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Halochromic Chiroptical Response of Novel Bis(9-acridinyl)-type Fluorophores with a Helical π Framework

Tatsuo Nehira,[1] Yasuyo Yoshimoto,[2] Kazuhisa Wada,[2] Hidetoshi Kawai,[2,3] Kenshu Fujiwara,[2] and Takanori Suzuki*[2]
[1]*Graduate School of Integrated Arts and Sciences, Hiroshima University, Higashi-hiroshima 739-8521*
[2]*Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810*
[3]*PRESTO, Japan Science and Technology Agency*

(Received December 14, 2009; CL-091109; E-mail: tak@sci.hokudai.ac.jp)

Acridine-based novel fluorophores **1/2** with a helical dihydrodibenzoxepin/azepine skeleton exhibit halochromic response upon addition of Brønsted acid in CH_2Cl_2, thus giving UV–vis and fluorescence spectral changes. By using the optically resolved species [(*M*)-**1/2**], circular dichroism (CD) and fluorescence detected-CD (FDCD) signals were also changed drastically, thus demonstrating four-way-output response thanks to configurational stability of helicity and efficient exciton coupling.

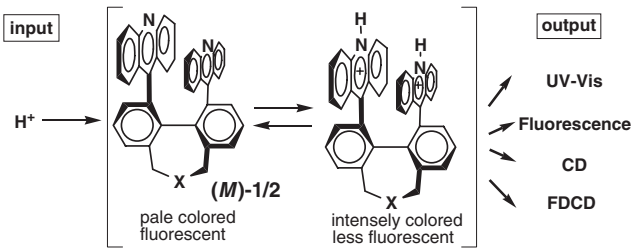
Chiral fluorophores are rare but interesting from the viewpoint of their unique chiroptical properties.[1] By adopting acridine as an excellent fluorophore,[2] we designed here novel diacridine-type molecules with an asymmetric π framework. They exhibit very strong circular dichroism (CD) signals when the helical π spacer can arrange the chromophores in a proper geometry for exciton coupling.[3]

On the other hand, upon treatment of acridines with Brønsted acid, protonation at the nitrogen atom can cause bathochromic shift of UV–vis spectra (halochromism).[4] The resulting acridiniums in general emit fluorescence in the longer wavelength region. Since their electron-accepting properties are much stronger than those of the corresponding acridines, fluorescence of the acridiniums would be quenched by intramolecular charge-shift when the π spacer attached has enough electron-donating properties.[5,7] Accordingly, the halochromism of acridine derivatives would be accompanied by fluorescence ON/OFF switching when designed suitably. These are the central points to prompt us to study novel diacridine derivatives **1/2** with the 5,7-dihydrodibenz[*c*,*e*]oxepin/azepine-1,11-diyl skeleton as new halochromic systems (Scheme 1). Here we report the details of the multioutput response[9] upon protonation of these chiral fluorophores.

Dihydroxepin *rac*-**1** (X = O) was prepared from 1,11-dibromodihydrodibenzoxepin according to a procedure we reported recently.[10] *N*-Methyldihydroazepine *rac*-**2**[11] (X = N-Me) was derived from 6,6′-diformylbiphenyl-2,2′-diylbis(9-acridine)[10] upon treatment with methylamine followed by reduction with DIBAH in 20% over two steps.[12] They are stable yellow crystalline materials [UV–vis (CH_2Cl_2): λ_{max} (log ε) 256 (4.89), 346 (3.93, sh), 366 (4.12), 377 (3.89, sh), 395 nm (3.62, sh) for **1**, and 257 (4.90), 346 (3.89, sh), 366 (4.09), 377 (3.90, sh), 395 nm (3.62, sh) for **2**, respectively].

