N-Aryl-2-nitrosoanilines as Intermediates in the Two-Step Synthesis of Substituted 1,2-Diarylbenzimidazoles from Simple Nitroarenes

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Abstract: *N*-Aryl-2-nitrosoanilines, easily available from reaction of nitroarenes with anilide anions, undergo base-promoted condensation reaction with substituted benzyl aryl sulfones, furnishing 1,2-diaryl-1*H*-benzimidazoles.

Key words: heterocycles, nitroso group, carbanions, condensation, sulfones, cyclization

Benzimidazoles are heterocyclic compounds of significant importance to medicinal chemistry.[1] Although those 1,2-disubstituted with aryl groups have been relatively less frequently reported, there is noticeable interest in their synthesis due to their potential biological activity and pharmacological applications. For example, they have been included in certain drug discovery programs, such as screening for anti-inflammatory activity[2] or selective ligands for ER-β.[3]

The chemistry of benzimidazoles is covered in several comprehensive reviews.[4] A number of methods reported for the general synthesis of benzimidazoles have been applied to obtain those at 1- and 2-positions disubstituted benzimidazoles, although examples of the synthesis of 1,2-diarylbenzimidazoles are less common. *ortho*-Phenylenediamine derivatives remain the most popular substrates, and two general methods leading to the benzimidazole system have been used. One of them involves the condensation of *N*-arylphenylenediamines with carboxylic acids, or their equivalents, followed by cyclization–dehydratation of the amides formed,[3,5] carried out as a two-step sequence[3,5a–5c] or in a one-pot process with the amide generated in situ.[5d,e] The cyclization step usually occurs under acidic conditions at elevated temperature.

Another common approach involves the condensation of *N*-aryl-*o*-phenylenediamines with aldehydes, followed by oxidative cyclization of the so-formed imines.[6,7] On the other hand, under reductive conditions, *o*-nitroanilines have been used as substrates in direct cyclization reactions with aldehydes.[8]

In most cases, however, the use of N-substituted *ortho*-arylenediamines requires their earlier synthesis from arylamines and nitroarenes bearing fluorine or other good leaving group in the *ortho* position, followed by the reduction of the nitro group. In addition, properly substituted *ortho*-halonitroarenes may be not easily available, and nucleophilic substitution of *ortho*-halogens with arylamines can be difficult, in certain cases.[9]

In recent times, alternative strategies for the synthesis of benzimidazoles have been revealed, which involve an N–C cross-coupling process leading to the formation of the fused imidazole ring. An intramolecular amination of *o*-halo-phenylamidines catalyzed by CuO or cobalt(II) complexes,[10] a CuI/L-proline-catalyzed coupling reaction of primary amines with 2-haloacetanilides,[11] and a tandem amination reaction between 1,2-differentiated dihaloarenes and N-substituted amidines[12] have been applied also for the synthesis of 1,2-diaryl derivatives.

In our studies on the synthesis of polycyclic nitrogen heterocycles from nitroarenes, we explore reactions which involve intermediate formation of σ^H adducts of anionic nucleophiles to the aromatic nitro compounds. Recently, we have described a reaction of nucleophilic substitution of hydrogen in nitroarenes with anilines, in which intramolecular oxidation of σ^H adducts occurs in expense of the nitro group, which in turn is transformed into a nitroso group.[13] The reaction readily takes place *ortho* to the nitro group, leading to variously substituted *N*-aryl-2-nitrosoanilines – stable, easy-to-handle compounds, which are potentially useful intermediates in the synthesis of polycyclic nitrogen heterocycles.

The value of *N*-aryl-2-nitrosoanilines in heterocyclic synthesis consists in their structure, containing two nitrogen functions of opposite reactivity, that is, the nucleophilic aniline group and the electrophilic nitroso group, located in proximity. Furthermore, positions of these groups in the benzene ring are defined towards other substituents, which is essential for regioselectivity of the formation of the new heterocyclic ring.

