

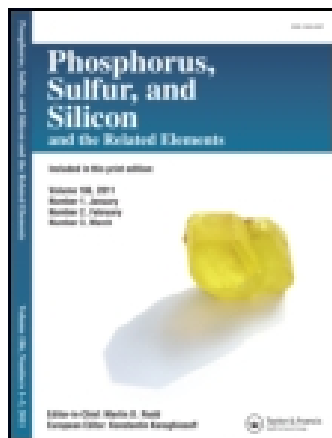
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Synthesis of Some New Thiazole, Thiophene, and 2,3-Dihydro-1,3,4-thiadiazole and Pyrimidino[1,2-b]indazole Derivatives

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Synthesis of Some New Thiazole, Thiophene, and 2,3-Dihydro-1,3,4-thiadiazole and Pyrimidino[1,2-b]indazole Derivatives

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Hydrazonoyl halides 4a–g reacted with methyl carbodithioate 3 thioanilide 10 to give 1,3,4-thiadiazoles 5a–g and 13a–g, respectively. Thioanilide 10 reacted with ω -bromoacetophenones 14a–e to give the acyclic product 15a–e, which was converted to the thiophenes 16a–e and to the thiazoles 17a–e, respectively. Structures of the newly synthesized compounds were elucidated on the basis of elemental analysis, spectral data, and alternative synthesis route whenever possible.

Keywords Dimidone; hydrazonoyl halides; thiophene; thiazoles; thiadiazoles

INTRODUCTION

Thiazoles^{1,2} and thiadiazoles have been found to exhibit diverse biological activities. They act as anticarcinogenic,³ fungicidal,^{4,5} herbicidal,^{6,7} lubricant,⁸ and antitumor⁹ agents. In continuation of our previous work,^{10–13} on the synthesis of different thiazoles, thiophenes, and 1,3,4-thiadiazoles with potential biological activities, we report the synthesis of some new thiazole, thiophene, 1,3,4-thiadiazole, and pyrimidino[1,2-b]indazole derivatives via the reaction of dimidone with different sulfur-containing compounds.

RESULTS AND DISCUSSION

The reaction of equimolar amounts of 3-{aza[(methylthiothioxomethyl) amino]methylene}-5,5-dimethylcyclohexane-1-one (**3**) (which was prepared from the reaction of dimidone and methylhydrazinecarbodithioate in isopropyl alcohol) and C-ethoxycarbonyl-N-phenylhydrazonoyl chloride (**4a**) in ethanolic triethylamine solution

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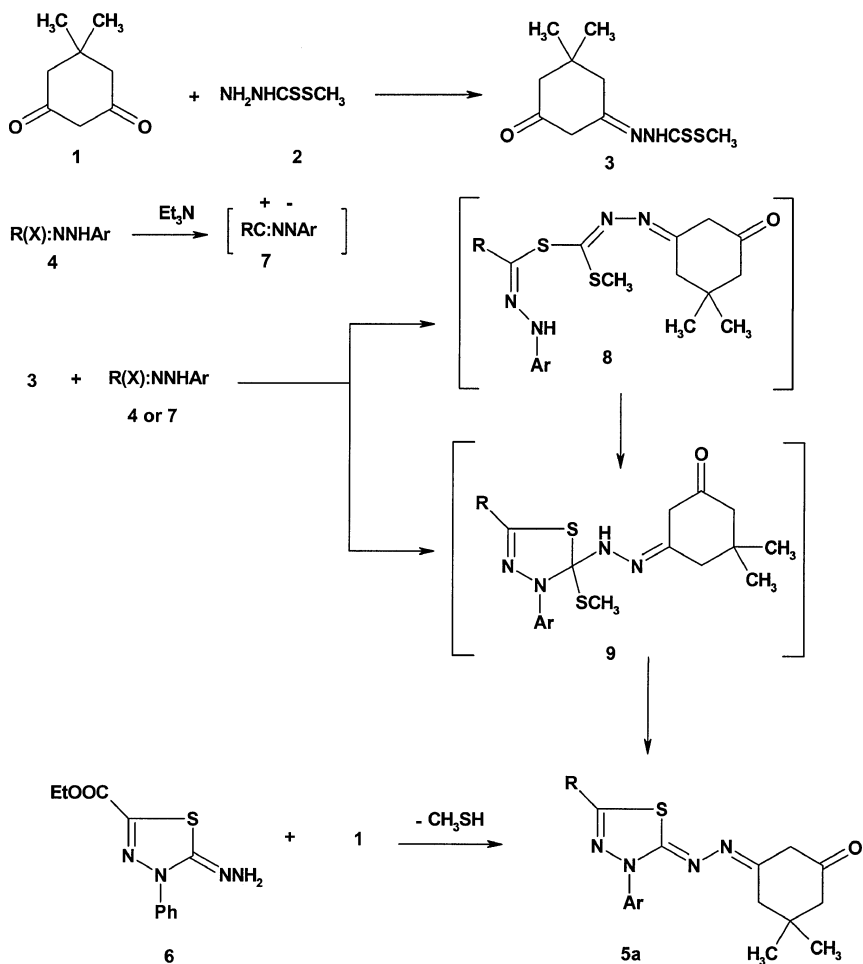
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afforded product **5a**. The structure **5a** was assigned as ethyl 2-[1,2-diaza-2-(5,5-dimethyl-3-oxocyclohexylidene)ethylidene]-3-phenyl-1,3,4-thiadiazoline-5-carboxylate based on elemental analysis, spectral data, and independent synthesis. ^1H NMR spectrum of **5a** showed signals at $\delta = 1.03$ (s, 6H, 2 CH_3), 1.37 (t, 3H, CH_2CH_3), 2.21 (s, 2H, CH_2), 2.34 (s, 2H, CH_2), 4.39 (q, 2H, CH_2CH_3), 4.22 (s, 2H, CH_2), and 7.25–7.80 (m, 5H, ArH's). Its IR spectrum (cm^{-1}) revealed absorption bands at 1723 and 1666 (CO's). Also, compound **5a** was obtained by the reaction of 2-hydrazino-2,3-dihydro-1,3,4-thiadiazole¹⁴ **6** with dimidone (Scheme 1).

