UNUSUAL SPONTANEOUS α→β ISOMERIZATION OF UNSYMMETRICAL BENZOINS

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α-Mixed aryl(furyl)benzoins undergo spontaneous thermal isomerization to β-isomers in the absence of a base. It is facilitated by two structural features viz. the presence of a *para*-halogen substituent in the aryl moiety and of a Me_2NN=CH-substituent at 5-position of the furan ring.

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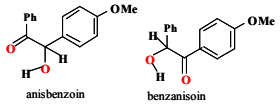
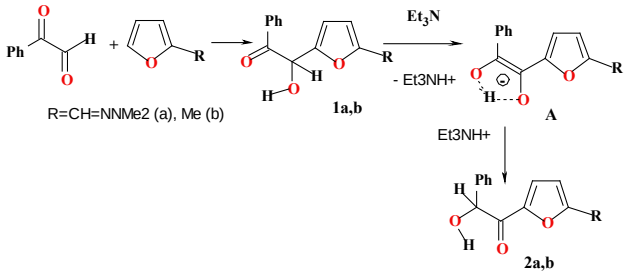
Introduction

Earlier we had reported that phenylglyoxal reacted with 2-R-furanes (R= CH= NNMe2 or Me) selectively yielding unsymmetrical α-benzoins, such as 2-furyl-1-arylethan-1-ones 1,[1-4] which cannot be synthesized by the usual way. There are two kinds of isomeric benzoins, α-benzoins and β-benzoins.[5] α-Benzoins are the lower-melting, less stable isomers, whereas β-benzoins are the higher-melting, more stable isomers.[5] The higher stability of β-benzoins is explained by the possibility of conjugation between the electron donor and the electron acceptor substituents via the aryl or heteroaryl ring. For example, anisbenzoin is α-benzoin and benzanisoin is β-benzoin.[5]



Scheme 1.

In the presence of a base α-benzoins are known to isomerize[5] to more stable β-benzoins, in which electron donor substituent of aryl moiety can conjugated with carbonyl group. It was found that α-benzoins **1** isomerized to 2-aryl-1-furylethan-1-ones **2** (β-benzoins) by the action of triethylamine [2-4] (Scheme 2). This isomerization may occur via the formation of the common anion **A**.



Scheme 2.

α-Benzoins **1** was synthesized by the interaction of phenylglyoxal with suitable furans.[2-4] But the reaction of these furans with other arylglyoxals has not been studied.

Experimental

^{1}H NMR spectra were recorded on a Varian VXP-300 spectrometer (300 MHz, internal standard – Me_4Si, chemical shifts in δ-scale (ppm), coupling constants in Hz). Mass spectra were recorded on a VG-70EQ 770 mass spectrometer in FAB mode (FAB).

2-Hydroxy-2-(2''-*N,N*-dimethylhydrazonyl-5''-furyl)-1-(2'-thienyl)ethanone-1 (3a). A solution of *N,N*-dimethylhydrazone of 2-furanecarbaldehyde (10.0 mmol, 1.38 g) in benzene (4 ml) was added to the 2-thienylglyoxal (10,0 mmol, 1.40 g) solution in PhH (14 ml), the reaction mixture was kept at 20 ^{0}C for 35 h, the precipitate was then filtered off and washed by benzene (4 ml), dried *in vacuo*, yielding 2.11 g (75.9 %) of 2-hydroxy-2-(2''-*N,N*-dimethylhydrazonyl-5''-furyl)-1-(2'-thienyl)ethanone-1 **3a**, yellow crystals, m.p. 119 – 120^{0}C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): 2.83 (s, 6H, NMe_2), 4.98 (d, 1H, CHOH, ^3J = 6.6 Hz), 5.92 (d, 1H, CHOH, ^3J = 6.6 Hz), 6.31 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.47 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 7.01 (s, 1H, CH=N), 7.16 (t, 1H, H_{Th}^4, ^3J = 5.1 Hz),7.90 (d, 1H, H_{Th}^5, ^3J = 5.1 Hz), 7.91 (d, 1H, H_{Th}^3, ^3J = 3.4 Hz). ^{1}H NMR (300 MHz, $(CD_3)_2SO$): 2.86 (s, 6H, NMe_2), 5.90 (d, 1H, CHOH, ^3J = 6.0 Hz), 6.26 (d, 1H, CHOH, ^3J = 6.0 Hz), 6.39 (d, 1H, H_{Fur}^3, ^3J = 3.0Hz), 6.49 (d, 1H, H_{Fur}^4, ^3J = 3.0 Hz), 7.10 (s, 1H, CH=N), 7.23 (t, 1H, H_{Th}^4, ^3J = 4.2 Hz), 8.02 (d, 1H, H_{Th}^3, ^3J = 3.0 Hz),

8.031 (d, 1H, H_{Th}^5, ^3J = 4.2 Hz). IR (ν, cm^{-1}): 3430 (OH), 1690 (C=O), 1578 (C=N). MS (EI, m/z, $I_{rel.}$, %): 279 $[M+H]^+$ (0.58), 278, M^+, (5.76), 277 $[M-H]^+$ (3.8), 276 (22.2), 167 (21.7), 166 (13.6), 165 (100), 151 (51.6), 111 (94.1). MS (FAB, m/z, $I_{rel.}$, %): 279 $[M+H]^+$ (42), 278, M^+, (52), 261 $[M+H-H_2O]^+$ (30), 167 (100), 111 (21). Found (%): C 56.25, H 5.17, N 9.98. Calc. for $C_{13}H_{14}N_2O_3S$ (%): C 56.10, H 5.07, N 10.06.

