Supporting Information:

Photoinduced cytotoxicity of photochromic symmetric diarylethene derivatives:

The relation of structure and cytotoxicity

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1. Materials

All commercial reagents were used as received unless otherwise stated. Diarylethenes (DAEs) **1o**[1], **2o**[2], **7o**[3], **8o**[4], **9o**[5], **10o**[6], and **11o**[7] were synthesized according to the procedure described in the literature. The DNA used was sodium salts of DNA from Salmon testes (average M_w: 1.3×10^6, ca. 2000 bp); SIGMA-ALDRICH D1626[8]. A_{260}/A_{280} is a measure of nucleic acid purity. DNA is known to absorb light at 260 nm, and the fact that ratios A_{260}/A_{280} ranged from 1.8 to 2.0 indicates that the sample is of good purity with little or no contamination.[9] The A_{260}/A_{280} ratio of the DNA used in this study in the mixture of solvent (Dulbecco's phosphate-buffered saline (D-PBS; pH 7.1-7.7, Wako, Osaka, Japan):DMSO = 95:5 (v/v)), ranged from 1.8 to 2.0.

2. Methods

^{1}H (400 MHz), ^{13}C (100 MHz), and ^{19}F NMR (376 MHz) spectra were recorded on a JEOL JNM-400 spectrometer. Chemical shifts are reported in ppm from the signals of tetramethylsilane (TMS) for ^{1}H NMR (TMS: 0.00 ppm, s)[10], solvent peak for ^{13}C NMR ($CHCl_3$: 77.16 ppm)[10], and hexafluorobenzene (C_6F_6) for ^{19}F NMR (C_6F_6: -164.9 ppm) in $CDCl_3$. In the case of molecules with perfluorocyclopentene rings, the ^{13}C NMR measurement by the ^{1}H decoupling method lacks signals from the fluorine-bonded carbon atoms. To measure these lacking signals, we performed ^{13}C NMR measurements using the ^{19}F decoupling method. However, the ^{13}C NMR using the ^{19}F decoupling method gave no clear data because the peaks were split by ^{1}H coupling. Note, therefore, that the ^{13}C NMR data in this paper were measured using the standard ^{1}H decoupling method. High resolution mass spectrometry (HRMS) was recorded on a JEOL JMS-S3000 SpiralTOF. Melting points were observed on a Yanaco MP-500D. Absorption spectra of the solutions were monitored on a Hitachi UH-4150 spectrophotometer. Fluorescence spectra of the solutions were monitored on a Hitachi F-7100 Fluorescence Spectrophotometer. For the UV light irradiation, a UV hand lamp SPECTROLINE Model EB-280C/J (λ = 313 nm) and an AS ONE Handy UV Lamp LUV-6 (dominant wavelength: 365 nm) were used. For visible light irradiation, a 500W USHIO SX-UI501XQ Xenon lamp with Toshiba color filters (Y-48, Y-44, UV-29: $\lambda > 480$ nm) was used. All measurements were performed at room temperature unless otherwise specified.

The Gaussian16 program package[11] was used for geometry optimization with density functional theory (DFT)[12] for ground states. The B3LYP[13-15] functionals were adopted as exchange-correlation terms of DFT. The gaussian 6-31G(d) basis set was adopted for all calculations. As for the solvent effect, a polarizable continuum model (PCM)[16] was employed for water.

The Avogadro ver. 1.2.0 (Hanwell et al., 2012)[17] was used for calculation of geometrical parameters of the DAE molecule obtained by DFT calculation.

HeLa cell line derived from human cervical adenocarcinoma was purchased from Riken Cell Bank (No. RCB0007). Light irradiation of HeLa cells in a medium containing each diarylethene was carried out using a PC-controlled micro-projection system (DESM-01, Engineering System Co.) installed in

an inverted research microscope (IX70, Olympus Co.).[18-21] Near-UV light with wavelength of 365 nm, blue light with wavelength of 436 nm or green light with wavelength of 546 nm was irradiated onto arbitrary areas of the sample as observed through the same objective lens.

3. X-ray crystallographic analysis

X-ray crystallographic analysis was performed with an X-ray diffractometer (**3o**, **4o**: Bruker AXS, D8 QUEST, Mo Kα radiation (λ = 0.71073 Å); **5o**: Bruker AXS, SMART APEX2 Ultra-Cu, Cu Kα radiation (λ = 1.54178 Å)). The crystals were cooled using a low-temperature controller (**3o**, **4o**: Japan Thermal Engineering, JAN 2-12; **5o**: Japan Thermal Engineering, TC-190CP-CS-K). The diffraction frames were integrated with the Bruker SAINT program. The cell constants were determined by global refinement. The data were corrected for absorption effects using the multi-scan method (SADABS). The structure was solved by the direct method and refined by the full-matrix least-squares method using the SHELX-2014 program. The positions of all hydrogen atoms were calculated geometrically and refined by the riding model. The crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. (CCDC 2095136-2095138).

4. Photoinduced cytotoxicity experiments

As a guidance in the comparing investigation to know the tendency of the structure dependent cytotoxicity of DAEs, we determined the lower limit concentration (LLC) of DAEs at which the photocytotoxicity started to appear clearly as follows.

1.The HeLa cells (5×10^5) were seeded in each well of 96 well plates together with 0.1 mL of a culture medium (MEM) containing a predetermined concentration of DAE (0.02, 0.05, 0.1, 0.2, 0.5, 1 and 2 ppm).

2. After incubation for 18 h, the dark cytotoxicity was evaluated from the number of live cells.

3. culture medium was replaced with a fresh one, and then blue light (λ = 436 nm, 180 mW cm^{-2}) was irradiated for 2 min.

4. The cells were observed 2 hours after irradiation, and the lower limit concentration expressing photoinduced cytotoxicity was determined with the criterion that more than 90% exhibited a change in appearance.

Since clear microscopic image was difficult to obtained for the cells in a well of 96 well plates, we used cell culture dish for the microscopic observation. Typical experimental conditions are as follows.

1. The HeLa cells (8×10^5) were seeded in a 35 mmϕ dish together with 2 mL of a medium (minimum essential media: MEM) containing a predetermined concentration of DAE.

2. After incubation for 18 h, the culture medium was replaced with a fresh one. Then, local light irradiation was carried out to achieve better distinction.

3. Changes in the appearance were observed 2 hours after irradiation.

The DAEs were added in the culture medium as ethanol solution due to their poor water solubility. The maximum amount of ethanol added to the medium was 0.5% and we had confirmed that the ethanol with those concentrations had no influence on the viability or growth of HeLa cells in advance.

5. DNA intercalation experiments[22,23]

Preparation of sample

To a 100 mL sample tube, 57 mL of D-PBS solution, 1.5 mL of DMSO, 1.77×10^{-3} g (4.49×10^{-6} mol) of ethidium bromide (EB), and 3.0×10^{-4} g (4.63×10^{-7} mol bp^{-1}, ca. 2000 bp) of DNA (sodium salts of DNA from salmon testes; SIGMA-ALDRICH D1626)[8] were added and stirred for 24 h at room temperature to form the DNA solution.

To a 10-mL sample tube, 1.5×10^{-6} mol of open- or closed-ring isomers of DAE derivatives dissolved in 1.5 mL of DMSO were added. These DMSO solutions and fresh DMSO were further mixed by changing the composition ratio and adjusting it to become 100 μL in total, and 3.9 mL of DNA solutions were added. The concentrations in the mixed solution were D-PBS/DMSO = 95:5 (v/v), DNA: 3.9 nM bp^{-1}, and EB: 75 μM. The concentrations of open- or closed-ring isomers of diarylethenes in the final mixed solutions were 0, 5, 10, 15, 20, and 25 μM (Table S1).

Measurement

Fluorescence spectra were measured three times just after the addition and 24 hours after the addition of the solutions of open-/closed-ring isomers of DAEs, and the fluorescence intensity of EB was recorded at λ_{em} = 610 nm (I).

Fluorescence spectra were monitored at constant concentrations of DNA and EB (3.9 nM bp^{-1} and 75 μM, respectively), while adding increasing amounts of diarylethenes (in the range of 0-25 μM) (Table S1).

Table S1. Mixed Ratio of DAE solutions and DMSO.

	DAE concentrations in final mixture					
	0 μM	5 μM	10 μM	15 μM	20 μM	25 μM
DAE solution / μL	0	20	40	60	80	100
DMSO / μL	100	80	60	40	20	0

6. Optimized structure by DFT calculation

To investigate the relationship between molecular bulkiness and DNA intercalation of the open- and closed-ring isomers of DAE derivatives, the optimized geometry of the open- and closed-ring isomers of each molecule were determined using DFT calculations. Note that in derivative **10**, the iodine ion was omitted, and thus charge of **10** was set to +2. The procedure consists of two steps:

1. Full optimization of ground state energies on the B3LYP/6-31G(d) level of theory. The effect of water as solvent was included using the polarizable continuum model (PCM).

2. Calculation of vibrational frequencies to confirm that the optimized structure corresponds to a minimum on the potential energy surface.

7. Synthesis

·Synthesis of 1,2-bis(5-methyl-2-phenylthiazol-4-yl)-3-trifluoromethylpentafluorocyclopentene (3o)

The derivative **3o** was obtained in 2% yield as a byproduct during the synthesis of 1,2-bis(5-methyl-2-phenylthiazol-4-yl)perfluorocyclohexene (**11o**).[7]

3o: m.p. 171.0−172.0°C

^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S1) δ 7.90-7.87 (m, 4H), 7.43-7.42 (m, 6H), 2.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S2) δ 166.0, 140.2, 137.5, 133.1, 130.5, 129.1, 126.6, 12.3. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S3) δ -76.2 (quin, J = 17 Hz, 3F), -105.5 (conformer A: q, J = 17 Hz) and -106.2 (conformer B: q, J = 17 Hz) (conformer A: conformer B = 2:3 (ratio of peak areas), 2F), -109.7 (conformer B: s) and -110.5 (conformer A: s) (conformer A: conformer B = 2:3 (ratio of peak areas), 2F), -184.8 (s, 1F). HRMS (MALDI, positive): *m/z* calcd. for $C_{26}H_{16}F_8N_2NaS_2^+$ $[M+Na]^+$: 595.05194, found: 595.05182.

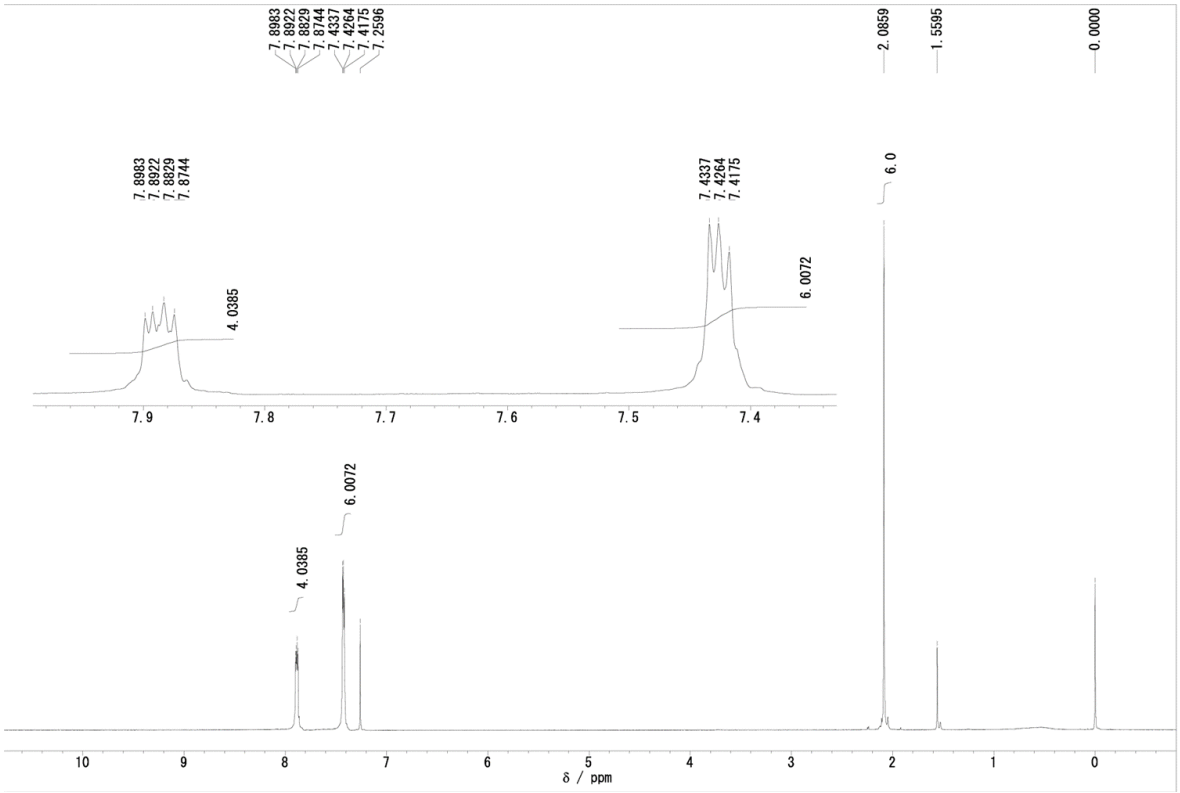


Figure S1. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl)-3-trifluoromethylpentafluorocyclopentene **(3o)**.

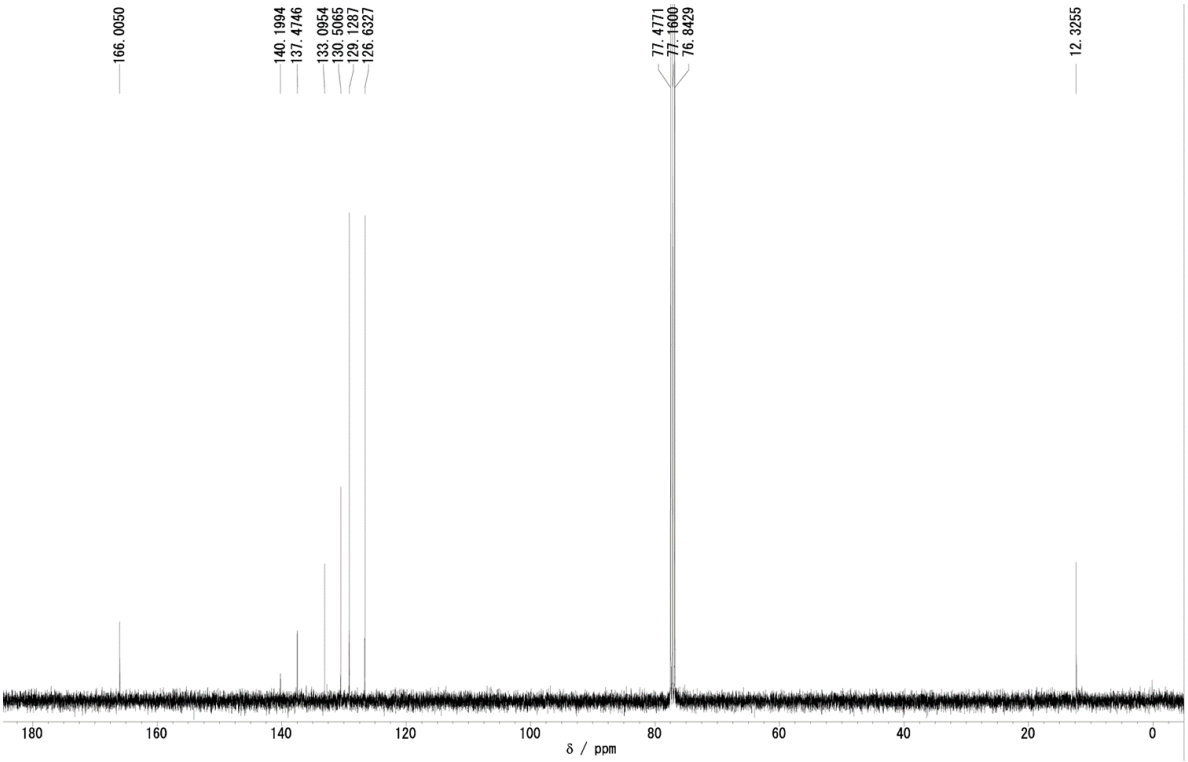


Figure S2. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl)-3-trifluoromethylpentafluorocyclopentene (**3o**).

