Green Chemistry

Accepted Manuscript

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DOI: 10.1039/C7GC02311A

Journal Name

ARTICLE

An environmentally benign and efficient synthesis of substituted benzothiazole-2-thiol, benzoxazole-2-thiol, benzimidazoline-2-thione in water

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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Dedicated to Prof. Herbert Mayr at Ludwig-Maximilians Universität on the occasion of his 70th birthday

An efficient and practical method for one-step synthesis of benzothiazole-2-thiols, benzoxazole-2-thiols and benzimidazoline-2-thione by cyclization of 2-aminothiophenols, 2-aminophenols, 1, 2-phenylenediamines with tetramethylthiuram disulfide (TMTD) in water was described. The features of this method include metal/ligand-free, exellent yield, short reaction time and broad substrate scope. The method provides a facile and convenient preparation of some potentially biologically active compounds.

Introduction

Benzoheterocycles containing mercapto group play an important role in synthetic chemistry due to their wide range of biological and pharmacological activities,[1-4] much attention was paid to the synthesis of benzothiazole-2-thiols, benzoxazole-2-thiols and benzimidazole-2-thiones which are key blocks of some medical agents or biologically active compounds (**Fig. 1**).[5-8] Conventionally, most of the reported procedures are only applicable for the synthesis of one type of benzoheterocycles.[9-13] Recently, some procedures were reported for the synthesis of the substituted benzoheterocycles mentioned above. Generally, these compounds are prepared through the reactions of 2-aminothiophenols, 2-aminophenols, 1,2-phenylenediamines with carbon disulfide,[14] potassium ethylxanthate[15] or phenyl chlorothionocarbonate,[16] respectively (**Scheme 1**).

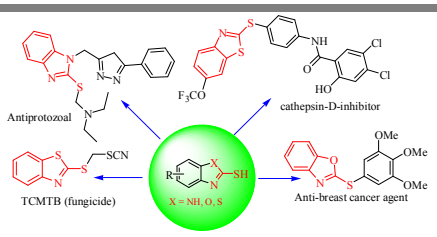
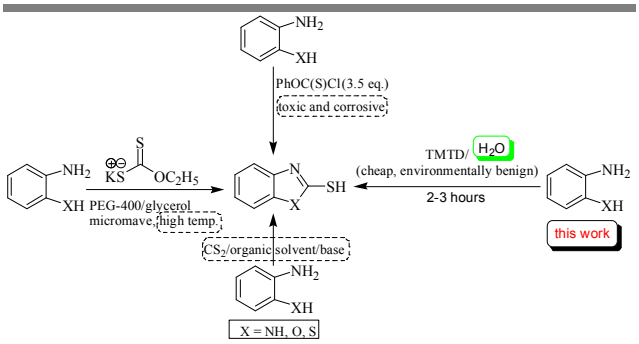


Fig. 1 Representative drugs containing benzothiazole-2-thiol, benzoxazole-2-thiol, benzimidazole-2-thiol skeletons.



Scheme 1 Synthetic route to benzothiazole-2-thiol, benzoxazole-2-thiol, benzimidazole-2-thiol.

However, these methods suffer from disadvantages such as high temperature, using large amount of organic solvents, toxic and obnoxious smelling reagent, heating under an inert atmosphere and tedious work-up. Therefore, the more facile and environmentally benign preparation methods for these compounds are still highly desirable. As part of our longstanding interests in developing phenylthioureas[17-18] and the relevant applications,[19] hereby we report an efficient and practical method for one-pot green synthesis of benzothiazole-2-thiols, benzoxazole-2-thiols and benzimidazoline-2-thione by reacting cheap and environmentally benign tetramethylthiuram disulfide (TMTD) with substituted anilines in water (**Scheme 1**).

