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MICROWAVE ASSISTED SYNTHESIS OF FUSED HETEROCYCLIC COMPOUNDS

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Abstract - Microwave assisted heating under controlled conditions has been proved beneficial for medicinal chemistry and drug discovery process since it dramatically reduces reaction times, from days or hours to minutes or even seconds. Also, microwave synthesis provides higher yields, lower cost, easy workups and greater purity as compared to lower yields, tedious workups, longer reaction times, lesser purity and termination of many by-products in the conventional thermal methods.

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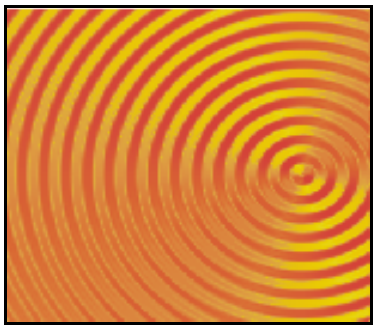
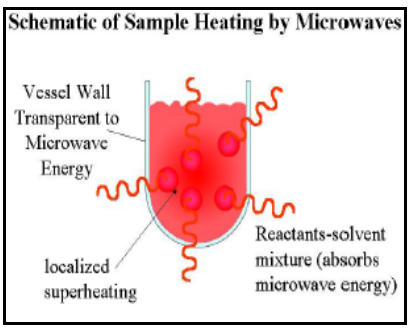
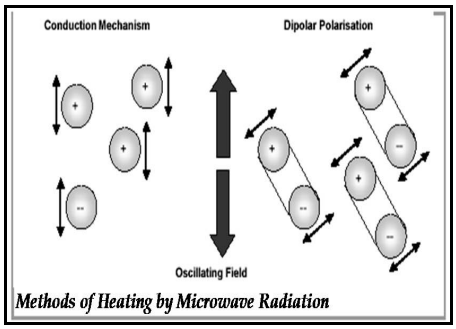
1. INTRODUCTION

In the new millennium, the concept of "Green Chemistry" will be forcing greater demands to meet the fundamental scientific challenges of protecting the health as well as environment, while maintaining the commercial viability. Exploration of alternative reaction conditions and media with minimal side products or waste and elimination of the use of hazardous solvents will be the main thrust area. Microwave technology has made greater residues now-a-days because of non-pollution, higher yields, lower cost, lesser time, easy workups and greater purity of final products.[1] Microwave assisted chemical synthesis has proved successful in remarkably cutting the required reaction time and improving the yields and purity of the desired products. It has emerged as a powerful technique to promote a variety of chemical reactions.[2] Microwave synthesis has the potential to influence medicinal chemistry efforts in at least three major phases of New Drug Discovery Research *i.e.* Generation of a discovery library, Hit-to-lead efforts and Lead optimization. On the other hand, it has become widely accepted that many classical reactions under microwave irradiation perform better than reactions under conventional heating.[3-7] Microwaves have a variety of applications such as in synthetic chemistry, degradation of natural products, quantitative analysis, etc. microwave assisted synthesis has become a powerful synthetic tool for rapid synthesis of a variety of organic compounds.[8-11] Microwave heating differs fundamentally from conductive heating. Microwaves couple directly with molecules within a reaction mixture, leading to rapid rise in temperature. The process is not dependent on the thermal conductivity of the vessel material resulting in instantaneous localized superheating of anything that will react to dipole rotation or ionic conduction, the mechanisms of energy transfer in microwave heating. The use of microwave energy reduces the heat-up and cool-down time for reactions and employs 50% less power than equivalent electric appliances.





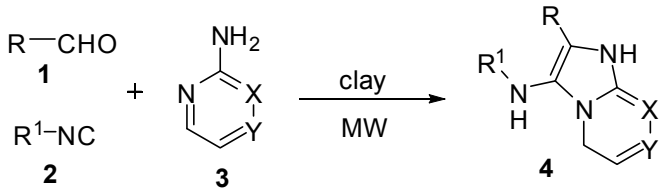


This review details the synthesis of a variety of fused heterocycles ($R/R_1/R_2/R_3/R_4$ = alkyl/aryl, X/Y = C/N/O/S/Halogens and Ar = aryl) under microwave assisted conditions and the results are compared with those carried out under conventional methods in the form of reaction times, temperature, reaction conditions and product yields.

2. MICROWAVE ASSISTED SYNTHESIS OF FUSED IMIDAZOLE DERIVATIVES

2.1. Imidazo[1,2-*a*]annulated pyridines, pyrazines and pyrimidines

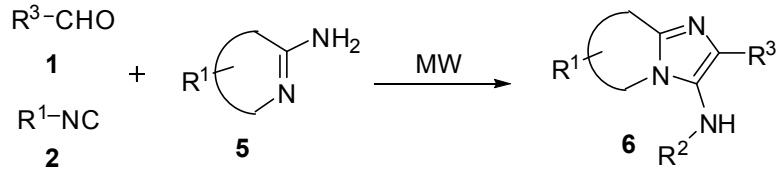
Aldehydes (**1**) and pyridine (**3**) were irradiated in a microwave oven by Varma *et al.*[1] for 1 min (900 W) in the presence of montmorillonite K 10 clay (Scheme 1). After addition of isocyanide (**2**), the reaction mixture was further irradiated followed by a cooling period of 1 min to give the final product (**4**).



Scheme 1. Conventional: 12 h, 30-37%; microwave: 3-4 min, 82-84%

2.2. Fused 3-aminoimidazoles

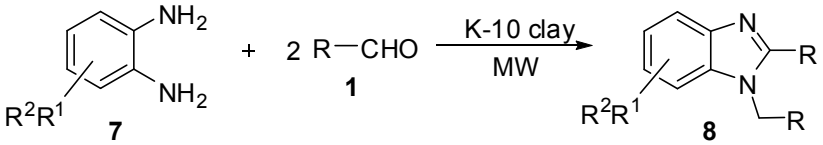
The reaction of heterocyclic amidines (**5**) with aldehydes (**1**) was carried out by the Ireland *et al.*[2] in methanol as solvent (Scheme 2). Immediate addition of the isocyanide (**2**) followed by microwave irradiation gave the product (**6**).



Scheme 2. Conventional: 72 h, 43-45%; microwave: 10 min, 75-87%

2.3. 2-Aryl-1-arylmethyl-1*H*-1,3-benzimidazoles

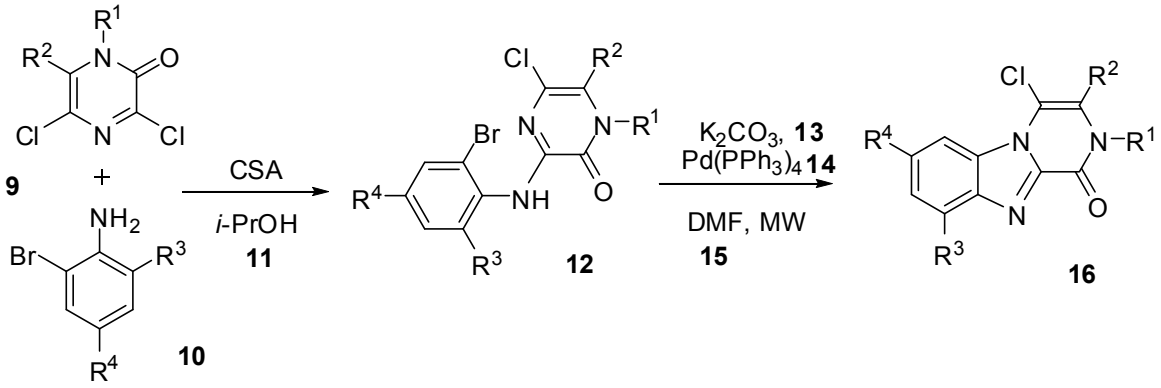
Perumal *et al.*[3] obtained 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles (**8**) in good yields by the reaction of *o*-phenylenediamine (**7**) with various aldehydes (**1**) in the presence of montmorillonite K-10 under microwave irradiation (Scheme 3) in the absence of solvent.



Scheme 3. Conventional: 10 min, 2-45%; microwave: 10 min, 78-96%

2.4. Pyrazino[1,2-*a*]benzimidazol-1(2*H*)ones

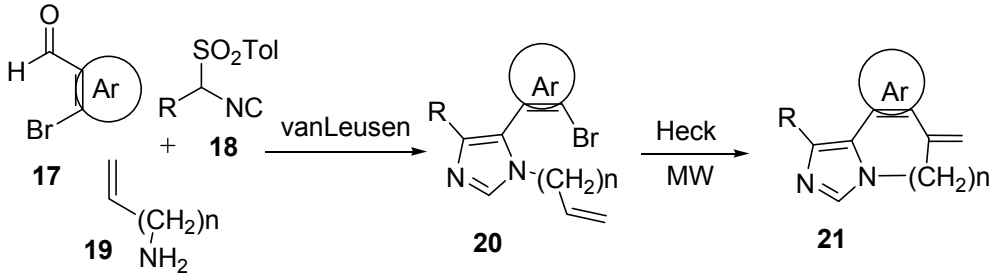
Alen *et al.*[4] refluxed substituted 3,5-dichloropyrazinone derivatives (**9**) and *o*-bromoanilino derivatives (**10**) in presence of *i*-propanol (**11**) for 48 h giving *o*-bromoanilinopyrazinone compounds (**12**). Using a power of 150W, precursors (**12**) were stirred at 150 °C for 25 min with 10% $Pd(PPh_3)_4$ (**14**) and anhydrous potassium carbonate (**13**) in DMF (**15**) in a microwave in 61-74% yields (Scheme 4) to give **16**.



Scheme 4. Conventional: 48 h, 32-48%; microwave: 25 min, 61-74%

2.5. Fused imidazo-pyridine and -azepine derivatives

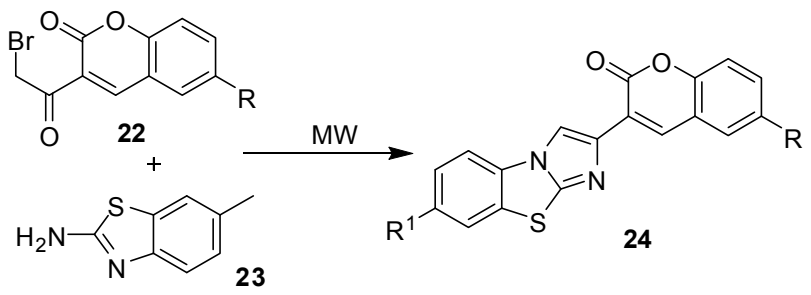
Beebe *et al.*[5] condensed an fused aldehyde (**17**) with an amine (**19**) and then treated with phenylTosMIC (**18**) in the presence of base to give imidazole (**20**) which was converted to the imidazo[1,5-*a*]pyridines (**21**) (Scheme 5).



Scheme 5. Conventional: 2-8 h, 7-24%; microwave: 12-16 min, 42-96%

2.6. Substituted imidazo[2,1-*b*]benzothiazoles

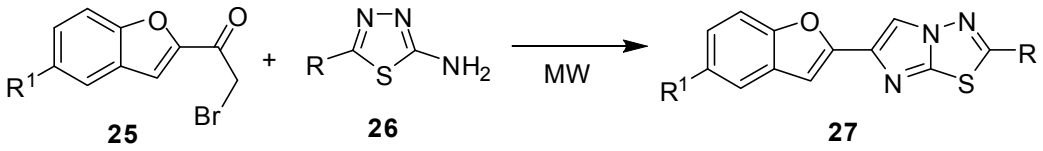
A series of substituted imidazo[2,1-*b*]benzothiazoles (**24**) have been synthesized by Jakhar *et al.*[6] by irradiating 3-(2'-bromoacetyl)-6-substituted coumarins (**22**) with 6-substituted-2-aminobenzothiazoles (**23**) by microwave irradiation in good yields (Scheme 6).



Scheme 6. Conventional: 4-6 h, 65-75%; microwave: 1.5-2.5 min, 81-90%

2.7. Substituted imidazo[2,1-*b*]-1,3,4-thiadiazoles

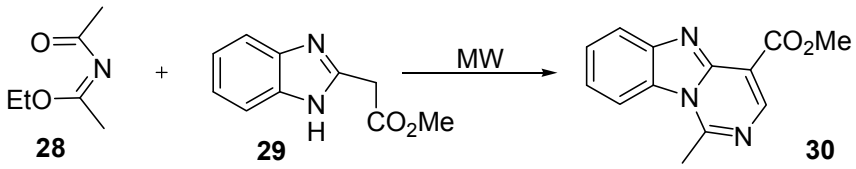
Rani *et al.*[7] synthesized 2-alkyl/aryl-6-benzofuranylimidazo[2,1-*b*]-1,3,4-thiadiazoles (**27**) by the condensation of 5-alkyl/aryl-2-amino-1,3,4-thiadiazoles (**26**) with 2-(2-bromoacetyl)benzofurans (**25**) (Scheme 7).



Scheme 7. Conventional: 4.5-6 h, 53-69%; microwave: 2-3 min, 58-77%

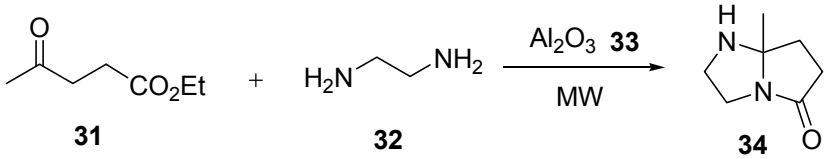
2.8. Pyrimidoimidazoles and pyrroloimidazolones

Rahmouni *et al.*[8] irradiated neat benzimidazole (**29**) and *N*-acylimidate (**28**) in an open vessel to give the product (**30**) (Scheme 8).



Scheme 8. Conventional: 5-6 h, 30-50%; microwave: 30 min, 86%

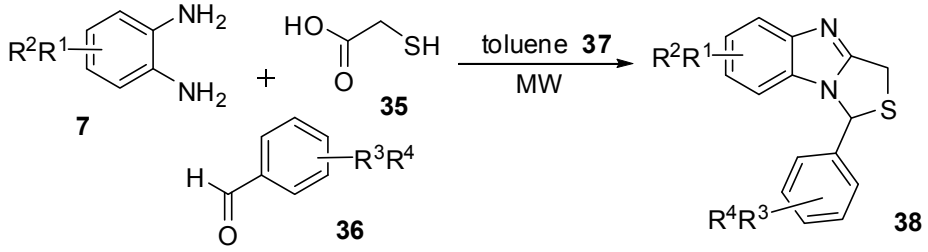
Irradiation of diamine (**32**) with keto-ester (**31**) in the presence of aluminium trioxide (**33**) led to the isolation of product (**34**). The reaction was carried out by supporting the reagents onto alumina and irradiating in an open vessel (Scheme 9).



