Facile Preparation of 3,7-Diazabicyclo[3.3.0]octane and 3,7,10-Triheterocyclic [3.3.3]Propellane Ring Systems from 1,5-Diazacyclooctane 3,7-Derivatives[1]

Paritosh R. Dave* and Farhad Forohar

GEO-CENTERS, INC at ARDEC, Building 3028, Picatinny Arsenal, New Jersey 07806-5000

Theodore Axenrod, Kajal K. Das, Lida Qi, Clara Watnick, and Hamid Yazdekhasti

Department of Chemistry, The City College of the City University of New York, New York, New York 10031

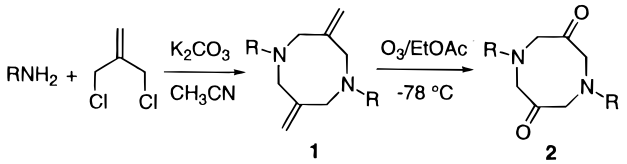
Received August 1, 1996[⊗]

The cyclodimerization of *p*-toluenesulfonamide and 3-chloro-2-(chloromethyl)-1-propene to prepare *N*,*N*′-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) and its ozonation to the corresponding 3,7-dione **2a** are reported. Unusual transannular cyclizations initiated by lithium aluminum hydride treatment or bromination of **1a** and oxidative coupling of the dioxime derived from **2a** are described. These reactions lead, respectively, to the following derivatives of the little-studied 3,7-diazabicyclo[3.3.0]octane ring system: 1,5-dimethyl-3,7-diazabicyclo[3.3.0]octane (**5**), *N*,*N*′-bis(*p*-toluenesulfonyl)-1,5-bis(bromomethyl)-3,7-diazabicyclo[3.3.0]octane (**8**), and *N*,*N*′-bis(*p*-toluenesulfonyl)-1,5-dinitro-3,7-diazabicyclo[3.3.0]octane, (**12**). Acid-catalyzed hydration of **1a**, in contrast, gives the expected 5-methyl-3,7-diazabicyclo[3.3.1]nonan-1-ol (**10**). Reaction of the dibromide **8** with the nucleophiles, sodium sulfide, sodium oxide, and sodium *p*-toluenesulfonamide conveniently delivers the corresponding novel 3,7,10-triheterocyclic [3.3.3]propellanes.

Introduction

The chemistry of 1,5-diazacyclooctanes has been investigated in these laboratories as part of a continuing program to synthesize novel high density energetic materials derived from functionalized small-[2] and medium-ring nitrogen heterocycles. As a class,[3] 1,5-diazacyclooctanes are versatile compounds important as pharmaceutical intermediates, polymerization accelerators, antiknock agents in motor fuels, and energetic materials.[4,5] In the course of this work, 1,5-diazacyclooctanes exhibited a marked propensity to undergo unusual transannular cyclizations to form the 3,7-diazabicyclo[3.3.0]octane ring system. With one notable exception, this same unexpected bicyclic ring system was formed by treatment of 1,5-diazacyclooctanes with several dissimilar reagents under conditions that doubtless proceed through different intermediates and by quite distinct reaction mechanisms. These cyclizations have been exploited to provide facile entry into the little-studied 3,7-diazabicyclo[3.3.0]octane ring system, which is easily transformed into polyheteroatom-containing tricyclic compounds conjoined in a carbon−carbon single bond (propellanes).[6] In this paper, we detail new synthetic routes to the 1,5-diazacyclooctane, 3,7-diazabicyclo[3.3.0]octane, and 3,7,10-triheterocyclic [3.3.3]propellane[6] ring systems that now become conveniently accessible.

Scheme 1



R = (a) p-$CH_3C_6H_4SO_2$, (b) CH_3SO_2

Results and Discussion

1,5-Diazacyclooctanes. Conspicuously absent from the many known 1,5-diazacyclooctanes are the 3,7-dimethylene and 3,7-diketo derivatives. These compounds were initially targeted as simple intermediates useful for the facile functionalization of the 3,7-ring positions. The sequence of steps outlined in Scheme 1 illustrates the synthetic method that was used to prepare these 3,7-dimethylene and 3,7-diketo derivatives. In this approach, when either *p*-toluenesulfonamide or methanesulfonamide was allowed to react with 3-chloro-2-(chloromethyl)-1-propene in the presence of potassium carbonate the corresponding cyclodimeric 3,7-bis(methylene)-1,5-diazacyclooctane derivatives **1** were easily obtained and isolated in moderate to good yields (∼50%).

The use of sulfonamides in this procedure is found to be superior to the previously described reactions of amines with 3-halo-2-(halomethyl)-1-propenes[7,8] or other bifunctional allylic compounds where the product is frequently a complex mixture consisting of the 3-methylene-1-azetidines, 3,7-bis(methylene)-1,5-diazacyclooctanes, and higher cyclic oligomers as well as noncyclic materials.[9,10] Ozonation of the exocyclic double bonds in

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1996.

(1) For a preliminary communication see: Dave, P. R.; Forohar, F. F.; Axenrod, T.; Qi, L.; Watnick, C.; Yazdekhasti, H. *Tetrahedron Lett.* **1994**, *35*, 8965.

(2) Axenrod, T.; Watnick, C.; Yazdekhasti, H.; Dave, P. R. *Tetrahedron Lett.* **1993**, *34*, 6677.

(3) For a review see Perlmutter, H. D. *Adv. Heterocycl. Chem.* **1989**, *46*, 1.

(4) Cichra, D. A.; Adolph, H. G. *Synthesis* **1983**, 830.

(5) Li-Hua, X.; Ming-xuan, W.; En-pu, W.; Hui-min, T.; BØ-ren, C. *Propellants, Explos., Pyrotech.* **1988**, *13*, 21.

(6) For a discussion of the use of this trivial nomenclature, see Knowles, P.; Harris, N. V. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1475. Altman, J.; Babad, E.; Itzchaki, J. Ginsburg, D. *Tetrahedron, Suppl. 8*, Part I, **1966**, 279.

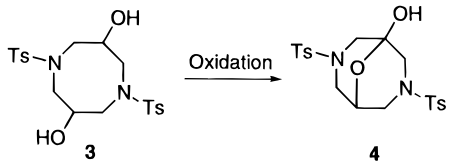
(7) Schulze, K.; Winkler, G.; Dietrich, W.; Mühlstädt, M. *Prakt. Chem.* **1977**, *319*, 463.

