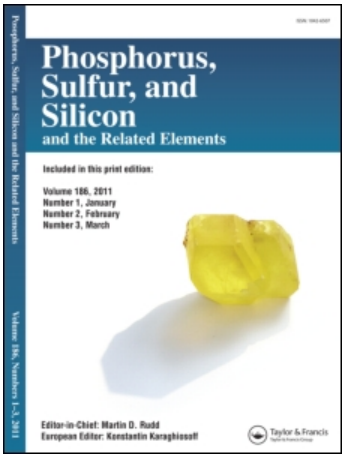

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Uses of 2-Amino-3-cyano-5,5-dimethyl-7-oxocyclohexano[*b*]thiophene in Heterocyclic Synthesis

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To cite this Article Wardakhan, Wagnat W. , Yousef, Adel M. and Hamed, Faten I.(2007) 'Uses of 2-Amino-3-cyano-5,5-dimethyl-7-oxocyclohexano[*b*]thiophene in Heterocyclic Synthesis', Phosphorus, Sulfur, and Silicon and the Related Elements, 182: 7, 1507 — 1523
To link to this Article: DOI: 10.1080/10426500701247052
URL: http://dx.doi.org/10.1080/10426500701247052

Phosphorus, Sulfur, and Silicon, 182:1507–1523, 2007

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701247052

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Uses of 2-Amino-3-cyano-5,5-dimethyl-7-oxocyclohexano[*b*]thiophene in Heterocyclic Synthesis

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*The reaction of 2-diazo-3-cyano-5,5-dimethyl-7-oxocycloheneno-[b]thiophene (**4**) with the active methylene reagents **2**, **5**, **12a,** or **12b** gave the hydrazo derivatives **6a,b** and **13a,b**, respectively. The reactivity of the latter products towards different reagents was studied to give pyrazole, pyridazine, 1,2,4-triazine, and thieno[3,4-d]pyridazine derivatives. The antimicrobial and antifungal activities of the newly synthesized products were measured against the three bacterial isolates (Bacillus Subtillis, Escherichia Coli, and Pseudomonas Aeruginosa) and the three fungal isolates (Candida Albicans, C. Glabrata, and A. Fumigatus).*

Keywords Dimedone; cyclohexeno[b]thiophene; pyrazole; pyridazine

INTRODUCTION

Interest in synthesising new benzo[*b*]thiophene derivatives continues as more of their biological activities, amongst other applications, have been discovered.[1] We investigated the formation of novel heterocycles derived from benzo[*b*]thiophene using tetrahydrobenzo[b]thiophenes as the starting materials.[2,3] The importance of such compounds is due to their diverse pharmaceutical activities including, antibacterial,[4] imminomodulatory[5] anti-inflammatory,[6] antiplatelet-activating factor,[7]and antiviral activities.[8]

Received September 18, 2006; accepted December 11, 2006.
W. W. Wardakhan thanks Professor Dr. V. Jager, University of Stuttgart, Germany, for his kind hospitality and affording facilities to complete this work.
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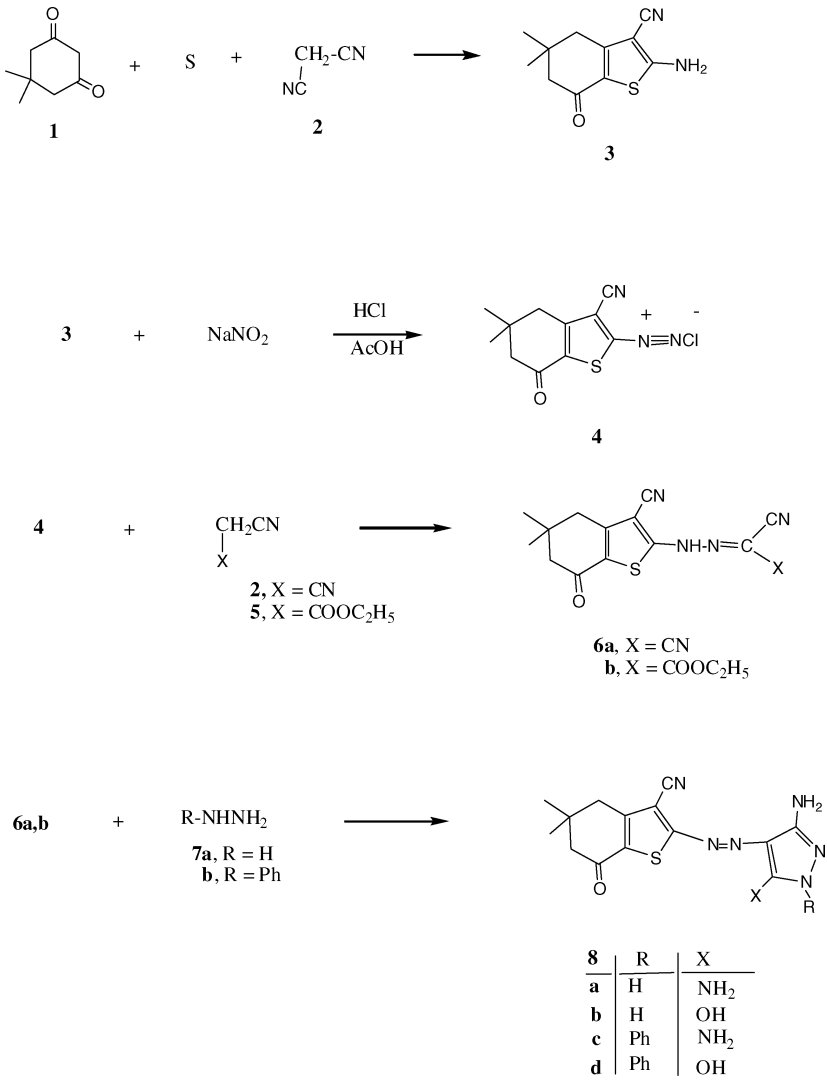
RESULTS AND DISCUSSION

In continuation of our previous work, we studied the uses of 2-amino-3-cyano-5,5-dimethyl-7-oxo-cyclohexano[b]thiophene (**3**) obtained according to literature procedures[9] through the reaction of dimedone (**1**) with malononitrile (**2**) and elemental sulphur in heterocyclic synthesis. Thus, the reaction of compound **3** with sodium nitrite at 0–5°C in acetic/HCl solution gave the non isolable diazonium salt **4**. The reaction of **4** with either malononitrile (**2**) or ethyl cyanoacetate (**5**) afforded the hydrazone derivatives **6a,b**, respectively. The structures of the latter products were based on analytical and spectral data. Thus, the ^{1}HNMR spectrum of **6a** showed two singlets at δ 0.90, 1.06 corresponding to two CH_3 groups, two multiplets at δ 2.45, 2.52 corresponding to two CH_2groups and a singlet at δ 8.40 corresponding to NH group. Further confirmations for the structure of either **6a** or **6b** were obtained through studying their reactivity towards some chemical reagents. Thus, the reaction of either **6a** or **6b** with either hydrazine hydrate (**7a**) of phenylhydrazine (**7b**) afforded the pyrazole derivatives **8a–d**, respectively (Scheme 1). The analytical and spectral data are consistent with the proposed structures (see Experimental section).

The reactivity of **6a,b** with cyanomethylene reagents was studied in the aim to form azine derivatives with potential biological activity. Thus, the reaction of either **6a** or **6b** with either malononitrile (**2**) or ethyl cyanoacetate (**5**) gave the pyridazine derivatives **9a–d**. The structures of the latter products were based on analytical and spectral data. On the other hand, the reaction of either **6a,b** with phenylisothiocyanate (**10**) gave the 1,2,4-triazine derivatives **11a** and **11b**, respectively.

