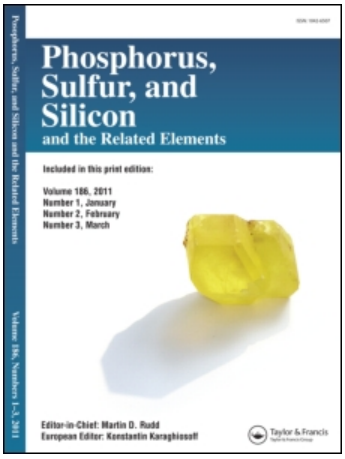

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Reactions with Hydrazonoyl Halides XXX: Synthesis of Some 2,3-Dihydro-1,3,4-Thiadiazoles and Unsymmetrical Azines Containing Benzothiazole Moiety

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REACTIONS WITH HYDRAZONOYL HALIDES XXX[1]: SYNTHESIS OF SOME 2,3-DIHYDRO-1,3,4-THIADIAZOLES AND UNSYMMETRICAL AZINES CONTAINING BENZOTHIAZOLE MOIETY

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C-Benzothiazoloyl-*N*-arylhydrazonoyl bromides **1a,b** have been caused to react with each of methyl 2-thiazolylcyanomethinecarbodithioate (**2**), alkyl carbodithioates **8–10**, and methyl thiocarbamates **14a-c** in the presence of triethylamine to give 2,3-dihydro-1,3,4-thiadiazoles in good yields. In contrast, hydrazonoyl bromides react with each of phenylthiourea (**19a**), phenylthiosemicarbazide (**19b**), and benzoylthiosemicarbazide (**19c**) afforded 5-arylazothiazole **22–24(a-c)** derivatives, respectively. Structures of the new compounds were elucidated on the basis of elemental analyses, spectral data, and alternative methods of synthesis whenever possible.

INTRODUCTION

Recently, a large number of thiazole derivatives have been found to exhibit pharmacological activity[2,3]. They also, used as an anthelmintic[4], fungicidal[5], antifungal activity, inhibiting in vivo the growth of Xanthomonas oryzae[6], and ingredient of herbicides[7]. As an extension of our study[8–10] and as a part of our program aiming at the synthesis of different thiadiazoles, unsymmetrical azines and thiazoles, we report here the reactivity of *C*-benzothiazoloyl-*N*-arylhydrazonoyl bromides towards some sulfur compounds.

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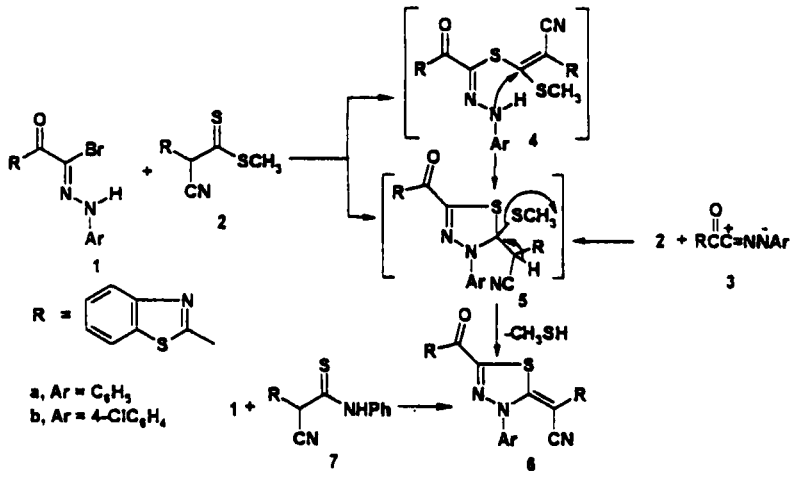
RESULTS AND DISCUSSION

