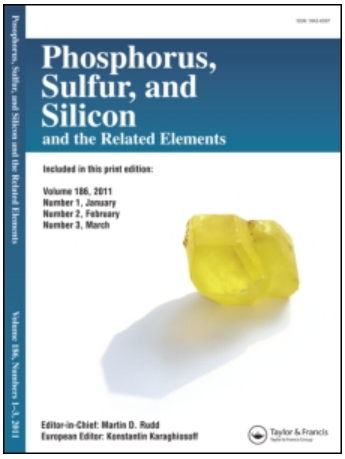


## Phosphorus, Sulfur, and Silicon and the Related Elements

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# Uses of 5,5-Dimethyl-7-oxocyclohexeno[b]thiophene Derivatives in Heterocyclic Synthesis

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# Uses of 5,5-Dimethyl-7-oxocyclohexeno[b]thiophene Derivatives in Heterocyclic Synthesis

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*The reaction of dimedone (**1**) with sulfur and the cyanomethylene reagents gave the cyclohexeno[b]thiophene derivatives. The reactivity of the latter products towards some chemical reagents was studied to give annulated derivatives. Their toxicity also was studied.*

**Keywords** cyanomethylene; pyrazole; thiazole; thiophene

## INTRODUCTION

During recent years, we have maintained a comprehensive program aimed at investigating the reaction of 4,5,6,7-tetrahydrobenzo-[*b*]thiophene derivatives with active methylene reagents to form fused hetrocyclic compounds. Such a synthetic route has proven to be easy and facile and is the sole approach for the synthesis of unreported derivatives of polyfunctionally substituted thiophenes, 2,3-dihydrothiazoles and thiazolidine.[1] The importance of such compounds is due to their diverse pharmacological activities including antibacterial,[2] immunomodulatory,[3] antiflammatory,[4] antidiabatic,[5,6] antiplatelet-activating factor,[7] and antiviral activities.[8,9]

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## RESULTS AND DISCUSSION

In continuation of our previous work, we wish to report on the scope and applicability of the 2-amino-5,5-dimethyl-7-oxotetrahydrobenzo-[*b*]thiophenes **3a,b**, which were synthesized according to the literature procedure,[10,11] through the reaction of dimedone (**1**) with either malononitrile (**2a**) or ethyl cyanoacetate (**2b**) and sulfur for the synthesis of annulated thiophene derivatives with potential pharmaceutical interest. The reaction of **3a**,**b** with benzaldehyde (**4**) in the presence of piperidine gave the schiff's bases **5a**,**b**.

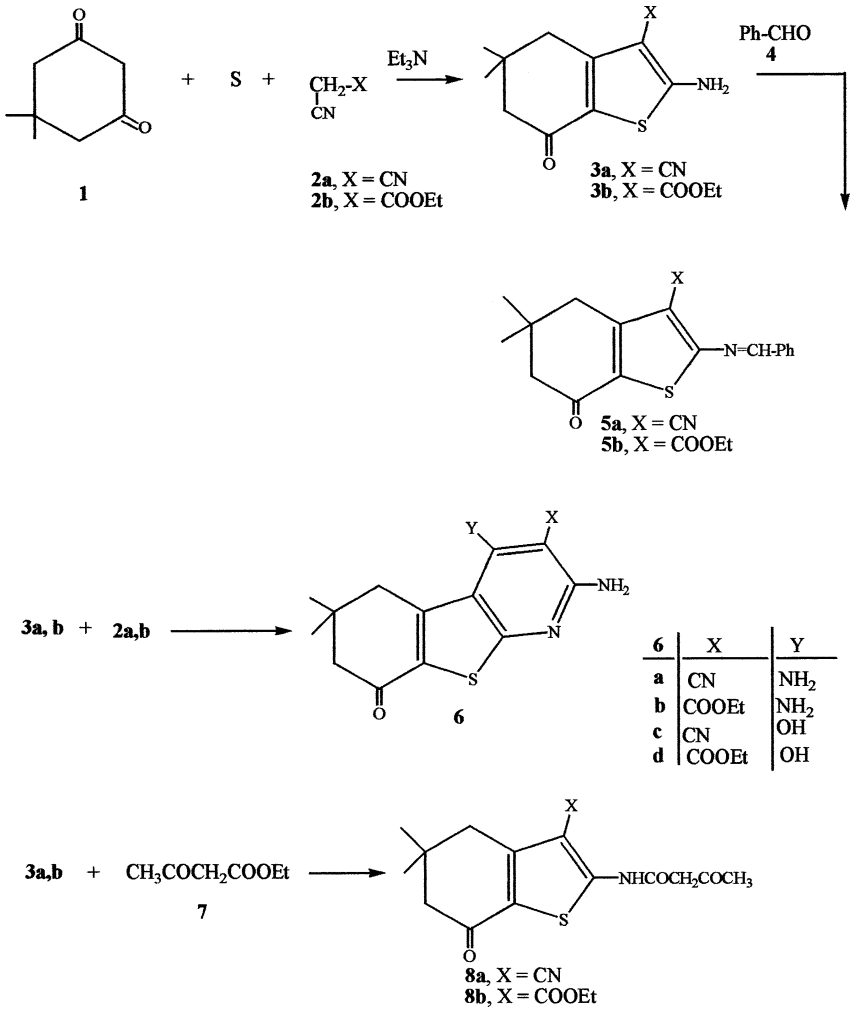
The reactivity of **3a**,**b** with cyanomethylene reagents was studied. Thus, the reaction of **3a**,**b** with either malononitrile (**2a**) or ethyl cyanoacetate (2b) gave the cyclohexeno[*b*]thieno[5,4:2,3]pyridine derivatives **6a–d**. Structures of **6a–d** were based on analytical and spectral data. Thus, the $H^1$NMR spectrum of **6a** showed two singlets at $\delta$ 1.66 and $\delta$ 1.72 for two $CH_3$ groups, two singlets at $\delta$ 2.70 and $\delta$ 3.08 for two $CH_2$ groups, and two singlets at $\delta$ 4.23 and $\delta$ 5.94 ($D_2O$ exchangeable) corresponding for two $NH_2$ groups.

The reaction of either **3a or 3b** with ethyl acetoacetate (**7**) in 1,4-dioxane containing triethylamine gave the amide derivatives **8a,b**. Structures of the latter products were confirmed on the basis of analytical and spectral data. The $^{13}$C NMR data of **8a** (as an example) showed $\delta$ 26.7, 26.9 (2 $CH_3$), 32.1 ($CH_3$), 54.8, 67.3, 82.9 (3 $CH_2$), 88.0 (C), 119.9 (CN), 122.4, 124.8, 140.1, 143.7 (thiopnene C), 177.2, and 179.5, and 180.2 (3 C=O).

Compounds **8a**,**b** underwent ready cyclization when heated in sodium ethoxide solution to give the 5,5-dimethyl-7-oxocyclohexeno-[*b*]thieno-[5,4:2,3]pyridine[*b*]thieno[5,4-*b*]pyrididine derivatives **9a**,**b**, respectively. Structures of compounds **9a–d** were based on analytical and spectral data. The $^{13}$C NMR spectrum of **9a** showed $\delta$ 26.8, 27.0, 29.9 (3 $CH_3$), 52.8, 66.9 (2 $CH_2$), 88.2 (C), 121.9, 124.3, 124.6, 133.8, 140.2, 144.9 (thiophene and pyridine-C), and 178.6 (C=O).

