Synthesis of a Wurster's Cyclophane: A Redox-Switchable Host for Nanotubes

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Abstract

Synthetic methods have been previously developed for a new class of macrocyclic hosts called Wurster's crowns. These compounds receive their name from the presence of a phenylenediamine structural subunit contained within the macrocyclic framework. Wurster's crowns have the ability to capture a guest and release it depending on the oxidation state of the ligand. This work involves the synthesis of a new Wurster's crown, formally a cyclophane, that is capable of encapsulating the purification of carbon nanotube mixtures.

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Introduction

Since their discovery, carbon nanotubes have attracted tremendous interest because of their unique tubular graphitic structure and their wide ranging potential application.[1] However, the range of tube diameters present in a typical sample and the strong propensity of nanotubes to form aggregate bundles make the study and use of specific sizes/types of nanotubes difficult at best. We are interested in the creation of a redox-active Wurster's crown-based structure that is of sufficient size and composition to encapsulate nanotubes of a certain diameter to facilitate their purification.

Wurster's crowns, named for the incorporation of functional equivalent(s) of the well-known redox center Wurster's reagent[2] (N,N,N',N'-tetramethyl-*p*-phenylenediamine or *p*-TMPD), are a class of macrocycles in which a phenylenediamine subunit is incorporated within the macrocyclic framework.[3] The phenylenediamine subunits undergo two reversible oxidations, thereby allowing for the modulation of the complexing abilities of Wurster's crowns. The goal of this work is to synthesize a phenylenediamine-based host (the Wurster's crown shown in Figure 1) and then use it to encapsulate nanotubes of a certain diameter. After separation of the encapsulated nanotubes from the bulk sample, the host can then release the now-purified nanotubes via oxidation. The key here is that the macrocyclic topology of the Wurster's crown will ensure capture of only nanotubes of the same diameter and the reversible electrochemistry of the phenylenediamines will allow for their release. To create this Wurster's crown, different schemes were used to prepare two fragments which will then be connected to complete the crown. This multi-step process was not completed, but the reactions completed provided a promising beginning because of the amount of precursors formed and the development of successful synthetic procedures.

Procedure

Chemicals.
All reagents and solvents were purchased commercially, of reagent grade quality, and used without further purification.

Instruments.
^{1}H NMR spectroscopy was performed on a Jeol 270 MHz NMR Spectrometer. Rotary evaporation was conducted on a Büchi Rotavapor model R-114 with water bath B-480.

*Synthesis of **1.1**.*
N, N'-dimethyl-*para*-phenylenediamine dihydrobromide (3.2 g, 11 mmol) was deprotonated by dissolving in water, basifying with the addition of NaOH, and subsequent extraction with dichloromethane. The dichloromethane solution was then dried with magnesium sulfate. Following filtration, the solvent was removed and the free

base form of the phenylenediamine was used directly. In a 250 mL round-bottomed flask, tosylaziridine (4.2 g, 25 mmol) was added to the N, N'-dimethyl-*para*-phenylenediamine. Acetonitrile was added and the resultant solution heated at reflux overnight. Upon cooling to room temperature, the solvent was concentrated by rotary evaporation and then placed in the freezer to allow crystals to form. The colorless crystals were filtered and washed with ethyl ether. After drying, the crystals of compound **1.1** were stored in a vial. Yield: 5.15 g (88%)

*Synthesis of **1.2**.*
N, N-dimethylformamide (DMF) and NaH as a 60% dispersion in mineral oil (2.0 g, 49 mmol), were added to compound **1.1** (5.15 g, 10 mmol) with subsequent heating at 90°C for one hour. After cooling to room temperature, the reaction mixture containing the deprotonated form of **1.1**, was placed in an ice bath. Iodomethane (3.2 mL) was then added dropwise with stirring overnight. The solvent was removed by distillation and the crude reaction mixture partitioned between dichloromethane and water. The organic layer was collected and dried with sodium sulfate. Following filtration of the drying agent, the filtrate was concentrated on a rotary evaporator. A thin layer chromatography (TLC) analysis showed impurities and a silica column was performed using an eluent of 2% methanol in chloroform. The fractions that contained pure material were retained while those that contained partially reacted starting material were combined and methylated again using the same procedure as before. When a TLC was performed after this second reaction, minor impurities still remained so a silica column was performed with 2% methanol in chloroform as the eluent. All fractions that contained pure material were combined.

