Supporting information for

Twisting of Aryl Groups Affects Thermal Back Reactivity of Diarylbenzene Photoswitches

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Contents

Abbreviations

Abbreviation	Meaning
HPLC	High-performance liquid chromatography
NMR	Nuclear magnetic resonance
TMS	Tetramethylsilane
HRMS	High-resolution mass spectra
UV	Ultraviolet
IR	Infrared
DFT	Density functional theory
IRC	Intrinsic reaction coordinates
HOMO	Highest occupied molecular orbital
DART	Direct analysis in real time

Experimental section

General

Commercially available reagents were used as they were for synthesis. Solvents used for spectroscopy were of spectroscopic grade or purified by distillation before use. High-performance liquid chromatography (HPLC) was carried out using a Hitachi L-7150/L-2400 HPLC system equipped with a Kanto Chemical Mightysil Si 60 Column. ^{1}H NMR (300 MHz) spectra and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AV-300N spectrometer with tetramethylsilane (TMS) as the internal standard. High-resolution mass spectra (HRMS) were measured on a JEOL AccTOF LC mass spectrometer. Single crystal X-ray crystallographic analysis was conducted using a Rigaku XtaLAB Synergy-S diffractometer with CuKα radiation (λ = 1.54184 Å). The crystal structures were solved by a direct method using SHELXS-97 and refined by the full-matrix least-squares method for F^2 with anisotropic displacement parameters for non-hydrogen atoms using SHELXL-2014. UV-Vis absorption spectra were recorded using a JASCO V-560 absorption spectrometer. Photoirradiation to solution was conducted using a 200 W mercury-xenon lamp (Moritex MUV-202) as the light source. Monochromatic light at 254 nm was obtained by passing the light through a bandpass filter. The solution samples were not degassed.

Theoretical calculations

DFT (Density functional theory) calculations (geometry optimizations and frequency calculations) of the open-ring isomers (Open), the closed-ring isomers (Closed), and transition states (TS) were carried out using Gaussian16 Rev.C.01 program package in a manner similar to procedures reported previously.[S1] The TS structure was optimized using Opt = TS keyword with Berny algorithm. To obey unrestricted Kohn–Sham solution, the broken-symmetry guess

was generated and followed using the keyword Guess (mix, always). The frequency calculation for the TS was carried out to confirm that there is only one imaginary frequency corresponding to the stretching vibration between the reactive carbon atoms. Then, the intrinsic reaction coordinates (IRC) calculations were performed and the geometry optimization of the endpoints in the IRC calculation was carried out to obtain the stable molecular structures of the open- and the closed-ring isomers. The frequency calculations for the obtained open- and the closed-ring isomers were performed to confirm that there are no imaginary frequencies. The M06-2X functional in combination with a 6-31G(d) basis set was used for all calculations.

Materials

1o was synthesized according to the procedures described in the previous work.[S1] **2o**–**7o** were also synthesized according to a similar procedure. The detailed procedures are described in the synthesis section below. All compounds were fully characterized by ^{1}H NMR, ^{13}C NMR, high-resolution mass spectrometry, and X-ray crystallographic analysis.

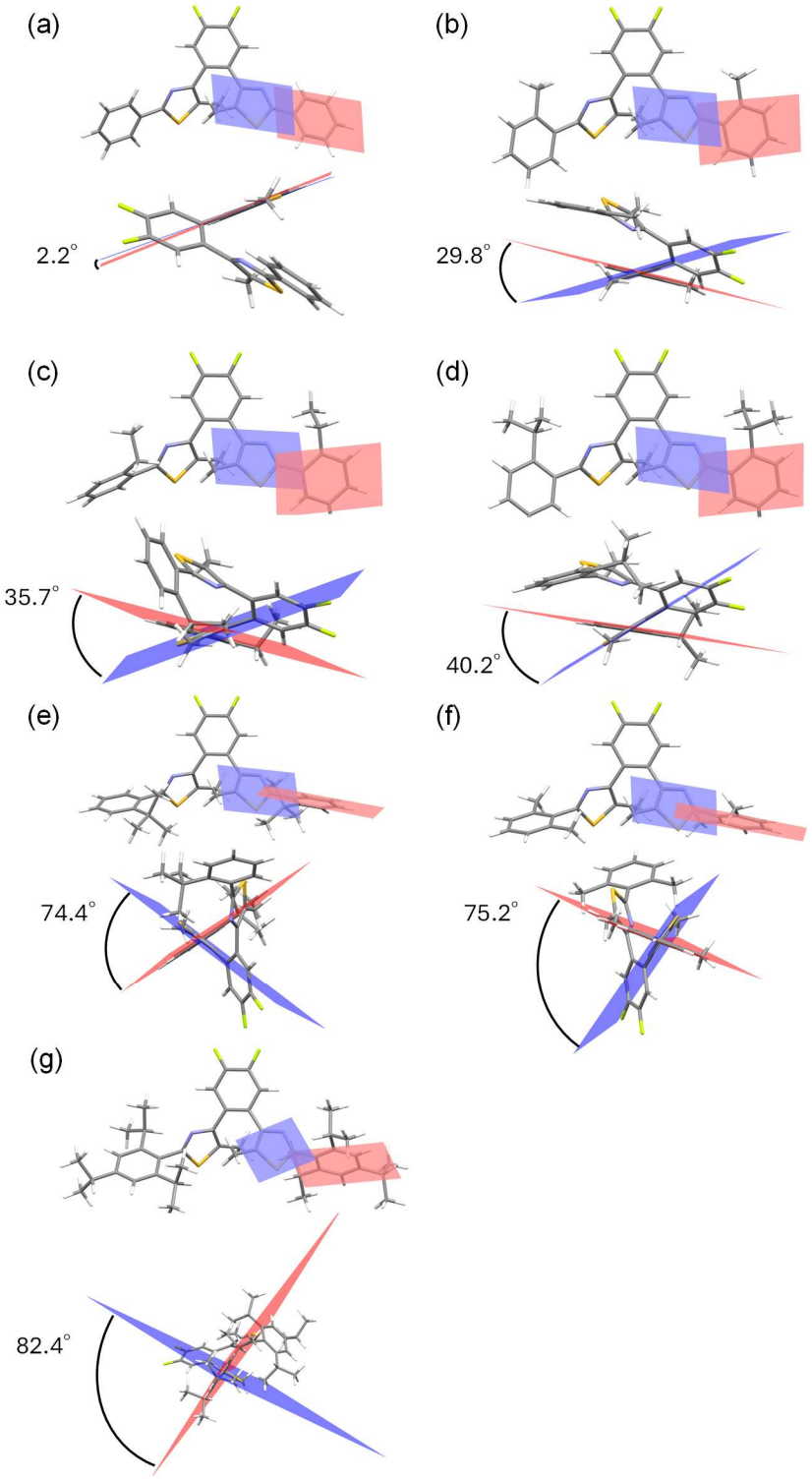


Fig. S1 Optimized structures of (a) **1o**, (b) **2o**, (c) **3o**, (d) **4o**, (e) **5o**, (f) **6o**, and (g) **7o** in the ground state using DFT calculations.

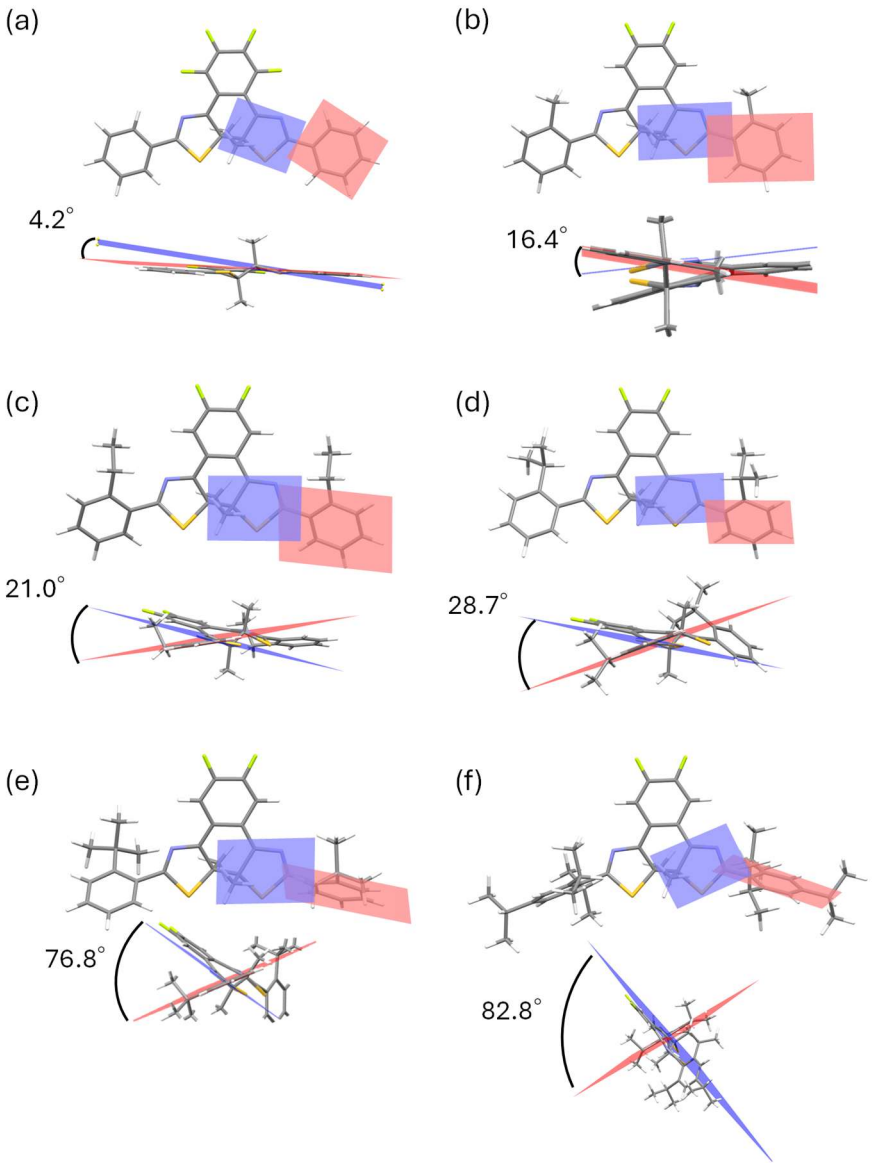


Fig. S2 Optimized structures of (a) **1c**, (b) **2c**, (c) **3c**, (d) **4c**, (e) **5c**, and (f) **7c** in the ground state using DFT calculations.

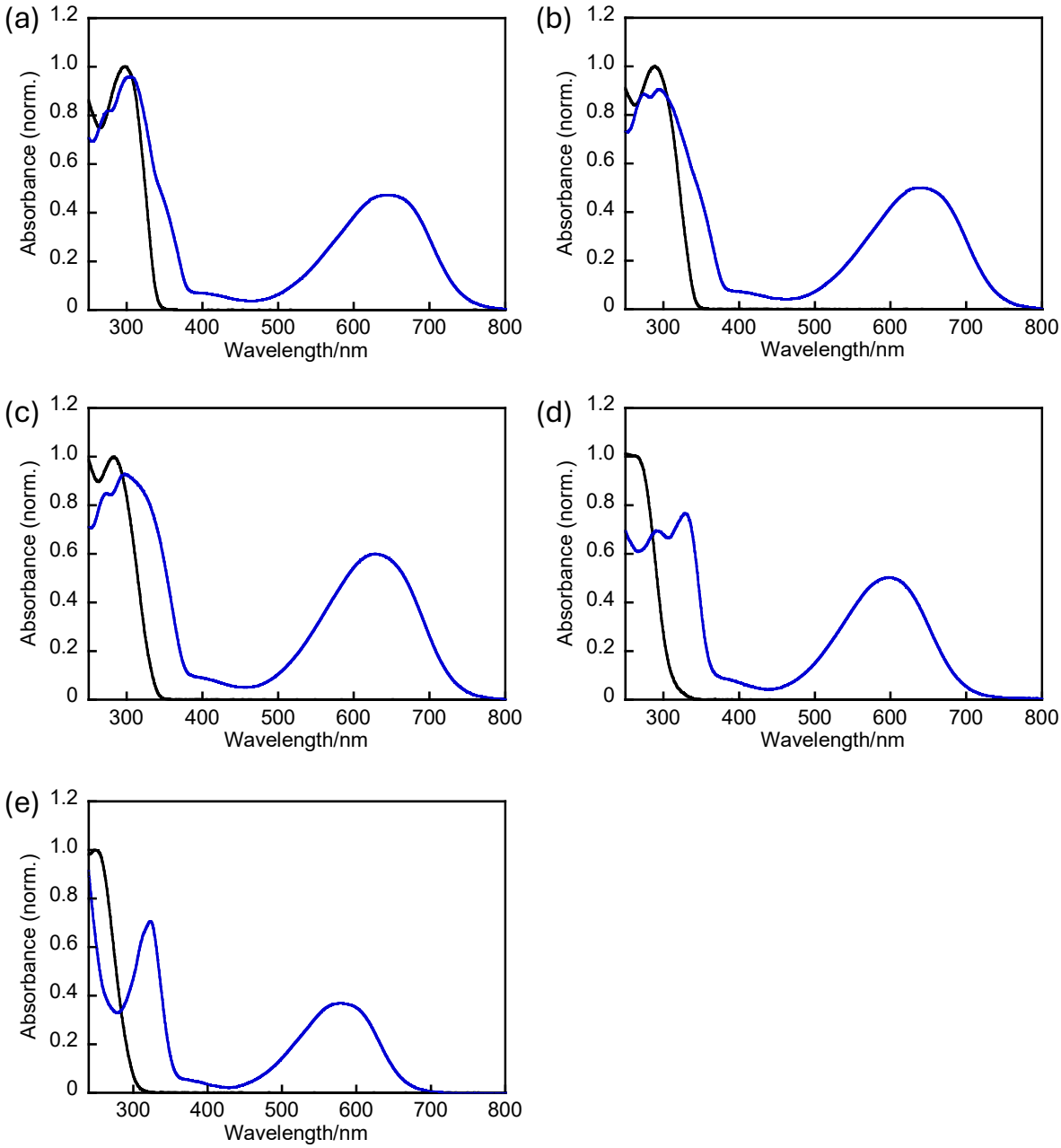


Fig. S3 Absorption spectral changes of (a) **2**, (b) **3**, (c) **4**, (d) **5**, and (e) **7** at 298 K in *n*-hexane: the open-ring isomer (black line) and the photostationary state upon irradiation with 254 nm light (blue line).

