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<td>Author(s)</td>
<td>Okada, Megumi; Nishiyori, Ryuichi; Kaneko, Shiho; Igawa, Kazunobu; Shirakawa, Seiji</td>
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KI-Tetraethylene Glycol Complex as an Effective Catalyst for the Synthesis of Cyclic Thiocarbonates from Epoxides and CS₂


Abstract: An efficient synthesis of cyclic thiocarbonates from epoxides and CS₂ under mild reaction conditions was achieved when a KI-tetraethylene glycol complex catalyst was used as a readily available and economical catalyst. The effects of glycols and alkali metal halides were investigated in the present work to clarify the importance of both KI and tetraethylene glycol. The reaction mechanisms for the cyclic thiocarbonate synthesis are discussed based on the stereochemistry of products.

Introduction

Alkali metal halides, such as potassium and sodium halides, are among the most abundant and economical natural resources. Accordingly, the development of organic reactions using potassium and sodium halide catalysts, which are promoted by utilizing the ionic nature of these salts, is very attractive because it promotes the development of green and sustainable chemistry.[1] However, an alkali metal halide alone is a less-reactive catalyst in organic synthesis, due to its neutrality and to a low level of solubility in organic solvents. To solve these problems and to activate alkali metal halides, polyether compounds, such as crown ethers and polyethylene glycols, are often used with alkali metal halides in organic synthesis.[2] Polyether compounds are known to form complexes with potassium and sodium halides, and these complexes are soluble in organic solvents. Furthermore, the halide anions in these complexes exist in a more naked and nucleophilic version. By utilizing these properties, KI-polyether complex catalysts are applied to CO₂ fixation reactions with epoxidation, which are important reactions in green and sustainable chemistry.[3–5] The drawback of these catalytic systems has been the harsh reaction conditions (high pressure and high temperature) that are required to promote efficient CO₂ fixation.[6,4,5] In our recent study on the CO₂ fixation reactions with epoxides 1 under mild reaction conditions,[6–7] we successfully developed a practical method for the synthesis of cyclic carbonates in the presence of a KI-tetraethylene glycol complex catalyst (Scheme 1).[8] Based on these findings, we were next interested in the synthesis of cyclic thiocarbonates by the reaction of epoxides 1 with CS₂, which is an isoelectronic analogue of CO₂.[9] Although these two reactions are similar, the reaction mechanisms are totally different. In the present article, we discuss and clarify the reaction mechanisms of the cyclic thiocarbonate synthesis based on the stereochemistry of products (Scheme 1).

Results and Discussion

Our initial aim was to clarify the utility of a KI-tetraethylene glycol complex catalyst in the synthesis of cyclic thiocarbonates under mild conditions. The effects of glycols and alkali metal halides were investigated in a reaction with epoxide 1a and CS₂ (Scheme 2). When a mixture of epoxide 1a, CS₂ (1.2 equiv), and KI (10 mol %) was stirred for 5 h in the absence of tetraethylene glycol at room temperature (25 °C), cyclic dithiocarbonate 2a was obtained in a low yield (2%). On the other hand, the KI-tetraethylene glycol complex catalyst efficiently promoted the reaction of 1a and CS₂ under the same reaction conditions to give product 2a in a high yield (88%). It is noteworthy that cyclic trithiocarbonate 3a was also isolated as a minor product in this reaction (4%). To clarify the role of hydroxy groups in tetraethylene glycol, we also examined the reactions with tetraethylene glycol dimethyl ether and 18-crown-6. Very low

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Supporting information for this article is given via a link at the end of the document.
catalytic activities were observed in these reactions, which gave dithiocarbonate 2a in low yields with trace amounts of trithiocarbonate 3a. The effect of alkali metal halides was also investigated in the reaction with CS₂. Although a KCl complex with tetraethylene glycol showed quite low reactivity, a KBr-tetraethylene glycol complex catalyst moderately promoted the reaction to give 2a in a 59% yield with 3a in a 2% yield. The tendency of this reactivity with KBr is different from the reaction with CO₂[8]. The NaCl complex showed comparable reactivity in the case of the KI complex, but the selectivity for dithiocarbonate 2a to trithiocarbonate 3a was lower (2a/3a = 6.4:1) than that attained with the KI complex (2a/3a = 22:1).

