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Potassium Periodate Mediated Oxidative Cyclodesulfurization toward Benzofused Nitrogen Heterocycles

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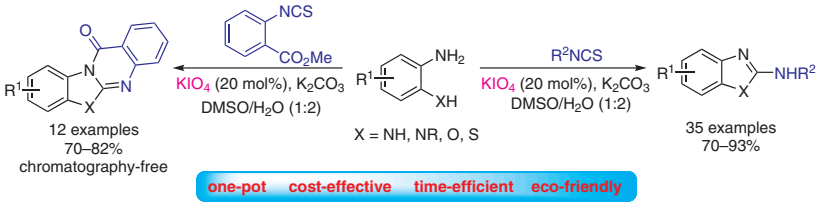

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Abstract A convenient oxidative cyclodesulfurization method toward the synthesis of benzofused nitrogen heterocycles using inexpensive and readily available potassium periodate as an oxidant was developed. Upon treating isothiocyanates with *ortho*-substituted anilines bearing *N*,*N*-, *N*,*O*-, and *N*,*S*-bis-nucleophiles, followed by an intramolecular cyclization of the in situ generated monothioureas, substituted 2-aminobenzazole series were rapidly accessible in good to excellent yields. The protocol can accommodate various substituents on both substrates while allowing more efficient, greener, and operational simpler process relative to other oxidative coupling reactions. Tetracyclic quinazolinone derivatives were also afforded in high yields in a single preparative step and chromatography-free.

Key words cyclization, oxidation, 2-aminobenzimidazoles, 2-aminobenzoxazoles, 2-aminobenzothiazoles, quinazolinones, periodate

Benzofused nitrogen heterocycles are prevalent in natural products as well as in synthetic bioactive molecules. Within this group of heterocycles, benzazoles are highly attractive due to their broad range of biological and pharmacological activities such as antimalarial,[1] antitubercular,[2] antiviral,[3] immunosuppressive,[4] antitumor,[5] as well as anticancer activities (Figure 1).[6] In drug discovery process, these key pharmacophores have often been incorporated in therapeutic leads to obtain desirable physicochemical properties, bioactivity, and the pK_a profiles.[7] Undoubtedly, benzazole scaffolds are present in several approved drugs[8] including Astemizole[9] and Suvorexant.[10] This class of heterocycles is thus of considerable importance as essential building blocks as well as synthetic targets in pharmaceutical and agrochemical industry.

In view of their broad spectrum of biological activities, several methods have been described in the literature for the synthesis of these compounds.[11] One of the most

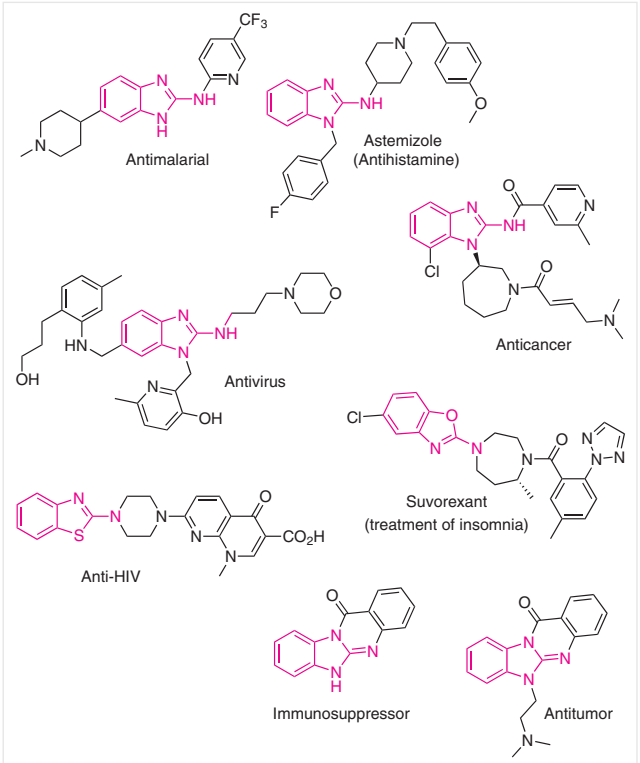

Figure 1 Examples of biologically active compounds with benzazole scaffolds

straightforward and convenient approaches is via cyclodesulfurization of the preformed monothioureas derived from the reaction of *ortho*-substituted aniline bis-nucleophiles with isothiocyanates. Desulfurization has been carried out using a variety of reagents such as HgO,[12] TsCl/NaOH,[13] triflic acid,[14] hypervalent iodine(III),[15] KO_2,[16] TBAI/H_2O_2,[17] I_2/K_2CO_3,[18] Ph_3P/I_2,[19] triphenylbismuth dichloride,[20] and BOP reagent.[21] These approaches provide reliable access to a

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range of benzazole derivatives; however, the reactions are carried out in organic solvents, using excess of toxic and expensive reagents, and/or required tedious product purification, which make the process undesirable based on the green chemistry perspective. With an increasing environmental and ecological concern, the development of a more practical, economical, and environmentally benign process is thus of urgent necessity.

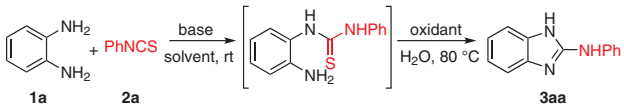
Periodate salts such as $NaIO_4$ or KIO_4 are a class of strong oxidants, which find widespread applications as bleach, detergents, soil conditioners, and waste water treatment.[22] They are commonly used as effective oxidizing agents in numerous elegant and valuable organic transformations, which are compatible with a wide range of functionalities.[22a] Apart from acting as oxidants in transition metal catalysis, they can act as oxidative mediators in metal-free reactions. Compared to organic hypervalent iodine reagents,[23] periodate salts are less expensive and easier to handle. Their water solubility also enables the application in water or aqueous organic solvents, which make the reagents as useful candidates to develop green and sustainable chemical process. Although periodate has been utilized in excess as a desulfurization agent in the synthesis of guanidines,[22a,24] to the best of our knowledge, this reagent has never been applied in cyclodesulfurization reaction toward *N*-heterocycles.

As part of our interests in the development of novel synthetic methods toward valuable heterocycles,[19,25] herein, we wish to report a convenient one-pot method for the synthesis of substituted 2-aminobenzazoles and the related benzofused quinazolinone derivatives from readily available precursors employing inexpensive KIO_4 as the desulfurizing agent.

To minimize hazardous waste generated from the use of excess reagent, in our preliminary study on optimization of the reaction conditions, oxidative cyclodesulfurization between *o*-phenylenediamine (**1a**) and phenyl isothiocyanate (**2a**) was carried out with less than stoichiometric amount of an oxidant. The reaction is typically carried out by treatment **1a** with **2a** in a specific solvent at room temperature. After complete formation of thiourea intermediate, an aqueous solution of the oxidant was added, followed by stirring at 80 °C for 1 hour. The results are summarized in Table 1.