Results and discussion

We began our investigations by using 2-aminothiophenols (**1a**) and tetramethylthiuram disulfide (TMTD, **2a**) to carry out the model reaction (**Table 1**). Reaction conditions were optimized

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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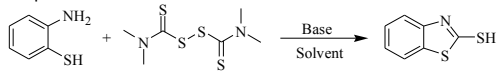
by varying the amount of base (K_2CO_3), reaction temperature, substrate ratio and solvents. Initially, various substrate ratio (1a:2a) were tested (Entries 1-5). The highest yield of the desired product 3a was obtained in 90 %, which showed that **1a** : **2a** = 1 : 0.6 was the optimal substrate ratio. When the amount of K_2CO_3 was dropped to 0.5 equiv (Entries 6-8), the yield of product **3a** was slightly decreased. However, product **3a** was obtained in excellent yield (Entry 9, 92 %) when K_2CO_3 was not added, which demonstrated that base was not crucial to the reaction. Next, different solvents were screened (Entries 9-16). To our delight, it showed that water could be served as environmentally friendly solvent, and the temperature survey (Entries 17-19) showed that 120 °C (*oil bath temperature*) was the optimal (Entry 16). The optimal reaction conditions were summarized in Entry 16. The subsequent control experiments revealed that 80 °C was most suitable temperature to 2-aminophenols and 110 °C was the best reaction temperature to 1,2-phenylenediamines.

Table 1 Optimization of the reaction conditions for the model reaction[a]



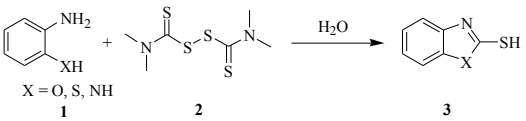
1a **2a** **3a**

Entry	base	T(°C)	Ratio[b]	Solvent	Yield(%)[c]
1	K_2CO_3 (3.0 eq)	120	1:1	DMF	79
2	K_2CO_3 (3.0 eq)	120	1:1.2	DMF	82
3	K_2CO_3 (3.0 eq)	120	1:0.8	DMF	86
4	K_2CO_3 (3.0 eq)	120	1:0.6	DMF	90
5	K_2CO_3 (3.0 eq)	120	1:0.5	DMF	76
6	K_2CO_3 (2.0 eq)	120	1:0.6	DMF	87
7	K_2CO_3 (1.0 eq)	120	1:0.6	DMF	87
8	K_2CO_3 (0.5 eq)	120	1:0.6	DMF	89
9	--	120	1:0.6	DMF	92
10	--	120	1:0.6	DMSO	62
11	--	120	1:0.6	DMAc	79
12	--	120	1:0.6	EtOH	18
13	--	120	1:0.6	Toluene	0
14	--	120	1:0.6	DMF:H_2O = 1:1	90
15	--	120	1:0.6	DMF:H_2O = 1:3	90
16	**--**	**120**	**1:0.6**	**H_2O**	**95**
17	--	130	1:0.6	H_2O	93
18	--	100	1:0.6	H_2O	89
19	--	80	1:0.6	H_2O	84

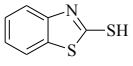
[a]Reaction conditions: **1a** (1.0 mmol), **2a** (0.6-1.2 mmol), base (K_2CO_3, 0-3 eq) and solvent (2.0 mL), stirred for 2-3 h. [b]Ratio is the mole ratio of **1a: 2a**. [c]Isolated yield based on **1a** after column chromatography.

