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# Pyridylazulenes: Synthesis, Color Changes, and Structure of the Colored Product

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A facile method for the synthesis of 1- and 2-pyridylazulenes, and of 1,3-dipyridylazulenes, is described. Color and spectral changes of these pyridylazulenes upon the addition of either acid or metal ions were investigated in detail. The color changed from blue to red upon the addition of trifluoroacetic acid or soft metal ions, depending on the substitution patterns of the pyridyl group on the azulene skeleton. The structures of the protonated or coordinated products were examined on the basis of the spectral data. It was found that the protonation or coordination of metal ions occurred on the nitrogen atom of the pyridine ring, but not on the carbon atom of azulene ring. The transition intervals of several pyridylazulenes for use as pH indicators were also determined.

## Introduction

Azulene is a non-alternant hydrocarbon well-known for its characteristic blue color. The blue color is caused by the compound's unusually low-lying first excited state ($S_1$), which is due to the small repulsive interaction between the two electrons in the nearly orthogonal HOMO and LUMO orbitals.[1] Azulene's unusual photophysical properties have stimulated significant research into the absorption spectra of azulene derivatives.[2]

Reactions that undergo color changes are important indicators in acid−base titrations, chelatometry, etc. Although it is well-known that adding protic acid or metal ions to azulene derivatives results in a color change,[3] little is known about the investigation on the structure of the colored product. The preparation of much simpler azulene derivatives that undergo a color change would be significant for furthering our understanding of azulenic chromophores, and for their commercialization as analytical reagents. Recent research on the synthetic

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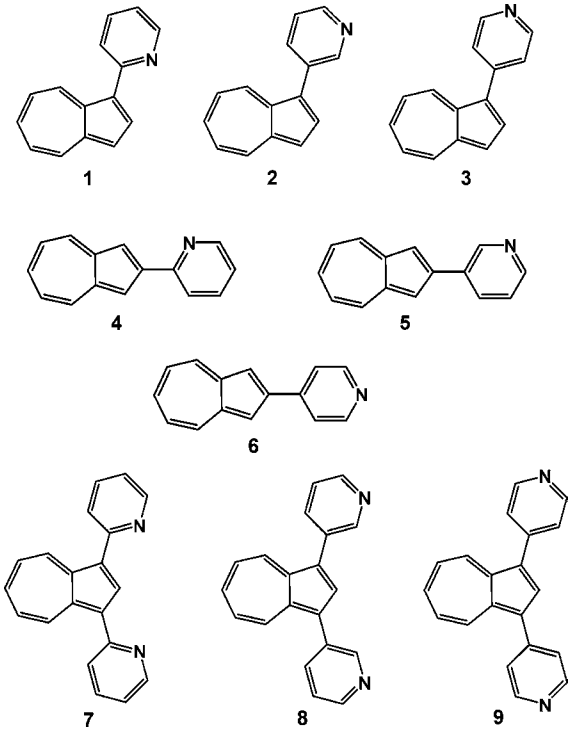
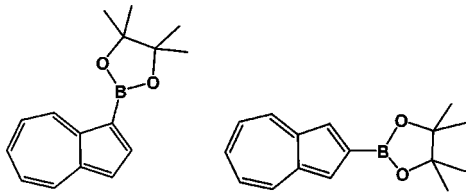
method of azulene derivatives[4] provides a facile route for synthesizing 1- and 2-pyridylazulenes, which potentially have utility as colorimetric reaction indicators. Comparing the color reactions of 1- and 2-pyridylazulene is attractive, because of the different locations of electrons in the HOMO and LUMO orbitals.[1,3g−i] In addition, investigation of color changes of 1,3-dipyridylazulenes is also of interest because successive influences on the azulenic chromophore by the two pyridyl groups, leading to multistep color changes, are expected. This paper describes the synthesis of 1- and 2-pyridylazulenes **1**−**6** and 1,3-dipyridylazulenes **7**−**9**, as well as the systematic studies on their color and UV/vis spectral changes upon the addition of either acid or metal salts. The structure of the colored product, preliminary applications of these azulenic chromophores as pH indicators, and simple rationalizations of the observed color changes are also presented.




## Results and Discussion

**Synthesis of Pyridylazulenes.** The synthesis of monopyridylazulenes **1** and **4**−**6** has been reported by Kuroda[5] and Yasunami,[6] respectively. However, these methods require multistep reactions and provide low overall yields. We chose the boryl-substituted azulene **10**[4c] as starting material for the synthesis of **1**−**3**, but not the halogenated ones, because 1-halogenated azulenes are unstable.[7] Compounds **1**−**6** could be easily prepared using the similar strategy in only one step from **10** or **11**.[4c] Thus, Suzuki coupling[8] of **10** with 2-bromopyridine, 3-bromopyridine, and 4-bromopyridine provided 1-substituted azulenes **1** (yield 52%, blue oil),[5] **2** (yield 60%, blue crystals, mp 81−83 °C), and **3** (yield 71%, blue crystals, mp 49−50 °C), respectively. The reaction of **11** with the corresponding bromopyridine provided 2-substituted azulenes as blue crystals (**4**, yield 33%, mp 116−118 °C; **5**, yield 92%, mp 182−183 °C; **6**, yield 81%, mp >200 °C).[6]




