ORGANIC
LETTERS

2007
Vol. 9, No. 20
3977−3980

A New Class of Chiroptical Molecular Switches Based on the Redox-Induced Conformational Changes

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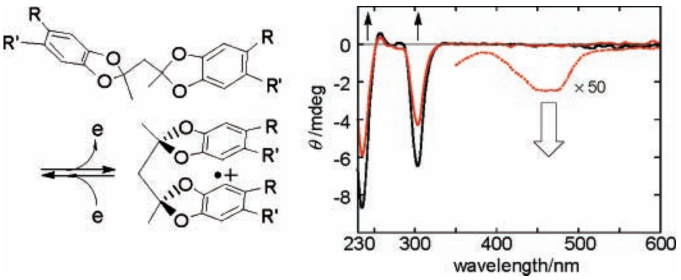
Received July 12, 2007

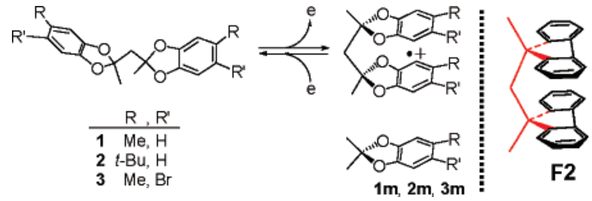
ABSTRACT



A series of optically active bis(catecholketal)s 1–3 were prepared, and their chiroptical properties were investigated experimentally and theoretically, demonstrating that they undergo conformational changes upon 1-e$^-$ oxidation and can be used as redox-responsive chiroptical molecular switches.

The design and synthesis of new π-stacked molecular arrays have been extensively investigated for potential applications in the emerging areas of molecular electronics and nanotechnology.[1] Our recent investigations have shown that polyfluorenes, in which the fluorene moieties are connected through a simple methylene linker, adopt rigid cyclophane-like π-stacked structures (see structure **F2** in Scheme 1).[2] In this context, structurally related bis(catecholketal)s of acetylacetone, which are readily available from an acid-catalyzed reaction of acetylacetone (1,3-diketone) with various catechols, are of particular interest due to the fact that they exist exclusively in an extended conformation in the neutral state unlike the π-stacked polyfluorenes (see Scheme 1).[3] Moreover, the bis(catecholketal)s undergo a ready transformation to the folded (π-stacked) conformation (similar to the π-stacked polyfluorenes) upon 1-e$^-$ oxidation (Scheme 1).[3]

Scheme 1. Chiral Bis(catecholketal)s and Comparison with a Representative π-Stacked Polyfluorene **F2**



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10.1021/ol701639u CCC: $37.00

This fact prompted us to prepare a series of chiral bis(catecholketal)s **1**−**3** (Scheme 1) to explore their potential as redox-responsive chiroptical switching molecules.[4] It is expected that the chiroptical properties of the neutral **1**−**3** (extended conformations) should be significantly different in comparison to the **1**−**3** cation radicals (folded or π-stacked conformation) which are easily generated by chemical or electrochemical oxidations.

Although redox-responsive chiroptical switching molecules have not been extensively investigated, a few successful examples are known. For example, Canary et al. have reported the inversion of the helical chirality in Cu(I)/Cu(II) complexes of *N*,*N*-dialkylmethionines.[5] Daub et al. have shown the chiroptical switching behavior of optically active binaphthyl boron dipyrromethanes.[6] Suzuki and coworkers showed that the two-electron oxidation/reduction of 2,2′-bis(diaryl-ethenyl)biphenyls can be used as a chiroptical switching device.[7] In comparison to the above systems, molecules **1**−**3** are relatively unique as they do not undergo any bond formation/breakage during the course of the redox cycle and they are rather easily accessible.[3]

Accordingly, herein, we report the preparation, separation of the enantiomers, redox behavior, and UV−vis/CD spectral changes, induced by 1-e$^-$ oxidation of various chiral bis(catecholketal)s **1**−**3**.