*Synthesis of **2.1** (Trial 1).*
N, N'-ditosyl-*para*-phenylenediamine (4.0 g, 10 mmol), ethylene carbonate (2.2 g, 24 mmol), and one crushed pellet of KOH were put into a round bottomed flask and heated with a stirring bar at 160°C for 3 hours. Little change was observed in the reaction as it was proceeding with the possible melting of the ethylene carbonate noted. After cooling, the reaction mixture was partitioned between dichloromethane and water. Magnesium sulfate, a drying agent, was used to dry the organic layer. A filter was used to remove the magnesium sulfate leaving the dichloromethane filtrate containing the anticipated product. A TLC analysis (confirmed by ^{1}H NMR spectroscopy) showed the presence of only starting material.

*Synthesis of **2.2**.*
Due to the previous unsuccessful attempt to synthesize compound **2.1**, an alternative procedure was pursued, first involving the synthesis of compound **2.2**. N, N'-ditosyl-*para*-phenylenediamine (2.0 g, 5.0 mmol), NaH as a 60% dispersion in mineral oil (0.5 g, 12 mmol), and DMF (30 mL) were heated at 90 °C for one hour. Then, 2-bromoethoxytetrahydropyran (2 mL) and DMF (20 mL) were mixed and added dropwise to the previous solution. The reaction was heated at 90 °C overnight. Next, a distillation was performed to remove the solvent, DMF. The resultant solid was dissolved in ethyl acetate and water. A separatory funnel was used to separate the ethyl acetate layer. A drying agent, magnesium sulfate, was added. Following filtration, the filtrate was

concentrated on a rotary evaporator. A TLC revealed multiple impurities. Therefore, an alumina column was performed using an eluent of 2% methanol in chloroform. Pure fractions were combined, concentrated, and placed on the high vacuum for final drying. This reaction was done twice to obtain more Compound 2.2, the intermediate step to the formation of Compound 2.1. Yield: 1.82 g (56.3%)

*Synthesis of **2.1** (Trial 2).*
To hydrolyze the THP protecting groups, a 4:2:1 solution of acetic acid (120 mL), tetrahydrofuran (60 mL), and water (30 mL) was added to compound **2.2** with heating at 45°C overnight. A distillation was then performed to remove the solvent. Dichloromethane and water were added to the resulting product along with 6 M NaOH which was used to neutralize the acid. Using a separatory funnel, the organic layer was separated and dried with sodium sulfate. Following filtration, the filtrate was collected and shown by TLC to contain impurities. So, an alumina column was employed to separate the product. A ^{1}H NMR analysis of fractions 3 and 4 revealed that the product obtained was, in fact, compound **2.1**. Fractions 1 and 2 appeared to still have either both or one THP protecting group, so they were reacted with the acetic acid, THF, and water solution again. Unfortunately, the amount of isolated compound **2.1** obtained was low. Yield: 0.33 g (24 %)

*Synthesis of **2.3**.*
A solution containing **2.1**, dichloromethane and one large pipette of pyridine was added to a round bottomed flask and cooled to in an ice bath. To this, a solution of *p*-toluenesulfonyl chloride (0.374 g, 2 mmol) in dichloromethane was added dropwise. The reaction was stirred overnight with subsequent warming to room temperature. To remove the pyridine, the reaction mixture was added to a 250 mL beaker along with ice, 4 pipettes of concentrated HCl and water. This mixture was stirred vigorously until all of the ice was melted. Using a separatory funnel, the organic layer was collected and dried with sodium sulfate. Following filtration, the filtrate was concentrated on a rotary evaporator.