With the effective catalysts in hand, the substrate generality of epoxides 1 for the synthesis of thiocarbonates was examined using a KI-tetraethylene glycol complex catalyst (Table 1). The reactions were efficiently promoted under mild reaction conditions, and dithiocarbonate products 2 were obtained in good-to-high yields. The selectivities for dithiocarbonates 2 to trithiocarbonates 3 were also good-to-high (2/3 = 4.3:1–>50:1).

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Conditions</th>
<th>Yield of 2 [%][b]</th>
<th>Yield of 3 [%][b]</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>n-Pr (1b)</td>
<td>40 °C, 24 h</td>
<td>65 (2b)</td>
<td>6 (3b)</td>
</tr>
<tr>
<td>2</td>
<td>CH₃CH₂CH₂ (1c)</td>
<td>40 °C, 16 h</td>
<td>65 (2c)</td>
<td>15 (3c)</td>
</tr>
<tr>
<td>3</td>
<td>CH₃=CHCH₂ (1d)</td>
<td>40 °C, 16 h</td>
<td>62 (2d)</td>
<td>12 (3d)</td>
</tr>
<tr>
<td>4</td>
<td>CH₃=CHCH₂OCH₂ (1e)</td>
<td>RT, 5 h</td>
<td>69 (2e)</td>
<td>4 (3e)</td>
</tr>
<tr>
<td>5</td>
<td>PhCH₂OCH₂ (1f)</td>
<td>RT, 5 h</td>
<td>63 (2f)</td>
<td>1 (3f)</td>
</tr>
<tr>
<td>6</td>
<td>CICO₂ (1g)</td>
<td>RT, 24 h</td>
<td>78 (2g)</td>
<td>trace (3g)</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: 1 (4.0 mmol), tetraethylene glycol (0.40 mol%), KI (0.40 mol%, 10 mol%), CS₂ (4.8 mmol, 1.2 equiv). [b] Yield of isolated products 2 and 3.

Enantiopure epoxides (1a, 1f, and 1h) were also submitted to the reaction with CS₂ under the influence of the KI-tetraethylene glycol complex catalyst (Scheme 3). To our delight, cyclic dithiocarbonates 2a, 2f, and 2h were obtained in good yields with a complete “retention” of the stereochemistry. On the other hand, cyclic trithiocarbonates 3a, 3f, and 3h were obtained in a complete “inversion” of the stereochemistry. The absolute configurations of the products 2 and 3 were determined by X-ray diffraction analysis of 2h and 3h.[10] Additionally, we proved that Werner’s catalytic system that uses a LiOBut catalyst [9j,k] also showed the same stereochemistry tendency demonstrated in the present reaction. It should be noted that this is a valuable example of the determination of absolute configurations for thiocarbonates in the reaction of enantiopure epoxides and CS₂.

Table 1. Substrate scope.[a]

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[a] Reaction conditions: 1 (4.0 mmol), tetraethylene glycol (0.40 mol%), KI (0.40 mol%, 10 mol%), CS₂ (4.8 mmol, 1.2 equiv). [b] Yield of isolated products 2 and 3.
intermediate trithiocarbonate retention of the stereochemistry. On the other hand, cyclic D
led to intermediate via hydrogen CO
the reaction with CS
1
reports,
Scheme
Based on these results and those of previous related reports,[6,11] the assumed mechanisms for the reaction of epoxides 1 and CS₂ were proposed in Schemes 4 and 5. The first step of the reaction with CS₂ is known to differ from the reaction with CO₂.[5] At first, an iodide anion attacks CS₂, which was activated via hydrogen-bonding with the hydroxyl groups of tetraethylene glycol (intermediate A). Subsequently, a nucleophilic attack by the resultant iododithioformate anion in intermediate B on epoxide 1 led to intermediate C. Intramolecular cyclization (intermediate C) and the subsequent elimination of the iodide anion (intermediate D(1)) led to the attainment of cyclic dithiocarbonate 2 and to the retention of the stereochemistry. On the other hand, cyclic trithiocarbonate 3 was obtained via the ring opening in intermediate D(2) to form intermediate E (Scheme 5). The intramolecular Sₓ2 reaction of the thiolate anion in intermediate E afforded thirane 4 with an inversion of the stereochemistry.[6,11] The reaction of thirane 4 with CS₂ under the influence of a KI-tetraethylene glycol complex gave product 3 in a catalytic cycle similar to that proposed for the reaction with epoxide 1 (Scheme 4).[9m,n,12] Note that trace amounts of thiranes 4 were observed in the crude NMR spectra of several examples in Table 1.

