Supplementary Information

Synthesis of Photochromic Diarylethnes Using Microflow System

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General Remarks. GC analysis was performed on a gas chromatograph (SHIMADZU GC-14B) equipped with a flame ionization detector using a fused silica capillary. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian Gemini 2000 (^{1}H 300 MHz, ^{13}C 75 MHz), Varian MERCURY plus-400 (^{1}H 400 MHz, ^{13}C 100 MHz, F^{19} 377 MHz), spectrometer with $CDCl_3$ as an internal standard unless otherwise noted. EI mass spectra were recorded on JMS-SX102A spectrometer. FAB mass spectra were recorded on JMS-HX110A spectrometer. The absorption spectra were measured using a Hitachi U-3410 spectrophotometer. Photo-irradiation was carried out using an USHIO 500W high-pressure mercury arc lamp. Light of appropriate wavelengths was isolated by passing the arc light through a monochromator (Jobin Yvon H-10 UV).

Thin-layer chromatography (TLC) was carried out by using Merck precoated silica gel F_{254} plates (thickness 0.25 mm). Flash chromatography was carried out using Kanto Chem. Co., Silica Gel N (spherical, neutral, 40-100 μm). Preparative recycling gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-908 equipped with a JAIGEL-1H column and a JAIGEL-2H column using $CHCl_3$ as eluent. All reactions were carried out under Ar atmosphere unless otherwise noted.

Materials. Dry THF (Kanto Chemical Co., Inc.), octafluorocyclopentene (Zeon Corporation), and a solution of butyllithium in hexane (Kanto Chemical Co., Inc.) were used as obtained.

General Procedure for the Synthesis of Diarylethenes using a Macro Batch System. Butyllithium (1.49M hexane solution, 0.700 mL, 1.04 mmol) was slowly added to a stirred THF solution (8.00 mL) of an aryl bromide (1.00 mmol) at –78 °C, and the mixture was stirred at –78 °C for 1 h. A THF solution of octafluorocyclopentene (0.660 M, 0.760 mL, 0.500 mmol) was then added slowly at –78 °C. The mixture was stirred at –78 °C for 2 h and then warmed to room temperature. The reaction mixture was poured into water and extracted with ethyl acetate. The organic extracts were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane or hexane/ethyl acetate) and/or GPC.

General Procedure for the Synthesis of Diarylethenes using Micro Flow System.
The reaction was carried out using a microflow system consisting of two T-shaped micromixers (**M1** and **M2**) (Swagelok Union Tee, inner diameter ϕ = 2.3 mm **(M1)**, ϕ = 1.3 mm **(M2**), and stainless microtube reactors (**R1**, and **R2**: ϕ = 800 μm x 1 **—** 2 m) as shown in Figure 1. A solution of aryl bromide (0.300 M) in THF and a solution of butyllithium (1.50 M) in hexane were introduced to **M1** at flow rate of 7.50 mL/min and 1.50 mL/min, respectively. The resulting mixture was allowed to react in **R1** (residence time: 3.4 **—** 6.7 sec). The outlet solution was introduced to **M2**, where a solution of octafluorocyclopentene (0.750 M) in THF was introduced (flow rate: 1.50 mL/min). The resulting mixture was allowed to react in **R2**, (residence time: 2.9 **—** 5.7 sec). The outlet solution was introduced to a flask containing ethyl acetate (10.0 mL), which was maintained at 0 ^{o}C. After a steady state was reached, an aliquot of the product solution was taken for 1.0 min and analyzed by ^{19}F NMR using trfluoromethylbenzene as an internal standard.

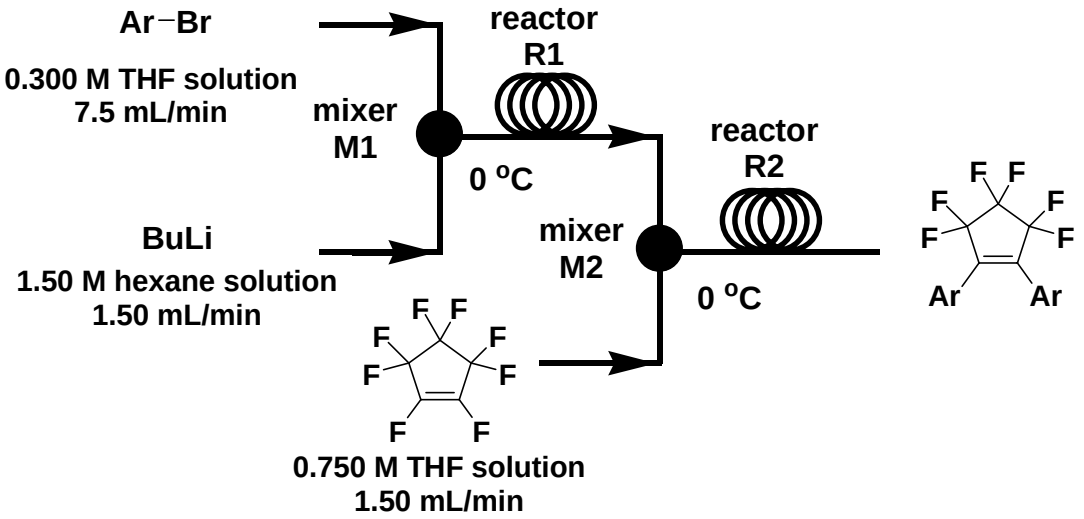
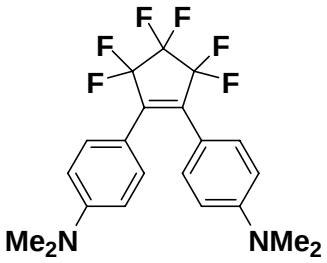


Figure 1. Microflow system for the synthesis of diarylethenes

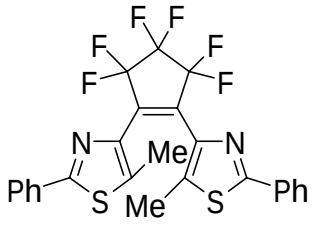
1,2-Bis(2-methyl-5-phenylthiophene-3-yl)hexafluorocyclopentene (1),[1] **and 1,2-bis(2-methylbenzothiophene-3-yl)hexafluorocyclopentene (2),**[2] **1,2-Bis(5-methyl-2-phenylthiazol-4-yl)hexafluorocyclopentene (3),**[3] **1,2-diphenylhexafluoro-cyclopentene (4),**[4] **1,2-bis(4-methylphenyl)hexafluorocyclopentene (5),**[4] **1,2-Bis(4-methoxyphenyl)- hexafluorocyclopentene (6)**[4]**,** were identified by comparison of their spectra data with those of authentic samples reported in the literature. 1,2-Bis(4-*N*,*N*-dimethylamino- phenyl)hexafluorocyclopentene (**7**) was an unknown compound and was identified by its spectral data as shown below.



1,2-Bis(4-*N*,*N*-dimethylaminophenyl)hexafluorocyclopentene (7): 51% yield from 4-bromo-*N*,*N*-dimethylaniline and octafluorocyclopentene, purified with flash chromatography (hexane / ethyl acetate: 10 / 1) and GPC, ^{1}H NMR (300 MHz) δ 3.00 (s, 12H), 6.63 (d, *J* = 9.0 Hz, 4H), 7.34 (d, *J* = 9.0 Hz, 4H); ^{13}C NMR (75 MHz) δ 39.9, 111.3 (tquint., *J* = 268.2 Hz, 25.1 Hz), 111.7, 115.6, 117.2 (tt, *J* = 253.4 Hz, 23.3 Hz), 130.4, 135.3 — 136.2 (m), 150.9; ^{19}F NMR (377 MHz) δ–132.0 — –131.9 (m, 2F), –110.4 — –110.3 (m, 4F); HRMS (EI) *m/z* calcd for $C_{21}H_{20}F_6N_2$: 414.1531, found: 414.1531.

