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Jun-ichi Matsuo,* Shun Sasaki, Takaya Hoshikawa, and Hiroyuki Ishibashi

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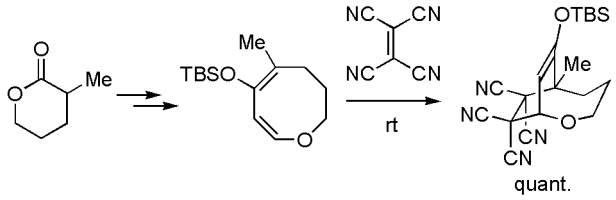

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Diels-Alder reaction of eight-membered cyclic siloxydienes

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Abstract— Eight-membered cyclic siloxydienes, 2-(*tert*-butyldimethylsiloxy)-1-methyl-5-oxacycloocta-1,3-diene and 2-(*tert*-butyldimethylsiloxy)-5-oxacycloocta-1,3-diene, were prepared from δ-valerolactone, and their Diels-Alder reactions with various dienophiles are reported.

Keywords: Diels-Alder reaction, Siloxydiene, Eight-membered cyclic compound, 8-Endo-dig cyclization

1. Introduction

The Diels-Alder reaction is one of the most powerful methods for constructing a cyclohexene ring in organic synthesis.[1] Although various types of dienes have been developed for the Diels-Alder reaction,[2] eight-membered cyclic dienes have rarely been employed since they are very poor enophiles. For example, it is very difficult to obtain the Diels-Alder adduct between cycloocta-1,3-diene and maleic anhydride.[3] It has also been reported that even tetracyanoethylene (TCNE), which is a much more reactive dienophile than maleic anhydride, reacted with cycloocta-1,3-diene too slowly to determine the reaction rate.[4] We considered that eight-membered siloxydienes **1** would be a more reactive enophile in Diels-Alder reactions than cycloocta-1,3-diene (Figure 1). In order to verify this hypothesis, we prepared eight-membered cyclic siloxydienes **1**, and investigated their reactivities in Diels-Alder reactions with various dienophiles. We report here the results obtained in the preparation and Diels-Alder reactions of **1**.

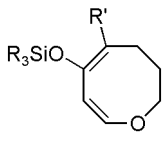

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Figure 1. Eight-membered cyclic siloxydiene **1**.

2. Results and discussion

2.1. Preparation of eight-membered cyclic siloxydienes 8 and 16

Eight-membered siloxydiene **8** was prepared from α-methyl-δ-valerolactone **2**, which was obtained by methylation of δ-valerolactone[5] (Scheme 1). α-Phenylsulfenylation of **2** in the presence HMPA gave **3** in 66% yield, and nucleophilic addition[6] of lithium trimethylsilylacetylide to **3** followed by treatment with saturated aqueous ammonium chloride gave trimethylsilylalkynyl ketone and the corresponding desilylated product **4** in 73 and 16% yields, respectively. Deprotection of the trimethylsilyl group of ethynyl ketone by TBAF gave **4** in 88% yield. It was noted that when the addition of lithium trimethylsilylacetylide to **3** was performed in a small scale (0.54 mmol of **3**), desilylated product **4** was directly obtained in 93% yield by successive treatment with aqueous ammonium chloride.

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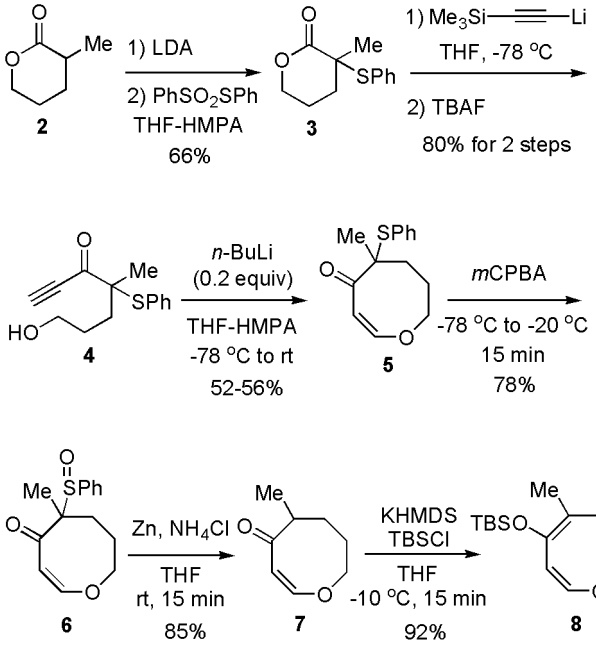
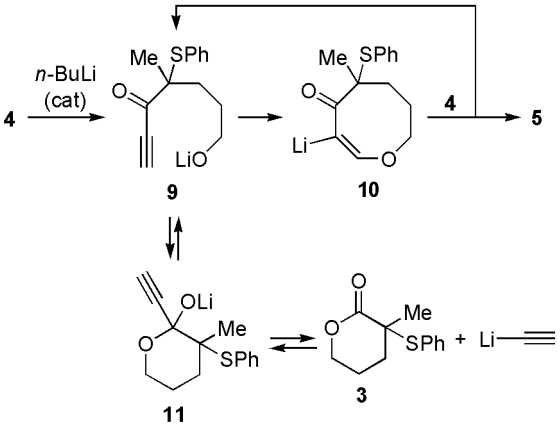


