Drastic change in racemization barrier upon redox reactions: novel chiral-memory units based on dynamic redox systems†

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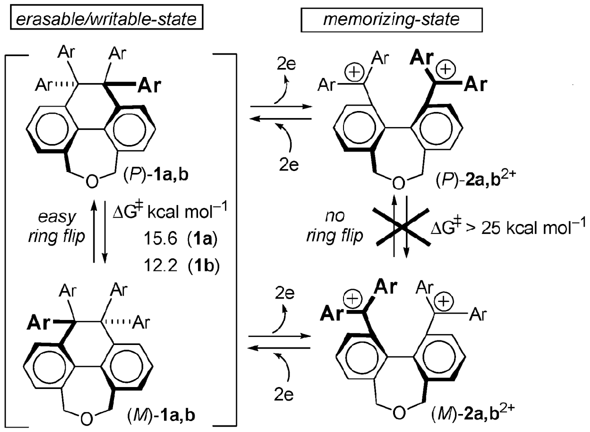
The helical configuration of dication dyes $\mathbf{2}^{2+}$ with a dihydrodibenzoxepin unit remained unchanged even at high temperature, whereas the corresponding neutral electron donors 1 with a tetrahydrophenanthroxepin skeleton easily underwent racemization. Due to their electrochemical bistability, electron exchange between 1 and $\mathbf{2}^{2+}$ is prohibited. Thus, the above electrochromic pairs can serve as novel chiral-memory units where redox reactions trigger switching between an "erasable/writable"-state (1) and a "memorizing"-state ($\mathbf{2}^{2+}$).

The intermolecular transmission of asymmetric information is one of the most important events in natural biological systems and in the field of supramolecular chirality.[1] Chiral-memory units play important roles in the above phenomenon, where they act as asymmetric-information receptors and store chiral information transmitted from the source.[2] To ensure this function, the chiral unit should be able to adopt an easily-racemized state ("erasable/writable"-state), but must also be intentionally interconvertible with the non-racemized state ("memorizing"-state) under certain conditions. Folded polymer chains with a helical structure[3] and some macrocyclic molecules[4] are important compounds that exhibit such switching by heating/cooling. However, much less has been reported on compounds whose interstate-switching[5] is achieved by electron transfer ("chiral redox memory").

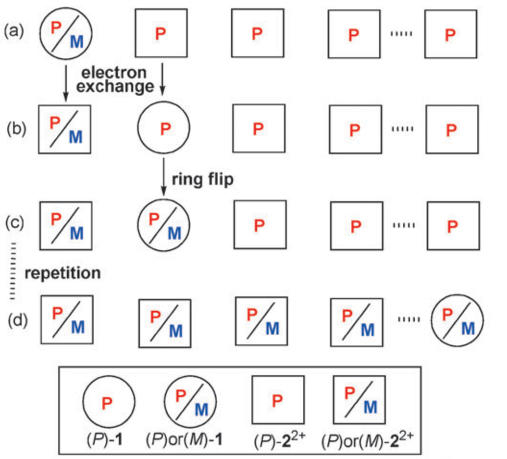
In the present study, we designed and prepared 5,7-dihydrodibenz[*c*,*e*]oxepin derivatives $\mathbf{2}^{2+}$ attached to two cationic chromophores at the 1,11-positions. These dications undergo reversible C–C bond formation ("dynamic redox properties")[6] to give electron donors **1** with a 4,6,10,11-tetrahydrophenanthr[4,5-*cde*]oxepin skeleton (Scheme 1). Colorless donors **1** would exist as an inseparable mixture of enantiomers by a facile ring flip,[6c,d] whereas the racemization of $\mathbf{2}^{2+}$ would be completely suppressed[7] by the large steric repulsion between the bulky Ar_2C^+ units at the bay region. In this way, only the neutral donors **1** would racemize ("erasable/writable") whereas the helicity in dications $\mathbf{2}^{2+}$ would be configurationally stable ("memorizing"). Furthermore, the oxidation of **1** and reduction of $\mathbf{2}^{2+}$ would occur at quite different potentials. Such separation of redox potentials would suppress electron-exchange between **1** and $\mathbf{2}^{2+}$, which should satisfy the requirement for a novel chiral-memory unit that works under redox conditions (Scheme 2).[6a,b]



