CHAPTER-4

tert-Butyl Nitrite Catalyzed Synthesis of Benzimidazoles From *o*-Phenylenediamine and Aldehydes at Room Temperature

4.1 Introduction

Benzimidazole motifs are present in many drugs, bioactive molecules and natural products [1]. For instance, benzimidazole derivatives are active pharmacophores which display anti-viral, anti-microbial, anti-cancer, anti-ulcer and anti-inflammatory properties (Figure 4.1) [2-5]. On the other hand, benzimidazole derivatives are well-used in synthetic organic chemistry as building blocks and ligands [6-9]. Moreover, benzimidazole based materials and polymers displayed promising applications in different fields, including optical sensing, energy storage, LED, dyes, etc [10-14]. Owing to their biological and chemical significance, the synthesis of benzimidazole derivatives has gained continuous interest in organic chemistry [15-33] Synthesis of benzimidazoles has been typically achieved by the condensation of *o*-phenylenediamine with carbonyl compounds in the presence of different reagents and oxidants [21, 27-32]. However, most of the reported methods uses metal catalysts [25, 26, 30, 31], stoichiometric amount of oxidants [22], higher reaction temperature [32], etc. In general, organocatalytic methods are attractive in organic synthesis due to their efficiency and selectivity [34-35].

tert-Butyl nitrite (TBN) is metal-free multi-tasking reagent extensively used in various organic transformations [36-38]. Besides diazotization and nitration, *tert*-butyl nitrite has been used as radical initiator, oxidant, etc [39-42]. Over the last few years, our research work is focused on the chemistry of *N*-nitrosamines [43-49] and we have reported TBN mediated solvent-free synthesis of *N*-nitrosamines [43], radical dimerization of thiobenzamide [48], transamidation of secondary amides [47], and nitration of *N*-alkyl anilines [44].

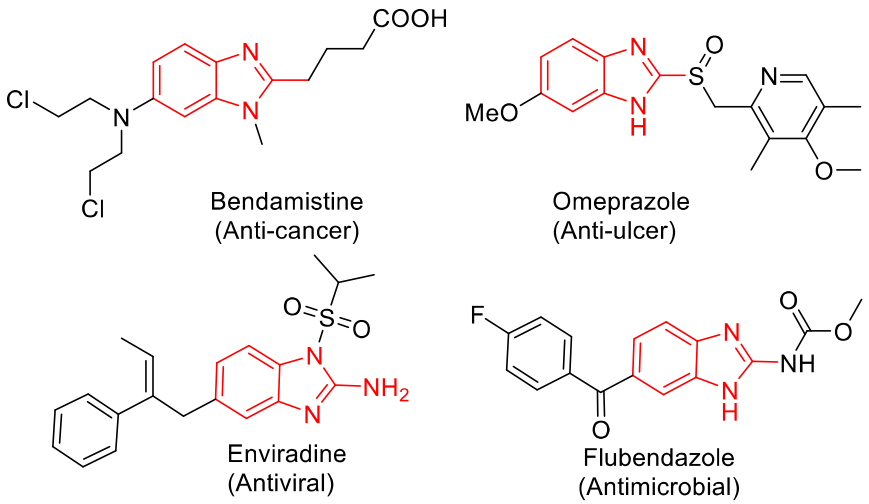
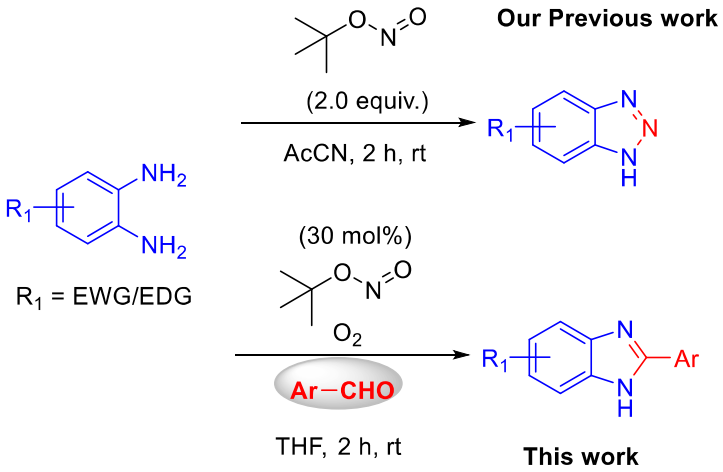


Figure 4.1 Pharmacological activities of benzimidazole derivatives

Recently, we have reported the synthesis of benzotriazoles from *o*-phenylenediamine using *tert*-butyl nitrite [49]. This method provides excellent yields of benzotriazoles under neutral conditions while several acid labile functional groups were found to be stable. In continuation of this work, here we report TBN catalysed transformation of *o*-phenylenediamines into benzimidazoles in the presence of aldehydes at room temperature.



Scheme 4.1 Synthesis of benzimidazoles

4.2 Results and discussion

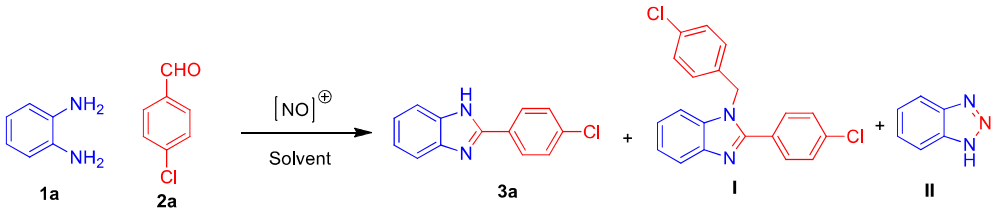
4.2.1 Optimization of the reaction conditions

At the outset, *o*-phenylenediamine (1a) and 4-chlorobenzaldehyde (2a) was chosen as model substrates and subjected to the condensation in the presence of *tert*-butyl nitrite (TBN) at room temperature (Table 4.1). The reaction was performed with one equiv. of *tert*-butyl nitrite in different solvents including dichloromethane, acetonitrile, toluene, 1,4-dioxane, methanol, THF, DMF and DMSO (Table 4.1, entries 1–8). Among these solvents, the reaction proceeded well in THF by providing the desired product 2- (4-chlorophenyl) benzimidazole (3a) in 80% yield in 30 mins (Table 4.1, entry 6). On the other hand, other solvents provided a mixture of products containing 1,2-substituted benzimidazole (I) and benzotriazole (II) in considerable yields. Also, in some solvents (e.g. DCM, toluene, etc.) the starting materials were remaining unreacted. Nevertheless, only a minimum amount of these side products were obtained in THF while compared with other solvents. Hence, the optimization was carried out in THF by varying the amount of TBN. The formation of benzotriazole (II) was observed in high amount when the reaction with 2.0 equiv. of TBN (Table 4.1, entry 9). Therefore, the reaction was performed with catalytic amount of TBN (i.e. 50 mol% to 10 mol%) in THF.

Although a decrease in benzotriazole (II) formation was observed with catalytic amount of TBN, the yield of the desired product was also dropped significantly (Table 4.1, entries 10–12). It is also important to note that the 3a was not observed in the absence of TBN (Table 4.1, entry 13). Considering the previous report on TBN mediated thiol oxidation [42], we performed the condensation reaction with molecular oxygen (i.e.

with oxygen balloon) in the presence of 50 mol% and 30 mol% of TBN (Table 4.1, entries 14 and 15). To our delight, the benzimidazole 3a was obtained in 90% yield under both the reaction conditions within 2 h at room temperature.

