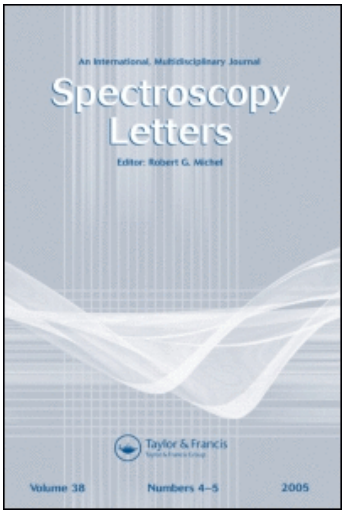

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Study of Chemical Shift Variations in Tricyclic Urazoles with a Norbornane Skeleton

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Abstract: Molecules related to norbornane commonly serve as useful models for stereochemical and conformational analysis, as well as for elucidation of steric and electronic substituent effects. Chemical shifts of their bridge protons are well tabulated and follow clear, easily predictable patterns. For example, the *exo* protons on a two-carbon bridge of these molecules are typically deshielded relative to the *endo* protons. Previously, some exceptions to this rule were noted and satisfactorily explained. In tricyclic urazoles, common precursors to cyclic diazenes, the order of chemical shifts of *exo* and *endo* bridge protons is reversed. In this paper, we use aromatic solvent induced shifts (ASIS) and homodecoupling experiments to assign ^{1}H-NMR signals in these urazoles and bridge proton signals in model molecules, and we discuss analysis of factors that influence chemical shifts in this polycyclic system.

Keywords: DBO, DBH, diazene, ^{1}H-NMR, NMR, stereochemical analysis, urazole

INTRODUCTION

Polycyclic molecules related to norbornane often serve as useful models for stereochemical and conformational analysis, as well as for elucidation of steric and electronic substituent effects.[1] Stereochemical assignment of their NMR signals is important because they are increasingly used as sources of new pharmaceuticals.[2] Assignment of NMR signals in these

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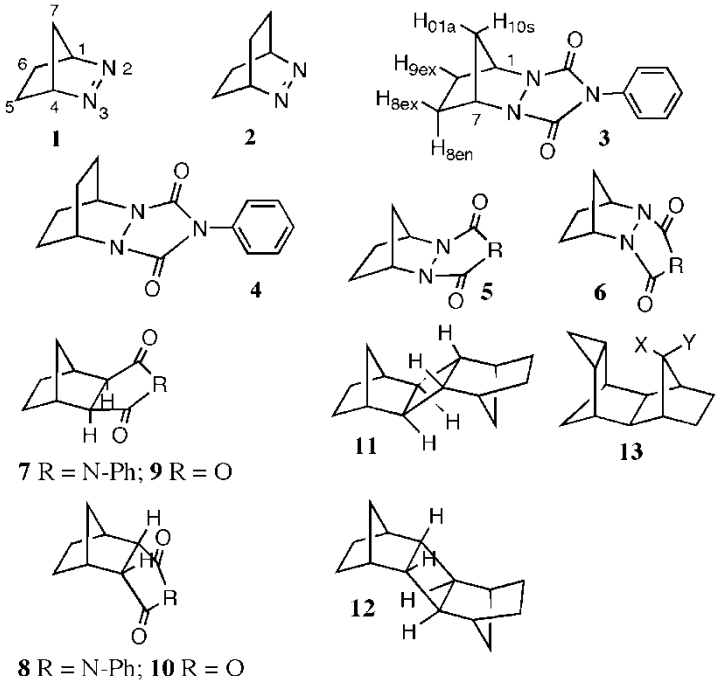
rigid, bicyclic structures is also crucial for structure elucidation in diazenes such as DBH (2,3-diazabicylo[2.2.1]heptene; **1**), DBO (2,3-diazabicyclo[2.2.2]octene; **2**), and related molecules (Scheme 1).

