g (0.25 mmol) of the epoxide **9b** in 1.0 mL of tetrahydrofuran was added, and the mixture was stirred with warming from −78 to −20 °C overnight. To the deep purple mixture was added 0.32 mL (1.88 mmol) of hexamethylphosphoric triamide at −20 °C. After 30 min, 0.031 g (0.25 mmol) of 4-(*N*,*N*-dimethylamino)pyridine and 0.191 g (1.20 mmol) of *tert*-butyldimethylsilyl chloride in 1.0 mL of tetrahydrofuran were added and the mixture was stirred for 4 h at −20 °C, then diluted with water, and extracted with ether. The combined ether layers were washed with water, dried over K_2CO_3, and concentrated. Flash chromatography on basic alumina (I) with hexane afforded 0.047 g (46%) of the ether, a 93:7 trans–cis mixture, as an oil: $[\alpha]^{23}_D$ −76.7° (*c* 2.58, $CHCl_3$); IR (film) ν 2900, 2840, 1465, 1260, 1080 cm^{-1}; ^1H NMR (90 MHz) 0.02 (s, CH_3Si), 0.86 (s, $(CH_3)_3C$), 0.95–1.55 (env, ring CH_2), 1.60–2.43 (m), 4.16 (AB q, J = 12.6 Hz, $\Delta\nu$ = 30.3 Hz, trans CH_2O), 4.05 (s, cis CH_2O) ppm. Anal. Calcd for $C_{26}H_{52}OSi$: C, 76.39; H, 12.82. Found: C, 76.45; H, 12.86. Integration of the ^1H NMR spectrum indicated a 93:7 mixture of trans–cis isomers.

(*R*)-(−)-2-Pentyl-1-((*tert*-butyldimethylsiloxy)methyl)-cyclohexadecene (15d). The procedure described above for **15b** was followed. Addition of 0.092 g (0.35 mmol) of the epoxide **9d** in 1.0 mL of tetrahydrofuran to the cuprate complex at −78 °C and stirring for 18 h at −78 to −20 °C followed by addition of 0.48 mL (2.75 mmol) of hexamethylphosphoric triamide, 0.043 g (0.35 mmol) of (dimethylamino)pyridine, and 0.272 g (1.80 mmol) of *tert*-butyldimethylsilyl chloride with stirring for 20 h gave upon workup and chromatography 0.072 g (48%) of the ether, a 93:7 trans–cis mixture, as an oil: $[\alpha]_D$ −62.9° (*c* 3.34, $CHCl_3$); IR (film) ν 2900, 2840, 1465, 1260, 1080 cm^{-1}; ^1H NMR (90 MHz) 0.03 (s, CH_3Si), 0.86 (s, $(CH_3)_3C$), 0.96–1.55 (env, ring CH_2), 1.66–2.50 (m), 4.16 (AB q, J = 11.7 Hz, $\Delta\nu$ = 28.3 Hz, trans CH_2O), 4.03 (s, cis CH_2O) ppm. GC/MS, *m/e* (M^+) 437, calcd (M^+) 436.8.

Acknowledgment. Support for this work was provided by a research grant (CHE-8026013) from the NSF. Funding for the AM-300 NMR spectrometer used in these studies was provided by NSF Instrument Grant CHE-8411172. We are indebted to Dr. M. Walla for helpful discussions of mass spectral data and to Dr. A. R. Garber for invaluable assistance in the measurement of ^{19}F NMR spectra.

Synthesis and Structure of Some Peri-Substituted 2,4,6,8-Tetraazabicyclo[3.3.0]octanes

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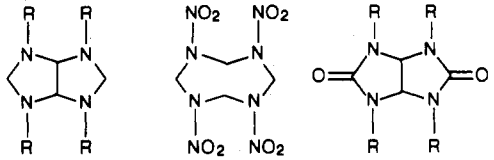
The synthesis and crystal structures of several substituted *cis*-2,4,6,8-tetraazabicyclo[3.3.0]octanes are reported. The stability of this ring system varies widely with the nature of the substituents present. Electrophilic substitution reactions on nitrogen are especially conducive to ring opening.

2,4,6,8-Tetraazabicyclo[3.3.0]octane-3,7-diones (glycolurils, **3**) have been investigated extensively and are often easily synthesized by condensation of ureas with glyoxal.[1] The parent ring compounds, the tetraazabicyclo[3.3.0]octanes, are far less well-known. A few 2,4,6,8-tetra-*n*-alkyl-2,4,6,8-tetraazabicyclo[3.3.0]octanes with *N*-methyl (**1a**), ethyl, and *n*-butyl substituents have been prepared by reduction of the corresponding glycolurils.[2a,b] *N*-Nitroso and *N*-nitro derivatives of this ring system, such as **1d**, are of interest as polycyclic analogues of the high-energy compound HMX (**2**). However, such compounds are unknown even though the corresponding 3,7-dione **3c** is readily available by nitration of glycoluril.[3]



1a. R=CH_3
b: R=$CH(CH_3)_2$
c: R=acetyl
d: R=NO_2

2

3a: R=CH_3
b: R=$CH(CH_3)_2$
c: R=NO_2

Initial synthesis efforts in our laboratory and elsewhere[4] indicated that the saturated tetraazabicyclooctane ring system **1** is not as easily formed by direct ring closure as the corresponding 3,7-diones. It appeared desirable to understand what structural factors affect its formation and stability. We now describe the synthesis, crystal structures, and selected properties of some potential precursors and structural analogues for **1d**.

Compounds **1a** and its higher *N*-alkyl homologues did not appear to be suitable precursors for **1d**, because no general method for replacement of *n*-alkyl by nitro exists. However, tertiary amines with *tert*-butyl or isopropyl groups undergo nitrolysis under mild conditions.[5] Therefore, the synthesis of **1b** and its *tert*-butyl analogue was attempted. *N*,*N*′-Diisopropylurea in the presence of acid readily condensed with glyoxal to a mixture of **3b** (≃50%) and *N*,*N*-diisopropylhydantoin (≃25%). The analogous reaction with *N*,*N*′-*tert*-butylurea was not successful. The glycoluril **3b** was reduced to **1b** with $LiAlH_4$ in dioxane at 90 °C. Pure **1b** can be stored in a closed container for a limited time. It is highly sensitive to acids.

(1) Petersen, H. *Synthesis* **1973**, 243.
(2) (a) Nelsen, S. F.; Hintz, P. J. *J. Am. Chem. Soc.* **1972**, *94*, 7108. (b) Suvorova, L. I.; Epishina, L. V.; Lebedev, D. V.; Khmelnitskii, L. I.; Novikov, S. S. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1979**, 2108.
(3) Boileau, J.; Emery, J. M. L.; Kehren, J. P. A. Ger. Offen. 2435651, 1975.
(4) Private communications by C. L. Coon, Lawrence Livermore National Laboratory, and R. L. Willer, Morton Thiokol Inc., Elkton Division.
(5) (a) Cichra, D. A.; Adolph, H. G. *J. Org. Chem.* **1982**, *47*, 2474. (b) Levins, D. A.; Bedford, C. D.; Staats, S. J. *Propellants, Explos., Pyrotech.* **1983**, *8*, 74.

