A Facile Method for the Synthesis of Hydrazine-4-oxothiazolidine and Imino-5-oxothiadiazine Derivatives from 1,4-Disubstituted Thiosemicarbazides

Alaa A. Hassan,[a]* Ashraf A. Aly,[a] Tarek I. M. Bedair,[a] Alan B. Brown[b] and Talaat I. El-Emary[c]

[a]Chemistry Department, Faculty of Science, Minia University, El-Minia 61519, Egypt
[b]Chemistry Department, Florida Institute of Technology, 150 W University BlvdMelbourne, Florida 32901
[c]Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt
*E-mail: alaahassan2001@yahoo.com

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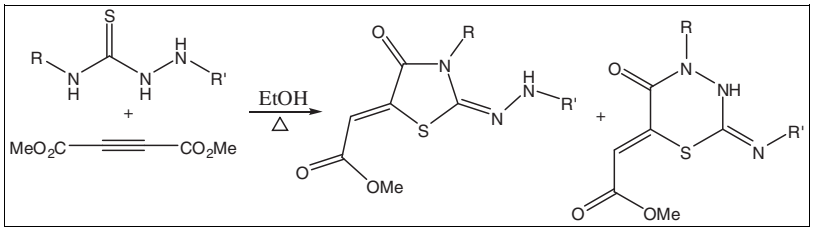

1,4-Disubstituted thiosemicarbazides reacted with dimethyl acetylenedicarboxylate with formation of (2-hydrazono-4-oxothiazolidin-5-ylidene)acetates and, in one case, a (2-imino-1,3,4-thiadiazin-5-on-6-ylidene)acetate. Several mechanistic options involving nucleophilic interaction are presented. The structures of all newly synthesized compounds were identified by ^{1}H NMR, ^{13}C NMR, COSY, HMQC and HMBC spectral data.

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INTRODUCTION

Acylthiosemicarbazides represent versatile synthons for various syntheses of nitrogen–sulfur heterocycles. The acylthiosemicarbazide moiety provides an opportunity to perform cyclocondensations as well as addition-cyclization reactions. The products of these reactions are thiazin-2-ylidene [1], thiazoline [2], triazole [3], and imidazolidine [4,5] derivatives. It has been reported that the reaction of dimethyl acetylenedicarboxylate with thiocarbamides led to 4-oxathiazolidine derivatives [6–9]. Thiazolidine-4-one ring systems are known to posses anti-bacterial [10], antituberculosis [11–13], antiviral [14–16], anticancer [17–20], and antioxidant [21] activities.

On the other hand, thiourea has been a subject of intensive investigations for its performance in the construction of anion receptors via double hydrogen-bonding interaction by thioureido-NH donors [22–25]. This interest has recently been enhanced because of the promising progress in thiourea-based organocatalysts, again via hydrogen bonding [26–29]. Obviously, the bonding ability of the thiourea moiety is an important parameter, which in principle depends on the acidity of thioureido-NH protons and the number of binding sites [30–32].

Recently, it has been reported that the acylthiosemicarbazides **1** reacted with tetracyanoethylene (TCNE, **2**), in dimethylformamide to form thiadiazoles **3** and oxadiazoles **4** [33]. Upon addition of TCNE to **1** (R = benzyl and allyl) in chlorobenzene, the thiadiazole, pyrazole, and oxadiazine derivatives **5–7**, respectively, were isolated (Scheme 1) [33].

In the present work, we have explored the effect of acyl group in acylthiosemicarbazides on the nucleophilicity of the nitrogen atoms by examining the reactions of selected acylthiosemicarbazides **1a–h** with dimethyl acetylenedicarboxylate and, in addition, by intramolecular cyclo-condensation under refluxing in ethanol. To elucidate the tautomeric states and structure of the products as well as to characterize the products and confirm the identities of the new compounds, we used IR, ^{1}H NMR and ^{13}C NMR, COSY, HMQC and HMBC as well as mass spectrometry.

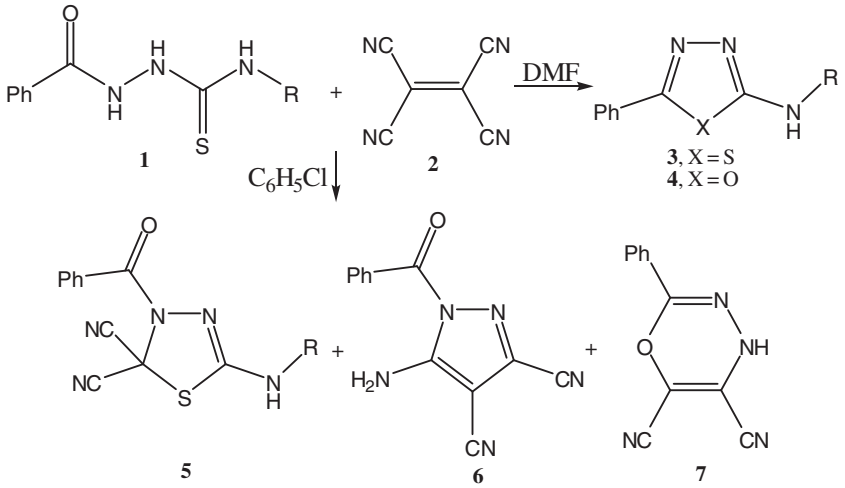
RESULTS AND DISCUSSION

Treatment of **1a–h** with one molar equivalent of dimethyl acetylenedicarboxylate (DMAD, **8**) in ethanol at reflux resulted in the formation of thiazolidinones **9a–h** as major products; the yields are 66–79% in all cases but **9a**. Adduct **9a** was isolated in 59% yield, along with thiadiazinone **10** (28%) as minor product (Scheme 2).

