1,3-Dihydro-1-ethoxy-1-methoxyisobenzofuran (5).[18] A mixture of 0.90 g (4.3 mmol) of **2** and 35 μL (0.21 mmol) of diisopropylamine in 12 mL of anhydrous ether under N_2 was cooled in an ice/salt bath. Methyllithium in ether (3.4 mL, 4.7 mmol) was added by syringe. After stirring for 0.5 h, a sample of the yellow solution, from which LiOEt had precipitated, was removed and examined by ^1H NMR, which indicated complete conversion of **2** to 1-ethoxyisobenzofuran (**8**): δ 6.45–6.90 (m, 2 H), 7.05–7.40 (m, 2 H), 7.45 (s, furan proton). These chemical shifts (in ether) are based on the observation that the broadened singlet aromatic absorption of **2** appears at essentially the same chemical shift in ether, THF, and $CDCl_3$ solvents. Methanol (20 mL) was added to the remaining reaction mixture, with stirring continued for 0.25 h at 0 °C, after which this solution was quenched and extracted in the usual way. Evaporation gave 724 mg of liquid residue, nearly pure **5** by NMR analysis. High-vacuum short-path distillation (60 °C) gave 665 mg (80%) of pure **5** as a colorless oil: ^1H NMR (300 MHz) δ 1.20 (t, 3 H), 3.28 (s, 3 H), 3.43 (dq, J = 9.3, 7.2 Hz, 1 H, diastereotopic -OCH_2CH$_3$), 3.64 (dq, 1 H), 5.09 (s, 2 H), 7.23–7.45 (m, 4 H); MS, m/z (relative intensity) 163 (54), 149 (100), 135 (81), 133 (37), 105 (23), 91 (17), 77 (20); calcd for $C_{10}H_{11}O_2$ (P – OMe) 163.0759; found 163.0769. Calcd for $C_9H_9O_2$ (P – OEt) 149.0602; found 149.0594.

3-Deuterio-1,3-dihydro-1-ethoxy-1-methoxyisobenzofuran (5-*d*). Samples of **5-*d*** were prepared either by addition of an ethereal solution of **8** to a large excess of CH_3OD or by addition of CH_3OD to a solution of **8** that had been filtered to remove precipitated LiOEt, with stirring at 0 °C for ca. 0.5 h prior to the usual workup. Yields are high in both cases; **5-*d*** has NMR characteristics identical with **5**, except for broadening of the benzylic proton due to deuterium coupling and the diminished integral of this peak. MS analysis was accomplished by examination of the appropriate M/(M + 1) ratios for the P – OEt and P – OMe peaks, taking into account ^{13}C contributions. These indicated 89% and 90% deuterium incorporation in the two samples; the m/z 149–151 peaks are the more pertinent for this analysis, since the 163, 164 peaks are affected by any unreacted **2** in the mixture, as observed in one run.

(18) In principle it should be possible to prepare **5** from **1** by using alcohol-free alkoxide in a solvent suitable for both the base and **1**. We have approached this by using LiOMe (prepared in methanol with subsequent vacuum removal of solvent) in acetonitrile, to which **1** was added as a solid. This gave a **4**:**5** ratio of 5:95. Further improvement should be possible by generating LiOR from stoichiometric amounts of alkyllithium and alcohol.

Acknowledgment. We thank Joel Baranski for performing some of the experiments described, Curt Breneman for assistance with NMR, Dr. Hugh Webb for obtaining MS data, and Prof. C. A. Bunton for helpful discussions. We also express our appreciation for the useful comments provided by Prof. R. A. McClelland (University of Toronto).

Registry No. **1**, 487-97-8; **3**, 89346-92-9; **4**, 59567-96-3; **5**, 89346-93-0; **5-d**, 89346-94-1; **8**, 75802-19-6; **15**, 41071-33-4.

peri-Nitrosamine Interactions. 2. *trans*-1,8-Dinitroso-1,8-diazadecalins

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An X-ray crystal structure of *trans*-1,8-dinitroso-1,8-diazadecalin (**5**) shows that in the crystal the nitroso groups adopt a syn,anti orientation and that the diazadecalin ring adopts a chair,twist-boat conformation. The chair,twist-boat conformation is apparently adopted so as to allow sufficient separation between the nitroso groups to avoid van der Waals interactions between them. Proton, ^{13}C, and ^{15}N NMR spectra of **5** and its 10-methyl analogue **6** show that they exist in solution mainly as the syn,anti rotamers with progressively lesser amounts of the anti,anti and syn,syn rotamers present. The results necessitate a reinterpretation of the previously reported "weak bonding interaction" between the nitroso groups of *trans*-1,4,5,8-tetranitroso-1,4,5,8-tetraazadecalin (**1**), which also shows a preference for syn,anti rotamers and which was assumed to exist in a chair,chair conformation.

Introduction

We recently reported on the unusual rotamer distribution and ^{15}N NMR chemical shifts of the nitroso nitrogens in *trans*-1,4,5,8-tetranitroso-1,4,5,8-tetraazadecalin[1] (**1**). We concluded that **1** exists in solution as an 88:12 mixture of rotamers **1c** and **1d** (see Figure 1) with perhaps a small amount of rotamers **1a** and **1b** present. We reasoned that both the rotamer distribution and ^{15}N chemical shifts could be explained by the existence of a "weak bonding interaction" between the oxygen atom of a syn nitroso group and the nitroso nitrogen of an anti nitroso group in a 1,8- (or 4,5-) syn,anti conformation (see Figure 2) and an electrostatic repulsion between like charges which destabilizes rotamer **1b**. We assumed that the three additional possible rotamers with 1,8- (or 4,5-) syn,syn conformations (i.e., **1e**–**1g**) were highly improbable since it was likely that the tetraazadecalin moiety of **1** was in a double chair conformation[2] and two oxygen atoms could not occupy the same space in the 1,8-syn,syn conformations. We will show, from new work reported in this paper and from recent work in other laboratories[3] on the related tetraacyltetraazadecalins, that the assumption that the tetraazadecalin moiety of **1** must adopt a double chair conformation is erroneous.

Further work on **1** to gain a better understanding of its unusual rotamer distribution and ^{15}N chemical shifts was hampered by its extremely low solubility and our inability

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(2) Fuchs, B.; Ellencweig, A. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 326.

