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Synthesis of Some 1,3-Thiazole, 1,3,4-Thiadiazole, Pyrazolo[5,1-*c*]-1,2,4-triazine, and 1,2,4-Triazolo[5,1-*c*]-1,2,4-triazine Derivatives Based on the Thiazolo[3,2-*a*]benzimidazole Moiety

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Summary. 3-(3-Methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile was synthesized by refluxing ethyl 3-methylthiazolo[3,2-*a*]benzimidazole-2-carboxylate, acetonitrile, and sodium hydride. Treatment of 3-(3-methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile with phenyl isothiocyanate, in the presence of KOH, furnished the corresponding potassium salt which was converted into thioacetanilide derivative upon neutralization. The thioacetanilide derivative reacts with α-chloroacetylacetone and ethyl α-chloroacetoacetate to give the 1,3-thiazole derivatives, while the reaction of the thioacetanilide derivative with hydrazonyl chlorides gave 1,3,4-thiadiazole derivatives. On the other hand, 3-(3-methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile reacted with the diazonium salt of both 3-phenyl-5-amino-(1*H*)-pyrazole and 5-amino-l,2,4-(1*H*)-triazole to afford the corresponding hydrazones. The latter hydrazones underwent an intramolecular cyclization upon boiling in pyridine to give pyrazolo[5,1-*c*]-1,2,4-triazine and 1,2,4-triazolo[5,1-*c*]-1,2,4-triazine derivatives. Moreover, the behavior of thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one towards phenyl isothiocyanate followed by the reaction with α-chloroketones or hydrazonyl chlorides was investigated. Some of the latter compounds exhibited moderate effects against some bacterial and fungal species.

Keywords. Heterocycles; Cyclizations; *Michael* addition; Hydrazonyl chlorides.

Introduction

Antibacterial [1–3], anti-inflammatory [4], antiulcer [5, 6], and antiviral [7, 8] effects have been shown with various thiazolo[3,2-*a*]benzimidazole derivatives. Furthermore, certain thiazolo[3,2-*a*]benzimidazole derivatives, such as tilomisole (WY-18,251) was largely studied [9, 10] demonstrating their anti-inflammatory [11] and immunomodulatory [12] activities. Recently, the gastric antisecretory activity of thiazolo[3,2-*a*]benzimidazol-1-oxide (WY-26,769) was reported [13]. Also, some thiazolo[3,2-*a*]benzimidazole derivatives were used for treatment of cancer [14], cerebral infarction [15], neurogenic pain [16], and bone diseases [17]. The above observations in connection with our research concerned with the synthesis of biologically active poly-substituted heterocycles [18–23] prompted us to synthesize some novel thiazolo[3,2-*a*]benzimidazole derivatives derived from 3-(3-methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile (**2**) and thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**18**) to evaluate their antimicrobial activities (Scheme 1).

Results and Discussion

Syntheses

The versatile, hitherto unreported 3-(3-methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile (**2**) was synthesized by refluxing equimolar quantities of 3-methylthiazolo[3,2-*a*]benzimidazole-2-carboxylic acid ethyl ester (**1**), acetonitrile and sodium hy-

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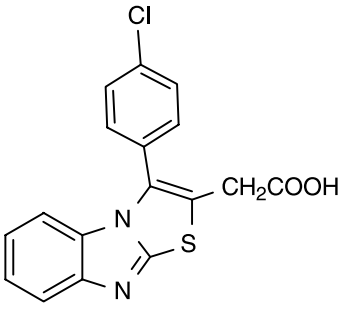
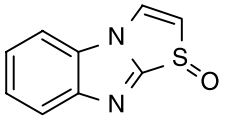
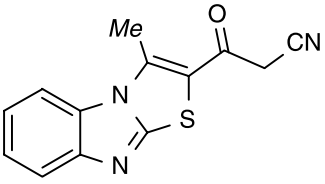


Tilomisole (WY-18,251)



WY-26,769



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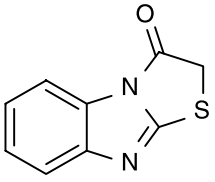

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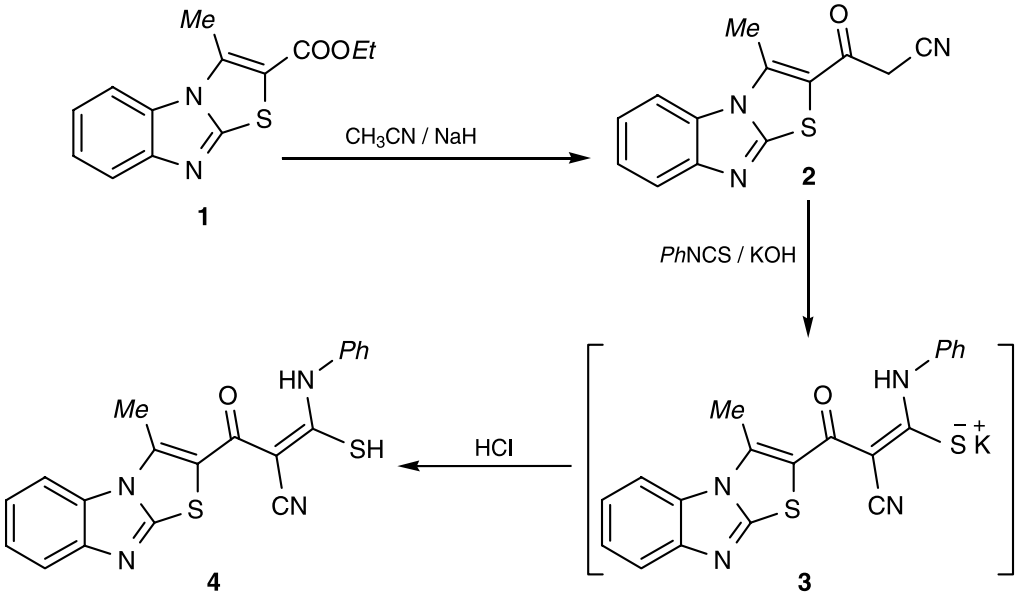
Scheme 1

dride in dry benzene (Scheme 2). Compound **2** was characterized by its elemental analysis and spectral data. Thus, its IR spectrum revealed two characteristic absorption bands at 2225 and 1681 cm^{-1} assignable to nitrile and carbonyl groups, whereas its ^1H NMR spectrum displayed a characteristic singlet signal at $\delta = 4.18$ due to active methylene protons in addition to aromatic protons in the region 7.21–8.01 ppm.