Scheme 1. Preparation of **8**.

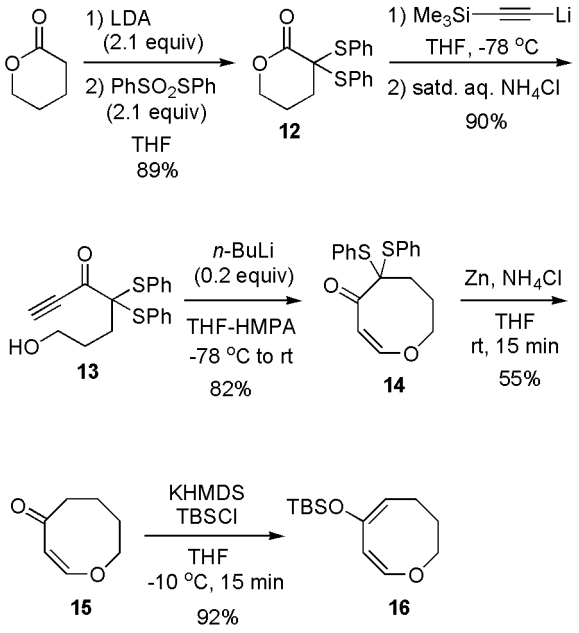
Intramolecular *8-endo-dig* cyclization of **4** by Schreiber's procedure[7] (the use of a stoichiometric amount of *n*-butyllithium in the presence of HMPA) gave **5** in 22-56% yields depending on the reaction scale. That is, the cyclization of 0.16 mmol of **4** gave **5** in 56% yield, whereas the same cyclization of 2.01 mmol of **4** gave **5** in 22% yield. We found that the use of a catalytic amount (0.2 equiv) of *n*-butyllithium in the presence of HMPA constantly gave the desired eight-membered enone **5** in 52–56% yields along with **3** in 10–22% yields. The suitable concentration of **4** for this cyclization was found to be 0.04 M, and a concentration lower than 0.04 M resulted in increased formation of **3**. These results suggest that this cyclization proceeds by the mechanism shown in Scheme 2. Alkoxide **9** generated by the reaction of **4** and a catalytic amount of *n*-butyllithium is cyclized to **10**, and **10** is protonated with unreacted **4** to give the desired product **5** and the intermediate **9**. The formation of **10** competes with the formation of **11** having a six-membered ring, and **11** equilibrates with **3** and lithium acetylide. Under the condition of a low concentration of **4** (lower than 0.04 M), it was difficult for intermolecular attack of lithium acetylide to **3** to take place, and **3** was obtained in increased yields.



Scheme 2. Possible Mechanism for cyclization of **4** to **5**.

Direct desulfurization of **5** to **7** by using zinc and ammonium chloride[8] did not proceed. Therefore, the phenylthio group of **5** was removed to afford desulfurized enone **7** by oxidation of **5** with *m*CPBA, followed by treatment of the resultant sulfoxide **6** with zinc and ammonium chloride. *tert*-Butyldimethylsilyl (TBS) enol ether **8** was prepared from **7** in 92% yield by using KHMDS and TBSCl at –10 °C.

