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METAL-FREE SYNTHESIS OF *N*-CONTAINING HETEROCYCLES FROM *o*-SUBSTITUTED ANILINE DERIVATIVES VIA 2,4,6-TRIHYDROXYBENZOIC ACID-CATALYZED OXIDATIVE DEHYDROGENATION OF BENZYLAMINES UNDER OXYGEN ATMOSPHERE

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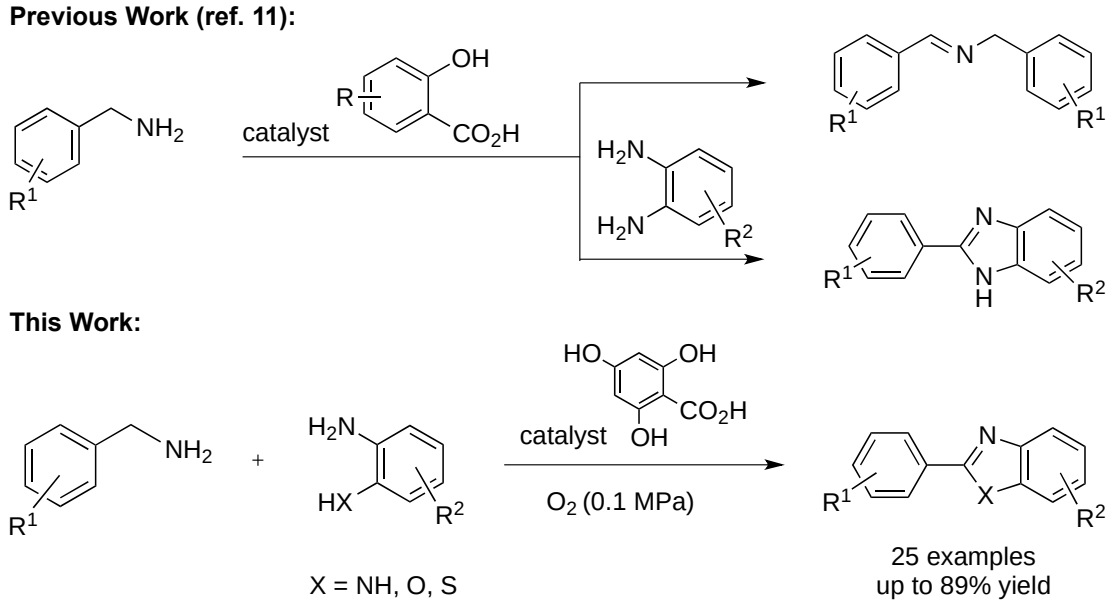
This paper is dedicated to Professor Kiyoshi Tomioka, Doshisha Women's College, on the occasion of his 70th birthday.

Abstract – A series of *N*-heterocycles, i.e., benzimidazoles, benzoxazoles, and benzothiazoles, can be conveniently synthesized by the oxidative cyclization of benzylamines with *o*-substituted aniline derivatives, i.e., *o*-phenylenediamines, *o*-aminophenols, and *o*-aminothiophenols, using 2,4,6-trihydroxybenzoic acid as an organocatalyst under an oxygen atmosphere. This approach provides a mild and efficient tool towards benzimidazoles and benzothiazoles with good yields and a broad substrate scope. The developed synthesis of *N*-heterocycles might proceed via the oxidative dehydrogenation of benzylamines ($ArCH_2NH_2$), generating the corresponding imines (ArCH=NH) as key intermediates.

INTRODUCTION

N–Heterocyclic compounds such as benzimidazoles and related heterocycles possess an important structural framework that is present in a large variety of naturally occurring compounds and pharmaceuticals.[1] Therefore, many methods for their syntheses have been reported. For example, condensation reactions between *o*-substituted aniline derivatives such as *o*-phenylenediamines and carboxylic acids[2] or aldehydes[3] are popular. In addition, the oxidative coupling between primary amines and *o*-phenylenediamines[4–9,10] is an excellent alternative, because of the high atom economy and high

selectivity of the products. During the last decade, transition metal (e.g., Pd,[4] Cu,[5] or Fe[6])-catalyzed processes have been developed for the oxidative coupling of amines and *o*-phenylenediamines. Recently, from the viewpoint of green chemistry, the use of metal-free catalysts in oxidative coupling reactions has garnered attention as a promising eco-friendly method. Organocatalysts such as bioinspired *ortho*-quinone[7] can be employed for the coupling of amines and *o*-phenylenediamines. Notably, ionic liquids have also been introduced for the metal-free synthesis of benzimidazoles. For example, imidazolium-based ionic liquid[8] shows high catalytic activities in this coupling reaction. Moreover, Nguyen's group synthesized benzimidazoles using a catalytic amount of acetic acid under an oxygen atmosphere.[9] We recently reported an efficient method for the oxidative coupling of benzylamines to imines using salicylic acid derivatives as organocatalysts under an oxygen atmosphere and applied the developed method to the synthesis of benzimidazoles.[11] Herein, we report the use of 2,4,6-trihydroxybenzoic acid as an organocatalyst to synthesize *N*-heterocycles such as benzimidazoles, benzoxazoles, and benzothiazoles, thereby significantly expanding the scope of the catalytic oxidation reaction with salicylic acid derivatives (Scheme 1).