Table 4.1 Optimization for synthesis of benzimidazole under various conditions



1a 2a 3a I II

S.No.	'NO' Source	Mol%	Additives	Solvent	Time (Hr)	Yield %[b]		
						3a	I	II
1	TBN	100	-	DCM[c]	0.5	26	24	20
2	TBN	100	-	CH_3CN	0.5	22	23	47
3	TBN	100	-	toluene[c]	0.5	17	10	16
4	TBN	100	-	1-4 dioxane[c]	0.5	46	20	15
5	TBN	100	-	MeOH	0.5	77	<5	14
6	TBN	100	-	THF	0.5	80	5	10
7	TBN	100	-	DMF	0.5	65	12	14
8	TBN	100	-	DMSO	0.5	62	12	17
9	TBN	200	-	THF	0.5	67	<10	21
10	TBN	50	-	THF[c]	0.5	65	<5	<5
11	TBN	30	-	THF[c]	0.5	59	<5	<5
12	TBN	10	-	THF[c]	1.0	40	<5	<5
13	TBN	00	-	THF[c]	2.0	<5	<5	nr
14	TBN	50	O_2	THF	2.0	90	<5	<5
15	TBN	30	O_2	THF	2.0	90	<5	<5
16	$NOBF_4$	30	O_2	THF[c]	2.0	trace	trace	<10
17	*Iso*-amylnitrite	30	O_2	THF	2.0	83	<5	<5
18	CF_3SO_3H	100	O_2	THF[c]	2.0	17	trace	trace

[a]Reaction conditions: Substrate **1a** & **2a** (1 mmol) and NO-source stirred in appropriate solvents (5 mL) at room temperature. [b]Isolated yield. [c]Imine was reminded in the reaction.

Furthermore, the condensation reaction was carried out with other nitrosating agents such as nitrosonium tetrafluoroborate ($NOBF_4$) and *iso*-amylnitrite in the presence of oxygen. The desired product 3a was not observed with $NOBF_4$ while *iso*-amyl nitrite gave the benzimidazole 3a in 83 % yield (Table 4.1, entry 16 and 17). Overall, the optimization study indicates that a catalytic amount of TBN (i.e. 30 mol %) in the presence of oxygen is sufficient for the efficient preparation of benzimidazoles from *o*-phenylenediamines and aryl aldehydes.

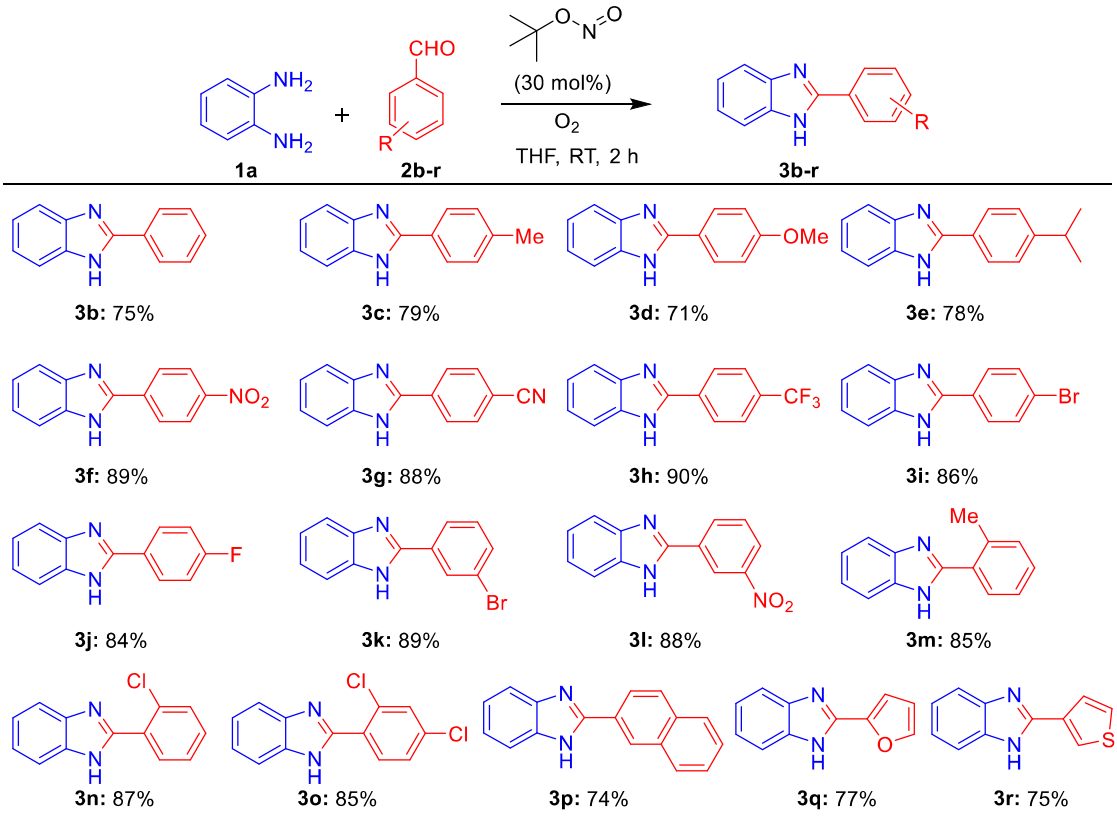
4.2.2 Substrate scope

With optimized conditions in hand, the scope of different aryl aldehydes was investigated for the preparation of benzimidazoles (Table 4.2). Initially, *o*-phenelenediamine was subjected to the condensation reaction with un-substituted as well as electron donating group substituted benzaldehydes in the presence of 30 mol% TBN. All these reactions underwent smoothly to provide the desired products 3b-3e in 71–79% yield. On the other hand, condensation of *o*-phenelenediamine with electron withdrawing group functionalized benzaldehydes (e.g. 4-NO_2, 4-CN, 4-CF_3, 4-F and 4-Br) provided corresponding benzimidazoles in 84–90% yields under the optimized conditions (Table 4.2, 3f-3j).

Furthermore, *meta*-substituted benzaldehydes (3-Br and 3-NO_2), sterically hindered *ortho*-substituted benzaldehydes (2-Me, 2-Cl and 2,4-diCl) as well as 2-naphthyl aldehyde also participated in the condensation reaction efficiently in the presence of TBN and provided the desired products in good to excellent yields (Table 4.2, 3k-3p). Overall, it was observed that the reaction proceeds smoothly irrespective of functional groups at the *ortho*, *para* and *meta*-positions of the aryl aldehydes. Similar to aryl

aldehydes, to our delight heterocyclic aldehydes such as 2-furaldehyde and 3-thiophene aldehyde also gave the corresponding benzimidazoles 3q and 3r in 75–77% yields (Table 4.2, 3q-3r).

Table 4.2 Scope of aryl aldehydes

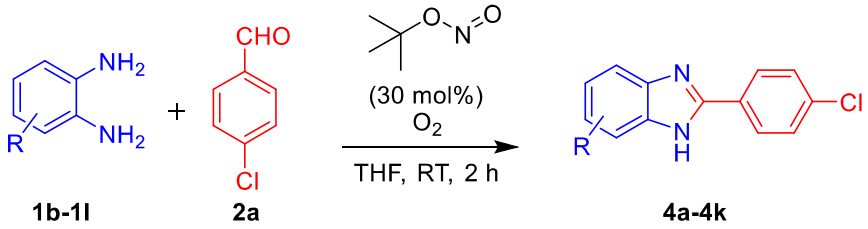


[a]Reaction conditions: Substrate **1a** & **2** (1 mmol) and TBN (30 mol%) in THF (5 mL) for 2 h at room temperature. [b]Isolated yield.

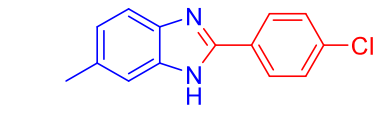
After exploring the scope of different aldehydes, a wide range of functionalized *o*-phenelenediamines was subjected to the condensation reaction with 4-chlorobenzaldehyde under optimized reaction conditions (Table 4.3). To our delight, *o*-phenylenediamines bearing electron donating groups (e.g. methyl, *tert*-butyl) and withdrawing groups (e.g. halogens, nitro, trifluoromethane, carbonyl, etc.) underwent cyclization smoothly. These reactions provided the corresponding

benzimidazoles in 82–89% yields within 2 h at room temperature (Table 4.3, 4a-4g). In addition, *o*-phenelenediamines bearing di-substitutions (i.e. 4,5-di-Me, 3,5-di-Me, 3,4- di-Me and 4,5-di-Cl) also participated efficiently in the reaction to provide the desired benzimidazoles in 86–89% yields (Table 4.3,4h-4k).