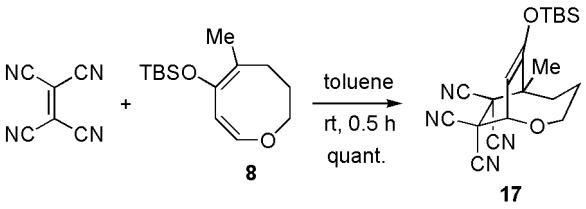
Similar to the synthesis of **8**, eight-membered siloxydiene **16** was prepared from δ-valerolactone (Scheme 3). Bis-α-phenylsulfenylation of δ-valerolactone gave **12** in 81% yield by using 2.1 equivalents of LDA and *S*-phenyl benzenethiosulfonate. Compound **13**, which was obtained by nucleophilic addition of lithium trimethylsilylacetylide followed by desilylation with aqueous ammonium chloride, was cyclized under the above-mentioned conditions of employing 0.2 equivalent of *n*-butyllithium in the presence of HMPA. The cyclization of **13** proceeded more efficiently than that of **4** and the desired product **14** was obtained in 82% yield. Direct desulfurization of **14** proceeded with zinc and ammonium chloride to give **15** in 55% yield, and eight-membered siloxydiene **16** was obtained by silylation with KHMDS and TBSCl.



Scheme 3. Preparation of **16**.

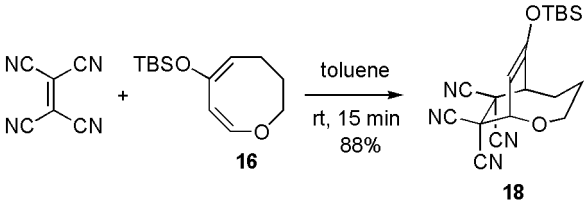
2.2. Diels-Alder reaction of eight-membered siloxydiene 8 and 16

The Diels-Alder reaction of **8** with tetracyanoethyene (TCNE)[9] at room temperature gave the corresponding Diels-Alder adduct **17** quantitatively (Scheme 4). The structure of **17** was confirmed by HMBC correlations. It has been reported that [4 + 2] and [2 + 2] cycloaddition competed in the reaction of TCNE and some substituted 1,3-butadienes.[9] However, only [4 + 2] cycloaddition proceeded efficiently in the reaction of **8** and TCNE.



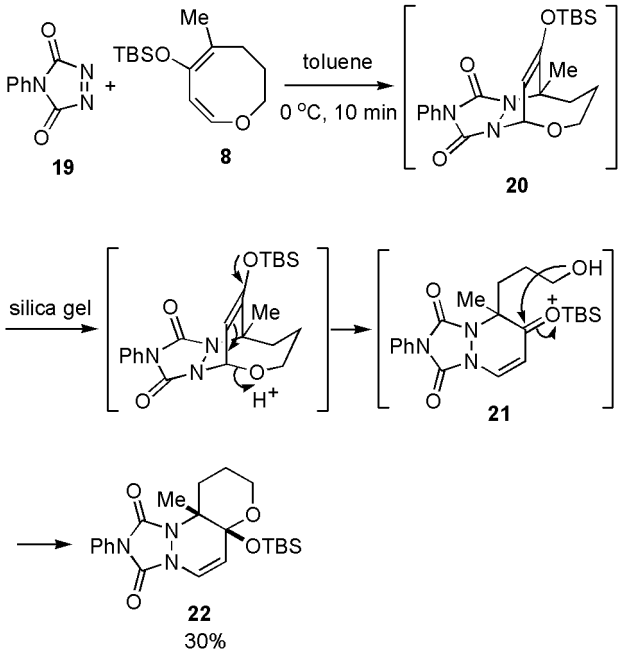
Scheme 4. Diels-Alder reaction of **8** and TCNE.

Eight-membered siloxydiene **16** also reacted with TCNE smoothly to afford the corresponding Diels-Alder adduct **18** in 88% yield (Scheme 5).



Scheme 5. Diels-Alder reaction of **16** with TCNE.

4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) **19**, which is known to be a better dienophile than TCNE,[10] reacted with **8** in toluene at 0 °C within 10 min. It was found that a major product was formed along with some by-products, and it was difficult to purify the major product without its isomerization on silica gel or neutral alumina. Therefore, the isomerization was led to completion by treating the crude product with silica gel in dichloromethane at room temperature to afford compound **22** in 30% yield (Scheme 6).[11] The structure of **22** was determined by HMBC correlations and NOE experiments. It was thought that the initial major product was Diels-Alder adduct **20**, and isomerization to **22** took place via intermediate **21**, which was formed by silica gel-catalyzed ring-opening of **20**.



Scheme 6. Diels-Alder reaction of **8** and PTAD (**19**).

