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1,2,3-BENZOTRIAZIN-4(3*H*)-ONES: SYNTHESIS, REACTIONS AND APPLICATIONS

**Zunera Khalid, Hafiz Adnan Ahmad, Munawar Ali Munawar,*
Misbah-ul-Ain Khan, and Salman Gul**

Institute of Chemistry, University of the Punjab, Lahore, 54590 Pakistan,
mamunawar.chem@pu.edu.pk

Abstract – An up-to-date review of 1,2,3-benzotriazin-4(3*H*)-ones including its synthesis, reactions and applications is presented. The title ring system deserves a special treatment due to its increasing importance in pharmaceuticals, imaging and recording materials.

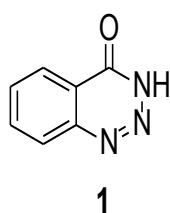
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1. INTRODUCTION

1,2,3-Benzotriazin-4(3*H*)-one (**1**) is an oxo derivative of benzotriazine; a bicyclic aromatic structure consisting of seven carbon and three nitrogen atoms. As will be seen later in the related section, it has been revealed as a good pharmacophore exhibiting various biological activities. Appearance of increasing publications dealing with the chemistry and diverse applications prompted us to survey this subject. This nucleus is known for the number of pharmacological activities including antimicrobial,¹ anti-inflammatory,² anti-depressant,³ anticancer,⁴ anti-ulcer,⁵ antidiarrhoeal⁶ and as anaesthetics.⁷ 3-Hydroxy-1,2,3-benzotriazin-4(3*H*)-one is a versatile reagent and has been successfully employed in peptide synthesis.⁸ Apart from the medicinal uses, it has been a part of dyeing,⁹ imaging and recording material.¹⁰ It has been treated in a small monograph and two review articles.¹¹⁻¹³ An overall view of **1** is presented here with more detailed development since 1976. The useful synthetic methods are followed by reactivity and applications.

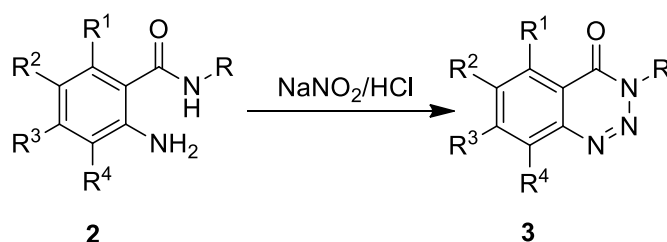
Figure 1. 1,2,3-Benzotriazin-4(3*H*)-one

2. Synthetic Methods

The general strategy employed for the construction of **1** is either by ring synthesis or by transformation from another ring. Mostly ring formation has been accomplished from starting materials such as; anthranilimides, anthranilic acids, alkyl anthranilates, acetophenones or azides.

2.1 From Anthranilamides

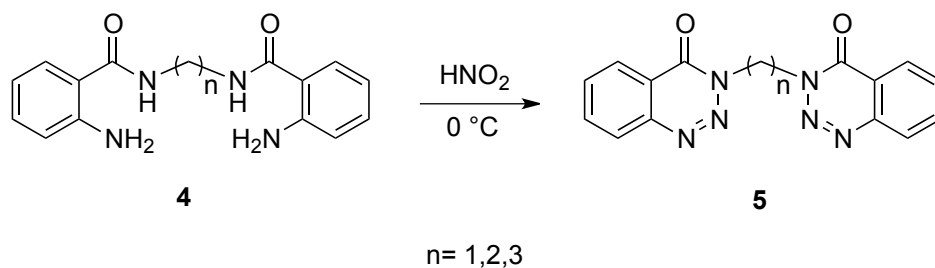
Most common and the oldest method used for 1,2,3-benzotriazin-4(3*H*)-ones (**3**) synthesis is the diazotization of anthranilamides (**2**) or as earlier termed benzazimides (Scheme 1).¹⁴⁻²³



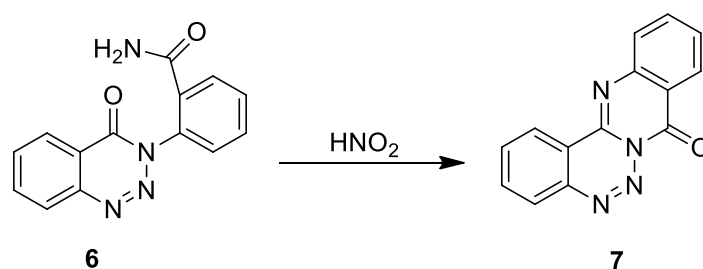
R= H, amino, alkyl, aryl *etc.* R¹- R⁴= H, alkyl, halo, cyano, nitro, amino, sulfonamido *etc.*

Scheme 1. Synthesis of 1,2,3-benzotriazin-4(3*H*)-ones from anthranilamides

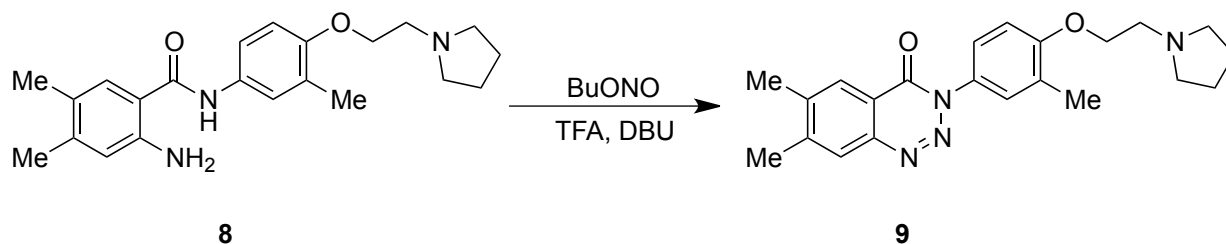
In a similar way, the synthesis of 2-bis-(4-oxo-3,4-dihydro-1,2,3-benzotriazin-3-yl)alkanes (**5**) have been carried out from bis amide (**4**) by diazotization and cyclization (Scheme 2).²⁴ Interestingly an analogous reaction of **6** with nitrous acid yielded **7** but alternative route for the cyclization of **6** by DABCO and dicyclohexylcarbodiimide failed to give the desired results (Scheme 3).²⁵ For aprotic diazotization, butyl nitrite was used for the preparation of **9** and DBU played a part to promote this reaction (Scheme 4).²⁶ In case of resin-bound anthranilamides (**10**) normal diazotization was problematic which was overcome by using *t*-butyl nitrite in acetic acid followed by treatment with 95% TFA to gain **11** in high yields (Scheme 5).^{27,28}



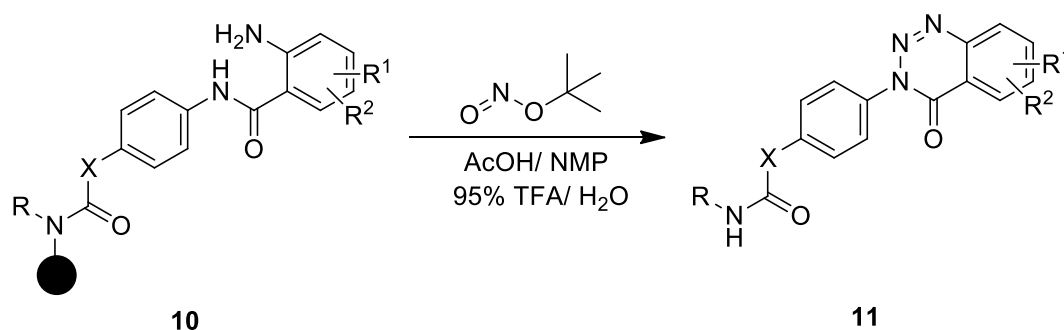
Scheme 2. Diazotization and cyclization of bis amide



Scheme 3. Intramolecular cyclization



Scheme 4. Diazotization and cyclization with base



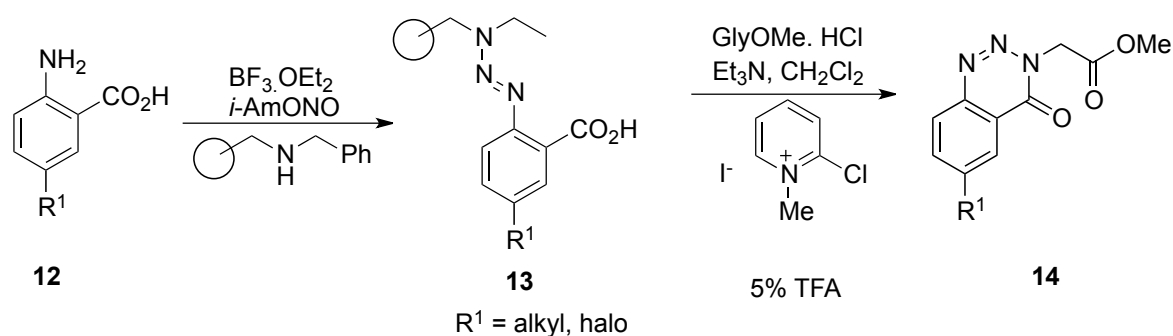
$R = \text{alkenyl, cycloalkyl, etc. } X = \text{alkyl, } R^1 = R^2 = \text{halo, nitro}$

Scheme 5. Synthesis of resins bound 1,2,3-benzotriazin-4(3*H*)one derivatives

2.2. From Anthranilic Acid

For the synthesis of 3 and 6 substituted 1,2,3-benzotriazin-4(3*H*)-ones (e.g.; **14**) a series of polymer-bound triazines (**13**) were prepared by the diazotization of different anthranilic acids (**12**) carried

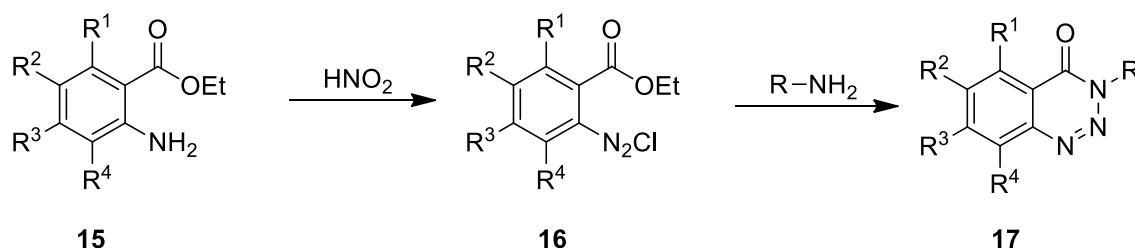
out with *iso*-amyl nitrite followed by reaction with benzylaminomethyl polystyrene. Which were coupled with different amines or amino acids or amino acid methyl ester by using of 2-chloro-1-methylpyridinium iodide as a coupling reagent. The resulting amides were subsequently cyclized to 1,2,3-Benzotriazinones (e.g.; **14**) (Scheme 6).²⁹



Scheme 6. Synthesis from anthranilic acid

2.3. From Alkyl Anthranilate

Diazotization of ethyl anthranilates (**15**) followed by cyclization by using ammonia or amine derivatives can lead to **17** (Scheme 7).³⁰⁻³² However, in case of amino hetaryl, cyclization requires a much stronger base, e.g.; sodium methoxide.³³⁻³⁷



R-R⁴ = H, alkyl, aryl, hetaryl, amino, nitro etc.

Scheme 7. Synthesis of 1,2,3-benzotriazin-4(3H)-ones from ethyl anthranilate

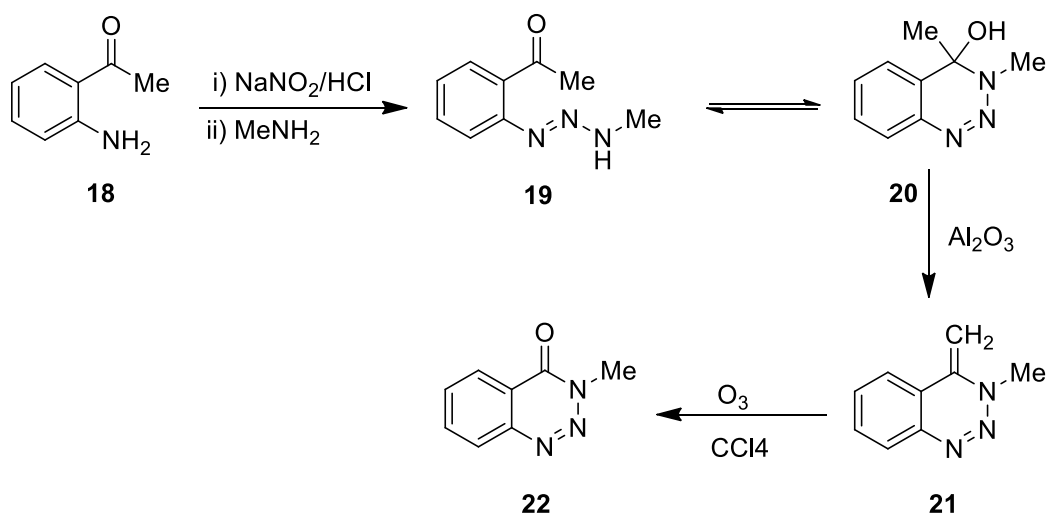
2.4. From 2-Aminoacetophenone

1-[2-(3-Methyltriaz-1-enyl)phenyl]ethanone (**19**) produced by reaction of 2-aminoacetophenone with nitrous acid followed by methyl amine was cyclodehydrated by neutral alumina to prepare 4-methylene-3,4-dihydrobenzo-1,2,3-triazine (**21**). Which was treated with ozone in CCl₄ to afford an orange residue of 3-methyl-1,2,3-benzotriazin-4(3H)-one (**22**) (Scheme 8).³⁸

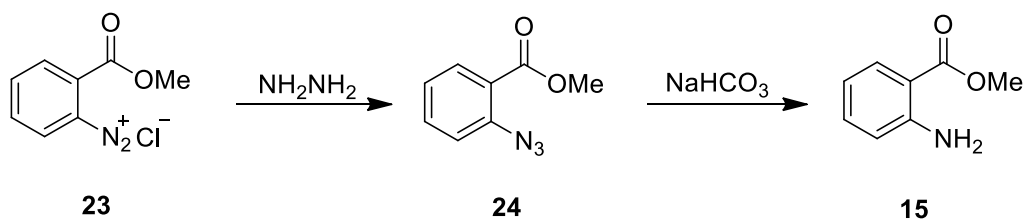
2.5. From Azides

Diazotized methyl anthranilate (**23**) was taken with hydrazine to afford 2-carbomethoxyphenyl azide (**24**)

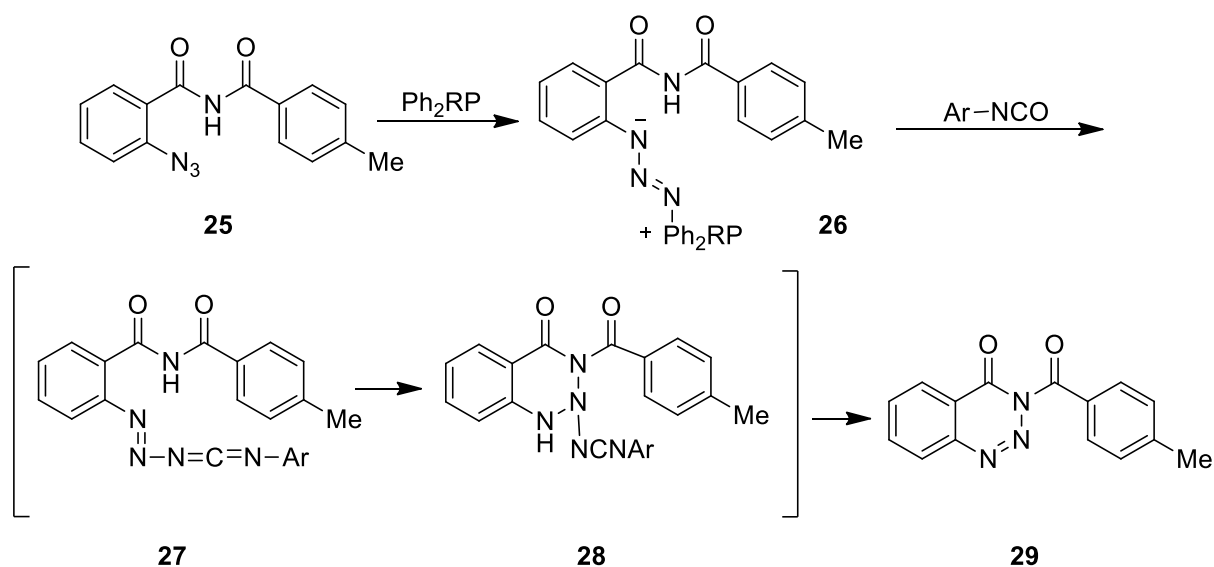
which resisted to cyclize and converted back to methyl anthranilate on treatment with sodium hydrogencarbonate solution (Scheme 9).³⁹



Scheme 8. Synthesis from 2-aminoacetophenone



Scheme 9. Diazotized methyl anthranilate reaction with hydrazine and sodium hydrogencarbonate

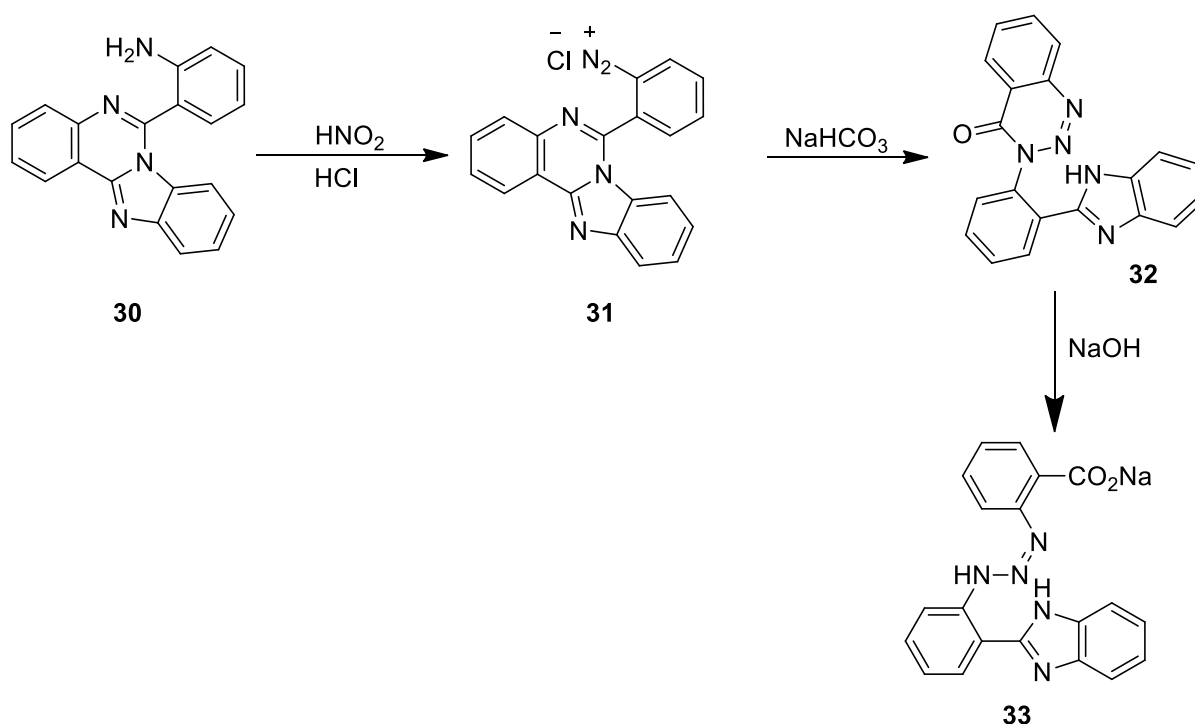


Scheme 10. Wittig type reaction

Velasco *et al.* have introduced a stable phosphazide (**26**) that can be stored for several weeks. A Staudinger reaction of the *N*-substituted *o*-azidobenzamide (**25**) with triphenylphosphine or diphenylmethylphosphine allowed the isolation of intermediate phosphazides (**26**) as crystalline solids. The phosphazides (**26**) was found to have zwitterionic character in which phosphorus have partial phosphonium character and nitrogen have a negative charge. Phosphazides were further reacted in an aza Wittig type fashion with isocyanates to form a 1,2,3-benzotriazin-4(3*H*)-one derivative **29** (Scheme 10).⁴⁰