(3) (a) Fuchs, B.; Weinman, S.; Shmueli, U.; Katritzky, A. R.; Patel, R. C. *Tetrahedron Lett.* **1981**, *22*, 3541. (b) Borremans, F.; Anteunis, M.; Shmueli, U.; Schleifer, L.; Shvo, H.; Fuchs, B. *J. Am. Chem. Soc.*, in press.

0022-3263/84/1949-1481$01.50/0

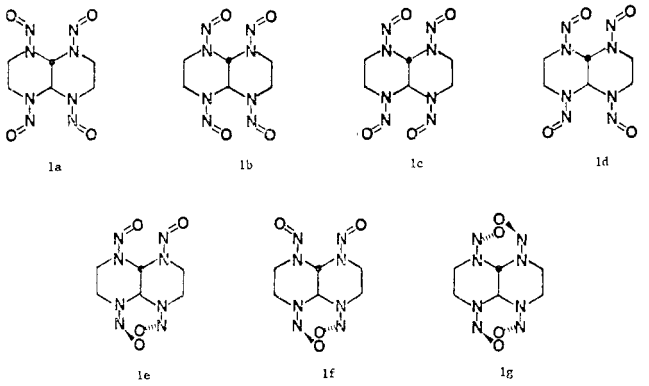


Figure 1. Possible rotational isomers of 1.

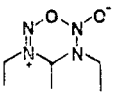
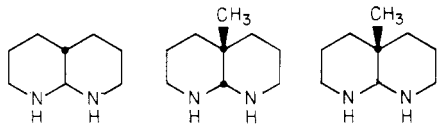


Figure 2. "Weak bonding interaction" in a 1,8-syn,anti conformation of a *peri*-dinitrosamine.

to grow crystals suitable for a single-crystal X-ray study. Therefore, we turned our attention to the related, but simpler, *trans*-1,8-dinitroso-1,8-diazadecalin system. Our main goal was to obtain a compound with the requisite peri nitrosamino interaction which would give suitable crystals for a single-crystal X-ray structure determination. We also hoped that the compound(s) would be sufficiently soluble in a variety of solvents to permit a solvent study of the interaction by NMR spectroscopy.

Results

trans-1,8-Diazadecalin (**2**) and a mixture of *cis*- and *trans*-10-methyl-1,8-diazadecalins (**3** and **4**) were synthesized by slight modifications of published literature procedures.[4] Both **2** and the mixture of **3** and **4** were nitrosated by using a procedure in which the stoichiometric amount of 1 N HCl is added to a mixture of the amine and sodium nitrite.[5] In each case, a single crystalline compound was isolated (**5** from **2**, and **6** from **3** and **4**), which gave a satisfactory elemental analysis for the corresponding dinitroso compound. Both **5** and **6** were also synthesized with the nitroso nitrogen enriched in ^{15}N by substituting enriched sodium nitrite in the preparation. Compound **5** was synthesized with the nitroso nitrogen enriched to 20% ^{15}N, and **6** was synthesized with the nitroso nitrogen enriched to 10% ^{15}N.



2 **3** **4**

X-ray Structure of *trans*-1,8-Dinitroso-1,8-diazadecalin (5). Crystals of **5** suitable for X-ray work were grown from methanol–water by the vapor diffusion technique. The compound crystallizes as elongated platelets, the direction of elongation being *b*. The space group was determined to be $P2_1/c$ ($Z = 4$) from precession and Weissenberg photographs and diffractometer data. The structure was solved by direct methods.[6,7] The final *R* value ($\sum[F_o - F_c]/\sum F_o$) was 0.074. Complete details of the structure solution are given in the experimental section. In Figure 3, a drawing of the molecular structure of **5** is given. The bond lengths and bond angles are summarized in Table I.

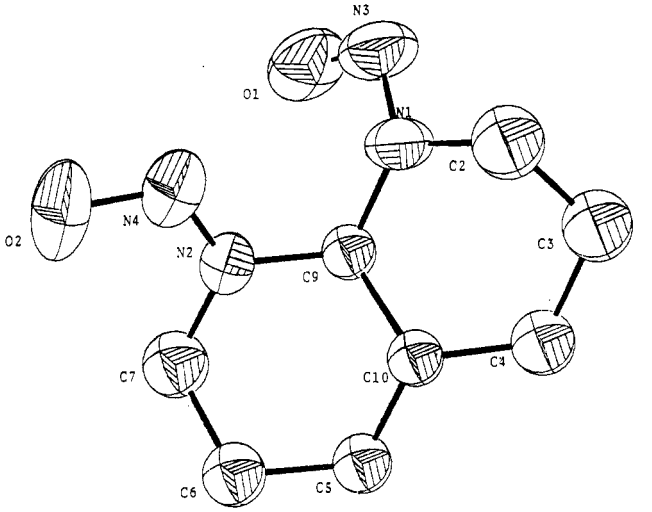


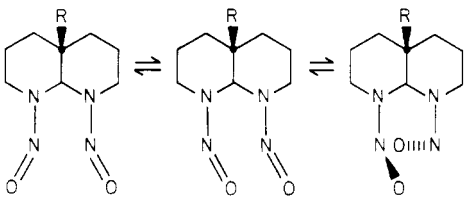
Figure 3. Drawing of *trans*-1,8-dinitroso-1,8-diazadecalin showing 50% motion probability ellipsoids.[6]

Table I. Bond Lengths and Bond Angles in 5[a]

N1-N3	1.322 (6) Å	C9-N1-C2	119.0 (3)°
N2-N4	1.306 (5) Å	O2-N4-N2	114.9 (4)°
O1-N3	1.222 (6) Å	N4-N2-C9	118.4 (3)°
O2-N4	1.242 (5) Å	N4-N2-C7	125.1 (3)°
N2-C9	1.461 (5) Å	C7-N2-C9	115.6 (3)°
N2-C7	1.458 (6) Å	N2-C9-C10	108.9 (3)°
N1-C9	1.442 (5) Å	N2-C9-N1	113.0 (3)°
N1-C2	1.469 (6) Å	N1-C9-C10	110.6 (3)°
C2-C3	1.495 (7) Å	N1-C2-C3	109.7 (4)°
C3-C4	1.526 (7) Å	C2-C3-C4	113.0 (4)°
C4-C10	1.523 (5) Å	C3-C4-C10	112.4 (4)°
C9-C10	1.521 (5) Å	C4-C10-C5	114.4 (3)°
C10-C5	1.516 (5) Å	C4-C10-C9	109.9 (3)°
C5-C6	1.524 (6) Å	C9-C10-C5	109.1 (3)°
C6-C7	1.512 (6) Å	C10-C5-C6	111.3 (3)°
O1-N3-N1	113.8 (5)°	C5-C6-C7	111.8 (4)°
N3-N1-C9	122.1 (4)°	C6-C7-N2	109.7 (3)°
N3-N1-C2	116.8 (4)°		

[a] Estimated standard deviation in parentheses.

