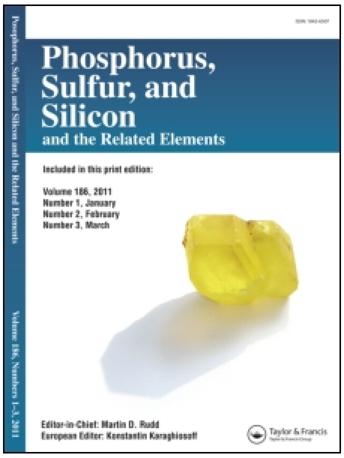

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Heteroaromatization with Sulfonamido Phenyl Ethanone, Part II: Synthesis of Novel Thiazolyl Acetonitriles and Thiazolyl Acrylonitriles and Their Derivatives Containing Dimethylsulfonamide Moiety

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Heteroaromatization with Sulfonamido Phenyl Ethanone, Part II: Synthesis of Novel Thiazolyl Acetonitriles and Thiazolyl Acrylonitriles and Their Derivatives Containing Dimethylsulfonamide Moiety

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Thiazolyl acetonitrile ***(2)*** *was prepared and converted to pyrazolo[5,1-c][1,2,4]triazine* ***(5)****, thiazoline-4-one derivatives* ***(10,12)****, thiazolo[3,2-a]pyridine* ***(13)****, coumarin* ***(14)****, and benzo[f]coumarin* ***(16)*** *derivatives through reactions with a variety of organic electrophiles and nucleophiles. Thiazolyl acrylonitrile derivatives* ***(17, 18, 21, 26–28, 31–33)*** *were also prepared, and their activity with a variety of reagents was investigated. The structure of these compounds was elucidated on the basis of elemental analysis, IR, ^{1}H-NMR, and mass spectra. The antimicrobial and antifungal activities of the prepared compounds are also reported.*

Keywords N,N-Dimethylbenzenesulfonamide; pyrazolo-[5,1-c][1,2,4]triazine; thiazoline-4-one; thiazolo[3,2-a]pyridine; thiazolyl acetonitrile; thiazolyl acrylonitrile

INTRODUCTION

Thiazole derivatives have attracted a great deal of interest owing to their antibacterial,[1] antifungal,[2] antiinflammatory,[3] and antiviral[4–6] activities. They are also useful as antiallergic,[7] anthelmintic[8] agents and as sedative hypnotics.[9] In addition to being used in the pharmaceutical industry, thiazoles also find a wide application in the dye[10] and photographic industry.[10] Sulfonamides also have a variety of biological activities such as antibacterial,[11] insulin releasing,[12] carbonic anhydrase inhibitory,[13,14] anti-flammatory,[15] and antitumor activities.[16] Thus, the present investigation deals with the synthesis of some new

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thiazoles containing a sulfonamide moiety using 4-(2-bromo acetyl)-N,N-dimethylbenzenesulfonamide **(1)**[17] as starting material (Table I).

RESULTS AND DISCUSSION

When 4-(2-bromoacetyl)-N,N-dimethylbenzenesulfonamide **(1)** was treated with 2-cyanothioacetamide in refluxing ethanol, the reaction afforded a single product identified as 4-(2-cyanomethylthiazol-4-yl)-N,N-dimethylbenzenesulfonamide (**2**) on the basis of its spectral data.

The methylene group in thiazolyl acetonitrile derivative **(2)** proved to be highly reactive. Thus, compound **(2)** underwent coupling with an equimolar amount of *p*-tolyl diazonium chloride in ethanol solution containing sodium acetate, at 0∼5°C, to afford a colored product for which two isomeric structures **(3)** or **(4)** seemed possible. However the appearance of (CN and NH) absorption bands at 2216 and 3190 cm^{-1}, respectively in the IR spectrum of the isolated product, the lack of the signal due to methylene protons, and the appearance of the signal due to the H-thiazole at 7.7 ppm. in the ^1H-NMR spectrum provided a firm support for structure **(3)** and ruled out the other possible isomer **(4)**. The structure **(3)** was also obtained via direct reaction of **(1)** with 2-cyano-2-*p*-tolylazo thioacetamide.

In the same manner, thiazolyl acetonitrile **(2)** couples with 4-cyano-3-methylthio-1H-pyrazole-5-diazonium chloride to afford the pyrazolo[5,1-c][1,2,4]triazine derivative **(5)** in moderate yields. The latter structure was established on the basis of its elemental analysis and spectral data (Scheme 1).

In contrast to their behavior, it has been found that a buffered solution of 1H-[1,2,4]-triazol-3-yl diazonium chloride couples smoothly, and in high yield, with compound **(2)** to afford a product for which two isomeric structures **(6)** or **(7)** seemed possible. However, the appearance of (CN and NH) absorption bands at 2220 and 3418 cm^{-1}, respectively, in the IR spectrum of the isolated product and the absence of any signals corresponding to (NH_2) group provided a firm support for structure **(6)** and ruled out the other possible isomer **(7)** (Scheme 1).

Formation of compounds **(8a–c)** is assumed to take place via the condensation of the active methylene group in **(2)** with aromatic aldehydes, namely benzaldehyde, *p*-chloro, and *p*-methoxy benzaldehyde, respectively. The structure of compounds **(8a–c)** was established on the basis of their elemental analysis and spectral data. A final evidence for the proposed structures comes from synthesizing compounds **(8a–c)** via reaction of phenacyl bromide derivative **(1)** with 2-cyano-3-aryl thioacrylamide **(a–c)** to afford products identical in all aspects (m.p.,

TABLE I Physical and Analytical Data for the Newly Prepared Compounds

Comp.	M.p.°C (Solvent of recrystallization)	Color (Yield%)	M. formula (M. Wt.)	Calculated/Found (%)				
				C	H	N	O	S
2	120	Yellow	$C_{13}H_{13}N_3O_2S_2$	50.79	4.26	13.67	10.41	20.86
	(Et.)	(60)	(307)	50.77	4.25	13.64	10.38	20.82
3	150	Yellow	$C_{20}H_{19}N_5O_2S_2$	56.45	4.50	16.46	7.52	15.07
	(Et./B.)	(78)	(425)	56.42	4.47	16.44	7.50	14.97
5	235	Brown	$C_{18}H_{16}N_8O_2S_3$	45.75	3.41	23.71	6.77	20.36
	(Et./B.)	(79)	(472)	45.73	3.38	23.68	6.74	20.33
6	233	White	$C_{15}H_{14}N_8O_2S_2$	44.77	3.51	27.84	7.95	15.93
	(Et./B.)	(80)	(402)	44.74	3.48	27.82	7.92	15.90
8a	227	White	$C_{20}H_{17}N_3O_2S_2$	60.74	4.33	10.62	8.09	16.22
	(Et.)	(70)	(395)	60.71	4.30	10.60	7.99	16.20
8b	192	Brown	$C_{20}H_{16}ClN_3O_2S_2$	55.87	3.75	9.77	7.44	14.92
	(Et.)	(72)	(429)	55.85	3.72	9.74	7.42	14.90
8c	160	Brown	$C_{21}H_{19}N_3O_3S_2$	59.27	4.50	9.87	11.28	15.07
	(Et.)	(80)	(425)	59.24	4.49	9.85	11.25	14.99
9	210	Black	$C_{13}H_{15}N_3O_2S_3$	45.73	4.43	12.31	9.37	28.17
	(Et./B.)	(70)	(341)	45.70	4.40	12.29	9.35	28.15
10	217	Black	$C_{16}H_{19}N_3O_3S_3$	48.34	4.82	10.57	12.07	24.20
	(Et./B.)	(82)	(397)	48.32	4.80	10.55	11.97	24.18
12	230	Yellow	$C_{24}H_{25}N_3O_4S_3$	55.90	4.89	8.15	12.41	18.65
	(Et./B.)	(80)	(515)	55.88	4.87	8.13	12.40	18.63
13	240	White	$C_{18}H_{15}N_5O_2S_3$	50.33	3.52	16.30	7.45	22.39
	(Et./B.)	(89)	(429)	50.31	3.50	16.27	7.43	22.37
14	270	White	$C_{20}H_{16}N_2O_4S_2$	58.24	3.91	6.79	15.52	15.55
	(Et./B.)	(92)	(412)	58.22	3.88	6.77	15.50	15.53
15	260	Orange	$C_{24}H_{19}N_3O_3S_2$	62.45	4.15	9.10	10.40	13.89
	(Et./B.)	(80)	(461)	62.43	4.13	9.08	10.35	13.87
16	300	White	$C_{24}H_{18}N_2O_4S_2$	62.32	3.92	6.06	13.84	13.86
	(DMF)	(79)	(462)	62.30	3.90	6.04	13.82	13.84
17	190	White	$C_{16}H_{17}N_3O_3S_2$	52.87	4.71	11.56	13.21	17.64
	(B.)	(70)	(363)	52.85	4.70	11.54	13.20	17.62
18	250	White	$C_{16}H_{18}N_4O_2S_2$	53.02	5.01	15.46	8.83	17.69
	(Et./B.)	(75)	(362)	52.99	4.98	15.44	8.81	17.67
19	298	White	$C_{16}H_{15}N_7O_2S_2$	47.87	3.77	24.42	7.97	15.97
	(D.)	(82)	(401)	47.85	3.74	24.40	7.95	15.94
20	300	Brown	$C_{19}H_{17}N_7O_2S_3$	48.39	3.63	20.79	6.79	20.40
	(D.)	(72)	(471)	48.35	3.60	20.77	6.77	20.38
21	220	Brown	$C_{14}H_{15}N_5O_2S_2$	48.12	4.33	20.04	9.16	18.35
	(Et.)	(69)	(349)	48.10	4.30	20.00	9.13	18.31
23	315	Yellow	$C_{14}H_{14}N_4O_3S_2$	47.99	4.03	15.99	13.70	18.30
	(Et./B.)	(80)	(350)	47.97	4.00	15.97	13.67	18.28
24	215	White	$C_{15}H_{16}N_6O_2S_2$	47.86	4.28	22.32	8.50	17.04
	(Et./B.)	(78)	(376)	47.85	4.24	22.30	8.48	17.00
25	320	White	$C_{23}H_{18}N_6O_2S_2$	58.21	3.82	17.71	6.74	13.51
	(DMF)	(89)	(474)	58.20	3.80	17.70	6.72	13.50

