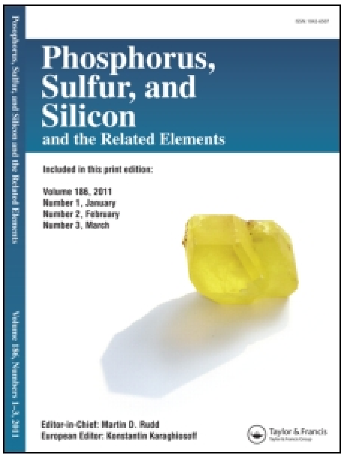

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Reaction of 3-Cyano-2-diazo-4,5,6,7-tetrahydrobenzo[b]thiophene with 3-Imino-butyronitrile: Synthesis of Pyridazines, Thiophenes and Their Fused Derivatives

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REACTION OF 3-CYANO-2-DIAZO-4,5,6,7-TETRAHYDROBENZO[*b*]THIOPHENE WITH 3-IMINO-BUTYRONITRILE: SYNTHESIS OF PYRIDAZINES, THIOPHENES AND THEIR FUSED DERIVATIVES

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The reaction of the 3-cyano-2-diazo-4,5,6,7-tetrahydrobenzo[b*]thiophene 1 with 3-imino-butyronitrile 2 gave the azo derivative (**3**). The reactivity of the latter product toward different reagents was studied to give fused derivatives with potential biological activities.*

Keywords: 3-Imino-butyronitrile; 4,5,6,7-tetrahydrobenzo[*b*]thiophene; pyridazines

During recent years we have maintained a comprehensive program aimed at investigation of the reaction of 2-diazo-4,5,6,7-terahydrobenzo[*b*]thiophene-3-carboxylate with active methylene reagents followed by heterocyclization of the resultant azo derivatives with simple, available regents. Such a synthetic route has been proved to be an easy facile and sole approach for the synthesis of either to unreported derivatives of polyfunctionally substituted thiophenes, 2,3-dihydrothiazoles and thiazolidine.[1,3]

The importance of such compounds is due to their diverse pharmacological activities including antibacterial,[4] immunodulatory,[5] antiflammatory,[6] antidiabatic,[7,8] antiplatelet activating factor,[9] and antiviral activities.[10,11]

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RESULTS AND DISCUSSION

In continuating of our previous work, we report here in the uses of 3-cyano-2-diazo-4,5,6,7-tetrahydrobenzo[*b*]thiophene 1[12] for the synthesis of a variety of azole, azine, or azoloazine derivatives incorporation a tetrahydrobenzo[*b*]thiophene moiety with anticipated biological activity.

The reaction of 3-cyano-2-diazo-4,5,6,7-tetrahydrobenzo[*b*]thiophene **1** with a cold solution (0–5°C) of 2-imino-butyronitrile **2**[13] in ethanol containing sodium acetate gave a single product with molecular formula $C_{13}H_{13}N_5S$. Three possible isomeric structures were proposed for this formula, **3, 4**, and **5**. Structures **4** and **5** were ruled out on the basis of the ^1H NMR spectrum of the reaction product that showed the presence of two singlets (D_2O exchangeable) at δ 8.97 and 9.23 ppm, corresponding to two NH groups together with the absence of any singlet due to a CH group or any NH_2 group stretching through the IR spectrum of the reaction product, which might be expected to appear if neither structure **4** or **5** were considered. The analytical and spectral data are in agree with structure **3**. Further conformation for structure **3** was obtained through studying its reactivity toward various chemical reagents. Thus, heating compounds in refluxing acetic/hydrochloric acid solution gave the *3-cyno-2-hydrazono (3-oxo-butyronitril-2-yl)-4,5,6,7-tetrahydrobenzo[* b*]thiophene* (**6**). The structure of compound **6** was based on analytical and spectral data. The oxo-group in compound **6** showed interesting reactivity toward cyano methylene reagents. Thus, the reaction of **6** with malononitrile in the presence of ammonium acetate gave the corresponding Knoevenagel condensation product **7**. The structure of **7** was established on the basis of IR spectrum, which showed the presence of four CN group stretching at 2225–2210 cm^{-1} and ^{13}C NMR data, which showed the presence of δ 23.2, 23.8 (cyclochexene C-2, C-3), 28.2 (CH_3), 29.7, 30.2 (cyclochexene C-1, C-4), 118.4, 118.6, 119.6, 120.9 (4 CN), 121.0, 122.6 (C=C),* 126.8, 132.2, 133.0, 138.2 (thiophene-C), 158.3 (C=N) ppm. Compound **7** underwent ready cyclization when heated under reflux in sodium ethoxide solution to give **9**. The latter product is formed through the intermediate formation of the 6-iminopyridazine **8** by Micheal addition and hydrolysis (Scheme 1).

