π-Conjugated Conjoined Double Helicene via a Sequence of Three Oxidative CC- and NN-Homocouplings

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Chiral π-conjugated systems with helically annelated aromatic rings possess extraordinary chiral properties.[1] Although significant advances in the synthesis of helical and doubly helical molecules have been made in recent years,[1−3] typical syntheses of such highly annelated molecules are tedious and produce relatively low yields. Novel efficient synthetic approaches to adequately functionalized, strongly chiral molecules are critical in enabling emerging applications for chiral π-conjugated materials.[4,5]

Herein we describe an efficient synthesis of a chiral π-conjugated dihydrazine **1**, in which the two [5]helicene-like fragments are annelated in their mid-sections to give a conjoined double helicene structure (Figure 1).
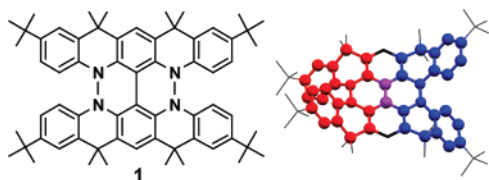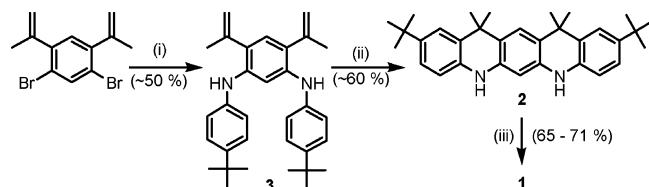
Figure 1. Dihydrazine **1**. Each of the two homochiral [5]helicene-like fragments is shown in stick-and-ball.

The synthesis of **1** was discovered during screening for the optimum routes to the dinitroxide, derived from diamine **2** (Scheme 1).[6] The remarkable aspect of this synthesis is that the chiral

Scheme 1 [a]

[a] (i) 4-*tert*-Butylaniline (2.2 equiv), *t*-BuONa (∼3 equiv), Pd(OAc)$_2$ (0.01 equiv), *t*-Bu$_3$P (0.03 equiv), toluene, under N$_2$, 90 °C for 12 h; (ii) H$_3$PO$_4$, 85 wt % in water, under N$_2$, 90 °C for 3−4 h; (iii) (PhCO$_2$)$_2$ (1.75−2.1 equiv), CH$_2$Cl$_2$, under air, 0 °C for 3 h.

structure **1** is obtained in high yield in a single, atom-efficient synthetic step from planarized diamine **2** via three oxidative homocouplings (one CC and two NN), and two annelating cyclizations, using a single reagent, such as benzoyl peroxide, (PhCO$_2$)$_2$.[7] Diamine **2** is prepared by annelation of **3** using electrophilic aromatic substitution.[8] **3** is obtained from 4,6-diisopropenyl-1,3-dibromobenzene[9] and 4-*tert*-butylaniline, using Pd-catalyzed CN bond cross-coupling.[10]

