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Synthesis of an *ortho*-Triazacyclophane: *N*,*N*′,*N*″-Trimethyltribenzo-1,4,7-triazacyclononatriene

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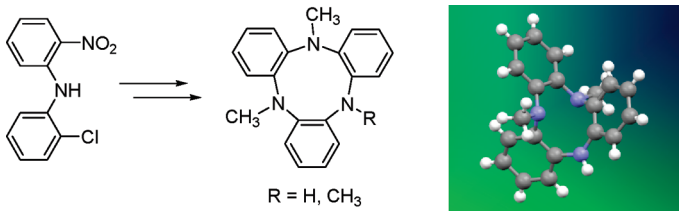

N,*N*′,*N*″-Trimethyltribenzo-1,4,7-triazacyclononatriene has been synthesized via sequential palladium-catalyzed Buchwald−Hartwig N-arylation reactions affording the 9-membered triaza *o*-cyclophane in 35% overall yield. An X-ray crystal structure shows the new cyclophane to have a C_2-symmetric saddle conformation, as compared to the crown conformation exhibited by the related carbocyclic cyclotriveratrylene (CTV).

Introduction

The area of supramolecular chemistry is of continued interest because of a wide variety of applications including materials technology, catalysis, medicine, analytical detection, and sensing. Cyclophanes, which are supramolecular structures comprised of aromatic units with bridging chains, have applications in molecular recognition as synthetic receptors[1] and have been used as building blocks for organic catalysts.[2] There is growing interest in the development of cyclophanes as hosts for ionic guests.[3−5]

The archetypal cyclophane cyclotriveratrylene (CTV, **1**), a [1.1.1]orthocyclophane, is a commonly employed scaffold in supramolecular chemistry[6] that is readily prepared from veratryl alcohol in acid and has been studied extensively for its capability of binding a number of smaller organic and organometallic guests within its bowl-shaped cleft.[7−9] CTV modification continues to be a significant area of study,[10−13] and it has been used as a building block enabling the construction of more complex cryptophanes.[14−17] Although CTV has proven to be quite useful, the molecule suffers from insolubility in aqueous systems and only limited opportunities for derivatization of the apical methylenes. Most derivatives of CTV have been prepared by varying the groups on the phenolic oxygens around the periphery of the molecule; Collet was among the first to transform CTV into cryptophanes in this manner.[18] Nierengarten addressed the aqueous insolubility of CTV by appending poly(ethylene glycol)

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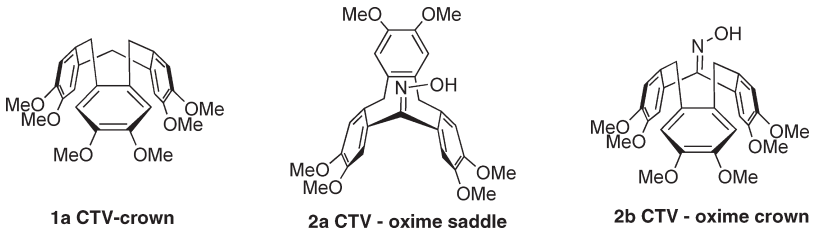

FIGURE 1. Cyclotriveratrylene (CTV) and CTV-oxime derivatives.

units via the peripheral oxygens toward derivatives with biomedical applications, specifically to aid in the biological delivery of fullerenes, although the derivatives were of high molecular weight (> 3000 to > 6000 amu).[19] As part of our own exploration of apex-modified CTV derivatives,[20] we have isolated the crown and saddle conformers of CTV-oxime (**2a**,**b**)[21] and studied the kinetics and thermodynamics of their interconversion between the crown and saddle CTV-oxime derivative **2a**,**b**[22] (Figure 1). CTV exists almost exclusively in its crown conformation (**1a**), and the saddle conformer of CTV was only recently isolated and characterized through high-temperature melt and quench techniques by Zimmermann, who also studied the thermodynamic and kinetic properties of the interconversion of the crown and saddle CTV conformers.[23] Holman[24] as well as Huber[25] have identified topoisomeric cryptophanes containing blended crown and saddle CTV moieties; Holman's cryptophane undergoes a conformational crown to saddle "implosion" upon thermal liberation of its tetrahydrofuran guest.

