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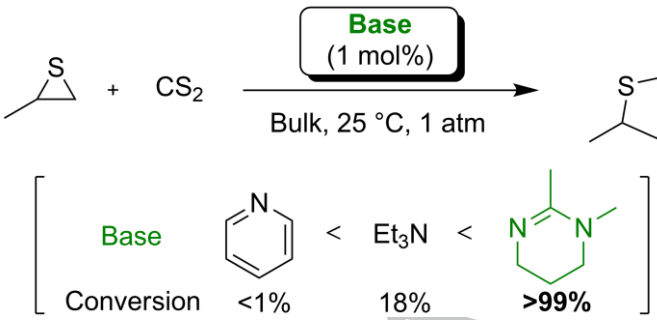

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Cyclic and linear amidine catalysts for the efficient synthesis of cyclic trithiocarbonates from carbon disulfide and episulfides under mild conditions

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ABSTRACT

Cyclic and linear amidines effectively catalyzed the reaction of carbon disulfide and episulfides under mild conditions, such as ordinary pressure and ambient temperature, to give the corresponding cyclic trithiocarbonates in high yields.

Introduction

Cyclic trithiocarbonates are key materials for the synthesis of tetrathiafulvalene derivatives,[1] sulfur-containing metal complexes,[2] crown thioethers,[3] dithiocarbonimidates[4] and dithiocarbamates,[5] which have recently attracted significant attention. Additionally, cyclic trithiocarbonates are used as reversible addition-fragmentation chain transfer (RAFT) agents, in order to synthesize amphiphilic multiblock co-polymers[6] and hyperbranched-linking-hyperbranched polymers[7] from vinyl monomers. However, efficient methods for the synthesis of cyclic trithiocarbonates are limited to only a few reports. One of the most common processes is alkylation of the trithiocarbonate anion with alkylene dihalides or alkylene dithiols in the presence of a phase-transfer catalyst.[8] This alkylation produces large amounts of by-products such as alkali halides and/or alkali trithiocarbonates because it requires excess amounts of carbon disulfide (CS_2) and bases. Another of the more simple processes is the incorporation of CS_2 into episulfides using catalytic triethylamine[9] or lithium *tert*-butoxide.[10] However, the triethylamine-catalyzed reaction requires high pressure and moderate to high temperature in order to achieve high efficiency. The lithium *tert*-butoxide-catalyzed reaction gives only moderate yields of cyclic trithiocarbonates. On the other hand, the ring-expansion addition of epoxides with CS_2 (1.8-7.0 equiv.) in the presence of a catalytic amount of the bimetallic aluminum(salen) complex give mixtures of cyclic dithiocarbonates and cyclic trithiocarbonates.[11] We have previously reported that isopropoxytitanatrane effectively catalyzed the reaction of cyclic ethers (epoxide or oxetane) and CS_2 (2 equiv.) to obtain the corresponding cyclic trithiocarbonates with high selectivity.[12] However, this reaction requires both high temperatures and long reaction times to obtain the cyclic trithiocarbonates in high yields. During the course of our research on the synthesis of cyclic trithiocarbonates using several basic catalysts, we found that cyclic and linear amidines efficiently catalyzed the ring-expansion addition of episulfides with CS_2 (Fig. 1). Herein, we report a novel and efficient method for the synthesis of cyclic trithiocarbonates from episulfides and CS_2 using catalytic amounts of cyclic and linear amidines under mild conditions, such as ordinary pressure and ambient temperature (Scheme 1).

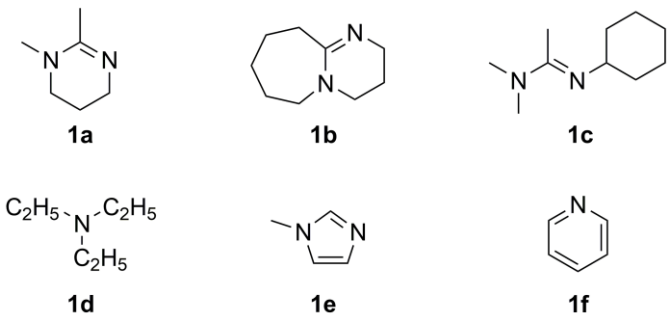

Figure 1. Amidines and amines used in this study.