(Continued on next page)

TABLE I Physical and Analytical Data for the Newly Prepared Compounds *(Continued)*

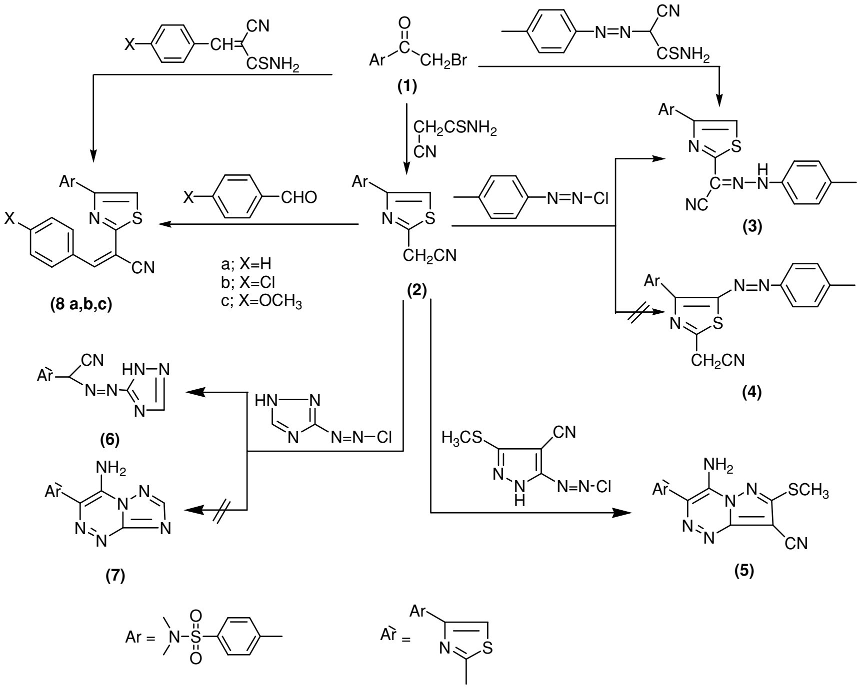
Comp.	M.p.°C (Solvent of recrystallization)	Color (Yield%)	M. formula (M. Wt.)	Calculated/Found (%)				
				C	H	N	O	S
26	275	Yellow	$C_{21}H_{20}N_4O_2S_3$	55.24	4.41	12.27	7.01	21.07
	(Et./B.)	(80)	(456)	55.21	4.40	12.25	7.00	21.02
27	210	Orange	$C_{24}H_{24}N_4O_4S_3$	54.53	4.58	10.60	12.11	18.20
	(Et.)	(75)	(528)	54.51	4.55	10.57	12.09	18.18
28	330	White	$C_{26}H_{23}N_5O_2S_2$	62.25	4.62	13.96	6.38	12.78
	(Et./B.)	(70)	(501)	62.22	4.60	13.93	6.34	12.74
29	350	Yellow	$C_{22}H_{18}N_4O_3S_3$	54.75	3.76	11.61	9.95	19.93
	(DMF)	(75)	(482)	54.73	3.73	11.60	9.91	19.90
31	160	Yellow	$C_{20}H_{18}N_4O_2S_3$	54.28	4.10	12.66	7.23	21.74
	(Et.)	(85)	(442)	54.25	4.08	12.64	7.20	21.71
32	130	White	$C_{14}H_{13}N_3O_2S_4$	43.84	3.42	10.96	8.34	33.44
	(Et.)	(80)	(383)	43.81	3.40	10.94	8.32	33.42
33	140	White	$C_{16}H_{17}N_3O_2S_4$	46.69	4.16	10.21	7.77	31.16
	(Et.)	(85)	(411)	46.67	4.14	10.20	7.75	31.14
34a	170	Brown	$C_{20}H_{16}N_4O_2S_3$	54.52	3.66	12.72	7.26	21.83
	(Et./B.)	(80)	(440)	54.50	4.73	12.70	7.24	21.80
34b	310	White	$C_{20}H_{16}N_4O_3S_2$	56.59	3.80	13.20	11.31	15.11
	(Et./B.)	(89)	(424)	56.57	3.78	13.18	11.30	15.10
34c	320	Yellow	$C_{20}H_{17}N_5O_2S_2$	56.72	4.05	16.54	7.56	15.14
	(Et./B.)	(79)	(423)	56.70	4.02	16.52	7.54	15.11
35a	265	Orange	$C_{17}H_{19}N_5O_2S_2$	52.42	4.92	17.98	8.22	16.46
	(Et./B.)	(70)	(389)	52.40	4.90	17.95	8.20	16.43
35b	250	Yellow	$C_{17}H_{19}N_5O_2S_2$	52.42	4.92	17.98	8.22	16.46
	(Et./B.)	(89)	(389)	52.39	4.91	17.97	8.19	16.45

B., benzene; D., dioxane; DMF, dimethylformamide; Et., ethanol.

TLC, IR, and mass spectra) with those obtained previously from the reaction of compound **(2)** with aromatic aldehydes as described before (Scheme 1).

Compound **(2)** was treated with H_2S gas in ethanol containing triethylamine as a catalyst at room temperature to afford 2-[4-(4-dimethylsulfamoylphenyl)thiazol-2-yl]thioacetamide **(9)**, which upon treatment with ethyl chloroacetate in refluxing ethanol contains fused sodium acetate afforded thiazolinone derivative **(10)**. The latter compound was also obtained via direct reaction of thiazolyl acetonitrile **(2)** with mercapto acetic acid in pyridine.

Efforts to cyclize **(10)** with *p*-methoxybenzylidine malononitrile to afford enaminonitriles **(11)** were not successful; instead the product was identified as 4-2-[5-(4-methoxy benzylidene)-4-oxo-4,5-dihydro thiazol-



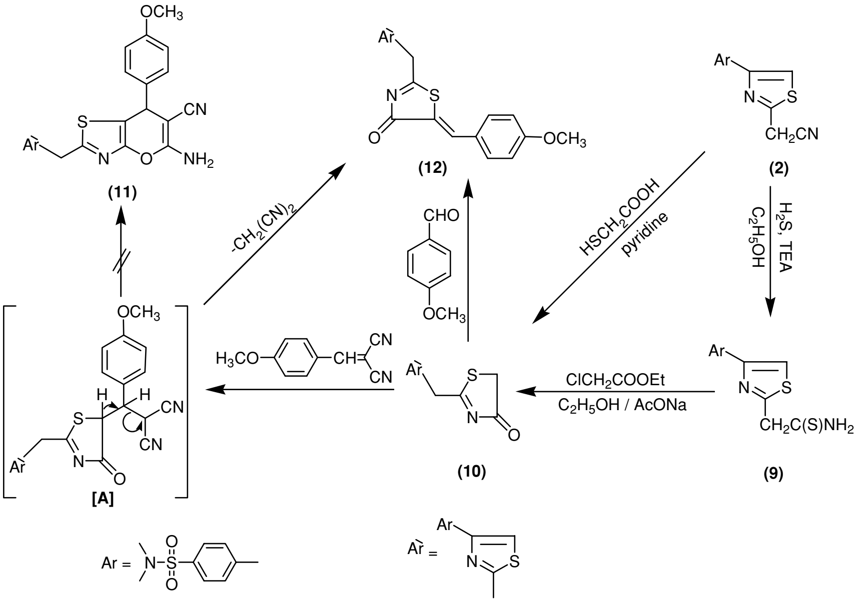
SCHEME 1

2-ylmethyl]thiazol-4-yl-N,N-dimethylbenzenesulfonamide **(12)** on the basis of elemental analysis and spectral data.

