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Synthesis and Structure of Benzotriazolyl Fluorenes

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1-(Fluoren-2-yl)-benzo[*d*][1,2,3]triazoles **5a-b** were synthesized starting from 2-nitrofluorene. 2-Nitrofluorenes **1a-b** were reduced by catalytic hydrogenation, reacted with 2,4-dinitrofluorobenzene followed by catalytic hydrogenation to afford 2-(*N*-2,4-diaminophenyl)aminofluorenes **4a-b**. Diazotization of **4a-b** with $NaNO_2/H_2SO_4$ followed by treatment with H_3PO_2 gave **5a-b**. Sulfonation of **5a-b** yielded 7-benzotriazol-1-yl-fluorene-2-sulfonic acids **6a-b**. The structures of **5b** and **6b** were firmly identified by X-ray crystal analysis in addition to ^{1}H NMR, ^{13}C NMR, and elemental analysis.

Key Words: 2-Aminofluorenes, 2-(*N*-2,4-Dinitrophenyl)aminofluorenes, 2-(*N*-2,4-Diaminophenyl)aminofluorenes, 1-(Fluoren-2-yl)-benzo[*d*][1,2,3]triazoles, 7-Benzotriazol-1-yl-fluorene-2-sulfonic acids

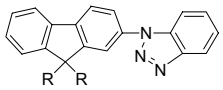
Introduction

The fluorene ring is a π-conjugated system that enables facile synthetic manipulation. The synthesis and characterization of fluorene derivatives have attracted much attention in recent years because of their interesting properties and potential applications in various fields, such as two-photon absorption dyes,[1-9] fluorescent probes,[10-17] and light-emitting materials.[18-21] It has also been shown that fluorene derivatives exhibit high binding affinity to human serum albumin,[13] β_2-integrins,[22] and β-amyloid.[23] These diverse applications of fluorene derivatives led us to explore synthesis of novel functional fluorene molecules.

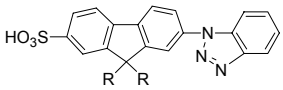
Derivatization of the fluorene ring has mostly been carried out at 2, 7, and 9 positions. Alkylation at the 9-position of the fluorene ring can be easily carried out utilizing the acidity of the hydrogens at the 9-position,[5,6,9,13-16,21] and introduction of substituents at 2- or 7-position was also effectively accomplished by electrophillic substitution of the fluorene ring.[5,9,12-15,21] Further manipulation at 2- or 7-position has been carried out by standard procedures starting from the appropriate fluorene compounds having diversely transformable substituents such as nitro and/or halogen group. In particular, various metal-catalyzed coupling reactions of bromo- or iodo-fluorenes with stannyl compounds (Stille reaction),[1,9] alkenes (Heck reaction),[1-3,5,6,15,16] arylboronic acid (Suzuki reaction),[10,18,21] terminal alkynes (Sonogashira reaction),[10] or amines (Buchwald-Hartwig or Ullmann reaction)[5,9,16] provided a variety of alkenyl-, aryl-, alkynyl-, or amino-substituted fluorene derivatives. However, further diversification of fluorene compounds is still highly desirable for the search of fluorene compounds of novel functionality.

The fluorene derivatives having heterocycle as a substituent have rarely been prepared: to the best of our knowledge, benzothiazole is an only example of heterocyclic substituents.[8-9] The benzothiazole-substituted fluorenes were prepared by coupling the preformed benzothiazole ring with fluorene derivatives.[8-9]

In this paper, we report the synthesis of new fluorene derivatives **5** having benzotriazole as a substituent *via in situ* formation of the heterocyclic ring. Introduction of sulfonic acid group to **5** gave water-soluble benzotriazole-substituted fluorenes **6**. Benzotriazole ring-containing compounds have been reported to show various biological activities such as potential inhibitors of protein kinase CK2,[24] cytosolic phospholipase $A_2\alpha$,[25] and cytochrome P450 14α-demethylase.[26]



