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Reusable Porphyrinatoiron(III) Complex Supported on Activated Silica as an Efficient Heterogeneous Catalyst for a Facile, One-Pot, Selective Synthesis of 2-Arylbenzimidazole Derivatives in the Presence of Atmospheric Air as a "Green" Oxidant at Ambient Temperature

Hashem Sharghi,*[a] Mohammad Hassan Beyzavi,[a] and Mohammad Mahdi Doroodmand[a]

Keywords: Iron / Porphyrinoids / Benzimidazoles / Heterogeneous catalysis / Activated silica gel / Oxidation

An efficient and highly selective synthesis of 2-arylbenzimidazoles by condensation of a wide range of aryl aldehydes bearing electron-donating or -withdrawing substituents and phenylenediamines in a single pot using a catalytic amount of (*meso*-tetrakis(*o*-chlorophenyl)porphyrinato)iron(III) chloride (5 mol-%) in excellent isolated yields is described. The reactions were performed in the presence of atmospheric air as a "green" oxidant at ambient temperature in ethanol without any additives. To benefit from the recovery and reuse of the catalyst, a new iron(III) porphyrin–silica heterogeneous catalyst was prepared by simple and successful impregnation of (*meso*-tetrakis(*o*-chlorophenyl)porphyrinato)iron(III) chloride onto activated commercial chromatographic silica gel. The silica was modified by treatment with HCl solution followed by NaOH solution, giving rise to the transformation of –O– strained siloxane atoms and silanol–OH groups into terminal negatively charged silanol–O^- groups. The heterogeneous catalyst was characterized by powdered X-ray diffraction (XRD), scanning electronic microscopy (SEM), atomic force microscopy (AFM), thermogravimetry (TG) to analyse for nitrogen adsorption, and Raman and FTIR spectroscopy. Leaching experiments showed that the catalyst is most strongly anchored to the activated support after 10 cycles. T(*o*-Cl)PPFe^{III}–SiO_2 was successfully used for all runs performed by the homogeneous catalyst and exhibited high isolated yields, selectivity, reusability, and the potential for large-scale synthesis. Mechanistically, the high-valent oxidoiron(IV)–porphyrin could be the key intermediate in this efficient and highly selective synthesis of benzimidazole derivatives.

Introduction

The benzimidazole ring is an important pharmacophore in modern drug discovery.[1] Benzimidazole derivatives exhibit significant activity against several viruses such as HIV,[2] herpes (HSV-1),[3] RNA,[4] influenza,[5] and human cytomegalovirus (HCMV).[2a] Substituted benzimidazole derivatives have found commercial applications in several therapeutic areas such as in antiparasitic,[6] antitumor,[7] antimicrobial,[8] and anti-inflammatory[9] agents as well as in antihelminthic agents in veterinarian medicine.[10] Furthermore, benzimidazoles are very important intermediates in organic reactions[11] and also can act as ligands to transition metals for modeling biological systems.[12] Therefore, the preparation of benzimidazoles has gained considerable attention in recent years.[13–15] Despite their importance from pharmacological, industrial, and synthetic points of view, there are only two general methods for the synthesis of 2-substituted benzimidazoles. One is the coupling of *o*-phenylenediamines (*o*-PDs) and carboxylic acids[16] or their derivatives (nitriles, imidates, or orthoesters),[17] which often requires strong acidic conditions such as polyphosphoric acid[18] or mineral acids,[19] PS–PPh_3/CCl_3CN[20] sometimes combined with very high temperatures (i.e., PPA, 180 °C) or the acid-promoted cyclization of *N*-(*N*-arylbenzimidoyl)-1,4-benzoquinoneimines,[21] or the use of microwave irradiation.[22] The other way involves a two-step procedure that includes the oxidative cyclo-dehydrogenation of aniline Schiff bases, which are often generated in situ from the condensation of phenylenediamines and aldehydes. Various oxidative reagents such as nitrobenzene (high-boiling-point oxidant/solvent),[23] 1,4-benzoquinone,[24] DDQ,[25] tetracyanoethylene,[26] benzofuroxan,[27] MnO_2,[28] $Pb(OAc)_4$,[29] Oxone®,[30] $NaHSO_3$,[31] I_2,[32] sulfamic acid,[33] IBD,[34] H_2O_2/HCl,[35] Me_2SBr_2,[36] IL,[37] $Sc(OTf)_3$,[38] $Yb(OTf)_3$,[39] $In(OTf)_3$,[40] and $Na_2S_2O_5$[41] have been employed. Partly due to the availability of a vast number of aldehydes, the latter method has been extensively used. The direct condensation of *o*-aryldiamines and aldehydes at room temperature is less developed.[42–46] However, many of these methods have some drawbacks such as low isolation yields, long reaction times, high reaction temperature, tedious work-up procedures, air-sensitive catalysts, toxic solvents, the

[a] Department of Chemistry, College of Science, Shiraz University,
Shiraz 71454, Iran
Fax: +98-711-2280926
E-mail: shashem@chem.susc.ac.ir
hashemsharghi@gmail.com

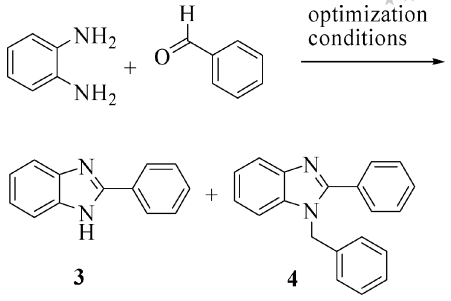
requirement of a stoichiometric or excess amount of oxidants, and the occurrence of several side-reactions. In some cases more than one step is involved in the synthesis of these compounds. Moreover, the main disadvantage of almost all the existing methods is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused. Therefore, the search continues for a better catalyst for the synthesis of benzimidazoles in terms of operational simplicity, reusability, economic viability, and greater selectivity. Metalloporphyrins have been the subject of many studies because these complexes show wide applicability[47] and in the past two decades the biomimetic catalysis of metalloporphyrins has increasingly attracted considerable attention.[48] Metalloporphyrins are chosen as the catalytic platform for several reasons. First, they are important catalysts in both biological and synthetic transformations. Secondly, they can tolerate many functional groups and solvents. Common polar groups such as hydroxy groups, amides, and ethers do not interfere with their catalytic activity. Thirdly, the phenyl groups in tetraphenylporphyrin are nearly perpendicular to the porphyrin plane, and introduction of functional groups with predictable spatial orientation on the phenyl rings is possible. Among them, porphyrinatoiron complexes, an important class of transition-metal complexes, continue to attract considerable attention because of their importance in biology and as catalysts. The roles played by these complexes in electron-transfer processes, metabolic control, transport, and versatile catalytic processes in vitro are surprisingly diverse. These compounds can also promote substrate oxidation by using molecular oxygen as the oxygen atom source[49–51] [Equation (1)]. High-valent oxido-iron–porphyrin complexes (**2**) have been recognized as the active intermediates in shunt cycles,[52] and the mechanism of oxygen-atom transfer from iron to substrates has been the subject of extensive investigation from various points of view, including kinetics,[53] stereoselectivity,[54] molecular rearrangement,[55] and deuterium isotope effects.[56]

$$\underset{\mathbf{1}}{PFe^{III}} + \text{oxidant} \longrightarrow \underset{}{PFe^{III}\text{-oxidant}} \longrightarrow \underset{\mathbf{2}}{PFe^{IV}{=}O} \qquad (1)$$

In this paper, we report a practical, facile, and selective synthesis of 2-arylbenzimidazoles starting from *o*-PDs and aromatic aldehydes in ethanol in the presence of catalytic amounts of porphyrinatoiron(III) in homogeneous and heterogeneous forms with molecular oxygen as the sole "green" oxidant without any additives at ambient temperature.

Results and Discussion

As a part of our ongoing project devoted towards the development of a practical synthesis of heterocyclic molecules of biological interest,[57] we have explored the possibility of synthesizing benzimidazole derivatives using metalloporphyrins as catalyst (Scheme 1).



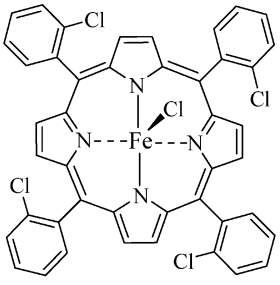
Scheme 1.

In order to establish the optimum conditions for this reaction, initially, various metalloporphyrin complexes were examined in a model reaction between *o*-PD and benzaldehyde in ethanol as solvent at room temperature with atmospheric air used as a "green" oxidant. Porphyrinatoiron(III) was found to be the most effective catalyst in terms of reaction rate, selectivity, and isolated yield of the product (Table 1, entry 1).

Table 1. Investigation of various metalloporphyrins (5 mol-%) in the synthesis of 2-phenylbenzimidazole from *o*-PD (1 mmol) and benzaldehyde (1 mmol) in ethanol at room temperature.