The structure of compound **9** was confirmed on the basis of analytical and spectral data. Thus, the IR spectrum of the reaction product showed the presence of two CN group stretching at 2225, 2220 cm^{-1}; moreover the ^1H NMR spectrum revealed, beside the two multiplets characteristic for the two CH_2 groups of the cyclohexene moiety, the

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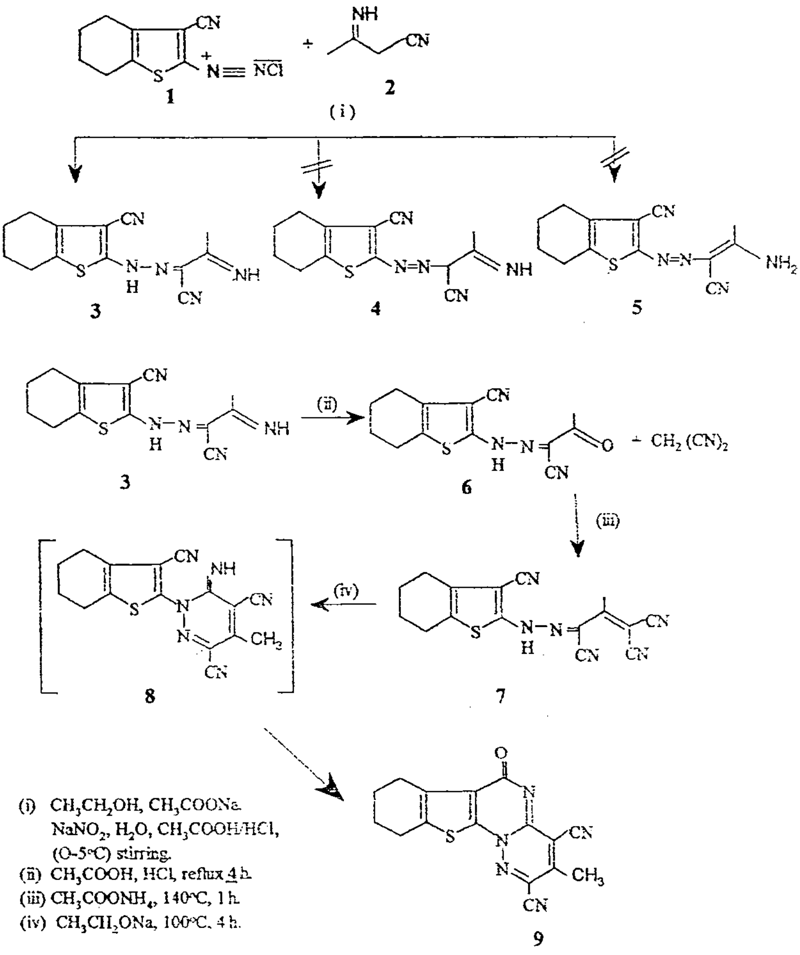
*The C=C group appears at low field due to its conjugation with C≡N and C=N—.

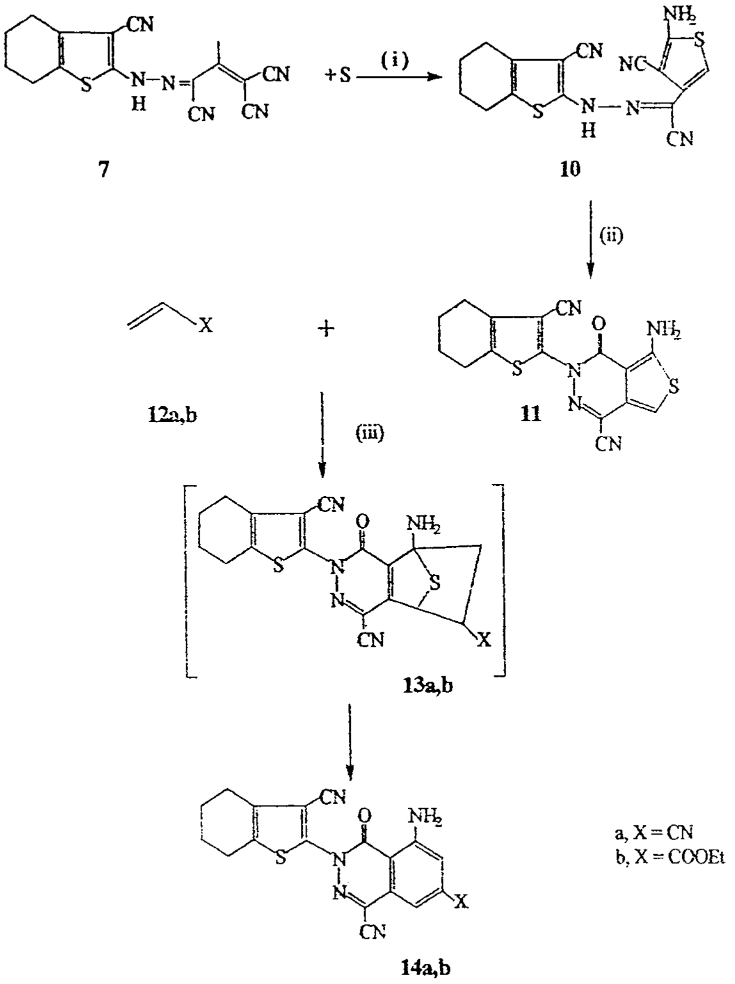


(i) CH_3CH_2OH, CH_3COONa. $NaNO_2$, H_2O, CH_3COOH/HCl, (0-5°C) stirring.
(ii) CH_3COOH, HCl, reflux 4 h.
(iii) CH_3COONH_4, 140°C, 1 h.
(iv) CH_3CH_2ONa, 100°C, 4 h.

SCHEME 1

presence of only a singlet at δ 2.19 ppm characteristic for a CH_3 group.