[**a**: Ar = 4-$MeOC_6H_4$; **b**: Ar_2C = 10-methyl-9-acridan]

Scheme 1

By reacting a dilithio compound derived from the known dibromide *rac*-**3**[8,9] with 4,4′-dimethoxybenzophenone, we obtained *rac*-diol **4**,† which gave the stable dication salt *rac*-$\mathbf{2a}^{2+}(BF_4^-)_2$† quantitatively under acidic dehydrating



(a) Chiral information is stored in configurationally stable (*P*)-$\mathbf{2}^{2+}$ molecules.
(b) Configurationally labile (*P*)-**1** is formed by electron-exchange.
(c) Ring flip of (*P*)-**1** furnishes partial loss of chiral information of the system.
(d) Repetition of the above process results in total racemization of $\mathbf{2}^{2+}$.
In the present case, (a) -> (b) is prohibited by the electrochemical bistability.

Scheme 2

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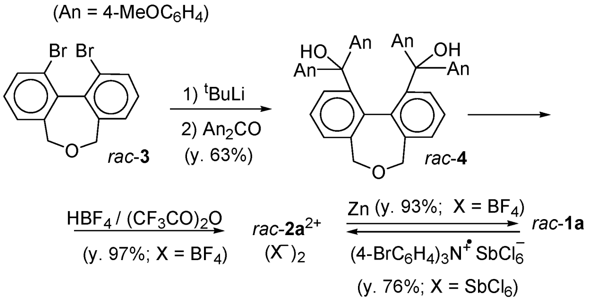
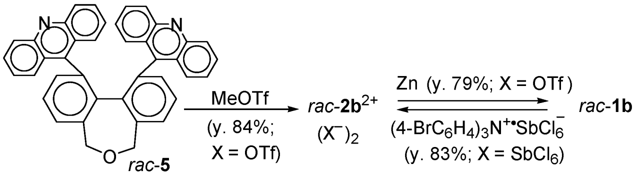
† Electronic supplementary information (ESI) available: X-Ray structure of **1b**, VT-NMR data of **1a**, spectral data of new compounds, and another route to dibromine **3**. CCDC 728166, 728167 and 762284. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc00026d.



Scheme 3



Scheme 4

conditions (Scheme 3). The deep red dication salt was then transformed into colorless donor **1a**† upon reduction with Zn dust, which regenerated starting dication $\mathbf{2a}^{2+}$ when treated with two equivalents of $(4\text{-BrC}_6\text{H}_4)_3\text{N}^{+\bullet}\text{SbCl}_6^-$. Their redox interconversion gave the products in good isolated yields. On the other hand, upon the bis(quaternization) of helical diacridine *rac*-**5** with TfOMe, the fluorescent yellow dye *rac*-$\mathbf{2b}^{2+}$ (Φ_f = 0.35 in CH_3CN) was obtained as a $(TfO^-)_2$ salt† (Scheme 4), which gave colorless dispiro donor **1b** upon reduction. Again, **1b** was reoxidized to give $\mathbf{2b}^{2+}(SbCl_6^-)_2$ salt,† which confirmed the reversible interconversion of **1b** and $\mathbf{2b}^{2+}$.

According to a voltammetric analysis (E/V *vs.* SCE), $\mathbf{2a}/\mathbf{b}^{2+}$ undergoes irreversible 2e-reduction at +0.29(CH_2Cl_2)/−0.20(MeCN) V (E^{red}), respectively, and the return peak in the far anodic region corresponds to the oxidation process of **1a**/**b** [E^{ox} = +1.46(CH_2Cl_2)/+0.14(MeCN) V] (Fig. 1). The observed separation of redox potentials provides the present pairs with high electrochemical bistability to prevent the loss of chiral information stored in $\mathbf{2}^{2+}$ even in the coexistence of **1** and $\mathbf{2}^{2+}$. Such characteristics were later confirmed experimentally (*vide infra*).