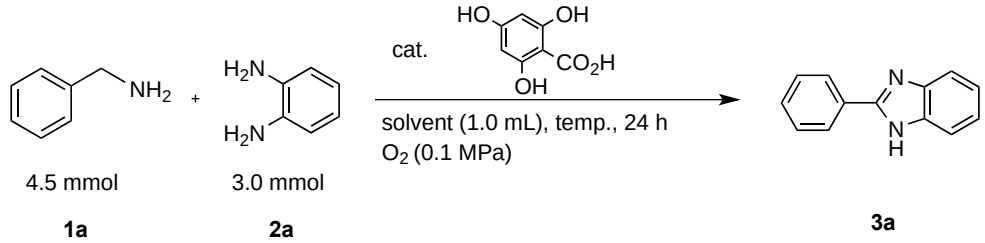
Scheme 1. Oxidation of benzylamines catalyzed by salicylic acid derivatives

RESULTS AND DISCUSSION

Initially, the oxidative coupling between benzylamine (**1**) and *o*-phenylenediamine (**2**) was examined under an oxygen atmosphere in the presence of 2,4,6-trihydroxybenzoic acid (10 mol%) as an organocatalyst. Compared with 4,6-dimethoxysalicylic acid, which was used previously, 2,4,6-trihydroxybenzoic acid has a higher oxidation ability and is less expensive. When this coupling reaction was conducted under neat conditions at room temperature, benzimidazole (**3a**) was not formed

(Table 1, entry 1). Fortunately, however, upon increasing the reaction temperature to 50 and 70 °C, the desired product **3a** was obtained in 15 and 75% yields, respectively (Table 1, entries 2 and 3). Next, the amount of catalyst was examined, and 10 mol% of 2,4,6-trihydroxybenzoic acid was found to be suitable (Table 1, entries 3–5). When the reaction was conducted in toluene, which was previously found to be the optimal solvent for the coupling reaction of benzylamines and imines,[11] **3a** was obtained in an improved yield of 94% (Table 1, entry 6). Without 2,4,6-trihydroxybenzoic acid as the catalyst, the coupling reaction did not proceed (Table 1, entry 7). Lower reaction temperatures or shorter reaction times hindered the formation of **3a** (Table 1, entries 8 and 9).

