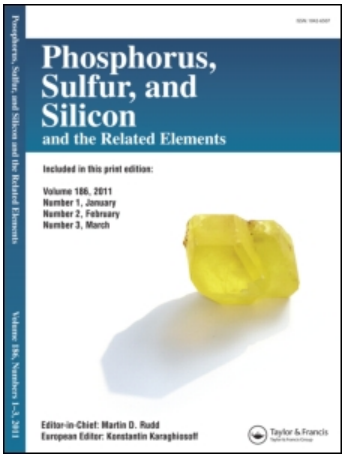

Phosphorus, Sulfur, and Silicon and the Related Elements

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Chemistry of 2-Cyanomethylbenzothiazole

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This review article includes the methods for the preparation of 2-cyanomethylbenzothiazole, its chemical reactivity towards different electrophiles and nucleophiles, and its use for the synthesis of heterocyclic compounds. Its biological activity and applications are also reported. This review includes 159 references.

Keywords 2-Cyanomethylbenzothiazole; benzothiazole; pyridobenzothiazole

INTRODUCTION

Benzothiazoles are derivatives of thiazole, which belong to an important group of heterocyclic compounds. Benzothiazoles with a cyanomethyl group at position 2 have been subject of extensive study in the recent past. Numerous reports have appeared in the literature, which highlight their chemistry and use.

Diverse biological activities such as bactericidal, pesticidal, fungicidal, insecticidal, anticonvulsant, tuberculostatic, anti-inflammatory, and antithyroidal have been found to be associated with thiazole and benzothiazole derivatives. In recent years, several new methods for the preparation of 2-cyanomethylbenzothiazole derivatives and reactions have been reported in the literature.

2-Cyanomethylbenzothiazole, in the presence of various reagents, undergoes different types of reactions to yield other heterocyclic compounds of biological and industrial interest. These advances warrant to review the chemistry and biological properties of 2-cyanomethylbenzothiazole and to highlight its potential in evolving synthetic uses.

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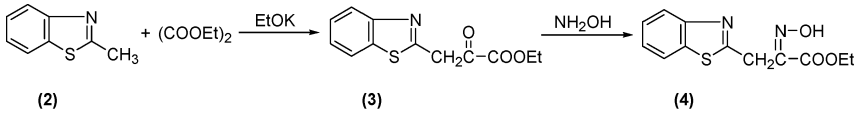
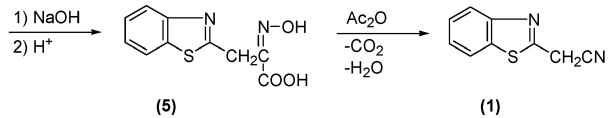
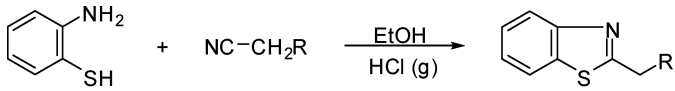
METHODS OF PREPARATION

The first trial for the preparation of 2-cyanomethylbenzothiazole (**1**) was reported in 1939.[1,2] Treatment of 2-methylbenzothiazole (**2**) with diethyloxalate in the presence of potassium ethoxide resulted in the formation of ethyl 2-benzothiazolyl pyruvate (**3**). The reaction of **3** with hydroxylamine gave the corresponding oxime (**4**) which on hydrolysis gave the oximino acid (**5**). Treatment of **5** with acetic anhydride afforded 2-cyanomethylbenzothiazole (**1**).

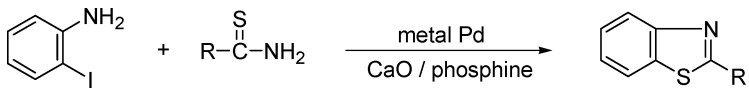




A convenient one-step cyclization reaction leading to the formation of 2-cyanomethylbenzothiazole (**1**) from o-aminothiophenol (**6**) has been reported.[3] Refluxing of **6** with malononitrile or ethyl cyanoacetate in ethanol in the presence of anhydrous hydrochloric acid gas gave the benzothiazole derivatives (**1**) or (**7**) in good yield.



Similar to the above reaction, substituted acetonitrile reacts with substituted aniline in ethanol in the presence of piperidine as a catalyst to give the isolable product **7**.[4] Recently, (**1**) was also prepared by reaction of o-haloaniline or o-aminothiophenol with thiocyanoacetamide.[5–7]

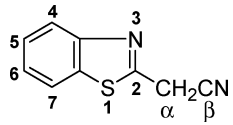


In addition M. Lorenz[8] prepared compound (**1**) by cyclocondensation of malononitrile in aqueous sodium hydroxide with 2-aminothiophenol.

CHEMICAL REACTIVITY

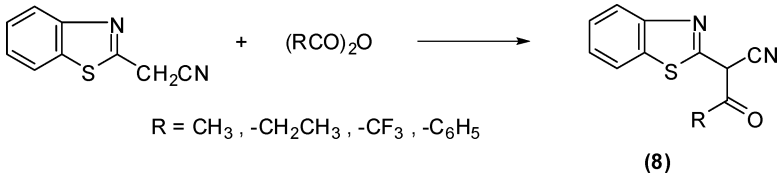
Reactions with Electrophilic Reagents

The presence of the cyano group and the benzothiazolyl group in 2-cyanomethylbenzothiazole (**1**) renders the α-carbon hydrogen very active. Thus, abstraction of these hydrogens by basic catalyst takes place quite readily; accordingly, electrophiles attack the α-carbon under comparatively mild conditions:



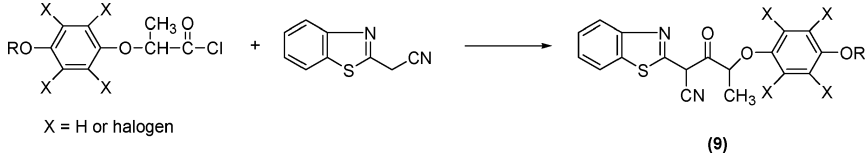
Acylation

It has been reported that acylation of compound **1** took place by reaction of 2-cyanomethylbenzothiazole (**1**) with aliphatic and/or aromatic acid anhydrides or with mixed esters of carboxylic acids[9] to afford the corresponding acyl derivative (**8**). In addition, acylation of **1** occurred also by the action of acid chlorides.[10–12] Formylation of compound **1** was reported by El Latif.[13]



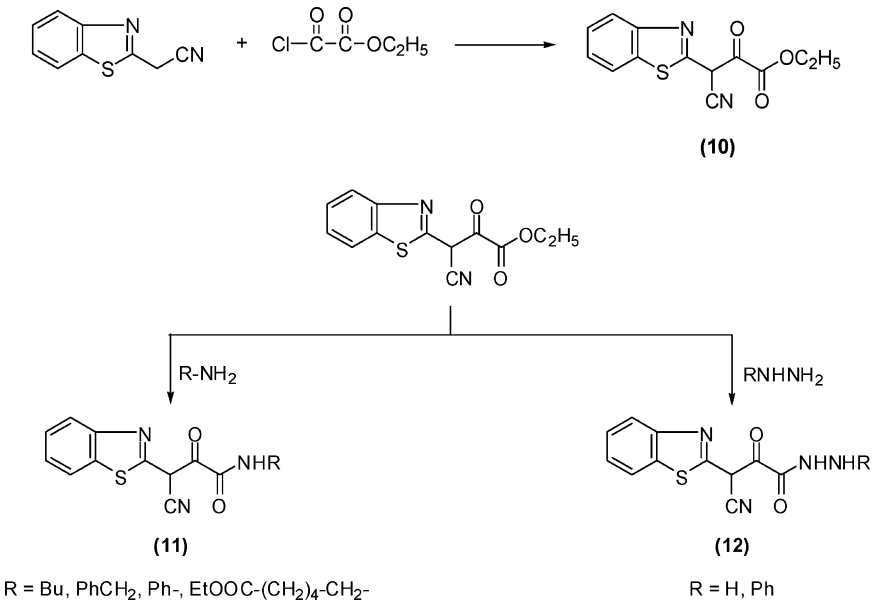
(8)

Some of the acylated products were found to possess biological activity, for example, compound **9** was used as herbicide.[14]

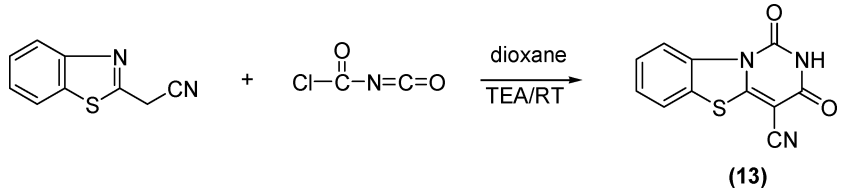


(9)

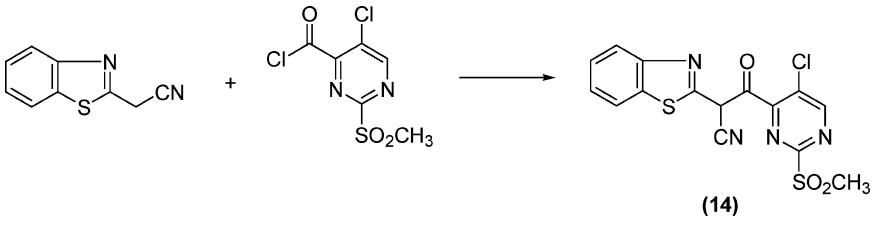
It was reported that the reaction of ethyl 2-chloro-2-oxoacetate with 2-cyanomethylbenzothiazole (**1**) was used as a route for the synthesis of amide (**11**) and hydrazide derivatives (**12**) via the α-keto ester intermediate (**10**).[15]



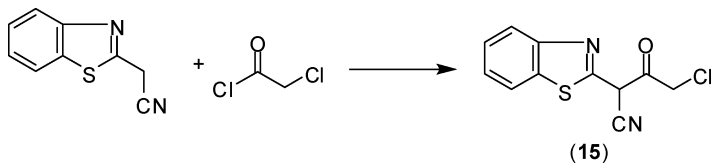
In addition, the acylation of **1** with chlorocarbonyl isocyanate yields the heterocyclic product **13.**[16,17]



Acylation of (**1**) by heterocyclic acid halide derivatives to form (**14**) was also reported.[18]

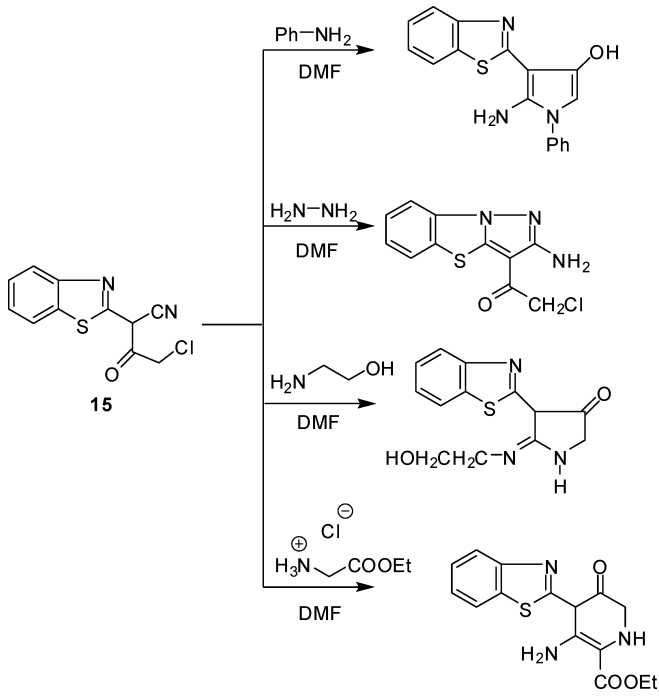


Recently, the acylation of **1** by chloroacetyl chloride to give 2-(benzothiazol-2-yl)-4-chloro-3-oxobutanenitrile (**15**) has been described.[19]



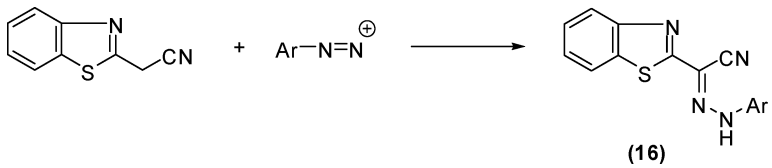
(**15**)

Compound **15** allows a fruitful one-step synthesis of several heterocyclic rings



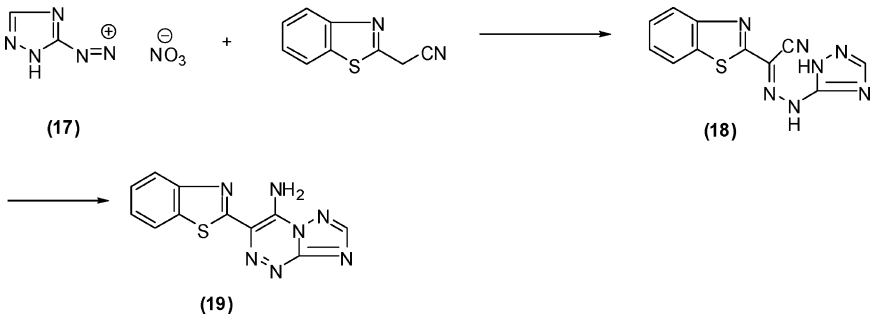
Reaction with Diazonium Chlorides

It has been found that coupling of aromatic diazonium salts with 2-cyanomethylbenzothiazole (**1**) afforded the corresponding hydrazono derivatives (**16**).[20,21]



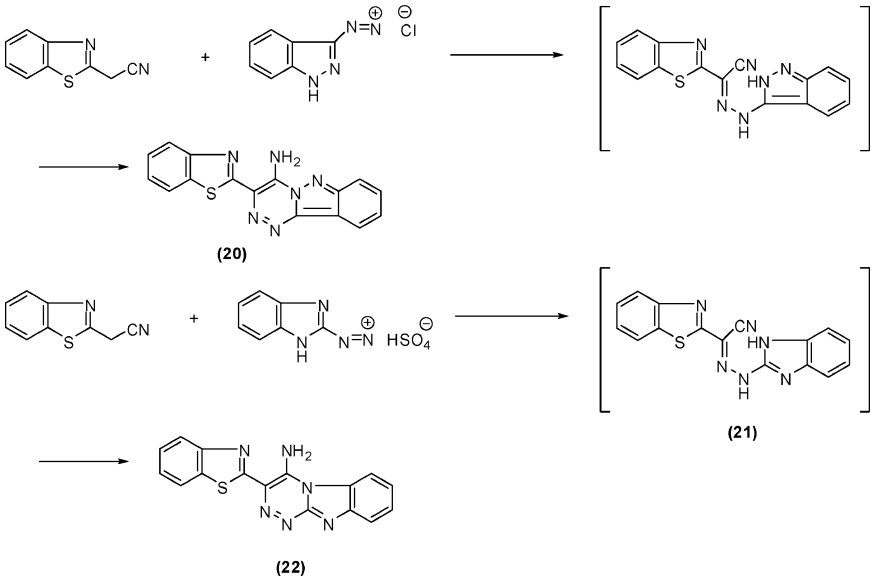
(**16**)

Moreover, coupling of **1** with diazonium salts containing NH at the α-carbon atom (**17**) was found to be followed by cyclization of the hydrazono derivative (**18**) to give the corresponding triazolotriazine derivative (**19**)[22].