Using periodate in the absence of base led to low conversion to benzimidazole **3aa** indicating the significance of base additive in the reaction (Table 1, entry 1). The reaction in the presence of $NaHCO_3$, a weak inorganic base, also gave low yield of the product (entry 2). While stronger base such as NaOH provided better product yield (entry 3), the reaction proceeded more effectively with K_2CO_3 (entry 4). Notably, the reaction carried out at room temperature was sluggish requiring extended reaction times with lower conversion. Interestingly, although periodate-mediated desulfurization of thioureas toward ureas has been reported,[26] we did not observe any urea product under the applied reaction conditions.

Table 1 Optimization of the Reaction Conditions[a]



1a 2a 3aa

Entry	Oxidant (mol%)	Base (1 equiv)	Solvent	Yield (%)
1	KIO_4 (20)	–	DMSO	20
2	KIO_4 (20)	$NaHCO_3$	DMSO	18
3	KIO_4 (20)	NaOH	DMSO	78
4	KIO_4 (20)	K_2CO_3	DMSO	92 (34)[b]
5	KIO_4 (20)	K_2CO_3	THF	68
6	KIO_4 (20)	K_2CO_3	H_2O	trace
7	KIO_4 (20)	K_2CO_3	MeCN	65
8	KIO_4 (20)	K_2CO_3	DMF	89
9	KIO_4 (10)	K_2CO_3	DMSO	78
10	KIO_4 (5)	K_2CO_3	DMSO	65
11	$NaIO_4$ (20)	K_2CO_3	DMSO	90
12	H_2O_2	K_2CO_3	DMSO	52
13	Oxone (20)	K_2CO_3	DMSO	9
14	MnO_2 (20)	K_2CO_3	DMSO	10

[a] Reaction at 80 °C, 1 h.
[b] Reaction at 25 °C, 12 h.

Solvent screening indicated that the first addition step required organic media and the best conversion was achieved in DMSO (Table 1, entries 4–8). In addition, reducing the loading of the periodate salt significantly decreases the product yield suggesting that periodate is the real terminal oxidant (entries 9, 10). Type of cation has no effect on the efficiency of the reaction as sodium periodate also gave comparative yield of **3aa** (entry 11). When comparing with other oxidizing agents, the reaction with H_2O_2 gave the product in much lower yields (entry 12). Additionally, low conversion was observed with Oxone or manganese oxide (entries 13 and 14).

To evaluate the scope and generality of this protocol, the reaction of *o*-phenylenediamines with a variety of aryl isothiocyanates was investigated under the above optimal reaction conditions (Table 1, entry 4). Through in situ formation of thioureas, followed by KIO_4-mediated oxidative cyclization, all examined substrates underwent clean conversion to the desired 2-aminobenzimidazoles **3** in good to excellent yields (Scheme 1).

The conditions were found to be compatible with a range of phenyl isothiocyanates bearing both electron-withdrawing groups (EWGs) and electron-donating groups (EDGs). The presence of EWGs (F, Br, NO_2) in phenyl isothiocyanates led to more favorable conversion whereas slightly

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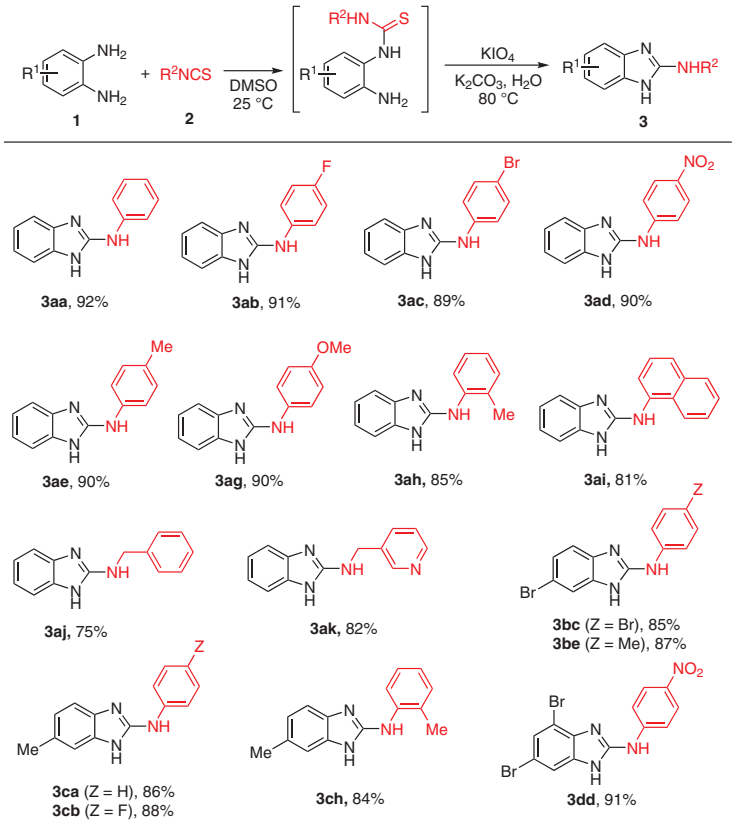

Scheme 1 Synthesis of substituted 2-aminobenzimidazoles **3**

longer reaction times were required with the substrates bearing EDGs (Me and OMe). The reaction toward **3ai** using relatively sterically hindered 1-naphthyl isothiocyanate also required extended times. Remarkably, replacement of aryl isothiocyanates with aliphatic derivatives did not affect the yield of the *N*-alkyl products **3aj** and **3ak**. The reaction can also accommodate various substituents on the phenylenediamines giving **3bc–dd** in satisfactory yields.

Since the substrate scope of this type of annulation processes is often limited to the *N*-unsubstituted diamines, we decided to further examine the compatibility of the conditions with *N*-substituted *o*-phenylenediamines. The conditions were proven to be general, reliable, and broadly applicable for the synthesis of N^1-substituted-2-aminobenzimidazoles **4**, which were afforded in high yields. The reaction proceeded well with both aryl and alkyl isothiocyanates (Scheme 2). It is important to note that, N^1-benzylated 2-aminobenzimidazoles are found in a variety of medicinally important compounds displaying potent biological activities (see Figure 1). Thus, the selective synthesis of this class of compounds from simple precursors in a one-pot procedure represents an attractive feature of our method over other previously employed routes.