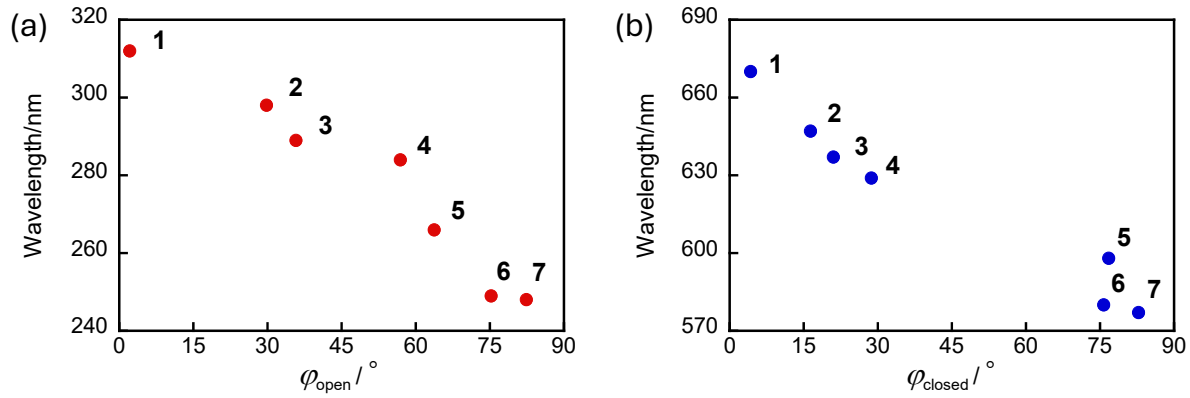


Fig. S4 Relationship between the absorption maximum and the dihedral angles in the aryl groups: (a) the open-ring isomers and (b) the closed-ring isomers.

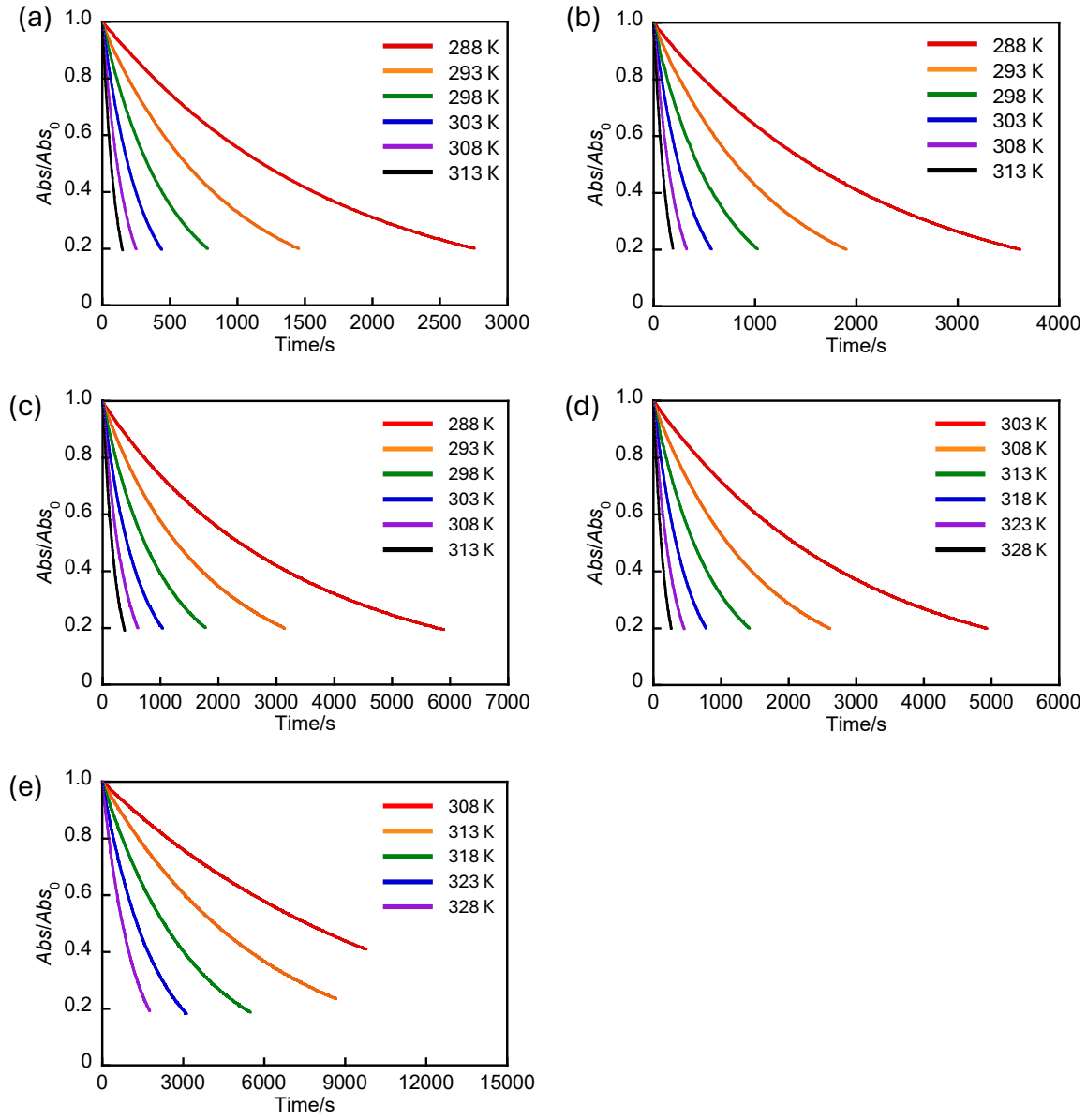


Fig. S5 Absorption decay curves at λ_{max} in *n*-hexane at various temperatures for (a) **2c**, (b) **3c**, (c) **4c**, (d) **5c**, and (e) **7c**.

Kinetic analysis of thermal back reaction

The reaction kinetics of the thermal back reaction was analyzed as follows: If the thermal back reaction from the closed-ring isomer to the open-ring isomer obeys a first-order kinetics, the kinetic equation is expressed as following equation by using Lambert-Beer law.

$$\ln\frac{A_t}{A_0} = -kt$$

where k is reaction rate constant, t is reaction time, and A_0 and A_t are absorbance of the closed-ring isomer at initial state (t = 0 s) and at arbitrary reaction time t, respectively. The k value can be calculated from the slope of the linear plot. The calculated k values are summarized in Tables S1–S6.

Eyring equation can be described as follows.

$$\ln(\frac{k}{T}) = -\frac{\Delta H^{\ddagger}}{R}\frac{1}{T} + \ln(\frac{k_B}{h}) + \frac{\Delta S^{\ddagger}}{R}$$

where R is gas constant, and T is absolute temperature, $\Delta H^{\ddagger}$ is enthalpy of activation, $\Delta S^{\ddagger}$ is entropy of activation, h is Planck constant, and k_B is Boltzmann constant. The linear relationship can be obtained by plotting $\ln(k/T)$ relative to $1/T$ as shown in Figs. 1d and S7. The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values can be determined from the slope and intercept of the linear plot. The Gibbs energy of activation ($\Delta G^{\ddagger}$) was also determined using the relationship of $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$. The results are summarized in Table 1.

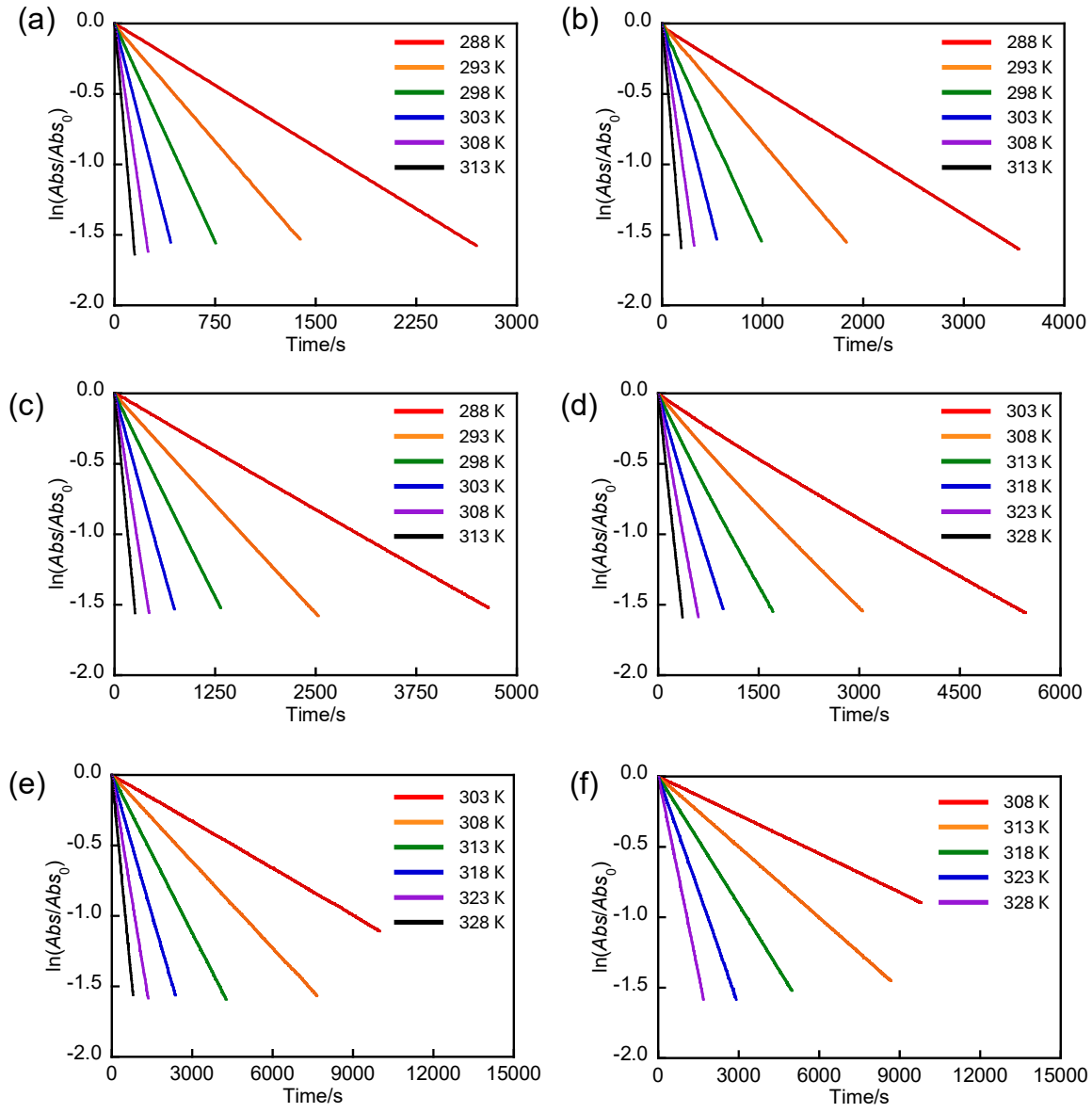


Fig. S6 First-order kinetics profiles of (a) **2c**, (b) **3c**, (c) **4c**, (d) **5c**, (e) **6c**, and (f) **7c** in *n*-hexane at various temperatures.

Table S1. First-order rate constants for the thermal back reaction of **2c**.

T/K	k/s^{-1}
288	0.000574
293	0.001092
298	0.002064
303	0.003637
308	0.006514

Table S2. First-order rate constants for the thermal back reaction of **3c**.

T/K	k/s^{-1}
288	0.000444
293	0.000817
298	0.001578
303	0.002788
308	0.004968

Table S3. First-order rate constants for the thermal back reaction of **4c**.

T/K	k/s^{-1}
288	0.000327
293	0.000618
298	0.001139
303	0.002059
308	0.003607

Table S4. First-order rate constants for the thermal back reaction of **5c**.

T/K	k/s^{-1}
303	0.000278
308	0.000498
313	0.000885
318	0.001563
323	0.002644

Table S5. First-order rate constants for the thermal back reaction of **6c**.

T/K	k/s^{-1}
303	0.000110
308	0.000204
313	0.000373
318	0.000651
323	0.001146

Table S6. First-order rate constants for the thermal back reaction of **7c**.

T/K	k/s^{-1}
308	0.000091
313	0.000167
318	0.000306
323	0.000544
328	0.000937

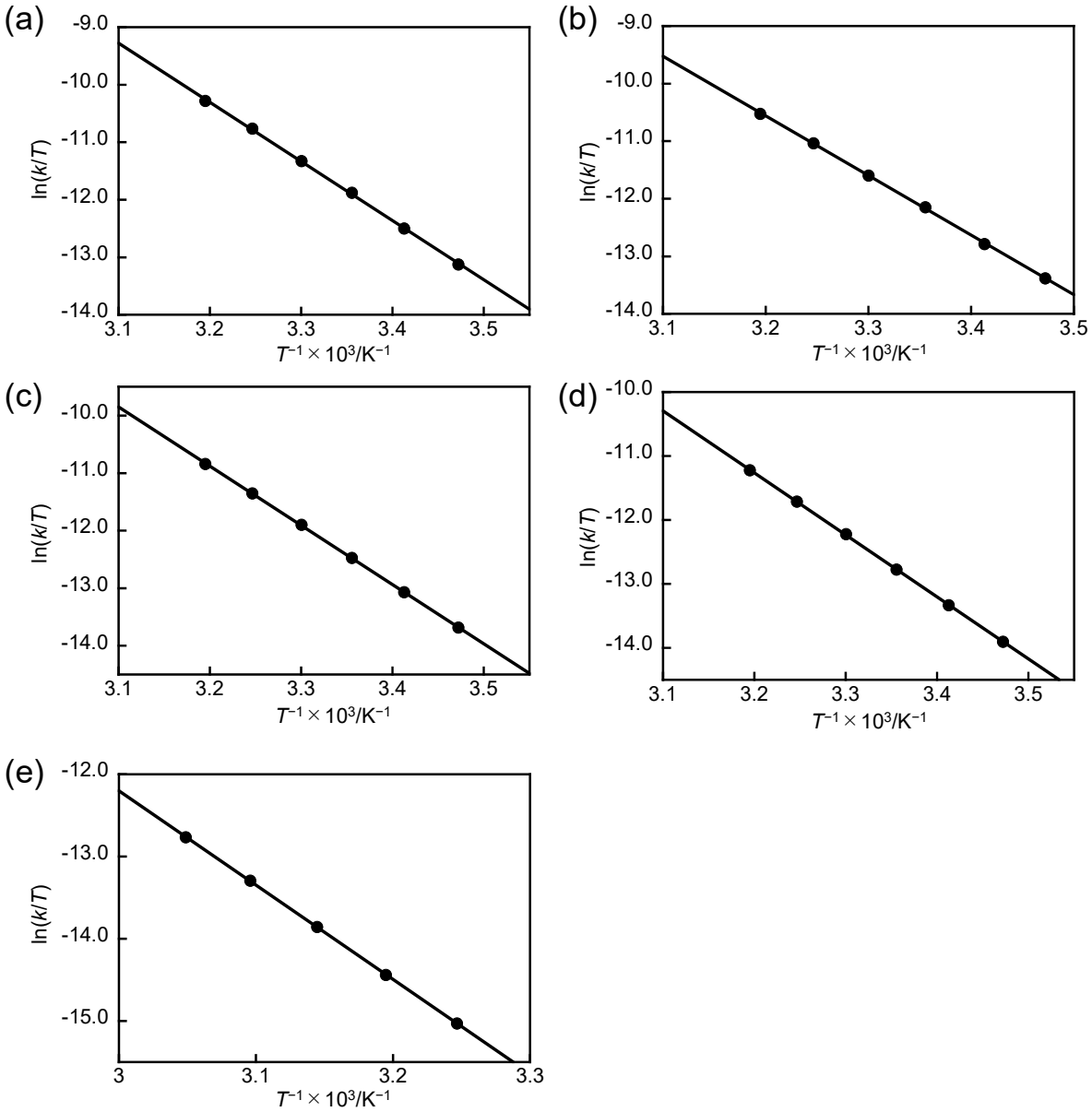


Fig. S7 Eyring plots for the thermal back reaction of (a) **2c**, (b) **3c**, (c) **4c**, (d) **5c**, and (e) **7c**.

