Reaction of Heteroaryl Thiols with Conjugated Azoalkenes: Regioselective Preparation of 4-(Heteroarylthio)-1*H*-pyrazol-5(2*H*)-ones. X-ray Crystal Structures of Methyl 2-((Pyrimid-2-yl)thio)acetoacetate (Aminocarbonyl)hydrazone and 1-(Aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one

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Heteroaryl thiols easily react with conjugated azoalkenes to give α-(heteroarylthio)hydrazones, by 1,4-addition to the azo–ene system. The treatment of the latter compounds with sodium methoxide and then with trifluoroacetic acid affords regioisomeric 4-(heteroarylthio)-1*H*-pyrazol-5(2*H*)-ones. In general, these reactions can be successfully executed in two as well as one pot procedures. X-ray diffraction studies of methyl 2-((pyrimid-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone unequivocally show that the preliminary 1,4-addition occurs by nucleophilic attack of the thiol function of heteroaryl thiols to the azo–ene system of conjugated azoalkenes. X-ray structure determination of 1-(aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one was carried out in order to determine the behavior of α-(heteroarylthio) hydrazones in the ring closure and the nature of the heterocycle. In particular, this investigation afforded information about the hydrogen bondings and the stereochemistry of this molecule and clarified some spectroscopic evidence. A detailed ^1H and ^{13}C NMR study of these compounds in DMSO-d_6 showed separate signals for the "NH" and "OH" tautomers, as well as a solvent effect on the enol–keto equilibrium. The conversion of the initial keto form to the related enol form was often complete. The equilibration was found to be extraordinarily slow, requiring in some cases 720 h at room temperature and corresponding to $\Delta G \approx 25-30$ kcal mol^{-1}. These findings suggest that the regioisomeric structure assignments reported in the literature for some 5- and 3-hydroxypyrazoles in solution should be reconsidered. In order to avoid misunderstandings about the correct nomenclature of heterocycle derivatives, we believe that such assignments should be supported, when possible, by the appropriate X-ray crystal structure determinations.

Introduction

It is known that β-nitrogen heteroaryl thiols may tautomerize into the relevant thioketo forms,[1,2] and in the literature different reaction behaviors ascribable to this tautomerism have been reported. However, several of these reports appear to be incongruent. In some cases, the different reactivities were related to the effect of the additional heteroatom (X = O or S).[2]

Indeed, on S nucleophilic attack is frequently difficult to distinguish from an N nucleophilic attack, given the very slight differences in the routine spectra. In fact,

only infrared spectroscopy provided immediate structural information, and unfortunately this technique is not sufficiently reliable, especially with complicated molecular structures.[1,2]

We decided to study the reaction of some β-nitrogen heteroaryl thiols[3–5] as a continuation of our previous investigations on conjugated azoalkenes. Our first goal was the determination of the much-debated mechanism of the nucleophilic attack of heteroaryl thiols on the azo–ene system of conjugated azoalkenes, to give the preliminary 1,4-addition products. Our second intent was the elucidation of the heterocyclization pathway of the heteroaryl thiol–azoalkene adducts in order to obtain bio-

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logically-interesting pyrazole derivatives.[6-16] Pyrazole derivatives have been used for the preparation of herbicides,[7] carbamate insecticides,[8] ulcer inhibitors,[9] cardiovascular agents,[10] muscimol analogs,[11] and bacterial metabolites of antipyrine.[12]

In the course of our investigations, we encountered difficulties in assigning, unequivocally, structures to the products obtained, due in part to the structural perplexities derived from the literature about the enol−keto tautomerism in these compounds. Frequently, we have observed that different authors have named substantially the same compounds 5-hydroxypyrazoles and/or pyrazol-5(2*H*)-ones, as well as 3-hydroxypyrazoles and/or pyrazol-3(2*H*)-ones. It is our belief that these differences have often arisen either due to the fact that structural determinations were made on compounds in the solution state or as a result of the solvents used in various spectroscopic techniques, and without examination of the crystalline state.[7-16] For these reasons, we decided to carry out an unequivocal X-ray structure determination for one of the compounds synthesized and then, on the basis of the data, to elucidate the variations with time of some ^1H and ^{13}C NMR spectral signals resulting from the tautomeric equilibrium for each of the heterocycle derivatives prepared.

In agreement with Katritzky,[17] we believe that heterocyclic tautomeric equilibria allow the existence of several hydroxy heterocycle derivatives, either as such or in the carbonyl form, depending on the physical state (vapor phase, solution, or crystalline state). However, in order to avoid confusion, in our opinion, the name and the structure of heterocyclic derivatives with tautomeric equilibria should refer primarily to the crystalline state. Then, if necessary, the regioisomer ratios pertinent to the specific tautomerism and related to the specific explorative conditions (solvent, time, temperature, etc.) could be emphasized, by determining the tautomeric constant as well.

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Scheme 1

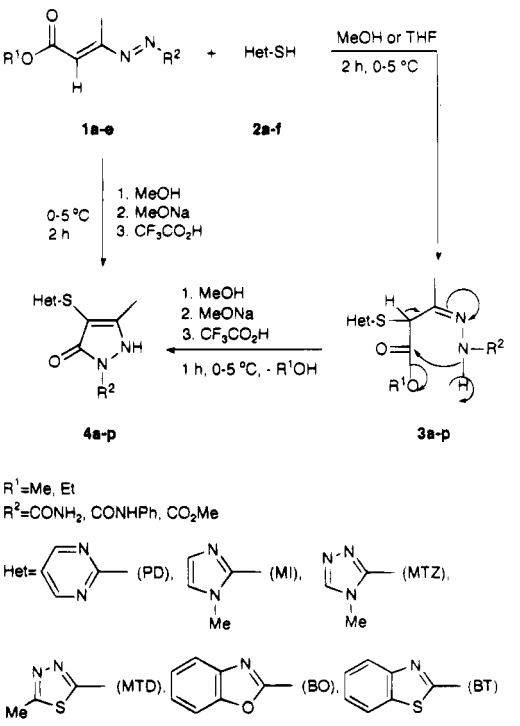


Table 1. Preparation of α-(Heteroarylthio)Hydrazones 3a−p

azoalkene			thiol		hydrazone	
1	R^1	R^2	2	Het	3	% yield
a	Me	$CONH_2$	a	PD	a	91
b	Et	$CONH_2$	a	PD	b	90
c	Me	CONHPh	a	PD	c	95
d	Et	CONHPh	a	PD	d	92
a	Me	$CONH_2$	b	MI	e	94
b	Et	$CONH_2$	b	MI	f	90
c	Me	CONHPh	b	MI	g	93
e	Me	CO_2Me	b	MI	h	92
a	Me	$CONH_2$	c	MTZ	i	85
b	Et	$CONH_2$	c	MTZ	j	92
c	Me	CONHPh	c	MTZ	k	91
d	Et	CONHPh	c	MTZ	l	91
e	Me	CO_2Me	c	MTZ	m	93
a	Me	$CONH_2$	d	MTD	n	92
a	Me	$CONH_2$	e	BO	o	93
b	Et	$CONH_2$	e	BO	p	91

Results and Discussion

Heteroaryl thiols **2a−e** readily reacted with conjugated azoalkenes **1a−e** in methanol or tetrahydrofuran at 0−5 °C with magnetic stirring, giving in good to excellent yields (90−95%, with the exception of 85% for **3i**) the α-(heteroarylthio) hydrazones **3a−p**, by efficient 1,4-addition of heteroaryl thiols to the azo−ene system of conjugated azoalkenes (see Scheme 1 and Table 1).

