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Visible-Light-Promoted Synthesis of Benzimidazoles

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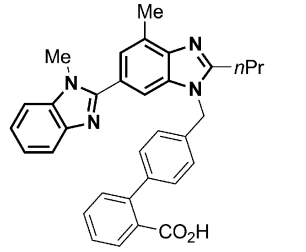
A simple and environmentally-friendly synthetic method for benzimidazoles, which are important structural motifs in many applications owing to their various biological functions, has been developed. The reaction of *o*-phenylenediamine and a variety of aliphatic/aromatic aldehydes in methanol proceeds at room temperature with only natural sources, molecular oxygen and visible light.

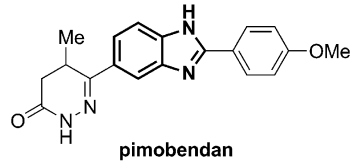
Introduction

The benzimidazole structural motif has been of great interest in many applications, especially in pharmaceuticals, owing to its broad range of biological functions (Figure 1),[1,2] and thus considerable effort has been expended to develop efficient methods for the preparation of benzimidazole derivatives.[3] Common methods involve condensation of *o*-phenylenediamine with carbonyl-containing compounds, such as aldehydes, carboxylic acid, and acid halides, in the presence of various oxidants [Scheme 1 (1)].[4] Despite their efficiency, many currently available methods have limitations, such as the use of hazardous and costly materials or the requirement for harsh reaction conditions (high temperature/pressure or the use of a microwave). Therefore, the development of more efficient, convenient, and eco-friendly methods is still desired. Herein, we present an efficient, green process,[5] which uses visible light irradiation,[6] for benzimidazole synthesis from *o*-phenylenediamine and a variety of aldehydes in the presence of molecular oxygen as oxidant [Scheme 1 (2)].

This synthetic strategy is eco-friendly with the following clear advantages: (1) It does not require any metal catalysts or hazardous materials; (2) It uses only natural sources, molecular oxygen (open to atmosphere) and visible light, aside from the starting materials; (3) Alcohol solvents, such as methanol and ethanol, are used instead of harmful organic solvents; and (4) The reaction conditions are very mild – room temperature and atmospheric pressure.



micardis
antihypertension drug



pimobendan
calcium sensitizer drug

Figure 1. Examples of pharmaceuticals that contain the benzimidazole structural motif.

Results and Discussion

Benzimidazole synthesis was examined by using *o*-phenylenediamine (**1**) and benzaldehyde (**2a**) as model compounds (Table 1). Desired benzimidazole product **3a** was obtained in the presence of molecular oxygen (air-equilibrated solution) under visible light irradiation with blue LEDs. Alcohols, such as ethanol and methanol, showed good reactivity as solvent (Table 1, Entries 5 and 6), whereas the reaction did not proceed in water, probably as a result of substrate insolubility (Table 1, Entry 4). The reaction proceeded optimally in MeOH at 0.1 M concentration (Table 1, Entry 6). The reaction concentration was critical to the reaction efficiency (Table 1, Entries 6–9). The reaction did not proceed in a reasonable time frame at concentrations lower than 0.05 M, whereas at higher concentrations the reaction gave lower yields of product **3a** with formation of diimine side product **B** from condensation of two

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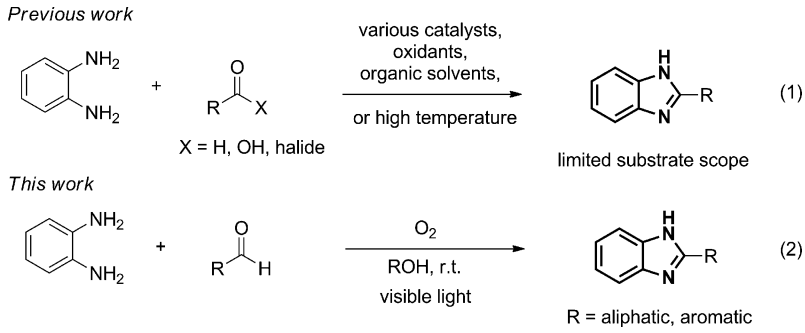
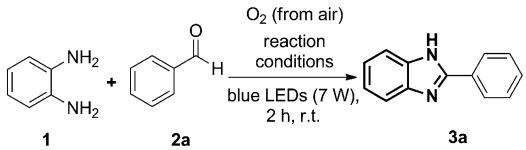


Scheme 1. Synthesis of benzimidazoles.