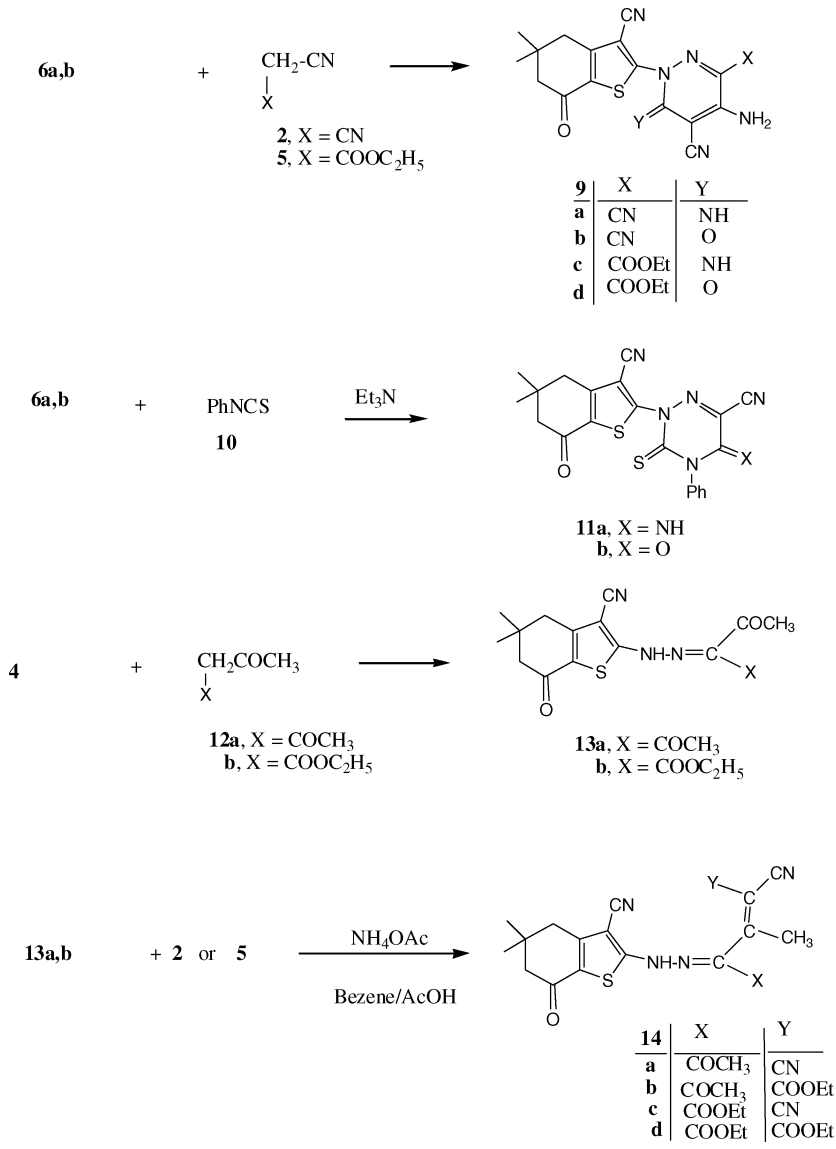
Next, we studied the coupling reaction of the diazoinum salt **3** with 1,3-dicarbonyl compounds. Thus, the reaction of **2** with either acetylactone (**12a)** or ethyl acetoacetate (**12b)** gave the hydrazone derivatives **13a** and **13b**, respectively. Structures of the latter products were established on the basis of analytical and spectral data. Thus the ^{1}HNMR of **13a** showed two singlets at δ 0.88, 0.98 corresponding to two CH_3 groups a multiplet at δ 2.19–2.24 corresponding to two CH_2 groups, two singlets at δ 2.67, 2.81 corresponding to two CH_3 groups, and a singlet at δ 8.02 corresponding to an NH group. Moreover, the ^{13}CNMR of **13b** showed δ at 18.5, 21.1, 27.4, 31.5 ($4CH_3$), 35.6 (C-5 cyclohexene) 50.8, 56.0 ($2CH_2$ cyclohexane); 60.6 (ester CH_2), 116.1 (CN); 102.9, 138.2, 144.4, 149.1 (thiophene carbons); 151.9 (C=N); 172.0, 190.4, 191.0 (3C=O). *DEPT* showed *Up lines* δ at 18.57, 21.1, 27.7, and 31.5 ($4CH_3$). *Down lines* at δ 50.8, 56.0, 60.6 ($3CH_2$), and 35.6 C-5 cyclohexene).

The acetyl group present in either **13a** or **13b**, underwent ready condensation with cyanomethylene reagents. Thus, with either



