J IRAN CHEM SOC (2014) 11:963–968
DOI 10.1007/s13738-013-0362-x

ORIGINAL PAPER

Reaction of arylglyoxals with pyrrole or indole in aqueous media: facile synthesis of heteroaryl α-acyloins

Mohammad Anary-Abbasinejad · Mahdiyeh Talebizadeh

Received: 30 June 2013 / Accepted: 25 September 2013 / Published online: 10 October 2013

Abstract Pyrrole or indole reacts with arylglyoxal monohydrates in aqueous media in the absence of any catalyst to produce pyrrol-2-yl or indol-3-yl α-acyloin derivatives in high yields as the only product. Reactions were clean and products were isolated by simple filtration. When the reactions were carried out in acetonitrile as solvent, different products were obtained.

Keywords Indole · Arylglyoxals · Electrophilic substitution · Benzoins

Introduction

Indole and pyrrole are among the most important chemical skeletons existing as the main core in the structure of various physiologically, pharmaceutically, and industrially important compounds [1–5]. For example indole derivatives involve beneficial estron metabolism promoter [1], inhibitor for human prostate cancer cells [2] and radical scavengers [3]. The importance of pyrrole containing natural products, such as heme, chlorophyl and vitamin B12 has stimulated extensive studies on the synthesis and chemical behavior of pyrrole derivatives [6].

Using water as solvent for chemical reactions has attracted much interests from chemists in recent years, because it offers a powerful tool for minimizing waste production and harmful organic solvent dispersal [7, 8]. Being naturally abundant, readily available and environmentally benign makes water an ideal solvent for chemical processes both in industry and laboratory [9–13]. Water also shows novel reactivity and selectivity for synthesis of chemically important and biologically active compounds in industry [14–17].

The electrophilic substitution reactions of indole and pyrrole have been extensively studied [18]. It is well-known that the reaction of indole with electrophiles almost always occurs on the C-3 position. In contrast, pyrrole usually reacts with electrophiles at C-2 position faster than C-3 position, although the electrophilic substitution on C-3 position is also observed. Aromatic aldehydes have been reported to react with two equivalents of indole or pyrrole in acidic media to produce diindolyl or dipyrrolylarylmthanes [19–22]. Although numerous methods have been reported for the reaction of indole with aromatic or aliphatic aldehydes or ketones and many acidic catalysts have been reported to affect these reactions, there are only a few reports on similar reaction between indole and arylglyoxals to produce diindolylethanones [23]. When neutral media is used, this reaction is occurred with 1:1 mol ratio between indole and arylglyoxals leading to heteroaryl α-acyloins [24]. Although the reaction between *N*-substituted pyrroles and arylglyoxals in neutral conditions has been reported to afford the related acyloins [24], the reaction of pyrrole itself with glyoxals has been reported to afford mixtures of mono- and di-substituted pyrrole derivatives [25]. The above mentioned reactions between indole or pyrrole derivatives and arylglyoxals for synthesis of heteroaryl α-acyloins have been done in boiling benzene as solvent, which is highly toxic, and moderate yields of products have been obtained. Indol-3-yl α-acyloins have also been reported as non-isolated intermediates, produced by the reaction between arylglyoxals and indole, which react with enaminones to afford functionalized pyrroles [26]. Here we wish to report that pyrrole or indole react with arylglyoxals

M. Anary-Abbasinejad (✉) · M. Talebizadeh
Department of Chemistry, Vali-e-Asr University, 77176 Rafsanjan, Iran
e-mail: m.anary@vru.ac.ir

in aqueous media in the absence of any catalyst to produce pyrrol-2-yl or indol-3-yl α-acyloin derivatives in high yields as the only product. Reactions are clean and products are isolated as pure compounds by simple filtration.

Experimental procedures

Materials and characterization techniques

All the utilized arylglyoxals were prepared by the SeO_2-oxidation of the related aryl methyl ketones on the basis of the reported procedure and used as their monohydrates [27]. All melting points are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-400 Avance spectrometer at 400 and 100 MHz, respectively. ^{1}H and ^{13}C NMR spectra were obtained on solution in d_6-DMSO using TMS as internal standard. The chemicals used in this work purchased from Fluka (Buchs, Switzerland) and were used without further purification. Structure of compounds **3d**, **3e**, **6c**, **6e** and **6f** were proved by comparing their physical and spectral data with the previously reported data. The other products were characterized using NMR and IR spectral and analytical data.

