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Synthesis and Structure of *m*-Terphenyl-Based Cyclophanes with Nitrogen Intra-annular Functional Groups

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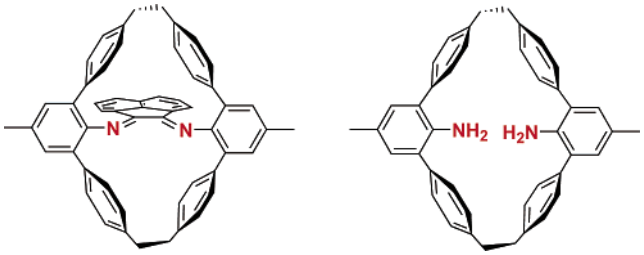
ABSTRACT



Herein we describe an efficient synthesis of cyclophanes comprised of intra-annular nitrogen functional groups through a template-promoted cyclization by ring-closing metathesis (RCM). The synthesis proceeds through condensation of *meta*-styryl anilines with acenaphthenequinone to form the templates, followed by RCM with Grubb's second-generation catalyst to afford cyclophanes with internal α-diimine functionality. Prolonged hydrogenation efficiently removes the template to provide a macrocycle containing the diamine functionality.

Cyclophanes, i.e., macrocycles containing aromatic groups, have received widespread attention due to their ability to host various metals and form many inclusion complexes.[1] The unique chemistry of cyclophanes was applied to molecular recognition, metal ion transport, and catalysis.[1] Cyclophanes containing intra-annular functionalities are critical for various applications due to the relative ease of tailoring selectivities for molecular recognition and complexation with ionic or neutral species. For example, the hydroxyl functionality of calixarenes has been exploited extensively for this purpose.[2] However, the difficulty involved in selective removal and modification of the hydroxyl moieties in the lower rim of calixarenes limits their synthetic potential because relatively harsh conditions are usually required to introduce new functional groups.[3] The increasing popularity of macrocycles similar to porphyrin and salen derivatives as ligands for metal-catalyzed reactions has prompted us and others[4] to investigate efficient synthetic routes of cyclophanes containing intra-annular functionalities. We wish to report here a facile synthesis of *m*-terphenyl-based cyclophanes containing amine and diimine groups at the core of the macrocycle. The presence of nitrogen functional groups at the core of cyclophanes is synthetically relevant for catalysis since nitrogen serves as a versatile binding site for a variety of metal complexes.[5] For example, bidentate and tridentate nitrogen ligands are important for

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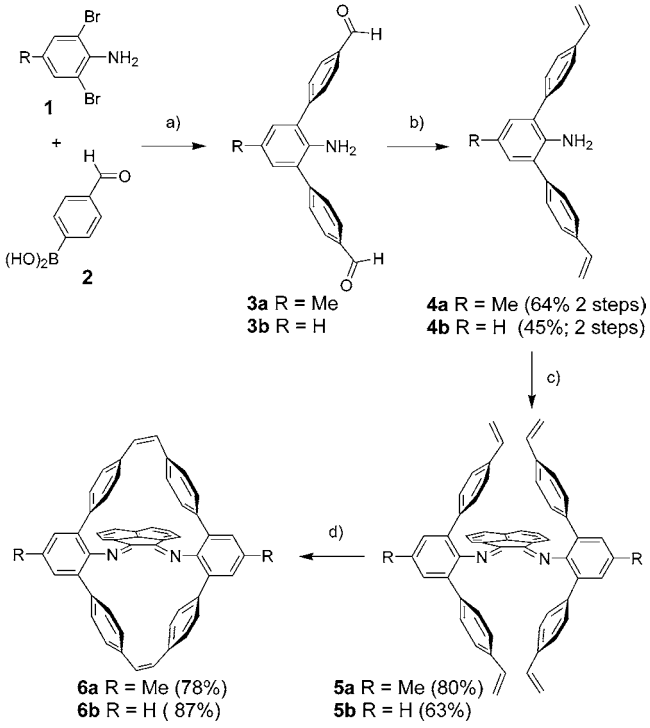
many catalytic transformations.[6] Moreover, for molecular recognition studies, the introduction of nitrogen functionalities at the core of cyclophanes offers new opportunities for functionalization and tailoring of binding selectivity.[7]

