A SYNTHETIC APPROACH TO BENZIMIDAZOLE DERIVATIVES AND THEIR POTENTIAL THERAPEUTIC USES: A REVIEW

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ABSTRACT:

Benzimidazole is an aromatic heterocyclic chemical molecule. The pharmacological actions of various molecules produced from the benzimidazole nucleus vary. Antivirals, antimicrobials, anticancer, antiparasitic, antioxidants, proton-pump inhibitors, anti-inflammatory, anticoagulants, antihypertensives, immunomodulators, and other therapeutic medications contain the benzimidazole nucleus. The substitution pattern around the nucleus of numerous benzimidazole derivatives with distinct pharmacological activities is detailed to assist medicinal chemists in creating a SAR on benzimidazole-derived drugs for each activity. Because of their similarity to naturally occurring nitrogenous bases, such as purine, benzimidazole and its derivatives demonstrated a extensive spectrum of biological uses. The current review focuses on the chemistry and pharmacology of substituted benzimidazoles.

Keywords: Benzimidazole, Heterocyclic Chemistry, Therapeutic Uses
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INTRODUCTION:

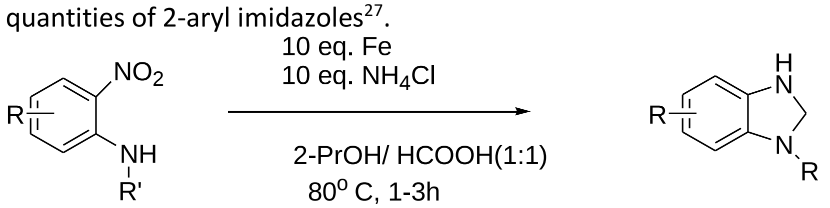
Benzimidazole moiety is imperative nitrogenous heterocycles that have been extensively researched and used in the pharmaceutical industry for medication development[1]. Because of their unique structural properties and electron-rich environment, bind to a number of different therapeutic targets[2]. As a result, they exhibit a wide variety of bioactivities. In clinical studies, benzimidazole-based medications have been widely used to treat a variety of disorders with promising therapeutic medicinal potential[3]. Benzimidazole derivatives have several pharmacological effects in the medical area, including anti-microbial, antiviral, anti-diabetic, and anti-cancer activity[4]. Benzimidazoles are highly effective compounds, with several biochemical and pharmacological studies demonstrating their effectiveness against a variety of bacteria[5-7].

The study and development of benzimidazole-based drugs is a lot more active and attractive field of medicinal chemistry because of their great pharmacological usefulness. This study looks at the chemistry and pharmacology of a variety of substituted benzimidazole derivatives[8-11]. Antioxidants are molecules that aid in the protection of cells against oxidative stress, which is a harmful physiological important component that occurs naturally[12]. These nutrients can be obtained naturally from a range of foods or as dietary supplements. They shield our bodies from the harm caused by oxygen-free radicals. Free radicals such as superoxide, hydroxyl, and peroxide radicals can cause damage to a wide range of biomolecules. They play a vital role in the development and progression of oxidative stress-associated illnesses such as carcinogenesis, Alzheimer's, inflammatory diseases, and cataracts. As a result, antioxidants may be considered free radical scavengers. When there is an excess of oxygen and its reduction is inadequate, reactive oxygen species (ROS) are produced. Naturally occurring antioxidants include flavonoids and phenolic acids[13]. Physiological tests such as melting point measurement, TLC, and percent yield were performed on the produced compounds[14, 15].

Newly synthesized compounds were evaluated physiologically against by E. coli and Staphylococcus aureus for antibacterial screening. The other in vitro effects investigated were anti-inflammatory and antioxidant capabilities. Benzimidazoles have biological features such as anti-inflammatory, anti-cancer, antifungal, antiviral, and anthelmintic activity. For many years, benzimidazole derivatives have been a key research area due to their great practical use[16-26].

SYNTHETIC SCHEME & GENERAL METHODS:

1. The direct arylation of C-H bonds of Imidazole with aryl-chloride is facilitated by a distinct NHC-Pd(II)-I complex. Several active and inactive aryl chlorides are used as arylation reagents to produce high quantities of 2-aryl imidazoles[27].



R:H,Ph,Et

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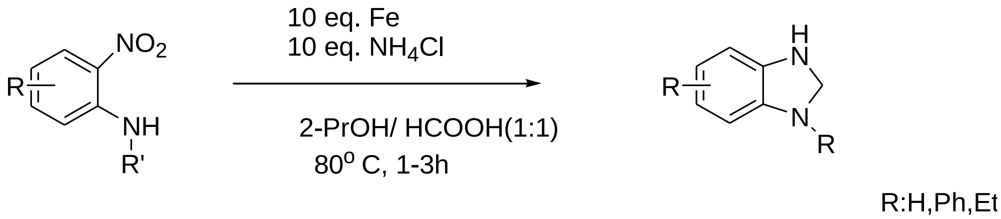
2. In a one-pot technique to convert bicyclic *2H* benzimidazoles from aromatic and 2- nitroamines (heteroaromatic), iron powder, formic acid and NH_4Cl function as additives that cause imidazole cyclization by reducing the nitro group, resulting in 1 to 2 hours, high-yielding conversions. The versatility of this molecule is proved by its ability to work with a wide range of functional groups[28].



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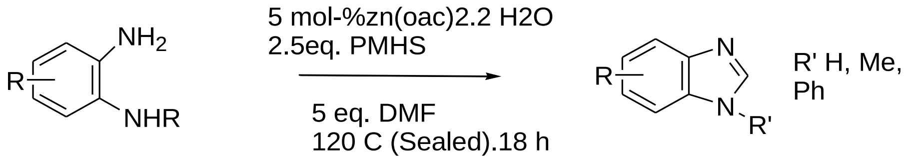
3. Benzimidazoles are produced in the zinc-catalyzed cyclization with good yields in the presence of poly(methyl-hydrosiloxane) using several O-phenylenediamine and N-substituted formamides as C1 sources. Benzoxazole and benzothiazole derivatives are also conceivable[29].



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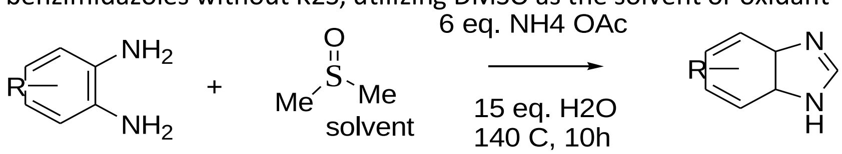
4. Non-substituted benzothiazoles are produced by a three-component reaction of o-iodoaniline or with K2S and DMSO in electron-rich aromatic amines in good isolate yields with sufficient functional group tolerance. In a similar procedure, o-phenylenediamine was utilized to synthesize 2-substituted benzimidazoles without K2S, utilizing DMSO as the solvent or oxidant[30].



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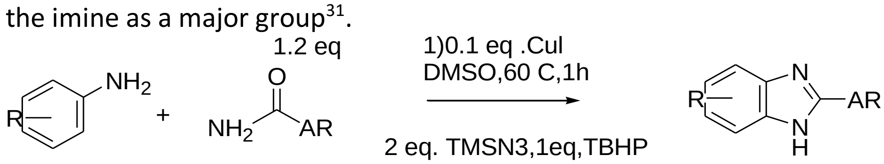
5. Commercial arylamines, aldehydes, and azides can be converted into useful benzimidazole structural units, using an active copper-catalyzed amination of N-aryl imines, by chelation with a metal base using the imine as a major group[31].



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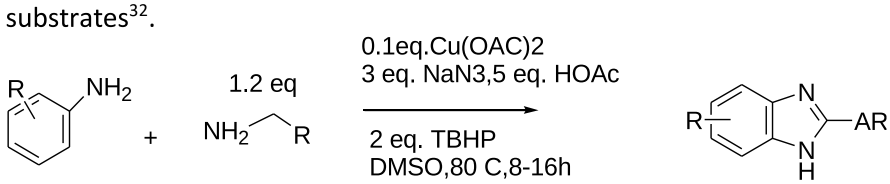
6. Anilines, primary alkyl amines, and sodium azide undergo a domino C-H functionalization, transamination, ortho-selective amination, and cyclization sequence in the presence of TBHP, resulting in benzimidazoles via a copper(II)-catalyzed oxidative cross-coupling of anilines, primary alkyl amines, and sodium azide. The reaction is functional group compatible and may be employed on a variety of substrates[32].



