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Utilization of α-Halocarbonyl Compounds in the Synthesis of Thiazole, Thiadiazole, and Thiophene Derivatives

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ABSTRACT: *The behavior of ethyl 2-phenylthiocarbamoyl acetate* **1** *toward a variety of several* α*-halocarbonyl compounds was investigated. Thus, reaction of* **1** *with* α*-bromoketones, hydrazonoyl bromides, and 2-chloro-N-arylacetamides afforded the corresponding dihydrothiazole, 1,3,4-thiadiazole, and thiophene derivatives, respectively. The synthesis of thiazolidin-4-one* **11**, *thiazolidin-5-one* **12**, *and some azo derivatives of thiazolidin-5-one were described. 5-Arylazothiazoles* **17** *and* **19** *were synthesized by condensation of hydrazonoyl bromides* **3** *with different thiourea derivatives.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:299–305, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20206

INTRODUCTION

α-Halocarbonyl compounds are highly versatile intermediates for the synthesis of a variety of heterocyclic compounds [1,2]. Thiazole derivatives have attracted continuing interest over the years because of their varied biological activities [3,4], recently found application in drug development for the treatment of allergies [5], hypertension [6], inflammation [7], schizophrenia [8], bacterial [9] and HIV infections [10], and very recently for the treatment of pain [11], as fibrinogen receptor antagonists with antithrombotic activity [12], as new inhibitors of bacterial DNA gyrase B [13]. Also, thiazoles were used as a building block of electrically and optically functional pi-conjugated polymers [14,15]. The demonstrated clinically effective antitumor activity of certain substituted-thiazole analogs [16–19] prompted us to explore an efficient and easily synthesis of some thiazole derivatives.

RESULTS AND DISCUSSION

In continuation of our interest in the synthesis of novel thiazole derivatives of industrial importance [20,21], we report here a facile one-pot synthesis of the title compounds via reaction of various α-halocarbonyl compounds with the thiocarbamoyl derivative **1**. Thus, treatment of ethyl 2-phenylthiocarbamoyl acetate **1** [22] with α-bromoketones, e.g., bromoacetone and phenacyl bromide in ethanol under reflux, afforded products identified as 2-(ethoxycarbonylmethylene)-2,3-dihydro-3-phenylthiazole derivatives **2** (Scheme 1). All of the isolated products **2a** and **2b** gave satisfactory elemental analyses and spectroscopic data (IR, ^{1}H NMR, and MS) consistent with their assigned structures. For example, the IR spectra of the products showed conjugated carbonyl absorption band near 1652 cm^{-1} and the absence of NH absorption band. The ^{1}H NMR spectrum of **2a** revealed ethyl ester protons as triplet and quartet signals at δ 1.40 and 4.40, a singlet signal at δ 1.75 due to methyl protons, olefinic CH singlet at δ 5.20, thiazole-5-CH proton at δ 6.60, in addition to a multiplet in the region δ 7.30–7.70 corresponding to the aromatic protons.

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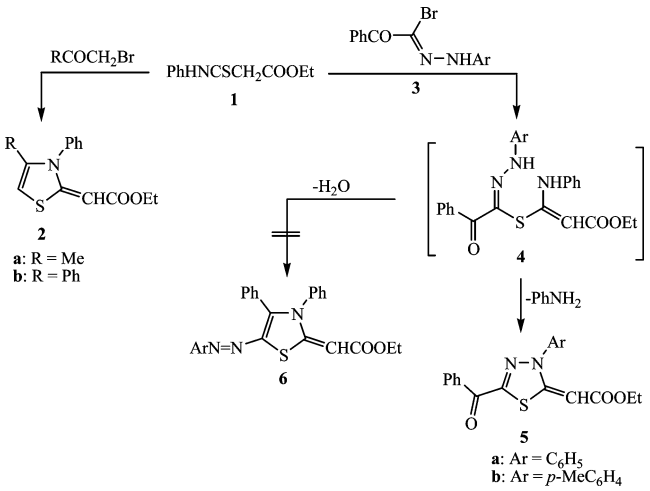
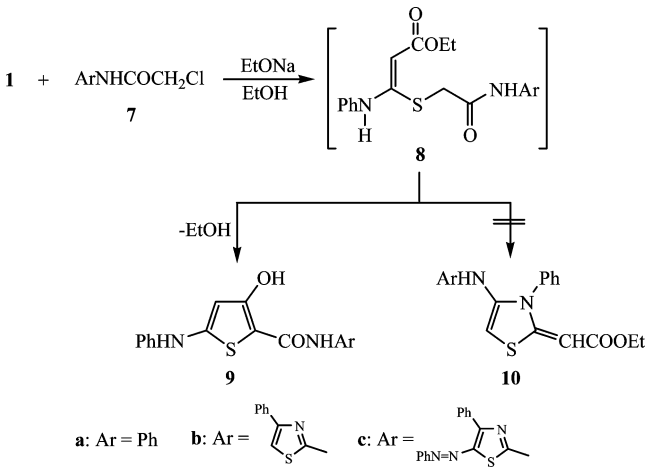