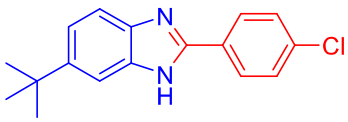
Table 4.3 Scope of *o*-phenelenediamines



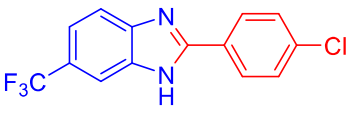
1b-1l **2a** **4a-4k**



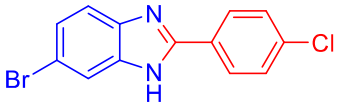
4a: 87%



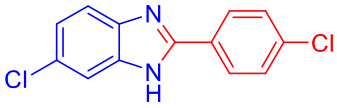
4b: 85%



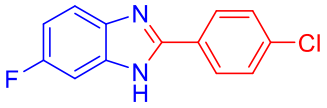
4c: 89%



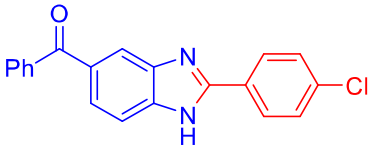
4d: 85%



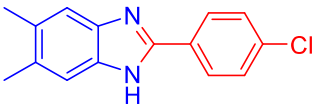
4e: 83%



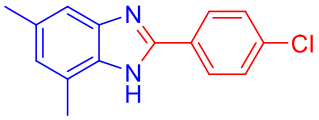
4f: 82%



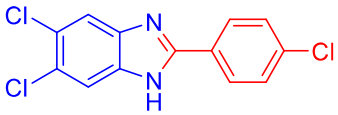
4g: 85%



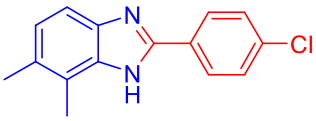
4h: 87%



4i: 89%



4j: 88%



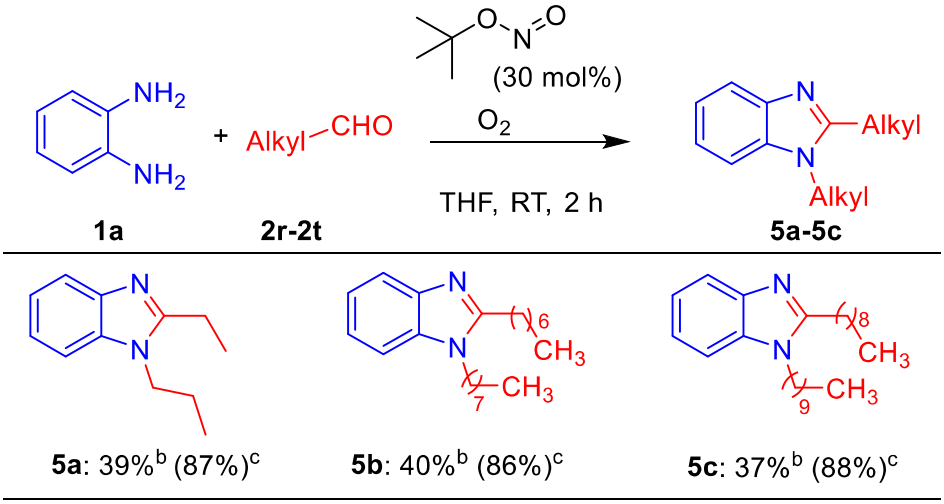
4k: 86%

[a]Reaction conditions: Substrate **1b-1l** & **2a** (1 mmol) and TBN (30 mol%) in THF (5 mL) for 2 h at room temperature. [b]Isolated yield.

Furthermore, we have investigated condensation of *o*-phenelenediamine with aliphatic aldehydes such as propanal, octanal and decanal under optimized conditions (Table 4.4). Interestingly, these aldehydes provided 1,2-disubstituted benzimidazoles

as a major product in 37–40% yields (Table 4.4, 5a–5c). It might be due to high reactivity of alkyl aldehydes over aryl aldehydes. Further, the reaction was carried out with 2.0 equiv. of aliphatic aldehydes which provided the 1,2-disubstituted benzimidazoles 5a–5c in 86– 88% yields.

Table 4.4 Scope of aliphatic aldehydes

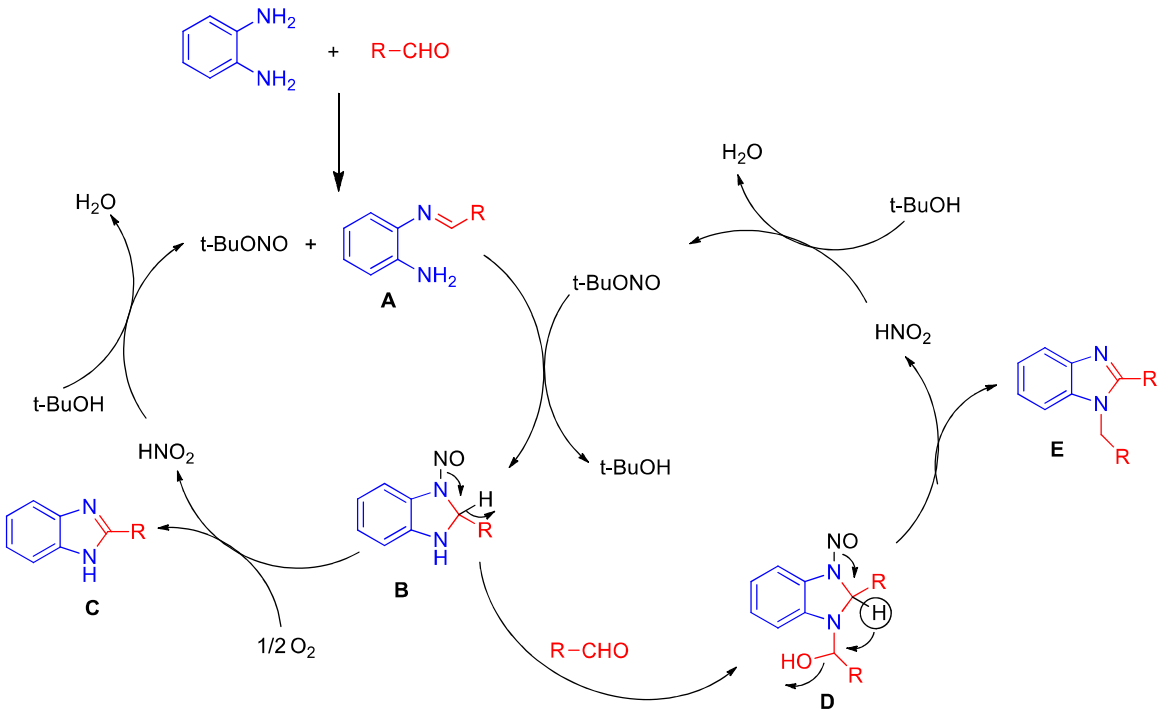


[a]Reaction conditions: Substrate **1a** (1 mmol) & aldehyde **2r-2t** (1 mmol) and TBN (30 mol%) in THF (5 mL) for 2 h at room temperature. [b]Isolated yield. [c]The reaction was carried out with 2.0 equiv. of aldehyde.

4.3 Plausible mechanism

A plausible mechanism for the reaction is depicted in Scheme 4.2. In the first step, *o*-phenylenediamine will react with benzaldehyde to form the imine intermediate (A). *tert*-Butyl nitrite (TBN) facilitates the formation of cyclic *N*-nitroso intermediate (B) from imine (A) *via N*-nitrosation [50]. The intermediate (B) delivers the desired product C (i.e. benzimidazole) and nitrous acid (HNO_2) in the presence of oxygen. In the case of formation of 1,2-disubstituted product, the intermediate (B) will react with another equivalent of aldehyde to form intermediate (D) which undergoes rearrangement [51-54] to generate 1,2-disubstituted product (E) and nitrous acid

(HNO_2). Further nitrous acid reacts with *tert*-butanol to provide the *tert*-butyl nitrite (TBN) [55] to resume the catalytic cycle.



