# Reactions with Hydrazonoyl Halides 62: Synthesis and Antimicrobial Evaluation of Some New Imidazo [1,2-*a*]pyrimidine, Imidazo [1,2-*a*]pyridine, Imdazo [1,2-*b*]pyrazole, and Quinoxaline Derivatives

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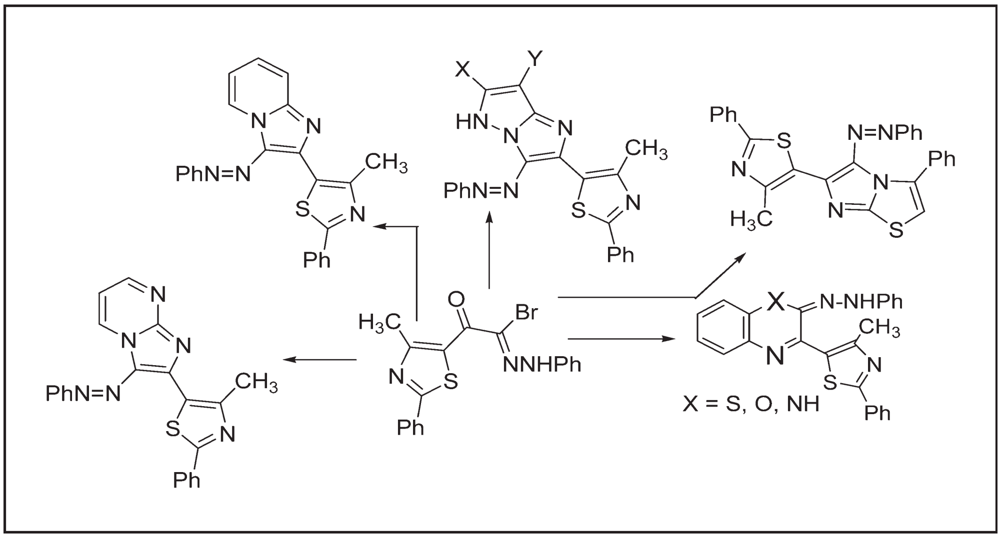


3-Arylazo-2-(4-methyl-2-phenylthiazol-5-yl)imidazo[1,2-*a*]pyrimidine, 2-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-3-phenylazoimidazo[1,2-*a*]pyridine, 3-arylazo-2-(4-methyl-2-phenylthiazol-5-yl)-6-phenyl-5*H*-imidazo[1,2-*b*]pyrazole, 6-(4-methyl-2-phenyl-thiazol-5-yl)-5-phenylazo3-phenyl-imidazo[2,1-*b*]thiazole, 3-(4-methyl-2-phenylthiazol-5-yl)-2-phenylhydrazino-(1*H*)-quinoxaline, 3-(4-methyl-2-phenylthiazol-5-yl)- 2-phenylazoquinoxaline, 3-(4-methyl-2-phenylthiazol-5-yl)-2-phenylhydrazinobenzo-[1,4] thiazine, 3-(4-methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazinobenzo[1,4]oxazine, and 3-(4-methyl-2-phenyl-thiazol-5-yl)-2-phenylazo-1*H*-pyrido[2,3-*b*]pyrazine derivatives were synthesized *via* reaction of 2-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-2-oxo-*N*-arylethanehydrazonoyl bromide with each of 2-aminopyrimidine, 2-aminopyridine, 3-aminopyrazoles, 2-amino-4-phenylthiazole, *o*-phenylenediamine, *o*-aminothiophenol, *o*-aminophenol, or 2, 3-diaminopyridine, respectively. All structures of the newly synthesized compounds were elucidated by elemental analysis, spectral data, and alternative synthetic route whenever possible. The entire newly synthesized compounds are tested toward different microorganisms.

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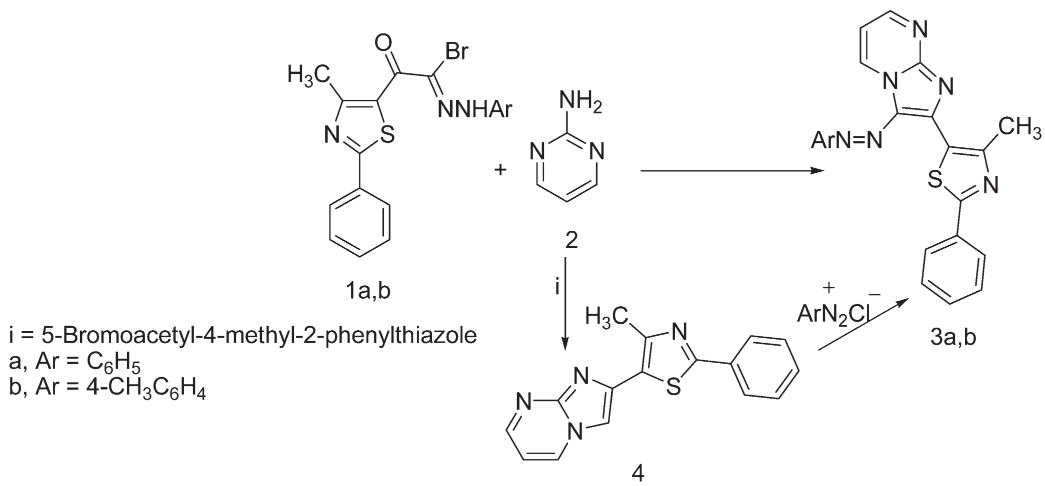
## INTRODUCTION