SCHEME 1



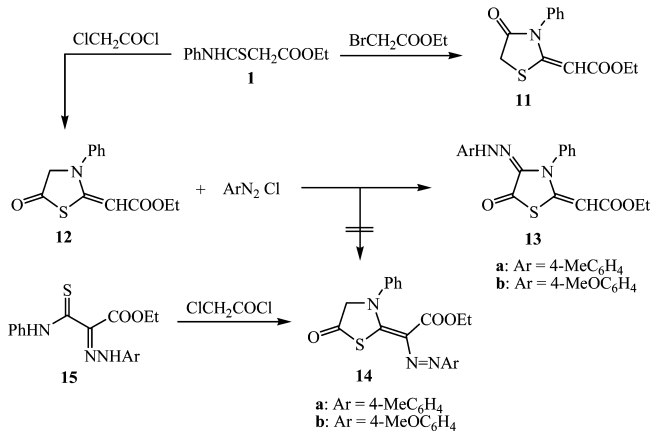
SCHEME 2

On the other hand, treatment of **1** with hydrazonoyl bromides **3** in ethanol in the presence of triethylamine under reflux, afforded a single product in each case, as evidenced by TLC. The structure of the isolated products was established by analytical and spectroscopic data (IR, ^{1}H NMR, and MS) and identified as 2-(ethoxycarbonylmethylene)-5-benzoyl-2,3-dihydro-3-aryl-1,3,4-thiadiazoles **5** instead of the arylazothiazole derivatives **6**. The formation of 1,3,4-thiadiazole derivatives **5** from the reaction of **1** with **3** seems to follow the sequence outlined in Scheme 1. It is suggested that the reaction starts with nucleophilic substitution of the bromine atom in **3** by the thiolate group of **1** to give the nonisolable intermediate **4** which cyclizes via elimination of aniline [23] to give **5** as end product. The IR spectrum of **5a** revealed two carbonyl absorption bands at 1667 (CO ester) and 1628 cm^{-1} (conjugated CO). The ^{1}H NMR spectrum of the same compound showed ethyl ester protons as triplet and quartet signals at δ 1.20 and 4.10, olefinic CH singlet at δ 5.30, in addition to a multiplet in the region δ 7.20–7.60 due to the aromatic protons. The mass spectra of the products **5a** and **5b** exhibited in each case a molecular ion peak with high intensity.

A different reaction path was observed when the anilide **1** reacts with 2-chloro-*N*-arylacetamides **7**. The reaction proceeds only in ethanolic sodium ethoxide solution under reflux to afford the corresponding thiophene derivatives **9** through nucleophilic attack of the thiolate group followed by ring closure and ethanol elimination (Scheme 2). The products were assigned the thiophene structure **9** and not the thiazole structure **10** on the basis of their elemental analysis and spectral data. Thus, e.g., the IR spectrum of **9a** showed three absorption bands at 3303, 3235, and 3192 cm^{-1} due to OH and two (NH) functions besides one carbonyl absorption band at 1671 cm^{-1}. Its ^{1}H NMR revealed a singlet at δ 6.20 due to thiophene 4-CH, multiplet at δ 6.90–7.60 corresponding to the aromatic protons, in addition to three exchangeable singlets at δ 9.20, 9.55, and 11.80 due to two NH and OH protons, respectively.

Treatment of **1** with ethyl bromoacetate and with chloroacetyl chloride afforded two different thiazolidinones according to their TLC, melting points, and spectral data. The structures of these thiazolidinones were clearly differentiated and identified as thiazolidin-4-one **11** and thiazolidin-5-one **12** on the basis of their IR, ^{1}H NMR, ^{13}C NMR and MS spectra. For example, in the IR spectra, there is a pronouncing difference: the carbonyl absorption frequency in the thiazolidin-4-one **11** appears at 1719 cm^{-1}, while in the thiazolidin-5-one **12** this absorption is shifted to higher frequency at 1742 cm^{-1}. The ^{1}H NMR spectra showed a strong chemical shift difference of methylene protons of about 1.00 ppm, thiazolidin-4-one **11** absorbs at lower chemical shift δ 3.90. The ^{13}C NMR spectra also showed a strong chemical shift difference of carbonyl carbon of about 12.84 ppm, thiazolidin-4-one **11** absorbs at lower chemical shift δ 171.72 (see Experimental).