Table 1. Optimization study for the synthesis of benzimidazole.[a]



Entry	Conditions	Solvent (concentration)	Product yield [%][b]
1	–	DMF (0.1 M)	trace
2	–	CH_2Cl_2 (0.1 M)	25
3	–	MeCN (0.1 M)	28
4	–	H_2O (0.1 M)	trace
5	–	EtOH (0.1 M)	81
6	–	MeOH (0.1 M)	95
7	–	MeOH (0.05 M)	46
8	–	MeOH (0.2 M)	88
9	–	MeOH (0.25 M)	56
10	–	solvent-free	trace
11	without O_2 (bubbling with Ar)	MeOH (0.1 M)	< 5
12	without visible light	$[D_4]$MeOH (0.1 M)	22[c]
13	$Ru(bpy)_3Cl_2$ (0.5 mol-%)	MeOH (0.1 M)	95
14	$Ru(phen)_3Cl_2$ (0.5 mol-%)	MeOH (0.1 M)	89
15	*fac*-Ir(ppy)$_3$ (0.5 mol-%)	MeOH (0.1 M)	62
16	$Ir(ppy)_2(dfbbpy)PF_6$ (0.5 mol-%)	MeOH (0.1 M)	72
17	$Ir(dfppy)_2(phen)PF_6$ (0.5 mol-%)	MeOH (0.1 M)	66

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.21 mmol). [b] The yields were determined by gas chromatography with dodecane as an internal standard. [c] The reaction was conducted in $[D_4]$MeOH, and the yield was determined by ^{1}H NMR spectroscopy; DMF = dimethylformamide.

molecules of **2a** with diamine **1** (see the structure of **B** in Figure 4). The use of oxygen as the oxidant was essential for the reaction to proceed: the reaction did not proceed after exclusion of oxygen from the solution through argon bubbling (Table 1, Entry 11). The reactivity was promoted significantly under visible light irradiation (Table 1, Entries 6 and 12). In the absence of visible light, a significant amount of diimine **B** as the side product was generated along with **3a** (see Supporting Information, Scheme S1 and Figure S1). As for a visible light source, the use of a fluorescent house lamp instead of a blue LED strip resulted in longer reaction time. The reaction was also attempted with several Ru and Ir complexes, which are known to be activated by visible light and lead to a variety of radical-mediated photoredox catalysis (Table 1, Entries 13–17).[7,8] Reactivity with 0.5 mol-% $[Ru(bpy)_3Cl_2]$ was as good as that of the reaction without a catalyst (Table 1, Entries 6 and 13).

To clearly assess the effect of a photocatalyst, a kinetic study was conducted in which reactions were set up in the presence and absence of $[Ru(bpy)_3Cl_2]$, and the results are shown in Figure 2. Product yields were detected by gas chromatography over 4 hours. Although the reaction initially proceeded slightly faster in the presence of 0.5 mol-%

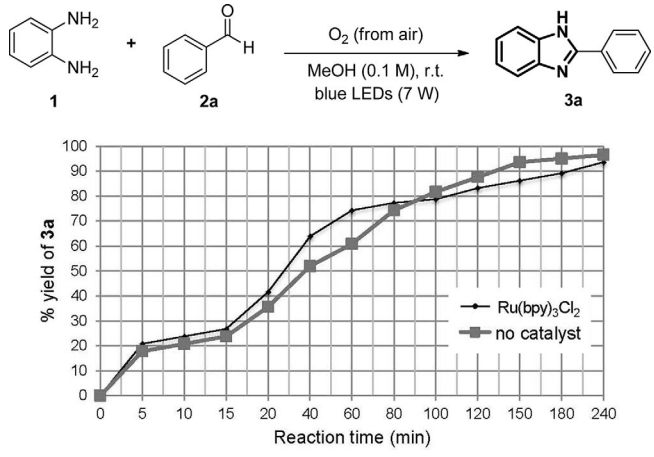


Figure 2. Kinetic study of **3a** in the presence and absence of $[Ru(bpy)_3Cl_2]$.