Scheme 9. Conventional: 12-15 h, 58%; microwave: 15 min, 86%

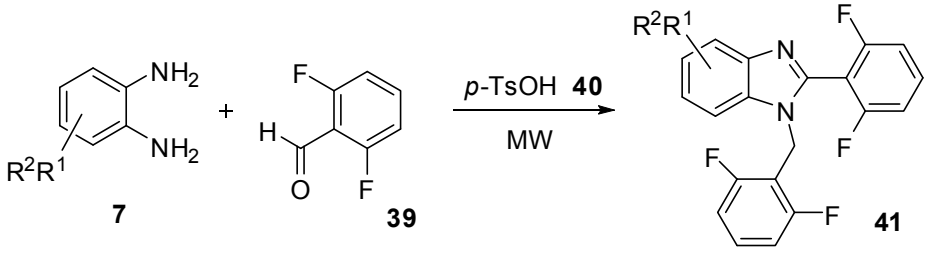
2.9. Thiazolobenzimidazole and benzylbenzimidazole derivatives

Rao *et al.*[9] carried the one-pot synthesis of 1*H*,3*H*-thiazolo[3,4-*a*]benzimidazoles (**38**) by the condensation cyclization reaction between the appropriate *o*-phenylenediamine (**7**) in the presence of toluene (**37**), substituted aromatic aldehyde (**36**) and 2-mercaptoacetic acid (**35**) (Scheme 10).



Scheme 10. Conventional: 24-48 h, 29-37%; microwave: 12 min, 40-64%

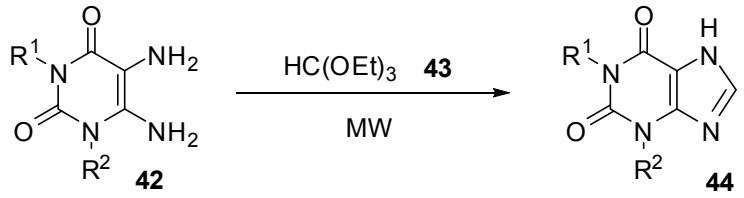
The same workers synthesized 2-aryl-1-benzylbenzimidazoles (**41**) by reacting a *o*-phenylenediamine (**7**) with an excess of 2,6-difluorobenzaldehyde (**39**) in the presence of a catalytic amount of *p*-toluenesulfonic acid (**40**) (Scheme 11).



Scheme 11. Conventional: 2 h, 20-70%; microwave: 6 min, 70-72%

2.10. Xanthine derivatives

Burbiel *et al.*[10] irradiated 5,6-diaminouracils (**42**) for 5 min with triethoxymethane (**43**) at 160 °C giving xanthine derivatives (**44**) in 76-90% yields (Scheme 12).

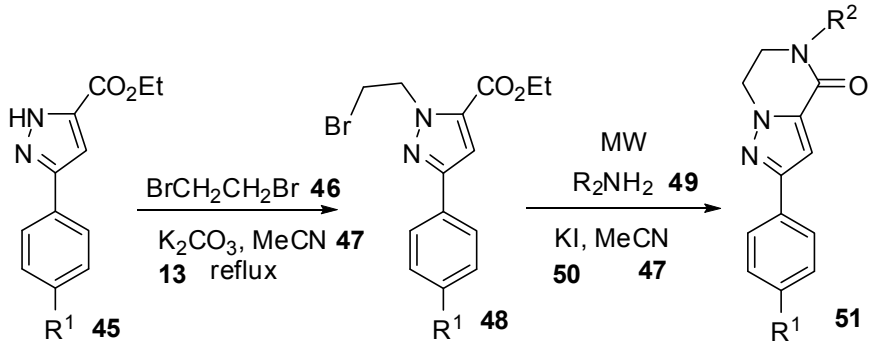


Scheme 12. Conventional: 1.5-3 h, 48-59%; microwave: 5 min, 76-90%

3. MICROWAVE ASSISTED SYNTHESIS OF FUSED PYRAZOLE DERIVATIVES

3.1. Pyrazolo[1,5-*a*]pyrazin-4(5*H*)-one derivatives

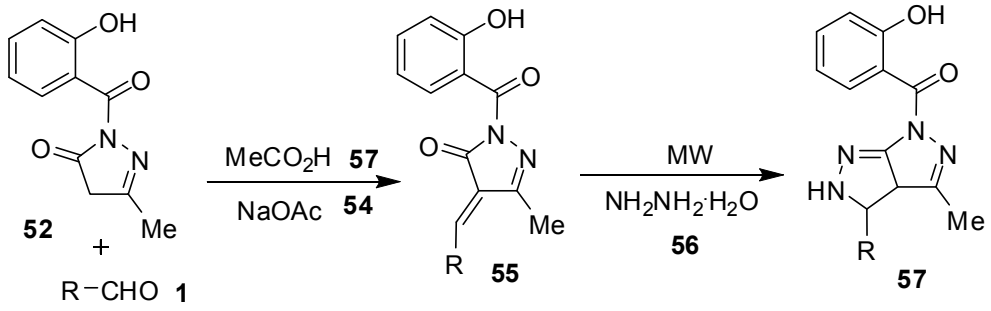
A series of novel pyrazolo[1,5-*a*]pyrazin-4(5*H*)-one derivatives (**51**) were synthesized by Zhang *et al.*[11] by the reaction of ethyl 3-aryl-1-(2-bromoethyl)-1*H*-pyrazol-5-carboxylate (**45**) with dibromoethane (**46**) in presence of potassium carbonate (**13**) and methyl cyanide (**47**), giving intermediate (**48**) which reacts with amine (**49**) in presence of potassium iodide (**50**) and methyl cyanide (**47**) (Scheme 13).



Scheme 13. Conventional: 3-17 h, 22-87%; microwave: 0.8-2.5 h, 54-94%

3.2. Tetrahydropyrazol[3,4-*c*]pyrazoles and thiazolo[5,4-*c*]-2,3-dihydropyrazoles

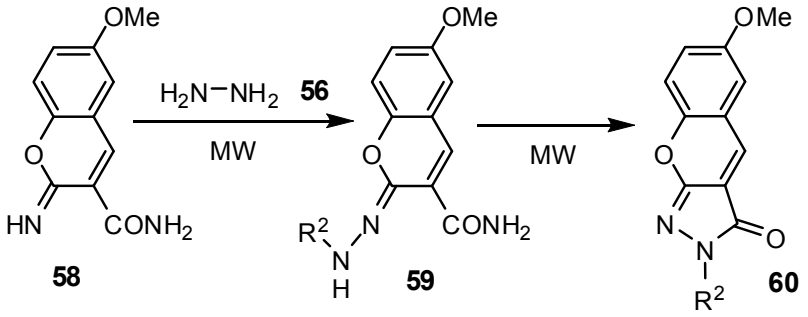
Pande *et al.*[12] reported the synthesis of 1-(2-hydroxybenzoyl)-3-methyl-4-aryl-1,3*a*,4,5-tetrahydropyrazol-[3,4-*c*]pyrazoles (**57**) by the condensation of hydrazine hydrate (**56**) with 4-alkylidene-2-(2-hydroxybenzoyl)-5-methyl-2,4-dihydropyrazol-3-ones (**55**) which is obtained from 2-(2-hydroxybenzoyl)-5-methyl-2,4-dihydropyrazol-3-ones (**52**) and aldehyde (**1**) in presence of acetic acid (**57**) and sodium acetate (**54**) (Scheme 14).



Scheme 14. Conventional: 40-50%, 12-16 h; microwave: 68-80%, 10-16 min

3.3. Benzopyrano[2,3-*c*]pyrazol-3(2*H*)-ones

Borisov *et al.*[13] reacted 1.50 mmol of 2-iminocoumarin-3-carboxamide (**58**) and 5% excess of the hydrazine (**56**) in acetic acid under microwave irradiation at 190 °C for 5 min to yield the benzopyrano[2,3-*c*]pyrazol-3(2*H*)-one library (**60**) *via* an intermediate (**59**) (Scheme 15).

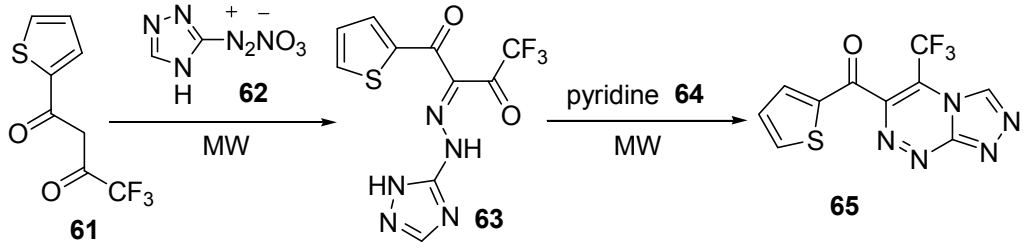


Scheme 15. Conventional: 6-36 h, 27-53%; microwave: 5-10 min, 49-85%

4. MICROWAVE ASSISTED SYNTHESIS OF FUSED TRIAZOLE DERIVATIVES

4.1. Triazolo[3,4-*c*]-1,2,4-triazine derivatives

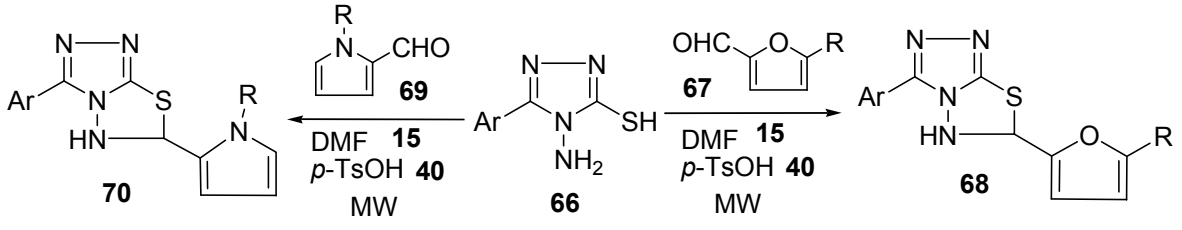
Shaaban *et al.*[14] coupled 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione (**61**) with diazonium salt of 1,2,4-aminotriazole (**62**), in pyridine (**64**), to give the corresponding hydrazone (**63**) which undergoes intramolecular cyclization in pyridine under microwave irradiation to give 6-thienoyl-5-(trifluoromethyl)-[1,2,4]triazolo[3,4-*c*][1,2,4]triazine (**65**) (Scheme 16).



Scheme 16. Conventional: 8-10 h, 48-56%; microwave: 13-18 min, 78-86%

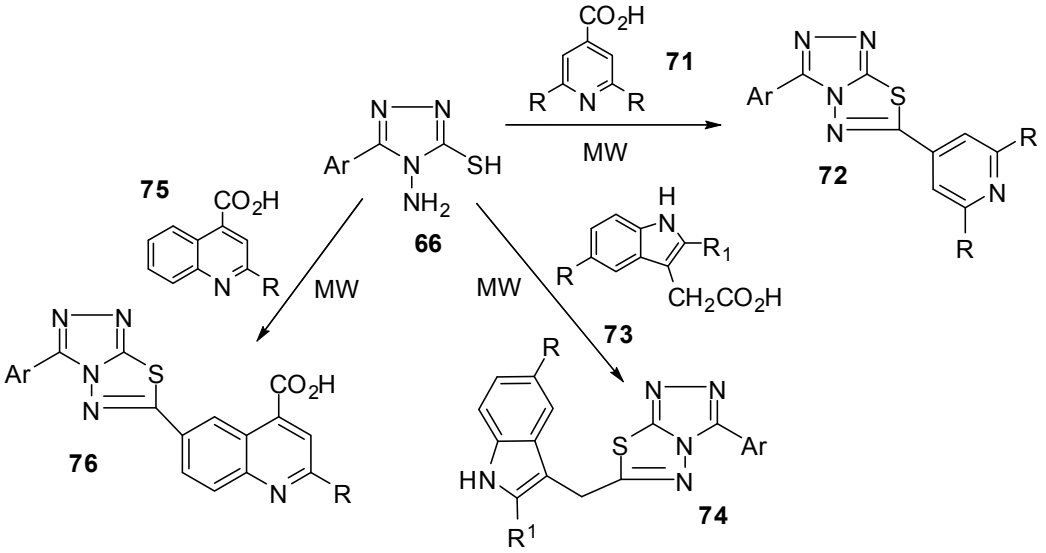
4.2. 3,6-Ddisubstituted-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazoles and their dihydro analogues

Mathew *et al.*[15] reported condensation of the triazoles (**66**) with heteroaromatic aldehydes (**67**, **69**) (Scheme 17), giving a series of 5,6-dihydrotriazolothiadiazoles (**68**, **70**) in presence of DMF (**15**) and *p*-TsOH (**40**) in 52-62% yields.



Scheme 17. Conventional: 6-12 h, 48-55%; microwave: 10-16 min, 52-62%

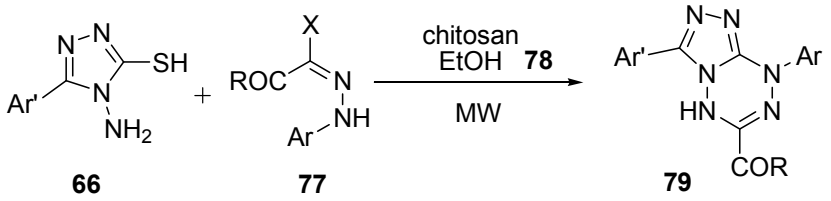
Condensation of the triazoles (**66**) with heteroaromatic acids (**71**, **73**, **75**) in the presence of phosphorous oxychloride produced a series of triazolothiadiazoles (**72**, **74**, **76**) in 49-64% yields (Scheme 18).