The structure of **(12)** was further confirmed by an independent synthesis of 4-thiazolinone derivative **(10)** with *p*-anisaldehyde in ethanolic piperidine solution.

The formation of **(12)** from 4-thiazolinone **(10)** and *p*-methoxy benzylidene malononitrile can be explained by the addition of an active methylene group of 4-thiazolinone **(10)** at the olefinic bond of benzylidene malononitrile forming the intermediate **[A]**, which undergoes spontaneous elimination of malononitrile to give the final product **(12)** (Scheme 2).

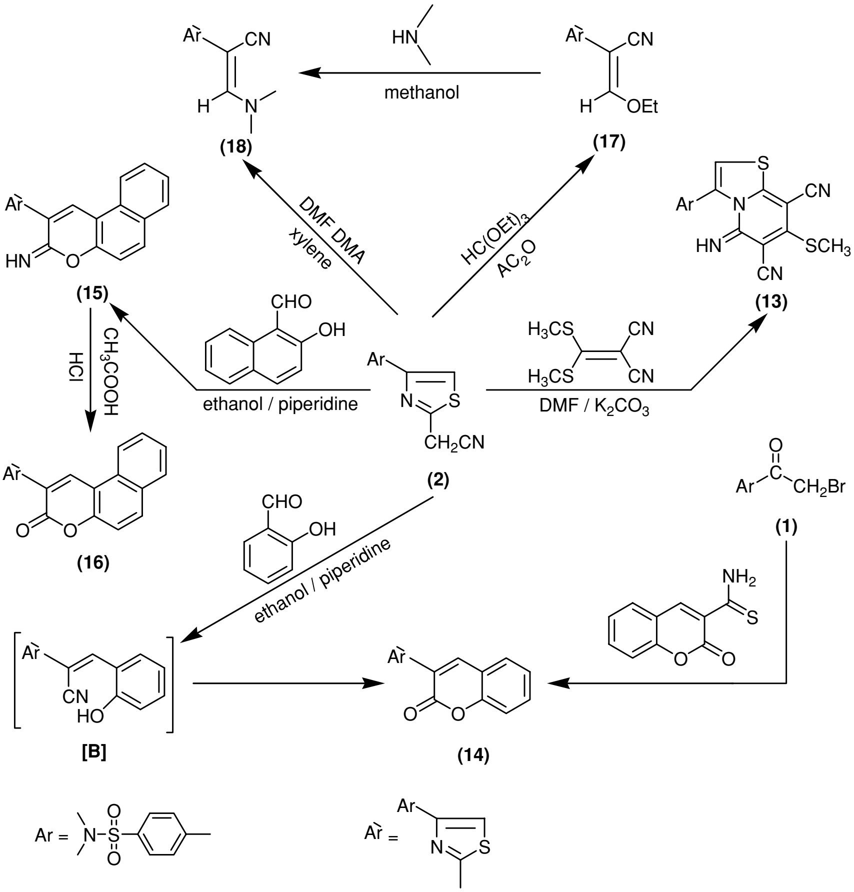
Reaction of **(2)** with 2-cyano-3,3-dimethyl thio acrylonitrile[18,19] in DMF in the presence of anhydrous potassium carbonate led to 4-(6,8-Dicyano-5-imino-7-methylsulfanyl-5H-thiazolo[3,2-a]pyridin-3-yl)-N,N-dimethylbenzenesulfonamide **(13)** (Scheme 3). The elemental analysis and spectral data of the latter structure were in agreement with its assigned structure.



SCHEME 2

Our investigation was also extended to study the reaction of **(2)** with o-phenolic aldehydes,[20] namely salicyaldehyde, and 2-hydroxy-1-naphthaldehyde. Thus, cyclocondensation of **(2)** with an equimolar amount of salicyaldehyde in boiling ethanol solution containing piperidine as a catalyst gave the corresponding N,N-di-methyl-4-[2-(2-oxo-2H-chromen-3-yl)thiazol-4-yl]benzenesulfonamide **(14)**. The formation of **(14)** was assumed to occur via the intermediacy of the Knovenagel condensed intermediate **[B]**, intramolecular cyclization via an anticipated Michael-type addition[21] of the acidic (OH) group to the (CN) function, and spontaneous hydrolysis of the imino function into a carbonyl function under the experimental reaction conditions employed. Similar hydrolysis phenomena have been previously reported[22,23] (Scheme 3).

The latter structure was established on the basis of its elemental analysis and spectral data. A final evidence for the proposed structure comes by boiling coumarin-3-carbothioc acid amide with phenacyl bromide derivative **(1)** in ethanol. But, when compound **(2)** was treated with 2-hydroxy-1-naphthaldehyde at the same reaction condition, the reaction afforded the isolable iminobenzocoumarin derivative **(15)**,



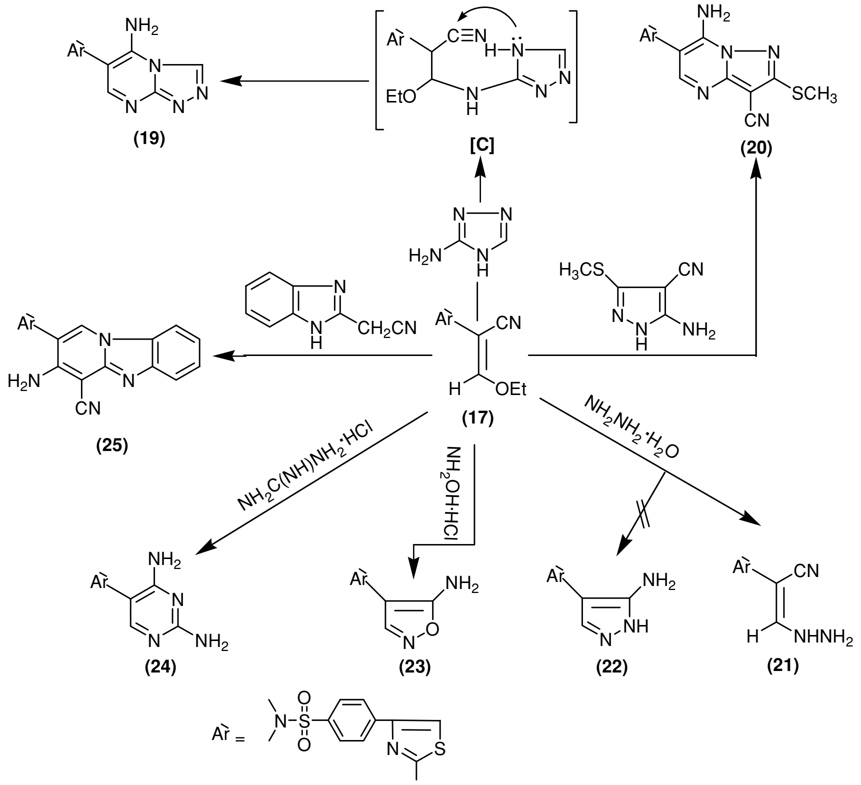
SCHEME 3

which when heated with glacial acetic acid in the presence of few drops of HCl afforded benzocoumarin derivative **(16)** (Scheme 3).

On the other hand, when compound **(2)** was allowed to react with triethyl orthoformate at reflux temperature, afforded 4-[2-(1-cyano-2-ethoxyvinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide **(17)**, which on treatment with dimethylamine in refluxing methanol afforded 1-cyano-2-dimethylaminovinylthiazolyl-N,N-dimethyl benzenesulfonamide **(18)**. The latter compound was also obtained via direct reaction of thiazolyl acetonitrile **(2)** with dimethylformamide-dimethylacetal in xylene (Scheme 3).

The behavior of 3-ethoxyacrylonitrile derivative **(17)** towards some heterocyclic amines are investigated, thus compound **(17)** reacted with

3-amino-1,2,4-triazole in DMF[24] under reflux to afford triazolo[4,3-a]pyrimidine derivative **(19)**. The formation of **(19)** is assumed to proceed through the addition of exocyclic amino group of aminotriazole to *α* ,*β* -unsaturated moiety of **(17)** to yield acyclic intermediate **[C]**, which undergoes intramolecular cyclization with elimination of ethanol to afford the final product triazolo[4,3-a]pyrimidine **(19)** (Scheme 4).



