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Synthesis and Reactions of Novel Pyrimido[4,5-*c*]pyridazine and *s*-Triazolo[3′,4′:2,3]pyrimido[4,5-*c*]pyridazine Derivatives

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Summary. The reaction of 3-chloro-5,6-diphenylpyridazine-4-carbonitrile with potassium thiocyanate gave the corresponding isothiocyanate derivative. This was reacted with aromatic amines in ethanol to afford pyrimido[4,5-*c*]pyridazine derivatives. The reaction of the latter compounds with hydrazine hydrate led to the formation of 6-hydrazino derivatives. One hydrazino compound was reacted with a variety of reagents to produce other new pyrimidopyridazines as well as a number of *s*-triazolo derivatives.

Keywords. Pyrimidopyridazine; *s*-Triazolopyrimidopyridazine; Heterocycles; Condensation.

Introduction

Pyridazine derivatives and heterocyclic annelated pyridazines continue to attract attention due to their wide variety of interesting biological activities [1]. Synthesis and utility of many pyridazine derivatives as analgesics, insecticidals [2], fungicidals [3, 4] cardiotonics [5], and bactericidals [6] have been reported. In view of the above mentioned benefits and in continuation of our work on the chemistry of pyridazine compounds [7], we report herein the synthesis of pyrimidopyridazine and triazolopyrimidopyridazine derivatives.

Results and Discussion

3-Chloro-5,6-diphenylpyridazine-4-carbonitrile (**1**), which was prepared according to Ref. [8] was reacted with potassium thiocyanate in acetic acid to yield (5,6-diphenyl-4-cyano pyridazin-2-yl)isothiocyanate (**2**). The reaction of **2** with different

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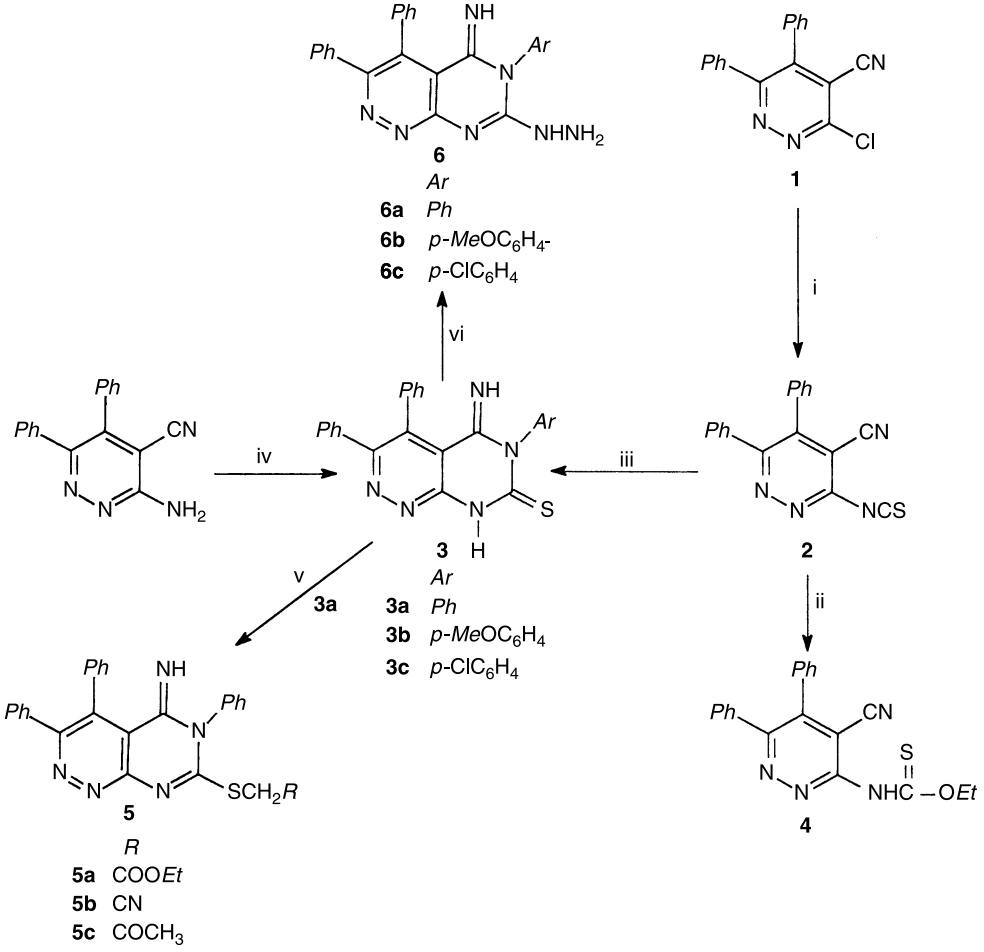
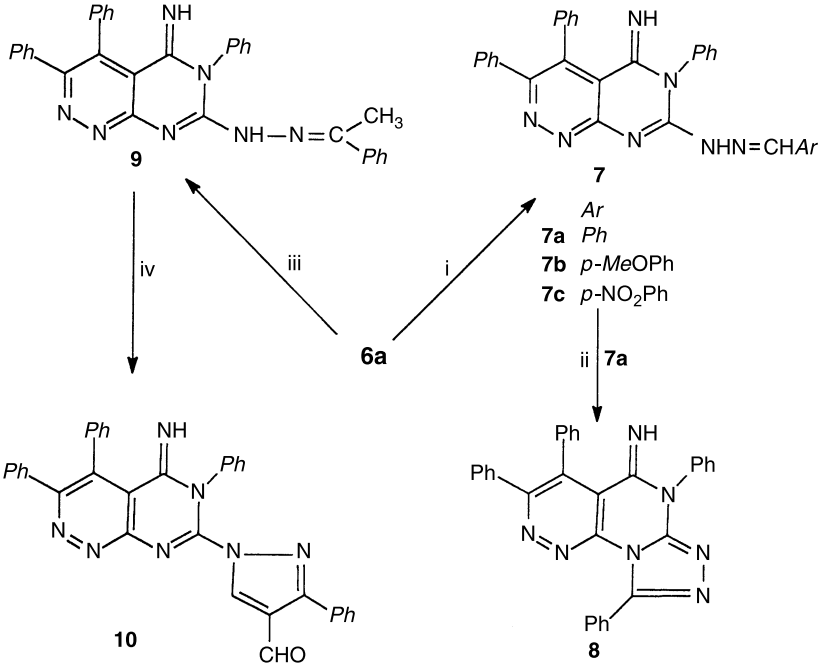
arylamines, namely aniline, *p*-anisidine, and 4-chloroaniline afforded the pyrimidopyridazine derivatives **3a**–**3c** [9]. Boiling of **2** in ethanol yielded the thiocarbamate derivative **4** in good yield.