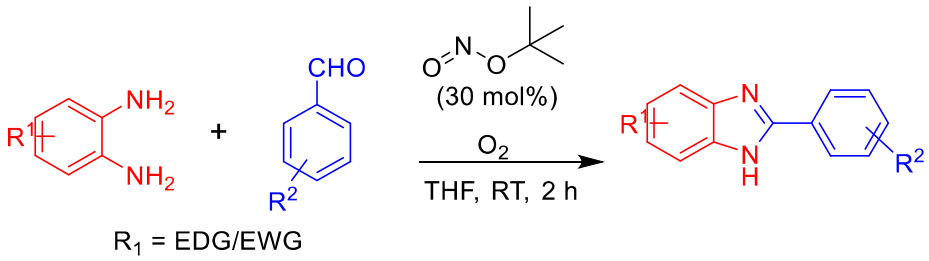
Scheme 4.2 Proposed mechanism of the reaction

4.4 Conclusion

In conclusion, an efficient catalytic method for the preparation of benzimidazoles from *o*-phenylenediamine and aldehydes in the presence of *tert*-butyl nitrite is demonstrated. All the reactions were carried out at room temperature in the presence of oxygen as an oxidant. This current methodology showed broad substrate scope while the desired products were obtained in good to excellent yields.

4.5 Experimental section

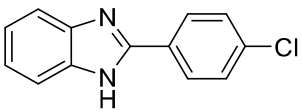
4.5.1 General experimental procedure for the synthesis of 2-substituted benzimidazoles.



o-phenylenediamine (**1**) (1.0 mmol; 1.0 equiv.) and aldehyde **2** (1.0 mmol; 1.0 equiv) were dissolved in THF (5 mL) and stirred at room temperature to which *tert*-butyl nitrite (30 mol%, 0.036 mL) was added. The resulting mixture was stirred under oxygen for 2 h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over sodium sulphate, concentrated and purified through column chromatography (SiO_2: ethyl acetate/hexane) to obtain the corresponding benzimidazole.

4.6 Analytical data of the products

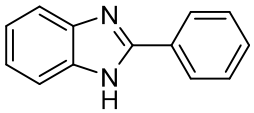
[4.6.1] 2-(4-Chlorophenyl)-1*H*-benzo[d]imidazole (3a)



The title compound was obtained as a white solid. M.p. 284–286 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), Rf = 0.57; Yield 90% (206 mg). 1H NMR (500 MHz, DMSO-d_6) δ = 12.99 (s, 1H), 8.18

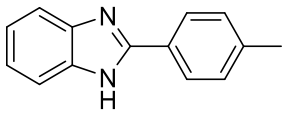
(d, J = 8.6 Hz, 2H), 7.73–7.60 (m, 3H), 7.59–7.51 (m, 1H), 7.22 (s, 2H). 13C NMR (125 MHz, DMSO-d_6) δ = 150.1, 143.6, 134.4, 131.1, 129.0, 129.0, 128.1, 122.7, 121.8, 118.9, 111.4. HRMS: Calc. for $C_{13}H_{10}ClN_2$ $[M+H]^+$: 229.0533, Obser.: 229.0530.

[4.6.2] 2-Phenyl-1*H*-benzo[d]imidazole (3b)



The title compound was obtained as a white solid. M.p. 286–288 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.55; Yield 75% (146 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.91 (s, 1H), 8.21–8.15 (m, 2H), 7.67 (d, J = 7.6 Hz, 1H), 7.59–7.52 (m, 3H), 7.49 (ddd, J = 7.3, 3.7, 1.2 Hz, 1H), 7.26–7.15 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.2, 143.7, 134.9, 130.1, 129.8, 128.9, 126.4, 122.5, 121.6, 118.8, 111.3. HRMS: Calc. for $C_{13}H_{11}N_2$ $[M+H]^+$: 195.0922, Obser.: 195.09200.

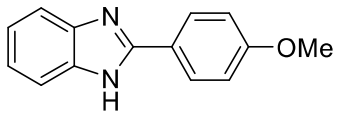
[4.6.3] 2-(*p*-Tolyl)-1*H*-benzo[d]imidazole (3c)



The title compound was obtained as a colourless solid. M.p. 266–268 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.58; Yield 79% (165 mg). ^{1}H

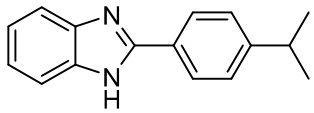
NMR (500 MHz, DMSO-d_6) δ = 12.81 (s, 1H), 8.07 (d, J = 8.1 Hz, 2H), 7.64 (d, J = 7.4 Hz, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 7.9 Hz, 2H), 7.22–7.16 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.3, 143.8, 139.5, 134.9, 129.4, 127.4, 126.3, 122.3, 121.5, 118.6, 111.1, 20.9. HRMS: Calc. for $C_{14}H_{13}N_2$ $[M+H]^+$: 209.1079, Obser.: 209.1073.

[4.6.4] 2-(4-Methoxyphenyl)-1*H*-benzo[d]imidazole (3d)



The title compound was obtained as a white solid. M.p. 222–224 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.48; Yield 71% (159 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.77 (s, 1H), 8.12 (d, J = 8.8 Hz, 2H), 7.56 (dd, J = 63.1, 6.9 Hz, 2H), 7.25–7.03 (m, 4H), 3.84 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 160.6, 151.3, 143.8, 134.9, 128.0, 122.6, 122.1, 121.5, 118.5, 114.4, 111.0, 55.3. HRMS: Calc. for $C_{14}H_{13}N_2O$ $[M+H]^+$: 225.1028, Obser.: 225.1020.

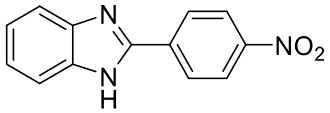
[4.6.5] 2-(4-Isopropylphenyl)-1*H*-benzo[d]imidazole (3e)



The title compound was obtained as a colourless solid. M.p. 255–257 °C. The residue was purified by column

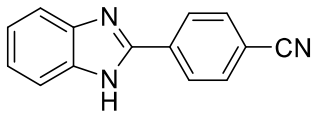
chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.56; Yield 78% (184 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.84 (s, 1H), 8.11 (d, J = 8.0 Hz, 2H), 7.59 (s, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.19 (dd, J = 5.9, 3.1 Hz, 2H), 2.95 (dt, J= 13.7, 6.8 Hz, 1H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.3, 150.3, 143.9, 135.0, 129.4, 127.8, 126.8, 126.5, 121.9, 118.6, 111.3, 33.3, 23.6. HRMS: Calc. for $C_{16}H_{10}N_2$ $[M+H]^+$: 237.1392, Obser.: 237.1387.

[4.6.6] 2-(4-Nitrophenyl)-1*H*-benzo[d]imidazole (3f)



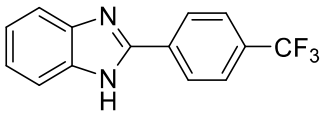
The title compound was obtained as a yellow solid. M.p. 302–304 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.37; Yield 89% (212 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.31 (s, 1H), 8.43 (s, 4H), 7.67 (d, J = 9.0 Hz, 2H), 7.28 (d, J = 3.3 Hz, 2H).^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.0, 147.8, 136.0, 135.3, 127.5, 127.4, 124.3, 122.8, 122.6, 119.4, 111.8. HRMS: Calc. for $C_{13}H_{10}N_3O_2$ $[M+H]^+$: 240.0773, Obser.: 240.0770.

[4.6.7] 4-(1*H*-Benzo[d]imidazol-2-yl) benzonitrile (3g)



The title compound was obtained as a colourless solid. M.p. 261–263 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.42; Yield 88% (193 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.19 (s, 1H), 8.34 (d, J = 8.5 Hz, 2H), 8.03 (d, J = 8.5 Hz, 2H), 7.65 (s, 2H), 7.30–7.22 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.3, 143.9, 134.2, 132.9, 126.9, 123.5, 122.9, 119.4, 118.5, 115.9, 111.8. HRMS: Calc. for $C_{14}H_{10}N_3$ $[M+H]^+$: 220.0875, Obser.: 220.0869.

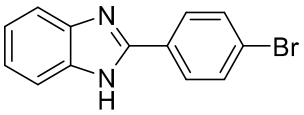
[4.6.8] 2-(4-(Trifluoromethyl)phenyl)-1*H*-benzo[d]imidazole (3h)



The title compound was obtained as a white solid. M.p. 264–265 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.47; Yield 90% (236 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.19 (s, 1H), 8.40 (d, J = 8.3 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.65 (s, 2H), 7.25 (dd, J = 5.9, 3.0 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.69, 143.82, 133.97, 129.69 (q, J = 31.25 Hz), 127.07, 126.88, 125.92 (q, J = 3.75 Hz), 124.14 (q, J = 270 Hz), 122.71, 119.14, 111.69.