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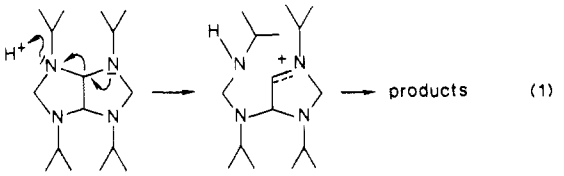
Solutions in dichloromethane exposed to the atmosphere decomposed completely over a 72-h period. Addition of a small amount of acetic acid (≃10% of **1b**) accelerated the decomposition to a half-life of 10 min or less. Since **1a** is stable under these conditions, the facile decomposition of **1b** must result from steric crowding due to the isopropyl groups. N-Protonation provides a low-energy path for ring opening and relief of this steric strain:



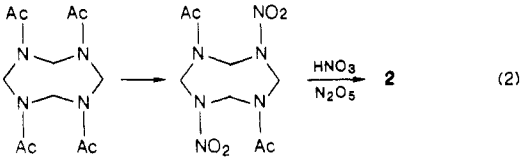
(1)

The ^{1}H NMR spectrum of **1b** clearly shows restricted rotation about the exocyclic C–N bonds (two CH_3 doublets). The presence of a methylene AB quartet is, as in the case of **1a**, indicative of the cis configuration at the ring junction. Upon addition of acetic acid to the NMR sample, the AB quartet quickly collapses into a singlet, and the methine ring proton signal is replaced by numerous low-intensity peaks. This change in the spectrum is consistent with the proposed ring-opening mechanism of decomposition.

The sensitivity of **1b** toward acids and electrophilic reagents in general precluded any attempts at its nitrolysis.

Reduction of **3c** to **1d** was also considered. Metal hydrides would be expected to give products resulting from cleavage of the urea moiety in analogy to the reactions of other nucleophiles[6,7] and were not investigated. Borane in THF with **3c** at room temperature gave only water-soluble degradation products. Catalytic hydrogenation of **3c** with palladium on carbon catalyst (30 psig) for 1 h gave products containing nitramine moieties, which are, at present, unidentified. The mixture does not contain **1d**, however, as evidenced by the absence of the appropriate signals in the NMR spectrum.

HMX, **2**, is prepared by nitrolysis of acyl precursors such as **4**:[8]



(2)

4

In an effort to mimic this approach, the synthesis of **1c** was attempted. Condensation of 1,3-diacetyl-4,5-dihydroxyimidazolidine[9] with *N,N'*-methylenebisacetamide (MBA) failed, probably because the forcing conditions required to effect the condensation caused fragmentation of the imidazolidine. When the imidazolidine was stabilized by acylation, the condensation with MBA proceeded readily, from the diacetyl as well as from the bis(trifluoroacetyl) derivative, to give **1c** in 58% and 30% yields, respectively. Compound **1c** is far more stable than **1a** and **1b**, even though the strain at the ring junction must be comparable to that in **1b**. This can be attributed to the lower basicity and decreased ability of the ring nitrogens

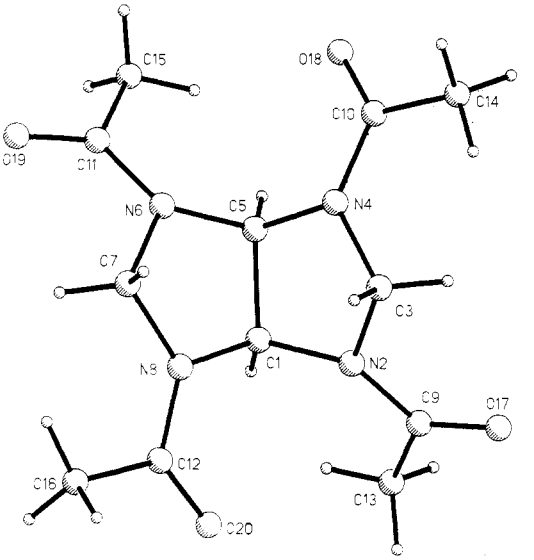
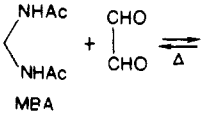
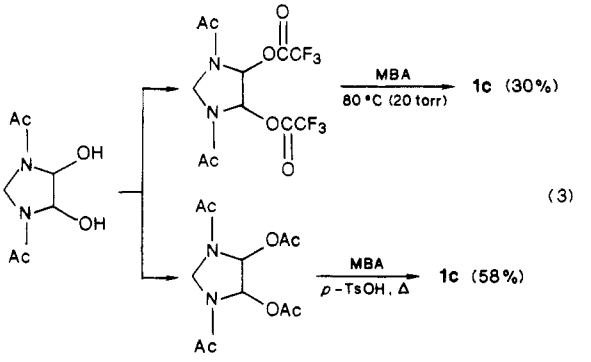


Figure 1. Crystal molecular structure of **1c**.

to stabilize the positive charge generated on heterolysis of a ring C–N bond. The ^{1}H NMR spectrum of **1c** exhibits





(3)

two broad methyl signals, a non-first-order multiplet for the methylene protons, and a singlet for the methine protons, in agreement with a cis ring junction, and restricted rotation about the acyl C–N bonds. The crystal structure determined by X-ray diffraction confirms this interpretation for the solid-state structure of **1c** (Figure 1 and Experimental Section). There appear to be no unusual bond lengths or angles in the molecule. Orientation of the two fused five-membered rings with respect to one another is folded-planar. Least-squares planes through each of the five-membered rings form a dihedral angle of 75.8°, with the average deviation of the atoms in each ring from its least-squares plane being only ±0.1 Å. The orientations of the four acetyl groups are defined by the torsion angles: O17–C9–N2–C3 = 165.8 (5)°, O18–C10–N4–C2 = 15.0 (4)°, O19–C11–N6–C7 = 179.7 (5)°, and O20–C12–N8–C7 = 13.4 (4)°. In two of the acetyl groups, the methyl groups face the ring junction, and in the other two, the oxygen atoms occupy this position.

Numerous attempts were made to nitrolyze **1c** to **1d** or to a partially nitrated intermediate, using the full scope of applicable nitrolysis agents[10] and conditions. In all cases

(6) Zhongji, P.; Daozheng, W. *Acta Armamentarii* **1980**, *3*, 23.
(7) Bachmann, W. E.; Horton, W. J.; Jenner, E. L.; MacNaughton, N. W.; Maxwell, C. E. *J. Am. Chem. Soc.* **1950**, *72*, 3132.
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(10) Gilbert, E. E.; Leccacorvi, J. R.; Warman, M. In *Industrial and Laboratory Nitrations*; Albright, L. F., Hanson, C., Eds.; ACS Symposium Series 22; American Chemical Society: Washington, DC, 1976; Chapter 23.