Eight-membered siloxydiene **8** did not react with maleic anhydride, *N*-phenylmaleimide, *p*-quinone, dimethyl acetylenedicarboxylate, and phenyl vinyl sulfone in refluxing toluene. It is considered that highly electrophilic dienophiles such as TCNE and PTAD[12] react with eight-membered siloxydienes by an asynchronous mechanism.[13] On the other hand, less electrophilic dienophiles such as maleic anhydride does not react with eight-membered siloxydienes because the diene moiety of eight-membered 1,3-dienes does not have planarity which is required for a synchronous [4 + 2] cycloaddition mechanism which works for less reactive dienophiles.

3. Conclusion

We established a method for the preparation of eight-membered silyloxydienes **8** and **16** from δ-valerolactone, and we found that they were more reactive than cycloocta-1,3-diene for the Diels-Alder reaction with TCNE. It was also found that PTAD reacted with **8** but the formed Diels-Alder adduct was considered to isomerize easily to six-membered ketal **22**. The reactivities of **8** and **16** in Diels-Alder reactions, which were disclosed by this research, will offer a part of basic information for the Diels-Alder reaction of medium-sized cyclic dienes.

4. Experimental

4.1. General

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100. ^{1}H NMR spectra were recorded on a JEOL JNM GSX500 (500 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; sext, sextet; m, multiplet. ^{13}C NMR spectra were recorded on a JEOL JNM GSX500 (500 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard $CDCl_3$. High resolution mass spectra (HRMS) were recorded on a JEOL JMS-SX-102A mass spectrometer (EI). Elemental analyses were carried out on a Yanaco CHN Corder MT-5. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Silica gel column chromatography was carried out on silica gel 60N (Kanto Kagaku Co., Ltd., spherical, neutral, 63–210 μm).

4.2. 2-Methyl-2-phenylsulfanylpentano-5-lactone (3)

To a stirred solution of diisopropylamine (5.93 mL, 42.3 mmol) in dry THF (141 mL) was added *n*-butyllithium (1.66 M in hexane, 25.5 mL, 42.3 mmol) at –78 °C and the resulting solution was stirred at –78 °C for 15 min. After the addition of HMPA (14.7 mL, 84.7 mmol), a solution of α-methyl-δ-varelolactone[5] (3.22 g, 28.2 mmol) in THF (10 mL) was added and the reaction mixture was stirred at –78 °C for 20 min. Then, a solution of *S*-phenyl benzenethiosulfonate[14] (10.6 g, 42.3 mmol) in THF (10 mL) was added at –78 °C, and the reaction mixture was stirred at 0 °C for 30 min and at room temperature for 30 min. The reaction was quenched with saturated aqueous ammonium chloride, and the mixture was extracted with ethyl acetate. The organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1 then 3 : 1) to afford **3** (4.52 g, 20.3 mmol, 72%) as colorless plates; mp 58.0–59.0 °C (hexane–ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 3H), 1.84–1.90 (m, 1H), 2.04–2.15 (m, 1H), 2.16–2.32 (m, 2H), 4.32–4.36 (m, 1H), 4.65–4.69 (m, 1H), 7.33-7.42 (m, 3H), 7.49–7.51 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.7, 26.4, 34.0, 50.5, 69.3, 128.8, 129.9, 130.1, 137.2, 171.4; IR ($CHCl_3$, cm^{-1}) 1720, 1269, 1119; Anal. Calcd for $C_{12}H_{14}O_2S$; C, 64.83; H, 6.35. Found: C, 64.55, H, 6.31.

4.3. 7-Hydroxy-4-methyl-4-phenylsulfanylhept-1-yn-3-one (4)

(Gram-scale preparation of **4**) To a stirred solution of trimethylsilylacetylene (3.37 mL, 24.4 mmol) in dry THF (70 mL) was added *n*-butyllithium (1.66 M in hexane, 14.7 mL, 24.4 mmol) at –78 °C, and the reaction mixture was stirred for 20 min. A solution of **3** (4.51 g, 20.3 mmol) in dry THF (5 mL) was added to the reaction mixture at –78 °C, and the reaction mixture was stirred at –78 °C for 15 min. A saturated aqueous ammonium chloride solution was added to the reaction mixture, and the resulting mixture was stirred at room temperature for 20 min, and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 3 : 1) to afford the corresponding trimethylsilylethynyl ketone (4.76 g, 14.9 mmol, 73%) and **4** (0.79 g, 3.18 mmol, 16%).