Scheme I. Rotamer Equilibrium in 5 and 6



a **b** **c**

5, R = H
6, R = CH_3

The crystal structure of **5** establishes three important points. The first is that, indeed, **5** is *trans*-1,8-dinitroso-1,8-diazadecalin. The second is that in the crystal **5** adopts the 1,8-syn,anti conformation for the dinitroso groups. The third, and most important point is that the *trans*-1,8-diazadecalin moiety of **5** adopts a chair,twist-boat conformation. This means that we cannot assume that the 1,8-syn,syn conformation is impossible and the rotamer equilibrium in **5** (and **6**) must be discussed in terms of the equation shown in Scheme I.

NMR of 1,8-Dinitroso-1,8-diazadecalins (5 and 6). The 500-MHz ^1H NMR spectrum of **5** in $CDCl_3$ is ex-

(4) Zondler, H.; Pfleiderer, W. *Leibigs Ann. Chem.* **1972**, *759*, 84.
(5) Evans, R. F. *Aust. J. Chem.* **1967**, *20*, 1643.
(6) SHELXTL (version 3.0A) Computer Program, July, 1981.
(7) Gilmore, C. J. In "Computational Crystallography"; Sayre, D., Ed.; Oxford University Press: New York, 1982; pp 136–137.

Table II. ^{13}C NMR Shifts, Assignments, and Isomer Distribution of 1,8-Dinitroso-1,8-diazadecalins[a]

isomer	solvent	%	C-2	C-3	C-4	C-5	C-6	C-7	C-9	C-10	CH_3
5a	$CDCl_3$		37.38	21.95	25.71	25.71	21.95	37.38	78.44	39.98	
	Me_2SO-d_6	9	37.83	22.37	25.85	25.85	22.37	37.83	78.30	*b*	
5b	$CDCl_3$		43.75	21.36	21.78	29.21	23.55	38.97	70.46	37.62	
	Me_2SO-d_6	89	44.15	21.68	22.02	29.17	24.07	37.69	70.72	39.44	
5c	$CDCl_3$		47.24	23.71	26.22	26.22	23.71	47.24	70.80	34.44	
	Me_2SO-d_6	2	47.64	(24.1)	26.27	26.27	(24.07)	47.64	71.05	34.90	
6a	$CDCl_3$	13	41.56	18.99	36.28	36.28	18.99	41.56	82.05	38.83	16.20
	Me_2SO-d_6	31	41.54	18.52	35.27	35.27	18.52	41.54	80.79	*b*	15.53
	acetone-d_6	24	42.17	19.82	36.75	36.75	19.82	42.17	82.36	39.49	16.25
6b	$CDCl_3$	85	44.39	19.84	39.53	29.92	20.10	39.58	73.96	36.46	18.25
	Me_2SO-d_6	67	44.18	19.44	36.04	28.86	19.48	39.28	73.42	38.47	17.81
	acetone-d_6	73	45.02	20.50	39.76	30.33	20.71	39.83	74 54	37.13	18.49
6c	$CDCl_3$	3	51.01	23.07	40.28	38.83	19.40	43.59	(74.0)	37.33	(18.3)
	Me_2SO-d_6	2	50.57	22.74	*b*	36.88	18.66	43.30	(73.4)	*b*	18.01
	acetone-d_6	3	51.43	23.81	40.45	37.82	20.02	44.11	74.48	38.79	17.69

[a] Figures in parentheses represent presumed shift values for weak lines which are obscured by more intense lines. [b] Obscured by Me_2SO-d_6 peaks.

tremely complex, yet it is easily interpreted as resulting from a 9:89:2 mixture of **5a**:**5b**:**5c**. Most notable is the existence of three downfield doublets at 4.72, 5.22, and 5.91 ppm all with a coupling constant of 10 Hz and an intensity ratio of 2:89:9. These can be assigned to **5c**, **5b**, and **5a**, respectively, on the basis of the known greater downfield shift of the protons anti to the nitroso oxygen.[8] Further confirmation of these assignments comes from the fact that the α-methylene protons on $C_{2,7}$ appear as four multiplets for the unsymmetrical isomer **5b**, while for the symmetrical isomers **5a** and **5c** they appear as two multiplets. The chemical shifts and assignments for the α-methylene protons are as follows: **5b** 2.62 (H_{7a}), 4.15 (H_{2a}), 5.04 (H_{2e}), and 5.11 ppm (H_{7e}); **5a** 3.85 ($H_{2a,7a}$, and 4.11 ppm ($H_{2e,7e}$); **5c** 4.41 ($H_{2a,7a}$) and 4.61 ppm ($H_{2e,7e}$).

The ^{13}C NMR spectrum of **5** also shows a mixture of the three isomers **5a**, **5b**, and **5c**. The spectrum consists of three sets of resonances in both $CDCl_3$ and Me_2SO-d_6. The most intense set, consisting of eight lines, can be readily assignment to the unsymmetrical isomer **5b**. The other two sets of resonances, each consisting of five lines, are assigned to the symmetric forms **5a** and **5c**. The chemical shifts, assignments, and isomer distribution in both $CDCl_3$ and Me_2SO-d_6 for **5a–c** are summarized in Table II. The assignments were made on the basis of substituent effects, symmetry arguments, single-frequency off-resonance decoupled (SFORD) spectra, and a 2-D INADEQUATE[9] experiment. The last technique was particularly valuable in sorting out the $C_{3,4,5,6}$ assignments which could not be distinguished by any a priori arguments.

