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New Synthetic Approaches to Condensed Pyridazinones: Alkylpyridazinyl Carbonitriles as Building Blocks for the Synthesis of Condensed Pyridazinones

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Abstract.— The pyridazinyl-5-carbonitriles (3a-d) were prepared via condensing the aryl hydrazones 2a-d with ethyl cyanoacetate. Similar condensation of 2a with malononitrile gives the pyrido[2,3-c]pyridazine derivative (8). Compounds 3a-d reacted with elemental sulphur in refluxing ethanolic solutions in the presence of triethylamine to yield the thieno[3,4-d]pyridazinones 9a-d. The 1,3,4-thiadiazaacenaphthene 12 was prepared via reacting 9e with diethyl fumarate. In contrast, only the phthalazines 14a-c were produced from the reaction of 13a-c with 9e. Compounds 9a-c reacted with benzaldehyde to yield 19a. Condensation of 3a, c, d with dimethylformamide dimethylacetal afforded 19b-d. Compound 19b cyclized into 20b when refluxed in acetic acid in the presence of ammonium acetate. This same product was obtained from the reaction of the amide 3g with formaldehyde in refluxing pyridine. The reaction of 3a, c with arylidenemalononitrile (23a, b) gives the tetrahydrophthalazines 25a-c. The pyridazin-4-ones 26a-d were prepared from the reaction of 2a-d with dimethylformamide dimethylformamide dimethylacetal in refluxing pridine.

INTRODUCTION

Fused pyridazinones comprise a very interesting class of compounds because of their significant biological and pharmaceutical activities.¹⁻⁵ As part of our studies aimed at developing simple and efficient syntheses of polyfunctional heteroaromatics from readily obtainable starting materials,⁶⁻⁸ we have previously reported the synthesis of 4-methyl-6-oxopyridazine-5-carbonitrile derivatives via condensation of active methylene nitriles with ethyl 2-arylhydrazono-3-oxobutyrates.^{6,8} The synthesized pyridazinones were shown to be excellent precursors for the synthesis of condensed polyfunctionally substituted pyridazinones.⁶

RESULTS AND DISCUSSION

In conjunction with our studies aimed at exploring the synthetic potentials of alkyl-6-oxopyridazin-5carbonitriles, we report here on the synthesis and reactivity of the 4-ethyl-6-oxopyridazine-5-carbonitrile derivatives **3a-d**. In addition, a new route for the synthesis of 5-methyl-4-pyridazinones is reported. The work has resulted in developing the synthesis of a variety of polyfunctionally substituted condensed pyridazines that looks interesting for utility in further chemical transformations as well as for biological evaluation. Thus, we have found that **2a-d**, prepared in excellent yields via coupling **2a**, **b** with aromatic diazonium salts, condensed readily with ethyl cyanoacetate to yield **3a-d** in good yields. This is a further extension of our pyridazine synthesis from the reaction of **2e** with active methylenenitriles.⁷⁻⁹



However, in contrast to the reported formation of 6-amino-5-cyano-4-methyl-l-phenylpyridazinium-3carboxylate from the reaction of ethyl 2-phenylhydrazono-3-oxobutyrate (2e) and malononitrile, the reaction of 2a with malononitrile in the presence of ammonium acetate, afforded a product with a molecular formula $C_{17}H_{15}N_7O$. This was thus considered to be 8. Formation of this product is assumed to result from condensation of 2a with the initially formed 4, resulting from dimerization of malononitrile in the presence of ammonium acetate, to yield 5 that readily afforded 6, and subsequently the ester 7. The latter, then reacts with ammonia yielding the final product 8. Self condensation of two molecules of malononitrile in the presence of ammonium acetate to yield 4 has been reported earlier.¹⁰ The difference in the behaviour between 2a and 2e is a result of decrease in reactivity of carbonyl group in 2a as compared to that of 2e, thus allowing initial self reaction of malononitrile.



Compound 3a-d reacted with elemental sulphur to yield the thieno[3,4-d]pyridazines 9a-d. The formation of 9a-d is a further demonstration of the scope of our thienoazine synthesis.⁶



9a, $R_1 = CH_3$, $R_2 = CO_2CH_3$, $Ar = C_6H_5$ 9b, $R_1 = CH_3$, $R_2 = CO_2CH_3$, $Ar = C_6H_4CH_3$ -p9c, $R_1 = CH_3$, $R_2 = CO_2CH_3$, $Ar = C_6H_4OCH_3$ -p9d, $R_1 = CH_3$, $R_2 = CN$, $Ar = C_6H_5$ 9e, $R_1 = H$, $R_2 = CO_2C_2H_5$, $Ar = C_6H_4OCH_3$ -p9f, $R_1 = H$, $R_2 = CO_2C_2H_5$, $Ar = C_6H_5$

In previous work we have shown that the thienopyridazine derivative 9e readily adds electron poor olefins to yield cycloadducts that readily decompose into phthalazines via elimination of hydrogen sulphide or hydrogen molecule, depending on both nature of olefin and applied reaction conditions.^{6,11} To our knowledge, this was the first successful cycloaddition of electron poor olefins and acetylenes to amino condensed thiophenes. Recently, Döpp et $al.^{12}$ have reported a second example of such addition. The reaction of aminothienobenzopyranimine with diethyl fumarate proceeded in a way similar to that reported by us.⁶ However, the reaction of this thienobenzopyranimine with dimethyl acetylenedicarboxylate resulted in rearrangement of the formed cycloadduct into thiepinobenzopyran.¹⁰ In order to see if such rearrangement can also occur with our systems we have investigated further the behavior of 9a-e toward electron poor olefins. The work enabled the development of a synthesis of polyfunctionally substituted 1,3,4-thiadiazaacenaphthene derivatives 12 and 18a, 18b via a new, previously unreported, reaction pathway. Thus, reacting 9e with diethyl fumarate, in refluxing dioxane in the presence of acetic acid, gave 12 in a moderate yield. Compound 12 is assumed to be formed via intermediacy of the cycloadduct 10 which first rearranges into 11 then undergoes autooxidation and cyclizes into 12 via loss of ethanol. In contrast, 9e reacted with the nitrostyrene derivatives 13a-c to yield the phthalazines 14a-c. Trials to isolate the product of the decomposition of the intermediary formed [4 + 2] cycloadduct with loss of hydrogen sulfide, as has been reported earlier, failed.¹¹



Compounds **9a-d** were recovered unreacted when refluxed with acrylonitrile in dioxane solution in the presence of acetic acid for two hours. In contrast to this, **9e** has been reported to add smoothly acrylonitrile under similar conditions.⁶ Although the introduction of methyl function at C7 of **9a-d** is expected to raise the HOMO-LUMO energy of the system, this same function interacts sterically with the substituents on the olefin, thus raising the energy needed to attain the transition state for the reaction. This seems to be the controlling factor.



