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PAPER

A straightforward synthesis of 2-aminobenzothiazoles from Herz compounds†‡

Ana G. Neo, Rosa M. Carrillo and Carlos F. Marcos*

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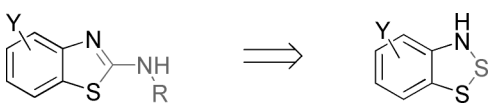
2-Aminobenzothiazoles are readily synthesised from anilines, sulfur monochloride and isocyanides. The key step consists of an iodine-catalysed insertion of isocyanides into the S–S bond of hydrolysed Herz salts, with concomitant extrusion of sulfur monoxide.

Introduction

2-Aminobenzothiazoles are recognised as an important class of heterocyclic compounds, which exhibit remarkable biological activities. For example, they have been proposed as antitumour agents,[1] and inhibitors of leukotriene and tromboxane biosynthesis.[2] Importantly, they have also shown neuroprotectant activity, and hence suggested for the treatment of chronic neurodegenerative disorders such as amyotrophic lateral sclerosis[3] and Huntington's disease.[4] On the other hand, they have shown a wide range of applications as reaction intermediates, and their chemistry has been recently revised.[5]

However, the available strategies for the synthesis of these compounds are rather limited. Unsubstituted aminobenzothiazoles can be obtained by oxidative *ortho*-thiocyanation of anilines followed by *in situ* cyclisation.[6] Alternatively, *N*-alkyl and *N*-aryl-2-aminobenzothiazoles are usually synthesised by oxidative cyclisation of substituted arylthioureas[7] or, more conveniently, by intramolecular C–S cross-coupling of *ortho*-iodo or *ortho*-bromo arylthioureas catalysed by palladium[8] or copper.[9] In any case, the precursor thioureas are in turn synthesised from aryl or alkylamines and noxious isothiocyanates.

In this work, we propose an alternative synthesis of 2-aminobenzothiazoles from 1,2,3-benzodithiazoles, by replacement of the S(2) atom with a C-NHR group (Scheme 1).



Scheme 1 Proposed retro-synthetic strategy for 2-aminobenzothiazoles.

Due to their unusual physical and chemical properties, 1,2,3-dithiazoles have been recognised as valuable building blocks in materials chemistry, and as starting materials in the synthesis of diverse heterocycles.[10] These compounds can be readily synthesised by reacting several organic precursors with the powerful sulfur transfer reagent sulfur monochloride.[10a] For example, 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) is conveniently prepared in this way from chloroacetonitrile,[11] while neutral fused 1,2,3-dithiazoles can be obtained from cyclic ketone oximes[12] or unsaturated cyclic 1-amino-2-carbonitriles.[13]

Besides, the Herz reaction[14] makes use of sulfur monochloride to transform anilines (**1**) into 1,2,3-benzodithiazolium chlorides (**2**), commonly called Herz compounds. Some derivatives of Herz salts have found important applications as new materials,[15] and have also been used as intermediates in the synthesis of other heterocycles. For example, they can be hydrolysed to 2-aminobenzenethioles, which upon condensation with aromatic aldehydes or acid chlorides give 2-arylbenzothiazoles.

The chemistry of monocyclic 1,2,3-dithiazole compounds, has been extensively studied. Hence, Appel salt is known to react with nucleophiles with cleavage of the dithiazole ring and elimination of one or two sulfur atoms.[10b] However, although Herz salts have been known for almost a century, examples of their direct condensation with other reagents are very scarce. For instance, treatment of Herz salts (**2**) with excess of nitrous acid was reported to give 1,2,3-benzothiadiazoles.[16] On the other hand, malononitrile[17] and amines[18] have been reported to react with the benzene ring of 1,2,3-benzodithiazolium chlorides (**2**) in low to moderate yields.

Herz compounds (**2**) can also be hydrolysed in mild conditions to stable 3*H*-1,2,3-benzodithiazole 2-oxides (**3**),[14b,19] which sometimes can be advantageously used in further reactions.[20]

Results and discussion

As a result of our double interest in the chemistry of isocyanides[21] and the use of sulfur monochloride[22] for the synthesis of heterocycles, we decided to explore the reaction of 3*H*-1,2,3-benzodithiazole 2-oxides (**3**) with isocyanides (**4**). We envisaged that isocyanides could insert in the dithiazole ring, with extrusion of sulfur monoxide to yield *N*-alkyl- or *N*-aryl-2-benzothiazolylamines (**5**).

