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Reactions of 5-mercaptoazoles and pyridine-2-thiones with acetylenic esters. Selectivity of the formation of novel fused thiazin-4-ones and thiazolidin-4-ones

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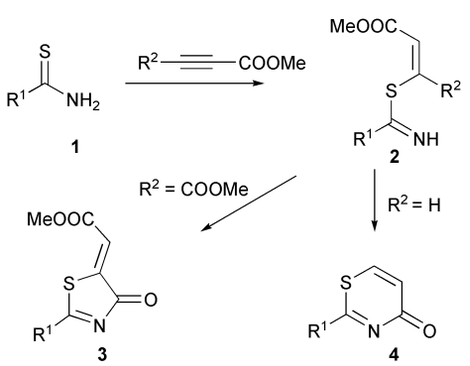
A systematic study of the reactions of dimethyl acetylenedicarboxylate (DMAD) and methyl propynoate with 5-mercaptoazoles and pyridine-2-thiones has been carried out and as a result, a number of novel imidazo[1,5-*b*]-thiazin-4-ones **6a**,**b**, pyrazolo[1,5-*b*] thiazin-4-ones **15a**–**f**, imidazo[1,5-*b*]thiazol-4-ones **7a**,**b** and thiazolo[3,2-*a*]-pyridines **21a**–**c** have been prepared. The influence of the size of the ring of the starting "cyclic" thioamides on the size of the fused ring in the reaction products has been established. The preferred formation of a six-membered thiazine ring took place in the reactions of 5-mercaptoazoles. In contrast, the five membered thiazolidine ring is formed in reactions of pyridine-2-thiones. In both cases the product is a five-membered ring fused to a six-membered heterocycle.

Introduction

The reactions of thioureas, thiosemicarbazides and thioamides with electron poor acetylenes are known as convenient and effective methods to prepare thiazolidin-4-ones and thiazin-4-ones.[1–12] The most probable mechanism of these reactions involves the addition of the sulfur atom of the thiocarbamoyl moiety onto the triple bond of the acetylenes, followed by cyclocondensation of the intermediate vinylthioimidates of type **2** *via* elimination of a molecule of methanol. Reactions of thioamides of various natures with DMAD have been shown to occur *via* one of two possible mechanisms where generally the α-situated ester group participates in the cyclization leading to a five-membered thiazolidine ring **3**.[3,4,6,10–12] An alternative possibility for the cyclization of intermediate **2** (R^2 = H) involves the reaction of the β-ester group to afford a thiazin-4-one ring.[4,6,10]



In previous work, we have shown that novel 2,5-dimethylenethiazolidin-4-one derivatives can be prepared by reaction of malonthioamide derivatives with DMAD[11] and a new synthetic approach to conjugated bicyclic heterocycles has been elaborated based on a similar reaction of heterocyclic thioamides.[12] Reactions of heterocyclic compounds where an endocyclic thioamide group is present with DMAD and methyl propynoate have only been reported once.[4] In order to find a general synthetic method to thiazin-4-ones and thiazolin-4-ones fused to azole and azine rings we have studied the reactions of 5-mercaptoimidazoles, -pyrazoles, -1,2,3-triazoles and tetrahydropyridine-2-thiones with DMAD and methyl propynoate.

Results and discussion

Reaction of 5-mercaptoimidazole-4-carboxamide **5a** with DMAD in principle could give both thiazine **6a** and thiazolidine **7a** rings. We have found that this reaction in methanol at room temperature results in the exclusive formation of fused thiazine **6a** in 66% yield. However, a mixture of thiazine **6a** and thiazolidine **7a** in a ratio of 7 to 3 was obtained when sodium methoxide was used as a catalyst. It should be noted that compound **5a** did not react with methyl propynoate in either circumstances.

The respective thiazin-4-one and thiazolin-4-one structures of products **6a** and **7a** are confirmed by their ^{1}H and ^{13}C NMR spectral data (Experimental section, Table 1). The ^{1}H NMR spectra for both products are very similar but all signals of thiazine **6a** are shifted 0.14–0.18 ppm downfield in comparison with those of **7a**. The signals in the ^{13}C NMR spectra are also very similar for both isomeric products **6a** and **7a**. The ^{1}H coupled ^{13}C NMR spectra of **6a** and **7a** show doublet signals at 119.0 and 118.8 ppm, respectively, with similar $^1J_{CH}$ coupling constants of 175 Hz, which is typical for CC units. The final decision in favor of the thiazolidine structure for **7a** and thiazine for **6a** can be made after considering the magnitudes of the ^{13}C–^{1}H coupling constants in the ^{13}C NMR spectra.[2,11,12] The C_6 and C_4 signals of **7a** are found in the coupled spectrum as doublets with $^2J_{C6–H5}$ coupling constants of 1.4 Hz and $^3J_{C4–H5}$ of 4.8 Hz. This shows the presence of an exocyclic double bond in the structure of thiazolidine **7a**. In contrast to this, the coupled spectrum of **6a** contains a doublet signal for C_4 with a $^2J_{C4–H5}$ coupling constant of 1.4 Hz, which confirms the structure of **6a** as thiazin-4-ones.