In this paper, we present the synthesis of 1,2-diaryl-1*H*-benzimidazoles, which takes advantage of the above features of *N*-aryl-2-nitrosoanilines (Scheme 1, Table 1).Together with the one-step method of preparation of the latter,[13] this provides a new way to 1,2-diaryl-1*H*-benzimidazoles, which is one of the shortest, and starts from simple nitroarenes with no leaving group at *ortho* position, required in the majority of other methods.

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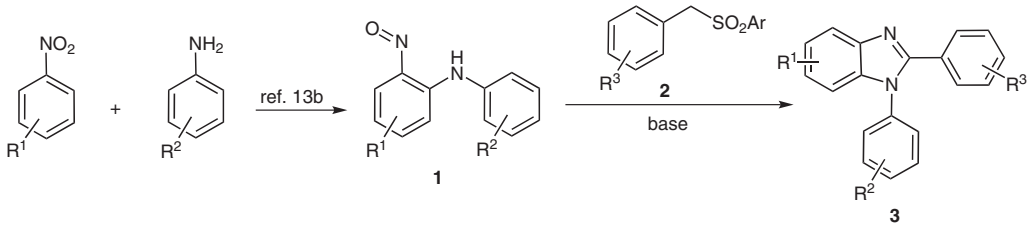


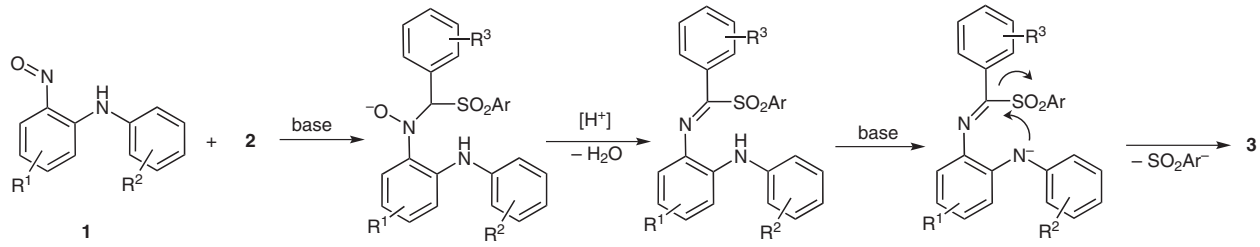
Scheme 1

Table 1 Synthesis of 1,2-Diaryl-1*H*-benzimidazoles **3**

	Nitrosoaniline **1**[a]			Sulfone **2**			Reaction conditions[b]		Benzimidazole **3**[16]	
Entry	R^1	R^2	**1**	Ar	R^3	**2**	Base/solvent	Time (h)[c]	**3**	Yield (%)[d]
1	4-Cl-2-MeO	4-EtO	**1a**	Ph	4-O_2N	**2a**	DBU/DMF[e]	24	**3a**	**42**
2	4-Cl-2-MeO	4-EtO	**1a**	Tol	2-O_2N-5-Cl	**2b**	DBU/DMF[e]	1	**3b**	**72**
3	4-Cl-2-MeO	4-EtO	**1a**	Tol	2-O_2N-5-Cl	**2b**	DBU/MeCN	1	**3b**	**31**
4	4-Cl-2-MeO	4-EtO	**1a**	Tol	2-O_2N-4-Me-5-MeO	**2c**	DBU/DMF	2	**3c**	**38**
5	4-Cl-2-MeO	4-EtO	**1a**	Ph	2-O_2N-4-*t*-Bu	**2d**	DBU/DMF	2	**3d**	**35**
6	4-Cl-2-MeO	4-EtO	**1a**	Tol	8-O_2N-quinoline-7	**2e**	DBU/DMF	2	**3e**	**51**
7	4-MeO	4-Me	**1b**	Ph	3,4-Cl_2	**2f**	DBU/DMF	96	**3f**	**81**
8	4-MeO	4-Me	**1b**	Tol	2-O_2N-5-Cl	**2b**	DBU/DMF	2	**3g**	**87**
9	4-MeO	4-Me	**1b**	Tol	2-O_2N-4-Me-5-MeO	**2c**	DBU/DMF	24	**3h**	**76**
10	4-MeO	4-Me	**1b**	Ph	2-O_2N-4-*t*-Bu	**2d**	DBU/DMF	24	**3i**	**72**
11	4-Cl	4-Cl	**1c**	Ph	3,4-Cl_2	**2f**	DBU/DMF	1	**3j**	**20**
12	4-Cl	4-Cl	**1c**	Tol	2-O_2N-5-Cl	**2b**	Et_3N/DMF	72	**3k**	**60**
13	4-Cl	4-Cl	**1c**	Tol	2-O_2N-5-Cl	**2b**	DBU/DMF	21	**3k**	**13**
14	4-Cl	4-Cl	**1c**	Ph	4-O_2N	**2a**	K_2CO_3/MeCN	6	**3l**	**81**
15	4-MeO	4-Me	**1b**	Tol	H	**2g**	$NaOH_{aq}$/PhMe[f]	1.5	**3m**	**46**

