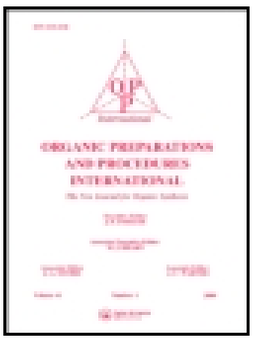

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Organic Preparations and Procedures International

The New Journal for Organic Synthesis

ISSN: 0030-4948 (Print) 1945-5453 (Online) Journal homepage: https://www.tandfonline.com/loi/uopp20

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To cite this article: Wei-wei Li & Hui Zheng (2019): A Highly Efficient Synthesis of 2-Benzimidazolthiones and Their Congeners under Mild Conditions, Organic Preparations and Procedures International, DOI: 10.1080/00304948.2019.1581717

To link to this article: https://doi.org/10.1080/00304948.2019.1581717

Published online: 09 Apr 2019.

Organic Preparations and Procedures International, 0:1–7,

ISSN: 0030-4948 print / 1945-5453 online
DOI: 10.1080/00304948.2019.1581717

A Highly Efficient Synthesis of 2-Benzimidazolthiones and Their Congeners under Mild Conditions

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2-Benzimidazolthiones and their congeners are significant motifs among heterocyclic compounds, and they have been broadly used as key building blocks in organic synthesis and in the pharmaceutical chemistry.[1–4] In the rubber industry, these compounds are promising ligands for metallic complexes used as important accelerators in rubber vulcanization.[5] In medicinal chemistry, these heterocyclic compounds have versatile bioactivities against tumors, ulcers, inflammatory conditions and infectious microbes.[6–8] Consequently, developing novel and efficient methods of preparing these heterocyclic derivatives are of increasing interest.

Common methods of synthesizing these materials have centered on the reactions of carbon disulfide with *o*-phenylenediamines, *o*-aminothiophenols and *o*-aminophenols.[9] 2-Benzoxazolthione derivatives also can be prepared from the reaction of *o*-haloanilines or *o*-aminothiophenols with disulfides.[10–12] These approaches often suffer from high temperatures, long reaction times, toxic solvents and metal catalysts.

As part of own ongoing interest in heterocyclic synthesis,[13] we now report a simple method for synthesizing 2-benzimidazolthiones, 2-benzothiazolthiones and 2-benzoxazolthiones *via* the reactions of CS_2 with appropriate precursors with a recyclable ionic liquid [DBUH][OAc] as catalyst and solvent, as shown in *Scheme 1*. The IL exhibited high catalytic ability under mild conditions with high yields, and it could be recycled at least six times and still keep good catalytic ability.

Initially, a number of bases (DBU, Et_3N, NaOH, KOH, K_2CO_3, K_3PO_4 and Cs_2CO_3) were investigated for the synthesis of 2-benzimidazolthione at room temperature for 30 minutes, and the results are summarized in *Table 1*. Some bases (NaOH, KOH, Cs_2CO_3, K_3PO_4, K_2CO_3, and Et_3N, *Table 1*, entries 3-8) had no catalytic ability in this reaction. It was found that DBU can catalyze the reaction with only 20% yield of the product 2-benzimidazolthione (*Table 1*, entry 2). Fortunately, the reaction went

Received November 16, 2017; in final form October 21, 2018.
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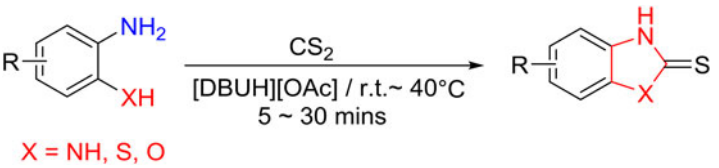
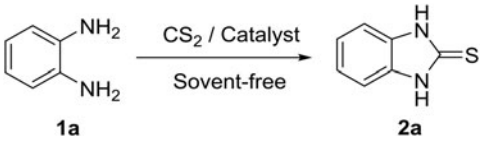


Scheme 1. The synthesis of the three types of derivatives.

Table 1
Synthesis of 2-benzimidazolthione with Different Catalysts



1a **2a**

Entry	Catalyst[a]	Yield[b](%)
1	None	0
2	DBU	20
3	Et_3N	0
4	NaOH	0
5	KOH	0
6	K_2CO_3	0
7	K_3PO_4	0
8	Cs_2CO_3	0
9	**[DBUH][OAc]**	**92**

[a]Reaction conditions: substrate 2 mmol, CS_2 3 mmol, catalyst 5 mmol, traditional solvent-free, r.t. 30 min.
[b]Isolated yield.

well and gave the product in high yield (92%) when [DBUH][OAc] was used as catalyst (*Table 1*, entry 9).