These heterosubstituted analogues of norbornane and bicyclo[2.2.2] octane are important sources of triplet and singlet 1,3- and 1,4-hydrocarbon biradicals.[3] Stereospecifically deuterated **1** and **2** are commonly used to analyze mechanisms of diazene photolysis and thermolysis,[4] test predictions of quasi-classical dynamics simulations,[5] and analyze conformational behavior of labeled intermediate biradicals.[4d,6]

In norbornene, bicyclo[2.2.2]octane, and most of their 2- and/or 3-substituted derivatives, the assignment of chemical shifts of bridge protons is fairly straightforward. The *exo* protons on a two-carbon bridge are deshielded relative to the isomeric *endo* protons, and the relative chemical shifts of the *syn* and *anti* one-carbon bridge protons are opposite of *exo* and *endo* pair. These chemical shift patterns are not absolute, and some *endo* substituents such as carbonyl[7] or aryl groups[8] may shift the *endo* protons of the opposite carbon of the bridge downfield of the *exo* signals by magnetic anisotropy effects. In norbornenes with no substituents at C-7, the chemical shift of the *syn* proton is highly dependent on the molecular geometry, because it lies on the diamagnetic-paramagnetic border of the double bond.[9]



Scheme 1.

Previously, we reported stereochemical assignment of bridge protons in **1** and its urazole precursor 4-phenyl-2,4,6-triazatricyclo[5.2.1.$0^{2,6}$]heptane-3,5-dione (**3**), and we described preliminary computational studies designed to determine the origin of differences in relative chemical shifts of *exo* and *endo* two-carbon bridge protons in diazenes **1** and **2** and urazoles **3** and **4**.[10] Analysis of chemical shifts of bridge protons in **1** and **3**, resolved in benzene-d_6 with the aid of significant aromatic solvent-induced shifts (ASIS),[11] suggested that in this solvent the *endo* protons are indeed deshielded relative to the isomeric *exo* protons in **3** but are more shielded relative to the *exo* protons in the spectrum of **1**. Thus, it appears that *both* the bicyclo[2.2.2]octene system of **2** and **4** and the bicyclo[2.2.1]heptene system of **1** and **3** interchange their *endo* and *exo* chemical shifts upon transformation of the respective urazole precursors into diazenes. The relative chemical shifts of *syn* and *anti* H-10 (H-7 in **1**) are *unaffected* upon changing the phenyltriazolinedione moiety to a diazene group (i.e., going from **3** to **1**).[10]

In general, the "unusual" chemical shifts of the *exo* and *endo* protons of urazoles **3** and **4** are difficult to explain. These molecules exist as a pair of interconverting *exo* and *endo* conformers **5** and **6**. Based on the experimental data for inversion barriers in various tricyclic hydrazines,[12] and considering the effect of the conjugated carbonyl groups, the inversion barrier in this system is expected to be much less than 10 kcal/mol. The chemical shifts of bridge protons in urazoles are likely influenced by numerous factors such as the relative population of conformers, the anisotropic effect of the phenyl group on N-4, and bridgehead N-2 and N-6. It is also possible that these shifts are entirely dominated by anisotropic interaction with the aromatic solvent. Therefore, four model polycyclic molecules were prepared to investigate various influences on the chemical shifts of bridge protons in **1**–**4**. These models, the *exo* and *endo* anhydrides 4-oxatricylco[5.2.1.$0^{2,6}$] heptane-3,5-diones, **9** and **10**, and *exo* and *endo* *N*-phenyl imides 4-phenyl-4-azatricyclo[5.2.1.$0^{2,6}$]heptane-3,5-diones, **7** and **8**, respectively, are rigid skeleton analogues of **3**. Although the electronic structures of **7**–**10** are quite different from **1** and **3**, they do permit the analysis of the effects of conformational changes, remote phenyl group, and aromatic solvent on the shifts of the bridge protons in these tricyclic systems.

