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# Conversion of 5-Aryl-3-phenylthio-2(3H)-furanones into Some Nitrogen- and Sulphur-Containing Heterocycles

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# Conversion of 5-Aryl-3-phenylthio-2(3*H*)-furanones into Some Nitrogen- and Sulphur-Containing Heterocycles

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*3-Phenylthio-5-aryl-2(3H)-furanones **4** were prepared from 2-phenylthio-**3**-aroylpropionic acids **3** by a ring closure using acetic anhydride. Benzylamine reacted with **4** to give the benzylamide derivatives **5**, which were cyclized to the corresponding 2(3H)-pyrrolones **6**. The isothiazolone derivatives **7** were obtained from the benzylamides **5** by the action of $SOCl_2$. A ring opening of furanone **4** with hydrazine hydrate gave the acid hydrazides **8**. The latter hydrazides were utilized as starting materials for the synthesis of pyridazinone derivatives **9** and **11**, 1,3,4-oxadiazoles **13**, and triazolone derivatives **14**.*

**Keywords** 2(3H)-furanones; 1,3,4-oxadiazales; 2(3H)-pyrrolones; pyridazinones; 1,2,4-triazolones

## INTRODUCTION

2(3H)-furanones represent an important type of five-membered heterocycles of synthetic and biological importance. The products of a ring opening of these compounds with nucleophiles are the precursors of a wide variety of biologically important heterocyclic systems viz. pyrrolones,[1,2] pyridazinones,[3,4] pyrazoles,[5] 1,3,4-oxadiazoles,[6,7] and triazoles.[8]

During an attempted ring opening of 3-aryl-5-phenyl-2(3H)-furanones **1** with nitrogen nucleophiles, some of our research group observed that instead of a ring opening, isomerization of furanones **1** into isomeric 2(5H)-furanones **2** occurred (Scheme 1).[9]

It was believed that such isomerization took place via the intermediacy of a carbanion intermediate initially formed at position 3, which by resonance stabilization affected the migration of the double bond.

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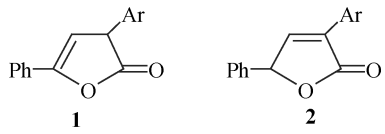


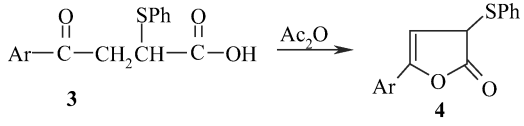

Ar = $C_6H_5$-; 4-$ClC_6H_4$-; 4-$CH_3OC_6H_4$-

**SCHEME 1**

In this investigation, it was thought that the presence of the phenylthio group at position 3 might exert a field effect, retarding the approach of the nucleophile (base). This would make an abstraction of a proton from position-3 difficult, and therefore, the ring opening should be the preferred route.

## RESULTS AND DISCUSSION

The starring materials for this study, 3-phenylthio-5-aryl-2(3H)-furanones **4**, were prepared from 2-phenylthio-3-aroylpropionic acids **3** (obtained from an addition of thiophenol to 3-aroylacrylic acids)[10] by a ring closure using the procedure previously described by one of us (Scheme 2).[11]




a, Ar = $C_6H_5$-; b, Ar = 4$ClC_6H_4$-; c, Ar = 4$CH_3OC_6H_4$-

**SCHEME 2**

The structure of furanones was inferred from analytical as well as spectral data (cf. Table I). IR spectra of these products showed an absorption band at 1773 $cm^{-1}$ characteristic of the five-membered lactone carbonyl group. $^1H$ NMR spectra of **4** showed characteristic signals of the methine, olefinic, and aromatic protons.

Benzylamine reacted with furanones **4**; the product obtained was found to depend mainly on the reaction conditions. Thus, when the reaction was carried out in ethanol at r.t. or in refluxing benzene for 1 h, the open-chain benzylamides **5** were obtained.

On the other hand, refluxing the reaction mixture in benzene for 3 h afforded the corresponding 2(3H)-pyrrolones **6**. The latter products were also obtained by a ring closure of the amides **5** using an HCl/AcOH mixture as a cyclizing agent.