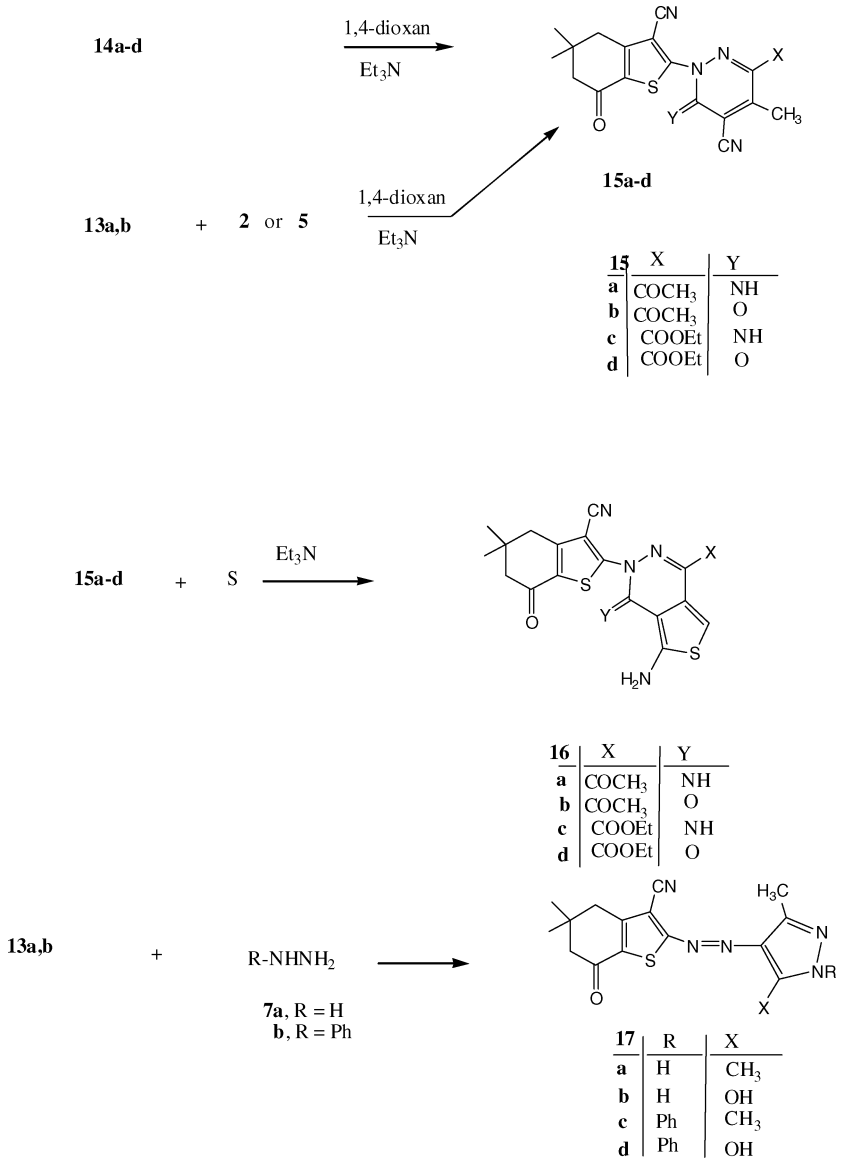
SCHEME 1

malononitrile (**2**) or ethyl cyanoacetate (**5**) in benzene/acetic acid containing ammonium acetate, the condensed derivatives **14a–d** were formed (Scheme 2). The structures of the latter compounds were based on analytical and spectral data. Thus the ^{13}C NMR spectrum of **14a** showed δ 18.1, 22.7, 26.5, 26.7 ($4CH_3$), 35.3 (C-5 cyclohexene), 34.1, 48.9 ($2CH_2$), 83.1, 88.4, 88.9, 145.1, 148.2, 163.8, (thiophene C, C=C), 116.7, 117.2, 118.7 (3CN), 156.8 (C=N), 194.1 (C=O).



SCHEME 2

Compounds **14a–d** underwent ready cyclization when heated under reflux in 1,4-dioxan solution containing a catalytic amount of triethylamine to give the pyridazine derivatives **15a–d**, respectively. The structures of the latter products were established on the basis of analytical and spectral data. Further confirmations were obtained through the



SCHEME 3

synthesis of **15a–d** via another reaction rout. Thus, the reaction of either **13a** or **13b** with either malononitrile (**2**) or ethyl cyanoacetate (**5**) in 1,4-dioxan containing a catalytic amount of triethylamine gave the same products **15a–d** (finger print IR, m.p., and mixed m.p.).

Compounds **15a–d** containing the o-methyl group to the cyano group showed interesting reactivity towards electrophilic reagents. Thus, compounds **15a–d** reacted with elemental sulfur in refluxing 1,4-dioxan and the presence of a catalytic amount of triethylamine to give the thieno[3,4-d]pyridazine derivatives **16a–d**. Similar thiophene derivatives were reported before in the literature.[10,11] Structures of **16a–d** were established on the basis of analytical and spectral data (see Experimental section). Compounds **13a** and **13b** reacted with either hydrazine hydrate (**7a**) or phenylhydrazine (**7b**) to give the pyrazol derivatives **17a–d** derivatives (Scheme 3).

Bioassay

There is considerable interest in the chemotherapeutic activity of azole and azine nucleus attached to a benzo[b]thiophene moiety. This includes anticancer,[12] antiviral,[13] anticonvulsant,[14] anti-inflammatory,[15] and antitubercular Agent.[16,17] In the present study, this strategy was used for the synthesis of these compounds in the hope that they may show different biological activities.

Screening for Antimicrobial and Antifungal Activity

Experimental Procedure

The preliminary antimicrobial activity of the synthesized derivatives was determined in vitro by filter paper disc method.[18] Three bacterial isolates (*Bacillus Subtillis, Escherichia Coli,* and *Pseudomonas Aeruginosa*) and three fungal isolates (*Candida Albicans*, *C. Glabrata,* and *A. Fumigatus*) were used as test organisms. The culture media were normal nutrient agar for bacteria, *Sabouraud* dextrose agar for Candida spp.and Czapek's Dox Agar for *A. Fumigatus*. Filter paper discs (7.0 mm diameter) and punched from No. 1 Whatman filter paper were sterilized by autoclaving followed by drying at 40°C for 1 h. It was then impregnated with 50 μg/ml tested compound in dimethylformamide (DMF). The sterile medium was inoculated onto the surface with the test organism so that each 100 ml of the medium received 1 mL of a 24 h culture of the bacterium or 3-day-old culture of spore suspension of the fungus. After the inoculum has dried, the dried discs were placed on the medium. A control disc (DMF) was also placed onto the medium. The plates were incubated at 37°C and the resulting inhibition zones were measured.

Results

As revealed from the results, most of the synthesized compounds showed antibacterial and/or antifungal activities. The most toxic

TABLE I Inhibition Zones in mm for Some of the Synthesized Compounds at Concentration Level of 50 ug/ml

Compd. no.	*B. Subtillis*	*E. Coli*	*P. Aeruginosa*	*C. Albicans*	*C. Glabrata*	*A. Fumigatus*
6a	3	4	5	—	—	—
6b	—	—	—	3	—	—
8a	3	4	5	—	—	—
8b	—	—	—	—	—	—
8c	26	20	6	10	12	3
8d	12	8	10	3	6	4
9a	7	5	8	4	6	3
9b	5	4	6	3	5	3
9c	11	11	11	5	6	4
9d	—	—	—	3	—	—
11a	24	20	29	14	16	22
11b	28	26	29	27	25	24
13a	11	9	9	7	7	5
13b	17	20	19	16	17	16
14a	11	11	11	5	6	4
14b	8	6	7	—	—	—
14c	18	16	20	24	14	12
14d	28	26	29	27	25	24
15a	8	6	7	—	—	—
15b	17	20	19	16	17	16
15c	11	11	11	5	6	4
15d	8	6	7	—	—	—
16a	—	—	—	—	—	—
16b	28	26	29	27	25	24
17a	8	6	7	—	—	—
17b	27	23	20	24	18	12
17c	24	22	29	20	28	24

—:no inhibition zone.

compounds (inhibition zone = 15–28 mm) against bacterial and fungal isolates were compounds **8c**, **8d**, **11a**, **11b**, **13b**, **14c**, **14d**, **15b**, **16b**, **17b,** and **17c**. The test microorganisms were less sensitive to compounds **6a**, **8a**, **9a**, **9c**, **13a**, **14a**, **14b,** and **15c**; these compounds were slightly effective only on *C. Albicans*. The test isolates were not sensitive to compounds **6b, 8b, 9d,** and**16a,** and these compounds did not exert inhibition zone against the bacterial or fungal isolates.

CONCLUSION

In this article describe's we the uses of 2-amino-3-cyano-5,5-dimethyl-7-oxo-cyclohexano[b]thiophene (**3**) to synthesize many heterocyclic compounds. Most of the synthesized products are pyridazines and pyrazoles. The collected data showed that many of the newly synthesized products have high toxicity.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded for (KBr) discs on Pye Unicam SP-1000 Spectrophotometer ^{1}HNMR Spectra were measured on a Varian EM-390-200 MHz and Bruker AVANCE DRX-500 in CD_3SOCD_3 as solvent using TMS as internal standard and chemical shifts are expressed as δ, ^{13}CNMR spectra were measured on Bruker AVANCE DRX-500.

3-Cyano-2-hydrazo(α-cyanoacetonitrilo)-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (6a), ethyl 2-hydrazo(α-ethoxycarbonylacetonitrilo)-5,5-dimethyl-7-oxocyclohexeno[b]thiophene (6b), 3-cyano-2-hydrazo(acetylacetono)-5,5-dimethyl-7-oxocyclohexeno[b]thiophene (13a) and 3-cyano-2-hydrazo(ethyl acetoacetato)-5,5-dimethyl-7-oxocyclohexeno[b]thiophene (13b) (General Procedure)

A cold solution (0–5°C) of compound **3** (0.01 mol, 2.2 g) in acetic acid/hydrochloric acid (1:3) 15 mL, sodium nitrite solution (1.38 g, 0.02 mol) was added. The reaction mixture was stirred for 15 min. The clear diazonium salt solution was then added dropwise to a solution of either malononitrile (0.66 g, 0.01 mol), ethyl cyanoacetate (1.13 g, 0.01 mol), acetyl acetone (1.0 g, 0.01 mol), or ethyl acetoacetate (1.29 g, 0.01 mol) in ethanol (50 mL) containing sodium acetate (4.0 g) at 0–5°C. After the addition of diazonium salt was completed, the reaction mixture was stirred at room temperature overnight, and the solid product formed; in each case, was collected by filtration.