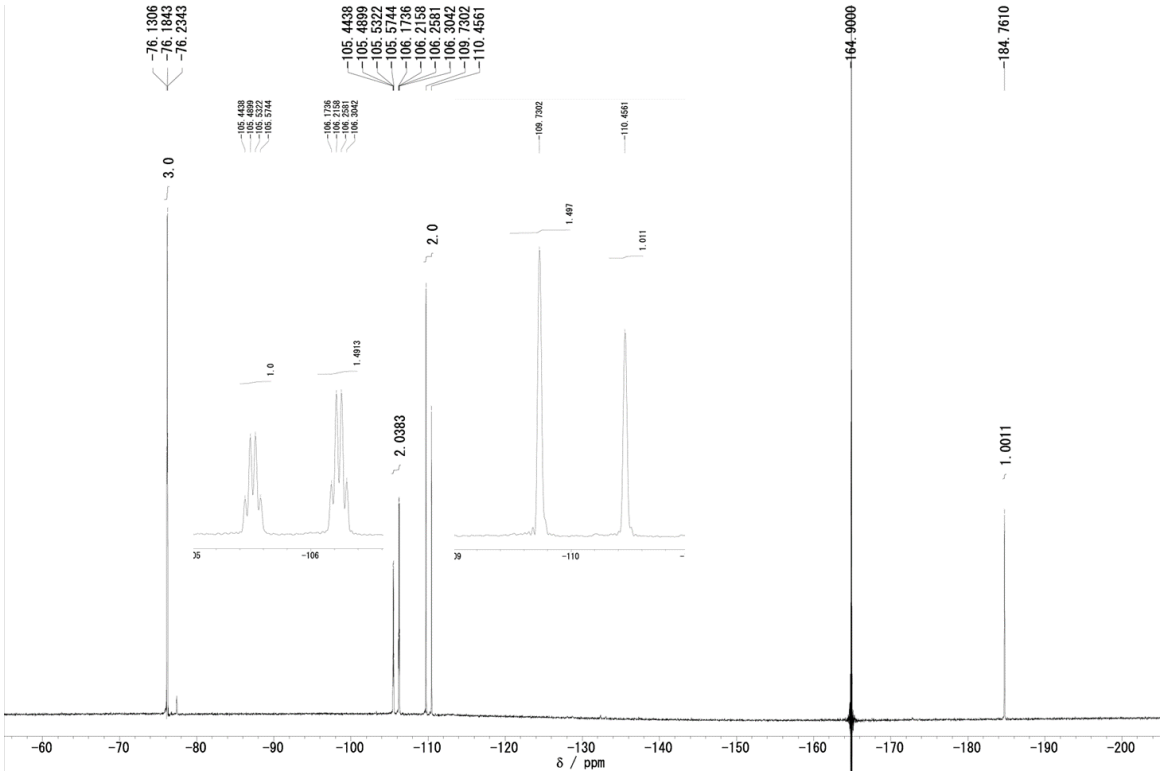
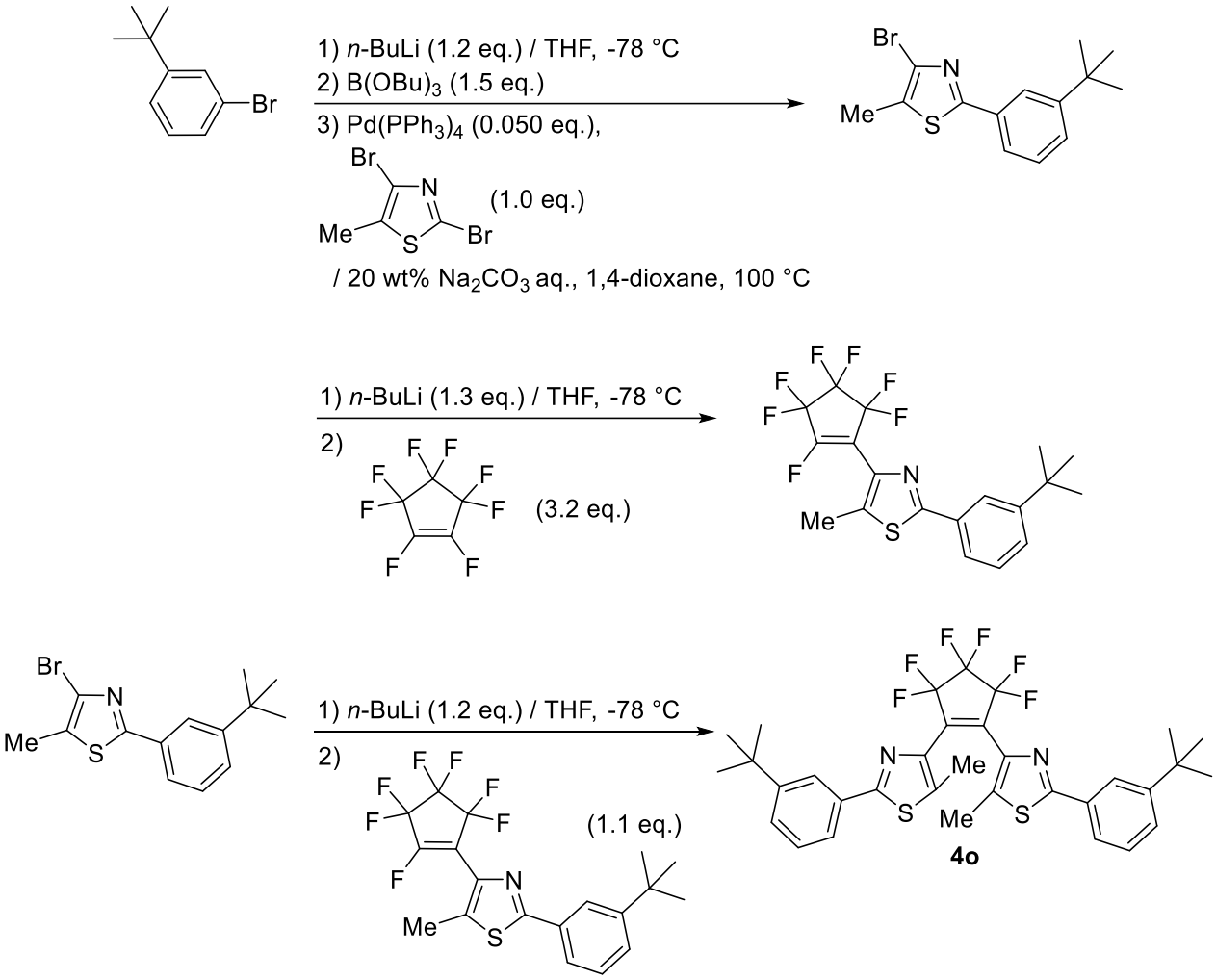


Figure S3. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl)-3-trifluoromethylpentafluorocyclopentene (**3o**).

·**Synthesis of 1,2-bis(5-methyl-2-(3-*tert*-butyl)phenylthiazol-4-yl)perfluorocyclopentene (4o)**

The total synthetic route of **4o** is shown in Scheme S1.



Scheme S1. Synthetic route of **4o**.

4-Bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole

Into a 200-mL three-neck flask, 1.66 g (7.79 mmol) of 1-bromo-3-*tert*-butylbenzene was added to 45 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 6.0 mL (9.60 mmol, 1.2 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. Then 3.2 mL (11.96 mmol, 1.5 eq.) of tributyl borate was added, followed by stirring another 10 min, after which the temperature of the reaction mixture was allowed to warm to room temperature. Then the mixture was stirred for 1 h at this temperature. After the reaction was completed, 2 mL of water was added, and the solvents were evaporated in vacuo. To the reaction mixture, we added 2,4-dibromo-5-methylthiazole[24] (2.00 g, 7.75 mmol, 1.0 eq.), tetrakis(triphenylphosphine)palladium(0) (0.45 g, 0.39 mmol, 0.050 eq.), a 20 wt% Na_2CO_3 aq. (15 mL), and 1,4-dioxane (30 mL), and the mixture was refluxed for 17 h. After the reaction was over, the reaction mixture was allowed to cool to room temperature. The mixture was extracted with 50 mL of diethyl ether four times. The organic layer was washed with 200 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents

were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using hexane as an eluent to obtain 1.77 g (5.71 mmol) of the 4-bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole as white solid in 73% yield.

m.p. 91.6−92.4°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S4) δ 7.90 (dd, J = 1.8, 1.8 Hz, 1H), 7.66 (ddd, J = 7.7, 1.8, 1.1 Hz, 1H), 7.46 (ddd, J = 7.7, 1.8, 1.1 Hz, 1H), 7.35 (dd, J = 7.7, 7.7 Hz, 1H), 2.44 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S5) δ 166.2, 152.2, 132.7, 128.8, 128.6, 127.6, 125.3, 123.5, 123.0, 34.9, 31.4, 13.1. HRMS (MALDI, positive): *m/z* calcd. for $C_{14}H_{17}NSBr^{+}$ $[M+H]^{+}$: 310.02596, found: 310.02563.

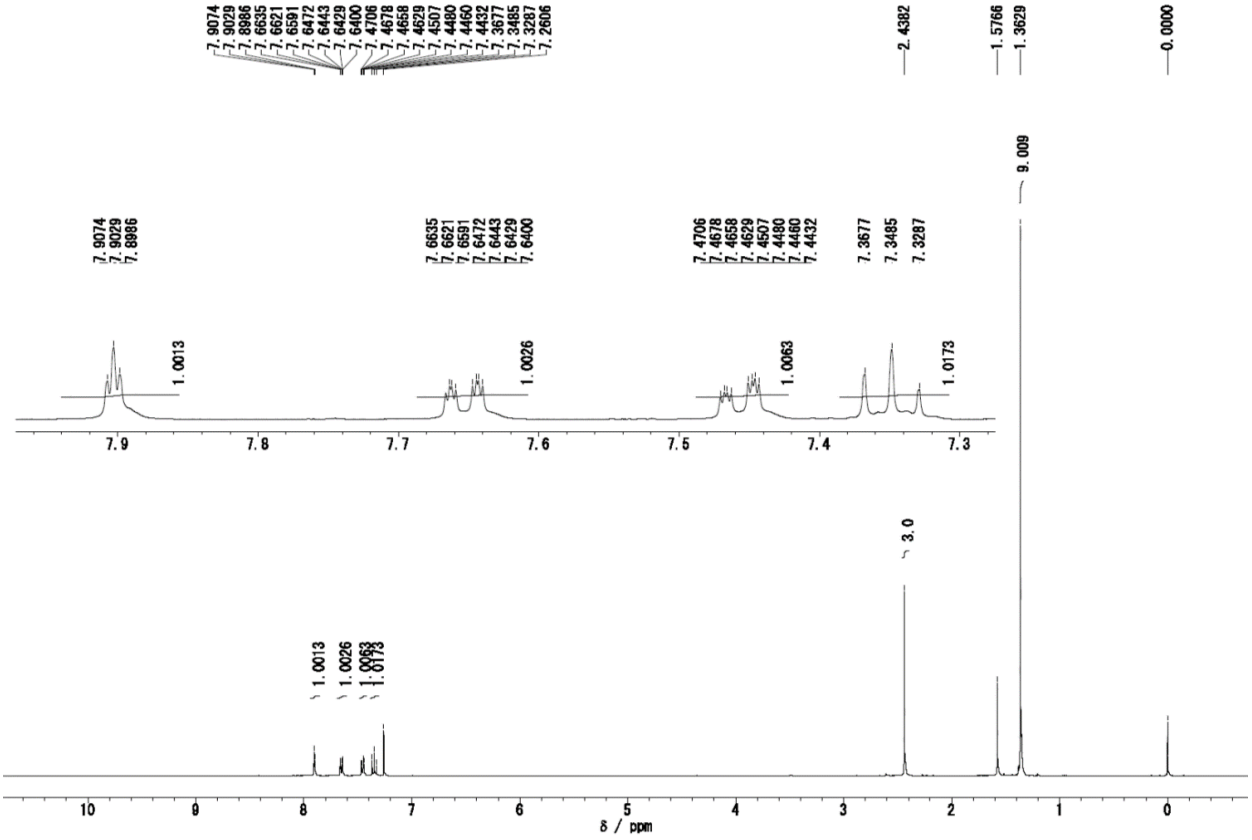


Figure S4. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 4-bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole.

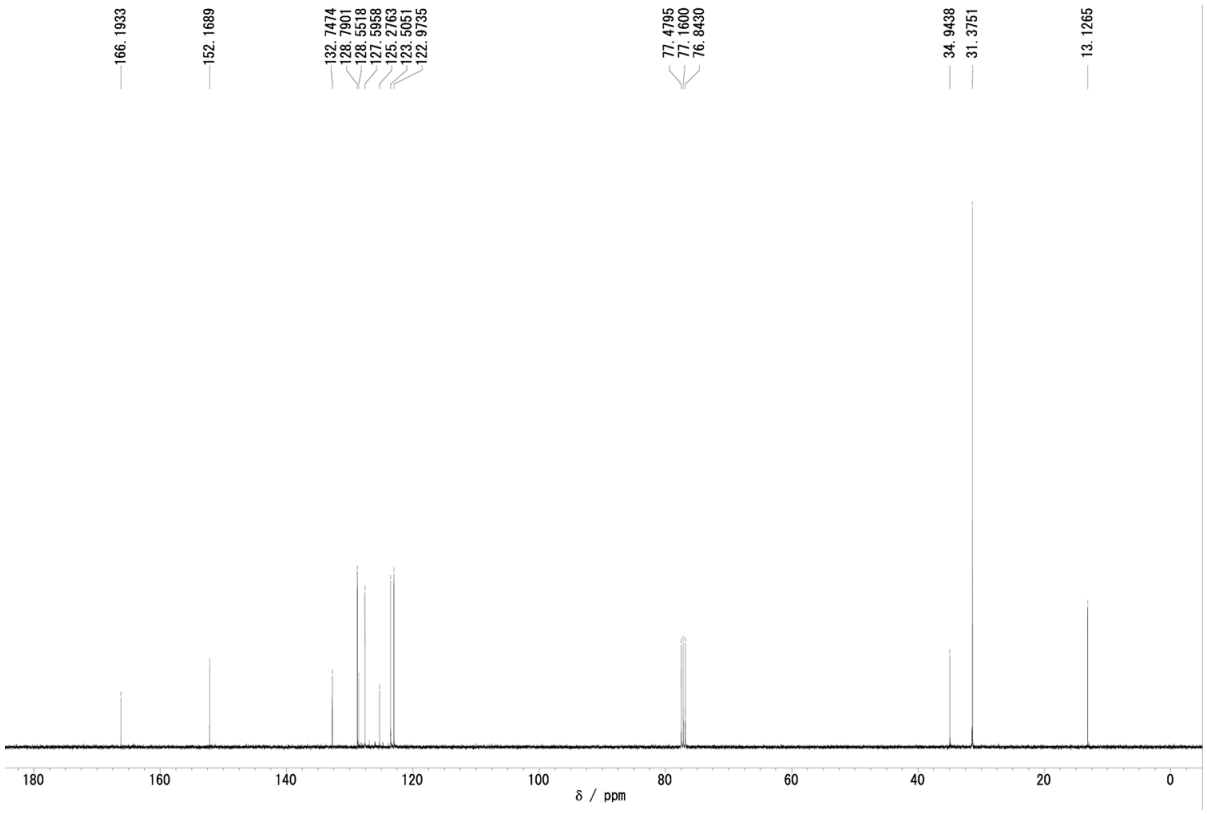


Figure S5. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 4-bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole.

4-(2,3,3,4,4,5,5-Heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole

Into a 200-mL three-neck flask, 1.50 g (4.83 mmol) of 4-bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole was added to 30 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 3.8 mL (6.08 mmol, 1.3 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. To the mixture, 1.3 mL (15.33 mmol, 3.2 eq.) of perfluorocyclopentene was gradually added, followed by stirring another 10 min. The temperature of the reaction mixture was allowed to warm to -40°C, then the solution was stirred another 4 h at this temperature. After the reaction was completed, 15 mL of water was added, and the mixture was allowed to warm to room temperature. Solvent of THF was evaporated in vacuo, then 300 mL of water was added. The mixture was extracted with 50 mL of diethyl ether four times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using hexane as an eluent to obtain 1.78 g (4.20 mmol) of the 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole as pale-yellow solid in 87% yield.

m.p. 61.7−62.5°C. ^1H NMR (400 MHz, $CDCl_3$, ppm: Figure S6) δ 7.93 (dd, J = 1.8, 1.8 Hz, 1H), 7.70 (ddd, J = 7.7, 1.8, 1.2 Hz, 1H), 7.49 (ddd, J = 7.7, 1.8, 1.2 Hz, 1H), 7.38 (dd, J = 7.7, 7.7 Hz, 1H), 2.54 (d, J = 2.7 Hz, 3H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S7) δ 148.4, 137.2, 121.6,

118.5, 118.3, 117.5, 115.7, 114.3, 113.8, 13.4, 40.6, 26.0. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S8) δ -111.3 (d, J = 11.6 Hz, 2F), -121.6 (d, J = 15.9 Hz, 2F), -128.2 (br s, 1F), -133.4 (s, 2F). HRMS (MALDI, positive): *m/z* calcd. for $C_{19}H_{17}F_7NS^+$ $[M+H]^+$: 424.09644, found: 424.09668.

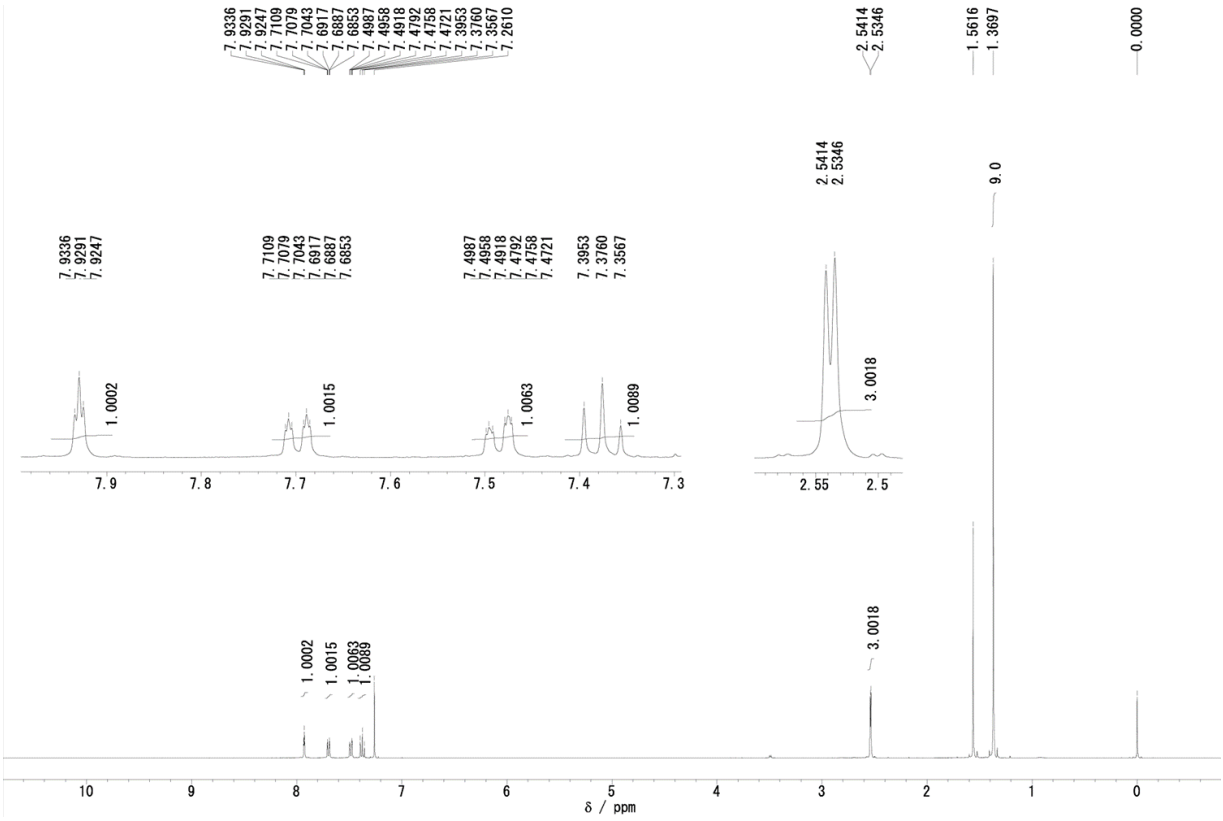


Figure S6. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole.

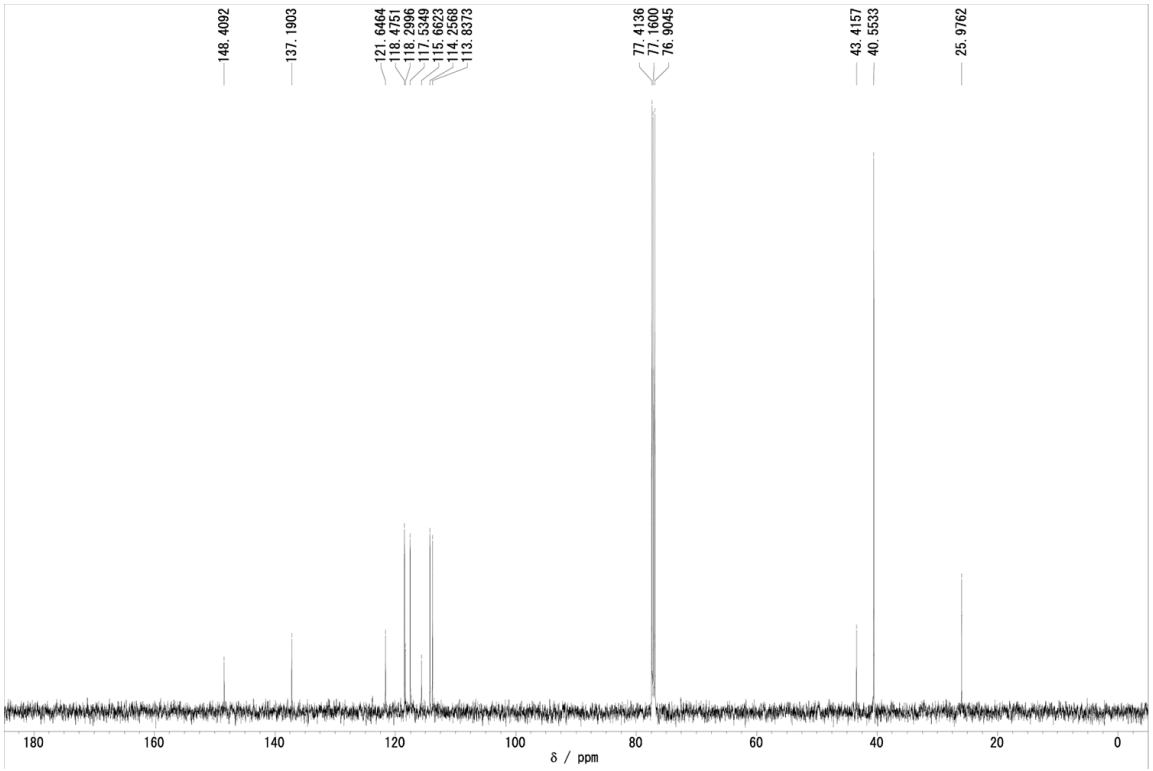


Figure S7. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole.