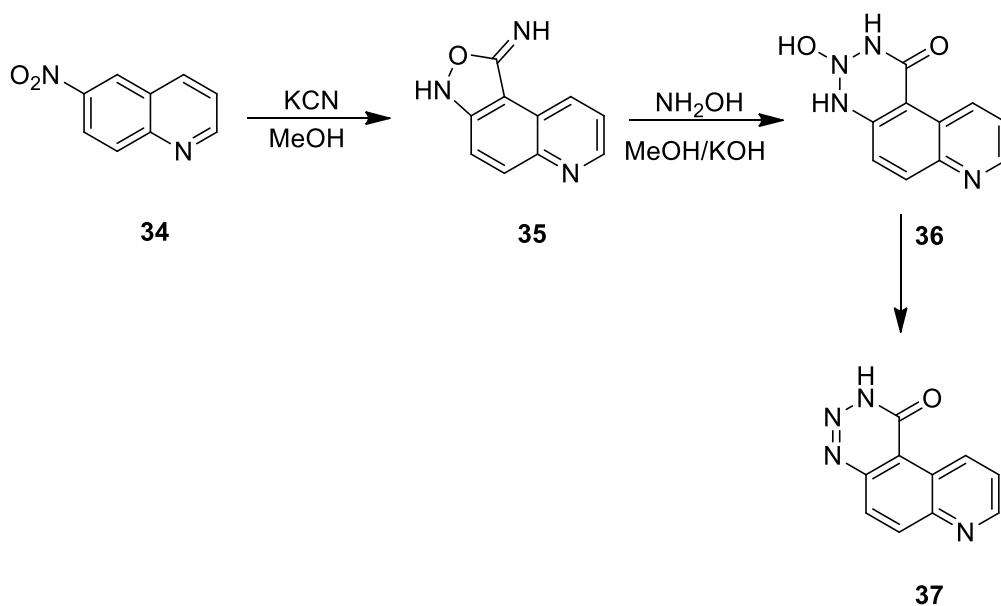
2.6. Ring Transformations

Treatment of 6-(2-aminophenyl)benzimidazo[1,2-*c*]quinazoline (**30**) with nitrous acid opens, the pyrimidine moiety to form 3-(2-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)benzo[1,2,3]triazin-4(3*H*)-one (**32**) (Scheme 11).⁴¹ Another publication deals with a ring transformation involves a successive *N*-chlorobenzotriazole oxidation, decomposition and thermally rearrangement to 3-phenyl-1,2,3-benzotriazin-4(3*H*)-one.⁴²



Scheme 11. Synthesis of 1,2,3-benzotriazin-4(3*H*)-ones system through intramolecular cyclization

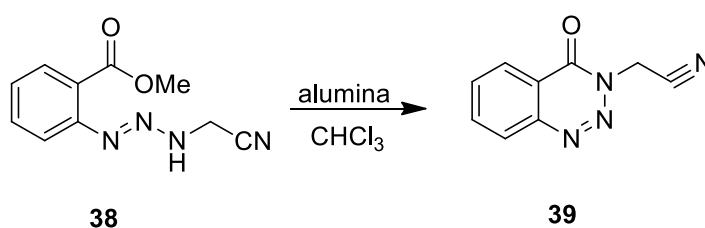
Another method used for the synthesis of a condensed 1,2,3-benzotriazin-4(3*H*)-one involves a ring transformation of an isoxazole ring into triazinone. Actually von Richter type reaction of 6-nitroquinoline (**34**) with methanolic potassium cyanide yield an isobenzoxazole (**35**). Its reaction with hydroxylamine gave **36** and produced [1,2,3]triazino[5,4-*f*]quinolin-1(2*H*)-one (**37**) after dehydration (Scheme 12).⁴³



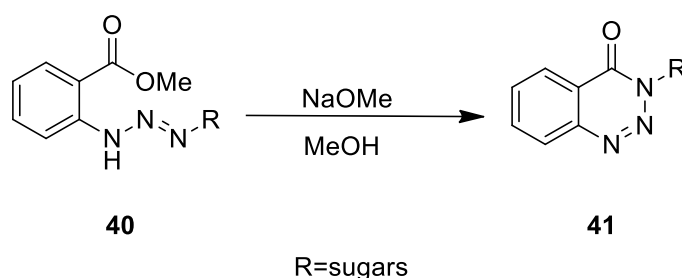
Scheme 12. Von-Richter type reaction

2.7. Miscellaneous

Basic alumina can easily transform (*E*)-methyl 2-(3-(cyanomethyl)triaz-1-enyl)benzoate (**38**) to 3-(cyanomethyl)-1,2,3-benzotriazin-4(3*H*)-one (**39**) (Scheme 13).⁴⁴ 1-Methyl-3-(2-carboethoxyphenyl)-triazene cyclization was also investigated in alkaline and acidic conditions. In 2 M sodium hydroxide reactant transformed to anthranilic acid whereas in 1 M H₂SO₄ changed to ethyl anthranilate (75%) and 3-methyl-1,2,3-benzotriazin-4(3*H*)-one (14%).⁴⁵ However with sodium methoxide in methanol, **40** successfully cyclized to **41** (Scheme 14).⁴⁶

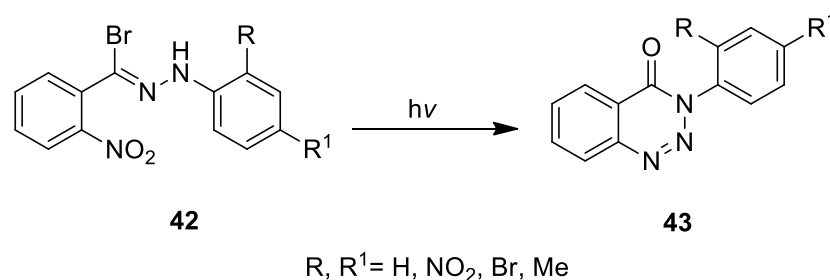


Scheme 13. Ring closure with basic alumina



Scheme 14. Cyclization by using sodium methoxide

Yoshifumi and Furuta have reported that **42** on photolysis transformed to *N*-substituted-1,2,3-benzotriazin-4(3*H*)-ones (**43**) with 40-55% yield (Scheme 15).⁴⁷

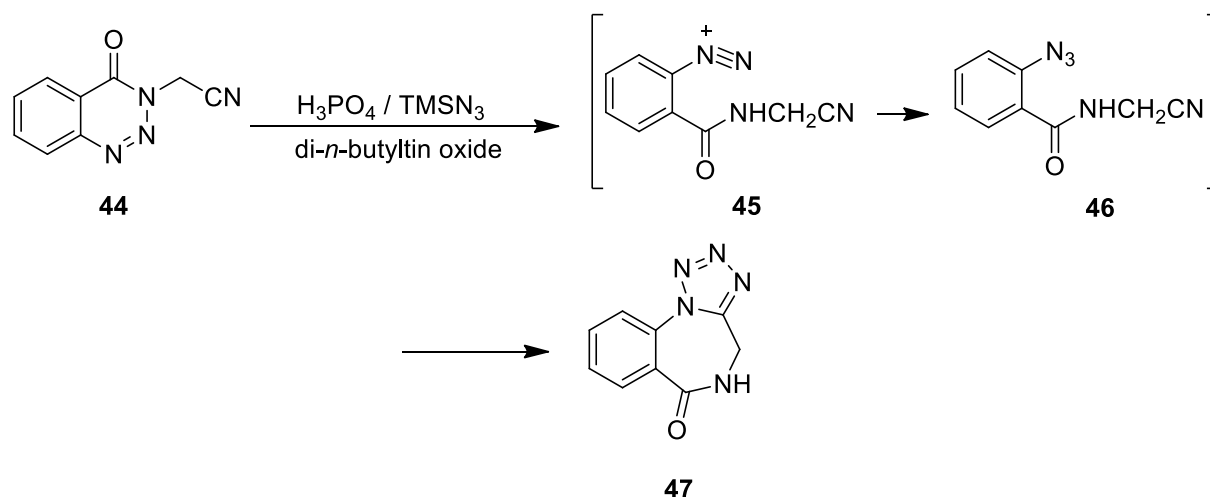


Scheme 15. Photolytic synthesis

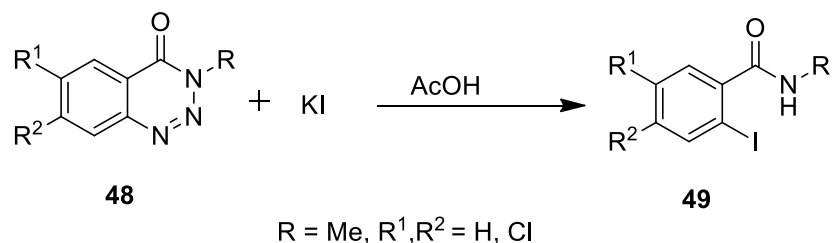
3. Chemical Reactions

3.1. Decomposition in Acids

Although 1,2,3-benzotriazin-4(3*H*)-one is a stable compound but some of its derivatives are sensitive towards acids or bases. On heating with phosphoric acid, 3-aryl-1,2,3-benzotriazin-4(3*H*)-ones were changed to 6-phenanthridone.⁴⁸ In the presence of trimethylsilyl azide and di-*n*-butyltin oxide along with phosphoric acid, **44** was converted to 4,5-dihydro-6*H*-tetrazolo[1,5-*a*][1,4]benzodiazepin-6-one (**47**) through intermediates (**45** and **46**) (Scheme 16).²³ In acetic acid with potassium iodide, 3-alkyl-1,2,3-benzotriazin-4(3*H*)-one derivative (**48**) has been reported to decompose to *O*-iodo-*N*-alkylbenzamides (**49**) (Scheme 17).⁴⁹



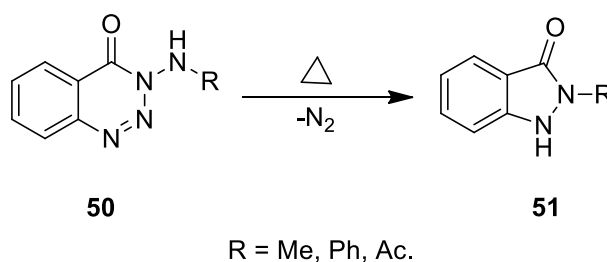
Scheme 16. Reaction with trimethylsilyl azide and di-*n*-butyltin oxide



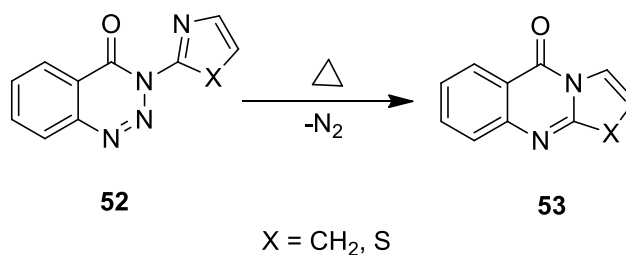
Scheme 17. Triazinone ring opens in potassium iodide and acetic acid solution

3.2. Thermolysis

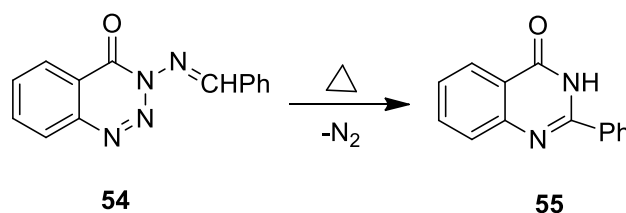
Thermolysis of 3-methyl, 3-phenyl or 3-acylamino-1,2,3-benzotriazin-4(3*H*)-one (**50**) may lead to the rearranged products 2-methyl, 2-phenyl or 2-acylindazolones (**51**) (Scheme 18).⁵⁰ Heterocyclic derivatives, 3-(α -pyridyl)- and 3-thiazol-2-yl-1,2,3-benzotriazin-4(3*H*)-one (**52**) under high temperature yielded pyrrolo[2,1-*b*]quinazolin-9(3*H*)-one and 5*H*-thiazolo[2,3-*b*]quinazolin-5-one (**53**) respectively (Scheme 19).⁵¹ While 3-(benzylideneamino)benzo-1,2,3-triazin-4(3*H*)-one (**54**) at high temperature transformed to 2-phenylquinazolin-4(3*H*)-one (**55**) (Scheme 20).



Scheme 18. Thermolysis

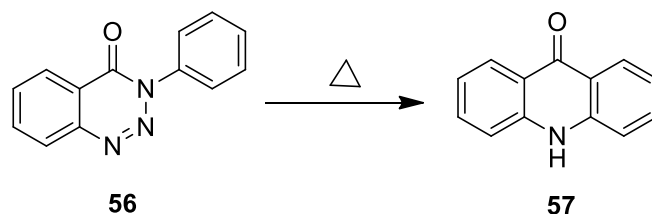


Scheme 19. Fused quinazolines synthesis through thermolysis of triazinone ring



Scheme 20. Transformation of triazinones to phenylquinazolinone

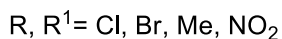
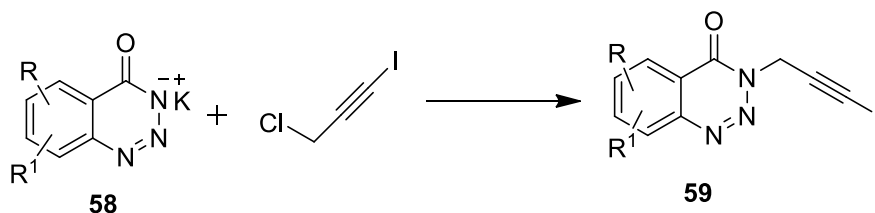
3-Phenyl-1,2,3-benzotriazin-4(3*H*)-one (**56**) underwent thermal decomposition and rearranged to 9-acridones (**57**) (Scheme 21) when refluxed in 1-methylnaphthalene, whereas in paraffin oil at 300 °C only benzanilide was obtained. When 3-(α -naphthyl)-1,2,3-benzotriazin-4(3*H*)-one was heated in paraffin oil, it converted to benzacridone and benzophenanthridone. Thermal rearrangement of 3-(1-propenyl) and 3-(β -styryl)-1,2,3-benzotriazin-4(3*H*)-one provided 12% 3-methyl- and 70% 3-phenylquinolin-4(1*H*)-one.⁵²



Scheme 21. Conversion of triazinone system to acridinone

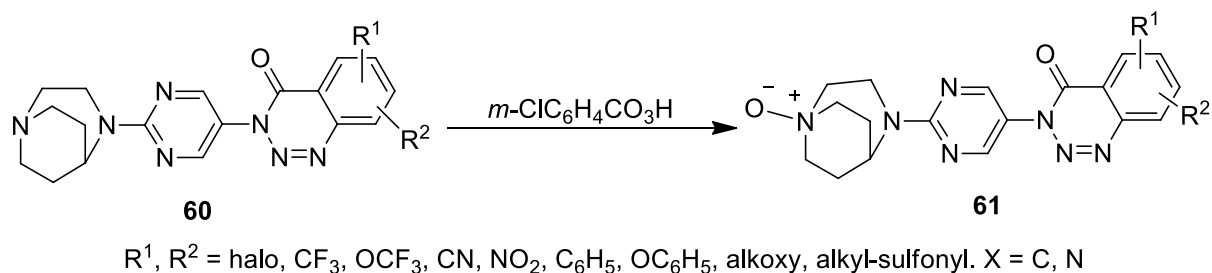
3.3. Salt Formation

1,2,3-Benzotriazin-4(3*H*)-ones are reported to be acidic compound, freely soluble in aqueous alkalis and give variety of metal salts.¹¹ Lithium salt can be prepared by reacting with lithium hydride while potassium salts after refluxing in 80% KOH ethanolic solution. The potassium salts have also been used to obtain 3-(3-iodopropargyl)-1,2,3-benzotriazin-4(3*H*)-ones derivatives (**59**) (Scheme 22).⁵³

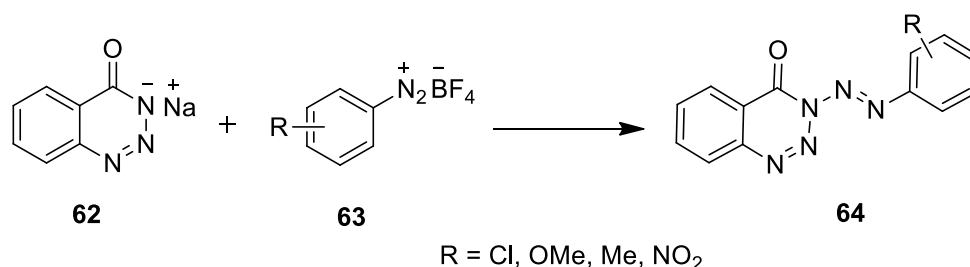


Scheme 22. Reaction with alkenyl halides

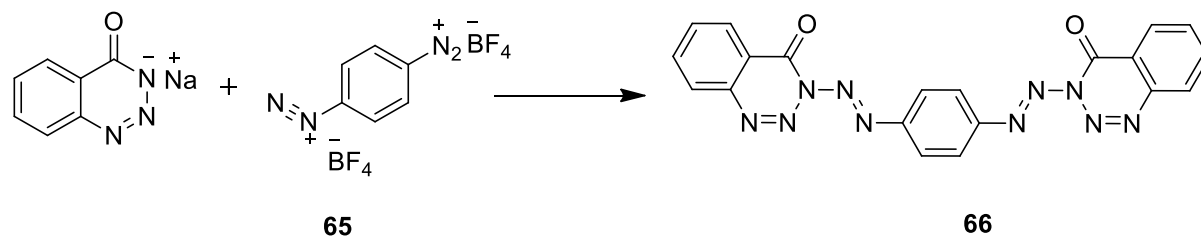
For direct pharmaceutical use, 3-(2-(1,4-diazabicyclo[3.2.2]nonan-4-yl)pyrimidin-5-yl)-benzo[1,2,3]triazin-4(3*H*)-one (**60**) were converted to their *N*-oxides (**61**) by reacting with meta-chloroperoxybenzoic acid and were tested for the treatment of neurodegenerative diseases (Scheme 23).⁵⁴⁻⁵⁶

Scheme 23. *N*-Oxides synthesis

Sodium salt of 1,2,3-benzotriazin-4(3*H*)-one, **62** underwent coupling with various arylazo tetrafluoroborate to give 3-(phenyldiazenyl)benzo[*d*][1,2,3]triazin-4(3*H*)-one derivatives (**64**) (Scheme 24) and with *p*-phenylene-bis(diazonium tetrafluoroborate) (**65**) to produce **66** (Scheme 25).⁵⁷