Pleasingly, other aniline substrates containing *O*-, and *S*-nucleophiles on reaction with isothiocyanates also gave the corresponding benzoxazoles **5** and benzothiazoles **6**, respectively, in good to excellent yields (Scheme 2). Bioactive compounds **5ma** and **5na**, which are 5-lipoxygenase (5-LOX) inhibitors[27] were rapidly afforded in one-pot. It should be noted that although the oxygen and sulfur analogues of **1a** are oxidation-sensitive, the reaction proceeded cleanly without detectable side reactions. Interestingly, the second cyclodesulfurization step was found to complete within 10–15 min with *O*- and *S*-nucleophiles.

With the success in the synthesis of 6,5-membered fused heterocycles, the developed protocol was further extended toward the synthesis of fused tetracyclic quinazolinone derivatives to demonstrate its synthetic utility. Quinazolinones are of great interest to synthetic and medicinal chemists in part due to their broad range of biological activities. Especially, benzimidazo[2,1-*b*]quinazoline-12(5*H*)-ones are known as potent immunosuppressors.[4] The compounds bearing different alkylamino side chains have also been reported to exhibit antiproliferative activity toward human tumor cell lines and promising activities in treating neurodegenerative disorders,[5] thereby serving as promising targets for therapeutic applications.

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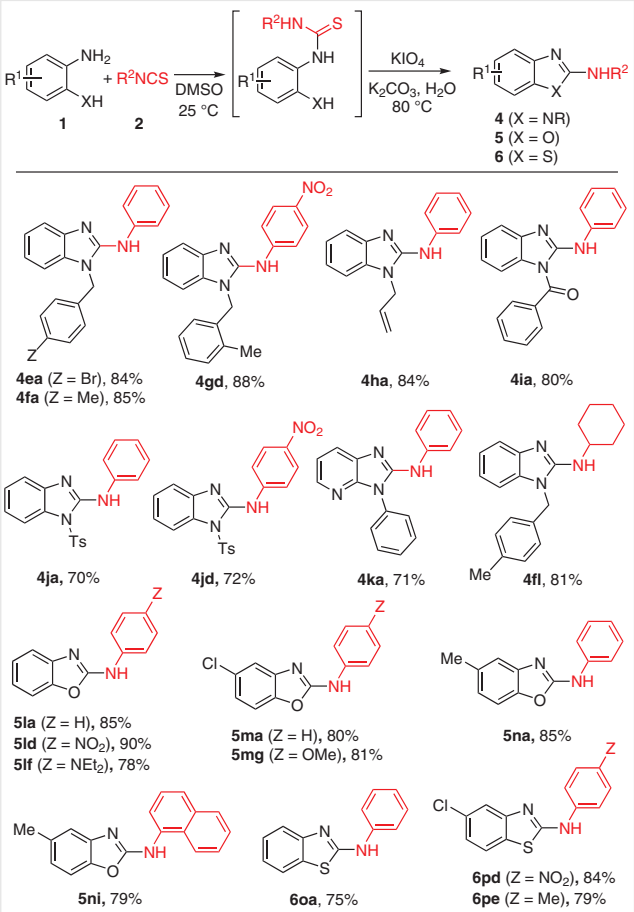
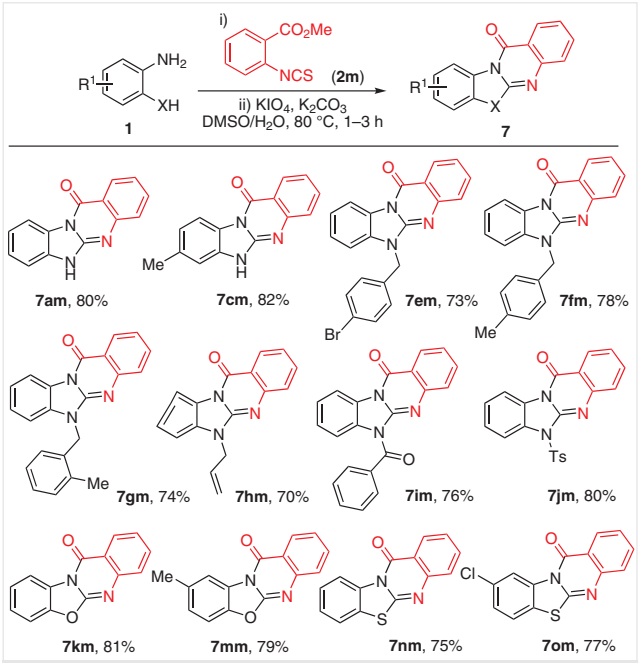


Scheme 2 Synthesis of N^1-substituted-2-aminobenzimidazoles **4**, benzoxazoles **5**, and benzothiazoles **6**

Only a few synthetic methods for the preparation of benzimidazoquinazolinones have been reported. These include microwave-assisted condensation of *o*-aryl isothiocyanate esters with *o*-phenylenediamines using 1,3-diisopropylcarbodiimide (DIC)/$Ba(OH)_2$,[28] copper-catalyzed annulation of iminophosphoranes[29] or (benzimidazol-1-yl)[2-(alkylamino)phenyl]methanones,[30] coupling between *N*-anilinoquinazolinones and aryl halides[31] or 2-bromo-*N*-(2-bromophenyl)benzamides with cyanamide,[32] as well as I_2/K_2CO_3-mediated reaction of 2-aminobenzoyl chlorides with benzimidazoles.[33] Nonetheless, these protocols still suffer from multi-step process, harsh reaction conditions, long reaction times, limited substrate scope, as well as difficulty in preparation of the key precursors.

Thus, by using a commercially available methyl ester of isothiocyanate as one of the coupling partners under the developed KIO_4-mediated cyclodesulfurization procedure, fused tetracyclic quinazolinones could be simply constructed through addition-double cyclization sequence. According to Scheme 3, when treating *o*-phenylenediamines with a commercially available isothiocyanate methyl ester **2m**, benzimidazoquinazolinones **7am** and **7cm** were successfully prepared in satisfactory yields. Similarly, with a sequential one-pot reaction, N^6-alkyl-substituted benzimidazoquinazolinones **7em–hm** were readily accessible without any modification of the reaction conditions. Likewise, the reaction toward N^6-benzoyl- and N^6-tosyl derivatives **7im** and **7jm** proceeded without difficulty. Gratifyingly, the protocol was proven to be highly versatile as both 2-aminophenols and 2-aminothiophenols were viable substrates in the reaction with **2m** leading to benzoxazoloquinazolinones **7km** and **7mm** and benzothiazoloquinazolinones **7nm** and **7om** in high yields. In addition, the reaction conditions are easily amendable to a large-scale synthesis, which provide compounds **7am** and **7fm** in 85% and 80% yield, respectively, using 10 mmol of the respective bis-amines. It is also worth mentioning that all products were obtained simply by precipitation in dichloromethane without requirement of chromatographic separation.



