Formation of 5-alkylidenepyrazol-4(1*H*)-ones and 3-amino-6-aryl-5-cyanopyridazine-4-carboxylates from arenealdehyde thiosemicarbazones and unsaturated 1,2-diesters

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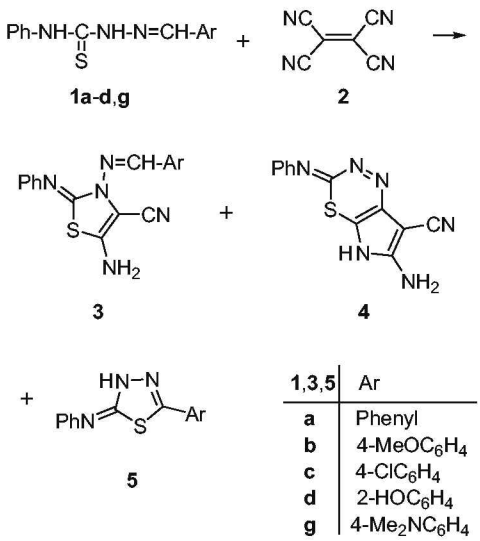
The reaction of arenealdehyde 4-phenylthiosemicarbazones **1a–f** with dimethyl ethynedicarboxylate (**6**) gave methyl [3-aryl-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1*H*-pyrazol-5-ylidene]ethanoates **10a–f** in 73–79% yield, while, by reaction with diethyl (*E*)-2,3-dicyanobutenedioate (**7**), compounds **1a–f** are transformed into ethyl [3-aryl-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1*H*-pyrazol-5-ylidene]cyanoacetates **15a–f** (54-61%) and ethyl 3-amino-6-aryl-5-cyanopyridazine-4-carboxylates **24a–f** (22–26%). Rationales for these transformations are presented.

Keywords: aza-enamine reactivity, conjugate addition, heterocyclisation, α,β-unsaturated diesters

Heterocyclisations of aldehyde thiosemicarbazones and related compounds to 1,2,4-triazolines and 1,3,4-thiadiazolines have been effected by oxidising agents,[1] especially oxidising transition metal salts,[2,3] and by sodium ethoxide.[4] Recently we reported that the reaction of various aldehyde 4-phenylthiosemicarbazones **1a–d,g** with ethenetetracarbonitrile (TCNE, **2**) effected the formation of the heterocyclic systems **3–5** (Scheme 1).[5] Thus, products originating from both incorporation of TCNE fragments (**3**, **4**) and of plain oxidative cyclisation (**5**) were found.[5]

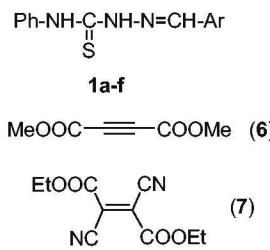


1,3,5	Ar
a	Phenyl
b	4-$MeOC_6H_4$
c	4-ClC_6H_4
d	2-HOC_6H_4
g	4-$Me_2NC_6H_4$

Scheme 1

This fascinating versatility in the reaction of **1** with **2** justifies further investigation of the reactivity of aldehyde 4-phenylthiosemicarbazones **1** towards other electron poor unsaturated compounds such as dimethyl ethynedicarboxylate (**6**) and diethyl (*E*)-2,3-dicyanobutenedioate (**7**) (Scheme 2). The latter two compounds offer C/C multiple bonds and the electrophilic carbonyl and nitrile carbon atoms for attack by nucleophiles, and compounds **1** may react at least with their sulfur atom, N2, and N4 as nucleophilic sites. Thus, several options for interactions between **1** and **6** or **7** may be envisaged, as will be outlined later.

In their reactions with acetylenic mono- and diesters, *N,S*-dinucleophiles as thioamides, thioureas, and thiosemicarbazides, clearly show the involvement of the thioxo group.[6] 1,3-Thiazin-4-ones are formed from **6** and propiolic

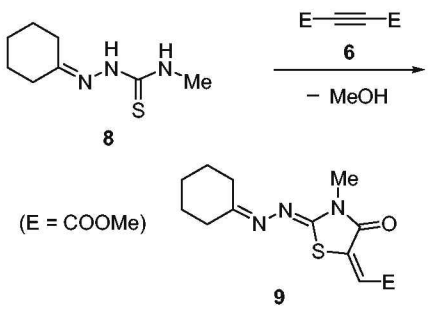


1	Ar
a	Phenyl
b	4-$MeOC_6H_4$
c	4-ClC_6H_4
d	2-HOC_6H_4
e	2-Thienyl
f	2-Furyl

Scheme 2

esters with primary thioamides,[7] and methyl phenylpropiolate and 1-acylthiosemicarbazides give triazolothiazinones.[8]

Less attention so far have received the reactions of thiosemicarbazones with acetylenic esters. Such reactions have been studied for isatine 3-thiosemicarbazone[9] and, after an earlier account on the transformation of cyclohexanone 4-methylthiosemicarbazone (**8**) with **6** yielding the thiazolidin-4-one **9** (Scheme 3),[10] more examples of the conversion of a series of aldehyde and ketone thiosemicarbazones (unsubstituted at N4) with **6** into analogous thiazolidinones under microwave activation have been reported.[11]



Scheme 3

Dialkyl (*E*)-2,3-dicyanobutenedioates ("dialkyl dicyanofumarates") as **7** have been recognised as viable and versatile alternatives to TCNE (**2**) as building blocks for the generation of molecule-based magnets.[12] Syntheses of nitrogen heterocycles starting from dicyanofumaric diesters and various vicinal diamines have also been reported.[13] These investigations have shown that, while the reactivity of **6** is based on the addition of nucleophiles to the triple bond and condensation of an XH-nucleophilic site with one of the ester groups, the dicyanofumarate offers both replacement of and nucleophilic attack at the cyano group as additional options.

In the light of the above mentioned findings, we undertook to investigate the reactions of thiosemicarbazones **1a–f** with

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Dedicated to Prof. Gerald Henkel on the occasion of his 60th birthday

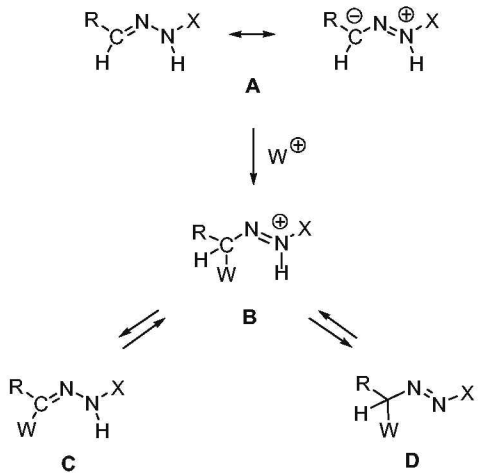
dimethyl ethynedicarboxylate (**6**) and diethyl dicyanofumarate (**7**) (see Scheme 2).