2-Hydroxy-2-(5''-methyl-2''-furyl)-1-(2'-thienyl)-ethanone-1 (3b). The solution of 2-thienylglyoxal (10.0 mmol, 1.40 g) and 2-methylfurane (27.77 mmol, 2.28 g) in PhH (9 ml) was kept in sealed tube at 18-20 ^{0}C for 44 days, the precipitate was then filtered off and washed by CH_2Cl_2, yielding 1.65 g (74.0 %) of 2-hydroxy-2-(5''-methyl-2''-furyl)-1-(2'-thienyl)ethanone-1 **3b**, colourless crystals, m.p. 141-142 ^{0}C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.24 (s, 3H, Me), 4.26 (br.s., 1H, CHOH), 5.75 c (1H, CHOH), 5.94 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 6.31 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 7.1 (t, 1H, H_{Th}^4, ^3J = 4.3 Hz), 7.67 (d, 1H, H_{Th}^3, ^3J = 4.3 Hz), 7.71 (d, 1H, H_{Th}^5, ^3J = 3.4 Hz). MS (FAB, m/z, $I_{rel.}$, %): 223 $[M+H]^+$ (6), 205 $[M+H-H_2O]^+$ (90), 111 (100). MS (FAB, Na^+, m/z, $I_{rel.}$, %): 245 $[M+Na]^+$ (100), 205 $[M+H-H_2O]^+$ (11), 111 (29). Found (%): C 59.52, H 4.41. Calc. for $C_{11}H_{10}O_3S$ (%): C 59.44, H 4.53.

2-Hydroxy-1-(4''-methoxyphenyl)-2-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanone-1 (4). A solution of *N,N*-dimethylhydrazone of 2-furanecarbaldehyde (1.712 mmol, 0.236 g) in PhH (2 ml) was added to a solution of 4-methoxyphenylglyoxal (1.8043 mmol, 0.2962 g) in PhH (3 ml) at -30°C. The reaction mixture was kept at 20°C for 11 days, and then filtered. The filtrate was evaporated *in vacuo* 30 Torr. The residue was washed by hexane (5 ml), dried *in vacuo* 7 Torr, yielding 0.444 g (85.7%) of 2-hydroxy-1-(4''-methoxyphenyl)-2-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanon-1 **4**, yellow crystals, m.p. 79-81 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 2.94 (s, 6H, Me_2N), 3.886 (s, 3H, OMe), 5.98 (s, 1H, CH), 6.25 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.33 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 6.89 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 9.0 Hz), 7.01 (s 1H, CH=N), 7.96 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 9.0 Hz). MS (FAB, m/z, $I_{rel.}$, %): 302 M^+ (35), 285 $[M+H-H_2O]^+$ (24), 167 (100), 135 (56). Found (%): C 63.64, H 6.28, N 9.31. Calc. for $C_{16}H_{18}N_2O_4$ (%): C 63.57, H 6.00, N 9.27. The process of synthesis of **2-Hydroxy-1-(4''-diphenyl)-2-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanone-1 (5)** was similar to that of compound **4**, yield 90%, yellow crystals, m.p. 108 – 109 °C (PhH). ^{1}H NMR (300 MHz, $CDCl_3$): 2.95 (s, 6H, NMe_2), 6.07 (s, 1H, CH), 6.31 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.35 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 7.03 (s, 1H, CH=N), 7.36 (s, 1H, OH), 7.43 (t, 1H, $H_{Ph}^{4'}$, ^3J = 6.6 Hz), 7.47 (t, 2H, $H_{Ph}^{3',5'}$, ^3J = 6.6 Hz), 7.60 (d, 2H, $H_{Ph}^{2',6'}$, ^3J = 6.6 Hz), 7.65 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.4 Hz), 8.05 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.4 Hz). MS (FAB, H^+, m/z, $I_{отн.}$, %): 349 $[M+H]^+$ (36), 348 M^+ (40), 331 $[M+H-H_2O]^+$ (29), 181 $PhC_6H_4C(O)^+$ (29), 167 (100). Found (%): C 72.35, H 6.08, N 8.31. Calc. for $C_{21}H_{20}N_2O_3$ (%): C 72.40, H 5.79, N 8.04.

2-Hydroxy-2-(4''-chlorophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanone-1 (6). A solution of *N,N*-dimethylhydrazone of 2-furanecarbaldehyde (31.59 mmol, 4.365 g) in PhH (5 ml) was added to a solution of 4-chlorophenylglyoxal (38.53 mmol, 6.500 g) in PhH (20 ml). The reaction mixture was kept at 20°C for 4 days, the precipitate was then filtered off, washed by PhH (7 ml), *i*-PrOH (15 ml), dried *in vacuo,* yielding 5.90 g (60.9 %) of 2-hydroxy-2-(4''-chlorophenyl)-1-(5'-*N,N*-dimethylhydrazonofuryl-2')-ethanone-1 **6**, red crystals, m.p. 150-151 °C (*i*-PrOH). ^{1}H NMR (300 MHz, $(CD_3)_2SO$): 3.00 (s, 6H, NMe_2), 5.72 (d, 1H, CHOH, ^3J = 5,1 Hz), 6.18 (d, 1H, CHOH, ^3J = 5.1 Hz), 6.56 (d, 1H, H_{Fur}^4, ^3J = 3.9 Hz), 7.10 (s, 1H, CH=N), 7.39 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.4 Hz), 7.49 (d, 2H, $H_{C6H4}^{2,6}$,, ^3J = 8.4 Hz), 7.68 (d, 1H, H_{Fur}^3, ^3J = 3.9 Hz). IR (ν, cm^{-1}): 3415 (OH); 1635 (C=O); 1555 (C=N). MS (EI, m/z, $I_{rel.}$, %): 308 M^+(0,5); 306 M^+, $[M-H_2]^+$ (4.9), 304 $[M-H_2]^+$(7.1), 166 (12.2), 165 (100), 143 (0.5), 141 (14.8), 139 (40.6), 113 (70.0), 111 (20.4), 109 (20.4). Found (%): C 58.84, H 4.72, N 9.02. Calc. for $C_{15}H_{15}ClN_2O_3$ (%): C 58.73, H 4.93, N 9.13.