Scheme 24. Coupling of benzotriazinone salts with diazonium tetrafluoroborates

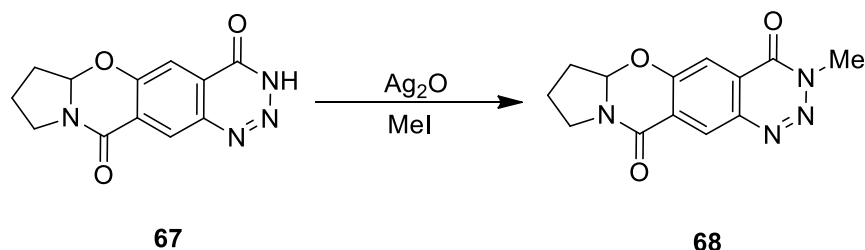


Scheme 25. Coupling of benzotriazinone salts with bis(diazonium tetrafluoroborates)

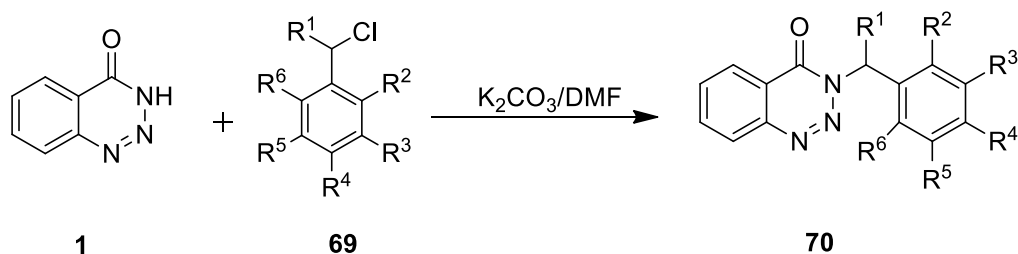
3.4. Alkylation

Although salt formation make an easy access to nucleophilic center but some direct reactions have been carried out on 1,2,3-benzotriazin-4(3*H*)-one (**1**) in the presence of different organic or inorganic bases. Previously, dimethyl sulfate and triethyloxonium tetrafluoroborate were used to alkylating agent but in each case two different products were formed.^{58,59} Recently methyl iodide with silver oxide have been used to obtain **68** from 6a,7,8,9-tetrahydro-3*H*-pyrrolo[2',1':2,3][1,3]oxazino[6,5-*g*][1,2,3]benzotriazine-4,11-dione (**67**) (Scheme 26).⁶⁰ When different benzyl halides (**69**) were made to react with **1** in the presence of potassium carbonate in microwave oven for few a minutes, 3-benzyl-1,2,3-benzotriazin-4(3*H*)-ones (**70**) were

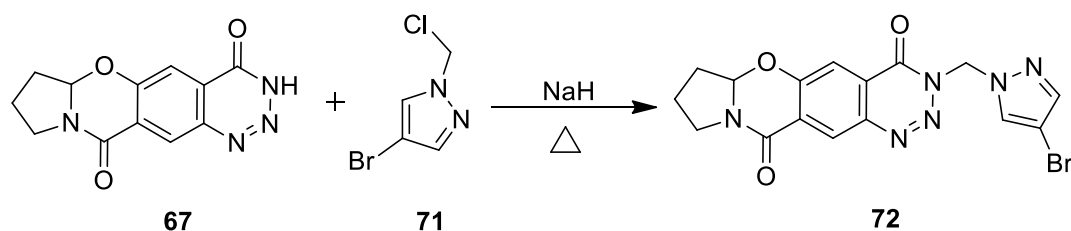
obtained (Scheme 27).⁶¹ Whereas thermal alkylation of **67** in the presence of sodium hydride afforded only **72** (Scheme 28).^{60,62}



Scheme 26. Direct alkylation

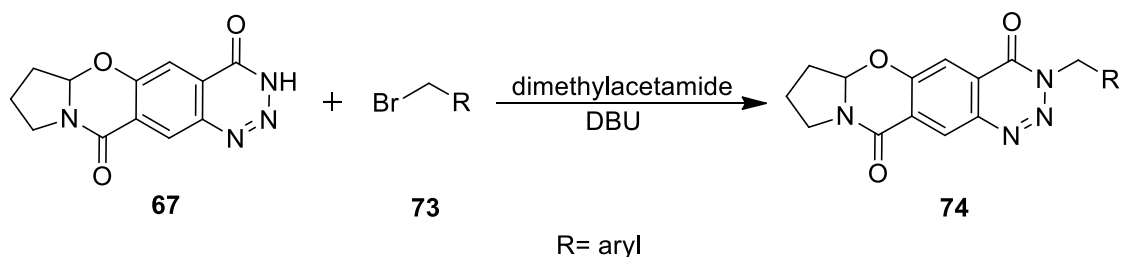


Scheme 27. Microwave assisted alkylation



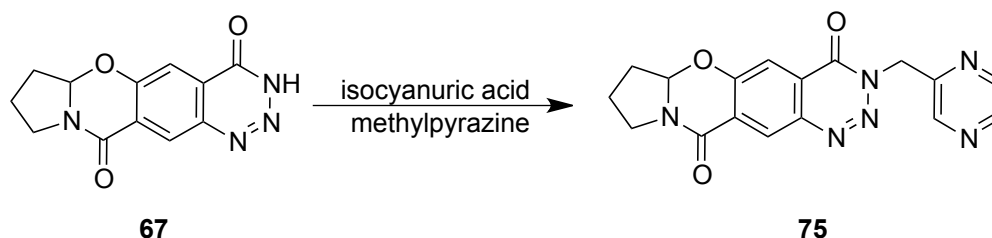
Scheme 28. N-Alkylation under thermal condition

DBU was found to be effective base for the reaction of **67** with a series of aryl or hetarylmethyl bromides (**73**) in dimethylacetamide to give **74** (Scheme 29).⁶⁰



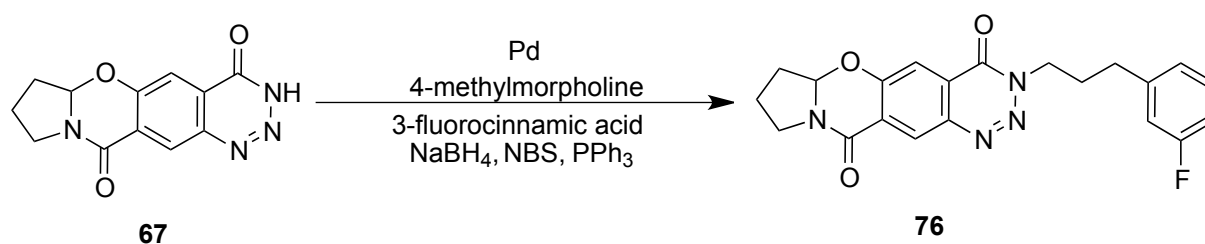
Scheme 29. N-Alkylation of benzotriazinones with DBU

The compound **67** was directly alkylated with methylpyrazine in the presence of isocyanuric acid to obtain **75** (Scheme 30).⁶⁰



Scheme 30. *N*-Alkylation with methylpyrazine

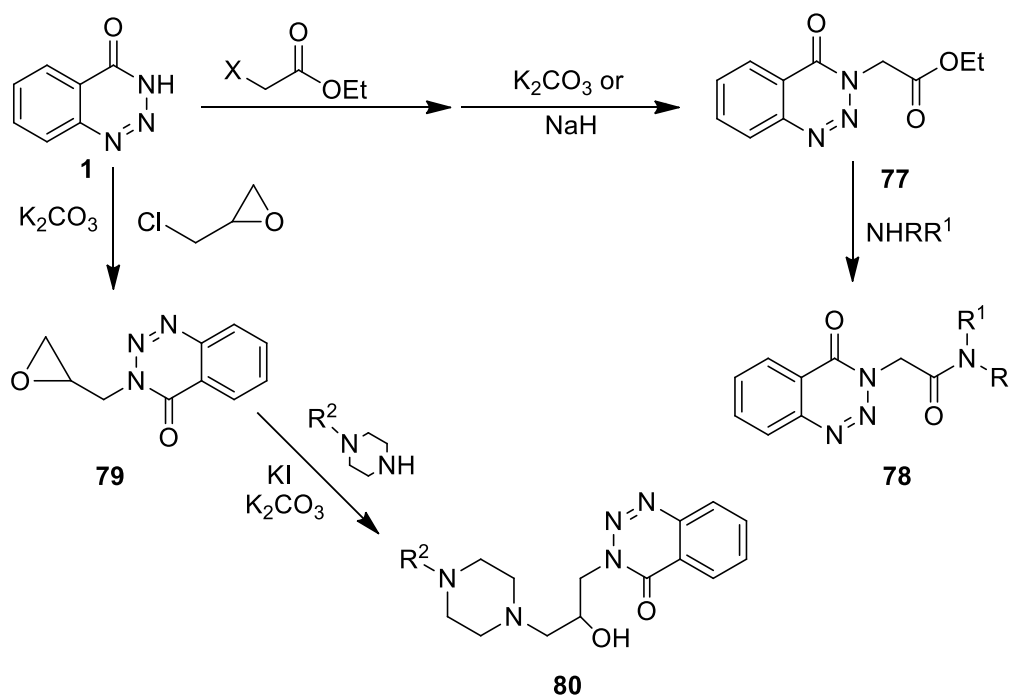
Palladium catalyzed coupling reaction of **67** with 3-fluorocinnamic acid using 4-methylmorpholine, NaBH₄, NBS and PPh₃ afforded **76** (Scheme 31).⁶⁰



Scheme 31. Palladium catalyzed coupling

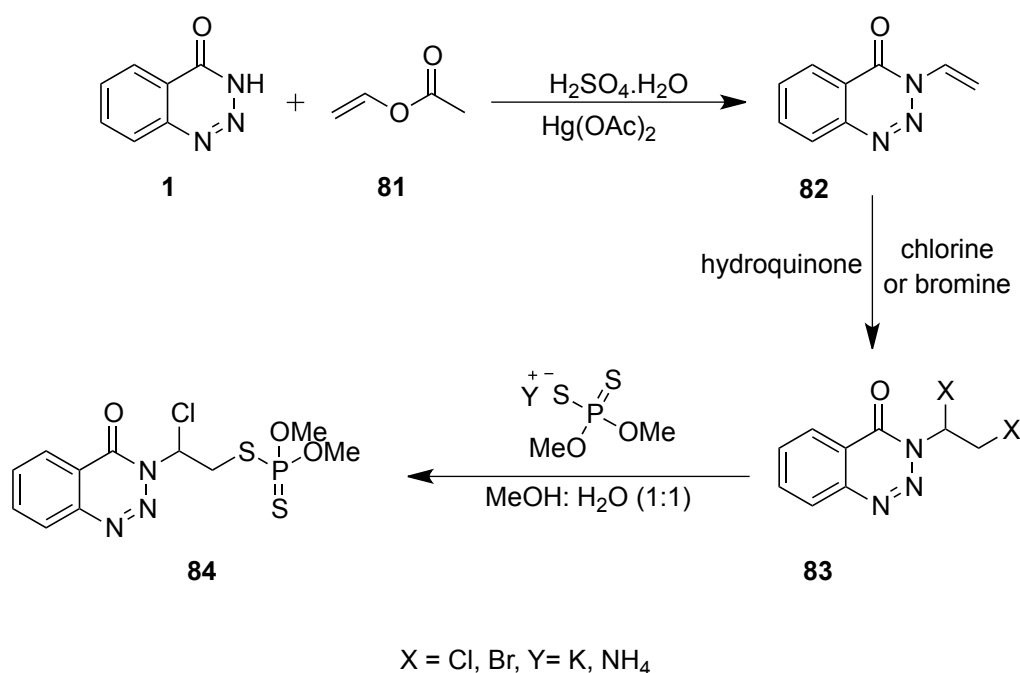
Compound **1** has been combined with different heterocycles through alkyl or acyl junctions to prepare bioactive compounds (Scheme 32). Ethyl 2-(4-oxobenzo[*d*][1,2,3]triazin-3(4*H*)-yl)acetate (**77**) was prepared by reaction of **1** with ethyl chloroacetate. The compound on reaction with amines or hydrazides afforded various amides or hydrazides (**78**) (Scheme 32).^{7,63} In a similar manner 2-chloromethyloxirane, **1** and potassium carbonate were heated at reflux to give 3-(oxiran-2-ylmethyl)-1,2,3-benzotriazin-4(3*H*)-one (**79**) which on further treatment with arylpiperazine and triethylamine in ethanol led to the formation of **80** (Scheme 32).⁶⁴ These derivatives have been claimed to have interesting biological activities such as, anesthetic or antidepressant.

Reaction of **1** with vinyl acetate using sulfuric acid and mercuric acetate led to the formation of 3-vinyl-1,2,3-benzotriazin-4(3*H*)-one (**82**). Halogenation of **82** provided **83** which on further treatment with potassium or ammonium *O,O*-dimethyl phosphorodithioate in aqueous methanol gave 2-chloro-2-(4-oxobenzo[*d*][1,2,3]triazin-3(4*H*)-yl)ethyl *O,O*-dimethyl phosphorodithioate (**84**) (Scheme 33).⁶⁵



X = Br, Cl, R = alkyl, aryl, NH₂, morpholine, pyridine, pyrrolidine, R¹ = H, alkyl, R² = substituted phenyl

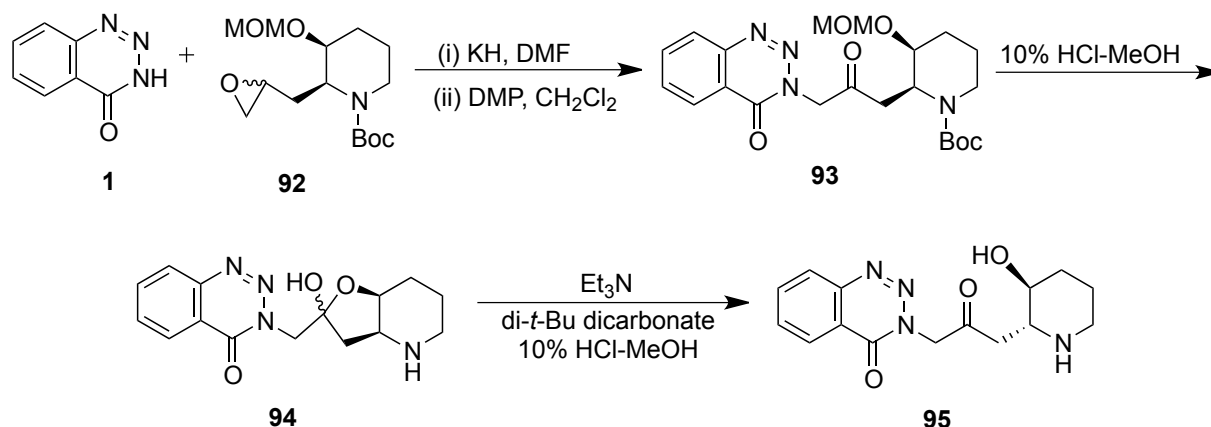
Scheme 32. Synthesis of bioactive benzotriazinone derivatives



Scheme 33. Synthesis of 2-chloro-2-(4-oxobenzo[*d*][1,2,3]triazin-3(4*H*)-yl)ethyl *O,O*-dimethyl phosphorodithioate

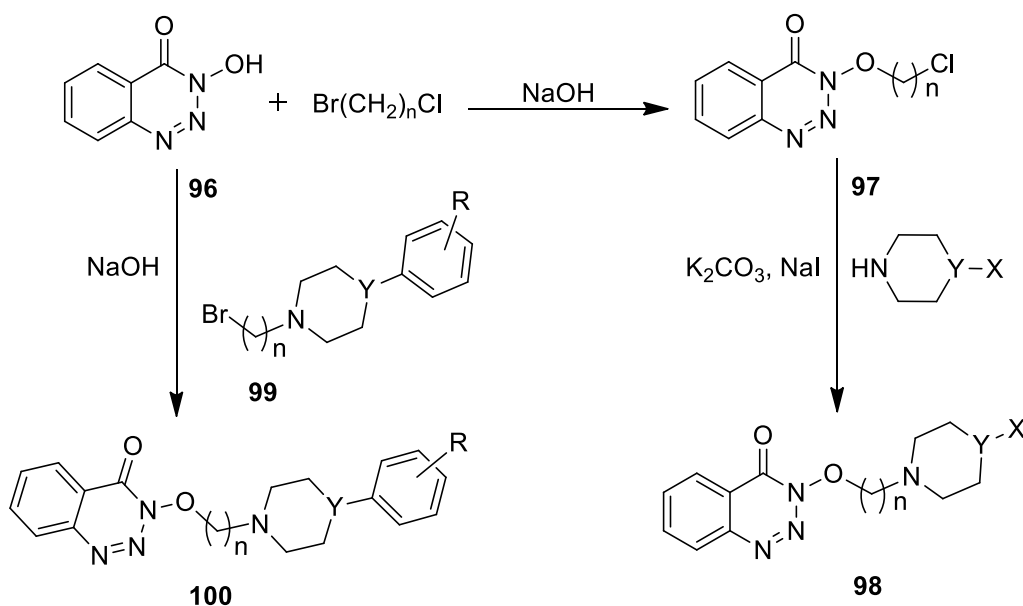
Alkylation of 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-ones (**85**) with long chain alkyl ω -bromoalkanoate (**86**) using sodium methoxide in methanol gave **87** in good yield (Scheme 34).^{66,67}

Epoxides have also been explored for the alkylation of **1**. An epoxide **92** using solution of potassium hydride in dimethylformamide followed by oxidation with Dess–Martin periodinane (DMP) in dichloromethane afforded **93**. The hydroxyl group protection was removed with methanolic hydrochloric acid prior to its conversion to **95** (Scheme 36).⁷³



Scheme 36. Reaction with epoxides

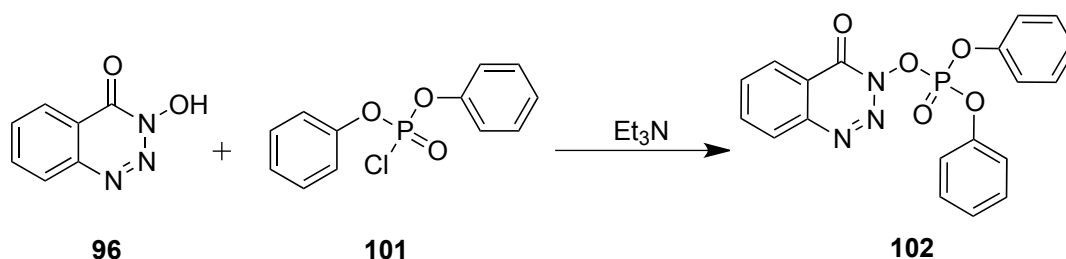
3-Hydroxy-1,2,3-benzotriazin-4(3H)-one (**96**) can be easily alkylated in basic solution. Its reaction with bromochloroalkanes gave 3-(chloroalkoxy) derivatives (**97**) which were further treated with piperidine or 1-chloropiperazine in the presence of potassium carbonate and sodium iodide to afford **98** (Scheme 37).^{6,74} Whereas another way to prepare the similar skeleton *i.e.* **100** was the reaction of **96** with **99** using sodium hydroxide as base (Scheme 37).⁷⁵



R = dialkylamine, pyridine, pyrrolidine. X = H, Cl, Y = C, N, R = H, halo, OMe

Scheme 37. Synthesis of benzotriazinones derivatives containing piperazine moiety