Compound 9a. To illustrate the structure elucidation of compounds **9a–h**, we choose **9a**, the major reaction product from equimolar quantities of **1a** and DMAD (**8**). IR spectra showed three carbonyl absorption bands at 1750, 1700 and 1660 cm^{-1}, and a band at 1615 cm^{-1} that was assigned to C=N vibration.

The ^{1}H NMR spectrum of **9a** showed one methoxyl group at $\delta_H = 3.82$, two phenyl groups in the range of $\delta_H = 6.97$–7.79, one vinylic proton at $\delta_H = 7.02$, and NH at $\delta_H = 9.42$. In principle, the reaction could form any of compounds

Scheme 1



1,**3** and **4**: R = PhCO, Ph, $PhCH_2$, CH_2=CH-CH_2, EtOOC
5: R = $PhCH_2$, CH_2=CH-CH_2

9a–13 (Figure 1), depending on the sites of nucleophilic attack. In each DMAD-derived substructure C-1″ is the lactam carbonyl, C-2″ is the proton-bearing carbon, and C-3″ is the (quaternary) carbon. Thus, in **11** and **12**, C-1″, 2″, 3″ are attached in that order; in **9a**, **10**, and **13**, C-3″ is between C-1″ and C-2″.

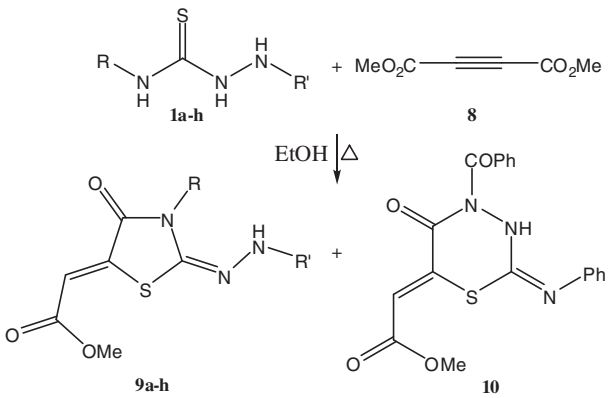
From the ^{13}C NMR data, structures with C═S double bonds, such as **11**, can be immediately ruled out: the C = X signals are not far enough downfield ($\delta_C \leq 166.03$). The methoxy protons ($\delta_H = 3.82$) give HMQC correlation with the attached carbon at $\delta_C = 52.71$ and HMBC correlation with the ester carbonyl at $\delta_C = 166.03$. The signal at $\delta_C = 161.90$, giving HMBC correlation with H-2″ at $\delta_H = 7.02$, must be the lactam carbonyl C-1″.

The aromatic carbon multiplicities show unambiguous positional assignments. The *para*-carbons C-4,4′ give double triplets, the *meta*-carbons C-3,3′ give double doublets, and the *ortho*-carbons H-2,2′ give double-double doublets, one doublet coupling constant being large in each case, The *ipso* carbons C-1,1′ appear as triplets with small coupling constants; the benzamide carbonyl does not show resolvable coupling, but gives HMBC correlation with H-3 and N-H. The coupling networks corresponding to each ring can be deduced from the correlation patterns.

Compound 10. The minor product of the same reaction is assigned as (Z)-methyl 2-((Z)-4-benzoyl-5-oxo-2-(phenylimino)-1,3,4-thiadiazinan-6-ylidene)acetate **10**, as one of the products from the reaction between **1a** and **8**. (It has been reported that compounds having thiadiazinan moiety showed potent antibacterial activity [36,37]).

Structures with C═S double bonds, such as **11**, can again be ruled out from the ^{13}C C = X chemical shifts ($\delta_C \leq 165.94$). The methoxyl protons are distinctive at $\delta_H = 3.81$; this signal gives HSQC correlation with the attached carbon at $\delta_C = 52.66$ and HMBC correlation with the ester carbonyl at $\delta_C = 165.94$. The signals at $\delta_C = 163.61$ and 163.52, giving HMBC correlation with H-2″ at $\delta_H = 6.87$ and H-2 at $\delta_H = 7.84$, must be lactam carbonyl C-1″ and benzamide carbonyl in some order. They almost overlap, in both the decoupled and ^{1}H-coupled spectra. In the coupled spectrum, the upfield of the two is a doublet or triplet with $J = 5.7$ Hz; the downfield signal is broadened by a coupling whose J is small. For structural assignment, the critical coupling is between C-I′ and H-2″, which would be a doublet coupling if observed; the coupling of the benzamide carbonyl to the

Scheme 2



1,9: a, R = Ph; R′ = PhCO; **b,** R = Ph; R′ = OC–N
c, R = Ph; R′ = O_2S–C_6H_4–CH_3
d, R = CH_2=CH-CH_2, R′ = O_2S–C_6H_4–CH_3
e, R = PhCO, R′ = O_2S–C_6H_4–CH_3 ; **f**, R = CH_2=CH-CH_2; R′ = PhCO
g, R = CH_2=CH-CH_2; R′ = OC–N ; **h**, R = R′ = PhCO