Table S7. The results of DFT calculations for **1**–**7** at the M06-2X/6-31G(d) level.

	Open /Hartree	Closed /Hartree	TS /Hartree	$\Delta G_{(calc)}$ /kJ mol^{-1}	$\Delta G^{‡}_{(calc)}$ /kJ mol^{-1}
1	−2106.284969	−2106.243631	−2106.209818	108.5	88.8
2	−2184.820220	−2184.778731	−2184.745130	108.9	88.2
3	−2263.351609	−2263.309338	−2263.275950	110.0	87.7
4	−2341.882819	−2341.840490	−2341.806140	111.1	90.2
5	−2420.395603	−2420.352038	−2420.316793	114.4	92.5
6	−2263.357477	−2263.316277	−2263.277018	108.2	103.1
7	−2813.092188	−2813.051056	−2813.012155	108.0	102.1

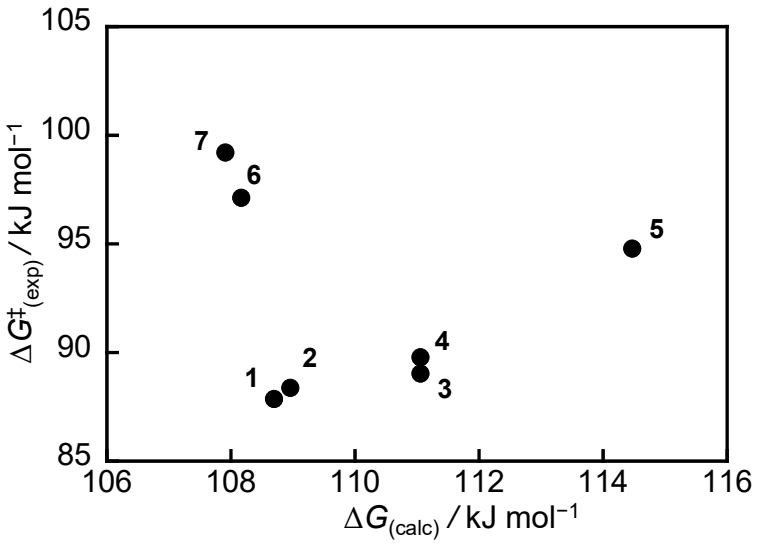


Fig. S8 Relationship between $\Delta G_{(calc)}$ and $\Delta G^{‡}_{(exp)}$.

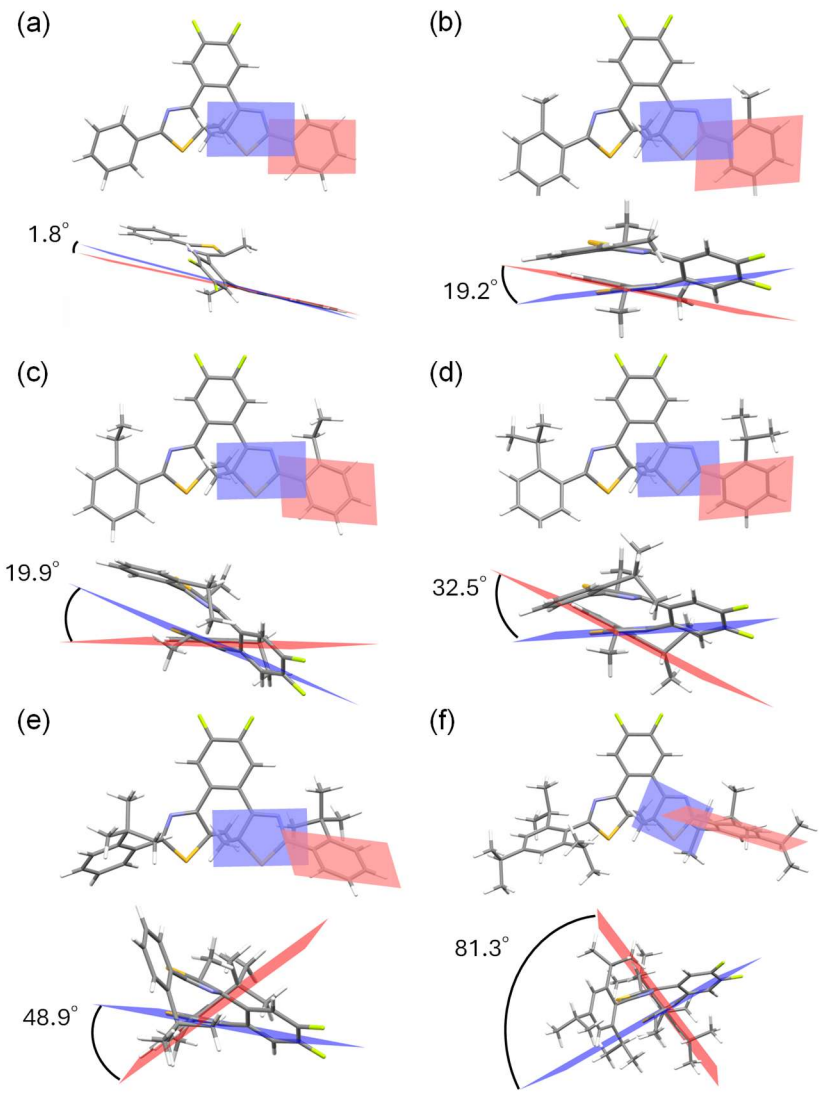


Fig. S9 Optimized structures of (a) **1**, (b) **2**, (c) **3**, (d) **4**, (e) **5**, and (f) **7** in the transition state using DFT calculations.

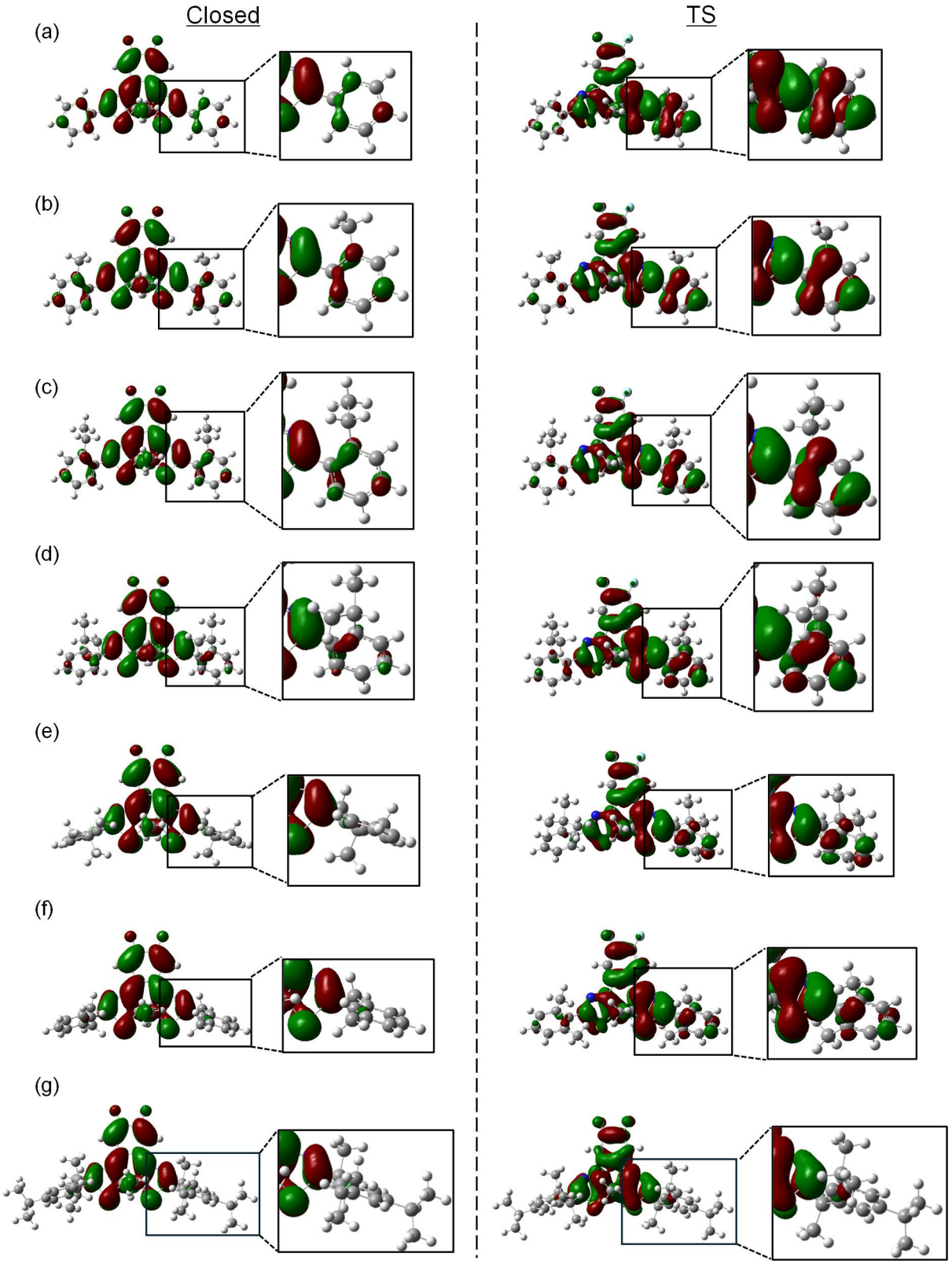
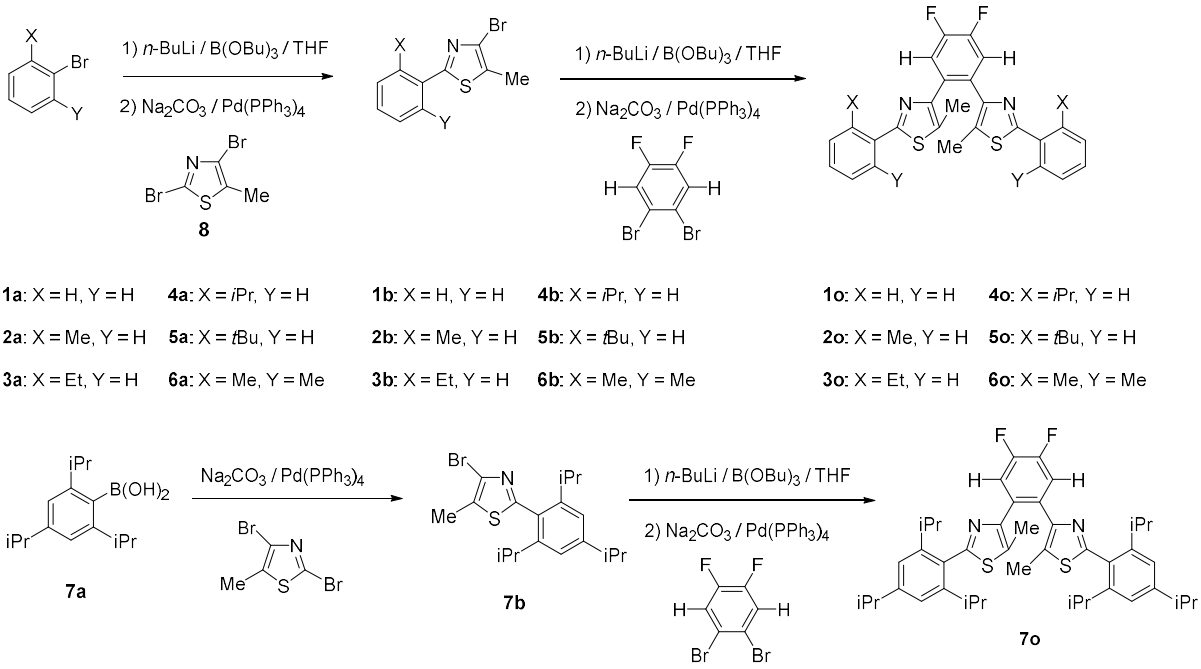


Fig. S10 Molecular orbital distribution of the closed-ring isomer and the transition state for (a) **1**, (b) **2**, (c) **3**, (d) **4**, (e) **5**, (f) **6**, and (g) **7** at the HOMO using DFT calculations.

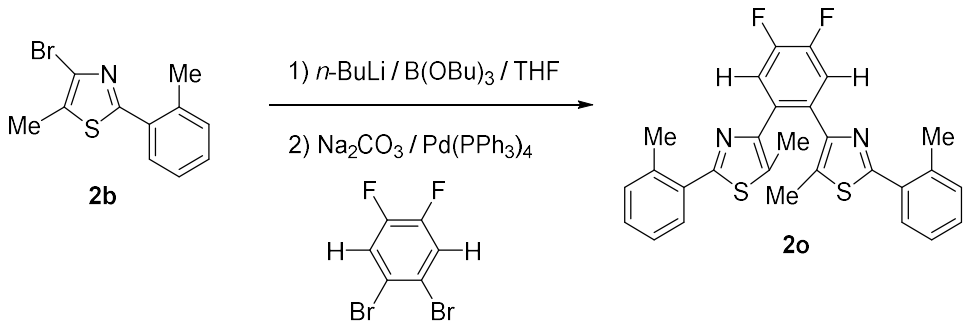
Synthesis

1o–**7o** were synthesized according to Scheme S1.



Scheme S1 Synthetic route of **1o**–**7o**.

1,2-Bis(2-(2-methylphenyl)-5-methyl-4-thiazolyl)-4,5-difluorobenzene (2o).



4-Bromo-5-methyl-2-(2-methylphenyl)thiazole (1.0 g, 3.7 mmol) was dissolved in anhydrous THF (15 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (2.8 mL, 4.5 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (1.2 mL, 4.5 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (480 mg, 4.5 mmol), tetrakis(triphenylphosphine)palladium (100 mg, 0.087 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 165 mg in 19% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 2.11 (s, 6H, C$H_{3(phenyl)}$), 2.48 (s, 6H, C$H_{3(thiazole)}$), 7.20–7.32 (m, 6H, Aromatic *H*), 7.45 (t, J_{HF} = 9.6 Hz, 2H, Aromatic *H*), 7.61 (d, *J* = 7.6 Hz, 2H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 11.9 (*C*$H_{3(thiazole)}$), 21.6 (*C*$H_{3(phenyl)}$), 119.9 (dd, $^2J_{CF}$ = 11.4 Hz, $^3J_{CF}$ = 7.3 Hz), 126.2, 129.3, 129.8, 130.8, 131.6, 131.8 (dd, $^3J_{CF}$ = 5.2 Hz, $^4J_{CF}$ = 5.2 Hz), 133.0, 136.5, 149.6 (dd, $^1J_{CF}$ = 252.0 Hz, $^2J_{CF}$ = 14.6 Hz), 149.8, 164.2. HRMS (DART+) *m/z* = 489.1280 (MH^+). Calc. for $C_{28}H_{23}F_2N_2S_2^+$ = 489.1271. Melting point: 77.1–78.1 °C.