Further chemical confirmation of the pyrimidopyridazine constitution of **3a** was achieved using an alternative route for the synthesis. Thus, when 3-amino-4-cyano-5,6-diphenylpyridazine [10] was allowed to react with phenyl isothiocyanate in pyridine for a long time, the pyrimidopyridazine **3a** was produced in a single step [11] (Scheme 1). When **3a** was reacted with different alkylating agents, namely ethyl chloroacetate, chloroacetonitrile, or chloroacetone in refluxing ethanol in the presence of sodium acetate, the corresponding *S*-alkylated derivatives **5a**–**5c** were obtained in excellent yield. Reaction of **3a**–**3c** with hydrazine hydrate in refluxing ethanol afforded the corresponding hydrazino compounds **6a**–**6c**.

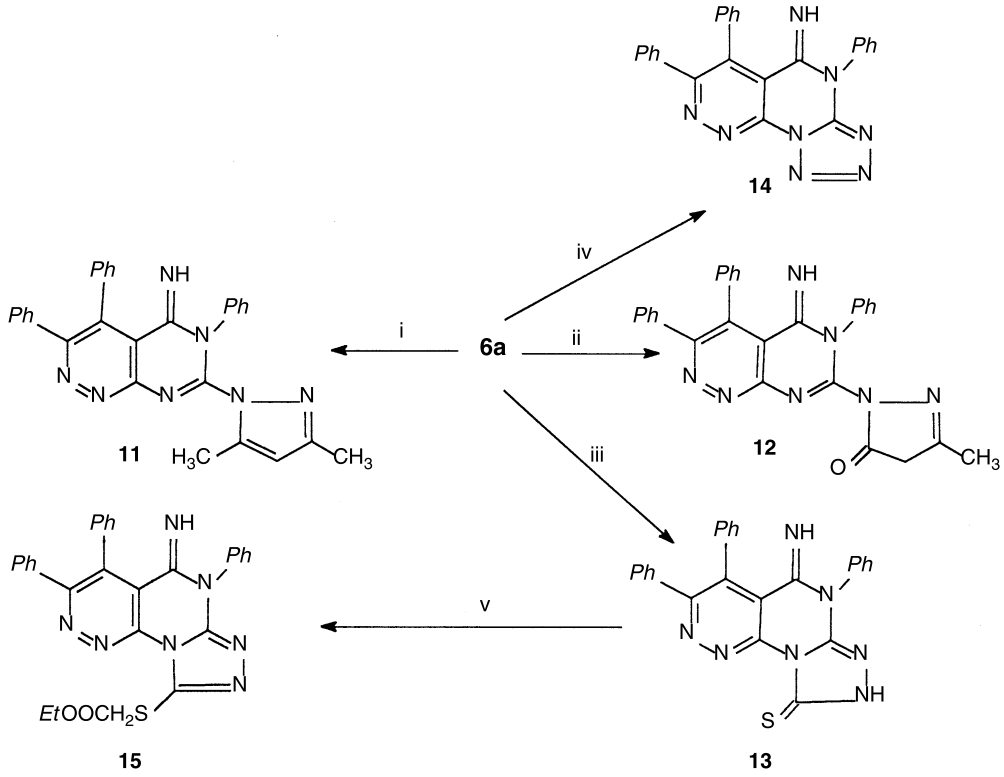
Condensation of **6a** with aromatic aldehydes in ethanol furnished 7-arylmethylenehydrazino derivatives **7a**–**7c**. When **7a** was treated with thionyl chloride, it underwent an intramolecular cyclization affording triazolopyrimidopyridazine **8** [12]. Condensation of **6a** with acetophenone in refluxing ethanol containing a



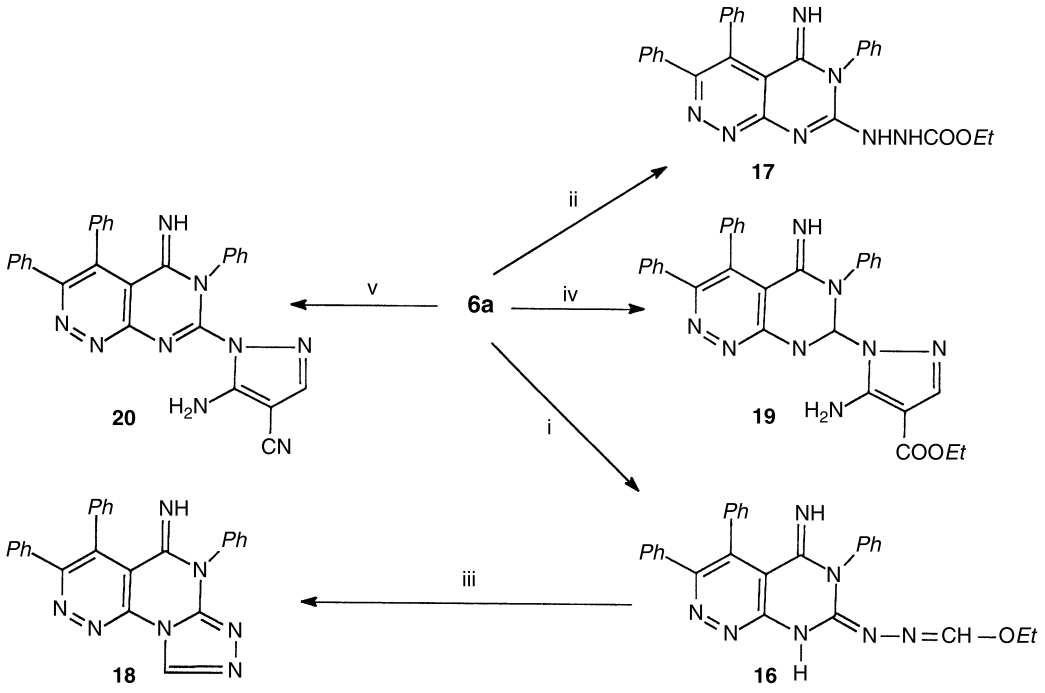
Scheme 1. i: KSCN/CH_3COOH; ii: *Et*OH; iii: $ArNH_2$/*Et*OH; iv: *Ph*NCS/pyridine; v: RCH_2Cl/*Et*OH/*Ac*ONa; vi: NH_2NH_2/*Et*OH