MATERIALS AND METHODS

Melting points were obtained on a Thomas–Hoover (Swedesboro, NJ) capillary melting point apparatus using Pyrex brand melting point tubes and are uncorrected. Infrared spectra were obtained on a Perkin Elmer (Wellesley, MA) 1600 FTIR (4 cm^{-1}) or Nicolet Avatar (Waltham, MA) 360 (0.5 cm^{-1}). Routine ^{1}H-NMR spectra were obtained at RT in C_6D_6, $CDCl_3$, or acetone-d_6 at 89.54 MHz on a JEOL (Peabody, MA) 90FTQ

instrument at Towson University, using 10 mg/mL^{-1} solutions in C_6D_6 (or $CDCl_3$). Pulse width of ca. 20° was used in all acquisitions. The spectral width was 1000.0 Hz, the data table size was 16K, with dwell time of 1000 μs.

High-resolution ^{1}H-NMR spectra were obtained at 300.13 MHz, 23°C, using 10 mg/mL^{-1} solutions in C_6D_6 on a Bruker (Billerica, MA) NMR instrument at Johns Hopkins University. Pulse width of ca. 30° was used in all acquisitions. The spectral width was either 3623.2 Hz or 6024.1 Hz, and the data table size was either 16K or 32K, with dwell time of 166 or 276 μs. TMS was used as the internal standard. All reported shifts are ±0.02 ppm.

Starting Materials

Maleic anhydride, dicyclopentadiene, *N*-phenylmaleimide, and all solvents were commercially available. All solvents were used as received. Maleic anhydride was recrystallized from $CHCl_3$. Cyclopentadiene was obtained by cracking dicyclopentadiene at 42°C, taking care to keep the cracked material at 0°C prior to use.

endo-4-Phenyl-4-azatricyclo[5.2.1.0^{2,6}]hept-8-ene-3,5-dione

This compound was prepared using a modified, scaled-up method of Wilcox and Wilcox[13]. *N*-phenylmaleimide, 5.8 g (0.03 mol), was dissolved in 50 mL of hot ligroin (bp 55–110°C). A minimum amount of ethyl acetate was added to aid dissolution. Cyclopentadiene (3.6 mL, ca. 0.04 mol) was added in 1 mL portions with continuous stirring. The solution was warmed under reflux for 5 min, or until the discharge of yellow of the maleimide, cooled to room temperature, and placed in ice/water bath. The precipitate was vacuum filtered and washed with 20 mL of hexanes. Recovered 7.4 g of white solid: mp 140.5–144°C; 92% yield. ^{1}H-NMR, acetone-d_6 (89.54 MHz) δ 0.79 (dm, H-10a), 1.20 (dm, H-10s), 2.62 (dd, 2H, H-1 and H-7), 2.98 (m, 2 H, H-2 and H-6), 5.89 (m, 2 H, H-8 and H-9), 6.99, 7.06, 7.26, 7.34 (m, 5H, aromatic); IR (Nujol) 1770, 1706, 1595, 1499, 1290, 1186, 848, 773, 740, 618 cm^{-1}.

exo-4-Phenyl-4-azatricyclo[5.2.1.0^{2,6}]hept-8-ene-3,5-dione

This *exo* adduct was obtained following a procedure similar to the *exo* anhydride (see below). The *endo* adduct was heated between 200°C–210°C for 3 hr. The crude material was recrystallized three times from benzene-ligroin, to a mp of 182–190.5°C, 92% yield, and was hydrogenated without further purification. ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 1.15 (m, 2 H, H-10a and H-10s), 2.18 (d, 2 H, H-1 and H-7), 3.02 (m, 2 H, H-2 and H-6), 5.74

(m, 2 H, H-8 and H-9), 6.99, 7.06, 7.26, 7.34 (m, 5H, aromatic); IR (Nujol) 1770, 1703, 1596, 1499, 1290, 840, 739, 620 cm^{-1}.

endo-4-Oxatricyclo[5.2.1.$0^{2,6}$]hept-8-ene-3,5-dione

This compound was prepared using a modified, scaled-up method from Wilcox and Wilcox.[13] Maleic anhydride, 19.6 g (0.2 mol), was dissolved in 50 mL of ethyl acetate with warming. Hexanes (50 mL, bp 68.5–70°C) were added and the solution cooled in an ice/water bath. Cyclopentadiene, (20 mL, ca. 0.25 mol) was added to the cooled reaction flask in 1-mL portions with stirring. After 0.5 hr, 27.6 g of white crystals were obtained, mp 162–164.5°C; 84% yield.[1] H-NMR, $CDCl_3$ (89.54 MHz) δ 1.58 (dt, H-10a), 1.78 (dt, H-10s), 3.51 (m, 2H, H-1 and H-7), 3.59 (dd, 2 H, H-2 and H-6), 6.32 (t, 2 H, H-8 and H-9); IR (Nujol) 1853, 1770, 1230, 1090 cm^{-1}.