Compounds 9a, 9b reacted with acrylonitrile when refluxed in acetic acid solution for twenty hours, to yield products of addition and methanol elimination. These are assigned structure 18, and are assumed to be formed via rearrangement of the initially formed cycloadduct 15 to 16. The latter is perhaps in equilibrium with 17. Cyclization of 16 via loss of methanol yields 18. This is different to the reported behaviour of 9e, 9f toward acrylonitrile where ready elimination of hydrogen sulfide or autooxidation of the formed cycloadduct has been observed.⁶ This difference in behaviour is the result of steric factors. Thus, if 17 would lose hydrogen sulphide to yield a phthalazine, the methyl and ester function in this product would experience large steric interactions. The structure proposed for compounds 18a, b was established with certainty by X-ray diffraction of a crystal of 18a (see later on). Furthermore ¹H NMR showed an AB multiplet near δ 3.00 ppm for CH₂ protons at position 8.



19a, R = Ar = C_6H_5 , X = CO_2H **19b**, R = N(CH_3)_2, Ar = C_6H_5 , X = CO_2CH_3 **19c**, R = N(CH_3)_2, Ar = $C_6H_4OCH_3$ -*p*, X = CO_2CH_3 **19d**, R = N(CH_3)_2, Ar = C_6H_5 , X = CN

Similar to the reported ready condensation of 3e with aromatic aldehydes to yield the styryl derivative 19a was formed on reacting 3a with benzaldehyde. Water separated during the condensation effects hydrolysis of methyl ester. Compound 19a was also formed from reaction of 3f with benzaldehyde. Compound 3f has been prepared by hydrolysis of 3a with acetic acid in the presence of hydrochloric acid.

Compounds 3a, 3c and 3d condensed with dimethylformamide dimethylacetal to yield the condensation products 19b-d. The reaction of 19d with acetic acid-hydrochloric acid mixture afforded a product that may be formulated as 20a or 21a. In order to establish the structure of this product, the amide 3g was synthesized via refluxing 3a with concentrated ammonia in DMF at 100°C for thirty minutes. This amide reacted with formaldehyde, in refluxing pyridine. However, instead of isolating 21a, an amide was formed. Thus, this amide may again be either 20b or 21b. In an other approach compound 3a was treated with dimethylformamide dimethylacetal and the product formed (19b) was treated with acetic acid in the presence of ammonium acetate. Again, the same amide was formed. Structure 20 was established for the reaction product 20a, b based on UV spectra which showed a pattern completely different to that of 22, recently obtained in our laboratory via reacting 3e with dimethylformamide dimethylacetal and treatment of the product with aniline.¹³ Thus, whereas 22 is a red compound with strong UV maxima at 430 nm, compounds 20a, 20b are yellow ones and do not absorb at above 400 nm. Their UV showed maxima at 371 and 365 nm, respectively.



The reaction of 3a, 3c with arylidenemalononitrile 23a, 23b afforded 1:1 adducts which may be formulated as 24 or 25. The tetrahydrophthazine structure 25 is established based on IR and ¹H NMR which revealed the presence of an amino group and the absence of CH multiplets in the range of δ 2-4 ppm other than the one for H-7, which would be present in the spectrum of 24. Formation of 25 from 23a, b and 3a, c is assumed to occur via initial formation of Michael adducts 24. Similar mechanism has been proposed earlier to account for the formation of phthalazines via reaction of 3e with 23.6.14-16 In contrast to this report, the formed adduct did not aromatize by losing hydrogen cyanide. It seems that the adducts 25 are more stable than the products of hydrogen cyanide elimination as in the latter products, several functional groups should be in one plane, and as such should experience strong steric interaction.



In order to investigate the activity of alkyls in pyridazin-4-ones, we have developed a new synthesis of 5methylpyridazin-4-ones. Thus, reacting **2a-d** with dimethylformamide dimethylacetal gives the pyridazinones **26a-d** in good yield. The IR spectra of **26a-d** did not show any band for ring CO above 1650 cm⁻¹. This may indicate the importance in this compound of the resonance form **27**. We have found that the methyl function in **26a-d** is inactive toward aldehydes.



X-Ray Crystallographic Study of Compound 18a.

The molecular structure and the numbering scheme is depicted in Fig. 1. The dihydrothiophene ring displays a similar pattern of bond distances and angles to that of thiophthalide (a dihydrobenzo[b]thiophenone, CSD refcode: THOPHT),¹⁷ the only similar ring reported so far. The observed distances in the 2-phenylpyridazinone are in good agreement with the mean values we have calculated from five structures containing this group (FEWBAK, GAXVIK, KUPNOY, PACVOE and PYRZON). The heteroring adopts a rather flat distorted boat conformation (Table 1) probably as a consequence of the fused rings as it happens in the PYRZON where a benzothiepine ring is sharing the C(3)-C(4) bond. The conformation of the dihydrothiophene ring as well as the other six-membered ring is defined by the ring puckering parameters,¹⁸ the rings show a distorted envelope and a 1,3-diplanar conformations respectively (Table 1).

The formation of the N-H intramolecular hydrogen bond to the carbonyl O6 atom weakens the C=O, displaying a length of 1.220(3) Å which aids π electron delocalization of the electron lone pairs giving rise to a C5-C6 bond shorter than the tabulated Csp²-Csp² of 1.465(18) Å in C=C-C(=O)(-C) fragments.^{19a} The phenyl ring, that makes an angle of 47.9(1)° with the pyridazinone one, allows the formation of the C19-H19--O6 interaction. The NH₂ group is involved in a bifurcated hydrogen bond (Table 2) with two O6 atoms giving rise to dimers (Fig 2) through symmetry centers. These dimers form piles along the c axis by means of weak C-H--O interactions. The crystal is built up of these piles that do no bear any interaction between them other than the van der Waals ones.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Shimadzu IR-740 spectrometer. ¹H and ¹³C NMR spectra were recorded on a Bruker AC-80 spectrometer (for compound **18a** a Varian Gemini 200 spectrometer was used) with [²H₆]DMSO as solvent and TMS as an internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on GS/MS INCOS XL Finnigan MAT. Microanalyses were performed on LECO CHNS-932. Compounds **3e** and **9e** were prepared using our recently published procedures.^{14,15}



Fig.1 .-Molecular structure showing the displacement parameters drawn at the 30% level. Hydrogen atoms are shown as spheres of arbitrary radii. Dotted line means hydrogen bond.