In contrast to **5a**, 5-mercapto-1,2,3-triazole-4-carboxamide does not react with DMAD and methyl propynoate. All our attempts to involve this compound in these reactions failed. We have shown that 5-mercapto substituted imidazole-4-thiocarboxamides can react with DMAD to form 2-imidazolyl-

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Table 1 ^{13}C NMR spectra

N	Chemical shifts (ppm), multiplicity						Coupling constants/Hz			
	C_2	C_4	C_5	C_6	C_7	Others	$J_{C5\text{-}H5}$	$J_{C4\text{-}H5}$	$J_{C8\text{-}H8}$	$J_{C6\text{-}H5}$
6a	124.2 d	156.4 d	118.8 d	143.5 s	162.5 s	54.3 q (OCH_3), 133.1 s (C_9), 133.9 d (C_8H), 162.0 s (C_{10})	175.0	<1.0	223.0	
6b	127.6 d	156.8 d	119.0 d	144.3 s	162.2 s	54.3 q (OCH_3), 133.2 s (C_9), 134.9 d (C_8H), 163.5 s (C_{10})	174.0	1.5	224.0	
7a	124.2 d	156.4 d	118.8 d	143.5 d	162.0 s	54.3 q (OCH_3), 127.6 s (C_9), 134.0 d (C_8H), 186.6 s (C_{10})	175.0	4.8	222.2	1.4
7b	127.6 d	158.2 d	112.7 d	144.3 s	160.1 s	54.3 q (OCH_3), 127.6 s (C_9), 132.7 d (C_8), 187.3 s (C_{10})	174.0	3.3	220.0	
15a	124.1	154.5	122.4	141.3	162.0	11.7 (C_{14}), 54.3 (OCH_3), 54.7 (OCH_3), 114.8 (C_{11}), 124.1 (C_{12}), 125.4 (C_8), 135.6 (C_{13}), 145.9 (C_{10}), 152.8 (C_9)				
15b	125.8	154.5	122.1	141.8	161.8	11.7 (C_{14}), 21.0 (CH_3), 54.3 (OCH_3), 121.8 (C_{11}), 130.1 (C_{12}), 136.5 (C_8), 141.8 (C_{13}), 149.8 (C_{10}), 153.1 (C_9)				
15c	127.0 s	155.3 br s	122.7 d	142.1 s	162.7 s	12.6 q (Me), 54.2 q (OCH_3), 136.5 s, 154.1 s ($C_{pyrazole}$), 123.5 d, 130.5 d, 132.3 s, 152.6 s (Ar)	173.6			
15d	125.9 s	154.9 d	122.6 d	142.1 s	161.9 s	12.0 q (Me), 54.3 q (OCH_3), 136.5 s, 154.6 s ($C_{pyrazole}$), 123.5 d, 129.4 d, 137.2 s, 150.6 s (Ar)	174.1	0.6		
15e	127.2	154.6	122.9	141.8	161.9	11.8 (C_{14}), 14.2 (CH_3), 54.5 (OCH_3), 61.2 (OCH_2), 123.0 (C_{11}), 130. (C_{12}), 136.0 (C_8), 141.6 (C_{13}), 153.8 (C_9), 153.8 (C_{10}), 165.2 (COOEt)				
15f	126.4 d	155.1 d	118.8 d	137.9 dd		12.0 q (Me), 136.5 s, 153.5 s ($C_{pyrazole}$), 123.4 d, 129.5 d, 137.0 s, 150.8 s (Ar)	173.1	10.6		2.3
19	122.6	154.6	121.8	141.2	162.2	11.8 (C_{14}), 53.9 (OCH_3), 119.2 (C_8), 151.7 s (C_9), 121.8 (C_{11}), 131.4 (C_{12}), 132.4 (C_{13}), 149.8 ($_{10}$)				
21a	137.7	166.1	113.7	143.1	166.2	52.3 (OCH_3), 66.0 (C_{10}), 109.7 (C_8), 119.2 (CN), 127.2, 127.6, 128.6, 144.9 (Ar), 147.6 (C_{11}), 164.5 (C_{12})				
21b	137.7	166.0	114.5	144.3	166.1	52.4 (OCH_3), 34.6 (C_9), 65.7 (C_{10}), 109.6 (C_8), 119.1 (CN), 147.9 (C_{11}), 147.3, 125.2, 125.5 d, 127.0 ($C_{thienyl}$), 164.5 (C_{12})				
21c	142.0 d	164.3 d	115.8 d	142.3 s	165.9 q	13.7 and 61.2 q (OCH_2CH_3), 52.5 q (OCH_3), 35.1 d, 65.7 m, 106.7 d, 147.6 d (C_{pyr}), 118.7 s (CN), 147.2 m, 127.0 d, 125.2 d, 125.1 d ($C_{thienyl}$)	172.8	5.6		

thiazolidines.[12] Therefore, we expected from the reaction of thioamide **5b** with DMAD the formation of the products of type **6**–**9** from the condensation with both the exocyclic and endocyclic thioamide groups.

