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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 8067–8070

Hydrogen bonding-mediated self-assembly of square and triangular metallocyclophanes

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Received 31 March 2005; revised 22 June 2005; accepted 27 June 2005
Available online 29 September 2005

Abstract—Intramolecular three-centered hydrogen bonding has been used to induce dipyridyl anthranilamide **5** and diphenylacetylene anthranilamide **11** to adopt rigid straight conformation. Compound **5** reacted with Pd(dppp)$(OTf)_2$ (**12a**) or Pt(dppp)$(OTf)_2$ (**12b**) in dichloromethane to afford square metallocyclophanes **13a** and **13b** in 70% and 40% yield, respectively. In contrast, the reaction of **11** with **12b** in dichloromethane gave triangular metallocyclophane **14** in 15% yield.

Although supramolecular chemistry emerged from the studies of macrocycles such as crown ethers, cryptands, and calixarenes,[1] in the past decade there has been increasing interest in constructing new kinds of macrocyclic species with well-established structures by making use of discrete non-covalent forces.[2] Among the other non-covalent forces, the coordination motif between transition metal ions and organic ligands has proven itself to be a highly efficient tool for the formation of new rigid and stable macrocyclic architectures.[3] Over years a large number of metallocyclophanes have been constructed. In order to overcome the entropic disadvantage during macrocyclization and also to achieve increased assembling efficiency, rigid aromatic molecules are usually used as ligands, examples of which include conjugated arylenes, arylene ethynylene, and vinylene oligomers.[4] Nevertheless, in many cases, the synthesis and modifications of ligands of such kinds are time consuming or even difficult, and there is a strong demand for the development of new kinds of rigid ligands for construction of new generation of supramolecular architectures and also for the investigation of assembling diversity.

In recent years, there have been increasing applications of intramolecular hydrogen bonding to control the folding or helical conformations of unnatural organic molecules.[5] Previously, we had reported that intramolecular hydrogen bonding could be utilized to induce linear oligoanthranilamides to adopt new unfolding, straight, or zigzag secondary structures in both the solid state and solutions.[6] The zigzag motif of the secondary structure has also been successfully applied to build new U-typed ligands for the self-assembly of a number of new planar and rigid metallocyclophanes, which represent a new generation of synthetic receptors for saccharide derivatives.[7] In this letter, we describe the synthesis of two new kinds of straight ligands and their applications in the self-assembly of rigid and planar square and triangular metallocyclophanes.

Straight conjugated dipyridyl derivatives have been extensively applied to assemble various metallocyclophanes.[4] In order to explore the possibility of making use of hydrogen bonding-induced non-conjugated dipyridyl compounds to construct metallocyclophanes, compound **5** was first designed and synthesized (Scheme 1). Thus, compound **1**[8] was first converted into nitrate **2** in 50% yield. The latter was then hydrogenated with Raney Ni as a catalyst to give amine **3** in quantitative yield. The treatment of excessive amount of the latter with diacyl chloride **4**[9] in refluxing chloroform in the presence of triethylamine produced **5** in 80% yield.[10]

Linear compound **11**, which is incorporated with two phenylacetylene units on both ends, was also prepared

Keywords: Coordination; Cyclophane; Hydrogen bonding; Molecular squares; Self-assembly.
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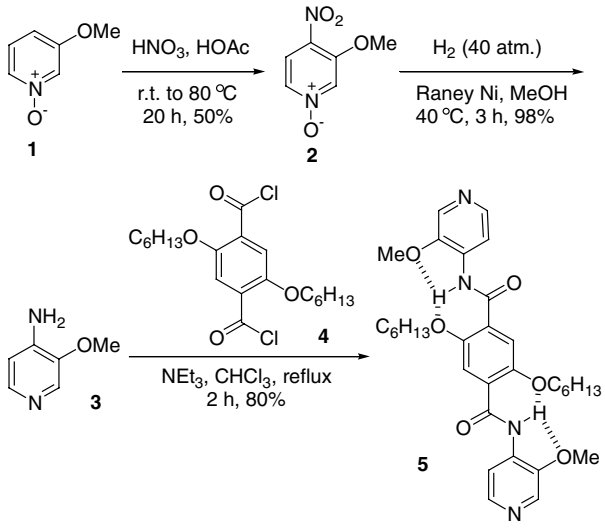
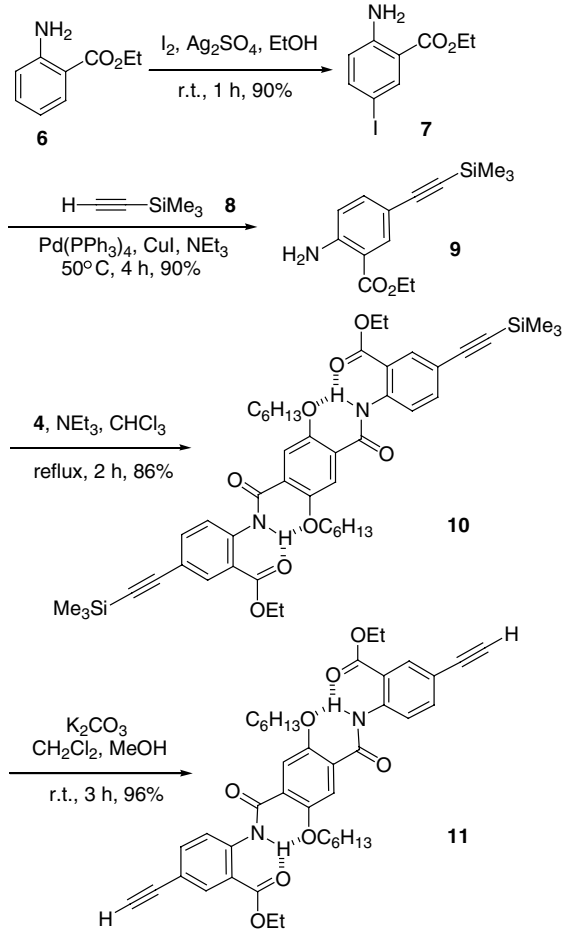
doi:10.1016/j.tetlet.2005.06.173