[a] Substituents numbered as in the starting nitroarene and aniline respectively, see Scheme 1.
[b] Except entry 15, procedure A was used.[14,]
[c] Reactions were carried out up to complete conversion of **1** or **2**.
[d] Isolated yields.
[e] No reaction was observed when Et_3N was used instead of DBU.
[f] Two-phase reaction, procedure B.[15]

Most likely, and according to the intended strategy, the reaction of carbanions, generated from substituted benzyl sulfones, with *N*-aryl-2-nitrosoanilines **1** consists of the Ehrlich–Sachs condensation[17] with the nitroso group, followed by a vinylic substitution of the sulfonyl entity with the aniline nucleophile (Scheme 2). Thus, the arylsulfonyl group plays the role of both an elctron-withdrawing group stabilizing the benzylic carbanion and a leaving group in the addition–elimination step constituting the five-membered ring.



Scheme 2

Although nitrosoanilines **1** are powerful electrophiles, they are also strong NH acids, which under basic conditions form anions, lacking their electrophilic activity. The positive result of the reaction could be expected when acidity of both reagents is balanced, and the base used is appropriate to acquire sufficient concentration of the carbanion of **2** and, at the same time, to retain no less than a fraction of the nitrosoaniline **1** neutral. Therefore, only acidic enough benzylic sulfones **2** and rather weak bases could be used in the reaction.

Following the above considerations, a choice of benzylic sulfones substituted with the nitro group in the aromatic ring (**2a**–**e**), and two other, much less acidic (**2f** and **2g**) were subjected to the reaction with a few, differently substituted nitrosoanilines (**1a**–**c**). After a very brief searching, DBU in DMF was chosen as a base/solvent system for most of the experiments.[14] While these reaction conditions were not optimized for individual pairs of reactants, selected reactions were attempted to proceed under different conditions. All reactions were performed at room temperature, up to complete conversion of the starting nitrosoaniline. Although, for that reason, particular reaction times combined with their yields do not reflect directly rates of these reactions, a comparison of the results allows for cautious formulating of some comments.

For nitrosoaniline **1b**, which is the less acidic substrate among being examined, satisfactory results were obtained in the reactions carried out in the DBU/DMF system (entries 7–10), with the rates of the overall reactions following roughly the anticipated acidity of the benzylic sulfones (**2b** > **2c** = ca. **2d** > **2f**). On the other hand, for nitrosoaniline **1c**, assumed as the most acidic one, such relatively strong basic system did not work well (entries 11 and 13). The reactions produced complex mixtures, and low yields of the desired benzimidazoles. A weaker base, such as triethylamine or potassium carbonate in acetonitrile, yielded better results (entries 12 and 14). Apparently, such bases provided low concentration of carbanions of **2**, at the same time as **1c** was not completely deprotonated, thus, suitable for nucleophilic addition.