Our interest in macrocycle synthesis stems from our study on α-diimine complexes for olefin polymerization.[8] The α-diimine ligands play a significant role in the efficient polymerization of ethylene, α-olefin, and polar comonomers catalyzed by late transition metals.[8,9] Modification of the α-diimine ligand structure was shown to significantly affect the rate of polymerization and the properties of the resultant polymers.[9] We are currently exploring a family of cyclophane-based diimine ligands for olefin polymerization catalysis.[10] In parallel with our catalysis studies, we are developing efficient syntheses of *m*-terphenyl-based cyclophanes containing amine and diimine functionalities at the core.[11]

The key strategy employed in our synthesis is the use of the *cis*-α-diimine as an organic template to facilitate the cyclization by ring-closing metathesis (RCM). RCM of olefins has shown to be a general strategy for the synthesis of macrocyclic compounds.[12] In the closure of medium-sized rings, template effects have been exploited to overcome the entropic barrier for the ring closing. In most cases, metal ions were used as temporary templates to promote macrocycle formation via RCM.[13] The use of organic templates to facilitate RCM seems to be less explored.[14]

Scheme 1. Synthesis of *m*-Terphenyl-Based Cyclophane[a]



[a] Conditions: (a) 12 mol % $Pd(PPh_3)_4$, 2 M Na_2CO_3, dioxane, EtOH, reflux; (b) Ph_3PMeBr, KO^{t}Bu, THF, −78 °C to rt; (c) acenaphthenequinone, *p*-TSA, benzene, azeotrope; (d) Grubbs second-generation catalyst, DCM (0.002 M) 50 °C.

The synthesis of the cyclophane (Scheme 1) began with Suzuki coupling of 2,6-dibromo aniline **1** and 4-formylphenylboronic acid **2** followed by conversion of the dialdehyde to divinyl via Wittig reaction to give the product **4**. Condensation of **4** with acenaphthenequinone gave the α-diimine **5**. Molecular modeling of **5** shows that the styryl phenyl rings are perpendicular to the aniline phenyl rings, setting the right conformation for an efficient RCM. RCM of **5** using the second-generation Grubbs catalyst[15] proceeded smoothly to afford the yellow-orange solids **6** in high yields within 6 h.

High-quality single crystals suitable for X-ray crystallography of macrocycle **6a** were obtained by slow evaporation of its $CHCl_3$ solution. The ORTEP drawing of **6a** is shown in Figure 1. The X-ray structure of **6a**[16] shows that

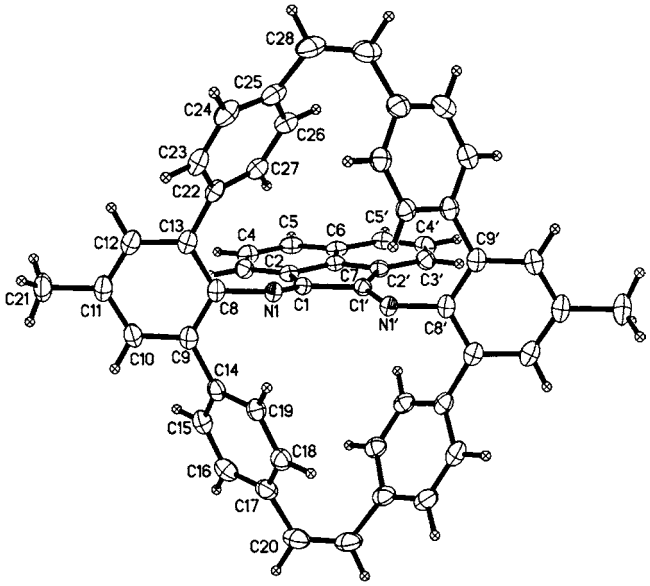


Figure 1. X-ray crystal structure of cyclophane α-diimine **6a**. Selected bond distances (Å): N(1)−C(1) 1.278(17); N(1)−C(8) 1.429(17); N(1)−N(1′) 2.875. Selected bond angles (deg): C(8)−C(9)−C(14) 122.20(13); C(8)−C(13)−C(22) 121.45(13); C(9)−C(8)−N(1) 119.97(13); C(19)−C(14)−C(9)−C(8) 44.4; C(23)−C(22)−(13)−C(8) 124.2.