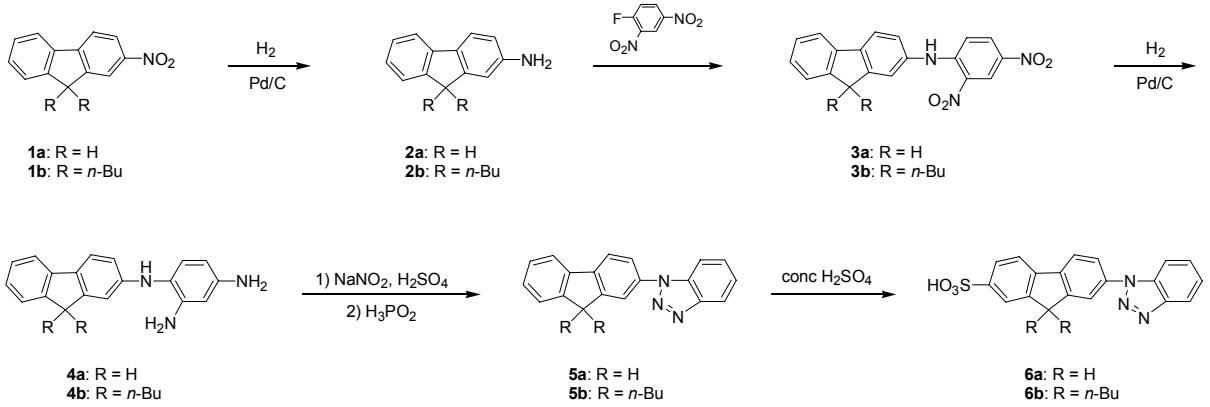
5a: R = H
5b: R = *n*-Bu



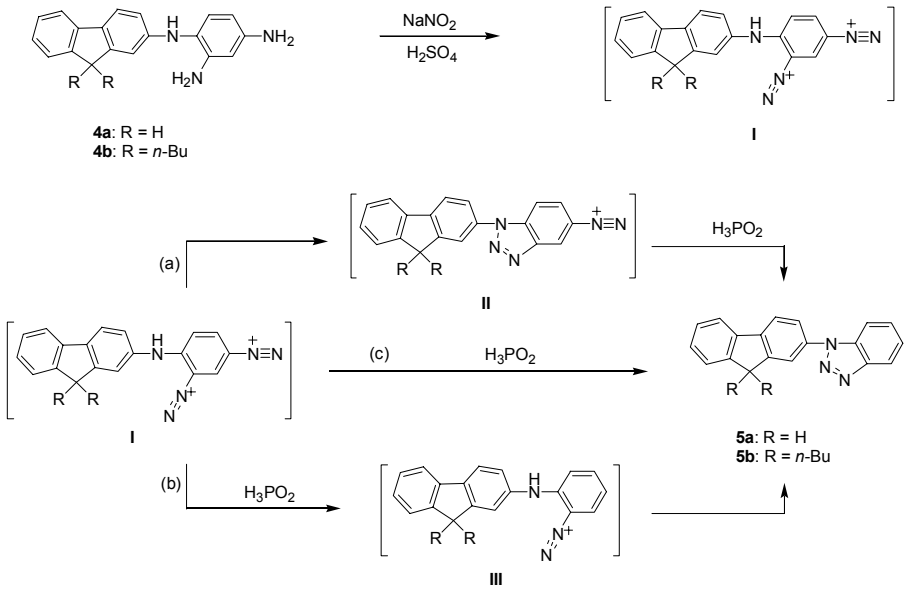
6a: R = H
6b: R = *n*-Bu

Results and Discussion

The synthetic pathway for the fluorene derivatives bearing benzotriazole substituent starting from 2-nitrofluorene **1a** or 2-nitro-9,9-dibutylfluorene **1b** is shown in Scheme 1. The compound **1b** was prepared by reacting **1a** with *n*-butyl bromide in DMF using cesium carbonate as a base as described previously.[13] Reduction of nitro group of **1a-b** with atmospheric hydrogen gas in the presence of 5% Pd/C at room temperature provided the corresponding 2-aminofluorenes **2a-b** in 85 ~ 96% yields. Nucleophilic aromatic substitution of 2,4-dinitrofluorobenzene with 2-aminofluorenes **2a-b** in DMSO at room temperature yielded 2-(*N*-2,4-dinitrophenyl)aminofluorene compounds **3a-b** in 90 ~ 97% yields. Catalytic reduction of the two nitro groups of **3a-b** with atmospheric hydrogen gas in the presence of 5% Pd/C at room temperature gave the corresponding 2-(*N*-2,4-diaminophenyl)aminofluorene compounds **4a-b**. Treatment of **4a-b** with $NaNO_2/H_2SO_4$ at 0 ~ 5 °C followed by treatment with H_3PO_2 at 0 ~ 5 °C and then room temperature gave 1-(fluoren-2-yl)-benzo[*d*][1,2,3]triazoles **5a-b**. The overall yields of **5a-b** starting from **3a-b** were 30 ~ 32%. Sulfonation of **5a-b** with concentrated sulfuric acid at room temperature provided 7-benzotriazol-1-yl-fluorene-2-sulfonic acids **6a-b** in 78 ~ 97% yields. The structures of all the new compounds were characterized by ^{1}H NMR, ^{13}C NMR, and elemental analysis except for **4a-b**: elemental analysis of **4a-b** was not carried out due to their lack of enough stability.



Scheme 1. Synthetic pathway of benzotriazolyl fluorene derivatives



Scheme 2. Possible mechanisms for conversion of **4a-b** to **5a-b**

The conversion of **4a-b** to **5a-b** indicates that the introduction of benzotriazole moiety as a substituent of the fluorene ring is accomplished through *in situ* formation of the heterocycle. It seems to occur *via* diazotization of both amino groups to diazonium group to give intermediate **I** and then the reaction of *p*-diazonium group with hypophosphorus acid and the coupling of *o*-diazonium group with the adjacent secondary