2-Hydroxy-2-(4''-bromophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanon-1 (7). A solution of *N,N*-dimethylhydrazone of 2-furanecarbaldehyde (2.70 mmol, 0.373 g) in PhH (2 ml) was added to a solution of 4-bromophenylglyoxal (2.70 mmol, 0,580 g) in PhH (20 ml). The reaction mixture was kept at 20°C for 4 days, and then evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and precipitated by an addition of hexane (10ml). The precipitate was filtered off and dried, yielding 0.51 g (54,0 %) of 2-hydroxy-2-(4''-bromophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanone-1 **7**, brown crystals, m.p. 127 – 129°C (with decomp.). ^{1}H NMR (300 Hz, $CDCl_3$): 3.08 (s, 6H, NMe_2), 5.79 (br. S, 1H, CHOH), 6.92 (br. s, 1H, CHOH,), 6.46 (d, 1H, H^4_{Fur}, ^3J = 3.9 Hz), 7.20 (d, 1H, H^3_{Fur}, ^3J = 3.9 Hz), 7.32 (s, 1H, CH=N), 7.35 (d, 2H, $H^{3,5}_{C6H4r}$, ^3J = 8,4 Hz), 7,45 (d, 2H, $H^{2,6}_{C6H4,}$, ^3J = 8.4 Hz). MS (EI, m/z, $I_{отн.}$, %): 351 M^+(28); 186 $Br\text{-}C_6H_4C^+H(OH)$ (30); 165 $Me_2NN{=}CH\text{-}C_4H_2O\text{-}C^+{=}O$ (100). Found (%): C 51.02, H 4.64, N 8.17. Calc. for $C_{15}H_{15}BrN_2O_3$ (%): C 51.30; H 4.31; N 7.98.

The filtrate was evaporated *in vacuo* yielding 0.20 g (22.0 %) of 2-(4''-bromophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethandione-1,2 **8** , red-brown solid. ^{1}H NMR (300 MHz, $CDCl_3$): 3.00 (s, 6H, NMe_2), 6.60 (d. 1H, H^4_{Fur}, ^3J = 3.6 Hz), 7.06 (s, 1H, CH=N), 7.48 (d, 1H, H^3_{Fur}, ^3J = 3.6 Hz), 7.74 (d, 2H, $H^{3,5}_{C6H4}$, ^3J = 8.7 Hz), 7.81 (d, 2H, $H^{2,6}_{C6H4,}$, ^3J = 8.7 Hz). MS (FAB, H^+, m/z, $I_{rel.}$, %): 350 $[M+H]^+$ (7.8), 348 $[M-H]^+$ (8.3), 165 (100).

2-Hydroxy-2-(5'-methylfuryl-2')-1-(4''-chlorophenyl)-ethanone-1 (9) A solution of 4-chlorophenylglyoxal (1.174 mmol, 0.198 g) and 2-methylfuran (4.215 mmol, 0.346 g) in CH_2Cl_2 (9 ml) in a sealed tube was kept at 20 – 23 °C in dark for 120 h, then the reaction mixture was concentrated *in vacuo* 30 Torr to 1 ml volume and hexane (5 ml) was added. After keeping at 5°C for 4 days, the precipitate was filtered off and dried yielding 0.269 g (91.0 %) of 2-hydroxy-2-(5'-methylfuryl-2')-1-(4''-chlorophenyl)ethanone-1 **9**, yellow crystals, m.p. 86 – 88 °C (hexane). ^{1}H NMR (300 MHz, $CDCl_3$): 2.22 (s, 3H, Me), 4.31 (d, 1H, CHOH, ^3J = 6.0 Hz), 5.90 (d and br. s, 2H, H_{Fur}^4 and OH, ^3J = 3.0 Hz), 6.21 (d, 1H, H_{Fur}^3, ^3J = 3.0 Hz), 7.41 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.1 Hz), 7.90 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.1 Hz). IR (υ, cm^{-1}): 3437 (OH), 1695 (C=O). MS (FAB, K^+, m/z, $I_{rel.}$,%): 291 $[M+K]^+$ (20), 289

$[M+K]^+$ (49), 235 $[M+H-H_2O]^+$ (45), 233 $[M+H-H_2O]^+$ (100), 141 $[ClC_6H_4C(O)^+]$ (14), 139 $[ClC_6H_4C(O)^+]$ (38). Found (%): C 62.10, H 4.55. Calc. for $C_{13}H_{11}ClO_3$ (%): C 62.29, H 4.42.