General procedure for synthesis of compounds **3a–e** and **5a–d**: A mixture of indole (2 mol, for preparation of **3a–e**) or pyrrole (2 mmol, for preparation of **5a–d**) and arylglyoxal monohydrate (2 mol) in water was stirred at room temperature for 5 h. The solid was filtered off and washed with diethyl ether (20 mL) to afford the pure product.

General procedure for synthesis of compounds **6a–f** and **7a–c**: A mixture of indole (4 mol, for preparation of **6a–f**)) or pyrrole (1 mmol, for preparation of **7a–c**) and arylglyoxal monohydrate (2 mol) in acetonitrile was stirred at room temperature for 5 h. The solvent was evaporated under reduced pressure and the solid was washed with diethyl ether to give the pure product.

Selected spectral data:

2-hydroxy-2-(1*H*-indol-3-yl)-1-(naphthalene-1-yl)ethanone **(3a)**: Yield: 90 %; white powder; m.p.177–182 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,415 and 3,309 (NH and OH), 1,654 (C=O). Calcd. for ($C_{20}H_{15}NO_2$): C, 79.72; H, 5.02; N, 4.65 %. Found: C, 79.7; H, 5.1; N,4.5 %. ^{1}H NMR (d_6-DMSO, 400 MHz): 5.68 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 6.43 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.98 (2 H, m), 7.25 (2 H, m), 7.49 (2 H, m), 7.68(1 H, d $^2J_{HH}$ = 8 Hz), 7.90 (1H, m), 8.00 (1H, d $^3J_{HH}$ = 8 Hz), 8.11 (1H, d $^3J_{HH}$ = 8 Hz), 8.20 (1H, m), 10.96 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 71.0 (C–OH), 111.4, 118.8, 119.2, 121.2, 124.5, 124.6, 125.0, 125.7, 126.2, 127.1, 127.3, 128.3, 129.9, 131.7, 133.3, 134.4, 135.9, 136.1, 202.6 (C=O).

2-hydroxy-2-(1*H*-indol-3-yl)-1-phenylethanone **(3b)**: Yield: 95 %; white powder; m.p.174–177 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,412 and 3,313 (NH and OH), 1,657 (C=O). Calcd. for ($C_{16}H_{13}NO_2$): C, 76.48; H, 5.21; N, 5.57 %. Found: C, 76.7; H, 5.1; N, 5.3 %. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.50 (1 H, braod s, OH), 6.37 (1 H, s, O–CH), 6.98 (1 H, t $^3J_{HH}$ = 8 Hz), 7.06 (1 H, t $^3J_{HH}$ = 8 Hz), 7.34 (2 H, m), 7.40 (2 H, m), 7.51 (1 H, m), 7.63 (1 H, d $^3J_{HH}$ = 8 Hz), 8.00 (2 H, m), 11.07 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 69.3 (C–OH), 111.5, 113.2, 118.8, 119.1, 121.2, 124.68, 124.8, 125.5, 128.4, 132.8, 134.9, 136.2 (aromatic carbons), 198.9 (C=O).

2-hydroxy-2-(1*H*-indol-3-yl)-1-(*p*-tolyl)ethanone **(3c)**: Yield: 89 %; white powder; m.p.154–158 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,415 and 3,309 (NH and OH), 1,654 (C=O). Calcd. for ($C_{17}H_{15}NO_2$): C, 76.96; H, 5.70; N, 5.28 %. Found: C, 76.7; H, 5.8; N, 5.5 %. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.28 (3 H, s, CH_3), 5.46 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 6.32 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.97 (1 H, m), 7.05 (1 H, m), 7.20 (2 H, d $^3J_{HH}$ = 8 Hz), 7.32 (1 H, m), 7.61 (1H, d $^3J_{HH}$ = 8 Hz), 7.90 (2 H, d $^3J_{HH}$ = 8 Hz), 11.04 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 21.0 (CH_3), 69.0 (C–OH), 111.5, 118.8, 119.1, 121.2, 124.6, 124.7, 125.5, 128.5, 128.9, 132.3, 136.2, 143.2 (aromatic carbons), 198.5 (C=O).

2-hydroxy-2-(1*H*-indol-3-yl)-1-(4-chlorophenyl)ethanone **(3d)** [24]: Yield: 97 %; white powder; m.p. 144–146 °C. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.65 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 6.36 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.99 (1 H, t $^3J_{HH}$ = 8 Hz,), 7.06 (1 H, t $^3J_{HH}$ = 8 Hz), 7.31 (1 H, d $^3J_{HH}$ = 8 Hz), 7.34 (1 H, s,), 7.44 (2 H, d $^3J_{HH}$ = 8 Hz), 7.60 (1 H, d $^3J_{HH}$ = 8 Hz), 8.10 (2 H, d $^3J_{HH}$ = 8 Hz), 11.07 (1 H, s, NH).