SCHEME 4

In the same manner, compound **(17)** reacted with 5-amino-3-methylthio-1(H)-pyrazole-4-carbonitrile[25] in refluxing DMF to give pyrazolo[1,5-a]pyrimidine derivative **(20)**.

The reactivity of compound **(17)** towards some nitrogen nucleophiles was also investigated. Thus, when **(17)** was treated with hydrazine hydrate in refluxing ethanol, the reaction afforded acyclic product 3-hydrazinoacrylonitrile derivative **(21)** and ruled out the amino pyrazole derivative **(22)**, due to the fact that the IR spectrum showed an absorption band for (CN) at 2196 cm^{-1}.

Similarly, compound **(17)** reacts with $NH_2OH{\cdot}HCl$ and guanidine·HCl in refluxing ethanol containing sodium acetate to afford aminoisoxazole derivative **(23)** and 2,4-diaminopyrimidine derivative **(24)** respectively (Scheme 4).

Moreover **(17)** reacts smoothly with 2-(1H)-benzimidazole acetonitrile in refluxing dioxane to afford only one isolable product, identified as benzo[4,5]imidazo[1,2-a]pyridine derivative **(25)**.

The IR spectrum of the latter product revealed absorption bands at 3460, 3374, 2200 cm^{-1} due to the NH_2 and CN.

The base-promoted nucleophilic addition of the thiazolyl acetonitrile **(2)** to an equimolar amount of phenyl isothiocyanate in dry DMF in the presence of KOH at room temperature afforded the non-isolable potassium salt **[D]**, which reacted with halogenated compounds (methyl iodide and ethyl bromoacetate) to give acyclic compound **(26,27)** derivatives, respectively (Scheme 5).

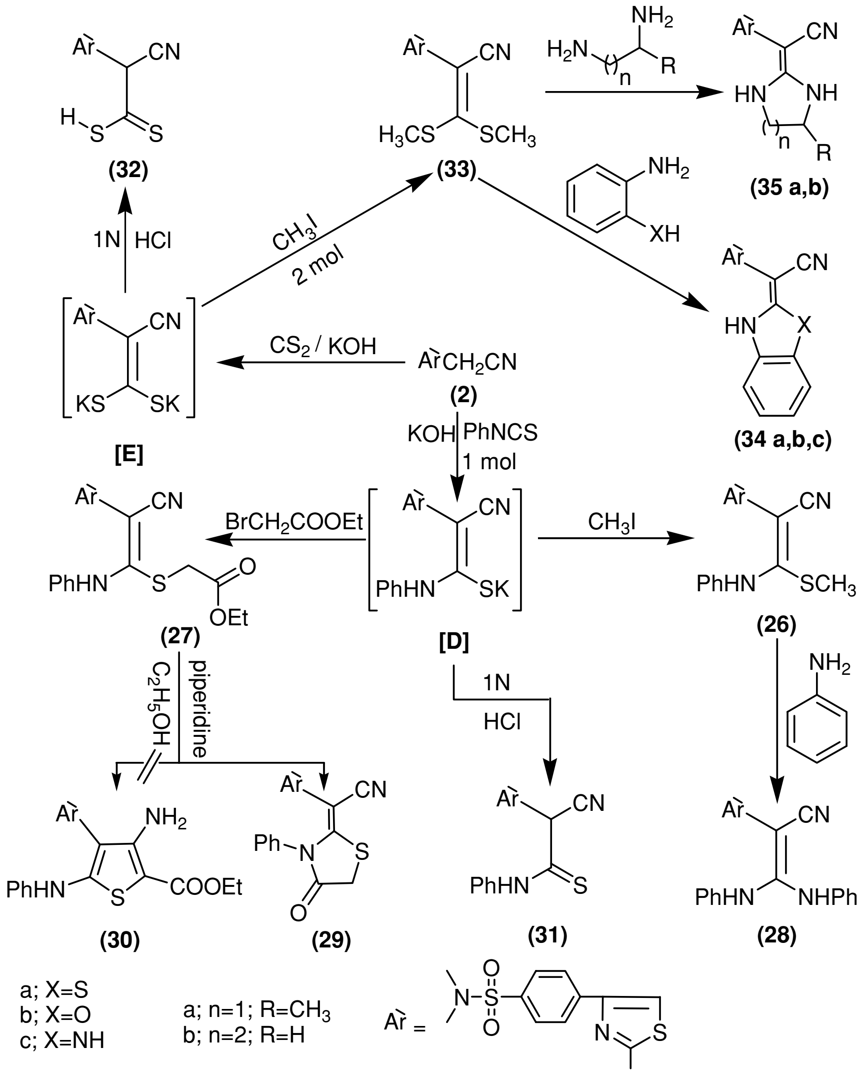
3-Methylsulfanyl-3-phenylaminoacrylonitrile derivative **(26)** reacted with aniline in refluxing ethanol afforded 3,3-bis phenyl amino acrylonitrile derivative **(28)**, which was established on the basis of elemental analysis and spectral data.

Compound **(27)**, when heated in ethanol in the presence of piperidine as a catalyst, afforded only one isolable product from two proposed structures 4-thiazolidinone **(29)** and thiophene **(30)**. IR spectrum indicated the disappearance of (NH_2) bands and showed absorption band for (CN) group at 2263 cm^{-1}, and ^{1}H-NMR spectrum showed the lack of the signal due to protons of ester group and the appearance of a signal due to the methylene group at 3.94 ppm. These spectral data provided a firm support for structure **(29)** and ruled out the other possible structure **(30)** (Scheme 5).

Acidified of intermediate **[D]** with 1N HCl yielded the N-phenyl cyanothioacetamide derivative **(31)**.

Additionally, when thiazolyl acetonitrile **(2)** was reacted with CS_2 (in the presence of potassium hydroxide) in DMF, the non-isolated potassium dithiolate **[E]** was obtained, and converted into cyano dithioacetic acid derivative **(32)** by treatment with 1N HCl. But when compound **(32)** was treated with 2 mol of methyl iodide afforded 3,3′-bis methylsulfanylacrylonitrile derivative **(33)** (Scheme 5).

Cyclization of ketendithioacetal **(33)** with o-substituted aniline (o-amino thiophenol, o-amino phenol, and o-phenylene diamine) afforded benzothiazole, benzoxazole, and benzoimidazole derivatives **(34 a–c)**, respectively.



SCHEME 5

Finally, the reaction of ketene **(33)** with 1,2-propane diamine and 1,3-propane diamine afforded 4-methylimidazolidine and tetrahydropyrimidine derivatives **(35 a,b)** respectively (Scheme 5).

From most the important routes, fragmentation patterns of the compounds are as follows. Loss of $N(CH_3)_2$ and SO_2 moieties from compounds **(2**, **8b**, **18**, **19**, **34c**, **35b)**;[26–28] loss of (H_2S, thiiran-2-one, 3-(4-methoxybenzylidene)thiiran-2-one, $CH_2=CH_2=CO$, NH_2CN, PhNCNPh, PhNCS, CS_2) from compounds **(9**, **10**, **12**, **17**, **21**, **28**, **31**, **32)** respectively to form thiazolyl acetonitrile derivative at m/e = 307; and loss of $R(CN)_2$ R= ($p-$ClPhCH=C, $N(CH_3)_2CH=C$, CH_2) from 2-substituted thiazole to form phenyl thiairidine ion at m/e = 133 for most prepared thiazole derivatives. The mass fragmentation pattern is depicted in Chart 1.[29–33]

Antimicrobial and Antifungal Activities

The results of antimicrobial screening (Table II) show that compounds **(2, 3, 5, 6, 8b, 13, 20, 21, 25, 34a**,**c)** are highly active compounds against antimicrobial activity, gram-positive (*B. subtilis, S. aureus, S. maxima*), gram-negative (*K. pneumonia, Salmonella, P. aeruginosa*), antifungal activity, unicellular fungi (*C. abicans*), and filamentous fungi (*Rhizopus, A. fumigatus*), while the compounds **(8a**,**c**, **15**, **17**, **18**, **23**, **24**, **28**, **29**, **34b)** showed moderately active, and the remaining compounds **(9, 10, 12, 14, 16, 19, 26, 27, 31–33, 35a,b)** showed weakly active. It seems that most activity was exhibited by derivatives with thiazole containing a sulfonamide moiety (Table II).

CONCLUSION

For synthesis of heterocyclic compounds containing sulfonamide moiety, which cannot be prepared by direct chlorosulfonation, the reaction of thiazolyl acetonitrile containg N,N-dimethylsulfonamide moiety with different electrophilic reagents afforded heterocyclic compounds with N,N-dimethyl-sulfonamide moiety, which cannot prepared by direct chlorosulfonation.

