2-HYDROXY-1-ARYL-2-(INDOL-3'-YL)ETHANONES: SYNTHESIS, SPECTRAL CHARACTERISTICS, STRUCTURE AND THEIR REARRANGEMENT INTO 2-HYDROXY-2-ARYL-1-(INDOL-3'-YL)ETHANONES

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Keywords: Arylglyoxals, α- and ß-benzoins, indole, synthesis, 2-hydroxy-1-aryl-2-(indol-3-yl)ethanones, 2-hydroxy-2-aryl-1-(indol-3-yl)ethanones, spectral characteristics.

A convenient method of synthesis of 2-hydroxy-1-aryl-2-(indol-3-yl)ethanones and their isomerization to 2-hydroxy-2-aryl-1-(indol-3-yl)ethanones in the presence of triethylamine on heating or in the presence of EtONa at room temperature have been studied. The spectral tests of isomers structures are presented. The structures of 2-hydroxy-1-phenyl-2-(indol-3-yl)ethanone and 2-hydroxy-2-phenyl-1-(indol-3-yl)ethanone have been studied by XRD technique.

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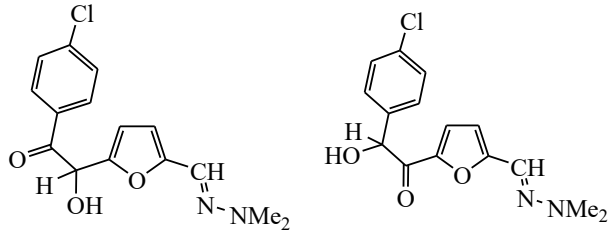
INTRODUCTION

Unsymmetrical arylbenzoins and aryl(heteryl)benzoins exist in two isomeric forms, α-benzoins and ß-benzoins,[1-8] for example aryl(furyl)benzoins **1a** and **1b** (Figure 1). [2,6-8] ß-Aryl(furyl)benzoin **1b** is more stable than **1a** due the possibility of the carbonyl group being in conjugation with π-donor furan ring.[2,7,8]

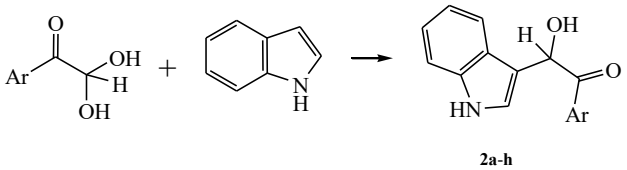


1a **1b**

Figure 1. Aryl(furyl)benzoins.

α-Aryl(furyl)benzoins can be easily obtained by arylglyoxals reaction with some furanes.[2,6-9] In many cases, they isomerize spontaneously into more stable ß-aryl(furyl)benzoins spontaneously,[7,8] however, in some cases, presence of a base and heating of reaction mixture are needed.[2,5-8]

It was first shown by Zhungietu[10,11] that phenylglyoxal hydrate and 2-thienylglyoxal hydrate react with indole in boiling benzene to give stable products α-ary(3-indolyl)benzoins **2a, b** (Scheme 1).[10,11] 4-Tolylglyoxal hydrate with indole forms α-benzoin **2c** in moderate yield.[11] Zhungietu had also reported that indole did not react with 4-methoxyphenylglyoxal in boiling benzene,[10] and with 4-chlorophenylglyoxal yields a 2:1 adduct, and not α-benzoin **2d**.[10] However, α-benzoins **2a-c** obtained by him have not been characterized by ^{1}HNMR and mass spectra. Later we have synthesized α-ary(3-indolyl)benzoins **2a,b,d,e** by interaction of indole with proper arylglyoxal hydrates or anhydrous arylglyoxals in benzene.[3,4,9,12] Their structure was confirmed by ^{1}HNMR and mass spectra data. Recently it was reported that indole reacted with arylglyoxals in 1,4-dioxane solution in the presence of $CuCl_2$ at room temperature forming α-ary(3-indolyl)benzoins **2a–h** in good yields.[13] Also recently Chinese chemists had reported that benzoic acid is an excellent catalyst of Friedel-Crafts alkylation of indole by arylglyoxals.[14] But earlier Iranian chemists had synthesized α-benzoins **2a,c-e** with excellent yields in aqueous media at room temperature in the absence of any acid catalyst,[15] this accords well with the earlier Zhungietu's reports.[10,11]



2a-h

Ar = Ph (**2a**), 2-thienyl (**2b**),4-MeC_6H_4 (**2c**), 4-ClC_6H_4 (**2d**), 4-BrC_6H_4 (**2e**), 4-FC_6H_4 (**2f**), 4-O_2NC_6H_4 (**2g**), 4-MeOC_6H_4 (**2h**)

Scheme 1. Synthesis of α-ary(3-indolyl)benzoins.

But the only reports about α→ß isomerization of α-aryl(indolyl)benzoins are our preliminary communications.[3,4] The development of efficient and general methodology for the synthesis of α-functionalized α-(indol-3-yl) ketones is highly desirable.[12] These compounds are possible precursors for the preparation of biologically

active molecules.[12] Therefore, we have investigated the synthesis of α-aryl(indolyl)benzoins and their isomerization to ß -aryl(indolyl)benzoins by the action of bases.

EXPERIMENTAL

^{1}H NMR spectra were recorded on VARIAN VXP-300, VARIAN JEMINI 400 and Bruker-Avance DRX 500 spectrometers (300, 400 and 500 MHz, respectively). ^{13}C NMR spectra were recorded on VARIAN VXP-300 spectrometer (75 MHz) and VARIAN JEMINI 400 spectrometer (100 MHz) with $(CD_3)_2SO$ as solvent and TMS as internal standard. Mass spectrum was recorded on VG 70-70EQ mass spectrometer in fast atom bombardment (FAB) mode and Kratos MS 890 mass spectrometer in electron impact (EI) mode (70 eV). Indole was sublimated under vacuum (3 Torr). The solvents were purified and dried according to standard procedures. Anhydrous arylglyoxals and 2-thienylglyoxal were obtained by rectification of proper arylglyoxal hydrates under vacuum 4 Torr.

Synthesis of α-aryl(indolyl)benzoins (2a,b)

A solution of 20 mmol anhydrous arylglyoxal and 20 mmol of indole in benzene (20 mL) was allowed to stand at 20 ºC for 72 h. The obtained precipitate was filtered off, washed by benzene (3 mL) and dried under vacuum (4 Torr.). The other α-aryl(indolyl)benzoins were synthesized in a similar manner.

2-Hydroxy-2-(indol-3'-yl)-1-phenylethanone (2a)

The compound was obtained as white crystals (66 %). m.p. 170-172°C (with decomp.) (lit. 170-172 °C,[10,11] 169-171 °C,[13] 174-177 °C[15]). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ = 5.549 (1H, d, ^3J = 5.6, CHOH), 6.379 (1H, d, ^3J = 5.6, CHOH), 6.991 (1H, t, ^3J = 7.4, H Ind), 7.065 (1H, t, ^3J = 7.4, H Ind), 7.327 (1H, d, ^3J = 8.0, H Ind), 7.355 (1H, d, ^3J = 2.4, C(2)H Ind), 7.399 (2H, t, ^3J = 7.6, C(3,5) H Ph), 7.507 (1H, t, ^3J = 7.6, C(4)H Ph), 7.645 (1H, d, ^3J = 7.6, H Ind), 8.013 (2H,d, ^3J = 7.2, C(2,6)H Ph), 11.075 (1H, s, NH).^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ = 69.5 (CHOH), 111.6, 113.3, 119.0, 119.2, 121.3, 124.9, 125.6, 128.47, 128.51, 132.9, 135.0, 136.3 (C Ph, Ind), 199.0 (C=O). MS (FAB) *m/z* 234 $[M+H-H_2O]^+$ (100), 206 $[M+H-H_2O-CO]^+$ (34), 146 (42), 118 (14), 105 Bz^+ (17). MS (FAB, KI) *m/z* 290 $[M+K]^+$ (100), 234 $[M+H-H_2O]^+$ (24), 206 $[M+H-H_2O-CO]^+$ (21), 146 (18), 105 Bz^+ (8). Anal. Calcd. for $C_{16}H_{13}NO_2$: N 5.57. Found: N 5.43.

