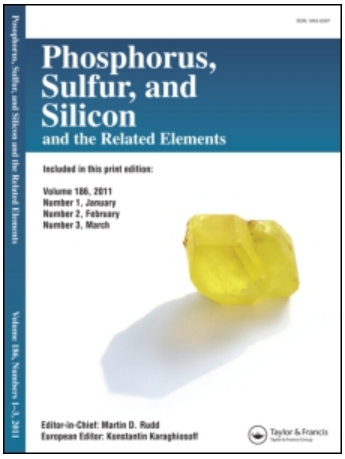

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The Reaction of Cyclohexan-1,3-dione with Cyanomethylenes: Synthesis of Thiophenes and Their Fused Derivatives with Antifungal Activities

Rafat M. Mohareb[ab]; Sherif M. Sherif[b]; Hosam El-Dean Moustafa[b]
[a] Department of Organic Chemistry, Faculty of Pharmacy, October University for Modern Sciences and Arts (MSA), October, A. R., Egypt [b] Department of Chemistry, Faculty of Science, Cairo University, Giza, A. R., Egypt

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The Reaction of Cyclohexan-1,3-dione with Cyanomethylenes: Synthesis of Thiophenes and Their Fused Derivatives with Antifungal Activities

Rafat M. Mohareb,[1,2] Sherif M. Sherif,[2] and Hosam El-Dean Moustafa[2]
[1]Department of Organic Chemistry, Faculty of Pharmacy, October University for Modern Sciences and Arts (MSA), October, A. R. Egypt
[2]Department of Chemistry, Faculty of Science, Cairo University, Giza, A. R. Egypt

*2-Amino-7-oxotetrahydrobenzo[b]thiophenes **3a,b** were prepared according to the Gewald procedure. Their reactivity toward a variety of chemical reagents was studied to give annulated heterocycles with potential bio-responses.*

Keywords Annulated derivatives; pyridine; thiazole; thiophene

INTRODUCTION

Benzothiophenes are one of the most common and consequently the most studied classes of aromatic heterocycles.[1] The occurrence of these heterocycles in a significant number of medicinal agents,[2] active in a variety of disease areas, has led to an enduring interest in the development of new methods for their synthesis.[3–5] Methods that utilize new classes of precursors are particularly valuable. Among the many syntheses available, transition metal catalyzed processes[6] and palladium-mediated methods in particular[7] feature heavily. Syntheses based on palladium-catalyzed cyclizations of appropriately substituted alkenyl or alkynyl phenols, or thiophenols, are versatile and have been used on many occasions.[8–10] Related tandem processes involving catalyzed C–C bond formation, usually employing Sonogashira-type reactions, before construction of the key C–S bond have also been developed.[11–14] The crucial bond-forming event in these processes is intramolecular attack

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Address correspondence to Rafat M. Mohareb, Department of Organic Chemistry, Faculty of Pharmacy, October University for Modern Sciences and Arts (MSA), El-Wahaat Road, October, A. R. Egypt. E-mail: raafat_mohareb@yahoo.com

of a nucleophilic oxygen or sulfur atom onto a palladium-activated C–C multiple bond, resulting in formation of the $X–C_2$ bond of the heterocycle. We aim to develop an alternative method for the synthesis of 2-amino-7-oxotetrahydrobenzo[*b*]thiophenes starting from cyclohexan-1,3-dione and cyanomethylene reagents.

RESULTS AND DISCUSSION

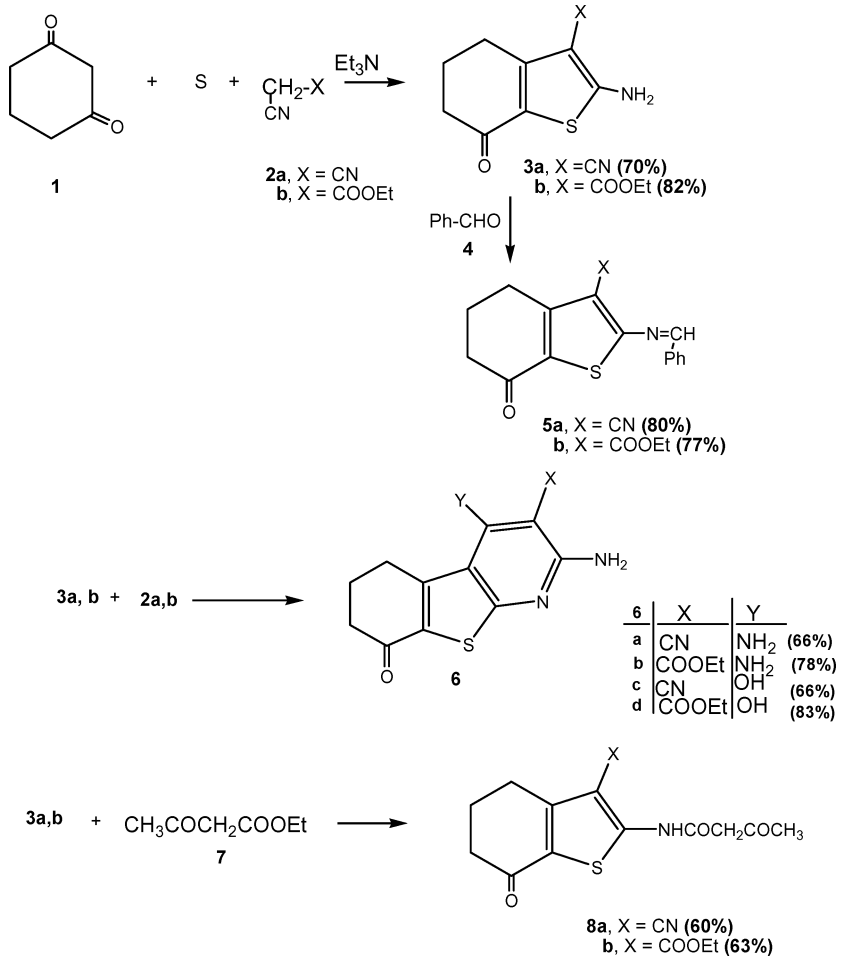
Chemistry

In continuation of our previous work,[15–17] we report herein on the scope and applicability of the 2-amino-7-oxotetrahydrobenzo[*b*]thiophenes **3a**,**b**, which were synthesized according to procedures in the literature[18,19] through the reaction of cyclohexan-1,3-dione (**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 results in the formation of Schiff's bases **5a**,**b**. (Scheme 1)

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 ^{1}H NMR spectrum of **6a** showed two multiplets at δ 2.70, 3.08 for two CH_2 groups and two singlets at δ 4.23, 5.94 (D_2O-exchangeable) corresponding to two NH_2 groups.

The reaction of either **3a** or **3b** with ethyl acetoacetate (**7**) in 1,4-dioxan containing piperidine gave the amide derivatives **8a**,**b**. The structures of the latter products were confirmed on the basis of analytical and spectral data. The downfield chemical shift of CH_3 groups in compounds **8a**,**b** are δ 3.14 and 3.20, respectively, is due to the existence of the $COCH_2CO$ moiety directly attached to the CH_3 group. The ^{13}CNMR data of **8a** showed signals at δ 34.1 (CH_3), 54.9, 64.3, 77.9 (3 CH_2), 90.0 (C), 120.9 (CN), 121.4, 123.8, 138.1, 140.7 (thiophene C), 176.5, 177.5, 183.0 (3 C=O).

