Organic LETTERS

Letter

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Redox-Regulated Rotary Motion of a Bis(9-triptycyl)-TTFV System

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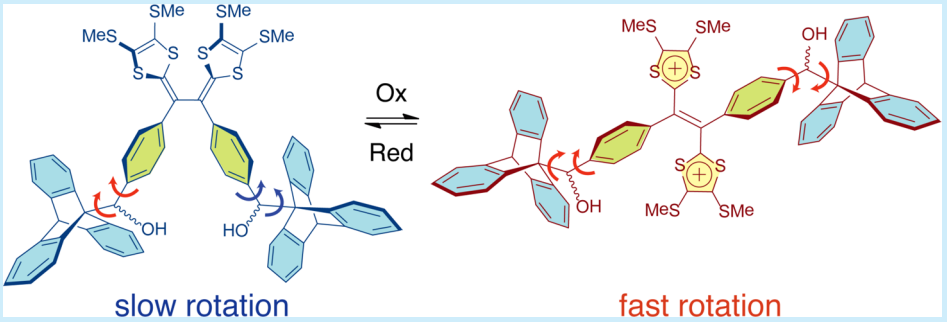
Supporting Information

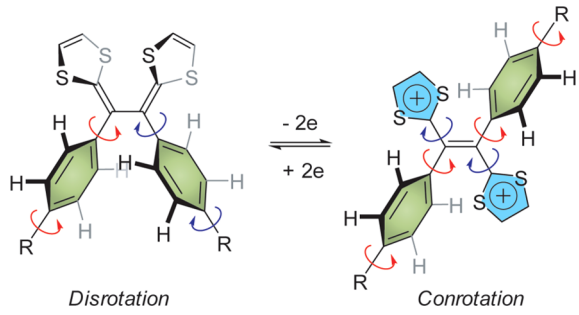


ABSTRACT: A tetrathiafulvalene vinylogue (TTFV) unit was covalently linked to two benzyltriptycene molecular rotors to form a molecular gearset. Dynamic NMR studies showed that reversible redox reactions at the TTFV central unit exerted regulation over the rotational properties of the 9-triptycyl rotors.

The study of molecular rotary devices has attracted considerable attention, driven by the challenging goal of attaining ultraminiaturized molecular machines.[1] The past few years have witnessed a large array of elegantly designed molecular rotary devices, including gears,[2] rotors,[3] motors,[4] clutches,[5] brakes,[6] and vehicles,[7] while the ambition to build more complex molecular machines continues to tantalize the mindset of both experimentalists and theoreticians. For a truly functioning molecular rotary machine, precise control over both rotational speed and direction is a feature highly desirable but very challenging to achieve. So far, suitable design principles and concepts for such kinds of molecular devices are far from being reliably established. Therefore, as the first step, it is imperative to design and investigate some new prototype models to expand our knowledge base.

In our recent studies, diphenyl-substituted tetrathiafulvalene vinylogues (TTFV)[8] have been identified as a class of potentially useful building blocks for making molecular rotary devices with controllability over rotational speed and/or direction. Our reasoning comes from the unique redox properties of diphenyl-TTFV, which generally shows a reversible two-electron transfer process on oxidation.[8,9] Associated with this redox reaction is a dramatic conformational change, as depicted in Scheme 1. Analysis of the purely concerted rotations among the aryl groups crowding together reveals interesting relationships; that is, the two phenyl groups favor *disrotation* in the neutral state and *conrotation* in the dicationic state. If such is the case, rotary components covalently linked to the two phenyl groups can thus be regulated by the oxidation state of the TTFV moiety in terms of both rotational speed and direction, assuming that the concerted rotational barriers in TTFV and [TTFV^{2+}] are distinctly different. In theory, such an assumption is reasonably