With the optimal reaction conditions in hand, the scope of the reaction was examined by checking the diverse substituted 2-aminothiophenols, 2-aminophenols, 1,2-phenylenediamines reacting with tetramethylthiuram disulfide (TMTD), and the results are summarized in **Table 2**. As for 2-aminothiophenols, chlorine atom on phenyl showed excellent group compatibility (Entry 2, yield 95%). Gratifyingly, 2-amino-ethanethiol could react with tetramethylthiuram disulfide (TMTD) furnishing the desired product with good yield (Entry 3). Then various 2-aminophenols were applied under the reaction conditions at 80 °C. In general, substituents ranging from weak electron-withdrawing groups, such as F, Cl, Br, to strong electron-withdrawing group, such as NO_2, along with electron-donating methyl and *tert*-butyl groups, all generated the corresponding benzoxazole-2-thiols in satisfying yields (Entries 4-14). When 2-amino-pyridin-3-ol was used, product **3p** was obtained in only 38 % yield (Entry 16). When it comes to 2-amino-ethanol, the temperature has to rise to 110 °C, and the isolation yield of product **3o** was 31 % (Entries 15). Subsequently, 1,2-phenylenediamine and its derivatives were submitted to react with TMTD under the standard reaction conditions. Substituents ranging from weak electron-withdrawing groups, such as F, Cl, Br, to strong electron-withdrawing groups, such as NO_2, CN, CF_3, along with electron-donating methyl and methoxyl groups, all furnished the desired benzoxazole-2-thiols in gratifying yields (Entries 17-28). It could be noted that the strong electron-withdrawing groups, such as NO_2, CN or CF_3 attaching to the aryl ring of 1,2-phenylenediamines (Entries 22-24) decreased the yields significantly, while the electron-donating groups could promote the yields (Entries 25-28). This further indicated that the strong electron-donating groups might activate the reactivity of NH_2 to give the possible intermediate phenylthioureas, which could be cyclized to benzimidazoline-2-thione. It is noteworthy that pyridine-2,3-diamine was also suitable to react with TMTD, giving product **3ze** with reasonable yield (76 %, Entry 31). Contrary to the results obtained in Entries 15, ethane-1,2-diamine and cyclohexane-1,2-diamine could be transformed to the corresponding imidazole-2-thiones with good yields (Entries 29-30).

Table 2 Synthesis of benzoheterocycles starting from substituted anilines and tetramethylthiuram disulfide (TMTD)[a]



1 **2** **3**

Entry	Substrate **1**	Product **3**	T(°C)	Yield(%)[b]
1			120	95
	1a	**3a**		

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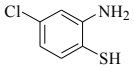
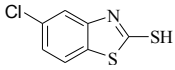
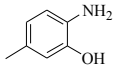
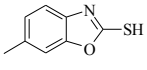
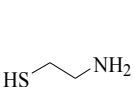
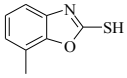
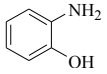
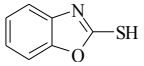
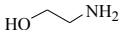
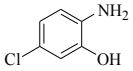
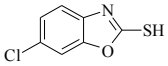
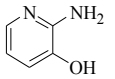
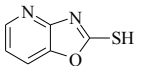
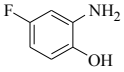
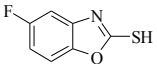
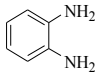
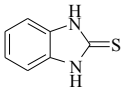
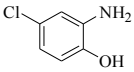
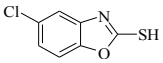
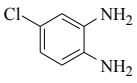
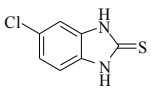
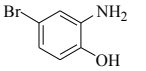
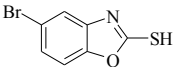
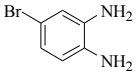
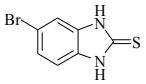
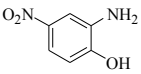
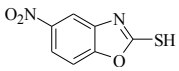
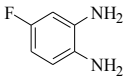
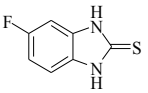
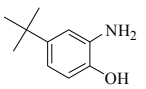
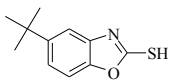
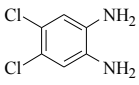
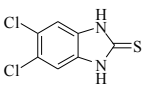
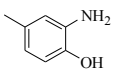
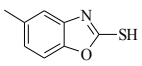
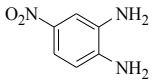
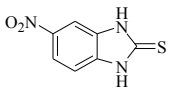
2	 **1b**	 **3b**	120	95	13	 **1m**	 **3m**	80	90
3	 **1c**	 **3c**	120	83	14	 **1n**	 **3n**	80	80
4	 **1d**	 **3d**	80	92	15	 **1o**	 **3o**	110	31
5	 **1e**	 **3e**	80	83	16	 **1p**	 **3p**	80	38
6	 **1f**	 **3f**	80	85	17	 **1q**	 **3q**	110	93
7	 **1g**	 **3g**	80	92	18	 **1r**	 **3r**	110	89
8	 **1h**	 **3h**	80	83	19	 **1s**	 **3s**	110	85
9	 **1i**	 **3i**	80	76	20	 **1t**	 **3t**	110	89
10	 **1j**	 **3j**	80	89	21	 **1u**	 **3u**	110	82
11	 **1k**	 **3k**	80	90	22	 **1v**	 **3v**	110	66
12	**1l**	**3l**	80	92					

