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Organocatalytic Syntheses of Benzoxazoles and Benzothiazoles using Aryl Iodide and Oxone via C−H Functionalization and C−O/S Bond Formation

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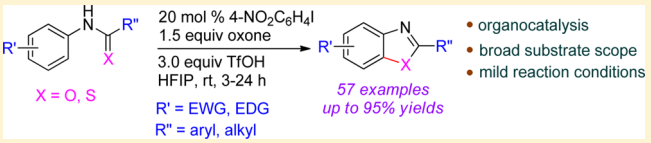
Supporting Information

ABSTRACT: An organocatalytic protocol for the syntheses of 2-substituted benzoxazoles and benzothiazoles is described from alkyl-/arylanilides and alkyl-/arylthioanilides using 1-iodo-4-nitrobenzene as catalyst and oxone as an inexpensive and environmentally safe terminal oxidant at room temperature in air via oxidative C−H functionalization and C−O/S bond formation. The procedure is simple and general and provides an effective route for the construction of functionalized 2-alkyl-/arylbenzoxazoles and 2-alkyl-/arylbenzothiazoles with moderate to high yields. The synthetic and mechanistic aspects have been described.



INTRODUCTION

The construction of benzoxazole and benzothiazole structural motifs has been a topic of immense interest in recent years due to their presence in a number of natural products and biologically active compounds. For examples, the benzoxazole scaffold is found in naturally occurring cytotoxic compounds, such as UK-1,[1] salvianen,[2] AJI9561,[3] and antimycrobacterial pseudopteroxazole.[4] Some of the recent medicinal chemistry applications of benzoxazoles and benzothiazoles include the HIV-1 reverse transcriptase inhibitors,[5a] melatonin receptor agonists,[5b] antitumor agents,[5c] $5HT_3$ receptor agonists,[5d] selective peroxisome proliferator-activated receptor γ antagonist JTP-426467,[5e] estrogen receptor-β agonist ERB-041,[5f] and orexin receptor antagonist[5g] (Figure 1). Furthermore, benzoxazoles are used as herbicides, such as Fenoxaprop, and as fluorescent probes such as bis-benzoxazolyl ethylenes and arenes.[6] The development of general and effective methods for the synthesis of functionalized benzoxazoles and benzothiazoles is thus important in organic synthesis.

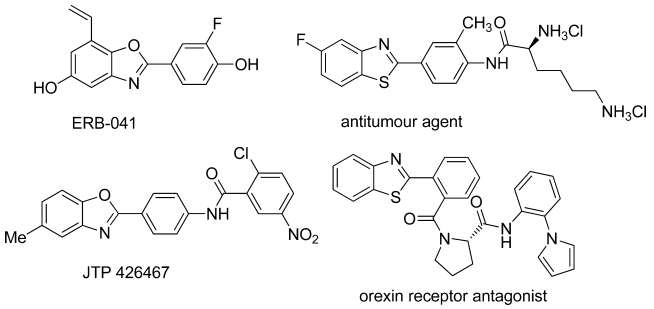


Figure 1. Examples of some biologically active substituted benzoxazoles and benzothiazoles.

The classical methods utilized for the synthesis of benzoxazoles and benzothiazoles involve the condensation of 2-aminophenol and 2-aminothiophenol with either aldehyde or carboxylic acid followed by oxidative cyclization.[7,8] However, these approaches often suffer due to limited substrate scope and sometimes with the harsh reaction conditions such as requirement of elevated temperature (~210 °C).[9] To overcome these drawbacks, considerable effort has been recently devoted to develop new approaches for the construction of C−O/S bonds via cross-coupling and C−H functionalization processes. For examples, copper-,[10] cobalt-,[11] and iron-catalyzed[12] C−O/S cross-coupling of 2-haloanilides/2-halothioanilides and copper-catalyzed[13] inter-/intramolecular domino C−N/O cross-coupling of 1,2-dihalobenzene with benzamides has been successfully utilized for the construction of benzoxazoles and benzothiazoles, while C−H functionalization followed by C−O/S bond formation has been explored for the synthesis of benzoxazoles and benzothiazoles using palladium-,[14] ruthenium-,[15] iron-,[16] and copper-based[17] catalytic systems as well as a stoichiometric amount of phenyliodinebis(trifluoroacetate) (PIFA).[18]

In recent years, hypervalent iodine catalyzed oxidative transformations have emerged as powerful strategies for carbon−carbon and carbon−heteroatom bond formation due to their unique features as mild, safe, and environmentally benign characterstics.[19−23] These processes are generally found to be effective in fluoro alcohols, as they have a high ionizing ability and low nucleophilicity and stabilize the cationic intermediates generated during the reactions.[20c−k] Herein, we wish to report an efficient organocatalytic protocol for the synthesis of substituted benzoxazoles and benzothiazoles from aryl-/alkylanilides and aryl-/alkylthioanilides using 1-iodo-4-

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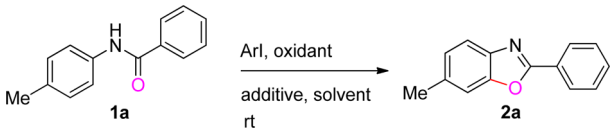
Table 1. Optimization of the Reaction Conditions[a]



entry	ArI (20 mol %)	oxidant (1.5 equiv)	additive (3.0 equiv)	solvent	conversion (%)[b]	yield (%)
1	PhI	oxone		HFIP	5	3
2	PhI	oxone	TfOH	HFIP	37	31
3	PhI	oxone	$BF_3{\cdot}Et_2O$	HFIP	24	19
4	PhI	oxone	TMSOTf	HFIP	25	16
5	PhI	oxone	$PTSA{\cdot}H_2O$	HFIP	n.d.	n.d.
6	PhI	$NaBO_3{\cdot}4H_2O$	TfOH	HFIP	4	2
7	PhI	30% H_2O_2	TfOH	HFIP	2	2
8	PhI	$Na_2S_2O_8$	TfOH	HFIP	10	7
9	PhI	*m*CPBA	TfOH	HFIP	23	21
10	**4-$NO_2C_6H_4I$**	**oxone**	**TfOH**	**HFIP**	**93**	**88**
11	4-MeC_6H_4I	oxone	TfOH	HFIP	17	10
12	4-$OMeC_6H_4I$	oxone	TfOH	HFIP	5	3
13	2-IC_6H_4COOH	oxone	TfOH	HFIP	31	24
14	4-$NO_2C_6H_4I$	oxone	TfOH	CH_2Cl_2	5	3
15	4-$NO_2C_6H_4I$	oxone	TfOH	THF	n.d.	n.d.
16	4-$NO_2C_6H_4I$	oxone	TfOH	toluene	n.d.	n.d.
17	4-$NO_2C_6H_4I$	oxone	TfOH	HFIP	63	56[c]
18	4-$NO_2C_6H_4I$	oxone	TfOH	HFIP	35	28[d]
19	4-$NO_2C_6H_4I$	oxone	TfOH	HFIP	70	61[e]
20	4-$NO_2C_6H_4I$	oxone	TfOH	HFIP	72	64[f]
21	4-$NO_2C_6H_4I$	$NaBO_3{\cdot}4H_2O$	TfOH	HFIP	12	7
22	4-$NO_2C_6H_4I$	30% H_2O_2	TfOH	HFIP	7	4
23	4-$NO_2C_6H_4I$	$Na_2S_2O_8$	TfOH	HFIP	12	9
24	4-$NO_2C_6H_4I$	*m*CPBA	TfOH	HFIP	43	38
25		oxone	TfOH	HFIP	n.d.	n.d.
26	4-$NO_2C_6H_4I$	oxone		HFIP	9	5

[a]Reaction conditions: **1a** (0.25 mmol), ArI (20 mol %), oxidant (0.37 mmol), additive (0.75 mmol), solvent (1.5 mL), room temperature, 12 h. n.d. = not detected. [b]Determined by 400 MHz ^{1}H NMR spectroscopy. [c]Oxone (0.25 mmol) was used. [d]TfOH (0.25 mmol) was used. [e]TfOH (0.5 mmol) was used. [f]4-$NO_2C_6H_4I$ (10 mol %) was used.

nitrobenzene as catalyst and oxone ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$) as the terminal oxidant in hexafluoro-2-propanol (HFIP) at room temperature. The protocol affords a potential route for the access of the target products with wide substrate scope.