the acenaphthene plane is roughly perpendicular to the imine phenyl rings. The *m*-terphenyl rings lie above and below the acenaphthene α-diimine plane. The α-diimine functionality

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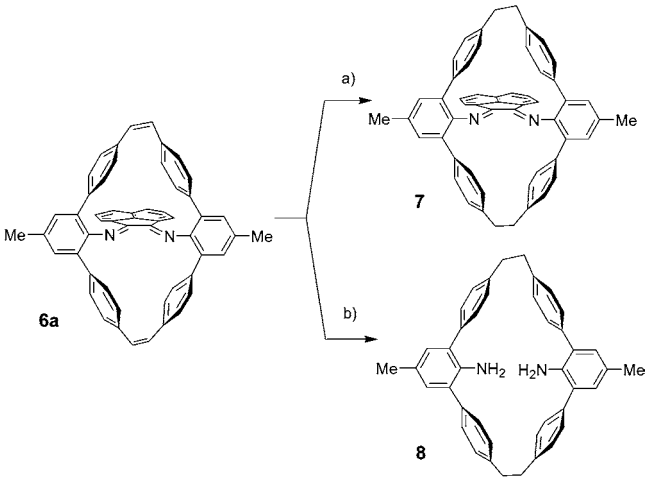
is encased in the core of the macrocylic ligand. The top view of the space-filling model indicates that the α-diimine is effectively shielded at the axial positions.

In addition to being used for olefin polymerization, α-diimines also serve as excellent ligands in metal-catalyzed alkyne dimerization,[17] alkyne cyclotrimerization,[18] coupling reactions,[19] and amination.[20] The unique architecture of **6a** should offer new opportunities of exploring metal-catalyzed reactions using cyclophane-based α-diimine ligands.

Hydrogenation of the cyclophane **6a** using Pd/C catalyst for 4 h gave the hydrogenated α-diimine cyclophane **7** as the major product. Complete hydrogenation of **6a** or **7** under the same conditions for an extended period of time (2−3 days) efficiently removes the diimine template to provide cyclophane **8** having two amino functionalities as a white solid in good yield. High-quality single crystals of **8** were

Scheme 2. Hydrogenation of the Cyclophane[a]



[a] Conditions: (a) H_2, 10% Pd on C, DCM−MeOH, rt, 4 h, 80%; (b) H_2 , 10% Pd on C, DCM−MeOH, rt, 60 h, 75%.

obtained from slow evaporation of its $CHCl_3$ solution and analyzed by X-ray crystallography. The ORTEP drawing of **8** is shown in Figure 2. The structure[21] shows that the diamine functionality is again encased in the cyclophane where the *m*-terphenyl rings lie above and below the diamines. The two aniline rings lie approximately on the same plane. The nitrogen intra-annular distance is 3.052 Å, which is longer

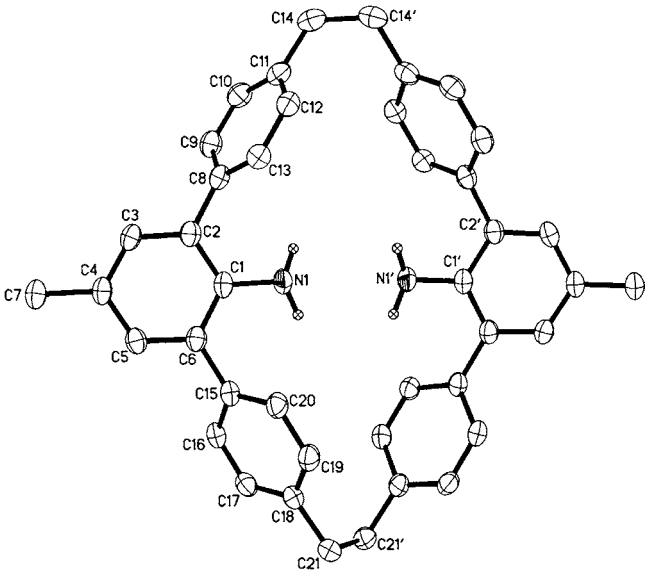


Figure 2. X-ray crystal structure of dianiline macrocycle **8**. Selected bond distances (Å) N(1)−C(1) 1.409(2); N(1)−N(1′) 3.052. Selected bond angles (deg): C(1)−C(6)−C(15) 121.09(15); C(1)−C(2)−C(8) 119.52(15); C(6)−C(1)−N(1) 120.50(16); C(1)−C(6)−C(15)−C(20) 53.0 (2); C(1)−C(2)−C(8)−C(9) 116.0(2).

