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Synthesis of cyclic di- and trithiocarbonates from epoxides and carbon disulfide catalyzed by *N*-heterocyclic carbene

Jinsong Cao · Meng Yu · Hanzhu Li · Liang Wang · Xu Zhu · Guangying Wang · Yanhui Shi · Changsheng Cao

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Abstract The synthesis of cyclic di- and trithiocarbonates from the reaction of epoxides and carbon disulfide catalyzed by *N*-heterocyclic carbene prepared in situ is described. 1,3-Oxathiolane-2-thiones or 1,3-dithiolane-2-thiones was obtained in high yield with good selectivity when the reactions were carried out with **4** in DMSO at 100 °C in the presence of K_2CO_3. The possible catalytic mechanism was proposed.

Keywords *N*-Heterocyclic carbene · Carbon disulfide · Epoxide · Dithiocarbonate · Trithiocarbonate

Introduction

N-Heterocyclic carbenes (NHCs) have been investigated with great intensity in recent years, and a large number of publications and reviews relating to NHC complexes have been published [1–5]. NHCs usually serve as extremely strong σ-donor, and have been widely applied in catalysis [6–13]. We have preciously reported that the combination of NHC prepared in situ with $ZnBr_2$ catalyzes the synthesis of cyclic carbonates in high yield from epoxides and carbon dioxide under mild conditions (atmospheric pressure or even 0.05 MPa of CO_2) [14].

Cyclic thiocarbonates have attracted much attention in material and biological science. For example, dithiocarbonates are important compounds utilized for the preparation of polymers [15, 16], and trithiocarbonates have been found to show radio protective and insecticidal activity [17, 18]. The reaction between epoxides

Jinsong Cao and Meng Yu have contributed equally to this work.

J. Cao · M. Yu · H. Li · L. Wang · X. Zhu · G. Wang · Y. Shi (✉) · C. Cao (✉)
School of Chemistry and Chemical Engineering and Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou 221116, Jiangsu, People's Republic of China
e-mail: yhshi@jsnu.edu.cn

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and carbon disulfide is known to lead to a range of products, including dithiocarbonates and trithiocarbonates [19, 20]. To extend the scope of reactions catalyzed by NHC, it was decided to study the synthesis of di- and trithiocarbonate from epoxides and carbon disulfide, and the results were reported herein.

Experimental

General procedures

Imidazol(in)ium chlorides were prepared using literature procedures [21, 22]. THF and 1,4-dioxane were distilled from sodium benzophenone ketyl prior to use. DMF was stirred over $MgSO_4$ overnight, filtered, and then distilled over 4 Å molecular sieves. DMSO was distilled over calcium hydride and stored with 4 Å molecular sieves. All other reagents were commercially available and were used without further purification. ^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer at room temperature and referenced to the residual ^{1}H signals of the solvent.

General procedure to synthesize 1,3-oxathiolane-2-thiones and 1,3-dithiolane-2-thiones

An oven-dried 4 mL of vial with stir bar was charged with **4** (0.021 g, 0.05 mmol) and K_2CO_3 (0.007 g, 0.05 mmol) in the glove box. The vial was capped and moved out from the glove box, then epoxide (1 mmol), CS_2 (3 mmol, 180 μL) and 2 mL of DMSO were injected into the vial by syringe. The reaction was stirred at 80 °C for 48 h. After the reaction was cooled down, and 100 mL of water was added in the reaction mixture. The organic layer was extracted with DCM (3 × 15 mL), and dried by anhydrous Mg_2SO_4. The product was isolated by chromatography (eluent: EtOAc/PE = 1:5).

Characterization data

*Synthesis of compound **6** [24]*

An oven-dried 4 mL of vial with stir bar was charged with **4** (0.021 g, 0.05 mmol) and K_2CO_3 (0.007 g, 0.05 mmol) in the glove box. The vial was capped and moved out from the glove box, then CS_2 (0.5 mmol, 30 μL) and 2 mL of THF were injected into the vial by syringe. The reaction was stirred at 80 °C for 24 h until a red solid was formed and precipitated. The resulting mixture was filtered through a plug of Celite, and washed by DCM. The volatiles were removed by rotavapor, and the product was isolated by chromatography with DCM as eluent with 95 % yield.