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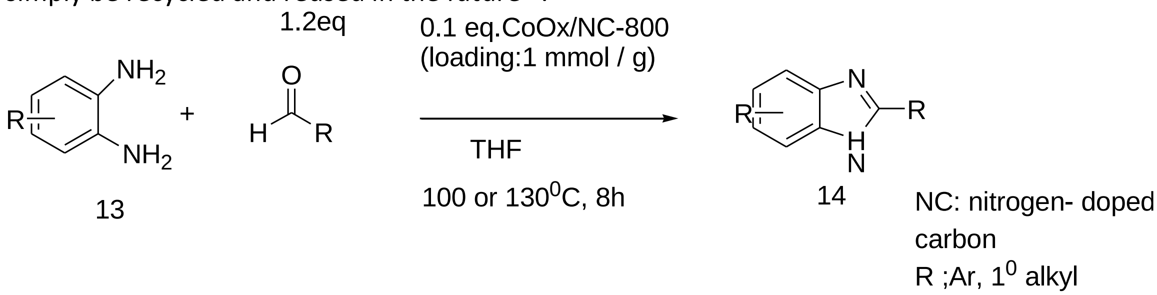
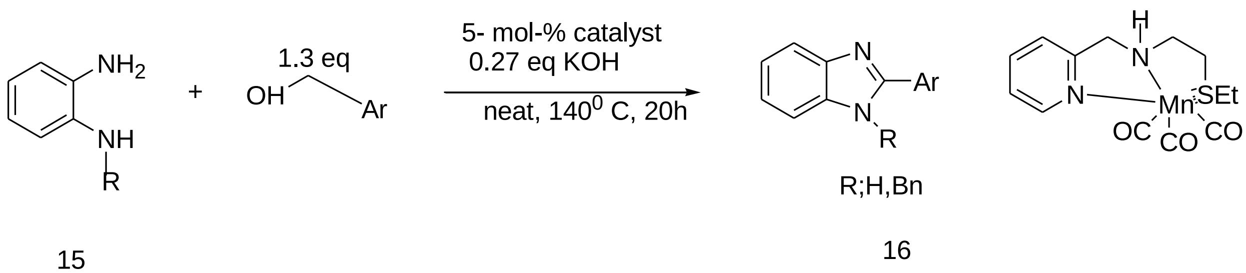
7. A very recyclable, non-degradable cobalt accelerates the coupling of phenylene-diamine with aldehydes to produce a broad spectrum of physiologically active benzimidazoles in good yields with

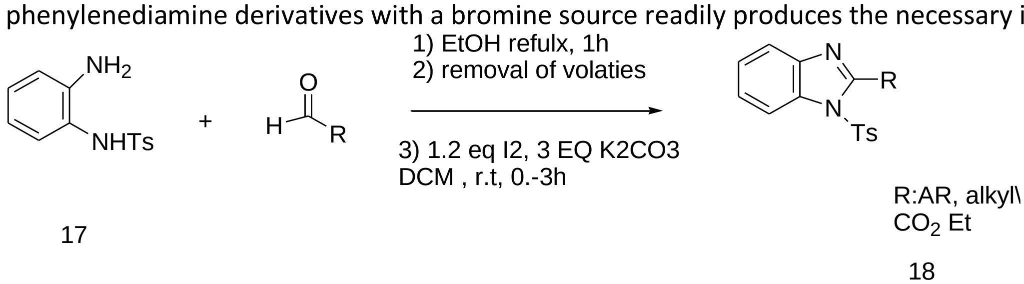
noteworthy functional group tolerances under additive and oxidant-free environments. The catalyst may simply be recycled and reused in the future[33].



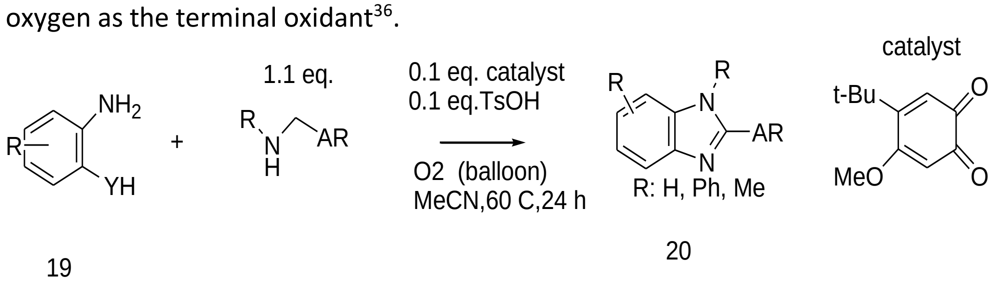
8. The selective synthesis of 2 and 1,2 substituted benzimidazoles is made possible by the dehydrogenative coupling of an aromatic diamine with a primary alcohol via an acceptor. This process is catalyzed by a manganese(I) complex derived from the phosphine-free tridentate NNS ligand[34].



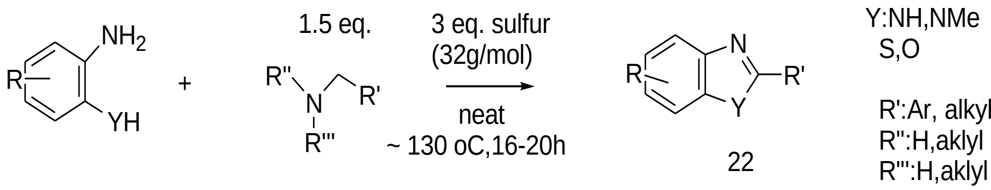
9. A functional molecular iodine-based intra-molecular CH modification technique provides transition metal-free cyclization of crude imine for the successive synthesis of N-protected benzimidazoles under modest conditions without removing least-stable condensation intermediates. The condensation of o-phenylenediamine derivatives with a bromine source readily produces the necessary imine substrates[35].



10. Bioinspired o-quinone catalyst has been utilized to oxidatively synthesize benzimidazoles, benzoxazole and quinoxaline from primary amines in good yields under mild situations and to employ oxygen as the terminal oxidant[36].



11. The utilize of essential sulphur as a traceless oxidizing agent facilitates the synthesis of benzoxazole from o-hydroxy/amino/mercaptan aniline and alkylamines without the need of solvents or catalysts[37].



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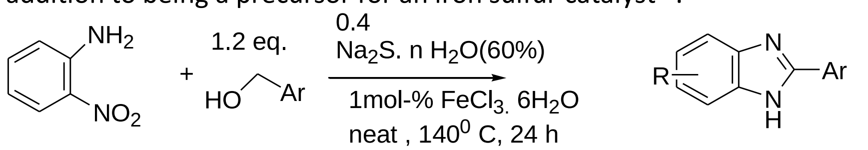
12. An imbalanced redox condensation reaction between o-nitro aniline and alcohols is promoted by sodium sulphide in mixture with iron (III) chloride hexahydrate, resulting in benzimidazole and quinoxaline heterocycles. Hydrated sodium sulphide is a solid noncompetitive multi-electron reducer in addition to being a precursor for an iron sulfur catalyst[38].



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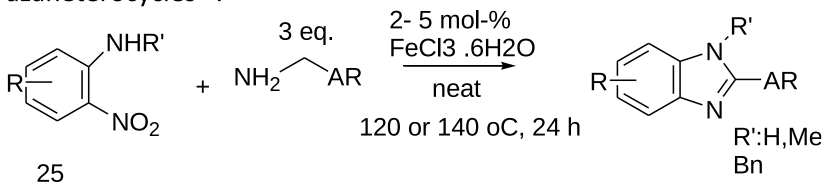
13. Through benzylamine condensation, oxidation, nitro reduction, and aromatization without the use of a reducing or oxidizing agent. It is possible to make an extensive spectrum of functionalized 2-aryl benzimidazoles using solvent free cobalt metal ions or iron catalyzed redox condensation of benzylamines and 2-nitro aniline. The procedure can be used to make a wide range of di-azaheterocycles[39].



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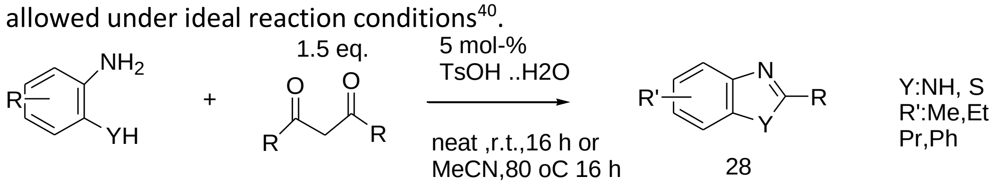
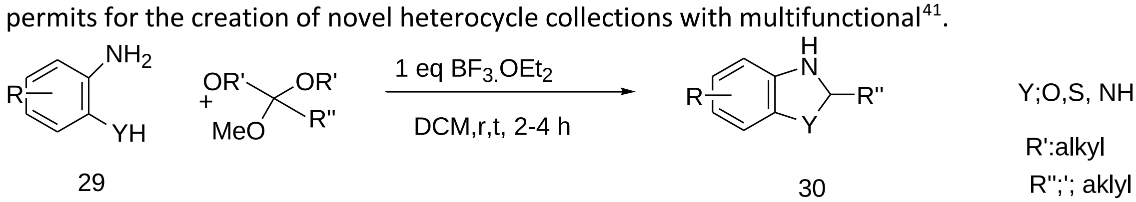
14. Bronsted acid catalyzed cyclization reactions of anilines and 2-amino thiophenols with diketones make good yields of benzimidazoles and 2-substituted benzothiazoles under metal-free and oxidant conditions. Various groups attached to benzene rings, such as nitro, methyl, methoxy, and chloro were allowed under ideal reaction conditions[40].



