# Studies and X-ray 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

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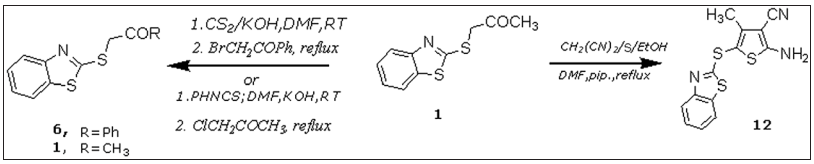


New route for the synthesis of 2-(benzothiazol-2-ylthio)-1-phenylethanone (**6**) and 2-(acetonylthio)benzothiazole (**1**) by using phenacyl bromide and α-chloroacetone, respectively, through carbon–sulfur bond cleavage reactions in a basic medium has been generated. Treatment of **1** with malononitrile and elemental sulfur afforded the corresponding derivative of 2-amino-3-cyanothiophene (**12**), whereas treatment of **1** with cyanoacetohydrazide afforded the corresponding derivative of cyanoacetylhydrazone derivative (**13**). The structure of the synthesis compounds has been established on the basis of elemental analyses, $^1$H-NMR, $^{13}$C-NMR, correlation spectroscopy, heteronuclear single quantum coherence, MS spectra, and X-ray crystallographic investigations.

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## INTRODUCTION

Benzothiazoles are bicycles ring system with varied biological activities and with greater scientific interest nowadays. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. The biological activities range from anti-microbial [1], anti-inflammatory [1], antibacterial [2], antitumor [3], and anticancer [4,5] to antifungal [6]. It is recently reported that 2-(benzothiazole −2-thio)-1-phenylethanone can be oxidized to β-keto-sulfones. The β-keto-sulfones can be used in the preparation of acetylene, allenes, chalcones, vinylsulfones, polyfunctionalized 4-H-pyrans, and ketones [7,8]. Encouraged by all these facts and in continuation of our research programmer dealing with synthesis of polyheterocyclic systems, particularly those containing S-acetyl incorporated with heteroaromatic [9–11], we decided to synthesize some novel substituted benzothiazole derivative in the hope of obtaining compounds that have biological and pharmacological applications.

## RESULTS AND DISCUSSION

Treatment of 2-(acetonylthio)benzothiazole (**1**) with an equimolar amount of carbon disulfide in solution DMF containing potassium hydroxide at room temperature and subsequent treatment of the reaction mixture with two molar amount of phenacylbromide afforded an orange crystal. We first thought that this orange crystal is alkylated 2,3-dithiothiophene **4**, by assuming the formation of non-isolated intermediate **2**, and subsequently, it reacted with two molar amount of phenacyl bromide, similar to the recent publication we reported [12]. However, the mass spectrum of the obtained product revealed a molecular ion peak ($M^+$) with *m/z* 285 and was compatible with the molecular formula $C_{15}H_{11}NS_2O$. Therefore, we considered the structure **6** for this reaction rather than the structure **4**. The isolated product was also conformed on the basis of elemental analysis and spectral data. The chemical shifts of the protons for the compound **6** were assigned using the correlation spectroscopy (COSY) measurement, which provided the proton–proton couplings. The $^1$H-NMR revealed, in addition to an aromatic multiple, a singlet signal integrated for two protons that appear at $\delta_H$ 5.00 ppm. Moreover, distrotionless enhancement by polarization transfer experiment shows seven signals arising from carbons in CH groups range between $\delta_C$ 121 and 133 ppm and point up words oppositely phased from those in $CH_2$ group. The signal from $CH_2$ group appears $\delta_C$ 40.97 ppm and points downwards. The chemical shifts of carbons for compound **6** were assigned using heteronuclear single quantum coherence (HSQC), and heteronuclear multiple bond coherence (HMBC) measurements (cf. Figures 1 and 2). The $^{13}$C-NMR spectrum for **6** is characterized by two signals at 192.9 and 41.0 ppm. The signal at δ 41.0 ppm was split into a triplet in the off-resonance spectrum, implying that the carbon atom bears two hydrogens.

The signal at highest frequency $\delta_C$ 192.86 ppm is assignable to the carbonyl carbon (cf. Figure 1). The structure of **6** was unambiguously confirmed by X-ray crystallography as

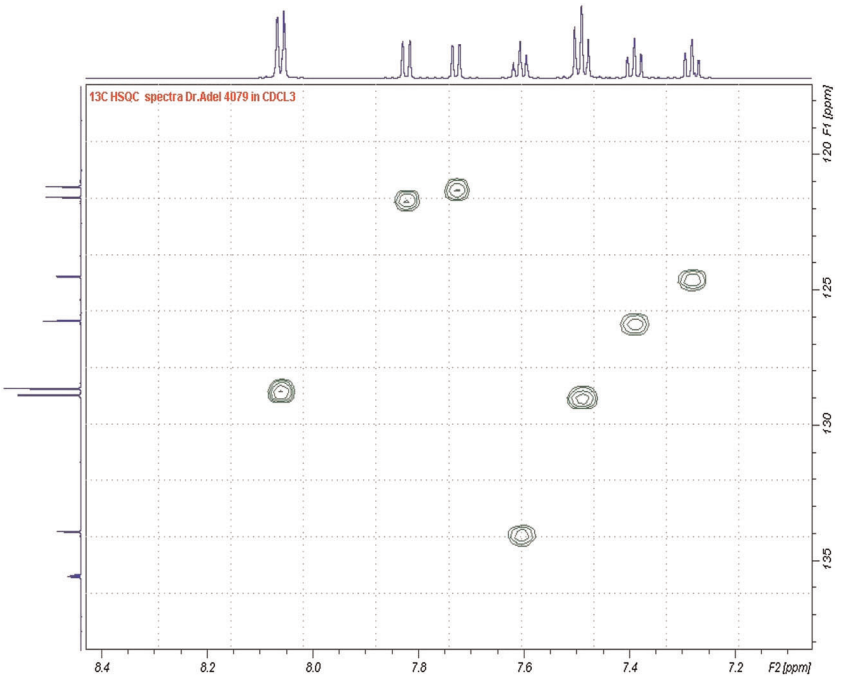



**Figure 1.** $^{13}$C-heteronuclear single quantum coherence (HSQC) spectra for the compound **6** in DMSO-$d_6$. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.

