Reactions of 3,4-bis(methoxycarbonyl)-1,2-dithiete (1) with various alkenes or alkynes formed 2,3-dihydro-1,4-dithiin or thiophenes, respectively. The reactions with alkenes were stereospecific, which indicates the concerted reaction between 1,2-bis(methoxycarbonyl)ethene-1,2-dithione (13), the valence isomer of the 1,2-dithiete, and the dienophiles. Theoretical study confirmed the reactions of 13 with alkenes and alkynes are of reverse electron demand hetero Diels–Alder type. The M0 calculations showed the 1,2-dithiete 1 was 5.8 kcal mol$^{-1}$ more stable than the corresponding ethane-1,2-dithione 13, and the tautomerization energy between the 1,2-dithiete and the ethane-1,2-dithione was also calculated to be 28.5 kcal mol$^{-1}$ from the 1,2-dithiete, which suggests the tautomerization from 1,2-dithiete 1 to ethane-1,2-dithione 13 is possible at least at high temperature. Reaction of 3,4,7,8-tetrakis(methoxycarbonyl)-1,2,5,6-tetrathiocin (2) or (Z,Z,Z,Z)-3,4,7,8,11,12,15,16-octakis-(methoxycarbonyl)-1,2,5,6,9,10,13,14-octathiacyclohexadeca-3,7,11,15-tetraene (3) with ethyl vinyl ether also formed the 2,3-dihydro-1,4-dithiin derivative, which is the same compound obtained by the reaction of 1,2-dithiete 1 with the ether. 1,2,5,6-Tetraethiole 2 and 16-membered cyclic compound 3 also reacted with diphenylacetylene to give the thiophene derivative. 

Introduction

Among the unsaturated cyclic compounds possessing disulfide linkage, the chemistry of 1,2-dithiete has been extensively studied and many reports have been published.$^{1-8}$ Especially, the relation with their valence isomers, ethane-1,2-dithiones, has been focused on.$^{5-8}$ Previously, we have succeeded in synthesizing 3,4-bis(methoxycarbonyl)-1,2-dithiete (1), 1,2,5,6-tetrathiocin 2, and 16-membered cyclic compound 3 by oxidation of the titanocene dithiolen complex with sulfuryl chloride, and the crystal structure of 1,2-dithiete 1 could be determined by X-ray crystallographic analysis.$^{9}$ Some reactions of 1,2-dithieties with alkenes have been examined to give 2,3-dihydro-1,4-dithiin derivatives.$^{10}$ However, it has not been clarified whether the alkenes react with 1,2-dithiete or ethane-1,2-dithione, which will be formed from the 1,2-dithiete. Recently, we started to examine the reaction of the 1,2-dithiete with various alkenes and alkynes. In this paper, we report the reactions of 1,2-dithiete 1 with alkenes and alkynes, and it was found that the reaction proceeded between ethane-1,2-dithione and the unsaturated compounds via a concerted path. Theoretical study also supports the reaction of reverse electron demand hetero Diels–Alder type. Activation energy for tautomerization between the 1,2-dithiete and the ethane-1,2-dithione is also discussed on the basis of ab initio MO calculations.

References


Results and Discussion

When a benzene solution of 1,2-dithiete 1 and ethyl vinyl ether was stirred at room temperature, 2,3-dihydro-1,4-dithiin 4 was obtained in 65% yield, as shown in Scheme 1. Although the reactions of 1 with (Z)- and (E)-bis(benzylthio)ethenes were very slow at room temperature, the reactions proceeded smoothly and stereospecifically in refluxing benzene to give cis- and trans-cycloadducts 5 and 6, respectively. The cis-geometry of 5 was confirmed by X-ray crystallographic analysis. Similarly, reactions of 1 with (E)-anethole and (E)-cinnamyl methyl ether also afforded only one of the stereoisomers 7 and 8, respectively, though the reactions were slow even in refluxing benzene. The reaction of 1 with N-phenylmaleimide also formed cycloadduct 9 although the yield was low (11%) together with tetrakis-(methoxycarbonyl)thiophene (10) in 38% yield. However, 1,2-dithiete 1 did not react with maleic anhydride even in refluxing benzene, and thiophene 10 was obtained in 26% yield after refluxing for 24 h.