(8) Schulze, K.; Vetter, A.; Dietrich, W.; Mühlstädt, M. *Z. Chem.* **1977**, *17*, 174.

(9) Lukin, S. S.; Levashova, V. I.; Bunina-Krivorukova, L. I.; Zlotskii, S. S. *J. Org. Chem. USSR* **1989**, 2210.

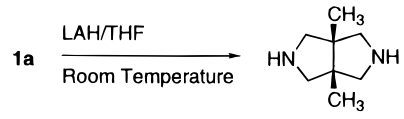
S0022-3263(96)01475-2 CCC: $12.00

Scheme 2



3 **4**

Scheme 3



5

the 3,7-bis(methylene)-1,5-diazacyclooctanes **1** produced the corresponding 1,5-diazacyclooctane-3,7-diones **2** in excellent yields.

Analysis of the respective ^{1}H and ^{13}C NMR spectra together with their mass spectra confirms that the cyclodimerization products of the reaction of *p*-toluenesulfonamide or methanesulfonamide with 3-chloro-2-(chloromethyl)-1-propene are the 3,7-bis(methylene)-1,5-diazacyclooctane derivatives **1** and not azetidines or some higher cyclic oligomers that are possible.

Although the stereoisomeric 1,5-diazacyclooctane-3,7-diols **3** are readily prepared from the reaction of *p*-toluenesulfonamide anion with epichlorohydrin or 1,3-dihalo-2-propanols, this route to the 1,5-diazacyclooctane-3,7-diones **2** is unsatisfactory because of the failure of the latter diols to undergo complete oxidation. Rather, as outlined in Scheme 2, chromic anhydride oxidation is reported[11] to give the transannular hemiketal **4** and, in our hands, oxidation under Swern conditions gives the same product.

In apparent contrast, the transannular hemiketal of 5-hydroxycyclooctanone is converted to the corresponding dione by Jones oxidation.[12]

3,7-Diazabicyclo[3.3.0]octanes. The convenient preparation of *N*,*N*′-bis(*p*-toluenesulfonyl) derivative **1a**, suggested N-detosylation followed by alkylation with appropriate electrophiles as a potential synthetic route to a variety of *N*,*N*′-disubstituted-3,7-bis(methylene)-1,5-diazacyclooctanes and their corresponding diketones. Precedents for the hydrolysis of sulfonamides[13] or their smooth reductive cleavage by hydride reagents[14] are available in the literature.

When **1a** was treated with lithium aluminum hydride, in an attempted reductive detosylation to prepare the parent 3,7-bis(methylene)-1,5-diazacyclooctane, the first indication of the pronounced tendency toward transannular cyclization in this system was detected. This normally predictable hydride reduction was found to follow an unexpected course. The reductive cleavage of the tosyl group proceeded smoothly as evidenced by the disappearance of the tosyl signals in the NMR spectrum of the product. However, surprisingly, this was accompanied by the simultaneous disappearance of the vinyl proton resonances at δ 5.19 and the emergence of a singlet at δ 0.99 in the methyl region along with an AB pattern centered at δ 2.71 and δ 2.92 (J = 11.2 Hz). The complete structure of this product was arrived at by analysis of its ^{1}H and ^{13}C NMR spectra including recording the DEPT and HETCORR spectra. From these determinations it was concluded that transannular bond formation, shown in Scheme 3, had occurred to afford 1,5-dimethyl-3,7-diazabicyclo[3.3.0]octane **5** in 82% yield. This conclusion is also supported by the measured mass spectrum of **5**.

Table 1. Results of Analysis of Deuterium Content of 1,5-Dimethyl-3,7-diazabicyclo[3.3.0]octanes-d_x 5 Obtained in Hydride Reduction of 1a

	products, **5**				
reactant[a]	LRMS[b]		δ ^{13}C{^{1}H}, ppm		
hydride/quench	m/z[c]	$(M+1)^+$	methyl	CH_2	C_q
LAH/H_2O	141	$C_8H_{17}N_2$	20.4,−	51.7	62.6
LAH/D_2O	142	$C_8H_{16}DN_2$	20.4, 20.0[d]	51.5	62.3
LAD/H_2O	142	$C_8H_{16}DN_2$	20.4, 20.0[d]	51.5	62.3
LAD/D_2O	143	$C_8H_{15}D_2N_2$−	−, 20.0[d]	51.5	62.1

[a] Compound **1a** in THF treated with indicated reagents. [b] Low resolution chemical ionization (NH_3) mass spectrum. [c] Base peak (100%); other isotopomeric $(M+1)^+$ ions less than 10%. [d] Triplet, $^1J(^{13}C-^2H)$ = 19.0 Hz.

To probe further the nature of this rather unexpected reductive cyclization, a series of experiments with lithium aluminum hydride and lithium aluminum deuteride was carried out, and the reaction mixtures were quenched with either H_2O or D_2O. The deuterium content of the several labeled reaction products was determined from the m/z value of the prominent $(M+1)^+$ ion in the chemical ionization (NH_3) mass spectra of the 1,5-dimethyl-3,7-diazabicyclo[3.3.0]octanes. Before mass measurement, azeotropic distillation of the reduction products with benzene containing added H_2O was employed to exchange any N−D species and convert them to the corresponding N−H compounds. The position of deuterium incorporation was determined by analysis of the carbon chemical shifts and multiplicities in the ^{13}C{^{1}H} spectra. These results are summarized in Table 1.

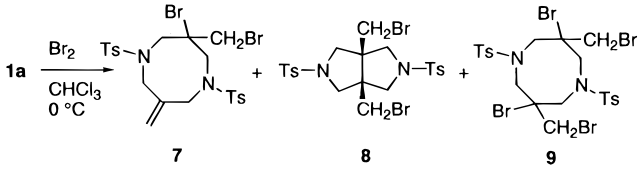
Analysis of the $(M+1)^+$ ions in the mass spectra of the various reaction products indicated that either one or two deuterium atoms were quantitatively introduced. Thus, reduction of **1a** with LAH and quenching with D_2O or reduction with LAD and quenching with H_2O afforded material having an m/z value equal to 142 corresponding to $C_8H_{15}DN_2$. Similarly, reduction with LAD followed by D_2O resulted in material having the composition $C_8H_{14}D_2N_2$. The isotope shifts and multiplicities in the ^{13}C{^{1}H} spectra establish unequivocally that the deuterium atoms appear, as the case may be, in either one or both of the methyls and then only as isotopically labeled CH_2D groups.