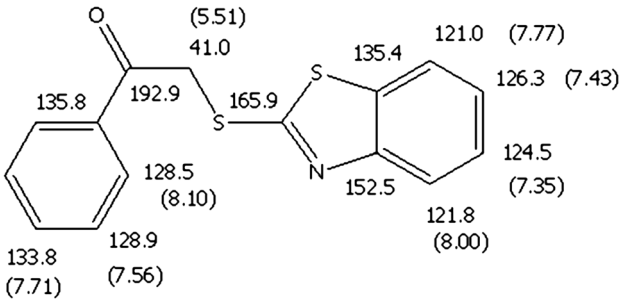



**Figure 2.** The complete assignment of $^{1}$H and $^{13}$C chemical shifts for **6** on the basis of the correlation spectroscopy, heteronuclear single quantum coherence, and heteronuclear multiple bond coherence experiments.

2-(benzothioazol-2-ylthio)-1-phenylethanone [22] (cf. Figure 3 and Tables 1–4). The conversion of 1-(benzothiazol-2′-ylthio) propan-2-one (**1**) to the corresponding 2-(benzothioazol-2-ylthio)-1-phenylethanone (**6**) is assumed to proceed *via* the carbon–sulfur bond cleavage under basic condition (potassium hydroxide) to give potassium benzothiazole-2-thiolet (**5**), which readily undergoes nucleophilic substitution reaction with phenacyl bromide to form **6** and potassium bromide. Several studies have pointed out that sulfide can readily undergo carbon–sulfur bonds cleaved and transformed to carbon–hydrogen bond under mildly basic condition [13–16]. The compound **6** could also be obtained *in situ via* a one-step process by heating of 2-mercaptobenzothiazole (**7**) with phenacyl bromide in acetone, and present anhydrous potassium carbonate afforded a product identical in all respects (mp and spectra) with that obtained previously from the reaction of **1** with phenacyl bromide (cf. Scheme 1).

Attempt to prepare compounds **8** and **9** by direct condensation of **6** with derivatives of nitrogen nucleophile

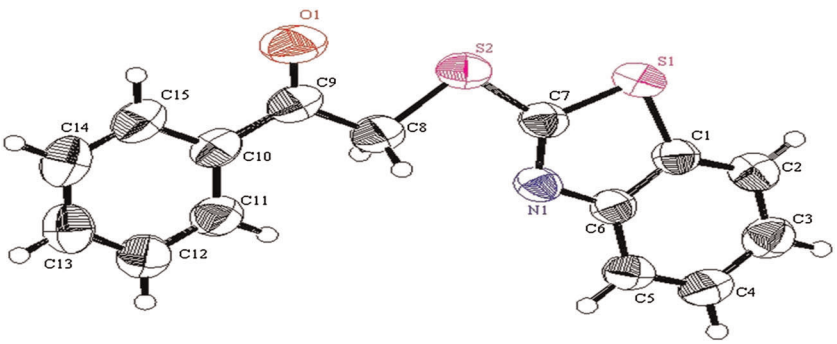



**Figure 3.** Perspective view and atom labeling of X-ray structure **6**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

**Table 1**

Bond lengths (Å) for compound **6**.

| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C1 | S1 | C7 | 88.97(13) | C7 | S2 | C8 | 98.31(13) |
| C6 | N1 | C7 | 110.2(2) | S1 | C1 | C2 | 129.7(2) |
| S1 | C1 | C6 | 109.4(2) | C2 | C1 | C6 | 121.0(3) |
| C1 | C2 | C3 | 118.4(3) | C2 | C3 | C4 | 120.7(3) |
| C3 | C4 | C5 | 121.2(3) | C4 | C5 | C6 | 119.2(3) |
| N1 | C6 | C1 | 115.4(3) | N1 | C6 | C5 | 125.2(3) |
| C1 | C6 | C5 | 119.5(3) | S1 | C7 | S2 | 117.72(14) |
| S1 | C7 | N1 | 116.1(2) | S2 | C7 | N1 | 126.1(2) |
| S2 | C8 | C9 | 110.2(2) | O1 | C9 | C8 | 120.1(3) |
| O1 | C9 | C10 | 121.5(3) | C8 | C9 | C10 | 118.4(3) |
| C9 | C10 | C11 | 122.3(3) | C9 | C10 | C15 | 119.5(3) |
| C11 | C10 | C15 | 118.2(3) | C10 | C11 | C12 | 121.0(3) |
| C11 | C12 | C13 | 119.5(3) | C12 | C13 | C14 | 120.4(4) |
| C13 | C14 | C15 | 120.5(4) | C10 | C15 | C14 | 120.4(3) |

**Table 2**

Bond lengths involving hydrogens (Å) compound **6**.

| Atom | Atom | Distance | Atom | Atom | Distance |
|---|---|---|---|---|---|
| C2 | H4 | 0.93 | C3 | H5 | 0.93 |
| C4 | H6 | 0.93 | C5 | H7 | 0.93 |
| C8 | H10A | 0.97 | C8 | H10B | 0.97 |
| C11 | H14 | 0.93 | C12 | H15 | 0.93 |
| C13 | H16 | 0.93 | C14 | H17 | 0.93 |
| C15 | H18 | 0.93 | | | |

or with carbon nucleophile in refluxing ethanol and the presence of a catalytic amount of piperidine for 3 h failed. The result supports the assumption that carbonyl carbon group in −2-(benzothioazol-2-ylthio)-1-phenylethanone (**6**) is not a reactive group because it is conjugated with the phenyl group (cf. Scheme 2).