Scheme 18. Conventional: 6-12 h, 48-55%; microwave: 10-16 min, 49-64%

4.3. Triazolo[4,3-*b*][1,2,4,5]tetrazines and triazolo[3,4-*b*][1,3,4]thiadiazines

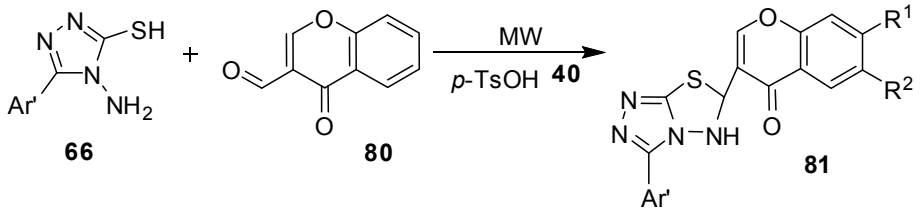
Gomha *et al.*[16] reported a novel approach to the synthesis of triazolo[4,3-*b*][1,2,4,5]tetrazines (**79**) *via* reactions of 4-amino-5-methyl-1,2,4-triazole-3(2*H*)-thione (**66**) with hydrazonoyl halides (**77**) in 78-88% yields using chitosan and ethanol (**78**) as a basic catalyst under microwave irradiation (Scheme 19).



Scheme 19. Conventional: 5-8 h, 30-35%; microwave: 14-18 min, 78-88%

4.4. Substituted triazolo[3,4-*b*][1,3,4]thiadiazoles

Rani *et al.*[17] prepared substituted triazolo[3,4-*b*][1,3,4]thiadiazoles (**81**) by the condensation of 3-akyl/aryl-4-amino-5-mercapto-*s*-triazoles (**66**) with chromon-3-carboxyaldehyde (**80**) in the presence of *p*-TsOH (**40**) (Scheme 20).

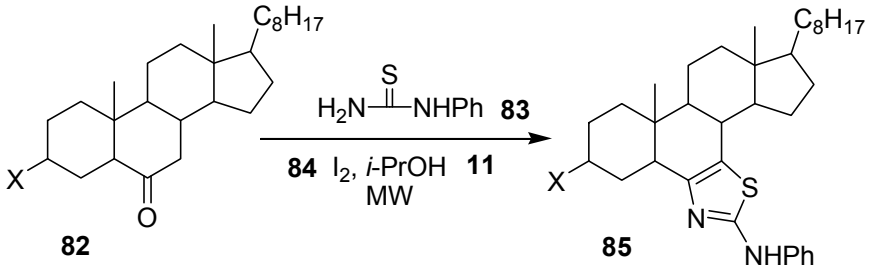


Scheme 20. Conventional: 8-9 h, 68-74%; microwave: 1.5-6.5 min, 73-79%

5. MICROWAVE ASSISTED SYNTHESIS OF FUSED THIAZOLE DERIVATIVES

5.1. 20-Amino-5*a*-cholest-6-eno[6,7-*d*]thiazole derivatives

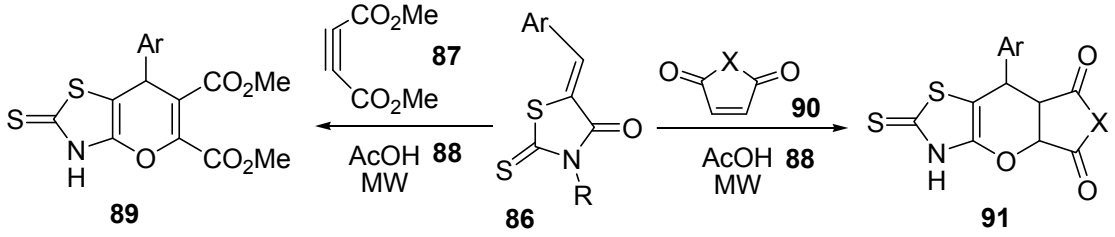
The synthesis of steroidal[6,7-*d*]thiazoles (**85**) was done by Khan *et al.*[18] under microwave irradiation using neutral alumina in anhydrous media in good yield. A slurry of steroidal ketones (**82**) (1 mmol), phenylthiourea (**83**) (1 mmol), iodine (**84**) (2 mmol) in isopropanol (**11**) (1 ml) was added to neutral aluminium oxide. The contents were then mixed thoroughly. The mixed contents were kept under microwave oven and irradiated (Scheme 21).



Scheme 21. Conventional: 18-25 h, 25-35%; microwave: 3-5 min, 70-76%

5.2. 2-Thioxopyrano[2,3-*d*][1,3]thiazoles by Diels-Alder reaction of arylidene rhodanines

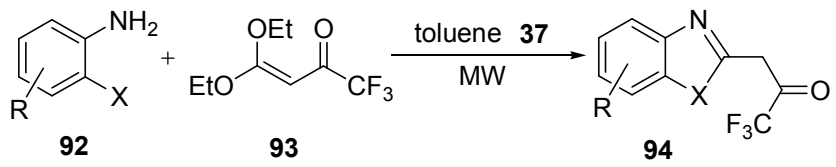
The reactions of 5-arylidene-1,3-thiazolidin-2,4-dithiones (**86**) with maleic anhydride or maleimide (**90**), dimethylacetylene dicarboxylate (**87**) and acrylonitrile in acetic acid (**88**) at room temperature have been reported by Yarovenko *et al.*[19] to yield thiopyrano[2,3-*d*]thiazolidin-2-thiones (**91**, **89**) (Scheme 22).



Scheme 22. Conventional: 6-8 h, 9-27%; microwave: 15-30 min, 72-90%

5.3. Benzthiazoles

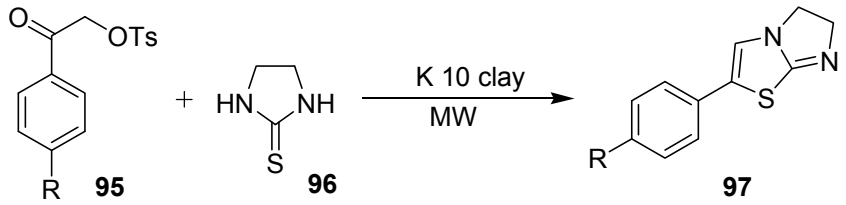
Chandra Sheker Reddy *et al.*[20] reacted *o*-substituted anilines (**92**) with butenones (**93**) to give benzthiazoles (**94**) in presence of toluene (**37**) under microwave conditions (Scheme 23).



Scheme 23. Conventional: 3.5 h, 40-80%; microwave: 9-11 min, 86-96%

5.4. Substituted thiazoles

Varma *et al.*[21] reacted α-tosyloxyketones (**95**) with ethylenethioureas (**96**) in a microwave oven to give thiazoles (**97**) (Scheme 24).

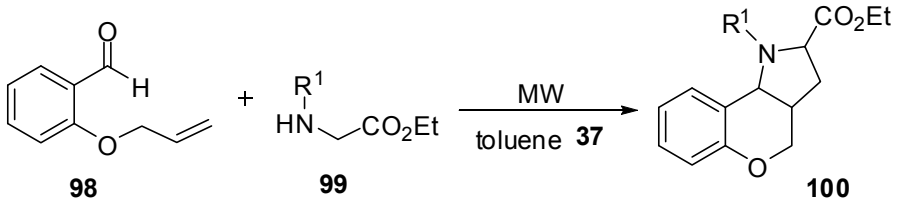


Scheme 24. Conventional: 29-58%, > 300 °C; microwave: 85-92%, 16-18 min

6. MICROWAVE ASSISTED SYNTHESIS OF FUSED PYROLLE DERIVATIVES

6.1. Hexahydrochromeno[4,3-*b*]pyrroles by cycloaddition

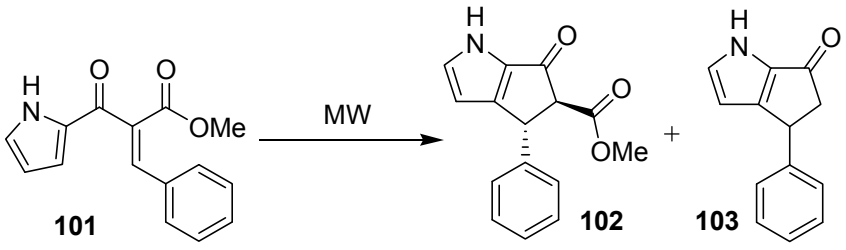
The cycloaddition reaction between aldehyde (**98**) and amine (**99**) was carried out by Pospisil *et al.*[22] to give **100** (Scheme 25) using toluene as a solvent (**37**).



Scheme 25. Conventional: 72 h, 48-69%; microwave: 15-60 min, 79-83%

6.2. Nazarov cyclization of pyrrole derivatives

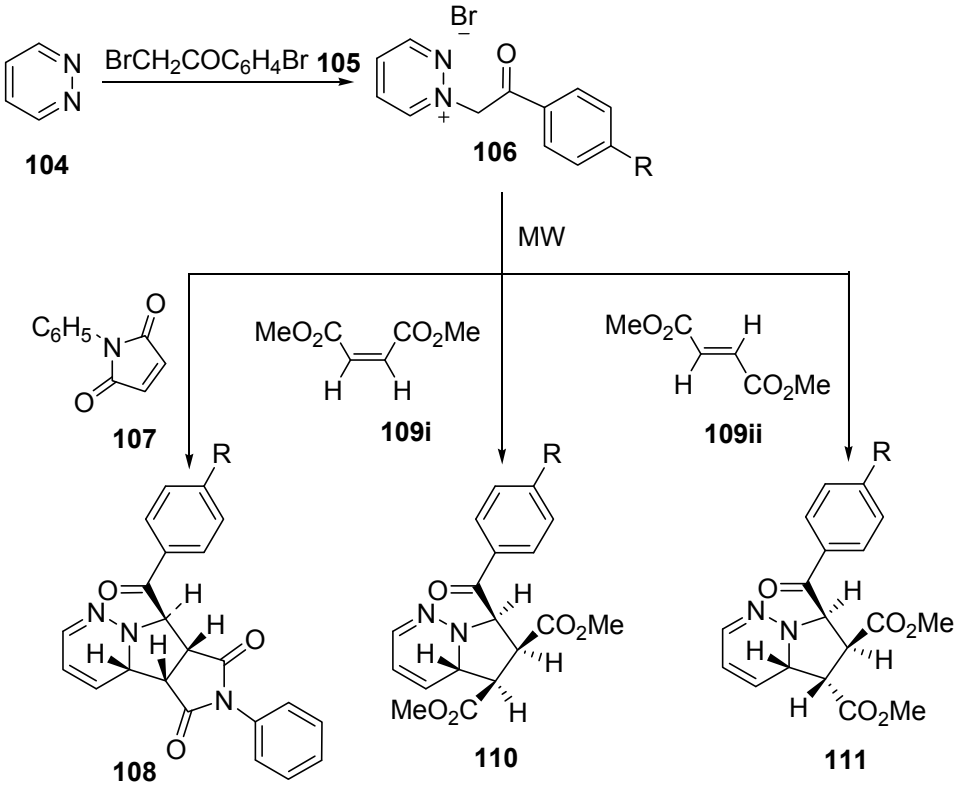
The Nazarov cyclization[8,23,24] is a very versatile process for the synthesis of cyclopentanones. Bachu *et al.*[25] treated **101** with 20 mol% TsOH at 80 °C. The enone underwent Nazarov cyclization to furnish **102** in low yields. The reaction at higher temperature with extended hours of heating resulted in the formation of a significant amount of decarboxylated compound of 4-phenyl-4,5-dihydrocyclopenta[*b*]pyrrol-6(1*H*)-one (**103**) (Scheme 26).



Scheme 26. Conventional: 12 h, 62%; microwave: 6 h, 81%

6.3. Pyrrolo[1,2-*b*]pyridazine derivatives

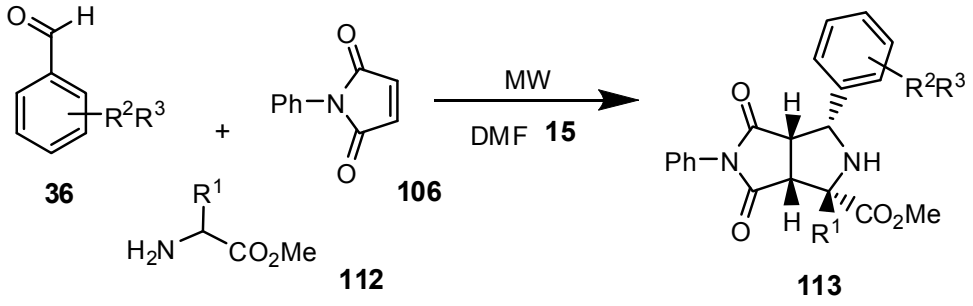
Butnariu *et al.*[26] reacted pyridazine (**104**) with 2-bromo-1-phenylethanone (**105**) to give ylide (**106**) which reacts with *N*-phenylmaleimide (**107**), maleic esters (**109i**) and fumaric esters (**109ii**) to give cycloadducts (**108**, **110**, **111**) (Scheme 27).



Scheme 27. Conventional: 2-3 h, 9-85%; microwave: 5 min, 9-93%

6.4. Bicyclic pyrrolidines

Rajendra Prasad *et al.*[27] synthesized, by microwave irradiation of an amine (**112**), aldehyde (**36**) and maleimide (**106**) in the presence of DMF (**15**) in one pot (Scheme 28) to give the desired product (**113**).

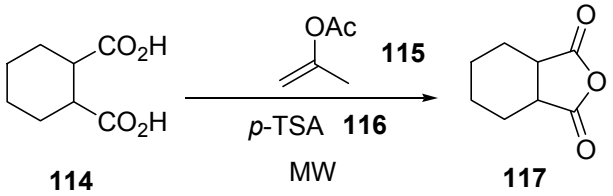


Scheme 28. Conventional: 30-48%, 10 h; microwave: 70-85%, 10 min

7. MICROWAVE ASSISTED SYNTHESIS OF FUSED BENZOFURAN DERIVATIVES

7.1. Cyclocondensed synthesis of benzofuran derivatives

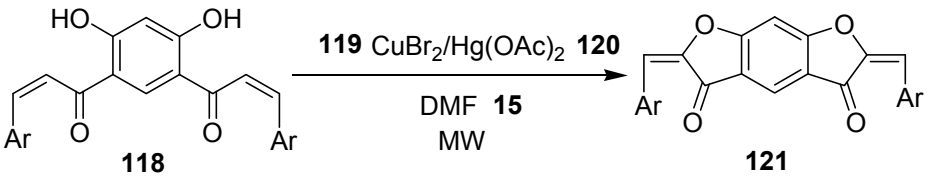
The condensation of diacids (**114**) to anhydrides (**115**) and *p*-TSA (**116**) has been reported by Villemin *et al.*[28] (Scheme 29) to form **117**.