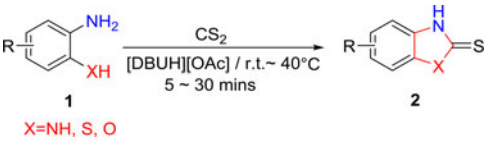
Having established the optimum conditions, different substrates were examined and the results are listed in *Table 2*. Different substrates of benzene-1,2-diamines bearing electron-donating or electron-withdrawing groups showed excellent reactivity with high yields (84-93%). Substrates bearing the electron-donating groups -OCH_3 and -CH_3 (*Table 2*, entries 2-5) reacted well with high yields (up to 93%). Compounds bearing electron-withdrawing groups -F, -Cl, -Br, -NO_2 and PhCO- (*Table 2*, entries 6-9 and 11) also gave very good yields. The bulky structure 1,8-naphthalenediamine (**1j**, *Table 2*, entry 10) reacted smoothly to give **2j** with a yield of 93%. Those results suggest that the electronic and steric effects had little influence on this system.

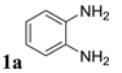
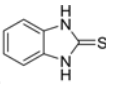
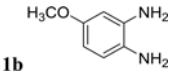
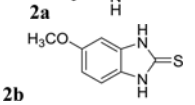
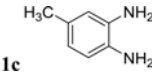
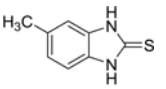
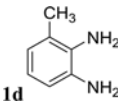
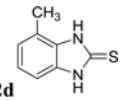
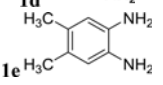
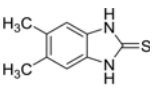
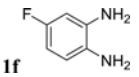
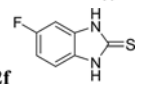
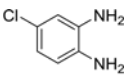
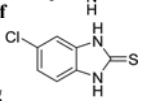
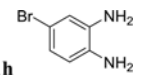
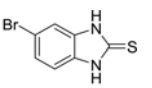
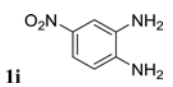
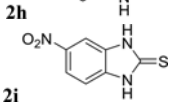
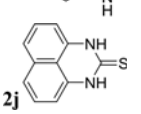
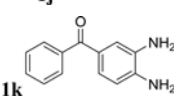
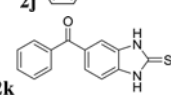
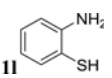
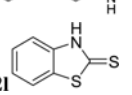
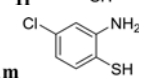
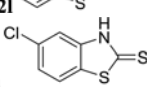
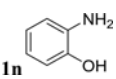
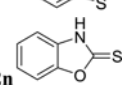
Encouraged by these results, other substrates (*o*-aminothiophenols and *o*-aminophenol) were employed. These kinds of substrates also performed well (*Table 2*, entries 12-16). Some substrates even reacted in 5 minutes at room temperature (*Table 2*, entries 12 and 13). [DBUH][OAc] retained high catalytic ability and gave 92% yield though six runs (*Table 2*, entry 1, notes e-i for runs 2-6).

In conclusion, a simple and highly efficient method was developed for the synthesis of 2-benzimidazolthiones and their congeners under mild conditions. This simple

Table 2

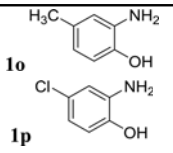
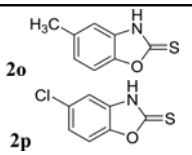
Synthesis of Different Benzimidazolthiones,[a] Benzothiazolthiones,[c] Benzoxazolthiones[d]



Entry	Substrate	Product	Yield[b](%)
1	 **1a**	 **2a**	92, 90[e], 93[f], 94[g], 92[h], 92[i]
2	 **1b**	 **2b**	90
3	 **1c**	 **2c**	90
4	 **1d**	 **2d**	91
5	 **1e**	 **2e**	91
6	 **1f**	 **2f**	88
7	 **1g**	 **2g**	87
8	 **1h**	 **2h**	89
9	 **1i**	 **2i**	84
10	 **1j**	 **2j**	93
11	 **1k**	 **2k**	89
12	 **1l**	 **2l**	96[c]
13	 **1m**	 **2m**	94[c]
14	 **1n**	 **2n**	94[d]
15			91[d]

(*Continued*)

Table 2
(*Continued*)

16	 **1o** **1p**	 **2o** **2p**	75[d]

[a]Reaction conditions: substrate 2 mmol, CS_2 3 mmol, [DBUH][OAc] 1 mL, r.t., 30 mins.
[b]Isolated yield.
[c]Reaction conditions: substrate 10 mmol, CS_2 15 mmol, [DBUH][OAc] 1 mL, r.t., 5 min.
[d]Reaction conditions: substrate 2 mmol, CS_2 3 mmol, [DBUH][OAc] 1 mL, 40°C, 30 mins.
[e-i]Yield of the product (runs: 2–6).

protocol employed inexpensive, convenient reactants to obtain the three kinds of heterocyclic compounds. The IL could be recycled at least six times and kept high catalytic activity.