27 28

15. In a compelling and connected strategy, o-substituted anilines mix with functionalized orthoesters to form derivatives of benzothiazole, benzoxazole, and benzimidazole. This technology's adaptability permits for the creation of novel heterocycle collections with multifunctional[41].



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16. Aromatic, heteroaromatic, and aliphatic aldehydes undergo ozone-mediated transformations from 2-aminobenzylamines to 2-substituted benzimidazoles at ambient temperature. After the first condensation of 2-aminobenzylamine with sufficient aldehydes generated a tetrahydroquinazoline

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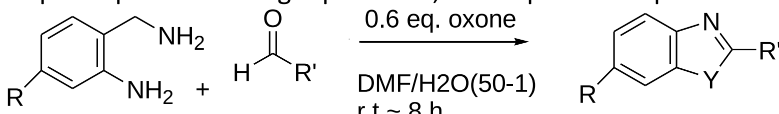
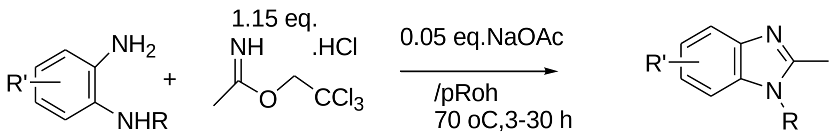
intermediate, which was subsequently subjected to ozone-mediated rings distortion to create the required products in high quantities, the required compounds were synthesized in high yields[42].



31 32

R:H,Me
Cl,Br
R':Ar,Me

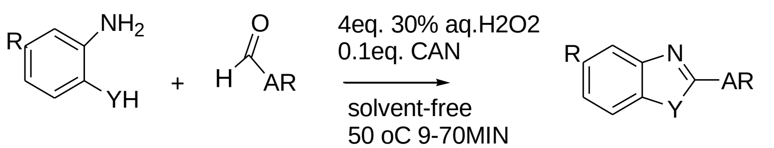
17. In isopropyl alcohol at 70°C, the acylating agents 2,2,2-trichloroethylene imitates are employed to produce benzimidazoles and imidazopyridines. When cyclization was sluggish, adding sodium acetate helped. For substrates with modest nucleophilicity, to use the more inert test-amyl alcohol produced better reactions[43].



33 34

R:H,alkyl,Ph

18. Short reaction durations, large-scale synthesis, simple compound identification, high chemo-selectivity, and high yields are all benefits of a simple approach for synthesizing 2-substituted benzimidazoles and benzothiazoles[44].



Y:S,NH

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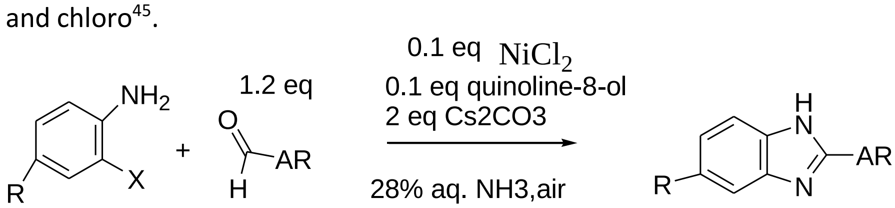
19. Benzimidazoles were generated in excellent yields using catalytic amounts of TMEDA and CuCl in DMSO at 120°C for 12 hours in a copper catalyzed, one pot 3-component synthesis comprising aldehydes, 2-haloanilines, and NaN3. The process contains many functional groups such as nitro, ester, and chloro[45].



X:I.Br

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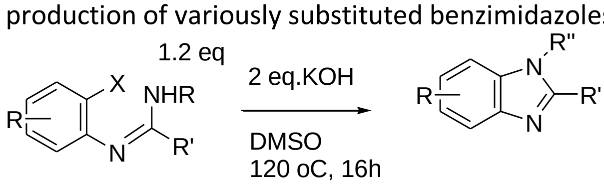
20. Intramolecular N-arylations of amidines generated by KOH in DMSO at 120°C allow for the high yield production of variously substituted benzimidazoles[46].



X: F, Br, I
R':alkyl,Ar
R": Ph, alkyl,
benzyl

39 40

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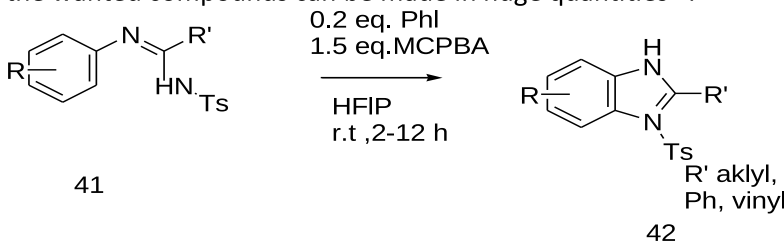
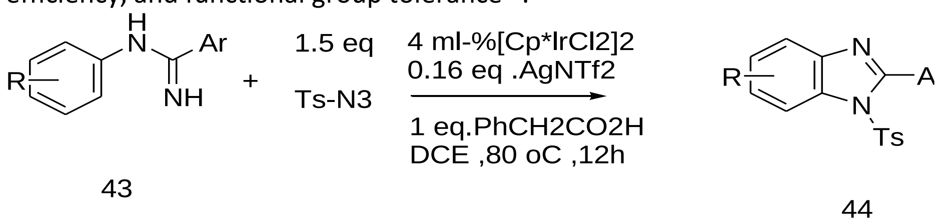
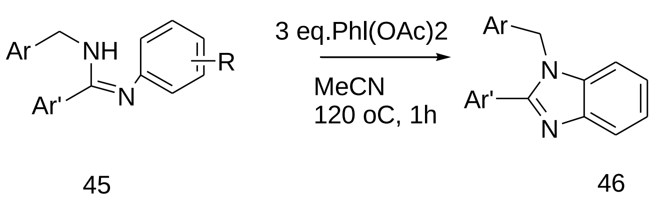
21. The benzimidazoles with 1,2-disubstituted are obtained via oxidative CH amination of N,N′-bis (aryl)amidines and N′-methylsulfonylamidines/N′′-aryl-N′-tosyl using mCPBA as a terminal oxidant at ambient temp with iodobenzene as a catalyst. The reaction can be used in a diversity of situations, and the wanted compounds can be made in huge quantities[47].



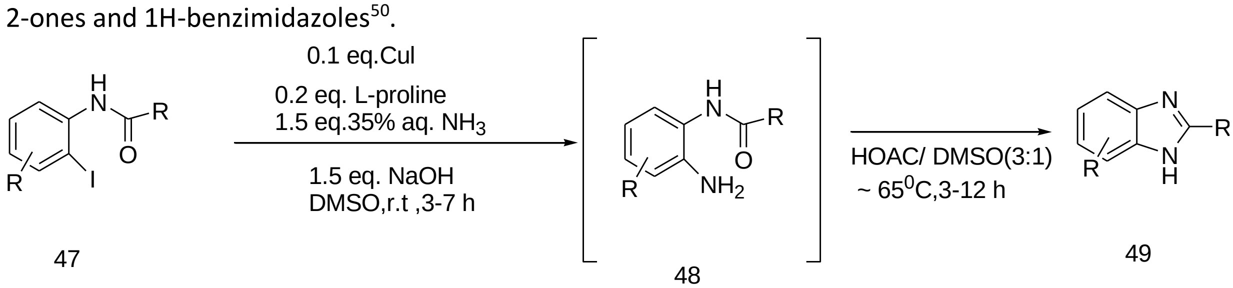
22. A moderate Iridium catalyzed annulation of imidamides with sulfonyl-azides provides substantial amounts of 1,2-disubstituted benzimidazoles. This approach is very selective in terms of regioselectivity, efficiency, and functional group tolerance[48].



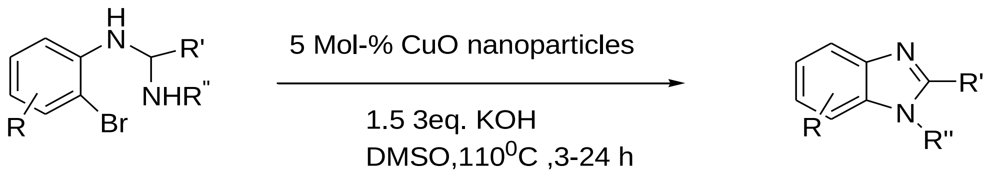
23. In nonpolar solvents, iodine (III) based oxidative produce sp3-sp2 bond converted amidines to benzimidazoles rapidly and easily, but polar fluids favoured formation of sp2-N bond to make quinazolines. K2S2O8 as an oxidant and TEMPO was used as a catalyst in a subsequent selective synthesis of quinazolines in polar solvent. There was no need for any base, metal, or other components[49].



