ORGANIC LETTERS

2005
Vol. 7, No. 1
87−90

Synthesis and Characterization of 9-(Cycloheptatrienylidene)fluorene Derivatives: Acid-Triggered "Switch on" of Fluorophores

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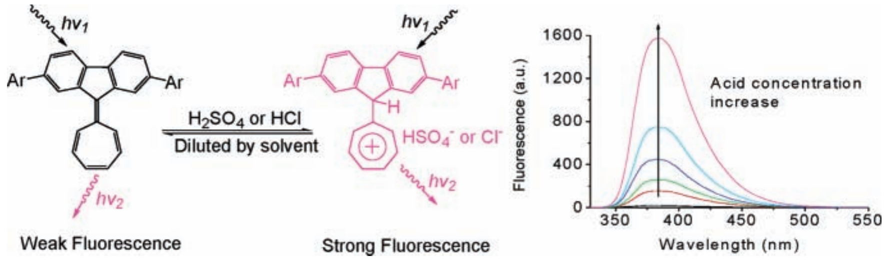
Received October 19, 2004

ABSTRACT



A series of 9-(cycloheptatrienylidene)fluorene derivatives were synthesized in good yields through the Suzuki or Sonogashira cross-coupling reactions. Fluorescence "off-on" behaviors of these compounds were investigated on the basis of variable acid concentrations. These compounds were shown to be acid-sensing fluorophores with utility as indicators in acidic environments.

Optical pH sensors, based on the measurement of fluorescence intensity,[1−2] fluorescence intensity ratios at two emission wavelengths,[3] and fluorescence lifetime[4] in response to environmental acidity, have been investigated and used to analyze biomolecules in living systems.[5] Many efforts have focused on designation and synthesis of pH-sensing fluorophores for this purpose.[6−8] Herein, we report new acid-sensing fluorophores based on a 9-(cycloheptatrienylidene)fluorene core.

Azulene and its derivatives,[9,10] nonbenzenoid aromatic systems, have improved electron affinity for formation of CT complexes. Compared to azulene, 9-(cycloheptatrienylidene)fluorene (9-CHF) has seven- and five-member rings but different connectivity. Little recent work on 9-CHFs has been reported.[11−13] Optical and electrochemical properties

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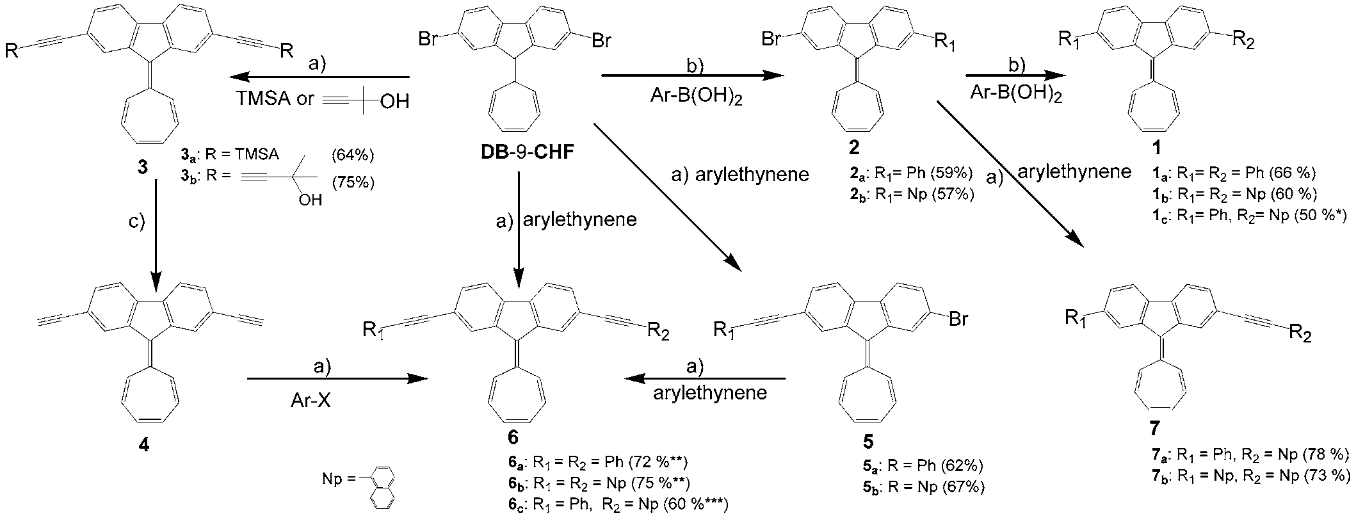
10.1021/ol047847a CCC: $30.25

