## Hindered Rotation

## **Optical Stability of Axially Chiral Push–Pull-Substituted Buta-1,3dienes: Effect of a Single Methyl Group on the C<sub>60</sub> Surface\*\***

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Axial chirality stems from the restricted rotation around a single bond, and the most abundant class of compounds featuring this type of chirality are biaryl derivatives. Biaryl structural motifs are encountered in a large number of optically active natural products,<sup>[11]</sup> and also provide the basis for some of the most versatile classes of enantiomerically pure ligands for asymmetric catalysis, such as 1,1'-binaphthalene derivatives.<sup>[2]</sup> A chiral axis is also found in substituted allenes,<sup>[3]</sup> alkylidenecycloalkanes, spiranes,<sup>[4]</sup> and buta-1,3-dienes. Only a few examples of sterically congested, axially chiral buta-1,3-dienes have been reported, and a summary of them, resulting in particular from early work by Köbrich, Mannschreck, and co-workers,<sup>[5]</sup> is included in Figure 1SI in the Supporting Information.

Over the past few years, we have prepared a large number of nonplanar push–pull-substituted buta-1,3-dienes by [2+2] cycloaddition of either tetracyanoethene (TCNE) or 7,7,8,8tetracyano-*p*-quinodimethane (TCNQ) with electron-donorsubstitued alkynes, and subsequent cycloreversion.<sup>[6-8]</sup> In several of these systems, the buta-1,3-diene moieties are highly sterically congested and NMR spectroscopy indicated the presence of different conformers undergoing slow exchange, resulting from hindered rotation about their central C–C single bond.<sup>[7]</sup> However, efforts to separate the axially chiral enantiomers were unsuccessful.

The stable and highly soluble nonplanar push–pull chromophores obtained by the TCNE and TCNQ additions are potent electron acceptors,<sup>[6]</sup> and this motivated us to conjugate them to  $C_{60}$  to improve the solubility of the carbon sphere and enhance its electron uptake capacity.<sup>[9]</sup>

Herein, we report the synthesis and X-ray structure of conjugates between  $C_{60}$  and push-pull chromophores obtained from TCNE and TCNQ by a cycloaddition/cyclo-reversion sequence. The focus lies on the remarkable stereochemical properties of the resulting axially chiral buta-1,3-dienes: a single methyl group attached to the full-

 [\*] Dr. M. Yamada, P. Rivera-Fuentes, Dr. W. B. Schweizer, Prof. Dr. F. Diederich Laboratorium für Organische Chemie, ETH Zürich Hönggerberg, HCI, 8093 Zürich (Switzerland) Fax: (+41)44-632-1109 E-mail: diederich@org.chem.ethz.ch Homepage: www.diederich.chem.ethz.ch erene surface is shown to raise the barrier for rotation about their chiral axis to such an extent that separation, isolation, and chiroptical characterization of the enantiomers of non-planar buta-1,3-diene-based charge-transfer (CT) chromophores are possible for the first time.<sup>[10]</sup>