Scheme 2. i: ArCHO/*Et*OH; ii: $SOCl_2$; iii: *Ph*$COCH_3$/*Et*OH; iv: $POCl_3$/*DMF*



Scheme 3. i: Ac_2CH_2/*Et*OH; ii: $CH_3COCH_2CO_2Et$/*Et*OH/KOH; iii: CS_2/pyridine; iv: $NaNO_2$/CH_3CO_2H; v: $ClCH_2CO_2$ *Et*/*Et*OH/*Ac*ONa



Scheme 4. i: $CH(OEt)_3$; ii: $ClCO_2Et$/pyridine; iii: CH_3CO_2H; iv: *Et*OCH=C(CN)CO_2Et; v: *Et*OCH=$C(CN)_2$/EtOH/*Ac*OH

few drops of acetic acid afforded 5,6-dihydro-7-[2-(methylphenylmethylene)hydrazino-5-imino-3,4,6-tri-phenylpyrimido[4,5-*c*]pyridazine (**9**). Upon treatment of **9** with $POCl_3$/*DMF* mixture (*Vilsmeier* reagent) at 60–70°C, the pyrazolylpyrimidopyridazine **10** was obtained [13]. Furthermore, the hydrazino derivative **6a** was condensed with acetylacetone or ethyl acetoacetate in refluxing ethanol in the presence of KOH to afford pyrazolylpyrimidopyridazines **11** or **12**.

Moreover, **6a** was used as a versatile compound for building a new heterocyclic system condensed with a pyridazine moiety. Thus, its reaction with carbon disulfide in pyridine and/or nitrous acid leads to the formation of the triazolopyrimidopyridazine **13** and tetrazolopyrimidopyridazine **14**. The thioxo derivative **13** was easily *S*-alkylated with ethyl chloroacetate in refluxing ethanol in the presence of sodium acetate to give the ester **15**. Furthermore, the reaction of **6a** with triethyl orthoformate and/or ethyl chloroformate afforded **16** and **17**. Compound **16** underwent an intramolecular cyclization when stirred in acetic acid at room temperature yielding triazolo[3′,4′:2,3]pyrimido[4,5-*c*]pyridazine (**18**). Finally, the reaction of **6a** with ethyl ethoxymethylenecyanoacetate or ethoxymethylenemalonitrile in refluxing ethanol in the presence of a few drops of *Ac*OH yielded pyrazolylpyrimidopyridazines **19** and **20**.

Experimental

Uncorrected Melting points were determined using a *Kofler* melting point apparatus. IR spectra were recorded on a Pye-Unicam spectrometer using KBr wafers. ^{1}H NMR spectra were recorded on a Varian 390 NMR spectrometer at 90 MHz using TMS as an internal standard. Mass spectra were recorded on

JEOL JMS 600 spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 C microanalyzer. They were found to agree favorably with the calculated values.

3-Chloro-5,6-diphenylpyridazine-4-carbonitrile (**1**) was prepared according to Ref. [8].

(5,6-Diphenyl-4-cyanopyridazine-2-yl)thiocyanate (**2**, $C_{18}H_{10}N_4S$)

A mixture of 2.91 g of **1** (0.01 mol) and 0.79 g of KSCN (0.01 mol) in acetic acid was stirred at room temperature. The precipitated product was collected by filtration as orange crystals in 82% yield; mp 175–177°C; IR: $\bar{\nu} = 2220$ (C≡N) and 1590 (C=N) cm^{-1}; EI: $m/z = 314$, base peak at 288 (M-26).

General Procedure for the Synthesis of ***3a–3c***

Method A: A suspension of 3.14 g of **2** (0.01 mol) and 0.01 mol of the respective arylamine in 35 cm^3 of absolute ethanol was heated under reflux for 2–4 h, and then allowed to cool. The solid product was collected by filtration and recrystallized from *Et*OH/$CHCl_3$ to give yellow-orange crystals.

5-Imino-5,6,7,8-tetrahydro-3,4,6-triphenylpyrimido[4,5-c]pyridazine-7-thion (**3a**, $C_{24}H_{17}N_5S$)

Yield 78%; mp 299–300°C; IR: $\bar{\nu} = 3450$, 3350 (NH) 1600 (C=N) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 7.5$–8.2 (m, 15ArH), 11.2 (s, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 147.2$, 156.4, 163.3 (3C=N), 114.9, 134.8 (C=C pyrimidine ring), 178.3 (C=S), 137.7 (N–C), 124.5, 125.3, 127.0, 128.5, 129.0, 136.5 (aromatic) ppm.