To a stirred solution of thus-obtained trimethylsilylethynyl ketone (4.74 g, 14.8 mmol) and methanol (5.98 mL, 148 mmol) in THF (80 mL) was added at –20 °C a solution of TBAF (1 M in THF, 5.91 mL, 5.91 mmol). The reaction mixture was stirred at –20 °C for 15 min and 0 °C for 15 min. The reaction was quenched by adding a solution of saturated aqueous ammonium chloride solution, and the resulting mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane / ethyl acetate = 2 : 1 then 1 : 1) to afford **4** (3.24 g, 13.0 mmol) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 3H), 1.49–1.57 (m, 1H), 1.69 (brs, 1H), 1.74–1.84 (m, 2H), 1.96–2.03 (m, 1H), 3.31 (s, 1H), 3.61-3.66 (m, 2H), 7.30–7.32 (m, 2H), 7.36–7.39 (m, 1H), 7.42–7.43 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.8, 27.8, 32.3, 60.2, 62.6, 79.8, 79.9, 129.0, 129.6, 129.8, 136.9, 138.0, 184.0; IR ($CHCl_3$, cm^{-1}) 3299, 2097, 1669; HRMS (EI) calcd for $C_{14}H_{16}O_2S$: 248.08710, found: 248.08680.

(Small scale preparation of **4**) To a stirred solution of trimethylsilylacetylene (0.09 mL, 0.65 mmol) in dry THF (2 mL) was added *n*-butyllithium (1.63 M in hexane, 0.39 mL, 0.64 mmol) at –78 °C, and the reaction mixture was stirred for 20 min. A solution of **3** (119 mg, 0.535 mmol) in dry THF (1 mL) was added to the reaction mixture at –78 °C, and the reaction mixture was stirred at –78 °C for 20 min. A saturated aqueous ammonium chloride solution was added to the reaction mixture, and the same workup

procedure described above gave **4** (123.8 mg, 0.499 mmol, 93%).

4.4. 8-Methyl-8-phenylsulfanyl-4-oxacyclooct-2-en-1-one (5)

To a stirred solution of *n*-butyllithium (1.55 M in hexane, 0.93 mL, 1.44 mmol) in dry THF (150 mL) and HMPA (12.5 mL, 71.8 mmol) was added at –78 °C a solution of **4** (1.79 g, 7.20 mmol) in dry THF (50 mL), and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated aqueous ammonium solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 10 : 1) to afford **3** (350 mg, 1.57 mmol, 22%) as a pale yellow oil and **5** (996 mg, 4.01 mmol, 56%) as colorless leaflets: mp 74.0–74.5 °C (hexane–ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.84–1.96 (m, 2H), 2.07–2.15 (m, 1H), 2.35 (dt, *J* = 3.9, 13.9 Hz, 1H), 3.64 (dt, *J* = 2.4, 12.9 Hz, 1H), 4.13 (ddd, *J* = 1.2, 4.9, 12.7 Hz, 1H), 5.06 (d, *J* = 8.1 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 7.32–7.43 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 26.5, 31.5, 60.3, 67.5, 100.9, 128.7, 129.8, 130.2, 137.4, 151.2, 199.2; IR ($CHCl_3$, cm^{-1}) 1657, 1624; HRMS (EI) calcd for $C_{14}H_{16}O_2S$: 248.08710, found: 248.08725.

4.5. 8-Methyl -4-oxacyclooct-2-en-1-one (7)

To a stirred solution of **5** (420 mg, 1.69 mmol) in dichloromethane (10 mL) was added at –78 °C a solution of *m*-CPBA (65%, 450 mg, 1.69 mmol) in dichloromethane (2 mL) and the mixture was stirred at –78 °C for 1 h and at –20 °C for 5 min. The reaction was quenched with 10% aqueous sodium thiosulfate solution at –20 °C, and the mixture was extracted with dichloromethane. The combined organic extracts were washed with saturated aqueous sodium hydrogencarbonate solution and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 3 : 1 then 2:1 then 1:1) to afford **6** (349 mg, 1.32 mmol, 78%) as yellow oil. To a solution of **6** (340.6 mg, 1.29 mmol) in THF (13 mL) was added activated zinc (5.02 g, 76.8 mmol) and saturated aqueous ammonium chloride solution (13 mL) at room temperature, and the mixture was stirred at room temperature for 15 min. The reaction mixture was filtered through a Celite pad, and the filtrate was extracted with ether. The combined organic extracts were washed with saturated aqueous sodium hydrogencarbonate solution and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ether = 7:1) to afford **7** (154.2 mg, 1.10 mmol, 85%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (d, *J* = 7.3 Hz, 3H), 1.71–1.78 (m, 1H), 1.87–1.90 (m, 2H), 1.99–2.07 (m, 1H), 2.53–2.60 (m, 1H), 3.93–4.02 (m, 2H), 4.91 (d, *J* = 7.8 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.9, 27.1, 27.8, 46.6, 68.9, 103.4, 153.7, 208.2; IR ($CHCl_3$, cm^{-1}) 1661, 1620; HRMS (EI) calcd for $C_8H_{12}O_2$: 140.08373, found: 140.08330.

