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Utilization of Thiazolylacetonitriles in the Synthesis of Thiophene, Thiazole, Pyrazolo[1,5-*a*]pyrimidine and Pyrazolo [5,1-*c*]triazine Derivatives

Abdou O. Abdelhamid, Hussein F. Zohdi, and Gaber S. Mohamed

Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt

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ABSTRACT: *Thiazolylcyanothioacetanilides react with α-haloketones and haloesters to give the corresponding thiophene or thiazole derivatives according to the reaction conditions. Pyrazolo[1,5-a]pyrimidines and pyrazolo[5,1-c]triazines were synthesized by reaction of 3-amino-4-(4′-arylthiazol-2′-yl)-5-phenylaminopyrazole with different reagents. Structures of the new compounds were confirmed by elemental analyses, spectral data, and alternative methods of synthesis whenever possible.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 508–516, 1999

INTRODUCTION

The interesting pharmacological properties of thiophene, thiazole, pyrazolo[1,5-*a*]pyrimidine and pyrazolo[5,1-*c*]triazine derivatives [1] in relation to the various changes in the structures of these compounds are important in the synthesis of some less toxic and more potent drugs. The present investigation deals with the synthesis of some such types of compounds, in continuation of our studies in the chemistry of these heterocycles [2–6]. The syntheses of several new heterocyclic derivatives are described.

RESULTS AND DISCUSSION

Treatment of 2-(4′-phenyl)thiazolylacetonitrile (**1a**), phenyl isothiocyanate, and potassium hydroxide in *N,N*-dimethylformamide with ω-bromoacetophenone afforded a product with the molecular formula $C_{26}H_{17}N_3S_2$. The IR (cm^{-1}) spectrum revealed a band at 2175 that was attributed to the presence of a cyano group, and there was no band between 3100 and 3500 or 1800 and 1650 because of the absence of each NH and CO groups [7]. Its ^{1}H NMR spectrum showed only a signal at $\delta = 7.21–7.88$ (m, ArHs, and thiazole H-5), and the mass spectrum revealed a peak at $m/z = 435$. Based on these facts, the product was assigned as: 1-[2′-(3′,4′-diphenyl)]thiazoline-2-cyano-2-(4′-phenyl)thiazolyethene (**3a**). However, Gewald et al. [8] reported that ω-bromoacetophenone reacted with **1a** and phenyl isothiocyanate in the presence of potassium ethoxide to give 3-amino-2-benzoyl-5-phenylamino-4-(4′-phenyl)thiazol-2′-yl-thiophene (**4a**). From the above data, product formation may be dependent on the reaction conditions (cf. Scheme 1). To clarify this situation, treatment of **2b** with ω-bromoacetophenone in ethanol at room temperature gave product **5**. The ^{1}H NMR spectrum of **5** showed signals at $\delta = 2.35$ (s, 3H, 4-$CH_3C_6H_4$), 3.39 (s, 2H, SCH_2), 7.25–8.05 (m, 15H, ArHs, and thiazole H-5) and 11.94 (s, br, 1H, NH). Its IR (cm^{-1}) spectrum revealed bands at 3441 (NH), 2209 (CN), 1666 (CO), and 1624 (C=N). Compound **5** was converted to the thiophene **4b** by boiling in ethanol containing triethylamine and to the thiazole **3b** by treatment with polyphosphoric acid (Scheme 1).

Similarly, ω-bromoacetophenone, chloroacetone, and ethyl chloroacetate reacted with the ap-

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Correspondence to: Abdou O. Abdelhamid. E-mail: *ABDOU@main-scc.cairo.eun.eg.*
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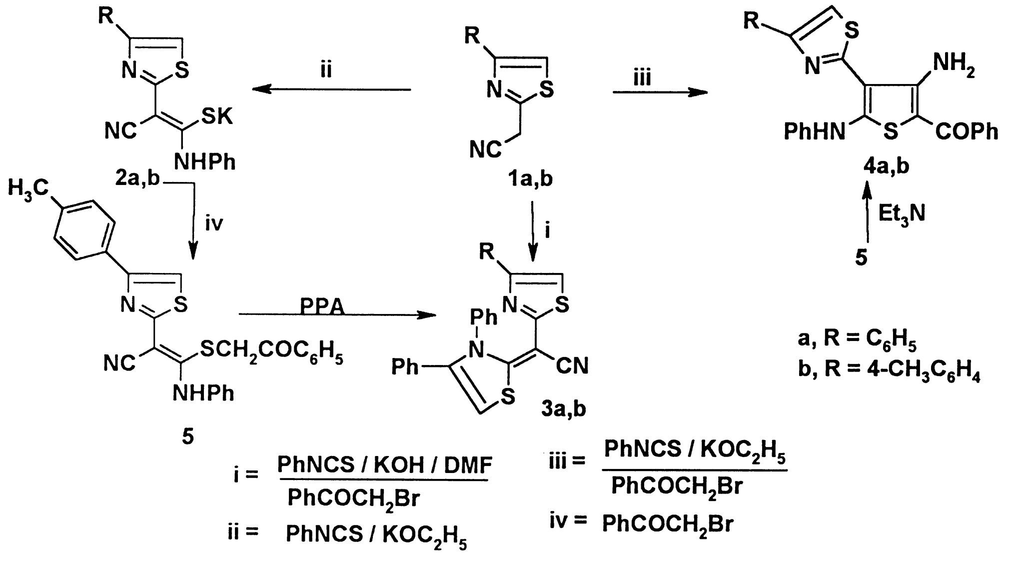
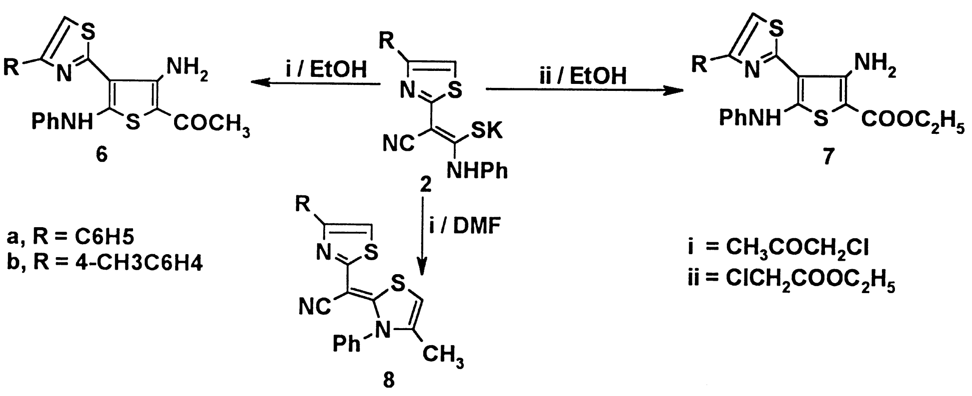
propriate potassium 2-(4′-arylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethyenylthiolates **2a,b** in ethanol to afford 3-amino-2-substituted-5-phenylamino-4-[4′-(aryl)thiazol-2′-yl]thiophenes **4**, **6**, and **7**, respectively, and *ω*-bromoacetophenone and chloroacetone reacted with the appropriate **2a,b** in *N,N*-dimethylformamide to give the [(3,4-disubstituted)thiazolidene-2-yl](4-arylthiazol-2-yl)acetonitriles **3** and **8**, respectively (cf. Scheme 2).