Intermediate, as to acidity, **1a** reacted easily in the DBU/DMF system, but the yields of the reactions were rather moderate and seem to depend on the acidity of the benzylic sulfones (**2b**, **2e** > **2c**, **2d**). Noteworthy, triethylamine in DMF did not work properly in attempted reactions of **1a** with sulfones **2a** and **2b**, giving not more than traces of the products after 24 hours of the reaction. This suggests that for the reaction of nitrosoaniline **1b** considerably higher concentration of the carbanion than in the case of **1c** is required.

When the less acidic benzyl tolyl sulfone (**2g**) was subjected to the reaction with **1b**, after several attempts with other base/solvent couples, the best yield was obtained in the catalytic two-phase system 50% NaOH/toluene/tetrabutylammonium bromide, according to procedure B (entry 15).[15]

The observations, based on the limited number of results in Table 1, seem to roughly support the predicted relationship between the acidity of both reagents and the observed efficiency of the reactions. However, since the reaction is multistage, also other aspects may have important influence on its course. For example, the rate of the elimination of water molecule from the initial adduct (Scheme 2), supposedly strongly depended on structural factors and reaction conditions, may govern the whole process considerably. Moreover, since more acidic sulfones are precursors of less reactive carbanions, and less acidic nitrosoanilines are believed to be also less electrophilic, the acid/base do not sufficiently explain the actual reaction course, and the results of any particular reaction may be difficult to predict. Apparently, also some side reactions play an important role and could be responsible for the observed low yield of the product despite of fast conversion of **1** (entry 11).

The starting nitrosoarenes **1** as well as benzylic sulfones **2** are easily available. Those of the latter, which are substituted with a nitro group, can be obtained by vicarious nucleophilic substitution of hydrogen (VNS) in appropriate nitroarenes with chloromethyl aryl sulfones.[18] By using the method described here, one can obtain highly substituted 1,2-diaryl-1*H*-benzimidazoles, suitable for further transformations and functionalization.

The presented synthesis of 1,2-diarylbenzimidazoles exhibits several features making it fairly distinctive among the others. The reaction occurs under very mild basic conditions, which may be suitable for reagents with labile, acid-sensitive substituents. Although sometimes prolonged, the reaction is carried out at room temperature. Further advantages of the reaction are clear, when it is considered as a part of the entire two-step synthetic route starting from simple nitroarenes (Scheme 1). Thus, the starting nitroarenes do not need to bear any leaving group, such as halogens, at *ortho* position, so they are much more easily available. Furthermore, there are no reducing or oxidazing agents involved in the synthesis, therefore it is presumably compatible with substrates sensitive to those processes.

The communication is a preliminary account of the new strategy of synthesis of 1,2-disubstituted benzimidazoles. This approach is presently a subject of our effort directed to extend its scope regarding nitrosoarenes and carbanionic reactants of general formula RCH_2Y which could be used as more versatile reagents for the synthesis of 2-substituted derivatives of *N*-arylbenzimidazoles.

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(14) **Procedure A**
To a solution of the nitrosoaniline **1** (0.5 mmol) and the sulfone (0.6 mmol) in a specified solvent (3 mL or 6 mL in the case of K_2CO_3 used as base) DBU (0.3 mL), Et_3N (0.3 mL), or K_2CO_3 (700 mg) was added, according to Table 1, and the mixture was stirred at r.t. for the time specified in Table 1. In the case when K_2CO_3 was used, it was then filtered off. The mixture was poured into 10% HCl aq (ca. 50 mL) and extracted with EtOAc. The extract was washed with H_2O and brine and dried with Na_2SO_4. After evaporation, the crude product mixture was subjected to column chromatography (SiO_2, hexane–EtOAc).

(15) **Procedure B**
A solution of nitrosoaniline **1b** (163 mg, 0.614 mmol) and benzyl tolyl sulfone (184 mg, 0.75 mmol) in toluene (3 mL) was vigorously stirred with 50% NaOH (1 mL) and TBAB (30 mg) at r.t. for 1.5 h. The mixture was then diluted with H_2O (100 mL) and extracted with EtOAc. The extracts were washed with H_2O three times, dried with Na_2SO_4, and evaporated. The mixture was subjected to column chromatography (SiO_2, hexane–EtOAc), and the crude **3m** was recrystallized from EtOAc.

