

The First Synthesis of 1-Fluoro- and 1,3-Difluoroazulenes

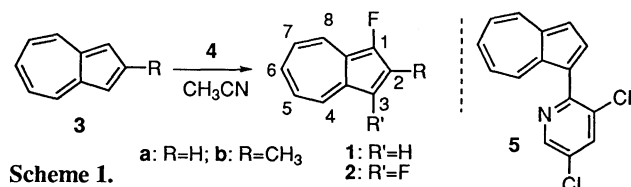
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(Received October 31, 1994)

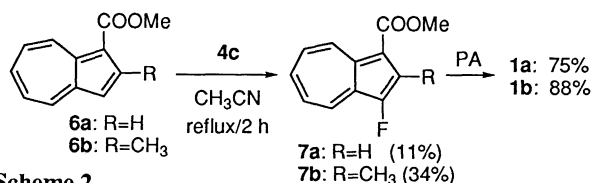
1-Fluoro- and 1,3-difluoroazulenes were synthesized by the reaction of azulene with *N*-fluoropyridinium salts in acetonitrile. Methyl azulene-1-carboxylates were also fluorinated to give the corresponding 3-fluoro derivatives. On the basis of the UV-visible absorption spectra, the fluorine atom acts as an electron-donating group to the azulene π -system due to the $+\pi$ effect.

Fluorinated organic compounds are a very interesting class of compounds in terms of biological activities as well as new organic materials.¹⁻³ Due to the strong electronegativity of the fluorine atom, fluoroazulenes would show unique properties and could be applied to novel functional dyes and bioactive agents. Dehmloew and Balschukat have reported the generation of three chlorofluoroazulenes by vacuum pyrolysis of halotricyclo-[7.1.0.0^{4,6}]deca-2,7-diene.⁴ Some spectroscopic properties were described, however, systematic synthesis has not been performed yet. We wish to report the first synthesis of 1-fluoro- and 1,3-difluoroazulenes by the reaction of azulene with commercially available *N*-fluoropyridinium salts (**4**),⁵ whose fluorinating power can easily be controlled by their substituents on the pyridine ring.

1-Fluoroazulenes (**1**) and 1,3-difluoroazulenes (**2**) were synthesized as follows and the results are summarized in Table 1: a solution of azulene⁶ (**3a**, 1.00 g, 7.80 mmol) and *N*-fluoro-2,4,6-trimethylpyridinium triflate (**4a**, 2.75 g, 1.2 equiv) in dry CH₃CN (50 mL) was heated under reflux for 1.5 h. After the usual aqueous workup, the green residue obtained was chromatographed on a reversed-phase HPLC column (YMC ODS-AM S-50, 20 $\times$ 500 mm, CH₃CN—water (7:3, v/v)) to give **1a** and **2a** as crystalline compounds.⁷ The yields of **1a** and **2a** decreased when more powerful fluorinating reagents (**4b,c**) were used.⁸ When **4d** was used (entry 4), 2-(1-azulenyl)-3,5-dichloropyridine (**5**)⁷ was obtained as a major product.⁹ Fluorination of 2-methylazulene (**1b**)^{10,11} gave better results (entry 5). Methyl azulene-1-carboxylates (**6a**,⁶ **6b**¹¹) were also fluorinated by the same reaction with **4c** to give methyl 3-fluoroazulene-1-carboxylates (**7a,b**)⁷ and their ester substituents were removed by heating in 100% H₃PO₄ (PA) to give the corresponding 1-fluoroazulenes (Scheme 2).



Scheme 1.



Scheme 2.