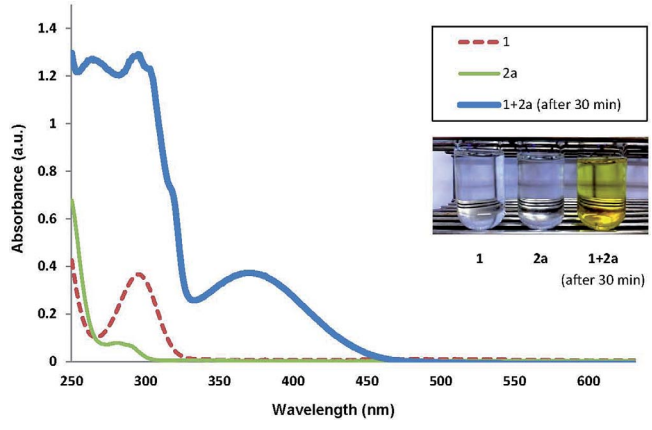


Figure 3. UV/Vis absorption spectra and visual appearance of the solution of **1**, **2a**, and the mixture (100 μM in MeOH).

of $[Ru(bpy)_3Cl_2]$, the difference in final yields was negligible. Therefore, metal-free conditions were chosen for further study owing to enhanced environmental benignity and compatibility. The most significant difference between this and previous works is the use of visible light as the energy source. In very recent work by Jiao and co-workers, a metal-free reaction was reported with molecular oxygen, which provided benzimidazoles from *o*-phenylenediamine and aliphatic aldehydes in toluene.[4e] However, the reaction has limited substrate scope, and works only for activated aliphatic aldehydes. In our current work, the limitation was overcome and reaction conditions were made more eco-friendly (e.g. the use of alcohol as solvent) by using visible light.[9]

An additional experiment with a UV/Visible spectrophotometer supported the fact that the reaction could be promoted by visible light (Figure 3).[10] Although *o*-phenylenediamine (**1**) and benzaldehyde (**2a**) did not show absorption in the visible light region, a mixture of **1** and **2a** resulted in a bathochromic shift, which indicates that an active intermediate was formed under visible light irradiation.[11] The formation of the active intermediate was confirmed visually

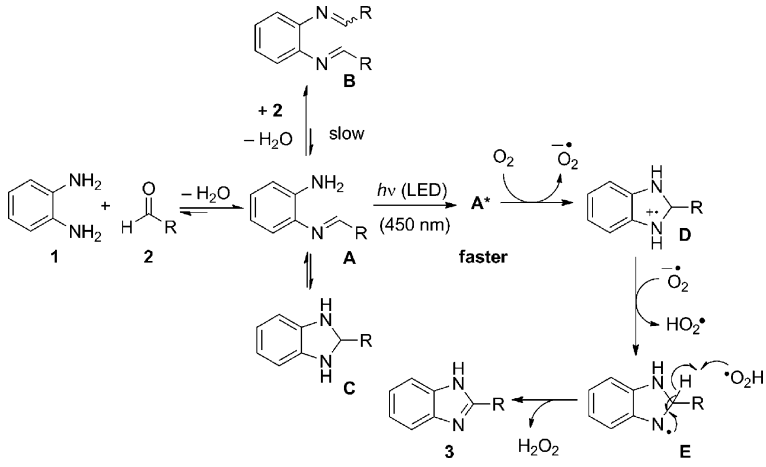
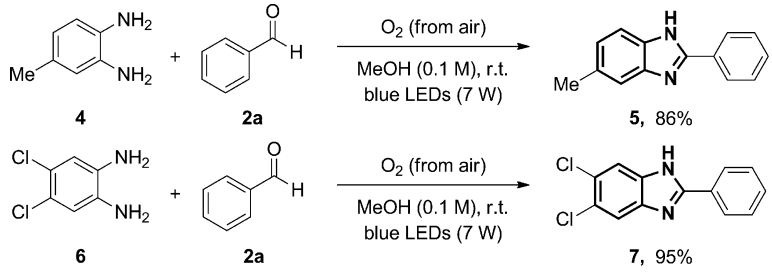
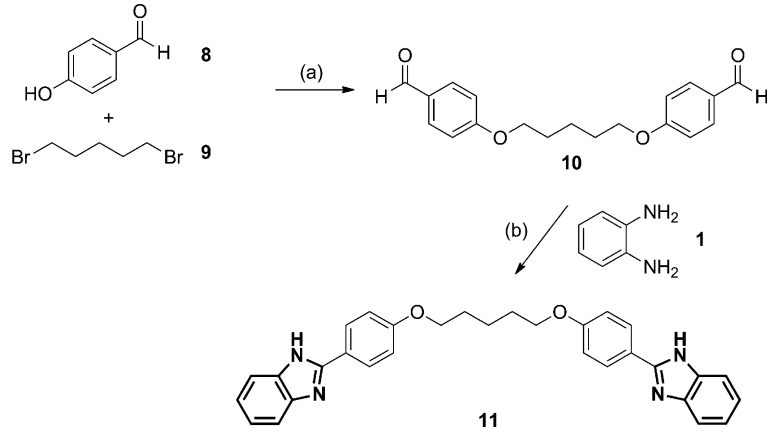