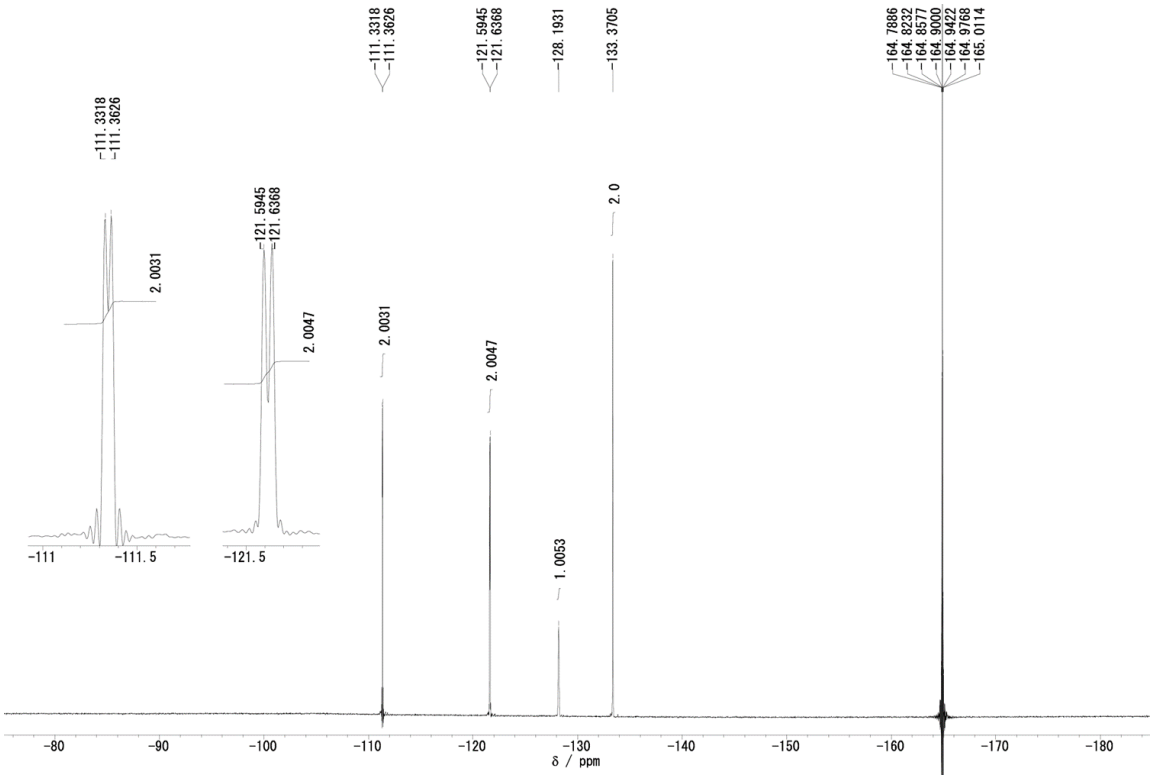


Figure S8. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole.

1,2-Bis(5-methyl-2-(3-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (4o)

Into a 100-mL three-neck flask, 0.83 g (2.68 mmol) of 4-bromo-5-methyl-2-(3-*tert*-butyl)phenylthiazole was added to 30 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 2.1 mL (3.36 mmol, 1.2 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. To the mixture, THF anhydrous solution containing 1.30 g (3.07 mmol, 1.1 eq.) of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(3-*tert*-buthylphenyl)thiazole was added, followed by stirring another 10 min. The temperature of the reaction mixture was allowed to warm to -40°C, then the solution was stirred another 5 h at this temperature. After the reaction was completed, 10 mL of water was added, and the mixture was allowed to warm to room temperature. Solvent of THF was evaporated in vacuo, then 300 mL of water was added. The mixture was extracted with 40 mL of diethyl ether four times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using a mixture of hexane and dichloromethane (3:1 (v/v)) as an eluent to obtain 1.12 g of crude product. By recrystallization from methanol, 0.87 g (1.37 mmol) of **4o** was obtained as colorless needle crystals in 51% yield.

m.p. 157.8−158.5°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S9) δ 7.86 (dd, J = 1.6, 1.6 Hz, 2H), 7.68 (ddd, J = 7.8, 1.6, 1.1 Hz, 2H), 7.46 (ddd, J = 7.8, 1.6, 1.1 Hz, 2H), 7.35 (dd, J = 7.7, 7.7 Hz, 2H), 2.12 (s, 6H), 1.33 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S10) δ 166.3, 152.2, 140.4, 137.0, 132.9, 128.8, 127.7, 124.0, 123.5, 34.9, 31.4, 12.3. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S11) δ -113.5 (s, 4F), -135.2 (s, 2F). HRMS (MALDI, positive): *m/z* calcd. for $C_{33}H_{32}F_6N_2NaS_2^+$ $[M+Na]^+$: 657.18033, found: 657.18024.

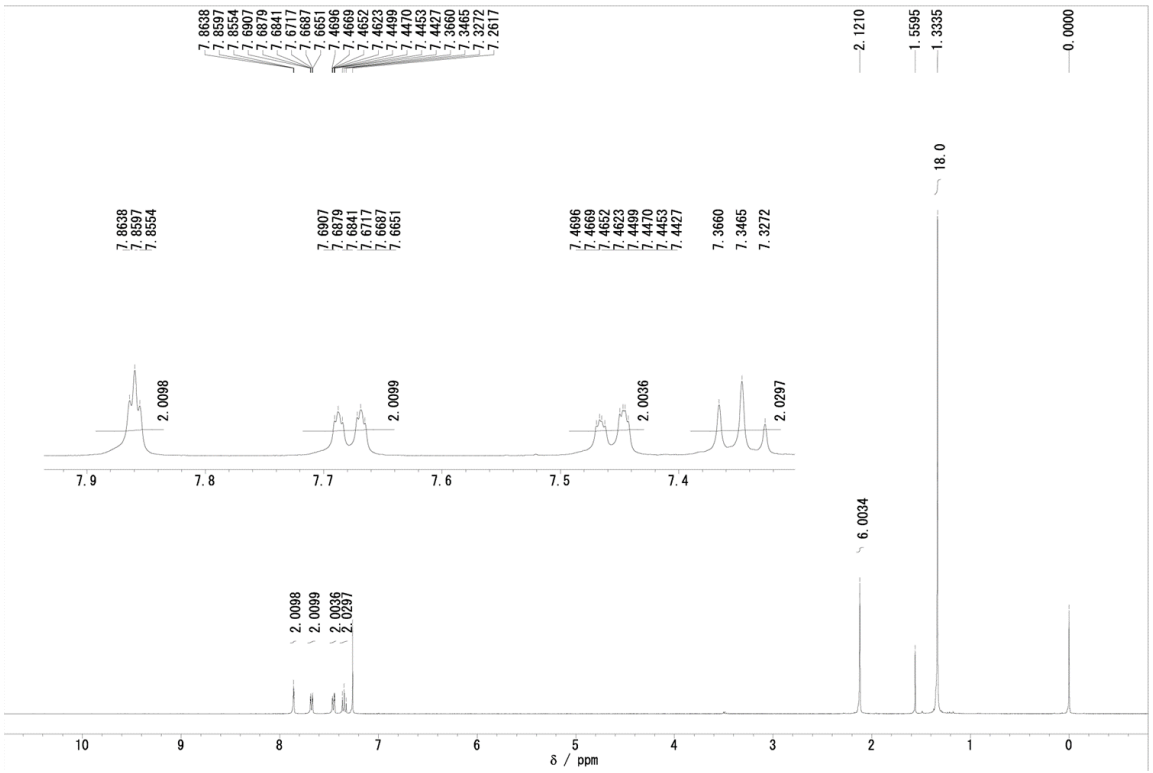


Figure S9. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1,2-bis(5-methyl-2-(3-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**4o**).

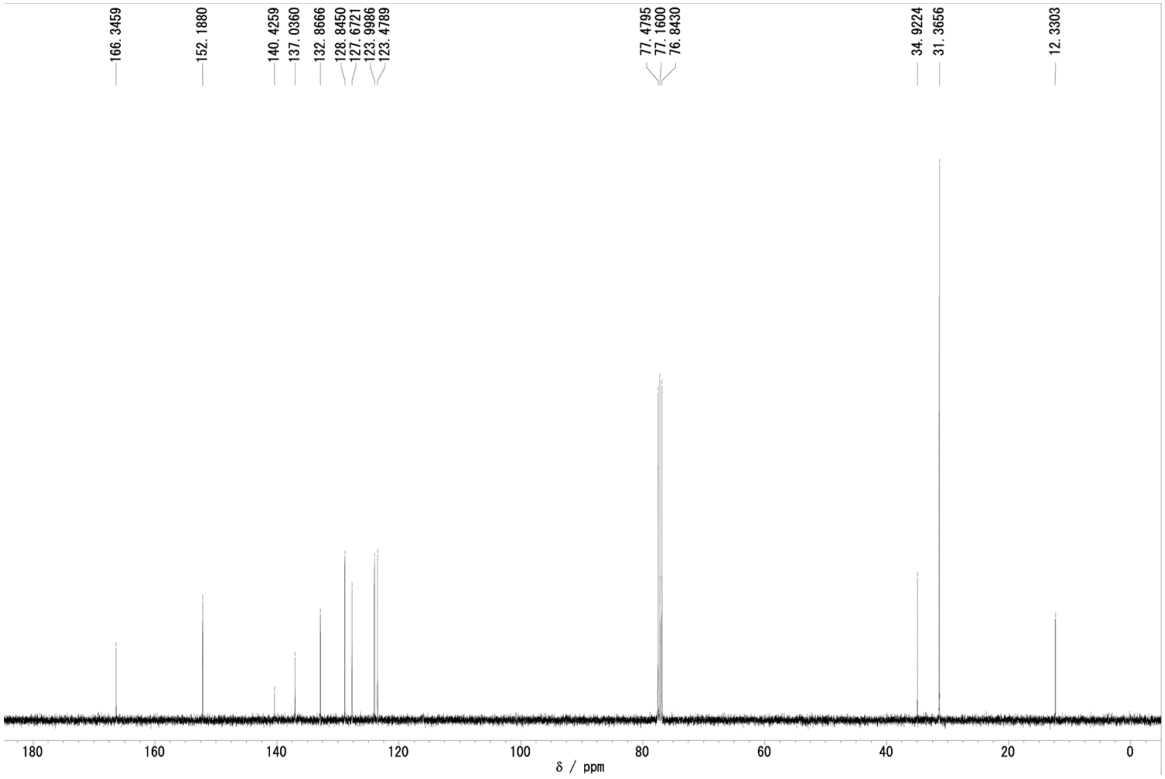


Figure S10. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1,2-bis(5-methyl-2-(3-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**4o**).

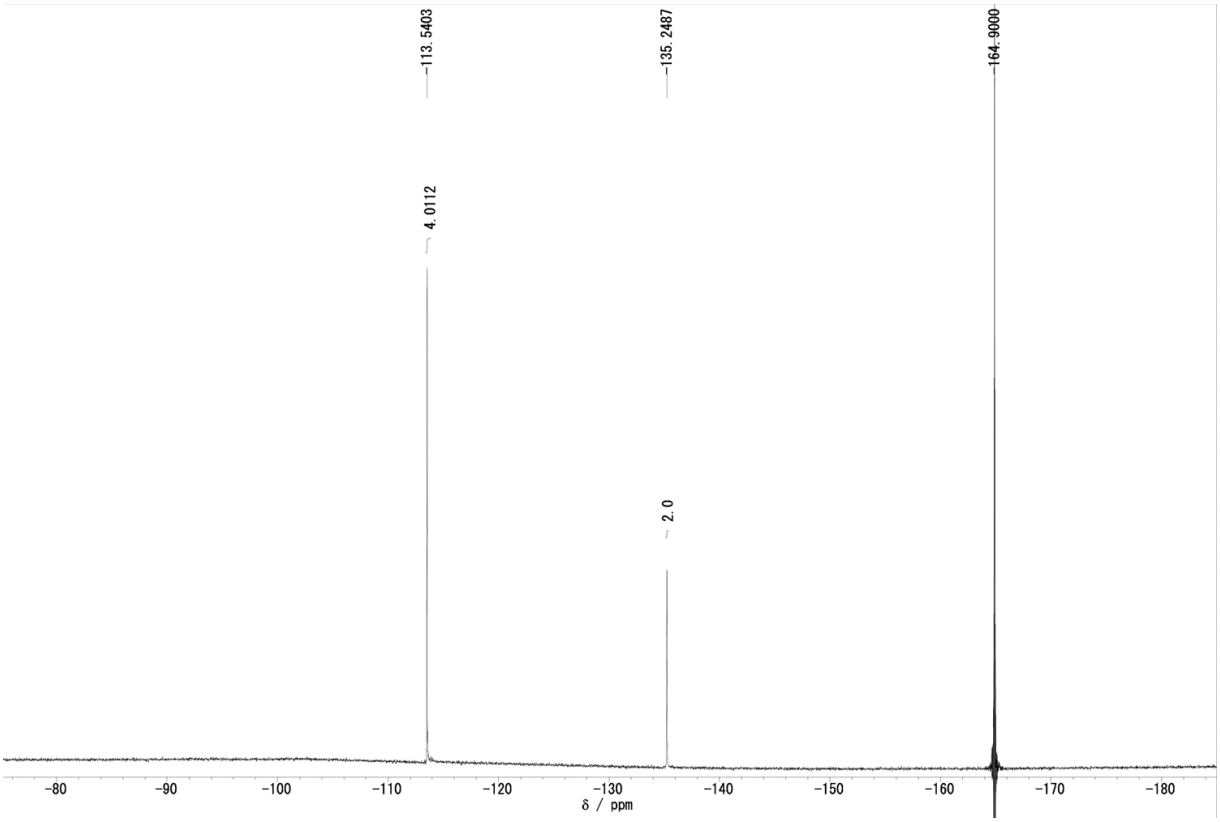
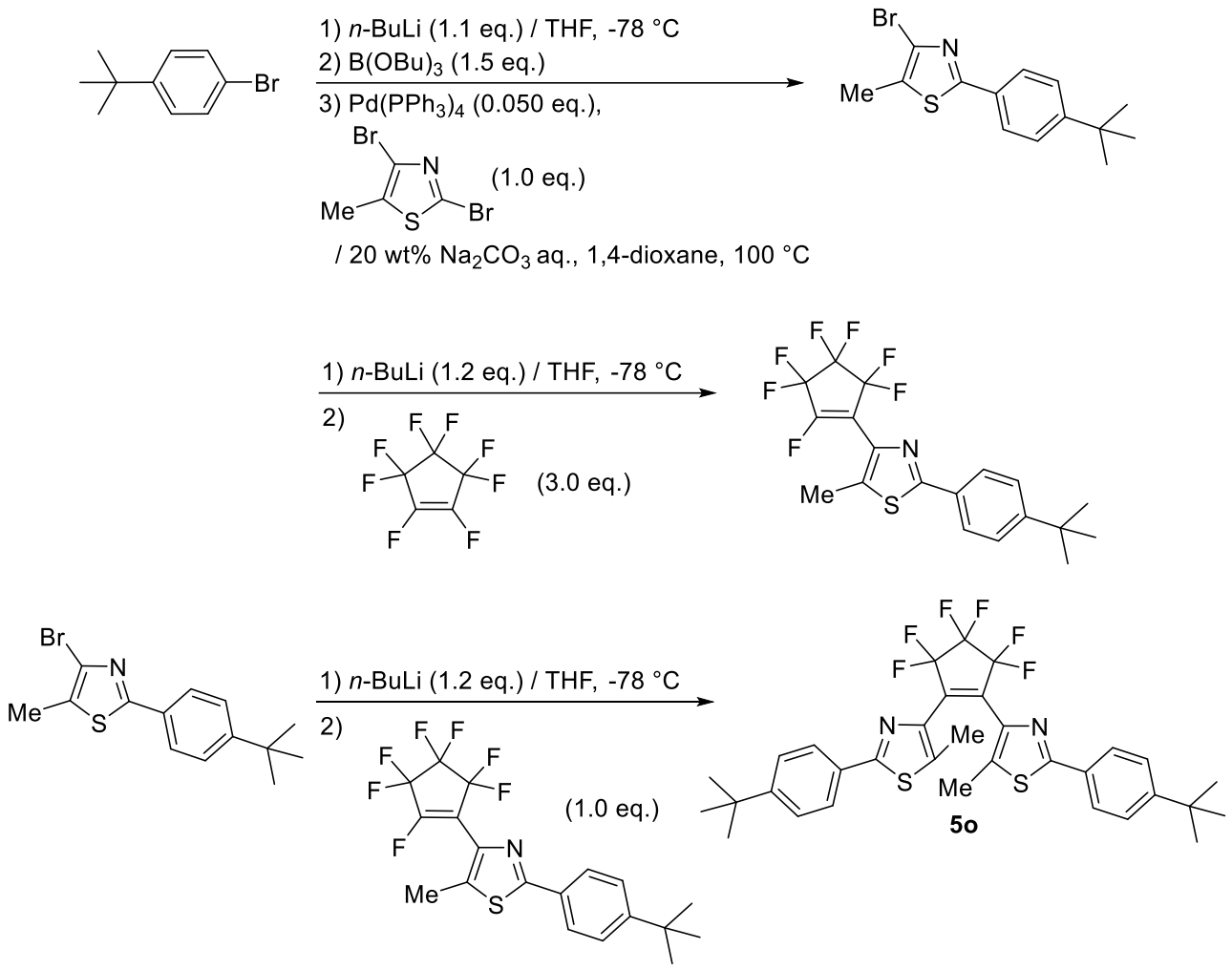


Figure S11. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 1,2-bis(5-methyl-2-(3-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**4o**).

·**Synthesis of 1,2-bis(5-methyl-2-(4-*tert*-butyl)phenylthiazol-4-yl)perfluorocyclopentene (5o)**

The total synthetic route of **5o** is shown in Scheme S2.



Scheme S2. Synthetic route of **5o**.

4-Bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole

Into a 300-mL three-neck flask, 1.66 g (7.79 mmol) of 1-bromo-4-*tert*-butylbenzene was added to 30 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 6.0 mL (9.60 mmol, 1.2 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. Then 3.2 mL (11.96 mmol, 1.5 eq.) of tributyl borate was added, followed by stirring another 10 min, and the temperature of the reaction mixture was allowed to warm to room temperature. Then the mixture was stirred for 1 h at this temperature. After reaction was completed, 10 mL of water was added, and the solvents were evaporated in vacuo. To the reaction mixture, we added 2,4-dibromo-5-methylthiazole[24] (2.00 g, 7.75 mmol, 1.0 eq.), tetrakis(triphenylphosphine)palladium(0) (0.45 g, 0.39 mmol, 0.050 eq.), a 20 wt% Na_2CO_3 aq. (16 mL), and 1,4-dioxane (30 mL), and this mixture was refluxed for 16 h. After reaction was over, the reaction mixture was allowed to cool to room temperature. The mixture was extracted with 30 mL of ethyl acetate four times. The organic layer was washed with 200 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo.