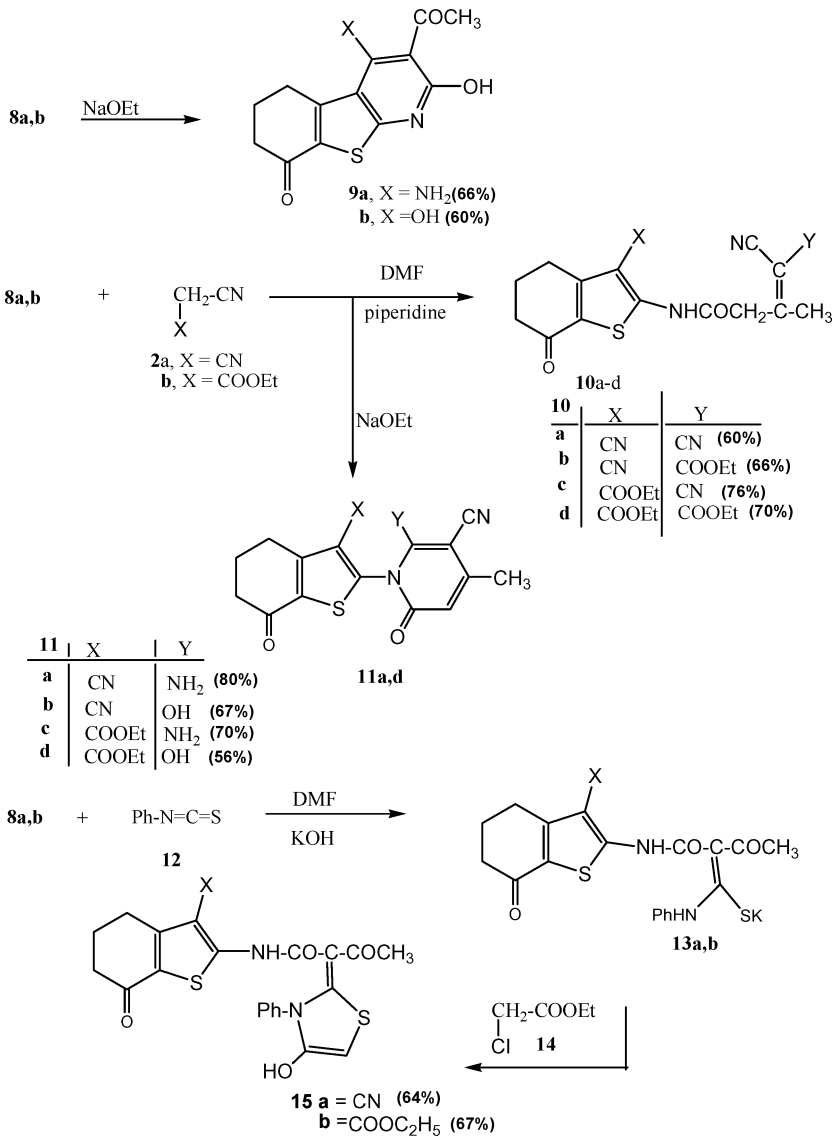
Compounds **8a**,**b** underwent ready cyclization when heated in sodium ethoxide solution to give the 7-oxocyclohexeno[*b*]thieno[5,4:2,3] pyridino[*b*]thieno[5,4-b]pyridine derivatives **9a**,**b** respectively. Structures of compounds **9a–b** were based on analytical and spectral data. The ^{13}C NMR spectrum of **9a** showed signals at δ 30.3 (CH_3), 50.6, 64.7 (2 CH_2), 88.2 (C), 120.6, 122.0, 122.8, 132.6, 142.7, 144.5 (thiophene and pyridine-C), 169.1, 176.9 (2C=O).



SCHEME 1

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

Recently our research group was interested in a series of reactions involving the reaction of phenyl isothiocyanate with active



SCHEME 2

methylene reagents followed by heterocyclization with α-haloketones. These reactions led to the formation of thiophene as well as thiazole derivatives.[20,21] In continuation of this program, we studied here the reactivity of either **8a**,**b** towards phenyl isothiocyanate (**12**) in basic

dimethylformamide to give the intermediate potassium sulfide salts **13a**,**b**. Reaction of either **13a** or **13b** with ethyl chloroacetate (**14**) gave the thiazole derivatives **15a**,**b**. The structures of the latter products were based on analytical and spectral data (see the Experimental section). Moreover, the reaction of **13a**,**b** with phenacyl bromide (**16**) gave the thiazolidene derivatives **17a**,**b**.

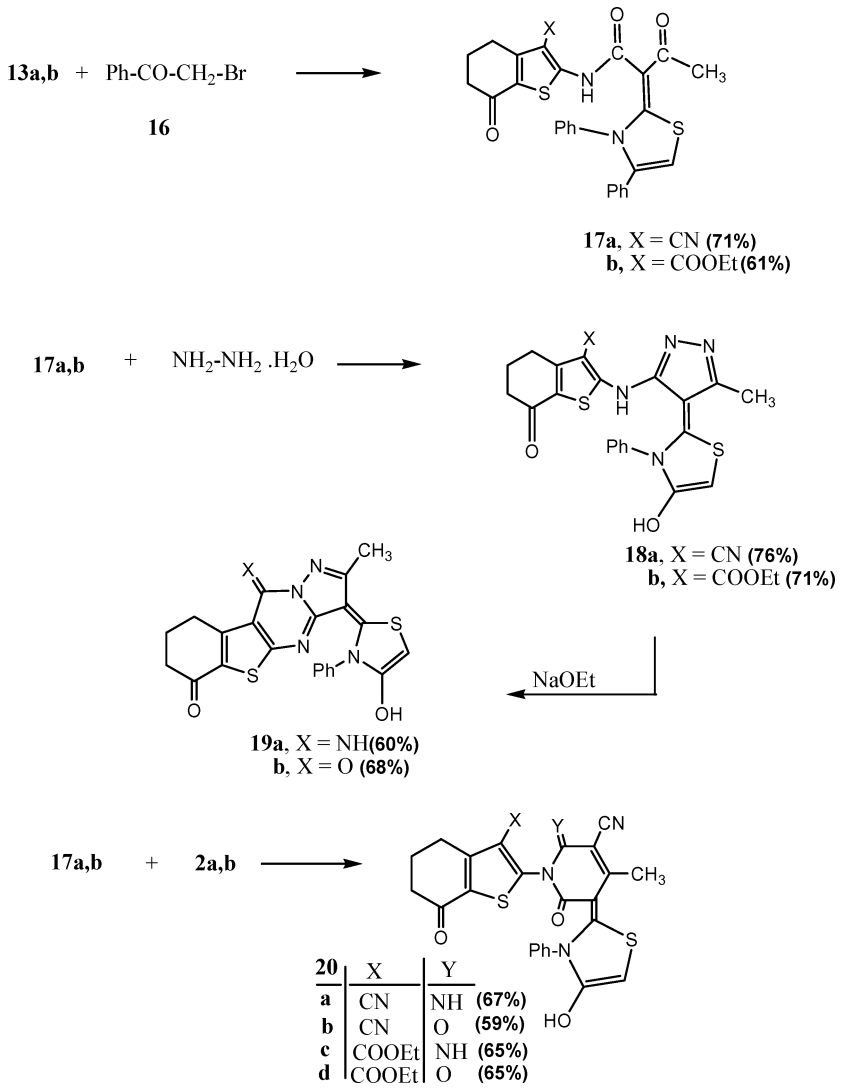
The reaction of either **17a** or **17b** with hydrazine hydrate gave the pyrazole derivatives **18a**,**b** respectively. Compounds **18a**,**b** underwent ready cyclization when heated in sodium ethoxide solution to give the corresponding cyclohexeno[*b*]thieno[5,4:2:3]pyrimidino [5,1:1,2]pyrazole derivatives **19a**,**b**, respectively. On the other hand, the reaction of **17a**,**b** with cyanomethylene reagents was studied, and thus the reaction of **17a**,**b** with either malononitrile (**2a**) or ethyl cyanoacetate (**2b**) gave the pyridine derivatives **20a–d**. The structures of the latter products were based on analytical and spectral data (Scheme 3).