However, the uncertainties regarding the behavior of analogous reactions[1,2] hindered us from immediately assigning an exact molecular structure to these products by the usual spectroscopic methods. Therefore, we carried out the X-ray diffraction study of methyl 2-((pyrimid-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (**3a**), as a model, in order to unequivocally determine both the mechanism of the nucleophilic attack of heteroaryl thiol on the conjugated azo−ene system and the molecular structure of this important reaction product and/or intermediate. In fact, as a consequence of the two possible preliminary attacks, by the SH or NH functions,

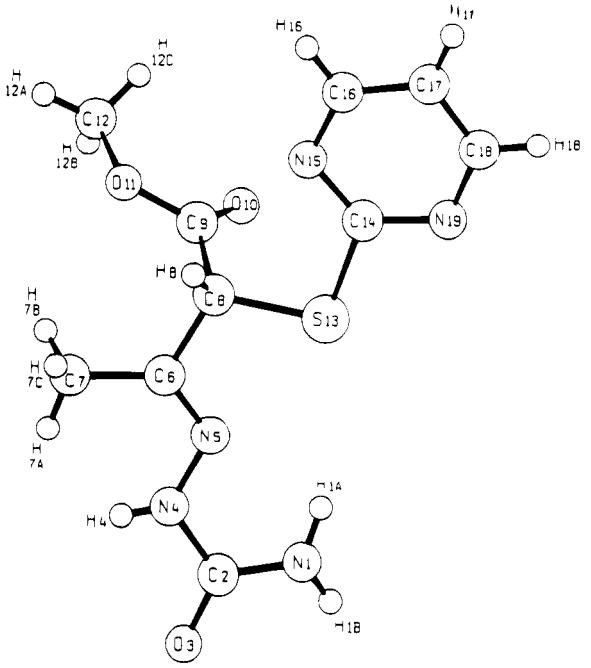


Figure 1. X-ray molecular structure of methyl 2-((pyrimid-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (**3a**) with the atom numbering system used in the crystallographic analysis.

some different reaction pathways resulting in different heterocyclization processes could be hypothesized.

The crystal structure of methyl 2-((pyrimid-2-yl)thio)-acetoacetate (aminocarbonyl)hydrazone (**3a**) is pictured in Figure 1.

The bond lengths C(8)–S(13) and S(13)–C(14) are 1.796 and 1.756 Å, respectively, undoubtedly showing pure C–S single bonds. Indeed, the carbon atom C(8) is clearly sp^3 hybridized. The sum of the bond angles of the pyrimidyl ring is 719.9°, supporting that this six-membered aromatic heterocycle is a perfectly planar hexagon of uniform bond lengths. The remaining bond lengths and angles are very regular for such a molecule.[21]

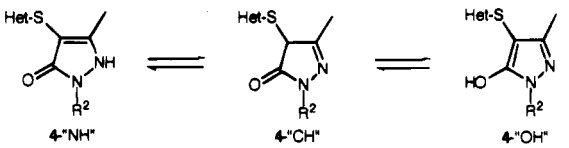
The results of this diffraction study helped us to correctly examine the spectroscopic data for all the synthesized α-(heteroarylthio) hydrazones **3** and to conclude that only the thiol function of heteroaryl thiols is involved in the nucleophilic attack on the azo–ene system of conjugated azoalkenes.

α-(Heteroarylthio) hydrazones **3a–p** were treated with a solution of sodium methoxide in methanol (30 wt %) and then acidified with a solution of trifluoroacetic acid at 0–5 °C with magnetic stirring, smoothly producing in good yields the interesting pyrazol-5-ones **4a,b, d–j,l** by an internal heterocyclization process. The intramolecular nucleophilic attack of the -NH- hydrazonic nitrogen atom on the alkoxycarbonyl group results in the pyrazolic ring closure with loss of an alcohol molecule (see Scheme 1). For this reason, the hydrazones **3a** and **3b**, **3c** and **3d**, **3e** and **3f**, **3i** and **3j**, **3k** and **3l**, **3o** and **3p** afforded the corresponding pyrazol-5-ones **4a**, **4b**, **4d**, **4g**, **4h**, and **4l**, respectively. More conveniently, the above-mentioned pyrazol-5-ones **4a,b,d–j,l** can be directly prepared in high yields (82–96%) by a one pot reaction of heteroaryl thiols **2a–c** and **2e** with conjugated azoalkenes **1a–c**, without the isolation of the corresponding hydrazone intermediate (see Scheme 1 and Table 2). This simple procedure was particularly successful (81–96% yields) in the synthesis of pyrazol-5-ones **4c,k,4m–p**. In fact, we observed the formation of the pyrazol-5-ones in the course of the preparation of the relevant hydrazonic intermediates (see Scheme 1 and Table 2).

Table 2. One-Pot Preparation of Pyrazol-5-ones 4a–p

azoalkene			thiol		pyrazolone	
1	R^1	R^2	**2**	Het	**4**	% yield
a	Me	$CONH_2$	**a**	PD	**a**	86
c	Me	CONHPh	**a**	PD	**b**	90
e	Me	CO_2Me	**a**	PD	**c**	96
a	Me	$CONH_2$	**b**	MI	**d**	92
c	Me	CONHPh	**b**	MI	**e**	85
e	Me	CO_2Me	**b**	MI	**f**	82
a	Me	$CONH_2$	**c**	MTZ	**g**	96
c	Me	CONHPh	**c**	MTZ	**h**	89
e	Me	CO_2Me	**c**	MTZ	**i**	82
a	Me	$CONH_2$	**d**	MTD	**j**	91
c	Me	CONHPh	**d**	MTD	**k**	93
b	Et	$CONH_2$	**e**	BO	**l**	91
c	Me	CONHPh	**e**	BO	**m**	87
a	Me	$CONH_2$	**f**	BT	**n**	92
c	Me	CONHPh	**f**	BT	**o**	88
e	Me	CO_2Me	**f**	BT	**p**	81

The spectroscopic techniques currently employed for the structure assignment still presented some interpretative difficulties ascribable to the enol–keto tautomerism of these and similar derivatives.[16] In principle, three tautomeric regioisomers should be possible:



In general, the ^1H and ^{13}C NMR spectra of compounds **4** in DMSO-d_6 reveal a mixture of two compounds with slightly different chemical shifts; the relative intensities of each group of signals vary with time. Since a systematic NMR study using different solvents was not possible given the very limited solubility of these compounds, and because in similar cases NMR spectroscopy is not able to unequivocally discriminate between the "OH" and "NH" forms, we determined the crystal structure by X-ray diffraction of one of the pyrazol-5-ones **4**. We selected the 1-(aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (**4a**), obtained by the heterocyclization of α-(heteroarylthio) hydrazone **3a**, which was also studied by X-ray diffraction.

The crystal structure of 1-(aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (**4a**) is pictured in Figure 2.