2-hydroxy-2-(1*H*-indol-3-yl)-1-(4-bromophenyl)ethanone **(3e)** [24]: Yield: 95 %; white powder; m.p. 159–161 °C. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.63 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 6.32 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.96 (1 H, t $^3J_{HH}$ = 8 Hz), 7.11 (1 H, t $^3J_{HH}$ = 8 Hz), 7.32 (1 H, d $^3J_{HH}$ = 8 Hz), 7.35 (1 H, d, 8 Hz), 7.37 (1 H, s,), 7.60 (2 H, d $^3J_{HH}$ = 8 Hz), 8.01 (2 H, d $^3J_{HH}$ = 8 Hz), 11.08 (1 H, s, NH).

2-hydroxy-2-(1*H*-pyrrol-2-yl)-1-(naphthalene-1-yl)ethanone **(5a)**: Yield: 95 %; white powder; m.p.106–108 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,460 and 3,349 (NH and OH), 1,667 (C=O). Calcd. for ($C_{16}H_{13}NO_2$): C, 76.48; H, 5.21; N, 5.57 %. Found: C, 76.6; H, 5.3; N, 5.6 %. ^{1}H NMR (d_6-DMSO, 400 MHz): 5.76 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 5.81 (2 H, m), 6.1 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.60 (1 H, m), 7.57 (4 H, m), 7.96 (2 H, m), 8.00 (1 H, d $^3J_{HH}$ = 8 Hz), 8.26 (1 H, m), 10.87 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 71.2 (C–OH), 106.7, 107.6, 118.2, 124.5,

125.0, 126.3, 127.1, 127.5, 128.0, 128.3, 129.8, 131.9, 133.2, 134.3 (aromatic carbons), 201.3 (C=O).

2-hydroxy-2-(1*H*-pyrrol-2-yl)-1-(naphthalene-2-yl)ethanone **(5b)**: Yield: 90 %; white powder; m.p.115–117 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,727 and 3,399 (NH and OH), 1,678 (C=O). Calcd. for ($C_{16}H_{13}NO_2$): C, 76.48; H, 5.21; N, 5.57 %. Found: C, 76.7; H, 5.2; N, 5.7 %. ^{1}H NMR (d_6-DMSO, 400 MHz): 5.74 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 5.89 (1 H, m), 6.24 (1 H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.68 (1 H, m), 7.58 (2 H, m), 7.77–8.11 (5 H, m), 8.69 (1 H, s), 10.94 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 69.5 (C–OH), 107.0, 107.6, 118.2, 124.1, 126.9, 127.5, 128.1, 128.5, 129.1, 129.5, 130.2, 131.9, 132.0, 134.8, 197.5 (C=O).

2-hydroxy-2-(1*H*-pyrrol-2-yl)-1-(phenyl)ethanone **(5c)**: Yield: 95 %; white powder; m.p.123–125 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,727 and 3,420 (NH and OH), 1,682 (C=O). Calcd. for ($C_{12}H_{11}NO_2$): C, 71.63; H, 5.51; N, 6.96 %. Found: C, 71.7; H, 5.4; N, 7.1 %. ^{1}H NMR (DMSO, 400 MH_Z): 5.64 (1 H, d $^3J_{HH}$ = 6 Hz, OH), 5.89 (2 H, m), 6.05 (1 H, d $^3J_{HH}$ = 6 Hz, O–CH), 6.68 (1 H, s), 7.45 (2 H, m), 7.57 (1 H, m), 7.96 (2 H, d $^3J_{HH}$ = 7 Hz), 10.89 (1 H, s, NH). ^{13}C NMR (DMSO, 100 MHz): δ = 69.5 (C–OH), 106.9, 107.5, 118.1, 118.2, 128.5, 133.0, 134.7 (aromatic carbons), 197.6 (C=O).

2-hydroxy-2-(1*H*-pyrrol-2-yl)-1-(*p*-tolyl)ethanone **(5d)**: Yield: 89 %; white powder; m.p.126–128 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,726 and 3,388 (NH and OH), 1,679 (C=O). Calcd. for ($C_{13}H_{13}NO_2$): C, 72.54; H, 6.09; N, 6.51 %. Found: C, 72.7; H, 6.0; N, 6.3 %. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.37 (3 H, s, CH_3), 5.57 (1 H, d $^3J_{HH}$ = 5 Hz, OH), 5.81 (1 H, m), 5.87 (1 H, m), 6.03 (1H, d $^3J_{HH}$ = 5 Hz, O–CH), 6.66 (1 H, m), 7.26 (2 H, d, $^3J_{HH}$ = 8 Hz), 7.86 (2 H, d, $^3J_{HH}$ = 8 Hz), 10.86 (1 H, s, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 21.1 (CH_3), 69.2 (C–OH), 96.3, 106.8, 107.5, 118.1, 128.6, 129.0, 132.1, 143.4 (aromatic carbons), 197.1 (C=O).