The formation of **5a** can be explained via elimination of methyl mercaptan from the corresponding cyclo adduct **9a**, which is assumed to be formed from 1,3 dipolar cycloaddition of **4a** to C=S in **3**. Alternatively, formation of **5a** can also be explained by the 1,3 addition of **3** to the nitrilium imide **7a** (which is prepared in situ by treatment of hydrazonoyl bromide **4a** with triethylamine) to give **8a** which readily cyclized to yield **9a**, which, in turn, affords **5a** by the loss of methyl mercaptan molecule. Similarly, compound **3** reacted with the appropriate hydrazonoyl halides **4b–g** to afford 2,3-dihydro-1,3,4-thiadiazole derivatives **5b–g**, respectively.

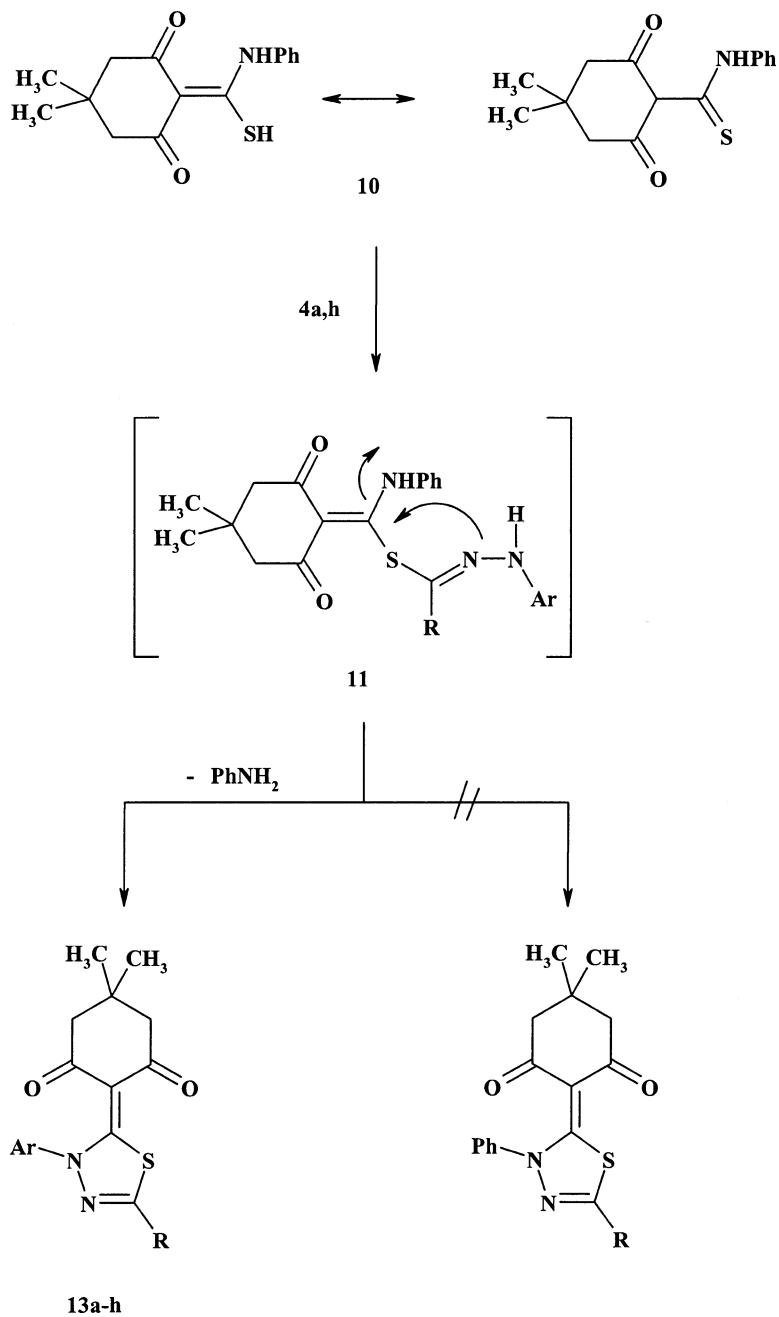
2-(Mercapto-phenylamino-methylene)-5,5-dimethyl-cyclohexane-1,3-dione¹⁵ (**10**) with C-ethoxycarbonyl-N-phenylhydrazonoyl chloride (**4a**) in N,N-dimethylformamide contains potassium hydroxide to give one isolable product, according to TLC, which seemed to be either **12** or **13**. The structure of the product was elucidated on the basis of elemental and spectral data. Thus, IR spectrum (cm^{-1}) revealed bands at 1710, 1616, and 1620 (3 CO's). Its ^1H NMR spectrum showed signals at $\delta = 1.10$ (s, 6H, 2 CH_3), 1.43 (t, 3H, CH_3CH_2), 2.33 (s, 2H, CH_2), 2.37 (s, 2H, CH_2), 4.48 (q, 2H, CH_3CH_2), and 7.13–7.32 (m, 5H, ArH's). More evidence of the structure **13** can be obtained from the reaction of **10** with C-ethoxycarbonyl-N-p-tolylhydrazonoyl chloride (**4h**) under the same condition which gave a product having an ^1H NMR spectrum which showed signals at $\delta = 1.10$ (s, 6H, 2 CH_3), 1.43 (t, 3H, CH_3CH_2), 2.33 (s, 2H, CH_2), 2.37 (s, 2H, CH_2), 2.43 (s, 3H, 4- $\text{CH}_3\text{C}_6\text{H}_4$), 4.48 (q, 2H, CH_3CH_2), and 7.13–7.32 (m, 5H, ArH's). Based on the spectral data and the elemental analysis, structure **12** was ruled out and the product was assigned as ethyl 2-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3-phenyl-1,3,4-thiadiazoline-5-carboxylate (**13a**). The formation of product **13a** can be explained via the reaction of **10** with hydrazonoyl chloride **4a** to form the intermediate **11**, which lost an aniline molecule¹¹ to give the final product **13a** (Scheme 2).

