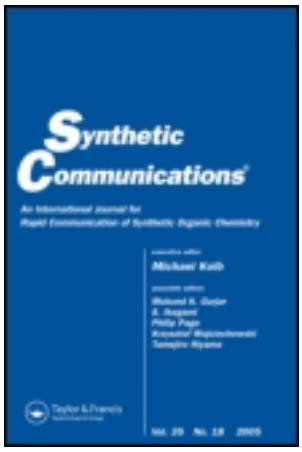

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SYNTHESIS OF NEW PYRIDAZIN- 6-ONES, PYRIDAZIN-6-IMINES, 4-PYRIDAZINALS, AND PYRIDINES

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SYNTHESIS OF NEW PYRIDAZIN-6-ONES, PYRIDAZIN-6-IMINES, 4-PYRIDAZINALS, AND PYRIDINES

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ABSTRACT

3-Dimethyl-1-[3-methyl-(4H)-5-phenylimidazol[2,1-b]thiazol-2-yl]prop-2-enone **4** couples smoothly with benzenediazonium chloride to yield propanal **5** which is a key intermediate for the synthesis of pyridazinones **9–13**, **16** and pyridazine-6-imine **8**, **19**. Pentadienonitrile **18** was converted into pyridine-3-carbonitrile **20** on refluxing in ethanolic sodium ethoxide solution. Pyrazole **24** was synthesized from the reaction of **5** with 1-chloro-2-phenylhydrazono propan-2-one **22**.

Key Words: Azo compounds; Active methylene; Hydrazonoyl chloride

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The biological and medicinal activity of pyridazines has stimulated considerable interest in the chemistry of the ring system.[1–8] As a part of our program aimed at developing the synthesis of functionally substituted heteroaromatices from readily obtainable starting materials, we have developed several novel and efficient syntheses of pyridazine derivatives from the readily obtainable 2-arylhydrazonoketones.[9,10] In conjunction with this work, we now report the synthesis of new, otherwise not readily obtainable pyridazinones and pyridazin-6-imines needed for the evaluation of their potential as new biodegradable agrochemicals.

Thus, we have found that 5-acetyl-2-amino-4-methylthiazole **1** readily reacts with phenacyl bromide **2** to afford 5-phenylimidazo[2,1-*b*]thiazol **3**. The formation of **3** was suggested to proceed through the intermolecular quaternization of phenacyl bromide on the thaizole ring nitrogen atom followed by dehydration to afford an intermediate which converted directly into anhydro base[11] 5-phenylimidazo[2,1-*b*]thiazol **3**. Compound **3** condensed readily with dimethylforamamide dimethylacetal as has been described earlier[12] affording 3-aminoenone derivative **4**. Compound **4** coupled smoothly with benzenediazonium chloride in the presence of sodium hydroxide[13] to yield the 2-phenylhydrazonopropanal **5**. Although the reactivity of methyl ketones toward nucleophilic reagents has been extensively studied,[14–16] to our knowledge this is first reported reaction of C-2 in 3-aminoenone derivatives **4** with electrophiles.

2-Phenylhydrazonopropanal **5** condensed readily with malononitrile **6a** to yield products that can be formulated as **7** or isomeric cyclic **8**. Structure **8** was established for the reaction products based on its stability under conditions reported to effect cyclization of compounds of structure similar to that of **7**.[17,18] For example, condensation product **8** was recovered unchanged after extensive reflux in acetic acid. Similar to the formation of pyridazine-6-imine **8**, compound **5** readily reacted with benzoylacetonitrile **6c** and cyanoacetamide **6d** to yield pyridazine-6-imines **10** and **11**, respectively. In contrast to the behaviour of **5** towards **6c**,**d**, treatment of **5** with ethyl cyanoacetate **6b** gave pyridazinone **9**.

Treatment of **5** with diethyl malonate **6e** in ethanol at room temperature in the presence of dimethylamine gave phenylazopyrane-2-one **12**; upon refluxing in ethanolic sodium ethoxide, the latter compound isomerized to **13** which was obtained directly from the reaction of **5** with **6e** in refluxing pyridine.