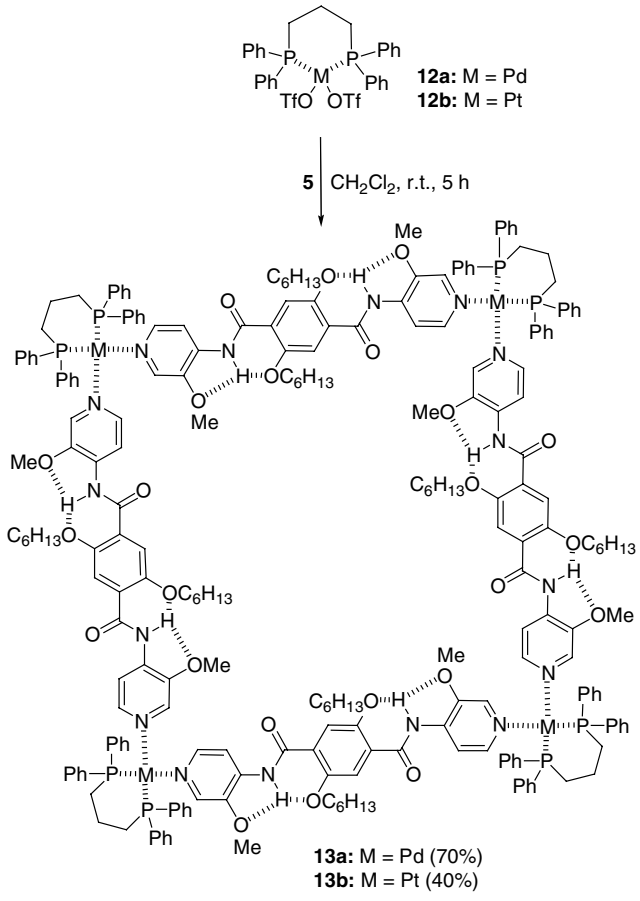
Scheme 1. Synthetic route of compound **5**.



Scheme 2. Synthetic route of compound **11**.

as shown in Scheme 2. Previous studies have demonstrated that straight conjugated diphenylacetylene derivatives are very efficient precursors for the construction of new metallocyclophanes.[6,11] The synthesis of **11** started from amine **6**, which was first converted into compound **7** with iodine in ethanol in the presence of silver sulfate in 90% yield.[12] Compound **7** was then coupled with acetylene **8** in triethylamine in the presence of $Pd(PPh_3)_4$ to afford aniline **9** in 90% yield. The reaction of **4** with excessive amount of **9** in refluxing chloroform with triethylamine as base produced compound **10** in 86% yield. Finally, treatment of **10** with potassium carbonate in dichloromethane and methanol afforded **11** in 96% yield.