Crystals of α-benzoin **2a** suitable for XRD study were grown from a solution in benzene at 10 ºC, monoclinic, $C_{16}H_{13}NO_2$ at 20°C ***a*** = 8.071(2), ***b*** = 8.513(3), ***c*** = 18.908(5) Å, β = 90.11(2)°, V = 1299.1(6) Å^3, M_r = 251.27, Z = 4, space group $P2_1/n$, d_{calc}= 1.285 g/cm^3, μ(MoKα) = 0.085 мм$^{-1}$, F(000) = 528. Cell parameters and intensities of 8638 reflections (2288 independent reflections, R_{int}=0.065) were measured using «Xcalibur 3» diffractometer (graphite-monochromated MoKα radiation, CCD detector, ***ω***-scan, 2 θ_{max}= 50°).

The structure was solved by direct method using SHELXTL program package.[16] Positions of hydrogen atoms were found from different synthesis of electronic density and refined using the riding model with U_{iso}=1.2U_{eqv} of non-hydrogen atom bonded with this hydrogen atom. Hydrogen atoms, taking place in hydrogen bonds formation, were refined in isotropic approximation. Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-hydrogen atoms to wR_2 = 0.154 for 2288 reflections (R_1 = 0.053 for 1647 reflections with F>4σ(F), S = 1.206). The final atomic coordinates, molecular geometry parameters, and crystallographic data of compound **2a** are deposited in the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2, 1EZ, UK (fax:+44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk) and is available on request quoting the deposition number CCDC 1864358).

2-Hydroxy-2-(indol-3'-yl)-1-(thien-2''-yl)ethanone (2b)

The compound was obtained as white crystals (75 %). m.p. 175-177 °C (with decomp.) (lit. 178-180 °C[10,11,13]). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ = 5.800 (1H, d, ^3J = 5.2, CHOH), 6.091 (1H, d, ^3J = 5.2, CHOH), 6.976 (1H, t•d, ^3J = 7.4, ^4J = 1.2, H Ind), 7.061 (1H, , t•d, ^3J = 7.5, ^4J = 1.2, H Ind), 7.134 (1H, d•d, ^3J = 4.8,^3J = 4.0, H(4) Th), 7.330 (1H, d, ^3J = 8.0, H Ind), 7.411 (1H, d,^3J = 2.8, C(2)H Ind), 7.643 (1H, d, ^3J = 7.6, H Ind), 7.9055 (1H, d•d, ^3J = 4.8,^4J = 1.2, H Th), 8.0035 (1H, d•d, ^3J = 4.0,^4J = 1.2, H Th), 11.085 (1H, s, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ =70.8 (CHOH), 111.6, 113.6, 119.0 119.4, 121.3, 124.8, 125.6, 128.4, 134.6, 136.3, 140.83 (C Th, Ind), 192.3 (C=O). MS (EI) *m/z* 257 M^+ (1.05), 256 (0.3), 255 (3.2), 241 (15), 240 (14), 239 (78), 212 (20), 211 (49), 210 (67), 146 (23), 145 (15), 144 (100), 130 (75),128 (16), 116 (15), 111 (87), 101 (30), 89 (17). MS (FAB) *m/z* 240 $[M+H-H_2O]^+$ (100), 212 $[M+H-H_2O-CO]^+$ (33), 146 (87), 111 $ThC^+=O$ (23). MS (FAB, KI) *m/z* 296 $[M+K]^+$ (67), 240 $[M+H-H_2O]^+$ (50), 146 (100), 111 (28). Anal. Calcd. for $C_{14}H_{11}NO_2S$: N 5.44. Found: N 5.31.

Benzoins **2a**,**b** also were identified by ^{1}H NMR spectra with the samplessynthesized by known method[10,11].

2-Hydroxy-2-(indol-3'-yl)-1-(thien-2''-yl)ethanone (2b)

The mixture of 2-thienylglyoxal hydrate (199 mg, 1.257 mmol), indole (147 mg, 1.257 mmol) and AcOH (7 mL) was stirred at 20 ºC for 23 h. The obtained precipitate was filtered off, washed by cold water (10 mL) and dried under vacuum (4 Torr) giving α-benzoin **2b** as colorless crystals (191 mg, 59 %), identified by its ^{1}H NMR spectrum.

2-Hydroxy-2-(indol-3'-yl)-1-(4''-methylphenyl)ethanone (2c)

4-Methylphenylglyoxal hydrate (221 mg, 1.327 mmol) was dissolved in boiling benzene (8 mL), then a solution of indole (178 mg, 1.518 mmol) was added, the reaction solution was boiled for 30 min, kept at 15 ºC for 19 h, then it was evaporated under vacuum (25 Torr) to a volume of 4 mL. To obtained residue, it was kept at 4 ºC for 2 days. The obtained precipitate was filtered off, washed by CCl_4 (0.5 mL) and dried under vacuum (4 Torr) giving 2-hydroxy-2-(indol-3'-yl)-1-(4''-methylphenyl)ethenone (**2c,** 128 mg, 36 %), as white crystals, m.p.146-147°C (benzene) (with

decomp.), (lit. 144-146°C,[13] 154-158°C[15]). ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ = 2.270 (3H, s, Me), 5.479 (1H, d, ^3J = 5.7, CHOH), 6.332 (1H, d, ^3J = 5.7, CHOH), 6.968 (1H, td, ^3J = 7.4, ^4J = 1.2, H Ind), 7.051 (1H, td, ^3J = 7.4,^4J = 1.2, H Ind),7.192 (2H, d, ^3J = 8.1, C(3,5)H C_6H_4Me), 7.324 (1H, d, ^3J = 7.5, H Ind), 7.332 (1H, d,^3J = 2.7 C(2)H Ind),7.616 (1H, d, ^3J = 7.5, H Ind), 7.906 (2H, d, ^3J = 8.1, C(2,6)H C_6H_4Me), 11.055 (1H, s, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ =21.1 (Me), 69.3 (CHOH), 111.6, 113.5, 118.9, 119.2, 121.3, 124.9, 125.6, 129.0, 132.4, 136.3, 143.3 (C Ind, C_6H_4), 198.6 (C=O). MS (FAB) *m/z* 248 $[M+H–H_2O]^+$ (100), 220 $[M+H–H_2O\text{-}CO]^+$ (71), 146 (20), 119 $MeC_6H_4C(O)^+$ (60), 118 (14). MS (FAB, KI) *m/z* 304 $[M+K]^+$ (100),248 $[M+H–H_2O]^+$ (34), 220 $[M+H–H_2O\text{-}CO]^+$ (61), 146 (20), 119 $MeC_6H_4C(O)^+$ (83), 118 (27).

To the filtrate CCl_4 (1 mL) was added, the obtained precipitate was filtered off, additionally yielding α-benzoin **2c** (30 mg, 8 %).

The compound was prepared by another method also. The solution of 4-methylphenylglyoxal hydrate (276 mg, 1.659 mmol) and indole (204 mg, 1.741 mmol) in benzene (5 mL) was boiled at 100 ºC for 1h in sealed tube, kept at 18 ºC for 23 h, then it was evaporated under vacuum (25 Torr) to 3 mL. To obtained residue, it was kept at 4 ºC for 2 days, the obtained precipitate was filtered off, washed with CCl_4 (1 mL) and dried under vacuum (4 Torr), giving 2-hydroxy-2-(indol-3'-yl)-1-(4''-methylphenyl)ethanone **2c** (276 mg, 63 %), as white crystals, m.p.146-148°C (benzene) (with decomp.)

