

Communication

Zirconocene-catalyzed alkylative dimerization of 2-methylene-1,3-dithiane via a single electron transfer process to provide symmetrical *vic*-bis(dithiane)s

Suguru Yoshida, Hideki Yorimitsu *, Koichiro Oshima *

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

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Abstract

A mixture of tertiary alkyl halide and 2-methylene-1,3-dithiane was treated with butylmagnesium bromide in the presence of a catalytic amount of zirconocene dichloride. The reaction resulted in alkylative dimerization to yield the corresponding *vic*-bis(dithiane). The reaction would proceed as follows. A single electron transfer from low-valent zirconocene to alkyl halide would generate the corresponding alkyl radical. The radical adds to 2-methylene-1,3-dithiane to afford the corresponding radical stabilized by the two sulfur atoms. A couple of the stable radicals finally undergo dimerization.

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1. Introduction

Since the discovery of a convenient method for generating a low-valent zirconocene complex $\text{Cp}_2\text{Zr}(\text{1-butene})$, so-called the Negishi reagent, organic synthesis by using the zirconocene complex has been extensively developed [1]. The reagent provides the corresponding zirconacycles upon treatment with unsaturated compounds such as alkene or alkyne. On the other hand, little attention has been paid to the reaction of $\text{Cp}_2\text{Zr}(\text{1-butene})$ with organic halides. Although the reactions with alkenyl or aryl halides result in the conventional oxidative addition reactions [2], the reactions are usually complicated when alkyl halides are subjected to the reactions. From a mechanistic point of view, Schwartz investigated oxidation of Cp_2ZrL_2 ($\text{L} = \text{PMePh}_2$ or PMe_2Ph) with RX ($\text{RX} = \text{alkyl halide}$) and showed that the formal oxidative addition product Cp_2ZrRX was formed [3]. It has been established that the

oxidative addition involves the intermediacy of alkyl radicals generated by single electron transfer from zirconocene complexes to alkyl halides. However, the synthetic utility of the zirconocene-mediated single electron transfer remains largely unexplored.

We have been interested in single electron transfer from low-valent zirconocene complexes to organic halides and have applied the zirconocene-mediated electron transfer to intramolecular radical cyclization reactions [4]. Here we report zirconocene-mediated intermolecular radical addition reactions of alkyl halides with 2-methylene-1,3-dithiane. The radical addition proceeded smoothly to yield *vic*-bis(dithiane)s through dimerization of the sulfur-stabilized radicals generated by the radical addition.

2. Results and discussion

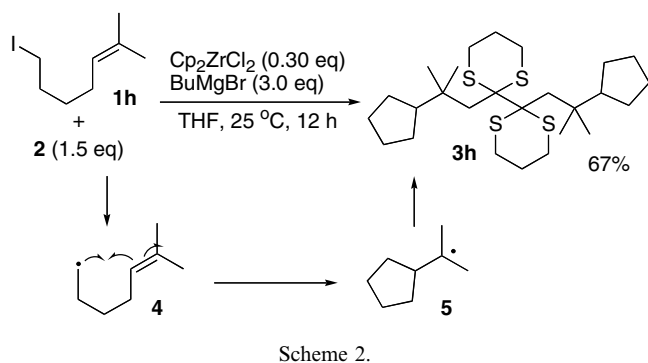
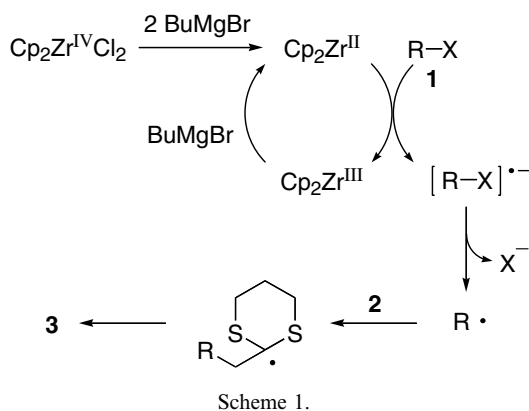
Treatment of *tert*-butyl bromide (**1a**, 0.50 mmol) and 2-methylene-1,3-dithiane (**2**, 0.60 mmol) with butylmagnesium bromide (1.2 mmol) in the presence of a catalytic amount of zirconocene dichloride (0.10 mmol) in THF at 25 °C provided *vic*-bis(dithiane) **3a** in 71% yield (Table

* Corresponding authors.

