

Relationship between aryl groups and proton stimuli-responsiveness of 4,4'-diaminodiphenylmethane-based fluorescent sensor including diarylmaleimide

Takaaki MIYAZAKI*, Shunsaku WATANABE, Shoko OKA,
and Osamu HAYASHIDA*

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Abstract

To reveal the relationship between the substituents in the aryl groups and the proton stimuli-responsiveness of the 4,4'-diaminodiphenylmethane-based fluorescent sensor including diarylmaleimide, **1R** (R = *i*Pr, H, and CF₃) were synthesized and measured the fluorescence spectra in CH₃CN, CH₂Cl₂, and toluene. The fluorescent behaviors of **1R** upon the addition of TFA depended on the substituents in the aryl group, and **1*i*Pr** responded to proton and its fluorescence intensity increased in CH₃CN, CH₂Cl₂, and toluene. While **1H** and **1CF₃** did not exhibit proton stimuli-responsiveness. Consequently, a donating substituent such as isopropyl groups is necessary on the DPM-based diarylmaleimide to apply as a proton sensor.

Keywords: Stimuli-responsive, Diarylmaleimide, Fluorescent sensor

1. Introduction

3,4-Diarylmaleimides are an attractive molecule because of their excellent fluorescent properties depending on the electronic properties of the aryl groups,[1–7] and easy introduction into molecules having an amino group. Chen's

group reported a series of *N*-methyl diarylmaleimide and its colorful fluorescent properties.[1] The advantages of diarylmaleimide, which is an excellent fluorophore and easy construction of the skeleton, are available to a sensing molecule. Our group has found that 4,4'-diaminodiphenylmethane (DPM)-based molecule having diarylmaleimide

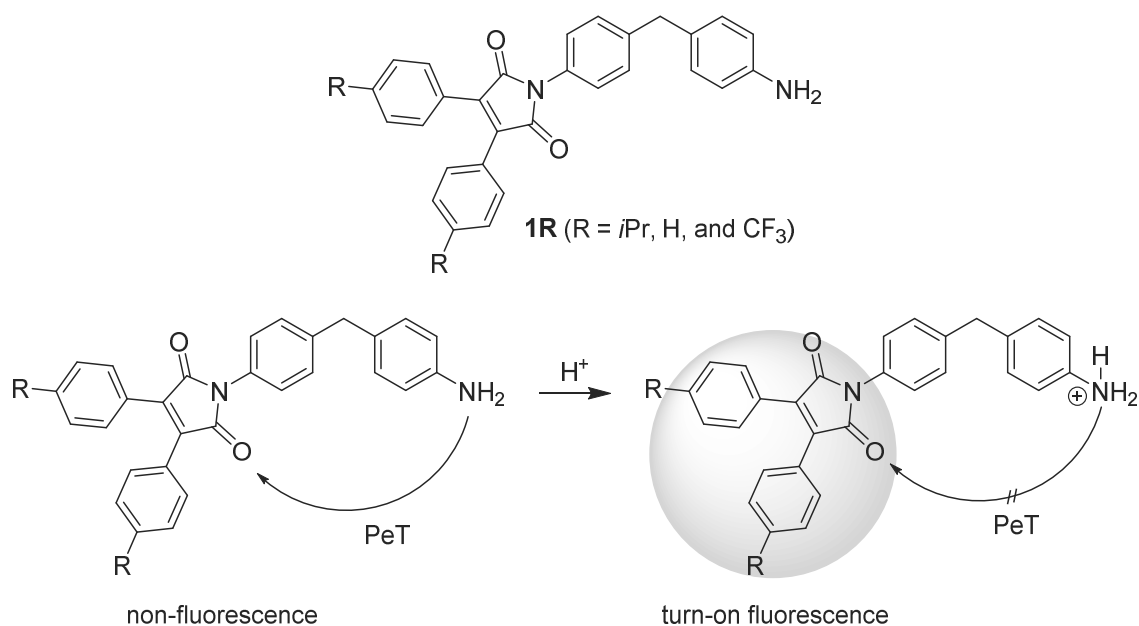


Fig. 1 Compound **1R** (R = *i*Pr, H, and CF₃) and mechanism of its turn-on fluorescence.