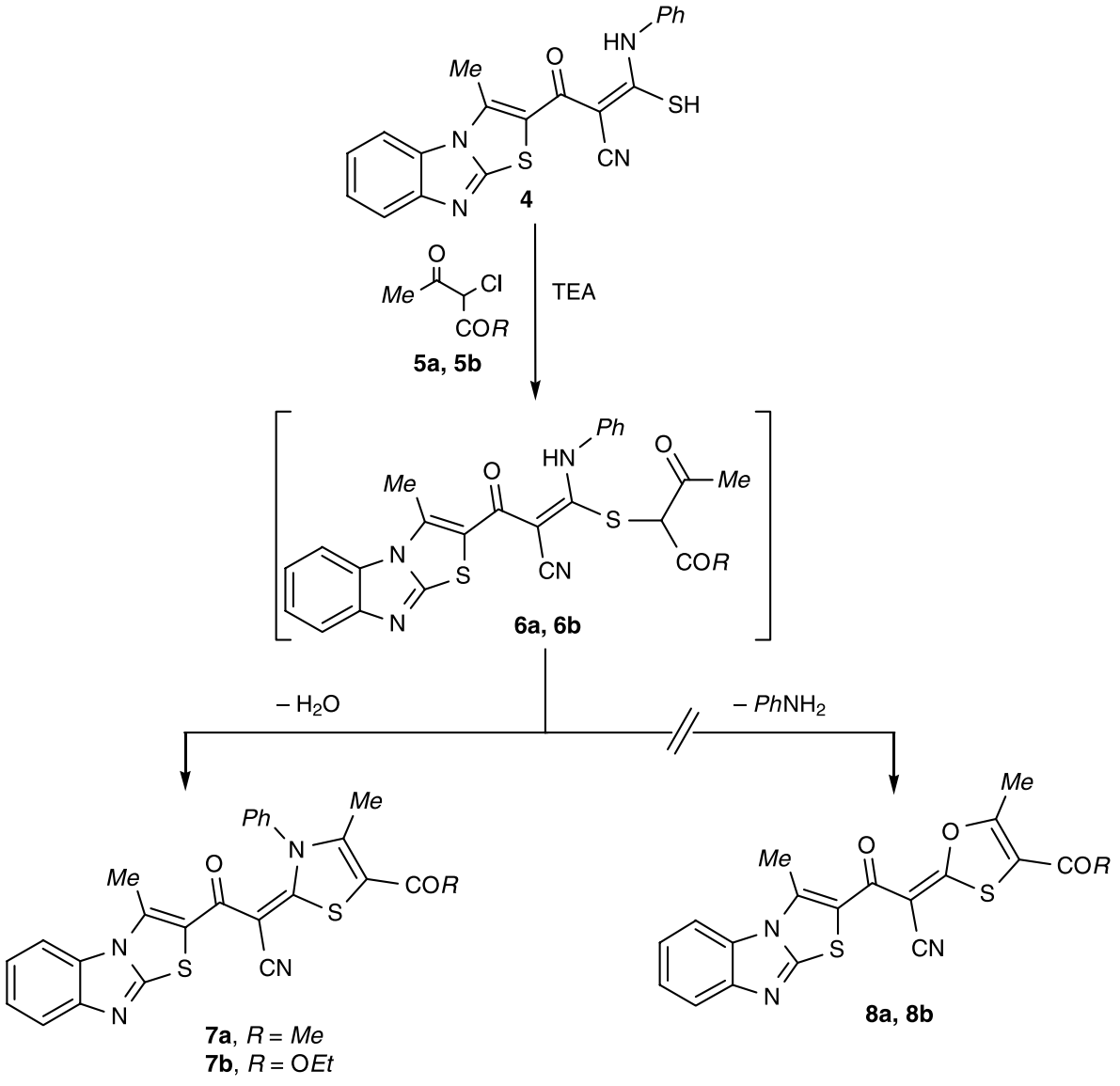
Next, treatment of compound **2** with phenyl isothiocyanate, in *DMF* and in the presence of KOH, at room temperature afforded the potassium salt **3** which was converted into the thioacetanilide derivative **4** upon treatment with dilute hydrochloric acid (Scheme 2). The structure of compound **4** was confirmed on the bases of its spectral data (*cf.* Experimental part).

Compound **4** reacted with α-chloroacetylacetone (**5a**) and ethyl α-chloroacetoacetate (**5b**) in refluxing ethanol and in the presence of a catalytic amount of triethylamine resulted in the formation of 1,3-thiazole derivatives **7a** and **7b** [19] not the other possible oxathiole structures **8a** and **8b** [22] according to the spectral data of the isolated products (Scheme 3). For example, the IR spectra of the isolated products revealed, in each case, two bands due to two carbonyl groups in the region 1703–1638 cm^{-1} and showed a nitrile absorption band in the region 2195–2172 cm^{-1}. The mass spectra of the same compounds showed peaks corresponding to their molecular ions. The latter reaction of the thioacetanilide **4** with α-chloroketones **5a** and **5b** proceeds, in each case, through loss of hydrogen chloride followed by elimination of a water molecule rather than elimination of aniline to afford 1,3-thiazole derivatives **7a** and **7b** not the other possible oxathiole structures **8a** and **8b**.

