Carbon Tetrabromide Promoted Reaction of Amines with Carbon Disulfide: Facile and Efficient Synthesis of Thioureas and Thiuram Disulfides

Fushun Liang,* Jing Tan, Chengri Piao, Qun Liu*

Department of Chemistry, Northeast Normal University, Changchun 130024, P. R. of China
Fax +86(431)5099759; E-mail: liangfs112@nenu.edu.cn

Received 30 June 2008; revised 1 August 2008

Abstract: A novel carbon tetrabromide promoted one-pot reaction of amines and carbon disulfide under mild conditions has been developed, which provides a straightforward and efficient access to thioureas and thiuram disufides, depending on the nature of the amines employed. The promotion effect is explained as the transient formation of a sulfenyl bromide intermediate from dithiocarbamate and carbon tetrabromide during the reaction.

Key words: carbon tetrabromide, thioureas, thiuram disulfides, sulfenyl bromide

Carbon tetrabromide is a commercially available and easily handled reagent and has found wide application in organic synthesis. For example, carbon tetrabromide can be used for the selective bromination of benzene hydrocarbons,[1a] terminal acetylenes,[1b,c] alkanes or arylalkanes,[1d,e] and active methylene compounds.[1f] In the presence of diacyl peroxide, carbon tetrabromide may add to the C=C bond of an olefin.[2] Carbon tetrabromide can also be used as a catalyst in the following reactions: regioselective ring-opening of epoxides with alcohols and water;[3a] photolytic deprotection of α-imidazole/benzimidazole ribonucleosides[3b] or acid-labile primary hydroxy protecting groups;[3c] and deprotection of β-(trimethylsilyl)ethoxymethyl ethers to the corresponding alcohols.[3d] Moreover, the combination of carbon tetrabromide and triphenylphosphine as a multifunctional reagent (Appel agent), has proven very effective for some important transformations. For instance, by reacting with Appel agents and analogues, aldehydes/ketones can be converted into 1,1-dihaloalkenes[4] or terminal alkynes by subsequent treatment with butyllithium (Corey–Fuchs reaction).[5] Additionally, the carbon tetrabromide–trisubstituted phosphine system can be used for selective cleavage of ketals and acetals,[6a] conversion of N-acylated α-aminonitriles into 2,4-disubstituted 5-halo-1*H*-imidazoles,[6b] condensation reaction of carbon dioxide with alcohols,[6c,d] and ring expansion of cyclopropyl amides to N-substituted pyrrolidin-2-ones,[6e] etc.

Thiourea derivatives are of great importance not only in medicinal chemistry due to their biological activity,[7] but they are also used as analytical reagents,[8] and as valuable building blocks in the synthesis of heterocycles.[9] Recently, some chiral thioureas have been used as highly efficient bifunctional organocatalysts in conjugate additions,[10a–d] and other reactions such as asymmetric Mannich reactions,[10e] asymmetric Strecker reactions,[10f] and asymmetric additions to oxocarbenium ions.[10g] The synthesis of symmetrical thioureas have been customarily carried out using carbon disulfide and primary amines in pyridine or ethanol as the simplest method, but the reactions usually require high reaction temperatures and a long reaction time.[11] Therefore, the development of mild, efficient, and convenient methods is still required. It has been reported that the utilization of catalysts such as sulfur or dimethylchloroformiminium chloride or the addition of hydrogen peroxide, iodine, or sodium hydroxide greatly increases the rate of thiourea formation.[12] Recently, in our exploration of the applications of carbon tetrabromide in organic synthesis, we presented an efficient and convenient C–S bond-forming reaction starting from two or three component coupling reactions of active methylene compounds with sulfur containing reagents (thiols, dithioacids, and dithiocarbamates) in the presence of carbon tetrabromide.[13] Herein, we would like to report our recent results, an interesting carbon tetrabromide pro-

Table 1 Carbon Tetrabromide Promoted Reactions of Primary Amines **1a–g** with Carbon Disulfide Leading to Thioureas **2**

1a–g **2a–g**

Entry	Primary amine[a] RNH_2	CBr_4 (equiv)	Time (h)	Product	Yield[b] (%)
1	$BuNH_2$ (**1a**)	0	13	**2a**	60
2	$BuNH_2$ (**1a**)	1.0	0.3	**2a**	91
3	$BnNH_2$ (**1b**)	1.0	1.4	**2b**	75
4	$PhNH_2$ (**1c**)	1.0	1.5	**2c**	80
5	4-$MeC_6H_4NH_2$ (**1d**)	0	20	**2d**	78
6	4-$MeC_6H_4NH_2$ (**1d**)	1.0	1.0	**2d**	90
7	4-$ClC_6H_4NH_2$ (**1e**)	1.0	1.5	**2e**	86
8	2-$ClC_6H_4NH_2$ (**1f**)	1.0	1.5	**2f**	71
9	4-$O_2NC_6H_4NH_2$ (**1g**)	1.0	20	**2g**	–[c]

[a] The feed ratio of amine to CS_2 is 2:1.
[b] Isolated yields.
[c] No reaction.