Scheme 1. Synthetic Routes to Various π-Conjugated Compounds with a 9-(Cycloheptatrienylidene)fluorene Core



of 9-CHF have not been studied systematically except for its reversible UV−vis absorption based on acidity, which was recently reported by our group.[14] To investigate the optoelectronic properties of 2,7-diaryl-substituted 9-(cycloheptatrienylidene)fluorenes (DA-9-CHFs), a series of DA-9-CHFs have been synthesized by palladium-catalyzed cross-coupling reactions. These reactions show unique advantage in the formation of sp^2−sp^2- and sp−sp^2-hybridized carbon−carbon single bonds. Among these are the Heck, Suzuki, and Sonagoshira reactions. The Suzuki cross-coupling reaction[15] shows specific advantages due to facile preparation of arylboronic acids, its nontoxicity, compatibility, and stability to air and moisture. Alternatively, the Sonagoshira reaction[16,17] provides an effective way to build π-systems with triple bonds. While aryl halides are typical substrates in both the Suzuki and Sonagoshira reactions, only a few examples of related nonbenzenoid aromatic halides have been reported.

On the basis of previous reports,[12,13] almost all 2,7-disubstituted-9-CHFs were constructed by two steps. The first step was the reaction between tropylium tetrafluoroborate and corresponding 2,7-disubstituted fluorenes in THF; the second step was oxidation. The drawback was the relatively low yields due to the acid- or base-sensitive 9-CHF core. In this paper, various DA-9-CHFs were prepared through the Suzuki or Sonogashira cross-coupling reactions starting from 2,7-dibromo-9-(cycloheptatrienylidene)fluorene (DB-9-CHF). DB-9-CHF was selected as starting material due to its easier preparation from 2,7-dibromo-9-lithiofluorene and tropylium tetrafluoroborate in THF and followed by oxidation with DDQ in benzene.[13] The 9-CHF core survived after both the Suzuki and Sonagoshira cross-coupling reactions because these were carried out under mild conditions. In this way, DA-9-CHFs could be prepared in 60−80% yields.

Pd-catalyzed cross-coupling reaction of DB-9-CHF with 3 equiv of phenylboronic acid or 1-naphthaleneboronic acid under Suzuki conditions afforded 2,7-diphenyl-9-(cycloheptatrienylidene)fluorene ($\mathbf{1_a}$) and 2,7-di(1-naphthyl)-9-(cycloheptatrienylidene)fluorene ($\mathbf{1_b}$) in 66 and 60% yields, respectively (Scheme 1). Under identical conditions, coupling of DB-9-CHF with 1.1 equiv of phenylboronic or 1-naphthaleneboronic acid produced monosubstituted compounds $\mathbf{2_a}$ and $\mathbf{2_b}$ in 59 and 57% yields, respectively. $\mathbf{2_a}$ and $\mathbf{2_b}$ could be used as intermediates for generating unsymmetrical DA-9-CHFs, for example, $\mathbf{1_c}$. The reaction of DB-9-CHF with 3 equiv of trimethylsilylacetylene (TMSA) or 2-methyl-3-butyn-2-ol leads to the formation of $\mathbf{3_a}$ and $\mathbf{3_b}$, in 64 and 75% yields, respectively, via the Sonogashira cross-coupling reaction. Subsequent treatment of $\mathbf{3_a}$ and $\mathbf{3_b}$ with appropriate base, followed by chromatography on silica gel using *n*-hexane/dichloromethane as an eluent, gave **4** in 90 and 41% yields, respectively. Both $\mathbf{3_a}$ and **4** could be used as substrates for the Hay coupling reaction[18,19] to get desired products. By analogy, DB-9-CHF could also be reacted with 1.1 or 3 equiv of arylethyne to produce 2-arylethynyl-7-bromo-9-CHFs ($\mathbf{5_a}$ and $\mathbf{5_b}$) and diarylethynyl-9-CHFs ($\mathbf{6_a}$ and $\mathbf{6_b}$) in moderate yields. When $\mathbf{5_a}$ or $\mathbf{5}_b$ was used as the substrate, unsymmetrical DA-9-CHFs (such as $\mathbf{6_c}$) could be obtained. Unsymmetrical compounds ($\mathbf{7_a}$ and $\mathbf{7_b}$) could also be prepared from intermediate **2** by the Sonogashira cross-coupling reaction.

