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Novel Solid-Phase Parallel Synthesis of *N*-Substituted-2-aminobenzo[*d*]thiazole Derivatives via Cyclization Reactions of 2-Iodophenyl Thiourea Intermediate Resin

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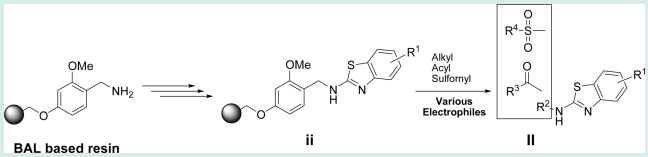
Supporting Information

ABSTRACT: A novel solid-phase methodology has been developed for the synthesis of *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole derivatives. The key step in this procedure involves the preparation of polymer-bound 2-aminobenzo[*d*]thiazole resins **5** by cyclization reaction of 2-iodophenyl thiourea resin **3**. The resin-bound 2-iodophenyl thiourea **3** is produced by addition of 2-iodophenyl isothiocyanate **2** to the amine-terminated linker amide resin **1**. These core skeleton 2-aminobenzo[*d*]thiazole resins **5** undergo functionalization reactions with various electrophiles, such as alkyl halides, acid chlorides, and sulfonyl chlorides to generate *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole resins **6**, **7**, and **8**, respectively. Finally, *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole derivatives **9**, **10**, and **11** are then generated in good yields and purities by cleavage of the respective resins **6**, **7**, and **8** using trifluoroacetic acid (TFA) in dichloromethane (DCM).



KEYWORDS: *2-5 aminobenzothiazole-based libraries, solid-phase synthesis, 2-aminobenzo[d]thiazole resins, Suzuki coupling reaction*

INTRODUCTION

Heterocyclic skeletons serve as ideal scaffolds on which pharmacophores can be appended to yield potent and selective drugs.[1] The development of unique five-membered heterocyclic core skeletons, is especially important to drug discovery research areas. In this respect, the potential of the benzothiazole scaffold to serve as a privileged structure for the generation of drug-like libraries in drug-discovery programs has been amply demonstrated in medicinal chemistry.[2] Although, benzothiazole derivatives are of particular interest in medicinal chemistry[3] and, consequently, have been the targets of several solution[4] and solid-phase[5] synthesis studies, the solid-phase synthesis of benzothiazoles with sufficiently high levels of diversity has not been reported in the drug discovery research area. Especially, the efficient solid-phase syntheses of *N*-substituted-2-aminobenzo[*d*]thiazoles using the Merrifield backbone resin have not been reported for the construction of drug-like libraries Therefore, we have previously concentrated our efforts on describing a facile and rapid solid-phase strategy for the preparation of a small molecule library based on the benzothiazole scaffold. As a result, we reported a useful method for the solid-phase synthesis of 2-aminobenzo[*d*]oxazole derivatives using thioether linkage as the safety-catch linker.[6] In our developed processes, the choice of the linker that serves to attach the library scaffold to the polymer support is critical. As a result, a variety of elegant linking methods have been developed (i.e., safety-catch linkers[7]) that enable additional diversity to be introduced into the products during the cleavage reactions. The sulfone linker is an example of a safety-catch linker that can be cleaved from resins by using nucleophilic substitution reactions with amines.[8] We have utilized this general methodology to produce amine-functionalized 2-aminobenzoxazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, and thiazole libraries through consecutive oxidation and amine-promoted cleavage of thioether linkages produced in carbon disulfide mediated reactions of the Merrifield resin.[9] However, our developed method suffered a limitation in that we could not efficiently introduce various substituents such as amine, amides, sulfone amides, and urea on the 2-position of benzo[*d*]oxazole core skeleton by nucleophilic substitution reaction at the last cleavage step, as shown in Scheme 1 (resin **i** → compound **I**). The nucleophile substitution reaction of the last cleavage step could only proceed with various amine nucleophiles, and not with alcohols or thiols. Moreover, we could not obtain the 2-aminobenzothiazole core skeleton using our developed solid-phase synthesis.[9] As a result of these limitations, we undertook an investigation aimed at developing efficient and simple parallel synthesis methods to produce various *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]-thiazole derivatives by a new type of solid-phase linker which can be used to introduce various electrophile substituents on the 2-position of benzothiazole at the last cleavage step. Herein we report our recent progress on this project which includes the first solid-phase synthesis protocol for *N*-alkyl, *N*-acyl, and

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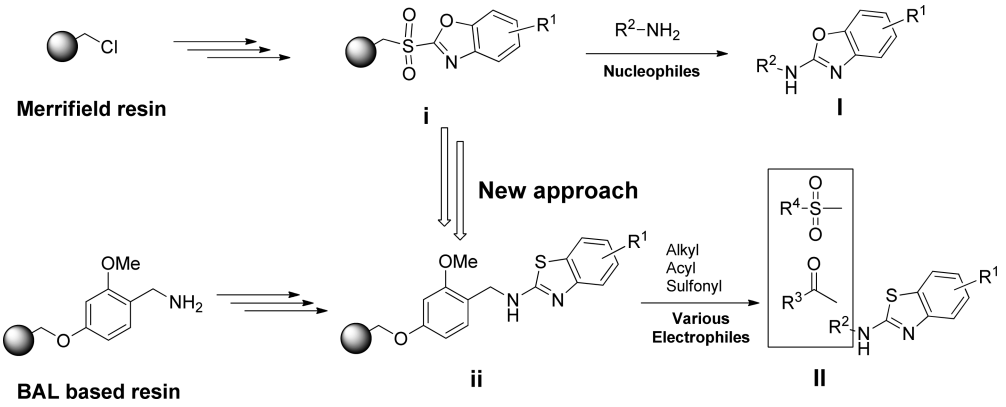
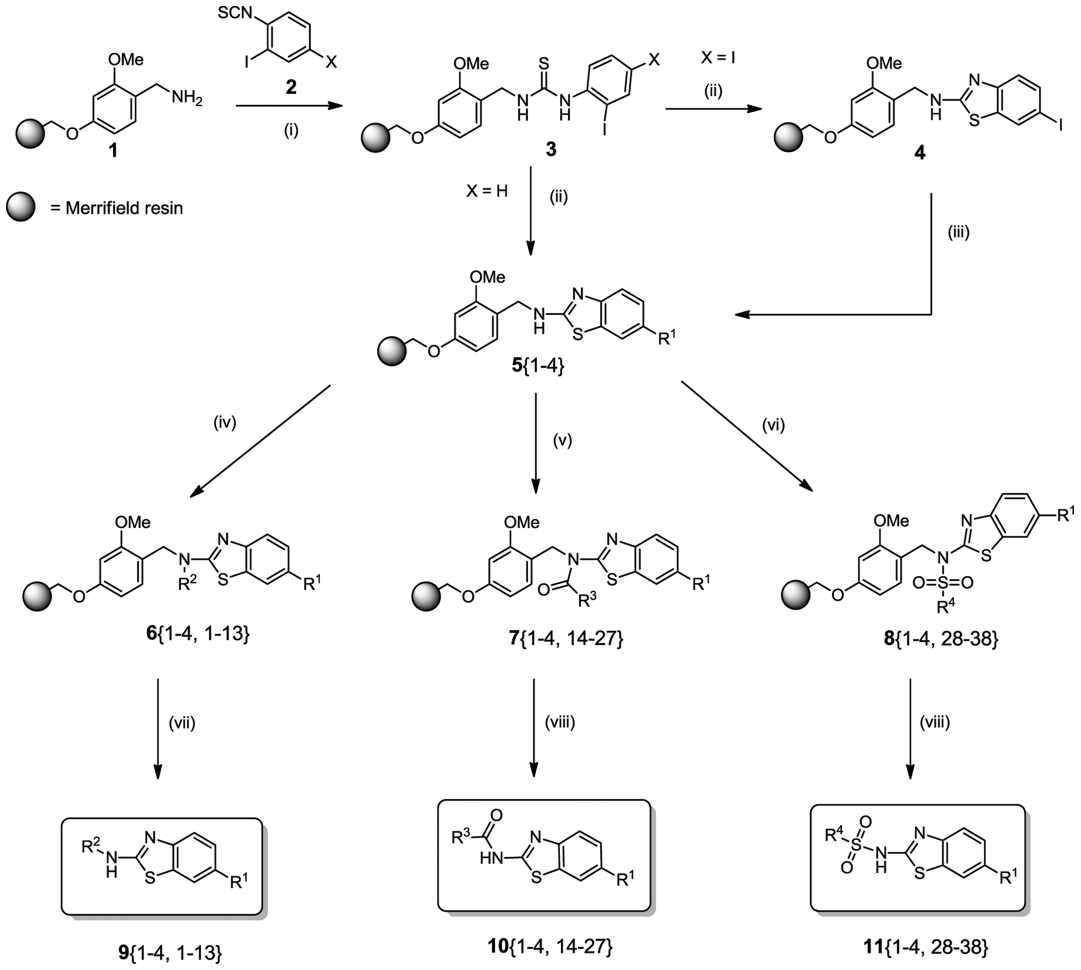
Scheme 1. Strategy Used to Make Various *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole Libraries



Scheme 2. Solid-Phase Synthesis Route to the Various *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-benzo[*d*]thiazole Derivatives[a]



[a]*Reagents and conditions*: (i) 2-iodophenyl isothiocyanate (or 2,4-diiodophenyl isothiocyanate), Et_3N, DCM, r.t., 0.5 h.; (ii) Cs_2CO_3, CuI(I), 1,4-dioxane, 70 °C, 1.5 h.; (iii) $R^1B(OH)_2$, K_3PO_4, $Pd(PPh_3)_4$, 1,4-dioxane:H_2O = 9:1, 15 h.; (iv) Alkyl halides, ^{t}BuOK, NMP, 60 °C, 24 h.; (v) Acyl halides, pyridine, 40 °C, 12 h.; (vi) sulfonyl halides, pyridine, 40 °C, 12 h.; (vii) TFA:DCM (1:4), 50 °C, 12 h.; and (viii) TFA:DCM (5:95), 50 °C, 3 h.