2-Hydroxy-2-(indol-3'-yl)-1-(4''-chlorophenyl)ethanone (2d)

The solution of 4-chlorophenylglyoxal hydrate (2.426 g, 13 mmol) and indole (1.524 g, 13 mmol) in benzene (17 mL) was boiled for 2 h under nitrogen, then it was kept at 20 ºC for 2 day. The obtained precipitate was filtered off, washed by CH_2Cl_2 (6 mL), dried under vacuum (2 Torr) to give **2d** as colorless crystals (2.226 g, 60 %), m.p. 145-146 ºC (benzene) (with. decomp.), (lit. 134-138 °C,[13] 144-146 °C).[15] ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ = 5.619 (1H, d, ^3J = 5.5, CHOH), 6.314 (1H, d, ^3J = 5.5, CHOH), 6.972 (1H, t, ^3J = 8.0, H Ind), 7.052 (1H, t, ^3J = 8.0, H Ind), 7.312 (1H, d, ^3J = 8.0, H Ind), 7.334 (1H, d,^3J = 2.0, C(2)H Ind), 7.464 (2H, d, ^3J = 9.0, H(3,5) C_6H_4Cl), 7.592 (1H, d, ^3J = 8.0 H Ind), 8.007 (2H,d, ^3J = 9.0, H(2,6) C_6H_4Cl), 11.077 (1H, s, NH). ^{13}C NMR (100 MHz $(CD_3)_2SO$) δ = 69.69 (CHOH); 111.53, 112.88 (C(2), C(3) Ind), 118.89, 119.07, 121.25 (C(5), C(6), C(4) Ind), 124.81 (C(7) Ind), 125.43 (C(1) C_6H_4Cl), 128.46 (C(3,5) C_6H_4Cl), 130.26 (C(2,6) C_6H_4Cl), 133.49, 136.19 (C(8), C(9) Ind), 137.68 (C(4) C_6H_4Cl), 197.83 (C=O). MS (FAB) *m/z* 270 $[M+H–H_2O]^+$ (34), 268 $[M+H–H_2O]^+$ (82), 242 $[M+H–H_2O\text{-}CO]^+$ (17), 240 $[M+H–H_2O\text{-}CO]^+$ (54), 145 (100). MS (FAB, KI) *m/z* 326 $[M+K]^+$ (15),324 $[M+K]^+$ (38), 270 $[M+H–H_2O]^+$ (17),268 $[M+H–H_2O]^+$ (47), 242 $[M+H–H_2O\text{-}CO]^+$ (6), 240 $[M+H–H_2O\text{-}CO]^+$ (17), 146 (100). Anal. Calcd. for $C_{16}H_{12}ClNO_2$: C 67.26, H 4.23, N 4.90. Found: C 67.42, H 4.27, N 4.72.

2-Hydroxy-2-(indol-3'-yl)-1-(4''-chlorophenyl)ethanone (2d)

The solution of 4-chlorophenylglyoxal hydrate (147 mg, 0.786 mmol) and indole (93 mg, 0.790 mmol) in AcOH (5 mL) was kept at 19 ºC for 1 h, then the solvent was evaporated under vacuum (4 Torr). The residue was extracted with water (10 mL) at 4 ºC. the obtained precipitate was filtered off, washed by water (5 mL), dried under vacuum (4 Torr), giving α-benzoin **2d** as white crystals (217 mg, 96 %), identified by its ^{1}H NMR spectrum.

2-Hydroxy-2-(indol-3'-yl)-1-(4''-bromophenyl)ethanone (2e)

The solution of 4-bromophenylglyoxal hydrate (808 mg, 3.5 mmol) and indole (410 mg, 3.5 mmol) in benzene (40 mL) was boiled for 2 h, then it was kept at 30 ºC for 3 day. The obtained reaction solution was evaporated to 80 % under vacuum, the obtained precipitate was filtered off, washed by cold benzene, giving 2-hydroxy-2-(indol-3'-yl)-1-(4''-bromophenyl)ethanone **2e** (673 mg, 58 %), as white crystals, m.p. 159-160ºC (with. decomp., benzene) (lit. 159-161°C[15]). ^{1}H NMR(400 MHz, $(CD_3)_2SO$) δ = 5.614 (1H, d, ^3J = 5.2, CHOH), 6.3055 (1H, d, ^3J = 5.2 CHOH), 6.971 (1H, t, ^3J = 7.2, H Ind), 7.054 (1H, t, ^3J = 7.2, H Ind), 7.314 (1H, d, ^3J = 8.8, H Ind), 7.3285(2H, d,^3J = 2.8, C(2)H), 7.589 (1H, d, ^3J = 8.0, H Ind), 7.6085 (2H, d, ^3J = 8.4, C(3,5)H C_6H_4Br), 7.9265 (2H, d, ^3J = 8.4, C(2,6)H C_6H_4Br), 11.073 (1H, s, NH). ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ = 69.7 (CHOH), 111.6, 113.0, 119.0, 119.2, 121.3, 124.9, 125.5, 127.0, 128.3, 130.5, 130.6, 131.5, 134.0 (C Ar, Ind), 136.3 (C-Br), 198.2 (C=O). MS (FAB) *m/z* 314 $[M+H–H_2O]^+$ (35), 312 $[M+H–H_2O]^+$ (31), 146 (100). MS (FAB, KI) *m/z* 370 $[M+K]^+$ (18),368 $[M+K]^+$ (20), 314 $[M+H–H_2O]^+$ (33),312 $[M+H–H_2O]^+$ (34), 146 (100). Anal. Calcd. for $C_{16}H_{12}BrNO_2$: C 58.20, H 3.66, N 4.24. Found: C 58.41, H 3.72, N 4.32.

2-Hydroxy-2-(indol-3'-yl)-1-(4''-bromophenyl)ethanone (2e)

The mixture of 4-bromophenylglyoxal hydrate (336 mg, 1.452 mmol), indole (172 mg, 1.471 mmol) and AcOH (9 mL) was stirred at 17 ºC for 50 min, the obtained solution was evaporated under vacuum (4 Torr) and the residue was extracted by water (10 mL) at 4 ºC. The obtained precipitate was filtered off, washed by water (8 mL) and dried under vacuum (4 Torr) to yield α-benzoin **2e** as white crystals (412 mg, 86 %), identified by its ^{1}H NMR spectrum.

2-Hydroxy-2-(indol-3'-yl)-1-(4''-fluorophenyl)ethanone (2f)

4-Fluorophenylglyoxal hydrate (110 mg, 0.648 mmol) was converted in anhydrous fluorophenylglyoxal by heating to 130 ºC under vacuum (10 Torr), then it was dissolved in benzene (5 mL) and indole (76 mg, 0.648 mmol) was added. The reaction solution was kept at 20 ºC for 88 h and then the solvent was evaporated under vacuum (25 Torr). The obtained residue was dissolved in CCl_4 (4 mL), the solution was filtered, and hexane (5 mL) was added. The obtained precipitate was filtered off, washed with hexane (5 mL) and dried under vacuum (4 Torr) to give 2-hydroxy-2-(indol-3'-yl)-1-(4''-fluorophenyl)ethanone **2f** (89 mg, 51 %), as white crystals, m.p.**2f•**PhH 116-117ºC (with. decomp., benzene). ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ = 5.618 (1H, d, ^3J = 5.4, CHOH), 6.345 (1H, d, ^3J = 5.4, CHOH), 6.987 (1H, t, ^3J = 7.0, H Ind), 7.066 (1H, t, ^3J = 7.0, H Ind), 7.227 (2H, dd, ^3J = 8.7, $^{H\text{-}F}J$ = 9.0, C(3,5)H C_6H_4F), 7.334 (1H, d, ^3J = 8.1, H Ind),), 7.3635 (1H, d,^3J = 2.1, C(2)H Ind),7.6305(1H, d, ^3J = 8.1, H Ind), 8.104 (2H, dd, ^3J = 8.7,$^{H\text{-}F}J$ = 5.7, C(2,6)H C_6H_4F), 11.090 (1H, s, NH). ^{13}C NMR (75 MHz$(CD_3)_2SO$)