BIOLOGICAL/FUNGICIDAL ACTIVITY

Sclerotium cepivorum Berk is a soilborne fungus that causes the white rot disease of 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 for long periods in unfavorable conditions in the soil. Although several heterocyclic compounds were tried against the sclerotium-forming fungi, however, the antifungal activity of these compounds depends on their chemical structure. Attempts have been made to increase the toxicity of biologically active compounds through introducing efficient functional groups. In this work, we succeeded in synthesizing fused thiophene derivatives and evaluated their bioactivity against the mycelial growth, sclerotial formation, and 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 then transferred to plates containing fresh potato-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 μg cm^{-3}).



SCHEME 3

For each treatment, three Erlenmeyer flasks (250 cm^3), each containing 90 mL of the previously prepared PDA medium, were melted and cooled to about 50°C. Each of the three flasks received 10 cm^3 of prepared stock solutions of thiophene derivatives. A suitable aliquot of each mixture was then poured into each of the six sterile plates (9 cm diameter)

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

Compound No.	Conc. [μg cm^{-3}] 4	Conc. [μg cm^{-3}] 12	Conc. [μg cm^{-3}] 30	Conc. [μg cm^{-3}] 75
5a	88.7	100.0	100.0	100.0
5b	27.5	47.8	72.7	87.4
6a	7.5	8.8	32.3	—
6b	22.3	33.4	37.9	44.1
6c	69.9	100.0	100.0	100.0
6d	25.2	39.8	44.7	88.5
8a	67.6	77.5	100.0	100.0
8b	1.5	4.7	7.8	12.6
9a	22.1	32.4	53.8	66.9
9b	80.0	100.0	100.0	100.0
10a	44.6	59.6	80.4	100.0
10b	33.1	48.1	62.6	74.2
10c	55.2	78.4	100.0	100.0
10d	2.3	4.5	14.7	19.4
11a	11.4	18.6	34.8	44.6
11b	1.8	4.4	22.7	36.4
11d	74.1	100.0	100.0	100.0
15a	69.4	78.5	100.0	100.0
15b	28.8	35.6	47.9	40.3
17a	5.2	7.6	29.5	30.3
17b	43.7	77.2	100.0	100.0
18a	2.5	4.7	16.8	31.7
18b	75.4	100.0	100.0	100.0
20a	21.3	33.8	46.1	88.3
20d	88.7	100.0	100.0	100.0

to form upon solidification, a thin layer at the bottom. Thirty-day-old sclerotia were then individually transferred under aseptic conditions to each of three plates for estimation of percentage germination. The other three plates of each treatment were used for estimation of mycelial growth, sclerotial formation, and sclerotial germination.

As can be seen from Table I, the effectiveness of the synthesized thiophene derivatives depends on the concentration and whether the structure contains either ethyl carboxylate or hydroxyl group. In most cases, the presence of the ethyl carboxylate group induced higher toxicity than the hydroxyl group. Compounds **9b** and **20d** showed the highest toxicity, as both of them bear the ethyl carboxylate and hydroxyl group.

EXPERIMENTAL

Chemistry

All melting points are uncorrected. IR spectra were recorded for (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 DMSO-d_6 as solvent and using TMS as internal standard, and chemical shifts are expressed as δ ppm. Analytical data were recorded at the Microanalytical Data Unit at Cairo University, Giza, Egypt.

Reaction of Compound 1 with Cyanomethylene Reagents: General Procedure for the Synthesis of 3a,b

To a solution of cyclohexan-1,3-dione (**1**) (1.12 g, 0.01 mol) in 1,4-dioxan (40 mL) containing triethylamine (1.0 mL) and sulfur (0.32 g, 0.01 mol), either malononitrile (**2a**) (0.66 g, 0.01 mol) or ethyl cyanoacetate (**2b**) (1.13 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 3 h, then poured onto ice water containing few drops of hydrochloric acid. The formed solid product was collected by filtration and crystallized from the proper solvent.

2-Amino-3-cyano-7-oxocyclohexeno[b]thiophene (3a)

Pale yellow crystals from ethanol, 70% yield (1.35 g), mp 145°C. IR (ν, cm^{-1}): 3058 (CH aromatic), 2985, 2893 (CH_3, CH_2), 2232 (CN), 1684 (C=O), 1650 (C=N), 1640 (C=C). ^{1}H NMR (δ, ppm): 2.72, 2.88 (2m, 4H, $2CH_2$), 2.92 (m, 2H, CH_2), 4.77 (s, 2H, NH_2). Calc. for $C_9H_8N_2OS$ (192.24): C, 56.23; H, 4.19; N, 14.57; S, 16.68. Found: C, 56.27; H, 4.21; N, 14.49; S, 16.70.

Ethyl 2-Amino-7-oxocyclohexeno[b]thiophene-3-carboxylate (3b)

Pale brown crystals from ethanol, 82.4% yield (1.97 g), mp 270°C. IR (ν, cm^{-1}): 3060 (CH aromatic), 2973, 2895 (CH_3, CH_2), 1698, 1680 (2C=O), 1645 (C=N), 1638 (C=C). ^{1}H NMR (δ, ppm): 1.13(t, 3H, $J = 7.22$ Hz, CH_3), 2.73, 2.79 (2m, 4H, $2CH_2$), 2.92 (m, 2H, CH_2), 4.24 (q, 2H, $J = 7.22$ Hz, CH_2), 4.79 (s, 2H, NH_2). Calc. For $C_{11}H_{13}NO_3S$ (239.29): C, 55.21; H, 5.48; N, 5.85; S, 13.40. Found: C, 55.26; H, 5.42; N, 6.04; S, 13.47.