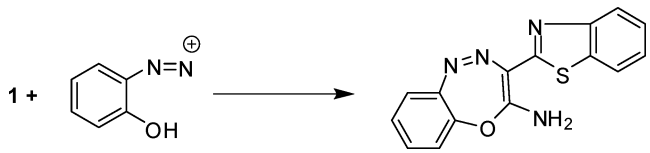
(17) (18) (19)

Many diazonium salts underwent diazocoupling reactions with **1** to give the corresponding triazinoindazole derivative **20** and triazinobenzimidazole derivative **22** via the intermediate **(21)** .[22]



(20) (21) (22)

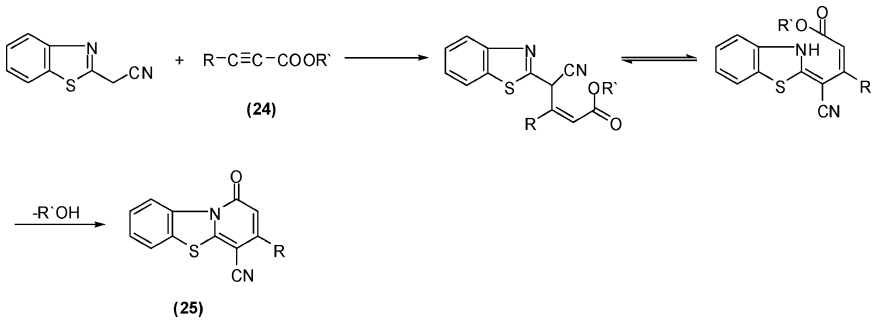
The diazonium salt of 2-aminophenol was coupled in situ with **1** to give 2-amino-3-(2-benzothiazolyl)-[1,4,5]benzoxadiazepine (**23**). [23]



(23)

Reaction with Acetylenic Compounds

2-Cyanomethylbenzothiazole (**1**) reacts with acetylenic compounds (**24**) affording new fused pyridinobenzothiazole derivatives (**25**) *via* Michael reaction.[24]

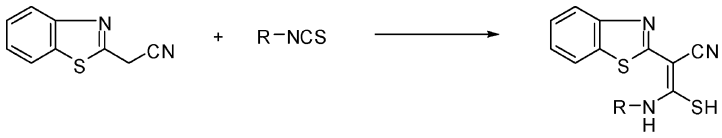


(25)

[R = -$COOCH_3$, Ph-, H-, $PhCH_2$-]
R` = -CH_3, CH_3CH_2-

Reaction with Isothiocyanates and Isocyanates

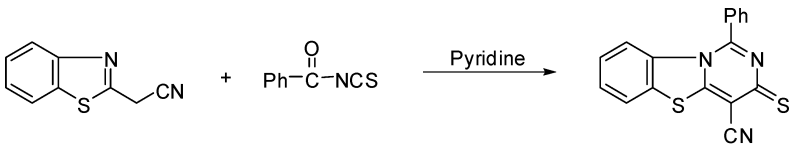
2-Cyanomethylbenzothiazole (**1**) reacts readily with isothiocyanates[25–29] to afford the thioketene derivatives (**26**).



(26)

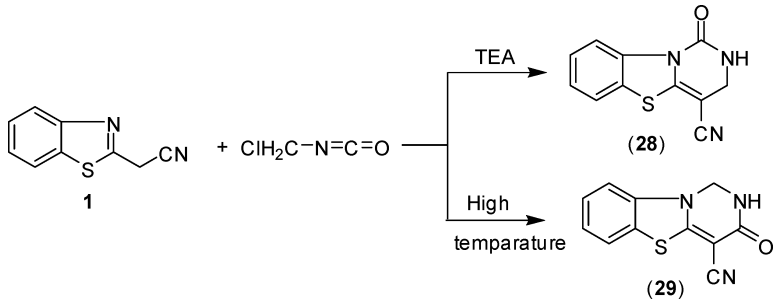
R = Ph, $PhCH_2$, C_6H_4-4-Cl-, C_6H_4-4-OCH_3, C_6H_4-4-CH_3, C_6H_4-3-CH_3, n- C_4H_9, C_6H_{11}

In addition, **1** reacts with benzoyl isothiocyanate to give the pyrimidobenzothiazole derivatives (**27**).[21,27]



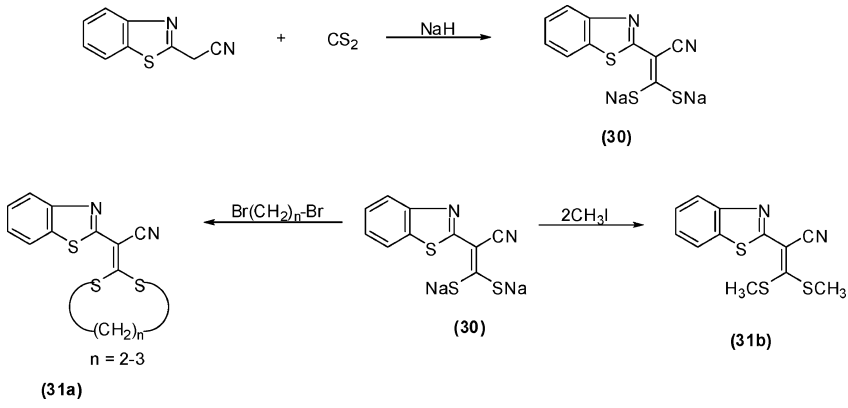
(27)

1-Chloromethyl isocyanate reacts with benzothiazolyl-2-acetonitrile (**1**) in the presence of triethylamine to give 4-cyano-2,3-dihydro-1*H*-pyrimido[6,1-*b*][1,3]benzothiazol-1-one (**28**). The same reaction at elevated temperature in the absence of a base yields the isomeric 4-cyano-2,3-dihydro-1*H*-pyrimido[6,1-*b*][1,3]benzothiazol-3-one (**29**).[30]



Reaction with Carbon Disulfide

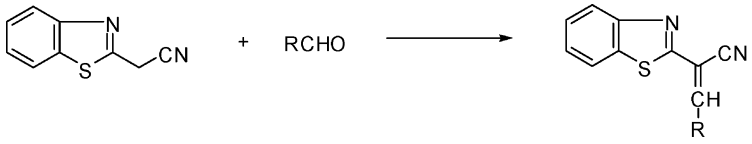
In addition, it was found that the reaction of (**1**) with carbon disulfide in the presence of sodium hydride[28,31] yields the dithiosodium salt (**30**) which was used as active intermediate for the synthesis of some 2-cyanomethylbenzothiazole derivatives (**31a,b**).



Reaction with Carbonyl Compounds

The reaction of (**1**) with carbonyl compounds was found to be dependent on the reaction conditions according to the type of the carbonyl compound.

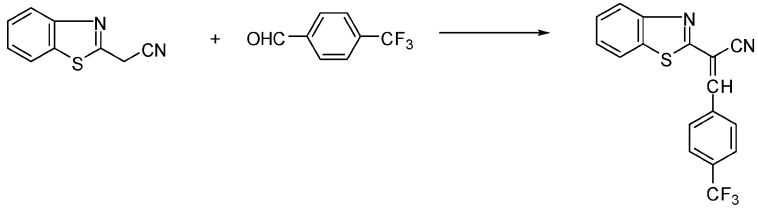
A variety of different aromatic aldehydes were used and the reaction proceeded generally by refluxing (**1**) with the aromatic aldehydes in the presence of catalytic amounts of base as catalyst[32–38] to give the corresponding arylidene derivatives (**32**).



(32)

R = Ph, p-$CH_3C_6H_4$-, p-$OCH_3C_6H_4$-, p-Cl-C_6H_4-, p-NO_2 or -C_6H_4- and Ph-CH=CH-

Some arylidene derivatives of **1** were used as electrophotographic receptors which showed high sensitivity, for example compounds (**33**)[39] and (**34**).[40]



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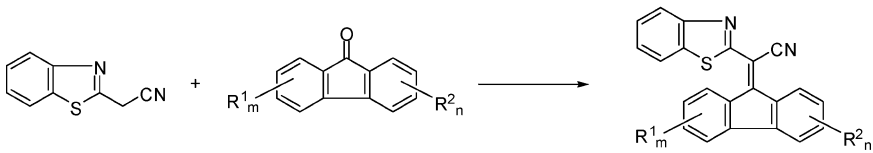
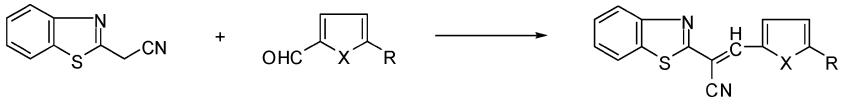


(34)

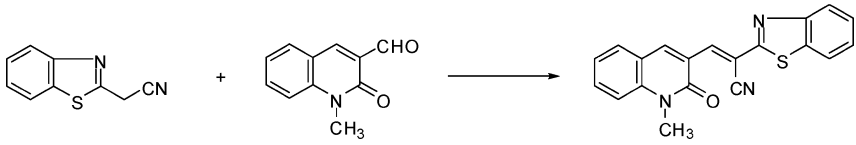
R^1, R^2= H, alkyl, alkoxy, alkoxyl carbonyl, acyl, -SO_2NH_2 $CONH_2$, halo, -CN, -NO_2, R^1 may be bonded to other atoms to form ring m,n 1-4.

In addition, it was found that (**1**) reacts with hetaryl aldehydes[35,36] forming the corresponding arylidene derivatives (**35**) [41] and (**36**).[42]



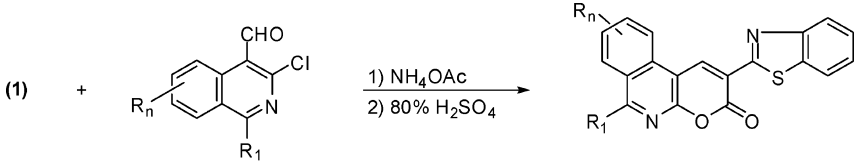
(35)

X = NH, O or S
R = H, CH_3, NO_2 or aliphatic alkyl



(36)

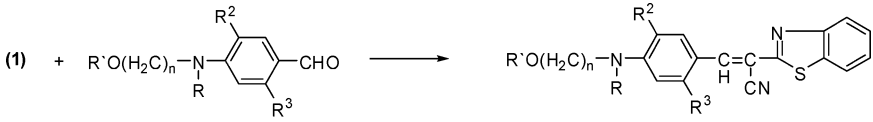
Some condensation products (**37**) of (**1**) with heterocyclic aldehydes have been used as dyes.[43]



(37)

R = H, halogen, alkyl, alkoxy, NO_2, NH_2 or CN
n = 1 or 2
R` = un(substituted) Ph, thienyl, pyridyl, naphthyl or pyrenyl

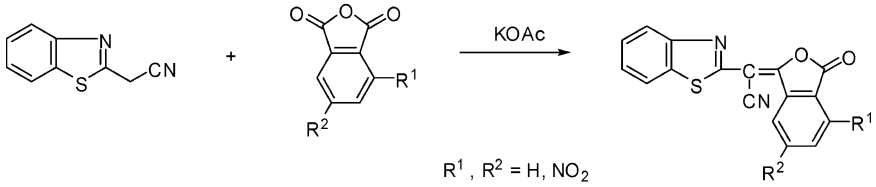
Similarly, the arylidene product (**39**) obtained from the reaction of (**1**) with the aldehyde (**38**) was used also as disperse dyestuff.[44]



(38) (39)

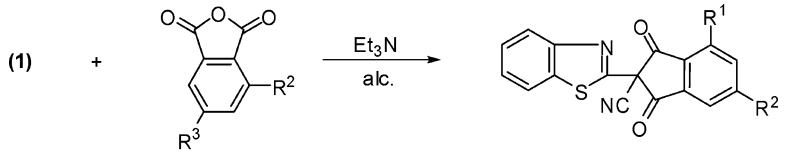
R = H, alkyl, aryl, cyclohexyl
R^1 = Ph or substituted phenyl
R^2 = H, Cl, lower alkyl or alkoxys
R^3 = substituted or unsubstituted heterocycles
n = 1-4

Moreover, compound (**1**) can undergo Aldol type condensation with dicarboxylic acid anhydrides to give the phthalides (**40**).[45]



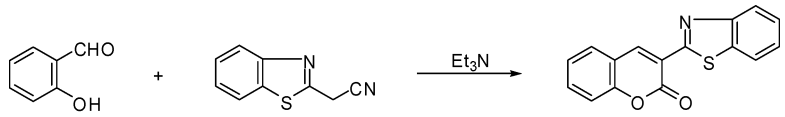
(40)

On the other hand, the reaction of compound **1** with phthalic anhydride derivatives in the presence of triethylamine afforded the indandione derivatives (**41**).[45]



(41)

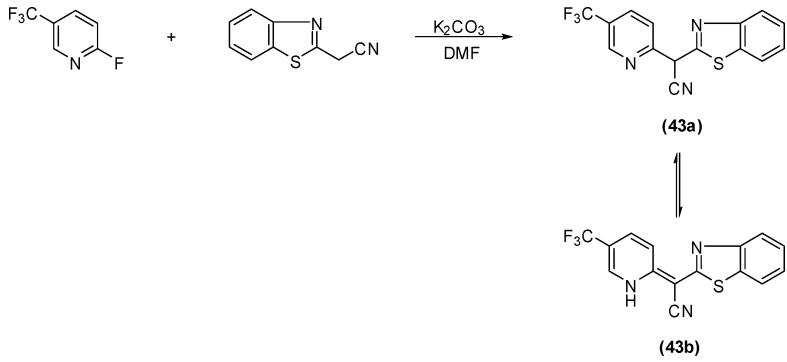
In addition, it was reported recently that **1** was reacted with quinolinic acid anhydride to give the corresponding 7-substituted furo[3,4-b]pyridine-5-one.[46] In addition, it was found that **1** reacts with salicylaldehyde or its derivatives to yield coumarine derivatives (**42**).[47,48] The reaction occurred in aprotic dipolar solvent (DMF or MeCN) in the presence of catalytic amounts of an organic base.