Results and discussion

Reaction with dimethyl ethynedicarboxylate (**6**)

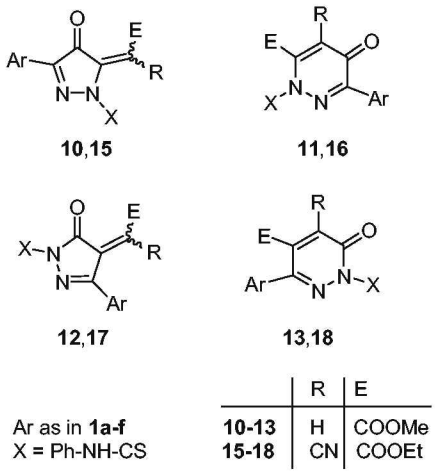
In methanol at reflux temperature, the thiosemicarbazones **1a–f** reacted to give one single product each in 73–79% yield. From the elemental analyses and the mass spectra a net release of methanol (MW 32) had occurred. The mass spectra showed the following four fragments common to all products: [M^+–31], *m/z* 150, *m/z* 135 [Ph–NCS^+], [M^+–ArCN]. In the IR spectra (see also Table 1) two carbonyl bands were seen in the ranges 1710–1720 cm^{-1} and 1680–1685 cm^{-1}, and a band between 1615 and 1630 cm^{-1} was assigned to a C=N vibration. The ^1H NMR spectra did reveal a vinylic CH between 6.78 and 6.62 ppm, while the azomethine CH for **1b** resonated at 8.1 ppm.[14] In four cases the ^{13}C NMR spectra have been obtained showing signals at 191.7–191.9 (C=O, ring), 178.4–178.8 (C=S), and 166.8–167.1 (C=O, ester) ppm. From these data it follows that the PhNHCS group was not changed, thus the thioxo sulfur did not act as a nucleophile. One ester group was converted into a ring carbonyl, and both the azomethine carbon and N2 of **1** had taken part in the heterocyclisation. Since **6** can offer only electrophilic sites for attack, the methine carbon of **1** had to act as a nucleophile in the sense of an "umpolung".

This behaviour is not unexpected, since aldehyde hydrazones (Scheme 4, **A**: R and X = H, alkyl, aryl) are known to react as aza-enamines[15-17] towards suitable electrophiles W^+, and this behaviour should consequently also be open to aldehyde thiosemicarbazones **10a–f** (Scheme 4, **A**: R = aryl), since the phenylthiocarbamoyl group is not a strong acceptor and may even be sterically hindered. Pick-up of an electrophile (W^+) would generate the iminium ion **B**, which may be deprotonated to both **C** an **D**. Product **C** is thus derived from **A** by substitution of the methine proton by W. The methine carbon of aldehyde hydrazones in this way may be attacked by various electrophiles as enones[17] α,β–unsaturated nitriles,[18,19] aldehydes,[20] aldimines,[21] sulfonyl isocyanates[15] and sulfenyl chlorides.[22]



Scheme 4

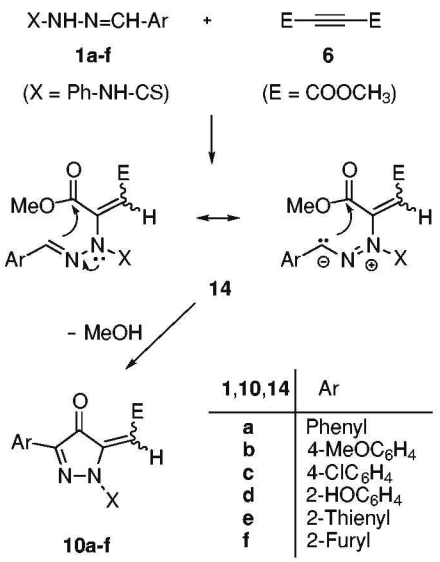
Taking all the restrictions from above into account, a total of four alternative product structures from two categories (Scheme 5) may be expected from the following reactions each involving two steps: (1) N2 attacks the triple bond, followed by attack of the methine CH on either the α- or β-ester group, giving rise to structures **10** or **11**, respectively. (2) The methine CH attacks the triple bond, followed by attack of N2 at either the α- or the β-ester group, respectively, giving rise to structures **12** or **13**, respectively.



Scheme 5

Of course, the same products would be formed if the order of the individual consecutive steps were interchanged. There is no way so far to experimentally discriminate between these options. As can be seen easily, structures **10–13** are all positional isomers. Only structure **10**, however, accomodates all spectral data listed above, especially the ^{13}C chemical shifts for the ring carbonyl C atoms (C4), see Table 1 for comparison of all relevant spectral data with literature data of suitable model substances for **10** and its alternatives **11–13.**

For the latter alternative structural types, in every case ring carbonyl ^{13}C resonances are considerably upfield to those which have been observed, and the IR frequencies to be expected are typical for such α,β-unsaturated esters which do not show any further conjugation to β-amino groups. This additional conjugation, shifting the ester IR frequencies to smaller wavenumbers, is, however, to be found for products **10**. The ring C=O frequencies observed rule out both pyridazinone structures (**11** and **13**) while they are agreeable also for structure **12**. The values found for the ester C=O ^{13}C resonances do not allow an assignment beyond doubt (see Table 1).



Scheme 6

A rationale for the formation of **10a–f** is given in Scheme 6 under the assumption that the process starts with the attack of N2 of **1** on the triple bond of **6** to generate intermediate **14**, and that the methine carbon atom displaces the methoxy group in its α-ester function. The remarkable feature is that

Table 1 (A) Experimental ^{13}C NMR (δ rel. to TMS [ppm]) and IR (ν [cm^{-1}], KBr) data for the C=O groups (ring and ester) in products **10a–f** and **15a–f** (this work) and (B) literature data[23-44] of compounds comparable to **10**, **15** and their structural alternatives **11–13**, **16–18** (see Scheme 5)

Sect.	Structures	Ring C=O		Ester C=O	
		^{13}C	IR	^{13}C	IR
A	Products **10a–f**	191.7–191.9[a]	1710–1720	166.8–167.1[a]	1680–1685
	Products **15a–f**	190.8–191.3	1710–1720	165.9–166.5	1675–1680
B	Pyrazol-4(1*H*)-ones comparable to **10**, **15**	188.6, 189.1[23] 203.4[24]	1700–1705[24] 1730,1735[33]	163.7, 164.7[23]	
	Comparable β-aminoacrylates	–	–	169.3–169.9[25]	1685,[b,26] 1677[27]
	Pyridazin-4(1*H*)-ones comparable to **11**, **16**	164.9,[28] 167.5[29]	1610,[30] 1590,[28] 1620[31]	[c]	1720[31]
	Pyrazol-3(2*H*)-ones comparable to **12**, **17**	160.3–163.4[23]	1710–1735[32]	[c]	[d]
	Pyridazin-3(2*H*)-ones comparable to **13**, **18**	161.4–163.7[34] 161,3–163.4,[35] 157.2[37] 159.5–160.0[40]	1680,[36] 1690,[37] 1649–1671[38,41] 1650–1670[39]	[c]	1720[38,41] 1730[36,42]

[a]Determined for **10a,b,e,f.** [b]For methyl 2-cyano-3-dimethylaminoacrylate. [c]Typical α,β-unsaturated esters: $\delta_{C=O}$ = 164.9, 166.0, 166.5 ppm.[43] [d]Typical α,β-unsaturated esters: ν = 1725-1750 cm^{-1}.[44]

the C=S group is not involved. This is in contrast to the report by Darehcordi *et al.*[11] who found the formation of 1,3-thiazolidin-4-ones from (albeit 4-unsubstituted) both arene aldehyde and ketone thiosemicarbazones and **6**.