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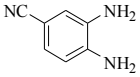
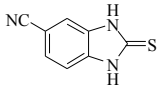
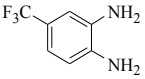
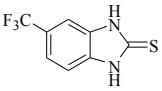
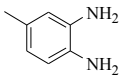
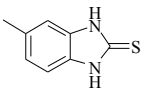
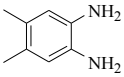
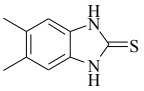
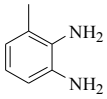
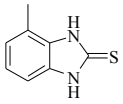
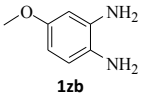
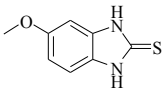
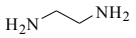
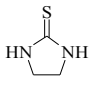
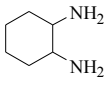
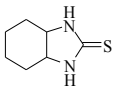
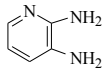
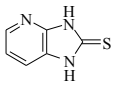
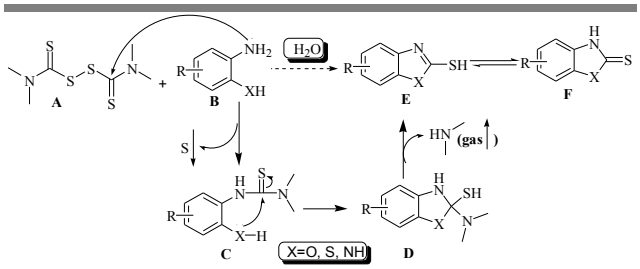
23	 **1w**	 **3w**	110	71
24	 **1x**	 **3x**	110	51
25	 **1y**	 **3y**	110	88
26	 **1z**	 **3z**	110	89
27	 **1za**	 **3za**	110	83
28	 **1zb**	 **3zb**	110	89
29	 **1zc**	 **3zc**	110	78
30	 **1zd**	 **3zd**	110	62
31	 **1ze**	 **3ze**	110	76

[a]Reaction conditions: **1** (1.0 mmol), **2** (0.6 mmol), H_2O (2.0 mL), stirred for 2-3 h. [b]Isolated yield.

Based on the experimental results and the reports from literature,[20] a plausible reaction pathway is outlined in **Scheme 2**. Tetramethylthiuram disulfide (TMTD) reacts with aniline to give intermediate thiourea **C**, the XH (X = O, S, NH) group of **C** undergoes intramolecular nucleophilic addition forming intermediate **D**. **D** undergoes intramolecular elimination by removing gas dimethylamine, forming target compound **E**. The isomerization between **E** and **F** could be a dynamical balance.



Scheme 2 Plausible mechanism of the reaction.

Conclusions

In summary, we have developed a simple, highly efficient and one-pot green synthetic method for the synthesis of benzoheterocycles by the treatment of various bifunctional 2-aminothiophenols, 2-aminophenols and 1,2-phenylenediamines with tetramethylthiuram disulfide (TMTD) using H_2O as solvent. The features of this method include easy performance, metal/ligand-free, nice yield, short reaction time, and broad substrate scope. The method provides a facile and convenient preparation for precursors of potentially biologically active compounds.

