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The Synthesis of Benzimidazoles via a Recycled Palladium Catalysed Hydrogen-Transfer under Mild Condition

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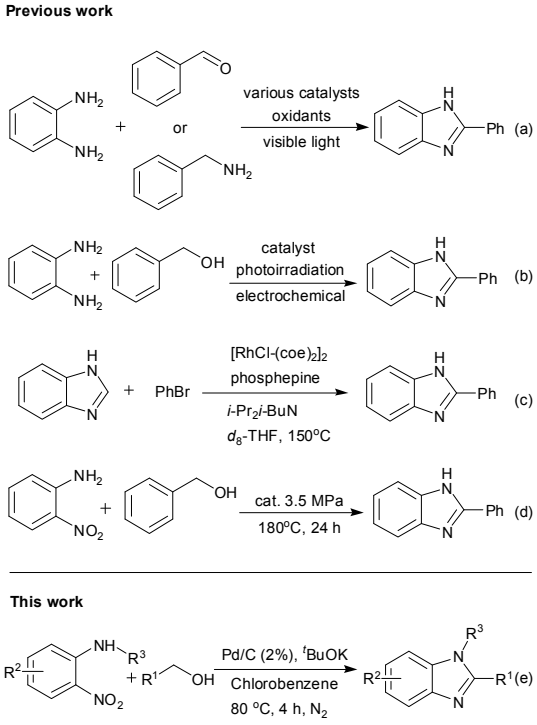
An efficient synthesis of benzimidazoles was developed by virtue of a recycled palladium catalyzed hyfrogen-transfer. The reaction can be carried out smoothly under mild conditions to give rise to a variety of benzimidazoles with good to excellent yields. The palladium catalyst could be recovered easily and reused for six times with great catalytic activity.

Introduction

N-Heterocycles[1] are pivotal scaffolds in biologically active natural products, drug intermediates, pharmaceuticals, and agrochemicals. In particular, benzimidazoles have been reported to possess a broad spectrum of biological activities and therapeutic potentialities,[2] such as antihypertensive,[3] antiulcer,[4] antihistaminic,[5] anticancer,[6] inotropic,[7] antifungal,[8] anti-HIV,[9] antiviral[10] and inhibitors.[11] Recent research indicate that 2-aryl benzimidazole conjugate can induce apoptosis in human breast cancer MCF-7 cells through caspase independent pathway.[12]

Much effort has been devoted by chemists to synthesize benzimidazole because of their widespread applications in different segments of science and technology. Over the last decade, the condensation of *o*-phenylenediamines with benzylamine[13] or benzaldehyde[14] has employed as an attractive strategy for the preparation of benzimidazole, in which oxidants and photo-catalyst were required (Scheme 1 a). Afterwards alcohols were developed as starting materials to react with *o*-phenylenediamines for the preparation of benzimidazoles (Scheme 1 b).[15] Also, benzimidazole was used as a starting material to obtain different substituent benzimidazoles by virtue of a Rh-catalyzed direct C-H bond arylation (Scheme 1 c).[16] In view of the importance of benzimidazoles, the development of alternative general methods from facile starting materials to synthesize benzimidazoles is highly desirable.[17] Recently the chemists have made progress in the synthesis of benzimidazole by virtue of the hydrogen-transfer pathway from benzyl alcohols and *o*-nitroanilines.[18] For instance, a synthesis of benzimidazole derivatives was realized via a hydrogen-transfer under catalysis of a multifunctional Cu–Pd/$_{\gamma}$-Al_2O_3 catalyst. (Scheme 1 d).[19] Recent studies on hydrogen-transfer reaction have revealed some advantages, such as, atomic economy, environmentally friendly and the recycle of catalyst. However, to the best of our knowledge, some of these hydrogen-transfer methods mentioned above suffer from narrow substrate scope and the request of high temperature, long reaction time and high pressure. Therefore, there is still a great demand for the development of more green and mild approaches. As a continuation of our interest in the heterogeneous catalysis,[20] herein we report a synthesis for benzimidazoles by a new hydrogen-transfer reaction of *N*-substituted 2-nitroanilines and alcohols catalyzed by Pd powder under mild condition (Scheme 1 e).



Scheme 1 Previous study and this work on hydrogen transfer reaction for the synthesis of benzimidazoles

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† Electronic Supplementary Information (ESI) available: Experimental procedures, compound characterization, X-ray crystal structure and analytical data (^{1}H NMR, ^{13}C NMR and HRMS) for all new compounds. CCDC 1551540. See DOI: 10.1039/x0xx00000x

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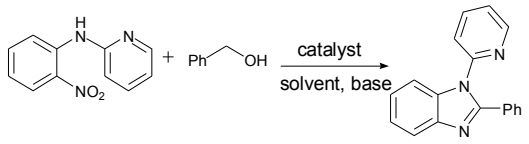
Results and discussion