It was of interest to the authors to convert amides **5** into the corresponding isothiazolone derivatives **7** by the action of thionyl chloride at

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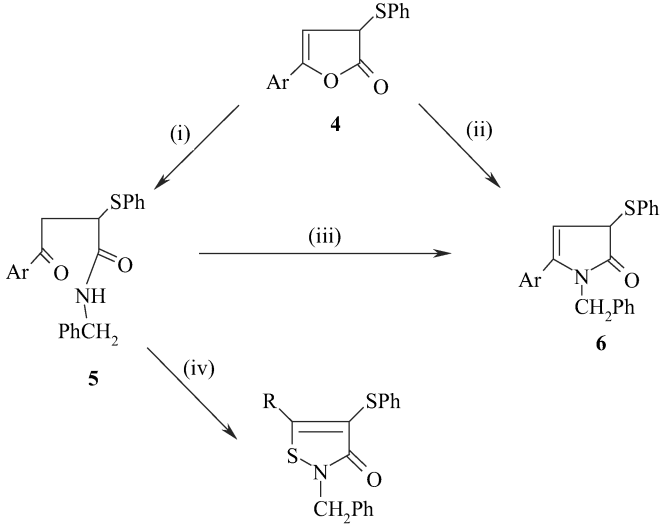
**TABLE I Infrared (IR) and $^1$H NMR (300 MHz) Spectral Data of Furanones 4**

| No. | IR ($\nu$ max) (KBr) $cm^{-1}$ $\nu_{C=O}$ | $^1$H NMR (DMSO-$d_6$) |
|---|---|---|
| **4a** | 1773 | $\delta = 3.73$ (d, 1, CH, $J = 1.36$ Hz), 6.72 (d, 1, =CH, $J = 1.56$ Hz), 7.20–7.53 (m, 10, ArH) |
| **4b** | 1772 | $\delta = 3.35$ (d, 1, CH, $J = 1.30$ Hz), 6.80 (d, 1, =CH, $J = 1.56$ Hz), 7.35–7.50 (m, 9, ArH) |
| **4c** | 1773 | $\delta = 3.30$ (d, 1, CH, $J = 1.30$ Hz), 3.70 (s, 3, $OCH_3$), 6.82 (d, 1, =CH, $J = 1.42$ Hz), 7.32–7.60 ( m, 9, ArH) |

r.t. Debenzoylation of the latter products **7a–c** was affected by refluxing with solid NaOH to give the isothiazolone derivative **7d**.

Structures of the products **5**,**6**, and **7** were elucidated from analytical and spectral data (cf. Table II). The foregoing reactions are represented by Scheme 3.




5, 6 a, Ar = $C_6H_5$- ; b, Ar = 4-Cl$C_6H_4$-

7 a, R = $C_6H_5CO$-; b, R = 4-Cl$C_6H_4$ CO-; C, R = 4-$CH_3$ $OC_6H_4CO$-; d, R = H

**SCHEME 3 Reagents and conditions:** (i) benzylamine in ethanol at r.t. or benzene/reflux for 1 h, (ii) benzylamine in benzene/reflux for 3 h, (iii) HCl/AcOH reflux 1 h, (iv) thionyl chloride at r.t.

Acid hydrazides represent a suitable functionality for obtaining a wide variety of biologically important heterocyclic systems. Dihydropyridazinones are known to have diverse pharmacological activities, e.g.,

**TABLE II Infrared (IR) and $^1$H NMR (300 MHz) Spectral Data of 5, 6, and 7**

| No. | IR ($\nu$ max) KBr ($cm^{-1}$) $\nu_{NH}$ | $\nu_{C=O}$ | $^1$H NMR (DMSO-$d_6$) |
|---|---|---|---|
| **5a** | 3300 | 1702<br>1665 | $\delta = 3.16$(d, 2, $CH_2CO$, $J = 7.2$ Hz), 4.10($AB_q$, 2, N-$CH_2$), 4.56(t, 1, CH, $J = 7.2$ Hz), 7.15–7.50 (m, 15, ArH), 8.50(br.s, NH, exchangeable) |
| **5b** | 3350 | 1702<br>1665 | $\delta = 3.20$(d, 2, $CH_2CO$, $J = 7.0$ Hz), 4.15($AB_q$, 2, N-$CH_2$), 4.56(t, 1, CH, $J = 7.0$ Hz), 7.10–7.63 (m, 14, ArH), 8.35(br.s, NH, exchangeable) |
| **5c** | 3330 | 1705<br>1675 | |
| **6a** | — | 1650 | $\delta = 3.80$($AB_q$, 2, N-$CH_2$), 4.82 (d, 1, CH, $J =$ 6.0 Hz), 6.59(d, 1, =CH, $J = 6.0$ Hz), 7.51–8.12 (m, 15, ArH) |
| **6b** | — | 1635 | |
| **6c** | — | 1639 | $\delta = 3.80$($AB_q$, 2, N-$CH_2$), 3.95 (s, 3, $OCH_3$), 4.84 (d, 1, CH, $J =$ 6.0 Hz), 6.50 (d, 1, =CH, $J =$ 6.0 Hz), 7.50–8.50 (m, 14, ArH) |
| **7a** | — | 1688 | $\delta = 3.95$( s, 2,N—$CH_2$), 7.25–7.55 (m, 15, ArH) |
| **7b** | — | 1690 | |
| **7c** | — | 1687 | $\delta = 3.95$(s, 3, $OCH_3$), 4.05 (s, 2,N—$CH_2$), 7.20–7.55 (m, 14, ArH) |
| **7d** | — | 1650 | $\delta = 3.95$( s, 2,N—$CH_2$), 6.62 (s, 1, =CH), 7.25–7.50, (m, 10, ArH) |