RESULTS AND DISCUSSION

First, the optimization of the reaction conditions was studied using *N*-*p*-tolylbenzamide (**1a**) as a model substrate in the presence of different aryl iodides, terminal oxidants, additives, and solvents at room temperature (Table 1). To our delight, the reaction occurred to give the target benzoxazole **2a** in 12 h with 5% conversion when the substrate **1a**, iodobenzene (0.2 equiv), and oxone (1.5 equiv) were stirred in HFIP (hexafluoro-2-propanol) at room temperature (entry 1). The use of TfOH (3.0 equiv, trifluoromethanesulfonic acid) as an additive led to increase the product **2a** formation to 37%, whereas $BF_3{\cdot}OEt_2$ and TMSOTf gave the target molecule with 24 and 25% conversions, respectively (entries 2−4). In contrast, $PTSA{\cdot}H_2O$ (*p*-toluenesulfonic acid) showed no effect and the starting material was recovered intact (entry 5). In a set of oxidants screened, oxone afforded superior results in comparison to those of $NaBO_3{\cdot}4H_2O$, *m*CPBA, $Na_2S_2O_8$, and 30% H_2O_2 (entries 6−9). Subsequent catalyst screening revealed that iodobenzene with a 4-nitro substituent exhibited greater reactivity, leading to **2a** in 93% conversion (entry 10). In contrast, iodobenzene with electron donating substituents (4-methyl and 4-methoxy) gave inferior results, whereas 2-iodobenzoic acid yielded **2a** in 31% conversion (entries 11−13). Solvent screening experiments showed that the choice of solvent was crucial and the best results were obtained using HFIP, while CH_2Cl_2, toluene, and THF were not effective, affording **2a** in <5% conversion (entries 14−16). Lowering the amount of either aryl iodide (10 mol %) or oxidant (1 equiv) or additive (2 equiv) led to the product formation in <72% conversion (entries 17−20). Furthermore, the screening of the oxidants $NaBO_3{\cdot}4H_2O$, *m*CPBA, $Na_2S_2O_8$, and 30% H_2O_2 with 1-iodo-4-nitrobenzene led to inferior results (entries 21−24). Control experiments confirmed that, in the absence of aryl iodide, no reaction was observed and the starting material was recovered intact (entry 25). In addition, the reaction using 1-iodo-4-nitrobenzene without TfOH as an additive yielded **2a** in 9% conversion (entry 26).

To explore the scope and functional group compatibility of this protocol, a series of alkyl-/arylanilides were subjected to the optimized reaction conditions (Table 2). First, the reactivity of unsubstituted arylanilide and the substrates equipped with electron-withdrawing and -donating groups in the anilide aryl ring was tested. The reaction of *N*-phenylbenzamide **1b** afforded benzoxazole **2b** in 12% yield. A similar result was observed with the substrate **1c**, having a 2-methoxy substituent.

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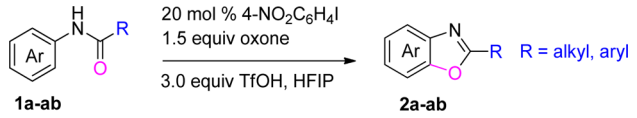
Table 2. 1-Iodo-4-nitrobenzene-Catalyzed Synthesis of Benzoxazoles with Oxone[a]



1a-ab 2a-ab

entry	Ar		R	time (h)	product (yield (%))
1	C_6H_5	**1b**	Ph	48	**2b** (12)
2	2-$OMeC_6H_4$	**1c**	Ph	48	**2c** (15)
3	3-$OMeC_6H_4$	**1d**	Ph	48	**2d** (n.d.)
4	3-$NO_2C_6H_4$	**1e**	Ph	48	**2e** (n.d.)
5	4-$OAcC_6H_4$	**1f**	Ph	1	**2f** (n.d.)
6	4-BrC_6H_4	**1g**	Ph	12	**2g** (88)
7	4-ClC_6H_4	**1h**	Ph	3	**2h** (91)
8	4-CNC_6H_4	**1i**	Ph	48	**2i** (19)
9	4-$CO_2EtC_6H_4$	**1j**	Ph	48	**2j** (14)
10	4-FC_6H_4	**1k**	Ph	5	**2k** (77)
11	4-$COMeC_6H_4$	**1l**	Ph	48	**2l** (n.d.)
12	4-$MeOC_6H_4$	**1m**	Ph	12	**2m** (82)
13	4-$NO_2C_6H_4$	**1n**	Ph	12	**2n** (n.d.)
14	4-$CF_3C_6H_4$	**1o**	Ph	48	**2o** (25)
15	2,4-$Me_2C_6H_3$	**1p**	Ph	12	**2p** (70)
16	3,4-$Me_2C_6H_3$	**1q**	Ph	12	**2qa,qb** (75)[b]
17	4-ClC_6H_4	**1r**	2-MeC_6H_4	12	**2r** (91)
18	4-ClC_6H_4	**1s**	3-MeC_6H_4	12	**2s** (84)
19	4-ClC_6H_4	**1t**	4-ClC_6H_4	12	**2t** (89)
20	4-ClC_6H_4	**1u**	4-$OMeC_6H_4$	12	**2u** (81)
21	4-ClC_6H_4	**1v**	4-MeC_6H_4	12	**2v** (82)
22	4-ClC_6H_4	**1w**	4-$NO_2C_6H_4$	24	**2w** (81)
23	4-ClC_6H_4	**1x**	1-naphthyl	12	**2x** (70)
24	4-ClC_6H_4	**1y**	2-furyl	8	**2y** (90)
25	4-ClC_6H_4	**1z**	Et	12	**2z** (63)
26	4-ClC_6H_4	**1aa**	^{i}Pr	20	**2aa** (80)
27	4-ClC_6H_4	**1ab**	^{t}Bu	24	**2ab** (45)

[a]Reaction conditions: **1a−ab** (0.36 mmol), 1-iodo-4-nitrobenzene (20 mol %), oxone (0.54 mmol), TfOH (1.08 mmol), HFIP (2.5 mL), room temperature. [b]Contained 6,7-dimethyl- (**2qa**) and 5,6-dimethyl-2-phenylbenzoxazoles (**2qb**) (1:2.2).

The substrate **1d** with a 3-methoxy group underwent decomposition, while **1e** substituted with a 3-nitro group failed to react and the starting material was recovered intact. However, the reactions of the substrates **1g,h,k,m** with 4-bromo, 4-chloro, 4-fluoro and 4-methoxy substituents readily occurred to furnish the corresponding substituted benzoxazoles **2g,h,k,m** in 77−91% yields, whereas **1i,j,o** having electron-withdrawing 4-cyano, 4-ester, and 4-trifluoromethyl groups were less reactive, giving the benzoxazoles **2i,j,o** in 14−25% yields. Furthermore, the substrate **1f** with a 4-acetoxy group underwent hydrolysis, while **1l,n** having 4-keto and 4-ntiro substituents showed no reaction and the starting materials were recovered. These results indicate the involvement of an electrophilic aromatic substitution process in the cyclization reaction. Furthermore, the reaction of the substrate **1p** with 2,4-dimethyl substituents provided the benzoxazole **2p** in 70% yield, whereas **1q** having 3,4-dimethyl substituents afforded a 1:2.2 mixture of 6,7-dimethyl-2-phenylbenzoxazole **2qa** and 5,6-dimethyl-2-phenylbenzoxazole **2qb** in 75% yield. These results suggest that the regioselectivity of the cyclization depends on the arene substituents. Next, the reactions of the substrates having electron-donating and -withdrawing groups in the amide aryl ring were studied. In general, these substrates smoothly underwent reaction with good yields. For examples, the reactions of the substrates **1r−w** with 2-methyl, 3-methyl, 4-chloro, 4-methoxy, 4-methyl, and 4-nitro substituents gave the corresponding 2-arylbenzoxazoles **2r−w** in 81−91% yields. Similarly, the substrates **1x,y** bearing R = 1-naphthyl and 2-furyl substituents underwent reaction to give the benzoxazoles **2x,y** in 70 and 90% yields, respectively. Then, the utility of the procedure for the synthesis of 2-alkylbenzoxazoles was explored. Interestingly, the reactions took place to furnish the desired 2-alkylbenzoxazoles with moderate to good yields. For examples, the substrates **1z,aa** with R = ethyl and isopropyl substituents underwent cyclization to give the benzoxazoles **2z,aa** in 63 and 80% yields, respectively, whereas the reaction of the substrate **1ab** with R = *tert*-butyl afforded 2-*tert*-butylbenzoxazole **2ab** in 45% yield.

The scope and utility of the protocol was further explored for the reaction of variously substituted analogous alkyl-/arylthioanilides (Table 3). The reactions readily occurred to give the desired 2-alkyl-/2-arylbenzothiazoles with enhanced yields. For examples, *N*-phenylthiobenzamide **3a** underwent reaction to afford 2-phenylbenzothiazole **4a** in 84% yield, while the substrate **3b** having a 2-methyl substituent afforded **4b** in 41% yield. The reaction of the substrate **3c** having a 3-methoxy group afforded a 1:32 mixture of 7-methoxy-2-phenylbenzothiazole **4ca** and 5-methoxy-2-phenylbenzothiazole **4cb** in 89% yield. A similar result was obtained with the substrate **3d** having a 3-methyl substituent, providing a 1:3.3 mixture of 7-methyl-2-phenylbenzothiazole (**4da**) and 5-methyl-2-phenylbenzothiazole (**4db**) in 79% yield. In contrast, the substrates **3e,m** with 3-nitro and 4-nitro substituents showed no reaction and the starting materials were recovered intact. However, the reaction of the substrates **3f,i−l,o,q** having 4-bromo, 4-chloro, 4-fluoro, 4-methoxy, 4-methyl, 2,4-dimethyl, and 3,5-dichloro substituents readily occurred to give the corresponding benzothiazoles **4f,i−l,o,q** in 61−89% yields, whereas the substrates **3g,h,n** having 4-cyano, 4-ester, and 4-trifluoromethyl substituents exhibited moderate reactivity, giving the target products in 38−44% yields. In addition, the substrate **3p** bearing 3,4-dimethyl substituents underwent reaction to give a 1:2.4 mixture of 6,7-dimethyl-2-phenylbenzothiazole **4pa** and 5,6-dimethyl-2-phenylbenzothiazole **4pb** in 75% yield. On the other hand, the substrates **3r−w** containing 2-methyl, 3-methyl, 4-fluoro, 4-methoxy, 4-methyl, and 4-nitro substituents on the thioamide aryl ring smoothly underwent reaction to give the corresponding 2-arylbenzothiazoles **4r−w** in 86−95% yields. Likewise, the cyclization of the substrates **3x−z** having 1-naphthyl and 2-furyl substituents could be carried out to afford the corresponding benzothiazoles **4x−z** in 75−88% yields. Furthermore, this protocol was compatible for the synthesis of 2-alkylbenzothiazoles. For examples, the substrates **3aa,ab**, with R = ethyl and isopropyl substituents, readily cyclized to provide the desired 2-alkylbenzothiazoles **4aa,ab** in 63 and 88% yields, respectively, whereas **3ac** having R = *tert*-butyl underwent reaction to give the target benzothiazole **4ac** in 81% yield.

