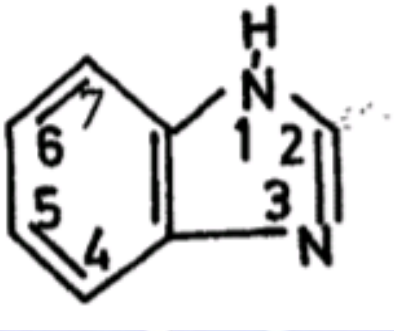


Figure 2: benzimidazole

The ring system in which a benzene ring is fused in the positions of imidazole is designated as benzimidazole.

2. METHODS FOR SYNTHESIS OF BENZIMIDAZOLES

Covering the synthesis and science of the two imidazoles and benzimidazoles have been distributed. Generally, benzimidazoles can be combined from an assortment of starting materials and a couple of them are recorded underneath in detail.

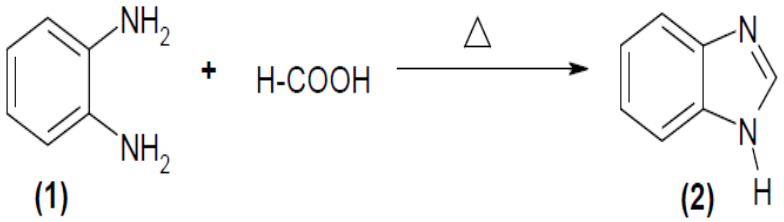
- *o*-Phenylenediamines
- *o*-(*N*-acylamino and *N*–aryolamino)arylamines and nitroarenes
- *o*-Nitroarylamines and o-dinitroarenes
- *o*-substituted-*N*-benzylideneanilines
- Amidines
- Other heterocyclic compounds

o-Phenylenediamine

O-Phenylenediamine (1) reacts with (a) carboxylic acids and their derivatives, (b)imino-ethers, (c) carbonyl compounds and (d) nitriles to yield differently substituted benzimidazoles.

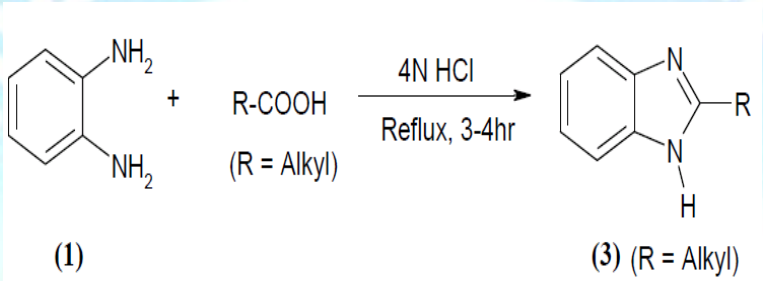
- **By reaction with carboxylic acids and their derivatives**

2-Substituted benzimidazoles may be synthesized in good yields by condensing *o*-phenylenediamine with carboxylic acids under a wide variety of conditions. Ladenburgfirst prepared 2, 5 (or 2, 6)-dimethylbenzimidazole by refluxing 4-methyl-*o*-phenylenediamine in glacial acetic acid. The parent benzimidazole (2) was preparedin 1878 by heating with formic acid(Scheme-1).



Scheme-1

Since then, a large number of benzimidazoles have been synthesized from 1 and aliphatic acids. The most satisfactory method for the synthesis of 2-alkylbenzimidazoles (3, R = alkyl) was developed, which involves refluxing equimolar quantities of the diamine and the aliphatic carboxylic acid in 4N hydrochloric acid for 3 to 4 hr (Scheme-2).