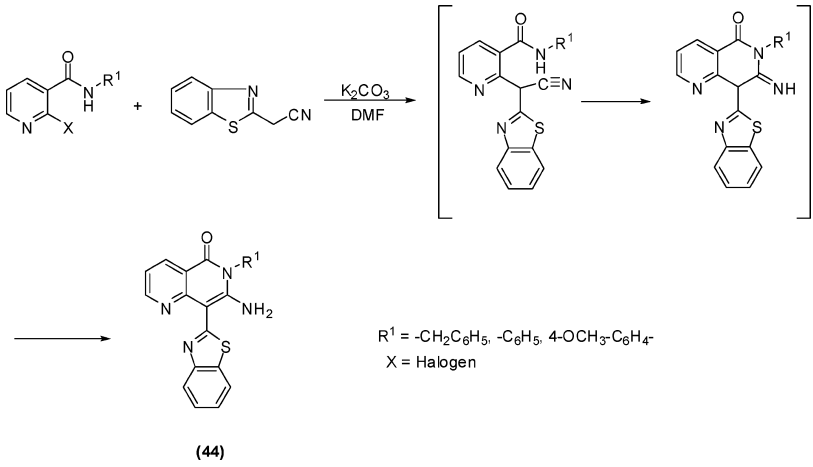
(42)

Reaction with Hetaryl Halides, Aryl Halides, and Alkyl Halides

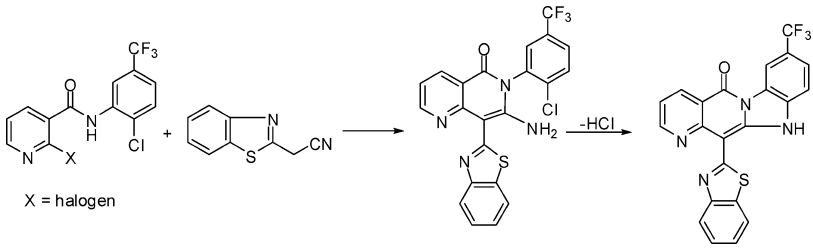
Pyridinylideneacetonitrile (**43**) were prepared by the reaction of (**1**) with 2-fluoro-5-(trifluromethyl)pyridine in the presence of K_2CO_3 in DMF.[49]



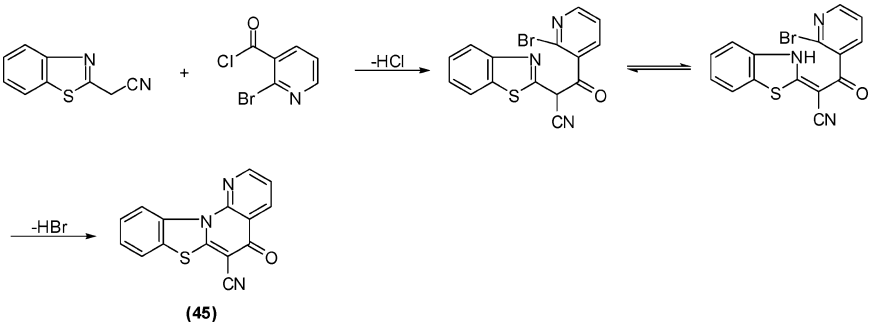
In the presence of a carboxamido substituent in ortho position to the halogen in the pyridine ring[50] or the aryl ring,[51] the reaction was followed by cyclization to give the corresponding 1,6-naphthyridine derivative (**44**).[50,51]



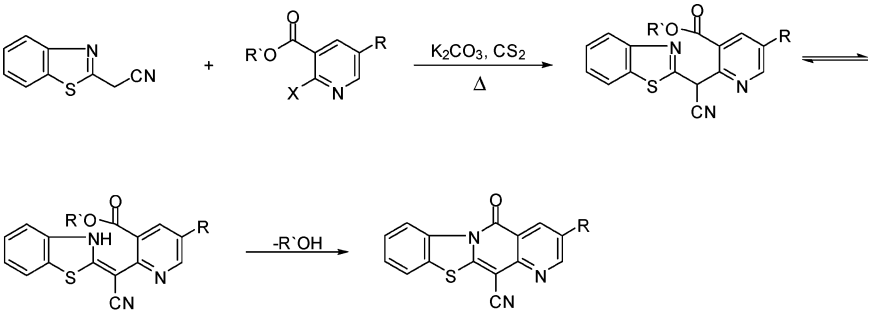
In case of R^1 = 2-Cl-5-CF_3 C_6H_3-, the reaction was assumed to proceed as follows:



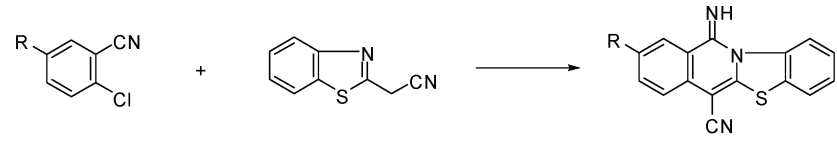
While, when 2-bromo-3-nicotnyl chloride was used, the benzothiazolo[3,2-a]1,8-naphthyridine derivative (**45**) was formed.[52–54]



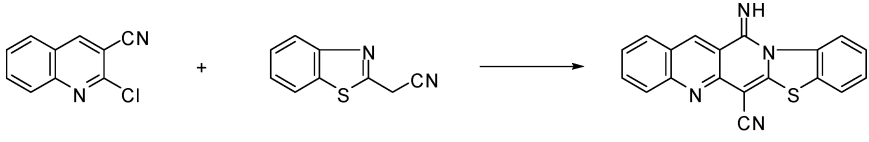
On the other hand, in case of an aryl halide containing ester group in the ortho position to halogen[54] the reaction proceeds under formation of the benzothiazolo[3,2-g]1,6-naphthyridine derivative (**46**).



The reaction of 2-cyanomethylbenzothiazole (**1**) with 2-halocarbonitrile was also reported to give (**47**) and(**48**).[55,56]

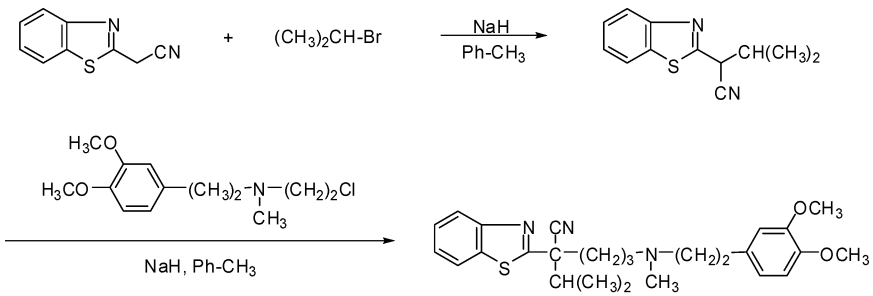


(47)



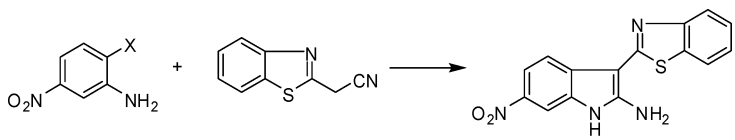
(48)

The substitution of the two acidic hydrogen atoms in compound (**1**) with different alkyl groups led to the formation of a very reactive anti-hypertension compound (**49**).[57]



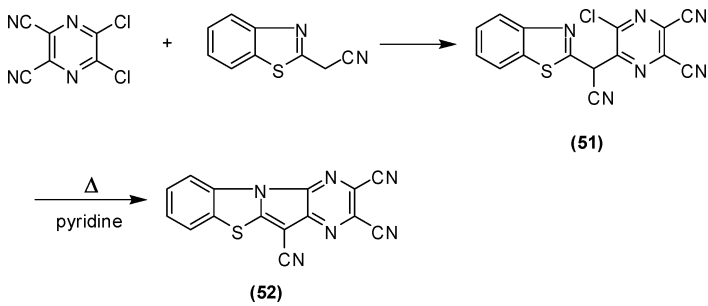
(49)

The reaction of a 2-amino-5-nitroaniline derivative with (**1**) led to the formation of the indole derivative **50.**[58]



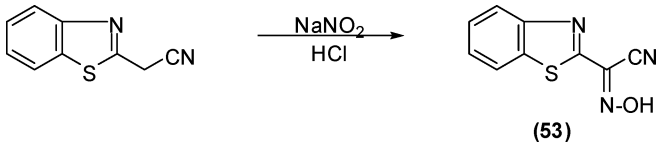
(50)

Reaction of **1** with 2,3-dichloro-5,6-dicyanopyrazine gave compound **51.** Subsequent heating in pyridine causes intramolecular cyclization to yield **52.**[59]



Reaction with Nitrous Acid

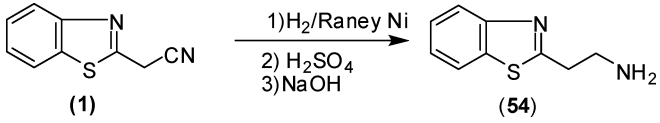
Syn and anti 2-oximino-2-cyanomethylbenzothiazole (**53**) were reported[60] to be formed by the reaction of **1** with nitrous acid.



The latter compound (**53**) was found to be a good multidenate ligand for metal complexes.[61]

Reduction of 2-Cyanomethylbenzothiazole

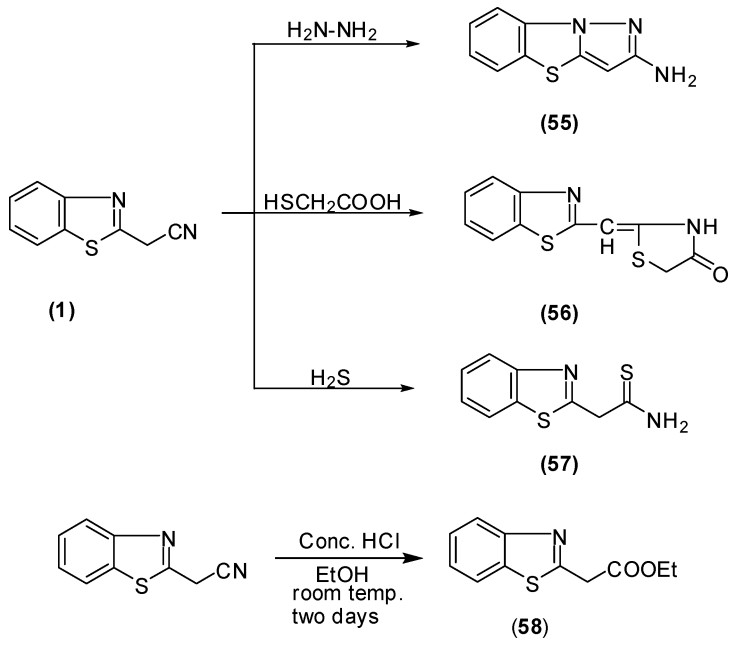
2-Benzothiazolylacetonitrile hydrogenated with Raney Ni, and treated with H_2SO_4 and NaOH gave the free amine from which 2-(2-benzothiazolyl)ethylamine (**54**) was formed.[62]



Reaction with Nucleophilic Reagents

Although reactions of nucleophilic reagents with 2-cyanomethylbenzoimidazole[63–69] have been reported only very few examples such as addition of hydrazine, thioglycolic acid and H_2S to form the benzothiazole derivatives (**55–57**), respectively have been described.[4,70,71]

Recently, the conversion of cyano group into the ethyl carboxylate **58** was reported[72]



UTILITY OF 2-CYANOMETHYLBENZOTHIAZOLE (1) IN HETEROCYCLIC SYNTHESIS

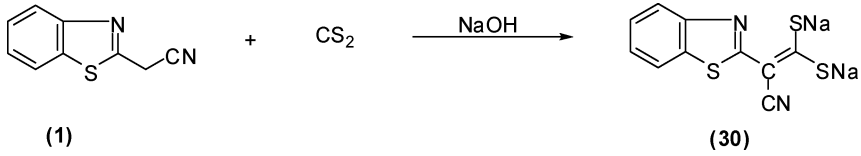
2-Cyanomethylbenzothiazole (**1**) was used in heterocyclic synthesis extensively. Interesting heterocycles were obtained by reaction of 2-cyanomethylbenzothiazole (**1**) with either monodentate or bidentate reagents.

Synthesis of 2-Substituted Benzothiazoles

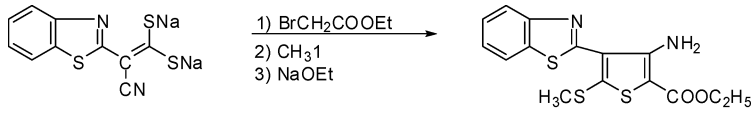
Formation of Five-Membered Rings Containing One Heteroatom

Synthesis of 2-[3-thienyl]benzothiazole derivatives. Thiophene derivatives in position 2- at the benzothiazole moiety were obtained via three pathways

i. Reaction of 2-cyanomethylbenzothiazole (**1**) with carbon disulfide in the presence of sodium hydroxide gave the sodium salt of 2-[2-benzothiazolyl]-3,3-disulphanylacrylonitriles (**30**).
Compound (**30**) was cyclized by treatment with ethyl bromoacetate followed by methylation to afford the thiophene (**59**).[32]

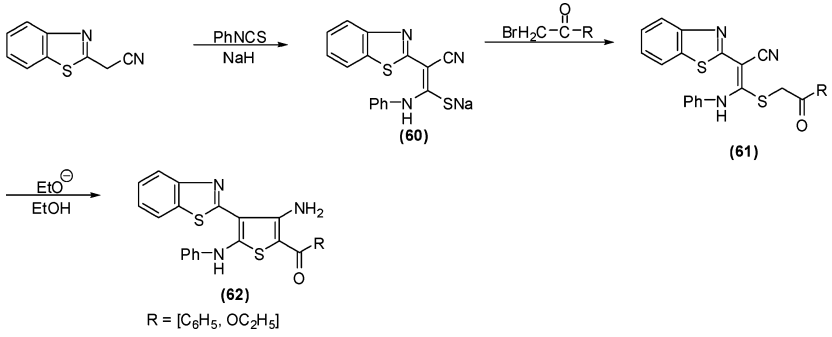


(1) (30)



(59)

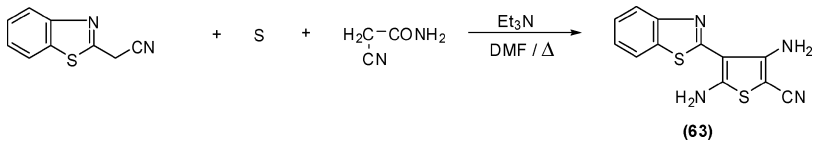
ii. 2-Cyanomethylbenzothiazole (**1**) reacts with phenyl isothiocyanate in the presence of sodium hydride to yield the sodium salt of 2-(2-benzothiazolyl)-3-phenylamino-3-sulfanylpropenenitrile (**60**), which on treatment with α-haloketones with subsequent cyclization afforded the thiophene derivatives (**62**) via the sulfide **61**.[25]



(60) (61) (62)

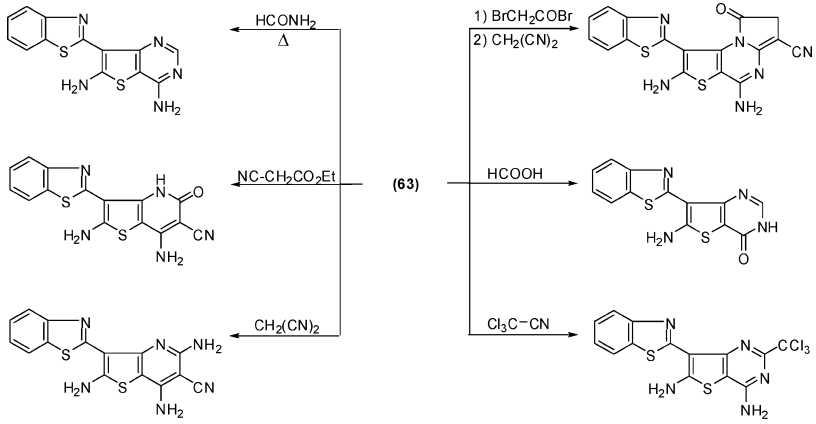
R = [C_6H_5, OC_2H_5]

iii. 2-Cyanomethylbenzothiazole (**1**) is used as a candidate for a facile synthesis of 2-[3,5-diamino-2-cyano-3-thienyl] benzothiazole (**63**) *via* Gewald reaction[73] as shown in the following equation:



(63)

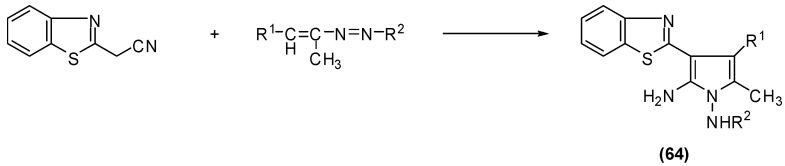
Thiophene derivative (**63**) could be successfully annelated[73] to polyfunctionally substituted thieno[3,2-b]pyridine, thieno[3,2-d]pyrimidine and some other fused thiophenes as shown in the following scheme.



Other thienyl benzothiazole derivatives have been reported.[74,75]

Synthesis of 2-[pyrrolyl]benzothiazoles. 2-[Pyrrolyl]benzothiazoles were prepared via two pathways

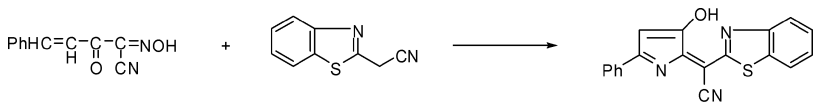
i. 2-Cyanomethylbenzothiazole (**1**) reacts with some conjugated azoalkene, of the general formula R^1-CH=C(CH_3)-N=N-R^2 to afford the intermediate 1,4- adduct which gave the corresponding pyrrole derivative (**64**) by cyclization.[76]



(64)

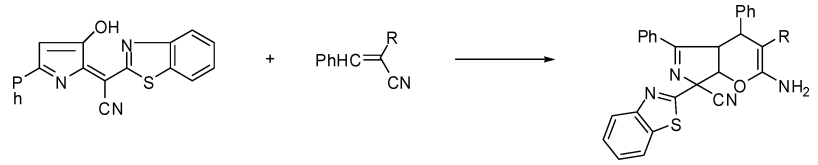
R^1 = -$COOCH_3$, -$COOC_2H_5$, R^2 = -$COOCH_3$, -$CONH_2$, -CONHPh

ii. The pyrrolyl ring system (**66**) was also synthesized by reaction of cinnamoyl (oximino)acetonitrile (**65**)[76] with 2-cyanomethylbenzothiazole (**1**).