2-Hydroxy-2-(5'-methylfuryl-2')-1-(4''-bromophenyl)ethanone-1 (10) was synthesized in a manner similar to that for compound **9**, yield 63 %, yellow crystals, m.p. 69 – 70 ˚C (CH_2Cl_2 - hexane). ^{1}H NMR (300 MHz, $CDCl_3$): 2.22 (s, 3H, Me), 4.30 (br. s, 1H, CHOH), 5.90 (br. s, 2H, H_{Fur}^4 and OH), 6.21 (d, 1H, H_{Fur}^3, ^3J = 3.0 Hz), 7.58 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.7 Hz), 7.82 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.7 Hz). IR (υ, cm^{-1}): 3440 (OH), 1700 (C=O). MS (FAB, H^+, m/z($I_{rel.}$,%): 297 $[M+H]^+$ (2), 295 $[M+H]^+$ (6), 293 $[M-H]^+$ (4), 279 $[M+H-H_2O]^+$ (84), 277 $[M+H-H_2O]^+$ (82), 111 Me-C_4H_3O-CH^+(OH) (100). MS (FAB, K^+, m/z($I_{rel.}$,%): 335 $[M+K]^+$ (50), 333 $[M+K]^+$ (60), 279 $[M+H-H_2O]^+$ (31), 277 $[M+H-H_2O]^+$ (28), 111 Me-C_4H_3O-CH^+(OH) (58), 39 K^+(100). Found (%): C 53.08, H 3.82. Calc. For $C_{13}H_{11}BrO_3$ (%): C 52.91, H 3.76.

2-Hydroxy-2-(5'-methylfuryl-2')-1-(4''-fluorophenyl)ethanone-1 (11) was synthesized in a manner similar to that for compound **9**, yield 84%, yellow crystals, m.p. 90 – 92 ˚C (CH_2Cl_2 – hexane). ^{1}H NMR (300 MHz, $CDCl_3$): 2.22 (s, 3H, Me), 4.34 (br. s, 1H, CHOH), 5.91 (br. s, 2H, H_{Fur}^4 and OH), 6.21 (d, 1H, H_{Fur}^3, ^3J = 3.0 Hz), 7.11 (dd, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.4 Hz, ^{H-F}J = 8.4 Hz), 8.00 (dd, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.4 Hz, ^{H-F}J = 8.4 Hz). IR (υ, cm^{-1}): 3440 (OH), 1698 (C=O). MS (EI, m/z ($I_{rel.}$,%)): 123 $[FC_6H_4C(O)^+]$ (100). MS (FAB, K^+, m/z($I_{rel.}$,%): 273 $[M+K]^+$ (16), 217 $[M+H-H_2O]^+$ (100), 123 $[FC_6H_4C(O)^+]$ (53). Found (%): C 66.31, H 4.93. Calc for $C_{13}H_{11}FO_3$ (%): C 66.66, H 4.73.

2-Hydroxy-1-(4''-chlorophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanon-1 (12). *N,N*-Dimethylhydrazone of 2-furanecarbaldehyde (3.90 mmol, 0.539 g) was added to a cooled (-20^{0}C) solution of 4-chlrophenylglyoxal (3.90 mmol, 0.650 g) in Et_2O (20 ml). The reaction mixture was kept for a week at -20^{0}C, and then evaporated *in vacuo*. The residue was washed by hexane and dried *in vacuo* 2 Torr, yielding 0.74 g (62 %) of 2-hydroxy-1-(4''-chlorophenyl)-2-(5'-*N,N*-dimethylhydrazonofuryl-2')ethanon-1 **12**, yellow viscous oil. ^{1}H NMR (300 MHz, $(CD_3)_2SO$): 2.85 (s, 6H, NMe_2), 6.13 (br. s, 2H, CHOH), 6.35 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.42 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 7.07 (s, 1H, CH=N), 7.58 (d, 2H, $H_{Ar}^{3,5}$, ^3J = 8.1 Hz), 8.01 (d, 2H, $H_{Ar}^{2,6}$,, ^3J = 8.1 Hz). ^{1}H NMR (300 MHz, $CDCl_3$): 2.96 (s, 6H, NMe_2), 6.01 (s, 1H, CH); 6.29 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.34 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 7.01 (s, 1H, CH=N), 7.15 (br. s, 1H, OH), 7.42 (d, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.7 Hz), 7.93 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.7 Hz). MS (FAB, m/z, $I_{отн.}$, %): 309 $[M+H]^+$ (5), 307 $[M+H]^+$ (16), 291 $[M+H-H_2O]^+$ (6), 289 $[M+H-H_2O]^+$ (20), 167 Me_2NN=CH-C_4H_2O-CH^+(OH) (100), 141 Cl-C_6H_4-C^+=O (13), 139 Cl-C_6H_4-C^+=O (33). Found (%): C 58.91, H 4.70, N 9.11. Calc. for $C_{15}H_{15}ClN_2O_3$ (%): C 58.73, H 4.93, N 9.13.

