Behavior of 3-Benzylamino-5-aryl-2(3*H*)-furanones Towards Some Nitrogen Nucleophiles

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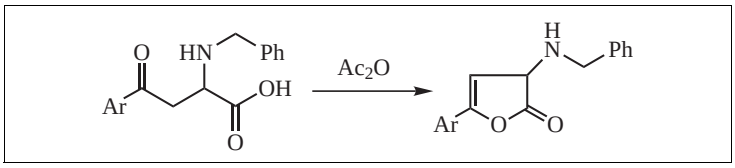

Ring closure of 2-*N*-benzylamino-3-aroylpropionic acids (**3**) with acetic anhydride afforded 3-*N*-benzylamino-5-aryl-2(3*H*)-furanones (**4**). The reaction of the furanones (**4**) with benzylamine in benzene was found to be time dependent. Thus refluxing the reaction mixture for 1 h only afforded the open-chain amides (**5a-c**). When the reaction was conducted for 3 h the 2(3*H*)-pyrrolones (**6**) were obtained. Hydrazine hydrate affected ring opening of the furanones to give the hydrazides (**5d-f**). Also, semicarbazide converted (**4**) into the corresponding semicarbazide derivatives (**5g-i**). The hydrazides (**5d-f**) were reacted with benzoyl chloride to give the corresponding diaroylhydrazines (**5j-l**). The open-chain derivatives (**5**) were converted into a variety of heterocycles: isothiazolones (**7**), dihydropyridazinones (**8**), 1,3,4-oxadiazoles (**9**) and 1,2,4-triazole derivatives (**10**) *via* cyclization reactions.

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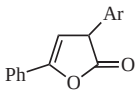
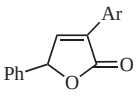
Introduction.

The chemistry of 2(3*H*)-furanones has received great attention in the last decades [1-5]. The importance of these compounds is due to facile opening of the lactone ring to give acyclic products which on recyclization can afford other heterocyclic systems. The conversion of 2(3*H*)-furanones into a variety of synthetically and biologically important heterocycles *e.g.* pyrrolones, pyridazinones, triazoles, oxadiazoles and isothiazolones was reported by a number of investigators [6-10]. It was reported that when 3-aryl-5-phenyl-2(3*H*)-furanones (**1**) were treated with benzylamine, isomerization occurred to give the thermodynamically more stable isomers 3-aryl-5-phenyl-2(5*H*)-furanones (**2**) [11].



1

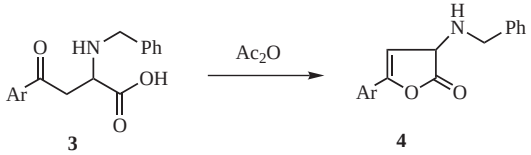


2

This isomerization was believed to occur *via* a carbanion intermediate, created by the effect of the amine, which is stabilized by the presence of aryl group at position 3. We wish to report here the behavior of some 2(3*H*)-furanones bearing a benzylamino group, a carbanion destabilizing group, towards some nitrogen nucleophiles.

Results and Discussion.

The starting materials 3-*N*-benzylamino-5-aryl-2(3*H*)-furanones (**4**) were prepared by ring closure of 2-*N*-benzylamino-3-aroylpropionic acids (**3**) [12] (obtained from addition of benzylamine to 3-aroylacrylic acids), using the method described previously by one of us [13].



3 **4**

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

The structure of compounds (**4a-c**) was elucidated from analytical and spectral data. Thus, the IR spectra of **4** showed a strong absorption at 1778 cm^{-1} characteristic of five membered lactone ring (Table 1). The ^1H NMR spectra of compounds (**4a-c**) showed absorptions correlated to methine, methylene and olefinic protons in addition to the NH and aromatic protons.