Entry	Catalyst	Yield[a] of product **3** [%]	Time [h]	Yield[a] of byproduct[b] **4** [%]
1	FeTPPCl[c]	92	0.6	0
2	CoTPP(OAc)	80	0.8	0
3	CrTPPCl	82	1	5
4	MgTPP	30	2	10
5	MnTPP(OAc)	65	2	0
6	ZnTPP	30	1.5	5
7	$SnTPPCl_2$	40	2	5
8	NiTPP	35	2	10
9	CuTPP	80	1	0
10	HgTPP	45	1.5	10
11	CdTPP	60	2	20
12	PbTPP	45	2	10
13	$FeCl_3$	20	24	20
14	–[d]	0	24	0

[a] Isolated yield. [b] Byproduct: 2-phenyl-1-phenylmethyl-1*H*-1,3-benzimidazole. [c] TPP = *meso*-tetraphenylporphyrinato dianion. [d] Under the same conditions but without catalyst.



T(*o*-Cl)PPFe^{III}Cl

Then the effect of the structure of various porphyrin ligands was investigated using a number of porphyrinatoiron(III) complexes (Table 2). As shown in Table 2, (entry 2), *meso*-tetrakis(*o*-chlorophenyl)porphyrin–Fe^{III}Cl

Table 2. Investigation of various ligand structures of the porphyrinatoiron complexes (5 mol-%) on the synthesis of 2-phenylbenzimidazole from *o*-PD (1 mmol) and benzaldehyde (1 mmol) in ethanol at room temperature.

Entry	Porphyrinatoiron(III) chlorides	Yield[a] of product **3** [%]	Time [min]	Yield[a] of byproduct[b] **4** [%]
1	*meso*-tetraphenylporphyrin–Fe	92	36	–
2	*meso*-tetrakis(2-chlorophenyl)porphyrin–Fe	97	30	–
3	*meso*-tetrakis(4-hydroxyphenyl)porphyrin–Fe	81	40	–
4	*meso*-tetrakis(3-hydroxyphenyl)porphyrin–Fe	85	40	–
5	*meso*-tetrakis(2-thiophenylphenyl)porphyrin–Fe	60	100	–
6	*meso*-tetrakis(9-anthracyl)porphyrin–Fe	60	120	–
7	*meso*-tetrakis(2-hydroxynaphthyl)porphyrin–Fe	75	40	–
8	*meso*-tetrakis(2,6-dichlorophenyl)porphyrin–Fe	95	40	–

[a] Isolated yield. [b] Byproduct = 2-phenyl-1-phenylmethyl-1*H*-1,3-benzimidazole.

[T(*o*-Cl)PPFe^{III}Cl] proved to be the most suitable catalyst and sterically crowded *meso*-tetrakis(9-anthracyl)porphyrin–Fe^{III}Cl the least reactive complex (entry 6).

During our optimization studies, various solvents were examined and it was found that the solvent plays a significant role in terms of reaction rate, isolated yield, and selectivity (Table 3). Ethanol clearly stands out as the solvent of choice with its fast reaction rate, high yield, selectivity, cheapness, and environmental acceptability.

Table 3. Investigation of the effect of various solvents on the synthesis of 2-phenylbenzimidazole from *o*-PD (1 mmol), benzaldehyde (1 mmol), and T(*o*-Cl)PPFe^{III}Cl (5 mol-%) at room temperature.

Entry	Solvent	Yield[a] of product **3** [%]	Time [h]	Yield[a] of byproduct[b] **4** [%]
1	acetonitrile	10	2	5
2	dioxane	15	2	10
3	ethanol	97	0.5	0
4	diethyl ether	10	2	5
5	chloroform	40	3	15
6	dmf	5	2	5
7	xylene	30	2	10
8	water	10	2	5
9	THF	25	2	10
10	DMSO	15	5	10

[a] Isolated yield. [b] Byproduct = 2-phenyl-1-phenylmethyl-1*H*-1,3-benzimidazole.

It should be noted that the optimal catalyst loading in the synthesis of 2-arylbenzimidazole is at a concentration of 5 mol-%. The product yields and catalyst TONs obtained under the optimal operating parameters are shown in Figure 1. The plot of the yield of 2-arylbenzimidazole versus the amount of catalyst has a turning point at a catalyst concentration of 20 mol-%. The self-polymerization of the porphyrinatoiron might account for this phenomenon.[58,59]

Using the optimized conditions, the effect of oxygen was investigated. Instead of a static atmosphere of air, a continuous flow of O_2 was bubbled through the reaction mixture, but the reaction rate was not accelerated showing that the O_2 dissolved in solvent and adsorbed by the surface of the reaction mixture is sufficient for an efficient reaction. Then, as a continuation of our study, the homogeneous catalyst was immobilized on a solid support in an effort to develop a heterogeneous catalyst that could be recovered and reused.

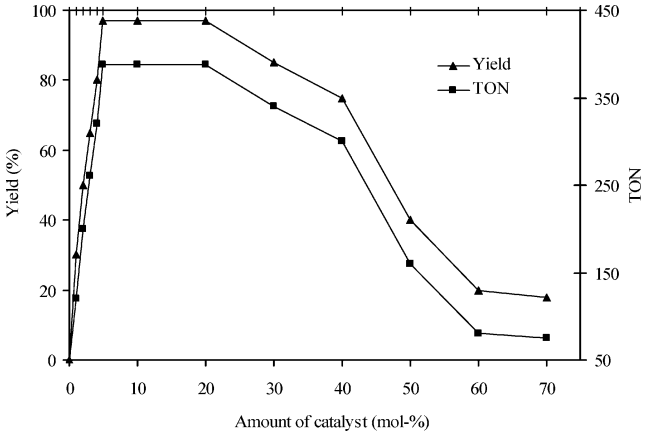


Figure 1. Plots of the yield of 2-phenylbenzimidazole and the TON versus the amount of T(*o*-Cl)PPFe^{III}Cl used as catalyst in the reaction of *o*-PD (1 mmol) and benzaldehyde (1 mmol) in ethanol at room temperature.

Immobilization of metalloporphyrin catalysts on insoluble organic and inorganic supports appears to be a good way to render them practicable and to improve their stability, selectivity, and the control of their reactivity through the microenvironment created by the support. There are also other advantages relating to the ease of catalyst removal from the reaction mixture and subsequent reuse. Supported metalloporphyrins also provide a physical separation of active sites, thus minimizing catalyst self-destruction and the dimerization of unhindered metalloporphyrins. Furthermore, in the era of "environmental amity chemistry", heterogeneous catalytic oxidation reactions have become an important target as these processes are used in industry, helping to minimize the problems of industrial waste treatment and disposal.[60–64]

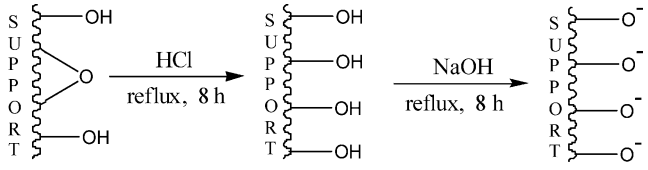
Five general methods have been used to anchor metalloporphyrins onto solid surfaces, namely, covalent binding,[65] coordinative binding,[66] ionic interactions,[67] intercalation,[67b,68] and entrapment.[69] Each of these has potential advantages depending on factors such as the strength of the attachment to the support, the ease of preparation, the general applicability to different metalloporphyrins, stability, and selectivity.

The use of inorganic solids has some advantages over other types of supports. The chemical and thermal stability

of inorganic supports make them compatible with the widest range of reagents and experimental conditions. Also, mechanical resistance of the solids makes these inorganic particles less prone to attrition due to stirring and solvent attack during their use in a chemical reactor under continuous operation. Another advantage relates to their inertness in oxidizing media. Besides the advantages mentioned above, silica has a high surface area (5–800 $m^2 g^{-1}$) compared with other inorganic supports, ranking these materials at the top of the list of high-surface area solids.[70] Because of its high surface area and porosity, silica gel is a common sorbent for the chromatographic separation of organic compounds. Furthermore, silica gel has found increasing application in organic synthesis.[71] Its surface contains silanol–OH groups, which are mainly responsible for adsorption, and –O– strained siloxane atoms.[72]

As T(*o*-Cl)PPFe^{III}Cl proved to be the best catalyst among the porphyrinatoiron complexes for benzimidazole synthesis, we set out to prepare a new heterogeneous catalyst by simple impregnation of activated commercial chromatographic silica gel with T(*o*-Cl)PPFe^{III}Cl.

In order to activate the silica gel, before direct use of the silica, its surface was modified by heating it at reflux with 37% hydrochloric acid to increase the terminal silanol–OH groups by transformation of the strained –O–siloxane atoms into these functional groups.[73] Then the support was heated at reflux with an aqueous solution of 0.04 M NaOH to change the terminal silanol–OH groups into negatively charged silanol–O^- groups (Scheme 2) to produce the desired activated silica to be impregnated by porphyrinatoiron(III) and thus form the heterogeneous catalyst (see the Exp. Sect. for details).