Scheme 1. Relationship of Concerted Rotations in Diphenyl-TTFV and Its Dication



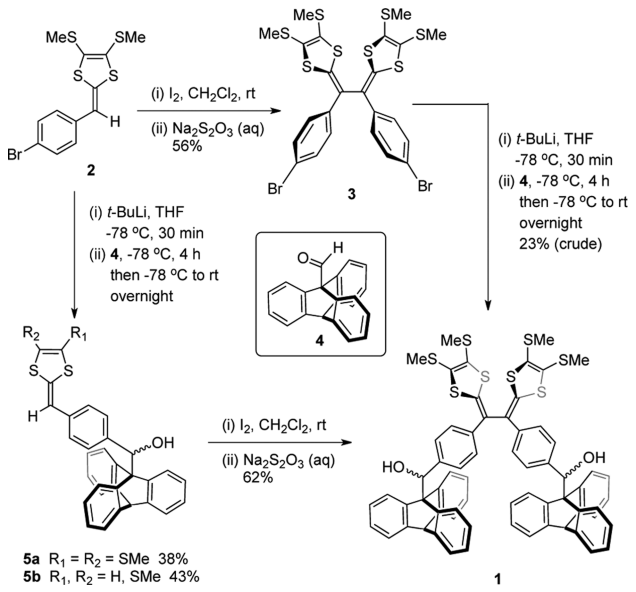
supported by the fact that both the steric crowding and electron density distribution of dipenyl-TTFV are substantially altered when it is switched from neutral to dicationic state. As such, the diphenyl-TTFV unit may act as a "molecular rotating regulator" under the control of redox stimuli.

Aiming at prototyping a diphenyl-TTFV-regulated molecular rotary device, we have designed and synthesized compound **1** (Scheme 2). The molecular structure of **1** is composed of two 9-triptycyl end groups and a diphenyl-TTFV central unit. The 9-benzyltriptycene segment was chosen because it has been well studied as a molecular gear, in which the phenyl and 9-triptycyl moieties favor geared (or concerted) rotation.[1a,10] Unlike many analogous molecular gear systems, in our design, a hydroxyl group is attached to the benzylic position. This feature was designed for a two-fold purpose. First, its synthesis can be easily undertaken reliably from aldehyde addition reaction.

Received: November 14, 2013
Published: January 14, 2014

   dx.doi.org/10.1021/ol403295q | *Org. Lett.* 2014, 16, 668–671

Scheme 2. Synthesis of Compound 1 via Two Different Routes



Second, the chirality of the benzylic carbon desymmetrizes the triptycyl unit, which in turn facilitates the study of rotational properties by dynamic ^{1}H NMR.

The synthesis of compound **1** was undertaken by two different routes, as illustrated in Scheme 2. The first route began with the oxidative dimerization of dithiafulvenyl (DTF)-substituted phenylbromide **2** promoted by iodine in CH_2Cl_2 at room temperature. The reaction afforded dibromo-TTFV **3** in 56% yield. Compound **3** was then subjected to a double lithium−halogen exchange with *t*-BuLi at low temperature. The in situ generated phenyl carbanion then underwent a nucleophilic addition with triptycene-9-carbaldehyde **4** to give the target compound **1** in a relatively low yield. Purification of compound **1** turned out to be extremely difficult, due to the formation of some inseparable byproducts. MS analysis revealed that the major byproduct(s) resulted from dethiomethylation of compound **1**, likely via a sulfur−lithium exchange mechanism.[11]

Alternatively, a second route was explored, in which compound **2** was first treated with *t*-BuLi, followed by an addition reaction with aldehyde **4**, to give compound **5a**. Again, the disfavored dethiomethylation reaction occurred noticeably in this reaction, leading to the formation of a byproduct **5b**. Fortunately, compounds **5a** and **5b** could be easily separated by column chromatography. Oxidative dimerization of pure **5a** with iodine then yielded compound **1** in a very good yield of 62%.

Since the structure of **1** carries two asymmetric benzylic carbons, it is possible that the product **1** resulting from oxidative dimerization of **5a** is composed of a pair of enantiomers (*RR*,*SS*) and a *meso* (*RS*) isomer, provided that the dimerization reaction proceeds without particular stereoselectivity. If such is the case, the ^{1}H NMR spectrum of **1** should be convoluted by these isomers and hence exhibit somewhat complex spectral patterns. Nevertheless, the actual ^{1}H NMR of **1** shows patterns much simpler than the expected mixture scenario. As can be seen from Figure 1A, all the aromatic protons of **1** are well-resolved and the spectral features appear to be similar to those of precursor **5b** (Figure 1B).