(16) **Analytical Data for the Products 3a–m**

6-Chloro-1-(4-ethoxyphenyl)-4-methoxy-2-(4-nitrophenyl)-1*H*-benzimidazole (3a)
Yellow crystals, mp 211–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.0 Hz, 3 H), 4.03 (s, 3 H), 4.10 (q, *J* = 7.0 Hz, 2 H), 6.74 (d, *J* = 1.8 Hz, 1 H), 6.92 (d, *J* = 1.8 Hz, 1 H), 7.09–7.13 (m, 2 H), 7.38–7.43 (m, 2 H), 7.75–7.79 (m, 2 H), 8.21–8.25 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 56.3, 63.5, 103.2, 105.4, 115.8, 123.6, 127.9, 128.7, 129.2, 130.0, 131.6, 135.6, 139.2, 147.6, 149.0, 151.8, 159.0. MS (EI): *m/z* (%) = 423 (95) [M$^+$], 422 (100), 394 (43), 376 (9), 348 (13). Anal. Calcd for $C_{22}H_{18}O_4N_3Cl$: C, 62.3; H, 4.3; N, 9.9. Found: C, 62.3; H, 4.3; N, 9.8.

6-Chloro-2-(5-chloro-2-nitrophenyl)-1-(4-ethoxyphenyl)-4-methoxy-1*H*-benzimidazole (3b)
Yellow solid, mp 145–148 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.33 (t, *J* = 7.0 Hz, 3 H), 4.00 (s, 3 H), 4.04 (q, *J* = 7.0 Hz, 2 H), 6.84 (d, *J* = 1.8 Hz, 1 H), 6.93 (d, *J* = 1.8 Hz, 1 H), 6.99–7.04 (m, 2 H), 7.23–7.28 (m, 2 H), 7.83 (dd, *J* = 8.7, 2.3 Hz, 1 H), 7.89 (d, *J* = 2.3 Hz, 1 H), 8.09 (d, *J* = 8.7 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.5, 56.3, 63.4, 103.02, 105.3, 115.5, 126.4, 126.5, 126.6, 128.2, 129.0, 131.3, 131.5, 132.7, 137.7, 138.2, 146.9, 147.1, 151.7, 158.7. MS (EI): *m/z* (%) = 459 (70), 457 (100) [M$^+$], 428 (23), 409 (13), 289 (34), 261 (45). HRMS (EI): *m/z* calcd for $C_{22}H_{17}O_4N_3{}^{35}Cl_2$ [M]$^+$: 457.0596; found: 457.0611.

6-Chloro-2-(5-methoxy-4-methyl-2-nitrophenyl)-1-(4-ethoxyphenyl)-4-methoxy-1*H*-benzimidazole (3c)
Creamy powder, mp 175–176 °C (hexane–EtOAc). ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.32 (t, *J* = 7.0 Hz, 3 H), 2.23 (s, 3 H), 3.87 (s, 3 H), 4.00 (s, 3 H), 4.02 (q, *J* = 7.0 Hz, 2 H), 6.81 (d, *J* = 1.7 Hz, 1 H), 6.92 (d, *J* = 1.7 Hz, 1 H), 6.96–6.99 (m, 2 H), 7.20–7.24 (m, 2 H), 7.31 (s, 1 H), 7.94 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.7, 16.1, 56.1, 56.3, 63.7, 103.5, 104.9, 113.7, 115.2, 125.7, 127.1, 127.2, 128.0, 129.5, 129.9, 131.7, 137.9, 140.7, 149.4, 151.7, 158.9, 161.2. MS (EI): *m/z* (%) = 467 (100) [M$^+$], 438 (14), 289 (68), 178 (21). HRMS (EI): *m/z* calcd for $C_{24}H_{22}O_5N_3{}^{35}Cl$ [M]$^+$: 467.1248; found: 467.1256.