Laboratorio de Química Orgánica y Bioorgánica (L.O.B.O.). Dept. Química Orgánica e Inorgánica. Facultad de Veterinaria. Universidad de Extremadura, 10071, Cáceres, Spain. E-mail: cfernan@unex.es

† Dedicated to the Memory of Antonio Fernández del Riego, who was professor of chemistry and oceanographer in the city of Vigo, Spain.

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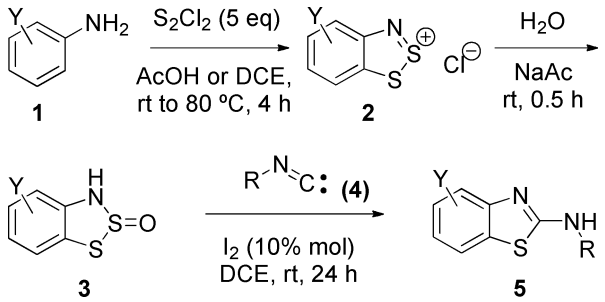
For that purpose, aniline **1a** was made to react with excess S_2Cl_2 in the classic Herz conditions,[14b] to yield the corresponding Herz salt **2a** (Scheme 2). Hydrolysis[20] of crude **2a** in 5% aqueous sodium acetate readily gave 3*H*-1,2,3-benzodithiazole 2-oxide (**3a**). Attempts to react sulfoxide **3a** with cyclohexyl isocyanide (**4a**), either at room temperature or in refluxing dichloroethane only allowed the recovery of untransformed starting materials.



Scheme 2 Synthesis of 2-aminobenzothiazoles from anilines.

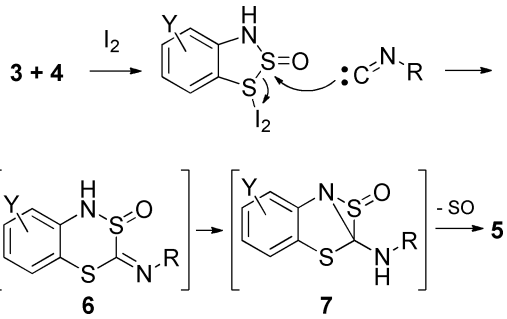
In order to activate the dithiazole ring for the attack of the isocyanide, we investigated the catalytic use of Lewis acids, such as $Sc(OTf)_3$. Unfortunately, they showed no significant effects on promoting the reaction.

In recent years, molecular iodine has received attention as a mild and readily available catalyst for a variety of organic transformations. Its catalytic activity has been attributed to its moderate Lewis acidity and oxidising capacity.[23] Furthermore, iodine has shown to activate disulfides for the sulfenylation of indoles.[24] Hence we decided to investigate the effect of iodine on the reaction of benzodithiazole oxides with isocyanides.

Interestingly, when a catalytic amount of iodine was added to an equimolar mixture of 6-chloro-3*H*-1,2,3-benzodithiazole 2-oxide (**3a**) and cyclohexyl isocyanide (**4a**) in dichloroethane, the required benzothiazolylamine (**5a**) was cleanly obtained as the sole product, after standing 24 h at room temperature (Scheme 2). The reaction could be accelerated by the use of microwave radiation; however this causes a considerable detriment in the yield.

We hypothesise that the reaction mechanism consists in an initial insertion of the isocyanide into the S–S bond, followed by loss of sulfur monoxide. However, neither a concerted process, nor a ring opening-ring closure mechanism can be totally ruled out. According to our hypothesis, the insertion of isocyanide (**4**) on benzodithiazole oxide (**3**) would give a six-membered heterocyclic intermediate (**6**), which would suffer a subsequent transannular nucleophilic attack to give thiaziridine oxide **7**. This would readily extrude sulfur monoxide, yielding the observed 2-amino-benzothiazole (**5**; Scheme 3). Although the insertion of isocyanides into the S–S bonds is a quite unusual process,[25] iodine has been reported to catalyse the cleavage of S–S bonds,[24] and probably plays a fundamental role in this initial step. On the other hand, the formation of thiirane intermediates is a common mechanism of sulfur extrusion, accepted in processes such as the Eschenmoser coupling[26] and in some ring contraction reactions.[22b,27]

