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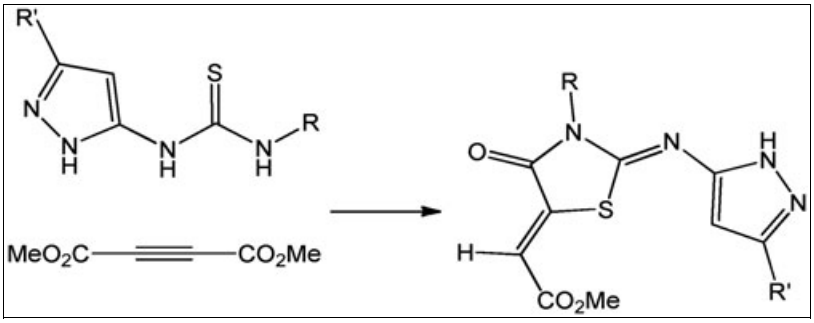

1-Substituted 3-[3-(methyl/phenyl)-1*H*-pyrazol-5-yl]thioureas react with the triple bond of dimethyl acetylenedicarboxylate forming (*Z*)-methyl 2-[(*Z*)-3-substituted-2-(3-(methyl/phenyl-1*H*-pyrazol-5-ylimino)-4-oxothiazolidin-5-ylidene)acetates. Rational for these conversations are presented.

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INTRODUCTION

Reactions of *N,N′*-disubstituted thioureas with dimethyl acetylenedicarboxylate (DMAD) have been reported to produce both five- [1–6] and six-membered heterocyclic systems [7,8].

Unsymmetrical *N,N′*-disubstituted thioureas with different N-substituents R and R′ possess two nonequivalent nucleophilic centers, so that their reactions could give rise to regioisomeric products. The pronounced reactivity of nitrogen containing heterocycles toward DMAD has been documented [9]. The reaction generally involves the initial addition of the N-heterocycle to DMAD to form a dipolar intermediate, which undergoes further reaction with DMAD leading to a variety of complex heterocyclic compounds; such reactions have been the subject of detailed investigations by a number of research groups [9–12].

On the contrary, a majority of the reactions have been carried out on heteroaromatic systems such as aryldiazenyl-1*H*-pyrazole-3,5-diamines with similar some π-deficient compounds [13–18]. Selective combination of two or more different compounds into one molecule leads to new composite electron donors with unique properties such as pyrazolylthioureas.

Recently, *N*-[(1-methyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)carbamothioyl]benzamide (**1**) reacted with DMAD (**2**) and ethyl propylate **3** to give mainly the corresponding fused 8-benzoyl-1-methyl-3,7-dioxo-2-phenyl-2,3,7,8-tetrahydro-1*H*-pyrazolo[3′,4′:4,5]pyrrolo-[1,2-*a*] pyrimidine-5-carboxylate (**4**) and 8-benzoyl-1-methyl-2-phenyl-1*H*-pyrazolo-[3′,4′:4,5]pyrrolo[1,2-*a*]-pyrimidine-3,7(2*H*,8*H*)-dione (**5**) (Scheme 1) [8].

Thiazolidin-4-ones are reported to act as analgesic, antibacterial, anticonvulsant, antiparasitic, anti-inflammatory, herbicidal agents [19–24], and as potent anti-HTV agents [25]. In the light of the above-mentioned findings, the authors have undertook to investigate the reactions of DMAD (**2**) with pyrazolylthioureas **6a–d**, which may react at sulfur atom, N^1 or N^3 of substituted thioureas, or the endocyclic pyrazole-NH as nucleophilic sites. On the contrary, compound **2** offers the C/C triple bond and the electrophilic carbonyl atoms for attack by nucleophiles. Thus, several methods of interaction between **6a–d** and **2** may be envisaged.

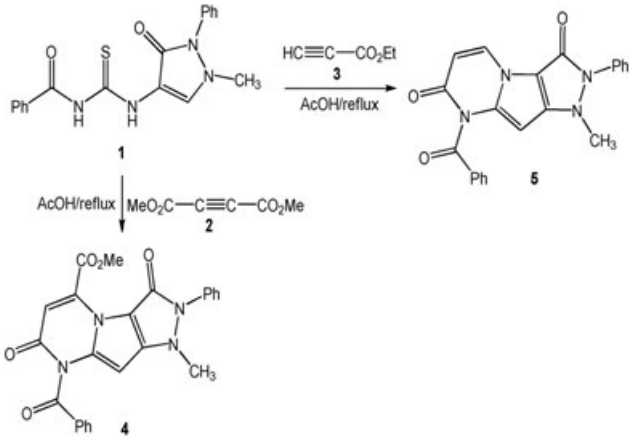
RESULTS AND DISCUSSION

In ethanol at reflux, or using microwave irradiation (MW), each pyrazolylthioureas **6a–d** reacted with DMAD (**2**) to give one single product **7a–d** (Scheme 2).

From elemental analyses and the mass spectra, a net release of methanol (MW-32) had occurred. The mass spectra showed three fragments common to all products: [M^+-$HCCO_2Me$], [M^+-RNCO], and 59 (CO_2Me).