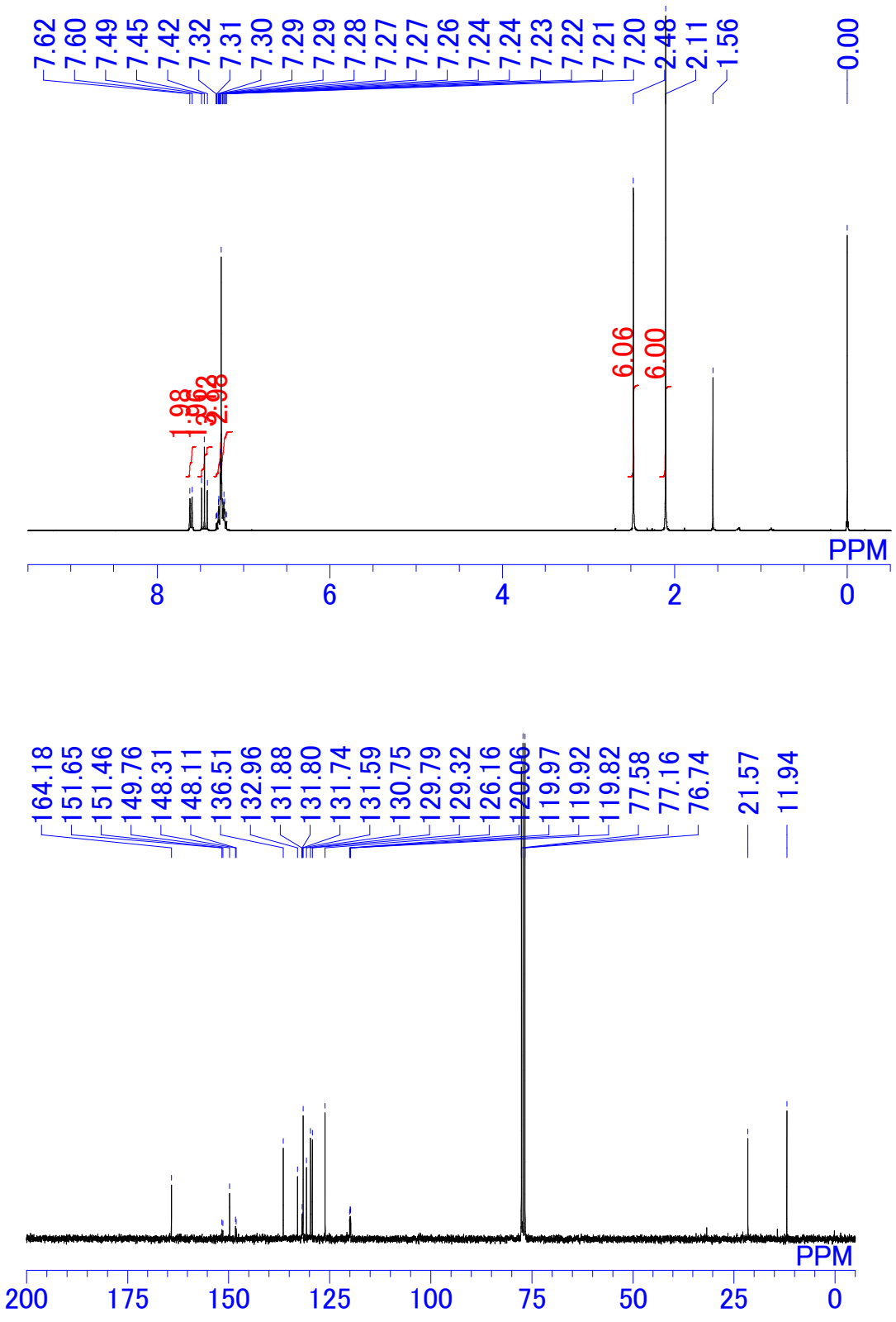
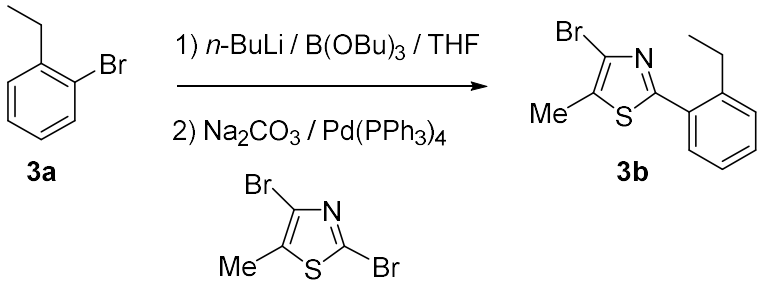


Fig. S11 ^{1}H NMR and ^{13}C NMR spectra of **2o** in $CDCl_3$.

4-Bromo-2-(2-ethylphenyl)-5-methylthiazole (3b).



1-Bromo-2-ethylbenzene (6.0 g, 33 mmol) was dissolved in anhydrous THF (60 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (22 mL, 35 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (9.3 mL, 35 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 2,4-Dibromo-5-methylthiazole[S2] (7.0 g, 27 mmol), tetrakis(triphenylphosphine)palladium (300 mg, 0.26 mmol), and 20wt% Na_2CO_3 aqueous solution (30 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 6.2 g in 79% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 1.20 (t, *J* = 7.5 Hz, 3H, C$H_{3(thiazole)}$), 2.45 (s, 3H, C$H_{3(phenyl)}$), 2.96 (q, *J* = 7.5 Hz, 2H, CH_2), 7.24 (t, *J* = 7.2 Hz, 1H, Aromatic *H*), 7.31 (d, *J* = 7.5 Hz, 1H, Aromatic *H*), 7.37 (t, *J* = 7.0 Hz, 1H, Aromatic *H*), 7.54 (d, *J* = 7.6 Hz, 1H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.0 (*C*$H_{3(thiazole)}$), 15.6 (*C*$H_{3(phenyl)}$), 26.8 (*C*H_2), 124.6, 126.1, 129.6, 129.8, 130.0, 130.1, 132.0, 142.9, 165.2. HRMS (DART+) *m/z* = 281.9960 (MH^+). Calc. for $C_{12}H_{13}BrNS^+$ = 281.9952.

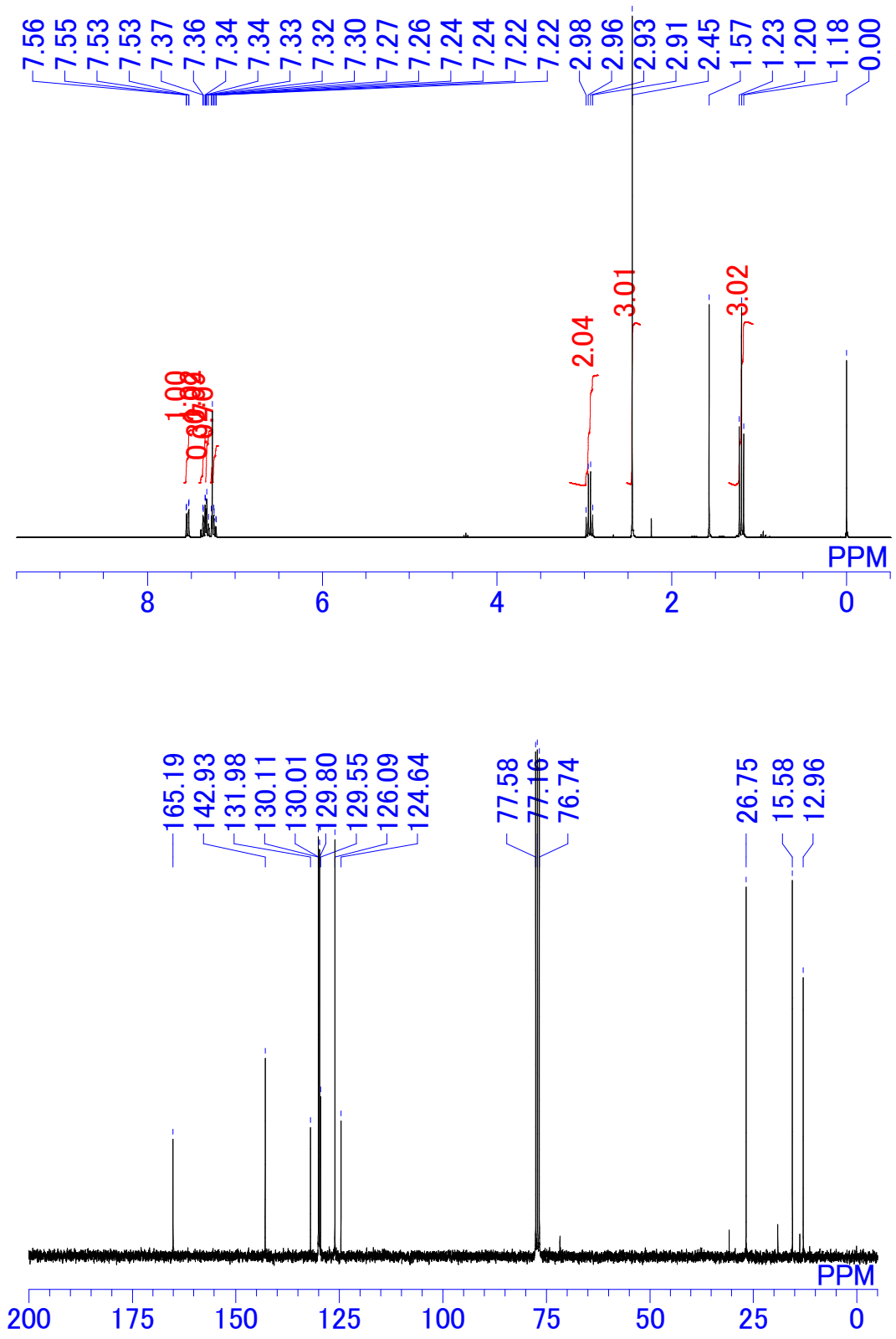
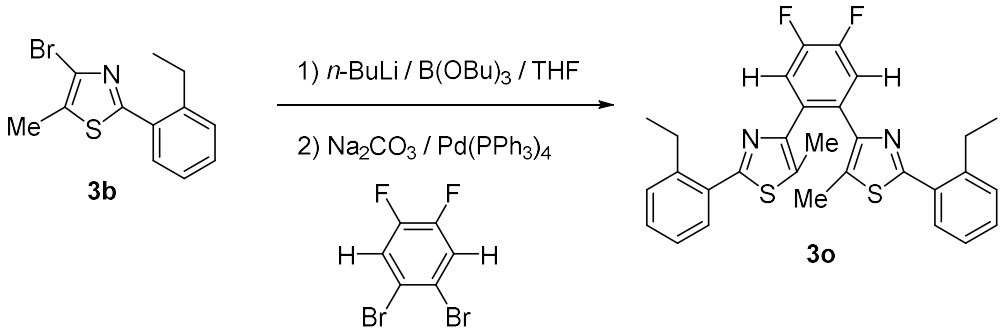


Fig. S12 ^{1}H NMR and ^{13}C NMR spectra of **3b** in $CDCl_3$.

1,2-Bis(2-(2-ethylphenyl)-5-methyl-4-thiazolyl)-4,5-difluorobenzene (3o).



4-Bromo-2-(2-ethylphenyl)-5-methylthiazole (1.4 g, 5.0 mmol) was dissolved in anhydrous THF (20 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (3.7 mL, 5.9 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (1.6 mL, 6.0 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (640 mg, 2.4 mmol), tetrakis(triphenylphosphine)palladium (100 mg, 0.087 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (95:5) as the eluent to give 120 mg in 9.9% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 1.18 (t, J = 7.5 Hz, 6H, C$H_{3(thiazole)}$), 2.06 (s, 6H, C$H_{3(phenyl)}$), 2.91 (q, J = 7.5 Hz, 4H, C$H_{2(phenyl)}$), 7.23–7.25 (m, 2H, Aromatic *H*), 7.29–7.35 (m, 4H, Aromatic *H*), 7.46 (t, J_{HF} = 9.5 Hz, 2H, Aromatic *H*), 7.53 (d, J = 7.6 Hz, 2H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 11.9 (*C*$H_{3(thiazole)}$), 15.8 (*C*$H_{3(phenyl)}$), 26.9 (*C*H_2), 119.9 (dd, $^2J_{CF}$ = 11.3 Hz, $^3J_{CF}$ = 7.4 Hz), 126.1, 129.6, 129.8, 130.3, 130.9, 131.6 (dd, $^3J_{CF}$ = 4.7 Hz, $^4J_{CF}$ = 4.7 Hz), 132.5, 142.9, 149.7, 149.9 (dd, $^1J_{CF}$ = 252.4 Hz, $^2J_{CF}$ = 15.1 Hz), 164.2. HRMS (DART+) *m/z* = 517.1594 (MH^+). Calc. for $C_{30}H_{27}F_2N_2S_2^+$ = 517.1583. Melting point: 101.7–102.7 °C.