The reactivity of thiazolidin-5-one derivative **12** toward the electrophilic substitution reaction by aromatic diazonium salts was also examined. The methylene group of the thiazolidine ring proved to be more reactive toward the azo coupling with diazonium salts than the olefinic methine group. Thus, an equimolar amount of aryl diazonium chlorides at 0–5°C reacted with compound **12** to yield the corresponding monohydrazono derivatives **13**

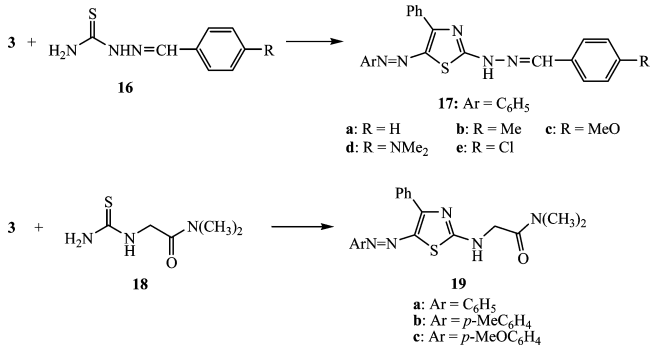


SCHEME 3

instead of the azo compounds **14** (Scheme 3). The azo compounds **14** were obtained in good yields from the reaction of ethyl 2-arylhydrazono-2-phenylthiocarbamoyl acetate derivatives **15** [24] with chloroacetyl chloride by stirring in DMF containing few drops of triethylamine as a catalyst. The molecular structures of the compounds **13** and **14** were established by elemental analyses and spectroscopic data.

Condensation of hydrazonoyl bromides **3** with thiosemicarbazone derivatives **16** by reflux in ethanol containing a catalytic amount of triethylamine afforded the corresponding 5-phenylazothiazole derivatives **17**. The chemical structures of **17a–e** were secured by their elemental analyses, IR, NMR, and MS spectra (see Experimental).

Finally, the appropriate hydrazonoyl bromides **3** were reacted with 1-[(dimethylcarbamoyl)methyl]-thiourea **18** to afford the corresponding 5-arylazothiazole derivatives **19** (Scheme 4). The structures of the highly functionalized thiazolyl dyes **19a–c** were assigned on the basis of their elemental analyses and spectral data. The IR spectra



SCHEME 4

of the dyes **19a–c** exhibited, in all cases, the presence of NH, carbonyl and azo stretching bands near 3284, 1656, and 1558 cm^{-1}, respectively. The ^1H NMR spectrum of **19c** (for example) revealed three singlet signals at δ 2.40, 3.00, and 4.20 corresponding to three CH_3 and one CH_2 protons in addition to abroad signal at δ 6.90 and a multiplet in the region δ 7.20–7.50 due to NH and aromatic protons, respectively.

CONCLUSION

In conclusion, several thiazole derivatives were prepared from the readily available thiocarbamoyl compound **1** and a variety of α-halocarbonyl compounds especially α-bromoketones, ethyl bromoacetate, and chloroacetyl chloride. The synthesis of 1,3,4-thiadiazoles was achieved by the reaction of **1** with hydrazonoyl bromides **3**. While the interaction of **1** with α-chloroacetamides furnished the corresponding thiophene derivatives. A large number of 5-arylazothiazole derivatives have been synthesized on useful paths. These highly functionalized derivatives may be of interest for dyeing purposes, yet to be explored.

EXPERIMENTAL

Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. IR spectra (KBr) were determined on a Mattson 5000 FTIR spectrometer (not all frequencies are reported). The ^1H NMR and ^{13}C NMR spectra were acquired using a Bruker WP 300 spectrometer at 300 MHz (^1H) or 75.5 MHz (^{13}C; in broad band mode) using TMS as an internal standard. Mass spectra were recorded on a Finnigan MAT 212 instrument. Elemental analyses were carried out at the microanalytical unit, Faculty of Science, University of Mansoura, Egypt. Due to the limited solubility of the products in common ^{13}C NMR solvents, the ^{13}C NMR spectra were recorded for **9a, 11, 12, 14c, 17c, 17d, 19a**, and **19b** only as representative examples of the series prepared.