Finally, the scaleup of the protocol was studied with **1a** as a representative example (Scheme 1). As expected, the reaction readily occurred to furnish the desired 2-arylbenzoxazole **2a** in 82% yield.

To investigate the reaction kinetics, an intermolecular competitive reaction between equimolar amounts of **1a**-d_2 and **1a** was conducted under the typical reaction conditions. At 23% conversion, the reaction revealed the intermolecular

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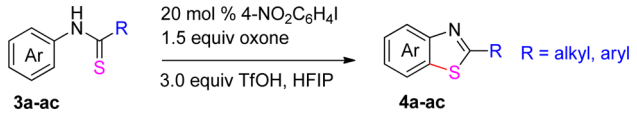
Table 3. 1-Iodo-4-nitrobenzene-Catalyzed Synthesis of Benzothiazoles with Oxone[a]

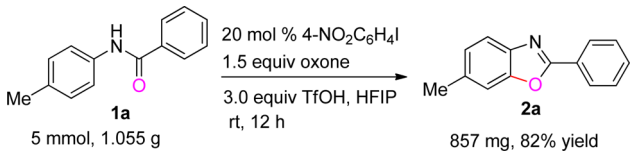


3a-ac 4a-ac

entry	Ar		R	time (h)	product (yield (%))
1	C_6H_5	**3a**	Ph	12	**4a** (84)
2	2-MeC_6H_4	**3b**	Ph	12	**4b** (41)
3	3-$MeOC_6H_4$	**3c**	Ph	6	**4ca,cb** (89)[b]
4	3-MeC_6H_4	**3d**	Ph	12	**4da,db** (79)[c]
5	3-$NO_2C_6H_4$	**3e**	Ph	48	**4e** (n.d.)
6	4-BrC_6H_4	**3f**	Ph	12	**4f** (89)
7	4-CNC_6H_4	**3g**	Ph	48	**4g** (41)
8	4-CO_2EtC6H4	**3h**	Ph	48	**4h** (38)
9	4-ClC_6H_4	**3i**	Ph	5	**4i** (88)
10	4-FC_6H_4	**3j**	Ph	12	**4j** (83)
11	4-$MeOC_6H_4$	**3k**	Ph	12	**4k** (87)
12	4-MeC_6H_4	**3l**	Ph	12	**4l** (89)
13	4-$NO_2C_6H_4$	**3m**	Ph	12	**4m** (n.d.)
14	4-$CF_3C_6H_4$	**3n**	Ph	48	**4n** (44)
15	2,4-$Me_2C_6H_3$	**3o**	Ph	12	**4o** (61)
16	3,4-$Me_2C_6H_3$	**3p**	Ph	12	**4pa,pb** (75)[d]
17	3,5-$Cl_2C_6H_3$	**3q**	Ph	12	**4q** (72)
18	4-ClC_6H_4	**3r**	2-MeC_6H_4	12	**4r** (95)
19	4-ClC_6H_4	**3s**	3-MeC_6H_4	12	**4s** (93)
20	4-ClC_6H_4	**3t**	4-FC_6H_4	8	**4t** (90)
21	4-ClC_6H_4	**3u**	4-$OMeC_6H_4$	12	**4u** (93)
22	4-ClC_6H_4	**3v**	4-MeC_6H_4	12	**4v** (89)
23	4-ClC_6H_4	**3w**	4-$NO_2C_6H_4$	24	**4w** (86)
24	1-naphthyl	**3x**	Ph	10	**4x** (88)
25	4-ClC_6H_4	**3y**	2-furyl	8	**4y** (81)
26	4-ClC_6H_4	**3z**	1-naphthyl	15	**4z** (75)
27	4-ClC_6H_4	**3aa**	Et	12	**4aa** (63)
28	4-ClC_6H_4	**3ab**	^{i}Pr	12	**4ab** (88)
29	4-ClC_6H_4	**3ac**	^{t}Bu	12	**4ac** (81)

[a]Reaction conditions: **3a–ab** (0.36 mmol), 1-iodo-4-nitrobenzene (20 mol %), oxone (0.54 mmol), TfOH (1.08 mmol), HFIP (2.5 mL), room temperature. [b]Contained 7-methoxy- (**4ca**) and 5-methoxy-2-phenylbenzothiazoles (**4cb**) (1:32). [c]Contained 7-methyl- (**4da**) and 5-methyl-2-phenylbenzothiazoles (**4db**) (1:3.3). [d]Contained 6,7-dimethyl- (**4pa**) and 5,6-dimethyl-2-phenylbenzothiazoles (**4pb**) (1:2.4).

Scheme 1. Gram-Scale Synthesis

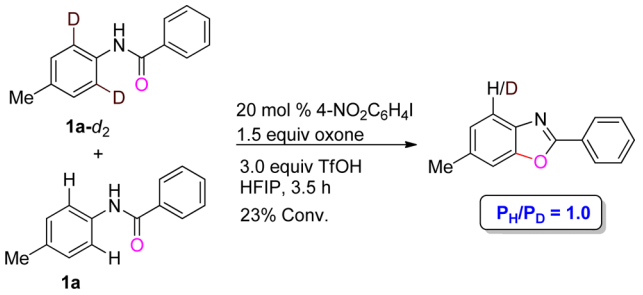


1a 2a

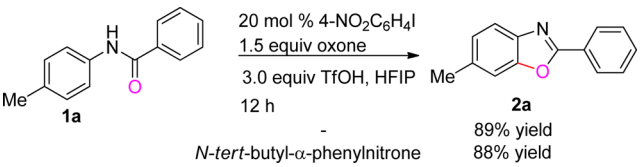
5 mmol, 1.055 g 857 mg, 82% yield

kinetic isotopic effect P_H/P_D = 1.0, which suggests that the C–H bond breaking step was not involved in the rate-determining step (Scheme 2).[22] Then, the application of a radical scavenger for I^{III} species, *N*-*tert*-butyl-α-phenylnitrone,[20c] was studied. However, the radical scavenger did not affect the reaction, and the target 2-arylbenzoxazole **2a** was obtained in 88% yield (Scheme 3). This result reveals that the radical was not involved in the cyclization process. Thus, the reaction of aryl iodide **A** with TfOH and oxone can generate an active hypervalent iodine(III) species, $PhI(OTf)_2$ (**B**),[23] that can

Scheme 2. Intermolecular Kinetic Isotope Experiment



Scheme 3. Radical Scavenger Experiment with *N*-*tert*-Butyl-α-phenylnitrone



catalyze the oxidative cyclization of the substrates **C** to give the intermediate **D**, which could be stabilized by HFIP.[20h,j] Intramolecular cyclization of **D** can give the cationic intermediate **E**, accompanied by the liberation of iodobenzene **A**, which could be reoxidized to **B**. The intermediate **E** can furnish the target products **2** and **4** by aromatization (Scheme 4).

CONCLUSIONS

In summary, we have developed a simple and general organocatalytic protocol for the synthesis of 2-arylbenzoxazoles and 2-arylbenzothiazoles using 1-iodo-4-nitrobenzene as catalyst in the presence of oxone as terminal oxidant at room temperature. This protocol can readily be extended to the construction of 2-alkylbenzoxazoles and 2-alkylbenzothiazoles.

EXPERIMENTAL SECTION

General Information. All chemicals and solvents were purchased from commercial suppliers and were used as received. Substituted anilides were prepared from anilines and acid chlorides.[24] Thiobenzanilides were prepared by thionation of the corresponding anilides with Lawesson's reagent.[14] Purification of the reaction products was carried out by column chromatography using silica gel (230–400 mesh). analytical TLC was performed on silica gel G/GF 254 plates. NMR spectra were recorded on 400 and 600 MHz NMR spectrometers using $CDCl_3$ as solvent and Me_4Si as internal standard, and the broad-band decoupling of carbon data was proton-decoupled $^{13}C\{^1H\}$. Chemical shifts (δ) are reported in ppm, and spin–spin coupling constants (J) are given in Hz. Melting points were determined using a melting point apparatus and are uncorrected. FT-IR spectra were recorded using an IR spectrometer. Elemental analyses were recorded using a CHNS analyzer. High-resolution mass spectra (HRMS) were recorded on a ESI-MS TOF instrument.