Some mechanisms are considered for the reactions of 1,2-dithiete 1 with the alkenes. Two mechanisms are via zwitterion intermediates 11 and 12 generated by the reaction of 1 or ethane-1,2-dithione 13 with the alkenes, and another is a concerted reaction of 13, the valence isomer of the 1,2-dithiete, with the alkenes. The present reactions are stereospecific, indicating the reactions are proceeding via a concerted path.

To clarify the mechanism, we calculated the FMO energy levels of the ethane-1,2-dithione 13 as a cisoid-form and the alkenes used for the reaction. The calculations were performed by the Hartree–Fock method with a 6-31G(d) basis set. The calculated FMO energy levels are summarized in Figure 1. Differences of energy levels between the LUMO of 13 and the HOMO of the alkenes are smaller than those of the ð orbital of 13 and the LUMO of the alkenes. This result indicates the reaction is of reverse electron demand hetero Diels–Alder type due to the low energy level of the LUMO (ð*) for ethane-1,2-dithione 13, and it can also explain the inert reactivity of maleic anhydride toward the dithione 13, in which the energy level of the HOMO of maleic anhydride is lower than those of the other alkenes.

Under this situation, the possibility of the formation of ethane-1,2-dithione 13 from 1,2-dithiete 1 arises to be a problem. 1H and 13C NMR spectra of 1 only showed the 1,2-dithiete structure, and no signal assigned to the ethane-1,2-dithione could be detected even at high temperature (80 °C in toluene-d8). However, it is no wonder because a trace amount of formation of ethane-1,2-dithione in the equilibrium may allow the reaction in the solution. There are some theoretical studies concerning stability of 1,2-dithietes and ethane-1,2-dithiones.4,6,8 However, these older studies used low levels of theory, and the many calculations used the simple model molecules substituted by a hydrogen or methyl group. Therefore, we attempted the comparison of the potential energy of 1,2-dithiete 1 and ethane-1,2-dithione 13 with the cisoid-form and estimated the activation energy of the interconversion between the isomers. The structural optimization and energy calculation were performed by the second-order Möller–Plesset perturbation method with a 6-31G(d) basis set. The calculation showed 1,2-dithiete 1 is 5.8 kcal mol–1 more stable than ethane-1,2-dithione 13, and the tautomerization energy was obtained to be 28.5 kcal mol–1 from the 1,2-dithiete 1 (Figure 2). This value of the activation energy supports the possibility of the tautomerization between 1,2-dithiete 1 and ethane-1,2-dithione 13 at least at high temperature.

When a p-xylene solution of 1,2-dithiete 1 was refluxed for 8 h, the thiophene 10 was obtained in 31% yield (Scheme 2). Therefore, the formation of thiophene 10 in the reaction of 1,2-dithiete 1 with N-phenylmaleimide or maleic anhydride can be explained...
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Figure 1. FMO energy levels of ethane-1,2-dithione 13 as a cisoid-form and alkenes calculated by the Hartree–Fock method with a 6-31G(d) basis set.

Scheme 2

![Scheme 2 diagram]

reaction of 1,2-dithiete 1 with ethane-1,2-dithione 13 because the desulfurization of the cycloadduct 14 probably forms 1,4-dithiin derivative followed by rearrangement and subsequent desulfurization to give thiophene 10. The calculated energy difference between the LUMO of 13 and the HOMO of 1 is 8.9 eV, and that between the π of 13 and the LUMO of 1 is 12.4 eV. Therefore, the reaction of 1,2-dithiete 1 with ethane-1,2-dithione 13 is also considered to be of reverse electron demand hetero Diels–Alder type. These results also clarified that 1,2-dithiete 1 and N-phenylmaleimide compete as the dienophiles toward the ethane-1,2-dithione 13 in the reaction of 1 with N-phenylmaleimide.