The synthesis of conjugates 1-6 (Scheme 1) begins with a protocol for fullerene alkynylation introduced in 1994 independently by Komatsu et al.<sup>[11]</sup> and our group.<sup>[12]</sup> Addition of lithiated N,N-dimethylanilino(DMA)-substituted acetylene to C<sub>60</sub>, and then either protonation (AcOH) or methylation (MeI), afforded intermediates 7 and 8; the latter was characterized by X-ray analysis (see Figure 2SI in the Supporting Information). Subsequent addition of TCNE and TCNQ, respectively, yielded the fullerene-CT chromophore conjugates 1-4 having the nonplanar push-pull buta-1,3-dienes directly attached to the carbon sphere. Conjugates 5 and 6, having an acetylenic spacer separating the CT chromophore and the fullerene, were obtained by addition of Me<sub>3</sub>Si-C=C-Li and subsequent deprotection to give 9, which then underwent oxidative hetero-Hay-coupling to yield 10 for subsequent cycloaddition/cycloreversion. All fullerene-CT chromophore conjugates are deeply colored solids that are stable at ambient temperature in air. Due to the nonplanarity of the push-pull butadiene moiety, they are highly soluble in common organic solvents such as CH<sub>2</sub>Cl<sub>2</sub>. The [6,6]-addition pattern (addition to the double bond shared by two sixmembered rings) on the fullerene was confirmed by the characteristic UV/Vis absorption maxima at  $\lambda_{max} = 431-434$ and 702 nm in the precursors 7, 8, and 10.<sup>[13]</sup> The UV/Vis spectra of 1-6 show intense broad CT bands with maxima between 450 and 700 nm (see Figures 18-23SI in the Supporting Information). Clear hypochromic shifts were observed after addition of CF<sub>3</sub>COOH, and the original CT bands were recovered upon addition of a base (Et<sub>3</sub>N or K<sub>2</sub>CO<sub>3</sub>).

The structures of the conjugates 2, 4, and 6 were additionally confirmed by X-ray structure analysis (Figure 1). The molecular structures confirmed not only the attachment of the two groups to the [6,6] junction, but also provided evidence for substantial bond length alternation in the DMA ring, indicative of efficient push-pull conjugation in the ground state (see Figure 3SI in the Supporting Information). The push-pull chromophores in 2, 4, and 6 are highly distorted from planarity, mainly by rotation around the chiral axis of the buta-1,3-diene moieties.

The NMR spectra of the conjugates recorded in  $C_2D_2Cl_4$ show large differences, depending on the nature of the second group on the fullerene surface (H or Me) and on the absence or presence of an acetylenic spacer (see the Supporting Information). Two rotational processes around C–C single bonds need to be considered: rotation about the bond



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only for 1, 3, 5, and 6. Nota-

bly, conjugates **1**, **3**, **5**, and **6** retain their  $C_s$  symmetry even at 193 K in a  $CD_2Cl_2$ solution. In contrast, conju-

gates 2 and 4, having a Me

group on the fullerene sur-

face and lacking an acety-

lenic spacer, are  $C_1$  symmetric according to the <sup>13</sup>C NMR spectra. The decrease in the molecular symmetry in **2** and

4 reflects hindered rotation

around the central buta-1,3-

diene C-C single bond, ren-

group, rigidly attached to

the fullerene surface, is the

origin of the axial chirality. When replaced by a H (as in 1 and 3), the rotation around the butadiene central bond becomes fast on the NMR

time scale. This is also the case, when the distance

between Me group and buta-

diene is increased by acety-

lene insertion (as in 5 and 6).

The axially chiral enantio-

meric pairs (P)-2/(M)-2 and (P)-4/(M)-4 are shown in

chiral

compounds

The

and

Me

the

dering

axially

 $C_1$  symmetric.



**Scheme 1.** a) 1. {[4-(*N*,*N*-dimethylamino)phenyl]ethynyl]lithium, THF, 20°C; 2. AcOH or Mel, 20°C or 40°C, 25% (**7**), 31% (**8**); b) 1. [(trimethylsilyl)ethynyl]lithium, THF, 20°C; 2. Mel, 40°C; 3.  $K_2CO_3$ , THF/MeOH (2:1), 20°C, 18% (**9**); c) 4-ethynyl-*N*,*N*-dimethylaniline, CuCl, O<sub>2</sub>, TMEDA, PhCl, 20°C, 61% (**10**); d) TCNE, 1,2-dichloroethane, 20°C, 39% (**1**), 80% (**2**); e) TCNQ, 1,2-dichloroethane or PhCl, 80°C, or 132°C, 62% (**3**), 94% (**4**); f) TCNE, PhCl, 20°C, 97% (**5**); g) TCNQ, PhCl, 80°C, 41% (**6**). TMEDA = *N*,*N*,*N*',*N*'-tetra-methylethylenediamine.

connecting the CT chromophore to the  $C_{60}$  core and rotation about the central bond of the buta-1,3-diene moiety. Although the conjugates **1–6** have inherently achiral  $C_{60}$ addition patterns, the <sup>13</sup>C NMR spectra reveal  $C_s$  symmetry Figure 2 below.