N-sulfonyl-2-aminobenzo[*d*]thiazole derivatives **9**, **10**, and **11** (Scheme 1; resin **ii** → compound **II**) via cyclization reactions of a 2-iodophenyl thiourea resin **3** by addition of 2-iodophenyl isothiocyanate to a terminated amine resin **1** and followed by functionalization of 2-aminobenzo[*d*]thiazole and cleavage on respective resins **6**, **7**, and **8** under trifluoroacetic acid (TFA) condition. We believe our efficient approach is suitable for the construction of drug-like *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole libraries **9**, **10**, and **11**, respectively, in a high throughput manner.

RESULTS AND DISCUSSION

The overall synthetic strategy used to prepare the target *N*-alkyl, *N*-acyl, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole ana-

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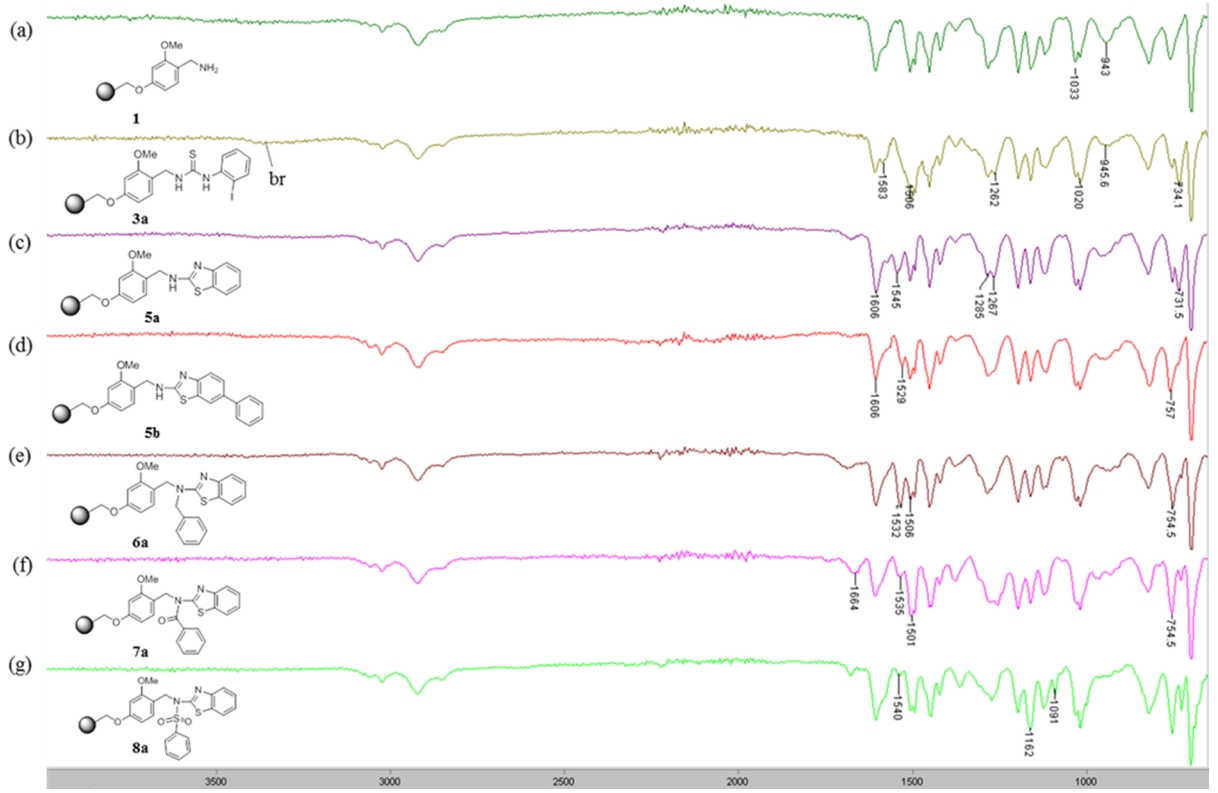
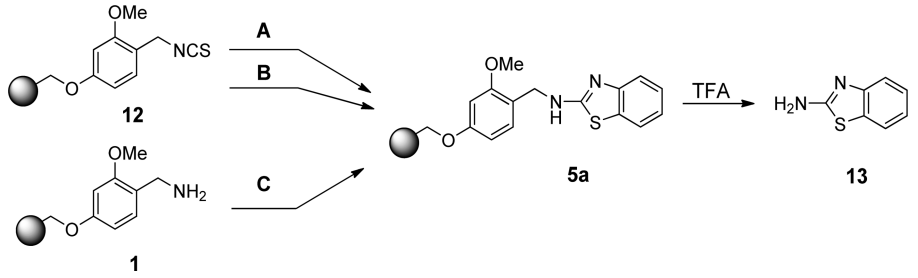


Figure 1. ATR-FTIR spectra on single beads of 2-aminobenzo[*d*]thiazole resins **1** (a), **3a** (b), **5a** (c), **5b** (d), **6a** (e), **7a** (f), and **8a** (g).

Table 1. Results of the Cyclization Condition Optimization[a]



entry	route	base	additive	solvent	time (h)	temp. (°C)	yields of **13** (%)
1	**A**	TEA		THF	24	80	trace
2[4a]	**A**			pyridine	24	80	trace
3[4d]	**A**		$FeCl_3$	THF	24	70	11
4[4e]	**A**		HgO, S	THF	24	60	8
5[4e]	**A**		HgO, S	1,4-dioxane	24	60	6
6[10]	**A**		EDC·HCl	THF	24	60	trace
7[4f]	**B**		TBAB/CuBr	DMSO	24	40	trace
8[4j,k]	**B**	Cs_2CO_3		1,4-dioxane	12	90	11
9[4g]	**C**	K_2CO_3	$CuCl_2·H_2O$	DMF	6	90	trace
10[4j,k]	**C**	Cs_2CO_3		1,4-dioxane	12	90	30
11[4l−o]	**C**	Cs_2CO_3	CuI	1,4-dioxane	1	70	62

[a]Reagents: (A) 2-aminothiophenol; (B) 2-iodoaniline; (C) 2-Iodophenyl isothiocyanate.

logues **9**, **10**, and **11** is outlined in Scheme 2. The initial solid phase synthesis route that we developed to prepare substances containing the benzothiazole scaffold involved the formation of the intermediate 2-aminobenzo[*d*]thiazole resins **4** and **5** from solid-supported 2-iodophenyl thiourea linker **3**, which was derived from the amine-terminated resin **1** with 2-iodophenyl isothiocyanate **2**. Next cyclization reaction of intermediate thiourea resin **3** in the presence of cesium carbonate (Cs_2CO_3) and copper(I) iodide (CuI) produced the solid bound 2-aminobenzo[*d*]thiazole **4** and **5** as the key intermediate resin. Subsequently, *N*-alkylation, *N*-acylation, and *N*-sulfonylation reactions of the 2-amino group proceeded to afford respective resins **6**, **7**, and **8** for effective diversification with various electrophiles. Toward further diversification, we tried to apply Suzuki coupling reaction. In the results, we successfully introduced phenyl and substituted phenyl groups on the

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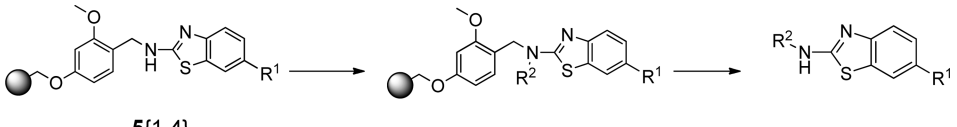
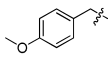
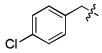
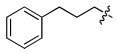
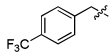
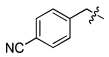
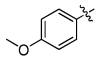
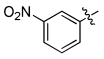
Table 2. Yields and Purities of the *N*-alkyl Benzothiazole Derivatives 9



5{1-4} 6{1-4, 1-13} 9{1-4, 1-13}

Code	R^1	R^2	Yield (%)[a]	Purity (%)[b]	Code	R^1	R^2	Yield (%)[a]	Purity (%)[b]
9a	H		45	>99	**9i**	H		29	>99
9b	H		38	99	**9j**	H		25	>99
9c	H		42	>99	**9k**	H		49	98
9d	H		33	>99	**9l**	H		28	>99
9e	H		45	>99	**9m**	H		50	>99
9f	H		47	>99	**9n**			15[c]	97
9g	H		23	98	**9o**			21[c]	94
9h	H		46	>99	**9p**			17[c]	97

[a]Four-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g). [b]All of the purified products were checked by LC/MS. [c]Five-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g).

benzothiazole ring **4**. Finally, the desired *N*-alkyl-, and *N*-acyl-, and *N*-sulfonyl-2-aminobenzo[*d*]thiazole derivatives **9**, **10**, and **11** were smoothly obtained by cleavage from the *N*-substituted resins **6**, **7**, and **8**, respectively, under the condition of dilute TFA in good yields and purities (Scheme 2).