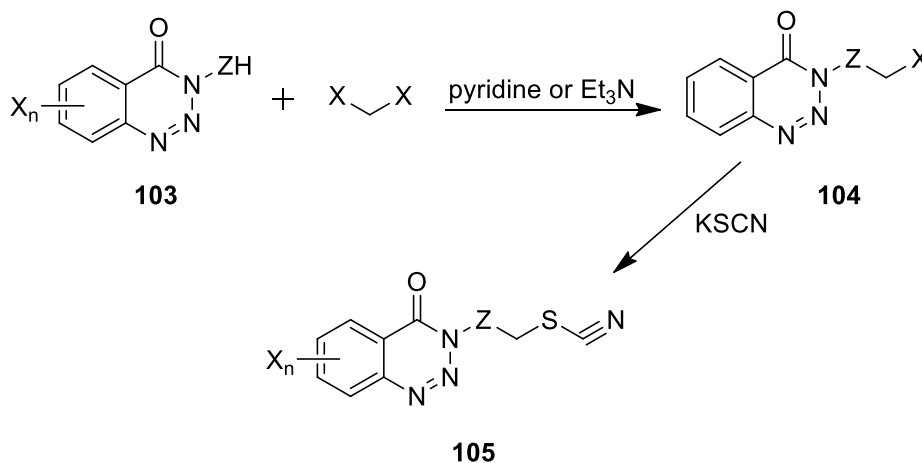
Some benzotriazinone derivatives have been also used as condensating agents like [(1,2,3-benzotriazin-4-one)-3-yl]diphenyl phosphate (**102**). It was prepared by the reaction of 3-hydroxy-1,2,3-benzotriazin-4(3*H*)one (**96**) with diphenyl phosphorochloridate (**101**) in the presence of triethylamine (Scheme 38).⁷⁶



Scheme 38. Synthesis of benzotriazinone based condensating agent

3.5. Thiocyanation

Reaction of 3-hydroxy or 3-thio-1,2,3-benzotriazin-4(3*H*)-ones with dihalomethane generate a reaction intermediate **104**, which reacted with potassium thiocyanate and produced **105** (Scheme 39).⁷⁷



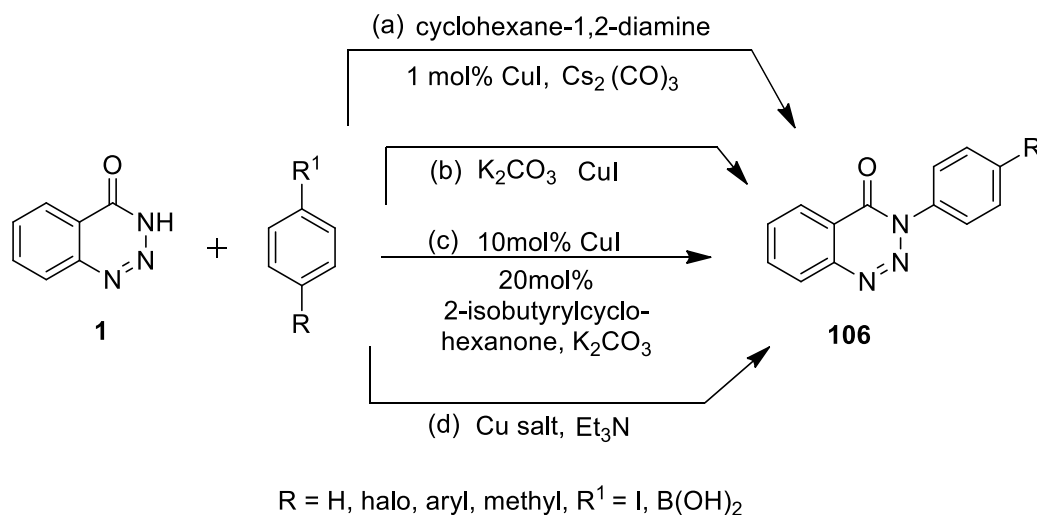
Z = O, S, n = 0-4, X = halo, alkyl, CF₃, OCF₃, CN, CO₂R

Scheme 39. Thiocyanation

3.6. N-Arylation

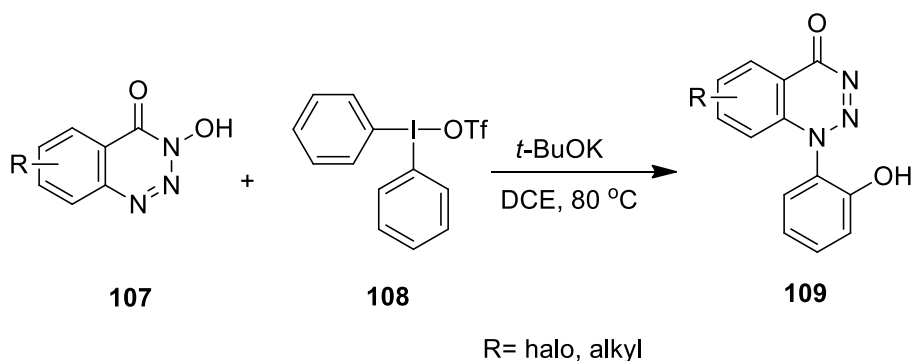
Ullman coupling of 1,2,3-benzotriazin-4(3*H*)-one (**1**) with iodobenzene was successfully carried out by using CuI in the presence of cesium carbonate and cyclohexanediamine (path: a) or with potassium carbonate (path: b) to afford *N*-aryl-1,2,3-benzotriazin-4(3*H*)-ones (**106**) (Scheme 40).^{78,79} Whereas arylation with 4-methyliodobenzene using CuI (10 mol%) and 2-isobutyrylcyclohexanone (20 mol%, path: c) mixture provided excellent 95% yield (Scheme 40).³⁷ Recently another method was designed for

the access of **106** by Cu-mediated coupling reaction of **1** with arylboronic acids (path: d), where different Cu salts were used for the synthesis of **106** and found that copper acetate gave better results as compare to CuBr, Cu(OAc)₂, Cu(OTf)₂ and CuI (Scheme 40).⁸⁰



Scheme 40. *N*-Arylation through coupling reactions

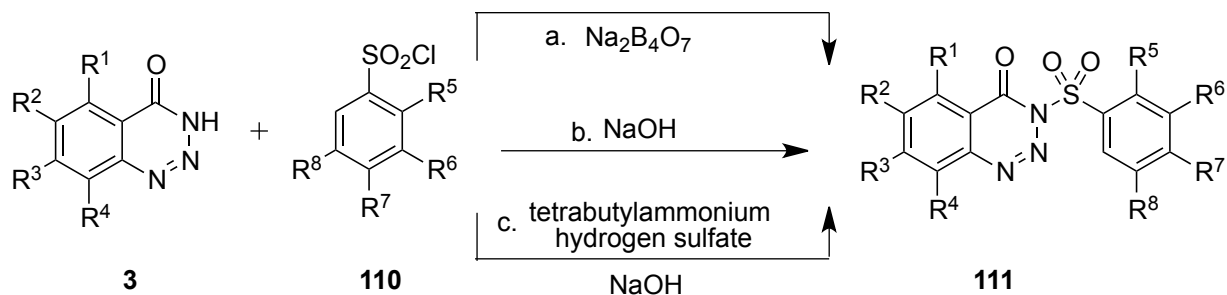
Recently Shi *et al.* have reported the *N*-arylation of 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-ones (**109**), through *O*-arylation of **107** with **108** followed by [3,3] rearrangement in good yield (Scheme 41).⁸¹



Scheme 41. *N*-Arylation of hydroxyl benzotriazinones followed by rearrangement

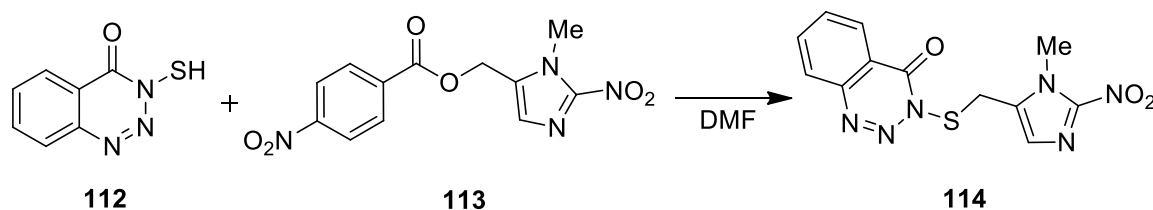
3.7. Sulfur Containing Derivatives

3-(Phenylsulfonyl)benzo[1,2,3]triazin-4(3*H*)-ones derivatives (**111**) have been prepared under different conditions by reacting **3** and benzenesulfonyl chloride (**110**). First reaction was studied in 24% aqueous sodium hydroxide but later better results were obtained using anhydrous borax or tetrabutylammonium hydrogen sulfate and sodium hydroxide mixture (Scheme 42).⁸²⁻⁸⁴



Scheme 42. Sulfonamide synthesis

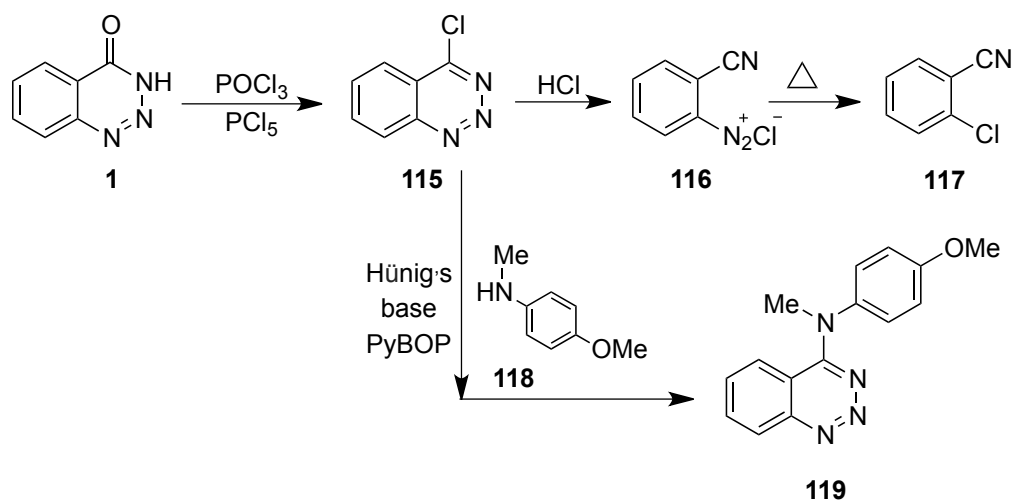
3-Thiobenzo[1,2,3]triazin-4(3*H*)-one (**112**) gave **114** when reacted with (1-methyl-2-nitro-1*H*-imidazol-5-yl)methyl 4-nitrobenzoate (**113**) in DMF (Scheme 43).^{85,86}

Scheme 43. *S*-Alkylation of mercaptobenzotriazinone

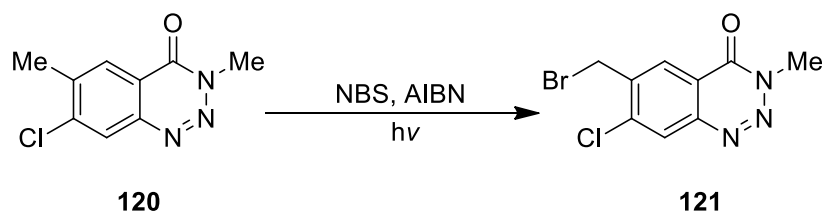
3.8. Halogenation

Treatment of **1** with a mixture of phosphoryl chloride and phosphorus pentachloride produced 4-chlorotriazine (**115**), which change into 2-chlorobenzonitrile (**117**) on decomposition through intermediate diazonium salt (**116**) (Scheme 44).^{48,87} 4-Chlorotriazine (**115**) have been reported to undergo normal nucleophilic substitution with *N*-methyl-4-methoxyaniline (**118**) in the presence of Hünig's base and PyBOP to give **119** (Scheme 44).^{88,89}

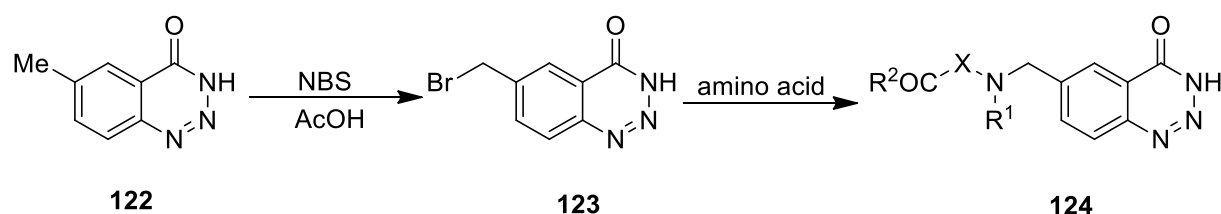
Bromination of 7-chloro-3,6-dimethyl-1,2,3-benzotriazin-4(3*H*)-one (**120**) under UV produced 7-chloro-6-bromomethyl-3-methyl-1,2,3-benzotriazin-4(3*H*)-one (**121**). The reaction was performed by treating the substrate with *N*-bromosuccinimide in the presence of (2,2-azobis(2-methylpropionitrile)) (AIBN) or benzoyl peroxide (Scheme 45).⁹⁰ In another reaction, 6-methyl-1,2,3-benzotriazin-4(3*H*)-one (**122**) was brominated with *N*-bromosuccinimide in glacial acetic acid giving 6-bromomethyl-1,2,3-benzotriazin-4(3*H*)-one (**123**), which was further converted into biologically active benzotriazinone-derived compounds containing amino acids and peptides moieties (**124**) (Scheme 46).^{18,19}



Scheme 44. Reaction with phosphoryl chloride



Scheme 45. Selective halogenation with NBS

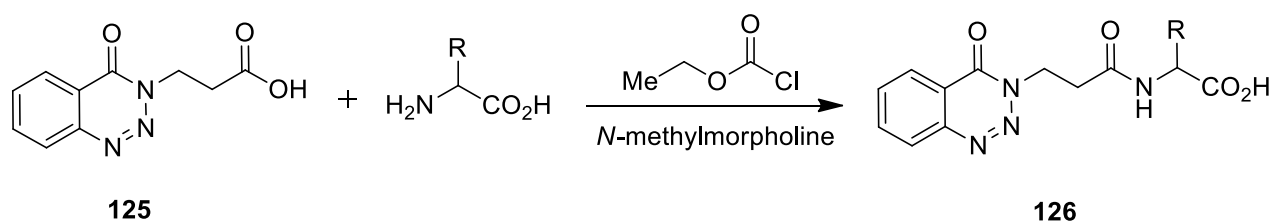
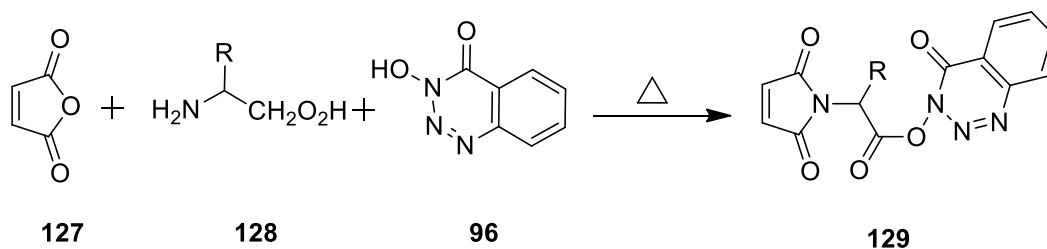


$R^1 = \text{H, alkyl, alkenyl, alkynyl}, R^2 = \text{H, OH, amino acids or peptide. X = aryl.}$

Scheme 46. Preparation of benzotriazinones derived compounds containing amino acids or peptide moieties

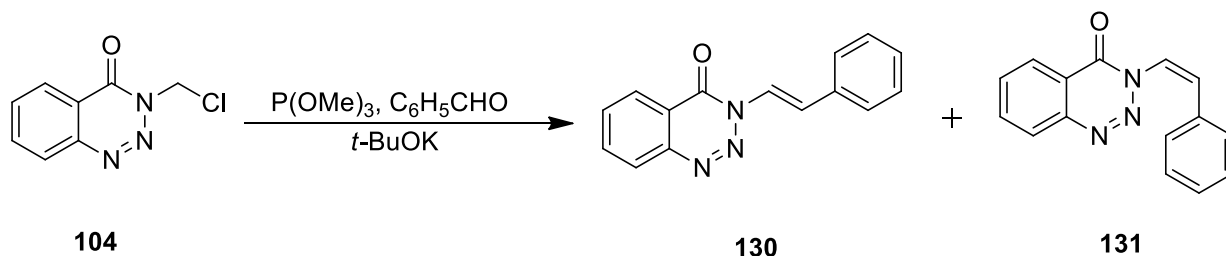
3.9. Condensation Reactions

3-(3,4-Dihydro-4-oxo-1,2,3-benzotriazin-3-yl)propanoyl amino acids (**126**) have been synthesized from 3-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)propionic acid (**125**) and amino acids or their hydrochlorides using ethyl chloroformate as a condensating agent in the presence of *N*-methylmorpholine (Scheme 47).⁶⁹ Thermal condensation of **1** or 6-chloro-1,2,3-benzotriazin-4(3*H*)-one with amino acids have been reported to provide 3*H*-1,4-benzodiazepin-(1*H*, 4*H*)-2,5-diones in moderate to good yield.⁹¹ In one pot reaction of **96** with amino acids (**128**) and maleic anhydride (**127**) yielded **129** as final product (Scheme 48).^{92,93}

Scheme 47. 3-(4-Oxobenzo[*d*][1,2,3]triazin-3(*4H*)-yl)propanoic acid reaction with amino acid

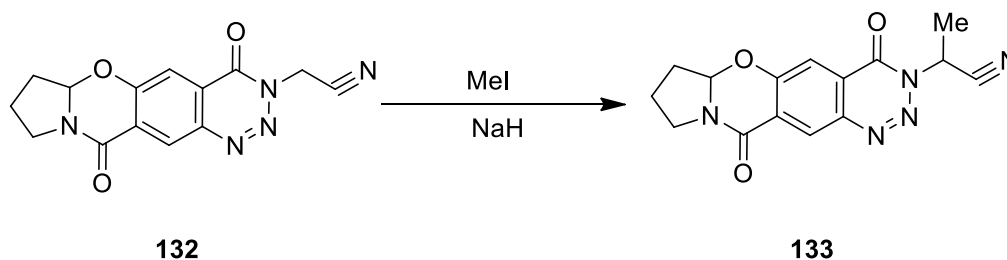
Scheme 48. 3-Hydroxy-1,2,3-benzotriazinone reaction with amino acids

3-*N*-Chloromethyl-1,2,3-benzotriazin-4(*3H*)-one (**104**) in combination with triethylphosphite, potassium *t*-butoxide and benzaldehyde generates both *E* and *Z* isomers two isomers of 3-styryl-1,2,3-benzotriazin-4(*3H*)-one (**130** and **131**) (Scheme 49).⁹⁴