Scheme 29. Conventional: 6-8 h, 50-60%; microwave: 3-4 min, 72-94%

7.2. Diaurones

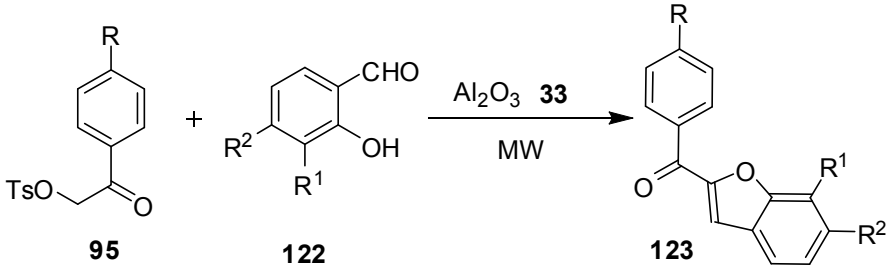
Ashok *et al.*[29] synthesized diaurones (**121**) by the oxidation of 4,6-dicinnamoyl resorcinols (**118**) using cupric bromide (**119**) or mercury (II) acetate (**120**) in DMF (**15**) in microwave (Scheme 30).



Scheme 30. Conventional: 6-10 h, 62-73%; microwave: 6-7 min, 88-95%

7.3. 2-Aroylbenzofurans

Varma *et al.*[21] obtained 2-aroylbenzofurans (**123**) from α-tosyloxyketones (**95**) and salicylaldehydes (**122**) in the presence of aluminium trioxide (**33**) using microwave irradiation (Scheme 31).

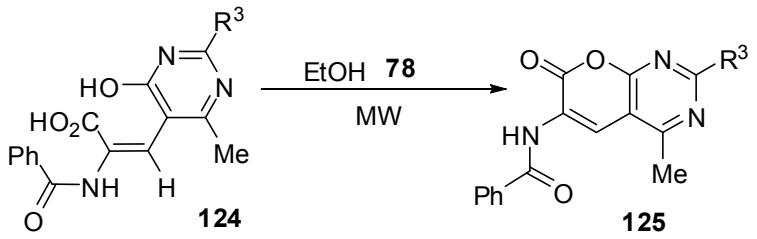


Scheme 31. Conventional: > 300 °C, 29-58%; microwave: 10-16 min, 85-92%

8. MICROWAVE ASSISTED SYNTHESIS OF FUSED PYRIMIDINE DERIVATIVES

8.1. Pyrano[2,3-*d*]pyrimidines

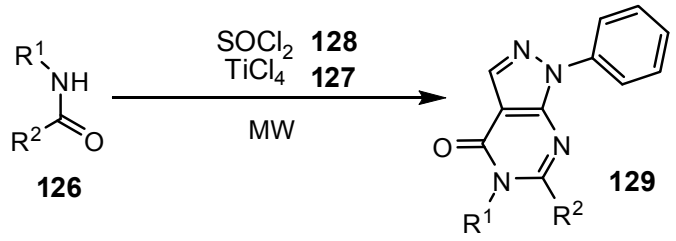
Hren *et al.*[30] synthesized pyrano[2,3-*d*]pyrimidines (**125**) from β-(4-hydroxypyrimidyl)-α,β-didehydro-α-amino acid derivatives (**124**) in ethanol (**78**) in a single step using microwave irradiation (Scheme 32).



Scheme 32. Conventional: 9 h, 76%; microwave: 120 min, 75-92%

8.2. Fused bicyclic 2,3-diarylpyrimidin-4(3*H*)-ones *via* Lewis acid

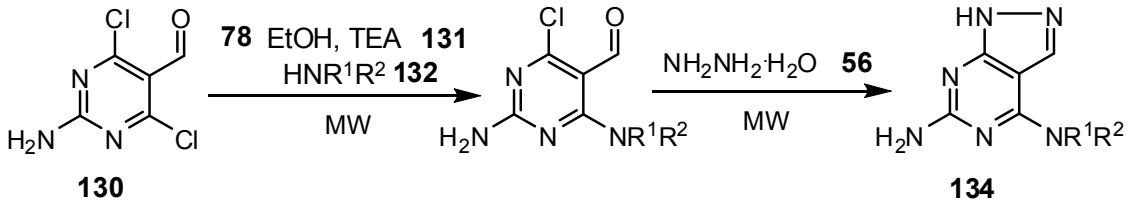
Yang *et al.*[31] carried out the synthesis of 1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones (**129**) from various amides (**126**), titanium (IV) chloride (**127**) and thionyl chloride (**128**) (Scheme 33).



Scheme 33. Conventional: 8 h, 50%; microwave: 20 min, 87%

8.3. Pyrazolo[3,4-*d*]pyrimidines

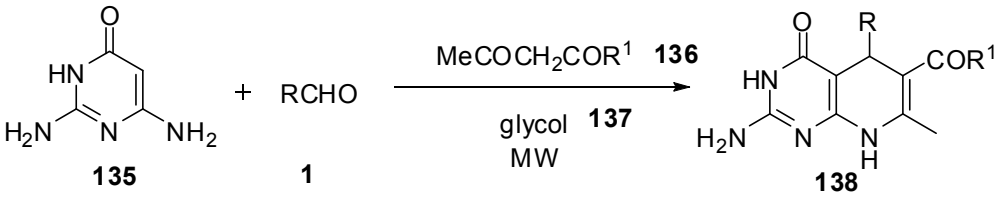
Quiroga *et al.*[32] reported a versatile synthesis of N^4-substituted-4,6-diaminopyrazolo[3,4-*d*]pyrimidines (**134**) using microwave in the absence of solvent from 2-amino-4,6-dichloropyrimidin-5-carbaldehyde (**130**) with secondary amine (**132**) with hydrazine hydrate (**56**) proceeding through **133** with good yields (Scheme 34).



Scheme 34. Conventional: 30 min, 45-55%; microwave: 1 min, 84-89%

8.4. 2-Amino-6,7-disubstituted-5-methyl-5,8-dihydropyrido[2,3-*d*]pyrimidin-4-(3*H*)-one

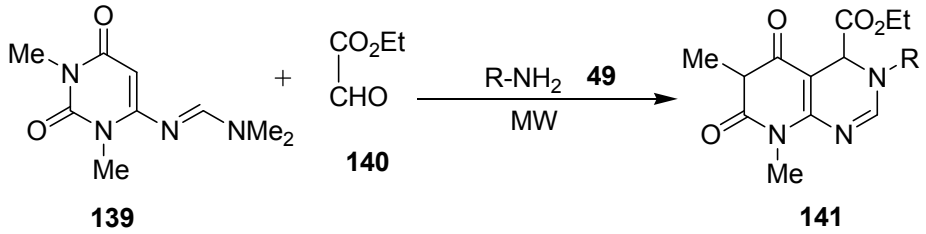
The reaction was carried out by Tu *et al.*[33] using diaminopyrimidines (**135**), aldehydes (**1**) and acyclic 1,3-dicarbonyl compound (**136**) and glycol (**137**) to afford dihydropyridopyrimidine derivatives (**138**) under microwave irradiation (Scheme 35).



Scheme 35. Conventional: 2 h, 59-78%; microwave: 4-7 min, 89-95%

8.5. Pyrimido[4,5-*d*]pyrimidines

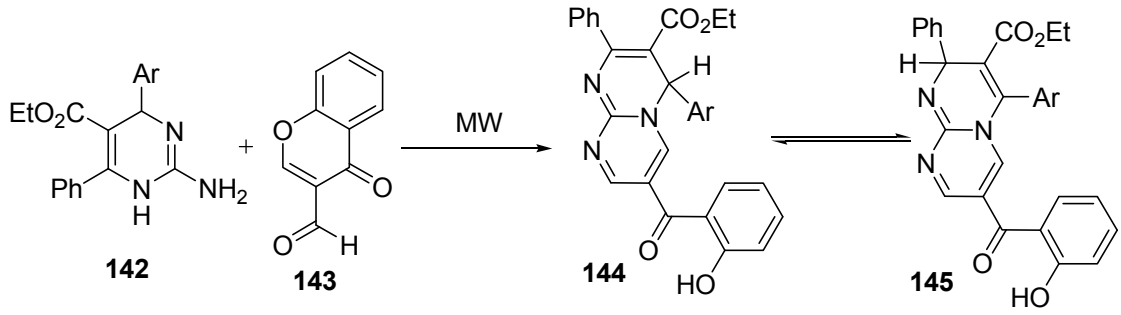
Prajapati *et al.*[34] placed a mixture of 6-[(dimethylamino)methylene]amino-1,3-dimethyl uracil (**139**) with an equimolar amount of ethyl glyoxylate (**140**) and aniline (**49**) in a reaction vessel which is irradiated in microwave at 110 °C, which gave, after elimination of dimethylamine, the pyrimido[4,5-*d*]pyrimidine (**141**) (Scheme 36) as the only product.



Scheme 36. Conventional: 5 h, 63%; microwave: 3.5 min, 95%

8.6. Pyrimido[1,2-*a*]pyrimidines

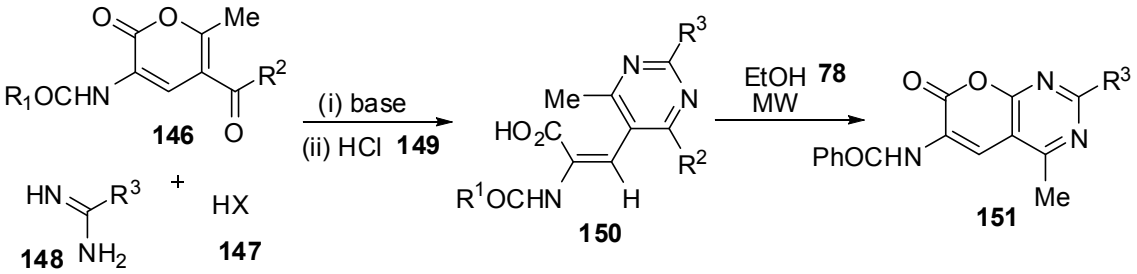
Pyrimido[1,2-*a*]pyrimidines (**144** or **145**) were worked on by Eynde *et al.*[35] and synthesized by reacting dihydroaminopyrimidines (**142**) and chromone-3-aldehydes (**143**) as is shown in Scheme 37.



Scheme 37. Conventional: 4 h, 60-70%; microwave: 20 min, > 95%

8.7. β-Pyrimidyl-α,β-didehydro-α-amino acid derivatives and pyrano[2,3-*d*]pyrimidines

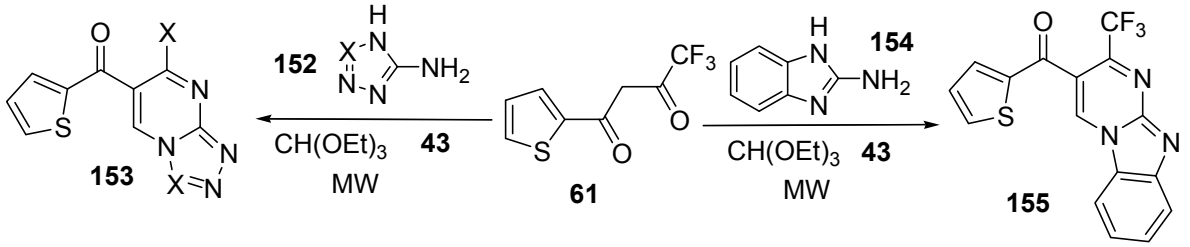
The reaction of 2*H*-pyran-2-one (**146**) with a slight excess of acetamidine hydrochloride (**148**) and haloacid (**147**) in the presence of a base was carried out by Hren *et al.*[30] to give pyrano[2,3-*d*]pyrimidines (**151**). Applying DBU as a base, the product was obtained (Scheme 38).



Scheme 38. Conventional: 76%, 9 h; microwave: 80-91%, 25-120 min

8.8. 1,2,4-Triazolo[1,5-*a*]pyrimidine derivatives

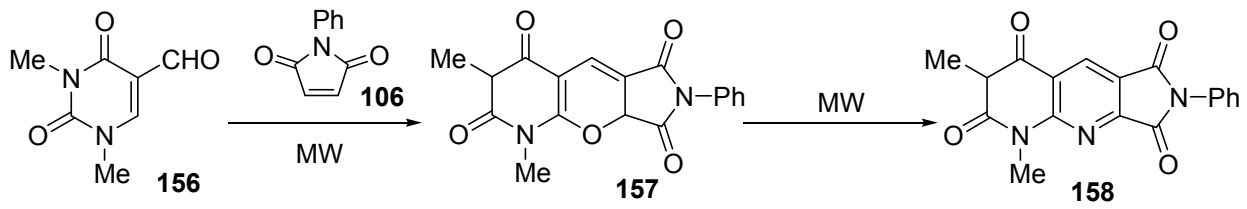
Shaaban *et al.*[36] reacted 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione (**61**) with 3-amino-5-substituted-1,2,4-triazole (**154**) and triethylorthoformate (**43**) to give 6-thienoyl-7-(trifluoromethyl)benzimidazo[1,2-*a*]pyrimidine (**155**). The same workers also reacted **61** with 2-aminobenzimidazole (**152**), under the same experimental conditions to afford only 6-thienoyl-7-(trifluoromethyl)[1,2,4]triazolo[4,3-*a*]pyrimidine (**153**) (Scheme 39).



Scheme 39. Conventional: 4-8 h, 39-55%; microwave: 15-18 min, 85-96%

8.9. Pyrido[2,3-*d*]- and pyrimido[4,5-*d*]- pyrimidines

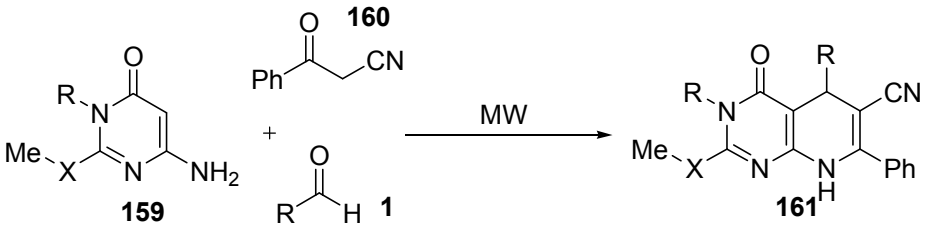
Devi *et al.*[37] reported the reaction of *N,N*-dimethyl-6-amino-5-formyluracil (**156**) with 1-phenyl-1*H*-pyrrole-2,5-dione (**106**) giving pyrido[2,3-*d*]pyrimidines (**158**) (Scheme 40).