Reactions of 1,2-dithiete 1 with acetylenes were also examined in refluxing p-xylene. The 1,4-dithiin derivative which is expected to be formed from the Diels–Alder reaction of 1,2-dithiete 1 with ethane-1,2-dithione 13 was not obtained in either reaction of 1 with dimethyl acetylenedicarboxylate or diphenylacetylene, and tetra-kis(methoxycarbonyl)thiophene (10) (25%) and 2,3-bis-(methoxycarbonyl)-4,5-diphenylthiophene (15) (44%) were yielded after 2 h (Scheme 3). Lack of isolation of

the 1,4-dithiin derivatives is also due to the high reactivity of the 1,4-dithiin derivatives under the conditions.\textsuperscript{7,10} The reaction of 3,4-di-tert-butyl-1,2-dithiete with acetylene was reported by Nakayama et al.\textsuperscript{7} to form two types of thiophenes; however, the reaction of 1\textsuperscript{1} with diphenylacetylene yielded only one isomer. In the reactions of 1,2-dithiete 1\textsuperscript{1} with acetylenes, two mechanisms are also considered just like mentioned by Nakayama et al.\textsuperscript{7} If the reaction proceeded via ionic pathway, dimethyl acetylenedicarboxylate may be a better reactant than diphenylacetylene. However, the result was the contrary. The FMO calculations of ethane-1,2-dithione 13 as a cisoid-form and alkenes, as shown in Figure 3, also indicate the higher reactivity of diphenylacetylene as the reverse electron demand hetero Diels–Alder reaction.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{FMO energy levels of ethane-1,2-dithione 13 as a cisoid-form and alkenes calculated by the Hartree–Fock method with a 6-31G(d) basis set.}
\end{figure}

\textbf{Scheme 3}

\begin{equation}
1 \xrightarrow{\text{p-xylene, reflux, 2 h}} Z
\end{equation}

\begin{equation}
10. \quad R = \text{CO}_{2}Me (25\%)
\end{equation}

\begin{equation}
15. \quad R = \text{Ph} (44\%)
\end{equation}

1,2,5,6-Tetrathiocin 2 and 16-membered cyclic compound 3 also reacted with ethyl vinyl ether at room temperature to give 2,3-dihydro-1,4-dithiin derivative 4 in 64 and 63% yields, respectively, as shown in Scheme 4. In these reactions, 1,2-dithiete 1\textsuperscript{1} is considered to be formed initially by nucleophilic reaction of ethyl vinyl ether to 2 or 3,\textsuperscript{9} and then the valence isomer 13 reacted with the ether. The reactions of 2 and 3 with diphenylacetylene in refluxing p-xylene also yielded thiophene derivative 15 in 49 and 41% yields, respectively, while the reaction did not proceed at room temperature. In these reactions, 1,2-dithiete 1\textsuperscript{1} is considered to be formed by heating since the compounds 2 and 3 are already known to be stable in nonpolar solvents at room temperature,\textsuperscript{9} although the ionic reaction via betaine intermediates 16 and 17 could not be completely excluded. However, even if the ionic reaction occurred initially, ethane-1,2-dithione 13 is formed as a side product of the 1,4-dithiin derivative. Thermal reactions of 2 and 3 in refluxing p-xylene also yielded thiophene 10 in similar yields with that by the thermal reaction of 1,2-dithiete 1, indicating the reaction is also proceeding via 1,2-dithiete 1.

\textbf{Conclusion}

Reactions of 3,4-bis(methoxycarbonyl)-1,2-dithiete (1) with various alkenes yielded 2,3-dihydro-1,2-dithiins, stereospecifically. It was clarified the reactions proceed between ethane-1,2-dithione, the valence isomer of the 1,2-dithiete, and alkenes via reverse electron demand hetero Diels–Alder reaction by experimental and theoretical study. The 1,2-dithiete was also found to react with alkenes to give thiophene derivatives. Reactions of 1,2,5,6-tetrathiocin 2 and 16-membered cyclic compound 3 with alkenes and alkynes were found to give the same products as those obtained from the reactions of the 1,2-dithiete with alkenes and alkynes.

