International Journal of Organic Chemistry, 2016, 6, 31-43
Published Online March 2016 in SciRes. http://www.scirp.org/journal/ijoc
http://dx.doi.org/10.4236/ijoc.2016.61004

Synthesis, Spectroscopy and X-Ray Characterization, of Novel Derivatives of Substituted 2-(Benzothiazol-2'-ylthio)acetohydrazide

Fatima Al-Omran*, Adel Abou El-Khair

Department of Chemistry, Faculty of Science, Kuwait University, Safat, Kuwait
Email: *fatima.alomran@ku.edu.kw, fatima7078@hotmail.com

Received 13 January 2016; accepted 14 March 2016; published 17 March 2016

Copyright © 2016 by authors and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY).
http://creativecommons.org/licenses/by/4.0/
Open Access

Abstract

Treatment of 2-(benzo[d]thiazol-2'-ylthio)acetohydrazide (3) with acetylacetone afforded *N*-(4-oxopentan-2-ylidine) acetohydrazide derivative 5. The acetohyrazide derivatives 3 and 5 were utilized as a key intermediate for the synthesis of a novel heterocyclic compounds. The synthesis of a novel series of condensation and substituted derivatives of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide in good yield has been reported. The newly synthesized compounds were characterized by elemental analysis ^{1}H-NMR, ^{13}C-NMR spectra and X-ray crystallographic investigations. The reported crystal structures of these novel 2-(benzo[*d*] thiazol-2'-ylthio)acetohydrazide derivatives are expected to be a remarkable contribution to the crystallographic database of heterocyclic compounds.

Keywords

Acetohydrazide, Benzothiazole, Pyrazole, 1,2,4-Triazolopyridine, *N*'-Acetylcinnamohydrazide

1. Introduction

Benzothiazole and its derivatives represent one of the most biologically active classes of compounds, displaying a remarkable diversity of bioactivities in the medical and the agrochemicals field [1]-[3]. Recently, several publications reported that hydrazide-hydrazones are valuable intermediates in the synthesis of heterocyclic compounds with potential pharmaceutical and biological activities [4] [5]. Based on those reports and in continuation of our

*Corresponding author.

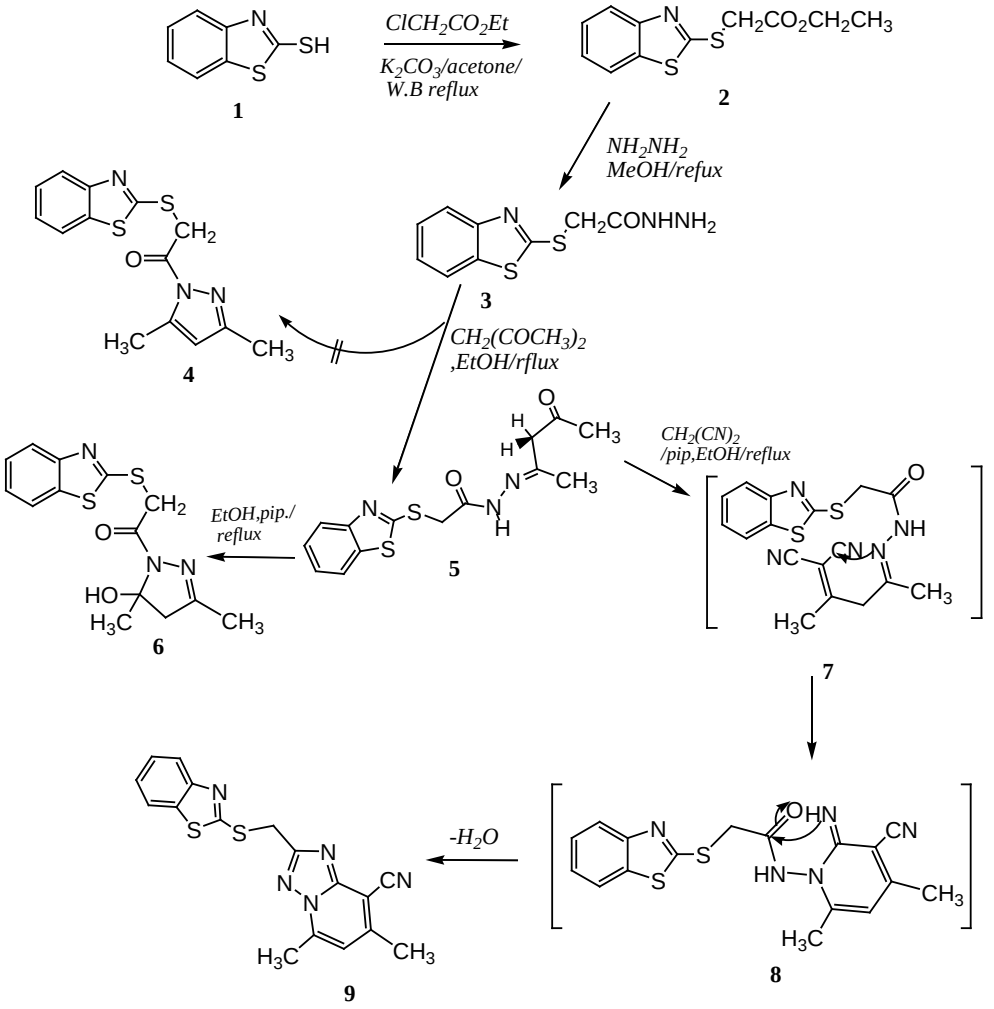
How to cite this paper: Al-Omran, F. and El-Khair, A.A. (2016) Synthesis, Spectroscopy and X-Ray Characterization, of Novel Derivatives of Substituted 2-(Benzothiazol-2'-ylthio)acetohydrazide. *International Journal of Organic Chemistry*, **6**, 31-43.
http://dx.doi.org/10.4236/ijoc.2016.61004

interest in the synthesis of heterocycles containing a 2-(benzo[*d*]thiazol-2'-ylthio) moiety [6]-[8], we reported herein the results of our study of the behavior the hitherto unreported of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide (**3**) towards a variety of reagents in order to synthesis of a novel 2,4-dihydropyrazole, 1,2,4-triazolopyridine, *N*'-acetyl cinnamohydrazide and 1,2,4-triazolo-3-(4*H*)thione bearing 2-(benzo[*d*]thiazol-2'-ylthio) in the hopes of obtaining compounds that have biological and pharmacological applications.

2. Results and Discussion

2.1. Synthesis

The 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide (**3**) proved to be a useful key intermediate in the synthesis of several heterocyclic nuclei [3]. Therefore, 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide (**3**) was prepared as previously described in the literature *via* treatment of 2-MBT (**1**) with ethyl chloroacetate yielded **2**. The latter compound reacted with hydrazine hydrate afforded **3** in good yield [3] [9]. The structure of **3** was confirmed on the basis of elemental analysis and spectral information. Treatment of **3** with acetylacetone in refluxing ethanol, afforded *N*-(4-oxopentan-2-ylidene)acetohydrazide derivative **5** and not the pyrazole derivative **4** as it reported in Literature [9]. The structure of **5** is confirmed by elemental analysis and spectral data. The mass spectrum showed the peak of the molecular ion at m/z 321[M+, 10.0%] corresponding to molecular formula $C_{14}H_{15}N_3O_2S_2$ (*cf*. **Scheme 1**). The ^{1}H NMR spectrum of **5** revealed, in addition to the aromatic benzothiazole protons, two doublets at δ H 2.97 and 2.84 ppm., with J = 16 Hz, as required for the methylene protons of H-3 indicating that



Scheme 1. Synthesis route of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide and their derivatives.

these protons are in a different environment. Likewise, the ^{1}H NMR spectrum exhibited two singlet signals at δH 4.58 and 10.70 ppm for -SCH_2-protons and NH group respectively. The assignments of ^{1}H and ^{13}C chemical shifts of compound **5** were registered in the **Experimental Section**. On the other hand, when the compound **5** heated in ethanol, containing a catalytic amount of piperidine, afforded 5-hydroxy-4, 5-dihydropyrazole derivative **6** in good yield. The mass spectrum of the obtained product revealed a molecular ion peak [M+] at m/z 321[15%] and it is compatible with the molecular formula $C_{14}H_{15}N_3O_2S_2$. It is worth mentioning that both compounds **5** and compound **6** have the same molecular formula, but has different melting points and spectral data (***cf***. **Scheme 1**). The complete assignments of ^{1}H and ^{13}C chemical shift for **6** based on COSY and HSQC were recorded in the **Experimental Section**. The structure of compound **6** was established based on X-ray crystallographic analysis, the pyrazole ring containing the chiral center (at C 10) and the benzothiazole moiety has located almost the same plane (*cf*. **Figure 1** and **Table 1**) [10].