2,2-di(1*H*-indol-3-yl)-1-(naphthalene-1-yl)ethanone **(6a)**: Yield: 90 %; white powder; m.p.234–239 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,411 (NH), 1,654(C=O). Calcd. for ($C_{28}H_{20}N_2O$): C, 83.98; H, 5.03; N, 7.00 %. Found: C, 83.7; H, 5.0; N, 7.2 %. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 6.66 (1 H, s), 6.96 (2 H, t $^3J_{HH}$ = 8 Hz), 7.05 (2 H, t $^3J_{HH}$ = 8 Hz), 7.26 (2 H, m), 7.33 (2 H, d $^3J_{HH}$ = 8 Hz), 7.49 (2 H, m), 7.58 (1 H, t $^3J_{HH}$ = 8 Hz), 7.66 (2 H, d $^3J_{HH}$ = 8 Hz), 7.94 (1 H, m), 8.05 (1H, d $^3J_{HH}$ = 8 Hz), 8.28 (1 H, m), 8.43 (1 H, d $^3J_{HH}$ = 8 Hz), 10.92 (2 H, 2 NH). ^{13}C NM (d_6-DMSO, 100 MHz): δ = 44.8 (CH), 111.4, 112.5, 118.4, 118.9, 121.0, 124.3, 124.7, 125.3, 126.2, 126.6, 126.9, 127.3, 128.3, 130.1, 131.8, 133.4, 136.2, 136.4 (aromatic carbons), 201.2 (C=O).

2,2-di(1*H*-indol-3-yl)-1-(naphthalene-2-yl)ethanone **(6b)**: Yield: 93 %; white powder; m.p. 268–270 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,407 (NH), 1,672 (C=O). Calcd. for ($C_{28}H_{20}N_2O$): C, 83.98; H, 5.03; N, 7.00 %. Found: C, 83.9; H, 5.2; N, 7.3 %. ^{1}H NMR (DMSO, 400 MHz): δ = 6.85 (1 H, s, CH), 6.95 (2 H, t, $^3J_{HH}$ = 8 Hz), 7.05 (2 H, t, $^3J_{HH}$ = 8 Hz), 7.24 (2 H, m), 7.34 (2 H, d, $^3J_{HH}$ = 8 Hz), 7.62 (4 H, m), 7.95 (2 H, m), 8.12 (2 H, m), 8.99 (1 H, s), 10.94 (2 H, NH): ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 41.4 (CH), 111.4, 112.9, 118.4, 119.0, 120.9, 124.4, 124.4, 126.4, 126.8, 127.5, 128.1, 128.5, 129.5, 129.9, 132.1, 133.7, 134.8, 136.2 (aromatic carbons), 197.8 (C=O).

2,2-di(1*H*-indol-3-yl)-1-phenylethanone **(6c)** [23]: Yield: 90 %; white powder; m.p. 205–207 °C. ^{1}H NMR (DMSO, 400 MHz): δ = 6.64 (1 H, s), 6.93 (2 H, t $^3J_{HH}$ = 7 Hz), 7.04 (2 H, t $^3J_{HH}$ = 7 Hz), 7.17 (2 H, s), 7.33 (2 H, d $^3J_{HH}$ = 8 Hz), 7.46 (2 H, d $^3J_{HH}$ = 7 Hz), 7.55 (3 H, d $^3J_{HH}$ = 3 Hz), 8.16 (2 H, d $^3J_{HH}$ = 8 Hz), 10.91 (2 H, 2 NH).