For the solid-phase parallel synthesis methodology, we selected the backbone amide linker (BAL) resin **1** as a polymer support since the amino group in the BAL resin **1** is suitable for the introduction of 2-iodophenyl isothiocyanate **2** through an addition reaction in the presence of Et_3N under mild condition, which can also serve as an efficient 2-iodophenyl thiourea linker **3** as a key intermediate resin. The progress of this addition reaction was monitored by using attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy to measure the growth of typical thiourea infrared-bands at 1585 cm^{-1} (Figure 1, **3a**(b)). We then attempted to obtain the 2-aminobenzo[*d*]thiazole core skeleton resin **5** by cyclization reaction in the presence of various bases (Et_3N, pyridine, K_2CO_3 etc.) and activation reagents (TBAB, $FeCl_3$, HgO, and $CuCl_2$, etc.) based on known benzothiazole synthesis methods.[4] However, we could not obtain the desired resin-bound 2-amio benzo[*d*]thiazole **4** and **5** core skeletons since the known reaction conditions of benzoxazoles were not suitable for solid-phase reactions. Therefore, our concern focused on the development of a resin-bound benzothiazole cyclization reaction under convenient reaction conditions (Table 1). From our results we determined an efficient cyclization condition in which 2-aminobenzo[*d*]thiazole resins **4** and **5** were afforded by cyclization of 2-iodophenyl thiourea resin **3** in the presence of Cs_2CO_3, CuI(I) at 70 °C for 1.5 h in 1,4-dioxane (Table 1 entry 11). The reaction protocol was modified from several known conditions.[4l−o] This process led to the formation of the 2-aminobenzo[*d*]thiazole resins **4** and **5**, whose single bead FTIR spectrum contained imine stretching bands at 1541 cm^{-1} and the absence of the thiourea band of resin **3** at 1585 cm^{-1}(Figure 1, **5a**(c)).

For the first diversification, we tried to introduce various electrophiles on the 2-amino group of benzo[*d*]thiazole core skeleton resins **4** and **5** using alkyl halides, acid chlorides, and sulfonyl chlorides. Initially, alkylation reaction of the 2-amino group on 2-aminobenzo[*d*]thiazole resins **4** and **5** provided the desired *N*-alkyl-2-benzo[*d*]thiazole resin **6** by reaction with alkyl halides in the presence of ^{t}BuOK at 60 °C for 24 h in *N*-methylpyrrolidone solvent.

In this step, the progress of this reaction (R^2 = Bn) was monitored by ATR-FTIR spectroscopy, which revealed the disappearance of the band at 1545 cm^{-1} (Figure 1, **5a** (d)). In the last step, the *N*-alkyl benzothiazole derivatives **9** was formed and cleaved from the resin **6** by treatment of TFA: DCM (1:4) at 50 °C for 12 h. The proton nuclear magnetic resonance (^{1}H NMR) spectroscopic properties of **9a**, following purification by passing through a short plug of silica, were identical to those of

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Chart 1. Building Block for Amine Capping

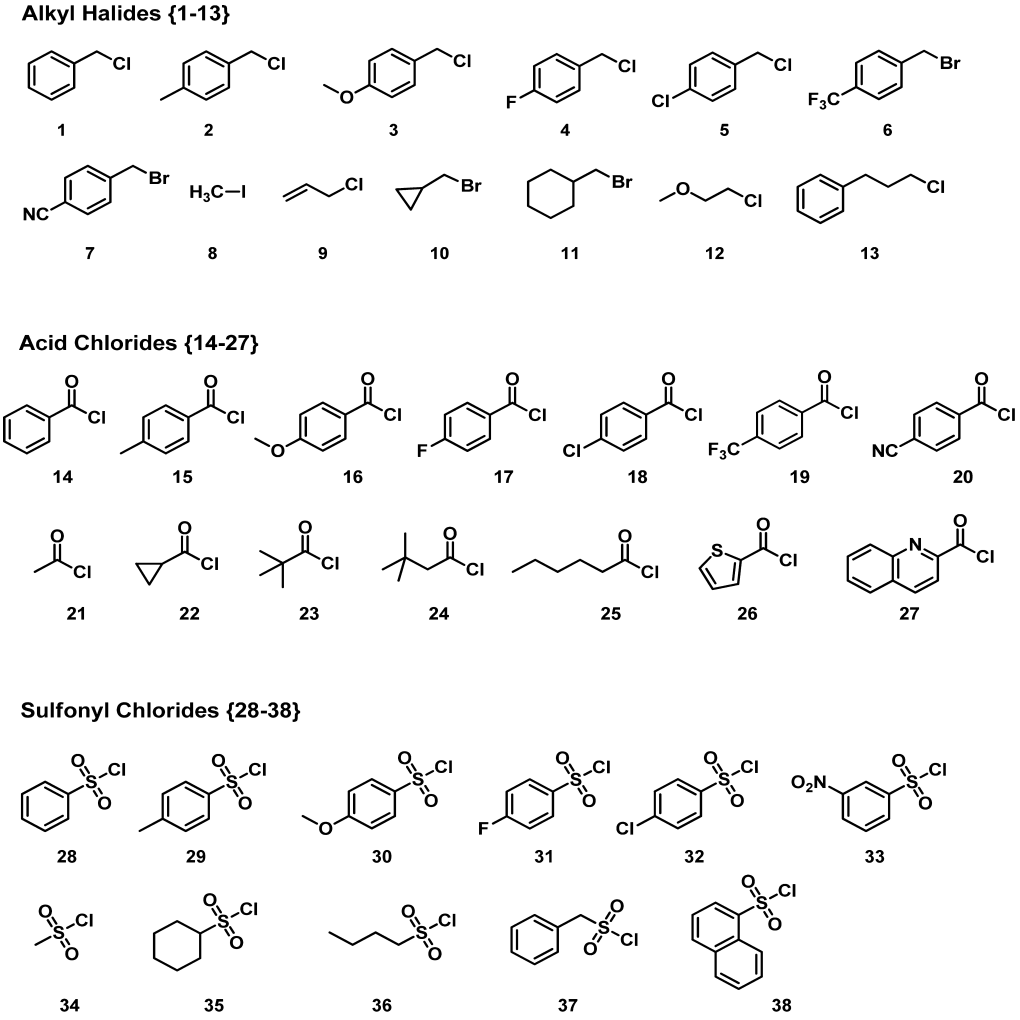
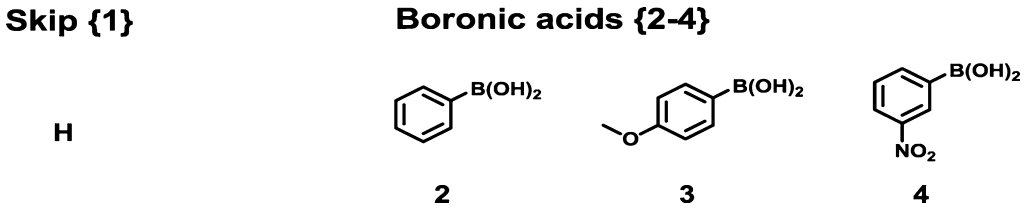


Chart 2. Building Block for Suzuki Coupling



the corresponding substances produced by using solution-phase synthesis routes. As shown by the data given in Table 2, the desired various *N*-alkyl-2-aminobenzo[*d*]thiazole derivatives **9** can be produced by this five-step route in high overall yields and purities. We successfully introduced various alkyl building blocks (Charts 1 and 2) on the 2-amino groups of the simple benzothiazole core skeleton ring (**9a**-**9m**) as well as R^1-substituted benzothiazole derivatives (**9n**-**9p**) by Suzuki coupling.

Next, the acylation reaction of 2-aminobenzo[*d*]thiazole resins **4** and **5** produced *N*-acyl-2-benzo[*d*]thiazole resin **7** with various acid chlorides in pyridine at 40 °C for 12 h. This progress step (R^3 = Ph) was also monitored by ATR-FTIR spectroscopy, which revealed the disappearance of the band at 1545 cm^{-1} and the appearance of an amide band at 1664 cm^{-1} (Figure 1, **7a**(e)). This *N*-acyl-2-aminobenzo[*d*]thiazole resin **7** easily gives the *N*-acyl-2-aminobenzo[*d*]thiazole derivatives **10** cleaved from the resin **7** by treatment of TFA:DCM (5:95) at 50 °C for 3 h. As shown by the data given in Table 3, various *N*-acyl-2-aminobenzo[*d*]thiazole derivatives **10** can be produced by introduction of various acid chloride building blocks on the 2-amino groups of the simple benzothiazole core skeleton ring (**10a**−**10n**) as well as R^1-substituted benzothiazole derivatives (**10o**−**10t**) by Suzuki coupling which were obtained in five-step overall yields and high purities.