antihypertensive,[12] analgesic, and antiinflammatory activities.[13] 1,3,4-oxadiazoles were reported to have carcinostatic activity against several types of tumors[14] and antiarrhythmic[15] and anticholesterolsmic[16] activities. Also 1,2,4-triazoles display some biological activities, such as an inhibition of cholinesterase,[17] interference with mitosis,[18] and reversible denaturation of serum proteins.[19] Since this investigation aims at converting 2(3H)-furanone derivatives **4** into other heterocyclic systems of biological importance, we believe that the key step is the conversion of **4** into the corresponding acid hydrazides.

Thus, the furanone **4** reacted with hydrazine hydrate in ethanol at r.t. to give 3-aroyl-2-phenylthiopropionic acid hydrazides **8**. The infrared spectra of these hydrazides (cf. Table III) showed absorption bands characteristic of the NH and amide C=O groups at 3200–3220 $cm^{-1}$ and 1670–1690$cm^{-1}$, respectively. Furthermore, the $^1$H NMR spectrum of **8a** showed signals characteristic of the different protons (cf. Table III).

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**TABLE III Infrared (IR) and 1H–NHR (300 MHz) Spectral data of 8–14**

| No. | IR ($\nu$ max) KBr($cm^{-1}$) $\nu_{NH}$ | $\nu_{C=N}$ | $\nu_{C=O}$ | $^1$H NMR (DMSO–$d_6$) |
|---|---|---|---|---|
| **8a** | 3250<br>3200 | | 1690<br>1672 | $\delta = 3.26$(d, 2, $CH_2CO$, $J = 6.0$ Hz), 4.85 (t, 1, CH, $J = 6.0$ Hz), 6.02 (br.s 2, $NH_2$, exchangeable), 7.69–8.02 (m, 10, ArH), 8.50 (br.s, NHCO, exchangeable) |
| **8b** | 3215<br>3190 | | 1695<br>1665 | |
| **8c** | 3220<br>3175 | | 1695<br>1670 | |
| **9a** | 3250 | | 1635 | $\delta = 2.90$(d, 2, CH-$CH_2$, $J = 6.0$ Hz), 4.89 (t, 1, CH-$CH_2$, $J = 6.0$ Hz), 7.49–7.90(m, 10, ArH), 10.49 (s, 1, NHCO, exchangeable) |
| **9b** | 3245 | | 1642 | |
| **9c** | 3290 | | 1630 | |
| **10a** | 3350 | | 1705<br>1659 | $\delta = 3.30$ (d, 2, $CH_2CO$, $J = 6.0$ Hz), 4.80(t, 2, $CH_2$-CH, $J = 6.0$ Hz), 7.35–7.89 (m, 15, ArH), 10.45(s, 2, CO-NH-NH-CO, exchangeable) |
| **10b** | 3390 | | 1699<br>1660 | $\delta = 3.45$(d, 2, $CH_2CO$, $J = 6.0$ Hz), 4.89(t, 2, $CH_2$-CH, $J = 6.0$ Hz), 7.20–7.65 (m, 14, ArH), 10.05(s, 2, CO-NH-NH-CO, exchangeable) |
| **10c** | 3400 | | 1710<br>1669 | |
| **11a** | 3324 | | 1630 | $\delta = 4.70$(d, 1, CH, $J = 6.2$ Hz), 6.60(d, 1, =CH, $J = 6.2$ Hz), 7.50–7.91(m, 15, ArH), 10.49(s, 1, NH–CO, exchangeable) |
| **11b** | 3320 | | 1635 | |

(*Continued on next page*)