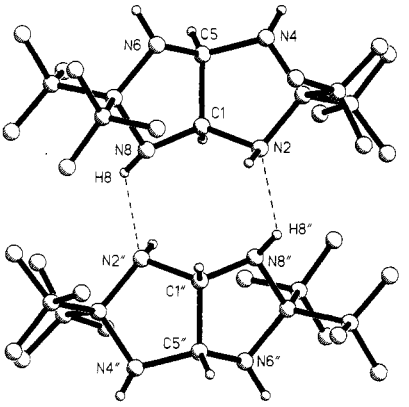
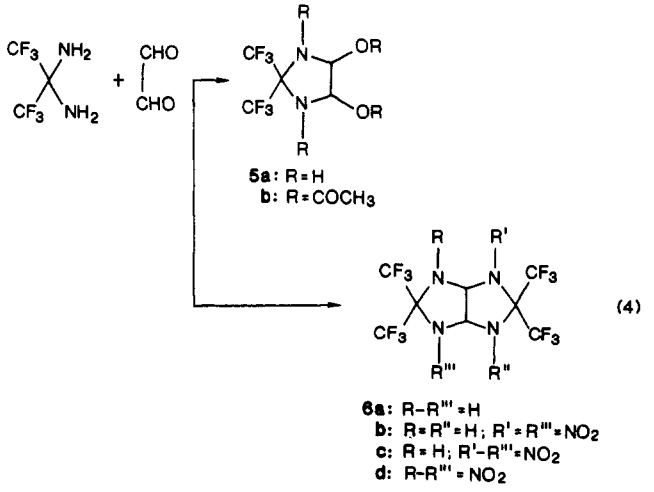


Figure 2. Crystal molecular structure of **6a** and intermolecular hydrogen bonding between two molecules in the crystal.

where starting material was consumed, only water-soluble decomposition products were observed. None of the expected *N*-nitro- or mixed *N*-nitro-*N*-acetyltetraazabicyclooctanes were found. A possible interpretation of these results is analogous to that of the acid decomposition of **1b** (eq 1). Attack by nitronium ion on a ring nitrogen in **1c** is followed by ring opening. This process is similarly favored by steric and electronic factors, with lesser contributions by the latter than in the case of **1b**.

Attempts were also made to remove the acetyl groups in **1c** by hydrolysis, aminolysis, and carbonyl reduction/addition reactions. In these cases, reaction should occur at the carbonyl carbon, and formation of the unsubstituted 2,4,6,8-tetraazabicyclo[3.3.0]octane was expected. However, here too, only decomposition products, including ammonia evolution, were observed, even at low temperatures (e.g., Birch reduction).

To obtain further information about the factors that determine the stability of the 2,4,6,8-tetraazabicyclo[3.3.0]octane ring system, the effect of alkyl substitution in the 3,7-positions was explored. Since 2,2-diaminohexafluoropropane was available,[11] its condensation with glyoxal to possible imidazolidine and tetraazabicyclooctane products was investigated. In this case, the well-known ring-stabilizing *gem*-dimethyl effect[12] should be amplified by the fluorine substitution on the methyl groups. The acid-catalyzed reaction between glyoxal and the diaminopropane proceeded readily in aqueous solution to give **6a** of excellent purity in 87% yield. Compound **6a**



(4)

(11) Middleton, W. J.; Krespan, C. G. *J. Org. Chem.* **1965**, *30*, 1398.
(12) Allinger, N. L.; Zalkov, V. *J. Org. Chem.* **1960**, *25*, 701.

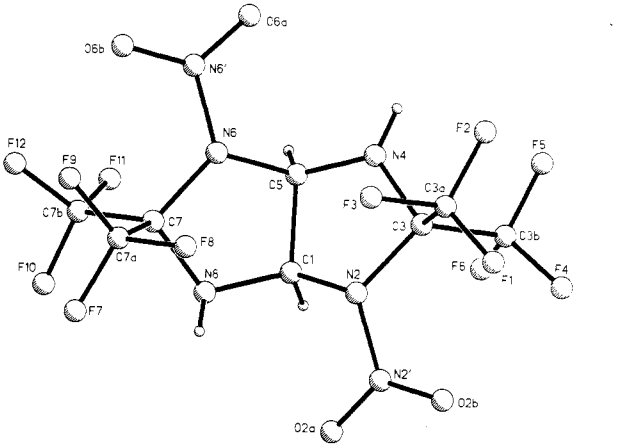
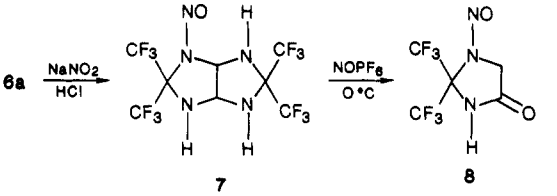


Figure 3. Crystal molecular structure of **6b**.

is a stable solid that can be recrystallized from dichloroethane without decomposition. The crystal structure (Figure 2 and Experimental Section) confirms the expected cis configuration. There are two distinct molecules of **6a** in the crystal. They are similar in conformation in all respects except for the orientation of the hydrogen on N2. These hydrogens are inverted with respect to each other to permit hydrogen bonding between N2″ and N8-H8.

Hexafluorodiaminopropane was also condensed with excess glyoxal in an effort to obtain **5a**, but this could not be isolated. However, addition of acetic anhydride to the reaction mixture gave **5b** in 18% yield as a mixture of cis and trans isomers.

Introduction of the first nitro groups into **6a** required careful control of the reaction conditions and was successful only at low temperatures to give **6b** in modest yield (42%). No unreacted starting material or other water-insoluble products were observed, an indication that degradation of the ring system must have occurred to a substantial degree. A similar observation was made in the attempted nitrosation of **6a**, which gave only the mononitroso derivative **7** in 43% yield and led to destruction of the ring system and formation of 8 under conditions



(5)

aimed at introduction of a second nitroso group. Attempted acetylation of **6a** was even less successful. Only starting material was recovered after treatment with acetyl chloride/triethylamine at ambient temperature or with acetic anhydride/pyridine at 100 °C. Reaction with acetic anhydride/BF_3·OEt_2 at 20 °C gave **5b** in 91% yield. Thus, the vulnerability of the ring system of **6a** in reactions involving electrophilic attack on nitrogen seems well-established. The failure of **6a** to undergo acetylation while **1c** can be prepared readily also provides evidence for steric crowding resulting from the presence of the trifluoromethyl groups. The crystal structures of **5b** and **8** were determined by X-ray diffraction (Experimental Section).