Finally, we tried to introduce a sulfonyl functional group on the 2- position of 2-aminobenzo[*d*]thiazole. The sulfonylation reaction of the 2-aminobenzo[*d*]thiazole resins **4** and **5** provided the desired *N*-sulfonyl-2-aminobenzo[*d*]thiazole resin **8** by reaction with sulfonyl chlorides in pyridine at 40 °C for 12 h. The progress of this reaction (R^4 = Ph) was monitored by ATR-FTIR spectroscopy (Figure 1, **8a**(g)),

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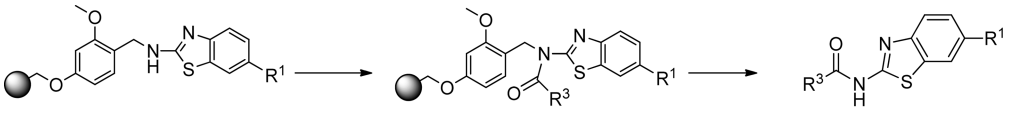
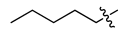
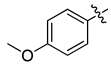
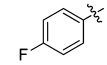
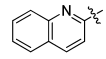
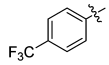
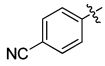
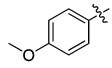
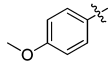
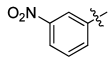
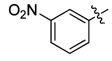
Table 3. Yields and Purities of the *N*-acyl-2-benzothiazole Derivatives 10



5{1-4} **7**{1-4, 14-27} **10**{1-4, 14-27}

Code	R^1	R^3	Yield (%)[a]	Purity (%)[b]	Code	R^1	R^3	Yield (%)[a]	Purity (%)[b]
10a	H		49	>99	**10k**	H		32	99
10b	H		37	>99	**10l**	H		26	89
10c	H		35	>99	**10m**	H		21	99
10d	H		31	95	**10n**	H		39	>99
10e	H		39	95	**10o**			33[c]	97
10f	H		29	>99	**10p**			32[c]	95
10g	H		33	95	**10q**			30[c]	>99
10h	H		51	>99	**10r**			30[c]	96
10i	H		23	>99	**10s**			25[c]	>99
10j	H		42	>99	**10t**			24[c]	92

[a]Four-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g). [b]All of the purified products were checked by LC/MS. [c]Five-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g).

which revealed the disappearance of the band at 1545 cm^{-1} and the appearance of sulfonamide band at 1162 cm^{-1}. This *N*-sulfonyl-2-aminobenzo[*d*]thiazole resin **8** easily gives the *N*-sulfonyl-2-aminobenzo[*d*]thiazole derivatives **11** cleaved from resin **8** by treatment of TFA:DCM (5:95) at 50 °C for 3 h. Although the sulfonylation affords lower yields compared to the alkylations and acylations, as shown by the data given in Table 4, various N-sulfonyl-2-aminobenzo[d]thiazole derivatives **11** (**11a−11q**) can be produced by this four or five-step route in fair yields.

To introduce additional diversification into this methodology, the aryl group containing 6-aryl-2-aminobenzo[*d*]-thiazole resin **5** was introduced by treatment with arylboronic acid in the presence of K_3PO_4 and $Pd(PPh_3)_4$ in 1,4-dioxane:H_2O (9:1) for 15 h. Functionalization of the 6-aryl-2-aminobenzo[*d*]thiazole resin **5** can be promoted by reactions with alkyl halides, acid chlorides or sulfonyl chlorides using conditions (iv), (v), and (vi) in Scheme 2 respectively to generate the corresponding substituted **6n**, **7n**, and **8n** resins. In each case, the desired 6-aryl-*N*-alkylamino-2-benzo[*d*]-thiazole **9n**, 6-aryl-*N*-acylamino-2-benzo[*d*]thiazole **10o**, and 6-aryl-*N*-sulfonylamino-2-benzo[*d*]thiazole **11l**, products are cleaved from the respective resins by subsequent treatment with TFA:DCM. As shown by the data given in Tables 2, 3, and 4, various 6-aryl-*N*-alkylamino-2-benzo[*d*]thiazole (**9n∼9p** in Table 2), 6-aryl-*N*-acylamino-2-benzo[*d*]thiazole (**10o∼10t** in Table 3), and 6-aryl-*N*-sulfonylamino-2-benzo[*d*]thiazole (**11l∼11p** in Table 4), derivatives can be produced by this five-step route in high overall yields and purities.

In this research, an efficient solid-phase methodology has been developed for the synthesis of 2-aminobenzothiazole-based libraries. This solid-phase synthesis route provided much more efficient generation of various 2-substituted alkyl/acyl/sulfonyl benzothiazole-based libraries **9**, **10**, and **11** than the standard solid-phase synthesis methods for benzothiazole derivatives. The key diversification step commences with a 2-aminobenzo[*d*]thiazole core skeleton resin **5** and relies on the alkylation, acylation, or sulfonylation of the 2 position on the 2-

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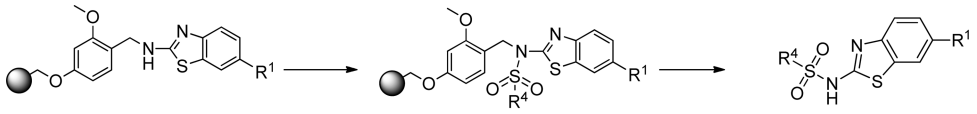
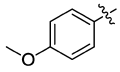
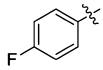
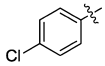
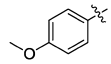
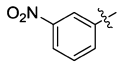
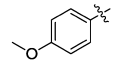
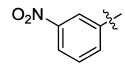
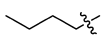
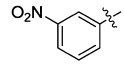
Table 4. Yields and Purities of the *N*-sulfonyl-2-aminobenzothiazole Derivatives 11



5{1-4} 8{1-4, 28-38} 11{1-4, 28-38}

Code	R^1	R^4	Yield (%)[a]	Purity (%)[b]	Code	R^1	R^4	Yield (%)[a]	Purity (%)[b]
11a	H		27	99	**11j**	H		trace	-
11b	H		19	>99	**11k**	H		6	98
11c	H		20	>99	**11l**			15[c]	94
11d	H		27	>99	**11m**			10[c]	91
11e	H		22	97	**11n**			10[c]	97
11f	H		16	96	**11o**			9[c]	96
11g	H		18	96	**11p**			12[c]	91
11h	H		8	98	**11q**			4[c]	92
11i	H		Trace	-					

[a]Four-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g). [b]All of the purified products were checked by LC/MS. [c]Five-step overall yields from BAL resin **1** (loading capacity of resin **1** is 1.16 mmol/g).

aminobenzo[*d*]thiazole ring. To introduce additional diversification into this methodology, the aryl group containing 6-aryl-2-amino-benzothiazole resin **5** was introduced by Suzuki coupling reaction. This strategy, based on an efficient solid-phase sequence, enables the construction of a large library and is potentially applicable for the preparation of other drug-like *N*-alkyl/acyl/sulfonyl-2-aminobenzo[*d*]thiazole ring systems. Finally, the calculated physicochemical properties of members of the library constructed by using this approach are well distributed within reasonable orally acceptable drug-like ranges. Further studies in this area are underway, the results of which will be reported in due course.

EXPERIMENTAL PROCEDURES

General Procedure for Synthesis. All chemicals were reagent grade and used as purchased. Reactions were monitored by thin layer chromatography (TLC) analysis using Merck silica gel 60 F-254 thin layer plates or attenuated ATR-FTIR analysis using Identify IR (Smiths Detection). Flash column chromatography was carried out on Merck silica gel 60 (230−400 mesh). The crude products were purified by high throughput chromatography using Isorea One (Biotage). ^{1}H NMR and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded in δ units relative to deuterated solvent as an internal reference using a Varian 400 MHz, Bruker 400 and 500 MHz NMR instrument. Liquid chromatography-tandem mass spectrometry (LC-MS/MS/Agilent6460 Triple Quad LC/MS) analysis was performed on an electrospray ionization (ESI) mass spectrometer with photodiode-array detector (PDA) detection. LC-MS/MS area percentage purities of all products were determined by LC peak area analysis (Poroshell 120 EC-C_{18} column, 4.6 mm × 100 mm, 2.7 Micron; PDA detector at 245 nm; 70% CH_3CN/H_2O). High-resolution mass spectrometry fast-atom bombardment (HRMS-FAB) spectra were obtained using an API 4000Q TRAP LC-MS/MS system (Applied Biosystems).

Representative Procedure for 2-Iodophenyl Thiourea Resin 3a. To a suspension of BOMBA resin **1** (5 g, 5.8 mmol,

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loading 1.16 mmol/g) in DCM (60 mL) was added successively triethylamine (TEA; 0.81 mL, 5.8 mmol), and 2-iodophenyl isothiocyanate **2** (0.64 g, 16 mmol) at 0 °C. The suspension was shaken for 0.5 h at room temperature under a nitrogen atmosphere. 2-Iodophenyl thiourea resin **3a** was filtered and washed with DCM (×2), MeOH (×2), DCM (×2) and dried under high vacuum. Resin **3a** was obtained as a orange solid. Single-bead ATR-FTIR: 1585, 1504, 1282, 957, 820, 732 cm^{-1}.

