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Chlorophyll-derived Thermochromic Sensor Based on α-Amino Alcohol Adduct Formation via Reversible Intramolecular Cyclization

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3-Trifluoroacetylchlorin possessing an ω-aminoalkyl chain at the 17-propionate residue was prepared to realize a chlorophyll-based supramolecule acting as a thermochromic switch. A THF solution of the synthetic sensor molecule appeared brown, while the solution color became purple at lower temperature due to the conversion of the trifluoroacetyl group to its α-amino alcohol adduct form in a molecule.

Chlorophyll(Chl)-*a* is a representative dye molecule in nature. Recent synthetic studies using Chl-*a* as a starting material include application towards photodynamic therapy[1] or dye-sensitized solar cells[2] as well as construction of supramolecular structures with self-assembling abilities for mimicking light-harvesting antennas.[3] We recently reported Chl-*a* derivative **1** (Figure 1) as a first example of a chemosensor using a chlorin skeleton as a main dye unit.[4,5] 3-Trifluoroacetylchlorin **1** showed a blue shift of the Q_y peak from 701 to 665 nm due to the formation of the corresponding α-amino alcohol as in **1**–$BuNH_2$ (see the upper drawing of Figure 1), accompanied by a visual color change from brown to purple. In contrast to the intermolecular system, introduction of an ω-aminoalkyl chain to a chlorin molecule seemed to be a reasonable strategy to create a new functional dye which forms a cyclophane structure as illustrated in the lower drawing of Figure 1. Because the adduct of **1** with $BuNH_2$ was formed temperature-dependently,[4] the intramolecular equilibrium between **2a** and **2b** is also expected to control the visual color of the solution by change of the temperature. The number of such supramolecular thermochromic dyes appears to be relatively limited.[6] Thus chlorin **2** was designed as a candidate of thermochromic switches using reversible intramolecular cyclization.

The length of the oligo(methylene) bridge in **2a** was considered to enable the intramolecular cyclization, based on our previous studies of strapped chlorophyll derivatives.[7] An amino group of 10-aminodecanol was protected by a *tert*-butoxycarbonyl (Boc) group, and the resulting alcohol was subjected to transesterification with the methyl ester of **1** using a tin catalyst in refluxing toluene (Figure 1).[8] A new chemosensor **2** was obtained after deprotection of the Boc group by 4 M HCl in EtOAc followed by neutralization.[9]

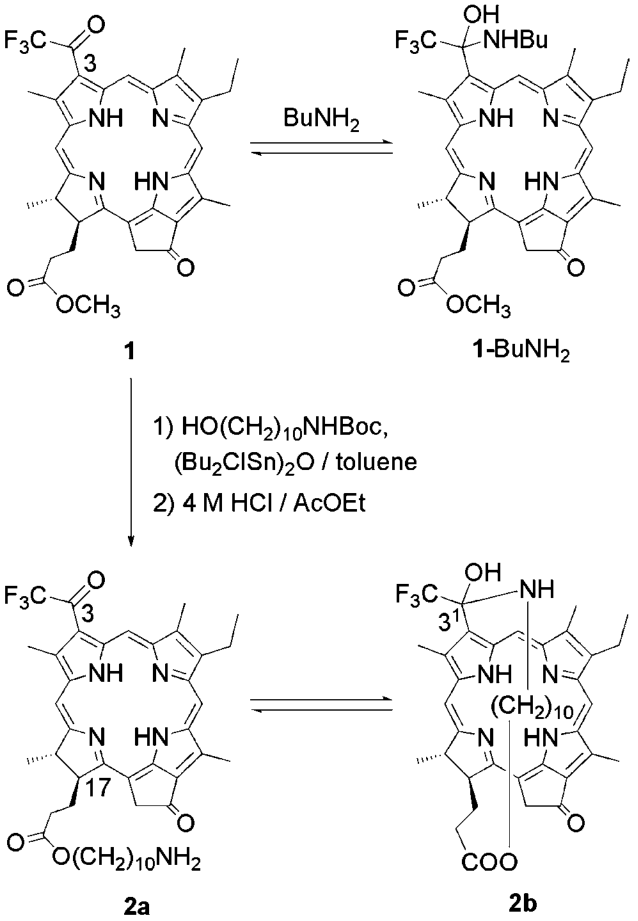

Figure 1. Synthetic route of trifluoroacetylchlorin **2** from **1**, and their equilibrium to α-amino alcohol forms.