By analogy, thioamide **10** reacted with the appropriate hydrazonoyl halides **4b–g** to afford the 2,3-dihydro-1,3,4-thiadiazoles derivatives **13b–g**, respectively. For example, the ^1H NMR spectrum of **13e** showed



- | | | | |
|------|---------------------------------------|--|--------|
| 4,5a | R = COOC ₂ H ₅ | Ar = Ph | X = Cl |
| 4,5b | R = CONHPh | Ar = Ph | X = Cl |
| 4,5c | R = Ph | Ar = Ph | X = Cl |
| 4,5d | R = COCH ₃ | Ar = Ph | X = Cl |
| 4,5e | R = COC ₆ H ₅ | Ar = Ph | X = Br |
| 4,5f | R = COC ₁₀ H ₇ | Ar = Ph | X = Br |
| 4,5g | R = COC ₄ H ₃ S | Ar = Ph | X = Br |
| 4h | R = COO ₂ H ₅ | Ar = 4-CH ₃ C ₆ H ₄ | X = Cl |

SCHEME 1



SCHEME 2

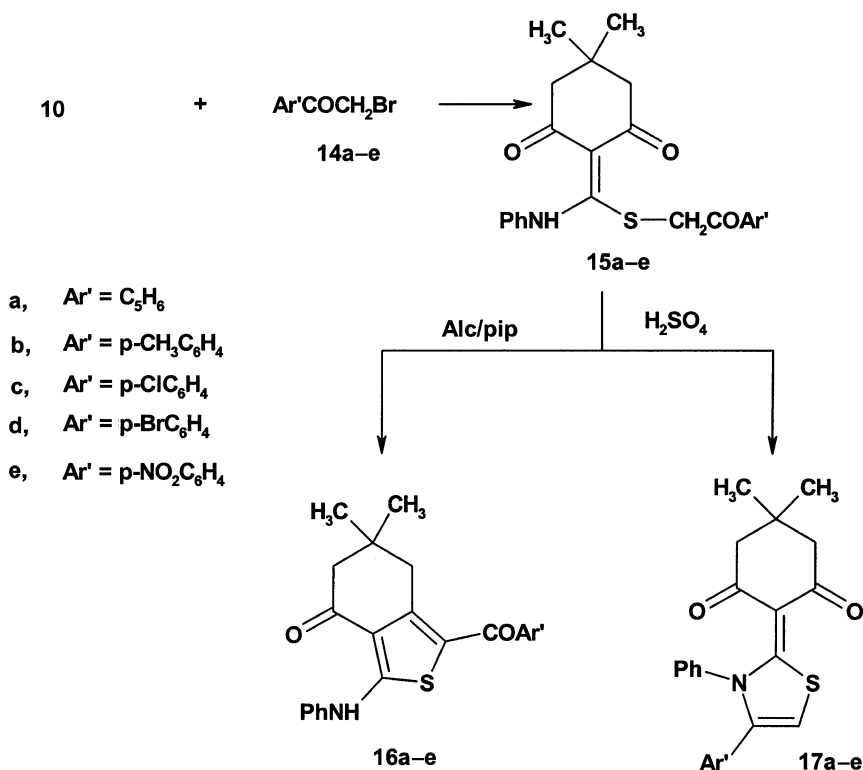
signals at $\delta = 1.06$ (s, 6H, 2 CH₃), 2.49 (s, 2H, CH₂), 2.65 (s, 2H, CH₂), and 7.15–7.50 (m, 10H, ArHs). Its ¹³C NMR spectrum showed signals at $\delta = 28.7, 31.1, 51.4, 105.7, 122.9, 128.9, 129.1, 130.8, 134.4, 134.8, 143.2, 183.3,$ and 191.9.