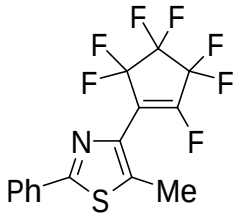
Synthesis of 1-(5-Methyl-2-phenylthiazol-4-yl)heptafluorocyclopentene (8) and 1,2-Bis(5-methyl-2-phenylthiazol-4-yl)hexafluorocyclopentene (3)[3] **using Macro Batch System.** Butyllithium (0.700 mL of a 1.49 M hexane solution, 1.04 mmol) was slowly added to a stirred THF solution (8.00 mL) of aryl bromide (1.00 mmol) at –78 °C, and the solution was stirred at –78 °C for 1 h. Octafluorocyclopentene (0.760 mL of a 0.660 M THF solution, 0.500 mmol) was then added slowly at –78 °C. The mixture was stirred at –78 °C to room temperature for 2 h. The reaction mixture was poured into water and the product was extracted with ethyl acetate. The organic extracts were dried over anhydrous magnesium sulfate and the solvent was evaporated under reduced pressure. The crude product was purified by GPC to obtain monothiazolyl compound **8** (95.3 mg 0.259 mmol, 52% yield) and bisthiazolyl compound **3** (25.7 mg,

0.0492 mmol, 10% yield).



1,2-Bis(5-methyl-2-phenylthiazol-4-yl)hexafluorocyclopentene (3)[3]

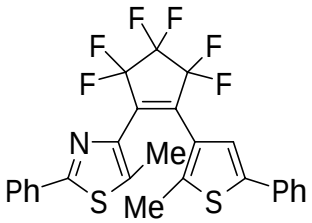
^{1}H NMR (400 MHz) δ 2.11 (s, 6H), 7.39-7.44 (m, 3H), 7.85-7.90 (m, 2H); ^{13}C NMR (100 MHz) δ 12.3, 111.3 (t with fine couplings, J = 269,2 Hz), 115.7 (t with fine couplings, J = 256.1 Hz), 126.4, 128.8, 130.2, 132.8, 135.8-136.6 (m), 136.9, 140.1, 165.5; ^{19}F NMR (377 MHz) δ –132.7 — –132.6 (m, 2F), –110.4 — –110.3 (m, 4F); HRMS (FAB) *m/z* calcd for $C_{25}H_{16}F_6N_2S_2$: 522.0659, found: 522.0657.



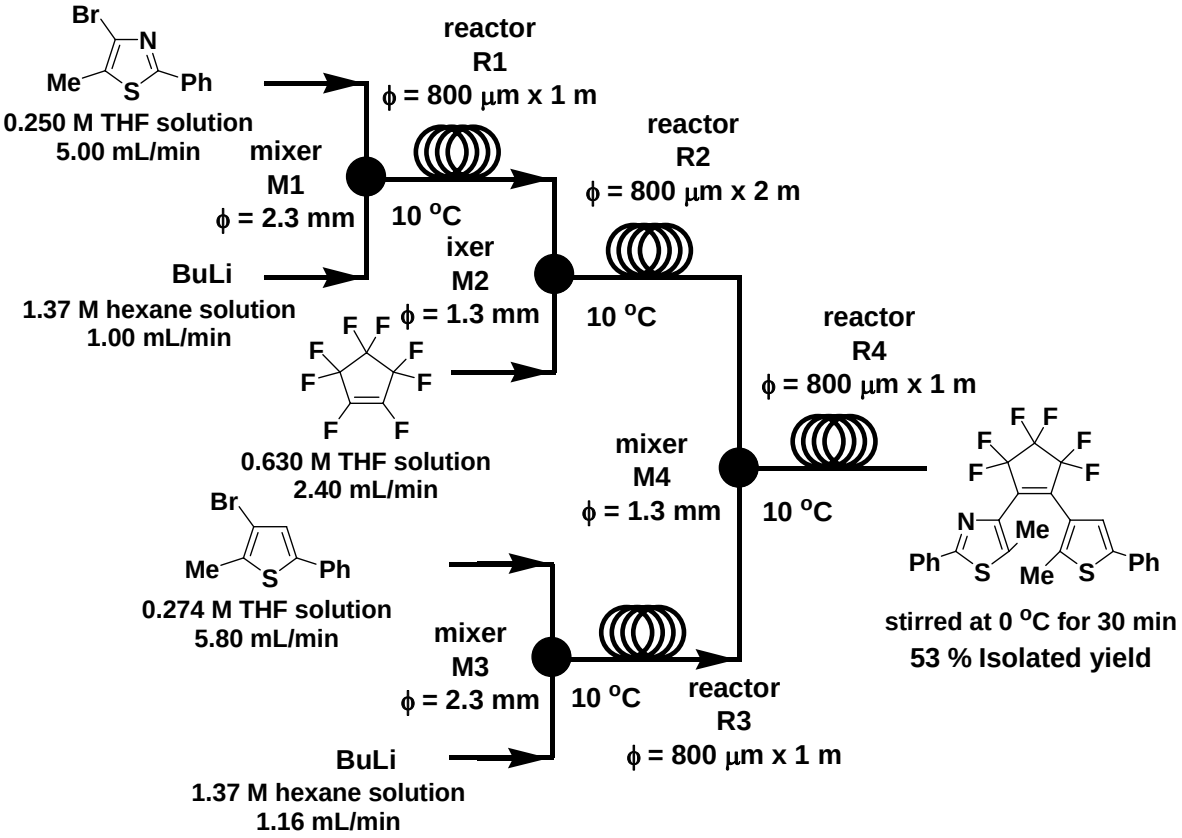
1-(5-Methyl-2-phenylthiazol-4-yl)heptafluorocyclopentene (8): ^{1}H NMR (400 MHz) δ 2.55 (d, J = 3.2 Hz, 3H), 7.43 — 7.47 (m, 3H), 7.89 — 7.93 (m, 2H); ^{13}C NMR (100 MHz) δ 12.4, 110.3 (t with fine couplings, J = 272.0 Hz), 110.8 (t with fine couplings, J = 255.9 Hz), 114.8 (t with fine couplings, J = 258.1 Hz), 117.7 — 118.4 (m), 126.4, 128.9, 130.4, 132.6, 135.6, 138.6, 151.6 (d with fine couplings, J = 297.6 Hz), 165.9; ^{19}F NMR (377 MHz) δ –130.9 — –130.8 (m, 2F), –125.7 — 125.5 (m, 1F), –119.2 — –119.1 (m, 2F), –109.1 — –109.0 (m, 2F); HRMS (FAB) *m/z* calcd for $C_{15}H_8F_7NS$: 367.0266, found: 367.0266.

Synthesis of 1,2-Bis(5-methyl-2-phenylthiazol-4-yl)hexafluorocyclopentene (3) using Micro Flow System. The reaction was carried out using a microflow system consisting of two T-shaped micromixers (**M1** and **M2**) (Swagelok Union Tee, channel width **M1**: ϕ = 2.3 mm, **M2**: ϕ = 1.3 mm), and stainless microtube reactors (**R1**: ϕ = 800 μm x 1 m, **R2:** ϕ = 800 μm x 2 m) as shown in Figure 1. A solution of 4-bromo-5-methyl-2-phenylthiazole (0.290 M) in THF and a solution of butyllithium (1.45 M) in hexane were introduced to the first micromixer (**M1**) at flow rate of 7.50 mL/min and 1.50 mL/min, respectively. The resulting solution was mixed with a solution of octafluorocyclopentene (0.670 M) in THF in the second micromixer (**M2**) (the 2nd step) (flow rate: 1.50 mL/min). The residence times were usually as follows: **R1**: 3.3 sec, **R2**: 5.8 sec. After a steady state was reached, an aliquot of the product solution was taken into a flask containing 10 mL of ethyl acetate at 0 ^{o}C. Evaporation of the solvent followed by column chromatography on silica gel (hexane) and GPC yielded the bisthiazolyl compound (419.1 mg, 0.802 mmol, 51% yield). The yield of monothiazolyl compound was determined by ^{19}F NMR of the crude product using an internal standard.