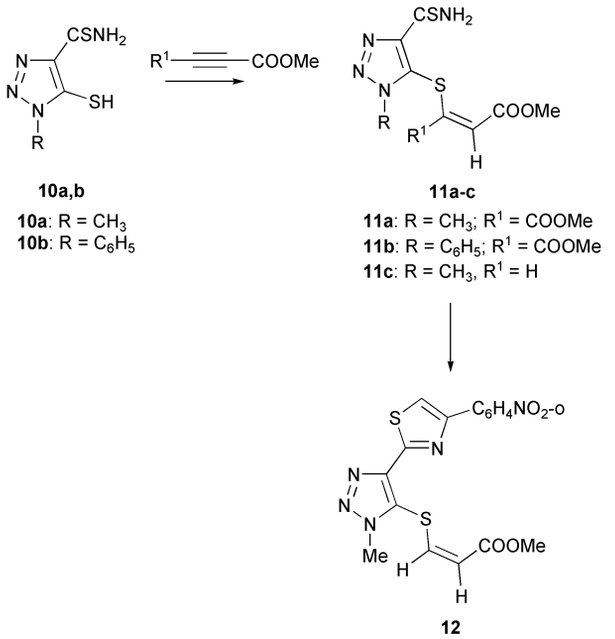
We have found that reaction of **5b** with DMAD in methanol, either with or without sodium methoxide, affords a mixture of thiazine **6b** and thiazolidine **7b** in a ratio of 9 to 1 in 50% yield. The ^1H and ^{13}C NMR spectra of products **6b**, **7b** are very similar to those of **7a** and **7b** (See Table 1). The downfield shift (0.5– 0.6 ppm) of the signals of C_8–H of **6b**, **7b** in comparison with the conjugated imidazolylthiazolidines[12] also confirmed the formation of fused imidazoles in this reaction. The ^{13}C NMR spectra of **7a** and **7b** contain signals at 186.8 and 187.3 ppm corresponding to signals of the unchanged thioamide groups.

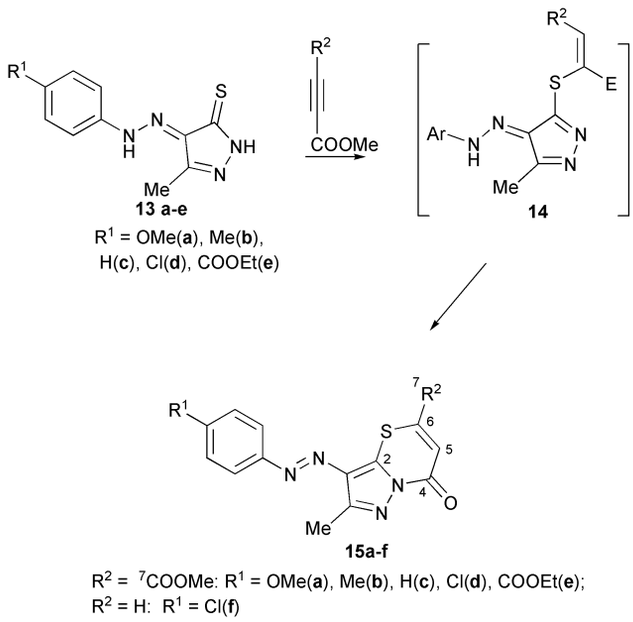
We have found that 5-mercapto-1,2,3-triazole-4-thiocarboxamides **10** are less active in the reaction with DMAD in comparison with 5-mercaptoimidazoles. Triazoles, that are unsubstituted at the ring nitrogen did not react either with DMAD or methyl propynoate. On the other hand 1-R-5-mercapto-1,2,3-triazoles reacted with both DMAD and methyl propynoate to form vinyl sulfide derivatives **11**. The presence of two ester groups and a vinyl moiety in compounds **11** was confirmed by the presence of two signals in their ^1H NMR spectra at 3.45–3.76 ppm, signals at 6.69 and 6.70 in spectra of **11a**,**b** respectively and of doublet signals at 6.10 and 7.25 with vicinal coupling constant of 8.6 Hz in spectra of **11c**. We did not manage to react compounds **11a**–**c** with a further equivalent of DMAD, although **11c** smoothly reacted with *o*-nitrophenacyl bromide to give 2-triazolylthiazole **12** in 74% yield.

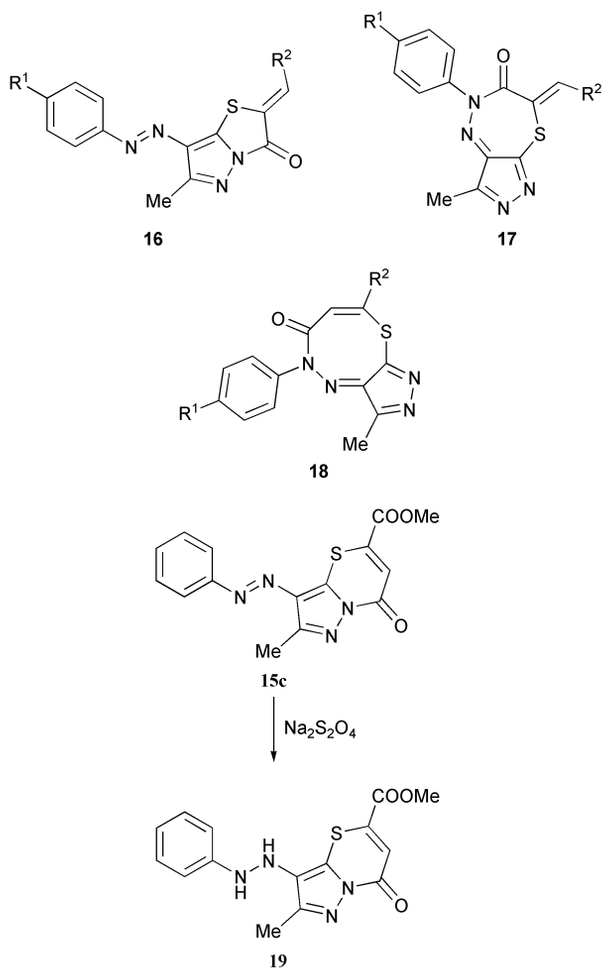
Indeed, reaction of DMAD with 5-mercaptoazole-4-thiocarboxamides **5b**,**10a**,**b** preferably occurs with participation of the endocyclic thioamide group, similar to the reaction of these compounds with alkylating agents.[13,14] This can be rationalized by the existence of **5b**,**10** in a zwitterionic tautomeric form where the negative charge is located at the 5-sulfur atom which should enhance an electrophilic attack to this center.