amino group at the 2-position of the fluorene ring. The possible mechanisms for the transformation are shown in Scheme 2: the replacement of the diazonium group by hydrogen atom and the coupling reaction to form the triazole ring can occur sequentially as shown in (a) and (b) or concurrently as in (c). The exact mechanism of the reaction is not clear at this point, and its clarification is beyond the scope of this work. We also attempted the reaction of 2-aminofluorenes **2a-b** with 2-nitrofluorobenzene instead of 2,4-dinitrofluorobenzene for the synthesis of **5a-b**, but the nucleophilic substitution reaction of the former compound by 2-aminofluorenes was quite sluggish even at 100 ~ 110 °C and gave complex mixtures.

It is worth to mention that ^{1}H NMR spectra of 9,9-dibutylated fluorene compounds **1b-6b** show interesting features in the alkyl region. All of them show a similar pattern of the peaks corresponding to the butyl groups, which are composed of four-proton multiplet (for the compounds **1b**,[13] **2b**, **4b**, and **5b**) or quintet (for **3b** and **6b**) at δ 0.4-0.7, six-proton triplet at δ 0.6-0.7, four-proton sextet at δ 1.0-1.1, and four-proton multiplet at δ 1.7-2.2. The portion of the spectrum of **5b** is given as a typical example in Figure 1. One noticeable feature of the butyl peaks of **1b-6b** is the unusually up-field multiplet (or quintet) at δ 0.4-0.7 (-$CH_2$$\underline{CH_2}$$CH_2CH_3$) and triplet at δ 0.6-0.7 (-$CH_2CH_2CH_2$$\underline{CH_3}$). These up-field shifts indicate that these protons lie in the shielding region generated by ring current of the aromatic nucleus.[27a] The other feature is the multiplet signal at δ 1.7-2.2 (-$\underline{CH_2}CH_2$ CH_2CH_3) rather than a usual triplet, which implies that the protons are diastereotopic. The diastereotopic protons have different chemical shifts and the proton is split by the other proton attached to the same carbon as well as the two protons attached to the next carbon.[27b] The peaks at δ 1.97-2.18 in Figure 1 can be viewed as two separate peaks centered at δ 2.02 and 2.12, respectively, and each peak is split into a doublet (by the other

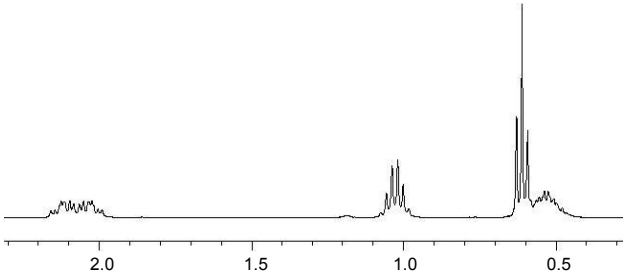


Figure 1. The portion of the ^{1}H NMR spectrum corresponding to the butyl group of **5b**.