(65) (66)

Pyrrolyl derivative (**66**) was used as useful intermediate for the synthesis of pyrano[2,3-c]pyrrole (**67**) by reaction with benzylidene nitrile.[76]

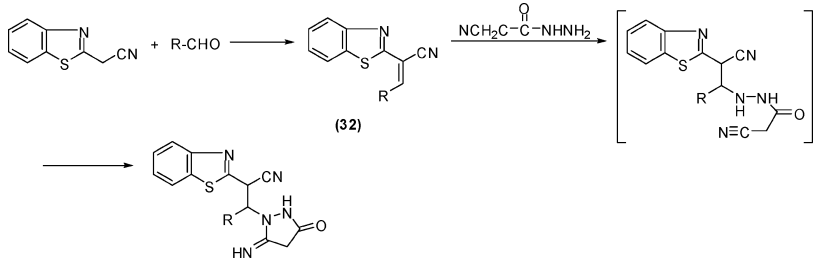


(66) (67)

R = CN, -$COOC_2H_5$

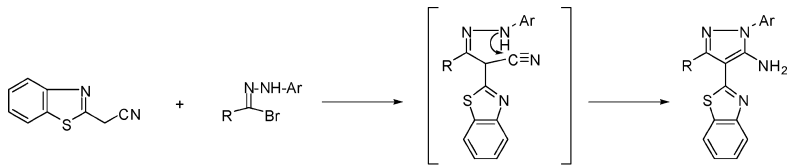
Formation of Five-Membered Rings Containing Two Heteroatoms

Synthesis of 2-[pyrazolyl]benzothiazole derivative. The pyrazole derivative (**68**) was prepared by reaction of the arylidene-2-cyanomethylbenzothiazole derivative (**32**) with cyanoacetyl hydrazide.[77]



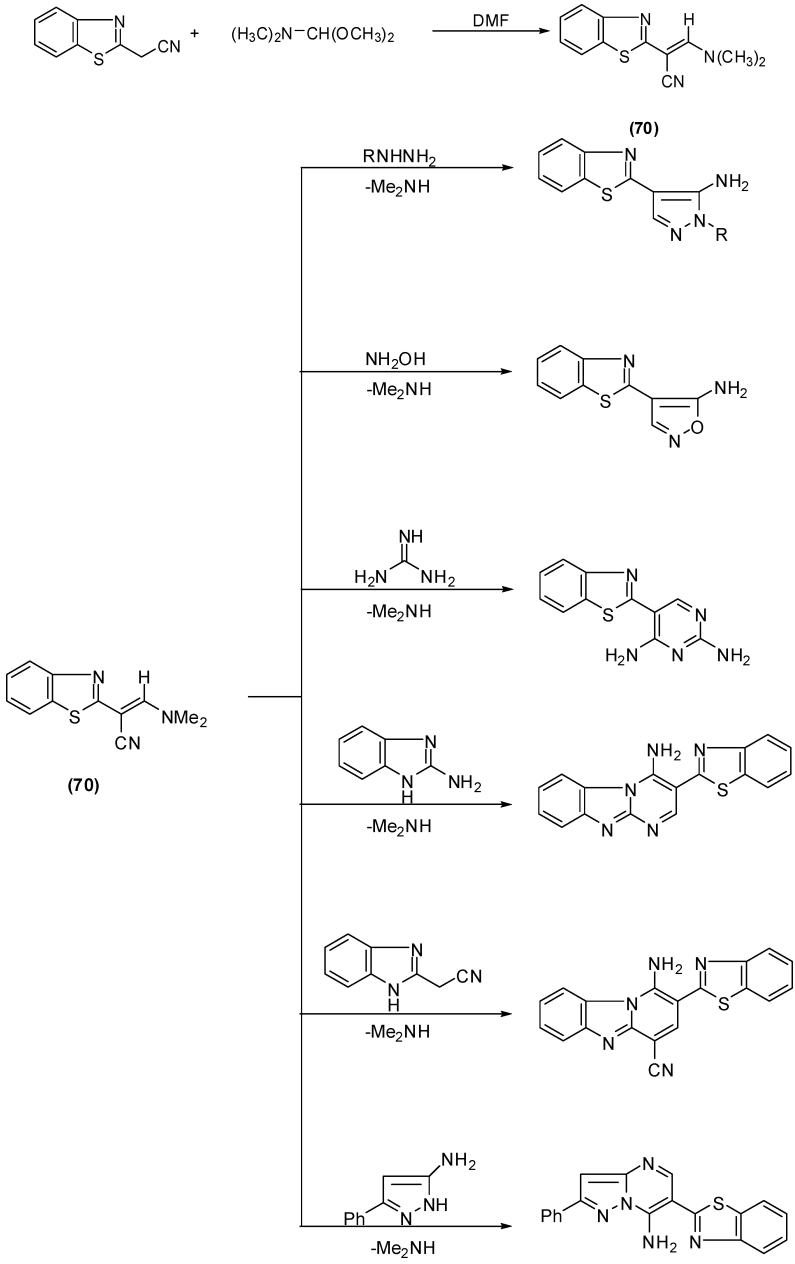
(32) (68)

Moreover, many pyrazole derivatives were prepared by treatment of **1** with hydrazonyl halide to give the aryl derivatives (**69**).[78–81]



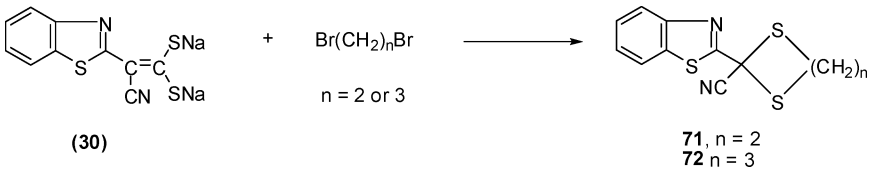
(69)

2-Pyrazolo and other 2-heterocyclic benzothiazole derivatives were also reported to be formed via the enaminonitrile intermediate (**70**).[82]



Some derivatives of pyrazolylbenzothiazoles were prepared and used as inhibitors of integrin-linked kinase as therapeutic agents for hyperproliferative and other disorders.[83]

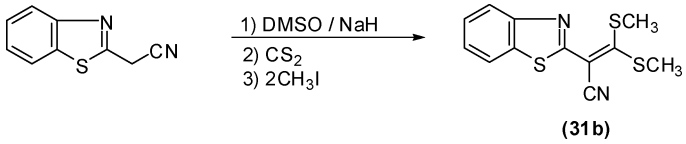
Synthesis of dithiole and dithione derivatives. Dithiole and dithione derivatives were prepared by reaction of acrylonitrile derivative (30) with ethylene bromide and/or 1,3-dibromopropane to give the corresponding dithiole (71) and dithione (72) derivatives, respectively.[28]



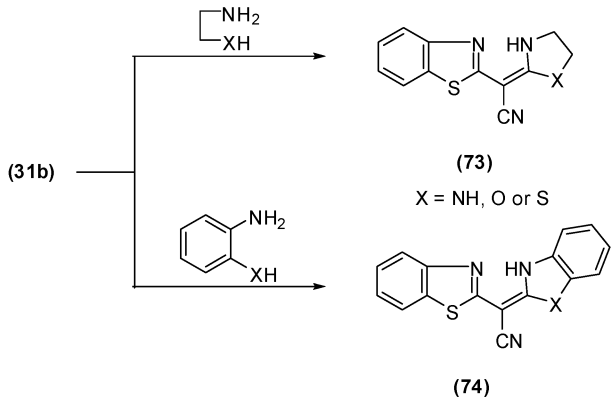
(30)

71, n = 2
72 n = 3

Synthesis of 2-imidazolinyl, 2-oxazolidinyl, and 2-thiazolidinylbenzothiazole derivatives. These heterocycles **73** and **74** could be prepared by reaction of 2-[2-benzothiazolyl]-3,3-bis(methylthio)-acrylonitrile (**31b**) with bifunctional reagents.[28]



(31b)



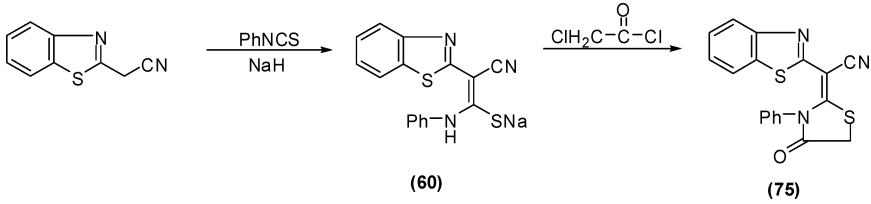
(73)

X = NH, O or S

(74)

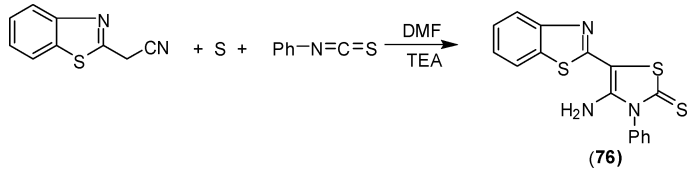
Chabaka, et al.[84] also prepared α-(heteroaryl)-2-benzothiazole acetonitriles. In addition, thiazolidine derivative (**75**) was reported to be

formed by the reaction of acrylonitrile derivative (**60**) with chloroacetyl chloride.[31]



(60) (75)

Recently, thiazoline **(76)** incorporating the benzothiazole moiety was prepared directly from compound **1** with elemental sulfur and phenyl isothiocyanate in the presence of an excess of triethylamine.[19]

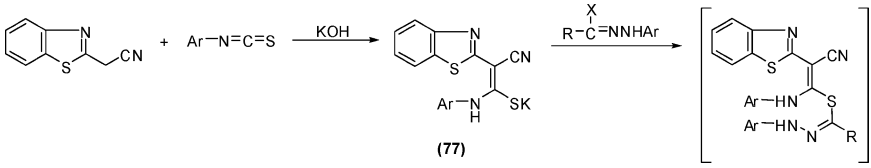


(76)

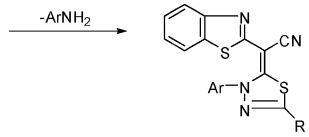
Formation of Five-Membered Rings with more than Two Heteroatoms

Synthesis of 2-thiadiazolylbenzothiazole derivatives.. There are two routes for the synthesis of thiadiazole derivatives

i. By the reaction of aryl isothiocyanates with 2-cyanomethylbenzothiazole (**1**) in the presence of potassium hydroxide to give the nonisolable 1:1 adduct (**77**) which was then subjected to react with hydrazonyl halide to give the corresponding 2,3-dihydro-1,2,3-thiadiazole derivatives (**78**).[28]



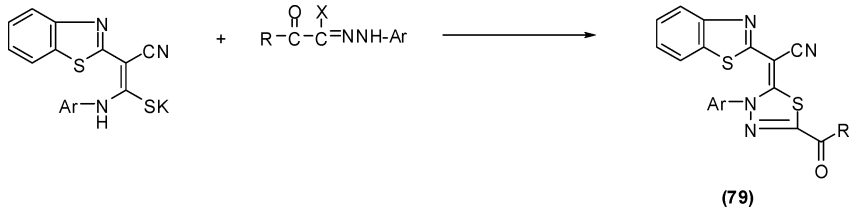
(77)



(78)

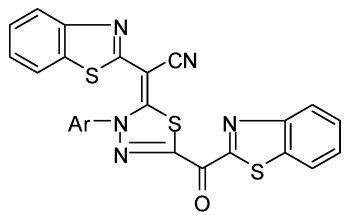
R	Ph-	PhCH=CH-	Ph-	CH_3	2-thienyl	2-furyl
Ar	Ph-	Ph-	4-NO-Ph-	4-NO_2-Ph	4-NO_2-Ph	4-NO_2-Ph

ii. Moreover, it has been found that α-ketohydrazonyl halides reacted with the nitrile (**77**) to afford the corresponding thiadiazole derivatives (**79**).[26]



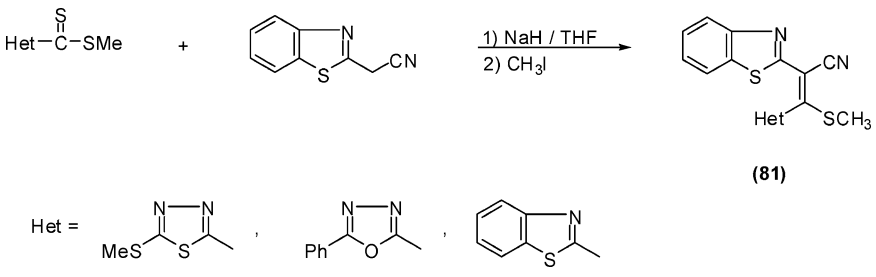
(79)

In case of R = 2-benzothiazolyl the above reaction gave the following compound (**80**).[24]



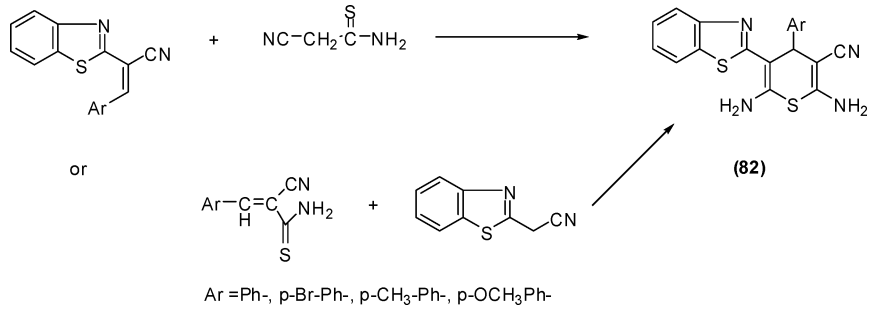
(80)

Miscellaneous five-membered rings with more than two heteroatoms. Heterocyclic methyl dithiocarboxylates react with (**1**) by Claisen condensation to form (**81**).[85]



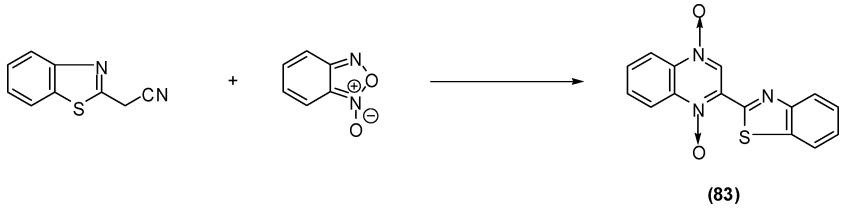
Formation of Six-Membered Rings

Synthesis of 2-thiopyranylbenzothiazole derivatives. It has been reported that thiopyranes (**82**) were obtained by reaction of arylidene derivatives of 2-cyanomethylbenzothiazole **(1)** with thiocyanoacetamide, or by reaction of (**1**) with arylidene of thiocyanoacetamide.[34]



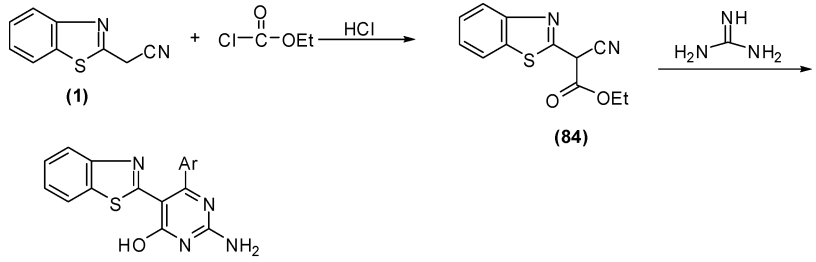
Synthesis of 2-pyridylbenzothiazole derivatives. As mentioned before, 2-cyanomethylbenzothiazole (**1**) reacts readily with pyridyl halide to form 2-[cyanopyridylmethyl]benzothiazole (**43**).[49]

Synthesis of quinoxalinylbenzothiazole derivatives. Under base catalyzed conditions, it was found that **1** reacts with benzofuroxane to yield quinoxaline 1,4-dioxide derivative (**83**).[86]



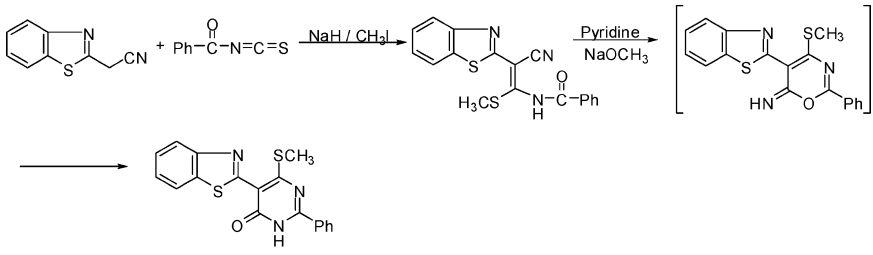
Synthesis of 2-pyrimidylbenzothiazole derivatives. Pyrimidyl benzothiazole derivatives were prepared by three different pathways.

