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INTRAMOLECULAR $[2\pi+2\pi]$ -PHOTOCYCLIZATION AND CONFORMATIONAL PREFERENCE OF 5-(2-BENZO[*b*]THIENYL)-5-ETHOXY-5*H*-DIBENZO[*a,d*]CYCLOHEPTENE

Motoko Akita, Sin-ya Mohri, Mai Takahashi, and Keiji Kobayashi*

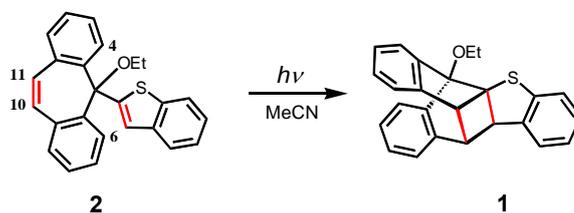
Department of Chemistry, Graduate School of Material Science, Josai University, Keyakidai, Sakado, Saitama 350-0295, Japan; E-mail: kobayak@josai.ac.jp

Abstract – The photoirradiation of 5-(2-benzo[*b*]thienyl)-5-ethoxy-5*H*-dibenzo[*a,d*]cycloheptene (**2**) in acetonitrile afforded a cagelike tetracyclic compound (**1**) via intramolecular $[2\pi+2\pi]$ -photocycloaddition. The molecular and crystal structures of **1** and **2** were characterized by a single-crystal X-ray diffraction study. The formation of the cycloadduct is discussed in relation to the preferable conformation of the central C-C bond in **2**, which was revealed to be in restricted rotation on the basis of the temperature-dependent ^1H NMR spectra.

Thiophene derivatives show versatile photoreactivity and wide mechanistic perspectives.¹ An unsaturated bond of the thiophene ring frequently exhibits photoreactivity as a 2π -electron component. A relevant example is the photoinduced electrocyclization of 1,2-di(2-thienyl)ethylenes to give a cyclohexadiene framework, which has been attracting considerable attention in relation to photochromic functions.² The thiophene ring of benzo[*b*]thiophenes also participates in inter- and intramolecular $[2\pi+2\pi]$ -cycloadditions.³ We previously reported the novel intramolecular photocyclization and di- π -methane rearrangement of tris(2-benzo[*b*]thienyl)methane derivatives.^{4,5} In the course of our continuous study, we have now found an unexpected intramolecular $[2\pi+2\pi]$ -photocyclization of 5-(2-benzo[*b*]thienyl)-5-ethoxy-5*H*-dibenzo[*a,d*]cycloheptene (**2**). Herein, we demonstrate the formation of **1**, a novel cagelike tetracyclic compound, from participation of the spatially remote olefinic bond in intramolecular $[2\pi+2\pi]$ -photocyclization,⁶ in which the conformation of the starting compound is preferable for the reaction to be induced.

An acetonitrile solution of **2** (ca 0.5 mM) was irradiated with a high-pressure Hg lamp through a Pyrex filter under nitrogen at 0 °C for 1 h. The chromatography of the resulting mixture on a silica gel gave **1**

in 54% yield (Scheme 1). The photoreaction proceeds rather cleanly without the formation of byproducts as indicated by the ^1H NMR spectrum of the photoreaction mixture.



Scheme 1

Single crystals of **1** suited for single-crystal structural analysis were isolated by recrystallization from ethanol. The crystal structure analysis of **1** confirms the formation of the cyclobutane ring, which arises from the intramolecular $[2\pi+2\pi]$ -cyclization of the $\text{C}_2=\text{C}_3$ double bond of the benzo[*b*]thiophene ring and the $\text{C}_{10}=\text{C}_{11}$ double bond of the dibenzocycloheptene ring (Scheme 1). The involvement of the double bond of the dibenzocycloheptene framework in intramolecular $[2\pi+2\pi]$ -photocycloaddition has been reported for photoreaction of tetrabenzoheptafulvalene,⁷ but such examples are rather rarely encountered. The cyclobutane ring of **1** is not planar but bent, and its four internal angles are all less than 90° . Although the results of the X-ray analysis are not good enough to estimate accurate structural parameters because of the poor crystallinity of the single crystal employed for data collection, they are still satisfactory for revealing the gross dihedral angles of $\text{H}_{58}\text{-C}_6\text{-C}_{13}\text{-H}_{53}$ and $\text{H}_{53}\text{-C}_{13}\text{-C}_2\text{-H}_{52}$ to be 93° and 33° , respectively (Figure 1).⁸ Thus, on the basis of the Karplus correlation, these geometries of hydrogen atoms provide a rational reason for their observed vicinal spin coupling constants in the ^1H NMR spectrum: $J_{\text{H}_{53}\text{-H}_{58}}=0$ and $J_{\text{H}_{52}\text{-H}_{53}}=5.6$ Hz.