Moreover, treatment of acetohydrazide derivative **5** with malononitrile in refluxing ethanolic piperidine afforded the [1,2,4]-triazolo[1,5-a]pyridine derivative **9** in good yield *via* the intermediary **7-8** (*cf*. **Scheme 1**).

Analytical and spectroscopic data confirmed the structure of compound **9**. The mass spectrum of **9** revealed the molecular ion peak (which is the base peak as well) at m/z value 351 [M+, 100%]. The complete assignments of the ^{1}H and ^{13}C chemical shift of the compound were recorded in the **Experimental Section**. It is worth noting that recently, [1,2,4]-triazolopyridine derivatives have been shown to be useful antifungal activities compare with the commercial pesticide [11].

On the other hand, treatment of acetohydrazide derivative **3** with 2,3-butanedione in refluxing ethanolic piperidine afforded the acetohydrazide derivative **10** in good yield (*cf*. **Scheme 2**). The analytical and spectral data of the last reaction product are entirely consistent with the proposed structure. The complete assignments of ^{1}H and ^{13}C chemical shifts of compound **10** based on COSY and HSQC experiments were recorded in the **Experimental Section.** Moreover, Nuclear Overhauser Effect (NOE) experiments were carried out to establish the configuration of acetohydrazide derivatives **10** whether it is (*E*) or (*Z*)isomers. Therefore, irradiation of a signal of the NH proton at δH 11.40 ppm,we observed increasing a signal of the methyl protons at δH 1.95 ppm. While, irradiation of a methyl signal at δH 1.95 ppm, increased the a NH signal at δ_H 11.40 ppm and have no effect on an acetyl signal at δH 2.41 ppm. Indicate the 2-(benzo[*d*]thiazol-2'-ylthio)acetamide moiety and the methyl group

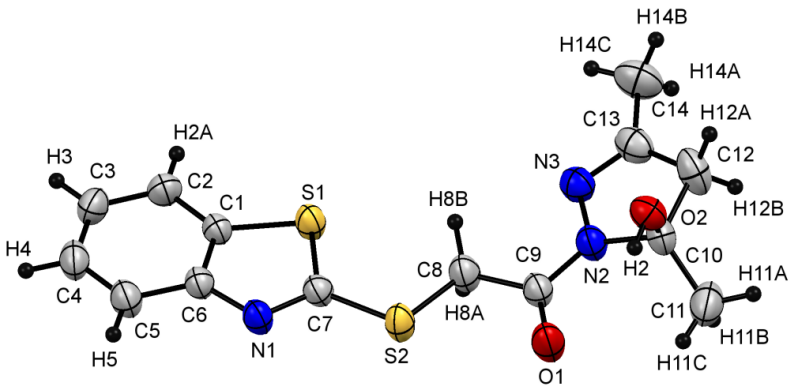
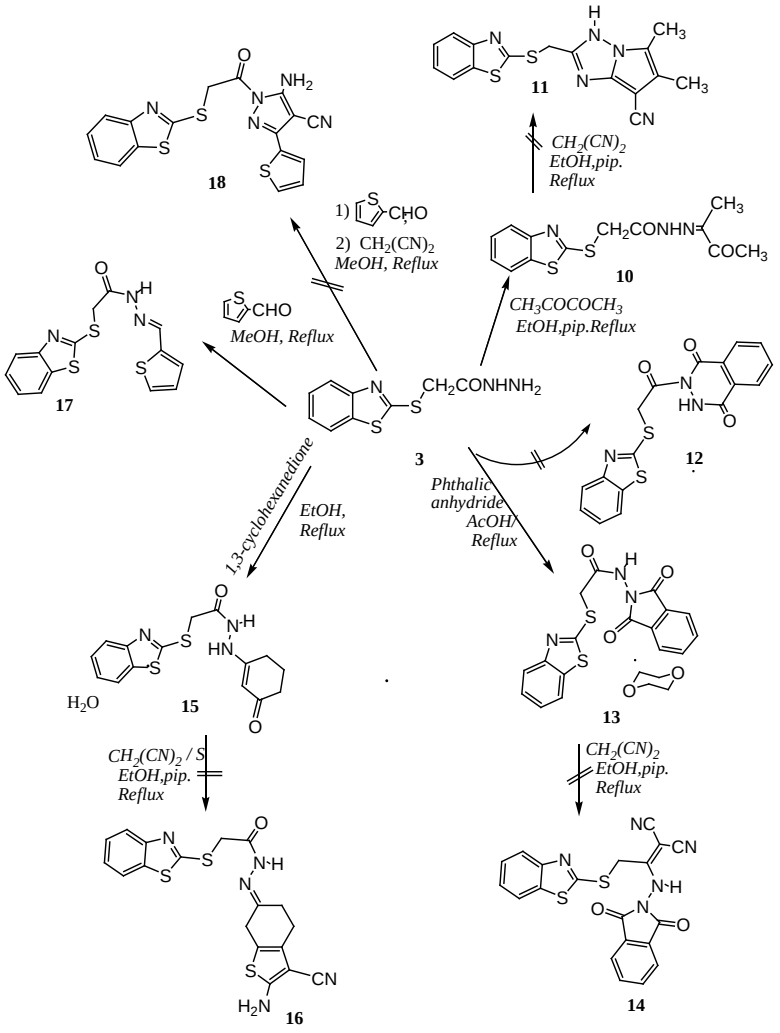


Figure 1. A general view and atom labeling of X-rays structure of **6**.

Table 1. Selected bond lengths (˚A) & bond angles for compound **6**.

Bond	Bond length (˚A)	Bond	Bond angle (˚)
S2-C7	1.734 (2)	C7-S2-C8	102.27 (11)
O2-C10	1.404 (3)	N3-C13-C14	121.3 (3)
C14-C13	1.487 (4)	C13-N3-N2	107.3 (2)
C13-N3	1.279 (3)	C9-N2-C10	125.35 (19)
N3-N2	1.399 (3)	O2-C10-C11	111.2 (2)
N2-C10	1.491 (3)	N2-C10-C12	99.30 (19)



Scheme 2. Reactions of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide with carbonyl compounds and phthalic anhydride.

are on opposite sides of the C=N, as required by an (*E*)-form. The crystal structure of **10** [12] depicted in **Figure 2**, besides to the selected bond lengths and bond angles was registered in **Table 2**. It observed from crystallographic image for the compound **10** that two molecules of **10** were shown in one asymmetric unit of these crystals; they are chemically same, only different in crystallographic point of view, due to nonequivalence in symmetry characteristics within the unit cell. In an attempt to obtain pyrolo[1,2-b][1,2,4]triazole derivative **11**, the compound **10** treated with malononitrile in refluxing ethanolic piperidine; it was found to be abortive.

Moreover, treatment of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide **3** with phthalic anhydride in refluxing acetic acid, afforded *N*-(1,3-dioxoisoindolin-2-yl)acetamide derivative **13** in good yield and not 2,3-dihydrophthalazine-1,4-dione derivative **12** as it reported in the literature [9] (**Scheme 2**). Complete assignments of ^{1}H and ^{13}C chemical shifts of compound **13** based on COSY and HSQC experiments were recorded in the **Experimental Section**. The crystal structure of **13** [13] depicted in **Figure 3**, beside to the selected bond lengths and bond angles was registered in **Table 3**. The crystal networks contain dioxane molecule as the space-filling solvent (crystalline solution). The phthalimide fraction is oriented nearly perpendicular to the plane of benzothiazole fraction (**Figure 3**). In an attempt to convert compound **13** to 1-aminoethylidine malononitrile derivatives **14** by treatment with malononitrile in refluxing ethanolic piperidine were ineffective.