SYNTHESIS 2008, No. 22, pp 3579–3584
Advanced online publication: 23.10.2008
DOI: 10.1055/s-0028-1083199; Art ID: F14808SS

moted reaction of amines and carbon disulfide under ambient conditions. It was found that when a primary amine was used, thioureas were obtained in high yields and with high purity in short reaction times. On the other hand, when secondary amines were introduced to this carbon tetrabromide promoted reaction, useful thiuram disulfides were obtained with high efficiency. The promotion effect was studied in detail and the reason for this was explained as the transient formation of a highly reactive sulfenyl bromide intermediate from dithiocarbamate and carbon tetrabromide during the process.

Initially, the reactions of primary amines with carbon disulfide leading to various thioureas were investigated (Table 1). In the model reaction of butylamine (**1a**) and carbon disulfide in the presence of carbon tetrabromide, *N*,*N*-dimethylformamide was the most efficient solvent. When other solvents like acetonitrile, tetrahydrofuran, and ethanol were used, the yields of **2a** were lower (12–61%). All the reactions were performed by mixing the reagents at 0 °C and then the mixture was stirred at room temperature. The role of carbon tetrabromide in the reactions was particularly examined. The reaction of butylamine (**1a**) and carbon disulfide without carbon tetrabromide needed 13 hours to go to completion and the yield of **2a** was 60% (Table 1, entry 1). When one equivalent of carbon tetrabromide was added, the reaction was complete within 15 minutes and **2a** was obtained in an excellent 91% yield (Table 1, entry 2). The same was observed for 4-methylaniline (**1d**) (Table 1, entries 6 and 7).

Table 2 Carbon Tetrabromide Promoted Reactions of Diamines **1h**,**j** or Hydroxy Amines **1i**,**k** with Carbon Disulfide

1h–k (X = O or NH) **2h–k**

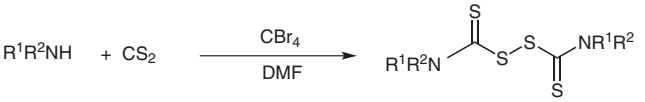
Entry	Primary amine[a]	CBr_4 (equiv)	Time (h)	Product	Yield[b] (%)
1	$H_2N(CH_2)_2NH_2$ (**1h**)	1.0	0.3	**2h**	98
2	$HO(CH_2)_2NH_2$ (**1i**)	1.0	0.5	**2i**	96
3	2-$H_2NC_6H_4NH_2$ (**1j**)	0	4	**2j**	53
4	2-$H_2NC_6H_4NH_2$ (**1j**)	1.0	0.4	**2j**	66
5	2-$HOC_6H_4NH_2$ (**1k**)	1.0	1.0	**2k**	64

[a] The feed ratio of amine to CS_2 is 1:1.
[b] Isolated yields.

Obviously, the reactions with carbon tetrabromide gave significantly shorter reaction times and higher yields than that without carbon tetrabromide. Carbon tetrabromide has marked acceleration effect on the reaction of carbon disulfide and primary amines. Comparatively, carbon tetrachloride gave no such promotion effect under the identical conditions. The reactions of both aliphatic and aromatic amines (2.0 equiv) with carbon disulfide (1.0 equiv) in the presence of carbon tetrabromide (1.0 equiv) proceeded efficiently, giving symmetrical thioureas **2a–f** in good to excellent yields (Table 1, entries 2–4 and 6–8). However, 4-nitroaniline (**1g**) gave no reaction under otherwise identical conditions (Table 1, entry 9), probably attributed to the strong electron-withdrawing effect of the nitro group that weakens the nucleophilicity of an aniline.

In the following work, primary amines **1h–k** containing an additional nucleophilic group were subjected to the reaction sequences (Table 2). As a result, the reactions of ethylenediamine (**1h**) and benzene-1,2-diamine (**1j**) with carbon disulfide (1.0 equiv) and carbon tetrabromide (1.0 equiv) led to the formation of imidazole-2-thiones **2h** and **2j**, respectively (Table 2, entries 1 and 4). The reactions of 2-hydroxyethylamine (**1i**) and 2-hydroxyaniline (**1k**) with carbon disulfide (1.0 equiv) and carbon tetrabromide (1.0 equiv) furnished oxazole-2-thiones **2i** and **2k**, respectively, in high yields (Table 2, entries 2 and 5). The promotion effect by carbon tetrabromide was also observed (Table 2, entries 3 and 4).