Treatment of **1** with phenyl isothiocyanate in N,N-dimethylformamide containing potassium hydroxide was followed by the appropriate ω -bromoacetophenones **14a–e** to afford the acyclic products **15a–e**, respectively. Structure **15** was established on the basis of elemental analysis, spectral data, and chemical transformation. For example, ¹H NMR spectrum of compound **15d** showed signals at $\delta = 1.09$ (s, 6H, 2 CH₃), 2.43 (s, 2H, CH₂), 2.80 (s, 2H, CH₂), 4.23 (s, 2H, SCH₂), 7.11–7.88 (m, 9H, ArH's), and 11.24 (s, 1H, NH). Its IR spectrum (cm⁻¹) revealed absorption bands at 1650, 1620, 1618 (CO's), and 3425 (NH). Thus, compound **15a–e** can be converted to the thiophenes **16a–e** by boiling in ethanol containing catalytic amount of piperidine. In contrast, the appropriate **15a–e**, when treated with conc. sulfuric acid at room temperature, was converted to the thiazoles **17a–e** respectively. The structure of these products was established on the basis of elemental analysis and spectral data (Scheme 3). For example, ¹³C NMR spectrum of **16c** showed signals at $\delta = 28.5, 34.3, 41.2, 52.0, 116.2, 118.3, 119.6, 125.0, 128.9, 129.9, 130.0, 138.1, 139.0, 139.3, 149.5, 162.4, 187.2,$ and 196.4. Its mass spectrum showed m/z peaks at 409, 410, 412, 394, 270, 214, 142, 139, and 77.

Compound **10** reacted with iodomethane in N,N-dimethylformamide containing potassium hydroxide to give 5,5-dimethyl-2-[methylthio(phenylamino)methylene]-cyclohexane-1,3-dione (**18**), which reacted with hydrazine hydrate in ethanol under reflux to give 6,6-dimethyl-3-phenylamino-2,5,6,7-tetrahydro-1H-indazol-4-one (**20**) (Scheme 4). Structure **20** was elucidated on the basis of elemental analysis and spectral data. Thus, ¹H NMR showed signals at $\delta = 1.03$ (s, 6H, 2 CH₃), 2.43 (s, 2H, CH₂), 2.60 (s, 2H, CH₂), 6.96–7.96 (m, 5H, ArHs), 9.13 (s, 1H, NH) and 12.40 (s, 1H, NH). Its mass spectrum showed m/z peaks 255, 212, 199, 170, 142, 115, 77, and 51 and the product obtained is free from sulfur. It was also prepared from the reaction of **10** with hydrazine hydrate in ethanol under reflux to give an identical product in all respects. (m.p., mixed m.p., and spectra). The reaction of **20** with ethylacetoacetate and with its trifluoro analogue in acetic acid afforded **21a** and **21b**, respectively.

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (on KBr discs) on a Shimadzu