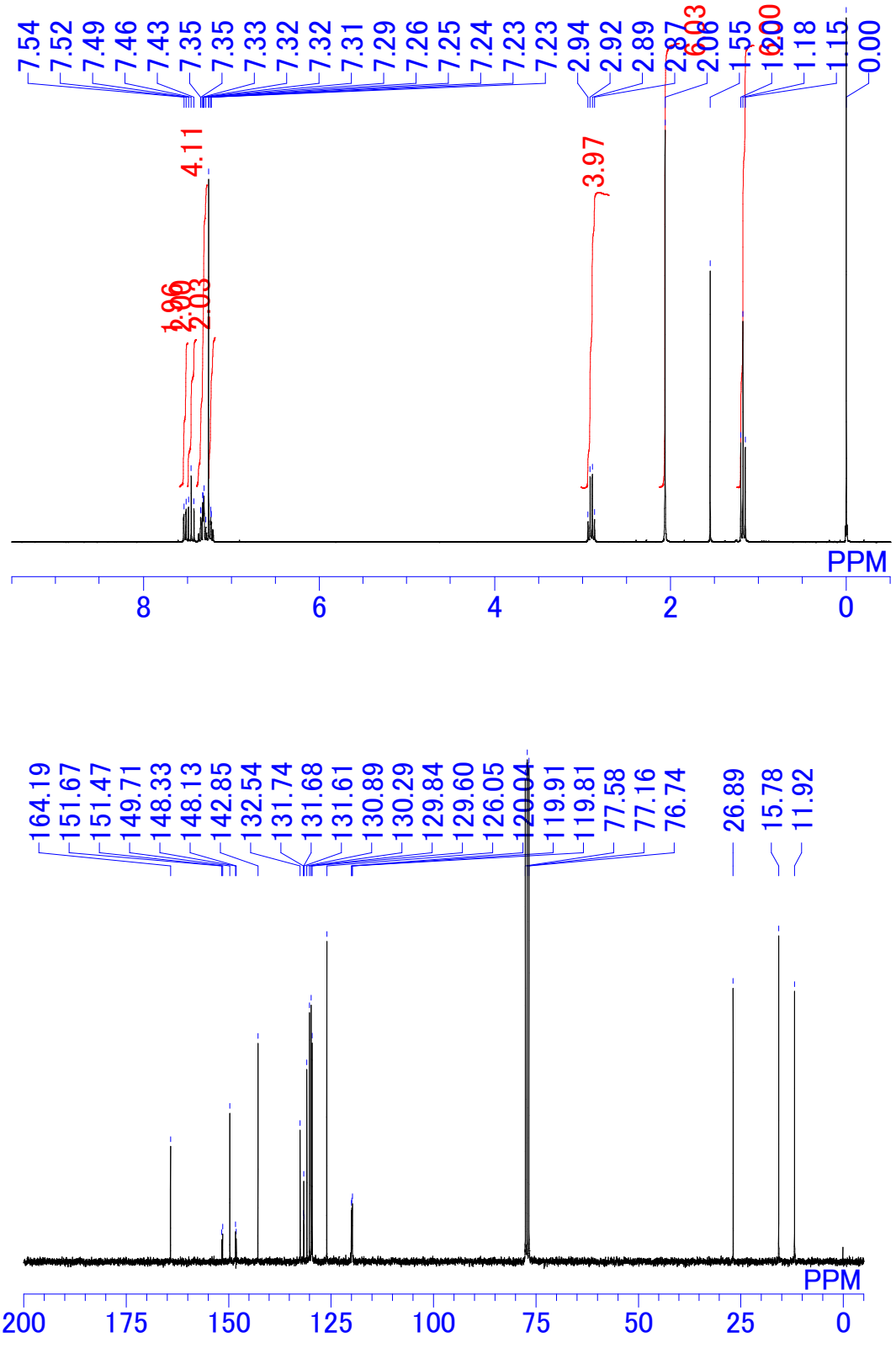
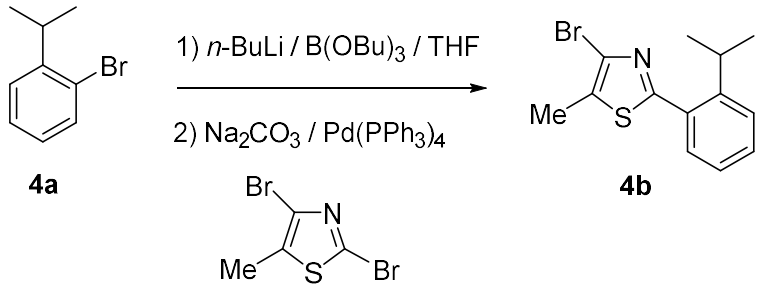


Fig. S13 ^{1}H NMR and ^{13}C NMR spectra of **3o** in $CDCl_3$.

4-Bromo-2-(2-isopropylphenyl)-5-methylthiazole (4b).



1-Bromo-2-isopropylbenzene (3.5 g, 18 mmol) was dissolved in anhydrous THF (40 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (13 mL, 21 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (5.4 mL, 20 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 2,4-Dibromo-5-methylthiazole[S2] (4.5 g, 18 mmol), tetrakis(triphenylphosphine)palladium (200 mg, 0.17 mmol), and 20wt% Na_2CO_3 aqueous solution (30 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (95:5) as the eluent to give 2.7 g in 51% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ =1.23 (d, *J* = 6.8 Hz, 6H, C$H_{3(phenyl)}$), 2.46 (s, 3H, C$H_{3(thiazole)}$), 3.56 (sep, *J* = 6.8 Hz, 1H, C*H*), 7.20–7.26 (m, 1H, Aromatic *H*), 7.41–7.45 (m, 3H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.0 (*C*$H_{3(thiazole)}$), 24.1 (*C*$H_{3(phenyl)}$), 29.3 (*C*H), 124.5, 125.8, 126.3, 129.9, 130.2, 130.4, 131.8, 147.7, 165.4. HRMS (DART+) *m/z* = 296.0099 (MH^+). Calc. for $C_{13}H_{15}BrNS^+$ = 296.0109.

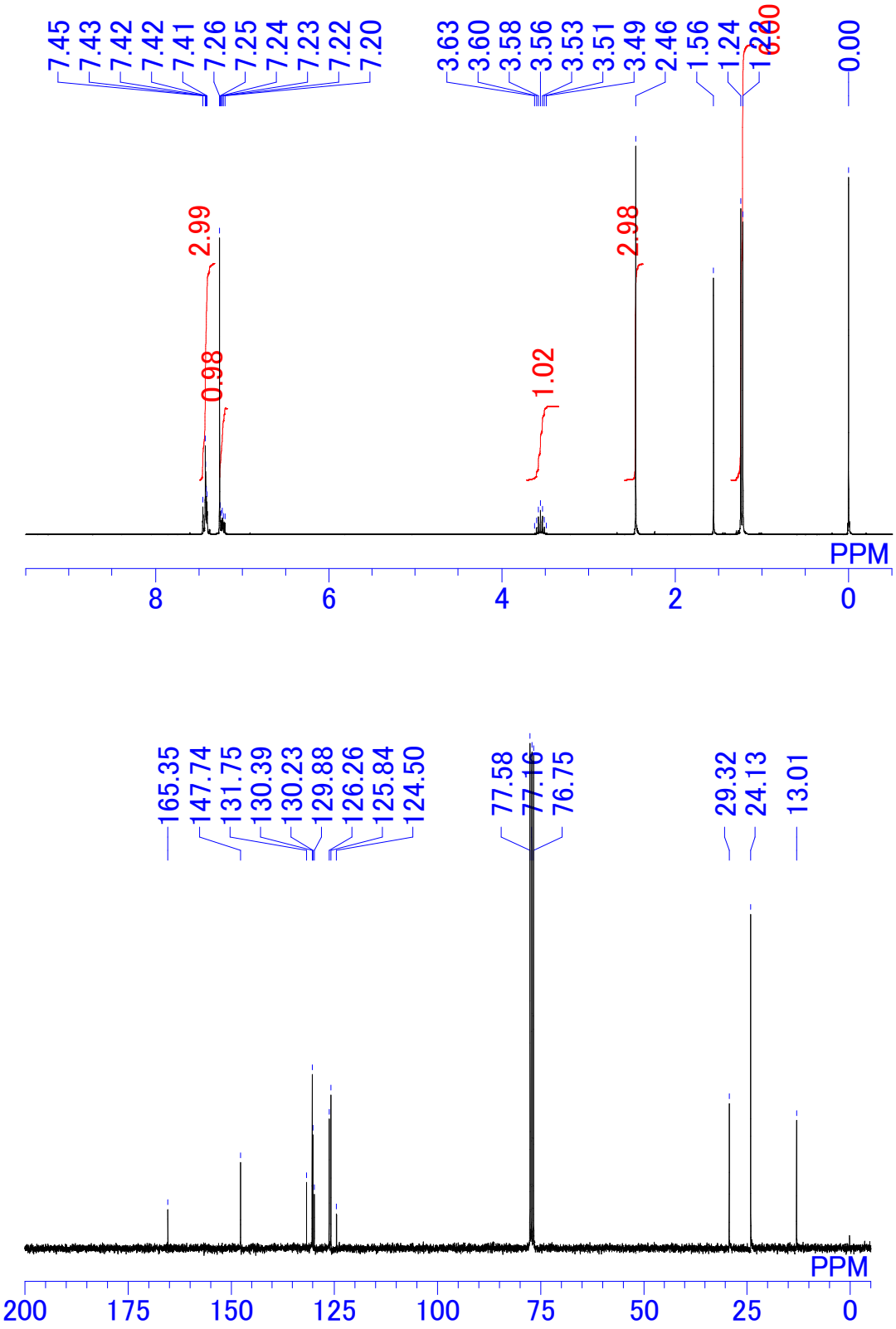
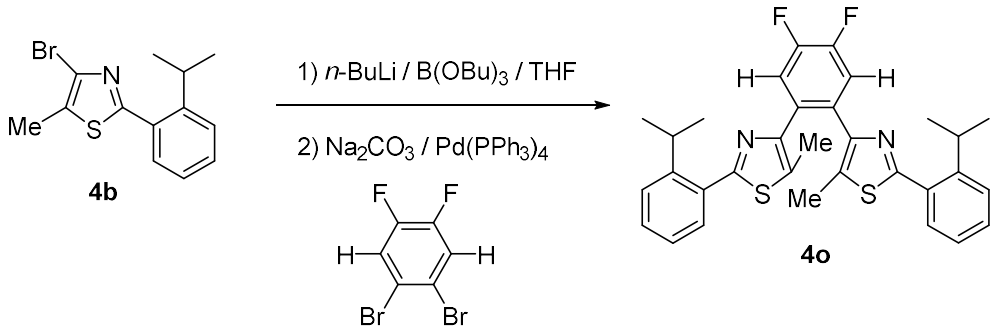


Fig. S14 ^{1}H NMR and ^{13}C NMR spectra of **4b** in $CDCl_3$.

1,2-Bis(2-(2-isopropylphenyl)-5-methyl-4-thiazolyl)-4,5-difluorobenzene (4o).



4-Bromo-2-(2-isopropylphenyl)-5-methylthiazole (2.4 g, 8.1 mmol) was dissolved in anhydrous THF (20 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (6.3 mL, 10 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (2.5 mL, 9.3 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (1.0 g, 3.7 mmol), tetrakis(triphenylphosphine)palladium (200 mg, 0.17 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (95:5) as the eluent to give 400 mg in 22% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 1.21 (d, J = 6.8 Hz, 12H, C$H_{3(phenyl)}$), 2.08 (s, 6H, C$H_{3(thiazole)}$), 3.54 (sep, J = 6.8 Hz 2H, C*H*), 7.21–7.26 (m, 2H, Aromatic *H*), 7.39–7.48 (m, 8H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 11.9 (C$H_{3(thiazole)}$), 24.2 (C$H_{3(phenyl)}$), 29.4 (*C*H), 119.9 (dd, $^2J_{CF}$ = 11.3 Hz, $^3J_{CF}$ =7.4 Hz), 125.8, 126.2, 129.8, 130.5, 131.2, 131.7 (dd, $^3J_{CF}$ = 5.2 Hz, $^4J_{CF}$ = 5.2 Hz,), 132.3, 147.6, 149.6, 149.9 (dd, $^2J_{CF}$ = 252.0 Hz, $^3J_{CF}$ =14.6 Hz), 164.3. HRMS (DART+) *m/z* = 545.1881 (MH^+). Calc. for $C_{30}H_{27}F_2N_2S_2^+$ = 545.1900. Melting point: 180.0–181.0 °C.

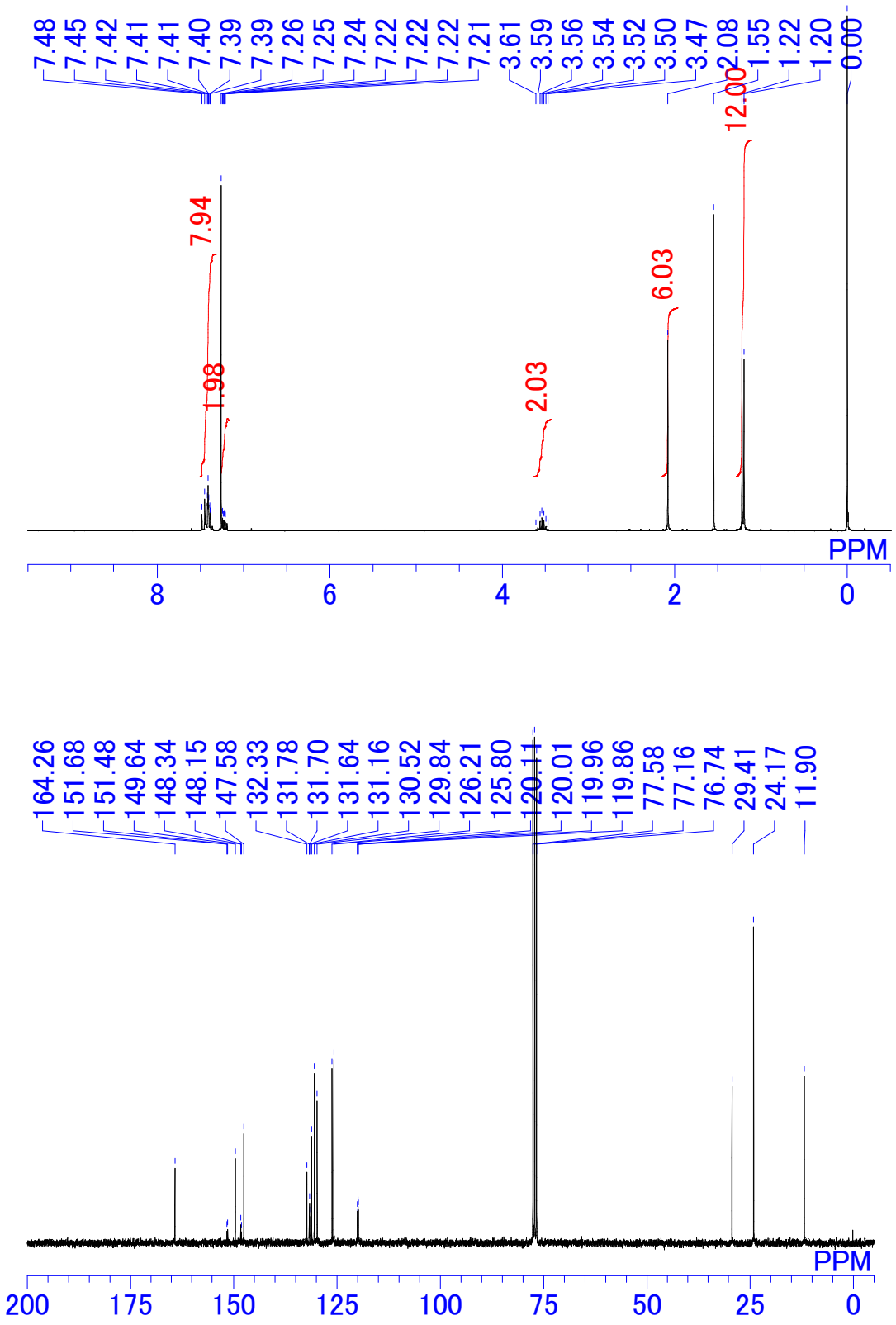
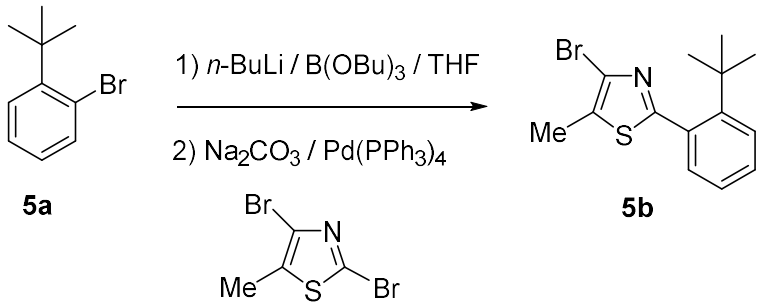


Fig. S15 ^{1}H NMR and ^{13}C NMR spectra of **4o** in $CDCl_3$.