The reaction of compound **7** with elemental sulfur in the presence of a catalytic amount of triethylamine gave the thiophene derivative **10**.[14,15] The latter underwent ready cyclization when refluxed in dimethylformamide containing triethylamine to give **11**. The structure of **11** was established on the basis of analytical and spectral data. Thus, the ^1H NMR spectrum of the reaction product showed the presence of two multiplets at δ 2.23–2.27 and 2.42–2.47 ppm due to two CH_2 group of the cyclohexene ring, a singlet at δ 5.38 ppm (D_2O exchangeable) corresponding to an NH_2 group and a singlet at δ 6.99 ppm due to the thiophene H-5 proton, moreover, the ^{13}C NMR spectrum, showed δ 23.1, 23.7 (cyclohexene C-2, C-3), 29.6, 30.8 (cyclohexene C-1, C-4), 119.6, 120.3 (2CN), 126.7, 132.2, 133.6, 139.8, 142.1 (pyridazine-C, thiophene-C), 178.40 (CO) ppm. Compound **11** showed an interesting reactivity toward cycloaddition reactions.[16] Thus, **11** reacted with either acrylonitrile **12a** or ethyl acrylate **12b** to give the phthalazine derivatives **14a** and **14b** respectively (Scheme 2). Formation of the



(i) Dioxane, Et$_3$N, S, reflux 4 h.
(ii) DMF, Et$_3$N, reflux 12 h.
(iii) Dioxane, Et$_3$N, reflux 6 h.

SCHEME 2

latter products is explained in terms of the intermediate formation of **13a** and **13b** followed by elimination of hydrogen sulphide. Structures **14a** and **14b** were based on analytical and spectral data (see Experimental).

The reaction of compound **7** with either benzaldehyde **15a** or 4-chlorobenzaldehyde **15b** gave the corresponding arylidene derivatives **16a** and **16b**, respectively, the analytical and spectral data of which are in agree with the proposed structures. The reaction of **16a** with either malononitrile or ethyl cyanoacetate in the presence of triethylamine gave the corresponding benzo[*d*]pyridiazine derivatives **18a** and **18b** respectively. Formation of the latter products was explained in terms of the intermediate formation of **17a** and **17b**, respectively, followed by Michael addition of NH to CN group, hydrolysis, and elimination of hydrogen cyanide. The structures of **18a** and **18b** were based on analytical and spectral data. Further conformation for the proposed structures was obtained through their synthesis via another reaction route. Thus, the reaction of **7** with cinnamonitrile derivatives **19a** and **19b** gave the same products **18a** and **18b** respectively (identical m.p. and mixed m.p.) (Scheme 3).

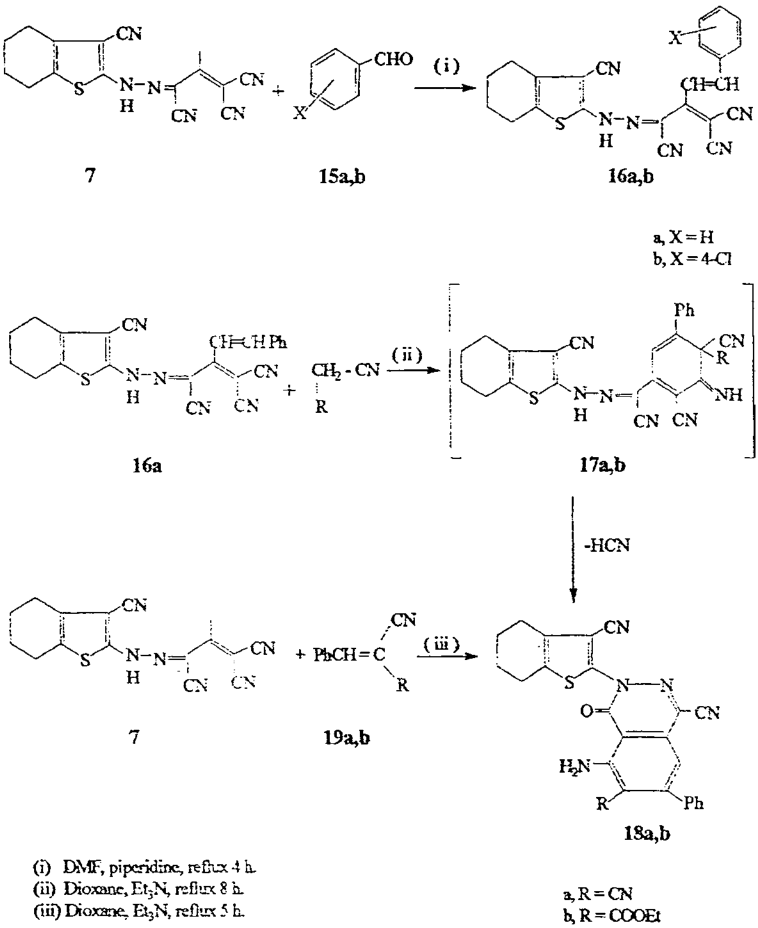
The reaction of compound **6** with ethyl cyanoacetate gave the pyridazine derivative **20**; its structure was based on analytical and spectral data. The latter product reacted with elemental sulfur to give a single product with molecular formula $C_{16}H_{11}N_5S_2O$. Two possible isomeric structures were considered, **11** and **21**. The reaction product was shown to be identical in all respects with compound **11** previously obtained (see Experimental).

The reaction of **20** with benzene diazomium chloride gave the phenylhydrazo derivative **22**. The latter product underwent ready cyclization when heated under reflux in ethanolic/sodium hydroxide solution to give the pyridazo[4,5-*d*]pyridazine derivative **24** via the intermediate formation of **23**.

The presence of the **1,3**-dicarbonyl moiety in compound **24** showed an interesting reactivity characteristic for such a series of compounds. Thus, the reaction of compound **24** with hydrazine hydrate afforded **25**. Moreover, with either urea or thiourea, compound **24** gave **26a** and **26b**, respectively; their structures were confirmed on the basis of analytical and spectral data (Scheme 4).