Low-temperature X-ray analyses[14] were conducted for *rac*-**1/2** to reveal the detailed structural features. Two equivalents of benzene are included as crystallization solvent in **1** and there are two crystallographically independent molecules of **2** (mol-1, mol-2) in the crystal. As shown in Figures 1 and 2, the dihydrodibenzoxepin/azepine moieties adopt a quite similar helical geometry [the twisting angle of biphenyl unit: 52.6(1), 55.5(1), and 55.8(1)° for **1**, **2** (mol-1), and **2** (mol-2), respectively]. Two acridine units are arranged to overlap almost in parallel with several interatomic contacts shorter than the sum of vdW radii [the dihedral angle and the shortest interatomic C···C contact: 6.5(1), 3.25(1); 4.5(1), 3.24(1); and 6.0(1)° and 3.24(1) Å for **1**, **2** (mol-1), and **2** (mol-2), respectively]. The short axes of the two acridine chromophores are arranged in a screwed manner, whose twisting angle (ca. 50°) is close to the ideal value for the maximum exciton coupling (70°).[3b]

The observed deeply coiled geometry in **1/2** suggests configurational stability of helicity, which is in accord with the *C*2- but not *C*2$_v$-symmetric ^{1}H NMR spectra in solution. By considering no spectral changes upon heating to 423 K in



Scheme 1.

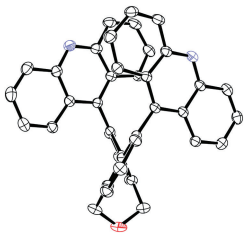


Figure 1. ORTEP drawing viewed along the long axis of biphenyl unit of (*M*)-**1** in *rac*-**1**·(benzene)$_2$ crystal determined at 153 K.

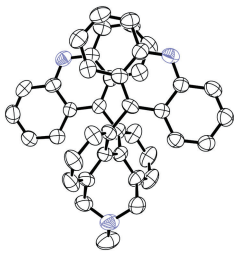


Figure 2. ORTEP drawing viewed perpendicular to the acridine plane of (*M*)-**2** (mol-2) in *rac*-**2** crystal determined at 153 K.

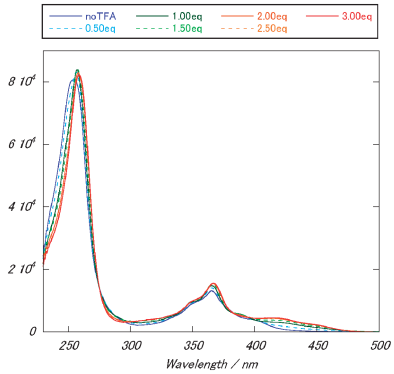


Figure 3. UV–vis spectral changes upon gradual addition of trifluoroacetic acid to a CH_2Cl_2 solution (1.5×10^{-5} mol dm^{-3}) of *rac*-**1** (0, 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 equiv).

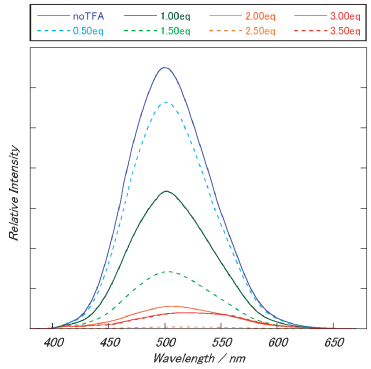
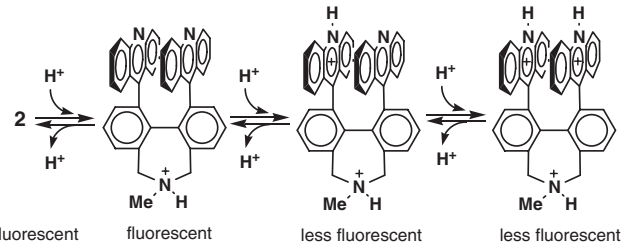


Figure 4. Fluorescence spectral changes upon gradual addition of trifluoroacetic acid to a CH_2Cl_2 solution (1.5×10^{-5} mol dm^{-3}) of *rac*-**2** (0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, and 3.5 equiv).



Scheme 2.

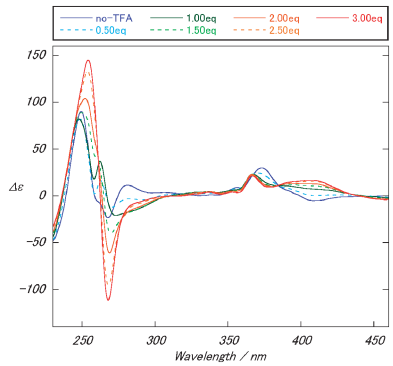


Figure 5. CD spectral changes upon gradual addition of trifluoroacetic acid to a CH_2Cl_2 solution (1.5×10^{-5} mol dm^{-3}) of (*M*)-**1** (100% ee) (0, 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 equiv).