Our initial study was carried out using (2-nitro-phenyl)-pyridin-2-yl-amine (**1a**) and benzyl alcohol (**2a**) in chlorobenzene at 120 °C (Table 1). With our continuous interest on nano-catalyzed reactions, we first screened various nano-catalysts. Interestingly, the desired product 2-phenyl-1-pyridin-2-yl-*1H*-benzoimidazole (**3aa**) was obtained in excellent yield when Pd/C was employed as a catalyst (Table 1, entry 5), while other catalysts such as carbon, CuO, Au/TiO_2 and Rh/Al_2O_3 showed no catalytic activity (entries 1-4). Moreover, the absolute configuration of the product **3aa** was confirmed by X-ray crystal diffraction.[21] Subsequently, the efficiency of different base sources was screened. Experimental results indicated that base had a great influence on the reaction. It was found that ^{t}BuOK was the best for this hydrogen-transfer reaction (entries 5-9). Temperature screening indicated that 80 °C was the optimal one to afford the desired product **3aa** with an excellent yield of 98%. Rising the temperature had no effect on the yield while lowing the reaction temperature decreased the yields largely (entries 10-12). Replacing chlorobenzene with other solvents resulted in the decrease of the reaction yields (entries 13-16). According to the results above, the optimal conditions were obtained as described in entry 11 of Table 1, that is, 1.0 equiv. of (2-nitro-phenyl)-pyridin-2-yl-amine (**1a**), 4.0 equiv. of benzyl alcohol (**2a**) as the reactants, 4.0 equiv. of ^{t}BuOK as the base, Pd/C (2 %) as the catalyst in chlorobenzene (1 mL) at 80 °C for 4 h.

With the optimized conditions established, the scope of the alcohols was first examined. R^1 as the substituent with aliphatic and aryl groups could react smoothly. Generally, the aryl groups afforded the desired product with higher yields than that of the aliphatic groups. Besides, when R^1 is a phenyl group, either electronic effect or the steric hindrance of the substituents at the phenyl ring showed little influence on the reaction (Table 2, **3aa**-**3am**). R^1 with 2,5-position substitution disfavoured this reaction, resulting a little decrease in the reaction yield perhaps due to the hindrance factor (**3an**, **3ap**). In contrast, multi-substituted alcohol **2o** could be tolerated in this conditions to give the corresponding product in good to excellent yield (**3ao**). It was noted that the condensation of **1a** with heterobenzylic alcohols such as **2r** and **2s** also afforded the corresponding product **3ar** and **3as** in excellent yields (91% and 92% respectively). When R^1 was the bulky naphthyl group, the reaction could work well to give the corresponding product in 95% yield (**3aq**). Moreover, simple aliphatic alcohols such as ethanol, propanol and butanol could also be the reaction substrates and the reactions can be carried out smoothly to afford the desired products although the yields were lower than that of benzylic alcohols (**3at**-**3av**). On the other hand, R^2 can be $-CF_3$ and $-CH_3$ substituents, which gave the desired product with an excellent yield regardless of the electron donation or withdrawing of this substituent (**3ba**, **3ca**). Next, the scope of the R^3 was examined. Generally, pyrindyl group favoured this reaction. The electron-donation group on this pyrindyl ring had little influence on the reaction (**3da**). When this pyrindyl substituent was replaced with other groups, it was found that electron-rich groups favoured this transformation to give the benzimidazoles with good yields (**3fa**, **3ga)**, while *N*- acetyl protected substrate was hardly converted to the desired product (**3ha**). Without protection at the amino group, that is, the 2-nitroaniline was employed as the substrate, the corresponding benzimidole can be obtained smoothly in spite of a lower yield (**3ea**).

Table 1 Optimization of the reaction conditions[a]



1a **2a** **3aa**

Entry	Catalyst	Solvent	Base	Temp. (°C)	Yield[b] (%)
1	Carbon	PhCl	NaOH	120	n.d.
2	CuO	PhCl	NaOH	120	n.d.
3	Au/TiO_2	PhCl	NaOH	120	n.d.
4	Rh/Al_2O_3	PhCl	NaOH	120	n.d.
5	Pd/C	PhCl	NaOH	120	83
6	Pd/C	PhCl	Et_3N	120	23
7	Pd/C	PhCl	$LiOH·H_2O$	120	29
8	Pd/C	PhCl	K_2CO_3	120	52
9	Pd/C	PhCl	^{t}BuOK	120	97
10	Pd/C	PhCl	^{t}BuOK	100	97
11	**Pd/C**	**PhCl**	**^{t}BuOK**	**80**	**98**
12	Pd/C	PhCl	^{t}BuOK	60	85
13	Pd/C	Toluene	^{t}BuOK	80	74
14	Pd/C	THF	^{t}BuOK	80	n.d
15	Pd/C	DMF	^{t}BuOK	80	16
16	Pd/C	CH_3CN	^{t}BuOK	80	n.d.

[a] The reactions were carried out with **1a** (1.0 equiv.,0.25 mmol), **2a** (4.0 equiv., 1.0 mmol), Base (4.0 equiv., 1.0 mmol), solvent (1.0 mL) and catalyst (metal: 2 %) for 4 h under N_2 atmosphere. [b] Isolated yield was based on **1a**, n.d. = not detected.

Encouraged by the successful hydrogen-transfer reaction, we then investigated the recycle of Pd/C catalyst. The catalyst could be recovered from the reaction by a simple phase separation and then washed with alcohol and deionized water. The recovered catalyst could then be reused in the next round. As shown in Table 3, little loss of catalytic activity was observed after the sixth round, giving the corresponding product with a yield of 95%.