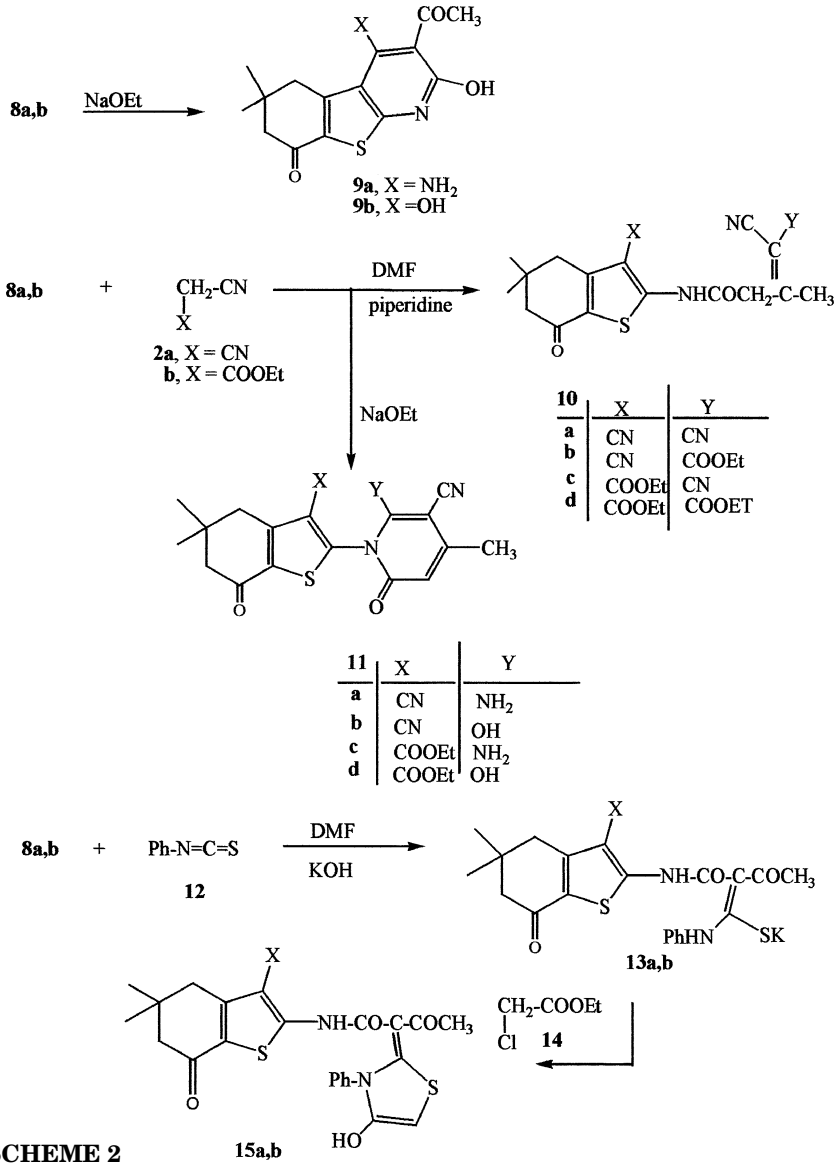
The reaction of either **8a** or **8b** with either **2a** or **2b** in dimethylformamide containing piperidine gave the Knoevenagel condensation products **10a–d**. Structures of the latter products were confirmed on the basis of analytical and spectral data (see experimental data). On the other hand, conducting the same reaction in sodium ethoxide/ethanol gave the pyridine derivatives **11a–d**.

Recently our research group was interested in a series of reactions involving the reaction of phenyl isothiocyanate with active methylene reagents followed by heterocyclization with $\alpha$-haloketones. These reactions led to the formation of thiophene as well as thiazole derivatives.[12,13] In continuation of this program, we studied the



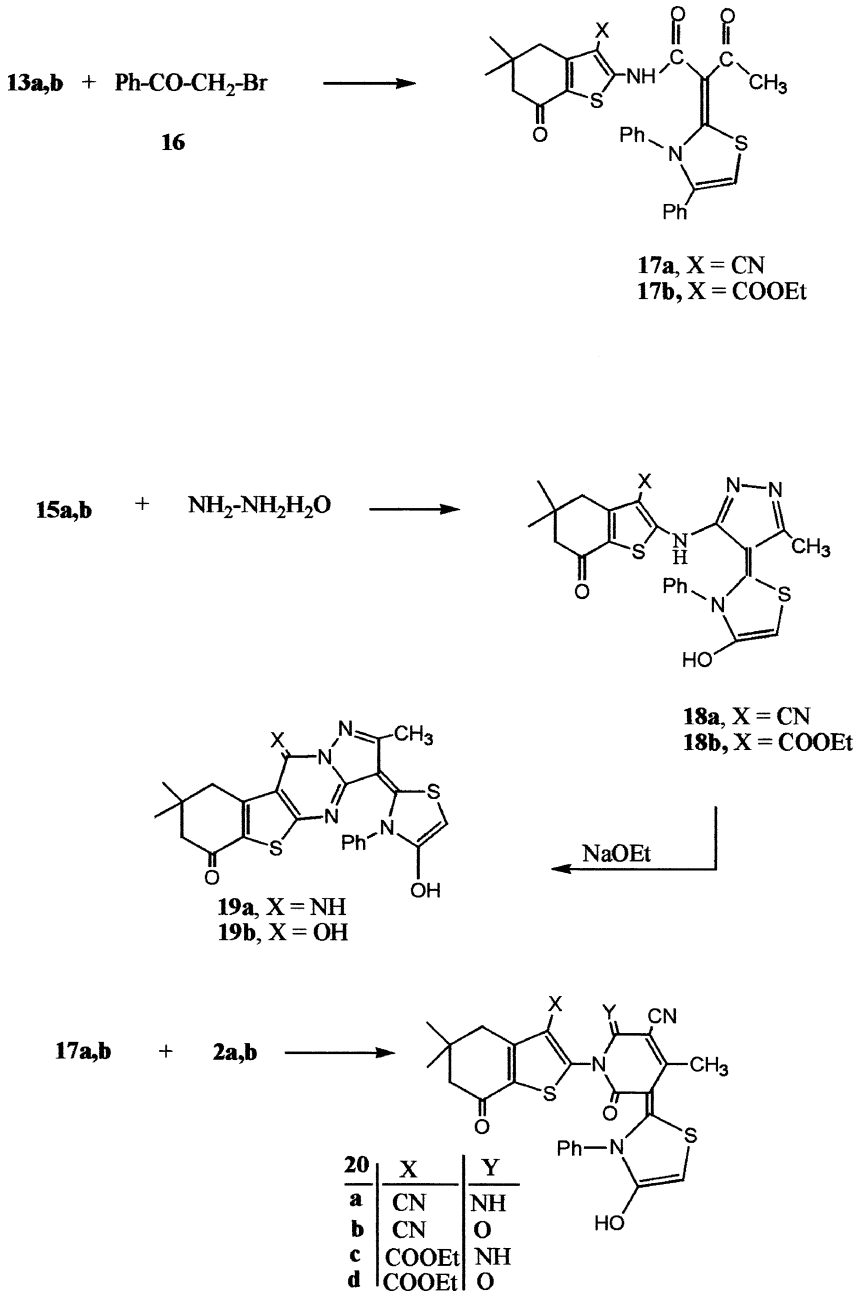

**SCHEME 1**

reactivity of either **8a** or **8b** towards phenyl isothiocynate (**12**) in basic dimethylformamide to give the intermediate potassium sulphide salts **13a**,**b.** Reaction of either **13a** or **13b** with ethyl chloroacetate (**14**) gave the thiazole derivatives **15a**,**b**. Structures of the latter products were based on analytical and spectral data (see experimental section). Moreover, the reaction of **13a**,**b** with phenacyl bromide (**16**) gave the thiazolidene derivatives **17a**,**b**.