On the other hand, condensation of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide (**3**) with 1,3-cyclohexadione yielded *N*'-(3-oxocylohex-1-enyl) acetohydrazide hydrate derivative (**15**) as depicted in **Scheme 2**. The structure

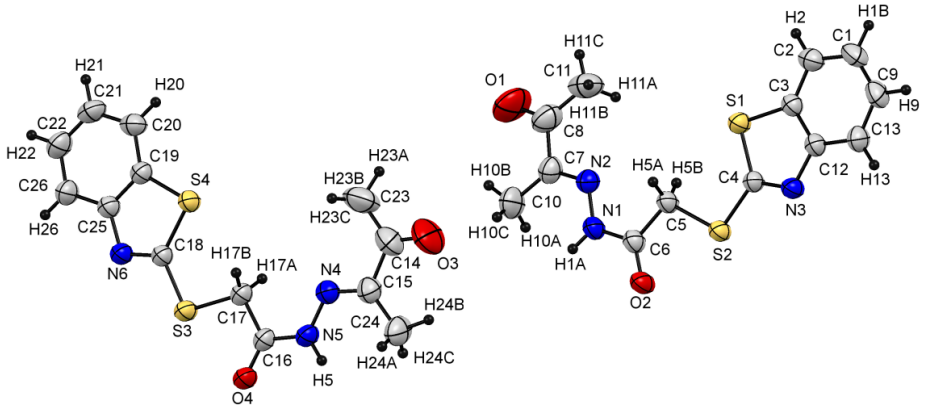


Figure 2. A general view and atom labeling of X-rays structure of **10**.

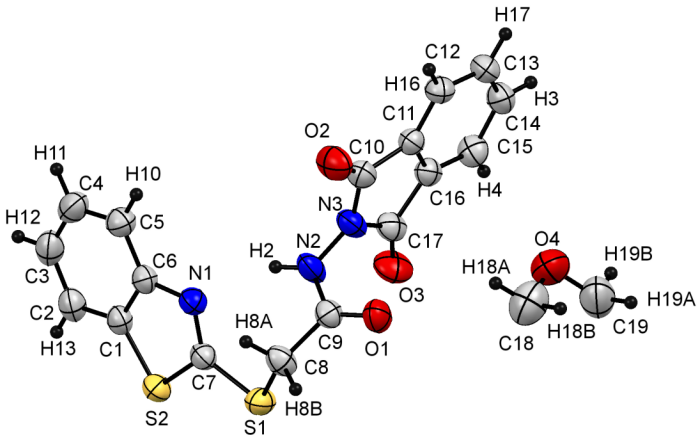


Figure 3. A general view and atom labeling of X-rays structure of **13**.

Table 2. Selected bond lengths (˚A) & bond angles for compound **10**.

Bond	Bond length (˚A)	Bond	Bond angle (˚)
S2-C5	1.804 (2)	C4-S2-C5	100.69 (10)
N1-C6	1.356 (3)	C6-N1-H1A	120.7
N1-N2	1.364 (3)	C7-N2-N1	117.4 (2)
N2-C7	1.282 (3)	C6-C5-S2	106.32 (15)
C5-C6	1.505 (3)	O1-C8-C11	122.5 (3)
C7-C8	1.497 (4)	N2-C7-C10	126.8 (3)

Table 3. Selected bond lengths (˚A) & bond angles for compound **13**.

Bond	Bond length (˚A)	Bond	Bond angle (˚)
S1-C7	1.7439 (16)	C7-S1-C8	101.81 (8)
O1-C9	1.204 (2)	N3-N2-H2	120.3
N2-N3	1.3788 (19)	C9-C8-S1	114.52 (11)
C8-H8A	0.97	C1-S2-C7	88.69 (8)
O3-C17	1.205 (2)	O1-C9-N2	122.94 (15)
C9-C8	1.512 (2)	O2-C10-C11	130.31 (16)

of this acetohydrazide hydrate derivative (**15**) deduced from its elemental analysis and spectroscopic data. The mass spectrum revealed a molecular ion peak at m/z 333[M+ -H_2O], which corresponds to a molecular weight consistent with a formula of $C_{15}H_{15}N_3O_2S_2$ (*cf.* **Experimental Section**). Furthermore, the X-ray crystallography provided an unambiguous evidence of structure **15** as proposed in **Scheme 2** [14] given in **Figure 4**.

The single crystal of **15** also contains water molecules in its network as space filling solvent. Based on bond length (**Table 4**) it is indicating the presence of keto-enol transformation from N3 to O2 through C10 and C11 as follows: the bond length between O1-C9 is 1.214 (6). While bond length between O2-C12 is 1.249 (6); elongated a little due to partial enol-form. Also, bond length between N2-C9 is 1.346 (6) while bond length between N3-C10 is 1.318 (7); reduced due to the partial double bond character. Besides, the two bond length between C10-C11 and C11-C12 are same [1.426 (6) and 1.422 (8) respectively] due to resonance. The inter conversion of the two forms involves the movement of the lone pair electrons on the N3 to the most electronegative atom (*cf.* **Figure 5**).

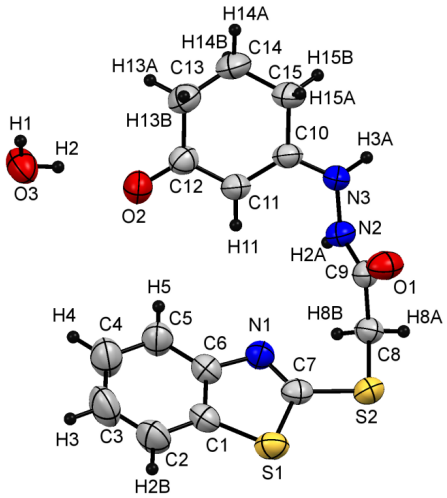


Figure 4. A general view and atom labeling of X-rays structure of **15**.

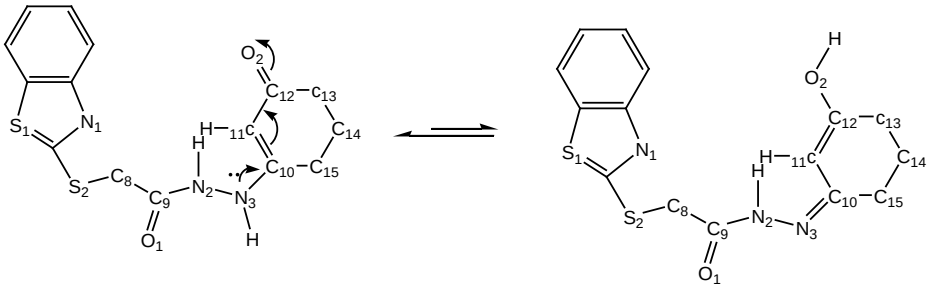


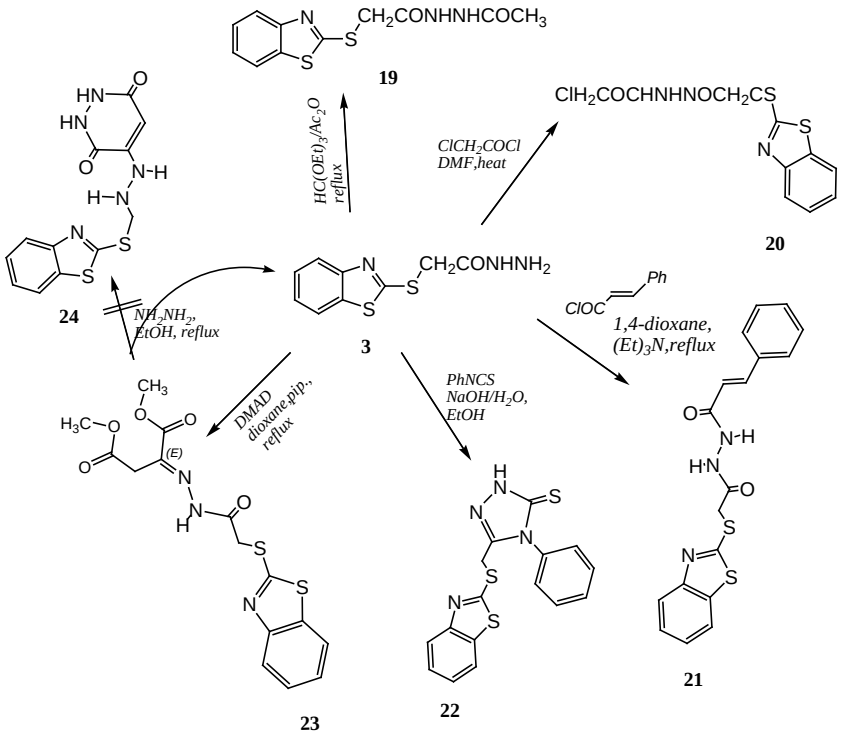
Figure 5. The keto-enol tautomeric forms of compound **15**.