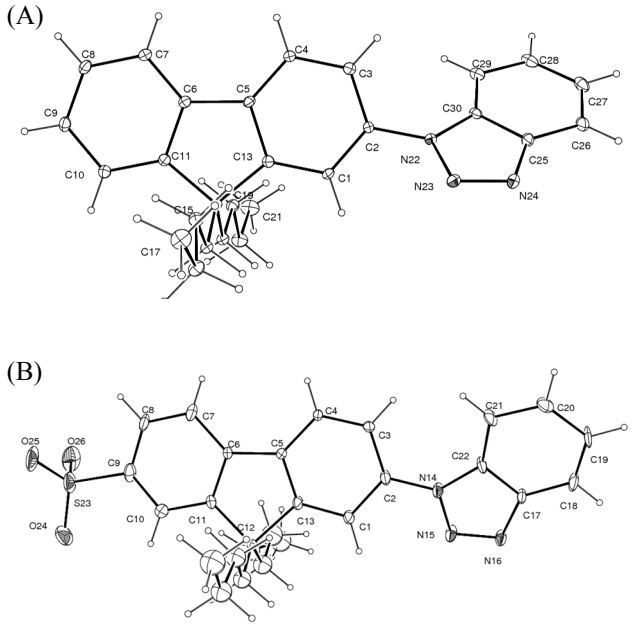


Figure 2. ORTEP diagrams of the compounds **5b** (A) and **6b** (B).

proton attached to the same carbon) of a triplet (by the two protons attached to the next carbon). It turned out that the methylene protons (-$CH_2\underline{CH_2}CH_2CH_3$) next to the aforementioned methylene group appear either as a multiplet (for the compounds **1b**,[13] **2b**, **4b**, and **5b**) or as a quintet (for **3b** and **6b**) at δ 0.4-0.7 depending on the detailed structure of the compound.

The structures of 1-(9,9-dibutylfluoren-2-yl)-benzo[*d*][1,2,3] triazole **5b** and 7-benzotriazol-1-yl-9,9-dibutylfluorene-2-sulfonic acid **6b** were further confirmed by single crystal X-ray analysis and their ORTEP diagrams are shown in Figure 2.[28] The fluorene ring is slightly puckered and benzotriazole ring is planar, and the two rings are twisted with a dihedral angle of 43.5° and 25.3° for **5b** and **6b**, respectively. It also shows that the protons of the methyl group (-$CH_2CH_2CH_2\underline{CH_3}$) and the methylene group (-$CH_2\underline{CH_2}CH_2CH_3$) separated by one carbon to the methyl group lie above the carbon atoms of the aromatic ring, justifying the aforementioned up-field shifts of those protons in the ^{1}H NMR spectra.

Conclusions

New fluorene derivatives **5a-b** having benzotriazole as a substituent were prepared *via in situ* formation of the heterocyclic ring, starting from 2-nitrofluorene. Sulfonation of **5a-b** with concentrated sulfuric acid yielded 7-benzotriazol-1-yl-fluorene-2-sulfonic acids **6a-b**. Their structures were characterized by ^{1}H NMR, ^{13}C NMR, and elemental analysis, and the structures of **5b** and **6b** were further confirmed by single crystal X-ray analysis. Fluorene derivatives and benzotriazole compounds are known to have various useful photophysical and biological properties, respectively, and thus the fluorene derivatives having benzotriazole substituent prepared in this study are expected to exhibit interesting characteristics.