General Procedure for 1-Iodo-4-nitrobenzene-Catalyzed Synthesis of Substituted Benzoxazoles/Benzothiazoles 2a–ab and 4a–ac. Oxone (1.5 equiv) was added to a stirred solution of anilide/thioanilide (0.36 mmol, 1.0 equiv), 4-nitroiodobenzene (20 mol %), and triflic acid (3.0 equiv) in HFIP (2.5 mL) at room temperature in air. The mixture was stirred, and the progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The reaction mixture was then treated with saturated $Na_2S_2O_3$ (1 mL) and $NaHCO_3$ (1 mL) solutions. The resultant mixture was extracted using ethyl acetate (3 × 10 mL) and washed with brine (2 × 5 mL) and water (1 × 5 mL). Drying (Na_2SO_4) and evaporation of the

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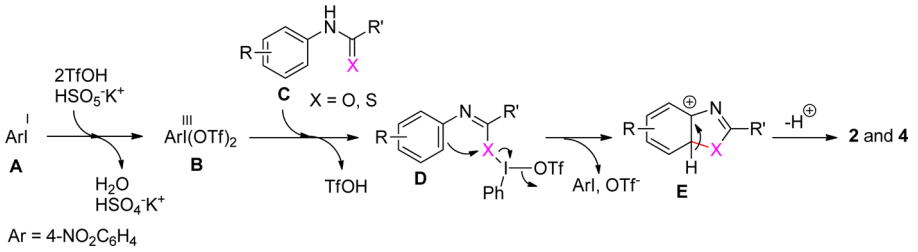
Scheme 4. Proposed Catalytic Cycle



solvent gave a residue that was purified by silica gel column chromatography using hexane and ethyl acetate as eluent to afford analytically pure substituted benzoxazoles and benzothiazoles.

*6-Methyl-2-phenylbenzo[d]oxazole (**2a**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.54; white solid; 66 mg, 88% yield; mp 91−92 °C (lit.[10a] mp 93 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.21 (m, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.51−7.50 (m, 3H), 7.37 (s, 1H), 7.16 (d, J = 8.4 Hz, 1H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.3, 150.8, 139.8, 135.2, 131.0, 128.6, 127.25, 127.2, 125.6, 119.1, 110.5, 21.5; FT-IR (KBr) 3054, 2919, 1647, 1615, 1554, 1482, 1448, 1337, 1247, 1173, 1126, 1052, 1021 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.29; H, 5.32; N, 6.73. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{14}H_{11}NOH$ 210.0913, found 210.0922.

*2-Phenylbenzo[d]oxazole (**2b**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.62; white solid; 8.0 mg, 12% yield; mp 102−103 °C (lit.[17] mp 102 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26−8.24 (m, 2H), 7.78−7.75 (m, 1H), 7.59−7.56 (m, 1H), 7.53−7.51 (m, 3H), 7.35−7.33 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 150.9, 142.2, 131.6, 129.0, 127.7, 127.3, 125.2, 124.7, 120.1, 110.7; FT-IR (KBr) 3063, 2920, 1722, 1615, 1550, 1448, 1345, 1284, 1239, 1194, 1145, 1104, 1055, 1022, 1002 cm^{-1}. Anal. Calcd for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17. Found: C, 79.92; H, 4.66; N, 7.21. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_9NOH$ 196.0757, found 196.0759.

*4-Methoxy-2-phenylbenzo[d]oxazole (**2c**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.46; white solid; 12 mg, 15% yield; mp 65−66 °C (lit.[17] mp 67 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31−8.29 (m, 2H), 7.52−7.50 (m, 3H), 7.31−7.26 (m, 1H), 7.22 (d, J = 8.0 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 4.07 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.1, 152.4, 151.8, 132.0, 131.5, 129.0, 127.8, 127.4, 125.9, 106.2, 103.6, 56.4; FT-IR (KBr) 3066, 2960, 1625, 1510, 1486, 1445, 1428, 1355, 1322, 1269, 1240, 1097, 1056, 1019 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.71; H, 4.90; N, 6.17. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{14}H_{11}NO_2H$ 226.0863, found 226.0859.

*6-Bromo-2-phenylbenzo[d]oxazole (**2g**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.60; white solid; 87 mg, 88% yield; mp 96−97 °C (lit.[17] mp 95 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.20 (m, 2H), 7.74 (d, J = 1.6 Hz, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.55−7.50 (m, 3H), 7.48 (dd, J = 8.4 Hz, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.8, 151.5, 141.6, 132.1, 129.2, 128.3, 127.9, 126.9, 121.2, 118.2, 114.4; FT-IR (KBr) 2960, 1638, 1557, 1506, 1449, 1422, 1328, 1257, 1041 cm^{-1}. Anal. Calcd for $C_{13}H_8BrNO$: C, 56.96; H, 2.94; N, 5.11. Found: C, 57.04; H, 2.92; N, 5.07. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_8BrNOH$ 273.9862, found 273.9860.

*6-Chloro-2-phenylbenzo[d]oxazole (**2h**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.63; white solid; 75 mg, 91% yield; mp 104−105 °C (lit.[10a] mp 107 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22−8.20 (m, 2H), 7.67 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 1.6 Hz, 1H), 7.54−7.51 (m, 3H), 7.33 (dd, J = 8.8 Hz, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 151.1, 141.1, 132.0, 130.9, 129.2, 127.9, 126.9, 125.5, 120.7, 111.4; FT-IR (KBr) 3059, 2926, 1618, 1552, 1488, 1450, 1331, 1263, 1051, 1022 cm^{-1}. Anal. Calcd for $C_{13}H_8ClNO$: C, 67.99; H, 3.51; N, 6.10. Found: C, 68.09; H, 3.49; N, 6.04. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_8ClNOH$ 230.0367, found 230.0367.

*2-Phenylbenzo[d]oxazole-6-carbonitrile (**2i**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.58; white solid; 15.0 mg, 19% yield; mp 198−199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.24 (m, 2H), 7.90 (d, J = 0.8 Hz, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.65 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.61−7.52 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 166.3, 150.3, 146.2, 132.9, 129.4, 129.1, 128.4, 126.3, 121.2, 119.0, 115.1, 108.4; FT-IR (KBr) 2924, 1700, 1630, 1601, 1552, 1517, 1482, 1456, 1409, 1351, 1327, 1292, 1225, 1111, 1047 cm^{-1}. Anal. Calcd for $C_{14}H_8N_2O$: C, 76.35; H, 3.66; N, 12.72. Found: C, 76.30; H, 3.65; N, 12.76. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{14}H_8N_2OH$ 221.0709, found 221.0711.

*Ethyl 2-phenylbenzo[d]oxazole-6-carboxylate (**2j**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.46; white solid; 13 mg, 14% yield; mp 76−77 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29−8.28 (m, 3H), 8.11 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.60−7.54 (m, 3H), 4.45 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 166.4, 165.8, 150.7, 146.2, 132.4, 129.3, 128.2, 127.8, 126.9, 126.6, 119.7, 112.5, 61.5, 14.6; FT-IR (KBr) 2980, 1713, 1614, 1582, 1476, 1447, 1431, 1365, 1346, 1318, 1292, 1262, 1226, 1187, 1051, 1020 cm^{-1}. Anal. Calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 71.85; H, 4.91; N, 5.30. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{16}H_{13}NO_3H$ 268.0968, found 268.0961.

*6-Fluoro-2-phenylbenzo[d]oxazole (**2k**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.62; white solid; 59 mg, 77% yield; mp 106−107 °C (lit.[10a] mp 109 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.18 (m, 2H), 7.69 (dd, J = 8.4 Hz, 4.8 Hz, 1H), 7.52−7.50 (m, 3H), 7.30 (dd, J = 7.6 Hz, 2.0 Hz, 1H), 7.11−7.06 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 162.1 (d, J = 242.5 Hz), 151.0 (d, J = 15.3 Hz), 138.6 (d, J = 1.6 Hz), 131.8, 129.1, 127.7, 127.1, 120.5 (d, J = 10.7 Hz), 112.8 (d, J = 24.4 Hz), 99.0 (d, J = 28.2 Hz); FT-IR (KBr) 3055, 2920, 1624, 1556, 1490, 1451, 1345, 1289, 1256, 1210, 1129, 1103, 1049, 1021 cm^{-1}. Anal. Calcd for $C_{13}H_8FNO$: C, 73.23; H, 3.78; N, 6.57. Found: C, 73.18; H, 3.77; N, 6.61. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{13}H_8FNOH$ 214.0663, found 214.0661.

*6-Methoxy-2-phenylbenzo[d]oxazole (**2m**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.54; white solid; 66 mg, 82% yield; mp 78−79 °C (lit.[25e] mp 75 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.17 (m, 2H), 7.63 (d, J = 9.2 Hz, 1H), 7.50−7.48 (m, 3H), 7.10 (d, J = 2.0 Hz, 1H), 6.95 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.4, 158.5, 151.9, 136.1, 131.3, 129.1, 127.6, 127.4, 120.2, 113.0, 95.7, 56.2; FT-IR (KBr) 3064, 2930, 1619, 1555, 1487, 1449, 1346, 1321, 1290, 1219, 1144, 1110, 1052, 1023 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.60; H, 4.93; N, 6.28. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{14}H_{11}NO_2H$ 226.0863, found 226.0862.

*2-Phenyl-6-(trifluoromethyl)benzo[d]oxazole (**2o**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.52; white solid; 24 mg, 25% yield; mp 100−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.25 (m, 2H), 7.86 (d, J = 9.2 Hz, 2H), 7.63 (d, J = 8.0 Hz, 1H), 7.58−7.52 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.6, 150.4, 145.1, 132.5, 129.3, 128.2, 127.5, 126.7, 123.5, 122.1, 120.6, 108.7 (q, J = 4.5 Hz); FT-IR (KBr) 2962, 1615, 1555, 1491, 1454, 1338, 1290, 1166, 1154, 1126, 1110, 1048 cm^{-1}. Anal. Calcd for $C_{14}H_8F_3NO$: C, 63.88; H, 3.06; N, 5.32. Found: C, 63.94; H, 3.04; N, 5.27. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{14}H_8F_3NOH$ 264.0631, found 264.0625.