To get further insight into the mechanism for this reaction, several control experiments were carried out under different conditions (Scheme 2). When the reaction time was shorten to 30 minutes, 10% of amine compound **1a'** and 61% of corresponding products **3aa** were observed. Moreover, the reaction of *N*-pyridin-2-yl-benzene-1,2-diamine (**1a'**) with

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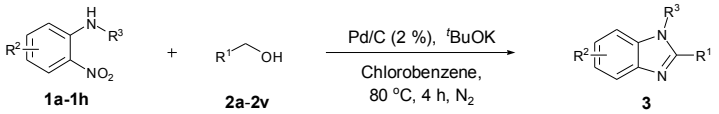
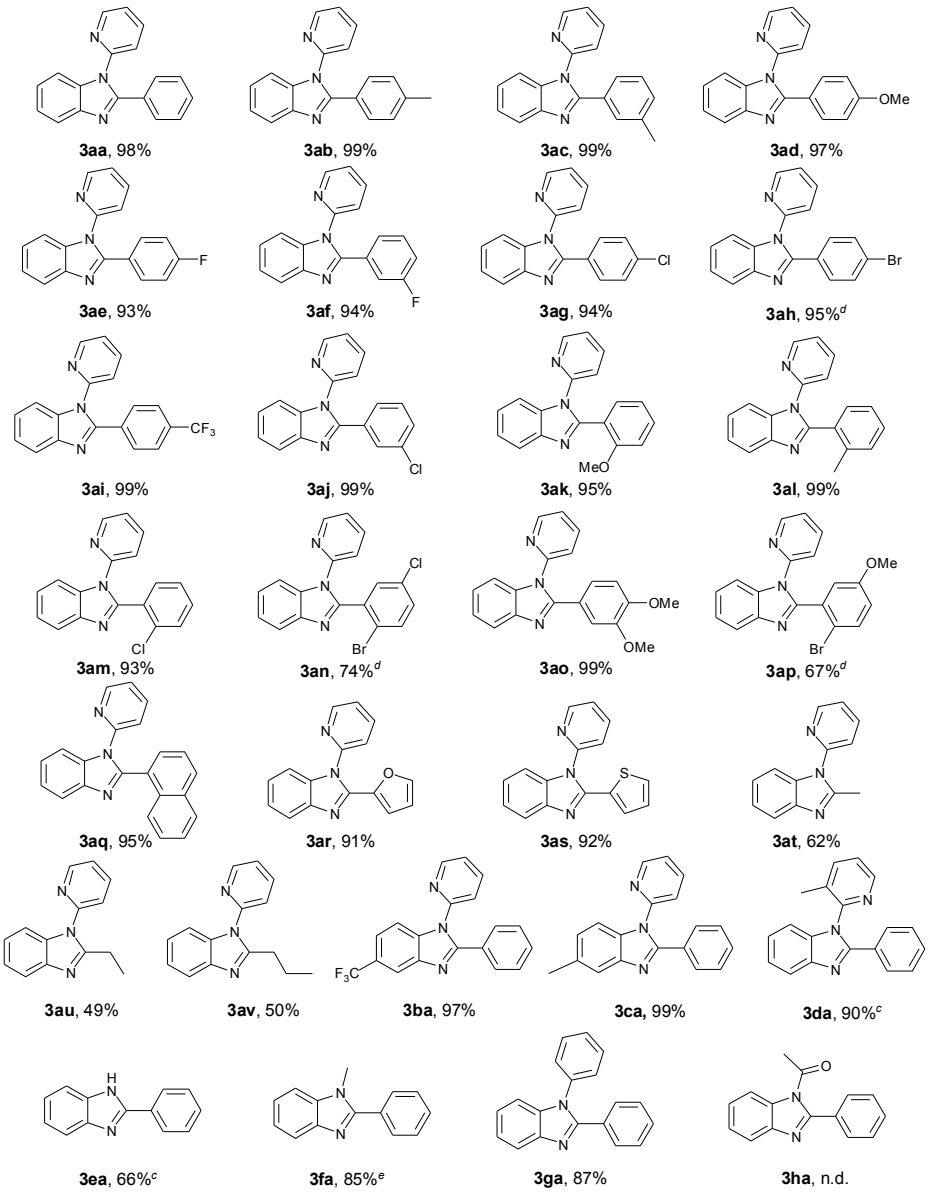
Table 2 Synthesis of benzimidazoles from alcohols and *N*-substituted 2-nitroanilines[a,b]





[a] The reactions were carried out with **1a** (1.0 equiv., 0.25 mmol), **2a** (4.0 equiv., 1.0 mmol), ^{t}BuOK (4.0 equiv., 1.0 mmol), 1.0 mL chlorobenzene and catalyst (Pd/C, Pd: 2 %) for 4 h under N_2 atmosphere. [b] Isolated yield was based on **1a**. [c] The reaction temperature was 100 °C. [d] The reaction temperature was 130 °C. [e]The reaction temperature was 100 °C, the solvent was water.