Reaction with diethyl dicyanofumarate (**7**)

Equimolar solutions of **1a–f** and **7** in ethyl acetate formed, on warming to reflux temperature for 14–18 hours, a major (54–61%) and a minor (22–26%) product in each case. From the mass spectral data and the elemental analyses, the following characteristics can be delineated:

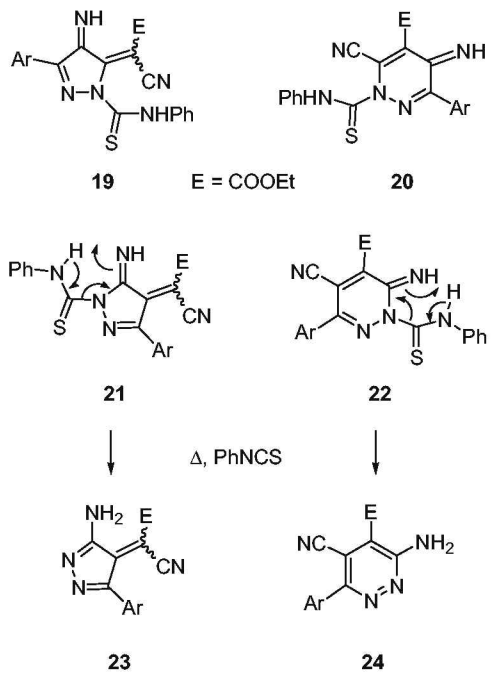
The *major products* are formed from the starting materials with loss of one molecule each of HCN and ethanol. As in the formation of **10**, the *N*-phenylthiocarbamoyl group remains intact as supported by the ^{13}C shift for the C=S group (approx. 178.6 ppm) and the ready loss of *m/z* 135 (PhNCS), thus the two sites of **1** involved in the addition/heterocyclisation again are N2 and the methine carbon of **1** by virtue of its azaenamine reactivity as outlined above. Again, no ^1H signal for a methine CH is found near 8.1 ppm.

One nucleophilic attack, namely that on the C=C bond of **7**, has to effect the displacement of HCN, the other that of EtOH from one of the ester groups in analogy to the formation of **10**. These restrictions point to options **15–18** for the structure of the main product (see Scheme 5). These options represent the products from the following four *a priori* possible reactions, sorted into two categories encompassing two options each: (1) N2 displaces HCN; the methine CH attacks either the α- or the β-ester group displacing EtOH, thus generating structures **15** or **16**, respectively. (2) The methine CH displaces HCN; N2 attacks either the α- or the β-ester group, thus generating structures **17** or **18**, respectively.

It should be stated again that the products do not allow to clarify the order of the individual steps in either case.

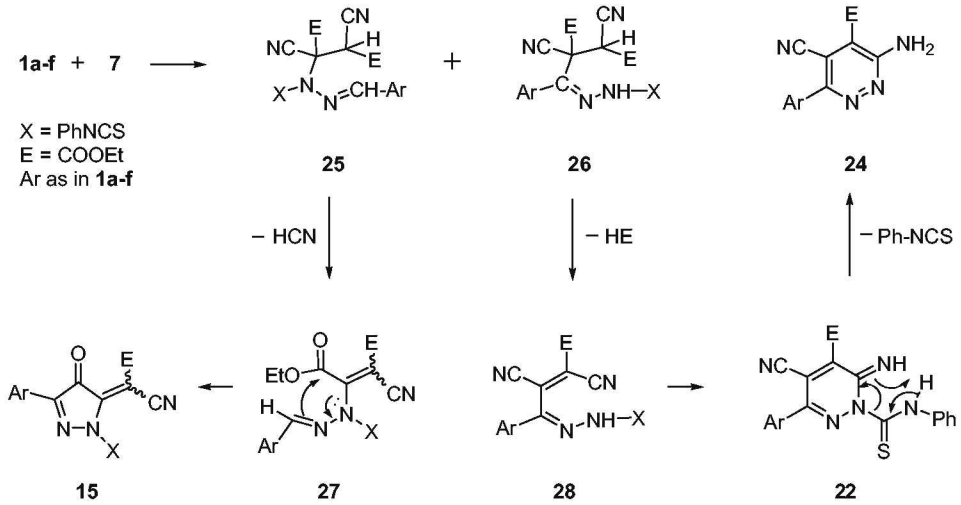
The spectroscopic data found for the major products fit best for structure **15** which is perfectly analogous to structure **10** discussed above. Again the ^{13}C chemical shifts for the ring protons at δ = 190.8–191.3 ppm are too high for the alternatives **16–18** with their amidic (**17**, **18**) or vinylogous amidic (**16**) substructures, and the δ (C=O) values reported[18] (168.3–169.9 ppm) for several *trans* β-(dialkylamino)acrylates match well with the resonances found for the ester C=O groups (see Table 1), and the same can be said about the IR absorptions for these groups.

Formation of the *minor products*, on the other hand, requires the loss of an ester function in the form of ethyl formate instead of HCN and also the ready loss of phenylisothiocyanate as can be accounted for by the elemental analyses and the mass spectra. Since there is no ring C=O group and one ester group is still present (δ ^{13}C=O = 167.2–167.6 ppm for the substituent pattern **a,b,e,f**, ^1H A_2X_3 patterns around δ 1.2 and 4.2 ppm for *one* ethoxy group), the heterocyclisation must involve one nitrile group generating a primary amino function (^1H NMR: δ = 6.23-6.31 ppm for 2H). These findings strongly suggest that the byproducts are formed from one of the four potential precursors **19–22** (Scheme 7).



Scheme 7

These precursors may have to be seen as formed from **7** and **1a–f** via the following two categories of reactions (all in either the given or in the inverted order): (3) N2 attacks the C=C bond and displaces H-COOEt; the methine CH adds to either the α- or the β-CN group, thus generating structures **19** or **20**, respectively. (4) The methine CH attacks the C=C bond



Scheme 8

displacing H-COOEt; N2 adds to either the α- or the β-CN group, thereby generating structures **21** or **22**, respectively.

A spontaneous thermal loss of phenyl isothiocyanate is conceivable for precursors **21** and **22**, respectively, giving rise to the final product structures **23** and **24**. But only in the latter case (**22** → **24**) this reaction is both kinetically favoured and driven by the maximum energy release due to aromatisation. This suggests structure **24** for the minor product. All spectral characteristics of **24** not mentioned so far (see Experimental) are also in accord with the suggested structure.

Scheme 8 outlines a rationale for the formation of both products **15** and **24** under the reasonable assumption, that **1a–f** and **7** form two types of adducts, namely **25** from N2 addition and **26** from CH addition to the C=C double bond. Adduct **25** releases HCN and forms the main product **15** via **27**, and **26** releases H-COOEt and undergoes heterocyclisation to precursor **22** via **28**. The pyridazine **24** is, in turn, formed from **22** via the most favourable pathway of phenylisothiocyanate release (see above and Scheme 7). Formation of the 4-alkylidene-4*H*-pyrrole **23** from the presumed precursor **21** (Scheme 7) is regarded less likely.