Red solid (DCM), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, J = 7.6 Hz, 2H), 7.17 (d, J = 7.6 Hz, 4H), 3.51–3.45 (m, 4H), 1.39 (d, J = 6.4 Hz, 12H), 1.29 (d, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 130.6, 124.9, 113.2, 51.3, 29.3, 26.7, 23.7.

5-Ethyl-1,3-oxathiolane-2-thione (***7a***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08–5.01 (m, 1H), 3.58 (dd, $J = 10.8$ Hz, $J = 6.4$ Hz), 3.40 (t, $J = 9.6$ Hz, 1H), 2.10–1.99 (m, 1H), 1.93–1.83 (m, 1H), 1.10 (t, $J = 7.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.1, 93.2, 39.4, 27.2, 10.2.

4-Ethyl-1,3-dithiolane-2-thione (***7b***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.35–4.29 (m, 1H), 3.98 (dd, $J = 12.0$ Hz, $J = 6.4$ Hz, 1H), 3.71 (dd, $J = 12.0$ Hz, $J = 7.6$ Hz, 1H), 2.03 (m, 2 H), 1.08 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 227.9, 62.6, 48.0, 26.9, 12.7.

5-Butyl-1,3-oxathiolane-2-thione (***8a***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.13–5.06 (m, 1H),3.58 (dd. $J = 11.2$ Hz, $J = 6.8$ Hz, 1H), 3.40 (t, $J = 9.6$ Hz, 1H), 2.17 (s, 1H), 2.07–1.98 (m, 1H), 1.86-1.78 (m, 1H), 1.48–1.35 (m, 3H), 0.94 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.1, 91.8, 39.3, 33.4, 27.4, 22.3, 13.8.

4-Butyl-1,3-dithiolane-2-thione (***8b***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.41–4.37 (m, 1H), 3.97 (dd, $J = 11.6$ Hz, $J = 5.2$ Hz, 1H), 3.71 (dd, $J = 12.0$ Hz, $J = 8.0$ Hz, 1H), 1.98–1.88 (m, 2H), 1.34–1.31 (m, 4H), 0.93 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 227.9, 60.9, 48.2, 33.2, 30.3, 22.4, 13.8.

5-Chloromethyl-1,3-oxathiolane-2-thione (***9a***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39–5.21 (m, 1H), 3.86 (d, $J = 5.8$ Hz, 2H), 3.76 (d, $J = 7.4$ Hz, 1H), 3.70 (dd, $J = 11.3$ Hz, $J = 7.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.9, 88.4, 42.9, 37.3.

4-Chloromethyl-1,3-dithiolane-2-thione (***9b***) *[19]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.98–4.82 (m, 1H), 4.60 (t, $J = 8.4$ Hz, 1H), 4.42 (dd, $J = 9.2$ Hz, $J = 6.0$ Hz, 1H), 3.75 (dd, $J = 6.0$ Hz, $J = 2.4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 228.5, 78.4, 43.1, 33.8.

4-Phenyl-1,3-dithiolane-2-thione (***10b***) *[19]* Yellow crystal, mp 114–116 °C (EtOAc/PE), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.39 (m, 5H), 5.64 (dd, $J = 9.6$ Hz, $J = 10.0$ Hz, 1H), 4.17 (t, $J = 11.6$ Hz, 1H), 4.03 (dd, $J = 5.6$ Hz, $J = 12.0$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 227.2, 135.3, 129.3, 129.2, 127.5, 64.2, 49.8.

2-Thioxo-1,3-oxathiolan-5-yl)methyl benzoate (***11a***) *[23]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, $J = 7.2$ Hz, 2H), 7.61 (t, $J = 7.6$ Hz, 1H), 7.47 (t, $J = 7.6$ Hz, 2H), 4.70–4.63 (m, 3H), 4.21 (dd, $J = 12.4$ Hz, $J = 4.4$ Hz, 1H), 3.93 (dd, $J = 12.0$ Hz, $J = 3.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.7, 165.8, 133.6, 129.7, 128.9, 128.5, 87.9, 68.6, 36.1.