Scheme 2. Activation of chromatography-grade silica with aqueous HCl followed by treatment with NaOH solution.

In order to examine the effect of the first step of the activation (refluxing with hydrochloric acid), a standard basic solution of NaOH (0.093 M, pH = 12.97) was prepared and added to silica treated with HCl and stirred for 24 hours in a sealed flask; a decrease in the pH of the aqueous solution from 12.97 to 10.56 was observed. The same procedure was used with unactivated silica. Calculations showed that the number of terminal silanol–OH in silica activated by HCl increases 13.18% in comparison with unactivated silica.

Preparation of the Silica Gel Supported T(*o*-Cl)PPFe^{III} Catalyst

Immobilization of the catalyst was undertaken by stirring a refluxing ethanolic solution of T(*o*-Cl)PPFe^{III}Cl with activated silica. The anchoring process was monitored by UV/

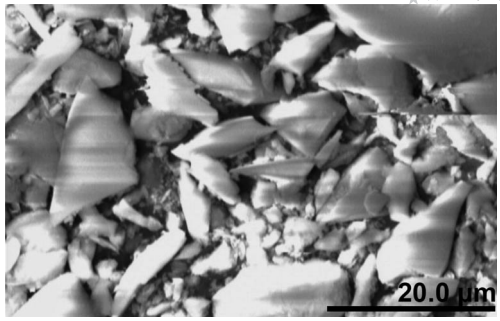


Figure 2. SEM image of T(*o*-Cl)PPFe^{III} supported on activated silica gel.

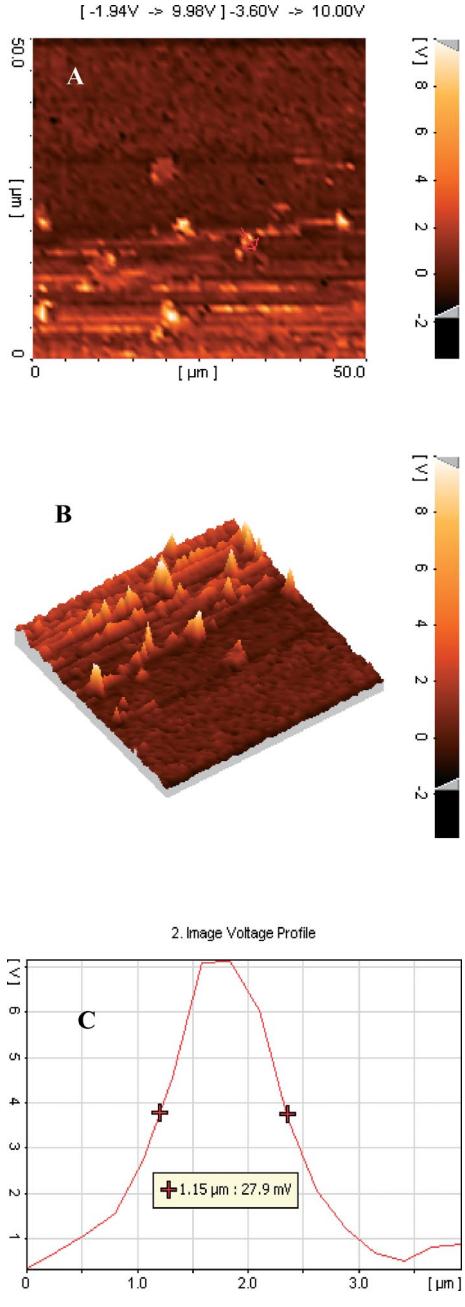


Figure 3. AFM Images of T(*o*-Cl)PPFe^{III} supported on activated silica gel. Part A: 2D image, part B: 3D image, C: voltage profile.

Vis spectrophotometry and a decrease in intensity of the Soret band at λ_{max} = 412.2 nm (ethanol) of the supernatant solution was observed. Removal of the solvent by rotary evaporation at 50 °C afforded the heterogeneous Fe catalyst as a pale-brown solid (see the Exp. Sect. for details). The FT-Raman analysis of T(*o*-Cl)PPFe^{III}–SiO_2 showed that the ν_{Si-O} stretches at 795 and 877 cm^{-1} and also the variations in wavenumber are related to the straightening of the tetrahedral chains and the corresponding changes in the Si–O bond lengths and O–Si–O angles caused by substitution of Na for Fe, which leads to broad bands. To evaluate the Fe content, the supported catalyst was treated with concentrated HCl and concentrated nitric acid to digest the metal complex and then analyzed by inductively coupled plasma (ICP) analysis. The Fe content was determined to be 0.600% w/w (see Exp. Sect. for details).

To obtain a visual image of the supported catalyst, scanning electron microscopy (SEM) and atomic force microscopy (AFM) of T(*o*-Cl)PPFe^{III}–SiO_2 were carried out. According to the SEM (Figure 2) and AFM images (Figure 3, see parts A and B), very different channels of porphyrinatoiron particles are dispersed molecularly on the silicone substrate.

The diameters of the complex were estimated to be several microns according to the voltage profile image of Fe catalysts (Figure 3, C). From the width of the band at half height of the peak, the diameter of particles was estimated to be about 1.15 μm.

The XRD pattern of the heterogeneous catalyst (Figure 4) shows a single-phase complex of a porphyrinatoiron structure and the amorphous nature of the SiO_2 substrate. The strongest peaks of the XRD pattern correspond to the SiO_2 plane with the other peaks indexed as the (220), (311), (400), (422), (511), and (440) planes of the porphyrinatoiron complex.

The FTIR transmission spectrum of the supported catalyst shows bands at around 1072, 802, and 470 cm^{-1}, which are presumably due to asymmetric stretching (ν_{as}), symmetric stretching (ν_s), and bending modes of Si–O–Si, respectively. The weak band at 1002 cm^{-1} is due to the nonbridging oxygen (Si–O) stretching vibration of silanol. In Figure 5, the band at 570.9 cm^{-1} is associated with the stretching vibration of Fe–O differentiated from the absorption of activated silica as substrate. Note that the intensity of the Fe–O band strongly depends on the weight percentage of Fe^{3+} in the T(*o*-Cl)PPFe^{III} sample. This implies that T(*o*-Cl)PPFe^{III} is well developed in this phase.[74] This result strongly supports the observed XRD patterns and shows that the porphyrinatoiron(III) complex is immobilized on the support by electrostatic interaction between the negatively charged surface of the activated inorganic solid and the positively electrically charged complex through the formation of a coordinative bond with the metal. To prove this kind of interaction, the T(*o*-Cl)PP ligand was similarly loaded onto the activated silica. A loading of about only 15% was achieved compared with that of T(*o*-Cl)PPFe^{III}Cl, which indicates the important role of the metal.

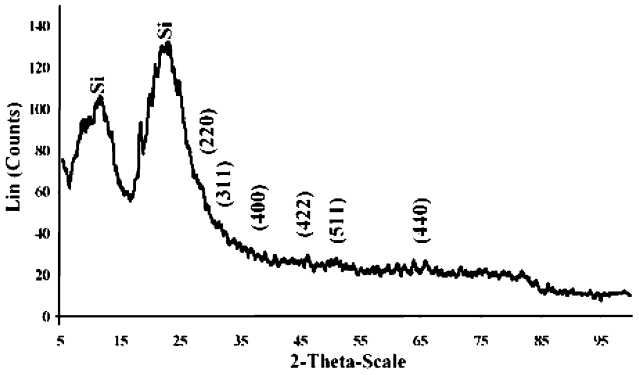


Figure 4. XRD pattern of T(*o*-Cl)PPFe^{III} supported on activated silica gel.

The adsorption behavior of nitrogen gas on both activated silica gel and on activated silica gel impregnated with T(*o*-Cl)PPFe^{III} was investigated by thermogravimetric analysis (TGA) under nitrogen (Figure 6). The results show that support of the Fe complex on activated silica gel reduces the adsorption of nitrogen gas by about 0.07 wt.-%.

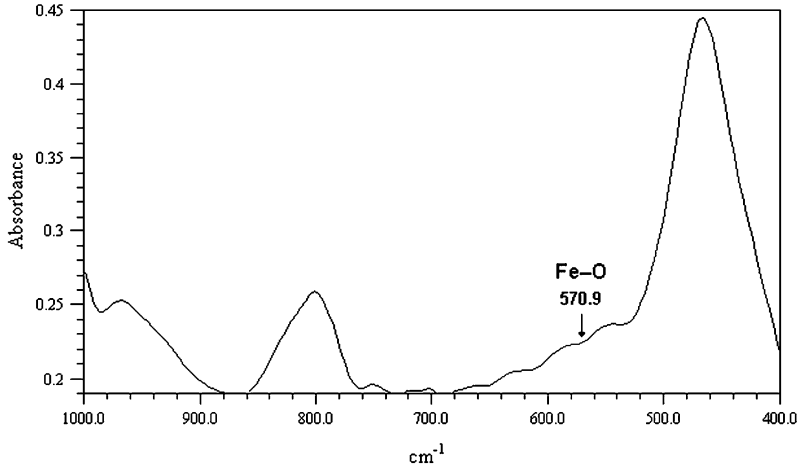


Figure 5. The FTIR spectrum of T(*o*-Cl)PPFe^{III}–SiO_2 differentiated from activated silica as substrate.