Scheme 40. Conventional: 5-6 h, 54-65%; microwave: 6-7 min, 80-85%

8.10. Dihydropyridopyrimidinones

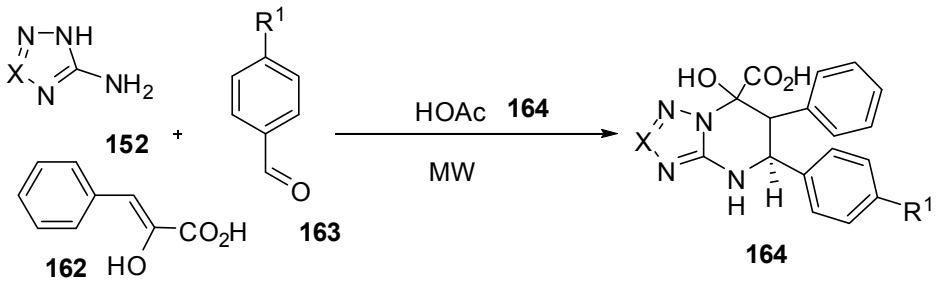
Quiroga *et al.*[38] synthesized dihydropyridopyrimidinones (**161**) by ring annulations of aminopyrimidinones (**154**) with phenylpropanenitrile (**160**) and aldehydes (**1**) (Scheme 41).



Scheme 41. Conventional: 40-48 h, 20-25%; microwave: 15-20 min, 70-76%

8.11. Triazolopyrimidines

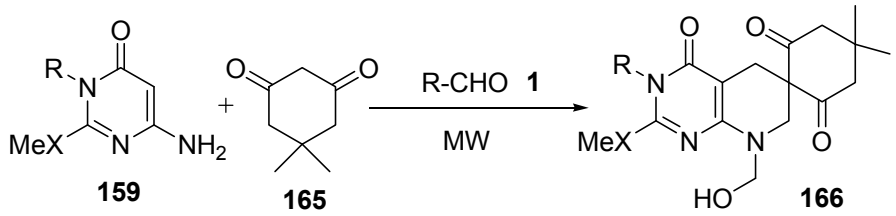
A Biginelli-like reaction of arylpyruvic acids with urea and aldehydes in the presence of catalytic amounts of acid to yield dihydropyrimidine carboxylic acids has also been reported in the literature.[39] Sakhno *et al.*[40] synthesized 5-aryl-7-hydroxy-6-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]-pyrimidine-7-carboxylic acids (**164**) from the reaction mixture after refluxing (~120 °C) equimolar amounts of aminotriazoles (**152**), phenylpyruvic acid (**162**) and aldehydes (**163**) in HOAc (**164**) for 2–3 min (Scheme 42).



Scheme 42. Conventional: 3 h, 56-75%; microwave: 2-3 min, 63-79%

8.12. Hexahydropyridopyrimidine–spirocyclohexanetriones

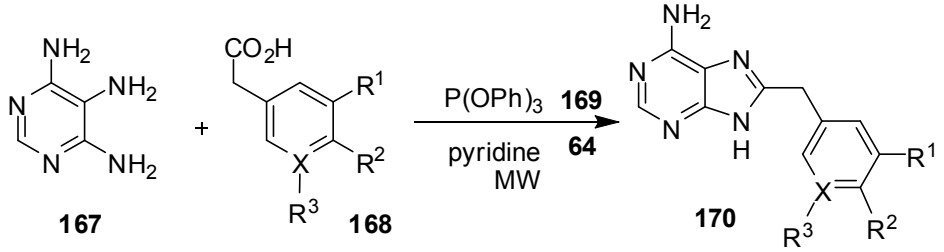
The synthesis of pyrimido[4,5-*b*]quinolines in a three-component reaction from 6-aminopyrimidines, dimedone and aromatic aldehydes was reported by Quiroga *et al.*[41] A facile one pot cyclocondensation takes place between 6-aminopyrimidines (**159**), dimedone (**165**) and aldehydes (**1**) affording pyridopyrimidinspirocyclohexanetriones (**166**) (Scheme 43).



Scheme 43. Conventional: 2-4 h, 35-59%; microwave: 1-3 min, 55-80%

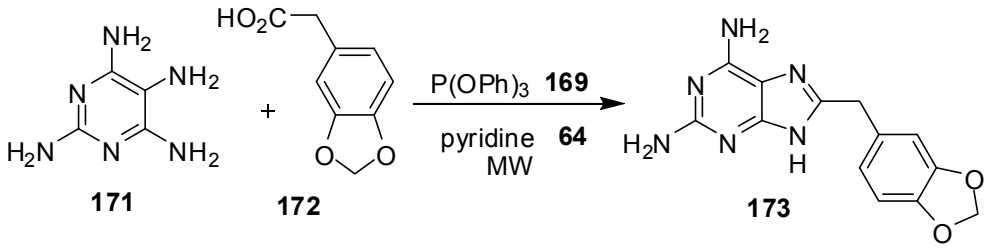
8.13. 8-Arylmethyl-9*H*-purin-6-amines

The synthesis was carried out by Tao *et al.*[42] consisting of irradiating 2-(benzo[*d*][1,3]dioxol-5-yl)acetic acid (**168**) (1.0 eq.) and pyrimidine-4,5,6-triamine (**167**) (1.2 eq.) at 220 °C for 15 min in the presence of $P(OPh)_3$ (**169**) (1.2 eq.) in pyridine (**64**), to give 8-(benzo[*d*][1,3]dioxol-5-ylmethyl)-9*H*-purin-6-amine (**170**) as the product (Scheme 44).



Scheme 44. Conventional: 12-24 h, 20%; microwave: 15 min, 87-98%

When the triamine pyrimidine substrate was replaced with its tetramine equivalent (**171**) and irradiated with dioxoloacetic acid (**172**) in presence of pyridine (**64**), the product (**173**) was formed in 62% isolated yield (Scheme 45).

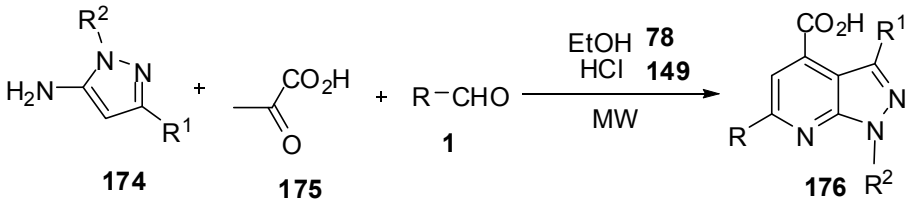


Scheme 45. Conventional: 20%, 5 h ethanol reflux; microwave: 15 min, 62%

9. MICROWAVE ASSISTED SYNTHESIS OF FUSED PYRIDINE DERIVATIVES

9.1. Multicomponent approaches to pyrazolopyridines

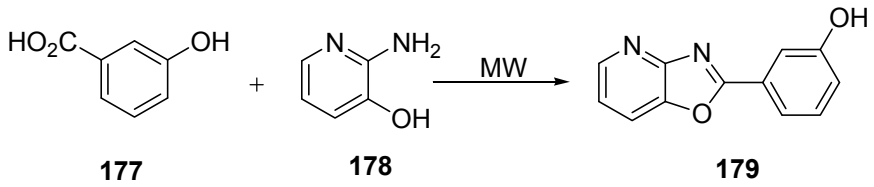
The three component reaction of 3-substituted 5-aminopyrazoles (**174**) with pyruvic acid (**175**) and aldehydes (**1**) was carried out in ethanol (**78**) by Chebanov *et al.*[43] using microwave to give pyrazolopyridines (**176**) (Scheme 46).



Scheme 46. Conventional: 9 h, 38-75%; microwave: 10 min, 75-92%

9.2. 2-Substituted oxazolo[4,5-*b*]pyridines

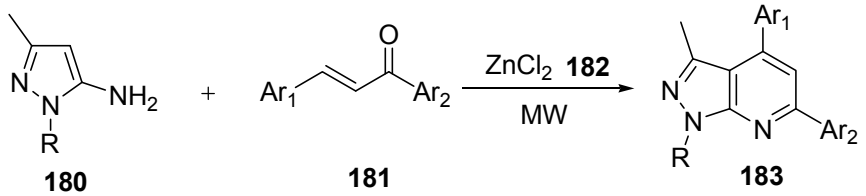
Myllymaki *et al.*[44] synthesized 2-phenyloxazolo[4,5-*b*]pyridines using palladium catalyzed C-2 arylation of oxazolo[4,5-*b*]pyridine. Condensation reaction of 3-hydroxybenzoic acid (**177**) and 2-aminopyridin-3-ol (**178**), shown in Scheme 47 also gives 2-phenyloxazolo[4,5-*b*]pyridines (**179**).



Scheme 47. Conventional: 18 h, 13%; microwave: 2 min, 77%

9.3. Pyrazolo[3,4-*b*]pyridine derivatives

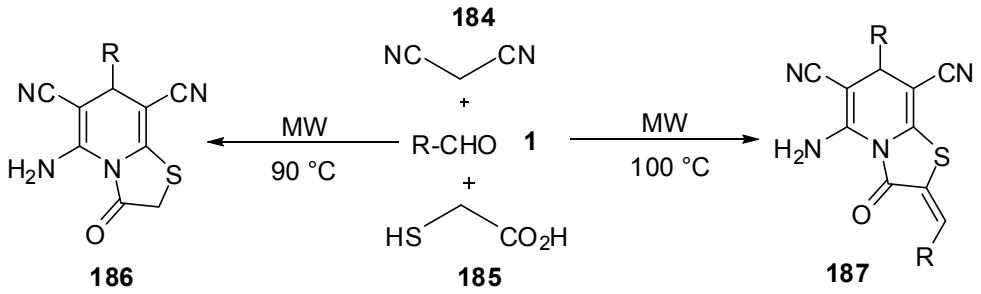
Zou *et al.*[45] developed a synthetic method of pyrazolo[3,4-*b*]pyridines (**183**) by the reaction of aminopyrazole (**180**) with chalcones (**181**) in one step under microwave irradiation in the presence of $ZnCl_2$ (**182**) leading to higher yields and shorter reaction times (Scheme 48).



Scheme 48. Conventional: 3 h, 70%; microwave: 8-12 min, 85-95%

9.4. Thiazolo[3,2-*a*]pyridine derivatives

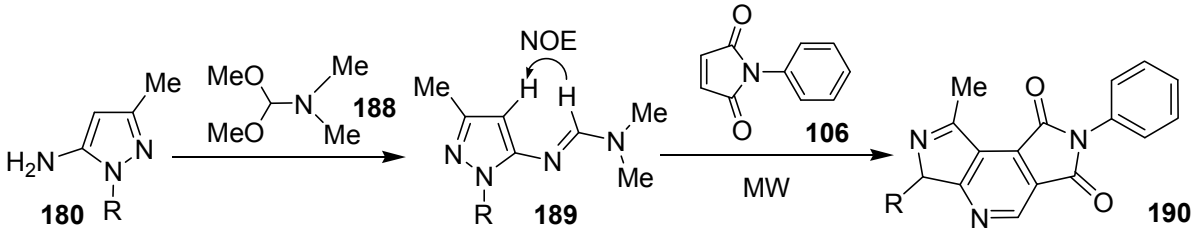
Shi *et al.*[46] carried out the synthesis of thiazolo[3,2-*a*]pyridines (**186**, **187**) *via* microwave assisted three component reactions of malononitrile (**184**) (2mmol), aldehydes (**1**) (1mmol) and 2-mercaptoacetic acid (**185**) (1mmol) in water with molar ratio of 2:1:1 (Scheme 49).



Scheme 49. Conventional: overnight reflux, 50%; microwave: 6-9 min, 80-89%

9.5. Pyrazolo[3,4-*b*]pyrrolo[3,4-*d*]pyridine derivatives

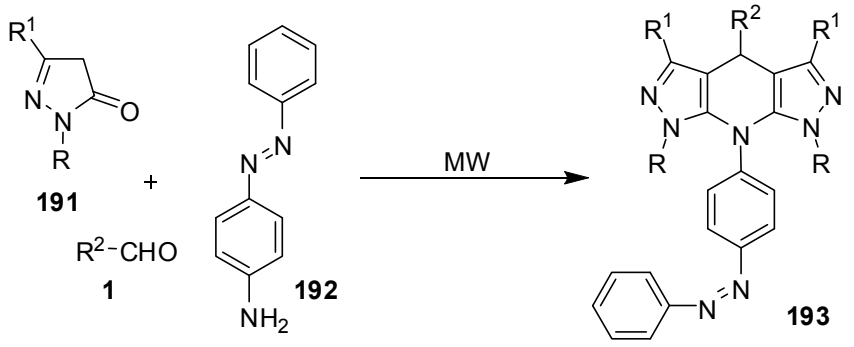
Pyrazolo[3,4-*b*]pyrrolo[3,4-*d*]pyridine derivatives were prepared in very low yields (20-35%), after long reaction time (48 h), through hetero Diels-Alder cycloaddition between the formamidine and the corresponding *N*-phenylmaleimide, under conventional heating, using AcOH or DMSO as solvent.[47] The same product (Scheme 50) was synthesized by Nascimento-Junior *et al.*[48] using pyrazol-5-amine (**180**) and *N,N*-dimethylmethanamine (**188**) to give an intermediate (**189**) which when reacted with pyrrole-2,5-dione (**106**) gives pyrazolo[3,4-*b*]pyrrolo[3,4-*d*]pyridine derivatives (**190**).