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**TABLE III Infrared (IR) and 1H–NHR (300 MHz) Spectral data of 8–14 (*Continued*)**

| No. | IR ($\nu$ max) KBr($cm^{-1}$) $\nu_{NH}$ | $\nu_{C=N}$ | $\nu_{C=O}$ | $^1$H NMR (DMSO–$d_6$) |
|---|---|---|---|---|
| **11c** | 3320 | | 1630 | $\delta = 3.75$(s, 3, $OCH_3$), 4.56(d, 1, CH, $J = 6.0$ Hz), 6.68 (d, 1, =CH, $J = 6.0$ Hz), 7.50–7.70(m, 14, ArH), 10.49 (s, 1, NH–CO, exchangeable) |
| **12a** | 3360 | | 1709<br>1670 | $\delta = 3.41$(d, 2, $CH_2CO$, $J = 6.3$ Hz), 4.89(t, 2, $CH_2$-CH, $J = 6.3$ Hz), 7.50–7.60 (m, 10, ArH), 8.60(br.s, 2, $H_2N$-CO, exchangeable), 10.45 (br.s, 2, CONHNHCO, exchangeable) |
| **12b** | 3356 | | 1710<br>1675 | $\delta = 3.60$(d, 2, $CH_2CO$, $J = 6.5$ Hz), 4.80(t, 2, $CH_2$-CH, $J = 6.5$ Hz), 7.50–7.60 (m, 9, ArH), 8.35(br.s, 2, $H_2N$-CO, exchangeable), 10.40 (br.s, 2, CONHNHCO, exchangeable) |
| **12c** | 3362 | | 1705<br>1675 | |
| **13a** | — | 1605 | 1675 | $\delta = 3.06$(d, 2, CH-$CH_2$, $J = 4.8$ Hz), 4.80 (t, 1, C$\underline{H}$-$CH_2$, $J = 4.8$ Hz), 7.55–8.01 (m, 15, ArH) |
| **13b** | — | 1600 | 1685 | $\delta = 3.30$(d, 2, CH-$CH_2$, $J = 5.3$ Hz), 4.80 (t, 1, C$\underline{H}$-$CH_2$, $J = 5.3$ Hz), 7.35–8.50 (m, 14, ArH) |
| **13c** | — | 1603 | 1670 | |
| **14a** | 3320 | 1600 | 1680 | $\delta = 3.21$(d, 2, $CH_2$, J = 6.0 Hz), 4.88(t, 1, $CH_2$-CH, $J = 6.0$ Hz), 7.22–7.39(m, 10, Ar), 13.04(br.s, 2, NHCONH, exchangeable) |
| **14b** | 3329 | 1600 | 1675 | |
| **14c** | 3300 | 1600 | 1677 | $\delta = 3.90$(s, 3, $OCH_3$), 3.15(d, 2, $CH_2$, $J = 6.2$ Hz), 4.68 (t, 1, $CH_2$-CH, $J = 6.2$ Hz), 7.05–7.30(m, 9, Ar), 12.09(br.s, 2, NHCONH, exchangeable) |

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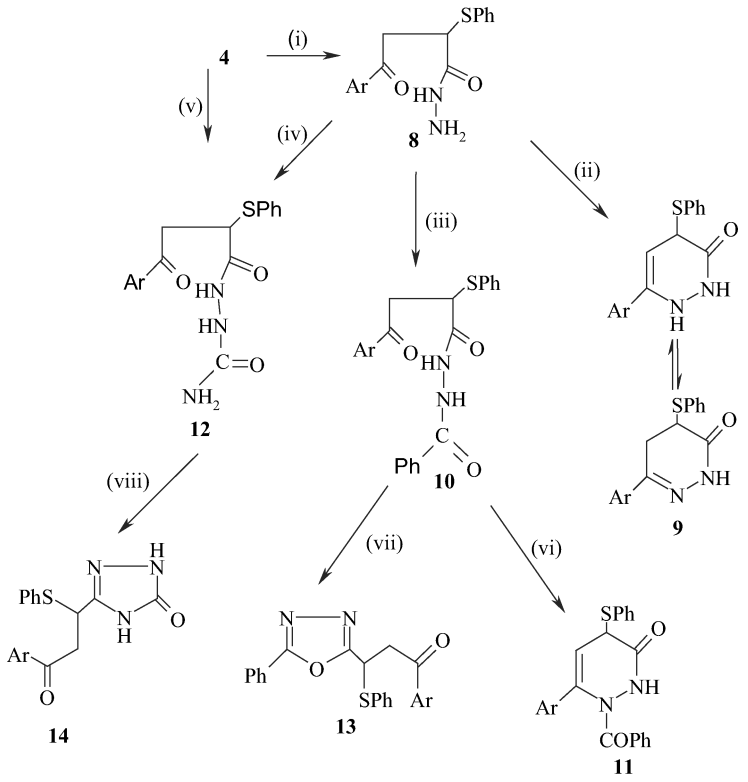
Hydrazides **8** were utilized for the synthesis of the following heterocyclic compounds (cf. Scheme 4):




a, Ar = $C_6H_5$-; b, Ar = 4-Cl $C_6H_4$-; c, Ar = 4-$CH_3OC_6H_4$-.