This drawing unquestionably reveals the proton on N(5) of the "NH" tautomeric form. The bond length C(9)–O(10) is 1.241 Å, typical for a nearly pure C=O double bond and quite different from the 1.43 Å appropriate for a C–O single bond. The bond length of C(8)–C(6) is 1.375 Å, in accordance with a C=C double bond. Furthermore, the sum of the bond angles of the five-membered heterocycle is 539.96°, indicating that this ring is a perfectly planar pentagon. This fact is clearly ascribable to three carbon atoms of the pyrazole ring having sp^2 hybridization. As for **3a**, the bond lengths C(8)–S(11) and S(11)–C(12) are 1.743 and 1.773 Å, respectively, clearly showing that they are pure C–S single bonds. However, the sum of the bond angles C(6)–C(8)–C(9), C(6)–C(8)–S(11), and C(9)–C(8)–S(11) is 359.95°, confirming that the carbon atom C(8) is sp^2 hybridized and excluding the "CH" form for this com-

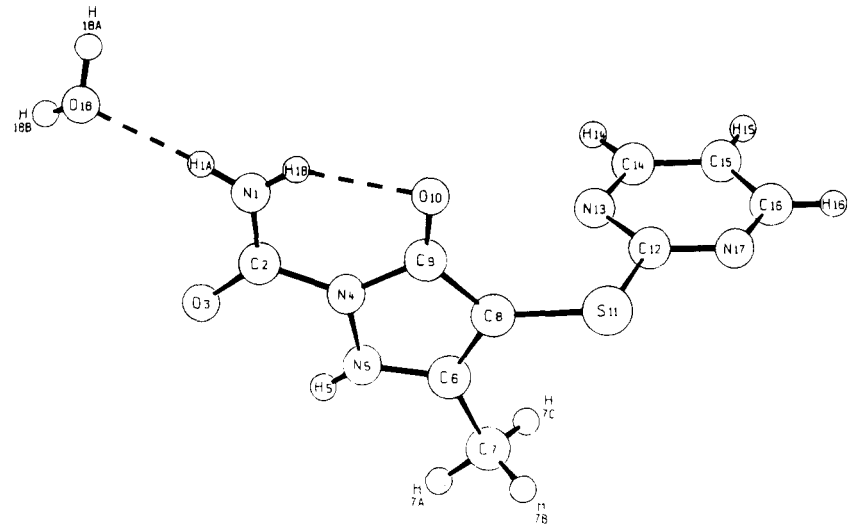


Figure 2. X-ray molecular structure of 1-(aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (**4a**) with the atom numbering system used in the crystallographic analysis.

pound. The situation of the pyrimidyl ring is the same as for **3a**. The intramolecular hydrogen bond N(1)–H(1B)–O(10) whose length is 2.106 Å and angle is 136.8° lends great stability to the "NH" tautomer, while the analogous intramolecular hydrogen bond N(5)–H(5)–O(3) is precluded for spatial reasons evidenced by the stereochemical data (see the supplementary material). This intramolecular organization is promoted by molecular packing due to the intermolecular hydrogen bondings N(5)–H(5)–O(3) of 1.950 Å, O(18)–H(18A)–0(10) of 2.050 Å, and O(18)–H(18B)–N(17) of 2.237 Å. Therefore, the sole, predictable intramolecular hydrogen bond in the "OH" tautomer should be O(3)–H(5)–O(10), probably leaving only the possibility of relatively weak intermolecular hydrogen bonds. In Figure 2 is also shown the intramolecular hydrogen bond N(1)–H(1A)–O(18) with hydration water molecule with length of 1.999 Å and angle of 170.7°. The remaining bond lengths and angles are as expected.[21]

On the basis of these X-ray data, we undertook a proton NMR investigation of all pyrazolones **4** which, in DMSO-d_6 solution, show well-separated signals for the "NH" and the "OH" tautomers (see Table 3). Since **4a** initially exhibits a single tautomeric form, it was assumed that this molecule, even in solution, is in the "NH" tautomeric form, in accordance with the X-ray results. This assumption was extended to all of the compounds **4**. The observed variations in the relative peak intensities for the methyl group on C-3 are ascribable to the progressive evolution toward a thermodynamic equilibrium between the "NH" or "OH" tautomers. It is known that polar aprotic solvents, such as DMSO-d_6, generally favor the "OH" form. The ratio between these two enol–keto regioisomers changes over several days (limit of 720 h) at different rates for different compounds, sometimes up to complete inversion, as unequivocably revealed by the proton NMR spectra (see Table 3). Due to the stereochemical consequences of the described hydrogen bondings, the tautomeric equilibration was found to be extraordinarily slow, requiring in some cases 720 h at room temperature to stabilize ($\Delta G \approx 25-30$ kcal mol^{-1}). In all other literature examples, only narrow averaged signals are observed for the "NH"/"OH" mixtures (even at low temperatures by ^{1}H NMR) with a $\Delta G^{\ddagger} \approx 5-10$ kcal mol^{-1} activation barrier separating the two tautomers.

Table 3. Enol–Keto Tautomerism of Pyrazol-5-ones 4a–p[a]

pyrazolone	R^2	% keto form (t_0)[b]	% keto form (t/h)[c]	δ_{Me}[e] (ppm)	δ_{Me}[f] (ppm)
4a	$CONH_2$	100	44 (720)[d]	2.16	2.07
4b	CONHPh	90	0 (350)	2.22	2.07
4c	CO_2Me	95	95 (0)	2.13	2.07
4d	$CONH_2$	99	41 (720)[d]	2.28	2.21
4e	CONHPh	100	31 (720)[d]	2.15	2.19
4f	CO_2Me	88	82 (24)	2.08	2.16
4g	$CONH_2$	100	50 (720)[d]	2.29	2.19
4h	CONHPh	100	22 (720)[d]	2.34	2.19
4i	CO_2Me	96	96 (0)	2.27	2.19
4j	$CONH_2$	100	43 (720)[d]	2.26	2.18
4k	CONHPh	98	0 (480)	2.32	2.17
4l	$CONH_2$	100	47 (720)[d]	2.28	2.19
4m	CONHPh	100	15 (720)[d]	2.34	2.19
4n	$CONH_2$	100	40 (720)	2.29	2.20
4o	CONHPh	100	9 (500)	2.35	2.20
4p	CO_2Me	100	85 (190)	2.01	2.07

[a] Conditions: DMSO-d_6, 10^{-2} M; temperature probe 25 °C. [b] Time (t_0) is the minimum time necessary for recording the first spectrum. [c] Time (t) from which no further changes in the enol–keto ratio were observed. [d] Time limit of recording although keto–enol conversion in progress. [e] ^{1}H NMR chemical shift for methyl on C-3 in the "NH" form. [f] ^{1}H NMR chemical shift for methyl on C-3 in the "OH" form.

In no case did we observe the "CH" tautomeric form. This enol–keto tautomerism appears to be dependent on the substituent on the nitrogen atom in position 1. The present qualitative study demonstrates that 1-((phenylamino)carbonyl)pyrazol-5-ones are converted to the corresponding enol form more easily than the analogous 1-(aminocarbonyl)pyrazol-5-ones, while 1-(alkoxycarbonyl)pyrazol-5-ones exhibit less transformation to the enol form. At present, further detailed kinetic investigations using UV spectroscopy are in progress in our laboratories.

These findings permit us to conclude that in the crystalline state, the products **4** exist predominantly as keto regioisomers and their spectral assignments reported in the Experimental Section correspond to the "NH" tautomeric form. In our opinion, the "OH" tautomeric form arises in different relative amounts and over variable times, depending on the solvent.