DMSO-d_6, the energy barrier for ring flip of the helical π spacer must be more than 25 kcal mol^{-1}, thus allowing the optical resolution of *P*- and *M*-enantiomers of **1/2** at room temperature.

By using chiral HPLC (Sumichiral OA-2000; CH_2Cl_2–0.5% EtOH, recycled), optical resolution of **1/2** was conducted. As indicated by the extended tails of the peaks in the chromatograms, the second fractions contain a certain amount of the corresponding antipode (ca. 35% ee) although the first-fraction components were obtained in high ee. Thus, the chiroptical studies were carried out for the enantiomers of the first-fraction components of **1/2** that exhibit very similar CD spectra with a negative Cotton effect for the first band at λ_{ext} 413–414 nm (vide infra). According to the TD-DFT calculations (B3LYP/6-31G(d)), the observed CD spectra of **1/2** well correspond to those calculated for (*M*)-**1/2** (Figures S1 and S2 in Supporting Information[13]), indicating that the first fraction of **1/2** has the *M*-configuration of helicity.

Halochromic response was first examined by using racemic compounds. Upon gradual addition of trifluoroacetic acid (TFA) (0.5 to 3.0/3.5 equiv) to a CH_2Cl_2 solution, pale yellow solutions turned orange with apparent decrease of fluorescence. Figure 3 shows the changes of UV–vis spectra of *rac*-**1** (1.5×10^{-5} mol dm^{-3}), where a new absorption band appeared in the visible region with λ_{max} at 415 and 450 (sh) nm. Very strong absorption of **1** at 256 nm was marginally red-shifted by 3 nm. Similar behavior was observed for *rac*-**2** (Figure S3 in Supporting Information[13]) although the spectral changes were sluggish at the early stage of acid addition.

More distinct difference between **1** and **2** was discernable in the fluorescence spectral changes (Figure 4; Figure S4 in Supporting Information[13]). Upon excitation with 366 nm light (1.5×10^{-5} mol dm^{-3}), both compounds emit fluorescence at 500 nm in CH_2Cl_2 (Φ: 0.15 for **1** and 0.16 for **2**, respectively), the intensity of which decreased upon gradual addition of TFA as expected. After addition of 2–3 equiv of TFA, only weak fluorescence remained, which centered at 540 nm. Inspection of the early stage of addition showed that the intensity was reduced to 40% and 20% of the original value upon addition of 0.5 and 1.0 equiv of TFA to **1**. On the other hand, the same amount of acid induced less degree of fluorescence quenching in **2**: 87% and 55% of intensity remained, respectively. The observed difference comes from the fact that the first protonation in **2** does not occur on the acridine chromophore but on the sp^3 nitrogen in the seven-membered ring (Scheme 2).[15] Such behavior can account for the presence of an acid threshold in **2** to exhibit halochromism. Regardless of the absence or presence of a threshold, the above spectral changes demonstrate that *rac*-**1/2** can serve as novel two-way-output response systems based on halochromism.

When optically resolved (*M*)-**1/2** were used, drastic changes were also induced for the CD spectra by TFA. As shown in Figure 5, the oxepin exhibits several Cotton effects [λ_{ext} ($\Delta\varepsilon$) = 414 (−7.44), 377 (+33.4), 358 (+9.78), 282 (+18.0), 268 (−30.6), 250 nm (+96.9)], some of which are very large due to exciton coupling of acridine chromophores although the precise assignment of transition awaits further examination. Upon gradual addition of TFA to a CH_2Cl_2 solution of (*M*)-**1** (1.5×10^{-5} mol dm^{-3}, 100% ee), the sign of the first band was

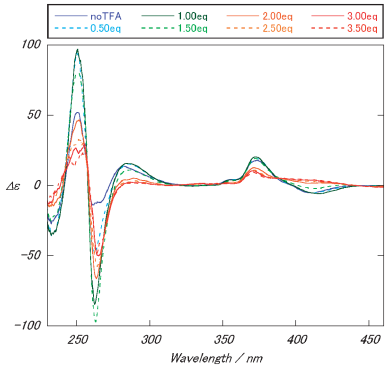


Figure 6. FDCD spectral changes upon gradual addition of trifluoroacetic acid to a CH_2Cl_2 solution (1.5×10^{-5} mol dm^{-3}) of (*M*)-**2** (80% ee) (0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, and 3.5 equiv).

reversed. At the same time, a negative couplet newly appeared around 265 nm, whose A-value is as large as 250. Similar changes were observed upon treatment of (*M*)-**2** with TFA (Figure S5 in Supporting Information;[13] a sample of 80% ee was used for the measurement).