EXPERIMENTAL

All melting points are uncorrected, the NMR spectra were recorded on a Varian Em-390 (90 MHz), and chemical shifts were expresed as δ values



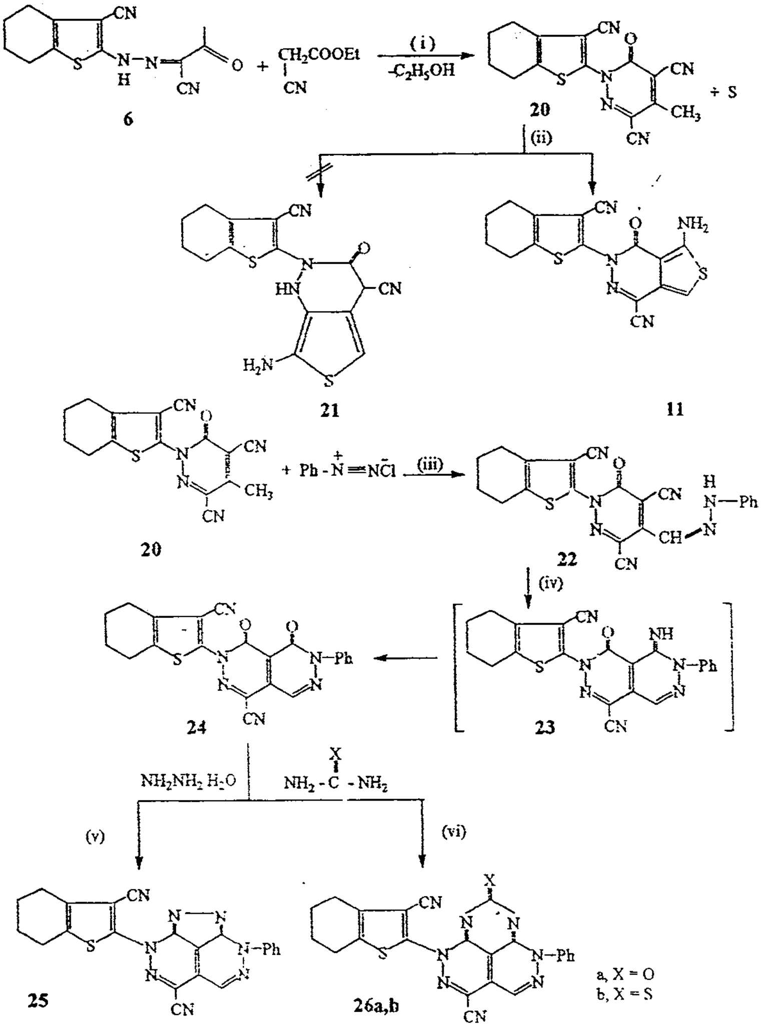
(i) DMF, piperidine, reflux 4 h.
(ii) Dioxane, Et_3N, reflux 8 h.
(iii) Dioxane, Et_3N, reflux 5 h.

SCHEME 3

against SiMe4 as internal standard. IR spectra were recorded as KBr pellets on a Pye Unicam spectrometer.

*3-Cyano-2-hydrazono(3-imino-butyronitril-2-yl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene (3)*

To a cold solution of compound **2** (0.82 g, 0.01 mol), in ethanol (50 ml), sodium acetate (0.82 g, 0.01 mol) and a cold solution of diazonium salt 1 (0.01 mol) (which was prepared by adding $NaNO_2$ [0.7 g, 0.01 mol] solution to a cold solution of the amine precursor 1 [1.47 g, 0.01 mol] in acetic acid [20 ml], HCl [5 ml]) was added dropwise with stirring for 1 h at 0–5°C. The formed solid product was collected by filtration, washed with water, dried, and crystallized from acetic acid, in 80%



(i) CH_3COONH_4, 140°C, 1 h.
(ii) DMF, Et_3N, S, stirring.
(iii) CH_3CH_2OH, 10% NaOH, 0-5°C, stirring.
(iv) CH_3CH_2OH, NaOH, reflux 5 h.
(v) Dioxane, reflux 2 h.
(vi) C_2H_5 ONa, 100°C, heat 5 h.

SCHEME 4

yield; m.p. 180–181°C. IR (KBr) cm^{-1}: 3564–3430 (2NH), 2972–2840 (CH_3, CH_2), 2225, 2220 (2CN); ^1H NMR (DMSO-d_6) ppm: 2.21–2.26 (2m, 4H, $2CH_2$), 2.30–2.34 (2m, 4H, $2CH_2$), 3.21 (s, 3H, CH_3), 8.97, 9.23 (2s, 2H, 2NH). Anal. Calcd. for $C_{13}H_{13}N_5S$ (271.00): C, 57.56; H, 4.97; N, 25.83; S, 11.80. Found: C, 57.50; H, 4.80; N, 25.81, S, 11.80.

3-Cyano-2-hydrazono(3-oxo-butyronitril-2-yl)-4,5,6,7-tetrahydrobenzo[b*]thiophene (6)*

A solution of compound **3** (2.71 g, 0.01 mol) in acetic acid (40 ml) containing HCl (5 ml) was heated under reflux for 4 h and then poured into an icewater mixture containing NaOH (to P^H6). The formed solid product was collected by filtration, washed with cold water several times, dried, and crystallized from acetic acid in 68% yield; m.p. 186–187°C. IR (KBr) cm^{-1}: 3480–3420 (NH), 2980, 2873 (CH_3, CH_2), 2225, 2220 (2CN), 1690 (CO); ^1H NMR (DMSO-d_6) ppm: 2.23–2.26 (2m, 4H, $2CH_2$), 2.33–2.38 (2m, 4H, $2CH_2$), 3.02 (s, 3H, CH_3), 8.90 (s, 1H, NH). Anal. Calcd. for $C_{13}H_{12}N_4OS$ (272): C, 57.35; H, 4.41; N, 20.58; S, 11.76. Found: C, 53.12; H, 4.11; N, 20.32, S, 11.56.