\textbf{Experimental Section}

\textbf{General Methods.} Benzene and p-xylene were distilled from sodium metal before use. All reactions were performed under nitrogen. Gel permeation chromatography (GPC) was

\begin{table}
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Reaction} & \textbf{Yield} & \textbf{Conditions} \\
\hline
2 \xrightarrow{\text{p-xylene, reflux, 2 h}} & 4 \xrightarrow{64\%} & \text{benzene, r.t., 40 h} \\
3 \xrightarrow{\text{p-xylene, reflux, 2 h}} & 4 \xrightarrow{63\%} & \text{benzene, r.t., 40 h} \\
2 \xrightarrow{\text{p-xylene, reflux, 2 h}} & 15 \xrightarrow{49\%} & \text{Ph} \xrightarrow{15} \text{Ph} \\
3 \xrightarrow{\text{p-xylene, reflux, 2 h}} & 15 \xrightarrow{41\%} & \text{Ph} \xrightarrow{15} \text{Ph} \\
2 \xrightarrow{\text{reflux, 8 h}} & 10 \xrightarrow{30\%} & \text{p-xylene} \\
3 \xrightarrow{\text{reflux, 8 h}} & 10 \xrightarrow{32\%} & \text{p-xylene} \\
\hline
\end{tabular}
\caption{Reactions of 3,4-bis(methoxycarbonyl)-1,2-dithiete (1) with various alkenes.}
\end{table}
performed using a J Al LC-08 and a LC-908 liquid chromatograph with two J AIGEL-1H columns (20 mm × 600 mm), and the products were eluted with chloroform.

**General Procedure for Reaction of 1,2-Dithieth with Alkenes and Alkynes**

A benzene solution (4 mL) of 1,2-dithieth 1 (41.2 mg, 200 μmol) and alkene (1.00 mmol) was stirred for desired period at desired temperature. After removal of the solvent in vacuo, products were purified by gel permeation chromatography.

**Reaction of 1,2-Dithieth with Alkenes and Alkynes**

164.0; IR (KBr) 1440, 1260, 1080, 1030 cm⁻¹; 1H, 3.81 (s, 3H), 3.82 (s, 3H), 4.51 (d, 1H, J = 6.4 Hz), 7.28 (m, 10H); 13C NMR (125 MHz, CDCl₃) δ 54.7, 46.5, 53.12, 53.16, 59.2, 73.0, 126.5, 127.9, 128.35, 128.39, 128.9, 133.6, 134.63, 164.4; IR (neat) δ 2970, 2970, 1740, 1550, 1450, 1440, 1420, 1250, 1080, 1020 cm⁻³ 2H; MS (EI, 70 eV) m/z 278 (M⁺), 143, 139, 91. HRMS calcd for C₂₂H₂₂O₄S₄: C, 55.20; H, 6.46. Found: C, 55.11; H, 4.66.

**trans-2,3-Bis(benzyloxy)-5,6-bis(methoxy carbonyl)-2,3-di hydrido-1,4-dithieth (5):** colorless oil; mp 107.5–108.0 °C (dichloromethane–hexane); 1H NMR (500 MHz, CDCl₃) δ 3.79 (s, 6H), 3.86 (d, 2H, J = 13.6 Hz), 3.94 (d, 2H, J = 13.6 Hz), 4.25 (s, 2H), 7.23–7.31 (m, 10H); 13C NMR (125 MHz, CDCl₃) δ 36.4, 51.0, 52.2, 127.2, 127.5, 128.7, 129.0, 136.4, 136.0 (KBr) δ 3040, 2950, 1740, 1540, 1400, 1460, 1440, 1430, 1240, 1070, 1010 cm⁻³ 2H; MS (EI, 70 eV) m/z 478 (M⁺), 357, 272, 232, 91; HRMS calcd for C₂₂H₂₂O₄S₄: C, 55.20; H, 6.43. Found: C, 55.11; H, 4.66.