The synthesis of 1,3-dipyridylazulenes was achieved using Stille coupling[9] of 1,3-diiodoazulene[10] and 2.2 equiv of 2-(tri-*n*-butylstannyl)pyridine, 3-(trimethylstannyl)pyridine,[11] or 4-(trimethylstannyl)pyridine[11] in the presence of cesium fluoride and copper iodide(I) to form **7** (yield 35%, blue oil), **8** (yield 51%, green crystals, mp 120−122 °C), and **9** (yield 38%, green crystals, mp >200 °C), respectively. The expected structures of **1**−**9** were fully supported by spectral data and elemental analysis; in addition, **1** and **4**−**6** had been previously identified.[5,6] All of these pyridylazulenes were stable and showed no deterioration after storage for 1 year at −30 °C.

**Acid-Induced Color Changes.** We studied changes in the spectral properties and colors of **1**−**9** upon addition of a moderately strong organic acid, trifluoroacetic acid (p$K_a$ 0.3). Under these conditions, protonation of the pyridine moiety was expected to enhance its electron-withdrawing ability and influence the $\pi$-conjugate system of azulene.[12] For 1-pyridylazulenes **1** and **3**, and 1,3-dipyridylazulenes **7** and **9** (which contain either the 2-pyridyl or the 4-pyridyl group), the addition of trifluoroacetic acid gradually produced a color change from blue to red. Upon the addition of 20 equiv of trifluoroacetic acid, UV/vis spectra showed strong blue-shifting of the $S_1$ band by 45 nm ($\Delta(\lambda^{-1}) = 1425$ cm$^{-1}$; **1**), 37 nm (1167 cm$^{-1}$; **3**), 67 nm (2164 cm$^{-1}$; **7**), and 53 nm (1900 cm$^{-1}$; **9**) with small changes in the $S_2$ and $S_3$ bands. Representative spectral and color changes are shown in Figure 1. It was found that the introduction of two pyridyl groups onto the azulene skeleton did not cause a two-step color change; moreover, the observed blue-shift did not reach twice the magnitude of that observed with monopyridylazulene.

1-(3-Pyridyl)azulene (**2**) and 1,3-di(3-pyridyl)azulene (**8**) showed relatively small blue shifts of 25 nm (750 cm$^{-1}$) and 40 nm (1170 cm$^{-1}$) with 20 equiv of trifluoroacetic acid, respectively. Neutralization of acidic solutions of **1**−**3** and **7**−**9**

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(11) Preparation of 3- or 4-(trimethylstannyl)pyridine: Yamamoto, Y.; Yanagi, A. *Chem. Pharm. Bull.* **1982**, *30*, 1731. Alternatively, we prepared these compounds from the reaction of 3- or 4-bromopyridine with *n*-butyllithium, followed by trimethylstannyl chloride.

(12) The basicity of pyridine (p$K_b$: 8.8) is considerably higher than that (p$K_b$: 16) of azulene. For azulene, see: Simon, W.; Naville, G.; Sulser, H.; Heilbronner, E. *Helv. Chim. Acta* **1956**, *132*, 1107.

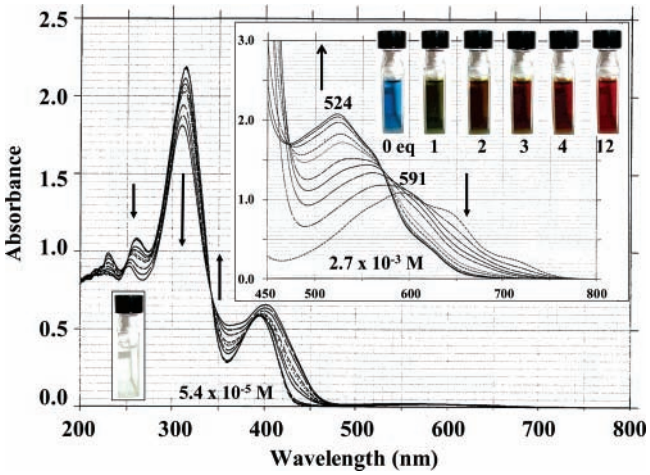
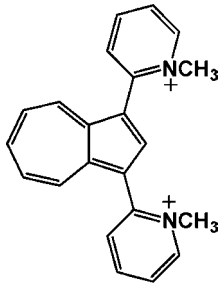



**FIGURE 1.** Spectral and color changes of **7** ($5.4 \times 10^{-5}$ M, $2.7 \times 10^{-3}$ M) upon the addition of trifluoroacetic acid in $CH_2Cl_2$, where the amount of trifluoroacetic acid varies from 1 to 20 equiv (1, 2, 3, 4, 6, 8, 12, 16, 20 equiv).

with triethylamine resulted in the color reverting back to blue, indicating that protonation is reversible. In contrast, little color change was observed by the naked eye for 2-pyridylazulenes **4**−**6**, although small red shifts (12, 7, 26 nm, respectively) were detected. Addition of a large excess (20−60 equiv) of trifluoroacetic acid to the compounds **1**−**9** did not cause any marked color change.