These conclusions also imply that a more general reconsideration of the previous structural assignments for similar derivatives may be necessary, especially if the

proton NMR spectra were not rapidly recorded, multiple times, in different solvents. We believe that several of the hydroxy heterocycles, and in particular some 5- and 3-hydroxypyrazoles,[7-16] reported in the literature and characterized in solution only by standard spectroscopic methods could in reality be derivatives in which the tautomeric ratio has been dictated by the solvent effect, while the structure in the crystalline state is probably the keto tautomer.

In our opinion, in order to avoid misunderstandings deriving from the assignment of two different structures and names to compounds in a state of tautomeric equilibrium, the name of such a compound should refer to the structure in its crystalline state, emphasizing the existence in solution of enol–keto tautomeric forms, in a specific ratio, depending on temperature, time, and the solvent used.

Experimental Section

General. Conjugated azoalkenes **1a–e** were prepared as previously reported.[18,19] Heteroaryl thiols **2a–f**, the solution of sodium methoxide in methanol (30 wt %), and trifluoroacetic acid were commercial materials (Aldrich or Janssen) and were used without further purification. Melting points were determined in capillary tubes with a Gallenkamp melting point apparatus and are uncorrected. IR spectra were obtained in Nujol mulls with a Perkin-Elmer 298 spectrophotometer. ^1H and ^{13}C NMR spectra of 200 MHz were recorded on a Bruker AC-200 in DMSO-d_6. Chemical shifts (δ) were reported in ppm downfield from internal TMS. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; D_2O-ex, D_2O exchange; PD, pyrimid-2-yl; MI, 1-methylimidazol-2-yl; MTZ, 4-methyl-1,2,4-triazol-3-yl; MTD, 5-methyl-1,3,4-thiadiazol-2-yl; BO, benzoxazol-2-yl; BT, benzothiazol-2-yl. Macherey-Nagel precoated silica gel SIL G-25 UV_{254} plates (0.25 mm) were employed for analytical thin-layer chromatography (TLC) and Baker silica gel (0.063-0.200 mm) for column chromatography.

Preparation of α-(Heteroarylthio) Hydrazones 3a–p. To a magnetically stirred solution of heteroaryl thiol (2 mmol) in methanol (4 mL) (**2a,c–e**) or tetrahydrofuran (4 mL) (**2b**) was added azoalkene **1a–e** (2 mmol) in small portions during 1 h at 0–5 °C. The reaction was continued for a further 1 h under the same conditions until azoalkene **1** disappeared (checked by TLC). In the cases in which the precipitate was formed during the reaction, the solid product was at first filtered off, and the filtrate, after evaporation of the solvent under reduced pressure, was separated by flash chromatography on silica gel column (eluent, ethyl acetate–cyclohexane mixtures), giving further product **3**. In the cases in which the reaction did not directly give the precipitate, after evaporation of solvent under reduced pressure, the product **3** was obtained by flash chromatography separation on a silica gel column (eluent, ethyl acetate–cyclohexane mixtures). Products **3a-p** were recrystallized from methanol/ethyl ether, dichloromethane/*n*-pentane, or tetrahydrofuran/*n*-pentane.

Methyl 2-((pyrimid-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3a): mp 128–129 °C; IR ν_{max} 3520, 3405, 3185, 3130, 3080, 1730, 1685, 1570, 1560, 1550, 1285 1158 cm^{-1}; ^1H NMR δ 1.97 (s, 3 H, Me), 3.70 (s, 3 H, OMe), 5.37 (s, 1 H, CH), 6.22 (s, 2 H, NH_2, D_2O-ex), 7.28 (t, 1 H, J = 5 Hz, PD), 8.65 (d, 2 H, J = 5 Hz, PD), 9.51 (s, 1 H, NH, D_2O-ex). Anal. Cacld for $C_{10}H_{13}N_5O_3S$: C, 42.40; H, 4.63; N, 24.72. Found: C, 42.56; H, 4.64; N, 24.65.

Ethyl 2-((pyrimid-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3b): mp 133–135 °C; IR ν_{max} 3465, 3280, 3180, 3120, 3080, 1730, 1675, 1580, 1560, 1550, 1290, 1170 cm^{-1}; ^1H NMR δ 1.16 (t, 3 H, J = 7 Hz, CH_2Me), 1.96 (s, 3 H, Me), 4.15 (q, 2 H, J = 7 Hz, CH_2Me), 5.35 (s, 1 H, CH), 6.20 (s, 2 H, NH_2, D_2O-ex), 7.26 (t, 1 H, J = 5 Hz PD), 8.64 (d, 2 H, J = 5 Hz, PD), 9.51 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{11}H_{15}N_5O_3S$: C, 44.44; H, 5.08; N, 23.55. Found: C, 44.27; H, 5.10; N, 23.62.

Methyl 2-((pyrimid-2-yl)thio)acetoacetate ((phenylamino)carbonyl)hydrazone (3c): mp 119-121 °C; IR ν_{max} 3365, 3195, 3090, 1745, 1695, 1590, 1550, 1530, 1268, 1150 cm^{-1}; ^1H NMR δ 2.02 (s, 3 H, Me), 3.72 (s, 3 H, OMe), 5.50 (s, 1 H, CH), 7.01–7.54 (m, 6 H, Ph and PD), 8.62 (s, 1 H, NH, D_2O-ex), 8.66 (d, 2 H, J = 5 Hz, PD), 9.97 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{16}H_{17}N_5O_3S$: C, 53.47; H, 4.77; N, 19.49. Found: C, 53.36; H, 4.76; N, 19.42.

Ethyl 2-((pyrimid-2-yl)thio)acetoacetate ((phenylamino)carbonyl)hydrazone (3d): mp 114–116 °C; IR ν_{max} 3380, 3180, 3070, 1735, 1680, 1590, 1560, 1548, 1515, 1270, 1165 cm^{-1}; ^1H NMR δ 1.19 (t, 3 H, J = 7 Hz, CH_2Me), 2.03 (s, 3 H, Me), 4.19 (q, 2 H, J = 7 Hz, CH_2Me), 5.48 (s, 1 H, CH), 7.02–7.55 (m, 6 H, Ph and PD), 8.62 (s, 1 H, NH, D_2O-ex), 8.68 (d, 2 H, J = 5 Hz, PD), 9.98 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{17}H_{19}N_5O_3S$: C, 54.68; H, 5.13; N, 18.75. Found: C, 54.81; H, 5.11; N, 18.70.

Methyl 2-((1-methylimidazol-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3e): mp 112–114 °C; IR ν_{max} 3460, 3280, 3180, 3085, 1730, 1710, 1586, 1260 cm^{-1}; ^1H NMR δ 1.87 (s, 3 H, Me), 3.63 (s, 3 H, NMe), 3.66 (s, 3 H, OMe), 4.84 (s, 1 H, CH), 6.20 (s, 2 H, NH_2, D_2O-ex), 6.96 (s, 1 H, MI), 7.29 (s, 1 H, MI), 9.38 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{10}H_{15}N_5O_3S$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.02; H, 5.32; N, 24.60.