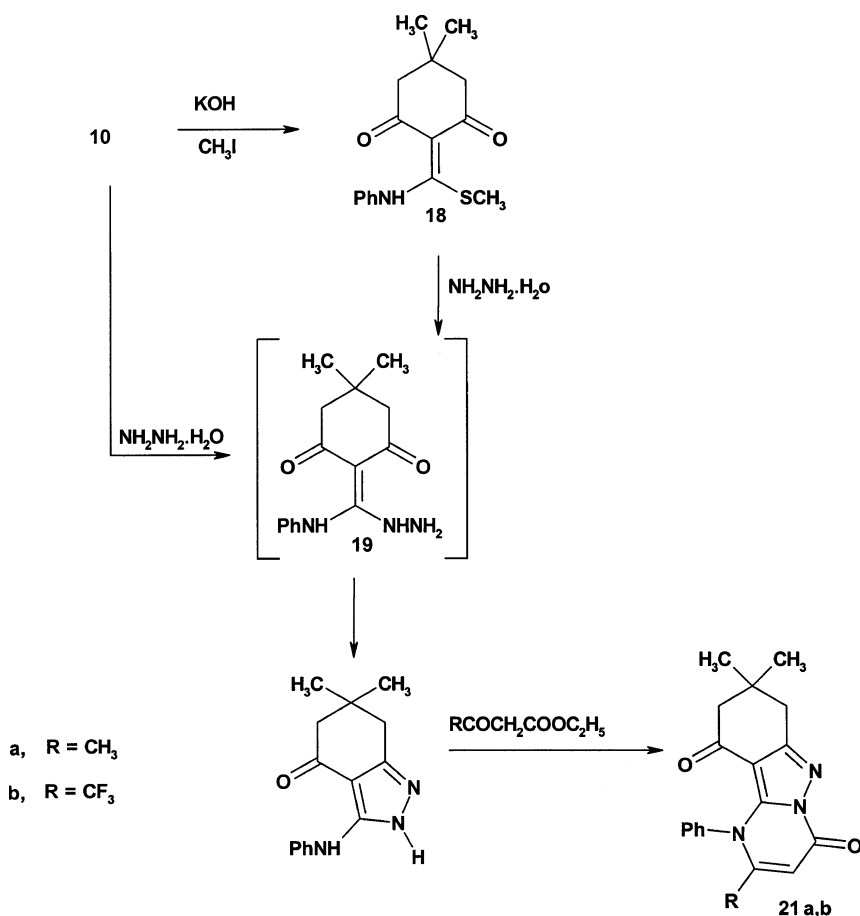


SCHEME 3

FT-IR 8201 PC spectrophotometer. ¹H NMR spectra were recorded in CDCl₃ and (CD₃)₂SO solutions on a Varian Gemini 300 MHz spectrometer and chemical shifts were expressed in δ using TMS as internal reference. ¹³C NMR spectra were recorded in CDCl₃ solutions on a Varian Gemini 75 MHz spectrometer and chemical shifts were expressed in δ using TMS as internal reference. MS spectra were recorded on a GC-MS HP 5889A. Elemental analysis was carried out at the Microanalytical Center, Cairo University. Thiadiazole¹⁴ **6**, thioanilide¹⁵ **10**, hydrazonoyl halides^{16–23} **4a–g**, and hydrazine carbodithioate²⁴ **2** were prepared as reported.

Synthesis of 3-{aza[(methylthiothioxomethyl)amino]methylene}-5,5-dimethylcyclohexane-1-one (**3**)

A mixture of dimidone **1** (0.05 mole) and methyl hydrazine carbodithioate²⁴ **2** (0.05 mole) was stirred in isopropyl alcohol for 1 h. The formed solid was collected by filtration and crystallized from acetic acid to give **3** (Tables I–III).



SCHEME 4

Synthesis of 2,3-Dihydro-1,3,4-thiadiazole Derivatives 5a–g

A mixture of **3** (0.005 mole), the appropriate hydrazoneyl halides^{16–23} **4a–g** (0.005 mole), and triethylamine (0.005 mole) in ethanol (20 mL) was stirred for 30 min. The resulting solid was collected and crystallized from the proper solvent to give **5a–g** (Tables I–III).

Synthesis of 2,3-Dihydro-1,3,4-thiadiazole Derivatives 13a–h

A mixture of **1** (0.01 mole), phenyl isothiocyanate (0.01 mole), and potassium hydroxide (0.01 mole) in N,N-dimethylformamide (20 mL) was stirred for 3 h at room temperature. The appropriate hydrazoneyl