5-Imino-5,6,7,8-tetrahydro-6-(4-methoxyphenyl)-3,4-diphenylpyrimido[4,5-c]pyridazine-7-thion (**3b**, $C_{25}H_{19}N_5SO$)

Yield 73%; mp 269–271°C; IR: $\bar{\nu} = 3450$, 3350 (NH), 1590 (C=N) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.4$ (s, OCH_3), 7.5–8.5 (m, 14ArH), 10.9 (s, 2NH) ppm.

6-(4-Chlorophenyl)-5-imino-5,6,7,8-tetrahydro-3,4-diphenylpyrimido[4,5-c]pyridazine-7-thion (**3c**, $C_{24}H_{16}N_5SCl$)

Yield 75%; mp 273–275°C; IR: $\bar{\nu} = 3450$–3350 (NH), 1600 (C=N) cm^{-1}.

Method B: A mixture of 2.5 g of 3-amino-4-cyano-5,6-diphenylpyridazine (0.01 mol) and 1.35 g of phenyl isothiocyanate (0.01 mol) in 20 cm^3 of pyridine was heated under refux for 10–12 h, and then allowed to cool. The solid product was collected by filtration and recrystallized from EtOH/$CHCl_3$ to give yellow crystals. The products were identical with those synthesized by method A.

Ethyl N-(4-Cyano-5,6-diphenylpyridazin-3-yl)thiocarbamate (**4**, $C_{20}H_{16}N_4OS$)

A sample of 2 g of **2** was boiled for 1 h in 30 cm^3 of ethanol and the reaction mixture was then allowed to cool. The solid product was filtered off and recrystallized from dioxane to give yellow crystals in 63% yield; mp 195–197°C; IR: $\bar{\nu} = 3310$ (NH), 2220 (C≡N) cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.5$ (t, $J = 7.0$ Hz, CH_3), 2.7 (q, $J = 7.0$ Hz, CH_2), 7.1–7.7 (m, 10ArH), 9.7 (s, NH) ppm; EI: $m/z = 360.5$.

General Procedure for the Synthesis of ***5a–5c***

A mixture of 2 g of **3a** (0.005 mol), 0.005 mol of the corresponding halo compound and 0.015 mol of sodium acetate in 30 cm^3 of ethanol was refluxed for 2 h, then allowed to cool, and poured into H_2O. The solid product was collected and recrystallized from ethanol to give white pale yellow crystals.

Ethyl (5,6-Dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazin-7-ylthio)acetate (**5a**, $C_{28}H_{23}N_5O_2S$)

Yield 87%; mp 193–195°C; IR: $\bar{\nu} = 3350$ (NH), 2900 (CH aliphatic), 1710 (C=O), 1600 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.5$ (t, $J = 7.0$ Hz, CH_3), 2.4 (q, $J = 7.0$ Hz, CH_2), 6.1 (s, CH_2), 7.5–8.6 (m, 15ArH), 10.9 (s, NH) ppm.

(5,6-Dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazin-7-ylthio)acetonitril (**5b**, $C_{26}H_{18}N_6S$)

Yield 81%; mp 173–175°C; IR: $\bar{\nu} = 3340$ (NH); 2220 (C≡N) and 1590 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.5$ (s, CH_2), 7.5–8.3 (m, 15ArH), 11.1 (s, NH) ppm.

(5,6-Dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazin-7-ylthio)aceton (**5c**, $C_{27}H_{21}N_5OS$)

Yield 85%; mp 181–183°C; IR: $\bar{\nu} = 3350$ (NH), 2900 (CH aliphatic), 1700 (C=O), 1590 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 2.9$ (s, CH_3), 4.1 (s, CH_2), 7.3–8.5 (m, 15ArH), 11.2 (s, NH) ppm.

*General Procedure for the Synthesis of **6a–6c***

A mixture of 0.01 mol of **3a–3c** and hydrazine hydrate (5 cm^3) was heated under reflux for 6 h, then 20 cm^3 of absolute ethanol were added and the mixture was refluxed for additional 1 h. The solid product was collected and recrystallized from ethanol to give orange crystals.

