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$AlCl_3$-Promoted Synthesis of 2-Mercapto Benzoheterocycles by Using Sodium Dimethyldithiocarbamate as Thiocarbonyl Surrogate

Xing Liu,[a] Shi-Bo Zhang,[a] Zhi-Bing Dong* [a, b]

Dedication ((optional))

Abstract: A simple, expeditious and high-efficiency synthetic method for the $AlCl_3$-mediated one-pot preparation of 2-mercapto benzoheterocycles (2-mercapto benzothiazoles, benzoxazoles and benzimidazoles) is described**.** By the treatment of a series of *S*, *O* and *N* heteroatoms containing bifunctional molecules with sodium dimethyldithiocarbamate in $AlCl_3$, the desired benzoheterocycles are obtained smoothly. The protocol can also be applied on the synthesis of a series of thiazolidine-2-thiones, imidazolidine-2-thiones. This novel synthetic approach has advantages such as ligand-free, high efficiency, short reaction time, readily available starting materials and simple experimental procedures.

Introduction

Heterocyclic compounds containing mercapto group play dominant role in drug discovery.[1] This heterocyclic compounds are the core structural elements of many natural products and approved pharmaceuticals.[2] It is already known that thioethers of 2-mercapto benzoheterocycles are a class of compounds endowed with broad and decisive biological and pharmacological activities.[3] They are extensively useful as fungicides, antiprotozoals, anticancer agents and enzyme inhibitors (Figure 1).[4] It is thus necessary to develop simple and effective synthetic methods for the construction of 2-mercapto benzoheterocycles.

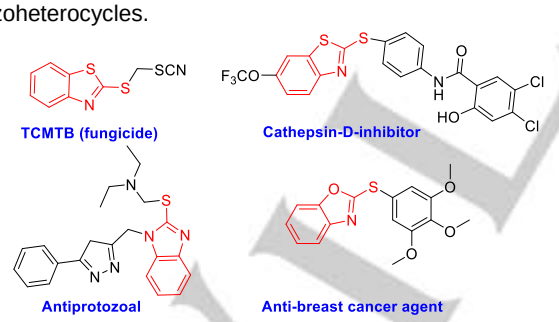

Figure 1. Bioactive benzofused N, O, S heterocycles.

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Although there has been intense development of synthetic methods for the preparation of 2-mercapto benzoheterocycles, most of the reported procedures are only applicable for the synthesis of one type of 2-mercapto benzoheterocycles.[5] The known synthetic procedures are based on the direct use of carbon disulfide (Figure **2a**), which is a toxic and obnoxious smelling thiocarbonyl surrogates, often requires drastic reaction conditions.[6] Therefore, the pursuance of more convenient and practical synthetic methods for these compounds still remains an active research area. Several methods are available for the synthesis of 2-mercapto benzoheterocycles. These compounds are prepared through the reactions of various bifunctional molecules with phenyl chlorothionocarbonate,[7] potassium ethylxanthate,[8] isopropyl-xanthicacipotassium salt,[9] respectively (Figure **2b**). Although these thiocarbonyl surrogates are effective for the synthesis of mercapto derivatives, there exist some drawbacks such as long reaction time, tedious work up procedures, commercially not available starting materials, use of additional microwave oven that utility and applicability are somehow limited. Therefore, the more expeditious and environmentally benign protocols for these compounds are still highly desirable.