2,2-di(1*H*-indol-3-yl)-1-(*p*-tolyl)ethanone **(6d)**: Yield: 90 %; white powder; m.p. 255–257 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,399 (NH), 1,674(C=O). Calcd. for ($C_{25}H_{20}N_2O$): C, 82.39; H, 5.53; N, 7.69 %. Found: C, 82.5; H, 5.4; N, 7.6 %. ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.32 (3 H, s, CH_3),6.63 (1 H, s), 6.94 (2 H, t $^3J_{HH}$ = 8 Hz,), 7.05 (2 H, t $^3J_{HH}$ = 8 Hz), 7.17 (2 H, m), 7.27 (2 H, d, $^3J_{HH}$ = 8 Hz), 7.34 (2 H, d, $^3J_{HH}$ = 8 Hz,), 7.56 (2 H, d, $^3J_{HH}$ = 8 Hz), 8.08 (2 H, d $^3J_{HH}$ = 8 Hz), 10.92 (2 H, 2 NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 21.0 (CH_3), 41.3, 111.4, 113.0, 118.4, 118.9, 120.9, 124.3, 126.4, 128.6, 129.1, 134.0, 136.2, 143.1 (aromatic carbons), 197.4 (C=O).

2,2-di(1*H*-indol-3-yl)-1-(4-chlorophenyl)ethanone **(6e)** [23]: Yield: 95 %; white powder; m.p. 195–197 °C. ^{1}H NMR (DMSO, 400 MHz): δ = 6.58 (1 H, s), 6.93 (2 H, t $^3J_{HH}$ = 7 Hz), 7.04 (2 H, t $^3J_{HH}$ = 7 Hz), 7.15 (2 H, d $^3J_{HH}$ = 2 Hz), 7.35 (2 H, d $^3J_{HH}$ = 8 Hz), 7.52 (2 H, d $^3J_{HH}$ = 8 Hz), 7.57 (2 H, d $^3J_{HH}$ = 8 Hz), 8.15 (2 H, d $^3J_{HH}$ = 8 Hz), 10.97 (2 H, 2 NH).

2,2-di(1*H*-indol-3-yl)-1-(4-bromophenyl)ethanone **(6f)** [23]: Yield: 90 %; white powder; m.p. 229–230 °C. ^{1}H NMR (DMSO, 400 MHz): δ = 6.35 (1 H, s), 6.87 (2 H, s), 6.95 (2 H, t $^3J_{HH}$ = 7 Hz), 7.09 (2 H, t $^3J_{HH}$ = 7 Hz), 7.25 (2 H, d $^3J_{HH}$ = 8 Hz), 7.40 (2 H, d $^3J_{HH}$ = 8 Hz), 7.45 (2 H, d $^3J_{HH}$ = 8 Hz), 7.86 (2 H, d $^3J_{HH}$ = 8 Hz), 10.20 (2 H, 2 NH).

2,2′-(1*H*-pyrrole-2,5-diyl)bis[2-hydroxy-1-(naphthalene-1-yl)]ethanone **(7a)**: 85 %; white powder; m.p. 100–105 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,623 and 3,343 (NH and OH), 1,617 (C=O). Calcd. for ($C_{28}H_{21}NO_4$): C, 77.23; H, 4.86; N, 3.22; %. Found: C, 77.4; H, 5.1; N, 3.1 %. Major isomer (55 %) ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.60 (2 H, d $^3J_{HH}$ = 4 Hz, 2 OH), 5.77 (2 H, m)*, 6.03 (2 H, d $^3J_{HH}$ = 5 Hz), 7.36 (2 H, t $^3J_{HH}$ = 8 Hz), 7.52 (4 H, m)*, 7.75 (2 H, d $^3J_{HH}$ = 8 Hz), 7.94 (2 H, m), 8.18 (2 H, m),

10.91 (1 H, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 71.6 (O–CH), 107.6, 124.9, 125.5, 126.8, 127.8, 128.0, 128.8*, 129.5, 130.3, 132.4, 133.7, 134.5* (aromatic carbons), 201.6 (C=O)*. Minor isomer (45 %): ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.64 (2 H, d $^3J_{HH}$ = 4 Hz, 2 OH), 5.77 (2 H, m)*, 6.13 (2 H, d $^3J_{HH}$ = 5 Hz), 7.44 (2 H, t $^3J_{HH}$ = 8 Hz), 7.52 (4 H, m)*, 7.83 (2 H, d $^3J_{HH}$ = 8 Hz), 8.03 (2 H,m), 8.22 (2 H, m), 11.02 (1 H, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): 71.5 (O–CH), 107.6, 124.9, 125.5, 126.7, 127.6, 127.9, 128.8*, 129.6, 130.2, 132.4, 133.7, 134.5* (aromatic carbons), 201.6 (C=O)*.