While we are aware of no precedent, the formation of this bicyclic system can be rationalized, mechanistically, in terms of a hydride attack at one of the exocyclic methylene carbons followed by carbanion addition to the proximal transannular double bond. The ring closure process is then completed by transfer of a proton to the newly generated intermediate methyl carbanion. This proposed interpretation is consistent with the results of these deuterium labeling experiments.

On the other hand, the smooth reduction of alkenes by $LiAlH_4$ in combination with catalytic quantities of such first-row transition metal salts as $CoCl_2$, $NiCl_2$, and $TiCl_3$

(10) Suzuki, M.; Lim, J.-C., Oguni, M.; Eberhardt, M.; Saegusa, T. *Polym. J.* **1990**, *22*, 815.
(11) Paudler, W. W.; Gapski, G. R.; Barton, J. M. *J. Org. Chem.* **1966**, *31*, 277.
(12) Bishop, R. *J. Chem. Soc. Perkin Trans. 1* **1974**, 2364.
(13) A mixture of acetic acid and 6 N hydrochloric acid has successfully been used to remove the *N*-tosyl groups in 3,7-disubstituted octahydrodiazocines over a four-week period; see for example, reference 16.
(14) Gold, E. H.; Babad. E. *J. Org. Chem.* **1972**, *37*, 2208.

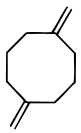
Scheme 4



7 8 9

is well-known. However, the low deuterium incorporation found when the product mixtures were quenched with D_2O suggests that the reactive intermediates arise from the homolytic dissociation of a transition metal−alkyl which subsequently abstracts hydrogen from the solvent.[15] This pathway is quite different from the present case where good yields and essentially quantitative deuterium incorporation are obtained in the absence of any added transition metal salts.

The 3,7-diazabicyclo[3.3.0]octane ring system has scarcely been investigated. The one reported example in the literature, of which we are aware, was prepared by a lengthy multistep synthesis.[6] While ring contractions to diazepines and piperidines have previously been observed in diazocine chemistry,[16] transannular cyclizations to bicyclic systems appear to be unknown. Thus, a significant contrast in behavior is observed in the electrophilic addition of bromine to the carbocycle, 1,5-bis(methylene) cyclooctane **6**, and its diaza analog **1a**.

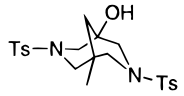


6

Both systems are disposed to undergo transannular cyclizations, but quite dissimilar ring skeletons are obtained. For example, carbocycle **6** is transformed by bromine into bridgehead substituted bicyclo[3.3.1]nonane derivatives,[12] whereas, as outlined in Scheme 4, **1a** gives an unexpected mixture of the 1,2- and 1,4-dibromo addition products, *N*,*N*′-bis(*p*-toluenesulfonyl)-3-bromo-3-(bromomethyl)-7-methylene-1,5-diazacyclooctane (**7**) and *N*,*N*′-bis(*p*-toluenesulfonyl)-1,5-bis(bromomethyl)-3,7-diazabicyclo[3.3.0]octane (**8**) together with very small quantities of the tetrabromide, *N*,*N*′-bis(*p*-toluenesulfonyl)-3,7-dibromo-3,7-bis(bromomethyl)-1,5-diazacyclooctane (**9**). The relative amounts of **7** and **8** formed are sensitive to the reaction conditions. Combination of molar equivalents by rapid dropwise addition of a solution of bromine to **1a** in CH_2Cl_2 at 0 °C affords mainly **7**, whereas slow addition of the bromine reverses the situation leading to **8** as the major product. Attempts to convert **7** to **8** by heating in DMSO at 110 °C for 16 h were unsuccessful, and the starting material was recovered.

The structures assigned to compounds **7**−**9** are confirmed by their ^1H and ^{13}C NMR properties and their mass spectra.

From carbonium ion considerations, the reaction of **1a** with bromine to give **7** and **8** is exceptional and clearly at variance with the anticipated and more readily rationalized formation of the 3,7-diazabicyclo[3.3.1]-nonane skeleton. In this connection, it is interesting to note that **1a** reacts with H_2SO_4 in a manner that parallels the behavior exhibited by carbocycle **6** toward electrophilic reagents. Thus, by treatment with acid, **1a** is quantitatively converted to the expected 5-methyl-3,7-diazabicyclo[3.3.1]nonan-1-ol **10**.



10

The structure of **10** has been deduced from its ^1H and ^{13}C NMR properties as well as analysis of its mass spectrum. The reaction path that leads to the formation of **10** highlights the apparent disparity in the behavior of **1a** toward acid-catalyzed hydration compared with the product of what is presumed to be electrophilic addition of bromine.

Transannular cyclizations in the diazacyclooctane system offer an attractive and viable synthetic route to the inaccessible 3,7-diazabicyclo[3.3.0]octane ring system. This property was utilized in the synthesis of 1,3,5,7-tetranitro-3,7-diazabicyclo[3.3.0]octane (**13**) shown in Scheme 5. Compound **2a** was converted to the corresponding dioxime **11** by standard method. NMR analysis showed the dioxime product so obtained to be a mixture of the *syn* (minor) **11a** and *anti* (major) **11b** stereoisomers, from which the latter could be isolated in pure form by recrystallization from 95% ethanol. Treatment of the stereoisomeric mixture of the dioximes **11** with *N*-bromosuccinimide in aqueous dioxane or with *m*-chloroperbenzoic acid in a buffered medium leads in both instances to ring-closure giving *N*,*N*′-bis(*p*-toluenesulfonyl)-1,5-dinitro-3,7-diazabicyclo[3.3.0]octane **12.** NMR and mass spectroscopic data provide evidence for the structure of compound **12**.

In a recent parallel report 3,7-dinitrotricyclo[3.3.1.$0^{3,7}$]-nonane has been prepared[17] from the dioxime of the corresponding bridgehead bicyclic diketone by oxidative coupling with *m*-chloroperbenzoic acid. Similar transannular reactions of bisoximes have also been described by Paquette[18] and Camps et al.[19]

Treatment of **12** with trifluoroacetyl nitrate in CH_2Cl_2 results in the nitrolysis of the tosyl groups affording the tetranitro compound **13**. The structure of **13** is supported by the presence of the expected AB system centered at δ 4.99 and δ 5.14 (J = 13.9 Hz) in the ^1H spectrum. Alternatively, compound **13** could be prepared directly from **11** by nitrolysis with 100% HNO_3. In this case considerable nitration of the tosyl groups was observed, but it proved possible to isolate pure **13** in 25% yield by preparative scale thin-layer chromatography. These assignments and the structure of **13** were further substantiated by X-ray crystallographic analysis.[20]

(15) See for example, Ganem, B.; Osby, J. O. *Chem. Rev.* **1986**, *86*, 763 and references cited therein.