E-mail addresses: yori@orgrxn.mbox.media.kyoto-u.ac.jp (H. Yorimitsu), oshima@orgrxn.mbox.media.kyoto-u.ac.jp (K. Oshima).

1, entry 1) [5,6]. No products of the direct dimerization or disproportionation of the alkyl halide were observed, which underscores the excellent reactivity of **2** as a radical acceptor. Other tertiary alkyl bromides participated in the reaction (entries 2–4). Unfortunately, the reactions of secondary alkyl bromides such as **1e** resulted in much lower yields (entry 5), which was due to lower conversions as well as formations of rather complicated mixtures of products. Use of secondary alkyl iodides led to full conversions, slightly improving the yields of **3** (entries 6 and 7). The reactions of activated tertiary alkyl bromides such as 2-bromo-*N,N*-diethyl-2-methylpropanamide afforded complex mixtures in which no desired products were observed.

We are tempted to assume the reaction mechanism as follows (Scheme 1), based on our previous reports [4b,4c]. A low-valent zirconocene complex $\text{Cp}_2\text{Zr}^{\text{II}}$ is initially formed. The zirconocene complex effected single electron transfer to an alkyl halide **1** to generate $\text{Cp}_2\text{Zr}^{\text{III}}$ and the radical anion of **1**. The radical anion immediately liberates a halide ion to yield an alkyl radical. The alkyl radical adds to **2** to generate the corresponding sulfur-stabilized radical. The radical is so stabilized and bulky that the radical is neither captured by $\text{Cp}_2\text{Zr}^{\text{III}}$ nor abstracts hydrogen from a solvent molecule. Pair of the long-lived radicals finally dimerize to yield **3** [7]. $\text{Cp}_2\text{Zr}^{\text{III}}$ would be reduced by the action of an excess of BuMgBr to form the initial low-valent $\text{Cp}_2\text{Zr}^{\text{II}}$, although the exact mechanism of the reduction process is not clear.



The following experiment justifies the intermediacy of alkyl radicals (Scheme 2). Treatment of **1h** under similar reaction conditions afforded **3h** having two cyclopentane rings in high yield. Single electron transfer to **1h** furnishes 6-methyl-5-heptenyl radical (**4**), which undergoes a well-known 5-*exo-trig* radical cyclization [8] to yield radical **5**. The following radical addition and dimerization provided **3h**.

3. Summary

The alkylative dimerization of 2-methylene-1,3-dithiane proceeds with the aid of the BuMgBr/cat. Cp_2ZrCl_2 combination. Tertiary alkyl bromides are the best alkyl sources. The transformation features single electron transfer from electron-rich zirconocene to alkyl halides. The products, *vic*-bis(dithiane)s, had not been readily accessible. The present easy preparation has made bis(dithiane)s accessible and hence being potentially interesting intermediates [9].

4. Experimental

4.1. Instrumentation and chemicals

^1H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.23 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. X-ray crystal structure analysis was carried out with a Bruker SMART APEX CCD diffractometer with Mo $\text{K}\alpha$ radiation. The structure was solved by direct methods and refined by full-matrix least squares methods on F^2 with the SHELXL-97. Mass spectra (FAB unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Zirconocene dichloride was purchased from TCI. Butylmagnesium bromide was prepared from magnesium metal and 1-bromobutane in THF. THF was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. All reactions were carried out under argon atmosphere. Halide **1h** was prepared according to the literature [10]. Dithiane **2** was prepared as described in the following section.