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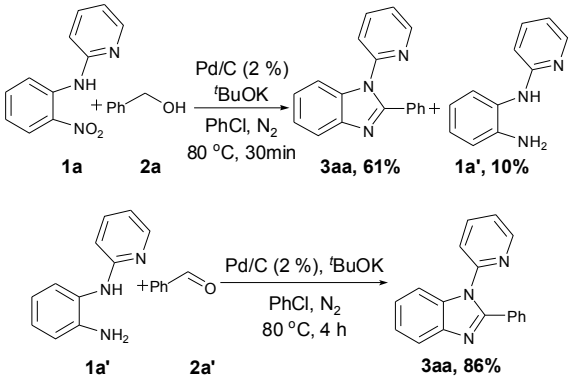
ARTICLE

Table 3 Recycling of Pd/C for the synthesis of 2-phenyl-1-pyridin-2-yl-1*H*-benzoimidazole [a,b]

Run	1	2	3	4	5	6
Yield[b](%)	98	98	97	96	96	95

[a] The reactions were carried out with **1a** (1.0 equiv., 0.25 mmol), **2a** (4.0 equiv., 1.0 mmol), ^{t}BuOK (4.0 equiv., 1.0 mmol), 1.0 mL chlorobenzene and catalyst (Pd/C, Pd: 2 %) for 4 h under N_2 atmosphere, 80 °C. [b] Isolated yield was based on **1a**.



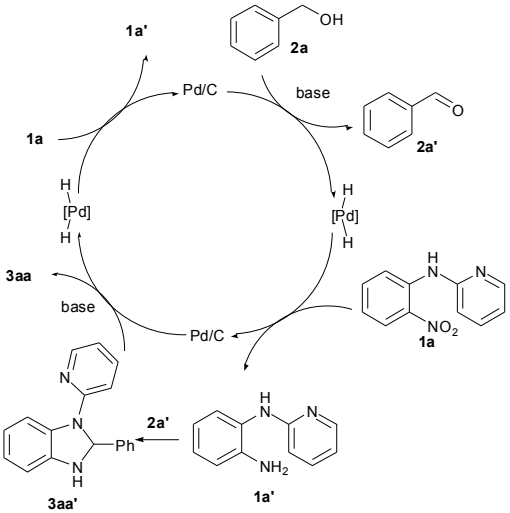
Scheme 2 Control experiments for the reaction

benzaldehyde (**2a'**) could give the desired product in 86% yield. These result implied that **1a'** and **2a'** are the key intermediates for this reaction.

On the basis of control experiments and the previous reports,[20] the possible mechanism was shown as below (Scheme 3). (2-nitro-phenyl)-pyridin-2-yl-amine (**1a**) is reduced to **1a'** in situ by a hydrogen-transfer process in the presence of Pd/C catalyst while the corresponding benzaldehyde (**2a'**) is obtained from the benzyl alcohol by an oxidation process at the same time. Then the condensation of **1a'** with **2a'** forms the intermediate **3aa'**. Subsequently, intermediate (**3aa'**) can be converted into the corresponding product **3aa** *via* a dehydrogenation process. And **1a** is reduced to **1a'** once again into the catalytic loop.

Conclusions

In conclusion, we developed a general and efficient method for the synthesis of benzimidazoles from cheap and readily available starting materials *via* a hydrogen-transfer strategy. A wide range of substrates were tolerated in this transformation, and the products were obtained in good to excellent yields under mild condition. Moreover, the catalyst



Scheme 3 The proposed reaction mechanism

can be recovered and reused for six times without obvious loss of the catalytic activity. Ongoing research including further mechanistic details, expanding the substrate scope and applications in organic synthesis is currently underway in our laboratory.

Experimental section

General remarks

All the chromatographic separations were carried out by using silica gel. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker-400MHz Spectrometer (^{1}H NMR: 400MHz, ^{13}C NMR: 100MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (*J*) were expressed in ppm and Hz, respectively. HRMS (ESI) were recorded on a WatersTM Q-TOF Premier. Commercially available compounds were used without further purification. Solvents were purified according to the standard procedures unless otherwise noted. Pd/C (10%) (CAS: 7440-05-3) was purchased from Shanghai Titan Technology Co., Ltd.

Typical experimental procedure

Solvent of chlorobenzene (1.0 mL) was added to the mixture of (2-Nitro-phenyl)-pyridin-2-yl-amine (0.25 mmol), benzyl alcohol (1.0 mmol), and metal catalyst (2 mol % Pd/C), ^{t}BuOK (1.0 mmol). The air in the reaction mixture was removed under vacuum and the reaction tube was refilled with N_2 under -30 °C. This procedure was repeated three times. The reaction mixture was then stirred under N_2 atmosphere at 80 °C for 4 h. After cooling to room temperature, the catalyst was recovered by filtering the solid from

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liquid phase and reused for the next round. Then, the liquid phase was removed under vacuum and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 5:1) to give the product as a white solid.

2-phenyl-1-(pyridin-2-yl)-1H-benzoimidazole (3aa)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 91 - 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 (dd, *J* = 4.8 Hz 1.3 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.76 (dt, *J* = 7.7 Hz 1.9 Hz, 1H), 7.57 – 7.53 (m, 3H), 7.41 – 7.29 (m, 6H), 7.07 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.2, 150.5, 149.7, 143.0, 138.5, 136.1, 130.1, 129.6, 129.4, 128.4, 123.8, 123.3, 123.1, 121.7, 119.9, 111.2. HRMS (ESI) m/z calcd for. $C_{18}H_{14}N_3$ $[M+H]^+$ 272.1188, found 272.1188.