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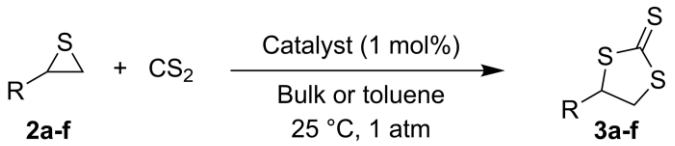


2a-f **3a-f**

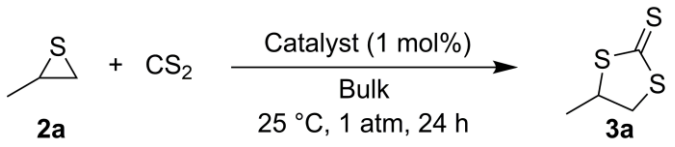
a: R = CH_3, **b**: R = $PhOCH_2$, **c**: R = CH_2=C(CH_3)CO_2CH_2, **d**: R = CH_2=$CHCH_2OCH_2$, **e**: R = $CH_3(CH_2)_3OCH_2$, **f**: R = $CH_3(CH_2)_9$

Scheme 1. Synthesis of cyclic trithiocarbonates from episulfides.

Results and Discussion

First, we investigated the effect of the structures of the catalysts on the ring-expansion addition of **2a** and CS_2 (2 equiv.) in bulk at 1 atm and ambient temperature (Table 1). In a typical experiment, CS_2 (2 mmol) was added to the catalyst (0.01 mmol), and the resulting mixture stirred at 25 °C. The colorless mixture changed to an orange solution within a few seconds, and then a blood red syrup gradually precipitated from the solution, indicating formation of the zwitterionic dithiocarbamate. After stirring for 10 minutes, **2a** (1 mmol) was added to the reaction mixture. The blood red syrup gradually dissolved, and then the color of the mixture changed from pale orange to pale yellow. The reaction was monitored by ^{1}H NMR spectroscopy. As shown in Table 1, strongly basic cyclic and linear amidines (**1a**, **1b** and **1c**) gave **3a** in quantitative yields (Entries 1-3).[13] In contrast, moderately basic triethylamine (**1d**) afforded **3a** in very low yield (Entry 4), as suggested by the fact that the reaction of **2a** and CS_2 (5 equiv.) with **1d** (10 mol%) required relatively severe conditions such as 8000 kg/cm^2 and 40 °C.[9] The use of weakly basic amines such as 1-methylimidazole (**1e**) and pyridine (**1f**) resulted in almost no reaction under mild conditions (Entries 5 and 6), which indicates that the high basicity of the amidine moiety is a prerequisite for catalysis.

Table 1. Effect of the structures of the catalysts on the synthesis of **3a** under ambient conditions without solvent.[a]



2a **3a**

Entry	Catalyst (pK_a /-)[b]	Yield **3a** (%)[c]
1	**1a** (13.42±0.20)	>99
2	**1b** (13.28±0.20)	99
3	**1c** (12.53±0.20)	>99
4	**1d** (10.62±0.25)	18
5	**1e** (7.01±0.1)	3
6	**1f** (5.23±0.1)	<1

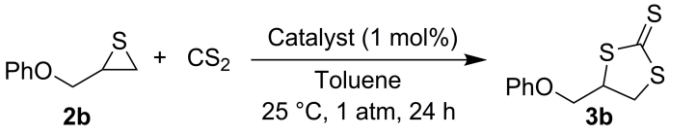
[a]Reagents and conditions: **2a** (1 mmol), CS_2 (2 mmol), catalyst (0.01 mmol), 25 °C, 24 h.

[b]pK_a values were obtained from SciFinder.[14]

[c]Determined by ^{1}H NMR spectroscopy.

Next, the ring-expansion addition of **2b** with CS_2 was carried out in toluene for the synthesis of **3b** as a solid product (Table 2). The episulfide (**2b**) was synthesized by our previous method.[15] As in the case of bulk conditions, cyclic and linear amidines (**1a**, **1b** and **1c**) also gave **3a** in quantitative yields (Entries 1-3). The use of **1d** resulted in a remarkably decreased yield of 24%, and the yield was decreased to less than 10% when **1e** and **1f** were used as catalysts (Entries 4-6). The catalytic activity was affected by the strongly basic amino group (pK_a > 12) on the catalysts, as shown by the result that the catalytic activity increased with increasing basicity of the amino group, that is, amidine > trialkylamine > nitrogen-containing aromatic heterocycle. A plausible mechanism for the catalytic synthesis of cyclic trithiocarbonates is shown in Scheme 2. Initially, the zwitterionic dithiocarbamate is formed by nucleophilic attack of the nitrogen atom of the amidine moiety onto the carbon atom of CS_2, and subsequent nucleophilic attack on the thiirane ring which leads to the ring-opened alkyl trithiocarbonate anion. Finally, ring-closure through elimination of the catalyst gives the cyclic trithiocarbonate.