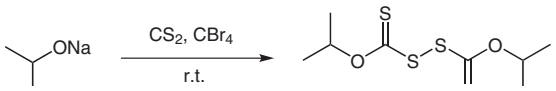
Table 3 Carbon Tetrabromide Mediated Reactions of Secondary Amines **3a–e** with Carbon Disulfide Leading to Thiuram Disulfides **4**



3a–e **4a–e**

Entry	Amine[a] R^1R^2NH	CBr_4 (equiv)	Time (h)	Product	Yield[b] (%)
1	Me_2NH (**3a**)	0	19.0	**4a**	48
2	Me_2NH (**3a**)	1.0	1.0	**4a**	95
3	Et_2NH (**3b**)	1.0	1.0	**4b**	96
4	Bu_2NH (**3c**)	1.0	1.5	**4c**	94
5	morpholine (**3d**)	1.0	2.0	**4d**	73
6	piperidine (**3e**)	1.0	2.5	**4e**	81
7	PhNHMe (**3f**)	1.0	19.0	**4f**	–[c]

[a] The feed ratio of amine to CS_2 is 2:1.
[b] Isolated yields.
[c] No reaction.



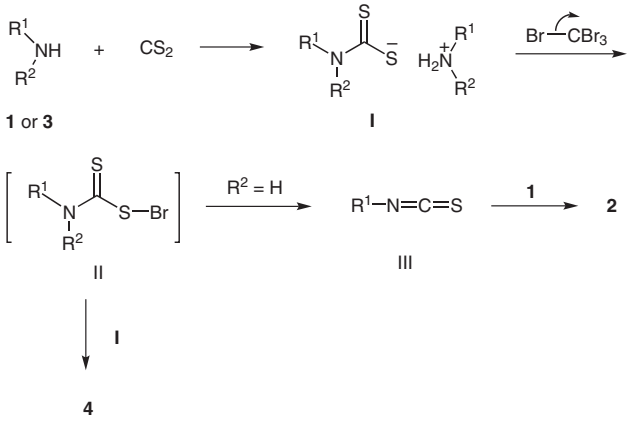
Equation 1

Next, the reactions of carbon disulfide with secondary amines were carried out under identical conditions. Gratifyingly, when a series of secondary amines like **3a–e** (2.0 equiv) were mixed with carbon disulfide (1.0 equiv) in the presence of carbon tetrabromide (1.0 equiv) at room tem-

perature, thiuram disulfides **4a–e** were achieved in good to excellent yields (73–96%, Table 3, entries 2–6). Thiuram disulfides may be used as the accelerator and vulcanization agents in the rubber industry[14] and are the precursor of organic dithiocarbamates.[15] Thus, an effective alternative route to thiuram disulfides was developed. Likewise, the remarkably promotion effect by carbon tetrabromide was observed in this S–S coupling reaction. In particular, in the absence of carbon tetrabromide, the reaction of dimethylamine (**3a**) with carbon disulfide needs 19 hours to go to completion, giving thiuram disulfide **4a** in 48% yield (Table 3, entry 1), while in the reaction with carbon tetrabromide, the reaction time was only one hour and the yield reached up to 95% (Table 3, entry 2). The significantly shorter reaction time (approx. 19-fold) and improved yield (nearly twofold) suggested that different reaction mechanisms are involved in the systems with and without carbon tetrabromide. The scope of the amines in the carbon tetrabromide mediated reactions leading to the thiuram disulfides was investigated. It was found that aliphatic secondary amines are effective in the reaction (Table 3, entries 2–6), while aromatic secondary amines, like *N*-methylaniline (**3f**), were inert to the reaction explored here regardless of the presence or absence of carbon tetrabromide (Table 3, entry 7). The use of thiocarbonyl thio compounds in free radical polymerization as agents that allow control of the molecular weight and polydispersity of polymers is now widespread.[16–18] The process is referred to as reversible addition fragmentation chain transfer (RAFT) mediated polymerization.[19] As an extension of the work on the synthesis of thiuram disulfides mentioned above, in the following work, the reaction of sodium isopropoxide (2.0 equiv) and carbon disulfide (2.0 equiv) in the presence of carbon tetrabromide (1.0 equiv) was tried and as a result, diisopropyl xanthogen disulfide (**5**) was successfully prepared in moderate yield (Equation 1). Clearly, such types of compounds could be readily synthesized utilizing this protocol. From above it can be concluded that this S–S coupling reaction is general to a wide range of thiuram disulfides and xanthate disulfides.

To understand the possible mechanism, some supplementary experiments were performed. The reaction of butylamine (**1a**), carbon disulfide, and carbon tetrabromide was performed in the dark under a nitrogen atmosphere. Consequently, the reaction rate exhibited almost no change and the corresponding product **2a** was obtained in comparable yield. In another isolated experiment, 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO), an efficient radical trapping agent, was added into the reaction mixture under otherwise identical conditions.