5,6-Dihydro-7-hydrazino-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**6a**, $C_{24}H_{19}N_7$)

Yield 77%; mp 195–197°C; IR: $\bar{\nu} = 3400$, 3350 (NH_2, NH), 1610 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 5.7$ (s, NH_2), 7.0–7.9 (m, 15ArH), 9.5–10.2 (2s, 2NH) ppm.

5,6-Dihydro-3,4-diphenyl-7-hydrazino-5-imino-6-(4-methoxyphenyl)pyrimido[4,5-c]pyridazine (**6b**, $C_{24}H_{21}N_7O$)

Yield 72%; mp 218–220°C; IR: $\bar{\nu} = 3400$, 3340 (NH_2, NH), 1610 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 3.5$ (s, CH_3), 5.5 (s, NH_2), 7.3–7.9 (m, 14ArH), 9.6, 10.2 (2s, 2NH) ppm.

5,6-Dihydro-3,4-diphenyl-7-hydrazino-5-imino-6-(4-chlorophenyl)pyrimido[4,5-c]pyridazine (**6c**, $C_{24}H_{18}N_7Cl$)

Yield 75%; mp 263–265°C; IR: $\bar{\nu} = 3410$, 3330 (NH_2, NH), 1590 (C=N) cm^{-1}.

*General Procedure for the Synthesis of **7a–7c***

A mixture of 0.01 mol of **6a** and 0.01 mol of the appropriate aromatic aldehyde in 30 cm^3 of ethanol was refluxed for 3 h, and then allowed to cool to room temperature. The solid product was collected and recrystallized from diluted CH_3COOH to give yellow crystals.

7-Benzylidenehydrazino-5,6-dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**7a**, $C_{31}H_{23}N_7$)

Yield 77%; mp >300; IR: $\bar{\nu} = 3450$, 3350 (NH), 1610 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta =$ 7.1–7.7 (m, 20ArH), 8.3 (s, N=CH), 10.5 (s, 2NH) ppm.

7-(4-Methoxybenzylidenehydrazino)-5,6-dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**7b**, $C_{32}H_{25}N_7O$)

Yield 79%; mp $>300°C$; IR: $\bar{\nu} = 3450$, 3350 (NH), 1605 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 3.2$ (s, $-OCH_3$), 7.2–7.7 (m, 19ArH), 8.3 (s, –N=CH), 10.7 (s, 2NH) ppm.

7-(p-Chlorobenzylidenehydrazino)-5,6-dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**7c**, $C_{31}H_{22}N_8O_2$)

Yield 69%; mp $>300°C$; IR: $\bar{\nu} = 3410$, 3350 (NH), 1610 (C=N) cm^{-1}.

5,6-Dihydro-5-imino-3,4,6,9-tetraphenyl-s-triazolo[3′,4′:2,3]pyrimido[4,5-c]pyridazine (**8**, $C_{31}H_{21}N_7$)

A mixture of 1.5 g of **7a** (0.003 mol) and 10 cm^3 of thionyl chloride was refluxed for 5 h, and then excessive thionylchloride was removed by evaporation. Cold saturated sodium bicarbonate was added and the reaction mixture was extracted several times with ether. The ether layer was washed with water and dried over anhydrous magnesium sulphate. The residue left after evaporation of the solvent, was recrystallized from dioxane to give yellow crystals in 54% yield; mp >300; IR: $\bar{\nu} = 3350$ (NH), 1590 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 7.2$–8.5 (m, 20ArH), 10.3 (s, NH) ppm.

5,6-Dihydro-7-[2-(methylphenylmethylen)hydrazino-5-imino-3,4,6-triphenylpyrimido[4,5-c]-pyridazine (**9**, $C_{32}H_{25}N_7$)

A mixture of 2 g of **6a** (0.005 mol) and 0.6 g of acetophenone (0.005 mol) in 20 cm^3 of absolute ethanol and a few drops of acetic acid was heated under reflux for 5 h. Upon cooling the precipitated product was filtered off and recrystallized from ethanol to give yellow crystals in 65% yield; mp 303–305°C; IR: $\bar{\nu} = 3250$ (NH), 1590 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 2.3$ (s, CH_3), 7.1–8.5 (m, 20ArH), 9.5, 11.1 (2s, 2NH) ppm.