Table 2. Effect of the structures of the catalysts on the synthesis of **3b** in toluene under ambient conditions.[a]



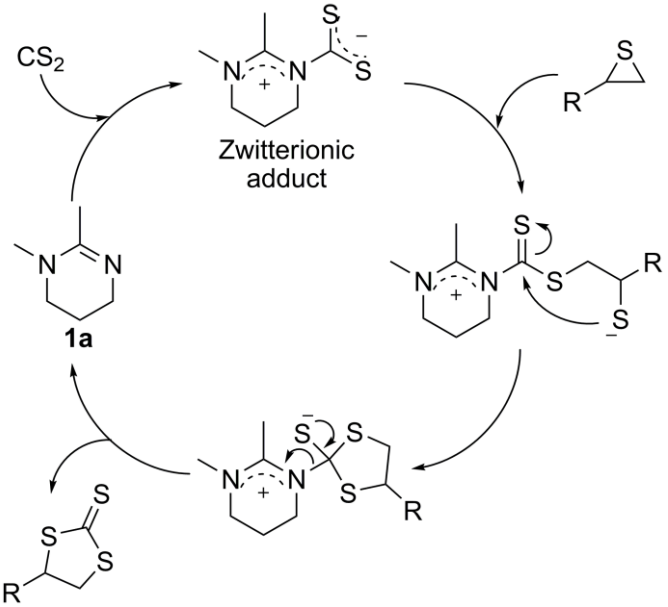
2b **3b**

Entry	Catalyst (pK_a /-)[b]	Yield **3b** (%)[c]
1	**1a** (13.42±0.20)	>99
2	**1b** (13.28±0.20)	97
3	**1c** (12.53±0.20)	>99
4	**1d** (10.62±0.25)	24
5	**1e** (7.01±0.1)	8
6	**1f** (5.23±0.1)	2

[a]Reagents and conditions: **2b** (1 mmol), CS_2 (2 mmol), catalyst (0.01 mmol), toluene (0.2 mL), 25 °C, 24 h.

[b]pK_a values were obtained from SciFinder.[14]

[c]Determined by ^{1}H NMR spectroscopy.

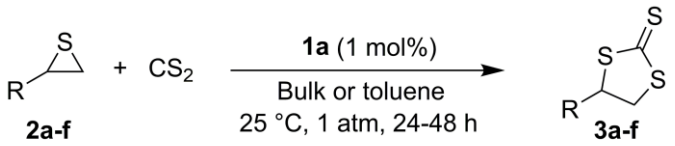


Scheme 2. Plausible mechanism for the catalyzed synthesis of cyclic trithiocarbonates from episulfides and CS_2.

Furthermore, we examined the synthesis of various cyclic trithiocarbonates from episulfides using **1a** (1 mol%) at 1 atm and 25 °C.[16] The episulfides (**2c**-**f**) were synthesized by our previous method.[15] As shown in Table 3, the cyclic trithiocarbonates (**3a** and **3b**) were isolated in high yield (97% and 98%) after short column chromatography on silica gel (Entries 1 and 2). 2-(Methacryloyloxymethyl)thiirane (**2c**), 2-(allyloxymethyl)thiirane (**2d**) and 2-(butoxymethyl)thiirane (**2e**) containing electron withdrawing groups on the carbon atom next

to the epoxy group were as reactive as **2b**, and the corresponding cyclic trithiocarbonates (**3c**, **3d** and **3e**) were isolated in high yields (Entries 3-6). The episulfide containing a long-chain alkyl group, 2-decylthiirane (**2f**), had a lower reactivity than the other episulfides (Entry 7). When the reaction time was extended from 24 to 48 h, the conversion of **2f** increased and the cyclic trithiocarbonate (**3f**) was isolated in high yield (Entry 8).