Figure 4. Proposed mechanism for the benzimidazole synthesis under visible light irradiation.

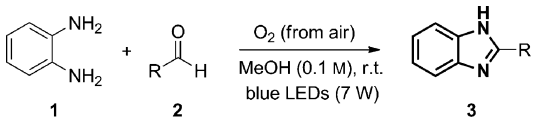


Scheme 2. Reactions of substituted *o*-phenylenediamines.



Scheme 3. Synthesis of 2,2′-[1,5-pentanediylbis(oxy-1,4-phenylene)]bis-1*H*-benzimidazole. Reaction conditions: (a) **8** (2.4 equiv.), **9** (1 equiv.), K_2CO_3 (3 equiv.), DMF, 100 °C, 12 h, 82%. (b) **10** (1 equiv.), **1** (2.5 equiv.), O_2, MeOH/MeCN (1:1, 0.05 M), blue LEDs (7 W), room temp., 10 h, 56%.

Table 2. Scope of 2-substituted benzimidazole synthesis.[a]



1 2 3

Entry	Product	Yield (%)[b]
1	**3a**	95
2	**3b**	95
3	**3c**	85
4	**3d**	70
5	**3e**	78
6	**3f**	95
7	**3g**	94
8	**3h**	99
9	**3i**	75
10	**3j**	71
11	**3k**	86

[a] Reaction conditions: **1** (1 mmol), **2a** (1.05 mmol), 4–7 h. [b] The given yields are the isolated yield and based on an average of two runs.

by the colour change in the mixed solution into a yellow-orange colour.

The isolation of the intermediate for further mechanistic studies was not possible probably owing to its high reactivity. However, we could detect an imine intermediate, which was generated from condensation between *o*-phenylenediamine (**1**) and benzaldehyde (**2a**), by ^{1}H NMR experiment done in [D$_4$]MeOH and by gas chromatography. In the ^{1}H NMR spectra no detectable amount of benzimidazoline, another possible intermediate, was observed.

Based on this evidence, we propose a plausible mechanism for the benzimidazole synthesis in Figure 4. Imine **A**, formed from the condensation between **1** and **2**, can be activated under visible light irradiation to **A*** (or **C***).[12] The species reduces O_2 to superoxide (O_2^{-}) and becomes a radical cation. Its intramolecular radical reaction with the imine moiety to form **D**, deprotonation by superoxide to **E**, and hydrogen abstraction by hydroperoxyl radical (HOO$^{\cdot}$) produces desired benzimidazole **3**. The H_2O_2 generated in the last step was detected with a H_2O_2 indicator.

With the optimized, environmentally benign conditions, we evaluated the reactions of *o*-phenylenediamine with a variety of aldehydes for the synthesis of 2-substituted benzimidazoles (Table 2). Reactions of both electron-rich and -poor aromatic aldehydes provided the corresponding benzimidazoles in good to excellent yields (Table 2, Entries 1–8). In addition, aliphatic aldehydes were also suitable substrates for the process (Table 2, Entries 9–11), which proves the reaction efficiency. The mild conditions allowed the reaction of aldehydes that contain a range of functional groups.