Experimental

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained at 400 and 100 MHz, respectively, using tetramethylsilane (in $CDCl_3$) or residual undeuterated solvent (in DMSO-d_6 and CD_2Cl_2) as an internal standard. Elemental analyses were carried out at Chungnam National University Center for Research Facilities.

Preparation of 2-amino-9,9-dibutylfluorene 2a-b. 2-Nitrofluorene **1a** or **1b**[13] (1.0 g) in methanol (10 mL) was reacted with atmospheric hydrogen gas in the presence of 5% Pd/C (0.50 g) at room temperature for 5 h. The reaction mixture was filtered, concentrated, and then purified by silica gel column chromatography (eluent : hexane : ethyl acetate = 4 : 1 for **2a**; hexane-ethyl acetate = 30 : 1 and then ethyl acetate for **2b**) to give 2-aminofluorenes (**2a**: 0.73 g, 85%; **2b**: 0.88 g, 96%) as pale yellow solids. **2a** is also commercially available.

2a: mp 133 ~ 134 °C (lit[29] 128 ~ 129 °C); ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 3.73 (s, 2H), 5.19 (s, 2H), 6.59 (d, 1H, *J* = 8.0 Hz), 6.77 (s, 1H), 7.10 (t, 1H, *J* = 7.4 Hz), 7.25 (t, 1H, *J* = 7.2 Hz), 7.42 (d, 1H, *J* = 7.6 Hz), 7.50 (d, 1H, *J* = 8.0 Hz), 7.59 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 36.2, 110.4, 112.8, 117.9, 120.5, 124.3, 124.7, 126.5, 129.6, 141.6, 142.3, 144.6, 148.4.

2b: mp 93 ~ 94 °C; ^{1}H NMR ($CDCl_3$) δ 0.54-0.70 (m, 4H), 0.67 (t, 6H, *J* = 7.2 Hz), 1.07 (sextet, 4H, *J* = 7.2 Hz), 1.82-1.97 (m, 4H), 3.69 (broad s, 2H), 6.66 (dd, 1H, *J* = 8.4, 2.0 Hz), 6.67 (s, 1H), 7.18 (t, 1H, *J* = 7.2 Hz), 7.24-7.28 (m, 2H), 7.48 (d, 1H, *J* = 8.0 Hz), 7.54 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.8, 23.1, 25.9, 40.4, 54.7, 109.9, 114.0, 118.3, 120.4, 122.5, 125.3, 126.5, 132.6, 141.5, 145.7, 149.7, 152.6. Anal. Calcd for $C_{21}H_{27}N$: C, 85.95; H, 9.27; N, 4.77. Found: C, 86.33; H, 9.51; N, 4.86.

Preparation of 2-(*N*-2,4-dinitrophenyl)aminofluorene compounds 3a-b. To a stirred solution of **2a-b** (0.5 g) in DMSO (5.0 mL) was added 2,4-dinitrofluorobenzene (1.1 molar ratio) under a nitrogen atmosphere and stirring was continued for 4 h at room temperature. The reaction mixture was diluted with cold water (20 mL), and then filtered. The collected precipitate was washed with cold water and then cold methanol, and dried under vacuum to give 2-(*N*-2,4-dinitrophenyl)aminofluorene compounds (**3a**: 0.87 g, 90%; **3b**: 0.76g, 97%) as pale yellow solids.

3a: mp 220 ~ 223 °C; ^{1}H NMR (CD_2Cl_2, residual solvent peak δ = 5.32) δ 3.98 (s, 2H), 7.23 (d, 1H, *J* = 9.6 Hz), 7.33-7.38 (m, 2H), 7.42 (t, 1H, *J* = 7.6 Hz), 7.51 (s, 1H), 7.60 (d,

1H, J = 7.6 Hz), 7.83 (d, 1H, J = 7.2 Hz), 7.90 (d, 1H, J = 8.0 Hz), 8.16 (dd, 1H, J = 9.2, 2.8 Hz), 9.15 (d, 1H, J = 2.8 Hz), 10.05 (broad s, 1H); ^{13}C NMR (CD_2Cl_2, solvent peak δ = 53.8) δ 37.3, 116.7, 120.4, 121.4, 122.6, 124.3, 124.6, 125.5, 127.3, 127.6, 130.1, 131.4, 135.6, 137.5, 140.8, 141.5, 143.8, 145.7, 147.7. Anal. Calcd for $C_{19}H_{13}N_3O_4$: C, 65.70; H, 3.77; N, 12.10. Found: C, 65.72; H, 4.15; N, 11.95.