Table 3. Synthesis of various cyclic trithiocarbonates using **1a** under ambient conditions.[a]



2a-f **3a-f**

a: R = CH_3, **b**: R = $PhOCH_2$, **c**: R = CH_2=C(CH_3)CO_2CH_2, **d**: R = CH_2=$CHCH_2OCH_2$, **e**: R = $CH_3(CH_2)_3OCH_2$, **f**: R = $CH_3(CH_2)_9$

Entry	Episulfide	Solvent	Time (h)	Yield[b] (%)
1	**2a**	Bulk	24	99 (97)[c]
2	**2b**	Toluene	24	>99 (98)[c]
3	**2c**	Bulk	24	99 (92)[c]
4	**2d**	Bulk	24	>99 (99)[c]
5	**2e**	Bulk	24	89
6	**2e**	Bulk	36	>99 (97)[c]
7	**2f**	Bulk	24	69
8	**2f**	Bulk	48	>99 (98)[c]

[a] Reagents and conditions: **2a-f** (5 mmol), CS_2 (10 mmol), **1a** (0.05 mmol), bulk or in toluene (1 mL), 25 °C, 24-48 h.

[b]Determined by ^{1}H NMR spectroscopy.

[c]Isolated yields are in parentheses.

Conclusion

We have demonstrated that cyclic and linear amidines effectively catalyzed the reactions of CS_2 and episulfides to afford the corresponding cyclic trithiocarbonates in high yields under mild conditions such as ordinary pressure and ambient temperature. The catalytic activity is highly affected by the strongly basic amino group on the catalysts; amidines efficiently catalyze the trithiocarbonate-forming reaction, in contrast triethylamine and heterocyclic aromatic compound such as 1-methylimidazole and pyridine show low reactivity. We believe that the results obtained in this study will serve as a basis for creating a mild and simple method for the synthesis of cyclic trithiocarbonate-containing organic compounds.

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13. *Synthesis of 1,2-dimethyl-1,4,5,6-tetrahydropyrimidine (**1a**):* The mixture of *N*-methyl-1,3-diaminopropane (4.41 g, 50 mmol) and *N*,*N*-dimethylacetamide dimethyl acetal (90% purity, 7.77 g, 52.5 mmol) was stirred at 80 °C without solvent. After 1 h, the mixture was evaporated *in vacuo*, and the residue was distilled under reduced pressure to give **1a** (5.33 g, 95%) as a colorless liquid; B.p. 62-64 °C/1.0 kPa. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ˚C) δ (ppm): 1.83 (quin, *J* = 6.0 Hz, 2H, $NCH_2CH_2CH_2N$), 1.96 (s, 3H, CCH_3), 2.88 (s, 3H, NCH_3), 3.13 (t, *J* = 6.0 Hz, 2H, $NCH_2CH_2CH_2NCH_3$), 3.29 (t, *J* = 6.0 Hz, 2H, $NCH_2CH_2CH_2NCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$, 25 ˚C) δ (ppm): 22.0 ($NCH_2CH_2CH_2N$), 22.7 (CCH_3), 38.7 (NCH_3), 44.2 ($NCH_2CH_2CH_2NCH_3$), 48.3 ($NCH_2CH_2CH_2NCH_3$), 155.8 (NCN).
14. The pK_a values were calculated using Advanced Chemistry Development (ACD/Labs) software V11.02 ((c)1994-2016 ACD/Labs).
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16. *Typical procedure of cyclic trithiocarbonates (**3a-f**):* A mixture of CS_2 (10 mmol) and **1a** (0.05 mmol) was stirred at 25 ℃ for 10 min, and then episulfide (5 mmol) or a dilute solution of episulfide in toluene (1 mL) was added dropwise to the mixture. After the mixture was stirred at 25 °C for 24-48 h, the reaction mixture was diluted with ethyl acetate (10 mL), and washed with water (10 mL). The aqueous phase was extracted with ethyl acetate (10 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/acetone = 3:1) to give cyclic trithiocarbonate as a yellow oil (**3a**, **3c-f**) or solid (**3b**).

Supplementary Material

Supplementary data (experimental data and NMR spectra of isolated compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2018.xxx.

Highlights

- Efficient synthesis of cyclic trithiocarbonates from episulfides with CS_2.
- Cyclic and linear amidines had high catalytic activity.
- Cyclic trithiocarbonates were obtained in high yields under mild conditions.