**cis-2,3-Bis(benzyloxy)-5,6-bis(methoxy carbonyl)-2,3-di hydrido-1,4-dithieth (5):** colorless oil; mp 107.5–108.0 °C (dichloromethane–hexane); 1H NMR (500 MHz, CDCl₃) δ 3.79 (d, 2H, J = 13.6 Hz), 3.81 (s, 6H), 3.95 (d, 2H, J = 13.6 Hz), 4.08 (s, 2H), 7.20–7.31 (m, 10H); 13C NMR (125 MHz, CDCl₃) δ 36.5, 50.1, 52.2, 127.2, 127.5, 128.7, 129.0, 136.4, 136.0 (KBr) δ 3040, 2950, 1740, 1540, 1400, 1440, 1430, 1240, 1070, 1010 cm⁻³ 2H; MS (EI, 70 eV) m/z 542 (M⁺), 323, 263, 233, 148, 117; HRMS calcd for C₂₂H₂₂O₄S₄: C, 55.09, 54.96, found 53.06.

**trans-2,3-Bis(methoxy carbonyl)-5-(4-methoxyphenyl)-6-methyl-5,6-dihydro-1,4-dithieth (7):** pale yellow oil; 1H NMR (500 MHz, CDCl₃) δ 1.18 (d, 3H, J = 6.8 Hz), 3.54 (qd, 1H, J = 6.8 Hz), 3.80 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 4.07 (d, 1H, J = 8.7 Hz), 6.89 (d, 2H, J = 6.7 Hz), 7.17 (d, 2H, J = 8.7 Hz); 13C NMR (125 MHz, CDCl₃) δ 18.7, 41.4, 51.2, 53.1, 55.1, 114.2, 126.8, 126.9, 129.8, 129.9, 135.7, 159.7, 164.4; IR (neat) δ 3060, 2970, 2850, 1730, 1610, 1550, 1510, 1440, 1260, 1080, 1030 cm⁻³ 3H; MS (EI, 70 eV) m/z 354 (M⁺), 326, 263, 233, 148, 117; HRMS calcd for C₂₂H₂₂O₄S₄: C, 55.09, 54.96, found 53.06.

**cis-2,3-Bis(methoxy carbonyl)-5-(4-methoxyphenyl)-6-methyl-5,6-dihydro-1,4-dithieth (7):** pale yellow oil; 1H NMR (500 MHz, CDCl₃) δ 3.32 (s, 3H), 3.16 (dd, 1H, J = 6.1, 16.1 Hz), 3.52 (dd, 1H, J = 6.1, 10.1 Hz), 3.59 (td, 1H, J = 6.1, 6.4 Hz), 3.81 (s, 3H), 3.82 (s, 3H), 4.51 (d, 1H, J = 6.4 Hz), 7.28–7.32 (m, 5H); 13C NMR (125 MHz, CDCl₃) δ 45.7, 46.5, 53.12, 53.16, 59.2, 73.0, 126.5, 127.9, 128.35, 128.39, 128.9, 133.6, 134.63, 164.4; IR (neat) δ 2970, 2970, 1740, 1560, 1440, 1420, 1130, 1030 cm⁻³ 2H; MS (EI, 70 eV) m/z 379 (M⁺), 349, 259, 232, 201, 173; HRMS calcd for C₂₂H₁₅NO₂S₄: 379.0184, found 379.0167.

**Theoretical Study.** MO calculations of 1,2-dithieth 1. Probable transition state for the tautomerization were carried out by the second-order Møller–Plesset perturbation method with a 6-31G(d) basis set. The structural optimization and energy calculation of 1, 13, and the transition state for the tautomerization were carried out by the second-order Møller–Plesset perturbation method with a 6-31G(d) basis set. All calculations were performed using the GAUSSIAN 94 program on an IBM RS/6000 computer.

**Acknowledgment.** The authors are grateful to Prof. J. Nakayama (Saitama University) for the gift of a reprint of their review (ref 1a) and Prof. S. Ikuta (Tokyo Metropolitan University) for discussion about the theoretical study. This work was financially supported by an MOC


Supporting Information Available: Detailed information of the X-ray crystallographic analysis of 5, including structure diagrams, details of data collection and reduction and structure solution and refinement, and tables of positional and thermal parameters, bond lengths and angles, and torsional angles, Cartesian coordinates of 1,2-dithietle 1, ethane-1,2-dithione 13, and the geometry at the transition state for the tautomerization between 1 and 13 calculated by the second-order Møller–Plesset perturbation method with the 6-31G(d) basis set, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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J 09908086