Relatively lower yields are obtained from $\mathbf{3_a}$ compared to $\mathbf{3_b}$ because the trimethylsilyl group was a better leaving group. Moreover, 20% yield of **4** was obtained as a byproduct during the preparation of $\mathbf{3_a}$. Compounds **6** could also be synthesized from **4** in excellent yields. However, unsymmetrical DA-9-CHFs ($\mathbf{1_c}$, $\mathbf{6_c}$, $\mathbf{7_a}$ and $\mathbf{7_b}$) were obtained in

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Table 1. Absorption and Emission Properties of DA-9-CHFs

DA-9-CHFs	UV−vis[a] λ_{max} (nm)/log ϵ	excitation[b] λ_{max} (nm)	emission[b] λ_{max} (nm)	quantum yield[c] (Φ_0)	relative fluorescence enhancement[d] (Φ_a)
$\mathbf{1_a}$	389/4.57	323	359, 375	0.008	1.2
$\mathbf{1_b}$	387/4.51	326	382	0.010	1.2
$\mathbf{1_c}$	388/4.18	321	383	0.030	1.1
$\mathbf{6_a}$	398/4.41	340	373, 392	0.013	2.1
$\mathbf{6_b}$	400/4.59	366	394, 418	0.025	2.8
$\mathbf{6_c}$	390/4.41	355	387, 409	0.054	2.6
$\mathbf{7_a}$	380/4.50	340	379, 399	0.014	1.9
$\mathbf{7_b}$	390/4.45	348	384	0.010	2.1

[a] UV−vis spectra were recorded in THF on a Shimadzu UV-2450 spectrophotometer. [b] Fluorescence spectra were recorded in THF on Shimadzu RF-5301PC spectrofluorophotometer. [c] Quantum yields were calculated in THF based on *trans*,*trans*-1,4-diphenylbuta-1,3-diene as the standard ($\Phi = 0.44$).[20] [d] Relative fluorescence enhancement (Φ_a) with respect to Φ_0 of the corresponding free dye was recorded in THF with 0.5 M H_2SO_4.

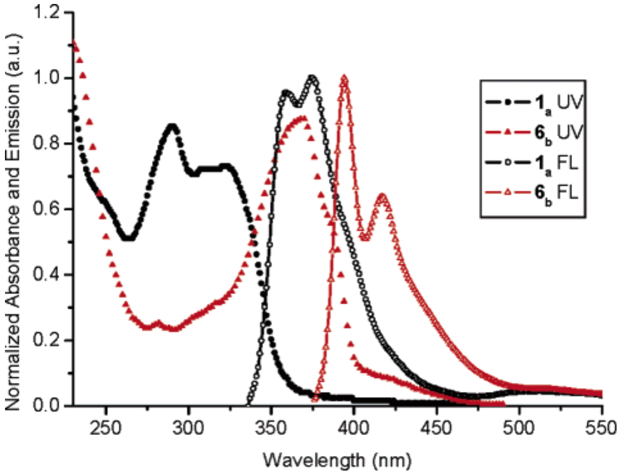

Figure 1. Normalized absorption and emission of $\mathbf{1_a}$ and $\mathbf{6_b}$ with 0.5 M H_2SO_4 in THF.

low yields. When $\mathbf{5_a}$ or $\mathbf{5_b}$ reacted with aryl boronic acid by Suzuki conditions, almost none of the corresponding coupling products were isolated.

On the basis of previous reports,[13,14] 9-CHFs showed reversible acid-dependent absorption spectra, but without emission. However, with DA-9-CHFs, weak purple-blue emissions were observed in THF. After acidification with sulfuric acid, the emission intensity increased dramatically. Table 1 lists maximum absorption and emission wavelengths for DA-9-CHFs in THF/H_2SO_4. Compound $\mathbf{6_b}$ exhibited indigo fluorescence with an emission at 394 and 418 nm, which was bathochromically shifted by 35 nm compared to the emission of $\mathbf{1}_a$ (Figure 1).

$\mathbf{1_b}$ illustrates the reversible acid-dependent absorption of DA-9-CHFs. Thus, when a THF solution of $\mathbf{1_b}$ was acidified by H_2SO_4, the solution color changed from yellow to colorless as the acid concentration increased. Increasing absorption at 325 nm was matched with decreasing absorption at 387 and 250 nm as H_2SO_4 concentration reached 0.75 mol L^{-1} (Figure 2). Moreover, the fluorescence intensity increased dramatically. Emission at 384 nm increased as the H_2SO_4 concentration reached 1.2 mol L^{-1} (Figure 3). When the acid solution was neutralized, the solution color changed back to yellow and fluorescence intensities decreased simultaneously.

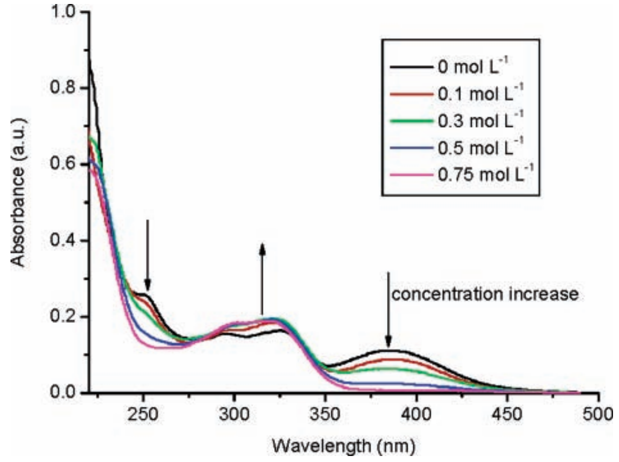

Figure 2. UV−vis spectra of $\mathbf{1_b}$ in THF with H_2SO_4 concentrations.