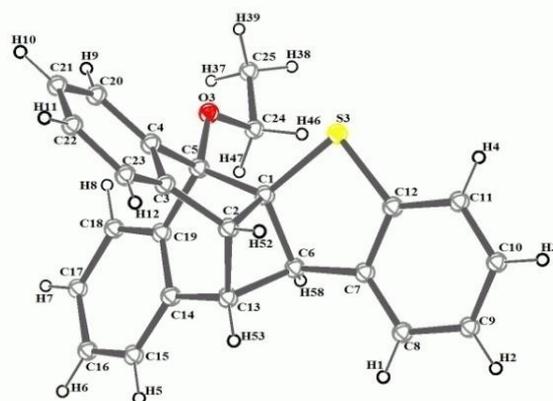


Figure 1. ORTEP drawing and atomic numbering of **1**.⁸ 20% thermal ellipsoids are shown. Selected distances [\AA] and angles [$^\circ$]: $\text{S}_3\text{-C}_1$ 1.819(5), $\text{S}_3\text{-C}_{12}$ 1.773(6), $\text{C}_1\text{-C}_2$ 1.548(8), $\text{C}_1\text{-C}_6$ 1.539(8), $\text{C}_6\text{-C}_{13}$ 1.565(7), $\text{C}_2\text{-C}_{13}$ 1.586(8), $\text{C}_6\text{-C}_7$ 1.490(8), $\text{C}_7\text{-C}_{12}$ 1.394(9), $\text{C}_1\text{-S}_3\text{-C}_{12}$ $88.6(3)$, $\text{C}_2\text{-C}_1\text{-C}_6$ $89.5(4)$, $\text{C}_1\text{-C}_6\text{-C}_{13}$ $85.1(4)$, $\text{C}_2\text{-C}_{13}\text{-C}_6$ $87.2(4)$, $\text{C}_1\text{-C}_2\text{-C}_{13}$ $84.0(4)$.

Intramolecular cyclization could be induced in the *syn* form with respect to the central C-C bond (Figure 2). Otherwise, the two 2π moieties are far apart to enter into the mutual reaction. The preference of an *sc* conformation was actually revealed by the X-ray crystallographic analysis of **2** (Figure 3).

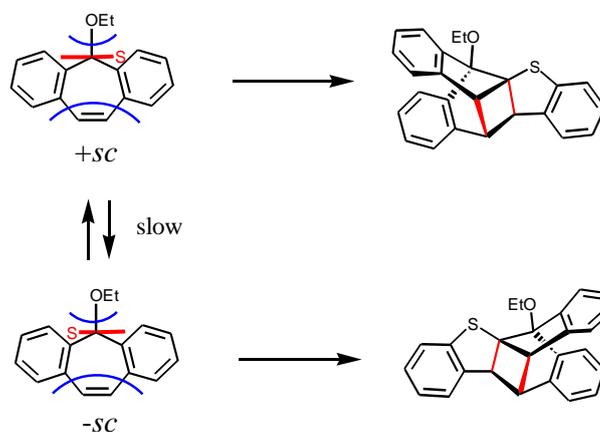


Figure 2. Schematic drawing of two equivalent *sc* forms of **2**, showing generation of chirality in photoproduct **1**. Blue bows indicate the steric congestion, restricting the rotation of the thieno[*b*]thiophene ring. See also Figure 3-a.