24. At room temperature, the coupling of aqueous ammonia with 2-iodophenylcarbamates and 2-iodoacetanilides catalyzed by l-proline/CuI yields aryl amination products, which are then additively cyclized in situ under acidic environments or heated to produce associated 1,3-dihydrobenzimidazozol-2-ones and 1H-benzimidazoles[50].

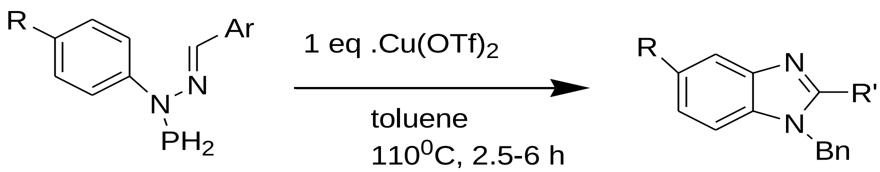


25. Through intramolecular cyclization of o-bromoaryl derivatives, copper (II) oxide nanoparticles in DMSO under air catalyse an experimentally modest, universal, practical, and ligand free synthesis of associated 2-aminobenzimidazoles, benzimidazoles, benzoxazoles and 2-aminobenzothiazoles. Without destroying activity, the heterogeneous catalyst can be retrieved and repurposed[51].



50 51 R'Me,Ph, NR'''
R'' : Bn,Ar,alkyl

26. Through intramolecular cyclization of o-bromoaryl derivatives, copper (II) oxide nanoparticles in DMSO under air catalyse an experimentally modest, universal, practical, and ligand free synthesis of associated 2-aminobenzimidazoles, benzimidazoles, benzoxazoles and 2-aminobenzothiazoles. The heterogeneous catalyst can be retrieved and used without destroying it[52].



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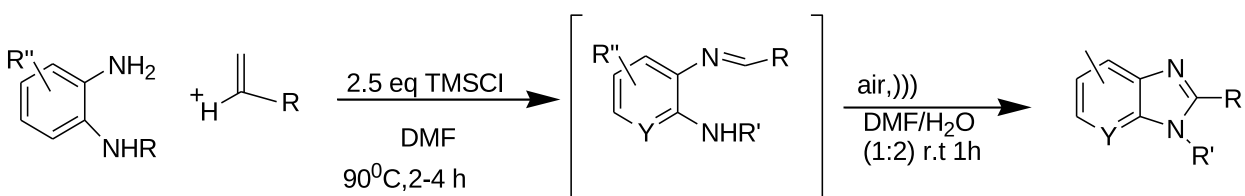
27. 3H-imidazo [4,5-b] pyridines, benzimidazoles, benzothiazoles, purines, and xanthines were typically synthesized from aromatic o-aminothiophenol or o-diamines and aldehydes in DMF utilizing chloro-trimethylsilane as a water-acceptor agent and supporter, then oxidised with air oxygen[53].



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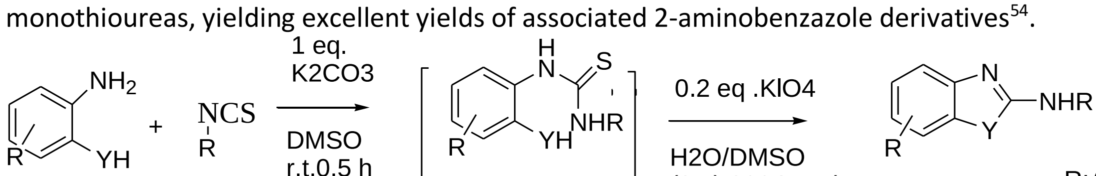
Y;CH,N

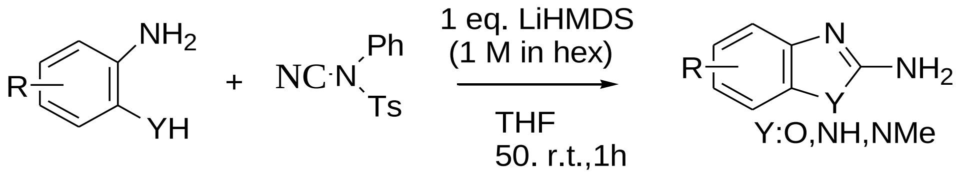
28. Isothiocyanates react with o-substituted anilines including N,S-bis-nucleophiles and N, N, N,O, tailed by intra-molecular, potassium-periodate facilitated oxidative cyclo-desulfurization of the in situ formed monothioureas, yielding excellent yields of associated 2-aminobenzazole derivatives[54].



R:Ar, BN
59 Y:NH,O,S,NR

57 58

29. The usage of N-cyano N-phenyl p-toluenesulfonamide (NCTS) as a harmless electrophilic cyanation agent while around lithium hexamethyldisilazane permits for the easy synthesis of 2-aminobenzoxazole and 2-aminobenzimidazole derivatives (LiHMDS). It's simple to set up and use, and it works rapidly[55].



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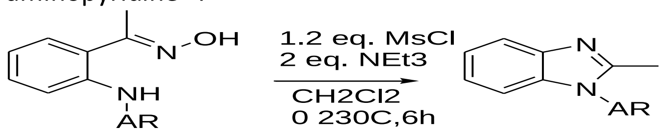
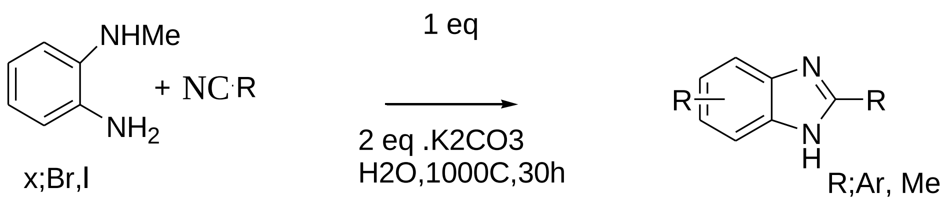
30. Depending on the base utilised in the process, numerous benzimidazoles and N-aryl 1H-indazoles were synthesised in good to outstanding yields from typical arylaminooximes. Triethylamine assisted the synthesis of benzimidazoles, while the development of N-arylindazoles was enhanced by 2-aminopyridine[56].



62 63

31. A collection of benzimidazoles is synthesised in good yields utilizing a simple, efficient, and sustainable intramolecular N-arylation technique with Cu2O as the catalyst, K2CO3 as the base and DMEDA as the ligand. Surprisingly, the reaction took place solely in water, making it both environmentally and economically beneficial[57].



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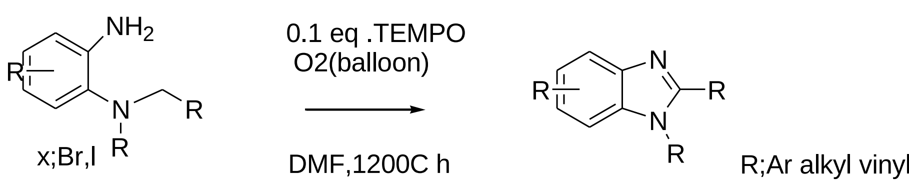
32. In the presence of oxygen and TEMPO, a metal-free oxidative C-N coupling between the free NH and sp3 CH of routinely available N1-benzyl/alkyl 1,2-phenylenediamines allows the formation of multi-substituted or fused tetracyclic benzimidazoles[58].