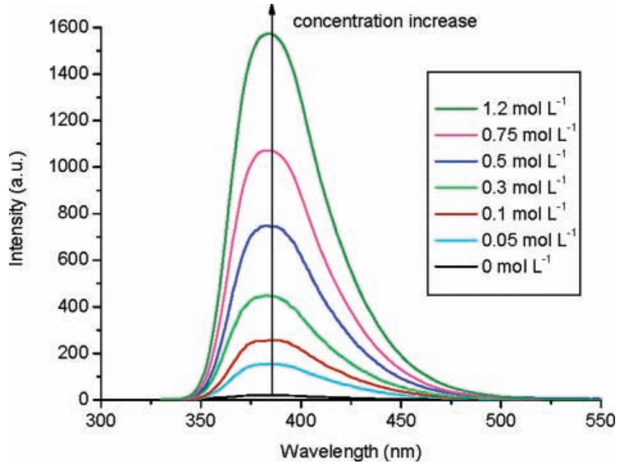

Figure 3. Fluorescence spectra of $\mathbf{1_b}$ in THF with relative H_2SO_4 concentrations, excited at 326 nm.

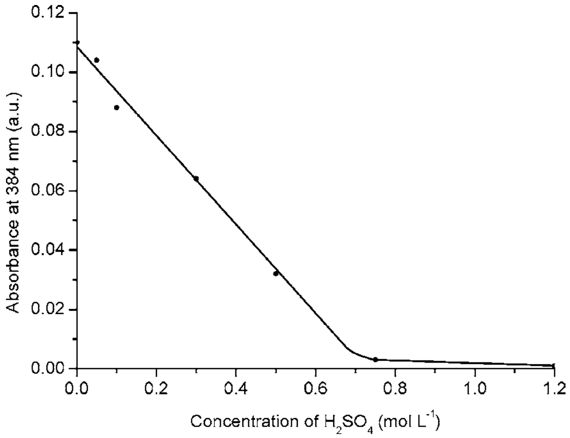

Figure 4. Absorption at 384 nm of $\mathbf{1_b}$ versus H_2SO_4 concentration.

Figure 4 shows the linear correlation between absorption at 384 nm of $\mathbf{1_b}$ and H_2SO_4 concentration. Suitable H_2SO_4 concentration for reversible change was between 0 and 0.75 mol L^{-1}. However, when the fluorescence technique was used instead of ultraviolet absorption, the suitable H_2SO_4 concentration for reversible change was between 0 and 1.2 mol L^{-1} (Figure 5). Obviously, $\mathbf{1_b}$ is an ideally acid-sensing fluorophore.

In conclusion, a series of DA-9-CHFs were synthesized by the Suzuki or Sonogashira cross-coupling reactions in moderate yields. Reversible changes were detected by both UV−vis absorption and emission on changing acidities. The acid-triggered “switch on” of emission intensity suggests that 2,7-diaryl-9-(cycloheptatrienylidene)fluorenes might be useful as acid-sensing fluorophores. Although this system is far from being an ideally broad pH sensor, it greatly complements normal pH sensors and supplies new indicators in extreme regions. Further work in this area would be beneficial to designing more excellent fluorophores for nonaqueous and aqueous systems.

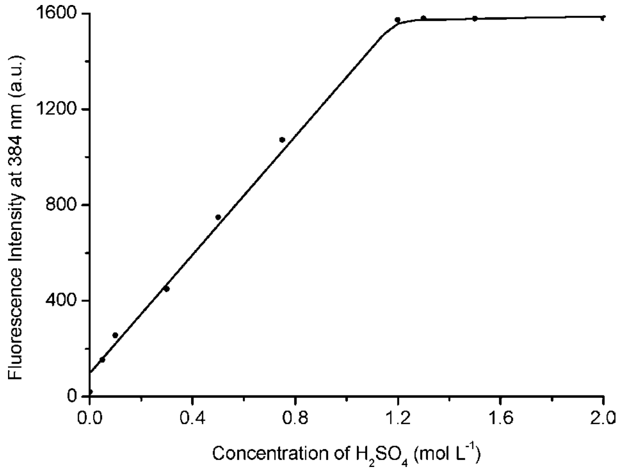

Figure 5. Emission at 381 nm of $\mathbf{1_b}$ versus H_2SO_4 concentration.

Acknowledgment. Ping Lu thanks National Science Foundation of China (20074032, 20374045) and Ministry of Education of China for financial support.

Supporting Information Available: Experimental details and characterization for new compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

OL047847A