Ethyl 2-((1-methylimidazol-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3f): mp 93–94 °C; IR ν_{max} 3460, 3330, 3180, 1725, 1690, 1580 cm^{-1}; ^1H NMR δ 1.15 (t, 3 H, J = 7 Hz, CH_2Me), 1.89 (s, 3 H, Me), 3.63 (s, 3 H, NMe), 4.10 (q, 2 H, J = 7 Hz, CH_2Me), 4.82 (s, 1 H, CH), 6.19 (s, 2 H, NH_2, D_2O-ex), 6.96 (s, 1 H, MI), 7.30 (s, 1 H, MI), 9.37 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{11}H_{17}N_5O_3S$: C, 44.14; H, 5.72; N, 23.40. Found: C, 44.04; H, 5.70; N, 23.47.

Methyl 2-((1-methylimidazol-2-yl)thio)acetoacetate ((phenylamino)carbonyl)hydrazone (3g): mp 169–170 °C; IR ν_{max} 3180, 3060, 1725, 1670, 1595, 1540, 1240 cm^{-1}; ^1H NMR δ 1.94 (s, 3 H, Me), 3.67 (s, 3 H, NMe), 3.70 (s, 3 H, OMe), 5.00 (s, 1 H, CH), 6.97–7.50 (m, 7 H, Ph and MI), 8.65 (s, 1 H, NH, D_2O-ex), 9.84 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{16}H_{19}N_5O_3S$: C, 53.17; H, 5.30; N, 19.38. Found: C, 53.29; H, 5.28; N, 19.44.

Methyl 2-((1-methylimidazol-2-yl)thio)acetoacetate (methoxycarbonyl)hydrazone (3h): mp 84–85 °C; IR ν_{max} 3140, 3120, 1735, 1550, 1230 cm^{-1}; ^1H NMR δ 1.91 (s, 3 H, Me), 3.63 (s, 3 H, NMe), 3.65 (s, 6 H, OMe), 4.84 (s, 1 H, CH), 6.95 (s, 1 H, MI), 7.28 (s, 1 H, MI), 10.08 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{11}H_{16}N_4O_4S$: C, 43.99; H, 5.37; N, 18.65. Found: C, 44.03; H, 5.38; N, 18.61.

Methyl 2-((4-methyl-1,2,4-triazol-3-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3i): mp 139–140 °C; IR ν_{max} 3460, 3200, 3146, 3110, 1735, 1700, 1580, 1570, 1285, 1160 cm^{-1}; ^1H NMR δ 1.90 (s, 3 H, Me), 3.63 (s, 3 H, NMe), 3.69 (s, 3 H, OMe), 5.02 (s, 1 H, CH), 6.22 (s, 2 H, NH_2, D_2O-ex), 8.62 (s, 1 H, MTZ), 9.43 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_9H_{14}N_6O_3S$: C, 37.76; H, 4.93; N, 29.35. Found: C, 37.70; H, 4.91; N, 29.29.

Ethyl 2-((4-methyl-1,2,4-triazol-3-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3j): mp 135–136 °C; IR ν_{max} 3465, 3190, 3130, 1725, 1700, 1570, 1296 cm^{-1}; ^1H NMR δ 1.15 (t, 3 H, J = 7 Hz, CH_2Me), 1.89 (s, 3 H, Me), 3.63 (s, 3 H, NMe), 4.13 (q, 2 H, J = 7 Hz, CH_2Me), 4.99 (s, 1 H, CH), 6.14 (s, 2 H, NH_2, D_2O-ex), 8.59 (s, 1 H, MTZ), 9.40 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{10}H_{16}N_6O_3S$: C, 39.99; H, 5.37; N, 27.98. Found: C, 39.90; H, 5.39; N, 28.03.

Methyl 2-((4-methyl-1,2,4-triazol-3-yl)thio)acetoacetate ((phenylamino)carbonyl)hydrazone (3k): mp 140–142 °C; IR ν_{max} 3280, 3190, 3110, 1735, 1600, 1550, 1300, 1205 cm^{-1}; ^1H NMR δ 1.96 (s, 3 H, Me), 3.68 (s, 3 H, NMe), 3.73 (s, 3 H, OMe), 5.18 (s, 1 H, CH), 7.01 (t, 1 H, Ph), 7.30 (t, 2 H, Ph), 7.56 (m, 2 H, Ph), 8.63 (s, 1 H, MTZ), 8.65 (s, 1 H, NH,

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D_2O-ex), 9.90 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{15}H_{18}N_6O_3S$: C, 49.71; H, 5.01; N, 23.19. Found: C, 49.80; H, 5.00; N, 23.14.

Ethyl 2-((4-methyl-1,2,4-triazol-3-yl)thio)acetoacetate ((phenylamino)carbonyl)hydrazone (31): mp 136–138 °C; IR ν_{max} 3385, 3200, 3120, 1725, 1675, 1600, 1590, 1300, 1215 cm^{-1}; ^1H NMR δ 1.19 (t, 3 H, J = 7 Hz, CH_2Me), 1.96 (s, 3 H, Me), 3.68 (s, 3 H, NMe), 4.18 (q, 2 H, J = 7 Hz, CH_2Me), 5.16 (s, 1 H, CH), 7.01 (t, 1 H, Ph), 7.29 (t, 2 H, Ph), 7.53 (d, 2 H, Ph), 8.63 (s, 2 H, NH and MTZ), 9.70 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{16}H_{20}N_6O_3S$: C, 51.05; H, 5.36; N, 22.33. Found: C, 51.00; H, 5.38; N, 22.36.

Methyl 2-((4-methyl-1,2,4-triazol-3-yl)thio)acetoacetate (methoxycarbonyl)hydrazone (3m): mp 105–107 °C; IR ν_{max} 3600, 3375, 3130, 3090, 1730, 1535, 1255, 1224 cm^{-1}; ^1H NMR δ 1.93 (s, 3 H, Me), 3.64 (s, 6 H, OMe), 3.68 (s, 3 H, NMe), 5.06 (s, 1 H, CH), 8.61 (s, 1 H, MTZ), 10.15 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{10}H_{15}N_5O_4S$: C, 39.86; H, 5.02; N, 23.24. Found: C, 39.80; H, 5.01; N, 23.20.

Methyl 2-((5-methyl-1,3,4-thiadiazol-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3n): mp 130–131 °C; IR ν_{max} 3460, 3190, 3140, 1745, 1695, 1580, 1280, 1150 cm^{-1}; ^1H NMR δ 1.93 (s, 3 H, Me), 2.69 (s, 3 H, Me-MTD), 3.72 (s, 3 H, OMe), 5.34 (s, 1 H, CH), 6.28 (s, 2 H, NH_2, D_2O-ex), 9.54 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_9H_{13}N_5O_3S_2$: C, 35.63; H, 4.32; N, 23.09. Found: C, 35.67; H, 4.31; N, 23.04.

Methyl 2-((benzoxazol-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3o): mp 143–144 °C; IR ν_{max} 3500, 3400, 3200, 3085, 1725, 1690, 1566, 1490, 1210, 1130 cm^{-1}; ^1H NMR δ 2.00 (s, 3 H, Me), 3.74 (s, 3 H, OMe), 5.52 (s, 1 H, CH), 6.28 (s, 2 H, NH_2, D_2O-ex), 7.28–7.37 (m, 2 H, BO), 7.59–7.68 (m, 2 H, BO), 9.59 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{13}H_{14}N_4O_4S$: C, 48.44; H, 4.38; N, 17.38. Found: C, 48.48; H, 4.39; N, 17.40.