In the reaction of 4-arylhydrazonopyrazole-5-thiones **13** with esters of acetylenecarboxylic acids one can theoretically expect the formation at least 4 products **15**–**18** because both thioamide and hydrazono groups of **13** are known to react with DMAD.[10–12,15] If we suppose that the most nucleophilic sulfur atom reacts first with the acetylene to form an intermediate vinylthioimidate of type **14** then the direction of its cyclization will govern the composition of the products **15**–**18**.

We have found that compounds **13a**–**f** readily react with DMAD and methyl propynoate to form **15a**–**f** as the only products in good yields. The assignments of the structures of compounds **15** as pyrazolo[1,5-*b*]thiazin-4-ones follows from the analysis of their ^1H and ^{13}C NMR spectra and from the reaction of **15d** with sodium dithionite. Mass spectra, and







decoupled ^{1}H and ^{13}C NMR spectra did not allow one to make a difference between structures **15**–**18**. At the same time, the similarity of the NMR spectra for the products obtained in the reaction of DMAD and methyl propynoate allowed us to assume that the same type of product was formed in both types of reactions. The spectrum of **15f** shows two doublets as an AB system with a coupling constant of 10.6 Hz which is typical for a CH=CH moiety. The C_4 and C_7 signals in the coupled spectrum of **15d** are found at δ = 154.9 ppm as doublets with a $^{2}J_{C4–H5}$ coupling constant of 0.6 Hz and at 161.9 ppm with $^{3}J_{C7–H5}$ of 3.8 Hz, respectively. These data allowed us to rule the structures **16** and **17** out of consideration, since one should observe an AB system in their spectra with a geminal constant of 18–22 Hz and a higher magnitude (2–5 Hz) for the coupling constant $J_{C4–H5}$.

An additional argument in favor of structure **15** was made from reduction of compound **15d** by sodium dithionite. The arylhydrazino derivative **19** was obtained, and hydrazines are typical reduction products of arylazo compounds. This finally eliminates structures **17** and **18**.

Thus, the novel imidazo[1,5-*b*]thiazin-4-ones **6a**,**b**, pyrazolo-[1,5-*b*]thiazin-4-ones **15a-f** and imidazo[1,5-*b*]thiazole-4-ones **7a**,**b** have been prepared by reactions of 5-mercaptoazoles with DMAD and methyl propynoate.

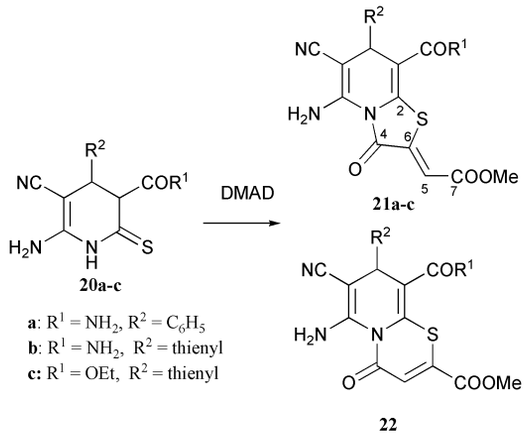
To study whether the size of the ring formed in the reaction of endocyclic thioamides with acetylene carboxylic esters depends on the type of ring in the starting compounds, we have carried out the reaction of 3,4-dihydropyridine-2(1H)-thiones **20a**–**c** with DMAD.

Reaction of 2(1*H*)-pyridinethiones with DMAD is known to give thiazolo[3,2-*a*]pyridinium salts. At the same time, the reaction of 2(1*H*)-pyridinethiones with methyl propynoate results in the acyclic condensation products.[16–18] 3,4-Dihydropyridin-2(1*H*)-ones have not been reacted with acetylene carboxylic acids so far.

By analogy with the reactions of malonthioamides and with the chemistry of the 5-mercaptoazoles mentioned above, one can expect the formation of both pyridothiazoles of type **21** and pyridothiazines **22** from the reaction of compounds **20** with DMAD. We have found that the reaction of pyridinethiones **20a**–**c** with DMAD in chloroform in the presence of triethylamine selectively affords thiazolo[3,2-*a*]pyridines **21a**–**c** in good yields. The structure assignment of the compounds prepared follows from their NMR spectra. ^{1}H NMR spectra of **21a**–**c** show signals at 6.65–6.78 ppm and the coupled ^{13}C NMR spectrum of **21c** contains doublets of C_4 with a $^{3}J_{CH}$ coupling constant of 5.6 Hz with the vinyl proton, and of C_7 with a $^{2}J_{CH}$ coupling constant of less than 1.0 Hz with the same vinyl proton. This is in accordance with the presence of an exocyclic double bond in the structures of compounds **21a**–**c**. Furthermore, the magnitude of the constant $^{3}J_{C4–H5}$ confirms the (*Z*)-configuration of this bond.

Conclusion

The data obtained allows us to make some conclusions. The size of the rings formed in the reactions of cyclic thioamides



with acetylenecarboxylic esters depends on the size of the starting heterocycle. Thus, a five-membered thiazolidine ring condenses onto the pyridine ring and a six-membered thiazine ring is fused onto a five-membered azole ring. In contrast to all reactions of thioamides of various structures,[9–12] including reactions of pyridinethiones with DMAD where the thiazolidin-4-ones are formed exclusively, the reactions of 5-mercaptoazoles with acetylenecarboxylic esters lead to the preferred formation of a six-membered thiazine ring. This exception to the general rule can be explained by the increased ring strain for two fused five-membered rings compared to a situation where a six-and five-membered ring are fused. This also implies that the reactions are under thermodynamic rather than kinetic control.