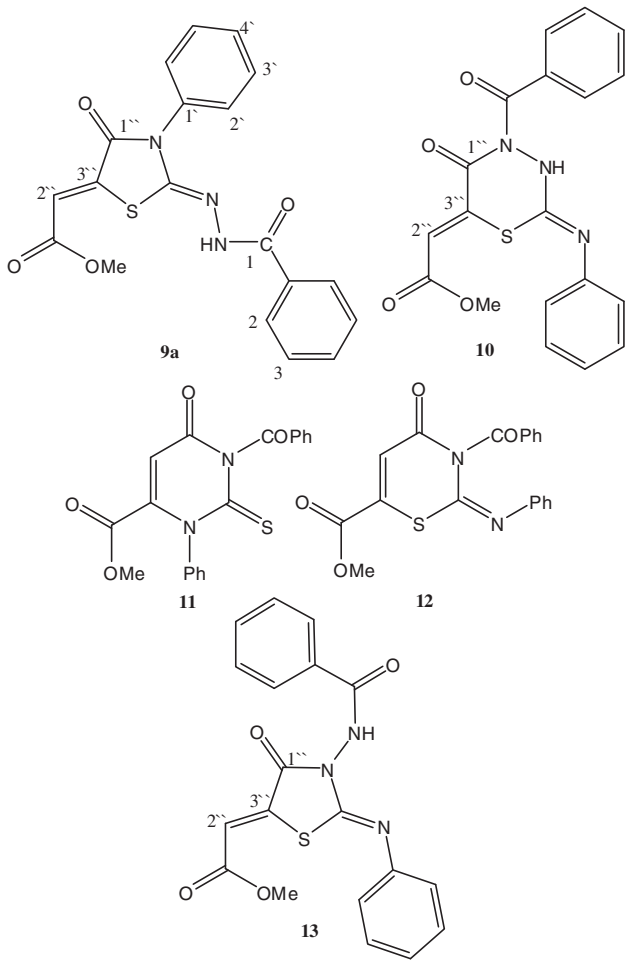


Figure 1. Possible products from the reaction between **1a–h** and dimethyl acetylenedicarboxylate (**8**).

ortho-protons would be a triplet coupling. We assign the coupling as a doublet and the upfield carbon as C-1″, based on the following reasoning (Figure 2).

In the decoupled ^{13}C spectrum, the signals are 9.3 Hz apart. In the coupled spectrum, if the upfield signal was a triplet, its center line should still be 9.3 Hz from the downfield signal, with smaller lines on either side. (The downfield line of the triplet might or might not be resolved from the other signal: the key observation is the line spacing.) On the other hand, if the upfield signal was a doublet, its downfield line should be 2.8 Hz from the original positions and 6.5 Hz from the downfield signal; there should be no line 9.3 Hz from the downfield signal, but the upfield line of the doublet should be 12.1–12.2 Hz from the downfield signal. The middle of the three observed lines is found to be 5.7 Hz from the downfield signal, and indeed there is no line 9 Hz from the downfield signal.

As in other compounds of the series, the magnitude of the coupling between C-1″ and H-2″ ($J = 5.6$) requires a three-bond not two-bond coupling [34,35], excluding structures **12**,

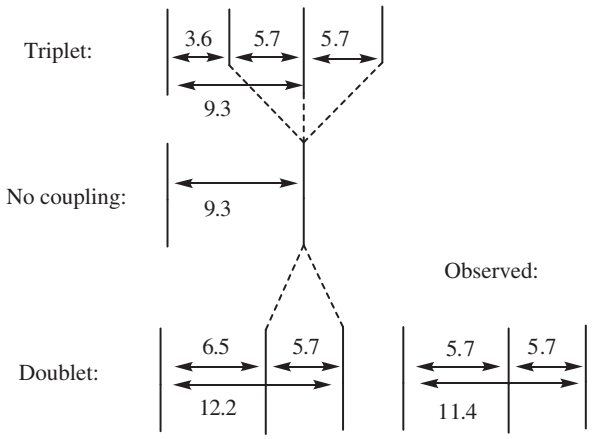


Figure 2. Coupling trees for amide carbons under various coupling scenarios.

and further argues that C-1″ and H-2″ are mutually *cis*, as depicted in structures **9** and **10**. Compound **9a** was assigned as (*Z*)-**9a**; the (*E*) isomer of **9a** is not expected to give a coupling this large, but (*Z*)-**10** is. Therefore, the structure is assigned as (*Z*)-**10**.

The aromatic signals are so close together that only partial assignment is possible. The signal at $\delta_C = 127.47$, which gives HSQC correlation with H-2, is assigned as C-2. The broadened double triplet at $\delta_C = 131.73$, which gives HMBC correlation with C-2, must be one of the other carbons in the benzamide ring, and its multiplicity requires it be the *para*-carbon C-4. The double-double doublet at $\delta_C = 128.20$, with three different coupling constants, is assigned as the remaining *ortho*-carbon C-2′ because of its multiplicity: the *ortho*-carbons of **9a** show similar coupling. The three signals between $\delta_C = 129.14$–128.48 must represent C-3,3′,4′; the smallest of the three ($\delta_C = 129.06$) is assigned as *para*-carbon C-4′, because the *meta*-carbon signals represent two carbons each. *Para*-carbons normally appear as double triplets, and this signal is therefore so assigned, although the downfield line is not resolved from the next signal downfield; it should be emphasized that the observed signals are consistent with this assignment. The two remaining signals must be the *meta*-carbons C-3,3′.