IR spectra of the isolated products showed two carbonyl absorption bands at about 1720–1715 and 1690–1685 cm^{-1}, a band between 1630 and 1610 cm^{-1}, which was assigned to a C=N vibration, and NH at 3330–3280 cm^{-1}.

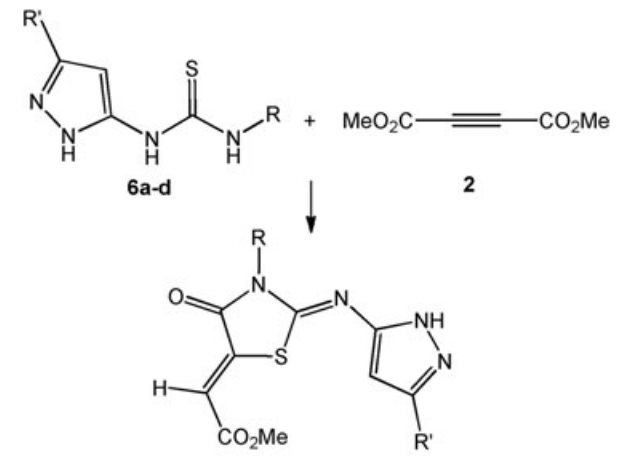
Scheme 1



All the new compounds contain a carbomethylidene side-chain (=CHCO$_2$Me). The ^{1}H-NMR spectra revealed a vinylic-CH singlet between 6.80 and 6.89 ppm, and a methoxy singlet at about 3.89–3.85 ppm. The products show one pyrazol-NH proton signal, for which the range of chemical shifts is relatively narrow (12.95–12.60 for compounds **7a–d**).

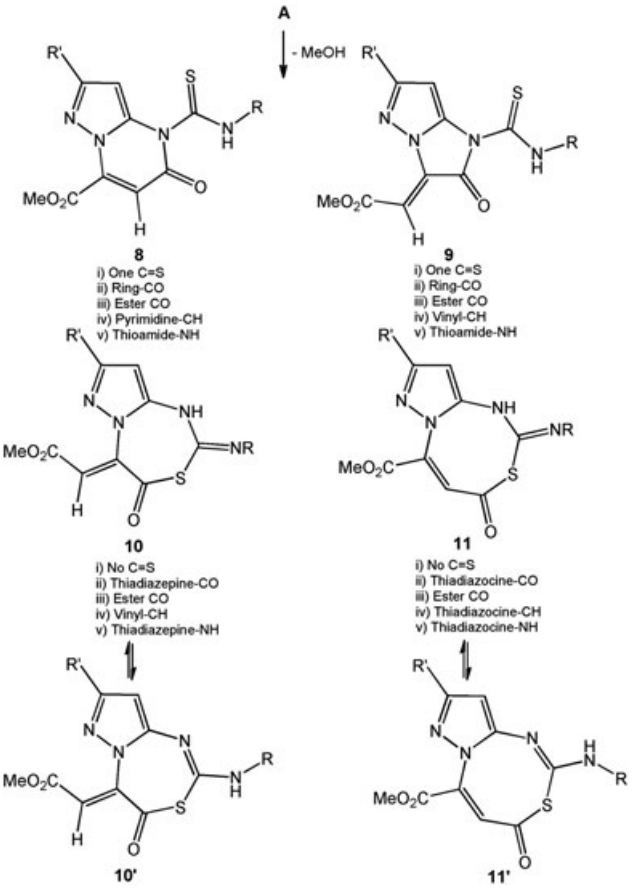
Compound **7c**, for example, the spectra show one methoxyl group, one methyl group, one N-allyl group, and one isolated vinylic-CH proton. The general pattern appears, as usual, to be conjugate addition to the alkyne followed by cyclization with loss of methanol. The ^{13}C-NMR spectra of all four products show five downfield lying lines at 166.77–165.73, 164.65–163.04, 148.90–148.17, 140.02–139.70, and 116.22–115.10 ppm, due to (C=O, ester), (C=O, ring), (C-2), pyrazole-C=N, and vinyl-CH, respectively.