Compound **5** readily reacted with hippuric acid **6f** in refluxing acetic anhydride to yield products that can be formulated as 2-phenyl-2-oxazolin-5-one **15a** or pyridazinone isomeric **16a**. Thus, initial cyclization of hippuric acid would generate in situ the oxazolone **14a**. This then condenses with **5** yielding the phenylhydrazone **15a**. This phenylhydrazone rearranges into

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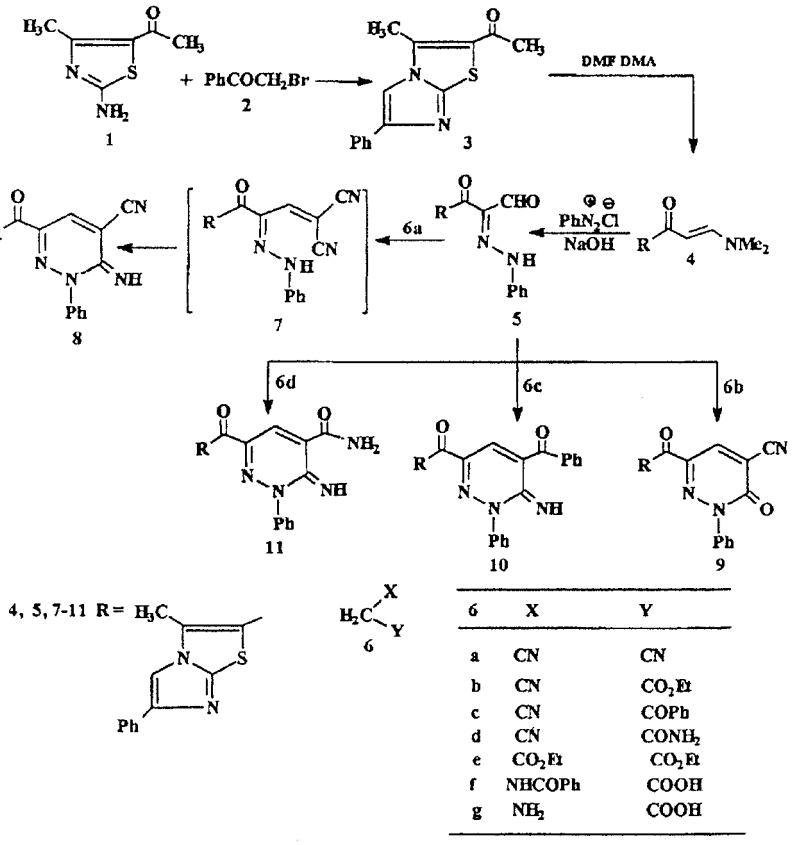
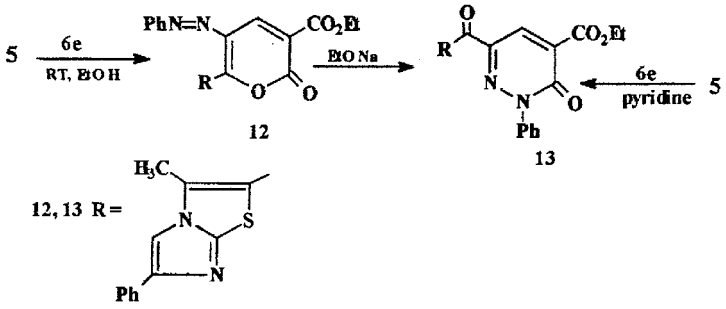


Scheme 1.



Scheme 2.