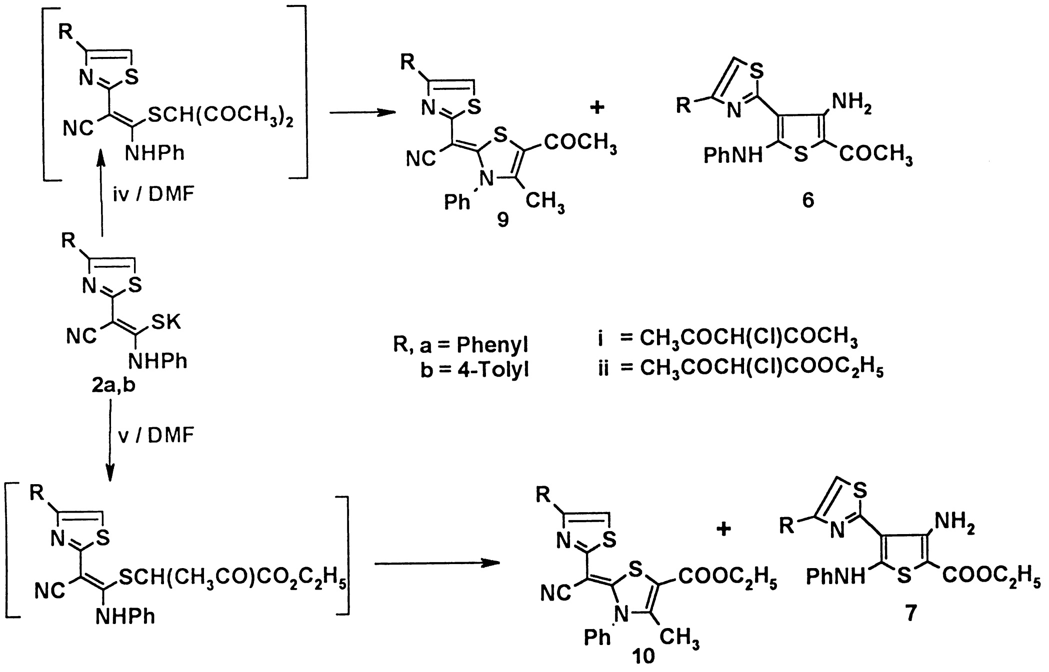
On the other hand, the appropriate potassium 2-(4′-arylthiazol-2′-yl)-2-cyano-1-(phenylamino) ethyenylthiolates **2a,b** reacted with 3-chloropentan-2,4-dione in *N,N*-dimethyformamide solution to afford two products (cf. Scheme 3). The first product was identical in all respects (m.p., mixed m.p., and spectra) with the corresponding thiophene **6** and the second product was formulated as 2-[2′-(5′-acetyl-4′methyl-3-phenyl]thiazolinyl-2-[2′-(4′-substituted)thiazolylcyanoethene **9**. The structure of **9** was confirmed on the basis of elemental analysis and spectral data. Thus, the ^{1}H NMR spectrum of **9a** showed signals at $\delta = 2.29$ (s, 3H, CH_3CO), 2.58 (s, 3H, thiazole CH_3), 7.26–7.70 (m, 10H, ArHs) and 8.20 (s, 1H, thiazole H-5). Its IR (cm^{-1}) spectrum revealed bands at 2191 (CN) and 1635 (CO conjugated), and no band was apparent near 3500–3100 because of the absence of the NH group. The formation of these products involves initial attack by one molecule of 3-chloropentan-2,4-dione on a molecule of the appropriate **2a,b** to give an intermediate, which cyclized to the final products, the thiophene **6** and the thiazole 9. Similarly, ethyl 2-chloro-3-oxobutanoate reacted with the appropriate potassium 2-(4′-arylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolates **2a,b** in *N,N*-dimethylformamide to give, in each case, the corresponding thiophenes **7** and