1-pyridin-2-yl-2-*p*-tolyl-1*H*-benzoimidazole (3ab)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 101 - 103 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.65 (s, 1H), 7.87 (d, *J* =7.8 Hz, 1H), 7.72 – 7.69 (m, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.4 Hz, 2H), 7.32 – 7.25 (m, 3H), 7.12 (d, *J* = 7.4 Hz, 2H), 7.03 (d, *J* = 7.8 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.3, 150.7, 149.7, 143.1, 139.7, 138.5, 136.1, 129.3, 129.1, 127.1, 123.6, 123.2, 123.0, 121.8, 119.7, 111.1, 21.3. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3$ $[M+H]^+$ 286.1344, found 286.1344.

1-pyridin-2-yl-2-*m*-tolyl-1*H*-benzoimidazole (3ac)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.66 (ddd, *J* = 4.9 Hz 1.9 Hz 0.8 Hz, 1H), 7.89 – 7.87 (m, 1H), 7.71 (dt, *J* = 7.6 Hz 2.0 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.36 – 7.26 (m, 3H), 7.19 – 7.14 (m, 3H), 7.05 (dt, *J* = 8.0 Hz 0.9 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.3, 150.5, 149.6, 142.9, 138.4, 138.3, 136.0, 130.3, 130.0, 129.8, 128.0 126.3, 123.6, 123.2, 123.0, 121.6, 119.7, 111.1, 21.2. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3$ $[M+H]^+$ 286.1344, found 286.1354.

2-(4-methoxy-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ad)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 127 - 129 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 – 8.67 (m, 1H), 7.87 – 7.85 (m, 1H), 7.74 (dt, *J* = 7.6 Hz 2.0 Hz, 1H), 7.52 – 7.50 (m, 1H), 7.49 – 7.46 (m, 2H), 7.36 – 7.25 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.86 – 6.83 (m, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 160.6, 152.1, 150.7, 149.7 143.0, 138.5, 136.0, 130.8, 123.4, 123.2, 123.0, 122.3, 121.8, 119.5, 113.8, 111.0, 55.2. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3O$ $[M+H]^+$ 302.1293, found 302.1291.

2-(4-fluoro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ae)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 160-163 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 (dd, *J* = 4.9 Hz 1.2 Hz, 1H), 7.88 (d, *J* =8.0 Hz, 1H), 7.80 (dt, *J* = 7.7 Hz 1.9 Hz, 1H), 7.56 -7.7.51 (m, 3H), 7.40 – 7.29 (m 3H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.06 – 7.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 163.5, (d, *J* = 249.2 Hz), 151.2, 150.4, 149.9, 142.9, 138.7, 136.1, 131.4(d, *J* = 21.8 Hz), 126.3 (d, *J* = 8.6 Hz), 123.9, 123.4, 123.3, 121.6, 119.9, 115.6 (d, *J* = 3.4 Hz), 111.1. HRMS (ESI) m/z calcd for. $C_{18}H_{13}FN_3$ $[M+H]^+$ 290.1093, found 290.1103.

2-(3-fluoro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3af)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 132 - 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 (ddd, *J* = 4.9 Hz 1.9 Hz 0.76 Hz, 1H), 7.90 – 7.88 (m, 1H), 7.81 (dt, *J* = 7.7 Hz 1.9 Hz, 1H), 7.53 – 7.51 (m, 1H), 7.42 – 7.28 (m,6H), 7.14 (dt, *J* = 8.0 Hz 0.8 Hz, 1H), 7.11 – 7.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 162.4 (d, *J* = 245.5 Hz), 150.8 (d, *J* = 2.7Hz), 150.2, 149.9, 142.9, 138.7, 136.1, 132.2 (d, *J* = 8.2 Hz), 130.0 (d, *J* = 8.4 Hz), 125.1 (d, *J* = 3.0 Hz), 124.1, 123.5, 123.4, 121.6, 120.1, 116.6 (d, *J* = 19.3 Hz), 116.4 (d, *J* = 21.6 Hz), 111.2. HRMS (ESI) m/z calcd for. $C_{18}H_{13}FN_3$ $[M+H]^+$ 290.1093, found 290.1093.

2-(4-chloro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ag)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 119 - 120 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.68 (dd, *J* = 4.9 Hz 1.2 Hz, 1H), 7.89 – 7.87 (m, 1H), 7.81 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.52 – 7.46 (m, 3H), 7.41 – 7.29 (m, 5H), 7.12 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 151.0, 150.2, 150.0, 142.8, 138.7, 136.1, 135.8, 130.6, 128.7, 128.5, 124.0, 123.5, 123.3, 121.6, 119.9, 111.1. HRMS (ESI) m/z calcd for. $C_{18}H_{13}ClN_3$ $[M+H]^+$ 306.0798, found 306.0796.