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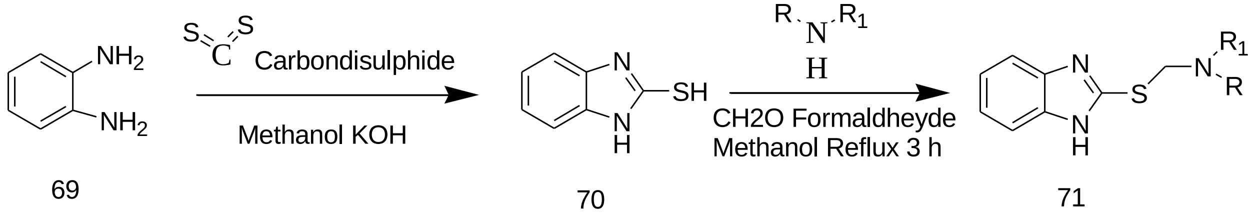
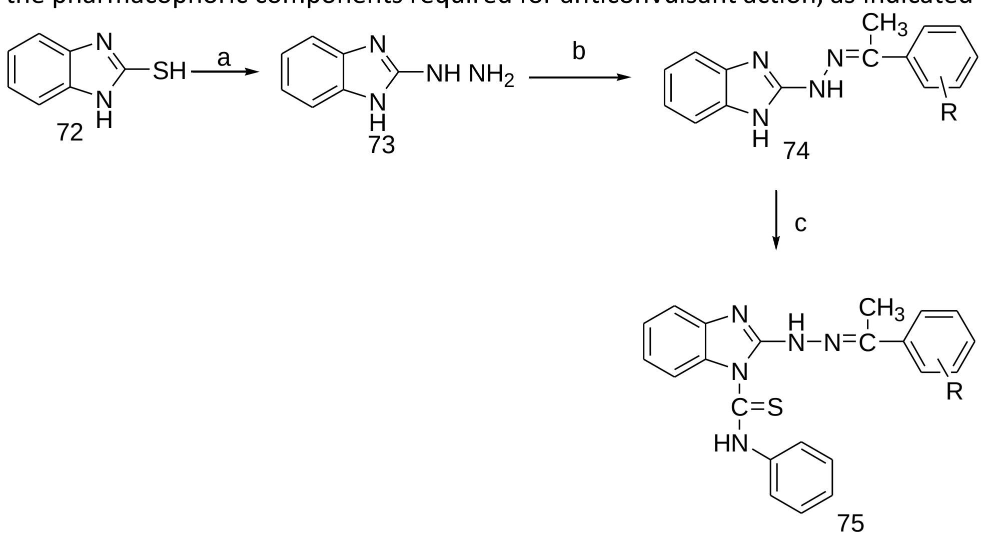
33. K.Anandarajagopal and colleagues Mannich reaction was used to create a novel series of 2-mercaptobenzimidazole derivatives from 2-mercaptobenzimidazole by reacting it with molecules containing secondary amine and formaldehyde. The maximal electrical shock-induced convulsion methodology was used to determine the anticonvulsant efficacy of newly synthesised 2-mercaptobenzimidazole derivatives. The majority of the produced compounds 71 had extremely substantial activity, as illustrated in Scheme 33[59].

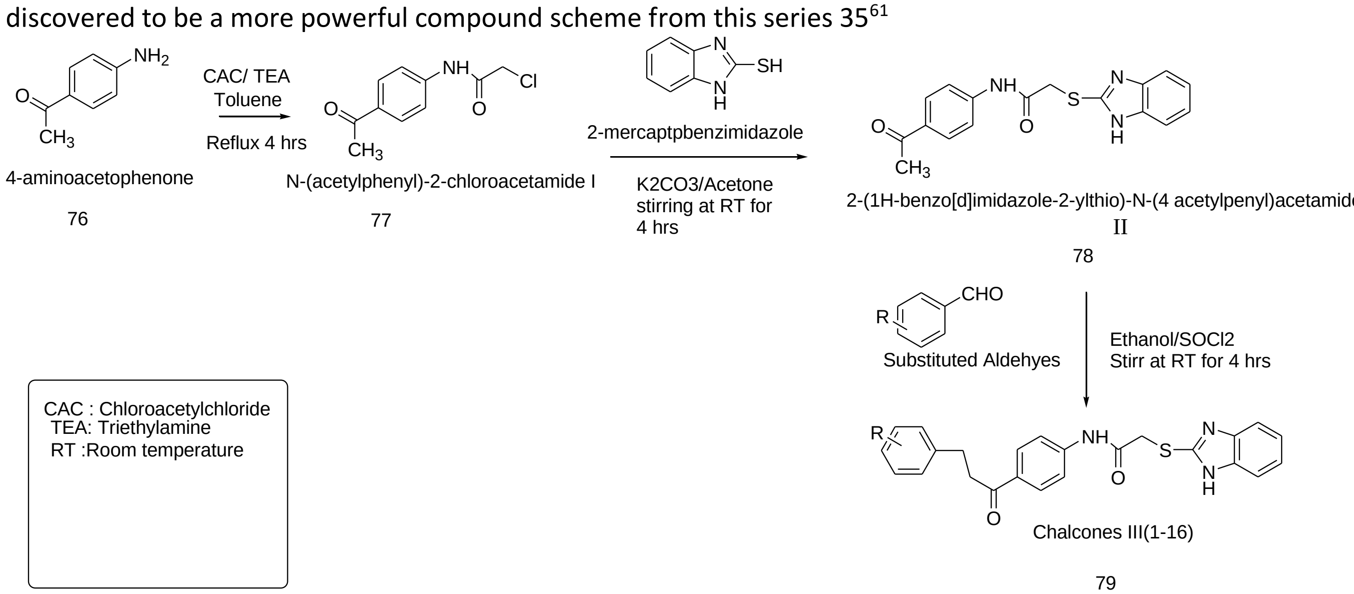


34. Bhanupriya Bhrigu *et al*. A novel family of 2-[(1-substituted phenylethylamine) hydrazine] -N-phenyl-1H-benzo[d] Compound 75 of imidazole-1-carbothioamides was developed and synthesized to contain the pharmacophoric components required for anticonvulsant action, as indicated in Scheme 34[60]

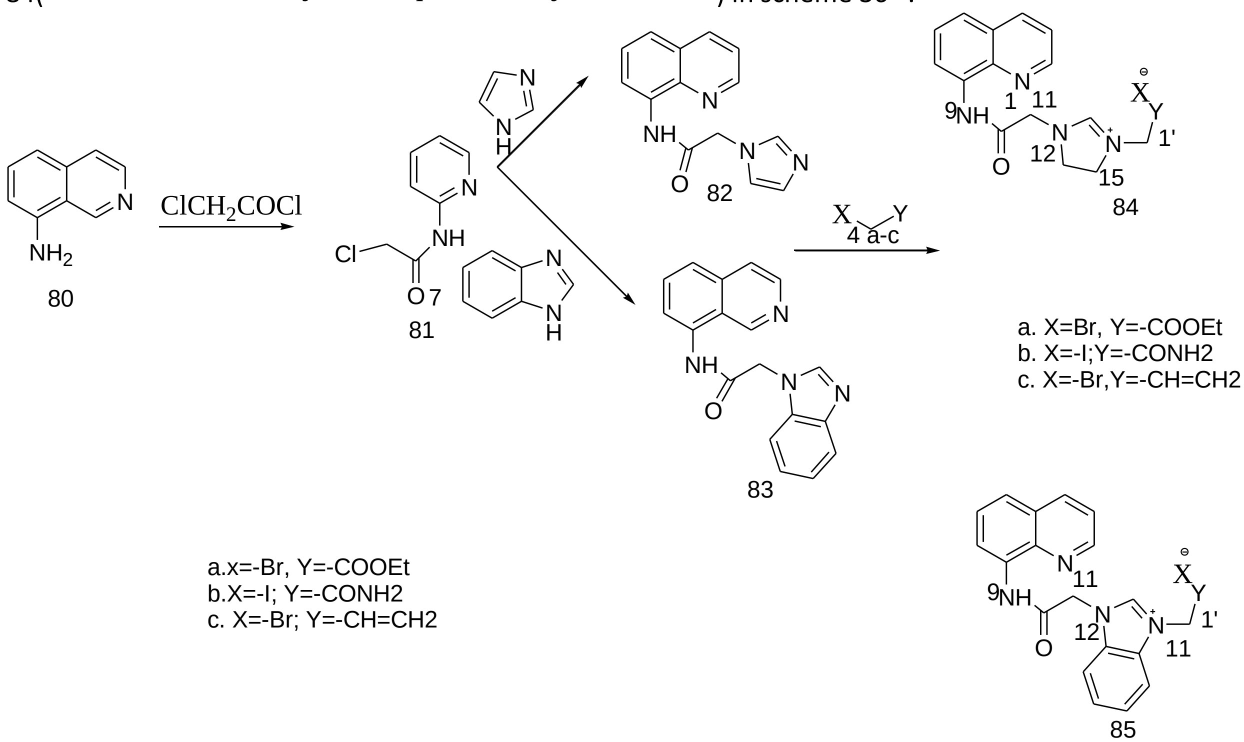


R=H,4-NH2, 4-OH,3-OH, 4-Br, 4-F, 2-Cl, 4NO2, 3-bR,4-Cl,5-di-OH

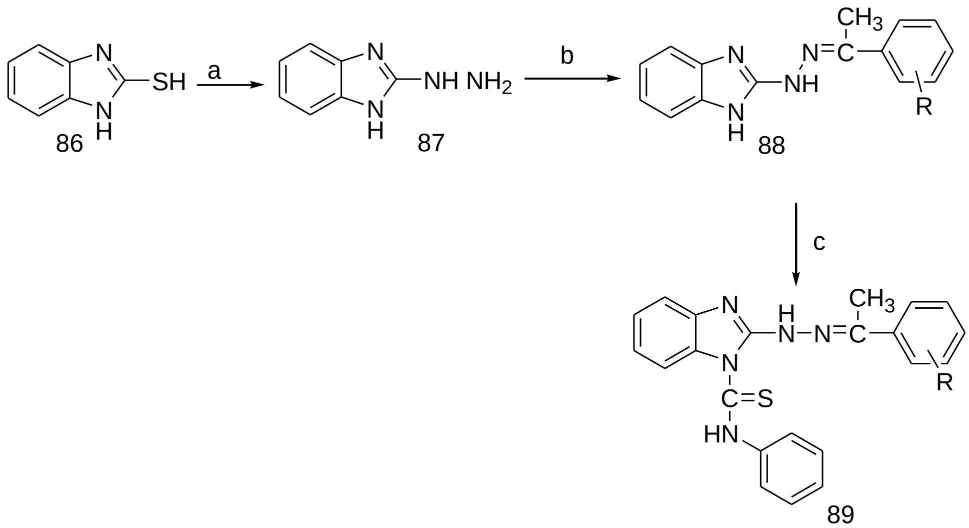
35. Kalpesh *et al*. Reported that on compound Chalcone III (79) was produced and tested for antibacterial and antifungal activity against S. aureus, E.coil, E.faecalis (Gram-positive bacteria), P.aeruginosa (Gram-negative bacteria), and Fungi C.albicans. The compound chalcone III (79) was discovered to be a more powerful compound scheme from this series 35[61]