The dinitro derivative **6b** is stable to storage as a solid and can be recrystallized from dichloroethane without decomposition. Crystal structure data are shown in Figure 3 and the Experimental Section. A discussion of the structure is given below together with those of **6c** and **6d**.

Further nitration of **6b** (HNO_3/Ac_2O) proceeded with little degradation of the ring system to give the trinitro

Table I. Selected Bond Distances and Angles for 6a–d

	6a	6b	6c	6d
⟨C–CF_3⟩ (Å)	1.529	1.544	1.575	1.582
⟨N–NO_2⟩ (Å)		1.386	1.405	1.413
⟨N–C–N⟩ (deg)	105.6	99.5	99.7	98.5
⟨CF_3 twist⟩[a]	2.7	6.8	18.3	28.0
⟨NO_2 twist⟩[a]		5.3	13.1	13.5
⟨C_1–C_5 twist⟩[a]	8.3, 16.8	18.9	15.9	29.6
N_2 bend[a]		29.4	6.6	34.7
N_4 bend[a]			30.3	6.4
N_6 bend[a]		28.9	24.4	11.5
N_8 bend[a]				22.3

[a] CF_3 twist measured away from a staggered conformation; NO_2 twist measured away from closest coplanarity with adjacent amino plane; C_1–C_5 bridgehead twist measured away from completely eclipsed conformation; N_2–N_8 amino bends defined as angle between N–NO_2 bond and adjacent C–N–C plane (ideal: 0° for sp^2, 54.8° for sp^3 hybridization).

compound **6c** in 90% yield, and this was nitrated with HNO_3/P_2O_5 to the tetranitro compound **6d** in 65% yield. We postulate that the two nitro groups in **6b** provide protection against the heterolytic ring opening discussed above, as one would expect on the basis of the proposed mechanism for this process. This electronic effect appears to be substantial because of the additional steric strain resulting from the insertion of the third and fourth nitro groups, which should favor ring opening. The trinitro compound **6c** is stable as a solid but decomposes in dichloromethane solution at room temperature in a matter of hours; **6d** is more stable but also decomposes gradually in dichloromethane solution (20% in 3 days at room temperature).

The ^1H NMR spectra of compounds **6a–d** show no unusual features. With the introduction of nitro groups, the CH signal is shifted progressively from δ 5.26 in **6a** to δ 7.40 in **6d**. The IR spectra, however, exhibit unusual features for the asymmetric NO_2 stretch absorption. The normally unresolved band near 1600 cm^{-1} (1570 cm^{-1} in 1,3,5-trinitrohexahydrotriazine) is split into two bands at 1595 and 1650 cm^{-1} in **6c** and into four bands between 1612 and 1662 cm^{-1} in **6d**. This blue shift in **6c** and **6d** is similar in magnitude to that observed in 2,4,6-tris(trifluoromethyl)-1,3,5-trinitrohexahydrotriazine.[13] It presumably results from the electron-withdrawing effect of the trifluoromethyl groups, which appears to outweigh the effect of the slight N–N bond lengthening in the series **6b**, **6c**, and **6d** (see Table I).

The crystal structures and associated crystallographic data for **6c** and **6d** are shown in Figure 4 and in the Experimental Section.

The crystal structures for compounds **1c** and **6a–d** represent the first X-ray structures of the completely saturated 2,4,6,8-tetraazabicyclo[3.3.0]octane ring system. Table I summarizes noteworthy bond distances and angles for **6a–d**. The data indicate progressive intramolecular crowding in this series, which leads to a number of intramolecular distortions having the effect of relieving this crowding: bonds to the nitro and CF_3 groups lengthen, the ring N–C–N angle sharpens, and the CF_3 groups rotate increasingly from a staggered conformation. In addition, in **6d** the bridge heads are twisted by almost 30° from the eclipsed conformation. While these effects lengthen some CF···O_2N distances, there are many such contacts in **6d** that are very short (more than 0.1 Å below the normal van der Waals contact): N2′···F6 (2.66 Å); O2b···C3b (2.85 Å); O2b···F1 (2.59 Å); O2b···F4 (2.63 Å); N4′···F5 (2.67 Å);

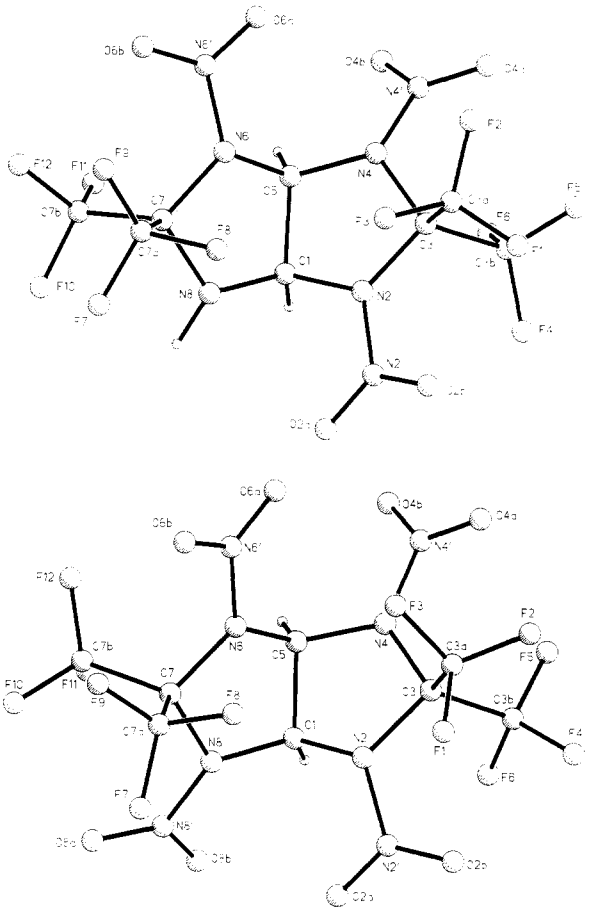


Figure 4. Crystal molecular structures of **6c** and **6d**.

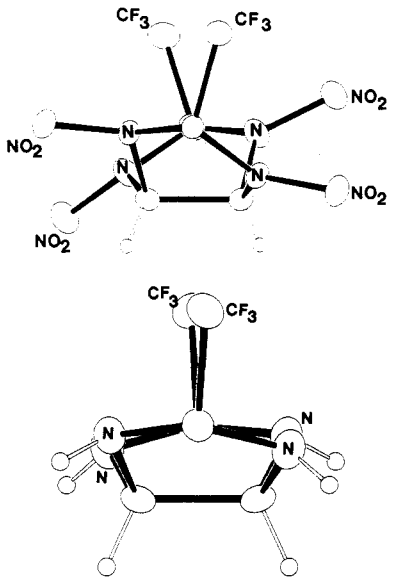


Figure 5. C3-end-on-view of **6a** and **6d** (for clarity, only one CF_3 group is shown on C3 and C7).