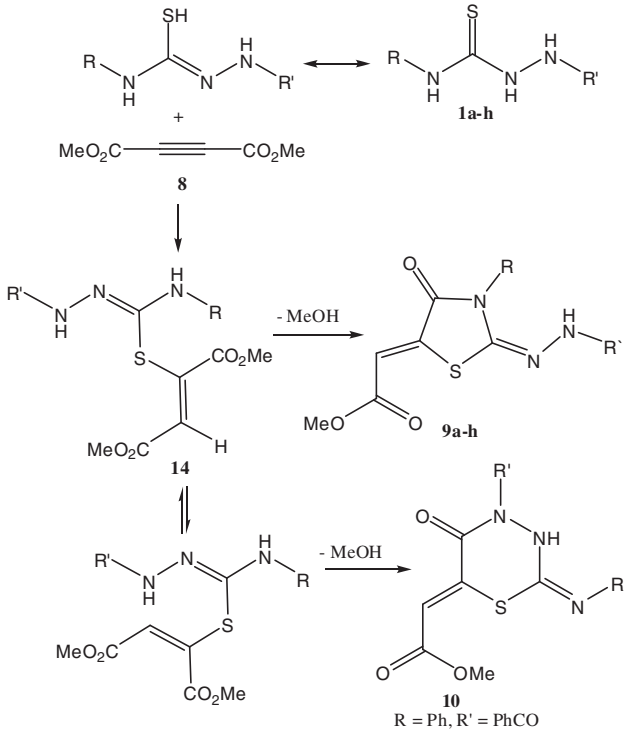
Most of the aromatic carbons are in an envelope that gives HSQC correlation with the signals at $\delta_H = 7.58$–7.51; the correlations are not resolved. C-4, which is downfield of the other protonated aromatic carbons, correlates only with the signal at $\delta_H = 7.58$, which therefore must include H-4. The signals at $\delta_H = 7.58$ and $\delta_H = 7.51$ have equal integrals; this requires that H-4′ also appear at $\delta_H = 7.58$, because all the other signals represent two protons. Because H-2 gives COSY correlation with $\delta_H = 7.51$ but not $\delta_H = 7.58$, H-3 must have $\delta_H = 7.51$. The proton integrals then require that one pair of the remaining protons H-2′,3′ has $\delta_H = 7.58$ and the other has $\delta_H = 7.51$ in some order.

The downfield of the two *ipso*-carbons, at $\delta_C = 134.08$, gives HMBC correlation with both $\delta_H = 7.58$ and $\delta_H = 7.51$;

the upfield *ipso*-carbon at $\delta_C = 132.89$ correlates with $\delta_H = 7.51$ only. Because the envelope at $\delta_H = 7.51$ contains *meta*-protons (and perhaps *ortho*) from both rings, whereas that at $\delta_H = 7.58$ contains neither H-2 nor H-3, the signal at $\delta_C = 134.08$ is assigned as C-1′ and that at $\delta_C = 132.89$ as C-1.

Although the starting materials **1a–h** possess four possible nucleophilic sites, namely the three nitrogens and the sulfur, both observed cyclization pathways appear to involve intermediate **14**, which would form by conjugate addition of the thiocarbonyl group to the C–C triple bond of **8** (Scheme 3). Attack on the proximal ester group by either N-1 or N-4 would then lead to **9a–h** or **10**, respectively. It is not obvious why **9a** alone furnishes a minor adduct of type **10**.

Scheme 3



CONCLUSION

Reactions of 1,4-disubstituted thiosemicarbazides **1a–h** with dimethyl acetylenedicarboxylate (**8**) lead to intermolecular nucleophilic attack on the C ≡ C triple bond of (**8**), followed by heterocyclization to give either oxothiazolidines (**9a–h**) or an oxothiadiazine (**10**), with elimination of a molecule of MeOH.

EXPERIMENTAL

Melting points were determined with a Gallenkamp melting point apparatus (Loughborough, UK) and were uncorrected. IR spectra were obtained in KBr disks on a Shimadzu 408 instrument (Kyoto, Japan); absorption frequencies (ν) are reported in cm^{-1}. NMR spectra (^1H, 400 MHz; ^{13}C, 100 MHz) were recorded at room temperature in $CDCl_3$ or DMSO-d_6 using a Bruker AV 400 spectrometer (Karlsruhe, Germany). Chemical shifts are expressed in δ (ppm) versus tetramethylsilane (TMS) = 0. Coupling constants are stated in Hz; ^1H-coupled ^{13}C NMR spectra were measured using gated decoupling. Correlations were established using ^1H-^1H COSY, HMBC, and HSQC experiments. Mass spectra were recorded with a Varian MAT CH-5 spectrometer (70 eV) (Germany). Elemental analyses were carried out at Microanalytical Center, Cairo University, Egypt. Preparative layer chromatography (plc) used air dried 1.0 mm thick layers of slurry applied silica gel (Merck Pf 254) on 48 × 20-cm glass plates using the solvents listed. Zones were detected by indicator fluorescence quenching upon 254 nm light and eluted with acetone.