Experimental

General

^{1}H and ^{13}C spectra were recorded at 400 and 100 MHz, respectively on a Bruker AMX 400 with $SiMe_4$ as an internal reference in ether DMSO-d_6 + CCl_4 or $CDCl_3$ solutions. Mass spectra were obtained on a Varian MAT 311A instrument using the electron impact ionization technique (40–200 °C, 70 eV). Reactions were monitored by TLC (Silufol®) on aluminium foil plates) in $CHCl_3$–EtOH (9 : 1), $CHCl_3$–EtOH–NH_4OH (15 : 8 : 1), acetone–hexane (3 : 5) visualized under UV light. All solvents were distilled prior to use.

General procedure. For reaction of 5-mercaptoazoles and pyridine-2-thiones with esters of acetylenecarboxylic and propiolic acids.

Method A. The acetylenecarboxylic ester (0.0015 mol) was added to a suspension of mercaptoheterocycle (0.001 mol) in methanol (10 mL). The reaction mixture was stirred at room temperature for 2–20 h until, according to TLC, all the starting materials had disappeared. On cooling, a precipitate was formed, that was filtered off and crystallized from methanol to afford the pure product.

Method B. The acetylenecarboxylic ester (0.0015 mol) was added to a solution of mercaptoheterocycle (0.001 mol) and sodium methoxide in methanol, which was prepared from Na (23 mg, 0.001 mol) and methanol (5 mL). The reaction mixture was stirred at room temperature for 8–10 h until, according to TLC, all the starting materials had disappeared. On cooling, a precipitate was formed, which was filtered off and the product was extracted with hot methanol. After cooling, the precipitate was collected.

Method C. The acetylenecarboxylic ester (0.0015 mol) was added to a suspension of mercaptoheterocycle (0.001 mol) in methanol (10 mL) or chloroform (10 mL) with triethylamine (0.001 mol). The reaction mixture was stirred at room temperature for 1–3 h until, according to TLC, all the starting material had disappeared. On cooling, a precipitate was formed, which was filtered off and crystallized from methanol to afford the pure product.

8-Carbamoyl-2-methoxycarbonyl-4-oxo-4*H*-imidazo[5,1-*b*]-[1,3]thiazine (6a). From 5-mercaptoimidazole-4-carboxamide **5a**[19] and DMAD. Yield 66% (method A), 43%. (method B). Yellow crystals, mp 218–221 °C. Mass spectrum, *m*/*z* (%): 253 (50) $M^{+\bullet}$. Found, %: C 42.55; H 2.90; N 16.93; S 12.21. $C_9H_7N_3O_4S$. Calcd, %: C 42.69; H 2.79; N 16.60; S 12.65; δ_H (DMSO-d_6) 3.97 (3H, s, OCH_3), 7.24 (1H, s, = $C_{(5)}$H), 7.63 (1H, s, NH), 7.83 (1H, s, NH), 8.80 (1H, s, = $C_{(8)}$H).

Methyl 2-(7-carbamoyl-3-oxoimidazo[5,1-*b*]thiazol-2-ylidene) acetate (7a). From 5-mercaptoimidazole-4-carboxamide **5a** and DMAD, method B. The precipitate, that was insoluble in hot methanol, was washed by methanol and dried. Yellow crystals, yield 60%. Mp 252–262 °C (decomp.). Mass spectrum, *m*/*z* (%): 253 (100) $M^{+\bullet}$.Found, %: C 42.60; H 2.70; N 16.04; S 12.23. $C_9H_7N_3O_4S$. Calcd, %: C 42.69; H 2.79; N 16.60; S 12.65; δ_H (DMSO-d_6) 3.79 (3H, s, OCH_3), 7.07 (1H, s, = $C_{(5)}$H), 7.45 (1H, s, NH), 7.65 (1H, s, NH), 8.63 (1H, s, = $C_{(8)}$H).

2-Methoxycarbonyl-4-oxo-8-thiocarbamoyl-4*H*-imidazo-[5,1-*b*][1,3]thiazine (6b) and methyl (3-oxo-7-thiocarbamoyl-imidazo[5,1-*b*]thiazol-2-ylidene) acetate (7b). Obtained as a mixture from 5-mercaptoimidazole-4-thiocarboxamide **5b**[19] and DMAD, yield 48% (method B). Yellow crystals, mp 268–270 °C (decomp.). Mass spectrum, *m*/*z* (%): 269 (100) $M^{+\bullet}$. Found, %: C 40.40; H 2.69; N 15.29; S 23.88. $C_9H_7N_3O_3S_2$. Calcd, %: C 40.14; H 2.62; N 15.60; S 23.81; **6b** δ_H (DMSO-d_6) 3.97 (3H, s, OCH_3), 7.27 (1H, s, = $C_{(5)}$H), 8.86 (1H, s, = $C_{(8)}$H), 9.41 (1H, s, NH), 9.70 (1H, s, NH); **7b** δ_H (DMSO-d_6) 3.76 (3H, s, OCH_3), 6.93 (1H, s, = $C_{(5)}$H), 8.70 (1H, s, = $C_{(8)}$H), 9.42 (1H, s, NH), 9.70 (1H, s, NH).