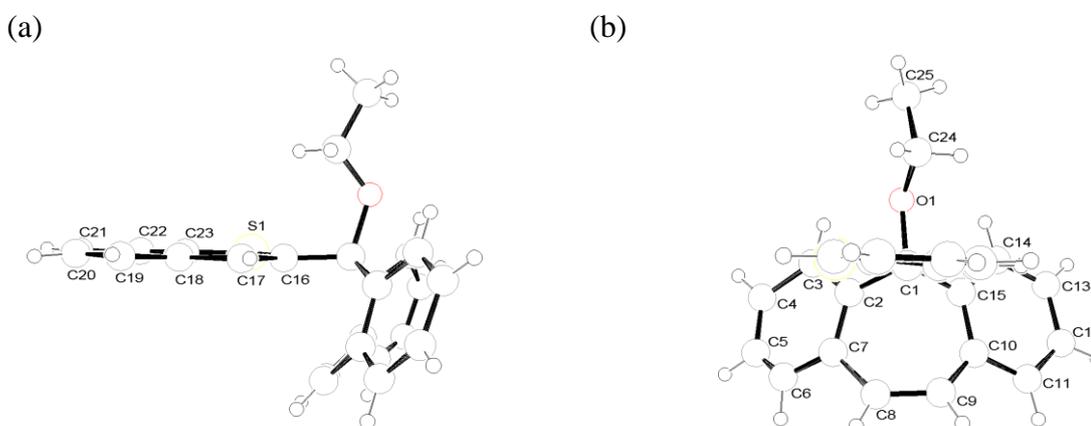


Figure 3. Molecular structure of **2** in the crystalline state:⁹ (a) side view. (b) top view.

Thus, judging from the molecular structure in the crystalline state, the intramolecular C---C distances associated with new bond formation (C8-C16 and C9-C17 of **2** in Figure 3) are 2.992 and 3.002 Å.^{9,10} The preference of the conformation, in which the C-S and C-O bonds are close to each other, is reasonable because of existence of attractive interactions between these two bonds.^{11,12} As seen in the side view of the molecular structure (Figure 3-a), the rotation of the planar thieno[*b*]thiophene ring about the central C-C bond suffers steric hindrance by both the C₁₀H=C₁₁H and C₂H₅O- moieties, resulting in restriction of the internal conversion between *+sc* and *-sc* forms (Figure 2). Such conformational

restriction is advantageous for the intramolecular $[2\pi+2\pi]$ -cycloaddition. Furthermore, the conformational fixation of the central bond of **2** at room temperature in the NMR time-scale was revealed by the temperature-dependent ^1H NMR spectra.

The ^1H NMR of **2** at room temperature displays distinct chemical shifts for H_{10} and H_{11} as well as for H_4 and H_6 (Scheme 1). As shown in Figure 4-a, when temperature was increased, the AB quartet signals at approximately 6.8 ppm due to H_{10} and H_{11} broadened and eventually coalesced at 60°. A similar behavior was also observed in the two doublet signals of H_4 and H_5 as shown in Figure 4-a. Thus, the single bond connecting the thieno[*b*]thiophene and dibenzocycloheptene rings of **2** has a high-energy barrier to rotation, which is attributed to the steric hindrance and the ground state stabilization of the *sc* form. A free-energy barrier (ΔG^\ddagger) for the rotation was estimated by the coalescence method to be 70 kJmol^{-1} at 60 °C, the coalescence temperature of the H_{10} and H_{11} signals.^{13,14}