2-Hydroxy-1-(4''-bromophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 (13). *N,N*-Dimethylhydrazone of 2-furanecarbaldehyde (2.30 mmol, 0.318 g) was added to the a solution of 4-bromophenylglyoxal (2.30 mmol, 0.480 g) in Et_2O (20 ml) at -20^{0}C, the reaction mixture was kept at -20^{0}C for a week, and then evaporated *in vacuo* 1 Torr at 10^{0}C. The residue was washed by hexane and dried *in vacuo* 1 Torr, yielding 0.72 g (86 %) of 2-hydroxy-1-(4''-bromophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 **13**, dark brown viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$): 2.96 (s, 6H, NMe_2), 6.00 (s, 1H, CH), 6.29 (d, 1H, H_{Fur}^3, ^3J = 3.3 Hz), 6.34 (d, 1H, H_{Fur}^4, ^3J = 3.3 Hz), 7.00 (s, 1H, CH=N), 7.58 (d, 2H, $_{C6H4}^{3,5}$, ^3J = 8.7 Hz), 7.84 (d, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.7 Hz). MS (FAB, m/z, $I_{rel.}$, %): 353 $[M+H]^+$ (21), 352 M^+ (23), 351 $[M+H]^+$ (28), 350 M^+ (24), 335 $[M+H-H_2O]^+$ (23), 333 $[M+H-H_2O]^+$ (23), 167 Me_2NN=CH-C_4H_2O-CH^+(OH) (100). 185 Br-C_6H_4-C^+=O (30). 183 Br-C_6H_4-C^+=O (30). Found (%): C 52.01, H 4.55, N 7.82. Calc. for $C_{15}H_{15}BrN_2O_3$ (%): C 51.30, H 4.31, N 7.98.

2-Hydroxy-1-(4''-fluorophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 (14).

(i) A solution of *N,N*-dimethylhydrazone of 2-furancarbaldehyde (1.404 mmol, 0.194 g) and 4-fluorophenylglyoxal (1.615 mmol, 0.245 g) in PhH (12 ml) under argon was kept in a sealed tube at 40˚C for 9h and at 24˚C for 80 h, and then evaporated *in vacuo* to a volume of 3 ml and hexane (10 ml) was added. The separated oil was extracted by CCl_4 (10 ml), the extract was evaporated *in vacuo* 2 Torr, yielding 0.302 g (74.3%) 2-hydroxy-1-(4''-fluorophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 **14,** red semi-solid substance. ^{1}H NMR (300 MHz, $CDCl_3$): 2.94 (s, 6H, NMe_2), 6.00 (s, 1H, CHOH), 6.28 (d, 1H, H_{Fur}^3, ^3J = 3.6 Hz), 6.33 (d, 1H, H_{Fur}^4, ^3J = 3.6 Hz), 7,00 (s, 1H, CH=N), 7.15 (dd, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.7 Hz, J = 8.7 Hz), 8.01 (dd, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.7 Гц, ^{F-H}J = 5.25 Hz). MS (EI, m/z, $I_{rel.}$(%)): 290 M^+ (24), 167 Me_2N-N+CH-C_4H_2O-C^+H(OH) (83), 123 $FC_6H_4C(O)^+$ (100). MS (FAB, H^+, m/z, $I_{rel.}$(%)): 291 $[M+H]^+$ (39), 290 M^+(38), 273 $[M+H-H_2O]^+$ (35), 167 Me_2N-N+CH-C_4H_2O-C^+H(OH) (100), 123 F-C_6H_4-C^+=O (54). Found (%): C 62.11, H 4.80, N 9.72. Calc. for $C_{15}H_{15}FN_2O_3$ (%): C 62.06, H 5.21, N 9.65.

From the hexane phase, 0.066 g (16.1%) 1-(5'-*N,N*-dimethylhydrazonylfuril-2')-2-(4''-fluorophenyl)-ethandione-1,2 **15** was isolated by crystallization as black-red solid. ^{1}H NMR (300 MHz, $CDCl_3$): 3.12 (s, 6H, NMe_2), 6.63 (d, 1H, H^4_{Fur}, ^3J = 3.9 Hz), 7.03 (s, 1H, CH=N), 7.18 (dd, 2H, $H_{C6H4}^{2,6}$, ^3J = 8.7 Hz, ^{F-H}J = 8.55 Hz), 7.40 (d, 1H, H^3_{Fur}, ^3J = 3.9 Hz), 8.12 (dd, 2H, $H_{C6H4}^{3,5}$, ^3J = 8.7 Hz, ^{F-H}J = 5.55 Hz). MS (EI, m/z, $I_{rel.}$(%)): 288 M^+ (27); 165 Me_2NN=CH-C_4H_2O-C^+=O (100), 123 $FC_6H_4C(O)^+$ (25). Found (%): N 9.70. Calc. for $C_{15}H_{13}FN_2O_3$ (%):N 9.72.

(ii) *N,N*-Dimethylhydrazone of 2-furancarbaldehyde (0.800 mmol, 0.110 g) was added to a solution of 4-fluorophenylglyoxal (0.800 mmol, 0.121 g) in Et_2O (20 ml) at -20˚C, the reaction mixture was kept at -20˚C for 4 days and then evaporated *in vacuo* 3 Torr, yielding 0.190 g (81.8%) 2-hydroxy-1-(4''-fluorophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 **14**, identified by ^{1}H NMR.