36. Dorina Mantu *et al*. Reported a novel series of compound syntheses of hybrid Imidazole, quinoline/benzimidazole. This shown and evaluation of their anti-cancer and antimycobacterial activity from this compound series were found to be the most potent compound is 84(2-Benzoimidazol-1-yl-*N*-isoquinolin-8-yl-acetamide) in scheme 36[62].

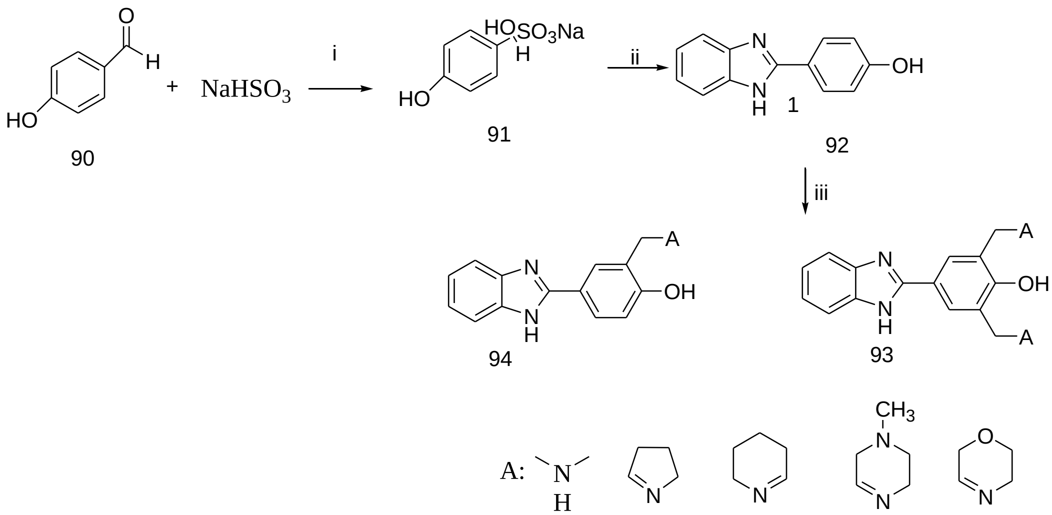


37. Bhanupriya Bhrigu *et al* A new class of chemicals has been developed. [(1-substituted phenylethylamine) hydrazine] 2-[(1-substituted phenylethylamine) hydrazine] -N-phenyl-1H-benzo[d] The pharmacophoric components required for anticonvulsant action were developed and synthesised in imidazole-1-carbothioamides (4a-n). Compound 89 in Scheme 37 is the most powerful compound in this scheme[63].

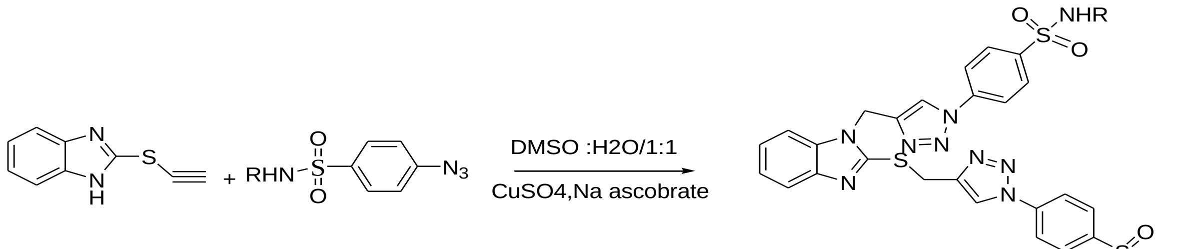


R=H,4-NH2, 4-OH,3-OH, 4-Br, 4-F, 2-Cl, 4NO2, 3-bR,4-Cl,5-di-OH

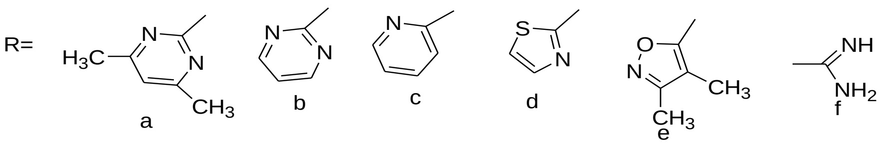
38. HALISE INCiGul et al. A novel benzimidazole molecule is obtained new compounds Many studies have demonstrated that the synthesis of 4-(1H-benzimidazole-2-yl)-2,6-bis[(morpholino-4-yl)methyl] phenol has a modest CA. Compound 94's inhibitory characteristics are demonstrated in this scheme in 38[64].



39. Fawziafaleh Al-blew *et al.* There has been a discovery of a novel benzimidazole chemical. In vitro tests were performed on the newly synthesized compounds for antibacterial and antiproliferative properties. The synthesis of 1,4-disubstituted bis-1,2,3-triazoles in this scheme 39 is the most successful chemical in this series. Antimicrobial and antiproliferative properties are found in compound 97[65].

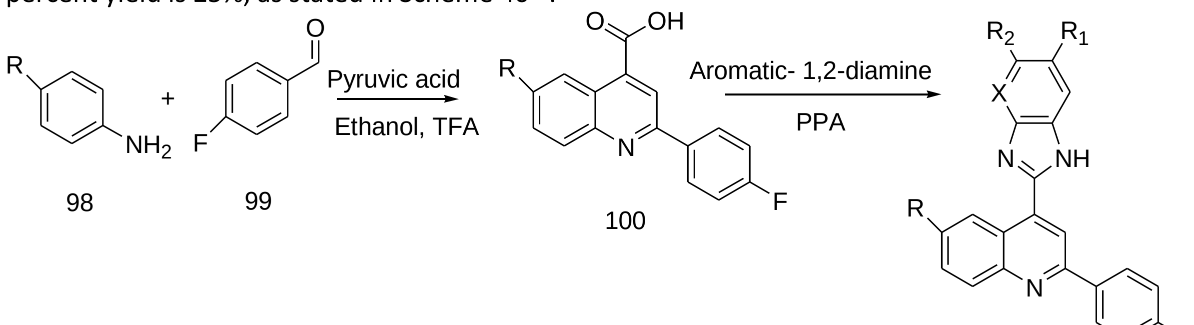


95 96 97



a b c d e f

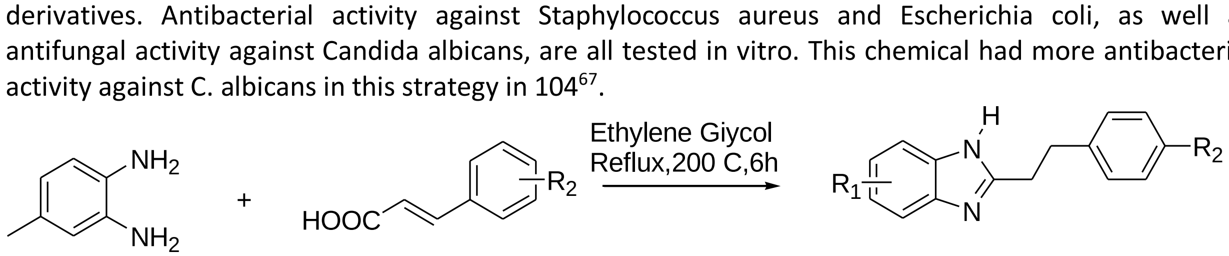
40. B.Garudachari *et al.* A new four-compound series has been created (1H-Benzimidazol-2-yl) -6-chloro-2-(4-fluorophenyl) In a multi-step synthesis that also yielded 6-substituted-4-carboxyquinoline, quinoline was synthesized from substituted aniline and isatin. In the well plate approach, the resulting product (101) was tested for (in-vitro) antibacterial and antifungal activities (zone inhibition). Molecule 101 was discovered to be a more powerful compound with effective antibacterial activity. The compound's percent yield is 25%, as stated in Scheme 40[66].