It was found that TEMPO has little influence on the reaction time and the product yield. Thus, a possible radical mechanism for the formation of thioureas **2** and thiuram disulfides **3** was excluded. To further understand the possible mechanism, the amount of carbon tetrabromide was examined. It was found that a catalytic amount of carbon



Scheme 1 Proposed mechanism for the formation of thioureas **2** and thiuram disulfides **4**

tetrabromide was insufficient to drive the reaction of butylamine (**1a**) and carbon disulfide to completion in a shorter time and a higher yield.

On the basis of the above experimental results and the work reported by us[13] and Abele et al.,[20] a possible mechanism for the formation of thiourea/thiones **2** and thiuram disulfides **4** was proposed (Scheme 1). Initially, nucleophilic attack of the mesomeric thioanion of **I** at the bromine atom of carbon tetrabromide produces the sulfenyl bromide **II**.[21] In the case of primary amines, isothiocyanates **III** may be formed (probably via the elimination of HSBr), followed by the addition of the amine, leading to the formation of thioureas **2**. When secondary amines are employed, the S–S coupling between sulfenyl bromide **II** and the dithiocarbamate anion **I** would take place, affording the disulfides **4** in high yields.[22] Sulfenyl bromides are highly reactive and electrophilic species, but rather unstable.[23] The proposed mechanism was supported by the isolation of trace amount of 4-tolyl isothiocyanate in the reaction of *p*-toluidine (**1d**) with carbon disulfide and carbon tetrabromide mentioned above (Table 1, entry 6). In addition, bromoform byproduct was identified in the experiments (a singlet at $\delta = 6.82$ in the ^{1}H NMR spectroscopy).

In conclusion, the carbon tetrabromide promoted reaction of amines with carbon disulfide has been disclosed. By this protocol, useful thioureas and thiuram disulfides were successfully prepared with high efficiency from primary and secondary amines, respectively. The advantages such as the high yields and short reaction times and mild conditions (no heating was required) make this reaction effective and practical. Further work on carbon tetrabromide mediated C–C coupling reactions is underway in our laboratory.

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. ^{1}H and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on a FT-IR spectrophotometer in the range of 400–4000 cm^{-1}. MS were recorded on a VG Platform mass spectrometer.

1,3-Dibutylthiourea (2a); Typical Procedure
CS_2 (0.06 mL, 1.0 mmol) was added to a soln of **1a** (0.20 mL, 2.0 mmol) in DMF (2.0 mL) in an ice-water bath; the mixture was stirred for 5 min. CBr_4 (331 mg, 1.0 mmol) was added to the mixture and it was stirred at r.t. for 0.3 h. The mixture was poured into ice-water (80 mL) with stirring and extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were concentrated and subjected to column chromatography (silica gel, petroleum ether–EtOAc, 15:1) to give **2a** (171 mg, 91%) as a white solid; mp 69–71 °C.

IR (KBr): 3734, 3219, 2960, 2928, 2860, 1568, 1520, 1247 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.5 Hz, 6 H), 1.34–1.42 (m, 4 H), 1.55–1.61 (m, 4 H), 3.39 (m, 4 H), 5.73 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 181.6, 44.4 (2 C), 31.3 (2 C), 20.3 (2 C), 14.0 (2 C).

MS: *m*/*z* $[M]^+$ calcd: 188.1; found: 189.0 $[M + 1]^+$.

Anal. Calcd for $C_9H_{20}N_2S$: C, 57.40; H, 10.70; N, 14.87. Found: C, 57.49; H, 10.74; N, 14.79.

1,3-Dibenzylthiourea (2b)
White solid; mp 146–148 °C.

IR (KBr): 3741, 3261, 3197, 1502, 1449, 1420, 1329, 1243, 1080, 914, 730, 692, 640 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.87 (d, *J* = 5.5 Hz, 4 H), 7.23–7.36 (m, 10 H), 8.36 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 180.9, 135.9 (2 C), 127.9 (4 C), 126.9 (2 C), 126.6 (4 C), 47.6 (2 C).

MS: *m*/*z* $[M]^+$ calcd: 256.1; found: 257.0 $[M + 1]^+$.

Anal. Calcd for $C_{15}H_{16}N_2S$: C, 70.27; H, 6.29; N, 10.93. Found: C, 70.16; H, 6.32; N, 11.02.

1,3-Diphenylthiourea (2c)
White solid; mp 153–154 °C.

IR (KBr): 3735, 3649, 3208, 3036, 1558, 1345, 698 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.43 (m, 10 H), 7.92 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 180.1, 137.3 (2 C), 129.9 (4 C), 127.4 (2 C), 125.6 (4 C).

MS: *m*/*z* $[M]^+$ calcd: 228.1; found: 229.0 $[M + 1]^+$.

Anal. Calcd for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30; N, 12.27. Found: C, 68.31; H, 5.28, N, 12.34.