3b: mp 193 ~ 194 °C; ^{1}H NMR (CD_2Cl_2, residual solvent peak δ = 5.32) δ 0.62 (quintet, 4H, J = 8.0 Hz), 0.69 (t, 6H, J = 7.6 Hz), 1.10 (sextet, 4H, J = 7.4 Hz), 1.93-2.07 (m, 4H), 7.21 (d, 1H, J = 9.6 Hz), 7.29-7.31 (m, 2H), 7.35-7.41 (m, 3H), 7.75 (d, 1H, J = 8.0 Hz), 7.82 (d, 1H, J = 8.8 Hz), 8.16 (dd, 1H, J = 9.6, 2.8 Hz), 9.16 (d, 1H, J = 2.8 Hz), 10.06 (broad s, 1H); ^{13}C NMR (CD_2Cl_2, solvent peak δ = 53.8) δ 14.0, 23.3, 26.4, 40.3, 55.7, 116.7, 120.2, 120.6, 121.3, 123.4, 124.4, 124.6, 127.4, 128.0, 130.1, 131.5, 136.0, 137.7, 140.3, 141.1, 147.8, 151.2, 153.4. Anal. Calcd for $C_{27}H_{29}N_3O_4$: C, 70.57; H, 6.36; N, 9.14. Found: C, 70.96; H, 6.17; N, 9.15.

Preparation of 1-(fluoren-2-yl)-benzo[*d*][1,2,3]triazoles 5a-b. 2-(*N*-2,4-Dinitrophenyl)aminofluorene compounds **3a-b** (0.50 g) in methanol (10 mL) was reacted with atmospheric hydrogen gas in the presence of 5% Pd/C (0.25 g) at room temperature for 5 h. Filtration and concentration of the reaction mixture gave **4a-b**, which was used in the next step without further purification.

4a: ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 3.72 (s, 2H), 4.48 (broad s, 2H), 4.69 (broad s, 2H), 5.87 (dd, 1H, J = 8.4, 2.4 Hz), 6.03 (1H, d, J = 2.4 Hz), 6.59 (dd, 1H, J = 8.0, 1.6 Hz), 6.65 (d, 1H, J = 8.0 Hz), 6.67 (s, 1H), 6.93 (s, 1H), 7.10 (t, 1H, J = 7.4 Hz), 7.25 (t, 1H, J = 7.4 Hz), 7.42 (d, 1H, J = 7.2 Hz), 7.53 (d, 1H, J = 8.4 Hz), 7.60 (d, 1H, J = 7.6 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 36.3, 100.6, 103.6, 109.1, 112.2, 116.3, 118.0, 120.3, 124.3, 124.7, 126.5, 128.1, 130.1, 141.7, 142.1, 144.4, 145.2, 147.0, 148.4.

4b: ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 0.43-0.63 (m, 4H), 0.64 (t, 6H, J = 7.2 Hz), 1.03 (sextet, 4H, J = 7.2 Hz), 1.72-1.92 (m, 4H), 4.47 (broad s, 2H), 4.67 (broad s, 2H), 5.86 (d, 1H, J = 8.0 Hz), 6.03 (s, 1H), 6.50 (d, 1H, J = 8.0 Hz), 6.60 (s, 1H), 6.67 (d, 1H, J = 8.0 Hz), 6.90 (s, 1H), 7.10 (t, 1H, J = 7.4 Hz), 7.19 (t, 1H, J = 7.2 Hz), 7.28 (d, 1H, J = 7.2 Hz), 7.44 (d, 1H, J = 8.0 Hz), 7.51 (d, 1H, J = 7.6 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 13.8, 22.5, 25.8, 39.6, 54.0, 100.8, 103.6, 107.3, 112.0, 116.6, 117.8, 120.3, 122.3, 124.7, 126.6, 126.9, 129.5, 141.6, 144.6, 146.6, 148.1, 149.0, 151.4.