(16) Paudler, W. W.; Zeiler, A. G.; Gapski, G. R. *J. Org. Chem.* **1969**, *34*, 1001.

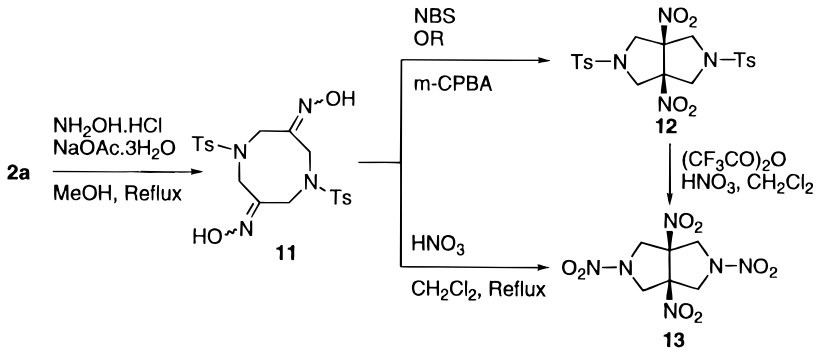
(17) Camps, P.; Munoz-Torrero, D. *Tetrahedron Lett.* **1994**, *35*, 3187; See also, Chapman, R. D.; Archibald, T. G.; Baum, K. Report No. ONR-7-1 (Interim), 1989; Fluorochem Inc., Azusa, CA; AD-A214106; available from the National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161.

(18) Waykole, L. M.; Shen, C. C.; Paquette, L. A. *J. Org. Chem.* **1988**, *53*, 4969.

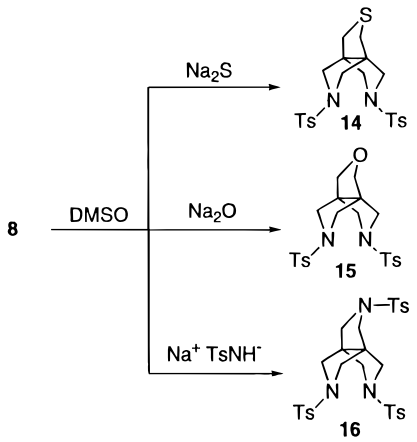
(19) Camps, P.; Munoz-Torrero, D., Munoz-Torrero, V. *Tetrahedron Lett.* **1995**, *36*, 1917. Camps, P.; Font-Bardia, M.; Munoz-Torrero, D.; Solans, X. *Liebigs Ann. Chem.* **1995**, 523.

(20) Ammon, H. L.; Zuyue, D.; Gilardi, R.; Dave, P. R.; Forohar, F.; Axenrod, T. *Acta Crystallogr. Sect. B* **1996**, *52*, 352.

Scheme 5



Scheme 6



3,7,10-Triheterocyclic [3.3.3]Propellanes. Polyamines, having the appropriate three-dimensional structure, such as that represented by the parent propellanes of **14**−**16**, have possible application as bifunctional catalysts in 1,3-proton transfer reactions. Thus, they are potentially important as mimics of transaminases in biological processes.[21] It has previously been observed that heterocyclic propellanes are difficult to prepare. In particular, it has been reported that angular halomethyl groups which form part of substituted neopentyl systems fail to undergo cyclization to the corresponding heterocyclic propellanes.[6] The ready availability of appropriate precursors in the present work prompted us to examine anew these ring-closures, which, if successful, would open a facile route to these desired heterocyclic propellanes. Although the reaction of **8** with nucleophiles was sluggish, this difficulty was surmounted by heating the reactants in dimethyl sulfoxide. Thus, as shown in Scheme 6, when **8** was heated with either Na_2S, Na_2O, or the preformed sodium salt of *p*-toluensulfonamide, cyclization could be induced to give the corresponding triheterocyclic propellanes. In this manner, propellanes **14**, **15**, and **16** were conveniently prepared in 80%, 75%, and 78% yield, respectively.

The ^1H and ^{13}C NMR spectral properties of these propellanes were consistent with the expected structures. The chemical shifts observed for the different carbons attached to nitrogen, oxygen, and sulfur in these propellanes also compare favorably with the trends reported for other related heteropolycycloalkanes.[22]

In conclusion, a convenient preparation of 3,7-functionalized *N,N′*-diarylsulfonyl and dialkylsulfonyl-1,5-diazacyclooctanes is described. Unusual transannular cyclizations in these systems leading to the little known 3,7-diazabicyclo[3.3.0]octane system have been examined. Procedures were developed that permit the ready conversion of the latter ring system to novel 3,7,10-triheterocyclic [3.3.3]propellanes. The methods reported constitute simple and efficient syntheses of otherwise inaccessible 3,7-diazabicyclo[3.3.0]octanes and various 3,7,10-triheterocyclic [3.3.3]propellanes.

Experimental Section

The chemical shifts in $CDCl_3$, DMSO-d_6, and acetone-d_6 are reported in δ (ppm) relative to TMS and were measured against the solvent as an internal standard. Melting points are uncorrected. THF was distilled from Na/benzophenone immediately prior to use. Other solvents and reagents were obtained from commercial sources and used without further purification.

***N,N′*-Bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (1a).** To a suspension of *p*-toluenesulfonamide (27.5 g, 160 mmol) and anhydrous K_2CO_3 (45.0 g) in anhydrous acetonitrile (250 mL) was added 3-chloro-2-(chloromethyl)-1-propene (20.0 g, 160 mmol) in acetonitrile (25.0 mL) over a 15 min period. After stirring the mixture at reflux for 4 h, the solvent was evaporated in vacuo, and the solid residue was extracted with hot ethyl acetate. Cooling the extract gave 21.5 g (60%) of colorless crystalline *N,N′*-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**): mp 194−197 °C; ^1H NMR ($CDCl_3$) δ 2.43 (s, 6H), 3.82 (s, 8H), 5.19 (s, 4H), 7.67 (d, J = 8.3 Hz, 4H), 7.31 (d, J = 8.3 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.5, 53.0, 118.1, 127.1, 129.7, 135.8, 141.8, 143.5. HRMS (FAB) calcd for $C_{22}H_{27}N_2O_4S_2$ $(MH)^+$ 447.1412; found m/z, 447.1402. Anal. Calcd for $C_{22}H_{26}N_2O_4S_2$: C, 59.17; H, 5.87; N, 6.27. Found: C, 59.21; H, 5.98, N, 6.54.