Scheme 50. Conventional: 48 h, 20-35%; microwave: 90 min, 80%

9.6. Dipyrazolopyridines

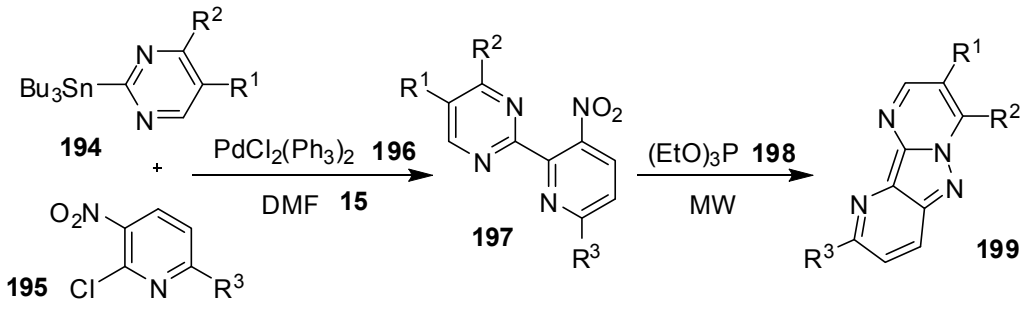
A new series of dipyrazolopyridines (**193**) has been synthesized by microwave irradiation by Thakre *et al.*[49] by the reaction of 2-pyrazolin-5-ones (**191**) with 4-aminoazobenzene **(192**) and aldehydes (**1**) (Scheme 51).



Scheme 51. Conventional: 8-10 h, 34-59%; microwave: 1-2 min, 64-89%

9.7. Pyrazolo[1,5-*a*]pyridines

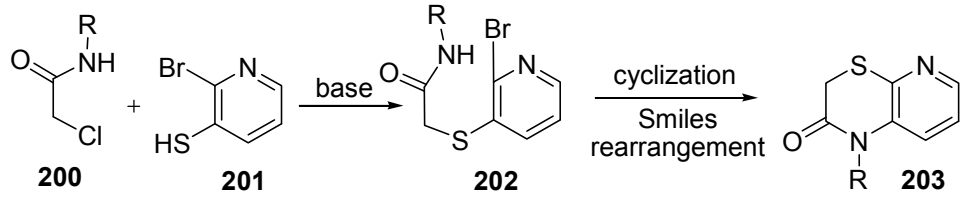
The Stille coupling between 2-tributylstannylpyridine (**194**) and 2-chloro-3-nitropyridine (**195**) was carried out by Nyffenegger *et al.*[50] and nitro bicycles (**197**) were synthesized. From this bicycle, **199** was formed (Scheme 52).



Scheme 52. Conventional: 2-6 h, 62%; microwave: 12-36 min, 86%

9.8. Pyrido[1,4]thiazinones based on the S–N type Smiles rearrangement.

Thiazinone fused pyridine derivatives (**203**) were synthesized *via* an intermediate (**202**) by Ma *et al.*[51] using *N*-substituted chloroacetamides (**200**) with 2-bromopyridin-3-thiol (**201**) (Scheme 53) in one pot.

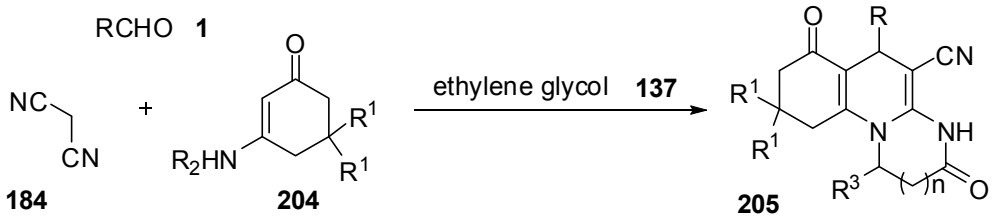


Scheme 53. Conventional: 30-70 min, 70%; microwave: 3-6 min, 83%

10. MICROWAVE ASSISTED SYNTHESIS OF FUSED QUINOLINE DERIVATIVES

10.1. Polysubstituent Pyrimido[1,2-*a*]quinolines

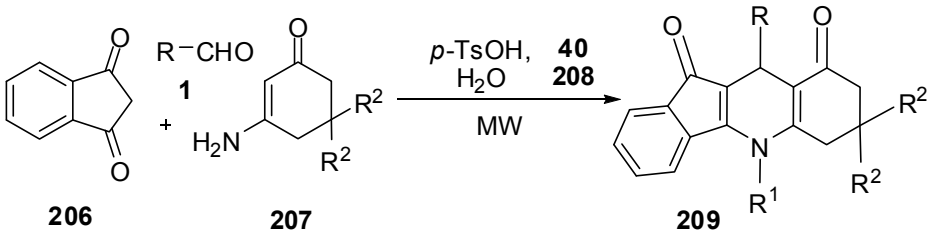
Using ethylene glycol (2.0 ml) as a solvent and 120 °C temperature, Tu *et al.*[52] carried out the reactions of different aldehydes (**1**), various enaminones (**204**) and malononitrile (**184**) to give pyrimido[1,2-*a*]quinolines (**205**) (Scheme 54).



Scheme 54. Conventional: 6-8 h, 56%; microwave: 4-8 min, 87%

10.2. Poly-substituted indeno[1,2-*b*]quinolines assisted by *p*-toluene sulfonic acid (*p*-TsOH)

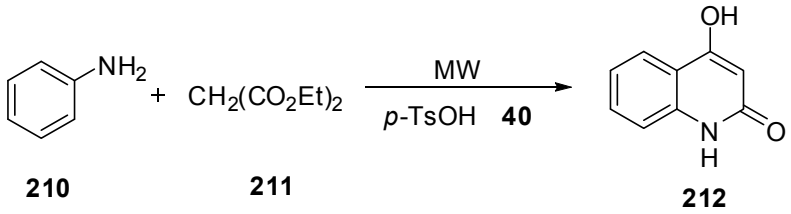
Tu *et al.*[53] reacted indane-1,3-dione (**206**), aldehyde (**1**) and substituted 3-amino-cyclohex-2-enone (**207**) in presence of *p*-TsOH (**40**) to give substituted indeno[1,2-*b*]quinolines (**209**) (Scheme 55).



Scheme 55. Conventional: 2 h, 75-87%; microwave: 2-6 min, 96%

10.3. 4-Methoxy-1-methyl-2-quinolinone and its analogs

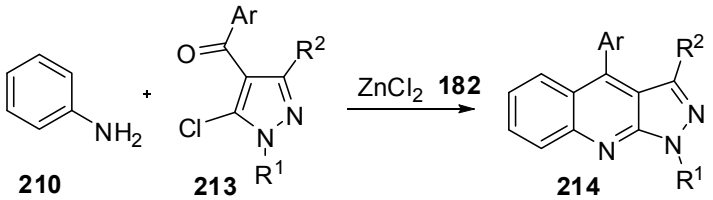
In the presence of a catalytic amount of *p*-toluenesulfonic acid (**40**), Nadaraj *et al.*[54] isolated quinolinone (**212**) in 84-96% yields in 6-11 min from a mixture of aniline (**210**) and diethylmalonate (**211**) (2:1 molar ratio) by irradiating under the microwave (Scheme 56).



Scheme 56. Conventional: 6-12 h, 55-65%; microwave: 6-11 min, 84-96%

10.4. 1*H*-Pyrazolo[3,4-*b*]quinolines

Danel *et al.*[55] heated aromatic amine (**210**) (0.02 mole), pyrazole (**213**) (0.01 mole), and anhydrous $ZnCl_2$ (**182**) (0.02 mole) in ethylene glycol in a microwave (800W) to give pyrazolo[3,4-*b*]quinolines (**214**) (Scheme 57).

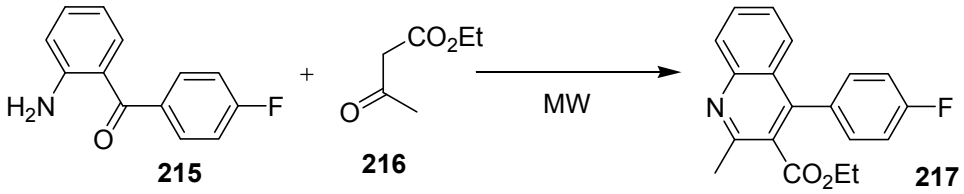


Scheme 57. Conventional: 5-8 h, 56%; microwave: 5-7 min, 80%

10.5. Poly-substituted quinolines

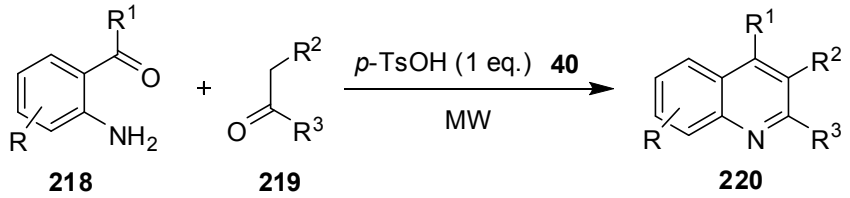
Jia *et al.*[56] reacted 2-amino-4'-fluorobenzophenone (**215**) and ethyl acetoacetate (**216**) to afford quinoline

(**217**) under microwave conditions (Scheme 58).



Scheme 58. Conventional: 3-5 min, 50-95%; microwave: 30-75 sec, 50-92%

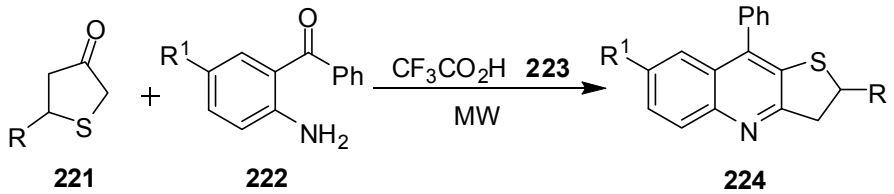
The same workers tried library synthesis of quinoline (**220**) from 2-aminoacetophenone (**218**) and various carbonyl compounds (**219**) under microwave conditions (Scheme 59).



Scheme 59. Conventional: 10-16 h, 68-69%; microwave: 10 min, 86-96%

10.6. 2,9-Diaryl-2,3-dihydrothieno[3,2-*b*]quinolines

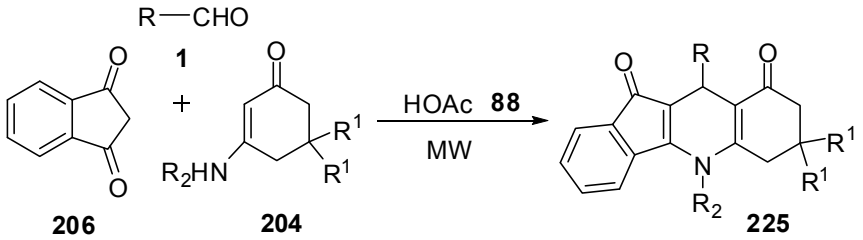
The synthesis of a series of 2,9-diaryl-2,3-dihydrothieno[3,2-*b*]quinolines (**224**) was initially investigated under thermal conditions.[57,58] Balamurugan *et al.*[59] heated a mixture of 5-aryldihydro-3(2*H*)-thiophenone (**221**), 2-aminobenzophenone (**222**) and trifluoroacetic acid (**223**) (Scheme 60) under microwave conditions to give **224**.



Scheme 60. Conventional: 2-2.5 h, 49-85%; microwave: 30 min, 60-98%

10.7. Indeno[1,2-*b*]quinoline-9,11(6*H*,10*H*)-dione derivatives by Michael addition

A series of aldehydes and enaminones were applied under microwave irradiation conditions by Tu *et al.*[61] to afford a newtype of heterocyclic compounds, the indeno[1,2-*b*]quinoline-9,11(6*H*,10*H*)-dione derivatives (**225**) from indane-1,3-dione (**206**), aldehyde (**1**) and cyclohexenone (**204**) (Scheme 61).

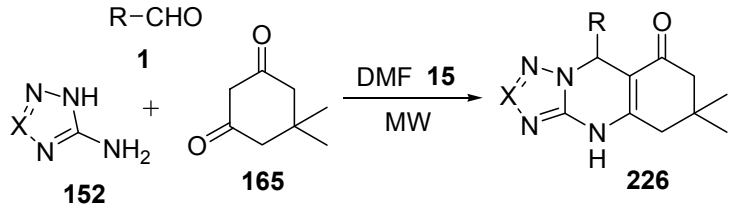


Scheme 61. Conventional: 1-5 h, 82-93%; microwave: 2-10 min, 85-93%

11. MICROWAVE ASSISTED SYNTHESIS OF FUSED QUINAZOLINE DERIVATIVES

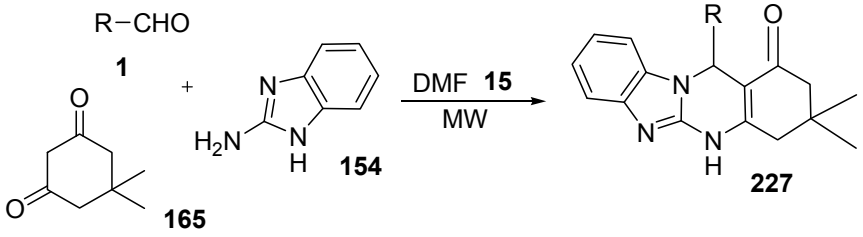
11.1. Synthesis of triazoloquinazolinones and benzimidazoquinazolinones

A general route to prepare 5,10-dihydro[1,2,4]triazolo[5,1-*b*]quinazolines (**226**) (Scheme 62) included the reaction of triazolamine (**152**), aldehydes (**1**) and cyclohexane-1,3-dione (**165**) in DMF (**15**) was reported by Mourad *et al.*[62]



Scheme 62. Conventional: 30-90 min, 60-76%; microwave: 3-10 min, 92-96%

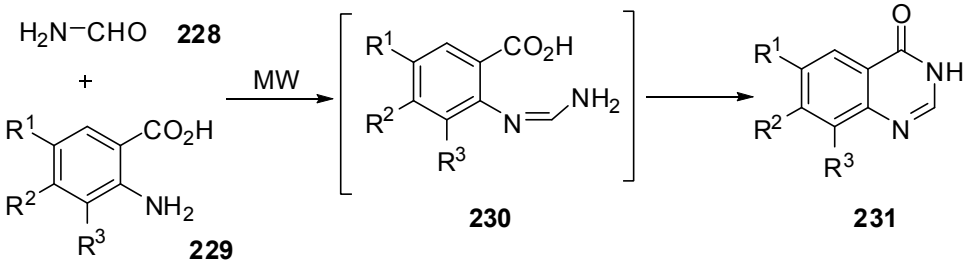
The same workers tried a microwave assisted synthesis of benzimidazoquinazolinones (**227**) from aldehydes (**1**), cyclohexane-1,3-dione (**165**) and benzoimidazol-2-amine (**154**) completed in 1-5 min and gave 90-96% yields (Scheme 63).