EXPERIMENTAL

Melting points are uncorrected. IR spectra (KBr) were recorded on FT-IR 5300 spectrometer and Perkin Elmer spectrum RXIFT-IR system (ν, cm^{-1}). The ^1H-NMR spectra were recorded at 300 MHz on a Varian Gemini NMR spectrometer (δ , ppm) using TMS as an internal standard. Mass spectra were obtained on GC Ms-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out by the Microanalytical Research Center, Faculty of Science, Cairo University and Al-Azhar University.

Chart 1

Fragmentation pattern for compounds

(2, 8b, 9, 10, 12, 17, 18, 19, 21, 24, 26, 28, 31, 32, 34c, 35b)

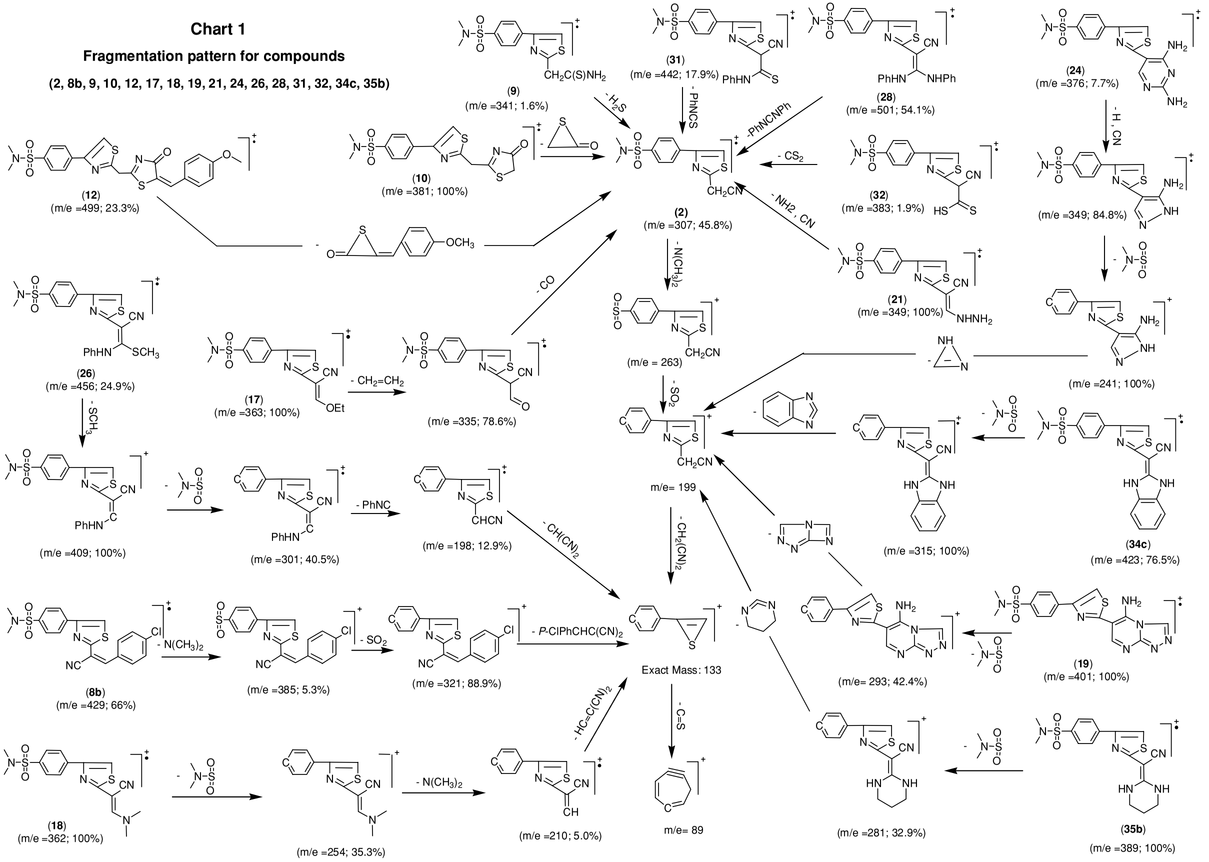


CHART 1

TABLE II Antimicrobial Activity and Antifungal Activity; Inhibition Zone Diameter (mm)

	Gram-Positive			Gram-Negative			Unicellular Fungi	Filamentous Fungi	
Compd. No.	B. Subtilis (NCTC-1040)	S. Aureus (NCTC-7447)	S. maxima (ATCC-33910)	K. Pneumonia (NCIMB-9111)	Salmonella	P. aeruginosa (ATCC-10145)	C. Abicans (IMRU-3669)	Rhizopus	A. Fumigatus
2	20	21	21	20	22	19	20	21	19
3	20	20	21	22	20	22	20	21	19
5	21	20	21	22	20	21	20	21	21
6	23	20	20	22	20	21	20	21	21
8a	17	18	17	17	19	20	17	18	17
8b	22	20	20	21	20	23	20	21	22
8c	19	18	18	19	17	17	18	17	17
9	13	12	17	17	12	15	15	14	16
10	17	12	13	13	14	15	14	14	15
12	14	13	17	13	15	12	16	12	13
13	21	20	22	23	22	24	24	20	20
14	17	12	15	16	12	11	12	13	11
15	19	18	18	17	17	19	18	17	16
16	16	17	15	11	12	13	15	17	12
17	18	20	18	18	19	19	18	16	16
18	17	18	19	18	16	20	19	18	16
Ampicillin (AMD) 25mg Calforan 30 mg.	26	25	27	27	26	25	24	25	25

(Continued on next page)

TABLE II Antimicrobial Activity and Antifungal Activity; Inhibition Zone Diameter (mm) ***(Continued)***

	Gram-Positive			Gram-Negative			Unicellular Fungi	Filamentous Fungi	
Compd. No.	B. Subtilis (NCTC-1040)	S. Aureus (NCTC-7447)	S. maxima (ATCC-33910)	K. Pneumonia (NCIMB-9111)	Salmonella	P. aeruginosa (ATCC-10145)	C. Abicans (IMRU-3669)	Rhizopus	A. Fumigatus
19	12	15	16	14	13	12	11	17	12
20	20	21	21	20	21	23	23	21	21
21	18	19	17	17	18	19	19	17	17
23	17	17	17	19	20	17	17	18	17
24	18	20	17	19	18	20	19	19	18
25	21	21	22	20	22	21	20	20	21
26	12	13	14	15	16	13	14	15	12
27	11	12	13	15	16	17	13	12	12
28	17	19	16	17	16	18	19	19	17
29	18	18	17	18	17	19	17	18	18
31	11	10	12	15	12	11	14	13	11
32	15	14	15	14	15	09	12	10	11
33	12	13	12	16	17	15	14	16	12
34a	21	20	20	19	20	20	22	21	20
34b	18	17	17	19	17	19	19	18	17
34c	20	20	22	20	21	19	20	21	22
35a	14	17	18	16	16	15	15	16	17
35b	11	12	13	14	15	09	10	11	10
Ampicillin (AMD) 25mg Calforan 30 mg.	26	25	27	27	26	25	24	25	25

24-20 mm: high active, 19-18 mm: moderate active, 17-12 mm: weak active.

4-(2-Cyanomethylthiazol-4-yl)-N,N-dimethylbenzenesulfonamide (2)

A mixture of phenacyl bromide derivative (**1**; 0.01 mol) and 2-cyanothioacetamide (0.01 mol) in ethanol (50 mL) was heated under reflux for 1 h. The solvent was concentrated, after cooling the solid product that formed was collected and recrystallized to give **(2)** (Table I). IR (film) $v = 3130$ (CH-arom.), 2964 (CH-aliph.), 2220 (CN), 1330, 1160 cm^{-1} (SO_2). MS: m/z (%) = 307 (45.8; M^+), 263 (19.4), 199 (100), 133 (12.2), 89(10.3).

4-[2-(Cyano(*p*-tolylhydrazono)methyl]thiazol-4-yl]-N,N-dimeth-ylbenzenesulfonamide (3)

Procedure (A)

p-Tolyl diazonium chloride (prepared by adding sodium nitrite (0.01 mol) to *p*-toluidine (0.01 mol) in conc. HCl (6 mL) at 0∼ 5°C under stirring) was added dropwise to a cold solution of thiazolyl acetonitrile derivative (**2**; 0.01 mol). In ethanol (20 mL) containing sodium acetate (0.08 mol), the obtained product was collected and recrystallized to give **(3)** (Table I).