1. Compound (**1**) reacts with ethyl chloroformate to give the corresponding ethyl α-cyano-α-benzothiazol-2-yl acetate (**84**) which was followed by reaction with guanidine to afford the pyrimidine derivatives (**85**).[27]



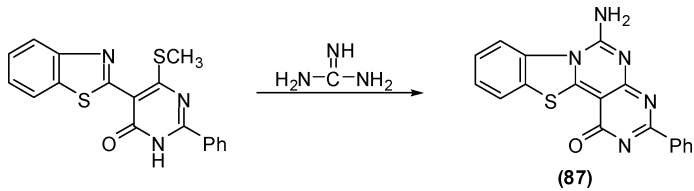
(1) (84) (85)

2. Reaction of benzoyl isothiocyanate with 2-cyanomethylbenzothiazole (**1**) in the presence of base, [27] yields the pyrimidine derivative (**86**).



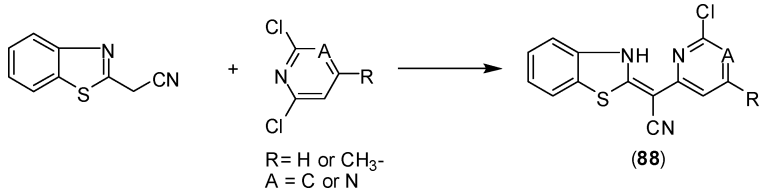
(86)

The product (**86**) was then cyclized by reaction with guanidine to give the pyrimidinobenzothiazole derivative (**87**)



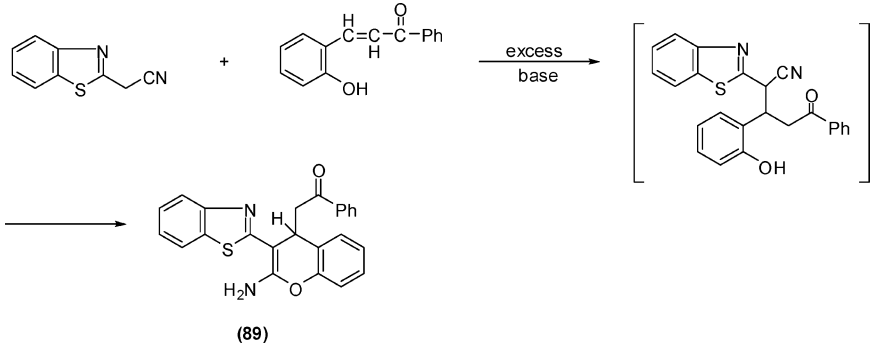
(87)

3. 3) Reaction of dichloropyrimidines or dichloropyridines with 2-cyanomethylbenzothiazole gave 1,3-benzothiazol-2-yl-(2-chloro-4-pyrimidinyl)acetonitrile(**88**).[72]



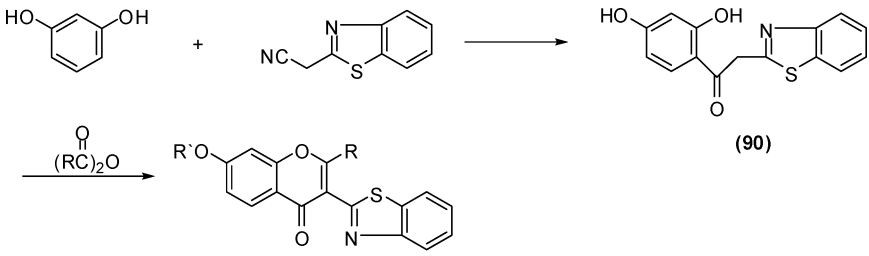
Synthesis of 2-Polycyclic Benzothiazoles

Synthesis of 2-benzopyrane derivatives. It has been reported that 2-cyanomethylbenzothiazole (**1**) reacts with arylidene acetophenone in basic medium to give the benzopyrane derivative (**89**).[37]



Synthesis of α and γ-chromone derivatives

Synthesis of γ-chromone. The interesting heterocyclic acetophenone (**90**) which was obtained by the nucleophilic addition of resorcinol to 2-cyanomethylbenzothiazole (**1**) was further subjected for cyclization with acid chlorides or anhydrides (acetic anhydride, trifluroacetic anhydride etc.) in pyridine solution to give the chromones (**91**) in good yield.[87] Also, substituted resorcinol was used to synthesize different chromone derivatives.[88–92]

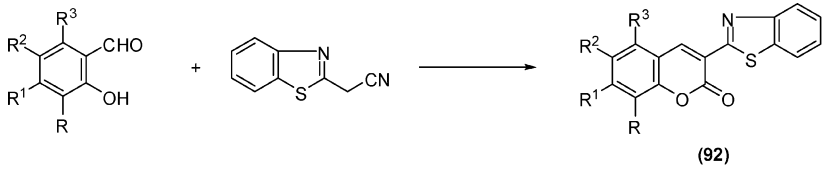


(90)

(91)

R = CH_3, CF_3, H, -COOEt R` = —$COCH_3$, —$COCF_3$, —COEt

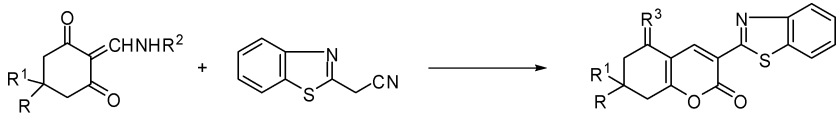
Synthesis of α-chromone (coumarine) derivatives. It has been reported that condensation of aromatic o-hydroxyaldehydes with (**1**) afforded the arylidene derivatives which was followed by intramolecular cyclization giving the corresponding coumarine derivatives (**92**).[37,47,48,93–103]



(92)

R = H, OH, R^1 = H, halogen, NO_2
R^3 = H or R^2 R^3 benzo

Coumarin derivatives (**94**) were also prepared from the enamine derivatives (**93**) by condensation with 2-cyanomethylbenzothiazole (**1**).[96,104,105]



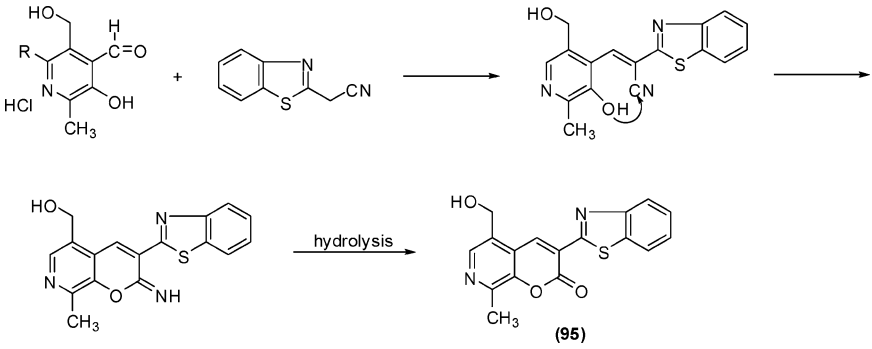
(93)

(94)

R = H, CH_3
R^1 = CH_3, Ph
RR^1 = $(CH_2)_5$

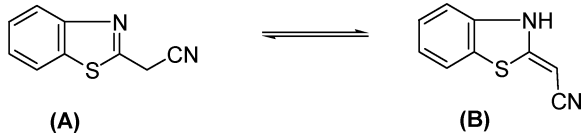
Synthesis of azacoumarine derivatives. Brufola et al.[106] prepared azacoumarine derivatives (**95**) by Knovenagel reaction of pyridoxal

hydrochloride with (**1**) in heterogeneous phase. The reaction gave better yields than obtained in homogenous alcoholic solution.



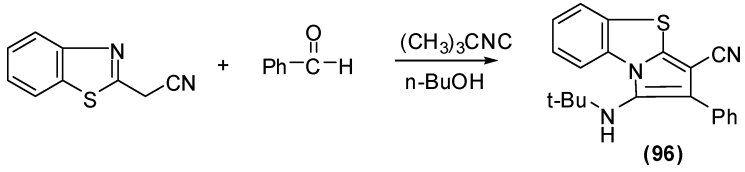
Synthesis of Fused Heterocycles

Most syntheses of fused heterocyclic benzothiazoles are based on the substitution of an acidic hydrogen of the methylene group by another group that can react with the enamine tautomer (B).



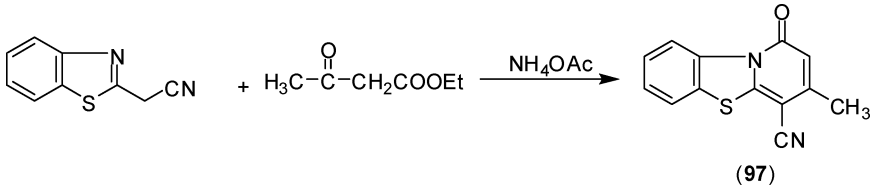
Synthesis of Pyrrolo[2,1-b]benzothiazole Derivatives

1-(tert-Butylamino)-2-phenyl-pyrrolo[2,1-b]benzothiazole-3-carbonitrile (**96**) was prepared by reaction of **1** with benzaldehyde and t-butylisonitrile in n-BuOH at 100°C for 16 h.[107]



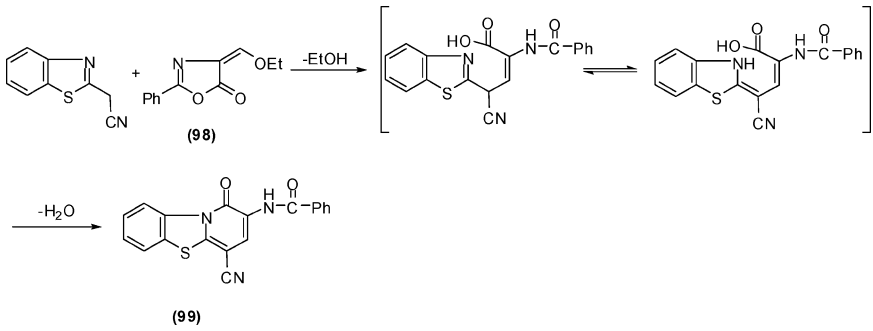
Synthesis of Pyrido[2,1-b]benzothiazole Derivatives

1. Reaction of ethyl acetoacetate with **1** in the presence of ammonium acetate gave annelated pyridine azaheterocyclic systems (**97**).[108]



(**97**)

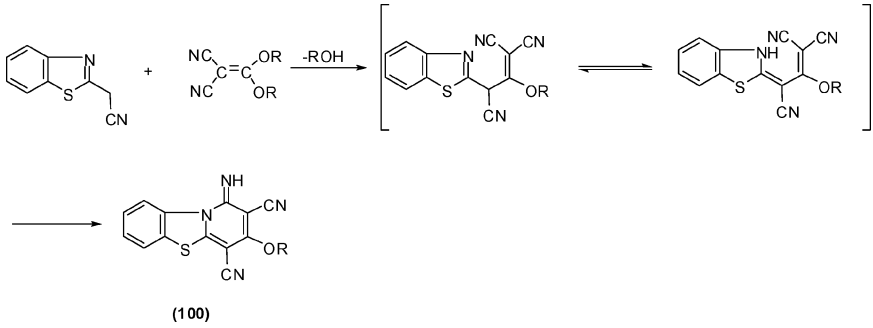
2. 2-Cyanomethylbenzothiazole (**1**) reacts readily with 4-ethoxymethylene-2-phenyl-5-oxazolone (**98**) to yield the corresponding pyrido[2,1-b]benzothiazole derivatives (**99**).[109]



(**98**)

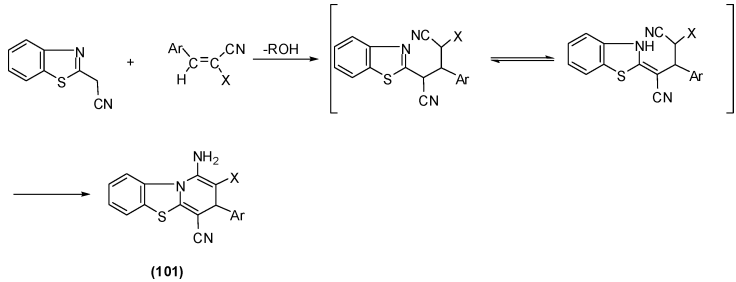
(**99**)

3. Moreover, it was found that **1** reacts with dialkoxymethylene-malonitrile to give pyrido[2,1-b]benzothiazole derivative (**100**).[32]



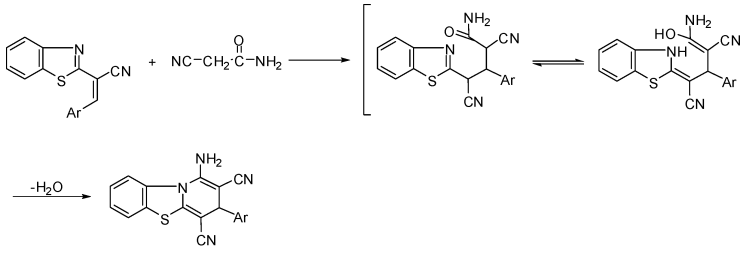
(**100**)

4. Similarly, pyrido[2,1-b]benzothiazole derivatives (**101**) were prepared by Michael addition of 2-cyanomethylbenzothiazole (**1**) to arylidene derivatives of malonitrile and/or ethyl cyanoacetate.[10]



(101)

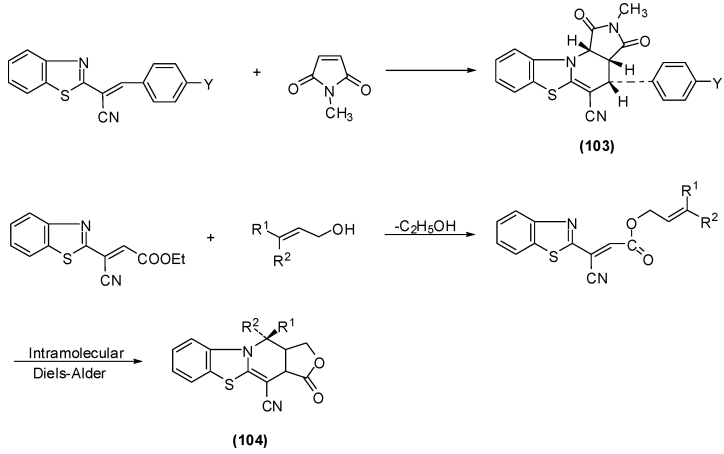
On the other hand, arylidene of 2-cyanomethylbenzothiazole (1) reacts readily with activated nitriles, e.g. cyanoacetamide, to give the corresponding pyrido[2,1-b]benzothiazole derivatives (**102**).