**SCHEME 2**

The reaction of either **15a** or **15b** with hydrazine hydrate gave the pyrazole derivatives **18a** and **18b**, respectively. Compounds **18a** and **18b** underwent ready cyclization when heated in sodium ethoxide/ethanol to give the cyclohexeno[b]thieno[5,4:2:3]pyrimidino[5,1:1,2]-pyrazole derivatives **19a** and **19b**, respectively. On the other hand, the




**SCHEME 3**

reaction of **17a**,**b** with either malononitrile **2a** or ethyl cyanoacetate **2b** gave the pyridine derivatives **20a–d**. Structures of the latter products were based on analytical and spectral data (see experimental section).

## BATERICIDAL ACTIVITY

*Sclerotium cepivorum* Berk. Is a soilborne fungus which causes the white rot disease of an onion. Primary inoculum of the pathogen results from spherical small black sclerotia. Sclerotia, which are formed by many other fungi, play a vital role in life cycle because they are the structures by which these fungi survive long periods in unfavorable conditions in the soil.[14,15] Although several heterocyclic compounds were tried against the sclerotium-forming fungi, the antifungal activity of these compounds depended upon their chemical structure. The structure–activity relationship has been was demonstrated by many workers.[16–19] Attempts have been made to increase the toxicity of biologically active compounds by introducing specific functional group(s). In this work, we succeeded in the synthesis-fused thiophene derivatives and evaluated their bioactivity against the mycelial growth, sclerotial formation, and the cellulolytic activity of *Sclerotium cepivorum*.



### Material and Methods

*Sclerotium cepivorum* Berk was isolated from an infected onion bulb (Allium cepa). The sclerotia were surface sterilized in 0.5% sodium hypochlorite for 20 min and then were transferred to plates containing fresh Potatoe-Dextrose Agar (PDA) medium. The plates were incubated at 20°C for 30 days after which the sclerotia were individually transferred to the experimental media. Twenty seven thiophene derivatives were used, each in four concentrations (namely 4, 12, 30, and 75 $\mu$g mL$^{-1}$). For each treatment, three Erlenmeter flasks (250 mL), each containing 90 mL of previously prepared PDA medium, were melted and cooled to about 50°C. Each of the three flasks received 10 mL of prepared stock solutions of thiophene derivatives. Suitable aliquots of each mixture were then poured into each six sterile plate (9 cm diameter) to form, upon solidification, a thin layer at the bottom of the plate. The sclerotia were then individually transferred under aseptic conditions to each of the three plates for an estimation of percentage germination. The other three plates of each treatment were used for estimation of mycelial growth, sclerotial formation, and Sclerotial germination.[20]

From Table I, it is obvious that the effectiveness of the synthesized thiophene derivatives depends on the concentration and where the

**TABLE I Effect of Different Concentrations of Thiophene Derivatives After 44 h on Percentage Inhibition of Germination of Slerotium Cepivorum**

| Compound no. | Conc. [$\mu$g mL$^{-1}$] 4 | Conc. [$\mu$g mL$^{-1}$] 12 | Conc. [$\mu$g mL$^{-1}$] 30 | Conc. [$\mu$g mL$^{-1}$] 75 |
|---|---|---|---|---|
| **5a** | 7.5 | 8.8 | 32.3 | 41.6 |
| **5b** | 28.8 | 35.6 | 47.9 | 73.9 |
| **6a** | 5.2 | 7.6 | 29.5 | 30.3 |
| **6b** | 25.2 | 39.8 | 44.7 | 88.5 |
| **6c** | 67.6 | 77.5 | 100.0 | 100.0 |
| **6d** | 88.7 | 100.0 | 100.0 | 100.0 |
| **8a** | 1.5 | 4.7 | 7.8 | 12.6 |
| **8b** | 69.4 | 78.5 | 100.0 | 100.0 |
| **9a** | 22.3 | 33.4 | 37.9 | 44.1 |
| **9b** | 88.7 | 100.0 | 100.0 | 100.0 |
| **10a** | 11.4 | 18.6 | 34.8 | 44.6 |
| **10b** | 2.3 | 4.5 | 14.7 | 19.4 |
| **10c** | 69.9 | 100.0 | 100.0 | 100.0 |
| **10d** | 55.2 | 78.4 | 100.0 | 100.0 |
| **11a** | 1.8 | 4.4 | 22.7 | 36.4 |
| **11b** | 27.5 | 47.8 | 72.7 | 87.4 |
| **11d** | 75.4 | 100.0 | 100.0 | 100.0 |
| **15a** | 2.5 | 4.7 | 16.8 | 31.7 |
| **15b** | 74.1 | 100.0 | 100.0 | 100.0 |
| **17a** | 22.1 | 32.4 | 53.8 | 66.9 |
| **17b** | 43.7 | 77.2 | 100.0 | 100.0 |
| **18a** | 21.3 | 33.8 | 46.1 | 88.3 |
| **18b** | 44.6 | 59.6 | 80.4 | 100.0 |
| **20a** | 33.1 | 48.1 | 62.6 | 74.2 |
| **20d** | 80.0 | 100.0 | 100.0 | 100.0 |



structures contain either an ethyl carboxylate or a hydroxyl group. In most cases, the presence of the ethyl carboxylate group induced higher toxicity than the hydroxyl group. Compounds **11d** and **20d** showed the highest toxicity since both compounds bear an ethyl carboxylate and a hydroxyl group as well.

## EXPERIMENTAL

All melting points are ucorrected. IR spectra were recorded as KBr discs on a Pye Unicam SP-1000 spectrophotometer. $^{1}$H NMR and $^{13}$C NMR spectra were measured on a Varian EM-390 (200 MHz) in $CD_3SOCD_3$ as solvent and using *TMS* as the internal standard.

### 3-Cyano-2-benzalamino-5,5-dimethyl-7-oxo-cyclohexeno[*b*]-thiophene (5a), and 2-benzalamino-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene-3-carboxylate (5b)

#### *General Procedure*

To a solution of either **3a** (2.20 g, 0.01 mol) or **3b** (2.67 g, 0.01 mole) in 1,4-dioxane (50 mL) containing piperidine (0.5 mL) **4** was added (1.10 g, 0.01 mol). The reaction mixture was heated under reflux for 5 h and then was evaporated in vacuum. The remaining semisolid product was triturated with ethanol. The solid product was collected by filtration.