The furanones (**4**) reacted with benzylamine in refluxing benzene to give products depending on the reaction time. Thus, when the reaction was conducted for 1 h, the open-chain amides (**5a-c**) were obtained; whereas refluxing for 3 h, afforded the pyrrolones (**6a-c**), which were also obtained *via* ring closure of (**5a-c**) by refluxing in HCl/CH_3COOH mixture. It is to be mentioned that the amides (**5a-c**) were also obtained when the reaction was carried out in ethanol at room temperature. Similarly, the furanones (**4**) reacted with the hydrazine hydrate and semicarbazide to give the hydrazide derivatives (**5d-f**) and the semicarbazide derivatives (**5g-i**), respectively. The latter products were obtained by an unambiguous route

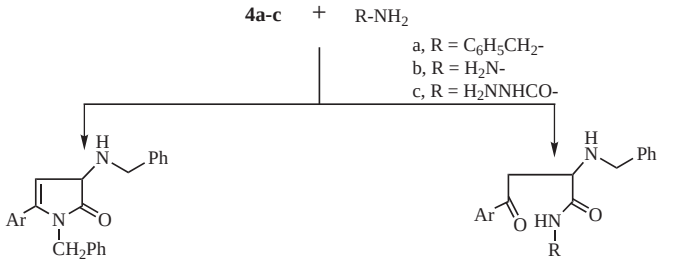
Table 1

IR and ^{1}H NMR (300 MHz) spectral data of compounds (**4** and **6**).

No.	IR (ν_{max}) (KBr) cm^{-1}		^{1}H-NMR (DMSO–d_6)
	ν_{NH}	$\nu_{C=O}$	
4a	3400	1778	δ = 3.40 (d, 1, CH, *J* = 1.4 Hz), 3.68 (d, 2, N-CH_2, *J* = 5.4 Hz), 3.80 (d, 1, CH, *J* = 1.5 Hz), 4.08 (d, 2, N-CH_2, *J* = 5.4 Hz), 6.78 (d, 1, =CH, *J* =1.6 Hz), 6.82 (d, 1, =CH, *J* = 1.4 Hz), 7.36-7.56 (m, 20, ArH), 8.69 (brs, NH, exchangeable)
4b	3380	1777	δ = 3.34 (d, 1, CH, *J* = 1.4 Hz), 3.68 (d, 2, N-CH_2, *J* = 5.4 Hz), 3.81 (d, 1, CH, *J* = 1.5 Hz), 3.81 (d, 1, CH, *J* = 1.5 Hz), 4.08 (d, 2, N-CH_2, *J* = 5.4 Hz), 6.80 (d, 1, =CH, *J* = 1.4 Hz), 6.83 (d, 1, =CH, *J* = 1.4 Hz), 7.32-7.61 (m, 18, ArH), 8.69 (brs, NH, exchangeable)
4c	3388	1779	δ = 3.36 (d, 1, CH, *J* = 1.4 Hz), 3.66 (d, 2, N-CH_2, *J* = 5.4 Hz), 3.76 (s, 3, OCH_3), 3.82 (d, 1, CH, *J* = 1.5 Hz), 4.08 (d, 2, N-CH_2, *J* = 5.4 Hz), 6.82 (1, =CH, *J* = 1.4 Hz), 6.85 (d, 1, =CH, *J* = 1.4 Hz), 7.32-7.61 (m, 18, ArH), 8.69 (brs, NH, exchangeable)
6a	3250	1651	δ = 3.71 (ABq, 2, N-CH_2), 3.92 (ABq, 2, N-CH_2), 4.09 (ABq, 2, N-CH_2), 4.88 (d, 1, CH, *J* = 6.0 Hz), 4.90 (d, 1, CH, *J* = 6.6 Hz), 6.63 (d, 1, =CH, *J* = 7.2 Hz), 6.65 (d, =CH, *J* = 6.9 Hz), 7.55-8.03 (m, 30, ArH), 8.18 (s, NH, exchangeable), 8.20 (s, NH, exchangeable)
6b	3350	1651	δ = 3.76 (ABq, 2, N-CH_2), 3.93 (ABq, 2, N-CH_2), 4.06 (ABq, 2, N-CH_2), 4.88 (d, 1, CH, *J* = 6.0 Hz), 4.90 (d, 1, CH, *J* = 7.2 Hz), 6.64 (d, 1, =CH, *J* = 7.2 Hz), 7.61-8.15 (m, 28, ArH), 8.18 (s, NH, exchangeable), 8.20 (s, NH, exchangeable)
6c	3250	1652	δ = 3.59 (s, 3, OCH_3), 3.71 (ABq, 2, N-CH_2), 3.92 (ABq, 2, N-CH_2), 4.12 (ABq, 2, N-CH_2), 4.88 (d, 1, CH, *J* = 6.0 Hz), 4.90 (d, 1, CH, *J* = 6.6 Hz), 6.62 (d, 1, =CH, *J* = 7.2 Hz), 6.64 (d, 1, =CH, *J* = 6.9 Hz), 7.61-8.15 (m, 28, ArH), 8.18 (s, NH, exchangeable), 8.20 (s, NH, exchangeable)

