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Reaction of benzoylpyruvate with a mixture of aromatic aldehydes and *p*-phenylenediamine

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Abstract: Reactions of benzoylpyruvate with a mixture of aromatic aldehydes and aromatic diamines, *p*-phenylenediamine or benzidine in a 1:1:1 molar ratio, afforded 1-(4-aminophenyl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1*H*-pyrrol-2-ones (**1a-c**) and 1-(4′-aminobiphen-4-yl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1*H*-pyrrol-2-ones (**2a-c**). 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)biphenyls (**4a-c**) were produced via similar reaction in a 2:2:1 molar ratio. The structure of the resulted products was confirmed by determination of the melting point and spectrophotometric techniques such as IR and ^{1}H-NMR, in some cases by using ^{13}C-NMR spectroscopy.

Keywords: Benzoylpyruvate, *p*-Phenylenediamine, Benzidine, Aromatic aldehydes, 1-Aminoaryl-4-acyl-5-aryl-3-hydroxy-3-pyrrolin-2-ones.

Introduction

N-Substituted 4-acyl-5-aryl-3-hydroxy-3-pyrrolin-2-ones have been synthesized via reactions of acylpyruvic acid esters with a mixture of aromatic aldehyde and amine [1-6]. The reaction of acylpyruvate esters with a mixture of aromatic aldehyde and aliphatic diamine, such as, 1,2-diaminoethane in equimolar amounts formed 1-(2-aminoethyl)-4-acyl-5-aryl-3-hydroxy-3-pyrrolin-2-ones [7,8]. While the three-component condensation between an acylpyruvate ester, aromatic aldehyde and 0.5 equiv of aliphatic diamine performed, both amino groups involved, and leads to formation of 1,2-bis(4-acyl-5-aryl-3-hydroxy-2-oxo-3-pyrroline-1-yl)ethanes [9,10].

1,4,5-Trisubstituted 3-hydroxy-3-pyrrolin-2-ones represent interesting derivatives of pyrroles from point of view of the syntheses of many further derivatives and biologically active compounds. In recent years, much effort has been done via V. L. Gain on the synthesis and biological evaluation of 1,4,5-trisubstituted tetrahydropyrrol-2,3-diones due to their possible applications. It is known that *N*-substituted 4-acyl-5-aryl-3-hydroxy-3-pyrrolin-2-ones possess various types of pharmacological activity such as antimicrobial [3-5,11-13], antiinflammatory [6,14,15], analgesic [6,15,16], antiviral [15,17], antiamnestic [14,18], nootropic [8], antiaggregant [19], and neurotropic [20,21]. 1-Substituted 4-aroyl-3-hydroxy-5-phenyl-1H-pyrrol-2(5H)-one has promising properties as inhibitors of the interaction between annexin A2 and S100A10 and may help to elucidate the cellular function of this protein interaction [22]. In continuation of the search for biologically active compounds among 4,5-substituted 1-aminoaryl-3-hydroxy-3-pyrrolin-2-ones, it seems interesting to study the reaction of acylpyruvates with a mixture of aromatic aldehyde and diaminoaromatic and to investigate the pharmacological activity of the products.

Herein, we wish to report a simple reaction between benzoylpyruvate with a mixture of aromatic aldehydes and aromatic diamines, *p*-phenylenediamine or