Scheme 2

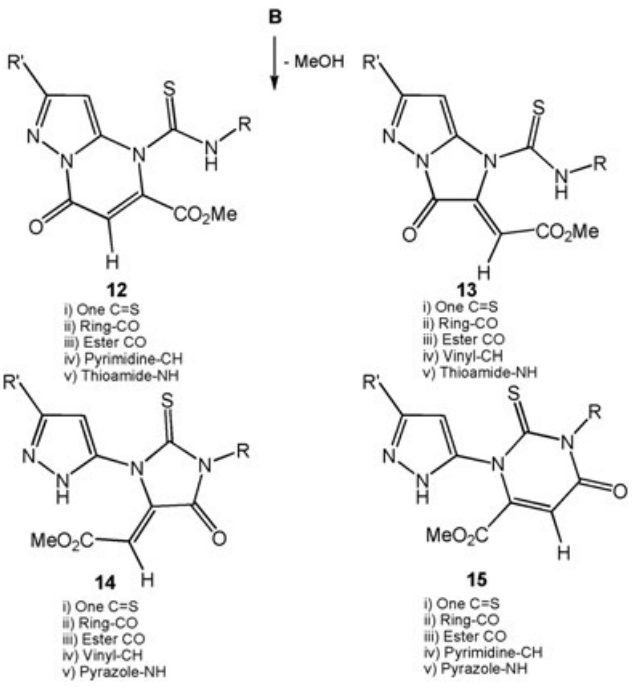


6,7: **a**, R = C_6H_5, R' = CH_3
b, R = $C_6H_5CH_2$, R' = CH_3
c, R = CH_2=CH-CH_2, R' = CH_3
d, R = R' = C_6H_5

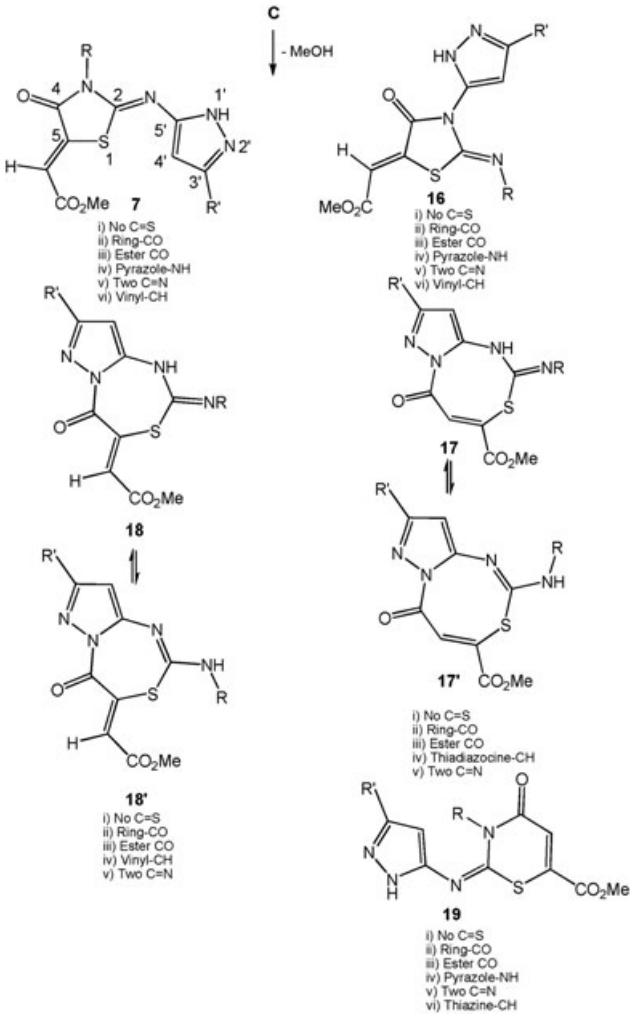
Scheme 3



Scheme 4



Scheme 5



There are possibilities for the formation of various isomers, which would behave very similarly spectroscopically (Schemes 2, 2–4). Similarly, all products observed are formed from one of the four labile (1:1) adducts (**A**–**D**) of **6** to **2** (Fig. 1).

Isomeric products **8–11** (Scheme 2) may be formed, if the reaction took place through intermediate **A** (Fig. 1).

The products **12–15** (Scheme 3) could be isolated via the intermediate **B** (Fig. 1).

If the SH attached C/C triple bond of **2** the intermediate **C** (or its tautomer, Fig. 1) could be formed, leading to the products **7, 16–19** (Scheme 5).

The products **20** and **21** (Scheme 6) could be isolated if the reaction involved the addition of thioureas-N^1 on the C/C triple bond of **2** via intermediate **D** (Fig. 1).

Structures **8**, **9**, **12–15**, **20,** and **21** could be ruled out according to by the absence of a C═S carbon from the ^{13}C-NMR data; thus, intermediates **B** and **D** are excluded.

The ring C═O resonances observed in ^{13}C-NMR rule out the thiadiazepinone **10** and thiadiazocinone **11** (which would be considerably downfield of those observed).

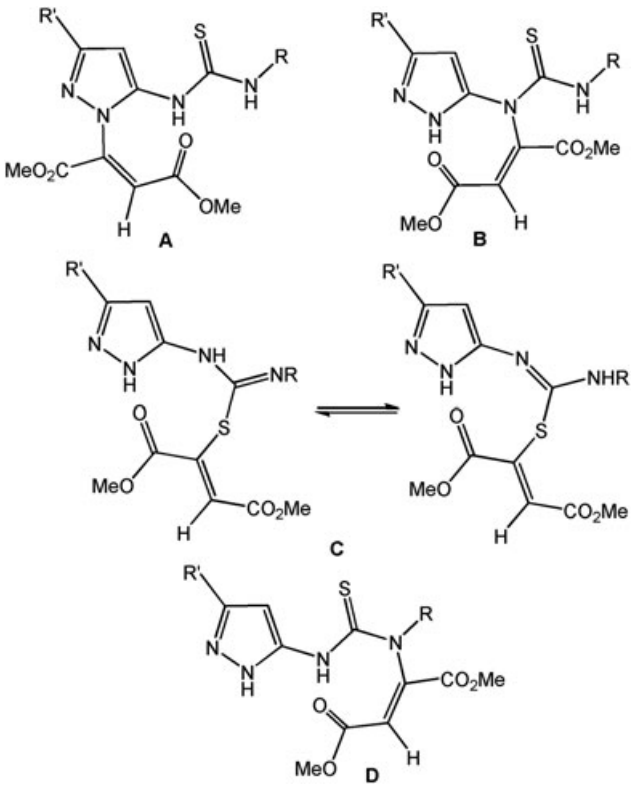
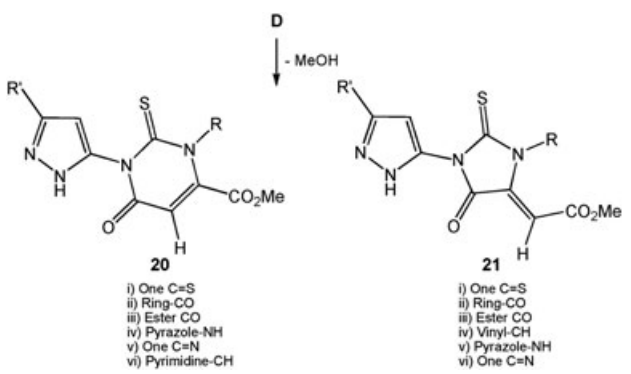