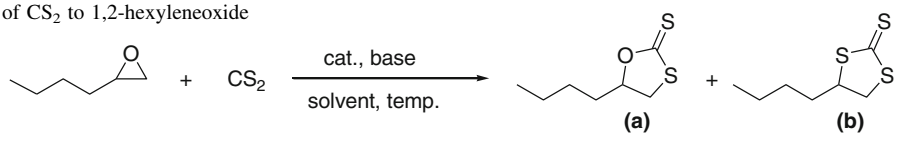
5-(Benzyloxymethyl)-1,3-oxathiolane-2-thione (***12a***) *[20]* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.31 (m, 5H), 4.59 (s, 2H), 4.48 (dd, $J = 8.4$ Hz, $J = 4.4$ Hz, 1H), 4.07 (dd, $J = 12.0$ Hz, $J = 5.6$ Hz, 1H), 3.96 (dd, $J = 12.0$ Hz,

$J = 4.8$ Hz, 1H), 3.86 (t, $J = 9.6$ Hz, 1H), 3.68 (dd, $J = 9.6$ Hz, $J = 5.6$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.9, 137.1, 128.5, 128.1, 127.8, 89.2, 73.7, 68.5, 36.1.

Results and discussion

Initially, the similar reaction conditions catalyzing the cycloaddition of epoxide with CO_2 [14] were tested for the reaction of epoxide with CS_2. When the reaction of 1,2-hexyleneoxide with carbon disulfide was carried out using 5 mol% of 4,5-dihydro-1,3-bis(2,4,6-trimethylphenyl)-1H-imidazolinium chloride (**2**), $ZnBr_2$, and K_2CO_3 in DMSO at 80 °C for 48 h, 58 % of 5-butyl-1,3-oxathiolane-2-thione and 4-butyl-1,3-dithiolane-2-thione was obtained in 68:32 ratio (Table 1, entry 1). However, it was found that Lewis acid has almost no effect on the yield and ratio of

Table 1 Screening of various of catalysts, solvents, bases, and Lewis acids for the cycloaddition reaction of CS_2 to 1,2-hexyleneoxide



Entry[a]	Cat.	CS_2 (eq.)	Lewis acid	Base	Solvent	Temp. (°C)	Yield (%)[b]	**a**:**b** ratio
1	**2**	3	$ZnBr_2$	K_2CO_3	DMSO	80	58	68:32
2	**2**	3	$AlCl_3$	K_2CO_3	DMSO	80	60	70:30
3	**2**	3	–	K_2CO_3	DMSO	80	60	70:30
4	**1**	3	–	K_2CO_3	DMSO	80	85	40:60
5	**3**	3	–	K_2CO_3	DMSO	80	78	66:34
6	**4**	3	–	K_2CO_3	DMSO	80	90	77:23
7	**5**	3	–	K_2CO_3	DMSO	80	92	52:48
8	**4**	3	–	Cs_2CO_3	DMSO	80	83	60:40
9	**4**	3	–	K_3PO_4	DMSO	80	50	65:35
10	**4**	3	–	*t*BuOK	DMSO	80	45	70:30
11	**4**	1	–	K_2CO_3	DMSO	80	73	14:86
12	**4**	1.5	–	K_2CO_3	DMSO	80	80	62:38
13	**4**	4.5	–	K_2CO_3	DMSO	80	88	75:25
14	**4**	6	–	K_2CO_3	DMSO	80	91	66:34
15	**4**	3	–	K_2CO_3	DMSO	50	70	70:30
16	**4**	3	–	K_2CO_3	DMSO	100	20	60:40
17	**4**	3	–	K_2CO_3	DMF	80	0	–
18	**4**	3	–	K_2CO_3	THF	80	0	–
19	**4**	3	–	K_2CO_3	1,4-dioxane	80	0	–

[a] Reaction conditions: the reaction was carried out in a 4 mL of vial containing 1,2-hexyleneoxide (127 μL, 1 mmol), CS_2 (1–6 mmol), the catalyst (0.05 mmol), base (0.05 mmol) and solvent (2 mL) with or without Lewis acid (0.05 mmol) at 50–100 °C for 48 h