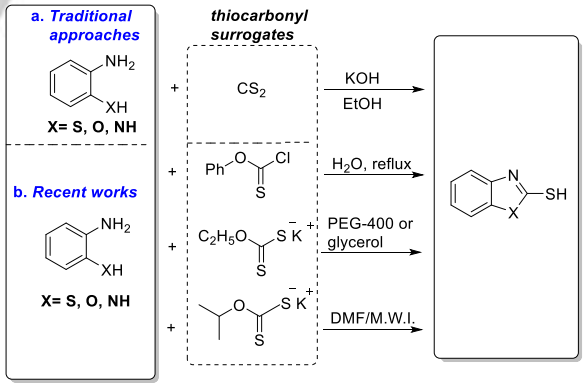
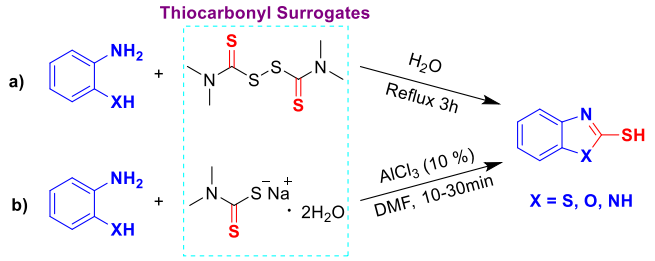


Figure 2. Some different strategies for the synthesis 2-mercapto benzoheterocycles.

Recently, construction of heterocycle thione with sulfur and chloroform as thiocarbonyl surrogates was reported by Tan and their co-workers.[10] For the continuous efforts on the study of C-S bond formation and related research,[11] we have reported a method for the synthesis of 2-mercapto benzoheterocycles by using TMTD (Tetramethylthiuram disulfide) as thiocarbonyl surrogates (Scheme **1a**).[12] For the research extension, we hereby wish to report an alternative protocol for the synthesis 2-mercapto benzoheterocycles by using sodium dimethyldithiocarbamate as surrogates (Scheme **1b**).

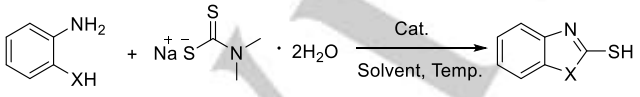


Scheme 1. Our previous (a) and present (b) strategies towards the synthesis of 2-mercapto benzoheterocycles.

Results and Discussion

To establish the optimal reaction conditions, we commenced our research by investigating the reaction using 2-aminothiophenol and sodium dimethyldithiocarbamate **2** as model substrates (Table 1). Initially, we treated 2-aminothiophenol with sodium dimethyldithiocarbamate **2** in DMF without any addition of catalyst. To our delight, we were able to obtain 2-mercaptobenzothiazole in 64% yield after the reaction mixture was stirred in DMF for 10 min at 120°C (entry 1). Encouraged by this initial result, several potential "catalysts" including $CuCl_2$, $Cu(OAc)_2$, $Cu(OTf)_2$, $CuSO_4$, $FeCl_3$, $AlCl_3$ were examined to evaluate their effect in the reaction (entries 2-7), and it revealed that $AlCl_3$ was found to be superior in furnishing the cyclized product in 94% yield (entry 7). Subsequently, to evaluate the solvent effect, the reaction was studied by performing the reaction in different solvents (entries 8-12). DMF was selected as the optimal solvent, giving 2-mercaptobenzothiazole in excellent yield after 10 minutes (entry 7). Based on these promising results, we further optimized the loading amount of $AlCl_3$. 2-Mercaptobenzothiazole was obtained in a lower yield (82%) when 5% equiv of $AlCl_3$ was used (entry 13). Thus, the loading of 10 % equiv of $AlCl_3$ was chosen to be the optimal. Screening of the reaction temperature showed that lower temperature led to lower yield, even when the reaction time was prolonged to 30 min. (entry 14). The optimal reaction conditions were also applied on the *O* and *N* heteroatoms containing bifunctional substrates (2-aminophenol, 1,2-phenylenediamine) to react with sodium salt **2**, furnishing the desired products in good yields (entries 15, 17).

