

# Electrochiroptical systems based on biphenyl-2,2'-diyl-type dicationic dyes: strong chiroptical signals through the transmission of point chirality to axial chirality

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**Abstract**—Huge CD amplitude ( $A = +538$ ) was attained by diastereomeric preference (50% de) for the title dication with two bis[4-(*R*)-*sec*-butoxyphenyl]methylum units in benzene at 23 °C. Intramolecular  $\pi$ - $\pi$  stacking is the origin for effective transmission of point chirality to axial chirality to attain the chiroptical enhancement of 400-times. Thanks to the strong CD signaling, chiroptical changes upon electrolysis could be readily detected, thus realizing a new class of electrochiroptical response systems. Chiroptical properties could also be modified by solvent polarity.

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The electrochiroptical systems are novel class of molecular response systems,<sup>1–4</sup> which, like advanced electrochromic systems,<sup>5</sup> can transduce electrochemical input into two kinds of spectral outputs, that is, UV–vis and circular dichroism (CD). To obtain strong chiroptical output, redox pairs with helicity or axial chirality are suitable since they can give very strong CD signals ( $\Delta\epsilon$  ca. 50–500) by an exciton-coupling mechanism,<sup>6</sup> whereas chiral organic molecules with simple point chirality only exhibit ellipticity, that is, too weak ( $\Delta\epsilon < 1$ ) to be detected. From this point of view, the electron-donating cross-clumped hexaphenylethane **1** is of interest which exhibits a drastic change in color upon two-electron oxidation by transforming into the bond-dissociated bis(triarylmethylum)-type dication **2**<sup>2+</sup> with a biphenyl skeleton.<sup>7</sup> Neutral donor **1** and dication **2**<sup>2+</sup> are endowed with helicity or axial chirality, respectively, so that this redox pair is a promising candidate for realizing electrochiroptical response (Scheme 1).

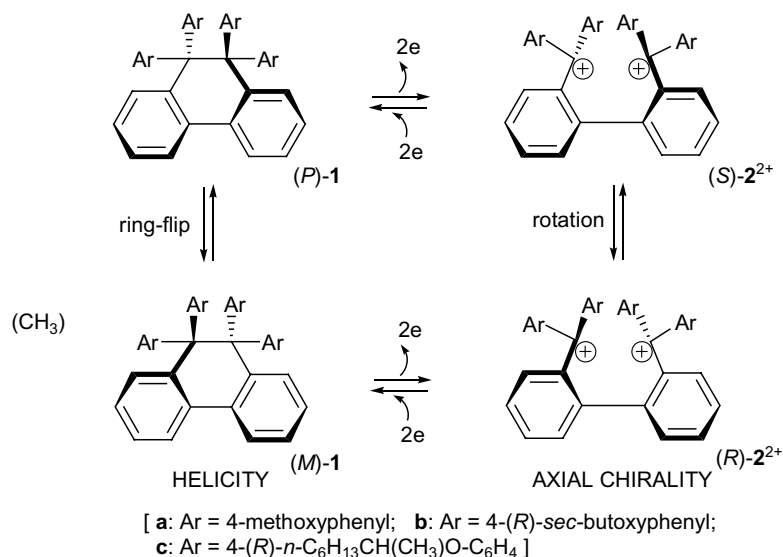
However, easy ring flip and rotation about the biphenyl axis ( $\Delta G^\ddagger$ : 12.6 and 16.6 kcal mol<sup>-1</sup>, respectively, for **1a** and **2a**<sup>2+</sup> with Ar = 4-MeOC<sub>6</sub>H<sub>4</sub>)<sup>7a</sup> make it difficult to

isolate their enantiomers.<sup>8</sup> To suppress the racemization, bulky groups are necessary to be attached at the proper positions as in the case of **3** and **4**<sup>2+</sup> (Scheme 2), by which the chiroptical response could be realized only after tedious optical resolution.<sup>2</sup> We are proposing in this Letter a new method to construct novel electrochiroptical response systems, for which very strong CD signals can be obtained without laborious optical resolution. The central point of our molecular design concept is based on the diastereomeric preference induced by transmission of point chirality to axial chirality<sup>9</sup> in the dication.<sup>10</sup> By simply attaching the chiral auxiliary such as (*R*)-*sec*-butoxy on the Ar groups, as much as 50% de has been achieved in the dication (*R,R,R,R*)-**2b**<sup>2+</sup>. Due to the exciton coupling of two bis(4-alkoxyphenyl)methylum chromophores on the biphenyl-2,2'-diyl skeleton, very strong CD signals are endowed in the visible region, which enables the strong chiroptical outputs upon electrolysis of (*R,R,R,R*)-**1b**. The details will be shown below.