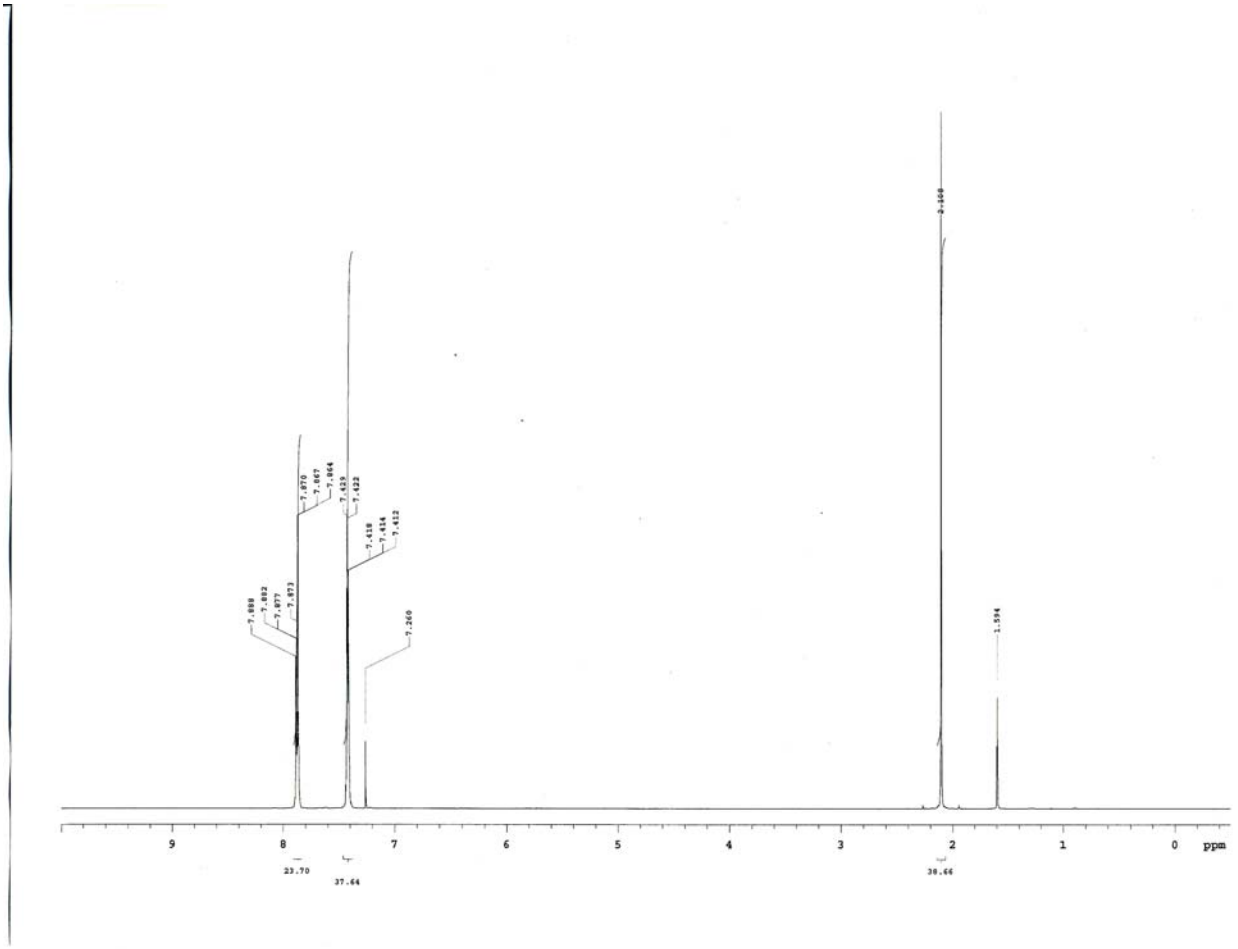
Synthesis of 1-(5-Methyl-2-phenylthiazol-4-yl)-2-(2-methyl-5-phenylthiophene-3-yl)hexafluorocyclopentene (9) using Micro Flow System.



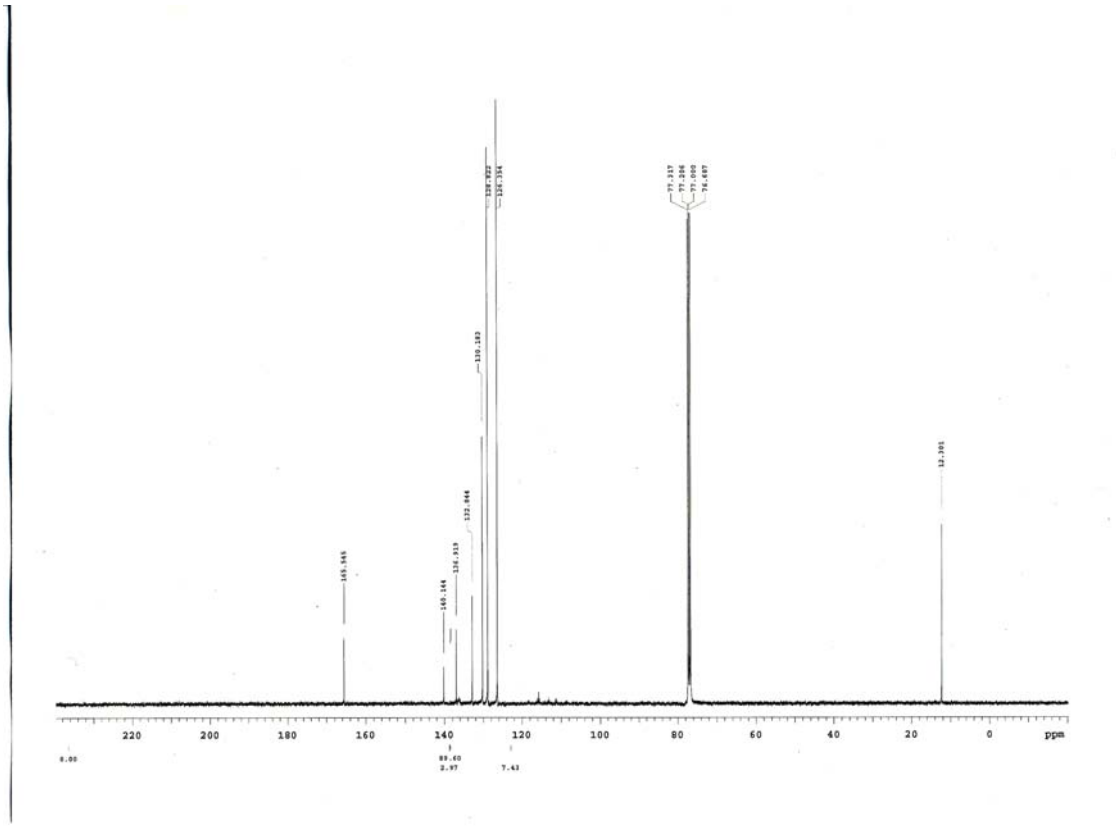
Synthesis of title compound was carried out using a microflow system consisting of four T-shaped micromixers (**M1, M2, M3** and **M4**) (Swagelok Union Tee, **M1** and **M3**: ϕ = 2.3 mm, **M2** and **M4**: ϕ = 1.3 mm) and stainless tube reactors (**R1**, **R3** and **R4**: ϕ = 800 μm x 1 m, **R2:** ϕ = 800 μm x 2 m), the temperature of which was maintained at 10 °C as shown in Figure 2. A solution of 4-bromo-5-methyl-2-phenylthiazole (0.250 M) in THF and a solution of butyllithium (1.37 M) in hexane were introduced to **M1** at flow rate of 5.00 mL/min and 1.0 mL/min, respectively. The resulting solution was allowed to react in **R1** (residence time: 5.0 sec). The outlet solution from **R1** was introduced to **M2**, where a solution of octafluorocyclopentene (0.630 M) in THF was introduced (flow rate: 2.40 mL/min). The resulting solution was allowed to react in **R2** (residence time: 7.2 sec). The outlet solution from **R2** was introduced **M4**. A solution of 3-bromo-2-methyl-5-phenylthiophene (0.274 M) in THF and a solution of butyllithium (1.37 M) in hexane were introduced to **M3** at flow rate of 5.80 mL/min and 1.16 mL/min, respectively. The resulting solution was allowed to react in **R3** (residence time: 4.3 sec). The outlet solution from **R3** was introduced to **M4**. In **M4** the solution from **R2** and that from **R3** were mixed and the resulting solution was allowed to react in **R4** (residence time: 2.0 sec). After a steady state was reached, the outlet solution from **R4** was introduced to an empty flask, which was maintained at 0 °C. The product solution in the flask was stirred for 0.5 h at 0 °C to ensure the completion of the reaction.