Reaction of Benzaldhyde with 3a,b: General Procedure for the Synthesis of 5a,b

To a solution of either **3a** (1.92 g, 0.01 mol) or **3b** (2.39 g, 0.01 mol) in 1,4-dioxan (30 mL) containing piperidine (0.50 mL), benzaldehyde (**4**)

(1.10 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 5 h then evaporated in vacuum, and the remaining semisolid product was triturated with ethanol. The formed solid product was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-benzalamino-7-oxocyclohexeno[b] thiophene (5a)

Pale yellow crystals from ethanol, 80.3% yield (2.25 g), mp 220°C. IR (ν, cm^{-1}): 3058 (CH aromatic), 2988, 2893 (CH_3, CH_2), 2235 (CN), 1688 (C=O), 1650 (C=N), 1640 (C=C). ^1H NMR (δ, ppm) = 2.75, 2.96 (2m, 4H, $2CH_2$), 2.99 (m, 2H, CH_2), 6.86 (s, 1H, CH=N), 7.03–7.29 (m, 5H, C_6H_5). Calc. For $C_{16}H_{12}N_2OS$ (280.34): C, 68.55; H, 4.31; N, 9.99; S, 11.44. Found: C, 68.71; H, 3.99; N, 9.96; S, 11.50**.**

Ethyl 2-benzalamino-7-oxocyclohexeno[b]thiophene-3-carboxylate (5b)

Pale brown crystals from ethanol, 77% yield (2.52 g), mp 190°C. IR (ν cm^{-1}): 3060 (CH aromatic), 2973, 2895 (CH_3, CH_2), 1698, 1680 (2C=O), 1645 (C=N), 1638 (C=C). ^1H NMR (δ, ppm): 1.14 (t, 3H, $J = 6.21$ *Hz*, CH_3), 2.71–3.02 (2m, 6H, $3CH_2$), 4.26 (q, 2H, J = 6.21 *Hz*, CH_2), 6.93 (s, 1H, CH=N), 7.32, 7.38 (m, 5H, C_6H_5). Calc. for $C_{18}H_{17}NO_3S$ (327.40): C, 66.03; H, 5.23; N, 4.28; S, 9.79. Found: C, 65.92; H, 5.05; N, 4.37; S, 10.01%.

Reaction of 3a,b with Cyanomethylene Reagents: General Procedure for the Synthesis of 6a–d

Equimolar amounts of either **3a** (1.92 g, 0.01 mol) or **3b** (2.39 g, 0.01 mol) in ethanol (40 mL) containing piperidine (0.50 mL), either malnonitrile (**2a**) (0.66 g, 0.01 mol) or ethyl cyanoacetate (**2b**) (1.13 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 8 h then evaporated in vacuum. The remaining product was triturated with ethanol, and the formed solid product was collected by filtration and crystallized from the proper solvent.

3-Cyano-2,4-diamino-8-oxo-cyclohexeno[b]thieno[5,4:2,3] pyridine (6a)

Pale brown crystals from acetic acid, 66.2% yield (1.71 g), mp 165°C. IR (ν, cm^{-1}): 3485, 3340 ($2NH_2$), 2990, 2875(CH_3, CH_2), 2225 (CN), 1680 (C=O), 1645 (C=N), 1630 (C=C). ^1H NMR (δ, ppm) = 2.70, 3.08 (2m, 4H, $2CH_2$), 3.17 (m, 2H, CH_2), 4.23, 5.94 (2s, 4H, $2NH_2$, D_2O exchangeable). Calc. for $C_{12}H_{10}N_4OS$ (258.30): C, 55.80; H, 3.90; N, 21.69; S, 12.41. Found: C, 55.97; H, 4.04; N, 21.89; S, 12.54%.

Ethyl 2,4-Diamino-8-oxo-cyclohexeno[b]thieno[5,4:2,3]pyridine -3-carboxylate (6b)

Orange crystals from 1,4-dioxan, 78.6% yield (2.40 g), mp 221°C. IR (ν, cm^{-1}) 3493–3360 ($2NH_2$), 2978, 2870 (CH_3, CH_2), 1690, 1680 (2C=O), 1660 (C=N), 1645 (C=C). ^1H NMR (δ, ppm): 1.13 (t, 3H, $J =$ 6.68 Hz, CH_3), 2.66, 3.09 (2m, 4H, $2CH_2$), 3.17 (m, 2H, CH_2), 4.26 (q, 2H, $J = 6.68$ Hz, CH_2), 5.31, 5.85 (2s, 4H, $2NH_2$). Calc. for $C_{14}H_{15}N_3O_3S$ (305.35): C, 55.07; H, 4.95; N, 13.76; S, 10.50. Found : C, 55.13; H, 5.08; N, 14.01; S, 10.54%.

2-Amino-3-cyano-4-hydroxy-8-oxo-cyclohexeno[b]thieno[5,4:2,3]-pyridine (6c)

Buff crystals from 1,4-dioxan, 66.4% yield (1.72 g), mp 190°C. IR (ν, cm^{-1}): 3580, 3353 (OH, NH_2) 2975, 2880 (CH_3, CH_2), 2223 (CN), 1698 (C=O), 1655 (C=N), 1630 (C=C). ^1H NMR (δ, ppm): 2.69, 3.12 (2m, 4H, $2CH_2$), 3.17 (m, 2H, CH_2), 5.63 (s, 2H, NH_2), 10.39 (s, 1H, OH). Calc. for $C_{12}H_9N_3O_2S$ (259.28): C, 55.59; H, 3.50; N, 16.21; S, 12.37. Found: C, 55.71; H, 3.67; N, 15.98; S, 12.45%.

Ethyl 2-amino-4-hydroxy-8-oxocyclohexeno[b]thieno[5,4:2,3]-pyridine-3-carboxylate (6d)

Pale yellow crystals from acetic acid, 82.6% yield (2.53 g). mp 150°C. IR (ν, cm^{-1}): 3590–3373 (NH_2, OH), 2960, 2882 (CH_3, CH_2), 1690–1680 (2 C=O), 1650 (C=N), 1640 (C=C). ^1H NMR (δ, ppm): 1.13 (t, 3H, $J =$ 5.68 Hz, CH_3), 2.62, 3.09 (2m, 4H, $2CH_2$), 3.12 (m, 2H, CH_2), 4.22 (q, 2H, $J = 5.68$ Hz , CH_2), 4.88 (s, 2H, NH_2), 10.01 (s, 1H, OH). Calc. for $C_{14}H_{14}N_2O_4S$ (306.34): C, 54.89; H, 4.61; N, 9.14; S, 10.47. Found: C, 54.73; H, 4.66; N, 9.30; S, 10.68%.

Reaction of 3a,b with Ethyl Acetoacetate: General Procedure for the Synthesis of 8a,b

To a solution of either **3a** (1.92 g, 0.01 mol) or **3b** (2.39 g, 0.01 mol) in 1,4-dioxan (60 mL) containing piperdine (1.0 mL), ethyl acetoacetate (**7**) (1.30 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 4 h then poured onto ice water containing few drops of hydrochloric acid. The formed solid product was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-(α-oxo-butyramido-N-yl)-7-oxocyclohexen[b]thiophene (8a)

Orange crystals from acetic acid, 60.5% yield (1.67 g), mp 147°C. IR (ν, cm^{-1}): 3460-3320 (NH), 2960, 2875 (CH_3, CH_2), 2222 (CN),

1696–1683 (C=O), 1640 (C=C). ^{1}H NMR (δ, ppm): 2.68, 2.84 (2m, 4H, $2CH_2$), 2.99 (m, 2H, CH_2), 3.14 (s, 3H, CH_3), 5.21 (s, 2H, CH_2), 8.83 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 34.1 (CH_3), 54.9, 64.3, 77.9 (3 CH_2), 90.0 (C), 120.9 (CN), 121.4, 123.8, 138.1, 140.7 (thiophene C), 176.5, 177.5, 183.0 (3C=O). Calc. for $C_{13}H_{12}N_2O_3S$ (276.31): C, 56.51; H, 4.38; N, 10.14; S, 11.60. Found: C, 56.70; H, 4.57; N, 9.92; S, 11.53%.