On the other hand, treatment at room temperature of 1-(benzothiazol-2′-ylthio)propanone **1** with phenyl isothiocyanate in *N*,*N*-dimethylformamide (DMF) containing potassium hydroxide and then subsequent treatment of the reaction mixture with an equimolar amount of α-chloroacetone, under refluxed for 3 h, afforded golden brown crystals. We first thought that this product is the thiophene derivative **11**, which assumed to proceed *via* formation of non-isolable intermediate potassium salt **10**, and then undergoes nucleophilic substitution reaction with α-chloroacetone. However, the mass spectrum of the new product revealed a molecular ion peak ($M^+$) with *m/z* 223 and was compatible with the molecular formula $C_{10}H_9NS_2O$. Therefore, we considered the structure **1** for this reaction rather than the structure **11**. The structure of isolated product **1** was confirmed on the basis of elemental analysis and spectral data. The chemical shifts of protons for **1** were assigned using the COSY measurement, which provided the proton–proton couplings. The $^1$H-NMR revealed, in addition to an aromatic multiplet, two singlet signals for methyl and methylene protons that appear, respectively, at $\delta_H$ 2.30 and 4.48 ppm. Moreover, the chemical shifts of

**Table 3**

Bond angles (°) compound **6**.

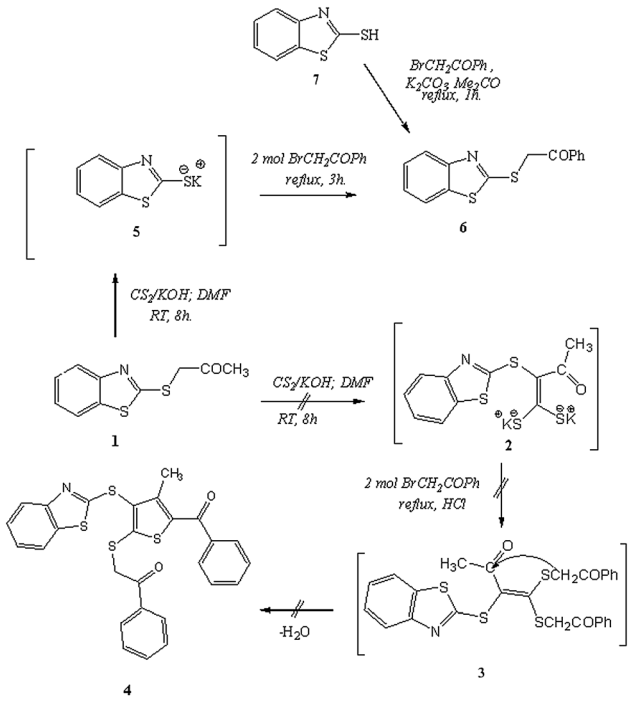
| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C1 | S1 | C7 | 88.97(13) | C7 | S2 | C8 | 98.31(13) |
| C6 | N1 | C7 | 110.2(2) | S1 | C1 | C2 | 129.7(2) |
| S1 | C1 | C6 | 109.4(2) | C2 | C1 | C6 | 121.0(3) |
| C1 | C2 | C3 | 118.4(3) | C2 | C3 | C4 | 120.7(3) |
| C3 | C4 | C5 | 121.2(3) | C4 | C5 | C6 | 119.2(3) |
| N1 | C6 | C1 | 115.4(3) | N1 | C6 | C5 | 125.2(3) |
| C1 | C6 | C5 | 119.5(3) | S1 | C7 | S2 | 17.72(14) |
| S1 | C7 | N1 | 116.1(2) | S2 | C7 | N1 | 126.1(2) |
| S2 | C8 | C9 | 110.2(2) | O1 | C9 | C8 | 120.1(3) |
| O1 | C9 | C10 | 121.5(3) | C8 | C9 | C10 | 118.4(3) |
| C9 | C10 | C11 | 122.3(3) | C9 | C10 | C15 | 119.5(3) |
| C11 | C10 | C15 | 118.2(3) | C10 | C11 | C12 | 121.0(3) |
| C11 | C12 | C13 | 119.5(3) | C12 | C13 | C14 | 120.4(4) |
| C13 | C14 | C15 | 120.5(4) | C10 | C15 | C14 | 120.4(3) |

**Table 4**

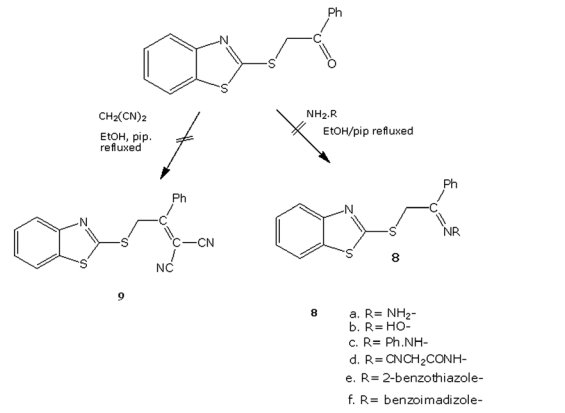
Bond angles involving hydrogens (°) compound **6**.

| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C1 | C2 | H4 | 120.8 | C3 | C2 | H4 | 120.8 |
| C2 | C3 | H5 | 119.7 | C4 | C3 | H5 | 119.7 |
| C3 | C4 | H6 | 119.4 | C5 | C4 | H6 | 119.4 |
| C4 | C5 | H7 | 120.4 | C6 | C5 | H7 | 120.4 |
| S2 | C8 | H10A | 109.6 | S2 | C8 | H10B | 109.6 |
| C9 | C8 | H10A | 109.6 | C9 | C8 | H10B | 109.6 |
| H10A | C8 | H10B | 108.1 | C10 | C11 | H14 | 119.5 |
| C12 | C11 | H14 | 119.5 | C11 | C12 | H15 | 120.3 |
| C13 | C12 | H15 | 120.3 | C12 | C13 | H16 | 119.8 |
| C14 | C13 | H16 | 119.8 | C13 | C14 | H17 | 119.7 |
| C15 | C14 | H17 | 119.7 | C10 | C15 | H18 | 119.8 |
| C14 | C15 | H18 | 119.8 | | | | |

**Scheme 1**




**Scheme 2**




carbons for compound **1** were assigned using HSQC and HMBC measurements (cf. Figures 4 and 5). The $^{13}$C-NMR spectrum for **1** is characterized by three signals at $\delta_C$ 201.6, 43.4, and $\delta_C$ 28.9 ppm for the ketone carbonyl carbon, methylene, and methyl groups. The structure of **1** was also confirmed by X-ray crystallography [17] (cf. Figure 6). The formation of the 1-(benzothiazol-2′-ylthio)propanone (**1**) from the previous reaction is assumed to proceed *via* the carbon–sulfur bond cleavage under basic condition (potassium hydroxide) to give potassium benzothiazole −2-thiolet (**5**), which readily undergoes nucleophilic substitution reaction with α-chloroacetone to form **1**.

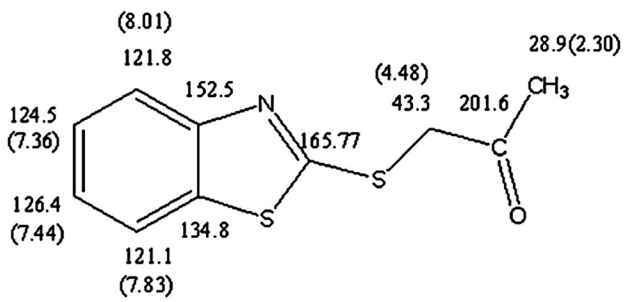



**Figure 4.** The complete assignment of $^{1}$H and $^{13}$C chemical shifts for 1 based on the correlation spectroscopy, heteronuclear single quantum coherence, and heteronuclear multiple bond coherence experiments.

The compound **1** can also be obtained *in situ*, *via* a one-step process by treatment of 2-mercaptobenzothiazole (**7**) with α-chloroacetone in refluxing acetone containing potassium carbonate and on the other hand, treatment of **1** with malononitrile in the refluxing dioxane containing a catalytic amount of acetic acid to afford 2-mercaptobenzothiazole (**7**). The structure of **7** was also confirmed by X-ray crystallography [23] (cf. Figure 7 and Tables 5–8).

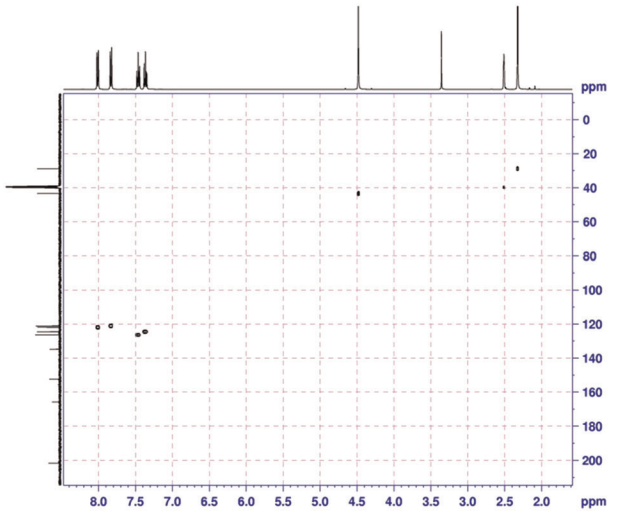



**Figure 5.** $^{13}$C-heteronuclear single quantum coherence spectra for the compound **1** in DMSO-$d_6$.

**Table 5**

Bond lengths (Å) compound **7**.

| Atom | Atom | Distance | Atom | Atom | Distance |
|---|---|---|---|---|---|
| S1 | C1 | 1.7446(16) | S1 | C7 | 1.7410(16) |
| S2 | C7 | 1.6644(17) | N1 | C6 | 1.392(2) |
| N1 | C7 | 1.340(2) | C1 | C2 | 1.386(3) |
| C1 | C6 | 1.393(2) | C2 | C3 | 1.375(3) |
| C3 | C4 | 1.391(3) | C4 | C5 | 1.377(3) |
| C5 | C6 | 1.386(3) | | | |

**Table 6**

Bond lengths involving hydrogens (Å) compound **7**.

| Atom | Atom | Distance | Atom | Atom | Distance |
|---|---|---|---|---|---|
| N1 | H1 | 0.860 | C2 | H2 | 0.930 |
| C3 | H3 | 0.930 | C4 | H4 | 0.930 |
| C5 | H5 | 0.930 | | | |

In continuation of our efforts to generate new synthetic routes to different polyfunctional thiophenes [9,11,12,17–19], we also used Gewald's reaction[20] for the synthesis of 2-amino −5-(benzothiazol-2′-thio) 4-methylthiophene-3-carbonitrile **12**. The compound **12** is obtained *in situ via* a one-step process by treatment of 2-(acetonylthio) benzothiazole **1** with malononitrile in refluxing ethanol and *N*,*N*-DMF containing an elemental sulfur and a catalytic amount of triethyl amine. The structure of **12** was established on the basis of its elemental analysis and spectral data. The mass spectrum of **12** revealed a molecular ion peak *m/z* at 303. However, the presence of the methyl singlet at $\delta_H$ 2.31 in the $^1$H-NMR spectrum indicates that methylene carbon in S-alkylated **1** is involved in the reaction. Moreover, the IR spectrum of the compound **12** showed strong absorption bands at $\nu_{max}$ 2200 and 3359–3424 cm$^{-1}$ corresponding to nitrile and amino groups, respectively. The absence of the carbonyl group absorption, in the IR spectrum, indicates that the carbonyl group is involved in the reaction (cf. Scheme 3).