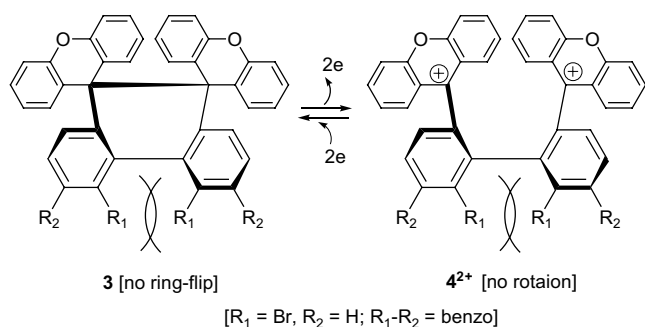
Dilithiobiphenyl was generated from diiodobiphenyl and *n*-butyllithium in THF, which was reacted with 4,4'-bis[(*R*)-*sec*-butoxy]benzophenone<sup>11</sup> to give diol (*R,R,R,R*)-**5b** in 46% yield. Upon treatment with 42% aqueous HBF<sub>4</sub>/(EtCO)<sub>2</sub>O, the dication salt (*R,R,R,R*)-**2b**<sup>2+</sup>(BF<sub>4</sub><sup>-</sup>)<sub>2</sub> was obtained as deep purple wax, which was reduced with Zn powder in MeCN to give colorless solid of (*R,R,R,R*)-**1b** in two-step yield

**Keywords:** Dynamic redox system; Hexaphenylethane; Chirality; Electrochiroptics; Chiroptical enhancement.

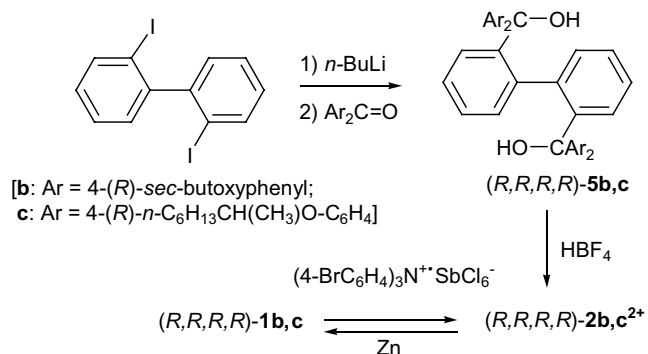
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Scheme 1.



Scheme 2.



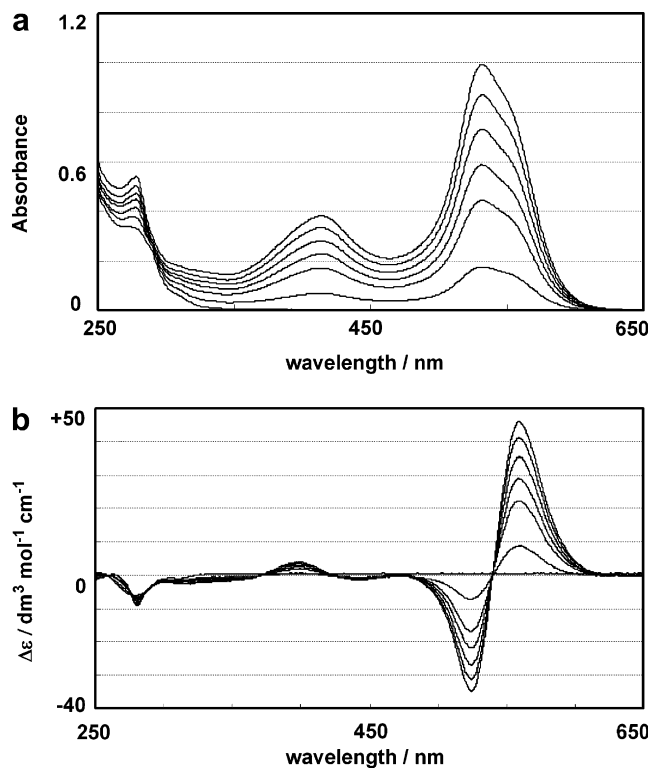
Scheme 3.