Ethyl 2-((benzoxazol-2-yl)thio)acetoacetate (aminocarbonyl)hydrazone (3p): mp 137–138 °C; IR ν_{max} 3460, 3150, 1740, 1690, 1578, 1506, 1270, 1130 cm^{-1}; ^1H NMR δ 1.16 (t, 3 H, J = 7 Hz, CH_2Me), 2.01 (s, 3 H, Me), 4.20 (q, 2 H, J = 7 Hz, CH_2Me), 5.50 (s, 1 H, CH), 6.28 (s, 2 H, NH_2, D_2O-ex) 7.30–7.37 (m, 2 H, BO), 7.62–7.65 (m, 2 H, BO), 9.81 (s, 1 H, NH, D_2O-ex). Anal. Calcd for $C_{14}H_{16}N_4O_4S$: C, 49.99; H, 4.79; N, 16.66. Found: C, 49.91; H, 4.78; N, 16.71.

One-Pot Procedure for the Synthesis of 4-(Heteroarylthio)-1*H*-pyrazol-5(2*H*)-ones 4a-p. To a magnetically stirred solution of heteroaryl thiol **2a-e** (2 mmol) in methanol (4 mL) was added azoalkene **1a-e** (2 mmol) in small portions during 0.5 h at 0–5 °C. The reaction was continued for 0.5 h until azoalkene **1** disappeared (checked by TLC), and then a solution of sodium methoxide (2 mmol) in methanol (30 wt %) was added at the same temperature. After being stirred for 1 h under the same conditions, the reaction mixture was acidified by addition of a solution of trifluoroacetic acid (2 mmol) in methanol (1 mL). In most cases the product **4** precipitated directly from the reaction mixture and was collected by filtration in good purity. The filtrate solution was evaporated under reduced pressure and the residue was separated by flash chromatography on a silica gel colum (eluent, ethyl acetate–methanol mixtures) giving further product **4**. In the case in which the reaction did not directly give the precipitate, after evaporation of the solvent under reduced pressure, the product **4** was obtained by flash chromatography on silica gel column (eluent, ethyl acetate–methanol mixtures). The products **4a–p** were recrystallized from methanol/tetrahydrofuran or tetrahydrofuran/*n*-pentane.

Procedure for the Synthesis of 4-(Heteroarylthio)-1*H*-pyrazol-5(2*H*)-ones 4a,b,d-j,l from α-Heteroarylthio Hydrazones 3a-p. To a magnetically stirred solution of α-(heteroarylthio) hydrazone **3** (2 mmol) in methanol (4 mL) was added a solution of sodium methoxide (2 mmol) in methanol (30 wt %) at 0–5 °C, and the reaction mixture was allowed to stand under these conditions for 1 h. The reaction mixture was then treated according to the above-described procedure, affording the products **4a,b,d-j,l**.

1(Aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4a): mp 205–207 °C; IR ν_{max} 3300, 3200, 3120, 1740, 1635, 1560, 1545, 1340 cm^{-1}; ^1H NMR δ 2.16 (s, 3 H, Me), 7.22 (t, 1 H, J = 5 Hz, PD), 7.93, 8.19 (brs, 2 H, NH_2, D_2O-ex), 8.58 (d, 2 H, J = 5 Hz, PD), 13.3 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.00 (Me), 88.01 (C4), 117.63 (PD), 148.97 (C3), 154.01 (C=O), 157.87 (PD), 161.96 (C5), 170.83 (PD). Anal. Calcd for $C_9H_9N_5O_2S$: C, 43.02; H, 3.61; N, 27.87. Found: C, 43.05; H, 3.60; H, 27.85.

1-(Anilinocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4b): mp 204–205 °C; IR ν_{max} 3450, 3190, 1725, 1590, 1550, 1200 cm^{-1}; ^1H NMR δ 2.23 (s, 3 H, Me), 7.14 (t, 1 H, Ph), 7.24 (t, 1 H, J = 5 Hz, PD), 7.39 (t, 2 H, Ph), 7.54 (d, 2 H, Ph), 8.61 (d, 2 H, J = 5 Hz, PD), 11.13 (s, 1 H, NH, D_2O-ex), 13.7 (brs, 1H, NH, D_2O-ex); ^{13}C NMR δ 11.07 (Me), 88.16 (C4), 117.72 (PD), 119.61 (Ph), 124.06 (Ph), 129.07 (Ph), 136.69 (Ph), 146.13 (C3), 154.88 (C=O), 157.92 (Pd), 162.29 (C5), 170.38 (PD). Anal. Calcd for $C_{15}H_{13}N_5O_2S$: C, 55.04; H, 4.00; N, 21.39. Found: C, 54.96; H, 3.99; N, 21.45.

1-(Methoxycarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4c): mp 151–152 °C; IR ν_{max} 3440, 1765, 1670, 1550, 1320, 1300, 1200, 1180 cm^{-1}; ^1H NMR δ 2.14 (s, 3 H, Me), 3.91 (s, 3 H, OMe), 7.23 (t, 1 H, J = 5 Hz, PD), 8.59 (d, 2 H, J = 5 Hz, PD), 12.7 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.66 (Me), 53.78 (OMe), 87.92 (C4), 117.72 (PD), 148.64 (C3), 157.02 (C=O), 157.82 (PD), 160.29 (C5), 170.66 (PD). Anal. Calcd for $C_{10}H_{10}N_4O_3S$: C, 45.11; H, 3.79; N, 21.04. Found: C, 45.01; H, 3.80; N, 21.07.

1-(Aminocarbonyl)-3-methyl-4-((1-methylimidazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4d): mp 214–216 °C; IR ν_{max} 3280, 3150, 3130, 3090, 1700, 1630, 1570, 1275, 1050 cm^{-1}; ^1H NMR δ 2.23 (s, 3 H, Me), 3.75 (s, 3 H, NMe), 7.42 (s, 1 H, MI), 7.60 (s, 1 H, MI), 7.91, 8.11 (brs, 2 H, NH_2, D_2O-ex), 13.0 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.37 (Me), 33.47 (NMe), 87.28 (C4), 123.42 (MI), 127.08 (MI), 140.38 (C3), 149.32 (MI), 153.14 (C=O), 162.21 (C5). Anal. Calcd for $C_9H_{11}N_5O_2S$: C 42.68; H, 4.38; N, 27.65. Found: C, 42.75; H, 4.39; N, 27.58.

1-(Anilinocarbonyl)-3-methyl-4-((1-methylimidazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4e): mp 196–198 °C; IR ν_{max} 3160, 3120, 1715, 1600, 1565, 1275, 1230, 1060 cm^{-1}; ^1H NMR δ 2.13 (s, 3 H, Me), 3.80 (s, 3 H, NMe), 7.05 (t, 1 H, Ph), 7.26 (s, 1 H, MI), 7.33 (t, 2 H, Ph), 7.49 (s, 1 H, MI), 7.51 (d, 2 H, Ph), 11.88 (s, 1 H, NH, D_2O-ex); ^{13}C NMR δ 12.42 (Me), 33.98 (NMe), 95.71 (C4), 119.11 (Ph), 123.02 (Ph), 123.92 (MI), 128.58 (MI), 128.87 (Ph), 137.94 (Ph), 142.50 (C3), 147.80 (MI), 152.96 (C=O), 164.30 (C5). Anal. Calcd for $C_{15}H_{15}N_5O_2S$: C, 54.70; H, 4.59; N, 21.26. Found: C, 54.80; H, 4.57; N, 21.31.