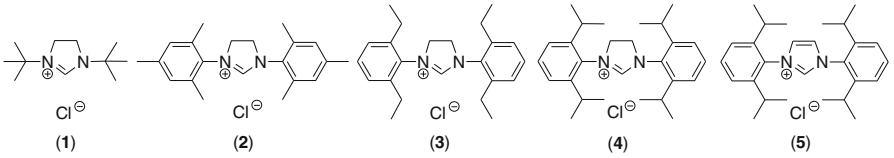
[b] Isolated yield with the average of two runs

the product (Table 1, entries 1–3). Therefore, no Lewis acid was added in further reactions. Screening tests, using a series of imidazol(in)ium chlorides (**1**–**5**, Scheme 1) with K_2CO_3 under the same conditions revealed that it seems that both steric issues and electronic properties of NHC play important roles in the cycloaddition (Table 1, entries 3–7). The best yield was attained by using diisopropyl substituted unsaturated *N*-phenyl imidazolinium chloride **5**; however, its saturated analogues **4** gave the better selectivity of the product. The base also affected the reaction (Table 1, entries 6, 8–10) and K_2CO_3 performed the best among all the bases tested. The solvent also has an effect on the reaction (entries 6, 17–19). The reaction was conducted in DMF, THF, and 1,4-dioxane providing no product, and the best solvent tested for the reaction is DMSO. To determine the optimum reaction conditions, the amount of CS_2 being used and reaction temperature were also tested in the cycloaddition reaction of 1,2-hexyleneoxide to CS_2 (Table 1, entries 6, 11–16). The results showed that the higher yield and better selectivity were obtained with 3 eq. of CS_2 at 80 °C for 48 h. Therefore, in the following studies, all the reactions were carried out with 5 mol% of **4** as catalyst, K_2CO_3 as base, 3 eq. of CS_2, and DMSO as a solvent at 80 °C for 48 h.

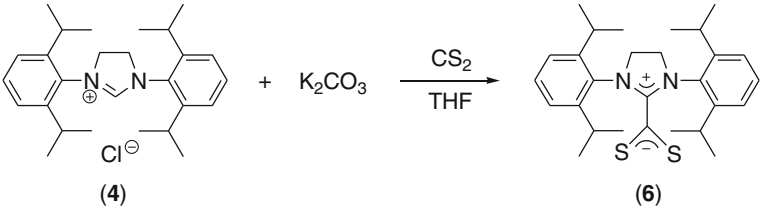
In order to better understand the reaction mechanism and determine the catalytic active species, the zwitterionic NHC-CS_2 adduct (**6**) (Scheme 2) was prepared and a few control experiments were conducted (Table 2) with the cycloaddition of hexyleneoxide to CS_2.

It can be seen from the Table 2 that no product was observed with only either imidazolinium chlorides **4** or base K_2CO_3 (Table 2, entries 1–2). The comparable yield and selectivity of products was observed by using **4**-CS_2 adduct and **4** with K_2CO_3, which suggests that the zwitterionic NHC-CS_2 adduct is probably the catalytic active species in the reaction.

To further probe the scope of the catalysis, a few selections of epoxides were screened under the optimum conditions (Table 3). All the reactions gave good total

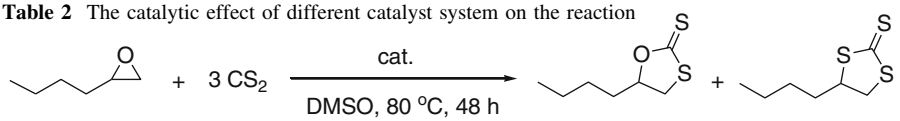


Scheme 1 Structure of imidazol(in)ium chlorides



Scheme 2 Synthesis of NHC-CS_2 adduct **6**

Table 2 The catalytic effect of different catalyst system on the reaction



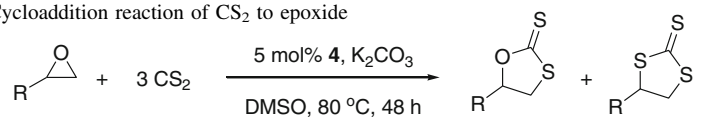
(**8a**) (**8b**)

Entry[a]	Catalytic system	Yield (%)[b]	**8a**:**8b** ratio
1	**4**	0	–
2	K_2CO_3	0	–
3	**4**, K_2CO_3	90	77:23
4	**4**-CS_2 adduct	91	72:28