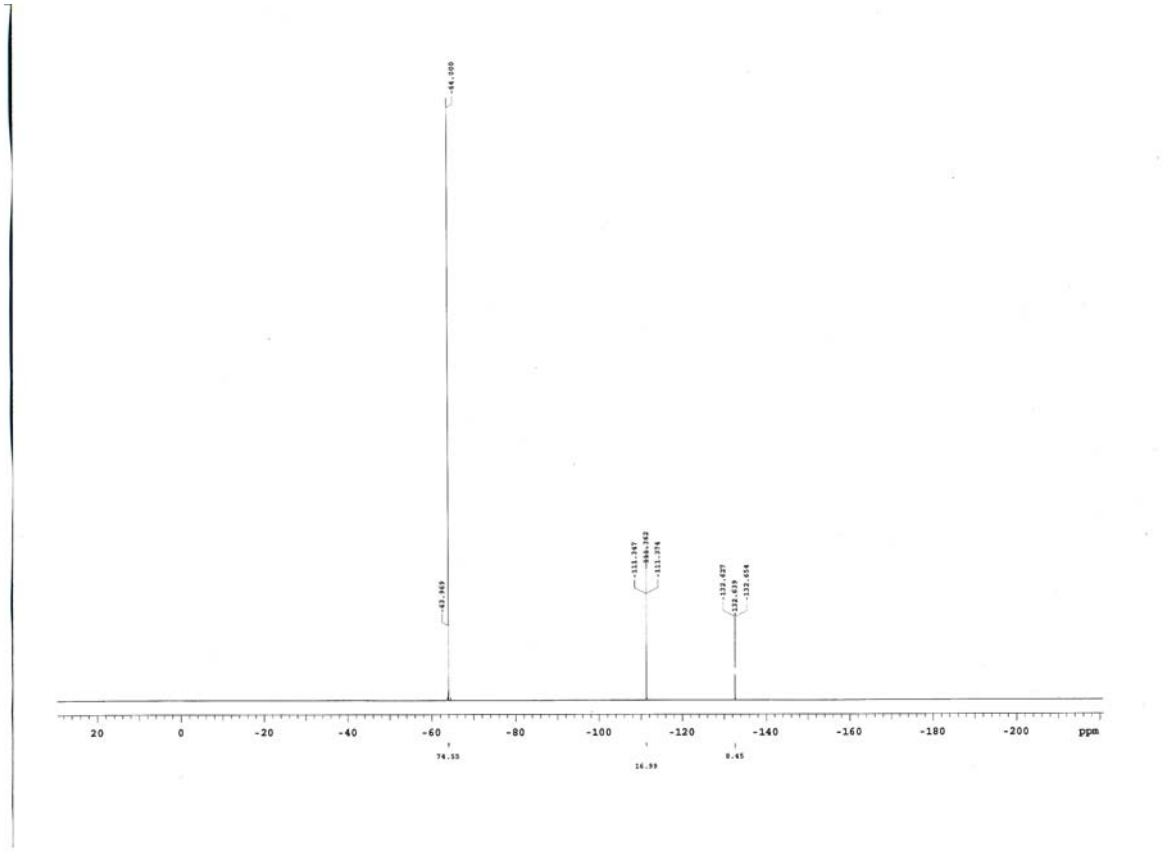
The pure product was isolated with flash chromatography (hexane) followed by GPC. ^{1}H NMR (400 MHz) δ 2.02 (s, 3H), 2.06 (s, 3H), 7.29 — 7.33 (m, 2H), 7.37 — 7.44 (m, 5H), 7.53 — 7.58 (m, 2H), 7.86 — 7.89 (m, 2H); ^{13}C NMR (100 MHz) δ 12.3, 14.4, 111.2 (t with fine couplings, J = 268.8 Hz), 115.8 (t with fine couplings, J = 255.7 Hz), 116.0 (t with fine couplings, J = 254.5 Hz), 122.5, 125.4, 125.7, 126.3, 127.8, 128.80, 128.84, 130.2, 132.8, 133.2, 134.9 — 135.7 (m), 136.6 — 137.4 (m), 136.7, 140.2, 141.2, 142.1, 165.5; ^{19}F NMR (377 MHz) δ–132.7 — –132.6 (m, 2F), –111.5 — –111.4 (m, 2F), –111.0 — –110.9 (m, 2F); HRMS (FAB) *m/z* calcd for $C_{26}H_{17}F_6NS_2$: 521.0707, found: 521.0707.



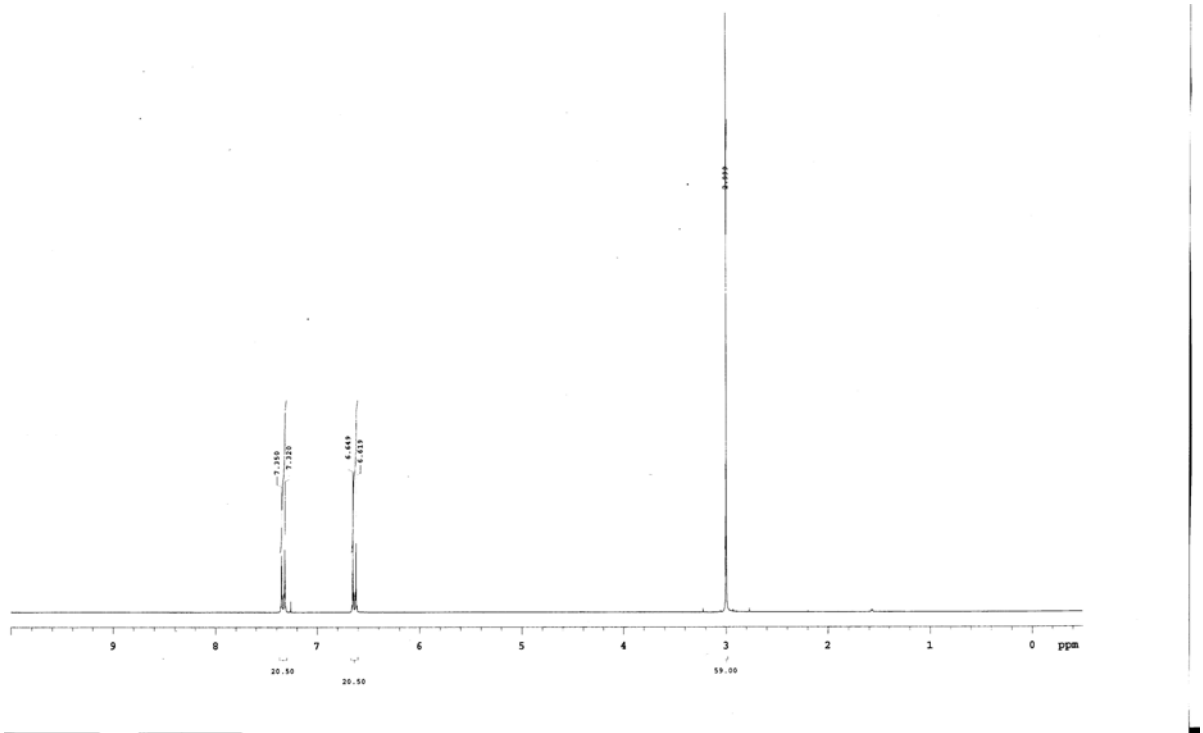
^{1}H NMR spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl))hexafluorocyclopentene (3).