The resulting crude product was purified by column chromatography on silica gel using a mixture of hexane and dichloromethane (3:1 (v/v)) as an eluent to obtain 1.72 g (5.54 mmol) of the 4-bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole as white solid in 71% yield.

m.p. 72.3−73.2°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S12) δ 7.80 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 2.43 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S13) δ 165.7, 153.9, 130.3, 128.8, 126.0, 125.9, 125.2, 35.0, 31.3, 13.2. HRMS (MALDI, positive): *m/z* calcd. for $C_{14}H_{17}NSBr^{+}$ $[M+H]^{+}$: 310.02596, found: 310.02566.

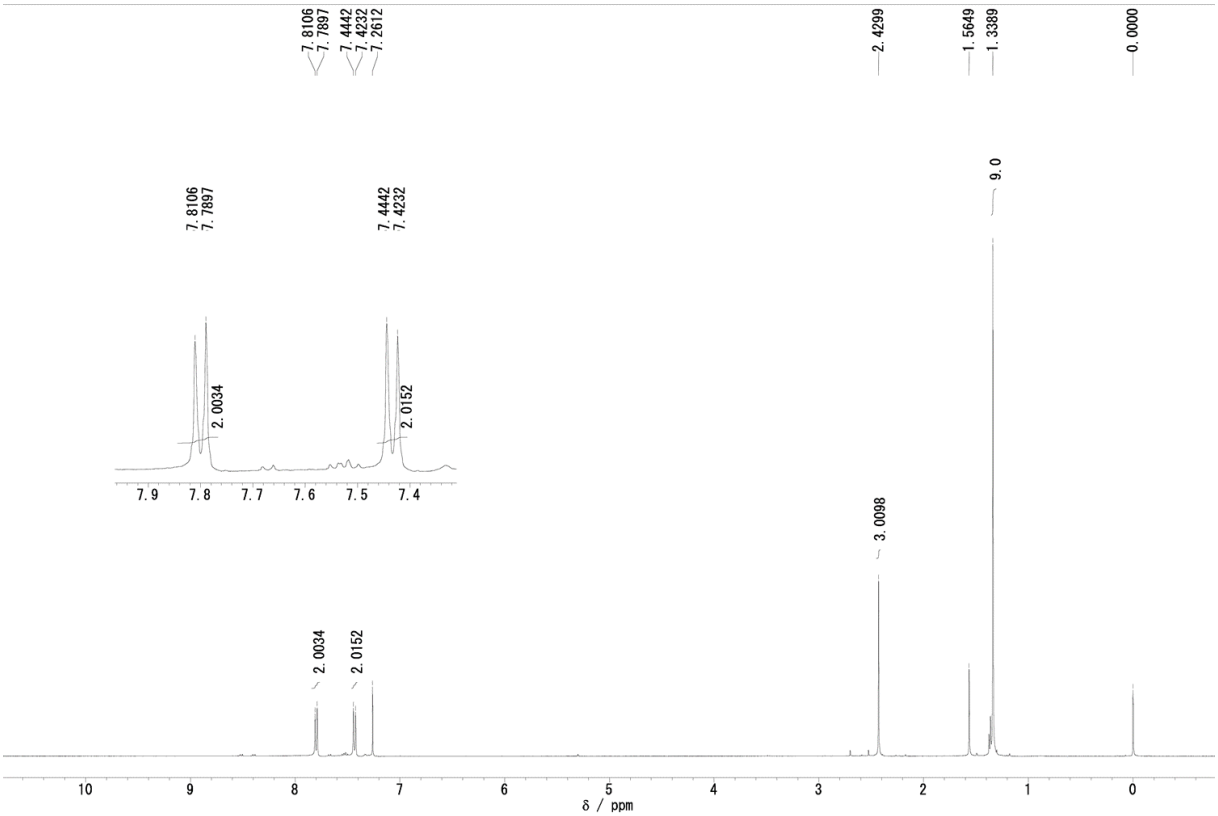


Figure S12. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 4-bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole.

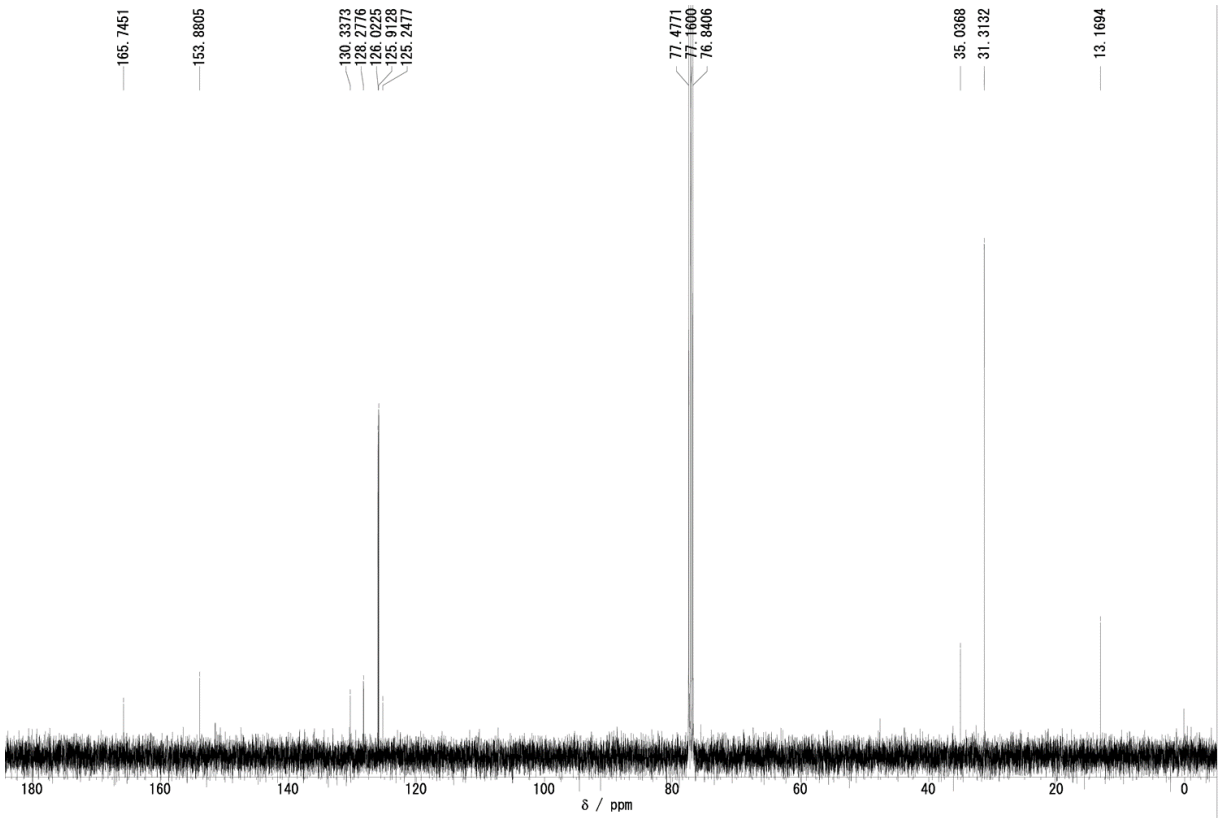


Figure S13. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 4-bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole.

4-(2,3,3,4,4,5,5-Heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole

Into a 200-mL three-neck flask, 2.00 g (6.45 mmol) of 4-bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole was added to 45 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 5.0 mL (8.00 mmol, 1.2 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. To the mixture, 1.64 mL (19.34 mmol, 3.0 eq.) of perfluorocyclopentene was gradually added, followed by stirring another 10 min. The temperature of the reaction mixture was allowed to warm to -40°C, then the solution was stirred another 4 h at this temperature. After reaction was completed, 15 mL of water was added, and the mixture was allowed to warm to room temperature. Solvent of THF was evaporated in vacuo, then 300 mL of water was added. The mixture was extracted with 50 mL of diethyl ether four times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using hexane as an eluent to obtain 2.25 g (5.31 mmol) of the 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole as pale-yellow solid in 82% yield.

m.p. 88.3−88.7°C. ^1H NMR (400 MHz, $CDCl_3$, ppm: Figure S14) δ 7.83 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 2.53 (d, J = 2.9 Hz, 3H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S15) δ 166.4, 154.2, 138.5, 135.7, 130.2, 126.4, 126.1, 35.1. 31.3, 12.5. ^{19}F NMR (376 MHz, $CDCl_3$, ppm:

Figure S16) δ -111.4 (d, J = 11.8 Hz, 2F), -121.6 (d, J = 15.9 Hz, 2F), -128.2 (br s, 1F), -133.4 (s, 2F). HRMS (MALDI, positive): *m/z* calcd. for $C_{19}H_{17}F_7NS^+$ $[M+H]^+$: 424.09644, found: 424.09591.

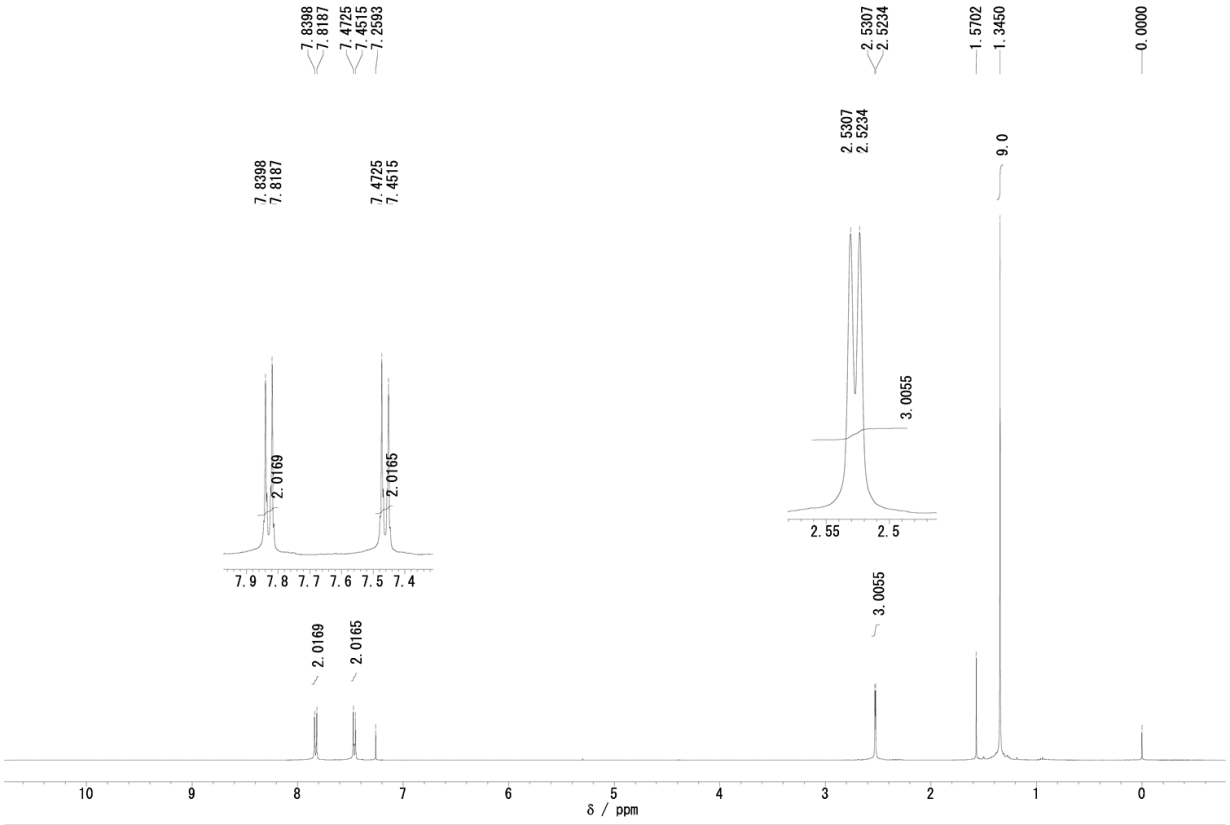


Figure S14. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole.

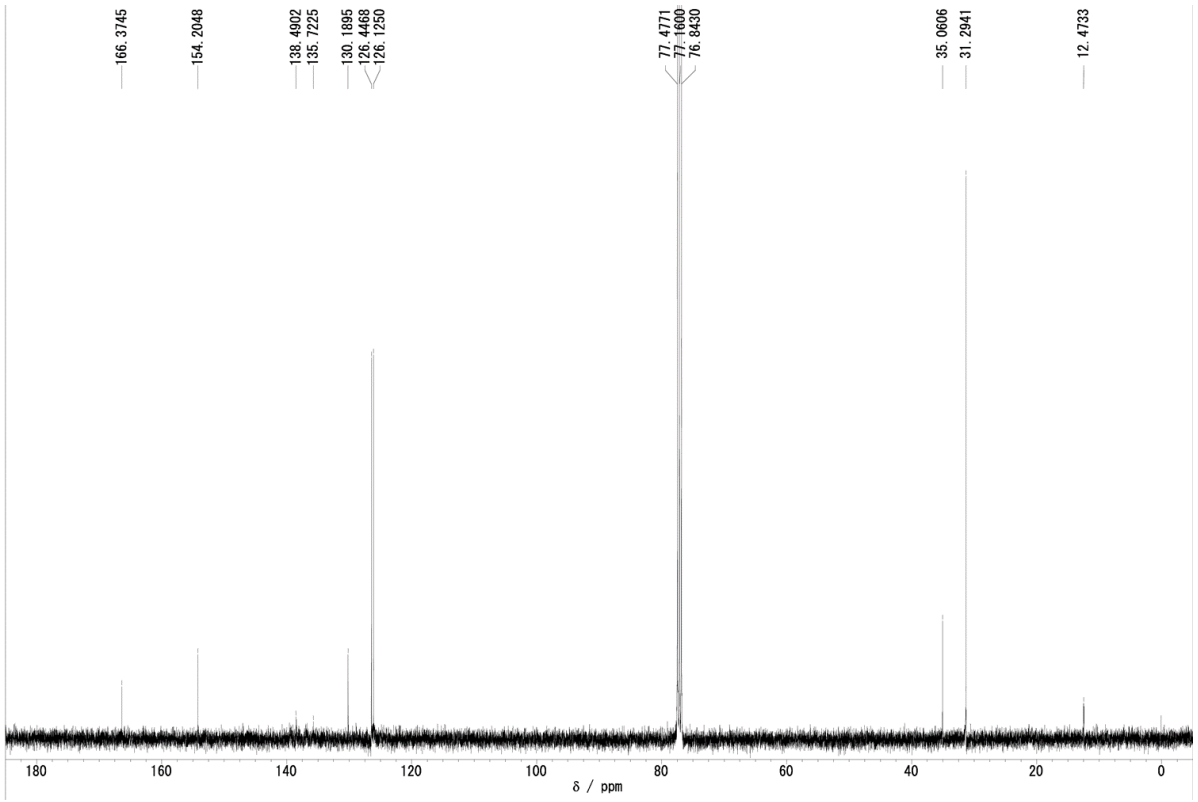


Figure S15. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole.

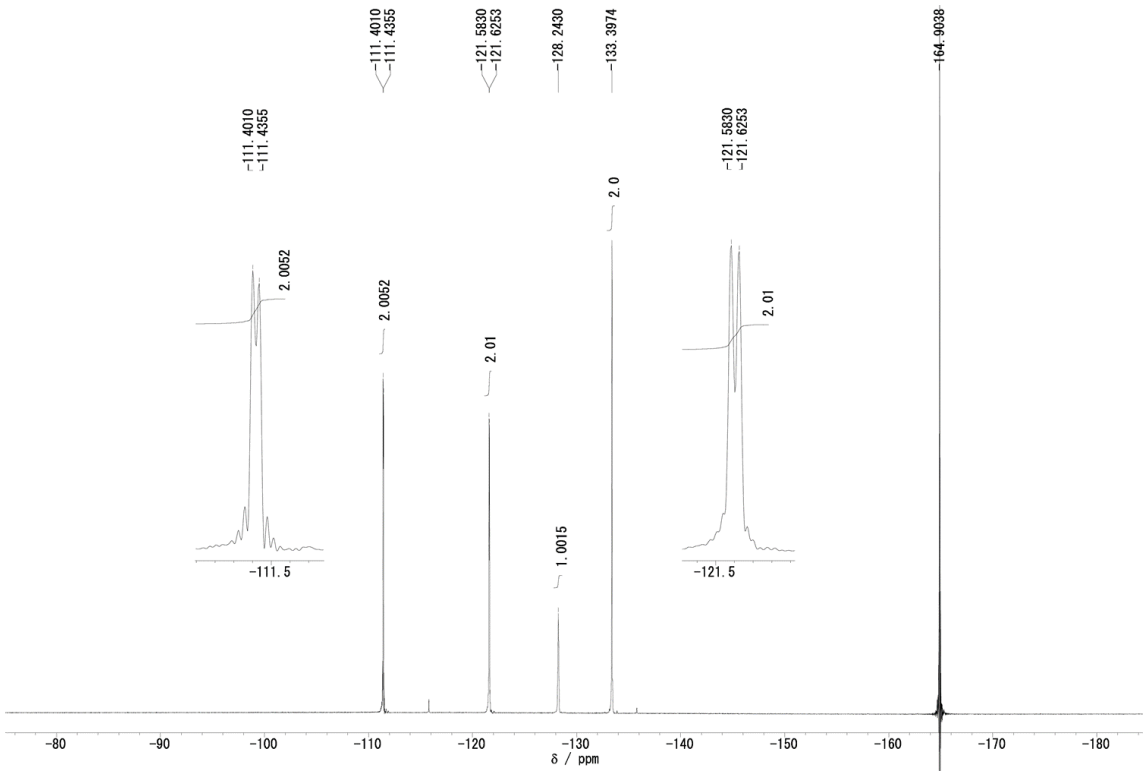


Figure S16. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole.

1,2-Bis(5-methyl-2-(4-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (5o)

Into a 100-mL three-neck flask, 1.20 g (3.87 mmol) of 4-bromo-5-methyl-2-(4-*tert*-butyl)phenylthiazole was added to 30 mL of THF anhydrous in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 2.9 mL (4.64 mmol, 1.2 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. To the mixture, THF anhydrous solution containing 1.64 g (3.87 mmol, 1.0 eq.) of 4-(2,3,3,4,4,5,5-heptafluorocyclopentenyl)-5-methyl-2-(4-*tert*-buthylphenyl)thiazole was added, followed by stirring another 30 min. The temperature of the reaction mixture was allowed to warm to -40°C, then the solution was stirred another 5 h at this temperature. After the reaction was completed, 10 mL of water was added, and the mixture was allowed to warm to room temperature. Solvent of THF was evaporated in vacuo, then 300 mL of water was added. The mixture was extracted with 40 mL of diethyl ether four times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using a mixture of hexane and dichloromethane (3:1 (v/v)) as an eluent to obtain 1.55 g of crude product. By recrystallization from ethyl acetate, 1.47 g (2.32 mmol) of **5o** was obtained as colorless needle crystals in 60% yield.

m.p. 189.3−189.7°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S17) δ 7.81 (dd, J = 8.5, 2.1 Hz, 4H), 7.44 (dd, J = 8.5, 2.1 Hz, 4H), 2.05 (s, 6H), 1.34 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S18) δ 166.0, 154.0, 140.4, 136.8, 130.5, 126.4, 126.0, 35.0, 31.3, 12.3. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S11) δ -113.8 (s, 4F), -135.2 (s, 2F). HRMS (MALDI, positive): *m/z* calcd. for $C_{33}H_{32}F_6N_2S_2^+$ $[M]^+$: 634.19056, found: 634.19030.