O4a···F5 (2.60 Å); N6′···F12 (2.68 Å); O6b···C7a (2.86 Å); N8′···F11 (2.73 Å); O8a···C7b (2.81 Å); O8a···F10 (2.58 Å); O6b···F12 (2.62 Å). This severe intramolecular crowding in **6c** and **6d** must account at least in part for the limited stability of these compounds. It follows from this assumption and the much greater stability of **1c** that compound **1d** should be more stable than **6d** and certainly should be capable of existence under ambient conditions. The conformation of nitro groups is also determined by response to crowding from the trifluoromethyl groups and peri interactions, but weak intermolecular H bonding to

(13) Young, J. A.; Schmidt-Collerus, J. J.; Krimmel, J. A. *J. Org. Chem.* **1971**, *36*, 347.

Table II. Deviations (Å) of the Two N Atoms from the Plane through the Three C Atoms in Each Five-Membered Ring[a]

molecule	N2	N4	N6	N8	av magnitude
1c	0.42	0.07	0.37	−0.03	0.22
6a-mol 1	−0.34	0.09	−0.35	0.05	0.21
6a-mol 2	−0.26	−0.06	−0.26	−0.06	0.16
6b	−0.32	0.06	−0.31	0.10	0.20
6c	−0.23	0.11	−0.32	0.04	0.18
6d	−0.43	0.34	−0.41	0.28	0.37
5b-mol 1	0.34	−0.38			0.36
5b-mol 2	0.38	−0.26			0.32

[a] A positive deviation is exo (out of the cleft of the two rings).

NH, present in the structures **6b** and **6c**, may also be a factor.

Table II and Figure 5 illustrate the twist of the five-membered rings, which serves to minimize peri interactions, especially in **6d**. This twist is also evident in the highly substituted **5b** (see Experimental Section for the crystal structure). It is noteworthy that the trifluoromethyl compounds all show the maximum deviations of the nitrogens in the endo direction, while **1c** exhibits an exo ring pucker.

Experimental Section

Melting points are uncorrected. IR spectra were taken on a Perkin-Elmer Model 283 grating spectrophotometer. ^{1}H NMR spectra were recorded at 90 MHz on a Varian Model EM-390 spectrometer (Me_4Si internal standard). Mass spectral data were obtained on a Finnigan Model 4000 instrument (CI, CH_4). Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

CAUTION: Compounds **6c** and **6d** are sensitive explosives and should be handled with care.

2,4,6,8-Tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (1a). This compound was prepared by the method of Nelsen and Hintz:[2] ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 2), 3.73, 3.15 (2 d of AB quartet, 4, J = 8 Hz), 2.45 (s, 12).

2,4,6,8-Tetraisopropyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (3b) and *N,N'*-Diisopropylhydantoin. A mixture of *N,N'*-diisopropylurea (2.88 g, 20 mmol), 40% aqueous glyoxal (1.45 g, 10 mmol), water (9 mL), and concentrated HCl (2 mL) was stirred at room temperature for 1 week and then filtered to yield a white solid (1.80 g). The solid was dissolved in CH_2Cl_2 and filtered through silica gel to remove some starting material. Evaporation of the solvent gave pure **3b** as a white solid (1.55 g, 50%): mp 150 °C (isopropyl ether); ^{1}H NMR (CD_2Cl_2) δ 5.01 (s, 2), 3.63 (m, 4), 1.26, 1.35 (2 d, 24). Anal. Calcd for $C_{16}H_{30}N_4O_2$: C, 61.90; H, 9.74; N, 18.05. Found: C, 62.10; H, 9.80; N, 18.13.

Evaporation of the original aqueous filtrate gave a solid residue, which was dissolved in CH_2Cl_2 and filtered through silica gel. Evaporation gave *N,N'*-diisopropylhydantoin as a white crystalline solid (0.46 g, 25%): mp 55–57 °C (lit.[14] mp 56–57 °C); ^{1}H NMR (CD_2Cl_2) δ 4.34 (m, 2), 3.74 (s, 2), 1.40 (d, 6), 1.18 (d, 6).

2,4,6,8-Tetraisopropyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (1b). A mixture of **3b** (7.0 g, 0.0226 mol), $LiAlH_4$ (8.5 g, 0.224 mol), and *p*-dioxane (300 mL) was heated, with stirring under nitrogen, for 24 h. Ethyl acetate (35 mL) was then added dropwise with stirring and ice cooling. After several hours, the mixture was filtered with suction and the filter cake washed with ether. Evaporation of the filtrate under vacuum gave the product (4.9 g, 76.9%) as a low-melting white solid, which was pure by NMR analysis: ^{1}H NMR (CD_2Cl_2) δ 4.40 (s, 2), 3.62, 3.30 (2 d of AB quartet, 4, J = 8 Hz), 2.96 (m, 4), 0.93–1.07 (2 d, 24). Because of its instability, **1b** was not analyzed further.

4,5-Diacetoxy-1,3-diacetylimidazolidine. A mixture of 1,3-diacetyl-4,5-dihydroxyimidazolidine[9] (18.8 g, 0.1 mol) and acetic anhydride (200 mL) was refluxed for 45 min. The solution was then evaporated to dryness under reduced pressure to leave a residue, which was triturated with ether (100 mL) and filtered to yield 20.8 g (76.4%) of white crystals: mp 136–139 °C (partial melting) and then 147–149 °C. The ^{1}H NMR spectrum ($CDCl_3$) showed a mixture of cis and trans isomers in approximately equal proportions: δ 6.54, 6.35 (2 s, 2, *cis*-CH), 6.33 (s, 2, *trans*-CH), 5.20, 4.90 (2 d of AB quartet, 2, J = 7 Hz, *cis*-CH_2), 5.04 (s, 2, *trans*-CH_2), 2.09 (m, 12, CH_3); mass spectrum, m/z (relative intensity) 313 (M + 41, 4), 301 (M + 29, 6), 273 (M + 1, 0.3), 213 (100). Anal. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.58; H, 6.02; N, 10.34.

2,4,6,8-Tetraacetyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (1c). A. From Diacetoxydiacetylimidazolidine. A solution of 4,5-diacetoxy-1,3-diacetylimidazolidine (13.61 g, 0.05 mol), *N,N'*-methylenebisacetamide (6.77 g, 0.052 mol), *p*-toluenesulfonic acid monohydrate (0.5 g), and CH_3CN (300 mL) was refluxed for 18 h, and the solvent was then evaporated under reduced pressure. The residue was dissolved in hot CH_3OH (70 mL) and cooled overnight in a refrigerator, and the solid was filtered to yield 8.2 g (58%) of white crystals: mp 243–245 °C; ^{1}H NMR (CD_2Cl_2) δ 6.25 (s, 2, CH), 5.54, 4.48 (2 d of AB quartet, 4, J = 7 Hz, CH_2), 2.30, 2.07 (2 br s, 12, CH_3); mass spectrum, m/z (relative intensity) 323 (M + 41, 4), 311 (M + 29, 4), 283 (M + 1, 17), 212 (100). Anal. Calcd for $C_{12}H_{18}N_4O_4$: C, 51.05; H, 6.53; N, 19.85. Found: C, 50.95; H, 6.54; N, 19.86.