4-Bromo-2-(2-(*tert*-butyl)phenyl)-5-methylthiazole (5b).



1-Bromo-2-(2-(*tert*-butyl))benzene (3.7 g, 18 mmol) was dissolved in anhydrous THF (60 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (13 mL, 21 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (5.4 mL, 20 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 2,4-Dibromo-5-methylthiazole[S2] (4.5 g, 18 mmol), tetrakis(triphenylphosphine)palladium (200 mg, 0.17 mmol), and 20wt% Na_2CO_3 aqueous solution (30 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 4.5 g in 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ =1.30 (s, 9H, C$H_{3(phenyl)}$), 2.46 (s, 3H, C$H_{3(thiazole)}$), 7.22–7.26 (m, 2H, Aromatic *H*), 7.36–7.41 (m, 1H, Aromatic *H*), 7.55 (d, *J* = 8.1 Hz, 1H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.0 (*C*$H_{3(thiazole)}$), 32.2 (*C*$H_{3(phenyl)}$), 36.7, 123.2, 125.3, 127.3, 129.9, 130.2, 132.5, 132.9, 149.9, 168.2. HRMS (DART+) *m/z* = 310.0262 (MH^+). Calc. for $C_{13}H_{15}BrNS^+$ = 310.0265.

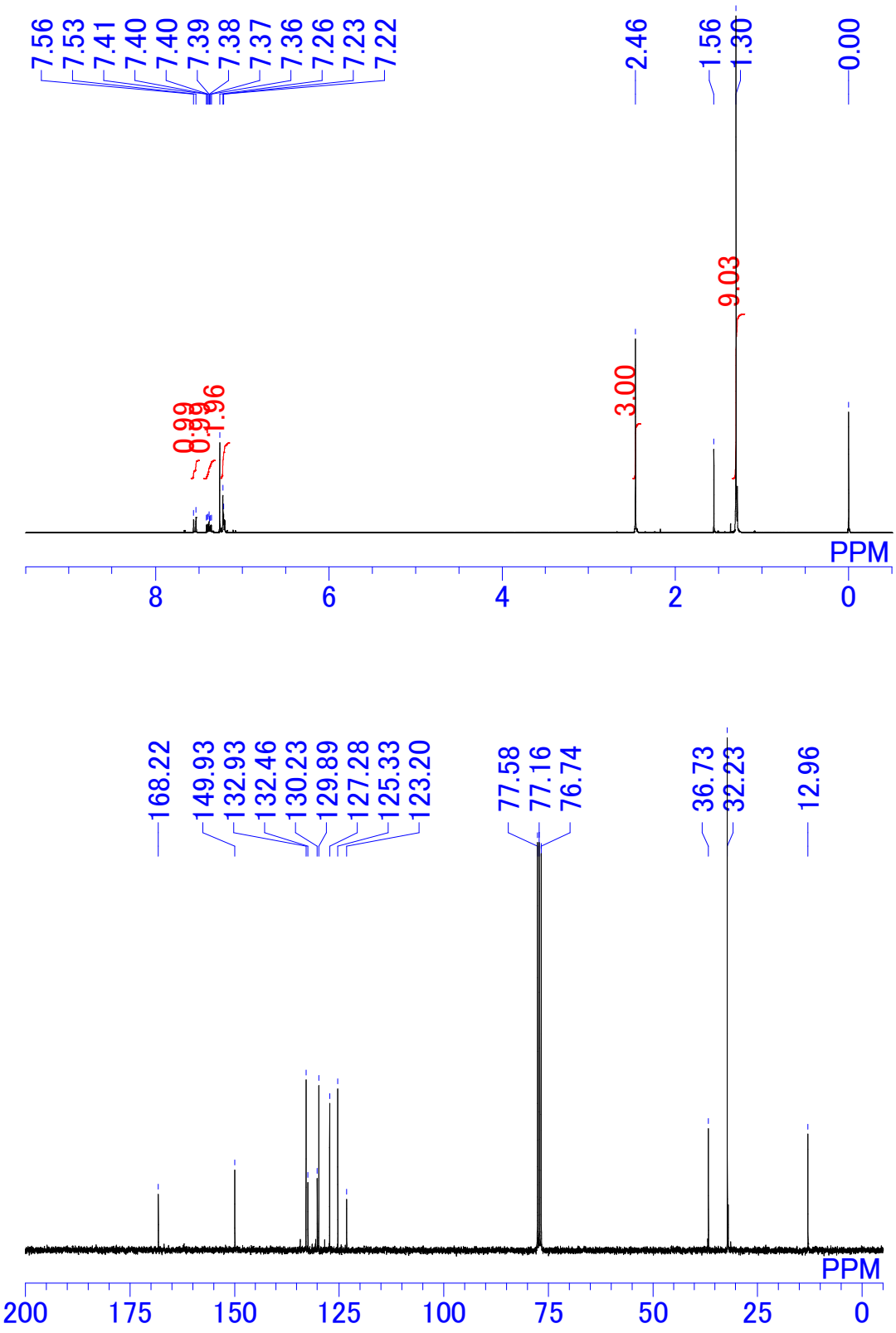
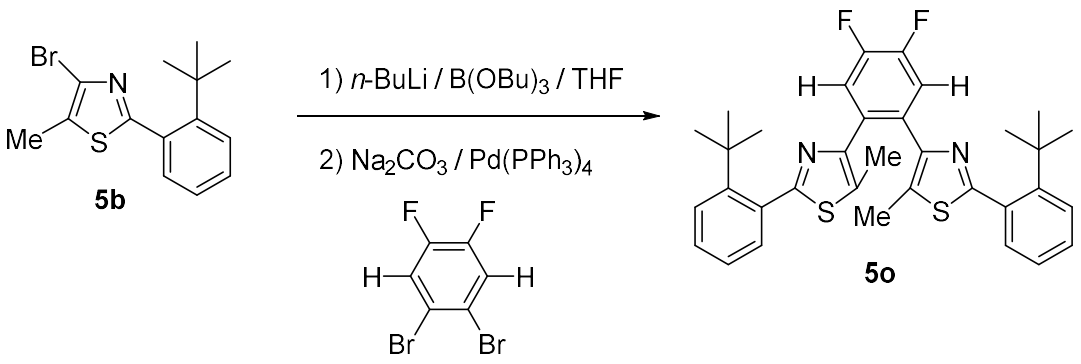


Fig. S16 ^{1}H NMR and ^{13}C NMR spectra of **5b** in $CDCl_3$.

1,2-Bis(2-(2-(*tert*-butyl)phenyl)-5-methyl-4-thiazolyl)-4,5-difluorobenzene (5o).



4-Bromo-2-(2-(*tert*-butyl)phenyl)-5-methylthiazole (1.1 g, 3.6 mmol) was dissolved in anhydrous THF (20 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (2.5 mL, 4.0 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (1.1 mL, 4.1 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (0.46 g, 1.7 mmol), tetrakis(triphenylphosphine)palladium (200 mg, 0.17 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (95:5) as the eluent to give 150 mg in 15% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 1.35 (s, 18H, C$H_{3(phenyl)}$), 2.02 (s, 6H, C$H_{3(thiazole)}$), 7.20–7.26 (m, 4H, Aromatic *H*), 7.39–7.46 (m, 4H, Aromatic *H*), 7.56 (d, *J* = 8.1 Hz, 2H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 12.1 (*C*$H_{3(thiazole)}$), 32.3 (*C*$H_{3(phenyl)}$), 36.8, 120.0 (dd, $^2J_{CF}$ = 11.1 Hz, $^3J_{CF}$ = 7.6 Hz), 125.3, 127.3, 129.6, 131.5 (dd, $^3J_{CF}$ = 5.2 Hz, $^4J_{CF}$ = 5.2 Hz), 131.6, 133.0, 133.1, 148.4, 149.6 (dd, $^2J_{CF}$ = 252.0 Hz, $^3J_{CF}$ = 14.6 Hz), 150.0, 167.3. HRMS (DART+) *m/z* = 573.2229 (MH^+). Calc. for $C_{30}H_{27}F_2N_2S_2^+$ = 573.2210. Melting point: 160.0–161.0 °C.

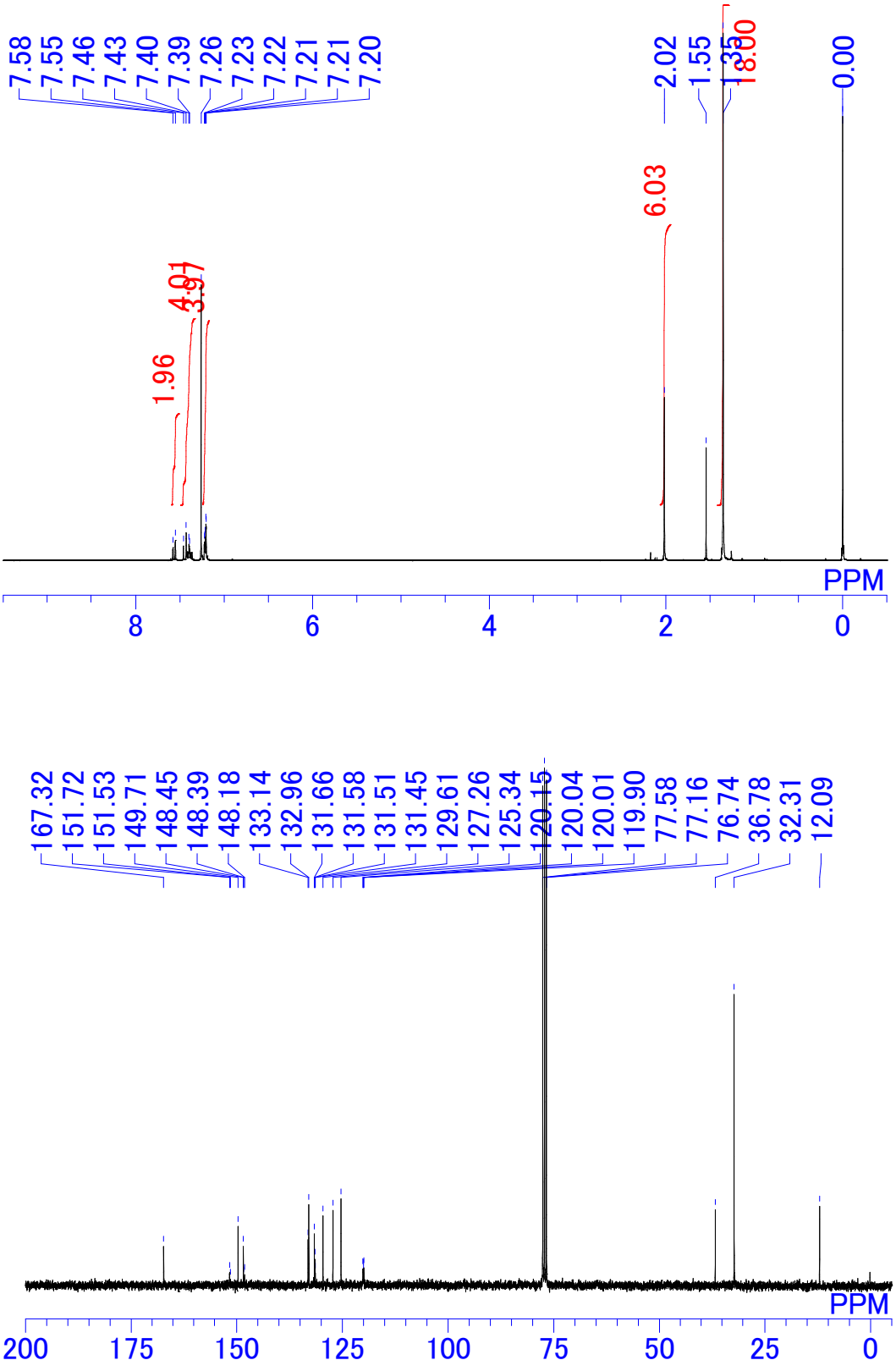
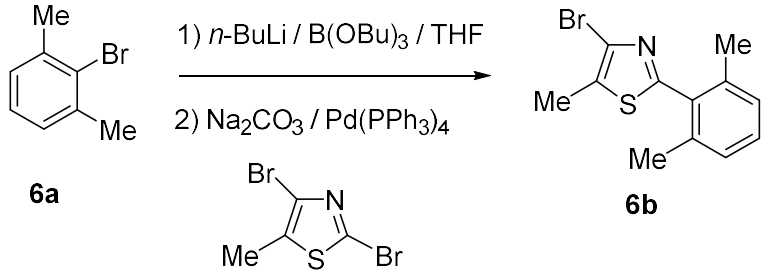


Fig. S17 ^{1}H NMR and ^{13}C NMR spectra of **5o** in $CDCl_3$.

4-Bromo-2-(2,6-dimethylphenyl)-5-methylthiazole (6b).



1-Bromo-2,5-dimethylbenzene (1.5 g, 8.2 mmol) was dissolved in anhydrous THF (50 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (5.3 mL, 8.5 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (2.3 mL, 8.6 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 2,4-Dibromo-5-methylthiazole[S2] (1.9 g, 7.5 mmol), tetrakis(triphenylphosphine)palladium (150 mg, 0.13 mmol), and 20wt% Na_2CO_3 aqueous solution (15 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 380 mg in 18% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 2.18 (s, 6H, C$H_{3(phenyl)}$), 2.47 (s, 3H, C$H_{3(thiazole)}$), 7.09 (d, *J* = 7.6 Hz, 2H, Aromatic *H*), 7.22 (t, *J* = 7.6 Hz, 1H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.1 (*C*$H_{3(thiazole)}$), 20.4 (*C*$H_{3(phenyl)}$), 124.3, 127.7, 129.6, 130.2, 130.0, 137.9, 164.5. HRMS (DART+) *m/z* = 281.9946 (MH^+). Calc. for $C_{12}H_{13}BrNS^+$ = 281.9952.