To study the scope of the reaction we prepared different 3*H*-1,2,3-benzodithiazole 2-oxides (**3**) through the Herz-hydrolysis sequence (Table 1). Hydrolysed Herz compounds **3a–e** were then condensed with different alkyl and aryl isocyanides (**4a–d**). In all the cases, the expected 2-aminobenzothiazoles (**5a–n**) were consistently obtained in moderate to good yields. The results are summarised in Table 2.



Scheme 3 Proposed mechanism of the reaction between isocyanides and 3*H*-1,2,3-benzodithiazole 2-oxides.

Table 1 Synthesis of benzo-1,2,3-ditiazole 2-oxides (**3**)

Entry	$ArNH_2$	Method	**3** (% yield)
1	4-Cl(C_6H_4)NH_2	A[a]	**3a**[20] (72)
2	2,4-Cl_2(C_6H_3)NH_2	A[a]	**3b**[20] (39)
3	4-CH_3O(C_6H_4)NH_2	B[b]	**3c**[28] (38)
4	4-CF_3(C_6H_4)NH_2	B[b]	**3d** (34)
5	2-naphthylamine	B[b]	**3e**[14b,19] (76)

[a] Representative procedure (Method A): To an ice-cooled solution of the aniline (**1**, 10 mmol) in of glacial acetic acid (1.6 mL), S_2Cl_2 (10 mmol) is cautiously added. The mixture is stirred at rt 30 min and then heated at 80 °C 4 h. The solution is cooled, toluene (25 mL) is added, and the resulting precipitate is filtered and washed with dry dichloromethane to yield the corresponding Herz compound (**2**).[14b] The Herz compounds, as obtained previously, are suspended in 5% aqueous NaOAc (25 mL). The mixture is stirred 30 min at rt, filtered, washed with water and dried under vacuum to yield the benzo-1,2,3-dithiazole 2-oxides (**3**).[20] [b] Method B: Same as Method A, except that the Herz reaction is carried out in dry dichloroethane (24 mL);[29] Herz salts (**2**) precipitate in dichloroethane without the need to add toluene, and hence are directly obtained by filtration.

Table 2 Synthesis of 2-aminobenzothiazoles (**5**)

				(% yield)	
Entry	**3**	Isocyanide (**4**)	**5**	MW[b]	rt[a]
1	**3a**	$C_6H_{11}NC$	**5a**	—	69
2	**3a**	^{t}BuNC	**5b**	30	47
3	**3a**	$PhCH_2NC$	**5c**	12	55
4	**3a**	2,5-$(CH_3)_2C_6H_3NC$	**5d**	9	45
5	**3b**	$C_6H_{11}NC$	**5e**	18	34
6	**3b**	^{t}BuNC	**5f**	12	26
7	**3c**	$C_6H_{11}NC$	**5g**	28	58
8	**3c**	^{t}BuNC	**5h**	28	57
9	**3d**	$C_6H_{11}NC$	**5i**	53	60
10	**3d**	^{t}BuNC	**5j**	—	52
11	**3d**	2,5-$(CH_3)_2C_6H_3NC$	**5k**	—	78
12	**3e**	$C_6H_{11}NC$	**5l**	27	54
13	**3e**	^{t}BuNC	**5m**	—	40
14	**3e**	2,5-$(CH_3)_2C_6H_3NC$	**5n**	—	79

[a] Procedure at room temperature: To a solution of **3** (0.5 mmol) in dry dichloromethane (3 mL) isocyanide (**4**, 0.5 mmol) and I_2 (10% mol) are added. The mixture is stirred at rt 24 h. Workup and purification by column chromatography gives **5**. [b] Procedure under microwave irradiation: Same as at room temperature, except that the mixture was irradiated at 100 W (max) and 100 °C in a closed vial during 20 min.