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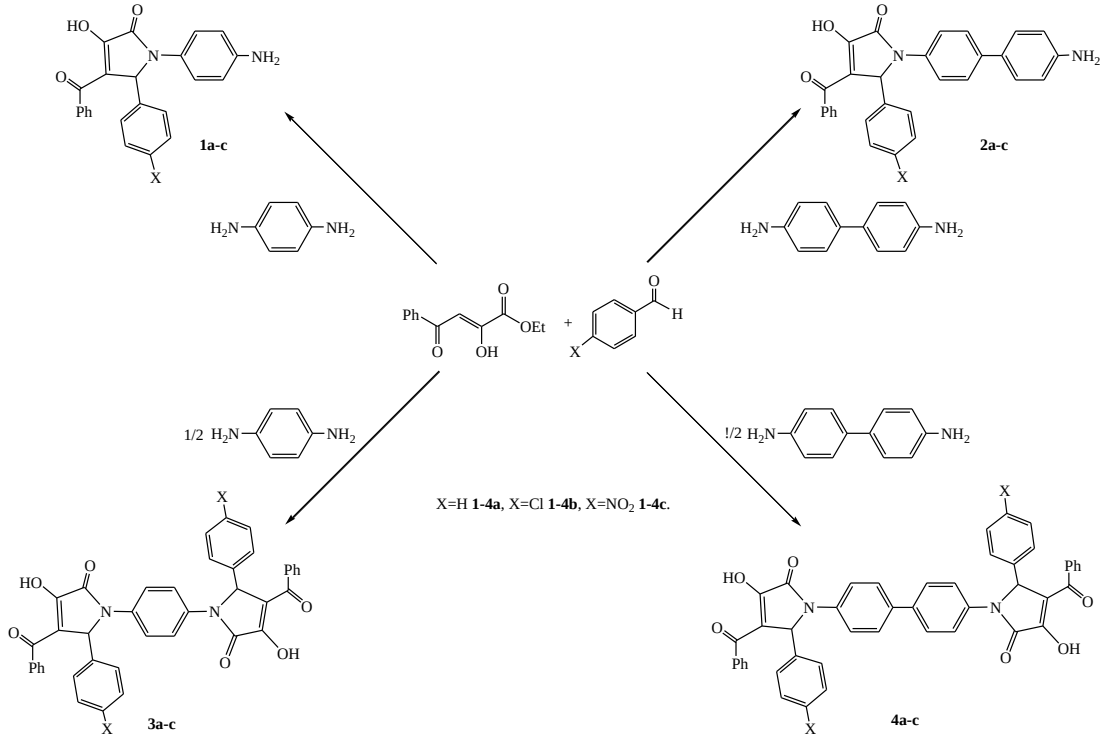
benzidine in 1:1:1 and 2:2:1 molar ratios, leading to 1-(aminoaryl)-5-aryl-4-benzoyl-3-hydroxy-3-pyrroline-2-ones (**1,2a-c**), 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-3-pyrroline-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-3-pyrroline-1-yl) biphenyls (**4a-c**).

Results and discussion

*1. Synthesis of 1-(4-aminophenyl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**1a-c**) and 1-(4′-aminobiphen-4-yl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**2a-c**)*

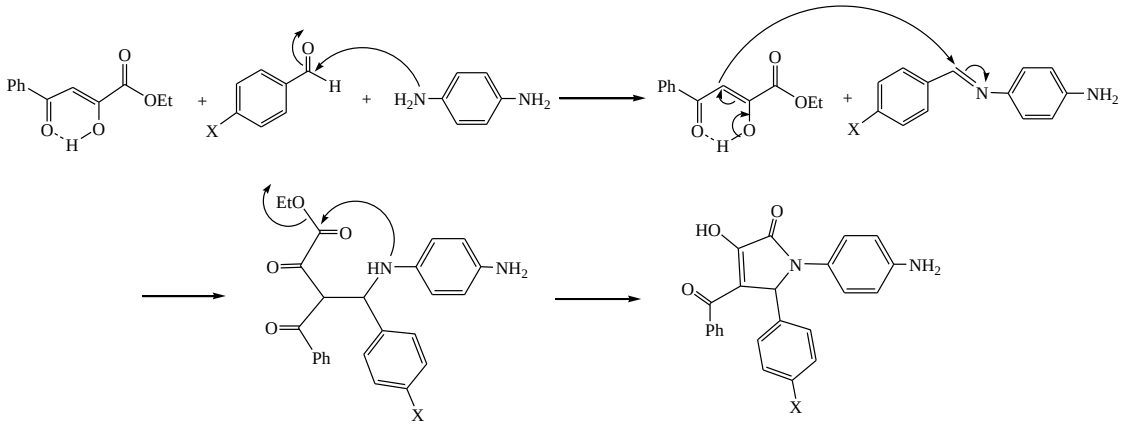
It seems reasonable to examine how the reactant ratio affects the direction of the above three-component reaction. For this purpose, benzoylpyruvate was used into reaction with a mixture of equimolar amounts of an aromatic aldehyde and aromatic diamines, *p*-phenylenediamine or benzidine. The reactions were carried out in acetic acid and the products were the corresponding 1-(4-aminophenyl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**1a-c**) and 1-(4′-aminobiphen-4-yl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**2a-c**) (Scheme **1**).



