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INTERACTION OF N,N-DIMETHYL-HYDRAZONOMETHYL AND α-HYDROXYKETONE GROUPS IN HETARYL ANALOGS OF UNSYMMETRICAL BENZOINS

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The reaction of phenylglyoxal hydrate with N,N-dimethylhydrazones of furfural and 1-methylpyrrole-2-carbaldehyde proceeds regioselectively at position 5 of the heterocycle. The hetaryl analogs of α-benzoins obtained are quantitatively isomerized into the isomeric β-benzoins. The N,N-dimethylhydrazonomethyl group, while activating the hetaryl residue, reduces the time for isomerization compared with unfunctionalized benzoins. The N,N-dimethylhydrazonomethyl group is readily transformed into an aldehyde or nitrile group and enters into a trans-hydrazonation reaction.

Keywords: benzoins, hydrazones, π-excess heterocycles, isomerization, electrophilic substitution.

The chemical properties of benzoins studied up to the present time are overwhelmingly linked in the majority of cases with the transformation of the α-hydroxyketone group and with the effect of (het)aryl residues on its reactivity. Consequently the desired substituents required in the (het)aryl residues are usually introduced at the stage of obtaining the benzoin, for example, in various modifications of the benzoin condensations [1-7], hydroxyalkylation of arylglyoxals of electron-rich benzenes and π-excess heterocycles [8-10]. Among the chemical properties affecting (het)aryl residues two types are known: the formation of benzofurans on photolysis of desyl esters of carboxylic, carbamic, and phosphoric acids, which occurs through intramolecular [2+2] cycloaddition of the carbonyl group to the double bond of the electron-rich aryl residue [11-14], and electrophilic substitution directly into the (het)aryl residue: formylation of furoin [15], and excessive hydroxymethylation of a pyrrole ring with phenylglyoxal [10]. The effect of an α-hydroxyketone group on the reactivity of substituents in the (het)aryl residue of isomeric benzoins remains unstudied.

It is interesting to study benzoins containing functional groups in the (het)aryl residues capable of further transformation within wide limits. One of the most promising groups, in our opinion, is the N,N-dimethylhydrazonomethyl group, which may readily be transformed into an aldehyde group [16], one of the most frequently used functional groups in organic synthesis [17]. At the same time the actual N,N-disubstituted hydrazonomethyl group is widely used in asymmetric synthesis [18, 19] and is a reactive nucleophilic substrate, similar to enamines according to the azaenamine concept [18].

However, in the case of hydrazones of aldehydes of π-excess five-membered heterocycles the trifluoroacetylation [20], and aminomethylation [21] reactions, and the interaction with electron-deficient unsaturated compounds [22-24], proceed regioselectively at position 5 of the ring, which is explained by

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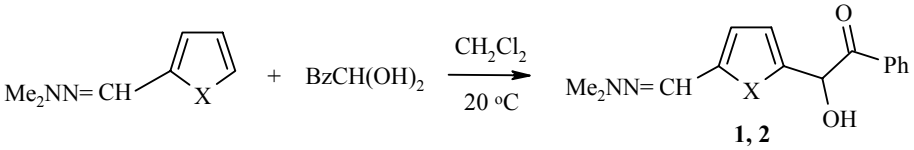
vinylology, such that the reaction proceeds at the most distant carbon atom of the conjugated system. In our opinion, a similar regioselectivity is linked with the fact that the N,N-dialkylhydrazonomethyl group is effectively conjugated with the ring and, while displaying high electron-donating properties, activates the heterocyclic ring which enabled us to carry out the reaction with milder electrophilic reagents, such as phosphorylation [25, 26] and trinitrophenylation [27].

Hydroxyalkylation of N,N-dimethylhydrazones of N-methylpyrrole-2-carbaldehyde and furfural with phenylglyoxal occurs regioselectively at position 5 of the heterocycle with the formation of the corresponding hetaryl analogs of the less stable α-benzoins **1**, **2** in high yield (Scheme 1). The activation of the heterocyclic ring by the hydrazonomethyl group enables reaction to be carried out smoothly with the less reactive phenylglyoxal hydrate at room temperature, which is uncharacteristic of unsubstituted heterocycles [28]. As a result of the difference in electron-donating properties of these heterocycles the formation of the pyrrole benzoin **2** occurs more rapidly.

Scheme 1



1, 2

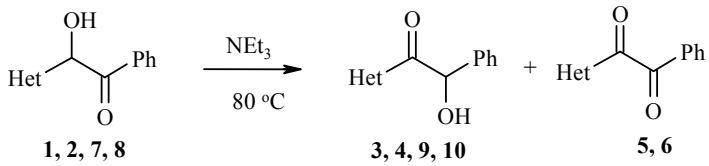
1 X = O, **2** X = NMe

The α-benzoins **1, 2** obtained are quantitatively isomerized in the presence of triethylamine as base into the corresponding β-benzoins **3, 4**. Benzils **5, 6**, products of oxidation of the benzoins by the oxygen of the air, are formed in small amount in parallel (Scheme 2) (Table 1, No. 1, 2). Assignment of the isomers was made on the basis of the signals of the protons of the unsubstituted phenyl ring in the ^{1}H NMR spectra of the benzoins and on the rules for the position and form of the signals of these protons depending on the isomer, which was proposed by us previously in [29]. In the ^{1}H NMR spectra of β-benzoins **3, 4** the signals were displaced towards high field in comparison with those in the spectra of α-benzoins **1, 2**.