Reactions of substituted *o*-phenylenediamines, such as 3,4-diaminotoluene (**4**) and 4,5-dichloro-*o*-phenylenediamine (**6**) also provided excellent yields of the corresponding benzimidazole products under the same conditions (Scheme 2).

The utility and practicality of this green process was proven by using it as the key step in the synthesis of a drug candidate that contains a benzimidazole motif, 2,2′-[1,5-pentanediylbis(oxy-1,4-phenylene)]bis-1*H*-benzimidazole (**11**; Scheme 3). The bis(oxyphenlene)benzimidazole structure is known to have pharmacological activities such as selective activity against *Leishmania donovani*.[13] Molecule **11** was obtained in two steps from commercially available compounds. Key substrate **10** was obtained by an S_N2 reaction between **8** and **9**,[14] and subjected to our reaction conditions. The reaction of *o*-phenylenediamine (**1**) with aldehyde **10** in air-equilibrated methanol under visible-light irradiation successfully provided desired benzimidazole product **11**.

Conclusions

An efficient and eco-friendly process for the synthesis of benzimidazoles was developed by using *o*-phenylenediamine and an aldehyde in MeOH. This remarkable process required only natural sources, molecular oxygen and visible light. The use of visible light significantly improved the reactivity, and thus the reaction worked for both aromatic and aliphatic aldehydes. In addition, the utility of this process was proved by successfully synthesizing a drug candidate. We present our protocol as an efficient and more eco-friendly alternative to the current methods of benzimidazole derivatisation.

Experimental Section

General Reagent Information: Anhydrous methanol (MeOH) in Sure-Seal bottles was purchased from Sigma Aldrich and degassed

by repeated sonication under reduced pressure and replenishing the atmosphere with argon.

o-Phenylenediamine and commercially available aldehydes were purchased from Sigma Aldrich, Alfa Aesar, or TCI, and used as received. Flash column chromatography was performed with Merck silica gel 60 (70–230 mesh).

General Analytical Information: The benzimidazole products were characterized by ^{1}H NMR, ^{13}C NMR, and FTIR spectroscopy. NMR spectra were recorded with a Bruker 400 MHz instrument (400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR). Copies of ^{1}H and ^{13}C NMR spectra can be found at the end of the Supporting Information. ^{1}H NMR spectroscopic data are referenced relative to residual DMSO (δ = 2.50 ppm) or chloroform (δ = 7.26 ppm) in the deuterated solvent. ^{13}C NMR spectra are reported in ppm relative to [D6]dimethyl sulfoxide (δ = 39.51 ppm) or deuteriochloroform (δ =77.23 ppm). ^{13}C NMR signals for carbons 3a, 4, 5, 6, 7a of benzimidazole moiety shown in Figure 5 are broad, and they are difficult or impossible to detect in some cases. FTIR spectra were recorded with a Bruker Alpha FTIR spectrometer with KBr plates. HRMS data were obtained on an Agilent 6530 Accurate-Mass Q-TOF LC/MS. UV/Vis spectra were obtained with a PDA UV/Vis Spectrophotometer (cell length: 1 cm).

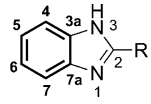


Figure 5. Structure of 2-substituted benzimidazole.

General Procedure for the Synthesis of Benzimidazoles: An open test tube equipped with a magnetic stir bar was charged with *o*-phenylenediamine (1.0 mmol). Then MeOH (10 mL, 0.1 M) and an aldehyde (1.05 mmol) were added. The open test tube was placed under blue LEDs (7 W) and stirred at room temperature for 4–7 h. Reaction progress was checked by thin layer chromatography (TLC) or gas chromatography (GC). The reaction mixture was concentrated in vacuo, and the benzimidazole products were purified by recrystallization (with hot ethanol and water) or flash column chromatography.