The ^{1}H and ^{13}C NMR data for **1** in solution are consistent with a conjoined double helicene structure, in which [5]helicene-like fragments are either homochiral or heterochiral (*meso*); that is, **1**
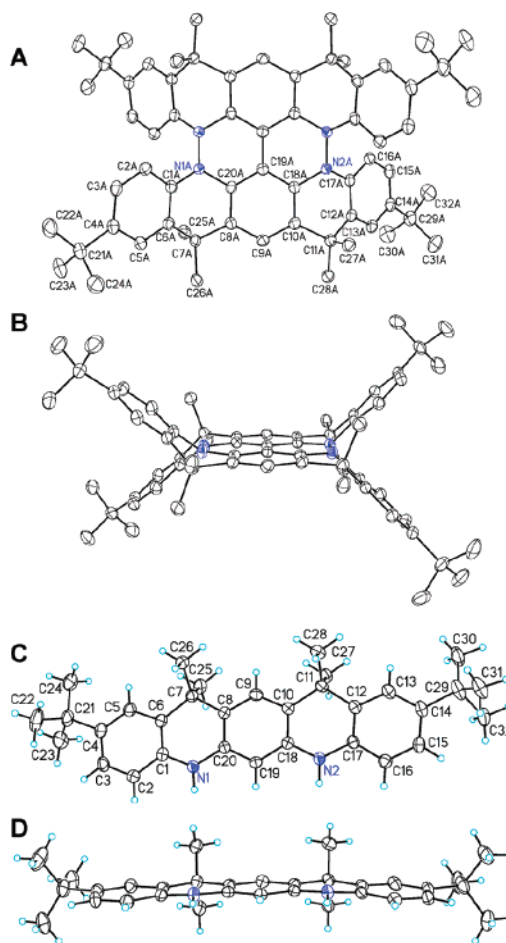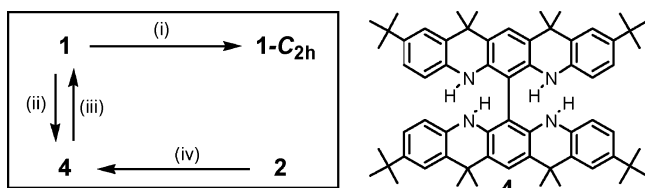
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Figure 2. Molecular structure and conformation for dihydrazine **1** and diamine **2**: (A) top view of **1**; (B) side view of **1**; (C) top view of **2**; and (D) side view of **2**. Carbon and nitrogen atoms are depicted with thermal ellipsoids set at the 50% probability level. Only one of the two unique molecules of **1**, in which hydrogen atoms are omitted for clarity, is shown. For **2**, disorder is omitted for clarity.

may possess either a D_2 (as in Figure 1) or C_{2h} point group. In particular, diastereotopic splitting ($\Delta\nu \approx 100$ Hz) for the methyl groups of the dihydropyridine rings is observed, with no line broadening up to at least 70 °C. However, upon addition of chiral shift reagent, ytterbium[tris(3-heptafluoropropylhydroxymethylene)-(+)-camphorate], the ^{1}H NMR (400 MHz, benzene-d_6) spectrum shows additional diastereomeric splittings, in particular, the methyl groups of the *t*-Bu groups appear as two well-resolved 1:1 singlets (e.g., $\Delta\delta \approx 0.01$ ppm). This precludes the achiral C_{2h} point group and indicates that the D_2-symmetric double helical structure of **1** is configurationally stable on the ^{1}H NMR time scale, providing the lower limit of 16 kcal mol^{-1} for the barrier for racemization in **1**.

Scheme 2 *a*

a (i) AcOH, 110 °C, 1 h, 66−73%; (ii) H$_2$NNH$_2$, AcOH, 110 °C, 10 min, quant.; (iii) (PhCO$_2$)$_2$ (2.0 equiv), CH$_2$Cl$_2$, under air, 0 °C, ∼4 h, ∼75%; (iv) (PhCO$_2$)$_2$ (0.75 equiv), CH$_2$Cl$_2$, under air, 0 °C, 3 h, 59−70%.

Structures of dihydrazine **1** and diamine **2** are confirmed by single-crystal X-ray analysis (Figure 2).

In diamine **2**, the annelated structure of five six-membered rings is approximately planar.[11a] Dihydrazine **1**, which may be viewed as a dimer of **2**, possesses an approximate D_2 point group. In the structure of **1**, each monomeric diamine moiety derived from **2** adopts a chairlike conformation, with the dihedral angles of 40.96-(3) and 43.90(3)° and dihedral angles of 40.85(3) and 43.64(3)° for the two independent molecules A and B, respectively. The two "chairs" are oriented antiparallel to each other, with their fused seats forming the approximately planar central part of the molecule, consisting of four six-membered rings.[11b] Therefore, the overall structure of **1** is conjoined helical, with two homochiral [5]helicene-like fragments annelated in their mid-sections (Figures 1 and 2).[12,13] Furthermore, the "four-armed" molecular shape of **1** results in inefficient crystal packing. It is conceivable that a single enantiomer may not crystallize but rather form an isotropic glassy material.[5b]