6a: Brown crystals (from EtOH), yield 67% (2.0 g), m.p. 201–204°C. IR (υ/cm^{-1})= 3652–3184 (NH), 2957–2870 (CH_3, CH_2), 2225–2211 (3CN), 1680 (C=O), 1656 (C=N), 1635 (C=C).^{1}HNMR δ= 0.90, 1.06 (2s, 6H, 2CH_3), 2.45-2.52 (m, 4H, 2CH_2), 8.40 (s, 1H, NH). ^{13}C NMR δ 27.3, 27.8 (2 CH_3), 31.2 (cyclohexene C-5), 38.1, 50.7 (2 CH_2), 114.2, 114.8, 118.4 (3 CN), 99.4, 142.1, 144.7, 147.4 (thiophene C), 162.3 (C=N), 188.3 (CO). *Calculated for* $C_{14}H_{11}N_5OS$ (297.34): C, 56.55; H, 3.73; N, 23.55; S, 10.78. Found: C, 56.39; H, 3.77; N, 23.89; S, 11.06.

6b: Orange crystals (from ethanol), yield 58% (2.0 g), m.p. 180°C. IR (υ/cm^{-1})= 3691–3131 (NH), 2932-2873 (CH_3, CH_2); 2222, 2212 (2CN), 1687, 1680 (2C=O), 1660 (C=N), 1614 (C=C). ^{1}HNMR δ= 0.89, 0.97 (2s, 6H, 2CH_3), 1.13 (t, 3H, J = 7.04 Hz, CH_3), 2.30–2.39 (m, 4H, 2CH_2), 4.22 (q, 2H, J = 7.04 Hz, CH_2), 8.93 (s, 1H, NH). ^{13}C NMR δ 16.6 (ester CH_3), 26.9, 27.3 (2 CH_3), 31.0 (cyclohexene C-5), 38.4, 50.2 (2 CH_2), 58.9 (ester CH_2), 114.8, 118.4 (2 CN), 99.2, 141.8, 143.2, 147.1 (thiophene C), 160.9 (C=N), 160.4, 190.3 (2 CO). *Calculated*

for $C_{16}H_{16}N_4O_3S$ (344.39): Calcd.: C, 55.80; H, 4.68; N, 16.27; S, 9.31. Found: C, 56.68; H, 4.90; N, 16.11; S, 9.62.

13a: Orange crystals (from acetic acid), yield 80% (2.65 g), m.p. 190°C. IR (υ/cm^{-1})= 3520–3313 (NH), 2931–2873 (CH_3, CH_2), 2210 (CN), 1692–1685, 1680 (3C=O), 1640 (C=N), 1612 (C=C). ^{1}HNMR δ= 0.88, 0.98 (2s, 6H, $2CH_3$), 2.19–2.24 (m, 4H, $2CH_2$), 2.67, 2.81 (2s, 6H, CH_3), 8.02 (s, 1H, NH). ^{13}C NMR δ= 18.5, 21.1, 26.6, 26.1 ($4CH_3$), 35.6 (cyclohexene C-5) 50.8, 56.0 (cyclohexene $2CH_2$); 115.8 (CN); 101.1, 138.82, 144.6, 148.8 (thiophene C); 152.6 (C=N); 185.2, 191.4, 194.3 (3C=O). *Calculated for* $C_{16}H_{17}N_3O_3S$ (331.39): C, 57.99; H, 5.17; N, 12.68; S, 9.68. Found: C, 58.05; H, 5.38; N, 12.96; S, 9.42.

13b: Reddish brown crystals (from EtOH), yield 49% (1.78 g), m.p. 198°C. IR (υ/cm^{-1})= 3649–3180 (NH), 2957–2871 (CH_3, CH_2), 2214 (CN), 1692–1685, 1670 (3C=O), 1650 (C=N), 1630 (C=C). ^{1}H NMR: δ= 0.87, 0.99 (2s, 6H, $2CH_3$), 1.36 (t, 3H, J = 6.55 Hz, CH_3), 2.17-2.26 (m, 4H, $2CH_2$), 2.60 (s, 3H, CH_3), 4.26 (q, 2H, J = 6.55 Hz, CH_2), 8.22 (s, 1H, NH).^{13}C NMR δ= 18.5, 21.1, 27.4, 31.5 ($4CH_3$), 35.6 (cyclohexene C-5) 50.8, 56.0 (cyclohexane $2CH_2$); 60.6 (ester CH_2), 116.1 (CN); 102.9, 138.2, 144.4, 149.1 (thiophene carbons); 151.9 (C=N); 172.0, 190.4, 191.0 (3C=O). *DEPT* showed *Up lines* δ 18.57, 21.1, 27.7, 31.5 ($4CH_3$). *Down lines* δ 50.8, 56.0, 60.6 ($3CH_2$), 35.6 (cyclohexene C-5). *Calculated for* $C_{17}H_{19}N_3O_4S$ (361.42): C, 56.50; H, 5.30; N, 11.63; S, 8.87. Found: C, 56.22; H, 5.69; N, 11.89; S, 8.93.

2-Diazo(3,5-diamino-1H-pyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclo-hexeno[b]thiophene (8a), 2-diazo(3-amino-5-hydroxy-1H-pyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiophene (8b), 2-diazo(3,5-diamino-1-phenylpyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (8c), 2-diazo(3-amino-5-hydroxy-1-phenyl-pyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiophene (8d), 2-diazo(3,5-di-methyl-1H-pyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (17a), 2-diazo(3-methyl-5-hydroxy-1H-pyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (17b), 2-diazo(3,5-di-methyl-1-phenylpyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (17c), and 2-diazo(3-methyl-5-hydroxy-1-phenylpyrazol-4-yl)-3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophene (17d) (General Procedure)

To a solution of either **6a** (2.97 g, 0.01 mol), **6b** (3.44 g, 0.01 mol), **13a** (3.31 g, 0.01 mol), or **13b** (3.61 g, 0.01 mol) in ethanol (50 mL) either

hydrazine hydrate (0.50 g, 0.01 mol) or phenylhydrazine (1.82 g, 0.01 mol) was added. The reaction mixture, in each case, was heated under reflux for 7h, and then poured onto ice/water mixture containing a few drops of hydrochloric acid. The solid product formed, in each case, was collected by filtration.

8a: Pale yellow crystals from 1,4-dioxan, yield 72% (2.38 g) and m.p. > 300°C. IR (υ/cm^{-1})= 3580 – 3323 ($2NH_2$), 2958, 2872 (CH_3, CH_2), 2212 (CN), 1689 (C=O), 1650 (C=N), 1629 (C=C). ^{1}H NMR δ 0.86, 0.95 (2s, 6H, $2CH_3$), 2.15–2.29 (m, 4H, $2CH_2$), 4.11, 4.45 (2s, 4H, $2NH_2$), 11.20 (s, 1H, NH). ^{13}C NMR δ = 24.7, 24.9 (2 CH_3), 32.6 (cyclohexene C-5), 37.6, 51.6 (2 CH_2), 88.3 (pyrazole C-4), 118.4 (CN), 133.9, 135.8, 144.7, 154.3, 157.0, 158.9 (thiophene C, pyrazole C-3, C-5), 189.5 (CO). *Calculated for* $C_{14}H_{15}N_7OS$ (329.38): C, 51.05; H, 4.59; N, 29.77; S, 9.73. Found: C, 50.88; H, 4.69; N, 29.88; S, 9.74.