from the hydrazides (**5d-f**) by the action of potassium cyanate. Also, the hydrazides (**5d-f**) were converted into the corresponding diaroylhydrazines (**5j-l**) by treatment with benzoyl chloride.

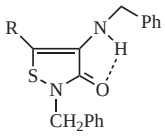
The structures of compounds (**5** and **6**) were substantiated from analytical and spectral data. Thus, the IR spectra of compounds (**5a,d,g** and **6a-c**) showed the functional groups correlated with the assigned structures (Tables 1 & 2). Moreover, the ^{1}H NMR spectra of compounds (**5a,d and g**) are in a good agreement with the proposed structure (Table 2). Evidently, the formation of compounds (**5** and **6**) indicates that existence of a benzylamino group at position 3 of the furanone nucleus rendered isomerization [11] less favorable and ring opening was the preferred pathway. It was of interest to the authors to convert the amides (**5a-c**) into the corresponding



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

a, Ar = $C_6H_5^-$, R = $C_6H_5CH_2^-$
b, Ar = 4-$ClC_6H_4^-$, R = $C_6H_5CH_2^-$
c, Ar = 4-$CH_3OC_6H_4^-$, R = $C_6H_5CH_2^-$
d, Ar = $C_6H_5^-$, R = H_2N
e, Ar = 4-$ClC_6H_4^-$, R = H_2N^-
f, Ar = 4-$CH_3OC_6H_4^-$, R = H_2N^-
g, Ar = $C_6H_5^-$, R = H_2NCONH^-
h, Ar = 4-$ClC_6H_4^-$, R = H_2NCONH^-
i, Ar = 4-$CH_3OC_6H_4^-$, R = H_2NCONH^-
j, Ar = $C_6H_5^-$, R = $PhCONH^-$
k, Ar = 4-$ClC_6H_4^-$, R = $PhCONH^-$
l, Ar = 4-$CH_3OC_6H_4^-$, R = PhCONH

isothiazolone derivatives (**7a-c**) by treatment with thionyl chloride at room temperature. Debenzoylation of (**7a-c**) was affected by heating with solid NaOH to give (**7d**).



7

a, R = C_6H_5CO
b, R = 4-$ClC_6H_4CO^-$
c, R = 4-$CH_3OC_6H_4CO^-$
d, R = H

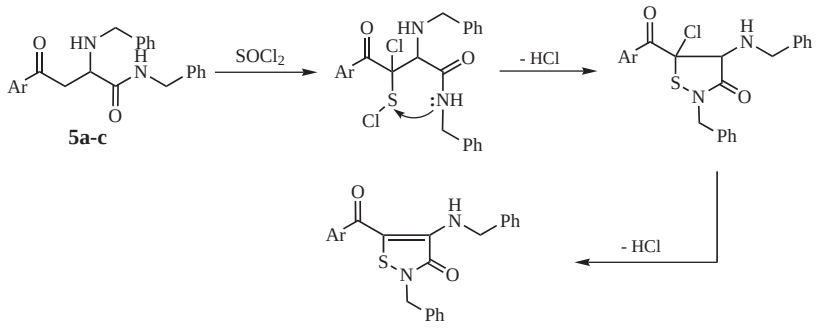
The structure of (**7**) was confirmed from analytical and spectral data. The IR spectra of compounds (**7a** and **7d**) showed absorption correlated to NH, C=O and C=C. Moreover, the ^{1}H NMR spectra showed absorptions corresponding to methylene, aromatic and NH protons for compounds (**7a** and **7d**) in addition to absorption for olefinic proton in case of compound (**7d**). Based on similar reports [11,14], the formation of isothiazolones (**7a-c**) can be represented as outlined in Scheme 1.