exo-4-Oxatricyclo[5.2.1.$0^{2,6}$]hept-8-ene-3,5-dione

The *exo* adduct was prepared using a modified method of Craig.[14] The *endo* adduct (27.5 g, 0.168 mol) was heated at 192°C in an open flask immersed in a hot oil bath for 1.5 hr and recrystallized three times from benzene. Recovered 3.6 g of white powder: mp 138.5–142°C; 13% yield, not optimized. ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 0.89 (m, 2H, H-10a and H-10s), 2.01 (m, 2H, H-1 and H-7), 2.77 (qd, 2 H, H-2 and H-6), 5.50 (dd, 2 H, H-8 and H-9); IR (Nujol) 1778, 1218, 1086, 941, 893, 734 cm^{-1}.

Preparation of Hydrogenated Compounds

All hydrogenations were performed using a Parr pressure reaction apparatus using commercially available 5% Pd on charcoal with THF as a solvent.

exo-4-Phenyl-4-azatricyclo[5.2.1.$0^{2,6}$]heptane-3,5-dione (7)

Fifty milliliters of THF, 200 mg of 5% palladium on carbon, and 1.4 g (0.006 mol) of corresponding unsaturated *exo*-isomer were placed in a standard Parr bottle. The bottle was pressurized to 60 psi with H_2 and flushed three times. The hydrogenation was carried out under an initial pressure of 80 psi. Once hydrogen uptake ceased, ca. 2 hr, the catalyst was gravity filtered, the solvent was removed under reduced pressure, and the residue was recrystallized from benzene. Recovered 0.25 g of **7**: mp 157–158°C, 17% yield, not optimized. Note that this material hydrolyzes rapidly in air and isomerizes to give **8** (by TLC and ^{1}H-NMR). It must be stored

under vacuum, in a dessicator, or under vacuum in an oven below its mp. ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 1.33-1.51 (m, 6 H, H-10s, H-10a, H-8ex, H-9ex, H-8en and H-9en), 2.81 (m, 2 H, H-1 and H-7), 3.03 (m, 2 H, H-2 and H-6), 7.18–7.57 (m, 5H, aromatic); IR (Nujol mull) 1706, 1192, 806, 750, 692, and 596 cm^{-1}.

endo-4-Phenyl-4-azatricyclo[5.2.1.0^{2,6}]heptane-3,5-dione (8)

This compound was prepared using 5.3 g (0.022 mol) of the corresponding unsaturated *endo*-isomer and following the procedure described above. Hydrogen uptake ceased after approximately 2.5 hr, and the crude material was recrystallized from benzene–ligroin, followed by recrystallization from ligroin. Recovered 4.6 g of white crystals: 85% yield. ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 1.37-1.79 (m, 6 H, H-10s, H-10a, H-8ex, H-9ex, H-8en and H-9en), 2.86 (m, 2 H, H-1 and H-7), 3.23 (m, 2 H, H-2 and H-6), 7.16–7.55 (m, 5H, aromatic); IR (Nujol mull) 1705, 1187, 736, and 692 cm^{-1}.

exo-4-Oxatricyclo[5.2.1.0^{2,6}]heptane-3,5-dione (9)

This compound was prepared using the same procedure as for the hydrogenated *endo* adduct below using 3.6 g (0.022 mol) of corresponding unsaturated *exo*-isomer. Hydrogen uptake ceased after 3.5 hr, and the crude material was recrystallized from benzene–ligroin, followed by recrystallization from ligroin. Recovered 2.6 g with mp 76.5–80°C; 72% yield. ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 1.34 (m, 3 H, H-8en, H-9en and H-10a), 1.72 (m, 3 H, H-8ex, H-9ex and H-10s), 2.84 (s, 2 H, H-1 and H-7), 2.90 (s, 2 H, H-2 and H-6); IR (Nujol mull) 1786, 1228, 1088, 946, and 908 cm^{-1}.