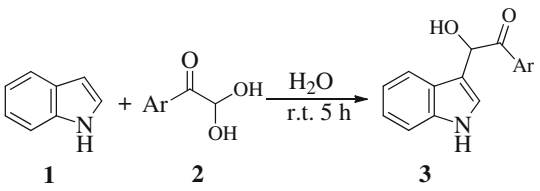
2,2′-(1*H*-pyrrole-2,5-diyl)bis[2-hydroxy-1-(naphthalene-2-yl)]ethanone **(7b)**: 90 %; white powder; m.p.127 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,623 and 3,357 (NH and OH), 1,676 (C=O). Calcd. for ($C_{28}H_{21}NO_4$): C, 77.23; H, 4.86; N, 3.22 %. Found: C, 77.4; H, 5.0; N, 3.3 %. Major isomer (60 %) ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 5.72 (2 H, m)*, 5.75 (2 H, d $^3J_{HH}$ = 6 Hz, 2 OH), 6.18 (2 H, d $^3J_{HH}$ = 6 Hz, 2 O–CH)), 7.50–8.20 (6 H, m)*, 8.57 (2 H, s), 11.16 (1 H, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 69.2 (O–CH), 107.4, 123.6*, 124.0, 126.8, 127.5, 128.0, 128.8, 129.4, 130.2*, 131.8, 131.9*, 134.8 (aromatic carbons), 197.1 (C=O). Minor isomer (40 %): δ = 5.72 (2 H, m)*, 5.77 (2 H, d $^3J_{HH}$ = 6 Hz, 2 OH), 6.23 (2 H, d $^3J_{HH}$ = 6 Hz, 2 O–CH)), 7.50 - 8.20 (6 H, m)*, 8.62 (2 H, s), 11.26 (1 H, NH). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 69.5, 107.4, 123.6*, 124.1, 126.7, 127.5, 127.9, 128.5, 129.4, 130.2*, 131.7, 131.9*, 134.7 (aromatic carbons), 197.3 (C=O).

2,2′-(1*H*-pyrrole-2,5-diyl)bis[2-hydroxy-1-(*p*-tolyl)]ethanone **(7c)**: Yield: 87 %; white powder; m.p.79–80 °C. IR (KBr) (υ_{max}, cm^{-1}): 3,407 and 3,370 (NH and OH), 1,676 (C=O). Calcd. for ($C_{22}H_{21}NO_4$): C, 72.71; H, 5.82; N, 3.85 %. Found: C, 72.4; H, 5.7; N, 3.9 %. Major isomer (66 %): ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.33 (6 H, s, CH_3), 5.60 (2 H, d $^3J_{HH}$ = 5 Hz, 2 OH), 5.67 (2 H, m,)*, 5.97 (2 H, d $^3J_{HH}$ = 5 Hz, 2 O–CH), 7.19 (4 H, d $^3J_{HH}$ = 8 Hz), 7.78 (4 H, d $^3J_{HH}$ = 8 Hz,), 10.97 (1 H, NH). Minor isomer (34 %): ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.23 (6 H, s, CH_3), 5.63 (2 H, d $^3J_{HH}$ = 5 Hz, 2 OH), 5.67 (2 H, m,)*, 6.00 (2 H, d $^3J_{HH}$ = 5 Hz, 2 O–CH), 7.25 (4 H, d $^3J_{HH}$ = 8 Hz), 7.84 (4 H, d $^3J_{HH}$ = 8 Hz,), 11.03 (1 H, NH).

*For two isomers

Results and discussion

To investigate the reaction between arylglyoxals and indole, at first a mixture of 1-naphthyl glyoxal monohydrate and indole in water was stirred at room temperature for 5 h (Scheme 1). Then the product was filtered off and washed with diethyl ether. The structure of product **3a** was



