Synthesis of 2-(*N*-Benzylpyrrolyl)-benzimidazoles Using Polyphosphoric Acid Prompted Cyclocondensation

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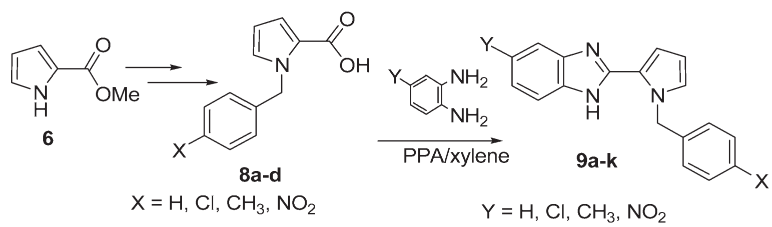

Synthesis of a series of 2-substituted benzimidazoles was carried out for screening anti-inflammatory activities. 2-(*N*-benzylpyrrolyl)-benzimidazoles **9a–k** were synthesized from *N*-benzyl-2-pyrrole carboxylic acids **8a–d** and 4-substituted-1,2-phenylenediamines by cyclocondensation utilizing polyphosphoric acid (PPA) as condensing agent. The *N*-benzyl-2-pyrrole carboxylic acids were prepared by standard method of *N*-benzylation of 2-pyrrole carboxylate using NaH/DMF and appropriately substituted benzyl halides followed by alkaline hydrolysis.

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INTRODUCTION

Benzimidazole derivatives are known to possess varied biological activities. Substituted benzimidazole derivatives have been reported to possess anticancer, antiulcer, antiviral, antifungal, antimicrobial, and anti-inflammatory activities [1–6]. Prostaglandins and leukotriens from oxidative metabolism of arachidonic acid play established roles in the pathophysiology of inflammatory disorders [7,8]. Pharmacological interference with cyclooxygenase (COX) and 5-lipooxygenase (5-LOX), enzymes involved in production of prostaglandins and leukotriens is a hallmark feature of virtually all marked nonsteroidal anti-inflammatory drugs (NSAIDs). This property is believed to play an important role in their therapeutic effects and certain mechanism-based side effects including gastrointestinal bleeding, nephrotoxicity, and cardiovascular problems in the case of highly selective cyclooxygenase-2 inhibitors [9–14]. There have been remarkable efforts in developing new classes of compounds to minimize the side effects of the existing NSAIDs. Recent investigations on triazole, imidazole, pyrrole, benzimidazole, and indole derivatives Figure 1 have shown that these classes of heterocycles received much attention as potential NSAIDs [15–25]. Literature survey also revealed that when one bioactive heterocyclic system was coupled with another, a molecule with enhanced biological activity was produced [26–28]. Based on these considerations, in the course of research devoted to the development of new classes of anti-inflammatory agents [29–31], we have speculated that incorporating pyrrole ring into the 2-position of benzimidazole moiety result in compounds with single

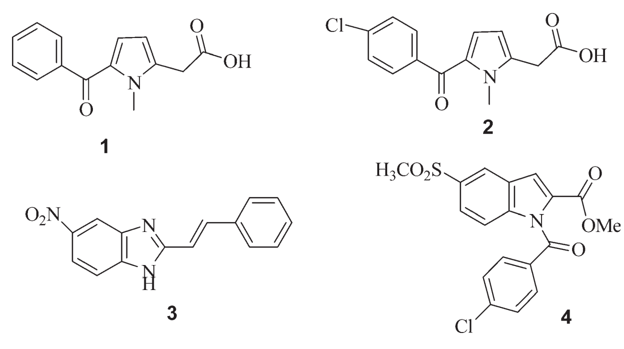


Figure 1. Structures of some pyrrole, benzimidazole, and indole derivatives with anti-inflammatory activity.

molecular scaffold that could enhance biological activities. Herein, we report the synthesis of this new class of compounds. The screening of anti-inflammatory activities of these compounds is underway.