The nitroso nitrogen region of the ^{15}N NMR spectrum of **5** consists of four lines. Two intense resonances for **5b**, a moderate single resonance for **5a** and a weak resonance for **5c**. The shifts, assignments, and isomer distribution in both $CDCl_3$ and Me_2SO-d_6 are summarized in Table III.

Unlike **5**, where we had an X-ray crystal structure to establish its stereochemistry, with **6** we could not be sure of the stereochemistry of the ring juncture, particularly since we started with a mixture of *cis*- and *trans*-10-methyl-1,8-diazadecalins. We have, however, come to the conclusion that **6** has the *trans* stereochemistry. This conclusion was reached on the basis of the similarities of the NMR spectra (particularly ^{13}C and ^{15}N) and the absence of any evidence for dynamic NMR behavior which one would expect of the cis compound.

Table III. ^{15}N NMR Chemical Shifts,[a] Assignments, and Isomer Distributions

compd	solvent	%	chemical shift, ppm -NO (syn)	chemical shift, ppm -NO (anti)
5a	$CDCl_3$	9.0		546.4
	Me_2SO-d_6	11.5		546.8
5b	$CDCl_3$	89.5	530.6	543.0
	Me_2SO-d_6	87.0	530.0	542.8
5c	$CDCl_3$	1.5	540.3	
	Me_2SO-d_6	1.5	541.2	
6a	$CDCl_3$	22.0		558.9
	Me_2SO-d_6	29.0		558.2
6b	$CDCl_3$	75.0	528.3	545.9
	Me_2SO-d_6	68.0	526.8	544.2
6c	$CDCl_3$	3.0	534.3, 536.5	
	Me_2SO-d_6	3.0	532.5, 534.5	

[a] Referred to liquid NH_3 = 0, using formamide in dimethyl-d_6 suifoxide as an intermediate spectrometer calibration standard. (Conversion factor = 108.5 ppm). Lichter, R. L. *J. Magn. Reson.* **1975**, *18*, 367.

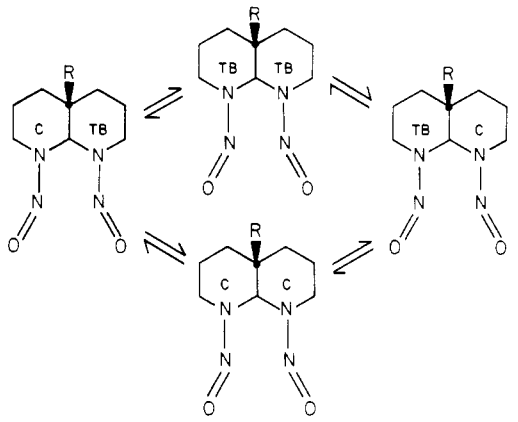
The ^1H NMR spectrum of **6** in $CDCl_3$ (360 MHz) is consistent with it existing in solution as a mixture of three rotamers. Most notable is the appearance of three methyl singlets at 0.98, 1.12, and 1.17 ppm in an intensity ratio of 4:1:14. However, only two of the expected three singlets for H_9 are observed. These appear at 5.26 and 5.75 ppm with an intensity ratio of 14:4. The missing H_9 resonance apparently is mixed in with one of the nearby signals for the α-methylene protons. The signals for the α-methylene protons of **6b** again appear as four multiplets at 2.82 (H_{7a}), 4.40 (H_{2a}), 5.15 (N_{2e}), and 5.20 (H_{7e}) ppm while the signals for the α-methylene of **5a** appear at 3.12 ($H_{2,7a}$) and 4.90 ($H_{2,7e}$) ppm. No assignments of the signals for the α-methylene protons of **5c** could be made because of their low intensity.

The ^{13}C NMR spectrum of **6** (Table II) was particularly informative. It consists of three sets of resonances in chloroform-*d*, acetone-d_6, benzene-d_6, or Me_2SO-d_6. The most intense set consists of nine resonances and is assigned to **6b**. The next most intense set consists of six resonances and is assigned to **6a**. The third set of resonances, surprisingly consists of nine lines. Initially, we were puzzled by this and wondered if the third set might be due to an impurity. However, samples of **6** which had been recrystallized repeatedly gave the same spectrum which convinced us that the third set of signals belonged to **6c**. The reason we believe **6c** shows nine resonances will be given below. The assignments in Table II were made on the basis of substituent effects, SFORD spectra, and symmetry

(8) (a) Brown, H. W.; Hollis, D. P. *J. Mol. Spectrosc.* **1964**, *13*, 305–312. (b) Karabatsos, G. J.; Taller, R. G. *J. Am. Chem. Soc.* **1964**, *86*, 4373–4378.

(9) (a) Bax, A.; Freeman, R.; Kempsell, S. P. *J. Am. Chem. Soc.* **1980**, *102*, 4849. (b) Bax, A.; Freeman, R.; Kempsell, S. P. *J. Magn. Res.* **1980**, *41*, 349.

Scheme II. Mechanism for Equilibration between the Enantiomeric Chair,Twist-boat Conformations of 5a and 6a



5, R = H
6, R = CH_3

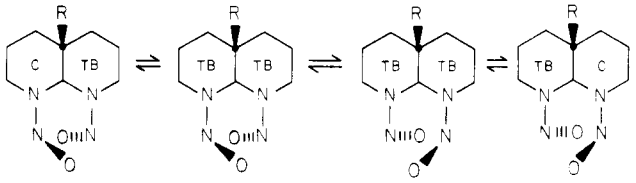
arguments. It should be noted that there is a large solvent dependence for the rotamer distribution in **6**, with **6a** being favored in more polar solvents.

The nitroso nitrogen region of the ^{15}N NMR spectrum of **6** (Table III) consists of five lines. Two intense signals for **6b**, one line for **6a**, and two weak signals for **6c**. Again, it is somewhat surprising that **6c** shows apparent molecular dissymmetry in solution.