Furthermore, the reaction of thioacetanilide derivative **4** with hydrazonyl chlorides **9a–9c** under the



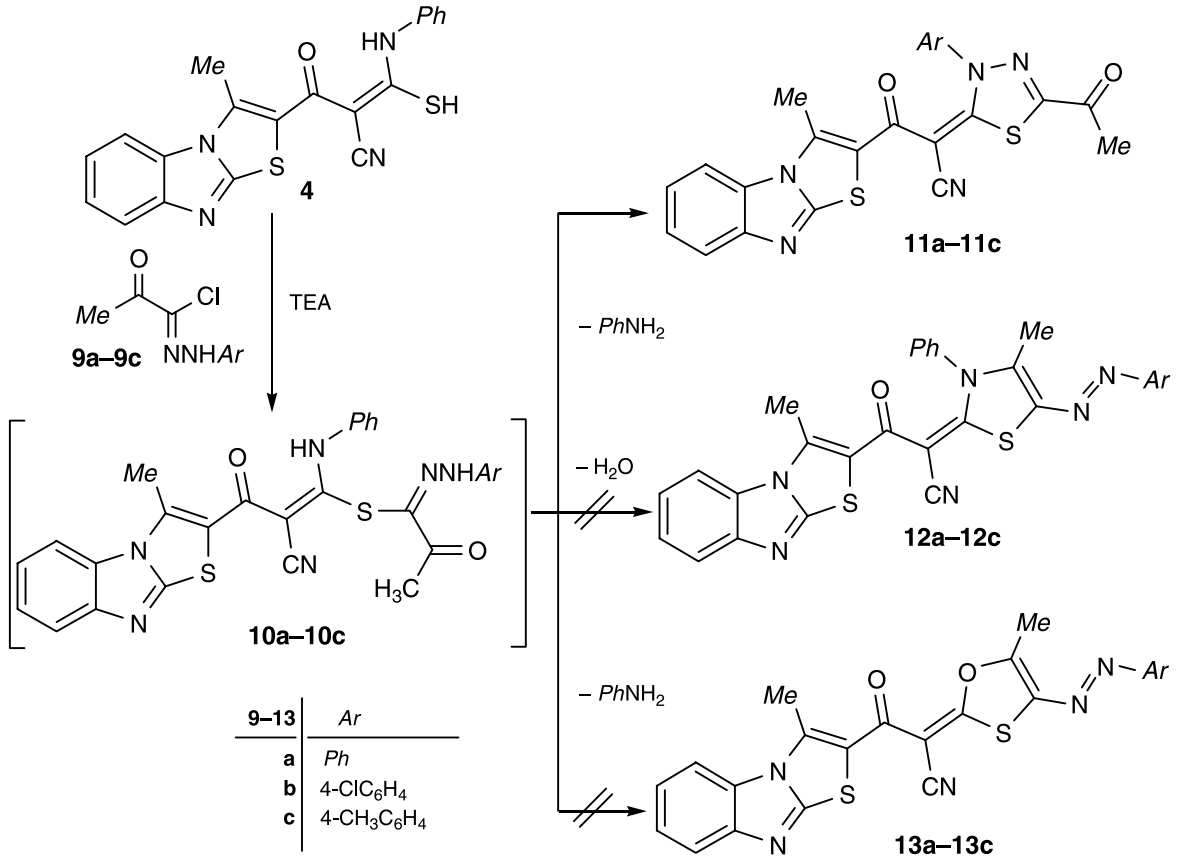
Scheme 2



Scheme 3

same reaction conditions afforded, in each case, only one isolable product. Scheme 4 depicts all the possible structures proposed for the reaction products. However, the elemental analyses and spectral data of the reaction products were compatible with the 1,3,4-thiadiazole structures **11a**–**11c**. For example, the IR spectra of the isolated products revealed, in each case, the appearance of two carbonyl absorption bands near 1695 and 1636 cm^{-1} in addition to a nitrile absorption band in the region 2205–2191 cm^{-1}. Their mass spectra revealed, in each case, a peak corresponding to the molecular ion. These results indicate that the reaction of the thioacetanilide **4** with hydrazonyl chlorides **9a**–**9c** proceeds in each case, *via* loss of hydrogen chloride to form the non-isolable intermediate **10a**–**10c** which cyclized by elimination of an aniline molecule to form the isolable 1,3,4-thiadiazole derivatives **11a**–**11c** [19, 22].

On the other hand, treatment of compound **2** with the diazonium salts of both 3-phenyl-5-amino-1*H*-pyrazole **14a** and 5-amino-1*H*-l,2,4-triazole **14b** [19, 24, 25] afforded hydrazones **15a** and **15b** (Scheme 5). The IR spectra of the isolated hydrazones exhibited, in each case, bands in the region 3325–3150 cm^{-1} corresponding to 2NH functions and a nitrile absorption band in the region 2225–2218 cm^{-1}, in addition to a strong carbonyl band in the region 1660–1646 cm^{-1}.