than the N1−N1′ distance of 2.875 Å in complex **6a**, indicating that the conformation of the macrocycle was relaxed after the removal of the acenaphthene backbone.

The diamine functionality at the core of cyclophane **8** can be readily functionalized for various nitrogen-based multidentate ligands that may potentially find applications in many metal-catalyzed transformations. Moreover, facile functionalization of the diamine at the core to amides and peptide-

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(16) Crystallographic data for **6a**: C_{54} H_{36} N_2, MW = 712.85, orthorhombic, space group *Pccn*, a = 14.5049(7) Å, b = 15.2026(7) Å, c = 17.1739(8) Å, $\alpha = \beta = \gamma = 90°$, V = 3787.1(3) Å^3, Z = 4, ρ_{calc} = 1.250 Mg/m^3, μ = 0.072 mm^{-1}, reflections collected 33 991, independent reflections 3861, $2\theta_{max} = 26.37°$, T = 163(2) K, GOF = 1.022, R_1 = 0.0371, wR_2 = 0.0781, ($I > 2\sigma(I)$), R_1 = 0.0632, wR_2 = 0.0911 (for all data); largest difference peak and hole 0.213 and −0.179 e/Å^3, respectively. Data collection was performed on a Bruker CCD platform diffractometer. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares techniques (SHELXTL). Hydrogen atoms were located from a difference Fourier map and refined. CCDC 223518 contains the supplementary crystallographic data. These data can be obtained free of charge via the Internet at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223−336−033; e-mail: deposit@ccdc.cam.ac.uk) upon quoting the full journal citation.

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based moieties offers opportunities to design new hosts for molecular recognition studies.

In summary, we have described a highly efficient synthetic route to prepare *m*-terphenyl-based cyclophanes containing intra-annular nitrogen functionalities. The key strategy employed in our synthesis is the use of the *cis*-α-diimine as a template to facilitate the cyclization by RCM. The strategic positioning of the α-diimine and diamine at the core opens new opportunities for investigating cyclophane-based metal catalysis and molecular recognition. The cyclic architecture, the bidentate nature, and the versatile coordination chemistry of diimine and diamine cyclophanes make them attractive ligands for new single-site catalysts. In addition, further functionalization of the nitrogen groups on the new cyclophanes should lead to the design of new molecular recognition hosts.

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Supporting Information Available: Experimental procedures, spectroscopic data, and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) Crystallographic data for **8**: $C_{42}H_{38}N_2$, MW = 570.74, monoclinic, space group *C*2/*c*, $a = 12.4590(9)$ Å, $b = 22.7629(17)$ Å, $c = 11.5262(9)$ Å, $\alpha = \gamma = 90°$, $\beta = 110.2560(10)°$, $V = 3066.7(4)$ Å^3, $Z = 4$, $\rho_{calc} = 1.236$ Mg/m^3, $\mu = 0.071$ mm^{-1}, reflections collected 12 679, independent reflections 2603, $2\theta_{max} = 24.71°$, $T = 163(2)$ K, GOF = 1.040, $R_1 = 0.0389$, w$R_2 = 0.0857$, ($I > 2\sigma(I)$), $R_1 = 0.0627$, w$R_2 = 0.1009$ (for all data); largest difference peak and hole 0.182 and −0.160 e/Å^3, respectively. Data collection was performed on a Bruker CCD platform diffractometer. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares techniques (SHELXTL). Hydrogen atoms were located from a difference Fourier map and refined. CCDC 223519 contains the supplementary crystallographic data. These data can be obtained free of charge via the Internet at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223−336−033; e-mail: deposit@ccdc.cam.ac.uk) upon quoting the full journal citation.