Table 1. Optimization of benzimidazole synthesis



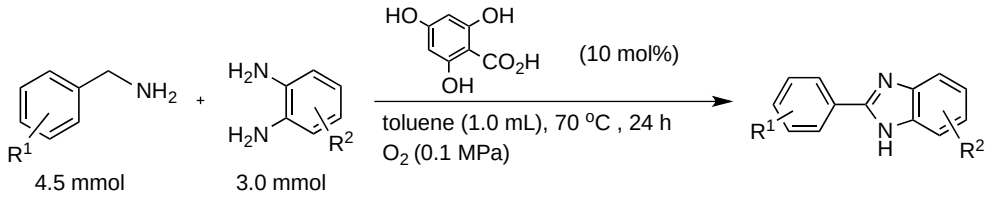
4.5 mmol **1a** 3.0 mmol **2a** **3a**

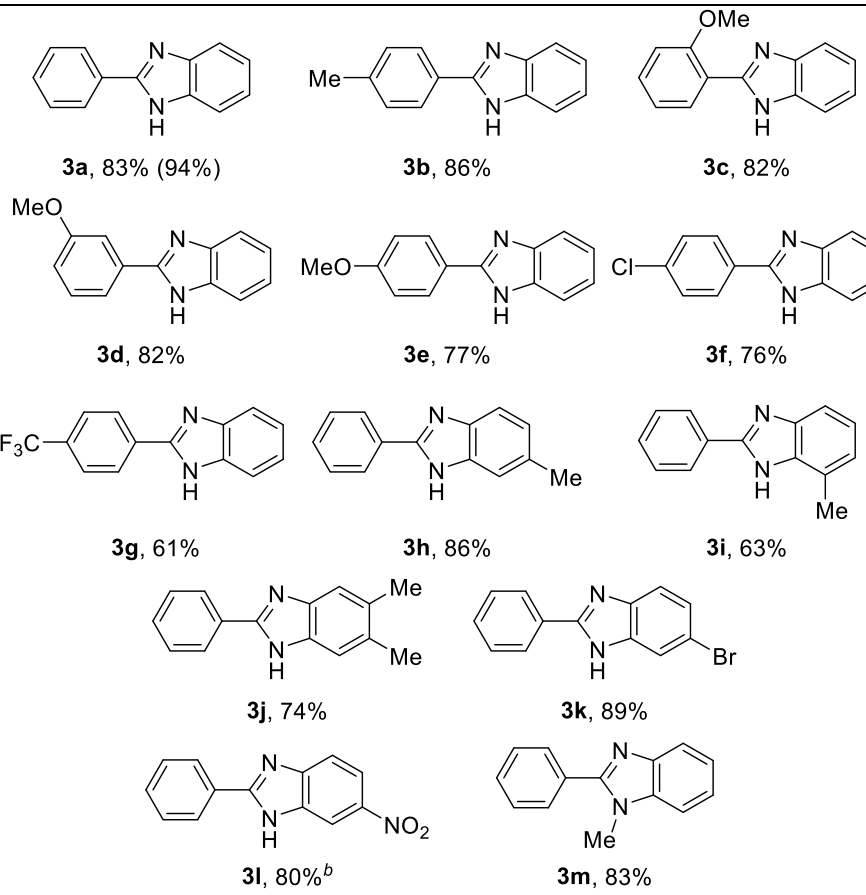
entry	solvent	cat. [mol%]	temp. [°C]	yield[a] [%] **3**
1	none	10	r.t.	N.D.
2	none	10	50	15
3	none	10	70	75
4	none	5	70	66
5	none	15	70	69
6	toluene	10	70	94 (83)
7	toluene	none	70	trace
8	toluene	10	50	61
9[b]	toluene	10	70	66

[a] Determined by ^{1}H NMR using 1,3,5-trioxane as the internal standard (isolated yield); yield of **3a** based on substrate **2a**. [b] Reaction time: 18 h.

Under the optimized conditions (Table 1, entry 6), the scope of the 2,4,6-trihydroxybenzoic acid-catalyzed oxidative coupling was examined with a range of benzylamines and *o*-phenylenediamines (Table 2). *p*-, *m*-, and *o*-Methoxy-substituted benzylamines oxidatively coupled with **2a** to afford benzimidazoles in 77–82% yields (Table 2, **3c**–**e**). Functional groups at the *para*-position of benzylamines, including methyl, chloro, and trifluoromethyl groups, were tolerated in the oxidative coupling reaction, producing benzimidazoles in 61–86% yields (Table 2, **3b**, **3f**, and **3g**). Moreover, several *o*-phenylenediamine derivatives were employed as substrates with benzylamine (**1a**). Under the developed conditions, *o*-phenylenediamines bearing electron-donating or electron-withdrawing groups on the aromatic ring could afford the desired benzimidazoles (**3**) in 63–89% yields (Table 2, **3h**–**3m**).

Table 2. Substrate scope of benzimidazole synthesis[a]



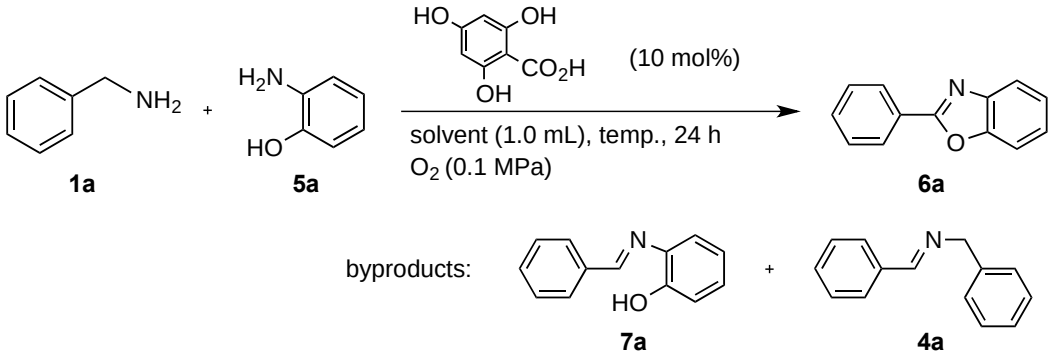


[a] Yield of the isolated product based on **2** (^{1}H NMR yield using 1,3,5-trioxane as the internal standard).
[b] Reaction conducted at 90 °C.