2-(4-bromo-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ah)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 137 - 139 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 – 8.67 (m, 1H), 7.89 – 7.87 (m, 1H), 7.81 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.52 – 7.46 (m, 3H), 7.63 – 7.29 (m, 5H), 7.12 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 157.1, 150.3, 150.0, 142.9, 138.7, 136.1, 131.7, 130.9, 129.0, 124.2, 124.0, 123.5, 123.4, 121.6, 120.0, 111.1. HRMS (ESI) m/z calcd for. $C_{18}H_{13}BrN_3$ $[M+H]^+$ 350.0293, found 350.0294.

1-pyridin-2-yl-2-(4-trifluoromethyl-phenyl)-1*H*-benzoimidazole (3ai)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether/ ethyl acetate = 5:1) to give the product as a white solid, mp = 155 - 157 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 – 8.68 (m, 1H), 7.92 – 7.90 (m, 1H), 7.84 (dt, *J* = 7.7 Hz 1.9 Hz,

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1H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.53 – 7.51 (m, 1H), 7.43 – 7.32 (m, 3H), 7.17 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 150.5, 150.1, 150.0, 142.9, 138.9, 136.1, 133.6, 131.3 (q, *J* =32.4 Hz), 129.6, 125.3 (q, *J* = 3.7 Hz), 124.3, 123.8 (q, *J* = 270.8 Hz), 123.7, 123.5, 121.5, 120.2, 111.1. HRMS (ESI) m/z calcd for. $C_{19}H_{13}F_3N_3$ $[M+H]^+$ 340.1062, found 340.1056.

2-(3-chloro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3aj)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 110 - 111 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.69 (dd, *J* = 4.8Hz 1.3Hz, 1H), 7.90 – 7.88 (m, 1H), 7.82 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.64 (t, *J* = 1.8 Hz, 1H), 7.53 – 7.51 (m, 1H), 7.42 – 7.30 (m, 5H), 7.27 – 7.22 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 150.7, 150.2, 150.0, 142.9, 138.7, 136.1, 134.5, 131.9, 129.7, 129.6, 129.5, 127.4, 124.2, 123.6, 123.4, 121.6, 120.1, 111.2. HRMS (ESI) m/z calcd for. $C_{18}H_{13}ClN_3$ $[M+H]^+$ 306.0798, found 306.0797.

2-(2-methoxy-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ak)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 129 - 131 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.61 – 8.59 (m, 1H), 7.89 – 7.87 (m, 1H), 7.80 (dd, *J* = 7.6 Hz 1.7 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.66 (dt, *J* = 7.6 Hz 1.8 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.36 – 7.30 (m, 2H), 7.26 – 7.23 (m, 1H), 7.10 (dt, *J* = 7.5 Hz 0.7 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 156.4, 151.2, 150.4, 149.0, 143.1, 137.8, 134.9, 132.1, 131.5, 123.6, 122.9, 122.1, 121.1, 120.0, 119.8, 118.9, 111.5, 110.7, 54.7. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3O$ $[M+H]^+$ 302.1293, found 302.1298.

1-pyridin-2-yl-2-*o*-tolyl-1*H*-benzoimidazole (3al)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 95 - 97 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.58 (s, 1H), 7.88 (d, *J* = 6.9 Hz, 1H), 7.77 (d, *J* = 7.0 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.38 – 7.19 (m, 7H), 6.81 (d, *J* = 7.8 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.0, 150.0, 149.2, 142.9, 138.0, 137.5, 134.6, 130.5, 130.3, 130.2, 129.6, 125.6, 123.6, 123.1, 122.2, 120.0, 119.7, 118.8, 19.7. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3$ $[M+H]^+$ 286.1344, found 286.1347.

2-(2-chloro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3am)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.56 (dd, *J* =4.8 Hz 1.6 Hz, 1H), 7.93 – 7.91 (m, 1H), 7.79 – 7.76 (m, 1H), 7.72 – 7.66 (m, 2H), 7.42 – 7.33 (m, 5H), 7.29 – 7.26 (m, 1H), 7.06 (d, *J* =8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 150.0, 149.8, 149.4, 142.8, 138.3, 134.6, 133.7, 132.6, 131.1, 130.4, 129.7, 127.0, 124.2, 123.4, 122.5, 120.2, 119.5, 111.8. HRMS (ESI) m/z calcd for. $C_{18}H_{13}ClN_3$ $[M+H]^+$ 306.0798, found 306.0796.

2-(2-bromo-5-chloro-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3an)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid, mp = 139 - 141 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.55 (dd, *J* = 4.7 Hz 1.4 Hz, 1H), 7.93 – 7.89 (m, 1H), 7.78 – 7.73 (m, 2H), 7.67 (d, *J* = 2.5, 1H), 7.45 (d, *J* = 8.6, 1H), 7.42 – 7.37 (m, 2H), 7.31 – 7.26 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 149.6, 149.6, 149.5, 142.8, 138.4, 134.4, 134.3, 133.9, 133.5, 132.6, 131.2, 124.4, 123.6, 122.7, 121.1, 120.4, 119.4, 111.8. HRMS (ESI) m/z calcd for. $C_{18}H_{12}BrClN_3$ $[M+H]^+$ 383.9903, found 383.9897.