To gain further insight into the structures of the pyridylazulene protonated products, $^1$H, $^{13}$C, $^{19}$F NMR, and UV/vis (vide supra) analyses of **7** in the presence of trifluoroacetic acid were performed and compared to those of the azulenyl *N*-methylpyridinium ion (**12**), which could be easily prepared from the reaction of **7** and methyliodide.[13] Figures S-18 and S-19 in the Supporting Information show the $^1$H and $^{19}$F NMR spectra of a mixture of an equimolar amount of **7** and hexafluorobenzene in $CDCl_3$, where **7** was protonated by 5 equiv of trifluoroacetic acid, respectively. Four features in these spectra are noteworthy. (1) The broad singlet signal due to two N−*H*'s of the pyridinium ion moiety was observed at 13.62 ppm in the $^1$H NMR spectrum. The main aromatic protons shown in Figure S-18 were found to be slightly shifted downfield (0.2−0.4 ppm for H-2, H-5, H-6 of azulene skeleton, 0.2−0.7 ppm for pyridinium ion moiety) or upfield (0.7 ppm for H-4 of azulene skeleton) as compared to **7**.[14] Similar shifts were also observed in the $^1$H NMR spectrum of **12** (downfield shifts by 0.1−0.5 ppm for H-2, H-5, H-6 of azulene skeleton, upfield shift by 0.9 ppm for H-4 of azulene skeleton, and downfield shifts by 0.4−1.0 ppm for pyridinium ion moiety, see Figure S-20 in the Supporting Information). (2) All of the $^{13}$C NMR signals of both protonated **7** and **12** were observed around 120−153 ppm. (3) The fluorine signal of the trifluoroacetate ion was observed at 86.1 ppm relative to a hexafluorobenzene standard in the $^{19}$F NMR spectrum, and trifluoroacetate/protonated **7** was estimated to be 2.1 from the integrated areas (Figure S-19). (4) The UV/vis spectrum of pyridylazulene **7** protonated by trifluoroacetic acid over 10 equiv in methylene chloride is quite similar to that of **12** in methanol (see Figure 1 and Figure S-21 in the Supporting Information). These observations suggest two important points. First, the protonation occurs on the nitrogen atom of the pyridine ring, but not on the carbon atom of the five-membered ring of azulene affording the tropylium ion **13** (Scheme 1), even in the case of adding excess trifluoroacetic acid. Second, the diprotonated species **15** was easily formed in the presence of trifluoroacetic acid over 5 equiv.




**12**

The observed shifts in the UV/vis spectra should be easily explained by the perturbation of the HOMO or LUMO of the azulene skeleton, which was done by Liu.[3i] Thus, the blue-shift in 1-substituted azulenes **1**−**3** and 1,3-disubstituted azulenes **7**−**9** could be explained by stabilization of the HOMO of the azulene skeleton, caused by the electron-withdrawing ability of the pyridinium ion moiety, because the azulene skeleton has large coefficients at the 1- and 3-positions in the HOMO.[1,3g−i] In contrast, the red-shift in 2-substituted azulenes **4**−**6** can be explained by the stabilization of the LUMO of the azulene skeleton, caused by the electron-withdrawing ability of the pyridinium ion moiety, because the azulene skeleton has a large coefficient at the 2-position in the LUMO.[1,3g−i]

**Transition Interval.** The determination of the transition interval is of great importance if a compound is to be used as a pH indicator. Because of the poor solubility of pyridylazulenes under alkaline conditions, investigations were conducted in a 1:1 mixture of aqueous buffer solution (1% phthalate or phosphate) and methanol at a concentration of $3 \times 10^{-3}$ mol/L.[15] When the pH of the solution containing compounds **1**, **3**, and **7** was increased from 2 to 8, the color gradually changed from red to blue via violet or green, indicating that the transition intervals are 4.6−5.7 for **1**, 4.9−6.8 for **3**, and 4.0−5.8 for **7**. Typical colors for **1** at the various pH's are shown in Figure 2. These results suggest that some pyridylazulenes could be utilized as pH indicators, which are superior to the other azulene derivatives, for example, 1,3-diformylazulene showing the color change from red to yellow with trifluoroacetic acid,[3i] because the present color change is visually clear-cut.

Upon protonation, dipyridylazulene **7** is expected to form two species, the monocation **14** and the dication **15** (Scheme 1). To clarify the formation of **14** and **15**, the DFT calculation at the B3LYP/6-31G* level of theory was conducted to provide an

(13) We thank one of the referees for suggestions of NMR and UV/vis experiments of **12**, which are very informative with respect to the structure of the protonated product.

(14) The small signals in Figure S-18 might arise from the small amount of monoprotonated species.