Several heteroatom analogues of CTV and the tribenzocyclononene core have been reported in which the methylene groups have been replaced (**3a**−**c**). Trithiacyclotriveratrylene (**3a**)[26,27] forms complexes with copper(I),[28] rhodium(III),[29] and platinum(II),[30] and it also exists in a temperature and solvent-dependent equilibrium of the crown and saddle forms. In addition, the trioxycyclononene **3b**[31,32] and trimercury cyclononene **3c**,[33] which is planar rather than crown-shaped, have also been described. Recently, the first apical methylene aza-substituted cyclophane was reported with the synthesis of

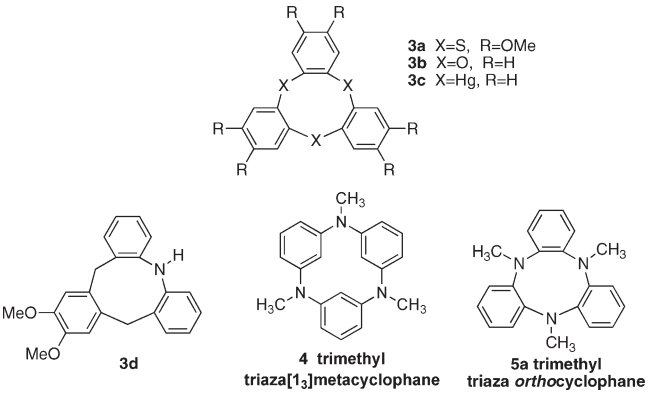

FIGURE 2. Analogues of CTV.

monoamine tribenzo-1-azacyclophane **3d**[34] which was prepared as a potential benzodiazepine receptor ligand, while Tanaka reported the synthesis of the trimethyl triaza[1_3]-metacyclophane **4**.[35] We envisioned a derivative of the tribenzotricyclononatriene core of CTV retaining its high (C_{3v}) symmetry with nitrogen atoms in place of the methylenes to provide a ready handle for apical functionalization and altering the charge on the scaffold, to enable modulation of host−guest properties, and to facilitate attachment to surfaces. Furthermore, the nitrogen atoms should function as a ligand for metals as described for the oxa- and thia-analogues above, ultimately providing a redox-switchable host molecule. Herein we describe the synthesis of the novel triazaorthocyclophane **5a** (Figure 2).

Results and Discussion

Looking retrosynthetically at the target tribenzo-1,4,7-triazacyclononatriene, we envisioned four unique synthetic approaches (Figure 3), with N−aryl bonds constructed potentially utilizing Buchwald−Hartwig,[36−39] Ullman,[40] or nucleophilic aromatic substitution (S_NAR) methodologies. Route A considers the direct trimerization of an ortho-substituted aniline. This highly convergent synthesis has literature precedent in the work of Tanaka[35] and co-workers who synthesized metacyclophane **4** in low yield directly from a meta-substituted aniline. Approaches B and C consider a diphenylamine derivative joining the third ring in a double-coupling. Finally, route D describes a linear construction of the molecule. The final intramolecular

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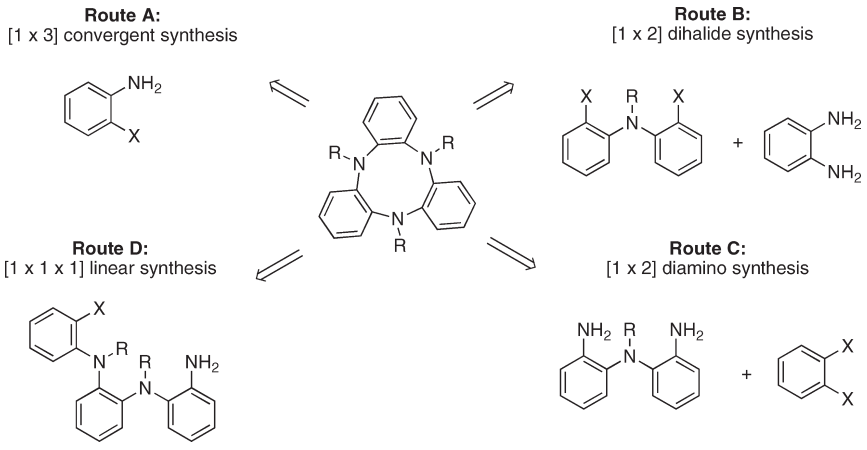