One question yet to be tackled is whether the azaenamine reactivity of the methine CH is probable to be retained or hampered in the intermediates from addition of N2 of **1a–f** to the electrophilic multiple bonds, *i.e.* in intermediates **14** (Scheme 6) and **27** (Scheme 8). These intermediates certainly do not show coplanarity of all unsaturated groups due to steric encumbering. Also, condensation of the methine CH with either ester group in **14** requires an out-of-plane attack. Finally, the question whether the products **10** and **15** have an *E*- or *Z*-configuration, has to be left unanswered at present.

Conclusion

The products obtained from the conjugate addition of arenealdehyde 4-phenylthiosemicarbazones to unsaturated diesters **6** and **7**, followed by heterocyclisation, are neither thiaheterocycles nor heterocyclic thiones. While neither the S–C–N + C_2 nor the N–C(S)–N + C_2 mode of cyclisation is found in this study, a novel C–N–N + C_2 mode is observed due to the aza-enamine reactivity shown by the starting materials **1**. This reactivity requires the availability of the methine proton, the reactions reported are thus not open to (and have not been found[10,11] for) ketone thiosemicarbazones.

Experimental

Melting points have been determined using open capillaries on a Gallenkamp melting point apparatus and are uncorrected. Elemental analyses were determined by Microanalytical centre, Cairo University, Egypt. The IR spectra were recorded with a Shimadzu 408 instrument using potassium bromide. 500 MHz ^{1}H and 125 MHz ^{13}C NMR spectra were recorded from DMSO-d_6 solutions on a Bruker DRX500 spectrometer. Chemical shifts are expressed as δ [ppm] with reference to tetramethylsilane as an internal standard, s = singlet, d = doublet, t = triplet, m = multiplet and br = broad. ^{13}C assignments were made with the aid of distortionless enhancement by polarisation transfer (DEPT) 135/90 spectra (qC = sp^2 quaternary carbon atoms). Mass spectra were recorded on a AMD 605 instrument in EI mode at 70 eV ionisation energy. Preparative layer chromatography (PLC) used air dried 1.0 mm thick layers of slurry applied silica gel (Merck PF_{254}) on 48 cm wide and 20 cm high glass plates using the solvents listed. Zones were detected by quenching of indicator fluorescence upon exposure to 254 nm light and eluted with acetone.

Starting materials

4-Phenylthiosemicarbazones **1a–f** were synthesised by reaction of 4-phenylthiosemicarbazide with the proper aldehyde according to published procedures: Benzaldehyde 4-phenylthiosemicarbazone (**1a**),[45] 4-methoxybenzaldehyde 4-phenylthiosemicarbazone (**1b**),[14] 4-chlorobenzaldehyde 4-phenylthiosemicarbazone (**1c**),[46] 2-hydroxybenzaldehyde 4-phenylthiosemicarbazone (**1d**),[47] thiophene-2-carbaldehyde 4-phenylthiosemicarbazone (**1e**)[48] and furan-2 carbaldehyde 4-phenylthiosemicarbazone (**1f**).[49]

Reactions of **1a–f** *with dimethyl ethynedicarboxylate* **(6)**: Into a 250 cm^3 two-necked flask containing (284 mg, 2.0 mmol) of **6** in 10 ml methanol, a solution of 2 mmol of **1a–f** in methanol (50 ml) was dropwisely added with stirring. The mixture was gently refluxed with stirring for 3 h. The resulting yellow precipitate was filtered off, washed with methanol, and recrystallised from a suitable solvent to give pure crystals of **10a–f**.

Methyl [3-phenyl-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]-ethanoate **(10a)**: Yellow crystals (0.59 g, 75%), m.p. 249–251 °C (methanol). ^{1}H NMR: δ = 9.92 (br, 1H, Ph–NH), 7.16–7.87 (m, 10H, phenyl H), 6.70 (s, 1H, methylene H), 3.75 (s, 3H, $COOCH_3$). ^{13}C NMR: δ = 191.94 (C–4), 178.83 (C=S), 166.79 (COO), 163.77 (C–5), 154.83 (C–3); 138.58, 134.74 (phenyl qC); 128.94, 128.86, 128.66, 128.41, 126.93, 126.58 (phenyl CH); 116.64 (methylene *C*H), 51.86 (OCH_3). IR (KBr): ν (cm^{-1}) = 3295 (NH), 1715 (CO), 1685 (COO), 1625 (C=N), 1565 (NH def. and C–N str.), 1355, 1000 (C=S and C–N). MS, *m/z* (%) = 365 [M$^+$] (49), 334 (31), 306 (29), 171 (27), 150 (48), 135 (71), 103 (69), 77 (100), 65 (82). $C_{19}H_{15}N_3O_3S$ (365.41): Calcd C, 62.45; H, 4.14; N, 11.50; S, 8.78. Found C, 62.22; H, 4.23; N, 11.71; S, 8.62%.

Methyl [3-(4-methoxyphenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]ethanoate **(10b)**: Yellow crystals (0.58 g, 79%), m.p. 289–291 °C (acetonitrile). ^{1}H NMR: δ = 9.89 (br, 1H, Ph–NH), 7.05–7.75 (m, 9H, aryl H), 6.68 (s, 1H, methylene H), 3.84 (s, 3H, OCH_3), 3.76 (s, 3H, $COOCH_3$). ^{13}C NMR: δ = 191.71 (C–4), 178.78 (C=S), 167.05 (COO), 163.69 (C–5), 160.65 (phenyl 4-MeO–*C*), 155.11 (C–3); 138.49, 133.26 (aryl qC); 129.94, 129.35, 128.46, 126.58, 126.23 (aryl CH), 116.72 (methylene *C*H), 55.69 (OCH_3), 51.88 ($COOCH_3$). IR (KBr): ν (cm^{-1}) = 3280 (NH), 1720 (CO), 1685 (COO), 1615 (C=N), 1575 (NH def. and C–N str.),

1360, 990 (C=S and C–N). MS: *m/z* (%) = 395 [M^+] (28), 364 (19), 336 (38), 201 (46), 150 (39), 135 (64), 133 (72), 93 (100), 77 (76). $C_{20}H_{17}N_3O_4S$ (395.43): Calcd C, 60.75; H, 4.33; N, 10.63; S, 8.11. Found C, 60.94; H, 4.22; N, 10.82; S, 8.26%.

Methyl [3-(4-chlorophenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]ethanoate **(10c)**: Pale yellow crystals (0.58 g, 73%), m.p. 302–304 °C (acetonitrile). ^{1}H NMR: δ = 9.90 (br, 1H, Ph–NH), 7.16–7.77 (m, 9H, aryl H), 6.69 (s, 1H, methylene H), 3.78 (s, 3H, $COOCH_3$). IR (KBr): ν (cm^{-1}) = 3275 (NH), 1710 (CO), 1685 (COO), 1620 (C=N), 1560 (NH def. and C–N str.), 1360, 1005 (C=S and C–N). MS: *m/z* (%) = 401/399 [M^+] (56), 363 (36), 332 (44), 304 (44), 169 (54), 150 (61), 138 (64), 135 (69), 91 (62), 77 (100), 65 (81). $C_{19}H_{14}ClN_3O_3S$ (399.85): Calcd C, 57.07; H, 3.53; Cl, 8.87; N, 10.51; S, 8.02. Found C, 56.88; H, 3.44; Cl, 9.06; N, 10.73; S, 7.84%.