Molecular Dissymmetry of the Syn,Syn Rotamer of *trans*-1,8-Dinitroso-10-methyl-1,8-diazadecalin (6c) in Solution. The crystal structure of **5** showed that the *trans*-1,8-diazadecalin ring system adopts a dissymmetric chain,twist-boat conformation. One might then expect that in solution both the anti,anti rotamers (**5a**,**6a**) and the syn,syn rotamers (**5c**, **6c**) would show molecular dissymmetry. Clearly, only **6c** shows molecular dissymmetry in solution and some mechanism must allow the enantiomeric forms of **5a**, **6a**, and **5c** to equilibrate. In the case of the anti,anti rotamers, this equilibration can occur through either the symmetric double chair or double twist-boat conformations as summarized in Scheme II. In the case of the syn,syn rotamers, the equilibration can only occur through double twist-boat conformations since the double chair conformation would require that the two oxygen atoms occupy the same space. Actually, the equilibration process in the syn,syn rotamers is even more complicated than this. Examination of molecular models shows that for equilibration to occur the intermediate double twist-boat conformation must undergo a change from a 2,10-6,9 double twist-boat conformation to a 3,9-7,10 double twist-boat conformation before conversion back to the enantiomeric chair,twist-boat conformation so that the process can avoid extremely unfavorable interactions between the nitroso groups. This is summarized in Scheme III. Apparently, this process is still of low enough energy that it occurs rapidly on the NMR time scale in **5c** and, thus, the molecule displays time-averaged molecular symmetry in its NMR spectrum. In **6c**, however, the introduction of the 10-methyl apparently raises the energy of the intermediate double twist-boat conformations (because of its unfavorable syn-axial type interaction[10] with C_2 and C_7) so that the equilibration becomes slow on the NMR time scale. Thus, **6c** shows molecular dissymmetry in solution.

(10) Eliel, E. L.; Allinger, N. L.; Angyal, S. I.; Morrison, G. A. "Conformational Analysis"; Interscience: New York, 1965; pp 51–52.

Scheme III. Mechanism for Equilibration between the Enantiomeric Chair,Twist-boat Conformations of 5c and 6c



5, R = H
6, R = CH_3

Solution Conformations of the Diazadecalin Rings. Since our previous assumption about the conformation of the tetraazadecalin ring in **1** proved erroneous, we wanted to definitely establish the solution conformation of the diazadecalin ring in each of the rotamers of **5** and **6**. Fortunately, this can be done from the NMR data. Most of the assignments rest on the chemical shifts and coupling constants for the protons on $C_{2,7}$.

In **5b** the α-methylene protons appear as four multiplets as already summarized. The signals for H_{7e} appear as a doublet (J = 13 Hz) further split by additional smaller couplings while the signal for H_{7a} appears as a triplet of doublets (J_T = 13 Hz, J_D = 5 Hz). This is consistent with a staggered ethylene fragment in a chair conformation. The signals for the protons on C_2 show a different pattern. The signal for H_{2e} appears as a doublet of doublets of doublets (J's = 14 Hz, 7 Hz, and 1 Hz) and H_{2a} also appears as a doblet of doublets of doublets (J's = 14 Hz, 12 Hz, and 7 Hz). These coupling constants are consistent with an ethylene fragment which is intermediate between a staggered and an eclipsed conformation, as would occur in a twist-boat conformation. Thus, the ^1H NMR data support **5b** existing in solution in the same conformaiton found in the X-ray structure. The chemical shifts and coupling constants for the $C_{2,7}$ protons on **6b** are very similar to those in **5b**, and we conclude that **6b** also exists in a chair,twist-boat conformation in solution.

The α-methylene signals for **5a** appear as two symmetric five-line multiplets with a small chemical shift difference between the two protons ($\Delta\delta$ = 0.24 ppm). This is consistent with **5a** being in a chair,twist-boat conformation and undergoing a rapid equilibration between the two enantiomeric forms. However, the signals for the α-methylene protons in **6a** indicate that this rotamer exists completely (or at least to a large extent) in a chair,chair conformation. This assignment is based on several points. First, there is a much larger difference between the chemical shifts of the two protons ($\Delta\delta$ = 1.78 ppm). Secondly, the multiplets are very similar in appearance to those of H_{7e} and H_{7a} in **5b**. There are also ^{13}C NMR data to support this assignment. The chemical shift of C_2 differs in **5a** and **6a** by 4.18 ppm while in **5b** and **6b** it differs by only 0.64 ppm. The greater downfield shift of C_2 in **6a** as compared to **5a** is consistent with **6a** being in a double chair conformation since C_2 would lose a γ-gauche interaction with C_{10} which is present in the chair,twist-boat conformation. The large (12 ppm) difference between the nitroso nitrogens in **5a** and **6a** also supports their being in different conformations. Thus, it seems clear that **5a** exists in solution in a chair,twist-boat conformation while **6a** is in a double chair conformation. The reason for **6a** being in the chair,chair conformation is the 1,3-syn-axial repulsion which occurs between the methyl group and C_2 in the chair,twist-boat conformation.

The ^{13}C and ^{15}N NMR data for **6c** are consistent with its existing in a chair,twist-boat conformation, since it

shows molecular dissymmetry in solution. The signal for the α-methylene protons of **5c** appears as two symmetric five-line multiplets essentially identical with those for **5a** with a very small chemical shift difference ($\Delta\delta$ = 0.29 ppm). Again, this is consistent with this rotamer existing in solution in a chair,twist-boat conformation and undergoing a rapid equilibrium between the enantiomeric forms. There is also ^{13}C NMR data to support this. The chemical shift of $C_{2,7}$ in **5c** (47.64 ppm) is essentially the average of the chemical shifts for C_2 and C_7 in **6c** [(51.01 + 43.59/2) = 47.30 ppm], which is in a chair,twist-boat conformation, but does not undergo the rapid equilibrium. Thus, we conclude that both **5c** and **6c** exist in solution in chair,twist-boat conformations.