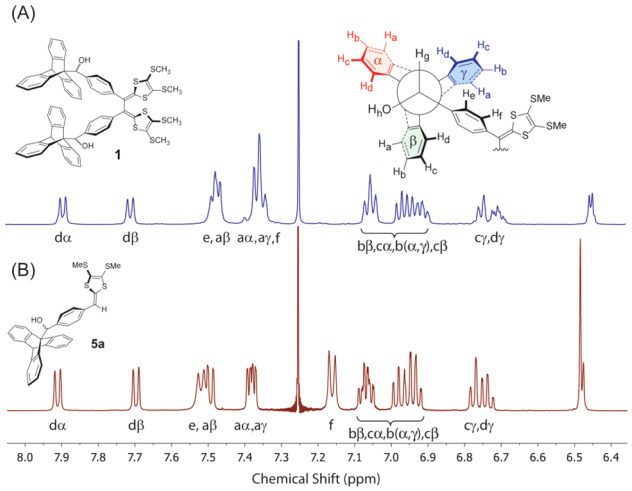


Figure 1. ^{1}H NMR (500 MHz, $CDCl_3$) spectra and assignments of signals in the aromatic regions for (A) compound **1** and (B) compound **5a**.

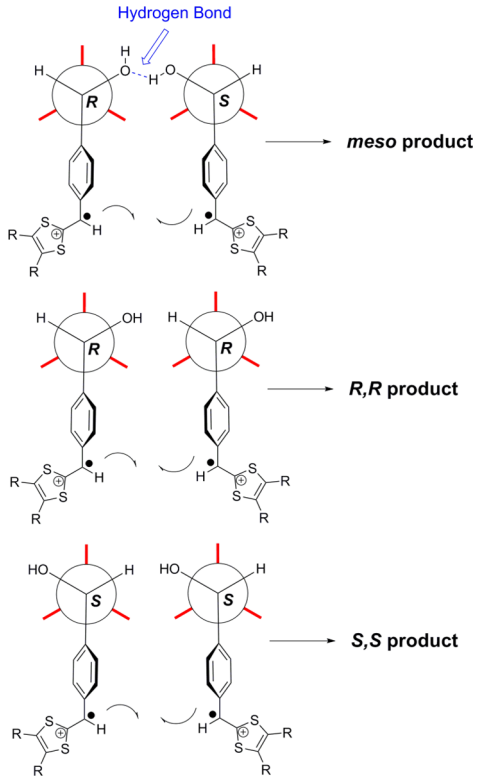
If the obtained product **1** is indeed a mixture of two enantiomers and one *meso* isomer, the only reasonable explanation for the clean ^{1}H NMR spectral features is that the chemical shift of each aromatic proton in the enantiomers is coincidentally identical to that of the corresponding proton in the *meso* isomer. The probability of such a scenario is obviously very low. On the other hand, if the dimerization of **5a** takes place via a stereoselective pathway, then the ^{1}H NMR results are in line with the reasoning that either the pair of enantiomers or the *meso* isomer is selectively formed. In conceiving the possible transition states involved in the oxidative dimerization of **5a**, one can easily find the preference for the *meso* product based on the hydrogen-bonding stabilization, as rationalized in Scheme 3. At this juncture, however, conclusive evidence for the optical purity of product **1** still awaits further investigation. Nevertheless, the clean and well-resolved spectral features observed in the aromatic region of the ^{1}H NMR spectrum of **1** indicate a two-fold symmetry, while such spectral simplicity indeed offers a great benefit to the subsequent dynamic NMR studies.