FIGURE 3. Retrosynthetic strategies toward the tribenzo-1,4,7-triazacyclononatriene ring system.

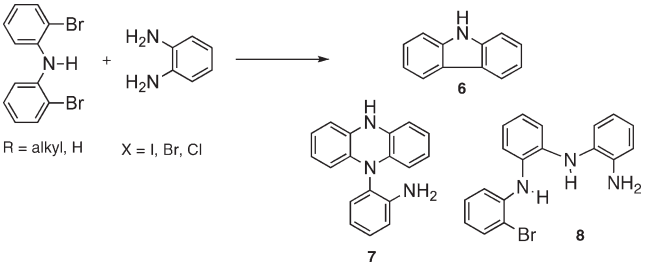
macrocyclization of the 9-membered ring should be aided by the limited degrees of freedom imposed by the aryl rings.

For the highly convergent approach (A), we subjected 2-iodoaniline and 2-bromoaniline to a variety of Buchwald−Hartwig cross-coupling conditions. Employing $Pd(OAc)_2$, $P(t\text{-}Bu)_3$ as the ligand, and sodium *tert*-butoxide as the base in dioxane under reflux as a typical example afforded only phenazine in 92% isolated yield via facile air oxidation of the metastable dihydrophenazine.[41] Tanaka was able to synthesize the triazametacyclophane **4** from the corresponding secondary *N*-methyl derivative but not from the unsubstituted (primary) aniline. Therefore, we attempted the convergent trimerization employing a secondary aniline utilizing similar Pd-catalyzed cross-coupling conditions. *N*-Methyl-2-bromoaniline under Buchwald−Hartwig conditions produced a complex mixture from which only dehalogenated dimer and dehalogenated tetramer were isolated in extremely low yields (0.3% and 2%, respectively). We were unable to detect the desired product in any mixture derived from the direct trimerization approach under a variety of Buchwald−Hartwig conditions, even when an authentic sample was available for direct comparison from the linear approach below.

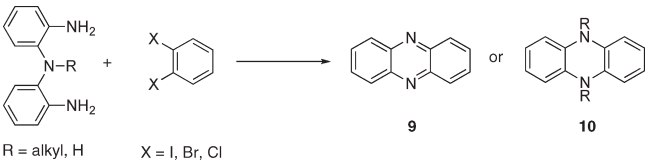
Given the facile formation of phenazine in the trimerization attempt, we focused on the moderately convergent [2 × 1] syntheses (routes B and C). Subjecting bis(2-bromophenyl)-amine to Buchwald−Hartwig conditions, carbazole **6** was formed as the major product via a reductive coupling in 65% yield. In addition, the phenazine derivative **7** was produced in 4% via intramolecular *N*-arylation involving a 6-membered ring formation. The monocoupled triaryl product **8** was also isolated in 4% yield (Scheme 1).

A similar convergent synthesis attempt beginning with *N*-(2-aminophenyl)-1,2-benzenediamine[42,43] is shown in Scheme 2. The diamine and the 1,2-dihalide were subjected to palladium-catalyzed N-arylation producing phenazine (**9**) in 20% yield as the only isolated product. When an *N*-methyl blocking group was added[44] to the central nitrogen, attempted *N*-arylation of the *N*-(2-aminophenyl)-*N*-methyl-1,2-benzenediamine with

SCHEME 1. 1 × 2 Synthesis Attempt from Bis(2-bromophenyl)-amine



SCHEME 2. 1 × 2 Synthesis Attempt from *N*-(2-Aminophenyl)-1,2-benzenediamine



1,2-dibromobenzene resulted in 5,10-dimethyldihydrophenazine (**10**) as the only isolated product (Scheme 2).