Experimental section

General Procedures

All reagents were used without further purification, which were purchased from commercial suppliers. All reactions were performed in an IKA parallel reactor, and were monitored by TLC. Column chromatography separations were carried out on silica gel (200-300 mesh). Melting points were measured with RY-1 m.p. machine without adjustment. ^{1}HNMR (in $CDCl_3$ or DMSO-d_6) and ^{13}CNMR (in $CDCl_3$ or DMSO-d_6) spectra were measured using TMS as internal standard on a Bruker 400 AC NMR spectrometer. The high-resolution mass spectra (ESI–HRMS) were determined on an Ion Spec (7.0 T) spectrometer. Yields refer to isolated compounds estimated to be > 95% pure as determined by ^{1}H NMR and capillary GC analysis.

Typical Procedure (TP) for Synthesis of Benzothiazole-2-thiol, Benzoxazole-2-thiol, Benzimidazole-2-thione Derivatives (3a-3z, 3za-3ze). **1** (1.0 mmol), **2** (0.6 mmol) was dissolved in H_2O (2mL) in a dried tube equipped with a magnetic stirring bar and a septum. The reaction mixture was then heated in oil bath and checked by TLC until the starting material was finished (2-3 hours). Then the reaction mixture was allowed to cool down to room temperature and was extracted with ethyl acetate, dried over anhydrous Na_2SO_4.

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The residue was purified by flash column chromatography to afford the desired product.

Characterization data for all products

Benzothiazole-2-thiol 3a[10]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3a** as a white solid (158 mg, 95%). Mp: 179-180 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.69 (brs, 1H), 7.64 (d, 1H, *J* = 8.0 Hz), 7.34 (d, 1H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 190.2, 141.7, 129.8, 127.6, 124.6, 122.2, 112.8. HRMS (ESI) Calcd for $C_7H_5NS_2$ (169.9863), found: 169.9871.

5-Chloro-benzothiazole-2-thiol 3b[10]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3b** as a white solid (192 mg, 95%). Mp: 203-204 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.86 (brs, 1H), 7.72 (d, 1H, *J* = 8.0 Hz), 7.35 (t, 1H, *J* = 4.0 Hz), 7.28 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 191.3, 142.6, 132.2, 128.7, 124.5, 123.6, 112.4. HRMS (ESI) Calcd for $C_7H_4ClNS_2$ (200.9474), found: 200.9456.

4,5-Dihydro-thiazole-2-thiol 3c[21]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3c** as a white solid (99 mg, 83%). Mp: 106-107 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 10.08 (brs, 1H), 3.88 (t, 2H, *J* = 8.0 Hz), 3.51 (t, 2H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 199.4, 51.9, 33.3. HRMS (ESI): Calcd for $C_7H_4ClNS_2$ (118.9863), found 118.9875.

Benzooxazole-2-thiol 3d[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3d** as a white solid (139 mg, 92%). Mp: 191-192 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.81 (brs, 1H), 7.44 (d, 1H, *J* = 8.0 Hz), 7.24-7.18 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.3, 148.3, 131.4, 125.3, 124.0, 110.7, 110.2. HRMS (ESI): Calcd for C_7H_5NOS (151.0092), found: 151.0076.

6-Chloro-benzooxazole-2-thiol 3e[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3e** as a yellow solid (153 mg, 83%). Mp: 224-225 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.92 (brs, 1H), 7.61 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.5, 148.6, 130.6, 128.2, 125.3, 111.4, 110.7. HRMS (ESI): Calcd for C_7H_4ClNOS (184.9702), found: 184.9731.

5-Fluoro-benzooxazole-2-thiol 3f[22]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3f** as a yellow solid (144 mg, 85%). Mp: 238-240 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.94 (brs, 1H), 7.44-7.41 (m, 1H), 7.04-6.97 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.2, 160.7 (d, 1C, *J* = 240 Hz), 144.5, 132.1 (d, 1C, *J* = 10 Hz), 110.8 (q, 1C, *J* = 30 Hz), 98.4 (d, 1C, *J* = 30 Hz), 79.3 (d, 1C, *J* = 30 Hz). HRMS (ESI): Calcd for C_7H_4FNOS (168.9998), found: 168.9978.