In conclusion, we have developed a novel and convenient synthesis of 2-aminobenzothiazoles by the reaction of Herz compounds with isocyanides. The target heterocycles can be readily obtained in just 3 reaction steps from simple *para*-substituted anilines. To the best of our knowledge this is the first time the insertion of an isocyanide into a S–S bond has been used in the synthesis of heterocycles.

Experimental section

General Techniques

Melting points are uncorrected. IR spectra were recorded in KBr pellets. Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were obtained on 400 MHz and 500 MHz spectrometers. Mass spectra (MS) were recorded using Electronic Impact (EI, 70 eV) or Chemical Ionization with CH_4. Commercial reagents and solvents were used as received with the exception of CH_2ClCH_2Cl and CH_2Cl_2 that were distilled from P_2O_5. Experiments under microwave irradiation were performed using a microwave reactor designed for synthetic chemistry (Discover from CEM). Liquid reagents were measured using positive-displacement micropipettes with disposable tips and pistons. Thin layer chromatography was performed on aluminium plates coated with silica gel, using 254 nm UV light or a mixture of *p*-anisaldehyde (2.5%), acetic acid (1%) and H_2SO_4 (3.4%) in 95% ethanol as developer.

Synthesis of benzo-1,2,3-dithiazole 2-oxides (3)

Benzo-1,2,3-dithiazole 2-oxides were prepared substantially following the procedure developed by Herz:[14b]

Method A. To a cooled (ice-water bath) solution of the aniline (**1**, 10 mmol) in of glacial acetic acid (1.6 mL), sulfur monochloride (10 mmol) is cautiously added. The mixture is stirred at rt 30 min and then heated at 80 °C 4 h. The solution is cooled, toluene (25 mL) is added, and the resulting precipitate filtered and washed with dry dichloromethane to yield the corresponding Herz compound (**2**). The Herz compounds, as obtained previously, are hydrolyzed following the procedure described by Sawhney.[20] Accordingly, they are suspended in 5% aqueous NaOAc (25 mL). The mixture is stirred 30 min at rt, filtered, washed with water and dried under vacuum to yield the benzo-1,2,3-dithiazole 2-oxides (**3**).

Method B. To a cooled (ice-water bath) solution of the aniline (**1**, 10 mmol) in dry dichloroethane (24 mL), sulfur monochloride (10 mmol) is cautiously added. The mixture is stirred at rt 30 min and then heated at 80 °C 4 h. The solution is cooled and filtered. The solid is washed with dry dichloromethane to yield the corresponding benzo-1,2,3-dithiazolium chloride (Herz compound, **2**). The Herz compounds, as obtained previously, are hydrolyzed following the same procedure as in *method A* to give the benzo-1,2,3-dithiazole 2-oxides (**3**).

6-Chloro-3*H*-benzo[*d*][1,2,3]dithiazole 2-oxide (3a)

(*Method A*, 72%) obtained as a violet solid; mp 91–96 °C (dec.) (lit.[20] 113–114 °C); IR (cm^{-1}) 3445, 1605, 1465, 1102, 810; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (bs, 1H), 7.39 (d, J = 2 Hz, 1H), 7.15 (dd, J = 8.5, 2 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.49 (C), 128.37 (C), 126.76 (CH), 123.00 (CH), 122.73 (C), 114.08 (CH); MS (EI) m/z (%) 207 (M$^+$, 13), 205 (M$^+$, 29), 190 (66), 188 (100), 171 (22), 158 (28), 154 (93); HRMS (EI) Calcd for $C_6H_4ClNOS_2$: 204.9423. Found: 204.9426.

4,6-Dichloro-3*H*-benzo[*d*][1,2,3]dithiazole 2-oxide (3b)

(*Method A*, 39%) obtained as a violet solid; mp 109–112 °C dec. (lit.[20] 129.5–130.5 °C dec.); IR (cm^{-1}) 3451, 1634, 1457, 1142; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (bs, 1H), 7.30 (d, J = 1.7 Hz, 1H), 7.26 (d, J = 1.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.42 (C), 128.21 (C), 126.42 (CH), 123.78 (C), 121.62 (CH), 118.86 (C); MS (EI) m/z (%) 241 (M$^+$, 24), 239 (M$^+$, 31), 224 (95), 222 (100), 166 (6), 164 (8), 158 (14), 156 (30).