Starting materials. Thiosemicarbazides **1a–h** were prepared according to the literature: **1a** [32,38], **1b** [31,39], **1c** [40], **1d** [41], **1e–g** [42], and **1h** [30]. DMAD (**8**) was bought from Fluka (Germany).

Reactions of 1,4-disubstituted thiosemicarbazides 1a–h with DMAD (8). A mixture of 1,4-disubstituted thiosemicarbazide (**1a–h**, 1 mmol) and DMAD (**8**, 1 mmol) in absolute ethanol was refluxed for 3 h. The solvent was evaporated and the residue was subjected to plc using toluene/ethyl acetate (10:3) as eluent to give two zones (in case of the reaction between **1a** and **8**), whereas only one zone was observed in the reactions between **1b–h** and **8**. The zones were removed and extracted to give the thiazolone and thiazinone derivatives **9** and **10**, respectively.

(Z)-Methyl 2-((E)-2-(2-benzoylhydrazono)-4-oxo-3-phenylthiazolidin-5-ylidene)acetate (9a). Pale yellow crystals (0.225 g, 59%), mp 192–194°C (ethanol). IR (KBr): 3245 (NH), 1750, 1700, 1660 (CO), 1615 (C═N), 1595 (Ar-C═C). ^1H NMR ($CDCl_3$) 9.42 (s, 1H; NH), 7.79 (d, $J = 7.6$, 2H; H-2), 7.47 (t, $J = 7.4$, 1H; H-4), 7.35 (t, $J = 8.0$, 2H; H-3′), 7.32 (t, $J = 7.9$, 2H; H-3), 7.19 (t, $J = 7.4$, 1H, H-4′), 7.02 (s, 1H; H-2″), 6.97 (d, $J = 7.6$, 2H; H-2′), 3.82 (s, 3H; OCH_3). ^{13}C NMR ($CDCl_3$) 166.03 (q, $J = 3.9$; **C**O_2CH_3), 165.13 (broad quin; PhCON), 161.90 (d, $J = 5.6$; C-1″), 149.60 (s; C═N), 146.08 (t, $J = 9.7$; C-1), 138.53 (s; C-3″), 132.82 (dt, $J_d = 162.1$, $J_t = 7.5$; C-4), 130.34 (t, $J = 8.1$; C-1′), 129.56 (dd, $J = 161.1$, 8.3; C-3′), 128.65 (dd, $J = 162.6$, 7.7; C-3), 127.79 (ddd, $J = 161.0$, 7.3, 6.4; C-2), 125.80 (dt, $J_d = 162.7$, $J_t = 7.6$; C-4′), 121.05 (ddd, $J = 160.3$, 7.5, 5.6; C-2′), 118.08 (d, $J = 173.6$; C-2″), 52.71 (q, $J = 148.0$; OCH_3). MS (EI): *m/z* (%) = 381 (21), 237 (17), 135 (24), 119 (41), 105 (100), 77 (67), 59 (56). *Anal.* $C_{19}H_{15}N_3O_4S$ (381.41): Calcd C, 59.83; H, 3.96; N, 11.02; S, 8.41. Found: C, 60.02; H, 4.09; N, 10.89; S, 8.29.

(Z)-Methyl 2-((Z)-4-benzoyl-5-oxo-2-(phenylimino)-1,3,4-thiadiazin-6-ylidene)acetate (10). Pale yellow crystals (0.106 g, 28%); mp 274–276°C (acetonitrile). IR (KBr): 3230 (NH), 1730, 1695, 1660 (CO), 1610 (C═N), 1590 (Ar-C═C). ^1H NMR (DMSO-d_6) 11.30 (s, 1H; N-H), 7.84 (d, $J = 7.1$, 2H; H-2), 7.58 (bt, $J = 6.9$, 4H; H-2′/3′,4,4′), 7.51 (m, 4H; H-3′/2′), 6.87 (s, 1H; H-2″), 3.81 (s, 3H; OCH_3). ^{13}C NMR (DMSO-d_6) 165.94 (q, $J = 3.4$; **C**O_2CH_3), 163.61 (b; Ph**C**ON), 163.52 (d, $J = 5.7$; C-1″), 157.56 (b; C═N), 140.91 (s; C-3″), 134.08 (bt, $J = 8.8$; C-1′), 132.89 (bt, $J = 8.8$; C-1), 131.73 (bdt, $J_d = 162.6$, $J_t = 8.7$; C-4), 129.14 (dd, $J = 163.2$, 7.8; C-3/3′), 129.06 (dt, $J = 159.5$, 7.1; C-4′), 128.48 (dd, $J = 162.0$, 6.7; C-3′/3), 128.20 (ddd, $J = 164.7$, 7.4, 5.1; C-2′), 127.47 (bd, $J = 161.7$; C-2), 115.12 (d, $J = 172.3$; C = 2″), 52.66 (q, $J = 148.1$; OCH_3). MS (EI): *m/z* (%) = 381 (22), 353 (36), 276 (19), 105 (82), 59 (100). *Anal.* $C_{19}H_{15}N_3O_4S$ (381.41): Calcd C, 59.83; H, 3.96; N, 11.02; S, 8.41. Found: C, 60.02; H, 4.09; N 10.87; S, 8.58.