SCHEME 1



SCHEME 2



SCHEME 3

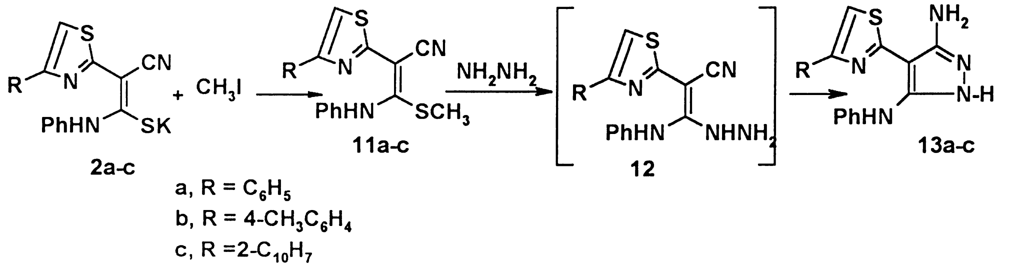
thiazoles **10**. Structures **7** and **10** were elucidated on the basis of elemental analyses, spectral data, and alternative methods of synthesis (cf. Experimental).

Also, treatment of the appropriate 2-(4-arylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolates **2a–c** reacted with methyl iodide to give the corresponding *S*-methyl derivative **11a–c**. The IR (cm^{-1}) spectrum of **11** revealed bands near 3350 (NH), 2200 (CN), and 1610 (C–N). The ^{1}H NMR spectrum of **11a** showed signals at δ = 2.7 (s, 3H, SCH$_3$), 7.36–8.22 (m, 11H, ArHs, and thiazole H-5) and 11.21 (s, br., 1H, NH). More information on the structure **11** came from its reaction with hydrazine hydrate in ethanol that was accompanied by the evolution of methanethiol and the conversion to the aminopyrazoles. The IR spectra of the products showed bands attributable to the NH$_2$ group and the absence of any absorption bands due to the nitrile group. Based on the above data, the products can be formulated as 3-amino-4-[2′-(4′aryl)thiazolyl]-5-(phenylamino)pyrazoles **13**. The formation of **13** proceeded most likely via the intermediacy of the corresponding 2-hydrazino derivatives **12**, which cyclized via an intramolecular addition of the hydrazine group to the nitrile function to afford the final product **13** (cf. Scheme 4).

Treatment of the appropriate **13a–c** with pentane-2,4-dione in boiling glacial acetic acid gave the corresponding 2,4-dimethylpyrazolo[1,5-*a*]pyrimidines **14a–c**, respectively (cf. Scheme 5). The structure of each **14** was elucidated on the basis of elemental analyses and spectral data. Thus, the IR (cm^{-1}) spectra of each compound **14a–c** revealed bands near 3265–3275 (NH) and 1640–1630 (C=N). The ^{1}H NMR spectrum of **14a** showed signals at δ = 2.44 (s, 3H, CH$_3$), 2.67 (s, 3H, CH$_3$), 6.61 (s, 1H, pyrimidine H-5), 7.31–7.82 (m, 10H, ArHs), 8.31 (s, 1H, thiazole H-5), and 11.32 (s, br., 1H, NH).

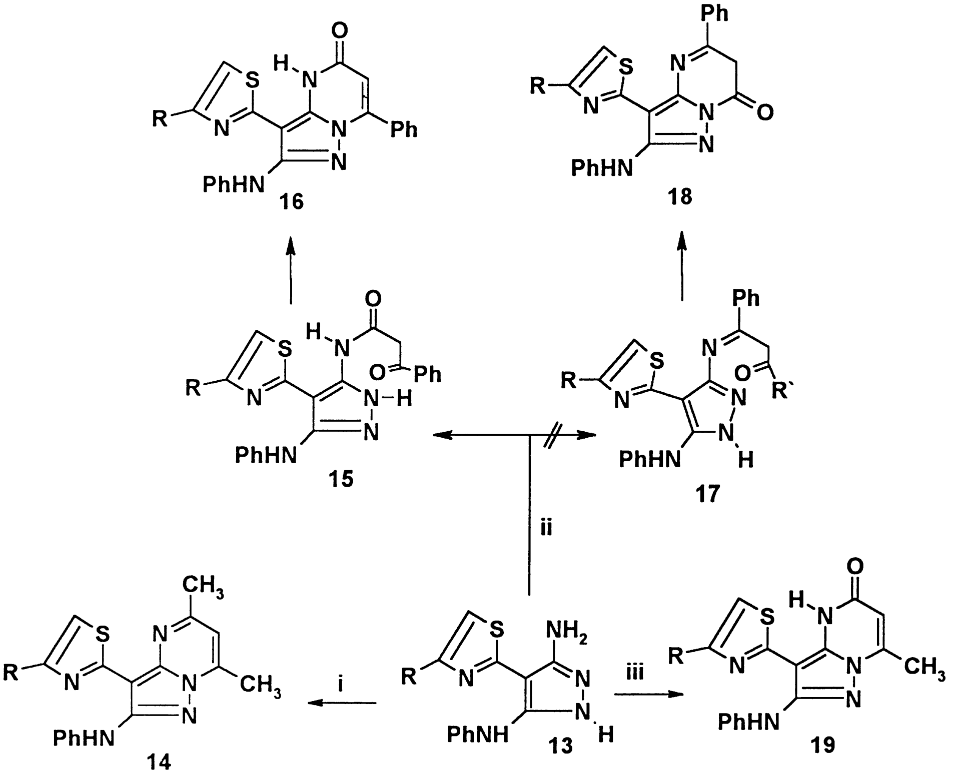
Unequivocal support for each structure **13** came from its reaction with β-ketoesters and β-ketoanilides in boiling acetic acid. Thus, the reaction of ethyl benzoylacetate or benzoylacetanilide with the appropriate aminopyrazole **13** afforded the identical product in all respects (m.p., mixed m.p., and spectra). The structure of the product could have been one of structures **15–18**. On the basis of the ^{1}H NMR spectrum, the structure **17** was eliminated because no signals attributable to the ethoxy group were evident. Thus, the reaction took place through the elimination of ethanol (or aniline) to give **15**, which cyclized to the pyrazolo[1,5-*a*]pyrimidine **16** by its treatment with concentrated sulfuric acid or by boiling with ethanolic piperidine solution (cf. Scheme 5).