The electronic properties of compound **1** were studied by UV−vis absorption spectroscopy (see Figure S-26 in the Supporting Information). Both the UV−vis spectra of **1** and **5a** show the same the maximum absorption wavelength at λ_{max} = 358 nm, suggesting little differences in the degree of π-electron delocalization. The electrochemical redox properties of compound **1** and precursor **5a** were examined by cyclic voltammetry (CV), and the data are shown in Figure 2.

In the cyclic voltammogram of **5a**, a prominent anodic peak (E_{pa} = +0.82 V) is observed in the forward scan, which can be assigned to the single-electron oxidation on the DTF unit that leads to the formation a DTF radical cation. In the reverse scan, a cathodic peak (E_{pc} = +0.49 V) emerges, which is consistent with the two-electron reduction of a typical TTFV dication.[8,9] The CV results thus point to an EC mechanism wherein the DTF radical cation is converted into [TTFV^{2+}] at the working electrode through a rapid electrochemical dimerization process.[8] The cyclic voltammogram of **1** shows a quasi-reversible redox wave pair (E_{pa} = +0.67 V, E_{pc} = +0.44 V), which closely resembles the CV features of other known diphenyl-TTFVs.[8,9] The results suggest that the presence of triptycyl and benzylic alcohol groups has little effect on the

dx.doi.org/10.1021/ol403295q | *Org. Lett.* 2014, 16, 668−671

Scheme 3. Proposed Transition States for the Oxidative Dimerization of 5a Leading to Three Different Stereoisomers



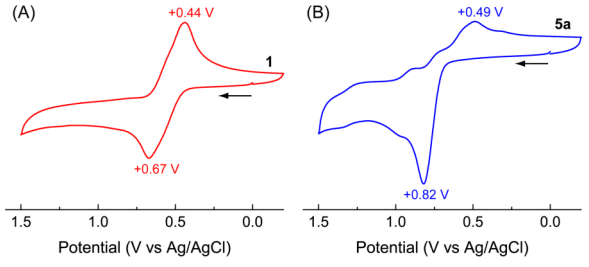


Figure 2. Cyclic voltammograms of (A) compound **1** and (B) **5a**. Experimental conditions: electrolyte, Bu_4NBF_4 (0.1 M); analyte (ca. 10^{-3} M); solvent, CH_2Cl_2; working electrode, glassy carbon; counter electrode, Pt wire; reference electrode, Ag/AgCl; scan rate, 0.2 V s^{-1}.

redox properties of the central TTFV unit, and the good electrochemical reversibility of **1** is indeed amenable to the study of redox-regulated rotatory motion within the molecular system.

The rotational properties of compound **1** and precursor **5a** were studied by variable temperature (VT)-NMR experiments. For compound **1**, at room temperature (298 K), each proton on the 9-triptycyl group appeared as distinctive signals as a result of very slow or restricted rotation between the triptycene wheel and the nearby phenyl paddle (see Figure 3). As the temperature is increased, significant peak broadening and merging can be seen due to faster rotation of the triptycene-benzyl molecular gear. For instance, the protons corresponding to H_d on the α and β phenyl rings of triptycene (for labeling, see Figure 1) appear as two sets of doublet of doublets (δ 7.88 and 7.76) at 298 K, which gradually merge into one broad singlet (δ 7.82) at temperatures above 338 K. Analysis of the VT-NMR data of **1** by simulation with the WinDNMR