Scheme 3 Synthesis of fused tetracyclic quinazolinone derivatives **7**

In attempts to understand the reaction mechanism, several control experiments were carried out. No conversion was observed in the absence of KIO_4 indicating that it is a terminal oxidant. When diphenylthiourea was subjected to KIO_4 under the standard conditions, only the corresponding carbodiimide was obtained in 73% yield without other isolable oxidized products. In addition, replacement of KIO_4 with KIO_3 (20 mol%) led to **3aa** in 63% suggesting that even after the oxidation reaction with KIO_4, the released iodate could also promote the reaction. The reaction of *o*-phenylenediamine (**1a**) with phenyl isothiocyanate (**2a**) in the presence of BHT [2,6-bis(1,1-dimethylethyl)-4-methyl-

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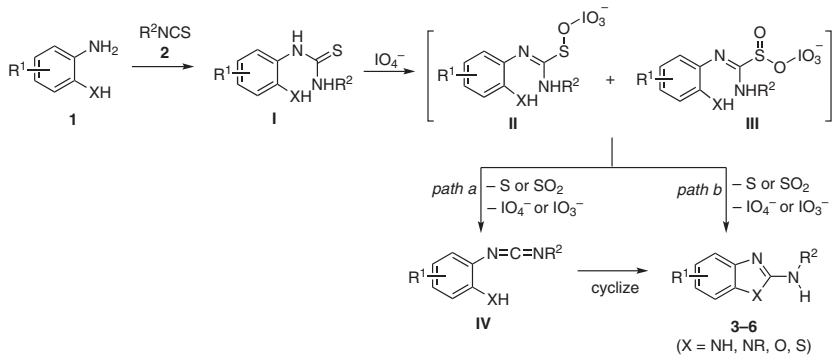

Scheme 4 Proposed reaction mechanism

phenol] also furnished **3aa** in 90% yield. This reaction indicates that cyclodesulfurization may not proceed through the radical intermediate.

Previous reports in the oxidation of sulfides to sulfoxides and sulfones suggested a one-step oxygen-transfer process proceed with sulfides as the electron donors and oxygens of periodate as electron acceptors.[22b,34] Thus, based on these data and control experiments, a tentative reaction mechanism for benzazole synthesis is proposed according to Scheme 4. First, addition of *o*-substituted aniline **1** to isothiocyanate **2** generates a thiourea intermediate **I**. Thiourea oxidation by KIO_4 under basic conditions then gives rise to oxidized species such as **II** and **III**, which could undergo elimination of sulfur or sulfur dioxide leading to carbodiimide **IV** before cyclization (path a). It is also possible that intramolecular cyclization within **II** or **III** could proceed directly to afford the benzazole products without the formation of **IV** (path b).

In summary, we have developed a facile and convenient one-pot approach for oxidative cyclodesulfurization toward various benzofused nitrogen heterocycles including potentially bioactive tetracyclic quinazolinones using periodate as a terminal oxidant. The use of sub-stoichiometric amount of easily handled and relatively low-cost periodate in aqueous organic media makes the method cost-effective, time-efficient, and eco-friendly, while the relatively mild reaction conditions can accommodate a broad range of substrates with good functional group tolerance.

All chemicals were obtained from Sigma-Aldrich Co., USA, and used without further purification. Bis-nucleophiles **1e–g**,[35a] **1h**,[35b] **1i**,[35c] **1j**,[35d] and **1k**[35e] were synthesized according to the reported procedures. The reaction was monitored by TLC carried out on silica gel plates (60F254, Merck, Germany) and visualized under UV light (245 nm). Column chromatography was performed over silica gel 60 (70–230 mesh, Merck, Germany). Melting points were determined using Sanyo, Gallenkamp apparatus and uncorrected. NMR measurements were recorded on a Bruker Avance™ (400 MHz for ^1H) using $CDCl_3$ as the solvent and TMS as an internal standard. Chemical shifts were reported in parts per million (ppm, δ) downfield from TMS. High-resolution mass spectra (HRMS) were recorded using time-of-flight (TOF) via the atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI).

Benzazoles 3–6; General Procedure

A solution of isothiocyanate **2** (0.27 mmol), aniline bis-nucleophile **1** (0.27 mmol), and K_2CO_3 (0.037 g, 0.27 mmol) in DMSO (1 mL) was stirred at rt for 30 min until thiourea was formed. A solution of KIO_4 (0.012 g, 0.05 mmol) in H_2O (2 mL) was then added to the mixture before raising the temperature to 80 °C and stirred until completion of the reaction. The crude mixture was concentrated under reduced pressure and then purified by short column chromatography using 10–40% EtOAc in hexane to give the desired product.

N-Phenyl-1*H*-benzo[*d*]imidazol-2-amine (3aa)[36a]

Brown solid; yield 0.0520 g (92%); mp 171–172 °C.

^1H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (2 drops)]: δ = 7.36 (dd, *J* = 8.0, 0.8 Hz, 2 H), 7.31–7.24 (m, 4 H), 7.09–7.05 (m, 2 H), 6.99 (t, *J* = 7.6 Hz, 1 H).

^{13}C NMR [100 MHz, $CDCl_3$ + MeOH-d_4 (2 drops)]: δ = 151.4, 139.6, 137.2, 129.4, 122.8, 121.1, 119.0, 112.7.

N-(4-Fluorophenyl)-1*H*-benzo[*d*]imidazol-2-amine (3ab)[19]

Brown solid; yield: 0.0558 g (91%); mp 156–157 °C.

^1H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.31–7.27 (m, 2 H), 7.24–7.21 (m, 2 H), 7.03–6.99 (m, 2 H), 6.93–6.88 (m, 2 H).

N-(4-Bromophenyl)-1*H*-benzo[*d*]imidazol-2-amine (3ac)[15]

Brown solid; yield: 0.0692 g (89%); mp 214–215 °C.

^1H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.34–7.25 (m, 6 H), 7.04–7.01 (m, 2 H).

N-(4-Nitropheny)-1*H*-benzo[*d*]imidazol-2-amine (3ad)[36]

Orange solid; yield: 0.0618 g (90%); mp 286–287 °C.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.63 (s, 1 H), 8.21 (d, *J* = 8.0 Hz, 2 H), 8.01 (d, *J* = 8.0 Hz, 2 H), 7.40 (br s, 2 H), 7.06 (br s, 2 H).

N-(*p*-Tolyl)-1*H*-benzo[*d*]imidazol-2-amine (3ae)[15]

Brown solid; yield: 0.0543 g (90%); mp 208–209 °C.

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^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.26–7.23 (m, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 7.02–7.01 (m, 2 H), 2.24 (s, 3 H).