The inability to produce the desired cyclophane utilizing convergent approaches led us to pursue a linear synthesis (route D) with sequential protection of the aniline nitrogens to avoid 6-membered ring formation. Scheme 3 outlines the successful synthesis of the *N*,*N*′,*N*″-trimethyltriazaorthocyclophane **5a** in 35% overall yield. A modification of the Buchwald−Hartwig N-arylation method used by Tietze[42] employing 1,2-bromochlorobenzene and *o*-nitroaniline gave 2-chloro-*N*-(2-nitrophenyl)benzenamine **11** in 99% yield. The aniline was protected by methylation using KOH and Me_2SO_4 in refluxing acetone[45] to give the *N*-methyldiphenylamine **12** in quantitative yield without the need for further purification. Compound **12** was easily reduced with the general method of Sanz[46] using CuCl and KBH_4 in dry MeOH at room temperature to give **13** in quantitative yield, again without further purification, whereas more common reduction methods such as Pd/C and H_2NNH_2 or hydrogenation gave dehalogenated or

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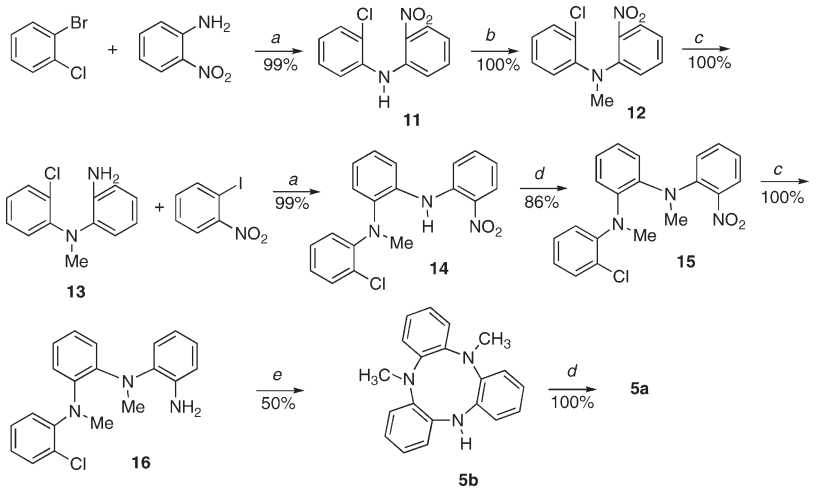
SCHEME 3.[a] **Linear Synthesis of *N*,*N*′,*N*″-Trimethyltribenzo-1,4,7-triazacyclononatriene 5a**



[a]Reaction conditions: (a) $Pd(dba)_2$, BINAP, tol, 24 h; (b) KOH, Me_2SO_4, acetone; (c) CuCl, KBH_4, MeOH; (d) KH, MeI, DMF; (e) $Pd(dba)_2$, BINAP, 1:5 *t*-BuOH/tol.

demethylated reduction products. The aniline **13** was coupled to iodonitrobenzene using the previously established Buchwald–Hartwig conditions to produce triarylamine **14** in 80% yield. Compound **14** was subjected to methylation using KH and MeI followed by reduction of the nitro group with CuCl and KBH_4 to give products **15** and **16**, respectively. The triarylaniline was successfully closed to the 9-membered cyclophane through the use of Buchwald–Hartwig coupling in a microwave reactor to afford the *N*,*N*′-dimethyltriazaorthocyclophane **5b** in 50% isolated yield after purification. The last step is a macrocyclization with unique steric demands and application of thermal conditions gave significant decomposition, low yields (< 5%), poor conversion and extremely long reaction times (> 5 days). However, we found that application of microwave conditions in this step gave moderate to good yields. The third apical nitrogen was methylated employing KH and MeI to give a quantitative yield of the *N*,*N*′,*N*″-trimethyltriazaorthocyclophane **5a** without the need for further purification (Scheme 3).