Scheme 1. Three-component condensations of benzoylpyruvate with a mixture of aromatic aldehydes and *p*-phenylenediamine or benzidine.

Structures **1a-c** and **2a-c** was assigned on the basis of their IR, ^{1}H NMR and in some cases ^{13}C NMR spectra. The IR spectra of compounds **1a-c** and **2a-c** have shown five characteristic absorption bands at 3485-3340, 3241-3134, 3110-3053, 1705-1681 and 1642-1618 cm^{-1} attributable to two bands for NH_2, enol OH, amide C=O and ketone C=O, functions, respectively. In the ^{1}H NMR spectra of **1a-c** and **2a-c** we have observed a singlet at δ 6.35-6.42 ppm for proton in position 5 of the pyrrole, a set of multiplet signals integrated for 14 (**1a**), 13 (**1b,c**) 18 (**2a**) and 17 (**2b,c**) protons at δ 6.68-8.06 ppm for aromatic protons, a broad singlet at δ 9.15-9.82 ppm for NH_2 protons and a broad singlet at δ 10.01-10.06 ppm for OH proton. For example, the ^{13}C NMR spectum of **1c** revealed four signals at δ 61.46 (C^5), 112.14 (C^4), 149.64 (C^3OH) and 164.42 (C^2=O) ppm due to the carbons of the pyrrole, besides twelve signals at δ 120.15-147.34 ppm attributable to the aromatic carbons and a signal at δ 185.35 ppm for the ketonic carbon. Compounds **1a-c** and **2a-c** give rise to brown-red color with an alcoholic solution of iron (III) chloride and pyridine, indicating that they exist in the enol form.

Presumably, the reaction mechanism includes formation of Schiff base from aromatic aldehyde and *p*-phenylenediamine or benzidine, followed by reaction with benzoylpyruvate to give 4-amino-3-benzoyl-2-oxobutanoic acid ester which then undergoes intramolecular ring closure to the final product (Scheme **2**). The yield depends on the substituent in the aryl fragment: electron-acceptor substituents favor the condensation.



Scheme 2. The reaction mechanism.

*2. Synthesis of 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)biphenyls (**4a-c**)*

When the three-component condensation was performed using 0.5 equiv of *p*-phenylenediamine or benzidine, both amino groups in the latter were involved, and we have isolated 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)biphenyles (**4a-c**) (Scheme **1**).

Structures **3a-c** and **4a-c** was assigned on the basis of their IR, ^{1}H NMR and in some cases ^{13}C NMR spectra. The IR spectra of compounds **3a-c** and **4a-c** have shown three characteristic absorption bands at 3115-3068, 1684-1661 and 1629-1618 cm^{-1} attributable to the enol OH, amide C=O and ketone C=O, functions, respectively. In the ^{1}H NMR spectra of **3a-c** and **4a-c** we have observed a singlet at δ 6.27-6.56 ppm for proton in position 5 of the pyrrole, a set of multiplet signals integrated for 24 (**3a**), 22 (**3b,c**) 28 (**4a**) and 26 (**4b,c**) protons at δ 7.09-8.08 ppm for aromatic protons and a broad singlet at δ 10.70-10.79 ppm for OH proton. For example, the ^{13}C NMR spectum of **3c** revealed four signals at δ 60.35 (C^{5}), 111.68 (C^{4}), 150.83 (C^{3}OH) and 165.93 (C^{2}=O) ppm due to the carbons of the pyrrole, besides ten signals at δ 119.49-146.52 ppm attributable to the aromatic carbons and a signal at δ 184.92 ppm for the ketonic carbon. Compounds **3a-c** and **4a-c** give rise to brown-red color with an alcoholic solution of iron (III) chloride and pyridine, indicating that they exist in the enol form.