Synthesis of 2,3-Dihydro-3-phenyl-1,3-thiazole Derivatives **2a,b**

A mixture of the thiocarbamoyl derivative **1** (5 mmol) and the appropriate α-bromoketone, bromoacetone or phenacyl bromide (5 mmol) in absolute ethanol (25 mL) was refluxed for 2 h, then allowed to cool. The precipitate that formed was filtered off, dried, and recrystallized from ethanol to give the dihydrothiazoles **2a** and **2b**, respectively.

2-(Ethoxycarbonylmethylene)-2,3-dihydro-4-methyl-3-phenyl-1,3-thiazole **2a**. Yellow crystals; yield 88%; mp 171–172°C; IR (ν/cm^{-1}) = 1652 (CO ester), 1596 (C=C); ^{1}H NMR (DMSO): δ = 1.40 (t, 3H, CH_3), 1.75 (s, 3H, CH_3), 4.40 (q, 2H, CH_2), 5.20 (s, 1H, =CH), 6.60 (s, 1H, thiazole 5-H), 7.30–7.70 (m, 5H, Ar-H); MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 262 (100). Calcd for $C_{14}H_{15}NO_2S$ (261.34): C, 64.34; H, 5.79; N, 5.36%. Found: C, 64.23; H, 5.71; N, 5.44%.

2-(Ethoxycarbonylmethylene)-2,3-dihydro-3,4-diphenyl-1,3-thiazole **2b**. Yellow crystals; yield 68%; mp 192–193°C; IR (ν/cm^{-1}) = 1646 (CO ester), 1598 (C=C); ^{1}H NMR (DMSO): δ = 1.40 (t, 3H, CH_3), 4.40 (q, 2H, CH_2), 5.20 (s, 1H, =CH), 6.60 (s, 1H, thiazole 5-H), 7.10–7.70 (m, 10H, Ar-H); MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 324 (100). Calcd for $C_{19}H_{17}NO_2S$ (323.41): C, 70.56; H, 5.30; N, 4.33%. Found: C, 70.38; H, 5.19; N, 4.28%.

Synthesis of 2,3-Dihydro-3-phenyl-1,3,4-thiadiazole Derivatives **5a,b**

To a mixture of the thiocarbamoyl derivative **1** (5 mmol) and the appropriate hydrazonoyl bromides **3a,b** (5 mmol) in absolute ethanol (25 mL), few drops of triethylamine was added as a catalyst. The mixture was refluxed for 4 h, then left to cool at room temperature. The solid that formed was collected by flirtation, dried, and recrystallized form ethanol to give the thiadiazoles **5a,b** in 78 and 74% yield, respectively.

2-(Ethoxycarbonylmethylene)-5-benzoyl-2,3-dihydro-3-phenyl-1,3,4-thiadiazole **5a**. Red crystals; yield 78%; mp 234–235°C; IR (ν/cm^{-1}) = 1667 (CO ester), 1628 (CO conjugated); ^{1}H NMR (DMSO): δ = 1.20 (t, 3H, CH_3), 4.10 (q, 2H, CH_2), 5.30 (s, 1H, =CH), 7.20–7.60 (m, 10H, Ar-H); MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 353 (80). Calcd for $C_{19}H_{16}N_2O_3S$ (352.41): C, 64.76; H, 4.58; N, 7.95%. Found: C, 64.86; H, 4.67; N, 7.81%.

2-(Ethoxycarbonylmethylene)-5-benzoyl-2,3-dihydro-3-(p-tolyl)-1,3,4-thiadiazole **5b**. Red crystals; yield 74%; mp 276–277°C; IR (ν/cm^{-1}) = 1662 (CO ester), 1630 (CO conjugated); ^{1}H NMR ($CDCl_3$): δ = 1.20 (t, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.10 (q, 2H, CH_2), 5.30 (s, 1H, =CH), 7.10–7.80 (m, 9H, Ar-H); MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 367 (67). Calcd for $C_{20}H_{18}N_2O_3S$ (366.43): C, 65.55; H, 4.95; N, 7.64%. Found: C, 65.73; H, 4.82; N, 7.76%.