#### Compound 5a

Pale yellow crystals from ethanol, yield 80% (2.46 g); m.p. 165–8°C. Found: C, 70.09; H, 4.89; N, 8.79; S, 10.08. $C_{18}H_{16}N_2OS$ (308.39). Calcd: C, 70.10; H, 5.23; N, 9.08; S, 10.40. IR: $\upsilon = 3058$ (CH aromatic), 2988, 2893 ($CH_3$, $CH_2$), 2235 (CN), 1688 (C=O), 1650 (C=N), 1640 (C=C). $^1$HNMR (DMSO-$d_6$) $\delta$ 1.62, 1.74 (2s, 6H, $2CH_3$), 2.75, 2.98 (2s, 4H, $2CH_2$), 6.86 (s, 1H, CH=N), 7.03–7.29 (m, 5H, $C_6H_5$).

#### Compound 5b

Pale brown crystals from ethanol, yield 83% (2.97 g), m.p. 270–2°C. Found: C, 67.45; H, 6.08; N, 3.66; S, 8.79. $C_{20}H_{21}NO_3S$ (355.45). Calcd: C, 67.58; H, 5.95; N, 3.94; S, 9.02. IR: $\upsilon = 3060$ (CH aromatic), 2973, 2895 ($CH_3$, $CH_2$) 1698, 1680 (2 C=O), 1645 (C=N), 1638 (C=C). $^1$HNMR (DMSO-$d_6$): $\delta = 1.14$ (t, 3H, $CH_3$), 1.59, 1.71 (2s, 6H, $2CH_3$), 2.71, 3.02 (2s, 4H, $CH_2$), 4.26 (q, 2H, $CH_2$), 6.93 (s, 1H, CH=N), 7.32, 7.38 (m, 5H, $C_6H_5$).

### 3-Cyano-2,4-diamino-6,6-dimethyl-8-oxocyclohexeno[*b*]-thieno[5,4:2,3]-pyridine (6a), Ethyl 2,4-diamino-6,6-dimethyl-8-oxocyclohexeno[*b*]thieno-[5,4:2,3]-pyridine-3-carboxylate (6b), 2-Amino-3-Cyano-4-hydroxy-6,6-dimethyl-8-oxo-cyclohexeno-[*b*]thieno[5,4:2,3]pyridine (6c), and Ethyl 2-amino-4-hydroxy-6,6-dimethyl-8-oxocyclohexeno[*b*]thieno[5,4:2,3]-pyridine-3-carboxylate (6d)

An equimolar amount of either **3a** (2.20 g, 0.01 mol) or **3b** (2.67 g, 0.01 mol) in ethanol (40 mL) containing piperidine (0.5 mL) was added either to **2a** (0.66 g, 0.01 mol) or **2b** (1.13 g, 0.01 mol). The reaction mixture was heated under reflux for 8h and then was evaporated in vacuum. The

remaining product was triturated with ethanol and the solid product was collected by filtration.

## Compound 6a

Pale brown crystals (from acetic acid), yield 80% (2.5 g), m.p. 190–192°C. Found: C, 58.79; H, 4.34; N, 19.85; S, 11.07. $C_{14}H_{14}N_4OS$ (286.35). Calcd: C, 58.72; H, 4.93; N, 19.57; S, 11.20. IR (KBr): $\upsilon$ = 3485, 3340 (2 $NH_2$), 2990, 2875($CH_3$, $CH_2$), 2225 (CN), 1680 (C=O), 1645 (C=N), 1630 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.66, 1.72 (2s, 6H, 2$CH_3$), 2.70, 3.08 (2s, 4H, 2$CH_2$), 4.23, 5.94 (2s, 4H, 2$NH_2$).

## Compound 6b

Orange crystals from 1,4-dioxane, yield 80% (2.3 g), m.p.170–2°C. Found: C, 57.88; H, 5.91; N, 12.32; S, 9.95. $C_{16}H_{19}N_3O_3S$ (333.58). Calcd: C, 57.64; H, 5.74; N. 12.60; S, 9.62. IR: $\upsilon$ = 3493–3360 (2 $NH_2$), 2978, 2870 ($CH_3$, $CH_2$), 1690, 1680 (2 C=O), 1660 (C=N), 1645 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13 (t, 3H, $CH_3$), 1.66, 1.79 (2s, 6H, 2$CH_3$), 2.66, 3.09 (2s, 4H, 2$CH_2$), 4.26 (q, 2H, $CH_2$), 5.31, 5.85 (2s, 4H, 2$NH_2$).

## Compound 6c

Buff crystals from 1,4-dioxane, yield 75% (2.15 g), m.p. 210–212°C. Found: C, 58.34; H. 4.37; N, 14.32; S, 10.86. $C_{14}H_{13}N_3O_2S$ (287.52). Calcd: C, 58.52; H, 4.56; N, 14.62; S, 11.16. IR: $\upsilon$ = 3580, 3353 (OH, $NH_2$) 2975, 2880 ($CH_3$, $CH_2$), 2223 (CN), 1698 (C=O), 1655 (C=N), 1630 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.69, 1.73 (2s, 6H, 2$CH_3$), 2.69, 3.12 (2s, 4H, 2$CH_2$), 5.63 (s, 2H, $NH_2$), 10.39 (s, 1H, OH).

## Compound 6d

Pale yellow crystals (from acetic acid), yield 70% (2.33 g), m.p.160–3°C. Found: C, 57.28; H, 5.11; N, 8.05; S, 9.41. $C_{16}H_{18}N_2O_4S$ (334.51). Calcd: C, 57.47; H, 5.43; N, 8.38; S, 9.59. IR: $\upsilon$ = 3590–3373 ($NH_2$, OH), 2960, 2882 ($CH_3$, $CH_2$), 1690–1680 (2 C=O), 1650 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$): $\delta$ 1.14 (t, 3H, $CH_3$), 1.66, 1.80 (2s, 6H, 2$CH_3$), 2.64, 3.11 (2 s, 4H, 2$CH_2$), 4.22 (q, 2H, $CH_2$), 5.29 (s, 2H, $NH_2$), 9.98 (s, 1H, OH).

### 3-Cyano-2-(α-oxo-butyramido-N-yl)-5,5-dimethyl-7-oxocyclohexeno-[*b*]thiophene (8a) and Ethyl 2-(β-oxo-butyramido-N-yl)-5,5-dimethyl-7-oxocyclohexeno [*b*]thiophene-3-carboxylate (8b)

Equimolar amounts of either **3a** (2.20 g, 0.01 mol) or **3b** (2.67 g, 0.01 mol) in 1,4-dioxane (60 mL) containing triethylamine (1.0 mL) was added **7** (1.30 g, 0.01 mol). The reaction mixture was heated under reflux for 4h and was poured into ice water containing a few drops of hydrochloric acid. The solid product was collected by filtration.

### Compound 8a

Orange crystals from acetc acid, yield 79% (2.40 g), m.p. 178–4°C. Found: C, 59.52; H, 5.06; N, 9.52; S, 10.75. $C_{15}H_{16}N_2O_3S$ (304.36). Calcd: C, 59.19; H, 5.30; N, 9.20; S, 10.54. IR: $\upsilon$ = 3460–3320 (NH), 2960, 2875 ($CH_3$, $CH_2$) 2222 (CN), 1696–1683 (C=O), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO–$d_6$) $\delta$ 1.66, 1.73 (2s, 6H, $CH_2$), 2.68, 2.99 (2m, 4H, $2CH_2$), 3.14 (s, 3H, $CH_3$), 5.21 (s, 2H, $CH_2$), 8.83 (s, 1H, NH). $^{13}$C NMR (DMSO) $\delta$ 26.7, 26.9 (2 $CH_3$), 32.1 ($CH_3$), 54.8, 67.3, 82.9 (3 $CH_2$), 88.0 (C), 119.9 (CN), 122.4, 124.8, 140.1, 143.7 (thiophene C), 177.2, 179.5, 180.2 (3 C=O).