Dihydropyridazinones are known to have diverse pharmacological activities, *e.g.* antihypertensive [15], analgesic and anti-inflammatory [16]. Also, 1,3,4-oxadiazoles were reported to have carcinostatic activity against several types of tumors [17], antiarrhythmic [18] and anticholesterolsmic [19] activities. These reported activities prompted us to use compounds (**5**) as precursors for these biologically active compounds. Thus, the hydrazides (**5d-f**) were cyclized into the corresponding dihydropyridazinones (**8a-c**) and the diaroylhydrazines (**5j-l**) were converted into (**8d-f**) by refluxing with HCl/AcOH mixture. Also, treatment of (**5j-l**) with phosphorus oxychloride afforded the corresponding 1,3,4-oxadiazoles (**9a-i**). The triazolone derivatives (**10a-c**) were obtained from (**5g-i**) by the action of aqueous sodium hydroxide.

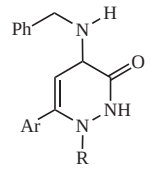
The structures of the above compounds were substantiated from analytical and spectral data. Thus, the IR spectra of (**8a,d**, **9a** and **10**) showed absorption bands characteristic of NH and carbonyl groups either for ketone or amide (Table 2).

Moreover, the ^{1}H NMR spectra of compounds (**8a,d**, **9a** and **10**) were in a good agreement with the assigned structure (Table 2). It is worth mentioning that the ^{1}H NMR spectrum of (**8a**) did not show any absorption corresponding to an olefinic proton but did show a splitting pattern for the CH_2–CH group. This inferred the existence of (**8a**) mainly in the tautomeric form **B**.

Scheme 1

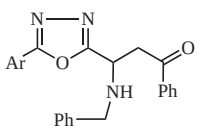


5a-c **7a-c**



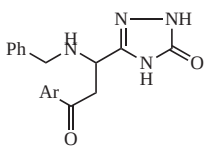
8

a, Ar = $C_6H_5^-$, R = H
b, Ar = 4-$ClC_6H_4^-$, R = H
c, Ar = 4-$CH_3OC_6H_4^-$, R = H
d, Ar = $C_6H_5^-$, R = $PhCO^-$
e, Ar = 4-$ClC_6H_4^-$, R = $PhCO^-$
f, Ar = 4-$CH_3OC_6H_4^-$, R = $PhCO^-$



9

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



10

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

Table 2

IR and ^{1}H NMR (300 MHz) spectral data of compounds (**5** and **7 – 10**).