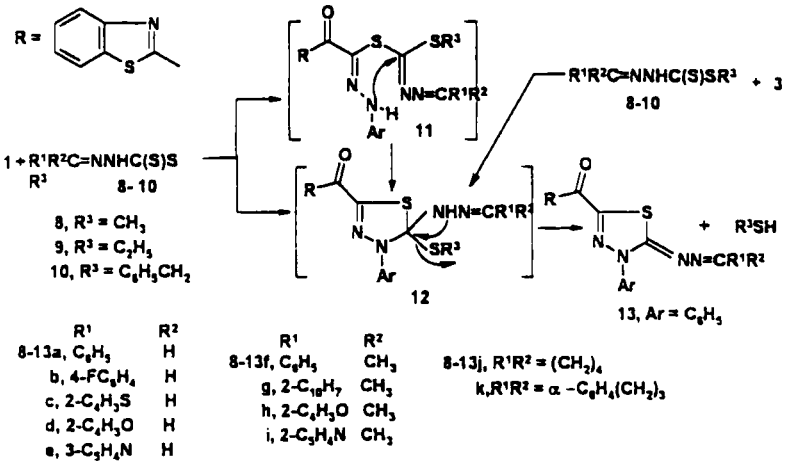
Treatment of the appropriate C-z-(benzothiazoloyl)-N-arylhydrazonoyl bromides **1a,b** with methyl 1-(2-benzothiazolyl)-1-cyanomethinecarbodithioate (**2**) in ethanolic triethylamine at room temperature afforded, in each case, one isolable product **6a,b**, respectively. ^{1}H NMR spectrum of the product showed one signal near δ_H 7.23–8.43 ppm due to aromatic protons. Its IR spectra revealed strong absorption bands near 2210 and 1670 cm^{-1} due to the nitrile and carbonyl groups, respectively. The product was identical in all respects (mp., mixed mp., and spectra) with authentic sample[11] [prepared via reaction of the appropriate **1a** with 2-benzothiazolylcyanothioacetanilide **7**]. Two possible pathways can account for the formation of **6**: i) 1,3-Addition of the thiol tautomer of **2** to the hydrazonoyl bromide **1** can give the thiohydrazonate ester **4**, which undergoes nucleophilic cyclization to yield **5**, which then affords **6** by loss of RSH. ii) Alternatively, 1,3-cycloaddition of the nitrilium imide **3** (which prepared in situ by treatment of **1** with triethylamine) to the C=S of **2** can give **5** directly (cf. Scheme 1).



SCHEME 1

Hydrazonoyl bromide **1a** reacts with the alkyl carbodithioate **8a** or **9a** or **10a** in ethanolic triethylamine afforded, in each case, the same isolable product (mp., mixed mp., and spectra). Scheme 2 depicts the proposed

mechanism for the reaction products. Structure **13a** was assigned to the isolated products on the basis of their elemental analyses and spectral data. For example, IR spectra of **13a** revealed, in each case, absorption band near 1670 cm^{-1} due to the carbonyl group. The ^1H NMR spectrum of **13a** showed signals at δ_H 7.12–8.42 ppm due to aromatic protons. The formation of **13a** is assumed to proceed via elimination of alkyl mercaptane from the non-isolable intermediate **12a** (Scheme 2). By similar route, the appropriate alkyl carbodithioates **8–10(b-k)** react with hydrazonoyl bromide **1a** to give unsymmetrical azines **13b-k**, respectively.