Scheme 3. Reaction with optically active epoxides.

Scheme 4. Assumed catalytic cycle to produce cyclic dithiocarbonate 2.

Scheme 5. Proposed mechanism to produce cyclic trithiocarbonate 3.

To expand the utility and further support the mechanism of the present reaction, 1,1- and 1,2-disubstituted epoxides 5 and cis-8 were submitted to the reaction (Scheme 6). The reaction with 1,1-disubstituted epoxide 5 was promoted by the KI-tetraethylene glycol complex catalyst to give dithiocarbonate 6 in a moderate yield (55%) with high selectivity (dithiocarbonate 7: ~0%). The reaction with 1,2-disubstituted epoxide cis-8 and CS₂ proceeded at room temperature to afford dithiocarbonate trans-9 (41%) and trithiocarbonate trans-10 (15%)[9p,4,14] Notably, the
reactivity and stereoselectivity were completely different by comparison with the reaction of cis-8 and CO₂ (Scheme 7). The reaction with CO₂ at 80 °C gave a cis-11, selectively, via double Sn2 inversions with activation of epoxide by the catalyst (intermediates F and H in Scheme 7). In sharp contrast, the product trans-9 was formed as a result of the single Sn2 inversion in the conversion of intermediate B' to C' (Scheme 8). The trans selectivity of trithiocarbonate 10 could be explained by the formation of thiirane cis-12, which was formed in the same reaction mechanism for the formation of thiirane 4 in Scheme 5. The reaction of thiirane cis-12 with CS₂ under the influence of the KI-tetraethylene glycol complex gave trans-10 in a mechanism that was similar to that proposed for the reaction with epoxide cis-8 (Scheme 8). These trans selectivities of thiocarbonates 9 and 10 from cis-8 fully support the reaction mechanisms proposed in Schemes 4, 5, and 8.

Scheme 6. Reaction with 1,1-disubstituted and 1,2-disubstituted epoxides.

Scheme 7. Reaction with epoxide cis-8 and CO₂.

Scheme 8. Proposed mechanism to produce cyclic thiocarbonates 9 and 10.

Conclusions

We have successfully developed an efficient method for the synthesis of cyclic thiocarbonates via a reaction of epoxides and CS₂ under mild reaction conditions using a KI-tetraethylene glycol complex catalyst. The effects of glycols and alkali metal halides
were investigated to clarify the essential points of the catalytic activity. The importance of both the hydroy groups of
tetraethylene glycol and the iodide of the alkali metal halide was clearly observed in the cyclic thiocarbonate synthesis. The reactions of various epoxides and CS2 provided cyclic dithiocarbonates in good yields. In these reactions, cyclic thiocarbocstes were also obtained as a minor product. The
optically active epoxides and 1,2-disubstituted epoxides were also submitted to the reactions with CS2 under the influence of a
Kl-tetraethylene glycol complex catalyst. Although the reaction with CO2 gave cyclic carbonates in retention of the stereochemistry,[8,13] different trends were observed in the reaction with CS2. Based on the stereochemistry of these two
reactions, the reaction mechanisms were discussed, and assumed catalytic cycles were proposed. The proposed reaction
mechanisms clearly explained the observed stereochemistry of cyclic thiocarbonates, and we concluded that the reactions with
CO2 and CS2 proceeded via different mechanisms.