Ethyl 2-(β-oxo-butyramido-N-yl)-7-oxocyclohexeno[b]thiophene-3-carboxylate (8b)

Reddish brown crystals (from acetic acid), 62.8% yield (2.03 g), mp 200°C. IR (ν, cm^{-1}): 3490–3330 (NH), 2973, 2890 (CH_3, CH_2), 1705–1680 (4C=O), 1630 (C=C). ^{1}H-NMR (δ, ppm): 1.14 (t, 3H, $J = 7.02$ Hz, CH_3), 2.73, 2.88 (2m, 4H, $2CH_2$), 2.98 (m, 2H, CH_2), 3.20 (s, 3H, CH_3), 4.24 (q, 2H, $J = 7.02$ Hz, CH_2), 4.53 (s, 2H, CH_2), 9.01 (s, 1H, NH). Calc. for $C_{15}H_{17}NO_5S$ (323.36): C, 55.71; H, 5.30; N, 4.33; S, 9.92. Found: C, 55.70; H, 5.62; N, 4.56; S, 10.03%.

General Procedure for the Synthesis of 9a,b

A solution of either **8a** (1.38 g, 0.005 mol) or **8b** (1.61 g, 0.005 mol) in sodium ethoxide (0.005 mol) [prepared by adding sodium metal (0.11 g, 0.005 mol) to absolute ethanol (20 mL)] was heated under reflux in a boiling water bath for 6 h. The reaction mixture was poured in to ice water containing few drops of hydrochloric acid (until pH = 6), and the formed solid product was collected by filtration and crystallized from the proper solvent.

3-Acetyl-4-amino-2-hydroxy-8-cyclohexeno[b]thieno[5,4:2,3]pyridine (9a)

Orange crystals from 1,4-dioxan, 66.6% yield (0.92 g), mp 233°C. IR (ν, cm^{-1}): 3560–3320 (OH, NH_2), 2960, 2873 (CH_3, $2CH_2$), 1696, 1685 (2C=O), 1655 (C=N), 1630 (C=C). ^{1}H NMR (δ, ppm): 2.65, 2.80 (2m, 4H, $2CH_2$), 2.93 (m, 2H, CH_2), 3.09 (s, 3H, CH_3), 4.53 (s, 2H, NH_2), 10.21 (s, 1H, OH). ^{13}C-NMR (DMSO-d_6): δ 30.3 (CH_3), 50.6, 64.7 (2 CH_2), 88.2 (C), 120.6, 122.0, 122.8, 132.6, 142.7, 144.5 (thiophene and pyridine-C), 169.1, 176.9 (2C=O). Calc. for $C_{13}H_{12}N_2O_3S$ (276.31): C, 56.51; H, 4.38; N, 10.14; S, 11.60. Found: C, 56.51; H, 4.70; N, 10.18; S, 11.54%.

3-Acetyl-2,4-dihydroxy-8-oxocyclohexeno-[b]thieno[5,4:2,3]pyridine (9b)

Yellow crystals from DMF, 60% yield (0.83 g), mp 182°C. IR (ν, cm^{-1}): 3575–3340 (2OH), 2890 (CH_2), 1695, 1683(2C=O), 1666 (C=N), 1640

(C=C). ^{1}H NMR (δ, ppm): 2.68, 2.76 (2m, 4H, $2CH_2$), 2.89 (m, 2H, CH_2), 3.09 (s, 3H, CH_3), 9.38, 10.02 (2s, 2H, 2OH). Calc. for $C_{13}H_{11}NO_4S$ (277.30): C, 56.31; H, 4.00; N, 5.05; S, 11.56. Found: C, 56.60; H, 4.16; N, 5.32; S, 11.38%.

Reaction of 8a,b with Cyanomethylene Reagents: General Procedure for the Synthesis of 10a–d

To a solution of either **8a** (1.38 g, 0.005 mol) or **8b** (1.61 g, 0.005 mol) in dimethylformamide (40 mL) containing piperidine (0.50 mL), either malononitrile (**2a**) (0.33 g, 0.005 mol) or ethyl cyanoacetate (**2b**) (0.56 g, 0.005 mol) was added. The reaction mixture was heated under reflux for 6 h then evaporated under vacuum, and the remaining product was triturated with ethanol. The formed solid product, in each case, was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-(α-dicyanomethino-β-ylidino-butyramido-N-yl)-7-oxo-cyclohexeno[b]thiophene (10a)

Pale brown crystals from 1,4-dioxan, 60% yield (0.97 g), mp 244°C. IR (ν, cm^{-1}): 3475–3365 (NH), 2973, 2885 (CH_3,CH_2), 2225, 2222–2218 (3CN) 1685, 1680 (2C=O), 1643 (C=C). ^{1}H NMR (δ ppm): 2.22, 2.67 (2m, 4H, $2CH_2$), 2.85 (m, 2H, CH_2), 3.25 (s, 3H, CH_3), 5.03 (s, 2H, CH_2), 8.73 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 29.5 (CH_3), 53.1, 66.4, 82.3 ($3CH_2$), 117.4, 118.0, 120.1 (3CN), 123.9, 124.0, 134.8, 140.0 (thiophene-C), 78.36, 180.4 (2C=O). Calc. for $C_{16}H_{12}N_4O_2S$ (324.36): C, 59.25; H, 3.73; N, 17.27; S, 9.89. Found: C, 59.40; H, 3.96; N, 17.45; S, 10.15%.

3-Cyano-2-(α-cyanoethoxycarbonylmethino-β-ylidinobutyramido-N-yl)-7-oxocyclohexeno[b]thiophene (10b)

Orange crystals from 1,4-dioxan, 66% yield (1.25 g), mp 222°C. IR (ν, cm^{-1}): 3460–3345 (NH), 2975, 2883 (CH_3, CH_2), 2225-2218(3CN), 1703, 1690–1680 (3C=O),1645 (C=C). ^{1}H NMR (δ, ppm): 1.13 (t, 3H, $J = 5.49$ Hz, CH_3), 2.65, 2.78 (2m, 4H, $2CH_2$), 2.91 (m, 2H, CH_2), 3.21 (s, 3H, CH_3), 4.22 (q, 2H, $J = 5.49$ Hz, CH_2), 4.83 (s, 2H, CH_2), 8.89 (s,1H, NH). Calc. for $C_{18}H_{17}N_3O_4S$ (371.20): C, 58.21; H, 4.61; N, 11.31; S, 8.63. Found: C, 58.34; H, 4.79; N, 11.57; S, 8.94%.

Ethyl 2-(α-Dicyano-methino-β-ylidino-butyramido-N-yl)-7-oxo-cyclohexeno[b]thiophene-3-carboxylate (10c)

Yellow crystals from 1,4-dioxan, 76% yield (1.41 g), mp 236°C. IR (ν, cm^{-1}): 3460–3345 (NH), 2975, 2883 (CH_3, CH_2), 2225-2218 (2CN),

1703, 1690–1680 (3C=O), 1645 (C=C). ^{1}H NMR (δ, ppm): 1.13(t, 3H, $J = 6.92$ Hz CH_3), 2.65, 2.78 (2m, 4H, $2CH_2$), 2.88 (m, 2H, CH_2), 3.21 (s, 3H, CH_3), 4.22 (q, 2H, $J = 6.92$ Hz, CH_2), 4.83 (s, 2H, CH_2), 8.89 (s, 1H, NH). Calc. for $C_{18}H_{17}N_3O_4S$ (371.20): C, 58.21; H, 4.61; N, 11.31; S, 8.63. Found: C, 58.54; H, 4.56; N, 11.42; S, 8.90%.