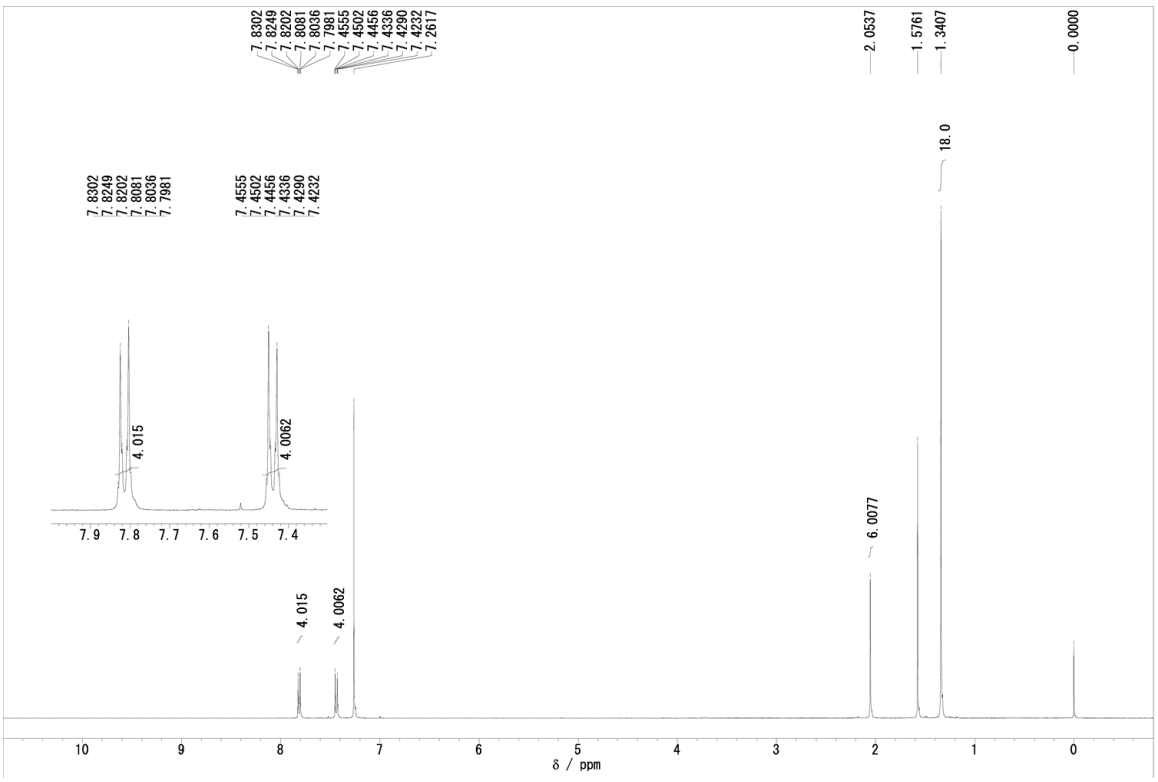


Figure S17. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1,2-bis(5-methyl-2-(4-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**5o**).

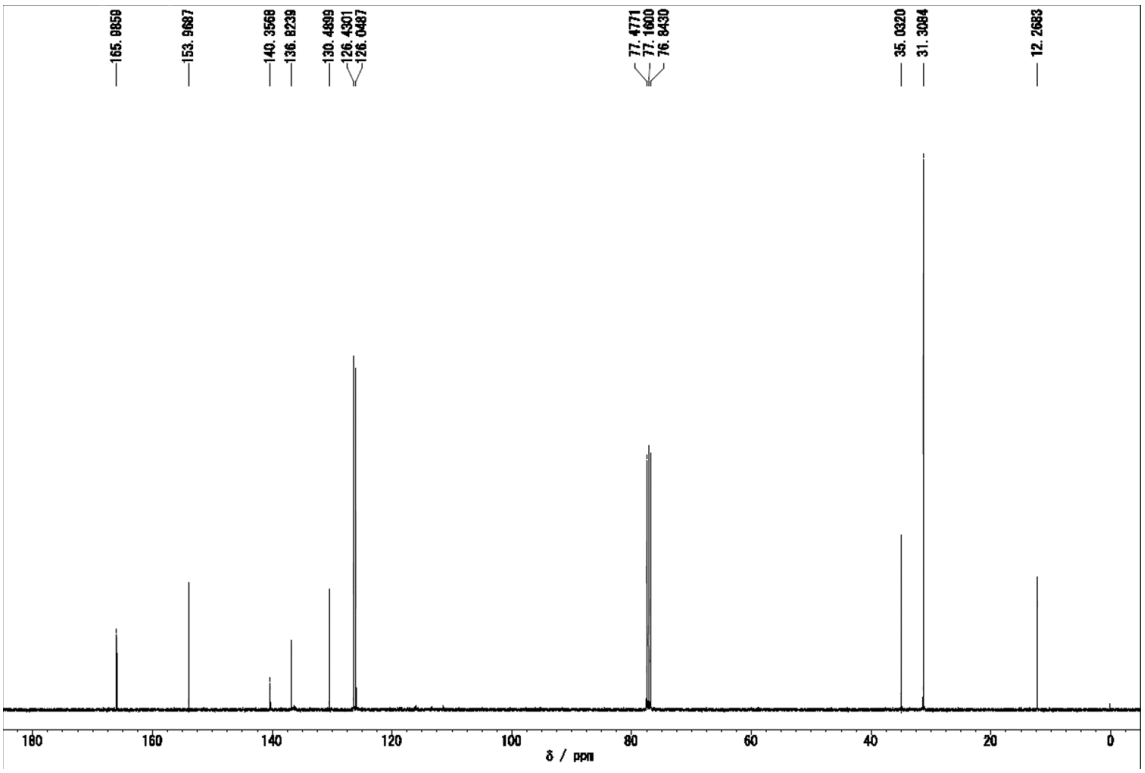


Figure S18. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1,2-bis(5-methyl-2-(4-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**5o**).

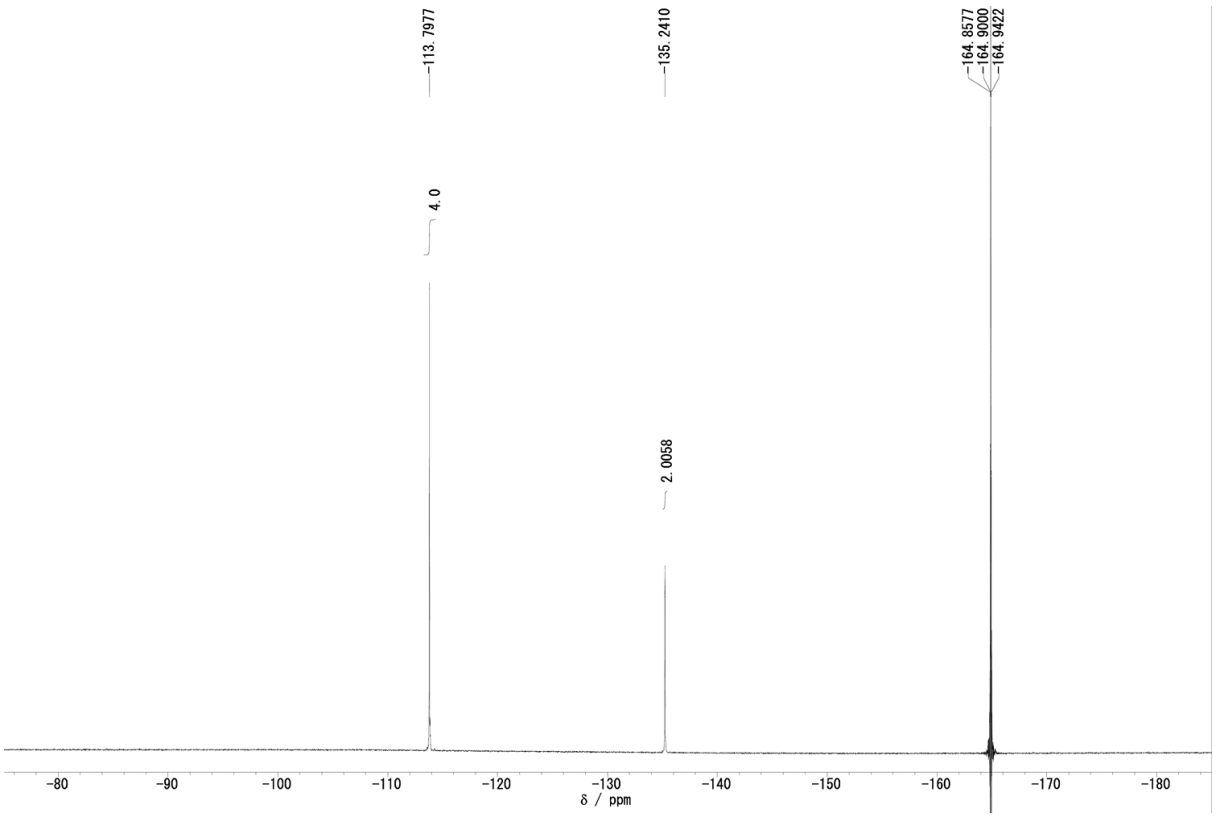
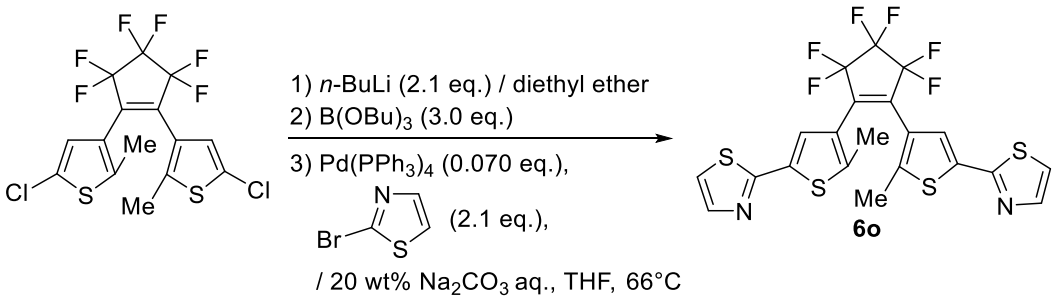


Figure S19. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 1,2-bis(5-methyl-2-(4-*tert*-butylphenyl)thiazole-4-yl)perfluorocyclopentene (**5o**).

·Synthesis of 1,2-bis(2-methyl-5-(2-thiaozoyl)lthiophen-3-yl)perfluorocyclopentene (6o)

The total synthetic route of **6o** is shown in Scheme S3.



Scheme S3. Synthetic route of **6o**.

1,2-Bis(2-methyl-5-(2-thiazolyl)thiophen-3-yl)perfluorocyclopenthene (6o)

Into a 200-mL four-neck flask, containing 1.00 g (2.29 mmol) of 1,2-bis(5-chloro-2-methylthiophen-3-yl)perfluorocyclopenthene[25] was added to 50 mL of dry diethyl ether in a dry ice-methanol bath at -20°C in an argon gas atmosphere. To the solution, 3.15 mL (5.04 mmol, 2.1 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h on the ice-salt bath at -4°C. After that, the mixture was cooled on a dry ice- methanol bath at -20°C. Then 1.84

mL (6.87 mmol, 3.0 eq.) of tributyl borate was added, followed by stirring another 10 min, and the temperature of the reaction mixture was allowed to warm to room temperature. Then the mixture was stirred for 1 h at this temperature. After reaction was completed, 10 mL of water was added, and the solvents were evaporated in vacuo. The reaction mixture was added to 2-bromothiazole (0.789 g, 4.81 mmol, 2.1 eq.), tetrakis(triphenylphosphine)palladium(0) (0.185 g, 0.16 mmol, 0.070 eq.), a 20 wt% Na_2CO_3 aq. (20 mL), and THF (20 mL), and the mixture was refluxed for 18 h. After reaction was over, the reaction mixture was allowed to cool to room temperature, and the solvent of THF was evaporated in vacuo. The mixture was extracted with 30 mL of diethyl ether with three times. The organic layer was dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using a mixture of hexane and chloroform (1:1 (v/v)) as an eluent to obtain 1.22 g of crude product. After recrystallization from hexane and dichloromethane (3:1 (v/v)), 0.819 g (1.53 mmol) of **6o** was obtained as pale-yellow solid in 67% yield.

m.p. 166.8−167.8°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S20) δ 7.77 (d, J = 3.3 Hz, 2H), 7.48 (s, 2H), 7.29 (d, J = 3.3 Hz, 2H), 2.00 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S21) δ 160.8, 144.3, 143.5, 135.8, 125.6, 118.8, 14.9. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S22) δ -113.3 (s, 4F), -135.0 (s, 2F). Anal. Calcd for $C_{21}H_{12}F_6S_4$: C, 47.18; H, 2.26; N, 5.24; Found: C, 46.94; H, 2.31; N, 5.17.

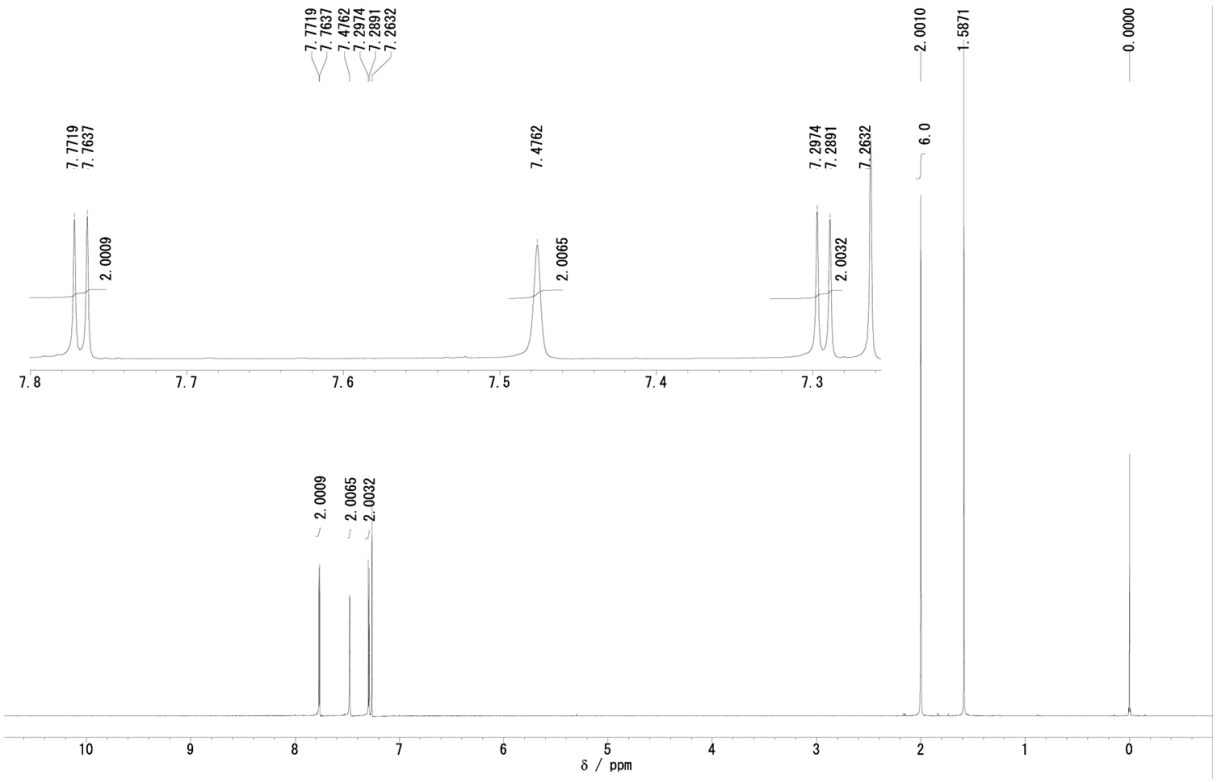


Figure S20. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1,2-bis(2-methyl-5-(2-thiazolyl)thiophen-3-yl)perfluorocyclopenthene (**6o**).

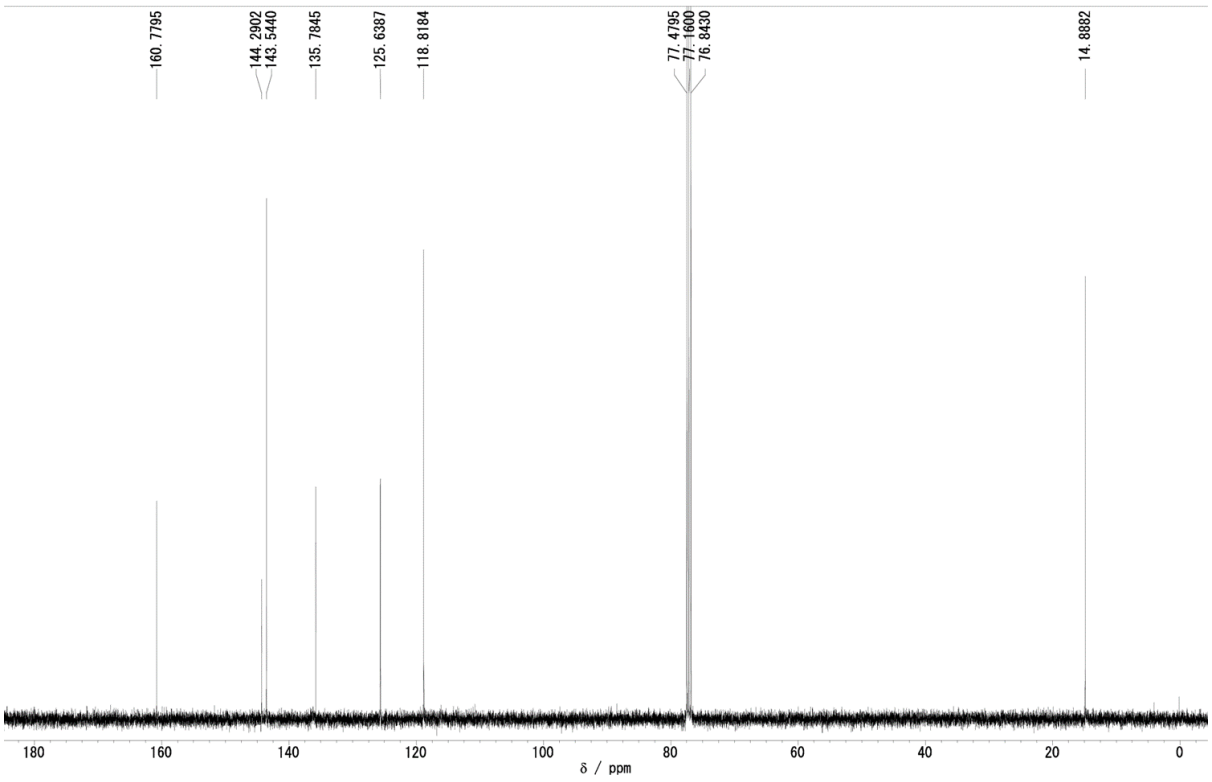


Figure S21. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1,2-bis(2-methyl-5-(2-thiazolyl)thiophen-3-yl)perfluorocyclopenthene (**6o**).