### Compound 8b

Redish brown crystals from acetic acid, yield 66% (2.31 g), m.p. 223–5°C. Found: C, 58.65; H, 5.59; N, 4.23; S, 9.52. $C_{17}H_{21}NO_5S$ (351.42). Calcd: C, 58.10; H, 6.02; N, 3.99; S, 9.12. IR: $\upsilon$ = 3490–3330 (NH), 2973, 2890 ($CH_3$, $CH_2$), 1705–1680 (4 C=O), 1630 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$): $\delta$ 1.13 (t, 3H, $CH_3$), 1.69, 1.75 (2s, 6H, $2CH_3$), 2.70, 2.88 (2m, 4H, $2CH_2$), 3.21 (s, 3H, $CH_3$), 4.22 (q, 2H, $CH_2$), 4.53 (s, 2H, $CH_2$), 8.86 (s, 1H, NH).

### 3-Acetyl-4-amino-2-hydroxy-6,6-dimethyl-8-oxocyclohexeno[*b*]thieno-[5,4:2,3]pyridine (9a) and 3-Acetyl-2,4-dihydroxy-6,6-dimethyl-8-oxo- cyclohexeno[*b*] thieno[5,4:2,3]-pyridine (9b)

#### *General Procedure*

A solution of either 8a (3.04 g, 0.01 mole) or 8b (3.51 g, 0.01 mole) in sodium ethoxide (0.01 mole) (prepared by adding sodium metal [0.23 g, 0.01 mole] to absolute ethanol [20 mL]) was heated under reflux in boiling water for 6h. The reaction mixture was poured into ice water

containing a few drops of hydrochloric acid (to pH = 6) and the solid product was collected by filtration.

## Compound 9a

Orange crystals from 1,4-dioxane, yield 70%; (2.13 g), m.p. 210–212°C. Found: C, 58.37; H, 5.09; N, 9.45; S, 10.83. $C_{15}H_{16}N_2O_3S$ (304.48). Calcd: C, 59.19; H, 5.30; N, 9.20; S, 10.54. IR (KBr): $\upsilon$ = 3560–3320 (OH, $NH_2$), 2960, 2873 ($CH_3$, $2CH_2$), 1696, 1685 (2 C=O), 1655 (C=N), 1630 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$): $\delta$ 1.66, 1.79 (2s, 6H, $2CH_3$), 2.65, 2.80 (2m, 4H, $2CH_2$), 3.09 (s, 3H, $CH_3$), 4.53 (s, 2H, $NH_2$), 10.21 (s, 1H, OH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 26.8, 27.0, 29.9 (3 $CH_3$), 52.8, 66.9 (2 $CH_2$), 88.2 (C), 121.9, 124.3, 124.6, 133.8, 140.2, 144.9 (thiophene and pyridine-C), 178.6 (C=O).



## Compound 9b

Yellow crystals from DMF, yield 60% (2.13 g); m.p. 200–3°C. Found: C, 58.72; H, 5.41; N, 4.89; S, 10.32. $C_{15}H_{15}NO_4S$ (305.42). Calcd: C, 59.00; H, 4.95; N, 4.59; S, 10.50. IR: $\upsilon$ = 3575–3340 (2OH), 2970, 2890 ($CH_3$, $CH_2$), 1695, 1683 (2C=O), 1666 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.64, 1.73 (2s, 6H, $2CH_3$), 2.68, 2.76 (2m, 4H, $2CH_2$), 3.09 (s, 3H, $CH_3$), 9.38, 10.02 (2s, 2H, 2OH).

## 3 Cyano-2-($\alpha$-dicyanomethino-$\beta$-ylidino-butyramido-N-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene (10a), 3-Cyano-2-($\alpha$-cyano ethoxycarbonyl-methino-$\beta$-ylidino-butyramido-N-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]-thiophene (10b), Ethyl 2-($\alpha$-dicyano-methino-$\beta$-ylidino-butyramido-N-yl) 5,5-dimethyl-7-oxocyclohexeno-[*b*]thiophene-3-carboxylate (10c) and Ethyl 2-($\alpha$-cyano ethoxycarbonylmethino-$\beta$-ylidino-butyramido-N-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]-thiophene-3-carboxylate (10d)

A solution of either **8a** (3.04 g, 0.01 mol) or **8b** (3.51 g, 0.01 mole) in dimethylformamide (40 mL) containing piperidine (0.5 mL) was added to either **2a** (0.66 g, 0.01 mole) or **2b** (1.13 g, 0.01 mole). The reaction mixture was heated under reflux for 6h and then was evaporated under vacuum. The remaining product was triturated with ethanol. The solid product, in each case, was collected by filtration.

## Compound 10a

Pale brown crystals from 1,4-dioxane, yield 74% (2.60), m.p. 255–8°C. Found: C, 61.09; H, 4.86; N, 16.64; S, 9.23. $C_{18}H_{16}N_4O_2S$ (352.65). Calcd: C, 61.35; H, 4.58; N, 15.90; S, 9.10. IR: $\upsilon$ = 3475–3365 (NH), 2973, 2885 ($CH_3$, $CH_2$), 2225, 2222–2218 (3 CN) 1685, 1680 (2 C=O), 1643 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.68, 1.73 (2s, 6H, $2CH_3$), 2.65, 2.80 (2m, 4H, $2CH_2$), 3.25 (s, 3H, $CH_3$), 5.03 (s, 2H, $CH_2$), 8.73 (s, 1H, NH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 26.4, 27.2, 29.5 (3 $CH_3$), 53.1, 66.4, 82.3 (3 $CH_2$), 118.8, 119.0, 1203 (3 CN), 122.9, 124.6, 133.8, 140.2 (thiophene-C), 178.6, 180.6 (2 C=O).

## Compound 10b

Orange crystals from 1,4-dioxane, yield 70% (2.79 g), m.p. 228–30°C. Found: C, 60.09; H, 5.21; N, 10.49; S, 7.67. $C_{20}H_{21}N_3O_4S$ (399.65). Calcd: C, 60.13; H, 5.30; N, 10.52; S, 8.03. IR: $\upsilon$ = 3460–3345 (NH), 2975, 2883 ($CH_3$, $CH_2$), 2225–2218 (3CN), 1703, 1690–1680 (3 C=O), 1645 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13 (t, 3H, $CH_3$), 1.66, 1.79 (2s, 6H, $2CH_3$), 2.65, 2.78 (2m, 4H, $2CH_2$), 3.21 (s, 3H, $CH_3$), 4.22 (q, 2H, $CH_2$), 4.83 (s, 2H, $CH_2$), 8.89 (s, 1H, NH).



## Compound 10c

Yellow crystals from DMF, yield 76% (3.03 g), m.p. 245–8°C. Found: C, 60.45; H, 5.11; N, 10.76; S, 7.79. $C_{20}H_{21}N_3O_4S$ (399.65). Calcd: C, 60.13; H, 5.30; N, 10.52; S, 8.03. IR: $\upsilon$ = 3460–3345 (NH), 2975, 2883 ($CH_3$, $CH_2$), 2225–2218 (2 CN), 1703, 1690–1680 (3 C=O), 1645 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13(t, 3H, $CH_3$), 1.66, 1.79 (2s, 6H, $2CH_3$), 2.65, 2.78 (2m, 4H, $2CH_2$), 3.21 (s, 3H, $CH_3$), 4.22 (q, 2H, $CH_2$), 4.83 (s, 2H, $CH_2$), 8.89 (s, 1H, NH).