endo-4-Oxatricyclo[5.2.1.0^{2,6}]heptane-3,5-dione (10)

This compound was prepared by hydrogenation of the corresponding unsaturated *endo* anhydride according to the procedure of Canonne, Bèlanger, and Lemay.[15] The unsaturated *endo* anhydride, 3.8 g (0.023 mol), was placed in a standard Parr bottle containing 200 mg of 5% palladium on charcoal and 40 mL of THF. The bottle was pressurized to 60 psi with H_2 and flushed three times. The hydrogenation was carried out under an initial pressure of 80 psi. Once hydrogen uptake ceased, ca. 4.5 hr, the catalyst was gravity filtered, the solvent was removed under reduced pressure, and the residue recrystallized from benzene–ligroin. Recovered 2.3 g of white crystals. mp 167–168°C; 58% yield; ^{1}H-NMR, $CDCl_3$ (89.54 MHz) δ 1.26–1.95 (m, 6H, H-10s, H-10a, H-8ex, H-9ex, H-8en and H-9en), 2.84

(m, 2 H, H-1 and H-7), 3.40 (m, 2 H, H-2 and H-6); IR (Nujol mull) 1790, 1724, 1311, 1294, 1213, 1079, 950, 906, 718, and 584 cm^{-1}.

RESULTS

Chemical shifts of bridge protons in **1**, **3**, and **4**, recorded at 500 MHz in C_6D_6, are listed in Table 1. Typically, the signals of bridge protons are unresolved when spectra of **1** and **3** are recorded in CCl_4, $CDCl_3$, or $(CD_3)_2CO$ at either 60,[4c] 90,[4e] 100,[4b] 250,[4a] 400,[4d] or 500 MHz.[10] Therefore, benzene was used as an NMR solvent, because it allows resolution of *all* bridge protons by ASIS.[10] Signal assignment in **1** and **3** is based on integrated

Table 1. Proton assignment in **1**, **2**, **3**, **4**, and **7**–**12**[a]

Molecule/ proton[b]	*syn*	*anti*	*endo*	*exo*	Bridgehead	Ref.
1[c]	0.68	0.35	0.56	0.84	4.67	10
3[c]	1.17	0.59	1.45	0.89	4.00	10
2[d,e]			1.27	1.55		6
4[d,e]			2.10	1.84		6
4			1.49	0.90	3.97	10
7[f]	1.04	0.69	0.76	1.10	2.06 (2.49)	This work
8[f]	0.98[f]	0.98[f]	1.33	1.15	2.41 (2.49)	This work
9	0.84	0.61	0.58	0.95	2.04 (2.27)	This work
10[c]	0.69	0.76	1.14	0.99	2.10 (2.36)	This work
	Δ(*syn*)	Δ(*anti*)	Δ(*endo*)	Δ(*exo*)		
3–**1**[h]	−0.49	−0.24	−0.89	−0.05		
8–**7**[i]	+0.06	−0.29	−0.57	−0.05		
10–**9**[i]	+0.15	−0.15	−0.56	−0.04		
12–**11**[i]	+0.87	−0.13	−0.86	−0.00		15

[a]Spectra recorded in C_6D_6, at 300 MHz unless indicated otherwise. The shifts are measured from the TMS signal at 0.00 ppm.

[b]Protons are *syn*/*anti* H-7 and *exo*/*endo* H-5,6 in **1** and **2** (bridgehead H-1,4), and are *syn*/*anti* H-10 and *exo*/*endo* H-8,9 [bridgehead H-1,7 (2,6)] in **3**, **4** and **7**–**10**.

[c]Spectra recorded in C_6D_6, at 500 MHz.