By analogy, the reaction of the appropriate of 3-amino-4-(4′-arylthiazol-2′-yl)-5-(phenylamino) pyrazoles **13a–c** with ethyl 3-oxobutanoate (or acetoacetanilide) in boiling acetic acid produces **19a–c**.



a, R = C_6H_5
b, R = $4\text{-}CH_3C_6H_4$
c, R = $2\text{-}C_{10}H_7$

SCHEME 4



i = $(CH_3CO)_2CO$
ii = $C_6H_5COCH_2COOC_2H_5$
iii = $CH_3COCH_2COOC_2H_5$

a, R = C_6H_5
b, R = $4\text{-}CH_3C_6H_4$
c, R = $2\text{-}C_{10}H_7$

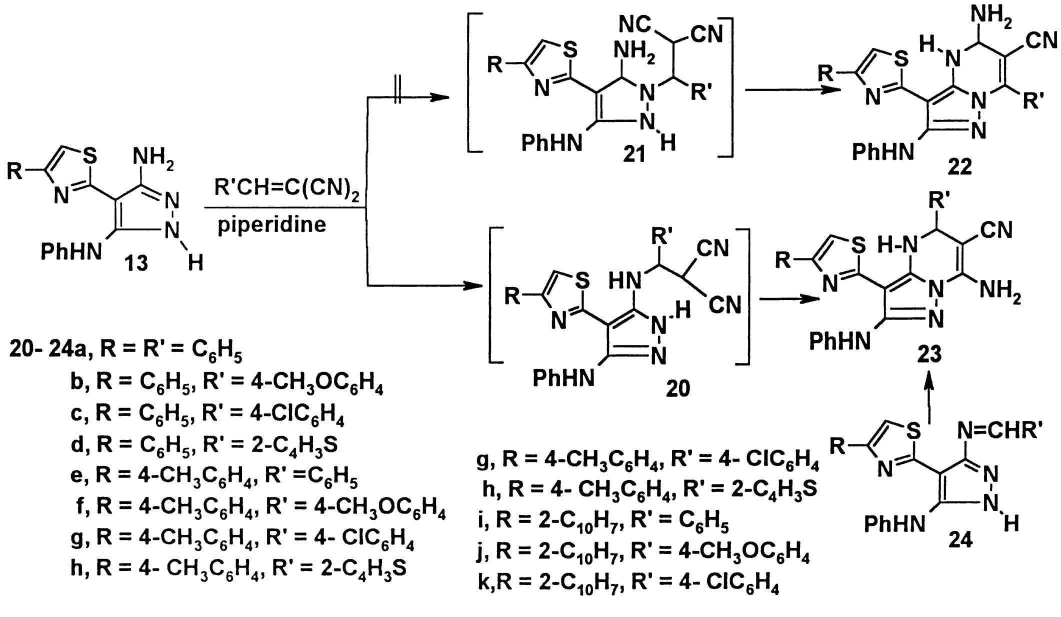
R' = $COOC_2H_5$

SCHEME 5

The structure **19** was elucidated on the basis of the elemental analysis and spectral data. Thus, the ^1H NMR spectrum of **19a** showed signals at $\delta = 2.67$ (s, 3H, CH_3), 6.61 (s, 1H, pyrimidine H-5), 7.31–7.82 (m, 10H, ArHs), 8.32 (s, 1H, thiazole H-5) and 11.82 (s, br., 2H, 2NH). Its IR (cm^{-1}) spectrum revealed bands at 3419 (NH), 1668 (CO), and 1620 (C–N).

Also, the appropriate **13a–c** reacted with the appropriate 1-cyano-2-substituted acrylonitriles in ethanol containing piperidine as a catalyst to afford a single product, in each case, according to thin-layer chromatography (TLC). The structure of each product was confirmed on the basis of elemental analyses, spectral data, and the alternative method of synthesis by reaction of the Schiff's base **24** with malononitrile (cf. Scheme 6).

Meanwhile, the appropriate diazonium chlorides **25a,b** were coupled with active methylene compounds such as acetylacetone, malononitrile, ethyl cyanoacetate, and ethyl 3-oxobutanoate in



SCHEME 6

ethanolic sodium acetate solution to afford pyrazolo[5,1-*c*][1,2,4]triazines **26–29**, respectively (cf. Scheme 7). The structures of **26–29** were established on the basis of elemental analysis and spectral data. Thus, the ^{1}H NMR spectrum of **26a** showed signals at δ = 2.25 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 7.31–8.31 (m, 11H, ArHs and thiazole H-5), and 9.52 (s, br., 1H, NH). Its mass spectrum revealed peaks at m/z = 426 (100%), 316 (12.9%), 134 (54.7%) and 77 (27%).

Similarly, the appropriate diazonium chlorides **25a,b** coupled with 3-chloropentan-2,4-dione and ethyl 2-chloro-3-oxobutanoate in cold ethanolic sodium acetate solution to give products **30a,b** and **31a,b**, respectively. Structures **30** and **31** were confirmed on the basis of spectral data and elemental analyses. The mass spectrum of **30a**, for example, revealed peaks at m/z = 420 (M-H_2O), 37.7%, and 418 (M-H_2O), 66.9%.