6-Chloro-2-(4-*tert*-butyl-2-nitrophenyl)-1-(4-ethoxyphenyl)-4-methoxy-1*H*-benzimidazole (3d)
Yellow powder, mp 162–163 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.18 (t, *J* = 7.1 Hz, 3 H), 1.31 (s, 9 H), 3.99 (s, 3 H), 4.03 (q, *J* = 7.1 Hz, 2 H), 6.81 (d, *J* = 1.8 Hz, 1 H), 6.91 (d, *J* = 1.8 Hz, 1 H), 6.99–7.03 (m, 2 H), 7.25–7.28 (m, 2 H), 7.60 (d, *J* = 8.1 Hz, 1 H), 7.81 (dd, *J* = 8.1, 1.9 Hz, 1 H), 7.98 (d, *J* = 1.9 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.0, 30.5, 35.0, 56.2, 63.4, 103.0, 105.2, 115.4, 121.1, 122.0, 126.9, 128.2, 128.7, 130.3, 131.5, 132.5, 137.9, 148.1, 148.9, 151.5, 154.5, 158.6. MS (EI): *m/z* (%) = 479 (100) [M$^+$], 450 (19), 289 (59) 260 (53). HRMS (EI): *m/z* calcd for $C_{26}H_{26}O_4N_3{}^{35}Cl$ [M]$^+$: 479.1612; found: 479.1606.

7-[6-Chloro-4-methoxy-1-(4-ethoxyphenyl)-1*H*-benzimidazol-2-yl]-8-nitroquinoline (3e)
Pale yellow crystals, mp 127–130 °C (hexane–EtOAc). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.31 (t, *J* = 7.0 Hz, 3 H), 4.02 (q, *J* = 7.0 Hz, 2 H), 4.04 (s, 3 H), 6.88 (d, *J* = 1.7 Hz, 1 H), 6.95 (d, *J* = 1.7 Hz, 1 H), 7.02–7.05 (m, 2 H), 7.33–7.36 (m, 2 H), 7.52 (d, *J* = 8.6 Hz, 1 H), 7.80 (dd, *J* = 8.4, 4.1 Hz, 1 H), 8.15 (d, *J* = 8.6 Hz, 1 H), 8.55 (dd, *J* = 8.4, 1.5 Hz, 1 H), 9.09 (dd, *J* = 4.1, 1.5 Hz, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 14.9, 56.8, 63.9, 103.6, 106.1, 116.0, 123.0, 124.7, 127.3, 127.4, 128.7, 129.2, 130.0, 130.8, 132.1,

137.0, 138.6, 138.7, 146.2, 148.1, 152.2, 154.0, 159.3. MS (EI): *m/z* (%) = 474 (100) [M$^+$], 429 (31), 289 (59), 261 (66), 155 (25). HRMS (EI): *m/z* calcd for $C_{25}H_{19}O_4N_4{}^{35}Cl$ [M]$^+$: 474.1095; found: 474.1089.

2-(3,4-Dichlorophenyl)-6-methoxy-1-(4-methylphenyl)-1*H*-benzimidazole (3f)

Yellow crystals, mp 173–177 °C (hexane–EtOAc). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.42 (s, 3 H), 3.73 (s, 3 H), 6.61 (d, *J* = 2.3 Hz, 1 H), 6.95 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.32–7.36 (m, 3 H), 7.39–7.46 (m, 2 H), 7.62 (d, *J* = 8.4 Hz, 1 H), 7.68 (d, *J* = 8.8 Hz, 1 H), 7.74 (d, *J* = 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.8, 55.5, 93.3, 112.7, 120.2, 127.2, 128.5, 130.4, 130.5, 130.6, 130.7, 131.1, 131.9, 133.4, 136.7, 137.9, 138.7, 148.4, 157.0. MS (EI): *m/z* (%) = 384 (71), 382 (100) [M$^+$], 367 (64), 159 (41). Anal. Calcd for $C_{21}H_{16}ON_2Cl_2$: C, 65.8; H, 4.2; N, 7.3. Found: C, 65.6; H, 4.2; N, 7.3.