Next, we examined the benzoxazole synthesis[7] using 2,4,6-trihydroxybenzoic acid-catalyzed oxidative coupling of benzylamine (**1a**) and *o*-aminophenol (**5a**) under an oxygen atmosphere. Table 3 shows the results of the optimization of the reaction conditions for the benzoxazole synthesis. Among the tested solvents, nonpolar and aprotic solvents such as toluene seemed to be suitable for the oxidative coupling (Table 3, entries 1–3), and elevated temperatures (90 °C) led to the formation of the desired benzoxazole **6a** in 17% yield along with uncyclized product **7a** and the homo-coupling product **4a** of benzylamine (**1a**) (Table 3, entry 4). Dilution resulted in an increase in the yield of **7a**, probably because oxygen easily dissolved in the solution (Table 3, entry 5). Increasing the temperature to 110 °C afforded 34% of **6a** along with 35% of **7a** (Table 3, entry 6). Decreasing the amount of **1a** (4 mmol) led to an increase in the

yield of **6a** (45%) (Table 3, entry 8). When the reaction was conducted at 140 °C using *p*-xylene, **6a** was formed in 50% yield; however, the material balance was lower unfortunately (Table 3, entry 10). Overall, in the synthesis of benzoxazoles, the oxidative coupling between benzylamine (**1a**) and the amino group of *o*-aminophenol (**5a**) proceeded efficiently; however, the decreased nucleophilicity of the phenolic -OH group might contribute to the increased difficulty of the cyclization process.

Table 3. Optimization of benzoxazole synthesis



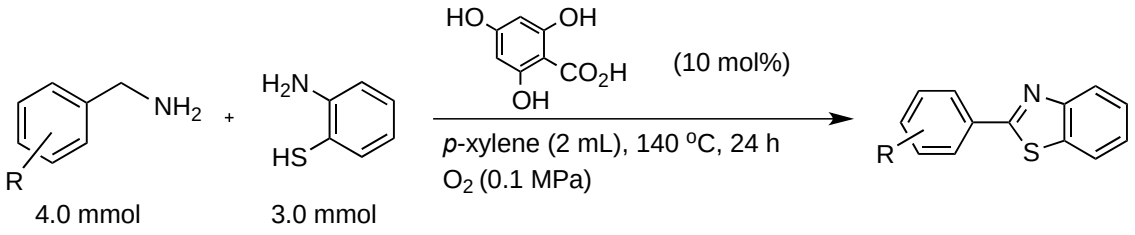
entry	solvent [mL]	**1a**/**5a** [mmol/mmol]	temp. [°C]	yield[a] [%] **6a**/**7a**/**4a**
1	toluene [1]	4.5/3.0	70	3/39/15
2	EtOAc [1]	4.5/3.0	70	1/21/2
3	MeCN [1]	4.5/3.0	70	4/14/1
4	toluene [1]	4.5/3.0	90	17/36/3
5	toluene [2]	4.5/3.0	90	13/61/7
6	toluene [2]	4.5/3.0	110	34/35/2
7	toluene [3]	4.5/3.0	110	24/56/2
8	toluene [2]	4.0/3.0	110	45/36/1
9	*p*-xylene [2]	4.5/3.0	140	44/1/1
10	*p*-xylene [2]	4.0/3.0	140	50/0/6

[a] Determined by ^{1}H NMR using 1,3,5-trioxane as the internal standard; yield of **3a** based on substrate **5a**.

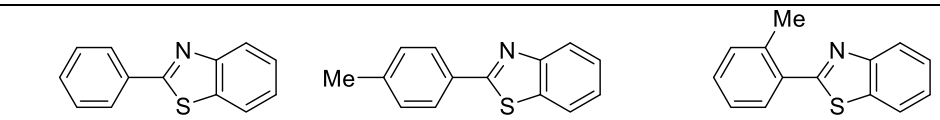
Since the nucleophilicity of -SH is much higher than that of -OH, the oxidative coupling between benzylamine (**1a**) and *o*-aminothiophenol (**8a**)[9,10] was expected to proceed via nucleophilic cyclization to afford benzothiazole (**9a**). Indeed, the reaction of **1a** (4 mmol) with **8a** (3 mmol) in the presence of 2,4,6-trihydroxybenzoic acid (10 mol%) in *p*-xylene (2 mL) under an O_2 atmosphere (0.1 MPa) at 140 °C for 24 h successfully afforded benzothiazole (**9a**) in 79% yield (Table 4, **9a**). In this reaction, the uncyclized product (PhCH=N-C_6H_4-SH-*o*, **10a**) was not obtained. The benzothiazole synthesis could be applied to a range of benzylamines (Table 4). For example, *p*- and *o*-methyl-substituted benzylamines underwent oxidative coupling to give the corresponding benzothiazoles in 83 and 80% yields, respectively (Table 4, **9b** and **9c**). *p*-, *m*-, and *o*-Methoxy-substituted benzylamines could oxidatively couple with **2a** to afford the desired benzothiazoles in 78–88% yields (Table 4, **9d**–**9f**). Functional groups such as *p*-Cl, *m*-Cl, and *p*-CF_3 were tolerated in this oxidative coupling reaction, and lead to the formation

of the desired benzothiazoles in 66–85% yields (Table 4, **9g**–**9i**). Moreover, *p*-*t*-butylbenzylamine and 1-naphthylmethylamine could be oxidized to the desired benzothiazoles in 87 and 72% yields, respectively (Table 4, **9j** and **9k**).