**SCHEME 4 Regents and conditions:** (i) Hydrazine hydrate/ethanol r.t.; (ii) HCl/AcOH reflux 1 h; (iii) PhCOCl/benzene reflux 2 h; (iv) $KNCO/H_2O$ r.t. 3 h; (v) $Cl^- {}^+NH_3$ $NHCONH_2$/AcONA (1.1 mol) ethanol, reflux 1 h; (vi) HCl/AcOH reflux 1 h; (vii) $POCl_3$/reflux 20 min; (viii) 2 N NaOH/reflux 2 h.

1. Pyridazinone derivatives **9** were obtained by a ring closure of the hydrazides **8** using an HCl/AcOH mixture as a cyclizing agent. The infrared spectra of these compounds (cf. Table III) showed an absorption band characteristic of the NH and amide C=O groups at 3245–3290 $cm^{-1}$ and 1630–1642 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **9a** showed signals characteristic of the different protons (cf. Table III).

2. 1-aroylpyridazinones **11** were synthesized from hydrazides **8** by two steps: (i) hydrazides **8** were converted by the action of benzoyl chloride into the corresponding diaroylhydrazines $\mathbf{10}^-$, and (ii) a ring closure of the latter products using HCl/AcOH afforded pyridazinones **11**. The infrared spectra of compounds **10** (cf. Table III) showed absorption bands characteristic of the NH and C=O groups at 3350–3400 $cm^{-1}$ and 1659–1710 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **10a** and **b** showed signals characteristic of the different protons (cf. Table III).
3. The infrared spectra of compounds **11** (cf. Table III) showed absorption bands characteristic of the NH and amide C=O groups at 3320–3324 $cm^{-1}$ and 1630–1635 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **11a** and **c** showed signals characteristic of the different protons (cf. Table III).
4. 1,3,4-oxadiazoles **13** were obtained by a ring closure of diaroylhydrazines using phosphorus oxychloride. Infrared spectra of compounds **13** (cf. Table III) showed absorption bands characteristic of the C=N and C=O groups at 1600–1605 $cm^{-1}$, and 1670–1685 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **13a** and **b** showed signals characteristic of the different protons (cf. Table III).
5. 1,2,4-triazolone derivatives **14** were obtained from hydrazides by two steps: (i) hydrazides **8** were reacted with pot. isocyanate to give the corresponding semicarbazide derivatives **12**. The infrared spectra of compounds **12** (cf. Table III) showed absorption bands characteristic of NH and C=O groups at 3356–3362 $cm^{-1}$ and 1675–1710 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **12a** and **b** showed signals characteristic of the different protons (cf. Table III). The latter products were also obtained by a ring opening of furanones **4** by semicarbazide in refluxing ethanol. (ii) Semicarbazides **12** were cyclized by means of sodium hydroxide to give triazolones **14**. The structures of compounds **14** were elucidated from their analytical as well as spectral data. Infrared spectra of compounds **14** (cf. Table III) showed absorption bands characteristic of NH and C=O groups at 3300–3329 $cm^{-1}$ and 1675–1680 $cm^{-1}$, respectively. Furthermore, the $^1H$ NMR spectrum of **14a** and **c** showed signals characteristic of the different protons (cf. Table III).

## EXPERIMENTAL

Melting points were measured on an electrothermal melting-point apparatus and are uncorrected. Elemental analyses were carried out at the Micro-Analytical Unit, Cairo University, Giza. IR spectra were measured on a Unicam SP-1200 spectrophotometer using the KBr-wafer

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technique. $^1$H NMR spectra were measured in DMSO-$d_6$ on a varian plus instrument (300 MHz).