According to an X-ray analysis,‡ the condensed heterocycle in **1a** adopts a helical structure, as expected (Fig. 2a). The biphenyl unit in the condensed heterocycle makes a dihedral angle of 32.83(5)°, and the polyarylated C10–C11 bond length is 1.631(2) Å. The latter value is much greater than the standard C_{sp3}–C_{sp3} bond length (1.54 Å) due to steric repulsion, which can explain its facile cleavage upon 2e-oxidation to $\mathbf{2a}^{2+}$. Two of the four methoxyphenyl groups are located at pseudo-axial positions, whereas the other two occupy pseudo-equatorial positions. They do not interconvert in the crystal, but do so in solution. VT-NMR analysis (C_6D_6, 300 MHz) of **1a** showed that two sharp resonances for the methoxy protons observed at 10 °C (3.09 and 3.28 ppm) coalesced upon heating to 40 °C (Fig. S1, ESI†), which corresponds to a $\Delta G^{\ddagger}$ of 15.6 kcal mol^{-1} for the ring flip (k = 22.5 s^{-1} at 25 °C). Thus, **1a** is proven to act as an easily-racemized "erasable/writable"-state. Similarly, the energy barrier for the racemization of **1b** was determined to be 12.2 kcal mol^{-1} (k = 7580 s^{-1} at 25 °C in CD_2Cl_2); the smaller value can be explained by considering the higher planarity of the helical tetracyclic core [dihedral angle of the biphenyl unit: 29.58(4)°] as determined by the X-ray analysis‡ of *rac*-**1b** (Fig. S2).†

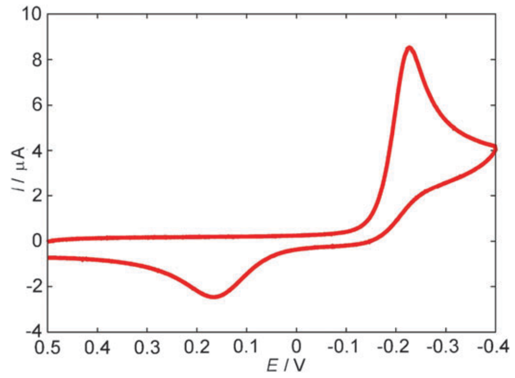


Fig. 1 Cyclic voltammogram of $\mathbf{2b}^{2+}(BF_4^-)_2$ salt in MeCN containing 0.1 mol dm^{-3} Et_4NClO_4 (E/V *vs.* SCE, Pt electrode, scan rate 100 mV s^{-1}).

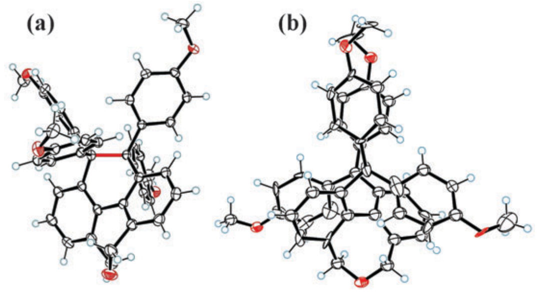


Fig. 2 ORTEP drawings of (a) (*M*)-**1a** in *rac*-**1** crystal and (b) (*M*)-$\mathbf{2a}^{2+}$ (mol-1) in *rac*-$\mathbf{2a}^{2+}(SbCl_6^-)_2$ crystal.

In the crystal of $\mathbf{2a}^{2+}(SbCl_6^-)_2$, there are two crystallographically independent molecules (mol-1, mol-2) with similar geometries. The separation between the two cationic centers is 3.52(4) or 3.53(3) Å, and the dihedral angle for the biphenyl unit in the condensed heterocycle is 56(3)° or 51(4)°, respectively, for mol-1 and mol-2. The π-conjugated system in $\mathbf{2a}^{2+}$ forms a helix-like structure with 1.5 turns (Fig. 2b), which makes the racemization of $\mathbf{2a}^{2+}$ very difficult. In fact, the NMR spectrum of $\mathbf{2a}^{2+}$ remained C_2-symmetric even at 150 °C in 1,2-dichlorobenzene-d_4, and thus the configuration of the "memorizing"-state would be quite stable. The same is true for bis(10-methylacridinium) dye $\mathbf{2b}^{2+}$.