## Compound 10d

Pale yellow crystals from acetic acid, yield 77% (3.43 g), m.p. 176–8°C. Found: C, 58.78; H, 5.46; N, 5.91; S, 7.53. $C_{22}H_{26}N_2O_6S$ (446.64). Calcd: C, 59.18; H, 5.87; N, 6.27; S, 7.18. IR: $\upsilon$ = 3475–3365 (NH), 2225 (CN), 1708–1685 (4 C=O), 2970, 2843 ($CH_3$, $CH_2$), 1645 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.12, 1.14 (2t, 6H, $2CH_3$), 1.64, 1.77 (2s, 6H, $2CH_3$), 2.66, 2.73 (2m, 4H, $2CH_2$), 2.83 (s, 3H, $CH_3$), 4.22, 4.26 (2q, 4H, $2CH_2$), 4.93 (s, 2H, $CH_2$), 8.31 (s, 1H, NH).

### 3-Cyano-2-(2-amino-3-cyano-4-methyl-6-oxopyridin-1-yl)-5,5-dimethyl-7-oxo-cyclohexeno[*b*]thiophene (11a), 3-Cyano-2-(3-Cyano-2-hydroxy-4-methyl-6-oxopyridin-1-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene (11b), Ethyl 2-(2-amino-3-cyano-4-methyl-6-oxopyridin-1-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene-3-carboxylate (11c) and Ethyl 2-(3-cyano-2-hydroxy-4-methyl-6-oxopyridin-1-yl)-5,5-dimethyl-7-oxocyclohexeno[*b*]-thiophene-3-carboxylate (11d)

A suspension of either **8a** (3.04 g, 0.01 mole) or **8b** (3.51 g, 0.01 mol) in sodium ethoxide ( prepared by dissolving sodium metal [0.23 g, 0.01 mol] to absolute ethanol [50 mL]) was added to either **2a** (0.66 g, 0.01 mole) or **2b** (1.13 g, 0.01 mol). The reaction mixture, in each case, was heated under reflux for 6h. The solid product that was formed, upon dilution with water containing hydrochloric acid (to pH = 6), was collected by filtration.



### Compound 11a

Orange crystals from ethanol, yield 77% (2.71 g); m.p. 274–3°C. Found: C, 61.09; H, 4.43; N, 16.21; S, 8.89. $C_{18}H_{16}N_4O_2S$ (352.65). Calcd: C, 61.35; H, 4.58; N, 15.90; S, 9.10. IR: $\upsilon$ = 3460–3345 ($NH_2$), 2978, 2883 ($CH_3$,$CH_2$), 2222–2220 (2 CN), 1695, 1680 (2 C=O), 1640 (C=O) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.65, 1.83 (2s, 6H, $2CH_3$), 2.61, 2.75 (2m, 4H, $2CH_2$), 3.24 (s, 3H, $CH_3$), 4.92 (s, 2H, $NH_2$), 6.63 (s, 1H, pyridine-H). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 26.2, 27.1 (2 $CH_3$), 53.8, 66.2 (2 $CH_2$), 118.9, 120.1 (2 CN), 122.3, 123.3, 124.9, 134.2, 143.0, 144.4 (thiophene and pyridine-C), 178.6, 179.9 (2 C=O).

### Compound 11b

Reddish brown crystals from ethanol, yield 74% (2.61 g), m.p. 286–4°C. Found: C, 60.87; H, 4.58; N, 12.27; S, 8.88. $C_{18}H_{15}N_3O_3S$ (353.58). Calcd: C, 61.18; H, 4.28; N, 11.89; S, 9.07. IR (KBr): $\upsilon$ = 3465–3340 (OH), 2978, 2883 ($CH_3$, $CH_2$), 2222–2220 (2 CN), 1695, 1680 (2 C=O), 1645 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.63, 1.84 (2s, 6H, $2CH_3$), 2.62, 2.77 (2m, 4H, $2CH_2$), 3.23 (s, 3H, $CH_3$), 6.67 (s, 1H, pyridine-H), 8.93 (s, 1H, OH).

### Compound 11c

Yellow crystals from ethanol, yield 66% (2.63 g), m.p. 210–2°C. Found: C, 60.45; H, 5.62; N, 10.87; S, 7.74. $C_{20}H_{21}N_3O_4S$ (399.65). Calcd: C, 60.13; H, 5.30; N, 10.52; S, 8.03. IR: $\upsilon$ = 3465–3340 ($NH_2$), 2978, 2883

($CH_3$, $CH_2$), 2222 (CN), 1695, 1690–1680 (3 C=O), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.16 (t, 3H, $CH_3$), 1.65, 1.83 (2s, 6H, $2CH_3$), 2.61, 2.75 (2m, 4H, $2CH_2$), 3.24 (s, 3H, $CH_3$), 4.26 (q, 2H, $CH_2$), 4.92 (s, 2H, $NH_2$), 6.63 (s, 1H, pyridine H-5).

## Compound 11d

Yellowish brown crystals from ethanol, yield 82% (3.28 g), m.p. 175–8°C. Found: C, 60.31; H, 4.87; N, 6.79; S, 8.53. $C_{20}H_{20}N_2O_5S$ (400.57). Calcd: C, 59.99; H, 5.03; N, 7.00; S, 8.02. IR: $\upsilon$ = 3460–3345 (OH), 2978, 2883 ($CH_3$, $CH_2$), 2220 (CN), 1695, 1690–1680 (3 C=O), 1695, 1690–1680 (3 C=O), 1640 (C=O) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$): $\delta$ = 1.16(t, 3H, $CH_3$), 1.65, 1.83 (2s, 6H, $2CH_3$), 2.61, 2.75 (2m, 4H, $2CH_2$), 3.24 (s, 3H, $CH_3$), 4.26 (q, 2H, $CH_2$), 6.63 (s, 1H, pyridine-H), 9.23 (s, 1H, OH).



## 3-Cyano-2-[$\alpha$-oxo-$\beta$-(3-phenyl-4-oxo-thiazolideno-2-ylideno)-butyramido-N-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]-thiophene (15a), Ethyl 2-[$\alpha$-oxo-$\beta$-(3-phenyl-4-oxo-thiazolideno-2-ylideno)butyramido-N-yl]-5,5-dimethyl-7-oxo-cyclohexen[*b*]thiophene-3-carboxylate (15b), 3-Cyano-2-[$\alpha$-oxo-$\beta$-(3,4-dipheno-thiazolo-2-ylidino)butyramido-N-yl]-5,5-dimethyl-7-oxo-cyclohexeno[*b*]thiophene (17a) and Ethyl 2-[$\alpha$-oxo-$\beta$-(3,4-dipheno-thiazolo-2-ylidino)butyramido-N-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene-3-carboxylate (17b)

A solution of either **10a** (3.04 g, 0.01 mole) or **10b** (3.51 g, 0.01 mole) in dimethylformamide (20 mL) was added to phenyl isothiocyanate (**12**) (1.35 g, 0.01 mole) and potassium hydroxide (0.57 g, 0.01 mol). The reaction mixture was heated under reflux on a water bath for 3 h. Then either **14** (1.20 g, 0.01 mol) or **16** (2.00 g, 0.01 mol) was added and the mixture was left over night. The solid product formed upon pouring the mixture into ice water containing a few drops of hydrochloric acid and was collected by filtration.