3-Cyano-2-hydrazono(3,3-dicyano-carbonylideno-butyronitril-2-yl)-4,5,6,7-tetrahydrobenzo[b*]thiophene (7)*

To compound **6** (2.88 g, 0.01 mol), malononitrile (0.66 g, 0.01 mol) and amonium acetate (0.77 g, 0.01 mol) were added. The reaction mixture was heated in an oil bath at 140°C for 1 h and left to cool. The solidified product washed with ethanol and collected by filtration, dried, and crystallized from ethanol in 96% yield; m.p. 210–211°C. IR(KBr) cm^{-1}: 3440–3360 (NH), 2990, 2875 (CH_3, CH_2), 2225–2210 (4CN); ^1H NMR (DMSO-d_6) ppm: 2.23–2.25 (m, 4H, $2CH_2$), 2.36–2.38 (m, 4H, $2CH_2$), 8.96 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) ppm: 23.2,23.8 (cyclohexene C-2, C-3), 28.2 (CH_3), 29.7, 30.2 (cyclohexene C-1, C-4), 118.4, 118.6, 119.6, 120.9 (4CN), 121.0, 122.6 (C=C), 126.8, 132.2, 133.0, 138.2 (thiophene-C) 158.3 (C=N). Anal. Calcd. for $C_{16}H_{12}N_6S$ (320): C, 60.00; H, 3.75; N, 26.25; S, 10.00. Found: C, 59.85; H, 3.59; N, 25.39; S, 10.17.

3,5-Dicyano-4-methyl-8-oxo-4,5,6,7-tetrahydrobenzo[b*]-thiophene[2,3:5,6]pyrimidino-[1,6-f]pyridazine (9)*

A suspension of compound **7** (3.2 g, 0.01 mol), in sodium ethoxide (which was prepared by adding sodium metal [0.23 g, 0.01 mol] to absolute ethanol [40 ml]) was heated in a boiling water bath for 3 h and poured into ice-water containing HCl (P^H6). The formed solid product was collected by filtration, dried, and crystallized from DMF in 62% yield; m.p. 158–159°C. IR (KBr) cm^{-1}: 2865 (CH_3), 2225, 2220 (2CN), 1706 (CO); ^1H NMR (DMSO-d_6) ppm: 2.19 (s, 3H, CH_3), 2.24–2.27

(m, 4H, 2CH$_2$), 2.35–2.38 (m, 4H, 2CH$_2$). Anal. Calcd. for $C_{16}H_{11}N_5OS$ (321): C, 59.81; H, 3.43; N, 21.81; S, 9.97. Found: C, 59.64; H, 3.31; N, 21.90; S, 9.81.

3-Cyano-2-hydrazono[(2-amino-3-cyanothiophen-4-yl)acetonitrilo-ylideno]-4,5,6,7-tetrahydrobenzo[b*]thiophene (10)*

To a solution of compound **7** (3.2 g, 0.01 mol), in dioxane (30 ml), Et$_3$N (0.5 ml) and elemental sulfur (0.32 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 4 h and left to cool. The formed solid product upon pouring into ice-water, was collected by filtration, washed with water, dried, and crystallized from ethanol in 63% yield; m.p. 190–191°C. IR (KBr) cm^{-1}: 3480, 3420 (NH$_2$, NH), 2855 (CH$_2$), 2225, 2220, 2215 (3 CN); ^{1}H NMR (DMSO-d_6) ppm: 2.20–2.24 (m, 4H, 2CH$_2$), 2.34–2.36 (m, 4H, 2CH$_2$), 5.55 (s; 2H, NH$_2$), 6.89 (s, 1H, thiophene H-5), 8.84 (s, 1H, NH). Anal. Calcd. for $C_{16}H_{12}N_6S_2$ (352): C, 54.54; H, 3.41; N, 23.86; S, 18.18. Found: C, 54.41; H, 3.32; N, 23.78; S, 18.20.

3-Cyano-2-(6-amino-3-cyano-7-oxo-thieno[3,4- d*]pyridazine)-4,5,6,7-tetrahydrobenzo[* b*]thiophene (11)*

A solution of either compound **10** (3.52 g, 0.01 mol) in DMF (30 ml) containing Et$_3$N (0.5 ml), or compound **20** (3.21 g, 0.01 mol) in DMF (30 ml) containing Et$_3$N (0.5 ml) and elemental sulfur (0.32 g, 0.01 mol) was heated under reflux for 12 h and then evaporated in vacuum. The remaining product was triturated with diethyl ether and the formed solid product was collected by filtration, dried, and crystallized from dioxane in 51% yield; m.p. >300°C. IR (KBr) cm^{-1}: 3470, 3350 (NH$_2$), 2975 (CH$_2$), 2225, 2220 (2CN), 1700 (CO), 1655 (C=N), 1644 (C=C); ^{1}H NMR (DMSO-d_6) ppm: 2.23–2.27 (m, 4H, 2CH$_2$), 2.42–2.47 (m, 4H, 2CH$_2$), 5.38 (s, 2H, NH$_2$), 6.99 (s, 1H, thiophene H-5); ^{13}C NMR (DMSO-d_6) ppm: 23.1, 23.7 (cyclohexene C-2, C-3), 29.6, 30.8 (cyclohexene C-1, C-4), 119.6, 120.3 (2CN), 126.7, 132.2, 133.6, 139.8, 142.1 (pyridazine-C and thiophene-C), 178.4 (CO). Anal. Calcd. for $C_{16}H_{11}N_5OS_2$ (353): C, 54.54; H, 3.41; N, 19.86; S, 18.18. Found: C, 54.43; H, 3.35; N, 19.72; S, 18.12.