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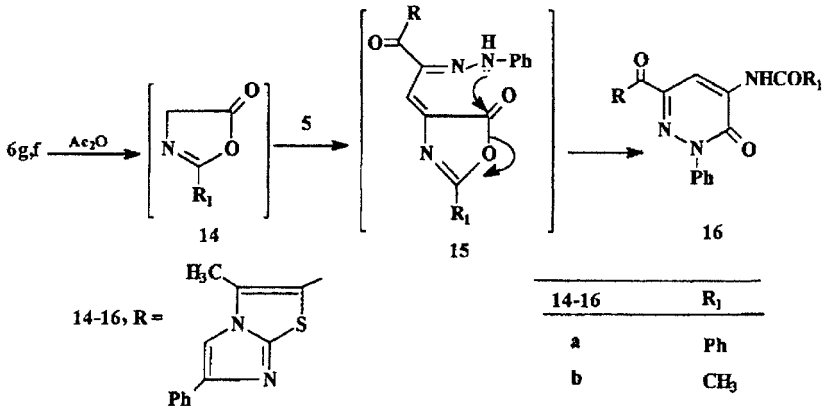
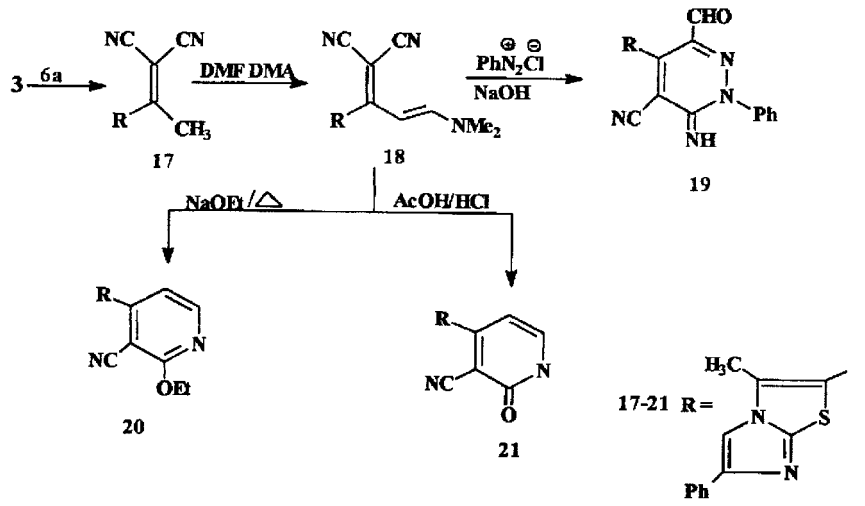
the pyridazinone **16a** via attack of the hydrazone moiety at the ring carbonyl group. Structure **16a** was preferred over **15a** based on the fact that the reaction product was recovered unchanged after extensive reflux under conditions reported to effect ring-opening[19] of 2-oxazolin-5-one. Similar to the formation of 5-benzoyl-aminopyridazine-6-one **16a**, compound **5** readily reacted with glycine **6g** in refluxing acetic anhydride to yield 5-acetylamino-pyridazin-6-one **16b**.



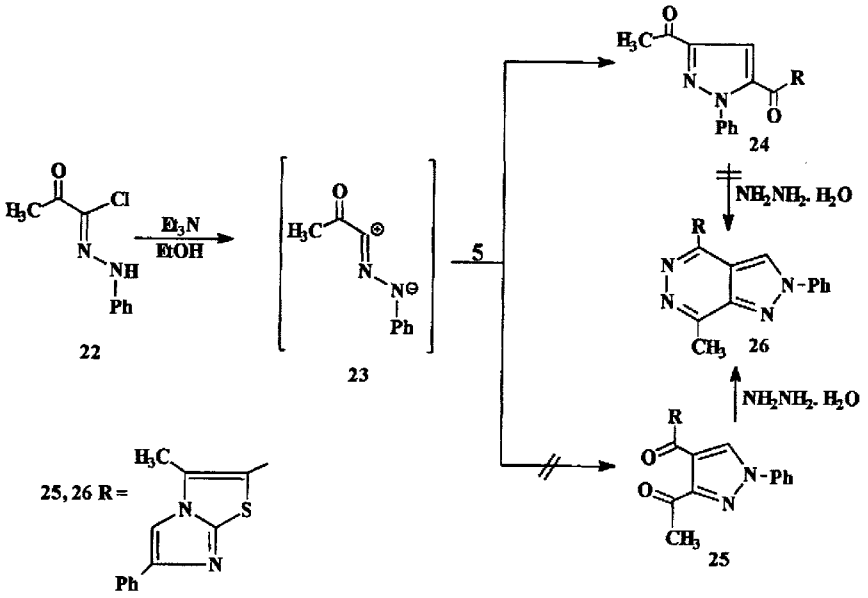
Scheme 3.