Table 4. Selected bond lengths (˚A) & bond angles for compound **15**.

Bond	Bond length (˚A)	Bond	Bond angle (˚)
O1-C9	1.214 (6)	N3-N2-C9	119.7 (4)
O2-C12	1.249 (6)	C10-C11-C12	120.6 (4)
N2-C9	1.346 (6)	O2-C12-C13	120.5 (6)
N3-C10	1.318 (7)	O1-C9-C8	123.8 (4)
C10-C11	1.426 (6)	C11-C10-C15	120.8 (5)
C11-C12	1.422 (8)	C10-N3-H3A	118.9

In continuation of our efforts to generate new routes to the different functional thiophenes [6], we have used Gewald's reaction [6] by treatment of compound **15** with malononitrile in refluxing ethanol containing an elemental sulfur and a catalytic amount of piperidine. Nevertheless, this procedure was found to be unsuccessful to obtain the expected 2-amino-3-cyanothiophene derivative **16**. Moreover, condensation of acetohydrazide derivative **3** with thiophene-2-carbaldehyde afforded a mixture of both configurations *E*/*Z* acetohydrazide derivative **17** in a ratio of 3:2 respectively, based on the ^{1}H-NMR spectrum. The ^{1}H-NMR spectrum, revealed, in addition to the expected aromatic signals, four downfield signals, two corresponding to the N=CH at δH 8.25 and 8.47 ppm. The other two signals corresponding to NH at δH 11.74 and 11.82 ppm. These protons assigned to the *E* and *Z*-configuration, respectively. The latter two signals underwent facile hydrogen, deuterium exchange upon addition of deuterium oxide. Also, the ^{1}H-NMR spectrum exhibited two singlet signals for methylene protons of two isomer *E* and *Z*-configuration at δH 4.63 and 4.23 ppm respectively. In an attempt to synthesize pyrazole derivative **18** by a one-pot reaction of acetohydrazide derivative **3** with thiophene-2-carbaldehyde in the refluxing methanol, followed by treatment with malononitrile, however, it was unsuccessful (*cf*. **Scheme 2**).

On the other hand, treatment of acetohydrazide derivative **3** with triethyl orthoformate, in refluxing acetic anhydride afforded *N*'-(acetyl) acetohydrazide derivative **19.** In a similar manner, upon treatment of acetohydrazide derivative **3** with chloroacetyl chloride in dimethylformamide (DMF), afforded the *N*'-(2-chloroacetyl)-acetohydrazide derivative **20** in good yield. The structure of **20** also confirmed by its spectral data. It should remark at this point that many publications have recently reported the broad spectrum of biological usefulness exhibited by *N*, *N*-diacylhydrazine derivatives such as anti-HIV, herbicidal and antifungal activities [15]. In contrast to the above-observed chemistry, the acetohydrazide derivative also reacted with cinnamoyl chloride in 1,4-dioxane and the presence of triethylamine afforded of *E*-configuration of *N*'-(acetyl cinnamohydrazide derivative **21**. Treatment of acetohydrazide derivative **3** with phenyl isothiocyanate in refluxing ethanolic sodium hydroxide solution, afforded the [1,2,4]-triazole-3(4*H*)-thione derivative **22**. The reaction of acetohydrazide derivative **3** with dimethyl acetylene dicarboxylate (DMAD) provided a mixture of both configuration (*E*/*Z*) acetyl hydrazono succinate derivative (**23**) in a ratio of 3:1 respectively (based on the ^{1}H-NMR spectrum). The chemical shift of protons **23** was assigned using COSY and HSQC measurements were recorded in the **Experimental Section** (*cf*. **Scheme 3**).



Scheme 3. Reactions of compound **3** with $HC(OEt)_3/Ac_2O$, $ClCH_2COCl$, cinnamoly chloride, PhNCS and DMAD.

Moreover, the ^{1}H-NMR spectrum showed in addition to the expected aromatic signals, two downfield signals at δH 11.74 and 11.44 ppm and two upfield signals at δH 4.71 and 4.45 ppm assignable to the *E* and *Z*-configuration for NH and methylene protons respectively. The crystal structure, bond lengths and bond angles data of **23** [16] depicted in **Figure 6** and **Table 5**. From single crystal X-ray crystallography of dimethyl 2-[2-(-2(benzo[*d*]thiazol-2'-ylthio)acetyl)hydrazono] succinate (**23**), it is indicated that the two acetate groups are present as tail units of the molecule. Out of which, one of the acetate group is oriented in the molecular plane of the benzothiazole, while the other acetate tail is situated perpendicular to this plane. Furthermore, the distortionless enhancement by polarization transfer (DEPT) experiment was too utilized for separate the carbon signals for the compound **23**. The DEPT spectrum of the aforementioned compound showed four positive signals δ126.8, 125.0, 122.3 and 121.6 for the aromatic benzothiazole carbon (CH) and two positive signals δ53.1 and 52.6 for methyl carbons , while two negative signals at δ35.8 and 32.6 for the methylene carbon. Also an attempt to prepare the dihydropyridine 3,6-dione **24** *via* condensation of **23** with hydrazine hydrate was unsuccessful and the product identified as 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide **3** (*cf.* **Scheme 3**).

3. Experimental Section

3.1. General Procedures

Melting points are reported uncorrected and determined on a Gallenkamp apparatus. The Infrared spectra recorded on a Jasco FT/IR-6300 FT-IR uses KBr disks. ^{1}H-NMR and ^{13}C-NMR spectra were measured on a Bruker DPX 400 MHz and Bruker AVANCE II 600 MHz spectrometers, with DMSO-d6 or $CDCl_3$ as solvent using TMS as an internal standard. The methods used for the purpose of NMR assignment were COSY, HSQC, DEPT and NOE. The chemical shifts expressed as a δ unit in parts per million (ppm) and TMS = 0.00 ppm. The following abbreviation is used: s = singlet, d = doublet, t = triplet; q = quartet; m = multiple; br. = broad. Mass spectra measured on GC/MS DFS, THERMO instrument. Microanalyses performed on a CHNS-Vario.

Micro Cube Analyzer; Single crystal X-ray crystallography was performed using Rigaku Rapid II and Bruker X8 Prospector diffractometers. The starting materials ethyl-2-(benzo[*d*]thiazol-2'-ylthio) acetate **2**, mp 59˚C (lit.

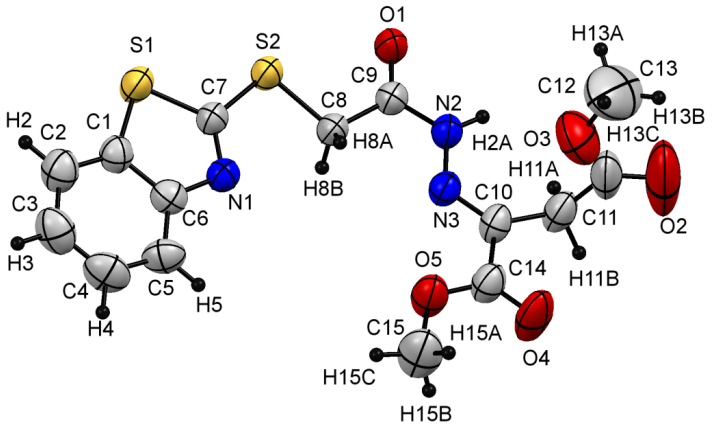


Figure 6. A general view and atom labeling of X-rays structure of **23**.