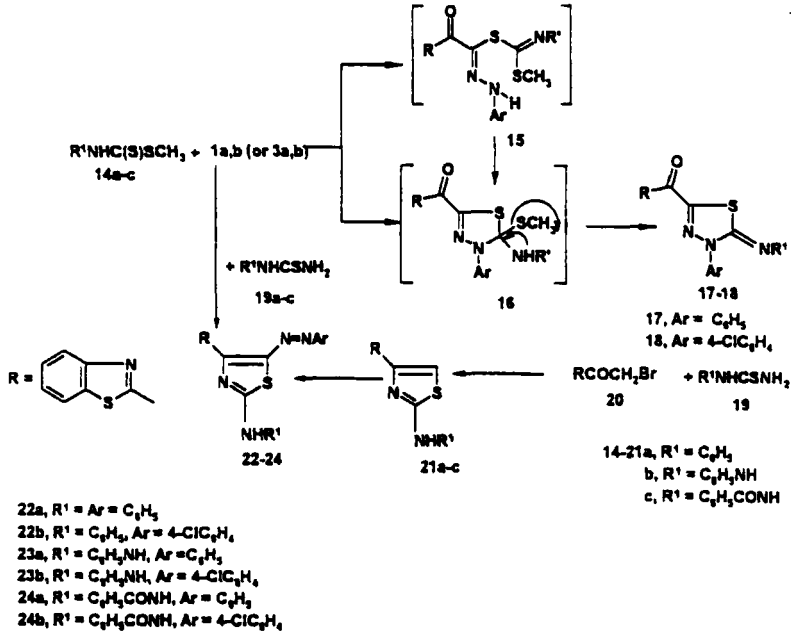


SCHEME 2

C-Thiazoloyl-*N*-phenylhydrazonoyl bromides (**1a**) react with the appropriate methyl thiocarbamate **14a** in ethanolic triethylamine at room temperature gave one isolable product **17a**. Structure **17a** was confirmed on the basis of elemental analysis and spectral data. IR spectrum of the product revealed absorption strong band at 1666 cm^{-1} due to CO function and no absorption band in the range 3100–3500 attributable the absence of NH group.

Analogy, the appropriate hydrazonoyl bromides **1a,b** react with the appropriate methyl thiocarbamates **14b,c** to give 2,3-dihydro-1,3,4-thiadiazole derivatives **17–18(b,c)**, respectively (cf. Scheme 3). Whereas, hydrazonoyl bromides **1a,b** react with phenylthiourea (**19a**) in ethanol

containing triethylamine gave 4-(z-benzothiazolyl)-2-phenylimino-5-phenylazothiazole **22a,b**. Structure **22** was elucidated on the basis of elemental analysis, spectral data, and alternative synthesis route. IR spectra of **22** showed no absorption bands between 1650–1800 due to the absence of CO group and revealed absorption of strong band at 3280 cm^{-1} assigned to the NH function. Thus, appropriate arenediazonium chloride couples with 4-(2-benzothiazolyl)-2-phenylaminothiazole (**21a**) in pyridine containing sodium hydroxide afforded product identical in all respects (mp., mixed mp., and spectra) with compounds **22a,b** (cf. Scheme 3).



SCHEME 3

Similar, treatment the appropriate hydrazonoyl bromides **1a,b** with the appropriate phenylthiosemicarbazide (**19b**) and benzoylthiosemicarbazide (**19c**) afforded the corresponding thiazole derivatives **23a,b** and **24a,b** respectively.

EXPERIMENTAL

All melting points were determined. on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz spectrometer and chemical shifts were expressed in δ units using TMS as internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University. All compounds gave satisfactory element analyses (±0.2%). Hydrazonoyl bromides[12] **1a,b**, alkyl carbodithioates[13–16] **8–10(a-k)**, phenylthiosemicarbazide[17], benzoylthiosemicarbazide[18], 2-bromoacetylbenzothiazole[19] and 4-benzothiazolyl-2-phenylaminothiazole[20] were prepared as previously reported.

Synthesis of methyl 1-benzothiazolyl-1-cyanomethinecarbodithioate (2)

Equimolar amount of 2-cyanomethylbenzothiazole, carbon disulfide and potassium hydroxide (5 mmol, each) in dry dimethylformamide (15 ml) were stirred for 3h at room temperature. Methyl iodide (0.71g; 0.32 ml) was added dropwise with stirring, the resulting solid was collected and crystallized from dimethylformamide gave **2** as yellow crystals (yield 82%); mp 256–58°C.

Synthesis of 2,3-Dihydro-1,3,4-thiadiazoles 6a,b, 17a-c, 18a-c and unsymmetrical azines 13a-k

General Procedure

Triethylamine (0.75 ml, 5 mmol) was added with stirring to a mixture of the appropriate hydrazonoyl bromides **1a,b**, the appropriate of methyl 1-benzothiazolyl-1-cyanomethinecarbodithioate (**2**), alkyl carbodithioates **8–10(a-k)**, and methyl thiocarbamates **14a-c** (5 mmol each) in ethanol (20 ml) at room temperature. Stirring was continued for 30 min., the resulting solid was collected, washed, and crystallized to give **6a,b, 13(a-k), 17a-c, and 18a-c**, respectively.