1-[3-Methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]-2,2-dicyano-1-methylvinyl **17** was prepared by condensing **6a** with imidazo[2,1-*b*]thiazolyl methyl ketone **3** in boiling dry benzene containing ammonium acetate and acetic acid using a Dean-stark water separator. Compound **17** reacted smoothly with dimethylformamide dimethylacetal in dioxane or with mixture of dimethylformamide/triethylorthoformate to afford pentadienonitrile **18**. The observation that C-2 in **4** couples with benzenediazonium chloride prompted us to investigate the behaviour of the enamine **18** toward benzenediazonium chloride to yield the pyridazinal **19**. Hydrolysis of the enamine **18** by the action of acetic acid/hydrochloric acid mixture afforded the pyridinone **21**,[20] but refluxing **18** in ethanolic sodium ethoxide solution afforded ethoxypyridine **20**.[21]

Nitrilimines, generated by the action of bases on hydrazonoyl halides have been reported to added to α,β-unsaturated carbonyl compounds to yield mixtures of isomeric pyrazolines.[22] In the present work, the reaction of nitrilimine **23** (generated in situ from 1-chloro-2-phenylhydrazono



Scheme 4.



Scheme 5.

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propan-2-one **22** and triethylamine) with **5** has afforded only one pyrazole derivative by cycloaddition and dimethylamine elimination. The derivative may be formulated as **24** or its isomer **25**. Structure **24** was established based on recovering unaffected after fused or long reflux with hydrazine hydrate. These finding provide firm support for structure **24**. Clearly the pyrazolo[3,4-*d*] pyridazine **26** could be obtained only from reaction of **25** and hydrazine hydrate.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Perkin-Elmer 1650 FT-IR Spectrometer. ^{1}H NMR spectra were measured on a Varian (200 MHz) Spectrometer with DMSO-d_6 as solvent and TMS as internal standard, chemical shifts are reported in δ units (ppm). Mass spectra were obtained by electron impact method. Microanalyses were obtained from the Microanalytical Data Unit at Cairo University. Compound **1**[10] and **22**[23] were prepared according to literature procedures.

2-Acetyl-3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazole (3): Equimolar amount of 2-amino-5-acetyl-4-methylthiazole **1** (1.56 g, 10 mmol) and phenacyl bromide (1.99 g, 10 mmol) in butanol (30 ml) were refluxed on water bath for 6–12 h, (TLC control). The solvent was evaporated under reduced pressure and the product obtained was triturated with ether, collected by filtration and crystallized from DMF.

Yield: 1.8 g (70%); mp 220–222°C; IR (KBr): $\nu = 1708\ cm^{-1}$ (C=O); ^{1}H NMR (DMSO-d_6): $\delta = 2.51$ (s, 3H, CH_3), 2.72 (s, 3H, $COCH_3$), 7.23–7.92 (m, $5H_{arom}$), 8.5 (s, $1H_{imidazo}$); MS: $m/z = 256$ (M^+).

		C	H	N	S
$C_{14}H_{12}N_2OS$	Calc.	65.60	4.72	10.93	12.51
(256.31)	Found	65.57	4.70	10.82	12.38

3-Dimethylamino-1-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]-prop-2-enone (4): The procedure used earlier was adopted.[12] An equimolar amount of dimethylformamide dimethylacetal (1.19 g, 10 mmol) was added to the thiazolyl methyl ketone **3** (2.56 g, 10 mmol) in *p*-xylene (50 ml), and the reaction mixture was refluxed for 4–6 h, (TLC control). The removal of solvent under reduced pressure yielded the crude product, which was crystallized from EtOH.

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Yield: 2.5 g (81%); mp 194–195°C; IR (KBr): $\nu = 1672\,cm^{-1}$ (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.35$ (s, 3H, CH_3), 2.81 (s, 6H, -N(CH_3)$_2$), 5.61 (d, 1H, -CH=C<u>H</u>-N, J = 13 Hz), 7.13–7.93 (m, 6H 5H_{arom} and -COC<u>H</u>=CH-), 8.51 (s, 1$H_{imidazo}$); MS: $m/z = 311$ (M^+).

		C	H	N	S
$C_{17}H_{17}N_3OS$	Calc.	65.57	5.50	13.49	10.30
(311.40)	Found	65.51	5.46	13.39	10.19

3-Oxo-2-phenylhydrazono-3-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazol-2-yl]propanal (5): A cold solution of benzenediazonium chloride (10 mmol) was prepared as described earlier[17] was stirring. The resulting solution of the benzenediazonium chloride was then added to a cold solution of enaminone **4** (3.11 g, 10 mmol) in ethanol (50 ml) containing sodium hydroxide (550 mg, 12.5 mmol, in (5 ml) water). The reaction mixture was stirred at room temperature for 3 h, crushed ice was added the solid separated was filtered off and crystallized from EtOH.