Ethyl 2-(α-Cyanoethoxycarbonylmethino-β-ylidino-butyramido-N-yl)-7-oxocyclohexeno[b]thiophene-3-carboxylate (10d)

Pale yellow crystals from acetic acid, 70% yield (1.47 g), mp 130°C. IR (ν, cm^{-1}): 3475–3365 (NH), 2220 (CN), 1708–1685 (4C=O), 2970, 2843 (CH_3, CH_2), 1645 (C=C). ^{1}H NMR (δ, ppm): 1.12, 1.14 (2t, 6H, $J = 7.04$ Hz, 6.44 Hz, $2CH_3$), 2.66, 2.73 (2m, 4H, $2CH_2$), 2.77 (m, 2H, CH_2), 2.82 (s, 3H, CH_3), 4.20, 4.27 (2q, 4H, $J = 7.04$ Hz, 6.44 Hz, $2CH_2$), 4.91 (s, 2H, CH_2), 8.30 (s, 1H, NH). Calc. for $C_{20}H_{22}N_2O_6S$ (418.46): C, 57.40; H, 5.30; N, 6.69; S, 7.66. Found: C, 57.23; H, 4.99; N, 7.00; S, 7.52%.

Cyclization of 8a,b with Cyanomethylene Reagents: General Procedure for Synthesis of 11a–d

To a suspension of either **8a** (1.38 g, 0.005 mol) or **8b** (1.61 g, 0.005 mol) in sodium ethoxide [prepared by dissolving sodium metal (0.11 g, 0.005 mol) in absolute ethanol (50 mL)], either malononitrile (**2a**) (0.33 g, 0.005 mol) or ethyl cyanoacetate (**2b**) (0.56 g, 0.005 mol) was added. The reaction mixture, in each case, was heated in a boiling water bath for 6 h. The solid product that formed upon dilution with water containing hydrochloric acid (until pH = 6) was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-(2-amino-3-cyano-4-methyl-6-oxopyridin-1-yl)-7-oxocyclohexeno[b]thiophene (11a)

Orange crystals from ethanol, 80% yield (2.3 g), mp 180°C. IR (ν, cm^{-1}): 3463–3340 (NH_2), 2978, 2883 (CH_3, CH_2), 2225-2220 (2CN), 1695, 1680 (2C=O), 1640 (C=O).^{1}H NMR (δ, ppm): 2.60, 2.78 (2m, 4H, $2CH_2$), 2.84 (m, 2H, CH_2), 3.22 (s, 3H, CH_3), 4.90 (s, 2H, NH_2), 6.63 (s, 1H, Pyridine H-5). ^{13}C NMR (DMSO) δ: 53.8, 66.2, 83.2 (3 CH_2), 118.9, 120.1 (2 CN), 122.0, 123.3, 124.9, 132.2, 142.0, 144.4 (thiophene and pyridine-C), 178.2, 180.5 (2C=O). Calc. for $C_{16}H_{12}N_4O_2S$ (324.36): C, 59.25; H, 3.73; N, 17.27; S, 9.89. Found: C, 59.28; H, 3.86; N, 16.98; S, 10.03%.

3-Cyano-2-(3-cyano-2-hydroxy-4-methyl-6-oxopyridin-1-yl)-7-oxocyclohexeno[b]thiophene (11b)

Reddish brown crystals from ethanol, 67% yield (1.19 g), mp > 300°C. IR (ν, cm^{-1}): 3460–3340 (OH), 2977, 2880 (CH_3, CH_2), 2222-2220 (2CN), 1692, 1685 (2C=O), 1645 (C=C). ^1H NMR (δ, ppm): 2.60, 2.77 (2m, 4H, $2CH_2$), 2.82 (m, 2H, CH_2), 3.26 (s, 3H, CH_3), 6.60 (s, 1H, pyridine-H-5), 8.90 (s, 1H, OH). Calc. for $C_{16}H_{11}N_3O_3S$ (325.34): C, 59.07; H, 3.41; N, 12.92; S, 9.86. Found: C, 59.02; H, 3.68; N, 16.91; S, 10.37%.

Ethyl 2-(2-Amino-3-cyano-4-methyl-6-oxopyridin-1-yl)-7-oxocyclo-hexeno[b]thiophene-3-carboxylate (11c)

Yellow crystals from ethanol, 70% yield (2.3 g), mp 182°C. IR (ν, cm^{-1}): 3465–3340 (NH_2), 2978, 2883 (CH_3, CH_2), 2222 (CN), 1695, 1690, 1680 (3C=O), 1640 (C=C). ^1H NMR (δ, ppm): 1.12 (t, 3H, CH_3), 2.60, 2.70 (2m, 4H, $2CH_2$), 2.84 (m, 2H, CH_2), 3.21 (s, 3H, CH_3), 4.22 (q, 2H, CH_2), 4.90 (s, 2H, NH_2), 6.66 (s, 1H, pyridine H-5). Calc. for $C_{18}H_{17}N_3O_4S$ (371.41): C, 58.21; H, 4.61; N, 11.31; S, 8.63. Found: C, 58.31; H, 4.74; N, 11.29; S, 8.75%.

Ethyl 2-(3-Cyano-2-hydroxy-4-methyl-6-oxopyridin-1-yl)-7-oxocyclohexeno[b]thiophene-3-carboxylate (11d)

Yellowish brown crystals from ethanol, 56% yield (1.0 g), mp 220°C. IR (ν, cm^{-1}): 3463-3343 (OH), 2975, 2880 (CH_3, CH_2), 2222 (CN), 1692, 1690, 1680 (3C=O), 1640 (C=O). ^1H-NMR (δ, ppm): 1.16 (t, 3H, $J = 6.48$ Hz, CH_3), 2.61, 2.75 (2m, 4H, $2CH_2$), 2.86 (m, 2H, CH_2), 3.24 (s, 3H, CH_3), 4.26 (q, 2H, $J = 6.48$ Hz, CH_2), 6.66 (s, 1H, pyridine-H-5), 10.20 (s, 1H, OH). Calc. for $C_{18}H_{16}N_2O_5S$ (372.40): C, 58.05; H, 4.33; N, 7.52; S, 8.61 Found: C, 58.14; H, 4.18; N, 7.82; S, 8.81%.

Reaction of 10a,b with Phenyl Isothiocyanate and α-Haloketones: General Procedure for Synthesis of 15a,b and 17a,b

To a solution of either **10a** (1.62 g, 0.005 mol) or **10b** (1.85 g, 0.005 mol) in DMF (20 mL), phenyl isothiocyanate (**12**) (0.67 g, 0.005 mol) and potassium hydroxide (0.28 g, 0.005 mol) were added. The reaction mixture was heated under reflux in a water bath for 3 h. To the reaction mixture, either ethyl chloroacetate (**14**) (0.60 g, 0.005 mol) or phenacyl bromide (**16**) (1.00 g, 0.005 mol) was added and left overnight. The solid product that formed upon pouring into an ice water mixture containing a few drops of hydrochloric acid was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-[α-oxo-β-(3-phenyl-4-oxo-thiazolideno-2-ylideno)-butyramido-N-yl]-7-oxocyclohexeno[b]thiophene (15a)

Yellow crystals from ethanol, 64% yield (1.45 g), mp 190°C. IR (ν, cm^{-1}): 3480–3375 (NH), 3060 (CH aromatic), 2970, 2884 (CH_3, CH_2), 2225 (CN), 1707, 1690–1680 (4C=O), 1640 (C=C). ^{1}H NMR (δ, ppm): 2.23–2.26 (m, 4H, $2CH_2$), 2.30–2.36 (m, 2H, CH_2), 3.28 (s, 3H, CH_3), 6.86 (s, 1H, thiazole H-5), 7.32–7.43 (m, 5H, C_6H_5), 8.81 (s, 1H, NH), 10.23 (s, 1H, OH). Calc. for $C_{22}H_{17}N_3O_4S_2$(451.52): C, 58.52; H, 3.79; N, 9.31; S, 14.20. Found: C, 58.47; H, 3.58; N, 9.34; S, 14.16%.