From this value it is estimated that the activated surface of silica gel is reduced by about 0.56 cm^3 when T(*o*-Cl)-$PPFe^{III}Cl$ is supported.

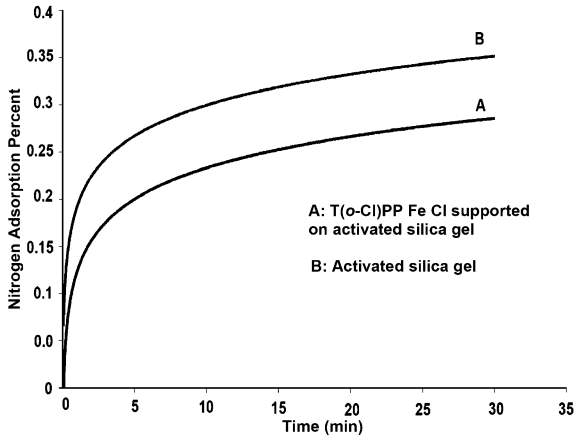
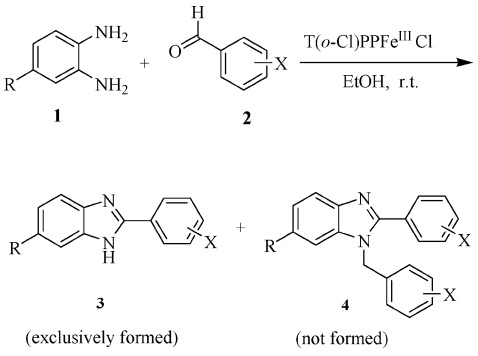


Figure 6. Comparison of adsorption of nitrogen on activated silica gel (B) and T(*o*-Cl)$PPFe^{III}$ supported on activated silica gel (A) at 25 °C.

The principle advantages of this immobilization technique include the absence of any complexity in the immobilization process, the widespread availability of silica inorganic supports (chromatography grade silica), the lack of any laborious need to alter the catalyst to facilitate the immobilization, the rapidity and experimental simplicity of the procedure by which the immobilization can be completed, and the fact that the purity of the immobilized complex can be better assessed.

Homogeneous and Heterogeneous Catalytic Benzimidazole Synthesis

Finally, under the optimized conditions, the condensation of *o*-PDs and aryl aldehydes was carried out in the presence of homogeneous and heterogeneous catalysts at room temperature and a ratio of 1:1 of *o*-PDs and aryl aldehydes was found to be optimum to give exclusively the corresponding 2-aryl-substituted benzimidazoles **3** in high yields (Scheme 3).



Scheme 3. Condensation of *o*-PDs and aromatic aldehydes under the optimized conditions.

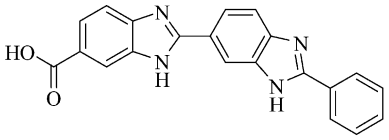
To test the generality and versatility of this procedure in the direct synthesis of 2-substituted benzimidazoles via the formation of Schiff bases, we examined the reactions of a number of substituted aromatic aldehydes and *o*-PDs under the optimized conditions in the presence of both homogeneous and heterogeneous catalysts. As shown in Table 4, aldehydes bearing electron-donating or -withdrawing substit-

Table 4. Selective synthesis of 2-arylbenzimidazoles from various *o*-PDs (1.0 mmol) and benzaldehydes (1.0 mmol) in the presence of homogeneous and heterogeneous T(*o*-Cl)$PPFe^{III}$ catalyst (5 mol-%) in ethanol solvent at room temperature.

Entry	*o*-PDs (R)	Aldehydes	Compound **3**	Method A[a]		Method B[b]	
				Yield[c] of product **3** [%]	Time [min]	Yield[c] of product **3** [%]	Time [h]
1	–	benzaldehyde	**3a**	97	30	95	1.5
2	–	2-chlorobenzaldehyde	**3b**	96	45	91	1.8
3	–	3-chlorobenzaldehyde	**3c**	95	55	90	2.0
4	–	4-chlorobenzaldehyde	**3d**	94	55	90	2.2
5	–	4-methylbenzaldehyde	**3e**	95	55	91	2.0
6	–	4-methoxybenzaldehyde	**3f**	95	90	92	2.6
7	–	4-isopropylbenzaldehyde	**3g**	95	80	90	2.5
8	–	4-cyanobenzaldehyde	**3h**	94	190	88	4.0
9	–	2-hydroxybenzaldehyde	**3i**	94	220	89	3.8
10	–	3-hydroxybenzaldehyde	**3j**	94	105	87	3.0
11	–	4-hydroxybenzaldehyde	**3k**	95	115	90	3.2
12	–	2,6-dichlorobenzaldehyde	**3l**	91	95	85	3.0
13	–	3-nitrobenzaldehyde	**3m**	92	230	88	4.5
14	–	4-nitrobenzaldehyde	**3n**	90	300	86	4.9
15	–	2-naphthaldehyde	**3o**	96	65	91	2.1
16	–	2-thiophenecarbaldehyde	**3p**	93	105	85	2.8
17	–	2-pyridinecarbaldehyde	**3q**	91	50	86	2.0
18	–	2-furancarbaldehyde	**3r**	90	110	84	2.9
19	CH_3	4-methylbenzaldehyde	**3s**	90	60	85	2.4
20	COC_6H_5	4-methylbenzaldehyde	**3t**	90	75	89	2.7
21	CO_2H	benzaldehyde	**3u**	90	180	86	3.4

[a] Reaction performed in the presence of homogeneous T(*o*-Cl)$PPFe^{III}Cl$. [b] Reaction performed in the presence of heterogeneous T(*o*-Cl)$PPFe^{III}$–SiO_2 containing 5 mol-% of catalyst (see the Exp. Sect. for details). [c] Isolated yield.

uents gave the desired benzimidazoles in high yields with both catalysts. Heteroaryl aldehydes, such as 2-thienyl, 2-pyridyl, acid-sensitive 2-furyl (Table 4, entries 16–18), and the sterically hindered 2-naphthaldehyde (Table 4, entry 15) tolerated these mild conditions. The method tolerates other functional groups such as hydroxy, methoxy, halides, nitro, and nitrile on the aryl aldehyde (Table 4, entries 2–14) and methyl, carbonyl, and carboxylic acid on *o*-PD (Table 4, entries 19–21). As expected, the carboxylic substituent on the *o*-PD did not participate in the reaction, resulting in the clean formation of 2-phenylbenzimidazole-6-carboxylic acid (Table 4, entry 21) with none of the dimeric derivative **5**, potentially formed from the participation of the carboxylic acid substituent, detected.



5

The reactivity of the heterogeneous catalyst in comparison with the homogeneous catalyst is slightly reduced, presumably because of its limited solubility in reaction media, but the selectivity remained unchanged (Table 4). The silica-supported porphyrinatoiron(III) complex was recovered by filtration after each experiment and could be reused for the benzimdazole synthesis in more than 10 successive reactions. After 10 consecutive reactions, the recovered T(*o*-Cl)-PPFe^{III}–SiO_2 was found to contain 0.586% (w/w) of Fe based on ICP analysis, which is comparable to the initial value of 0.600 % (w/w), indicative of less than 2% leaching during the reaction cycles (see the Exp. Sect. for details).

As shown in Figure 7, the catalytic activity of T(*o*-Cl)-PPFe^{III}–SiO_2 remained largely unchanged for 10 successive runs. The heterogeneous catalyst was also recycled up to 20 times without any significant reduction in activity in the synthesis of benzimidazoles in ethanol as solvent with a total of 388 turnovers being achieved.