Table 5. Selected bond lengths (˚A) & bond angles for compound **23**.

Bond	Bond length (˚A)	Bond	Bond angle (˚)
N2-C9	1.359 (6)	S2-C8-C9	109.3 (3)
O2-C12	1.205 (11)	O1-C9-N2	120.5 (4)
N2-N3	1.348 (4)	O2-C12-C11	116.6 (6)
N3-C10	1.285 (6)	O5-C14-C10	115.2 (4)
C10-C14	1.478 (5)	C9-N2-H2A	120.9
C11-C12	1.536 (8)	C10-C11-C12	114.8 (5)

mp. 58˚C) [3] and 2-(benzo[*d*]thiazol-2'-ylthio)acetohydrazide (**3**), mp. 192˚C - 194˚C (lit mp. 193˚C) [3] were prepared according to the indicated literature method.

3.2. Procedures for the Synthesis of 2-(Benzothiazol-2'-ylthio)acetohydrazide Derivatives

3.2.1. 2-(Benzo[*d*]thiazol-2'-ylthio)-*N*'-(4-oxopentan-2-ylidene)acetohydrazide (5)

A mixture of compound **3 (**2.39 gm 10.0 mmol) and 2,4-pentanedione (1.0 g, 10 mmol) in ethanol (20 mL) was refluxed for 3 h. The reaction was allowed to cool to room temperature for 24 h. The solid product formed was collected by filtration and crystallized from ethanol as white crystal. Yield: 2.40 g (75%); mp 182˚C - 184˚C; FT-IR ν_{max} (cm^{-1}): 3186 - 3568 (br, NH), 1690 (C=O ketone),1670(C=O amide); ^{1}H NMR (DMSO-d_6) δ ppm: 10.7 (s, 1H, NH, D_2O exchangeable), 8.02 (d, *J* = 8 Hz, 1H, H-4'), 7.85 (d, *J* = 8 Hz, 1H, H-7'), 7.46 (t, *J* = 8 Hz, 1H, H-6'), 7.36 (t, *J* = 8 Hz, 1H, H-5'), 4.58 (s, 2H, -SCH_2), 2.97 (d, *J* = 16, 1H, H-3), 2.84 (d, *J* = 16, 1H, H-3a), 2.01 (s,3H, CH_3), 1.77 (s, 3 H, CH_3); ^{13}C NMR (DMSO-d_6) δ ppm: 168.1 (C=O), 166.4 (C=O), 165.1(C-2'), 155.9 & 152.6 (C-2 &C-3a'), 135.1 (C-7a'), 126.4 (C-6'), 124.6 (C-5'), 121.9 (C-4'), 121.2 (C-7'), 52.2 (CH_2), 37.9 (CH_2), 23.0 (CH_3), 14.1 (CH_3). EI-MS m/*z* [relative intensity]: 321 [M^+, 10], 264 [15%], 208 [100%], 180 [62%]. Anal. Calcdfor $C_{14}H_{15}N_3O_2S_2$ (321.42): C, 52.32; H, 4.70; N, 13.07%. Found: C, 52.16; H, 4.53; N, 13.39%.

3.2.2. 2-(Benzo[*d*]thiazol-2'-ylthio)-1-(5-hydroxy-3,5-dimethyl-4,5-dihydropyrazole-1-yl) ethanone (6)

A solution of **5** (3.21 g, 10 mmol) in ethanol (20 mL) containing a few drops of piperidine was refluxed for 3 h. The reaction was allowed to cool to room temperature for 24 h. The solid product formed, was collected by filtration and crystallized from ethanol as yellow crystal. Yield: 2.34 g (73%); mp 123˚C - 125˚C; FT-IR ν_{max} (cm^{-1}): 3090 - 3998 (br, OH), 1670(C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 7.90 (d, *J* = 8 Hz, 1H, H-4'), 7.78 (d, *J* = 8 Hz, 1H, H-7'), 7.47 (t, *J* = 8 Hz, 1H, H-6'), 7.31 (t, *J* = 8 Hz, 1H, H-5'), 6.55 (s, 1H, OH, D_2O exchangeable), 4.58 (dd, *J* = 20, 2H, SCH_2), 2.98 (d, *J* = 16, 1H, H-4 *pyrazole*), 2.82 (d, *J* = 16, 1H, H-4'*pyrazole*), 2.01 (s, 3H, CH_3), 1.76 (s, 3 H, CH_3); ^{13}C NMR (DMSO-d_6) δ ppm: 166.5 (C=O), 163.7 (C-2'), 155.8 (C-3), 152.7 (C-3a'), 134.7 (C-7a'), 126.4 (C-6'), 124.4 (C-5'), 121.8 (C-4'), 121.1 (C-7'), 90.7 (C-5 *pyrazole*), 52.2 (C-4*pyrazole*), 37.9 (SCH_2),), 25.9 (CH_3), 15.9 (CH_3). EI-MS *m/z* [relative intensity]: 321 [M^+, 15%], 264 [18%], 230 [3%], 208 [100%], 180 [62%]. Anal. Calcdfor $C_{14}H_{15}N_3O_2S_2$ (321.42): C, 52.32; H, 4.70; N, 13.07%. Found: C, 52.21; H, 4.55; N, 13.08%.

3.2.3. 2-[(Benzo[*d*]thiazol-2'-ylthio)methy]-5,7-dimethyl-[1,2,4]triazole-[1,5-a] pyridine-8-carbonitrile (9)

A mixture of **5** (3.21 g, 10.0 mmol) and malononitrile (0.66 g, 10 mmol) in ethanol (20 mL) containing a few drops of piperidine was refluxed for 4 h. The reaction was allowed to cool to room temperature. The solid product formed, was collected by filtration and crystallized from ethanol as brown crystals. Yield: 2.56 g (73%); mp 258˚C - 260˚C; FT-IR ν_{max} (cm^{-1}): 2227 (CN); ^{1}H-NMR (DMSO-d_6) δ ppm: 7.94 (d, *J* = 8 Hz, 1H, H-4'), 7.84 (d, *J* = 8 Hz, 1H, H-7'), 7.47 (t, *J* = 8 Hz, 1H, H-6'), 7.36 (t, *J* = 8 Hz, 1H, H-5'), 7.10 (s,1H, 6-H *pyridine*), 4.18 (s,2H, SCH_2), 2.29 (s,, 3 H, CH_3), 2.21 (s, 3 H, CH_3); ^{13}C NMR (DMSO-d_6) δ ppm: 163.4, 160.7, 153.1, 151.6, 149.5, 143.5, 135.5, 126.8, 125.1, 122.2, 121.8, 116.3, 114.4, 107.8 (arom. Carbons & CN), 30.7 (SCH_2), 20.0 (CH_3), 17.9 (CH_3). EI-MS *m/z* (relative intensity): 351 [M^+, 100%], 318 [23%], 274 [2%], 236 [4%]. Anal. Calcd. for $C_{17}H_{13}N_5S_2$ (351.45): C, 58.10; H, 3.73; N, 19.93; Found: C, 58.18; H, 3.83; N, 19.73.

3.2.4. (E) 2-[Benzo[*d*]thiazol-2'-ylthio]-*N*'-(3-oxobutan-2-ylidine)acetohydrazide (10)

A mixture **3** (2.39 g, 10.0 mmol) and 2,3-butanedione (0.87 g, 10.0 mmol) in ethanol (20 mL) containing a few drops of piperidinewas refluxed for 1 h. The reaction mixture was allowed to cool to room temperature. The product formed was collected by filtration and recrystallized from ethanol as yellow crystals. Yield: 2.64 g (86%); mp 198˚C - 199˚C. FT-IR ν_{max} (cm^{-1}): 3188 - 3448 (br, NH), 1680 (C=O ketone), 1612 (C=O amide); ^{1}H NMR (DMSO-d_6) δ ppm: 11.40 (s, 1H, NH, D_2O exchangeable), 8.02 (d, *J* = 8 Hz, 1H, H-4') 7.81 (d, *J* = 8 Hz, 1H, H-7'), 7.46 (t, *J* = 8 Hz, 1H, H-6'), 7.36 (t, *J* = 8Hz, 1H, H-5'), 4.75 (s, 2H, SCH_2), 2.41(s, 3H, $COCH_3$), 1.95 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6) δ ppm: 196.9 (C=O ketone), 169.8 (C=O amide), 166.0 (C-2'), 152.4

(C-3a'), 147.4 (C-2), 134.7 (C-7a'), 126.3 (C-6'), 124.6 (C-5'), 121.9 (C-4'), 121.1 (C-7'), 35.3 (SCH_2), 24.3 ($COCH_3$), 9.8 (CH_3). EI-MS *m/z* [relative intensity]: 307 [M^+, 10%], 264 [100%], 231 [13%], 208 [11%]. Anal. Calcd. for $C_{13}H_{13}N_3O_2S_2$ (307.39): C, 50.79; H, 4.26; N, 13.67%. Found: C, 50.53; H, 4.39; N, 13.45%.