Methyl [3-(2-hydroxyphenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]ethanoate **(10d)**: Yellow crystals (0.57 g, 75%), m.p. 278–279 °C (acetonitrile). ^{1}H NMR: δ = 9.94 (br, 1H, Ph–NH), 9.58 (br, 1H, OH), 7.08–7.73 (m, 9H, aryl H), 6.72 (br, 1H, methylene H), 3.75 (s, 3H, $COOCH_3$). IR (KBr): ν (cm^{-1}) = 3465 (OH), 3285 (NH), 1720 (CO), 1680 (COO), 1620 (C=N), 1570 (NH def. and C–N str.), 1355, 995 (C=S and C–N). MS: *m/z* (%) = 381 [M^+] (56), 350 (34), 332 (25), 197 (39), 150 (53), 135 (66), 129 (45), 93 (100), 77 (86), 65 (79). $C_{19}H_{15}N_3O_4S$ (381.41): Calcd C, 59.83; H, 3.96; N, 11.02; S, 8.41. Found C, 60.09; H, 4.05; N, 10.84; S, 8.63%.

Methyl [3-(2-thienyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]ethanoate **(10e)**: Pale yellow crystals (0.56 g, 76%), m.p. 263–264 °C (acetonitrile). ^{1}H NMR: δ = 9.88 (br, 1H, Ph–NH), 7.17–7.73 (m, 8H, phenyl and thienyl H), 6.70 (s, 1H, methylene H), 3.76 (s, 3H, $COOCH_3$). ^{13}C NMR: δ = 191.75 (C–4), 178.65 (C=S), 167.12 (COO), 163.65 (C–5), 155.26 (C–3); 138.59, 133.26 (aryl qC), 129.18, 128.41, 127.43, 127.28, 126.64, 126.26 (phenyl and thienyl *C*H), 116.83 (methylene *C*H), 52.04 ($COOCH_3$). IR (KBr): ν (cm^{-1}) = 3285 (NH), 1715 (CO), 1685 (COO), 1625 (C=N), 1565 (NH def. and C–N str.), 1360, 1000 (C=S and C–N). MS: *m/z* (%) = 371 [M^+] (53), 340 (27), 312 (44), 177 (56), 150 (52), 135 (71), 109 (65), 77 (100), 65 (53). $C_{17}H_{13}N_3O_3S_2$ (371.43): Calcd C, 54.97; H, 3.53; N, 11.31, S, 17.27. Found C, 55.16; H, 3.43; N, 11.16; S, 17.45%.

Methyl [3-(2-furyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]ethanoate **(10f)**: Pale yellow crystals (0.52 g, 73%), m.p. 237–238 °C (acetonitrile). ^{1}H NMR: δ = 9.83 (br, 1H, Ph–NH), 6.98–7.64 (m, 8H, phenyl and furyl H), 6.70 (s, 1H, methylene H), 3.78 (s, 3H, $COOCH_3$). ^{13}C NMR: δ = 191.65 (C–4), 178.83 (C=S), 167.10 (COO), 163.58 (C–5), 155.18 (C–3), 143.86 (furyl C-2), 141.65 (furyl C-5), 138.62 (phenyl qC); 129.36, 128.51, 126.64, 125.94, 125.76 (phenyl and furyl CH); 116.82 (methylene *C*H), 51.79 ($COOCH_3$). IR (KBr): ν (cm^{-1}) = 3275 (NH), 1720 (CO), 1680 (COO), 1620 (C=N), 1570 (NH def. and C–N str.), 1360, 995 (C=S and C–N). MS: *m/z* (%) = 355 [M^+] (31), 324 (19), 296 (43), 161 (55), 150 (48), 135 (59), 93 (86), 77 (100), 65 (53). $C_{17}H_{13}N_3O_4S$ (355.37): Calcd C, 57.46; H, 3.69; N, 11.82, S, 9.02. Found C, 57.67; H, 3.58; N, 12.06; S, 8.89%.

Reactions of **1a–f** *with diethyl (E)-2,3-dicyanobutenedioate* **(7)**: A solution of 222 mg (1.0 mmol) of **7** in 20 ml ethyl acetate was treated with 1.0 mmol of **1a–f** (in 20 ml of ethyl acetate). The mixture was refluxed for 14–18 hours with stirring (the reaction was monitored by TLC). The reaction time of **1a–f** with **7** was as follows for **1a** (15 h), **1b**, **c** (14 h), **1d** (16 h), **1e** (17 h) and **1f** (18 h). After concentration of the reaction mixture to dryness, the residues were dissolved in 5 ml of acetone and subjected to PLC using toluene/ethyl acetate (4:1) as eluent. Chromatographic separation of the residue gave numerous zones, two of which (with high intensity) were removed and extracted. The fastest moving zone contained compounds **24a–f**, while the slowest moving zone contained the pyrazolone derivatives **15a–f.** Extraction of the zones with acetone and crystallisation gave the pure compounds.

Ethyl [3-phenyl-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]-cyanoacetate **(15a)**: Yellowish brown crystals (0.234 g, 58%), m.p. 287–289 °C (acetonitrile). ^{1}H NMR: δ = 9.94 (br, 1H, Ph–NH), 7.26–7.86 (m, 10H, phenyl H), 4.21 (q, 2H, OCH_2, *J* = 7.05 Hz), 1.18 (t, 3H, CH_3, *J* = 7.05 Hz). ^{13}C NMR: δ = 191.28 (C–4), 179.19 (C=S), 170.16 (C–5), 166.33 (COO), 156.17 (C–3); 138.64, 133.29 (phenyl qC); 130.76, 129.54, 129.14, 128.80, 128.44, 127.16 (phenyl CH); 117.96 (CN), 103.22 (methylene qC), 61.02 (OCH_2), 14.36 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3275 (NH), 2220 (CN), 1720 (CO), 1680 (COO), 1625 (C=N), 1565 (NH-def. and C–N str.), and 1365, 985 (C=S and C–N). MS: *m/z* (%): 404 [M^+] (34), 269 [M^+-PhNCS] (57), 224 (41), 180 (21), 154 (19), 150 (56), 135 (94), 103 (79), 91 (100), 77 (74), 65 (63). $C_{21}H_{16}N_4O_3S$ (404.44): Calcd C, 62.36; H, 3.99; N, 13.85; S, 7.93. Found C, 62.18; H, 4.12; N, 14.06; S, 8.11%.