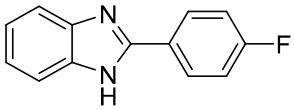
HRMS: Calc. for $C_{13}H_{10}F_3N_2$ $[M+H]^+$: 263.0796, Obser.: 263.0793 HRMS: Calc. for $C_{14}H_{10}F_3N_2$ $[M+H]^+$: 263.0796, Obser.: 263.0793.

[4.6.9] 2-(4-Bromophenyl)-1*H*-benzo[d]imidazole (3i)



The title compound was obtained as a white solid. M.p. 294–296 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.52; Yield 86% (234 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.00 (s, 1H), 8.13 (dd, J = 8.5, 2.6 Hz, 2H), 7.77 (dd, J = 8.4, 1.4 Hz, 2H), 7.67 (d, J = 6.3 Hz, 1H), 7.54 (d, J = 6.3 Hz, 1H), 7.22 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 150.2, 143.7, 135.0, 131.9, 129.3, 128.3, 123.2, 122.7, 121.8, 118.9, 111.4. HRMS: Calc. for $C_{13}H_{10}BrN_2$ $[M+H]^+$: 273.0027, Obser.: 273.0027.

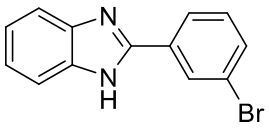
[4.6.10] 2-(4-Fluorophenyl)-1*H*-benzo[d]imidazole (3j)



The title compound was obtained as a white solid. M.p. 250–252 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.54; Yield 84% (178 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.92 (s, 1H), 8.26–8.17 (m, 2H), 7.60 (s, 2H), 7.40 (t, J = 8.8 Hz, 2H),

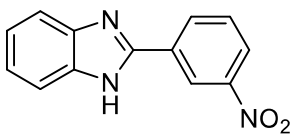
7.20 (dd, J = 5.9, 3.1 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 163.05 (q, 245 Hz), 150.3, 128.71 (d, J = 8.05 Hz), 126.78 (d, J = 5.0 Hz), 122.1, 118.6, 116.0 (d, J = 22.5 Hz), 111.1. HRMS: Calc. for $C_{13}H_{10}FN_2$ $[M+H]^+$: 213.0828, Obser.: 213.0824.

[4.6.11] 2-(3-Bromophenyl)-1H-benzo[d]imidazole (3k)



The title compound was obtained as a colourless solid. M.p. 249–251 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.55; Yield 89% (243 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.05 (s, 1H), 8.38 (t, J = 1.8 Hz, 1H), 8.19 (ddd, J = 7.8, 1.5, 1.0 Hz, 1H), 7.68 (ddd, J = 8.0, 2.0, 1.0 Hz, 2H), 7.53 (dt, J = 15.8, 5.7 Hz, 2H), 7.23 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.6, 143.6, 135.0, 132.4, 132.4, 131.1, 128.9, 125.3, 122.9, 122.2, 121.9, 119.0, 111.5. HRMS: Calc. for $C_{13}H_{10}BrN_2$ $[M+H]^+$: 273.0027, Obser.: 273.0024.

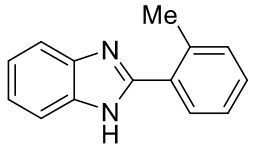
[4.6.12] 2-(3-Nitrophenyl)-1*H*-benzo[d]imidazole (3l)



The title compound was obtained as a yellow solid. M.p. 280–282 °C. The residue was purified by column chromatography in silica gel eluting with hexane:

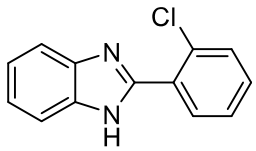
EtOAc (70:30), R_f = 0.38; Yield 88% (210 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.29 (s, 1H), 9.04–8.98 (m, 1H), 8.63–8.58 (m, 1H), 8.32 (ddd, J = 8.2, 2.2, 0.8 Hz, 1H), 7.84 (t, J = 8.0 Hz, 1H), 7.72 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.25 (dt, J = 14.9, 6.7 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.0, 148.3, 143.5, 135.0, 132.4, 131.7, 130.6, 124.2, 123.2, 122.1, 120.8, 119.2, 111.6. HRMS: Calc. for $C_{13}H_{10}N_3O_2$ $[M+H]^+$: 240.0733, Obser.: 240.0730.

[4.6.13] 2-(*o*-Tolyl)-1*H*-benzo[d]imidazole (3m)



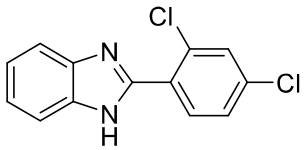
The title compound was obtained as a colourless solid. M.p. 222–223 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.56; Yield 85% (177 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.63 (s, 1H), 7.75 (d, J = 7.3 Hz, 1H), 7.68 (s, 1H), 7.55 (s, 1H), 7.41–7.34 (m, 3H), 7.21 (d, J = 3.8 Hz, 2H), 2.62 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.9, 143.7, 136.9, 134.3, 131.2, 130.0, 129.4, 129.2, 125.9, 122.3, 121.3, 118.8, 111.2, 20.9. HRMS: Calc. for $C_{14}H_{13}N_2$ $[M+H]^+$: 209.1079, Obser.: 209.1072.

[4.6.14] 2-(2-Chlorophenyl)-1*H*-benzo[d]imidazole (3n)



The title compound was obtained as a white solid. M.p. 225–226 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.59; Yield 87% (198 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.75 (s, 1H), 7.92 (dd, J = 7.3, 2.1 Hz, 1H), 7.68–7.50 (m, 5H), 7.25 (dd, J = 5.8, 2.8 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.0, 143.1, 134.6, 132.0, 131.6, 131.1, 130.3, 129.9, 127.4, 122.5, 121.9, 118.9, 111.6. HRMS: Calc. for $C_{13}H_{10}ClN_2$ $[M+H]^+$: 229.0533, Obser.: 229.0528.

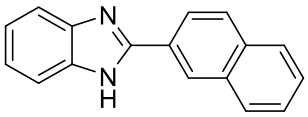
[4.6.15] 2-(2,4-Dichlorophenyl)-1*H*-benzo[d]imidazole (3o)



The title compound was obtained as a white solid. M.p. 220–222 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.63; Yield 85% (223 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.79 (s, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 2.0 Hz, 1H), 7.75–7.54 (m, 3H), 7.28–7.21 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 148.0, 143.1, 134.9, 134.6, 133.2, 132.5, 129.8, 128.8, 127.7, 122.9, 121.9, 119.1, 111.7. HRMS: Calc. for $C_{13}H_9Cl_2N_2$ $[M+H]^+$: 263.0143,

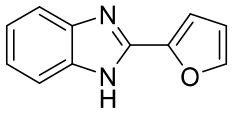
Obser.: 263.0141.

[4.6.16] 2-(Naphthalen-2-yl)-1*H*-benzo[d]imidazole (3p)



The title compound was obtained as a white solid. M.p. 216–218 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.62; Yield 74% (180 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ= 13.12 (s, 1H), 8.77 (s, 1H), 8.35 (dd, J = 8.6, 1.5 Hz, 1H), 8.11–8.03 (m, 2H), 8.01–7.95 (m, 1H), 7.72–7.56 (m, 4H), 7.24 (dd, J = 5.9, 3.0 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.2, 143.9, 135.2, 133.4, 132.8, 128.5, 128.5, 127.8, 127.6, 127.0, 126.9, 125.8, 124.0, 123.9, 122.2, 118.8, 111.5. HRMS: Calc. for $C_{17}H_{13}N_2$ $[M+H]^+$: 245.1079, Obser.: 245.1075.

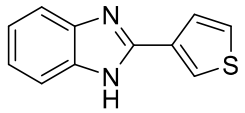
[4.6.17] 2-(Furan-2-yl)-1*H*-benzo[d]imidazole (3q)



The title compound was obtained as a pale yellow solid. M.p. 286–288 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.50; Yield 77% (142 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.90 (s, 1H), 7.95–7.92 (m, 1H), 7.56 (s, 2H), 7.20 (dd, J = 6.0, 3.2 Hz, 3H), 6.73 (dd, J = 3.4, 1.8 Hz, 1H). ^{13}C

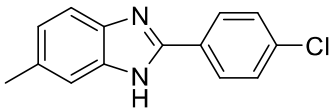
NMR (125 MHz, DMSO-d_6) δ = 145.5, 144.5, 143.6, 133.9, 122.1, 118.7, 112.2, 110.4. HRMS: Calc. for $C_{11}H_9N_2O$ $[M+H]^+$: 185.0715, Obser.: 185.0712.