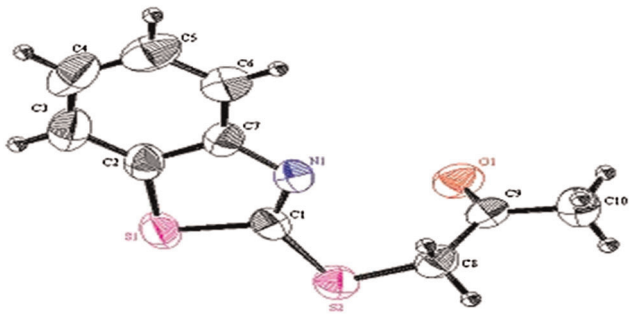



**Figure 6.** Perspective view and atom labeling of X-ray structure **1**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

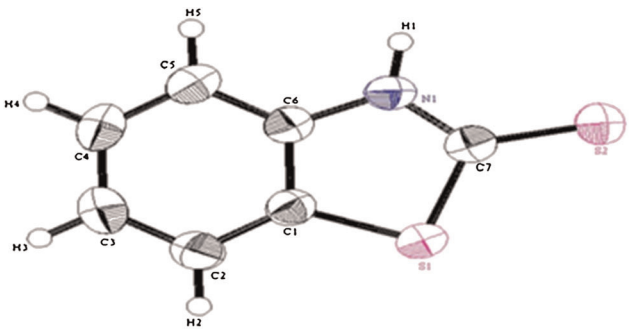



**Figure 7.** Perspective view and atom labeling of X-ray structure **7**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Furthermore, treatment of 1-(benzothiazol-2′-ylthio)propanone (**1**) with cyanoacetohydrazide in 1,4-dioxane at reflux temperature afforded the corresponding 1-(benzothiazol-2′-ylthio)propanone cyanoacetyl hydrazone **13**[20]. The structure of **13** was established on the basis of its elemental analysis and spectral data. The IR spectrum of the isolated product showed an amino, nitrile, and carbonyl absorption bands at 3232, 2264, and 1697 cm$^{-1}$, respectively. The mass spectrum of **13** revealed a molecular ion peak (M+) with *m/z* 304. The chemical shifts of protons for **13** were assigned using the COSY measurement, which provided the proton–proton couplings. The $^1$H-NMR revealed, in addition to an aromatic multiplet, three singlet signals for methyl and two methylene protons that appear at $\delta_H$ 2.04, 4.04, and 4.25 ppm, respectively. Moreover, the chemical shifts of carbons for compound **13** were assigned using HSQC and HMBC measurements. The $^{13}$C-NMR spectrum for **13** is characterized by two signals at $\delta_c$ 165.9 and 115.9 ppm for carbonyl carbon and cyano groups (cf. Experimental section).the structure of **13** was

**Table 7**

Bond angles (°) compound **7**.

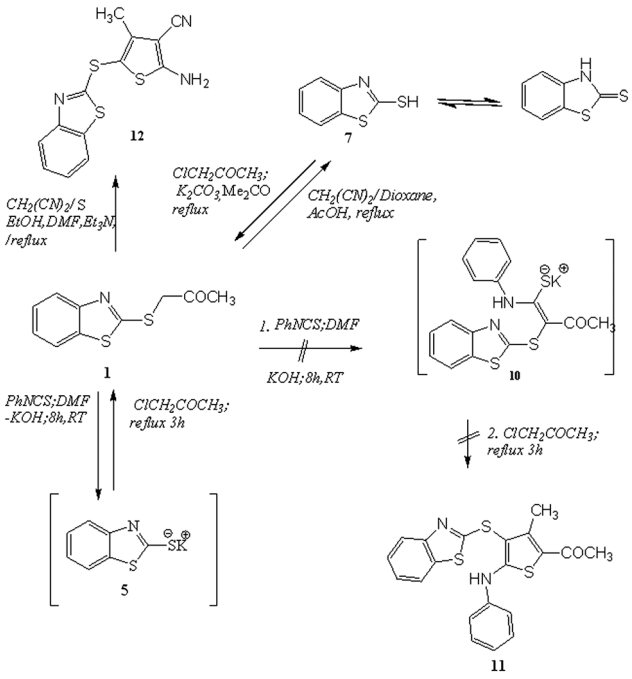
| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C1 | C7 | C7 | 92.30(8) | C6 | N1 | C7 | 116.79(13) |
| S1 | C1 | C2 | 129.42(12) | S1 | C1 | C6 | 109.80(12 |
| C2 | C1 | C6 | 120.77(15) | C1 | C2 | C3 | 118.30(16) |
| C2 | C3 | C4 | 120.69(18) | C3 | C4 | C5 | 121.59(16) |
| C4 | C5 | C6 | 117.72(16) | N1 | C6 | C1 | 111.75(13) |
| N1 | C6 | C5 | 127.33(15) | C1 | C6 | C1 | 120.91(16) |
| S1 | C7 | S2 | 123.03(9) | S1 | C7 | N1 | 109.34(12) |
| S2 | C7 | N1 | 127.63(12) | | | | |

**Table 8**

Bond angles involving hydrogens (°) compound **7**.

| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C6 | N1 | H1 | 121.6 | C7 | N1 | H1 | 121.6 |
| C1 | C2 | H2 | 120.8 | C3 | C2 | H2 | 120.9 |
| C2 | C3 | H3 | 119.7 | C4 | C3 | H3 | 119.7 |
| C3 | C4 | H4 | 119.2 | C5 | C4 | H4 | 119.2 |
| C4 | C5 | H5 | 121.1 | C6 | C5 | H5 | 121.1 |

**Scheme 3**




unambiguously confirmed by X-ray crystallography [24] (cf. Figure 8 and Tables 9–12; Scheme 4).