1-(Methoxycarbonyl)-3-methyl-4-((1-methylimidazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4f): mp 167–168 °C; IR ν_{max} 3380, 3110, 1725, 1660, 1580, 1330, 1280, 1145, 1050 cm^{-1}; ^1H NMR δ 2.06 (s, 3 H, Me), 3.70 (s, 3 H, NMe), 3.75 (s, 3 H, OMe), 7.15 (s, 1 H, MI), 7.40 (s, 1 H, MI); ^{13}C NMR δ 13.08 (Me), 33.62 (NMe), 52.36 (OMe), 79.21 (C4), 123.06 (MI), 125.58 (MI), 142.79 (C3), 150.32 (MI), 155.36 (C=O), 163.93 (C5). Anal. Calcd for $C_{10}H_{12}N_4O_3S$: C, 44.77; H, 4.51; N, 20.88. Found: C, 44.69; H, 4.49; N, 20.80.

1-(Aminocarbonyl)-3-methyl-4-(4-methyl-1,2,4-triazol-3-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4g): mp 218–220 °C; IR ν_{max} 3360, 3200, 3130, 3080, 1710, 1660, 1578, 1340, 1210 cm^{-1}; ^1H NMR δ 2.30 (s, 3 H, Me), 3.73 (s, 3 H, NMe), 7.95, 8.15 (s, 2 H, NH_2, D_2O-ex), 8.53 (s, 1 H, MTZ), 13.4 (s, 1 H, NH, D_2O-ex); ^{13}C NMR δ 10.95 (Me), 31.14 (NMe), 87.50 (C4), 146.15 (MTZ), 148.60 (MTZ), 148.70 (C3), 153.57 (C=O), 161.45 (C5). Anal. Calcd for $C_8H_{10}N_6O_2S$: C, 37.79; H, 3.96; N, 33.05. Found: C, 33.70; H, 3.97; N, 33.10.

1-(Anilinocarbonyl)-3-methyl-4-((4-methyl-1,2,4-triazol-3-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4h): mp 197–198 °C; IR ν_{max} 3250, 3070, 1710, 1620, 1570, 1218, 1198, 1060 cm^{-1}; ^1H NMR δ 2.35 (s, 3 H, Me), 3.75 (s, 3 H, NMe), 7.14 (t, 1 H, Ph), 7.38 (t, 2 H, Ph), 7.5 (d, 2 H, Ph), 8.55 (s, 1 H, MTZ), 11.08 (s, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.15 (Me), 31.22 (NMe), 87.28 (C4), 119.61 (Ph), 124.06 (Ph), 129.05 (Ph), 136.71 (Ph), 146.04 (C3), 146.19 (MTZ), 148.60 (MTZ), 153.37 (C=O), 161.91 (C5). Anal. Calcd for $C_{14}H_{14}N_6O_2S$: C, 50.90; H, 4.27; N, 25.44. Found: C, 51.04; H, 4.29; N, 25.50.

1-(Methoxycarbonyl)-3-methyl-4-((4-methyl-1,2,4-triazol-3-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4i): mp 141–142 °C;

IR ν_{max} 3340, 3120, 1735, 1675, 1560, 1510, 1300, 1180, 1150 cm^{-1}; ^1H NMR δ 2.25 (s, 3 H, Me), 3.72 (s, 3 H, NMe), 3.86 (s, 3 H, OMe), 8.51 (s, 1 H, MTZ); ^{13}C NMR δ 11.48 (Me), 31.14 (NMe), 53.86 (OMe), 87.85 (C4), 146.11 (MTZ), 148.34 (MTZ), 148.54 (C3), 156.63 (C=O), 159.72 (C5). Anal. Calcd for $C_9H_{11}N_5O_3S$: C, 40.14; H, 4.12; N, 26.01. Found: C, 40.04; H, 4.11; N, 26.09.

1-(Aminocarbonyl)-3-methyl-4-((5-methyl-1,3,4-thiadiazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4j): mp 187–189 °C; IR ν_{max} 3280, 3100, 3050, 1706, 1680, 1580, 1540 cm^{-1}; ^1H NMR δ 2.27 (s, 3 H, Me), 2.60 (s, 3 H, Me-MTD), 8.03, 8.12 (s, 2 H, NH_2, D_2O-ex), 13.7 (brs, 1 H, NH, D_2O-ex), ^{13}C NMR δ 10.85 (Me), 15.07 (Me-MTD), 88.45 (C4), 148.58 (C3), 153.19 (C=O), 160.99 (C5), 165.42 (MTD), 169.64 (MTD). Anal. Calcd for $C_8H_9N_5O_2S_2$: C, 35.42; H, 3.34; N, 25.81. Found: C, 35.46; H, 3.34; N, 25.76.

1-(Anilinocarbonyl)-3-methyl-4-((5-methyl-1,3,4-thiadiazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4k): mp 180–181 °C; IR ν_{max} 3450, 3210, 1730, 1600, 1550, 1200 cm^{-1}; ^1H NMR δ 2.32 (s, 3 H, Me), 2.60 (s, 3 H, Me-MTD), 5.26 (brs, 1 H, NH, D_2O-ex), 7.19 (t, 1 H, Ph), 7.40 (t, 2 H, Ph), 11.09 (s, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.18 (Me), 15.04 (Me-MTD), 87.65 (C4), 119.54 (Ph), 124.07 (Ph), 129.03 (Ph), 136.78 (Ph), 146.21 (C3), 153.79 (C=O), 160.79 (C5), 165.39 (MTD). Anal. Calcd for $C_{14}H_{13}N_5O_2S_2$: C, 48.40; H, 3.77; N, 20.16. Found: C, 48.46; H, 3.76; N, 20.11.

1-(Aminocarbonyl)-3-methyl-4-((benzoxazolyl-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (41): mp 184–186 °C; IR ν_{max} 3340, 3200, 1730, 1640, 1580, 1500, 1340, 1228, 1125 cm^{-1}; ^1H NMR δ 2.30 (s, 3 H, Me), 7.32 (m, 2 H, BO), 7.63 (m, 2 H, BO), 8.04, 8.16 (s, 2 H, NH_2, D_2O-ex), 13.7 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 10.96 (Me), 83.54 (C4), 110.15 (BO), 118.32 (BO), 123.95 (BO), 124.15 (BO), 124.47 (BO), 141.30 (BO), 148.70 (C3), 151.32 (BO), 153.75 (C=O), 161.37 (C5). Anal. Calcd for $C_{12}H_{10}N_4O_3S$: C, 49.65; H, 3.47; N, 19.30. Found: C, 49.54; H, 3.49; N, 19.24.

1-(Anilinocarbonyl)-3-methyl-4-((benzoxazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4m): mp 194–196 °C; IR ν_{max} 3200, 3130, 1720, 1640, 1600, 1560, 1190 cm^{-1}; ^1H NMR δ 2.36 (s, 3 H, Me), 7.15 (t, 1 H, Ph), 7.29–7.43 (m, 4 H, Ph and BO), 7.54–7.68 (m, 4 H, Ph and BO), 11.03 (s, 1 H, NH, D_2O-ex), 13.3 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.19 (Me), 83.48 (C4), 110.18 (BO), 118.34 (BO), 119.65 (Ph), 123.95 (BO), 124.08 (Ph), 124.18 (BO), 124.49 (BO), 129.05 (Ph), 136.69 (Ph), 141.30 (BO), 146.09 (C3), 151.33 (BO), 154.53 (C=O), 161.99 (C5). Anal. Calcd for $C_{18}H_{14}N_4O_3S$: C, 59.01; H, 3.85; N, 15.29. Found: C, 59.10; H, 3.85; N, 15.33.