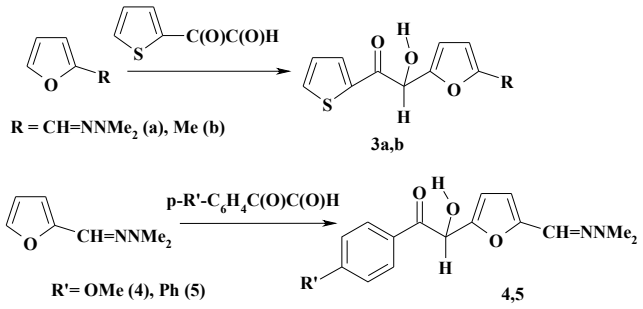
(iii) A solution of *N,N*-dimethylhydrazone of 2-furancarbaldehyde (1.615 mmol) and 4-fluorophenylglyoxal (1.717 mmol) in PhH (10 ml) was kept at 20˚C in a sealed tube for 7 days and then evaporated *in vacuo*. The residue was washed by hexane

and dried *in vacuo*, yielding 0.464 g (99%) of 2-hydroxy-1-(4''-fluorophenyl)-2-(5'-*N,N*-dimethylhydrazonylfuril-2')-ethanone-1 **14**, identified by ^{1}H NMR.

2-Hydroxy-2-(4''-fluorophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanone-1 (16). A sample of 2-hydroxy-1-(4''-fluorophenyl)-2-(5'-5'-*N,N*-dimethylhydrazonylfuryl-2'-)-ethanone-1 **14** was kept at 10°C in dark for 4 months. A quantitative isomerization took place to 2-hydroxy-2-(4''-fluorophenyl)-1-(5'-*N,N*-dimethylhydrazonylfuryl-2')-ethanon-1 **16**, red solid, m.p. 117-120°C (with decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): 3.08 (s, 6H, NMe_2), 5.73 (s, 1H, CH), 6.47 (d, 1H, H_{Fur}^4, ^3J = 3.9 Hz), 6.93 (s, 1H, CH=N), 7.02 (dd, 2H, $H_{Ar}^{2,6}$, ^3J = 8.7 Hz, J = 8.7 Hz), 7.19 (d, 1H, H_{Fur}^3, ^3J = 3.9 Hz), 7.42 (dd, 2H, $H_{Ar}^{3,5}$, ^3J = 8.7 Hz, ^{F-H}J = 5.25 Hz). IR (ν, cm^{-1}): 1640 (C=O), 1600 (C=N). MS (EI, m/z, $I_{rel.}$(%)): 290 M^+ (10); 166 $Me_2NN{=}CH\text{-}C_4H_2O\text{-}CH{=}O^{+\cdot}$ (81), 124 $FC_6H_4CH(=O)^{+\cdot}$ (100). MS (FAB, H^+, m/z, $I_{rel.}$(%)): 289 $[M+H]^+$ (58), 245 (38), 165 (76), 154 (100), 136 (80), 123 (53). Found (%): C 62.25, H 5.42. Calc. for $C_{15}H_{15}FN_2O_3$ (%): C 62.06, H 5.21.

Results and Discussion

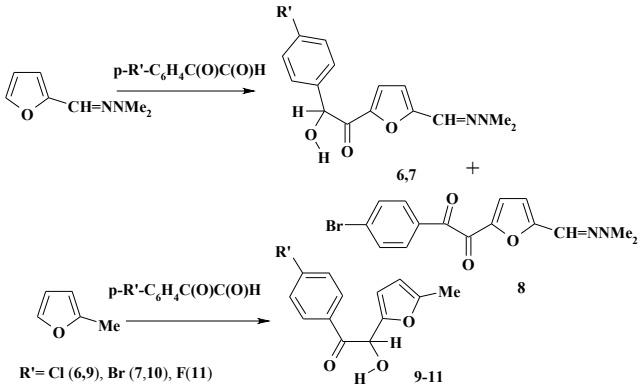
By the investigating the reaction of arylglyoxal with the 2-R-furanes, we have established that the 4-R'-phenylglyoxales (R'=OMe, Ph,) and 2-thienylglyoxal react in similar manner with *N,N*-dimethylhydrazone of 2-furancarbaldehyde and 2-methylfurane yielding α-benzoins, such as 2-furyl-1-arylethan-1-ones **3**-**5**, at room temperature (Scheme 3).



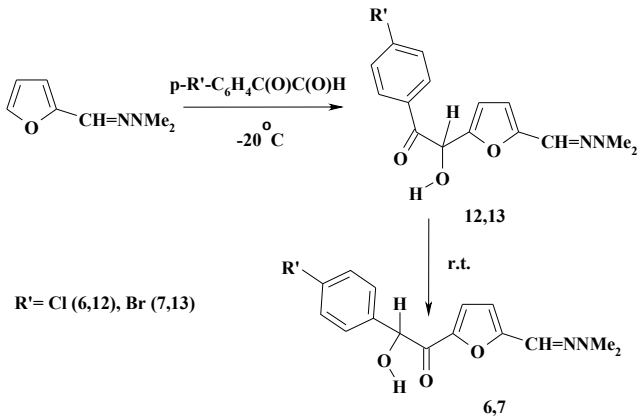
Scheme 3

However, it was found that 4-chlorophenylglyoxal and 4-bromophenylglyoxal react with *N,N*-dimethylhydrazone of 2-furancarbaldehyde yielding β-benzoins, such as 2-aryl-1-furylethan-1-ones **6**,**7** if this reaction carries out at room temperature (18 - 28°C) in dichloromethane or benzene solution. This reaction also yielded some 1,2-diketone **8** in the last case. Under the similar conditions 4-X-phenylglyoxals (X=Cl, Br, F) react with 2-methylfuran yielding only α-benzoins, 2-furyl-1-arylethan-1-ones **9**-**11** (Scheme 4).