## The Preparation of 2-Phenylthio-3-aroylpropionic Acids (3a–c)

These compounds were prepared according to the procedure described by previous investigators.[10]

## The Preparation of 3-Phenylthio-5-aryl-2(3H) Furanones (4a–c)

A mixture of 2-phenylthio-3-aroylpropionic acids (3a–c)[10] (0.1 mol) and acetic anhydride (27 mL, 0.3 mol) was heated under reflux for 20 min. The reaction mixture was cooled, poured onto ice, and filtered off, and the product was recry stallized from a suitable solvent to give **(4a–c)** (cf. Table IV).

## The Reaction of 3-Phenylthio-5-aryl-2(3H)-furanones (4a–c) with Benzylamine

To a solution of the furanones **(4a–c)** (0.01 mol) in benzene or ethanol (20 mL), benzylamine (1.1 mL, 0.01 mol) was added. The reaction mixture was refluxed in benzene at 60°C for 1 h or left at r.t. for 5 min in ethanol. The products obtained were shown to be 2-phenylthio-3-aroyl-N-benzyl-propionamides **(5a–c)**, (cf. Table IV). When the reaction mixture was heated at 100°C for 3 h, the product obtained was filtered off, washed with benzene, and recrystallized from the suitable solvent (cf. Table IV). 1-benzyl-3-phenylthio-5-aryl-2(3H)-pyrrolones **(6a–c)** were obtained.

## The Conversion of Amides (5a–c) into Isothiazolones (7a–c)

A mixture of N-benzylamide derivatives **(5a–c)** (0.001 mol) and thionyl chloride (20 mL, 0.17 mol) was stirred at r.t. for 24 h. The excess thionyl chloride then was evaporated under vacuum. The solid obtained was filtered off and recrystallized from a suitable solvent (cf. Table IV) to give 2-benzyl-4-phenylthio-5-aroyl-3 (2H)-isothiazolones **(7a–c)**.

## Debenzoylation of (7a–c)

A mixture of **(7a–c)** (0.01 mol) and solid NaOH (0.1 g, 0.0025 mol) in 20 mL of benzene was stirred at r.t. for 1 h. When a fading of the initial yellowish color was observed, the benzene layer was separated and concentrated under vacuum to give a solid residue, which was

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**Table IV Physical and Analytical Data of Compounds 4–14**

| No. | M.P. °C (solvent) | Yield % | (Calcd/Found) % C | H | N | S |
|---|---|---|---|---|---|---|
| **4a** | 120–122 | 40 | 71.64 | 4.48 | — | 11.94 |
| | (ethanol) | | 71.60 | 4.48 | | 11.89 |
| **4b** | 160–163 | 50 | 63.47 | 3.64 | — | 10.58 |
| | (ethanol) | | 63.42 | 3.60 | | 10.56 |
| **4c** | 140–141 | 25 | 68.46 | 4.70 | — | 10.74 |
| | (ethanol) | | 68.69 | 4.65 | | 10.69 |
| **5a** | 145–147 | 65 | 73.60 | 5.60 | 3.73 | 8.53 |
| | (ethanol) | | 73.50 | 5.60 | 3.70 | 8.50 |
| **5b** | 190–191 | 62 | 67.40 | 4.88 | 3.42 | 7.80 |
| | (ethanol) | | 67.35 | 4.86 | 3.40 | 7.80 |
| **5c** | 165–166 | 55 | 71.11 | 5.68 | 3.46 | 7.90 |
| | (ethanol) | | 70.95 | 5.67 | 3.44 | 7.87 |
| **6a** | 130–132 | 75 | 77.31 | 5.32 | 3.92 | 8.96 |
| | (ethanol) | | 77.20 | 5.30 | 3.88 | 8.95 |
| **6b** | 160–162 | 70 | 70.50 | 4.60 | 3.58 | 8.17 |
| | (ethanol) | | 70.45 | 4.62 | 3.64 | 8.15 |
| **6c** | 140–142 | 72 | 74.42 | 5.43 | 3.62 | 8.27 |
| | (ethanol) | | 74.39 | 5.46 | 3.60 | 8.24 |
| **7a** | 250–252 | 40 | 68.49 | 4.22 | 3.47 | 15.88 |
| | (ethanol) | | 68.67 | 4.23 | 3.54 | 15.85 |
| **7b** | 230–233 | 35 | 63.09 | 3.66 | 3.20 | 14.63 |
| | (ethanol) | | 63.216 | 3.69 | 3.31 | 14.60 |
| **7c** | 257–258 | 40 | 66.51 | 4.39 | 3.23 | 14.78 |
| | (ethanol) | | 66.60 | 4.38 | 3.21 | 14.77 |
| **7d** | 195–197 | 45 | 64.21 | 4.35 | 4.68 | 21.40 |
| | (ethanol) | | 64.35 | 4.33 | 4.68 | 21.37 |
| **8a** | 150–153 | 72 | 64.00 | 5.33 | 9.33 | 10.67 |
| | (benzene) | | 64.12 | 5.35 | 9.50 | 10.65 |
| **8b** | 185–186 | 75 | 57.40 | 4.48 | 8.37 | 9.57 |
| | (benzene) | | 57.57 | 4.48 | 8.40 | 954 |
| **8c** | 165–166 | 70 | 61.82 | 5.45 | 8.48 | 9.69 |
| | (benzene) | | 61.80 | 5.43 | 8.42 | 9.65 |
| **9a** | 145–146 | 55 | 68.09 | 4.96 | 9.93 | 11.35 |
| | (ethanol) | | 68.15 | 4.97 | 9.97 | 11.33 |
| **9b** | 156–159 | 45 | 60.66 | 4.11 | 8.85 | 10.11 |
| | (ethanol) | | 60.78 | 4.10 | 8.89 | 10.10 |
| **9c** | 183–185 | 50 | 65.38 | 5.13 | 8.97 | 10.26 |
| | (ethanol) | | 65.50 | 5.13 | 8.95 | 10.25 |
| **10a** | 250–251 | 40 | 68.32 | 4.95 | 6.93 | 7.92 |
| | (benzene/ethanol) | | 68.35 | 4.93 | 6.90 | 7.90 |
| **10b** | 258–259 | 45 | 62.94 | 4.33 | 6.39 | 7.29 |
| | (benzene/ethanol) | | 62.89 | 4.31 | 6.38 | 7.27 |
| **10c** | 265–266 | 35 | 66.36 | 5.07 | 6.45 | 7.37 |
| | (benzene/ethanol) | | 66.34 | 5.04 | 6.46 | 7.35 |