(15) The pH solutions were prepared by adding HCl aq or NaOH aq to 1:1 mixtures of aqueous buffer solution (1% phthalate or phosphate) and methanol. Although the readings on the pH meter in mixed solvents should not represent the "true" pH values, the pH values shown in Figure 2 were measured by means of a pH meter, which was calibrated by using standard buffers at pH 4.10 (phthalate) and pH 6.86 (phosphate). When the experiment was carried out in an aqueous buffer, blue precipitates were formed above pH 5. However, the resulting transition interval was almost the same as in the mixture of aqueous buffer and methanol.

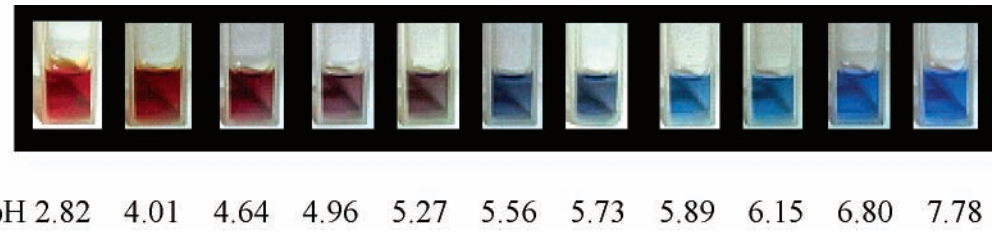
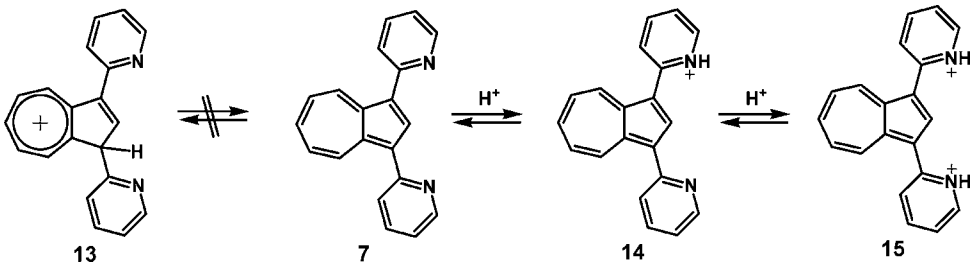



**FIGURE 2.** Colors of **1** in buffer (1% phthalate or phosphate)−methanol (1:1) solution at various pH's.

**SCHEME 1. Equilibrium of 7 in Acidic Solution**




estimate of the p$K_a$.[16] Interestingly, the calculated p$K_a$ values of **14** and **15** are almost the same (5.7 and 5.5, respectively), suggesting that the second protonation to form the diprotonated species might occur as easily as the monoprotonation step. Thus, it appears that **7** is in equilibrium with an approximately equal amount of **14** and **15** in the transition interval. Under more acidic conditions, the equilibrium seems to shift toward **15**.

**Color Changes Induced by Metal Salts.** The affinity of the pyridylazulenes for groups I ($Li^+$ and $Na^+$), II ($Ca^{2+}$), XII ($Zn^{2+}$, $Cd^{2+}$, $Hg^{2+}$), and XIV ($Pb^{2+}$) metal ions, and for transition metal ions ($Cr^{3+}$, $Cu^{2+}$), is of great interest because the $\pi$-conjugate system of azulene and the pyridine moiety in the pyridylazulene might serve as efficient Lewis bases for metal ions.[17]

Five metal ions ($Li^+$, $Na^+$, $Ca^{2+}$, $Zn^{2+}$, $Cd^{2+}$) were individually added in excess as nitrate salts. Negligible changes were observed in the absorption spectra of **1** and **7**−**9** dissolved in a mixture of acetone−water (2:1) or methanol−water (2:1). In contrast, **1** (blue), **7** (green), and **9** (green) turned red or reddish brown in acetone when a small amount of $Pb^{2+}$, $Hg^{2+}$, $Cu^{2+}$, and $Cr^{3+}$ ions was individually added as perchlorate salts.[18] For example, the absorption spectrum of **7** showed a substantial blue shift (ca. 65 nm) with 2 equiv of $Hg(ClO_4)_2$ (Figure 3). Strong interactions between the **7** and $Hg^{2+}$ ion are corroborated by MS studies of **7**·$Hg^{2+}$ complexes. ESI-TOF-MS of the **7**·$Hg^{2+}$ complex in acetone provided a weak charged peak at *m*/*z* 641, corresponding to [**7**·Hg·acetone·$ClO_4$]$^+$. The observed isotopic distribution was in close agreement with the theoretical one (see Figure S-43 in the Supporting Information). Furthermore, MALDI-TOF-MS measurement, using HABA [2-(4-hydroxyphenylazo)benzoic acid] as a matrix, afforded the heaviest mass at *m*/*z* 765 (weak intensity), corresponding to [**7**·Hg·**7** − H]$^+$. The observed and theoretical isotopic distributions were also in close agreement (see Figure S-44 in the Supporting Information). In contrast, **8** exhibited relatively small color changes from greenish blue to green or blackish green upon the addition of $Pb^{2+}$, $Hg^{2+}$, $Cu^{2+}$, and $Cr^{3+}$ ions, similar to that observed with trifluoroacetic acid, indicating that these metal ions have little or no interaction with the $\pi$-conjugate system of azulene.[19] The HSAB principle[20] may be helpful for rationalizing the trends observed with the cations tested: the relatively soft pyridine base is easily coordinated with soft acids such as $Pb^{2+}$ and $Hg^{2+}$ ions.[21]