of 97% (Scheme 3). According to the voltammetric analysis in CH<sub>2</sub>Cl<sub>2</sub>, the irreversible redox waves for (*R,R,R,R*)-**1b** and **-2b**<sup>2+</sup> appeared at +1.56 V and +0.14 V versus SCE, respectively, which are close to those of 4-methoxyphenyl derivatives (**1a** +1.44 V; **2a**<sup>2+</sup> +0.21 V) measured under the similar conditions. A large separation of redox potentials is not due to decomposition of the material but due to the dynamic redox behavior,<sup>12</sup> where reversible C–C bond formation/breaking is accompanied by electron transfer. In fact, the prepara-

tive interconversion of the redox pair proceeds nearly quantitatively, upon treatment of **1b** with 2 equiv of (4-BrC<sub>6</sub>H<sub>4</sub>)<sub>3</sub>N<sup>+</sup>SbCl<sub>6</sub><sup>-</sup> (yield 97%) and of **2b**<sup>2+</sup> (SbCl<sub>6</sub><sup>-</sup>)<sub>2</sub> with excess Zn powder (yield 97%).

The chiral donor is colorless with only absorption in the UV region ( $\lambda_{\text{max}}$  274 nm,  $\log \epsilon = 4.27$  in CH<sub>2</sub>Cl<sub>2</sub>), whereas the dication exhibits very strong absorption in the longer-wavelength region (538 nm, 5.05), thanks to the triarylmethyl cation chromophores (Fig. S1). These features are similar to those of achiral redox pair of **1a** and **2a**<sup>2+</sup>. In the CD spectrum, (*R,R,R,R*)-**1b** exhibits only weak Cotton effect ( $\lambda_{\text{ext}}$  278 nm,  $\Delta \epsilon -6.3$ ) similar to bis[4-(*R*)-*sec*-butoxyphenyl]phenylmethanol (*R,R*)-**6b** (277 nm,  $-1.0$ ),<sup>13</sup> suggesting that the chiral auxiliaries on the aryl groups in (*R,R,R,R*)-**1b** are not biasing the helicity of the dihydrophenanthrene skeleton. In contrast, a positive couplet in (*R,R,R,R*)-**2b**<sup>2+</sup> ( $\lambda_{\text{ext}}$  564 nm,  $\Delta \epsilon +31$ ; 531 nm,  $-23$  at 23 °C in CH<sub>2</sub>Cl<sub>2</sub>) is evident at 545 nm with an amplitude  $A$  of +54 (Fig. S2), which is absent in bis[4-(*R*)-*sec*-butoxyphenyl]phenylmethyl cation (*R,R*)-**7b**<sup>+</sup> ( $\lambda_{\text{ext}}$  508 nm,  $\Delta \epsilon -1.3$ ).<sup>13,14</sup> Thus, the couplet is surely the result of exciton coupling between two bis(4-alkoxyphenyl)methyl cation chromophores. On the basis of the exciton chirality method,<sup>6</sup> the (*S*)<sub>ax</sub>-diastereomer of (*R,R,R,R*)-**2b**<sup>2+</sup> is predicted to exist in major since it is most probably that the dication **2b**<sup>2+</sup> adopts the geometry where two chromophores are partly overlapped in a face-to-face manner with the biphenyl moiety twisted by about 70° (vide infra).