3.2.5. 2-(Benzo[*d*]thiazol-2'-ylthio)-*N*'-(1,3-dioxoisoindolin-2-yl)acetamide (13)

A mixture of **3 (**2.39 g 10.0 mmol) and phthalic anhydride (1.48 g, 10 mmol) in acetic acid (10 mL) was heated under refluxed for 2 - 3 h. The solid product, so formed, was collected by filtration and recrystallized from 1,4-dioxane as white crystal solid. Yield: 2.69 mg (73%); mp 176˚C - 178˚C; FT-IR ν_{max} (cm^{-1}): 3215 (br, NH), 1793 & 1743 (2C=O),1662 (C=O *amide*); ^{1}H NMR (DMSO-d_6) δ ppm : 11.22 (s, 1H, NH, D_2O exchangeable), 8.01 (d, *J* =8 Hz, 1H, H-4') ,7.94 (d, *J* = 7.4 Hz, 2H, H-4 & H-7), 7.93 (d, *J* = 8 Hz, 1H, H-7'), 7.91 (t, *J* = 7.4 Hz, 2H, H-5 & H-6), 7.48 (t, *J* = 8 Hz, 1H, H-6'), 7.37 (t, *J* = 8 Hz, 1H, H-5'), 4.49 (s, 2H, SCH_2); ^{13}C NMR (DMSO-d_6) δ ppm: 166.5 (2C=O amide) 165.3 (C=O amide), 164.9 (C-2'), 152.5 (C-3a'), 135.2 (C-5 & C6), 134.9 (C-7a'), 129.4 (C-4a & C-7a), 126.4 (C-6'), 124.5 (C-5'), 123.7 (C-4 & C-7), 121.8 (C-4'), 121.3 (C-7'), 34.3 (SCH_2). EI-MS *m/z* [relative intensity]: 369 [M^+, 295 [11%], 250 [9%], 208 [100%]. Anal. Calcd. for $C_{17}H_{11}N_3O_3S_2$ (369.42): C, 55.27; H, 3.00; N, 11.37%. Found: C, 54.90; H, 3.00; N, 11.22%.

3.2.6. 2-(Benzo[*d*]thiazol-2'-ylthio)-*N*'-(3-oxocylohex-1-enyl)acetohydrazide hydrate (15)

A mixture of **3** (2.39 g 10.0 mmol) and 1,3-cyclohexanedione (1.12 g, 10.0 mmol) in ethanol (20 mL) was refluxed for 2 - 3 h. The reaction mixture was allowed to cool to room temperature. The product formed was collected by filtration and recrystallized from ethanol as yellow crystals. Yield: 2.63 g (79%); mp 185˚C - 187˚C; FT-IR ν_{max} (cm^{-1}):3433 (OH), 3198 (NH), 1695(C=O), 1657 (C=O); NMR (DMSO-d_6) δ ppm: 10.29 (s, 1H, NH, D_2O exchangeable), 8.96 (s, 1H, NH, D_2O exchangeable), 8.02 (d, *J* = 8 Hz, 1H, H-4'), 7.96 (d, *J* = 8 Hz, 1H, H-7'), 7.47 (t, *J* = 8 Hz, 1H, H-6'), 7.37 (t, *J* = 8 Hz, 1H, H-5'), 5.15 (s, 1H, H-2) 4.23 (s, 2H, SCH_2), 2. 32 (t, *J* = 8, 2 H, H-4), 2.11 (t, *J* = 8, 2 H, H-6) 1.8 (t , *J* = 8, 2H, H-5); ^{13}C NMR (DMSO-d_6) δ ppm: 196.2 (C=O ketone), 170.5 (C=O amide), 166.0 (C-2), 164.6 (C-1), 152 (C-3a'), 135.1 (C-7a'), 126.0 (C-6'), 124.0 (C-5'), 122.1 (C-4'), 121 (C-7'), 99.7 (C-2), 37.1 (SCH_2), 26.0 (C-4), 22.1 (C-6), 19.2 (C-5). EI-MS *m/z* [relative intensity]: 333 [M^+-H_2O, 10%], 315 [7%], 223 [3%], 208 [47%], 180 [56%]. Anal.Calcd.for $C_{15}H_{17}N_3O_3S_2$ (351.34): C, 51.26; H, 4.88; N, 11.92%. Found: C, 51.08; H, 4.74; N, 11.92%.

3.2.7. (*E*)-2-[Benzo[*d*]thiazol-2'-ylthio]-*N*'-(2-thiophene-2-yl-methylene)acetohydrazide (17)

A mixture of **3** (2.39 g, 10.0 mmol), and thiophene-2-carbaldehyde (1.12 g, 10.0 mmol) in methanol (20 mL) was refluxed for 1 h. The reaction mixture was allowed to cool to room temperature. The product formed was collected by filtration and crystallized from ethanol as yellow crystals. Yield: 2.53 g (76%); mp 134˚C - 136˚C; FT-IR ν_{max} (cm^{-1}): 3295 (NH); 1658 (CO); ^{1}H-NMR (DMSO-d_6) δ ppm: 11.74 (s, 1H, D_2O exchangeable, NH), 8.25 (s, 1 H, HC=N), 7.10 - 8.00 (m, 7H, Ar-H), 4.63 (s, 2H, SCH_2); ^{13}C NMR (DMSO-d_6) δ ppm: 167.9 (C=O), 165.3 (C-2'), 152.5 (-3a'), 142.4, 139.1, 134.8, 131.3, 130.7, 128.7, 127.8, 126.3, 124.4, 121.8 (*arom.* & HC=N), 35.8 (SCH_2). EI-MS *m/z* [relative intensity]: 333 [M^+, 12%], 259 [4%], 223 [3%], 208 [100%], 180 [71%]. Anal. Calcd. for $C_{14}H_{11}N_3OS_3$ (333.38): C, 50.43; H, 3.33; N, 12.60%. Found: C, 50.33; H, 3.27; N, 12.61%.

3.2.8. 2-(Benzo[*d*]thiazol-2'-ylthio)-*N*'-(acetyl)acetohydrazide (19)

A mixture of **3** (2.39 g 10.0 mmol) and triethyl orthoformate (1.6 g, 10.0 mmol) in acetic anhydride (20 mL) was refluxed for 2 h. The reaction was allowed to cool to room temperature, then poured in ice cold water. The solid product formed was collected by filtration and crystallized from ethanol as white crystals. Yield: 1.9 g (71%); mp 202˚C - 204˚C; FT-IR ν_{max} (cm^{-1}): 3205 (2NH), 1685, 1641 (2C=O amide);^{1}H-NMR (DMSO-d_6) δ ppm: 10.28 (s, 1H, NH, D_2O exchangeable), 9.99 (s, 1H, NH, D_2O exchangeable), 8.02 (d, *J* = 8 Hz, 1H, H-4'), 7.85 (d, *J* = 8 Hz, 1H, H-7'), 7.48 (t, *J* = 8 Hz, 1H, H-6'), 7.38 (t, *J* = 8Hz, 1H, H-5'), 4.23 (s, 2H, SCH_2), 1.92 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δC 167.9 (C=O), 165.9 (C=O), 165.4 (C-2'), 152.5 (C-3a'), 134.8 (C-7a'), 126.4 (C-6'), 124.6 (C-5'), 121.9 (C-4'), 121.2 (C-7'), 34.7 (SCH_2), 20.5 (CH_3). EI-MS *m/z* [relative intensity]: 281 [M^+, 12%], 236 [4%], 208 100%], 180 [37%]. Anal. Calcd. for $C_{11}H_{11}N_3O_2S_2$ (281.35): C, 46.96; H, 3.94; N, 14.93%. Found: C, 46.81; H, 3.95; N, 14.92%.