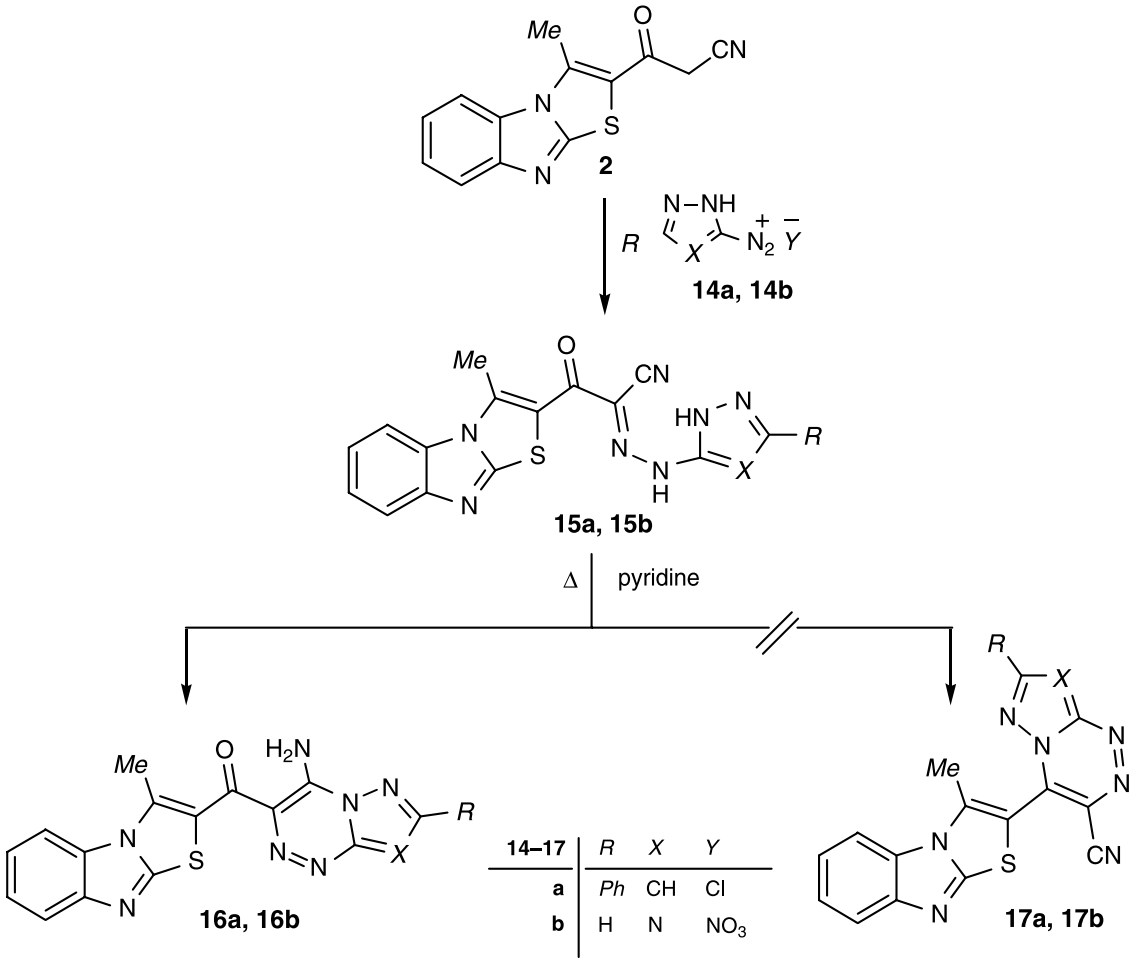


Scheme 4

Compounds **8a** and **8b** underwent an intramolecular cyclization upon boiling in pyridine *via Michael* type addition of the endocyclic NH of the hydrazones **8a** and **8b** to the triple bond of a nitrile function to afford the corresponding pyrazolo[5,1-*c*]-1,2,4-triazine and 1,2,4-triazolo[5,1-*c*]-1,2,4-triazine derivatives **16a** and **16b** (Scheme 5). Their IR spectra revealed, in each case, the lack of band corresponding to nitrile absorption and revealed the presence of amino and carbonyl functions, whereas, their ^{1}H NMR showed, in each case, the appearance of a D_2O exchangeable signal in the region 8.55–9.06 ppm due to the amino function (*cf.* Experimental part).

The behavior of thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**21**) towards phenyl isothiocyanate followed by the reaction with α-chloroacetylacetone (**5a**), ethyl α-chloroacetoacetate (**5b**), or hydrazonyl chlorides **9a**–**9c** was investigated. Thus, treatment of thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**18**) with phenyl isothiocyanate, in *DMF* and in the presence of KOH, at ambient temperature furnished the non-isolable potassium salt **19** which reacts *in situ* with α-chloroacetylacetone (**5a**) and ethyl α-chloroacetoacetate (**5b**) to give 1,3-thiazole derivatives **20a** and **20b** (Scheme 6). In a similar manner, hydrazonyl chlorides **9a**–**9e** reacted with the non-isolable potassium salt **19** under the same reaction conditions, to afford 1,3,4-thiadiazole derivatives **21a**–**21e**. The structures of the latter compounds were confirmed by their IR, ^{1}H NMR, and mass spectra (*cf.* Experimental part). The latter reactions of the non-isolable potassium salt **19** with α-chloroketones **5a** and **5b** or hydrazonyl chlorides **9a**–**9c** proceeds in the same sequence of these reactions depicted in Schemes 3 and 4, respectively, except elimination of potassium chloride instead of hydrogen chloride [19, 26].

Compound **18** couples smoothly with 3-phenyl-1*H*-pyrazole-5-diazonium chloride (**14a**) and 1*H*-l,2,4-triazole-5-diazonium nitrate **14b** to afford the corresponding hydrazones **22a** and **22b** (Scheme 6). The structures of the latter hydrazones were deduced by their elemental analyses and spectral data. For example, the IR spectrum of the hydrazone deriva-