In fact, optically pure salts of dication $\mathbf{2a}/\mathbf{b}^{2+}$ were obtained as follows. We succeeded in the optical resolution of the precursor diol *rac*-**4** by using chiral HPLC at 25 °C (Sumichiral OA-2000, AcOEt : CH_2Cl_2 : hexane = 1 : 2 : 4 with 0.5% Et_3N, recycled) (Fig. S3, ESI†). Optically pure (−)-**4** {first fraction, $[\alpha]_D^{23}$ = −186 (c = 0.3 in $CHCl_3$)} was converted to the chiral dication salt $\mathbf{2a}^{2+}(BF_4^-)_2$ as in the case of the racemic compound. In the circular dichroism (CD) spectrum, it showed a very strong positive couplet in the visible region [λ_{ext} 559 nm (Δε +182), 518 (−133) in CH_2Cl_2] (Fig. 3), which is due to effective exciton coupling between the two cationic chromophores [An_2CPh^+: UV-Vis (CH_2Cl_2): λ_{max} 525 nm (log ε 4.71)] arranged in a helical configuration.[10] The CD signals did not show any decay over several days at 25 °C ($\Delta G^{\ddagger}$ > 25 kcal mol^{-1}), which confirmed the long-lasting chiral memory of this unit.

An optically pure salt of (*M*)-$\mathbf{2b}^{2+}(OTf^-)_2$ was prepared from the resolved precursor (*M*)-$\mathbf{5}^{11}$ by *N*-methylation with

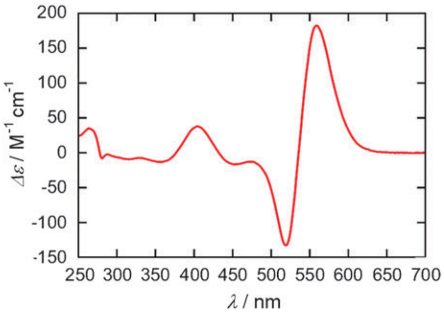


Fig. 3 CD spectrum of optically pure $\mathbf{2a}^{2+}(BF_4^-)_2$ prepared from (−)-**4**.

TfOMe. It exhibits a large negative couplet in the CD spectrum [λ_{ext} 270 nm ($\Delta\varepsilon$ −36.4), 258 (+33.0) in CH_2Cl_2], and again the Cotton effects remained unchanged over several days at 25 °C. This material was subjected to electrochemical reduction, and the changes were followed by three kinds of spectroscopy at 25 °C. The UV-Vis spectral changes of $\mathbf{2b}^{2+}$ into neutral donor **1b** exhibit several isosbestic points with a loss of absorptions in the visible region, which were regenerated upon reoxidation (Fig. 4a). Fluorescence of (*M*)-$\mathbf{2b}^{2+}$ was also lost upon reduction to **1b**, yet recovered completely upon reversal of the polarity of the electrodes (Fig. 4b), which demonstrates clean interconversion between **1b** and $\mathbf{2b}^{2+}$. In contrast, the CD signals of (*M*)-$\mathbf{2b}^{2+}$ disappeared gradually upon reduction, and were not reproduced upon reoxidation (Fig. 4c), which demonstrates that the resulting (*M*)-**1b** was easily racemized to lose chiral information. These findings successfully demonstrate the electrochemical response of a novel chiral memory unit ("erasing"-process of chiral memory). If the electron-exchange between **1b** and $\mathbf{2b}^{2+}$ (Scheme 2) was a facile process, the CD signals should have shown current-independent decay in the middle of electrolysis, but this was not the case (Fig. S4, ESI†).