Representative Procedure for 2-Aminobenzo[*d*]-thiazole Resin 5a. To a suspension of 2-iodophenyl thiourea resin **3a** (6.4 g, 5.8 mmol) in 1,4-dioxane (65 mL) was added Cs_2CO_3 (7.5 g, 23.2 mmol), and CuI (0.22 g, 1.16 mmol). The mixture was shaken for 1.5 h at 70 °C. The suspension was filtered, and the precipitate containing the 2-aminobenzo[*d*]-thiazole resin **5a** was washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. Resin **5a** was obtained as a dark yellow solid. Single-bead ATR-FTIR: 1542, 1492, 1450, 1419, 1375, 750, 725 cm^{-1}.

Representative Procedure for the Suzuki Coupling Reaction. Formation of 6-Phenyl-2-aminobenzo[*d*]-thiazole Resin 5b. To a suspension of 6-iodo-2-aminobenzo [*d*]thiazole resin **4a** was added successively K_3PO_4 (1.4 g, 6.8 mmol), phenylboronic acid (0.8 g, 6.8 mmol) in 1,4-dioxane:H_2O (9:1), and $Pd(PPh_3)_4$ (0.2 g, 0.2 mmol) was added under nitrogen atmosphere. The suspension was shaken for 15 h at 80 °C. 6-Phenyl-2-aminobenzo[*d*]thiazole resin **5b** was filtered and washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. Resin **5b** was obtained as a dark brown solid. Single-bead ATR-FTIR: 1527, 1506, 1493, 1450, 1419, 872, 758, 698 cm^{-1}.

Representative Procedure for the First-Generation Alkylation Reaction Step iv, the Preparation of *N*-benzyl-2-aminobenzo[*d*]thiazole Resin 6a. To a suspension of 2-aminobenzo[*d*] thiazole resin **5a** (150 mg, 0.15 mmol) in NMP (4 mL) was added ^{t}BuOK (168 mg, 1.5 mmol). After shaking for 1 h, benzyl chloride (0.17 mL, 1.5 mmol) was added to the mixture which was then shaken for 24 h at 60 °C. *N*-benzyl-2-aminobenzo[*d*]thiazole resin **6a** was filtered and washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. Resin **6a** was obtained as a yellow-orange solid. Single-bead ATR-FTIR: 1682, 1534, 1504, 1493, 1450, 1376 cm^{-1}.

Representative Procedure for the First-Generation Alkylation Reaction Step iv, Preparation of 6-Phenyl-*N*-benzyl-2-aminobenzo[*d*]thiazole Resin 6n. To a suspension of 6-phenyl-2-aminobenzo[*d*] thiazole resin **5b** (150 mg, 0.14 mmol) in 1,4-dioxane (4 mL) were added LiHMDS (234 mg, 1.4 mmol). After shaking for 1 h, benzyl chloride (0.17 mL, 1.5 mmol) was added to the mixture which was then shaken for 24 h at 60 °C. 6-Phenyl-*N*-benzyl-2-aminobenzo[*d*]thiazole resin **6n** was filtered and washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. Resin **6n** was obtained as a dark brown solid. Single-bead ATR-FTIR: 1682, 1534, 1504, 1493, 1450, 1376 cm^{-1}.

Representative Procedure for the Second-Generation Acylation Reaction Step v, the Preparation of *N*-benzoyl-2-aminobenzo[*d*]thiazole Resin 7a. To a suspension of 2-aminobenzo[*d*]thiazole resin **5a** (150 mg, 0.15 mmol) in pyridine (4 mL) was added benzoyl chloride (0.17 mL, 1.5 mmol) and catalytic amounts of DMAP. The mixture was shaken for 12 h at 40 °C. *N*-benzoyl-2-aminobenzo [*d*]thiazole resin **7a** was filtered and washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. Resin **7a** was obtained as a yellow-orange solid. Single-bead ATR-FTIR: 1719, 1655(C═O), 1502, 1492, 1450, 1376, 1253, 972 cm^{-1}.

Representative Procedure for the Third-Generation Sulfonylation Reaction Step vi, the Preparation of *N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole Resin 8a. To a suspension of 2-aminobenzo[*d*]thiazole resin **5a** (150 mg, 0.15 mmol) in pyridine (4 mL) was added benzenesulfonyl chloride (0.18 mL, 1.5 mmol) and catalytic amounts of DMAP. The mixture was shaken for 12 h at 40 °C. *N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole resin **8a** was filtered and washed with water, MeOH (×3), and DCM (×3) and dried under high vacuum. **8a** was obtained as a yellow-orange solid. Single-bead ATR-FTIR: 1676, 1603, 1503, 1492, 1445, 1362, 1270 cm^{-1}.

Representative Procedure for the Cleavage Step vii: the Preparation of *N*-benzyl-2-aminobenzo [*d*]thiazole 9a from Resin 6a. A mixture of *N*-benzyl-2-aminobenzo [*d*]thiazole resin **6a**(150 mg, 0.15 mmol) and 3 mL of cleavage cocktail (TFA:DCM = 1:4, v/v) was shaken at 50 °C for 12 h. The resin was filtered, and the filtrate was concentrated in vacuum to give a residue that was dissolved in DCM. The organic filtrates were neutralized by adding saturated $NaHCO_3$ solution. The filtrate was washed with water and dried over $MgSO_4$. The solution was concentrated under reduced pressure, and the residue was purified by column silica gel chromatography to afford **9a** (14 mg, 45%, four-step overall yield from BOMBA resin, loading capacity 1.16 mmol/g) as a white solid. mp 161−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 7.9, 0.7 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.42−7.38 (m, 2H), 7.38−7.26 (m, 4H), 7.11−7.04 (m, 1H), 6.24 (s, 1H), 4.63 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 152.3, 137.5, 130.5, 128.8, 127.9, 127.7, 126.0, 121.6, 120.8, 119.0, 49.4; LC-MS/MS (ESI): m/z = 241.0 $[M+1]^+$. HRMS (EI): $[M+1]^+$ calcd for $C_{14}H_{13}N_2S$, 241.0794; found, 240.963.

***N*-(4-methylbenzyl)-2-aminobenzo[*d*]thiazole (9b).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.33−7.26 (m, 3H), 7.17 (d, J = 7.8 Hz, 2H), 7.08 (t, J = 7.6 Hz, 1H), 5.77 (s, 1H), 4.59 (s, 2H), 2.35 (s, 3H); LC-MS/MS (ESI): m/z = 255.0 $[M+1]^+$.

***N*-(4-methoxybenzyl)-2-aminobenzo[*d*]thiazole (9c).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.9 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.37−7.26 (m, 3H), 7.08 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.6 Hz, 2H), 5.84 (s, 1H), 4.56 (s, 2H), 3.80 (s, 3H); LC-MS/MS (ESI): m/z = 271.0 $[M+1]^+$.

***N*-(4-fluorobenzyl)-2-aminobenzo[*d*]thiazole (9d).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.9 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.37 (dd, J = 8.5, 5.4 Hz, 2H), 7.33−7.27 (m, 1H), 7.13−6.99 (m, 3H), 5.70 (s, 1H), 4.62 (s, 2H); LC-MS/MS (ESI): m/z = 259.0 $[M+1]^+$.

***N*-(4-chlorobenzyl)-2-aminobenzo[*d*]thiazole (9e).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.8 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.31−7.26 (m, J = 7.7 Hz, 1H), 7.13−7.07 (m, J = 7.6 Hz, 1H), 6.02 (s, 1H), 4.62 (s, 2H); LC-MS/MS (ESI): m/z = 274.9 $[M+1]^+$.

***N*-(4-trifluoromethylbenzyl)-2-aminobenzo[*d*]thiazole (9f).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.56 (m, J = 11.8, 8.1 Hz, 3H), 7.55−7.46 (m, J = 13.4, 8.1 Hz, 3H), 7.33−7.26 (m, 1H), 7.14−7.07 (m, J = 11.0, 4.2 Hz, 1H), 6.12 (s, 1H), 4.72 (s, 2H); LC-MS/MS (ESI): m/z = 309.0 $[M+1]^+$.

***N*-(4-cyanobenzyl)-2-aminobenzo[*d*]thiazole (9g).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 7.9 Hz, 1H), 7.52 (dd, J = 8.2, 2.8 Hz, 3H), 7.34−7.27 (m, J = 7.7 Hz, 1H), 7.15−7.09 (m, J = 7.6 Hz, 1H), 5.86 (s, 1H), 4.75

(s, 2H); ^{13}C NMR (126 MHz, DMSO) δ 166.6, 152.7, 145.6, 132.8, 131.0, 128.5, 126.1, 121.7, 121.5, 119.4, 118.7, 110.2, 47.1; LC-MS/MS (ESI): m/z = 266.0 $[M+1]^+$.

***N*-methyl-2-aminobenzo[*d*]thiazole (9h).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 7.9, 0.7 Hz, 1H), 7.57−7.52 (m, 1H), 7.33−7.27 (m, 1H), 7.12−7.05 (m, J = 7.8, 1.1 Hz, 1H), 5.65 (s, 1H), 3.11 (s, 3H); LC-MS/MS (ESI): m/z = 165.0 $[M+1]^+$.