5-Chloro-benzooxazole-2-thiol 3g[22]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3g** as a white solid (170 mg, 92%). Mp: 275-276 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.92 (brs, 1H), 7.44 (d, *J* = 12.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.7, 146.9, 132.4, 129.2, 123.4, 111.1, 110.3. HRMS (ESI): Calcd for C_7H_4ClNOS (184.9702), found: 184.9733.

5-Bromo-benzooxazole-2-thiol 3h[23]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3h** as a red solid (190 mg, 83%). Mp: 283-284 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.59 (brs, 1H), 7.49-7.41 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.0, 147.8, 133.4, 126.7, 117.4, 113.5, 112.1. HRMS (ESI): Calcd for C_7H_4BrNOS (228.9197), found: 228.9186.

5-Nitro-benzooxazole-2-thiol 3i[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3i** as a white solid (149 mg, 76%). Mp: 244-245 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 8.14 (d, *J* = 8.0 Hz, 1H), 7.89 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.8, 152.4, 145.1, 132.6, 120.4, 110.7, 106.1. HRMS (ESI): Calcd for $C_7H_4N_2O_3S$ (195.9943), found: 195.9971.

5-tert-Butyl-benzooxazole-2-thiol 3j[24]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3j** as a red solid (184 mg, 89%). Mp: 127-128 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.08 (brs, 1H), 7.22 (s, 3H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.0, 149.4, 146.8, 130.3, 121.8, 109.7, 107.4, 35.0, 31.5. HRMS (ESI): Calcd for $C_{11}H_{13}NOS$ (207.0718), found: 207.0733.

5-Methyl-benzooxazole-2-thiol 3k[8]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3k** as a white solid (149 mg, 90%). Mp: 216-217 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.65 (brs, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.1, 146.2, 134.7, 131.1, 124.2, 110.4, 109.3, 20.8. HRMS (ESI): Calcd for C_8H_7NOS (165.0248), found: 165.0236.

4-Methyl-benzooxazole-2-thiol 3l[34]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3l** as a white solid (151 mg, 92%) Mp: 93-94 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.83 (brs, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.01 (t, 1H, *J* = 8.0 Hz), 6.94 (d, *J* = 8.0 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.0, 147.8, 130.3, 125.8, 123.5, 121.0, 107.1, 16.0. HRMS (ESI): Calcd for C_8H_7NOS (165.0248), found: 165.0229.

6-Methyl-benzooxazole-2-thiol 3m[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3m** as a white

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DOI: 10.1039/C7GC02311A

solid (148 mg, 90%). Mp: 209-210 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.61 (brs, 1H), 7.17 (s, 1H), 6.97 (s, 2H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 179.8, 148.2, 133.5, 128.7, 125.5, 110.1, 109.8, 20.8. HRMS (ESI): Calcd for C_8H_7NOS (165.0248), found: 165.0256.

7-Methyl-benzooxazole-2-thiol 3n[35]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3n** as a red solid (132 mg, 80%). Mp: 243-245 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.69 (brs, 1H), 7.04 (t, 1H, *J* = 8.0 Hz), 6.92 (t, 2H, *J* = 8.0 Hz), 2.25 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.9, 147.9, 131.7, 125.9, 125.8, 120.9, 108.9, 15.2. HRMS (ESI): Calcd for C_8H_7NOS (165.0248), found 165.0241.

4,5-Dihydro-oxazole-2-thiol 3o[25]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3o** as a white solid (32 mg, 31%). Mp: 99-100 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 10.11 (brs, 1H), 3.88 (t, 2H, *J* = 8.0 Hz), 3.52 (t, 2H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 199.4, 51.9, 33.3. HRMS (ESI): Calcd for C_3H_5NOS (103.0092), found: 103.0109.