Table 1. Optimization of the reaction conditions.[a]



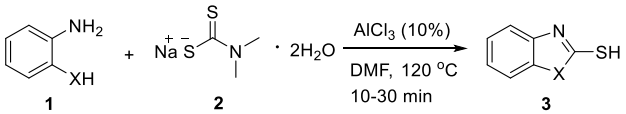
1 **2** **3**

Entry	X	Catalyst	Solvent	Temp (°C)	Time (min)	Yield[b] (%)
1	S	--	DMF	120	10	64
2	S	$CuCl_2$	DMF	120	10	83
3	S	$Cu(OAc)_2$	DMF	120	10	82
4	S	$Cu(OTf)_2$	DMF	120	10	81
5	S	$CuSO_4$	DMF	120	10	78
6	S	$FeCl_3$	DMF	120	10	76
7	**S**	**$AlCl_3$**	**DMF**	**120**	**10**	**94**
8	S	$AlCl_3$	H_2O	120	10	70
9	S	$AlCl_3$	toluene	120	10	trace
10	S	$AlCl_3$	THF	80	10	51
11	S	$AlCl_3$	EtOH	100	10	56
12	S	$AlCl_3$	MeCN	100	10	54
13[c]	S	$AlCl_3$	DMF	120	10	82
14	S	$AlCl_3$	DMF	100	30	81
15	**O**	**$AlCl_3$**	**DMF**	**120**	**20**	**83**
16	O	$AlCl_3$	DMF	100	60	76
17	**NH**	**$AlCl_3$**	**DMF**	**120**	**30**	**73**
18	NH	$AlCl_3$	DMF	100	60	56

[a]Reaction conditions: **1** (1.0 mmol), **2** (2.5 mmol), cat. (10 mol %), solvent (2.0 mL). [b]Isolated yield based on **1a** after column chromatography. [c]In the presence of $AlCl_3$ (5 mol%).

With the optimal conditions in hand, we investigated the substrate scope to obtain 2-mercapto benzofused heterocycles (Table 2). Firstly, the scope of 2-aminothiophenols were explored. Starting materials **1b** and **1c** reacted with sodium salt **2** successfully under the optimal reaction conditions to provide the desired products **3b** (95%) and **3c** (45%), respectively (entries 2-3). Subsequently, the scope of 2-aminophenol derivatives were also surveyed. Electron-withdrawing substituted 2-aminophenol substrates furnished **3e, 3f** and **3g** in moderate yield (entries 5-7). Electron-donating substituted 2-aminophenol substrates gave **3h, 3j, 3k** and **3l** in good yield (entries 8, 10-12) . The results indicated that electron-donating groups were more favored (generally) for the reaction than electron-withdrawing groups. Unfortunately, heterocycle substrate **1m** was not suitable for the transformation (entry 13). Finally, substituted 1,2-phenylenediamines bearing electron-withdrawing as well as electron-donating groups were submitted for evaluation of their compatibility in this reaction. It could be seen that the desired products were obtained in general moderate yields (entries 14-21). It is noteworthy that heterocycle substrate **1v** could be converted to the corresponding product **3v** in 30% yield (entry 22). To our delight, akyl-diamines **1w** and **1x** were also suitable for the transformation to afford **3w** and **3x** in good yields (entries 23-24). In general, the results allow the present procedure to be used as an easy and useful protocol for the preparation of 2-mercapto benzoheterocycles.