4.2. Preparation of 2-methylene-1,3-dithiane (**2**)

Butyllithium (1.60 M in hexane, 15.9 mL, 25.4 mmol) was added to a solution of 2-trimethylsilyl-1,3-dithiane (4.19 g,

22.1 mmol) in THF (20 mL) at $-40\text{ }^{\circ}\text{C}$. After stirring for 2 h at the same temperature, paraformaldehyde (0.90 g, 30.0 mmol) was added to the resulting solution. The reaction was allowed to warm to room temperature gradually for 12 h. Water (20 mL) was added to the reaction mixture, and the mixture was extracted with ethyl acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure. Distillation ($51\text{ }^{\circ}\text{C}/0.1\text{ Torr}$) in the presence of hydroquinone (a few milligram) gave 2-methylene-1,3-dithiane (**2**, 1.68 g, 12.7 mmol, 58%). The product showed the identical NMR spectrum in the literature [11].

4.3. Typical procedure for zirconocene-catalyzed alkylative dimerization (Table 1)

Zirconocene dichloride (29.0 mg, 0.10 mmol) was placed in a flask under an atmosphere of argon. A THF (1.0 mL) solution of 2-methylene-1,3-dithiane (**2**, 80.0 mg, 0.61 mmol) and *tert*-butyl bromide (67.6 mg, 0.49 mmol) was added. A THF solution of butylmagnesium bromide (0.86 M, 1.40 mL, 1.2 mmol) was added, and the mixture was stirred at $25\text{ }^{\circ}\text{C}$ for 1 h. The reaction mixture was poured into satu-

rated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification by chromatography on a silica gel column provided 2,2'-bis(2,2-dimethylpropyl)-2,2'-bi-1,3-dithianyl (**3a**, 66.0 mg, 71%).

4.4. Characterization data


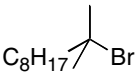

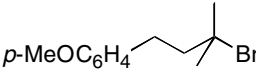
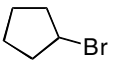


4.4.1. 2-Bromo-4-(4-methoxyphenyl)-2-methylbutane (**1d**)

IR (neat) 2931, 1613, 1514, 1456, 1248, 1038 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.83 (s, 6H), 2.05–2.08 (m, 2H), 2.79–2.82 (m, 2H), 3.81 (s, 3H), 6.85 (dd, $J = 6.5, 2.0\text{ Hz}$, 2H), 7.14 (dd, $J = 6.5, 2.0\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3) δ 32.2, 34.6, 50.0, 55.6, 67.9, 114.2, 129.6, 133.9, 158.2. HRMS (FAB⁺) (m/z) Observed: 256.0460 ($\Delta = -1.2\text{ ppm}$). Calcd for $\text{C}_{12}\text{H}_{17}\text{OBr}$ [M^+]: 256.0463.

4.4.2. 1-Iodo-6-methyl-5-heptene (**1h**)

IR (neat) 2929, 2855, 1436, 1377, 1224 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.44 (tt, $J = 7.5, 7.5\text{ Hz}$, 2H), 1.61 (s, 3H), 1.70 (d, $J = 1.0\text{ Hz}$, 3H), 1.83 (tt, $J = 7.5, 7.5\text{ Hz}$, 2H), 2.01 (dt, $J = 7.5, 7.5\text{ Hz}$, 2H), 3.20 (t, $J = 7.5\text{ Hz}$, 2H), 5.10 (dt, $J = 7.5, 1.0\text{ Hz}$, 1H); ^{13}C NMR (CDCl_3) δ 7.4,

Table 1
Zirconocene-mediated alkylative dimerization of 2-methylene-1,3-dithiane (**2**)

Entry	R-X	1	3	Yield (%)
1		1a	3a	71
2		1b	3b	69
3		1c	3c	50
4		1d	3d	52
5		1e	3e	21 ^a
6		1f	3f	44 ^b
7		1g	3g	42 ^b

^a The reaction was performed for 4 h.

^b 1.5 equiv of **2** was used.