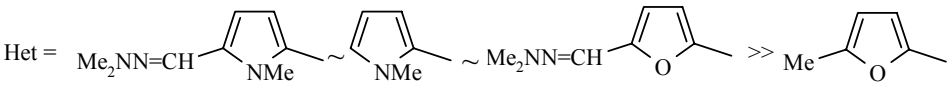
It was shown previously in the example of derivatives of π-excess heterocycles, that an increase in the electron-donating properties of the hetaryl residue assists α→β-isomerization of unsymmetrical benzoins [29]. Activation of the hetaryl residue in α-benzoins **1, 2** by the introduction of a N,N-dimethylhydrazonomethyl group reduces the isomerization time compared with the unfunctionalized hetaryl-α-benzoins **7, 8** correspondingly (in the Scheme the hetaryl residues are placed in increasing order of isomerization time).

The activating influence of the N,N-dimethylhydrazonomethyl group shows up to a larger extent on the furan ring than on the pyrrole, which is probably linked with the transmission effect [30]. The furan hydrazone **1** is comparable in reactivity with pyrroles **7** and **2** in the isomerization reaction (Table 2, Nos. 1-3).

Scheme 2



1, 2, 7, 8 **3, 4, 9, 10** **5, 6**



2, 4, 6 **7, 9** **1, 3, 5** **8, 10**

TABLE 1. Yields of β-Benzoins **3,4** and Benzils **5, 6** under Various Conditions

No.	Reaction	Products (yield, %)	
1	Isomerization in the presence of NEt_3	**3** (92)	**5** (5)
2	Ditto	**4** (91)	**6** (5)
3	Autoisomerization	**3** (53)	**5** (33)
4	Ditto	**4** (45)	**6** (38)
5	Hydroxymethylation at 80°C	**3** (22)	**5** (45)
6	Ditto	**4** (10)	**6** (50)

TABLE 2. Isomerization Conditions for α-Benzoins **1, 2, 7, 8** in the Presence of Triethylamine

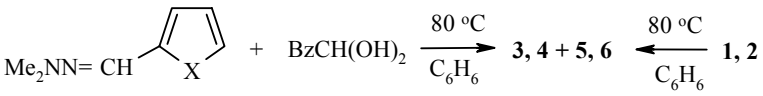
No.	Initial	Product	Solvent	Time, h*
1	**1**	**3**	C_6H_6	1.5
2	**2**	**4**	C_6H_6	1.5
3 [29]	**7**	**9**	EtOH	1.5
4 [29]	**8**	**10**	EtOH	9

* Time was determined at the disappearance of the spot for the starting material on TLC (every 0.5 h).

Activation of the hetaryl residue leads to the situation that in the case of the hydrazones isomerization proceeds successfully in nonpolar benzene, unlike the isomerization of α-benzoins **7** and **8**, which was carried out in ethyl alcohol [29]. In the more polar alcohol α-benzoins **1, 2** were completely oxidized by the oxygen of the air to benzils **5** and **6** respectively, while the more stable β-benzoins **3, 4** were stable in boiling alcohol.

The presence of the basic dimethylamino group in the molecule of benzoins **1**, **2** leads to them being isomerized in the absence of an external base on heating in benzene solution, but the yields of β-benzoins **3, 4** were lower (Scheme 3) (Table 1, Nos. 3, 4). It is interesting to note that in the hydroxymethylation reaction at increased temperature the reaction products proved to be the β-isomers **3, 4** and the oxidation products benzils **5** and **6** (Table 1, Nos. 5, 6) for the same reason.