6-Methoxy-3*H*-benzo[*d*][1,2,3]dithiazole 2-oxide (3c)

(*Method B*, 38%) obtained as a violet solid; mp 86–90 °C (lit. 115–118 °C,[28] 150 °C[20]); IR (cm^{-1}) 3444, 1634, 1486, 1225, 1103; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (bs, 1H), 6.99 (d, J = 8.7 Hz, 1H), 6.91 (d, J = 2.4 Hz, 1H), 6.72 (dd, J = 8.7, 2.4 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.12 (C), 134.88 (C), 122.49 (C), 114.34 (CH), 113.08 (CH), 108.16 (CH), 55.98 (CH_3); MS (EI) m/z (%) 201 (M$^+$, 21), 184 (100), 169 (49), 141 (38); HRMS (EI) Calcd for $C_7H_7NO_2S_2$: 200.9918. Found: 200.9924.

6-(Trifluoromethyl)-3*H*-benzo[*d*][1,2,3]dithiazole 2-oxide (3d)

(*Method B*, 34%) obtained as a violet solid; mp 126–128 °C; IR (cm^{-1}) 3134, 1334, 1180, 1138, 1080, 830; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.71 (s, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 143.23 (C), 125.82 (q, J = 33.2 Hz, C), 124.22 (q, J = 3.5 Hz, CH), 123.35 (q, J = 271.94 Hz, C), 121.65 (C), 120.87 (q, J = 3.9 Hz, CH), 113.15 (CH); MS (EI) m/z (%) 239 (M$^+$, 12), 222 (93), 203 (12), 189 (15), 172 (16), 149 (28), 71 (100); HRMS (EI) Calcd for $C_7H_4F_3NOS_2$: 238.9686. Found: 238.9687.

3*H*-Naphtho[2,1-*d*][1,2,3]dithiazole 2-oxide (3e)

(*Method B*, 76%) obtained as a violet solid; mp 136–139 °C (lit.[14b,19] 142–143 °C); IR (cm^{-1}) 3446, 3219, 1620, 1096, 1081, 811, 740; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.2 Hz, 1H), 7.77 (bs, 1H), 7.74 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.54 (C), 130.36 (C), 128.89 (C), 128.68 (CH), 127.95 (CH), 127.55 (CH), 124.73 (CH), 124.35 (CH), 114.40 (C), 113.90 (CH); MS (EI) m/z (%) 221 (M$^+$, 13), 204 (100), 172 86), 171 (5), 146 (12), 145 (10), 102 (14); HRMS (EI) Calcd for $C_{10}H_7NOS_2$: 220.9969. Found: 220.9968.

Synthesis of 2-aminothiazoles (5)

To a solution of benzo-1,2,3-dithiazole 2-oxide (**3**, 0.5 mmol) in dry dichloromethane (3 mL) isocyanide (**4**, 0.5 mmol) and I_2 (10% mol) are added. The mixture is stirred at rt 24 h (*Method A*) or, alternatively, subjected to microwave irradiation at 100 W (max) and 100 °C, for 20 min, in a closed vial (*Method B*). Water (10 mL) is then added, and the resulting mixture extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases are dryed

(Na_2SO_4) and concentrated, and the residue is purified by flash column chromatography (SiO_2, hexane : EtOAc gradient) to give compound **5**.

6-Chloro-*N*-cyclohexylbenzo[*d*]thiazol-2-amine (5a).

(*Method A*, 69%) obtained as a white solid; mp 98–101 °C; IR (cm^{-1}) 3205, 3019, 2925, 2856, 1593, 1568, 1524, 1446, 1213, 807; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 2.1 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.25 (dd, J = 8.6, 2.1 Hz, 1H), 5.45 (bs, 1H), 3.62–3.49 (m, 1H), 2.33–1.04 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.98 (C), 149.79 (C), 130.70 (C), 126.68 (C), 126.56 (CH), 120.55 (CH), 118.86 (CH), 55.00 (CH), 33.06 (CH_2), 25.36 (CH_2), 24.64 (CH_2); MS (EI) m/z (%) 266 (M^+, 14), 184 (100), 149 (12); HRMS (EI) Calcd for $C_{13}H_{15}ClN_2S$: 266.0644. Found: 266.0652.