(*Continued on next page*)

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**Table IV Physical and Analytical Data of Compounds 4–14 (*Continued*)**

| No. | M.P. °C (solvent) | Yield % | (Calcd/Found) % C | H | N | S |
|---|---|---|---|---|---|---|
| **11a** | 190–192 | 30 | 71.50 | 4.66 | 7.25 | 8.29 |
| | (ethanol) | | 71.56 | 4.65 | 7.20 | 8.28 |
| **11b** | 178–179 | 35 | 65.64 | 4.04 | 6.66 | 7.61 |
| | (ethanol) | | 65.69 | 3.97 | 6.61 | 7.64 |
| **11c** | 192–193 | 45 | 69.23 | 4.81 | 6.73 | 7.69 |
| | (ethanol) | | 69.20 | 4.89 | 6.79 | 7.65 |
| **12a** | 110–112 | 35 | 59.48 | 4.96 | 12.24 | 9.33 |
| | (benzene/ethanol) | | 59.47 | 4.94 | 12.20 | 9.30 |
| **12b** | 125–126 | 50 | 54.01 | 4.24 | 11.13 | 8.48 |
| | (benzene/ethanol) | | 54.09 | 4.25 | 11.11 | 8.46 |
| **12c** | 130–133 | 40 | 57.91 | 5.09 | 11.26 | 8.58 |
| | (benzene/ethanol) | | 57.96 | 5.07 | 11.26 | 8.55 |
| **13a** | 180–181 | 50 | 71.50 | 4.66 | 7.25 | 8.29 |
| | (ethanol) | | 71.52 | 4.62 | 7.26 | 8.28 |
| **13b** | 175–177 | 54 | 65.64 | 4.04 | 6.66 | 7.61 |
| | (ethanol) | | 65.66 | 4.06 | 6.64 | 7.60 |
| **13c** | 185–186 | 50 | 69.23 | 4.81 | 6.73 | 7.69 |
| | (ethanol) | | 69.20 | 4.80 | 6.70 | 7.69 |
| **14a** | 219–120 | 52 | 62.77 | 4.92 | 12.92 | 9.85 |
| | ( ethanol) | | 62.73 | 4.90 | 12.95 | 9.84 |
| **14b** | 213–114 | 65 | 56.75 | 4.17 | 11.68 | 8.90 |
| | (ethanol) | | 56.69 | 4.15 | 11.67 | 8.92 |
| **14c** | 225–126 | 50 | 60.85 | 5.07 | 11.83 | 9.01 |
| | (ethanol) | | 60.82 | 5.07 | 11.80 | 9.00 |

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crystallized from ethanol (cf. Table IV) to give 2-benzyl-4-phenylthio-3(2H)-isothiazolone **(7d)**.