[4.6.18] 2-(Thiophen-3-yl)-1*H*-benzo[d]imidazole (3r)



The title compound was obtained as a white solid. M.p. 58–60 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (90:10), R_f = 0.57; Yield 75% (150 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.79 (s, 1H), 8.24 (dd, J = 2.9, 1.2 Hz, 1H), 7.78 (dd, J = 5.0, 1.2 Hz, 1H), 7.73 (dd, J = 5.0, 2.9 Hz, 1H), 7.57 (s, 2H), 7.19 (dd, J = 6.0, 3.1 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 147.9, 145.5, 144.5, 143.6, 132.5, 127.5, 126.2, 124.9, 121.9, 112.2, 110.4. HRMS: Calc. for $C_{11}H_9N_2S$ $[M+H]^+$: 201.0486, Obser.: 201.0481.

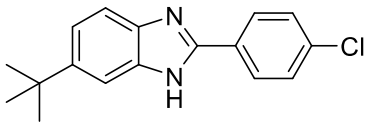
[4.6.19] 2-(4-Chlorophenyl)-6-methyl-1*H*-benzo[d]imidazole (4a)



The title compound was obtained as a white solid. M.p. 220 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.52; Yield 87% (210 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.84 (s, 1H), 8.17 (d, J = 8.6 Hz, 2H), 8.01–7.87 (m, 1H), 7.61 (d, J =

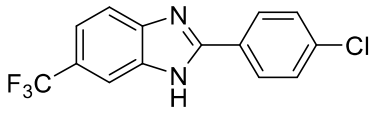
8.5 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 167.3, 149.7, 134.2, 132.7, 130.8, 129.2, 129.1, 128.9, 128.5, 127.9, 123.7, 118.5, 111.2, 21.2. HRMS: Calc. for $C_{14}H_{12}ClN_2$ $[M+H]^+$: 243.0689, Obser.: 243.0685.

[4.6.20] 6-(*tert*-Butyl)-2-(4-chlorophenyl)-1*H*-benzo[d]imidazole (4b)



The title compound was obtained as a white solid. M.p. 122–125 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.52; Yield 85% (241 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.02–7.96 (m, 2H), 7.56 (s, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.35–7.28 (m, 3H), 1.33 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.8, 146.8, 138.6, 137.1, 136.0, 129.2, 128.3, 127.9, 121.3, 114.6, 111.1, 34.8, 31.6. HRMS: Calc. for $C_{17}H_{18}ClN_2$ $[M+H]^+$: 285.1159, Obser.: 285.1178.

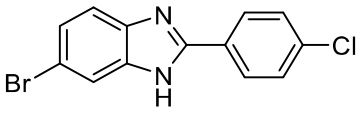
[4.6.21] 2-(4-Chlorophenyl)-6-(trifluoromethyl)-1*H*-benzo[d]imidazole (4c)



The title compound was obtained as a white solid. M.p. 105–115 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.62; Yield 89% (263 mg). ^{1}H

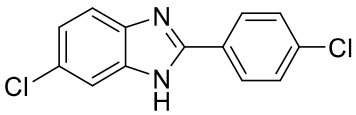
NMR (500 MHz, DMSO-d_6) δ = 13.39 (s, 1H), 8.20 (d, J = 8.6 Hz, 2H), 8.07–7.68 (m, 2H), 7.63 (d, J = 8.6 Hz, 2H), 7.52 (d, J = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 166.43, 152.6, 142.9, 136.02 (q, J = 370 Hz) 135.2, 129.1, 128.4, 128.3, 124.99 (q, J = 270 Hz), 122.88 (q, J = 31.25 Hz) 114.28 (q, J = 480 Hz). HRMS: Calc. for $C_{14}H_9ClF_3N_2$ $[M+H]^+$: 297.0406, Obser.: 297.0397.

[4.6.22] 6-Bromo-2-(4-chlorophenyl)-1*H*-benzo[d]imidazole (4d)



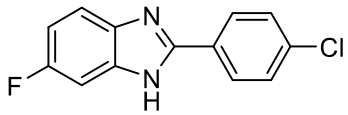
The title compound was obtained as a white solid. M.p. 210–215 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.51; Yield 85% (260 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.17 (d, J = 17.7 Hz, 1H), 8.17 (d, J = 8.6 Hz, 2H), 7.86 (s, 1H), 7.66–7.44 (m, 3H), 7.35 (d, J = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.5, 151.1, 145.1, 142.7, 136.2, 134.8, 134.1, 129.0, 128.5, 128.2, 125.3, 124.8, 121.2, 120.6, 114.9, 114.0, 113.1. HRMS: Calc. for $C_{13}H_9BrClN_2$ $[M+H]^+$: 306.9638, Obser.: 306.9659.

[4.6.23] 6-Chloro-2-(4-chlorophenyl)-1*H*-benzo[d]imidazole (4e)



The title compound was obtained as a white solid. M.p. 202–205 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.58; Yield 83% (218 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.16 (s, 1H), 8.18 (d, J = 8.1 Hz, 2H), 7.82–7.46 (m, 4H), 7.25 (d, J = 15.3 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 151.7, 144.6, 134.8, 133.8, 129.0, 128.5, 128.2, 122.8, 122.2, 120.1, 118.2, 112.7, 111.0. HRMS: Calc. for $C_{13}H_9Cl_2N_2$ $[M+H]^+$: 263.0143, Obser.: 263.0139.

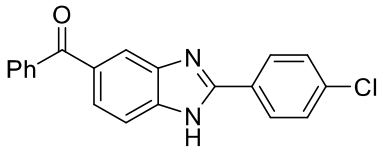
[4.6.24] 2-(4-Chlorophenyl)-6-fluoro-1*H*-benzo[d]imidazole (4f)



The title compound was obtained as a white solid. M.p. 105–110 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.56; Yield 82% (202 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.12 (s, 1H), 8.17 (d, J = 8.6 Hz, 2H), 7.73–7.30 (m, 4H), 7.07 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 166.46, 158.57 (d, J = 250 Hz), 151.52 (d, J = 92.5 Hz), 144.1, 140.4, 137.7, 134.6, 131.39 (d, J = 71.25 Hz), 129.0, 128.72 (d, J = 5 Hz), 128.1, 119.8, 112.0, 110.46 (d, J = 63.75

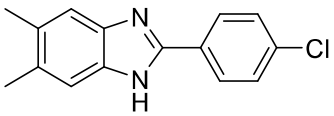
Hz), 104.4, 97.7. HRMS: Calc. for $C_{13}H_9ClFN_2$ $[M+H]^+$: 247.0438, Obser.: 247.0421.

[4.6.25] (2-(4-Chlorophenyl)-1*H*-benzo[d]imidazol-5-yl)(phenyl)methanone (4g)



The title compound was obtained as a white solid. M.p. 260 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (30:40), R_f = 0.47; Yield 85% (282 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.34 (s, 1H), 8.20 (s, 2H), 8.05–7.87 (m, 1H), 7.84–7.49 (m, 9H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 195.4, 152.4, 142.9, 138.0, 135.1, 132.0, 131.0, 129.4, 129.1, 128.6, 128.3, 128.3, 124.6, 121.7, 118.7, 114.2, 111.5. HRMS: Calc. for $C_{20}H_{14}ClN_2O$ $[M+H]^+$: 333.0795, Obser.: 333.0814.

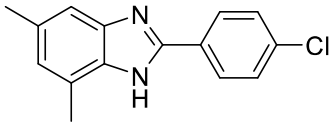
[4.6.26] 2-(4-Chlorophenyl)-5,6-dimethyl-1*H*-benzo[d]imidazole (4h)



The title compound was obtained as a white solid. M.p. 142–145 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.60; Yield 87% (222 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.71 (s, 1H), 8.18–8.11 (m, 2H), 7.60 (d, J = 8.7 Hz, 2H), 7.47–7.27 (m, 2H), 2.33 (s, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ =

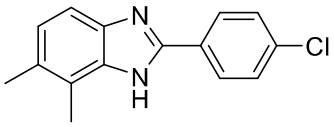
149.2, 142.5, 134.0, 131.1, 130.0, 129.3, 128.9, 128.6, 127.8, 118.9, 111.3, 20.0. HRMS: Calc. for $C_{15}H_{14}ClN_2$ $[M+H]^+$: 257.0846, Obser.: 257.0861.