8b: Yellow crystals from 1,4-dioxan, yield 83% (2.75 g), m.p. 230–233°C. IR (υ/cm^{-1})= 3564, 3422 (OH, NH_2); 2925–2857 (CH_3, CH_2), 2212 (CN), 1690 (C=O), 1646 (C=N), 1630 (C=C). ^{1}H NMR δ= 0.88, 0.97 (2s, 6H, $2CH_3$), 2.10–2.26 (m, 4H, $2CH_2$), 4.45 (s, 2H, NH_2), 11.20 (s, 1H, NH), 13.36 (s, 1H, OH). *Calculated for* $C_{14}H_{14}N_6O_2S$ (330.36): C, 50.90; H, 4.27; N, 25.44; S, 9.71. Found: C, 51.21; H, 4.47; N, 25.67; S, 9.84.

8c: Buff crystals from ethanol, yield 78.5% (3.18 g) and m.p. 164°C. IR (υ/cm^{-1})= 3568–3250 ($2NH_2$), 3060 (CH aromatic), 2931, 2869 (CH_3, CH_2), 2210 (CN), 1685 (C=O), 1660 (C=N), 1616 (C=C). ^{1}H NMR δ= 0.84, 0.94 (2s, 6H, $2CH_3$), 2.13–2.25 (m, 4H, $2CH_2$), 4.23, 4.47 (2s, 4H, $2NH_2$), 7.30–7.38 (m, 5H, C_6H_5).^{13}C NMR δ = 24.4, 24.8 (2 CH_3), 32.2 (cyclohexene C-5), 37.3, 51.1 (2 CH_2), 88.6 (pyrazole C-4), 117.2 (CN), 122.3, 124.6, 129.1, 129.8, 133.3, 135.5, 146.5, 152.0, 156.9, 158.8 (benzene, thiophene C, pyrazole C-3, C-5), 190.3 (CO). *Calculated for* $C_{20}H_{19}N_7OS$ (405.48): C, 59.24; H, 4.72; N, 24.18; S, 7.91. Found: C, 59.44; H, 4.82; N, 24.08; S, 8.32.

8d: Orange crystals from ethanol yield 84% (3.43 g) and m.p. 202-205oC. IR (υ/cm^{-1})= 3560, 3232 (NH_2, OH), 3055 (CH aromatic), 2954, 2869 (CH_3, CH_2), 2214 (CN), 1688 (C=O), 1651 (C=N), 1596 (C=C). ^{1}H NMR δ= 0.88, 0.96 (2s, 6H, $2CH_3$), 2.14–2.28 (m, 4H, $2CH_2$), 4.44 (s, 2H, NH_2), 7.28–7.37 (m, 5H, C_6H_5), 13.25 (s, 1H, OH). *Calculated for* $C_{20}H_{18}N_6O_2S$ (406.46): C, 59.10; H, 4.46; N, 20.68; S, 7.89. Found: C, 58.89; H, 4.35; N, 20.55; S, 7.65.

17a: Pale yellow crystals from acetic acid, yield 65% (2.13 g), m.p. 245oC. IR (υ/cm^{-1})= 3651–3397 (NH), 2956–2871 (CH_3, CH_2), 2211 (CN), 1680 (C=O), 1660 (C=N), 1630 (C=C). ^{1}H NMR δ= 0.88, 0.92 (2s, 6H, $2CH_3$), 2.14-2.28 (m, 4H, $2CH_2$), 2.72, 2.81 (2s, 6H, $2CH_3$), 7.33–7.39

(m, 5H, C_6H_5), 11.24 (s, 1H, NH). ^{13}C NMR δ = 9.6, 10.3 (2 CH_3), 24.3, 24.7 (2 CH_3), 32.3 (cyclohexene C-5), 37.6, 51.0 (2 CH_2), 101.2 (pyrazole C-4), 116.9 (CN), 120.3, 130.4, 136.1, 145.9, 150.9, 154.6, 159.6 (thiophene C, pyrazole C-3, C-5), 191.6 (CO). *Calculated for* $C_{16}H_{17}N_5OS$ (327.40): C, 58.70; H, 5.23; N, 21.39; S, 9.79. Found: C, 58.56; H, 5.07; N, 21.62; S, 10.04.

17b: Yellow crystals from acetic acid, yield 73% (2.40 g), m.p. 222–225°C. IR (υ/cm^{-1})= 3588–3325 (OH, NH), 2988, 2867 (CH_3, CH_2), 2222 (CN), 1687 (CO), 1655 (C=N), 1640 (C=C). ^{1}H NMR δ= 0.89, 0.94 (2s, 6H, 2CH_3), 2.19–2.28 (m, 4H, 2CH_2), 2.67 (s, 3H, CH_3), 11.23 (s, 1H, NH), 13.45 (s, 1H, OH). *Calculated for* $C_{15}H_{15}N_5O_2S$ (329.38): C, 54.70; H, 4.59; N, 21.26; S, 9.74. Found C, 55.05; H, 4.83; N, 21.45; S, 9.67.

17c: Yellow crystals from acetic acid, yield 66% (2.9 g), m.p. 150–152°C. IR (υ/cm^{-1})= 3056 (CH aromatic), 2928, 2869 (CH_3, CH_2), 2211 (CN), 1685 (C=O), 1633 (C=N); 1599 (C=C). ^{1}H NMR δ= 0.86, 0.98 (2s, 6H, 2CH_3), 2.16–2.26 (m, 4H, 2CH_2), 2.66, 2.82 (2s, 6H, 2CH_3), 7.26–7.42 (m, 5H, C_6H_5). *Calculated for* $C_{22}H_{21}N_5OS$ (403.50): C, 65.49; H, 5.25; N, 17.36; S, 7.95. Found: C, 65.33; H, 5.08; N, 17.69; S, 8.22.

17d: Pale brown crystals from acetic acid, yield 61% (2.7 g), m.p. 166 °C. IR (υ/cm^{-1})= 3270 (OH), 3053 (CH aromatic), 2931, 2873 (CH_3, CH_2), 2211 (CN), 1680 (C=O), 1650 (C=N), 1613 (C=C). ^{1}H NMR δ= 0.87, 0.96 (2s, 6H, 2CH_3), 2.18–2.30 (m, 4H, 2CH_2), 2.80 (s, 3H, CH_3), 7.28–7.40 (m, 5H, C_6H_5). *Calculated for* $C_{21}H_{19}N_5O_2S$ (405.47): C, 62.21; H, 4.72; N, 17.27; S, 7.91. Found: C, 61.89; H, 4.48; N, 17.07; S, 8.35.