Oxazolo[4,5-b]pyridine-2-thiol 3p[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the target compound **3p** as a white solid (58 mg, 38%). Mp: 238-240 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 14.47 (brs, 1H), 8.21 (s, 1H), 7.86 (s, 1H), 7.25 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.8, 147.5, 144.6, 142.1, 119.5, 117.5. HRMS (ESI): Calcd for $C_6H_4N_2OS$ (152.0044), found: 152.0056.

1,3-Dihydro-benzoimidazole-2-thione 3q[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3q** as a yellow solid (139 mg, 93%). Mp: 298-300 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.48 (brs, 2H), 7.10 (s, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.5, 132.6, 122.7, 109.9. HRMS (ESI): Calcd for $C_7H_6N_2S$ (150.0252), found: 150.0263.

5-Chloro-1,3-dihydro-benzoimidazole-2-thione 3r[26]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3r** as a gray solid (164 mg, 89%). Mp: 298-300 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.70 (d, *J* = 8 Hz, 2H), 7.14 (d, 3H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.7, 133.7, 131.7, 127.1, 122.6, 111.0, 109.6. HRMS (ESI): Calcd for $C_7H_5ClN_2S$ (183.9862), found: 183.9878.

5-Bromo-1,3-dihydro-benzoimidazole-2-thione 3s[27]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3s** as a gray solid (194 mg, 85%). Mp: 301-302 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.70 (d, *J* = 12 Hz, 2H), 7.27 (d, *J* = 4.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.5, 134.1, 132.0, 125.4, 114.8, 112.3, 111.4. HRMS (ESI): Calcd for $C_7H_5BrN_2S$ (227.9357), found: 227.9369.

5-Fluoro-1,3-dihydro-benzoimidazole-2-thione 3t[28]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3t** as a white solid (149 mg, 89%). Mp: 284-285 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.64 (d, *J* = 12.0 Hz, 2H), 7.13-7.09 (m, 1H), 6.96 (t, 2H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.8, 160.1 (d, 1C, *J* = 235 Hz), 133.2 (d, 1C, *J* = 13 Hz), 129.3, 110.5 (d, 1C, *J* = 10 Hz), 109.8 (d, 1C, *J* = 25 Hz), 97.4 (d, 1C, *J* = 28 Hz). MS (EI): Calcd for $C_7H_5FN_2S$ (168.0157), found: 168.0169.

5,6-Dichloro-1,3-dihydro-benzoimidazole-2-thione 3u[29]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3u** as a yellow solid (179 mg, 82%). Mp: 350-351 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.81 (brs, 2H), 7.32 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 170.7, 132.6, 125.1, 110.9. HRMS (ESI): Calcd for $C_7H_4Cl_2N_2S$ (219.9472), found: 217.9486.

5-Nitro-1,3-dihydro-benzoimidazole-2-thione 3v[26]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3v** as a yellow solid (128 mg, 66%). Mp: 273-275 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.08 (brs, 2H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.85 (s, 1H), 7.26 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 172.2, 143.0, 137.8, 132.6, 119.3, 109.6, 105.1. HRMS (ESI): Calcd for $C_7H_5N_3O_2S$ (195.0102), found: 195.0121.

2-Thioxo-2,3-dihydro-1H-benzoimidazole-5-carbonitrile 3w[30]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3w** as a white solid (124 mg, 71%). Mp: 315-316 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.00 (brs, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 171.1, 136.1, 132.8, 127.4, 119.7, 113.3, 110.6, 104.7. HRMS (ESI): Calcd for $C_8H_5N_3S$ (175.0204), found: 175.0217.