Atropisomerism about the C–C single bond connecting the butadiene moiety to the fullerene core is observed by <sup>1</sup>H NMR analysis of **1–3** at 298 K. The two atropisomers of  $C_s$ -



Figure 1. ORTEP drawings of a) 2, b) 4, and c) 6 with thermal ellipsoids shown at the 50% probability level for 173–223 K. Solvate molecules are omitted for clarity. Selected dihedral angles [°]: a) C78-C63-C62-C73 74.1, C78-C63-C64-C65 46.0; b) C64-C63-C62-C84 79.8, C64-C63-C73-C78 54.0; c) C72-C62-C83-C85 60.1, C72-C62-C63-C64 26.6.

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## Communications

symmetric **1** are observed in a 1.0:0.65 ratio ( $\Delta G = 0.3$  kcal mol<sup>-1</sup>). Increased broadening of the peaks is observed upon heating the sample to 368.2 K (see Figure 24SI in the Supporting Information). Since the coalescence temperature is higher than 368.2 K, it is estimated that the free enthalpy of activation,  $\Delta G^{\neq}$ , is larger than 17.2 kcalmol<sup>-1</sup> based on the Eyring equation. The <sup>1</sup>H NMR spectrum of  $C_1$ -symmetric 2 also exhibits two sets of signals assignable to atropisomers in a ratio of 1.0:0.19, yielding  $\Delta G = 1.0 \text{ kcal mol}^{-1}$ . Again, peak broadening is observed upon heating and  $\Delta G^{\neq}$  is estimated larger than 17.6 kcalmol<sup>-1</sup>. A similar atropisomerism (ratio 1.0:0.48;  $\Delta G = 0.4 \text{ kcal mol}^{-1}$ ) was observed for  $C_s$ -symmetric **3**. Here, the coalescence temperature  $(T_c)$  was reached  $[T_c =$  $(345 \pm 5)$  K] and  $\Delta G^{\neq}$  calculated as  $(16.1 \pm 0.3)$  kcal mol<sup>-1</sup>. In contrast, the <sup>1</sup>H NMR spectrum of **4** only shows one  $C_1$ symmetric atropisomer; the equilibrium is shifted because of the steric repulsion between the methyl group on  $C_{60}$  and the cyclohexa-2,5-diene-1,4-diylidene moiety. The energy difference between the two atropisomers of 4 was estimated to be 4.2 kcal mol<sup>-1</sup> by density functional theory (DFT) calculations at the B3LYP/6-31G\* level of theory (see the Supporting Information). Notably, the calculated structures of the preferred atropisomers of **2** and **4** closely resembles the one observed by X-ray crystallography.

The remaining question was whether the barrier for rotation around the chiral axis in 2 and 4 would be sufficiently large to allow separation of the  $C_1$ -symmetrical conjugates into their enantiomers. This could indeed be accomplished with an enantiomeric ratio (e.r.) of greater than 99:1 by HPLC methods using the chiral stationary phase (S,S)-WHELK-O1 (see Figure 28SI in the Supporting Information). Large optical rotations at  $\lambda = 589$  nm were measured: +770 for (+)-2 and +5800 for (+)-4. The CD spectra of (+)-2/(-)-2and (+)-4/(-)-4, respectively, are mirror images along the abscissa and show Cotton effects associated with the CT absorptions (Figure 2). This observation gives conclusive evidence that  $(\pm)$ -2 and  $(\pm)$ -4 are axially chiral butadienes. The CD curves of (+)-2/(-)-2 change drastically upon acidification with TFA and were fully recovered after neutralization with Et<sub>3</sub>N (see Figure 29SI in the Supporting Information). In contrast, acidification of a CH<sub>2</sub>Cl<sub>2</sub> solution of (+)-4/(-)-4 with TFA and subsequent neutralization with Et<sub>3</sub>N caused a large decrease in intensity of the CD features (see Figure 30SI in the Supporting Information). Apparently the barrier for racemization of (+)-4/(-)-4 is lower than for



(+)-2/(-)-2.