1,3-Di-4-tolylthiourea (2d)
White solid; mp 177–179 °C.

IR (KBr): 3151, 2921, 1557, 1508, 1249, 1142 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.35 (s, 6 H), 7.19–7.26 (m, 8 H), 7.80(s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 180.5, 137.5 (2 C), 134.6 (2 C), 130.4 (4 C), 125.8 (4 C), 21.4 (2 C).

MS: *m*/*z* $[M]^+$ calcd: 256.1; found: 257.0 $[M + 1]^+$.

Anal. Calcd for $C_{15}H_{16}N_2S$: C, 70.27; H, 6.29; N, 10.93. Found: C, 70.16; H, 6.27; N, 10.88.

1,3-Bis(4-chlorophenyl)thiourea (2e)
White solid; mp 172–174 °C.

IR (KBr): 3174, 3016, 2883, 2770, 1593, 1535, 1486, 1400, 1311, 1281, 1224, 1086, 823, 727 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.5 Hz, 4 H), 7.39 (d, *J* = 8.5 Hz, 4 H), 7.77(s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 180.1, 135.6 (2 C), 132.6 (2 C), 129.7 (4 C), 126.5 (4 C).

MS: *m*/*z* $[M]^+$ calcd: 296.0; found: 297.0 $[M + 1]^+$.

Anal. Calcd for $C_{13}H_{10}Cl_2N_2S$: C, 52.54; H, 3.39; N, 9.43. Found: C, 52.81; H, 3.41; N, 9.40.

1,3-Bis(2-chlorophenyl)thiourea (2f)
White solid; mp 125–126 °C.

IR (KBr): 3196, 3014, 2978, 1587, 1541, 1512, 1330, 1306, 1226, 1058, 722 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.25 (m, 2 H), 7.35 (m, 2 H), 7.47 (m, 2 H), 7.83 (s, 2 H), 7.94 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 179.6, 134.0 (2 C), 130.2 (2 C), 129.3 (2 C), 128.1 (2 C), 127.6 (2 C), 127.3 (2 C).

MS: *m*/*z* $[M]^+$ calcd: 296.0; found: 297.0 $[M + 1]^+$.

Anal. Calcd for $C_{13}H_{10}Cl_2N_2S$: C, 52.54; H, 3.39; N, 9.43. Found: C, 52.69; H, 3.38; N, 9.38.

4,5-Dihydro-1*H*-imidazole-2-thiol (2h)
White solid; mp 198–200 °C.

IR (KBr): 3370, 1506, 1446, 1419, 1133, 931, 746 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.62 (s, 1 H), 2.88 (s, 2 H), 2.96 (s, 2 H), 8.02 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 36.7, 31.7.

MS: *m*/*z* $[M]^+$ calcd: 102.0; found: 103.0 $[M + 1]^+$.

Anal. Calcd for $C_3H_6N_2S$: C, 35.27; H, 5.92; N, 27.42. Found: C, 35.33; H, 5.95; N, 27.38.

Oxazolidine-2-thione (2i)
White solid; mp 97–99 °C.

IR (KBr): 3292, 3047, 1621, 1490, 1475, 1335, 1064, 991, 648 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.55 (m, 4 H), 2.17 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.5, 31.2, 0.23.

MS: *m*/*z* $[M]^+$ calcd: 103.0; found: 104.0 $[M + 1]^+$.

Anal. Calcd for C_3H_5NOS: C, 34.93; H, 4.89; N, 13.58. Found: C, 34.86; H, 4.87; N, 13.65.

1,3-Dihydro-2*H*-benzimidazole-2-thione (2j)
White solid; mp >250 °C.

IR (KBr): 3155, 3116, 2982, 1558, 1514, 1468, 1358, 1180, 744, 602 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.71 (m, 4 H), 13.15 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.5, 131.7 (2 C), 121.8 (2 C), 109.0 (2 C).

MS: *m*/*z* $[M]^+$ calcd: 150.0; found: 151.0 $[M + 1]^+$.

Anal. Calcd for $C_7H_6N_2S$: C, 55.97; H, 4.03; N, 18.65. Found: C, 56.04; H, 4.04; N, 18.69.

Benzoxazole-2(3*H*)-thione (2k)
White solid; mp 192–194 °C.

IR (KBr): 3327, 1506, 1447, 1132, 1096, 931, 747 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.25–7.39 (m, 4 H), 11.44 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 181.0, 149.0, 130.5, 125.6, 124.8, 110.8, 110.5.

MS: *m*/*z* $[M]^+$ calcd: 151.0; found: 152.0 $[M + 1]^+$.

Anal. Calcd for C_7H_5NOS: C, 55.61; H, 3.33; N, 9.26. Found: C, 55.54; H, 3.37; N, 9.30.