exhibits a turn-on fluorescent property responding to proton and pH.[8] DPM has been used as a component of cyclophanes[9–12] and polymers,[13–16] and the applications of the DPM-based polymer are expected to be available as sensors. The fluorescent properties of diarylmaleimide strongly depend on the electronic property of substituents. The aryl groups of diarylmaleimide, therefore, are modified to various substitutes, and an investigation of their stimuli-responsiveness is an interesting issue. In this paper, we report the relationship between the aryl groups of diarylmaleimide and their proton stimuli-responsive properties by using compounds **1R** including 4-isopropylphenyl (R = *i*Pr), phenyl (R = H), and 4-trifluoromethylphenyl (R = CF₃) groups as the aryl group (Figure 1).

2. Experimental section

2.1. Synthesis of **3iPr**

A mixture of **2** (134 mg, 0.30 mmol), 4-isopropylphenyl boronic acid (121 mg, 0.74 mmol), palladium acetate (7.2 mg, 0.032 mmol), XPhos (31.0 mg, 0.062 mmol), tripotassium phosphate (128 mg, 0.60 mmol), and toluene (6.0 mL) was heated at 100 °C in a nitrogen atmosphere for 1 day. After cooling to room temperature, the reaction mixture was directly charged in silica gel chromatography and purified (EtOAc/Hexane = 1:6) to give **3iPr** (148 mg, 80%) as yellow powder. ¹H NMR (400 MHz, CDCl₃): δ 1.26 (d, *J* = 6.9 Hz, 12H), 1.51 (s, 9H), 2.92 (sep, *d* = 6.9 Hz, 2H), 3.97 (s, 2H), 6.42 (br, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 4H), 7.26–7.30 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 23.7, 28.4, 34.1, 40.9, 80.4, 118.8, 126.2, 126.7, 129.4, 129.6, 129.9, 130.0, 135.2, 135.5, 136.6, 140.9, 150.9, 152.8, 170.0; LRMS (MALDI-TOF) *m/z*: [M+Na]⁺ calcd for C₄₀H₄₂N₂O₄Na 637.30; Found 637.68. Anal. Calcd for C₄₀H₄₂N₂O₄: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.15; H, 7.01; N, 4.63.

2.2. Synthesis of **3H**

This compound was synthesized by the similar procedure to those of **3iPr**. (75%) Yellow powder; ¹H NMR (400 MHz, CDCl₃): δ 1.51 (s, 9H), 3.97 (s, 2H), 6.41 (br, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.26–7.30 (m, 4H), 7.34–7.42 (m, 8H), 7.50–7.53 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 28.4, 40.9, 80.4, 118.9, 126.2, 128.5, 128.6, 129.5, 129.6, 129.8, 130.0, 130.0, 135.2, 136.3, 136.6, 141.0, 152.8, 169.6; LRMS (MALDI-TOF) *m/z*: [M+Na]⁺ calcd for C₃₄H₃₀N₂O₄Na 553.21; Found 553.67. Anal. Calcd for C₃₄H-

₃₀N₂O₄: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.07; H, 5.70; N, 5.31.

2.3. Synthesis of **3CF₃**

This compound was synthesized by the similar procedure to those of **3iPr**. (64%) Yellow powder; ¹H NMR (400 MHz, CDCl₃): δ 1.51 (s, 9H), 3.98 (s, 2H), 6.42 (br, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.28–7.31 (m, 4H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 4H), 7.67 (d, *J* = 8.4 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 28.4, 40.9, 80.5, 115.5, 118.9, 119.6, 122.3, 125.0, 125.7, 125.8, 125.8, 125.9, 126.1, 127.7, 129.3, 129.6, 130.4, 131.5, 131.7, 132.0, 132.3, 132.6, 135.0, 136.3, 136.7, 141.6, 152.8, 168.7; ¹⁹F NMR (376 MHz, CDCl₃): δ -63.6; LRMS (MALDI-TOF) *m/z*: [M+Na]⁺ calcd for C₃₆H₂₈F₆N₂O₄Na 689.19; Found 689.55. Anal. Calcd for C₃₆H₂₈F₆N₂O₄: C, 64.86; H, 4.23; N, 4.20. Found: C, 64.94; H, 4.52; N, 4.34.