***N*-*tert*-Butyl-6-clorobenzo[*d*]thiazol-2-amine (5b)**

(*Method A*, 47%; *Method B*, 30%) obtained as a white solid; mp 84–87 °C; IR (cm^{-1}) 3420, 3270, 3227, 3035, 2966, 2932, 1592, 1563, 1530, 1447, 1363, 1258, 1214, 811; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 2.1 Hz, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.24 (dd, J = 8.6, 2.2 Hz, 1H), 5.20 (s, 1H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.59 (C), 151.16 (C), 131.90 (C), 126.59 (C), 126.14 (CH), 120.11 (CH), 119.64 (CH), 53.61 (C), 29.04 (CH_3); MS (EI) m/z (%) 240 (M^+, 23), 218 (19), 184 (100), 149 (14); HRMS (EI) Calcd for $C_{11}H_{13}ClN_2S$: 240.0488. Found: 240.0490.

***N*-Benzyl-6-clorobenzo[*d*]thiazol-2-amine (5c)**

(*Method A*, 55%; *Method B*, 12%) obtained as a white solid; mp 180–190 °C (lit.[30] 207–208 °C); IR (cm^{-1}) 3441, 2928, 1620, 1574, 1448, 1355, 1264, 820, 746; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 1.9 Hz, 1H), 7.52 (d, J = 8.7 Hz, 1H), 7.74–7.17 (m, 7H), 4.63 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.03 (C), 134.13 (C), 129.53 (C), 129.19 (CH), 128.75 (CH), 128.37 (CH), 127.82 (CH), 125.80 (C), 125.76 (C), 121.53 (CH), 116.97 (CH), 50.53 (CH_2); MS (EI) m/z (%) 274 (M^+, 21), 170 (10), 149 (25), 91 (100); HRMS (EI) Calcd for $C_{14}H_{11}ClN_2S$: 274.0331. Found: 274.0342.

6-Cloro-*N*-(2,6-dimethylphenyl)benzo[*d*]thiazol-2-amine (5d)

(*Method A*, 45%; *Method B*, 9%) obtained as a white solid; mp 204–207 °C; IR (cm^{-1}) 3443, 2920, 1649, 1592, 1522, 1496, 1473, 1445, 1315, 1194, 770; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.31–7.11 (m, 5H), 6.26 (bs, 1H), 2.33 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.89 (C), 150.15 (C), 137.20 (C), 136.46 (C), 131.20 (C), 129.07 (CH), 128.67 (CH), 126.91 (C), 126.57 (CH), 120.68 (CH), 118.86 (CH), 18.17 (CH_3); MS (EI) m/z (%) 288 (M^+, 100), 273 (21), 220 (18), 132 (28); HRMS (EI) Calcd for $C_{15}H1_3ClN_2S$: 288.0488. Found: 288.0496.

4,6-Dichloro-*N*-cyclohexylbenzo[*d*]thiazol-2-amine (5e)

(*Method A*, 34%; *Method B*, 18%) obtained as a white solid; IR (cm^{-1}) 3445, 2931, 2856, 1594, 1554, 1539, 1432, 774; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.34 (s, 1H), 6.14 (bs, 1H), 3.43–3.32 (m, 1H), 2.15–1.21 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.32 (C), 147.08 (C), 131.39 (C), 126.55 (C), 126.44 (CH), 122.98 (C), 119.19 (CH), 55.54 (CH), 32.89 (CH_2), 25.24 (CH_2), 24.44 (CH_2); MS (EI) m/z (%) 300 (M^+, 16), 218 (100), 191 (10), 156 (16); HRMS (EI) Calcd for $C_{13}H_{14}Cl_2N_2S$: 300.0255. Found: 300.0265.