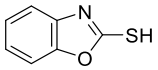
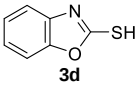
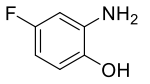
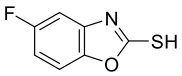
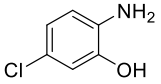
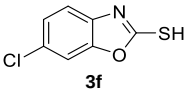
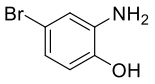
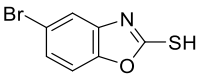
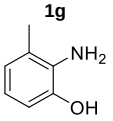
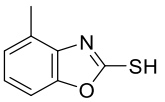
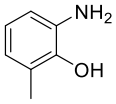
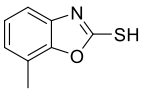
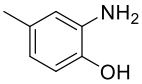
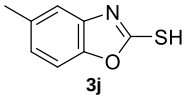
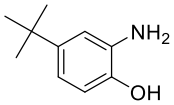
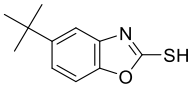
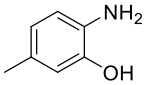
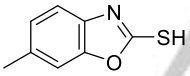
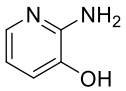
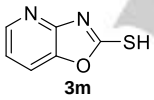
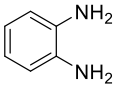
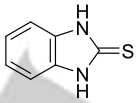
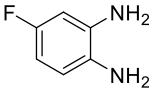
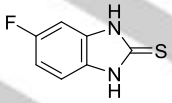
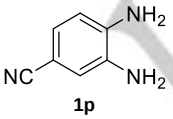
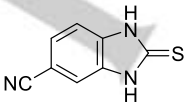
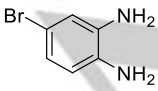
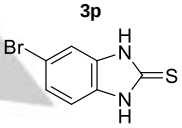
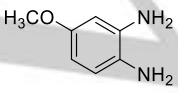
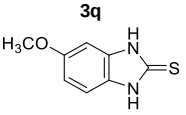
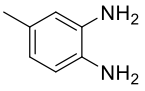
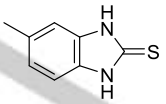
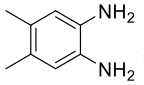
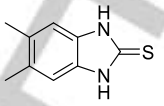
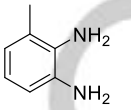
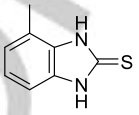
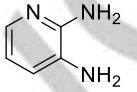
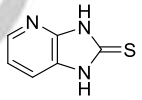
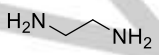
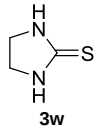
Table 2. Synthesis of benzoheterocycles starting from substituted anilines and sodium dimethyldithiocarbamate.[a]



1 **2** **3**

X = S, O, NH

Entry	Substrate 1	Product	Yield (%)[b]
1	**1a**	**3a**	94
2	**1b**	**3b**	95
3	**1c**	**3c**	45

4	 **1d**	 **3d**	83
5	 **1e**	 **3e**	55
6	 **1f**	 **3f**	55
7	 **1g**	 **3g**	60
8	 **1h**	 **3h**	69
9	 **1i**	 **3i**	32
10	 **1j**	 **3j**	78
11	 **1k**	 **3k**	88
12	 **1l**	 **3l**	75
13	 **1m**	 **3m**	0
14	 **1n**	 **3n**	73
15	 **1o**	 **3o**	56
16	 **1p**	 **3p**	30
17	 **1q**	 **3q**	49
18	 **1r**	 **3r**	53
19	 **1s**	 **3s**	58
20	 **1t**	 **3t**	67
21	 **1u**	 **3u**	54
22	 **1v**	 **3v**	30
23	 **1w**	 **3w**	92
24	**1x**	**3x**	65

[a]Reaction conditions: **1** (1.0 mmol), **2** (2.5 mmol), $AlCl_3$ (10 mol %), DMF (2.0 mL). [b]Isolated yield based on **1** after column chromatography.

A plausible reaction mechanism for this transformation is proposed. Initially, $AlCl_3$ coordinates with thiocarbonyl moiety of sodium dimethyldithiocarbamate **A**, enhancing the electrophilicity at carbonyl-carbon of **A** and facilitates amino-group of bifunctional molecule **B** to attack at this position to generate the intermediate dimethylphenylthiourea **C**. Secondly, the intramolecular cyclization of **C** generates target product **E,** which is the dynamical isomer of **F** (Scheme 2).

Scheme 2. The possible reaction mechanism.