Redox properties of **1**−**3** were evaluated by cyclic voltammetry (CV) in dichloromethane at 25 °C, and the results were compared with the achiral analogue **4** (R, R′ = Me) as follows. Thus, the cyclic voltammograms of both **2** and **3** showed two reversible 1-e$^-$ oxidation waves, whereas Me-substituted derivative **1** showed only an irreversible redox profile (see Figure S1 in Supporting Information). The irreversibility of **1** can be easily reconciled by the fact that it contains substitution-labile hydrogens para to the oxygen atoms and thus can undergo reaction with weak nucleophiles, dimerization, etc. Note that in **2** these hydrogens are protected by steric hindrance of the adjacent *tert*-butyl groups. As expected, the monomeric model compounds **1m**−**3m**, containing only one catechol moiety, showed only one 1-e$^-$ oxidation wave in their cyclic voltammograms. Moreover, the first oxidation potentials of **1**−**3** were lowered by 50−110 mV when compared to the corresponding model compounds **1m**−**3m** (see Table 1).[8]

These cyclic voltammetric observations are compatible with the formation of π-stacked structures and the subsequent stabilization through the effective electronic coupling between the two cofacially oriented catechol moieties in the cation radicals of **1**−**3** (i.e., Scheme 1). It is also noted that the degree of stabilization of a single cationic charge ($\Delta G = -F \times \Delta E$) is relatively smaller for **2** and **3** than for **1** or **4** and most likely caused by the steric hindrance of larger substituents in the folded conformations.

Table 1. Redox Properties of Bis(catecholketal)s **1**−**4**[a]

	monomer	bis(catecholketal)		
	E_{ox} (V)	E_{ox}(I) (V)	E_{ox}(II) (V)	ΔG (kcal/mol)
1	+1.39[b]	+1.28[b]	+1.61[b]	−2.6
2	+1.38	+1.33	+1.59	−1.2
3	+1.47[b]	+1.42 (1.41[b])	+1.76	−1.4
4	+1.23[c]	+1.13[c]	+1.50[c]	−2.3

[a] Oxidation potentials were obtained by cyclic voltammetry in dichloromethane at 25 °C, unless otherwise stated. [b] From Osteryoung square-wave voltammetry. [c] See: Rathore et al. in ref 3.

The (+)-, *meso*-, and (−)-**3** were readily separated on chiral HPLC using Chiralcel OJ−RH to afford the three fractions in a 26:47:27 ratio (i.e., Figure 1). The (+)-**2** was also successfully isolated by chiral HPLC (Chiralpak IB); however, the *meso*-**2** and (−)-**2** were inseparable under a variety of conditions examined. Also, note that (+)-**2** and a mixture of (−)-**2**/*meso*-**2** were obtained in 21:89 ratio when detected at 254 nm.[9] Hence, only (+)-**2** and both (+)- and (−)-**3** of >99.5% enantiomeric excess were subjected to the following studies.

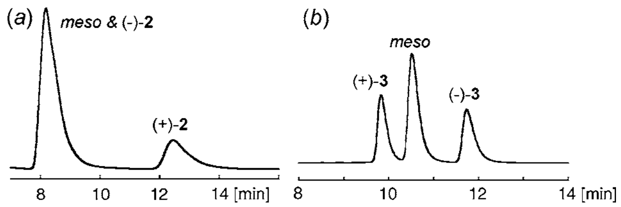

Figure 1. Chiral HPLC traces for **2** and **3**. (a) Chiralcel OJ−RH, MeOH/H_2O = 97:3, 1.0 mL/min. (b) Chiralpak IB, $C_6H_{14}/CHCl_3$ = 99.8:0.2, 1.0 mL/min.

UV−vis spectra of the neutral **2** and **3** exhibited typical benzenoid characteristics of the ^1L_b, ^1L_a, and ^1B_b transitions. However, the CD profile significantly deviated from the UV profile, most likely due to the cancellation of the oppositely signed spectra of the relevant conformers (i.e., Figure 2).