## EXPERIMENTAL

All melting points are reported uncorrected. The IR spectra were recorded on a Jasco FT/IR-6300 (Italy) using KBr disks. $^1$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker DPX 400 MHz and Bruker AVANCE II 600 MHz (Switzerland), spectrometers in DMSO-$d_6$ or $CDCl_3$ as solvent using TMS as an internal standard. The methods used for the purpose of NMR assignment were COSY, HSQC, and HMBC. The chemical shifts are reported as δ unit in (ppm) and TMS = 0.00 ppm. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiple, and br. = broad. Mass spectra were measured on GC/MS DFS, THERMO instrument. Microanalyses were performed on a CHNS-Vario Micro Cube analyzer. The single crystal X-ray crystallography was performed using a RIGAKU RAPID II located at the Chemistry Department of Kuwait University. Abbreviations are as follows: $Me_2CO$ = acetone, EtOH = ethanol, $Et_3N$ = triethylamine, DMF = *N*, *N*-dimethylformamide, $DMSO_4$-$d_6$ = dimethyl-$d_6$-sulfoxide. Compound **1** was prepared according to our recent reference [9], and its X-ray data were reported in reference [17].

**2-(benzothiazol-2′-ylthio)-1-phenylethanone (6)**

***Method A.*** A mixture of **1** (2.23 g, 10 mmoles), carbon disulfide (0.76 g, 10 mmoles), and potassium hydroxide (0.56 g, 10 mmoles) in DMF (20 mL) was stirred at room temperature for 10 h. To a stirred solution, phenacyl bromide (3.98 g, 20 mmoles) was added, then refluxed for 6 h. The reaction mixture was allowed to cool at room temperature and then poured onto a beaker containing an ice/water. The mixture was neutralized with HCl (10%). The solid product, so formed, was collected by filtration and crystallized from EtOH/DMF (2:1, v/v) as orange crystals, 2.63 g (93%).

***Method B.*** A mixture of **7** (1.67 g, 10 mmoles), phenacyl bromide (1.99 g, 10 mmoles), and anhydrous potassium carbonate (1.38 g, 10 mmoles) in $Me_2CO$ (100 mL) were refluxed in water bath for 3 h. The solvent was then evaporated under reduced pressure. The solid product, so formed, was collected by filtration and crystallized from EtOH as white crystals, 2.56 g, (90%), mp 110–112 C. IR: $\nu_{max}$ 1681 $cm^{-1}$ (CO); $^1$H-NMR (DMSO-$d_6$): $\delta_H$ 5.51 (s, 2H, $CH_2$), 7.35 (t, 1H, $J$ = 8.0 Hz, H-5′), 7.43 (t, 1H, $J$ = 8.0 Hz, H-6′), 7.56 (t, 2H, $J$ = 8.0 Hz, H-3), 7.71(t, 1H, $J$ = 7.6 Hz, H-4), 7.77 (d, 1H, $J$ = 8.0 Hz, H-7′), 8.00 (d, 1H, $J$ = 8.0 Hz, H-4′), 8.10 (d, 1H, $J$ = 8.0 Hz, H-2) ppm; $^{13}$C NMR(DMSO-*d*6): $\delta_C$ 192.9 (CO),165.9 (C-2′), 152.5 (C-3a′), 135.8(C-1), 135.4 (C-7a′),133.8 (C-4), 128.9 (C-3), 128.5 (C-2), 126.3 (C-6′), 124.5 (C-5′), 121.8 (C-4′), 121.0 (C-7′), 41.0 (CH2) ppm; ms: *m/z* 285[M]. *Anal.* Calcd. for $C_{15}H_{11}NS_2O$ (285.37): C, 63.11; H, 3.88; N, 4.90. Found: C, 63.30; H, 3.97; N, 5.11.

**2-Mercaptobenazothiazole (7).** A mixture of **1** (2.23 g, 10 mmoles) and malononitrile (0.66 g, 10 mmoles) in dioxane (20 mL) and acetic acid (1 mL) was refluxed for 3 h. The reaction mixture was allowed to cool at room temperature. The solid product, so formed, was collected by filtration and crystallized from EtOH as yellow crystals,1.3 g (78%), mp 178–180°C, (lit

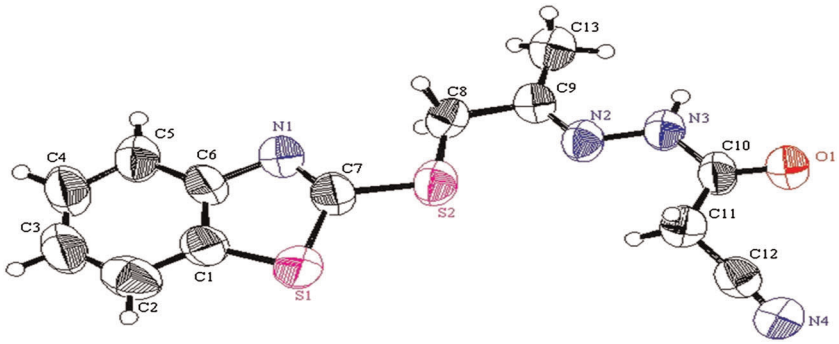



**Figure 8.** Perspective view and atom labeling of X-ray structure **13**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

**Table 9**

Bond length (Å) for compound **13**.