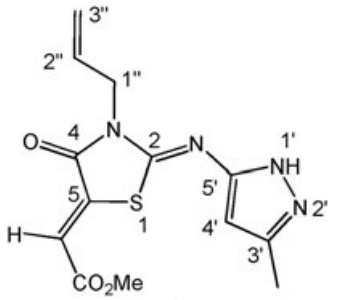
Figure 1. Four labile (1:1) adducts (**A-D**) observed from the reaction between **6a–d** and **2**.

Because of the ^{1}H-NMR chemical shifts of the endocyclic pyrazole-NH (δ_H = 12.95–12.60), the alternative structures **8**–**13**, **17,** and **18** could be ruled out. The values for exocyclic-NHR groups depend on the nature of R: around 10.59 ppm, for R=phenyl, 8.40 ppm, for R=benzyl, 7.9 ppm, for R=allyl (see experimental). This logic excludes intermediate **A**; thus, the products must form from intermediates of type **C**.

The remainder of the structural assignments was made using a combination of 2D NMR correlations and ^{1}H–^{13}C coupling constants. For example, in compound **7c**, the signal at δ_H = 3.85 is assigned as the methoxyl (Table 1); this

Scheme 6





7c

Figure 2. The structure of compound **7c**.

signal gives HSQC correlation with the attached carbon at δ_C = 52.40 and HMBC correlation with the ester carbonyl at δ_C = 165.73 ppm (Table 2). The chemical shift and HMBC correlations of the signal next farthest downfield, at δ_C = 163.64, require it be C-4. Under gated decoupling, C-4 couples to vinyl-CH with J = 5.7 Hz, a value which requires a three- not two-bond coupling [1], [26]; thus, structure **19** can also be ruled out. The magnitude of this coupling further argues that C-4 and vinyl-CH are mutually cis [1] as depicted in structures **7**. The carbon (δ_C = 115.10) giving HSQC correlation to vinyl-CH is assigned as vinyl-C, and the carbon (δ_C = 143.34) giving HMBC correlation to vinyl-CH is assigned as C-5 (Table 2). The observation of coupling and HMBC correlation between C-4 and the allylic methylene protons (δ_H = 4.52) requires that the overall structure be **7** rather than **16**. The rest of the signals can be assigned in full, and support the structural assignment. The pyrazole-CH_3 protons are distinctive at δ_H = 2.36 ppm (Table 1); this signal gives HSQC correlation with the attached carbon at δ_C = 10.62 ppm and HMBC correlation with C-5′ at δ_C = 153.17, C-3′ at δ_C = 139.75, and C-4′ at δ_C = 100.43. C-4′ gives HSQC correlation to the attached proton at δ_H = 6.02 and HMBC correlation to the N–H at δ_H = 12.60; C-3′ gives quartet coupling to CH_3, while C-5′ is a double-doublet coupled to N–H and H-4′ but not pyrazole-CH_3. The ring C═N gives HMBC correlation and triplet coupling to the allylic methylene protons, consistent with the assigned connectivity (although this particular connectivity would also be present in **16**). The allyl signals are assigned straightforwardly.

The NMR spectra showed that only one stereoisomer was present for all products indicating that the reaction is stereoselective.

As shown in Table 3, MW irradiation provided higher yields than direct heating, along with greater selectivity and easier manipulation.

CONCLUSION

Reaction of DMAD (**2**) with pyrazolylthioureas **6a–d** can involve possible competition between nucleophilic addition of several sites (N^1,N^3 and SH of thioamide group) to the triple bond of the activated acetylenic compound. The authors found that the sulfur atom is incorporated into the ring and the thia-hetrocyclic N–C–S + C_2 mode of cyclization is favored with thioureas characterized by increased negative charge on sulfur atom. Comparison of ^{1}H-NMR, ^{13}C-NMR, and HMBC chemical shifts for the possible sets of isomers may serve as a useful supplementary tool in finding the correct structure of a heterocycle.