B. Via 1,3-Diacetyl-4,5-bis(trifluoroacetoxy)imidazolidine. A stirred mixture of 4,5-dihydroxy-1,3-diacetylimidazolidine (0.95 g, 5.05 mmol), pyridine (0.8 g, 10.1 mmol), and CH_2Cl_2 (5 mL), under N_2, was cooled in an ice bath during the dropwise addition of trifluoroacetic anhydride (1.75 mL, 2.6 g, 12.4 mmol). After the mixture was stirred at room temperature overnight, the volatiles were removed under vacuum, methylenebisacetamide (0.66 g, 5.08 mmol) was added, and the mixture was slowly stirred under vacuum (20 mm) at 75–80 °C overnight. After cooling to room temperature, methanol (10 mL) was added and the solution cooled to −20 °C for several hours. Filtration gave 0.42 g (30%) of white solid, which was identical (melting point and NMR) with the product isolated above.

3,3,7,7-Tetrakis(trifluoromethyl)-2,4,6,8-tetraazabicyclo-[3.3.0]octane (6a). A stirred solution of 2,2-diaminohexafluoropropane[11] (7.20 g, 40 mmol) and 40% aqueous glyoxal (2.80 g, 19 mmol) in H_2O (20 mL) was cooled in an ice bath during the dropwise addition of a solution of concentrated H_2SO_4 (2.0 g) in H_2O (20 mL). After the mixture was stirred overnight at room temperature, the crystalline precipitate was filtered, washed with H_2O, and dried ($CaSO_4$) to yield **6a** (6.63 g, 87%): mp 92–93.5 °C (from 1,2-dichloroethane); ^{1}H NMR ($CDCl_3$) δ 5.26 (br s, 2), 2.80 (br s, 2); mass spectrum, m/z (relative intensity) 387 (6, M + 1), 367 (15), 347 (2), 317 (7), 222 (39), 57 (100). Anal. Calcd for $C_8H_6F_{12}N_4$: C, 24.88; H, 1.57; F, 59.04; N, 14.51. Found: C, 24.78; H, 1.69; F, 58.86; N, 14.50.

2,2-Bis(trifluoromethyl)-4,5-diacetoxy-1,3-diacetylimidazolidine (5b). A. By Condensation of 2,2-Diaminohexafluoropropane with Glyoxal. A stirred solution of 2,2-diaminohexafluoropropane (360 mg, 2.0 mmol), 40% aqueous glyoxal (420 mg, 3.0 mmol), and acetic acid (2.0 mL) containing 1 drop of concentrated H_2SO_4 was heated at 90 °C for 30 min and then cooled to room temperature, and acetic anhydride (4.0 g, 39 mmol) was added. After 16 h, the solution was evaporated under vacuum at 50 °C and the yellow liquid residue was triturated with ether to give **5b** (150 mg, 18%): mp 144–146 °C. Its NMR spectrum was identical with that of a recrystallized (ethyl ether) sample with mp 169–170 °C: ^{1}H NMR ($CDCl_3$) δ 6.51 (s, 2), 2.28 (s, 6), 2.20 (s, 6). Anal. Calcd for $C_{13}H_{14}F_6N_2O_6$: C, 38.24; H, 3.46; F, 27.92; N, 6.86. Found: C, 38.25; H, 3.30; F, 27.90; N, 6.77.

B. By Acetylation of 6a. A mixture of **6a** (390 mg, 1.0 mmol), acetic anhydride (4 mL), and boron trifluoride etherate (130 mg, 1.14 mmol) was stirred at room temperature for 16 h. The solution was then stirred with water until the acetic anhydride layer disappeared, and the solid was extracted with CH_2Cl_2. The dried ($MgSO_4$) extract yielded **5b** (370 mg, 91%): mp 142–152 °C.

This and the material from method A are probably mixtures of cis and trans isomers. Samples melting as high as 174–176 °C were obtained by recrystallization from $CHCl_3$/hexane. The ^{1}H NMR spectra of the differently melting samples were identical.

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The highest melting samples were found to have the trans configuration by X-ray diffraction analysis.

2,6-Dinitro-3,3,7,7-tetrakis(trifluoromethyl)-2,4,6,8-tetraazabicyclo[3.3.0]octane (6b). The bicyclic amine **6a** (2.0 g, 0.0052 mol) was added in portions over 20 min, with stirring, to absolute (100%) nitric acid (13 mL, 19.5 g, 0.31 mol), with the solution temperature kept at −35 to −40 °C. The temperature was then allowed to rise to −30 °C (10 min) and then to −15 °C (15 min). The solution was poured onto ice (45 g), and the solid was filtered, washed with H_2O, and dried ($CaCl_2$, 20 °C (1 mm)) to give **6b** (1.04 g, 42%): mp 167–168 °C; IR (KBr) 1585 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ 6.13 (s, 2), 4.17 (br s, 2); mass spectrum, m/z (relative intensity) 477 (M + 1, 0.2), 415 (0.3), 220 (0.8), 57 (30), 48 (82), 46 (43), 44 (100).

2-Nitroso-3,3,7,7-tetrakis(trifluoromethyl)-2,4,6,8-tetraazabicyclo[3.3.0]octane (7). A solution of **6a** (190 mg, 0.5 mmol) in ether (4 mL) was added to a solution of sodium nitrite (280 mg, 4.0 mmol) in H_2O (2 mL). The mixture was cooled in an ice bath during the dropwise addition of 1.0 M HCl (5 mL). After 2 h at room temperature, the solution was poured into a dish and the ether was allowed to evaporate. The precipitated solid was extracted with CH_2Cl_2, and the extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated to yield almost pure **7** (90 mg, 43%). Recrystallization ($CHCl_3/CCl_4$) gave the pure material: mp 52–54 °C; ^1H NMR ($CDCl_3$) δ 5.77, 5.49 (2 m, 1, C_1-H), 5.28 (br s, 1, C_5-H), 3.63, 3.38 (2 br s, 1, N_8-H), 2.90 (br s, 2, $N_{4,6}$-H); mass spectrum, m/z (relative intensity) 416 (M + 1, 16), 387 (78), 367 (43), 317 (37), 222 (75), 205 (29), 58 (100).