## Compound 15a

Yellow crystals from ethanol, yield 75% (3.59 g), m.p. 197–200°C. Found: C, 60.54; H, 4.56; N, 8.94; S, 13.85. $C_{24}H_{21}N_3O_4S_2$ (479.76). Calcd: C, 60.11; H, 4.41; N, 8.76; S, 13.37. IR: $\upsilon$ = 3480–3375 (OH, NH), 3060 (CH aromatic), 2970, 2884 ($CH_3$, $CH_2$), 2225 (CN), 1707, 1690–1680 (4 C=O), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.65, 1.73 (2s, 6H,

$2CH_3$), 2.63, 2.80 (2m, 4H, $2CH_2$), 3.28 (s, 3H, $CH_3$), 5.91 (s, 2H, $CH_2$), 7.32–7.43 (m, 6H, $C_6H_5$, thiazole CH), 8.81 (s, 1H, NH), 10.21 (s, 1H, OH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 26.8, 27.6, 33.3 (3 $CH_3$), 54.8, 67.2, 89.4 (3 $CH_2$), 120.5 (CN), 124.3, 126.7, 124.9, 134.0, 144.9 (thiophene and thiazole-C), 178.9, 179.0, 179.8, 180.0 (4 C=O).

## Compound 15b

Pale yellow crystals from 1,4-dioxane, yield 82% (4.31 g), m.p. 215–7°C (1,4-dioxane). Found: C, 59.09; H, 5.22; N, 5.63; S, 12.63. $C_{26}H_{26}N_2O_6S_2$ (526.75 g) . Calcd: C, 59.30; H, 4.98; N, 5.32; S, 12.18. IR: $\upsilon$ = 3480–3375 (OH, NH), 3060 (CH aromatic), 2983, 2879 ($CH_3$, $CH_2$) 1710, 1690–1675 (5 C=O), 1640 (C=C) cm$^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13 (t, 3H, $CH_3$), 1.64, 1.79 (2s, 6H, $2CH_3$), 2.64, 2.81 (2m, 4H, $2CH_2$), 3.24 (s, 3H, $CH_3$), 5.69 (s, 2H, $CH_2$), 7.32, 7.40 (m, 6H, $C_6H_5$, thiazole CH), 8.89 (s, 1H, NH), 10.29 (s, 1H, OH).



## Compound 17a

Orange crystals from 1,4-dioxane, yield 70% (3.78 g), m.p. 270–3°C. Found: C, 66.89; H, 4.89; N, 8.02; S, 12.03. $C_{30}H_{25}N_3O_3S_2$(539.67). Calcd: C, 66.77; H, 4.67; N, 7.79; S, 11.88. IR: $\upsilon$ = 3480–3364 (NH), 3050 (CH aromatic), 2990, 2870 ($CH_3$, $CH_2$), 2227 (CN), 1704–1680 (3 C=O), 1640 (C=C) cm$^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.64, 1.78 (2s, 6H, $2CH_3$), 2.64, 2.82 (2m, 4H, $2CH_2$), 3.20 (s, 3H, $CH_3$), 6.99 (s, 1H, thiazole H-5), 7.32–7.40 (m, 10H, 2 $C_6H_5$), 8.94 (s, 1H, NH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 26.4, 27.0, 35.6 (3 $CH_3$), 53.5, 66.9 (2 $CH_2$), 120.1 (CN), 123.9, 126.4, 125.3, 133.8, 136.7, 145.6 (thiophene and thiazole-C), 178.2, 179.6, 181.3 (3 C=O).

## Compound 17b

Pale yellow crystals from ethanol, yield 69% (4.05 g), m.p. 195–7°C. Found: C, 65.25; H, 4.86; N, 4.91; S, 11.28. $C_{32}H_{30}N_2O_5S_2$ (586.85). Calcd: C, 65.51; H, 5.15; N, 4.77; S, 10.93. IR: $\upsilon$ = 3480–3364 (NH), 3050 (CH aromatic), 2994, 2878 ($CH_3$, $CH_2$), 2225 (CN), 1700–1684 (3 C=O), 1638 (C=C) cm$^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.16 (t, 3H, $CH_3$) 1.64, 1.78 (2s, 6H, $2CH_3$), 2.64, 2.82 (2m, 4H, $2CH_2$), 3.20 (s, 3H, $CH_3$), 4.25 (q, 2H, $CH_2$), 6.92 (s, 1H, thiazole H-5), 7.32–7.40 (m, 10H, 2 $C_6H_5$), 8.94 (s, 1H, NH).

### 3-Cyano-2-[5-methyl-4-ylideno-(4-oxo-3-phenyl-thiazolideno-2-yl)pyrazolo-3-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]-thiophene (18a) and Ethyl 2-[5-methyl-4-ylideno-(4-oxo-3-phenyl-thiazolideno-2-yl)pyrazolo-3-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene-3-carboxylate (18b)

#### *General Procedure*

A solution of either **15a** (4.68 g, 0.01 mole) or **15b** (5.15 g, 0.01 mole) in ethanol (50 mL) was added to hydrazine hydrate (0.5 mL, 0.01 mole). The reaction mixture was heated under reflux for 7 h. The mixture was poured into ice water containing a few drops of hydrochloric acid. The solid product was collected by filtration.

### Compound 18a

Orange crystals from acetic acid, yield 76% (3.61 g), m.p. 264–7°C. Found: C, 60.23; H, 4.52; N, 14.87; S, 13.07. $C_{24}H_{21}N_5O_2S_2$ (475.89). Calcd: C, 60.61; H, 4.45; N, 14.73; S, 13.48. IR (KBr): $\upsilon$ = 3470–3384 (NH), 3060 (CH aromatic), 2988, 2884 ($CH_3$, $CH_2$), 2225 (CN), 1706, 1685 (2 C=O), 1663 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.59, 1.76 (2s, 6H, $2CH_3$), 2.66, 2.81 (2m, 4H, $2CH_2$), 3.21 (s, 3H, $CH_3$), 5.89 (s, 2H, $CH_2$), 7.34–7.39 (m, 5H, $C_6H_5$), 8.81 (s, 1H, NH).

### Compound 18b

Yellow crystals from acetic acid, yield 70% (3.65 g), m.p. 235–8°C. Found: C, 59.57; H, 4.87; N, 10.95; S, 11.81. $C_{26}H_{26}N_4O_4S_2$ (522.88). Calcd: C, 59.75; H, 5.01; N, 10.72; S, 12.27. IR: $\upsilon$ = 3460–3385 (NH), 3068 (CH aromatic), 2973, 2898 ($CH_3$, $CH_2$), 1703, 1690–1680 (3 C=O), 1655 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.14 (t, 3H, $CH_3$), 1.54, 1.78 (2s, 6H, $2CH_3$) 2.64, 2.77 (2m, 4H, $2CH_2$), 3.11 (s, 3H, $CH_3$), 4.26 (q, 2H, $CH_2$), 5.81 (s, 2H, $CH_2$), 7.32–7.37 (m, 5H, $C_6H_5$), 8.84 (s, 1H, NH).