N1-N2	1.346(2)	N2-C3	1.304(2)	 C3-C4	1.401(3)
C4-C5	1.355(3)	C5-C6	1.451(2)	N1-C6	1.410(3)
C6-O6	1.220(3)	C3-C7	1.490(2)	C7-07	1.201(3)
\$1-C7	1.785(2)	S1-C8	1.845(2)	C4-C8	1.500(2)
C8-C12	1.531(2)	C8-C9	1.526(3)	C9-C10	1.519(3)
C10-C13	1.416(3)	C13-N13	1.145(3)	C10-C11	1.373(2)
C11-N11	1.351(2)	C11-C5	1.471(3)	N1-C14	1.443(2)
N2-N1-C14	114.6(1)	N2-N1-C6	126.2(1)	C6-N1-C14	119.1(1)
C3-N2-N1	115.2(2)	C4-C3-N2	124.6(2)	C4-C3-C7	113.7(1)
C7-C3-N2	121.6(2)	C8-C4-C5	123.2(2)	C5-C4-C3	120.6(2)
C8-C4-C3	116.2(2)	C11-C5-C6	123.2(2)	C11-C5-C4	119.3(2)
C4-C5-C6	117.4(2)	C5-C6-N1	115.0(2)	N1-C6-O6	119.8(2)
C5-C6-O6	125.2(2)	S1-C7-C3	108.0(1)	C3-C7-O7	127.3(2)
S1-C7-07	124.7(2)	C8-S1-C7	95.0(1)	S1-C8-C4	103.6(1)
S1-C8-C9	114.2(1)	S1-C8-C12	108.2(1)	C9-C8-C4	108.2(2)
C12-C8-C4	110.1(1)	C12-C8-C9	112.2(2)	C8-C9-C10	109.6(2)
C9-C10-C11	123.0(2)	C9-C10-C13	119.2(2)	C13-C10-C11	117.4(2)
C10-C13-N13	176.5(2)	C10-C11-C5	116.9(2)	C10-C11-N11	124.1(2)
N11-C11-C5	119.1(2)	C15-C14-C19	122.0(2)		
N1-N2-C3-C4	2.0(3)	N2-C3-C4-C5	-8.6(3)	C3-C4-C5-C6	5.2(3)
C4-C5-C6-N1	3.3(2)	C5-C6-N1-N2	-10.5(3)	C6-N1-N2-C3	7.8(2)
C3-C7-S1-C8	11.7(1)	C7-S1-C8-C4	-16.7(1)	S1-C8-C4-C3	18.6(2)
C8-C4-C3-C7	-11.2(2)	C4-C3-C7-S1	-2.6(2)	C5-C4-C8-C9	-38.8(2)
C4-C8-C9-C10	48.8(2)	C8-C9-C10-C11	-35.4(2)	C9-C10-C11-C5	3.1(3)
C10-C11-C5-C4	12.9(2)	C11-C5-C4-C8	6.8(3)	N2-N1-C14-C15	-45.3(2)

Table 1. Selected geometrical parameters $(\text{\AA}, ^{\circ})$.



Fig.2.-Crystal packing down the c axis.

Х-НҮ	Х-Н	XY	HY	Х-НҮ
N11-H111O6	0.86(3)	2.773(2)	2.12(3)	132(3)
С19-Н19Об	0.98(3)	2.861(3)	2.60(3)	95(2)
N11-H111O6(-x+1,-y+1,-z)	0.86(3)	3.033(2)	2.30(3)	143(3)
C12-H121O7(x,y,z-1)	0.96(3)	3.357(2)	2.63(3)	134(2)

Table 2. Hydrogen interactions. (Å,°).

General procedure for the preparation of Methyl 2-arylhydrazono-3-oxopentanoates (2a-c) and 3-oxo-2-phenylhydrazonopentanonitrile (2d). To a solution of 1a or 1b (0.1 mol) in ethanol (100 mL) 20 sodium acetate (20.0 g, 0.3 mol) were added. The mixture was then treated gradually with stirring at room temperature with a solution of the appropriate aryldiazonium salt (prepared from 0.1 mol of aromatic amine and the appropriate quantities of hydrochloric acid and sodium nitrite). The product was separated on standing, collected by filtration and crystallised from ethanol.

Methyl 2-phenylhydrazon-3-oxo-pentanoate (2a). Compound 2a was obtained as yellow crystals from ethanol (94%); m.p. 74°C; IR: 3500-3450 (NH), 1685 (ester CO) and 1660 cm⁻¹ (acyl CO); ¹H NMR: δ 1.10 (t, 3H, CH₃, J = 7 Hz), 2.90 (q, 2H, CH₂, J = 7 Hz), 3.80 (s, 3H, OCH₃), 7.20-7.60 (m, 5 H, Ar-H) and 11.8 ppm (br, 1H, NH); MS: m/z 234 (M⁺); Anal. Calcd. for C₁₂H₁₄N₂O₃ (234.25): C, 61.52; H, 6.02; N, 11.96. Found: C, 61.87; H, 6.08; N, 12.16.

Methyl 2-(p-methylphenylhydrazone)-3-oxopentanoate (2b). Compound 2b was obtained as yellow crystals from ethanol (92%); m.p. 71.5°C; IR: 3450-3300 (NH), 1700 (ester CO) and 1660 cm⁻¹ (acyl CO); ¹H NMR: δ 1.10 (t, 3H, CH₃, J = 7 Hz), 2.30 (s, 3H, CH₃), 2.90 (q, 2H, CH₂, J = 7 Hz), 3.80 (s, 3H, OCH₃), 7.00-7.60 (m, 4H, Ar-H) and 11.7 ppm (br, 1H, NH); Anal. Calcd. for C₁₃H₁₆N₂O₃ (248.28): C, 62.88; H, 6.49; N, 11.28. Found: C, 62.87; H, 6.45; N, 11.30.

Methyl 2-(*p*-methoxyphenylhydrazone)-3-oxopentanoate (2c). Compound 2c was obtained as red crystals from ethanol (96%); m.p. 90°C; IR: 3450-3300 (NH), 1700 (ester CO) and 1680 cm⁻¹ (acyl CO); ¹H NMR: δ 1.10 (t, 3H, CH₃, J = 7 Hz), 2.95 (q, 2H, CH₂, J = 7 Hz), 3.75 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 6.80-7.60 (m, 4H, Ar-H) and 11.8 ppm (br, 1H, NH); Anal. Calcd. for C₁₃H₁₆N₂O₄ (264.27): C, 59.08; H, 6.10; N, 10.60. Found: C, 58.77; H, 6.08; N, 10.63.

2-Phenylhydrazono-3-oxo-pentanonitrile (2d). Compound **2d** was obtained as yellow crystals from ethanol (73%); m.p. 127-129°C; IR: 3450-3000 (NH), 2225 (CN) and 1670 cm⁻¹ (CO); ¹H NMR: δ 1.20 (t, 3H, CH₃, J = 7 Hz), 2.90 (q, 2H, CH₂, J = 7 Hz), 7.10-7.40 (m, 5H, Ar-H) and 9.65 ppm (br, 1H, NH); ¹³C NMR: δ 195.70 (CO), 142.42, 129.89, 125.27, 116.06 (phenyl carbons), 113.47 (CN), 111.33 (C=N), 29.89 (CH₂), 8.49 (CH₃); Anal. Calcd. for C₁₁H₁₁N₃O (201.22): C, 65.67; H, 5.51; N, 20.88. Found: C, 65.71; H, 5.70; N, 20.85.

General procedure for the preparation of methyl 1-aryl-5-cyano-4-ethyl-1,6-dihydro-6oxopyridazin-3-carboxylates (3a-c) and 4-ethyl-1,6-dihydro-6-oxo-l-phenyl-pyridazin-3,5dicarbonitrile (3d). In a 100 mL flask, a suspension of 2a-d (0.01 mol) in benzene (50 mL) was treated with ammonium acetate (5.0 g) and acetic acid (2.0 mL). The reaction flask was then provided with a device for continual elimination of water, then heated under reflux for 6 h. The benzene layer was then evaporated. The resulting solid product was triturated with ethanol then collected by filtration and crystallized from ethanol.