2.4. Synthesis of **1iPr**

A mixture of **3iPr** (123 mg, 0.20 mmol), trifluoroacetic acid (2.0 mL), and CH₂Cl₂ (40 mL) was stirred at room temperature for 2 hours. The reaction mixture was washed with saturated NaHCO₃ aq. The organic layer was dried with MgSO₄, filtered and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/Hexane = 1:4) to give **1iPr** (101 mg, 98%) as orange powder. ¹H NMR (400 MHz, CDCl₃): δ 1.26 (d, *J* = 6.9 Hz, 12H), 2.92 (sep, *J* = 6.9 Hz, 2H), 3.92 (s, 2H), 6.66 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 4H), 7.28 (d, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 23.7, 34.1, 40.7, 115.4, 126.1, 126.2, 126.7, 129.4, 129.7, 129.9, 130.0, 130.7, 135.5, 141.5, 144.6, 150.9, 170.0; LRMS (MALDI-TOF) *m/z*: [M+H]⁺ calcd for C₃₅H₃₅N₂O₂ 515.27; Found 515.81. Anal. Calcd for C₃₅H₃₄N₂O₂: C, 81.68; H, 6.66; N, 5.44. Found: C, 81.45; H, 6.79; N, 5.39.

2.5. Synthesis of **1H**

This compound was synthesized by the similar procedure to those of **1iPr**. (quant.) Orange powder; ¹H NMR (400 MHz, CDCl₃): δ 3.92 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.33–7.42 (m, 8H), 7.50–7.53 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 40.7, 115.4, 126.1, 128.6, 128.6, 129.4, 129.6, 129.9, 130.0, 130.0, 130.6, 136.3, 141.7, 144.5, 169.7; LRMS (MALDI-TOF) *m/z*: [M+H]⁺ calcd for C₂₉H₂₃N₂O₂ 431.18; Found 431.95. Anal. Calcd for C₂₉H₂₂N₂O₂: C, 80.91; H, 5.15; N,

6.51. Found: C, 80.70; H, 5.29; N, 6.44.

2. 6. Synthesis of 1CF₃

This compound was synthesized by the similar procedure to those of **1iPr**. (71%) Red powder; ¹H NMR (400 MHz, CDCl₃): δ 3.93 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 4H), 7.67 (d, *J* = 8.5 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 40.7, 115.4, 119.6, 122.3, 125.0, 125.7, 125.8, 125.8, 126.1, 127.7, 128.8, 129.1, 129.6, 129.9, 130.4, 130.9, 131.5, 131.7, 132.0, 132.3, 132.6, 136.2, 142.3, 144.7, 168.7; ¹⁹F NMR (376 MHz, CDCl₃): δ -63.6; LRMS (MALDI-TOF) *m/z*: [M+H]⁺ calcd for C₃₁H₂₁F₆N₂O₂ 567.15; Found 567.63. Anal. Calcd for C₃₁H₂₀F₆N₂O₂: C, 65.73; H, 3.56; N, 4.95. Found: C, 66.02; H, 3.68; N, 4.81.