Our continuous interest in the chemistry of hydrazonoyl halides [1–9] originates from our persistent trials to obtain pyridines, pyrimidines, pyridazines, and their analogs. The importance of such compounds lies in their diverse pharmaceutical activities, namely antibacterial [10,11], antidiabetic [12], anti-HIV [13], antiviral [14,15], and analgesic activities. We report herein the reactivity of 2-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-2-oxo-*N*-arylethanehydrazonoyl bromides toward 2-aminopyrimidine, 2-aminopyridine, 3-aminopyrazoles, 2-amino-4-phenylthiazole, *o*-phenylenediamine, *o*-aminothiophenol, *o*-aminophenol, and 2,3-diaminopyridine.

## RESULTS AND DISCUSSION

Treatment of 2-aminopyrimidine (**2**) with the appropriate 2-(4-methyl-2-phenylthiazol-5-yl)-2-oxo-*N*-arylethanehydrazonoyl bromide (**1a**, **b**) in ethanol gave 3-arylazo-2-(4-methyl-2-phenylthiazol-5-yl)imidazo[1,2-*a*] pyrimidine (**3a**, **b**) in a good yield (Scheme 1). Structure **3** was elucidated by elemental analysis, spectral

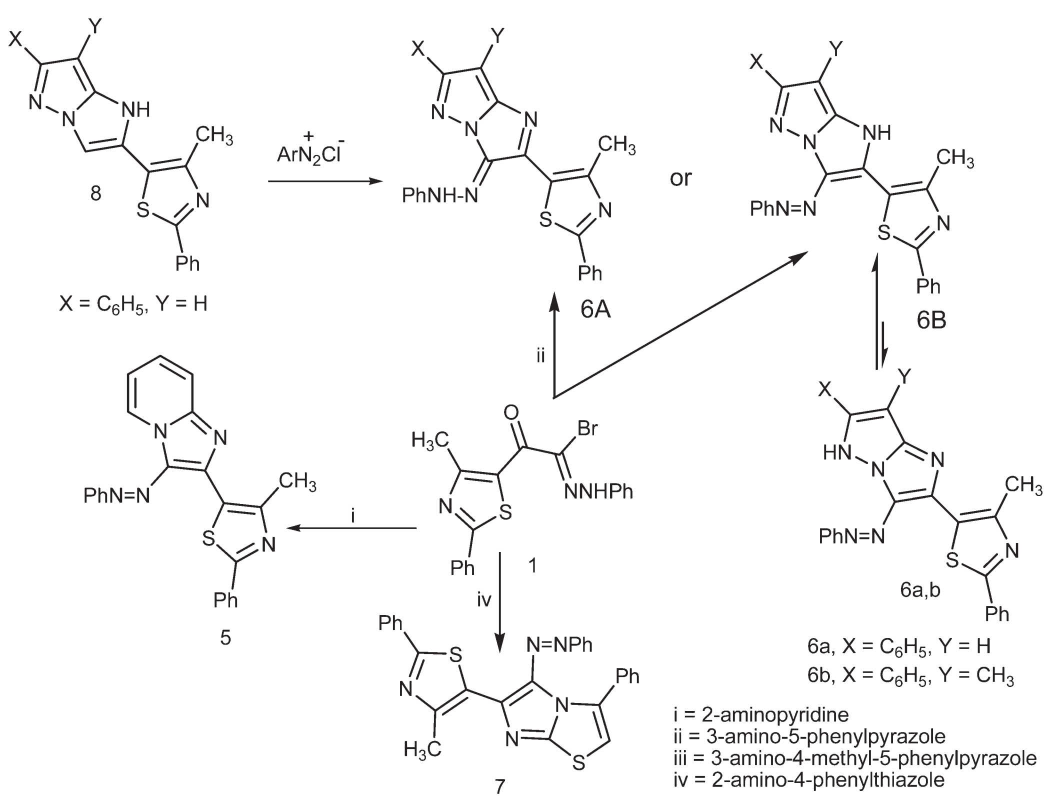
**Scheme 1**



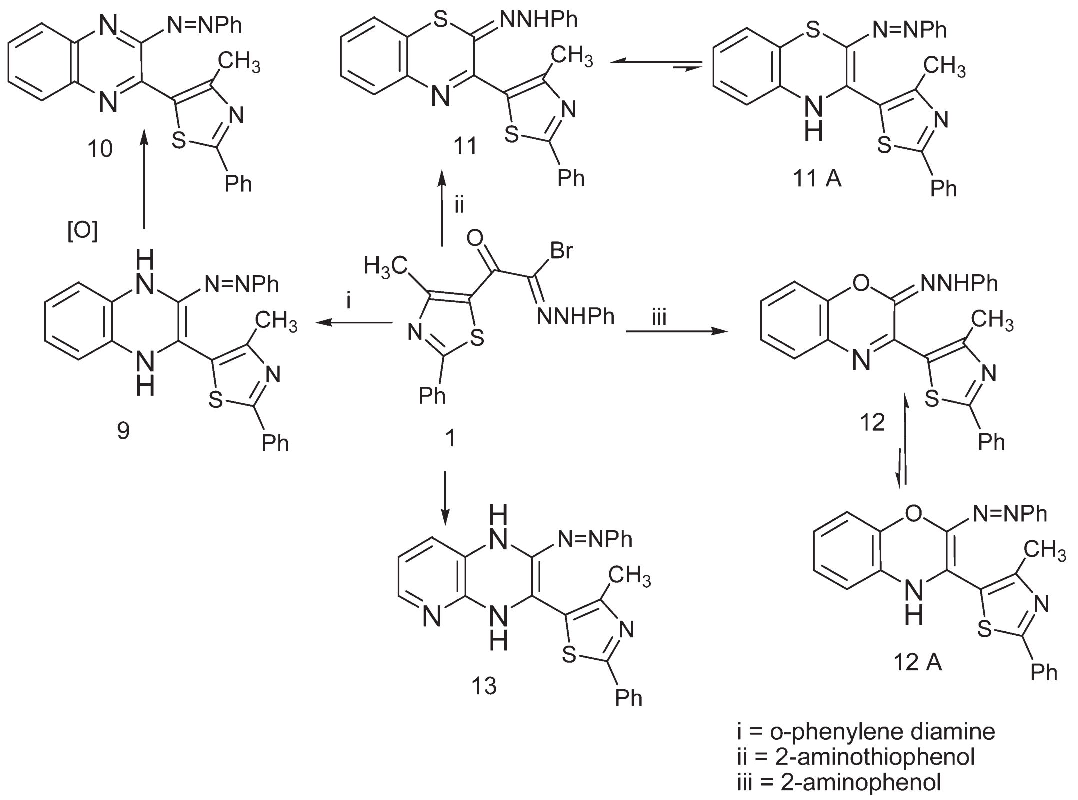

data, and alternative synthesis. [1]H-NMR spectrum of **3a** showed signals at δ = 2.46 (s, 3H, 4-methylthiazole), 6.86–6.70 (t, 3H, pyrimidine H-5), 7.36–7.37 (d, 2H, ArH), 7.62–7.67 (m, 3H, ArH), 7.70–7.81 (m, 3H, ArH), 8.53–8.54 (d, 1H, pyrimidine H-4), 8.65–8.66 (d, 1H, pyrimidine H-6). Its IR ($cm^{-1}$) spectrum revealed bands at 3060, 2923 (CH), 1645 (C=N), 1599 (C=C), 1321 ($CH_3$), and no band between 1800 and 1650 $cm^{-1}$ attributed the absence of carbonyl group. Thus, treatment of 2-(4-methyl-2-phenylthiazol-5-yl)imidazo[1,2-*a*]pyrimidine (**4**), which was synthesized *via* reaction of 2-aminopyrimidine with 2-bromo-1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)ethanone, with the appropriate arenediazonium chloride in ethanolic sodium acetate gave a product identical in all aspects (mp., mixed mp., and spectra) with **3a** and **3b**, respectively.

Analogously, the appropriate 2-aminopyridine, 3-amino-5-phenylpyrazole, 3-amino-4-methyl-5-phenylpyrazole, or 2-

**Scheme 2**



**Scheme 3**




amino-4-phenylthiazole was reacted with 2-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-2-oxo-*N*-phenylethanehydrazonoyl bromide (**1a**) in boiling ethanol gave 3-phenylazo-2-(4-methyl-2-phenylthiazol-5-yl)imidazo[1,2-*a*]pyridine (**5**), 3-phenylazo-2-(4-methyl-2-phenyl-thiazol-5-yl)-6-phenyl-5*H*-imidazo [1,2-*b*]pyrazole (**6a**), 2-(4-methyl-2-phenyl-thiazol-5-yl)-5-methyl-6-phenyl-3-phenylazo-5*H*-imidazo[1,2-*b*]pyrazole (**6b**), and 6-(4-methyl-2-phenyl-thiazol-5-yl)-5-phenylazo3-phenylimidazo[2,1-*b*]thiazole (**7**), respectively (Scheme 2).