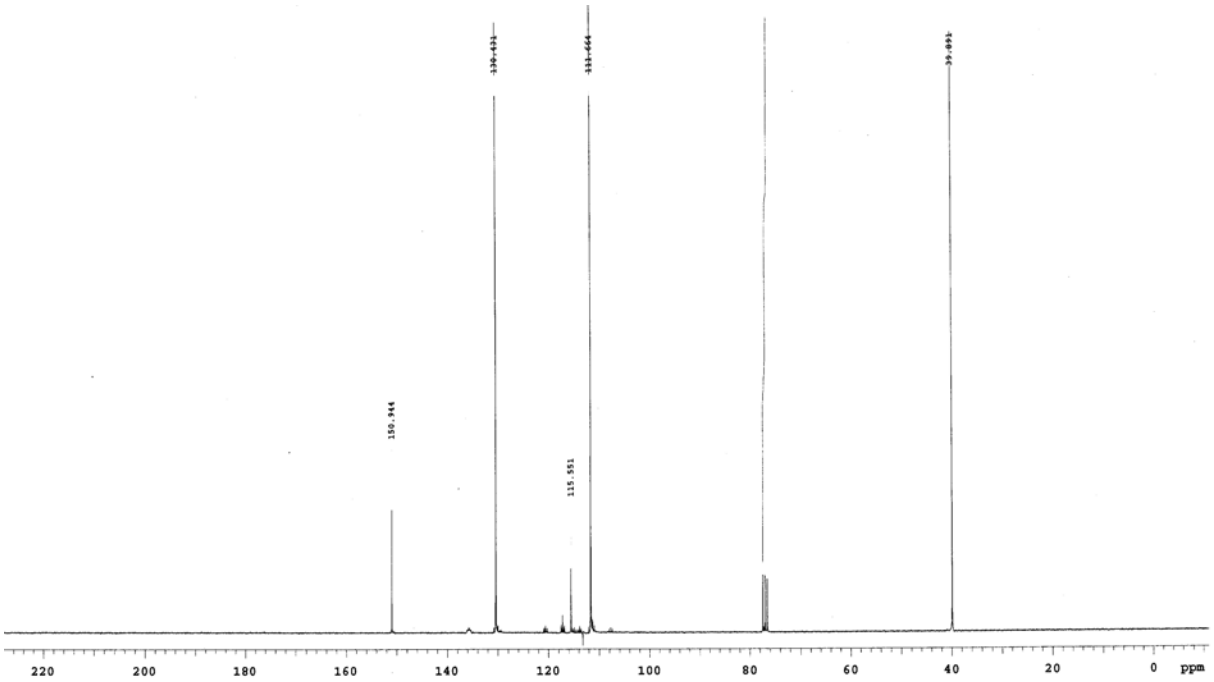
^{13}C NMR spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl))hexafluorocyclopentene (3).



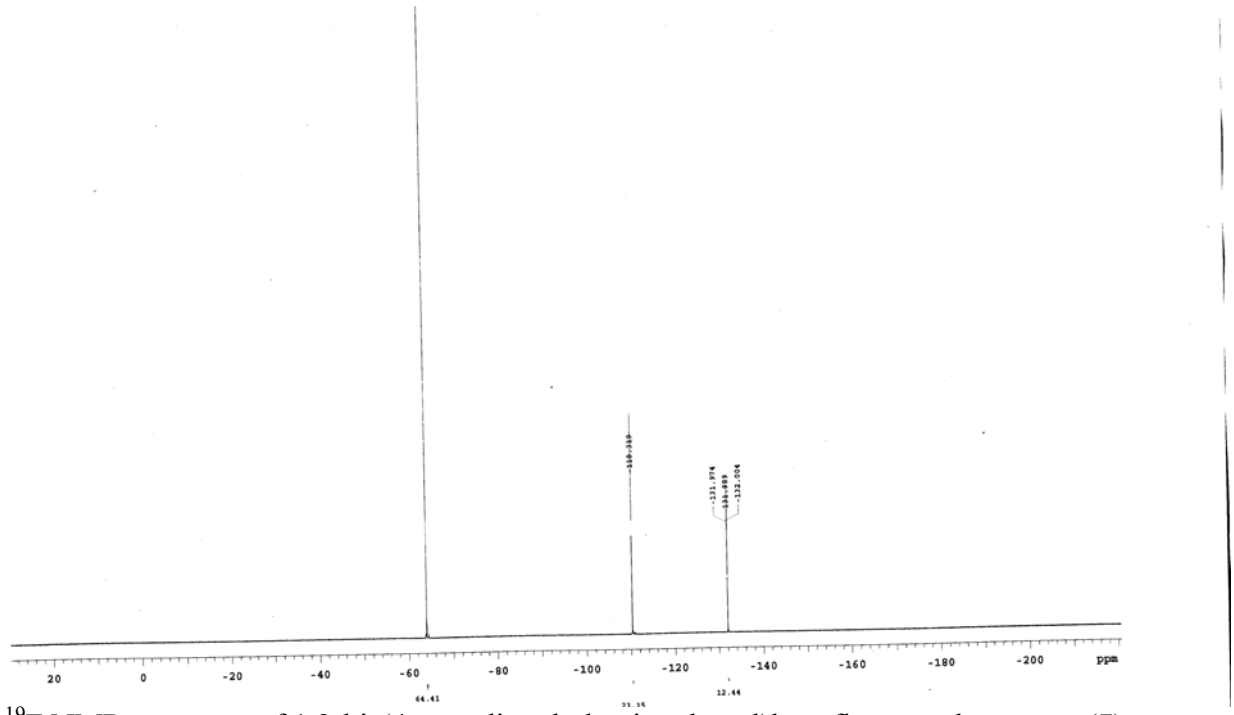
^{19}F NMR spectrum of 1,2-bis(5-methyl-2-phenylthiazol-4-yl))hexafluorocyclopentene (3).