No.	IR (ν_{max}) (KBr) cm^{-1} ν_{NH}	$\nu_{C=O}$	^{1}H NMR (DMSO–d_6)
5a	3330	1700(sh.) 1685	δ = 3.16 (d, 2, CH_2CO, *J* = 7.2 Hz), 3.80 (brs, 2, N-CH_2), 4.16 (brs, 2, N-CH_2), 4.78 (t, 1, CH, *J* = 7.2 Hz), 5.89 (brs, NH, exchangeable), 7.24-7.48 (m, 15, ArH), 8.51 (br s, NH, exchangeable).
5d	3201 3170	1695 (sh) 1668	δ = 3.20 (d, 2, CH_2CO, *J* = 6.0 Hz), 3.92 (ABq, 2, N-CH_2, *J* = 6.0 Hz), 4.21 (br s, NH, exchangeable), 4.88 (t, 1, CH, *J* = 6.3 Hz), 6.02 (brs, 2, NH_2, exchangeable), 7.60-8.14 (m, 10, ArH), 8.50 (br s, 1, NHCO, exchangeable)
5g	3390	1702 (sh) 1675	δ = 3.41 (d, 2, CH_2CO, *J* = 6.3 Hz), 4.33 (s, 2, CH_2-N), 4.78 (s, 1, NH-CH_2, exchangeable), 4.89 (t, 2, CH_2-C*H*, J = 6.3 Hz), 7.50-7.60 (m, 10, ArH), 8.64 (s, 2, H_2N–CO, exchangeable), 10.49 (s, 2, CO–NH–NHCO, exchangeable)
5j	3400 3325	1705 (sh) 1662	δ = 3.38 (d, 2, CH_2CO, *J* = 6.3 Hz), 4.29 (s, 2, CH_2-N), 4.89 (t, 2, CH_2-C*H*, *J* = 6.3 Hz), 6.64 (br s, 1, NH-CH_2, exchangeable), 7.50-7.95 (m, 15, ArH), 10.49 (s, 2, CO-NH-NH-CO, exchangeable)
7a	3380	1687	δ = 3.91 (s, 2, N-CH_2), 3.99 (s, 2, N-CH_2), 7.34-7.54 (m, 15, ArH), 8.64 (br s, NH, exchangeable)
7d	3293	1638	δ = 3.99 (s, 4, 2N-CH_2), 6.64 (s, 1, =CH), 7.24-7.53 (m, 10, ArH), 8.58 (br s, NH, exchangeable)
8a	3294	1639	δ = 2.97 (d, 2, CH-C*H*$_2$, *J* = 6.3 Hz), 3.76 (ABq, 2, N-CH_2), 4.89 (t, 1, C*H*-CH_2, *J* = 6.3 Hz), 7.50-7.95 (m, 10, ArH), 8.64 (br s, NH, exchangeable), 10.49 (s, NHCO, exchangeable)
8d	3294	1630	δ = 3.92 (s, 2, N-CH_2), 4.78 (s, 1, -CH-), 6.64 (s, 1, =CH), 7.36 (s, 1, N*H*-CH_2, exchangeable), 7.50-7.95 (m, 15, ArH), 10.49 (s, 1, NHCO, exchangeable)
9a	3150	1679	δ = 3.06 (d, 2, C*H*$_2$-CH, *J* = 4.8 Hz), 3.98 (s, 2, NCH_2), 4.21 (br s, NH, exchangeable), 4.89 (t, CH_2C*H*, *J* = 4.8 Hz), 7.60-8.14 (m, 15, ArH)
10a	3324	1718, 1679	δ = 3.19 (d, 2, C*H*$_2$–CH, *J* = 6.3 Hz), 3.85 (ABq, 2, N-CH_2), 4.15 (s, NH, exchangeable), 4.88 (t, 1, CH_2C*H*, *J* = 6.3 Hz), 7.26-7.45 (m, 10, ArH), 13.04 (br s, 2, NHCONH, exchangeable)

A **B**

Table 3

Physical and analytical data of compounds (**4**-**7**).

No.	mp°C (Solvent)	Yield %	(Calcd./Found) C	H	N
4a	185-187 (benzene/ethanol)	80	76.98 77.12	5.66 5.64	5.28 5.35
4b	266-268 (benzene/ethanol)	85	68.11 68.10	4.67 4.59	4.67 4.69
4c	170-173 (benzene/ethanol)	65	73.2 72.9	5.76 5.80	4.75 4.76
5a	200-202 (ethanol)	60	77.40 77.56	6.40 6.41	7.50 7.47
5b	290-292 (ethanol)	60	70.80 70.85	5.66 5.71	6.89 6.85
5c	193-195 (ethanol)	50	74.60 74.90	6.47 6.48	6.97 6.94
5d	134-136 (ethanol)	80	68.69 68.61	6.39 6.41	14.14 14.19
5e	178-180 (ethanol)	80	61.54 61.50	5.43 5.51	12.67 12.71

Table 3 (continued)