(102)

Ar = C_6H_5-, 4-BrC_6H_4-, 4-ClC_6H_4-, 4-CH_3-C_6H_4- and 4-$OCH_3C_6H_4$-

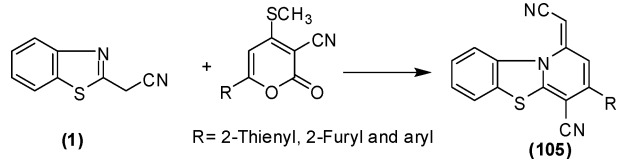
5. Furthermore, pyrido[2,1-b]benzothiazole derivatives (**103**) and (**104**) were prepared by reaction of arylidene derivatives of 2-cyanomethylbenzothiazole (**1**) as diene with different dienophiles, e.g N-methylmalemide,[110] allyl alcohol, methyl vinyl ether, methyl acrylate, p-methoxy styrene and 2,3-dihydrofurane.[111]



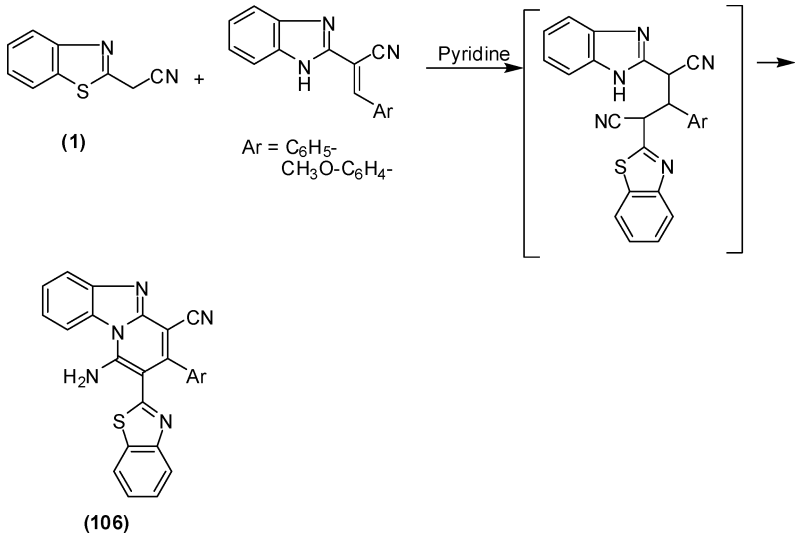
(103)

(104)

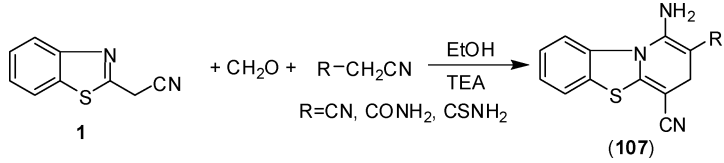
6. Pyrido[2,1-b] benzothiazole derivatives **(105)** were prepared by reaction of compound **1** with 6-alkyl-3-cyano-4-methylthio-2H-2-pyrone.[112]



Compound **1** was also used for the preparation of pyrido[1,2-a] benzimidazole derivatives **106.**[113]

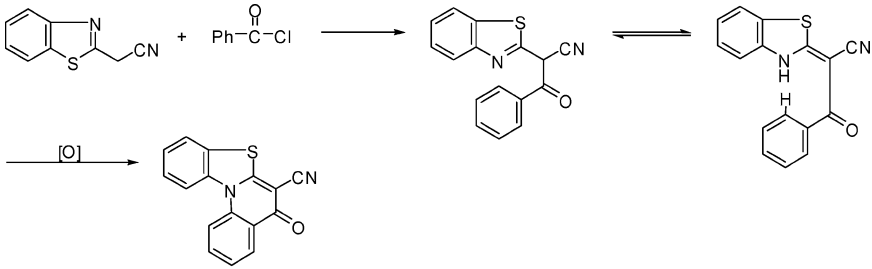


A variety of pyrido[2,1-b]benzothiazole derivatives (**107**) could be prepared by reaction of **1,** with formaldehyde and various active methylene reagents.[114]



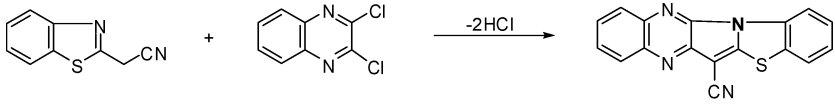
Moreover, compound **1** was also used in the synthesis of polyfunctionally substituted pyridine.[115,116]

7. Benzothiazolo[3,2-a]quinoline derivative (**108**) was prepared by benzoylation of the active methylene group of compound (**1**) which followed by oxidative cyclization with the benzene ring.[12]



(108)

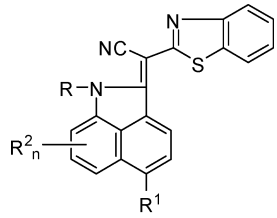
Other fused heterocyclic compounds such as (**109**) were prepared by reaction of 2,3-dichloroquinoxaline with 2-cyanomethylbenzothiazole (**1**).[117]



(109)

APPLICATIONS

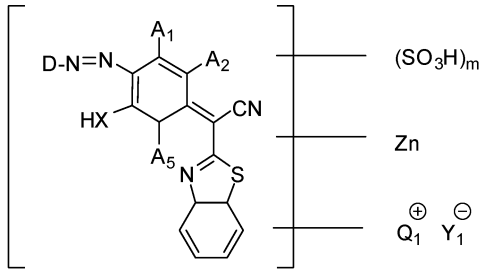
2-Cyanomethylbenzothiazole derivatives have found wide-spread applications as dyes, polymers, antibacterial and antiviral agents. A series of dyes (**110**) have been synthesized to be used as dyestuffs for dyeing polyamide, polyester, and acrylic fibers.[3,118,119]



(110)

2-Cyanomethylbenzothiazole **1** was also used to prepare the cationic, reactive, or acid dyes of general structure (**111**)[120] which are applied

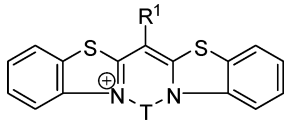
for dyeing and printing of macromolecule compounds including natural fibers with good general fastness results.



(111)

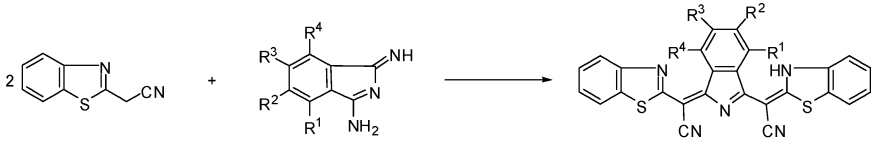
A_1, A_2 = H or A_1, A_2 cyclic groups, A_5 = H or NH_2
X = O or N, Q^+ = ammonium, Y^- = anion, D = cyclic diazo component

In addition, 2-cyanomethylbenzothiazole was used for the synthesis of complexes having the general structure (**112**), which may be further substituted to form analogs of monomethine cyanine dyes and are useful for importing fluorescent properties to materials by covalent and non covalent association.[121]



(112)

Reaction of one mole of 1-amino-3-iminoisoindolines with two moles of **1** afforded dyes of the general structure (**113**)[122] which were used as a pigment for thermoplastics during extrusion.

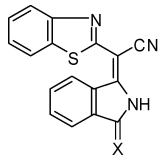


(113)

R^1-R^4 = H, NO_2, Ph, -OPh, alkyl, alkoxy

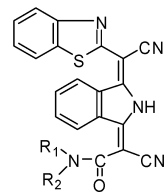
Also, it has been reported that 1-amino-3-iminoisoindolenine was condensed with cyanoacetic acid piperidide and the product was further condensed with **1** to give (**114**)[123] which provided polyesters with a light

fast greenish yellow shade while dyes (**115**)[124] provided polyesters with a light fast fluorescent yellow shade.



(**114**)

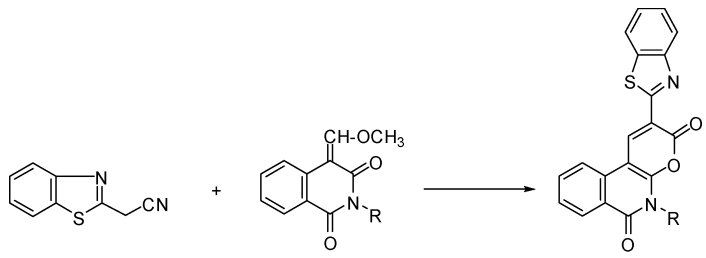
X= NH
= CH-COOR



(**115**)

R_1 = C_1-C_{10} aliphatic
R_2 = H, aryl
R_1, R_2 may form a heterocycle with N

A series of red to violet dyes (**117**) have been prepared by reaction of **1** with isoquinoline derivative (**116**).[125]



(**116**) (**117**)

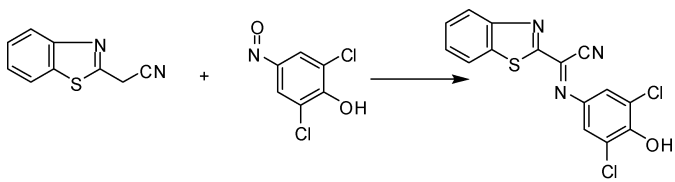
R = H, CH_3

Kluger et al.[126] prepared compounds, which are used to identify the dyed wool by irradiation.

Recently, compound **1** was used for the preparation of dyes with many applications.[127–135] Compound **1** was also used for color diffusion, transfer photographic materials, and formation of images.[136]

Some of the dyes were uses as photographic material.[137–139]

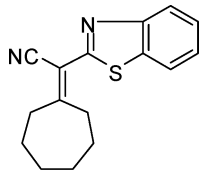
A hair dye **118** compound is provided as direct dye and prepared as follows:



(**118**)

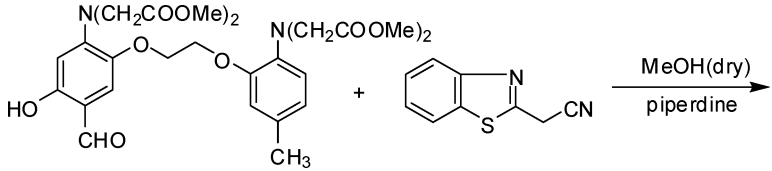
The hair dye compound is capable of strongly dyeing the hair with a vivid color tone without causing decomposition of the dye during the dyeing process, it exhibits an excellent resistance against sunlight, hair washing, perspiration, friction and heat, has a high stability against alkali and oxidizing agents, has a high dyeing property and less color fading after the passage of time.[140]

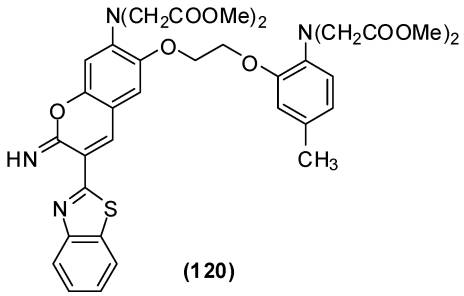
Also **1** was used to prepare compound (**119**) by reaction with cycloheptanone. Compound (**119**) was used in crystallography and molecular structure determination.[141]



(119)

2-Cyanomethylbenzothiazole was used to prepare compounds with high biological activity as antiviral,[142] antibacterial,[143,144] antihypertensive,[145] herbicides,[146–148] antineurodegenerative disease,[149] treatment of circulatory organ disease.[150] Iminocoumarin-based fluorescent Ca^{2+} indicators (**120**) were synthesized and the spectral profiles of their free and Ca^{2+} bound forms were studied.[151]





(120)

2-Cyanomethylbenzothiazole was also used in the preparation of metal complexes[152], JNK modulators,[153] corrosion inhibitor,[154] electro organic synthesis,[155]polymethine dyes [156] and polymers.[157–159]

REFERENCES

[1] W. Borsche and W. Doeller, *Ann.* **537**, 39–52 (1938); *Chem. Abstr.,* **33,** 1740 (1939).
[2] J. D. Kendall and D. J. Fry, *GB*. **577,** 295 (1946); *Chem. Abstr.,* **42,** 24976 (1948).
[3] P. Loew, H. Schwander, and H, Kristinsson, (Ciba-Geigy A.-G., Switz.). *Ger. Offen.* (1977), 15 pp.; *Chem. Abstr.,* **88,** 105342 (1978).
[4] A. K. El-Shafai and A. M. El-Sayed, *Gazz. Chim. Ital.*, **117**(7), 385 (1987); *Chem. Abstr.,* **108,** 112274 (1988).
[5] K. Takagi, T. Iwachido, and N. Hayama, *Chem. Letters*, **5,** 839 (1987); *Chem. Abstr.,* **108,** 37716 (1988).
[6] K. Takagi, T. Iwachimichi, and N. Hayama. *Jpn. Kokai Tokkyo Koho Jp*., **01**, 75, 234, 276, (1987); *Chem. Abstr.,* **112,** 35842 (1990).
[7] K. R. Nivalkar and S. H. Mashsraqui, *Synth. Commun*., **26** (19), 35 (1996); *Chem. Abstr.,* **125,** 275749 (1996).
[8] M. Lorenz, *(Bayer A.-G., Germany). Ger. Offen* (1998), 6 pp.; *Chem. Abstr.,* **129,** 4646 (1998).
[9] F. S. Babichev and Yu. M. Volovenko, *Ukr. Khim., Zh* (Russ) **43** (1), 41–43 (1977); *Chem. Abstr.,* **86,** 171330 (1977).
[10] F. S. Babichev, V. K. Patratii, Yu. M. Volovenko, N. G. Prodanckuk, V. G. Sinchenko, and A. G. Nemazanyi, *Khim. Farm. Zh*., **22** (10), 1223–1225 (1988); *Chem. Abstr.,* **111,** 7285 (1989).
[11] Yu. M. Volovenko, E. V. Blyumin, T. V. Shokol, G. G. Dubinina, and F. S. Babidev. *Chem. Heterocycl. Compd*., **33** (4), 445–447 (1997); *Chem. Abstr.,* **128,** 88845 (1998).
[12] Yu. M. Volovenko, A. G. Nemazanyi, I. G. Ryabokon, and F. S. Babichev, *Ukr. Khim. Zh.*, **54**(3), 295–300, (1988); *Chem. Abstr.,* **110,** 38921 (1989).
[13] M. Abd. El Latif, Fawi, *Phosphorus, Sulfur Silicon Relat. Elem*., **167,** 267–274 (2000); *Chem. Abstr.,* **135,** 107313 (2001).
[14] M. Ishizaki and S. Osada. *Jpn. Kokai Tokkyo Koho Jp*, **06,** 128, 213 (1994), Appl. 92/278, 871, 1992; 31 pp.; *Chem. Abstr.,* **121,** 205215 (1994).
[15] Yu. M. Volovenko, T. V. Shokol, I. B. Kulik, and F. S. Babichev. *Ukr. Khim. Zh*., **61**(7–8), 131–134 (1995); *Chem. Abstr.,* **125,** 275737 (1996).
[16] W. Lindner and A. Haberkorn. *Eur. Pat.* Appl. (1990), 38 pp.; *Chem. Abstr.,* **113,** 152471 (1990).
[17] H. Galal Elgemeie, R. Samia El-Ezbawy, and A. Hany Ali. *Synth.. Commun.* **31** (22), 3459–3467 (2001); *Chem. Abstr.,* **136,** 102359 (2002).
[18] Yu. M. Volovenko and E. V. Blyumin. *Chem. Heterocycl. Compd.*, **34** (3), 324–328 (1998); *Chem. Abstr.,* **130,** 25020 (1999).
[19] M. E. A. Zaki, A. A. Fadda, K. Samir, and F. A. Amer, *Phosphorus, Sulfur, and Silicon and the Related Elements*, **181** (8), 1815–1823 (2006).
[20] P. Loew and S. Koller. *Ger. Offen*, (1976) 33 pp.; *Chem. Abstr.,* **86,** 56736 (1977).
[21] G. H. El-Gemie and F. A. Abd-El-Al, *Heterocycles*, **24** (2), 349–353 (1986); *Chem. Abstr.,* **106,** 84531 (1987).
[22] A. M. Farag. *J. Chem. Res. Synop* (**3**) 96-7 (1995). *Chem. Abstr.,* **123,** 557330 (1995).
[23] E. A. El-Rady. *Journal of Heterocyclic Chemistry*, **39**(5), 1109–1110 (2002), *Chem. Abstr.,* **138,** 238146 (2003).