[a] Reaction conditions: the reaction was carried out in a 4 mL of vial containing 1,2-hexyleneoxide (127 μL, 1 mmol), CS_2 (180 μL, 3 mmol), the catalyst (0.05 mmol) and DMSO (2 mL) at 80 °C for 48 h

[b] Isolated yield with the average of two runs

Table 3 Cycloaddition reaction of CS_2 to epoxide



(**a**) (**b**)

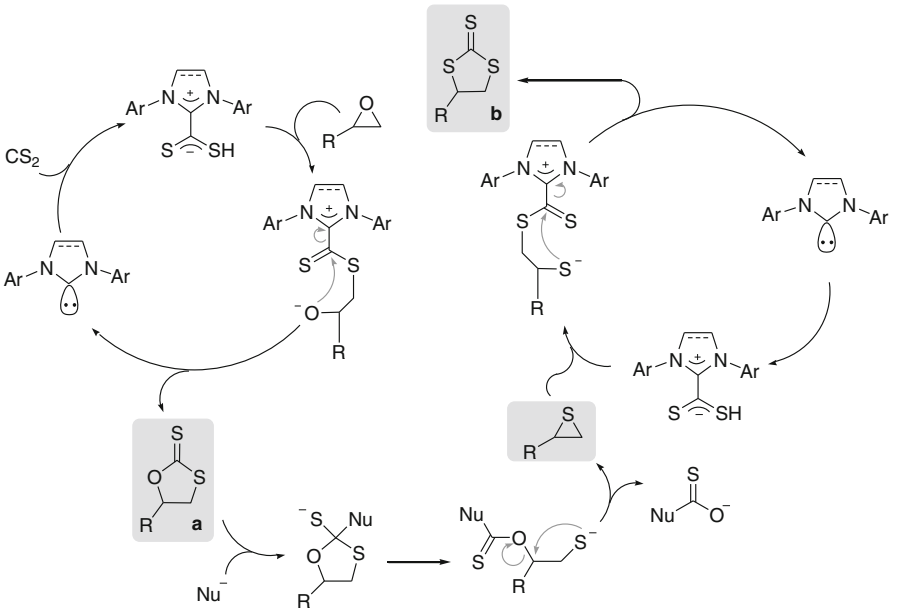
Entry[a]	R	Product	Yield[b]	**a**:**b** ratio
1	Et	**7a** + **7b**	92	75:25
2	*n*-Bu	**8a** + **8b**	90	77:23
3	$ClCH_2$	**9a** + **9b**	93	70:30
4	Ph	**10b**	95	<1:99
5	$PhCOOCH_2$	**11a**	89	>99:1
6	$PhCH_2OCH_2$	**12a**	86	>99:1

[a] Reaction conditions: the reaction was carried out in a 4 mL of vial containing epoxide (1 mmol), CS_2 (180 μL, 3 mmol), **4** (0.021 g, 0.05 mmol), K_2CO_3 (0.007 g, 0.05 mmol) and DMSO (2 mL) at 80 °C for 48 h

[b] Isolated yield with the average of two runs

yield of dithiocarbonates and trithiocarbonates (over 85 %). Interestingly, the reactions with alkyl substituted epoxides preferred dithiocarbonates over trithiocarbonates, and it is worth mentioning that only dithiocarbonates were achieved with oxiran-2-ylmethyl benzoate and 2-(benzyloxymethyl)oxirane as starting materials. However, the reaction with phenyl substituted epoxides gave only trithiocarbonates as the product in good yield.

Based on previous reports and our study, we proposed the possible mechanism of the cycloaddition reaction shown in Scheme 3. The possible nucleophile (Nu) in the catalytic cycle would be the base carbonate ion.



Scheme 3 The mechanism of the cycloaddition reaction of CS_2 and epoxide

In conclusion, we have demonstrated that NHC prepared in situ is a catalyst for the cycloaddition of CS_2 to epoxides. High conversions with good selectivity towards cyclic thiocarbonates were achieved using NHC precursor, 4,5-dihydro-1,3-bis(2, 6-diisopropylphenyl)-1H-imidazolinium chloride (**4**) with K_2CO_3 as base. The catalytic active species was investigated and the possible mechanism was proposed.

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