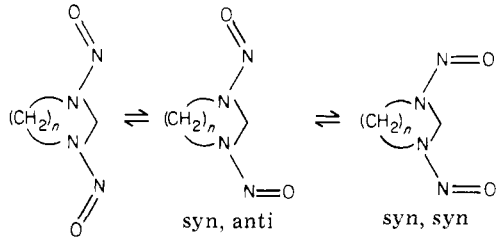
Discussion

The main goal of this study was to obtain the crystal structure of a compound which had a peri nitrosamino interaction so that we could gain a better understanding of the nature of this interaction. In our previous study of **1**, we concluded that this interaction was of an attractive nature. This conclusion was largely based upon the assumption that the tetraazadecalin (TAD) moiety of **1** adopted a double chair conformation. The crystal structure of **5** and the recently determined crystal structure of *trans*-1,4,5,8-tetraacetyl-1,4,5,8-tetraazadecalin[3] (**7**) in which the TAD moiety was found to be in a double twist-boat conformation clearly shows that this assumption about the conformation of the TAD moiety in **1** is incorrect.

The new results show that, in fact, these interactions are part repulsive and part attractive in nature. The principal repulsive interaction is between the peri nitroso nitrogens (in **1**, **5**, and **6**) and the carbonyl carbons (in **7**). This is a typical peri interaction. From the fact that it is strong enough to force one ring of the diazadecalin ring system of **5a** into the more energetic twist-boat conformation but not strong enough to do it in **6a**, which has an additional syn-axial type interaction, (~3.7 kcal/mol) between C_2 and the methyl group, one can establish that the strength of this interaction lies between 5 and 9 kcal/mol, with a reasonable guess being 8–9 kcal/mol. The net result of the conversion of the 1,8-diazadecalin ring into a chair,-twist-boat conformation is to move the nitroso nitrogens apart to relieve this repulsive interaction. In an idealized double chair conformation, the nitroso nitrogens in **5** (or **6**) would be about 2.5 Å apart, which is well within the sum of their van der Waals radii of 3.0 Å.[11] In the actual chair, twist-boat conformation of **5b**, the nitroso nitrogens are 3.14 Å apart, which is slightly larger than the sum of their van der Waals radii. In the case of **1** and **7**, both rings must convert into twist-boat conformations in order to relieve both repulsive interactions. In addition to this repulsive interaction, there are attractive interactions which control the rotamer distribution in **5** and **6**.

Relative Stability of the Rotamers 5 and 6. In both compounds, the relative order of stability of the rotamers is **b** > **a** > **c**. It is useful in discussing the stability of the rotamers to use the anti,anti isomer of **5** (i.e., **5a**) as a reference point. In this rotamer, the strong interaction between the two nitroso nitrogens has been relieved by the diazadecalin ring converting to a chair,twist-boat conformation. This rotamer has no additional interaction between the nitroso groups. In **5** the syn,anti rotamer is more stable than the anti,anti rotamer. Our previous explanation for this preference was the "weak bonding interaction". However, in the actual structure of **5b**, the intramolecular interatomic distance between the N and O atoms is 3.09 Å (O1 to N4, Figure 3). Since this distance is slightly greater than the sum of their van der Waals (2.9 Å) radii there is no possibility for any bonding occurring between these atoms. It should be pointed out that the distance between the oxygen and the nitrogen really depends upon which ring of the diazadecalin converts into a twist-boat conformation. In the actual structure, the ring bearing the syn nitroso group is the one which is in the twist-boat conformation. A model of the other possibility, with the ring bearing the anti nitroso group in a twist-boat, shows that while the peri nitrogens are still about 3.1 Å apart the oxygen–nitrogen separation would be only about 2.0 Å. Thus, it appears that a mutual repulsion causes the oxygen to be separated by the greater distance. In actuality, it would seem that this preference for the 1,8-syn,anti conformation is due to a sort of internal solvation or electrostatic attraction. The large difference of ^{15}N chemical shifts of the nitroso nitrogens gives a clear indication that there is a substantial interaction between them in the 1,8-syn,anti conformation and not in the anti,anti or syn,syn conformations. Further confirmation of the unusualness of the shifts of the nitroso nitrogen in the 1,8-syn,anti conformations is apparent in comparing their shifts to the chemical shifts in 1,3-dinitroso-1,3-diazacycloalkanes. Here, a similar type of rotational isomerism occurs (see Scheme IV), but the shifts of the nitroso nitrogen in all three rotamers span only a 2–5 ppm range.[12] The larger difference in the chemical shift difference of **5b** and **6b** (13 vs. 18 ppm) may well reflect the fact that **6b** is less able to deform because of the severe interaction between C_2 and the methyl group in the chair,twist-boat conformation. This would also account for the reduced stability of **6b** compared to **6a**. Compound **6a** can convert to chair,chair conformation to relieve this interaction while **6b** cannot, since it would force the syn nitroso oxygen very close to the anti nitroso nitrogen. It would appear that the strength of the attractive interaction between the oxygen and nitrogen atoms in the 1,8-syn,anti conformation is approximately 1.5–2.0 kcal/mol.

Scheme IV. Rotational Isomerization in 1,3-Dinitroso-1,3-diazacycloalkanes



In both **5** and **6**, the least stable rotamer is the syn,syn rotamer. It differs from the syn,anti rotamer in having an additional O–N interaction and an O–O interaction. A molecular model shows that the interatomic distance between the O and the N would be only 2.5 Å if the molecule remained in a chair,twist-boat conformation. This rather small separation and resulting severe steric interaction easily explains the reduced stability of the syn,syn rotamers.

A Reexamination of the Rotamer Distribution in *trans*-1,4,5,8-Tetranitroso-1,4,5,8-tetraazadecalin (1).

(11) Pauling, L. "The Nature of the Chemical Bond", 2nd ed.; Cornell University Press: New York, 1948; p 189.

(12) Willer, R.; Moore, D. W., to be published.

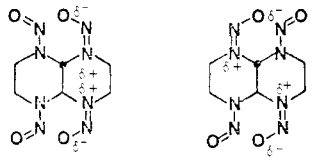


Figure 4. Cross-ring interactions in 1.