***N*-*tert*-Butyl-4,6-dichlorobenzo[*d*]thiazol-2-amine (5f)**

(*Method A*, 26%; *Method B*, 12%) obtained as a yellow oil; IR (cm^{-1}) 3417, 2970, 1593, 1538, 1433, 1388, 1258, 1219, 837; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.36 (s, 1H), 6.55 (bs, 1H), 1.54 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.06 (C), 147.40 (C), 132.29 (C), 126.39 (C), 126.27 (CH), 123.46 (C), 118.77 (CH), 53.57 (C), 28.86 (CH_3); MS (EI) m/z (%) 274 (M^+, 10), 218 (74), 156 (13), 141 (13), 71 (100); HRMS (EI) Calcd for $C_{11}H_{12}Cl_2N_2S$: 274.0098. Found: 274.0102.

***N*-Cyclohexyl-6-methoxybenzo[*d*]thiazol-2-amine (5g)**

(*Method A*, 58%; *Method B*, 28%) obtained as a white solid; mp 98–100 °C; IR (cm^{-1}) 3422, 2928, 2853, 1604, 1542, 1471, 1246, 827; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 2.4 Hz, 1H), 6.90 (dd, J = 8.8, 2.5 Hz, 1H), 5.23 (bs, 1H), 3.83 (s, 3H), 3.63–3.49 (m, 1H), 2.21–1.17 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.99 (C), 155.02 (C), 146.64 (C), 131.28 (C), 119.05 (CH), 113.36 (CH), 105.47 (CH), 55.92 (CH_3), 54.37 (CH), 33.36 (CH_2), 25.51 (CH_2), 24.73 (CH_2); MS (EI) m/z (%) 262 (M^+, 39), 191 (10), 180 (100), 165 (89); HRMS (EI) Calcd for $C_{14}H_{18}N_2OS$: 262.1140. Found: 262.1141.

***N*-*tert*-Butyl-6-methoxybenzo[*d*]thiazol-2-amine (5h)**

(*Method A*, 57%; *Method B*, 28%) obtained as a white oil; IR (cm^{-1}) 3375, 2964, 2922, 1605, 1572, 1551, 1469, 1429, 1256, 1213; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 2.5 Hz, 1H), 6.90 (dd, J = 8.8, 2.6 Hz, 1H), 5.10 (bs, 1H), 3.83 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.09 (C), 155.16 (C), 146.46 (C), 131.62 (C), 119.34 (CH), 113.28 (CH), 105.10 (CH), 55.92 (CH_3), 53.28 (C), 29.16 (CH_3); MS (CI) m/z (%) 237 (M^++ 1, 14), 181 (17), 149 (86), 71 (100); HRMS (CI) Calcd for $C_{12}H_{17}N_2OS$: 237.1062. Found: 237.1073.

***N*-Cyclohexyl-6-(trifluoromethyl)benzo[*d*]thiazol-2-amine (5i)**

(*Method A*, 60%; *Method B*, 53%) obtained as a white solid; mp 101–102 °C; IR (cm^{-1}) 3433, 3236, 2932, 2855, 1639, 1581, 1550, 1321, 1274, 1167, 1109; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.61–7.51 (m, 2H), 5.88 (bs, 1H), 3.65–3.52 (m, 1H), 2.20–1.18 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.48 (C), 154.66 (C), 130.25 (C), 125.90 (C), 123.57 (C), 123.46 (q, J = 3.6 Hz, CH), 118.31 (q, J = 4.0 Hz, CH), 54.94 (CH), 33.10 (CH_2), 25.35 (CH_2), 24.66 (CH_2); MS (EI) m/z (%) 300 (M^+, 14), 257 (6), 243 (7), 218 (100), 149 (38); HRMS (EI) Calcd for $C_{14}H_{15}F_3N_2S$: 300.0908. Found: 300.0905.

***N*-*tert*-Butyl-6-(trifluoromethyl)benzo[*d*]thiazol-2-amine (5j)**

(*Method A*, 52%) obtained as a yellow oil; IR (cm^{-1}) 3421, 2967, 2926, 1577, 1540, 1319, 1288, 1163, 1119, 826; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.60 (bs, 2H), 6.80 (bs, 1H), 1.56 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.72 (C), 146.63 (C), 126.63 (C), 125.45 (d, J = 34.2 Hz, C), 124.53 (CH), 122.61 (C), 118.72 (CH), 116.60 (CH), 54.94 (C), 28.38 (CH_3); MS (EI) m/z (%)

274 (M^+, 14), 218 (100), 191 (8), 149 (18); HRMS (EI) Calcd for $C_{12}H_{13}F_3N_2S$: 274.0752. Found: 274.0753.