Ethyl [3-(4-methoxyphenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]cyanoacetate **(15b)**: Brown crystals (0.265 g, 61%), m.p. 316–318 °C (methanol). ^{1}H NMR: δ = 9.9 (br, 1H, Ph–NH), 7.09–7.74 (m, 9H, aryl H), 4.22 (q, 2H, OCH_2, *J* = 7.08 Hz), 3.84 (s, 3H, OCH_3), 1.21 (t, 3H, CH_3, *J* = 7.08 Hz). ^{13}C NMR: δ = 190.76 (C–4), 178.84 (C=S), 170.84 (C–5), 166.51 (COO), 160.63 (phenyl 4-MeO-*C*), 155.89 (C–3), 138.76, 137.96 (aryl qC); 129.54, 128.66, 127.66, 127.24, 126.63 (aryl CH); 118.06 (CN), 103.14 (methylene qC), 60.94 (OCH_2), 55.10 (OCH_3), 14.29 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3280 (NH), 2220 (CN), 1715 (CO), 1675 (COO), 1630 (C=N), 1570 (NH-def. and C–N str.), and 1360, 990 (C=S and C–N). MS: *m/z* (%): 434 [M^+] (26), 299 (41), 268 (26), 223 (46), 179 (52), 152 (36), 150 (64), 135 (71), 133 (58), 91 (88), 77 (100), 65 (69). $C_{22}H_{18}N_4O_4S$ (434.47): Calcd C, 60.82; H, 4.18; N, 12.90; S, 7.38. Found C, 61.04; H, 4.09; N, 13.14; S, 7.59%.

Ethyl [3-(4-chlorophenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]cyanoacetate **(15c)**: Pale brown crystals (0.228 g, 56%), m.p. 326–328 °C (acetonitrile). ^{1}H NMR: δ = 9.90 (br, 1H, Ph–NH), 7.24–7.77 (m, 9H, aryl H), 4.22 (q, 2H, OCH_2, *J* = 7.05 Hz), 1.19 (t, 3H, CH_3, *J* = 7.05 Hz). ^{13}C NMR: δ = 190.86 (C–4), 178.56 (C=S), 171.05 (C–5), 165.96 (COO), 155.87 (C–3); 138.56, 136.64, 131.28 (aryl qC); 130.26, 129.22, 128.96, 128.28, 127.44 (aryl CH); 117.98 (CN), 103.11 (methylene qC), 60.96 (OCH_2), 14.23 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3270 (NH), 2220 (CN), 1710 (CO), 1675 (COO), 1625 (C=N), 1570 (NH-def. and C–N str.), and 1360, 995 (C=S and C–N). MS. *m/z* (%) = 440/438 [M^+] (54), 402 (29), 267 (44), 222 (56), 178 (18), 152 (37), 150 (64), 139 (74), 135 (56), 91 (100), 77 (74), 65 (66). $C_{21}H_{15}ClN_4O_3S$ (438.89): Calcd C, 57.47; H, 3.44; Cl, 8.08; N, 12.77; S, 7.31. Found C, 57.29; H, 3.58; Cl, 7.92; N, 12.56; S, 7.54%.

Ethyl [3-(2-hydroxyphenyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]cyanoacetate **(15d)**: Brown crystals (0.235 g, 56%), m.p. 308–309 °C (methanol). ^{1}H NMR: δ = 9.92 (br, 1H, Ph–NH), 9.54 (br, 1H, OH), 7.98–7.68 (m, 9H, aryl H), 4.19 (q, 2H, OCH_2, *J* = 7.03 Hz), 1.24 (t, 3H, CH_3, *J* = 7.03 Hz). ^{13}C NMR: δ = 190.94 (C–4), 178.65 (C=S), 170.72 (C–5), 165.96 (COO), 161.16 (aryl C–OH), 156.09 (C–3); 138.76, 134.83 (aryl qC); 130.11, 129.76, 129.12, 128.46, 127.55, 127.12, 126.56 (aryl CH); 118.12 (CN), 102.96 (methylene qC), 61.11 (OCH_2), 14.26 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3465 (OH), 3260 (NH), 2215 (CN), 1715 (CO), 1680 (COO), 1620 (C=N), 1566 (NH-def. and C–N str.), and 1355, 980 (C=S and C–N). MS: *m/z* (%) = 420 [M^+] (42), 285 (39), 240 (28), 196(34), 170 (18), 150 (49), 135 (66), 119 (74), 93 (100), 77 (86), 65 (44). $C_{21}H_{16}N_4O_4S$ (420.44): Calcd C, 59.99; H, 3.84; N, 13.33; S, 7.63. Found C, 60.16; H, 3.71; N, 13.12; S, 7.81%.

Ethyl [3-(2-thienyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-yli-dene]cyanoacetate **(15e)**: Yellowish brown crystals (0.234 g, 57%), m.p. 299–301 °C (ethanol). ^{1}H NMR: δ = 9.89 (br, 1H, Ph–NH), 7.14–7.72 (m, 8H, phenyl and thienyl H), 4.23 (q, 2H, OCH_2, *J* = 7.10 Hz), 1.21 (t, 3H, CH_3, *J* = 7.10 Hz). ^{13}C NMR: δ = 190.82 (C–4), 178.61 (C=S), 170.64 (C–5), 165.83 (COO), 155.76 (C–3), 138.57 (phenyl qC), 136.14 (thienyl C–2); 129.22, 128.41, 127.74, 127.36, 126.55, 126.38 (phenyl and thienyl CH); 118.16 (CN), 103.18 (methylene qC), 61.08 (OCH_2), 14.25 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3280 (NH), 2220 (CN), 1705 (CO), 1675 (COO), 1620 (C=N), 1560 (NH-def. and C–N str.), and 1355, 990 (C=S and C–N). MS. *m/z* (%) = 410 [M^+] (61), 275 (48), 230 (52), 186 (39), 160 (17), 150 (33), 135 (67), 109 (81), 91 (86), 77 (100), 65 (74). $C_{19}H_{14}N_4O_3S_2$ (410.47): Calcd C, 55.60; H, 3.44; N, 13.65; S, 15.62. Found C, 55.42; H, 3.58; N, 13.86; S, 15.40%.

Ethyl [3-(2-furyl)-4-oxo-1-(phenylthiocarbamoyl)-4,5-dihydro-1H-pyrazol-5-ylidene]cyanoacetate **(15f)**: Pale brown crystals (0.213 g, 54%), m.p. 278–279 °C (ethanol). ^{1}H NMR: δ = 9.90 (br, 1H, Ph–NH), 7.04–7.66 (m, 8H, aryl and furyl-H), 4.22 (q, 2H, OCH_2, *J* = 7.05 Hz), 1.18 (t, 3H, CH_3, *J* = 7.05 Hz). ^{13}C NMR: δ = 190.92 (C–4), 178.56 (C=S), 170.93 (C–5), 165.88 (COO), 155.54 (C–3), 143.22 (furyl C–2), 141.72 (furyl CH-5), 138.67 (aryl qC); 129.29, 128.67, 128.44, 126.14, 125.97 (phenyl and furyl CH), 117.89 (*C*N), 102.92 (methylene qC), 60.93 (OCH_2), 14.19 (CH_3). IR (KBr): ν (cm^{-1}) = 3265 (NH), 2215 (CN), 1710 (CO), 1680 (COO), 1625 (C=N), 1565 (NH-def. and C–N str.), and 1360, 995 (C=S and C–N). MS: *m/z* (%) = 394 [M^+] (35), 259 (27), 214 (56), 170 (61), 150 (48), 144 (19), 135 (76), 93 (66), 77 (100), 65 (64). $C_{19}H_{14}N_4O_4S$ (394.07): Calcd C, 57.86; H, 3.58; N, 14.21; S, 8.13. Found C, 58.11; H, 3.69; N, 13.98; S, 18.36%.