Scheme 3

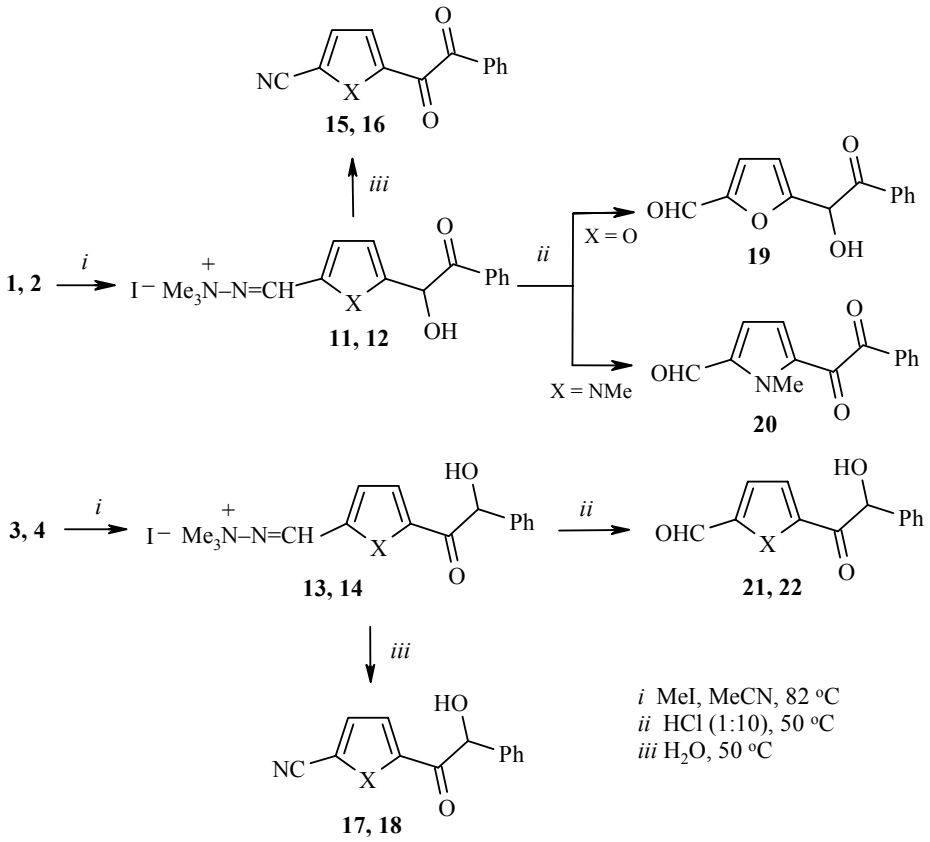


It is probable that in autocatalysis the dimethylamino group plays the role of a base only for the initial hydrazones or α-benzoins, but not for β-benzoins, which is linked with the reduction of basicity of the dimethylamino group in the latter due to conjugation with the carbonyl group.

The formation of a conjugated system in β-benzoins and the reduction thereby of the electron density on the nitrogen atom of the dimethylamino group leads to the fact that alkylation of β-benzoins **3, 4** with methyl iodide occurs only on extended boiling, while α-benzoins **1, 2** are readily alkylated on brief heating. The salts obtained may readily be transformed into nitriles or aldehydes by briefly heating their aqueous solutions in

neutral or weakly acidic media respectively. In this way salts **11** and **12** form benzil derivatives **15, 16, 19, 20,** as a result of the high inclination towards oxidation of the same α-benzoins in the majority of cases, while the salts of β-benzoins **13, 14** readily form derivatives of α-hydroxyketones **17, 18, 21**, and **22**.

Scheme 4



11, 13, 15, 17, 21 X = O; **12, 14, 16, 18, 22** X = NMe

There are two reactive centers in the obtained aldehydes **19, 21**, and **22**, capable of reacting with N-nucleophiles. These are primarily the aldehyde group and the hydroxyketone group, which may form substitution products in reactions with N-nucleophiles, both at the carbonyl carbon atom, to give hydroxyamines [8], and at the hydroxyl atom, to give an amino ketone. This is linked with the isomerization of the intermediate hydroxyenamines in the course of the reaction [31].

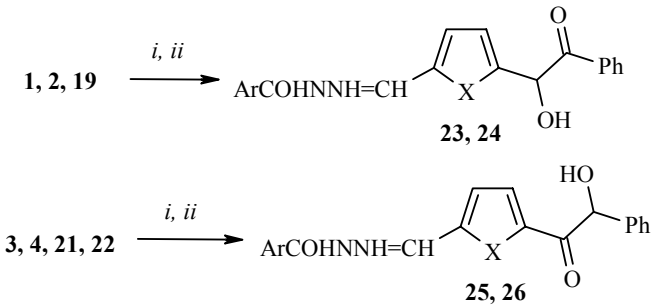
The reaction of aldehydes **19, 21**, and **22** with *para*-bromobenzhydrazides in boiling ethyl alcohol occurs regioselectively in all cases at the most reactive aldehyde group. In this situation the reactivity of the carbonyl of the α-hydroxyketone group is somewhat reduced, so that hydrazones **1-4** enter into a transhydrazonation reaction with the hydrazide both in neutral and in acidic media. The α-hydroxyketone group remains unaffected by this.

As is evident from Table 3 the reactivity of the β-derivatives, aldehydes or hydrazones, in the reaction with *para*-bromobenzhydrazide surpasses that of the corresponding α-derivatives and does not depend on the reaction conditions. This is linked with the acceptor effect of the carbonyl of the α-hydroxyketone group through the heterocyclic ring. In the case of both α- and β-isomers, the reactivity of the furan derivatives is greater than that of the pyrrole, which is linked with the greater electron-donating effect of pyrrole.

TABLE 3. Times of Formation and Yields of Hydrazones **23-26** under Various Conditions

Initial	Product	Method	Reaction time, h	Yield, %
19	**23**	*i*	1.5	70
21	**25**	*i*	0.75	75
22	**26**	*i*	2	62
1	**23**	*i*	2	63
1	**23**	*ii*	1.5	89
2	**25**	*i*	5	55
2	**25**	*ii*	3	62
3	**26**	*i*	0.75	80
3	**26**	*ii*	0.75	99
4	**24**	*i*	2	91
4	**24**	*ii*	2	85

Scheme 5



i $H_2NNHCOAr$, EtOH, 78°C; *ii* $H_2NNHCOAr$, H^+, EtOH, 78°C (only for **1-4**);
23, 25 X = O; **24, 26** X = NMe; Ar = 4-BrC_6H_4