EXPERIMENTAL

General procedures. Melting points (uncorrected) were determined in open glass capillaries on a Gallenkamp melting point apparatus. The IR spectra were recorded from potassium bromide disks with a Shimadzu 408. NMR spectra (400 MHz for ^{1}H, 100 MHz for ^{13}C) were observed in DMSO-d_6 on Bruker AM400 or AV400 spectrometers with tetramethylsilane as the internal standard. The ^{13}C signals were assigned with the aid of DEPT 135/90, HMBC, and HMQC experiments. Mass spectra (70 eV, electron impact mode) were recorded on a Finnigan MAT instrument. A START Labstation for microwave enhanced chemistry oven was used at its full power 1400 W, and the temperature was controlled at 80°C for the experiments recorded for this study. TLC were performed on analytical Merck 9385 silica aluminum sheets (Kiesegel 60) with Pf_{254} indicator-TLC's were viewed λ_{max} = 254 nm. Elemental analyses were carried out at the Microanalytical Center, Cairo University, Egypt.

Starting materials. DMAD (**2**) was bought from Fluka. Pyrazolylthioureas **6a–d** were prepared according to the following procedure:

Procedure: preparation of pyrazolylthioureas 6a–d. A solution of substituted isothiocyanates (0.1 mol) in 5 mL DMF was added dropwise with stirring at room temperature to (0.1 mol) 3-(methyl/phenyl)-1*H*-pyrazol-5-amine in 5 mL DMF and the reaction mixture was left standing for overnight. Then, the reaction mixture was poured into a 500-mL beaker containing 200 mL cold water, pyrazolylthioureas **6a–d** were separated. The resulting solid material was filtered and the precipitate was washed with cold water, dried, and recrystallized from ethanol.

Table 1

^{1}H-NMR and COSY data for compound **7c**.

^{1}H-NMR (DMSO-d_6)	COSY	Assignment
12.60 (bs; 1H)	6.02, 2.36	N—H
6.81 (s; 1H)		viny—CH
6.02 (s; 1H)	12.60, 2.36	H—4′
5.95 (ddt, Jd = 17.0, 10.5, Jt = 5.3; 1H)	5.22, 5.20, 4.52	Allyl—CH═
5.22 (d, J = 9.5; 1H)	5.95, 5.20, 4.52	Allyl—CH_2═(*cis*)
5.20 (d, J = 17.5; 1H)	5.95, 5.22, 4.52	Allyl—CH_2═(*trans*)
4.52 (d, J = 4.7; 2H)	5.95, 5.22, 5.20	Allyl—CH_2N
3.85 (s; 3H)		CO_2CH_3
2.36 (s; 3H)	12.60, 6.02	Pyrazole—CH_3

Table 2

HSGC data.

^{13}C NMR (DMSO-d_6)	HSQC	HMBC	Assignment
165.73 (dq, Jd = 1.7, Jq = 3.6)		3.85	CO_2CH_3
163.64 (dt, Jd = 5.7, Jt = 2.9)		6.81, 4.52	C—4
153.17 (dd, *J* = 10.5, 3.5)		12.60, 6.02, 2.36	C—5′
148.26 (t, *J* = 3.4)		4.52	C═N
143.34 (s)		6.81	C—5
139.75 (ddq, *J* = 7.0, 7.0, 7.0)		12.60, 6.02, 2.36	C—3′
131.37 (ddt, Jd = 158.6, 4.7, Jt = 4.7)	5.95	5.22, 5.20, 4.52	Allyl—CH═
117.00 (ddt, Jd = 159.3, 154.5, Jt = 4.6)	5.22, 5.20	4.52	Allyl—CH_2═
115.10 (d, *J* = 171.6)	6.81	3.85	vinyl—CH
100.43 (dt, Jd = 176.0, Jt = 3.6)	6.02	12.60, 2.36	C—4′
52.50 (q, *J* = 148.0)	3.85		OCH_3
44.28 (dddt, Jd = 12.9, 7.4, 5.8, Jt = 141.9)	4.52	5.95, 5.22, 5.20	Allyl—CH_2N
10.62 (q, *J* = 128.4)	2.36		Pyrazol—CH_3

1-(3-Methyl-1H-pyrazol-5-yl)-3-phenylthiourea (6a). This compound was obtained as colorless crystals (ethanol), mp 206–208°C; IR: NH 3300, 3295, Ar-CH 3090, Ali-CH 2990, C═N 1690, Ar-C═C 1600 cm^{-1}; ^{1}H NMR: δ 2.22 (s, 1 H, CH_3), 5.81 (s, 1 H, pyrazole-CH), 7.18–7.64 (m, 5 H, Ar-H), 10.59 (s, br, 1 H, phenyl-NH), 11.78 (s, br, NH-CS), 12.33 (s, br, pyrazole-NH); ^{13}C NMR: δ 10.39 (CH_3), 93.54 (pyrazole-C4), 123.94, 125.05, 128.39 (Ar-CH), 138.99 (pyrazole-C5), 139.45 (Ar-C), 149.63 (C═N), 176.12 (C═S); ms: *m/z* 232 (M^+, 100), 155 (47), 135 (86), 97 (24), 77 (75), 74 (16). Anal. Calcd. for $C_{11}H_{12}N_4S$: C, 56.87; H, 5.21; N, 24.12; S, 13.80. Found: C, 56.70; H, 5.33; N, 24.32; S, 13.66.