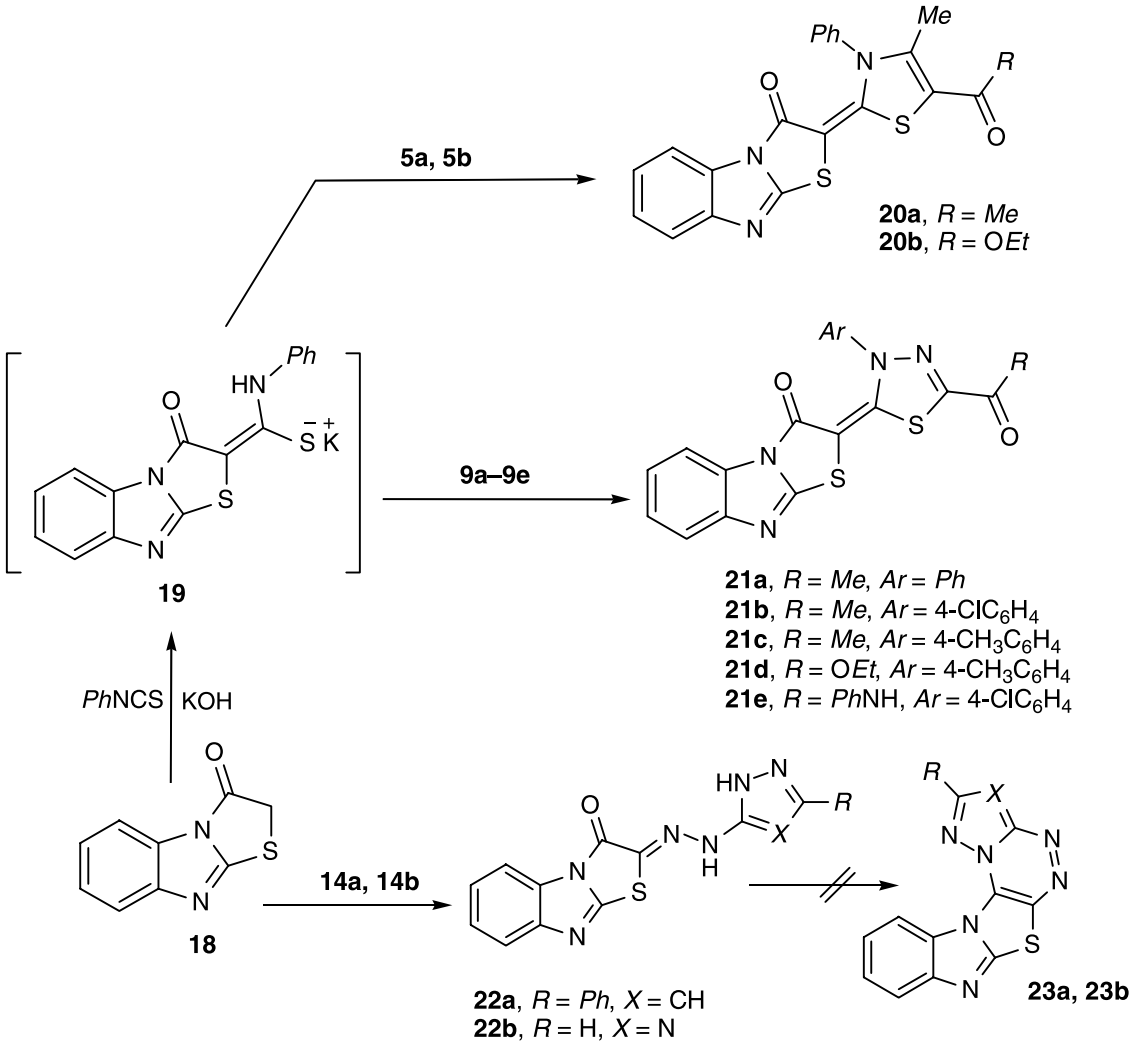


Scheme 5

tive **22a** showed bands at 3208 and 3112 cm^{-1} due to two NH groups and exhibited a strong absorption band at 1701 cm^{-1} corresponding to a carbonyl group while its ^1H NMR revealed two D_2O exchangeable signals of two NH functions at $\delta = 8.65$, 10.44 ppm. All attempts to cyclize the hydrazones **22a** and **22b** to their corresponding fused heterocyclic ring systems **23a** and **23b** were unsuccessful.

Antimicrobial Activity

The antibacterial and antifungal activities were carried out at the Regional Center for Mycology and Biotechnology at Al-Azhar University, Cairo, Egypt. Some of the newly synthesized compounds were screened for their antimicrobial activity using the diffusion agar technique [27], where ten compounds were tested against four fungal species namely *Aspergillus fumigatus* (*A.f.*), *Penicillium italicum* (*P.i.*), *Syncephalastrum racemosum* (*S.r.*), and *Candida albicans* (*C.a.*) as well as against four bacterial species namely *Staphylococcus aureus* (*S.a.*), *Pseudomonas aeruginosa* (*P.a.*), *Bacillus subtilis* (*B.s.*), and *Escherichia coli* (*E.c.*) for their antimicrobial activity using 5 mg/cm^3 of each compound in *DMF*. Inhibition zone diameter (IZD) in cm was taken as the criterion for antimicrobial activity. The antimicrobial activity was assayed biologically using a spore suspension of the fungal species (1 cm^3 of sterile water containing approximately 10^8 conidia) or spreading bacterial suspension over a solidified malt agar medium. The layer was allowed to set for 30 min. A solution of each of the tested compounds (5 mg/cm^3) was placed onto sterile 5 mm filter paper discs and allowed to dry, then the discs were placed onto the center of the malt agar plate and incubated at the optimum incubation temperature, $28 \pm 2°C$. A clear zone around the disc was taken as an indication



Scheme 6

Table 1. Antimicrobial activities of the tested compounds

Compd.[a]	Inhibitions[b]				Inhibitions[b]			
	Fungal species				Bacterial species			
	(*A.f.*)	(*P.i.*)	(*S.r.*)	(*C.a.*)	(*S.a.*)	(*P.a.*)	(*B.s.*)	(*E.c.*)
7b	0	0	+	+	0	0	+	0
11c	0	+	0	+	0	+	0	0
16a	0	0	+	+	0	+	0	0
20b	0	+	++	+	+	++	++	+
21c	+	0	+	+	0	+	0	+
22b	+	+	0	+	0	+	++	0
Stand.[c]	+++	+++	+++	++	++	+++	+++	++

[a] The biological activity of the other compounds **7a**, **11a**, **16b**, and **21d** revealed no inhibition activities against all species
[b] Inhibition value = 0.1–0.5 cm beyond control = +, 0.6–1.0 cm = ++, 1.1–1.5 cm = +++ and 0 = not detected
[c] The fungicide *Terbinafin* and the bactericide *Chloramphenicol* were used as standards

of the inhibition of the test organism growth. The size of the clear zone is proportional to the inhibitory action of the compound under investigation. The fungicide *Terbinafin* and the bactericide *Chloramphenicol* were used as references to evaluate the potency of the tested compounds under the same conditions. Measurements were considered after 72 h for fungi and 24 h for bacteria. The results are contained in Table 1.

The results of antimicrobial activity showed that compound **20b** exhibited moderate effects against *Syncephalastrum racemosum* (*S.r.*), *Pseudomonas aeruginosa* (*P.a.*) and *Bacillus subtilis* (*B.s.*). Also, the hydrazone derivative **22b** showed a moderate effect against *Bacillus subtilis* (*B.s.*). Most of tested compounds exhibited slightly effects against *Candida albicans* (*C.a.*) and *Pseudomonas aeruginosa* (*P.a.*). However, the activities of the tested compounds are less than those of the standard agents used (Table 1).

Experimental

Melting points were measured with a Gallenkamp apparatus. IR spectra were recorded on a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^{1}H NMR spectra were determined in *DMSO*-d_6 at 300 MHz on a Varian Mercury VX 300 NMR spectrometer using *TMS* as an internal standard. Mass spectra were measured on a GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses (C, H, N, and S) were performed using the Elmentar varu EL Germany Instrument. Their results agreed favourably with the calculated values. 3-Methylthiazolo[3,2-*a*]benzimidazole-2-carboxylic acid ethyl ester (**1**) [28], thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**18**) [29], hydrazonyl chlorides **9a–9c** [30], **9d** [31], and **9e** [32] were prepared according to the reported methods.