δ = 66.7 (CHOH), 111.6, 113.2, 115.4, 119.0, 119.2, 121.3, `124.9, 125.6 (C Ind, C_6H_4F),131.5 (d, *J* = 9.0, C(3,5)C_6H_4F), 136.3 (C(1) C_6H_4F), 164.7 5 (d, *J* = 249.0, C(4)C_6H_4F), 197.6 (C=O). MS (FAB) *m/z* 252 $[M+H–H_2O]^+$ (93), 224 $[M+H–H_2O\text{-}CO]^+$ (100), 146 (59), 123 $FC_6H_4C(O)^+$ (51), 118 (46). MS (FAB, KI) *m/z* 308 $[M+K]^+$ (100),252 $[M+H–H_2O]^+$ (53), 224 $[M+H–H_2O\text{-}CO]^+$ (69), 146 (51), 123 $FC_6H_4C(O)^+$ (61), 118 (45).

2-Hydroxy-2-(indol-3'-yl)-1-(4''-nitrophenyl)ethanone (2g)

The solution of 4-nitrophenylglyoxal hydrate (146 mg, 0.740 mmol) and indole (87.3 mg, 0.745 mmol) in AcOH (5 mL) was kept at 19ºC for 1 h, then AcOH was evaporated under vacuum (4 Torr) at 19 ºC. The obtained residue was washed by water (10 mL) at 5ºC for 1 h. The obtained precipitate was filtered off, washed by water (5 mL) and dried under vacuum (4 Torr) to yield 2-hydroxy-2-(indol-3'-yl)-1-(4''-nitrophenyl)ethanone **2g** (215 mg, 98 %), as yellow crystals, **2g**•benzene, m.p. 126-127°C (benzene).^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ = 5.798 (1H, d, ^3J = 5.2, CHOH), 6.394 (1H, d, ^3J = 5.2, CHOH), 6.992 (1H, t, ^3J = 7.4, H Ind), 7.064 (1H, t, ^3J = 7.4, H Ind),7.320 (1H, d, ^3J = 8.0, H Ind), 7.369 (1H, d,^3J = 2.4 C(2)H Ind),7.604 (1H, d, ^3J = 8.0, H Ind), 8.193 – 8.228 (4H, m as 8.21 s, H(2,3,5,6) $C_6H_4NO_2$), 11.116 (1H, s, NH). ^{13}C NMR (75 MHz$(CD_3)_2SO$) δ = 70.3(CHOH), 111.7, 112.3, 119.1, 121.5, 123.6, 125.2, 125.5, 128.4, 129.8, 136.4, 140.1, 149.6 (C Ar, Ind), 198.2 (C=O). MS (FAB) *m/z* 279 $[M+H–H_2O]^+$ (100), 146 (75).

The compound was prepared by another process also. Mixture of 4-nitrophenylglyoxal hydrate (127 mg, 0.645 mmol) and water (15 mL) was stirred at 30 ºC for 1 h, then indole (72 mg, 0.614 mmol) was added. The reaction mixture was stirred at 30 ºC for 3 h, the aqueous phase was separated from resin, was kept at 30 ºC for 20 h, at 10 ºC for 2 h, then the yellow precipitate was filtered off, washed by cold water (2 mL) and dried under vacuum (2 Torr) to yield **2g** (56 mg, 31 %).

2-Hydroxy-2-(indol-3'-yl)-1-(4''-methoxyphenyl)ethanone (2h)

The solution of 4-methoxyphenylglyoxal hydrate (198 mg, 1.086 mmol) and indole (141 mg, 1.196 mmol) in toluene (6 mL) was boiled for 1h, was then kept at 15 ºC for 19 h. It was then it was evaporated under vacuum (25 Torr) to 2 mL and CCl_4 (5 mL) was added. The obtained mixture was kept at 4 ºC for 24 h, the formed precipitate was filtered off, washed by cold CCl_4 (3 mL), dried under vacuum (4 Torr) to give **2h** (160 mg, 52 %), as white-pink crystals (unstable at storing). ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ = 3.754 (3H, s, Me), 5.437 (1H, d, ^3J = 5.7, CHOH), 6.292 (1H, d, ^3J = 5.7, CHOH), 6.915 (2H, d, ^3J = 8.7, C(3,5)H C_6H_4OMe), 6.966 (1H, td, ^3J = 7.5, ^4J = 1.2, H Ind), 7.050 (1H, td, ^3J = 7.4,^4J = 1.5, H Ind),7.312 (1H, d, ^3J = 7.8, H Ind), 7.333 (1H, d,^3J = 2.7 C(2)H Ind),7.612 (1H, d, ^3J = 7.8, H Ind), 7.997 (2H, d, ^3J = 8.7, C(2,6)H C_6H_4OMe), 11.049 (1H, d,^3J = 2.1, NH). ^{13}C NMR (75 MHz$(CD_3)_2SO$) δ = 55.4 (MeO), 69.2(CHOH), 111.6 (C Ind), 113.7 (C(3,5) C_6H_4), 113.8, 118.9, 119.3, 121.3, 124.7, 125.6, 127.5 (C Ind), 130.9 (C(2,6) C_6H_4), 136.3 (C(1) C_6H_4), 162.9 (C(4) C_6H_4), 197.5 (C=O). MS (FAB) *m/z* 264 $[M+H–H_2O]^+$ (100), 236 $[M+H–H_2O\text{-}CO]^+$ (72), 146 (58), 135 $MeOC_6H_4C(O)^+$ (58), 118 (7). MS (FAB, KI) *m/z* 320 $[M+K]^+$ (100),264 $[M+H–H_2O]^+$ (15), 236 $[M+H–H_2O\text{-}CO]^+$ (35), 146 (17), 135 $MeOC_6H_4C(O)^+$ (37), 118 (13).

2-Hydroxy-1-(indol-3'-yl)-2-phenylethanone (3a)

The solution of compound **2a** (554 mg, 2.205 mmol) and Et_3N (363 mg, 3.585 mmol) in EtOH (5 mL) was boiled for 5 h under nitrogen, kept at 20ºC during 20 h and then it was evaporated under vacuum (15 Torr). The residue was washed by Et_2O (7 mL), recrystallized from i-PrOH (5 mL), the obtained crystal were filtered off and dried under vacuum (3 Torr), to give **3a** (310 mg, 56 %), colorless crystals, m.p. 167-168ºC (benzene). ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ = 5.791 (1H, d, ^3J = 5.5, CHOH), 5.909 (1H, d, ^3J = 5.5, CHOH), 7.152–7.221 (3H, C(4)H Ph and C(5,6)H Ind), 7.296 (2H, t, ^3J = 7.5, C(3,5)H Ph), 7.451 (1H, d, ^3J = 8.0, H Ind), 7.528 (2H, d, ^3J = 7.5, C(2,6)H Ph), 8.179 (1H, d, ^3J = 8.0, H Ind), 8.544 (1H, s, C(2)H Ind), 11.984 (1H, s, NH).^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ = 76.24 (CHOH); 112.10, 113.06 (C(2), C(3) Ind), 121.27, 121.86, 122.91 (C(5), C(6), C(4) Ind), 125.88 (C(7) Ind), 126.74 (C(3,5) Ph),127.18 (C(4) Ph), 128.08 (C(2,6) Ph), 134.70, 136.18 (C(8), C(9) Ind), 141.45 (C(1) Ph), 194.34 (C=O). MS (FAB) *m/z* 252 $[M+H]^+$ (63), 236 (6), 206 $[M+H–H_2O\text{-}CO]^+$ (100), 145 (48), 91 (29). Anal. Calcd. for $C_{16}H_{13}NO_2$: N 5.57. Found: N 5.64.