This unusual formation of 2-aryl-1-furylethan-1-ones **6**,**7** from 4-chloro- and 4-bromophenylglyoxals must have arisen from the formation of α-benzoins, 2-furyl-1-arylethan-1-ones **12**,**13**, in the first stage. IN the second stage, α-benzoins **12**, **13** spontaneously isomerize into β-benzoins **6**, **7** at room temperature (Scheme 5).



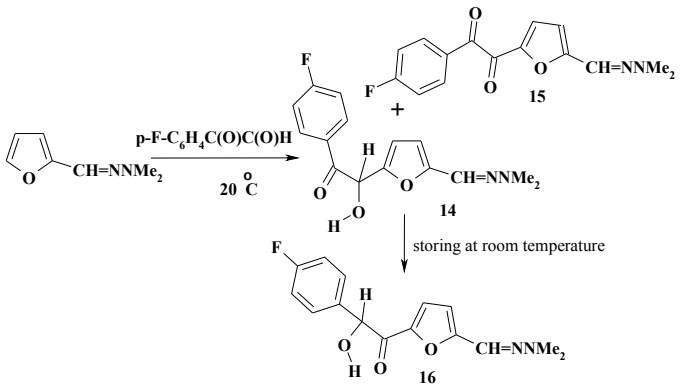
Scheme 4



Scheme 5.

Actually, it was found that at -23 - -20°C, 4-chloro- and 4-bromophenylglyoxals react with *N,N*-dimethylhydrazone of 2-furancarbaldehyde selectively yielding unstable 2-furyl-1-arylethan-1-ones **12**,**13**, which spontaneously isomerize in 2-aryl-1-furylethan-1-ones **6**,**7** at room temperature. The unstable α-benzoins **12**,**13** had been characterized by ^{1}H NMR and MS spectra.

4-Fluorophenylglyoxal reacts with *N,N*-dimethylhydrazone of 2-furancarbaldehyde at 20-40^{0}C range yielding mainly α-benzoin **14** (Scheme 6). At 40^{0}C some 1,2-diketone **15** is also formed.



Scheme 6

Table 1. The characteristic ^{1}H NMR chemical shifts of α-benzoins **3a**,**4**,**5**,**12-14** and β-benzoins **6**,**7**,**16** in $CDCl_3$

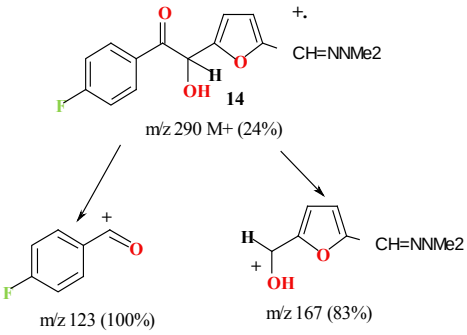
Compound		Resonance, σ, ppm				
Number	X in 4-X-C_6H_4	H_{Furane}		C_6H_4		Me_2N
		H^3_{Fur}	H^4_{Fur}	$H^{3,5}$	$H^{2,6}$	
α-**3a***	2-thienyl	6.31	6.47	-	-	2.83
α-**3a****	2-thienyl	6.39	6.49	-	-	2.86
α-**4**	OMe	6.27	6.35	6.91	7.98	2.96
α-**5**	Ph	6.31	6.35	7.65	8.05	2.95
α-**12****	Cl	6.35	6.42	7.58	8.01	2.85
α-**12**	Cl	6.29	6.34	7.42	7.93	2.96
α-**13**	Br	6.29	6.34	7.58	7.84	2.96
α-**14**	F	6.28	6.33	7.15	8.01	2.94
β-**6****	Cl	6.56	7.68	7.39	7.49	3.00
β-**7**	Br	6.46	7.20	7.35	7.45	3.08
β-**16**	F	6.47	7.19	7.42	7.02	3.08

*) in $(CD_3)_2CO$, **) in $(CD_3)_2SO$

Mixed α-benzoin **14** is more stable than mixed α-benzoins **12**,**13** and can exist for 1-2 months at 20°C. However, after that period α-benzoin **14** spontaneously isomerizes to β-benzoin **16** in solid state as well as in solution. On storing at 5-6°C for 4–5 months, α-benzoin **14** isomerizes into β-benzoin **16**.

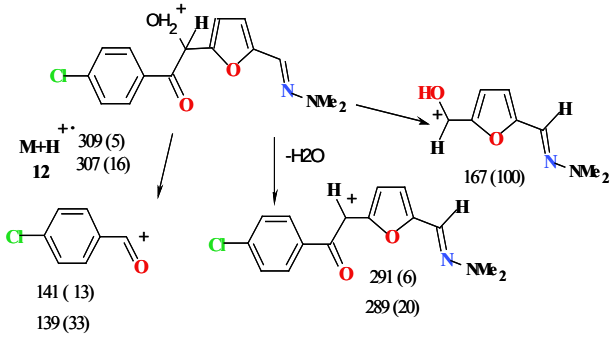
On the other hand, α-benzoins **1a**, **3a**,**b**, **4**,**5** and **9-11** remained unchanged after storing at 5°C for more than five years.

The structures of the compounds **3-16** were confirmed by data of ^{1}H NMR spectrometry and MS data. ^{1}H NMR spectra of α-benzoins **3a**,**4**,**5**,**12-14** and β-benzoins **6**,**7**,**16** are given in the Table 1.