Table IV. Predicted Rotamer Populations in 1 Based upon Experimental Rotamer Distribution in 5[13] in Me_2SO

rotamer	$P_1 \times P_2 \times S$		population, %
1a	(0.09 × 0.09) × 100	=	0.81
1b	(0.89 × 0.89)/2 × 100	=	39.60
1c	(0.89 × 0.89)/2 × 100	=	39.60
1d	(0.89 × 0.09) × 2 × 100	=	16.02
1e	(0.02 × 0.89) × 2 × 100	=	3.56
1f	(0.02 × 0.09) × 2 × 100	=	0.36
1g	(0.02 × 0.02) × 100	=	0.04
			99.99

Table V. Crystal Data for *trans*-1,8-Dinitroso-1,8-diazadecalin

formula, $C_8H_{14}N_4O_2$
space group, $P2_1/c$ ($Z = 4$)
unit cell, $a = 7.444$ (2) Å, $b = 9.546$ (3) Å, $c = 13.801$ (6) Å, $\beta = 97.34$ (3)°
crystal size for data collection (approx), 0.02 × 0.2 × 0.6 mm³
wavelength, Mo $K\alpha_1$ 0.70926 Å, Mo $K\alpha_2$ 0.71354 Å
μ, 0.94 cm⁻¹
$F(000)$, 423.88

It is possible with the rotamer distribution in **5** established to predict what the rotamer distribution in **1** should be on a purely statistical basis.[13] This type of prediction assumes no cross-ring interaction. In Table IV, this predicted rotamer population distribution is summarized.

This prediction makes several points. The first is that, as we have said,[1] rotamers **1b** and **1c** should be of equal energy. The low population (or maybe even complete absence) of **1b** must mean that there is some type of cross-ring interaction. Although it is certainly not as strong as would have been implied by our "weak bonding interaction" scheme,[1] it must be at least on the order of 2 kcal/mol to account for the population difference between **1b** and **1c**. Perhaps, a better representation of this cross-ring interaction is that it is an electrostatic one as represented pictorially in Figure 4. An alternative explanation for the lowered preference for **1b** could be that **1c** has a lower dipole moment than **1b**. This does not seem to be a reasonable explanation in light of the small energy difference (0.24–0.38 kcal/mol) between the cis and trans forms of dinitrosopiperazine.[14a,b]

The analysis also predicts that isomer **1e** (one of those which we had considered as impossible because it had a 1,8-syn,syn conformation) should be the next most stable rotamer after **1c** and **1d**. Indeed, when the ^{15}N NMR spectra of **1** are reexamined, the peaks which had been assigned to **1a** and **1b** could also be assigned to **1e**. However, without additional data it is impossible to assign any of the minor peaks (unambiguously) to **1a**, **1b**, or **1e**. It is perhaps more correct to say that the actual rotamer distribution in **1** is approximately 88% **1c** and 12% **1d** with some other minor component(s) present, but it is

Table VI. Atomic Coordinates and Thermal Parameters[a,b] for *trans*-1,8-Dinitroso-1,8-diazadecalin

atom	x/a	y/b	z/c	U/U_{eq}	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C2	0.18778 (66)	-0.05285 (52)	0.90479 (33)	0.0667 (13)						
C3	0.26964 (65)	0.08013 (50)	0.94724 (34)	0.0666 (13)						
C4	0.35981 (61)	0.16657 (47)	0.87396 (29)	0.0583 (12)						
C5	0.43498 (57)	0.17846 (44)	0.69868 (26)	0.0503 (11)						
C6	0.42587 (57)	0.09849 (48)	0.60261 (30)	0.0566 (11)						
C7	0.23592 (62)	0.04851 (51)	0.56759 (33)	0.0647 (13)						
C9	0.16232 (49)	0.05245 (40)	0.73707 (25)	0.0432 (9)						
C10	0.35573 (47)	0.09336 (41)	0.77568 (24)	0.0426 (9)						
N1	0.08012 (49)	-0.02381 (36)	0.81013 (26)	0.0569 (13)	0.0511 (21)	0.0534 (22)	0.0695 (24)	-0.0047 (17)	0.0203 (17)	-0.0127 (16)
N2	0.16323 (44)	-0.02600 (35)	0.64623 (22)	0.0505 (12)	0.0533 (21)	0.0515 (22)	0.0460 (20)	-0.0057 (15)	0.0031 (15)	-0.0043 (16)
N3	-0.09736 (63)	-0.03881 (50)	0.80553 (38)	0.0850 (20)	0.0603 (28)	0.0896 (33)	0.1100 (38)	-0.0169 (29)	0.0294 (26)	-0.0229 (25)
N4	0.12727 (49)	-0.15986 (40)	0.64653 (26)	0.0634 (14)	0.0644 (25)	0.0563 (24)	0.0666 (25)	-0.0142 (20)	-0.0026 (18)	0.0006 (19)
O1	-0.18106 (49)	0.00060 (44)	0.72838 (34)	0.0966 (18)	0.0503 (20)	0.1178 (33)	0.1190 (34)	-0.0178 (28)	0.0009 (21)	-0.0078 (20)
O2	0.14657 (51)	-0.22241 (39)	0.56961 (25)	0.0918 (16)	0.1131 (31)	0.0808 (25)	0.0791 (25)	-0.0396 (20)	0.0032 (20)	-0.0005 (21)

[a] The estimated standard deviation of the last digits are given in parentheses. [b] The thermal parameters are for the expressions: $\exp[-8\pi^2 U(\sin\theta_{hkl}/\lambda)^2]$ (isotropic) or $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$ (anisotropic). The equivalent isotropic U (U_{eq}) is one-third of the trace of the orthogonalized U_{ij} tensor.

(13) Aitkens, A. C. "Statistical Mathematics"; Interscience Publishers, Inc.: New York, 1939; pp 13–15.
(14) (a) Harris, R. K. *J. Mol. Spectrosc.* **1965**, *15*, 100–102. (b) Lambert, J. B.; Gosnell, J. L.; Bailey, D. S.; Henkin, B. M. *J. Org. Chem.* **1969**, *34*, 4147.

unclear which ones these are.

Experimental Section

NMR spectra were recorded on Nicolet 200WB, 300NB, 360WB, and 500NB spectrometers in the FT mode. ^1H and ^{13}C NMR spectra are reported as ppm downfield from internal Me_4Si. The ^{15}N NMR spectra are reported on the ammonia scale (liquid NH_3 = 0). The actual reference was formamide in dimethyl-d_6 sulfoxide. A conversion factor of 108.5 ppm was used to convert the data to the ammonia scale.[15] Infrared spectra were recorded as KBr pellets on a Nicolet 7000 FTIR spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Melting points are uncorrected.