Synthesis of 3-Hydroxy-5-(phenylamino)-thiophene-2-carboxamide Derivatives **9a–c**

General Procedure. To a solution of **1** (5 mmol) in ethanolic sodium ethoxide (5 mmol) (prepared by dissolving sodium metal (0.12 g) in absolute ethanol (30 mL)), the appropriate 2-chloro-*N*-arylacetamides **7a–c** were added. The reaction mixture was heated under reflux for 4 h. The reaction mixture was poured into cold water, neutralized with dilute HCl, and the solid product that formed was filtered off and recrystallized from dioxane to afford the corresponding thiophene derivatives **9a–c**.

3-Hydroxy-N-phenyl-5-(phenylamino)thiophene-2-carboxamide **9a**. White crystals; yield 68%; mp 196–197°C; IR (ν/cm^{-1}) = 3303 (OH), 3235 (NH), 3192 (NH), 1671 (CO amide); ^{1}H NMR (DMSO): δ = 6.20 (s, 1H, thiophene 4-H), 6.90–7.60 (m, 10H, Ar-H), 9.20 (s, 1H, NH), 9.55 (s, 1H, NH), 11.80 (s, 1H, OH); ^{13}C NMR (DMSO): δ = 96.05, 99.38, 116.89 (2C), 119.42 (2C), 121.40, 122.83, 128.72 (2C), 129.40 (2C), 138.86, 141.74, 151.41, 157.55, 161.14; MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 311 (78). Calcd for $C_{17}H_{14}N_2O_2S$ (310.37): C, 65.79; H, 4.55; N, 9.03%. Found: C, 65.62; H, 4.43; N, 8.86%.

3-Hydroxy-5-(phenylamino)-N-(4-phenylthiazol-2-yl)thiophene-2-carboxamide **9b**. White crystals; yield 58%; mp 211–212°C; IR (ν/cm^{-1}) = 3294 (OH), 3244 (NH), 3146 (NH), 1677 (CO amide); ^{1}H NMR (DMSO): δ = 6.20 (s, 1H, thiophene 4-H), 6.90–7.80 (m, 11H, Ar-H, thiazole 5-H), 9.20 (s, 1H, NH), 9.70 (s, 1H, NH), 11.90 (s, 1H, OH). Calcd for $C_{20}H_{15}N_3O_2S_2$ (393.48): C, 61.05; H, 3.84; N, 10.68%. Found: C, 61.22; H, 3.93; N, 10.77%.

3-Hydroxy-5-(phenylamino)-N-(4-phenyl-5-phenylazothiazol-2-yl)thiophene-2-carboxamide **9c**. Red crystals; yield 62%; mp 184–185°C; IR (ν/cm^{-1}) = 3303 (OH), 3235 (NH), 3182 (NH), 1671 (CO amide); ^{1}H NMR (DMSO): δ = 6.20 (s, 1H, thiophene 4-H), 7.00–7.80 (m, 15H, Ar-H), 9.20 (s, 1H, NH), 9.60 (s, 1H, NH), 11.70 (s, 1H, OH). Calcd for $C_{26}H_{19}N_5O_2S_2$ (497.59): C, 62.76; H, 3.85; N, 14.07%. Found: C, 62.58; H, 3.94; N, 14.18%.

Synthesis of 2-(Ethoxycarbonylmethylene)-3-phenyl-1,3-thiazolidin-4-one **11**

A mixture of **1** (5 mmol) and ethyl bromoacetate (5 mmol) in ethanol (30 mL) containing fused sodium acetate (0.40 g) was refluxed for 4 h. The reaction mixture was left to cool to room temperature. The solid product was collected by filtration,

washed with water, and recrystallized from ethanol to give **11** as follows.

White crystals; yield 78%; mp 161–162°C; IR (ν/cm^{-1}) = 1719 (CO ring), 1683 (CO ester); ^{1}H NMR ($CDCl_3$/DMSO): δ = 1.20 (t, 3H, CH_3), 3.90 (s, 2H, CH_2), 4.10 (q, 2H, CH_2), 5.10 (s, 1H, =CH), 7.15–7.55 (m, 5H, Ar-H); ^{13}C NMR ($CDCl_3$/DMSO): δ = 14.02, 31.79, 59.65, 92.36, 127.68 (2C), 129.45, 129.86 (2C), 134.61, 158.76, 167.21, 171.72; MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 264 (100). Calcd for $C_{13}H_{13}NO_3S$ (263.06): C, 59.30; H, 4.98; N, 5.32%. Found: C, 59.13; H, 4.85; N, 5.18%.