4-Amino-3,5-dicyano-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiophen-2-yl)-6-iminopyridazine (9a), 4-amino-3,5-dicyano-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiophen-2-yl)-6-oxopyridazine (9b), ethyl 4-amino-5-cyano-1-(3-cyano-5,5-dimethyl-7-oxo-cyclohexeno[b]thiophen-2-yl)-6-iminopyridazin-3-carboxylate (9c), ethyl 4-amino-5-cyano-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiophen-2-yl)-6-oxopyridazin-3-carboxylate (9d), 3-acetyl-5-cyano-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiophen-2-yl)-6-imino-4-methylpyridazine (15a), 3-acetyl-5-cyano-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]-thiophen-2-yl)-4-methyl-6-oxopyridazine (15b), ethyl 5-cyano-1-(3-cyano-5,5-dimethyl-7-

oxocyclohexeno[b]thiophen-2-yl)-4-methyl-6-oxopyridazin-3-carboxylate (15d) (General Procedure) (*Continued*)

An equimolar amount of either **6a** (2.97 g, 0.01 mol), **6b** (3.44 g, 0.01 mol), **13a** (3.31 g, 0.01 mol), or **13b** (3.61 g, 0.01 mol) in 1,4-dioxan (40 mL) containing triethylamine (0.5 mL) either malononitrile (0.66 g, 0.01 mol) or ethyl cyanoacetate (1.13 g, 0.01 mol) was added. The reaction mixture, was heated under reflux for 6 h, and then poured onto ice/water mixture containing a few drops of hydrochloric acid. The solid product formed, and in each case, was collected by filtration.

Cyclization of 14a–d into 15a–d

A solution of either **14a** (3.79 g, 0.01 mol), **14b** (4.26 g, 0.01 mol), **14c** (4.09g, 0.01 mol), and **14d** (4.56 g, 0.01 mol) in 1,4-dioxan (40 mL) containing triethylamine (1.0 mL) was heated under reflux for 8 h then left to cool. The solid product formed in each case, upon pouring onto ice/water containing few drops of hydrochloric acid was collected by filtration.

9a: Pale brown powder 1,4-dioxan yield 77% (2.8 g), m.p. > 300°C. IR (υ/cm^{-1})= 3733–3328 (NH_2, NH), 2927, 2873 (CH_3, CH_2), 2225–2220, 2206 (3CN), 1680 (C=O), 1662 (C=N), 1640 (C=C). ^{1}H NMR δ= 0.89, 0.97 (2s, 6H, 2CH_3), 2.16–2.33 (m, 4H, 2CH_2), 4.44 (s, 2H, NH_2), 8.56 (s, 1H, NH). ^{13}C NMR δ= 24.8, 24.9 (2 CH_3), 32.8 (cyclohexene C-5), 37.8, 51.6 (2 CH_2), 113.6, 114.2, 116.9 (3 CN), 89.9, 101.7, 122.3, 134.6, 149.6, 155.4, 157.7, 160.8 (thiophene, pyridazine C), 166.2 (C=N), 189.7 (CO). *Calculated for* $C_{17}H_{13}N_7OS$ (363.40): C, 56.19; H, 3.61; N, 26.98; S, 8.82. Found: C, 55.87; H, 3.92; N, 27.31; S, 9.05.

9b: Orange crystals from acetic acid, , yield 66% (2.4 g) and m.p. 140°C. IR (υ/cm^{-1})= 3488-3334 (NH_2); 2931, 2873 (CH_3, CH_2); 2222, 2214 (2CN); 1688, 1684 (2C=O), 1660 (C=N), 1612 (C=C). ^{1}H NMR δ= 0.84, 0.93 (2s, 6H, 2CH_3), 2.13–2.36 (m, 4H, 2CH_2), 4.46 (s, 2H, NH_2). *Calculated for* $C_{17}H_{12}N_6O_2S$ (364.38): Calcd: C, 56.04; H, 3.32; N, 23.06; S, 8.80. Found: C, 55.86; H, 3.59; N, 22.85; S, 8.69.

9c: Orange crystals from acetic acid, yield 63% (2.6 g,) and m.p. > 300oC. IR (υ/cm^{-1})= 3494–3322 (NH_2, NH); 2970, 2888 (CH_3, CH_2); 2225, 2220 (2CN), 1690, 1686 (2C=O), 1668 (C=N), 1633 (C=C). ^{1}H NMR δ= 0.87, 0.99 (2s, 6H, 2CH_3), 1.33 (t, 3H, J = 6.89 Hz, CH_3), 2.16–2.34 (m, 4H, 2CH_2), 4.23 (q, 2H, J = 6.89 Hz, CH_2), 4.45 (s, 2H, NH_2), 8.89 (s, 1H, NH). ^{13}C NMR δ= 14.6 (ester CH_3), 24.6, 24.7 (2

CH_3), 32.9 (cyclohexene C-5), 37.3, 51.5 (2 CH_2), 60.3 (ester CH_2), 114.5, 116.2 (2 CN), 90.2, 102.4, 121.0, 135.6, 149.2, 156.4, 157.3, 160.1 (thiophene, pyridazine C), 164.8 (C=N), 173.1, 190.2 (2 CO). *Calculated for* $C_{19}H_{18}N_6O_3S$ (410.45): C, 55.60; H, 4.42; N, 20.48; S, 7.81. Found: C, 55.83; H, 4.71; N, 20.73; S, 8.22.

9d: Pale yellow crystals from acetic acid, yield 70% (2.88g), m.p. 207–210°C. IR(υ/cm^{-1})= 3420, 3201 (NH_2), 2930, 2872 (CH_3, CH_2), 2220, 2211 (2CN), 1690, 1688 (2 C=O), 1651 (C=N), 1617 (C=C). ^{1}HNMR δ= 0.97, 1.07 (2s, 6H, 2CH_3), 1.22 (t, 3H, J = 7.34 Hz, CH_3), 2.4, 2.51 (2s, 4H, CH_2), 4.25 (q, 2H, J = 7.34 Hz, CH_2), 5.22 (s, 2H, NH_2). *Calculated for* $C_{19}H_{17}N_5O_4S$ (411.43): C, 55.47; H, 4.16; N, 17.02; S, 7.79. Found: C, 55.81; H, 4.07; N, 16.84; S, 8.11.

15a: Yellow crystals from acetic acid, yield 77% (2.92 g), 60% (2.27 g) from **14a**; m.p. 200–203°C. IR(υ/cm^{-1})= 3465–3222 (NH), 2933, 2879 (CH_3, CH_2), 2227, 2210 (2CN), 1688 (C=O), 1670 (C=N), 1633 (C=C). ^{1}HNMR δ= 0.94, 1.09 (2s, 6H, 2CH_3), 2.22, 2.53 (2s, 4H, CH_2), 2.67, 3.11 (2s, 6H, 2CH_3), 8.76 (s, 1H, NH). ^{13}C NMR δ= 25.2, 25.4 (2 CH_3), 26.8 ($\underline{CH_3}$-CO), 33.1 (cyclohexene C-5), 37.4, 51.4 (2 CH_2), 115.8, 116.6 (2 CN), 88.7, 103.2, 124.3, 134.4, 148.2, 157.2, 158.2, 160.8 (thiophene, pyridazine C), 166.0 (C=N), 1908, 193.5 (2 CO). *Calculated for* $C_{19}H_{17}N_5O_2S$ (379.44): C, 60.14; H, 4.52; N, 18.46; S, 8.45. Found: C, 60.42; H, 4.37; N, 18.79; S, 8.32.

15b: Yellow crystals from acetic acid, yield 66% (2.50 g), 73% (2.77 g) from **14b**; m.p. 116°C. IR (υ/cm^{-1})= 2964, 2866 (CH_3, CH_2), 2220, 2205 (2CN), 1693–1687, 1680 (3C=O), 1660 (C=N); 1632 (C=C). ^{1}HNMR δ= 0.92, 1.11 (2s, 6H, 2CH_3), 2.25, 2.54 (2s, 4H, CH_2), 2.69, 3.19 (2s, 6H, 2CH_3).*Calculated for* $C_{19}H_{16}N_4O_3S$ (380.42): C, 59.99; H, 4.24; N, 14.73; S, 8.43. Found: C, 60.31; H, 4.54; N, 14.89; S, 8.51.