To elucidate the contribution of possible conformers of **2** and **3** in solution, we performed dispersion-corrected DFT calculations[10] on all the possible conformations. Rotations around the two central C−C bonds (*trans*, *gauche*+, and *gauche*−) lead to six possible conformations, i.e., *Tt*, *Tg*+, *Tg*−, *G*+*g*+, *G*+*g*−, and *G*−*g*−. Table 2 summarizes the

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(8) All E_{ox} values were obtained for solutions of **1**−**3** as diastereomeric mixtures. Note that the values were not sensitive to the diastereoisomerism as the CV's were identical for *dl*- and *meso*-**3**.

(9) All attempts to separate the enantiomers of **1** were unsuccessful. We tested the following chiral columns with a variety of eluents, i.e., Daicel Chiralcel OD−H, OJ, AD, IA, IB, OJ−RH, and OD−RH as well as Sumichiral OA−2000 and OA−3300.

(10) (a) Grimme, S.; Antony, J.; Schwabe, T.; Mück-Lichtenfeld, C. *Org. Biomol. Chem.* **2007**, *5*, 741. (b) Grimme, S. *J. Comput. Chem.* **2004**, *12*, 1463.

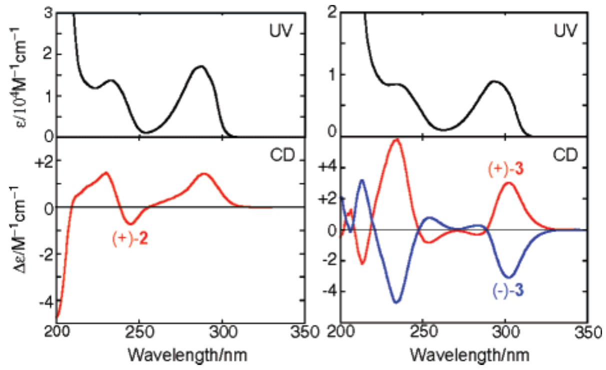

Figure 2. UV−vis and CD spectra of **2** and **3** in acetonitrile at 20 °C.

Table 2. Calculated SCS-MP2/TZVPP and DFT-B-LYP/TZV2P Energies on the DFT-D-B-LYP/TZV2P Optimized Conformers of **2** and **3**

	2			**3**		
conf	E (hartree)	E_{rel}[a]	% pop[b]	E (hartree)	E_{rel}[a]	% pop[b]
Tt	−1270.2117	≡ 0 (+9.2)	---	−6178.8282	≡ 0 (+6.4)	---
Tg−	−1270.2058	+3.7 (+1.8)	11.4	−6178.8215	+4.2 (+1.6)	47.4
G−*g*−	−1270.2070	+3.0 (≡ 0)	38.5	−6178.8209	+4.6 (≡ 0)	24.1
G+*g*+	−1270.2071	+2.9 (+0.0)	45.8	−6178.8207	+4.7 (+0.0)	20.0
Tg+	−1267.5275	>10 (>10)	0.0	−6178.8198	+5.3 (+2.5)	7.3
G+*g*−	−1270.2049	+4.3 (+2.1)	4.3	−6178.8180	+6.3 (+2.9)	1.1

[a] Relative SCS-MP2/TZVPP energies in kcal/mol. Relative DFT-B-LYP/TZV2P energies in parentheses. [b] Boltzmann distribution among five extended conformers based on the relative SCS-MP2 energies.

relative SCS-MP2/TZVPP and DFT-B-LYP/TZV2P energies of the DFT-D-B-LYP/TZV2P optimized structures of **2** and **3**. (Also, see Figure 3 for various conformers of **3**.)

The SCS-MP2 single-point energy calculations, which are thought to give very accurate relative energies comparable to the CCSD(T) limit,[11] show that the *Tt* conformer (i.e., folded conformation) is the most stable (in the gas phase). However, such a theoretical prediction most likely arises due to the absence of the solvent effect in the calculations, which generally overestimate the $\pi-\pi$ interactions such as in the *Tt* conformer. The following provide evidence in support of the fact that **2** and **3** exist largely in the extended conformer in solution, analogous to their achiral analogues:[3] (1) the X-ray structural studies of an achiral analogue (**4**; R, R = Me) in the solid state; (2) the charge-transfer interaction with chloranil as an acceptor in solution, which showed that the charge-transfer transition for the bichromophoric achiral donors **4** and **5** (R, R′ = H) occurred at a wavelength identical to its monochromophoric model compound; (3) similarity of the ^{1}H NMR chemical shifts to the corresponding monomeric model compounds (compare Table S1 in the Supporting Information); and (4) an excellent CD spectral reproduction by the simulation without including the *Tt* conformer (vide infra).