Ethyl 2-[α-Oxo-β-(3-phenyl-4-oxo-thiazolideno-2-ylideno)-butyramido-N-yl]-7-oxocyclohexen[b]thiophene-3-carboxylate (15b)

Pale yellow crystals (from 1,4-dioxan), 67% yield (1.67 g), mp 200°C. IR (ν, cm^{-1}): 3480–3375 (NH), 3060 (CH aromatic), 2983, 2879 (CH_3, CH_2) 1710, 1690-1675 (4C=O), 1640 (C=C). ^{1}H-NMR (δ, ppm): 1.14 (t, 3H, $J = 6.40$ Hz, CH_3), 2.30–2.36 (m, 2H, CH_2), 2.64, 2.80 (2m, 4H, $2CH_2$), 3.24 (s, 3H, CH_3), 4.21 (q, 2H, $J = 6.40$ Hz, CH_2), 5.69 (s, 2H, CH_2), 6.81 (s, 1H, thiazole H-5), 7.30, 7.40 (m, 5H, C_6H_5), 8.76 (s, 1H, NH), 10.04 (s, 1H, OH). Calc. for $C_{24}H_{22}N_2O_6S_2$(498.57): C, 57.82; H, 4.45; N, 5.62; S, 12.86. Found: C, 57.90; H, 4.42; N, 5.78; S, 12.73%.

3-Cyano-2-[α-oxo-β-(3,4-dipheno-thiazolo-2-ylidino)-butyramido-N-yl-7-oxocyclohexeno[b]thiophene (17a)

Orange crystals from 1,4-dioxan, 71% yield (1.82 g), mp 168°C. IR (ν, cm^{-1}): 3480–3364 (NH), 3050 (CH aromatic), 2990, 2870 (CH_3, CH_2), 2227 (CN), 1704–1680 (3C=O), 1640 (C=C). ^{1}H-NMR (δ, ppm): 2.24–2.26 (m, 4H, $2CH_2$), 2.34–2.38 (m, 2H, CH_2), 3.20 (s, 3H, CH_3), 6.99 (s, 1H, thiazole H-5), 7.32–7.40 (m, 10H, $2C_6H_5$), 8.94 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 35.0 (CH_3), 50.5, 68.9 (2 CH_2), 120.1 (CN), 120.9, 126.4, 125.3, 133.8, 136.1, 145.8 (thiophene and thiazole-C), 177.2, 179.6, 180.3 (3C=O). Calc. for $C_{28}H_{21}N_3O_3S_2$(511.37): C, 65.80; H, 4.10; N, 8.21; S, 12.53. Found: C, 65.64; H, 3.86; N, 8.45; S, 12.84%.

Ethyl 2-[α-Oxo-β-(3,4-dipheno-thiazolo-2-ylidino)butyramido-N-yl]-7-oxocyclohexeno[b]thiophene-3-carboxylate (17b)

Pale yellow crystals from ethanol, 60.75% yield (1.69 g), mp 170°C. IR (ν, cm^{-1}): 3483–3368 (NH), 3050 (CH aromatic), 2990, 2870 (CH_3, CH_2), 2227 (CN), 1704–1680 (3C=O), 1640 (C=C). ^{1}H-NMR (δ, ppm): 1.13 (t, 3H, $J = 5.68$ Hz, CH_3), 2.64, 2.80 (2m, 4H, $2CH_2$), 3.01 (m, 2H, CH_2), 3.22 (s, 3H, CH_3), 4.26 (q, 2H, $J = 5.68$ Hz, CH_2), 6.99 (s, 1H, thiazole H-5), 7.31–7.37 (m, 10H, 2 C_6H_5), 8.77 (s, 1H, NH). Calc. for

$C_{30}H_{26}N_2O_5S_2$(558.37): C, 64.52; H, 4.65; N, 5.01; S, 11.48. Found: C, 64.44; H, 4.87; N, 5.24; S, 11.25%.

Reaction of Hydrazine Hydrate with 17a,b: General Procedure for the Synthesis of 18a,b

To a solution of either **17a** (2.55 g, 0.005 mol) or **17b** (2.79 g, 0.005 mol) in ethanol (50 mL), hydrazine hydrate (0.25 g, 0.005 mol) was added. The reaction mixture was heated under reflux for 4 h, then it was poured in to ice water containing a few drops of hydrochloric acid. The formed solid product was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-[5-methyl-4-ylideno-(4-oxo-3-phenyl-thiazolideno-2-yl)pyrazolo-3-yl]-7-oxocyclohexeno[b]thiophene (18a)

Orange crystals from acetic acid, 76% yield (1.70 g), mp 264–266°C. IR (ν, cm^{-1}): 3466–3380 (NH), 3060 (CH aromatic), 2988, 2884 (CH_3, CH_2), 2225 (CN), 1706, 1685 (2C=O), 1663 (C=N), 1640 (C=C). ^1H NMR (δ, ppm): 2.66, 2.81 (2m, 4H, $2CH_2$), 3.21 (s, 3H, CH_3), 2.89 (s, 2H, CH_2), 6.97 (s, 1H, thiazole H-5), 7.31–7.39 (m, 5H, C_6H_5), 8.33 (s, 1H, NH), 10.23 (s, 1H, OH). Calc. for $C_{22}H_{17}N_5O_2S_2$(447.32): C, 59.06; H, 3.80; N, 15.64; S, 14.33. Found: C, 60.15; H, 4.06; N, 15.99; S, 14.68%.

Ethyl 2-[5-methyl-4-ylideno-(4-oxo-3-phenyl-thiazolideno-2-yl)-pyrazolo-3-yl]-7-oxocyclohexeno[b]thiophene-3-carboxylate (18b)

Yellow crystals from acetic acid, 70.8% yield (1.75 g), mp 235°C. IR (ν, cm^{-1}): 3460–3385 (NH), 3068 (CH aromatic), 2973, 2898 (CH_3, CH_2), 1703, 1690–1680 (3C=O), 1655 (C=N), 1640 (C=C). ^1H NMR (δ, ppm): 1.16 (t, 3H, CH_3), 2.61, 2.77 (2m, 4H, $2CH_2$), 3.11 (s, 3H, CH_3), 4.24 (q, 2H, CH_2), 2.32 (s, 2H, CH_2), 6.96 (s, 1H, thiazole H-5), 7.30–7.37 (m, 5H, C_6H_5), 8.36 (s, 1H, NH), 10.03 (s, 1H, OH). Calc. for $C_{24}H_{22}N_4O_4S_2$ (494.32): C, 58.31; H, 4.45; N, 11.32; S, 12.97. Found: C, 58.29; H, 4.36; N, 11.49; S, 13.01%.

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

A suspension of either **18a** (2.23 g, 0.005 mol) or **18b** (2.47 g, 0.005 mol) in sodium ethoxide solution (0.005 mol) was heated in a boiling water bath for 2 h. The reaction mixture was poured in to ice water containing few drops of hydrochloric acid (until pH = 7) and the formed solid

product was collected by filtration and crystallized from the proper solvent.