Scheme 49. 3-Styryl-1,2,3-benzotriazin-4(*3H*)-one synthesis

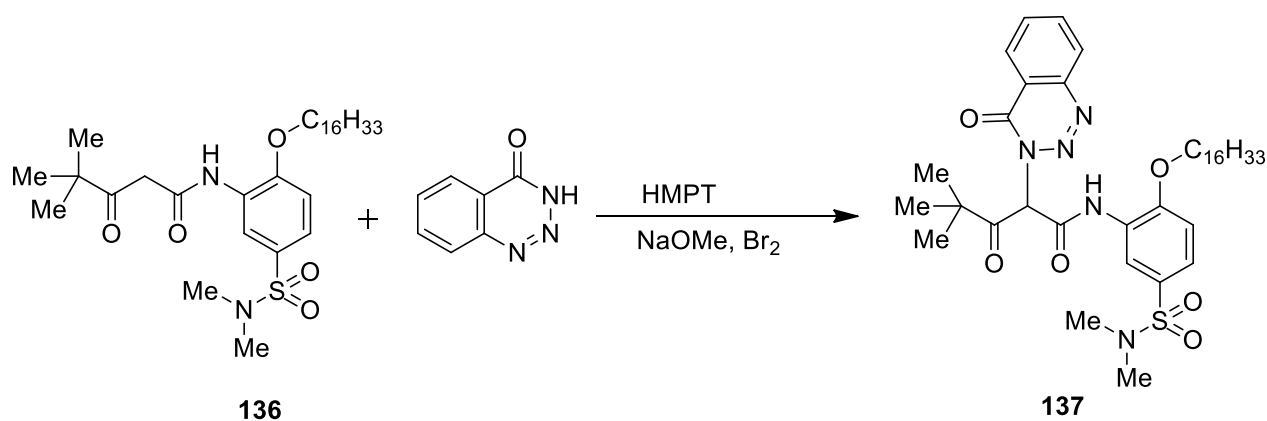
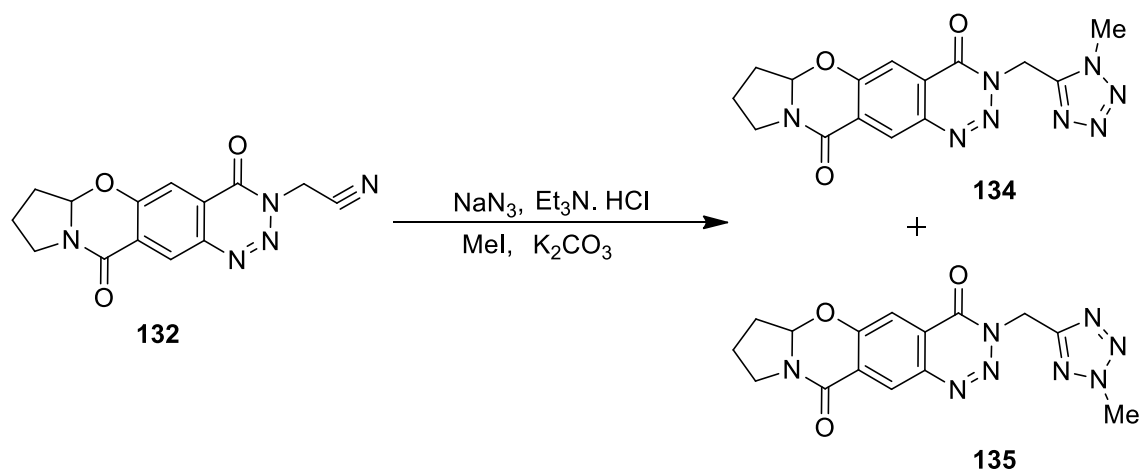
3.10. Active Methylene Derivatives

The compound **132** when reacted with methyl iodide in the presence of sodium hydride gave **133** (Scheme 50).



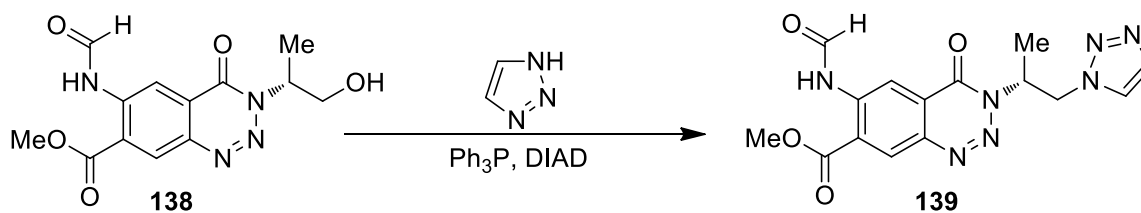
Scheme 50. Methylation reaction

While reaction with sodium azide in the presence of triethylamine hydrochloride yielded a tetrazol substituted benzotriazinone derivative. Which produced two isomeric compounds **134** and **135** after methylation with methyl iodide in the presence of potassium carbonate (Scheme 51).⁶⁰ While 2-hexadecyloxy-5-dimethylaminosulfonyl-pivaloylacetyl-anilide (**136**) on reaction with 1,2,3-benzotriazin-4(3*H*)-one (**1**) in bromine, sodium methoxide and hexamethylphosphoric triamide (HMPT) gives **137** (Scheme 52).⁹⁵⁻⁹⁷

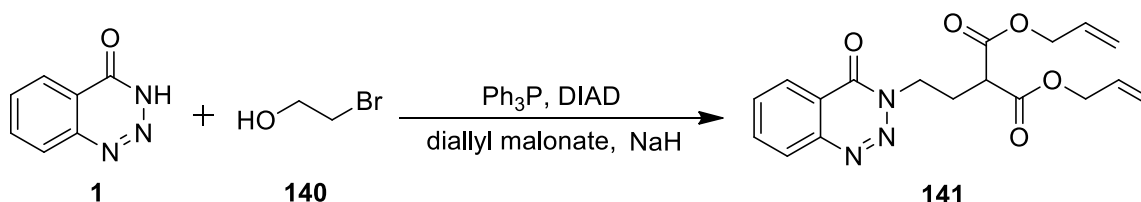


3.11 Mitsunobu Reactions

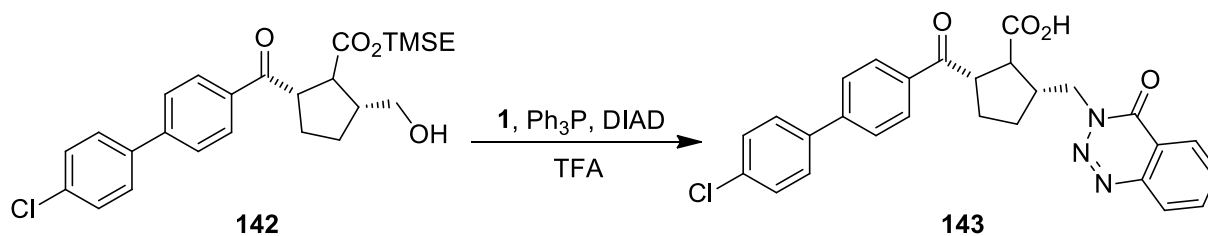
1,2,3-Triazole has been introduced to produce **139** from **138** using Mitsunobu reaction (Scheme 53).⁹⁸ Mitsunobu reaction has been also successfully used for the synthesis of 3-(2-bromoethyl)-1,2,3-benzotriazin-4(3*H*)-one, which was further reacted with diallyl malonate using sodium hydride as a base to form 2-(2-((3*H*)-benzo-1,2,3-triazin-4-on-3-yl)ethyl)malonate (**141**) (Scheme 54).⁹⁹ Similarly, **142** underwent Mitsunobu reaction with **1** to produce **143** (Scheme 55).^{100,101}



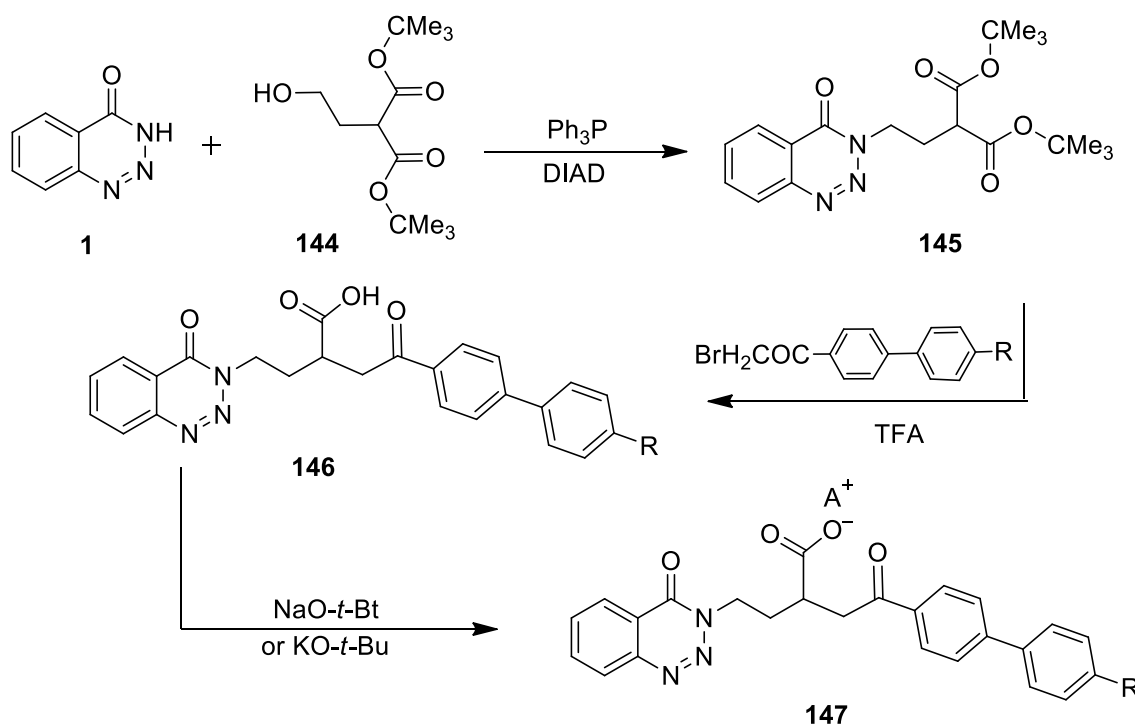
Scheme 53. Mitsunobu reaction with triazole



Scheme 54. Mitsunobu reaction with diallyl malonate



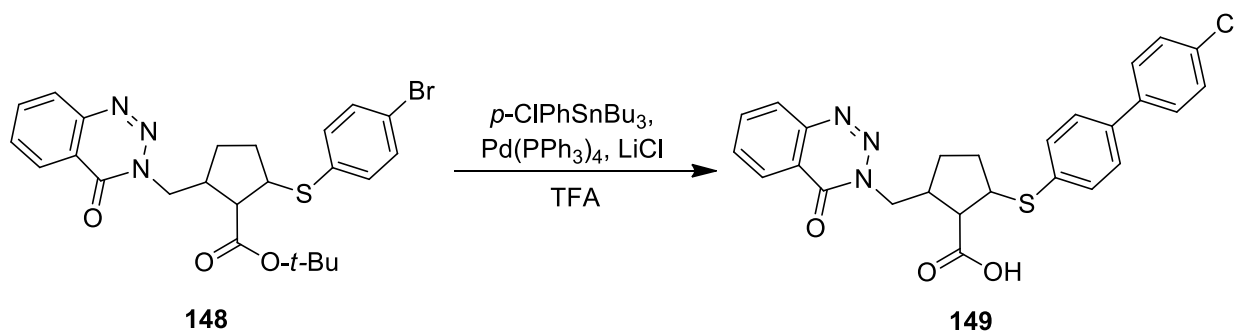
Scheme 55. Reaction with triphenylphosphine and further hydrolysis by TFA



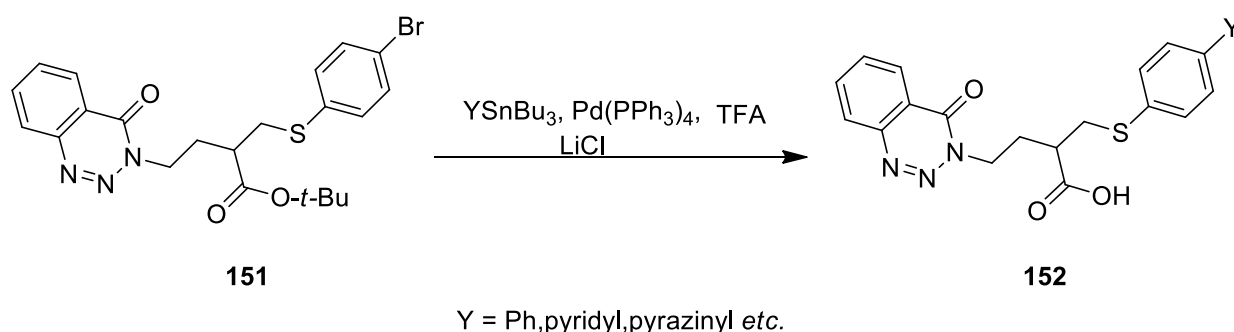
R = OEt, Br, Me, Et, Bu, A^+ = Na, K

Scheme 56. Mitsunobu reaction with di(*t*-butyl) 2-(2-hydroxyethyl)malonate

In another reaction **1** was taken with di(*t*-butyl)-2-(2-hydroxyethyl)malonate (**144**) in the presence of triphenylphosphine and DEAD to afford **145** as a precursor for the synthesis of **146** and their sodium or potassium salts (**149**) (Scheme 56).^{102,103} In the same fashion, **148** and **150** were prepared and further converted into **149** (Scheme 57)¹⁰⁴ and **151** respectively (Scheme 58).¹⁰⁵



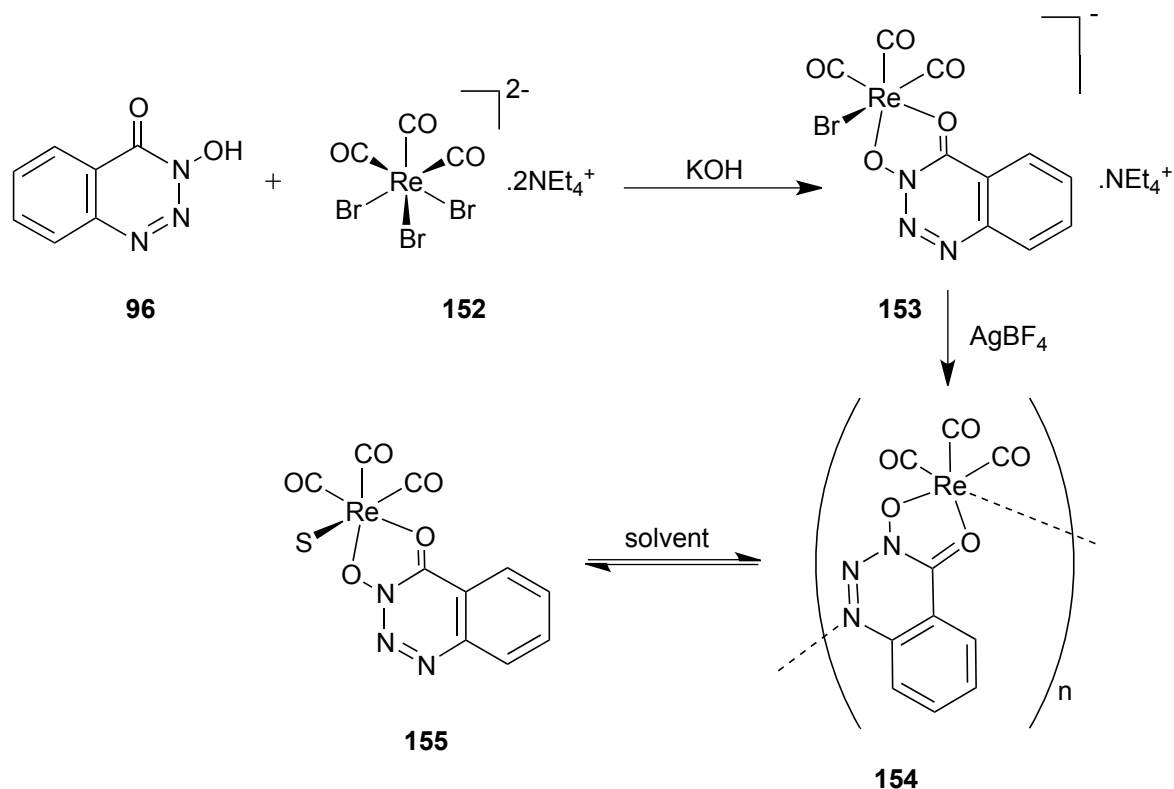
Scheme 57. Stille coupling reaction

Scheme 58. Stille coupling with tri-*n*-butyltin hydride

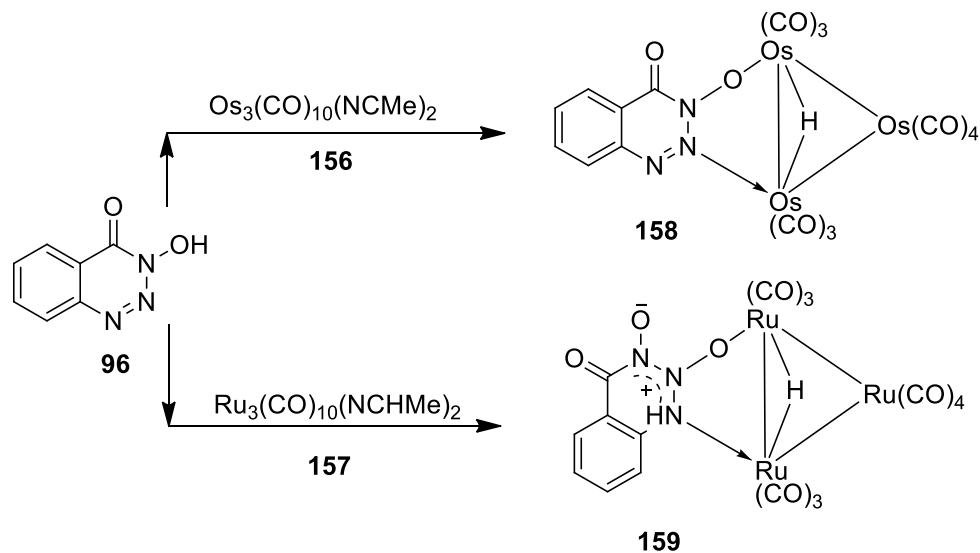
3.12. Metal Complexes

3-Hydroxy-1,2,3-benzotriazin-4(3*H*)-one (**96**) has been investigated for the formation of metal complexes. The ionic rhenium complex $[\text{ReBr}(\text{C}_7\text{H}_4\text{N}_3\text{O}_2)(\text{CO})_3][\text{NEt}_4]$ (**153**) was synthesized from **96** and $[\text{ReBr}_3(\text{CO})_3][\text{NEt}_4]_2$ (**152**) using potassium hydroxide as a base. The structure of **153** was confirmed by crystallography and when stirred with AgBF_4 , a polymeric entity **154** was obtained. On exposure of **154** to polar solvents, such as methanol produced the monomeric adduct **155** (Scheme 59).¹⁰⁶

Kumaresan *et al.* have reported the 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-one complexes with osmium and ruthenium clusters. Lightly ligated complex $\text{Os}_3(\text{CO})_{10}(\text{NCMe})_2$ (**156**) with 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-one (**96**) in dichloromethane gave $(\mu\text{-H})\text{Os}_3(\text{CO})_{10}(\mu_2\text{-}(2.3\text{-}\eta^2)\text{-}(\text{O})\text{NNNC}_7\text{H}_4\text{O})$ (**158**) (Scheme 61). Whereas $\text{Ru}_3(\text{CO})_{10}(\text{NCMe})_2$ complex (**157**) with **96** in dichloromethane afforded *N*-oxide complex $(\mu\text{-H})\text{Ru}_3(\text{CO})_{10}(\mu_2\text{-}(1.2\text{-}\eta^2)\text{-}(\text{O})\text{NNN}(\text{O})\text{C}_7\text{H}_4\text{O})$ (**159**) with 11% yield (Scheme 60).¹⁰⁷