Table 4. Benzothiazole synthesis[a]



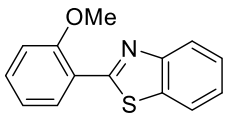
1 **8a** **9**



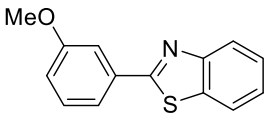
9a, 79% (91%)

9b, 83% (97%)

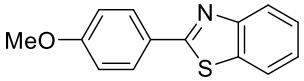
9c, 80% (99%)



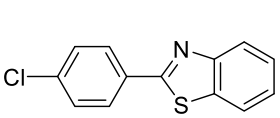
9d, 85% (71%)



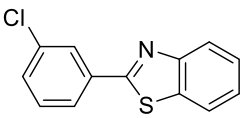
9e, 78% (77%)



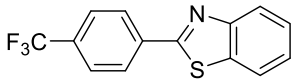
9f, 88% (79%)



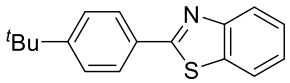
9g, 66% (87%)

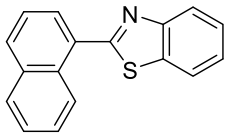


9h, 85% (68%)



9i, 77% (81%)

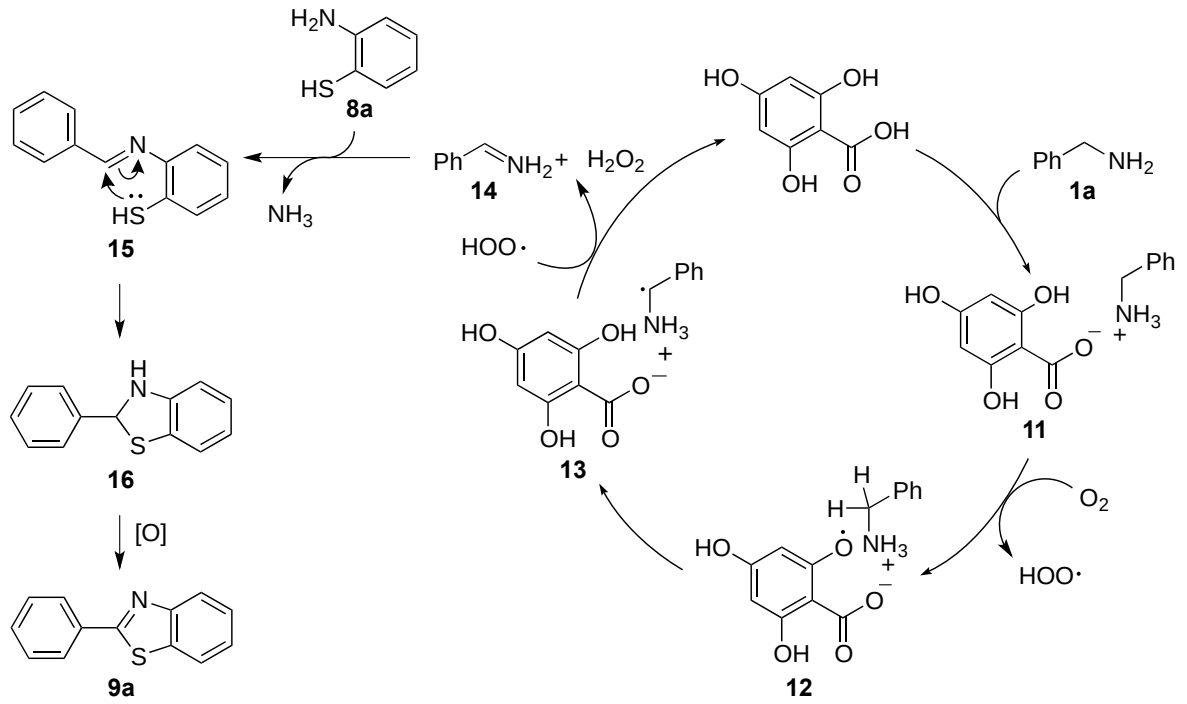




9j, 87% (71%) **9k**, 72% (82%)

[a] Yield of isolated product based on **8a**; ^{1}H NMR yield determined using 1,3,5-trioxane as internal standard provided in parenthesis.