No.	mp°C	Yield %	(Calcd./Found) C	H	N
5f	160-162 (ethanol)	80	66.05 66.12	6.40 6.40	12.84 12.85
5l	259-260 (ethanol)	55	69.60 69.58	5.80 5.80	9.74 9.65
6a	190-192 (benzene)	80	81.35 81.36	6.20 6.21	7.90 7.79
6b	270-271 (benzene)	73	74.10 74.14	5.40 5.40	7.20 7.35
6c	161-162 (benzene)	65	78.13 78.15	6.25 6.29	7.29 7.30
7a	260-261 (ethanol)	45	72.00 72.10	5.00 5.02	7.00 6.94
7b	254-25 (ethanol)	57	66.28 66.21	4.37 4.35	6.44 6.45
7c	276-278 (ethanol)	60	69.77 70.01	5.12 5.13	6.51 6.55
7d	170-172 (ethanol)	75	68.91 68.90	5.41 5.46	9.45 9.35

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 KBr wafer

Table 4

Physical and analytical data of compounds (**8**-**10**).

No.	mp°C (Solvent)	Yield %	(Calcd./Found) C	H	N
8a	160-162 (ethanol)	50	73.12 73.19	6.09 6.11	15.05 15.12
8b	158-160 (ethanol)	50	65.18 65.17	5.11 5.10	13.42 13.40
8c	165-166 (ethanol)	50	69.90 69.92	6.15 6.11	13.59 13.52
8d	182-183 (benzene)	60	75.19 75.05	5.48 5.45	10.97 10.11
8e	179-180 (benzene/ethanol)	62	68.98 68.85	4.79 4.72	10.06 10.15
8f	185-187 (benzene/ethanol)	60	72.64 72.55	5.57 5.51	10.17 10.01
9a	140-142 (ethanol)	70	75.19 75.30	5.48 5.46	10.97 11.02
9b	152-153 (ethanol)	65	68.98 69.00	4.79 4.75	10.06 10.02
9c	159-160 (ethanol)	75	72.64 72.57	5.57 5.55	10.17 10.21
10a	230-231 (ethanol)	45	67.08 67.10	5.59 5.61	17.39 17.34
10b	242-244 (ethanol)	40	60.59 60.62	4.77 4.76	15.71 15.73
10c	235-236 (ethanol)	40	64.77 64.75	5.68 5.67	15.91 15.88

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

2-*N*-Benzylamino-3-aroylpropionic acids (**3a-c**).

These compounds were prepared according to the procedure described by previous investigators [12].

3-*N*-Benzylamino-5-aryl-2(3*H*)-furanones (**4a-c**).

A mixture of 2-*N*-benzylamino-3-aroyl propionic acids (**3a-c**) [12] (1 mol) and acetic anhydride (270 mL, 3 mol) was heated under reflux for 20 min, the reaction was then cooled, poured onto ice, collected by filtration and the product was recrystallized from a suitable solvent to give (**4a-c**) (Table 3).

General Procedure for the Reactions of 3-*N*-Benzylamino-5-aryl-2(3*H*)-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 rt for 5 min in ethanol. The product was shown to be 2-*N*-benzylamino-3-aroyl-*N*-benzyl–propion-amides (**5a-c**), (Table 3). When the reaction mixture was heated at 100 °C for 3 h, the product obtained was collected by filtration, washed with benzene and recrystallized from the suitable solvent (Table 3) to give 1-benzyl-3-*N*-benzyl amino-5-aryl-2(3*H*)-pyrrolones (**6a-c**).

General Procedure for the Conversion of the 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 rt for 24 h. The excess thionyl chloride was then evaporated under vacuum. The solid obtained was collected by filtration and recrsytallized from a suitable solvent (Table 3) to give 2-benzyl-4-*N*-benzylamino-5-aroyl-3(2*H*)-isothiazolones (**7a-c**).

General Procedure for the 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 rt for 1 h. When a fading of the initial yellowish colour was observed, the benzene layer was separated and concentrated under vacuum to give a solid residue which was recrystallized from ethanol (Table 3), to give 2-benzyl-4-*N*-benzylamino-3(2*H*)-isothiazolone (**7d**).