| Atom | Atom | Distance | Atom | Atom | Distance |
|---|---|---|---|---|---|
| S1 | C1 | 1.718 (11) | S1 | C7 | 1.774 (10) |
| S2 | C7 | 1.743 (12) | S2 | C8 | 1.788 (10) |
| O1 | C10 | 1.213 (15) | N1 | C6 | 1.409 (15) |
| N1 | C7 | 1.285 (14) | N2 | N3 | 1.406 (13) |
| N2 | C9 | 1.282 (13) | N3 | C10 | 1.354 (13) |
| N4 | C12 | 1.123 (16) | C1 | C2 | 1.415 (18) |
| C1 | C6 | 1.410(13) | C2 | C3 | 1.38 (3) |
| C3 | C4 | 1.347 (18) | C4 | C5 | 1.366(19) |
| C5 | C6 | 1.367 (17) | C8 | C9 | 1.519 (17) |
| C9 | C13 | 1.460 (14) | C10 | C11 | 1.502 (14) |
| C11 | C12 | 1.444 (16) | | | |

**Table 10**

Bond lengths (Å) for compound **13**.

| Atom | Atom | Distance | Atom | Atom | Distance |
|---|---|---|---|---|---|
| N3 | H3 | 0.86 | C2 | H2 | 0.93 |
| C3 | H3A | 0.93 | C4 | H4 | 0.93 |
| C5 | H5 | 0.93 | C8 | H8A | 0.97 |
| C8 | H8B | 0.97 | C11 | H11A | 0.97 |
| C11 | H11B | 0.97 | C13 | H13A | 0.96 |
| C13 | H13B | 0.96 | C13 | H13C | 0.96 |

[21] mp 180°C; IR: $\nu_{max}$ 3437 $cm^{-1}$ (NH); $^1$H-NMR (DMSO-$d_6$): $\delta_H$, 7.28 (d, 1H, $J$ = 8.0 Hz, H-5), 7.31 (d, 1H, $J$ = 8.0 Hz, H-6), 7.41(d, 1H, $J$ = 8.0 Hz, H-7)), 7.69 (d, 1H, $J$ = 8.0 Hz, H-4), 13.8 (bs., 1H, SH, $D_2O$ exchangeable) ppm; $^{13}$C NMR(DMSO-$d_6$): $\delta_C$ 189.8 (C-2), 141.2 (C-3a), 129.3 (C-7a), 127.1 (C-6), 124.2 (C-5), 121.7 (C-4), 112.4 (C-7) ppm; ms: *m/z* 167 [$M^+$]. *Anal*. Calcd. for $C_7H_5NS_2$ (167.25): C, 50.27; H, 3.01; N, 8.37. Found: C, 50.33; H, 3.02; N, 8.72.

**Reaction of 1 with phenyl isothiocyanate and KOH**

***Method A.*** A mixture of **1** (2.23 g, 10 mmoles), phenyl isothiocyanate (1.35 g 10 mmoles), and potassium hydroxide (0.56 g, 10 mmoles) in DMF (20 mL) was stirred at room temperature for 8 h. To a stirred solution, chloroacetone (7.9 g, 10 mmoles) was added and refluxed for 3 h. The reaction mixture was allowed to cool at room temperature, then poured into ice-cold water and neutralized with HCl (10%). The solid product, so formed, was collected by filtration and crystallized from a mixture of DMF: EtOH (2:1,v/v) as golden brown crystals, 1.67 g (75%).

***Method B.*** A mixture **7** (1.67 g, 10 mmoles), α-chloroacetone (7.9 g, 10 mmoles), and anhydrous potassium carbonate (1.38 g, 10 mmoles) in $Me_2CO$ (100 mL) was refluxed in water bath for 3 h. The solvent was then evaporated under reduced pressure. The solid product, so formed, was collected by filtration and crystallized from EtOH as white crystals of 1-(benzothiazol-2-ylthio)propanone (**1**), 1.47 g, (66%), mp 67–68°C, (lit [21] mp 67°C; IR: $_{vmax}$ 1721 $cm^{-1}$ (keto CO); $^1$H-NMR (DMSO-$d_6$): $\delta_H$ 2.30 (1H, 3H, $CH_3$), 4.48 (s, 2H, $CH_2$), 7.36 (t, 1H, $J$ = 8.0 Hz, H-5), 7.44 (t, 1H, $J$ = 8.0 Hz, H-6), 7.83 (d, 1H, $J$ = 8.0 Hz, H-7), 8.01 (d, 1H, $J$ = 8.0 Hz, H-4) ppm; $^{13}$C NMR (DMSO-$d_6$): $\delta_C$ 201.6 (CO),165.9 (C-2), 152.5 (C-3a), 134.8 (C-7a), 126.4 (C-6), 124.5 (C-5), 121.8 (C-4), 121.1 (C-7), 43.3 ($CH_2$), 28.9 ($CH_3$) ppm; ms: *m/z* 223 [$M^+$]. *Anal*. Calcd. for $C_{10}H_9NS_2O$ (223.31): C, 53.87; H, 4.06; N, 6.27. Found: C, 53.97; H, 3.97; N, 6.38.

**2-Amino-5-(benzothiazol-2′-yl thio)-4-methylthiophene-3-carbonitrile (12).** A mixture of **1** (2.23 g, 10 mmoles), malononitrile (0.66 g,10 mmoles) and elemental sulfur (0.32 g, 10 mmoles) in DMF: EtOH (2:1, v/v) containing $Et_3N$, (1 mL) was refluxed for 3 h. The reaction mixture was left to cool at room temperature. The solid product, so formed, was collected by filtration and crystallized from EtOH as brown crystals, 2.5 g (83%); mp 158-160°C. IR: $\nu_{max}$ 3359–3424 ($NH_2$), 2200 (CN) $cm^{-1}$; $^1$H-NMR (DMSO-$d_6$): $\delta_H$ 2.31 (s, 3H, $CH_3$), 7.22–7.93 (m, 4H, aromatic protons), 13.75 (bs., 2H, $NH_2$, $D_2O$ exchangeable) ppm; $^{13}$C NMR (DMSO-$d_6$): δ 31.2 ($CH_3$), 109.3, 112.9, 116.1, 122.1, 124.6, 127.5, 129.8, 141.1, 141.7, 142.3, 147.6, 158.1 (aromatic carbons and CN), ppm; ms *m/z* 303 [$M^+$]. *Anal*. Calcd. for $C_{13}H_9N_3S_3$ (303.42): C, 51.46; H, 2.99; N, 13.84. Found: C, 51.50; H, 2.91; N, 13.82.