Crystals of ß-benzoin **3a** suitable for XRD study were grown from a solution in benzene at 10 ºC, monoclinic, $C_{16}H_{13}NO_2$, at 20°C ***a*** = 8.144(1), ***b*** = 7.5178(7(3), ***c*** = 21.738(3) Å, β = 99.17(1)°, V = 1313.8(3) Å^3, M_r = 251.27, Z = 4, space group $P2_1/n$, d_{calc}= 1.270 g/cm^3, μ(MoKα) = 0.084 мм$^{-1}$, F(000) = 528. Cell parameters and intensities of 13188 reflections (3835 independent reflections, R_{int}=0.081) were measured using «Xcalibur 3» diffractometer» (graphite-monochromated MoKα radiation, CCD detector, ***ω***-scan,$2\theta_{max}$= 60°). The structure was solved by direct method using SHELXTL program package.[16] Positions of hydrogen atoms were found from different synthesis of electronic density and refined using the riding model with U_{iso}=1.2U_{eqv} of non-hydrogen atom bonded with this hydrogen atom. Hydrogen atoms, taking place in hydrogen bonds formation, were refined in isotropic approximation. Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-hydrogen atoms to wR_2 = 0.135 for 3745 reflections (R_1 = 0.052 for 1882 reflectionswith F>4σ(F), S = 0.884). The final atomic coordinates, molecular geometry parameters, and crystallographic data of compound **3a** were deposited in the Cambridge Crystallographic Data Center, 12 Union Road, CB2, 1EZ, UK (fax:+44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk and is available on request quoting the deposition number CCDC 1864359).

2-Hydroxy-1-(indol-3'-yl)-2-(thien-2''-yl)ethanone (3b)

The solution of compound **2b** (611 mg, 2.375 mmol) and Et_3N (363 mg, 3.585 mmol) in i-PrOH (8 mL) in sealed tube was heated at 100ºC for 5 h, then it was concentrated under vacuum (20 Torr) to a volume of 5 mL. The obtained precipitated was filtered off, washed by CH_2Cl_2 (4 mL) and dried under vacuum (4 Torr), giving 2-hydroxy-1-(indol-3'-yl)-2-(thien-2''-yl)ethanone **3b** (318 mg, 52 %), colorless

crystals, m.p. 162–163ºC (with. decomp.).^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ = 6.058 (1H, d, ^3J = 5.5, CHOH), 6.128 (1H, d, ^3J = 5.5, CHOH), 6.928 (1H, t, ^3J = 4.0, C(4)H Th), 7.110 (1H, d, ^3J = 3.0, H Th), 7.189 (1H, t, ^3J = 7.0, H Ind), 7.219 (1H, t, ^3J = 7.0, H Ind), 7.391 (1H, d, ^3J = 5.0, H Th), 7.475 (1H, d, ^3J = 7.0, H Ind),8.193 (1H, d, ^3J = 7.0, H Ind), 8.563 (1H, s, C(2)H Ind), 12.042 (1H, s, NH).^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ = 72.4 (CHOH), 112.3, 112.8, 121.4, 122.1, 123.1, 125.2, 125.5, 126.0, 126.6, 134.9, 136.4, 145.2 (C Ar, Ind), 193.1 (C=O). MS (EI) *m/z* 257 M^+ (0.76), 256 (2.43), 255 (9.82), 239 (22.7), 210 (26.3), 145 (49.6), 144 (100), 116 (53.3). MS (FAB) *m/z* 258 $[M+H]^+$ (34), 240 $[M+H–H_2O]^+$ (19), 212 $[M+H–H_2O\text{-}CO]^+$ (55), 144 (100). Anal. Calcd. for $C_{14}H_{11}NO_2S$: N 5.44, S 12.46. Found: N 5.25, S 12.53.

2-Hydroxy-1-(indol-3'-yl)-2-(4''-chlorophenyl)ethanone (3d)

The solution of compound **2d** (576 mg, 2.226 mmol) and Et_3N (363 mg, 3.585 mmol) in i-PrOH (7 mL) in a sealed tube was heated at 82 ºC for 4 h, then it was evaporated under vacuum (12 Torr), the residue was recrystallized from i-PrOH (4 mL), the obtained crystals were filtered off, washed by cold i-PrOH (2 mL) and dried under vacuum (2 Torr), giving **3d** (414 mg, 72 %), colorless crystals, m.p. 165- 167ºC (with decomp., benzene**)**. ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ = 5.8315 (1H, d, ^3J = 5.1, CHOH), 6.0655 (1H, d, ^3J = 5.1, CHOH), 7.151–7.234 (2H, m,H Ind), 7.3675 (2H, d,^3J = 7.5, C(2,6)H C_6H_4Cl), 7.472 (1H, d,^3J = 7.2, H Ind), 7.5625 (2H, d,^3J = 7.5, C(3,5)H C_6H_4Cl), 8.194 (1H, d,^3J = 7.2, H Ind), 8.586 (1H, s, C(2)H Ind), 12.044 (1H, s, NH).^{13}C NMR (75 MHz $(CD_3)_2SO$) δ = 75.5 (CHOH), 112.2, 113.1, 121.3, 122.0, 123.1, 126.0 (C Ind), 128.2, 128.6 (C(2,3,5,6) C_6H_4Cl), 131.9, 134.9 (C Ind), 136.3 (C(1) C_6H_4Cl), 140.5 (C(4) C_6H_4Cl), 194.1 (C=O). MS (EI) *m/z*) 287 M^+ (1.64), 285M^+ (3.49), 283 (1.70), 271 (0.63), 269 (2.11), 144 (100), 116 (29.2). MS (FAB) *m/z* 288 $[M+H]^+$ (9), 286 $[M+H]^+$ (34), 242 $[M+H–H_2O\text{-}CO]^+$ (23), 244 $[M+H–H_2O\text{-}CO]^+$ (75), 145 (100). Anal. Calcd. for $C_{16}H_{12}ClNO_2$: N 4.90. Found: N 4.94.

This compound **3d** was prepared by another method also. α-Benzoin **2d** (113 mg, 0.395 mmol) was dissolved in freshly obtained solution of Na (20 mg, 0.870 g-atom) in EtOH (5 mL), the reaction mixture was kept at 16 ºC for 20 min, then AcOH (57 mg, 0.957 mmol) was added, the reaction mixture was evaporated under vacuum (10 Torr). The solid residue (**C**) was extracted by CH_2Cl_2 (12 mL), CH_2Cl_2-extract was evaporated under vacuum(10 Torr), the residue was washed by water (10 mL) and the solid residue was dried under vacuum (2 Torr), giving ß-benzoin **3d** (49 mg, 43 %), which was identified by ^{1}H NMR spectrum.

Solid residue of CH_2Cl_2-extraction (**C**) was washed by water (10 mL), the unsolved white precipitate was dried under vacuum (2 Torr), additionally giving ß-benzoin **3d** (16 mg, 14 %).