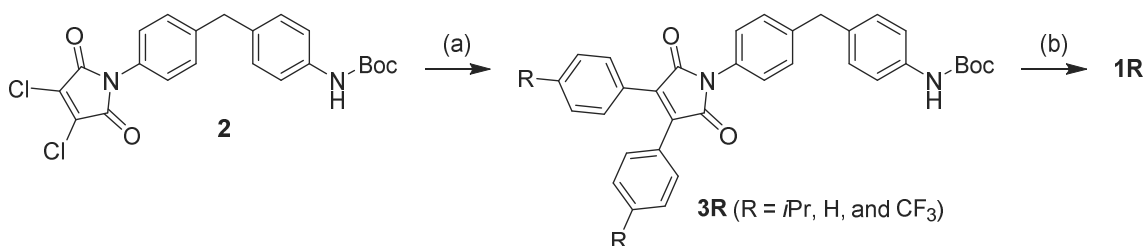
3. Result and Discussion

Diarylmaleimides having 4-isopropylphenyl, phenyl, and 4-trifluoromethylphenyl groups **1R** were synthesized as shown in Scheme 1. The synthesis of **2** was completed by our group[8]. **2** was carried out Suzuki coupling with the corresponding boronic acid to get **3R**, and the Boc group was deprotected by trifluoroacetic acid (TFA) to produce **1R**.

The absorption spectra of **1R** were measured in CH₃CN, CH₂Cl₂, and toluene (Figure 2), and the results were summarized in Table 1. The absorption peak at the longest wavelength region of **1iPr** in CH₃CN appeared at 375 nm, and the corresponding peaks of **1H** and **1CF₃** were not determined due to their weak broad bands. The onsets of their bands were blue-shifted with a weakening of the electron-donating ability (**1iPr**, ca. 450 nm; **1H**, ca. 420 nm; **1CF₃**, ca. 400 nm). A slight change in the absorption bands of **1R** was observed upon the addition of TFA to these solutions, suggesting that the diarylmaleimide units were not protonated. An almost similar spectral change was

shown in CH₂Cl₂ and toluene, and the protonated position was not dependent on the solvent polarity.

The fluorescent properties of **1R** were evaluated in CH₃CN, CH₂Cl₂, and toluene (Figure 3). In each case, the fluorescence band was not observed, indicating the possibility that the photo-induced electron transfer (PeT) between the aniline and imide units might quench the fluorescence. To evaluate the proton responsiveness of **1R**, TFA titration (10-100 equiv.) was carried out. A slight rise of the fluorescence band of **1iPr** appeared at ca. 550 nm in CH₃CN, indicating the responsiveness to TFA. A larger increase of the fluorescence intensity of **1iPr** in CH₂Cl₂ and toluene was observed at ca. 550 nm compared with that in CH₃CN. The fluorescence of **1iPr** is derived from a charge-transfer type, which is generally weaker with increasing solvent polarity, between the imide and 4-isopropylphenyl groups, thus it is considered that the fluorescence of **1iPr** exhibited a solvent dependence. Although the proton responsiveness of **1iPr** was revealed, **1H** and **1CF₃** having non-donating substituents in the aryl groups observed no fluorescent spectral change upon the addition of TFA. The fluorescence properties of *N*-methyl diphenyl and 4-trifluoromethylphenyl maleimide were reported, and their fluorescence bands were observed at 503 nm and 487 nm in CH₂Cl₂, respectively, along with the moderate quantum yields (31% and 26%, respectively)[1]. The reason, therefore, why **1H** and **1CF₃** did not show the fluorescent properties before and after adding TFA is considered to be a lack of an electron-donating group on the *N*-phenyl diarylmaleimide skeleton rather than the contribution of PeT. *N*-methyl 1,8-naphthalimide is a weak fluorophore due to an intersystem crossing (ISC) from the S₁ to T_n states in the excited state, however, the introduction of an electron-withdrawing group to the methyl substituent led to the increase of the fluorescence intensity, because the energy gap between the S₁ and T_n states is expanded leading that the ISC pathway was inhibited.[17] It is considered that, therefore, **1H** and **1CF₃** are affected by the inherent properties of *N*-phenyl diarylmaleimide skeleton as



Scheme 1 Synthesis of **1R**. (a) aryl boronic acid, Pd(OAc)₂, XPhos, K₃PO₄, toluene, 100 °C, 1 d, 80% for **3iPr**, 75% for **3H**, 64% for **3CF₃**. (b) TFA, CH₂Cl₂, rt, 2 h, 98% for **1iPr**, quant. for **1H**, 71% for **1CF₃**.