N-(4-Methoxyphenyl)-1H-benzo[d]imidazol-2-amine (3ag)[15]

White solid; yield: 0.0581 g (90%); mp 176–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 7.24–7.22 (m, 2 H), 7.05–7.03 (m, 2 H), 6.78 (d, *J* = 8.8 Hz, 2 H), 3.72 (s, 3 H).

N-(o-Tolyl)-1H-benzo[d]imidazol-2-amine (3ah)[36c]

Brown solid; yield: 0.0512 g (85%); mp 181–182 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.5 Hz, 1 H), 7.25 (s, 2 H), 7.21–7.17 (m, 2 H), 7.06 (s, 3 H), 2.22 (s, 3 H).

N-(Naphthalen-1-yl)-1H-benzo[d]imidazol-2-amine (3ai)[36c]

Yellow solid; yield: 0.0567 g (81%); mp 286–287 °C.

^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 8.06 (br s, 1 H), 7.84 (br s, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.67 (d, *J* = 8.0 Hz, 1 H), 7.46 (br s, 3 H), 7.26 (br s, 2 H), 7.04 (br s, 2 H).

N-Benzyl-1H-benzo[d]imidazol-2-amine (3aj)[36d]

Brown solid; yield: 0.0452 g (75%); mp 165–166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.53 (m, 2 H), 7.47–7.43 (m, 1 H), 7.26–7.19 (m, 5 H), 7.01–6.99 (m, 1 H), 4.54 (s, 2 H).

N-(Pyridin-3-ylmethyl)-1H-benzo[d]imidazol-2-amine (3ak)[36e]

Brown oil; yield: 0.0497g (82%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 9.0 Hz, 1 H), 7.22 (d, *J* = 9.0 Hz, 1 H), 7.18 (d, *J* = 8.0 Hz, 1 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 6.87 (s, 1 H), 6.86 (d, *J* = 9.0 Hz, 1 H), 6.82 (t, *J* = 8.0 Hz, 1 H), 5.60 (s, 1 H), 3.83 (s, 2 H).

6-Bromo-N-(4-bromophenyl)-1H-benzo[d]imidazol-2-amine (3bc)[36f]

Brown solid; yield: 0.0842 g (85%); mp 155–156 °C.

^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.34–7.25 (m, 5 H), 7.04–7.01 (m, 2 H).

6-Bromo-N-(p-tolyl)-1H-benzo[d]imidazol-2-amine (3be)

Brown solid; yield: 0.0710 g (87%); mp 173–174 °C.

^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.36 (d, *J* = 2.8 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 7.11–7.06 (m, 4 H), 2.24 (s, 3 H).

^{13}C NMR [100 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 152.2, 138.7, 136.4, 135.8, 132.7, 129.7, 123.6, 119.5, 115.4, 113.4, 113.2, 20.5.

TOF-HRMS: *m*/*z* calcd for $C_{14}H_{13}{}^{81}BrN_3$ (M + H)$^+$: 304.0273; found: 304.0277; *m*/*z* calcd for $C_{14}H_{13}{}^{79}BrN_3$ (M + H)$^+$: 302.0293; found: 302.0297.

6-Methyl-N-phenyl-1H-benzo[d]imidazol-2-amine (3ca)[21]

Brown solid; yield: 0.0518 g (86%); mp 134–135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 7.6 Hz, 2 H), 7.26 (t, *J* = 7.6 Hz, 2 H), 7.14 (d, *J* = 8.0 Hz, 1 H), 7.06 (s, 1 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 2.35 (s, 3 H).

N-(4-Fluorophenyl)-6-methyl-1H-benzo[d]imidazol-2-amine (3cb)[36g]

Brown solid; yield: 0.0573 g (88%); mp 184–185 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.24 (m, 2 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 7.03 (s, 1 H), 6.91 (t, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 2.35 (s, 3 H).

6-Methyl-N-(o-tolyl)-1H-benzo[d]imidazol-2-amine (3ch)[36g]

Brown oil; yield: 0.0538 g (84%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.0 Hz, 1 H), 7.21–7.14 (m, 3 H), 7.07 (s, 1 H), 7.06 (t, *J* = 7.5 Hz, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 2.39 (s, 3 H), 2.23 (s, 3 H).

4,6-Dibromo-N-(4-nitrophenyl)-1H-benzo[d]imidazol-2-amine (3dd)[19]

Yellow solid; yield: 0.1012 g (91%); mp 288 °C (dec.).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.23 (d, *J* = 9.2 Hz, 2 H), 7.95 (d, *J* = 9.2 Hz, 2 H), 7.54 (s, 1 H), 7.43 (s, 1 H).

1-(4-Bromobenzyl)-N-phenyl-1H-benzo[d]imidazol-2-amine (4ea)

White solid; yield: 0.0858 g (84%); mp 151–152 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.5 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 7.5 Hz, 2 H), 7.29 (t, *J* = 7.5 Hz, 1 H),7.27 (d, *J* = 7.5 Hz, 1 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.15–7.10 (m, 2 H), 7.04 (d, *J* = 8.0 Hz, 2 H), 7.00 (d, *J* = 7.5 Hz, 1 H), 5.17 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$: δ = 149.8, 134.3, 133.8, 132.4, 132.3, 129.3, 128.5, 128.2, 122.8, 122.3, 122.1, 121.2, 118.7, 108.0, 45.7.

TOF-HRMS: *m*/*z* calcd for $C_{20}H_{17}{}^{81}BrN_3$ (M + H)$^+$: 380.0586; found: 380.0592; *m*/*z* calcd for $C_{20}H_{17}{}^{79}BrN_3$ (M + H)$^+$: 378.0606; found: 378.0601.

1-(4-Methylbenzyl)-N-phenyl-1H-benzo[d]imidazol-2-amine (4fa)

White solid; yield: 0.0756 g (85%); mp 173–174 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 7.5 Hz, 2 H), 7.24 (br s, 4 H), 7.20–7.04 (m, 4 H), 6.96 (t, *J* = 7.5 Hz, 1 H), 6.87 (d, *J* = 7.5 Hz, 1 H), 6.24 (s, 1 H), 5.13 (s, 2 H), 2.30 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.3, 135.9, 134.0, 132.9, 131.1, 129.2, 128.4, 126.9, 126.3, 122.4, 121.9, 120.8, 118.5, 117.7, 108.0, 44.8, 19.2.

TOF-HRMS: *m*/*z* calcd for $C_{21}H_{20}N_3$ (M + H)$^+$: 314.1652; found: 314.1654.