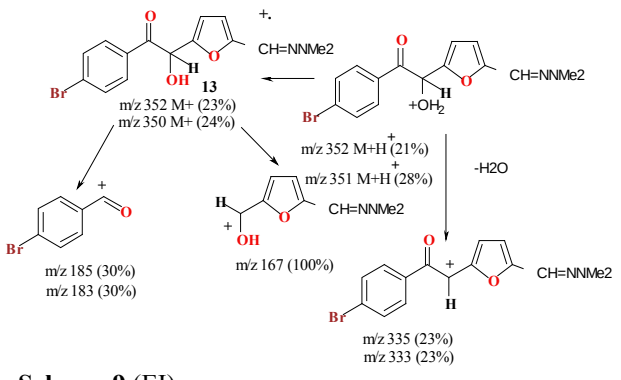
Scheme 7 (EI)

For β-benzoins **6**,**7**,**16** the differences of chemical shifts of H^4- and H^3 furan protons are substantial more, 0.72-1.12 ppm, whereas that for α-benzoins **3a**,**4**,**5**,**12-14**, is 0.04-0.16 ppm. That is caused by the possibility of the conjugation of Me_2N-moiety with carbonyl group in β-benzoins. In α-benzoins this possibility is absent. The other consequence of this conjugation is some low field shift of the resonance of Me_2N-group protons for β-benzoins **6**,**7**,**16**.



Scheme 8 (FAB)

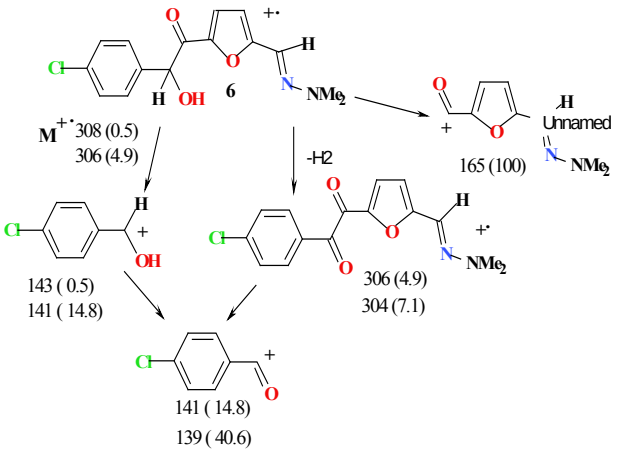
Conversely, the difference of the chemical shifts of $H^{2,6}$ and ^{3,5}H of *para*-substituted benzene ring for α-benzoins **4**,**5**,**12-14** is substantially more, 0.40-1.07 ppm (but for α-benzoin **13** – only 0.26 ppm), whereas that for β-benzoins **6**,**7** is only 0.10 ppm (excluding β-benzoin **16** – 0.40 ppm). This phenomenon is caused by the possibility of the conjugation of *para*-substituent with carbonyl group in α-benzoins. In β-benzoins this possibility is absent.



Scheme 9 (EI)

Mass spectra may also differentiate between α- and β-benzoins as was shown ealier for α-benzoin **1a** and β-benzoin **1b**[2]. For α-benzoins, in mass spectra the furan "benzylic' ions with m/z 167 and and *para*-substituted aroyl cations dominate (Scheme 7,8,9). Similar fragmentation was observed for unsubstituted α-benzoin **1a.**[2]

On the other hand, MS spectrum of β-benzoin **6** is dominated by the furoyl cation with m/z 165 (Scheme 10). Similar fragmentation was observed for unsubstituted β-benzoin **1b** [2].



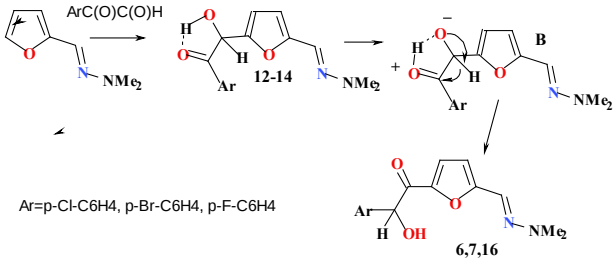
Scheme 10. (EI)

Only one case of the α→β benzoin isomerization by heating has been reported earlier[6]. Anisbenzoin isomerizes to benzanisoin by heating the former above its melting point (89^{0}C) or by distillation in vacuum[6]. But the spontaneous α→β benzoin isomerization at the room temperature was not reported.

Therefore, it may be supposed that this spontaneous α→β benzoins rearrangement of these mixed aryl(furyl)benzoins is caused by two reasons. First, the presence of a *para*-halogen substituent in the aryl moiety and secondly the presence of Me_2NN=CH-substituent at 5-position of furan ring. This spontaneous α→β benzoins rearrangement takes place in the absence of bases. The Me_2N-group of β-benzoins 6,7,16 cannot been regarded as base center because it presence in α-benzoins 1a, 3a,b, 4,5 and 9-11 does not cause their spontaneous α→β rearrangement.

An alternative mechanism for the spontaneous α→β benzoins isomerisation of α-benzoins which does not involve the formation of the intermediate anion A is depicted in Scheme 11.

Probably, intramolecular hydroxyl group protonation of the oxygen atom of carbonyl group increases the electron density on σ^*_{C-H} orbital. The H-atom becomes intramolecular nucleophilic center. The latter causes the synchronous 1,2-hydride shift as nucleophilic attack on carbonyl group finally yielding β-benzoins 6,7,16.



Scheme 11.

Thus, the new kind of α→β benzon isomerization was found. It is independent of base catalyst and takes place at temperature growth from -20°C to room temperature.

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