Thus, both amino groups are involved in the reaction of *p*-phenylenediamine or benzidine with 2 equiv of an aromatic aldehyde, whereas successive reaction first at one and then at the other reaction center seems to be improbable.

Conclusion

In the present work, it has been shown that benzoylpyruvate reacted with a mixture of aromatic aldehydes and aromatic diamines, *p*-phenylenediamine or benzidine in 1:1:1 and 2:2:1 molar ratios, to form cyclocondensation products that were heterocyclic compounds of 1-(2-aminophenyl)-, 1-(4′-aminobiphen-4-yl)-5-aryl-4-benzoyl-3-hydroxy-3-pyrroline-2-ones (**1,2a-c**), 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-3-pyrroline-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-3-pyrroline-1-yl)biphenyls (**4a-c**).

Experimental

Melting points were measured in open capillaries and are reported uncorrected. Infrared spectra were measured from KBr disk using a FT-IR Perkin Elmer GX spectrometer and frequencies are reported in cm^{-1}. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Ultra Shield^{TM}-500MHz instrument using TMS as an internal standard. Chemical shifts are reported in ppm. Column chromatography was performed on silica gel L 100/250. Thin-layer chromatography was

performed on "Silufol-UV 254" plates. Ethyl 2,4-dioxo-4-phenylbutanoate was prepared from diethyl oxalate and the acetophenone by known methods [23].

*2. Synthesis of 1-(4-aminophenyl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**1a-c**) and 1-(4′-aminobiphen-4-yl)-5-aryl-4-benzoyl-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**2a-c**). General Procedure*

To a solution of 1.0 mmol 1,4-diaminobenzene or benzidine and 1.0 mmol of the aromatic aldehyde in 10 ml of glacial acetic acid was added with boiling a solution of 1.0 mmol 2,4-dioxo-4-phenylbutanoate in 10 ml of glacial acetic acid and the mixture was refluxed for 2 hours. Then the solvent was evaporated and the residue washed with warm 2-propanol to give **1a-c** and **2a-c**, respectively [6].

*1-(4-Aminophenyl)-4-benzoyl-3-hydroxy-5-phenyl-2,5-dihydro-1H-pyrrol-2-ones (**1a**):*

Yellow powder (Yield 54%), m.p. 208-210°C (decom.); IR: 3367, 3134 (NH_2), 3110 (OH), 1694 (C=O, amide), 1638 (C=O, ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.37 (1H, s, C^5H), 6.68 (2H, d, $^3J_{HH}$=7.86 Hz, $2CH_{ortho}$ of Ph-NH_2), 6.98 (2H, d, $^3J_{HH}$=7.86 Hz, $2CH_{ortho}$ of Ph-N), 7.12-7-84 (8H, m, of 2Ph), 8.05 (2H, d, $^3J_{HH}$=7.83 Hz, $2CH_{ortho}$ of Ph-CO), 9.82 (2H, br.s, NH_2, exchangeable with D_2O), 10.04 (1H, br.s, OH, exchangeable with D_2O) ppm.