Yield: 3 g (77%); mp. 160–162°C; IR (KBr): $\nu = 3335$–3450 (NH), $1662\,cm^{-1}$ (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.43$ (s, 3H, CH_3), 7.16–7.98 (m, 10H_{arom}), 8.49 (s, 1$H_{imidazo}$), 9.85 (s, 1H, CHO), 11.16 (brs, 1H, NH); MS: $m/z = 389$ ($M^+ + 1$).

		C	H	N	S
$C_{21}H_{16}N_4O_2S$	Calc.	64.93	4.15	14.42	8.25
(388.443)	Found	64.85	4.11	14.32	8.16

5-Substituted-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazoloyl]-6-imino-1-phenylpyridazines (8, 10, 11); General Procedure: A mixture of 3-oxo-2-phenylhydrazono-3-[3-methyl-(4H)-5-phenylimidazo-[2,1-*b*]thiazol-2-yl]propanal **5** (3.88 g, 10 mmol) malononitrile, benzoylacetonitrile and/or cyanoacetamide (10 mmol) and a few drops of piperidine (0.5 ml) in absolute ethanol (50 ml) were refluxed for 4–6 h. (TLC control). The reaction mixture was cooled to room temperature, evaporated till dryness and the residue redissolved in cold water (25 ml) containing dilute HCl (if necessary) and kept over night. The solid product, so formed, was collected by filtration and crystallized from EtOH.

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1,6-Dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]-6-imino-1-phenylpyridazine-5-carbonitrile (8): Yield: 3.2 g (73.5%); mp 175–176°C; IR (KBr): $\nu = 3295$ (NH), 2225 (CN), 1668 cm^{-1} (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.45$ (s, 3H, CH_3), 7.16–8.46 (m, 12H, $10H_{arom}$; 4-H and $1H_{imidazo}$), 10.27 (brs, 1H, NH); MS: $m/z = 436$ (M^+).

		C	H	N	S
$C_{24}H_{16}N_6OS$	Calc.	66.04	3.69	19.25	7.34
(436.49)	Found	65.94	3.62	19.19	7.26

5-Benzoyl-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]-6-imino-1-phenylpyridazine (10): Yield: 3.1 g (60%); mp 201–203°C; IR (KBr): $\nu = 3380$ (NH), 1662, 1645 cm^{-1} (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.45$ (s, 3H, CH_3), 7.21–8.76 (m, 17H, $15H_{arom}$; 4-H and $1H_{imidazo}$), 9.98 (brs, 1H, NH); MS: $m/z = 516$ ($M^+ + 1$).

		C	H	N	S
$C_{30}H_{21}N_5O_2S$	Calc.	69.89	4.11	13.58	6.22
(515.59)	Found	69.86	4.13	13.51	6.15

5-Amino-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]-6-imino-1-phenylpyridazine (11): Yield: 3.3 g (72%); mp 194–195°C; IR (KBr): $\nu = 3246$, 3125 (NH and NH_2), 1673 (C=O), 1640 cm^{-1} (amide C=O); ^1H NMR (DMSO-d_6): $\delta = 2.51$ (s, 3H, CH_3), 7.22–8.46 (m, 14H, $10H_{arom}$; 4-H and $1H_{imidazo}$ and NH_2), 9.72 (brs, 1H, NH); MS: $m/z = 454$ (M^+).

		C	H	N	S
$C_{24}H_{18}N_6O_2S$	Calc.	63.42	4.00	18.49	7.05
(454.505)	Found	63.39	3.98	18.35	6.91

1,6-Dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]-6-imino-5-oxo-1-phenylpyridazine (9): To a suspension of **5** (3.88 g, 10 mmol) in dioxane (35 ml), ethyl cyanoacetate (1.13 g, 10 mmol), a few drops of

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triethylamine were added. The reaction mixture was refluxed for 4–6 h (TLC control), then concentrated to half of its volume, poured into crushed ice containing dilute HCl (if necessary). The solid product, so formed on standing was collected by filtration and crystallized from DMF.