Tetramethylthiuram Disulfide (4a); Typical Procedure
CS_2 (0.12 mL, 1.0 mmol) was added to a soln of **3a** (0.30 mL, 2.0 mmol) in DMF (2.0 mL) in an ice-water bath and the mixture was stirred for 5 min. CBr_4 (331 mg, 1.0 mmol) was added and the mixture was stirred at r.t. for 0.5 h and then poured into ice-water (80 mL) with stirring. The mixture was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were concentrated and subjected to column chromatography (silica gel, petroleum ether–EtOAc, 10:1) to give **4a** (228 mg, 95%) as a white solid; mp 154–156 °C.

IR (KBr): 2931, 2785, 1506, 1458, 1400, 1375, 1236, 1149, 970, 849 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.60 (s, 6 H), 3.63 (s, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.92, 47.82, 42.31.

MS: *m/z* $[M]^+$ calcd: 240.0; found: 241.0 $[M + 1]^+$.

Anal. Calcd for $C_6H_{12}N_2S_4$: C, 29.97; H, 5.03; N, 11.65. Found: C, 30.11; H, 5.01; N, 11.62.

Tetraethylthiuram Disulfide (4b)
White solid; mp 70–72 °C.

IR (KBr): 2974, 2915, 2869, 1506, 1497, 1457, 1418, 1375, 1350, 1272, 1195, 1149, 1060, 966, 912, 817, 669 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 6.5 Hz, 6 H), 1.48 (t, *J* = 6.5 Hz, 6 H), 4.02 (q, *J* = 7.0, 7.5 Hz, 8 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.91, 52.28, 47.84, 13.72, 11.70.

MS: *m/z* $[M]^+$ calcd: 296.1; found: 297.0 $[M + 1]^+$.

Anal. Calcd for $C_{10}H_{20}N_2S_4$: C, 40.50; H, 6.80; N, 9.45. Found: C, 40.34; H, 6.81; N, 9.48.

Tetrabutylthiuram Disulfide (4c)
Yellow liquid.

IR (KBr): 2958, 2930, 2871, 1488, 1457, 1416, 1367, 1291, 1248, 1221, 1179, 1146, 1091, 1111, 1002, 935, 905, 863, 733, 669, 418 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.0, 7.5 Hz, 6 H), 1.00 (t, *J* = 7.0, 7.5 Hz, 6 H), 1.33 (q, *J* = 7.0, 7.5 Hz, 4 H), 1.44 (q, *J* = 7.5 Hz, 4 H), 1.72 (m, 4 H), 1.88 (m, 4 H), 3.93 (m, 8 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.68, 55.18, 50.99, 27.97, 25.89, 17.83, 17.79, 11.52, 11.47.

MS: *m/z* $[M]^+$ calcd: 408.2; found: 409.0 $[M + 1]^+$.

Anal. Calcd for $C_{18}H_{36}N_2S_4$: C, 52.89; H, 8.88; N, 6.85. Found: C, 53.01; H, 8.90; N, 6.84.

Bis(3-oxapentamethylene)thiuram Disulfide (4d)
White solid; mp 120–122 °C.

IR (KBr): 2961, 2916, 2853, 1739, 1688, 1645, 1514, 1473, 1419, 1300, 1263, 1227, 1110, 1061, 1030, 977, 908, 858, 797, 674, 533 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.84 (t, *J* = 5.0 Hz, 8 H), 4.30 (s, 8 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.07, 66.65, 54.14, 52.00.

MS: *m/z* $[M]^+$ calcd: 324.0; found: 325.0 $[M + 1]^+$.

Anal. Calcd for $C_{10}H_{16}N_2O_2S_4$: C, 37.01; H, 4.97; N, 8.63. Found: C, 37.28; H, 4.99; N, 8.65.

Dipentamethylenethiuram Disulfide (4e)
White solid; mp 124–126 °C.

IR (KBr): 2939, 2854, 1653, 1636, 1558, 1506, 1479, 1454, 1429, 1362, 1281, 1257, 1242, 1221, 1137, 1107, 1019, 1005, 958, 892, 852, 599, 512, 458, 418 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.76 (s, 12 H), 4.22 (m, 8 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.91, 56.10, 52.87, 26.74, 25.72, 24.46.

MS: *m/z* $[M]^+$ calcd: 320.0; found: 321.0 $[M + 1]^+$.

Anal. Calcd for $C_{12}H_{20}N_2S_4$: C, 44.96; H, 6.29; N, 8.74. Found: C, 45.21; H, 6.28; N, 8.77.

Diisopropyl Xanthogen Disulfide (5)
Na (0.046 g, 2.0 mmol) was added to anhyd *i*-PrOH (2 mL) in an ice-water bath. After the Na had dissolved, CS_2 (0.12 mL, 2.0 mmol) was then added followed by CBr_4 (331 mg, 1.0 mmol). The mixture was stirred at r.t. for 1.0 h and then poured into ice water (80 mL) with stirring. The mixture was extracted with CH_2Cl_2 (3 × 60 mL) and the combined organic layers were concentrated and subjected to column chromatography (silica gel, petroleum ether–EtOAc, 24:1) to give **5** (137 mg, 51%) as a yellow solid; mp 52–54 °C.