1-(3-Methyl-1H-pyrazol-5-yl)-3-benzylthiourea (6b). This compound was obtained as colorless crystals crystals (ethanol), mp 162–164°C; IR: NH 3290, 3285, Ar-CH 3085, Ali-CH 2990, C═N 1690 cm^{-1}; ^{1}H NMR: δ 2.12 (s, 1H, CH_3), 4.51 (benzyl-CH_2), 5.61 (s, 1H, pyrazole-CH), 7.38–7.67 (m, 5H, Ar-H), 8.40 (s, br, 1H, benzyl-NH), 11.56 (s, br, NH-CS), 12.02 (s, br, pyrazole-NH); ^{13}C NMR: δ 10.22 (CH_3), 42.32 (benzyl-CH_2), 92.84 (pyrazole-C4), 124.92, 125.15, 128.77 (Ar-CH), 138.02 (pyrazole-C5), 139.41 (Ar-C), 149.03 (C═N), 176.62 (C═S); ms: *m/z* 246 (M^+, 56), 155 (37), 149 (22), 97 (36), 91 (25), 77 (56). Anal. Calcd. for $C_{12}H_{14}N_4S$: C, 58.51; H, 5.73; N, 22.74; S, 13.02. Found: C, 58.65; H, 5.90; N, 22.86; S, 12.85.

1-(3-Methyl-1H-pyrazol-5-yl)-3-allylthiourea (6c). This compound was obtained as colorless crystals (ethanol), mp 128–130°C; IR: NH 3300, 3295, Ar-CH 3090, Ali-CH 2990, C═N 1690, Ar-C═C 1600 cm^{-1}; ^{1}H NMR: δ 2.22 (s, 1H, CH_3), 4.50–4.56 (m, 2H, allyl-CH_2N), 5.18–5.26 (m, 2H, allyl-CH_2═), 5.86–5.90 (m, 1H, allyl-CH═), 5.96 (s, 1H, pyrazole-CH═), 7.90 (s, br, 1H, allyl-NH), 11.23 (s, br, NH-CS), 12.01 (s, br, pyrazole-NH); ^{13}C NMR: δ 10.39 (CH_3), 43.12 (allyl-CH_2N), 92.84 (pyrazole-C4), 115.36 (ally-CH_2═), 130.21 (allyl-CH═), 138.11 (pyrazole-C5), 148.93 (C═N), 175.89 (C═S); ms: *m/z* 196 (M^+, 100), 99 (45), 97 (54), 74 (36). Anal. Calcd. for $C_8H_{12}N_4S$: C, 48.96; H, 6.16; N, 28.55; S, 16.34. Found: C, 49.15; H, 6.33; N, 28.30; S, 16.26.

1-(3-Phenyl-1H-pyrazol-5-yl)-3-phenylthiourea (6d). This compound was obtained as pale yellow crystals (ethanol), mp 182–184°C; IR: NH 3310, 3300, Ar-CH 3085, Ali-CH 2995, C═N 1690, Ar-C═C 1600 cm^{-1}; ^{1}H NMR: δ 2.23 (s, 1H, CH_3), 5.99 (s, 1H, pyrazole-CH), 7.28–7.66 (m, 10H, Ar-H), 10.85 (s, br, 1H, phenyl-NH), 11.88 (s, br, NH-CS), 12.36 (s, br, pyrazole-NH); ^{13}C NMR: δ 11.02 (CH_3), 93.14 (pyrazole-C4), 125.22, 128.29, 128.66, 129.23, 129.40 (Ar-CH), 139.09 (pyrazole-C5), 131.66, 139.55 (Ar-C), 149.60 (C═N), 175.99 (C═S); ms: *m/z* 294 (M^+, 42), 155 (100), 135 (38), 97 (21), 77 (55), 74 (26). Anal. Calcd. for $C_{16}H_{14}N_4S$: C, 65.28; H, 4.79; N, 19.03; S, 10.89. Found: C, 65.40; H, 4.66; N, 19.12; S, 10.77.

Reactions of 6a–d with dimethyl ethynedicarboxylate (2).

(i) **Method (A):** Conventional heating under refluxing in ethanol: into a 250-round bottom flask containing (142 mg, 1 mmol) of **2** in 10 mL of ethanol, a solution of 1 mmol of **6a–d** in ethanol (20 mL) was dropwise added with stirring. The mixture was gently refluxed with stirring for 2–5 h. The resulting yellow precipitate was filtered off, washed with ethanol, and recrystallized from a suitable solvent to give pure crystals of **7a–d**.

(ii) **Method (B):** Heterocyclization by microwave irradiation: Equimolar amounts of **6a–d** (1 mmol) and **2** (142 mg, 1 mmol) were well-mixed in ethanol (10 mL). The mixture

Table 3

Conventional heating under reflux (A) and MW irradiation (B) of pyrazolothiourea **6a–d** and dimethyl acetylenedicarboxylate (**2**).