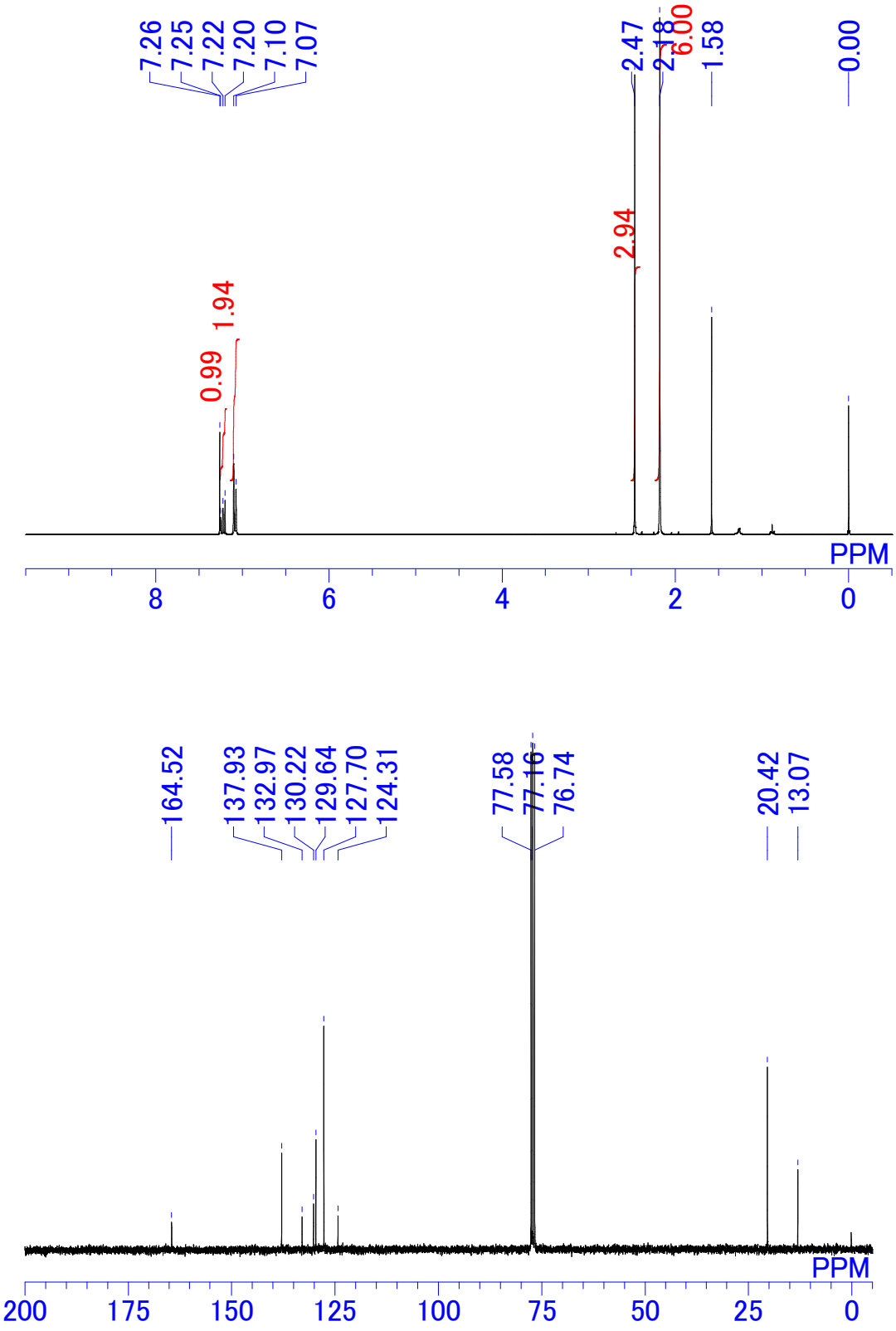
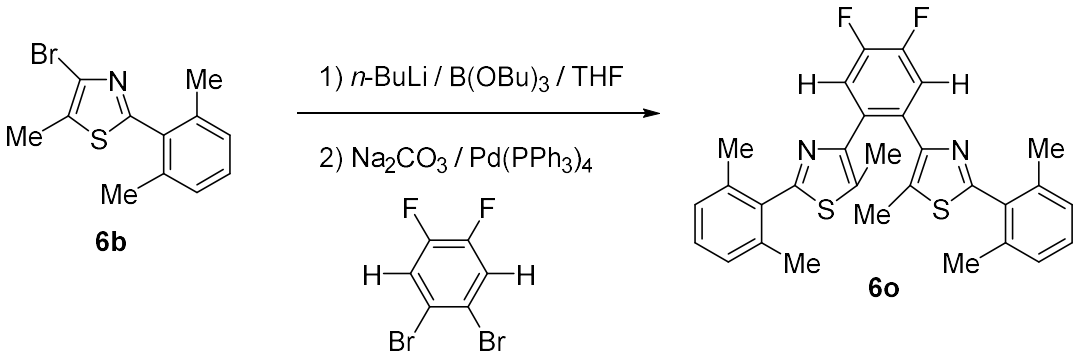


Fig. S18 ^{1}H NMR and ^{13}C NMR spectra of **6b** in $CDCl_3$.

1,2-Bis(2-(2,5-dimethyl)-5-methyl-4-thiazolyl)-4,5-difluorobenzene (6o).



4-Bromo-2-(2,6-dimethylphenyl)-5-methylthiazole (0.80 g, 2.8 mmol) was dissolved in anhydrous THF (20 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (2.0 mL, 3.2 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (0.90 mL, 3.4 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (0.35 g, 1.3 mmol), tetrakis(triphenylphosphine)palladium (100 mg, 0.087 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 50 mg in 13% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 2.07 (s, 12H, C$H_{3(phenyl)}$), 2.20 (s, 6H, C$H_{3(thiazole)}$), 7.11 (d, J = 7.7 Hz, 4H, Aromatic *H*), 7.23 (t, J = 7.5 Hz, 2H, Aromatic *H*), 7.46 (t, J_{HF} = 9.6 Hz, 2H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 12.1 (*C*$H_{3(thiazole)}$), 20.6 (*C*$H_{3(phenyl)}$), 120.1 (dd, $^2J_{CF}$ = 11.1 Hz, $^3J_{CF}$ =7.6 Hz), 127.8, 129.4, 131.4, 131.4 (dd, $^3J_{CF}$ = 5.2 Hz, $^4J_{CF}$ = 5.2 Hz), 133.5, 137.6, 149.5, 150.0 (dd, $^2J_{CF}$ = 252.5 Hz, $^3J_{CF}$ =14.6 Hz), 163.7. HRMS (DART+) *m/z* = 517.1595 (MH^+). Calc. for $C_{30}H_{27}F_2N_2S_2^+$ = 517.1584. Melting point: 220.8–221.8 °C.

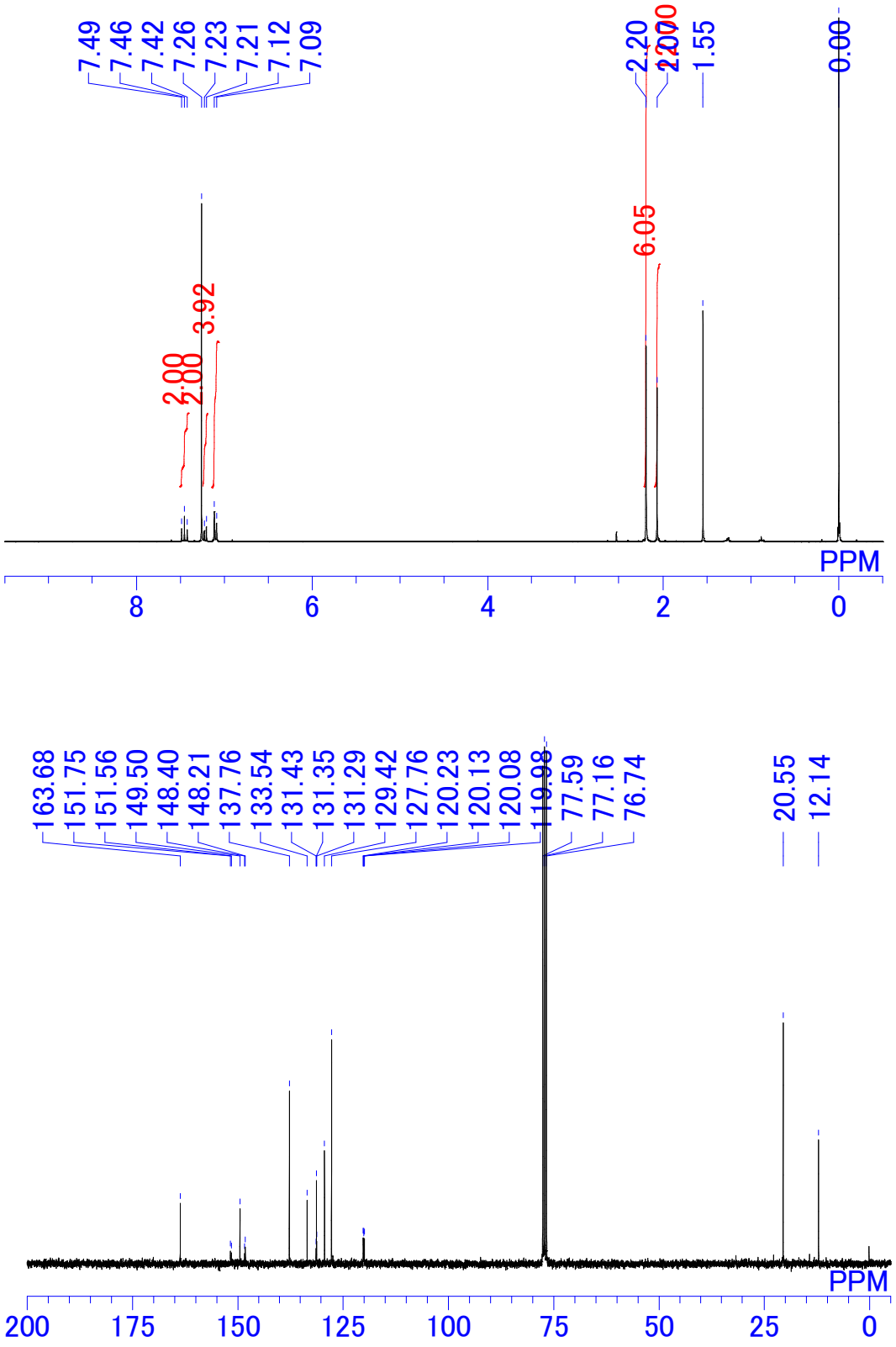
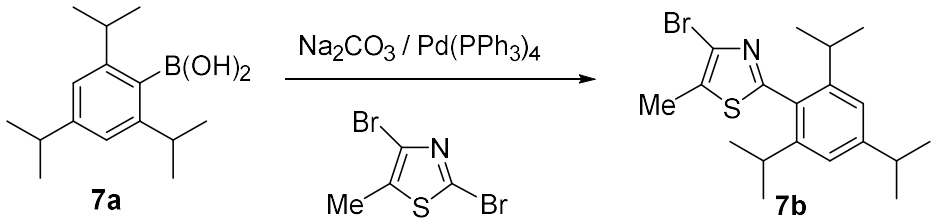


Fig. S19 ^{1}H NMR and ^{13}C NMR spectra of **6o** in $CDCl_3$.

4-Bromo-5-methyl-2-(2,4,6-triisopropylphenyl)thiazole (7b).



2,4-Dibromo-5-methylthiazole[S2] (4.1 g, 16.0 mmol), (2,4,6-triisopropylphenyl)boronic acid (4.0 g, 16 mmol), tetrakis(triphenylphosphine)palladium (300 mg, 0.26 mmol), and 20wt% Na_2CO_3 aqueous solution (15 mL) were added to THF (50 mL), and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 450 mg in 7.4% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ =1.16 (d, J = 7.0 Hz, 12H, C$H_{3(o\text{-phenyl})}$), 1.26 (d, J = 7.0 Hz, 6H, C$H_{3(p\text{-phenyl})}$), 2.46 (s, 3H, C$H_{3(\text{thiazole})}$), 2.66 (sep, J = 6.8 Hz, 2H, C$H_{(o\text{-phenyl})}$), 2.91 (sep, J = 6.8 Hz, 1H, C$H_{(p\text{-phenyl})}$), 7.04 (s, 2H, Aromatic *H*). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.1 (*C*$H_{3(\text{thiazole})}$), 24.1 (*C*$H_{3(p\text{-phenyl})}$), 24.4 (*C*$H_{3(o\text{-phenyl})}$), 30.8 (*C*$H_{(o\text{-phenyl})}$), 34.6 (*C*$H_{(p\text{-phenyl})}$), 121.0, 123.9, 128.1, 130.0, 148.5, 150.9, 164.9. HRMS (DART+) *m/z* = 380.1055 (MH^+). Calc. for $C_{30}H_{27}F_2N_2S_2^+$ = 380.1048.

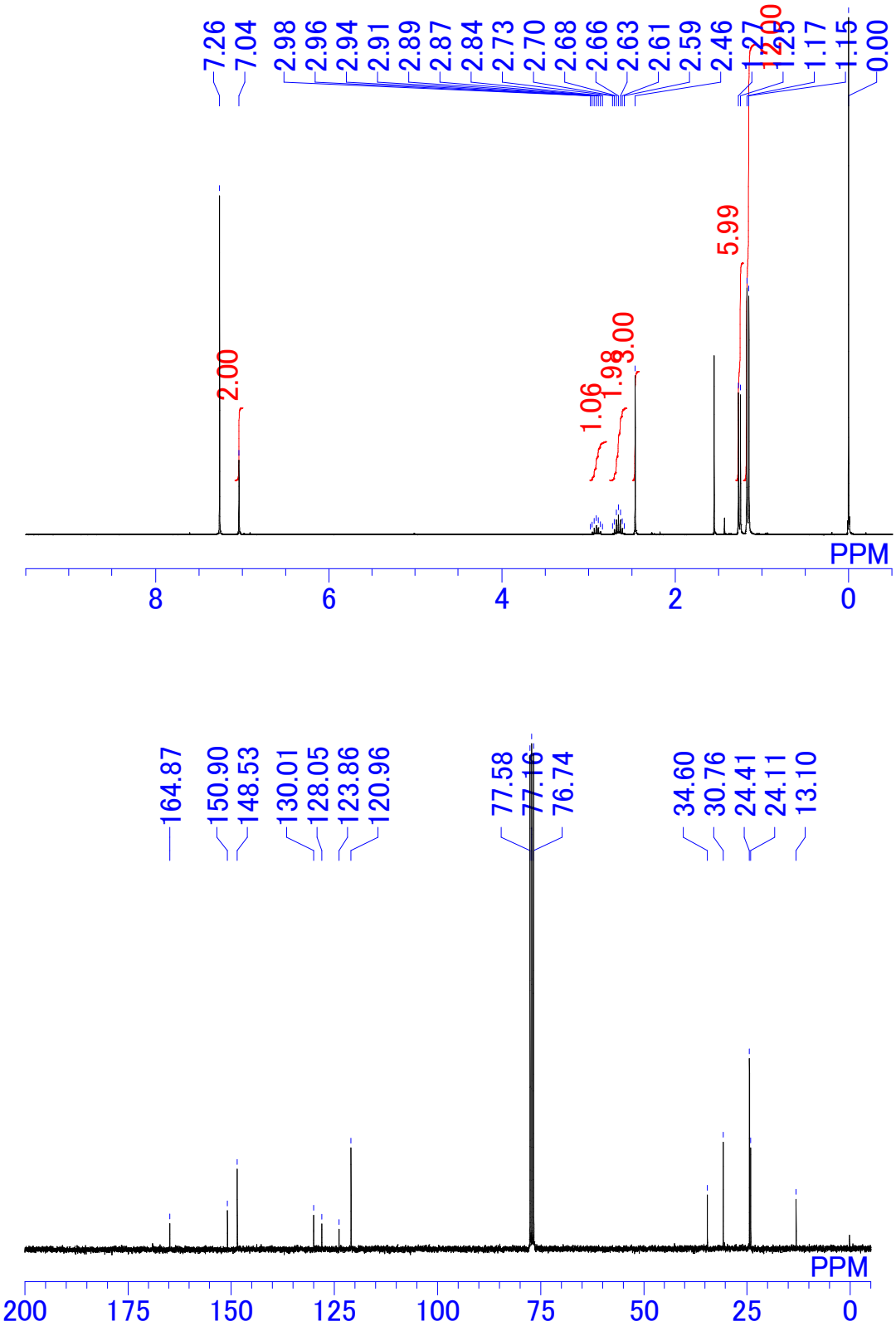
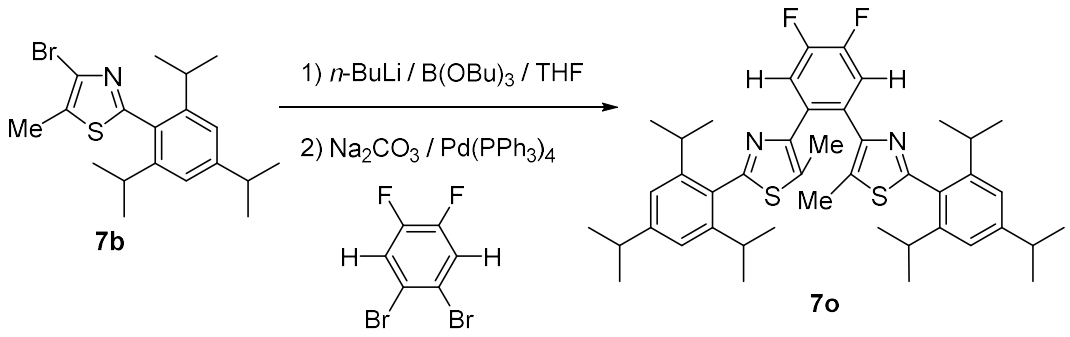


Fig. S20 ^{1}H NMR and ^{13}C NMR spectra of **7b** in $CDCl_3$.