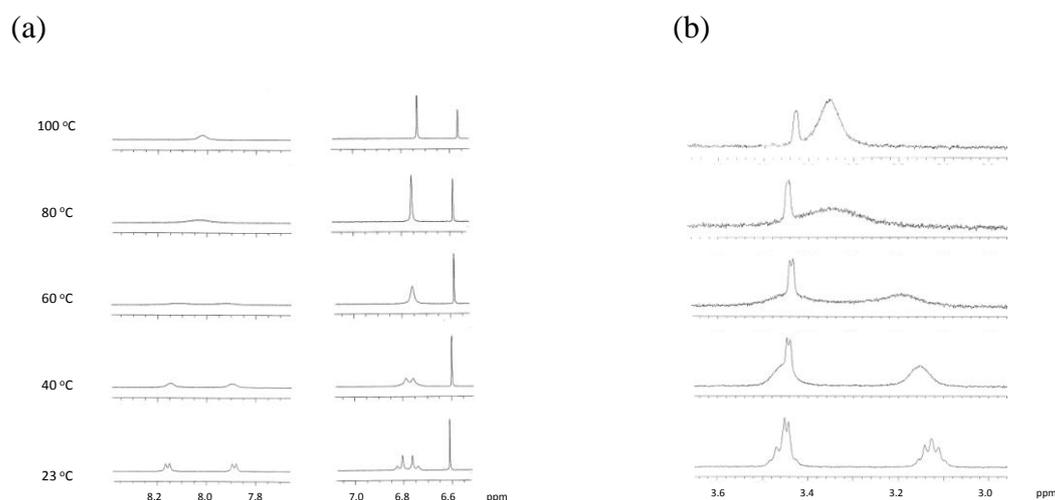
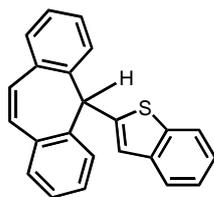


Figure 4. Variable-temperature ^1H NMR of **2** (in $\text{CDCl}_2\text{CDCl}_2$)
(a) low-field region and (b) methylene proton region.

The restricted rotation around the central bond was also indicated in the methylene protons of the ethoxy group, which occur at 3.12 and 3.45 ppm as double triplet signals, respectively (Figure 4-b). These signals showed averaging to coalesce at about 80 °C. The conformational rigidity is also shown by ^{13}C NMR spectra of **2**, in which twenty five signals are observed because of the nonequivalency of the dibenzo moiety.

Upon irradiation for 4 hours under nitrogen, no photoreaction was induced in **3**, a compound analogous to **1** but bearing no ethoxy substituent. Furthermore, **3** indicated no restricted rotation in its ^1H NMR spectra. Thus, the photoreactivity of **2** could be partially attributed to the preferable conformation, the *sc* form, which is considered to be persistent enough to undergo the photocyclization.

**3**

In summary, we described a novel photochemical reaction, *i.e.*, the intramolecular $[2\pi+2\pi]$ -cycloaddition between the unsaturated bond of the thieno[*b*]thiophene ring and the C=C double bond of the dibenzocycloheptene moiety. The fascinating cage-like structure of the intramolecular cycloadduct was elucidated by X-ray crystallographic structural analysis. The conformational preference and rigidity of the starting compound, revealed by X-ray analysis and dynamic ^1H NMR spectroscopy, respectively, are suggested to have effect on the intramolecular photocycloaddition.

EXPERIMENTAL

All the melting points were determined using a Yanaco MS-500V apparatus and are uncorrected. The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using a Varian 400-MR spectrometer. Chemical shifts are given in δ values (ppm) using TMS as the internal standard. Mass spectra were taken on a Shimadzu GCMS-QP5050A mass spectrometer. Elementary combustion analyses were recorded using a Yanaco CHN CORDER MT-6 analyzer. All reactions were monitored by TLC employing a 0.25 mm silica gel plate (Merck 60F 254). Column chromatography was carried out on silica gel (Merck 60N spherical).

Photoreaction: A solution of **2** (0.035 g, 0.095 mmol) in acetonitrile (200 mL) was degassed with nitrogen for 20 min prior to irradiation with 100W Hg vapor lamp. Photoirradiation was carried out through Pyrex filter for 20 min under nitrogen. After evaporation to dryness the residue was purified by silica gel chromatography to afford **1** (0.019 g, 54%) as colorless prisms.