***N*-allyl-2-aminobenzo[*d*]thiazole (9i).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 18.1, 8.0 Hz, 2H), 7.29 (t, J = 7.7 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 5.98 (ddd, J = 22.0, 10.6, 5.5 Hz, 1H), 5.67−5.46 (m, 1H), 5.35 (d, J = 17.1 Hz, 1H), 5.23 (d, J = 10.3 Hz, 1H), 4.07 (d, J = 5.4 Hz, 2H); LC-MS/MS (ESI): m/z = 190.9 $[M+1]^+$.

***N*-(cyclopropylmethyl)-2-aminobenzo[*d*]thiazole (9j).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.44 (m, 2H), 7.34−7.26 (m, 1H), 7.12−7.04 (m, 1H), 5.55 (s, 1H), 3.29 (d, J = 7.1 Hz, 2H), 1.22−1.08 (m, 1H), 0.63−0.54 (m, 2H), 0.34−0.26 (m, 2H); LC-MS/MS (ESI): m/z = 205.1 $[M+1]^+$.

***N*-(cyclohexylmethyl)-2-aminobenzo[*d*]thiazole (9k).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.32−7.26 (m, 1H), 7.07 (td, J = 8.1, 1.0 Hz, 1H), 5.45 (s, 1H), 3.25 (d, J = 6.8 Hz, 2H), 1.86−1.60 (m, J = 22.3, 18.4, 10.1 Hz, 7H), 1.32−1.14 (m, 3H), 1.01 (qd, J = 12.1, 2.9 Hz, 2H); LC-MS/MS (ESI): m/z = 247.0 $[M+1]^+$.

***N*-(methylethylether)-2-aminobenzo[*d*]thiazole (9l).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 10.7, 8.0 Hz, 2H), 7.33−7.26 (m, 1H), 7.12−7.05 (m, 1H), 5.61 (s, 1H), 3.70−3.58 (m, 4H), 3.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 152.4, 130.5, 125.9, 121.6, 120.8, 119.0, 70.8, 58.8, 44.8. LC-MS/MS (ESI): m/z = 209.0 $[M+1]^+$.

***N*-(3-phenylpropyl)-2-aminobenzo[*d*]thiazole (9m).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 8.1 Hz, 1H), 7.41−7.26 (m, 3H), 7.24−7.16 (m, J = 12.5, 4.2 Hz, 3H), 7.12−7.03 (m, 1H), 5.50 (s, 1H), 3.45 (t, J = 7.0 Hz, 2H), 2.75 (t, 2H), 2.03 (dt, J = 14.4, 7.2 Hz, 2H); LC-MS/MS (ESI): m/z = 269.1 $[M+1]^+$.

6-Phenyl-*N*-benzyl-2-aminobenzo[*d*]thiazole (9n). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 1.6 Hz, 1H), 7.61−7.52 (m, 4H), 7.44−7.31 (m, 8H), 5.89 (s, 1H), 4.66 (s, J = 8.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 151.8, 141.1, 137.4, 135.3, 131.3, 128.9, 128.8, 127.9, 127.7, 127.0, 126.9, 125.5, 119.3, 119.1, 49.4; LC-MS/MS (ESI): m/z = 317.0 $[M+1]^+$. HRMS (EI): $[M+1]^+$ calcd for $C_{20}H_{17}N_2S$, 317.1107; found, 316.992.

6-(4-Methoxyphenyl)-*N*-benzyl-2-aminobenzo[*d*]-thiazole (9o). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 1.7 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.53−7.48 (m, 3H), 7.43−7.30 (m, 5H), 6.97 (d, J = 8.8 Hz, 2H), 4.65 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 158.8, 151.2, 137.4, 134.9, 133.6, 131.2, 128.8, 128.0, 127.9, 127.7, 125.1, 119.0, 118.8, 114.2, 55.4, 49.4; LC-MS/MS (ESI): m/z = 347.0 $[M+1]^+$.

6-(3-Nitrophenyl)-*N*-benzyl-2-aminobenzo[*d*]thiazole (9p). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (t, J = 2.0 Hz, 1H), 8.17 (ddd, J = 8.2, 2.2, 0.9 Hz, 1H), 7.91 (ddd, J = 7.8, 1.6, 1.0 Hz, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.65−7.52 (m, 3H), 7.45−7.30 (m, 5H), 5.76 (s, 1H), 4.68 (s, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.7, 153.4, 148.9, 142.3, 139.2, 133.3, 132.2, 131.1, 130.9, 128.9, 127.9, 127.6, 125.2, 121.9, 121.1, 120.1, 118.9, 47.7; LC-MS/MS (ESI): m/z = 361.9 $[M+1]^+$.

Representative Procedure for the Cleavage Step viii; Preparation of *N*-benzoyl-2-aminobenzo [*d*]thiazole 10a from Resin 7a. A mixture of *N*-benzoyl-2-aminobenzo [*d*]thiazole resin **7a**(150 mg, 0.15 mmol) and 3 mL of cleavage cocktail (TFA:DCM = 5:95, v/v) was shaken at 50 °C for 3 h. The resin was filtered, and the filtrate was concentrated in vacuum to give a residue that was dissolved in DCM. The organic filtrates were adjusted to pH 5−6 by adding saturated $NaHCO_3$ solution. The filtrate was washed with water and dried over $MgSO_4$. The solution was concentrated under reduced pressure, and the residue was purified by column silica gel chromatography to afford **10a** (19 mg, 49%, four-step overall yield from BOMBA resin, loading capacity 1.16 mmol/g) as a white solid. mp 187−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.68 (s, 1H), 8.00 (d, J = 7.3 Hz, 2H), 7.88−7.80 (m, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.31−7.26 (m, 1H), 7.25 (d, J = 3.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 159.6, 147.9, 133.1, 132.1, 132.0, 129.0, 127.9, 126.1, 124.0, 121.4, 120.7; LC-MS/MS (ESI): m/z = 254.9 $[M+1]^+$. HRMS (EI): $[M+1]^+$ calcd for $C_{14}H_{11}N_2OS$, 255.0587; found, 254.749.

***N*-(4-methylbenzoyl)-2-aminobenzo[*d*]thiazole (10b).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1H), 7.92−7.86 (m, 2H), 7.86−7.78 (m, 1H), 7.44−7.34 (m, 1H), 7.34−7.27 (m, 2H), 7.23 (d, J = 7.9 Hz, 2H), 2.39 (s, 3H); LC-MS/MS (ESI): m/z = 269.0 $[M+1]^+$.

***N*-(4-methoxybenzoyl)-2-aminobenzo[*d*]thiazole (10c).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (s, 1H), 7.96 (d, J = 8.8 Hz, 2H), 7.89−7.80 (m, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.38−7.27 (m, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H); LC-MS/MS (ESI): m/z = 282.9 $[M+1]^+$.

***N*-(4-fluorobenzoyl)-2-aminobenzo[*d*]thiazole (10d).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H), 8.05−7.97 (m, 2H), 7.89−7.82 (m, 1H), 7.39−7.29 (m, 3H), 7.14−7.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6 (d, J = 255.1 Hz), 165.1, 160.1, 147.4, 131.8, 130.6 (d, J = 9.3 Hz), 128.3 (d, J = 3.1 Hz), 126.1, 124.2, 121.5, 120.4, 116.2 (d, J = 22.2 Hz); LC-MS/MS (ESI): m/z = 273.0 $[M+1]^+$.

***N*-(4-chlorobenzoyl)-2-aminobenzo[*d*]thiazole (10e).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.43 (s, 1H), 7.95−7.90 (m, 2H), 7.88−7.83 (m, 1H), 7.42−7.38 (m, 2H), 7.38−7.29 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 160.0, 147.3, 139.5, 131.7, 130.5, 129.4, 129.3, 126.2, 124.2, 121.5, 120.4; LC-MS/MS (ESI): m/z = 288.9 $[M+1]^+$.

***N*-(4-trifluoromethylbenzoyl)-2-aminobenzo[*d*]-thiazole (10f).** ^{1}H NMR (500 MHz, DMSO) δ = 13.19 (s, 1H), 8.35 (d, J = 7.6 Hz, 2H), 8.04 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 7.7 Hz, 2H), 7.82 (d, J = 7.9 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 165.36, 159.23, 147.59, 135.85, (q, J = 32.0 Hz), 131.29, 129.28, 126.28, 125.51(q, J = 3.5 Hz), 123.79 (q, J = 272.7 Hz), 123.82, 121.84, 120.10; LC-MS/MS (ESI): m/z = 322.9 $[M+1]^+$.

***N*-(4-cyanobenzoyl)-2-aminobenzo[*d*]thiazole (10g).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (s, 1H), 8.09 (d, J = 8.5 Hz, 2H), 7.90−7.85 (m, 1H), 7.77 (d, J = 8.5 Hz, 2H), 7.55−7.50 (m, 1H), 7.43−7.33 (m, 2H); LC-MS/MS (ESI): m/z = 280.0 $[M+1]^+$.