6a: crystallized from acetic acid as violet crystals (yield, 92%), m.p. 318–320°C. **6b**: crystallized from acetic acid as violet crystals (yield,

92%), m.p. 330–32°C. **13a**: crystallized from acetic acid as deep orange crystals (yield, 88%), m.p. 195–97°C. ^{1}H NMR (δ) = 7.39–8.46 (m). **13b**: crystallized from acetic acid as red crystals (yield, 85%), m.p. 200–2°C. **13c**: crystallized from acetic acid as orange crystals (yield, 87%), m.p. 204–6°C. **13d**: crystallized from acetic acid as brown crystals (yield, 89%), m.p. 178–79°C. **13e**: crystallized from acetic acid as orange crystals (yield, 92%), m.p. 143–45°C. **13f**: crystallized from acetic acid as red crystals (yield, 91%), m.p. 173–75°C. ^{1}H NMR (δ) = 2.52 (s) and 7.25–8.37 (m) **13g**: crystallized from acetic acid as orange crystals (yield, 87%), m.p. 208–10°C. **13h**: crystallized from acetic acid as orange crystals (yield, 85%), m.p. 165–67°C. ^{1}H NMR (δ) = 4.1 (s), 6.51 (d), 6.93 (d) and 7.25–8.37 (m). **13i**: crystallized from acetic acid as brown crystals (yield, 81%), m.p. 208–10°C. **13j**: crystallized from acetic acid as red crystals (yield, 86%), m.p. 208–10°C. ^{1}H NMR (δ) = 1.82 (m), 2.56 (t) and 7.33–8.36 (m). **13k**: crystallized from acetic acid as red crystals (yield, 78%), m.p. 235–36°C. ^{1}H NMR (δ) = 1.98 (m), 2.85 (t), 2.99 (t) and 7.26–8.36 (m). **17a**: crystallized from acetic acid as orange crystals (yield, 72%), m.p. 158–60°C. **17b**: crystallized from acetic acid as violet crystals (yield, 78%), m.p. 178–80°C. **17c**: crystallized from acetic acid as red crystals (yield, 81%), m.p. 157–58°C. **18a**: crystallized from acetic acid as red crystals (yield, 68%), m.p. 133–35°C. **18b**: crystallized from acetic acid as violet crystals (yield, 75%), m.p. 158–60°C. **18c**: crystallized from acetic acid as red crystals (yield, 82%), m.p. 245–47°C.

Synthesis of 5-Arylazo-4-(z-benzothiazolyl)-2-substituted aminothiazoles 22–24(a,b)

Method A

Triethylamine (0.75 ml, 5 mmol) was added with stirring to a mixture of the appropriate hydrazonoyl halides **1a,b** and the appropriate phenylthiourea (**19a**), phenylthiosemicarbazide (**19b**), and benzoylthiosemicarbazide (**19c**) (5 mmol) in ethanol (20 ml) at room temperature and stirring was continued for 2h. The resulting solid was collected, washed, and crystallized to give **22–24(a,b)**.

22a: crystallized from acetic acid as red. crystals (yield, 72%), m.p. 250–52°C. **22b**: crystallized from acetic acid as red crystals (yield, 69%), m.p. 273–75°C. **23a**: crystallized from acetic acid as red crystals (yield,

74%), m.p. 310–213°C. **23b**: crystallized from acetic acid as red crystals (yield, 71%), m.p. 252–53°C. **24a**: crystallized from acetic acid as red crystals (yield, 76%), m.p. 240–42°C. **24b**: crystallized from acetic acid as red crystals (yield, 71%), m.p. 248–50°C.

Method B

The appropriate arenediazonium chlorides were added to a cold solution contains equimolar amount of the appropriate 4-benzothiazolyl-2-substituted thiazoles **21a-c** and sodium hydroxide (5 mmol) in pyridine (20 ml) with stirring. The reaction mixture was stirred for 3h with temperature kept below 5°C then the resulting solid was collected. Crystallized from acetic acid gave identical products (mp., mixed mp., and spectra) with those obtained above.

Synthesis of 4-(z-benzothiazolyl)-2-substituted thiazole 21b,c

A mixture of equimolar amount of 2-bromoacetylthiazole and the appropriate phenylthiosemicarbazide or benzoylthiosemicarbazide (10 mmol) in ethanol (25 ml) was refluxed for 2h, then poured onto ice cold water (100 ml) containing few drops of ammonia. The resulting solid was collected and crystallized to give **21b** and **21c**.

21b: crystallized from acetic acid as pale brown crystals (yield, 76%), m.p. 215–17°C.

21c: crystallized from acetic acid as buff crystals (yield, 78%), m.p. 233–35°C.

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