[4.6.27] 2-(4-Chlorophenyl)-5,7-dimethyl-1*H*-benzo[d]imidazole (4i)



The title compound was obtained as a white solid. M.p. 150–155 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.54; Yield 89% (228 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.63 (d, J = 102.9 Hz, 1H), 8.19 (dd, J = 36.4, 8.4 Hz, 2H), 7.61 (t, J = 7.5 Hz, 2H), 7.19 (d, J = 69.4 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 2.53 (s, 3H), 2.38 (d, J = 9.9 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.8, 148.7, 143.8, 141.3, 134.8, 134.1, 134.0, 132.7, 131.9, 130.8, 129.3, 128.9, 128.8, 128.2, 127.9, 127.9, 124.9, 123.7, 120.8, 116.0, 108.5, 21.3, 21.1, 17.0, 16.5. HRMS: Calc. for $C_{15}H_{14}ClN_2$ $[M+H]^+$: 257.0846, Obser.: 257.0832.

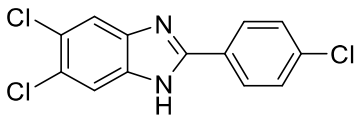
[4.6.28] 2-(4-Chlorophenyl)-6,7-dimethyl-1*H*-benzo[d]imidazole (4j)



The title compound was obtained as a white solid. M.p. 130–135 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.57; Yield 88% (225 mg). ^{1}H

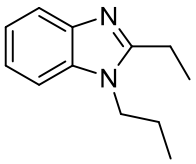
NMR (500 MHz, DMSO-d_6) δ = 12.59 (d, J = 175.7 Hz, 1H), 8.22 (d, J = 12.9 Hz, 2H), 7.69–7.53 (m, 2H), 7.48–7.17 (m, 1H), 7.01 (d, J = 8.1 Hz, 1H), 2.50 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 149.6, 149.2, 143.6, 141.9, 135.3, 134.1, 132.8, 130.0, 129.3, 128.8, 128.1, 128.0, 126.3, 124.8, 124.2, 118.9, 115.7, 107.9, 19.0, 13.9, 13.1. HRMS: Calc. for $C_{15}H_{14}ClN_2$ $[M+H]^+$: 257.0846, Obser.: 257.0832.

[4.6.29] 5,6-Dichloro-2-(4-chlorophenyl)-1*H*-benzo[d]imidazole (4k)



The title compound was obtained as a white solid. M.p. 270 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.67; Yield 86% (255 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.27 (s, 1H), 8.14 (d, J = 8.5 Hz, 2H), 7.90 (s, 1H), 7.73 (s, 1H), 7.61 (d, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 152.6, 143.3, 135.1, 131.1, 129.1, 128.3, 128.1, 119.9, 112.7. HRMS: Calc. for $C_{13}H_8Cl_3N_2$ $[M+H]^+$: 296.9753, Obser.: 296.9743.

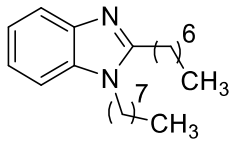
[4.6.30] 2-Ethyl-1-propyl-1*H*-benzo[d]imidazole (5a)



The title compound was obtained as a yellow liquid. The residue was purified by column chromatography

in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.70; Yield 87% (163 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.75–7.71 (m, 1H), 7.31–7.27 (m, 1H), 7.21 (dd, J = 6.1, 3.0 Hz, 2H), 4.09–4.02 (m, 2H), 2.89 (q, J = 7.5 Hz, 2H), 1.88–1.79 (m, 2H), 1.47 (t, J = 7.5 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 155.9, 142.5, 135.0, 121.8, 121.5, 119.1, 109.1, 45.0, 23.0, 20.7, 11.8, 11.3. HRMS: Calc. for $C_{12}H_{17}N_2$ $[M+H]^+$: 189.1392, Obser.: 189.1392.

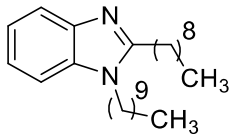
[4.6.31] 2-Heptyl-1-octyl-1*H*-benzo[d]imidazole (5b)



The title compound was obtained as a Brown liquid. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.65; Yield 86% (282 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79–7.65 (m, 1H), 7.30–7.26 (m, 1H), 7.21 (ddd, J = 6.4, 3.9, 1.8 Hz, 2H), 4.1–4.04 (m, 2H), 2.87–2.81 (m, 2H), 1.94–1.85 (m, 2H), 1.82–1.73 (m, 2H), 1.45 (dd, J = 10.4, 5.2 Hz, 2H), 1.35 (ddd, J = 14.4, 7.1, 4.7 Hz, 6H), 1.31–1.27 (m, 6H), 1.25 (s, 4H), 0.88 (td, J = 7.0, 3.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 155.0, 142.6, 134.9, 121.7, 121.5,

119.0, 109.1, 43.5, 31.6, 31.6, 29.8, 29.5, 29.1, 29.0, 28.9, 27.8, 27.4, 26.9, 22.5, 22.5, 14.0, 13.9. HRMS: Calc. for $C_{22}H_{37}N_2$ $[M+H]^+$: 329.2957, Obser.: 239.2949

[4.6.32] 1-Decyl-2-nonyl-1*H*-benzo[d]imidazole (5c)



The title compound was obtained as a Brown liquid. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (70:30), R_f = 0.67; Yield 88% (338 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76–7.68 (m, 1H), 7.30–7.26 (m, 1H), 7.24–7.17 (m, 2H), 4.12–4.00 (m, 2H), 2.90–2.78 (m, 2H), 1.89 (dt, J = 15.5, 7.7 Hz, 2H), 1.78 (dt, J = 14.9, 7.6 Hz, 2H), 1.45 (dd, J = 10.5, 4.9 Hz, 3H), 1.38–1.31 (m, 6H), 1.29–1.23 (m, 17H), 0.87 (t, J = 7.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 155.0, 142.6, 134.9, 121.7, 121.5, 119.0, 109.1, 43.5, 31.8, 31.7, 29.8, 29.5, 29.4, 29.3, 29.3, 29.2, 29.1, 27.8, 27.4, 26.9, 226, 22.5, 14.0. HRMS: Calc. for $C_{26}H_{45}N_2$ $[M+H]^+$: 385.3583, Obser.: 385.3572.