Experimental Section

Typical procedure for the reaction of epoxides 1 with CS2 catalyzed by a Kl-tetraethylene glycol complex: To a mixture of glycidyl phenyl
ether 1a (0.542 mL, 4.00 mmol), tetraethylene glycol (69.1 μL, 0.400 mmol, 10 mol %), and potassium iodide (66.4 mg, 0.400 mmol, 10 mol %) was
added CS2 (0.289 mL, 4.80 mmol) at room temperature. The reaction mixture was stirred for 5 h at room temperature (25 °C). The resulting
reaction mixture was purified by flash column chromatography on silica gel (hexane/ EtOAc = 20:1 as eluent) to afford cyclic dithiocarbonate 2a
(797 mg, 3.52 mmol; R = 0.42 in hexane/EtOAc = 2:1) and trithiocarbonate 3a
(38.8 mg, 0.16 mmol; Rf = 0.67 in hexane/EtOAc = 2:1).

2a[9] Spectral data completely matched with reported data. 1H NMR (400 MHz, CDCl3): δ = 7.31 (t, J = 8.0 Hz, 2H), 7.01 (t, J = 7.6 Hz, 1H). 6.92 (d, J = 8.8 Hz, 2H), 5.39–5.46 (m, 1H), 4.24–4.34 (m, 2H), 3.69–3.81 (m, 2H).
13C NMR (100 MHz, CDCl3): δ = 211.2, 157.7, 129.7, 121.9, 114.5, 67.7, 66.3, 36.3; IR (neat) 3060, 3038, 2924, 2870, 1597, 1597, 1494, 1240, 1228, 1181, 1042, 751, 689 cm
–1.

3a[9] Spectral data completely matched with reported data. 1H NMR (400 MHz, CDCl3): δ = 7.32 (t, J = 8.0 Hz, 2H), 7.02 (t, J = 7.6 Hz, 1H). 6.93 (d, J = 8.8 Hz, 2H), 4.61–4.67 (m, 1H). 4.37 (t, J = 9.6 Hz, 1H). 4.23 (dd, J = 5.8, 12.2 Hz, 1H). 4.20 (dd, J = 5.4, 9.8 Hz, 1H), 4.08 (dd, J = 4.0, 12.0 Hz, 1H). 13C NMR (100 MHz, CDCl3): δ = 226.4, 157.7, 129.7, 121.8, 114.6, 66.4, 57.2, 44.9; IR (neat) 3046, 1599, 1587, 1496, 1264, 1329, 1078, 1041, 732, 702, 690 cm
–1.

2b: 1H NMR (400 MHz, CDCl3): δ = 5.08–5.15 (m, 1H), 3.59 (dd, J = 6.6, 10.8 Hz, 1H), 3.40 (dd, J = 9.4, 11.0 Hz, 1H). 1.98–2.07 (m, 1H), 1.75–1.84 (m, 1H), 1.45–1.65 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ = 212.2, 91.6, 39.3, 35.7, 18.7, 13.7; IR (neat) 2959, 2932, 2872, 1102, 846, 830, 647 cm
–1; HRMS (FAB) m/z calcd for C8H8O2S: 162.0173 (M+) found 162.0172.

3b: 1H NMR (400 MHz, CDCl3): δ = 4.38–4.45 (m, 1H), 3.97 (dd, J = 5.6, 11.6 Hz, 1H), 3.71 (dd, J = 8.0, 12.0 Hz, 1H). 1.84–2.01 (m, 2H), 1.47 (sextet, J = 7.6 Hz, 2H), 0.99 (t, J = 7.4 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ = 228.0, 60.7, 42.8, 35.3, 21.5, 13.8; IR (neat) 2956, 2926, 2869, 1461, 1421, 1090, 1048, 874 cm
–1; HRMS (FAB) m/z calcd for C10H10O4S: 177.9945 (M+) found 177.9945.


Efficient synthesis of cyclic thiocarbonates from epoxides and CS$_2$ was achieved when a KI-tetraethylene glycol complex was used as an economical catalyst. The mechanism for this reaction was discussed based on the stereochemistry of products.