[e]The *syn*/*anti* pair in **2** and **4** is same as the *endo*/*exo* pair due to higher symmetry of the molecule. The spectra of **2** and **4** in Ref. 6 were recorded at 220 MHz in $CDCl_3$. The signals from bridgehead protons were not tabulated.

[f]Chemical shifts of aromatic protons in **7** and **8** are listed in the "Materials and Methods" part of the paper.

[g]Signals unresolved, confirmed by integration.

[h]All values are ±0.03 ppm. Chemical change from the urazole (**3**) to diazene (**1**).

[i]Structural change from rigid *endo*-isomer (**8**, **10**, **12**) to the *exo*-isomer (**7**, **9**, **11**).

signal intensities and on comparison with the C_6D_6 spectrum of **4**, whose *exo* and *endo* protons have been previously assigned by Samuel et al.[6] The appearance of *syn* and *anti* protons in **1** and **3** is almost identical to that of corresponding resolved signals in norbornene recorded at 100 MHz.[16] In **1** and **3**, the *anti* proton, typically a clean doublet due to geminal coupling to the *syn* proton, is the most shielded signal based on the accepted norbornene model. This assignment is also supported by the splitting pattern of the *syn* proton, that of a doublet of quintets. The larger coupling constant, 10.2 Hz, is due to geminal coupling to the *anti* partner, consistent with values previously observed in 2,3-substituted bicyclo[2.2.2]octane and norbornane skeletons.[1] The smaller constant of 1.9 Hz is the result of combined coupling to bridgehead protons on carbons 1 and 4(7) ($^3J_{HH}$ lit. value 1.7–1.8 Hz)[1] and W-type $^4J_{HH}$ coupling to *endo* protons (lit. value 2.2 Hz).[17] In accord with literature data on norbornane and norbornene, the *anti* doublet is broadened by small, unresolved long-range coupling to other nuclei.[1]

Table 1 also presents detailed assignment of protons in model molecules **7**–**10**. The latter are paired as *exo*- and *endo*-N-phenylimide isomers **7** and **8** and as *exo*- and *endo*-isomers of anhydrides **9** and **10**. In these molecules, the *syn*/*anti* and *endo*/*exo* pairs are discernible by their integrals and leaning patterns. Each partner within a pair is assigned based on the examination of coupling patterns, aided by homonuclear decoupling. For example, the spectra of *endo* anhydride 4-oxatricyclo-[5.2.1.$0^{2,6}$]heptane-3,5-dione (**10**) recorded without (a) and with decoupling of the H-1,7 protons (b) are shown in Fig. 1. The *exo* protons at 0.99 ppm are identified by their large

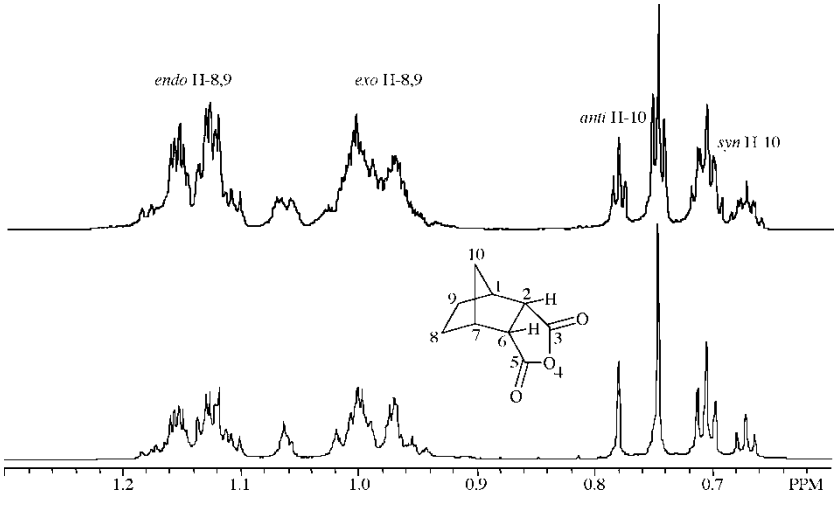


Figure 1. Spectra of *endo* anhydride 4-oxatricylco[5.2.1.$0^{2,6}$]heptane-3,5-dione (**10**) recorded without (a) and with decoupling of the H-1,7 protons (b).