1-(4-Hydroxy-3phenyl-3H-thiazol-2-ylidene)-4-imino-2-methyl-1,4,6,7-tetrahydro-5H-9-thia-3,3a,10-triaza-cyclopenta[b]-fluoren-8-one (19a)

White crystals from ethanol, 60% yield (1.35 g), mp 180°C. IR (ν, cm^{-1}): 3475–3360 (NH), 3063 (CH aromatic), 2970, 2882 (CH_3, CH_2), 1720, 1691 (2C=O), 1670 (exocyclic C=N), 1635 (C=C). ^{1}H NMR (δ, ppm): 2.22–2.25 (m, 4H, $2CH_2$), 2.36 (s, 2H, CH_2), 3.22 (s, 3H, CH_3), 6.20 (s, 1H, thiazole H-5), 7.30–7.42 (m, 5H, C_6H_5), 8.92 (s, 1H, NH), 10.05 (s, 1H, OH). Calc. for $C_{22}H_{17}N_5O_2S_2$(447.08): C, 59.04; H, 3.83; N, 15.65; S, 14.33. Found: C, 59.01; H, 3.65; N, 15.78; S, 14.44%.

1-(4-Hydroxy-3phenyl-3H-thiazol-2-ylidene)-2-methyl-6,7-dihydro-1H,5H-9-thia-3,3a,10-triaza-cyclopenta[b]fluoren-4,8-dione (19b)

Yellow crystals from 1,4-dioxan, 68% yield (1.52 g), mp 170°C. IR (ν, cm^{-1}): 3056 (CH aromatic), 2972, 2878 (CH_3 , CH_2), 1710, 1706, 1688 (3C=O), 1663 (C=N), 1643 (C=C). ^{1}H-NMR (δ, ppm): 2.65–2.80 (2m, 6H, $3CH_2$), 3.07 (s, 3H, CH_3), 6.22 (s, 1H, thiazole H-5), 7.30–7.32 (m, 5H, C_6H_5), 10.10 (s, 1H, OH). Calc. for $C_{22}H_{16}N_4O_3S_2$(448.07): C, 58.91; H, 3.60; N, 12.49; S, 14.30. Found : C, 58.71; H, 3.80; N, 12.59; S, 14.28%.

Reaction of 17a,b with Cyanomethylenes: General Procedure for the Synthesis of 20a–d

To a solution of either **17a** (2.55 g, 0.005 mol) or **17b** (2.79 g, 0.005 mol) in ethanol (40 mL) containing piperidine (0.50 mL), either malononitrile (**2a**) (0.33 g, 0.005 mol) or ethyl cyanoacetate (**2b**) (0.56 g, 0.005 mol) was added. The reaction mixture, in each case, was heated under reflux for 6 h, then evaporated in vacuum. The remaining product was triturated with ethanol, and the formed solid product was collected by filtration and crystallized from the proper solvent.

3-Cyano-2-[3-cyano-4-methyl-2-imino-6-oxo-5-(3-phenyl-4-oxo-thia-zolideno-2-ylideno)pyridin-1-yl]-7-oxocylohexeno[b]-thiophene (20a)

Brown crystals from acetic acid, 67% yield (1.68g), mp 176°C. IR (ν, cm^{-1}): 3463–3384 (OH, NH) , 3053 (CH aromatic), 2983, 2890 (CH_3, CH_2), 2227–2220 (2CN), 1702–1685 (3C=O), 1650 (C=N), 1630 (C=C). ^{1}H-NMR (δ, ppm): 2.66–2.79 (2m, 6H, $3CH_2$), 3.43 (s, 3H, CH_3), 6.26 (s,

1H, thiazole H-5), 7.34–7.80 (m, 5H, C_6H_5), 8.93(s, 1H, NH), 10.38 (s, 1H, OH). Calc. for $C_{25}H_{17}N_5O_3S_2$(499.34): C, 60.12; H, 3.40; N, 14.01; S, 12.84. Found: C, 59.98; H, 3.26; N, 13.87; S, 13.02%.

3-Cyano-2-[3-cyano-4-methyl-2,6-dioxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-7-oxocylohexeno[b]thiophene (20b)

Orange crystals from 1,4-dioxan, 59% yield (1.47 g), mp 180°C. IR (ν, cm^{-1}): 3520–3330 (OH), 3056 (CH aromatic), 2934, 2866 (CH_3, CH_2), 2225, 2220 (2CN), 1720, 1685–1682 (4C=O), 1643 (C=C). ^{1}HNMR (δ, ppm): 2.64, 2.80 (2m, 4H, $2CH_2$), 3.32 (s, 3H, CH_3), 6.28 (s, 1H, thiazole H-5), 6.45 (s, 2H, CH_2), 7.32–7.36 (m, 5H, C_6H_5), 10.32 (s, 1H, OH). Calc. for $C_{25}H_{16}N_4O_4S_2$(500.33): C, 60.01; H, 3.19; N, 11.19; S, 12.81. Found: C, 59.77; H, 3.35; N, 11.16; S, 12.72%.

Ethyl 2-[3-Cyano-4-methyl-2-imino-6-oxo- 5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-7-oxocylohexeno[b]-thiophene-3-carboxylate (20c)

Yellow crystals from 1,4-dioxan, 65% yield (1.77 g), mp 190°C. IR (ν, cm^{-1}): 3455–3365 (NH), 3053 (CH aromatic), 2968, 2875 (CH_3, CH_2), 2223 (CN), 1695–1680 (3C=O), 1648 (C=N), 1640 (C=C). ^{1}H-NMR (δ, ppm): 1.13 (t, 3H, $J = 7.30$ Hz, CH_3), 2.64–2.82 (2m, 6H, $3CH_2$), 3.25 (s, 3H, CH_3), 4.26 (q, 2H, $J = 7.30$ Hz, CH_2), 6.34 (s, 1H, thiazole H-5), 7.30–7.35 (m, 5H, C_6H_5), 8.55 (s, 1H, NH), 10.28 (s, 1H, OH). Calc. for $C_{27}H_{22}N_4O_5S_2$(546.34): C, 59.35; H, 4.02; N, 10.25; S, 11.73. Found: C, 59.44; H, 4.10; N, 10.19; S, 12.00%.

Ethyl 2-[3-Cyano-4-methyl-2,6-dioxo-5-(3-phenyl-4-oxo-thiazolideno-2-ylideno)pyridin-1-yl]-7-oxocylohexeno[b]-thiophene-3-carboxylate (20d)

Reddish brown crystals from 1,4-dioxan, 65% yield (1.82 g), mp 155°C. IR (ν, cm^{-1}): 3053 (CH aromatic), 2968, 2875 (CH_3, CH_2), 2223 (CN), 1695–1680 (4C=O), 1648 (C=N), 1640 (C=C). ^{1}H NMR (δ, ppm): 1.13 (t, 3H, $J = 7.22$ Hz, CH_3), 2.64, 2.82 (2m, 6H, $3CH_2$), 3.23 (s, 3H, CH_3), 4.22 (q, 2H, $J = 7.22$ Hz, CH_2), 6.34 (s, 1H, thiazole H-5) 7.30–7.33 (m, 5H, C_6H_5), 10.34 (s, 1H, OH). Calc. for $C_{27}H_{21}N_3O_6S_2$(547.09): C, 59.22; H, 3.87; N, 7.67; S, 11.71. Found: C, 59.54; H, 3.58; N, 8.00; S, 11.73%.

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