## The Reaction of 3-Phenylthio-5-aryl-2(3H)-furanones (4a–c) with Hydrazine Hydrate

To a solution of furanones **(4a–c)** (1 mol) in ethanol (20 mL), hydrazine hydrate (35.5 mL, 1.1 mol) was added at r.t. for 5 min. The product obtained was filtered off and washed with ethanol, and the product was shown to be 2-phenylthio-3-aroylpropionic acid hydrazides **(8a–c)** (cf. Table IV). When the reaction mixture was refluxed in ethanol, the product was shown to be 6-aryl-4-phenylthio-4,5-dihydropyridazin-3-(2H)-one derivatives **(9a–c)**, which were recrystallized from a suitable solvent (cf. Table IV).

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## The Reaction of Hydrazides (8a–c) with Potassium Isocyanate

A solution of potassium isocyanate (1.78 g, 0.02 mol) in water (10 mL) was added dropwise with stirring at 0°C to a solution of hydrazide derivative **(8a–c)** (0.02 mol) in an acetic acid–water (1:1) mixture. The reaction mixture was stirred at r.t. for 3 h. The product obtained was filtered off, washed thoroughly with water, and finally recrystallized from a suitable solvent (cf. Table IV) to give 2-phenylthio-3-aroylpropionic acid semicarbazides **(12a–c)**.

The same semicarbazide derivatives **(12a–c)** were also obtained from heating a solution of 2(3H)-furanones **(4a–c)** (0.01 mol) in ethanol (30 mL) and a mixture of semicarbazide hydrochloride (1.12 g, 0.01 mol), and anhydrous sodium acetate (0.82 g, 0.01 mol) under reflux at 70°C for 1 h. The solid was obtained, filtered off, and recrystallized from a suitable solvent (cf. Table IV). The products obtained were identical in all respects (m.p., mixed m.p., and TLC) with the previously discussed products obtained from the reaction between hydrazides **(8a–c)** and potassium isocyanate.

## The Reaction of Hydrazide (8a–c) with Benzoyl Chloride

To a solution of hydrazide **(8a–c)** (0.01 mol) in 50 mL of benzene, dry benzoyl chloride (1.5 mL, 0.01 mol) was added. The reaction mixture was heated under reflux for 2 h. The solvent was distilled off under reduced pressure. The yellow solid obtained was washed thoroughly with water, drained, and recrystallized from the suitable solvent (cf. Table IV) to give 1-benzoyl-2-[$\alpha$-phenylthio-$\beta$-aroyl] propionyl hydrazines **(10a–c)**.

## Ring Closure of Compounds (5a–c) and (8a–c)

A solution of **(5a–c)** or **(8a–c)** (1 g) in a mixture of (HCl–$CH_3COOH$) (1:1) (30 mL) or ethanol (30 mL) was heated under reflux for 1 h and then left to cool. The solid obtained was filtered off, washed with water, and recrystallized from the suitable solvent (cf. Table IV) to give 1-benzyl-3-phenylthio-5-aryl-2(3H)-pyrrolone **(6a–c)** in the case of **(5a–c)** and 6-aryl-4-phenylthio-4,5-dihdropyridazin-3(2H)-ones **(9a–c)** in the case of **(8a–c)** (cf. Table IV).

## Ring Closure of Diaroylhydrazine (10a–c)

Phosphorus oxychloride (10 mL, 0.065 mol) was added dropwise to 1g of the diaroylhydrazine **(10a–c)**. The reaction mixture was refluxed for

20 min, left to cool, and poured onto crushed ice. The solid obtained was filtered off, washed with water, and recrystllized from a suitable solvent (cf.Table IV) to give 2-aryl-5-[$\alpha$-phenylthio-$\beta$-benzoyl] ethyl-1,3,5-oxadiazoles **(13a–c)**.

## Ring Closure of the Semicarbazide Derivatives

A solution of 2 N NaOH (40 mL, 0.08 mol) was added to the semicarbazide derivatives **(12a–c)** (0.01 mol). The reaction mixture was refluxed for 2 h, filtered while hot, acidified with hydrochloric acid, and diluted with 60 mL of water. The solid formed was separated out, filtered off, washed with water, and recystallized from a suitable solvent (cf. Table IV) to give 3-($\alpha$-phenylthio-$\beta$-aroyl) ethyl-4,5-dihydro-1,2,4-triazol-5-ones **( 14a–c)**.

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