1-Nitroso-2,2-bis(trifluoromethyl)imidazolidin-4-one (8). A stirred suspension of **7** (2.0 g, 5 mmol) in CH_3NO_2 (15 mL) was cooled to 0 °C while a solution of $NOPF_6$ (4.0 g, 22 mmol) in CH_3NO_2 (15 mL) was added dropwise. After 1 h at 0 °C, the mixture was warmed to room temperature and then poured onto ice and extracted with CH_2Cl_2. The dried ($MgSO_4$) extract was evaporated to leave a mixture of liquid and solid, which was recrystallized from 1,2-dichloroethane to yield **8** (110 mg, 9%) as a white solid: mp (sealed capillary) 179–180 °C dec; ^1H NMR (Me_2CO-d_6) δ 4.48 (s, 2); mass spectrum, m/z (relative intensity) 292 (M + 41, 11), 280 (M + 29, 18), 252 (M + 1, 100), 222 (19).

3,3,7,7-Tetrakis(trifluoromethyl)-2,4,6-trinitro-2,4,6,8-tetraazabicyclo[3.3.0]octane (6c). A nitration solution was prepared by the dropwise addition of acetic anhydride (4 mL, 4.33 g, 0.042 mol) to absolute (100%) nitric acid (8 mL, 12 g, 0.19 mol) at −15 °C. The solution was warmed to 0 °C (30 min) and then cooled to −10 °C during the addition of **6b** (1.0 g, 2.1 mmol) in portions. After 30 min at −10 °C and 4 h at 0 °C, the solution was poured onto ice (50 g) and the precipitated solid was filtered, washed with H_2O, and dried ($CaCl_2$, 20 °C (1 mm)) to give **6c** (960 mg, 88%) as a white solid: mp 109–110 °C dec; IR (Fluorolube) 1650 and 1595 cm^{-1} (NO_2); ^1H NMR (CD_2Cl_2) δ 7.35 (d, 1, J = 6 Hz), 6.30 (m, 1), 4.58 (br s, 1).

3,3,7,7-Tetrakis(trifluoromethyl)-2,4,6,8-tetranitro-2,4,6,8-tetraazabicyclo[3.3.0]octane (6d). Absolute (100%) nitric acid (5 mL, 7.5 g, 119 mmol) was slowly added to P_2O_5 (2.6 g, 17.6 mmol) under N_2. After the exothermic reaction had subsided, **6c** (0.25 g, 0.48 mmol) was added and the solution temperature was then raised from 25 to 55 °C during 15 min and held at 55–60 °C for 20 min. The mixture was poured onto ice and the precipitated white solid filtered and dried ($CaCl_2$, 20 °C (1 mm)) to give **6d** (180 mg, 67%): mp 110–111 °C dec; IR (KBr) 1662, 1653, 1626, 1612 cm^{-1} (NO_2); ^1H NMR (CD_2Cl_2) δ 7.40 (s).

X-ray Diffraction. Crystallographic information summaries for seven compounds are presented below. Unless noted otherwise, the diffraction experiments were performed on a Nicolet R3m automatic diffractometer at the Naval Research Laboratory using Cu Kα radiation, λ = 1.541 78 Å, and an incident beam graphite monochromator. Unit cell dimensions reported below were calculated from a least-squares fit of the coordinates of 25 centered reflections. The scan speed varied from 4° to 30° min^{-1}, depending on the intensity, and the scan range was from [$2\theta(K\alpha_1)$ − 1/0] to [$2\theta(K\alpha_2)$ + 1.0]. Three check reflections were collected after every 60 observations to check for deterioration or instability. The structures were solved by direct methods[15] as implemented in the SHELXTL system[16] of computer programs, and refined by the SHELXTL blocked-cascade full-matrix least-squares method, which shifts up to 103 structural parameters during each cycle of minimization. All refinements were continued until all shifts were less than 0.5 esd (and usually <0.1 esd).

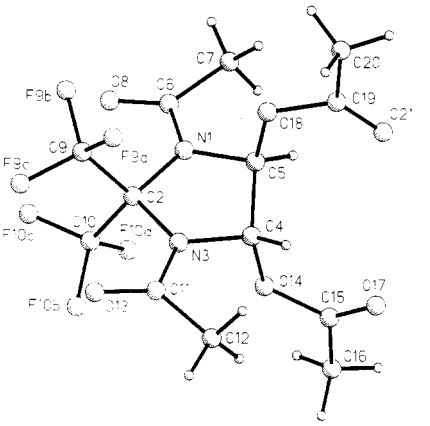

Figure 6. Crystal molecular structure of **5b**.

Compound 1c: $C_{12}H_{18}N_4O_4$, fw = 282.30. Clear, colorless crystal (0.32 × 0.33 × 0.30 mm) crystallized from CH_3CN. Unit cell: a = 17.848 (6) Å, b = 7.738 (2) Å, c = 19.682 (6) Å, V = 2718.2 (14) Å^3. Space group: $Pbca$, Z = 8 (1 molecule/asymmetric unit), D(X-ray, calcd) = 1.379 mg mm^{-3}. Least-squares refinement of 236 structural parameters gave agreement factors of R = 0.051, R_w = 0.045 for 1456 unique observed reflections. (Another 313 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples between −0.21 and 0.22 e Å^{-3}, were observed in the final difference map.

A different crystal form of **1c** was obtained from ethanol, with space group $Pca2_1$ and unit cell dimensions a = 17.616 Å, b = 9.723 (3) Å, and c = 7.977 (2) Å. A structure solution was obtained but was not fully refined. The $Pca2_1$ cell resembles one-half of the $Pbca$ cell in the packing arrangement of the molecules; the molecular conformation is essentially the same in both cells.

Compound 5b: $C_{13}H_{14}F_6N_2O_6$, fw = 408.25. Clear, colorless prism (0.25 × 0.15 × 0.12 mm) crystallized from ethylene dichloride. Unit cell: a = 10.069 (2) Å, b = 22.076 (4) Å, c = 16.071 (2) Å, β = 105.68 (1)°, V = 3439.1 (9) Å^3. Space group: $P2_1/n$, Z = 8 (2 molecules/asymmetric unit), D(X-ray, calcd) = 1.577 mg mm^{-3}. Least-squares refinement of 512 structural parameters gave agreement factors of R = 0.072, R_w = 0.080 for 4032 unique observed reflections. (Another 1463 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.35 to 0.33 e Å^{-3}, in the final difference map.

The diazacyclopentane rings differ slightly in conformation in the two independent molecules found in the unit cell: in one, an acetoxy-substituted carbon lies 0.41 Å from a plane that passes to within 0.01 Å of each of the other ring atoms; in the other, no four atoms fit a plane well. The two acetoxy sites lie +0.30, −0.19 Å on either side of the N1–C2–N3 plane. (See Figure 6.)