***N*-acetyl-2-aminobenzo[*d*]thiazole (10h).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (s, 1H), 7.85 (ddd, J = 7.9, 1.1, 0.5 Hz, 1H), 7.80−7.74 (m, 1H), 7.46 (ddd, J = 8.2, 7.3, 1.2 Hz,

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1H), 7.34 (ddd, J = 8.3, 7.4, 1.1 Hz, 1H), 2.30 (s, 3H); LC-MS/MS (ESI): m/z = 193.0 $[M+1]^+$.

***N*-cyclopropanecarbonyl-2-aminobenzo[*d*]thiazole (10i).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.15 (s, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.47−7.41 (m, 1H), 7.35−7.29 (m, 1H), 1.77−1.69 (m, 1H), 1.30−1.23 (m, 2H), 1.01−0.94 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 160.4, 147.7, 131.9, 126.3, 123.9, 121.7, 120.0, 15.2, 9.5; LC-MS/MS (ESI): m/z = 219.0 $[M+1]^+$.

***N*-trimethylacetyl-2-aminobenzo[*d*]thiazole (10j).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.49−7.40 (m, 1H), 7.36−7.28 (m, 1H), 1.36 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 158.3, 148.2, 132.2, 126.2, 123.9, 121.4, 120.8, 39.4, 27.2; LC-MS/MS (ESI): m/z = 235.0 $[M+1]^+$.

***N*-hexanoyl-2-aminobenzo[*d*]thiazole (10k).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.88 (s, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.49−7.41 (m, 1H), 7.38−7.30 (m, 1H), 2.55−2.39 (m, 2H), 1.71 (dt, J = 14.4, 7.2 Hz, 2H), 1.31−1.22 (m, 4H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 159.2, 147.9, 132.0, 126.3, 124.0, 121.6, 120.5, 36.5, 31.2, 24.7, 22.2, 13.8; LC-MS/MS (ESI): m/z = 249.0 $[M+1]^+$.

***N*-(3,3-dimethylbutyryl)-2-aminobenzo[*d*]thiazole (10l).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (s, J = 188.0 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.50−7.43 (m, 1H), 7.38−7.30 (m, 1H), 2.33 (s, 2H), 0.94 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 159.5, 147.7, 131.9, 126.3, 124.0, 121.6, 120.5, 49.8, 31.4, 29.4; LC-MS/MS (ESI): m/z = 249.1 $[M+1]^+$.

***N*-(2-thienoyl)-2-aminobenzo[*d*]thiazole (10m).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, J = 3.9, 1.0 Hz, 1H), 7.92−7.84 (m, J = 5.2, 4.0 Hz, 2H), 7.78 (dd, J = 5.0, 1.0 Hz, 1H), 7.60 (ddd, J = 8.4, 7.4, 1.1 Hz, 1H), 7.55−7.46 (m, 1H), 7.28 (dd, J = 4.9, 4.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.5, 159.8, 147.5, 136.5, 133.1, 132.0, 130.8, 128.3, 126.3, 124.1, 121.5, 120.6; LC-MS/MS (ESI): m/z = 260.9 $[M+1]^+$.

***N*-(2-quinolinecarbonyl)-2-aminobenzo[*d*]thiazole (10n).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.55 (s, 1H), 8.48−8.36 (m, 2H), 8.23−8.15 (m, 1H), 7.94 (dd, J = 8.2, 0.8 Hz, 1H), 7.91−7.80 (m, 3H), 7.70 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.54−7.44 (m, 1H), 7.39−7.31 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 157.4, 148.9, 147.1, 146.4, 138.1, 132.4, 130.8, 129.9, 129.8, 128.9, 127.8, 126.3, 124.0, 121.5, 121.2, 118.7; LC-MS/MS (ESI): m/z = 306.0 $[M+1]^+$.

6-Phenyl-*N*-benzoyl-2-aminobenzo[*d*]thiazole (10o). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 8.07−7.98 (m, 3H), 7.66−7.59 (m, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.47 (ddd, J = 23.9, 12.4, 5.0 Hz, 5H), 7.36 (t, J = 7.4 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 159.7, 147.2, 140.7, 137.5, 133.1, 132.8, 132.0, 129.1, 128.9, 127.9, 127.4, 127.3, 125.7, 120.8, 119.7; LC-MS/MS (ESI): m/z = 331.0 $[M+1]^+$. HRMS (EI): $[M+1]^+$ calcd for $C_{20}H_{15}N_2OS$, 331.0900; found, 331.001.

6-Phenyl-*N*-acetyl-2-aminobenzo[*d*]thiazole (10p). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.15 (s, 1H), 8.05 (d, J = 1.7 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 8.4, 1.7 Hz, 1H), 7.64 (d, J = 7.3 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 159.4, 147.2, 140.6, 137.7, 132.8, 128.9, 127.4, 127.3, 126.0, 120.7, 120.0, 23.6; LC-MS/MS (ESI): m/z = 269.0 $[M+1]^+$.

6-(4-Methoxyphenyl)-*N*-benzoyl-2-aminobenzo[*d*]thiazole (10q). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.10 (s, 1H), 8.05−7.96 (m, J = 5.9, 4.5 Hz, 3H), 7.63−7.54 (m, 3H), 7.53−7.45 (m, 3H), 7.43 (d, J = 8.5 Hz, 1H), 7.04−6.96 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.4, 159.3, 159.0, 158.6, 136. 2, 133.4, 133.0, 132.8, 132.4, 129.1, 128.8, 128.4, 125.3, 121.0, 119.5, 114. 9, 55.6; LC-MS/MS (ESI): m/z = 361.0 $[M+1]^+$.

6-(4-Methoxyphenyl)-*N*-acetyl-2-aminobenzo[*d*]thiazole (10r). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70−10.42 (m, 1H), 7.98 (d, J = 1.6 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.64 (dd, J = 8.5, 1.8 Hz, 1H), 7.61−7.54 (m, 2H), 7.01 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 159.3, 158.8, 146.8, 137.3, 133.2, 132.8, 128.3, 125.7, 120.7, 119.7, 114.4, 55.4, 23.6; LC-MS/MS (ESI): m/z = 299.0 $[M+1]^+$.

6-(3-Nitrophenyl)-*N*-benzoyl-2-aminobenzo[*d*]thiazole (10s). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.03−10.75 (m, 1H), 8.50 (t, J = 1.9 Hz, 1H), 8.22 (ddd, J = 8.2, 2.2, 0.9 Hz, 1H), 8.10 (d, J = 1.5 Hz, 1H), 8.06−8.00 (m, 2H), 7.97 (ddd, J = 7.7, 1.6, 1.0 Hz, 1H), 7.67−7.58 (m, 3H), 7.52 (dd, J = 15.5, 7.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO) δ 166.6, 160.51, 149.2, 149.0, 142.0, 133.8, 133.8, 133.4, 133.2, 132.3, 131.0, 129.1, 128.8, 125.9, 122.4, 121.6, 121.3, 120.9; LC-MS/MS (ESI): m/z = 376.0 $[M+1]^+$.

6-(3-Nitrophenyl)-*N*-acetyl-2-aminobenzo[*d*]thiazole (10t). ^{1}H NMR (400 MHz, DMSO) δ 12.44 (s, 1H), 8.52 (t, J = 1.9 Hz, 1H), 8.46 (s, 1H), 8.22 (dd, J = 7.9, 1.7 Hz, 2H), 7.85 (d, J = 1.0 Hz, 2H), 7.78 (t, J = 8.0 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 170.1, 159.6, 149.3, 149.0, 142.1, 133.8, 133.6, 133.1, 131.0, 125.8, 122.4, 121.6, 121.4, 120.8, 40.5, 40.3, 40.2,40.0, 39.8, 39.6, 39.5, 23.3; LC-MS/MS (ESI): m/z = 314.0 $[M+1]^+$.

Representative Procedure for the Cleavage Step viii, Preparation of *N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole 11a from Resin 8a. A mixture of *N*-benzenesulfonyl-2-aminobenzo [*d*]thiazole resin **8a**(150 mg, 0.15 mmol) and 3 mL of cleavage cocktail (TFA:DCM = 5:95, v/v) was shaken at 50 °C for 3 h. The resin was filtered, and the filtrate was concentrated in vacuum to give a residue that was dissolved in DCM. The organic filtrates were adjusted to pH 5−6 by saturated adding $NaHCO_3$ solution. The filtrate was washed with water and dried over $MgSO_4$. The solution was concentrated under reduced pressure, and the residue was triturated with ether and the solid was collected to give **11a** (12 mg, 27%, four-step overall yield from BOMBA resin, loading capacity 1.16 mmol/g) as an ivory solid. mp 269−270 °C; ^{1}H NMR (400 MHz, DMSO) δ 13.22 (s, 1H), 7.91−7.84 (m, 2H), 7.81 (d, J = 7.6 Hz, 1H), 7.64−7.60 (m, 1H), 7.60−7.52 (m, 2H), 7.44−7.36 (m, 1H), 7.32−7.24 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 167.5, 142.5, 136.69, 132.9, 129.6, 127.7, 126.3, 125.2, 124.2, 123.2, 113.3; LC-MS/MS (ESI): m/z = 290.9 $[M+1]^+$. HRMS (EI): $[M+1]^+$ calcd for $C_{13}H_{11}N_2O_2S_2$, 291.0256; found, 290.844.