4a-b (0.33 g) was added to an aqueous sulfuric acid solution (prepared by mixing 1 mL of 98 wt % sulfuric acid and 3 mL of distilled water), stirred at room temperature for 0.5 h, and then cooled to 0 ~ 5 °C. To this was added slowly an aqueous solution (1.5 mL) of $NaNO_2$ (2.5 molar ratio), stirred for 0.5 h, and then added H_3PO_2 (50 wt %, 5.0 mL) and stirred for 6 h maintaining the temperature at 0 ~ 5 °C. After further stirring at room temperature for 16 h, the reaction mixture was diluted with distilled water (10 mL) and then extracted with dichloromethane (4 × 20 mL). The combined organic layers were dried, concentrated, and then purified by column chromatography (eluent : hexane : ethyl acetate = 4 : 1 for **5a**; 10 : 1 for **5b**) to give 1-(fluoren-2-yl)-benzo[*d*][1,2,3]triazoles (**5a**: 0.13 g, 32% based on **3a**; **5b**: 0.13 g, 30% based on **3b**) as pale yellow solids.

5a: mp 150 ~ 152 °C; ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 4.10 (s, 2H), 7.39 (dt, 1H J = 7.6, 1.2 Hz), 7.45 (t, 1H, J = 7.6 Hz), 7.53 (t, 1H, J = 7.6 Hz), 7.64-7.69 (m, 2H), 7.89 (dd, 1H, J = 8.0, 2.0 Hz), 7.99 (t, 1H, J = 8.4 Hz), 8.03 (d, 1H, J = 8.0 Hz), 8.08 (d, 1H, J = 2.0 Hz), 8.19 (d, 1H, J = 8.0 Hz), 8.20 (d, 1H, J = 8.4 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 36.7, 111.1, 119.7, 119.9, 120.6, 121.2, 121.8, 124.7, 125.3, 127.0, 127.5, 128.7, 132.0, 134.9, 140.0, 141.6, 143.6, 144.9, 145.7; LCMS m/z (relative intensity), 113.2 (6), 282.3 (6), 284.1 (MH^+, 100), 285.1 (20). Anal. Calcd for $C_{19}H_{13}N_3$: C, 80.54; H, 4.62; N, 14.83. Found: C, 80.37; H, 4.91; N, 14.65.

5b: mp 129 ~ 131 °C; ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 0.46-0.60 (m, 4H), 0.61 (t, 6H, J = 7.2 Hz), 1.03 (sextet, 4H, J = 7.2 Hz), 1.97-2.18 (m, 4H), 7.37-7.40 (m, 2H), 7.47-7.50 (m, 1H), 7.53 (t, 1H, J = 7.6 Hz), 7.69 (t, 1H, J = 7.6 Hz), 7.83 (dd, 1H, J = 8.4, 2.0 Hz), 7.90 (d, 1H, J = 8.4 Hz), 7.92-7.95 (m, 1H), 7.96 (d, 1H, J = 1.6 Hz), 8.10 (d, 1H, J = 8.0 Hz), 8.21 (d, 1H, J = 8.4 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 13.7, 22.3, 25.8, 39.0, 55.2, 111.0, 117.7, 119.7, 120.4, 121.1, 121.8, 123.0, 124.7, 127.1, 127.9, 128.7, 131.9, 135.3, 139.4, 141.1, 145.8, 150.5, 152.1; LCMS m/z (relative intensity), 282.3 (15), 396.3 (MH^+, 100), 397.2 (28). Anal. Calcd for $C_{27}H_{29}N_3$: C, 81.99; H, 7.39; N, 10.62. Found: C, 81.61; H, 7.57; N, 10.75.

Crystal data for 5b:[28] crystal color, colorless; habit, plate; crystal dimensions, 0.11 × 0.10 × 0.03 mm^3; crystal system, monoclinic; space group, $P2_1/n$; cell parameters, a = 8.9243(8) Å, b = 25.137(2) Å, c = 10.4656(11) Å , α = 90.0, β = 98.78(1), γ = 90.0; V = 2320.2(4) Å^3; λ (Mo-Kα) = 0.71073 Å; $R_1(I > 2\sigma(I))$ = 0.070.