Because of the possible cooperativity in double chair-to-chair flips and inversion of configuration for both [5]helicene-like fragments, the barrier for the racemization of **1** is likely to be much higher than the lower limit estimate by ^{1}H NMR spectroscopy. Analogous cooperativity may be demonstrated for the double chair-to-boat flips, corresponding to the isomerization of the D_2-symmetric **1** to its C_{2h}-symmetric diastereomer (**1-**C_{2h}). Such isomerization occurs readily in acetic acid at moderate temperatures (Scheme 2), indicating that **1-**C_{2h} is the thermodynamic product. However, in the absence of acid, **1** isomerizes to **1-**C_{2h} with a half-life of ∼3 h at 180 °C in naphthalene solution. This corresponds to a free energy barrier of ∼35 kcal mol^{-1} for the inversion of one of the [5]helicene-like fragments in the D_2-symmetric structure **1**. This relatively high barrier, compared to the barrier of 24.1 kcal mol^{-1} in [5]helicene,[14] may be indicative of cooperativity in the conversion from two chairs in D_2 to two boats in the C_{2h} point group.[15]

Dihydrazine **1** is reduced to achiral tetraamine **4** (Scheme 2). Oxidation of **4** with (PhCO$_2$)$_2$ gives exclusively dihydrazine **1**; upon partial oxidation of **4**, only **1** and unreacted **4** are detected. Interestingly, **4** is obtained in good isolated yield via partial oxidation of diamine **2**. These results suggest that **4**, that is, CC-monocoupling product of **2**, is an intermediate in the oxidation pathway from **2** to **1**.[16]

UV/vis absorption spectra in *n*-heptane showed the expected red shift from λ_{max} = 275 nm (sh 333 nm) for diamine **2** to λ_{max} = 409 nm (sh 439 nm) for dihydrazine **1**.[17] A blue fluorescence is found for **1** in *n*-heptane, with quantum efficiency, $\Phi_F \approx$ 15%, at λ_{max}^{em} = 472 nm (excitation in the λ^{exc} = 289 and 409 nm).[17]

In summary, the synthesis of **1** provides a novel, highly efficient approach to a chiral π-conjugated conjoined double helicene with remarkable configurational stability. Considering the molecular shape, the hydrazine moieties of **1**, and the possible analogues of **1**, organic materials that are strongly chiral, electroactive, and isotropic may be envisioned. Resolution and syntheses of analogues of **1** with extended conjoined helical structures are being pursued.[18]

References

(1) (a) Meurer, P. P.; Vögtle, F. *Top. Curr. Chem.* **1985**, *127*, 1−76. (b) Oxidative coupling: Larsen, J.; Bechgaard, K. *J. Org. Chem.* **1996**, *61*, 1151−1152. (c) Katz, T. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 1921−1923. (d) Han, S.; Bond, A. D.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitener, G. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3223−3227. (e) Urbano, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3986−3989. (f) Schmuck, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2448−2452. (g) Rajca, A.; Miyasaka, M.; Pink, M.; Wang, H.; Rajca, S. *J. Am. Chem. Soc.* **2004**, *126*, 15211−15222.

(2) π-Conjugated double helices: (a) Rajca, A.; Safronov, A.; Rajca, S.; Schoemaker, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 488−491. (b) Marsella, M. J. *Acc. Chem. Res.* **2002**, *35*, 944−951. (c) An, D. L.; Nakano, T.; Orita, A.; Otera, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 171−173.

(3) Triple and double helicenes: (a) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **2000**, *2*, 1629−1632. (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **2003**, *5*, 1863−1866. (c) Gomez-Lor, B.; Echavarren, A. M. *Org. Lett.* **2004**, *6*, 2993−2996.

(4) Selected examples: (a) Zahn, S.; Swager, T. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4225−4230. (b) Percec, V.; Glodde, M.; Bera, T. K.; Miura, Y.; Shiyanovskaya, I.; Singer, K. D.; Balagurusamy, V. S. K.; Heiney, P. A.; Schnell, I.; Rapp, A.; Spiess, H.-W.; Hudson, S. D.; Duan, H. *Nature* **2002**, *419*, 384−387. (c) Field, J. E.; Muller, G.; Riehl, J. P.; Venkat-araman, D. *J. Am. Chem. Soc.* **2003**, *125*, 11808−11809.

(5) Chiral optical waveguides using chiral isotropic glasses: (a) Herman, W. N. *J. Opt. Soc. Am. A* **2001**, *18*, 2806−2818. (b) Miyasaka, M.; Rajca, A.; Pink, M.; Rajca, S. *Chem.−Eur. J.* **2004**, *10*, 6531−6539.