$[2\pi+2\pi]$ -Photocycloadduct (1**):** colorless solids; mp 163 °C; MS m/z = 368; IR (KBr) 1445, 1223, 1196 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.39 (3H, t, J = 6.7 Hz), 3.62 (1H, s), 3.83 (1H, quint, J = 6.9 Hz), 4.05 (1H, d, J = 5.6 Hz), 4.10 (1H, quint, J = 6.9 Hz), 4.44 (1H, d, J = 5.6 Hz), 6.99 (1H, d, J = 7.3 Hz), 7.02 (1H, d, J = 7.3 Hz), 7.04 (1H, t, J = 7.3 Hz), 7.10 (1H, t, J = 7.3 Hz), 7.12 (1H, t, J = 6.8 Hz), 7.15 (1H, t, J = 6.8 Hz), 7.18 (1H, t, J = 7.6 Hz), 7.22 (1H, t, J = 7.3 Hz), 7.26 (1H, d, J = 7.6 Hz), 7.38 (1H, d, J = 7.3 Hz), 7.42 (1H, d, J = 7.3 Hz), 7.48 (1H, d, J = 7.6 Hz); ^{13}C NMR (CDCl_3) δ 15.50, 49.51, 58.06, 58.50, 61.54, 88.52, 119.98, 122.32, 124.22, 124.81, 125.64, 125.87, 126.87, 126.93, 127.47, 127.54, 127.66, 128.36, 135.42, 138.90, 139.56, 141.60, 144.07, 154.72. Anal. Calcd for $\text{C}_{25}\text{H}_{20}\text{OS}$: C; 81.48, H; 5.47. Found: C; 81.58, H; 5.53.

X-ray data for 1: 223 K: C₂₅H₂₀OS, *M* = 368.49, monoclinic, *P*2₁/*n* (#14), *a* = 10.396(3) Å, *b* = 30.936(5) Å, *c* = 17.575(4) Å, β = 91.323(10)°, *Z* = 12, *V* = 5651(2) Å³. *D*_{calcd} = 1.299 g/cm³. *R*1(*I* > 2.00σ(*I*)) = 0.0614, *wR*2(*I* > 3.00σ(*I*)) = 0.1241.

Preparation of 2: 5-(2-Benzo[*b*]thienyl)-5-ethoxy-5*H*-dibenzo[*a,d*]cycloheptene (**2**) was prepared by ethanolysis of 5-(2-benzo[*b*]thienyl)-5-hydroxy-5*H*-dibenzo[*a,d*]cycloheptene (**4**).

To a solution of benzo[*b*]thiophene (1.34 g, 10.0 mmol) in 120 mL of dried THF (100 mL), was added 8.2 mL of a solution of *n*-butyllithium (1.6 M in hexane) under nitrogen at 0 °C. After addition, the mixture was stirred for 30 min at this temperature. To this solution a solution of dibenzosuberone (2.06 g, 10 mmol) in 60 mL of THF was added dropwise at 0 °C. After being stirred for 1 h at room temperature the solution was refluxed for 4 h under nitrogen. The reaction mixture was then poured into water and treated with CH₂Cl₂ and the aqueous layer was extracted twice with 40 mL of CH₂Cl₂. The combined organic layer was dried over anhydrous magnesium sulfate and concentrated. The residue was chromatographed on silica using CH₂Cl₂ as eluent to give (**4**) (2.83 g, 83%) as colorless solids.

5-(2-Benzo[*b*]thienyl)-5-hydroxy-5*H*-dibenzo[*a,d*]cycloheptene (4**)**: mp 150 °C; MS *m/z* = 340; IR (KBr) 3460, 1302, 1159 cm⁻¹; ¹H NMR (CDCl₃) 2.62 (1H, s), 6.57 (1H, s), 6.80 (2H, s), 7.20-7.23 (2H, m), 7.34-7.40 (4H, m), 7.48-7.53 (3H, m), 7.59 (1H, d, *J* = 8.0 Hz), 8.20 (2H, d, *J* = 7.9 Hz); ¹³C NMR (CDCl₃) δ 75.70, 122.15, 123.10, 123.50, 124.04, 124.19, 124.42, 127.27, 128.11, 128.73, 131.28, 133.54, 138.75, 139.18, 141.81, 151.84. Anal. Calcd for C₂₃H₁₆SO: C, 81.15; H, 4.74; S, 9.42. Found: C, 81.29; H, 4.77; S, 9.46.

A solution of **4** (0.68 g, 2.00 mmol) in 80 mL EtOH was refluxed with conc H₂SO₄ (ca. 0.2 mL) for 3 h. The reaction mixture was then poured into water, treated with 50 mL of brine and with 80 mL of CHCl₃, and the aqueous layer was extracted twice with 40 mL of CHCl₃. The combined organic layer was dried over anhydrous MgSO₄ and concentrated. The residue was chromatographed on silica gel using CH₂Cl₂ as eluent to give **2** (0.57 g, 78%) as colorless solids.