Methyl 5-cyano-1,6-dihydro-4-ethyl-6-oxo-1-phenylpyridazin-3-carboxylate (3a). Compound 3a was obtained as pale yellow crystals (85%); m.p. 139.2°C; IR: 2225 (CN), 1730 (ester CO) and 1670 cm⁻¹ (ring CO); ¹H NMR: δ 1.13 (t, 3H, CH₃, J = 7 Hz), 3.00 (q, 2H, CH₂, J = 7 Hz), 3.90 (s, 3H, OCH₃) and 7.50-7.60 ppm (m, 5H, Ar-H); ¹³C NMR: δ 162.18 (ester CO), 156.06 (C-4), 155.54 (C-1), 136.11 (C-6), 140.14,

129.22, 128.89, 125.61 (phenyl carbons), 114.20 (CN), 112.95 (C-5), 53.00 (OCH₃), 25.26 (CH₂), 13.33 (CH₃); MS: m/z 283 (M⁺); Anal. calcd. for C₁₅H₁₃N₃O₃ (283.28): C, 63.59; H, 4.63; N, 14.83. Found: C, 63.64; H, 4.63; N, 14.83.

Methyl 5-cyano-1,6-dihydro-4-ethyl-1-(*p*-methylphenyl)-6-oxopyridazine-3-carboxylate (3b). Compound 3b was obtained as pale yellow crystals from ethanol (81%); m.p. 133-134°C; IR: 2225 (CN), 1730 (ester CO) and 1680 cm⁻¹ (ring CO); ¹H NMR: δ 1.30 (t, 3H, CH₃, J = 7 Hz), 2.40 (s, 3H, CH₃), 3.00 (q, 2H, CH₂, J = 7 Hz), 3.90 (s, 3H, OCH₃), and 7.20-7.50 ppm (m, 4H, Ar-H); Anal. calcd. for C₁₆H₁₅N₃O₃ (297.30): C, 64.63; H, 5.09; N, 14.14. Found: C, 64.88; H, 5.02; N,14.05.

Methyl 5-cyano-1,6-dihydro-4-ethyl-1-(*p*-methoxyphenyl)-6-oxopyridazine-3-carboxylate (3c). Compound 3c was obtained as orange crystals from ethanol (90%); m.p. 109°C; IR: 2225 (CN), 1730 (ester CO) and 1680 cm⁻¹ (ring CO); ¹H NMR: δ 1.30 (t, 3H, CH₃, J = 7 Hz), 3.00 (q, 2H, CH₂, J = 7 Hz), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), and 7.10-7.50 ppm (m, 4H, Ar-H); Anal. calcd. for C₁₆H₁₅N₃O₄ (313.30): C, 61.33; H, 4.83; N, 13.51. Found: C, 61.24; H, 4.88; N, 13.51.

1,6-Dihydro-4-ethyl-6-oxo-1-phenylpyridazine-3,5-dicarbonitrile (3d). Compound **3d** was obtained as violet crystals from ethanol (50%); m.p. 145-147°C; IR: 2225 (CN) and 1680 cm⁻¹ (ring CO); ¹H NMR δ 1.40 (t, 3H, CH₃, J = 7 Hz), 2.95 (q, 2H, CH₂, J = 7 Hz), and 7.20-7.50 (m, 5H, Ar-H); Anal. calcd. for C₁₄H₁₀N₄O (250.25): C, 67.19; H, 4.03; N, 22.19. Found: C, 67.33; H, 4.48; N, 21.89.

Preparation of 5-amino-6-cyano-7,8-dihydro-4-ethyl-7-imino-1-phenylpyrido[2,3*c*]pyridazine -3-carboxamide (8). A mixture of 2a (0.01 mol), malononitrile (0.66 g, 0.01 mol) and ammonium acetate (5.0 g) was heated at 180° for 30 min. The solid product formed on cooling, was triturated with water, collected by filtration and crystallized from ethanol. Compound 8 was obtained as violet crystals (45%); m.p. > 200°C; IR: 3600-3400 (NH and NH₂), 2225 (CN) and 1665 cm⁻¹ (amide CO); ¹H NMR: δ 1.20 (t, 3H, CH₃, J = 7 Hz), 2.95 (q, 2H, CH₂, J = 7 Hz), 7.30-7.60 (m, 10H, Ar-H, NH and NH₂); Anal. calcd. for C₁₇H₁₅N₇O (333.35): C, 61.25; H, 4.53; N, 29.41. Found: C, 61.30; H, 4.64; N, 29.30.

Preparation of methyl 5-amino-3-aryl-3,4-dihydro-7-methyl-4-oxothieno[3,4-d]pyridazine-1carboxylate (9a-c) and 5-amino-3,4-dihydro-7-methyl-3-phenyl-4-oxothieno[3,4-d]pyridazine-1-carbonitrile (9d). To a suspension of 3a-d (0.05 mol) in dioxane (30 mL), elemental sulfur (0.05 mol) and few drops of triethylamine were added. The reaction mixture was refluxed for 3 h then poured onto water. The solid product, so formed, was then collected by filtration and crystallized from ethanol.

Methyl 5-amino-3,4-dihydro-7-methyl-4-oxo-3-phenylthieno[3,4-*d*]pyridazine-1-carboxylate (9a). Compound 9a was obtained as brown crystals from ethanol (77%); m.p. 186°C; IR: 3550-3300 (NH₂), 1730 (ester CO) and 1640 cm⁻¹ (ring CO); ¹H NMR: δ 2.30 (s, 3H, CH₃), 3.90 (s, 3H, OCH₃), 7.20-7.60 ppm (m, 7H, Ar-H and NH₂); ¹³C NMR: δ 164.02 (ester CO), 160.07 (C-4), 158.15 (C-1), 135.92 (C-5), 140.48, 128.32, 126.96, 125.82 (phenyl carbons), 121.00 (C-7), 115.17 (C-7a), 104.04 (C-4a), 52.71 (OCH₃), 12.94 (CH₃); Anal . calcd . for C₁₅H₁₃N₃O₃S (315.34): C, 57.14 ; H , 4.16 ; N, 13.33 ; S, 10.17. Found: C, 56.93; H, 4.20; N, 13.32; S, 10.15.

Methyl 5-amino-3,4-dihydro-7-methyl-3-(*p*-methylphenyl)-4-oxothieno[3,4-*d*]pyridazine-1carboxylate (9b). Compound 9b was obtained as brown crystals from ethanol (61%); m.p. 178°C; IR: 3500-3300 (NH₂),1730 (ester CO) and1640 cm⁻¹ (ring CO); ¹H NMR: δ 2.30 (s, 3H, CH₃), 2.35 (s, 3H, CH₃), 3.90 (s, 3H, OCH₃) and 7.05-7.40 ppm (m, 6H, Ar-H and NH₂); ¹³C NMR: δ 164.09 (CO), 159.99 (C-4), 158.25 (C-1), 136.36 (C-5), 138.09, 135.78, 128.78, 125.65 (phenyl carbons), 121.10 (C-7), 115.04 (C-7a), 104.22 (C-4a), 52.69 (OCH₃), 20.55 (CH₃), 12.98 (CH₃); Anal. calcd. for C₁₆H₁₅N₃O₃S (329.36): C, 58.35; H, 4.59; N, 12.76. Found: C, 58.19; H, 4.72; N,12.67.