In summary, a simple route for the synthesis of pyridylazulenes has been developed. In the presence of trifluoroacetic acid, azulene derivatives **1**, **3**, **7**, and **9** containing the 2-pyridyl or 4-pyridyl group at the 1- or 1,3-positions were a deep red color, in sharp contrast to derivatives **4**−**6** containing the pyridyl group at the 2-position. Pyridylazulenes **1**, **3**, and **7** might be useful as pH indicators. The addition of soft metal ions such as $Pb^{2+}$, $Hg^{2+}$, $Cu^{2+}$, and $Cr^{3+}$ to **1**, **7**, and **9** produced similar color changes, whereas little color change was effected by $Li^+$, $Na^+$, $Ca^{2+}$, $Zn^{2+}$, or $Cd^{2+}$ ion salts. The present color changes are caused by the protonation or coordination of metal ions on the nitrogen atom of the pyridine ring, but not on the carbon atom of azulene ring. Therefore, the present study may be helpful in the construction of novel analytical reagents bearing the azulenic chromophore.

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(18) The addition of nitrate instead of perchlorate salt afforded considerable brownish precipitate and a reddish-brown solution. The use of acetonitrile, methylene chloride, or aqueous methanol as solvent also provided a suspension, even when perchlorates were added. To the degree investigated, the addition of perchlorates in acetone gave clear red solutions.

(19) Even if a large excess of metal ions were added to the compounds, we could not see any marked color change due to the coordination on azulene ring. Otherwise, the reactions of pyridylazulenes with boron compounds were also examined. Among the various boron compounds studied, the addition of triethylborane to **1**, **7**−**9**, and the parent azulene resulted in a yellow color. However, analysis of the reaction mixture of azulene and triethylborane in $CH_2Cl_2$ and THF revealed the formation of unidentified compounds.

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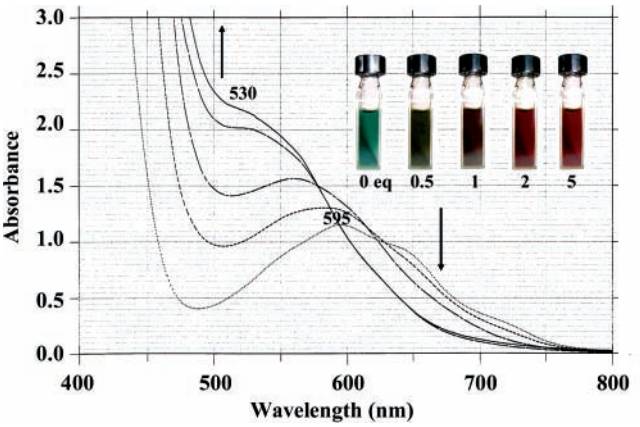


**FIGURE 3.** Spectral and color changes of **7** ($2.8 \times 10^{-3}$ M) upon the addition of $Hg(ClO_4)_2$ in acetone, where the amount of $Hg(ClO_4)_2$ varies from 0.5 to 5 equiv.

## Experimental Section

**Cross-Coupling Reactions: Typical Procedure A. 1-(2-Pyridyl)azulene (1).** The suspension of $(Ph_3P)_2PdCl_2$ (74 mg, 0.11 mmol), 2-(1-azulenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**10**)[4c] (190 mg, 0.75 mmol), $Ba(OH)_2$ $8H_2O$ (526 mg, 1.67 mmol), and 2-bromopyridine (200 mg, 1.27 mmol) in DME−$H_2O$ (50:1) (20 mL) was stirred at 95 °C for 2 h. The reaction mixture was poured into water (10 mL) and extracted with ethylacetate (40 mL, 20 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The crude product was subjected to silica gel column chromatography [silica gel (4 g), benzene → benzene-ether] to afford the blue oil **1** (80 mg, 52%) (lit.[5] purple oil).

$^1$H NMR (400 MHz, $CDCl_3$): 7.09−7.13 (m, 1H), 7.19 (t, 1H, $J$ = 9.8 Hz), 7.30 (t, 1H, $J$ = 9.8 Hz), 7.40 (d, 1H, $J$ = 4.1 Hz), 7.62 (t, 1H, $J$ = 9.8 Hz), 7.68−7.72 (m, 2H), 8.24 (d, 1H, $J$ = 4.2 Hz), 8.34 (d, 1H, $J$ = 9.5 Hz), 8.73 (d, 1H, $J$ = 4.6 Hz), 9.56 (d, 1H, $J$ = 10.0 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 117.8, 120.2, 123.0, 124.1, 125.1, 127.9, 136.3, 136.9, 137.4, 137.7, 138.5, 143.1, 149.3, 156.6. EIMS (70 eV): 205 ($M^+$, 55), 204 ($M^+ - 1$, 100%). The $^1$H, $^{13}$C NMR, and EIMS data matched those previously reported.[5] HRMS (EI): $m/z$ calcd for $C_{15}H_{11}N$ 205.0891, found 205.0938. IR (neat): 1586, 1561, 1505, 1476, 1456, 1397 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 237 ($\epsilon$ 19 500), 303 (27 000), 377 (12 100), 585 (350), 635 (sh), 705 nm (sh).