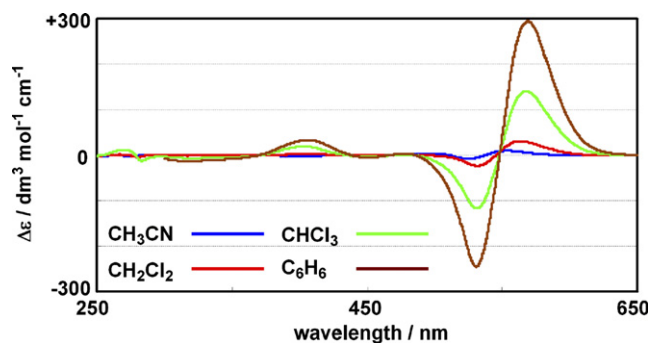
Strong CD activity based on the diastereomeric preference in the dication makes it possible to use the chiral redox pair of (*R,R,R,R*)-**1b** and **-2b**<sup>2+</sup> as a novel electrochiroptical response system. Upon electrochemical oxidation of the colorless donor in CH<sub>2</sub>Cl<sub>2</sub>, the UV–vis spectrum changed gradually into that of the deep purple dication (Fig. 1a), thus exhibiting electrochromic behavior. At the same time, continuous changes with several



**Figure 1.** Changes in (a) UV-vis and (b) CD spectra upon constant-current electrochemical oxidation (24 micro A, every 20 min) of  $(R,R,R,R)$ -**1b** (3.5 mL,  $1.8 \times 10^{-5}$  mol dm<sup>-3</sup>) to  $(R,R,R,R)$ -**2b**<sup>2+</sup> in CH<sub>2</sub>Cl<sub>2</sub> containing 0.05 mol dm<sup>-3</sup> *n*-Bu<sub>4</sub>NBF<sub>4</sub> as a supporting electrolyte. Reversal of current caused conversion of **2b**<sup>2+</sup> to **1b**.

isosbestic points were observed in the CD spectrum (Fig. 1b), indicating the clean conversion from  $(R,R,R,R)$ -**1b** to **-2b**<sup>2+</sup>. In this way, we could demonstrate the validity of our molecular design concept, by which the transmission of point chirality to axial chirality induces the diastereomeric preference to enhance the CD activity ('chiroptical enhancement'<sup>15</sup>).

It is noteworthy that the CD amplitude (*A*) of the couplet around 545 nm in  $(R,R,R,R)$ -**2b**<sup>2+</sup> shows significant solvent effects<sup>16</sup> (Fig. 2). In much polar MeCN, the *A* value is smaller (+19) than in CH<sub>2</sub>Cl<sub>2</sub> (Table 1). On the other hand, in the solvents with a smaller dielectric



**Figure 2.** CD spectra of  $(R,R,R,R)$ -**2b**<sup>2+</sup>(SbCl<sub>6</sub><sup>-</sup>)<sub>2</sub> salt measured in several solvents with different dielectric constant (*c* 1.2–2.1 × 10<sup>-5</sup> mol dm<sup>-3</sup>) at 23 °C.

**Table 1.** CD Amplitude (*A*)<sup>a</sup> and diastereomeric excess (de)<sup>b</sup> of  $(R,R,R,R)$ -**2b**<sup>2+</sup>(SbCl<sub>6</sub><sup>-</sup>)<sub>2</sub> in several solvents with a different dielectric constant (*ε*)

	CH <sub>3</sub> CN	CH <sub>2</sub> Cl <sub>2</sub>	CHCl <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>
<i>ε</i>	37.5	8.9	4.8	2.3
<i>A</i> <sup>a</sup>	+19	+54	+258	+538
de <sup>c</sup>	— <sup>d</sup>	5%	25%	50%

<sup>a</sup> Amplitude (*A*) for the positive couplet is obtained as Δε(+)-Δε(-) at 23 °C.

<sup>b</sup> Determined by <sup>1</sup>H NMR spectrum measured in deuterated solvent at 23 °C. Exchange of diastereomers is slower than the NMR time scale. The ratio of diastereomers was estimated by integration of the methine proton on the chiral auxiliary with the aid of nonlinear least-square fitting (Fig. S3).