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*4,6-Dimethyl-2-phenylbenzo[d]oxazole (**2p**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.75; white solid; 56 mg, 70% yield; mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24−8.21 (m, 2H), 7.50−7.48 (m, 3H), 7.19 (s, 1H), 6.96 (s, 1H), 2.61 (s, 3H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0, 151.1, 139.5, 135.3, 131.2, 130.0, 129.0, 127.8, 127.6, 126.6, 108.2, 22.0, 16.7; FT-IR (KBr) 3059, 2922, 1614, 1554, 1489, 1447, 1337, 1291, 1264, 1224, 1069, 1049, 1019 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.61; H, 5.89; N, 6.31. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{13}NOH$ 224.1070, found 224.1071.

*6,7-Dimethyl-2-phenylbenzo[d]oxazole (**2qa**) and 5,6-Dimethyl-2-phenylbenzo[d]oxazole (**2qb**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.63; white solid; 60 mg, 75% yield; mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25−8.20 (m, 4H), 7.51−7.46 (m, 8H), 7.34 (s, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 2.48 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 162.5, 149.6, 140.5, 139.8, 134.6, 134.0, 133.5, 131.4, 131.3, 129.1, 128.4, 128.0, 127.73, 127.7, 127.62, 127.6, 126.5, 120.2, 119.6, 116.6, 111.1, 20.8, 20.5, 19.5, 12.5; FT-IR (KBr) 3057, 2922, 1613, 1552, 1488, 1464, 1446, 1334, 1262, 1152, 1049, 1020, 999 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.64; H, 5.86; N, 6.30. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{13}NOH$ 224.1070, found 224.1072.

*6-Chloro-2-(o-tolyl)benzo[d]oxazole (**2r**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.70; white solid; 80 mg, 91% yield; mp 89−90 °C (lit.[25g] mp 85 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 1.6 Hz, 1H), 7.41−7.39 (m, 1H), 7.35−7.31 (m, 3H), 2.78 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 164.2, 150.7, 141.2, 139.2, 132.1, 131.4, 130.8, 130.1, 126.3, 126.0, 125.3, 120.8, 111.3, 22.4; FT-IR (KBr) 2957, 2923, 1614, 1547, 1461, 1325, 1255, 1235, 1165, 1059, 1023 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNO$: C, 69.00; H, 4.14; N, 5.75. Found: C, 69.06; H, 4.12; N, 5.68. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{10}ClNOH$ 244.0524, found 244.0524.

*6-Chloro-2-(m-tolyl)benzo[d]oxazole (**2s**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; white solid; 74 mg, 84% yield; mp 98−99 °C (lit.[25g] mp 99 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 1.6 Hz, 1H), 7.41−7.35 (m, 2H), 7.32 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.1, 151.0, 141.1, 139.0, 132.8, 130.7, 129.0, 128.4, 126.7, 125.4, 125.0, 120.5, 111.4, 21.5; FT-IR (KBr) 3059, 2922, 1618, 1553, 1485, 1428, 1327, 1264, 1242, 1072 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNO$: C, 69.00; H, 4.14; N, 5.75. Found: C, 68.95; H, 4.13; N, 5.79. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{10}ClNOH$ 244.0524, found 244.0526.

*6-Chloro-2-(4-chlorophenyl)benzo[d]oxazole (**2t**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.70; white solid; 84 mg, 89% yield; mp 148−149 °C (lit.[25g] mp 148 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.12 (m, 2H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.50−7.47 (m, 2H), 7.34 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.9, 151.1, 141.0, 138.3, 131.1, 129.5, 129.1, 125.7, 125.4, 120.7, 111.5; FT-IR (KBr) 3064, 2923, 1616, 1594, 1551, 1482, 1460, 1403, 1328, 1282, 1260, 1230, 1109, 1090, 1047, 1010 cm^{-1}. Anal. Calcd for $C_{13}H_7Cl_2NO$: C, 59.12; H, 2.67; N, 5.30. Found: C, 59.03; H, 2.70; N, 5.33. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_7Cl_2NOH$ 263.9977, found 263.9977.

*6-Chloro-2-(4-methoxyphenyl)benzo[d]oxazole (**2u**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.52; white solid; 76 mg, 81% yield; mp 147−148 °C (lit.[25i] mp 140 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.1, 162.8, 151.1, 141.3, 130.3, 129.7, 125.3, 120.3, 119.4, 114.7, 111.3, 55.7; FT-IR (KBr) 3073, 2924, 1621, 1602, 1505, 1454, 1440, 1333, 1263, 1257, 1177, 1055, 1024 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.39. Found: C, 64.82; H, 3.87; N, 5.32. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{10}ClNO_2H$ 260.0473, found 260.0473.

*6-Chloro-2-p-tolylbenzo[d]oxazole (**2v**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.70; white solid; 72 mg, 82% yield; mp 129−130 °C (lit.[25g] mp 126 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.32−7.29 (m, 3H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 163.9, 150.8, 142.4, 140.9, 130.3, 129.7, 127.6, 125.1, 123.8, 120.2, 111.1, 21.6; FT-IR (KBr) 2920, 2853, 1616, 1554, 1500, 1440, 1426, 1408, 1329, 1257, 1234, 1170, 1119, 1050, 1013 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNO$: C, 69.00; H, 4.14; N, 5.75. Found: C, 68.95; H, 4.13; N, 5.80. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{10}ClNOH$ 244.0524, found 244.0524.

*6-Chloro-2-(4-nitrophenyl)benzo[d]oxazole (**2w**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.72; white solid; 80 mg, 81% yield; mp 182−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41−8.36 (m, 4H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.40 (dd, *J* = 8.0 Hz, 2.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5, 151.4, 150.0, 140.9, 132.5, 132.3, 128.7, 126.2, 124.4, 121.4, 111.8; FT-IR (KBr) 3087, 1947, 1603, 1595, 1554, 1518, 1460, 1409, 1349, 1327, 1312, 1263, 1109, 1048, 1011 cm^{-1}. Anal. Calcd for $C_{13}H_7ClN_2O_3$: C, 56.85; H, 2.57; N, 10.20. Found: C, 56.81; H, 2.56; N, 10.24. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_7ClN_2O_3H$ 275.0218, found 275.0216.

*6-Chloro-2-(naphthalen-1-yl)benzo[d]oxazole (**2x**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.72; yellow solid; 70 mg, 70% yield; mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (d, *J* = 8.8 Hz, 1H), 8.41 (dd, *J* = 7.6 Hz, 0.8 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.72−7.68 (m, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.61−7.56 (m, 2H), 7.37 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 163.6, 150.5, 141.3, 134.2, 132.9, 131.1, 130.8, 129.6, 128.9, 128.3, 126.8, 126.4, 125.4, 125.1, 123.3, 120.9, 111.4; FT-IR (KBr) 3045, 2926, 1895, 1609, 1589, 1541, 1508, 1459, 1427, 1395, 1323, 1263, 1250, 1131, 1108, 1073, 1054, 966 cm^{-1}. Anal. Calcd for $C_{17}H_{10}ClNO$: C, 72.99; H, 3.60; N, 5.01. Found: C, 72.93; H, 3.62; N, 5.06. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{10}ClNOH$ 280.0524, found 280.0523.

*6-Chloro-2-(furan-2-yl)benzo[d]oxazole (**2y**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.40; pale yellow solid; 71 mg, 90% yield; mp 78−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.62 (m, 2H), 7.55 (d, *J* = 2.0 Hz, 1H), 7.33 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 7.27 (d, *J* = 3.2 Hz, 1H), 6.62−6.60 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.9, 150.4, 146.2, 142.2, 140.6, 131.0, 125.7. 120.7, 114.9, 112.5, 111.3; FT-IR (KBr) 3062, 3039, 1635, 1606, 1538, 1455, 1427, 1326, 1290, 1264, 1232, 1160, 1089, 1057, 1011 cm^{-1}. Anal. Calcd for $C_{11}H_6ClNO_2$: C, 60.16; H, 2.75; N, 6.38. Found: C, 60.24; H, 2.73; N, 6.33. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_6ClNO_2H$ 220.0160, found 220.0163.

*6-Chloro-2-ethylbenzo[d]oxazole (**2z**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.50; colorless liquid; 41 mg, 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.27 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 2.96 (q, *J* = 8.0 Hz, 2H), 1.44 (t, *J* = 8.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.1, 151.2, 140.4, 130.3, 124.9, 120.2, 111.2, 22.3, 11.0; FT-IR (KBr) 3104, 2920, 1618, 1576, 1466, 1451, 1358, 1267, 1225, 1152, 1075, 1055 cm^{-1}. Anal. Calcd for C_9H_8ClNO: C, 59.52; H, 4.44; N, 7.71. Found: C, 59.45; H, 4.46; N, 7.74. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for C_9H_8ClNOH 182.0367, found 182.0365.

*6-Chloro-2-isopropylbenzo[d]oxazole (**2aa**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.52; colorless liquid; 56 mg, 80% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.8 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.26−7.24 (m, 1H), 3.24−3.17 (m, 1H), 1.44 (d, *J* = 7.2 Hz, 6H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 172.2, 151.2, 140.3, 130.3, 124.9, 120.3, 111.2, 29.1, 20.4; FT-IR (KBr) 3098, 2988, 1614, 1570, 1465, 1446, 1367, 1266, 1232, 1138, 1083, 1054 cm^{-1}. Anal. Calcd for $C_{10}H_{10}ClNO$: C, 61.39; H, 5.15; N, 7.16. Found: C, 61.46; H, 5.14; N, 7.12. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{10}H_{10}ClNOH$ 196.0524, found 196.0525.