**2-(benzothiazol-2-yl-thio)propanone cyanoacetyl hydrazone (13).** A mixture of **1** (2.23 g, 10 mmoles) and cyanoacetohydrazide (0.99 g, 10 mmoles) in 1,4-dioxane (20 mL) was refluxed for 3 h. The reaction mixture was left to cool at room temperature for 24 h. The solid product, so formed, was collected by filtration and crystallized from mixture of EtOH: dioxane (2:1, v/v) as yellow crystals, 2.67 g (78.8%), mp 177–179.IR: $\nu_{max}$ 3232 (NH), 2264 (CN), 1696 (C═O) $cm^{-1}$; $^1$H-NMR (DMSO-$d_6$): $\delta_H$ 2.04 (s, 3H,$CH_3$),4.04 (s,2H,$COCH_2$) 4.25 (s,2H,$SCH_2$), 7.38 (t, 1H, $J$ = 8.0 Hz, H-5), 7.48 (t, 1H, $J$ = 8. Hz, H-6), 7.87 (d, 1H, $J$ = 8.0 Hz, H-7), 8.00 (d, 1H, $J$ = 8.0 Hz, H-4), 10.98 (bs., 1H, NH, D2O exchangeable) ppm; $^{13}$C NMR (DMSO-$d_6$): $\delta_C$ 165.3 and 165.9 (C-2 and C═O),159.1 (C═N), 152.2 (C-3a),

**Table 11**

Bond angles (°) for compound **13**.

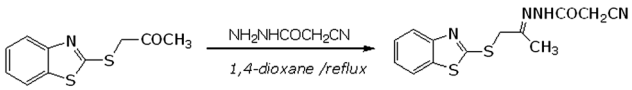
| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| C1 | S1 | C7 | 88.5 (5) | C7 | S2 | C8 | 98.9 (5) |
| C6 | N1 | C7 | 109.5 (8) | N3 | N2 | C9 | 116.3 (8) |
| N2 | N3 | C10 | 118.6 (8) | S1 | C1 | C2 | 130.5 (8) |
| S1 | C1 | C6 | 110.0 (8) | C2 | C1 | C6 | 119.4 (10) |
| C1 | C2 | C3 | 118.3 (11) | C2 | C3 | C4 | 120.9 (14) |
| C3 | C4 | C5 | 122.0 (13) | C4 | C5 | C6 | 119.8 (10) |
| N1 | C6 | C1 | 115.1 (10) | N1 | C6 | C5 | 125.3 (9) |
| C1 | C6 | C5 | 119.6 (10) | S1 | C7 | S2 | 115.1 (6) |
| S1 | C7 | N1 | 116.8 (9) | S2 | C7 | N1 | 128.1 (8) |
| S2 | C8 | C9 | 111.6 (8) | N2 | C9 | C8 | 114.1 (9) |
| N2 | C9 | C13 | 128.9 (11) | C8 | C9 | C13 | 117.0 (10) |
| O1 | C10 | N3 | 120.0 (9) | O1 | C10 | C11 | 124.4 (10) |
| N3 | C10 | C11 | 115.6 (10) | C10 | C11 | C12 | 111.3 (10) |
| N4 | C12 | C11 | 177.7 (11) | | | | |

**Table 12**

Bond angles involving hydrogens (°) for compound **13**.

| Atom | Atom | Atom | Angle | Atom | Atom | Atom | Angle |
|---|---|---|---|---|---|---|---|
| N2 | N3 | H3 | 120.7 | C10 | N3 | H3 | 120.7 |
| C1 | C2 | H2 | 120.9 | C3 | C2 | H2 | 120.9 |
| C2 | C3 | H3A | 119.5 | C4 | C3 | H3A | 119.5 |
| C3 | C4 | H4 | 119 | C5 | C4 | H4 | 119 |
| C4 | C5 | H5 | 120.1 | C6 | C5 | H5 | 120.1 |
| S2 | C8 | H8A | 109.3 | S2 | C8 | H8B | 109.3 |
| C9 | C8 | H8A | 109.3 | C9 | C8 | H8B | 109.3 |
| H8A | C8 | H8B | 108 | C10 | C11 | H11A | 109.4 |
| C10 | C11 | H11B | 109.4 | C12 | C11 | H11A | 109.4 |
| C12 | C11 | H11B | 109.4 | H11A | C11 | H11B | 108 |
| C9 | C13 | H13A | 109.5 | C9 | C13 | H13B | 109.5 |
| C9 | C13 | H13C | 109.5 | H13A | C13 | H13B | 109.5 |
| H13A | C13 | H13C | 109.5 | H13B | C13 | H13C | 109.5 |

**Scheme 4**




1 13

134.8 (C-7a), 126.4 (C-6), 124.6 (C-5), 121.9 (C-4), 121.1 (C-7), 115.9 (CN),40.1 ($SCH_2$–), 24.3 ($COCH_2$–), 15.5 ($CH_3$) ppm; ms: *m/z* 304 [M+]. *Anal*. Calcd. for $C_{13}H_{12}N4S_2O$ (304.39): C, 51.29; H, 3.97; N, 18.40. Found: C, 51.22; H, 3.97; N, 18.10.

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[22] CCDC 859123 contains the supplementary crystallographic data for compound **6** in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk.

[23] CCDC 859125 contains the supplementary crystallographic data for compound **7** in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk.

[24] CCDC 859124 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.