Experimental Section

All the commercial reagents were purchased from Alfa Aesar, TCI or Sigma-Aldrich and used directly without further purification. NMR was carried out with a Bruker AV400 (500 MHz) spectrometer in DMSO-d_6 using TMS as internal standard. Chemical shifts are reported in ppm. The melting points were determined using a XT-4 melting point apparatus and were uncorrected. IR spectra were recorded on a Bruker Equinox-55 spectrophotometer using KBr discs in the 4,000-400 cm^{-1} region.

General procedure for synthesizing [DBUH][OAc] ionic liquid: 40 mmol of DBU was placed in a 250 mL three-necked flask. Then 40 mmol acetic acid was slowly dropped into the flask over an ice bath, which was removed when the addition was finished. The reaction system was stirred at room temperature for 24 h. The oily product was dried in vacuum at 60°C for one day. The light yellow, viscous liquid of [DBU][OAc] IL was obtained. The characterization data accorded with the literature.[15]

The basic procedure for preparing all products was similar. Taking the entry **1** in *Table 2* as an example: **1a** (2 mmol) and [DBUH][OAc] (1 mL) were added to a 10 mL flask and stirred at room temperature. After 30 minutes, adding 5 mL water into the flask dispersed the solid product, which could be separated by filtration. The solid was recrystallized from an ethyl acetate and petroleum ether mixture (v/v, 1/1) to get **2a**. The aqueous residue was evaporated under vacuum at 50°C for 8 h and reused in the next run. All the products were known compounds, and the characteristic data accorded with the relevant literature.

2-Benzimidazolthione (2a).[15] Mp >300°C, *lit.*[16] mp 302°C; IR (KBr, cm^{-1}) ν_{max} 3153, 3119, 2982, 1558, 1462; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.48 (s, 2H), 7.14 -7.12 (m, 4H).^{13}C NMR (126 MHz, DMSO-d_6) δ 168.71, 132.86, 122.68, 109.93

5-Methoxybenzimidazolthione (2b). Mp 257–258°C, *lit.*[17] mp 255–256°C; IR (KBr, cm^{-1}) ν_{max} 3155, 3122, 2989, 1559, 1518, 1468; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.41 (d, $J = 19.7$ Hz, 2H), 7.05 (d, $J = 8.6$ Hz, 1H), 6.98 – 6.60 (m, 2H), 3.76 (s, 3H).^{1}H NMR (500 MHz, DMSO-d_6) δ 168.21, 156.20, 133.52, 126.82, 110.43, 110.18, 94.88, 55.99.

5-Methyl-2-benzimidazolthione (2c). Mp 292–294°C, *lit.*[16] mp 296°C; IR (KBr, cm^{-1}) ν_{max} 3156, 3125, 2987, 1557, 1514, 1467; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.41 (s, 1H), 7. 03 – 6.92 (m, 3H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.24, 132.94, 132.12, 130.67, 123.66, 110.07, 109.58.

4-Methyl-2-benzimidazolthione (2d). Mp >300°C, *lit.*[18] mp >300°C; IR (KBr, cm^{-1}) ν_{max} 3155, 3121, 2989, 1559, 1516, 1468; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.54 (d, $J = 63.4$ Hz, 2H), 7.03–6.90 (m, 3H), 2.37 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.40, 132.39, 131.99, 123.63, 122.81, 120.16, 107.38, 16.71.

4,5-Dimethyl-2-benzimidazolthione (2e). Mp 227–228°C, *lit.*[19] mp 225°C; IR (KBr, cm^{-1}) ν_{max} 3275, 3134, 2988, 1626, 1432; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.28 (s, 2H), 6.93 (s, 2H), 2.23 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.71, 131.07, 130.93, 110.50, 20.01.

5-Fluoro-2-benzimidazolthione (2f). Mp 277-278°C, *lit.*[20] mp 280°C; IR (KBr, cm^{-1}) ν_{max} 3160, 3087, 2986, 1633, 1434; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.63 (d, $J = 15.7$ Hz, 2H), 7.14-6.95 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.80, 159.00 (d, $J = 236.6$ Hz), 133.22 (d, $J = 13.1$ Hz), 110.51 (d, $J = 9.9$ Hz), 109.73 (d, $J = 24.8$ Hz), 97.33 (d, $J = 27.9$ Hz).