*2-(tert-Butyl)-6-chlorobenzo[d]oxazole (**2ab**):*[25j] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; colorless liquid; 34 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.29 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 1.49 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.4, 151.2, 140.2, 130.2, 124.8, 120.4, 111.2, 34.4, 28.6; FT-IR (KBr) 2977, 2870, 1614,

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1569, 1458, 1428, 1364, 1326, 1259, 1232, 1129, 1109, 1053 cm^{-1}. Anal. Calcd for $C_{11}H_{12}ClNO$: C, 63.01; H, 5.77; N, 6.68. Found: C, 63.07; H, 5.78; N, 6.63. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{12}ClNOH$ 210.0680, found 210.0686.

*2-Phenylbenzo[d]thiazole (**4a**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.62; white solid; 64 mg, 84% yield; mp 101−102 °C (lit.[10e] mp 99 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09−8.05 (m, 3H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.50−7.46 (m, 4H), 7.39−7.35 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.2, 154.3, 135.2, 133.8, 131.1, 129.2, 127.7, 126.5, 125.3, 123.4, 121.8; FT-IR (KBr) 3034, 1634, 1510, 1479, 1454, 1445, 1434, 1314, 1225, 1159, 1071, 1028 cm^{-1}. Anal. Calcd for $C_{13}H_9NS$: C, 73.90; H, 4.29; N, 6.63; S, 15.18. Found: C, 73.99; H, 4.27; N, 6.59; S, 15.15. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_9NSH$ 212.0528, found 212.0528.

*4-Methyl-2-phenylbenzo[d]thiazole (**4b**):*[16] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.80; white solid; 33 mg, 41% yield; mp 41−42 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11−8.09 (m, 2H), 7.73−7.71 (m, 1H), 7.49−7.47 (m, 3H), 7.27−7.26 (m, 2H), 2.80 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.8, 153.7, 135.2, 134.2, 133.6, 130.9, 129.2, 127.7, 127.0, 125.3, 119.2, 18.6; FT-IR (KBr) 3061, 2920, 1577, 1478, 1445, 1314, 1223, 1179, 1072, 970 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NS$: C, 74.63; H, 4.92; N, 6.22; S, 14.23. Found: C, 74.70; H, 4.90; N, 6.20; S, 14.20. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{11}NSH$ 226.0685, found 226.0682.

*7-Methoxy-2-phenylbenzo[d]thiazole (**4ca**) and 5-Methoxy-2-phenylbenzo[d]thiazole (**4cb**). Characterization Data for **4cb**:* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.54; white solid; 77 mg, 89% yield; mp 71−72 °C (lit.[14a] mp 75 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−8.04 (m, 2H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.55 (s, 1H), 7.46 (s, 3H), 7.03 (d, *J* = 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.5, 159.3, 155.6, 133.9, 131.0, 129.2, 127.6, 127.1, 122.0, 115.7, 105.7, 55.8; FT-IR (KBr) 2936, 1601, 1558, 1465, 1430, 1329, 1279, 1248, 1160, 1139, 1076, 1025, 969 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80; S, 13.29. Found: C, 69.75; H, 4.60; N, 5.78; S, 13.25. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{11}NOSH$ 242.0634, found 242.0634.

*7-Methyl-2-phenylbenzo[d]thiazole (**4da**)*[25f] *and 5-methyl-2-phenylbenzo[d]thiazole (**4db**):*[18a] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.72; white solid; 64 mg, 79% yield; mp 129−130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11−8.05 (m, 3H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.50−7.45 (m, 7H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.21−7.16 (m, 2H), 2.59 (s, 3H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.3, 167.7, 154.7, 154.2, 136.6, 135.8, 134.0, 132.2, 131.9, 131.1, 131.0, 129.2, 129.15, 127.71, 127.7, 127.0, 126.7, 126.3, 125.6, 123.4, 121.3, 120.9, 21.7, 21.6; FT-IR (KBr) 3066, 2921, 1601, 1502, 1476, 1441, 1313, 1276, 1230, 1152, 1071, 967 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NS$: C, 74.63; H, 4.92; N, 6.22; S, 14.23. Found: C, 74.57; H, 4.91; N, 6.26; S, 14.26. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{11}NSH$ 226.0685, found 226.0686.

*6-Bromo-2-phenylbenzo[d]thiazole (**4f**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.66; white solid; 93 mg, 89% yield; mp 146−147 °C (lit.[14b] mp 150 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06−8.04 (m, 2H), 8.02 (d, *J* = 2.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.58 (dd, *J* = 8.8 Hz, 2.0 Hz, 1H), 7.49−7.47 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.7, 153.2, 136.8, 133.3, 131.4, 130.0, 129.3, 127.7, 124.5, 124.3, 118.9; FT-IR (KBr) 3074, 1637, 1509, 1478, 1445, 1395, 1304, 1276, 1248, 1225, 1091, 1072 cm^{-1}. Anal. Calcd for $C_{13}H_8BrNS$: C, 53.81; H, 2.78; N, 4.83; S, 11.05. Found: C, 53.72; H, 2.80; N, 4.85; S, 11.11. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_8BrNSH$ 289.9634, found 289.9634.

*2-Phenylbenzo[d]thiazole-6-carbonitrile (**4g**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.64; white solid; 35 mg, 41% yield; mp 193−194 °C (lit.[14a,b] mp 195 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.11−8.08 (m, 3H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.53−7.51 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 172.5, 156.7, 135.7, 133.0, 132.3, 130.0, 129.5, 128.1, 126.6, 124.1, 118.9, 108.8; FT-IR (KBr) 2954, 2229, 1632, 1506, 1475, 1441, 1405, 1311, 1260, 1061, 970 cm^{-1}. Anal. Calcd for $C_{14}H_8N_2S$: C, 71.16; H, 3.41; N, 11.86; S, 13.57. Found: C, 71.24; H, 3.39; N, 11.87; S, 13.50. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_8N_2SH$ 237.0481, found 237.0482.

*Ethyl 2-phenylbenzo[d]thiazole-6-carboxylate (**4h**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.56; white solid; 39 mg, 38% yield; mp 192−193 °C (lit.[14a] mp 196 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 0.8 Hz, 1H), 8.17 (dd, *J* = 8.8 Hz, 1.6 Hz, 1H), 8.10−8.06 (m, 3H), 7.51−7.48 (m, 3H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H);; $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 171.5, 166.3, 157.1, 135.1, 133.4, 131.7, 129.3, 127.9, 127.7, 127.4, 123.9, 123.0, 61.4, 14.5; FT-IR (KBr) 2975, 1708, 1684, 1628, 1506, 1477, 1441, 1408, 1390, 1325, 1273, 1226, 1133, 1056, 1030 cm^{-1}. Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94; S, 11.32. Found: C, 67.72; H, 4.64; N, 4.98; S, 11.38. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{13}NO_2SH$ 284.0740, found 284.0749.

*6-Chloro-2-phenylbenzo[d]thiazole (**4i**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.64; white solid; 78 mg, 88% yield; mp 156−157 °C (lit.[15] mp 160 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06−8.04 (m, 2H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 2.0 Hz, 1H), 7.50−7.48 (m, 3H), 7.45 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.7, 152.9, 136.4, 133.4, 131.4, 131.3, 129.3, 127.7, 127.3, 124.1, 121.4; FT-IR (KBr) 3076, 2923, 1587, 1545, 1479, 1438, 1306, 1246, 1224, 1104, 1072, 1053 cm^{-1}. Anal. Calcd for $C_{13}H_8ClNS$: C, 63.54; H, 3.28; N, 5.70; S, 13.05. Found: C, 63.48; H, 3.26; N, 5.73; S, 13.09. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_8ClNSH$ 246.0139, found 246.0142.

*6-Fluoro-2-phenylbenzo[d]thiazole (**4j**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.62; white solid; 68 mg, 83% yield; mp 133−134 °C (lit.[15] mp 137 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−8.02 (m, 2H), 8.01 (dd, *J* = 9.2 Hz, 4,8 Hz, 1H), 7.57 (dd, *J* = 7.6 Hz, 2.4 Hz, 1H), 7.49−7.47 (m, 3H), 7.23 (td, *J* = 8.8 Hz, 2.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.9 (d, *J* = 3.0 Hz), 161.8 (d, *J* = 244.8 Hz), 150.9 (d, *J* = 1.5 Hz), 136.2 (d, *J* = 11.4 Hz), 133.4, 131.2, 129.2, 127.6 (d, *J* = 4.6 Hz), 124.3 (d, *J* = 9.1 Hz), 115.2 (d, *J* = 25.2 Hz), 108.1 (d, *J* = 26.6 Hz); FT-IR (KBr) 3078, 2921, 1896, 1608, 1562, 1513, 1482, 1454, 1443, 1316, 1307, 1276, 1260, 1249, 1118, 1072, 1050, 1029 cm^{-1}. Anal. Calcd for $C_{13}H_8FNS$: C, 68.10; H, 3.52; N, 6.11; S, 13.99. Found: C, 68.15; H, 3.51; N, 6.14; S, 13.94. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_8FNSH$ 230.0434, found 230.0438.