2,2′-[1,5-Pentanediylbis(oxy-1,4-phenylene)]bis-1*H*-benzimidazole (11): An open test tube equipped with a magnetic stir bar was charged with *o*-phenylenediamine (0.5 mmol). Then MeOH/MeCN (1:1, 0.05 M), and 1,5-pentanediylbis(oxy)dibenzaldehyde (**10**, 0.2 mmol) were added to it. The open test tube was placed under blue LEDs (7 W) and stirred at room temperature for 10 h. Reaction progress was checked by TLC. The reaction mixture was concentrated in vacuo, and desired product **11** (yellow solid) was purified by flash column chromatography.

2-Phenyl-1*H*-benzimidazole (3a): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.95 (br. s, 1 H), 8.17 (d, J = 6.0 Hz, 2 H), 7.70–7.45 (m, 5 H), 7.20 (d, J = 6.0 Hz, 2 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 151.31, 143.83, 135.05, 130.17, 129.98, 129.07, 126.51, 122.65, 121.81, 118.92, 111.45 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3367, 2255, 2128, 1654, 1002 cm^{-1}. R_f = 0.41 (hex/EtOAc, 2:1).

2-(4-Methoxyphenyl)-1*H*-benzimidazole (3b): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.75 (br. s, 1 H), 8.12 (dd, J = 8.0, 4.0 Hz, 2 H), 7.62 (d, J = 8.0 Hz, 1 H), 7.49 (d, J = 8.0 Hz, 1 H), 7.20–7.13 (m, 2 H), 7.11 (d, J = 8.0 Hz, 2 H), 3.84 (s, 3 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 151.37, 143.89, 134.98, 128.02, 122.69, 122.09, 121.48, 118.50, 114.38, 111.06, 55.34, 14.10 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3448, 2251, 2125, 1656, 1047 cm^{-1}. HRMS (ESI): m/z calcd. for $C_{14}H_{12}N_2O$ [M + H]$^+$ 225.0950; found 225.1015. R_f = 0.38 (hex/EtOAc, 1:1).

2-{4-[(*tert*-Butyldimethylsilyl)oxy]phenyl}-1*H*-benzimidazole (3c): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.77 (br. s, 1 H), 8.07 (d, J = 8.8 Hz, 2 H), 7.60–7.50 (m, 2 H), 7.20–7.14 (m, 2 H), 7.02 (d, J = 8.8 Hz, 2 H), 0.97 (s, 9 H), 0.24 (s, 6 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 159.18, 151.80, 143.83, 135.05, 128.16, 121.67, 121.13, 118.33, 115.70, 111.10, 25.84, 17.84, –3.16 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3368, 2255, 2128, 1654, 1005 cm^{-1}. R_f = 0.60 (EtOAc).

2-[4-(1-Methylethoxy)phenyl]-1*H*-benzimidazole (3d): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.88 (br. s, 1 H), 8.13 (d, J = 8.2 Hz, 2 H), 7.70–7.50 (m, 2 H), 7.40 (d, J = 8.2 Hz, 2 H), 7.20–7.18 (m, 2 H), 2.93 (heptet, J = 6.8 Hz, 1 H), 1.22 (d, J = 6.8 Hz, 6 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 151.43, 150.38, 143.87, 135.06, 127.87, 126.91, 126.55, 122.23, 121.68, 118.67, 111.26. 33.39, 23.69 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3442, 2250, 2124, 1661, 1063 cm^{-1}. R_f = 0.51 (hex/EtOAc, 2:1).

2-(4-Bromophenyl)-1*H*-benzimidazole (3e): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 13.05 (br. s, 1 H), 8.11 (d, J = 8.6 Hz, 2 H), 7.76 (d, J = 8.6 Hz, 2 H), 7.76–7.55 (m, 2 H), 7.26–7.17 (m, 2 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 150.24, 131.99, 129.40, 128.38, 123.27, 122.35 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3298, 2257, 2129, 1650, 1026, 827 cm^{-1}. R_f = 0.49 (hex/EtOAc, 2:1).