Dimethyl 2-(3-methyl-5-thiocarbamoyl-3*H*-[1,2,3]triazol-4-yl-thio)but-2-enedioate (11a). From 1-methyl-5-mercapto-1,2,3-triazole-4-thiocarboxamide **10a**[20] and DMAD, yield 43% (method A). Yellow crystals, mp 175–178 °C. Mass spectrum, *m*/*z* (%): 316 (60) $M^{+\bullet}$. Found, %: C 37.70; H 3.91; N 17.72; S 20.65. $C_{10}H_{12}N_4O_4S_2$. Calcd, %: C 37.97; H 3.82; N 16.70; S 20.27; δ_H (DMSO-d_6) 3.48 (3H, s, OCH_3), 3.76 (1H, s, OCH_3), 4.08 (3H, s, NCH_3), 6.69 (1H, s, =CH), 9.50 (1H, s, NH), 9.72 (1H, s, NH).

Dimethyl 2-(5-thiocarbamoyl-3-phenyl-3*H*-[1,2,3]triazol-4-yl-thio)but-2-enedioate (11b). From 1-phenyl-5-mercapto-1,2,3-triazole-4-thiocarboxamide **10b**[20] and DMAD, yield 44% (method A). Yellow crystals, mp 100–105 °C (ethanol). Found, %: C 47.85; H 3.91; N 14.44; S 17.32. $C_{15}H_{14}N_4O_4S_2$. Calcd, %: C 47.61; H 3.73; N 14.81; S 16.93; δ_H (DMSO-d_6) 3.45 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 6.70 (1H, s, =CH), 7.20–7.45 (5H, m, Ph), 9.53 (1H, s, NH), 9.79 (1H, s, NH).

Methyl 2-(3-methyl-5-thiocarbamoyl-3*H*-[1,2,3]triazol-4-yl-thio)acrylate (11c). From 1-methyl-5-mercapto-1,2,3-triazole-4-thiocarboxamide **10a** and methyl propynoate, yield 43% (method A). Yellow crystals, mp 167–170ºC (from ethanol). Mass spectrum, *m*/*z* (%): 258 (71) $M^{+\bullet}$. Found, %: C 36.78; H 4.0; N 22.14. $C_8H_{10}N_4O_2S_2$. Calcd, %: C 37.2; H 3.88; N 21.71; δ_H (DMSO-d_6) 3.78 (3H, s, OCH_3), 4.04 (3H, s, NCH_3), 6.10(1H, d, *J* = 8.6 Hz, =CH), 7,25 (1H, d, 8.6, =CH), 9.56 (1H, s, NH), 9.80 (1H, s, NH).

Methyl 2-{3-methyl-5-[4-(2-nitrophenyl)thiazol-2-yl]-3*H*-[1,2,3]triazol-4-ylthio}acrylate (12). 0.245 g (0.001 mol)

o-nitrophenacyl bromide was added to a suspension of 0.316 g (0.001 mol) triazole **11c** in 10 mL ethanol. The reaction mixture was refluxed for 1 h. After cooling, the precipitate was filtered off. The product was crystallized from ethanol. Yield 74%, mp 180–183 °C. Found, %: C 47.62; H 3.50; N 17.74; S 16.32. $C_{16}H_{15}N_5O_4S_2$. Calcd, %: C 47.63; H 3.25; N 17.36; S 15.88; δ_H (DMSO-d_6) 3.79 (3H, s, OCH_3), 4.14 (3H, s, NCH_3), 6.19(1H, d, J = 9.6, =CH), 7.40 (1H,d, J = 9.6 Hz, =CH), 7.73 (1H, t, ArH), 8.15–8.22 (1H, m, ArH), 8.35–8.41 (1H, m, ArH), 8.50 (1H, s, $H_{thiazole}$), 8.77 (1H, t, ArH).

5-Methoxycarbonyl-3-(4-methoxyphenylazo)-2-methyl-7-oxo-7*H*-pyrazolo[5,1-*b*][1,3]thiazine (15a). From pyrazole **13a** and DMAD in methanol by method C, yield 73%, mp 218–220 °C. Found, %: C, 53.81; H, 4.01; N, 15.71; S, 9.00. $C_{16}H_{14}N_4O_4S$. Calcd, %: C, 53.63; H, 3.91; N, 15.64; S, 8.94; δ_H (DMSO-d_6) 2,59 (3H, s, Me), 3.89 (3H, s, OMe), 4.0 (3H, s, COOMe), 7.33 (1H, s, $C_{(5)}H$), 7.81 and 7.04 (4H, AA′XX′, J = 9.3 Hz, ArH).

5-Methoxycarbonyl-2-methyl-7-oxo-3-*p*-tolylazo-7*H*-pyrazolo[5,1-*b*][1,3]thiazine (15b). From pyrazole **13b** and DMAD in methanol by method C, yield 80%, mp 183–185 °C. Found, %: C, 56.25; H, 4.12; N, 16.52; S, 9.50. $C_{16}H_{14}N_4O_3S$. Calcd, %: C, 56.14; H, 4.09; N, 16.37; S, 9.36; δ_H (DMSO-d_6) 2,44 (3H, s, Me), 2.70 (3H, s, Me), 3.99 (3H, s, COOMe), 7.36 (1H, s, $C_{(5)}H$), 7.74 and 7.33 (4H, AA′XX′, J = 8.0 Hz, ArH).