***N*-toluenesulfonyl-2-aminobenzo[*d*]thiazole (11b).** ^{1}H NMR (400 MHz, DMSO) δ 13.18 (s, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.75 (d, J = 8.2 Hz, 2H), 7.43−7.34 (m, 3H), 7.33−7.22 (m, 2H), 2.36 (s, 3H); LC-MS/MS (ESI): m/z = 305.0 $[M+1]^+$.

***N*-(4-methoxybenzene)sulfonyl-2-aminobenzo[*d*]thiazole (11c).** ^{1}H NMR (400 MHz, DMSO) δ 13.12 (s, 1H), 7.79 (d, J = 8.9 Hz, 3H), 7.42−7.36 (m, 1H), 7.30 (d, J = 7.9 Hz, 1H), 7.27−7.22 (m, 1H), 7.12−7.04 (m, 2H), 3.81 (s, 3H);

^{13}C NMR (101 MHz, DMSO) δ 167.1, 162.6, 137.0, 134.4, 128.4, 127.6, 125.3, 123.9, 123.1, 114.7, 113.3, 56.1; LC-MS/MS (ESI): m/z = 321.0 $[M+1]^+$.

***N*-(4-fluorobenzene)sulfonyl-2-aminobenzo[*d*]thiazole 11d.** ^{1}H NMR (400 MHz, DMSO) δ 7.96−7.87 (m, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.41−7.28 (m, 4H), 7.24−7.15 (m, 1H); ^{13}C NMR (101 MHz, DMSO) δ 171.7, 167.6, 164.3 (d, J = 249.9), 139.7 (d, J = 3.1), 129.2 (d, J = 9.3), 127.2, 126.8, 123.4, 122.7, 116.4 (d, J = 22.5), 114.4; LC-MS/MS (ESI): m/z = 308.9 $[M+1]^+$.

***N*-(4-chlorobenzene)sulfonyl-2-aminobenzo[*d*]thiazole 11e.** ^{1}H NMR (400 MHz, DMSO) δ 13.29 (s, 1H), 7.92−7.85 (m, 2H), 7.82 (d, J = 7.6 Hz, 1H), 7.70−7.60 (m, 2H), 7.45−7.37 (m, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.30−7.24 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 167.8, 141.4, 137.6, 136.9, 129.7, 128.2, 127.8, 125.3, 124.2, 123.2, 113.5; LC-MS/MS (ESI): m/z = 324.9 $[M+1]^+$.

***N*-(3-nitrobenzene)sulfonyl-2-aminobenzo[*d*]thiazole 11f.** ^{1}H NMR (400 MHz, DMSO) δ 13.30 (s, 1H), 7.87 (dt, J = 4.4, 1.3 Hz, 2H), 7.82 (d, J = 7.6 Hz, 1H), 7.68−7.60 (m, 2H), 7.44−7.38 (m, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.31−7.25 (m, 1H); ^{13}C NMR (101 MHz, DMSO) δ 168.3, 148.3, 144.1, 137.0, 132.3, 131.8, 127.8, 127.4, 125.4, 124.4, 123.3, 120.9, 113.7; LC-MS/MS (ESI): m/z = 335.9 $[M+1]^+$.

***N*-methanesulfonyl-2-aminobenzo[*d*]thiazole 11g.** ^{1}H NMR (400 MHz, DMSO) δ 7.77 (d, J = 7.8 Hz, 1H), 7.43−7.35 (m, 1H), 7.32 (d, J = 7.4 Hz, 1H), 7.26−7.18 (m, 1H), 2.99 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 166.9, 136.8, 127.6, 125.3, 123.8, 123.1, 113.0; LC-MS/MS (ESI): m/z = 228.9 $[M+1]^+$.

***N*-butanesulfonyl-2-aminobenzo[*d*]thiazole 11h.** ^{1}H NMR (400 MHz, DMSO) δ 13.00 (s, 1H), 7.76 (d, J = 7.4 Hz, 1H), 7.41−7.35 (m, 1H), 7.31 (d, J = 7.4 Hz, 1H), 7.26−7.19 (m, 1H), 3.12−3.02 (m, 2H), 1.67 (ddd, J = 12.3, 10.3, 6.5 Hz, 2H), 1.47−1.32 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, HDMSO) δ 167.2, 138.2, 127.3, 126.0, 123.5, 122.8, 113.4, 53.0, 25.9, 21.4, 14.0; LC-MS/MS (ESI): m/z = 271.0 $[M+1]^+$.

***N*-(1-naphthalenesulfonyl)-2-aminobenzo[*d*]thiazole 11k.** ^{1}H NMR (400 MHz, DMSO) δ 13.25 (s, 1H), 8.73 (d, J = 8.5 Hz, 1H), 8.26 (dd, J = 7.3, 1.2 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.4 Hz, 1H), 7.73 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.70−7.61 (m, 2H), 7.40−7.32 (m, 1H), 7.31−7.20 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 167.3, 137.0, 136.7, 134.3, 134.0, 129.2, 128.2, 128.2, 127.9, 127.7, 127.3, 126.0, 125.2, 124.9, 124.1, 123.2, 113.3; LC-MS/MS (ESI): m/z = 341.0 $[M+1]^+$.

6-Phenyl-*N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole 11l. ^{1}H NMR (400 MHz, DMSO) δ 13.28 (s, 1H), 8.14 (d, J = 1.6 Hz, 1H), 7.91−7.86 (m, 2H), 7.69 (dd, J = 8.4, 1.8 Hz, 1H), 7.68−7.64 (m, 2H), 7.62−7.55 (m, 3H), 7.48 (t, J = 7.6 Hz, 2H), 7.41−7.35 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 167.6, 142.6, 139.8, 136.6, 136.4, 132.8, 129.6, 129.5, 127.9, 127.1, 126.5, 126.4, 126.3, 121.2, 113.7; LC-MS/MS (ESI): m/z = 366.9 $[M+1]^+$.

6-Phenyl-*N*-methanesulfonyl-2-aminobenzo[*d*]thiazole 11m. ^{1}H NMR (400 MHz, DMSO) δ 13.02 (s, 1H), 8.12 (d, J = 1.6 Hz, 1H), 7.73−7.65 (m, 3H), 7.48 (t, J = 7.6 Hz, 2H), 7.42−7.34 (m, 2H), 3.02 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.0, 164.7, 138.7, 135.2, 135.1, 128.4, 126.8, 126.0, 125.2, 120.1, 112.3; LC-MS/MS (ESI): m/z = 305.0 $[M+1]^+$.

6-(4-Methoxyphenyl)-*N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole 11n. ^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.93−7.84 (m, 2H), 7.69−7.53 (m, 6H), 7.34 (d, J = 8.4 Hz, 1H), 7.08−6.99 (m, 2H), 3.80 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.9, 158.8, 141.9, 135.7, 132.3, 131.5, 129.0, 127.6, 125.7, 125.6, 125.5, 120.1, 114.4, 113.0, 55.1; LC-MS/MS (ESI): m/z = 397.0 $[M+1]^+$.

6-(4-Methoxyphenyl)-*N*-methanesulfonyl-2-aminobenzo[*d*]thiazole 11o. ^{1}H NMR (400 MHz, DMSO) δ 12.99 (s, 1H), 8.06 (s, 1H), 7.70−7.55 (m, 3H), 7.36 (d, J = 8.4 Hz, 1H), 7.04 (d, J = 8.6 Hz, 2H), 3.80 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.9, 159.4, 136.0, 135.6, 132.2, 128.2, 126.3, 125.8, 120.5, 114.9, 113.3, 55.7; LC-MS/MS (ESI): m/z = 335.0 $[M+1]^+$.

6-(3-Nitrophenyl)-*N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole 11p. ^{1}H NMR (400 MHz, DMSO) δ 13.33 (s, 1H), 8.46 (s, 1H), 8.31 (s, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.92−7.74 (m, 5H), 7.65−7.56 (m, 4H), 7.42 (d, J = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 167.7, 148.9, 142.3, 141.4, 137.0, 133.9, 133.6, 133.0, 131.1, 129.7, 126.7, 126.5, 126.3, 122.6, 121.8, 121.5, 113.8; LC-MS/MS (ESI): m/z = 411.9 $[M+1]^+$.

6-(3-Nitrophenyl)-*N*-benzenesulfonyl-2-aminobenzo[*d*]thiazole 11q. ^{1}H NMR (400 MHz, DMSO) δ 13.11 (s, 1H), 8.47 (t, J = 1.9 Hz, 1H), 8.29 (d, J = 1.7 Hz, 1H), 8.23 (dd, J = 8.2, 2.2 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.83 (dd, J = 8.4, 1.8 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 3.04 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.5, 148.4, 140.8, 135.4, 133.0, 133.0, 130.5, 130.4, 126.1, 122.0, 121.1, 120.8, 112.9, 41.0; LC-MS/MS (ESI): m/z = 349.9 $[M+1]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full experimental procedures and analytical data of compounds, along with copies of ^{1}H, ^{13}C NMR, LC-MS, and high resolution-MS spectra of compounds **9a**, **10a**, and **11a**, and ^{1}H NMR, and LC-MS spectra of compounds **9b**−**9s**, **10b**−**10u**, and **11b**−**11q**, and ATR-FTIR spectra of resins **1**−**7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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