Conclusions

In summary, we have developed an $AlCl_3$-promoted one-pot synthesis of 2-mercapto heterocycles (benzothiazoles, benzoxazoles, benzimidazoles, thiazolidine-2-thiones and imidazolidine-2-thiones). The reactions were readily facilitated to

afford the desired compounds smoothly under easy conditions. Features of this protocol are 1) easy performance, 2) commercially available, inexpensive, easy-to-handle and chemically stable thiocarbonyl surrogates, 3) the ability to prepare structurally diverse 2-mercapto heterocycles (benzothiazoles, benzoxazoles, benzimidazoles, thiazolidine-2-thiones and imidazolidine-2-thiones).

Experimental Section

General remarks: 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 an RY-1 m.p. machine without adjustment. ^{1}H NMR (in $CDCl_3$ or DMSO-d_6) and ^{13}C NMR (in $CDCl_3$ or DMSO-d_6) spectra were recorded using TMS as an 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 the isolated compounds estimated to be >95% pure as determined by ^{1}H NMR and capillary GC analysis.

Typical procedure (TP) for synthesis of 2-mercapto benzothiazoles, benzoxazoles and benzimidazoles. (3a-3x): 1 (1.0 mmol), 2 (2.5 mmol) and $AlCl_3$ (0.1 mmol) were dissolved in DMF (2 mL) in a dried tube equipped with a magnetic stirring bar and a septum. The reaction mixture was then heated in an oil bath and checked by TLC until the starting material was consumed (about 10-30min). Then the reaction mixture was allowed to cool down to room temperature, quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The residue was purified by flash column chromatography to afford the desired product.

Benzothiazole-2-thiol (3a): 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 (yield = 94%). m.p: 180-182°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.71 (brs, 1H), 7.59 (d, 1H, *J* = 4.0 Hz), 7.30-7.17 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 190.2, 141.8, 129.9, 127.7, 124.7, 122.3, 112.9. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_6NS_2$ (170.9936), found: 170.9939.

5-Chloro-benzothiazole-2-thiol (3b): 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 (yield = 95%). m.p: 201-203°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.81 (brs, 1H), 7.67 (d, 1H, *J* = 8.0 Hz), 7.31-7.25 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 191.3, 142.6, 132.2, 128.6, 124.4, 123.5, 112.3. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_5ClNS_2$ (201.9547), found: 201.9545.

thiazolidine-2-thione (3c): 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 (yield = 45%). m.p: 106-108°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 10.09 (brs, 1H), 3.87 (t, d = 8.0 Hz, 2H), 3.51 (t, d = 8.0 Hz 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 199.4, 51.9, 33.3. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_3H_6NS_2$ (119.9936), found 119.9932.

Benzooxazole-2-thiol (3d): 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 (yield = 83%). m.p: 192-193°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.92 (brs, 1H), 7.47 (d, 1H, *J* = 8.0 Hz), 7.29-7.20 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.5, 148.5, 131.6, 125.5, 124.2, 110.9, 110.4. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_7H_6NOS (152.0165), found: 152.0162.

5-Fluoro-benzooxazole-2-thiol (3e): 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 (yield = 55%). m.p: 189-190°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.99 (brs, 1H), 7.50-7.47 (m, 1H), 7.10-7.02 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.6, 159.9 (d, 1C, *J* = 238 Hz), 144.9 (d, 1C, *J* = 1 Hz), 132.5 (d, 1C, *J* = 13 Hz), 111.1 (q, 1C, *J* = 38 Hz), 98.7 (d, 1C, *J* = 29 Hz). HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_7H_5FNOS (170.0071), found: 170.0075.

6-Chloro-benzooxazole-2-thiol (3f): 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 (yield = 55%). m.p: 224-225°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 14.01 (brs, 1H), 7.72 (d, *J* = 4 Hz, 1H), 7.35-7.32 (m, 1H), 7.23 (d, *J* = 8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.9, 148.9, 130.9, 128.4, 125.6, 111.7, 111.0. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_7H_5ClNOS (185.9775), found: 185.9772.