(6) Oxidation of **2** to the corresponding dinitroxide will be reported elsewhere.

(7) Two NN-homocouplings in cyclodehydrogenation of tetra(benzimidazol-2-yl)benzenes: Wu, W.; Grimsdale, A. C.; Müllen, K. *Chem. Commun.* **2003**, 1044−1045.

(8) Hellwinkel, D.; Schmidt, W. *Chem. Ber.* **1980**, *113*, 358−384.

(9) Rajca, A.; Utamapanya, S. *J. Org. Chem.* **1992**, *57*, 1760−1767.

(10) Goodson, F. E.; Hauck, S. I.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 7527−7539.

(11) (a) In diamine **2**, the mean deviation from a calculated least-squares plane, including all five six-membered rings (C1−C20, N1, N2) is 0.0834 Å. (b) In dihydrazine **1**, the mean deviations from a calculated least-squares plane, including the two center benzene rings and the nitrogens (C7, C8, C9, C10, C11, C18, C19, C20, N1, N2, C7$^{#1}$, C8$^{#1}$, C9$^{#1}$, C10$^{#1}$, C11$^{#1}$, C18$^{#1}$, C19$^{#1}$, C20$^{#1}$, N1$^{#1}$, N2$^{#1}$, with symmetry operation #1: $-x$, y, 0.5 − z), are 0.0237 and 0.0314 Å for the two independent molecules.

(12) With the middle benzene ring of the [5]helicene-like fragment as a reference, the inner helix climbs 3.3 Å and turns in-plane by 280°.

(13) Benzo[*c*]benzo[3,4]cinnolino[1,2]cinnoline: (a) Neugebauer, F. A.; Ku-hnhäuser, S. *Angew. Chem., Int. Ed.* **1985**, *24*, 596−597. (b) Fischer, H.; Krieger, C.; Neugebauer, F. A. *Angew. Chem., Int. Ed.* **1986**, *25*, 374−375. (c) Dietrich, M.; Heinze, J.; Krieger, C.; Neugebauer, F. A. *J. Am. Chem. Soc.* **1996**, *118*, 5020−5030.

(14) Goedicke, C.; Stegemeyer, H. *Tetrahedron Lett.* **1970**, 937−940.

(15) (a) Double nitrogen inversion in the hydrazine moiety may contribute to the cooperativity. (b) Racemization of **1** would involve double nitrogen inversion in both hydrazine moieties. (c) Nelsen, S. F.; Frigo, T. B.; Kim, Y.; Thompson-Colon, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 7926−7934.

(16) Formation of **4** may involve either the CC-homocoupling via radical cation (or diradical dication) of **2** or the NN-homocoupling followed by benzidine rearrangement (e.g., [3,3]-sigmatropic shift): Cepanec, I. *Synthesis of Biaryls*; Elsevier: Amsterdam, 2004; Chapter 6, pp 209−239.

(17) (a) **1**: UV/vis (*n*-heptane): λ_{max}/nm (ϵ_{max}/L mol^{-1} cm^{-1}) = 289 (7.4 × 10^4), 333 (sh, ∼8 × 10^3), 409 (∼4 × 10^3, ∼3 × 10^3). Fluorescence (*n*-heptane): λ_{max}^{em}/nm (λ_{exc}/nm, Φ_F/%) = 472 (289, ∼15), 472 (409, ∼15); the emission spectra for **1** are concentration independent (6.0 × 10^{-6} − 1.5 × 10^{-5} M, λ_{exc}/nm = 409). (b) **2**: UV/vis (*n*-heptane): λ_{max}/nm (ϵ_{max}/L mol^{-1} cm^{-1}) = 275 (∼3 × 10^4), 333 (sh, ∼3 × 10^3); the data for **2** are only qualitative, due to its very low solubility in *n*-heptane.

(18) Our approach is based upon replacement of 4-*tert*-butylaniline with 2,4-disubstituted anilines and angularly connected aromatic amines in the synthetic route in Scheme 1, for example, using 1-aminonaphthalene to obtain the conjoined double helicene of [7]helicene-like fragments.

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