Synthesis of 2-(Ethoxycarbonylmethylene)-3-phenyl-1,3-thiazolidin-5-one **12**

To a solution of **1** (5 mmol) in *N*,*N*-dimethylformamide (20 mL) containing drops of triethylamine, chloroacetyl chloride (10 mmol) was added dropwise with stirring. After complete addition, the reaction mixture was stirred for 2 h and then poured into ice-cooled water. The solid product was collected by filtration and recrystallized from ethanol to give **12** as follows.

Yellow crystals; yield 84%; mp 137–138°C; IR (ν/cm^{-1}) = 1742 (CO ring), 1688 (CO ester); ^{1}H NMR ($CDCl_3$/DMSO): δ = 1.20 (t, 3H, CH_3), 4.10 (q, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.10 (s, 1H, =CH), 6.95–7.80 (m, 5H, Ar-H); ^{13}C NMR ($CDCl_3$/DMSO): δ = 13.85, 43.14, 59.65, 106.74, 128.06 (2C), 129.11, 130.74 (2C), 137.42, 158.94, 168.36, 184.56. Calcd for $C_{13}H_{13}NO_3S$ (263.06): C, 59.30; H, 4.98; N, 5.32%. Found: C, 59.08; H, 4.79; N, 5.23%.

Synthesis of 3-Phenyl-4-(arylhydrazono)-1,3-thiazolidin-5-ones **13a,b**

An aqueous solution of the appropriate arenediazonium chloride (5 mmol) was added portionwise to a stirred solution of **12** (5 mmol) in pyridine (30 mL) at 0–5°C. The reaction mixture was stirred for 2 h, the resulting solid was collected, washed with water, and recrystallized from ethanol to give **13a,b** in 71 and 66% yield, respectively.

2-(Ethoxycarbonylmethylene)-3-phenyl-4-(p-tolylhydrazono)-1,3-thiazolidin-5-one **13a**. Red crystals; yield 71%; mp 253–254°C; IR (ν/cm^{-1}) = 1711 (CO ring), 1686 (CO ester); ^{1}H NMR (DMSO): δ = 1.10 (t, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.10 (q, 2H, CH_2), 5.10 (s, 1H, =CH), 7.10–7.80 (m, 9H, Ar-H), 8.90 (s, 1H, NH). Calcd for $C_{20}H_{19}N_3O_3S$ (381.45): C, 62.97; H, 5.02; N, 11.02%. Found: C, 62.84; H, 5.09; N, 11.11%.

2-(Ethoxycarbonylmethylene)-3-phenyl-4-(p-methoxyphenylhydrazono)-1,3-thiazolidin-5-one **13b**. Reddish brown crystals; yield 66%; mp 231–232°C; IR (ν/cm^{-1}) = 1709 (CO ring), 1682 (CO ester); ^{1}H NMR (DMSO): δ = 1.10 (t, 3H, CH_3), 3.85 (s, 3H, OCH_3), 4.10 (q, 2H, CH_2), 5.10 (s, 1H, =CH), 6.90–7.60 (m, 9H, Ar-H), 8.80 (s, 1H, NH). MS ($M^+ + H$; CI *iso*-butane) *m*/*z* (%): 398 (100). Calcd for $C_{20}H_{19}N_3O_4S$ (397.45): C, 60.44; H, 4.82; N, 10.57%. Found: C, 60.30; H, 4.88; N, 10.63%.

Synthesis of 2-[Ethoxycarbonyl(aryldiazenyl)-methylene]-thiazolidin-5-ones **14a,b**

To a solution of **15** (5 mmol) in *N*,*N*-dimethylformamide (20 mL) containing drops of triethylamine, chloroacetyl chloride (10 mmol) was added dropwise with stirring. After complete addition, the reaction mixture was stirred for 2 h and then poured into ice-cooled water. The solid product was collected by filtration and recrystallized from EtOH/DMF mixture (2:1) to give **14a,b**.

2-[Ethoxycarbonyl(p-tolyldiazenyl)methylene]-3-phenyl-1,3-thiazolidin-5-one **14a**. Orange crystals; yield 83%; mp 161–162°C; IR (ν/cm^{-1}) = 1731 (CO ring), 1706 (CO ester); ^{1}H NMR (DMSO): δ = 1.10 (t, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.50 (q, 2H, CH_2), 5.10 (s, 2H, CH_2), 7.10–7.70 (m, 9H, Ar-H). Calcd for $C_{20}H_{19}N_3O_3S$ (381.45): C, 62.97; H, 5.02; N, 11.02%. Found: C, 63.17; H, 5.12; N, 10.94%.