4.7 Spectral data of few products

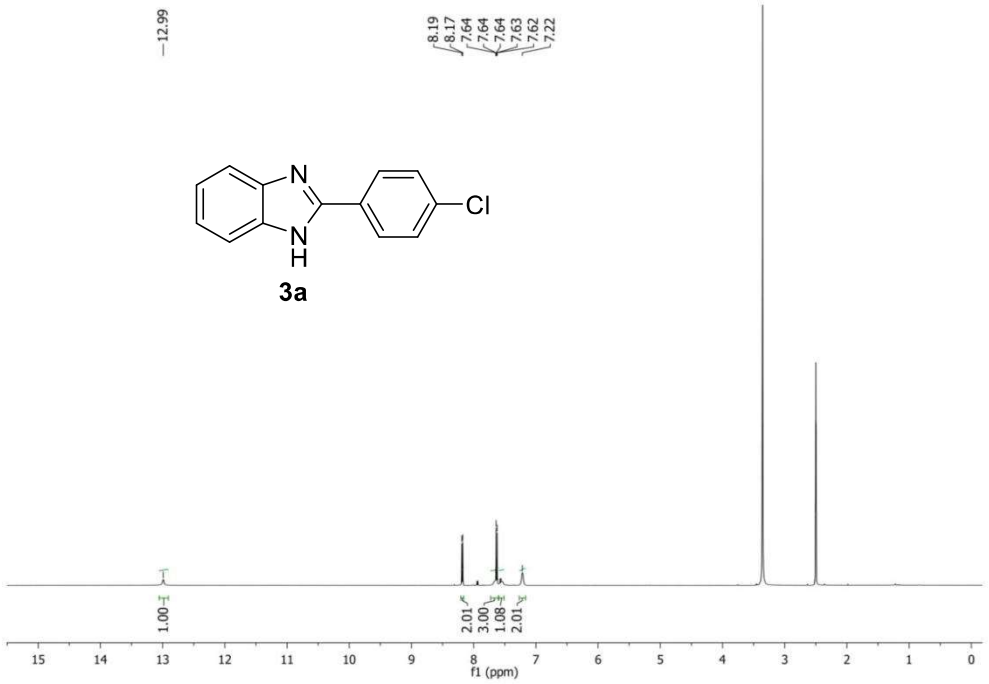


Figure 4.2 ^{1}H NMR of product **3a** in **DMSO-d$_6$**

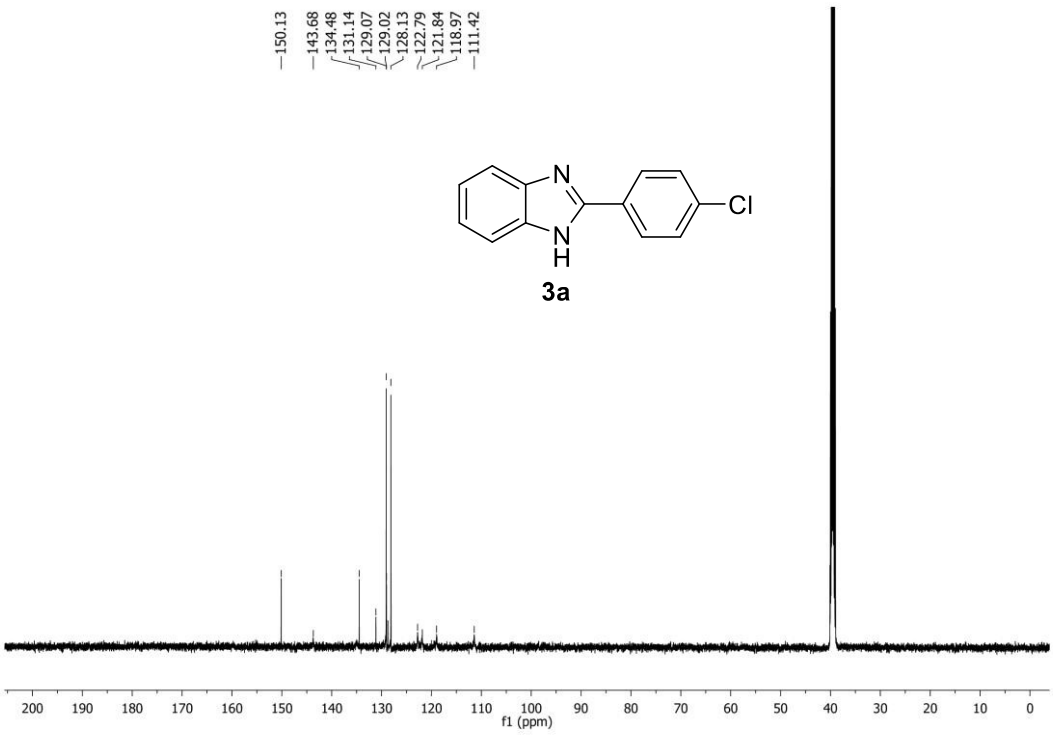


Figure 4.3 ^{13}C NMR of product **3a** in **DMSO-d$_6$**

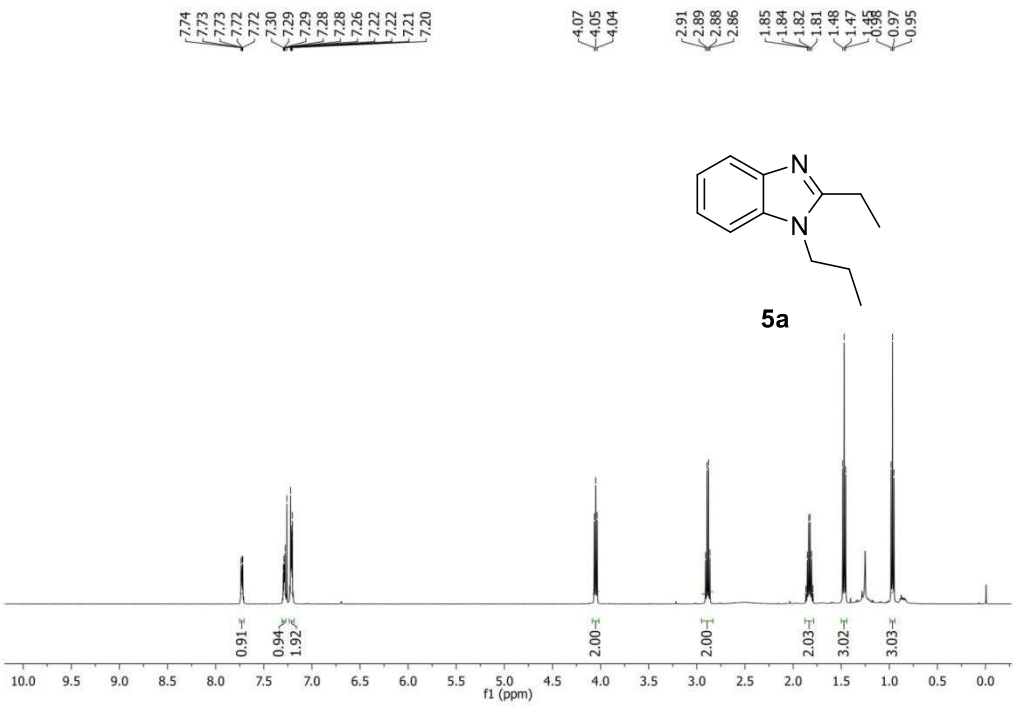


Figure 4.4 ^{1}H NMR of product **5a** in **$CDCl_3$**

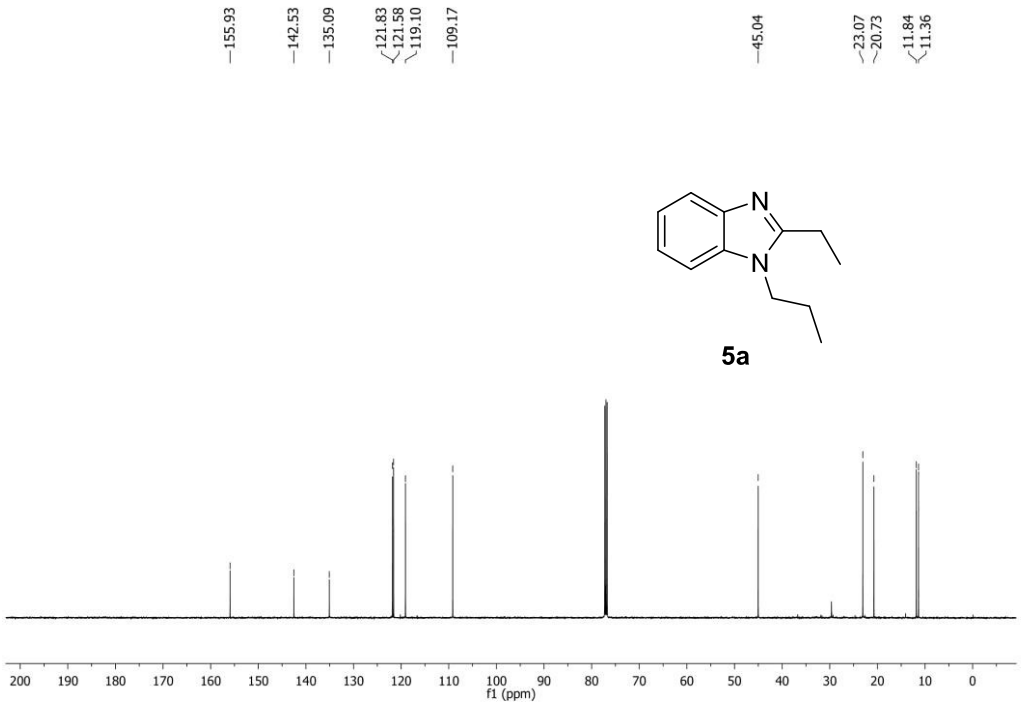


Figure 4.5 ^{13}C NMR of product **5a** in **$CDCl_3$**

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