Fluorescence detected-CD (FDCD)[16] is a relatively new technique to utilize chiroptical properties as molecular response.[9b,9c] High sensitivity is the most important feature of this method, which provides reason for its use to study isolated single molecules.[2c,2d] It has been revealed here that protonation of (*M*)-**1**/**2** by TFA causes drastic changes in FDCD spectra (Figure 6; Figure S6 in Supporting Information[13]).

These results demonstrate that optically resolved helical diacridines **1**/**2** can be regarded as novel transducers, by which four-way-output signals of UV–vis, fluorescence, CD, and FDCD are modified by chemical input of proton ("multioutput halochromism"). By incorporating an amine group, which is protonated prior to the acridine fluorophore, halochromic response is induced only when supplied protons exceed a threshold in **2**. Such nonlinear response is often found in other chromic systems containing both sp^2 and sp^3 nitrogens,[17] which leads to highly sensitive yet error-tolerant response.

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11 Data of *rac*-**2**: mp 295 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, $J = 8.8$ Hz, 2H), 7.59–7.53 (m, 4H), 7.54 (dd, $J = 7.5$, 1.3 Hz, 2H), 7.40 (ddd, $J = 8.8$, 6.6, 1.3 Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 2H), 7.10 (ddd, $J = 8.8$, 6.6, 1.3 Hz, 2H), 6.82 (dd, $J = 7.6$, 1.3 Hz, 2H), 6.69 (ddd, $J = 8.8$, 6.6, 1.3 Hz, 2H), 5.76 (d, $J = 8.8$ Hz, 2H), 4.93 (d, $J = 12.1$ Hz, 2H), 4.73 (d, $J = 12.1$ Hz, 2H), 2.63 (s, 3H); IR (KBr): 3061, 2934, 2849, 2792, 1735, 1628, 1558, 1539, 1517, 1460, 1437, 1411, 1355, 1239, 1014, 861, 782, 755, 743, 681, 661, 649, 637, 628, 619, 603, 542 cm^{-1}. CD spectrum of (*M*)-**2** (CH_2Cl_2): λ_{ext} ($\Delta\varepsilon$) = 413 (−4.84), 375 (+19.04), 358 (+6.20), 280 (+13.6), 268 (+1.09), 261 (+11.8), 251 nm (+29.6).

12 Details of experimental procedures and spectral data are given in Supporting Information (Ref. 13).

13 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

14 Crystal data of **1**·(benzene)$_2$: $C_{46}H_{32}N_2O$, $M_r = 628.77$, triclinic, $P\bar{1}$, $a = 10.903(2)$, $b = 12.804(3)$, $c = 12.890(3)$ Å, $\alpha = 88.52(1)$, $\beta = 67.526(8)$, $\gamma = 74.665(9)°$, $V = 1597.9(6)$ Å^3, $Z = 2$, $D_{calcld} = 1.307$ g cm^{-3}, $T = 153$ K, independent reflection 7006 (all), 4588 (2σ), $R = 4.4\%$, CCDC 755387. Crystal data of **2**: $C_{41}H_{29}N_3$, $M_r = 563.70$, monoclinic, $P2_1/c$, $a = 9.798(4)$, $b = 34.27(1)$, $c = 16.885(7)$ Å, $\beta = 94.376(4)°$, $V = 5652.3(3)$ Å^3, $Z = 8$, $D_{calcld} = 1.325$ g cm^{-3}, $T = 153$ K, independent reflection 11442 (all), 9877 (2σ), $R = 5.8\%$, CCDC 755388.

15 Stepwise addition of TsOH to $CDCl_3$ solutions of **1**/**2** was followed by ^{1}H NMR spectroscopy, which demonstrated first protonation at the azepine nitrogen in **2**. ^{1}H NMR spectral changes are given as Figure S7 in Supporting Information (Ref. 13).

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