*1-(4-Aminophenyl)-4-benzoyl-5-(4-chlorophenyl)-3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**1b**)*:

Yellow powder (Yield 61%), m.p. 223-225°C (decom.); IR: 3415, 3238 (NH_2), 3053 (OH), 1681 (C=O, amide), 1642 (C=O, ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.35 (1H, s, C^5H), 6.74 (2H, d, $^3J_{HH}$=7.53 Hz, $2CH_{ortho}$ of Ph-NH_2), 6.93 (2H, d, $^3J_{HH}$=7.53 Hz, $2CH_{ortho}$ of Ph-N), 7.25 (2H, t, $^3J_{HH}$=7.65 Hz, $2CH_{meta}$ of Ph-CO), 7.34 (1H, t, $^3J_{HH}$=7.65 Hz, CH_{para} of Ph-CO), 7.54 (2H, d, $^3J_{HH}$=8.22 Hz, $2CH_{ortho}$ of Ph-C^5H), 7.82 (2H, d, $^3J_{HH}$=8.22 Hz, $2CH_{ortho}$ of Ph-Cl), 8.06 (2H, d, $^3J_{HH}$=7.65 Hz, $2CH_{ortho}$ of Ph-CO), 9.80 (2H, br.s, NH_2, exchangeable with D_2O), 10.05 (1H, br.s, OH, exchangeable with D_2O) ppm.

*1-(4-Aminophenyl)-4-benzoyl-3-hydroxy-5-(4-nitrophenyl)-2,5-dihydro-1H-pyrrol-2-ones (**1c**)*:

Yellow powder (Yield 69%), m.p. 239-241°C (decom.); IR: 3485, 3224 (NH_2), 3076 (OH), 1686 (C=O, amide), 1626 (C=O, ketone), 1518, 1354 (NO_2) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.38 (1H, s, C^5H), 7.40 (2H, t, $^3J_{HH}$=7.40 Hz, $2CH_{meta}$ of Ph-CO), 7.43 (1H, t, $^3J_{HH}$=7.40 Hz, CH_{para} of Ph-CO), 7.46 (2H, d, $^3J_{HH}$=7.53 Hz, $2CH_{ortho}$ of Ph-NH_2), 7.52 (2H, d, $^3J_{HH}$=7.92 Hz, $2CH_{ortho}$ of Ph-C^5H), 7.60 (2H, d, $^3J_{HH}$=7.53 Hz, $2CH_{ortho}$ of Ph-N), 7.68 (2H, d, $^3J_{HH}$=7.40 Hz, $2CH_{ortho}$ of Ph-CO), 8.03 (2H, d, $^3J_{HH}$=7.92 Hz, $2CH_{ortho}$ of Ph-NO_2), 9.82 (2H, br.s, NH_2, exchangeable with D_2O), 10.05 (1H, br.s, OH, exchangeable with D_2O) ppm; ^{13}C NMR (DMSO-d_6) δ: 61.46 (C^5), 112.14 (C^4), 120.15, 121.53, 122.68, 123.02, 125.93, 127.11, 128.78, 129.34, 133.57, 141.22, 143.79, 147.34 (18C, 3Ph), 149.64 (C^3OH), 164.42 (C^2=O), 185.35 (COPh) ppm.

*1-(4′-Aminobiphen-4-yl)-4-benzoyl-3-hydroxy-5-phenyl-2,5-dihydro-1H-pyrrol-2-ones (**2a**):*

Yellow powder (Yield 53%), m.p. 214-216°C (decom.); IR: 3340, 3241 (NH_2), 3063 (OH), 1694 (C=O, amide), 1635 (C=O, ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.40 (1H, s, C^5H), 6.79 (2H, d, $^3J_{HH}$=7.91 Hz, $2CH_{ortho}$ of Ph-NH_2), 6.94 (2H, d, $^3J_{HH}$=7.91 Hz, $2CH_{meta}$ of Ph-NH_2), 7.11-7-96 (12H, m, 4Ph), 8.02 (2H, d, $^3J_{HH}$=7.67 Hz, $2CH_{ortho}$ of Ph-CO), 9.15 (2H, br.s, NH_2, exchangeable with D_2O), 10.03 (1H, br.s, OH, exchangeable with D_2O) ppm.