A plausible mechanism for the present oxidative cyclization reaction is proposed in Scheme 2. The salicylic acid catalyst first reacts with benzylamine (**1a**) to form the corresponding salt **11**. Under an oxygen atmosphere, the salt **11** may be oxidized to form phenoxyl radical **12**, which abstracts H· from benzylamine to generate **13**. Meanwhile, the formed HOO· abstracts another H· from amino group to afford phenylmethanimine (**14**) with regeneration of the salicylic acid catalyst.[11,12] The intermediate **14** undergoes amino group exchange reaction with *o*-aminothiophenol (**8a**) to form imine **15**. The intramolecular cyclization of **15** leads to the formation of **16**, followed by oxidative aromatization to afford the product **9a**.



Scheme 2. A plausible mechanism for the oxidative cyclization reaction

In summary, we developed a simple, metal-free synthetic route towards benzimidazoles from benzylamines and *o*-phenylenediamines using 2,4,6-trihydroxybenzoic acid as an organocatalyst under an oxygen atmosphere. This cyclization method was successfully applied for the synthesis of benzoxazoles and benzothiazoles. The versatility of salicylic acid catalysts was demonstrated in a new oxidative process. Further efforts towards developing metal-free oxidations are currently under way in our laboratory and will be reported in due course.

EXPERIMENTAL

Unless otherwise stated, benzylamine derivatives, *o*-phenylenediamine derivatives, *o*-aminophenol, *o*-aminothiophenol, and 4,6-dihydroxysalicylic acid were obtained from commercial suppliers. All solvents were distilled and degassed with nitrogen prior to use. ^{1}H NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) FT NMR system or JEOL JNM-ECX400 (400 MHz) FT NMR system in $CDCl_3$ and DMSO-d_6 with Me_4Si as the internal standard. ^{13}C NMR spectra were recorded on a JEOL JNM-ECX400 (100 MHz) FT NMR or JEOL JNM-ECS400 (100 MHz) FT NMR in $CDCl_3$ and DMSO-d_6.

Experimental Procedure for the Synthesis of Benzimidazole Derivatives 3. To a two-necked flask, benzylamine derivatives **1** (4.5 mmol), *o*-phenylenediamine derivatives **2** (3.0 mmol), 4,6-dihydroxysalicylic acid (10 mol%), and distilled toluene (1.0 mL) were added, and then the reaction

vessel was connected to an O_2 balloon at room temperature. The mixture was stirred at 70 °C under an O_2 atmosphere for 24 h. The resulting mixture was transferred into a round-bottom flask using methanol (MeOH) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (basified with Et_3N (25 wt%) (eluent: hexane/EtOAc with 1.0 v/v% Et_3N) to give the product **3**.

*2-Phenyl-1H-benzimidazole (**3a**)*.[13] Yellow solid, 484 mg, 83% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.98 (br, 1H), 8.23–8.21 (m, 2H), 7.63–7.53 (m, 4H), 7.49–7.46 (m, 1H), 7.23–7.19 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 151.2, 130.2, 129.8, 128.9, 126.4, 122.1 [note: The signals of quaternary carbon atoms at 150–130 ppm and at 120–110 ppm could not be clearly observed due to broadening].

*2-(4-Methylphenyl)-1H-benzimidazole (**3b**)*.[13] Yellow solid, 537 mg, 86% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.83 (br, 1H), 8.08 (d, J = 8.0 Hz, 2H), 7.65–7.50 (m, 2H), 7.35 (d, J = 7.5 Hz, 2H), 7.29–7.18 (m, 2H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 151.3, 143.8, 139.5, 134.9, 129.5, 127.4, 126.3, 122.3, 121.5, 118.7, 111.1, 20.9.

*2-(2-Methoxyphenyl)-1H-benzimidazole (**3c**)*.[13] Yellow solid, 552 mg, 82% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.17 (br, 1H), 8.37 (dd, J = 1.8, 7.8 Hz, 1H), 7.65 (dd, J = 6.4, 13.2 Hz, 2H), 7.48–7.43 (m, 1H), 7.22–7.10 (m, 4H), 4.01 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 156.7, 149.0, 142.7, 134.7, 131.2, 129.7, 122.0, 121.5, 120.8, 118.4, 118.1, 112.0, 111.9, 55.7.

*2-(3-Methoxyphenyl)-1H-benzimidazole (**3d**)*.[13] Brown solid, 579 mg, 82% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.92 (br, 1H), 7.79–7.77 (m, 2H), 7.61 (br, 2H), 7.46 (t, J = 8.20 Hz, 1H), 7.22–7.20 (m, 2H), 7.07–7.04 (m, 1H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 159.6, 151.1, 143.7, 134.9, 131.5, 130.1, 122.2, 118.7, 115.8, 111.4, 55.3.