4.6. 2-(*tert*-Butyldimethylsiloxy)-1-methyl-5-oxacycloocta-1,3-diene (8)

To a stirred solution of **7** (155 mg, 1.11 mmol) and TBSCl (201 mg, 1.33 mmol) in dry THF (5 mL) was added at –10 °C a solution of KHMDS (0.5 M in toluene, 2.65 mL, 1.33 mmol) and the mixture was stirred at –10 °C for 15 min. The reaction was quenched with saturated aqueous ammonium chloride solution, and the resulting mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 55 : 1) to afford **8** (260 mg, 1.02 mmol, 92%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.16 (s, 3H), 0.96 (s, 9H), 1.57 (brs, 2H), 2.30 (brs, 2H), 4.20 (brs, 2H), 4.41 (dd, *J* = 1.2, 8.5 Hz, 1H), 6.08 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –3.6, 16.2, 18.2, 22.4, 25.9, 29.3, 66.0, 100.7, 112.2, 142.5, 145.3; IR ($CHCl_3$, cm^{-1}) 1630, 1119; HRMS (EI) calcd for $C_{14}H_{26}O_2Si$: 254.17021, found: 254.17096.

4.7. Bis(2-phenylsulfanyl)pentano-5-lactone (12)

To a stirred solution of diisopropylamine (4.35 mL, 31.0 mmol) in dry THF (74 mL) was added at –78 °C a solution of *n*-butyllithium (1.59 M in hexane, 19.5 mL, 31.0 mmol) and the reaction mixture was stirred at the same temperature for 15 min. Then, a solution of freshly distilled δ-valerolactone (1.48 g, 14.8 mmol) in dry THF (5 mL) was added at –78 °C and the mixture was stirred at –78 °C for 30 min. A solution of *S*-phenyl benzenethiosulfonate (7.77 g, 31.0 mmol) in dry THF (8 mL) was added at –78 °C and the reaction mixture was stirred at –20 °C for 50 min. The reaction was quenched with saturated aqueous ammonium chloride solution, and the resulting mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 5 : 1) to afford **12** (4.17 g, 13.2 mmol, 89%) as colorless crystals: mp 126.5–127.0 °C (hexane–ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97 (sext, *J* = 6.1 Hz, 2H), 2.16 (t, *J* = 6.4 Hz, 2H), 4.36 (t, *J* = 6.1 Hz, 2H), 7.36–7.44 (m, 6H), 7.66–7.67 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9, 33.6, 64.5, 69.7, 128.9, 129.9, 130.4, 136.6, 167.0; IR ($CHCl_3$, cm^{-1}) 1278; Anal. Calcd for $C_{17}H_{18}O_2S_2$; C, 64.53; H, 5.10; N, 0.00. Found: C, 64.48, H, 5.10, N, 0.00.

4.8. 7-Hydroxy-bis(4-phenylsulfanyl)hept-1-yn-3-one (13)

To a stirred solution of trimethylsilylacetylene (1.34 mL, 9.69 mmol) in dry THF (55 mL) was added *n*-butyllithium (1.66 M in hexane, 6.09 mL, 10.1 mmol) was added at –78 °C, and the mixture was stirred for 15 min. A solution of **12** (2.66 g, 8.42 mmol) in dry THF (5 mL) was then added at –78 °C, and the mixture was stirred at –78 °C for 15 min. Saturated aqueous ammonium chloride solution was then added at –78 °C, and the mixture was stirred at room temperature for 20 min. The resulting mixture was extracted with ethyl acetate, and combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 2 : 1) to afford **13** (2.61g, 7.62 mmol, 90%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (brs, 1H), 1.77–1.80 (m, 2H), 1.88–1.95 (m, 2H), 3.40 (s, 1H), 3.49 (t, *J* = 6.3 Hz, 2H), 7.33–7.41 (m, 6H), 7.61 (d, *J* = 7.6 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7, 29.2, 62.3, 74.0, 79.9, 81.3, 129.1, 129.5, 129.9, 136.1, 179.6; IR ($CHCl_3$, cm^{-1}) 3299, 2099, 1669; HRMS (EI) calcd for $C_{19}H_{18}O_2S_2$: 342.07483, found: 342.07371.