*1-(4′-Aminobiphen-4-yl)-4-benzoyl-5-(4-chlorophenyl) -3-hydroxy-2,5-dihydro-1H-pyrrol-2-ones (**2b**):*

Yellow powder (Yield 65%), m.p. 232-234°C (decom.); IR: 3353, 3235 (NH_2), 3075 (OH), 1687 (C=O, amide), 1618 (C=O, ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.42 (1H, s, C^5H), 6.86 (2H, d, $^3J_{HH}$=8.07 Hz, $2CH_{ortho}$ of Ph-NH_2), 7.06 (2H, d, $^3J_{HH}$=8.07 Hz, $2CH_{meta}$ of Ph-NH_2), 7.16 (2H, d, $^3J_{HH}$=7.58 Hz, $2CH_{meta}$ of Ph-N), 7.58 (2H, t, $^3J_{HH}$=7.55 Hz, $2CH_{meta}$ of Ph-CO), 7.64 (1H, t, $^3J_{HH}$=7.55 Hz, CH_{para} of Ph-CO), 7.70 (2H, d, $^3J_{HH}$=8.23 Hz, $2CH_{ortho}$ of Ph-C^5H), 7.75 (2H, d, $^3J_{HH}$=7.58 Hz, $2CH_{ortho}$ of Ph-N), , 7.85 (2H, d, $^3J_{HH}$=8.23 Hz, $2CH_{ortho}$ of Ph-Cl), 7.98 (2H, d, $^3J_{HH}$=7.55 Hz, $2CH_{ortho}$ of Ph-CO), 9.18 (2H, br.s, NH_2, exchangeable with D_2O), 10.06 (1H, br.s, OH, exchangeable with D_2O) ppm.

*1-(4′-Aminobiphen-4-yl)-4-benzoyl-3-hydroxy-5-(4-nitrophenyl)-2,5-dihydro-1H-pyrrol-2-ones (**2c**):*

Yellow powder (Yield 71%), m.p. 247-249°C (decom.); IR: 3452, 3157 (NH_2), 3062 (OH), 1705 (C=O, amide), 1631 (C=O, ketone), 1520, 1349 (NO_2) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.42 (1H, s, C^5H), 6.92 (2H, d, $^3J_{HH}$=7.48 Hz, $2CH_{ortho}$ of Ph-NH_2), 7.15 (2H, d, $^3J_{HH}$=7.48 Hz, $2CH_{meta}$ of Ph-NH_2), 7.41 (2H, d,

$^3J_{HH}$=7.95 Hz, 2CH$_{meta}$ of Ph-N), 7.52 (2H, t, $^3J_{HH}$=7.41 Hz, 2CH$_{meta}$ of Ph-CO), 7.59 (1H, t, $^3J_{HH}$=7.41 Hz, CH$_{para}$ of Ph-CO), 7.69 (2H, d, $^3J_{HH}$=8.52 Hz, 2CH$_{ortho}$ of Ph-C^{5}H), 7.72 (2H, d, $^3J_{HH}$=7.95 Hz, 2CH$_{ortho}$ of Ph-N), 7.75 (2H, d, $^3J_{HH}$=7.41 Hz, 2CH$_{ortho}$ of Ph-CO), 8.02 (2H, d, $^3J_{HH}$=8.52 Hz, 2CH$_{ortho}$ of Ph-NO$_2$), 9.15 (2H, br.s, NH$_2$, exchangeable with D$_2$O), 10.01 (1H, br.s, OH, exchangeable with D$_2$O) ppm; ^{13}C NMR (DMSO-d_6) δ: 59.74 (C^5), 111.46 (C^4), 119.46, 120.56, 122.86, 123.45, 124.05, 128.07, 128.85, 129.41, 131.55, 132.74, 133.87, 135.87, 137.25, 142.67, 144.53, 147.59 (24C,4Ph), 150.47 (C^{3}OH), 166.23 (C^2=O), 188.91 (COPh) ppm.