3-(3-Methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**2**, $C_{13}H_9N_3OS$)
To 26.0 g 3-methylthiazolo[3,2-*a*]benzimidazole-2-carboxylic acid ethyl ester (**1**) (100 mmol) dissolved in 250 cm^3 dry benzene, 10 cm^3 *DMF*, 4.1 g acetonitrile (100 mmol), and 4.8 g sodium hydride (60%) were added. The reaction mixture was refluxed for 4 h, then allowed to cool. The solid that precipitated was collected by filtration, washed with ether, and dried. The solid product was dissolved in water and the resulting solution was acidified with concentrated HCl until it became neutral (*pH* 7). The precipitated solid was collected by filtration, washed with water, and dried. Recrystallization of the crude product from *Et*OH/*DMF* gave 3-(3-methylthiazolo[3,2-*a*]benzimidazol-2-yl)-3-oxopropionitrile (**2**) as white powder in 58% yield, mp 210–212°C; IR (KBr): $\bar{\nu} = 2225$ (C≡N), 1681 (C=O), 1612 (C=N) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 3.04$ (s, 3H, CH_3), 4.18 (s, 2H, CH_2), 7.21–8.01 (m, 4H, ArH) ppm; MS (70 eV): $m/z = 256$ ($M^+ + 1$), 255 (M^+), 189 (100%), 118, 67.

3-Mercapto-2-(3-methylthiazolo[3,2-a]benzimidazol-2-oyl)-3-phenylamino-acrylonitrile (**4**, $C_{20}H_{14}N_4OS_2$)
To a stirred solution of 0.56 g KOH (10 mmol) in 20 cm^3 *DMF*, 2.55 g propionitrile derivative **2** (10 mmol) was added. After stirring for 30 min 1.35 g phenyl isothiocyanate (10 mmol) was added to the resulting mixture. Stirring was continued for 6 h, then poured over crushed ice containing HCl. The solid product so formed was filtered off, washed with water, dried, and finally crystallization from *Et*OH/*DMF* afforded compound **4** as yellow solid in 86% yield, mp 221–223°C; IR (KBr): $\bar{\nu} = 3206$ (NH), 2183 (C≡N), 1635 (C=O), 1558 (C=N) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 3.01$ (s, 3H, CH_3), 7.26–8.12 (m, 9H, ArH), 10.70 (s, 1H, NH, D_2O exchangeable), 12.50 (s, 1H, SH, D_2O exchangeable) ppm; MS (70 eV): $m/z = 391$ ($M^+ + 1$), 390 (M^+), 224 (100%), 188, 134, 77.

*Reaction of Thioacetanilide **4** with α-Chloroketones **5a, 5b**. General Procedure*
To 0.39 g **4** (1 mmol) dissolved in 20 cm^3 ethanol, the appropriate α-chloroacetylacetone (**5a**) or ethyl α-chloroacetoacetate (**5b**) (1 mmol), and 0.5 cm^3 triethylamine were added. The mixture was refluxed for 8 h, then allowed to cool. The formed solid was filtered off, washed with ethanol, and recrystallized from *DMF*/H_2O to afford the corresponding 1,3-thiazole derivatives **7a** and **7b**.

2-[5-Acetyl-4-methyl-3-phenyl-3H-thiazol-2-ylidene]-3-(3-methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**7a**, $C_{25}H_{18}N_4O_2S_2$)
This compound was produced as yellow crystals, yield 54%, mp 271–273°C; IR (KBr): $\bar{\nu} = 2195$ (C≡N), 1654, 1638 (2C=O), 1587 (C=N) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.24$ (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.81 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.81 (s, 3H, CH_3), 7.24–8.12 (m, 9H, ArH) ppm; MS (70 eV): $m/z = 471$ ($M^+ + 1$), 470 (M^+), 380 (100%), 225, 153, 118, 98.

2-[1-Cyano-2-(3-methylthiazolo[3,2-a]benzimidazol-2-yl)-2-oxoethylidene]-4-methyl-3-phenyl-2,3-dihydrothiazole-5-carboxylic acid ethyl ester (**7b**, $C_{26}H_{20}N_4O_3S_2$)
This compound was produced as yellow crystals, yield 57%, mp 241–242°C; IR (KBr): $\bar{\nu} = 2172$ (C≡N), 1703, 1655 (2C=O), 1598 (C=N) cm^{-1}; ^{1}H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.02$ (t, 3H, $J = 7.26$ Hz, CH_3), 2.98 (s, 3H, CH_3), 4.13 (q, 2H, $J = 7.26$ Hz, CH_2), 7.22–8.09 (m, 9H, ArH) ppm; MS (70 eV): $m/z = 501$ ($M^+ + 1$), 500 (M^+), 225 (100%), 188, 132, 68.

*Reaction of Thioacetanilide **4** with Hydrazonyl Chlorides **9a–9c***
This reaction was carried out by the same procedure described above using the appropriate hydrazonyl chlorides **9a–9c** instead of the α-chloroketones **5a** and **5b**. The solid product was recrystallized from *DMF*/H_2O to afford the corresponding 1,3,4-thiadizole derivatives **11a** and **11b**.

2-[5-Acetyl-3-phenyl-3H-1,3,4-thiadiazol-2-ylidene]-3-(3-methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**11a**, $C_{23}H_{15}N_5O_2S_2$)
Yellow crystals, yield 76%, mp 277–279°C; IR (KBr): $\bar{\nu}=$ 2205 (C≡N), 1695, 1636 (2C=O), 1580 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=2.43$ (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 7.13–7.95 (m, 9H, ArH) ppm; MS (70 eV): $m/z=458$ ($M^+ + 1$), 457 (M^+, 100%), 241 (7.4%), 77.

2-[5-Acetyl-3-(4-chlorophenyl)-3H-1,3,4-thiadiazol-2-ylidene]-3-(3-methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**11b**, $C_{23}H_{14}ClN_5O_2S_2$)
Yellow crystals, yield 72%, mp >300°C; IR (KBr): $\bar{\nu}=2191$ (C≡N), 1686, 1640 (2C=O), 1573 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=2.49$ (s, 3H, CH_3), 2.92 (s, 3H, CH_3), 7.27–7.06 (m, 8H, ArH) ppm; MS (70 eV): $m/z=493$ ($M^+ + 2$), 492 ($M^+ + 1$), 491 (M^+), 342 (100%), 243, 187, 113.