1-(2-Methylbenzyl)-N-(4-nitrophenyl)-1H-benzo[d]imidazol-2-amine (4gd)

Yellow oil; yield: 0.0852 g (88%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.5 Hz, 2 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.23 (t, *J* = 7.5 Hz, 3 H), 7.24–7.09 (m, 6 H), 6.82 (d, *J* = 7.5 Hz, 1 H), 5.19 (s, 2 H), 2.28 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.2, 146.5, 141.6, 140.6, 135.9, 133.6, 132.5, 131.2, 128.6, 126.9, 126.2, 125.4, 122.6, 122.0, 117.8, 116.9, 108.8, 45.1, 19.2.

TOF-HRMS: *m*/*z* calcd for $C_{21}H_{19}N_4O_2$ (M + H)$^+$: 359.1508; found: 359.1511.

1-Allyl-N-phenyl-1H-benzo[d]imidazol-2-amine (4ha)

White solid; yield: 0.0565 g (84%); mp 203–204 °C.

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^{1}H NMR [500 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 7.44 (d, *J* = 5.5 Hz, 1 H), 7.26–7.16 (m, 5 H), 7.04 (t, *J* = 7.0 Hz, 2 H), 6.89 (t, *J* = 7.0 Hz, 1 H), 5.80–5.74 (m, 1 H), 5.25 (d, *J* = 10.5 Hz, 1 H), 5.11 (d, *J* = 17.5 Hz, 1 H), 4.63 (s, 2 H).

^{13}C NMR [125 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 148.0, 136.9, 131.5, 131.1, 129.8, 129.3, 125.3, 124.2, 123.4, 121.1, 119.2, 113.8, 109.9, 46.0.

TOF-HRMS: *m*/*z* calcd for $C_{16}H_{16}N_3$ (M + H)$^+$: 250.1344; found: 250.1340.

Phenyl[2-(phenylamino)-1*H*-benzo[*d*]imidazol-1-yl]methanone (4ia)[18]

Yellow oil; yield: 0.0677 g (80%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.73 (s, 1 H), 7.82 (d, *J* = 7.5 Hz, 2 H), 7.70 (t, *J* = 7.5 Hz, 3 H), 7.56 (t, *J* = 7.5 Hz, 2 H), 7.51 (d, *J* = 7.5 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 7.17 (t, *J* = 7.5 Hz, 1 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 6.80 (t, *J* = 7.5 Hz, 1 H), 6.18 (d, *J* = 8.0 Hz, 1 H).

***N*-Phenyl-1-tosyl-1*H*-benzo[*d*]imidazol-2-amine (4ja)**[18]

Brown oil; yield: 0.0687 g (70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 7.87–7.79 (m, 5 H), 7.49 (d, *J* = 8.0 Hz, 1 H), 7.45 (t, *J* = 8.0 Hz, 2 H), 7.29–7.23 (m, 3 H), 7.20–7.14 (m, 2 H), 2.35 (s, 3 H).

***N*-(4-Nitrophenyl)-1-tosyl-1*H*-benzo[*d*]imidazol-2-amine (4jd)**[18]

Yellow solid; yield: 0.0794 g (72%); mp 265–266 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.13 (s, 1 H), 8.30 (d, *J* = 7.5 Hz, 2 H), 7.97 (d, *J* = 7.5 Hz, 2 H), 7.78 (d, *J* = 7.5 Hz, 3 H), 7.51 (d, *J* = 7.5 Hz, 1 H), 7.27 (d, *J* = 7.5 Hz, 4 H), 7.22 (t, *J* = 7.5 Hz, 1 H), 2.36 (s, 3 H).

***N*,3-Diphenyl-3*H*-imidazo[4,5-*b*]pyridin-2-amine (4ka)**

White solid; yield: 0.0549 g (71%); mp 206–207 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 5.5 Hz, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.65 (t, *J* = 8.0 Hz, 4 H), 7.56 (t, *J* = 8.0 Hz, 3 H), 7.35 (t, *J* = 8.5 Hz, 2 H), 7.14 (t, *J* = 5.5 Hz, 1 H), 7.07 (t, *J* = 5.5 Hz, 1 H), 6.45 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.7, 147.9, 141.0, 138.4, 135.1, 132.9, 130.7, 129.6, 129.3, 127.7, 123.8, 123.2, 118.9, 118.5.

TOF-HRMS: *m*/*z* calcd for $C_{18}H_{15}N_4$ (M + H)$^+$: 287.1297; found: 287.1293.

***N*-Cyclohexyl-1-(4-methylbenzyl)-1*H*-benzo[*d*]imidazol-2-amine (4fl)**[36h]

Colorless oil; yield: 0.0734 g (81%).

^{1}H NMR [500 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.22 (t, *J* = 7.5 Hz, 1 H), 7.17 (d, *J* = 7.0 Hz, 1 H), 7.15 (s, 2 H), 7.12 (d, *J* = 7.5 Hz, 1 H), 7.08 (d, *J* = 7.0 Hz, 1 H), 6.88 (s, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 4.06 (s, 2 H), 2.37 (s, 3 H), 2.07 (d, *J* = 11.0 Hz, 2 H), 1.75 (d, *J* = 12.5 Hz, 2 H), 1.65 (d, *J* = 12.5 Hz, 2 H), 1.42 (q, *J* = 11.5 Hz, 2 H), 1.22 (t, *J* = 11.5 Hz, 3 H).

***N*-Phenylbenzo[*d*]oxazol-2-amine (5la)**[15]

Brown solid; yield: 0.0482 g (85%); mp 99–101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (s, 1 H), 7.64 (d, *J* = 7.6 Hz, 2 H), 7.52 (d, *J* = 7.6 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 1 H), 7.27 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.19–7.11 (m, 2 H).

***N*-(4-Nitrophenyl)benzo[*d*]oxazol-2-amine (5ld)**[14]

Brown solid; yield: 0.0621 g (90%); mp 239–240 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 9.2 Hz, 2 H), 7.78 (d, *J* = 9.2 Hz, 2 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.34 (d, *J* = 7.6 Hz, 1 H), 7.23 (t, *J* = 7.6 Hz, 1 H), 7.14 (t, *J* = 7.6 Hz, 1 H).

***N*^{1}-(Benzo[*d*]oxazol-2-yl)-*N*^{4},*N*^{4}-diethylbenzene-1,4-diamine (5lf)**

Brown solid; yield: 0.0593 g (78%); mp 105–106 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (s, 1 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 1 H), 7.18 (t, *J* = 8.0 Hz, 1 H), 7.06 (t, *J* = 8.0 Hz, 1 H), 6.73 (d, *J* = 8.0 Hz, 2 H), 3.35 (q, *J* = 7.0 Hz, 4 H), 1.16 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8, 149.1, 145.0, 142.8, 126.3, 124.0, 122.1, 116.7, 112.9, 108.9, 44.7, 12.5.