***N,N′*-Bis(methanesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (1b).** To a well-stirred refluxing suspension of methanesulfonamide (15.2 g, 160 mmol) and anhydrous K_2CO_3 (48.5 g) in acetonitrile (150 mL) was added 3-chloro-2-(chloromethyl)-1-propene (20.0 g, 160 mmol). The mixture was heated at reflux for 4 h and then cooled and filtered, and the filtrate was concentrated to give a solid residue, which was extracted with CH_2Cl_2 (100 mL). The CH_2Cl_2 solution was washed with 5% NaOH (50 mL) and water, dried ($MgSO_4$), and evaporated to give 4.96 g (22%) of crude *N,N′*-bis(methanesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1b**). Recrystallization from ethyl acetate afforded a colorless crystalline solid: mp 136−137 °C; ^1H NMR ($CDCl_3$) δ 2.88 (s, 6H), 3.99 (s, 8H), 5.28 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 38.1, 52.8, 119.3, 141.2. HRMS (FAB) calcd for $C_{10}H_{19}N_2O_4S_2$ $(MH)^+$ 295.0786; found m/z, 295.0781. Anal. Calcd for $C_{10}H_{18}N_2O_4S_2$: C, 40.80; H, 6.16; N, 9.52. Found: C, 41.11; H, 5.87, N, 9.32.

***N,N′*-Bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-dione (2a).** A mixture of ozone in oxygen was bubbled through a solution of *N,N′*-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) (1.0 g, 2.24 mmol) in CH_2Cl_2 (20 mL) at −78 °C until the blue color persisted. The

(21) Wu, Y.; Ahlberg, P. *Acta Chem. Scand.* **1992**, *46*, 60.
(22) Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH Publishers: New York, **1987**; p 277.

mixture was stirred for 1 h and then allowed to warm to 0 °C. Oxygen was bubbled through the mixture to remove excess ozone, and then excess dimethyl sulfide was added. After stirring at rt for 1 h the mixture was concentrated, and the residue was dissolved in CH_2Cl_2, washed with water and brine, dried ($MgSO_4$), and concentrated. The residue was recrystallized from acetone/hexanes to give pure *N,N′*-bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-dione (**2a**) (0.86 g, 85%): mp 275 °C dec; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 6H), 4.08 (s, 8H), 7.72 (d, J = 8.3 Hz, 4H), δ 7.36 (d, J = 8.3 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.6, 59.9, 127.1, 130.3, 133.9, 145.1, 204.3; HRMS (FAB) calcd for $C_{20}H_{23}N_2O_6S_2$ $(MH)^+$ 451.0998; found m/z 451.0990. Anal. Calcd for $C_{20}H_{22}N_2O_6S_2$: C, 53.32; H, 4.92; N, 5.93. Found: C, 53.61; H, 5.09, N, 5.93.

If the reaction mixture was not worked up until the next day, a sticky white substance was obtained; addition of CH_2Cl_2 or ether resulted in the formation of a white precipitate in 6% yield, that was identified as the cyclic hydrate of the diketone: ^{1}H NMR (acetone-d_6) δ 2.42 (s, 6H), 2.30 (d, J = 11 Hz, 4H), 3.66 (d, J = 11 Hz, 4H), 7.45 (d, J = 7.3 Hz, 4H), 7.65 (d, J = 7.3 Hz, 4H); ^{13}C NMR (acetone-d_6) δ 21.4, 52.0, 93.7, 128.6, 130.4, 133.1, 145.5. Heating the hydrate with benzene with azeotropic removal of water resulted in smooth dehydration to **2a**.

***N,N′*-Bis(methanesulfonyl)-1,5-diazacyclooctane-3,7-dione (2b).** A mixture of ozone in oxygen was bubbled through a suspension of *N,N′*-bis(methanesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1b**) (1.0 g, 3.34 mmol) in CH_2Cl_2 (50 mL) at −78 °C until the blue color of ozone persisted. The mixture was stirred for 1 h and then allowed to warm to 0 °C. Oxygen was then bubbled through the reaction mixture to remove excess ozone. Excess dimethyl sulfide was then added, and the mixture was stirred at rt for 1 h to decompose the ozonide. The mixture was then filtered, and the collected solid was washed with a small amount of CH_2Cl_2 to give 0.94 g of *N,N′*-bis(methanesulfonyl)-1,5-diazacyclooctane-3,7-dione (**2b**) (93%): mp 305 °C dec; ^{1}H NMR (DMSO-d_6) δ 3.36(s, 6H), 4.18 (s, 8H); ^{13}C NMR (DMSO-d_6)) δ 38.7, 59.1, 206.5. HRMS (FAB) calcd for $C_8H_{15}N_2O_6S_2$ $(MH)^+$ 299.0372; found m/z, 299.0379. Anal. Calcd for $C_8H_{14}N_2O_6S_2$: C, 32.21; H, 4.73; N, 9.39. Found: C, 32.47; H, 4.48, N, 9.81.

Oxidation of Stereoisomeric *N,N′*-Bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-diols (3). A solution of pyridine sulfur trioxide complex (0.88 g, 5.54 mmol), triethylamine (0.82 g, 8.72 mmol), and a stereoisomeric mixture of the *N,N′*-bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-diols (0.20 g, 0.44 mmol) in DMSO (6.91 g, 88.5 mmol) stirred at rt for 1 h and then poured over ice and extracted with ethyl acetate (4 × 10 mL). The combined extracts were washed with water (5 × 10 mL), dried ($MgSO_4$), and concentrated to give an oil which solidified on standing. Recrystallization from ethanol/hexane gave 0.41g (41%) of **4** as a colorless solid: mp 215−217 °C (lit. mp[11] 217 °C); ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 6H), 2.53 (d, 2H), 2.88 (m, 2H), 3.51 (d, J = 11 Hz, 2H), 3.71 (d, J = 11 Hz, 2H), 4.21 (m, 1H), 7.69 (d, J = 8.2 Hz, 4H), 7.33 (d, J = 8.2 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.6, 46.1, 52.3, 68.8, 90.4, 128.1, 129.9, 132.1, 144.2. LRMS (CI-NH_3) 453 (M + 1), 470 (M + 18).