98 99 100 101

R1= H, Cl, F; R2=H Cl; X= CH, N

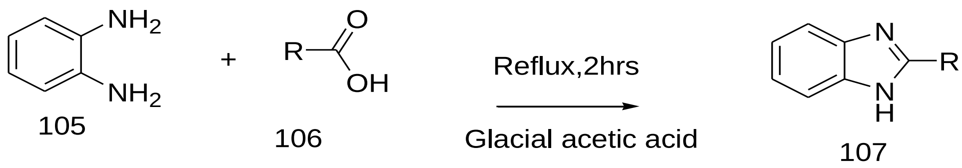
41. Love Kumar Soni *et al*. 5-(nitro/chloro)-2-styryl-benzimidazoles are a new class of benzimidazole derivatives. Antibacterial activity against Staphylococcus aureus and Escherichia coli, as well as antifungal activity against Candida albicans, are all tested in vitro. This chemical had more antibacterial activity against C. albicans in this strategy in 104[67].



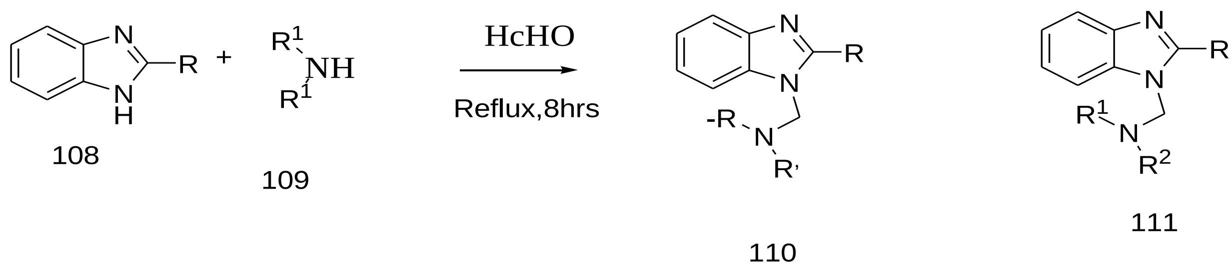
102 103 104

42. Sekar Vinoth Kumar *et al.* A brand-new class of benzimidazole derivatives Compound of 2-[(Dimethyl amino) methyl]-1H-benzimidazol-2-yl benzoic acid (118) Among the most effective compounds generated, the anti-microbial assays were done using the micro broth dilution technique, which was

revealed by spectrum data. The more effective compound (111) against all bacteria tested. In scheme 42, this chemical demonstrated full bacterial DNA cleavage and was non-toxic[68].

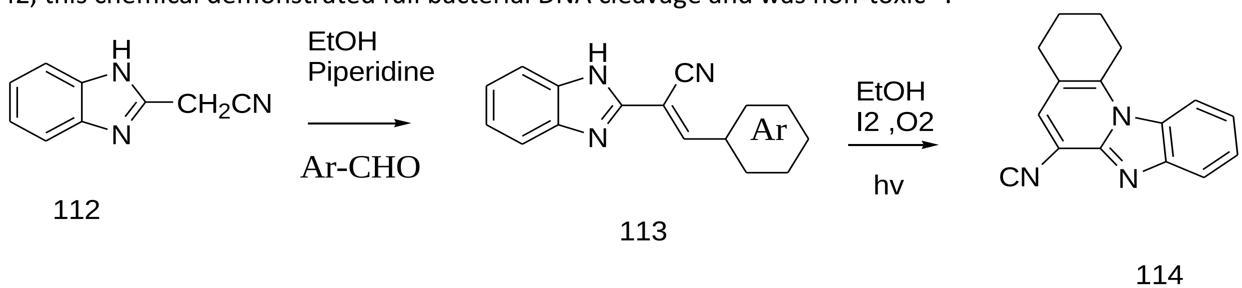


3A=R=-H,3B=R=-CH3,3C= R=-C6H5,3D= R=-C6H4(OH), 3E=R=-C6H3(OH)SO20H
3F=R=--COOH,3G=R=-C6H4COOH

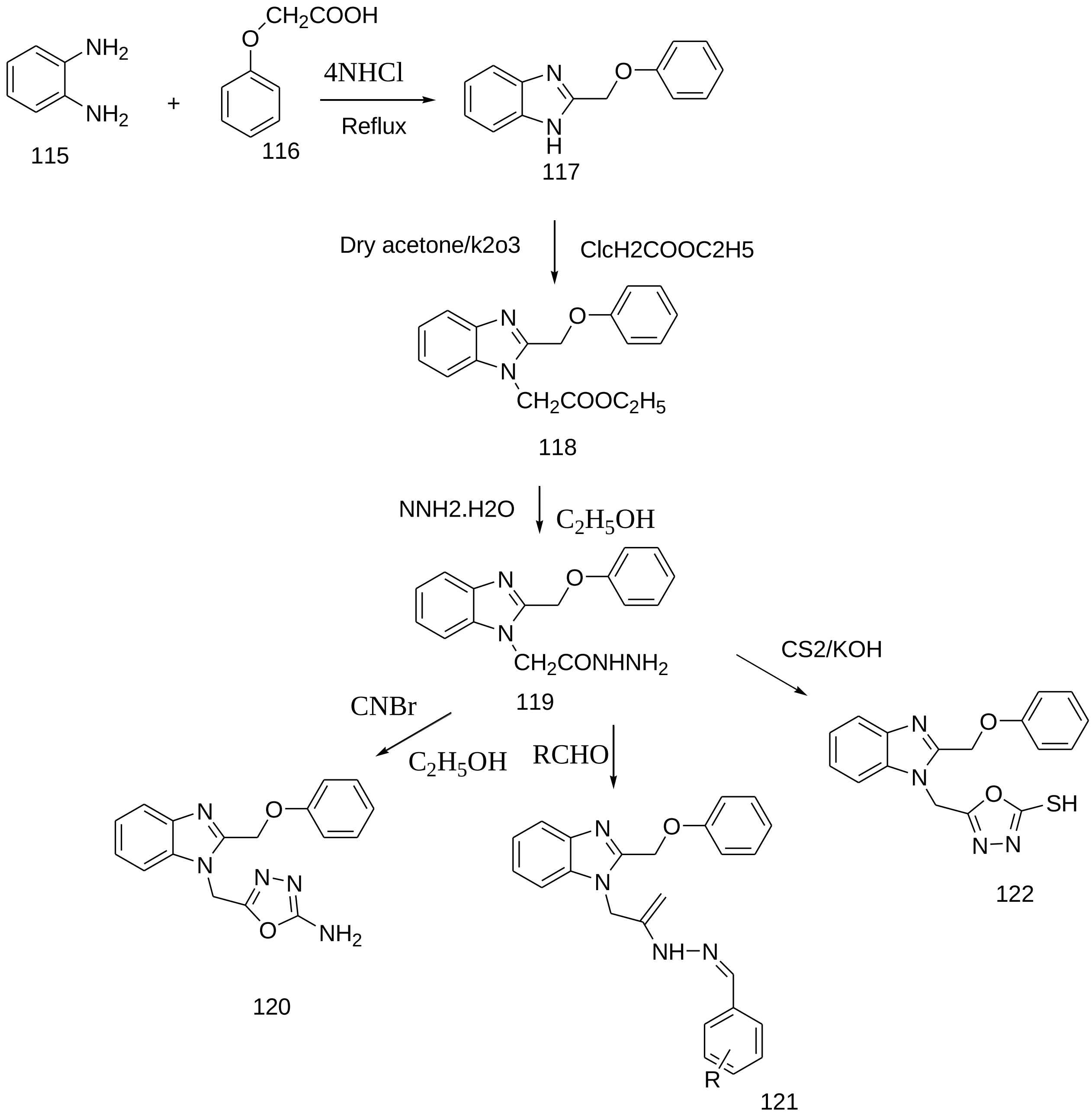


COMPOUNDS	R	R1	R2
5E(a)	$-C_6H_3(2\text{-}OH)(5\text{-}SO_2OH)$	$-CH_3$	$-CH_3$
5E(b)	$-C_6H_3(2\text{-}OH)(5\text{-}SO_2OH)$	$-C_2H_5$	$-C_2H_5$

43. Marijana Hranjec *et al*. A brand-new class of benzimidazole derivatives compound of 2-[(Dimethyl amino) methyl]-1H-benzimidazol-2-yl benzoic acid (118) Among the most effective compounds generated, the anti-microbial assays were done using the micro broth dilution technique, which was revealed by spectrum data. The more effective compound (114) against all bacteria tested. In scheme 42, this chemical demonstrated full bacterial DNA cleavage and was non-toxic[69].