Yield: 3 g (68.5%); mp 215–216°C; IR (KBr): $\nu = 2198$ (CH), 1693 (C=O), 1635 cm^{-1} (ring C=O); ^1H NMR (DMSO-d_6): $\delta = 2.51$ (s, 3H, CH_3), 7.25–8.48 (m, 12H, $10H_{arom}$; 4-H and $1H_{imidazo}$); MS: $m/z = 437$ (M^+).

		C	H	N	S
$C_{24}H_{15}N_5O_2S$	Calc.	65.89	3.46	16.01	7.33
(437.47)	Found	65.87	3.45	15.89	7.26

Ethyl 2-Oxo-5-phenylazo-6-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]-4H-pyrane-3-carboxylate (12): To stirred solution of **5** (3.88 g, 10 mmol) in ethanol (30 ml) containing dimethylamine diethyl malonate **6e** (1.6 g, 10 mmol) was added. The reaction mixture was kept under stirring for 24 h, at room temperature during which the solid formed was filtered and washed with ethanol and crystallized from methanol.

Yield: 3.6 g (75%); mp 124–125°C; IR (KBr): $\nu = 1732$ (ester CO), 1644 cm^{-1} (ring C=O); ^1H NMR (DMSO-d_6): $\delta = 1.35$ (t, 3H, $J = 8$ Hz, CH_3), 2.47 (s, 3H, CH_3), 4.34 (q, 2H, $J = 8$ Hz, OCH_2), 7.34–8.52 (m, 12H, $10H_{arom}$; 4-H and $1H_{imidazo}$); MS: $m/z = 484$ (M^+).

		C	H	N	S
$C_{26}H_{20}N_4O_4S$	Calc.	64.45	4.16	11.56	6.62
(484.53)	Found	64.41	4.12	11.48	6.58

Ethyl 1,6-Dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]-6-oxo-1-phenylpyridazine-5-carboxylate (13) Method A: To a suspension of **5** (3.88 g, 10 mmol) in pyridine (35 ml), diethyl malonate (1.6 g, 10 mmol) was added. The reaction mixture was refluxed for 3–6 h, (TLC control), then concentrated to half of its volume, poured into crushed ice containing dilute HCl (if necessary). The solid product, so formed on standing was collected by filtration and crystallized from EtOH.

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Yield: 3.3 g (68%); mp 170–172°C; IR (KBr): ν = 1728 (ester CO), 1665 (C=O), 1634 cm^{-1} (ring C=O); ^1H NMR (DMSO-d_6): δ = 1.32 (t, 3H, J = 8.6 Hz, CH_3), 2.47 (s, 3H, CH_3), 4.31 (q, 2H, J = 8 Hz, OCH_2), 7.34–8.58 (m, 12H, $10H_{arom}$; 4-H and $1H_{imidazo}$); MS: $m/z = 485$ ($M^+ + 1$).

		C	H	N	S
$C_{26}H_{20}N_4O_4S$	Calc.	64.45	4.16	11.56	6.62
(484.53)	Found	64.38	4.14	11.47	6.53

Method B: A solution of **12** (4.84 g, 10 mmol) in absolute ethanol (50 ml) was treated with sodium ethoxide (0.25 mmol). The reaction mixture was heated for 4 h, then allow to cool to room temperature and acidified with dilute HCl. The solid product thus formed was collected by filtration and crystallization from ethanol to afford a compound identical in all respects (mp, mixed mp and spectral data) with that obtained by Method A.

5-Substituted-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazoloyl]-6-oxo-1-phenylpyridazine (16a,b): General procedure: A solution of **5** (3.88 g, 10 mmol) and hippuric acid (1.79 g, 10 mmol) or glycine (0.8 g, 10 mmol) in dry acetic anhydride (45 ml) was refluxed for 3–5 h, left to cool then poured into water. After complete decomposition of excess acetic anhydride the remaining was triturated with methanol, collected by filtration and crystallized from EtOH.

5-Benzoamido-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazoloyl]-6-oxo-1-phenylpyridazine (16a): Yield: 4.3 g (81%); mp 288–289°C; IR (KBr): ν = 3375 (NH), 1698 (CO), 1675 (ring C=O), 1660 cm^{-1} (amide C=O); ^1H NMR (DMSO-d_6): δ = 2.49 (s, 3H, CH_3), 7.31–8.52 (m, 17H, $15H_{arom}$; 4-H and $1H_{imidazo}$), 10.11 (brs, 1H, NH); MS: $m/z = 531$ (M^+).