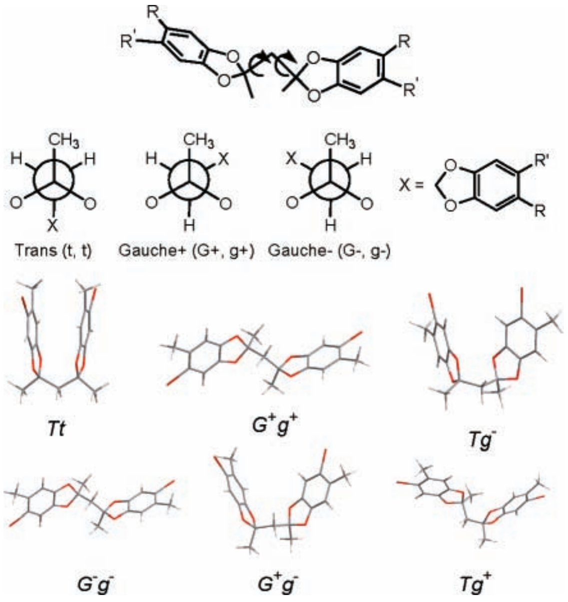

Figure 3. DFT-D-B-LYP/TZV2P optimized structures of all possible conformations of **3**. Conformers were denoted as small or capital letters by dihedral angles around the C−C*−C−X bond.

Among the five extended conformations, the *Tg*+ and *G*+*g*− conformers are energetically less important for both compounds. For **2**, the *G*+*g*+ conformation was found to be the most stable; this conformation has been obtained in the X-ray crystallographic structure of the corresponding tetramethyl analogue **4**. In the case of brominated **3**, the *Tg*− conformation was found to be the most stable, possibly owing to the bromine−bromine interaction in this conformation.

Following TD−DFT calculations with BH-LYP functionals on all the possible conformers afforded the theoretical UV−vis and CD spectra,[12] which were averaged by using the Boltzmann distribution based on the relative SCS-MP2 energies. Comparison of the theoretical and experimental CD spectra revealed that (+)-**2** possesses the *S*,*S* configuration, whereas (+)-**3** has the *R*,*R* configuration (Figure 4). The effect of solvents on the CD behavior was also examined, and the results are compared in Figure S2 in the Supporting Information. By simply changing the solvent from nonpolar methylcyclohexane to a water−methanol mixture (1:3), the observed Cotton effects were significantly changed, reflecting the sensitive nature of the equilibrium of the conformers in solution.

Chemical oxidation[13] of the optically pure **2** and **3** was performed as follows. A 50 mL flask equipped with a

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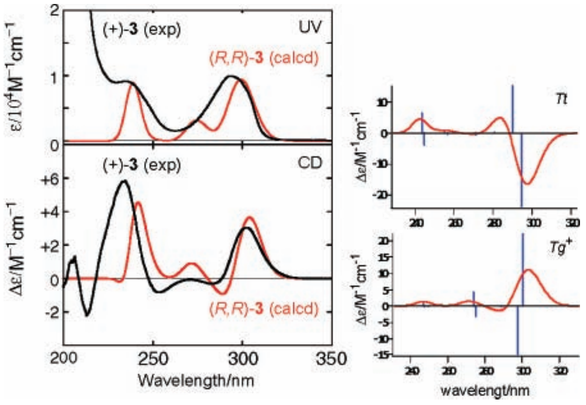

Figure 4. Left: Comparison of theoretical (averaged) and experimental UV−vis and CD spectra of **3**. Right: Computed CD spectra for selected conformers of **3**.