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. The IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. The ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ on a Varian Gemini 200 MHz spectrometer, and chemical shifts were expressed in δ units using TMS as an internal reference. The MS spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of the University of Cairo, Giza, Egypt. The 2-(4′-aryl)thiazolylacetonitrile **1a,c** and potassium 2-(4′-arylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolates **2a,2c** were prepared as previously reported [6,9].

2-(4′-P-tolyl)thiazolylacetonitrile (1b)

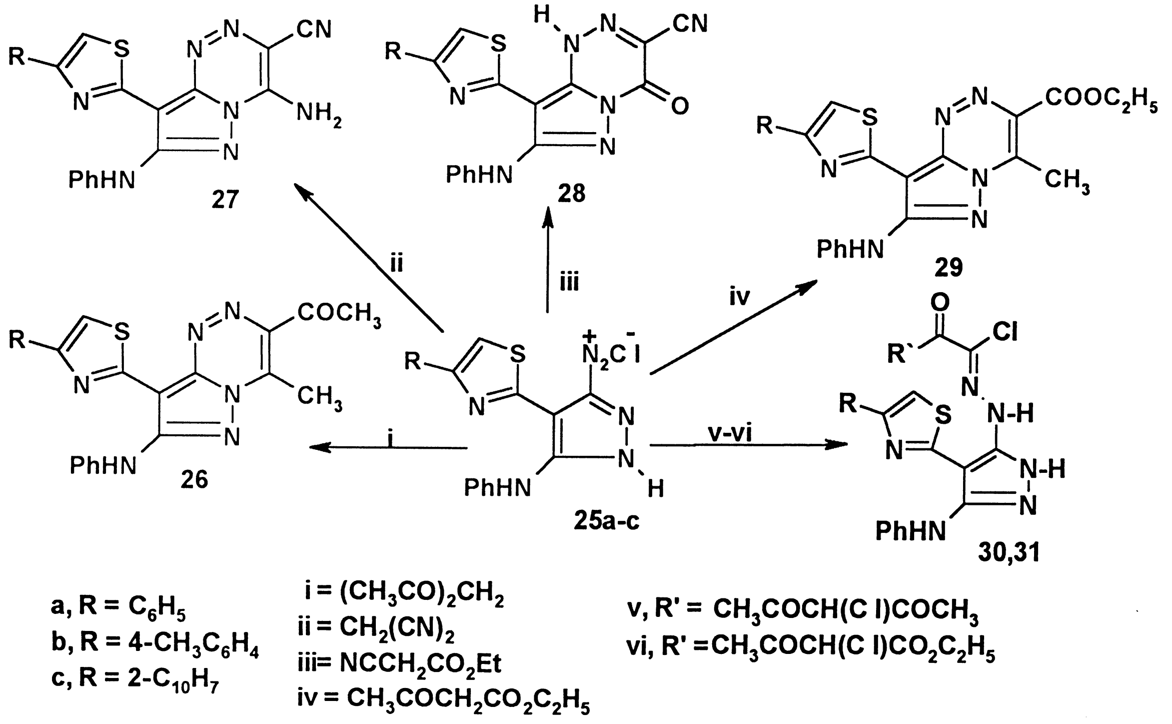
Equimolar amounts of ω-bromo-*p*-methylacetophenone (21.3 g, 0.01 mol) and cyanothioacetamide (10 g, 0.1 mol) in ethanol (50 mL) were refluxed for 30 minutes. The reaction mixture was cooled and poured onto ice cold water containing two drops of ammonium hydroxide (100 mL). The resulting solid was collected and crystallized from ethanol to give thiazole **1b**, in a 65% yield (cf. Table 1).

Potassium 2-(4′-p-tolylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolates 2b

Potassium ethoxide solution, which was prepared via reaction of potassium metal (1 g) in absolute ethanol (10 mL), was added to the mixture of the thiazole **1b** (2.15 g, 0.01 mol) and phenyl isothiocyanate (1.35 g, 0.01 mol) in ethanol (20 mL) with stirring. The resulting solid was collected and washed with diethyl ether.

1-[2′-(3′,4′-Disubstituted)]thiazoline-2-cyano-2-(4′-aryl)thiazolyethene 3a,b *and* 8a,b

A mixture of each appropriate 2-cyanomethylthiazole **1a,b**, phenyl isothiocyanate, and potassium hydroxide (0.05 mol, each) in *N,N*-dimethylformamide



SCHEME 7

was stirred for 4 hours at room temperature. The ω-bromoacetophenone or chloroacetone (0.05 mol) was added, and stirring was continued for 2 hours. The resulting solid, after dilution with water, was collected and crystallized from dimethylformamide to give the corresponding thiazoles **3a,b** and **8a,b**, respectively, in a 62–64% yield (cf. Tables 1 and 2).

3-Amino-5-phenylamino-2-substituted-4-[4′-(aryl)thiazol-2′-yl]thiophenes 4a,b *and* 6a,b

The appropriate ω-bromoacetophenone, chloroacetone, or ethyl chloroacetate (0.05 mol) was added to the appropriate potassium salts **2a,b** (0.05 mol) in ethanol (20 mL) with stirring. The solid that formed after 4 hours was collected and then crystallized from a proper solvent to give the thiophenes **4a,b** and **6a,b**, in 60–62% yields, respectively (cf. Tables 1 and 2).