Methy] 5-amino-3,4-dihydro-7-methyl-3-(*p*-methoxyphenyl)-4-oxothieno[3,4-d]pyridazine-1carboxylate (9c). Compound 9c was obtained as golden brown crystals from ethanol (69%); m.p. 162°C; IR: 3500-3400, 3300 (NH₂), 1730 (ester CO) and 1680 cm⁻¹ (ring CO); ¹H NMR: δ 2.30 (s, 3H, CH₃), 3.80 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃) and 6.80-7.50 ppm (m, 6H, Ar-H and NH₂); Anal. calcd. for C₁₆H₁₅N₃O₄S (345.36): C, 55.65; H, 4.38; N, 12.17; S, 9.27. Found: C, 56.08; H, 4.77; N, 12.15; S, 9.63.

5-Amino-3,4-dihydro-7-methyl-3-phenyl-4-oxothieno[3,4-*d*]pyridazine-l-carbonitrile (9d). Compound 9d was obtained as dark crystals from ethanol (88%); m.p. 235°C; IR: 3450, 3300 (NH₂), 2225 (CN), and 1670 cm⁻¹ (ring CO); ¹H NMR: δ 2.60 (s, 3H, CH₃), and 7.30-7.70 ppm (m, 7H, Ar-H and NH₂); Anal. calcd. for C₁₄H₁₀N₄OS (282.69): C, 59.48; H, 3.56; N, 19.81; S, 11.34. Found: C, 59.70; H, 3.95; N, 19.60; S, 11.23.

Diethyl 6-amino-4,5-dihydro-2,5-dioxo-4-(*p*-methoxyphenyl)-1,3,4-thiadiazaacenaphthene-7,8-dicarboxylate (12). A suspension of 9e (0.01 mol) in dioxane (30 mL) and acetic acid (5 mL) was treated with diethyl fumarate (0.01 mol). The reaction mixture was refluxed for 5 h then poured onto water. The solid product, so formed, was collected by filtration and crystallized from ethanol. This compound was obtained in 62% yield as orange crystals, m.p. 192-193°C; IR: 3600-3400 (NH₂), 1720 (thiolacetone CO), 1695 (ester CO) and 1640 cm⁻¹ (ring CO); ¹H NMR: δ 1.25 (t, 3H, CH₃, J = 7 Hz); 1.30 (t, 3H, CH₃, J = 7 Hz), 3.85 (s, 3H, OCH₃); 4.25 (q, 2H, OCH₂, J = 7 Hz), 4.40 (q, 2H, OCH₂, J = 7 Hz), 7.1-7.6 (m, 4H, Ar-H) and 7.70 ppm (br, 2H, NH₂); ¹³C NMR: δ 191.85 (C-2), 169.60 (ester CO), 168.72 (ester CO), 163.45 (C-5), 163.39 (C-2a), 152.03, 143.08, 137.87, 136.16, 133.51, 131.76, 118.04, 117.56, 116.97, 115.95 (Aromatic carbons), 66.57 (CH₂), 65.85 (CH₂), 59.57 (OCH₃), 17.93 (CH₃) and 17.70 (CH₃); MS: m/z 470 (M⁺); Anal. calcd. for C₂₂H₁9N₃O₇S (469.65): C, 56.29; H, 4.07; N, 8.98. Found: C, 56.25; H, 4.07; N, 8.98.

General procedure for the preparation of ethyl 5-amino-7-aryl-3,4-dihydro-3-(*p*-methoxyphenyl)-8-mercapto-6-nitro-4-oxophthalazine-1-carboxylates (14a-c). A suspension of 9e (0.01 mL) in dioxane (30 mL) and acetic acid (5 mL) was treated with 13a-c. The reaction mixture was refluxed for 6 h then poured onto water. The solid product was collected by filtration and crystallized from ethanol.

Ethyl 5-amino-3,4-dihydro-3-(*p*-methoxyphenyl)-7-(*p*-methylphenyl)-8-mercapto-6-nitro-4oxophthalazine-1-carboxylate (14a). Compound 14a was obtained as brown powder from ethanol (67%); m.p. 143-145°C; IR: 3560-3300 (NH₂), 1720 (ester CO) and 1650 cm⁻¹ (ring CO); ¹H NMR: δ 1.16 (t, 3H, CH₃, J = 7 Hz), 2.30 (s, 3H, CH₃), 3.70 (s, 3H, OCH₃), 4.30 (q, 2H, OCH₂ J = 7 Hz), 5.20 (br, 1H, SH) and 6.80-7.60 ppm (m, 10H, Ar-H and NH₂); Anal. calcd. for C₂₅H₂₂N₄O₆S (506.53): C, 59.28; H, 4.37; N, 11.06. Found: C, 58.91; H, 4.72; N, 11.05.

Ethyl 5-amino-3,4-dihydro-3,7-di-(p-methoxyphenyl)-6-nitro-4-oxophthalazine-1-carboxylate (14b). Compound 14b was obtained as dark brown crystal from ethanol (42%); m.p.112-114°C; IR: 3550-3400 (NH₂), 1720 (ester CO) and 1650 cm⁻¹ (ring CO); ¹H NMR: δ 1.16 (t, 3H, CH₃, J = 7 Hz), 3.75 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 4.30 (q, 2H, OCH₂ J = 7Hz), 5.20 (brs, 1H, SH) and 6.70-7.60 ppm (m, 10H, Ar-H and NH₂); Anal. calcd. for C₂₅H₂₂N₄O₇S (522.53): C, 57.46; H, 4.24; N, 10.72. Found: C, 57.33; H, 4.32; N, 10.65.

Ethyl 5-amino-3,4-dihydro-3-(*p*-methoxyphenyl)-8-mercapto-4-oxo-7-phenylphthalazine-1carboxylate (14c) .Compound 14c was obtained as brown crystals from ethanol (61%); m.p. 190-192°C; IR: 3420-3320 (NH₂), 1710 (ester CO) and 1660 cm⁻¹ (ring CO); ¹H NMR: δ 1.30 (t, 3H, CH₃, J = 7 Hz), 3.80 (s, 3H, OCH₃), 4.30 (q, 2H, OCH₂ J = 7 Hz), 5.30 (brs, 1H, SH) and 6.90-7.70 ppm (m, 10H, Ar-H and NH₂); Anal. calcd. for C₂₄H₂₀N₄O₆S (492.51): C, 58.52; H, 4.09; N, 11.37; S, 6.50. Found: C, 58.70; H, 4.07; N, 11.11; S, 6.17.