5,6-Dihydro-5-imino-7-(3-phenyl-4-carboxaldehydepyrazol-1-yl)-3,4,6-triphenyl-pyrimido[4,5-c]pyridazine (**10**, $C_{34}H_{23}N_7O$)

To a *Vilsmeier* reagent which was prepared from *DMF* (10 cm^3) and $POCl_3$ (0.012 mol), 2 g of **9** (0.004 mol) were added. The mixture was stirred at 60–70°C for 6 h, and then poured into an ice/H_2O mixture. The product which separated upon neutralization with $NaHCO_3$ solution was filtered off and recrystallized from ethanol to give pale yellow crystals in 52% yield; mp 318–320°C; IR: $\bar{\nu} = 3350$ (–NH), 1640 (C=O), 1590 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 7.1$–7.8 (m, 20ArH), 8.2 (s, CH pyrazole), 9.1 (s, CHO), 9.9 (s, NH) ppm.

5,6-Dihydro-7-(3,5-dimethylpyrazol-1-yl)-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**11**, $C_{29}H_{23}N_7$)

A mixture of 2 g of **6a** (0.005 mol) and 0.5 g of acetylacetone (0.005 mol) was refluxed in ethanol (30 cm^3) for 6 h. The solid product was separated from the hot mixture, filtered off and recrystallized from acetic acid to give yellow crystals in 78% yield; mp 277–279°C; IR: $\bar{\nu} = 3400$ (NH), 1610 (C=N) cm^{-1}; ^1H NMR (CF_3COOD): $\delta = 2.4$, 2.7 (2s, $2CH_3$), 6.2 (s, CH pyrazol), 7.5–8.9 (m, 15ArH) ppm.

5,6-Dihydro-5-imino-7-(3-methyl-5-oxo-pyrazol-1-yl)-3,4,6-triphenylpyrimido[4,5-c]pyridazine (**12**, $C_{28}H_{21}N_7O$)

A mixture of 2 g of **6a** (0.005 mol) and 0.65 g of ethyl acetoacetate (0.005 mol) in ethanol (30 cm^3) was refluxed for 5 h. After cooling the solid product was filtered off and recrystallized from ethanol/$CHCl_3$ to give yellow crystals in 71% yield; mp $>300°C$; IR: $\bar{\nu} = 3100$ (NH), 1670 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 2.1$ (s, CH_3), 4.5 (s, CH_2), 7.5–8.9 (m, 15ArH), 9.3 (s, NH) ppm.

4,5-Dihydro-5-imino-4,6,7-triphenyl-s-triazolo[3′,4′:2,3]pyrimido[4,5-c]pyridazine-1(2H)-thione (**13**, $C_{25}H_{17}N_7S$)

A sample of 2 g of **6a** (0.005 mol) and carbon disulphide (3 cm^3) in pyridine (20 cm^3) was heated on a water bath for 8 h, and then allowed to cool. The solid product was collected and recrystallized from dioxane to give yellow crystals in 65% yield; mp 255°C; IR: $\bar{\nu} = 3310$ (NH), 1610 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 7.5$–8.4 (m, 15ArH), 9.8, 10.3 (2s, 2NH) ppm.

5,6-Dihydro-5-imino-3,4,6-triphenyltetrazolo[5′,1′:2,3]pyrimido[4,5-c]pyridazine (**14**, $C_{24}H_{16}N_8$)

To a cooled sample of 0.5 g of **6a** in glacial acetic acid (15 cm^3), a cold solution of sodium nitrite (0.3 g in 5 cm^3 of H_2O) was added dropwise with stirring. Stirring was continued for 3 h at room temperature, the solid product was filtered off, and recrystallized from dioxane to give pale brown crystals in 62% yield; mp 285°C (decomposed); IR: $\bar{\nu} = 3310$ (NH), 1610 (C=N) cm^{-1}; ^1H NMR (CF_3COOD): $\delta = 7.3$–7.8 (m, 15ArH) ppm. EI: $m/z = 416.5$.

4,5-Dihydro-1-ethoxycarbonylmethylthio-5-imino-4,6,7-triphenyl-s-triazolo[3′,4′:2,3]-pyrimido[4,5-c]pyridazine (**15**, $C_{28}H_{23}N_7O_2S$)

A mixture of 4.47 g of **13** (0.01 mol), 1.5 g of ethyl chloroacetate (0.01 mol), and 0.98 g of sodium acetate (0.012 mol) in 30 cm^3 of ethanol was heated under reflux for 4 h, and then allowed to cool. The solid product was collected by filtration as white crystals in 77% yield; mp 193–192°C; IR: $\bar{\nu} = 3410$ (–NH), 1715 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.5$ (t, $J = 7.0$ Hz, CH_3), 4.2 (q, $J = 7.0$ Hz, CH_2), 4.7 (s, CH_2), 7.3–8.1 (m, 15ArH), 9.7 (s, NH) ppm.