Benzo[*d*]pyridazine Derivatives (14a,b) (General Procedure)

Equimolecular amounts of compound **11** (3.53 g, 0.01 mol) and either acrylonitrile **12a** (0.53 g, 0.01 mol), or ethyl acrylate **12b** (1.14 g, 0.01 mol) in dioxane (40 ml) containing Et$_3$N (0.5 ml) were heated under reflux for 6 h until all hydrogen sulfide was liberated. The remaining product, obtained upon evaporating the solution under vacuum, was triturated with ethanol and the formed solid product was collected by filtration, dried, and crystallized from the proper solvent to produce **14a,b**.

*3-Cyano-2-(7-amino-3,5-dicyano-8-oxo-benzo[*d*]pyridazine)-4,5,6,7-tetrahydrobenzo[* b*]thiophene (14a)*

14a crystallized from dioxane in 59% yield; m.p. 233–234°C. IR (KBr) cm^{-1}: 3480, 3360 (NH_2), 2890 (CH_2), 2225, 2215, 2210 (3CN), 1703 (CO), 1645 (C=N), 1638 (C=C); ^1H NMR (DMSO-d_6) ppm: 2.21–2.26 (m, 4H, $2CH_2$), 2.30–2.38 (m, 4H, $2CH_2$), 5.20 (s, 2H, NH_2), 7.32–7.41 (m, 2H, C_6H_2). Anal. Calcd. for $C_{19}H_{12}N_6OS$ (372): C, 61.29; H, 3.22; N, 22.58; S, 8.60. Found: C, 61.22; H, 3.18; N, 22.43; S, 8.57.

*3-Cyano-2-(7-amino-3-cyano-5-ethoxy-carbonyl-8-oxo-benzo[*d*]pyridazine)-4,5,6,7-tetrahydrobenzo[* b*]thiophene (14b)*

14b crystallized from acetic acid in 69% yield; m.p. >300°C. IR (KBr) cm^{-1}: 3480, 3365 (NH_2), 2980, 2880 (CH_3, CH_2), 2225, 2222 (2CN), 1703, 1680 (2 CO), 1645 (C=N), 1638 (C=C); ^1H NMR (DMSO-d_6) ppm: 1.66 (t, 3H, $J = 6.2$ Hz, CH_3), 2.21–2.27 (m, 4H, $2CH_2$), 2.30–2.37 (m, 4H, $2CH_2$), 4.22 (q, 2H, $J = 6.2$ Hz, CH_2),5.20 (s, 2H, NH_2), 7.30–7.38 (m, 2H, C_6H_2). Anal. Calcd. for $C_{21}H_{17}N_5O_3S$ (419): C, 60.14; H, 4.07; N, 16.70; S, 7.37. Found: C, 60.10; H, 4.00; N, 16.81; S, 7.29.

4,5,6,7-Tetrahydrobenzo[*b*]thiophene Derivatives (16a,b) (General Procedure)

To a solution of compound **7** (3.2 g, 0.01 mol) in DMF (40 ml) containing piperidine (0.5 ml), either benzaldehyde (1.06 g, 0.01 mol) or 4-chlorobenzaldehyde (1.41 g, 0.01 mol) was added. In each case the reaction mixture was heated under reflux for 4 h and evaporated in vacuum. The remaining products were collected by filtration and crystallized from the proper solvent to produce **16a,b**.

3-Cyno-2-hydrazono(3,3-dicyano-carbonyl-ideno-4-benzal-butyronitril-2-ylideno)-4,5,6,7-tetrahydrobenzo[b*]-thiophene (16a)*

16a crystallized from ethanol in 80% yield; m.p. 210–211°C. IR (KBr) cm^{-1}: 3461–3340 (NH), 2890 (CH_2), 2225–2210 (4CN), 1640 (C=N); ^1H NMR (DMSO-d_6) ppm: 2.24–2.27 (m, 4H, $2CH_2$), 2.30–2.35 (m, 4H,

$2CH_2$), 6.20–6.23 (d, 2H, J = 3.50 Hz, CH=CH) 7.32–7.40 (m, 5H, C_6H_5), 8.75 (s, 1H, NH). Anal. Calcd. for $C_{23}H_{16}N_6S$ (408): C, 67.64; H, 3.92; N, 20.58; S, 7.84. Found: C, 67.81; H, 3.98; N, 20.43; S, 7.72.

3-Cyano-2-hydrazono[3,3-dicyano-carbonyl-ideno-4-(4-chlorobenzal)-butyronitril-2-ylideno]-4,5,6,7-tetrahydrobenzo[b*]thiophene (16b)*

16b crystallized from ethanol in 72% yield; m.p. 185–186°C. IR (KBr) cm^{-1}: 3520–3330 (NH), 2893 (CH_2), 2225–2212 (4CN), 1642 (C=N), 1638 (C=C); ^1H NMR (DMSO-d_6) ppm: 2.21–2.25 (m, 4CH, $2CH_2$), 2.36–2.39 (m, 4H, $2CH_2$), 6.23–6.27 (d, 2H, J = 3.50 Hz, CH=CH), 7.33–7.40 (m, 4H, C_6H_4), 8.81 (s, 1H, NH). Anal. Calcd. for $C_{23}H_{15}ClN_6S$ (442.5): C, 62.37; H, 3.38; Cl, 8.02; N, 18.98; S, 7.23. Found: C, 62.28; H, 3.41; Cl, 8.12; N, 18.81; S, 7.11.