General procedure for the preparation of 6-amino-4-aryl-8,8a-dihydro-2,5-dioxo-8a-methyl-1, 3,4-thiadiazaacenaphthene-7-carbonitriles (18a, b): A solution of 9a-b (0.01 mol) in acetic acid (50 mL) was treated with acrylonitrile (0.01 mol). The reaction mixture was refluxed for 20 h, then evaporated *in vacuo*. The remaining product was triturated with water, and the resulting solid product was collected by filtration and crystallized from dioxane.

6-Amino-8a-methyl-8,8a-dihydro-2,5-dioxo-8a-methyl-4-phenyl-1,3,4-thiadiazaacenaphthene-7-carbonitrile (18a): Compound 18a was obtained as red crystals (90%); m.p. 224°C; IR: 3500~3250 (NH₂), 2195 (CN), 1710 (ester CO), 1665 (ring CO) and 1625 cm⁻¹ (NH₂); ¹H NMR: δ 2.10 (s, 3H, CH₃), 2.81 and 3.06 (AB system, 2H, CH₂, $J_{AB} = -15.5$ Hz),7.35 (s, 2H, NH₂) and 7.80 ppm (m, 6H, Ar-H and OH); ¹³C NMR: δ 193.19 (C-2), 161.28 (C-5), 153.03 (C-2a), 144.89 (C-6), 143.90, 133.29, 132.90, 130.08 (phenyl carbons), 124.02 (C-5a), 123.73 (CN), 101.17 (C-7), 75.58 (C-8a), 52.61 (C-8) and 29.54 (CH₃); Anal. calcd for C₁₇H₁₂N₄O₂S (336.30): C, 60.34; H, 3.90; N, 16.77, S, 9.33. Found: C,60.71; H, 3.60; N, 16.66; S, 9.53.

6-Amino-8,8a-dihydro-2,5-dioxo-8a-methyl-4-methoxyphenyl-1,3,4-thiazaacenaphthene-7carbonitrile (18b): Compound **18b** was obtained as red crystals (85%); m.p. 275°C; IR: 3500-3300 (NH₂), 2195 (CN), 1715 (ester CO), 1665 (ring CO) and 1640 cm⁻¹ (NH₂); ¹H NMR: δ 2.90 (s, 3H, CH₃), 3.00 (s, 2H, CH₂), 7.10 (s, 2H, NH₂) and 7.2-7.5 ppm (m, 5H, Ar-H); Anal. calcd for C₁₉H₁₆N₄O₃S (350.32): C, 61.51; H, 4.45; N, 16.01; S, 9.15. Found: C, 61.71; H, 4.03; N, 16.00; S, 9.15.

5-Cyano-1,6-dihydro-4-(1-methylstyryl)-6-oxo-1-phenylpyridazine-3-carboxylic acid (19a). A solution of **3a** or **3f** (0.01 mol) in pyridine (30 mL) was treated with benzaldehyde (0.01 mol) then refluxed for 6 hours. The reaction mixture was left to cool to room temperature then poured onto water. The solid product, so formed, was collected by filtration and crystallized from ethanol. This compound was obtained in 69% yield as yellow crystals, m.p. 202-204°C; IR: 3500-3300 (OH dimer), 1710 (carboxylic CO) and 1675 cm⁻¹ (ring CO); ¹H NMR: δ 2.20 (s, 3H, CH₃), 6.70 (s, 1H, C=CH), 7.35-7.70 (m, 10H, Ar-H) and 8.6 ppm (brs, 1H, OH); Anal. calcd. for C₂₁H₁₅N₃O₃ (357.36): C, 70.58; H, 4.23; N, 11.76. Found: C, 70.63; H, 4.39; N, 12.15.

5-Cyano-1,6-dihydro-4-ethyl-6-oxo-1-phenylpyridazine-3-carboxylic acid (3f). A solution of 3a (0.01 mol) in acetic acid-hydrochloric acid (2:1) mixture (30 mL) was refluxed for 1 h, then poured onto water. The solid product, so formed, was collected by filtration and crystallized from ethanol. This compound was obtained in 91% yield as yellow crystals; m.p. 230-231.5°C; IR: 3500-3350 (OH dimer), 2225 (CN), 1760 (carboxylic CO) and 1660 cm⁻¹ (ring CO); ¹H NMR: δ 1.30 (t, 3H, CH₃, J = 7 Hz), 3.00 (q, 2H, CH₂, J = 7 Hz) 4.00 (brs, 1H, OH) and 7.60 ppm (m, 5H, Ar-H); Anal. calcd. for C₁₄H₁₁N₃O₃ (269.25): C, 62.45; H, 4.12; N, 15.61. Found: C, 62.56; H, 4.18; N, 15.68.

Reaction of 3c, 3d with dimethylformamide dimethylacetal. A solution of **3c, 3d** (0.01 mol) in acetic anhydride (30 mL) was treated with dimethylformamide dimethylacetal (0.01 mol). The reaction mixture was then refluxed for 10-15 min. After cooling down to room temperature it was poured onto water. The solid precipitate was collected by filtration and crystallized from ethanol.

Methyl 5-cyano-1,6-dihydro-4-[2-(N,N-dimethylamino-1-methylethenyl)]-6-oxo-1-(p-methoxyphenyl)pyridazine-3 carboxylate (19c). Compound 19c was obtained as dark brown crystals from ethanol (70%); m.p. 169-170°C; IR: 2225 (CN), 1730 (ester CO) and 1656 cm⁻¹ (ring CO); ¹H NMR: δ 1.95 (s, 3H, CH₃), 3.00 (s, 6H, N(CH₃)₂), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 6.85 (s, 1H, C=CH) and 7.00-7.60 ppm (m, 4H, Ar-H); Anal. calcd. for C₁₉H₂₀N₄O₄ (368.39): C, 61.94; H, 5.47; N, 15.20. Found: C, 61.72; H, 5.52; N, 14.73.

1,6-Dihydro-4-[2-(*N*,*N*-dimethylamino-1-methylethenyl)]-6-oxo-1-phenyl-pyridazine-3,5-dicarbonitrile (19d). Compound 19d was obtained as red crystals from ethanol (71%); m.p. 205°C; IR: 2225 (CN) and 1660 cm⁻¹ (ring CO); ¹H NMR: δ 2.25 (s, 3H, CH₃), 3.15 (s, 6H, N(CH₃)₂), 7.10 (s, 1H, C=CH); and 7.30-7.70ppm (m, 5H, Ar-H); Anal. calcd. for $C_{17}H_{15}N_5O$ (305.33): C, 66.87; H, 4.95; N, 22.94. Found: C, 66.93; H, 4.89; N, 22.92.

5-Cyano-1,6-dihydro-4-ethyl-6-oxo-1-phenylpyridazine-3-acetamide (3g). To 3a (0.05 mol) dissolved in DMF, an excess of ammonia was added. The mixture was refluxed for 30 min, then kept at room temperature overnight. The mixture was then poured onto water and the solid product, so formed, was filtered and crystallized from ethanol. Compound 3g was obtained as colorless crystals (83%); m.p. 187-189°C, IR: 3375-3205 (NH₂), 2230 (CN) and 1670-1650 (ring and amide CO); ¹H NMR: δ 1.28 (t, 3H, CH₃, J = 7 Hz), 2.95 (q, 2H, CH₂, J = 7 Hz) and 7.2-8.2 ppm (m, 7H, Ar-H and NH₂); Anal. calcd. for C₁₄H₁₂N₄O₂ (268.27): C, 62.68; H, 4.51; N, 20.89. Found: C, 62.60; H, 4.59; N, 21.03.