15c: Orange crystals from acetic acid, yield 64% (2.60 g), 55% (2.25 g) from **14c**; m.p. 140°C. IR (υ/cm^{-1})= 3440–3321 (NH), 2977, 2860 (CH_3, CH_2), 2222, 2209 (2CN), 1690, 1683 (2C=O), 1665 (C=N); 1630 (C=C). ^{1}HNMR δ= 0.93, 1.14 (2s, 6H, 2CH_3), 1.16 (t, 3H, J = 7.77 Hz, CH_3), 2.22, 2.48 (2s, 4H, CH_2), 2.67, 3.16 (2s, 6H, 2CH_3), 4.23 (q, 2H, J = 7.77 Hz, CH_2), 8.72 (s, 1H, NH). *Calculated for* $C_{20}H_{19}N_5O_3S$ (409.46): C, 58.67; H, 4.68; N, 17.10; S, 7.83. Found: C, 58.55; H, 4.51; N, 16.89; S, 8.21.

15d: Orange crystals from acetic acid, yield 61% (1.50 g), 68% ((2.78 g); m.p. 140°C. IR (υ/cm^{-1})= 2931, 2873 (CH_3, CH_2), 2210 (CN), 1688–1686, 1680 (3C=O), 1658 (C=N), 1631 (C=C). ^{1}HNMR δ= 0.91, 1.13 (2s, 6H, 2CH_3), 1.15 (t, 3H, J = 6.89 Hz, CH_3), 2.26, 2.45 (2s, 4H, CH_2), 2.68 (s, 3H, CH_3), 4.26 (q, 2H, J = 6.89 Hz, CH_2). *Calculated for* $C_{20}H_{18}N_4O_4S$ (410.45): C, 58.53; H, 4.42; N, 13.65; S, 7.81. Found: C, 58.69; H, 4.71; N, 13.97; S, 8.11.

6-Cyano-4,5-dihydro-4-imino-5-phenyl-3-thioxo-2-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiopheno)-1,2,4-triazine (11a) and 6-Cyano-4,5-dihydro-4-oxo-5-phenyl-3-thioxo-2-(3-cyano-5,5-dimethyl-7-oxocyclo-hexeno[b]thiopheno)-1,2,4-triazine (11b) (General Procedure)

To a solution of either **6a** (2.97 g, 0.01 mol) or **6b** (3.44 g, 0.01mol) in 1,4-dioxan (30 mL) containing triethylamine (0.5 mL) and phenylisothiocyanate (1.35 mL, 0.01 mol) was added. The reaction mixture was heated under reflux for 3h then poured onto ice/water mixture containing few drops of hydrochloric acid and the formed solid product; in each case, it was collected by filtration.

11a: Pale yellow from ethanol yield 55% (2.37 g), m.p. 160°C. IR (υ/cm^{-1})= 3465–3322 (NH), 3060 (CH aromatic), 2970, 2866 (CH_3, CH_2), 2227, 2214 (2CN), 1690–1680 (2C=O), 1650 (C=N), 1612 (C=C).^{1}HNMR δ= 0.97, 1.07 (2s, 6H, $2CH_3$), 2.41, 2.52 (2s, 4H, $2CH_2$), 7.01–7.41 (m, 5H, C_6H_5), 8.63 (s, 1H, NH). *Calculated for* $C_{21}H_{16}N_6OS_2$ (432.08): C, 58.31; H, 3.73; N, 19.43; S, 14.83. Found: C, 58.55; H, 4.01; N, 19.77; S, 15.04.

11b: Yellowish white crystals from ethanol, yield 60% (2.59 g), m.p. 173–176°C. IR (υ/cm^{-1})= 3056 (CH aromatic), 2931, 2873 (CH_3, CH_2), 2220, 2213 (2CN), 1686, 1680 (2C=O), 1650 (C=N), 1613 (C=C). ^{1}HNMR δ= 0.95, 1.11 (2s, 6H, $2CH_3$), 2.38, 2.44 (2s, 4H, $2CH_2$), 7.27–7.38 (m, 5H, C_6H_5). *Calculated for* $C_{21}H_{15}N_5O_2S_2$ (433.07): C, 58.18; H, 3.49; N, 16.16; S, 14.79. Found: C, 57.88; H, 3.74; N, 16.21; S, 15.18.

3-Cyano-5,5-dimethyl-2-hyrazo(γ-acetylα-cyano-β-methylcrtono-nitril-γ-ylideno)-7-oxocyclohexeno[b]thiophene (14a), 3-cyano-5,5-dimethyl-2-hyrazo(ethyl γ-acetylβ-methyl-α-nitrilocrtonoat-γ-ylideno)-7-oxocyclo-hexeno[b]thiophene (14b), 3-cyano-5,5-dimethyl-2-hyrazo(γ-ethoxy-carbonylβ-methylcrtononitril-γ-ylideno)-7-oxocyclo-hexeno-[b]thiophene (14c), 3-cyano-5,5-dimethyl-7-oxo-2-hyrazo(ethyl γ-ethoxycarbonylβ-methylcrtonoat-γ-ylideno)-7-oxocyclohexeno-[b]thiophene (14d). (General Procedure)

To an equimolar amounts of either **13a** (3.31 g, 0.01 mol) or **13b** (3.61 g, 0.01 mol) in a mixture of benzene (60 mL), glacial acetic acid (20

mL), and ammonium acetate (3.0 g) either malononitrile (0.66 g, 0.01 mol) or ethyl cyanoacetate (1.13 g, 0.01 mol) was added. The reaction mixture, in each case, was heated under reflux using isotropic water separator for 6 h, water is separated during the reaction course, then evaporated under vacuum. The remaining product was triturated with dietylether and the formed solid product was collected by filtration.

14a: Pale yellow crystals from 1,4-dioxan, yield 72% (2.72 g), m.p. 180-183°C. IR (υ/cm^{-1})= 3456–3324 (NH), 2976, 2861 (CH_3, CH_2), 2228–2220, 2210(3CN), 1690, 1686 (2C=O), 1656 (C=N), 1638 (C=C). ^{1}HNMR δ= 0.96, 1.07 (2s, 6H, $2CH_3$), 2.24, 2.39 (2s, 4H, $2CH_2$), 2.70, 3.11 (2s, 6H, $2CH_3$), 8.44 (s, 1H, NH). ^{13}C NMR δ= 18.1, 22.7, 26.5, 26.7 ($4CH_3$), 35.3 (cyclohexene C-5), 34.1, 48.9 ($2CH_2$), 83.1, 88.4, 88.9, 145.1, 148.2, 163.8, (thiophene C, C=C), 116.7, 117.2, 118.7 (3CN), 156.8 (C=N), 194.1 (C=O). *Calculated for* $C_{19}H_{17}N_5O_2S$ (379.44): C, 60.14; H, 4.52; N, 18.46; S, 8.45. Found: C, 59.88; H, 4.82; N, 18.33; S, 8.31.

14b: Yellowish white crystals from 1,4-dioxan, yield 63% (2.68 g), m.p. 180–184°C. IR (υ/cm^{-1})= 3555–3326 (NH), 2988, 2876 (CH_3, CH_2), 2227, 2218 (2CN), 1688, 1686 (2C=O), 1660 (C=N), 1632 (C=C). ^{1}HNMR δ= 0.92, 1.12 (2s, 6H, $2CH_3$), 1.14 (t, 3H, J = 6.99 Hz, CH_3), 2.27, 2.41 (2s, 4H, $2CH_2$), 2.68, 3.14 (2s, 6H, $2CH_3$), 4.22 (q, 2H. J = 6.99 Hz, CH_2), 8.46 (s, 1H, NH). *Calculated for* $C_{21}H_{22}N_4O_4S$ (426.49): C, 59.14; H, 5.20; N, 13.14; S, 7.52. Found: C, 59.33; H, 3.22; N, 7.68; S, 7.31.