Compound 6a: $C_8H_6F_{12}N_4$, fw = 336.14. Clear, colorless crystal (0.35 × 0.22 × 0.15 mm) crystallized from CH_2Cl_2 at 5 °C. Unit cell: a = 10.431 (4) Å, b = 7.050 (2) Å, c = 25.778 (14) Å, β = 90.80 (4)°, V = 1895.7 (13) Å^3. Space group: $P2/n$, Z = 6 (3/2 molecules/asymmetric unit), D(X-ray, calcd) = 2.029 mg mm^{-3}. Least-squares refinement of 361 structural parameters gave agreement factors of R = 0.053, R_w = 0.056 for 2294 unique observed reflections. (Another 818 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.32 to 0.26 e Å^{-3}, were observed in the final difference map. One molecule lies on a crystallographic 2-fold symmetry axis, while another occupies a general position in the unit cell, and they differ in conformation. The most striking difference is in the disposition of the amino hydrogen atoms. The symmetric molecule has all N–H bonds bent exo to the cleft, with bend angles (defined as in Table I) ranging from 46 (1) to 54 (1)°; in the other molecule

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(shown in Figure 2), the N2–H2 bend is 54° endo, and the three others are exo with 51–54° bend angles. All of the amino hydrogens were prominent in a difference map with densities from 0.5 to 0.7 e Å^{-3}, well above background, 0.26 e Å^{-3}; the "anomalous" endo H atom was one of the strongest of these peaks. The only hydrogen bonding in the crystal involves the endo-bent N2 as an acceptor; a centrosymmetric dimer results, which is shown in Figure 2. The N···N and H···N distances are 3.25 Å and 2.55 Å, and the N–H···N angle is 139°.

Compound 6b: $C_8H_4F_{12}N_6O_4$, fw = 476.14. Clear, colorless prism (0.10 × 0.15 × 0.65 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 20.073 (4) Å, β = 7.353 (1) Å, c = 10.832 (2) Å, V = 1598.7 (4) Å^3. Space group: $Pna2_1$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 1.978 mg mm^{-3}. Least-squares refinement of 283 structural parameters gave agreement factors of R = 0.064, R_w = 0.089 for 1205 unique observed reflections. (Another 58 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.28 to 0.34 e Å^{-3}, were observed in the final difference map. The two N–H groups each donate in H-bonds to nitro oxygen acceptors. One, N4–H4···O2a (x,y−1,z), has H···O and N···O distances of 2.28 Å and 3.06 Å, and an N–H···O angle of 165°. The other, O6a···H8–N8 (x,y−1,z), has H···O, N···O, and N–H···O values of 2.51 Å and 126°. The latter should be the weaker, due to its nonlinearity; both H-bonds go to the same neighboring molecule and are repeated by the lattice ad infinitum along the b axis.

Compound 6c: $C_8H_3F_{12}N_7O_6$, fw = 521.13. Clear, colorless prism (0.62 × 0.23 × 0.35 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 6.990 (6) Å, b = 19.090 (2) Å, c = 12.347 (1) Å, β = 95.38 (1)°, V = 1640.1 (3) Å^3. Space group: $P2_1/c$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 2.110 mg mm^{-3}. Least-squares refinement of 367 structural parameters gave agreement factors of R = 0.049, R_w = 0.074 for 2168 unique observed reflections. (Another 91 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.19 to 0.27 e Å^{-3}, were observed in the final difference map. There is one amino hydrogen that H-bonds to a nitro oxygen on a neighboring molecule at (x−1,y,z); the N···O, H···O, and N–H···O values are 3.18 Å, 2.39 Å, and 140°.

Compound 6d: $C_8H_2F_{12}N_8O_8$, fw = 566.13. Clear, colorless crystal (0.50 × 0.35 × 0.12 mm) crystallized from CH_2Cl_2/hexane. Unit cell: a = 34.074 (5) Å, b = 7.456 (1) Å, c = 13.877 (2) Å, β = 102.41 (1)°, V = 3443.1 (8) Å^3. Space group: $C2/c$, Z = 8 (1 molecule/asymmetric unit), D(X-ray, calcd) = 2.184 mg mm^{-3}. Least-squares refinement of 333 structural parameters gave agreement factors of R = 0.041, R_w = 0.068 for 2799 unique observed reflections. (Another 31 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.24 to 0.23 e Å^{-3}, were observed in the final difference map.

Compound 8: $C_5H_3F_6N_3O_2$, fw = 251.09. Clear, colorless, needle-shaped crystal (0.10 × 0.20 × 0.70 mm) grown by sublimation at 90 °C (200 mmHg). Unit cell: a = 10.214 (2) Å, b = 10.986 (3) Å, c = 7.614 (2) Å, V = 854.4 (3) Å^3. Space group: $Pna2_1$, Z = 4 (1 molecule/asymmetric unit), D(X-ray, calcd) = 1.952 mg mm^{-3}. Least-squares refinement of 150 structural parameters gave agreement factors of R = 0.051, R_w = 0.061 for 524 unique observed reflections. (Another 59 reflections, with $F_o < 3\sigma(F_o)$, were considered unobserved.) No significant features, only ripples from −0.25 to 0.28 e Å^{-3}, were observed in the final difference map.

Crystals of **8** are volatile and sublime completely at room temperature in 24 h. Rapid data collection was used to obtain a data set in 3 h; all peaks were scanned at a rate of 30° min^{-1}. Three monitor reflections, remeasured after every 60 observations, decreased uniformly from 100% to 87% in intensity, presumably because of sublimation; a smoothed curve of the monitor decrement ratios was used to correct all data.

Acknowledgment. This work was supported by the Office of the Chief of Naval Research, Mechanics Division (Code 1132P).

Supplementary Material Available: Tables of atomic coordinates, temperature parameters, and bond distances and angles for compounds **1c**, **5b**, **6a–d**, and **8** (22 pages). Ordering information is given on any current masthead page.

A Photochemical Approach to the Taxanes

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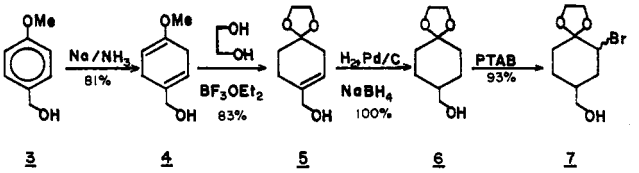
The de Mayo sequence has been applied to the inter- and intramolecular photocycloaddition of various cycloalkenes with homocamphorquinone derivatives to generate a model for the A, B, and C rings of the taxanes. A model sequence of reactions applicable to the construction of the oxetane (D-ring)–tertiary acetate grouping of baccatin III (taxol, cephalomannine) has also been accomplished.

The de Mayo sequence,[1a] photocycloaddition of the enol of a β-diketone and an alkene, followed by retroaldol or other cyclobutane ring fragmentation has been employed extensively for the synthesis of natural products.[1b–l] Its application[2] to the synthesis of the taxane[3] skeleton **1** is

Scheme I



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