*6-Methoxy-2-phenylbenzo[d]thiazole (**4k**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.50; white solid; 76 mg, 87% yield; mp 114−115 °C (lit.[15] mp 116 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.47−7.44 (m, 3H), 7.34 (d, *J* = 2.8 Hz, 1H), 7.09 (dd, *J* = 9.2 Hz, 2.8 Hz, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.7, 157.9, 148.9, 136.6, 133.9, 130.7, 129.1, 127.4, 123.9, 115.8, 104.3, 55.9; FT-IR (KBr) 3072, 2970, 1602, 1558, 1511, 1483, 1464, 1280, 1266, 1225, 1118, 1097, 1059, 999 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80; S, 13.29. Found: C, 69.61; H, 4.60; N, 5.84; S, 13.33. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{11}NOSH$ 242.0634, found 242.0632.

*6-Methyl-2-phenylbenzo[d]thiazole (**4l**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.62; white solid; 72 mg, 89% yield; mp 124−125 °C (lit.[15] mp 126 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07−8.05 (m, 2H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.68 (s, 1H), 7.49−7.46 (m, 3H), 7.30−7.28 (m, 1H), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.2, 152.5, 135.5, 135.4, 133.9, 130.9, 129.2, 128.1, 127.6, 122.9, 121.5, 21.7; FT-IR (KBr) 3053, 2914, 1603, 1552, 1480, 1309, 1256, 1227, 1125, 1075, 1062, 971 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NS$: C, 74.63; H, 4.92; N, 6.22; S, 14.23. Found: C, 74.73; H, 4.90; N, 6.17; S, 14.20. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{11}NSH$ 226.0685, found 226.0683.

*2-Phenyl-6-(trifluoromethyl)benzo[d]thiazole (**4n**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.52; white solid; 44 mg, 44% yield; mp 157−158 °C (lit.[10e] mp 152 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.14−8.08 (m, 3H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.52−7.50 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 171.4, 156.3, 135.3, 133.3, 131.9, 129.4 (2C), 128.0, 123.7, 123.6, 123.5, 119.6 (q, *J* = 4.5 Hz); FT-IR (KBr) 3036, 1512, 1482, 1461, 1415, 1320, 1252, 1225, 1167, 1109, 1086, 970 cm^{-1}. Anal. Calcd for

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$C_{14}H_8F_3NS$: C, 60.21; H, 2.89; N, 5.02; S, 11.48. Found: C, 60.27; H, 2.90; N, 5.00; S, 11.44. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_8F_3NSH$ 280.0402, found 280.0406.

*4,6-Dimethyl-2-phenylbenzo[d]thiazole (**4o**):*[25h] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; white solid; 53 mg, 61% yield; mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09−8.07 (m, 2H), 7.50 (s, 1H), 7.47−7.44 (m, 3H), 7.09 (s, 1H), 2.75 (s, 3H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.7, 151.9, 135.4, 135.3, 134.3, 132.9, 130.7, 129.1, 128.7, 127.6, 118.9, 21.7, 18.5; FT-IR (KBr) 3051, 2914, 1595, 1510, 1480, 1439, 1310, 1281, 1222, 1177, 1094, 1069, 1031, 973 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85; S, 13.40. Found: C, 75.36; H, 5.48; N, 5.81; S, 13.35. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}NSH$ 240.0841, found 240.0840.

*6,7-Dimethyl-2-phenylbenzo[d]thiazole (**4pa**) and 5,6-dimethyl-2-phenylbenzo[d]thiazole (**4pb**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.60; white solid; 65 mg, 75% yield; mp 113−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09−8.04 (m, 4H), 7.83 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.63 (s, 1H), 7.49−7.45 (m, 6H), 7.29 (d, J = 8.4 Hz, 1H), 2.50 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.1, 166.8, 153.1, 152.5, 136.7, 135.7, 134.9, 134.03, 134.0, 133.1, 132.6, 131.1, 130.8, 130.76, 129.5, 129.1, 129.0, 127.5, 127.2, 123.5, 121.7, 120.4, 20.4, 20.3, 19.7, 19.4; FT-IR (KBr) 3056, 2974, 1507, 1476, 1448, 1309, 1275, 1228, 1023, 947 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85; S, 13.40. Found: C, 75.21; H, 5.49; N, 5.88; S, 13.42. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}NSH$ 240.0841, found 240.0841.

*5,7-Dichloro-2-phenylbenzo[d]thiazole (**4q**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.72; white solid; 73 mg, 72% yield; mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−8.05 (m, 2H), 7.93 (d, J = 1.6 Hz, 1H), 7.51−7.50 (m, 3H), 7.38 (d, J = 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 170.6, 155.1, 134.0, 133.0, 132.8, 131.9, 129.4, 127.9, 127.4, 125.3, 121.8; FT-IR (KBr) 3060, 2921, 1570, 1537, 1507, 1441, 1424, 1379, 1262, 1098, 1067, 984 cm^{-1}. Anal. Calcd for $C_{13}H_7Cl_2NS$: C, 55.73; H, 2.52; N, 5.00; S, 11.44. Found: C, 55.82; H, 2.51; N, 4.95; S, 11.39. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_7Cl_2NSH$ 279.9749, found 279.9749.

*6-Chloro-2-(o-tolyl)benzo[d]thiazole (**4r**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; white solid; 89 mg, 95% yield; mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 2.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.46 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 7.37−7.30 (m, 3H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.7, 152.6, 137.6, 136.9, 132.8, 131.9, 131.3, 130.7, 130.5, 127.2, 126.4, 124.3, 121.2, 21.6 ; FT-IR (KBr) 2924, 2853, 1604, 1591, 1480, 1441, 1382, 1305, 1220, 1100, 1050 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNS$: C, 64.73; H, 3.88; N, 5.39; S, 12.34. Found: C, 64.69; H, 3.90; N, 5.36; S, 12.37. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}ClNSH$ 260.0295, found 260.0295.

*6-Chloro-2-(m-tolyl)benzo[d]thiazole (**4s**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; white solid; 87 mg, 93% yield; mp 121−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 9.2 Hz, 1H), 7.88 (s, 1H), 7.85 (d, J = 2.0 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.44 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 169.0, 152.9, 139.1, 136.4, 133.3, 132.2, 131.2, 129.2, 128.1, 127.2, 125.0, 124.0, 121.4, 21.5; FT-IR (KBr) 3056, 2924, 1593, 1512, 1441, 1400, 1306, 1249, 1170, 1104, 1024 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNS$: C, 64.73; H, 3.88; N, 5.39; S, 12.34. Found: C, 64.67; H, 3.87; N, 5.43; S, 12.38. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}ClNSH$ 260.0295, found 260.0298.

*6-Chloro-2-(4-fluorophenyl)benzo[d]thiazole (**4t**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.68; white solid; 85 mg, 90% yield; mp 151−152 °C (lit.[25c] mp 151 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−8.02 (m, 2H), 7.94 (d, J = 9.2 Hz, 1H), 7.85 (d, J = 2.0 Hz, 1H), 7.44 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.19−7.15 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.3, 166.0, 163.5, 152.8, 136.4, 131.3, 129.8 (d, J = 9.2 Hz), 127.4, 124.1, 121.4, 116.5 (d, J = 22.1 Hz); FT-IR (KBr) 3034, 2914, 1598, 1548, 1521, 1484, 1441, 1408, 1305, 1231, 1155, 1096, 1052, 965 cm^{-1}. Anal. Calcd for $C_{13}H_7ClFNS$: C, 59.21; H, 2.68; N, 5.31; S, 12.16. Found: C, 59.12; H, 2.67; N, 5.35; S, 12.19. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_7ClFNSH$ 264.0045, found 264.0041.

*6-Chloro-2-(4-methoxyphenyl)benzo[d]thiazole (**4u**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.54; white solid; 92 mg, 93% yield; mp 137−138 °C (lit.[25c] mp 135 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 9.2 Hz, 2H), 7.91 (d, J = 8.8 Hz, 1H), 7.83 (d, J = 2.0 Hz, 1H), 7.42 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 6.99 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.5, 162.3, 153.0, 136.2, 130.7, 129.3, 127.1, 126.2, 123.6, 121.3, 114.6, 55.7; FT-IR (KBr) 3024, 2923, 1602, 1522, 1483, 1458, 1440, 1429, 1309, 1260, 1225, 1171, 1101, 1051, 1027, 966 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNOS$: C, 60.98; H, 3.66; N, 5.08; S, 11.63; Found: C, 61.07; H, 3.65; N, 5.05; S, 11.59. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}ClNOSH$ 276.0244, found 276.0244.

*6-Chloro-2-p-tolylbenzo[d]thiazole (**4v**):*[25k] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.64; white solid; 83 mg, 89% yield; mp 158−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 3H), 7.84 (d, J = 2.0 Hz, 1H), 7.43 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.9, 152.9, 142.0, 136.3, 131.0, 130.7, 130.0, 127.6, 127.2, 123.9, 121.3, 21.7; FT-IR (KBr) 2918, 1610, 1542, 1481, 1426, 1308, 1232, 1210, 1098, 1048, 962 cm^{-1}. Anal. Calcd for $C_{14}H_{10}ClNS$: C, 64.73; H, 3.88; N, 5.39; S, 12.34; Found: C, 64.79; H, 3.86; N, 5.42; S, 12.29. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}ClNSH$ 260.0295, found 260.0295.