Structures **5–7** were elucidated by elemental analyses, spectral data, and alternative synthetic route. Thus, treatment of 2-(4-methyl-2-phenylthiazol-5-yl)-6-phenyl-1*H*-imidazo[1,2-*b*]pyrazole (**8**), which was synthesized from 2-bromo-1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)ethanone with 3(5)-amino-5(3)-phenylpyrazole in boiling ethanol, with benzenediazonium chloride in ethanolic sodium acetate solution gave product identical in all aspects (mp., mixed mp., and spectra) with **6a**.

Attention was then turned to the tautomeric structure of the product **6a** as they can exist in the tautomeric hydrazone form **A** or phenylazoenamine form **B** (Scheme 2). Unfortunately, their spectra (IR and $^1$H-NMR) were not of too much help to decide the actual tautomeric form of the compound in question. This problem was solved by examining UV spectrum and M.O. calculation. The electronic absorption of compound **6a** in ethanol was also compatible with the azo form **B**. The product exhibits in ethanol two bands at $\lambda_{nm} = 315$ (log $\varepsilon$ = 3.3416) and 466 (log $\varepsilon$ = 4.1734). Such an absorption pattern is similar to that of typical azo-form [16,17]. M.O. calculation using HyperChem semi-empirical method AM1, for structure **6A**, showed $E = -6034.948$ kcal/mol and heat formation = 365.522 kcal/mol, for structure **6B** showed $E = -6096.498$ kcal/mol and heat formation = 303.972 kcal/mol, and for structure **6a**, $E = -6113.009$ kcal/mol and heat formation = 287.460 kcal/mol. These results indicted that the structure **6a** was more compatible tautomeric form.

Treatment of **1a** with *o*-phenylenediamine in boiling ethanol under reflux gave 3-(4-methyl-2-phenylthiazol-5-yl)-2-phenylhydrazino-(1*H*)-quinoxaline (**9**). Structure **9** was confirmed by elemental analysis, spectral data, and its oxidation with hydrogen peroxide in acetic acid to afford 3-(4-methyl-2-phenyl-thiazol-5-yl)-2-phenylazoquinoxaline (**10**) (Scheme 3).

Analogously, treatment of **1a** with the appropriate of each of 2-aminothiophenol, 2-aminophenol, or 2,3-diaminopyridine gave 3-(4-methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazinobenzo[1,4]thiazine (**11**), 3-(4-methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazinobenzo[1,4]oxazine (**12**), and 1-(1,4-dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-2-phenylazopyrido[2,3-*b*]pyrazine (**13**), respectively. Structures **11A** and **12A** were ruled out according to UV spectra. Thus, UV spectra of **11** and **12** exhibit

**Table 1**

Response of various microorganisms to some synthesized compounds *in vitro* culture.

| Comp no. | *S. aureus* | *B. subitis* | *E. coli* | *Ps. aeruginosa* | *C. albicans* |
|---|---|---|---|---|---|
| **3a** | ≥1600 | ≥800 | ≥800 | ≥400 | ≥400 |
| **3b** | ≥1600 | ≥800 | ≥800 | ≥800 | ≥400 |
| **4** | ≥1600 | ≥400 | ≥800 | ≥800 | ≥800 |
| **5** | ≥800 | ≥800 | ≥800 | ≥400 | ≥800 |
| **6a** | ≥800 | ≥800 | ≥400 | ≥800 | >800 |
| **6b** | ≥1600 | ≥800 | ≥800 | ≥400 | ≥400 |
| **7** | ≥1600 | ≥400 | ≥800 | ≥800 | ≥800 |
| **8** | ≥1600 | ≥800 | ≥800 | ≥800 | ≥400 |
| **9** | ≥1600 | ≥400 | ≥800 | ≥400 | ≥800 |
| **10** | ≥1600 | ≥400 | ≥400 | ≥800 | ≥800 |
| **11** | ≥1600 | ≥800 | ≥800 | ≥800 | ≥400 |
| **12** | ≥1600 | ≥400 | ≥400 | ≥400 | ≥800 |
| **13** | ≥1600 | ≥400 | ≥800 | ≥400 | ≥800 |
| **DMSO** | >1600 | >400 | >800 | >800 | >400 |
| Ciprofloxacin | ≤100 | ≤25 | ≤25 | 400 | ≥800 |
| Triflucan | ≥800 | ≥800 | ≥800 | ≥800 | ≤25 |

$\lambda_{max}$ = 357 (log ε = 4.022) and 345 (log ε = 2.716), whereas spectrum of **13** exhibits two bands at $\lambda_{max}$ = 345 (log ε = 4.0177) and 466 (log ε = 4.6467).