RESULTS AND DISCUSSION

The synthetic routes for the title compounds are outlined in Scheme 1. Pyrrolylbenzimidazoles, **9a–k** were synthesized starting from the commercially available 2-pyrrole carboxylic acid in four steps. Esterification of an acid by refluxing in thionylchloride/methanol mixture afforded the corresponding ester **6**. *N*-benzylation of **6** by treating with NaH/DMF followed by appropriately substituted benzyl halides afforded the corresponding *N*-benzyl-2-pyrrole carboxylates **7a–d**. Alkaline hydrolysis of **7** using 30% aqueous potassium hydroxide gave the carboxylic acids **8a–d**, as key intermediates for the preparation of the targeted benzimidazoles. Cyclocondensation of **8** with 4-substituted-1,2-phenylenediamine carried out utilizing polyphosphoric acid (PPA) as condensing agent afforded the titled compounds in fair to good yield. The chemical structures of all new compounds were established by infrared (IR), ^{1}H NMR spectra as well as elemental analysis. The IR-spectral characteristics (all spectra taken in KBr) are quite similar and could be summarized as: ν (N—H): 3150–3185 cm^{-1}; ν (C—H) 2900 cm^{-1}; ν (—C═N—): 1620–1760 cm^{-1}. Detailed ^{1}H NMR spectra of the targeted and intermediate compounds is given in the experimental section. The elemental analysis indicated by the symbols of the elements was within ±0.4% of theoretical values. Relevant physical data of the targeted compounds were collected and summarized in Table 1.

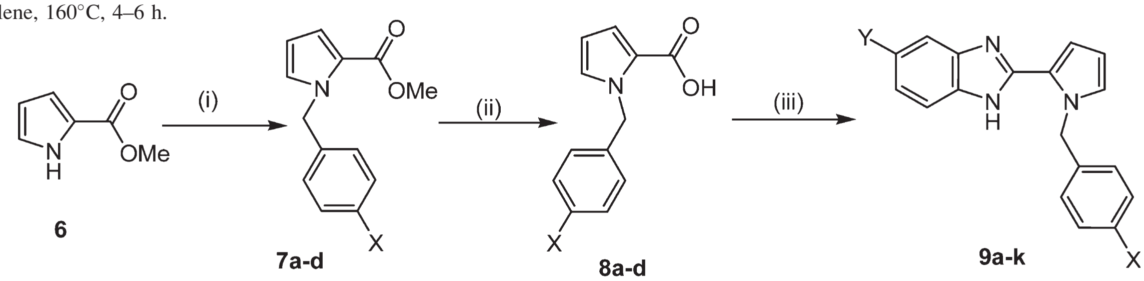
EXPERIMENTAL

Melting points (mp) were determined on Gallenkamp melting point apparatus and are uncorrected. Reagents and solvents were purchased from Sigma-Aldrich Chemical Company (Milwaukee, WI) and used as received. The structures of the products described were confirmed by IR, ^{1}H NMR, and elemental analysis data. The IR spectra were run with KBr pellets on Perkin-Elmer 1430 FT spectrometer and are reported in cm^{-1}. ^{1}H NMR spectra were recorded on Varian Gemini HX-300 MHz spectrometer. All ^{1}H chemical shifts (in ppm) are reported relative to tetramethylsilane as internal standard for solutions in DMSO-d_6 and $CDCl_3$ as the solvent unless otherwise specified. Elemental microanalysis was performed in Galbraith Laboratories (Knoxville, Tennessee). Analysis indicated by the symbols of the elements was within ±0.4% of the theoretical values. Analytical thin layer chromatography was performed on 250 μm-layer flexible plates. Spots were visualized under Ultraviolet illumination. Reaction products were purified, when necessary, by column chromatography on silica gel 60 (200–425 mesh), with the solvent system indicated. Solvents were evaporated *in vacuo*. Anhydrous sodium sulphate was used as drying agent.

Preparation of *N*-benzyl-2-pyrrole carboxylates (7a–d); general procedure A. To a cooled solution of methyl-2-pyrrol carboxylate **6** (1 equiv, 10 mmol), in 12 mL of DMF, NaH (1.5 equiv, 15 mmol) was added in small portions. The reaction mixture was stirred at 0°C for 20 min, the appropriately substituted benzyl halide (1 equiv, 10 mmol) in 0.6 mL DMF was added dropwise. The mixture was warmed to room temperature and stirred for 2 h. Excess hydride was decomposed with a small amount of methyl alcohol. After evaporation to dryness under reduced pressure, the crude residue was washed with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, and the solvent was evaporated *in vacuo*. The resulting solid was purified by column chromatography (ethyl acetate: hexane) to afford *N*-(4-substitutedbenzyl)-2-pyrrole carboxylates (**7a–d**).

Methyl-N-benzylpyrrole-2-carboxylate (7a). Isolated as white crystalline solid, yield 1.86 g (86.5%); ^{1}H NMR (300

Scheme 1. Reagents and conditions: (i) NaH, DMF, $PhCH_2Br$, 0–65°C, 2–4 h, (ii) 30% KOH/MeOH, reflux, 1–2 h. (iii) *O*-phenylene diamine, PPA/xylene, 160°C, 4–6 h.