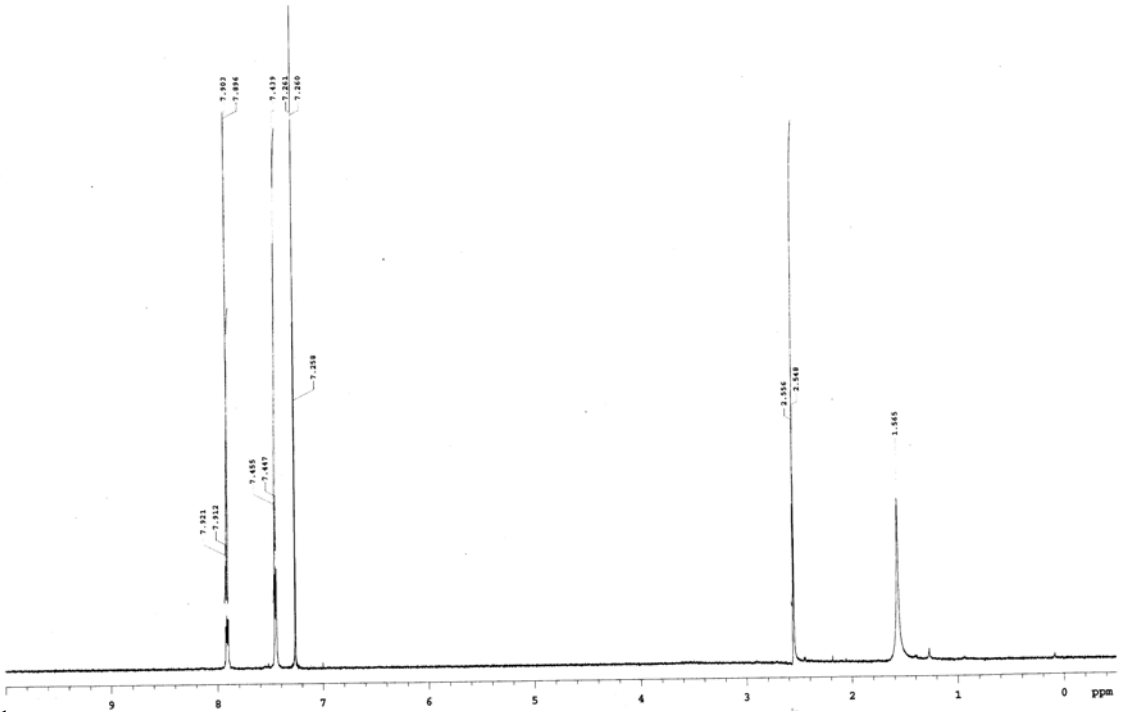
^{1}H NMR spectrum of 1,2-bis(4-*N*,*N*-dimethylaminophenyl)hexafluorocyclopentene (**7**).



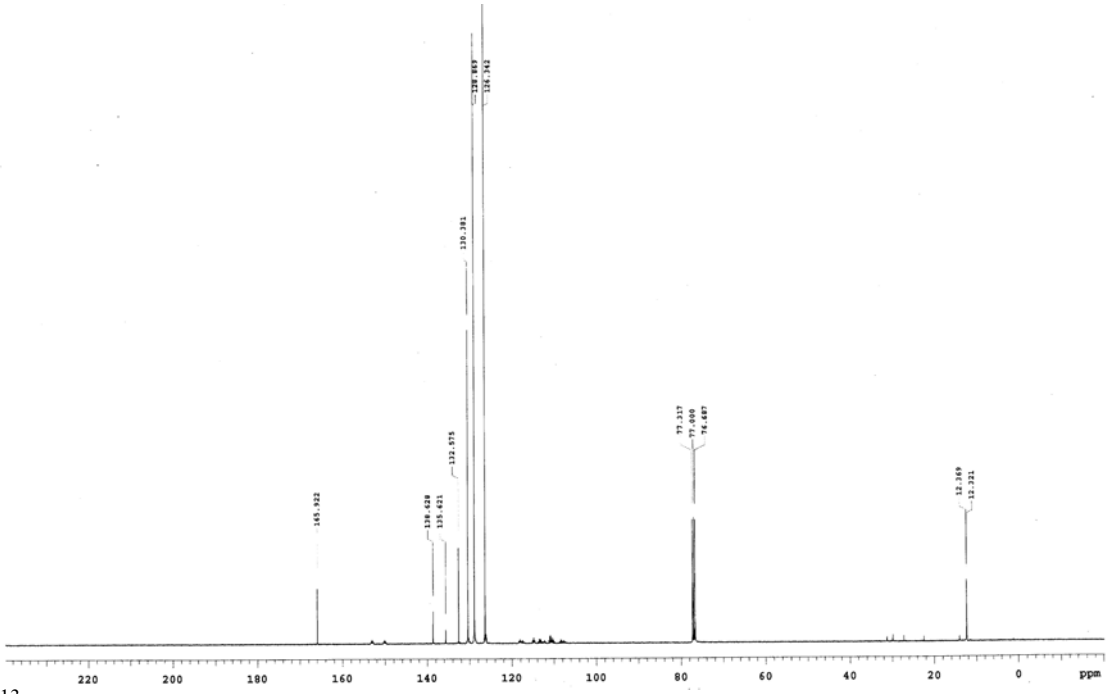
^{13}C NMR spectrum of 1,2-bis(4-*N*,*N*-dimethylaminophenyl)hexafluorocyclopentene (**7**).



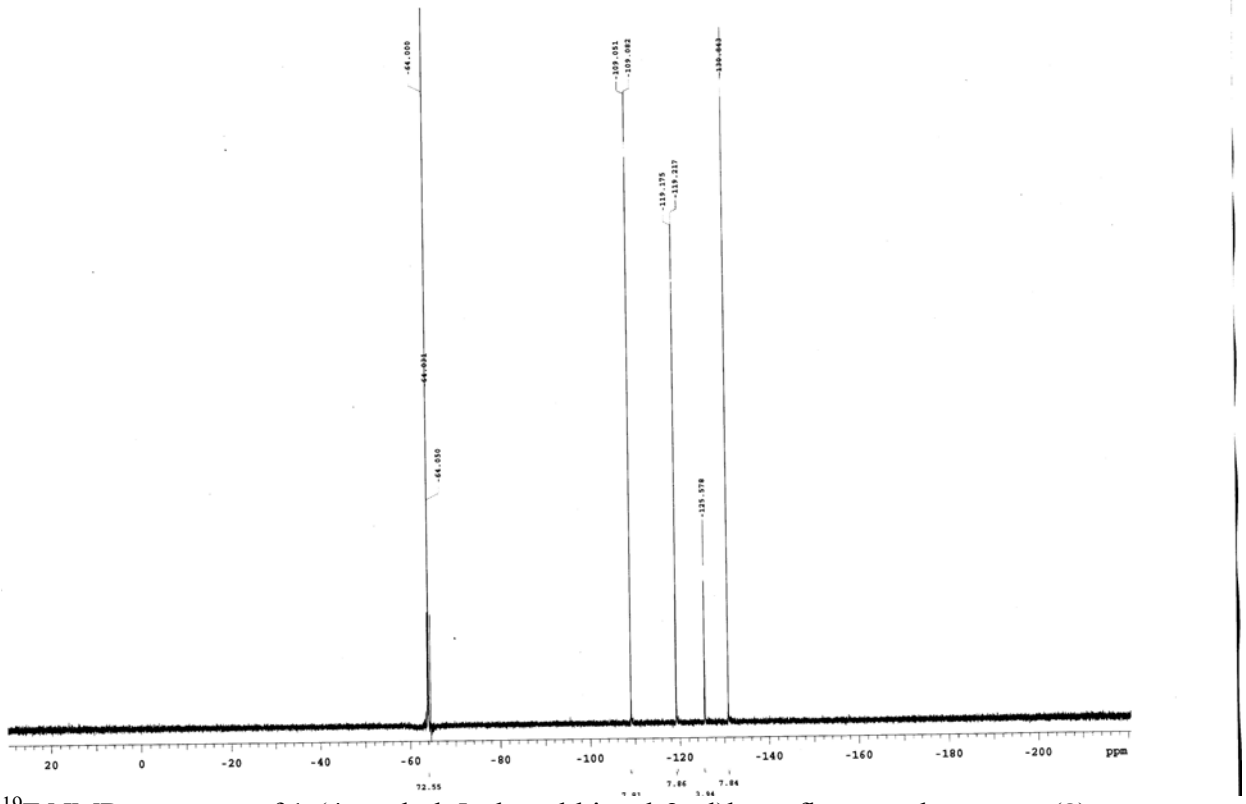
^{19}F NMR spectrum of 1,2-bis(4-*N*,*N*-dimethylaminophenyl)hexafluorocyclopentene (7).