1-(Aminocarbonyl)-3-methyl-4-((benzothiazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4n): mp 176–178 °C; IR ν_{max} 3310, 3190, 1735, 1660, 1580, 1340 cm^{-1}; ^1H NMR δ 2.30 (s, 3 H, Me), 7.32–7.47 (m, 2 H, BT), 7.81 (d, 1 H, BT), 7.93 (d, 1 H, BT), 8.06, 8.18 (s, 2 H, NH_2, D_2O-ex), 13.7 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 10.87 (Me), 87.49 (C4), 121.09 (BT), 121.52 (BT), 124.02 (BT), 126.11 (BT), 134.72 (BT), 148.70 (C3), 153.82 (C=O), 154.29 (BT), 161.34 (C5). Anal. Calcd for $C_{12}H_{10}N_4O_2S_2$: C, 47.05; H, 3.29; N, 18.29. Found: C, 46.97; H, 3.28; N, 18.34.

1-(Anilinocarbonyl)-3-methyl-4-((benzothiazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4o): mp 192–194 °C; IR ν_{max} 3440, 3180, 1720, 1640, 1600, 1550 cm^{-1}; ^1H NMR δ 2.36 (s, 3 H, Me), 7.16 (t, 1 H, Ph), 7.32–7.60 (m, 6 H, Ph and BT), 7.82 (d, 1 H, BT), 7.93 (d, 1 H, BT), 11.06 (s, 1 H, NH, D_2O-ex), 13.8 (brs, 1 H, NH, D_2O-ex); ^{13}C NMR δ 11.14 (Me), 75.16 (C4), 119.63 (Ph), 121.11 (BT), 121.53 (BT), 123.77 (BT), 124.06 (Ph), 126.12 (BT), 129.08 (Ph), 134.74 (BT), 136.70 (Ph), 146.18 (C3), 154.26 (BT), 154.49 (C=O), 162.03 (C5). Anal. Calcd for $C_{18}H_{14}N_4O_2S_2$: C, 56.53; H, 3.69; N, 14.65. Found: C, 56.41; H, 3.67; N, 14.62.

1-(Methoxycarbonyl)-3-methyl-4-((benzothiazol-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4p): mp 164–166 °C; IR ν_{max} 3250, 1755, 1730, 1650, 1600, 1575, 1305 cm^{-1}; ^1H NMR δ 2.07 (s, 3 H, Me), 3.82 (s, 3 H, OMe), 7.26–7.39 (m, 2 H, BT), 7.74 (d, 1 H, BT), 7.87 (d, 1 H, BT); ^{13}C NMR δ 12.74 (Me), 52.79 (OMe), 80.57 (C4), 120.70 (BT), 121.27 (BT), 123.41 (BT), 125.71 (BT), 134.86 (BT), 150.36 (C3), 154.75 (BT), 155.39 (C=O), 163.77 (C5). Anal. Calcd for $C_{13}H_{11}N_3O_3S_2$: C, 48.59; H, 3.45; N, 13.08. Found: C, 48.66; H, 3.46; N, 13.04.

X-ray Analysis of Methyl 2-((Pyrimid-2-yl)thio)acetoacetate (Aminocarbonyl)hydrazone (3a). Intensity data were collected by a CAD4 diffractomer using a $\omega/2\theta$ scan, range $2.56° < \theta < 27.97°$. Precise unit cell dimensions were determined by a least-squares refinement on diffractometer angles for 25 automatically centered reflections $8° < \theta < 13°$.

Crystal Data of Methyl 2-((Pyrimid-2-yl)thio)acetoaceate (aminocarbonyl)hydrazone (3a): crystal dimensions, 0.8 × 0.6 × 0.3 mm; $C_{10}H_{13}N_5O_3S$; M_r 283.31; triclinic; space group *P*-1; a = 8.308(2) Å, b = 10.545(3) Å, c = 8.187(2) Å, α = 107.26(4)°, β = 97.86(3)°, γ = 73.41(3)°, V = 655.4(3) $Å^3$, D_c = 1.436 mg/m^3, Z = 2, Mo Kα radiation, λ = 0.71069 Å, μ(MoKα) = 0.260 mm^{-1}, F(000) = 296; number of reflections collected, 3314; number of independent reflections 3138 [R(int) = 0.0130].

Structure Determination and Refinement of Methyl 2-((Pyrimid-2-yl)thio)acetoacetate (Aminocarbonyl)hydrazone (3a). The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELX program packages.[20] Goodness of fit on F^2 1.062. In refinements were used weights in accordance with the scheme $w = 1/[\sigma^2(F_o^2) + (0.0641P)^2 + 0.1223P]$ where $P = (F_o^2 + 2F_c^2)/3$. All the hydrogen atoms were revealed in the Fourier difference map, but not refined. The final agreement indices for 8188 reflections [$I > 2\sigma(I)$] were R1 = 0.0365, wR2 = 0.0995. Largest difference peak and hole was 0.306 and −0.323 e $Å^{-3}$; Δ/σ = 0.011.

X-ray Analysis of 1-(Aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4a). Intensity data were collected by a CAD4 diffractometer using a $\omega/2\theta$ scan, range $2.45° < \theta < 25.01°$. Precise unit cell dimensions were determined by a least-squares refinement on diffractometer angles for 25 automatically centered reflections $8° < \theta < 13°$.

Crystal Data of 1-(Aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4a): crystal dimensions, 0.8 × 0.4 × 0.2 mm; $C_9H_9N_5O_2S{\cdot}H_2O$; M_r 269.29; monoclinic; space group $P2_1/n$; a = 8.436(2) Å, b = 16.651(4) Å, c = 8.485(2) Å, β = 92.68(5)°, V = 1190.6(5) $Å^3$, D_c = 1.502 mg/m^3, Z = 2, Mo Kα radiation, λ = 0.71069 Å, μ(MoKα) = 0.282 mm^{-1}, F(000) = 560; number of reflections collected, 2225; number of indipendent reflections 2081 [R(int) = 0.0144].

Structure Determination and Refinement of 1-(Aminocarbonyl)-3-methyl-4-((pyrimid-2-yl)thio)-1*H*-pyrazol-5(2*H*)-one (4a). The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELX program packages.[20] Goodness of fit on F^2 1.119. In refinements were used weights in accordance with the scheme $w = 1/[\sigma^2(F_o^2) + (0.0623P)^2 + 0.3970P]$ where $P = (F_o^2 + 2F_c^2)/3$. All the hydrogen atoms were revealed in the Fourier difference map, but not refined. The final agreement indices for 1814 reflections [$I > 2\sigma(I)$] were R1 = 0.0347, wR2 = 0.1016. Largest difference peak and hole was 0.260 and −0.264 e $Å^{-3}$; Δ/σ = 0.020.

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(21) The authors have deposited atomic coordinates for structures **3a** and **4a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.