2-(5-Chloro-2-nitrophenyl)-6-methoxy-1-(4-methylphenyl)-1*H*-benzimidazole (3g)

Yellow crystals, mp 155–158 °C (hexane–EtOAc). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H), 3.75 (s, 3 H), 6.73 (d, *J* = 2.2 Hz, 1 H), 6.96 (dd, *J* = 8.8, 2.2 Hz, 1 H), 7.22–7.26 (m, 2 H), 7.28–7.34 (m, 2 H), 7.68 (d, *J* = 8.8 Hz, 1 H), 7.80 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.84 (d, *J* = 2.3 Hz, 1 H), 8.06 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.6, 55.6, 93.3, 112.7, 120.4, 126.4, 126.6, 127.1, 130.4, 131.0, 132.1, 132.5, 136.6, 136.9, 137.9, 138.4, 146.2, 147.2, 157.1. MS (EI): *m/z* (%) = 393 (38) [M$^+$], 348 (9), 225 (100), 182 (20). Anal. Calcd for $C_{21}H_{16}N_3O_3Cl$: C, 64.0; H, 4.1; N, 10.7. Found: C, 63.8; H, 4.2; N, 10.6.

6-Methoxy-2-(5-methoxy-4-methyl-2-nitrophenyl)-1-(4-methylphenyl)-1*H*-benzimidazole (3h)

Yellow crystals, mp 200–201 °C (EtOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 2.37 (s, 3 H), 3.80 (s, 3 H), 3.91 (s, 3 H), 6.73 (d, *J* = 2.3 Hz, 1 H), 6.99 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.04–7.08 (m, 3 H), 7.17 (m, 2 H), 7.76 (d, *J* = 8.8 Hz, 1 H), 7.80 (d, *J* = 0.8 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.1, 21.2, 55.9, 56.2, 93.8, 112.5, 113.5, 120.5, 126.0, 126.5, 127.1, 129.4, 130.2, 132.6, 136.9, 137.1, 138.5, 140.8, 148.9, 157.4, 161.2. MS (EI): *m/z* (%) = 403 (50) [M$^+$], 361 (16), 225 (100), 182 (15). Anal. Calcd for $C_{23}H_{21}N_3O_4$: C, 68.5; H, 5.2; N, 10.4. Found: C, 68.4; H, 5.2; N, 10.4.

2-(4-*tert*-Butyl-2-nitrophenyl)-6-methoxy-1-(4-methylphenyl)-1*H*-benzimidazole (3i)

Yellow crystals, mp 184–188 °C (hexane–EtOAc). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.31 (s, 9 H), 2.34 (s, 3 H), 3.75 (s, 3 H), 6.70 (d, *J* = 2.3 Hz, 1 H), 6.94 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.24–7.33 (m, 4 H), 7.54 (d, *J* = 8.1 Hz, 1 H), 7.65 (d, *J* = 8.8 Hz, 1 H), 7.77 (dd, *J* = 8.1, 1.9 Hz, 1 H), 7.96 (d, *J* = 1.9 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.7, 30.5, 35.0, 55.6, 93.4, 112.4, 120.2, 121.0, 122.5, 126.6, 130.1, 130.4, 132.3, 132.5, 136.6, 137.0, 138.2, 147.4, 149.1, 154.2, 156.8. MS (EI): *m/z* (%) = 415 (53) [M$^+$], 370 (17), 225 (100), 182 (13). Anal. Calcd for $C_{25}H_{25}N_3O_4$: C, 72.3; H, 6.1; N, 10.1. Found: C, 72.1; H, 6.2; N, 9.9.