Scheme 59. Rhenium complex

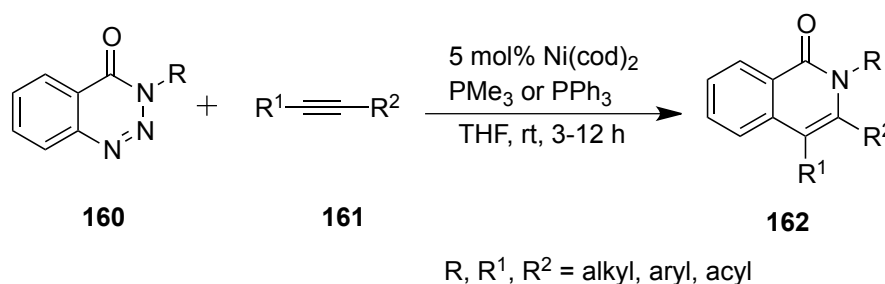


Scheme 60. Osmium and ruthenium complexes

3.13. Ring Transformations

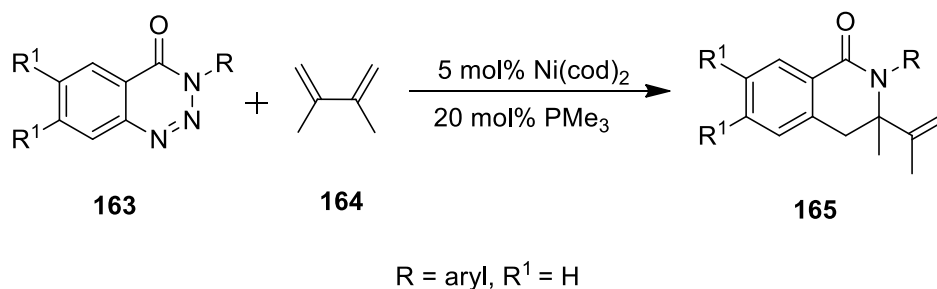
Under certain conditions 1,2,3-benzotriazin-4(3H)-ones or their derivatives can be transformed into other heterocyclic systems. For example, 1,2,3-benzotriazin-4(3H)-one and its 6-chloro derivative on thermal condensation with amino acids produced 3H-1,4-benzodiazepine-(1H,4H)-2,5-diones with moderate to

good yield. This cyclocondensation is believed to proceed through the formation of an iminoketene.⁹¹ Transition-metal catalyzed annulation reactions have been described to be a powerful methodology for the construction of substituted 1(2*H*)-isoquinolines from 1,2,3-benzotriazin-4(3*H*)-ones. Under Nickel (0) and phosphine ligand catalytic effect **160** was found to lose nitrogen and insert acetylenes (**161**) to give a wide range of substituted 1(2*H*)-isoquinolones (**162**) (Scheme 61).¹⁰⁸ Recently Wang and co-workers have reported the detailed mechanism of this transformation using DFT calculations and explained that this process involved nitrogen extrusion, carbometalation, Ni–C bond insertion, (rate determining step) and reductive elimination.¹⁰⁹

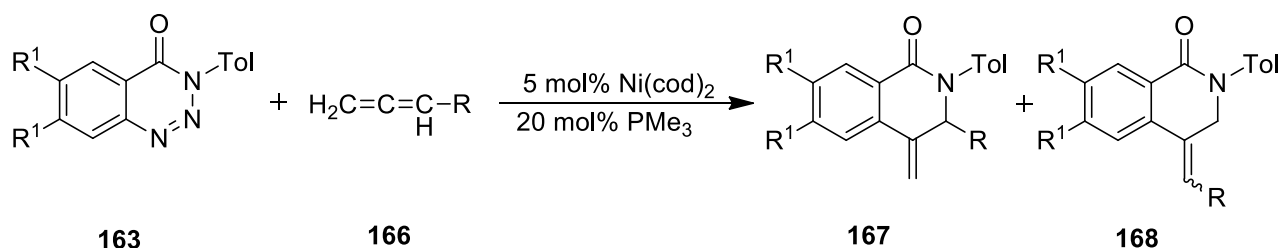


Scheme 61. Insertion reaction of alkynes

Instead of alkynes, when alkenes (**164**) or allenes (**166**) were used, 3-substituted 3,4-dihydroisoquinolin-1(2*H*)-ones (**165**, **169**, **169**) were obtained (Schemes 62 and 63). Many phosphine ligands including PMe_2Ph , PMePh_2 , PPh_3 , $\text{P}(t\text{-Bu})_3$, dppb (1,4-bis(diphenylphosphino)butane), were used to study their effects on product yield and selectivity. Results shown that allenes and unsymmetrical alkenes produced regio or enantio-isomers, however selectivity increased when dppf (1,10-bis(diphenylphosphino)ferrocene) was employed as a phosphine ligand.^{37,110} When annulation reaction of **163** ($\text{R}^1=\text{H}$) was performed with isocyanides (**169**) then 3-(arylimino)-2-*p*-tolylisoindolin-1-one (**170**) was obtained as the product. This reaction was examined with different palladium catalysts; $\text{CpPd}(\pi\text{-allyl})$ with PMe_3 showed best results with 94% yield while other phosphine ligands gave inferior results: $\text{P}(n\text{-Bu})_3$ (92%), PCy_3 (92%), $\text{P}(t\text{-Bu})_3$ (11%), PPh_3 (17%), dppf (15%) and even the reaction fails to occur in the presence of $\text{Ni}(\text{cod})_2$ and $\text{P}(\text{Me})_3$ mixture (Scheme 64).¹¹¹

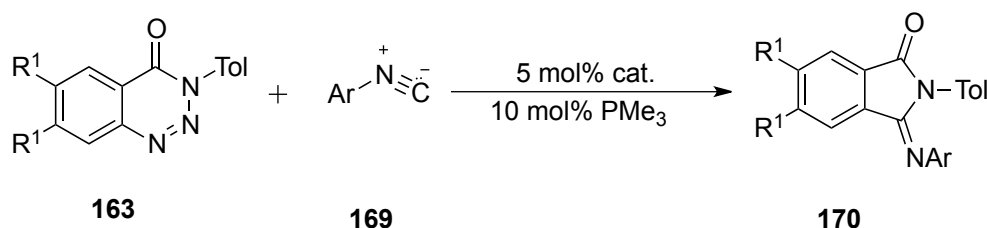


Scheme 62. Insertion reaction of 1,3-dialkene



R = (CH₂)₂OBn, (CH₂)₂OSi^t-BuMe₂, (CH₂)₂OH, (CH₂)₃CN, Hex, *t*-Bu, Si^t-BuMe₂, R¹ = Me

Scheme 63. Reaction with unsymmetrical allenes

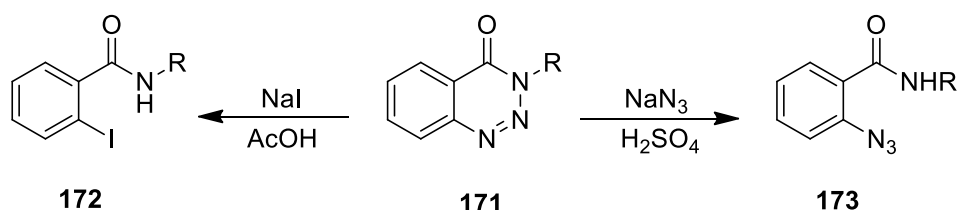


R¹ = H, Ar = 2,6-xylyl

Scheme 64. Reaction with isocyanides

3.14. Oxidation and Reduction

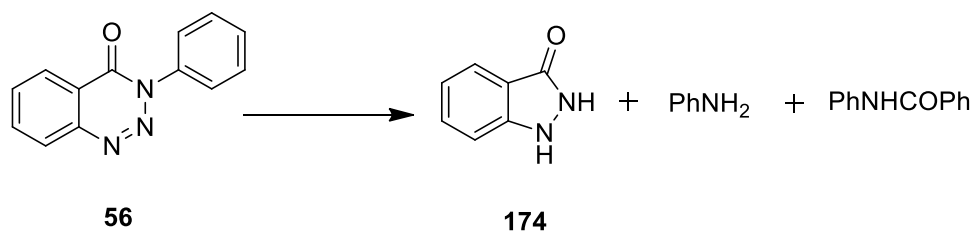
Under Schmidt reaction conditions (sodium azide and sulfuric acid) 3-aryl-1,2,3-benzotriazin-4(3H)-ones decomposed to **173** (Scheme 65) while using sodium iodide in acetic acid **171** transformed to **172** (Scheme 65).^{112,113} 3-(2-Azidobenzoyl)benzo[1,2,3]triazin-4(3H)-one has been reported to alter into benzazetidinone after lose of N₂ molecule, which produced 2-(2-azidophenyl)-3,1-benzoxazin-4-ones after valence tautomerization and electrocyclization on boiling in *O*-cresol.¹¹⁴



R = H, aryl

Scheme 65. Decomposition of benzotriazinones ring

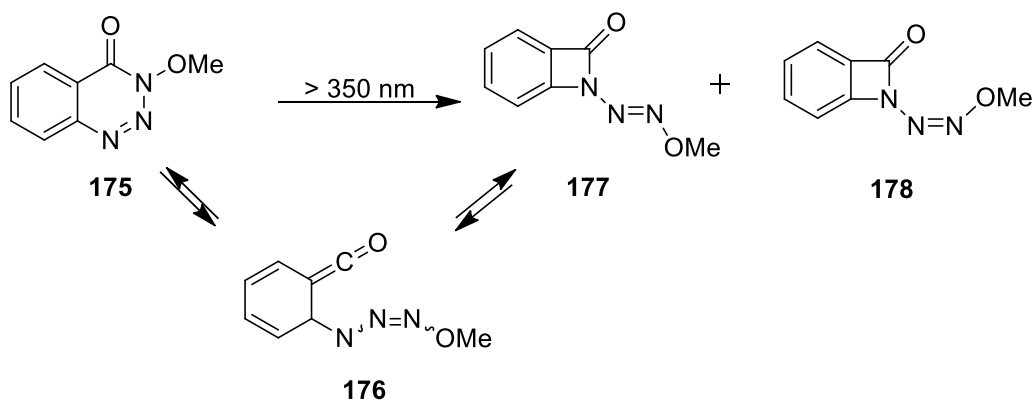
Electrochemical reduction of 3-phenyl-1,2,3-benzotriazinone (**56**) in aqueous alcoholic solution with HCl at a Hg electrode produced **176** as the major product along with aniline and benzanilide. However in DMF, the only isolated product was benzanilide (Scheme 66).¹¹⁵



Scheme 66. Electrochemical reduction reaction

3.15. Photolysis

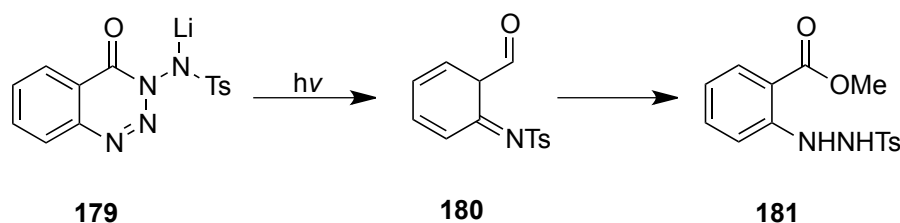
Photolysis of 3-phenylbenzotriazinones in THF has been reported to give 9-acridones.⁵² Whereas 3-methoxy- and 3-*N*-butoxy-1,2,3-benzotriazin-4(3*H*)-ones under irradiation ($\lambda > 350$ nm) at 10 K have been monitored by infrared spectroscopy, indicated that carbonyl peak of precursor decreased with the appearance of new carbonyl band at 1823 and 1806 cm^{-1} . These peaks suggested that **175** transformed into a mixture of *Z* and *E* isomers of 1-(methoxyazo)benzazetidinones (**177**, **178**), which were found to be interconvertible and also revert to starting material (Scheme 67). Tomioka and Komatsu explained the mechanism involving the formation of cyclohexadienylienes (**176**) as a reverse reaction of 1,3-sigmatropic shift initiated photo cleavage of CO-N bond followed by cyclization to azetidinones (**177**, **178**). Alkyl derivative of **1** was also checked for photo reaction but no change was observed. This study proved that alkoxy group at third position exerts a special effect on the reaction process.¹¹⁶

Scheme 67. Photolysis of *N*-methoxy-1,2,3-benzotriazinone

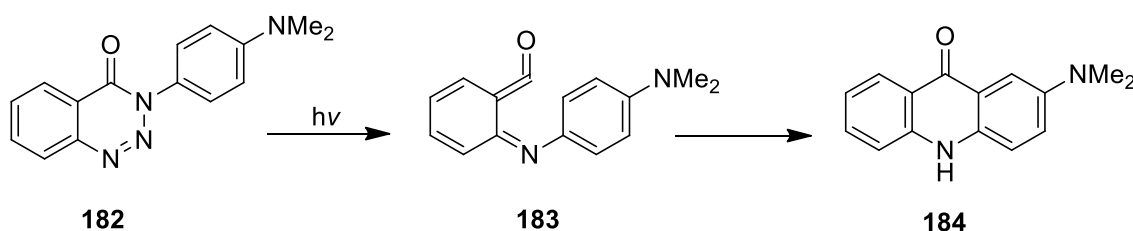
The photochemical reactivities of 3-hydroxy-1,2,3-benzotriazinone and tris[3-hydroxy-1,2,3-benzotriazin-4(3*H*)-one]iron(III) have been studied in solution at low temperature. During photoexcitation N_2 released and generated oxime ketenes from the collapse of diradicals as precursor for the formation of 4-membered lactam ring. It was observed that the kinetics for the formation and decay of the ketene were strongly influenced by the presence of Fe(III) center, which leads to an increase the life time of the diradical in solution, persisting sufficiently long to react with solution

substrates.¹¹⁷ It has been claimed that, under visible wavelength tris[3-hydroxy-1,2,3-benzotriazin-4(3*H*)one]iron(III) released N₂ molecule and produce localized radical intermediates capable of cleaving DNA, which can be a new approach to photo nuclease design for biological applications.¹¹⁸

On photolysis, the compound **179** was found to be converted into methyl 2-(2-tosylhydrazinyl)benzoate (**181**) through intermediate iminoketene (**180**).¹¹⁹ While under photochemical reaction **182** changed into **184** through reaction intermediate **183** (Scheme 69).¹²⁰⁻¹²²



Scheme 68. Photolytic reaction of lithium (4-oxobenzo[1,2,3]triazin-3(4*H*)-yl)(tosyl)amide (**179**)



Scheme 69. Photolytic conversion of 3-(4-(dimethylamino)phenyl)benzo[1,2,3]triazin-4(3*H*)-one to 2-(dimethylamino)acridin-9(10*H*)-one

4. APPLICATIONS

Although in the beginning study of 1,2,3-benzotriazin-4(3*H*)-one (**1**) and its diverse applications lead to the discovery of azinphos-methyl (**185**) (Figure 2) as an organophosphorus insecticide and a number of its phosphorus and sulfur containing analogues derivatives were synthesized. Because of the adverse effects **185** and allied compounds were banned. In this review, 1,2,3-benzotriazin-4(3*H*)-one applications in other fields than agriculture have been highlighted. A variety of 1,2,3-benzotriazin-4(3*H*)-ones derivatives exhibits pharmacological and imaging properties which are discussed below.

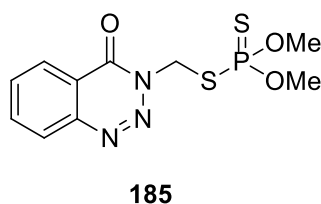


Figure 2. Azinphos-methyl

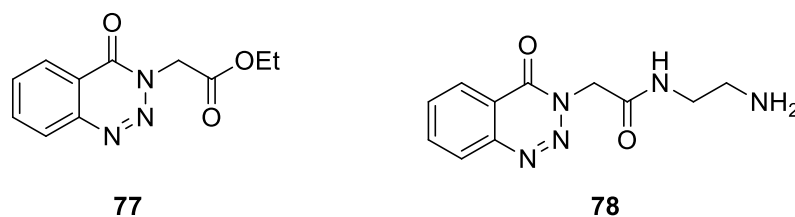
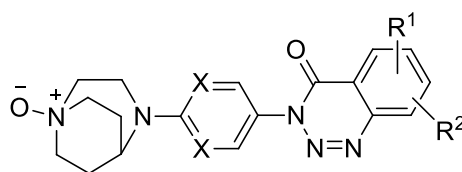


Figure 4. Anesthetic agent

4.1.3. CNS disordering curing Agents

1,2,3-Benzotriazin-4(3H)-one derivatives like **61** have been found to inhibit 3H- α -bungarotoxine binding in rat brain and may be useful for pharmaceutical compositions as cholinergic ligands at the nicotinic acetylcholine receptors, modulators of monoamine receptors and transporters (Figure 5). Thus these compounds have been claimed to be effective for disorder of central and peripheral nervous system related to muscle contractions, endocrine diseases or neurodegenerative diseases related to pain or inflammation.^{54-56,124,125}

**61**

$R^1, R^2 = H, \text{ halo, trifluoromethyl, alkyl, sulfonyl etc. } X = C, N$

Figure 5. 3H- α -Bungarotoxine binding inhibitor

Some compounds with structures like **188-190** (Figure 6) have been claimed as useful agent for the prevention and treatment of cerebral insufficiency, in regulation of breathing cognitive abilities related to memory impairment and imbalances in neuronal activity between different brain regions. Actually these act as enhancing agents of glutamatergic synaptic response in brain networks which is responsible for basic and higher behavior orders.^{60,98}

Matrix metalloproteinases (MMPs) are a class of zinc dependent proteolytic enzyme involved in the turnover of extracellular matrix. Up regulation of MMPs has been associated with various pathologies including arthritis (MMP-1) and cancer (MMP-2). Activity of **149** was checked on mouse metastasis model and the result displayed that it inhibits MMPs and may be valuable for therapeutic approach.¹⁰⁵ Compounds, **147** and **143**, have also been found to be matrix metalloproteinase inhibitors and have been suggested as drugs for the treatment and prevention of cerebral diseases (Figure 6).^{100,102,103}