General Procedure for the Reactions of 3-*N*-Benzylamino-5-aryl-2(3*H*)-furanones (**4a-c**) with Hydrazine Hydrate.

To a solution of the furanones (**4a-c**) (1 mol) in ethanol (20 mL), (100%) hydrazine hydrate (35.5 mL, 1.1 mol) was added at rt for 5 min. The product obtained was collected by filtration, washed with ethanol and the product was shown to be 2-*N*-benzylamino-3-aroylpropionic acid hydrazides (**6d-f**), (Table 3). When the reaction mixture was refluxed in ethanol the product was shown to be 6-aryl-4-*N*-benzylamino-4,5-dihydropyridazin-3-(2*H*)-one (**8a-c**) which were recrystalized from suitable solvents (Table 4).

General Procedure for the Reaction of Hydrazides (**6d-f**) with Potassium Isocyanate.

A solution of potassium isocyanate (1.78 g, 0.022 mol) in water (10 mL) was added dropwise with stirring at 0 °C to a solution of the hydrazide derivatives (**5d-f**) (0.02 mol) in acetic acid-water (1:1) mixture. The reaction mixture was stirred at rt for 3 h, the product obtained was collected by filtration, washed thoroughly with water, and finally recrystallized from a suitable solvent (Table 3) to give 2-*N*-benzylamino-3-aroylpropionoyl acid semicarbazides (**5g-i**).

The same semicarbazide derivatives (**5g-i**) were also obtained from heating a solution of 2(3*H*)-furanones (**4a-c**) (0.01 mol) in ethanol (30 mL) and a mixture of semicarbazide hydrochloride (1.12 g, 0.01 mol), sodium acetate anhydrous (0.82 g, 0.01 mol) under reflux at 70 °C for 1 h. The solid obtained was collected by filtration and recrystallized from a suitable solvent (Table 3). The solid obtained was identical in all respects (mp, mixed mp and TLC) with the product obtained above from the reaction between hydrazides (**5d-f**) and potassium isocyanate.

General Procedure for the Reaction of Hydrazides (**5d-f**) with Benzoyl Chloride.

To a solution of hydrazides (**5d-f**) (0.01 mol) in 50 mL of dry benzene, 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 (Table 3) to give 1-benzoyl-2-[α-*N*-benzylamino-β-aroyl]propionylhydrazines (**5j-l**).

General Procedure for the Ring Closure of Compounds (**5a-f**).

A solution of (**5a-f**) (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 collected by filtration, washed with water and recrystallized from a suitable solvent (Table 3) to give 1-benzyl-3-*N*-benzylamino-5-aryl-2(3*H*)-pyrrolone (**6a-c**) in case of (**5a-c**), 6-aryl-4-*N*-benzylamino-4,5-dihydropyri-dazin-3(2*H*)-ones (**8a-c**) in case of **5d-f** (Table 4).

General Procedure for the Ring Closure of Diaroylhydrazines (**5j-l**).

Phosphorus oxychloride (10 mL, 0.065 mol) was added dropwise to 1 g of the diaroylhydrazines (**5j-l**). The reaction mixture was refluxed for 20 min, left to cool, and poured onto crushed ice. The solid obtained was collected by filtration, washed with water and recrystallized from a suitable solvent (Table 4) to give 2-aryl-5-[α-*N*-benzylamino-β-benzoyl]ethyl-1,3,5-oxadiazoles (**9a-c**).

Ring Closure of the Semicarbazide Derivatives.

A solution of 2 *N* NaOH (40 mL, 0.08 mol) was added to the semicarbazide derivatives (**5g-i**) (0.01 mol). The reaction mixture was refluxed for 2 h, filtered while hot and acidified with hydrochloric acid, diluted with 60 mL of water. The solid formed was collected by filtration, washed with water and recrystallized from the suitable solvent (Table 4) to give 3-(α-*N*-benzylamino-β-aroyl)ethyl-4,5-dihydro-1,2,4-triazol-5-ones (**10a-c**).

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