Starting materials (conditions)	Products	Yielding % A	Yielding % B
6a + 2			
(A: Reflux in EtOH, 2 h)	**7a**	62%	82%
(B: MW, 3 min)	**7a**		
6b + 2			
(A: Reflux in EtOH, 3 h)	**7b**	45%	78%
(B: MW, 5 min)	**7b**		
6c + 2			
(A: Reflux in EtOH, 5 h)	**7c**	42%	75%
(B: MW, 6 min)	**7c**		
6d + 2			
(A: Reflux in EtOH, 4 h)	**7d**	58%	79%
(B: MW, 4 min)	**7d**		

was irradiated in a microwave oven in an open glass tube (the time of irradiation as monitored in Table 2). After completion of the reaction as monitored by TLC, the residue was separated as reported above. Comparison of the yields from method **A** and method **B** (Table 3).

(Z)-Methyl 2-[(Z)-3-phenyl-2-(3-methyl-1H-pyrazol-5-yl-imino)-4-oxothiazolidin-5-ylidene]acetate (7a). This compound was obtained as yellow crystals (acetonitrile), mp 251–253°C; IR: NH 3290, CO 1715,1690, C=N 1620, Ar-C=C 1600 cm^{-1}; ^1H NMR: δ 2.30 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 6.12 (s, 1H, pyrazol-CH), 6.84 (s, 1H, vinyl-CH), 7.28–7.62 (m, 5H, phenyl-CH), 12.65 ppm (bs, 1H, pyrazole-NH); ^{13}C NMR: δ 10.70 (CH_3), 52.51 (OCH_3), 101.40 (pyrazol-C-4′), 116.02 (vinyl-CH), 127.57, 128.09, 129.26 (Ar-CH), 135.70 (Ar-C), 139.70 (pyrazol-C-3′), 143.44 (C-5), 148.86 (C-2), 154.11 (pyrazol-C-5′), 163.04 (CO, ring), 166.34 ppm (CO, ester); ms: *m/z* 342 (M^+, 100), 283 (75), 270 (20), 261 (28), 223 (22), 119 (25), 81 (22), 77 (16), 72 (18), 59 (56). Anal. Calcd. for $C_{16}H_{14}N_4O_3S$: C, 56.13; H, 4.12; N, 16.36; S, 9.37. Found: C, 56.29; H, 4.01; N, 16.21; S, 9.41.

(Z)-Methyl 2-[(Z)-3-benzyl-2-(3-methyl-1H-pyrazol-5-yl-imino)-4-oxothiazolidin-5-ylidene]acetate (7b). This compound was obtained as yellow crystals (acetonitrile), mp 212–214°C; IR: NH 3280, CO 1720, 1685, C=N 1610, Ar-C=C 1595 cm^{-1}; ^1H NMR: δ 2.35 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 5.12 (benzyl-CH_2), 6.20 (s, 1H, pyrazol-CH), 6.80 (s, 1H, vinyl-CH), 7.30–7.70 (m, 5H, phenyl-CH), 12.70 ppm (bs, 1H, pyrazole-NH); ^{13}C NMR: δ 11.01 (CH_3), 44.56 (CH_2), 52.51 (OCH_3), 101.45 (pyrazol-C-4′), 116.12 (vinyl-CH), 127.97, 128.19, 129.01 (Ar-CH), 135.69 (Ar-C), 139.81 (pyrazol-C-3′), 144.04 (C-5), 148.90 (C-2), 154.31 (pyrazol-C-5′), 164.65 (CO, ring), 166.27 ppm (CO, ester); ms: *m/z* 356 (M^+, 100), 297 (34), 284 (22), 275 (18), 233 (37), 133 (50), 91 (36), 81 (42), 77 (18), 72 (51), 59 (65). Anal. Calcd. for $C_{17}H_{16}N_4O_3S$: C, 57.29; H, 4.52; N, 15.72; S, 9.00. Found: C, 57.33; H, 4.41; N, 15.66; S, 9.11.

(Z)-Methyl 2-[(Z)-3-allyl-2-(3-methyl-1H-pyrazol-5-yl-imino)-4-oxothiazolidin-5-ylidene]acetate (7c). This compound was obtained as yellow crystals (acetonitrile); mp 200–202°C; IR: NH 3300, Ali-CH 2295, CO 1715, 1685, C=N 1615, Ar-C=C 1595 cm^{-1}; ^1H NMR and ^{13}C NMR (see Tables 1 and 2); ms: *m/z* 306 (M^+, 59), 247 (100), 234 (18), 223 (37), 83 (56), 81 (24), 72 (28), 59 (66), 31 (36). Anal. Calcd. for $C_{13}H_{14}N_4O_3S$: C, 50.97; H, 4.61; N, 18.29; S, 10.47. Found: C, 51.02; H, 4.75; N, 18.21; S, 10.33.