Scheme 63. Conventional: 6-12 min, 62-74%; microwave: 1-5 min, 90-96%

11.2. Quinazolines by Niementowski reaction

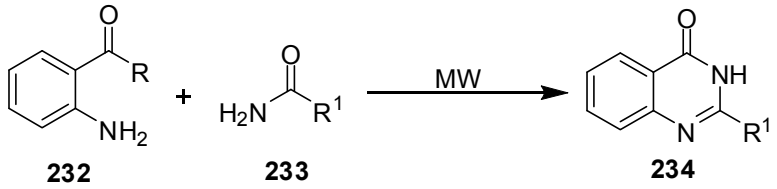
The most common synthetic method of the 3*H*-quinazolin-4-one ring (**231**) is based on the Niementowski reaction.[63] Alexandre *et al.*[64] fused anthranilic acid (**229**) with formamide (**228**) proceeding *via* an *o*-amidine intermediate (**230**) (Scheme 64).



Scheme 64. Conventional: 6 h, 59%; microwave: 20 min, 90%

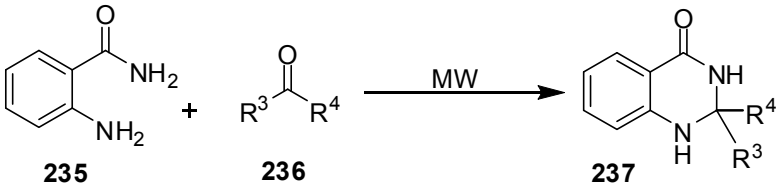
11.3. Quinazolin-4(3*H*)-one derivatives

Li *et al.*[65] reacted anthranilic acids (**232**) and anthranilamides (**233**) to give 2-substituted quinazolin-4(3*H*)-ones (**234**) (Scheme 65).



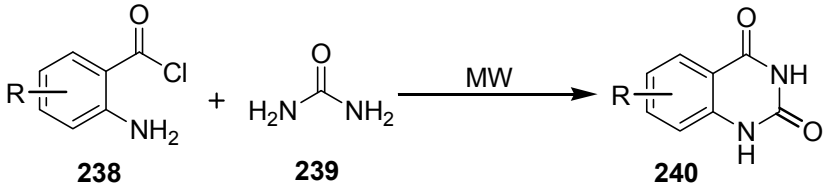
Scheme 65. Conventional: 1 h, 86%; microwave: 5-20 min, 77-93%

The same workers tried to react different benzamides (**235**) with carbonyl compounds (**236**) to give 2,2-disubstituted-2,3-dihydroquinazolin-4(1*H*)-ones (**237**) (Scheme 66).



Scheme 66. Conventional: 1-1.5 h, 23-46%; microwave: 5-20 min, 66-95%

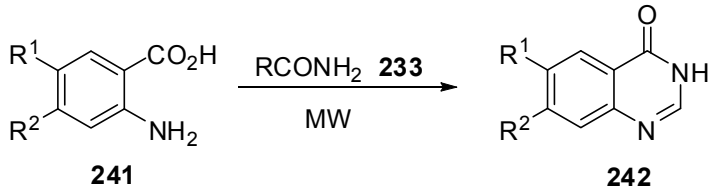
The same workers tried to react different benzoyl chlorides (**238**) with urea (**239**) giving 1*H*,3*H*-quinazolin-2,4-dione (**240**) (Scheme 67).



Scheme 67. Conventional: 1 h, 56-66%; microwave: 5-10 min, 66-88%

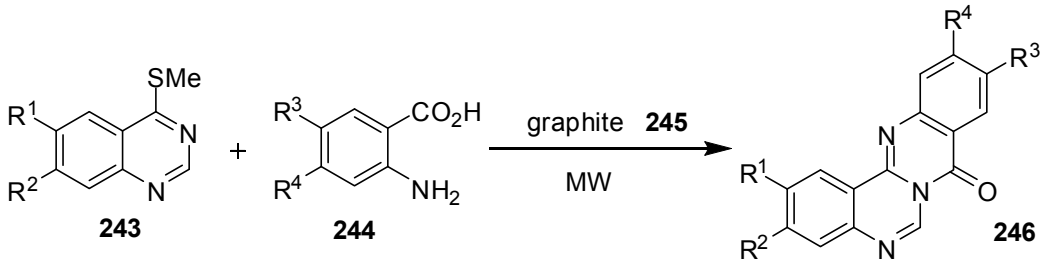
11.4. 8*H*-Quinazolino[4,3-*b*]quinazolin-8-ones *via* two Niemen-towski condensations

Novel tetracyclic 8*H*-quinazolino[4,3-*b*]quinazolin-8-ones were prepared from anthranilic acids, by fusing the quinazolinone and the quinazoline rings. The synthesis of various congeners was performed *via* two Niementowski condensations.[63] Alexandre *et al.*[66] condensed amide (**233**) with various anthranilic acids (**241**) to afford substituted quinazolinones (**242**) (Scheme 68) in the first step.



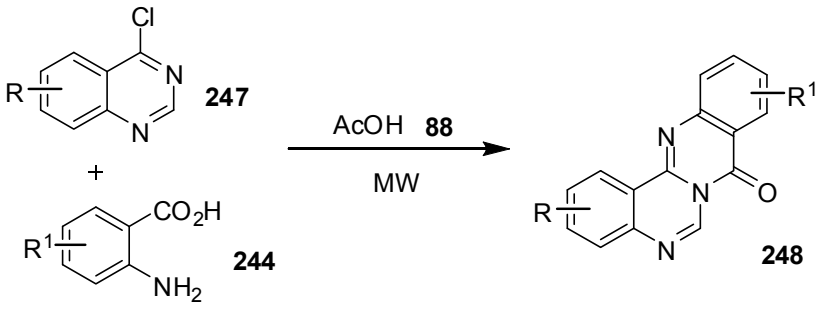
Scheme 68. Conventional: 18 h, 54-68%; microwave: 15-40 min, 70-90%

The second step involves the preparation of 8*H*-quinazolino[4,3-*b*]quinazolin-8-ones (**246**) consisting of microwave irradiation of a mixture of the 4-(thiomethyl)quinazoline (**243**) with an excess of anthranilic acid (**244**) (6 eq.), adsorbed on graphite (Scheme 69). This procedure led to the cyclised compounds (**246**) in good yields and in a shorter time.



Scheme 69. Conventional: 18-20 h, 60%; microwave: 30 min, 84-90%

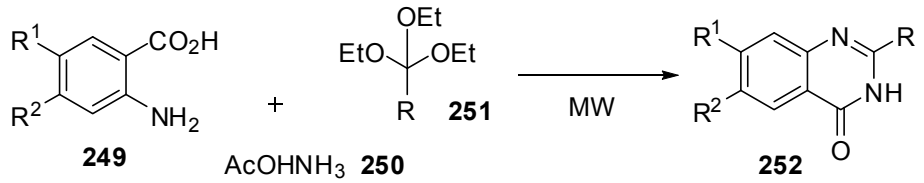
The same workers tried 4-chloroquinazoline (**247**) with an excess of anthranilic acid (**244**) (6 eq.) to get adsorbed on graphite (Scheme 70). This procedure led to the cyclised compounds (**248**) in good yields and in a shorter time.



Scheme 70. Conventional: 18 h, 48-62%; microwave: 10 min, 78-88%

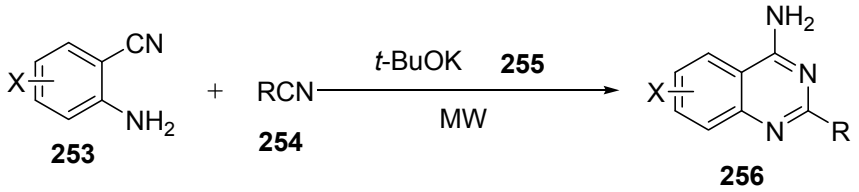
11.5. Quinazolinones and quinazolines

Rad-Moghadam *et al.*[67] performed the condensation of anthranilic acid (**249**), ammonium acetate (**250**) and the orthoesters (**251**), which gives access to the 2-substituted-4(3*H*)-quinazolinone (**252**) (Scheme 71) under microwave conditions.



Scheme 71. Conventional: 6-8 h, 26-54%; microwave: 5 min, 76-89%

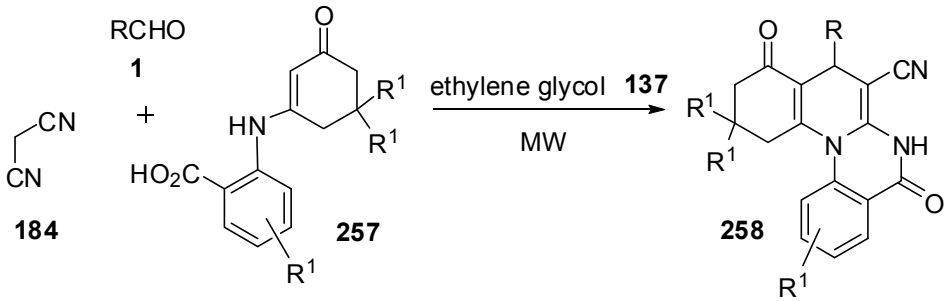
A microwave promoted synthesis of 4-aminoquinazolines (**256**) by reacting cyanoaromatic compounds (**253**) with anthranilonitrile (**254**) in a microwave oven was carried out by Seijas *et al.*[68] (Scheme 72).



Scheme 72. Conventional: 48 h, 40%; microwave: 1-3 min, 73-93%

11.6. Polysubstituent Quinolino[1,2-*a*]quinazolines

Under the optimal conditions of ethylene glycol (2.0 ml) as a solvent and 120 °C, Tu *et al.*[52] performed the reactions of different aldehydes (**1**), various enaminones (**257**) and malononitrile (**184**) (Scheme 73) to give quinolino[1,2-*a*]quinazolines (**258**).

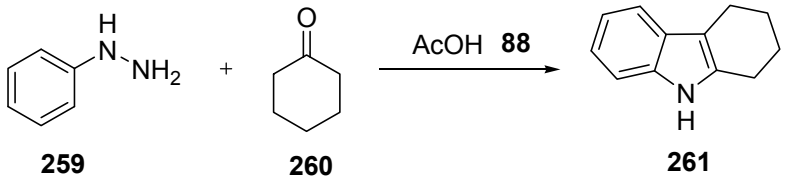


Scheme 73. Conventional: 14-16 h, 56%; microwave: 5-8 min, 78%

12. MICROWAVE ASSISTED SYNTHESIS OF FUSED INDOLE DERIVATIVES

12.1. Indole derivatives

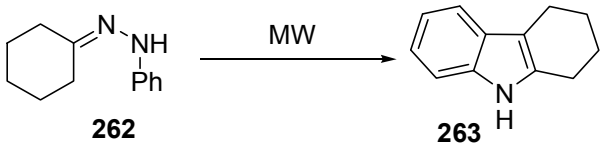
Sridar *et al.*[69] synthesized indoles (**261**) from an aryl hydrazine (**259**) and a ketone (**260**) in acetic acid (**88**) (Scheme 74).



Scheme 74. Conventional: 2 h, 59%; microwave: 30 sec, 68-89%

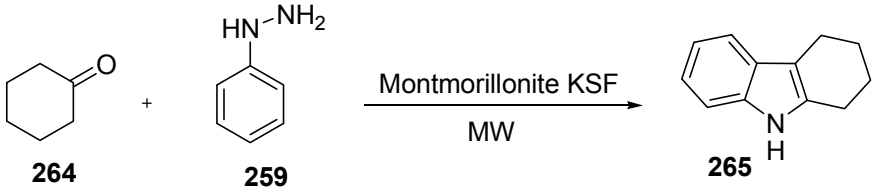
12.2. Carbazole derivatives

The Abrarnovitch group[70] have irradiated **262** in formic acid in a Parr bomb and produced the product (**263**) in excellent yields (Scheme 75).



Scheme 75. Conventional: 3-4 h, 30-50%; microwave: 30-90 sec, 70-85%

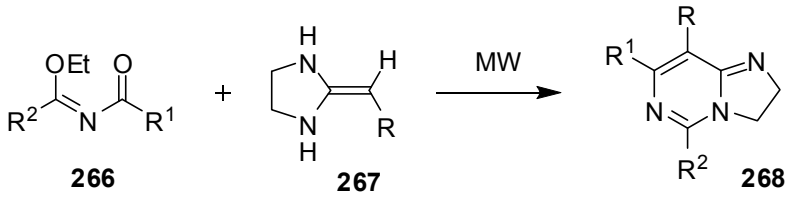
Villemin and co-workers[71] have illustrated the utility of this procedure in the synthesis of **265** from cyclohexanone (**264**) and phenyl hydrazine (**259**) (Scheme 76).



Scheme 76. Conventional: 3-4 h, 25-50%; microwave: 30-90 sec, 60-85%

12.3. Imidazo[1,2-*f*]pyrimidine derivatives

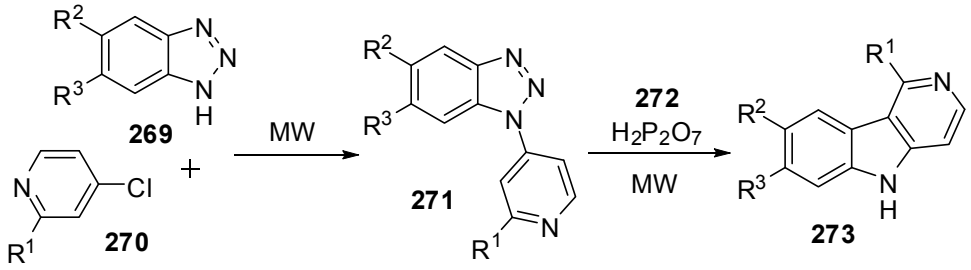
Rahmouni *et al.*[72] have synthesised 2,3-dihydroimidazo[1,2-*c*]pyrimidines (**268**) under microwave irradiation in moderate yields from *N*-acylimidates (**266**) and activated 2-benzimidazoles (**267**) (Scheme 77).