IR (KBr): 2981, 2930, 1693, 1378, 1265, 1087, 1007, 897, 796 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.39 (s, 6 H), 1.40 (s, 6 H), 5.69 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.7 (2 C), 80.3 (2 C), 21.1 (4 C).

MS: *m/z* $[M]^+$ calcd: 270.0; found: 271.0 $[M + 1]^+$.

Anal. Calcd for $C_8H_{14}O_2S_4$: C, 35.53; H, 5.22. Found: C, 35.39; H, 5.19.

Acknowledgment

Financial support of this research by NSFC (20672019), NENU-STB07007 and Science Foundation for Young Teachers of Northeast Normal University (20060313) is gratefully appreciated.

References

(1) (a) Hunter, W. H.; Edgar, D. E. *J. Am. Chem. Soc.* **1932**, *54*, 2025. (b) Abele, E.; Rubina, K.; Abele, R.; Gaukhman, A.; Lukevics, E. *J. Chem. Res., Synop.* **1998**, 618. (c) Abele, E.; Fleisher, M.; Rubina, K.; Abele, R.; Lukevics, E. *J. Mol. Catal. A: Chem.* **2001**, *165*, 121. (d) Schreiner, P. R.; Lauenstein, O.; Kolomitsyn, I. V.; Nadi, S.; Fokin, A. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 1895. (e) Fokin, A. A.; Schreiner, P. R. *Adv. Synth. Catal.* **2003**, *345*, 1035. (f) Camps, X.; Schönberger, H.; Hirsch, A. *Chem. Eur. J.* **1997**, *3*, 561.

(2) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *J. Am. Chem. Soc.* **1946**, *68*, 154.

(3) (a) Yadav, J. S.; Reddy, B. V. S.; Harikishan, K.; Madan, C.; Narsaiah, A. V. *Synthesis* **2005**, 2897. (b) Chandra, T.; Brown, K. L. *Tetrahedron Lett.* **2005**, *46*, 8617. (c) Chen, M.-Y.; Patkar, L. N.; Jan, M.-D.; Lee, A. S.-Y.; Lin, C.-C. *Tetrahedron Lett.* **2004**, *45*, 635. (d) Chen, M.-Y.; Lee, A. S.-Y. *J. Org. Chem.* **2002**, *67*, 1384.

(4) (a) Appel, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801. (b) Rabinowitz, R.; Marcus, R. *J. Am. Chem. Soc.* **1962**, *84*, 1312.

(5) (a) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769. (b) Mori, M.; Tonogaki, K.; Kinoshita, A. *Org. Synth.*, Vol. 81; John Wiley & Sons: London, **2005**, 1. (c) Marshall, J. A.; Yanik, M. M.; Adams, N. D.; Ellis, K. C.; Chobanian, H. R. *Org. Synth.*, Vol. 81; John Wiley & Sons: London, **2005**, 157. (d) Donovan, P. M.; Scott, L. T. *J. Am. Chem. Soc.* **2004**, *126*, 3108.

(6) (a) Johnstone, C.; Kerr, W. J.; Scott, J. S. *Chem. Commun.* **1996**, 341. (b) Zhong, Y.-L.; Lee, J.; Reamer, R. A.; Askin, D. *Org. Lett.* **2004**, *6*, 929. (c) Kadokawa, J.; Habu, H.; Fukamachi, S.; Karasu, M.; Tagaya, H.; Chiba, K. *Macromol. Rapid Commun.* **1998**, *19*, 657. (d) Kadokawa, J.; Habu, H.; Fukamachi, S.; Karasu, M.; Tagaya, H.; Chiba, K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2205. (e) Yang, Y.-H.; Shi, M. *J. Org. Chem.* **2005**, *70*, 8645.

(7) Smith, J.; Liras, J. L.; Schneider, S. E.; Anslyn, E. V. *J. Org. Chem.* **1996**, *61*, 8811.

(8) (a) Hennrich, G.; Sonnenschein, H.; Resch-Genger, U. *J. Am. Chem. Soc.* **1999**, *121*, 5073. (b) Pedireddi, V. R.; Chatterjee, S.; Ranganathan, A.; Rao, C. N. R. *J. Am. Chem. Soc.* **1997**, *119*, 10867. (c) Burrows, A. D.; Menzer, S.; Michael, D.; Mingos, P.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Dalton Trans.* **1997**, 4237. (d) Smith, J.; Liras, J. L.; Schneider, S. E.; Anslyn, E. V. *J. Org. Chem.* **1996**, *61*, 8811.