2-[Ethoxycarbonyl(p-methoxyphenyldiazenyl)methylene]-3-phenyl-1,3-thiazolidin-5-one **14b**. Orange crystals; yield 78%; mp 153–154°C; IR (ν/cm^{-1}) = 1734 (CO ring), 1698 (CO ester); ^{1}H NMR (DMSO): δ = 1.00 (t, 3H, CH_3), 3.45 (q, 2H, CH_2), 3.80 (s, 3H, OCH_3), 5.25 (s, 2H, CH_2), 6.95–7.80 (m, 9H, Ar-H); ^{13}C NMR (DMSO): δ = 13.15, 44.47, 55.51, 61.29, 113.99 (2C), 124.05 (2C), 126.82, 128.45, 128.74 (2C), 130.85 (2C), 138.55, 139.33, 159.94, 160.88, 169.11, 185.90; MS (M^+ + H; CI *iso*-butane) *m*/*z* (%): 398 (60). Calcd for $C_{20}H_{19}N_3O_4S$ (397.45): C, 60.44; H, 4.82; N, 10.57%. Found: C, 60.26; H, 4.71; N, 10.49%.

Synthesis of 5-Phenylazo-1,3-thiazole Derivatives **17** *and* **19**

General Procedure. A mixture of hydrazonoyl bromides **3** (2 mmol) and the appropriate thiosemicarbazones **16** or thiourea derivative **18** (2 mmol) in absolute ethanol (20 mL), in the triethylamine (0.2 mL), was refluxed for 2 h, then left to cool. The precipitated product was filtered off, dried, and

finally recrystallized from EtOH/DMF mixture (2:1) to afford the corresponding thiazoles **17a–e** and **19a–c**.

2-(Benzylidenehydrazino)-4-phenyl-5-phenylazo-1,3-thiazole **17a**. Red crystals; yield 60%; mp 217–218°C; IR (ν/cm^{-1}) = 3153 (NH), 1601 (C=N), 1561 (N=N); ^{1}H NMR (DMSO): δ = 7.05–7.55 (m, 12H, Ar-H, NH), 7.80 (d, 2H, Ar-H), 8.30 (d, 2H, Ar-H), 8.40 (s, 1H, N=CH); MS (M$^+$; EI) *m/z* (%): 383 (100). Calcd for $C_{22}H_{17}N_5S$ (383.47): C, 68.91; H, 4.47; N, 18.26%. Found: C, 69.02; H, 4.54; N, 18.34%.

2-(p-Methylbenzylidenehydrazino)-4-phenyl-5-phenylazo-1,3-thiazole **17b**. Red crystals; yield 62%; mp 204–205°C; IR (ν/cm^{-1}) = 3168 (NH), 1607 (C=N), 1571 (N=N); ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3H, CH_3), 7.10–7.70 (m, 15H, Ar-H, NH), 8.40 (s, 1H, N=CH); MS (M$^+$; EI) *m/z* (%): 397 (100). Calcd for $C_{23}H_{19}N_5S$ (397.50): C, 69.50; H, 4.82; N, 17.62%. Found: C, 69.58; H, 4.87; N, 17.71%.

2-(p-Methoxybenzylidenehydrazino)-4-phenyl-5-phenylazo-1,3-thiazole **17c**. Red crystals; yield 82%; mp 215–216°C; IR (ν/cm^{-1}) = 3246 (NH), 1602 (C=N), 1553 (N=N); ^{1}H NMR ($CDCl_3$/CF_3COOD): δ = 3.85 (s, 3H, OCH_3), 6.95 (d, 2H, Ar-H), 7.40–8.05 (m, 12H, Ar-H), 8.20 (s, 1H, N=CH); ^{13}C NMR ($CDCl_3$/CF_3COOD): δ = 55.56, 114.79 (2C), 121.39 (2C), 121.96, 124.63, 127.95, 129.36 (2C), 129.79 (2C), 130.20 (2C), 130.57 (2C), 131.03, 133.00, 137.15, 147.49, 154.33, 163.17, 170.04; MS (M$^+$; EI) *m/z* (%): 413 (100). Calcd for $C_{23}H_{19}N_5OS$ (413.49): C, 66.81; H, 4.63; N, 16.94%. Found: C, 66.86; H, 4.68; N, 16.87%.