The structure of the *N*,*N*′-dimethyl derivative **5b** was assigned on the basis of the equivalent methyls in the ^{1}H NMR at δ 2.68 (6H, s) and the appropriate exact mass (MH^+) observed by mass spectrometry. The structure was ultimately confirmed by single-crystal X-ray analysis revealing a C_2-symmetric saddle (Figure 4). The ^{1}H NMR of the *N*,*N*′,*N*″-trimethyl dervative **5a** reveals the high C_{3v} symmetry with signals at δ 6.90 (12H, s) and δ 2.91 (9H, s) and manifesting the similarity of protons ortho and meta to the nitrogen, leading to a fortuitous singlet for all 12 aromatic protons.

In conclusion, we have constructed the new triazacyclophane, tribenzo-1,4,7-triazacyclononatriene **5b**, in seven steps via palladium-catalyzed C–N amination, followed by alkylation and reduction, and reiteration of this sequence in order to obtain the triaryl precursor to the final palladium-catalyzed cyclization to the 9-membered cyclophane. Alkylation of **5b** gives the C_{3v}-symmetric *N*,*N*′,*N*″-trimethyltriazaorthocyclophane and demonstrates the ability to functionalize the cyclophane at the apex in order to modulate its physicochemical properties. We envision that the new triazacyclophane will complement the familiar carbocyclic framework of CTV with greater versatility, including the ability to bind cationic species in the apex analogous to metal complexes of the well-known triazacyclononene (TACN) derivatives that have utility as MRI contrast agents[47,48] and radioimmunotherapy agents.[49] These studies are in progress and will be reported in due course.

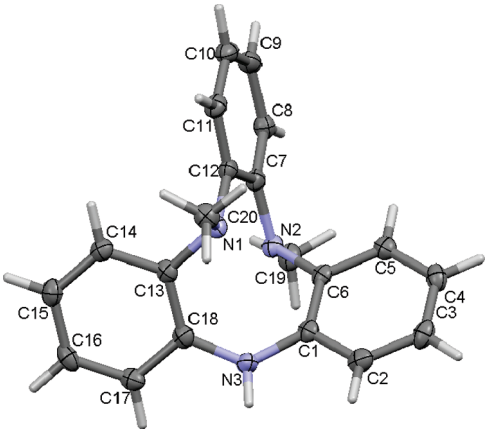


FIGURE 4. X-ray structure of compound **5b** with atom labels; thermal ellipsoids are at the 50% probability level.

Experimental Section

General Experimental Methods. All solvents were distilled prior to use. All reagents were used without further purification unless otherwise noted. All Pd- and Cu-catalyzed reactions were conducted under an inert atmosphere of argon, and all other reactions were conducted under a nitrogen atmosphere. Sorbent Technologies silica gel 60A, 40–75 μm (200 × 400 mesh) was used for column chromatography. Sorbent Technologies

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aluminum-backed silica gel 200 μm plates were used for TLC. ^{1}H NMR spectra were obtained utilizing a 300 MHz spectrometer with trimethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were obtained using a 75 MHz spectrometer. A CEM Discover Microwave model no. 908005 was used for all microwave (MW) reactions. Infrared (IR) spectra were determined as a solution in $CHCl_3$. Single-crystal X-ray diffraction data were collected on a charge-coupled-device (CCD) diffractometer with a liquid nitrogen vapor cooling device. Data were collected at 100 K with graphite-monochromated Mo Kα X-ray radiation (λ = 0.71073 Å). Data were collected, reduced, and corrected for absorption using multiscan methods. The structure was solved by direct methods and refined by full matrix least-squares against F^2 with all reflections. Non hydrogen atoms were refined anisotropically. C−H hydrogen atom positions were idealized. Additional details of the structure determination can be found in the Supporting Information.