¹H and ¹⁹F NMR data of fluoroazulenes are summarized in Table 2. In ¹⁹F NMR analysis **1a** resonates significantly at a higher field than 1-fluoronaphthalene ($\delta_F = -123.8$)¹² because of the higher electron density at the 1-position of the azulene ring. On the basis of differential NOE experiments for **1a**, H-3 and H-4 were unambiguously assigned and the other protons were assigned by an H,H-COSY experiment. Long-range ¹⁹F-¹H couplings were observed for H-3 and H-4 due to the W and zig-zag arrangement of the coupled nuclei, respectively. These characteristic long-range couplings are similar in the case of 1-fluoronaphthalene,¹³ except for H-2 and H-8.¹⁴ Substituent effects in ¹³C NMR indicate that the fluorine atom acts as a strongly electron-withdrawing group. Characteristic low-field shifts were observed at the 1-position with a large ¹J_{FC} coupling constant [**1a**: $\delta = 151.0$ (¹J_{FC} = 261.6 Hz); **2a**: $\delta = 146.0$ (¹J_{FC} = 265.5 Hz and ³J_{FC} = 8.0 Hz)].

Comparing the visible absorptions of **1a** and **2a** together with **3a** (Figure 1), one fluorine atom seems to cause approximately 75 nm-bathochromic shift due to the so-called $+\pi$ effect of the fluorine atom.^{15,16} This significant spectroscopic property

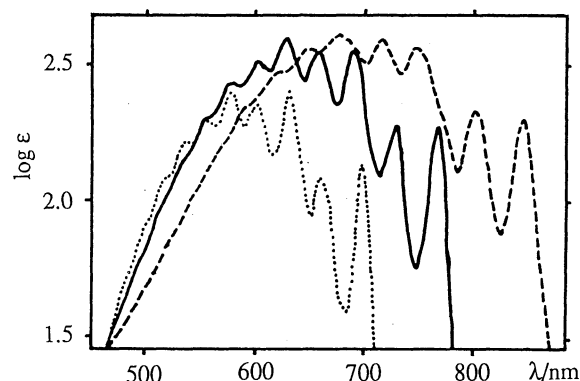
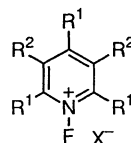


Figure 1. Visible absorption spectra of **1a** (—), **2a** (---), and **3a** (·····) in hexane.

Table 1. Results on the Fluorination of Azulenes (**3**)

Entry	3	Conditions	Yield/% ^a			Recov. of 3 /%
			1	2	5	
1	3a	4a / reflux/1.5 h	17	5	—	2
2	3a	4b / 60 °C/ 1.5 h	8	3	—	—
3	3a	4c / 60 °C/ 1.5 h	4	2	—	—
4	3a	4d / 0 °C/ 0.5 h	<1	<1	49	—
5	3b	4a / reflux/ 6 h	46	12	—	11

^a Isolated yield based on **3**.



4a: R¹ = CH₃, R² = H, X = TfO
4b: R¹ = R² = H, X = TfO
4c: R¹ = R² = H, X = BF₄⁻
4d: R¹ = H, R² = Cl, X = TfO

Table 2. ^1H NMR^a and ^{19}F NMR^b Data of **1**, **2**, and **7**

	H-2	H-3	H-4	H-5	H-6	H-7	H-8	2-CH ₃	3-COOCH ₃	^{19}F
1a	7.50d (4.5)	7.13dd (4.5, 4.5)	8.15dd (9.7, 3.3)	6.98dd (9.7, 9.7)	7.51dd (9.7, 9.7)	6.99dd (9.7, 9.7)	8.26d (9.7)	—	—	-148.0d (4.5)
1b	—	7.00d (4.8)	8.06dd (9.6, 3.3)	7.01dd (9.6, 9.6)	7.47dd (9.6, 9.6)	7.01dd (9.6, 9.6)	8.17d (9.6)	2.59s	—	-152.7m
2a	7.16s	—	8.17dd (9.9, 1.5)	6.80ddd (9.9, 9.9, 2.2)	7.46dd (9.9, 9.9)	6.80ddd (9.9, 9.9, 2.2)	8.17dd (9.9, 1.5)	—	—	-149.4dd (1.4, 1.4)
2b	—	—	8.10d (9.8)	6.82dd (9.8, 9.8)	7.41dd (9.8, 9.8)	6.82dd (9.8, 9.8)	8.01d (9.8)	2.48s	—	-154.9 br.s
7a	7.93s	—	9.59ddd (9.8, 0.7, 2.8)	7.45dd (9.8, 9.8)	7.80dd (9.8, 9.8)	7.37dd (9.8, 9.8)	8.44dd (9.8, 0.8)	—	3.95s	-149.9d (2.8)
7b	—	—	9.48dd (9.8, 2.8)	7.40dd (9.8, 9.8)	7.68dd (9.8, 9.8)	7.31dd (9.8, 9.8)	8.30d (9.8)	2.73s	3.97s	-154.3m