5-Bromo-benzooxazole-2-thiol (3g): 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 red solid (yield = 60%). m.p: 283-284°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.93 (brs, 1H), 7.47-7.41 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.0, 147.8, 133.3, 126.8, 117.4, 113.5, 112.1. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_7H_5BrNOS (229.9270), found: 229.9274.

4-Methyl-benzooxazole-2-thiol (3h): 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 white solid (yield = 69%) m.p: 218-219°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.93 (brs, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.15-7.06 (t, *J* = 8 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.5, 148.3, 130.8, 126.4, 124.0, 121.5, 107.6, 16.5. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_8H_8NOS (166.0321), found: 166.0328.

7-Methyl-benzooxazole-2-thiol (3i): 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 red solid (yield = 32%). m.p: 203-205°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.76 (brs, 1H), 7.17 (t, *J* = 8 Hz, 1H), 7.05 (t, *J* = 8 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.3, 147.4, 131.2, 125.4, 125.3, 120.4, 108.3, 14.7. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_8H_8NOS (166.0321), found 166.0323.

5-Methyl-benzooxazole-2-thiol (3j): 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 white solid (yield = 78%). m.p: 214-216°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.94 (brs, 1H), 7.56 (d, *J* = 12 Hz, 1H), 7.25 (d, *J* = 4 Hz, 2H), 2.57 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 181.6, 147.7, 136.2, 132.6, 125.7, 111.9, 110.8, 22.2. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_8H_8NOS (166.0321), found: 166.0316.

5-tert-Butyl-benzooxazole-2-thiol (3k): 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 red solid (yield = 88%). m.p: 126-128°C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 12.20 (brs,

1H), 7.34 (m, 3H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 181.4, 149.9, 147.3, 130.8, 122.4, 110.3, 108.2, 35.6, 32.1. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{11}H_{14}NOS$ (208.0791), found: 208.0788.

6-Methyl-benzooxazole-2-thiol (3l): According to the 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 (yield = 75%). m.p: 208-210°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.68 (brs, 1H), 7.24 (s, 1H), 7.03 (s, 2H), 2.3 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 180.3, 148.7, 134.0, 129.2, 126.0, 110.6, 110.3, 21.3. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for C_8H_8NOS (166.0321), found: 166.0324.

1,3-Dihydro-2H-benzoimidazole-2-thione (3n): According to the TP, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3n** as a white solid (yield = 73%). m.p: 298-300°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.42 (brs, 2H), 7.00 (t, *J* = 4.0 Hz, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.1, 133.2, 123.3, 110.5. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_7N_2S$ (151.0325), found: 151.0321.

5-Fluoro-1,3-dihydro-2H-benzoimidazole-2-thione (3o): According to the TP, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3o** as a white solid (yield = 56%). m.p: 284-286°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.61 (d, *J* = 8.0 Hz, 2H), 7.13-7.10 (m, 1H), 6.98-6.93 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.7, 160.1 (d, 1C, *J* = 236 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). HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_6FN_2S$ (169.0230), found: 169.0227.

2-Thioxo-2,3-dihydro-2H-benzoimidazole-5-carbonitrile (3p): According to the TP, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give the target compound **3p** as a white solid (yield = 30%). m.p: 315-316°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.95 (d, *J* = 20.0 Hz, 2H), 7.53-7.51 (m, 2H), 7.25 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 171.0, 136.0, 132.7, 127.4, 119.7, 113.3, 110.6, 104.6. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_6N_3S$ (176.0277), found: 176.0273.

5-Bromo-1,3-dihydro-2H-benzoimidazole-2-thione (3q): According to the 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 gray solid (yield = 49%). m.p: 302-303°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.65 (d, *J* = 16 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 169.4, 134.0, 132.0, 125.4, 114.8, 112.4, 111.5. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_6BrN_2S$ (228.9430), found: 228.9434.