1 **2** **3**

3	Ar	yield%*
a	1-naphthyl	90
b	Ph	95
c	4-MeC_6H_4	89
d	4-ClC_6H_4	97
e	4-BrC_6H_4	95

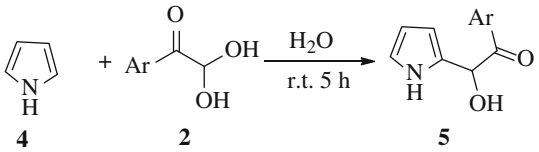
*Isolated yields

Scheme 1 Reaction between indole and arylglyoxals in water

deduced from IR and NMR spectral and analytical data. The ^{1}H NMR spectrum of **3a** exhibited two doublets ($^3J_{HH}$ = 5 Hz) at 5.68 and 6.43 ppm, respectively, for OH and O–CH protons. The NH proton resonated at 10.96 ppm as a broad single signal. The aromatic protons resonated between 6.98 and 8.20 ppm. When the spectrum was prepared after addition of a few drops of D_2O to d_6-DMSO solution of compound **3a**, the signals related to the OH and NH protons were disappeared and the signal related to the O–CH proton converted to a single signal, showing the spin–spin coupling between OH and O–CH protons. ^{13}C NMR spectrum of **3a** shows twenty distinct signals consistent with the proposed structure, the methine (O–CH) and carbonyl carbons resonating at 71.0 and 202.6 ppm, respectively. The structure of compound **3a** was also confirmed by its IR spectrum, which exhibited two absorption bands at 3,415 and 3,309 cm^{-1} for NH and OH bonds and an absorption band at 1,654 cm^{-1} for the carbonyl group. This reaction was also examined between indole and other arylglyoxals and as shown in Scheme 1 the expected benzoin derivatives were obtained in excellent yields.

We also examined similar reaction between pyrrole and arylglyoxals in aqueous media. As shown in Scheme 2, the reaction is compatible for pyrrole as for indole and excellent yields of pyrrol-2-yl α-acyloin derivatives **5a–d** were obtained in good yields.

The reaction of indole or pyrrole was also examined with more reactive dehydrated arylglyoxals in water, but no improvement in reaction time or yield of products was observed and the related benzoins were isolated in high yields. However, no reaction was observed between indole or pyrrole and general aldehydes such as 4-bromobenzaldehyde or even electron-deficient 4-nitrobenzaldehyde in water in the obscene of any catalyst and starting materials were isolated after 24 h stirring at room temperature.

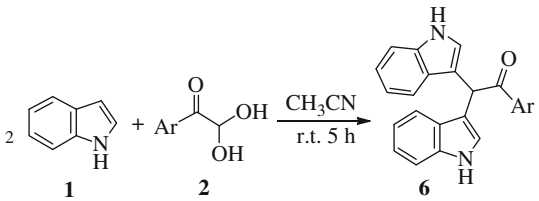


4 2 5

5	Ar	yield%*
a	1-naphthyl	95
b	2-naphthyl	90
c	Ph	95
d	4-MeC_6H_4	89

*Isolated yields

Scheme 2 Reaction between pyrrole and arylglyoxals in water



1 2 6

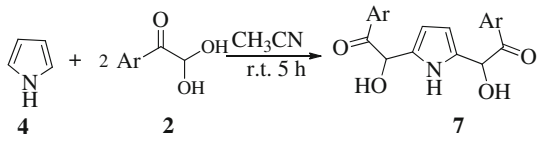
6	Ar	yield%*
a	1-naphthyl	90
b	2-naphthyl	93
c	Ph	90
d	4-MeC_6H_4	90
e	4-ClC_6H_4	95
f	4-BrC_6H_4	90

*Isolated yields

Scheme 3 Reaction between indole and arylglyoxals in acetonitrile

To explore the role of water as the solvent of reaction between indole or pyrrole and arylglyoxals, the above reactions were investigated in acetonitrile as solvent. When indole was reacted with 1-naphthylglyoxal hydrate in acetonitrile, after 5 h stirring at room temperature, evaporating the solvent and washing the residue with diethyl ether a pure solid product was obtained. The analytical and NMR spectral data showed that the product is 2,2-bis(indol-3-yl)-1-(1-naphthyl)ethanone **6a** (Scheme 3). We could not isolate any traces of compound **3a** from this reaction. The reaction was also examined with other arylglyoxal hydrates and good yields of the corresponding 2,2-bis(indol-3-yl)-1-(aryl)ethanone derivatives were obtained (Scheme 3).

When pyrrole was reacted with arylglyoxals in acetonitrile, different products were obtained. For example, from the reaction between pyrrole and 1-naphthylglyoxal in acetonitrile at room temperature, compound **7a** was isolated as the only product in 85 % yield (Scheme 4). Compound **7a** possesses two stereogenic centers and may exist as two



4 2 7

7	Ar	yield%*
a	1-naphthyl	85
b	2-naphthyl	90
c	4-MeC_6H_4	87

*Isolated yields

Scheme 4 Reaction between pyrrole and arylglyoxals in acetonitrile

diastereomers. The NMR spectra of **7a** show the existence of both isomers. The ^{1}H NMR spectrum of compound **7a** exhibited two double signals ($^3J_{HH} = 5$ Hz) at 5.60 and 6.03 ppm for OH and O–CH protons of the major isomer (the corresponding signals for the minor isomer were observed as two doublets at 5.64 and 6.13 ppm). Two broad single signals were observed at 10.91 and 11.02 ppm for the NH protons of two isomers. When the spectrum was prepared after addition of a few drops of D_2O to d_6-DMSO solution of compound **7a**, the signals related to the OH and NH protons were disappeared and the signal related to the O–CH protons converted to single signals. ^{13}C NMR spectrum of compound **7a** exhibited two sets of 14 distinct signals for two isomers in consistent with the proposed structure. As shown in Scheme 4 the reaction of pyrrole was also examined with 2-naphthylglyoxal and 4-methyl phenyl glyoxal in acetonitrile and the corresponding 2,5-disubstituted pyrrole derivatives **7b** and **7c** were obtained in good yields both of them as two diastereomers.