^a 200 or 600 MHz, δ in CDCl_3 . The values in parentheses denote coupling constants in Hz. Values printed in italics denote J_{FH} . Numbering of protons is referred to **1a** to prevent complexity. ^b 188 MHz, δ in CDCl_3 . PhCF_3 was used as internal standard ($\delta = -63$). The values in parentheses denote J_{FH} in Hz.

implies that fluoroazulenes can be used as starting materials for new types of dyes with extended performances.

We thank Takasago International Corp. and Central Glass Co. Ltd. for donating chemicals.

References and Notes

- # Fellowships of the Japan Society for the Promotion of Science for Japanese Junior Scientists.
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- 7 All new compounds gave satisfactory analytical and spectroscopic data. Selected data are as follows. **1a**: Blue crystals, mp 58.5–59.5 °C; MS (EI, 70 eV) m/z 146 (M^+ , 100%); UV-VIS (hexane) 237 (log ϵ 4.21), 254 (sh, 4.33), 270 (4.65), 273 (4.64), 316 (sh, 3.13), 328 (3.44), 333 (3.40), 342 (3.58), 357 (3.17), 530 (sh, 2.13), 551 (sh, 2.29), 576 (2.43), 600 (2.52), 626 (2.60), 656 (2.55), 689 (2.55), 728 (2.29), 767 (2.28) nm; Found: m/z 146.0537. Calcd for $\text{C}_{10}\text{H}_7\text{F}$: M, 146.0532. **1b**: Blue oil; MS (EI, 70 eV) m/z 160 (M^+ , 100%); UV-VIS (hexane) 212 (log ϵ 3.99), 239 (4.18), 274 (4.70), 278 (4.70), 299 (3.86), 313 (3.60), 331 (3.53), 347 (3.60), 566 (sh, 2.41), 584 (sh, 2.47), 604 (2.53), 618 (2.51), 641 (2.48), 664 (2.47), 683 (sh, 2.30), 710 (2.17), 738 (2.11) nm; Found: m/z 160.0694. Calcd for $\text{C}_{11}\text{H}_9\text{F}$: M, 160.0688. **2a**: Green crystals, mp 47–48 °C; MS (EI, 70 eV) m/z 164 (M^+ , 100%); UV-VIS (hexane) 232 (log ϵ 4.27), 258 (sh, 4.58), 268 (4.76), 313 (3.20), 320 (3.27), 327 (3.47), 355 (3.46), 343 (3.65), 358 (3.14), 586 (sh, 2.34), 617 (sh, 2.47), 646 (2.56), 672 (2.61), 713 (2.59), 744 (2.57), 799 (2.34), 842 (2.31) nm; Found: m/z 164.0433. Calcd for $\text{C}_{10}\text{H}_6\text{F}_2$: M, 164.0438. **2b**: Green crystals, mp 26–27 °C; MS (EI, 70 eV) m/z 178 (M^+ , 100%); UV-VIS (hexane) 217 (log ϵ 4.07), 236 (sh, 4.20), 271 (4.81), 317 (3.18), 331 (3.54), 339 (3.41), 346 (3.65), 586 (sh, 2.42), 605 (sh, 2.49), 625 (2.56), 646 (2.61), 667 (2.58), 693 (2.58), 717 (2.55), 741 (2.37), 775 (2.29), 808 (2.18) nm; Found: m/z 178.0599. Calcd for $\text{C}_{11}\text{H}_8\text{F}_2$: M, 178.0594. **5**: Green needles (hexane), mp 91–91.5 °C. **7a**: Blue prisms (hexane), mp 69–69.5 °C. **7b**: Violet prisms (hexane), mp 90–91 °C.
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