5-Chloro-2-benzimidazolthione (2g). Mp >300°C, *lit.*[21] mp >300°C; IR (KBr, cm^{-1}) ν_{max} 3186, 3063, 2987, 1636, 1435; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.65 (d, $J = 12.6$ Hz, 2H), 7.16 – 7.13 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.83, 133.72, 131.73, 127.16, 122.67, 110.98, 109.64.

5-Bromo-2-benzimidazolthione (2h). Mp 288-289°C, *lit.*[22] mp 289–292°C; IR (KBr, cm^{-1}) ν_{max} 3201, 3069, 2987, 1634, 1436; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.64 (d, $J = 18.5$ Hz, 2H), 7.66–6.73 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.69, 134.13, 132.09, 125.40, 114.77, 112.38, 111.46.

5-Nitro-2-benzimidazolthione (2i). Mp 269-271°C, *lit.*[22] mp 272°C; IR (KBr, cm^{-1}) ν_{max} 3235, 3101, 2988, 1645, 1457; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.07 (d, $J = 46.1$ Hz, 2H), 8.08–8.05 (m, 1H), 7.88-7.85 (m, 1H), 7.30 – 7.25 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.29, 143.06, 137.82, 132.70, 119.33, 109.63, 105.07.

1H,3H-Perimidin-2-thione (2j). Mp >300°C, *lit.*[16] mp >300°C; IR (KBr, cm^{-1}) ν_{max} 3213, 3167, 2981, 1637, 1447; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.39 (s, 2H), 7.25–6.15 (m, 4H), 6.63 (d, $J = 7.3$ Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 173.34, 135.73, 134.44, 128.74, 119.48, 116.54, 105.04.

5-Benzoyl-2-benzimidazolthione (2k). Mp 255-257°C, *lit.*[23] mp 254-256°C; IR (KBr, cm^{-1}) ν_{max} 3202, 2988, 1640, 1454; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.85 (d, $J = 65.9$ Hz, 2H), 7.72–7.27 (m, 8H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 195.45, 170.80, 138.26, 136.30, 132.69, 132.66, 131.49, 129.82, 128.94, 125.84, 111.30, 109.60.

2-Benzothiazolthione (2l). Mp 187-189°C, *lit.*[24] mp189-190°C; IR (KBr, cm^{-1}) ν_{max} 3158, 2989, 1562, 1488; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.73 (s, 1H), 7.70–7.64 (m, 1H), 7.42-7.26 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 190.31, 141.73, 129.83, 127.61, 124.66, 122.22, 112.89.

5-Chloro-2-benzothiazolthione (2m). Mp 199–201°C, *lit.*[25] mp 201–202°C; IR (KBr, cm^{-1}) ν_{max} 3155, 2986, 1569, 1481; ^1H NMR (500 MHz, DMSO-d_6) δ 13.82 (s, 1H), 7.72 (d, $J = 8.5$ Hz, 1H), 7.36–7.28 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 191.41, 142.70, 132.28, 128.71, 124.53, 123.68, 112.41.

2-Benzoxazolthione (2n). Mp 190–193°C, *lit.*[26] mp 193–195°C; IR (KBr, cm^{-1}) ν_{max} 3182, 2989, 1462, 1239; ^1H NMR (500 MHz, DMSO-d_6) δ 13.84 (s, 1H), 7.51 (d, $J = 7.7$ Hz, 1H), 7.32–7.24 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.63, 148.64, 131.69, 125.61, 124.24, 110.95, 110.45.

5-Methy-2-lbenzoxazolthione (2o). Mp 215–217°C, *lit.*[27] mp 217–218°C; IR (KBr, cm^{-1}) ν_{max} 3381, 3022, 2919, 1645, 1453; ^1H NMR (500 MHz, DMSO-d_6) δ 13.74 (s, 1H), 7.37 (d, $J = 8.1$ Hz, 1H), 7.06 (d, $J = 6.7$ Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.73, 146.86, 135.30, 124.82, 111.03, 109.97, 21.29.

5-Chloro-2-benzoxazolthione (2p). Mp 275–277°C, *lit.*[28] mp 278–280°C; IR (KBr, cm^{-1}) ν_{max} 3075, 2934; ^1H NMR (500 MHz, DMSO-d_6) δ 14.00 (s, 1H), 7.53 (d, $J = 8.2$ Hz, 1H), 7.31 (d, $J = 8.3$ Hz, 2H). ^3C NMR (126 MHz, DMSO-d_6) δ 181.26, 147.46, 133.08, 129.80, 123.99, 111.68, 110.85.

Acknowledgments

The authors are grateful to the Zhejiang higher education classroom teaching reform project (kg20160714), Pandeng Plan Foundation of Hangzhou Normal University for Youth Scholars of Materials, Chemistry and Chemical Engineering, and Zhejiang Provincial Natural Science Foundation of China (LY19B060007) for providing financial support.

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