2-Hydroxy-1-(indol-3'-yl)-2-(4''-bromophenyl)ethanone (3e)

The solution of compound **2e** (270 mg, 0.817 mmol) and Et_3N (132 mg, 1.307 mmol) in i-PrOH (5 mL) in sealed tube was heated at 82 ºC for 4 h, kept at 20 ºC for 24 h and then it was evaporated under vacuum (12 Torr). The residue was extracted with boiling CH_2Cl_2 (3 mL), cooled, the obtained precipitate was filtered off, then it was extracted with boiling CH_2Cl_2 (2 mL), cooled, the obtained precipitate was washed by CH_2Cl_2 (1 mL) and dried under vacuum, giving **3e** (69 mg, 26 %), white crystals, m.p. 175-177ºC (with decomp.). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ = 5.789 (1H, d, ^3J = 5.6, CHOH), 6.038 (1H, d, ^3J = 5.6, CHOH), 7.186 (2H, quint•d, ^3J = 7.4, ^4J = 1.6, C(5,6)H Ind), 7.439–7.473 (1H, m, H Ind), 7.475–7.520 (4H, m, C_6H_4Br), 8.1595 (1H, d•d, ^3J = 6.8, ^4J = 1.6, H Ind), 8.564 (1H, d,^3J = 6.8, C(2)H Ind), 12.025 (1H, s, NH).^{13}C NMR (75 MHz $(CD_3)_2SO$) δ = 75.5 (CHOH), 112.1, 113.1, 120.5, 121.2, 121.9, 123.0, 125.9, 128.9, 131.0, 134.8, 136.2 (C Ar,Ind), 140.9 (C-Br), 194.0 (C=O). MS (FAB) *m/z* 332 $[M+H]^+$ (22), 330 $[M+H]^+$ (22), 286 $[M+H–H_2O\text{-}CO]^+$ (31), 284 $[M+H–H_2O\text{-}CO]^+$ (30), 144 (100). Anal. Calcd. for $C_{16}H_{12}BrNO_2$: N 4.24. Found: N 4.14.

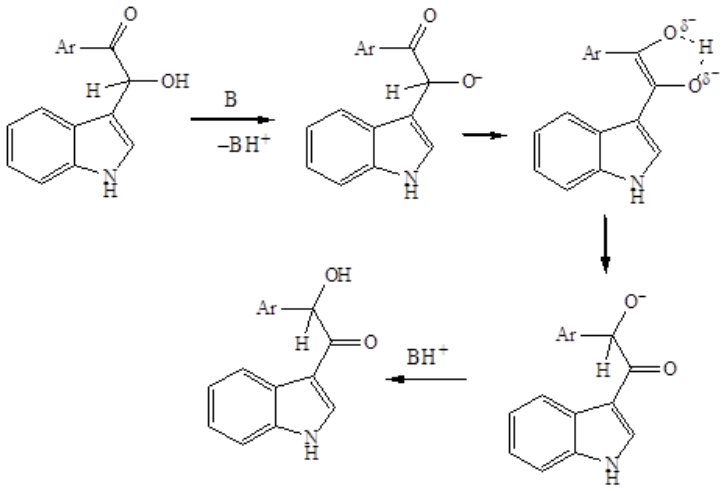
This compound **3e** was prepared by another method also. Compound **2e** (105 mg, 0.371 mmol) was dissolved in the freshly obtained solution of EtONa [obtained by sodium (25.8 mg, 1.122 mmol) dissolved in EtOH (4 mL)], the reaction mixture kept at 8 ºC for 2 h and then a solution of AcOH (80 mg, 1.333 mmol) in EtOH (1 mL) was added. The solvent was evaporated under vacuum (5 Torr). The residue was extracted CH_2Cl_2 (16 mL), the CH_2Cl_2 extract was concentrated under vacuum to 6 mL, the obtained white precipitate was filtered off and dried under vacuum, giving **3e** (33 mg, 32 %), white crystals, which was identified by its ^{1}H NMR spectrum.

RESULTS AND DISCUSSION

We had synthesized known[10,11] α-phenyl(indol-3-yl)benzoin **2a** and α-(thien-2-yl)l(indol-3'-yl)benzoin **2b** with moderate yields (Scheme 1) by reaction of indole and appropriate arylglyoxals in benzene at room temperature or in acetic acid solution at room temperatures. α-Aryl(indolyl)benzoin **2c** has been synthesized with moderate yield in boiling benzene accordingly Zhungietu's methodic.[10,11] But, if this reaction was carried out at 100ºC in sealed tube, the yield of α-benzoin **2c** was higher. α-Aryl(indolyl)benzoins **2d**,**e** had been synthesized as by known method,[4,9] in acetic acid solution at room temperature by keeping the reagents for 1 h.

α-(4-Fluorophenyl)(indolyl)benzoin **2f** was obtained by an interaction of 4-fluorophenylglyoxal with indole in benzene at room temperature. α-(4-Nitrophenyl)(indolyl)benzoin **2g** was obtained by an interaction of 4-nitrophenylglyoxal hydrate with indole in acetic acid at 19 ºC for not more than 1 h. Increasing the interaction with acetic solution increases yields of by products. α-Benzoin **2g** also was synthesized in aqueous media, as reported earlier.[15]

α-(4-Methoxyphenyl)(indolyl)benzoin **2h** was synthesized with moderate yield by an interaction of 4-methoxyphenylglyoxal hydrate with indole in boiling toluene. In all cases, presence of copper(II) chloride[13] or benzoic acid[14] were not necessary. This reaction occurs with good yields in absence of any catalyst in organic solvent and with excellent yield in aqueous media.[15]



Scheme 2. Isomerization of 2-hydroxy-1-aryl-2-(indol-3'-yl)ethanones) into ß-aryl(indolyl)benzoins.

Structure of α-aryl(indolyl)benzoins **2a**–**h** was consistent with by data of ^{1}H and ^{13}C NMR spectra, and mass spectra (see further).

We have found that all α-aryl(indolyl)benzoins **2a**,**b**,**d**,**e** (2-hydroxy-1-aryl-2-(indol-3'-yl)ethanones) readily isomerize into ß-aryl(indolyl)benzoins **3a**,**b**,**d**,**e** (2-hydroxy-2-aryl-1-(indol-3'-yl)ethanones) in presence of triethylamine in alcohol solution by heating (Scheme 2). The reaction must be protected from air oxygen, in a sealed tube or else under nitrogen.

Evidently α→ß isomerization α-aryl(indolyl)benzoins **2a**,**b**,**d**,**e** occurs as transformation of anion of α-benzoin **A** via mutual anion **B** to anion **C** of ß-benzoin (Scheme 2). The similar route to ß-aryl(indolyl)benzoins **3d**,**e** is isomerization of α-aryl(indolyl)benzoins **2d**,**e** in the presence of EtONa in ethanol solution at room temperature during short time. But in other cases this method did not gave positive results (e.g. for **2g**).

Structure of isomeric 2-hydroxy-2-aryl-1-(indol-3'-yl)ethanones(ß-aryl(indolyl)benzoins) **3a**,**b**,**d**,**e** was confirmed by ^{1}H and ^{13}C NMR spectra and MS.

The substantial difference was observed in NMR MS of α-aryl(indol-3-yl)benzoin **2** and ß-aryl(indolyl)benzoins **3**. In ^{1}H NMR spectra 2-hydroxy-2-aryl-1-(indol-3'-yl)ethanones **3a**,**b**,**d**,**e** the chemical shifts of C(2)H indolyl proton and NH proton lie in lower field than the chemical shifts of proper protons of 2-hydroxy-1-aryl-2-(indol-3'-yl)ethanones **2a**–**h** (Table 1). Probably, this phenomenon is caused by conjugation of indol-3-yl moiety with carbonyl group in ß-aryl(indolyl)benzoins **3a**,**b**,**d**,**e**.