[24] D. Konwar and R. Boruah, *Heterocycles*, **24** (2), 3364–3372 (1988); *Chem. Abstr.,* **106,** 213814 (1987).
[25] M. Augustin and W. Dolling, *J. Prakt Chem.*, **324** (2) 322–328 (1982); *Chem. Abstr.,* **97,** 92199 (1982).
[26] H. M. Hassaneen, A. S. Shawali, and T. A. Abdallah, *Sulfur Letters,* **15** (3), 103–109 (1992); *Chem. Abstr.,* **118,** 1244549 (1993).
[27] G. A. M. Nawwar, M. E. A. Zaki, and L. M. Chabaka. *Phosphorus, Sulfur, and Silicon,* **79** (1–4), 195–205 (1993); *Chem. Abstr.,* **120,** 164052 (1994).
[28] M. Augustin and W. Dolling, *J. Prakt Chemie*, **324** (1), 3–11 (1982); *Chem. Abstr.,* **97,** 55732 (1982).
[29] A. A. Fadda, F. A. Amer, M. E. A. Zaki, and Kh. Samir, *Phosphorous, Sulfur and Silicon,* **155,** 59–66 (1999); *Chem. Abstr.,* **33,** 281720 (2000).
[30] M. V. Vovk, P. S. Lebed, V. A. Sukach, and M. Y. Kornilov, *Russian Journal of Organic Chemistry*, **39** (12)**,** 1781–1788 (2003); *Chem. Abstr.,* **141,** 277585 (2004).
[31] M. Augustin and W. Dolling. *Z. Chem.*, **21** (6), 216–217 (1981); *Chem. Abstr.,* **95,** 115332 (1981).
[32] S. Kambe and K. Saito. *Synthesis*, **7,** 601–602 (1984).
[33] V. Drynaska, *Sulfur Letters,* **5** (2) 47–50 (1981); *Chem. Abstr.,* **108,** 75272 (1988).
[34] N. M. Fathy, F. M. Abed El-Motti, and G. E. H. Elgemeie, *Arch. Pharmacie*, **321** (9) 509–12(1988), **110,** 23775.
[35] M. Sakamoto, A. Nozak, M. Shimamoto, Y. Suzuki, S. Yashiok, and M. Nagano, *J. Chem. Soc. Perkin Trans 1*, **13,** 1759–1770 (1995); *Chem. Abstr.,* **123,** 313802 (1995).
[36] V. Dryanska, *Khim. Fak.,* **80,** 63–70 (1992); *Chem. Abstr.,* **121,** 57370 (1994).
[37] G. A. M. Nawwar, H. F. Zohdi, R. H. Swellem, and S. A. Osman, *Heterocycles*, **34** (3) 547–564 (1992); *Chem. Abstr.,* **117,** 90208 (1992).
[38] H. Galal Elgemeie, Z. Hoda Shams, M. Yehya Elkholy, and S. Neerrmeen Abbas, *Phosphorus, Sulfur, Silicon Relat. Elem.*, **165,** 265–272 (2000); *Chem. Abstr.,* **134,** 295766.
[39] K. Teramura, M. Shoji, and A. Kojima, *Jpn. Kokai Tokkyo Koho Jp.*, **07,** 258, 236, (1995); Appl. **99**, 50, 427, (1994) 19 pp.; *Chem. Abstr.,* **124,** 176077 (1996).
[40] K. Teramura, M. Shoji, and A. Kojima, *Jpn. Kokai Tokkyo Koho Jp.*, **07,** 157, 476, (1995) Appl. 93, 339, 380, (1993), 58pp.; *Chem. Abstr.,* **123,** 213103 (1995).
[41] R. Kada, D. Ilavasky, I. Goljer, and G. Peter, *Collect Czech Chem. Commun.*, **56** (2), 418–419 (1991); *Chem. Abstr.,* **115,** 8649 (1991).
[42] M. M. Ismail, A. M. Abdel-Halim, and M. Abass, *J. Serb. Chem. Soc.*, **62** (10), 977–986 (1997); *Chem. Abstr.,* **128,** 13217 (1998).
[43] H. M. Deger and E. Konz, *Ger. Offen. DE* **3**, 210, 776, 1983, Appl., (1982) 31 pp.; *Chem. Abstr.,* **100,** 53203 (1984).
[44] K. Hunt, *Brit. UK Pat. Appl. GB* **2,** 077, 751 23 Dec. 1981, Appl. 80, (1980); *Chem. Abstr.,* **96,** 182763 (1982).
[45] M. Lacova and P. Chabrecek, *Chemical Papers*, **41** (5), 709–717 (1987); *Chem. Abstr.,* **109,** 377732 (1988).
[46] A. A. Fadda, H. M. Refat, M. E. A. Zaki, and H. H. Abdel Razik, *Synth. Commun.*, **29**(21), 3773-3779 (1999); *Chem. Abstr.,* **131**, 351251 (1999).
[47] P. Loew, *Ger. Offen,* **2,** 710, 285 , 1977, Swiss Appl. 76, 3, 035, (1976); *Chem. Abstr.,* **87,** 168083 (1977).
[48] V. Dryanska, *Synth. Commun.*, **17** (2) 203–209 (1987); *Chem. Abstr.,* **107,** 198012 (1987).
[49] Yu. M. Volovenko, T. V. Shokol, L. I. Vlasyk, and N. G. Prodanchuk, *Ukr. Khim. Zh.*, **58** (5), 430–432 (1992); *Chem. Abstr.,* **117,** 233799 (1992).

[50] A. Nemazanyi and N. Haider, *J. Heterocyclic Chem.*, **34** (2), 397–400 (1997); *Chem. Abstr.,* **127,** 50555 (1977).
[51] A. G. Nemazanyi, Yu. M. Volovenko, T. A. Silaeva, M. Yu. Kornilov, and F. S. Babichev, *Khimiya Geterotsiklicheskikh Soedinenii*, **8,** 1104–1106 (1991); *Chem. Abstr.,* **116,** 194121 (1992).
[52] F. S. Babichev and Yu. M. Volovenko, *Ukr. Khim. Zh.*,**52** (5), 506–509 (1986); *Chem. Abstr.,* **107,** 7092 (1987).
[53] Yu. M. Volovenko, A. G. Nemazanyi, G. L. Vesel Sikayo, and F. S. Babichev, *Khim. Biol. Nauki*, **6,** 35–38 (1986); *Chem. Abstr.,* **106,** 176303 (1987).
[54] A. Nemazanyi and N. Haider, *Journal of Heterocyclic Chemistry*, **33** (4), 1147–1151 (1996); *Chem. Abstr.,* **125,** 300843 (1996).
[55] A. G. Nemazanyi, Yu. M. Volovenko, T. A. Silaeva, and F. S. Babichev, *Dokl. Akad Nauk SSR*, **310** (5), 1135–1137 (1990); *Chem. Abstr.,* **113,** 78221 (1990).
[56] Yu. M. Volovenko.; T. A. Volovenko, A. P. Kozynchenko, and F. S. Babichev, *Ukr. Khim. Zh.*, **62,** (1–2), 124–127 (1996); *Chem. Abstr.,* **126,** 157445 (1997).
[57] K. Saito, T. Goto, A. Kobayashi, K. Kojo, S. Oguchi, and S. Narita, *Jpn. Tokkyo Koho Jp.,* (1987), 8 pp.; *Chem. Abstr.,* **109,** 110408 (1988).
[58] Yu. M. Volovenko and T. A. Volovenko, *Chemistry of Heterocyclic Compounds*, **37** (9), 1092–1095 (2001); *Chem. Abstr.,* **137,** 47170 (2002).
[59] Yu. M. Volovenko and G. G. Dubinina, *Chem. Heterocycl. Compd.*, **35** (9), 1089–1093 (1999) (Pub. 2000); *Chem. Abstr.,* **132,** 334426 (2000).
[60] A. A. Mokhir, V. V. Polovinko, and K. V. Domasevich, *Zh. Obshch. Khim.*, **65** (6), 1038–41, (1995); *Chem. Abstr.,* **124,** 145973 (1996).
[61] A. A. Mokhir, K. V. Domasevich, N. K. Dalley, X. Kou, N. N. Gerasmichuk, and O. A. Gerasimchuk, *Inorg. Chim. Acta,* **284** (1) 85–98 (1999); *Chem. Abstr.,* **130,** 223202 (1999).
[62] W. Ried and H. Schiller, *Chem. Ber.,* **86,** 730–734 (1953); *Chem. Abstr.,* **48,** 68070 (1954).
[63] A. Lukszczyk, H. Martin, P. G. Diel, W. Fory K. Gatzi, H. Kristinsson, B. Muller, W. R. Munt, and J. P. Pachlatko, *Eur. Pat.* Appl. EP, **12,** 158, (1980), CH Appl. 78/9, 255, 1978; 72 pp.; *Chem. Abstr.,* **97,** 140287 (1982).
[64] R. A. B. Copeland and A. R. Day, *J. Amer. Chem. Soc.*, **65,** 1072 (1943).
[65] L. Bukowski, *Acta Pol. Pharm.*, **35** (3), 295–259 (1978).
[66] S. Galinowski and J. Lenartowicz, *J. Pol.,* **95,** 878, 31 (1978); *Chem. Abstr.,* **90,** 139069 (1979).
[67] T. Ozden, A. Ayalap, and S. Ozden, *FABAD Farm, Bilimler Derg.*, **9** (1), 25–34 (1984); *Chem. Abstr.,* **101,** 110816 (1984).
[68] L. Hans, F. Werner, and P. Jerker, *Chem. Ber.*, **84,** 719–729 (1951).
[69] R. W. Balsiger, H. Hanni, and O. Schinder, *Helv. Chim. Acta,* **49** (2), 889–891 (1966).
[70] K. V. Domasevich, *Russ. J. Org. Chem.*, **33** (4), 569–570 (1997); *Chem. Abstr.,* **128,** 192583 (1998).
[71] M. A. A. Eneairy, T. M. Abdel-Rahman, and A. M. Hammad, *J. Chem. Res.; Synop.*, **11,** 684–685 (1998); *Chem. Abstr.,* **130,** 81447 (1999).
[72] G. Pascale, J. E. Isabelle A. Vittoria, A. A. Steve, and C. Yve, *J. Med. Chem.*, **48,** 4596–4607 (2005).
[73] S. M. Mourad, *Monatsch. Chem.*, **127,** 955–962 (1996); *Chem. Abstr.,* **126,** 8069 (1997).
[74] M. A. Raslan, M. A. Khalil, S. M. Sayed, and A. M. Farag, *Heterocycl. Commun.*, **5**(2), 167–171 (1999); *Chem. Abstr.,* **131,** 116183 (1999).
[75] Y. M. El-Kholy, *Phosphorus, Sulfur Silicon Relat. Elem.*, **177** (1)**,** 115–122 (2002).

[76] O. Attansi, Z. M. Liao, S. S. Alexender, and Z. Serra, *J. Chem. Soc. Perkin Trans. 1*, **3,** 315–320 (1993); *Chem. Abstr.,* **118,** 212802 (1993).
[77] G. A, M. Nawwar, R. H. Swellem, and L. M. Chabaka, *Heterocycles*, **38** (1), 71–80 (1994); *Chem. Abstr.,* **120,** 270177 (1994).
[78] K. M. Ghoneim, S. El-Basil, A. N. Osman M. M. Said, and S. A. Megahed, *Rev. Roum. Chim.*, **36** (11–12), 1355–1361 (1991); *Chem. Abstr.,* **117,** 131111 (1992).
[79] A. M. Farag, K. M. Dawood, and Z. E. Kandeel, *J. Chem. Res. Synop.,* **9,** 416–417 (1996).
[80] M. A. Abdallah, A.N. Mosselhi, S. M. Riyadh, and A. S. Shawali, *Indian J. Chem. Sect. B: Org. Chem. Incl. Med.*, **36** (12), 1175–1177 (1997); *Chem. Abstr.,* **128,** 308432 (1998).
[81] K. M. Dawood, *J. Chem. Res. Synop*., **3** 128–129 (1998); *Chem. Abstr.,* **129,** 16081 (1998).
[82] K. M. Dawood, Z. E. Kandeel, and A. M. Farag, *J. Res., Synop.*, **4,** 208–209 (1998).
[83] Z. Zhang, S. T. Daynard, S. Wang, X. Du, B. G. Chopiuk, J. Yan, J. Chen, and V. S. Sviridov, (Kinetek Pharmaceuticals, Inc., Can.). *PCT Int. Appl.*, (2004), 171 pp.; *Chem. Abstr.,* **140,** 163862 (2004).
[84] L. M. Chabaka, R. H. Swellem, and N. A. Shafik, *Pol. J. Chem*., **68** (7), 1317–1328 (1994); *Chem. Abstr.,* **122,** 81325 (1995).
[85] R. Mayer, H. Hartenhanuer, and M. Gruner, *J. Prakt. Chem*., **333** (1) 35–40 (1991); *Chem. Abstr.,* **115,** 92172 (1991).
[86] H. N. Borah and J. S. Sandhu, *Heterocycles*, **24** (4), 979–982 (1986); *Chem. Abstr.,* **106,** 67240 (1987).
[87] V. P. Khilya, L. G. Grishko, and T. N. Sokolova, *Khim. Geterotskikl. Soedin*, **12**, 1593–1595 (1975); *Chem. Abstr.,* **84,** 105486 (1976).
[88] N. V. Gorbulenko, N. N. Shimko, and V. P. Khilya, *Doklady Akademii Nauk Ukrainskoi SSR*, **5,** 117–123 (1991); *Chem. Abstr.,* **115,** 182897 (1991).
[89] N. V. Gorbulenko, M. S. Fransinyuk, and V. P. Khilya, *Khim. Geterotiskil Soedin*, **4** 464–471 (1994); *Chem. Abstr.,* **122,** 290759 (1995).
[90] M. S. Frasinyuk, M. S. A. V. Turov, and V. P. Khilya, *Chem. Heterocycl. Comp.*, **34** (8), 923–928 (1998) (Pub) (1999); *Chem. Abstr.,* **130,** 282026 (1999).
[91] M. A. El-Sayed Yakout, *Egypt J. Chem*., **45**(6), 1029–1042 (2003).
[92] G. Brufola, F. Frinuelli, O. Piermatti, and F. Pizo, *Heterocycles*, **43** (6), 1257–1266 (1996); *Chem. Abstr.,* **125,** 142352 (1996).
[93] R. Suzuki, A. Otsuji, T. Uragami, and H. Takum, *Jpn. Kokai, Tokkyo Koho, Jp*., **09,** 291, 087, 1997, Appl. 96, 105, 126 , (1996); *Chem. Abstr.,* **128,** 68505 (1998).
[94] G. H. Elgemie, *Chem. Ind*., **19,** 653–654 (1989); *Chem. Abstr.,* **112,** 158179 (1990).
[95] H. Harnisch, *Ger. Offen. DE* **3,** 044, 128 (1982), Appl. (1980); 21 pp.; *Chem. Abstr.,* **97,** 146218 (1982).
[96] V. Dryanska, *Phosphorus, Sulfur, Silicon Rel. elements,* **61** (3–4), 325–329 (1991); *Chem. Abstr.,* **115,** 207902 (1991).
[97] M. H. Elnagdi, S. O. Abdallah, K. M. Ghoneium, E. M. Ebied, and K. N. Kassab, *J. Chem. Res. Synop*, **2,** 44–45 (1997); *Chem. Abstr.,* **126,** 1326365 (1997).
[98] T. Ohyama, K. Murayama, and K. Kato, *Eur. Pat. Appl. Ep*. **435,** 261, (1991), Jp Appl. 89, 338, 282, 1989; 15 pp.; *Chem. Abstr.,* **115,** 232232 (1991).
[99] H. Mitekura, Y. Danoh, Y. Ooga, N. Mori, S. Suga, Y. Taniguchi, T. Koyama, C. Adachi, T. Saitou, and M. Satusuki, *PCT Int. Appl. WO* 99 40, 086, 1999, Jp. Appl. 1998/297, 521 (1998), 57 pp.; *Chem. Abstr.,* **131,** 137985 (1999).
[100] T. Nakaya, T. Yamauchi, Takao; T. Saikawa, A. Tajima, and H. Mori, *Jpn. Kokai Tokkyo Koho JP* 2002 **114,** 773. 16 Apr 2002, Appl. 2000/301,040, 29 Sep 2000; 28 pp.; *Chem. Abstr.,* **136,** 309849.