4.9. Bis(8-phenylsulfanyl)-4-oxacyclooct-2-en-1-one (14)

To a stirred solution of *n*-butyllithium (1.66 M in hexane, 0.99 mL, 1.64 mmol) in dry THF (200 mL) and HMPA (14.3 mL, 82.2 mmol) was added a solution of **13** (2.816 g, 8.22 mmol) in dry THF (6 mL) at –78 °C, and the mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous ammonium chloride solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 10 : 1) to afford **14** (2.31 g, 6.75 mmol, 82%) as a white powder: mp 159.5–160.0 °C (hexane–ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.93 (brs, 2H), 2.10 (brs, 2H), 3.99 (brs, 2H), 4.97 (d, *J* = 8.1 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 7.36–7.43 (m, 6H), 7.71 (brs, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 28.6, 67.9, 78.3, 99.7, 128.8, 129.4, 131.2, 135.6, 151.8, 193.8; IR ($CHCl_3$, cm^{-1}) 1661, 1624; HRMS (EI) calcd for $C_{19}H_{18}O_2S_2$: 342.07483, found: 342.07438.

4.10. 4-Oxacyclooct-2-en-1-one (15)

To a stirred solution of **14** (2.10 g, 6.13 mmol) in THF (35 mL) was added activated zinc (9.2 g, 141 mmol) and saturated aqueous ammonium chloride solution (35 mL) at room temperature, and the resulting suspension was stirred at room temperature for 15 min. After filtration through a Celite pad, the filtrate was extracted with diethyl ether. The combined organic extracts were washed with saturated aqueous sodium hydrogencarbonate and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ether = 5 : 1 then 1 : 1) to afford **15** (342 mg, 2.71 mmol, 44%) and a mixture containing a partially reduced compound (868 mg). The mixture containing a partially reduced compound was treated with zinc and ammonium chloride by the same procedure to give **15** (86 mg, 0.68 mmol, 11%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88–1.99 (m, 4H), 2.53–2.55 (m, 2H), 4.09 (t, *J* = 5.6 Hz, 2H), 4.92 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 8.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.0, 30.6, 42.0, 69.3, 104.3, 155.0, 204.0; IR ($CHCl_3$, cm^{-1}) 1641, 1617, 1302; HRMS (EI) calcd for $C_7H_{10}O_2$: 126.06808, found: 126.06840.

4.11. 2-(*tert*-Butyldimethylsiloxy) -5-oxacycloocta-1,3-diene (16)

To a stirred solution of **15** (59.3 mg, 0.47 mmol) and TBSCl (77.9 mg, 0.517 mmol) in dry THF (2.5 mL) was added a solution of KHMDS (0.5 M in toluene, 1.13 mL, 0.565 mmol) at –10 °C, and the reaction mixture was stirred at the same temperature for 15 min. The reaction was quenched with saturated aqueous ammonium chloride solution, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ether = 50 : 1) to afford **16** (104 mg, 0.433 mmol, 92%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.16 (s, 6H), 0.94 (s, 9H), 1.52–1.58 (m, 2H), 2.29–2.34 (m, 2H), 4.33 (t, *J* = 5.4 Hz, 2H), 4.36 (d, *J* = 8.3 Hz, 1H), 4.70 (t, *J* = 8.3 Hz, 1H), 6.14 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –4.3, 18.1, 22.2, 24.0, 25.7, 66.5, 100.0, 104.9, 146.9, 150.2; IR ($CHCl_3$, cm^{-1}) 1635, 1163, 1117; HRMS (EI) calcd for $C_{13}H_{24}O_2Si$: 240.15456, found: 240.15388.