Reaction of 2a,b *with 3-Chloropentane-2,4-dione and Ethyl 2-chloro-3-oxobutanoate*

3-Chloropentane-2,4-dione or ethyl 2-chloro-3-oxobutanoate was added to the appropriate thiazoles **2a,b** (5 mmol each) in *N,N*-dimethylformamide (20 mL) with stirring at room temperature for 4 hours and left overnight. The resulting solid was collected by filtration, and fractional crystallization gave [3′,4′,5′-tri-substituted)thiazolidene-2-yl](4-aryl-thiazl-2-yl)cyanoethene **9a,b** or **10a,b** and thiophenes **6a,b** or **7a,b** in 30–50% yields (cf. Tables 1 and 2).

Synthesis of 5

A mixture of ω-bromo-4-methylphenacyl bromide (1.01 g, 0.005 mol) and potassium 2-(4′-*p*-tolylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolate (**2b**) (1.92 g, 0.005 mol) in ethanol (20 mL) was stirred for 1 hour at room temperature. The resulting solid was collected and crystallized from benzene to give compound **5** in a 68% yield (cf. Tables 1).

Cyclization of 5: Formation of 3-Amino-2-benzoyl-5-phenylamino-4-(4′-p-tolyl)thiazol-2′-ylthiophene (4b)

To a solution of **5** (1 g) in ethanol (20 mL), triethylamine (0.5 mL) was added, and the reaction mixture was refluxed for 30 minutes. The solid, so formed, was collected and crystallized from benzene to give the corresponding thiophene **4b** (cf. Tables 1 and 2).

Cyclization of 5: 1-[2′-(3′,4′-Diphenyl)]thiazoline-2-cyano-2-(4′-p-tolyl)thiazolyethene (3b)

Compound **5** (1 g) was mixed with polyphosphoric acid, which was prepared by dissolving P_2O_5 (1 g) in

TABLE 1 Characterization Data of the Newly Synthesized Compounds

Compd No.	*M.P. (°C) color*	*Compd No.*	*M.P. (°), color*	*Compd No.*	*M.P. (°) color*	*Compd No.*	*M.P. (°C) color*
1b	103–105 Brown	**11b**	156–158 Yellow	**23c**	>320 Yellow	**24h**	258–260 Yellow
3a	28–283 Yellow	**11c**	215–217 [9] Yellow	**23d**	>320 Orange	**24i**	248–250 Brown
3b	255–257 Yellow	**13a**	220–222 White	**23e**	>320 Yellow	**24j**	253–255 Yellow
4a	198–199 [8] Yellow	**13b**	216–218 White	**23f**	>320 Yellow	**24k**	289–290 Yellow
4b	204–206 Yellow	**13c**	226–228 [9] White	**23g**	>320 Yellow	**26a**	241–243 Black
5	152–153 Yellow	**14a**	233–235 Yellow	**23h**	244–246 Red	**26b**	176–178 Black
6a	205–207 White	**14b**	255–257 Yellow	**23i**	>320 Yellow	**27a**	>320 Dark green
6b	206–207 White	**14c**	282–284 Yellow	**23j**	>320 Yellow	**27b**	246–248 Black
7a	176–178 White	**15c**	148–150 Green	**23k**	>320 Yellow	**28a**	255–257 Dark green
7b	175–176 White	**16a**	238–240 Green	**24a**	230–231 Yellow	**28b**	258–260 Black
8a	245–247 Yellow	**16b**	263–265 Green	**24b**	212–214 Yellow	**29a**	308–310 Red
8b	263–265 Yellow	**16c**	265–267 Green	**24c**	263–265 Yellow	**29b**	240–243 Black
9a	271–273 Yellow	**19a**	332–334 White	**24d**	225–227 Brown	**30a**	182–184 Black
9b	>320 Yellow	**19b**	>325 White	**24e**	243–245 Orange	**30b**	238–240 Black
10a	272–274 Orange	**19c**	>325 White	**24f**	253–255 Yellow	**31a**	172–174 Dark red
10b	280–282 Orange	**23a**	>320 Yellow	**24g**	265–266 Yellow	**31b**	213–215 Red
11a	196–198 Yellow	**23b**	>320 Yellow				

Crystallization solvents: a = acetic acid; b = benzene; c = *N,N*-dimethylformamide; d = dioxin; e = ethanol.
Microanalytical data are satisfactory: ±0.2%.

ortho-phosphoric acid (3 mL; 85%), and heated at 110C°C for 1 hour. The reaction mixture was poured onto ice-cold water (30 mL), and the resulting solid was collected and crystallized to give the corresponding thiazole **3b** (cf. Tables 1 and 2).

1-Cyano-1-(4′-substituted)thiazol-2′-yl-2-phenylamino-2-thiomethylethene **11a–c**

Methyl iodide (0.71 g, 0.005 mol) was added to the appropriate 2-(4-arylthiazol-2′-yl)-2-cyano-1-(phenylamino)ethenylthiolates **2a–c** (0.005 mol) in *N,N*-dimethylformamide (20 mL) with stirring. The reaction mixture was stirred for 1 hour, and the resulting solid was collected and crystallized from acetic acid to give products **11a–c** in 72–75% yields, respectively (cf. Tables 1 and 2).

3-Amino-4-(4′-substituted)thiazol-2′-yl-5-phenylaminopyrazoles **13a–c**

A mixture of the appropriate **11a–c** (0.01 mol) and hydrazine hydrate (5 mL, 0.02 mol) in ethanol (20 mL) was refluxed for 6 hours. The resulting solid was collected and crystallized from ethanol (or dioxane) to give the corresponding aminopyrazoles **13a–c** in 66–68% yields, respectively (cf. Tables 1 and 2).