6-(Trifluoromethyl)-*N*-(2,6-dimethylphenyl)benzo[*d*]thiazol-2-amine (5k)

(*Method A*, 78%) obtained as a yellow solid; mp 246–250 °C; IR (cm^{-1}) 3451, 2859, 1621, 1581, 1560, 1319, 1272, 1160, 1118, 771; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.34–7.19 (m, 4H), 2.37 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.33 (C), 152.27 (C), 136.93 (C), 135.75 (C), 129.31 (C), 129.22 (CH), 129.15 (CH), 125.61 (C), 124.46 (q, J = 32.8 Hz, C), 123.82 (CH), 123.80 (q, J = 3.7 Hz, 1H), 118.66 (q, J = 3.9 Hz, 1H), 117.89 (CH), 18.10 (CH_3); MS (EI) m/z (%) 322 (M^+, 25), 307 (10), 162 (7), 149 (8), 131 (20), 57 (100); HRMS (EI) Calcd for $C_{16}H_{13}F_3N_2S$: 322.0752. Found: 322.0756.

N-Cyclohexylnaphtho[2,1-*d*]thiazol-2-amine (5l)

(*Method A*, 54%; *Method B*, 27%) obtained as a white solid; mp 81–83 °C; IR (cm^{-1}) 3441, 2930, 2851, 1597, 1571, 1507, 1450, 809, 741; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.1 Hz, 1H), 7.81–7.66 (m, 3H), 7.53 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 6.08 (bs, 1H), 3.65–3.55 (m, 1H), 2.38–1.09 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.11 (C), 148.54 (C), 129.54 (C), 129.01 (CH), 128.05 (C), 126.96 (CH), 126.80 (CH), 124.07 (CH), 123.80 (C), 123.55 (CH), 118.77 (CH), 55.29 (CH), 33.05 (CH_2), 25.43 (CH_2), 24.71 (CH_2); MS (EI) m/z (%) 282 (M^+, 30), 239 (6), 225 (5), 200 (100), 155 (10), 146 (16); HRMS (EI) Calcd for $C_{17}H_{18}N_2S$: 282.1191. Found: 282.1196.

N-*tert*-Butylnaphtho[2,1-*d*]thiazol-2-amine (5m)

(*Method A*, 40%) obtained as a yellow oil; IR (cm^{-1}) 3407, 2971, 2927, 1615, 1563, 1541, 1505, 1219, 811, 745; ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 8.7 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 6.81 (bs, 1H), 1.59 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.55 (C), 129.94 (C), 129.21 (CH), 128.04 (CH), 127.49 (CH), 124.99 (CH), 123.09 (CH), 116.65 (CH), 54.33 (C), 28.50 (CH_3); MS (EI) m/z (%) 256 (M^+, 13), 200 (72), 149 (11), 146 (13), 57 (100); HRMS (EI) Calcd for $C_{15}H_{16}N_2S$: 256.1034. Found: 256.1034.

N-(2,6-Dimethylphenyl)naphtho[2,1-*d*]thiazol-2-amine (5n)

(*Method A*, 79%) obtained as a white solid; mp 270–272 °C (dec.); IR (cm^{-1}) 3432, 3046, 2849, 1604, 1571, 1507, 1450, 1429, 1286, 1248, 813, 769, 747; ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.71–7.61 (m, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 1H), 7.35–7.23 (m, 3H), 6.53 (bs, 1H), 2.42 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.33 (C), 140.24 (C), 136.37 (C), 135.41 (C), 130.25 (C), 129.57 (CH), 129.38 (CH), 129.33 (CH), 128.91 (CH), 127.94 (CH), 127.41 (C), 125.69 (CH), 122.80 (CH), 120.01 (C), 115.58 (CH), 18.05 (CH_3); MS (EI) m/z (%) 304 (M^+, 20), 289 (8), 143 (19), 131 (17), 57 (100); HRMS (EI) Calcd for $C_{19}H_{16}N_2S$: 304.1034. Found: 304.1034.

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