4.12. 7-*tert*-Butyldimethylsiloxy-9,9,10,10-tetracyano-6-methyl-2-oxabicyclo[4.2.2]dec-7-ene (17)

A solution of TCNE (13.8 mg, 0.108 mmol) in toluene (1 mL) was added **8** (17.6 mg, 69.2 μmol) at room temperature, and the resulting yellow solution was stirred at room temperature for 30 min. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 30 : 1 then 5:1) to afford **17** (26.5 mg, 69.3 μmol, quant) as a white solid: mp 137.0–137.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.30 (s, 3H), 0.33 (s, 3H), 0.99 (s, 9H), 1.65 (s, 3H), 1.70–1.78 (m, 1H), 1.93-2.13 (m, 3H), 3.65–3.69 (m, 1H), 3.94 (dd, *J* = 6.1, 12.8 Hz, 1H), 4.96 (d, *J* = 7.3 Hz, 1H), 5.20 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –4.8, –4.8, 18.2, 25.4, 26.9, 27.3, 31.9, 36.1, 46.9, 47.2, 50.0, 63.0, 74.2, 94.4, 110.3, 110.6, 111.9, 113.1, 159.9; IR ($CHCl_3$, cm^{-1}) 2253, 1649; HRMS (EI) calcd for $C_{20}H_{26}O_2N_4Si$ (*m*/*z*) 382.18250, found 382.18272.

4.13. 7-*tert*-Butyldimethylsiloxy-9,9,10,10-tetracyano-2-oxabicyclo[4.2.2]dec-7-ene (18)

To the stirred solution of **16** (20.8 mg, 86.5 μmol) in toluene (2 mL) was added tetracyanoethylene (16.7 mg, 0.13 mmol) at room temperature, and the mixture was stirred at room temperature for 15 min. After the solvent was evaporated, the crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 5 : 1) to afford **18** (28.2 mg, 76.5 μmol, 88%) as a white solid: mp 107.5–108.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.30 (s, 3H), 0.32 (s, 3H), 0.97 (s, 9H), 1.81–1.89 (m, 1H), 1.98–2.03 (m, 2H), 2.31–2.36 (m, 1H), 3.29 (dd, *J* = 2.4, 5.9 Hz, 1H); 3.67–3.72 (m, 1H), 3.92 (dt, *J* = 3.9, 13.4 Hz, 1H), 5.03 (d, *J* = 7.8 Hz, 1H), 5.21 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –4.7, –4.7, 17.9, 25.3, 26.1, 26.7, 42.3, 46.4, 47.6, 63.1, 75.0, 95.2, 110.1, 110.3, 112.3, 113.1, 158.6; IR ($CHCl_3$, cm^{-1}) 2253, 1661, 1256; HRMS (EI) calcd for $C_{19}H_{24}O_2N_4Si$ (*m*/*z*) 368.16685, found 368.16585.

4.14. (±)-(4a*R**,8a*R**)-4a-*tert*-Butyldimethylsiloxy-8a-methyloctahydro-5-oxa- *N*-phenyl-1,2-cinnolinedicarboximide (22)

To a solution of **8** (20.9 mg, 82.1 μmol) in toluene (1 mL) was added at 0 °C a solution of PTAD (14.6 mg, 83.4 μmol) in toluene (1 mL) and the resulting red solution was stirred at 0 °C for 15 min. After evaporation of the solvent, silica gel (1 g) and dichloromethane (3 mL) were added. The suspension was stirred at room temperature for 20 min, and it was filtered through a Celite pad. The filtrate was concentrated, and the crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 7 : 1) to afford **22** (10.7 mg, 24.9 mmol, 30%) as a white solid: mp 138.0–143.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.23 (s, 3H), 0.27 (s, 3H), 0.97 (s, 9H), 1.33 (s, 3H), 1.54–1.57 (m, 1H), 2.03–2.17 (m, 2H), 2.93–2.97 (m, 1H), 3.68–3.72 (m, 1H), 3.90–3.95 (m, 1H), 5.25 (d, *J* = 8.3 Hz, 1H), 6.98 (dd, *J* = 0.5, 8.3 Hz, 1H), 7.37–7.39 (m, 1H), 7.45-7.50 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –3.0, –2.5, 18.5, 21.2, 21.7, 25.9, 28.1, 60.8, 62.8, 94.0, 107.7, 117.8, 125.8, 128.3, 129.1, 130.9, 145.6, 149.8; IR ($CHCl_3$, cm^{-1}) 1775, 1717, 1659, 1412; HRMS (EI) calcd for $C_{22}H_{31}O_4N_3Si$ (*m*/*z*) 429.20839, found 429.20770.

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