5-Chloro-*N*-phenylbenzo[*d*]oxazol-2-amine (5ma)[36i]

White solid; yield: 0.0529 g (80%); mp 210–211 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 7.53 (s, 1 H), 7.50–7.41 (m, 5 H), 7.33–7.28 (m, 2 H).

5-Chloro-*N*-(4-methoxyphenyl)benzo[*d*]oxazol-2-amine (5mg)[36j]

White solid; yield: 0.0601 g (81%); mp 185–186 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.0 Hz, 2 H), 7.33 (s, 1 H), 7.19 (d, *J* = 7.5 Hz, 1 H), 7.05 (d, *J* = 8.5 Hz, 1 H), 6.87 (d, *J* = 8.0 Hz, 2 H), 3.75 (s, 3 H).

5-Methyl-*N*-phenylbenzo[*d*]oxazol-2-amine (5na)[27]

Brown solid; yield: 0.0515 g (85%); mp 213–214 °C.

^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 7.50 (d, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.6 Hz, 2 H), 7.17 (s, 1 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 7.00 (t, *J* = 7.6 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 2.34 (s, 3 H).

5-Methyl-*N*-(naphthalen-1-yl)benzo[*d*]oxazol-2-amine (5ni)[36k]

Brown solid; yield: 0.0585 g (79%); mp 176–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12–8.09 (m, 1 H), 7.94 (d, *J* = 7.2 Hz, 1 H), 7.91–7.88 (m, 1 H), 7.72 (d, *J* = 8.4 Hz, 1 H), 7.56–7.51 (m, 3 H), 7.17 (d, *J* = 8.4 Hz, 1 H), 7.14 (s, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 146.2, 142.0, 134.3, 134.0, 133.2, 128.6, 127.3, 126.33, 126.23, 125.8, 125.3, 122.4, 121.43, 121.40, 119.13, 119.10, 117.0, 108.5, 21.4.

***N*-Phenylbenzo[*d*]thiazol-2-amine (6oa)**[36k]

White solid; yield: 0.0459 g (75%); mp 161–162 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.29 (s, 1 H), 7.62 (d, *J* = 7.5 Hz, 1 H), 7.54 (d, *J* = 7.5 Hz, 1 H), 7.50 (d, *J* = 7.5 Hz, 2 H), 7.40 (br s, 2 H), 7.31 (s, 1 H), 7.16 (t, *J* = 7.5 Hz, 2 H).

5-Chloro-*N*-(4-nitrophenyl)benzo[*d*]thiazol-2-amine (6pd)

Yellow solid; yield: 0.0693 g (84%); mp 278–279 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 8.25 (d, *J* = 8.0 Hz, 2 H), 7.87 (d, *J* = 8.0 Hz, 2 H), 7.75 (s, 1 H), 7.59 (d, *J* = 8.0 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR [125 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 152.66, 145.94, 145.08, 142.07, 132.20, 128.75, 125.44, 123.57, 121.39, 120.45, 117.38.

TOF-HRMS: *m*/*z* calcd for $C_{13}H_9{}^{37}ClN_3O_2S$ (M + H)$^+$: 308.0074; found: 308.0082; *m*/*z* calcd for $C_{13}H_9{}^{35}ClN_3O_2S$ (M + H)$^+$: 306.0104; found: 306.0107.

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5-Chloro-*N*-(*p*-tolyl)benzo[*d*]thiazol-2-amine (6pe)

White solid; yield: 0.0586 g (79%); mp 219-210 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56 (s, 1 H), 7.50 (d, *J* = 8.5 Hz, 1 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 8.5 Hz, 1 H), 2.37 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.2, 152.9, 136.7, 134.9, 132.0, 130.2, 128.4, 122.5, 121.4, 120.9, 119.4, 21.0.

Fused Tetracyclic Quinazolinones 7; General Procedure

Following the above described general procedure for the synthesis of benzazoles, methyl 2-isothiocyanatobenzoate (**2m**; 0.0521 g, 0.27 mmol) was reacted with amino derivative **1**. After completion of the reaction, the mixture was treated with CH_2Cl_2 (2 mL). The resulting precipitate was filtered, washed with CH_2Cl_2, and oven-dried at 80 °C.

Benzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7am)[29]

White solid; yield: 0.0508 g (80%); mp >300 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 8.63 (d, *J* = 8.0 Hz, 1 H), 8.47 (d, *J* = 8.0 Hz, 1 H), 7.96 (t, *J* = 8.0 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.71 (d, *J* = 8.0 Hz, 1 H), 7.64–7.57 (m, 3 H).

^{13}C NMR [125 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 156.8, 144.2, 137.3, 137.0, 128.6, 128.5, 126.7, 125.8, 125.7, 118.1, 113.52, 113.46, 111.3.

8-Methylbenzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7cm)[36l]

Brown solid; yield: 0.0552 g (82%); mp >300 °C.

^{1}H NMR [400 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 8.31 (t, *J* = 8.4 Hz, 2 H), 7.69 (t, *J* = 7.6 Hz, 1 H), 7.51–7.41 (m, 1 H), 7.30 (t, *J* = 7.6 Hz, 1 H), 7.20 (s, 1 H), 7.08 (d, *J* = 7.6 Hz, 1 H), 2.46 (s, 3 H).

6-(4-Bromobenzyl)benzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7em)

White solid; yield: 0.0797 g (73%); mp 288–290 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 8.75 (d, *J* = 8.0 Hz, 1 H), 8.48 (d, *J* = 8.0 Hz, 1 H), 7.97 (t, *J* = 8.0 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.64 (br s, 3 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 1 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 5.77 (s, 2 H).

^{13}C NMR [125 MHz, $CDCl_3$ + TFA (3 drops)]: δ = 156.5, 143.6, 137.5, 137.3, 132.7, 130.5, 129.7, 128.5, 128.4, 127.1, 126.6, 125.7, 123.5, 114.6, 111.2, 47.4.

TOF-HRMS: *m*/*z* calcd for $C_{21}H_{15}{}^{81}BrN_3O$ (M + H)$^+$: 406.0368; found: 406.0363; *m*/*z* calcd for $C_{20}H_{17}{}^{79}BrN_3O$ (M + H)$^+$: 404.0398; found: 404.0396.

6-(4-Methylbenzyl)benzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7fm)[36m]

White solid; yield: 0.0748 g (78%); mp 225–226 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 (d, *J* = 7.5 Hz, 1 H), 8.43 (d, *J* = 8.0 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.36 (d, *J* = 7.5 Hz, 1 H), 7.35–7.30 (m, 2 H), 7.28–7.17 (m, 2 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 7.02 (d, *J* = 7.5 Hz, 1 H), 6.96 (d, *J* = 7.5 Hz, 1 H), 5.50 (s, 2 H), 2.47 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 149.2, 146.7, 135.8, 134.4, 132.9, 131.8, 130.8, 127.9, 127.0, 126.5, 126.4, 126.1, 126.0, 125.8, 123.1, 122.3, 116.9, 116.3, 109.0, 43.9, 19.4.