Preparation of 7-benzotriazol-1-yl-fluorene-2-sulfonic acids 6a-b. A reaction mixture of 1-(fluoren-2-yl)-benzo[*d*][1,2,3] triazole **5a-b** (60 mg) and concentrated sulfuric acid (0.5 mL, Aldrich, 99.999 wt %) was stirred at room temperature for 5 h and then poured slowly into icy water (5.0 mL) to obtain precipitates. The precipitates were filtered, washed with cold water, and put in water and then basified with saturated Na_2CO_3 solution to obtain a clear solution. The solution was acidified with 2 N HCl to produce precipitates, which were filtered, washed with water and then vacuum-dried to give **6a** (60 mg, 78%) as pale yellow solid. In case of **6b**, the reaction mixture diluted with icy water was extracted with ethyl acetate (4 × 5 mL). The organic layers were dried, concentrated, and then purified by column chromatography (eluent : hexane : ethyl acetate = 4 : 1) to give **6b** (70 mg, 97%) as pale yellow solid.

6a: mp 287 °C (dec); ^{1}H NMR (DMSO-d_6, residual solvent peak δ = 2.50) δ 4.12 (s, 2H), 7.54 (t, 1H, J = 7.4 Hz), 7.66-7.72 (overlapped d + t, 2H), 7.89-7.91 (overlapped s + d, 2H), 7.99 (d, 1H, J = 8.4 Hz), 8.02 (d, 1H, J = 8.4 Hz), 8.10 (s, 1H), 8.20 (d, 1H, J = 8.0 Hz), 8.21 (d, 1H, J = 8.4 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 36.8, 111.2, 119.7, 119.8, 120.0, 121.5, 121.9, 122.6, 124.7, 124.8, 128.8, 132.0, 135.0, 140.1, 141.2, 143.2, 145.6, 145.8, 147.5. Anal. Calcd for $C_{19}H_{13}N_3O_3S \cdot 3H_2O$: C, 54.67; H, 4.59; N, 10.07; S, 7.68. Found: C, 54.64; H, 4.35; N, 10.02; S, 7.70.

6b: mp 174 °C (dec); ^{1}H NMR (DMSO-d_6, residual solvent

peak δ = 2.50) δ 0.56 (quintet, 4H, J = 7.6 Hz), 0.64 (t, 6H, J = 7.4 Hz), 1.07 (sextet, 4H, J = 7.6 Hz), 1.98-2.18 (m, 4H), 7.54 (t, 1H, J = 7.6 Hz), 7.66-7.72 (overlapped s + d + t, 3H), 7.84 (d, 1H, J = 8.4 Hz), 7.91 (d, 2H, J = 8.4 Hz), 7.98 (s, 1H), 8.11 (d, 1H, J = 8.4 Hz), 8.21 (d, 1H, J = 8.0 Hz); ^{13}C NMR (DMSO-d_6, solvent peak δ = 39.5) δ 13.8, 22.4, 25.8, 39.3, 55.3, 111.0, 117.8, 119.70, 119.74, 119.9, 121.4, 121.9, 124.8, 125.1, 128.7, 132.0, 135.4, 139.6, 140.6, 145.8, 148.0, 150.0, 152.7. Anal. Calcd for $C_{27}H_{29}N_3O_3S{\cdot}3H_2O$: C, 61.23; H, 6.66; N, 7.93; S, 6.05. Found: C, 61.11; H, 6.67; N, 7.74; S, 6.04.

Crystal data for 6b:[28] crystal color, colorless; habit, block; crystal dimensions, 0.10 × 0.10 × 0.05 mm^3; crystal system, triclinic; space group, P-1; cell parameters, a = 9.5199(19) Å, b = 12.255(3) Å, c = 25.823(5) Å, α = 79.61(3), β = 85.49(3), γ = 77.95(3); V = 2895.3(10) Å^3; λ (Mo-Kα) = 0.71073 Å; R_1 ($I > 2\sigma(I)$) = 0.175.

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