Procedure (B)

A mixture of phenacyl bromide derivative (**1**; 0.01 mol) and 2-cyano-2-*p*-tolylazo thioacetamide (0.01 mol) in ethanol (50 mL) was heated under reflux for 1 h. The resulting solid was collected to give the compound (**3**), m.p. and mixed m.p. determined with authentic sample, which was obtained in procedure **(A)** gave no depression. IR (film) $v = 3190$ (NH), 3096 (CH-arom.), 2917 (CH-aliph.), 2216 (CN), 1340, 1162 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): $\delta = 2.40$ (s, 3H, CH_3), 2.78 (s, 6H, $N(CH_3)_2$), 7.20 and 7.35 (dd, 4H, AB-ArH), 7.73 (s, 1H, CH-thiazole), 7.91 and 8.04 (dd, 4H, AB-ArH; J=8.1 Hz), 13.98 ppm (s, 1H, NH).

General Procedure for Preparation of (5,6)

To a stirred solution of (**2**; 0.01 mol) in ethanol (50 mL) containing sodium acetate (3 g) pyrazole diazonium salt, or triazole diazonium salt (prepared by adding sodium nitrite (0.01 mol) to heterocyclic amines (0.01 mol) in conc. HCl (6 mL) at 0∼ 5°C under stirring) was added dropwise while cooling to 0∼ 5°C and stirring. The reaction mixture was then left at room temperature for 2 h, and the solid product formed was collected by filtration and recrystallized from the appropriate solvent to give **(5,6)**, respectively (Table I).

4-[2-(4-Amino-8-cyano-7-methylsulfanylpyrazolo[5,1-c][1,2,4]-triazin-3-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (5)

IR (film) v = 3483, 3305 (NH_2), 3198 (CH-arom.), 2916 (CH-aliph.), 2224 (CN), 1340, 1160 cm^{-1} (SO_2). MS: m/z (%) = 472 (100; M^+), 409 (33.1), 374 (21.4), 308 (28.9), 240 (28.2), 185 (58.3).

4-{2-[Cyano(2H-[1,2,4]triazol-3-ylazo)methyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (6)

IR (film) v = 3418 (NH), 3106 (CH-arom.), 2922 (CH-aliph.), 2220 (CN), 1332, 1156 cm^{-1} (SO_2). MS: m/z (%) = 403 (100; M^++1), 402 (91.7; M^+), 294 (60.3), 197 (26.0), 134 (19.1).

General Procedure for Preparation of (8a–c)

Procedure (A)

A mixture of (**2**; 0.01 mol) and the appropriate aromatic aldehyde (0.01 mol) in ethanol (40 mL) containing few drops of piperidine was refluxed for 2 h The obtained product that formed was collected by filtration and recrystallized from the appropriate solvent to give **(8a–c)** (Table I).

Procedure (B)

A mixture of phenacyl bromide derivative (**1**; 0.01 mol) and the appropriate arylidine (0.01 mol) in ethanol (40 mL) was refluxed for 2 h. The product obtained was collected and recrystallized. M.p. and mixed m.p. determined with authentic sample gave no depression.

4-[2-(1-Cyano-2-phenylvinyl)thiazol-4-yl]-N,N-dimethylbenz-enesulfonamide (8a)

IR (film) v = 3100 (CH-arom.), 2920 (CH-aliph.), 2222 (CN), 1334, 1158 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): δ =2.74 (s, 6H, $N(CH_3)_2$), 7.51 and 8.02 (m, 5H, ArH), 7.73 (s, 1H, CH-thiazole), 7.84 and 8.16 (dd, 4H, AB-ArH; J=8.2 Hz), 8.27 ppm (s, 1H, C=CH).

4-{2-[2-(4-Chlorophenyl)-1-cyanovinyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (8b)

IR (film) v = 3100 (CH-arom.), 2930 (CH-aliph.), 2216 (CN), 1326, 1154 cm^{-1} (SO_2). MS: m/z (%) = 429 (66.0; M^+), 385 (5.3), 321 (88.9), 133 (12.9) 89(12.3).

4-{2-[1-Cyano-2-(4-methoxyphenyl)vinyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (8c)

IR (film) $\upsilon = 3104$ (CH-arom.), 2926 (CH-aliph.), 2214 (CN), 1334, 1164 cm^{-1} (SO_2).

^{1}H-NMR ($CDCl_3$): $\delta = 2.75$ (s, 6H, $N(CH_3)_2$), 3.91 (s, 3H, OCH_3), 7.02 and 7.86 (dd, 4H, AB-ArH; J=8.4 Hz), 7.69 (s, 1H, CH-thiazole), 8.03 and 8.15 (dd, 4H, AB-ArH; J=8.1 Hz), 8.20 ppm (s, 1H, C=CH).

2-[4-(4-Dimethylsulfamoylphenyl)thiazol-2-yl] thioacetamide (9)

To a solution of (**2**; 0.01 mol) in ethanol (30 mL) triethyl amine (0.1 mol) was added, and the mixture was saturated with H_2S for 3 h and then left overnight. The precipitated solid was separated by filtration and purified by recrystallization to give **(9)** (Table I). IR (film) $\upsilon = 3402$, 3307 (NH_2), 3117 (CH-arom.), 2917 (CH-aliph.), 1576 (CS), 1340, 1160 cm^{-1} (SO_2). MS: m/z (%) = 341 (1.6; M^+), 307 (24.1), 263 (26.3), 199 (33.8), 133 (6.3), 89 (21.1).

N,N-Dimethyl-4-[2-(4-oxo-4,5-dihydrothiazol-2-ylmethyl)-thiazol-4-yl]benzenesulfonamide (10)

Procedure (A)

A mixture of (**9**; 0.01 mol) and ethyl chloroacetate (0.01 mol) in ethanol (20 mL) containing (1 g) of sodium acetate was refluxed for 2 h. The obtained product that formed was collected and recrystallized to give **(10)**.

Procedure (B)

A mixture of (**2**; 0.01 mol) and thioglycolic acid (0.01 mol) in pyridine (10 mL) was refluxed for 45 min. The solid obtained was filtered off and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression (Table I). IR (film) $\upsilon = 3108$ (CH-arom.), 2872 (CH-aliph.), 1708 (CO), 1336, 1158 cm^{-1} (SO_2). MS: m/z (%) =381 (100; M^+), 307 (28.5), 199 (52.8), 133 (29.1), 89 (5.8).

4-{2-[5-(4-Methoxybenzylidene)-4-oxo-4,5-dihydrothiazol-2-ylmethyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (12)

Procedure (A)

A mixture of (**10**; 0.01 mol) and 2-(4-methoxy benzylidene) malononitrile (0.01 mol) in ethanol (50 mL) was refluxed for 2 h. The solid obtained was filtered off and recrystallized to give **(12)**.

Procedure (B)

A mixture of (**10**; 0.01 mol) and p-anisaldehyde (0.01 mol) in ethanol (20 ml) and few drops of piperidine was refluxed for 3 h. The mixture was cooled, and the separated solid was filtered off and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression (Table I). IR (film) $v =$ 3110 (CH-arom.), 2870 (CH-aliph.), 1658 (CO), 1336, 1168 cm^{-1} (SO_2). MS: m/z (%) = 499 (23.3; M$^+$), 307 (8.6), 199 (28.7), 133 (21.5), 89 (74.2).

4-(6,8-Dicyano-5-imino-7-methylsulfanyl-5H-thiazolo[3,2-a]-pyridin-3-yl)-N,N-dimethylbenzenesulfonamide (13)

A mixture of (**2**; 0.01 mol), anhydrous potassium carbonate (0.012 mol), and 2-cyano-3,3-dimethyl thio acrylonitrile (0.01 mol) in DMF (30 mL) was heated at 50$\sim$ 60°C with stirring until odor of the methane thiol is ceased. After cooling, the reaction mixture poured into crushed ice (100 g) then acidified with 1N HCl. The solid product that formed was collected and recrystallized to give **(13)** (Table I). IR (film) $v =$ 3282 (NH), 3046 (CH-arom.), 2916 (CH-aliph.), 2202, 2197 (2CN), 1334, 1162 cm^{-1} (SO_2). MS: m/z (%) =429 (28.0; M$^+$), 428 (73.2; M$^+$ -1), 367 (21.8), 333 (35.0), 261 (11.4), 212 (17.2), 170 (100).

N,N-Dimethyl-4-[2-(2-oxo-2H-chromen-3-yl)thiazol-4-yl]benzenesulfonamide (14)

Procedure (A)

To a mixture of (**2**; 0.01 mol) and salicyldehyde (0.01 mol) in ethanol (50 mL), a few drops of piperidine was added as a catalyst. The reaction mixture was refluxed for 3 h, and the solid product was collected by filtration and recrystallized to give **(14)**.