3-(4′-Aryl)thiazol-2′-5,7-disubstituted-2-phenylaminopyrazolo[1,5-a]pyrimidines **14a–c, 16a–c***, and* **19a–c**

A mixture of the appropriate 3-aminopyrazoles **13a–c** (5 mmol) and the appropriate pentane-2,4-dione or ethyl 3-oxo-4-phenylpropanoate (or benzoylacetanilide) or ethyl 3-oxobutanoate (or acetoacetanilide) (0.005 mol) in acetic acid (20 mL) was refluxed for 3 hours. The solid was collected and crystallized from the proper solvent to give the corresponding pyrazolo[1,5-*a*]pyrimidine **14a–c**, **16a–c**, and **19a–c** in 70–75% yields, respectively (cf. Tables 1 and 2). In the reaction of **13c** with 3-oxo-4-phenylpropanoate, the filtrate was diluted with water and **15c** was isolated.

Synthesis of Schiff's Bases **24a–k**

General Procedure. A mixture of the appropriate aminopyrazoles **13a–c** and the appropriate aldehyde (0.005 mol each) in ethanol (20 mL) containing 3 drops of piperidine was refluxed for 4 hours. The resulting solid was collected and crystallized from the proper solvent to give the products **26a–k** in 70–75% yields, respectively (cf. Tables 1 and 2).

7-Amino-3-(4-aryl)thiazol-2′-yl-6-cyano-5-substituted-2-phenylaminopyrazolo[1,5-a]-pyrimidines 23

General Procedure. Method A: Equimolar amounts of the appropriate aminopyrazoles **13a–c**, 1-cyano-1-substituted acrylonitrile (0.005 mol each), and 3 drops of piperidine in ethanol (20 ml) were refluxed for 4 hours. The resulting solid was collected and crystallized from the proper solvent to give 7-amino-3-(4′-aryl)thiazol-2′-yl-6-cyano-5-substituted-2-phenylaminopyrazolo[1,5-*a*]-pyrimidines

TABLE 2 IR and ^{1}H NMR Spectra of the Newly Synthesised Compounds

Compd.	*IR (cm^{-1})*	^{1}H NMR (δ)
3b	2175 (CN)	2.44 (s, 3H, 4-CH$_3$C$_6$H$_4$) and 7.22–7.92 (m, 16H, ArHs, and thiazole)
4b	3433 (NH$_2$), 1650 (CO) and 1600 (C=C)	2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 7.22–7.92 (m, 17H, ArHs, thiazole H-5, and NH$_2$) and 11.94 (s, 1H, NH)
6a	3247 (NH), 1635 (CO)	2.28 (s, 3H, CH$_3$), 7.12–7.19 (m, 13H, ArHs), thiazole H-5, and NH$_2$) and 11.94 (s, 1H, NH)
6b	3247 (NH), 1640 (CO)	2.28 (s, 3H, CH$_3$), 2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 7.12–7.19 (m, 12H, ArHs, thiazole H-5, and NH$_2$) and 11.94 (s, 1H, NH).
7a	3408, 3311 (NH2), 1715 (CO).	1.13 (t, 3H, CH$_2$CH$_3$), 4.22 (q, 2H, CH$_2$CH$_3$), 7.22–7.72 (m, 13H, ArHs, thiazole H-5, and NH$_2$) and 11.85 (s, 1H, NH).
7b	3396, 3319 (NH2) and 1733 (CO).	1.13 (t, 3H, CH$_2$CH$_3$), 2.45 (s, 3H, CH$_3$) 4.22 (q, 2H, CH$_2$CH$_3$), 7.22–7.72 (m, 12H, ArHs, thiazole H-5, and NH$_2$) and 11.85 (s, 1H, NH)
8a	2177 (CN)	2.57 (s, 3H, CH$_3$), 7.21–7.82 (m, 12H, ArHs, and thiazole).
8b	2171 (CN)	2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.57 (s, 3H, CH$_3$) and 7.22–7.86 (m, 11H, ArHs and thiazole)
9b	2191 (CN) and 1635 (CO).	2.29 (s, 3H, CH$_3$), 2.42 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.59 (s, 3H, CH$_3$), 7.26–7.70 (m, 9H, ArHs), and 8.64 (s, 1H, thiazole)
10a	2189 (CN), 1703 (CO), and 1606 (C=N)	1.44 (t, 3H, CH$_2$CH$_3$), 2.21 (s, 3H, CH$_3$), 4.35 (q, 2H, CH$_2$CH$_3$), and 7.27–7.39 (m, 11H, ArHs)
10b	2183 (CN), 1708 (CO), and 1608 (C=N)	1.44 (t, 3H, CH$_2$CH$_3$), 2.21 (s, 3H, CH$_3$), 2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 4.35 (q, 2H, CH$_2$CH$_3$), and 7.27–7.39 (m, 10H, ArHs)
11b	3350 (NH), 2230 (CN), and 1610 (C=N)	2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.7 (s, 3H, SCH$_3$), 7.36–8.22 (m, 10H, ArHs, and thiazole H-5) and 11.21 (s, br., 1H, NH).
13a	3199 3122 (NH2) and 1618 (C=N)	5.62 (s, 2H, NH$_2$), 7.21–7.772 (m, 11H, ArHs), 8.22 (s, br., 1H, NH), and 8.45 (s, br., 1H, NH)
13b	3199, 3122 (NH2) and 1618 (C=N)	2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 5.62 (s, 2H, NH$_2$, 7.21–7.77 (m, 10H, ArHs), 8.22 (s, br., 1H, NH), and 8.45 (s, br., 1H, NH).
14b	3276 (NH) and 1626 (C=N)	2.44 (s, 3H, CH$_3$), 2.45 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.67 (s, 3H, CH$_3$), 6.61 (s, 1H, pyrimidine H-4), 7.22–7.77 (m, 10H, AHs, and thiazole), and 8.34 (s, br., 1H, NH)
14c	3276 (NH) and 1626 (C=N)	2.44 (s, 3H, CH$_3$), 2.67 (s, 3H, CH$_3$), 6.61 (s, 1H, pyrimidine H-4), 7.22–7.77 (m, 13H, AHs, and thiazole) and 8.34 (s, br., 1H, NH)
19b	3417 (NH), 3186 (NH), 1666 (CO), and 160 (C=N).	2.44 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.67 (s, 3H, CH$_3$), 6.61 (s, 1H, pyrimidine H-5), 7.31–7.82 (m, 9H, ArHs), 8.32 (s, 1H, thiazole H-5), and 11.82 (s, br., 2H, 2NH).
19c	3417 (NH), 3186 (NH), 1666 (CO), and 1604 (C=N).	2.67 (s, 3H, CH$_3$), 6.6 (s, 1H, pyrmidine H-5), 7.31–7.82 (m, 12H, ArHs), 8.32 (s, 1H, thiazole H-5), and 11.82 (s, br., 2H, 2NH)
23b	3448, 3292, 3199 (NH, NH$_2$), 2216 (CN).	2.74 (s, 1H, CH), 2.89 (s, 1H, NH), 3.87 (s, 3H, OCH$_3$), 7.00–8.05 (m, 15H, ArHs, and thiazole), 8.98 (s, 2H, NH$_2$), and 10.14 (s, 1H, NH)
23f	3448, 3292, 3199 (NH, NH$_2$), 2216 (CN)	2.45 (s, 3H, 4-CH$_3$C$_6$H$_5$), 2.74 (s, 1H, CH), 2.89 (s, 1H, NH), 3.80 (s, 3H, CH$_3$OC$_6$H$_4$), 7.00–8.05 (m, 14H, ArHs and thiazole), 8.98 (s, 2H, NH$_2$), and 10.14 (s, 1H, NH)
24b	3261 (NH).	3.85 (s, 3H, OCH$_3$), 7.21–8.03 (m, 17H, ArHs thiazole and NH), and 8.52 (s, 1H, CH=N)
24e	3273 (NH).	2.42 (s, 3H, CH$_3$), 7.21–8.03 (m, 17H, ArHs, thiazole, and NH) and 8.52 (s, 1H, CH=N)
24f	3265 (NH).	2.42 (s, 3H, CH$_3$), 3.85 (s, 3H, OCH$_3$), 7.21–8.03 (m, 16H, ArHs, thiazole, and NH) and 8.52 (s, 1H, CH=N)
29a	3350 (NH), 1720 (CO), and 1611 (C=N)	1.03 (t, 3H, CH$_2$CH$_3$), 1.95 (s, 3H, CH$_3$), 4.22 (q, 2H, CH$_2$CH$_3$), 7.01–7.75 (m, 10H, ArHs), 8.31 (s, 1H, thiazole H-5), and 9.57 (s, br., 1H, NH)