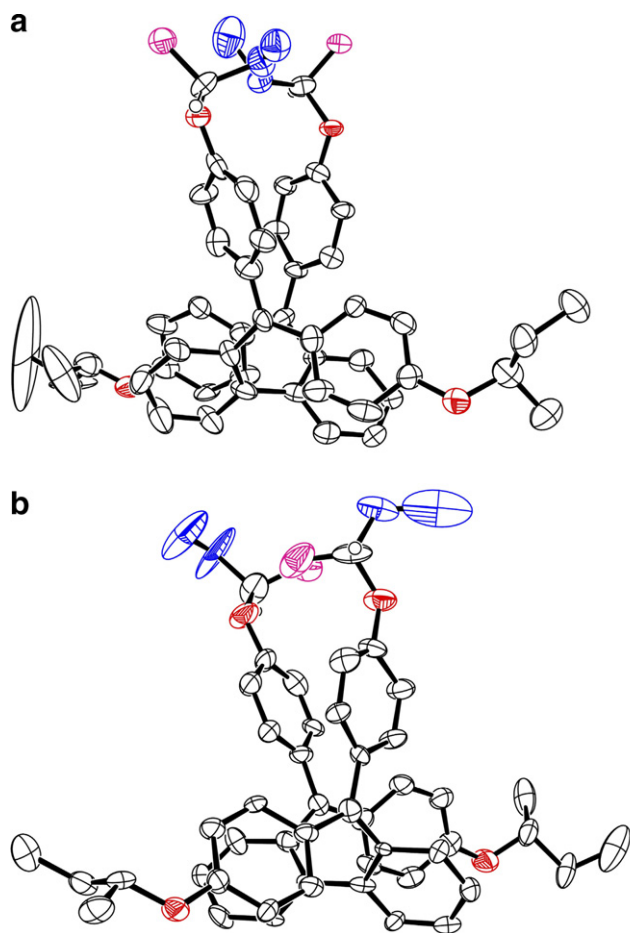
<sup>c</sup> Due to partial overlap of the resonance and/or solubility problem, the estimations include about 10% of errors.

<sup>d</sup> Could not be determined since the peaks for the diastereomers are inseparable.

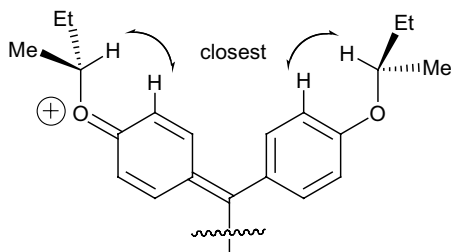
constant, the amplitude is larger. The CD amplitude and the diastereomeric excess (de) correlate almost linearly, the latter of which was determined on the basis of the <sup>1</sup>H NMR analyses. Thus, (*R*)<sub>ax</sub>- and (*S*)<sub>ax</sub>-diastereomers of  $(R,R,R,R)$ -**2b**<sup>2+</sup> exhibit nearly mirror-imaged CD signals at least for the couplet around 545 nm. The enormous *A* value (+538) in benzene corresponds to 50% de, demonstrating effective transmission of point chirality to axial chirality despite the fact that the chiral auxiliaries are attached far from the biphenyl axis. To get the clue to understand the origin of the presumed preference for (*S*)<sub>ax</sub>-diastereomer, the X-ray analysis<sup>17</sup> of the dication salt was conducted.

Fortunately, by recrystallization of salt from CH<sub>2</sub>Cl<sub>2</sub>, we succeeded in obtaining the crystal of  $(R,R,R,R)$ -**2b**<sup>2+</sup>(SbCl<sub>6</sub><sup>-</sup>)<sub>2</sub> that contains both of (*R*)<sub>ax</sub>- and (*S*)<sub>ax</sub>-diastereomers in a 1:1 ratio (*P*<sub>2</sub><sub>1</sub>, *Z* = 4), which enables us direct comparisons of their detailed geometries (Fig. 3). There are several common structural features: (1) twisting of biphenyl axis with *syn*-arrangement of substituents [dihedral angles of 72.8(5)<sup>o</sup> and 71.9(4)<sup>o</sup> for (*R*)<sub>ax</sub>- and (*S*)<sub>ax</sub>-isomers, respectively], (2) parallel arrangement of two cationic chromophores with the face-to-face overlap at one of the two 4-(*R*)-*sec*-butoxyphenyl groups in each, (3) nearly coplanar location of the asymmetric carbon with the phenoxy moieties due to oxonium-type sp<sup>2</sup>-hybridization of phenoxy oxygen. Among the three substituents on the asymmetric center, the methine proton is closest to the phenyl proton without exception as shown in Figure 4.