2-(4-Fluorophenyl)-1*H*-benzimidazole (3f): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.98 (br. s, 1 H), 8.24 (dd, J = 8.8, 5.6 Hz, 2 H), 7.65–7.56 (m, 2 H), 7.40 (dd, J = 8.8, 8.7 Hz, 2 H), 7.24–7.17 (m, 2 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 163.12 (d, J = 248.3 Hz), 150.46, 143.96, 135.18, 128.78 (d, J = 8.7 Hz), 126.84 (d, J = 3.0 Hz), 122.21, 119.34, 116.05 (d, J = 21.9 Hz), 111.38 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3441, 2251, 2125, 1659, 1020, 824 cm^{-1}. R_f = 0.42 (hex/EtOAc, 2:1).

2-[3-(Trifluoromethyl)phenyl]-1*H*-benzimidazole (3g): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 13.21 (br. s, 1 H), 8.53 (s, 1 H), 8.48 (d, J = 7.6 Hz, 1 H), 7.85 (d, J = 7.6 Hz, 1 H), 7.79 (dd, J = 7.6, 7.5 Hz, 1 H), 7.70–7.60 (m, 2 H), 7.30–7.20 (m, 2 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 172.25, 149.77, 131.21, 130.31, 129.93 (q, J = 32.0 Hz), 126.86 (q, J = 273.7 Hz), 126.33 (q, J = 3.7 Hz), 122.89 (q, J = 3.7 Hz) ppm. IR (neat): $\tilde{\nu}_{max}$ = 3425, 2253, 2127, 1656, 1026, 825 cm^{-1}. R_f = 0.47 (hex/EtOAc, 2:1).

2-(4-Pyridinyl)-1*H*-benzimidazole (3h): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 13.32 (br. s, 1 H), 8.76 (d, J = 6.0 Hz, 2 H), 8.12 (dd, J = 6.0, 1.4 Hz, 2 H), 7.72–7.63 (m, 2 H), 7.28–7.24 (m, 2 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 172.19, 150.54, 148.88, 139.42, 137.22, 122.99, 120.43 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3432, 2251, 2125, 1606, 1028 cm^{-1}. R_f = 0.60 (EtOAc).

2-Heptyl-1*H*-benzimidazole (3i): Brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.04 (br. s, 1 H), 7.55 (dd, J = 6.0, 2.8 Hz, 2 H), 7.24–7.18 (m, 2 H), 2.94 (td, J = 7.6, 2.4 Hz, 2 H), 1.86 (tt, J = 7.6, 7.5 Hz, 2 H), 1.40–1.31 (m, 2 H), 1.30–1.16 (m, 6 H), 0.83 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.76, 138.74, 122.25, 114.78, 31.84, 29.58, 29.53, 29.17, 28.59, 22.76, 14.21 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3425, 2252, 2126, 1659, 1027 cm^{-1}. R_f = 0.37 (hex/EtOAc, 2:1).

2-(2-Phenylethyl)-1*H*-benzimidazole (3j): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.23 (br. s, 1 H), 7.54–7.49 (m, 1 H), 7.44–7.49 (m, 1 H), 7.30–7.24 (m, 4 H), 7.20–7.15 (m, 1 H), 7.14–7.07 (m, 2 H), 3.13–3.10 (m, 4 H) ppm. ^{13}C NMR (400 MHz, DMSO): δ = 154.39, 143.31, 141.05, 134.27, 128.41, 128.28, 126.09, 121.50, 120.89, 118.15, 110.79, 33.35, 30.42 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3442, 2251, 2125, 1659, 1059 cm^{-1}. R_f = 0.32 (hex/EtOAc, 1:1).

2-Cyclohexyl-1*H*-benzimidazole (3k): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.12 (br. s, 1 H), 7.51 (d, J = 6.6 Hz, 1 H), 7.39 (d, J = 6.6 Hz, 1 H), 7.09 (m, 2 H), 2.83 (tt, J = 11.3, 3.6 Hz, 1 H), 2.05–1.97 (m, 2 H), 1.85–1.75 (m, 2 H), 1.74–1.54 (m, 3 H), 1.44–1.20 (m, 3 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 158.91, 143.06, 134.18, 121.35, 120.73, 118.19, 110.75, 37.72, 31.27, 25.59, 25.54 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3442, 2251, 2125, 1660, 1025 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{13}H_{16}N_2$ $[M + H]^+$ 201.1313; found 201.1377. R_f = 0.49 (hex/EtOAc, 1:1).

