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

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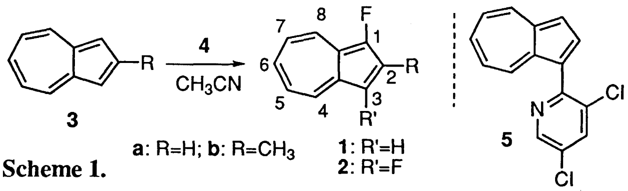
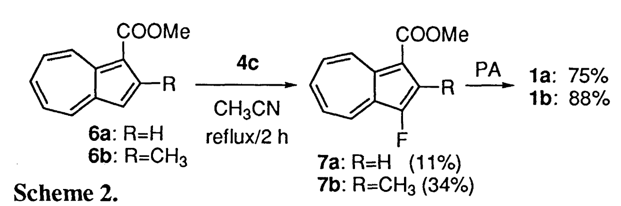
1-Fluoro- and 1,3-difluoroazulenes were synthesized by the reaction of azulene with *N*-fluoropyridinium salts in acetonitrile. Methyl azulene-1-carboxylates were also fluorinated to give the corresponding 3-fluoro derivatives. On the basis of the UV-visible absorption spectra, the fluorine atom acts as an electron-donating group to the azulene π-system due to the +Iπ 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. Dehmlow 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 azulene[6] (**3a**, 1.00 g, 7.80 mmol) and *N*-fluoro-2,4,6-trimethylpyridinium triflate (**4a**, 2.75 g, 1.2 equiv) in dry CH_3CN (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 x 500 mm, CH_3CN—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% H_3PO_4 (PA) to give the corresponding 1-fluoroazulenes (Scheme 2).



Scheme 1.



Scheme 2.

^{1}H and ^{19}F NMR data of fluoroazulenes are summarized in Table 2. In ^{19}F 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 ^{19}F-^{1}H 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 ^{13}C 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**: δ=151.0 ($^1J_{FC}$=261.6 Hz); **2a**: δ=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 +Iπ effect of the fluorine atom.[15,16] This significant spectroscopic property

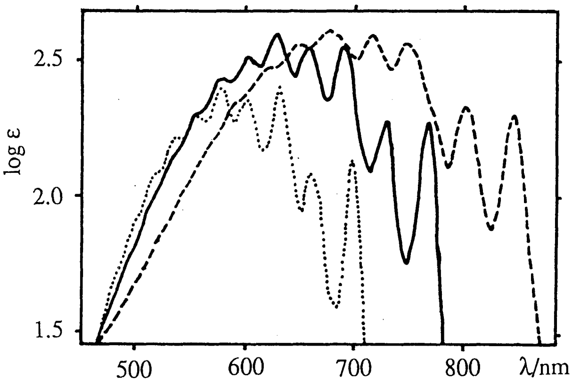
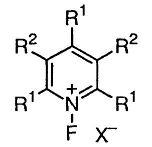


Figure 1. Visible absorption spectra of **1a** (——), **2a** (------), and **3a** (······) in hexane.

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: R^1=CH_3, R^2=H, X=TfO
4b: R^1=R^2=H, X=TfO
4c: R^1=R^2=H, X=BF_4
4d: R^1=H, R^2=Cl, X=TfO

Table 2. ^{1}H 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	$2\text{-C}\underline{\text{H}}_3$	$3\text{-COOC}\underline{\text{H}}_3$	^{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 (δ= –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.

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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 $C_{10}H_7F$: 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 $C_{11}H_9F$: 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 $C_{10}H_6F_2$: 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 $C_{11}H_8F_2$: 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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