[101] X. Luo, C. Song, and H. Lubai, *Science in China, Series B*: Chemistry, **44** (5), 532–539 (2001); *Chem. Abstr.,* **136,** 356371 (2002).
[102] O. V. Khilya, M. S. Frasinyuk, A. V. Turov, and V. P. Khilya, *Chemistry of Heterocyclic compounds*, **37** (8), 1029–1037 (2001); *Chem. Abstr.,* **136,** 401550 (2002).
[103] W. Czajkowski and M. Kazmierska, *Przemysl Chemiczny*, **81** (3), 177–180 (2002); *Chem. Abstr.,* **137,** 95150 (2002).
[104] I. Trummer, E. Ziegler, and O. S. Wolfbeis, *Synthesis*, **3,** 225–227 (1981); *Chem. Abstr.,* **95,** 42829 (1981).
[105] A. Knierzinger and O. S. Wolfbies, *J. Heterocyclic Chem*., **17** (2), 225–229 (1980); *Chem. Abstr.,* **93,** 133811 (1980).
[106] G. Brufola, F. Frinuelli, O. Piermatti, and F. Pizzo, *Heterocycles*, **45** (9), 1715–1721 (1997); *Chem. Abstr.,* **127,** 278158 (1997).
[107] K. Bedjeguelal, H. Bienayme, P. Schmitt, and S. Grisoni, *(Urogene, Fr.). PCT Int. Appl*. (2004), 89 pp.; *Chem. Abstr.,* **142,** 56369 (2005).
[108] Yu. M. Volovenko and T. V. Shokol, *Chemistry of Heterocyclic Compounds*, **39** (4), 545–546 (2003)**;** *Chem. Abstr.,* **140,** 287326 (2004).
[109] T. Chiba, T. Tahahashe, and C. Kanno, *Chem. Pharm. Bull*, **33** (9) 4002–4004 (1985); *Chem. Abstr.,* **105,** 97378 (1986).
[110] M. Sakamoto, A. Nazaka M. Shimamoto, H. Ozaki, Y. Suzuki, S. Yoshioka, M. Nagano, K. Okamura, T. Date, and O. Tamura, *J. Chem. Soc. Perkin Trans. 1,* **13,** 1759–1770 (1995); *Chem. Abstr.,* **123,** 313802 (1995).
[111] M. Sakamoto, M. Nagano, Y. Suzuki, K. Satoh, and O. Tamura, *Tetrahedron*, **52** (3) 733–742 (1996); *Chem. Abstr.,* **124,** 202089 (1996).
[112] J. V. Ram, P. Srivastava, and N. Agarwal, *J. Chem. Res. (S)*, **10,** 421–423 (2001); *Chem. Abstr.,* **136,** 247518 (2002).
[113] M. A. Raslan, *J. Chin. Chem. Soc.*, **47** (4B), 961–965 (2000); *Chem. Abstr.,* **134,** 222689 (2001).
[114] M. E. A. Zaki, A. A. Fadda, K. Samir, and F. A. Amer, *Chemistry of Heterocylic Compounds,* **39 (**9) 1413–1419 (2003); *Chem. Abstr.,* **141,** 225372 (2004).
[115] A. A. Fadda and H. M. Refat, *Monatsh. Chem*., **130** (12), 1487–1492 (1999); *Chem. Abstr.,* **132,** 222418 (2000).
[116] A. A. M. Elneairy, A. M. Abdel-Fattah, *Phosphorus, Sulfur and silicon and the Related Elements*, **175,** 15–33 (2001); *Chem. Abstr.,* **136,** 247556 (2002).
[117] A. P. Kozyrchenko, Yu. M. Volovenko, F. S. Babichev, and V. K. Drgmonenkov, *Khim. Geterotisl. Soedin*, **1,** 85–87 (1990); *Chem. Abstr.,* **113,** 132129 (1990).
[118] H. Schwander, C. Zickendraht, and P. Loew, *Ger. Offen*, **2,** 55, 575, (1976) Swiss. Appl. 74, 15, 368, (1974), 14 pp.; *Chem. Abstr.,* **85,** 64799 (1976).
[119] H. Schwander and C. Zickendraht, *Ger Offen*, **2,** 724, 540, (1977) Swiss Appl.; *Chem. Abstr.,* **88,** 91049 (1978).
[120] R. Hamprecht, *Ger. Offen. DE* **19** 535, 501, (1997), Appl. **19,** 535, 501, (1995), 73 pp.; *Chem. Abstr.,* **126,** 306381 (1997).
[121] A. S. Waggoner, B. M. Karandikar, and R. B. Mujumdar, *Eur. Pat.* Appl. EP **747,** 448, (1996) US Appl. 474. 057, 1995, 37 pp.; *Chem. Abstr.,* **126,** 119061 (1997).
[122] J. Eibl and H. Harnish, *Ger. Offen*, DE, **3,** 309, 653, 1984, Appl., (1983). 18 pp.; *Chem. Abstr.,* **102,** 8250 (1985).
[123] M. Lorenz and K. W. Wanken, *Eur. Pat*. Appl. EP **684,** 289, 1995. DE Appl. 4, 418, 148, 1994, 31 pp.; *Chem. Abstr.,* **124,** 120119 (1996).
[124] M. Lorenz, *Eur. Pat*. Appl. Ep. **811,** 662, (1997), DE Appl. 19, 622, 356, 1996 21 pp.; *Chem. Abstr.,***128,** 62841 (1998).
[125] O. S. Wolfbeis, I. Trummer, and A. Knierzinger, *Liebigs Ann. Chem.*, (**5**), 811–818 (1981); *Chem. Abstr.,* **95,** 63658 (1981).

[126] E. W. Kluger, P. D. Moore, J. B. Hines, and J. G. Lever, *U.S., US.* **4,** 992, 204, 1991, Appl. 397, 079, (1989), 74 pp.; *Chem. Abstr.,* **115,** 94032 (1991).
[127] E. Daltrozzo and A. Reiss, *Eur. Pat* Appl. Ep **1,** 054, 039, 22 Nov (2000), DE Appl. 19, 923, 168, 20 May (1999); 27 pp.; *Chem. Abstr.,* **134,** 5912 (2001).
[128] T. Kawagishi and Y. Yabuki, *Jpn. Kokai Tokkyo Koho JP* 2001 279, 123, 10 Oct (2001). Appl. 2000/91,621, 29 Mar 2000; 49 pp.; *Chem. Abstr.,* **135,** 290296 (2001).
[129] A. Monden, E. Kobe, M. Shinkai, S. Sasaki, S. Yamamiya, and Y. Abe, *Jpn. Kokai Tokkyo koho Jp* (2001) 219,650. 14 Aug 2001, Appl 2000/32, 010, 9 Feb 2000; 16 pp.; *Chem. Abstr.,* **135,** 173039 (2001).
[130] Y. Ishiwata and T. Katsumata, *Jpn. Koki Tokkyo Koho JP* (2002) 38, 041. 6 Feb (2002), Appl. 2000/229,457, 28 Jul 2000; 60 pp.; *Chem. Abstr.,* **136,** 175413 (2002).
[131] O. Uchida, Osamu, and Y. Ishiwata, *Jpn. Kokai Tokkyo Koho Jp* (2002) **38,** 042. (2002), Appl. 2000/224, 563, 25 Jul 2000; 57 pp. (Japan); *Chem. Abstr.,* **136,** 158760 (2002).
[132] H. Schwander and C. Zickendraht, (Ciba-Geigy A.-G., Switz.). *Ger. Offen.* (1977), 114 pp.; *Chem. Abstr.,* **88,** 106757 (1978).
[133] H. Schwander and C. Zickendraht, (Ciba-Geigy A.-G., Switz.). *Ger. Offen.* (1977), 58 pp.; *Chem. Abstr.,* **88,** 1049 (1978).
[134] H. Harnisch, (Bayer, A.-G., Fed. Rep. Ger.). *Ger. Offen.* (1977), 49 pp.; *Chem. Abstr.,* **87,** 186076 (1977).
[135] W. Franke and, C. Dr. Adox-Fotowerke, *Photographische Korrespondenz*, **94,** 154–156 (1958); *Chem. Abstr.,* **53,** 43975 (1959).
[136] K. Taguchi, *Jpn. Kokai Tokkyo Koho Jp* (2001) 183, 786, 6 Jul 2001, Appl. 1999/364,903, 22 Dec 1999; 57 pp.; *Chem. Abstr.,* **135,** 99776 (2001).
[137] Y. Ishiwata, O. Uchida, and A. Ogasawara, *Jpn, Kokai Tokkyo Koho JP* 2001 261,988. 26 Sep 2001, Appl. 2000/70,558, 14 Mar 2000; 50 pp.; *Chem. Abstr.,* **135,** 280421 (2001).
[138] O. Uchida, Y. Ishiwata, and T. Katsumata, *Jpn. Koki Tokkyo Koho JP,* **321,** 732 (2000).
[139] T. Kamosaki and H. Naruse, *Jpn. Kokai Tokkyo koho Jp* 2001 201,834. 27 Jul 2001, Appl. 2000/12,229, 20 Jan 2000; 62 pp.; *Chem. Abstr.,* **135,** 129516 (2001).
[140] D. Pratt and T. Kawagishi, (Kao Corporation, Japan; Fuji Photo Film Co., Ltd.). *Eur. Pat. Appl.* (2004); *Chem. Abstr.,* **140,** 326609 (2004).
[141] O. Cox, Y. J. Li Gao1, and W. J. Hernandez, *J. Crystallogr. Spectroscopic Res*., **23** (10), 825–828 (1993); *Chem. Abstr.,* **120,** 216305 (1994).
[142] S. Shigeta, M. Hosoya, and S. Mochizuki, *Ciba, Tokkyo Yakugak Zasshi*, **108** (9), 856–859 (1988).
[143] W. R. Sabins and D. W. Rangnekar, *Indian J. Technol*., **28** (2), 54–58 (1990).
[144] L. Orosova, V. Sutoris, P. Foltinova, and S. Haviarova, *Chem. Zvesti*., **30** (2), 186–194 (1976); *Chem. Abstr.,* **87,** 16433 (1977).
[145] H. Okujima, T. Niifuku, H. Betsushor, A. Kyonor, J. Hayashi, A. Tobeand, and M. Kobayashi, *Jpn-Kokai Tokkyo Koho JP* **05,** 59, 003, (1993), Appl. 91, 224, 411, 1991; 18 pp.; *Chem. Abstr.,* **119,** 159902 (1993).
[146] M. Ikcguchi, K. Kto, M. Sawaki, and Y. Morishima, *PCT Int. Appl. W* **094, 13,** 665, (1994). *Chem. Abstr.,* **121,** 179616 (1994).
[147] M. Ikeguchi, M. Sawaki, H. Yoshii, K. Maeda, and Y. Morishima, *Nippon Noyaku Gakkaishi*, **25** (2), 107–116 (2000); *Chem. Abstr.,* **134,** 203719 (2001).
[148] M. Ikegychi, K. Ito, and Y. Morishima, *Jpn. Kokai Tokkyo Koho, JP* 06, 25, 160, 1994, Appl. 92, 226, 335, 1992, 36 pp, *Chem. Abstr.,* **123,** 9330 (1995).

[149] K. Kato, S. Miki, K. Naruo, and H. Takahashi, *Eur. Pat. Appl. EP* **737,** 671, 1996 Jp Appl. 95, 215, 932, (1995); 83 pp.; *Chem. Abstr.,* **126,** 7829 (1997).

[150] T. Goto, Y. Manome, M. Murata, S. Suzuki, and K. Kojo, *Jpn Koki Tokkyo Koho Jp* **11** 80, 155, (1999), Appl. 97, 261, 096, 1997, 20 pp.; *Chem. Abstr.,* **130,** 282066 (1999).

[151] F. Liepouri, E. Foukaraki, T. G. Deligeorgiev, and H. E. Katerinopoulos, *Cell Calcium,* **30** (5), 331–335 (2001).

[152] K. V. Domasevitch, V. V. Ponomareva, A. A. Mokhir, E. B. Rusanov, J. Sieler, and E. Hoyer, *Z. Naturforsch.*, B.: Chem. Sci., **52** (3), 323–330 (1997); *Chem. Abstr.,* **127,** 12552 (1997).

[153] S. Halazy, D. Church, M. Camps, P. Gaillard, and P. G. Gotteland, *Eur. Pat.* Appl. EP **1,110,**957 27 Jun (2001), Appl. 1999/811,207, 24 Dec 1999; 31 pp.; *Chem. Abstr.,* **135,** 61322 (2001).

[154] S. S. El-Rehim, S. A. M. Abd; Refaey, F. Taha, M. B. Saleh, and R. A. Ahmed, *J. Appl. Electrochem.*, **31** (4), 429–435 (2001); *Chem. Abstr.,* **135,** 140374 (2001).

[155] M. A. Azzem, G. E. H. Elgemaie, M. A. Neguid, H. M. Fahmy, and Z. M. El-Massry, *J. Chem. Soc. Perkin Trans (2)*, **4,** 445-50 (1990); *Chem. Abstr.,* **113,** 31026 (1990).

[156] A. A. Tolmachev, L. N. Babichenko, and A. K. Sheinkman, *Ukr. Khim. Zh.*, **57** (2) 183–186 (1991); *Chem. Abstr.,* **115,** 282053 (1991).

[157] Sekisui Chemical Co. Ltd., *Jpn. Kokai Tokkyo Koho Jp* 59, 178, 448 1984, Appl. 83, 54, 709, (1983); *Chem. Abstr.,* **102,** 158058 (1985).

[158] T. Oyama, K. Murayama, Y. Matsuzaki, S. Kasamotsu, H. Takumoand, and K. Kato, *Jpn. Kokai Tokkyo Koho Jp* **03,** 200, 785, (1991), Appl. 89, 338, 281, (1989); 9 pp.; *Chem. Abstr.,* **116,** 265713 (1992).

[159] Y. Z. Lu, S. T. Yuan, L. Y. Chen, Q. X. Wei, G. W. Zhu, G. Wei, and G. M. Xie, *Chinese Chemical Letters*, **13** (7), 674–677 (2002); *Chem. Abstr.,* **137,** 279579 (2002).