1,5-Dimethyl-3,7-diazabicyclo[3.3.0]octane (5). A slurry of *N,N′*-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) (2.22 g, 4.98 mmol), in THF (75 mL) containing $LiAlH_4$ (1.90 g, 50 mmol), was stirred under N_2 for 42 h. The reaction mixture was quenched with 20% NaOH (4.5 mL) with external cooling. Stirring was continued at rt for 3 h, and the white granular precipitate that formed was removed by filtration and washed with anhydrous ether (3 × 50 mL). The combined organic extracts were concentrated to give 0.574 g (82%) of **5** as a colorless oil which slowly solidified: mp ∼ 30 °C; ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 6H), 2.71 (d, J = 11.2 Hz, 4H), 2.92 (d, J = 11.2 Hz, 4H), 2.61 (s, 2H, br); ^{13}C NMR ($CDCl_3$) δ 20.4, 51.7, 62.6. HRMS (FAB) calcd for $C_8H_{17}N_2$ $(MH)^+$ 141.1392; found m/z, 141.1388. Treatment of an ethanolic solution of **5** with picric acid afforded the picrate as a yellow solid, mp 258 °C.

1,5-Dimethyl-3,7-diazabicyclo[3.3.0]octane-d_1. The procedure used to prepare **5** was modified by the use of deuterated reagents in two separate experiments.

(a) *N,N′*-Bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) (0.223 g, 0.50 mmol) in THF (50 mL) was treated with $LiAlH_4$ (0.25 g, 6.6 mmol). Quenching of the reaction mixture with D_2O (1.0 mL) followed by 40% NaOD (0.5 mL) gave, after workup, 0.052 g (82%) of **5**-d_1 as a colorless oil.

(b) Procedure a was repeated using $LiAlD_4$ and H_2O followed by 40% NaOH to give 0.57 g of **5**-d_1 (82%).

Prior mass spectral measurement, the crude products were dissolved in benzene (25 mL) to which was added H_2O (3 × 1 mL), and the mixtures were independently subjected to azeotropic distillation using a Dean−Stark trap. Analysis of these samples by a DEPT experiment and their respective mass spectra confirmed the presence of only one deuterium atom and a CH_2D group. LRMS (EI) 141 (M).

1,5-Dimethyl-3,7-diazabicyclo(3.3.0)octane-d_2. A suspension of *N,N′*-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) (0.446 g, 1.00 mmol) in THF (50 mL) and $LiAlD_4$ (0.427 g, 10.2 mmol, 99% ^{2}H atom-enrichment) in THF (50 mL) afforded 0.152 g of crude product after quenching with D_2O, followed by NaOD, and workup as described for the preparation of **5**. Prior to mass spectral measurement, the crude product was azeotropically distilled with benzene and water as described above.

***N,N′*-Bis(*p*-toluenesulfonyl)-3-bromo-3-(bromomethyl)-7-methylene-1,5-diazacyclooctane (7), *N,N′*-Bis(*p*-toluenesulfonyl)-1,5-bis(bromomethyl)-3,7-diazabicyclo[3.3.0]-octane (8), and *N,N′*-Bis(*p*-toluenesulfonyl)-3,7-dibromo-3,7-bis(bromomethyl)-1,5-diazacyclooctane (9).** A solution of bromine (3.2 g, 20 mmol) in CH_2Cl_2 (50 mL) was added dropwise over a 4 h period to a stirred solution of **1a** (8.92 g, 20 mmol) in CH_2Cl_2 (250 mL) at 0 °C. The reaction mixture was then stirred for an additional 6 h and then it was washed successively with 5% $Na_2S_2O_3$ (100 mL), saturated $NaHCO_3$ (100 mL), and water. The organic phase was dried ($MgSO_4$) and concentrated at reduced pressure to give a residue which was treated with ice-cold acetone (15 mL). Pure **8** (8.2 g, 68%) was isolated as crystalline material which remained insoluble in the acetone: mp 228−231 °C; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 6H), 3.16 (d, J = 10.5 Hz, 4H), 3.31 (d, J = 10.5 Hz, 4H), δ 7.33 (d, J = 8.4 Hz, 4H), δ 7.64 (d, J = 8.3 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.6, 34.0, 56.0, 57.3, 127.7, 130.0, 131.9, 144.5; HRMS (FAB) calcd for $C_{22}H_{27}N_2O_4S_2Br_2$ $(MH)^+$ 604.9778, found m/z, 604.9768. Anal. Calcd for $C_{22}H_{26}N_2O_4S_2Br_2$: C, 43.58; H, 4.32; N, 4.62. Found: C, 43.66; H, 4.73, N, 4.96.

Concentration of the acetone mother liquor deposited the tetrabromide **9** (0.30 g, 2%) as colorless crystals: mp 210−212 °C; ^{1}H NMR ($CDCl_3$) δ 2.48 (s, 6H), 3.33 (d, J = 15.6 Hz, 4H), 4.18 (s, 4H), 4.35 (d, J = 15.6 Hz, 4H), 7.38, 7.40, 7.75, 7.77; ^{13}C NMR ($CDCl_3$) δ 21.61, 39.85, 61.13 67.07, 127.93,-130.22, 133.96,144.89; LRMS (EI) 762 (M).

After separating the undissolved **9**, column chromatography of the mother liquor on silica gel using hexane−ethyl acetate (4:1) as the elution solvent afforded the dibromide **7** (3.6 g, 30%): mp 192−197 °C; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 6H), 3.45 (d, J = 12.6 Hz, 2H), 3.88 (d, J = 12.6 Hz, 2H), 3.56 (d, J = 15.7 Hz, 2H), 3.85 (d, J = 15.7 Hz, 2H), 4.11 (s, 2H), 5.24 (s, 2H), 7.33, 7.35, 7.69, 7.72; ^{13}C NMR ($CDCl_3$) δ 21.55, 42.61, 55.28, 55.58, 67.29, 124.23, 127.66, 130.03, 134.04, 139.33, 144.27; HRMS (FAB) calcd for $C_{22}H_{27}N_2O_4S_2Br_2$ $(MH)^+$ 604.9779; found m/z, 604.9779. Anal. Calcd for $C_{22}H_{26}N_2O_4S_2Br_2$: C, 43.58; H, 4.32; N, 4.62. Found: C, 43.25; H, 4.95, N, 4.90.

Attempts to convert **7** to its isomer **8** by heating at 110 °C for 16 h in anhydrous DMSO lead to the recovery of the starting material.