The absorption spectra in Figure 2a show that chlorin **2** dominantly exists as its keto-form **2a** in $CHCl_3$ at room temperature ($Q_y = 701$ nm, solid line), while the equilibrium partially shifted to its α-amino alcohol form **2b** at $-40\,^\circ C$ ($Q_y = 669$ nm, dotted line). The 1:1 mixture of chlorin **1** and $BuNH_2$ in $CHCl_3$ did not show such spectral changes (Figure S2 in SI),[10] so the α-amino alcohol formation of **2** occurred intramolecularly. Figure 2b shows the temperature dependence of the absorption spectra of **2** in THF. Since the α-amino alcohol form **2b** was more stable in polar solvents,[11] the Q_y band of **2a** (696 nm at room temperature) almost disappeared at $-50\,^\circ C$. Thus the color change was visualized in THF from brown ($60\,^\circ C$) to purple ($-70\,^\circ C$) as shown in the drawing of the Graphical Abstract. The present thermochromism was fully reversible in the above range of examined temperature in the liquid phase of THF, because the on–off mechanism depends on the reversible covalent bond formation at the 3^1-position in **2b**.[12]

To further confirm the intramolecular cyclization as illustrated in **2b** (Figure 1), ^1H NMR spectra of **2** in $CDCl_3$ were measured at different temperatures. Proton signals of the oligo(methylene) bridge appeared in the up-field region at lower temperatures due to the shielding effect of the chlorin π-system

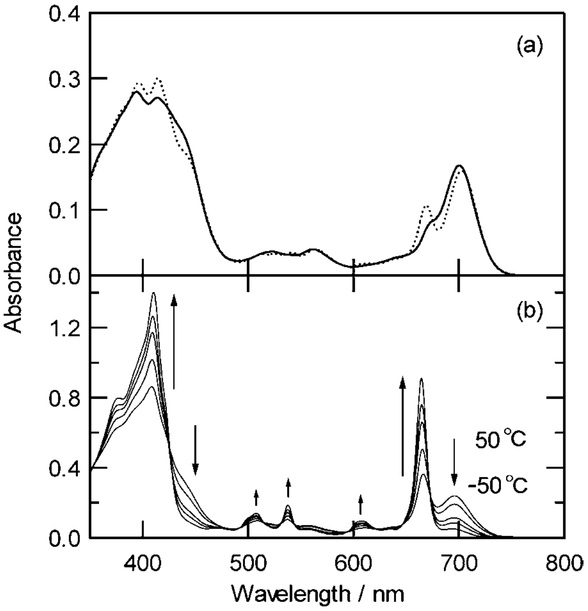

Figure 2. Absorption spectra of chlorin **2** (a) in CHCl$_3$ (5 µM) at 20 °C (solid line) and −40 °C (dotted line), and (b) in THF (13 µM) at various temperatures.

(Figures S3C and S3D in SI),[10] which is characteristic of face-protected chlorin derivatives.[7] This observation supports the cyclophane structure as in **2b**, namely, the α-amino alcohol formation proceeds to form an intramolecular bridge rather than intermolecular complexation. Because the highly concentrated sample for ^{1}H NMR (ca. 0.05 M) showed such a phenomenon, it is reasonable to assume that the contribution of intermolecular binding was ruled out in the diluted solutions for Figure 2 and the detection of visible color changes as shown in the Graphical Abstract (ca. 0.1 mM).

In conclusion, we have demonstrated an example of a supramolecular design concept of a thermochromic switch using an interesting α-amino alcohol formation.

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9 Spectral data of chlorin **2**: Vis (MeOH) $\lambda_{\max}$ 667 (relative intensity, 60%), 610 (9), 540 (12), 509 (11), 407 nm (100); ^{1}H NMR (CDCl$_3$, 50 °C) δ 9.82, 9.57, 8.87 (each 1H, s, 5-, 10-, 20-H), 5.33, 5.18 (each 1H, d, $J = 19$ Hz, 13^1-CH$_2$), 4.60 (1H, q, $J = 7$ Hz, 18-H), 4.40 (1H, br-m, 17-H), 4.04, 3.94 (each 1H, m, 17^2-COOCH$_2$), 3.70 (2H, q, $J = 8$ Hz, 8-CH$_2$), 3.69, 3.67, 3.26 (each 3H, s, 2-, 7-, 12-CH$_3$), 2.74, 2.59, 2.35, 2.33 (each 1H, m, 17-CH$_2$CH$_2$), 2.63 (2H, t, $J = 7$ Hz, 17^2-COOC$_9$CH$_2$), 1.87 (3H, d, $J = 7$ Hz, 18-CH$_3$), 1.71 (3H, t, $J = 8$ Hz, 8^1-CH$_3$), 1.48–1.20 (16H, m, 17^2-COOC(CH$_2$)$_8$), −0.23, −1.97 (each 1H, br, NH × 2); MS (APCI) *m/z*: 760 ([M + H]$^+$). See also Figure S1 in SI[10] for the ^{1}H NMR spectrum.

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

11 The association constants of **1** with BuNH$_2$ in CDCl$_3$ and in THF were determined to be 8 and 7800 M^{-1}, respectively (see Ref. 4a).

12 By the van't Hoff plot based on Figure 2b, thermodynamic parameters of **2a** → **2b** in THF were roughly estimated to be $\Delta H = -16\,\mathrm{kJ\,mol^{-1}}$ and $\Delta S = -48\,\mathrm{J\,K^{-1}\,mol^{-1}}$; $\Delta G = -2\,\mathrm{kJ\,mol^{-1}}$ (at 20 °C).