(Z)-Methyl 2-((E)-2-(2-isonicotinoylhydrazono)-4-oxo-3-phenylthiazolidin-5-ylidene)acetate (9b). Pale yellow crystals (0.260 g, 68%); mp 201–203°C (ethanol). IR (KBr): 3210 (NH), 1735, 1695, 1655 (CO), 1610 (C═N), 1590 (Ar-C═C). ^{1}H NMR ($CDCl_3$) 9.17 (b, 1H; NH), 8.76 (d, J = 5.6, 2H; H-3), 7.71 (t, J = 5.1, 2H; H-2), 7.37 (t, J = 7.8, 2H; H-3′), 7.21 (t, J = 7.5, 1H; H-4′), 7.05 (s, 1H; H-2″), 6.97 (d, J = 7.6, 2H; H-2′), 3.84 (s, 3H; OCH_3). ^{13}C NMR ($CDCl_3$) 165.98 (q, J = 4.3; **C**O_2CH_3), 163.60 (dt, J_d = 4.1, J_t = 2.5; C-1″), 161.48 (t, J = 5.0; PyCON), 150.80 (bdd, J_d = 182.3, 10.7; C-2), 148.73 (b; C═N), 145.95 (bt; C-1′), 138.27 (s; C-3″), 137.85 (t, J = 5.9; C-1), 129.62 (dd, J = 161.3, 8.3; C-3′), 125.93 (dt, J_d = 162.7, J_t = 8.5; C-4′), 121.31 (dddd, J = 164.7, 7.6, 7.6, 1.9; C-3), 120.96 (ddd, J = 158.7, 7.6, 7.6; C-2′), 118.37 (d, J = 173.9; C-2″), 52.80 (q, J = 148.2; OCH_3). MS (EI): *m/z* (%) = 382 (34), 354 (19), 276 (12), 106 (87), 59 (100). *Anal*. $C_{18}H_{14}N_4O_4S$ (382.39): Calcd C, 56.54; H, 3.69; N, 14.65; S, 8.39. Found: C, 56.39; H, 3.78; N, 14.81; S, 8.25.

(Z)-Methyl 2-((E)-4-oxo-3-phenyl-2-(2-tosylhydrazono)-thiazolidin-5-ylidene)acetate (9c). Pale yellow crystals (0.327 g, 76%); mp 220–222°C (acetonitrile). IR (KBr): 3250 (NH), 1730, 1695 (CO), 1610 (C═N), 1590 (Ar-C═C). ^{1}H NMR ($CDCl_3$) 10.38 (b, 1H; NH), 7.54 (d, J = 8.2, 2H; H-2), 7.52 (t, J = 7.6, 2H; H-3′), 7.48 (t, J = 7.1, 1H; H-4′), 7.35 (d, J = 7.1, 2H; H-2′), 7.31 (d, J = 8.1, 2H; H-3), 6.85 (s, 1H; H-2″), 3.84 (s, 3H; OCH_3), 2.37 (s, 3H; CCH_3). ^{13}C NMR ($CDCl_3$) 165.92 (q, J = 3.5; **C**O_2CH_3), 163.50 (d, J = 5.6; C-1″), 157.61 (s; C═N), 143.66 (tq, $J_t = J_q$ = 6.6; C-4), 140.90 (d, J = 1.0; C-3″), 134.79 (t, J = 8.6; C-1), 133.67 (tt, J = 9.3, 2.3; C-1′), 129.10 (ddd, J = 161.3, 5.9, 5.2; C-3), 128.92 (dt, J_d = 162.0, J_t = 7.6; C-4′), 128.83 (dd, J = 163.5, 7.6; C-3′), 127.95 (dd, J = 166.0, 3.5; C-2), 127.90 (ddd, J_d = 165.7, 6.8, 6.8; C-2′), 115.48 (d, J = 172.7; C-2″), 52.70 (q, J = 148.1; OCH_3), 21.00 (tq, J_t = 4.2, J_q = 127.1; C**C**H_3). MS (EI): *m/z* (%) = 431 (23), 276 (28), 247 (36), 155 (670, 135 (45), 112 (77), 59 (100). *Anal*. $C_{19}H_{17}N_3O_5S_2$ (431.49): Calcd C, 52.89; H, 3.97; N, 9.74; S, 14.86. Found: C, 53.08; H, 4.09; N, 9.69; S, 14.78.