		C	H	N	S
$C_{30}H_{21}N_5O_3S$	Calc.	67.78	3.98	13.17	6.03
(531.59)	Found	67.87	3.78	13.01	5.92

5-Acetamido-1,6-dihydro-3-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazoloyl]-6-oxo-1-phenylpyridazine (16b): Yield: 3.4 g (72%);

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mp 145–147°C; IR (KBr): ν = 3315 (NH), 1692 (CO), 1679 (ring CO), 1656 cm^{-1} (amide CO); ^1H NMR (DMSO-d_6): δ = 2.28 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 7.38–8.63 (m, 12H, 10H_{arom}; 4-H and 1$H_{imidazo}$), 9.98 (brs, 1H, NH); MS: $m/z = 470$ ($M^+ + 1$).

		C	H	N	S
$C_{25}H_{19}N_5O_3S$	Calc.	63.95	4.08	14.92	6.83
(469.52)	Found	63.87	3.98	14.79	6.72

1-(3-Methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]ethylidenemalononitrile (17): A suspension of **3** (2.56 g, 10 mmol) in dry benzene (30 ml), ammonium acetate (0.5 g) and acetic acid (2 ml) was treated with malononitrile (0.67 g, 10 mmol). The reaction mixture was heated under reflux using a Dean-stark water separator until water ceased to be collected. The solid product obtained was crystallized from EtOH.

Yield: 2.5 g (82%); mp 207–209°C; IR (KBr): ν = 2210 cm^{-1} (CN); ^1H NMR (DMSO-d_6): δ = 2.51 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 7.32–7.96 (m, 5H_{arom}), 8.45 (s, 1$H_{imidazo}$); MS: $m/z = 304$ (M^+).

		C	H	N	S
$C_{17}H_{12}N_4S$	Calc.	67.09	3.98	18.41	10.53
(304.37)	Found	66.98	3.68	18.19	10.42

2-Cyano-5-(*N*,*N*-dimethylamino)-3-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]-thiazol-2-yl]-2,4-pentadienonitrile (18) Method A: A suspension of each of **17** (3.04 g, 10 mmol) was treated with *N*,*N*-dimethyl-formamide (15 ml) and triethylorthoformate (15 ml). The reaction mixture was refluxed for 4–6 h, then poured into water. The oily product thus formed was triturated with methanol and left aside for two days. The solid product was filtered off and crystallized from dioxane.

Method B: A suspension of each of **17** (3.04 g, 10 mmol) in dioxane (35 ml), dimethylformamide dimethylacetal (1.19 g, 10 mmol) was added. The reaction mixture was refluxed for 3 h, (TLC control). The solid product thus formed was collected by filtration and crystallized from dioxane to afford a compound identical in all respects (mp, mixed mp and all spectra data) with that obtained by Method A.

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Yield: 2.4 g (67%); mp 200–201°C; IR (KBr): $\nu = 2225\,cm^{-1}$ (CN); ^1H NMR (DMSO-d_6): $\delta = 2.48$ (s, 3H, CH_3), 3.10 (s, 3H, NCH_3), 3.19 (s, 3H, NCH_3), 5.68 (d, 1H, -CH=C<u>H</u>-N, J = 13 Hz), 7.23–8.52 (m, 7H, $5H_{arom}$ and –COC<u>H</u>=CH-, $1H_{imidazo}$). MS: $m/z = 359$ (M^+).

		C	H	N	S
$C_{20}H_{17}N_5S$	Calc.	66.83	4.77	19.48	8.92
(359.45)	Found	66.81	4.58	19.21	8.82

1,6-Dihydro-3-formyl-6-imino-4-[3-methyl-(4H)-5-phenylimidazo-[2,1-*b*]thiazol-2-yl]-1-phenylpyridazine-5-carbonitrile (19): A solution of 2-cyano-5-(*N*,*N*-dimethylamino)-3-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]- thiazol-2-yl]- 2,4-pentadienonitrile **18** (3.59 g, 10 mmol) in ethanol (50 ml) containing sodium hydroxide solution (0.5 g, in (10 ml) water) was treated with a cold solution of benzenediazonium chloride (10 mmol) prepared according to literature.[13] The reaction mixture was stirred at room temperature for 48 h, crushed ice was added (50 g), the solid separated was filtered and crystallization from EtOH.