17.9, 26.0, 27.1, 30.9, 33.4, 124.1, 132.3. Anal. Calc. for $C_8H_{15}S_4$: C, 40.35; H, 6.35. Found: C, 40.12; H, 6.30%.

4.4.3. 2,2'-Bis(2,2-dimethylpropyl)-2,2'-bi-1,3-dithianyl (3a)

Mp 119–120 °C; IR (nujol) 2925, 2855, 1464, 1456 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.21 (s, 18H), 1.80–2.30 (m, 8H), 2.73 (ddd, $J = 13.5, 4.5, 4.5$ Hz, 4H), 3.20–3.80 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 23.1, 30.4, 31.9, 33.3, 52.3, 67.9. Anal. Calc. for $C_{18}H_{34}S_4$: C, 57.08; H, 9.05. Found: C, 57.24; H, 9.11%. Crystal data. CCDC 627902, $C_{18}H_{34}S_4$, $M = 378.69$, orthorhombic, $a = 12.0851(13)$, $b = 11.1164(12)$, $c = 15.2028(17)$ Å, $V = 2042.4(4)$ Å³, $T = 293(2)$ K, space group $Pbca$, $Z = 4$, $\mu(Mo K\alpha) = 0.461$ mm⁻¹, 10,778 reflections measured, 2214 unique ($R_{int} = 0.0273$) which were used in all calculations. The final $wR(F^2)$ was 1.136 (all data). The largest residual electron density hole was -0.181 e Å⁻³.

4.4.4. 2,2'-Bis(2,2-dimethyldecyl)-2,2'-bi-1,3-dithianyl (3b)

IR (neat) 2925, 2854, 1468, 1456 cm^{-1} ; 1H NMR ($CDCl_3$) δ 0.87 (t, $J = 7.0$ Hz, 6H), 1.18 (s, 12H), 1.19–1.33 (m, 24H), 1.43–1.48 (m, 4H), 1.70–2.50 (m, 8H), 2.62–2.78 (m, 4H), 3.00–3.90 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 14.4, 23.0, 23.3, 24.5, 29.4, 29.7, 30.0, 30.7, 30.9, 32.2, 36.1, 45.2, 50.3, 68.3. Anal. Calc. for $C_{32}H_{62}S_4$: C, 66.83; H, 10.87. Found: C, 66.57; H, 10.67%.

4.4.5. 2,2'-Di[(1-methylcyclohexyl)methyl]-2,2'-bi-1,3-dithianyl (3c)

Mp 107–108 °C; IR (nujol) 2925, 2855, 1456, 1448 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.34 (s, 6H), 1.38–1.68 (m, 20H), 1.80–2.50 (m, 8H), 2.73 (ddd, $J = 13.5, 4.5, 4.5$ Hz, 4H), 3.20–3.80 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 22.4, 23.3, 24.8, 26.6, 30.8, 36.2, 40.5, 52.8, 68.5. HRMS (FAB⁺) (m/z) Observed: 459.2242 ($\Delta = -1.3$ ppm). Calcd for $C_{24}H_{43}S_4$ [MH^+]: 459.2247.

4.4.6. 2,2'-Bis[4-(4-methoxyphenyl)-2,2-dimethylbutyl]-2,2'-bi-1,3-dithianyl (3d)

IR (neat) 2919, 2859, 1506, 1464, 1456, 1247, 1176, 1039 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.28 (s, 12H), 1.60–2.50 (m, 12H), 2.55–2.65 (m, 4H), 2.65–2.70 (m, 4H), 3.00–3.60 (m, 4H), 3.79 (s, 6H), 6.82 (dd, $J = 6.5, 2.0$ Hz, 4H), 7.14 (dd, $J = 6.5, 2.0$ Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 29.7, 30.3, 30.8, 31.8, 36.3, 47.1, 49.5, 55.5, 66.4, 113.9, 129.5, 136.1, 157.7. Anal. Calc. for $C_{34}H_{50}O_2S_4$: C, 65.97; H, 8.14. Found: C, 65.80; H, 8.04%.