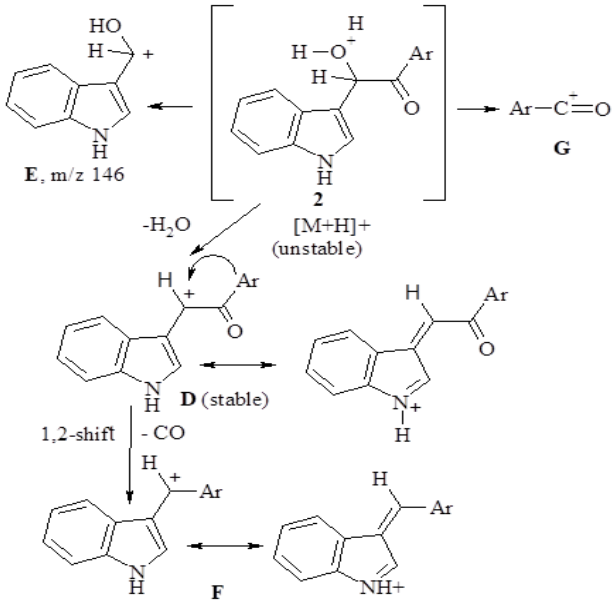
In ^{13}C NMR spectra of α-aryl(indolyl)benzoins **2** and ß-aryl(indolyl)benzoins **3** shifts of **C**HOH carbon and **C**=O carbon atoms can be regard as the characteristic carbon shifts (Table 2). In ß-aryl(indolyl)benzoins **3** shift of C=O carbon lies in some upper field than of C=O carbon of α-aryl(indolyl)benzoins **2** due to more conjugation of carbonyl group with 3-indolyl moiety. Shift of CHOH carbon forß-aryl(indolyl)benzoins **3** is observed yo some lower field than that of α-aryl(indolyl)benzoins **2**.

Table 1. The characteristic ^{1}H NMR chemical shifts of α-aryl(indolyl)benzoins and ß-aryl(indolyl)benzoins.

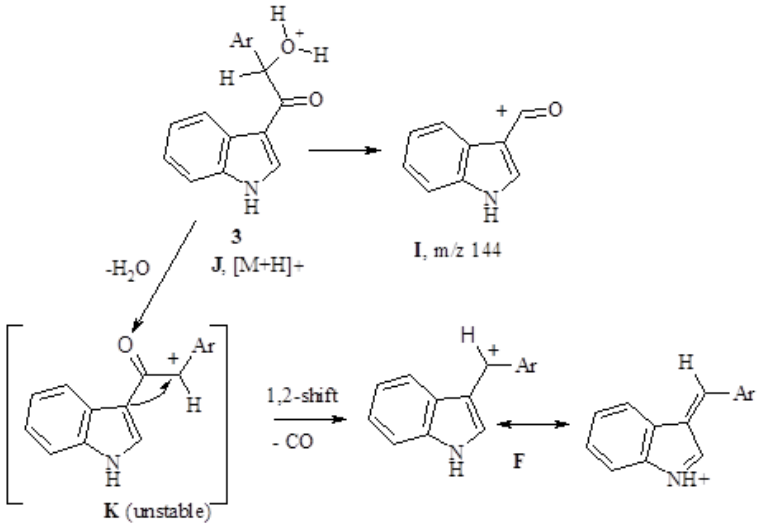
Resonance, σ, ppm					
α-Benzoins			ß-Benzoins		
Ar	**C(2)$_{ind}$H**	**NH**	**Ar**	**C(2)$_{ind}$H**	**NH**
2a	7.355	11.075	**3a**	8.544	11.984
2b	7.411	11.085	**3b**	8.563	12.042
2d	7.334	11.077	**3d**	8.586	12.044
2e	7.3285	11.073	**3e**	8.564	12.025
2f	7.3635	11.090			
2c	7.332	11.055			
2g	7.369	11.116			
2h	7.333	11.049			

Table 2. The characteristic ^{13}C NMR chemical shifts of α-aryl(indolyl)benzoins and ß-aryl(indolyl)benzoins.

Resonance, ^{13}C chemical shift, ppm					
α-Benzoins			ß-Benzoins		
Ar	**CHOH**	**C=O**	**Ar**	**CHOH**	**C=O**
2a	69.5	199.0	**3a**	76.2	194.3
2b	70.8	192.3	**3b**	72.4	193.1
2c	69.3	198.6			
2d	69.7	197.8	**3d**	75.5	194.1
2e	69.7	198.2	**3e**	75.5	194.0
2f	66.7	197.6			
2g	70.3	198.2			
2h	69.2	197.5			



Scheme 3. Fragmentation pattern of α-aryl(3-indolyl)benzoins **2** under MS (FAB).



Scheme 4. Fragmentation pattern of ß-aryl(3-indolyl)benzoins **3** under MS (FAB).

Probably, it is caused by more electronegativity of the aryl groups compare to indol-3-yl moiety.

Earlier MS spectra α- and ß-aryl(3-indolyl)benzoins[3,4,17] and α- and ß-aryl(2-furyl)benzoins[7,18] were obtained in EI regime, and peaks of M^+ ions were recorded in all cases. It was found that main direction of molecular ion fragmentation was breaking of C–C bond between CHOH group and C=O group yielding stable acyl and benzyl cations. In EI regime relative intensity of peaks depends of temperature of their generation.

As FAB regime of ionization is not connected with heating, it was used for the compounds **2** and **3** characterization.

Protonation of aryl(3-indolyl)benzoins molecules in FAB-MS conditions causes substantial difference of their FAB–MS spectra relatively to their EI–MS spectra. In FAB–MS spectra of α-aryl(indolyl)benzoins **2** peaks of $[M+H]^+$ ions are absent **(**Scheme 3), but KI addition to the samples yields peaks of $[M+K]^+$ions, whereas in FAB-MS spectra of ß-aryl(indolyl)benzoins **3** $[M+H]^+$ peaks of cations **J** are observed (Scheme 4).

The analysis of linked scanning (B/E linked scanning and B^2/E linked scanning) gave main directions of fragmentation of protonated molecular ions of α- and ß-aryl(3-indolyl)benzoins **2** and **3** (Scheme 3 and 4).

In MS spectra (FAB regime) of α-aryl(indolyl)benzoins **2,** peaks of stable indolylions **D** $[M+H-H_2O]^+$ and "benzylic" ion **E** with m/z 146 are dominating (Scheme 3).

In this case of α-aryl(indolyl)benzoins **2** the cations $[M+H-H_2O-CO]^+$ **F** are observed, presumably obtaining from cations **D** by synchronous 1,2-shieft of aryl moiety to caution center and CO elimination. Acyl cations **G** are also observed. However, in MS spectra of ß-aryl(indolyl)benzoins **3** peaks of ions $[M+H]^+$ **J,** $[M+H-H_2O-CO]^+$ **F** and acyl cation **I** with *m/z* 144 are dominating (Scheme 4). In this case aryl(indolyl) cations **F** are observed too, presumably obtaining from cations **J** by H_2O elimination and unstable cations **K** formation. Peaks ions $[M+H-H_2O]^+$ **K** have low intensity. Further cations **K** convert into stable cations **F** probably by route of synchronous 1,2-shieft of indolyl moiety to cation center and CO elimination (Scheme 4).

As shown by Scheme 3 and 4, the water molecule elimination from protonated molecules benzoins **2** and **3** leads to the formation of ions having cation center in α-position to the indol-3-yl moiety in the case of α-aryl(indolyl)benzoins **2** and in α-position to the aryl moiety in the case of ß-aryl(indolyl)benzoins **3**. Seemingly, the indolyl moiety much effectively stabilized the positive charge than the aryl moiety. This phenomenon causes the high stability of ions **D** and low stability of ions **K**. Probably, the first causes the absence of $[M+H]^+$ ions in FAB-MS spectra of α-aryl(indolyl)benzoins **2**.

With an aim of understanding α→ß aryl(indol-3-yl)benzoins isomerization, XRD study of α-phenyl(indol-3-yl)benzoin **2a** and ß-phenyl(indol-3-yl)benzoin **3a** were made.