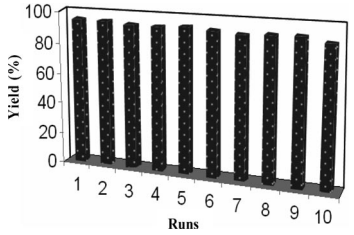
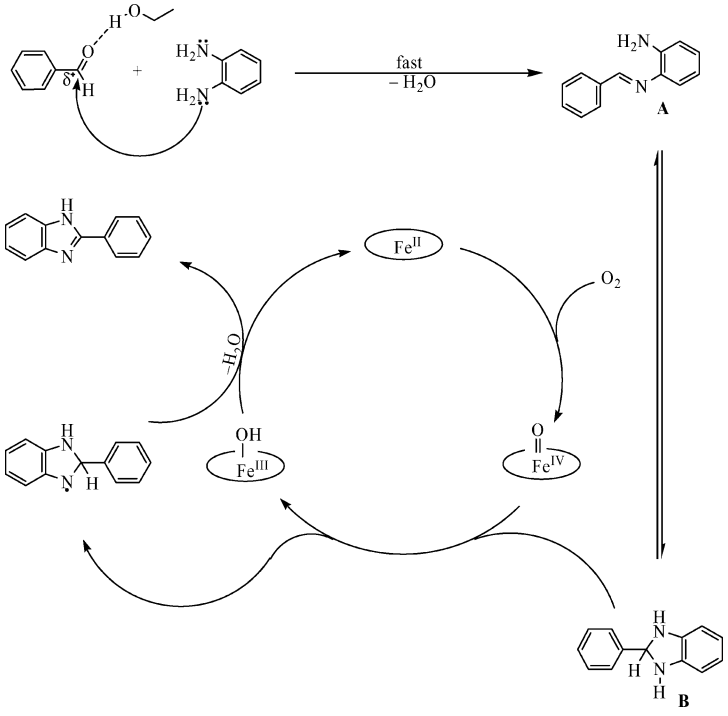


Figure 7. Recyclability of T(*o*-Cl)PPFe^{III}–SiO_2 in the synthesis of 2-phenylbenzimidazole.

Note that the anchoring of T(*o*-Cl)PPFe^{III}Cl onto unactivated silica or silica activated by only HCl resulted in 42 and 34% leaching, respectively, after one run, which shows the importance of the whole activation process for the successful immobilization of the catalyst.

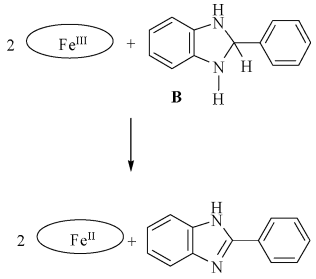
To assess the feasibility of applying this method on a preparative scale, we coupled *o*-PD with benzaldehyde on a 100 mmol scale in the presence of the heterogeneous catalyst. As expected, the reaction proceeded similarly to the smaller-scale reaction (Table 4, entry 1), and the desired 2-phenylbenzimidazole was obtained in 92% isolated yield in 1.8 h. Continuous bubbling of O_2 through the reaction mixture instead of the static atmosphere of air did not accelerate the reaction rate, as mentioned above for the smaller-scale reaction.



Scheme 4. Proposed mechanism for the porphyrinatoiron-catalyzed synthesis of benzimidazole.

To explore the mechanism of the reaction, aldehyde consumption was monitored by GC analysis and we found that the Schiff base is formed very rapidly (within the first 3 minutes of the beginning of reaction) and the rate-determining step (RDS) was found to be the oxidative cyclization step. Furthermore, we found that it is not necessary to prepare Schiff bases in advance. We can directly use equimolar amounts of *o*-PDs and aromatic aldehydes as starting materials in the presence of porphyrinatoiron(III) complexes, which should be synthetically useful and practical.

A plausible pathway for the formation of benzimidazoles involves the formation of intermediate Schiff bases **A** from which the cyclic adduct **B** (hydrobenzimidazole) is produced by intramolecular participation of the *o*-amino group (Scheme 4).[35,75] In the initial step of the catalytic reaction, we propose that T(*o*-Cl)PPFe^{III}Cl is reduced to the T(*o*-Cl)PPFe^{II} state by an outer-sphere electron transfer from hydrobenzimidazole **B** to the porphyrin periphery (a peripheral π transfer). Both the N–H and α-C–H positions in compound **B** are essential for this reduction (Scheme 5).[76] To validate our proposal, the reaction progress was monitored from the beginning of the reaction by UV/Vis spectrophotometry under strictly anaerobic conditions and the T(*o*-Cl)PPFe^{III} Soret band at λ_{max} = 412.2 nm (ethanol) was observed to gradually shift to the corresponding T(*o*-Cl)-PPFe^{II} Soret band at λ_{max} = 427.7 nm (ethanol) in several minutes (Figure 8). In 1984, Balch and co-workers identified the irreversible oxidation of (TMP)Fe^{II} (TMP = *meso*-tetramesitylporphyrin dianion) by molecular oxygen at a low temperature[77] and confirmed the previous proposal.[78] The oxygen-bound porphyrinatoiron complex reacts with another T(*o*-Cl)PPFe^{II} to give the μ-peroxo complex. Subsequent O–O bond cleavage gives the high-valent oxo iron(IV) porphyrin complex, T(*o*-Cl)PPFe^{IV}=O (Scheme 6). The subsequent oxidative dehydrogenation of adduct **B** in the presence of the porphyrin–iron(IV)-oxido complex affords the desired 2-arylbenzimidazoles (Scheme 4).



Scheme 5.

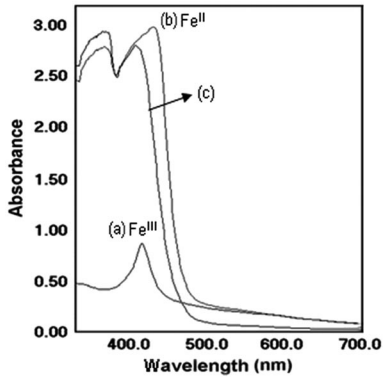
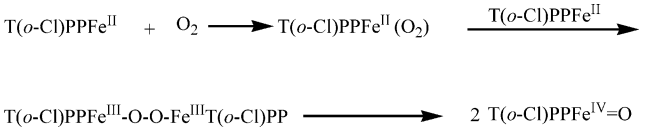


Figure 8. The UV/Vis spectra change from (a) T(*o*-Cl)PPFe^{III} Cl (λ_{max} = 412.2 nm) to (b) T(*o*-Cl)PPFe^{II}Cl (λ_{max} = 427.7 nm) due to electron transfer under strictly anaerobic conditions in the presence of *o*-PD and benzaldehyde in a 1:1 ratio in ethanol as solvent at 25 °C (t = 10 min). (c) Absorbtion spectrum of intermediate Schiff base **A** (λ_{max} = 404.9 nm) separately prepared in the absence of the catalyst in ethanol solvent. Spectrum (c) overlays spectra (a) and (b).



Scheme 6.

Conclusions

In summary, we have presented the first example of a porphyrinatoiron-catalyzed synthesis of benzimidazoles under mild conditions. This new and efficient catalytic method provides a protocol that enables the synthesis of 2-arylbenzimidazoles in a regioselectively pure form while displaying good functional group tolerance. The advantage of this procedure is the employment of atmospheric air as the oxidant. No toxic reagent(s) or byproduct(s) was involved and no laborious purifications were necessary. This procedure is ideally suited to automated applications because the entire synthetic sequence can be carried out at room temperature in the presence of a reusable heterogeneous catalyst. These conditions are also environmentally friendly, cost effective, and possess high generality, which makes our methodology suitable for industrialization as a valid contribution to the existing processes in the field of benzimidazole synthesis, an important class of heterocycles.

Experimental Section

General: NMR spectra were recorded with a Bruker Avance DPX-250 spectrometer (^{1}H NMR 250 MHz and ^{13}C NMR 62.9 MHz) in pure deuteriated solvents with tetramethylsilane (TMS) as the internal standard. Scanning electron micrographs were obtained by SEM (SEM, XL-30 FEG SEM, Philips, at 20 KV). An atomic forced microscope (AFM, DME-SPM, version 2.0.0.9) was also used to obtain AFM images. Spectroscopic methods including Raman spectrometry (Thermo Nicolet AlmegaY dispersive, Raman Spectrometer) and X-ray diffraction (XRD, D8, Advance, Bruker, axs) data were used to characterize the heterogeneous catalyst. TGA of the samples was performed with a laboratory-made TGA instrument. Infrared spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Metal contents were obtained with an ICP analyzer (Varian, vista-pro). Mass spectra were determined with a Shimadzu GCMS-QP 1000 EX instrument at 70 or 20 eV. Melting points were determined in open capillary tubes in a Buchi-535 circulating oil melting point apparatus. UV/Vis spectra were

obtained with an Ultrospec 3000 UV/Vis spectrometer. Elemental analyses were performed with a Thermo Finnigan CHNS-O 1112 series analyzer. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel coated (PolyGram SILG/UV_{254}) plates or by GC with a Shimadzu Gas Chromatograph GC-10A instrument with a flame-ionization detector using a column of 15% carbowax 20 M chromosorb-W acid washed 60–80 mesh. Column chromatography was carried out on short columns of silica gel 60 (70–230 mesh) in glass columns (2–3 cm diameter) using 15–30 gram of silica gel per gram of the crude mixture. Chemicals were either prepared in our laboratories or purchased from Fluka, Aldrich, or Merck.