2-(3,4-dimethoxy-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ao)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.71 – 8.70 (m, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.75 (m, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.39 – 7.26 (m, 3H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.01 (dd, *J* = 8.4 Hz 2.0 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.1, 150.8, 150.1, 149.7, 148.7, 142.9, 138.5, 136.1, 123.5, 123.2, 123.0, 122.4, 122.4, 122.0, 120.0, 112.2, 110.9, 110.7, 55.8, 55.7. HRMS (ESI) m/z calcd for. $C_{20}H_{18}N_3O_2$ $[M+H]^+$ 332.1399, found 332.1400.

2-(2-bromo-5-methoxy-phenyl)-1-pyridin-2-yl-1*H*-benzoimidazole (3ap)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 164 - 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.58 (dd, *J* = 4.9 Hz 1.2 Hz, 1H), 7.92 – 7.90 (m, 1H), 7.81 – 7.79 (m, 1H), 7.68 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.41 – 7.36 (m, 3H), 7.28 – 7.25 (m, 1H), 7.16 (d, *J* = 3.0 Hz, 1H), 7.06 (d, *J* = 4.0 Hz, 1H), 6.86 (dd, *J* = 8.8 Hz 3.1 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 158.7, 150.7, 149.9, 149.2, 142.8,138.2, 134.4, 133.6, 133.2, 124.2, 123.4, 122.4, 120.2, 120.0, 118.0, 117.3, 113.6, 112.0, 55.6. HRMS (ESI) m/z calcd for. $C_{19}H_{15}BrN_3O$ $[M+H]^+$ 380.0398, found 380.0392.

2-naphthalen-1-yl-1-pyridin-2-yl-1*H*-benzoimidazole (3aq)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.58 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.98 – 7.91 (m, 2H), 7.87 – 7.80 (m, 2H), 7.55 (d, *J* = 6.4 Hz, 1H), 7.45 – 7.41 (m, 6H), 7.15 – 7.14 (m, 1H), 6.75 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 151.1, 150.2, 149.3, 143.1, 138.1, 135.0, 133.5, 131.7, 130.2, 129.5, 128.2, 127.8, 127.1, 126.3, 125.6, 124.8, 124.0, 123.4, 122.4, 120.4, 120.0, 111.9. HRMS (ESI) m/z calcd for. $C_{22}H_{16}N_3$ $[M+H]^+$ 322.1344, found 322.1348.

2-furan-2-yl-1-pyridin-2-yl-1*H*-benzoimidazole (3ar)

The title compound was prepared according to the general

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working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.73 – 8.71 (m, 1H), 7.93 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.86 (dd, *J* = 7.8 Hz 0.9 Hz, 1H), 7.49 (ddd, *J* = 7.5 Hz 4.9 Hz 0.9 Hz, 1H), 7.42 – 7.25 (m, 5H), 6.63 – 6.62 (m, 1H), 6.43 (dd, *J* = 3.5 Hz 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 149.9, 149.8, 144.5, 144.1, 143.5, 142.9, 138.7, 135.9, 123.9, 123.4, 121.8, 119.9, 112.7, 111.6, 110.6. HRMS (ESI) m/z calcd for. $C_{16}H_{12}N_3O$ $[M+H]^+$ 262.0980, found 262.0986.

1-pyridin-2-yl-2-thiophen-2-yl-1*H*-benzoimidazole (3as)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 93 - 95 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.76 – 8.74 (m, 1H), 7.91 (dt, *J* = 7.7 Hz 1.7 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 7.4 Hz 5.0 Hz, 1H), 7.39 – 7.23 (m, 5H), 6.95 – 6.92 (m, 1H), 6.88 – 6.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 150.1, 149.9, 146.8, 142.8, 139.0, 136.5, 132.1, 128.6, 128.5, 127.5, 124.1, 123.7 123.3, 122.5, 119.6, 110.4. HRMS (ESI) m/z calcd for. $C_{16}H_{12}N_3S$ $[M+H]^+$ 278.0752, found 278.0760.

2-methyl-1-pyridin-2-yl-1*H*-benzoimidazole (3at)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.70 (d, *J* =4.7 Hz, 1H), 7.76 – 7.74 (m, 1H), 7.75 (d, *J* = 3.9 Hz, 1H), 7.48 (d, *J* =8.0 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.31 – 7.22 (m, 2H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 151.5, 149.9, 149.7, 142.5, 138.8, 134.8, 123.0, 122.9, 122.8, 120.0, 119.1, 110.2, 15.3. HRMS (ESI) m/z calcd for. $C_{13}H_{12}N_3$ $[M+H]^+$ 210.1031, found 210.1031.

2-ethyl-1-pyridin-2-yl-1*H*-benzoimidazole (3au)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.70 (d, *J* = 4.8 Hz, 1H), 7.96 (dt, *J* = 7.8 Hz 1.7 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.35 – 7.21 (m, 3H), 3.03 (q, *J* = 7.5 Hz, 2H), 1.38 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 156.2, 150.0, 149.8, 142.6, 138.8, 135.1, 123.1, 122.9, 122.7, 120.2, 119.3, 110.0, 21.9, 11.9. HRMS (ESI) m/z calcd for. $C_{14}H_{14}N_3$ $[M+H]^+$ 224.1188, found 224.1186.