(Z)-Methyl 2-[(Z)-3-phenyl-2-(3-phenyl-1H-pyrazol-5-yl-imino)-4-oxothiazolidin-5-ylidene]acetate (7d). This compound was obtained as yellow crystals (acetonitrile); mp 238–240°C; IR: NH 3330, CO 1720, 1685, C=N 1630, Ar-C=C 1605 cm^{-1}; ^1H NMR: δ 2.37 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.32 (s, 1H, pyrazol-CH), 6.89 (s, 1H, vinyl-CH), 7.21–7.82 (m, 10H, phenyl-CH), 12.95 ppm (bs, 1H, pyrazole-NH); ^{13}C NMR: δ 11.05 (CH_3), 52.65 (OCH_3), 100.99 (pyrazol-C-4′), 116.22 (vinyl-CH), 125.40, 128.09, 128.75, 129.08, 129.17 (Ar-CH), 129.33, 134.16 (Ar-C), 140.02 (pyrazol-C-3′), 143.54 (C-5), 148.17 (C-2), 154.22 (pyrazol-C-5′), 164.14 (CO, ring), 166.77 ppm (CO, ester); ms: *m/z* 404 (M^+, 100), 373 (49), 345 (38), 332 (22), 285 (54), 143 (25), 119 (23), 77 (20), 72 (27), 59 (24), 31 (72). Anal. Calcd. for $C_{21}H_{16}N_4O_3S$: C, 62.36; H, 3.99; N, 13.85; S, 7.93. Found: C, 62.23; H, 4.11; N, 13.92; S, 8.11.

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REFERENCES AND NOTES

[1] Danilina, N. A.; Mikhailov, L. E.; Lvin, B. A. Russ J Org Chem 2006, 42, 783.

[2] Hassan, A. A; Shehata, H. S.; Döpp, D. J. Chem Res 2008, 12, 725.

[3] Fâbian, B.; Csâmpas, A.; Nagy, T. Z.; Czugler, M.; Sohör, P. J. Organomet Chem 2009, 694, 3732.

[4] Darehkordi, A.; Saidi, K.; Islami, M. R. Arkivoc 2007, 1, 180.

[5] Tozkoparan, B.; Aktay, G.; Yesilade, E. Farmaco, 2002, 57, 145.

[6] Ibrahim, Y. R. J. Chem Res 2009, 602.

[7] Fâbian, B.; Kudar, V.; Csâmpas, A.; Nagy, T. Z.; Sohár, P. J Organomet Chem 2007, 692, 5621.

[8] Aly. A. A.; Ahmed. E. K.; El-Mokadem, E. M. J Heterocycl Chem 2007, 44, 1431.

[9] Acheson, R. M.; Elmore, N. F. Adv Heterocycl Chem 1978, 23, 263.

[10] Nair, V.; Sreekanth, A. R.; Abhilash, N.; Bhadbhade, M. M.; Gonnada, R. C. Org Lett 2002, 4, 3575.

[11] Nair, V.; Sreekanth, A. R.; Biju, A. T.; Rath, N. P. Tetrahedron Lett 2003, 44, 729.

[12] Yavaria, I.; Pilatan, M.; Moradi, L. Tetrahedron, 2009, 65, 2067.

[13] Hassan, A. A.; Ibrahim, Y. R.; Mohamed, N. K.; Mourad, A. E. J Prakt Chem 1990, 332, 1049.

[14] Hassan, A. A.; Mohamed, N. K.; Ibrahim, Y. R.; Mourad, A. E.; Fetouh, S. A. Spectrochim Acta 1991, 47A, 1635.

[15] Hassan, A. A.; Ibrahim, Y. R.; Mohamed, N. K.; Mourad, A. E. Liebigs Ann Chem, 1993, 71.

[16] Mohamed, N. K.; Ibrahim, Y. R.; Hassan, A. A.; Mourad, A. E. Arch Pharm (Weinheim) 1993, 326, 245.

[17] Hassan, A. A.; Mohamed, N. K.; Ibrahim, Y. R.; Mourad, A. E. Liebigs Ann Chem 1991, 695.

[18] Ibrahim, Y. R. J. Chem Res 2009, 495.

[19] KucuKguzel, G.; Kocatepe, A.; De Clercq, E.; Sahin, F.; Gulluce, M. Eur J Med Chem 2006, 41, 353.

[20] Tenorio, R. P.; Carvalho, C. S.; Pessanha, C. S.; de Lima, J. G.; de Faria, A. R.; Alves, A. J.; de Melo, E. J. T.; Goes, A. J. S. Bioorg Med Chem Lett 2005, 15, 2575.

[21] Kato, T.; Ozaki, T.; Tsuzuki, K.; Ohi, N. Org Process Res Dev 2001, 5, 122.

[22] Kucukguzel, S. G.; Oruc, E. E.; Rollas, S.; Sahin, F.; Ozbek, A. Eur J Med Chem 2002, 37, 197.

[23] Shih, M.-H.; Ke, F.-Y. Bioorg Med Chem 2004, 12, 4633.

[24] Kato, T.; Ozaki, T.; Tamura, K.; Snzuki, Y.; Akima, M.; Ohi, N. J Med Chem 1999, 42, 3134.

[25] Barreca, M. L.; Balzarini, J.; Chimirri, A.; De Clercq, E.; De Luca, L.; Holtje, H. D.; Holtje, M.; Monforte, A. M.; Monforte, P.; Pannecouque, C.; Rao, A.; Zappala, M. J Med Chem 2002, 45, 5410.

[26] Vögeli, U.; von Philipsborn, W.; Nagarajan, K.; Nair, M.D. Helv Chim Acta 1978, 61, 607;. (b) Danilkina, N. A.; Mikhailov, L. E.; Ivin, B. A. Russ J Org Chem 2006, 42, 783.