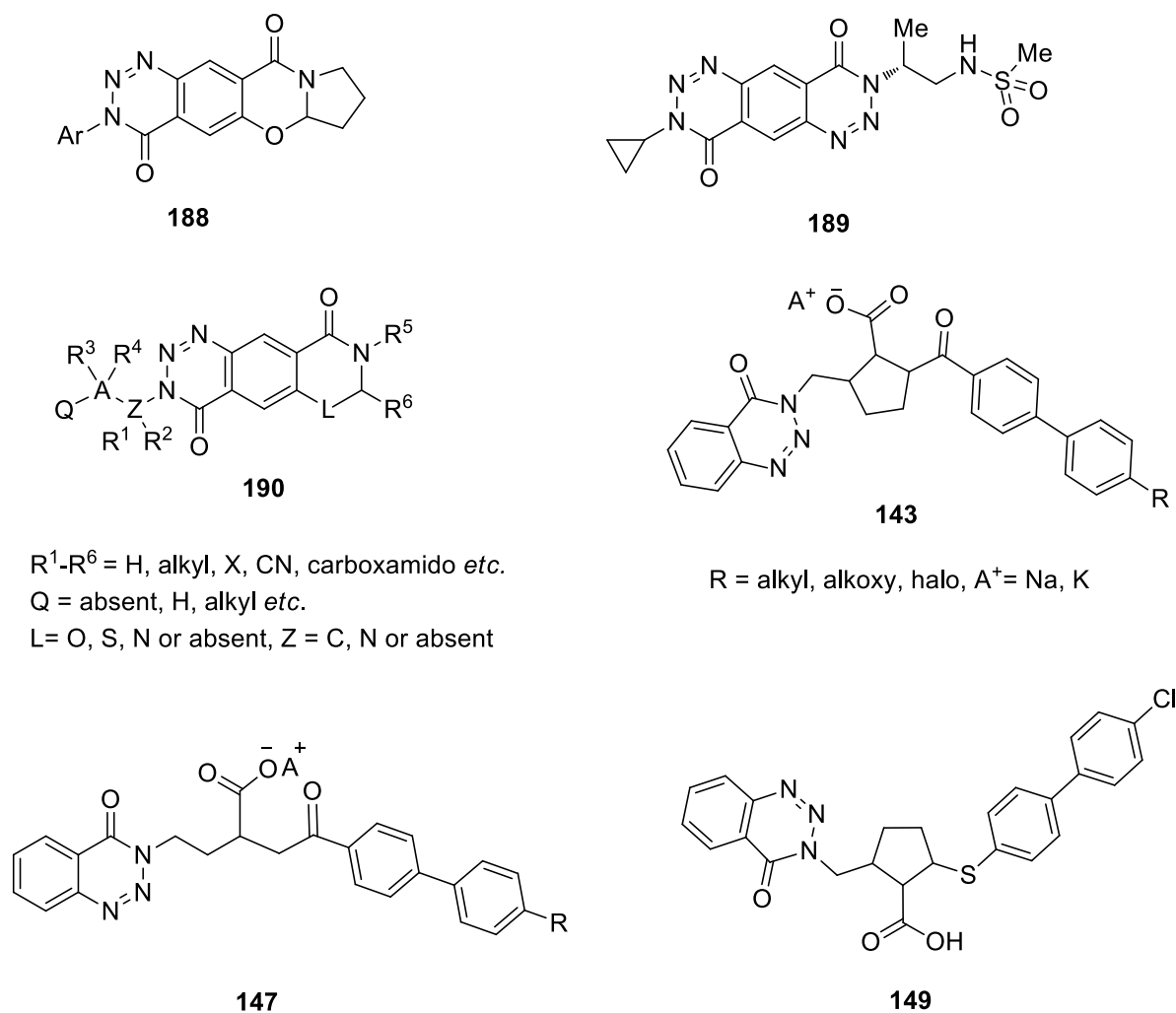


Figure 6. CNS disordering curing benzotriazinones derivatives

4.1.4. Anti-hypertensives

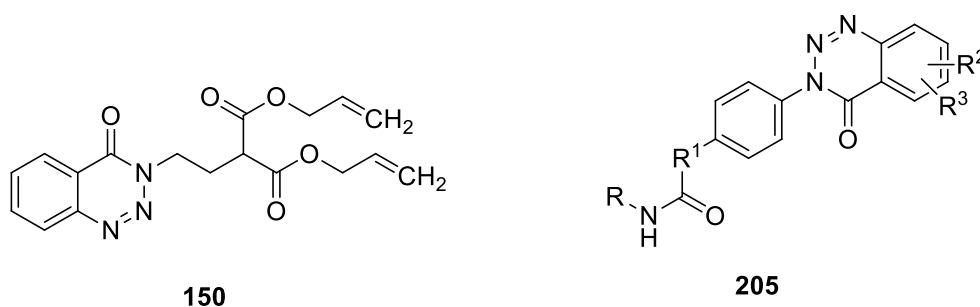
The structures of some anti-hypertensive compounds have been shown in Figure 7. Some derivatives of **191** (Figure 7) were tested on rats and shown good potency as an anti-hypertensive agents.⁵ While 3-(4-(1*H*-imidazol-1-yl)butyl)benzo[1,2,3]triazin-4(3*H*)-one (**192**) (Figure 7) have good anti-hypertensive activity due to their inhibitory effect on thromboxane (TX) synthetase.¹²⁶ The **191** also revealed good antiulcer and anti-inflammatory activity. Some other amino acid containing compounds (*i.e.*; **193**) (Figure 7) have been claimed as angiotensin converting enzyme inhibitors.¹²⁷

Some carbamate derivatives of **1** were discovered as active antithrombotic and elastase inhibitors.¹²⁸ The compounds **194**, **195** and **196** (Figure 7) were evaluated as thromboxane synthase inhibitors. About 51-100% inhibition was observed. Compound **200** (Figure 7) showed excellent 97% inhibition of thromboxane A₂ synthase with rat platelet generation and reduced arterial blood pressure. Among these some are pharmaceutically acceptable and may be useful in treating ischemia, thrombosis, hypertension, and migraine.¹²⁹

Some new derivatives of 1,2,3-benzotriazine-4(3*H*)ones (**203**) (Figure 10) were studied as antitumor drugs in comparison to temozolomide and mitozolomide, but none of the compounds was significantly more cytotoxic than lead structures.²⁰ The compound **204** (Figure 10) was studied for its *in vitro* antiproliferation activity against cell lines. This pharmacologically screenings bear out that it possess antiproliferation activity with growth inhibition.⁴

4.1.6. Anti-inflammatory Compounds

For the treatment of inflammation in osteoarthritis or rheumatoid arthritis, compounds **143** and **150** have shown good activity by the inhibition of matrix metalloproteases which are involved in inflammation process.^{99,100,103} A series of compounds (**205**) (Figure 11) were tested for α -4 integrin inhibitory effect and has been recommended to be useful as remedies for diseases related to inflammation.²⁸ 3-(Pyrazol-5-yl)-1,2,3-benzotriazin-4(3*H*)-ones and quinazolin-4(3*H*)-ones were tested and found to be analgesic, anti-exudative and have anti-edema activities with induction of lesion in the gastric mucosa.² Even some derivatives were found to be more effective than commercial medicines with comparative lower ulcer genic activity.²¹



R = cycloalkyl, alkenyl, R¹ = alkyl, R², R³ = halo, nitro

Figure 11. Anti-inflammatory compounds containing 1,2,3-benzotriazinone skeleton

In beginning, *N*-alkylated-1,2,3-benzotriazin-4(3*H*)-ones were analyzed for COX inhibition and good results were observed.² When the alkyl was changed to a hetaryl, **206** (Figure 12) was formed and found to be selective COX-1 and COX-2 inhibitor in comparison to celecoxib with acute toxicity.¹³¹ Another series of compounds (**207** and **208**) (Figure 12) have ability to inhibit 3 α -hydroxysteroid dehydrogenase of rat liver cytosol and found to be more active than phenylbutazone with no ulcerogenic effect and low systemic toxicity.^{132,133} Although 1,2,3-benzotriazinones with pyrazole moiety exhibited activity but with oxazole ring (**209**) and benzopyrimidine pyridylmethyl (**210**) (Figure 12) no significant activity was observed.^{134,135} 3-Morpholino derivative (**211**) (Figure 12) was found to be more useful as an analgesic superior to phenacetin and aminopyrine with lower acute toxicity.¹³⁶

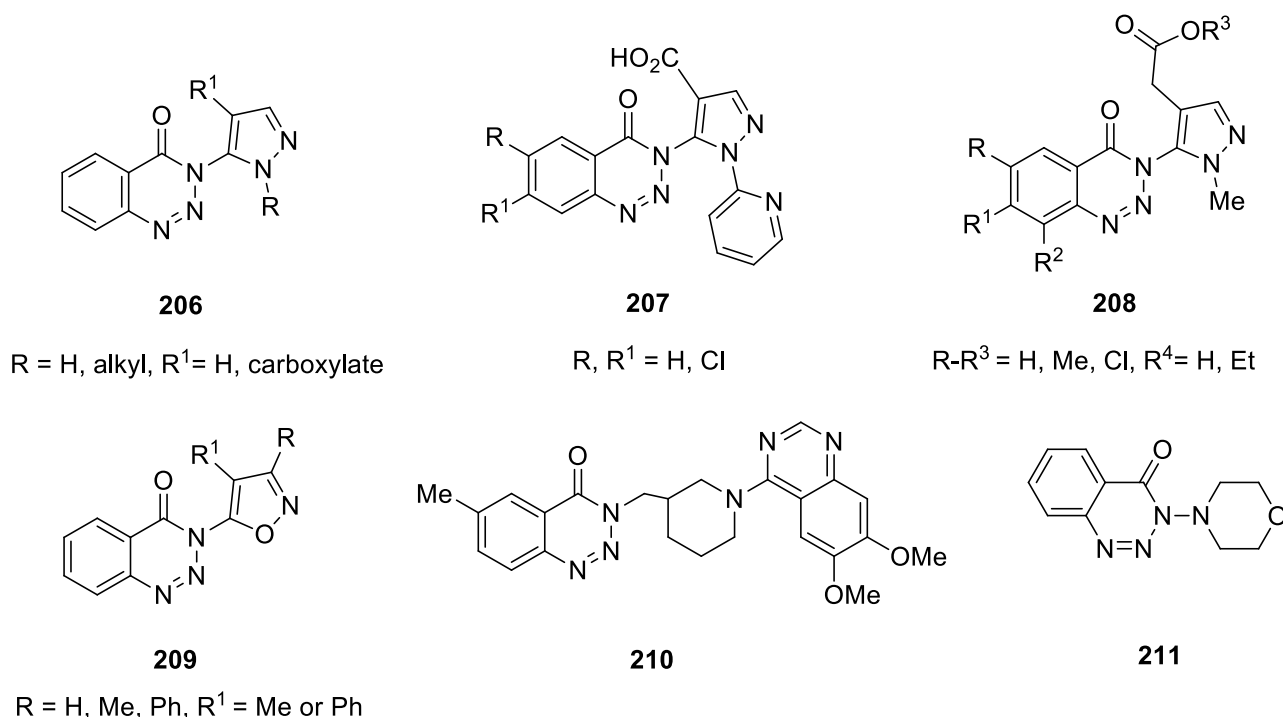


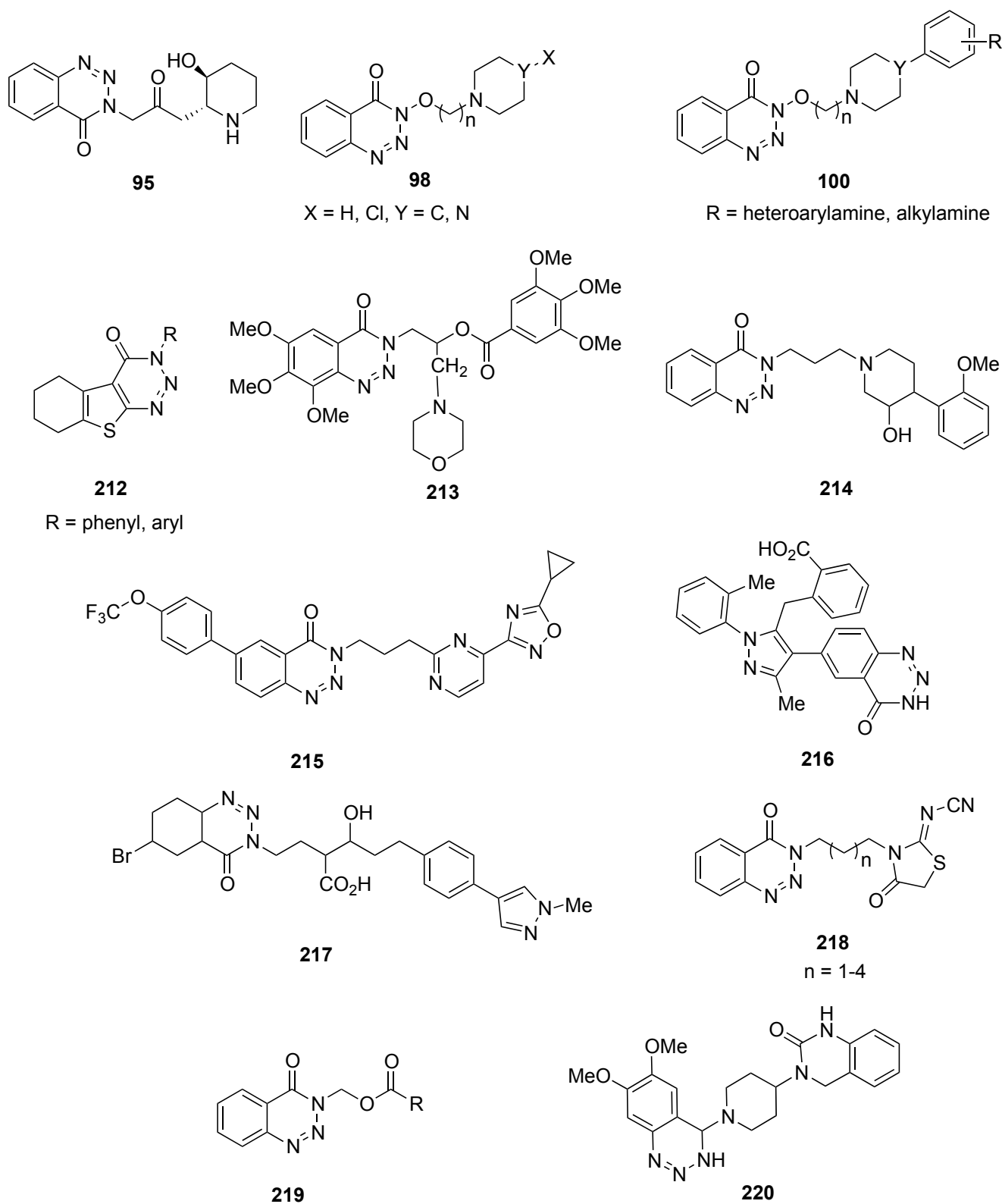
Figure 12. Benzotriazinones derivatives as selective enzyme inhibitor

4.1.7. Miscellaneous

Compounds like **212** (Figure 13) have been reported for their specific antihistaminic action.¹³⁷ 3-[3-(3-Hydroxypiperidin-2-yl)-2-oxopropyl]benzo[*d*][1,2,3]triazin-4(3*H*)-one (**95**) was evaluated for antimalarial activities, therapeutic selectivity both *in vitro* and *in vivo* tests was observed.⁷³ Pharmaceutically acceptable salts of **210** have been claimed to be responsible for increasing erythropoiesis in hemodialysis to prevent anemia.¹³⁸ They have been also evaluated for the inhibition of cellular uptake of adenosine and thereby found to be useful for treating heart muscles from anoxia or low oxygen diseases such as ischemia or reperfusion disorders and to prevent and treat inflammation of foot edema.¹³⁹ *In vitro*, **106** was evaluated for chorismate mutase inhibitory properties and a moderate activity was observed.⁸⁰ Razinodil (**213**) is a possible new drug for ischemic myocardial diseases. It is coronary vasodilator, increased the coronary blood flow of the canine heart lung without increasing the myocardial consumption. It increases the myocardial blood flow especially in the endocardial region.¹⁴⁰ Poly(*N-p*-methacryloxybenzoyloxy-4-oxo-3,4-dihydro-1,2,3-benzotriazine) is useful as carriers of immobilization of enzymes, especially trypsin.¹⁴¹

Compound **214** has been found to be adrenergic receptors antagonists, which can be used to treat benign prostatic hyperplasia and have been also suggested to treat diseases of lower urinary tract that may or may not be associated with BPH and related symptoms.⁶⁴ Some compounds like **98** and **100** (Figure 13) have shown good results both *in vivo* and *in vitro* in comparison to loperamide for antidiarrhoeal activity⁶ and

3-aryl-1,2,3-benzotriazin-4(3*H*)-ones have been claimed as potential antituberculotic.¹⁴² Benzotriazinone derivatives like **215** (Figure 13) were evaluated as sodium channel modulators.¹⁴³



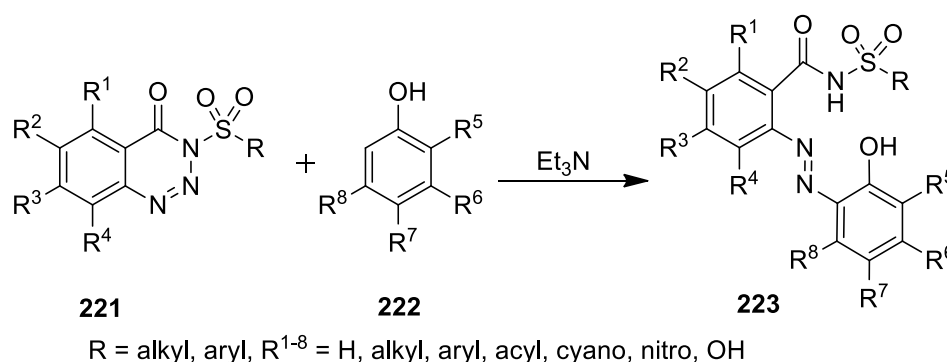
R = phenyl, 2-thienyl, Me, 2-furfuryl, (Ph)₂CH.

Figure 13. Miscellaneous bioactive 1,2,3-benzotriazinones analogs

Pyrazole substituted benzotriazinones like **216** evaluated as adenosine A1 receptor antagonists.¹⁴⁴ Its uronic acid derivative **219** (Figure 13) claimed as metalloproteinase inhibitor.¹⁴⁵ Nematicidal assays of **218** (Figure 13) *in vivo* showed that they exhibits excellent control efficacy against *Meloidogyne incognita* that causes cucumber root-knot nematode disease.¹⁴⁶ Some 1,2,3-benzotriazin-4(3*H*)-ones esters **219** (Figure 13) were synthesized and tested for kinase inhibition. Some of the compounds showed significant antitubercular activity *in vitro*. The compound 6,7-dimethoxy-1,2,3-benzotriazinone **220** (Figure 13) was found as cardiotoxic agent.¹⁴⁷

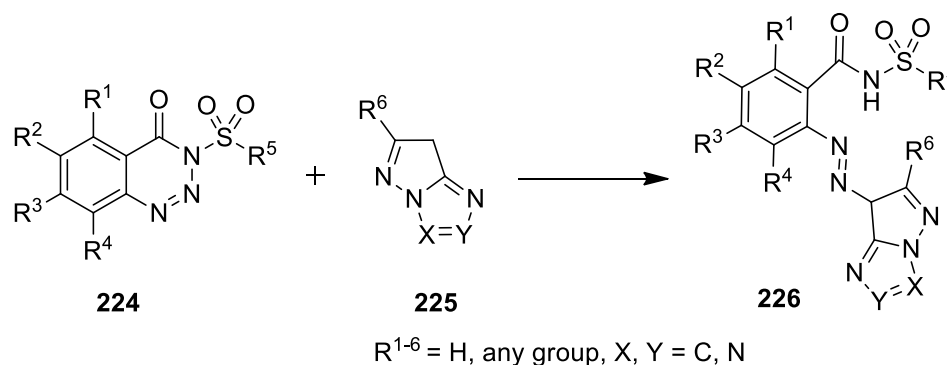
4.2. Dyes

1,2,3-Benzotriazin-4(3*H*)-ones derivatives have been also tested for diverse non-pharmacological applications including as pigments and their usefulness as recording and imaging materials, as indicated in the past section. 1,2,3-Benzotriazin-4(3*H*)-ones are called Pologenowe dyes because they have masked diazonium moiety. Azo dye **223** and their tautomers can be easily prepared by reaction of 3-sulfonylbenzo[*e*]-1,2,3-benzotriazin-4(3*H*)-ones (**221**) and phenols (**222**) (Scheme 70).⁹



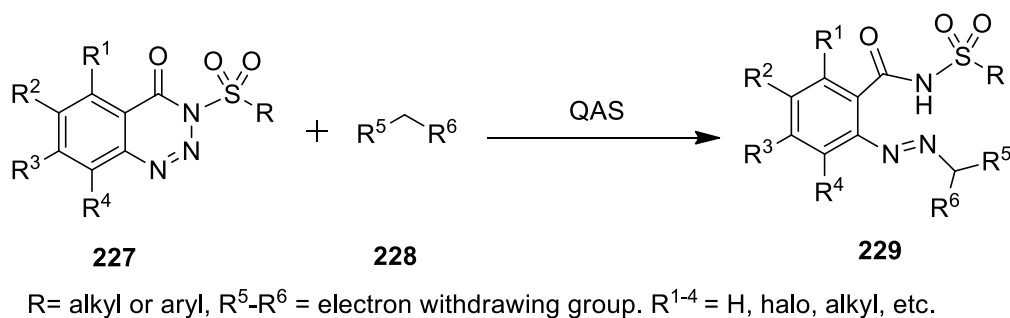
Scheme 70. Pologenowe dyes synthesis

Dyes like **226** prepared from **225** and **224** are being used as printing ink with good light fastness (Scheme 72).^{148,149} These compounds have been also microencapsulated to improve the shelf life of the thermal recording material.