Results and Conclusions

The goal of this research was the development of a Wurster's crown with the ability to capture nanotubes of a certain diameter. Once achieved, the crown host will then be placed in a sample of nanotubes to form threaded rotaxane complexes with nanotubes of one diameter. The encapsulated nanotubes can then be separated from the rest of the sample due to their enhanced solubility and ejected from the crown host via oxidation, thereby forming a pure sample of nanotubes with the same diameter. The first two schemes show the synthesis of the two acyclic fragments to be used to eventually form the crown. The final scheme shows the proposed completion of the crown by reaction of the two products from Schemes 1 and 2.

The first scheme began with the reaction of N, N'-dimethyl-*para*-phenylenediamine and tosylaziridine. Before reaction with tosylaziridine, the free base form of N, N'-dimethyl-*para*-phenylenediamine, was generated by deprotonation of the dihydrobromide salt

using sodium hydroxide. The successful reaction with tosylaziridine resulted in an 88% yield of compound **1.1**. This product was then methylated to form compound **1.2** in N, N-dimethylformamide (DMF) using NaH and iodomethane. Due to the presence of several impurities as detected by thin layer chromatography (TLC), column chromatography was performed on the reaction mixture. Fractions 8 and 9 contained pure **1.2** while fractions 10 through 15 contained a mixture of **1.2** and the monomethylated by-product. As such, these latter fractions were reacted further with iodomethane to complete the conversion to compound **1.2**. Another silica column was performed after the second reaction and fractions 1 through 7 of this second column were added to the previous fractions 8 and 9 to give **1.2**. To reach the final compound of this scheme, necessary to form the complete Wurster's crown, four more reactions will follow. Due to time constraints, compound **1.6** was not achieved.

Scheme 2 describes the synthesis of the other half of the Wurster's crown. Hoping to create compound **2.1** in a one-step process, N, N'-ditosyl-*para*-phenylenediamine was reacted with ethylene carbonate in a melt reaction at 160 ^{o}C. However, after TLC and ^{1}H NMR analysis, it was apparent that little to no reaction had occurred. This may have been a result of the high melting point (> 160 ^{o}C) of the tosylated precursor. The next attempt to synthesize **2.1** involved the reaction of N, N'-ditosyl-*para*-phenylenediamine with tetrahydropyranyl (THP) protected 2-bromoethanol in the presence of NaH and DMF to form the intermediate THP protected form of compound **2.1**. A TLC analysis of the reaction mixture showed impurities so an alumina column was performed. Pure fractions 1 and 2 were combined with subsequent solvent removal. The ^{1}H NMR analysis showed that they were, in fact, the desired target, compound **2.2**. However, due to the small amount obtained, the reaction was repeated giving a total percent yield of 56%. The deprotection of the THP adduct, compound **2.2**, was performed in a 4:2:1 solution of acetic acid, THF, and water respectively to give compound **2.1**. After TLC, it appeared that much of compound **2.2** with the THP arms had not reacted or had reacted partially with only one THP arm removed. Therefore, the 4:2:1 acetic acid, THF, and water reaction was repeated. However, the final yield of the reaction to form compound **2.1** was only 24%. Continuing despite the small amount of compound **2.1** obtained, *p*-toluenesulfonyl chloride was added along with pyridine in dichloromethane. A TLC was performed and showed many different products including Compound **2.3** and a partially tosylated compound (presumably the singly tosylated species). For purification, the reaction mixture was mixed into cold water containing concentrated HCl to remove pyridine. The dichloromethane layer was collected using a separatory funnel with the water soluble components of the reaction mixture eliminated. Compound **2.3** was obtained, however more thorough purification is needed.

Scheme 3 incorporates the final products of the first two schemes and shows the ultimate formation of the actual target Wurster's crown that is predicted to capture nanotubes. No reactions in this scheme were performed since the final product, compound **1.6**, of Scheme 1 was never achieved due to the small amount of time available. If the scheme were carried out, the two final products of Schemes 1 and 2 would connect to form a ring which would then be detosylated using sodium amalgam. Methylation will then give compound **3.3**.