2-(p-N,N-Dimethylaminobenzylidenehydrazino)-4-phenyl-5-phenylazo-1,3-thiazole **17d**. Red crystals; yield 86%; mp 212–213°C; IR (ν/cm^{-1}) = 3164 (NH), 1599 (C=N), 1578 (N=N); ^{1}H NMR ($CDCl_3$): δ = 3.05 (s, 6H, $2CH_3$), 6.65 (d, 2H, Ar-H), 7.00–7.75 (m, 13H, Ar-H, NH), 8.40 (s, 1H, N=CH); ^{13}C NMR ($CDCl_3$): δ = 40.05 (2C), 111.59 (2C), 114.21 (2C), 121.76, 122.70, 128.32 (2C), 129.51 (2C), 130.24, 130.66 (2C), 130.93 (2C), 131.91, 141.04, 142.82, 152.67, 161.42, 168.61, 172.02; MS (M$^+$; EI) *m/z* (%): 426 (100). Calcd for $C_{24}H_{22}N_6S$ (426.54): C, 67.58; H, 5.20; N, 19.70%. Found: C, 67.44; H, 5.12; N, 19.62%.

2-(p-Chlorobenzylidenehydrazino)-4-phenyl-5-phenylazo-1,3-thiazole **17e**. Red crystals; yield 76%; mp 207–208°C; IR (ν/cm^{-1}) = 3182 (NH), 1599 (C=N), 1548 (N=N); ^{1}H NMR ($CDCl_3$/CF_3COOD): δ = 7.30–8.00 (m, 14H, Ar-H), 8.25 (s, 1H, N=CH); MS (M$^+$; EI) *m/z* (%): 417 (100). Calcd for $C_{22}H_{16}ClN_5S$ (417.91): C, 63.23; H, 3.86; N, 16.76%. Found: C, 63.06; H, 3.74; N, 16.68%.

2-(4-Phenyl-5-phenylazo-thiazol-2-ylamino)-N,N-dimethylacetamide **19a**. Red crystals; yield 91%; mp 209–210°C; IR (ν/cm^{-1}) = 3284 (NH), 1656 (CO), 1558 (N=N); ^{1}H NMR ($CDCl_3$): δ = 3.00 (s, 6H, $2CH_3$), 4.20 (s, 2H, CH_2), 6.90 (s, 1H, NH), 7.30–7.50 (m, 6H, Ar-H), 7.70 (d, 2H, Ar-H), 8.25 (d, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ = 35.75, 35.87, 45.38, 122.44 (2C), 128.22 (2C), 128.98 (2C), 129.14, 129.32, 130.38 (2C), 134.69, 141.44, 152.82, 154.52, 167.07, 167.37; MS (M$^+$; EI) *m/z* (%): 365 (100). Calcd for $C_{19}H_{19}N_5OS$ (365.45): C, 62.44; H, 5.24; N, 19.16%. Found: C, 62.50; H, 5.28; N, 19.12%.

2-(4-Phenyl-5-(p-tolylazo)thiazol-2-ylamino)-N,N-dimethylacetamide **19b**. Red crystals; yield 82%; mp 220–221°C; IR (ν/cm^{-1}) = 3288 (NH), 1655 (CO), 1542 (N=N); ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3H, CH_3), 3.00 (s, 6H, $2CH_3$), 4.20 (s, 2H, CH_2), 6.90 (s, 1H, NH), 7.20–7.50 (m, 9H, Ar-H); ^{13}C NMR ($CDCl_3$): δ = 21.37, 35.73, 35.86, 45.35, 122.39 (2C), 128.20 (2C), 129.16, 129.67 (2C), 130.32 (2C), 134.20, 139.56, 141.56, 150.90, 153.70, 167.03, 167.14. Calcd for $C_{20}H_{21}N_5OS$ (379.48): C, 63.30; H, 5.58; N, 18.46%. Found: C, 63.24; H, 5.52; N, 18.53%.

2-(4-Phenyl-5-(p-methoxyphenylazo)-thiazol-2-ylamino)-N,N-dimethylacetamide **19c**. Red crystals; yield 87%; mp 224–225°C; IR (ν/cm^{-1}) = 3238 (NH), 1651 (CO), 1581 (N=N); ^{1}H NMR ($CDCl_3$/CF_3COOD): δ = 3.00 (s, 6H, $2CH_3$), 3.80 (s, 3H, OCH_3), 4.35 (s, 2H, CH_2), 6.90 (d, 2H, Ar-H), 7.40–7.90 (m, 7H, Ar-H); MS (M$^+$; EI) *m/z* (%): 395 (100). Calcd for $C_{20}H_{21}N_5O_2S$ (395.48): C, 60.74; H, 5.35; N, 17.71%. Found: C, 60.68; H, 5.30; N, 17.78%.

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