6-Methyl-2-phenyl-1*H*-benzimidazole (5): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.80 (br. s, 1 H), 8.15 (d, J = 8.0 Hz, 2 H), 7.54 (t, J = 8.0 Hz, 2 H), 7.47 (t, J = 8.0 Hz, 1 H), 7.44–7.40 (m, 2 H), 7.02 (d, J = 8.0 Hz, 1 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 151.35, 130.67, 130.18, 129.41, 126.76, 123.89, 118.82, 21.79 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3424, 2252, 2126, 1657, 1027 cm^{-1}. R_f = 0.42 (hex/EtOAc, 2:1).

5,6-Dichloro-2-phenyl-1*H*-benzimidazole (7): Brown solid. ^{1}H NMR (400 MHz, DMSO): δ = 8.16 (d, J = 8.0 Hz, 2 H), 7.83–7.80 (m, 2 H), 7.55 (dd, J = 8.0, 4.0 Hz, 3 H), 3.49 (br. s, 1 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 153.82, 130.52, 129.27, 129.04, 126.73, 124.49 ppm. IR (neat): $\tilde{\nu}_{max}$ = 3425, 2252, 2126, 1659, 1026 cm^{-1}. R_f = 0.51 (hex/EtOAc, 2:1).

4,4′-[1,5-Pentanediylbis(oxy)]bis-benzaldehyde (10): White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.86 (s, 2 H), 7.82 (d, J = 8.0 Hz, 4 H), 6.89 (d, J = 8.0 Hz, 4 H), 4.07 (t, J = 4.0 Hz, 4 H), 1.90 (tt, J = 8.0, 7.9 Hz, 4 H), 1.73–1.63 (m, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.09, 164.30, 132.24, 130.03, 114.93, 68.27, 28.99, 22.88 ppm. IR (neat): $\tilde{\nu}_{max}$ = 2945, 1690, 1427, 1318, 1122, 1067 cm^{-1}. R_f = 0.55 (EtOAc).

2,2′-[1,5-Pentanediylbis(oxy-1,4-phenylene)]bis-1*H*-benzimidazole (11): Yellow solid. ^{1}H NMR (400 MHz, DMSO): δ = 12.79 (br. s, 1 H), 8.10 (d, J = 8.8 Hz, 4 H), 7.74–7.64 (m, 4 H), 7.19–7.14 (m, 4 H), 7.10 (d, J = 8.8 Hz, 4 H), 4.10 (t, J = 6.2 Hz, 4 H), 1.83 (tt, J = 6.2, 6.1 Hz, 4 H), 1.70–1.58 (m, 2 H) ppm. IR (neat): $\tilde{\nu}_{max}$ = 3426, 2251, 2125, 1638, 1027 cm^{-1}. R_f = 0.61 (hex/EtOAc, 1:1).

Supporting Information (see footnote on the first page of this article): Details of the synthesis of benzimidazole without visible-light irradiation, the UV/Vis absorption spectra of the solution of **1**, **2a**, and the mixture, and NMR spectra of all new compounds are provided.

Acknowledgments

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[10] UV/Vis absorption spectra with molar absorptivity (ε) as the vertical axis is provided in the Supporting Information Figure S2.

[11] Recently the Melchiorre group described the photochemical activity of in-situ-formed electron donor-acceptor complexes under visible light irradiation, see: E. Arceo, I. D. Jurberg, A. Álvarez-Fernández, P. Melchiorre, *Nat. Chem.* **2013**, *5*, 750.

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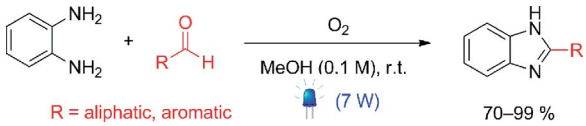

A simple and eco-friendly synthetic method for benzimidazoles, which are important structural motifs in many applications owing to their various biological functions, has been developed. The reaction of *o*-phenylenediamine and a variety of aliphatic/aromatic aldehydes in methanol proceeds at room temperature with only natural sources, molecular oxygen and visible light.

Keywords: Synthetic methods / Photochemistry / Nitrogen heterocycles