^{1}H NMR spectrum (400 MHz) in chloroform-*d* revealed that all the NH protons of compounds **5**, **10**, and **11** are involved in the three-centered hydrogen bonding because their signals were displayed typically at the very downfield area (10.72, 12.20, and 12.21 ppm, respectively). ^{1}H NMR dilution experiments in chloroform-*d* at 25 °C revealed very small concentration dependence (<0.008 ppm) within the range of 30–0.4 mM for compounds **5** and **11**. Temperature-variable ^{1}H NMR experiments also showed a relatively low temperature dependence for the chemical shifts of the amide protons of both **5** and **11** ($<3.5\times10^{-3}$ ppm/K within the range of −10 to 50 °C investigated in chloroform-*d*).[13] In addition, the NH stretching frequencies (ν) of their IR spectrum, obtained both with the KBr disk method or in chloroform (5 mM), are $<3315\ cm^{-1}$ and independent of the concentration changes in chloroform.[14] All these observations support that these linear compounds adopt rigid planar conformations due to the existence of the

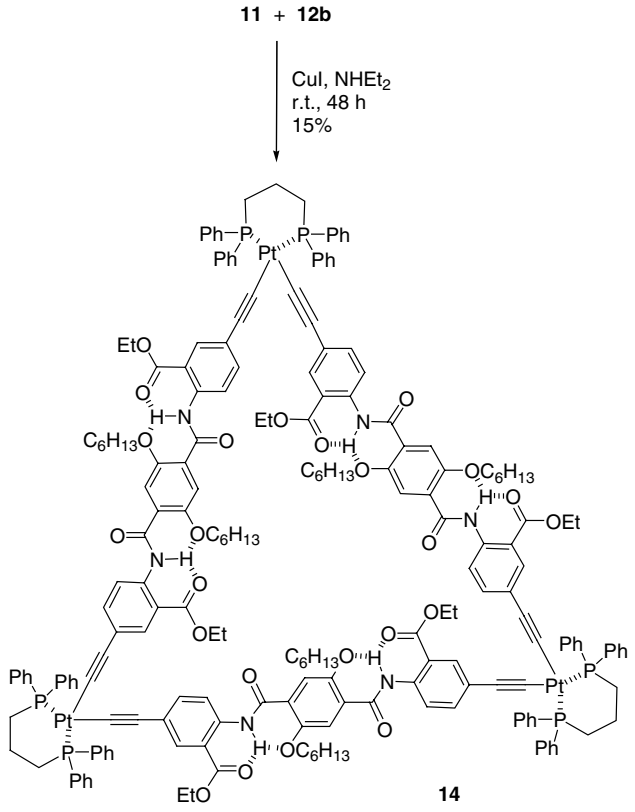


Scheme 3. Synthetic route of metallocyclophanes **13a** and **13b**.

intramolecular three-centered hydrogen bonding,[15,16] as shown in Schemes 1 and 2.

The possibility of constructing rigid metallomacrocyclic structures from **5** and **11** were then investigated. Treatment of dipyridyl **5** with complex **12a**[17] or **12b**[18] in dichloromethane at room temperature afforded molecular squares **13a** and **13b** in 70% and 40% yield, respectively (Scheme 3).[19] In contrast, compound **11** reacted with **12b** at room temperature in diethylamine in the presence of cupric iodide gave triangular cyclophane **14** in 15% yield (Scheme 4). No square metallocyclophane or other products were obtained from this reaction. The fact that only triangular cyclophane was formed might reflect the facts that the steric hindrance of the acetylene ligand is remarkably reduced compared to that of the pyridine-based ligand **5** and the formation of smaller rings is favorable entropically than larger ones from the same ligand in the absence of templating effect. Such result has been observed frequently in the synthesis of crown ethers.[20] The low yield of triangular **14** compared with that of square **13a** and **13b** may be the result of the fact that the intramolecular hydrogen bonding-driven straight ligand is still more flexible than fully conjugative linear ligand.[21]

The structures of the cyclophanes have been characterized by ^{1}H NMR and MS spectroscopy, and microanalysis (for **13a** and **13b**). All the three cyclophanes are moderately soluble in chloroform but not in polar acetone or methanol. Upon coordination, the resolution of their ^{1}H NMR spectrum is also reduced compared to the rigid precursors, but the amide protons give their signals at downfield area (>11.0 ppm), indicating that they are still involved in intramolecular hydrogen bonding.



Scheme 4. Synthetic route of triangular metallocyclophane **14**.

In summary, we have demonstrated that intramolecular three-centered hydrogen bonding can be applied to rigidify the unfolding conformation of linear dipyridyl and diphenylacetylene derivatives and consequently facilitate the self-assembly of two square and one triangular metallocyclophanes. In principle, this non-covalent approach may be further utilized to control functionalized linear molecules to adopt discrete kinds of rigid conformations, which should find applications in constructing new generation of functional supramolecular architectures and for the development of new synthetic receptors for molecular recognition.

Acknowledgments

We are grateful to the Ministry of Science and Technology (G2000078101), the Natural Science Foundation of China, and the Chinese Academy of Sciences for financial support.