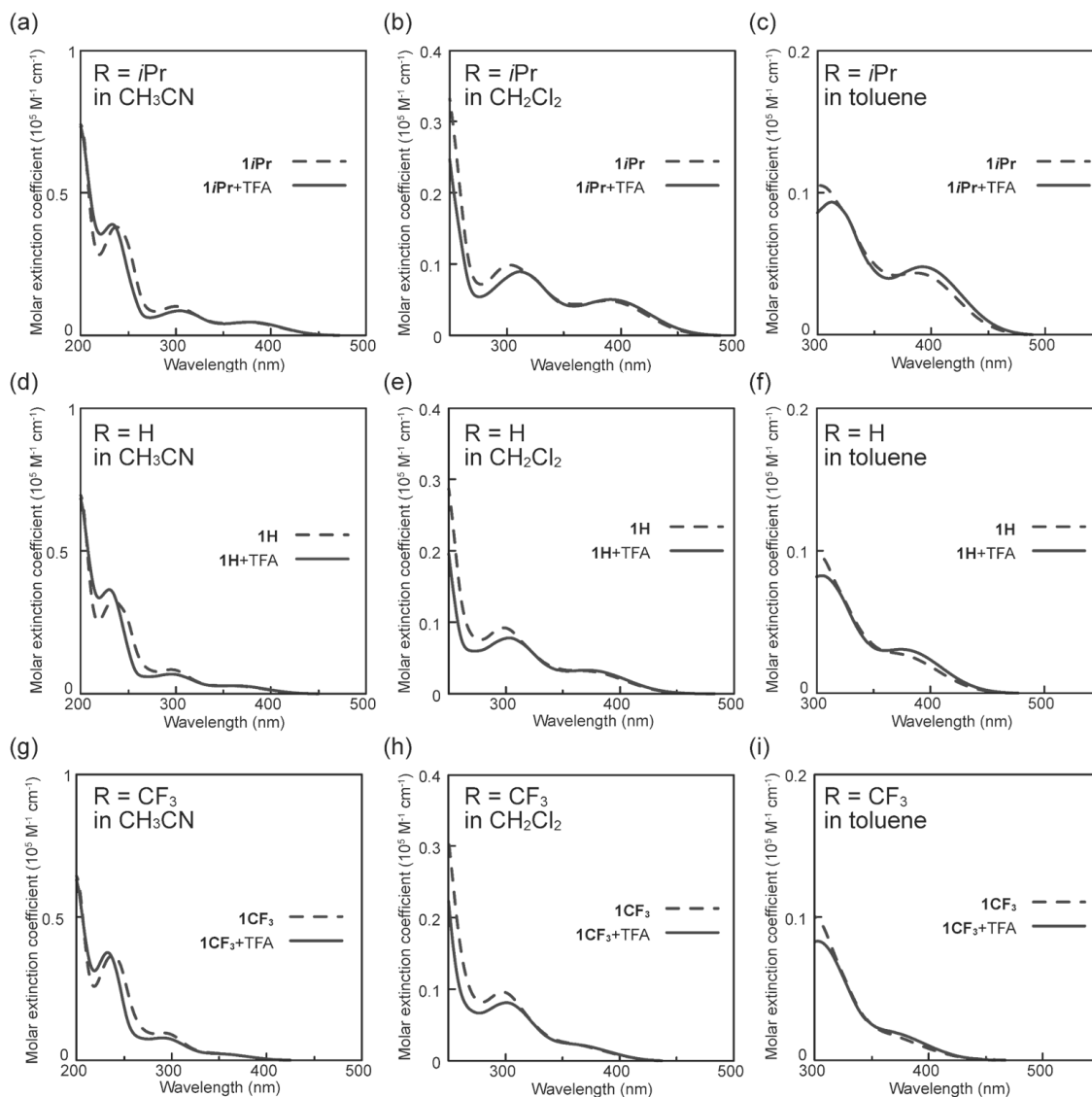


Fig. 2 Absorption spectral change of **1R** upon the addition of TFA in (a) $R = iPr$, CH_3CN , (b) $R = iPr$, CH_2Cl_2 , (c) $R = iPr$, toluene, (d) $R = H$, CH_3CN , (e) $R = H$, CH_2Cl_2 , (f) $R = H$, toluene, (g) $R = CF_3$, CH_3CN , (h) $R = CF_3$, CH_2Cl_2 , and (i) $R = CF_3$, toluene.