(2′-Chlorophenyl)(2-nitrophenyl)amine (11). Compound **11** was synthesized according to the general procedures outlined by Tietze et al.[42] A pressure tube was charged with *o*-nitroaniline (0.690 g, 5 mmol), *o*-bromochlorobenzene (0.60 mL, 5.00 mmol), $Pd(dba)_2$ (0.144 g, 5%), BINAP (0.233 g, 7.5%), Cs_2CO_3 (3.26 g, 10 mmol), and toluene (10 mL). The mixture was purged with argon for 10 min at rt, and the pressure tube was sealed. The reaction was sealed and placed in a preheated oil bath. The temperature was brought to 120 °C and the reaction stirred for 24 h. TLC showed complete consumption of *o*-nitroaniline, and the reaction mixture was filtered through a pad of SiO_2 using 5/5/90 EA/DCM/petroleum ether as the eluent. The solvent was removed under vacuum and no further purification was needed to give the product as an orange solid (1.24 g, 100%) which was identical to the material reported in the literature[42] by ^{1}H NMR.

2-Chloro-*N*-methyl-*N*-(2-nitrophenyl)aniline (12). Following the general method of Wilshire,[45] compound **11** (1.25 g, 5 mmol) was stirred at rt in acetone (16 mL), and freshly crushed KOH (1.23 g, 22.0 mmol) was added to the stirring mixture. After the reaction was brought to reflux, Me_2SO_4 (2.18 mL, 23 mmol) was added dropwise via syringe over 10 min. The mixture was allowed to stir at reflux for 1 h. The reaction was cooled to rt, and 20 mL of 10 M NaOH was added to the solution. After 1 h, the mixture was quenched with 10 mL of H_2O and extracted with 3 × 10 mL of DCM. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum, and the mixture was placed in an 80 °C oil bath under vacuum to remove excess Me_2SO_4. No further purification was needed to obtain the desired compound **12** as an off-white solid (1.31 g, 100%): mp 73−75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (1H, dd, J = 8.1, 1.5 Hz), 7.54 (1H, ddd, *J* = 8.7, 7.3, 1.7 Hz), 7.42 (1H, dd, *J* = 7.8, 1.5 Hz), 7.19 (1H, dd, *J* = 7.7, 1.7 Hz), 7.14−7.11 (2H, m), 7.06 (1H, dd, *J* = 7.7, 1.9 Hz), 7.0 (1H, ddd, *J* = 8.2, 7.3, 1.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 143.0, 133.2, 131.3, 130.9, 128.7, 127.9, 126.7, 126.2, 125.9, 120.8, 120.6, 41.1; IR ($CDCl_3$) 1520 (NO_2); HRMS (MH^+) calcd for $C_{13}H_{11}O_2N_2Cl$ 263.0509, found 263.0604.

***N*^{1}-(2-Chlorophenyl)-*N*^{1}-methylbenzene-1,2-diamine (13).** Following the general procedure of Sanz,[46] CuCl (0.137 g, 1.38 mmol) was added to a stirring solution of compound **12** (0.121 g, 0.46 mmol) in MeOH (4.6 mL) at rt. KBH_4 (0.174 g, 3.22 mmol) was then added in portions. The reaction was stirred at rt until the solution became clear (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 15 mL of 90/10 EA/DCM. The organic layers were combined and dried over Na_2SO_4, and the solvent was removed to give the desired product as a brown oil (0.107 g, 100%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J* = 7.8, 1.4 Hz), 7.25 (1H, dd, *J* = 7.3, 1.7 Hz), 7.22 (1H, dd, *J* = 7.1, 1.7 Hz), 7.16 (1H, dd, *J* = 8.0, 1.6 Hz), 7.00−6.95 (2H, m), 6.76 (1H, ddd, *J* = 9.3, 7.7, 1.4 Hz), 6.67 (1H, ddd, *J* = 8.9, 7.6, 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 142.2, 136.9, 130.7, 130.68, 127.4, 125.5, 123.6, 121.9, 118.6, 115.8, 41.1; IR ($CDCl_3$) 3440 (NH_2), 3351 (NH_2); HRMS (MH^+) calcd for $C_{13}H_{13}N_2Cl$ 233.0767, found 233.0791.