(Z)-Methyl 2-((E)-3-allyl-4-oxo-2-(2-tosylhydrazono)-thiazolidin-5-ylidene)acetate (9d). Pale yellow crystals (0.312 g, 79%), mp 212–214 °C (acetonitrile). IR (KBr): 3200 (NH), 1720, 1700 (CO), 1610 (C═N), 1590 (Ar-C═C). ^{1}H NMR (DMSO-d_6) 10.43 (s, 1H; NH), 7.73 (d, J = 8.2, 2H; H-2), 7.43 (d, J = 8.1, 2H; H-3), 6.80 (s, 1H; H-2″), 5.72 (ddt, J_d = 17.1, 10.3, J_t = 5.5, 1H; H-2′), 5.13 (dd, J = 10.3, 1.1, 1H; H-3′-*trans* [43]), 5.05 (dd, J = 17.2, 1,2, 1H; H-3′-*cis* [43]), 4.25 (d, J = 5.4, 2H; H-1′), 3.81 (s, 3H; OCH_3), 2.40 (s, 3H; CCH_3). ^{13}C NMR (DMSO-d_6) 165.72 (q, J = 4.6; **C**O_2CH_3), 163.41 (dt, J_d = 5.4, J_t = 2.7; C-1″), 156.56 (b; C═N), 143.66 (dt, $J_d = J_t$ = 6.8; C-1), 140.35 (s; C-3″), 134.89 (t, J = 7.9; C-4), 130.35 (dddt, J_d = 159.2, 3.3, 3.3, J_t = 3.3; C-2′), 129.26 (ddq, J_d = 161.8, 5.5, J_q = 5.5; C-3), 127.91 (dd, J = 166.2, 4.9; C-2), 117.91 (dd, J_d = 159.9, 154.9, J_t = 5.5; C-3′), 115.62 (d, J = 172.7; C-2″), 52.61 (q, J = 148.2; OCH_3), 44.61 (dddt, J_d = 13.4, 6.4, 6.1. J_t = 142.7; C-1′), 20.96 (tq, J_t = 4.2, J_q = 127.1). MS (EI): *m/z* (%) = 395 (17), 240 (100), 211 (53), 116 (39), 91 (88), 65 (56). *Anal*. $C_{16}H_{17}N_3O_5S_2$ (395.45): Calcd C, 48.60; H, 4.33; N, 10.63; S, 16.22. Found: C, 48.44; H 4.42; N, 10.76; S, 16.07.

(Z)-Methyl 2-((E)-2-(benzoylimino)-3-(4-methylbenzene-sulfonamido)-4-oxothiazolidin-5-ylidene)acetate (9e). Pale yellow crystals (0.325 g, 71%), mp 237–239°C (acetonitrile). IR (KBr): 3265 (NH), 1745, 1700, 1665 (CO), 1620 (C═N), 1595 (Ar-C═C). ^{1}H NMR (DMSO-d_6) 11.47 (b, 1H; NH), 7.90 (dd, J = 7.2, 1.1, 2H; H-2′), 7.75 (d, J = 8.3, 2H; H-2), 7.68 (t, J = 7.4, 1H; H-4′), 7.48 (d, J = 7.8, 2H; H-3′), 7.21 (d, J = 8.1, 2H; H-3), 7.04 (s, 1H; H-2″), 3.83 (s, 3H; OCH_3), 2.21 (s, 3H; CCH_3). ^{13}C NMR (DMSO-d_6) 175.91 (t, J = 3.9; PhCON), 165.27 (q, J = 4.5; CO_2CH_3), 163.93 (s; C═N), 161.38 (d, J = 5.8; C-1″), 143.99 (sextet, J = 6.7; C-4), 138.00 (s; C-3″), 137.12 (t, J = 8.6; C-1), 134.01 (dt, J_d = 164.0, J_t = 7.0; C-4′), 133.50 (t, J = 7.6; C-1′), 130.19 (dt, J_d = 163.5, J_t = 6.6; C-2′), 129.65 (ddq, J_d = 162.1, 5.6, J_q = 5.6; C-3), 128.38 (dd, J_d = 163.7, 7.3; C-3′), 127.43 (dd, J = 165.9, 5.5; C-2), 120.93 (d, J = 173.2; C-2″), 52.86 (q, J = 148.4; OCH_3), 20.81 (tq, J_t = 4.3, J_q = 127.1; C**C**H_3). MS (EI): *m/z* (%) = 459 (42), 304 (18), 296 (28), 163 (54), 105 (100), 77 (76), 59 (81). *Anal*. $C_{20}H_{17}N_3O_6S_2$ (459.50): Calcd C, 52.28; H, 3.73; N, 9.14; S, 13.96. Found: C, 52.15; H, 3.81; N, 8.99; S, 14.11.

(Z)-Methyl 2-((E)-3-allyl-2-(2-benzoylhydrazono)-4-oxo-thiazolidin-5-ylidene)acetate (9f). Pale yellow crystals (0.228 g, 66%), mp 202–204°C (acetonitrile). IR (KBr): 3240 (NH), 1720, 1700, 1660 (CO), 1610 (C═N), 1585 (Ar-C═C). ^{1}H NMR (DMSO-d_6) 11.34 (s, 1H; NH), 7.87 (d, J = 6.9, 2H; H-2), 7.60 (t, J = 7.2, 1H; H-4), 7.52 (dd, J = 7.4, 7.4, 2H; H-3), 6.82 (s, 1H; H-2″), 5.92 (m, 1H; H-2′), 5.221 (d, J = 15.4, 1H; H-3′-*cis* [43]), 5.216 (d, J = 11.2, 1H; H-3′-*trans* [43]), 4.48 (m, 2H; H-1′), 3.78 (s, 3H; OCH_3). ^{13}C NMR (DMSO-d_6) 165.75 (q, J = 4.3; **C**O_2CH_3), 163.61 (t, J = 3.8; PhCON), 163.29 (dt, J_d = 6.3, J_t ~ 5; C-1″), 155.55 (b; C═N), 140.40 (s; C-1), 132.81 (t, J = 8.2; C-3″), 131.67 (dt, J_d = 162.9, J_t = 6.6; C-4), 130.65 (dt, J_d = 159.9, J_t = 6.2; C-2′), 128.40 (dd, J = 161.9, 7.3; C-3), 127.45 (dm, J_d = 162.1; C-2), 117.56 (ddt, J_d = 154.2, 154.2, J_t = 5.7; C-3′), 115.20 (dm, J_d = 172.7; C-2″), 52.55 (q, J = 148.2; OCH_3), 44.62 (dddt, J_d = 12.8, 6.4, 6.4, J_t = 143.0; C-1′). MS (EI): *m/z* (%) = 345 (27), 262 (32), 178 (19), 105 (100), 83 (41), 77 (52), 59 (27), 41 (76). *Anal*. $C_{16}H_{15}N_3O_4S$ (345.37): Calcd C, 55.64; H, 4.38; N, 12.17; S, 9.28. Found: C, 55.45; H, 4.48; N, 11.99; S, 9.17.