*3. Synthesis of 1,4-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)benzenes (**3a-c**) and 4,4′-bis(5-aryl-4-benzoyl-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)biphenyles (**4a-c**). General Procedure*

To a solution of 1.0 mmol 1,4-diaminobenzene or benzidine and 1.0 mmol of the aromatic aldehyde in 10 ml of glacial acetic acid was added with boiling a solution of 0.5 mmol 2,4-dioxo-4-phenylbutanoate in 10 ml of glacial acetic acid and the mixture was refluxed for 2 hours. Then the solvent was evaporated and the residue washed with warm 2-propanol (**3a-c**) or ethanol (**4a-c**) to give **3a-c** and **4a-c**, respectively [6].

*1,4-Bis(4-benzoyl-3-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1H-pyrrol-1-yl)benzene (**3a**):*

Yellow powder (Yield 56%), m.p. 185-187°C (decom.); IR: 3092 (OH), 1673 (C=O, amide), 1629 (C=O, ketone) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.27 (2(1H), s, 2C^{5}H), 7.11 (2(2H), d, $^3J_{HH}$=8.24 Hz, 4CH$_{meta}$ of Ph-CO), 7.18-7.85 (2(8H), m, 5Ph), 7.95 (2(2H), d, $^3J_{HH}$=7.58 Hz, 4CH$_{ortho}$ of Ph-CO), 10.71 (2(1H), br.s, 2OH, exchangeable with D$_2$O) ppm.

*1,4-Bis(4-benzoyl-5-(4-chlorophenyl)-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)benzene (**3b**):*

Yellow powder (Yield 68%), m.p. 203-205°C (decom.); IR: 3071 (OH), 1661 (C=O, amide), 1618 (C=O, ketone) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.30 (2(1H), s, 2C^{5}H), 7.22 (2(2H), t, $^3J_{HH}$=7.42 Hz, 4CH$_{meta}$ of Ph-CO), 7.34 (2(1H), t, $^3J_{HH}$=7.42 Hz, 2CH$_{para}$ of Ph-CO), 7.54 (2(2H), d, $^3J_{HH}$=8.65 Hz, 4CH$_{ortho}$ of Ph-C^{5}H), 7.59 (2(2H), s, 4CH$_{ortho}$ of Ph-N), 7.84 (2(2H), d, $^3J_{HH}$=8.65 Hz, 4CH$_{ortho}$ of Ph-Cl), 8.03 (2(2H), d, $^3J_{HH}$=7.42 Hz, 4CH$_{ortho}$ of Ph-CO), 10.70 (2(1H), br.s, 2OH, exchangeable with D$_2$O) ppm.

*1,4-Bis(4-benzoyl-3-hydroxy-5-(4-nitrophenyl)-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)benzene (**3c**):*

Orange powder (Yield 72%), m.p. 235-237°C (decom.); IR: 3068 (OH), 1682 (C=O, amide), 1625 (C=O, ketone), 1518, 1348 (NO$_2$) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.32 (2(1H), s, 2C^{5}H), 7.26 (2(2H), t, $^3J_{HH}$=7.22 Hz, 4CH$_{meta}$ of Ph-CO), 7.33 (2(1H), t, $^3J_{HH}$=7.22 Hz, 2CH$_{para}$ of Ph-CO), 7.55 (2(2H), d, $^3J_{HH}$=8.83 Hz, 4CH$_{ortho}$ of Ph-C^{5}H), 7.56 (2(2H), s, 4CH$_{ortho}$ of Ph-N), 7.73 (2(2H), d, $^3J_{HH}$=7.22 Hz, 4CH$_{ortho}$ of Ph-CO), 8.00 (2(2H), d, $^3J_{HH}$=8.83 Hz, 4CH$_{ortho}$ of Ph-NO$_2$), 10.71 (2(1H), br.s, 2OH, exchangeable with D$_2$O) ppm; ^{13}C NMR (DMSO-d_6) δ: 60.35 (2C^5), 111.68 (2C^4), 119.49, 122.04, 123.18, 126.53, 127.23, 129.12, 129.96, 134.49, 141.46, 146.52 (30C, 5Ph), 150.83 (2C^{3}OH), 165.93 (2C^2=O), 184.92 (2COPh) ppm.