14c: Orange crystals from 1,4-dioxan/acetic acid, yield 70% (2.68 g), m.p. 234–236°C. IR (υ/cm^{-1})= 3543–3321 (NH), 2982, 2880 (CH_3, CH_2), 2229–2219 (3CN), 1689, 1684 (2C=O), 1655 (C=N), 1636 (C=C). ^{1}HNMR δ= 0.90, 1.08 (2s, 6H, $2CH_3$), 1.13 (t, 3H, J = 7.02 Hz, CH_3), 2.24, 2.39 (2s, 4H, $2CH_2$), 2.73 (s, 3H, CH_3), 4.23 (q, 2H. J = 7.02 Hz, CH_2), 8.34 (s, 1H, NH). *Calculated for* $C_{20}H_{19}N_5O_3S$ (409.46): C, 58.67; H, 4.68; N, 17.10; S, 7.83. Found: C, 58.77; H, 4.71; N, 7.33; S, 8.05.

14d: Pale yellow crystals from ethanol, yield 75% (3.42 g), m.p. 140oC. IR (υ/cm^{-1})= 3552–3321 (NH), 2976, 2863 (CH_3, CH_2), 2219, 2211 (2 CN), 1691, 1686 (3 C=O), 1660 (C=N), 1632 (C=C). ^{1}HNMR δ= 0.92, 1.11 (2s, 6H, $2CH_3$), 1.12, 1.15 (2t, 6H, J = 6.66, 7.16 Hz, $2CH_3$), 2.22, 2.40 (2s, 4H, $2CH_2$), 2.70 (s, 3H, CH_3), 4.23, 4.25 (2q, 4H, J = 6.66, 7.16 Hz, $2CH_2$), 8.30 (s, 1H, NH). *Calculated for* $C_{22}H_{24}N_4O_5S$ (456.51): C, 57.88; H, 5.30; N, 12.27; S, 7.02. Found: C, 58.26; H, 3.05; N, 11.99; S, 7.25.

3-Acetyl-6-amino-7-imino-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno-[b]thiopheno)-thieno[3,4-d]pyridazine (16a), 3-acetyl-6-amino-7-oxo-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]thiopheno)-thieno[3,4-b]pyridazine (16b), ethyl 6-amino-7-imino-1-(3-cyano-5,5-dimethyl-7-oxo-cyclohexeno[b]thiopheno)-thieno[3,4-d]pyridazin-3-carbnxylate (16c), ethyl 6-amino-7-oxo-1-(3-cyano-5,5-dimethyl-7-oxocyclohexeno[b]-thiopheno)-thieno[3,4-d]pyridazin-3-carbnxylate (16d) (General Procedure)

To a solution of either **15a** (3.79 g, 0.01 mol), **15b** (3.80 g, 0.01 mol), **15c** (4.09 g, 0.01 mol), or **15d** (4.10 g, 0.01 mol) in 1,4-dioxan (40 mL) containing triethylamine (1.00 mL), elemental sulfur (0.32 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, in each case, was collected by filtration.

16a: Orange crystals from acetic acid, yield 80% (3.28 g), m.p. 190–192°C. IR (υ/cm^{-1})= 3588–3323 (NH_2, NH), 2976, 2877 (CH_3, CH_2), 2225 (CN), 1692, 1686 (2 C=O), 1670 (C=N), 1634 (C=C). ^{1}HNMR δ= 0.92, 1.18 (2s, 6H, $2CH_3$), 2.21, 2.39 (2s, 4H, $2CH_2$), 3.07 (s, 3H, CH_3), 4.56 (s, 2H, NH_2), 6.88 (s, 1H, thiophene H-2), 10.20 (s, 1H, NH). ^{13}C NMR: δ= 21.3 ($\underline{CH_3}$-CO), 24.6, 24.8 (2 CH_3), 32.8 (cyclohexene C-5), 37.7, 51.8 (2 CH_2), 114.6 (CN), 88.6, 122.3, 124.6, 127.8, 124.9, 141.6, 148.5, 157.3, 159.7, 160.3 (thiophenes, pyridazine C), 190.7, 196.6 (2 CO). *Calculated for* $C_{19}H_{17}N_5O_2S_2$ (411.08): C, 55.46; H, 4.16; N, 17.02; S, 15.58. Found: C, 55.73; H, 4.21; N, 16.84; S, 15.73.

16b: Yellow crystals from acetic acid, yield 69% (2.84 g), m.p. 245–248°C. IR (υ/cm^{-1})= 3576–3318 (NH_2, NH), 2986, 2865 (CH_3, CH_2), 2220 (CN), 1695–1688, 1686 (3C=O), 1661 (C=N), 1638 (C=C). ^{1}HNMR δ= 0.90, 1.12 (2s, 6H, $2CH_3$), 2.25, 2.36 (2s, 4H, $2CH_2$), 3.12 (s, 3H, CH_3), 4.54 (s, 2H, NH_2), 6.67 (s, 1H, thiophene H-2), 10.09 (s, 1H, NH). *Calculated for* $C_{19}H_{16}N_4O_3S_2$ (412.07): C, 55.32; H, 3.91; N, 13.58; S, 15.55. Found: C, 55.43; H, 4.09; N, 13.84; S, 15.82.

16c: Orange crystals from acetic acid, yield 73% (3.22 g), m.p. 130°C. IR (υ/cm^{-1})= 3566–3338 (NH_2, NH), 2987, 2885 (CH_3, CH_2), 2220 (CN), 1693, 1688 (2 C=O), 1668 (C=N), 1637 (C=C). ^{1}HNMR δ= 0.92, 1.11 (2s, 6H, $2CH_3$), 1.34 (t, 3H, J = 7.26 Hz, CH_3), 2.20, 2.33 (2s, 4H, $2CH_2$), 4.22 (q, 2H, J = 7.26 Hz, CH_2), 4.50 (s, 2H, NH_2), 6.64 (s, 1H, thiophene H-2), 9.88 (s, 1H, NH). *Calculated for* $C_{20}H_{19}N_5O_3S_2$ (441.09): C, 54.41; H, 4.34; N, 15.86; S, 14.52. Found: C, 54.25; H, 4.29; N, 15.66; S, 14.72.

16d: Orange crystals from acetic acid, yield 56% (2.47 g), m.p. 180–184°C. IR (υ/cm^{-1})= 3562–3329 (NH), 2977, 2862 (CH_3, CH_2), 2223

(CN), 1693–1688, 1684 (3C=O), 1659 (C=N), 1636 (C=C). ^{1}HNMR δ= 0.90, 1.12 (2s, 6H, $2CH_3$), 1.13 (t, 3H, J = 7.11 Hz, CH_3), 2.23, 2.40 (2s, 4H, $2CH_2$), 4.25 (q, 2H, J = 7.11 Hz, CH_2), 4.53 (s, 2H, NH_2), 6.39 (s, 1H, thiophene H-2). *Calculated for* $C_{20}H_{18}N_4O_4S_2$ (442.08): C, 54.28; H, 4.10; N, 12.66; S, 14.49. Found: C, 54.37; H, 3.86; N, 12.94; S, 14.52.

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