***trans*-1,8-Diazadecalin (2).** This compound was synthesized by a modification of the procedure of Zondler and Pfleiderer.[4] The bis(β-cyanoethyl)acetaldehyde ethylene glycol acetal was reduced to the bis(α-aminopropyl)acetaldehyde ethylene glycol acetal at low pressure (50 psi) using a 10% Pd/C catalyst instead of at high pressure (2,000 psi) using a Raney Nickel catalyst.

***cis*- and *trans*-10-Methyl-1,8-diazadecalin (3 and 4).** This mixture was synthesized by the same modification of the procedure of Zondler and Pfleiderer employed for the synthesis of **2**.

***trans*-1,8-Dinitroso-1,8-diazadecalin (5).** A solution of 1.40 g of **2** (10 mmol) and 1.38 g of sodium nitrite (20 mmol) dissolved in 20 mL of water was prepared. This was cooled to 0 °C and while the solution was stirred 20 mL of 1 N HCl was added in one portion. The product slowly precipitated. After 1 h of stirring at 0 °C, the product was collected and recrystallized from methanol–water to give 1.40 g (7 mmol, 70%) of light yellow crystals with a melting point of 68–70 °C: IR (KBr) 2950 (s), 2900 (m), 2870 (m), 1468 (s), 1445 (s), 1419 (s), 1389 (s), 1340 (s), 1330 (s), 1320 (s), 1307 (s), 1296 (s), 1285 (s), 1209 (s), 1185 (m), 1152 (s), 1133 (s), 1103 (sh), 1083 (s), 1040 (m), 1031 (m), 1000 (sh), 987 (m), 947 (m), 894 (w), 868 (sh), 858 (m), 848 (sh), 818 (w), 781 (w), 747 (m), 678 (w), 509 (w).

Anal. Calcd. for $C_8H_{14}N_4O_2$: C, 48.47; H, 7.11;, N, 28.27. Found: C, 48.58; H, 7.23; N, 28.42.

***trans*-10-Methyl-1,8-dinitroso-1,8-diazadecalin (6).** A solution of 1.54 g of mixture of **3** and **4** (10 mmol) and 1.38 g of sodium nitrite in 20 mL of water was prepared. This was cooled to 0 °C and while stirred 20 mL of 1 N HCl was added. The solution was stirred for 1 h and the product was collected and recrystallized from ethanol–water to give 1.40 g of **6**, with a melting point of 82–84 °C: IR (KBr) 2930 (m), 2860 (m), 1462 (s), 1421 (s), 1397 (s), 1362 (w), 1329 (m), 1316 (m), 1289 (m), 1251 (w), 1228 (sh), 1214 (w), 1192 (s), 1176 (m), 1166 (m), 1157 (sh), 1115 (w), 1100 (m), 1090 (sh), 1065 (m), 1051 (sh), 1037 (w), 1014 (w), 978 (w), 945 (w), 866 (w), 758 (w).

(15) Lichter, R. L. *J. Magn. Reson.* **1975**, *18*, 367.

Anal. Calcd for $C_9H_{16}H_4O_2$: C, 50.92; H, 7.60; N, 26.40. Found: C, 51.10; H, 7.63; N, 26.56.

Crystallography of *trans*-1,8-Dinitroso-1,8-diazadecalin. Crystals of *trans*-1,8-dinitroso-1,8-diazadecalin (**5**) crystallized from methanol–water solution as elongated platelets with well-defined crystal faces. As determined from precession and Weissenberg photographs and diffractometer data, **5** crystallizes in the monoclinic space group $P2_1/c$ (Z = 4). The unit cell dimensions, listed in Table V, were calculated from a symmetry-constrained least-squares fit of 25 computer-centered reflections. Intensity data for the four octants $\bar{h}k\bar{l}$, $\bar{h}kl$, hkl, $hk\bar{l}$ were collected on a Nicolet XRD R3 four-circle diffractometer with graphite-monochromatized Mo Kα radiation from 4° (2θ) to 50° (2θ) with 2θ/θ scans. The scan speed varied from 2° (2θ)/min to 10°/min depending on the intensity of the reflection. Scan ranges were from 1° < $K\alpha_1(2\theta)$ to 1° > $K\alpha_2(2\theta)$. Backgrounds were measured at the beginning and end of each scan for a total background counting time equivalent to that of the scan time. Three check reflections were collected every 45 reflections during the data collection to check for stability. No crystal decay or large intensity variations were observed. The 3908 measured reflections were corrected for Lorentz and polarization effects but *not* for absorption or extinction effects. The check reflections were deleted and the remaining reflections combined to give a unique data set of 1687 unique reflections. Reflections with $I < 0.5\sigma(I)$ were reset to $I = 0.25\sigma(I)$. Five hundred and thirty-eight reflections with $F_0 < 4\sigma(F_0)$ were retained but flagged as "unobserved" reflections.[6] The direct methods part of SHELXTL,[6,7] with an E-Fourier iterative recycling procedure, was used to find the "best" solution. The resulting E map clearly indicated atomic positions of the C, N, O atoms of **5**. These initial atomic positions were refined using unit weights and a blocked-cascade (103 parameter full-matrix blocks) least-squares minimization of $\sum[w(F_0 - F_c)^2]$.[6] During the final cycles of refinement, hydrogen atoms were included with a fixed (calculated) geometry relative to their respective carbon atoms but were allowed to "ride" on the carbon atoms and have variable temperature factors. During the final cycles of refinement the weights used were $w = 1/[\sigma F^2 + gF^2]$ with $g = 0.001$. The refinement converged for the 101 parameters with all shifts less than 0.1 esd on the final cycle. $R = (\sum[F_0 - F_c]/\sum F_0) = 0.074$ for 1149 reflections with $|F_0| > 4\sigma(F_0)$. The resulting atomic coordinates and temperature factors are listed in Table VI. Only the nitrogen and oxygen atoms were refined with anisotropic temperature factors. Atomic numbering is summarized in Figure 3. Bond length and angles are summarized in Table I.

Registry No. **1**, 81898-35-3; **2**, 13993-60-7; **3**, 89178-53-0; **4**, 89178-54-1; **5**, 89178-55-2; **6**, 89178-56-3.

Supplementary Material Available: Table of observed and calculated structure factors (7 pages). Ordering information is given on any current masthead page.