TABLE I Characterization Data of the Newly Synthesized Compounds

| Compound no. | Mp., °C solvent | Colour yield % | Mol. formula (Mol. Wt.) | % Analyses, calcd./found | | | |
|--------------|-----------------|----------------|--|--------------------------|------|-------|-------|
| | | | | C | H | N | S |
| 3 | 210–13 | Yellow | C ₁₀ H ₁₆ N ₂ OS ₂ | 49.15 | 6.60 | 11.46 | 26.24 |
| | ACOH | 89 | (244.38) | 49.00 | 6.50 | 11.30 | 26.10 |
| 5a | 115–17 | Yellow | C ₁₉ H ₂₂ N ₄ O ₃ S | 59.05 | 5.74 | 14.50 | 8.30 |
| | EtOH | 65 | (386.48) | 59.20 | 5.90 | 14.70 | 8.50 |
| 5b | 180–83 | Yellow | C ₂₃ H ₂₃ N ₅ O ₂ S | 63.72 | 5.35 | 16.15 | 7.40 |
| | EtOH | 67 | (433.54) | 63.50 | 5.10 | 15.90 | 7.20 |
| 5c | 155–56 | Yellow | C ₂₂ H ₂₂ N ₄ OS | 67.67 | 5.68 | 14.35 | 8.21 |
| | EtOH | 59 | (390.51) | 67.80 | 5.80 | 14.50 | 8.00 |
| 5d | 140–43 | Orange | C ₁₈ H ₂₀ N ₄ O ₂ S | 60.65 | 5.66 | 15.72 | 9.00 |
| | EtOH | 55 | (356.45) | 60.40 | 5.40 | 15.50 | 8.90 |
| 5e | 80–83 | Red | C ₂₃ H ₂₂ N ₄ O ₂ S | 66.01 | 5.30 | 13.39 | 7.66 |
| | EtOH | 59 | (418.52) | 66.30 | 5.50 | 13.50 | 7.80 |
| 5f | 185–86 | Red | C ₂₇ H ₂₄ N ₄ O ₂ S | 69.21 | 5.16 | 11.96 | 6.84 |
| | EtOH | 55 | (468.58) | 69.00 | 4.90 | 11.70 | 6.60 |
| 5g | 120–22 | Brown | C ₂₁ H ₂₀ N ₄ O ₂ S ₂ | 59.41 | 4.75 | 13.20 | 15.11 |
| | EtOH | 75 | (424.55) | 59.60 | 4.80 | 13.40 | 15.30 |
| 13a | 138–40 | Yellow | C ₁₉ H ₂₀ N ₂ O ₄ S | 61.27 | 5.41 | 7.52 | 8.61 |
| | EtOH | 75 | (372.45) | 61.40 | 5.30 | 7.30 | 8.60 |
| 13b | 245–47 | Yellow | C ₂₃ H ₂₁ N ₃ O ₃ S | 65.85 | 5.05 | 10.02 | 7.64 |
| | DMF | 79 | (419.51) | 65.60 | 4.90 | 9.90 | 7.40 |
| 13c | 138–40 | Yellow | C ₂₂ H ₂₀ N ₂ O ₂ S | 70.19 | 5.35 | 7.44 | 8.52 |
| | EtOH | 73 | (376.48) | 70.30 | 5.10 | 7.20 | 8.30 |
| 13d | 199–200 | Orange | C ₁₈ H ₁₈ N ₂ O ₃ S | 63.14 | 5.30 | 8.18 | 9.36 |
| | EtOH | 80 | (342.42) | 63.30 | 5.00 | 8.00 | 9.20 |
| 13e | 209–11 | Orange | C ₂₃ H ₂₀ N ₂ O ₃ S | 68.30 | 4.98 | 6.93 | 7.93 |
| | ACOH | 75 | (404.49) | 68.10 | 5.00 | 6.70 | 7.80 |
| 13f | 147–50 | Orange | C ₂₇ H ₂₂ N ₂ O ₃ S | 71.35 | 4.88 | 6.16 | 7.05 |
| | ACOH | 79 | (454.55) | 71.50 | 5.00 | 6.00 | 6.90 |
| 13g | 217–20 | Yellow | C ₂₁ H ₁₈ N ₂ O ₃ S ₂ | 61.44 | 4.42 | 6.82 | 15.62 |
| | ACOH | 78 | (410.52) | 61.20 | 4.20 | 6.60 | 15.40 |
| 15a | 138–40 | White | C ₂₃ H ₂₃ NO ₃ S | 70.20 | 5.89 | 3.56 | 8.15 |
| | EtOH | 85 | (393.51) | 70.40 | 6.00 | 3.70 | 8.30 |
| 15b | 145–46 | White | C ₂₄ H ₂₅ NO ₃ S | 70.73 | 6.18 | 3.44 | 7.87 |
| | EtOH | 87 | (407.54) | 70.90 | 6.30 | 3.60 | 7.90 |
| 15c | 160–62 | White | C ₂₃ H ₂₂ ClNO ₃ S | 64.55 | 5.18 | 3.27 | 7.49 |
| | ACOH | 83 | (427.95) | 64.20 | 4.90 | 3.10 | 7.50 |
| 15d | 159–60 | Yellow | C ₂₃ H ₂₂ BrNO ₃ S | 58.48 | 4.49 | 2.96 | 6.79 |
| | ACOH | 85 | (472.40) | 58.40 | 4.50 | 2.90 | 6.70 |
| 15e | 190–92 | Orange | C ₂₃ H ₂₂ N ₂ O ₅ S | 63.00 | 5.06 | 6.39 | 7.31 |
| | ACOH | 78 | (438.51) | 63.20 | 5.20 | 6.50 | 7.50 |
| 16a | 150–51 | Yellow | C ₂₃ H ₂₁ NO ₂ S | 73.57 | 5.64 | 3.73 | 8.54 |
| | EtOH | 80 | (375.49) | 73.30 | 5.40 | 3.50 | 8.30 |
| 16b | 180–82 | Yellow | C ₂₄ H ₂₃ NO ₂ S | 74.01 | 5.95 | 3.60 | 8.23 |
| | EtOH | 75 | (389.52) | 73.90 | 6.00 | 3.50 | 8.20 |

TABLE I Characterization Data of the Newly Synthesized Compounds (Continued)