2-propyl-1-pyridin-2-yl-1*H*-benzoimidazole (3av)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.71 – 8.69 (m, 1H), 7.95 (dt, *J* = 7.8 Hz 2.0 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.42 (ddd, *J* = 7.5 Hz 4.9 Hz 0.8 Hz, 1H), 7.34 – 7.20 (m, 3H), 2.98 (t, *J* = 7.8 Hz, 2H), 1.86 – 1.77 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 155.1, 149.9, 149.7, 142.6, 138.8, 135.0, 123.1, 122.8, 122.6, 120.3, 119.3, 110.0, 30.2, 21.1, 13.9. HRMS (ESI) m/z calcd for. $C_{15}H_{16}N_3$ $[M+H]^+$ 238.1344, found 238.1343.

2-phenyl-1-pyridin-2-yl-5-trifluoromethyl-1*H*-benzoimidazole (3ba)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 134 - 136 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.72 (dd, *J* = 4.8 Hz 1.4 Hz, 1H), 8.16 (s, 1H), 7.79 (dt, *J* = 7.8 Hz 1.9 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.56 – 7.53 (m, 3H), 7.45 – 7.40 (m, 2H), 7.38 – 7.34 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 154.0, 150.0, 149.9, 142.5, 138.7, 138.0, 130.2, 129.5, 129.4, 128.6, 125.8 (q, *J* = 32.1 Hz), 124.7 (q, *J* = 270.0 Hz), 123.6, 121.7, 120.6 (q, *J* = 3.6 Hz), 117.5 (q, *J* = 4.2 Hz), 111.8. HRMS (ESI) m/z calcd for. $C_{19}H_{13}F_3N_3$ $[M+H]^+$ 340.1062, found 340.1067.

5-methyl-2-phenyl-1-(pyridin-2-yl)-1*H*-benzoimidazole (3ca)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.68 – 8.66 (m, 1H), 7.75 – 7.70 (m, 1H), 7.67 – 7.66 (m, 1H), 7.55 – 7.52 (m, 2H), 7.45 – 7.43 (m, 1H), 7.39 – 7.30 (m, 4H), 2.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.1, 150.7, 149.7, 143.4, 138.4, 134.2, 133.0, 130.3, 129.5, 129.4, 128.4, 125.2, 122.9, 121.6, 119.7, 110.8, 21.6.

1-(3-methyl-pyridin-2-yl)-2-phenyl-1*H*-benzoimidazole (3da)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a yellow solid, mp = 127 – 129 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.56 (d, *J* = 4.7 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 – 7.55 (m, 2H), 7.39 – 7.23 (m, 6H), 7.07 (*J* = 8.0 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.1, 149.3, 147.7, 143.0, 140.5, 136.3, 131.3, 130.2, 129.6, 128.5, 128.4, 124.5, 123.5, 123.0, 119.8, 110.4, 16.9. HRMS (ESI) m/z calcd for. $C_{19}H_{16}N_3$ $[M+H]^+$ 286.1344, found 286.1346.

2-phenyl-1*H*-benzoimidazole (3ea)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid; ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ = 12.96 (s, 1H), 8.21 – 8.19 (m, 2H), 7.63 – 7.49 (m, 5H), 7.24 – 7.20 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6, ppm): δ = 152.1, 131.1, 130.8, 129.9, 127.4, 123.1. HRMS (ESI) m/z calcd for. $C_{13}H_{11}N_2$ $[M+H]^+$ 195.0922, found 195.0920.

Reference: J. Liu, Q. Liu, H. Yi, C. Qin, R. Bai, X. Qi, Y. Lan, A.-W. Lei, *Angew. Chem.*, 2014, **126**, 512; H.-B. Wang, J.-M. Huang, *Adv. Synth. Catal.*, 2016, **358**, 1975.

methyl-2-phenyl-1*H*-benzoimidazole (3fa)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.85 – 7.82 (m, 1H), 7.79 – 7.75 (m, 2H), 7.56 – 7.51 (m, 3H), 7.42 – 7.39 (m, 1H),

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7.36 – 7.30 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 154.1, 143.1, 136.8, 130.4, 130.1, 129.8, 129.0, 123.1, 122.8, 120.1, 110.0, 32.0. HRMS (ESI) m/z calcd for. $C_{14}H_{14}N_2$ $[M+H]^+$ 209.1079, found 209.1081.

1,2-diphenyl-1*H*-benzoimidazole (3ga)

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.90 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.56 (m, 2H), 7.52 – 7.44 (m, 3H), 7.37 – 7.24 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 152.7, 143.3, 137.5, 137.3, 130.2, 130.2, 129.8, 128.9, 128.6, 127.7, 123.7, 123.3, 120.2, 110.8. HRMS (ESI) m/z calcd for. $C_{19}H_{15}N_2$ $[M+H]^+$ 271.1235, found 271.1234.

Conflicts of interest

There are no conflicts to declare.

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21 Details of the crystal structure analysis are provided as Supporting Information. CCDC-**1551540** contains the supplementary crystallo-graphic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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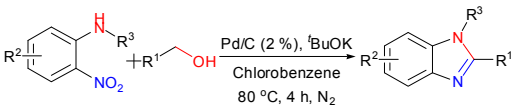

R^2 = CF_3, CH_3 R^1 = aryl, alkyl
R^3 = H, aryl, alkyl, pyridyl

29 examples
up to 99% yield
reused six times with excellent catalytic activity