Rapid Addition of Bromine to 1a. To an ice-cooled (−5 to 0 °C) solution of *N,N′*-bis(*p*-toluenesulfonyl)-3,7-bis(methylene)-1,5-diazacyclooctane (**1a**) (2.68 g, 6.0 mmol) in CH_2Cl_2 (80 mL) was added a solution of bromine (0.96 g, 6.0 mmol) in CH_2Cl_2 (15 mL) over a 30 min period. The reaction mixture was stirred at 0 °C for an additional 5 h and then was washed successively with 5% sodium bicarbonate (30 mL), 5% sodium

bisulfite (30 mL), brine, and water. The organic layer was dried ($MgSO_4$), and the solvent was removed on a rotary evaporator to give 2.07 g of a crude mixture of **7** and **8**. NMR analysis showed this material to be an 88:12 mixture of **7** and **8**.

5-Methyl-3,7-diazabicyclo[3.3.1]nonan-1-ol (10). A solution of **1a** (112 mg, 0.25 mmol) in chloroform (2.0 mL) was stirred at rt for 24 h with concd H_2SO_4 (4.0 mL). The reaction mixture was poured into ice−water (60 mL) and extracted with chloroform (3 × 25 mL). The chloroform layer was washed with saturated sodium bicarbonate, dried ($MgSO_4$), and evaporated to leave 115 mg of crude product which was essentially pure **10**. Recrystallization from alcohol afforded needle-shaped crystals: mp 238−240 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H), 1.33 (s, 2H), 1.62 (s, br, 1H), 2.32 (d, 2H, J = 11.2 Hz), 2.41 (s, 6H), 2.48 (d, 2H, J = 10.7 Hz), 3.43 (d, 2H, J = 11.2 Hz), 3.66 (d, 2H, J = 10.7 Hz), 7.30, 7.33, 7.67, 7.69; ^{13}C NMR ($CDCl_3$) δ 21.54, 24.76, 33.19, 45.38, 54.08, 54.35, 66.57, 127.91, 129.78, 133.03, 143.67. HRMS (FAB) calcd for $C_{22}H_{29}N_2O_5S_2$ $(MH)^+$ 465.1518; found m/z, 465.1510. Anal. Calcd for $C_{22}H_{28}N_2O_5S_2$: C, 56.88; H, 6.07; N, 6.03. Found: C, 56.68; H, 5.78, N, 5.72.

Stereoisomeric Mixture of *N,N′*-Bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-dione Dioximes (11). A suspension of *N,N′*-bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-dione (**2a**) (0.900 g, 2.00 mmol), hydroxylamine hydrochloride (0.556 g, 8.00 mmol), and sodium acetate trihydrate (2.18 g, 16.0 mmol) in ethanol (70 mL) was stirred under reflux for 5 d. The ethanol was removed, and the residue was washed with water and dried over P_2O_5 in vacuo to give 0.710 g (74%) of **11** as a colorless solid comprised of two geometric isomers (syn, minor, **11a** and anti, major, **11b**).

A sample of crude **11** was recrystallized from ethanol to give the pure anti isomer **11b**: mp 239 °C dec; ^{1}H NMR (DMSO-d_6) δ 2.41 (s, 6H), 3.84 (s, 4H), 4.09 (s, 4H), 7.46 (d, J = 7.9 Hz, 4H), 7.69 (d, J = 7.9 Hz, 4H), 11.3 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 21.0, 47.0, 52.3, 126.6, 130.0, 134.6, 143.9, 152.9. HRMS (FAB) calcd for $C_{20}H_{25}N_4O_6S_2$ $(MH)^+$ 481.1216; found m/z, 481.1198.

***N,N′*-Bis(*p*-toluenesulfonyl)-1,5-dinitro-3,7-diazabicyclo[3.3.0]octane (12) by *N*-Bromosuccinimide Oxidation of 11.** A mixture of sodium bicarbonate (7.4 g, 88.1 mmol), NBS (6.6 g, 37.1 mmol), and a stereoisomeric mixture of the dioximes **11** (3.5 g, 7.3 mmol) in 5% aqueous dioxane (200 mL) was stirred at rt for 4 d. The reaction mixture was partitioned between CH_2Cl_2 (150 mL) and 5% sodium hydroxide (150 mL), and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were successively treated with 5% NaOH (2 × 50 mL), water (2 × 100 mL), and brine, dried (Na_2SO_4), and concentrated in vacuo to give 2.06 g of a slightly yellow solid, most of which dissolved on treatment with acetone (70 mL). The acetone solution was concentrated in vacuo to give 1.89 g of **12** as a slightly yellow solid (48%). Recrystallization from acetone/water gave crystalline needles of **12**: mp 154−156 °C; ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 6H), 3.89 (d, J = 11.5 Hz, 4H), 4.00 (d, J = 11.5 Hz, 4H), 7.40 (d, J = 8.3 Hz, 4H), 7.70 (d, J = 8.3 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.7, 55.1, 94.0, 127.5, 130.4, 131.8, 145.5. HRMS (FAB) calcd for $C_{20}H_{23}N_4S_2O_8$ $(MH)^+$ 511.0957; found m/z, 511.0955.

***N,N′*-Bis(*p*-toluenesulfonyl)-1,5-dinitro-3,7-diazabicyclo[3.3.0]octane (12) by m-CPBA Oxidation of 11.** A mixture of urea (0.02 g, 0.3 mmol), disodium hydrogen phosphate (0.8 g, 5.6 mmol), and the dioxime **11** (0.240 g, 0.5 mmol) in anhydrous acetonitrile (5.0 mL) was stirred at reflux for 10 m, and then m-chloroperbenzoic acid (0.3 g, 1.8 mmol) was slowly added over 1 h. The suspension was heated under reflux for 2 h and concentrated at reduced pressure, and the residue was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with a saturated sodium bicarbonate solution (4 × 15 mL), water (4 × 15 mL), and brine (2 × 30 mL), dried (Na_2SO_4), and concentrated to give compound **12** (0.064 g, 24%). The properties of **12** obtained in this experiment were identical with those exhibited by compound **12** isolated from the NBS oxidation of **11**.