**Antimicrobial screening.** Ten selected compounds were screened for their antimicrobial activity using five selected standard isolates, which have been chosen as representative examples of different types of microorganisms as follows: Gram-positive both nonsporulated bacteria as *Staphylococus aureus* and sporulated as *Bacillus subtilis*, Gram-negative as *Escherichia coli* and *Pseudomonas aeruginosa*, and a fungus as *Candida albicans*.

***Method: Agar dilution technique.*** The appropriate volume of membrane filtered stock solution of 0.05 g/5 mL of each compound was prepared by the twofold dilution method to obtain the concentrations: 400, 200, 100, 50, and 25 μg/mL [18]. The volumes were added to the molten LB agar (about 50°C). After mixing, the media were allowed to harden and dry by placing in an incubator at 37°C for 10 min. Plates containing serial dilutions of each compound were inoculated with a sterile multi-inoculator onto the surface of the agar medium so that the final inoculum of each isolate on the agar surface was in the order of $10^4$–$10^5$ CFU/spot. Ciprofloxacin and triflucan were used as positive controls and the solvent, dimethylsulfoxide (DMSO), as negative control. Minimum inhibitory concentrations (MICs) were read after 18 h incubation at 37°C for bacteria and 25°C for fungus. The MIC is reported as the lowest concentration of the compound that prevents the growth of visible colonies. The obtained MICs of 10 representative examples are presented in Table 1.

As shown in Table 1, there is variability in the susceptibilities of the different organisms to the different compounds. *S. aureus* was the most resistant organism. Some compounds showed antibacterial activity, whereas others showed antifungal activity.

## EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FTIR 8201 PC Spectrophotometer. $^1$H-NMR and $^{13}$C-NMR spectra were recorded in $CDCl_3$ solution on a Varian Mercury 300 MHz spectrometer, and chemical shifts are expressed as δ using TMS as an internal reference. The ultraviolet spectrum was recorded using Shimadzu UV–vis 1601 PC double beam spectrophotometer. Mass spectra were recorded on a GC-MS QP1000. Elemental analyses were carried out at the Micro analytical center of Cairo University. The hydrazidoyl bromides **1**(**a**, **b**) were prepared as previously reported [19].

**General procedure for the synthesis of (3a, b), (5), (6a, b), (7), (9), (11), (12), and (13).** A mixture of the appropriate hydrazonoyl bromide **1a**, **b** (5 mmol), the appropriate 2-aminopyrimidine, 2-aminopyridine, 3-amino-5-phenylpyrazole, 3-amino-4-methyl-5-phenylpyrazole, 2-amino-4-phenylthiazole, *o*-phenylenediamine, 2-aminothiophenol, 2-aminophenol or 2,3-diaminopyridine (6 mmol), and triethylamine (0.5 g, 0.75 mL, 5 mmol) in ethanol (25 mL) was heated under reflux for 3 h and then cooled. The solid precipitated was collected, washed with water, and then crystallized from the appropriate solvent to give **3**(**a**, **b**), **5**, **6**(**a**, **b**), **7**, **8**, **11**–**13**, respectively.

***3-Phenylazo-2-(4-methyl-2-phenylthiazol-5-yl)imidazo[1,2-*a*] pyrimidine (3a).*** This compound was obtained as violet crystals (DMF-EtOH), mp > 300°C, yield (69%); IR (cm$^{-1}$): 3060, 2923 (CH), 1623 (C=N), 1599 (C=C), 1321 ($CH_3$). $^1$H-NMR $(CD_3)_2SO$: δ = 2.46 (s, 3H, 4-methylthiazole), 7.07–7.13 (t, 3H, *J* = 5.6 Hz, pyrimidine H-5), 7.49–7.51 (d, 2H, *J* = 4.0 Hz, ArH), 7.94–7.97 (m, 3H, ArH), 8.27 (m, 3H, ArH), 8.56–8.58 (d, 1H, *J* = 4.0 Hz, pyrimidine H-4), 8.95–

8.98 (d, 1H, $J$ = 4.0 Hz, pyrimidine H-6). $^{13}$C-NMR: δ = 14.71 ($CH_3$), 110.64, 156.19, 160.11 (thiazole), 113.45, 120.45, 145.78 (imidazole), 122.04, 125.11, 127.31, 129.21, 130.12, 131.18, 135.20, 154.68 (aromatic carbons), 108.12, 134.45, 152.67 (pyrimidine). Anal. Calcd. for $C_{22}H_{16}N_6S$ (396.46): C, 66.72; H, 4.07; N, 21.20; S, 8.09. Found: C, 66.60; H, 4.00; N, 21.40; S, 8.20.