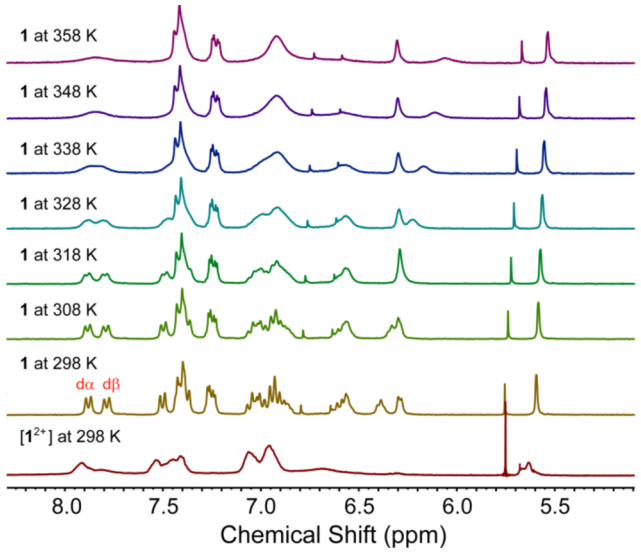
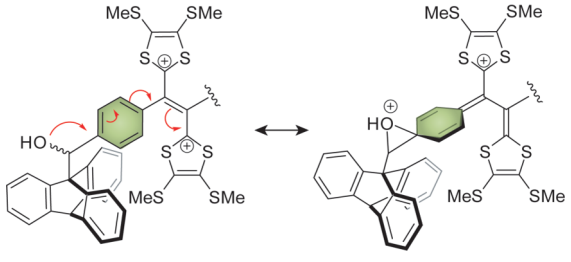


Figure 3. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **1** recorded at varying temperatures and the spectrum of [$\mathbf{1}^{2+}$] at 298 K.

program[12] allows the kinetic constants related to rotation to be calculated, which through the Erying plot give the activation energy for rotation as $\Delta H^{\ddagger}$ = 22.0 ± 1.2 kcal mol^{-1} and $\Delta S^{\ddagger}$ = 17 ± 4 cal mol^{-1} K^{-1} (see the Supporting Information for details). These values are very close to results of DTF precursor **5a** ($\Delta H^{\ddagger}$ = 18.8 ± 1.3 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 3 ± 3 cal mol^{-1} K^{-1}), suggesting that the TTFV linker does not add a significant amount of "torque" or "friction" to the rotation of the two benzyl-triptycene gears.

To test the redox-regulated rotational properties for compound **1**, dicationic [$\mathbf{1}^{2+}$] was first generated by addition of iodine (3 equiv) in a DMSO-d_6 solution of **1** at room temperature. The ^{1}H NMR spectrum of the resulting [$\mathbf{1}^{2+}$] was immediately recorded (see the bottom trace in Figure 3). Interestingly, the spectral pattern of the triptycyl protons in [$\mathbf{1}^{2+}$] bears close resemblance to the spectrum of neutral **1** measured above the coalescent temperature. VT-NMR analysis of [$\mathbf{1}^{2+}$], unfortunately, did not give meaningful data for exact calculation of its rotational energy barriers due to significant line shape broadening of signals. However, qualitative assessment on the change in rotational properties before and after TTFV oxidation can still be clearly made; that is, after the central TTFV unit is oxidized, the energy barrier for triptycyl of rotation is lowered and the rotation speed is considerably accelerated at room temperature. Rationalization for this oxidation-accelerated rotational property can be made based on an anchimeric assistance effect elicited by the benzylic hydroxyl group. As illustrated in Scheme 4, the interaction of

Scheme 4. Anchimeric Assistance Effect in [$\mathbf{1}^{2+}$] Which Facilates the Rotation of the Triptycyl Group



dx.doi.org/10.1021/ol403295q | Org. Lett. 2014, 16, 668–671

the hydroxyl electron lone pair with adjacent carbocation is expected to cause a wider bond angle between the triptycyl rotor and the adjacent phenyl paddle and hence results in much easier rotation of the triptycyl group.

In summary, we have prepared a prototype molecular gearset **1** designed to give redox-regulated rotatory motion. Dynamic NMR studies have shown that oxidation of the TTFV moiety in compound **1** causes its two triptycyl rotors to rotate at a faster rate than in the neutral state. At this juncture, the performances of this molecular gearset are far from being well-tuned and controlled since there are still many factors and fundamental issues that need to be investigated and understood. The current work is a promising small step contributing to the giant leap for achieving controllable and truly functioning artificial molecular rotary devices.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic procedures and spectroscopic characterizations for all new compounds and detailed dynamic ^{1}H NMR analysis of **1** and **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge NSERC, Canada Foundation of Innovation (CFI), and Memorial University for financial support.