Benzo[*d*]pyridazine Derivatives (18a,b) (General Procedure)

Method A. For an equimolecular amounts of compound **16a** (4.08 g, 0.01 mol) in dioxane (40 ml) containing Et_3N (0.5 ml) either malonitrile (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 for 8 h. The solid product, formed upon pouring into ice-water containing few drops of HCl, was collected by filtration, dried, and crystallized from appropriate solvent to produce **18a,b**.

Method B. To a solution of compound **7** (3.2 g, 0.01 mol) in dioxane (50 ml), containing Et_3N (0.5 ml), either **19a** (1.54 g, 0.01 mol) or **19b** (2.01 g, 0.01 mol) of the cinnamonitrile derivatives was added. The reaction mixture in each case was heated under reflux for 5 h and poured into ice-water containing a few drops of HCl. The solid product formed was collected by filtration, washed with cold water, dried, and crystallized from appropriate solvent to produce **18a,b**.

*3-Cyano-2-(7-amino-3,6-dicyano-5-phenyl-8-oxo-benzo[*d*]-pyridazine)-4,5,6,7-tetrahydrobenzo[* b*]thiophene (18a)*

18a crystallized from acetic acid in 60% yield; m.p. 158–159°C. IR (KBr) cm^{-1}: 3480–3360 (NH_2), 2880 (CH_2), 2225, 2222, 2217 (3CN), 1697 (CO), 1650 (C=N); ^1H NMR (DMSO-d_6) ppm: 2.25–2.28 (m, 4H, $2CH_2$), 2.36–2.39 (m, 4H, $2CH_2$), 5.50 (s, 2H, NH_2), 7.30–7.38 (m, 6H, C_6H_5, benzene CH). Anal. Calcd. for $C_{25}H_{16}N_6OS$ (448): C, 66.96; H, 3.57; N, 18.75; S, 7.14. Found: C, 66.90; H, 3.41; N, 18.91; S, 7.11.

3-Cyano-2-[7-amino-3-cyano-6-(ethoxy-carbonyl)-5-phenyl-8-oxo-benzo[d]pyridazine]-4,5,6,7-tetrahydrobenzo[b]-thiophene (18b)

18b crystallized from acetic acid in 50% yield; m.p. 222–223°C. IR (KBr) cm^{-1}: 3480–3365 (NH_2) 2878 (CH_2), 2225, 2220 (2 CN), 1685 (CO), 1660 (C=N), 1640 (C=C), 1635 (CO); ^{1}H NMR (DMSO-d_6) ppm: 1.64 (t, 3H, J = 7.0 Hz, CH_3), 2.25–2.27 (m, 4H, $2CH_2$), 2.35–2.39 (m, 4H, $2CH_2$), 4.24 (q, 2H, J = 7.0 Hz, CH_2), 5.42 (s, 2H, NH_2), 7.30–7.41 (m, 6H, C_6H_5, benzene CH). Anal. Calcd. for $C_{27}H_{21}N_5O_3S$ (495): C, 65.45; H, 4.24; N, 14.14; S, 6.46. Found: C, 65.35; H, 4.12; N, 14.00; S, 6.51.

3-Cyano-2-(3,5,-dicyano-4-methyl-6-oxo-pyridazin-1-yl)-4,5,6,7-tetrahydrobenzo[b]thiophene (20)

To a dry solid of compound **6** (2.88 g, 0.01 mol), ethyl cyanoacetate (1.13 g, 0.01 mol) and ammonium acetate (0.77 g, 0.01 mol) were added. The reaction mixture was heated in an oil bath at 140°C for 1 h and left to cool. The solidified product washed with ethanol and collected by filtration, dried, and crystallized from dioxane in 65% yield; m.p. 148–149°C. IR (KBr) cm^{-1}: 2982, 2873 (CH_3, CH_2), 2225, 2220, 2215 (3CN), 1695 (CO), 1655 (C=N), 1640 (C=C); ^{1}H NMR (DMSO-d_6) ppm: 2.20 (s, 3H, CH_3), 2.24–2.26 (2m, 4H, $2CH_2$) 2.36–2.40 (2m, 4H, $2CH_2$). Anal. Calcd. for $C_{16}H_{11}N_5OS$ (321): C, 59.81; H, 3.42; N, 21.80; S, 9.96. Found: C, 59.72; H, 3.37; N, 21.70; S, 9.94.

3-Cyano-2-[3,5,-dicyano-4-(phenylhydrazono-methino)-6-oxo-pyridazin-1-yl]-4,5,6,7-tetrahydrobenzo[b]thiophene (22)

To a cold (0–5°C) solution of compound **20** (3.21 g, 0.01 mol) in ethanol (50 ml) containing NaOH solution (10 ml, 10%), a solution of benzene diazonium chloride (0.01 mol) (which was prepared by $NaNO_2$ [0.79 g, 0.01 mol], in water [2 ml] was added to a cold solution of aniline [0.93 g, 0.01 mol] containing the appropriate amount of HCl with stirring) was added with continuous stirring. The formed solid product was collected by filtration, dried, and crystallized from acetic acid in 70% yield; m.p. 198–199°C. IR (KBr) cm^{-1}: 3460–3330 (NH) 2895 (CH_2), 2225, 2220, 2215 (3 CN), 1695 (CO), 1655 (C=N), 1640 (C=C); ^{1}H NMR (DMSO-d_6) ppm: 2.30–2.34 (m, 4H, $2CH_2$), 2.38–2.41 (m, 4CH, $2CH_2$), 6.58 (s, 1H, CH), 7.30–7.38 (m, 5H, C_6H_5), 8.20 (s, 1H, NH). Anal. Calcd. for $C_{22}H_{15}N_7OS$ (425): C, 62.12; H, 3.53; N, 23.05; S, 7.52. Found: C, 61.98; H, 3.41; N, 23.00; S, 7.41.