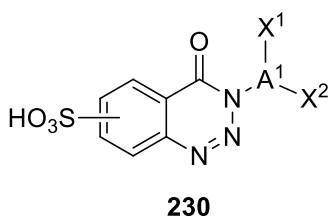
Scheme 71. Synthesis of printer ink

In the same fashion, a series of dyes have been reported to be prepared from 3-(4-chlorophenyl)-4-(2,6-di-*t*-butyl-4-methyl)cyclohexyloxycarbonyl-5-aminopyrrole and related compounds.¹⁵¹ Reactions of 1,2,3-benzotriazin-4-one sulfone derivatives (**227**) with active methylenes (**228**) have resulted **229** with good color hue and light resistant properties (Scheme 72).¹⁵¹



Scheme 72. Synthesis of dye having light resistant properties

Different dyes like **230** (Figure 14) have been found to produce good desired colors, when fabric was immersed twice in the dye followed by squeezing, drying, steaming, and washing.¹⁵²



A¹ = aryl, X¹, X² = H, halo, alkyl, cyano.

Figure 14. 1,2,3-Benzotriazinone base Dyes

4.3. Recording and Imaging Materials

Heat-sensitive layer normally contains 1,2,3-benzotriazin-4(3*H*)-one derivatives as diazo compounds with couplers. Compounds **231** (Figure 15) produce magenta-coloring layer and give good full-color thermal recording material, which are easy to handle and also durable.¹⁵³ The compounds **231** and **232** (Figure 15) have been also used in the preparation of heat-developable recording material with improved yellow color formation with background whiteness.¹⁵⁴ Combination of these compounds with fog inhibitors and polymer latex have displayed good photographic properties and storage stability.¹⁰

In photo thermographic material, some components like **233** (Figure 16) have been found to be useful as color tone-control material which generates pure black images.¹⁵⁵ Certain 1,2,3-benzotriazin-4(3*H*)-ones derivatives are reported to act as gelatin hardeners in photographic layers. These hardeners are inexpensive and are prepared readily.¹⁵⁶ Polymers **233** and **234** (Figure 16) have a plurality of first group which expose maximum area towards imaging material to form an image.¹⁵⁷

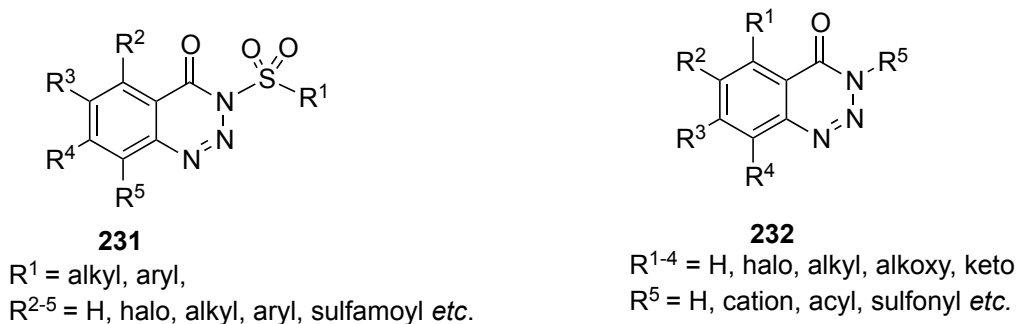


Figure 15. Thermal recording materials

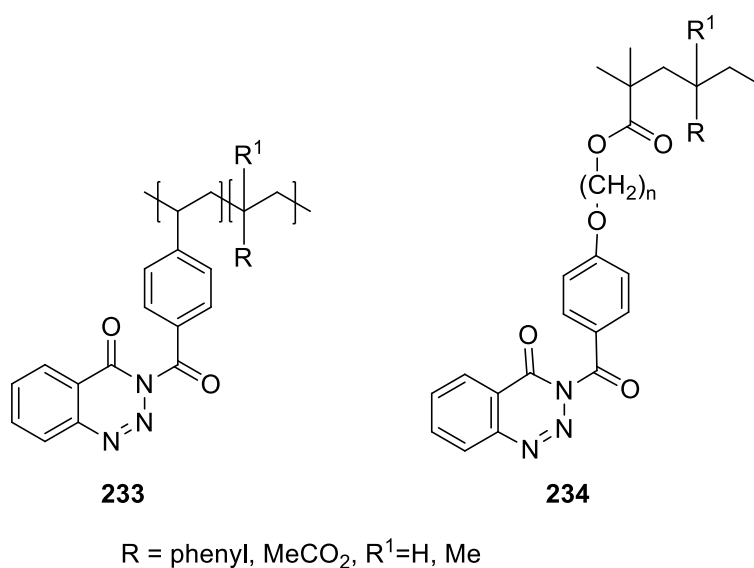


Figure 16. Imaging material

Pivaloylacetanilides derivatives (*i.e.*; **235**) (Figure 17) have been tested as two equivalent couplers for photography. These couplers have excellent reactivity and found to be good as photographic recording materials.⁹⁶ While some other derivatives (*i.e.*; **236**) (Figure 17) employed as two equivalent yellow photographic couplers provide dye images with a high color density and a high sensitivity.⁹⁵

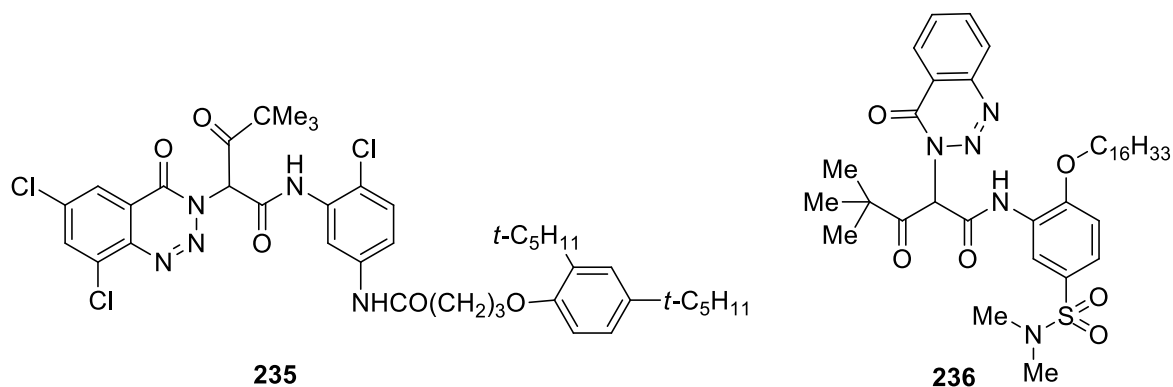


Figure 17. Photographic recording materials

1,2,3-Benzotriazin-4(3*H*)-ones derivatives are also valuable in photoconductor as photo generating layer of charge transport component.¹⁵⁸ The compounds like **237** (Figure 18) have been used as thermoplastic organic polymer binder,¹⁵⁹ and as heat sensitive diazo imaging material.¹⁶⁰ Such derivatives have been also used in thermal recording layer as coupler for coloring. These compounds possess photo fix ability and are excellent in light resistance for imaging parts.^{82,161,162} Copper complex **238** (Figure 18) was used in recording medium for optical information and results showed that it afforded good storage stability in solution and good light resistance with good recording characteristics.¹⁶³

As thermal recording materials **239** and **240** (Figure 18) with couplers have shown improved color develop ability and light stability.^{164,165} Another compounds like **241** (Figure 18) have also high stability to 350 nm light and have good storage stability.¹⁶⁶ The compounds **242** (Figure 18) have been proved to be useful for negative imaging recording material for planographic printing plate preparation.¹⁶⁷ Polymeric 1,2,3-benzotriazin-4(3*H*)-ones derivatives (**243**) (Figure 18) are found to be useful for direct printing by using an IR laser. They have been used as negative type photo imaging materials for lithographic printing plates with long shelf life and good printability.^{168,169,170} As negative-working image-forming compounds, **244** (Figure 18) for presensitized lithographic plate material have shown good storage stability and are found to be useful for direct plate making by IR digital data.¹⁷¹ Compounds **243** are also reported to be useful for negative-working image-forming material for pre sensitized lithographic plates and showed good storage stability. They have ability to suppress corrosion of metals with good adhesion.¹⁷²

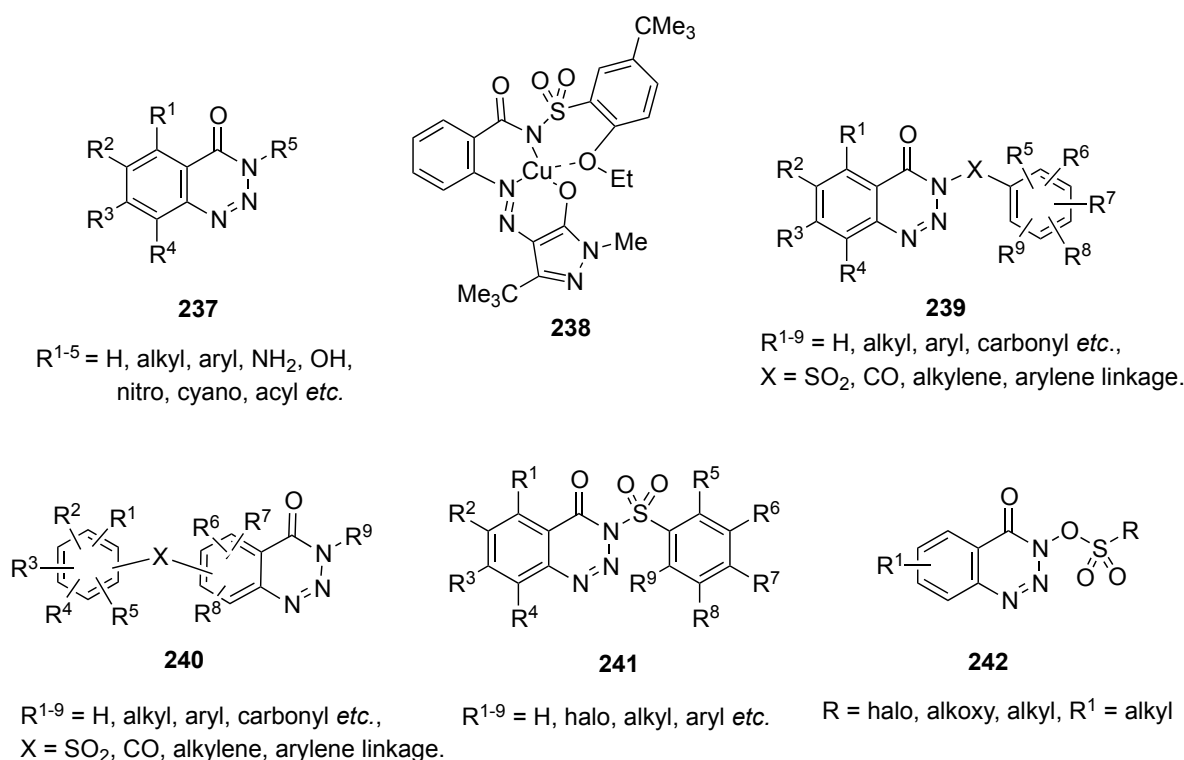
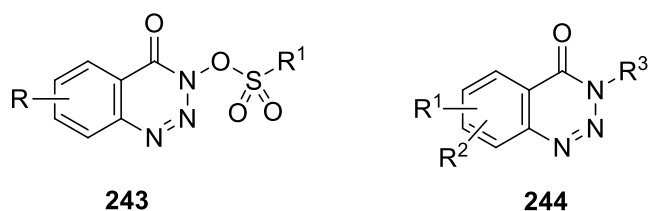


Figure 18. (Continued)



R = halo, alkoxy, alkyl, R¹ = polymer R¹⁻³ = H, alkyl, alkoxy

Figure 18. Miscellaneous recording and imaging materials

4.4. Fluorescence and Chemiluminescence

Photo physical properties of both *E* and *Z* isomers of 3-styryl-1,2,3-benzotriazin-4(3*H*)-one (**130** and **131**) (Figure 19) were investigated as fluorescent material but spectral studies did not displayed such property. 1,2,3-Benzotriazine-4(3*H*)-one derivatives were also evaluated for their catalytic efficiency in the peroxyoxalate chemiluminescence (PO-CL) reaction by using bis(2,4,6-trichlorophenyl)oxalate (TCPO) as reagent but no detectable chemiluminescence was observed.¹⁷³

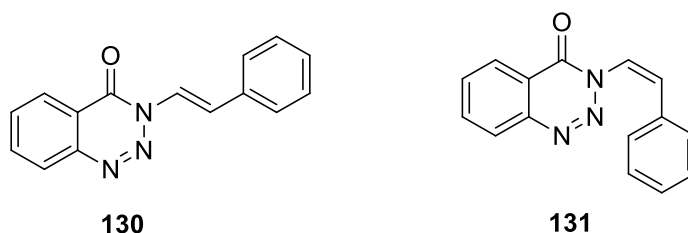
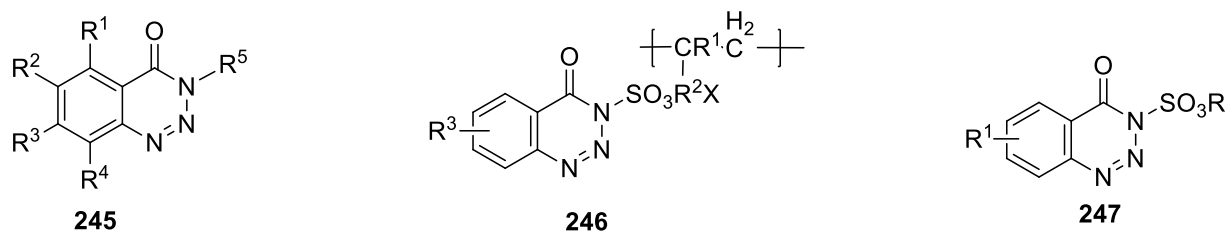


Figure 19. Poor fluorescent material

4.5. Printing

The compounds **245** (Figure 20) encapsulated in a polyurea shell have been used on a heat-sensitive recording sheet for improving print density.¹⁷⁴ The polymeric materials **246** (Figure 20) have been reported to be useful for direct printing by using an IR laser.¹⁶⁹ *N*-Sulfonate esters of benzotriazin-4(3*H*)-ones, (**249**) (Figure 20) have been found to be useful for printing since they can record images by using IR laser and are suitable for making lithographic printing plate with long shelf life and good printability.^{169,175}



R¹⁻⁵ = H, alkyl, aryl, ether, thio, etc. R¹⁻³ = H, alkyl, halo, alkoxy, X = carbonyl

R = alkyl, R¹ = halo, alkyl, alkoxy

Figure 20. 1,2,3-Benzotriazinon analogs useful in printing

4.4 Conclusion

This review expounding the synthetic methods, reactions and applications of 1,2,3-benzotriazin-4(3*H*)-ones in diverse fields. This versatile molecule can be synthesized easily and transforms to other valuable heterocycles. Many of its biologically active derivatives have been explored and still there is need for further research. Especially as recording and imaging materials benzotriazinones have been found to be very effective agent. It is hoped that this review will provoke more research work for the synthesis of numerous derivatives of benzotriazinones and exploration of their applications in new fields.

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Zunera Khalid was born in 1985 in Lahore. She completed her Bachelor and Master Studies from University of the Punjab, Lahore. During Master studies she worked on the synthesis of benzothiazinones derivatives with potential to be Anti-HIV. Now she is working on the synthesis of bio active compounds containing benzotriazinone moiety in the same institute as a part of her Ph.D studies. Her major research interests include synthesis of bioactive heterocyclic compounds and their biological evaluation.



Hafiz Adnan Ahmad was born and raised in Lahore, Pakistan. He received M.Sc degree in organic chemistry from the institute of chemistry, University of Punjab, Lahore in 2014. At the same year, he again joined the same institute as M.Phil student. Now he has been doing his research under the supervision of Prof. Dr. Munawar Ali Munawar. His research interests include development of new reactions methodologies, synthesis of heterocyclic compounds especially sulfonamides and their computational studies.



Prof. Dr. Munawar Ali Munawar obtained his master degree in chemistry with distinction from The Islamia University, Bahawalpur and joined the same as lecturer in 1983. He obtained M. Phil degree from Institute of Chemistry, University of the Punjab in 1987. He earned his Ph.D. degree from University of Wales UK in 1996. He joined the Institute of Chemistry, University of the Punjab in 2002. To his credit he holds more than 150 publications including one patent. He was awarded post-doctoral fellowship at University of Florida (USA) by Higher Education Commission of Pakistan for the year 2008-2009 where he worked on benzotriazole mediated synthesis of amino acid conjugates of bioactive compounds. His research interests include: synthesis of dyes and heterocyclic compounds of biological and industrial importance, conversion of polymer and agro waste into value added products.



Dr. Misbahul Ain Khan, Professor Emeritus at The Islamia University of Bahawalpur, Pakistan, is a former Vice Chancellor of the University and a former Chairman of Pakistan Council of Scientific and Industrial Research, Pakistan. He was born at Lahore (Pakistan) in 1935, Got his early education at Karachi and M.Sc. in Chemistry from the University of Karachi (1959) and an M.Sc from Memorial University and Ph.D. from The University of Tasmania (1967). After a Post-doctoral fellowship at St. Francis Xavier University, Canada and a Liverhulme Trust Visiting Lecturership at UWIST, Cardiff, he joined Military Engineering Institute, Rio de Janeiro, Brazil where he was a Professor till 1984 when he returned to Pakistan and the Islamia University as a Professor and Dean of the Faculties of Science and Arts. He was Visiting Professor at the Federal Fluminense University, Rio de Janeiro, Brazil during 1998-1999. He has supervised 30 Ph.D. Thesis and published around 300 research papers in national and International journals.



Salman Gul is an Organic Chemist, working on heterocycles synthesis these days. Born in 1982, he earned his MSc in Chemistry from Institute of Chemistry, University of the Punjab, Lahore, Pakistan in 2006. After completing his eighteen year education he was awarded degree of MPhil in Chemistry in 2009 from the Institute of Chemistry. Currently he is working as PhD research scholar in the same institute for the last six years under the guidance of Professor Dr. Munawar Ali Munawar. Having eight publications on his credit, recently he is doing research on synthesis of active thiazines, Benzothiazines, Sulfonamides and pyrazole ring systems.