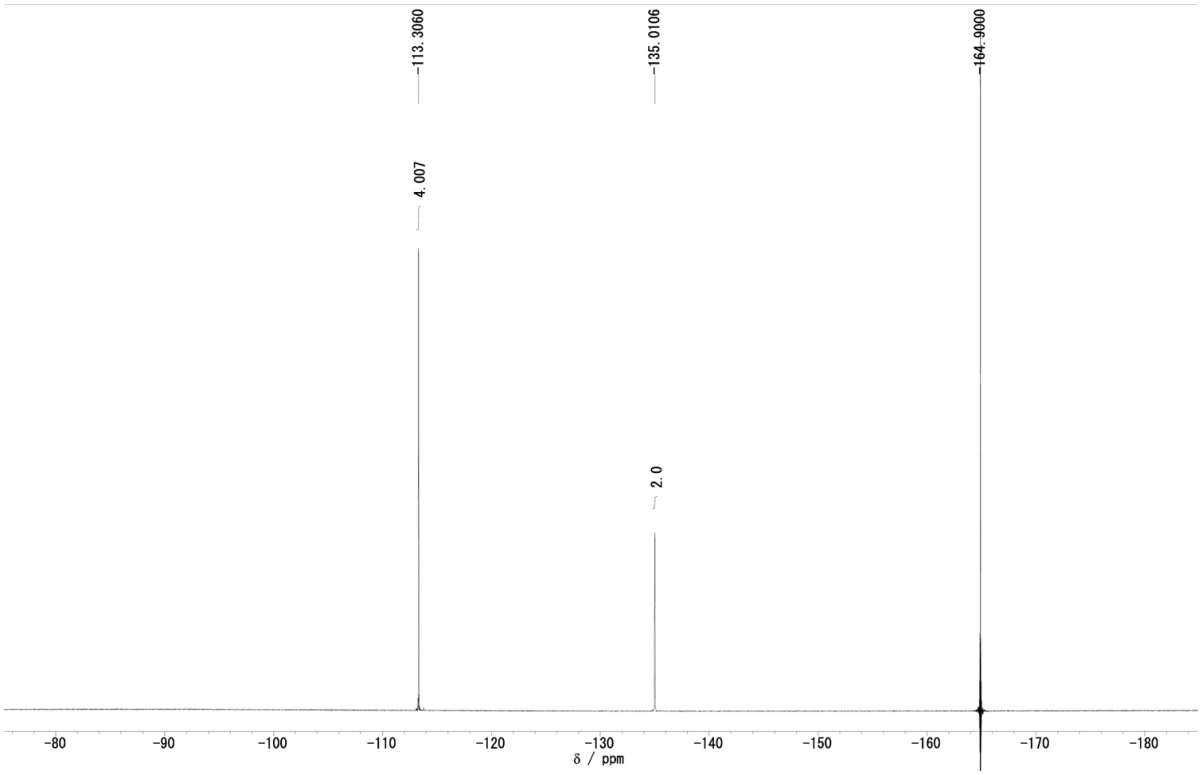
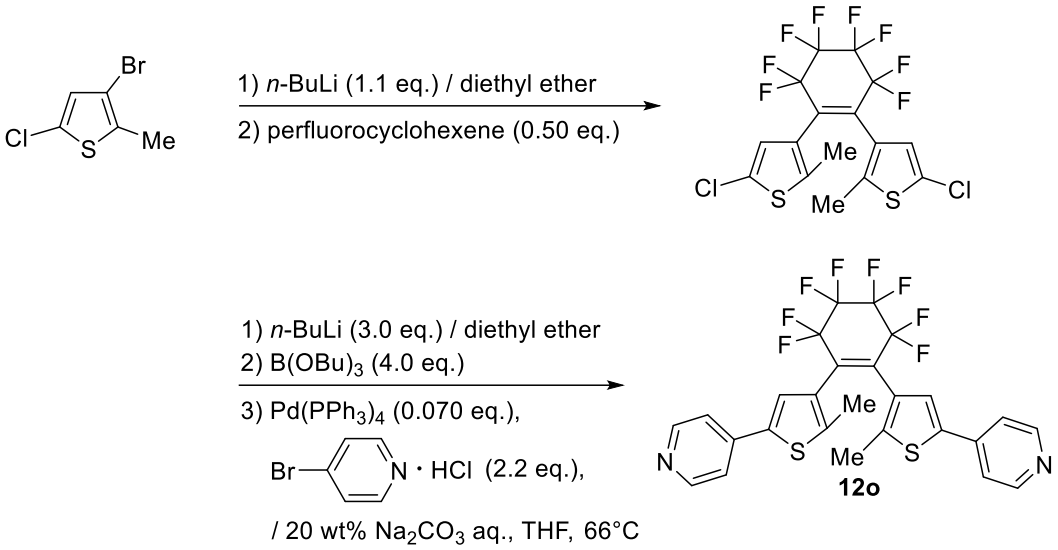


Figure S22. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 1,2-bis(2-methyl-5-(2-thiazolyl)thiophen-3-yl)perfluorocyclopenthene (**6o**).

·**Synthesis of 1,2-bis(2-methyl-5-(pyrid-4-yl)thien-3-yl)perfluorocyclohexene (12o)**

The total synthetic route of **12o** is shown in Scheme S4.



Scheme S4. Synthetic route of **12o**.

1,2-Bis(5-chloro-2-methylthien-3-yl)perfluorocyclohexene

Into a 100-mL three-neck flask, 2.00 g (9.46 mmol) of 3-bromo-5-chloro-2-methylthiophene[25] was added to 30 mL of dry diethyl ether in a dry ice-methanol bath at -78°C in an argon gas atmosphere. To the solution, 6.5 mL (10.41 mmol, 1.1 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. To the mixture, 1.24 g (4.73 mmol, 0.50 eq.) of perfluorocyclohexene in 10 mL of dry diethyl ether was gradually added, followed by stirring another 3 h at this temperature. After the reaction was completed, 30 mL of water was added, and the mixture was allowed to warm to room temperature. The mixture was extracted with 30 mL of diethyl ether five times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using hexane as an eluent to obtain 1.58 g of yellow oily crude product. Since further purification was difficult, it was used as is for the next reaction.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.71 (s, 2H), 2.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 139.3, 127.7, 126.2, 125.4, 13.9.

1,2-Bis(2-methyl-5-(pyrid-4-yl)thien-3-yl)perfluorocyclohexene (12o)

Into a 100-mL four-neck flask, 1.31 g (2.69 mmol) of 1,2-bis(5-chloro-2-methylthiophen-3-yl)perfluorocyclohexene was added to 50 mL of dry diethyl ether on the ice-salt bath at -10°C in an argon gas atmosphere. To the solution, 5.1 mL (8.16 mmol, 3.0 eq.) of 1.6 N *n*-BuLi hexane solution was gradually added while maintaining the temperature and stirred for 1 h at this temperature. Then

2.9 mL (10.84 mmol, 4.0 eq.) of tributyl borate was added, followed by stirring another 10 min, and the temperature of the reaction mixture was allowed warm to room temperature. Then the mixture was stirred for 1 h at this temperature. After reaction was completed, 10 mL of water was added, and the solvents were evaporated in vacuo. The reaction mixture was added to 4-bromopyridine hydrochloride (1.15 g, 5.92 mmol, 2.2 eq.), tetrakis(triphenylphosphine)palladium(0) (0.22 g, 0.19 mmol, 0.070 eq.), a 20 wt% Na_2CO_3 aq. (20 mL), and THF (20 mL), and the mixture was refluxed for 16 h. After the reaction was over, the reaction mixture was allowed to cool to room temperature, and the solvent of THF was evaporated in vacuo. The mixture was extracted with 30 mL of diethyl ether five times. The organic layer was washed with 100 mL of brine and dried over sodium sulfate anhydrous. After removal of sodium sulfate by filtration, the solvents were removed in vacuo. The resulting crude product was purified by column chromatography on silica gel using a mixture of hexane and ethyl acetate (3:7 (v/v)) as an eluent to obtain 0.88 g (1.52 mmol) of **12o** as pale-yellow oil in 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm: Figure S23) δ 8.58 (dd, J = 4.6, 1.6 Hz, 4H), 7.48 (dd, J = 4.6, 1.6 Hz, 4H), 7.31 (s, 2H), 2.21 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm: Figure S24) δ 150.6, 142.4, 140.4, 138.6, 127.2, 125.3, 119.6, 14.7. ^{19}F NMR (376 MHz, $CDCl_3$, ppm: Figure S25) δ -109.3 (conformer A: s) and -113.8 (conformer B: s) (conformer A: conformer B = 1:1 (ratio of the peak areas), 4F), -135.1 (conformer A: s) and -138.1 (conformer B: s) (conformer A: conformer B = 1:1 (ratio of the peak areas), 4F). Anal. Calcd for $C_{26}H_{16}F_8N_2S_2$: C, 54.54; H, 2.82; N, 4.89; Found: C, 54.37; H, 2.82; N, 4.84.

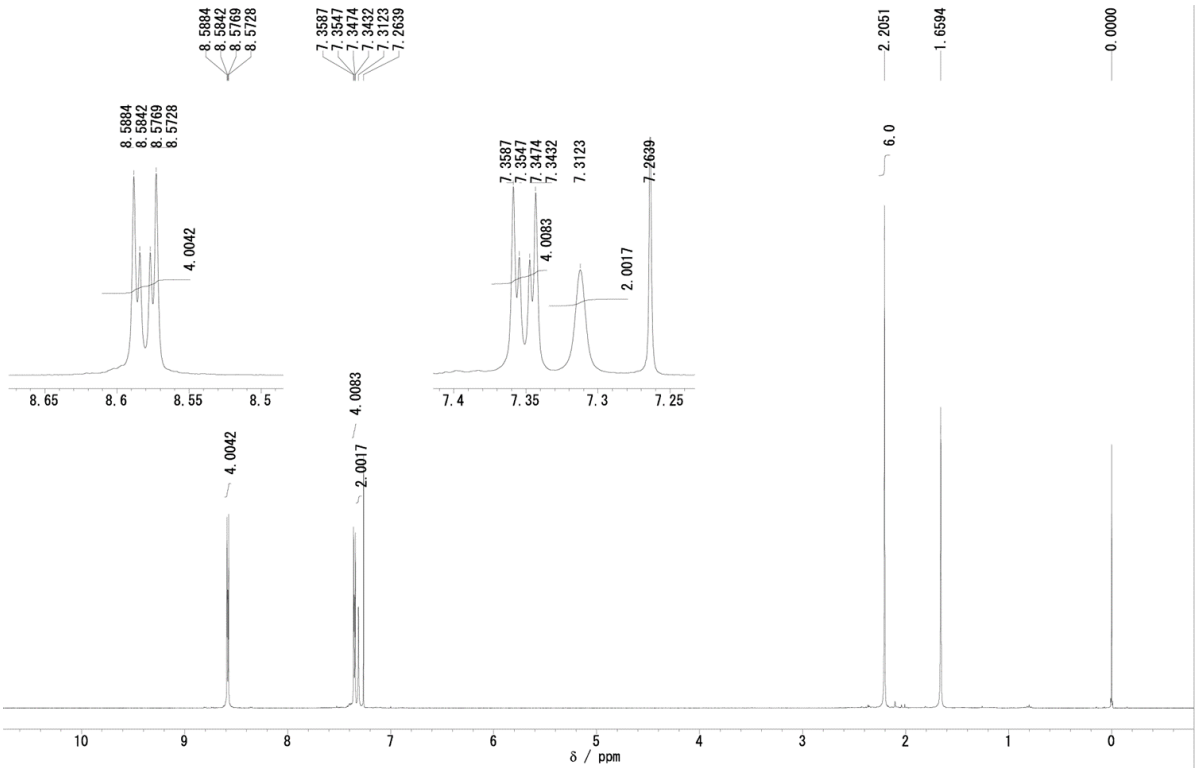


Figure S23. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 1,2-bis(2-methyl-5-(pyrid-4-yl)thien-3-yl)perfluorocyclohexene (**12o**).

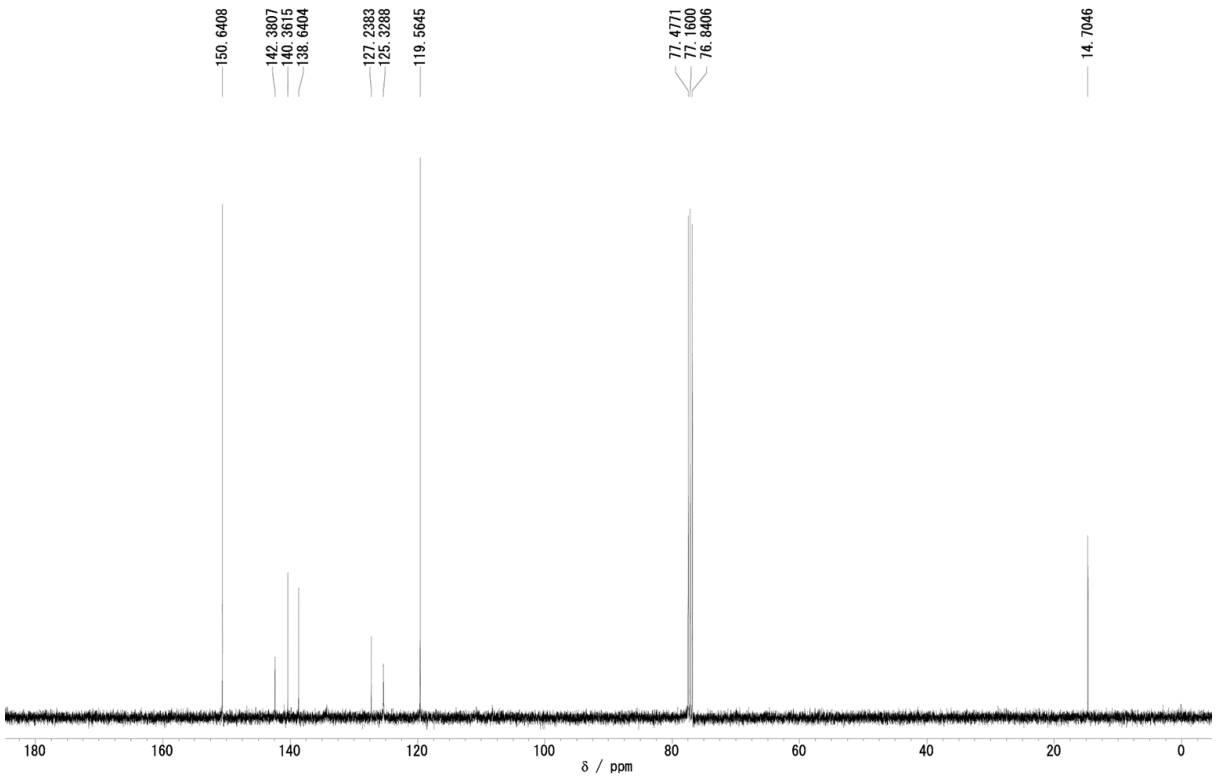


Figure S24. ^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of 1,2-bis(2-methyl-5-(pyrid-4-yl)thien-3-yl)perfluorocyclohexene (**12o**).

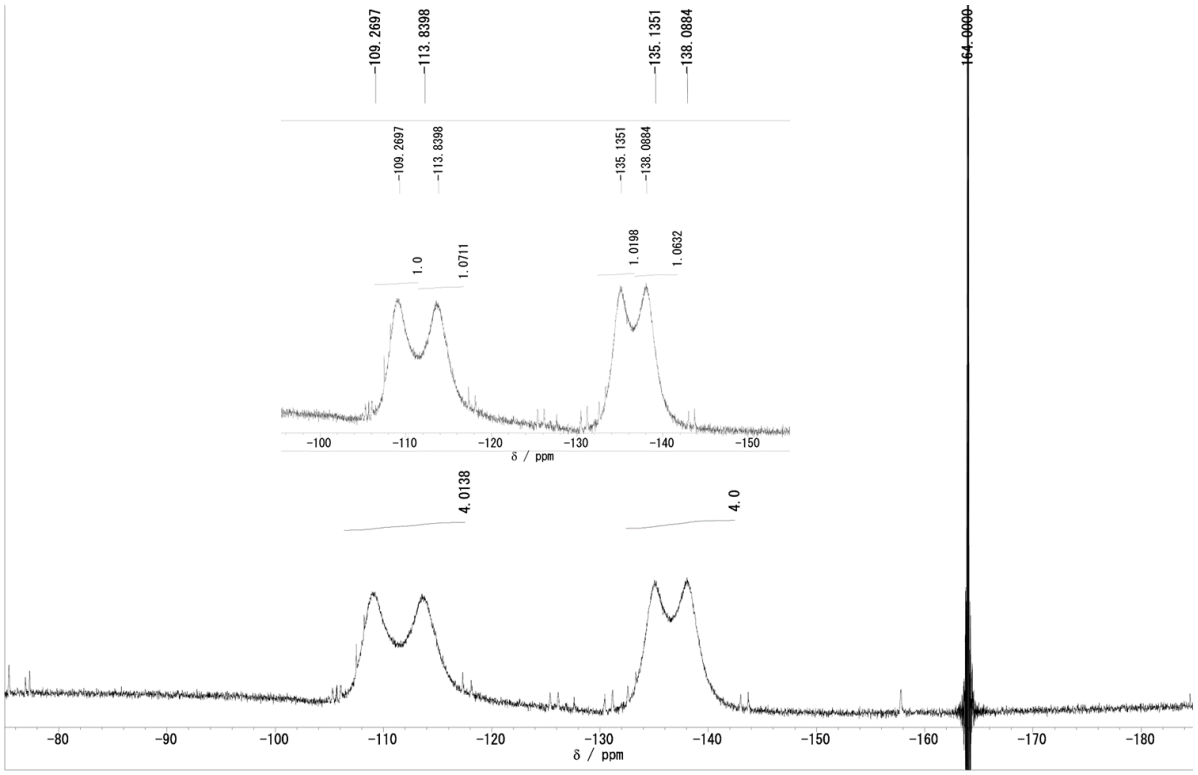


Figure S25. ^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of 1,2-bis(2-methyl-5-(pyrid-4-yl)thien-3-yl)perfluorocyclohexene (**12o**).

8. Crystal data of 3o, 4o, and 5o.

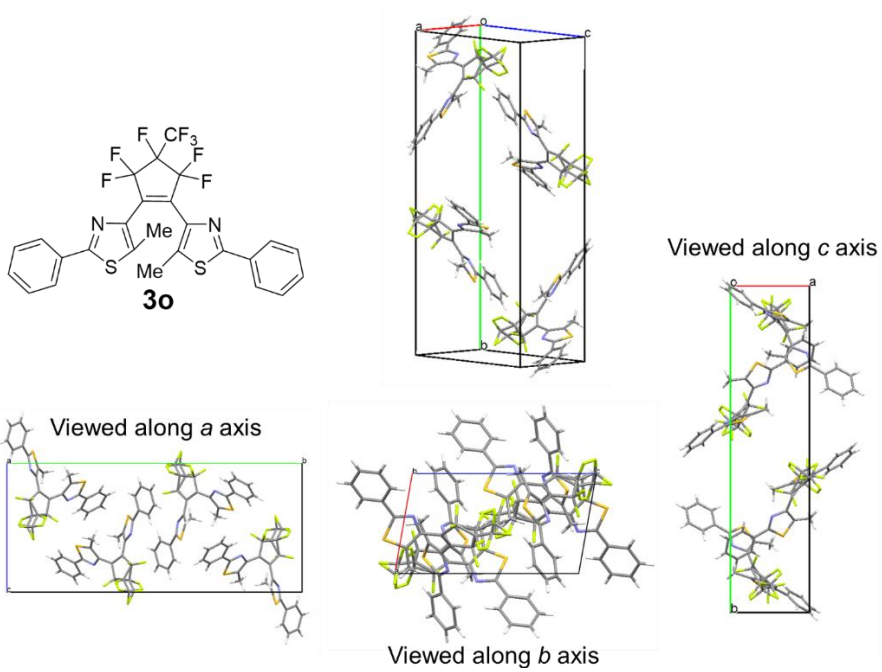


Figure S26. Molecular packing of **3o** crystal.