5-(2-Benzo[*b*]thienyl)-5-ethoxy-5*H*-dibenzo[*a,d*]cycloheptene (2**)**: mp 96-97 °C; MS *m/z* = 368; ¹H NMR (CDCl₃) δ 1.39 (3H, t, *J* = 7.0 Hz), 3.17 (1H, m), 3.48 (1H, m), 6.61 (1H, s), 6.78 (2H, q, *J* = 9.4 Hz), 7.22 (2H, m), 7.33 (4H, m), 7.46-7.52 (3H, m), 7.60 (1H, d, *J* = 5.2 Hz), 7.90 (1H, d, *J* = 7.9 Hz), 8.17 (1H, d, *J* = 7.9 Hz); ¹³C NMR (CDCl₃) δ 15.21, 60.50, 122.11, 123.45, 124.03, 124.15, 124.28, 124.53, 125.98, 126.70, 126.99, 127.85, 128.12, 128.70, 128.78, 128.88, 130.50, 131.82, 133.76, 133.90, 138.33, 139.53, 140.01, 142.40, 146.41. Anal. Calcd for C₂₅H₂₀SO: C, 81.48; H, 5.47. Found: C, 81.48; H, 5.47.

X-ray data for 2: 93 K: C₂₅H₂₀OS, *M* = 368.49, orthorhombic, *P*2₁2₁2₁ (#19), *a* = 7.151(3) Å, *b* = 14.398(4) Å, *c* = 17.328(8) Å, *Z* = 4, *V* = 1784.2(11) Å³. *D*_{calcd} = 1.372 g/cm³. *R*1(*I* > 2.00σ(*I*)) = 0.0813,

$wR2 (I > 1.50\sigma(I)) = 0.2320$.

Preparation of 3: A mixture of **4** (1.7 g, 5.0 mmol) and hydriodic acid (57%) (2.5 mL) in AcOH (100 mL) was refluxed under nitrogen for 4 h at 110 °C. The reaction mixture was poured into a aqueous solution of Na₂S₂O₃ and extracted twice with CH₂Cl₂. The combined organic layer was dried over anhydrous MgSO₄ and concentrated. The residue was chromatographed on silica gel using benzene and hexane (1:1) as eluent to give **3** (1.39 g, 86%) as colorless crystals.

5-(2-Benzo[*b*]thienyl)-5*H*-dibenzo[*a,d*]cycloheptene (3): mp 168-169 °C; MS $m/z = 324$; ¹H NMR (CDCl₃) δ 5.55 (1H, s), 6.36 (1H, s), 6.78 (2H, s), 7.14 (1H, t, $J = 7.5$ Hz), 7.19 (1H, t, $J = 7.5$ Hz), 7.34-7.45 (7H, m), 7.50 (2H, d, $J = 7.5$ Hz), 7.57 (1H, d, $J = 8.1$ Hz). Anal. Calcd for C₂₃H₁₆S: C, 85.14; H, 4.97, S, 9.88. Found: C, 85.40; H, 5.02; S, 9.92.

Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre. **1:** CCDC 912714. **2:** CCDC 928802.

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8. The molecules of **1** are packed in the space group $P2_1/c$ (#14), and there are three crystallographically independent molecules of **1**, *i.e.*, **A**, **B**, and **C**, in a unit cell. These molecules exhibit essentially the same structure with respect to the rigid carbon framework, but take somewhat different conformation with respect to the ethoxy moiety. **A** molecule makes a centrosymmetric pairing with its own enantiomeric molecule, aligning along the *a*-axis. On the other hand, **B** and **C** make no pairing with their own enantiomers, which align in separate lines along the *a*-axis. Figure 1 shows the molecular structure of **A**.
9. A flip-flop disorder is involved in the benzo[*b*]thiophene ring. The existence of this disorder gave rather poor results in the X-ray analysis.
10. Despite of these short distances, **2** showed no photoreactivity in the solid state.
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