*2-(4-Methoxyphenyl)-1H-benzimidazole (**3e**)*.[13] Yellow solid, 518 mg, 77% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.76 (br, 1H), 8.13–8.11 (m, 2H), 7.61–7.50 (m, 2H), 7.17–7.09 (m, 4H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 160.6, 151.3, 143.8, 134.9, 128.0, 122.7, 122.0, 121.4, 118.4, 114.3, 111.0, 55.3.

*2-(4-Chlorophenyl)-1H-benzimidazole (**3f**)*.[13] Yellow solid, 521 mg, 76% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.99 (br, 1H), 8.19 (d, J = 8.55 Hz, 2H), 7.62 (d, J = 8.55 Hz, 4H), 7.21 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 150.1, 143.7, 135.0, 134.4, 129.0, 128.8, 128.1, 122.6, 121.9, 118.9, 111.3.

*2-(4-(Trifluoromethyl)phenyl)-1H-benzimidazole (**3g**)*.[3b] Yellow solid, 480 mg, 61% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.18 (br, 1H), 8.39 (d, J = 7.94 Hz, 2H), 7.92 (d, J = 7.94 Hz, 2H), 7.72–7.56 (m, 2H), 7.28–7.21 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 149.6, 143.7, 135.1, 133.9, 129.8, 129.5, 127.0, 125.9, 125.5, 123.2, 122.7, 122.0, 119.2, 111.6.

*6-Methyl-2-phenyl-1H-benzimidazole (**3h**)*.[13] Yellow solid, 537 mg, 86% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.80 (br, 1H), 8.19–8.17 (m, 2H), 7.55–7.36 (m, 5H), 7.02 (d, J = 7.9 Hz, 1H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 150.9, 141.9, 130.3, 129.9, 129.6, 128.9, 126.3, 123.9, 123.3, 118.4, 111.0, 21.3.

*7-Methyl-2-phenyl-1H-benzimidazole (**3i**)*.[14] Yellow solid, 394 mg, 63% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.82 (br, 0.5H), 12.56 (br, 0.5H), 8.24–8.20 (m, 2H), 7.56–7.35 (m, 2H), 7.09 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 7.5 Hz, 1H), 2.58 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 150.3, 143.1, 134.5, 130.3, 129.6, 128.8, 128.3, 126.4, 123.0, 122.3, 121.8, 116.2, 108.7, 16.7.

*5,6-Dimethyl-2-phenyl-1H-benzimidazole(**3j**)*.[10] Yellow solid, 493 mg, 74% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.66 (br, 1H), 8.16 (d, J = 7.4 Hz, 2H), 7.54–7.31 (m, 5H), 2.31 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 150.3, 142.5, 133.6, 131.1, 130.5, 129.9, 129.4, 128.8, 126.2, 118.9, 111.3, 20.0.

*6-Bromo-2-phenyl-1H-benzimidazole (**3k**)*.[3c] Yellow solid, 729 mg, 89% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.17 (br, 1H), 8.17 (d, J = 8.0 Hz, 2H), 7.79 (s, 1H), 7.57–7.50 (m, 4H), 7.35–7.32 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 152.5, 130.2, 129.7, 129.0, 126.7, 125.0, 114.4. [note: The signals of quaternary carbon atoms at 150–130 ppm and at 120–110 ppm could not be clearly observed due to broadening].

*6-Nitro-2-phenyl-1H-benzimidazole (**3l**)*.[10] Yellow solid, 574 mg, 80% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.43 (s, 1H), 8.20–8.19 (m, 2H), 8.10–8.07 (m, 1H), 7.71 (d, J = 9.2 Hz, 1H) 7.58–7.52 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 155.8, 142.6, 130.8, 129.0, 126.9, 117.8, 114.5, 112.0.

*1-Methyl-2-phenyl-1H-benzimidazole (**3m**)*.[3a] Yellow solid, 519 mg, 83% (isolated yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.86–7.84 (m, 2H), 7.69 (d, J = 7.0 Hz, 1H), 7.61–7.55 (m, 4H), 7.32–7.23 (m, 2H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 152.9, 142.4, 136.5, 130.1, 129.6, 129.2, 128.6, 122.3, 121.8, 118.9, 110.5, 31.6.

Experimental Procedure for the Synthesis of Benzothiazole Derivatives 9. To a two-necked flask, benzylamine derivatives **1** (4.0 mmol), *o*-aminothiophenol (**8a**) (3.0 mmol), 4,6-dihydroxysalicylic acid (10 mol%), and distilled *p*-xylene (2.0 mL) were added, and then the reaction vessel was connected to an O_2 balloon at room temperature. The mixture was stirred in 140 °C under O_2 atmosphere for 24 h. The resulting mixture was transferred into a round-bottom flask using ethyl acetate (EtOAc) and concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: hexane/EtOAc) to give product **9**.