6-(2-Methylbenzyl)benzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7gm)

White solid; yield: 0.0678 g (74%); mp 225–226 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.67 (d, *J* = 6.1 Hz, 1 H), 8.42 (d, *J* = 8.0 Hz, 1 H), 7.72 (t, *J* = 7.2 Hz, 1 H), 7.63 (d, *J* = 8.0 Hz, 1 H), 7.36–7.29 (m, 3 H), 7.25–7.18 (m, 2 H), 7.08 (t, *J* = 7.2 Hz, 1 H), 7.01 (d, *J* = 6.1 Hz, 1 H), 6.95 (d, *J* = 7.5 Hz, 1 H), 5.48 (s, 2 H), 2.46 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 149.2, 146.7, 135.8, 134.4, 132.9, 131.8, 130.8, 127.9, 127.0, 126.5, 126.4, 126.1, 126.0, 125.8, 123.1, 122.3, 116.9, 116.3, 109.0, 43.9, 19.4.

TOF-HRMS: *m*/*z* calcd for $C_{22}H_{18}N_3O$ (M + H)$^+$: 340.1450; found: 340.1446.

6-Allylbenzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7hm)[4a]

White solid; yield: 0.0520 g (70%); mp 205–206 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (d, *J* = 8.0 Hz, 1 H), 8.41 (d, *J* = 8.0 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 1 H), 7.35–7.26 (m, 3 H), 6.07–6.00 (m, 1 H), 5.30 (t, *J* = 7.5 Hz, 2 H), 4.93 (s, 2 H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 160.1, 149.2, 146.3, 134.4, 131.6, 131.0, 127.0, 126.0, 125.9, 125.7, 123.0, 122.2, 118.4, 116.8, 116.3, 108.7, 44.3.

6-Benzoylbenzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7im)[4]

White solid; yield: 0.0696 g (76%); mp >340 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + TFA (5 drops)]: δ = 8.60 (d, *J* = 8.0 Hz, 2 H), 8.45 (d, *J* = 8.0 Hz, 2 H), 7.94 (t, *J* = 7.5 Hz, 2 H), 7.81 (d, *J* = 8.0 Hz, 2 H), 7.72 (d, *J* = 8.0 Hz, 2 H), 7.66–7.55 (m, 5 H).

^{13}C NMR [125 MHz, $CDCl_3$ + TFA (5 drops)]: δ = 156.7, 144.3, 137.16, 137.10, 128.7, 128.47, 128.45, 126.5, 125.7, 118.2, 116.3, 114.6, 113.6.

6-Tosylbenzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one (7jm)

White solid; yield: 0.0841 g (80%); mp 210–211 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 8.58 (d, *J* = 7.7 Hz, 1 H), 8.32 (d, *J* = 7.7 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H), 8.15 (d, *J* = 7.5 Hz, 2 H), 7.82–7.76 (m, 2 H), 7.49 (t, *J* = 7.5 Hz, 1 H), 7.51–7.39 (m, 2 H), 7.30 (d, *J* = 7.5 Hz, 3 H), 2.36 (s, 3 H).

^{13}C NMR [125 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 159.3, 147.5, 146.5, 143.4, 134.8, 134.0, 129.7, 128.7, 128.5, 126.9, 126.9, 126.7, 126.5, 125.2, 125.1, 118.2, 116.2, 113.6, 21.7.

TOF-HRMS: *m*/*z* calcd for $C_{21}H_{16}N_3O_3S$ (M + H)$^+$: 390.0912; found: 390.0908.

12*H*-Benzo[4,5]oxazolo[2,3-*b*]quinazolin-12-one (7km)[36n]

White solid; yield: 0.0517 g (81%); mp 233–235 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 7.5 Hz, 2 H), 7.80 (t, *J* = 7.5 Hz, 1 H), 7.72 (d, *J* = 5.5 Hz, 1 H), 7.51–7.40 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.3, 152.0, 147.5, 144.7, 135.1, 127.1, 126.9, 126.8, 126.5, 125.4, 125.0, 118.5, 116.0, 110.8.

9-Methyl-12*H*-benzo[4,5]oxazolo[2,3-*b*]quinazolin-12-one (7mm)

White solid; yield: 0.0534 g (79%); mp 214–215 °C.

^{1}H NMR [500 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 8.34 (d, *J* = 7.5 Hz, 1 H), 8.15 (s, 1 H), 7.77 (t, *J* = 7.2 Hz, 1 H), 7.68 (d, *J* = 7.2 Hz, 1 H), 7.45 (t, *J* = 7.2 Hz, 1 H), 7.33 (d, *J* = 7.2 Hz, 1 H), 7.20 (d, *J* = 7.5 Hz, 1 H), 2.47 (s, 3 H).

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^{13}C NMR [125 MHz, $CDCl_3$ + MeOH-d_4 (3 drops)]: δ = 159.2, 152.3, 147.2, 142.6, 135.3, 135.1, 127.3, 126.9, 126.5, 126.2, 125.3, 118.2, 116.1, 110.2, 21.4.

TOF-HRMS: *m*/*z* calcd for $C_{15}H_{11}N_2O_2$ (M + H)$^+$: 251.0821; found: 251.0827.

12*H*-Benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one (7nm)[29]

Yellow solid; yield: 0.0511 g (75%); mp 187–188 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.05 (d, *J* = 8.0 Hz, 1 H), 8.45 (d, *J* = 8.0 Hz, 1 H), 7.81 (t, *J* = 8.0 Hz, 1 H), 7.69 (d, *J* = 8.0 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.53–7.49 (m, 2 H), 7.46 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.9, 157.0, 147.3, 136.2, 135.0, 127.2, 126.9, 126.8, 126.0, 125.9, 123.8, 121.9, 119.3, 118.6.

9-Chloro-12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one (7om)

White solid; yield: 0.0597 g (77%); mp 237–238 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 8.44 (d, *J* = 8.0 Hz, 1 H), 7.83 (t, *J* = 8.0 Hz, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.56–7.50 (m, 2 H), 7.44 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.7, 156.7, 147.1, 136.7, 135.3, 133.0, 127.3, 127.1, 126.2, 126.1, 122.5, 122.1, 119.6, 118.5.

TOF-HRMS: *m*/*z* calcd for $C_{14}H_8ClN_2OS$ (M + H)$^+$: 287.0046; found: 287.0051.

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Supporting Information

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