It has therefore been shown that the reaction of phenylglyoxal hydrate with the N,N-dimethylhydrazones of furfural and pyrrole-2-carbaldehyde occurs regioselectively at position 5 of the heterocycle. The N,N-dimethylhydrazonomethyl group, activating the hetaryl residue, reduces the time for α→β-isomerization of unsymmetrical benzoins compared to nonfunctionalized hetaryl benzoin analogs. In β-benzoins conjugation is observed between the acceptor carbonyl of the α-hydroxyketone and the hydrazonomethyl groups, which leads to a reduction in the electron density on the tertiary nitrogen atom and activation of the carbon atom towards nucleophilic attack in the hydrazonomethyl group.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Varian VXR 300 (300 MHz) instrument in DMSO-d_6, internal standard was TMS. The IR spectra were taken on a UR 20 instrument in KBr disks, and the UV spectra in 95% ethanol solution on a Specord M 40 instrument at an absorbing layer thickness of 1 cm. The mass spectra were recorded on a MX 1321 instrument in electron impact mode (70 eV). A check on the progress of reactions and the purity of the compounds obtained was effected by TLC on Silufol UV 254 plates in the system benzene–acetone, 5:1.

Preparation of α-Benzoins 1, 2 (General Procedure). A solution of the N,N-dimethylhydrazone (5.00 mmol) in dichloromethane (5 ml) was added to a solution of phenylglyoxal hydrate (0.76 g, 5.00 mmol) in dichloromethane (5 ml). The mixture was left at room temperature for 3 days, then evaporated in vacuum. The residue was crystallized from hexane.

2-[5-(Dimethylhydrazonomethyl)-2-furyl]-2-hydroxy-1-phenylethanone. (1). Yield 86%, yellow powder; mp 136.5-137°C. UV spectrum, λ_{max}, nm (log ε): 244.9 (3.94); 308.3 (4.23). IR spectrum, ν, cm^{-1}: 3430, 3140, 3000, 2940, 2875, 2805, 1690, 1600, 1575, 1290, 1230. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.87 [6H, s, $N(CH_3)_2$]; 5.00 (1H, d, *J* = 6.5, CHOH); 6.19 (1H, d, *J* = 6.5, CHOH); 6.32 (1H, d, *J* = 3.4, H-3 Fur); 6.45 (1H, d, *J* = 3.4, H-4 Fur); 7.05 (1H, s, CH=N); 7.49 (2H, t, *J* = 7.8, H-3,5 Ph); 7.62, (1H, d, *J* = 7.8, H-4 Ph); 8.05 (2H, d, *J* = 7.8, H-2,6 Ph). Mass spectrum, *m/z* (I_{rel}, %): 272 (14) $[M]^+$, 167 (100), 165 (11), 105 (16), 77 (13), Found, %: C 66.32; H 5.81. $C_{15}H_{16}N_2O_3$. Calculated, %: C 66.16; H 5.92.

2-[5-(Dimethylhydrazonomethyl)-1-methyl-1H-pyrrol-2-yl]-2-hydroxy-1-phenylethanone (2). Yield 88%, yellow powder; mp 136-137°C. UV spectrum, λ_{max}, nm (log ε): 243.9 (4.06), 305.3 (4.20). IR spectrum, ν, cm^{-1}: 3175, 2970, 2868, 1682, 1597, 1261, 1234, 1200, 1155, 1070, 1042, 1013, 990, 952, 920. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.30 (3H, s, 1-CH_3 Pyr); 3.81 [6H, s, $N(CH_3)_2$]; 5.63 (1H, d, *J* = 7.6, CHOH); 5.70 (1H, d, *J* = 4.0, H-3 Pyr); 6.03 (1H, d, *J* = 4.0, H-4 Pyr); 6.17 (1H, d, *J* = 7.6, CHOH); 7.25 (1H, s, CH=N); 7.43 (2H, t, *J* = 8.6, H-3,5 Ph); 7.57 (1H, d, *J* = 8.6, H-4 Ph); 7.90 (2H, d, *J* = 8.06, H-2,6 Ph). Mass spectrum, *m/z* (I_{rel}): 285 (16) $[M]^+$, 180 (100). Found, %: C 67.36; H 6.71. $C_{16}H_{19}N_3O_2$. Calculated, %: C 67.35; H 6.71.

β-Benzoins 3, 4 (Table 1). A. Isomerization of benzoins **1, 2**. A solution of α-benzoin (1.50 mmol), triethylamine (0.25 ml, 1.80 mmol) or without it, in benzene (6 ml) was boiled for 1 h 30 min. The solid β-benzoin precipitated on cooling was filtered off, and crystallized from benzene. The filtrate was evaporated in vacuum, the residue was treated with carbon tetrachloride (5 ml), the solution was evaporated in vacuum, and benzils were obtained.

B. Interaction of phenylglyoxal hydrate with furfural hydrazones and pyrrole-2-carbaldehyde. A solution of phenylglyoxal hydrate (0.76 g, 5.00 mmol) and the hydrazone (5.00 mmol) in benzene (8 ml) was boiled for 1 h 30 min. Further treatment was by method A.