4,5-Dioxo-8-methyl-3-phenyl-3,4,5,6-tetrahydropyrido[**3,4-***d*]**pyridazine-1-carbonitrile** (**20a**). A solution of **19e** (0.01 mol) was added to a mixture acetic acid- hydrochloric acid (2:1) (30 mL). The reaction mixture was refluxed for 1 h then poured onto water. The solid product, so formed, was then collected by filtration and crystallized from ethanol. Compound **20a** was obtained as yellow crystals (78%); m.p. 268°C; IR: 3435-3220 (NH), 2225 (CN) and 1703, 1673 cm⁻¹ (ring CO); ¹H NMR: δ 2.30 (s, 3H, CH₃), 7.30-7.75 (m, 5H, Ar-H), 7.80 (s, 1H, ring H-7) and 11.6 ppm (brs, 1H, NH); Anal. calcd. for C₁₅H₁₀N₄O₂ (278.27): C, 64.74; H, 3.62; N, 20.13. Found: C, 64.70; H, 3.82; N, 19.89.

Preparation of 4,5-dioxo-8-methyl-3-phenyl-3,4,5,6-tetrahydropyrido[3,4-d]pyridazine-1carboxamide (20b). Method A: A suspension of 3g (0.01 mol) in pyridine (30 mL) was treated with formaldehyde (0.01 mol). The mixture was refluxed for 4 h and left to cool, then poured onto water. The so formed product was filtered and crystallized from ethanol. Method B: A suspension of 3a (0.01 mol) in dioxane (30 mL) was treated with dimethyl formamide dimethylacetal (0.01 mol) and refluxed for 30 min. Then, to the refluxed solution, acetic acid (0.01 mol) and ammonium acetate were added and the solution was further refluxed for 2 hours. When cooled, the solution was poured onto water and the solid product, so formed, was filtered and crystallized from ethanol. Compound 20b was obtained as brown crystals (85%); m.p. 235°C; IR: 3460-3260 (NH₂); 1699 (amide CO); 1662 cm⁻¹ (ring CO); ¹H NMR: δ 2.35 (s, 3H, CH₃); 7.30 (s, 1H, ring H-7), 7.60 (s, 7H, Ar-H and NH₂), and 11.50 (brs, 1H, NH); Anal. Calcd. for C₁₅H₁₂N₄O₃ (296.28): C, 60.80; H, 4.08; N, 18.91. Found: C, 60.83; H, 4.26; N, 18.79.

General procedure for the preparation of methyl-5-amino-3,7-diaryl-6,6-dicyano-8-methyl-4oxo-3,4,6,7-tetrahydrophthalazine-1-carboxylate (25a-c). A solution of 3a, c (0.01 mol) in pyridine (20 mL) was treated with 23a, b (0.01 mol). The reaction mixture was refluxed for five hours then poured onto water. The solid product, so formed, was collected by filtration and crystallized from ethanol.

Methyl 5-amino-6,6-dicyano-8-methyl-4-oxo-3,7-diphenyl-3,4,6,7-tetrahydrophthalazine-1carboxylate (25a). Compound 25a was obtained as brown powder from ethanol (63%); m.p. 243°C; IR: 3420-3300 (NH₂), 2225 (CN), 1745 (ester CO) and 1660 cm⁻¹ (ring CO); ¹H NMR: δ 1.90 (s, 3H, CH₃), 2.50 (m, 1H, phthalazine H-7), 3.90 (s, 3H, OCH₃), 7.20-7.70 (m, 10H, Ar-H) and 8.00 ppm (brm, 2H, NH₂); Anal. calcd. for C₂₅H₁₉O₃N₅ (437.45): C, 68.64; H, 4.37; N, 16.01. Found: C, 68.98; H, 4.40; N, 15.91.

Methyl 5-amino-7-(*p*-chlorophenyl)-6,6-dicyano-8-methyl-4-oxo-3-pheny-3,4,6,7-tetrahydrophthalazine-1-carboxylate (25b). Compound 25b was obtained as gray crystals from methanol (57%); m.p. 185°C; IR: 3500-3450 (NH₂), 2200 (CN) and 1660-1640 cm⁻¹ (ester and ring CO); ¹H NMR: δ 1.60 (s, 3H, CH₃), 2.50 (m, 1H, phthalazine H-7), 3.80 (s, 3H, OCH₃) and 7.20-7.80ppm (m, 11H, Ar-H and NH₂); Anal . calcd . for C₂₅H₁₈ClN₅O₃ (471.89) : C, 63.63; H, 3.84; N, 14.84 . Found: C, 63.91; H, 5.08; N, 14.93.

Methyl 5-amino-7-(*p*-chlorophenyl)-6,6-dicyano-8-methyl-3-(*p*-methoxyphenyl)-4-oxo-3,4,6, 7-tetrahydrophthalazine-1-carboxylate (25c). Compound 25c was obtained as dark green crystals from ethanol (69%); m.p. 192°C; IR: 3500-3400 (NH₂), 2220 (CN) and 1750 cm⁻¹ (ester CO); ¹H NMR: δ 2.10 (s, 3H, CH₃), 2.50 (m, 1H, phthalazine H-7), 3.80 (s, 3H, OCH₃), 6.90-7.90 ppm (m, 8H, Ar-H) and 8.30 ppm (brm, 2H, NH₂); Anal. calcd. for C₂₆H₂₀ClN₅O₄ (501.92): C, 62.21; H, 4.01; N, 13.95. Found: C, 61.74; H, 4.17; N, 14.07.

General procedure for the preparation of methyl 1-aryl-1,4-dihydro-5-methyl-4oxopyridazine-3-carboxylate (26a-c) and 1,4-dihydro-5-methyl-4-oxo-1-phenyl-pyridazine-3carbonitrile (26d). A solution of 2a-d (0.01 mol) in dioxane (30 mL) was treated with dimethylformamide dimethylacetal (0.01 mol). The reaction mixture was refluxed for 10 h then the solvent was evaporated. The solid product so formed was washed and crystallized from ethanol. Methyl 1,4-dihydro-5-methyl-4-oxo-1-phenylpyridazine-3-carboxylate (26a). Compound 26a was obtained as yellow crystals (86%); m.p. 161°C; IR: 1735 cm⁻¹ (ester CO); ¹H NMR: δ 2.1 (s, 3H, CH₃), 3.90 (s, 3H, OCH₃), 7.30-7.60 (m, 5H, Ar-H) and 8.30ppm (s, 1H, pyridazine H-6); Anal. calcd. for C₁₃H₁₂N₂O₃ (244.24): C, 63.85; H, 4.95; N, 11.47. Found: C, 63.56; H ,5.20; N,11.36.