**1-(3-Pyridyl)azulene (2).** Yield: 60%; blue crystals; mp 81−83 °C. $^1$H NMR (300 MHz, $CDCl_3$): 7.21 (dt, 2H, $J$ = 11.8, 2.0 Hz), 7.41 (ddd, 1H, $J$ = 0.9, 5.0, 7.9 Hz), 7.47 (d, 1H, $J$ = 3.9 Hz), 7.64 (t, 1H, $J$ = 9.9 Hz), 7.90 (dt, 1H, $J$ = 1.7, 8.3 Hz), 8.02 (d, 1H, $J$ = 3.9 Hz), 8.39 (d, 1H, $J$ = 9.4 Hz), 8.49 (d, 1H, $J$ = 9.4 Hz), 8.58 (dd, 1H, $J$ = 1.7, 4.8 Hz), 8.88 (d, 1H, $J$ = 1.7 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): 117.8, 123.5, 123.7, 123.9, 127.2, 133.3, 135.2, 136.6, 137.0, 137.6, 138.5, 141.9, 147.3, 150.4. EIMS (70 eV): $m/z$ 205 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{15}H_{11}N$ 205.0891, found 205.0842. IR (KBr): 1588, 1570, 1509, 1478, 1414, 1402, 1314, 1293, 1192, 1022 cm$^{-1}$. UV/vis (EtOH): $\lambda_{max}$ 201 ($\epsilon$ 14 400), 235 (19 300), 295 (30 500), 347 (5810), 467 (7210), 587 (310), 637 (sh), 705 nm (sh). Anal. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.81; H, 5.32; N, 6.86.

**1-(4-Pyridyl)azulene (3).** Yield: 71%; blue crystals; mp 49−50 °C. $^1$H NMR (400 MHz, $CDCl_3$): 7.27 (dt, 2H, $J$ = 9.8, 3.2 Hz), 7.46 (d, 1H, $J$ = 3.9 Hz), 7.54 (dd, 2H, $J$ = 4.4, 1.5 Hz), 7.68 (t, 1H, $J$ = 9.8 Hz), 8.07 (d, 1H, $J$ = 3.9 Hz), 8.41 (d, 1H, $J$ = 9.5 Hz), 8.62 (d, 1H, $J$ = 9.8 Hz), 8.68 (dd, 2H, $J$ = 4.6, 1.7 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): 118.1, 124.0, 124.2, 124.4, 127.7, 135.1, 135.6, 137.0, 137.7, 138.6, 142.6, 144.9, 149.9. EIMS (70 eV): $m/z$ 205 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{15}H_{11}N$ 205.0891, found 205.0850. IR (KBr): 1592, 1572, 1395 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 237 ($\epsilon$ 22 800), 280 (21 600), 304 (32 600), 373 (10 900), 582 (380), 630 (sh), 700 nm (sh). Anal. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.47; H, 5.31; N, 6.84.

**2-(2-Pyridyl)azulene (4).** Yield: 33%; blue crystals; mp 116−118 °C. $^1$H NMR (400 MHz, $CDCl_3$): 7.15 (t, 2H, $J$ = 9.8 Hz), 7.21 (dd, 1H, $J$ = 4.9, 7.3 Hz), 7.53 (t, 1H, $J$ = 10.0 Hz), 7.74 (td, 1H, $J$ = 1.7, 7.8 Hz), 7.92 (s, 2H), 7.96 (d, 1H, $J$ = 8.1 Hz), 8.33 (d, 2H, $J$ = 9.5 Hz), 8.75 (d, 1H, $J$ = 4.6 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 115.5, 122.2, 122.5, 123.7, 136.5, 137.4, 137.5, 141.2, 148.9, 150.1, 154.7. EIMS (70 eV): $m/z$ 205 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{15}H_{11}N$ 205.0891, found 205.0906. IR (KBr): 1586, 1572, 1563, 1426, 1406, 1337, 1210, 1190 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 238 ($\epsilon$ 10 500), 298 (47 200), 310 (54 700), 366 (9770), 384 (13 000), 433 (86), 585 (350), 627 (350), 685 nm (160).