***N*^{1}-(2-Chlorophenyl)-*N*^{1}-methyl-*N*^{2}-(2-nitrophenyl)benzene-1,2-diamine (14).** Compound **13** (0.842 g, 3.62 mmol), *o*-iodonitrobenzene (1.35 g, 5.43 mmol), $Pd(dba)_2$ (0.104 g, 5% mol), BINAP (0.170 g, 7.5%), Cs_2CO_3 (2.35 g, 7.42 mmol), and 12 mL of toluene were placed in a pressure tube. The mixture was purged with argon at rt for 15 min, and the tube was then sealed and placed in a preheated oil bath at 80−90 °C for 30 h. After TLC showed consumption of **13**, the reaction mixture was filtered through a pad of silica gel eluting with 90/10 EA/DCM. The solvent was then removed under vacuum. The crude product was then purified by column chromatography on silica gel eluting with 1/99 Et_2O/petroleum ether to afford the desired product **14** as a red crystalline solid (0.785 g, 80%): mp 141−145 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.03 (1H, bs), 8.07 (1H, dd, *J* = 8.7, 1.5 Hz), 7.32−7.19 (4H, m), 7.12−6.99 (5H, m), 6.90 (1H, ddd, *J* = 8.0, 6.9, 2.2 Hz), 6.68 (1H, ddd, *J* = 8.4, 6.9, 1.2 Hz), 3.16 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 145.1, 142.4, 135.2, 131.6, 130.7, 129.5, 127.4, 126.5, 126.5, 126.0, 124.8, 124.0, 123.2, 121.7, 117.0, 115.8, 40.6; IR ($CDCl_3$) 3344 (NH), 1503 (NO_2); HRMS (MH^+) calcd for $C_{19}H_{16}N_3O_2Cl$ 354.1009, found 354.0961.

***N*^{1}-(2-Chlorophenyl)-*N*^{1},*N*^{2}-dimethyl-*N*^{2}-(2-nitrophenyl)benzene-1,2-diamine (15).** A solution of compound **14** (0.405 g, 1.14 mmol) in 4 mL of DMF was added to KH (0.46 g, 3.42 mmol). Upon addition, the solution turned from orange to deep purple. The mixture was stirred at rt for 10 min, and then MeI (0.4 mL, 5.7 mmol) was added dropwise via syringe. The reaction was stirred at rt until the solution returned to a yellow color. The reaction was then quenched with H_2O and extracted with 3 × 15 mL of EA. The organic layers were combined and washed with 3 × 15 mL of H_2O, brine, and then H_2O again to remove excess DMF. The organic layer was then dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the desired product as a yellow powder with no further purification necessary (0.362 g, 86%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (1H, dd, *J* = 8.0, 1.7 Hz), 7.36 (1H, ddd, *J* = 8.8, 7.3, 1.8 Hz), 7.29−7.19 (2H, m), 7.12 (1H, dd, *J* = 8.2, 1.7 Hz), 7.07−6.92 (5H, m), 6.88 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz), 6.81 (1H, dd, *J* = 7.8, 1.2 Hz), 3.32 (3H, s), 3.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.5, 143.5, 142.1, 138.8, 132.7, 131.0, 128.7, 127.6, 126.2, 124.2, 124.1, 123.7, 123.1, 120.4, 118.8, 38.5, 38.1; IR ($CDCl_3$) 1520 (NO_2); HRMS (MH^+) calcd for $C_{20}H_{18}N_3O_2Cl$ 368.1166, found 368.1091.