5,6-Dihydro-7-ethoxymethylenehydrazino-5-imino-3,4,6-triphenylpyrimido[4,5-c]-pyridazine (**16**, $C_{27}H_{23}N_7O$)

A mixture of 2 g of **6a** (0.005 mol), triethyl orthoformate (3 cm^3), and 1 cm^3 of glacial acetic acid was heated under reflux for 3 h, and then cooled. The solid product was filtered off and recrystallized from acetic acid to give pale yellow crystals in 64% yield; mp 185°C; IR: $\bar{\nu} = 3410$, 3350 (NH), 2900 (CH aliphatic), 1590 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.5$ (t, $J = 7.0$ Hz, CH_3), 3.7 (q, $J = 7.0$ Hz, CH_2), 7–7.5 (m, 15ArH), 11.1 (s, 2NH) ppm.

Ethyl [5,6-Dihydro-5-imino-3,4,6-triphenylpyrimido[4,5-c]pyridazine-7-yl]carbazate (**17**, $C_{27}H_{23}N_7O_2$)

A mixture of 2 g of **6a** (0.005 mol), ethyl chloroformate (10 cm^3), and 2.0 cm^3 of pyridine was refluxed for 4 h, the excess ethyl chloroformate was removed by distillation and the solid product which formed after adding ethanol was crystallized from dioxane to give pale yellow crystals in 71% yield; mp 173–175°C; IR: $\bar{\nu} = 3400$, 3150 (NH), 1710 (C=O), 1600 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.3$ (t, $J = 7.0$ Hz, CH_3), 4.1 (q, $J = 7.0$ Hz, CH_2), 7.3–8.1 (m, 15ArH) 10.5 (s, 2NH); 11.2 (s, NH) ppm.

5,6-Dihydro-3,4,6-triphenyl-s-triazolo[3′,4′:2,3]pyrimido[4,5-c]pyridazine (**18**, $C_{25}H_{17}N_7$)

A sample of 2 g of **16** in glacial acetic acid (10 cm^3) was stirred at room temperature for about 4 h. The solid product which formed during stirring was collected and recrystallized from acetic acid to give dirty white crystals in 52% yield; mp >300; IR: $\bar{\nu} = 3300$ (NH), 1610 (C=N) cm^{-1}; EI: $m/z = 415$.

5,6-Dihydro-5-imino-7-(5-amino-4-ethoxycarbonylpyrazol-1-yl)-3,4,6-triphenyl-pyrimido[4,5-c]pyridazine (**19**, $C_{30}H_{24}N_8O_2$)

A mixture of 2 g of **6a** (0.005 mol) and 0.85 g of ethyl ethoxymethylene cyanoacetate (0.005 mol) in 30 cm^3 of ethanol was refluxed in the presence of 1 cm^3 of glacial acetic acid for 4 h. After cooling the solid product was filtered off and recrystallized from dioxane to give brown crystals in 67% yield; mp 260–263°C; IR: $\bar{\nu} = 3300$ (NH), 3400, 3480 (NH_2), 1690 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.5$ (t, $J = 7.0$ Hz, CH_3), 2.5 (q, $J = 7.0$ Hz, CH_2), 5.5 (s, NH_2), 7.2–7.9 (m, 15ArH) ppm.

5,6-Dihydro-5-imino-7-(5-amino-4-cyanopyrazol-1-yl)-3,4,6-triphenylpyrimido[4,5-c]-pyridazine (**20**, $C_{28}H_{19}N_9$)

A mixture of 2 g of **6a** (0.005 mol) and 0.6 g of ethoxymethylenemalonitrile (0.005 mol) in 30 cm^3 of ethanol was refluxed in the presence of 1 cm^3 of glacial acetic acid for 4 h. After cooling the brown solid product was collected and recrystallized from dioxane to give brown crystals in 53% yield; mp 253–255°C; IR: $\bar{\nu} = 3100$, 3300, 3450 (NH, NH_2), 2220 (C≡N) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta =$ 4.5 (s, NH_2), 7.3–7.9 (m, 15ArH), 9.3 (s, NH) ppm.

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