6-Chloro-1-(4-chlorophenyl)-2-(3,4-dichlorophenyl)-1*H*-benzimidazole (3j)

Yellow solid, mp 176–178 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.29 (d, *J* = 2.2 Hz, 1 H), 7.37 (dd, *J* = 8.4, 2.2 Hz, 1 H), 7.38 (dd, *J* = 8.8, 2.2 Hz, 1 H), 7.54–7.58 (m, 2 H), 7.66–7.70 (m, 3 H), 7.79 (d, *J* = 2.2 Hz, 1 H), 7.84 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 111.0, 121.5, 124.0, 128.9, 129.5, 129.9, 130.2, 130.7, 131.2, 131.5, 131.8, 133.2, 134.4, 134.8, 138.1, 141.6, 151.0. MS (EI): *m/z* (%) = 408 (100), 407 (89), 406 (76) [M$^+$], 372 (20), 370 (20), 336 (7). Anal. Calcd for $C_{19}H_{10}N_2Cl_4$: C, 55.9; H, 2.5; N, 6.9. Found: C, 55.9; H, 2.7; N, 6.8.

6-Chloro-1-(4-chlorophenyl)-2-(5-chloro-2-nitrophenyl)-1*H*-benzimidazole (3k)

Pale yellow crystals, mp 148–149 °C (hexane–EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15–7.18 (m, 2 H), 7.27 (d, *J* = 1.9 Hz, 1 H), 7.35 (dd, *J* = 8.6, 1.9 Hz, 1 H), 7.40–7.43 (m, 2 H), 7.58 (dd, *J* = 2.3, 8.8 Hz, 1 H), 7.68 (d, *J* = 2.3 Hz, 1 H), 8.62 (d, *J* = 8.6 Hz, 1 H), 7.99 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.5, 121.5, 124.3, 126.2, 127.2, 128.1, 130.3, 130.4, 131.1, 132.9, 133.0, 135.3, 136.6, 140.1, 141.5, 146.7, 148.4. MS (EI): *m/z* (%) = 419 (24), 417 (25) [M$^+$], 372 (27), 249 (100), 214 (22), 169 (16), 138 (18), 111 (28). HRMS (EI): *m/z* calcd for $C_{19}H_{10}O_2N_3{}^{35}Cl_3$ [M]$^+$: 416.9839; found: 416.9842.

6-Chloro-1-(4-chlorophenyl)-2-(2-nitrophenyl)-1*H*-benzimidazole (3l)

Yellow crystals, mp 274–275 °C (MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 2.0 Hz, 1 H), 7.25–7.29 (m, 2 H), 7.36 (dd, *J* = 8.8, 2.0 Hz, 1 H), 7.53–7.58 (m, 2 H), 7.72–7.76 (m, 2 H), 7.81 (d, *J* = 8.8 Hz, 1 H), 8.18–8.22 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.6, 121.3, 123.7, 124.6, 128.4, 130.1, 130.5, 130.8, 134.3, 135.2, 135.7, 137.7, 141.4, 148.2, 150.3. MS (EI): *m/z* (%) = 383 (100) [M$^+$], 336 (39), 302 (15), 266 (12). HRMS (EI): *m/z* calcd for $C_{19}H_{11}O_2N_3{}^{35}Cl_2$ [M]$^+$: 383.0228; found: 383.0216.

6-Methoxy-1-(4-methylphenyl)-2-phenyl-1*H*-benzimidazole (3m)

Solid, mp 166–167 °C (EtOAc). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.40 (s, 3 H), 3.72 (s, 3 H), 6.61 (d, *J* = 2.4 Hz, 1 H), 6.93 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.28–7.39 (m, 7 H), 7.47–7.50 (m, 2 H), 7.67 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.7, 55.5, 93.4, 112.1, 119.9, 127.2, 128.3, 128.8, 129.1, 130.1,130.5, 133.9, 136.9, 137.8, 138.3, 150.9, 156.6. MS (EI): *m/z* (%) = 314 (100) [M$^+$], 299 (50). Anal. Calcd for $C_{21}H_{18}ON_2$: C, 80.2; H, 5.8; N, 8.9. Found: C, 79.9; H, 5.7; N, 8.9.

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