3-Cyano-2-[3-cyano-7,8-dioxo-6-phenyl-pyridazo(4,5-d) pyridiazin-1-yl]-4,5,6,7-tetrahydrobenzo[b]thiophene (24)

A solution of compound **22** (4.25 g, 0.01 mol) in ethanol (50 ml) containing NaOH (0.5 g) was heated under reflux for 5 h and poured into ice-water containing a few drops of HCl. The solid product formed was collected by filtration, washed with cold water, dried, and crystallized from dioxane in 60% yield; m.p. 210–211°C. IR (KBr) cm^{-1}: 2890 (CH_2), 2225, 2215 (2CN), 1700, 1685 (2CO), 1660 (C=N), 1650 (C=C); ^1H NMR (DMSO-d_6) ppm: 2.25–2.28 (m, 4H, $2CH_2$), 2.33–2.36 (m, 4H, $2CH_2$), 7.30–7.37 (m, 6H, C_6H_5, and pyridazine H). Anal. Calcd. for $C_{22}H_{14}N_6O_2S$ (426): C, 61.97; H, 3.28; N, 19.72; S, 7.51. Found: C, 61.82; H, 3.17; N, 19.70; S, 7.48.

3-Cyano-2-(3-cyano-7-phenyl-1,2,6,7,9,10,-hexazaace-napthalen-1-yl)-4,5,6,7-tetrahydrobenzo[b]thiophene (25)

To a solution of compound **24** (4.26 g, 0.01 mol) in dioxane (30 ml) hydrazine hydrate (0.52 g, 0.01 mol) was added. The reaction mixture was heated under reflux for 2 h and poured into ice-water containing a few drops of HCl. The solid product formed was collected by filtration, dried, and crystallized from ethanol in 60% yield; m.p. 280–281°C. IR (KBr) cm^{-1}: 2893 (CH_2), 2225, 2215 (2CN), 1660 (C=N), 1635 (C=C); ^1H NMR (DMSO-d_6) ppm: 2.24–2.26 (m, 4H, $2CH_2$), 2.33–2.38 (m, 4H, $2CH_2$), 7.31–7.36 (m, 6H, C_6H_5 and pyridazine H). Anal. Calcd. for $C_{22}H_{14}N_8S$ (422): C, 62.55; H, 3.31; N, 26.54; S, 7.58. Found: C, 62.42; H, 3.20; N, 26.42; S, 7.52.

3-Cyano-2-(1,2,6,7,9,11-hexazaphenanthren-1-yl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene Derivatives (26a,b) (General Procedure)

To a suspension of compound **24** (4.26 g, 0.01 mol) in sodium ethoxide (prepared by dissolving sodium metal in absolute ethanol [40 ml]), either urea (0.6 g, 0.01 mol) or thiourea (0.76 g, 0.01 mol) was added. The reaction mixture was heated in boiling water bath for 5 h and poured into ice-water containing HCl (P^H6). The formed solid product in each case was collected by filtration, dried, and crystallized from appropriate solvent to produce **26a,b**.

3-Cyano-2-(3-cyano-7-phenyl-10-oxo-1,2,6,7,9,11-hexaza-phenanthren-1-yl)-4,5,6,7-tetrahydrobenzo[b]thiophene (26a)

26a crystallized from dioxane in 62% yield; m.p. 210–211°C. IR (KBr) cm^{-1}: 2880 (CH_2), 2225, 2218 (2CN), 1689 (CO), 1655 (C=N), 1640

(C=C); ^{1}H NMR (DMSO-d_6) ppm: 2.26–2.28 (m, 4H, 2CH$_2$), 2.32–2.36 (m, 4H, 2CH$_2$), 7.28–7.36 (m, 6H, C_6H_5, and pyridazine H). Anal. Calcd. for $C_{23}H_{14}N_8OS$ (450): C, 61.33; H, 3.11; N, 24.88; S, 7.11. Found: C, 61.16; H, 3.09; N, 24.81; S, 7.10.

3-Cyano-2-(3-cyano-7-phenyl-10-thioxo-1,2,6,7,9,11-hexazaphenanthren-1-yl)-4,5,6,7-tetrahydrobenzo[b*]thiophene (26b)*

26b crystallized from dioxane in 70% yield; m.p. 180–181°C. IR (KBr) cm^{-1}: 2880 (CH$_2$), 2220, 2218 (2CN), 1694 (C=S), 1650 (C=N), 1640 (C=C); ^{1}H NMR (DMSO–d_6) ppm: 2.27–2.32 (m, 4H, 2CH$_2$), 2.39–2.41 (m, 4H, 2CH$_2$), 7.26–7.35 (m, 6H, C_6H_5 and pyridazine H). Anal. Calcd. for $C_{23}H_{14}N_8\ S_2$ (466): C, 59.22; H, 3.00; N, 24.03; S, 13.73. Found: C, 59.13; H, 2.88; N, 24.00; S, 13.61.

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