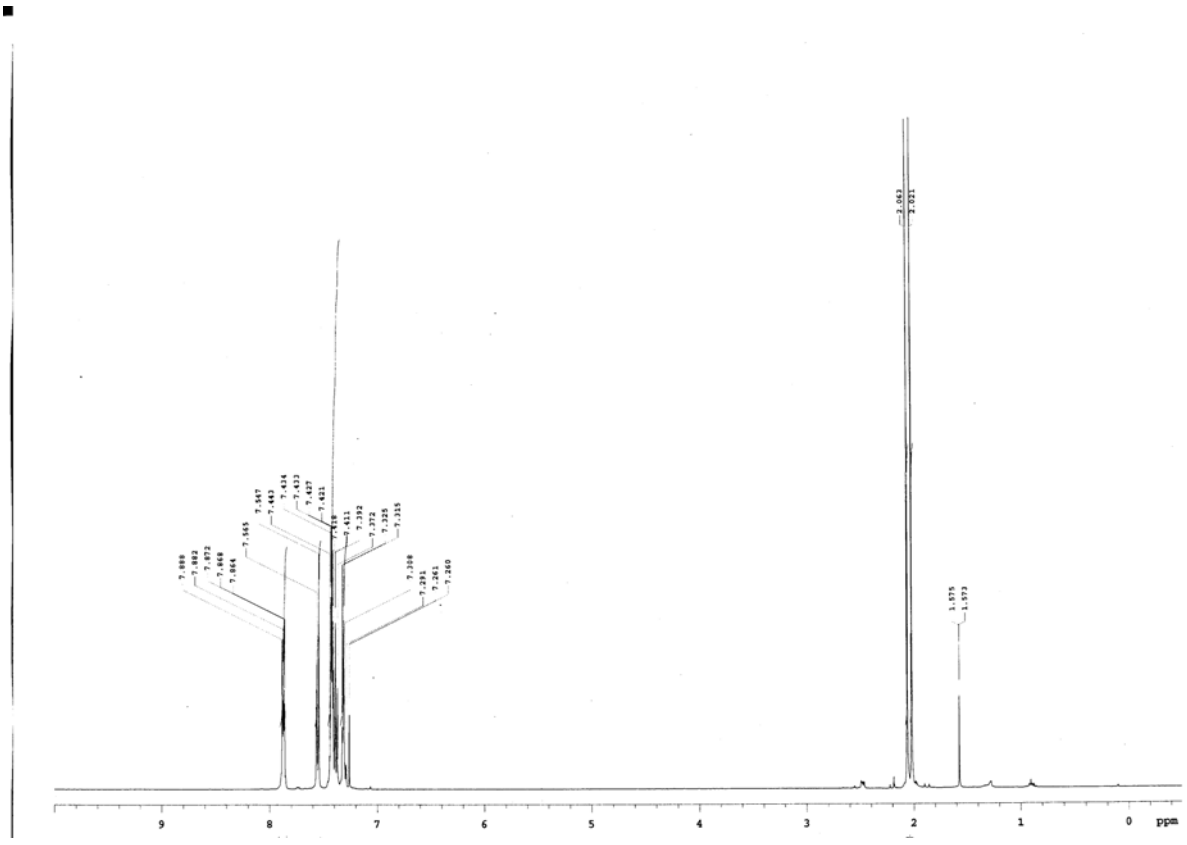
^{1}H NMR spectrum of 1-(4-methyl-5-phenylthiazol-2-yl)heptafluorocyclopentene (**8**).



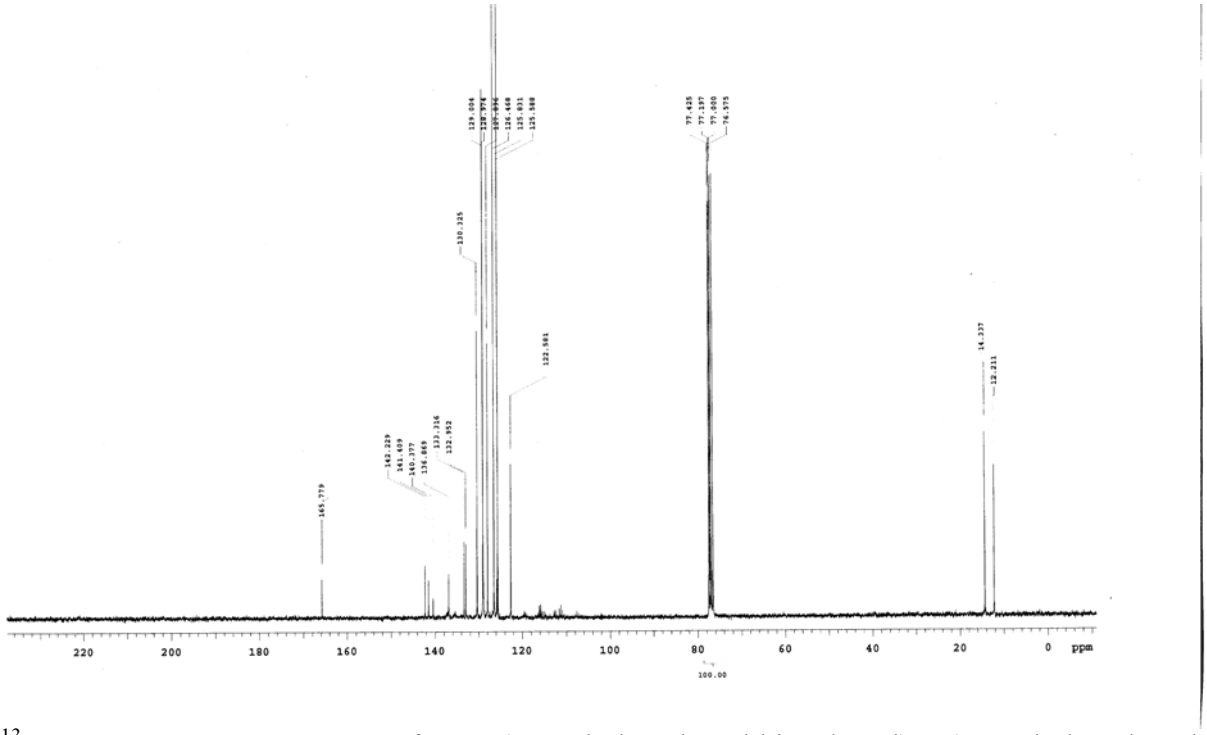
^{13}C NMR spectrum of 1-(4-methyl-5-phenylthiazol-2-yl)heptafluorocyclopentene (**8**).