***3-[4-Methylphenylazo)-2-(4-methyl-2-phenylthiazol-5-yl)imidazo [1,2-*a*]pyrimidine (3b).*** This compound was obtained as red crystals (AcOH), mp 272–74°C, yield (66%); IR ($cm^{-1}$): 3060, 2968 (CH), 1625 (C=N), 1599 (C=C), 1321 ($CH_3$). $^1$H-NMR $(CD_3)_2SO$: δ = 2.46 (s, 3H, 4-methylthiazole), 2.53 (s, 3H, 4-$CH_3C_6H_4$), 6.86–6.70 (t, 3H, pyrimidine H-5), 7.36–7.37 (d, 2H, ArH), 7.62–7.67 (m, 3H, ArH), 7.70–7.81 (m, 2H, ArH), 8.53–8.54 (d, 1H, pyrimidine H-4), 8.65–8.66 (d, 1H, pyrimidine H-6). Anal. Calcd. for $C_{23}H_{18}N_6S$ (410.49): C, 67.30; H, 4.42; N, 20.47; S, 7.81. Found: C, 67.55; H, 4.53; N, 20.12; S, 7.68.

***2-(4-Methyl-2-phenyl-1,3-thiazol-5-yl)-3-phenylazoimidazo [1,2-a]pyridine (5).*** This compound was obtained as violet crystals (DMF/EtOH), mp 223–26°C, yield (55%); $^1$H-NMR $(CD_3)_2SO$: δ = 2.46 (s, 3H, 4-methylthiazole), 6.85 (t, 1H, pyridine H-5), 7.15 (d, 1H, pyridine H-3), 7.37 (t, 1H, pyridine H-4), 7.62–7.84 (m, 10 H, ArH), 8.78 (d, 1H, pyridine H-6). $^{13}$C-NMR: δ = 14.85 ($CH_3$), 111.21, 155.71, 160.32 (thiazole), 111.62, 121.45, 144.10 (imidazole), 122.10, 125.00, 126.58, 128.84, 130.54, 131.10, 136.24, 154.44 (aromatic carbon), 112.12, 117.89, 123.77, 126.28 (pyridine). Anal. Calcd. for $C_{23}H_{17}N_5S$ (395.48): C, 69.85; H, 4.33; N, 17.71; S, 8.11. Found: C, 69.70; H, 4.09; N, 17.55; S, 8.00.

***3-Phenylazo-2-(4-methyl-2-phenylthiazol-5-yl)-6-phenyl-5*H*-imidazo[1,2-*b*]pyrazole (6a).*** This compound was obtained as red crystals (DMF/EtOH), mp > 300°C, yield (89%); IR ($cm^{-1}$): 3424 (NH), 1633 (C=N), 1607 (C=C). $^1$H-NMR: δ = 2.46 (s, 3H, 4-methylthiazole), 6.19 (s, 1H, pyrazole H-4), 7.36–7.91 (m, 16 H, ArH and NH proton). Anal. Calcd. for $C_{27}H_{20}N_6S$ (460.55): C, 70.41; H, 4.38; N, 18.25; S, 6.96. Found: C, 70.40; H, 4.02; N, 18.41; S, 7.02.

***2-(4-Methyl-2-phenyl-thiazol-5-yl)-5-methyl-6-phenyl-3-phenylazo-5*H*-imidazo[1,2-*b*]pyrazole (6b).*** This compound was obtained as red crystals (DMF/EtOH), mp > 300°C, yield (67%); $^1$H-NMR: δ = 2.46 (s, 3H, 4-methylthiazole), 2.50 (s, 3H, 4-$CH_3C_6H_4$), 6.15 (s, 1H, pyrazole H-4), 7.36–8.10 (m, 14H, ArH), 8.42 (s, br., 1H, NH). $^{13}$C-NMR: δ = 14.45 ($CH_3$), 21.21 ($CH_3$), 83.89, 142.67, 159.14 (pyrazole), 108.00, 122.45 (imidazole, 114.23, 160.45, 163.57 (thiazole), 122.12, 122.57, 128.42, 129.23, 130.12, 134.45, 139.57, 153.38 (aromatic carbons). Anal. Calcd. for $C_{28}H_{22}N_6S$ (474.58): C, 70.86; H, 4.67; N, 17.71; S, 6.76. Found: C, 71.14; H, 4.73; N, 17.66; S, 6.66.