Preparation of Activated Silica Gel: Silica gel 60 (5.00 g, 0.063–0.200 mm, 70–230 mesh ASTM, CAS No. 60740, Fluka) was heated at reflux with 37% hydrochloric acid (30 mL) for 8 h to change the –O– strained siloxane atoms into terminal silanol–OH groups. Then the silica was thoroughly washed with diionized water until the pH of the eluent reached 6. As the final step, the silica was heated at reflux with an aqueous solution of 0.04 M NaOH (30 mL) for 8 h to transform the terminal silanol–OH groups into negatively charged silanol–O^- groups. Then it was washed with dionized water until a constant pH 8 to afford a white solid powder that was dried at 110 °C in an oven overnight under vacuum.

Preparation of the Silica-Supported T(*o*-Cl)PPFe^{III} Catalyst: Immobilization of the catalyst was undertaken by stirring a refluxing ethanolic solution (15 mL) of T(*o*-Cl)PPFe^{III} (0.10 g) with activated silica (1.00 g) for 8 h. The anchoring process was monitored by UV/Vis spectrophotometry and a decrease in the intensity of the Soret band at λ_{max} = 412.2 nm (ethanol) of supernatant solution was observed. Removal of the solvent by rotary evaporation at 50 °C afforded the heterogeneous T(*o*-Cl)PPFe^{III}–SiO_2 catalyst as a pale-brown solid. In order to remove any physisorbed complex, the resulting heterogeneous catalyst was purified by Soxhlet extraction with ethanol for 8 h.

General Procedure for the Synthesis of 2-Substituted Benzimidazoles in the Presence of a Catalytic Amount of T(*o*-Cl)PPFe^{III}–SiO_2 and Recycling of the Heterogeneous Catalyst: The gel-supported T(*o*-Cl)PPFe^{III} catalyst was subjected to 10 successive reuses under the reaction conditions: For each reaction, *o*-PD (1 mmol) and aryl aldehyde (1 mmol) was stirred in EtOH (96%, 5 mL) in the presence of the heterogeneous catalyst (5 mol-%, 0.470 g) at room temperature. According to the ICP analysis, the Fe content in the heterogeneous catalyst was determined to be 0.600% (w/w). Therefore, each gram of heterogeneous catalyst includes 0.000107 mmol of iron or porphyrinatoiron complex. For 1 mmol of reactants, 0.05 mmol of catalyst is needed, which is equal to 0.470 g of the heterogeneous catalyst. The reactions were monitored by TLC using *n*-hexane/ethyl acetate (8:1). After the reaction was complete the whole reaction mixture was centrifuged and the supernatant solution was decanted to separate the catalyst, which was washed several times with ethanol. The reaction vessel containing the heterogeneous catalyst was recharged with *o*-PD, aryl aldehyde, and ethanol for another reaction run. The combined supernatant and organic washings were purified by silica gel column chromatography employing *n*-hexane/ethyl acetate (8:1) as the eluent.

General Procedure for the Synthesis of *meso*-Tetrakis(*o*-chlorophenyl)porphyrin: Our recent methods for the synthesis of *meso*-tetraarylporphyrins were used.[79] A standard reaction was performed in a 150-mL three-necked round-bottomed flask fitted with a septum port, a reflux condenser, and a gas inlet port. The inlet port consisted of a glass disk immersed in solution with nitrogen flow rates maintained at about 2 mL/min. The flask was charged with distilled CH_2Cl_2 (100 mL), aryl aldehyde (1 mmol), and pyrrole (0.07 mL, 1 mmol). The resulting solution was magnetically stirred at room temperature. After stirring the solution for 5–10 min, an appropriate amount of CF_3SO_2Cl (0.1 mL, 1 mmol) was added through a syringe. After 1 h, the yield of the porphyrinogen was a maximum. Then the gas inlet line was switched to filtered house air and the mixture was aerated for 4 h (39 °C). During this time, the mixture became dark purple, and the porphyrinogen under aerobic oxidation was converted into the product. The solution was concentrated by rotary evaporation and purified by chromatography (silica gel; with CH_2Cl_2/petroleum ether, 1:1) to give the product in 35% yield.

Preparation of [*meso*-Tetrakis(*o*-chlorophenyl)porphyrinato]iron(III) Chloride: A three-necked round-bottomed flask equipped with a thermometer, reflux condenser, and magnetic force stirrer was charged with DMF (20 mL), T(*o*-Cl)PP (0.27 mmol), and anhydrous $FeCl_3$ (0.30 mmol). The mixture was stirred under reflux for 2 h at 165 °C. TLC revealed the complete disappearance of the starting material. Deionized water (20 mL) and 10% HCl (30 mL) were added to the cooled mixture, and a crystalline product formed. After overnight deposition, followed by filtration and drying in a vacuum, the crude product (180 mg) was obtained. This was dissolved in CH_2Cl_2 and purified by column chromatography (neutral Al_2O_3, CH_2Cl_2 as eluent), and T(*o*-Cl)PPFe^{III}(Cl) was obtained as a powder (160 mg). Other metalloporphyrin complexes were prepared by reported procedures, and their spectroscopic and physical data were compared with those reported in the literature.[80]

General Procedure for the Synthesis of 2-Substituted Benzimidazoles in the Presence of a Catalytic Amount of the T(*o*-Cl)PPFe^{III}Cl Complex: For each reaction, *o*-PD (1 mmol) and aryl aldehyde (1 mmol) were stirred in EtOH (5 mL) in the presence of catalyst (5 mol-%) at room temperature. The reactions were monitored by TLC using *n*-hexane/ethyl acetate (8:1). After completion of the reaction the solvent was evaporated to give the crude product, which was purified by silica gel column chromatography employing *n*-hexane/ethyl acetate (8:1) as the eluent.

All the benzimidazoles produced were characterized in detail by IR, ^1H and ^{13}C NMR, mass spectroscopy, and elemental analysis.

2-Phenyl-1*H*-benzimidazole (3a): Colorless solid; 97% yield (0.188 g). M.p. 290–292 °C (ref.[81] m.p. 292 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3444 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 250 MHz): δ = 7.14–7.25 (m, 2 H), 7.44–7.61 (m, 5 H), 8.20 (d, J = 7.2 Hz, 2 H), 12.94 (s, 1 H) ppm. ^{13}C NMR ([D_6]DMSO, 62.9 MHz): δ = 122.1, 126.4, 128.4, 128.9, 129.2, 129.8, 130.1, 151.2 ppm. MS: *m*/*z* (%) = 194 (97.4) $[M]^+$, 149 (45.6), 115 (20.2), 97 (27.2), 73 (46.5), 57 (100.0). $C_{13}H_{10}N_2$ (194.235): C 80.39, H 5.19, N 14.42; found C 80.30, H 5.25, N 14.39.

2-(2-Chlorophenyl)-1*H*-benzimidazole (3b): Colorless solid; 96% yield (0.219 g). M.p. 233–234 °C (ref.[81] m.p. 234 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3445 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 250 MHz): δ = 7.20–7.24 (m, 2 H), 7.48–7.51 (m, 2 H), 7.54–7.68 (m, 3 H), 7.89–7.93 (m, 1 H), 12.74 (s, 1 H) ppm. ^{13}C NMR ([D_6]DMSO, 62.9 MHz): δ = 111.7, 119.0, 121.7, 122.7, 127.3, 129.9, 130.3, 131.1, 131.6, 132.0, 134.6, 143.1, 149.1 ppm. MS: *m*/*z* (%) = 230 (2.3) $[M + 2]^+$, 229 (13.5) $[M + 1]^+$, 228 (44.6) $[M]^+$, 167 (24.2), 149 (68.5), 129 (20.4), 112 (19.2), 91 (41.2), 57 (100.0). $C_{13}H_9ClN_2$ (228.681): C 68.28, H 3.97, N 12.25; found C 68.31, H 4.07, N 12.20.

2-(3-Chlorophenyl)-1*H*-benzimidazole (3c): Colorless solid; 95% yield (0.217 g). M.p. 230–232 °C. IR (KBr): $\tilde{\nu}$ = 1623 (C=N), 3445

(NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.21 (m, 2 H), 7.49–7.64 (m, 4 H), 8.13 (dd, J_1 = 6.6, J_2 = 1.8 Hz, 1 H), 8.21 (s, 1 H), 13.04 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 111.5, 119.0, 122.0, 122.9, 125, 126, 129.5, 130.9, 132.1, 133.7, 143.5, 149.7 ppm. MS: *m*/*z* (%) = 230 (16.1) $[M + 2]^+$, 229 (25.0) $[M + 1]^+$, 228 (38.6) $[M]^+$, 167 (20.5), 149 (62.8), 111 (19.6), 94 (99.8), 71 (37.3), 55 (100.0). $C_{13}H_9ClN_2$ (228.681): C 68.28, H 3.97, N 12.25; found C 68.21, H 4.09, N 12.18.