Yield: 2.7 g (63%); mp 140–142°C; IR (KBr): $\nu = 3395$ (NH), 2225 (CN), 1695 cm^{-1} (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.51$ (s, 3H, CH_3), 7.92–8.62 (m, 11H, $10H_{arom}$, $1H_{imidazo}$), 8.72 (s, 1H, CHO), 8.98 (brs, 1H, NH); MS: $m/z = 436$ (M^+).

		C	H	N	S
$C_{24}H_{16}N_6OS$	Calc.	66.04	3.69	19.25	7.34
(436.49)	Found	66.12	3.62	19.01	7.21

2-Ethoxy-4-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]pyridine-3-carbonitrile (20): A solution of **18** (3.59, 10 mmol) in absolute ethanol (50 ml) was treated with the sodium ethoxide (0.25 mmol). The reaction mixture was heated for 4 h, then allowed to cool to room temperature and triturated with cold water containing dilute HCl. The solid product thus formed was collected by filtration and crystallized from ethanol.

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Yield: 2 g (58%); mp 222–223°C; IR (KBr): $\nu = 2218\,cm^{-1}$ (CN); ^1H NMR (DMSO-d_6): $\delta = 1.40$ (t, 3H, J = 8 Hz, CH_3), 2.43 (s, 3H, CH_3), 4.71 (q, 2H, J = 8 Hz, OCH_2), 7.92–8.62 (m, 6H, $5H_{arom}$, pyridyl H-5), 8.53 (m, 2H, $1H_{imidazo}$ pyridyl H-6); MS: $m/z = 361$ ($M^+ + 1$).

		C	H	N	S
$C_{20}H_{16}N_4OS$	Calc.	66.65	4.47	15.54	8.89
(360.43)	Found	66.61	4.42	15.41	8.82

1,2-Dihydro-2-oxo-4-[3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazol-2-yl]-pyridine-3-carbonitrile (21): A solution of **18** (3.59 g, 10 mmol) in acetic acid/hydrochloric acid (3/1) mixture (30 ml) was refluxed for 4 h, then poured into water. The solid product thus formed was collected by filtration and crystallized from dioxane.

Yield: 2.4 g (72%); mp 194–196°C; IR (KBr): $\nu = 3298$ (NH), 2226 (CN), 1658 cm^{-1} (amide CO): ^1H NMR (DMSO-d_6): $\delta = 2.48$ (s, 3H, CH_3), 6.34 (d, 1H, pyridyl H-5), 7.24–7.98 (m, 6H, $5H_{arom}$, pyridyl H-6), 8.51 (s, $1H_{imidazo}$), 12.51 (brs, 1H, NH); MS: $m/z = 332$ (M^+).

		C	H	N	S
$C_{18}H_{12}N_4OS$	Calc.	65.05	3.64	16.86	9.64
(332.38)	Found	64.88	3.58	16.49	9.58

3-Acetyl-1-phenyl-5-[2-(3-methyl-(4H)-5-phenylimidazo[2,1-*b*]thiazoloyl]pyrazole (24): A solution of **5** (3.88 g, 10 mmol) in ethanol (30 ml) and **22** (1.96 g, 10 mmol) in ethanol (30 ml) was treated with triethylamine (2 ml). The solution was left over night under stirring, then reflux for 4 h. The solvent was then evaporated and the remaining product was triturated with methanol. The product that formed, was collected by filtration and crystallized from ethanol.

Yield: 2.5 g (58%); mp 235–236°C; IR (KBr): $\nu = 1693$, 1662 cm^{-1} (C=O); ^1H NMR (DMSO-d_6): $\delta = 2.49$ (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 7.14–8.06 (m, $10H_{arom}$), 8.49 (s, $1H_{imidazo}$), 8.92 (s, 1H, H-5); MS: $m/z = 426$ (M^+).

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		C	H	N	S
$C_{24}H_{18}N_4O_2S$	Calc.	67.59	4.25	13.14	7.52
(426.49)	Found	67.31	4.58	13.11	7.46

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