■ REFERENCES

(1) (a) Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281. (b) Michl, J.; Sykes, E. C. H. *ACS Nano* **2009**, *3*, 1042.

(2) (a) Frantz, D. K.; Linden, A.; Baldridge, K. K.; Siegel, J. S. *J. Am. Chem. Soc.* **2012**, *134*, 1528. (b) Manzano, C.; Soe1, W.-H.; Wong, H. S.; Ample, F.; Gourdon, A.; Chandrasekhar, N.; Joachim, C. *Nat. Mater.* **2009**, *8*, 576.

(3) (a) Arcos-Ramos, R.; Rodríguez-Molina, B.; Romero, M.; Méndez-Stivalet, J. M.; Ochoa, M. E.; Ramírez-Montes, P. I.; Santillan, R.; Garcia-Garibay, M. A.; Farfán, N. *J. Org. Chem.* **2012**, *77*, 6887. (b) Kao, C.-Y.; Hsu, Y.-T.; Lu, H.-F.; Chao, I.; Huang, S.-L.; Lin, Y.-C.; Sun, W.-T.; Yang, J.-S. *J. Org. Chem.* **2011**, *76*, 5782.

(4) (a) Ruangsupapichat, N.; Pollard, M. M.; Harutyunyan, S. R.; Feringa, B. L. *Nat. Chem.* **2011**, *3*, 53. (b) van Delden, R. A.; ter Wiel, M. K. J.; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. *Nature* **2005**, *437*, 1337. (c) Kanazawa, H.; Higuchi, M.; Yamamoto, K. *J. Am. Chem. Soc.* **2005**, *127*, 16404.

(5) Setaka, W.; Nirengi, T.; Kabuto, C.; Kira, M. *J. Am. Chem. Soc.* **2008**, *130*, 15762.

(6) Sun, W.-T.; Huang, S.-L.; Yao, H.-H.; Chen, I.-C.; Lin, Y.-C.; Yang, J.-S. *Org. Lett.* **2012**, *14*, 4154.

(7) Kudernac, T.; Ruangsupapichat, N.; Parschau, M.; Maciá, B.; Katsonis, N.; Harutyunyan, S. R.; Ernst, K.-H.; Feringa, B. L. *Nature* **2011**, *479*, 208.

(8) (a) Lorcy, D.; Carlier, R.; Robert, A.; Tallec, A.; Le Maguerès, P.; Ouahab, L. *J. Org. Chem.* **1995**, *60*, 2443. (b) Hapiot, P.; Lorcy, D.; Carlier, R.; Tallec, A.; Robert, A. *J. Phys. Chem.* **1996**, *100*, 14823. (c) Yamashita, Y.; Tomura, M.; Zaman, M. B. *Chem. Commun.* **1998**, 1657. (d) Bellec, N.; Boubekeur, K.; Carlier, R.; Hapiot, P.; Lorcy, D.; Tallec, A. *J. Phys. Chem. A* **2000**, *104*, 9750.

(9) (a) Chen, G.; Mahmud, I.; Dawe, L. N.; Zhao, Y. *Org. Lett.* **2010**, *12*, 704. (b) Chen, G.; Mahmud, I.; Dawe, L. N.; Daniels, L. M.; Zhao, Y. *J. Org. Chem.* **2011**, *76*, 2701. (c) Zhao, Y.; Chen, G.; Mulla, K.; Mahmud, I.; Liang, S.; Dongare, P.; Thompson, D. W.; Dawe, L. N.; Bouzan, S. *Pure Appl. Chem.* **2012**, *84*, 1005.

(10) (a) Yamamoto, G. *Pure Appl. Chem.* **1990**, *62*, 569. (b) Yamamoto, G. *Tetrahedron* **1990**, *46*, 2761. (c) Yamamoto, G.; Oki, M. *J. Org. Chem.* **1983**, *48*, 1233.

(11) Foubelo, F.; Yus, M. *Chem. Soc. Rev.* **2008**, *37*, 2620.

(12) Reich, H. J. *J. Chem. Educ.* **1995**, *72*, 1086.