23a–k in 73–75% yields, respectively (cf. Tables 1 and 2).

Method B. Equimolar quantities of each the appropriate aminopyrazoles **13a–c** and the appropriate **24a–j** (5 mmol each) in ethanol (20 mL) containing 3 drops of piperidine as a catalyst was refluxed for 4 hours. The resulting solid was collected and crystallized to give products identical in all respects (m.p., mixed m.p., and spectra) with those corresponding in method A.

3,4-Disubstituted-8(4′-aryl)thiazol-2′-yl-7-phenylaminopyrazolo[5,1-c]-1,2,4-triazines **26–29***, and hydrazonoyl chlorides* **31a,b** *and* **32a,b**

The appropriate aminopyrazolediazonium chlorides, **25a,b** (ca. 0.01 mol) which were prepared by adding concentrated hydrochloric acid (3 mL, 12 M) to a cold solution of the appropriate aminopyrazole **13a,b** (0.01 mol) in acetic acid (2 ml) followed by treatment with a cold solution of sodium nitrite (0.7 g, 0.01 mol) in water (5 mL), was added dropwise with stirring at 0–5°C to a cold solution of each of acetylacetone or malononitrile or ethyl cyanoacetate or ethyl 3-oxobutanoate or 3-chloropentane-2,4-dione or ethyl 2-chloro-3-oxobutanoate (0.01 mol) in ethanol (50 mL) containing sodium acetate trihydrate (1.3 g, 0.01 mol). The reaction mixture was stirred for 3 hours, and the precipitated was filtered off, washed with water, dried, and crystallized from acetic acid (or DMF) to give **29,31–32** in 63–65% yields, respectively (cf. Tables 1 and 2).

REFERENCES

[1] Katritzky, A. R., Ed. Comprehensive Heterocyclic Chemistry, Pergamon Press: Elsmford, NY, 1984.

[2] Hassan, N. M.; Abdelhamid, A. O. J Chem Res 1997 (S), 350 (M), 2244.

[3] Emam, H. A.; Abdelhamid, A. O. Indian J Chem 1997, 36B, 880.

[4] Farag, A. M.; Dawood, K. M.; Abdelhamid, A. O. Tetrahedron 1997, 53, 17461.

[5] Zohdi, H. F.; Rateb, N. M.; Sallam, M. M. M.; Abdelhamid, A. O. J Chem Res 1998, (S) 742, (M), 3329.

[6] Abdelhamid, A. O.; Mohamed, G. S. Heteroatom J 1999, (in press).

[7] Williams, D. H.; Fleming, I. Spectroscopic Methods in Organic Chemistry, 2nd ed.; McGraw-Hill: Maidenhead, UK, 1973.

[8] Schafer, V. H.; Gewald, K. J Prakt Chemie 1974, 316, 686.

[9] Abdelhamid, A. O.; Al-Shieri, S. M. J Chem Res 1997, (S) 240, (M) 16812.