A kinetic study was carried out to determine the activation parameters for racemization. Both compounds (+)-2/(-)-2 and (+)-4/(-)-4racemized readily upon moderate heating, with the former being the more optically stable conjugate. The racemization processes of the (+)- and (-)-enantiomers were monitored by CD spectroscopy of 1,2dichloroethane solution, and the firstorder rate constants were obtained by linear line-fitting plots of the molar circular dichloism  $\Delta \varepsilon$  as a function of time at different temperatures (see Figures 31SI-41SI in the Supporting Information). From the Arrhenius plot and the Eyring equation, the activation parameters were obtained (Table 1). As already deduced

**Figure 2.** a) Top: CD spectra of enantiopure (+)-2 (black line) and (-)-2 (gray line). Bottom: UV/Vis spectrum. b) Top: CD spectra of enantiopure (+)-4 (black line) and (-)-4 (gray line). Bottom: UV/Vis spectrum. All spectra recorded for compounds in  $CH_2CI_2$  solutions.

**Table 1:** Kinetic parameters obtained from Arrhenius plots and from the Eyring equation.<sup>[a]</sup>

[	[]		[u]
<b>2</b> 27.6±2.3 9.7±6.7 2	$24.8 \pm 0.3$	$28.2 \pm 2.2 \\ 12.4 \pm 1.0$	$5.9 \pm 2.4$
<b>4</b> 11.8±1.0 -38.3±3.2 2	23.3 ± 0.1		$1.2 \pm 0.1$

[a] All data represent an average value obtained from three measurements.

from qualitative observations, the activation free enthalpy  $(\Delta G^{\neq})$  for racemization of (+)-2/(-)-2 (half-life at 313 K  $\tau_{1/2} = 5.9$  h) is approximately 1.5 kcal mol<sup>-1</sup> larger than that for (+)-4/(-)-4 ( $\tau_{1/2} = 1.2$  h). This difference can be attributed to the fact that the cyclohexa-2,5-diene-1,4-diylidene moiety is more flexible, and its distortion by bending out of plane is energetically less disfavored, as compared to the dicyanovinyl moiety.

The absolute configuration of the axially chiral butadienes was determined through comparison of the experimental CD spectra with spectra obtained in theoretical calculations (time-dependent DFT (TD/DFT) using the the B3LYP<sup>[14]</sup> functional and the 6-31G\* basis set). As shown in Figure 46SI in the Supporting Information, the basic patterns of the CD curves of (-)-2 and (-)-4 (sign, magnitude, and position of Cotton effects) are in agreement with the TD/DFT calculations of (M)-2 and (M)-4, respectively. Therefore, the absolute configurations of both (-)-2 and (-)-4 were determined as M. In addition, the TD/DFT calculations are in agreement with the absorption spectra of 2 and 4 (see Figures 42SI and 43SI in the Supporting Information).

In summary, we have prepared a new family of axially chiral buta-1,3-dienes involving conjugation of nonplanar push–pull chromophores to  $C_{60}$ , separated their enantiomers, and determined their absolute configuration. This investigation adds a new aspect to fullerene chirality, in which the surface of the carbon sphere plays a key role.<sup>[10,15]</sup> It reveals a particularly dramatic difference between a Me and a H—both rigidly fixed on the fullerene surface—in sterically affecting the rotation around a neighboring single bond. This study clearly demonstrates that the integrity of  $C_{60}$  can serve as powerful steric force to control molecular configurations and opens up a new avenue of chiral buta-1,3-diene chemistry.

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