(9) (a) Kearney, P. C.; Frenandez, M.; Flygare, J. A. *J. Org. Chem.* **1998**, *63*, 196. (b) Boga, C.; Forlani, L.; Silvestroni, C.; Corradi, A. B.; Sagarabotto, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1363. (c) Patil, D. G.; Chedekel, M. R. *J. Org. Chem.* **1984**, *49*, 997. (d) Paul, S.; Gupta, M.; Gupta, R.; Loupy, A. *Synthesis* **2002**, 75.

(10) Selected examples: (a) Song, J.; Wang, Y.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 6048. (b) Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X.; Takemoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 119. (c) Wang, J.; Li, H.; Duan, W.; Zu, L.; Wang, W. *Org. Lett.* **2005**, *7*, 4713. (d) Cao, C.-L.; Ye, M.-C.; Sun, X.-L.; Tang, Y. *Org. Lett.* **2006**, *8*, 2901. (e) Okino, T.; Nakamura, S.; Furukawa, T.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 625. (f) Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 10012. (g) Reisman, S. E.; Doyle, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 7198.

(11) (a) Wagner-Jauregg, T.; Arnold, H.; Rauen, H. *Ber. Dtsch. Chem. Ges. B* **1941**, *74*, 1372. (b) Chinchilla, R.; Nájera, C.; Sánchez-Agulló, P. *Tetrahedron: Asymmetry* **1994**, *5*, 1393. (c) Shriner, R. L.; Snow, C. D. *Org. Synth. Coll. Vol. III*; John Wiley & Sons: London, **1955**, 394.

(12) (a) Ballabeni, M.; Ballini, R.; Bigi, F.; Maggi, R.; Parrini, M.; Predieri, G.; Sartori, G. *J. Org. Chem.* **1999**, *64*, 1029. (b) Dunn, A. D.; Rudorf, W. D. *Carbon Disulphide in Organic Chemistry*; Ellis Horwood: Chichester, **1997**, 226–315. (c) Yamazaki, N.; Tomioka, T.; Higashi, F. *Synthesis* **1975**, 384. (d) Ranu, B. C.; Dey, S. S.; Bag, S. *ARKIVOC* **2003**, *(ix)*, 14; http://www.arkat-usa.org/home.

(13) Tan, J.; Liang, F.; Wang, Y.; Cheng, X.; Liu, Q.; Yuan, H. *Org. Lett.* **2008**, *10*, 2485.

(14) Thorn, G. D.; Ludwig, R. A. *The Dithiocarbamates and Related Compounds*; Elsevier: Amsterdam, **1962**.

(15) Gronowitz, S.; Hörnfeldt, A.-B.; Temciuc, M. *Synthesis* **1993**, 483.

(16) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379.

(17) Moad, G.; Chiefari, J.; Chong, B. Y.; Krstina, J.; Mayadunne, R. T.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polym. Int.* **2000**, *49*, 993.

(18) Webera, W. G.; McLeary, J. B.; Sandersona, R. D. *Tetrahedron Lett.* **2006**, *47*, 4771.

(19) Chiefari, J.; Chong, Y. K. B.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559.

(20) Abele, E.; Abele, R.; Lukevics, E. *J. Chem. Res., Synop.* **1999**, 624.

(21) Selected examples for sulfenyl halides, see: (a) Koval', I. V. *Russ. Chem. Rev. (Engl. Transl.)* **1995**, *64*, 731. (b) Schroll, A. L.; Eastep, S. J.; Barany, G. *J. Org. Chem.* **1990**, *55*, 1475. (c) Kharasch, N.; Gleason, G. I.; Buess, C. M. *J. Am. Chem. Soc.* **1950**, *72*, 1796. (d) Kharasch, N.; Langford, R. B. *J. Org. Chem.* **1963**, *28*, 1903. (e) Romano, R. M.; Della Vedova, C. O.; Downs, A. J.; Greene, T. M. *J. Am. Chem. Soc.* **2001**, *123*, 5794. (f) Kuhle, E. *Synthesis* **1970**, 561. (g) Kato, S.; Komatsu, Y.; Miyagawa, K.; Ishida, M. *Synthesis* **1983**, 552.

(22) Goto, K.; Holler, M.; Okazaki, R. *Chem. Commun.* **1998**, 1915.

(23) The sulfenyl bromide intermediate is highly active and can not be isolated easily. Also refer to: (a) Tudge, M.; Tamiya, M.; Savarin, C.; Humphrey, G. R. *Org. Lett.* **2006**, *8*, 565. (b) Schlosser, K. M.; Krasutsky, A. P.; Hamilton, H. W.; Reed, J. E.; Sexton, K. *Org. Lett.* **2004**, *6*, 819. (c) Goto, K.; Holler, M.; Okazaki, R. *Chem. Commun.* **1998**, 1915.