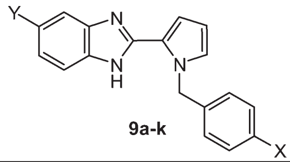


6 7a-d 8a-d 9a-k

9a X = Y = H	9g X = Cl, Y = H
9b X = H, Y = CH_3	9h X = Cl, Y = NO_2
9c X = H, Y = NO_2	9i X = NO_2, Y = H
9d X = H, Y = Cl	9j X = NO_2, Y = CH_3
9e X = CH_3, Y = H	9k X = NO_2, Y = Cl
9f X = CH_3, Y = NO_2	

Table 1

Physical and analytical data of *N*-benzyl-2-pyrrolylbenzimidazoles.



9a-k

Entry	X	Y	Yield (%)	mp (°C)	M. Formula	Analysis (%) (Calc./Found) C	H	N
9a	H	H	77.4	121–123	$C_{18}H_{15}N_3$	79.10	5.53	15.37
						79.14	5.52	15.36
9b	H	CH_3	80.1	133–134	$C_{19}H_{17}N_3$	79.41	5.96	14.62
						79.07	5.92	14.36
9c	H	NO_2	67	151–153	$C_{18}H_{14}N_4O_2$	67.91	4.43	17.60
						67.87	4.52	17.44
9d	H	Cl	79	167–168	$C_{18}H_{14}ClN_3$	70.24	4.58	13.65
						70.07	4.52	13.36
9e	CH_3	H	74	176–177	$C_{19}H_{17}N_3$	79.41	5.96	14.62
						79.15	5.98	14.76
9f	CH_3	NO_2	74.7	204–205	$C_{19}H_{16}N_4O_2$	68.66	4.85	16.86
						68.35	4.98	16.76
9g	Cl	H	78.8	233–235	$C_{18}H_{14}ClN_3$	70.24	4.58	13.65
						70.19	4.52	13.44
9h	Cl	NO_2	61.9	239–241	$C_{18}H_{13}ClN_4O_2$	61.28	3.71	15.88
						61.15	3.88	15.74
9i	NO_2	H	61.6	202–205	$C_{18}H_{14}N_4O_2$	67.91	4.43	17.60
						67.77	4.41	17.63
9j	NO_2	CH_3	63.8	246–248	$C_{19}H_{16}N_4O_2$	68.66	4.85	16.86
						68.35	4.98	16.76
9k	NO_2	Cl	63.6	222–224	$C_{18}H_{13}ClN_4O_2$	61.28	3.71	15.88
						61.15	3.88	15.74

MHz, $CDCl_3$): δ 7.78 (d, J = 7.6 Hz, 2H, $C_{3'}$,$C_{5'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.15–7.22 (m, 3H, $C_{2'}$, $C_{4'}$, $C_{6'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 4.98 (s, 2H, benzyl-CH_2), 3.77 (s, 3H, —$COOCH_3$).

Methyl-N-(4-methylbenzyl)-pyrrole-2-carboxylate (7b). Isolated as light yellow oily liquid. Crystallized from absolute ethanol as white crystalline solid, yield 1.68 g (73.3%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.0–7.4 (m, 4H, $C_{2'}$,$C_{3'}$$C_{5'}$,$C_{6'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-$C_{4'}$H), 5.08 (s, 2H, benzyl-CH_2), 3.72 (s, 3H, —$COOCH_3$), 2.32 (s, 3H, Ar-CH_3).

Methyl-N-(4-chlorobenzyl)-pyrrole-2-carboxylate (7c). Isolated as white solid, yield 1.52 g (60.8%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (d, J = 8.1 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.26 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.20 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-$C_{4'}$H), 5.28 (s, 2H, benzyl-CH_2), 3.67 (s, 3H, —$COOCH_3$).

Methyl-N-(4-nitrobenzyl)-pyrrole-2-carboxylate (7d). Isolated as white solid, yield 1.68 g (64.6%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (d, J = 8.1 Hz, 2H, $C_{3'}$,$C_{5'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.20 (d, 2H, J = 8.4 Hz, $C_{2'}$, $C_{6'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.58 (s, 2H, benzyl-CH_2), 3.77 (s, 3H, —$COOCH_3$).

Preparation of *N*-benzyl-2-pyrrole carboxylic acids (8a–d): general procedure B. A suspension of the *N*-benzyl-pyrrole-2-carboxylates **7a–d** (1 equiv, 10 mmol) was dissolved in MeOH/H_2O (3:1) and 30% KOH (4 equiv). The mixture was heated under reflux for 1–2 h. After cooling to room temperature, the reaction mixture was acidified using 2*N* HCl. The resulting precipitate was filtered and washed with water and petroleum ether to give the desired acids **8a–d**.

N-benzyl-2-pyrrol carboxylic acid (8a). Isolated as white solid, yield 1.92 g (95.5%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.66 (br, s, 1H, —COOH), 7.7 (d, J = 7.6 Hz, 2H, $C_{3'}$,$C_{5'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.25–7.32 (m, 3H, $C_{2'}$, $C_{4'}$, $C_{6'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 4.98 (s, 2H, benzyl-CH_2).

N-(4-methylbenzyl)-2-pyrrole carboxylic acid (8b). Isolated as white solid, yield 2.07 g (96.2%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.78 (br, s, 1H, —COOH), 7.06–7,4 (m, 4H, $C_{2'}$,$C_{3'}$ $C_{5'}$, $C_{6'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 6.38 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.20 (m, 1H, pyrrole-C_4'H), 5.58 (s, 2H, benzyl-CH_2), 2.32 (s, 3H, Ar-CH_3).

N-(4-chlorobenzyl)-2-pyrrole carboxylic acid (8c). Isolated as white solid, yield 2.18 g (93%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.80 (br, s, 1H, —COOH), 7.11 (d, J = 8.1 Hz, 2H, $C_{3'}$,$C_{5'}$ Ar-H), 7.27 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.20 (d, 2H, J = 8.4 Hz, $C_{2'}$, $C_{6'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.21 (m, 1H, pyrrole-C_4'H), 5.52 (s, 2H, benzyl-CH_2).

N-(4-nitrobenzyl)-2-pyrrole carboxylic acid (8d). Isolated as white solid, yield 2.22 g (90.2%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.78 (br, s, 1H, —COOH), 7.96 (d, J = 8.1 Hz, 2H, $C_{3'}$,$C_{5'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.20 (d, 2H, J = 8.4 Hz, $C_{2'}$, $C_{6'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.58 (s, 2H, benzyl-CH_2).

Preparation of *N*-benzylpyrrole-2-benzimidazoles (9a–k); general procedure C. To a suspension of PPA (5.2 g) in xylene (15 mL) at 80°C, 4-substituted-1,2-phenylenediamine (1 equiv, 0.2 mmol) and the corresponding acid **(8a–d)** (1 equiv, 0.2 mmol) were added. The temperature was raised to 145°C and stirred for 4 h. The reaction mixture was cooled and diluted with hot water with stirring. The hot reaction mixture was filtered through a Buchner funnel and solid was isolated. The solid was taken in water (60 mL) and neutralized with $NaHCO_3$. The solid was filtered and washed with hot water (2 × 40 mL) and recrystallized from THF.

2-(N-benzyl-2-pyrrolyl)-benzimidazole (9a). Isolated as white solid, yield 2.06 g (75.4%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.59 (d, 2H, J = 8.7 Hz, Bzi-C_4,C_7—H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.33 (d, 2H, J = 8.7 Hz, Bzi-C_5,C_6—H), 7.02–7.16 (m, 5H, Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.28 (s, 2H, benzyl-CH_2), 5.02 (br, s, 1H, NH).

2-(N-benzyl-2-pyrrolyl)-5-methylbenzimidazole (9b). Isolated as white solid, yield 1.15 g (80.14%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.52 (d, 1H, J = 8.7 Hz, Bzi-C_7H), 7.34 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.13 (s, 1H, Bzi-C_4H), 7.05 (d, 1H, J = 8.7 Hz, Bzi-C_6H), 6.98–7.02 (m, 5H, Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.56 (s, 2H, benzyl-CH_2), 5.11 (br, s, 1H, NH), 2.30 (s, 3H, Bzi-CH_3).

2-(N-benzyl-2-pyrrolyl)-5-nitrobenzimidazole (9c). Isolated as pale yellow solid, yield 1.06 g (67%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.59 (d, 1H, J = 8.7 Hz, Bzi-C_7H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.32 (s, 1H, Bzi-C_4H), 7.23 (d, 1H, J = 8.7 Hz, Bzi-C_6H), 6.98–7.11 (m, 5H, Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.39 (s, 2H, benzyl-CH_2), 5.06 (br, s, 1H, NH).

N-benzyl-2-pyrrole-5-chlorobenzimidazole (9d). Isolated as yellow solid, yield 1.21 g (79%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.59 (d, 1H, J = 8.7 Hz, Bzi-C_7H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.33 (s, 1H, Bzi-C_4H), 7.23 (d, 1H, J = 8.7Hz, Bzi-C_6H), 7.02–7.16 (m, 5H, Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.44 (s, 2H, benzyl-CH_2), 5.11 (br, s, 1H, NH).

2-[N-(4-methylbenzyl)-2-pyrrolyl]-benzimidazole (9e). Isolated as white solid, yield 1.07 g (74%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.61 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.59 (d, 2H, J = 8.7 Hz, Bzi-C_4,C_7—H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.33 (d, 2H, J = 8.7 Hz, Bzi-C_5,C_6—H), 7.22 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.43 (s, 2H, benzyl-CH_2), 5.0 (br, s, 1H, NH), 2.32 (s, 3H, Ar-CH_3).

N-(4-methylbenzyl)-2-pyrrolyl-5-nitrobenzimidazole (9f). Isolated as white solid, yield 1.24 g (74.7%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.64 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.61 (d, 1H, J = 8.7 Hz, Bzi-C_7H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 7.33 (s, 1H, Bzi-C_4H), 7.23 (d, 1H, J = 8.7 Hz, Bzi-C_6H), 7.22 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 5.48 (s, 2H, benzyl-CH_2), 5.04 (br, s, 1H, NH), 2.42 (s, 3H, Ar-CH_3).

N-(4-chlorobenzyl)-2-pyrrolylbenzimidazole (9g). Isolated as white solid, yield 1.21 g (78.8%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.60 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.58 (d, 2H, J = 8.7 Hz, Bzi-C_4,C_7—H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.33 (d, 2H, J = 8.7 Hz, Bzi-C_5,C_6—H), 7.22 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 5.52 (s, 2H, benzyl-CH_2), 5.0 (br, s, 1H, NH).

N-(4-chlorobenzyl)-2-pyrrolyl-5-nitrobenzimidazole (9h). Isolated as white solid, yield 1.09 g (61.9%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.61 (d, 2H, J 7.6 Hz, $C_{2'}$,$C_{6'}$ Ar-H), 7.62 (d, 1H, J = 8.7 Hz, Bzi-C_7H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.31 (d, 1H, J = 8.7 Hz, Bzi-C_4H), 7.23 (d, 1H, J = 8.7 Hz, Bzi-C_6H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-C_4'H), 7.22 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 5.49 (s, 2H, benzyl-CH_2), 5.06 (br, s, 1H, NH).

N-(4-nitrobenzyl)-2-pyrrolylbenzimidazole (9i). Isolated as white solid, yield 0.98 g (61.6%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 (d, 2H, J = 8.4 Hz, $C_{3'}$, $C_{5'}$-Ar-H), 7.59 (d, 2H, J = 8.7 Hz, Bzi-C_4,C_7—H), 7.54 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 7.33 (d, 2H, J = 8.7 Hz, Bzi-C_5,C_6—H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-$C_{4'}$H), 5.35 (s, 2H, benzyl-CH_2), 5.20 (br, s, 1H, NH).

N-(4-nitrobenzyl)-2-pyrrolyl-5-methylbenzimidazole (9j). Isolated as white solid, yield 1.06 g (63.85%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 (d, 2H, J = 8.4 Hz, $C_{3'}$, 7.59 (d, 1H, J = 8.7 Hz, Bzi-C_7H), $C_{5'}$-Ar-H), 7.54 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-$C_{4'}$H), 7.33 (d, 1H, J = 8.7 Hz, Bzi-C_4H), 7.23 (d, 1H, J = 6 Hz, C_6H). 5.44 (s, 2H, benzyl-CH_2), 5.20 (br, s, 1H, NH), 2.51 (s, 3H, Ar-CH_3).

N-(4-nitrobenzyl)-2-pyrrolyl-5-chlorobenzimidazole (9k). Isolated as white solid, yield 1.12 g (63.6%); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 (d, 2H, J = 8.4 Hz, $C_{3'}$,$C_{5'}$-Ar-H), 7.59 (d,1H, J = 8.7 Hz, Bzi-C_7H), 7.54 (d, J 7.6 Hz, 2H, $C_{2'}$,$C_{6'}$ Ar-H), 7.37 (d, 1H, J = 1.5 Hz, pyrrole-$C_{5'}$H), 6.4 (d, 1H, J = 1.5 Hz, pyrrole-$C_{3'}$H), 6.23 (m, 1H, pyrrole-$C_{4'}$H), 7.33 (d, 1H, J = 8.7 Hz, Bzi-C_4H), 7.23 (d, 2H, J = 6 Hz, C_6H). 5.51 (s, 2H, benzyl-CH_2), 5.18 (br, s, 1H, NH).

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