5-Methoxy-1,3-dihydro-2H-benzoimidazole-2-thione (3r): According to the 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 yellow solid (yield = 53%). m.p: 255-257°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.38 (d, *J* = 12.0 Hz,, 2H), 7.05 (d, *J* = 12.0 Hz, 1H), 6.72 (t, *J* = 8.0 Hz, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.0, 156.2, 133.4, 126.7, 110.5, 110.2, 94.9, 55.9. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_9N_2OS$ (181.0430), found: 181.0425.

5-Methyl-1,3-dihydro-2H-benzoimidazole-2-thione (3s): According to the 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 white solid (yield = 58%). m.p: 294-295°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.41 (brs, 2H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.93 (t, *J* = 8.0 Hz, 2H,), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.1, 132.9, 132.1, 130.6, 123.6, 110.0, 109.6, 21.4. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_9N_2S$ (165.0481), found: 165.0479.

5,6-Dimethyl-1,3-dihydro-2H-benzoimidazole-2-thione (3t): According to the 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 brown solid (yield = 67%). m.p: 325-326°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.29 (brs, 2H), 6.92 (s, 2H), 2.19 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 167.4, 131.0, 131.0, 110.5, 20.0. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_9H_{11}N_2S$ (179.0638), found: 179.0643.

4-methyl-1,3-dihydro-2H-benzoimidazole-2-thione (3u): According to the 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 brown solid (yield = 54%). m.p: decomposed; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.58 (s, 1H), 12.46 (s, 1H), 7.02-6.88 (m, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 168.2, 132.3, 131.9, 123.6, 122.8, 120.1, 107.4, 16.7. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_9N_2S$ (165.0481), found: 165.0484.

1,3-dihydro-2H-imidazo[4,5-b]pyridine-2-thione (3v): According to the 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 white solid (yield = 30%). m.p: 322-324°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.13 (brs, 1H), 12.71 (brs, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.14-7.10 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 170.2, 146.8, 142.7, 125.9, 118.6, 116.7. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_6H_6N_3S$ (152.0277), found: 152.0273.

imidazolidine-2-thione (3w): According to the 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 (yield = 92%). m.p: 204-205°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 7.95 (brs, 2H), 3.48 (s, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 184.4, 45.1. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_3H_7N_2S$ (103.0325), found: 103.0321.

octahydro-2H-benzoimidazole-2-thione (3x): According to the 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 (yield = 65%). m.p: 159-161°C; ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 8.26 (brs, 2H), 3.02 (t, *J* = 4.0 Hz, 2H), 1.91 (d, *J* = 12.0 Hz, 2H), 1.68 (d, *J* = 8.0 Hz, 2H), 1.34-1.22 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 186.9, 64.2, 29.2, 23.9. HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_7H_{13}N_2S$ (157.0794), found: 157.0797.

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Keywords: aluminium chloride • mercapto benzoheterocycle • dimethyldithiocarbamate • surrogate • thione

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Cyclization: synthesis of 2-mercapto benzoheterocycles*

*X. Liu, S. B. Zhang, Z. B. Dong**

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$AlCl_3$-Promoted Synthesis of 2-Mercapto Benzoheterocycles by Using Sodium Dimethyldithiocarbamate as Thiocarbonyl Surrogate

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A simple, expeditious and high-efficiency synthetic method for the $AlCl_3$-mediated one-pot preparation of 2-mercapto benzoheterocycles (2-mercapto benzothiazoles, benzoxazoles and benzimidazoles) is described. By the treatment of a series of *S*, *O* and *N* heteroatoms containing bifunctional molecules with sodium dimethyldithiocarbamate in $AlCl_3$, the desired 2-mercapto benzoheterocycles were synthesized smoothly. The protocol can also be applied on the synthesis of a series of thiazolidine-2-thiones, imidazolidine-2-thiones.