4.4.7. 2,2'-Di(cyclopentylmethyl)-2,2'-bi-1,3-dithianyl (3e)

Mp 118–119 °C; IR (nujol) 2924, 2854, 1456, 1416, 1377, 1284 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.18–1.25 (m, 4H), 1.47–1.64 (m, 8H), 1.90–1.97 (m, 2H), 1.98–2.05 (m, 6H), 2.24 (d, $J = 5.5$ Hz, 4H), 2.37–2.46 (m, 2H), 2.84 (ddd, $J = 14.0, 7.5, 5.0$ Hz, 4H), 3.12 (ddd, $J = 14.0, 7.5, 5.0$ Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 23.4, 25.0, 28.8, 35.3,

38.2, 45.3, 68.3. Anal. Calc. for $C_{20}H_{34}S_4$: C, 59.64; H, 8.51. Found: C, 59.37; H, 8.25%.

4.4.8. 2,2'-Di(2-methylpropyl)-2,2'-bi-1,3-dithianyl (3f)

Mp 126–127 °C; IR (nujol) 2926, 2857, 1456 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.07 (d, $J = 8.0$ Hz, 12H), 1.92 (doublet of septet, $J = 8.0, 4.5$ Hz, 2H), 1.99 (d, $J = 4.5$ Hz, 4H), 2.03–2.10 (m, 2H), 2.29–2.36 (m, 2H), 2.81 (ddd, $J = 14.5, 7.0, 5.0$ Hz, 4H), 3.18 (ddd, $J = 14.5, 9.0, 4.5$ Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 23.7, 25.7, 26.5, 29.2, 47.8, 68.9. Anal. Calc. for $C_{18}H_{30}S_4$: C, 54.80; H, 8.62. Found: C, 54.77; H, 8.70%.

4.4.9. 2,2'-Di(cyclohexylmethyl)-2,2'-bi-1,3-dithianyl (3g)

Mp 114–115 °C; IR (nujol) 2917, 2848, 1654, 1559, 1457 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.00–1.06 (m, 4H), 1.13–1.18 (m, 2H), 1.26–1.34 (m, 4H), 1.55–1.68 (m, 6H), 1.88–2.00 (m, 12H), 2.01–2.10 (m, 2H), 2.79 (ddd, $J = 14.0, 6.5, 4.5$ Hz, 4H), 3.17 (ddd, $J = 14.0, 9.0, 5.0$ Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 23.7, 26.6, 26.9, 29.3, 35.7, 36.1, 46.4, 69.0. Anal. Calc. for $C_{22}H_{38}S_4$: C, 61.34; H, 8.89. Found: C, 61.30; H, 8.91%.

4.4.10. 2,2'-Di(2-cyclopentyl-2-methylpropyl)-2,2'-bi-1,3-dithianyl (3h)

Mp 131–132 °C; IR (nujol) 2924, 2855, 1684, 1653, 1558 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.25–1.32 (m, 16H), 1.41–1.50 (m, 8H), 1.61–1.68 (m, 4H), 1.70–2.40 (m, 10H), 2.73 (ddd, $J = 13.5, 4.5, 4.5$ Hz, 4H), 3.00–3.80 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 23.3, 25.8, 26.2, 27.4, 30.8, 37.8, 50.0, 53.6, 68.4. Anal. Calc. for $C_{26}H_{46}S_4$: C, 64.14; H, 9.52. Found: C, 63.96; H, 9.26%.

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- [5] In the absence of zirconocene dichloride and **2**, no reaction between **1a** and butylmagnesium bromide took place. The reaction of **1a** with butylmagnesium bromide in the presence of zirconocene dichloride and in the absence of **2** afforded a mixture of 2-methyl-1-decene (24%), 2-methyl-2-decene (10%), 2-methyldecane (34%), and 9,9,10,10-tetramethyloctadecane (8%).
- [6] Use of 0.05 mmol of zirconocene dichloride resulted in a slightly lower yield (65%). Much lower catalyst loadings such as 0.025 mmol led to poor reproducibility.
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