**2-(3-Pyridyl)azulene (5).** Yield: 92%; blue crystals; mp 182−183 °C. $^1$H NMR (400 MHz, $CDCl_3$): 7.20 (t, 2H, $J$ = 10.0 Hz), 7.38 (dd, 1H, $J$ = 4.6, 7.8 Hz), 7.57 (t, 1H, $J$ = 9.8 Hz), 7.68 (s, 2H), 8.19 (dt, 1H, $J$ = 1.7, 8.1 Hz), 8.33 (d, 2H, $J$ = 9.5 Hz), 8.33 (d, 2H, $J$ = 9.5 Hz), 8.57 (dd,1H, $J$ = 1.5, 4.9 Hz), 9.21 (d, 1H, $J$ = 2.0 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): 114.3, 123.8, 124.1, 132.2, 134.5, 136.7, 137.3, 141.3, 146.1, 148.88, 148.95. EIMS (70 eV): $m/z$ 205 ($M^+$, 100%). IR (KBr): 1588, 1541, 1458, 1410, 1211, 1019 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 238 ($\epsilon$ 14 000), 298 (59 300), 307 (60 900), 366 (10 000), 384 (12 300), 433 (190), 575 (400), 615 (400), 670 nm (180). Anal. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.70; H, 5.25; N, 6.74.

**2-(4-Pyridyl)azulene (6).** Yield: 81%; blue crystals; mp >200 °C. $^1$H NMR (400 MHz, $CDCl_3$): 7.21 (t, 2H, $J$ = 9.8 Hz), 7.60 (t, 1H, $J$ = 9.8 Hz), 7.71 (s, 2H), 7.79 (d, 2H, $J$ = 4.9 Hz), 8.35 (d, 2H, $J$ = 9.8 Hz), 8.69 (d, 2H, $J$ = 4.9 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 114.8, 121.8, 124.2, 128.3, 134.4, 137.6, 138.1, 141.2, 150.5. EIMS (70 eV): $m/z$ 205 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{15}H_{11}N$ 205.0891, found 205.0896. IR (KBr): 1595, 1576, 1541, 1410, 1219 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 237 ($\epsilon$ 10 000), 296 (36 700), 304 (37 900), 362 (6280), 379 (8370), 412 (220), 437 (310), 584 (240), 623 (250), 680 nm (110).

**Cross-Coupling Reactions: Typical Procedure B. 1,3-Di(2-pyridyl)azulene (7).** To the mixture of 1,3-diiodoazulene[10] (214 mg, 0.563 mmol), $Pd(PPh_3)_4$ (65 mg, 0.056 mmol), CuI (24 mg, 0.126 mmol), and CsF (335 mg, 2.21 mmol) was added a solution of 2-(tri-*n*-butylstannyl)pyridine (460 mg, 1.250 mmol) in DMF (6 mL). The mixture was bubbled with Ar for 15 min and stirred at 90 °C for 0.5 h. The reaction mixture was poured into water (20 mL) and extracted with ethylacetate (50 mL). The organic layer was washed with brine (20 mL × 2), dried over $MgSO_4$, and concentrated. The crude product (586 mg) was subjected to silica gel column chromatography [silica gel (7.7 g), ethylacetate-hexane (1:8 → 1:4 → 1:2)] to afford the blue oil **7** (56 mg, 35%). $^1$H NMR (400 MHz, $CDCl_3$): 7.17 (dt, 2H, $J$ = 4.9, 1.7 Hz), 7.36 (t, 2H, $J$ = 9.8 Hz), 7.68−7.80 (m, 5H), 8.58 (s, 1H), 8.76 (d, 2H, $J$ = 3.7 Hz), 9.56 (d, 2H, $J$ = 9.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 120.5, 123.3, 126.2, 127.4, 136.4, 137.0, 138.2, 139.0, 139.7, 149.4, 156.2. EIMS (70 eV): $m/z$ 282 ($M^+$, 100%), 204 ($M^+$ − pyridine, 63%). HRMS (EI): $m/z$ calcd for $C_{20}H_{14}N_2$ 282.1157, found 282.1192. IR (KBr): 1586, 1561, 1522, 1487, 1417, 1368, 782 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 260 ($\epsilon$ 20 200), 314 (40 600), 393 (10 900), 591 (400), 640 (320, sh), 728 nm (80, sh).

**1,3-Di(3-pyridyl)azulene (8).** Yield: 51%; green crystals; mp 120−122 °C. $^1$H NMR (400 MHz, $CDCl_3$): 7.25 (t, 2H, $J$ = 10.0 Hz), 7.45 (dd, 2H, $J$ = 7.8, 4.9 Hz), 7.69 (t, 1H, $J$ = 9.8 Hz), 7.94 (dt, 2H, $J$ = 7.8, 2.0 Hz), 8.12 (s, 1H), 8.52 (d, 2H, $J$ = 9.8 Hz), 8.63 (dd, 2H, $J$ = 4.9, 1.5 Hz), 8.91 (d, 2H, $J$ = 2.0 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 123.6, 124.7, 126.8, 132.7, 136.1, 136.8, 136.9, 137.3, 139.7, 147.7, 150.36, 150.42. EIMS (70 eV): $m/z$ 282 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{20}H_{14}N_2$ 282.1157, found 282.1114. IR (KBr): 1570, 1489, 1474, 1433, 1362, 1321, 1020, 806, 714 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 225 (18 300), 248 (23 100), 302 (36 500), 380 ($\epsilon$ 8700), 605 (360), 650 (310, sh), 730 nm (100,

sh). Anal. Calcd for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.63; H, 4.89; N, 9.81.