*2-Phenylbenzothiazole (**9a**)*.[13] White solid, 500 mg, 79% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06–8.01 (m, 3H), 7.75 (d, J = 8.4 Hz, 1H), 7.43–7.36 (m, 4H), 7.28–7.25 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ167.7, 153.9, 134.8, 133.3, 130.6, 128.7, 127.2, 126.0, 124.9, 122.9, 121.3.

*2-(4-Methylphenyl)benzothiazole (**9b**)*.[13] White solid, 559 mg, 83% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.42–7.38 (m, 1H), 7.28–7.24 (m, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.9, 153.9, 141.1, 134.7, 130.7 129.4, 127.2, 125.9, 124.7, 122.8, 121.3 21.2.

*2-(2-Methylphenyl)benzothiazole (**9c**)*.[15] Purple solid, 547 mg, 80% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.72 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.45–7.41 (m, 1H), 7.33–7.21 (m, 4H), 2.63 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.9, 153.7, 137.2, 135.5, 133.0, 131.4, 130.4, 129.9, 126.07, 126.05, 125.0, 123.3, 121.3, 21.3.

*2-(2-Methoxyphenyl)benzothiazole (**9d**)*.[13] White solid, 616 mg, 85% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, *J* = 7.6 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.46–7.29 (m, 3H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.9, 157.0, 152.0, 135.9, 131.6, 129.3, 125.7, 124.4, 122.6, 122.0, 121.0, 120.9, 111.4, 55.4.

*2-(3-Methoxyphenyl)benzothiazole (**9e**)*.[13] Purple solid, 563 mg, 78% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.65–7.59 (m, 2H), 7.47–7.43 (m, 1H), 7.35–7.32 (m, 2H), 6.99 (dd, *J* = 8.2, 1.8 Hz, 1H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.7, 159.9, 153.9, 134.9, 134.7, 129.8, 126.1, 125.0, 123.1, 121.4, 120.0, 117.1, 111.8, 55.3.

*2-(4-Methoxyphenyl)benzothiazole (**9f**)*.[13] White solid, 627 mg, 88% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, 3H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.46–7.42 (m, 1H), 7.33–7.29 (m, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.7, 161.7, 154.1, 134.7, 128.9, 126.3, 126.0, 124.6, 122.7, 121.4, 114.2, 55.3.

*2-(4-Chlorophenyl)benzothiazole (**9g**)*.[13] White solid, 627 mg, 88% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.46–7.31 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.4, 153.9, 136.8, 134.9, 131.9, 129.0, 128.5, 126.3, 125.2, 123.1, 121.5.

*2-(3-Chlorophenyl)benzothiazole (**9h**)*.[13] White solid, 617 mg, 85% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06–8.02 (m, 2H), 7.86–7.81 (m, 2H), 7.47–7.30 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.0, 153.8, 135.0, 134.98, 134.94, 130.6, 130.0, 127.2, 126.3, 125.5, 125.4, 123.3, 121.5.

*2-(4-(Trifluoromethyl)phenyl)benzothiazole (**9i**)*.[10] White solid, 643 mg, 77% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.0 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.9, 153.9, 136.6, 135.1, 132.3 (q, *J* = 32.4 Hz), 127.6, 126.5, 125.9 (q, *J* = 3.8 Hz), 125.7, 123.7 (q, *J* = 271.7 Hz), 123.5, 121.6.

*2-(4-tert-Butylphenyl)benzothiazole (**9j**)*.[15] White solid, 694 mg, 87% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.47–7.41 (m, 3H),

7.32–7.28 (m, 1H), 1.32 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 168.2, 154.5, 154.3, 135.1, 131.0, 127.4, 126.3, 126.0, 125.1, 123.2, 121.7, 35.0, 31.3.

*2-(Naphthalen-1-yl)benzothiazole (**9k**)*.[13] Purple oil, 557 mg, 72% (isolated yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.93 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.98–7.90 (m, 4H), 7.61–7.52 (m, 4H), 7.45–7.41 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 167.5, 154.1, 135.4, 133.9, 131.0, 130.8, 130.6, 129.3, 128.3, 127.6, 126.4, 126.2, 125.8, 125.2, 124.9, 123.5, 121.3.

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12. We have already performed a screening of salicylic acid catalysts for oxidation of benzylamines[11] and found that 2,4,6-trihydroxybenzoic acid exhibits the most effective catalytic activity compared with other related acids. Based on these results, we consider that introduction of electron-donating groups (–OH) to salicylic acid is effective to improve its catalytic activity. This may be because increasing electron density promotes the generation of the phenoxyl radical from salicylic acid to oxidize benzylamine.[16]
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