| | $\lambda_{max} / nm (\epsilon / 10^3 M^{-1} cm^{-1})$ | | |
|----------------------------|---|--|------------------------------|
| | CH_3CN | CH_2Cl_2 | Toluene |
| 1Pr | 375 (4.48), 300 (10.1), 237 (37.8) | 388 (4.83), 303 (9.81), 240 (38.6) | 386 (4.34) |
| 1Pr+TFA | 378 (4.60), 304 (8.53), 233 (40.5) | 391 (5.00), 311 (8.88), 236 (38.7) | 393 (4.76), 312 (9.38) |
| 1H | — ^a 295 (8.41), 234 (32.4) | — ^a 298 (9.21), 237 (35.5) | — ^a |
| 1H+TFA | 361 (2.78), 296 (6.81), 230 (37.4) | 371 (3.30), 303 (7.79), 233 (37.7) | 373 (3.07), 304 (8.35) |
| 1CF₃ | — ^a 292 (9.61), 238 (36.7) | — ^a 298 (9.57), 239 (36.9) | — ^a |
| 1CF₃+TFA | — ^a 290 (7.95), 233 (40.2) | — ^a 301 (8.06), 234 (38.8) | — ^a 304 (8.05) |

Table 1 Summary of the absorption spectral peaks of **1R** in CH_3CN , CH_2Cl_2 , and toluene before and after the addition of excess amount of TFA. ^a λ_{max} could not be determined because of a weak broad band.