2-[5-Acetyl-3-(4-tolyl)-3H-1,3,4-thiadiazol-2-ylidene]-3-(3-methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**11c**, $C_{24}H_{17}N_5O_2S_2$)
Yellow needles, yield 78%, mp >300°C; IR (KBr): $\bar{\nu}=2199$ (C≡N), 1679, 1646 (2C=O), 1584 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=2.23$ (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 7.07–7.73 (m, 8H, ArH) ppm; MS (70 eV): $m/z=472$ ($M^+ + 1$), 471 (M^+, 100%), 346, 294, 146, 94, 51.

*Reaction of 3-(3-Methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxopropionitrile (**2**) with 3-Phenyl-1H-pyrazole-5-diazonium Chloride (**14a**) and 1H-1,2,4-Triazole-5-diazonium Nitrate (**14b**). General Procedure*
To 2.55 g **2** (10 mmol) dissolved in 30 cm^3 pyridine, the appropriate diazonium salt **14a** or **14b** (10 mmol) was added. The addition was carried out portion-wise with stirring at 0–5°C over a period of 30 min. After complete addition, the reaction mixture was stirred for further 4 h, then kept in an ice-chest for 12 h, and finally diluted with H_2O. The precipitated solid was collected by filtration, washed with water and dried. Recrystallization from *Et*OH/*DMF* afforded the corresponding hydrazone derivatives **15a** and **15b**.

3-(3-Methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxo-2-[(5-phenyl-2H-pyrazol-3-yl)hydrazono]propionitrile (**15a**, $C_{22}H_{15}N_7OS$)
Yellow solid, yield 61%, mp >300°C; IR (KBr): $\bar{\nu}=3325$, 3163 (2NH), 2218 (C≡N), 1660 (C=O), 1620 (C=N) cm^{-1}; MS (70 eV): $m/z=426$ ($M^+ + 1$), 425 (M^+, 100%), 302, 291, 77.

3-(3-Methylthiazolo[3,2-a]benzimidazol-2-yl)-3-oxo-2-[2H-1,2,4-triazol-3-yl)hydrazono] propionitrile (**15b**, $C_{15}H_{10}N_8OS$)
Yellow solid, yield 57%, mp >300°C; IR (KBr): $\bar{\nu}=3282$, 3150 (2NH), 2225 (C≡N), 1646 (C=O), 1616 (C=N) cm^{-1}; MS (70 eV): $m/z=352$ ($M^+ + 2$), 351 ($M^+ + 1$), 350 (M^+, 100%), 189, 91.

*Intramolecular Cyclization of the Heterocyclic Hydrazones **15a** and **15b**. General Procedure*
A solution of the appropriate hydrazone **15a** and **15b** (1 mmol) in 15 cm^3 pyridine was refluxed for 6 h, then left to cool. The solid that formed was filtered off, washed with ethanol, and dried. Recrystallization from *DMF*/H_2O afforded the corresponding fused heterocyclic **16a** and **16b**.

2-(4-Amino-7-phenylpyrazolo[5,1-c]-1,2,4-triazin-3-oyl)-3-methylthiazolo[3,2-a]benzimidazole (**16a**, $C_{22}H_{15}N_7OS$)
Brown solid, yield 67%, mp >300°C; IR (KBr): $\bar{\nu}=3130$, 3235 (NH_2), 1624 (C=O), 1558 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=3.10$ (s, 3H, CH_3), 6.57 (s, 1H, pyrazole), 7.21–8.03 (m, 9H, ArH), 9.06 (br, s, 2H, NH_2, D_2O exchangeable) ppm; MS (70 eV): $m/z=427$ ($M^+ + 2$), 426 ($M^+ + 1$), 425 (M^+, 100%), 324, 291, 187, 105, 77.

2-(4-Amino-1,2,4-triazolo[5,1-c]-1,2,4-triazin-3-oyl)-3-methylthiazolo[3,2-a]benzimidazole (**16b**, $C_{15}H_{10}N_8OS$)
Pale brown solid, yield 65%, mp >300°C; IR (KBr): $\bar{\nu}=$ 3233, 3105 (NH_2), 1612 (C=O), 1535 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=3.14$ (s, 3H, CH_3), 7.24–8.02 (m, 4H, ArH), 8.28 (s, 1H, triazole), 8.55 (br, s, 2H, NH_2, D_2O exchangeable) ppm; MS (70 eV): $m/z=352$ ($M^+ + 2$), 351 ($M^+ + 1$), 350 (M^+), 284, 188, 118 (100%), 105, 91, 72.

*Reaction of Thiazolo[3,2-a]benzimidazol-3(2H)-one (**18**) with Phenyl isothiocyanate*
To 0.06 g KOH (1 mmol) in 20 cm^3 *DMF*, thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**18**) (1 mmol) was added. After stirring for 30 min 0.135 g phenyl isothiocyanate (1 mmol) were added to the resulting mixture. Stirring was continued for 6 h, then the appropriate α-chloroketones **5a** and **5b** or hydrazonyl chlorides **9a**–**9e** (1 mmol) was added portion-wise over a period of 30 min. After the addition was complete, the reaction mixture was stirred for 12 h. The yellowish colored precipitate was filtered off, washed with H_2O, and dried. Crystallization from *Et*OH/*DMF* afforded the corresponding 1,3-thiazole derivatives **20a** and **20b**, and 1,3,4-thiadiazole derivatives **21a**–**21e**.

2-[5-Acetyl-4-methyl-3-phenyl-3H-thiazol-2-ylidene]-3-oxothiazolo[3,2-a]benzimidazole (**20a**, $C_{21}H_{15}N_3O_2S_2$)
Yellow crystals, yield 55%, mp >300°C; IR (KBr): $\bar{\nu}=1666$, 1638 (2C=O), 1612 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta=2.22$ (s, 3H, CH_3), 3.16 (s, 3H, CH_3), 7.23–8.01 (m, 9H, ArH) ppm; MS (70 eV): $m/z=407$ ($M^+ + 2$), 406 ($M^+ + 1$), 405 (M^+, 100%), 365, 244, 188, 164, 107, 77.