*6-Chloro-2-(4-nitrophenyl)benzo[d]thiazole (**4w**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.76; white solid; 90 mg, 86% yield; mp 208−209 °C (lit.[10d] mp 216 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.40−8.36 (m, 5H), 8.15 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 7.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 166.1, 152.2, 148.9, 137.9, 136.6, 130.9, 128.5, 127.7, 124.64, 124.6, 122.4; FT-IR (KBr) 2920, 1684, 1653, 1597, 1518, 1403, 1346,1322, 1302, 1237, 1017, 969 cm^{-1}. Anal. Calcd for $C_{13}H_7ClN_2O_2S$: C, 53.71; H, 2.43; N, 9.64; S, 11.03. Found: C, 53.79; H, 2.42; N, 9.61; S, 10.98. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_7ClN_2O_2SH$ 290.999, found 290.995.

*2-Phenylnaphtho[1,2-d]thiazole (**4x**):*[16] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.70; white solid; 83 mg, 88% yield; mp 97−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 8.4 Hz, 1H), 8.20−8.17 (m, 2H), 7.95−7.90 (m, 2H), 7.81 (d, J = 8.8 Hz, 1H),7.70−7.66 (m, 1H), 7.60−7.56 (m, 1H), 7.53−7.48 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.2, 150.6, 134.2, 132.2, 131.9, 130.8, 129.2, 129.0, 128.3, 127.5, 127.1, 126.3, 126.1, 124.2, 119.2; FT-IR (KBr) 3047, 2922, 1509, 1472, 1442, 1394, 1361, 1251, 1069, 1025, 972 cm^{-1}. Anal. Calcd for $C_{17}H_{11}NS$: C, 78.13; H, 4.24; N, 5.36; S, 12.27. Found: C, 78.23; H, 4.23; N, 5.30; S, 12.24. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{11}NSH$ 262.0685, found 262.0685.

*6-Chloro-2-(furan-2-yl)benzo[d]thiazole (**4y**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.48; white solid; 69 mg, 81% yield; mp 115−116 °C (lit.[25c] mp 119 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.8 Hz, 1H), 7.84 (d, J = 2.0 Hz, 1H), 7.60 (d, J = 1.2 Hz, 1H), 7.44 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.18 (d, J = 3.6 Hz, 1H), 6.59−6.58 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.1, 152.5, 148.5, 145.2, 135.7, 131.2, 127.5, 123.9, 121.4, 112.8, 112.0; FT-IR (KBr) 3131, 1600, 1578, 1548, 1502, 1470, 1435, 1304, 1281, 1250, 1222, 1132, 1099, 1077, 1019 cm^{-1}. Anal. Calcd for $C_{11}H_6ClNOS$: C, 56.06; H, 2.57; N, 5.94; S, 13.60; Found: C, 56.00; H, 2.56; N, 5.99; S, 13.58. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_6ClNOSH$ 235.9931, found 235.9931.

*6-Chloro-2-(naphthalen-1-yl)benzo[d]thiazole (**4z**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.60; yellow solid; 80 mg, 75% yield; mp 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J = 8.8 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.93−7.90 (m, 3H), 7.62−7.48 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.4, 153.0, 136.8, 134.3, 131.62, 131.6, 130.8, 130.6, 129.7, 128.7, 128.0, 127.3, 126.8, 126.0, 125.2, 124.5, 121.2; FT-IR (KBr) 3059, 2924, 1618, 1552, 1488, 1450, 1426, 1331, 1263, 1051, 1022 cm^{-1}. Anal. Calcd for $C_{17}H_{10}ClNS$: C, 69.03; H, 3.41; N, 4.74; S,

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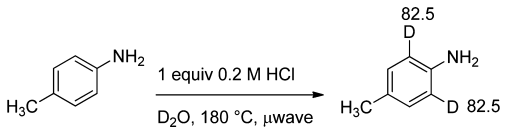
10.84; Found: C, 69.11; H, 3.40; N, 4.70; S, 10.79. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{10}ClNSH$ 296.0295, found 296.0297.

*6-Chloro-2-ethylbenzo[d]thiazole (**4aa**):*[25b] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.58; colorless liquid; 45 mg, 63% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 1.6 Hz, 1H), 7.39 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 3.14 (q, J = 7.6 Hz, 2H), 1.46 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.2, 152.0, 136.5, 130.7, 126.8, 123.4, 121.3, 27.9, 13.8; FT-IR (KBr) 2968, 1592, 1519, 1441, 1400, 1301, 1270, 1169, 1096, 1049 cm^{-1}. Anal. Calcd for C_9H_8ClNS: C, 54.68; H, 4.08; N, 7.09; S, 16.22; Found: C, 54.61; H, 4.10; N, 7.14; S, 16.20. HRMS (ESI) m/z: $[M + H]^+$ calcd for C_9H_8ClNSH 198.0139, found 198.0139.

*6-Chloro-2-isopropylbenzo[d]thiazole (**4ab**):* analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.60; yellow liquid; 67 mg, 88% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 2.0 Hz, 1H), 7.39 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 3.40−3.36 (m, 1H), 1.46 (d, J = 7.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.2, 151.9, 136.1, 130.6, 126.7, 123.5, 121.3, 34.2, 22.9; FT-IR (KBr) 2968, 1592, 1517, 1463, 1443, 1310, 1298, 1265, 1100, 1037, 1001 cm^{-1}. Anal. Calcd for $C_{10}H_{10}ClNS$: C, 56.73; H, 4.76; N, 6.62; S, 15.15. Found: C, 56.81; H, 4.74; N, 6.58; S, 15.11. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{10}H_{10}ClNSH$ 212.0295, found 212.0296.

*2-(tert-Butyl)-6-chlorobenzo[d]thiazole (**4ac**):*[25c] analytical TLC on silica gel, 1/9 ethyl acetate/hexane R_f = 0.72; colorless liquid; 66 mg, 81% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 2.0 Hz, 1H), 7.39 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 1.49 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.6, 152.0, 136.4, 130.6, 126.7, 123.6, 121.2, 38.6, 30.9; FT-IR (KBr) 2966, 1592, 1505, 1473, 1438, 1399, 1365, 1299, 1272, 1127, 1043, 1013 cm^{-1}. Anal. Calcd for $C_{11}H_{12}ClNS$: C, 58.53; H, 5.36; N, 6.20; S, 14.20. Found: C, 58.60; H, 5.34; N, 6.17; S, 14.15. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}ClNSH$ 226.0452, found 226.0447.

Scheme 5



Preparation of *p*-Toluidine-d_2 (Scheme 5).[22a] In a microwave reaction vial equipped with a magnetic stir bar, *p*-toluidine (2 mmol, 214 mg), D_2O (2.5 mL) and 0.2 M HCl (1 equiv) were added. The vial was then capped, sealed, and heated in the microwave synthesis apparatus for 0.5 h at 180 °C. The reaction mixture was transferred to a round-bottom flask, and the solvent was removed on a rotary evaporator to afford the DCl salt of the *p*-toludine. The residue was treated with 3 M NaOH (3 mL), and the solution was extracted using diethyl ether (10 mL), and washed with brine (3 mL). Drying (Na_2SO_4) and evaporation of the solvent under reduced pressure afforded the deuterated *p*-toluidine, and the deuterium incorporation (82.5%) was determined by ^1H NMR analysis of the mixture.[22e] Characterization data for the deuterated product: analytical TLC on silica gel, 1/4 ethyl acetate/hexane R_f = 0.32; pale brown solid; 185 mg, 85% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 2H), 3.47 (bs, 2H), 2.23 (s, 3H).

Preparation of *N*-(*p*-Tolyl)benzamide-d_2 (1a-d_2). To a stirred solution of *p*-toluidine-d_2 (1.5 mmol, 163 mg) in THF (3 mL) at 0 °C was added dropwise benzoyl chloride (1.65 mmol, 192 μL). The resulting solution was warmed to room temperature, and stirring was continued for an additional 24 h. The solvent was evaporated on a rotary evaporator, and the residue was treated with ethyl acetate (5 mL). The solution was successively washed with aqueous $NaHCO_3$ (2 mL) and brine (2 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was recrystallized using ethanol: analytical TLC on silica gel, 3/7 ethyl acetate/hexane, R_f = 0.25; white solid; 236 mg, 74% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (bs, 1H), 7.85−7.82 (m, 2H), 7.53−7.42 (m, 3H), 7.14 (s, 2H), 2.32 (s, 3H); HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}D_2NO$ 214.1201, found 214.1207.

Intermolecular Competition Reaction. Oxone (0.75 mmol) was added to a stirred solution of *N*-(*p*-tolyl)benzamide (**1a**; 0.2 mmol, 42.2 mg) and *N*-(*p*-tolyl)benzamide-d_2 (**1a**-d_2; 0.3 mmol, 63.9 mg, 82.5% deuterated), 1-iodo-4-nitrobenzene (0.1 mmol, 12.45 mg), and triflic acid (1.5 mmol, 132 μL) in HFIP (3.5 mL) at room temperature in air. The reaction was stopped at 23% conversion (3.5 h) and the mixture then treated with saturated $Na_2S_2O_3$ (1 mL) and $NaHCO_3$ (1 mL) solutions. The mixture was extracted with ethyl acetate (3 × 10 mL) and washed with brine (2 × 5 mL) and water (1 × 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified by silica gel column chromatography using hexane and ethyl acetate as eluent (19% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 8.23−8.21 (m, 1.88H), 7.63 (d, J = 8.0 Hz, 0.46H), 7.52−7.49 (m, 2.93H), 7.37 (s, 0.90H), 7.16−7.14 (m, 0.91H), 2.49 (s, 3H). The ^1H NMR analysis showed the kinetic isotopic effect (KIE) value P_H/P_D = 1.0.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving NMR (^1H and ^{13}C) spectra of the products **2a−ab** and **4a−ac**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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