Schlenk adapter was charged with $(C_2H_5)_3O^+SbCl_6^-$ (3 equiv), to which an anhydrous dichloromethane solution of bis(catecholketal) (+)-**2** or (−)-**3** (2 equiv) was added at 0 °C under an argon atmosphere. The reaction mixture immediately took on a yellow coloration, indicating the formation of the corresponding cation radicals, and the mixture was stirred at ∼0 °C for an additional 12 h. At this stage, the oxidation proceeded to an extent of ca. 10−20% as estimated from the UV−vis spectral comparison with the known achiral analogue **4**. The radical cations of **2** and **3** were sensitive to air and/or moisture due to their relatively higher oxidation potentials and lack of sterical protection.

The solutions of oxidized **2** and **3** thus obtained were diluted with anhydrous dichloromethane for UV and CD spectral analyses. The spectra were recorded in a 1 mm quartz cell (230−330 nm) or in a 1 cm quartz cell (330−600 nm) at 20 °C under an argon atmosphere and are shown in Figure 5. New absorption bands at 350−500 nm were ascribed to the D−D transitions of the corresponding radical cations resulting from **2** and **3**. It turned out that the magnitude of the negative Cotton effects induced by this transition is as small as the typical rotatory strength of the D−D transition,[14] but it is significant enough for chiroptical sensing. It should be noted for monitoring purposes that a change from zero to finite value is much more sensitive than in the cases where simply the strength of signals changes! Also, the reason for observing the same negative Cotton effects in the 350−500 nm region for both (*S*,*S*)-(+)-**2** and (*S*,*S*)-(−)-**3** can be ascribed to the same absolute configuration for (+)-**2** and (−)-**3**. The reason for the opposite signs in specific rotations for (*S*,*S*)-**2** and (*S*,*S*)-**3** is not clear at the present time.

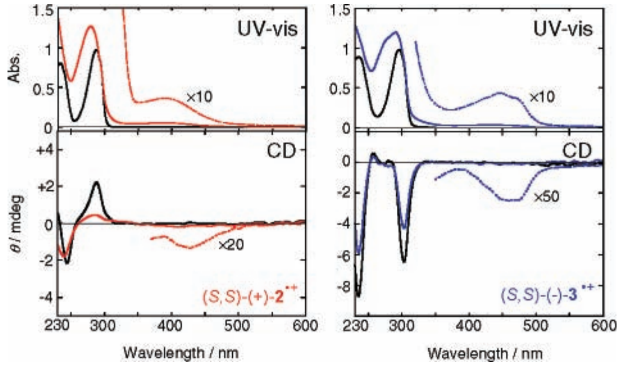

Figure 5. UV−vis and CD spectral changes of **2** and **3** upon oxidation with $(C_2H_5)_3O^+SbCl_6^-$ in dichloromethane at 20 °C.

It is also interesting to note that the Cotton effects at the ^1L_b and ^1L_a transitions become much smaller upon oxidation. This is most likely due to the formation of the folded conformers in the oxidized states, which reduces the population of the extended conformations. It is important to mention that **2** and **3** can be quantitatively regenerated by reduction of the oxidized **2** and **3** using zinc duct, and the redox cycle (i.e., oxidation using $(C_2H_5)_3O^+SbCl_6^-$ and reduction using Zn dust) was repeated at least three times without any sign of decomposition of **2** and **3**.

In summary, we have demonstrated that the new chiral bis(catecholketal)s (**2** and **3**) show significantly altered CD spectra when oxidized to their cation radicals. Moreover, the observed redox-induced chiroptical switching is based on the spontaneous conformational changes upon 1-e$^-$ oxidation and is distinctly different from the precedents that employ the bond forming/breaking processes in their redox cycles. Further studies are in progress to obtain chiral derivatives based on the bis(catecholketal) system which will allow easy separation of the enantiomers as well as quantitative preparation of their robust cation−radical salts.

Acknowledgment. T.M. thanks the Alexander von Humboldt-Stiftung for the fellowship and a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan for financial support. R.R. thanks NSF (CAREER award) for financial support. We also thank Ms. Yumi Origane for technical assistance in the chiral HPLC separation.

Supporting Information Available: Preparation of **1**−**3**, detailed experimental results, and summary of the theoretical calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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