| Compound no. | Mp., °C solvent | Colour yield % | Mol. formula (Mol. Wt.) | % Analyses, calcd./found | | | |
|--------------------------|-----------------|----------------|--|--------------------------|------|-------|-------|
| | | | | C | H | N | S |
| 16c | 159–60 | Yellow | C ₂₃ H ₂₀ ClNO ₂ S | 67.39 | 4.92 | 3.42 | 7.81 |
| | EtOH | 79 | (409.94) | 67.20 | 4.70 | 3.20 | 7.60 |
| 16d ¹⁵ | 165–67 | Yellow | C ₂₃ H ₂₀ BrNO ₂ S | 60.80 | 4.44 | 3.08 | 7.06 |
| | EtOH | 75 | (454.39) | 60.60 | 4.20 | 2.90 | 7.00 |
| 16e | 188–90 | Yellow | C ₂₃ H ₂₀ N ₂ O ₄ S | 65.70 | 4.79 | 6.66 | 7.63 |
| | EtOH | 84 | (420.49) | 65.50 | 4.60 | 6.40 | 7.40 |
| 17a | 250–53 | White | C ₂₃ H ₂₁ NO ₂ S | 73.57 | 5.64 | 3.73 | 8.54 |
| | EtOH | 75 | (375.49) | 73.40 | 5.50 | 3.60 | 8.30 |
| 17b | >340 | White | C ₂₄ H ₂₃ NO ₂ S | 74.01 | 5.95 | 3.66 | 8.23 |
| | EtOH | 73 | (389.52) | 73.90 | 6.00 | 3.50 | 8.20 |
| 17c | 296–300 | Yellow | C ₂₃ H ₂₀ ClNO ₂ S | 67.39 | 4.92 | 3.42 | 7.82 |
| | EtOH | 69 | (409.94) | 67.30 | 4.90 | 3.30 | 7.60 |
| 17d | 282–85 | Yellow | C ₂₃ H ₂₀ BrNO ₂ S | 60.80 | 4.44 | 3.08 | 7.06 |
| | EtOH | 75 | (454.39) | 60.70 | 4.30 | 3.10 | 7.00 |
| 17e | 269–70 | Yellow | C ₂₃ H ₂₀ N ₂ O ₄ S | 65.70 | 4.79 | 6.66 | 7.63 |
| | EtOH | 79 | (420.49) | 65.60 | 4.70 | 6.50 | 7.50 |
| 18 | 135–37 | White | C ₁₆ H ₁₉ NO ₂ S | 66.41 | 6.62 | 4.84 | 11.08 |
| | EtOH | 55 | (289.40) | 66.20 | 6.40 | 4.60 | 10.90 |
| 20 | 235–36 | Yellow | C ₁₅ H ₁₇ N ₃ O | 70.56 | 6.71 | 16.46 | |
| | EtOH | 79 | (255.32) | 70.40 | 6.50 | 16.20 | |
| 21a | 278–80 | Yellow | C ₁₉ H ₁₉ N ₃ O ₂ | 71.01 | 5.96 | 13.07 | |
| | ACOH | 65 | (321.38) | 71.00 | 6.00 | 13.00 | |
| 21b | 268–70 | Yellow | C ₁₉ H ₁₆ F ₃ N ₃ O ₂ | 60.80 | 4.30 | 11.19 | |
| | ACOH | 63 | (375.35) | 60.60 | 4.10 | 11.00 | |

halides **4a–h** (0.01 mole) were added and stirring was continued for 2 h. The reaction mixture was diluted with water and the solid that was precipitated was collected and crystallized from the proper solvent to give **13a–g** (Tables I–III).

Synthesis of 5,5-Dimethyl-2-[(2-oxo-2-arylethylthio)(phenyl-amino)-methylene] cyclohexane-1,3-dione **15a–e**

A mixture of **1** (0.01 mole), phenyl isothiocyanate (0.01 mole), and potassium hydroxide (0.01 mole) in N,N-dimethylformamide (20 mL) was stirred for 3 h at room temperature. The appropriate *o*-bromoacetophenones **14a–e** (0.01 mole) was added and stirring was continued for 2 h. The formed solid was collected and crystallized from the proper solvent to give **15a–e** (Tables I–III).

TABLE II ^1H NMR Spectrum of Some Newly Synthesized Compounds

| Compound no. | ^1H NMR (δ ppm) |
|--------------|---|
| 3 | 1.03 (s, 6H, 2 CH ₃), 2.07 (s, 2H, CH ₂), 2.21 (s, 2H, CH ₂), 2.31 (s, 3H, SCH ₃), 4.28 (s, 2H, CH ₂), and 11.56 (s, 1H, NH). |
| 5e | 1.06 (s, 6H, 2 CH ₃), 2.44 (s, 2H, CH ₂), 2.68 (s, 2H, CH ₂), 4.22 (s, 2H, CH ₂) and 7.39–8.23 (m, 10H, ArHs). |
| 13b | 1.03 (s, 6H, 2 CH ₃), 2.30 (s, 2H, CH ₂), 2.50 (s, 2H, CH ₂), 7.20–7.80 (m, 10H, ArHs) and 10.81 (s, 1H, NH). |
| 13d | 1.01 (s, 6H, 2 CH ₃), 2.33 (s, 3H, CH ₃ CO), 2.50 (s, 2H, CH ₂), 2.66 (s, 2H, CH ₂) and 7.15–7.50 (m, 5H, ArHs). |
| 15a | 1.21 (s, 6H, 2 CH ₃), 2.35 (s, 2H, CH ₂), 2.96 (s, 2H, CH ₂), 4.23 (s, 2H, SCH ₂), 7.07–8.05 (m, 10H, ArHs), and 11.28 (s, 1H, NH). |
| 15b | 1.25 (s, 6H, 2 CH ₃), 2.33 (s, 2H, CH ₂), 2.52 (s, 2H, CH ₂), 2.32 (s, 3H, 4-CH ₃ C ₆ H ₄), 4.26 (s, 2H, SCH ₂), 7.07–7.91 (m, 9H, ArHs) and 11.26 (s, 1H, NH). |
| 15c | 1.04 (s, 6H, 2 CH ₃), 2.08 (s, 2H, CH ₂), 2.20 (s, 2H, CH ₂), 4.75 (s, 2H, SCH ₂), 7.06–8.03 (m, 9H, ArHs), and 11.23 (s, 1H, NH). |
| 15d | 1.09 (s, 6H, 2 CH ₃), 2.43 (s, 2H, CH ₂), 2.80 (s, 2H, CH ₂), 4.30 (s, 2H, SCH ₂), 7.11–7.88 (m, 9H, ArHs), and 11.24 (s, 1H, NH). |
| 16b | 1.00 (s, 6H, 2 CH ₃), 2.32 (s, 2H, CH ₂), 2.31 (s, 3H, 4-CH ₃ C ₆ H ₄), 2.70 (s, 2H, CH ₂), 7.01–7.69 (m, 9H, ArHs), and 11.32 (s, 1H, NH). |
| 21a | 1.06 (s, 6H, 2 CH ₃), 2.29 (s, 2H, CH ₂), 2.68 (s, 2H, CH ₂), 2.92 (s, 3H, CH ₃), and 7.07–8.05 (m, 6H, ArH's and CH). |
| 21b | 1.06 (s, 6H, 2 CH ₃), 2.29 (s, 2H, CH ₂), 2.68 (s, 2H, CH ₂), and 7.07–8.05 (m, 6H, ArH's and CH). |