In conclusion, the procedure to create this Wurster's crown, which will hopefully separate nanotubes of a certain diameter, involves many steps and requires considerable purification. Though many of the reactions were not completed, Scheme 1 displayed promise in yielding much of the desired product. Scheme 2 was more unreliable with very little product being produced and some failed reactions. The target macrocycle has yet to be completed; however, so far, the successful synthesis of these intermediates gives hope for the formation of this Wurster's crown.

Works Cited

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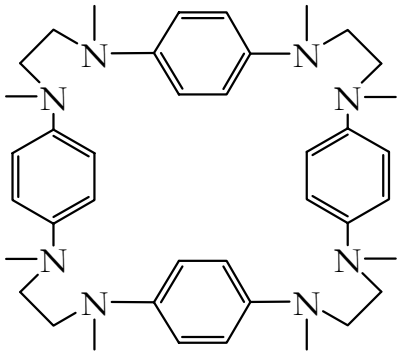
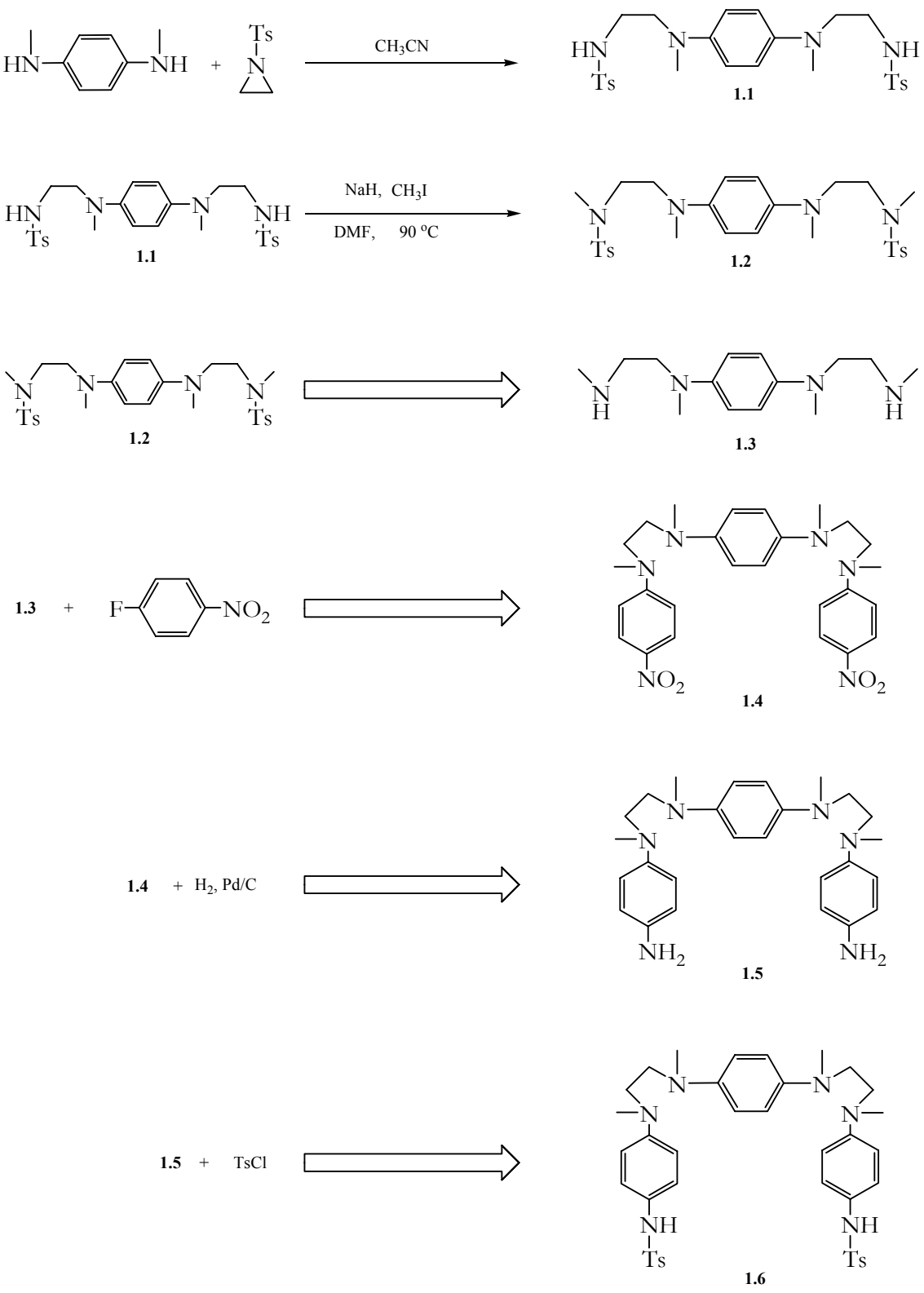
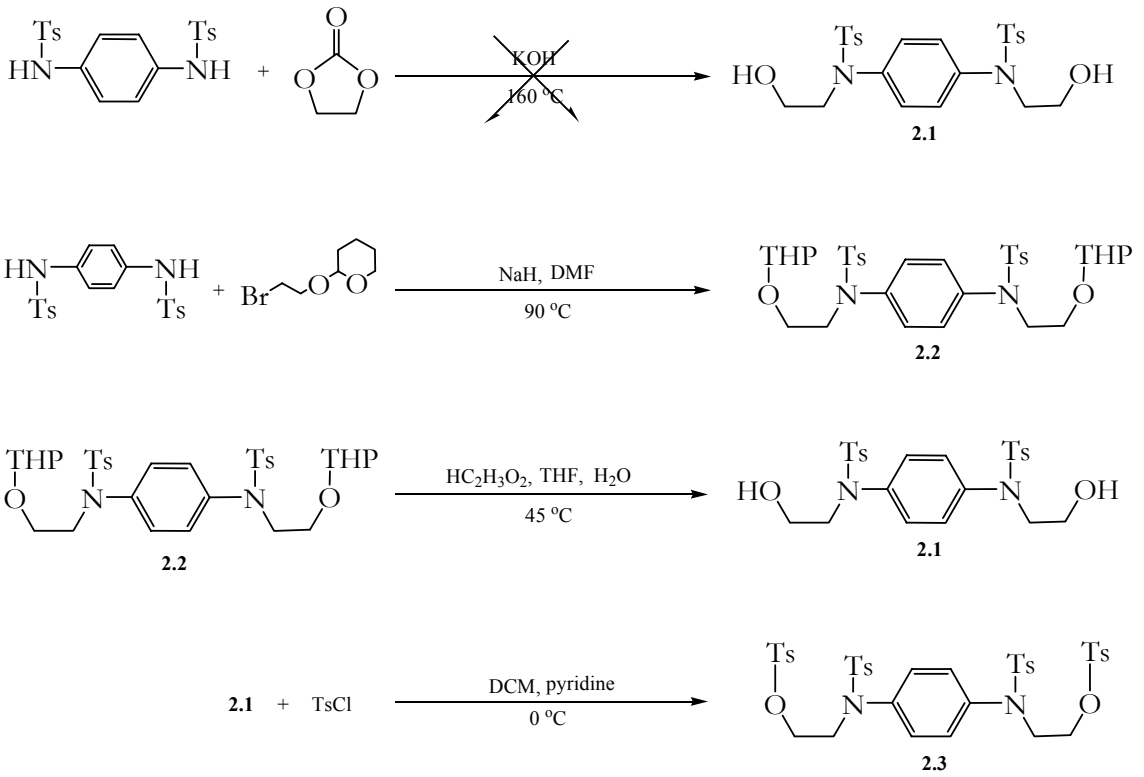


Figure 1. Compound **3.3**.

Scheme 1



Scheme 2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HN
NH
Ts
+
O
O
O
KOH
160 °C
HO
N
OH
2.1
HN
NH
Ts
Ts
+
Br
O
O
NaH, DMF
90 °C
THP
O
2.2
HC2H3O2, THF, H2O
45 °C
2.1 + TsCl
DCM, pyridine
0 °C

Scheme 3