*4,4′-Bis(4-benzoyl-3-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1H-pyrrol-1-yl)biphenyles (**4a**):*

Yellow powder (Yield 54%), m.p. 206-208°C (decom.); IR: 3110 (OH), 1675 (C=O, amide), 1637 (C=O, ketone) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.36 (2(1H), s, 2C^{5}H), 7.09 (2(2H), d, $^3J_{HH}$=7.85 Hz, 4CH$_{meta}$ of Ph-CO), 7.15-7.88 (2(10H), m, 6Ph), 7.98 (2(2H), d, $^3J_{HH}$=7.58 Hz, 4CH$_{ortho}$ of Ph-CO), 10.76 (2(1H), br.s, 2OH, exchangeable with D$_2$O) ppm.

*4,4′-Bis(4-benzoyl-5-(4-chlorophenyl)-3-hydroxy-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)biphenyles (**4b**):*

Yellow powder (Yield 65%), m.p. 248-250°C (decom.); IR: 3082 (OH), 1679 (C=O, amide), 1625 (C=O, ketone) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.38 (2(1H), s, 2C^{5}H), 7.25 (2(2H), d, $^3J_{HH}$=8.10 Hz, 4CH$_{meta}$ of Ph-N), 7.46 (2(2H), t, $^3J_{HH}$=7.46 Hz, 4CH$_{meta}$ of Ph-CO), 7.49 (2(1H), t, $^3J_{HH}$=7.46 Hz, 2CH$_{para}$ of Ph-CO), 7.59 (2(2H), d, $^3J_{HH}$=8.73 Hz, 4CH$_{ortho}$ of Ph-C^{5}H), 7.72 (2(2H), d, $^3J_{HH}$=8.10 Hz, 4CH$_{ortho}$ of Ph-N), 7.95 (2(2H), d, $^3J_{HH}$=8.73 Hz, 4CH$_{ortho}$ of Ph-Cl), 8.08 (2(2H), d, $^3J_{HH}$=7.46 Hz, 4CH$_{ortho}$ of Ph-CO), 10.79 (2(1H), br.s, 2OH, exchangeable with D$_2$O) ppm.

*4,4′-Bis(4-benzoyl-3-hydroxy-5-(4-nitrophenyl)-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)biphenyles (**4c**):*

Orange powder (Yield 71%), m.p. 266-267°C (decom.); IR: 3115 (OH), 1684 (C=O, amide), 1624 (C=O, ketone), 1519, 1349 (NO$_2$) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 6.56 (2(1H), s, 2C^{5}H), 7.45 (2(2H), d, $^3J_{HH}$=8.04 Hz, 4CH$_{meta}$ of Ph-N), 7.57 (2(2H), t,

$^3J_{HH}$=7.32 Hz, 4CH$_{meta}$ of Ph-CO), 7.60 (2(1H), t, $^3J_{HH}$=7.32 Hz, 2CH$_{para}$ of Ph-CO), 7.72 (2(2H), d, $^3J_{HH}$=8.61 Hz, 4CH$_{ortho}$ of Ph-C^{5}H), 7.75 (2(2H), d, $^3J_{HH}$=8.04 Hz, 4CH$_{ortho}$ of Ph-N), 7.77 (2(2H), d, $^3J_{HH}$=7.32 Hz, 4CH$_{ortho}$ of Ph-CO), 8.05 (2(2H), d, $^3J_{HH}$=8.61 Hz, 4CH$_{ortho}$ of Ph-NO$_2$), 10.79 (2(1H), br.s, 2OH, exchangeable with D_2O) ppm; ^{13}C NMR (DMSO-d_6) δ: 60.70 (2C^5), 112.34 (2C^4), 119.60, 123.04, 123.93, 128.62, 129.18, 129.66, 133.17, 135.90, 136.45, 138.32, 145.11, 147.59 (36C, 6Ph), 151.42 (2C^{3}OH), 165.13 (2C^2=O), 189.44 (2COPh) ppm.

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