Synthesis of 6,6-Dimethyl-3-(phenylamino)-1-(arylcarbonyl)-5,6,7-trihydrobenzo[2,1-c]thiophen-4-one 16a–e

Compounds **15a–e** (0.005 mole) were refluxed in ethanol (20 mL) that contained a catalytic amount of piperidine for 1 h. The resulting solid was collected and crystallized from the proper solvent to give **16a–e** (Tables I–III).

Synthesis of 2-(4-(Substituted)-3-Phenyl-(1,3-thiazolin-2-ylidene))-5,5-dimethyl-cyclohexane-1,3-dione 17a–e

A mixture of **15a–e** (0.005 mole) with conc. sulfuric acid (10 mL) was stirred for 1 h at room temperature and then poured on to ice. The formed solid was collected and crystallized from the proper solvent to give **17a–e** (Tables I–III).

Synthesis of 5,5-Dimethyl-2-[methylthio(phenylamino)methylene]-cyclohexane-1,3-dione (18)

A mixture of **1** (0.01 mole), phenyl isothiocyanate (0.01 mole), and potassium hydroxide (0.01 mole) in N,N-dimethylformamide (20 mL) was

TABLE III Mass Spectra of Some Newly Synthesized Compounds

| Compound no. | M+ m/z |
|--------------|--|
| 3 | 244, 196, 171, 146, 110, 83, 55. |
| 5b | 433, 404, 377, 323, 296, 244, 188, 110, 91, 77. |
| 5d | 356, 357, 341, 328, 313, 300, 255, 205, 187, 135, 110, 77. |
| 5e | 418, 403, 375, 313, 255, 198, 161, 105, 77. |
| 5f | 468, 385, 331, 312, 242, 155, 127, 77. |
| 5g | 424, 381, 288, 276, 196, 171, 111, 83. |
| 13f | 454, 407, 225, 155, 127, 77. |
| 13g | 410, 326, 313, 245, 217, 143, 111, 77. |
| 15b | 407, 374, 313, 274, 226, 165, 119, 91. |
| 16a | 375, 376, 360, 214, 149, 105, 77. |
| 16e | 420, 405, 150, 104, 77. |
| 17b | 389, 375, 362, 329, 273, 238, 214, 152, 105, 84. |
| 17c | 409, 410, 411, 412, 353, 312, 285, 247, 214, 168, 136, 77, 55. |
| 17d | 453, 455, 358, 356, 275, 247, 180, 103, 77, 55. |
| 17e | 420, 364, 323, 321, 147, 89, 55. |

stirred for 3 h at room temperature. Iodomethane (0.01 mole) was added and stirring was continued for 2 h. The formed solid was collected and crystallized from ethanol to give **18** (Tables I and II).

Synthesis of 6,6-Dimethyl-3-(phenylamino)-2,5,6,7-tetrahydro-1H-indazol-4-one (**20**)

A mixture of **18** (or **10**) and hydrazine hydrate (0.01 mole) was refluxed in ethanol (20 mL) for 2 h. The formed solid was collected and crystallized from ethanol to give **20** (Tables I and II).

Synthesis of 2-Substituted-7,7-dimethyl-1,6,7,8,4a-pentahydropyrimidino[1,2-b] 1H-indazole-4, 9-dione **21a,b**

A mixture of **20** and ethylacetoacetate and trifluoromethyl ethylacetoacetate was refluxed in acetic acid for 3 h. The formed solid was collected and crystallized from acetic acid to give **21a** and **21b**, respectively

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