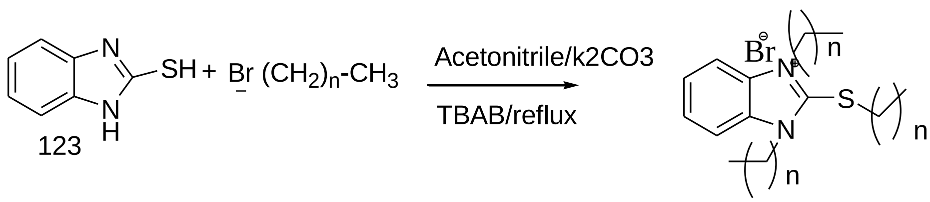


44. Mohammad Shaharyar *et al.* N0 -[(Z)-(4-nitrophenyl) methylidene] N0 -[(Z)-(4-nitrophenyl) methylidene] N0 -[(Z)-(4-nitrophenyl) methylidene] N0 -[(Z)- Where the chemical has more strong activity revealed in the elemental analysis is -2- [2-(phenoxy methyl)-1H-benzimidazol-1-yl] aceto hydrazide. In *VIVO* anticonvulsant screening was carried out using MES and scPTZ. It revealed that the compounds (121) were successful in both screens and their protective index in yield 69 in scheme 43[70].



R=H,2-Cl,4-Cl ,4-OCH_3,3,4-diOCH_3, 4-F, 4-NH_2, 4,4-dimetylamino, NO_2

45.Terence Nguema Ongone *et al.* Novel benzimidazole 1,3-dialkyl-2-alkylthio-1H-benzimidazolium bromides were described. The chemical (124) yields 74 percent in scheme 44 due to its high action in terms of acute toxicity and analgesic, psychotropic activities[71].



123

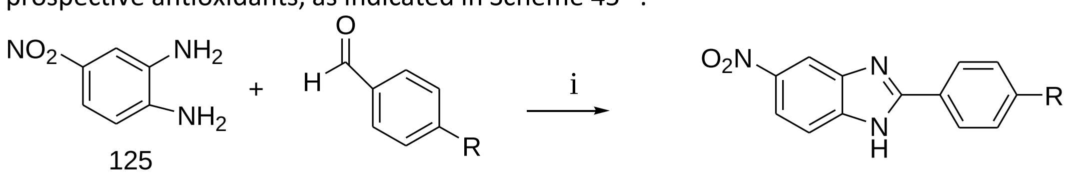
124

a;n=7
b;n= 8
c;n=9
d;n=11

2;n=7
3;n=8
4;n=9
5;n=11

Synthesis of 1,3-dialkyl-2-alkythio-1h-benzimidazolium bromides

46. Sabrina Rahman Archie *et al.* A new series of benzimidazole compounds (127) with strong action was described. The molecule (127) demonstrated strong antioxidant activity with IC_{50} values ranging from 3.17 to 7.59 mg/ml, whereas the compound (127) may serve as a future leader in the creation of prospective antioxidants, as indicated in Scheme 45[72].



125

126

127

2a(R=Cl), 2b(R=Br)

2c (r=f),2d (R=OMe)

R	product
Cl	3a
Br	3b
F	3c
OMe	3d

Reagent and condition: (1) $NA_2S_2O_5$, absolute ethanol, reflux 4h

Biological Activities of Benzimidazole Derivatives:

The benzimidazole moiety is exceedingly adaptable, and it has been exploited in the development of various clinically useful medications with high therapeutic potency and commercial value, such as antihypertensive, antiulcer, and other therapeutic agents.

Antihypertensive Agents: Biphenyl benzimidazoles exhibit a powerful antihypertensive effect as compared to prior comparable medicines owing to greater oral availability; the 2-position of biphenyl is crucial for the activity. Angiotensin-II AT1 receptor antagonistic activity has been observed in 5 substituted aryl or alkyl carboxamides derivatives, making them effective antihypertensive medicines[73-78].

Antiulcer Activity: The proton pump in Parietal cells and the H+/K+ ATPase are both inhibited by substituted benzimidazoles. They can also inhibit the secretion of stomach acid in response to specific stimuli. The sulfoxide, methylene, and heterocycle groups are essential for activity[73-78].

Antiviral activity: Several studies using a variety of virus strains, including HIV, human cytomegalovirus (HCMV), and hepatitis B and C virus, have indicated antiviral activity of benzimidazole derivatives. Bis(5-amidino-2-benzimidazolyl) methane (BABIM) and other amino-substituted benzimidazoles have also been demonstrated to block respiratory syncytial virus-induced cell fusion. Adding an amidino moiety to a benzimidazole ring has also been shown to have significant antibacterial and anti-protozoal activity[73-78].

Antimicrobial Activity: Isoxazolyl substituted compounds were tested for efficacy against Gram-negative bacteria such as E.coli and Proteus Vulgaris, as well as gram-positive bacteria such as Bacillus mycoides and Staphylococcus aureus. Some benzimidazole compounds with hydrazone moiety were examined to see whether they have any antibacterial action[73-78].

Antifungal Activity: These are the medications that are used to treat superficial and deep fungal infections. Mycoses are fungal infections that are classified as superficial (skin, nails, and scalp) or systemic (deeper tissues and organs). Some disorders include blastomycosis, histoplasmosis, candidiasis, coccibiomycosis, and others[73-78].

Anthelmintic: These are the medications that either kill or expel helminths. Many benzimidazole-based wide spectrum anthelmintics as compounds with the therapeutic prospective of benzimidazole in parasite chemotherapy were recognised after the advent of thiabendazole and carbendazim, including mebendazole, cyclobendazole, flubendazole, fenbendazole, oxibendazole, oxfendazole, nocodazole and albendazole[73-78].

Antioxidant activity: Some dihydrochlorides have been shown to exhibit antioxidant action; these salts also have moderate platelet and erythrocyte antiaggregant activity[73-78].

Antitumor activity: Several novel nitro-benzimidazoles with cytotoxic efficacy against breast cancer has been found. The described study also discovered that chemicals such as thiadiazole, tetrazole, triazines, and imidazoles had action[73-78].

Anti-inflammatory activity: Benzimidazole is a potential heteroaryl moiety that has generated numerous effective medications such as omeprazole and mebendazole. Benzimidazole-2-carboxylic acid derivatives were developed because the benzimidazole moiety with carboxylic acid substitution at position 2 matches the minimal and desirable structural criteria observed in the bulk of commercialised anti-inflammatory drugs. They were tested for immediate anti-inflammatory effectiveness in a carrageenan-induced rat paw edoema paradigm. Carrageenan's anti-inflammatory efficacy on edoema suggests that prostaglandin synthesis inhibition is the most likely mechanism of action[73-78].

Benzimidazole Derivatives Under Clinical Trial

The development of benzimidazole based medicines is a fascinating topic that is drawing more and more researchers. A rising number of benzimidazole compounds have been studied, and interesting research is now being conducted. Pharmaceutical firms have identified a huge number of medicine candidates that are now undergoing clinical trials at various stages. As a consequence, the benzimidazole nucleus might be tweaked to provide safer, new, and additional effective treatments for fungal infection patients. Triazole-based antifungal medicines have received a lot of attention in recent years because they have better antifungal action[73-78].

Conclusion: The benzimidazole ring is an essential pharmacophore in modern drug development. The synthesis of benzimidazole compounds is gaining popularity. The benzimidazole ring is an essential pharmacophore in drug development. Many clinical studies are now being conducted to investigate the promise and low toxicity of medications. These surveys or research were determined to be successful in establishing techniques to synthesize the benzimidazole derivate reaction process. Some benzimidazole derivative medicines with substituted benzimidazole action are more powerful. The synthesis of benzimidazole derivatives is a privileged scaffold with a wide range of therapeutic applications, together with antifungal, antiviral, antiparasitic, antihistamine, anticancer, and usage in cardiovascular disease, neurology, and endocrinology.

Future Prospects: In the future approach, novel and potent chemical entities with immense promise for the therapy of many illnesses can be investigated by combining benzimidazole scaffolds. In the coming-century, this has the potential to alter medical practise. Existing medications must be improved or changed to meet issues including resistance, toxicity, and poor absorption, resulting in a significant improvement or change in activity. Prodrugs can also be used to increase the bioavailability of pharmaceuticals that are already on the market.

In recent years, there has been a lot of interest in benzimidazole derivatives. The most active medications were created by combining the changes at positions 1, 2, and 5 of the molecule. The 4-, 6-, and 7-positions of benzimidazole, on the other hand, need to be investigated further for new entities with intriguing biological activity. Consequently, we expect the combination of benzimidazole-triazole-based heterocycles to lead to new drug discovery. This idea could be the next important step in the development of more potent and less toxic broad-spectrum antifungal drugs. These findings are expected to encourage further research into new and more effective treatments.

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