It was found that in α-phenyl(indol-3-yl)benzoin **2a** (**Figure 2**) 3-indolylmethyl moiety was situated in the plane which orthogonaly oriented to the benzoyl group plane.

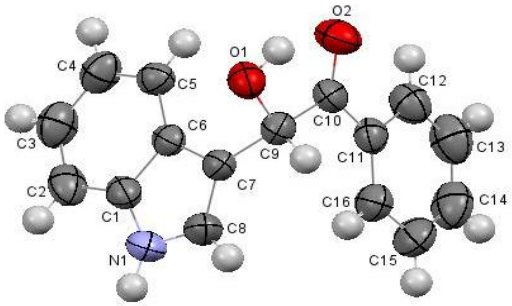


Figure 2. The molecular structure of 2-hydroxy-2-(indol-3'-yl)-1-phenylethanone **2a**

The angle between these fragments planes is 89º. The weak steric repulsion occurs between phenyl group and C(9) atom (the H16…C9 length is 2.69 Å whereas the vander Waals radii sum is 2.87 Å.[19] This steric repulsion causes some weak carbonyl group rolling toward phenyl moiety plane (the O2–C10–C11–C12 torsion angle is -9.7(3)º). HO-Group is coplanar oriented to C=O carbonyl due to intramolecular hydrogen bonding O1–H…O2 (H…O 2.24 Å, OH…O 104º). The length of C=O bond (C10=O2 bond) is 1.218(2) Å (the average length of C=O is 1.210 Å[20]). That means the negligible C=O bond deformation is due to its conjugation with benzene ring. The length of C10–C11 bond is 1.480(3) Å.

In the crystal molecules of compound **2a** form centrosymmetric dimmer due to O1-H…O2' (2-x, 2-y, 1-z) (H…O 2.12 Å, O-H…O 157º) intermolecular hydrogen bond. The dimmers are bonded in the links due to intermolecular bond N1-H…O1' (1.5-x, -0.5+y, 1.5-z) (H…O 2.10 Å, N-H…O 165º) (Figure 3).

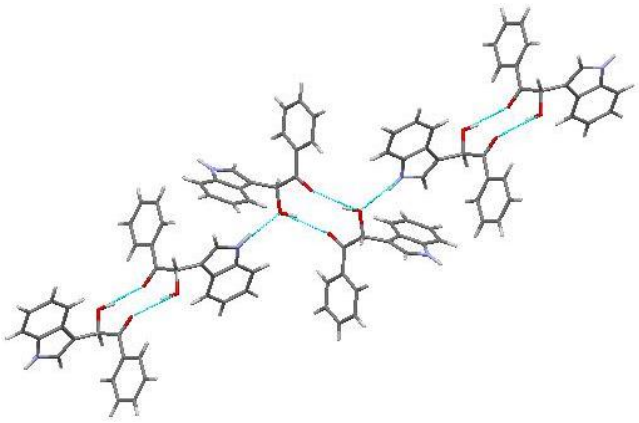


Figure 3. The packing of molecules of α-benzoin **2a** in the crystal

In ß-phenyl(indol-3-yl)benzoin **3a** (Figure 4) 3-indolyl substituent and carbonyl group C(9)=O(1) are coplanar (the C6–C7–C9–O1 torsion angle is 6.9(2)º). The phenyl substituent is orthogonally oriented to the mutual plane of indolyl moiety and carbonyl C(9)=O(1) group (the O1–C9–C10–C11 torsion angle is -97.0(2)º).

The C7–C9 bond $(C(3)^{Ind}–C(=O))$ is some shortened (1.439(2) Å) compare to average this bond length 1.455 Å[20] and C(9)=O(1) bond is substantially elongated to 1.242(2) Å compare to average length of C=O (1.210 Å[20]).

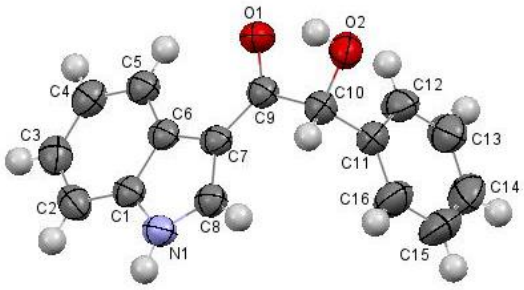


Figure 4. The molecular structure of 2-hydroxy-1-(indol-3'-yl)-2-phenylethanone **3a**.

This phenomena is caused by strong degree of conjugation of the carbonyl group with the indolyl moiety compare to degree of conjugation of the carbonyl group with phenyl substituent inα-phenyl(indol-3-yl)benzoin **2a**.

In indolyl substituent of ß-benzoin **3a** C7–C8 bond ($C(3)^{Ind}$–$C(2)^{Ind}$ bond) is elongated to 1.389(2) Å compare to that bond in α-benzoin **2a** (1.355(3) Å). And vice versa, in ß-benzoin **3a** N1–C8 bond (($N(1)^{Ind}$–$C(2)^{Ind}$ bond) is shortened to 1.349(2)Å compared to the same bond of α-benzoin **2a** (1.422(2) Å).

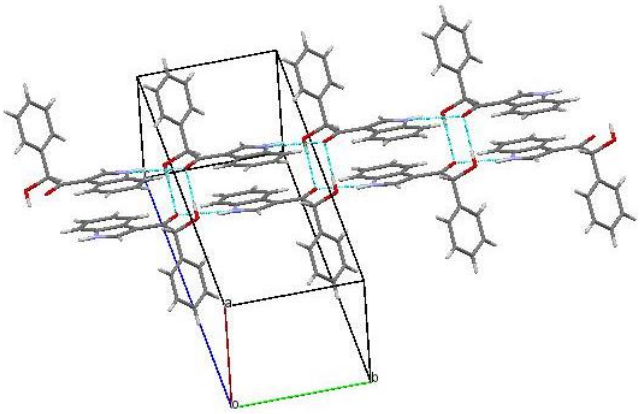


Figure 5. The packing of molecules of ß –benzoin **3a** in the crystal.

Earlier the same elongation of carbonyl group (1.236(5)Å) and shortening of $C(2)^{Fur}$–C(=O) (1.433(5)Å) has been established for ß-aryl(fur-2-yl)benzoin **1b**.[8] In compound **1b** the furan ring, carbonyl group and N,N-dimethylhydrazonyl moiety are situated in the same plane too. This data show on stronger conjugation of C=O group with hetaryl moiety in ß-benzoins **1b**, **3a** relatively to conjugation of C=O group with aryl substituent in α-benzoins **1a**, **2a**. Evidently, that realization of strong conjugation is moving force of α→ß benzoin rearrangement.

In the crystal lmolecules of compound **3a** form twice links (Figure 5) due to intermolecular hydrogen bond O2-H…O1' (2-x, 2-y, 1-z) H…O 2.07 Å O-H…O 167º and bifurcate hydrogen bonds with participating NH-group as proton donor (N1-H…O1' (x, y-1, z) H…O 2.26 Å N-H…O 141º; N1-H…O2' (x, y-1, z) H…O 2.29 Å N-H…O 147º).

The isomerization ofα-aryl(indolyl)benzoins can be regarded as convenient method of synthesis of ß-aryl(indolyl)benzoins which can not obtained from proper aldehydes by usual benzoin condensation.[1]

Conclusion

A convenient method of synthesis of 2-hydroxy-1-aryl-2-(indol-3-yl)ethanones, their isomerization in 2-hydroxy-2-aryl-1-(indol-3-yl)ethanones in presence of triethylamine on heating or in presence of EtONa at room temperature and spectral data of both isomers were discussed. The spectral tests of isomers structure were found. The structure of α- and ß-benzoins has been studied.

This work was supported by Department of Education and Science of Ukraine (grant no 0116U001722).

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Received: 18.09.2018
Accepted: 13.10.2018.