5-Trifluoromethyl-1,3-dihydro-benzoimidazole-2-thione 3x[31]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3x** as a white solid (111 mg, 51%). Mp: decomposed; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.94 (d, *J* = 12 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.38 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 170.9, 135.5, 132.7, 127.7 (d, 1C, *J* = 270 Hz), 123.3 (d, 1C, *J* = 32 Hz), 119.9 (d, 1C, *J* = 4 Hz), 110.1, 106.5 (d, 1C, *J* = 3 Hz). HRMS (ESI): Calcd for $C_8H_5F_3N_2S$ (218.0126), found: 218.0137.

5-Methyl-1,3-dihydro-benzoimidazole-2-thione 3y[15]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3y** as a white solid (144 mg, 88%). Mp: 293-294 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.43 (brs, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.94 (t, 2H, *J* = 8.0 Hz), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.2, 132.95, 132.1, 130.6, 123.6, 110.0, 109.5, 21.4. HRMS (ESI): Calcd for $C_8H_8N_2S$ (164.0408), found: 164.0417.

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DOI: 10.1039/C7GC02311A

5,6-Dimethyl-1,3-dihydro-benzoimidazole-2-thione 3z[27]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3z** as a brown solid (159 mg, 89%). Mp: 325-326 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.35 (brs, 2H), 6.94 (s, 2H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 167.6, 131.0, 130.9, 110.4, 20.0. HRMS (ESI): Calcd for $C_9H_{10}N_2S$ (178.0565), found: 178.0577.

4-Methyl-1,3-dihydro-benzoimidazole-2-thione 3za[31]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3za** as a brown solid (136 mg, 83%). Mp: decomposed; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.56 (s, 1H), 12.44 (s, 1H), 6.96-6.86 (m, 3H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.3, 132.3, 131.9, 123.6, 122.8, 120.1, 107.3, 16.7. HRMS (ESI): Calcd for $C_8H_8N_2S$ (164.0408), found: 164.0421.

5-Methoxy-1,3-dihydro-benzoimidazole-2-thione 3zb[32]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3zb** as a yellow solid (160 mg, 89%). Mp: 256-258 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.46 (s, 1H), 12.42 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.77-6.72 (m, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.2, 156.2, 133.5, 126.8, 110.4, 110.1, 94.9, 56.0. HRMS (ESI): Calcd for $C_8H_8N_2OS$ (180.0357), found: 180.0367.

Octahydro-benzoimidazole-2-thione 3zc[14]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3zc** as a white solid (80 mg, 78%). Mp: 203-205 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 7.91 (brs, 2H), 3.44 (s, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 183.8, 44.5. HRMS (ESI): Calcd for $C_3H_6N_2S$ (102.0252), found: 102.0267.

Octahydro-benzoimidazole-2-thione 3zd[32]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3zd** as a white solid (97 mg, 62%). Mp: 158-160 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 8.26 (brs, 2H), 3.02 (d, *J* = 8.0 Hz, 2H), 1.91 (d, *J* = 12.0 Hz, 2H), 1.69 (d, *J* = 8.0 Hz, 2H), 1.35-1.26 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 186.9, 64.2, 29.2, 23.9. HRMS (ESI): Calcd for $C_7H_{12}N_2S$ (156.0721), found: 156.0734.

1,3-Dihydro-imidazo[4,5-b]pyridine-2-thione 3ze[33]: According to **TP**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3ze** as a white solid (115 mg, 76%). Mp: 320-323 °C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.14 (brs, 1H), 12.72 (brs, 1H), 8.13 (d, *J* = 4.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.15 (t, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 170.3, 146.9, 142.7, 125.9, 118.5, 116.6. HRMS (ESI): Calcd for $C_6H_5N_3S$ (151.0204), found: 151.0221.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank the foundation support from National Natural Science Foundation of China (21302150) Hubei Provincial Department of Education (D20131501), Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry [2012]1707, foundation of Chutian distinguished fellow from Hubei Provincial Department of Education. We thank Prof. Aiwen Lei at Wuhan University for generous NMR analysis support. We also thank Prof. Paul Knochel at Ludwig-Maximilians-Universität for helpful discussions.

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