2-(4-Chlorophenyl)-1*H*-benzimidazole (3d): Colorless solid; 94% yield (0.214 g). M.p. 292–293 °C (ref.[81] m.p. 292 °C). IR (KBr): $\tilde{\nu}$ = 1626 (C=N), 3445 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.18–7.21 (m, 2 H), 7.60 (m, 4 H), 8.17 (d, J = 8.6 Hz, 2 H), 12.99 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 111.4, 118.9, 121.9, 122.7, 128.1, 129, 134.5 150.1 ppm. MS: *m*/*z* (%) = 230 (21.1) $[M + 2]^+$, 229 (36.3) $[M + 1]^+$, 228 (54.9) $[M]^+$, 193 (13.5), 167 (7.0), 149 (25.0), 129 (11.1), 111 (15.4), 85 (33.2), 57 (100.0). $C_{13}H_9ClN_2$ (228.681): C 68.28, H 3.97, N 12.25; found C 68.23, H 4.05, N 12.24.

2-(4-Methylphenyl)-1*H*-benzimidazole (3e): Colorless solid; 95% yield (0.197 g). M.p. 270–272 °C (ref.[82] m.p. 270–272 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3649 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 2.35 (s, 3 H), 7.15–7.20 (m, 2 H), 7.33 (d, J = 8.1 Hz, 2 H), 7.46–7.56 (m, 2 H), 8.07 (d, J = 8.1 Hz, 2 H), 12.84 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 20.9, 121.9, 126.3, 127.4, 128.9, 129.4, 139.5, 151.3 ppm. MS: *m*/*z* (%) = 208 (66.5) $[M]^+$, 149 (49.1), 111 (18.0), 83 (44.9), 57 (100.0). $C_{14}H_{12}N_2$ (208.262): C 80.74, H 5.81, N 13.45; found C 80.69, H 5.90, N 13.38.

2-(4-Methoxyphenyl)-1*H*-benzimidazole (3f): Colorless solid; 95% yield (0.213 g). M.p. 226 °C (ref.[83] m.p. 226–227 °C). IR (KBr): $\tilde{\nu}$ = 1612 (C=N), 3422 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 3.78 (s, 3 H), 7.10 (d, J = 8.8 Hz, 2 H), 7.16 (q, J = 3.01 Hz, 2 H), 7.50 (m, 2 H), 8.12 (d, J = 8.8 Hz, 2 H), 12.76 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 55.2, 111.0, 114.3, 118.4, 121.5, 122.0, 122.6, 128.0, 151.3, 160.5 ppm. MS: *m*/*z* (%) = 225 (86.4) $[M + 1]^+$, 224 (92.4) $[M]^+$, 210 (51.8), 182 (51.0), 149 (30.9), 129 (17.8), 97 (30.4), 69 (100.0). $C_{14}H_{12}N_2O$ (224.261): C 74.98, H 5.39, N 12.49; found C 74.93, H 5.42, N 12.45.

2-(4-Isopropylphenyl)-1*H*-benzimidazole (3g): Colorless solid; 95% yield (0.224 g). M.p. 250–251 °C. IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3417 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 1.22 (d, J = 6.9 Hz, 6 H), 2.93 (m, 1 H), 7.17 (m, 2 H), 7.40 (d, J = 8.15 Hz, 2 H), 7.51–7.62 (m, 2 H), 8.10 (d, J = 8.2 Hz, 2 H), 12.83 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 23.6, 33.3, 111.2, 118.6, 121.5, 122.3, 126.4, 127.7, 150.3, 151.3 ppm. MS: *m*/*z* (%) = 237 (40.1) $[M + 1]^+$, 236 (67.3) $[M]^+$, 221 (100.0), 194 (11.6), 110 (17.6), 92 (29.5), 65 (31.2). $C_{16}H_{16}N_2$ (236.316): C 81.32, H 6.82, N 11.85; found C 81.25, H 6.90, N 11.78.

4-(1*H*-Benzimidazol-2-yl)benzonitrile (3h): Colorless solid; 94% yield (0.206 g). M.p. 262 °C (ref.[82] m.p. 261–262 °C). IR (KBr): $\tilde{\nu}$ = 1612 (C=N), 2230 (CN) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.22–7.24 (m, 2 H), 7.50–7.70 (m, 2 H) 7.97 (d, J = 8.3 Hz, 2 H), 8.31 (d, J = 8.3 Hz, 2 H), 13.17 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 62.9 MHz): δ = 111.8, 118.5, 119.3, 122.2, 123.2, 126.4, 126.9, 132.9, 134.2, 149.3 ppm. MS: *m*/*z* (%) = 220 (9.7) $[M + 1]^+$, 219 (14.1) $[M]^+$, 149 (18.6), 97 (19.6), 69 (100.0), 57 (82.1). $C_{14}H_9N_3$ (219.245): C 76.70, H 4.14, N 19.17; found C 76.63, H 4.21, N 19.11.

2-(1*H*-Benzimidazol-2-yl)phenol (3i): Yellow solid; 94% yield (0.197 g). M.p. 240–242 °C (ref.[81] m.p. 242 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3247 (OH, NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 6.97–7.04 (m, 2 H), 7.25–7.45 (m, 3 H), 7.63–7.67 (m, 2 H), 8.02 (d, J = 7.8 Hz, 1 H), 13.07 (s, 2 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 111.5, 112.5, 117.1, 117.9, 119.1, 122.4, 123.2, 126.1, 131.7, 151.6, 157.9 ppm. MS: *m*/*z* (%) = 211 (60.5) $[M + 1]^+$, 210 (84.1) $[M]^+$, 181 (43.2), 149 (52.7), 129 (16.8), 94 (42.3), 73 (39.5), 57 (100.0). $C_{13}H_{10}N_2O$ (210.234): C 74.27, H 4.79, N 13.33; found C 74.24, H 4.82, N 13.28.

3-(1*H*-Benzimidazol-2-yl)phenol (3j): Colorless solid; 94% yield (0.197 g). M.p. 182–183 °C (ref.[84] m.p. 181–184 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3261 (OH, NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 6.86–6.89 (m, 1 H), 7.16–7.19 (m, 2 H), 7.32 (t, J = 8.1 Hz, 1 H), 7.55–7.58 (m, 4 H), 9.81 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 112.6, 117.0, 117.2, 122.1, 129.6, 131.2, 151.4, 157.7 ppm. MS: *m*/*z* (%) = 212 (1.5) $[M + 2]^+$, 211 (8.2) $[M + 1]^+$, 210 (14.6) $[M]^+$, 150 (9.9), 137 (15.2), 111 (19.0), 97 (38.6), 83 (56.4), 70 (23.7), 55 (100.0) $C_{13}H_{10}N_2O$ (210.234): C 74.27, H 4.79, N 13.33; found C 74.19, H 4.85, N 13.32.

4-(1*H*-Benzimidazol-2-yl)phenol (3k): Pale-yellow solid; 95% yield (0.199 g). M.p. 254–255 °C (ref.[85] m.p. 254.1–256.6 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3256 (OH, NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 6.93 (dd, J_1 = 8.5, J_2 = 1.2 Hz, 2 H), 7.10–7.22 (m, 2 H), 7.52–7.53 (m, 2 H), 8.02 (d, J = 8.6 Hz, 2 H), 10.07 (s, 1 H), 12.65 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 115.7, 121.0, 121.6, 128.1, 151.8, 159.1 ppm. MS: *m*/*z* (%) = 211 (55.2) $[M + 1]^+$, 210 (100.0) $[M]^+$, 181 (24.8), 105 (20.9), 64 (26.4). $C_{13}H_{10}N_2O$ (210.234): C 74.27, H 4.79, N 13.33; found C 74.19, H 4.85, N 13.32.

2-(2,6-Dichlorophenyl)-1*H*-1,3-benzimidazole (3l): Colorless solid; 91% yield (0.239 g). M.p. 279 °C. IR (KBr): $\tilde{\nu}$ = 1627 (C=N), 3447 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 7.11–7.30 (m, 7 H), 7.54 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 115.4, 122.2, 128.3, 130.4, 132.4, 135.0, 137.0, 146.6 ppm. MS: *m*/*z* (%) = 265 (7.0) $[M + 2]^+$, 263 (100.0) $[M]^+$, 228 (58.0), 193 (71.0). $C_{13}H_8Cl_2N_2$: C 59.34, H 3.06, N 10.65; found C 59.16, H 3.15, N 10.63.

2-(3-Nitrophenyl)-1*H*-benzimidazole (3m): Pale-yellow solid; 92% yield (0.219 g). M.p. 206–207 °C (ref.[86] m.p. 207–208 °C). IR (KBr): $\tilde{\nu}$ = 1346, 1516 (NO_2), 1620 (C=N), 3368 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.21 (m, 2 H), 7.61 (m, 2 H), 7.74–7.84 (m, 1 H), 8.23–8.32 (m, 1 H), 8.52–8.57 (m, 1 H), 8.95 (s, 1 H), 13.24 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 116.0, 120.8, 122.7, 124.2, 130.6, 131.6, 132.4, 136.9, 148.3, 149.0 ppm. MS: *m*/*z* (%) = 239 (3.3) $[M]^+$, 209 (14.4), 167 (10.5), 149 (25.4), 129 (13.9), 111 (12.7), 84 (29.7), 55 (100.0). $C_{13}H_9N_3O_2$ (239.232): C 65.27, H 3.79, N 17.56; found C 65.22, H 3.83, N 17.49.