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10. *Experimental procedures*: A solution of 2,5-dihexoxyterephthalic acid (0.95 g, 2.60 mmol) in thionyl chloride (50 mL) was heated under reflux for 3 h and then concentrated in vacuo. The resulting compound **4** was dissolved in chloroform (20 mL) and the solution added to a hot solution of compound **3** (0.77 g, 6.20 mmol) in chloroform (20 mL) and triethylamine (0.5 mL). The reaction mixture was refluxed for 2 h, and then cooled. After removal of the solvent under reduced pressure, the resulting residue was triturated with dichloromethane (30 mL). The organic phase was washed with water, brine, dried over sodium sulfate. After the solvent was removed, the crude product was purified by column chromatography (dichloromethane/ethyl acetate 10:1) to afford compound **5** as a white solid (1.2 g) in 80% yield. Mp 192–194 °C: ^{1}H NMR (400 MHz, $CDCl_3$): 10.72 (s, 2H), 8.58 (d, $J = 5.1$ Hz, 2H), 8.30 (d, $J = 3.3$ Hz, 4H), 7.99 (s, 2H), 4.29 (t, $J = 6.9$ Hz, 4H), 4.04 (s, 6H), 2.00 (t, $J = 6.6$ Hz, 4H), 1.49–1.35 (m, 12H), 0.89 (t, $J = 7.2$ Hz, 6H). IR (film, KBr): *v* 3315, 2955, 2927, 2857, 2677, 2605, 2498, 1670, 1591, 1521, 1482, 1415, 1394, 1232, 1211. MS (EI): *m/z* 578 $[M]^+$. Anal. Calcd for $C_{32}H_{42}N_4O_6$: C, 66.42; H, 7.31; N, 9.68. Found: 66.11; H, 7.38; N, 9.58.
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19. *Experimental procedures:* Under an atmosphere of nitrogen, to a flask (100 mL) equipped with a stir bar, containing a solution of Pd(dppp)$(OTf)_2$ (**12a**, 40 mg, 0.5 mmol) in dichloromethane (35 mL) was added compound **5** (28 mg, 0.5 mmol). The mixture was stirred at room temperature for 5 h and then the solid was filtered off through celite. The solid was washed with dichloromethane (10 mL) and the filtrate was concentrated to about 25 mL. To the solution was added slowly diethyl ether (about 15 mL), and the resulting precipitate was filtered and dried in vacuo. Compound **13a** was obtained as a colorless solid (47 mg, 70%). Mp >250 °C. ^{1}HNMR (400 MHz, $CDCl_3$): δ 11.32 (s, 8H), 9.17 (d, $J = 6.9$ Hz, 8H), 8.54 (s, 8H), 8.42 (d, $J = 6.6$ Hz, 8H), 8.01 (s, 8H), 7.60 (br, 32H), 7.32 (br, 48H), 4.37 (t, $J = 7.2$ Hz, 16H), 4.20 (s, 24H), 2.77 (br, 8H), 2.01–2.05 (m, 16H), 1.52–1.27 (m, 64H), 0.89 (t, $J = 15.3$ Hz, 24H). MS (ESI): *m/z* 1143 $[M-4OTf-dppp]^{4+}$, 968 $[M-5OTf]^{5+}$. Anal. Calcd for $C_{244}H_{272}F_{24}N_{16}O_{48}P_8Pd_4S_8$: C, 52.49; H, 4.91; N, 4.01. Found: C, 52.77; H, 4.89; N, 3.60. In analogy with the preparation of compound **13a**, treatment of compound **5** (28 mg, 0.5 mmol) with Pt(dppp)$(OTf)_2$ (46 mg, 0.5 mmol) in dichloromethane (40 mL) at room temperature for 5 h produced compound **13b** as a colorless solid (30 mg, 40%) after workup. Mp >260 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.28 (s, 8H), 9.17 (d, $J = 6.9$ Hz, 8H), 8.58 (s, 8H), 8.43 (d, $J = 6.9$ Hz, 8H), 8.01 (s, 8H), 7.71–7.75 (m, 32H), 7.44–7.48 (m, 48H), 4.36 (t, $J = 6.9$ Hz, 16H), 4.19 (s, 24H), 3.20 (br, 16H), 2.56 (br, 8H), 2.02 (t, $J = 6.6$ Hz, 16H), 1.50–1.34 (m, 48H), 0.91 (t, $J = 7.8$ Hz, 24H). MS (ESI): *m/z* 837 $[M-6OTf]^{6+}$, 593 $[M-8OTf]^{8+}$. Anal. Calcd for $C_{244}H_{272}N_{16}O_{48}F_{24}P_8Pt_4S_8$: C, 49.36; H, 4.62; N, 3.77. Found: C, 49.79; H, 4.99; N, 3.66.
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