**1,3-Di(4-pyridyl)azulene (9).** Yield: 38%; green crystals; mp > 200 °C. $^1$H NMR (600 MHz, $CDCl_3$): 7.33 (t, 2H, $J$ = 10.3 Hz), 7.56 (d, 4H, $J$ = 5.9 Hz), 7.75 (t, 1H, $J$ = 9.8 Hz), 8.17 (s, 1H), 8.64 (d, 2H, $J$ = 9.6 Hz), 8.72 (d, 4H, $J$ = 4.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): 121.4, 124.3, 125.7, 127.7, 136.3, 136.9, 137.9, 140.1, 144.4, 150.0, 150.6. EIMS (70 eV): $m/z$ 282 ($M^+$, 100%). HRMS (EI): $m/z$ calcd for $C_{20}H_{14}N_2$ 282.1157, found 282.1102. IR (KBr): 1593, 1570, 1420, 1368, 1221, 992, 818, 745 cm$^{-1}$. UV/vis ($CH_2Cl_2$): $\lambda_{max}$ 245 ($\epsilon$ 24 100), 305 (39 300), 383 (9380), 590 (340), 635 (290, sh), 715 nm (90, sh).

**Reaction Product of 1,3-Di(2-pyridyl)azulene (7) and Trifluoroacetic Acid.** To a solution of **7** (11 mg, 0.037 mmol) in $CH_2Cl_2$ (1 mL) was added a solution of trifluoroacetic acid in $CDCl_3$ (0.539 M, 0.32 mL, 0.17 mmol) at room temperature. The successive coevaporations with benzene, $CHCl_3$, and acetone gave the reddish solid (20 mg). The addition of the solution of hexafluorobenzene in $CDCl_3$ (0.537 M, 0.070 mL, 0.037 mmol) followed by the $^1$H, $^{13}$C, and $^{19}$F NMR analyses afforded the following data. $^1$H NMR (600 MHz, $CDCl_3$): 7.62−7.75 (m, 4H), 8.05 (t, 1H, $J$ = 9.5 Hz), 8.19 (d, 2H, $J$ = 8.1 Hz), 8.39 (td, 2H, $J$ = 8.1, 1.5 Hz), 8.80 (s, 1H), 8.89 (d, 2H, $J$ = 9.9 Hz), 8.96 (d, 2H, $J$ = 5.9 Hz), 13.62 (bs, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$): 120.6, 123.2, 127.3, 130.4, 137.7, 140.1, 140.6, 142.6, 143.1, 144.3, 149.9. $^{19}$F NMR (560 MHz, $CDCl_3$, $C_6F_6$ as internal standard): 86.1.

**2,2′-(Azulene-1,3-diyl)bis(*N*-methylpyridinium)diiodide (12).** Methyliodide (750 $\mu$L, 12.1 mmol) was added dropwise to a stirred solution of **7** (38 mg, 0.135 mmol) in acetone (1 mL) at room temperature.[22] The mixture was stirred for 2 days at room temperature. Evaporation of the solvent gave a reddish brown solid (72 mg, 94%). $^1$H NMR (400 MHz, $CD_3OD$): 4.34 (s, 6H), 7.86 (t, 2H, $J$ = 10.0 Hz), 8.14 (t, 2H, $J$ = 6.3 Hz), 8.23 (t, 1H, $J$ = 10.0 Hz), 8.30 (d, 1H, $J$ = 7.8 Hz), 8.65 (d, 2H, $J$ = 7.8 Hz), 8.70 (d, 2H, $J$ = 10.0 Hz), 8.71 (s, 1H), 9.15 (d, 2H, $J$ = 6.1 Hz). $^{13}$C NMR (100 MHz, $CD_3OD$): 119.8, 127.6, 131.3, 133.3, 139.7, 140.7, 141.4, 143.9, 146.2, 148.6, 152.8. UV/vis ($CH_3OH$): $\lambda_{max}$ 282 ($\epsilon$ 23 700), 377 (12 800), 524 nm (620).

**General Procedures for the Titration Experiments by UV/Vis Spectroscopy.** Screw-capped quartz cells were used to prevent the volatilization of solvent and to mix up the samples. To a solution of azulene derivative in methylene chloride ($2 \times 10^{-3}$ M, 3 mL) was added a 2.23 M solution of trifluoroacetic acid in methylene chloride using a pipet at ambient temperature. After the solution was mixed, the changes of color were checked by the naked eye, and UV/vis spectra were measured.

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**Supporting Information Available:** General method, the detail for DFT calculations, $^1$H NMR spectra of **1**−**9**, protonated **7**, **12**, $^{19}$F NMR spectrum of protonated **7**, UV/vis spectra of **12**, colors of **3**, **7** at various pH's, UV/vis spectral and color changes of **1**−**9** with trifluoroacetic acid and metal ions, and ESI-TOF-MS, MALDI-TOF-MS spectra of **7** with $Hg(ClO_4)_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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