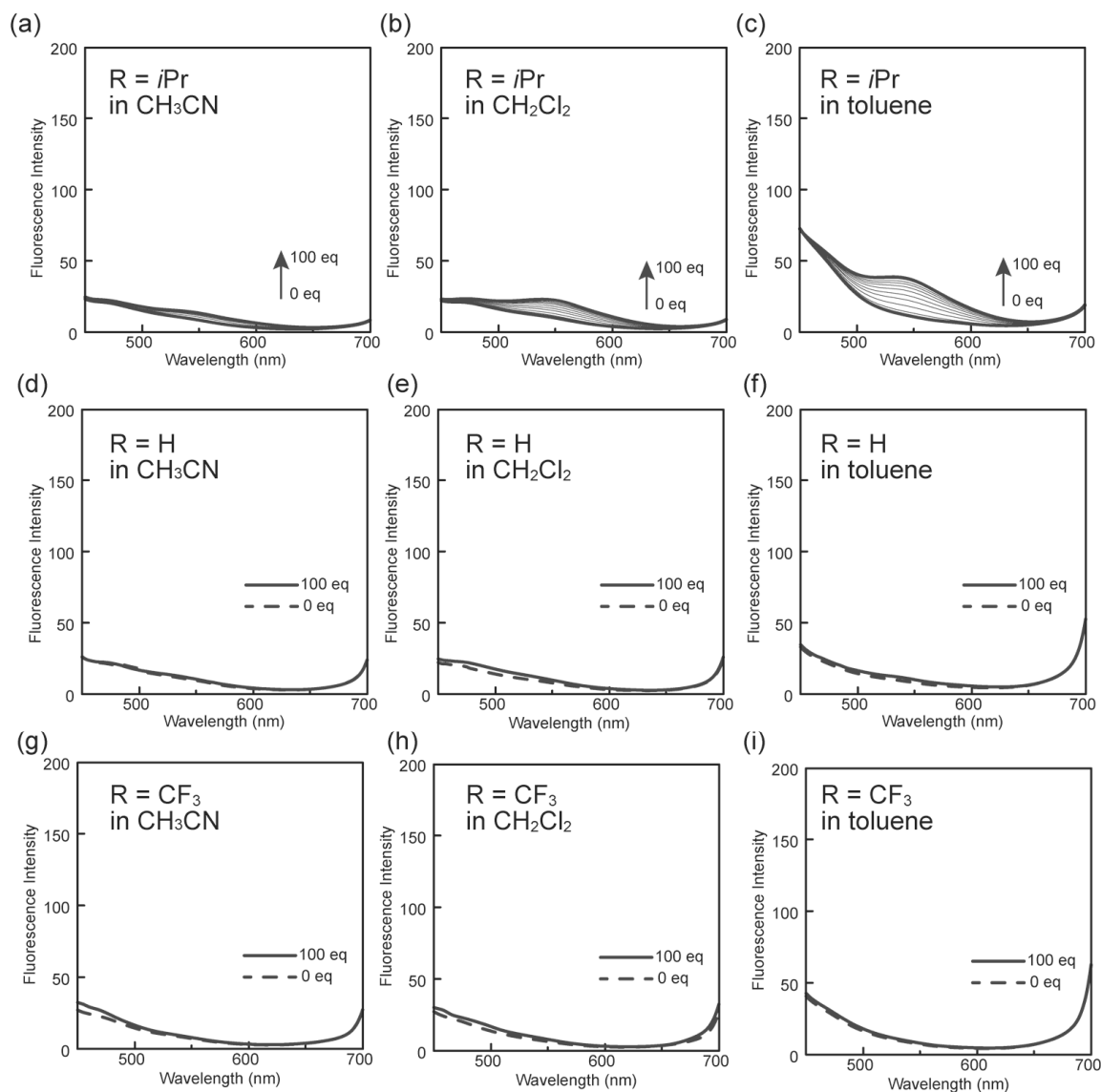


Fig. 3 Fluorescence spectral change of **1R** (50 μ M) upon the gradual addition of TFA in (a) $R = iPr$, CH_3CN ($\lambda_{ex} = 375$ nm), (b) $R = iPr$, CH_2Cl_2 ($\lambda_{ex} = 375$ nm), (c) $R = iPr$, toluene ($\lambda_{ex} = 375$ nm), (d) $R = H$, CH_3CN ($\lambda_{ex} = 370$ nm), (e) $R = H$, CH_2Cl_2 ($\lambda_{ex} = 370$ nm), (f) $R = H$, toluene ($\lambda_{ex} = 370$ nm), (g) $R = CF_3$, CH_3CN ($\lambda_{ex} = 370$ nm), (h) $R = CF_3$, CH_2Cl_2 ($\lambda_{ex} = 370$ nm), and (i) $R = CF_3$, toluene ($\lambda_{ex} = 370$ nm).

well as the ISC from the S_1 to T_n states in the excited state, resulting in the non-fluorescent property, although *N*-methyl diphenyl and 4-trifluoromethylphenyl maleimides are good fluorophores. Consequently, DPM-based proton sensors including diarylmaleimide as a fluorophore exhibited the proton stimuli-responsiveness depending on the substituent on the aryl group, that is, to respond to proton and increase the fluorescence intensity, a donating substituent such as isopropyl groups is necessary on the diarylmaleimide unit.

4. Conclusion

To evaluate the substituent effect in the aryl groups for the proton stimuli-responsiveness of the DPM-based fluorescent sensor including diarylmaleimide, **1R** ($R = iPr, H,$

and CF_3) were synthesized and measured their absorption and fluorescence spectral change upon the addition of TFA in CH_3CN , CH_2Cl_2 , and toluene. The onset of the absorption bands of **1R** was blue-shifted with reducing the donating ability of the substituent, and a small change in absorption spectra upon adding TFA in **1R** was observed. The fluorescent behaviors of **1R** upon the addition of TFA revealed the substituent effect, that is, **1iPr** responded to proton and its fluorescence intensity was increased in CH_3CN , CH_2Cl_2 , and toluene. While **1H** and **1CF₃** including no donating substituents did not exhibit proton stimuli-responsiveness. This is probably because the ISC from the S_1 to T_n states in these excited states occurred derived from the *N*-phenyl maleimide skeleton. To apply as a proton sensor, a donating substituent such as isopropyl groups is necessary on the

DPM-based diarylmalimide.

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