Conclusions

In summary, we report herein that the reaction between indole or pyrrole with arylglyoxals in aqueous media provides a facile and efficient route for synthesis of indol-3-yl or pyrrol-2-yl α-acyloins in good yields. The advantages of the method are readily available starting materials, neutral reaction conditions, using water as an environmentally green solvent and simple isolation and purification of products. The reaction of indole with arylglyoxals in acetonitrile as solvent afforded bis(indolyl) arylethanones in good yields. Reaction between pyrrole and arylglyoxals in acetonitrile afforded disubstituted pyrrole derivatives.

References

1. R.J. Sundberg, *The chemistry of indoles* (Academic Press, New York, 1970), p. 1

2. Y.C. Chang, J. Riby, G. Chang, B. Peng, G.L. Firestone, L.F. Bjeldanes, Biochem. Pharmacol. **58**, 825 (1999)
3. S.H. Benabadji, R. Wen, J. Zheng, X. Dong, S. Yuan, Acta Pharmacol. Sin. **25**, 666 (2004)
4. J.A.H. Lainton, J.W. Hoffman, D.R. Martin, D.R. Compton, Tetrahedron Lett. **36**, 1401 (1995)
5. C.Y. De Leon, B.A. Ganem, Tetrahedron **53**, 7731 (1997)
6. R.A. Jones, G.P. Bean, *The chemistry of pyrroles* (Academic Press, London, 1977)
7. P. Tundo, P.T. Anastas, *Green chemistry: challenging perspectives* (Oxford University Press, Oxford, 1999)
8. J.M. DeSimone, Science **297**, 799 (2002)
9. B.L. Mojet, S.D. Ebbesen, L. Lefferts, Chem. Soc. Rev. **39**, 4643 (2010)
10. C.J. Li, Acc. Chem. Res. **43**, 581 (2010)
11. M. Lamblin, L. Nassar-Hardy, J.C. Hierso, E. Fouquet, F.X. Felpin, Adv. Syn. Catal. **33**, 352 (2010)
12. A. Chanda, V.V. Fokin, Chem. Rev. **109**, 725 (2009)
13. D. Burtscher, K. Grela, Angew. Chem. Int. Ed. **48**, 442 (2009)
14. C.J. Li, Chem. Rev. **105**, 3095 (2005)
15. K. Manabe, S. Limura, X.M. Sun, S. Kobayashi, J. Am. Chem. Soc. **124**, 11971 (2002)
16. S.V. Chankeshwara, A.K. Chakraborti, Org. Lett. **8**, 3259 (2006)
17. G.L. Khatik, R. Kumar, A.K. Chakraborti, Org. Lett. **8**, 2433 (2006)
18. T.L. Gilchrist, *Heterocyclic chemistry*, 2nd edn. (Wiley & Sons, New York, 1992), p. 188
19. M. Zahran, Y. Abdin, H. Salama, Arkivoc **XI**, 256 (2008)
20. B. Karmakar, A. Nayak, B. Chowdhury, J. Banerji, Arkivoc **XII**, 209 (2009)
21. R. Naik, P. Joshi, S.P. Kaiwar, R.K. Deshpande, Tetrahedron **59**, 2207 (2003)
22. A.M. Ganecheva, V. Terlemezyan, L. Tanyeli, L.C. Toppare, Eur. Poly. J. **44**, 2567 (2008)
23. M.H. Mosslemin, A. Movahhed, E J. Chem. **9**, 301 (2012)
24. S.P. Ivonin, A.V. Lapandin, A.A. Anishchenko, V.G. Shtamburg, Synth. Commun. **34**, 451 (2004)
25. T. Seuerin, I. Ipuch, Chem. Ber. **108**, 1768 (1975)
26. J.Y. Liu, Q.Y. Li, B. Jiang, S.J. Tu, RSC Adv. **3**, 5056 (2013)
27. H.A. Riley, A.R. Gray, in *Organic syntheses,* Vol. II (Wiley & Sons: New York, 1943), Collect, p 509