Methyl 1,4-dihydro-5-methyl-1-(*p*-methylphenyl)-4-oxopyridazine-3-carboxylate (26b). Compound 26b was obtained as yellow crystals (90%); m.p. 138-140°C; IR: 1730 cm⁻¹ (ester CO); ¹H NMR: δ 2.0 (s, 3H, CH₃), 2.30 (s, 3H, CH₃), 3.95 (s, 3H, OCH₃), 7.20-7.70 (2d, 4H, Ar-H) and 8.8 ppm (s, 1H, pyridazine H-6); Anal. calcd. for C₁₄H₁₄N₂O₃ (258.27): C, 65.10; H, 5.46; N, 10.86. Found: C, 65.02; H, 5.46; N,10.84.

Methyl 1,4-dihydro-l-(*p*-methoxyphenyl)-5-methyl-4-oxopyridazine-3-carboxylate (26c). Compound 26c was obtained as orange crystals (85%); m.p. 142-144°C; IR: 1730 cm⁻¹ (ester CO); ¹H NMR: δ 2.05 (s, 3H, CH₃), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 7.00-7.50 (2d, 4H, Ar-H) and 8.8 ppm (s, 1H, pyridazine H-6); ¹³C NMR: δ 167.40 (C-4), 164.02 (ester CO), 159.43 (C-3), 146.28 (C-6), 139.28, 136.61, 130.96, 114.99 (phenyl carbons), 123.06 (C-5), 55.95 (OCH₃), 52.81 (OCH₃), 39.28 (CH₃); Anal. calcd. for C₁₄H₁₄N₂O (274.26): C,61.31; H,5.14; N,10.21. Found: C, 61.11; H, 5.13; N, 10.26.

1,4-Dihydro-5-methyl-4-oxo-1-phenylpyridazine-3-carbonitrile (26d). Compound **26d** was obtained as violet crystals (65%); m.p. 201°C; IR: 2225 cm⁻¹ (CN); ¹H NMR: δ 2.10 (s, 3H, CH₃), 7.40-7.70 (m, 5H, Ar-H) and 9.00 ppm (s, 1H, pyridazine H-6); Anal. calcd. for C₁₂H₉N₃O (211.22): C, 68.23; H, 4.31; N, 19.72. Found: C, 68.06; H,4.31, N,19.72.

X ray Analysis.- A summary of data collection and refinement process is given in Table 3. All non-hydrogen atoms were found by direct methods (SIR92)^{19b} and the structure was refined with a full matrix least-squares procedures on Fobs using anisotropic displacement parameters. All hydrogens were located on a difference Fourier synthesis and included and refined isotropically in the last cycles. The scattering factors were taken from the International Tables for X-Ray Crystallography.²⁰ Table 4 lists the final atomic coordinates and equivalent thermal factors for non-hydrogen atoms. The calculations were carried out with the XTAL,²¹ PESOS²² and PARST²³ set of programs running on a VAX 6410 computer.

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Table 3. Crystal analysis parameters at room temperature.

Crystal data					
Chemical formula	$C_{17}H_{12}N_4O_2S$	Crystal system	Triclinic		
Mr	336.367	Space group	P-1		
a (Å)	12.5258(13)	α(°)	98.761(4)		
b (Å)	9.7370(8)	β(°)	83.463(4)		
c (Å)	6.6076(3)	γ́(°)	105.775(7)		
Z	2	Dx (gr/cm ³)	1.46		
V (Å ³)	764.26(8)	Radiation	CuKa		
Wavelength (Å)	1.5418	No. of reflections for			
θ range for lattice parameters (°)	3-45	lattice parameters:	62		
Absorption coefficient (cm ⁻¹)	20.4	Temperature (K)	295		
Crystal colour	Deep red	Crystal description	Prism		
Crystal size (mm)	0.50 x 0.17 x 0.23				
Data collection					
Diffractometer type	Philips PW1100, four circle. Graphite oriented monochromator.				
Measurement time	1 min./reflection	Detector apertures (°)	1 x 1		
Collection method	ω/2θ scans	θmax (°)	65		
No. of standard reflections (interval)	2 (90 min.). No decay	Scan width (°)	1.5		
No. of independent reflections	2612	No. of observed reflections, I>20(I)	2452		
Refinement					
Treatment of hydrogen atoms	See experimental part	ull matrix			
Secondary extinction correction (10 ⁴)	0.23(2)	-			
R	0.038	No. of parameters refined	266		
wR	0.044	Degrees of freedom	2186		
$(\Delta \rho)$ max (e/Å ³)	0.32	Ratio of freedom	9.2		
<shift error=""></shift>	0.001	Max. thermal value (Å ²)	U33[C22]=0.122(2)		
Weighting scheme: Empirical as to give	ve no trends in <∞∆2F> vs. <i< td=""><td>Fobsi> and $<\sin\theta/\lambda>$.</td><td></td></i<>	Fobsi> and $<\sin\theta/\lambda>$.			

Table 4. Final atomic coordinates and Ueq= $(1/3)\Sigma[\text{Uij}\cdot a_i \cdot \cdot a_j \cdot a_i \cdot a_j \cdot \cos(a_i,a_i)] \times 10^3$

Atom	x	у	z	Ueq	Atom	x	у	z	Ueq
S1	0.21947(4)	-0.04618(5)	0.65086(7)	49.6(2)	C10	0.1755(1)	0.1618(2)	0.1737(3)	42.7(6)
NI	0.5481(1)	0.2933(2)	0.3932(2)	39.9(5)	C11	0.2836(1)	0.2342(2)	0.1251(3)	39.7(5)
N2	0.5162(1)	0.2031(2)	0.5372(2)	40.7(5)	N11	0.3161(1)	0.3131(2)	-0.0329(2)	46.7(5)
C3	0.4140(1)	0.1236(2)	0.5331(2)	39.4(5)	C12	0.2375(2)	-0.1175(2)	0.2333(3)	48.9(6)
C4	0.3404(1)	0.1244(2)	0.3889(2)	37.6(5)	C13	0.0927(2)	0.1792(2)	0.0578(3)	49.0(6)
C5	0.3678(1)	0.2240(2)	0.2563(3)	39.1(5)	N13	0.0291(2)	0.2002(2)	-0.0371(4)	71.5(8)
C6	0.4788(1)	0.3205(2)	0.2586(3)	44.8(6)	C14	0.6636(1)	0.3728(2)	0.3896(3)	41.7(5)
06	0.5140(1)	0.4197(2)	0.1558(3)	71.2(6)	C15	0.7090(2)	0.4359(2)	0.5722(4)	53.4(7)
C7	0.3629(2)	0.0290(2)	0.6945(3)	45.5(6)	C16	0.8214(2)	0.5082(3)	0.5656(5)	70.7(9)
07	0.4075(1)	0.0078(2)	0.8340(2)	59.4(5)	C17	0.8847(2)	0.5177(3)	0.3814(5)	76.5(10)
C8	0.2316(1)	0.0117(2)	0.3942(2)	41.0(5)	C18	0.8380(2)	0.4517(3)	0.2008(5)	74.1(10)
C9	0.1403(1)	0.0803(2)	0.3592(3)	45.3(6)	C19	0.7267(2)	0.3774(2)	0.2032(3)	54.6(7)

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