Table S2. Crystal data of **3o** crystal.

	3o
formula	$C_{26}H_{16}F_8N_2S_2$
formula weight	572.53
T / K	128(2)
crystal system	monoclinic
space group	$P2_1/c$
a / Å	6.9257(3)
b / Å	28.2706(15)
c / Å	12.4537(6)
α / °	90
β / °	99.8416(17)
γ / °	90
V / Å^3	2402.5(2)
Z	4
R_1 (I > 2σ(I))	0.0398
wR_2 (I > 2σ(I))	0.0979
R_1 (all data)	0.0594
wR_2 (all data)	0.1150
CCDC No.	2095136

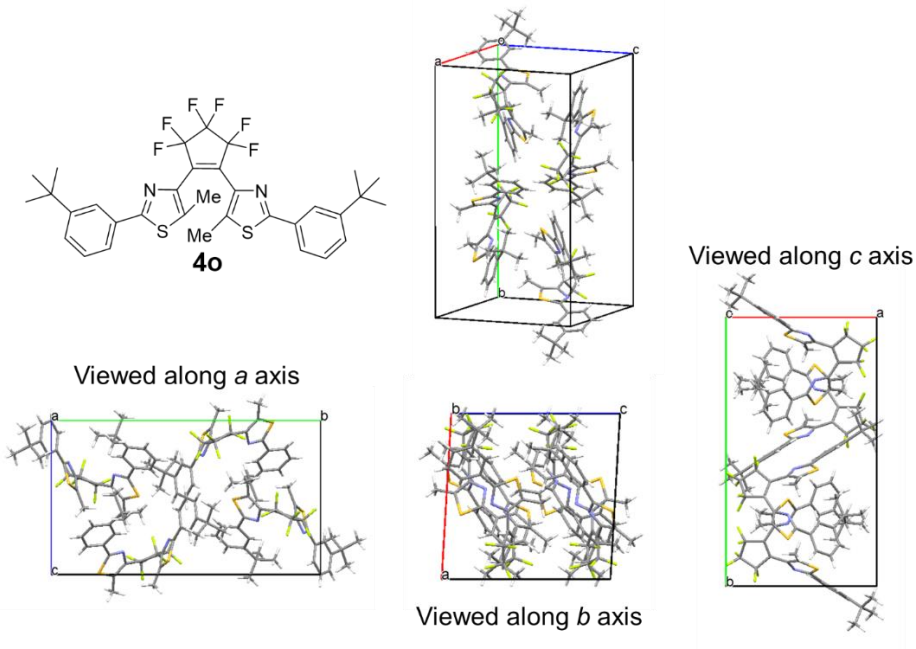


Figure S27. Molecular packing of **4o** crystal.

Table S3. Crystal data of **4o** crystal.

	4o
formula	$C_{33}H_{32}F_6N_2S_2$
formula weight	634.72
T / K	173(2)
crystal system	monoclinic
space group	$P2_1/C$
a / Å	11.9900(5)
b / Å	21.3155(10)
c / Å	12.2134(5)
α / °	90
β / °	93.3338(17)
γ / °	90
V / Å^3	3116.1(2)
Z	4
R_1 (I > 2σ(I))	0.0554
wR_2 (I > 2σ(I))	0.1504
R_1 (all data)	0.0637
wR_2 (all data)	0.1576
CCDC No.	2095138

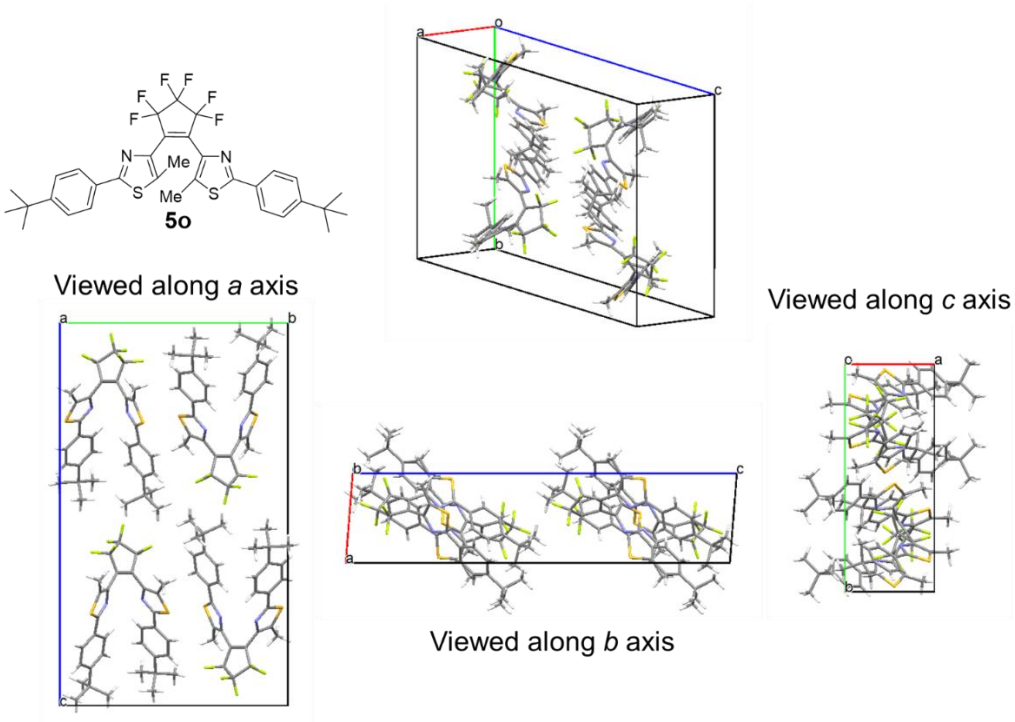


Figure S28. Molecular packing of **5o** crystal.

Table S4. Crystal data of **5o** crystal.

	5o
formula	$C_{33}H_{32}F_6N_2S_2$
formula weight	634.72
T / K	93(2)
crystal system	monoclinic
space group	$P2_1/c$
a / Å	6.57040(10)
b / Å	16.6413(3)
c / Å	28.0569(5)
α / °	90
β / °	94.4663(6)
γ / °	90
V / Å^3	3058.43(9)
Z	4
R_1 (I > 2σ(I))	0.0325
wR_2 (I > 2σ(I))	0.0848
R_1 (all data)	0.0329
wR_2 (all data)	0.0854
CCDC No.	2095137

9. Absorption spectral changes of 1-12 in organic solvents

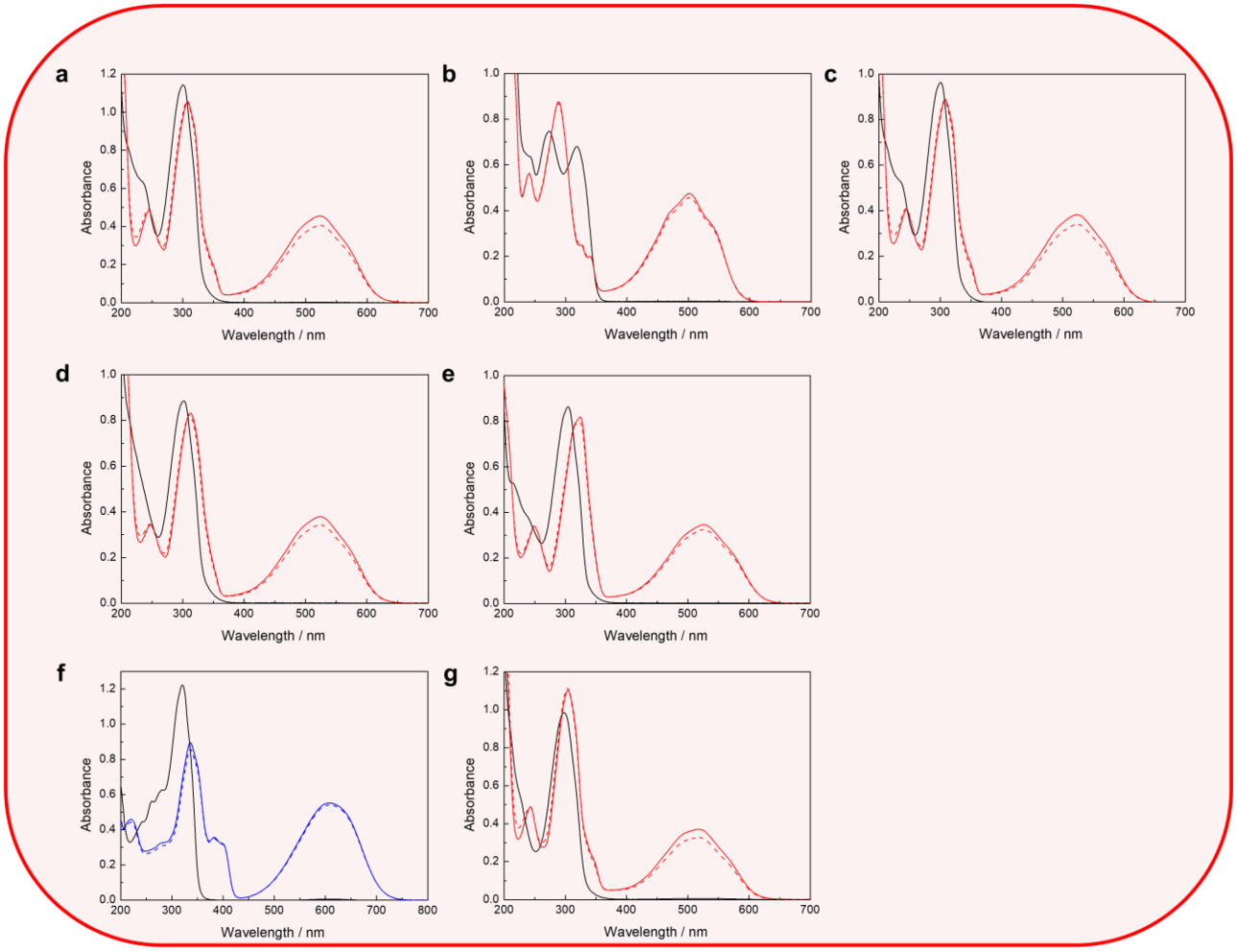


Figure S29. Absorption spectral changes of derivatives having thiazole group (**1** (a), **2** (b), **3** (c), **4** (d), **5** (e), **6** (f), and **11** (g)) in hexane. Absorption spectra of open-ring isomers: black solid line, closed-ring isomers: red or blue solid line, photostationary state (PSS) upon UV light ($\lambda = 313$ nm) irradiation: red or blue broken line. See Table 1 for detailed values of PSS. The color of the lines shows the color of the solution.

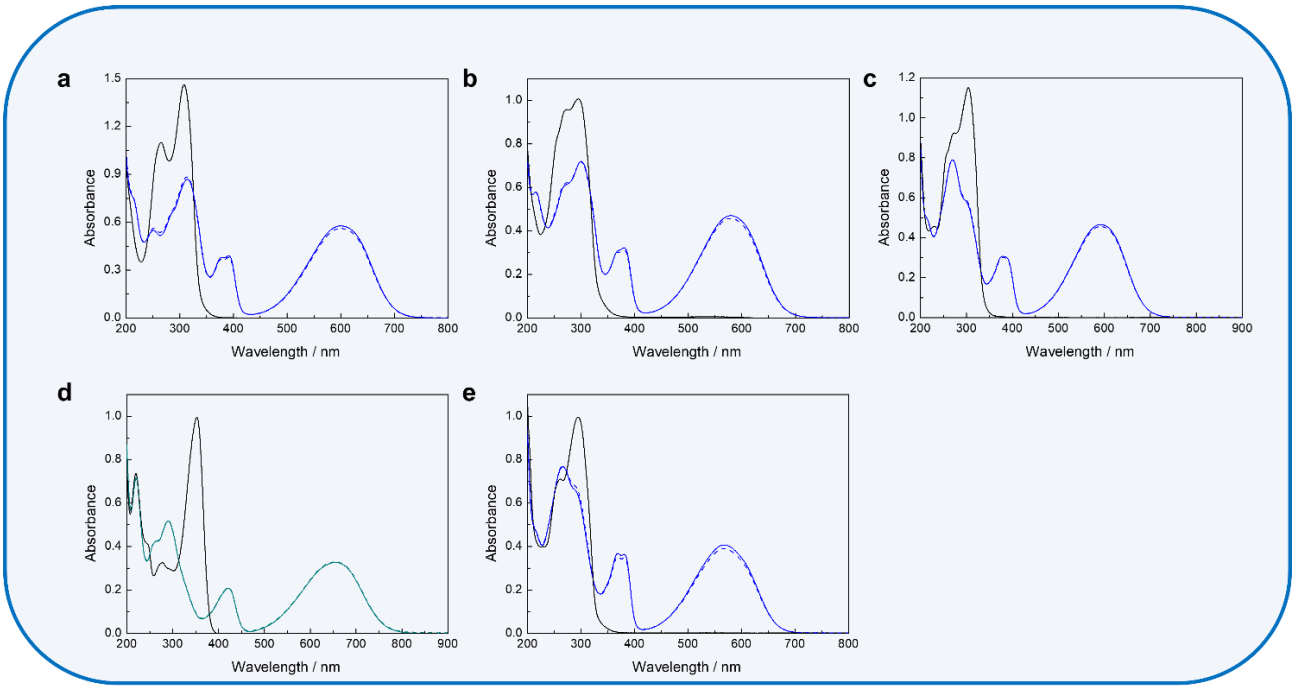


Figure S30. Absorption spectral changes of derivatives having pyridine group (**7** (a), **8** (b), **9** (c), **10** (d), and **12** (e)) in methanol. Absorption spectra of open-ring isomers: black solid line, closed-ring isomers: blue or emerald green solid line, photostationary state (PSS) upon UV light (λ = 313 or 365 nm) irradiation: blue or emerald green broken line. See Table 1 for detailed values of PSS. The color of the lines shows the color of the solution.

10. Absorption spectra, reversibility, and thermal stability of diarylethene derivatives having thiazole or pyridine rings in water/ethanol = 3:7 (v/v).

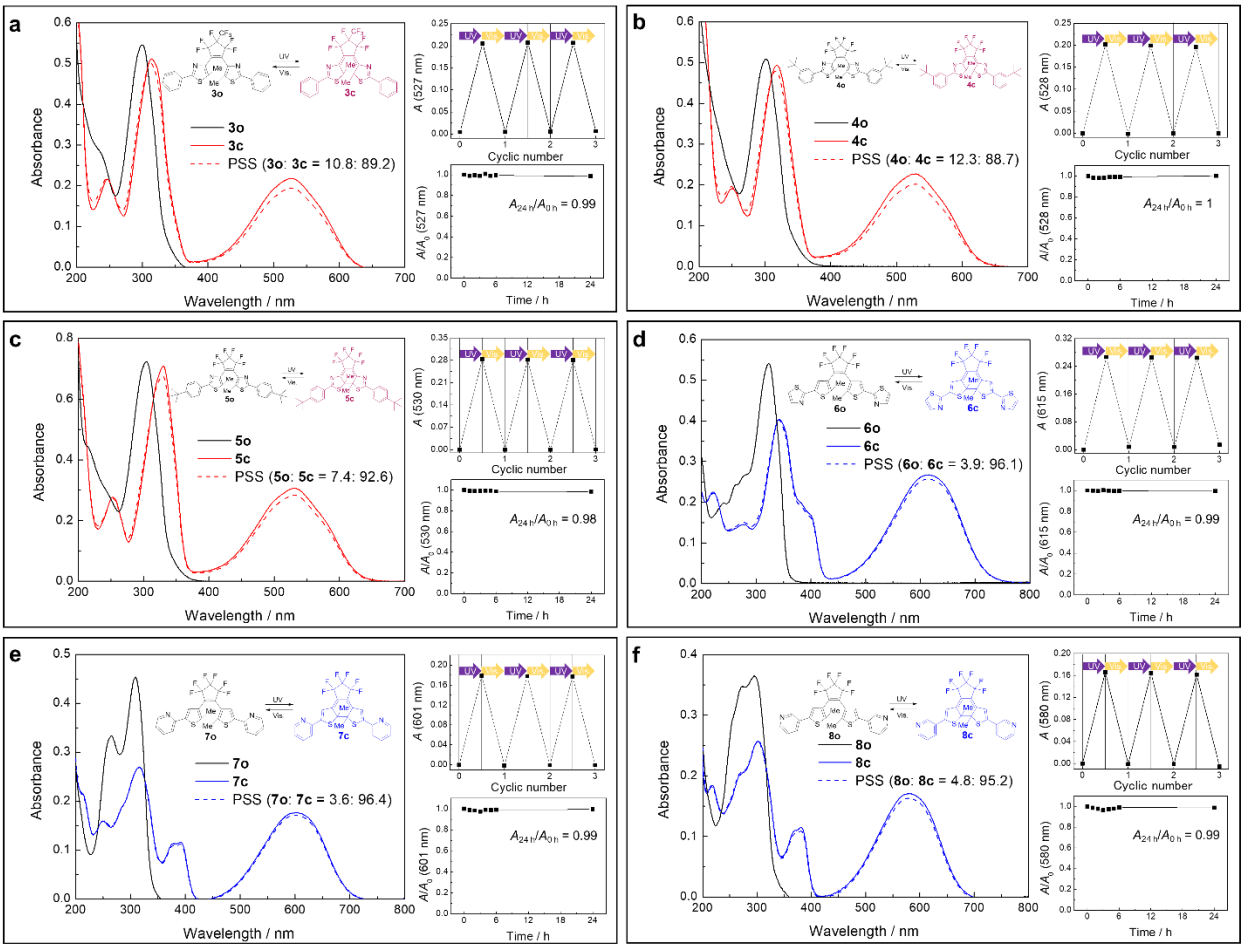


Figure S31. Absorption spectra, reversibility, and thermal stability of diarylethene derivatives having thiazole (a-d) or pyridine rings (e and f) in water/ethanol = 3:7 (v/v). The absorption spectra of the open- (black solid line) and closed-ring isomers (colored solid lines other than black) and the PSSUV (broken line) are shown. In each panel the reversibility (top right) and thermal stability (bottom right) are shown. To obtain the PSS^{UV} absorption spectra, the samples were irradiated with their optimal wavelength (see Table 2). For the reversibility, the samples were alternately irradiated with UV (λ = 313 nm) and visible light (λ > 480 nm). For the thermal stability, the samples of each closed-ring isomer were kept at 37 °C. These data were measured at 15 μM.