1,3,5,7-Tetranitro-5,7-diazabicyclo[3.3.0]octane (13) by Nitrolysis of 12. Over a 2 min period 100% nitric acid (0.9 g, 14.2 mmol) was added to a stirred solution of trifluoroacetic anhydride (2.9 g, 14.1 mmol) in CH_2Cl_2 (10 mL) at −10 °C. To this mixture, maintained at −10 °C, was added a solution of **12** (0.36 g, 0.7 mmol) in CH_2Cl_2 (4 mL) was added over 0.5 h, and stirring was continued for 2.5 h. The reaction mixture was poured into ice−water (35 g) and extracted with CH_2Cl_2 (35 mL). The combined organic layers were washed successively with 5% sodium carbonate (50 mL) and water (50 mL), dried (Na_2SO_4), and evaporated to give a crude yellowish product (0.26 g) which was chromatographed on silica gel and eluted with acetone−hexane to give 0.06 g of **13** (36%), as colorless crystals: mp 222−224 °C; ^{1}H NMR (acetone-d_6) δ 5.14 (d, J = 13.9 Hz, 4H), 4.99 (d, J = 13.9 Hz, 4H); ^{13}C NMR (acetone-d_6) δ 56.6, 94.0.

1,3,5,7-Tetranitro-5,7-diazabicyclo[3.3.0]octane (13) from the Nitrolysis of *N,N′*-Bis(*p*-toluenesulfonyl)-1,5-diazacyclooctane-3,7-dione Dioxime (11). A solution of 98% nitric acid (5 mL) in CH_2Cl_2 (10 mL) containing catalytic quantities of urea and ammonium nitrate was added to a refluxing solution of dioxime **11** (0.3 g, 0.6 mmol) in CH_2Cl_2 (50 mL). The reaction mixture was heated under reflux for 1 h, initially developing a blue-green color which changed to dark brown as the reaction progressed. The reaction mixture was cooled to rt and poured over ice, and the organic layer was washed with water (50 mL), saturated sodium bicarbonate solution (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on silica gel and eluted with acetone−hexane. The appropriate fractions were combined and recrystallized from acetone−hexane to give **13** (0.045 g, 25%) which was identical in all respects with the material isolated from the reaction of **12** with trifluoroacetyl nitrate. Although no other pure material was isolated, NMR evidence indicated byproducts arising from nitration of the aromatic rings.

***N,N′*-Bis(*p*-toluenesulfonyl)-3-thia-7,10-diaza[3.3.3]propellane (14).** To a solution of **8** (150 mg, 0.25 mmol) in DMSO (15 mL) was added sodium sulfide (100 mg, 0.42 mmol). After heating at 125 °C for 1.5 h, the mixture was cooled to rt and poured into water (45 mL). The aqueous medium was extracted with ethyl acetate (2 × 20 mL), the combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo, and the resulting residue was recrystallized from acetone/hexanes to give **14** (0.95 g, 80%): mp 195−6 °C; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 6H), δ 2.96 (d, J = 9.5 Hz, 4H), 3.01 (d, J = 9.5 Hz, 4H), 2.73 (s, 4H), 7.33 (d, J = 8.0 Hz, 4H), 7.58 (d, J = 8.0 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.61, 42.22, 57.15, 65.88, 127.93, 129.93, 131.10, 144.34; HRMS (FAB) calcd for $C_{22}H_{27}N_2O_4S_3$ $(MH)^+$ 479.1133; found m/z, 479.1119. Anal. Calcd for $C_{22}H_{26}N_2O_4S_3$: C, 55.21; H, 5.47; N, 5.85. Found: C, 55.37; H, 5.29, N, 6.14.

***N,N′*-Bis(*p*-toluenesulfonyl)-3-oxa-7,10-diaza[3.3.3]propellane (15).** To a solution of **8** (0.20 g, 0.33 mmol) in anhydrous DMSO (15 mL) was added anhydrous sodium oxide (0.021 g, 3.3 mmol). The reaction mixture was heated for 20 h at 120 °C under N_2. The solvent was removed under vacuum and the residue taken up in water (30 mL) which was extracted with ethyl acetate (2 × 25 mL). The combined organic extracts were washed with water (2 × 25 mL) and dried (Na_2SO_4), and the solvent was removed under vacuum. After triturating the residue with cold ethyl acetate, **15** was obtained as a white solid (0.114 g, 75%): mp 212−216 °C; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 6H), 2.95 (d, J = 9.5 Hz, 4H), 3.01 (d, 9.5 Hz, 4H), 3.62 (2H), 7.33 (d, J = 8.0 Hz, 4H), 7.59 (d, J = 8.0 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.62, 56.03, 63.53, 76.19, 127.95, 129.99, 131.05, 144.45; HRMS (FAB) calcd for $C_{22}H_{27}N_2O_5S_2$ $(MH)^+$ 463.1361; found m/z, 463.1349. Anal. Calcd for $C_{22}H_{26}N_2O_5S_2$: C, 57.12; H, 5.67; N, 6.06. Found: C, 56.93; H, 5.89, N, 6.41.

***N,N′,N″*-Tris(*p*-toluenesulfonyl)-3,7,10-triaza[3.3.3]propellane (16).** *p*-Toluenesulfonamide (0.865 g, 5.05 mmol) was added to a solution of metallic sodium (115 mg, 5.05 mmol) in anhydrous methanol (50 mL), the solvent was removed under vacuum, and the residue was dissolved in DMSO (50 mL). The freshly prepared sodium salt solution was added

dropwise to a heated solution of dibromide **8** (1.0 g, 1.65 mmol) in anhydrous DMSO (25 mL) under N_2. After heating the solution for 16 h at 110 °C the solvent was removed and the residue taken up in chloroform (50 mL), washed with water (3×50 mL), and dried ($MgSO_4$). Removal of the solvent under vacuo gave pure **16** (0.79 g, 78%): mp 208−210 °C; ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 9H), 2.99 (s, 12H), 7.29 (d, J = 8.3 Hz, 6H), 7.51 (d, J = 8.3 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 21.47, 56.08, 60.73, 127.70, 129.92, 130.85, 144.44; HRMS (FAB) calcd for $C_{29}H_{34}N_3O_6S_3$ $(MH)^+$ 616.1610; found m/z, 616.1606. Anal. Calcd for $C_{29}H_{33}N_3O_6S_3$: C, 56.57; H, 5.40; N, 6.82. Found: C, 56.73; H, 5.56, N, 7.05.

Acknowledgment. The assistance of Mr. William Cao is gratefully acknowleged. P.R.D. and F.F. thank Drs. T. DeAngelis, G. Doyle, and R. Surapaneni for their support. Financial support for this work was provided in part by ARDEC, and in part by the Office of Naval Research and the Ballistic Missile Defense Organization.

Supporting Information Available: Copies of the ^{1}H NMR spectra of **5**, **9**, **11**, and **13** as well as ^{13}C NMR spectra of **5**, **7**−**9**, **10**, and **12**−**16** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9614755