3.2.9. 2-(Benzo[*d*]thiazol-2'-ylthio-)-*N*'-(2-chloroacetyl)acetohydrazide (20)

A mixture **3** (2.39 g, 10.0 mmol) and chloroacetyl chloride (1.12 g, 10.0 mmol) in DMF (20 mL) was heated for

2 h. The mixture was allowed to cool to room temperature. The solid product formed was collected by Filtration and crystallized from ethanol as yellow crystals. Yield: 2.28 g (82%); mp 162˚C - 164˚C; FT-IR ν_{max} (cm^{-1}): 3174 (2NH), 1659 (2C=O amide); ^{1}H-NMR (DMSO-d_6) δ ppm: 10.56 (s, 1H, NH, D_2O exchangeable) 10.52 (s, 1H,NH, D_2O exchangeable), 8.03 - 7.35 (m, 4H, ArH), 4.52 (s, 2H, CH_2), 4.26 (s, 2H, CH_2); ^{13}C-NMR (DMSO-d_6) δC ppm: 165.7 (C=O), 165.3 (C=O), 162.3 (C-2'), 152.5 (C-3a'), 135.8 (C-7a'), 126.4 (C-6'), 124.6 (C-5'), 121.8 (C-4'), 121.2 (C-7'), 40.8 (CH_2Cl), 34.6 (SCH_2). EI-MS *m/z* [relative intensity]: 316 [M^+, 13%], 279 [2%], 241 [2%], 208 [100%]. Anal. Calcd. for $C_{11}H_{10}ClN_3O_2S_2$ (315.80): C, 41.84; H, 3.19; N, 13.31%. Found: C, 41.72; H, 3.23; N, 13.43%.

3.2.10. *N*'[-2-(Benzo[*d*]thiazol-2'-ylthio)acetyl]cinnamohydrazide (21)

A mixture of **3** (2.39 g 10.0 mmol) and cinnamoyl chloride (1.66 g, 10.0 mmol) in 1,4 dioxane (20 mL) containing a few drops of triethylamine was refluxed for 2 h .The solid product formed, was collected by filtration and crystallized from ethanol as white crystals. Yield: 2.80 g (76%); mp 164˚C - 166˚C; FT-IR ν_{max} (cm^{-1}): 3207 (2NH), 1672 (C=O), 1641 (CO-amide); ^{1}H-NMR (DMSO-d_6) δ_H: 10.60 (s, 1H,NH, D_2O exchangeable), 10.39 (s, 1H, NH, D_2O exchangeable), 8.03 (d, *J* = 8 Hz, 1H, H-4'), 7.87 (d, *J* = 8 Hz, 1H, H-7'), 7.88 - 7.37 (m, 8H, Ar-H & vinylic-H), 6.70 (d, 1H, *J* = 16, vinylic-H), 4.28 (s, 2H, SCH_2); ^{13}C-NMR (DMSO-d_6) δ_C ppm: 165.8 & 165.0 (2C=O), 163.3, 152.5, 140.3, 134.8, 134.5, 129.8, 129.0, 127.7, 126.4, 124.6, 121.8, 121.2, 119.2 (arom. carbons) 34.7 (CH_2). EI-MS *m/z* [relative intensity]: 369 [M^+, 7%], 208 [51%] 180 [9%], 148 [3%], 131 [100%]. Anal. Calcd. for $C_{18}H_{15}N_3O_2S_2$ (369.46): C, 58.52; H, 4.09; N, 11.37%. Found: C, 58.32; H, 4.09; N, 11.39%.

3.2.11. 5-[(Benzo[*d*]thiazol-2'-ylthio)methyl]-4-phenyl-2H-1,2,4-triazole-3(4*H*)-thione (22)

A mixture of **3** (2.39 g 10.0 mmol) and phenyl isothiocyanate (1.99 g, 10.0 mmol) in ethanol (20 mL) and sodium hydroxide solution (2 g in 20 mL water) was refluxed for 2 h. The reaction mixture was allowed to cool to room temperature then acidify with 10% HCl. The product formed was collected by filtration and crystallized from ethanol as yellow crystals. Yield: 2.99 g (84%); mp 140˚C - 142˚C; FT-IR ν_{max} (cm^{-1}): 3061(NH); ^{1}H-NMR (DMSO-d_6) δ_H ppm: 7.17 - 7.95 (m, 10H, ArH & NH), 4.54 (s, 2H, SCH_2). EI-MS [relative intensity]: 356 [M^+, 71%], 323 [8%] 265 [3%], 224 [7%].190 [12%]. *Anal*. Calcd. for $C_{16}H_{12}N_4S_3$ (356.46): C 53.91; H, 3.39; N, 15.72%. Found: C, 53.97; H, 3.46; N, 15.92%.

3.2.12. (*E*)-Dimethyl 2-[2-(-2(benzo[d]thiazol-2'-ylthio)acetyl)hydrazono] succinate (23)

Mixture of **3** (2.39 g, 10.0 mmol) and dimethylacetylene dicarboxylate (1.12 g, 10.0 mmol) in 1,4 dioxane (20 mL) containing a few drops of triethylamine was refluxed for 3 h. The mixture was allowed to cool to room temperature. The solid product formed, was collected by filtration and crystallized from methanol as pale yellow crystals. Yield: 2.85 g (75%); mp 147˚C - 148˚C; FT-IR ν_{max} (cm^{-1}): 3182 (NH), 1749,1710 (2C=O *ester*), 1683 (C=O amide); ^{1}H NMR (DMSO-d_6) δppm: 11.74 (s, 1H, NH, D_2O exchangeable), 7.98 (d, *J* = 8 Hz, 1H, H-4'), 7.84 (d, *J* = 8 Hz, 1H, H-7'), 7.45 (t, *J* = 8 Hz, 1H, H-6'), 7.35 (t, *J* = 8 Hz, 1H, H-5'), 4.71 (s, 2H, SCH_2), 3.83 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3); ^{13}C-NMR (DMSO-d_6) δ_C/ppm: 170.0 (amide C=O), 166.4 (ester C=O), 165.2 (ester C=O), 164.5 (C-2'), 152.9 (C-3a'), 136.3 (C=N), 135.2 (C-7a'), 126.8 (C-6'), 125.0 (C-5'), 122.3 (C-4'), 121.6 (C-7'), 53.1 (OCH_3), 52.6 (OCH_3), 35.8 (SCH_2), 32.6 ($COCH_2$). EI- MS *m/z* [relative intensity]: 381 [M^+, 10%], 323 [71%], 272 [2%], 250 [12%], 208 [41%]. Anal. Calcd. for $C_{15}H_{15}N_3O_5S_2$ (381.32): C, 47.23; H, 3.96; N, 11.02%. Found: C, 47.13; H, 3.85; N, 11.21%.

3.3. Single Crystal X-Ray Diffraction Studies

Crystal structure of compounds **6** [10], **10** [12], **13** [13], **15** [14] and **23** [16], as well as their packing pattern were successfully developed by single crystal X-ray diffraction analysis. The molecular structure information of all these molecules, obtained from the X-diffraction method is in perfect agreement with their predicted synthetic protocol and other characterization techniques like ^{1}HNMR and ^{13}C NMR and mass spectroscopy.

Table 6 summarizes the crystal nature, unit cell descriptions and crystallographic refinement parameters of all crystal samples studied in this work.

4. Conclusions

We have corrected the wrong literature structures formed from reactions 2-(benzo[*d*]thiazol-2'-ylthio) acetohy-

Table 6. Precise crystal data for **6**, **10**, **13**, **15** and **23**.