(Z)-Methyl 2-((E)-3-allyl-2-(2-isonicotinoylhydra-zono)-4-oxothiazolidin-5-ylidene)acetate (9g). Pale yellow crystals (0.256 g, 74%), mp 194–196°C (acetonitrile). IR (KBr): 3200 (NH), 1740, 1700, 1655 (CO), 1605 (C═N), 1590 (Ar-C═C). ^{1}H NMR (DMSO-d_6) 11.65 (s, 1H; NH), 8.77 (d, J = 5.6, 2H; H-3), 7.78 (d, J = 5.4, 2H; H-2), 6.84 (s, 1H; H-2″), 5.92 (ddt, J_d = 17.1, 10.4, J_t = 5.2, 1H; H-2′), 5.223 (d, J = 16.5, 1H; H-3′-*cis* [43]), 5.216 (d, J = 11.0, 1H; H-3′-*trans* [43]), 4.49 (b, 2H; H-1′), 3.79 (s, 3H; OCH_3). ^{13}C NMR (DMSO-d_6) 165.74 (q, J = 3.5; **C**O_2CH_3), 163.32 (t, J = 2.5; PyCON), 163.32 (d, J = 5.1; C-1″), 155.89 (b; C═N), 140.40 (bs; C-3″), 139.79 (quin, J = 3.2; C-1), 130.65 (ddt, J_d = 158.9, 4.3, J_t = 4.3; C-2′), 121.30 (ddd, J = 161.4, 8.2, 4.1; C-2), 117.58 (ddt, J_d = 159.8, 154.7, J_t = 5.3; C-3′), 115.46 (d, J = 172.6; C-2″), 52.58 (q, J = 148.2; OCH_3), 44.64 (dddt, J_d = 13.6, 6.3, 6.3, J_t = 142.6; C-1′). MS (EI): *m/z* (%) = 346 (27), 247 (19), 240 (45), 112 (55), 106 (63), 99 (57), 59 (81), 41 (100). *Anal*. $C_{15}H_{14}N_4O_4S$ (346.36): Calcd C, 52.02; H, 4.07; N, 16.18; S, 9.26. Found: C, 51.88; H, 3.98; N, 16.29; S, 9.38.

(Z)-Methyl 2-((E)-3-benzoyl-2-(2-benzoylhydrazono)-4-oxothiazolidin-5-ylidene)-acetate (9h). Pale yellow crystals (0.311 g, 76%), mp 230–232°C (acetonitrile). IR (KBr): *v* 3240 (NH), 1745, 1705, 1665 (CO), 1610 (C═N), 1590 (Ar-C═C) cm^{-1}. ^{1}H NMR (DMSO-d_6) 11.90 (s, 1H; NH), 8.10 (d, J = 7.3, 2H; H-2), 8.04 (d, J = 7.3, 2H; H-2′), 7.73 (t, J = 7.3, 1H; H-4′), 7.67 (t, J = 7.4, 1H; H-4), 7.64 (dd, J = 7.5, 7.5, 2H; H-3′), 7.52 (dd, J = 7.7, 7.7, 2H; H-3), 7.13 (s, 1H; H-2″), 3.86 (s, 3H; OCH_3). ^{13}C NMR (DMSO-d_6) 176.20 (t, J = 3.9; PhCON), 165.21 (q, J = 3.7; **C**O_2CH_3), 165.10 [b; (PhCON)′], 163.89 (s; C═N), 161.67 (d, J = 5.7; C-1″), 137.49 (s; C-3″), 134.17 (dt, J_d = 162.8, J_t = 7.5; C-4), 133.72 (t, J = 4.9; C-1′), 132.95 (dt, J_d = 158.6, J_t = 7.2; C-4′), 130.66 (t, J = 7.7; C-1), 129.71 (ddd, J = 162.6, 6.6,

6.6; C-2), 128.86 (dd, $J = 162.8$, 7.3; C-3/3′), 128.82 (dd, $J = 163.1$, 7.5; C-3′/3), 127.80 (ddd, $J = 161.7$, 6.7, 6.7; C-2′), 121.36 (d, $J = 173.5$; C-2″), 52.55 (q, $J = 148.4$; OCH_3). MS (EI): *m/z* (%) = 409 (32), 275 (23), 163 (41), 114 (19), 105 (100), 77 (62), 59 (48). *Anal*. $C_{20}H_{15}N_3O_5S$ (409.42): Calcd C, 58.67; H, 3.69; N, 10.26; S, 7.83. Found: C, 58.79; H, 3.58; N, 10.41; S, 7.98.

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