Scheme 77. Conventional: 4-6 h, 58-70%; microwave: 15 min, 85-91%

12.4. γ-Carboline and Pyrido[4,3-*b*]indole derivatives

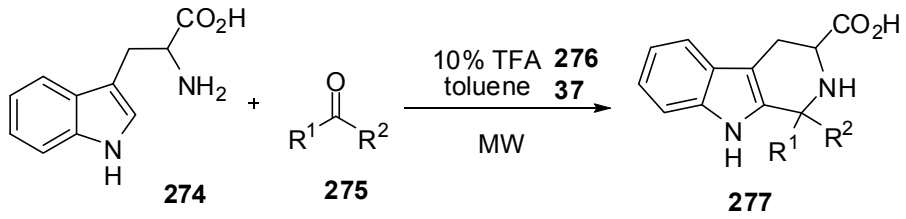
Molina *et al.*[73] converted 1-arylbenzotriazoles into carbazoles or their heterocyclic analogs under microwave conditions (Scheme 78) where the 1-(4-pyridyl)benzotriazole (**269**) reacts with 4-chloropyridine (**270**) to give γ-carboline (**273**).



Scheme 78. Conventional: 1.5 h, 28-80%; microwave: 15 min, 30-76%

12.5. Pictet–Spengler reactions for preparation of 1,1-disubstituted tetrahydro-β-carbolines

Kuo *et al.*[74] reacted tryptophan (**274**) with ketones (**275**) by microwaves to produce 1,1-disubstituted tetrahydro-β-carbolines (**277**) in much shorter reaction times with good to excellent isolated yields (Scheme 79).



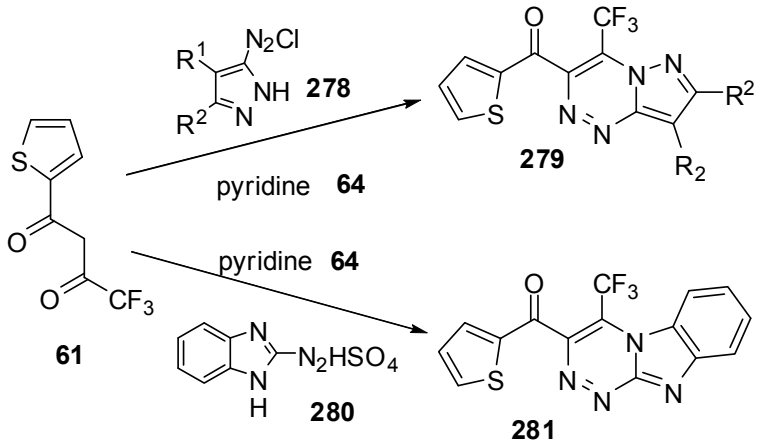
Scheme 79. Conventional: 1-96 h, 86-99%; microwave: 10-20 min, 91-99%

13. MICROWAVE ASSISTED SYNTHESIS OF FUSED TRIAZINE DERIVATIVES

13.1. Synthesis of pyrazolo[5,1-*c*]triazine and benzimidazo[5,1-*c*]-1,2,4-triazine derivatives

Shaaban *et al.*[14] coupled thiazole compound (**61**) with the diazonium salt of aminopyrazole derivatives

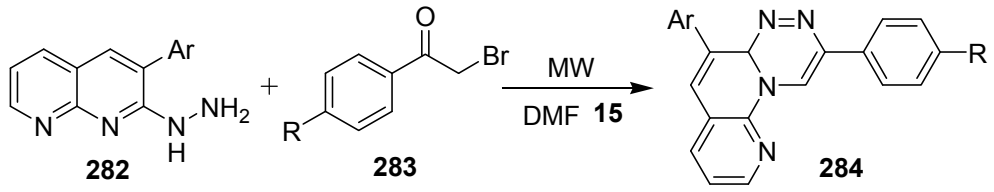
(**278**) and 2-aminobenzimidazole (**280**) under same conditions. In each case, 6-thienoyl-4-(trifluoromethyl)pyrazolo[5,1-*c*][1,2,4]triazines (**279**) and 3-thienoyl-4-(trifluoromethyl)-benzimidazo[2,1-*c*][1,2,4]triazine (**281**) was obtained (Scheme 80).



Scheme 80. Conventional: 9-10 h, 43-59%; microwave: 5 min, 57-84%

13.2. Triazino[4,3-*a*][1,8]naphthyridines

Mogilaiah *et al.*[75] reported a rapid and efficient protocol for the synthesis of novel triazino[4,3-*a*][1,8]naphthyridines (**284**) by the reaction of 3-Aryl-2-hydrazino-1,8-naphthyridines (**282**) with ω-bromoacetophenones (**283**) in the presence of catalytic amount of DMF (**15**) in solvent free conditions under microwave irradiation (Scheme 81).

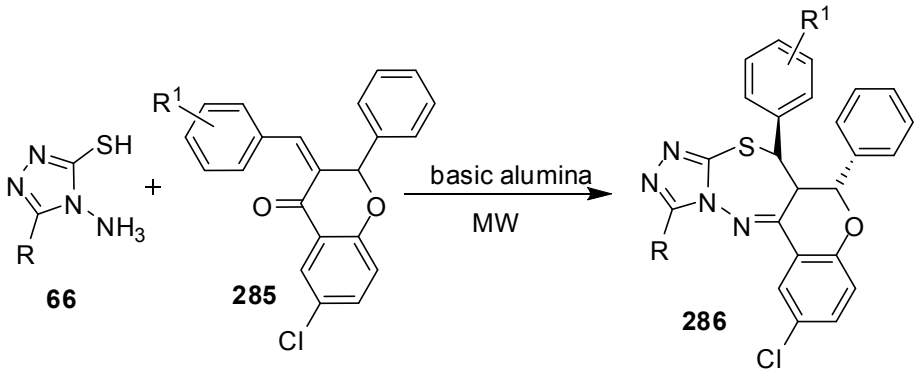


Scheme 81. Conventional: 6-8 h, 49-58%; microwave: 3-4 min, 85-90%

14. MICROWAVE ASSISTED SYNTHESIS OF FUSED AZEPINE DERIVATIVES

14.1. Fluorine containing benzopyranotriazolothiadiazepines

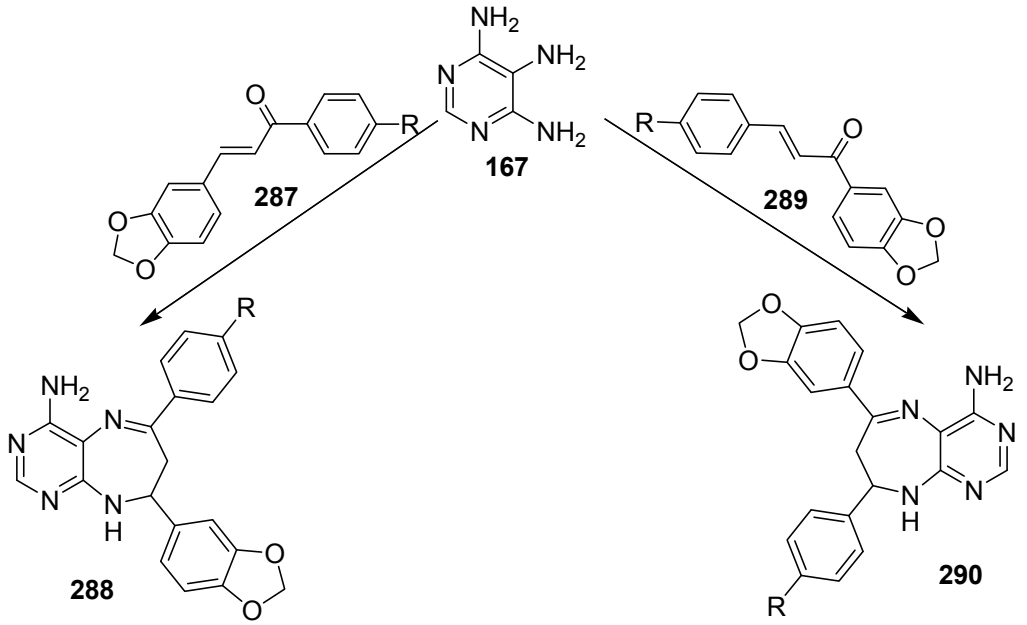
Dandia *et al.*[76] developed the reaction of 3-arylidene flavanones (**285**) with 4-amino-5-alkyl-3-mercaptotriazole (**66**) involving the formation of intermediate followed by condensation of the carbonyl group with the aromatic primary amine to give a seven membered ring system leading to the formation of a new class of tetracyclic ring system (**286**) (Scheme 82).



Scheme 82. Conventional: 60-65 h, 40-47%; microwave: 3-5 min, 72-82%

14.2. 8,9-dihydro-7*H*-pyrimido[4,5-*b*][1,4]diazepines

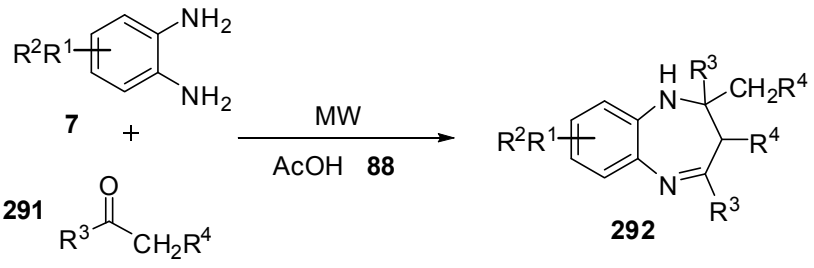
Insuasty *et al.*[77] irradiated an equimolar mixture of 4,5,6-triaminopyrimidine (**167**) and chalcones (**287**, **289**) in presence of catalytic amounts of DMF (1 ml) to afford the desired products (**288**, **290**) (Scheme 83).



Scheme 83. Conventional: 5-7 h, 35-40%; microwave: 14-18 min, 60-77%

14.3. 1,5-benzodiazepine derivatives

A very few methods for the preparation of 1,5-benzodiazepines are reported in the literature.[78-80] Pozarentzi *et al.*[81] synthesized 2,3-dihydro-1*H*-1,5-benzodiazepines (**292**) by condensation of ketones (**291**) with *o*-phenylenediamines (**7**) in acetic acid (**88**) (Scheme 84) by microwave irradiation.

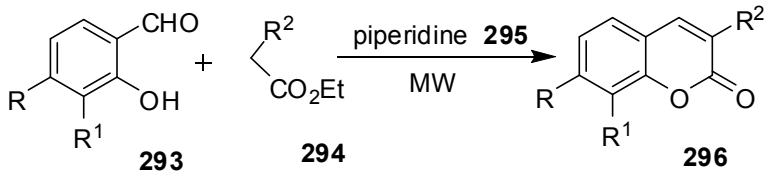


Scheme 84. Conventional: 7-8 h, 35-55%; microwave: 2-7 min, 90-99%

15. MICROWAVE ASSISTED SYNTHESIS OF FUSED CHROMENE DERIVATIVES

15.1. Synthesis of 5-nitrofurfurylidine

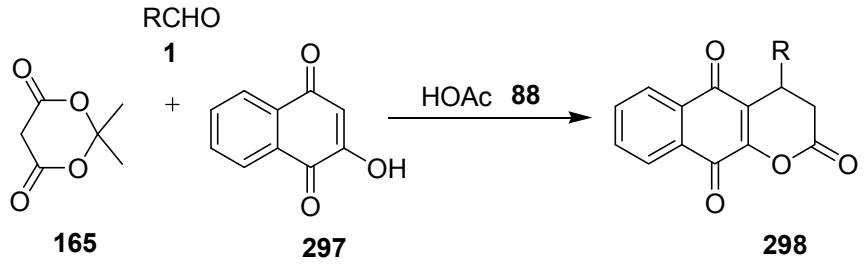
Villemin and Martin[82] have synthesized 5-nitrofurfurylidine by the condensation of 5-nitrofurfuraldehyde with active methylene compounds under microwave irradiation using K 10 and $ZnCl_2$ as a catalyst. Singh *et al.*[83] developed solventless systems wherein salicylaldehydes (**293**) undergo Knoevenagel condensation with a variety of ethyl acetate derivatives (**294**) piperidine (**295**) to afford coumarins (**296**) (Scheme 85).



Scheme 85. Conventional: 9-11 h, 30-40%; microwave: 14-18 min, 65-85%

15.2. α-Lapachone derivatives

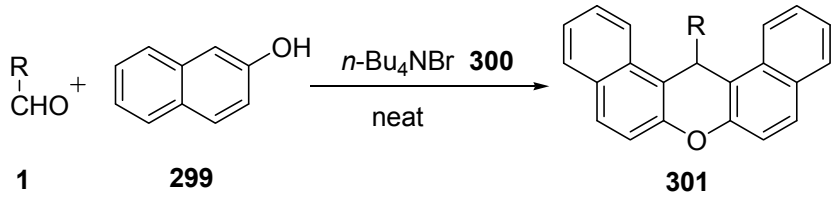
A new class of α-lapachone derivatives (**298**) with diversed structure in one pot was developed by Wei *et al.*[84] (Scheme 86). The reaction of a variety of substituted aldehydes (**1**), dioxandione (**165**) and naphthalenedione (**297**) as reactants using AcOH (**88**) as a solvent was performed in a microwave.



Scheme 86. Conventional: 12-15 h, 60-65%; microwave: 4-6 min, 83-93%

15.3. Aryl-14*H*-dibenzo[*a*,j]xanthenes

Kantevari *et al.*[85] reacted β-naphthol (**299**) and TBAB (**300**) (10 mol%) with various aldehydes (**1**) to yield various aryl-14*H*-dibenzo[*a*,*j*]xanthenes (**301**) (Scheme 87).



Scheme 87. Conventional: 60-90 min, 78-96%; microwave: 4-6 min, 75-95%

16. CONCLUSIONS

This review deals with microwave assisted synthesis of a variety of five membered fused heterocycles like imidazoles, pyrazoles, triazoles, thiazoles, pyrroles and benzofurans. The review also deals with microwave assisted synthesis of a variety of six and seven membered fused heterocycles like pyrimidines, pyridines quinolines, quinazolines, indoles, imidazoles, pyrazoles, triazoles, triazines, azepines, thiazoles, pyrolles, benzofurans and chromenes. Deliberate attempts were made to compare the microwave assisted synthesis with those of the conventional conditions. Microwave assisted conditions proved to be faster in terms of reaction times, dramatically decrease the reaction times and improve the product yields and purity as compared to the conventional conditions.

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