Compound	6	10	13	15	23
Crystal Dimension/mm	0.07 × 0.13 × 0.25	09 × 0.13 × 0.19	0.10 × 0.20 × 0.34	0.20 × 0.20 × 0.20	0.10 × 0.25 × 0.25
Crystal Color and Shape	Light colorless, block-like	Lightcolorless, block-like	Lightcolorless, block-like	Colorless, Prism	Colorless, block like
Formula weight	$C_{14}H_{15}N_3O_2S_2$	$C_{13}H_{13}N_3O_2S_2$	$C_{19}H_{15}N_3O_4S_2$	$C_{15}H_{17}N_3O_3S_2$	$C_{15}H_{15}N_3O_5S_2$
Crystal system	Triclinic	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	P-1	P 121/c 1	P-1	P-1	P-1
T/K	296	296	296	296	296
a/Å	7.8168 (5)	12.5590 (7)	7.5866 (6)	7.646 (2)	7.7601 (5)
b//Å	8.6997 (6)	29.3421 (17)	11.5021 (9)	10.020 (2)	10.5935 (6)
c/Å	11.6038 (7)	7.9023 (5)	11.7568 (9)	11.640 (2)	12.6829 (9)
α/deg	88.409 (3)	90	99.111 (2)	72.136 (5)	65.372 (5)
β/deg	73.837 (3)	93.870 (3)	106.564 (3)	77.211 (6)	72.296 (5)
γ/deg	82.013 (3)	90	102.689 (3)	78.761 (6)	78.930 (6)
V/Å^3	750.51 (8)	2905.4 (3)	932.16 (13)	820.0 (2)	900.3 (1)
Z	2	8	2	2	2
μ/mm^{-1}	3.287	3.371	2.874	3.421	3.240
ρ_{calcd}/g·cm^{-3}	1.422	1.405	1.473	1.423	1.403
$Theta_{max/deg}$	61.15	66.66	66.28	25.00	26.35
Reflections collected	3851	14154	11244	6464	8085
Unique reflections	2218	4962	3177	2870	3645
R_{int}	0.0170	0.0276	0.0353	0.0481	0.0244
R (I > 2σ)	0.0346	0.0425	0.0357	0.0664	0.0679
R (all data)	0.0355	0.0501	0.0361	0.1071	0.0972
R_w (all data)	0.1005	0.1392	0.0937	0.2302	0.2426
Peak max/e Å^{-3}	0.234	0.391	0.250	0.45	0.93

drazide (**3**) with acetyl acetone and phthalic anhydride. We have also reported that both compounds **3** and **5** were utilized as a key intermediate for the synthesis of a novel heterocyclic compounds. We also reported the synthesis of a novel series of condensation and substituted derivatives of 2-(benzo[*d*]thiazol-2'-ylthio) acetohydrazide in good yield. The structures of the newly synthesized compounds were confirmed by elemental analysis, ^{1}H-NMR, ^{13}C-NMR spectra, Ms, and X-ray crystallographic investigations.

Acknowledgements

This work financed by the University of Kuwait research grant SC10/13. We are grateful to the Faculty of Science, Chemistry Department, and the SAF facility for the spectral and analytical data (Project GS01/10, GS03/08, GS01/03, GS 01/05). The CCDC file numbers for all crystal data are given in the reference section.

Author Contributions

F.A. is the Principal Investigator, designed the research work, collected the analysis of the spectroscopic data and wrote the manuscript. A.A. is the research associate performed the work in the laboratory. All authors have

read and approved the final manuscript.

Conflicts of Interest

The authors declare, they have no conflict of interests regarding the publication.

References

[1] Mahran, M.A., El-Nassry, S.M.F., Allam, S.R. and El-zawawy, L.A. (2003) Synthesis of Some New Benzothiazole Derivatives as Potential Antimicrobial and Antiparasitic Agents. *Die Pharmazie*, **58**, 527-530.

[2] Wang, W., Zhang, G.-P., Song, B.-A., Wang, H., Jin, L.-H., Hu, D.-Y. and Yang, S. (2007) Synthesis and Anti-Tobacco Mosaic Virus Activity of O,O'-Dialkyl-α-(substituted benzothia-zol-2-yl)amino-(substituted phenylmethyl) Phosphonate. *Chinese Journal of Chemistry*, **26**, 279-284. http://sioc-journal.cn/Jwk_yjhx/EN/Y2007/V26/I02/279

[3] Kaur, H., Kaur, S., Singh, I., Saxena, K.K. and Kumar, A. (2010) Synthesis, Characterization and Biological Activity of Various Substituted Benzothiazole Derivatives. *Digest Journal of Nanomaterials and Biostructures*, **5**, 67-76.

[4] Wardakhan, W.W., El-Sayed, N.N. and Mohareb, R.M. (2013) Synthesis and Anti-Tumor Evaluation of Novel Hydrazide and Hydrazide-Hydrazone Derivatives. *Acta Pharmaceutica*, **63**, 45-57. http://dx.doi.org/10.2478/acph-2013-0004

[5] Mohareb, R.M., Fleita, D.H. and Sakka, O.K. (2011) Novel Synthesis of Hydrazide-Hydrazone Derivatives and Their Utilization in the Synthesis of Coumarin, Pyridine, Thiazole and Thiophene Derivatives with Antitumor Activity. *Molecules*, **16**, 16-27. http://dx.doi.org/10.3390/molecules16010016

[6] Al-Omran, F., Abou El-Khair A. (2013)Studies and X-rays Determinations with 2-(Acetonylthio)benzothiazole: Synthesis of 2-(Benzothiazol-2-ylthio)-1-phenylethanone and 2-(Acetonylthio)benzothiazole by C-S Bond Cleavage of 2-(Acetonylthio)benzothiazole in KOH. *Journal Heterocyclic Chemistry*, **51**, 62-70. http://dx.doi.org/10.1002/jhet.1693

[7] Al- Omran, F., Mohareb, R.M. and Abou El-khair, A. (2011) Synthesis and E/Z Configuration Determination of Novel Derivatives of 3-Aryl-2-(benzothiazol-2'-ylthio) acrylonitrile, 3-(Benzothiazol-2'-ylthio)-4-(furan-2"- yl)-3-buten-2-one and 2-(1-(Furan-2"-yl)-3'-oxobut-1"-en-2-ylthio)-3-phenylquinazolin-4(3H)-one. *Molecules*, **16**, 6129-6147. http://dx.doi.org/10.3390/molecules16076129

[8] Mohareb, R.M. and Al-Omran, F. (2012) Reaction of Pregnenolone with Cyanoacetylhydrazine. Novel Synthesis of Hydrazide-Hydazone, Pyrazole, Pyridine, Thiazole, Thiophene Derivatives and Their Cytotoxicity Evaluations. *Steroids*, **77**, 1551-1559. http://dx.doi.org/10.1016/j.steroids.2012.09.007

[9] AL-Saadi, M.A.E. and AL-Bayati, R.H.I. (2006) Synthesis and Characterization of Some New Derivatives of 2-Mercapto Benzothiazole and Evaluation Their Biological Activity. *National Journal of Chemistry* (*NJC*), **23**, 390-404.

[10] The CCDC File 1012540 Contains the Supplementary Crystallographic Data for Compounds **6** in This Paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk

[11] Liu, X.-H., Sun, Z.-H., Yang, M.-Y., Tan, C.-X., Weng, J.-Q., Zhang, Y.-G. and Ma, Y. (2014) Microwave Assistant One Pot Synthesis, Crystal Structure, Antifungal Activities and 3D-QSAR of Novel 1,2,4-Triazolo [4,3-a] pyridines. *Chemical Biology & Drug Design*, **84**, 342-347. http://dx.doi.org/10.1111/cbdd.12323

[12] The CCDC file 1012539 contains the supplementary crystallographic data for compounds **10** in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk

[13] The CCDC file 1012538 contains the supplementary crystallographic data for compound **13** in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk

[14] The CCDC file 1012541 contains the supplementary crystallographic data for compound **15** in this report. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk

[15] Sun, G.-X., Sun, Z.-H., Yang, M.-Y., Liu, X.-H., Ma, Y. and Wei, Y.-Y. (2013) Design, Synthesis, Biological Activities and 3D-QSAR of New *N*,*N*'-Diacylhydrazines Containing 2,4-Dichlorophenoxy Moieties. *Molecules*, **18**, 14876-14891. http://dx.doi.org/10.3390/molecules181214876

[16] The CCDC file 1032664 contains the supplementary crystallographic data for compound **23** in this report. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk