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SYNTHESIS OF 2-(3-FURYL)-1H-BENZIMIDAZOLES FROM 2-PHENACYL-1H-BENZIMIDAZOLES

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C-Alkylation at the active methylene group of 2-phenacyl-1H-benzimidazoles with phenacyl bromides proceeds highly selectively with the formation of the corresponding 1,4-diketones, which on heating with hydrochloric acid are cyclized with the formation of the previously unknown 2-(2,5-diaryl-3-furyl)-1H-benzimidazoles.

Keywords: benzimidazoles, phenacyl bromides, furans, C-alkylation, selectivity, cyclocondensation.

2-(2-Furyl)benzimidazole possesses marked antimicrobial activity and has been intensively subject to structural modification by chemists [1-10]. On the other hand its structural analogs with 3-furyl substituents are little known, only two compounds of this type have been reported. The unsubstituted 2-(3-furyl)-benzimidazole was synthesized from furan-3-carboxylic acid and its derivatives [11, 12] or from furan-3-carbaldehyde [13]. Its derivative substituted with hydroxyl groups at positions 2 and 4 of the furan ring was obtained from the product of C-acylation of (2-benzimidazolyl)acetonitrile with chloroacetyl chloride [14]. It is impossible to exclude that the development of the practical usefulness of 2-(3-furyl)benzimidazoles will aid broadening of the series of their representatives and the development of preparatively convenient and fairly general methods for their synthesis. The chemical part of this problem is solved in the present work mainly by the conversions of 2-phenacyl-1H-benzimidazoles **1a-d**, which have already recommended themselves as convenient reagents in the synthesis of new compounds with a benzimidazole fragment [15, 16].

We have found that compounds **1a-d** are alkylated at the active methylene group by phenacyl bromides **2a-d** with the formation of 1,4-diketo compounds **3a-g**. The obtained products on subsequent heating with hydrochloric acid readily undergo cyclocondensation and give salts of the previously unknown 2-(3-furyl)benzimidazoles **4a-g** (compound **4c** was isolated as the better crystallizing hydrobromide), from which the free bases **5a-g** were obtained after treatment with ammonia.

Such a scheme of synthesis was not obvious. It was shown previously that the direction of the acylation reaction of 2-phenacyl-1H-benzimidazole **1a** depends on the nature of the acylating reagent. With benzoyl chloride dibenzoylation occurs with the participation of the nitrogen atom of the benzimidazole ring and the oxygen atom of the phenacyl fragment [17]. With acetyl chloride monoacetylation occurs at the active methylene group [18]. The selectivity of C-alkylation with phenacyl bromides, as we have established, depends on the reaction conditions and is reduced on increasing the electron-withdrawing properties of the aryl substituents Ar and Ar′ in the initial reactants. On interacting compounds **1a** and **2a** in boiling acetone over potassium carbonate (under conditions typical of alkylating with bromoketones), in addition to the desired

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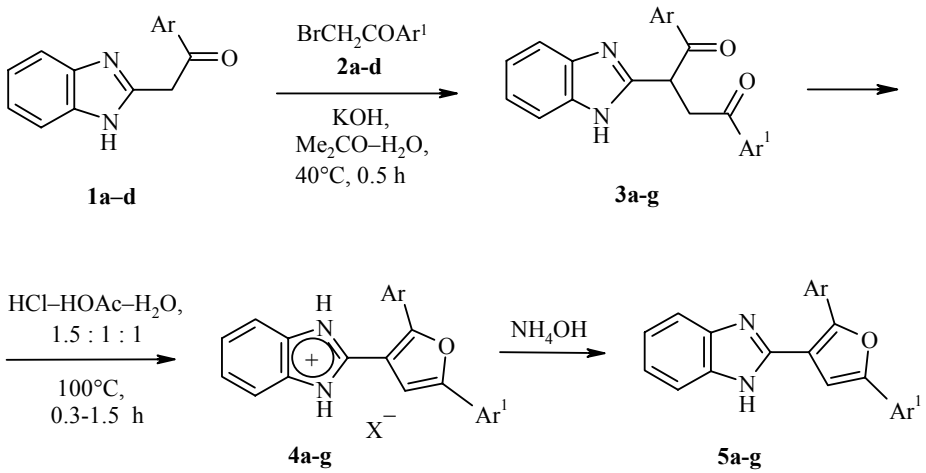
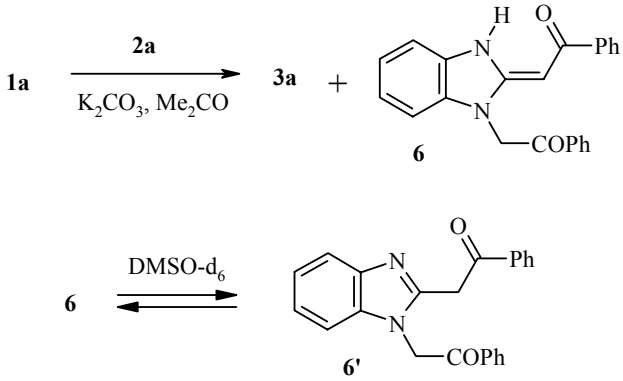


1a–d **3a-g** **4a-g** **5a-g**

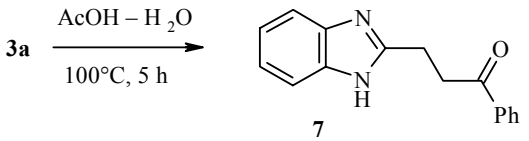
1 a Ar = Ph, **b** Ar = 4-$MeOC_6H_4$, **c** Ar = 3,4,5-$(MeO)_3C_6H_2$, **d** Ar = 4-BrC_6H_4; **2 a** Ar^1 = Ph, **b** Ar^1 = 3,4-$(MeO)_2C_6H_3$, **c** Ar^1 = 4-ClC_6H_4, **d** Ar^1 = 3-$O_2NC_6H_4$; **3–5 a** Ar = Ar^1 = Ph, **b** Ar = 4-$MeOC_6H_4$, Ar^1 = Ph, **c** Ar = 3,4,5-$(MeO)_3C_6H_2$, Ar^1 = Ph, **d** Ar = 4-BrC_6H_4, Ar^1 = Ph, **e** Ar = Ph, Ar^1 = 3,4-$(MeO)_2C_6H_3$, **f** Ar = Ph, Ar^1 = 4-ClC_6H_4, **g** Ar = Ph, Ar^1 = 3-$O_2NC_6H_4$; **4 a**, **b**, **d–g** X = Cl, **c** X = Br

diketone **3a** the product of N-alkylation **6** is also formed, which was successfully isolated, and which, as we found, exists in solution in equilibrium with the tautomeric form **6′**. The reaction becomes highly selective on carrying it out in an aqueous acetone solution of potassium hydroxide (stronger base).



The desired products **3** were isolated from the reaction mixture in high yield (77-85%) in the majority of examples without contamination by products of N-alkylation and purification was not required. An exception was the alkylation of compound **1d** containing the most electron-withdrawing aryl substituent (Ar = 4-BrC_6H_4) in the series of reactants **1** used. The corresponding product **3** precipitated from the reaction mixture together with the product of N-alkylation (^{1}H NMR data) in 91% overall yield, and after purification by crystallization was obtained in the pure state in 63% yield. Interaction of compound **1a** with *m*-nitrophenacyl bromide **2d** readily gave a pure C-alkylation product **3g** in satisfactory yield (50%), which is probably caused by undesired consumption of the highly reactive bromo ketone on interacting with alkali.

The cyclocondensation of diketo compounds of type **3** with closure of the furan ring by a Paal-Knorr reaction scheme occurs on heating in a mixture of hydrochloric and acetic acids in water at volume ratios of 1 : 1.5 : 1 and is complete after 1 h, uncomplicated by side reactions (such as cyclocondensation involving the



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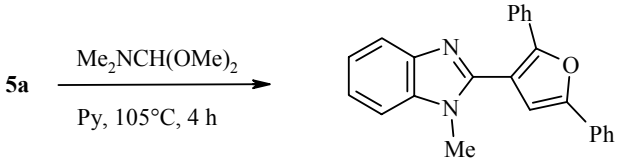

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_{23}H_{18}N_2O_2$	77.88 / 77.95	5.03 / 5.12	7.82 / 7.90	210.5-212	85
3b	$C_{24}H_{20}N_2O_3$	74.77 / 74.98	5.32 / 5.24	7.08 / 7.29	200-201.5	75
3c	$C_{26}H_{24}N_2O_5$	70.12 / 70.26	5.35 / 5.44	6.18 / 6.30	221.5-223	81
3d	$C_{23}H_{17}BrN_2O_2$	63.57 / 63.76	4.06 / 3.95	6.32 / 6.47	225-227.5	63
3e	$C_{25}H_{22}N_2O_4$	72.33 / 72.45	5.47 / 5.35	6.57 / 6.76	210-211.5	77
3f	$C_{23}H_{17}ClN_2O_2$	70.88 / 71.04	4.28 / 4.41	7.06 / 7.20	208-209.5	79
3g	$C_{23}H_{17}N_3O_4$	69.03 / 69.17	4.18 / 4.29	10.37 / 10.52	206.5-208	50
4a	$C_{23}H_{17}ClN_2O$	73.95 / 74.09	4.55 / 4.60	7.42 / 7.51	232-234	94
4b	$C_{24}H_{19}ClN_2O_2$	71.38 / 71.55	4.49 / 4.75	6.72 / 6.95	226.5-228	91
4c	$C_{26}H_{23}BrN_2O_4$	61.38 / 61.55	4.62 / 4.57	5.43 / 5.52	219-221	57
4d	$C_{23}H_{16}BrClN_2O$	61.12 / 61.15	3.45 / 3.57	6.14 / 6.20	271.5-273	91
4e	$C_{25}H_{21}ClN_2O_3$	69.29 / 69.36	4.93 / 4.89	6.58 / 6.47	214-215.5	96
4f	$C_{23}H_{16}Cl_2N_2O$	67.69 / 67.83	3.81 / 3.96	6.72 / 6.88	226.5-228	93
4g	$C_{23}H_{16}ClN_3O_3$	66.02 / 66.11	3.93 / 3.86	9.95 / 10.06	223-224.5	76
5a	$C_{23}H_{16}N_2O$	82.04 / 82.12	4.58 / 4.79	8.27 / 8.33	215-217	95
5b	$C_{24}H_{18}N_2O_2$	78.58 / 78.67	4.83 / 4.95	7.52 / 7.65	228-229.5	96
5c	$C_{26}H_{22}N_2O_4$	73.18 / 73.23	5.12 / 5.20	6.45 / 6.57	225.5-227	96
5d	$C_{23}H_{15}BrN_2O$	66.47 / 66.52	3.72 / 3.64	6.58 / 6.75	271.5-273	91
5e	$C_{25}H_{20}N_2O_3$	75.60 / 75.74	5.12 / 5.08	7.02 / 7.07	215-216.5	92
5f	$C_{23}H_{15}ClN_2O$	74.37 / 74.49	4.14 / 4.08	7.43 / 7.55	187.5-189	93
5g	$C_{23}H_{15}N_3O_3$	72.48 / 72.43	3.94 / 3.96	10.97 / 11.02	259-260.5	91
6	$C_{23}H_{18}N_2O_2$	77.82 / 77.95	5.05 / 5.12	7.86 / 7.90	138.5-140	7
7	$C_{16}H_{14}N_2O$	76.69 / 76.78	5.56 / 5.64	11.08 / 11.19	219-220.5 (229 [17])	86
8	$C_{24}H_{18}N_2O$	82.18 / 82.26	5.07 / 5.18	7.86 / 7.99	153.5-155	85

benzimidazole nitrogen atom). The desired compounds **4** and **5** were successfully isolated in yields mainly exceeding 90%. It should be noted that mineral acid plays a significant role in the reaction. As we have established, cyclization does not take place on heating compound **3a** in a mixture of acetic acid and water, but deacylation with the formation of 2-(β-benzoylethyl)-1H-benzimidazole **7** occurs. The C-alkylation carried out by us is confirmed by this conversion, the more so since product **7** is a compound already described (obtained by the condensation of β-benzoyl-propionic acid with *o*-phenylenediamine [19]). The structure of compound **5a** was also confirmed by a chemical conversion, by methylation at the benzimidazole nitrogen atom with the formation of the corresponding derivative **8**.

The composition and structures of the synthesized compounds were confirmed by data of elemental analysis (Table 1) and ^{1}H NMR spectra (Table 2).

In the ^{1}H NMR spectra of compounds of type **3** the most convincing signals with regard to C-alkylation being accomplished were the three doublets of doublets in the high field region, corresponding to the signal of the protons of the diastereomeric methylene group and the neighboring methine group. On the other hand, in the spectrum of the N-alkylation product **6** there were, corresponding to its structure, singlet signals of the phenacyl methylene (6.12 ppm) and vinyl methine group
(6.36 ppm) , and also corresponding to tautomer **6′** singlet signals of two nonequivalent phenacyl methylene groups (4.71 and 6.02 ppm). According to the ratio of the integral intensities of these signals the content of tautomer **6′** amounted to ~8%. Signals are displayed in approximately in the same regions and in the same ratio of integral intensities in the unpurified product **3d**, together with its signals (see Table 2) and the signals of the contamination by the N-alkylation product (~11%), which disappear after purification of the compound by crystallization. The spectra of compounds of types **4**, **5**, **7**, and **8** have no special features. The signal H-4′ of the furan ring of the desired salts **4** is displayed at 7.55-7.95 and of their bases of type **5** at 7.36-7.82 ppm all regularly displaced towards low field with the increase of electron-withdrawing properties of substituents Ar and Ar′.

2-Phenacyl-1H-benzimidazoles are therefore highly selectively alkylated at the methylene group by phenacyl bromides in an aqueous acetone solution of potassium hydroxide with the formation of the corresponding 1,4-diketo compounds, which are fairly efficient reagents in the synthesis of the previously unknown 2-(2,5-diaryl-3-furyl)-1H-benzimidazoles.

EXPERIMENTAL

A check on the progress of reactions and the purity of the synthesized compounds was carried out by TLC on Silufol UV 254 plates in benzene–ethanol, 9:1, visualizing in UV light. The ^{1}H NMR spectra were recorded on a Bruker Avance DRX 500 (500 MHz) in DMSO-d_6, standard was TMS. Before determining the elemental analysis and spectral investigations of compound **6** it was dried for 24 h at 40-45^{o}C, and the remaining compounds were dried for 4-5 h at 125^{o}C.

2-(1H-Benzimidazol-2-yl)-1,4-diphenylbutane-1,4-dione (3a). Bromo ketone **2a** (0.440 g, 2.2 mmol) was added during 5 min to a stirred solution of compound **1a** (0.472 g, 2 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in water (2 ml) and acetone (4 ml) at 40-45°C. Stirring was continued at the same temperature for 25-30 min and the mixture then left to cool to 15-20°C. The solid was filtered off, washed with water–acetone, 1 : 1, and dried. Product (0.604 g) was obtained, which was used without purification in subsequent conversions.

Compounds 3b-g were obtained analogously from reactants **1a-d** and the appropriate bromo ketone **2a-d**. Compound **3d** was recrystallized from pyridine–ethyl acetate, 1 : 2. IR spectrum, $\nu_{C=O}$, cm^{-1}: 1675 (**3a**), 1680 (**3b**), 1680 (**3c**), 1690 (**3d**), 1675 (**3e**), 1680 (**3f**), 1685 (**3g**).

TABLE 2. ^{1}H NMR Spectra of the Synthesized Compounds

Compound	Chemical shifts, δ, ppm (*J*, Hz)
1	2
3a	3.75 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 4.23 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.64 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.07-7.16 (2H, m, H-5,6); 7.46-7.57 (6H, m, H-4,7 + 4 H_{Ph}-*m*); 7.62 and 7.67 (2 × 1H, two t, *J* = 7.5, 2 H_{Ph}-*m*); 8.03 and 8.10 (2 × 2H, two d, *J* = 8.0, 4 H_{Ph}-*o*); 12.56 (1H, s, NH*)
3b	3.67 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 3.81 (3H, s, H_3CO); 4.24 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.58 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.03 (2H, d, *J* = 7.5, 2 H_{Ar}-*m*); 7.04-7.15 (2H, m, H-5,6); 7.44 (1H, d, *J* = 7.5, H-7); 7.50 (1H, d, *J* = 7.5, H-4); 7.51 (2H, t, *J* = 8.0, 2 H_{Ph}-*m*); 7.66 (1H, t, *J* = 7.5, H_{Ph}-*p*); 8.02 and 8.08 (2 × 2H, two d, *J* = 8.0, 2 H_{Ar}-*o* and 2 H_{Ph}-*o*); 12.54 (1H, s, NH)
3c	3.70 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 3.71 (3H, s, H_3CO-*p*); 3.85 (6H, s, H_3CO-*m*); 4.24 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.65 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.15 (2H, m, H-5,6); 7.42 (2H, s, 2 H_{Ar}); 7.45-7.57 (4H, m, H-4,7 + 2 H_{Ph}-*m*); 7.67 (1H, t, *J* = 7.0, H_{Ph}-*p*); 8.04 (2H, d, *J* = 8.0, 2 H_{Ph}-*o*); 12.58 (1H, s, NH)
3d	3.77 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 4.23 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.60 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.06-7.17 (2H, m, H-5,6); 7.47-7.51 (2H, m, H-4,7); 7.55 (2H, t, *J* = 8.0, H_{Ph}-*m*); 7.67 (1H, t, *J* = 7.0, H_{Ph}-*p*); 7.74 (2H, d, *J* = 8.0, 2 H_{Ar}-*m*); 8.03 (4H, d, *J* = 8.0, 2 H_{Ar}-*o* + 2 H_{Ph}-*o*); 12.56 (1H, s, NH)
3e	3.71 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 3.79 and 3.85 (2 × 3H, two s, 2 H_3CO); 4.19 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.60 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.09 (1H, d, *J* = 7.5, H_{Ar}-5); 7.14 (2H, m, H-5,6); 7.45-7.48 (3H, m, H-4,7 + H_{Ar}-2); 7.52 (2H, t, *J* = 8.0, H_{Ph}-*m*); 7.61 (1H, t, *J* = 7.0, H_{Ph}-*p*); 7.72 (1H, d, *J* = 7.5, H_{Ar}-6); 8.08 (2H, d, *J* = 8.0, 2 H_{Ph}-*o*); 12.55 (1H, s, NH)
3f	3.73 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 4.22 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.62 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.12 (2H, m, H-5,6); 7.48 (2H, m, H-4,7); 7.52 (2H, t, *J* = 8.0, H_{Ph}-*m*); 7.61-7.63 (3H, m, H_{Ph}-*p* + 2 H_{Ar}-*m*); 8.05 and 8.09 (2 × 2H, two d, *J* = 8.5 and *J* = 7.0, 2 H_{Ar}-*o* and 2 H_{Ph}-*o*); 12.57 (1H, s, NH)
3g	3.86 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(A)}$ = 4.0, H_A); 4.30 (1H, dd, $J_{H(A)-H(B)}$ = 18.5, $J_{H-H(B)}$ = 10.0, H_B); 5.67 (1H, dd, $J_{H-H(B)}$ = 10.0, $J_{H-H(A)}$ = 4.0, CH); 7.10-7.15 (2H, m, H-5,6); 7.34-7.49 (2H, m, H-4,7); 7.52 (2H, t, *J* = 8.0, H_{Ph}-*m*); 7.62 (1H, m, H_{Ph}-*p*); 7.85 (1H, t, *J* = 7.0, H_{Ar}-5); 8.10 (2H, d, *J* = 8.0, H_{Ph}-*o*); 8.47 and 8.49 (2×1H, two d, *J* = 8.0, H_{Ar}-4 and H_{Ar}-6); 8.72 (1H, s, H_{Ar}-2); 12.59 (1H, s, NH)
4a	7.42 (1H, t, *J* = 7.5, $H_{5'-Ph}$-*p*); 7.47-7.50 (7H, m, H-5,6 + 2 $H_{5'-Ph}$-*m* + 3 $H_{2'-Ph}$-*p*,-*m*); 7.67 (1H, s, H-4'); 7.75-7.80 (2H, m, H-4,7); 7.57-7.89 (4H, m, 4 H_{Ph}-*o*)
4b	3.83 (3H, s, H_3CO); 7.08 (2H, d, *J* = 7.5, 2 H_{Ar}-*m*); 7.40 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.48-7.54 (4H, m, H-5,6 + 2 H_{Ph}-*m*); 7.62 (1H, s, H-4'); 7.75-7.77 (2H, m, H-4,7); 7.83 (2H, d, *J* = 7.5, 2 H_{Ar}-*o*); 7.88 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*)
4c	3.75 (3H, s, H_3CO-*p*); 3.78 (6H, s, 2 H_3CO-*m*); 7.31 (2H, s, 2 H_{Ar}-*o*); 7.43 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.51-7.56 (4H, m, H-5,6 + 2 H_{Ph}-*m*); 7.61 (1H, s, H-4'); 7.77-7.79 (2H, m, H-4,7); 7.89 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*)
4d	7.43 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.51-7.55 (4H, m, H-5,6 + 2 H_{Ph}-*m*); 7.69 (1H, s, H-4'); 7.71 (2H, d, *J* = 7.5, 2 H_{Ar}-*m*); 7.78-7.80 (2H, m, H-4,7); 7.85-7.89 (4H, m, 2 H_{Ph}-*o* + 2 H_{Ar}-*o*)
4e	3.65 and 3.75 (2 × 3H, two s, 2 H_3CO); 7.09 (1H, d, *J* = 9.0, H_{Ar}-5); 7.38 (1H, s, H_{Ar}-2); 7.42 (1H, d, *J* = 9.0, H_{Ar}-6); 7.46-7.53 (5H, m, H-5,6 + 3 H_{Ph}-*m*,-*p*); 7.55 (1H, s, H-4'), 7.77-7.90 (2H, m, H-4,7); 7.85 (2H, d, *J* = 8.0, 2 H_{Ph}-*o*)
4f	7.50-7.54 (5H, m, H-5,6 + 3 H_{Ph}-*m*,-*p*); 7.60 (2H, d, *J* = 7.5, 2 H_{Ar}-*m*); 7.71 (1H, s, H-4'); 7.78-7.80 (2H, m, H-4,7); 7.87-7.89 (4H, m, 2 H_{Ph}-*o* + 2 H_{Ar}-*o*)
4g	7.51-7.54 (5H, m, H-5,6 + 3 H_{Ph}-*m*,-*p*); 7.78-7.80 (2H, m, H-4,7); 7.82 (1H, m, H_{Ar}-5); 7.91 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*); 7.94 (1H, s, H-4'); 8.22 (1H, d, *J* = 7.5, H_{Ar}-4); 8.30 (1H, d, *J* = 7.5, H_{Ar}-6); 8.58 (1H, s, H_{Ar}-2)
5a	7.22-7.24 (2H, m, H-5,6); 7.36-7.42 (2H, m, 2 H_{Ph}-*p*); 7.47-7.52 (5H, m, 4 H_{Ph}-*m* + H-7); 7.55 (1H, s, H-4'); 7.61 (1H, m, H-4); 7.88 (2H, d, *J* = 9.0, 2 $H_{5'-Ph}$-*o*); 8.26 (2H, d, *J* = 9.0, 2 $H_{2'-Ph}$-*o*); 12.74 (1H, s, NH*)
5b	3.81 (3H, s, H_3CO); 7.05 (2H, d, *J* = 8.5, 2 H_{Ar}-*m*); 7.21 (2H, m, H-5,6); 7.36 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.49-7.50 (3H, m, 2 H_{Ph}-*m* + H-7); 7.51 (1H, s, H-4'); 7.67 (1H, m, H-4); 7.84 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*); 8.28 (2H, d, *J* = 9.0, 2 H_{Ar}-*o*); 12.66 (1H, s, NH)
5c	3.73 (3H, s, H_3CO-*p*); 3.88 (6H, s, 2 H_3CO-*m*); 7.20-7.26 (2H, m, H-5,6); 7.39 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.51-7.55 (3H, m, 2 H_{Ph}-*m* + H-7); 7.59 (1H, s, H-4'); 7.64 (1H, m, H-4); 7.88 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*); 8.01 (2H, s, 2 H_{Ar}-*o*); 12.72 (1H, s, NH)

TABLE 2. (continued)

1	2
5d	7.23 (2H, m, H-5,6); 7.39 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.50-7.53 (3H, m, 2 H_{Ph}-*m* + H-7); 7.57 (1H, s, H-4'); 7.68 (3H, d, *J* = 7.0, H-4 + 2 H_{Ar}-*m*); 7.87 (2H, d, *J* = 7.0, 2 H_{Ph}-*o*); 8.31 (2H, d, *J* = 9.0, 2 H_{Ar}-*o*); 12.76 (1H, s, NH)
5e	3.81 and 3.88 (2 × 3H, two s, 2 H_3CO); 7.09 (1H, d, *J* = 9.0, H_{Ar}-5); 7.19-7.24 (2H, m, H-5,6); 7.36-7.49 (6H, m, 2 H_{Ar}-*o* + 3 H_{Ph}-*m*,-*p* + H-4'); 7.52 (1H, d, *J* = 7.5, H-7); 7.67 (1H, d, *J* = 7.5, H-4); 8.25 (2H, d, *J* = 8.0, 2 H_{Ph}-*o*); 12.70 (1H, s, NH)
5f	7.19-7.25 (2H, m, H-5,6); 7.40 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.46-7.48 (2H, m, H_{Ph}-*m*); 7.52 (1H, d, *J* = 7.5, H-7); 7.57 (2H, d, *J* = 7.0, H_{Ar}-*m*); 7.57 (1H, s, H-4'); 7.68 (1H, d, *J* = 7.5, H-4); 7.88 (2H, d, *J* = 7.5, 2 H_{Ar}-*o*); 8.24 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*); 12.70 (1H, s, NH)
5g	7.23 (2H, m, H-5,6); 7.42 (1H, t, *J* = 7.5, H_{Ph}-*p*); 7.48-7.51 (2H, m, H_{Ph}-*m*); 7.53 (1H, m, H-7); 7.68 (1H, m, H-4); 7.78-7.81 (1H, m, H_{Ar}-5); 7.82 (1H, s, H-4'); 8.19 (1H, d, *J* = 7.5, H_{Ar}-4); 8.27-8.30 (3H, m, H_{Ph}-*o* + H_{Ar}-6); 8.57 (1H, s, H_{Ar}-2); 12.74 (1H, s, NH)
6	4.71 (0.16H, s, CH_2C-6'); 6.02 (0.16H, s, CH_2N-6'); 6.12 (1.84H, s, CH_2); 6.36 (0.92H, s, CH); 7.12-7.22 (2H, m, H-5,6); 7.42-7.55 (4H, m, H-4,7 + 2 H_{Ph}-*m*); 7.61-7.77 (4H, m, 2 H_{Ph}-*m* + 2 H_{Ph}-*p*); 7.92 and 8.03 (1.84H and 0.16H, two d, *J* = 8.0, 2 H_{Ph}-*o* and 2 H_{Ph}-*o*-6'); 8.11 and 8.16 (0.16H and 1.84H, two d, *J* = 8.0, 2 H_{Ph}-*o*-6' and 2 H_{Ph}-*o*); 12.25 (0.92H, s, NH)
7	3.18 (2H, t, *J* = 7.0, H_2C-Het); 3.63 (2H, t, *J* = 7.0, H_2C-CO); 7.09 (2H, m, H-5,6); 7.44 (2H, m, H-4,7); 7.52-7.55 (2H, m, 2 H_{Ph}-*m*); 7.63-7.66 (1H, m, H_{Ph}-*p*); 8.01 (2H, d, *J* = 7.5, 2 H_{Ph}-*o*); 12.23 (1H, s, NH)
8	3.64 (3H, s, 1-CH_3); 7.28 (1H, t, *J* = 7.5, $H_{5'\text{-}Ph}$-*p*); 7.31-7.35 (2H, m, H-5,6); 7.37-7.40 (3H, m, 2 $H_{2'\text{-}Ph}$-*m* + H-7); 7.44 (1H, s, H-4'); 7.49-7.52 (2H, m, $H_{5'\text{-}Ph}$-*m*); 7.61-7.65 (3H, m, 2 $H_{5'\text{-}Ph}$-*o* + $H_{2'\text{-}Ph}$-*p*); 7.71 (1H, d, *J* = 8.5, H-4); 7.91 (2H, d, *J* = 7.5, $H_{2'\text{-}Ph}$-*o*)

*Subjected to deuterium exchange.

2-(3-Furyl-2,5-diphenyl)benzimidazolium Chloride (4a). A mixture of compound **3a** (0.354 g, 1 mmol), glacial acetic acid (1.5 ml), water (1 ml), and concentrated hydrochloric acid (1 ml) was maintained at 100-105°C for 1 h. After cooling the reaction mixture, the solid formed was filtered off, washed with 2-propanol, and dried. Analytically pure product (0.350 g) was obtained.

Compounds **4b-g** were obtained analogously from compounds **3b-g** respectively. To isolate bromide **4c** the reaction mixture was diluted with 48% hydrobromic acid (1 ml) before cooling.

2-(3-Furyl-2,5-diphenyl)-1H-benzimidazole (5a). A mixture of salt **4a** (0.2 g), 20% aqueous ammonia solution (0.5 ml), and pyridine (1.5 ml) was heated to boiling with stirring. Water (4 ml) was added dropwise slowly to the boiling mixture during 2-3 min. After cooling, the solid was filtered off, washed with water, and dried. Analytically pure product (0.17 g) was obtained.

Compounds **5b,d-g** were obtained analogously from compounds **4b,d-g** respectively. Products **5e,f** crystallized better if acetonitrile (2.5 ml) was used as solvent in place of pyridine.

2-[3-Furyl-5-phenyl-2-(3,4,5-trimethoxyphenyl)]-1H-benzimidazole (5c). A mixture of compound **3a** (0.444 g, 1 mmol), glacial acetic acid (1.5 ml), water (1 ml), and concentrated hydrochloric acid (1 ml) was maintained at 100-105°C for 1 h. The reaction mixture was cooled to 40-45°C, diluted with acetone (2 ml) with stirring, and made alkaline with 20% aqueous ammonia solution (5 ml). After cooling, the resulting solid was filtered off, washed with water, and dried. Analytically pure product (0.411 g) was obtained.

2-[(2*E*)-2-Phenacyl-2,3-dihydro-1H-benzimidazol-2-ylidene]-1-benzoylethane (6). A mixture of compound **1a** (1.18 g, 5 mmol), bromo ketone **2a** (1.19 g, 6 mmol), finely powdered potassium carbonate (0.552 g, 4 mmol), and acetone (15 ml) was boiled with stirring for 2 h, then diluted with water (7.5 ml), and left for 2 h slowly cooling to 15°C. The colorless solid compound **3a** (1.26 g, 71%) was filtered off. A second solid

separated from the filtrate left at 15°C for 2 h. The yellow solid was filtered off, washed with acetone–water, 1:1, recrystallized from acetone–water, 2:1, and dried. Pure product **6** (0.132 g) was obtained. IR spectrum, $\nu_{C=O}$, cm^{-1}: 1630, 1690.

2-(β-Benzoylethyl)-1H-benzimidazole (7). A mixture of compound **3a** (0.354 g, 1 mmol), glacial acetic acid (1.5 ml), and water (1 ml) was maintained at 100-105°C for 5 h. The reaction solution was cooled, diluted with acetone (2 ml), and made alkaline by stirring in 20% aqueous ammonia solution (5 ml). The precipitate was filtered off, washed with water, and recrystallized from pyridine–ethanol, 1:1. After drying, product **7** (0.215 g) was obtained. IR spectrum, $\nu_{C=O}$, cm^{-1}: 1680 (lit. 1685 [17]).

2-(3-Furyl-2,5-diphenyl)-1-methyl-1H-benzimidazole (8). A mixture of compound **5a** (0.168 g, 0.5 mmol), DMF dimethylacetal (0.5 ml), and anhydrous pyridine (0.5 ml) was maintained at 105-110°C for 4 h. The reaction solution was diluted with 2-propanol (1 ml) and water (3 ml), and heated with stirring until crystallization began. After cooling, the solid was filtered off, washed with a mixture of 2-propanol–water, 1:1, and dried. Analytically pure product (0.148 g) was obtained.

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