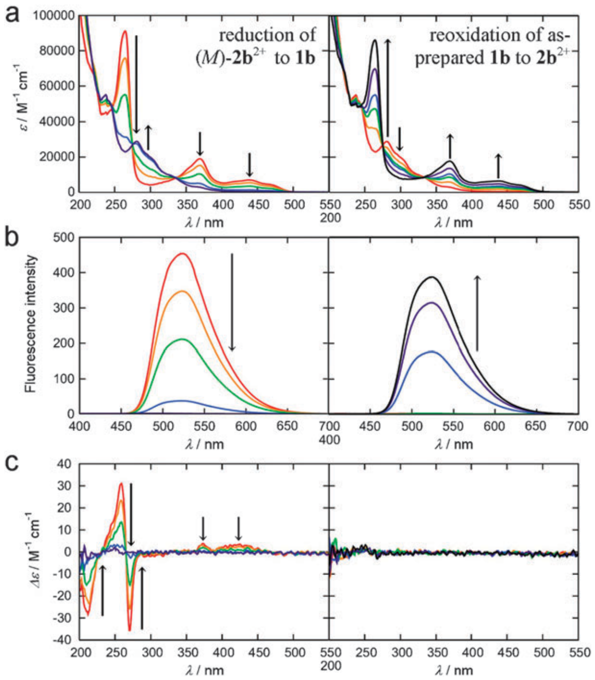


Fig. 4 (left) Changes in the (a) UV-Vis, (b) fluorescence (λ_{exc} 370 nm), and (c) CD spectra of (*M*)-$\mathbf{2b}^{2+}$ (9.0×10^{-6} M) in MeCN (containing 0.05 M Et_4NClO_4) upon constant-current electrochemical reduction (37 μA at 2.5 min interval, at 25 °C). Figures on the right show the changes upon reoxidation of the as-prepared **1b** (37 μA at 3 min interval).

The intermolecular transmission of asymmetric information into these chiral memory units is the next step in our project, and the catalytic asymmetric induction of **1** (biasing of the *P*/*M* ratio) followed by oxidation to configurationally stable $\mathbf{2}^{2+}$ is now being studied to demonstrate the "writing"-process for the present chiral memory unit.

Notes and references

‡ Crystal data of **1a**: $C_{44}H_{38}O_5$, *M* 646.78, monoclinic, $P2_1/n$, a = 12.331(2), b = 20.121(4), c = 13.178(2) Å, β = 94.0081(9)°, V = 3261.6(10) Å^3, Z = 4, D_c 1.317 g cm^{-3}, independent reflection 7479 (all), 4304 (2σ), T = 153 K, R = 3.6%, CCDC 728167. Crystal data of *rac*-$\mathbf{2a}^{2+}(SbCl_6^-)_2$: $C_{44}H_{38}Cl_{12}O_5Sb_2$, *M* 1315.72, triclinic, $P\bar{1}$, a = 12.073(4), b = 15.599(6), c = 27.406(11) Å, α = 81.941(18)°, β = 80.772(18)°, γ = 79.240(18)°, V = 4972(3) Å^3, Z = 4, D_c 1.757 g cm^{-3}, independent reflection 23827 (all), 2969 (2σ), T = 153 K, R = 5.8%, CCDC 728166. Crystal data of **1b** benzene solvate (1 : 1): $C_{48}H_{38}N_2O$, *M* 658.84, monoclinic, $C2/c$, a = 23.560(4), b = 11.900(2), c = 13.927(2) Å, β = 120.2315(5)°, V = 3373.5(9) Å^3, Z = 4, D_c 1.297 g cm^{-3}, independent reflection 3776 (all), 3289 (2σ), T = 153 K, R = 7.0%, CCDC 762284.

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9 Dibromide **3** was more conveniently prepared from 1,3-dibromobenzene *via* 2,2′,6,6′-tetrabromobiphenyl as shown in Scheme S1 of ESI†.

10 Based on the Flack parameter in the preliminary crystallographic study of the resolved $\mathbf{2a}^{2+}(SbCl_6^-)_2$, helicity would be M for the enantiomer with the positive couplet shown in Fig. 3.

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