1-[5-(Dimethylhydrazonomethyl)-2-furyl]-2-hydroxy-2-phenylethanone (3). Yield 53%, yellow powder; mp 160-162°C. UV spectrum, λ_{max}, nm (log ε): 293.8 (3.88), 375.4 (4.14). IR spectrum, ν, cm^{-1}: 3425, 3115, 2955, 2880, 1650, 1560, 1510, 1350, 1275. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.99 [6H, s, $N(CH_3)_2$]; 5.70 (1H, d, *J* = 5.1, CHOH); 6.06 (1H, d, *J* = 5.1, CHOH); 6.54 (1H, d, *J* = 3.6, H-4 Fur); 7.09 (1H, s, CH=N); 7.28 (1H, d, *J* = 7.5, H-4 Ph); 7.32 (2H, t, *J* = 7.5, H-3,5 Ph); 7.47 (2H, d, *J* = 7.5, H-2,6 Ph); 7.65 (1H, d, *J* = 3.6, H-3 Fur). Mass spectrum, *m/z* (I_{rel}): 272 (28) $[M]^+$, 167 (10), 165 (100), 77 (11). Found, %: C 66.15; H 5.89. $C_{15}H_{16}N_2O_3$. Calculated, %: C 66.16; H 5.92.

1-[5-(Dimethylhydrazonomethyl)-1-methyl-1H-pyrrol-2-yl]-2-hydroxy-2-phenylethanone (4). Yield 45%, yellow crystals; mp 140-141°C. UV spectrum, λ_{max}, nm (log ε): 254.1 (3.74), 367.1 (4.42). IR spectrum, ν, cm^{-1}: 3390, 3136, 2940, 2885, 2800, 1616, 1568, 1494, 1446, 1400, 1360, 1340, 1297, 1207, 1180, 1056, 1000, 931, 909. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.33 [6H, s, $N(CH_3)_2$]; 3.69 (3H, s, 1-CH_3 Pyr); 5.66 (1H, d, *J* = 6.9, CHOH); 5.77 (1H, d, *J* = 6.9, CHOH); 6.31 (1H, d, *J* = 4.5, H-4 Pyr); 7.17 (1H, s, CH=N); 7.23 (1H, d, *J* = 4.5, H-3 Pyr); 7.30 (1H, d, *J* = 9.0, H-4 Ph); 7.37 (2H, t, *J* = 9.0, H-3,5 Ph); 7.46 (2H, d, *J* = 9.0, H-2,6 Ph). Mass spectrum, *m/z* (I_{rel}, %): 285 (23) $[M]^+$, 178 (100). Found, %: C 67.28; H 6.59. $C_{16}H_{19}N_3O_2$. Calculated, %: C 67.35; H 6.71.

1-[5-(Dimethylhydrazonomethyl)-2-furyl]-2-phenylethane-1,2-dione (5). Viscous red liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.04 [6H, s, $(CH_3)_2$]; 6.67 (1H, d, *J* = 3.9, H-4 Fur); 7.14 (1H, s, CH=N); 7.53 (1H, d, *J* = 3.9, H-3 Fur); 7.61 (2H, t, *J* = 7.5, H-3,5 Ph); 7.68 (1H, d, *J* = 7.5, H-4 Ph); 7.94 (2H, d, *J* = 7.5, H-2,6 Ph). Found, %: C 67.01; H 5.51. $C_{15}H_{14}N_2O_3$. Calculated, %: C 66.66; H 5.22.

1-[5-(Dimethylhydrazonomethyl)-1-methyl-1H-pyrrol-2-yl]-2-phenylethane-1,2-dione (6). Red powder (hexane); mp 82-83°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.32 [6H, s, $(CH_3)_2$]; 4.15 (3H, s, 1-CH_3 Pyr); 6.39 (1H, d, *J* = 4.9, H-4 Pyr); 6.74 (1H, d, *J* = 4.9, H-3 Pyr); 7.22 (1H, s, CH=N); 7.59 (2H, t, *J* = 8.1, H-3,5 Ph); 7.74 (1H, d, *J* = 8.1, H-4 Ph); 7.93 (2H, d, *J* = 8.1, H-2,6 Ph). Found, %: C 67.82; H 6.04. $C_{16}H_{17}N_3O_2$. Calculated, %: C 67.83; H 6.05.

Alkylation of Benzoins 1-4 (General Procedure). A solution of benzoin (0.82 g, 3.00 mmol) in a mixture of acetonitrile (5 ml) and iodomethane (3 ml) was boiled for 1 h (in the case of the α-isomer) or 24 h (in the case of the β-isomer). In the case of the α-benzoins the solid precipitated on cooling was filtered off, and in the case of the β-benzoins the solution was evaporated in vacuum.

N'-[5-(1-Hydroxy-2-oxo-2-phenylethyl)-2-furylmethylene]-N,N,N-trimethylhydrazonium Iodide (11). Yield 100%, white powder; mp 160-162°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz); 2.08 [9H, s, $N(CH_3)_3$]; 6.31 (1H, d, *J* = 6.3, CHOH); 6.47 (1H, d, *J* = 6.3, CHOH); 6.82 (1H, d, *J* = 4.0, H-3 Fur); 7.33 (1H, d, *J* = 4.0, H-4 Fur); 7.52 (2H, t, *J* = 8.1, H-3,5 Ph); 7.65 (1H, d, *J* = 8.1, H-4 Ph); 8.03 (2H, d, *J* = 8.1, H-2,6 Ph); 8.89 (1H, s, CH=N). Found, %: C 46.38; H 4.63. $C_{16}H_{19}IN_2O_3$. Calculated, %: C 46.39; H 4.62.