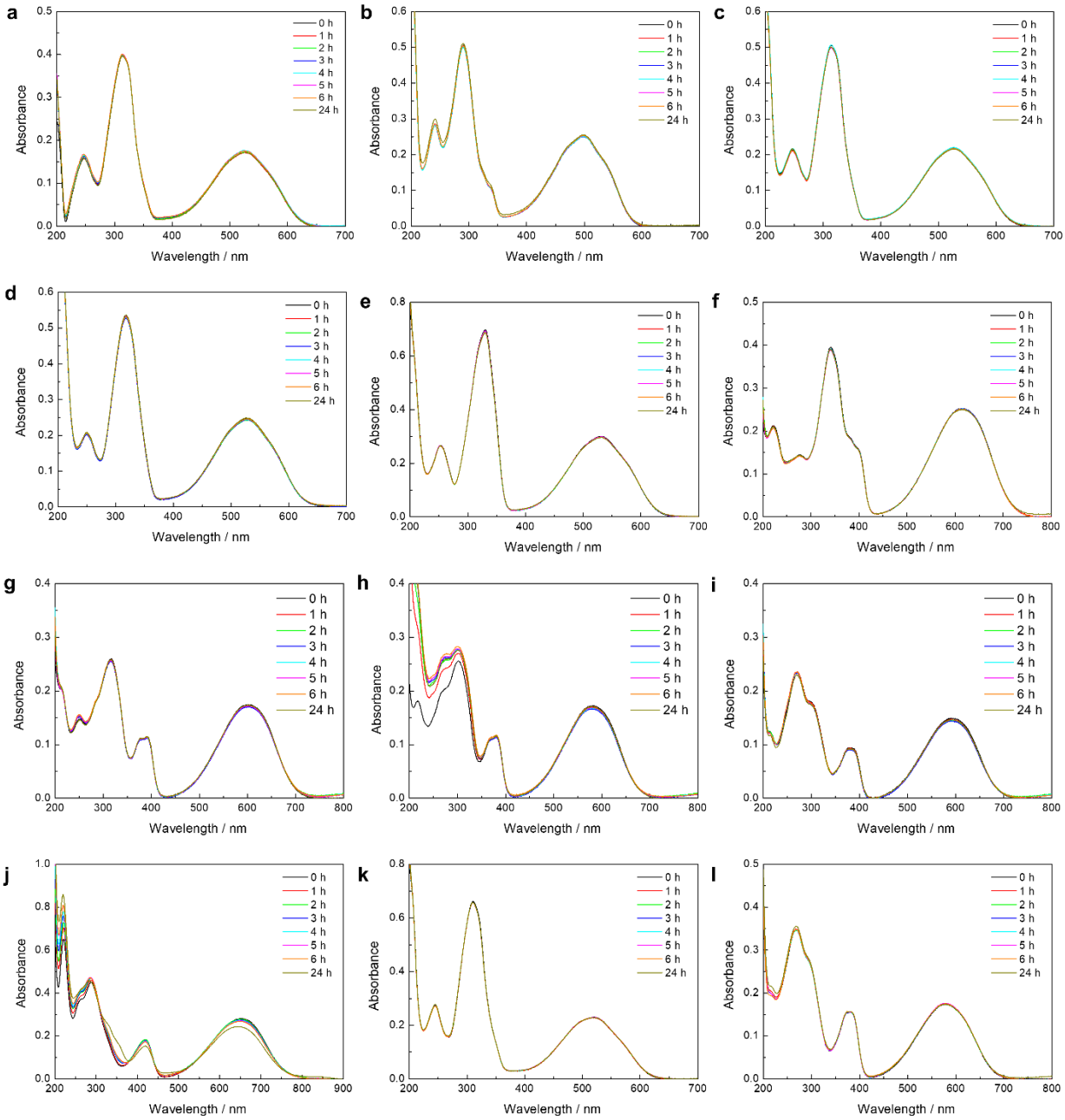


Figure S32. Time-dependent absorption spectral changes of **1-12** in water/ethanol = 3:7 (v/v) at 37°C. **1c** (a), **2c** (b), **3c** (c), **4c** (d), **5c** (e), **6c** (f), **7c** (g), **8c** (h), **9c** (i), **10c** (j), **11c** (k), and **12c** (l).

11. Cytotoxicity of diarylethenes without light irradiation

The potential cytotoxicity of diarylethene without light irradiation was evaluated in the same way as done for photoinduced cytotoxicity (Table S5). These cytotoxicities were evaluated at the lower limit concentration, where the cells begin to show affect. Note that this potential cytotoxicity is dependent on the ratio of the number of moles of closed-ring isomer/number of cells.

Table S5. Concentration at which cytotoxicity is observed without light irradiation (cytotoxicity in the dark) for the closed-ring isomers of **1**-**12**.

	Cytotoxicity in dark / ppm
1c	0.2
2c	1
3c	2
4c	>2
5c	>2
6c	0.5
7c	>2
8c	>2
9c	>2
10c	>2
11c	1
12c	1

12. Molecular structures of open- and closed-ring isomers of 1-12 by DFT calculation

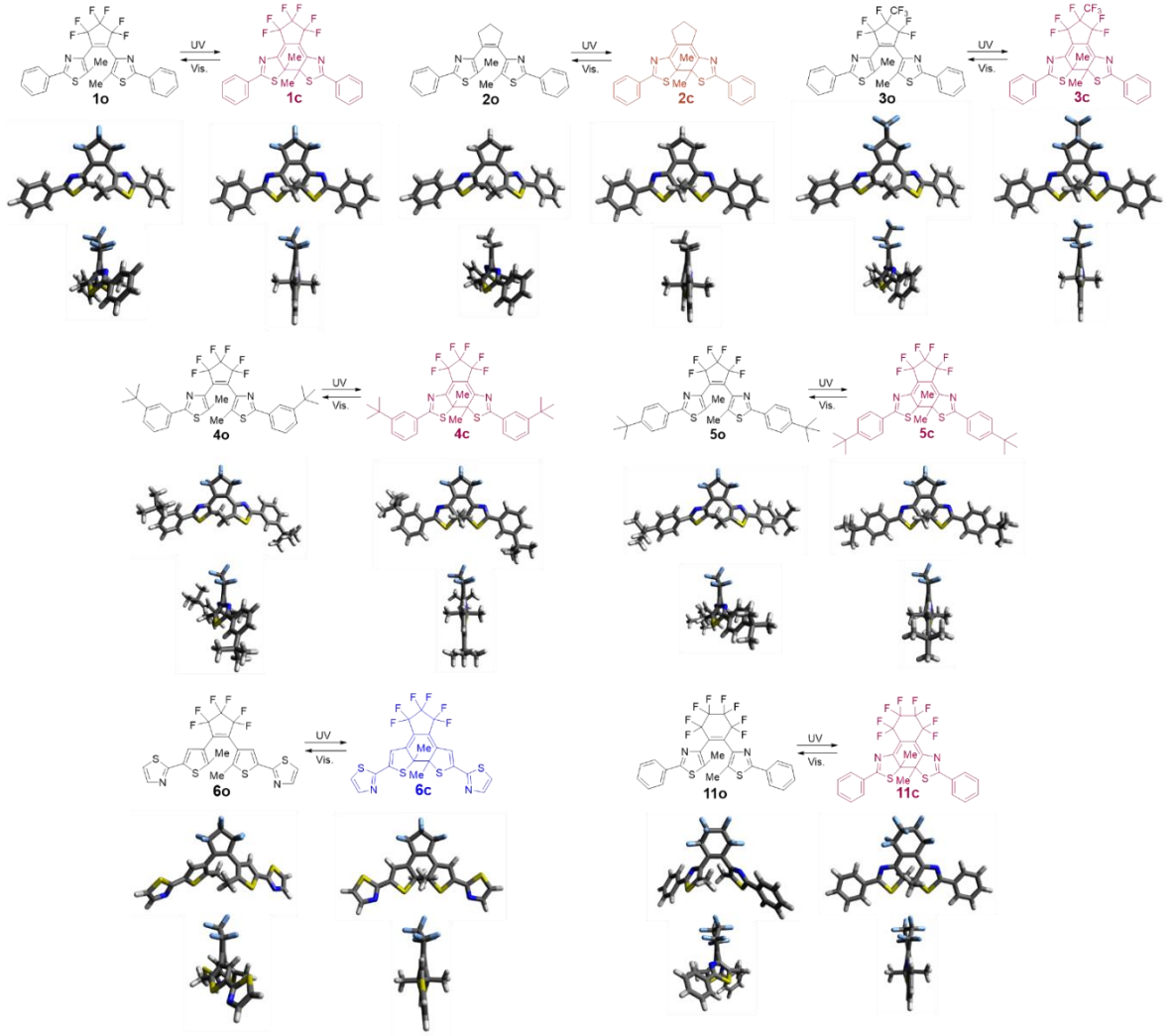


Figure S33. Structures of open- and closed-ring isomers of derivatives having thiazole group optimized on the B3LYP/PCM(water)//6-31G(d) level of theory.

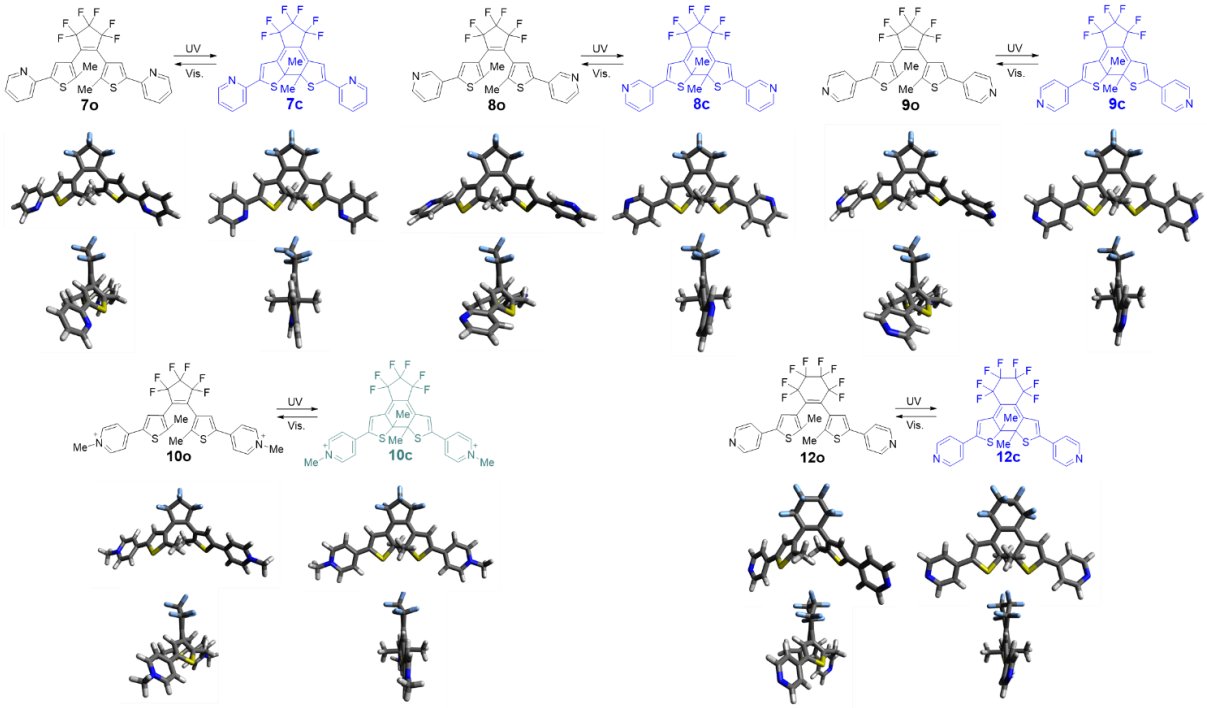
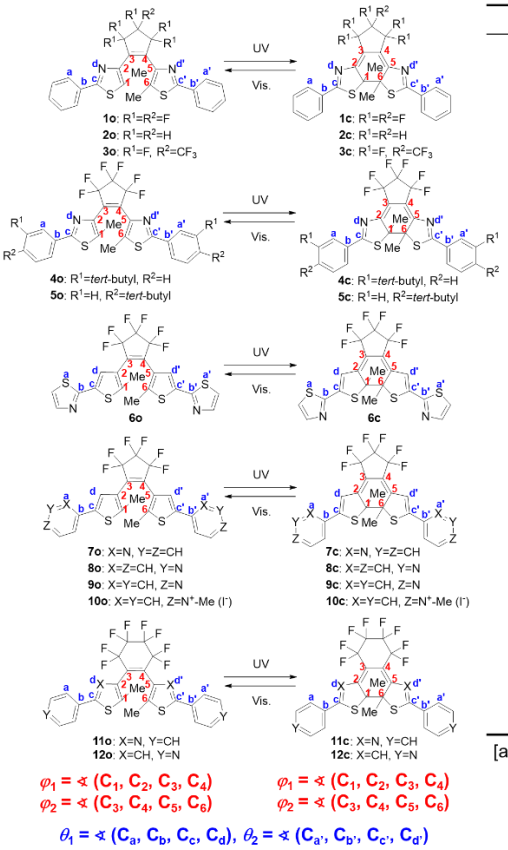


Figure S34. Structures of open- and closed-ring isomers of derivatives having pyridine group optimized on the B3LYP/PCM(water)//6-31G(d) level of theory.

Table S6. Geometric parameters of optimized structures of open- and closed-ring isomers of **1-12** on the B3LYP/PCM(water)/6-31G(d) level of theory.



		ΔE [kJ/mol]	$r_{C1\text{-}C6}$ [Å]	φ_1 / φ_2 [°]	θ_1 / θ_2 [°]
1	Open-ring	47.667	3.675	-47.4 / -44.2	5.5 / 3.5
	Closed-ring		1.548	7.8 / 7.3	2.5 / 3.4
2	Open-ring	36.219	3.646	-48.3 / -47.9	2.7 / 2.4
	Closed-ring		1.542	6.3 / 6.8	6.4 / 7.3
3	Open-ring	48.782	3.681	-44.0 / -47.0	3.5 / 4.4
	Closed-ring		1.549	7.7 / 7.5	2.6 / 3.3
4	Open-ring	46.742	3.677	-47.4 / -44.3	5.5 / 2.5
	Closed-ring		1.548	7.7 / 7.3	3.1 / 3.6
5	Open-ring	44.796	3.674	-47.3 / -44.0	3.0 / 1.9
	Closed-ring		1.549	7.9 / 7.3	2.7 / 2.9
6	Open-ring	57.858	3.705	-49.3 / -46.5	-0.3 / -0.2
	Closed-ring		1.549	-8.8 / -7.6	3.2 / 3.1
7	Open-ring	59.234	3.700	46.0 / 48.8	0 / -0.1
	Closed-ring		1.549	-8.4 / -7.3	6.2 / 6.1
8	Open-ring	56.650	3.702	46.5 / 49.3	26.4 / 26.4
	Closed-ring		1.549	-8.8 / -7.7	-20.1 / -20.5
9	Open-ring	62.781	3.708	46.8 / 49.6	16.3 / 16.3
	Closed-ring		1.549	-8.9 / -7.6	-16.1 / -15.5
10	Open-ring	82.288	3.745	51.2 / 48.1	-1.6 / 2.7
	Closed-ring		1.549	-9.3 / -7.8	-6.1 / -8.0
11	Open-ring	34.930	3.702	57.4 / 57.4	-2.7 / -2.7
	Closed-ring		1.543	-5.4 / -5.4	-3.6 / -3.6
12	Open-ring	48.097	3.713	59.0 / 59.0	-17.6 / -17.6
	Closed-ring		1.542	-6.1 / -6.1	-17.4 / -17.4

[a] Energy of the closed-ring isomers compared to the open-ring isomers.

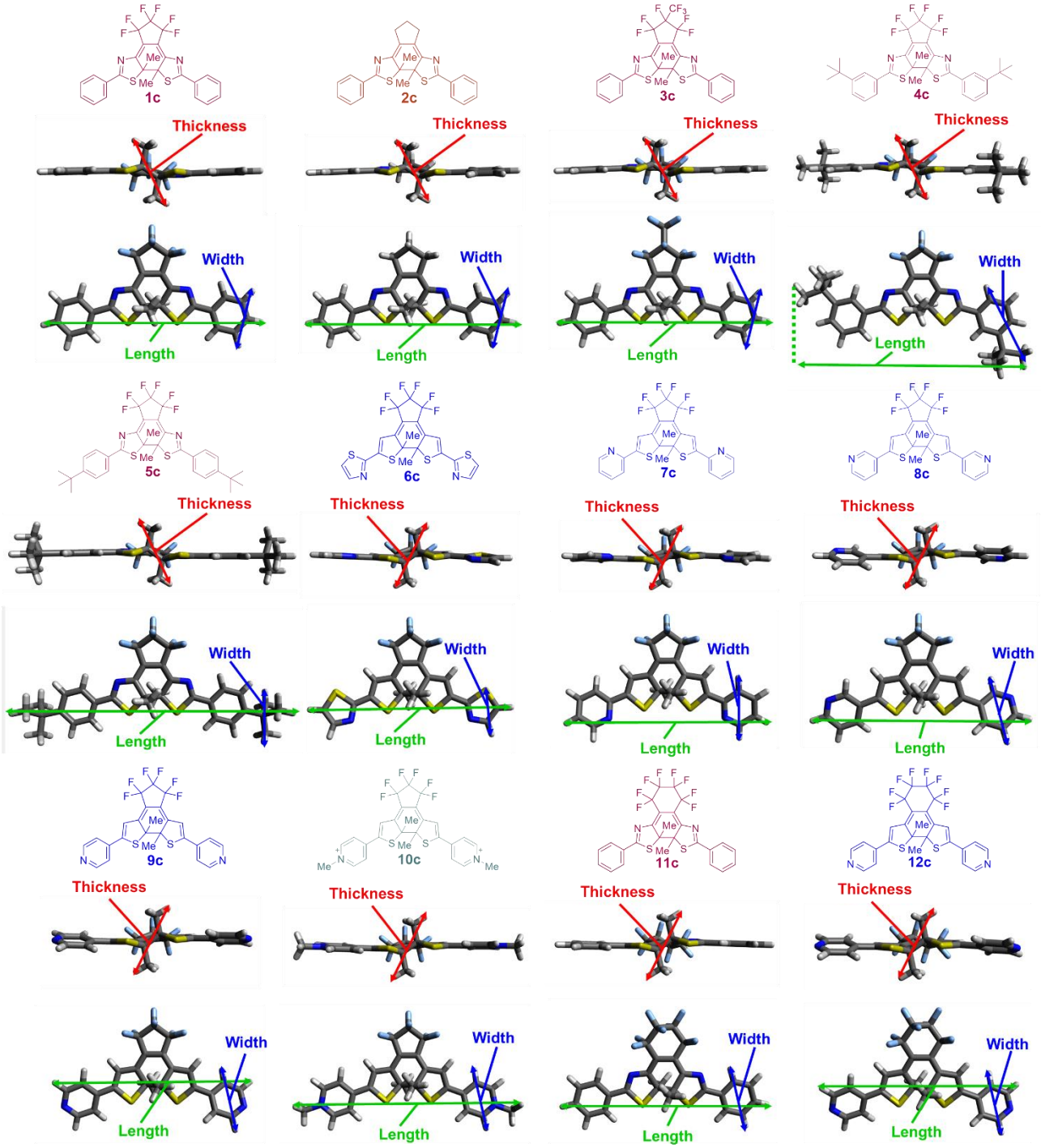


Figure S35. Structures of closed ring isomers of **1-12** optimized on the B3LYP/PCM(water)/6-31G(d) level of theory used to calculate molecular sizes. Molecular thickness (red line), width (blue line), and length (green line).

Table S7. Molecular size parameters of optimized structures of closed-ring isomers of **1**-**12** on the B3LYP/PCM(water)/6-31G(d) level of theory.

	Thickness [Å]	Width [Å]	Length [Å]
1c	5.646	4.306	16.739
2c	5.622	4.297	16.686
3c	5.642	4.306	16.739
4c	5.646	**7.291**	18.553
5c	5.646	4.356	**21.145**
6c	5.646	3.603	16.043
7c	5.644	4.903	15.954
8c	5.644	4.896	16.497
9c	5.645	4.892	15.648
10c	5.650	4.907	18.256
11c	5.644	4.967	16.705
12c	5.643	4.892	15.595

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