1,2-Bis(5-methyl-2-(2,4,6-triisopropylphenyl)-4-thiazolyl)-4,5-difluorobenzene (7o).



4-Bromo-5-methyl-2-(2,4,6-triisopropylphenyl)thiazole (0.50 g, 1.3 mmol) was dissolved in anhydrous THF (15 mL) under argon atmosphere. 1.6 M *n*-BuLi hexane solution (0.80 mL, 1.3 mmol) was slowly added dropwise to the solution at −78 °C, and the mixture was stirred for 1.5 h. Tri-*n*-butyl borate (0.40 mL, 1.5 mmol) was slowly added to the solution at the temperature, and the mixture was stirred for 1.5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. 1,2-Dibromo-4,5-difluorobenzene (0.33 g, 1.2 mmol), tetrakis(triphenylphosphine)palladium (100 mg, 0.087 mmol), and 20wt% Na_2CO_3 aqueous solution (10 mL) were added, and the mixture was refluxed for 24 h. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate (9:1) as the eluent to give 100 mg in 25% yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ =1.22 (d, J = 6.8 Hz, 24H, C$H_{3(o\text{-phenyl})}$), 1.28 (d, J = 6.8 Hz, 12H, C$H_{3(p\text{-phenyl})}$), 2.00 (s, 6H, C$H_{3(\text{thiazole})}$), 2.77 (sep, J = 6.8 Hz, 4H, C$H_{(o\text{-phenyl})}$), 2.94 (sep, J = 6.8 Hz, 2H, C$H_{(p\text{-phenyl})}$), 7.08 (s, 4H, CH), 7.45 (t, J_{HF} = 9.6 Hz, 2H, CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 11.9 (C$H_{3(\text{thiazole})}$), 24.1 (C$H_{3(p\text{-phenyl})}$), 24.4 (C$H_{3(o\text{-phenyl})}$), 31.0 (C$H_{(o\text{-phenyl})}$), 34.6 (C$H_{(p\text{-phenyl})}$), 120.2 (dd, $^2J_{CF}$ = 11.1 Hz, $^3J_{CF}$ =7.6 Hz), 121.0, 128.7, 131.0, 131.1 (dd, $^3J_{CF}$ = 5.2 Hz, $^4J_{CF}$ = 5.2 Hz), 148.2, 148.4, 149.9 (dd, $^2J_{CF}$ = 244.9 Hz, $^3J_{CF}$ = 22.6 Hz), 150.7, 164.3. HRMS (DART+) *m/z* = 735.3593 (MNa^+). Calc. for $C_{44}H_{54}F_2N_2NaS_2^+$ = 735.3594. Melting point: 220.5–221.5 °C.

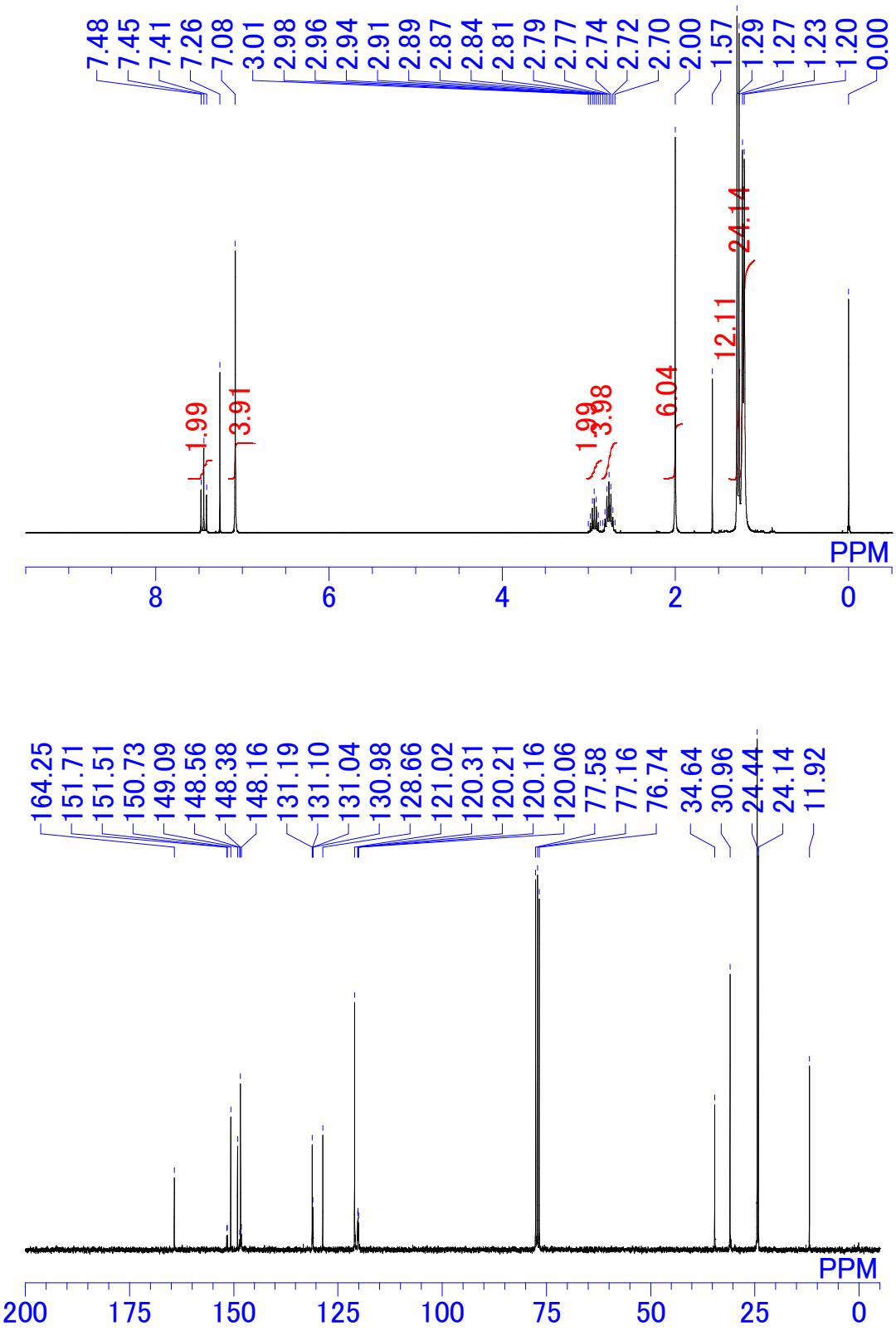


Fig. S21 ^{1}H NMR and ^{13}C NMR spectra of **7o** in $CDCl_3$.

X-ray crystallographic analysis

Crystals **2o**–**7o** were prepared by recrystallization from *n*-hexane.

Table S8 X-ray crystallographic data for the open-ring isomers **2o**–**4o**.

	2o	**3o**	**4o**
Formula	$C_{28}H_{22}F_2N_2S_2$	$C_{30}H_{26}F_2N_2S_2$	$C_{32}H_{30}F_2N_2S_2$
Formula weight	488.59	516.65	544.70
Temperature/K	100.0(1)	100.0(1)	100.0(1)
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$C2/c$	$C2/c$
Unit cell dimensions			
a/Å	11.2940(1)	19.4157(5)	19.0612(3)
b/Å	22.7558(2)	10.9681(1)	12.1912(1)
c/Å	9.1549(1)	13.8257(3)	13.5755(2)
α/deg	90	90	90
β/deg	92.8389(8)	121.068(3)	121.113(2)
γ/deg	90	90	90
Volume/Å^3	2349.96(4)	2521.89(11)	2700.86(8)
Z	4	4	4
Density/g cm^{-3}	1.381	1.361	1.340
Goodness-of-fit on F^2	1.062	1.069	1.040
R ($I > 2\sigma(I)$)	$R_1 = 0.0297$ $wR_2 = 0.0763$	$R_1 = 0.0314$ $wR_2 = 0.0327$	$R_1 = 0.0318$ $wR_2 = 0.0808$
R (all data)	$R_1 = 0.0319$ $wR_2 = 0.0777$	$R_1 = 0.0787$, $wR_2 = 0.0796$	$R_1 = 0.0334$ $wR_2 = 0.0820$
CCDC No.	2452875	2452876	2452877

Table S9 X-ray crystallographic data for the open-ring isomers **5o**–**7o**.

	5o	**6o**	**7o**
Formula	$C_{34}H_{34}F_2N_2S_2$	$C_{30}H_{26}F_2N_2S_2$	$C_{44}H_{54}F_2N_2S_2$
Formula weight	572.75	516.65	713.01
Temperature/K	100.0(1)	100.0(1)	100.0(1)
Crystal system	Monoclinic	Orthorhombic	Triclinic
Space group	$P2_1/n$	$Pbcn$	$P\bar{1}$
Unit cell dimensions			
a/Å	14.5230(1)	21.4133(3)	11.6733(3)
b/Å	10.6398(1)	13.7635(2)	13.4099(3)
c/Å	19.0421(2)	8.9630(1)	13.5210(3)
α/deg	90	90	76.6459(18)
β/deg	91.6399(8)	90	74.5390(19)
γ/deg	90	90	85.3589(19)
Volume/Å^3	2941.21(5)	2641.59(6)	1984.37(8)
Z	4	4	2
Density/g cm^{-3}	1.293	1.299	1.193
Goodness-of-fit on F^2	1.050	1.062	1.064
R ($I > 2\sigma(I)$)	$R_1 = 0.0390$ $wR_2 = 0.0969$	$R_1 = 0.0344$ $wR_2 = 0.0942$	$R_1 = 0.0322$ $wR_2 = 0.0829$
R (all data)	$R_1 = 0.0416$ $wR_2 = 0.0984$	$R_1 = 0.0369$ $wR_2 = 0.0965$	$R_1 = 0.0350$ $wR_2 = 0.0847$
CCDC No.	2452878	2452879	2452880

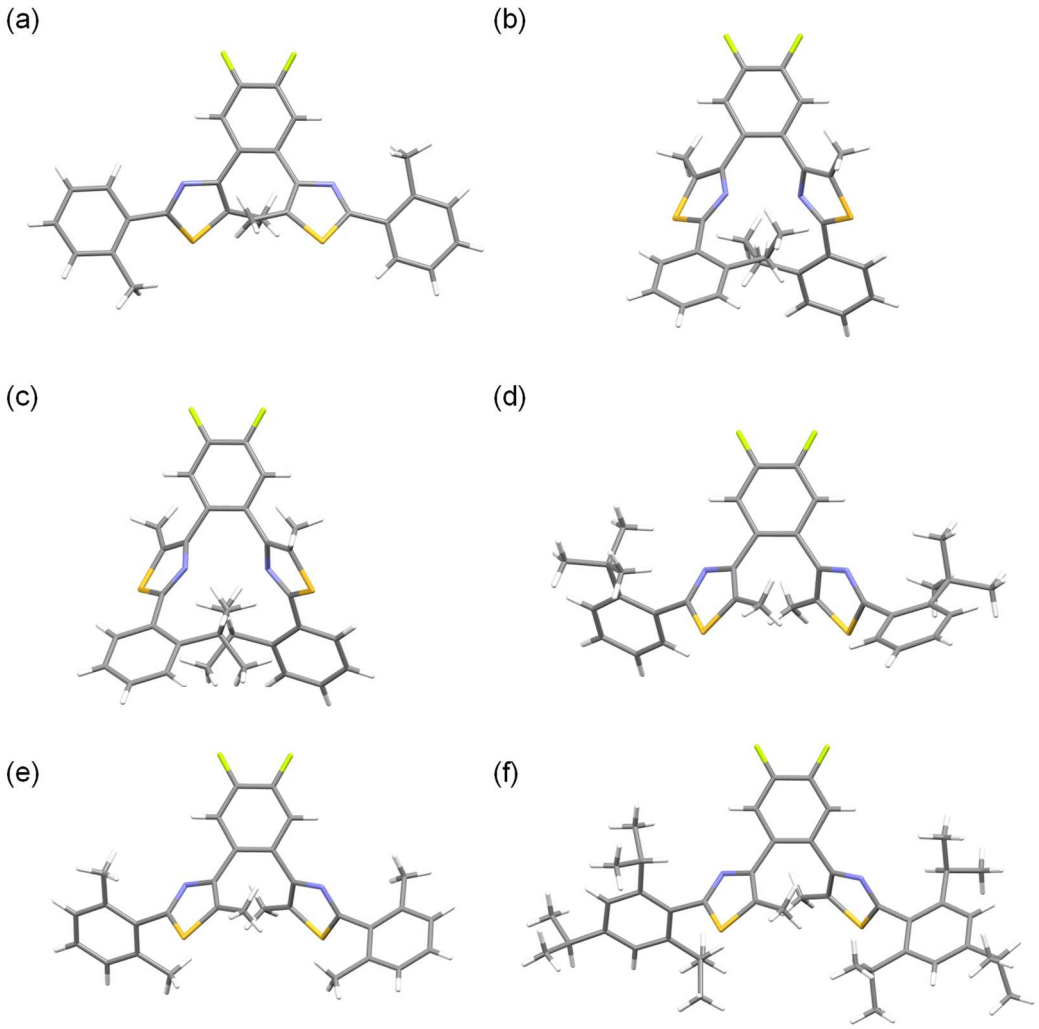


Fig. S22 Molecular structures of **2o**–**7o** in the crystals.

References

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