N'-[5-(1-(Hydroxy-2-oxo-2-phenylethyl)-1-methyl-1H-pyrrol-2-ylmethylene]-N,N,N-trimethylhydrazonium Iodide (12). Yield 100%, white powder; mp 199-201°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.46 [9H, s, $N(CH_3)_3$]; 3.92 (3H, s, 1-CH_3 Pyr); 6.09 (1H, d, *J* = 4.2, H-3 Pyr); 6.14 (1H, d, *J* = 6.9, CHOH); 6.35 (1H, d, *J* = 6.9, CHOH); 6.77 (1H, d, *J* = 4.2, H-4, Pyr); 7.49 (2H, t, *J* = 8.1, H-3,5 Ph); 7.62 (1H, d, *J* = 8.1, H-4 Ph); 7.97 (2H, d, *J* = 8.1 H-2,6 Ph); 8.85 (1H, s, CH=N). Found, %: C 47.70; H 5.16. $C_{17}H_{22}IN_3O_2$. Calculated, %: C 47.79; H 5.19.

N'-[5-(2-Hydroxy-2-phenylacetyl)-2-furylmethylene]-N,N,N-trimethylhydrazonium Iodide (13). Yield 86%, light brown powder; mp 117-118°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.33 [9H, s, $(CH_3)_3$]; 5.82 (1H, d, *J* = 5.7, CHOH); 6.37 (1H, d, *J* = 5.7, CHOH); 7.26 (1H, d, *J* = 4.2, H-3 Fur); 7.36 (1H, d, *J* = 8.1, H-4 Ph); 7.46 (2H, t, *J* = 8.1, H-3,5 Ph); 7.47 (2H, d, *J* = 8.1, H-2,6 Ph); 7.81 (1H, d, *J* = 4.2, H-4 Fur); 9.05 (1H, s, CH=N). Found, %: C 46.29; H 4.60. $C_{16}H_{19}IN_2O_3$. Calculated, %: C 46.39; H 4.62.

N'-[5-(2-Hydroxy-2-phenylacetyl)-1-methyl-1H-pyrrol-2-ylmethylene]-N,N,N-trimethylhydrazonium Iodide (14). Yield 87%, light brown powder; mp 115-117°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.57 [9H, s, $(CH_3)_3$]; 4.04 (3H, s, CH_3 Pyr); 5.86 (1H, d, *J* = 5.7, CHOH); 5.88 (1H, d, *J* = 5.7, CHOH); 6.89 (1H, d, *J* = 4.5, H-3 Pyr); 7.26 (1H, d, *J* = 6.9, H-4 Ph); 7.33 (2H, t, *J* = 6.9, H-3,5 Ph); 7.41 (1H, d, *J* = 4.5, H-4 Pyr); 7.44 (2H, d, *J* = 6.9, H-2,6 Ph); 8.98 (1H, s, CH=N). Found, %: C 47.65; H 5.08. $C_{17}H_{22}IN_3O_2$. Calculated, %: C 47.79; H 5.19.

Preparation of Nitriles 15-18 (General Procedure). A solution of the appropriate salt **11-14** (0.80 mmol) in water (15 ml) was heated on a water bath at 50°C (bath temperature) for 1 h. The solid precipitated on cooling was filtered off. In the case of α-benzoins the product was chromatographed on a column (Al_2O_3, dichloromethane), and crystallized from hexane.

5-(2-Oxo-2-phenylacetyl)furan-2-carbonitrile (15). Yield 82%, yellow powder; mp 107-108°C. IR spectrum, ν, cm^{-1}: 3150, 3129, 2248, 1663, 1594, 1491, 1445, 1366, 1315, 1237, 1205, 1180, 1041. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.63 (2H, t, *J* = 8.1, H-3,5 Ph); 7.78 (1H, d, *J* = 8.1, H-4 Ph); 7.80 (1H, d, *J* = 4.2, H-3 Fur); 7.86 (1H, d, *J* = 4.2, H-4 Fur); 8.01 (2H, d, *J* = 8.1, H-2,6 Ph). Found, %: C 69.27; H 3.10. $C_{13}H_7NO_3$. Calculated, %: C 69.33; H 3.13.

1-Methyl-5-(2-oxo-2-phenylacetyl)-1H-pyrrole-2-carbonitrile (16). Yield 75%, light brown powder; mp 108-109°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.13 (3H, s, 1-CH_3 Pyr); 6.98 (1H, d, *J* = 5.1, H-3 Pyr); 7.09 (1H, d, *J* = 5.1, H-4 Pyr); 7.62 (2H, t, *J* = 8.7, H-3,5 Ph); 7.79 (1H, d, *J* = 8.7, H-4 Ph); 7.98 (2H, d, *J* = 8.7, H-2,6 Ph). Found, %: C 70.49: H 4.22. $C_{14}H_{10}N_2O_2$. Calculated, %: C 70.58; H 4.23.