5-Methoxycarbonyl-2-methyl-7-oxo-3-phenylazo-7*H*-pyrazolo[5,1-*b*][1,3]thiazine (15c). From pyrazole **13c** and DMAD by method C, yield 69%, mp 198–200 °C. Found, %: C, 55.01; H, 3.71; N, 17.07; S, 9.81. $C_{15}H_{12}N_4O_3S$. Calcd, %: C, 54.85; H, 3.66; N, 17.15; S, 9.76; δ_H (DMSO-d_6) 2,71 (3H, s, Me), 3.99 (3H, s, COOMe), 7.52 (1H, s, $C_{(5)}H$), 7.3–7.26 (3H, m, ArH), 7.84 (2H, dd, J = 8.3, J = 2.3 Hz, ArH).

3-(4-Chlorophenylazo)-2-methyl-7-oxo-7*H*-pyrazolo[5,1-*b*]-[1,3]thiazine-5-carboxylic acid methyl ester (15d). From pyrazole **13d** and DMAD by method C, yield 85%, mp 224–226 °C. Found, %: C, 49.83; H, 3.10; N, 15.37; S, 8.75. $C_{15}H_{11}ClN_4O_3S$. Calcd, %: C, 49.66; H, 3.03; N, 15.45; S, 8.83; δ_H (DMSO-d_6) 2.71 (3H, s, Me), 3.99 (3H, s, COOMe), 7.39 (1H, s, $C_{(5)}H$), 7.85 and 7.54 (4H, AA′XX′, J = 8.8 Hz, ArH).

3-(4-Ethoxycarbonylphenylazo)-5-methoxycarbonyl-2-methyl-7-oxo-7*H*-pyrazolo[5,1-*b*][1,3]thiazine (15e). From pyrazole **13e** and DMAD by method C, yield 71%, mp 195–197 °C. Found, %: C, 53.82; H, 3.93; N, 14.10; S, 7.93. $C_{18}H_{16}N_4O_5S$. Calcd, %: C, 54.00; H, 4.00; N, 14.00; S, 8.00; δ_H (DMSO-d_6) 1.41 (3H, t, 7.0, CH_2CH_3), 2.72 (3H, s, Me), 4.00 (3H, s, COOMe), 4.37 (2H, q, J = 7.0 Hz, OCH_2), 7.39 (1H, s, $C_{(5)}H$), 8.09 and 7.88 (4H, AA′XX′, J = 8.5 Hz, ArH).

3-(4-Chlorophenylazo)-2-methyl-7*H*-pyrazolo[5,1-*b*][1,3]thiazin-7-one (15 f). From pyrazole **13d** and methyl propynoate in ethanol by method C, yield 73%, mp 248–249 °C. Found, %: C, 51.40; H, 3.11; N, 18.10; S, 10.71. $C_{18}H_{16}N_4O_5S$. Calcd, %: C, 51.23; H, 2.96; N, 18.39; S, 10.51; δ_H ($CDCl_3$) 2.81 (3H, s, Me), 7.73 and 6.85 (2H, AA′XX′, J = 10.6 Hz, $C_{(5)}H$ + $C_{(6)}H$), 7.84 and 7.49 (4H, AA′XX′, J = 8.4 Hz, ArH).

5-Methoxycarbonyl-2-methyl-7-oxo-3-(2-phenylhydrazino)-7*H*-pyrazolo[5,1-*b*][1,3]thiazine (19). A mixture of sodium dithionite (0.4 g, 0.0023 mol) and azo compound **15c** (0.3 g, 0.0009 mol) in acetone (40 mL) and water (10 mL) was refluxed for 3 hours. The solvents were evaporated and the residue was crystallized from MeOH–DMF. Yield 30%, mp 175–176 °C. Found, %: C, 54.55; H, 4.24; N, 16.97; S, 9.70. $C_{15}H_{14}N_4O_3S$. Calcd, %: C, 54.40; H, 4.11; N, 17.14; S, 9.91; δ_H (DMSO-d_6) 2.34 (3H, s, Me), 3.88 (3H, s, COOMe), 6.82 (1H, dd, J = 7.5, J = 7.3 Hz, H_{17}), 6.84 (2H, d, J = 7.5 Hz, H_{13}, H_{14}), 7.01(1H, s, $C_{(5)}H$), 7.14 (2H, dd, J = 7.5, J = 7.3 Hz, $H_{15}H_{16}$), 7.44 (1H, s, NH), 7.80 (1H, s, NH).

Methyl (5-amino-8-carbamoyl-3-oxo-7-phenyl-6-cyano-7*H*-thiazolo[3,2-*a*]pyridin-2-ylidene)acetate (21a). From pyridinethione **20a**[21] and DMAD in chloroform, yield 42% (method C). Yellow crystals, mp 305–307 °C. Found, %: C 56.56; H 3.75; N 14.60; S 8.95. $C_{18}H_{14}N_4O_4S$. Calcd, %: C 56.54; H 3.69; N 14.69; S 8.41; δ_H (DMSO-d_6) 3.81 (3H, s,OCH_3), 4.76 (1H, s, CH), 6.66 (1H, s, $C_{(5)}H$), 7.25–7.35 (5H, m, ArH), 7.27 (2H, s NH_2).