***6-(4-Methyl-2-phenyl-thiazol-5-yl)-5-phenylazo3-phenylimidazo[2,1-*b*]thiazole (7).*** This compound was obtained as red crystals (AcOH), mp > 300°C, yield (80%); $^1$H-NMR: δ = 2.46 (s, 3H, 4-methylthiazole), 7.24 (s, 1H, thiazole H-5), 7.36–7.97 (m, 15H, ArH), $^{13}$C-NMR: δ = 13.57 ($CH_3$), 14.57 ($CH_3$), 103.25, 111.23, 126.32, 158.74, 159.62, 145.43 (thiazole rings), 114.25, 120.85 (imidazole), 122.12, 125.42, 127.61, 128.08, 130.24, 131.75, 135.28, 155.35 (aromatic carbons). Anal. Calcd. for $C_{27}H_{19}N_5S_2$ (477.60): C, 67.90; H, 4.01; N, 14.66; S, 13.43. Found: C, 67.80; H, 4.96; N, 14.30; S, 13.07.

***3-(4-Methyl-2-phenylthiazol-5-yl)-2-phenylazo-(1*H*)-quinoxaline (9).*** This compound was obtained as orange crystals (EtOH), mp 240–42°C, yield (80%); IR ($cm^{-1}$): 3399 (NH), 3047, 2964 (CH), 1632 (C=N), 1605 (C=C). $^1$H-NMR: δ = 2.57 (s, 3H, 4-methylthiazole), 7.08–7.89 (m, 14H, ArH), 8.92 (s, br., 1H, NH), 9.22 (s, br., 1H, NH). Anal. Calcd. for $C_{24}H_{19}N_5S$ (409.51): C, 70.93; H, 4.68; N, 17.10; S, 7.83. Found: C, 70.50; H, 4.56; N, 17.39; S, 7.70.

***3-(4-Methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazinobenzo [1,4]thiazine (11).*** This compound was obtained as shiny green crystals (DMF/EtOH), mp 280–82°C, yield (89%); IR: 3422 (NH), 3058, 2982 (CH), 1655 (C=N), 1602 (C=C). $^1$H-NMR: δ = 2.62 (s, 3H, 4-methylthiazole), 7.18–8.29 (m, 14H, ArH), 13.09 (s, br., 1H, NH). MS: 426 (4.98%), 384 (11%), 360 (16%), 354 (59%), 319 (17.8%), 302 (38%), 372 (18%), 270 (100%), 226 (15%), 212 (22%), 196 (12%), 148 (54.9%), 122 (27%), 94 (23%), 63 (20%). Anal. Calcd. for $C_{24}H_{18}N_4S_2$ (426.56): C, 67.58; H, 4.25; N, 13.13; S, 15.03. Found: C, 67.90; H, 4.55; N, 13.33; S, 15.21.

***3-(4-Methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazinobenzo [1,4]oxazine (12).*** This compound was obtained as yellow crystals (DMF/EtOH), mp 202–204°C, yield (72%); IR ($cm^{-1}$): 3422 (NH), 2924 (CH), 1634 (C=N), 1602 (C=C). $^1$H-NMR: δ = 2.59 (s, 3H, 4-methylthiazole), 7.18–8.29 (m, 14H, ArH), 9.32 (s, br., 1H, NH). $^{13}$C-NMR: δ = 15.57 ($CH_3$), 112.32, 158.85, 162.10 (thiazole), 129.23, 139.53, 144.71, 150.82 (oxazine), 115.24, 118.35, 119.85, 127.45, 128.68, 129.28, 130.30, 130.45, 13.90, 133.72, 143.68 (aromatic carbons). Anal. Calcd. for $C_{24}H_{18}N_4OS$ (410.49): C, 70.22; H, 4.42; N, 13.56; S, 7.81. Found: C, 70.44; H, 4.56; N, 13.72; S, 7.65.

***3-(4-Methyl-2-phenyl-thiazol-5-yl)-2-phenylhydrazino-1*H*-pyrido [2,3-*b*]pyrazine (13).*** This compound was obtained as red crystals (DMF/EtOH), mp > 300°C, yield (70%); IR ($cm^{-1}$): 3382 (NH), 3060, 2969 (CH), 1632 (C=N), 1595 (C=C). $^1$H-NMR: δ = 2.56 (s, 3H, 4-methylthiazole), 7.18–8.35 (m, 13H, ArH), 10.51 (s, br., 2H, NH). MS: 409 (4.9%), 308 (22.8%), 228 (10.5%), 213 (22.4%), 205 (17.8%), 183 (16%), 182 (100%), 179 (14.6%), 153 (16.5%), 140 (77%), 125 (14%), 124 (20%). Anal. Calcd. for $C_{23}H_{18}N_6S$ (410.49): C, 67.30; H, 4.42; N, 20.47; S, 7.81. Found: C, 67.11; H, 4.10; N, 120.12; S, 7.55.