4-Methyl-2-(3-oxothiazolo[3,2-a]benzimidazol-2-ylidene)-3-phenyl-2,3-dihydrothiazole-5-carboxylic acid ethyl ester (**20b**, $C_{22}H_{17}N_3O_3S_2$)
Yellow needles, yield 59%, mp >300°C; IR (KBr): $\bar{\nu}=$ 1684, 1649 (2C=O), 1607 (C=N) cm^{-1}; ^1H NMR (300 MHz,

DMSO-d_6): $\delta = 1.32$ (t, 3H, $J = 7.25$ Hz, CH_3), 2.18 (s, 3H, CH_3), 4.31 (q, 2H, $J = 7.25$ Hz, CH_2), 7.26–7.99 (m, 9H, ArH) ppm; MS (70 eV): $m/z = 437$ ($M^+ + 2$), 436 ($M^+ + 1$), 435 (M^+, 100%), 407, 363, 258, 231, 187, 77.

2-(5-Acetyl-3-phenyl-3H-1,3,4-thiadiazol-2-ylidene)-3-oxothiazolo[3,2-a]benzimidazole (**21a**, $C_{19}H_{12}N_4O_2S_2$)
Yellow needles, yield 56%, mp 290–292°C; IR (KBr): $\bar{\nu} = 1689$, 1663 (2C=O), 1609 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.34$ (s, 3H, CH_3), 7.28–8.00 (m, 9H, ArH) ppm; MS (70 eV): $m/z = 394$ ($M^+ + 2$), 393 ($M^+ + 1$), 392 (M^+, 100%), 291, 243, 205, 143, 103, 77.

2-[5-Acetyl-3-(4-chlorophenyl)-3H-1,3,4-thiadiazol-2-ylidene]-3-oxothiazolo[3,2-a]benzimidazole
(**21b**, $C_{19}H_{11}ClN_4O_2S_2$)
Yellow needles, yield 60%, mp 227–229°C; IR (KBr): $\bar{\nu} =$ 1693, 1655 (2C=O), 1593 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.34$ (s, 3H, CH_3), 7.27–7.81 (m, 8H, ArH) ppm; MS (70 eV): $m/z = 428$ ($M^+ + 2$), 427 ($M^+ + 1$), 426 (M^+, 100%), 316, 283, 225, 146, 109.

2-[5-Acetyl-3-(4-tolyl)-3H-1,3,4-thiadiazol-2-ylidene]-3-oxothiazolo[3,2-a]benzimidazole (**21c**, $C_{20}H_{14}N_4O_2S_2$)
Yellow needles, yield 53%, mp 280–282°C; IR (KBr): $\bar{\nu} =$ 1703, 1648 (2C=O), 1602 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 2.30$ (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 7.24–7.78 (m, 8H, ArH) ppm; MS (70 eV): $m/z = 407$ ($M^+ + 1$), 406 (M^+, 100%), 299, 196, 109.

5-(3-Oxothiazolo[3,2-a]benzimidazol-2-ylidene)-4-(4-tolyl)-4,5-dihydro-1,3,4-thiadiazole-2-carboxylic acid ethyl ester
(**21d**, $C_{21}H_{16}N_4O_3S_2$)
Yellow crystals, yield 64%, mp 220–222°C; IR (KBr): $\bar{\nu} =$ 1741, 1683 (2C=O), 1593 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 1.26$ (t, 3H, $J = 7.26$ Hz, CH_3), 2.33 (s, 3H, CH_3), 4.22 (q, 2H, $J = 7.26$ Hz, CH_2), 7.19–7.77 (m, 8H, ArH) ppm; MS (70 eV): $m/z = 437$ ($M^+ + 1$), 436 (M^+), 377 (100%), 324, 164, 105.

2-(Phenylcarboxamido)-4-(4-chlorophenyl)-5-(3-oxothiazolo[3,2-a]benzimidazol-2-ylidene)-4,5-dihydro-1,3,4-thiadiazole (**21e**, $C_{24}H_{14}ClN_5O_2S_2$)
Pale yellow solid, yield 62% mp >300°C; IR (KBr): $\bar{\nu} =$ 3165 (NH), 1692, 1638 (C=O), 1577 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 7.21$–7.94 (m, 14H, ArH), 8.64 (br. s, 1H, NH, D_2O exchangeable) ppm; MS (70 eV): $m/z = 507$ ($M^+ + 4$), 505 ($M^+ + 2$), 504 ($M^+ + 1$), 503 (M^+), 355 (100%), 218, 151, 86.

Reaction of Thiazolo[3,2-a]benzimidazol-3(2H)-one (***18***) *with Diazonium Salts of Heterocyclic Amines* ***14a*** *and* ***14b***. *General Procedure*
This procedure is similar to the method that was used in synthesis of compounds **15a** and **15b** above using thiazolone derivative **18** instead of compound **2**. The corresponding hydrazones **22a** and **22b** were crystallized from *DMF*/H_2O.

2-[(5-Phenyl-2H-pyrazol-3-yl)hydrazono]-3-oxothiazolo-[3,2-a]benzimidazole (**22a**, $C_{18}H_{12}N_6OS$)
Yellow solid, yield 64%, mp >300°C; IR (KBr): $\bar{\nu} = 3208$, 3112 (2NH), 1701 (C=O), 1616 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 5.65$ (s, 1H, pyrazole), 7.31–7.93 (m, 9H, ArH), 8.65 (s, 1H, NH, D_2O exchangeable), 10.44 (s, 1H, NH, D_2O exchangeable) ppm; MS (70 eV): $m/z = 363$ ($M^+ + 3$), 362 ($M^+ + 2$), 361 ($M^+ + 1$), 360 (M^+, 100%), 318, 176, 160, 148, 77.

2-[(2H-1,2,4-Triazol-3-yl)hydrazono]-3-oxothiazolo[3,2-a]-benzimidazole (**22b**, $C_{11}H_7N_7OS$)
Yellow solid, yield 59%, mp >300°C; IR (KBr): $\bar{\nu} = 3233$, 3105 (2NH), 1705 (C=O), 1620 (C=N) cm^{-1}; ^1H NMR (300 MHz, *DMSO*-d_6): $\delta = 7.15$ (s, 1H, NH, D_2O exchangeable), 7.31–7.94 (m, 4H, ArH), 8.27 (s, 1H, triazole), 8.80 (s, 1H, NH, D_2O exchangeable) ppm; MS (70 eV): $m/z = 287$ ($M^+ + 2$), 286 ($M^+ + 1$), 285 (M^+, 100%), 257, 176, 160, 148, 90.

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