2-(4-Nitrophenyl)-1*H*-benzimidazole (3n): Yellow solid; 90% yield (0.215 g). M.p.312–314 °C (ref.[81] m.p. 316 °C). IR (KBr): $\tilde{\nu}$ = 1338, 1516 (NO_2), 1620 (C=N), 3421 (NH) cm^{-1}. ^1H NMR ([D$_6$]-DMSO, 250 MHz): δ = 7.22–7.26 (m, 2 H), 7.62 (m, 2 H), 8.38 (m, 4 H), 13.27 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 111.7, 119.3, 122.3, 123.4, 124.1, 127.2, 135.9, 147.6, 148.9 ppm. MS: *m*/*z* (%) = 240 (4.3) $[M + 1]^+$, 210 (7.9), 181 (3.5), 150 (6.6), 123 (10.2), 97 (32.6), 57 (100.0). $C_{13}H_9N_3O_2$ (239.232): C 65.27, H 3.79, N 17.56; found C 65.19, H 3.86, N 17.52.

2-(2-Naphthyl)-1*H*-1,3-benzimidazole (3o): Colorless solid; 96% yield (0.234 g). M.p. 217 °C. IR (KBr): $\tilde{\nu}$ = 1625 (C=N), 3445 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 7.19 (dd, J_1 = 6.0, J_2 = 3.0 Hz, 2 H), 7.37–7.40 (m, 2 H), 7.59–7.77 (m, 5 H), 8.11 (dd, J_1 = 8.6, J_2 = 1.7 Hz, 1 H), 8.49 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 115.2, 123.2, 123.6, 126.5, 126.8, 127.2,

127.8, 128.5, 129.0, 134.2, 138.1, 145.9, 151.6 ppm. MS: *m/z* (%) = 245 (43) $[M + 1]^+$, 244 (100) $[M]^+$, 153 (58). $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; found C 83.40, H 4.97, N 11.42.

2-(2-Thienyl)-1*H*-benzimidazole (3p): Yellow solid; 93% yield (0.186 g). M.p. 329–331 °C (ref.[87] m.p. 330 °C). IR (KBr): $\tilde{\nu}$ = 1620 (C=N), 3447 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.16–7.22 (m, 3 H), 7.48–7.58 (m, 2 H), 7.73 (d, J = 3.1 Hz, 1 H), 7.82 (d, J = 2.7 Hz, 1 H), 12.96 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 62.9 MHz): δ = 111.0, 118.4, 121.7, 122.6, 126.6, 128.2, 128.7, 133.6, 134.6, 147.0 ppm. MS: *m/z* (%) = 201 (2.4) $[M + 1]^+$, 200 (5.4) $[M]^+$, 167 (5.6), 149 (29.9), 123 (11.4), 94 (23.6), 73 (49.1), 57 (100.0). $C_{11}H_8N_2S$ (200.258): C 65.98, H 4.03, N 13.99; found C 65.95, H 4.09, N 13.92.

2-(2-Pyridyl)-1*H*-benzimidazole (3q): Colorless solid; 91% yield (0.177 g). M.p. 218 °C (ref.[81] m.p. 218 °C). IR (KBr): $\tilde{\nu}$ = 1621 (C=N), 3444 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.16–7.24 (m, 2 H), 7.47–7.71 (m, 3 H), 7.98 (dd, J_1 = 7.7, J_2 = 1.7 Hz, 1 H), 8.30–8.34 (m, 1 H), 8.71 (d, J = 6.9 Hz, 1 H), 13.01 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 112.0, 119.2, 121.4, 121.9, 123.1, 124.6, 134.8, 137.5, 143.7, 148.4, 149.3, 150.7 ppm. MS: *m/z* (%) = 196 (42.8) $[M + 1]^+$, 195 (100.0) $[M]^+$, 167 (25.1), 105 (11.8), 78 (31.6), 51 (28.3). $C_{12}H_9N_3$ (195.223): C 73.83, H 4.65, N 21.52; found C 73.77, H 4.72, N 21.48.

2-(2-Furyl)-1*H*-benzimidazole (3r): Colorless solid; 90% yield (0.165 g). M.p. 287–288 °C (ref.[81] m.p. 288 °C). IR (KBr): $\tilde{\nu}$ = 1627 (C=N), 3447 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 6.69 (dd, J_1 = 3.4, J_2 = 1.7 Hz, 1 H), 7.16–7.20 (m, 4 H), 7.53 (d, J = 3.1 Hz, 1 H), 7.56 (d, J = 3.1 Hz, 1 H), 7.89 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 110.6, 112.3, 115.0, 122.3, 138.8, 143.6, 144.6, 145.3 ppm. MS: *m/z* (%) = 186 (3.0) $[M + 2]^+$, 185 (15.5) $[M + 1]^+$, 184 (23.7) $[M]^+$, 156 (18.8), 129 (17.9), 94 (40.4), 73 (55.9), 57 (100.0). $C_{11}H_8N_2O$ (184.19): C 71.73, H 4.38, N 15.21; found C 71.68, H 4.29, N 15.15.

6-Methyl-2-(4-methylphenyl)-1*H*-benzimidazole (3s): Pale-yellow solid; 90% yield (0.199 g). M.p. 101–102 °C (ref.[88] m.p. 101–103 °C). IR (KBr): $\tilde{\nu}$ = 1622 (C=N), 3444 (NH) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.21 (s, 3 H), 2.34 (s, 3 H), 6.99–7.08 (m, 3 H), 7.48 (s, 1 H), 7.54 (d, J = 8.1 Hz, 1 H), 8.15 (d, J = 8.1 Hz, 2 H), 12.65 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 21.4, 21.5, 113.9, 114.4, 124.1, 125.5, 127.3, 129.8, 134.1, 134.6, 135.9, 141.7, 150.8 ppm. MS: *m/z* (%) = 223 (40.1) $[M + 1]^+$, 222 (62.3) $[M]^+$, 221 (42.0), 170 (2.5), 149 (35.2), 110 (17.3), 105 (17.9), 83 (33.3), 55 (100.0). $C_{15}H_{14}N_2$ (222.285): C 81.05, H 6.35, N 12.60; found C 81.01, H 6.38, N 12.56.

[2-(4-Methylphenyl)-1*H*-benzimidazol-6-yl](phenyl)methanone (3t): Colorless solid; 90% yield (0.280 g). M.p. 234 °C. IR (KBr): $\tilde{\nu}$ = 1612 (C=N), 1643 (C=O), 3244 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 2.05 (s, 3 H), 7.37 (d, J = 7.4 Hz, 2 H), 7.55 (d, J = 7.4 Hz, 2 H), 7.61–7.75 (m, 5 H), 7.94 (s, 1 H), 8.09 (d, J = 7.4 Hz, 2 H), 8.29 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 20.9, 79.1, 114.6, 117.6, 124.3, 126.2, 126.8, 128.3, 129.4, 129.6, 131.1, 131.9, 138.0, 138.3, 140.6, 141.9, 153.8, 195.4. MS: *m/z* (%) = 314 (16.1) $[M + 2]^+$, 313 (87.6) $[M + 1]^+$, 312 (66.6) $[M]^+$, 311 (34.0), 250 (2.8), 237 (32.1), 236 (100.0), 235 (91.4), 207 (23.3), 181 (13.9) 149 (19.5), 97 (37.0), 71 (43.3) ppm. $C_{21}H_{16}N_2O$ (312.365): C 80.75, H 5.16, N 8.97; found C 80.71, H 5.19, N 8.92.

2-Phenyl-1*H*-benzimidazole-6-carboxylic Acid (3u): Colorless solid; 90% yield (0.214 g). M.p. 325 °C. IR (KBr): $\tilde{\nu}$ = 1628 (C=N), 1655 (C=O), 2450–3250 (OH), 3549 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 7.47–7.66 (m, 4 H), 7.84 (d, J = 8.4 Hz, 1 H), 8.17–8.20 (m, 3 H), 12.79 (s, 1 H), 13.19 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 62.9 MHz): δ = 122.7, 123.5, 124.0, 125.0, 126.7, 128.3, 129.2, 129.6, 130.3, 142.4, 153.7, 168.0 ppm. MS: *m/z* (%) = 239 (8.6) $[M + 1]^+$, 238 (9.2) $[M]^+$, 221 (7.1), 193 (1.9), 152 (5.6), 111 (16.2), 83 (41.4), 57 (100.0). $C_{14}H_{10}N_2O_2$ (238.244): C 70.58, H 4.23, N 11.76; found C 70.52, H 4.28, N 11.72.

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