Ethyl 3-amino-6-phenyl-5-cyanopyridazine-4-carboxylate **(24a)**: Reddish brown crystals (0.067 g, 25%), m.p. 196–197 °C (acetonitrile). ^{1}H NMR: δ = 7.33–7.76 (m, 5H, phenyl H), 6.30 (br, 2H, NH_2), 4.24 (q, 2H, OCH_2, J = 7.12 Hz), 1.21 (t, 3H, CH_3, J = 7.12 Hz). ^{13}C NMR: δ = 167.56 (COO), 154.16 (C–3), 148.82 (C–6), 136.76 (C–4), 133.52 (phenyl C-1); 129.66, 128.76, 128.32 (phenyl CH); 120.18 (C–5), 118.42 (CN), 60.96 (OCH_2), 14.18 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3370 (NH_2), 2222 (CN), 1680 (CO), 1620 (C=N). MS: *m/z* (%) = 268 [M$^+$] (62), 242 (46), 197 (64), 165 (34), 153 (28), 103 (72), 77 (100). $C_{14}H_{12}N_4O_2$ (268.27): Calcd C, 62.68; H, 4.51; N, 20.88. Found C, 62.51; H, 4.63; N, 21.09%.

Ethyl3-amino-6-(4-methoxyphenyl)-5-cyanopyridazine-4-carboxylate **(24b)**: Reddish brown crystals (0.075 g, 26%), m.p. 244–246 °C (acetonitrile). ^{1}H NMR: δ = 7.10–7.64 (m, 4H, aryl H), 6.25 (br, 2H, NH_2), 4.21 (q, 2H, OCH_2, J = 7.07 Hz), 3.85 (s, 3H, OCH_3), 1.19 (t, 3H, CH_2CH_3, J = 7.07 Hz). ^{13}C NMR: δ = 167.44 (COO), 160.64 (phenyl 4–MeO–*C*), 154.28 (C–3), 149.12 (C–6), 136.54 (C–4), 133.64 (aryl C–1); 128.56, 126.83 (aryl CH), 120.33 (C–5), 118.57 (CN), 61.14 (OCH_2), 55.64 (OCH_3), 14.18 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3360 (NH_2), 2220 (CN), 1675 (CO), 1625 (C=N). MS: *m/z* (%) = 298 [M$^+$] (58), 267 (44), 241 (26), 196 (55), 165 (52), 152 (36), 133 (62), 77 (100). $C_{15}H_{14}N_4O_3$ (298.30): Calcd C, 60.40; H, 4.73; N, 18.78. Found C, 60.18; H, 4.84; N, 18.94%.

Ethyl 3-amino-6-(4-chlorophenyl)-3-cyanopyridazine-4-carboxylate **(24c)**: Pale brown crystals (0.066 g, 22%), m.p. 259–260 °C (acetonitrile). ^{1}H NMR: δ = 7.32–7.79 (m, 4H, aryl H), 6.23 (br, 2H, NH_2), 4.25 (q, 2H, OCH_2, J = 7.10 Hz), 1.23 (t, 3H, CH_3, J = 7.10 Hz). IR (KBr): ν (cm^{-1}) = 3385 (NH_2), 2210 (CN), 1675 (COO), 1610 (C=N). MS: *m/z* (%) = 304/302 [M$^+$] (41), 266 (27), 240 (24), 195 (56), 165 (66), 151 (49), 138 (51), 77 (100). $C_{14}H_{11}ClN_4O_2$ (302.72): Calcd C, 55.55; H, 3.66; Cl, 11.71 N, 18.51. Found C, 55.81; H, 3.78; Cl, 11.52; N, 18.29%.

Ethyl 3-amino-6-(2-hydroxyphenyl)-5-cyanopyridazine-4-carboxylate **(24d)**: Reddish brown crystals (0.068 g, 24%), m.p. 227–228 °C (ethanol). ^{1}H NMR: δ = 9.56 (br, 1H, OH), 7.07–7.75 (m, 4H, aryl H), 6.27 (br, 2H, NH_2), 4.20 (q, 2H, OCH_2, J = 7.03 Hz), 1.23 (t, 3H, CH_3, J = 7.03 Hz). IR (KBr): ν (cm^{-1}) = 3455 (OH), 3365 (NH_2), 2215 (CN), 1675 (COO), 1620 (C=N). MS: *m/z* (%) = 284 [M$^+$] (23), 258 (30), 213 (41), 169 (21), 165 (55), 119 (64), 93 (100), 77 (75), 65 (62). $C_{14}H_{12}N_4O_3$ (284.09): Calcd C, 59.15; H, 4.25; N, 19.71. Found C, 58.94; H, 4.36; N, 19.49%.

Ethyl 3-amino-6-(2-thienyl)-5-cyanopyridazine-4-carboxylate **(24e)**: Brown crystals (0.066 g, 24%), m.p. 211–212 °C (ethanol). ^{1}H NMR (DMSO-d_6): δ = 7.14–7.72 (m, 3H, thienyl H), 6.31 (br, 2H, NH_2), 4.21 (q, 4H, OCH_2, J = 7.02 Hz), 1.25 (t, 3H, CH_3, J = 7.02 Hz). ^{13}C NMR: δ = 167.23 (COO), 153.86 (C–3), 140.17 (thienyl–C–2), 148.96 (C–6), 136.44 (C–4); 128.65, 128.19, 127.64 (thienyl CH); 121.12 (C–5), 118.72 (*C*N), 61.14 (OCH_2), 14.26 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3360 (NH_2), 2220 (CN), 1680 (COO), 1625 (C=N). MS: *m/z* (%): 274 [M$^+$] (32), 225 (25), 185 (44), 165 (71), 159 (24), 109 (56), 45 (100). $C_{12}H_{10}N_4O_2S$ (274.30): Calcd C, 52.54; H, 3.67; N, 20.43; S, 11.69. Found C, 52.36; H, 3.75; N, 20.64; S, 11.82%.

Ethyl 3-amino-6-(2-furyl)-5-cyanopyridazine-4-carboxylate **(24f)**: Pale brown crystals (0.059 g, 23%), m.p. 187–188 °C (ethanol). ^{1}H NMR: δ = 7.18–7.82 (3H, furyl H), 6.27 (br, 2H, NH_2), 4.21 (q, 2H, OCH_2, J = 7.10 Hz), 1.22 (t, 3H, CH_3, J = 7.10 Hz). ^{13}C NMR: δ = 167.23 (COO), 157.26 (furyl C-2), 154.21 (C–3), 148.35 (C–6), 143.12 (furyl C-5), 136.74 (C–4); 125.65, 124.84 (furyl C–3,4), 120.84 (C–5), 118.26 (CN), 60.92 (OCH_2), 14.16 (OCH_2CH_3). IR (KBr): ν (cm^{-1}) = 3360 (NH_2), 2215 (CN), 1675 (COO), 1625 (C=N). MS: *m/z* (%) = 258 [M$^+$] (33), 232 (25), 187 (45), 165 (74), 143 (22), 93 (100), 45 (74). $C_{12}H_{10}N_4O_3$ (258.23): Calcd C, 55.81; H, 3.90; N, 21.70. Found C, 55.57; H, 4.12; N, 21.92%.