Scheme-2

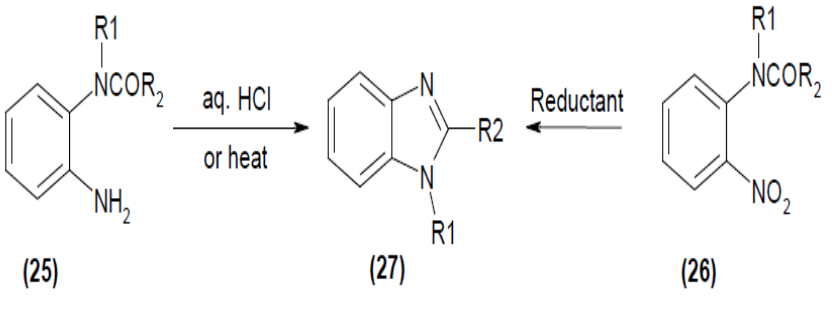
The mechanistic pathway for the formation of benzimidazoles by the reaction of with natural acids has just been considered. Further, the job of hydrochloric corrosive in the reaction has likewise been investigated. The synergist action of hydrochloric corrosive is explained based on enactment of the carboxyl gathering by the protonation of oxygen. The intermediate in the reaction is the expansion item framed by the assault of the unshared electron pair of nitrogen on to the carbonyl gathering of the protonated corrosive. In any case, Phillips inferred that the monoacyl subsidiary was the important key intermediate for formation of benzimidazole ring.

For aromatic carboxylic acids, however, Phillips procedure fails to give any respectable yields of 2-arylbenzimidazoles. Aromatic carboxylic acids were reportedto give good yields of 2-arylbenzimidazoles (4, R = Ar) when heated with in a sealed tube at 180-190 ^{o}C. A superior methodology for the preparation of 2-arylbenzimidazoles from and fragrant carboxylic corrosive involves the utilization of polyphosphoric corrosive (PPA) or polyphosphate ester (PPE) as dehydrating specialist. On the other hand, phosphorus pentoxide has additionally been accounted for as a dehydrating operator for the preparation of 2-arylbenzimidazole derivatives(Scheme-3).

from o-(*N*-acylamino and *N*-aroylamino) arylamines and nitroarenes

The formation of benzimidazoles by the reaction of 1 with carboxylic acids and related compounds is dared to involve the formation of (monoaroylamino) arylamines. Various benzimidazole compounds (27) have been incorporated by cyclisation of N-monoacyl-o-phenylenediamines (25), under corrosive catalyzed conditions or in uncatalysed warm conditions. Compound 27 can likewise be

produced in situ from the proper o-nitroarylamine (26) by using an assortment of reducing specialists, for example, (Scheme-3).

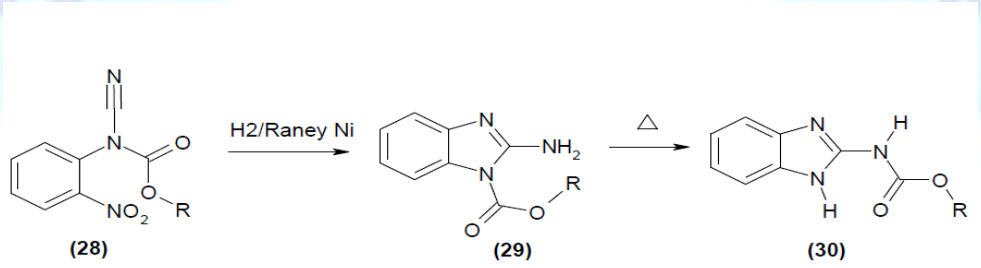


Scheme-3

Thus, differently substituted benzimidazoles (27) and related compoundshave been synthesized by the cyclisation of *N*-monoacyl-*o*-phenylenediamines (25).

from*o*-Nitroarylamines and *o*-dinitroarenes

Benzimidazoles have been synthesized in a single step from *o*-nitroarylamine or *o*-dinitroarenes by using reductants such as N_aHSO_3,$BaSO_4$/Pd/H_2, Zn,$Na_2S_2O_5$ and Na_2SO_3. Benzimidazoles are also obtained by the thermolysis of nitroarenes and alcohol mixtures in the gas phase. Since reasonable yields are obtained, these processes have got commercial importance. When *o*-nitroanilines are used in thermolysis, a secondary reaction occurs which converts the 2-alkylbenzimidazoles into 1, 2-dialkylbenzimidazoles. *O-Dinitroarenes* behave in a similar fashion with alcohols over alumino–copper or vanadium, but in this case the products are exclusively 2-alkylbenzimidazoles (3). The direct reductive method from the carbanilic acid derivatives (28) leading to alkyl esters of 2-amino-1-benzimidazolecarboxylic acids (29) is of commercial value, since products of the latter type are transformed thermally into alkyl esters of benzimidazole-2-carbamic acids (30) (Scheme-4).