Procedure (B)

A mixture of (**1**; 0.01 mol) and coumarin-3-carbothioic acid amide (0.01 mol) in ethanol (50 mL) was refluxed for 2 h. The solid obtained was filtered off and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression (Table I). IR (film) $v = 3047$ (CH-arom.), 2900 (CH-aliph.), 1720 (CO), 1340, 1162 cm^{-1} (SO_2). MS: m/z (%) =412 (100; M^+), 378 (68.3), 304 (93.4), 241 (32.4), 134 (21.1).

4-[2-(3-Imino-3H-benzo[f]chromen-2-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (15)

To a mixture of (**2**; 0.01 mol) and 2-hydroxy-1-naphthaldehyde (0.01 mol) in ethanol (50 mL), a few drops of piperidine was added as catalyst. The reaction mixture was refluxed for 5h. The isolated product was collected and recrystallized to give (**15**) (Table I). IR (film) v =3308 (NH), 3050 (CH-arom.), 2910 (CH-aliph.), 1340, 1158 cm^{-1} (SO_2). MS: m/z (%) =461 (67.2; M^+), 444 (100), 336 (17.1), 193 (15.3), 133 (3.6).

N,N-Dimethyl-4-[2-(3-oxo-3H-benzo[f]chromen-2-yl)thiazol-4-yl]benzenesulfonamide (16)

To a mixture of 30 mL acetic acid and 3 mL of HCl, 0.01 mol of compound **(15)** was added and refluxed for 2 h. The precipitate obtained after cooling was filtered off and recrystallized to give **(16)** (Table I). IR (film) $v = 3108$ (CH-arom.), 2872 (CH-aliph.), 1708 (CO), 1336, 1158 cm^{-1} (SO_2).

4-[2-(1-Cyano-2-ethoxyvinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (17)

A mixture of (**2**; 0.01 mol) and triethyl orthoformate (0.01 mol) in acetic anhydride (0.01 mol) was refluxed for 3 h. The reaction mixture was concentrated to 10 mL. After cooling, the solid product was collected by filtration and washed with ethanol then recrystallized to give **(17)** (Table I). IR (film) $v = 3100$ (CH-arom.), 2950 (CH-aliph.), 2218 (CN), 1342, 1162 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): $\delta = 1.52$ (t, 3H, CH_3), 2.72 (s, 6H, $N(CH_3)_2$), 4.42 (q, 2H, CH_2), 7.43 (s, 1H, C=CH), 7.65 (s, 1H, CH-thiazole), 7.81 and 8.12 ppm (dd, 4H, AB-ArH; J = 8.1 Hz). MS: m/z (%) = 363 (100; M^+), 335 (78.6), 307 (15.1), 263 (1.0), 199 (29.3), 133 (9.6).

4-[2-(1-Cyano-2-dimethylaminovinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (18)

Procedure (A)

A mixture of (**17**; 0.01 mol) and dimethyl amine (0.01 mol) in methanol (40 mL) was refluxed for 3 h. The mixture was then cooled, and the separated solid was collected by filtration and recrystallized to give **(18)**.

Procedure (B)

A mixture of (**2**; 0.01 mol) and DMF-DMA (0.01 mol) in dry xylene (30 ml) was refluxed for 3 h. Then the cooled precipitated product was filtered off, washed with light petroleum ether, and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression (Table I). IR (film) $\upsilon = 3098$ (CH-arom.), 2960 (CH-aliph.), 2200 (CN), 1340, 1162 cm^{-1} (SO_2). MS: m/z (%) = 362 (100; M$^+$), 254 (35.3), 210 (5.0), 133 (12.1).

4-[2-(5-Amino[1,2,4]triazolo[4,3-a]pyrimidin-6-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (19)

A mixture of (**17**; 0.01 mol) and 3-amino-1,2,4-triazole (0.01 mol) in DMF (30 mL) was refluxed for 3 h. After cooling, the product was collected by filtration then washed with ethanol and recrystallized to give **(19)** (Table I). IR (film) $\upsilon = 3422$, 3306 (NH_2), 3190 (CH-arom.), 2917 (CH-aliph.), 1340, 1160 cm^{-1} (SO_2). MS: m/z (%) = 401 (100; M$^+$), 293 (42.4), 237 (4.4), 199 (25.8), 133 (11.1), 89 (4.6).

4-[2-(7-Amino-3-cyano-2-methylsulfanylpyrazolo[1,5-a]pyrimidin-6-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (20)

The same experimental procedure described above for the synthesis of **(19)** has been followed except for using 5-amino-3-methylthio-1H-pyrazole-4-yl carbonitrile instead of 3-amino-1,2,4-triazole (Table I). IR (film) $\upsilon = 3382$, 3360 (NH_2), 3099 (CH-arom.), 2970 (CH-aliph.), 2216 (CN), 1338, 1164 cm^{-1} (SO_2). ^{1}H-NMR (DMSO): $\delta = 2.67$ (s, 6H, $N(CH_3)_2$), 2.80 (s, 3H, SCH_3), 7.86 and 8.27 (dd, 4H, AB-ArH; J = 7.8 Hz), 8.41 (s, 1H, CH-thiazole), 8.83 (s, 1H, CH-pyrimidine), 9.31 ppm (br, 2H, NH_2).

4-[2-(1-Cyano-2-hydrazinovinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (21)

To a solution of the (**17**; 0.01 mol) in ethanol (20 mL) hydrazine hydrate (99%, 0.01 mol) was added. The reaction mixture was refluxed for 2 h, then cooled. The solid product formed was filtered off, washed with ethanol, and dried, then recrystallized to give **(21)** (Table I). IR (film) $v = 3310, 3238$ (NH_2), 3182 (NH), 3106 (CH-arom.), 2975 (CH-aliph.), 2196 (CN), 1336, 1152 cm^{-1} (SO_2). MS: m/z (%) = 349 (100; M^+), 307 (24.0), 199 (48.5), 133 (18.0), 89 (5.8).

4-[2-(5-Aminoisoxazol-4-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (23)

To a mixture of (**17**; 0.01 mol) and $NH_2OH{\cdot}HCl$ (0.015 mol) in ethanol (30 mL), sodium acetate (0.025 mol) was added. The resulting mixture was refluxed for 3 h and then allowed to cool to room temperature and diluted with water (20 mL). The solid product so formed was collected by filtration, washed with water, and dried, then recrystallized to give **(23)** (Table I). IR (film) $v = 3410, 3364$ (NH_2), 3107 (CH-arom.), 2966 (CH-aliph.), 1338, 1162 cm^{-1} (SO_2). MS: m/z (%) = 350 (13.9; M^+), 286 (11.6), 249 (15.1), 237 (18.6), 163 (29.1), 131 (47.7).

4-[2-(2,4-Diaminopyrimidin-5-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (24)

The same experimental procedure described above for the synthesis of **(23)** has been followed except for using guanidine HCl (0.01 mol) instead of $NH_2OH{\cdot}HCl$ (Table I). IR (film) $v = 3400, 3350, 3256, 3190$ ($2NH_2$), 3100 (CH-arom.), 2955 (CH-aliph.), 1330, 1160 cm^{-1} (SO_2). MS: m/z (%) =376 (7.7; M^+), 349 (84.8), 241 (100), 199 (20.0), 133 (10.1).

4-[2-(3-Amino-4-cyanobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (25)

A mixture of (**17**; 0.01 mol) and 2-(1H)-benzoimidazole acetonitrile (0.01 mol) in dioxane (50 mL) was refluxed for 5 h. The solid product that was obtained after cooling was collected by filtration and recrystallized to give (**25**) (Table I). IR (film) $v = 3460, 3374$ (NH_2), 3110 (CH-arom.), 2965 (CH-aliph.), 2200 (CN), 1350, 1161 cm^{-1} (SO_2). MS: m/z (%) =473 (3.5; M^+ -1), 430 (3.0), 365 (3.1), 199 (17.2), 160 (15.6).

General Procedure for Preparation of (26,27)

To a cooled suspension of finely grounded KOH (0.01 mol) in dry DMF (40 mL), thiazolyl acetonitrile (**2**; 0.01 mol) and subsequently phenyl isothiocyanate (0.01 mol) were added. The reaction mixture was stirred overnight at room temperature, then treated with the appropriate halo compound (0.01 mol), and left at room temperature for an additional 24 h. The reaction mixture was then triturated with cold H_2O (50 mL) and neutralized with 1N HCl. The resulting precipitated solid was collected by filtration, washed with water, dried, and recrystallized from an appropriate solvent (Table I).