5-(2-Hydroxy-2-phenylacetyl)furan-2-carbonitrile (17). Yield 83%, yellow powder; mp 140-141°C. IR spectrum, ν, cm^{-1}: 3449, 3415, 3151, 3113, 2252, 1674, 1493, 1452, 1395, 1269, 1228, 1210, 1187, 1045, 1024, 972. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.90 (1H, d, *J* = 6.0, CHOH); 6.40 (1H, d, *J* = 6.0, CHOH); 7.30

(1H, d, *J* = 8.1, H-4 Ph); 7.36 (2H, t, *J* = 8.1, H-3,5 Ph); 7.46 (2H, d, *J* = 8.1, H-2,6 Ph); 7.74 (1H, d, *J* = 4.2, H-4 Fur); 7.78 (1H, d, *J* = 4.2, H-3 Fur). Found, %: C 68.70; H 3.95. $C_{13}H_9NO_3$. Calculated, %: C 68.72; H 3.99.

5-(2-Hydroxy-2-phenylacetyl)-1-methyl-1H-pyrrole-2-carbonitrile (18). Yield 74%, light brown powder; mp 112-114°C. IR spectrum, ν, cm^{-1}: 3390, 3360, 3120, 2919, 2895, 2238, 1682, 1475, 1444, 1382, 1334, 1273, 1236, 1210, 1189, 1103, 1050, 1004, 919. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.91 (3H, s, 1-CH_3 Pyr); 5.84 (1H, d, *J* = 5.1, CHOH); 6.07 (1H, d, *J* = 5.1, CHOH); 6.99 (1H, d, *J* = 5.1, H-3 Pyr); 7.25 (1H, d, *J* = 8.7, H-4 Ph); 7.33 (2H, t, *J* = 8.7, H-3,5 Ph); 7.37 (1H, d, *J* = 5.1, H-4 Pyr); 7.45 (2H, d, *J* = 8.7, H-2,6 Ph). Found, %: C 69.95; H 4.98. $C_{14}H_{12}N_2O_2$. Calculated, %: C 69.99; H 5.03.

Preparation of Aldehydes 19-22 (General Procedure). A solution of the appropriate salt **11-14** in dilute (1:10) hydrochloric acid was heated on a water bath at 50°C (bath temperature) for 1 h. The solid precipitated on cooling was filtered off, and crystallized from hexane.

5-(1-Hydroxy-2-oxo-2-phenylethyl)furan-2-carbaldehyde (19). Yield 76%, light yellow needles; mp 87-88°C. IR spectrum, ν, cm^{-1}: 3391, 3378, 3127, 2948, 2820, 1675, 1591, 1516, 1456, 1393, 1270, 1222, 1200, 1175, 1098, 1025, 980, 959. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.31 (1H, d, *J* = 6.3, CHOH); 6.51 (1H, d, *J* = 6.3, CHOH); 6.76 (1H, d, *J* = 3.9, H-3 Fur); 7.49 (1H, d, *J* = 3.9, H-4 Fur); 7.53 (2H, t, *J* = 7.8, H-3,5 Ph); 7.64 (1H, d, *J* = 7.8, H-4 Ph); 8.02 (2H, d, *J* = 7.8, H-2,6 Ph); 9.51 (1H, s, CH=O). Found, %: C 67.80; H 4.37. $C_{13}H_{10}O_4$. Calculated, %: C 67.82; H 4.38.

1-Methyl-5-(2-oxo-2-phenylacetyl)-1H-pyrrole-2-carbaldehyde (20). Yield 61%, orange powder; mp 74-75°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.32 (3H, s, 1-CH_3 Pyr); 6.92 (1H, d, *J* = 4.5, H-3 Pyr); 7.08 (1H, d, *J* = 4.5, H-4 Pyr); 7.62 (2H, t, *J* = 7.5, H-3,5 Ph); 7.79 (1H, d, *J* = 7.5, H-4 Ph); 7.97 (2H, d, *J* = 7.5, H-2,6 Ph); 9.95 (1H, s, CH=O). Found, %: C 6.68; H 4.55. $C_{14}H_{11}NO_3$. Calculated, %: C 69.70; H 4.60.

5-(2-Hydroxy-2-phenylacetyl)furan-2-carbaldehyde (21). Yield 83%, light yellow needles; mp 165-166°C. IR spectrum, ν, cm^{-1}: 3463, 3428, 3152, 3110, 2820, 1680, 1650, 1252, 1214, 1183, 1060, 1025, 970. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.82 (1H, d, *J* = 4.8, CHOH); 6.34 (1H, d, *J* = 4.8, CHOH); 7.29 (1H, d, *J* = 7.5, H-4 Ph); 7.35 (2H, t, *J* = 7.5, H-3,5 Ph); 7.47 (2H, d, *J* = 7.5, H-2,6 Ph); 7.58 (1H, d, *J* = 4.2, H-4 Fur); 7.74 (1H, d, *J* = 4.2, H-3 Fur); 9.75 (1H, s, CH=O). Found, %: C 67.79; H 4.38. $C_{13}H_{10}O_4$. Calculated, %: C 67.82; H 4.38.

5-(2-Hydroxy-2-phenylacetyl)-1-methyl-1H-pyrrole-2-carbaldehyde (22). Yield 89%, light brown powder; mp 108-109°C. IR spectrum, ν, cm^{-1}: 3500, 3130, 2965, 2830, 2800, 1679, 1655, 1488, 1452, 1413, 1377, 1336, 1280, 1235, 1210, 1174, 1097, 1060, 1007. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.08 (3H, s, 1-CH_3 Pyr); 5.82 (1H, d, *J* = 4.9, CHOH); 5.88 (1H, d, *J* = 4.9, CHOH); 7.01 (1H, d, *J* = 4.8, H-4 Pyr); 7.25 (1H, d, *J* = 9.00, H-4 Ph); 7.35 (2H, t, *J* = 9.0, H-3,5 Ph); 7.36 (1H, d, *J* = 4.8, H-3 Fur); 7.45 (2H, d, *J* = 9.0, H-2,6 Ph); 9.77 (1H, s, CH=O). Found, %: C 69.07; H 5.31. $C_{14}H_{13}NO_3$. Calculated, %: C 69.12; H 5.39.