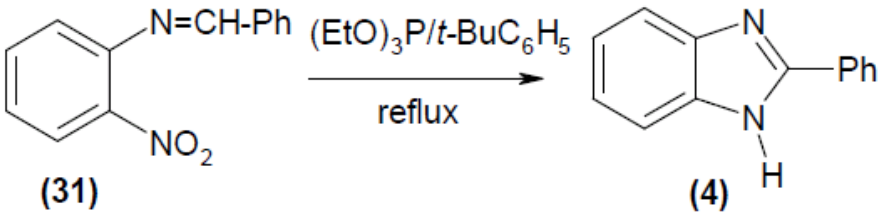


Scheme-4

from*o*-substituted-*N*-benzylideneanilines

The decrease of fragrant nitro compounds by triethylphosphite and related reagents has been generally utilized as a simple and successful course to an assortment of nitrogen containing heterocycles. Derivatives of N-benzylidene-2-nitroaniline (31) were changed over into substituted (4) thusly and the

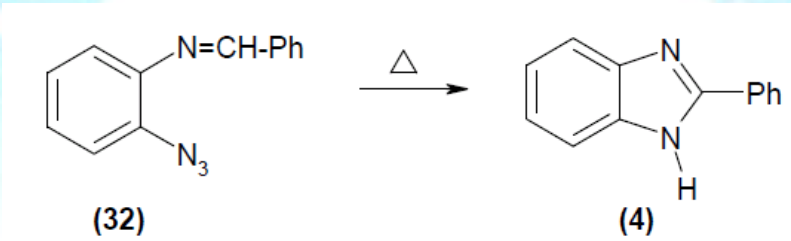
yields were somewhat higher than those obtained by the utilization of established Weidenhagen aldehyde strategy (Scheme-5).



(31) (4)

Scheme-5

Good yields of benzimidazoles can be obtained by heating *N*-benzylidene-2-azidoanilines (**32**) in 1; 2–dichlorobenzeneor dimethylformamideand the method can be used to prepare 2-substituted benzimidazoles (Scheme-6).

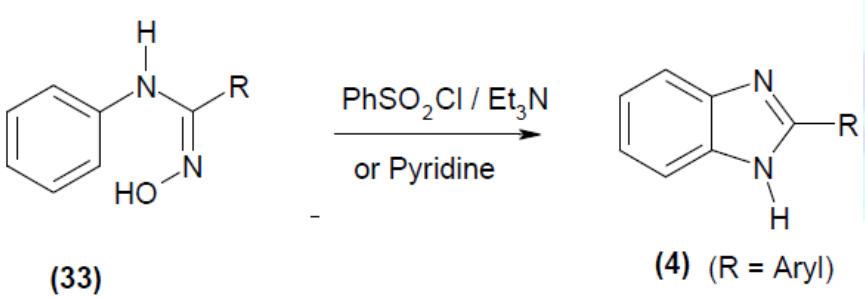


(32) (4)

Scheme-6

fromAmidines

Generally benzimidazoles are synthesized from 1 and its derivatives. Their preparation from *N*'-aryl-*N*-hydroxylamidines(33) is unusual in the sense that both nitrogen atoms of the imidazole ring arise from one side chain (Scheme-7).



(33) (4) (R = Aryl)

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Scheme-7

The reactions are carried out under mild conditions using benzene sulfonyl chloride in pyridine or triethylamine giving good yields .This method has been used to prepare a variety of compounds with substiutuents in the aryl ring.

from other heterocyclic compounds

Benzimidazole derivatives can be prepared by reductive cyclisation of *o*-benzoquinonedibenzimide by using triphenylphosphine. Benzimidazoles are also formed during the photolysis of indazoles.

4. CONCLUSION

Through different studies of benzimidazole subordinates, obviously there is impressive enthusiasm from scientific experts and drug specialists. The reason is because of their qualities and numerous responses of these mixes. Subsidiaries have numerous utilizations in different fields of life, for example, prescription, drug store, horticulture, industry and others. They are countless and studies of properties, techniques for arrangement of benzimidazoles subordinates since the center of the only remaining century. There were great outcomes in the learning of the properties and there were numerous strategies for readiness that have plans to encourage and lessen costs during the time spent planning of these mixes. Rapid and large scientific development must be a far reaching survey of the techniques for planning of this kind of mixes.

5. REFERENCES

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