Methyl (5-amino-8-carbamoyl-3-oxo-7-thienyl-6-cyano-7H-thiazolo[3,2-*a*]pyridin-2-ylidene)acetate (21b). From pyridinethione **20b**[21] and DMAD in chloroform, yield 71% (method C). Yellow crystals, mp 292–295 °C. Found, %: C 49.55; H 3.02; N 14.93; S 16.00. $C_{16}H_{12}N_4O_4S_2$. Calcd, %: C 49.48; H 3.11; N 14.42; S 16.51; δ_H (DMSO-d_6) 3.80 (3H, s, OCH_3), 5.18 (1H, s, CH), 6.67 (1H, s, $=C_{(5)}H$), 6.92–6.94 (1H, m, $H_{thienyl}$), 7.03–7.04 (1H, m, NH), 7.28–7.31 (2H, m, $H_{thienyl}$), 7.33 (1H, s, NH), 7.43 (2H, s, NH_2).

Methyl (5-amino-8-ethoxycarbonyl-3-oxo-7-thienyl-6-cyano-7*H*-thiazolo[3,2-*a*]pyridin-2-ylidene)acetate (21c). From pyridinethione **20c**[22] and DMAD in chloroform, yield 48% (method C). Yellow crystals, mp 249–252 °C. Found, %: C 51.98; H 3.55; N 10.51; S 14.95. $C_{18}H_{15}N_3O_5S$. Calcd, %: C 51.79; H 3.62; N 10.06; S 15.36; δ_H (DMSO-d_6) 1.21 (3H, t, CH_3), 3.83 (3H, s, OCH_3), 4.18 (2H, q, CH_2), 4.86 (1H, s, CH), 6.77 (1H, s, $=C_{(5)}H$), 6.90–6.95 (2H, m, $H_{thienyl}$), 7.25–7.30 (1H, m, $H_{thienyl}$), 7.35 (2H, s, NH_2).

General method for the synthesis of arylazopyrazolethiones 13a-e

Arylazopyrazolones[23] (0.004 mol) were refluxed about 30 min in toluene (50 mL) with Lawesson's reagent (0.0022 mol). The solution was cooled and the solid filtered off. The product was crystallized from ethanol.

4-(4-Methoxyphenylazo)-5-methyl-2,4-dihydropyrazole-3-thione (13a). Yield 81%, mp 201–202 °C. Mass spectrum, *m*/*z* (%): 248 (78) $M^{+\bullet}$.Found, %: C 53.45; H 4.77; N, 22.58; S, 12.90. $C_{11}H_{12}N_4OS$. Calcd, %: C 53.21; H 4.87; N, 22.67; S, 13.00; δ_H (DMSO-d_6) 2.26 (3H, s, Me), 3.89 (3H, s, OMe), 7.52 and 7.01 (4H, AA′BB′, J = 8.8 Hz, ArH), 12.99 (1H, s, NH), 16.78 (1H, s, NH).

4-(4-Methylphenylazo)-5-methyl-2,4-dihydropyrazole-3-thione (13b). Yield 85%, mp 190–193 °C. Mass spectrum, *m*/*z* (%): 232 (50) $M^{+\bullet}$.Found, %: C 56.69; H 5.37; N, 24.14; S, 13.79. $C_{11}H_{12}N_4S$. Calcd, %: C 56.87; H 5.21; N, 24.03; S, 13.86; δ_H (DMSO-d_6) 2.38 (3H, s, Me), 2.53 (3H, s, Me), 7.59 and 7.27 (4H, AA′BB′, J = 8.8 Hz, ArH), 13.00 (1H, s, NH), 16.70 (1H, s, NH).

4-Phenylazo-5-methyl-2,4-dihydropyrazole-3-thione (13c). Yield 83%, mp 171–172 °C. Mass spectrum, *m*/*z* (%): 218 (75) $M^{+\bullet}$. Found, %: C 55.15; H 4.80; N, 25.69; S, 14.68. $C_{10}H_{10}N_4S$. Calcd, %: C 55.03; H 4.62; N, 25.71; S, 14.90; δ_H (DMSO-d_6) 2.26 (3H, s, Me), 7.27 (1H, dd, *J*-7.5, J = 7.3 Hz, ArH), 7.44 (2H, dd, J = 7.5, J = 7.3 Hz, ArH), 7.56 (2H, d, J = 7.7 Hz, ArH), 13.03 (1H, s, NH), 16.58 (1H, s, NH).

4-(4-Chlorophenylazo)-5-methyl-2,4-dihydropyrazole-3-thione (13d). Yield 93%, mp 205–208 °C. Mass spectrum, *m*/*z* (%): 252 (85) $M^{+\bullet}$. Found, %: C 47.33; H 3.88; N, 22.18; S, 12.67. $C_{10}H_9ClN_4S$. Calcd, %: C 47.53; H 3.59; N, 22.11; S, 12.80;

δ_H (DMSO-d_6) 2.30 (3H, s, Me), 7.75 and 7.56 (4H, AA′BB′, J = 8.8 Hz, ArH), 13.10 (1H, s, NH), 16.55 (1H, s, NH).

4-(4-Ethoxycarbonylphenylazo)-5-methyl-2,4-dihydropyrazole-3-thione (13e). Yield 85%, mp 195–197 °C. Mass spectrum, *m/z* (%): 290 (89) $M^{+\bullet}$.Found, %: C 54.01; H 4.98; N, 19.31; S, 11.09. $C_{13}H_{14}N_4O_2S$. Calcd, %: C 53.78; H 4.86; N, 19.54; S, 11.35; δ_H (DMSO-d_6) 1.38 (3H, q, J = 7.0 Hz, CH_2CH_3), 2.26 (3H, s, Me), 4.32 (2H, q, J = 7.0 Hz, CH_2CH_3), 8.02 and 7.60 (4H, AA′BB′, J = 9.0 Hz, ArH), 13.21 (1H, s, NH), 16.43 (1H, s, NH).

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