4-[2-(1-Cyano-2-methylsulfanyl-2-phenylaminovinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (26)

IR (film) $v = 3448$ (NH), 3102 (CH-arom.), 2924 (CH-aliph.), 2200 (CN), 1336, 1158 cm^{-1} (SO_2). MS: m/z (%) = 456 (24.9; M^+), 409 (100), 301 (40.5), 198 (12.9), 133 (18.7).

{*2-Cyano-2-[4-(4-dimethylsulfamoylphenyl)thiazol-2-yl]-1-phenylaminovinylsulfanyl*}*Acetic Acid Ethyl Ester (27)*

IR (film) $v = 3114$ (NH), 3130 (CH-arom.), 2917 (CH-aliph.), 2198 (CN), 1736 (CO), 1338, 1162 cm^{-1} (SO_2). ^1H-NMR ($CDCl_3$): $\delta = 1.35$ (t, 3H, $CH_2\underline{CH_3}$), 2.76 (s, 6H, $N(CH_3)_2$), 4.27 (q, 2H, $\underline{CH_2}CH_3$), 6.15 (s, 2H, SCH_2), 7.18 (m, 5H, ArH), 7.52 (s, 1H, CH-thiazole), 7.84 and 8.02 (dd, 4H, AB-ArH; J=7.9 Hz), 11.48 ppm (s, 1H, NH).

4-[2-(1-Cyano-2,2-bisphenylaminovinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (28)

A mixture of 1-cyano-2-methylsulfonyl-2-phenylamino vinyl (**26**; 0.01 mol) and aniline (0.01 mol) in ethanol (50 mL) was refluxed for 3 h after cooling The solid product which formed was collected by filtration and recrystallized to give (**28**) (Table I). IR (film) $v = 3428$, 3348 (2NH), 3126 (CH-arom.), 2968 (CH-aliph.), 2186 (CN), 1338, 1156 cm^{-1} (SO_2). MS: m/z (%) = 501 (54.1; M^+), 307 (60.0), 263 (22.7), 199 (89.9), 133 (72.6), 93 (100).

4-{2-[Cyano-(4-oxo-3-phenylthiazolidin-2-ylidene)methyl] thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (29)

To a mixture of (30 mL) ethanol and (1 mL) of piperidine, (0.01 mol) of compound **(27)** was added and refluxed for 3 h. The precipitate obtained after cooling was filtered off and recrystallized to give **(29)** (Table I).

IR (film) $\upsilon = 2952$ (CH-arom.), 2858 (CH-aliph.), 2263 (CN), 1701 (CO), 1332, 1172 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): $\delta = 2.69$ (s, 6H, $N(CH_3)_2$), 3.94 (s, 2H, CH_2), 6.30 (s, 1H, CH-thiazole), 7.61 (m, 5H, ArH), 7.79 and 7.86 ppm (dd, 4H, AB-ArH; J = 6.6 Hz).

2-Cyano-2-[4-(4-dimethylsulfamoylphenyl)thiazol-2-yl]-N-phenyl Thioacetamide (31)

The same experimental procedure described above for the synthesis of **(26,27)** has been followed, except the halo compounds were not used (Table I). IR (film) $\upsilon = 3348$ (NH), 3135 (CH-arom.), 3064 (CH-aliph.), 2188 (CN), 1344, 1162 cm^{-1} (SO_2). MS: m/z (%) =442 (17.9; M^+), 307 (36.4), 263 (11.3), 199 (39.0), 133 (39.5).

Cyano[4-(4-dimethylsulfamoylphenyl)thiazol-2-yl]dithio Acetic Acid (32)

Carbon disulphide (0.01 mol) was added gradually to a cold solution of thiazolyl acetonitrile (**2**; 0.01 mol) in DMF (20 mL) containing finely ground KOH (0.02 mol). The reaction mixture left at room temperature for an additional 24 h. The reaction mixture was then triturated with cold H_2O (50 mL) and neutralized with 1N HCl. The resulting precipitated solid was collected by filtration, washed with water, dried, and recrystallized to give **(32)** (Table I). IR (film) $\upsilon = 2941$ (CH-arom.), 2854 (CH-aliph.), 2220 (CN), 1334, 1167 cm^{-1} (SO_2). MS: m/z (%) = 383 (1.9; M^+), 307 (3.0), 263 (2.3), 199 (4.1), 133 (4.4), 76 (100).

4-[2-(1-Cyano-2,2-bismethylsulfanylvinyl)thiazol-4-yl]-N,N-dimethylbenzenesulfonamide (33)

The same experimental procedure described above for the synthesis of **(32)** has been followed except methyl iodide was added (0.02 mol) before the reaction mixture was left at room temperature (Table I). IR (film) $\upsilon = 3116$ (CH-arom.), 2920 (CH-aliph.), 2214 (CN), 1340, 1158 cm^{-1} (SO_2). MS: m/z (%) = 411 (50.8; M^+), 378 (100), 288 (36.7), 212 (44.0), 134 (21.4).

General Procedure for Preparation of (34a–c)

A mixture of ketene dithio acetal (**33**; 0.01 mol) and the appropriate o-substituted aniline (0.01 mol) in ethanol (50 mL) was refluxed for 3 h. The obtained product was collected by filtration and recrystallized from an appropriate solvent (Table I).

4-{2-[(3H-Benzothiazol-2-ylidene)cyanomethyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (34a)

IR (film) $v = 3370$ (NH), 3064 (CH-arom.), 2922 (CH-aliph.), 2200 (CN), 1335, 1150 cm^{-1} (SO_2). MS : m/z (%) = 440 (56.9; M^+), 378 (100), 288 (25.1), 242 (21.8), 134 (14.0).

4-{2-[(3H-Benzooxazol-2-ylidene)cyanomethyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (34b)

IR (film) $v = 3394$ (NH), 2924 (CH-arom.), 2851 (CH-aliph.), 2215 (CN), 1338, 1162 cm^{-1} (SO_2). MS: m/z (%) = 424 (17.2; M^+), 392 (22.4), 355 (36.2), 327 (25.8), 281 (24.1), 194 (29.3), 152 (25.8), 69 (100).

4-{2-[Cyano-(1,3-dihydrobenzoimidazol-2-ylidene)methyl] thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (34c)

IR (film) $v = 3214$, 3200 (2NH), 2964 (CH-arom.), 2850 (CH-aliph.), 2172 (CN), 1334, 1156 cm^{-1} (SO_2). MS: m/z (%) = 423 (76.5; M^+), 315 (100), 199 (27.9), 133 (34.8), 89 (25.7).

General Procedure for Preparation of (35a,b)

A mixture of (**33**; 0.01 mol) and the appropriate diamine (0.01 mol) in ethanol (50 mL) was refluxed for 5 h. The obtained product was collected by filtration and recrystallized from an appropriate solvent (Table I).

4-{2-[Cyano-(4-methyl imidazolidin-2-ylidene)methyl] thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (35a)

IR (film) $v = 3326$, 3300 (2NH), 3130 (CH-arom.), 2917 (CH-aliph.), 2178 (CN), 1338, 1164 cm^{-1} (SO_2). ^{1}H-NMR (DMSO): $\delta = 1.30$ (s, 3H, CH_3), 2.68 (s, 6H, $N(CH_3)_2$), 3.15 (br, 2H, CH_2), 3.86, 4.11 (2br, 2H, 2NH), 7.77 (s, 1H, CH-imidazolidine), 7.79 (s, 1H, CH-thiazole), 7.75 and 8.21 ppm (dd, 4H, AB-ArH; J = 7.5 Hz).

4-{2-[Cyano(tetrahydropyrimidin-2-ylidene)methyl]thiazol-4-yl}-N,N-dimethylbenzenesulfonamide (35b)

IR (film) $v = 3354$, 3118 (2NH), 2930 (CH-arom.), 2874 (CH-aliph.), 2168 (CN), 1334, 1156 cm^{-1} (SO_2). MS: m/z (%) = 389 (100; M^+), 281 (32.9), 199 (7.3), 133 (4.0).

Antimicrobial and Antifungal Screening

The prepared compounds were evaluated for their antimicrobial activity using the agar diffusion technique.[34,35] A mg/mL solution in DMF was used. The test organisms were Gram-positive *Bacillus subtilis* (NCTC-1040), *Staphylococcus aureus* (NCTC-7447), *Sarcina maxima* (ATCC-33910); Gram-negative *Klebsiella pneumonia* (NCIMB-9111), *Salmonella*, *Pseudomonas aeruginosa* (ATCC-10145); and antifungal activity unicellular fungi *Candida abicans* (IMRU-3669), filamentous fungi *Rhizopus*, and *Asperigillus fumigatus*. DMF showed no inhibition zones. The reference antibiotics were Ampicillin (AMD) and Calforan. The inhibition zones (IZ) of these compounds are listed in (Table II).

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