Preparation of Hydrazones 23-26 (General Procedure) (Table 3). A solution of the appropriate compound (see Table 3) (0.90 mmol), *p*-bromobenzoic acid hydrazide (0.19 g, 0.90 mmol), concentrated sulfuric acid (0.05 ml), or without it, in ethanol (8 ml) was boiled. The solid precipitated on cooling was filtered off, and crystallized from ethanol.

4-Bromobenzoic Acid [5-(1-Hydroxy-2-oxo-2-phenylethyl)-2-furylmethylene]hydrazide (23). Light brown powder; mp 165-166°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.25 (1H, d, *J* = 6.3, CHOH); 6.29 (1H, d, *J* = 6.3, CHOH); 6.59 (1H, d, *J* = 3.0, H-3 Fur); 6.89 (1H, d, *J* = 3.0, H-4 Fur); 7.51 (2H, t, *J* = 7.2, H-3,5 Ph); 7.63 (1H, d, *J* = 7.2, H-4 Ph); 7.75 (2H, d, *J* = 8.5, H-3,5 Ar); 7.84 (2H, d, *J* = 8.5, H-2,6 Ar); 8.02 (2H, d, *J* = 7.2, H-2,6 Ph); 8.23 (1H, s, CH=N); 11.84 (1H, s, NH). Found, %: C 56.20; H 3.54. $C_{20}H_{15}BrN_2O_4$. Calculated, %: C 56.22; H 3.54.

4-Bromobenzoic Acid [5-(1-Hydroxy-2-oxo-2-phenylacetyl)-1-methyl-1H-pyrrol-2-ylmethylene-hydrazide (24). Brown powder; mp 164-165°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.01 (3H, s, 1-CH_3 Pyr); 5.65 (1H, d, *J* = 3.5, H-3 Pyr); 5.75 (1H, d, *J* = 5.3, CHOH); 6.13 (1H, d, *J* = 5.3, CHOH); 6.80 (1H, d, *J* = 3.5, H-4 Pyr); 7.49 (2H, t, *J* = 7.7, H-3,5 Ph); 7.65 (1H, d, *J* = 7.7, H-4 Ph); 7.77 (2H, d, *J* = 8.1, H-3,5 Ar); 7.91

(2H, d, *J* = 8.1, H-2,6 Ar); 8.00 (2H, d, *J* = 7.7, H-2,6 Ph); 8.37 (1H, s, CH=N); 11.77 (1H, s, NH). Found, %: C 57.19; H 4.08. $C_{23}H_{18}BrN_3O_3$. Calculated, %: C 57.29; H 4.12.

4-Bromobenzoic Acid [5-(2-Hydroxy-2-phenylacetyl)-2-furylmethylene]hydrazide (25). Orange powder; mp 176-177°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.78 (1H, d, *J* = 4.6, CHOH); 6.25 (1H, d, *J* = 4.6, CHOH); 7.10 (1H, d, *J* = 3.0, H-4 Fur); 7.25 (1H, d, *J* = 3.0, H-3 Fur); 7.30 (2H, t, *J* = 7.2, H-3,5 Ph); 7.35 (1H, d, *J* = 7.2, H-4 Ph); 7.49 (2H, d, *J* = 7.2, H-2,6 Ph); 7.76 (2H, d, *J* = 7.6, H-3,5 Ar); 7.86 (2H, d, *J* = 7.6, H-2,6 Ar); 8.36 (1H, s, CH=N); 12.13 (1H, s, NH). Found, %: C 56.19; H 3.50. $C_{20}H_{15}BrN_2O_4$. Calculated, %: C 56.22; H 3.54.

4-Bromobenzoic Acid [5-(2-Hydroxy-2-phenylacetyl)-1-methyl-1H-pyrrol-2-ylmethylene]-hydrazide (26). Orange powder; mp 178-179°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.34 (3H, s, 1-CH_3 Pyr); 5.83 (1H, d, *J* = 5.7, CHOH); 5.87 (1H, d, *J* = 5.7, CHOH); 6.64 (1H, d, *J* = 3.3, H-3 Pyr); 7.25 (1H, d, *J* = 7.5, H-4 Ph); 7.32 (2H, t, *J* = 7.5, H-3,5 Ph); 7.40 (1H, d, *J* = 3.3, H-4 Pyr); 7.47 (2H, d, *J* = 7.5, H-2,6 Ph); 7.75 (2H, d, *J* = 7.8, H-3,5 Ar); 7.85 (2H, d, *J* = 7.8, H-2,6 Ph); 8.49 (1H, s, CH=N); 11.93 (1H, s, NH). Found, %: C 57.15; H 4.10. $C_{21}H_{18}BrN_3O_3$. Calculated, %: C 57.29; H 4.12.

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