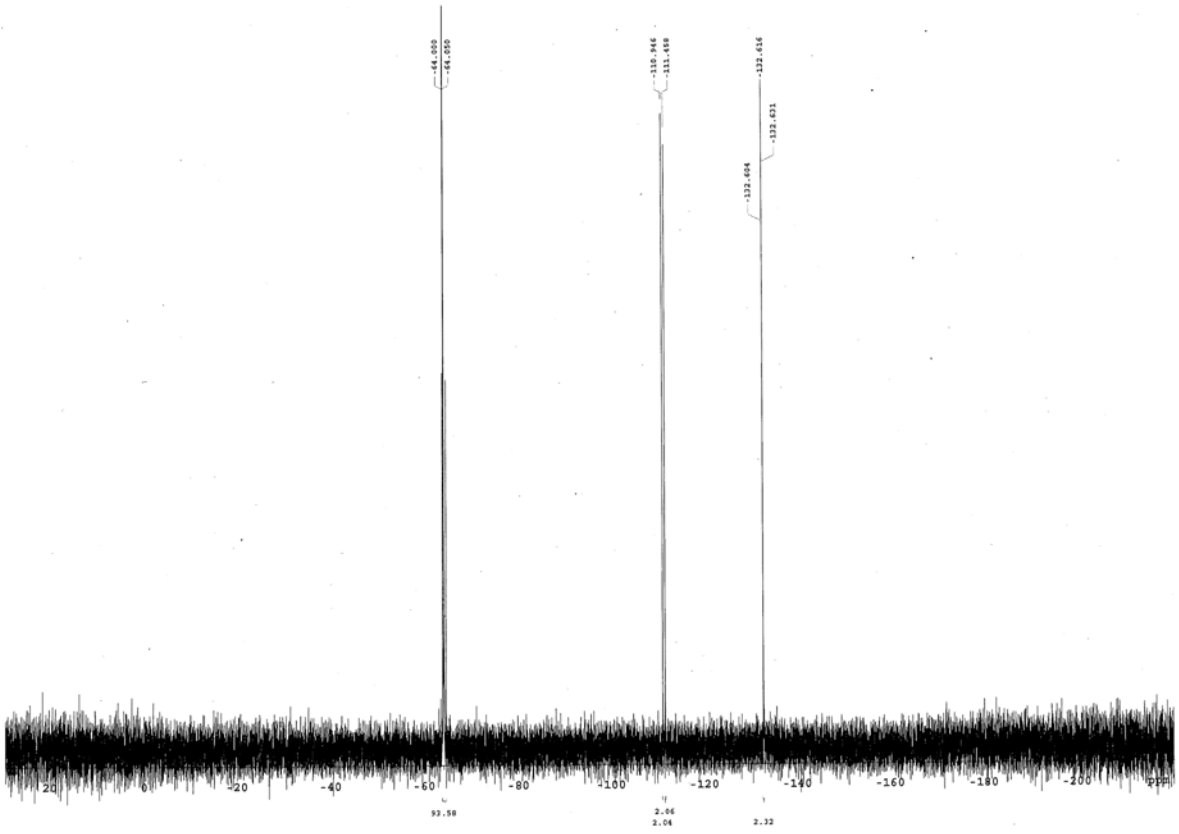
^{19}F NMR spectrum of 1-(4-methyl-5-phenylthiazol-2-yl)heptafluorocyclopentene (**8**).



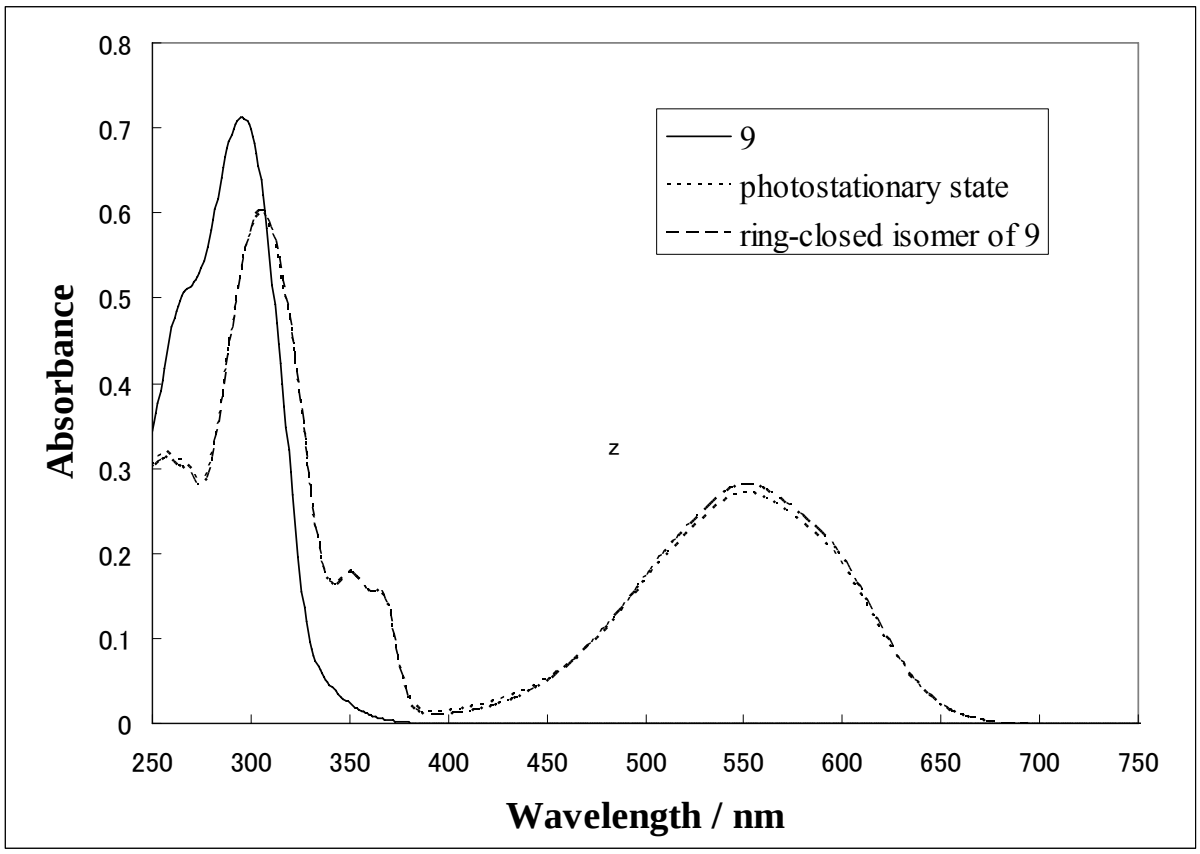
^{1}H NMR spectrum of 1-(5-methyl-2-phenylthiazol-4-yl)-2-(2-methyl-5-phenylthiophene-3-yl)hexafluorocyclopentene (**9**).



^{13}C NMR spectrum of 1-(5-methyl-2-phenylthiazol-4-yl)-2-(2-methyl-5-phenylthiophene-3-yl)hexafluorocyclopentene (**9**).



^{19}F NMR spectrum of 1-(5-methyl-2-phenylthiazol-4-yl)-2-(2-methyl-5-phenyl- thiophene-3-yl)hexafluorocyclopentene (**9**).



Absorption spectral change of **9** in heptane (2.1×10^{-5} M) upon irradiation with 313 nm light: **9** (─), **9** in the photostationary state under irradiation with 313 nm light (·····), and the ring-closed isomer of **9** (---).

The picture shown in the paper was taken using hexane solutions of the ring-closed isomers of **1**, **9**, and **3** (2×10^{-3} M).

References

(1) de Jong, J. J. D.; Lucas, L. N.; Hania, R.; Pugzlys, A.; Kellogg, R. M.; Feringa, B. L.; Duppen, K.; van Esch, J. H. *Eur. J. Org. Chem.* **2003**, 1887.
(2) WO 2004/113469 A1
(3) Uchida, K.; Ishikawa, T.; Takeshita, M.; Irie, M. *Tetrahedron* **1998**, *54*, 6627.
(4) Yamada, S.; Konno, T.; Ishihara, T.; Yamanaka, H. *J. Fluorine Chem.* **2005**, *126*, 125.