The second point is diagnostic to suggest that the molecules in solution adopt the similar geometry to the solid-state structures. In the <sup>1</sup>H NMR spectra, two resonances are assigned to the methine proton of the chiral auxiliary for each diastereomer (Fig. S3), one of which is shifted to the lower field than the ordinary position. This observation is best accounted for by π-π overlap of two alkoxyphenyl pendants, whose alkoxy parts are deshielded by the diamagnetic ring current of the other. The third point is directly related with the diastereomeric preference. The bulkier ethyl groups have to be made to face each other in the π-π overlap of (*R*)<sub>ax</sub>-isomer (Fig. 3a)

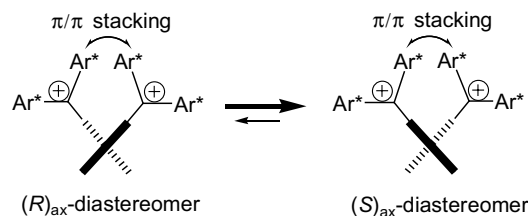


**Figure 3.** ORTEP drawings of (a)  $(R)_{ax}$ - $(R,R,R,R)$ - $2b^{2+}$  and (b)  $(S)_{ax}$ - $(R,R,R,R)$ - $2b^{2+}$  determined by the low-temperature X-ray analysis of  $(R,R,R,R)$ - $2b^{2+}$  ( $SbCl_6^-$ )<sub>2</sub> salt. Both diastereomers coexist in the same crystal in a 1:1 ratio.



**Figure 4.** Schematic drawing of the geometry for bis[4-(*R*-*sec*-butoxyphenyl)methyl]methyl unit commonly observed for both diastereomers in  $(R,R,R,R)$ - $2b^{2+}$  ( $SbCl_6^-$ )<sub>2</sub> crystal.

whereas the smaller methyl groups are positioned in proximity in the  $(S)_{ax}$ -isomer (Fig. 3b). Such a geometrical consideration provides one of the reasons that can account for the presumed  $(S)_{ax}$ -configuration preference for  $(R,R,R,R)$ - $2b^{2+}$  (Scheme 4). In the less polar solvents, solvation of the cationic moieties is not so effective that the closer overlap is expected to gain stability through  $\pi$ - $\pi$  interaction in these solvents. In this way, the higher *de* in the less polar solvents can be rationalized by larger energy difference between diastereomers, since the steric repulsion in  $(R)_{ax}$ -isomer becomes much severer.



**Scheme 4.**

In summary, we are successfully demonstrating the novel electrochiroptical response system that can output huge CD activity. Just by attaching simple chiral auxiliaries on the aryl pendants, chiroptical enhancement is realized through diastereomeric preference in terms of axial chirality via  $\pi$ - $\pi$  interaction of aryl pendants. Not only  $(R)$ -*sec*-butoxy group but also  $n$ - $C_6H_{13}$ - $CH(CH_3)O$  group is effective to induce the similar degree of diastereomeric preference in  $(R,R,R,R)$ - $2c^{2+}$ , and stronger CD signals were obtained by lowering the temperature of the solutions. Works on the multi-input–multi-output response systems are now in progress based on this novel molecular design concept.

### Supplementary data

Crystallographic data (excluding structure factors) for the structure in this Letter have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication No. CCDC 636050. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Selected spectral data of new compounds; UV–vis (Fig. S1) and CD spectra (Fig. S2) of  $(R,R,R,R)$ - $1b$  and  $-2b^{2+}$  ( $SbCl_6^-$ )<sub>2</sub>;  $^1H$  NMR spectrum of  $(R,R,R,R)$ - $2b^{2+}$  ( $SbCl_6^-$ )<sub>2</sub> in  $CD_2Cl_2$  at 23 °C (Fig. S3), which are available in PDF format. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.080.

### References and notes

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