### Synthesis of the Cyclohexeno[*b*]thieno[5,4:2:3]pyrimidino-[5,1:1,2]-pyrazole derivatives 19a and 19b

A suspension of either **18a** (4.7 g, 0.01 mol) or **18b** (5.2 g, 0.01 mol) in sodium ethoxide (0.01 mol) in ethanol was heated in boiling water for 2h. The reaction mixture was poured into ice water containing few drops of hydrochloric acid (to pH = 7) and the formed solid product was collected by filtration.

## Compound 19a

White crystals from DMF, yield 60% (2.85 g), m.p. 180–2°C. Found: C, 60.98; H, 4.61; N, 14.94; S, 13.17. $C_{24}H_{21}N_5O_2S_2$ (475.87). Calcd: C, 60.61; H, 4.45; N, 14.73; S, 13.48. IR: $\upsilon$ = 3475–3360 (NH), 3063 (CH aromatic), 2977, 2880 ($CH_3$, $CH_2$), 1700, 1690 (2C=O), 1673 (exocyclic C=N), 1635 (C=C). $^1$HNMR (DMSO-$d_6$) $\delta$ 1.55, 1.72 (2s, 6H, $2CH_3$), 2.69, 2.80 (2m, 4H, $2CH_2$), 3.22 (s, 3H, $CH_3$), 5.74 (s, 2H, $CH_2$), 7.30–7.42 (m, 5H, $C_6H_5$), 8.92 (s, 1H, NH).

## Compound 19b

Yellow crystals from 1,4-dioxane, yield 61% (2.90 g), m.p. 195–7°C. Found: C, 60.21; H, 3.87; N, 11.92; S, 13.21. $C_{24}H_{21}N_4O_3S_2$ (477.88). Calcd: C, 60.49; H, 4.23; N, 11.76; S, 13.46. IR: $\upsilon$ 3060 (CH aromatic), 2978, 2880 ($CH_3$, $CH_2$), 1710, 1706, 1688 (3 C=O), 1663 (C=N), 1643 (C=C) cm$^{-1}$. $^1$HNMR (DMSO-$d_6$): $\delta$ = 1.54, 1.71 (2s, 6H, $2CH_3$), 2.65, 2.80 (2m, 4H, $2CH_2$), 3.19 (s, 3H, $CH_3$), 5.78 (s, 2H, $CH_2$), 7.30–7.37 (m, 5H, $C_6H_5$).



## 3-Cyano-2-[3-cyano-4-methyl-2-imino-6-oxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene (20a), 3-Cyano-2-[3-cyano-4-methyl-2,6-dioxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)-pyridin-1-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene (20b), Ethyl 2-[3-cyano-4-methyl-2-imino-6-oxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-5,5-dimethyl-7-oxocyclohexeno[*b*]thiophene-3-carboxylate (20c) and Ethyl 2-[3-cyano-4-methyl-2,6-dioxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-5,5-dimethyl-7-oxocyclohexeno-[*b*]thiophene-3-carboxylate (20d)

An equimolar amount of either **15a** (4.68 g, 0.01 mole) or **15b** (5.15 g, 0.01 mole) in ethanol (40 mL) containing piperidine (0.5 mL) was added to either malononitrile **2a** (0.66 g, 0.01 mole) or ethyl cyanoacetate **2b** (1.13 g, 0.01 mol). The reaction mixture, in each case, was heated under reflux for 6h and evaporated in a vacuum. The remaining product was triturated with ethanol and the formed solid product was collected by filtration.

## Compound 20a

Brown crystals from acetic acid, yield 69% (3.63 g), m.p. 176–8°C. Found: C, 61.83; H, 3.76; N, 13.09; S, 15.52. $C_{27}H_{21}N_5O_3S_2$ (527.91). Calcd: C, 61.46; H, 4.01; N, 13.27; S, 12.15. IR: $\upsilon$ = 3469–3384 (NH),

3050 (CH aromatic), 2973, 2898 ($CH_3$, $CH_2$), 2225, 2222 (2 CN), 1705–1685 (3 C=O), 1650 (C=N), 1630 (C=C). $^1$HNMR (DMSO-$d_6$) $\delta$ 1.68, 1.74 (2s, 6H, $2CH_3$), 2.66, 2.79 (2m, 4H, $2CH_2$), 3.48 (s, 3H, $CH_3$), 5.38 (s, 2H, $CH_2$), 7.33–7.83 (m, 5H, $C_6H_5$), 8.91 (s, 1H, NH).

## Compound 20b

Orange crystals from 1,4-dioxane, yield 72% (3.80 g), m.p. 196–8°C. Found: C, 61.55; H, 4.09; N, 10.84; S, 12.42. $C_{27}H_{20}N_4O_4S_2$ (528.85). Calcd: C, 61.35; H, 3.81; N, 10.60; S, 12.13. IR: $\upsilon = 3060$ (CH aromatic), 2965, 2874 ($CH_3$, $CH_2$), 2225, 2248 (2 CN), 1740, 1695–1680 (4 C=O), 1648 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.69, 1.74 (s, 6H, $2CH_3$), 2.64, 2.80 (2m, 4H, $2CH_2$), 3.39 (s, 3H, $CH_3$), 6.49 (s, 2H, $CH_2$), 7.30–7.36 (m, 5H, $C_6H_5$).



## Compound 20c

Yellow crystals from 1,4-dioxane, yield 80% (4.59 g), m.p. 215–8°C (acetic acid). Found: C, 60.55; H, 4.82; N, 10.08; S, 10.89 $C_{29}H_{26}N_4O_5S_2$ (574.92). Calcd: C, 60.61; H, 4.56; N, 9.75; S, 11.16. IR: $\upsilon = 3455$–3365 (NH), 3053 (CH aromatic), 2968, 2875 ($CH_3$, $CH_2$), 2223 (CN), 1695–1680 (3 C=O), 1648 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13 (t, 3H, $CH_3$), 1.63, 1.75 (2s, 6H, $2CH_3$), 2.64, 2.82 (2m, 4H, $2CH_2$), 3.25 (s, 3H, $CH_3$), 4.26 (q, 2H, $CH_2$), 6.63 (s, 2H, $CH_2$), 7.32–7.39 (m, 5H, $C_6H_5$), 8.83 (s, 1H, NH).

## Compound 20d

Reddish brown crystals from 1,4-dioxane, yield 68% (3.91 g), m.p. 182–5°C (acetic acid). Found: C, 60.78; H, 4.69; N, 7.09; S, 10.94. $C_{29}H_{25}N_3O_6S_2$ (575.89). Calcd: C, 60.51; H, 4.38; N, 7.30; S, 11.14. IR: $\upsilon = 3053$ (CH aromatic), 2968, 2875 ($CH_3$, $CH_2$), 2223 (CN), 1695–1680 (5C=O), 1648 (C=N), 1640 (C=C) $cm^{-1}$. $^1$HNMR (DMSO-$d_6$) $\delta$ 1.13 (t, 3H, $CH_3$), 1.63, 1.75 (2s, 6H, $2CH_3$), 2.64, 2.82 (2m, 4H, $2CH_2$), 3.25 (s, 3H, $CH_3$), 4.26 (q, 2H, $CH_2$), 6.63 (s, 2H, $CH_2$), 7.32–7.39 (m, 5H, $C_6H_5$).

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