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References

1 M. Gruttadauria, F. Bucheri, G. Cusmano, P. Lo Meo, R. Noto and G. Werber, *J. Heterocyclic Chem.*, 1993, **30**, 765.
2 R. Noto, P. Lo Meo, M. Gruttadauria and G. Werber, *J. Heterocyclic Chem.*, 1996, **33**, 863.
3 R. Noto, P. Lo Meo, M. Gruttadauria and G. Werber, *J. Heterocyclic Chem.*, 1999, **36**, 667.
4 S. Ernst, C. Richter, A. Hobert, G.G. Mariam and K. Schulze, *J. Heterocyclic Chem.*, 1995, **32**, 275.
5 M.A.M. Gomaa, A.A. Hassan and H.S. Shehatta, *Heteroatom Chem.*, 2006, **17**, 261.
6 N.A. Danilkina, L.E. Mikhailov and B.A. Ivin, *Russ J. Org. Chem.*, 2006, **42**, 783.
7 Yu. A. Rabukhin, O.B. Kozhavina and K.F. Suzdalev, *Adv. Heterocycl. Chem.*, 1996, **66**, 131.
8 N.A. Danilkina, L.E. Mikhailov and B.A. Ivin, 3rd. *Euro-Asian heterocyclic meeting*, 12-17 September 2004, Novosibirsk, Russia.
9 A.S.A. Youssef, *Phosphorus, Sulfur, Silicon Relat. Elem.*, 2002, **177**, 173.
10 V. Ya. Kauss, E.E. Liepins, I. Kalvin and E. Lukevics, *Khim. Geterotsikl. Soedin.*, 1990, 120; *Chem. Abstr.* 1990, **113**, 132061. – *Chem. Heterocycl. Compounds* (Engl. Transl.), 1990, **26**, 103.
11 A. Darehcordi, K. Saidi and M.R. Islami, *ARKIVOC*, 2007 (i), 180.
12 B.B. Kaul, W.S. Durfee and G.T. Yee, *J. Am. Chem. Soc.*, 1999, **121**, 6862.
13 Y. Yamada, H. Yasuda and M. Kasai, *Heterocycles*, 1999, **51**, 2453, and papers by the same group cited therein.
14 K.M.M.S. Prakash, D.L. Prabhakar and D. Vankata Reddy, *Anal. Lett.*, 1987, **20**, 959.
15 R. Brehme and A. Kleemann, *Tetrahedron*, 1987, **43**, 4113.
16 D. Enders, G. Syrig, G. Raabe, R. Fernandez, J.M. Lassaletta and J.M. Llera, *Synthesis*, 1996, 48.
17 E. Diez, R. Fernandez, C. Gasch, J.M. Lassaletta, J.M. Llera, E. Markín-Zamora and J. Vasquez, *J. Org. Chem.*, 1997, **62**, 5144.
18 S.A. Ghozlan, I.A. Abdelhamid, H.M. Hassaneen and M.H. Elnagdi, *J. Heterocyclic Chem.*, 2007, **44**, 105.
19 S.I. Aziz, H.F. Anwar, M.A. El-Apasery and M.H. Elnagdi, *J. Heterocyclic Chem.*, 2007, **44**, 877.
20 L. El-Kaim, L. Gautier, L. Grimaud and V. Michaut, *Synlett*, 2003, 1844.
21 M. Rueping, E. Sugiono, T. Theissmann, A. Kuenkel, A. Köckritz, A. Pews-Davtyan, N. Namati and M. Beller, *Organic Letters*, 2007, **9**, 1065.
22 M. Mühlstädt, L. Weber and P. Birner, *J. Chem. Soc., Perkin Trans. 2*, 1988, 821.
23 M. Kirschke, P. Hübner, G. Lutze, E. Gundermann and M. Ramm, *Liebigs Ann. Chem.*, 1994, 159.
24 P. Cuadrado, A.M. González-Nogal and S. Matinez, *Tetrahedron*, 1997, **53**, 8585.
25 R.K. Vohra, J.L. Renaud and C. Brunéau, *Synthesis*, 2007, 731.
26 L. Crombie and R.V. Dove, *J. Chem. Soc., Perkin Trans. 1*, 1979, 686.
27 A. Gómez Sánchez and J. Bellanato, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1561.
28 Y. Kamitori, M. Hojo, R. Masuda and T. Ikemura, *Tetrahedron Lett.*, 1993, **34**, 5135.
29 G.V. Subbaraju, K.S. Rao, G.S. Reddy and Z. Urbanczyk-Lipkowska, *Indian J. Chem.*, 1995, **34B**, 342.
30 S. Gelin and R. Gelin, *J. Heterocyclic Chem.*, 1977, **14**, 75.
31 C.W. Bird, *Tetrahedron*, 1976, **32**, 269.
32 G. Tacconi, A.G. Invernizzi, P.P. Righetty and G. Desmony, *J. Prakt. Chem.*, 1980, **322**, 711.
33 W.H. Pirkle and D.J. Hoover, *J. Org. Chem.*, 1980, **45**, 3407.
34 H. McNab and I. Stobie, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1845.
35 H. McNab, J. Chem. Soc., Perkin Trans. 1, 1983, 1203.
36 E. Sotelo, N. Fraiz, M. Yáñez, V. Terrades, R. Laguna, E. Cano and E. Raviña, *Bioorg. Med. Chem.*, 2002, **10**, 2873.
37 L.F. Marcos, S. Maraccini, R. Pepino, C. Polo and T. Torroba, *Synthesis*, 2003, 691.
38 V. Dal Piaz, M.P. Giovannoni, G. Ciciani, D. Barlocco, G. Giardina, G. Petrone and G.D. Clarke, *Eur. J. Med. Chem.*, 1996, **31**, 65.
39 V. Dal Piaz, M.P. Giovannoni, R. Laguna and E. Cano, *Eur. J. Med. Chem.*, 1994, **29**, 249.
40 A. Coelho, E. Sotelo and E. Raviña, *Tetrahedron*, 2003, **59**, 2477.
41 F. Fariña, M.V. Martín, M. Romañach and F. Sanchez, *Heterocycles*, 1988, **27**, 1431.
42 E. Sotelo, E. Raviña and E. Estevez, *J. Heterocyclic Chem.*, 1999, **36**, 985.
43 M. Hesse, H. Meier and B. Zeeh, *Spektroskopische Methoden in der Organischen Chemie*, 7th edn, Stuttgart, 2005 p.220.
44 M. Hesse, H. Meier and B. Zeeh, *Spektroskopische Methoden in der Organischen Chemie*, 7th edn, Stuttgart, 2005 p.53.
45 N.K. Kaushik, A.K. Mishra, *Indian J. Chem.*, 2003, **42A**, 2762.
46 R. Beckert, M.G. Gruner, I. Seidel, R. Kuban, *Monatsh. Chem.* 1989, **120**, 1125.
47 J.T. Wang, Y.W. Zhang, Y.M. Xu, Z.W. Wang, *Heteroatom Chem.* 1995, **6**, 443.
48 B. Singh, H. Misra, *J. Indian Chem. Soc.* 1986, **63**, 1069.
49 P. Umpathy, A.P. Budhkar, C.R. Dorai, *J. Indian Chem. Soc.* 1986, **63**, 714.