**General procedure for the synthesis of 4 and 8.** A mixture of 2-bromo-1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)ethanone [20] (1.48 g, 5 mmol) and 2-aminopyrimidine (0.48 g, 6 mmol) or 2-amino-4-phenylthiazole (0.56 g, 6 mmol) in ethanol (25 mL) was heated under reflux for 3–4 h. The resulting solid was neutralized with sodium bicarbonate solution, collected by filtration, and then was crystallized from ethanol to give **4** and **8**, respectively.

***2-(4-Methyl-2-phenylthiazol-5-yl)imidazo[1,2-a]pyrimidine (4).*** This compound was obtained as yellow crystals (EtOH), mp 223–26°C, yield (62%); IR ($cm^{-1}$): 3060.3, 2928 (CH), 1655 (C=N), 1599 (C=C), 1369 ($CH_3$). $^1$H-NMR: δ = 2.46 (s, 3H, 4-methylthiazole), 6.91 (d, 1H, pyrimidine H-5), 7.62 (t, 2H, ArH), 7.68 (t, 1H, ArH), 7.76 (d, 2H, ArH), 7.91 (s, 1H, imidazole H-4), 8.50 (d, 1H, pyrimidine H-6), 8.57 (d, 1H, pyrimidine H-4). $^{13}$C-NMR: δ = 13.85 ($CH_3$), 114.21, 150.71, 160.82 (thiazole), 111.62, 124.45, 149.10 (imidazole), 125.00, 126.58, 131.10, 136.24 (phenyl), 110.12, 135.77, 151.28 (pyrimidine). MS: 293 (8.8%), 292 (30%), 202 (19.9%), 203 (10%), 188 (22.9), 144 (15.9), 92 (7.1%), 66 (10.6%). Anal. Calcd. for $C_{16}H_{12}N_4S$ (292.36): C, 65.73; H, 4.14; N, 19.16; S, 10.97. Found: C, 65.90; H, 4.33; N, 19.02; S, 10.70.

***2-(4-Methyl-2-phenylthiazol-5-yl)-6-phenyl-1*H*-imidazo[1,2-*b*]pyrazole (8).*** This compound was obtained as orange crystals (DMF), mp 244–47°C, yield (60%); $^{1}$H-NMR $(CD_3)_2SO$: $\delta$ = 2.46 (s, 3H, 4-methylthiazole), 6.15 (s, 1H, pyrazole H-4), 7.40 (s, 1H, imidazole H-4), 7.45–7.92 (m, 10H, ArH), 8.42 (s, br., 1H, NH). Anal. Calcd. for $C_{21}H_{16}N_4S$ (356.44): C, 70.67; H, 4.52; N, 15.72; S, 9.00. Found: C, 70.55; H, 4.31; N, 15.50; S, 9.07.

***Alternative synthesis of 3a, b and 6a.*** A solution of the appropriate arenediazonium chloride (10 mmol) was added dropwise to a stirred solution of the appropriate reactant (**4**, **8**) (10 mmol) in ethanol (50 mL) containing sodium acetate trihydrate (1.3g, 10 mmol) at 0–5°C. The reaction mixture was stirred for 3 h at 0°C, the resulting solid was collected and crystallized from ethanol to give **3**(**a**, **b**) and **6a**, respectively.

***3-(4-Methyl-2-phenyl-thiazol-5-yl)-2-phenylazoquinoxaline (10).*** A mixture of compound **9** (0.5 g) in ethanol (20 mL) and hydrogen peroxide (3 mL, 30%) was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure, the resulting solid was collected and recrystallized to give **10**. This compound was obtained as red crystals (DMF/EtOH), mp > 300°C, yield (78%); $^{1}$H-NMR $(CD_3)_2SO$: $\delta$ = 2.46 (s, 3H, 4-methylthiazole), 7.26–8.13 (m, 14H, ArH). $^{13}$C-NMR: $\delta$ = 15.57 ($CH_3$), 109.58, 162.11, 167.00 (thiazole), 138.32, 139.54, 146.61, 145.45 (pyrazine), 124.12, 125.54, 126.28, 129.23, 129.65, 129.89, 132.52, 133.21, 154.94 (phenyl groups). Anal. Calcd. for $C_{24}H_{117}N_5S$ (407.49): C, 70.74; H, 4.21; N, 17.19; S, 7.87. Found: C, 70.90; H, 4.31; N, 17.33; S, 7.60.

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