***N*^{1}-(2-Aminophenyl)-*N*^{2}-(2-chlorophenyl)-*N*^{1},*N*^{2}-dimethylbenzene-1,2-diamine (16).** Following the general procedure of Sanz,[46] CuCl (0.460 g, 4.65 mmol) was added to a stirring solution of compound **15** (0.570 g, 1.55 mmol) in MeOH (15.5 mL) at rt. KBH_4 (0.836 g, 15.5 mmol) was then added in portions. The reaction stirred at rt until the solution became clear, 2−4 h. The reaction was then quenched with H_2O and extracted 3 × 30 mL of 90/10 EA/DCM. The organic layers were combined and dried over Na_2SO_4, and the solvent was removed to give the desired product as a reddish-brown oil (0.450 g, 86%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3 (1H, dd, *J* = 8.0, 1.9 Hz), 7.15 (1H, 8.5, 7.3, 1.7 Hz), 7.06−6.88 (7H, m), 6.83−6.73 (2H, m), 6.60 (1H, dd, *J* = 7.3, 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 143.4, 142.2, 141.1, 136.7, 131.1, 128.2, 127.3, 124.6, 124.4, 124.3, 123.4, 123.4, 123.2, 122.6, 122.5, 118.7, 116.1, 39.4, 38.6; IR ($CDCl_3$) 3441 (NH_2), 3368 (NH_2); HRMS (MH^+) calcd for $C_{20}H_{20}N_3Cl$ 338.1424, found 338.1379.

N-Methyl-2-(10-methylphenazin-5(10*H*)-yl)aniline (5b). Compound **16** (0.090 g, 0.27 mmol), $Pd(dba)_2$ (0.016 g, 10% mol), BINAP (0.034 g, 20% mol), and Cs_2CO_3 (0.132 g, 0.41 mmol) in 3 mL of 1:1 toluene/*t*-BuOH were added to a 10 mL microwave tube. The mixture was purged with Ar for 5 min while stirring at rt. The MW settings were as follows: *P* = 250 W, time = 60 min, temp = 130 °C; PSI = 250. The reaction mixture was checked by TLC after each 60 min run. When TLC showed consumption of

starting material **16** (240 min total), the mixture was filtered through a pad of silica gel eluting with 90/10 EA/DCM. The solvent was removed under reduced pressure. The product was then purified by column chromatography eluting with DCM/petroleum ether gradient to give the cyclized product **5b** as a white powder (41 mg, 50%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05−6.95 (6H, m), 6.87 (1H, d, J = 1.1 Hz), 6.84 (1H, d, J = 1.1 Hz), 6.75−6.73 (4H, m), 5.82 (1H, bs), 2.68 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 141.4, 140.2, 127.8, 126.1, 121.9, 121.1, 118.4, 117.5, 39.9; IR ($CDCl_3$) 3382 (NH), 1499 (C═C); HRMS (MH^+) calcd for $C_{20}H_{19}N_3$ 302.1579, found 302.1573. Single crystals for X-ray structural analysis were grown by the slow evaporation of a solution of **5b** DCM.

5,10,15-Trimethyl-10,15-dihydro-5*H*-tribenzo[*b*,*e*,*h*][1,4,7]triazonine (5a). A solution of *N*,*N*′-dimethyl triazacyclophane **5b** (0.018 g, 0.07 mmol) in 0.2 mL of DMF was added to KH (0.028 g, 0.21 mmol). Upon addition, effervescence ensued, and the solution turned a pale pinkish-purple color. The mixture was stirred at rt until effervescence ceased (about 5 min), and MeI (0.022 mL, 0.35 mmol) was added dropwise via syringe. The reaction was allowed to stir at rt for 2 h, during which time the solution became faint yellow. The reaction mixture was quenched with deionized H_2O and extracted with EA (3 × 10 mL). The organic layers were combined and dried over Na_2SO_4, and the solvent was removed under reduced pressure to give the product **5a** as a pale yellow oil (0.021 g, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (12H, s), 2.93 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 122.9, 121.0, 40.6; IR ($CDCl_3$) 3052 (CH), 1605 (C═C) HRMS (MH^+) calcd for $C_{21}H_{21}N_3$ 316.1808, found 316.1799.

Supporting Information Available: X-ray crystal structure coordinates and files for compound **5b** (CIF). ^{1}H and ^{13}C NMR spectra are available for all compounds in the eight-step linear synthesis. This material is available free of charge via the Internet at http://pubs.acs.org.