(3.2–3.4 Hz)[1] coupling constant to H-1,7, and the *endo* protons remain almost unaffected because they couple to H-1,7 with at most 0.5 Hz.[1] The *syn* H-10 proton at 0.69 ppm is identified by its larger (1.7 Hz) coupling constant to H-1,7. The corresponding *anti* proton exhibits a smaller coupling of 1.5 Hz. Although this difference is within the digital resolution of the spectra, it is nonetheless in very good agreement with averaged tabulated data for some 26 related 2,3-disubstituted norbornane and norbornene compounds listed in Ref. [1], that is, 1.8 ± 0.2 Hz from H-1,7 to the *syn* proton and 1.4 ± 0.1 Hz from H-1,7 to the *anti* proton.

DISCUSSION

In order to correctly assign the protons in these molecules, it is necessary to discuss the role of the aromatic solvent. As was mentioned earlier, the bridge protons are not resolved at fields up to 500 MHz in noncomplexing solvents such as acetone or chloroform[10] (see also data in the "Materials and Methods" section). The possibility exists that the chemical shifts observed in C_6D_6 are influenced in part by the aromatic solvent (ASIS), that is, the shifts are being scrambled as they are resolved. That this is not the case is strongly suggested by the following observations:

(a) Similar anomalous chemical shifts were observed in cyclic diazene **2** and its derivatives. Specifically, Samuel et al. reported that in urazole precursor to **2**, 4-phenyl-2,4,6-triazatricyclo[5.2.2.$0^{2,6}$]octane-3,5-dione (**4**), the *endo* H-8,9 protons are deshielded by about 0.25 ppm relative to the isomeric *exo* counterparts,[6] contrary to what would be expected from the norbornane model.[1] However, in the diazene **2**, the relative chemical shifts of *exo* and *endo* H-5,6 were ordered as expected. These results are fully in accord with the observations reported here for *endo* and *exo* chemical shifts in urazole **3** when compared with diazene **1**. (Note that the tricyclic ring system of **3** and **4** is indexed differently, that is, the two carbon bridge protons 5 and 6 in **1** and **2** are numbered 8 and 9 in **3**, **4**). In Ref.[6], the stereochemical assigment was carried out in *noncomplexing solvents* ($CDCl_3$) using lanthanide induced shifts and $^{15}N\{^1H\}$ NOE studies. Therefore, it appears that a change to a *complexing, aromatic solvent* doesn't change the order of chemical shifts in **1** and **3**.

(b) In rigid model molecules studied here (**7**, **8** and **9**, **10**) the change from the *endo*- to the *exo*-isomer within each pair results in *nearly identical* chemical shifts when recorded in benzene (Table 1). The shape and electronic properties of these two sets of isomers are *very different*. It would be highly coincidental that such regularity would be observed if the aromatic solvent were the sole cause of the shifts discussed here, that is, that the aromatic solvent would interact identically with these model compounds.

Our confidence in correct assignment of chemical shifts in model molecules is based on the following observations. First, as seen in Table 1, the substitution of the N-phenyl group for an oxygen in these molecules

(i.e., changing **7** to **9** and **8** to **10**) leads to the consistent 0.21 ± 0.05 ppm upfield shift for all the protons. This would not be likely in the case of incorrect stereochemical assignment. Second, chemical shifts presented in this work are in very good agreement with literature data on other rigid *exo* and *endo* isomers of a tricyclic norbornane system. For example, a thorough study of all possible isomers of fully saturated norbornene dimers, such as **11** and **12**,[18] shows that the *endo* protons are upfield of the *exo* partners in the all-*exo* isomer **11** but move downfield in **12** (see Table 1). Likewise, the chemical shift of the *endo* protons in the *exo* isomer of a variety of 10-substituted decahydrotrimethanonaphtalenes **13**[19] ranges from 1.00 to 1.40 ppm, always upfield of the *exo* protons (1.65–1.93 ppm).

It appears from Table 1 that the chemical transformation from the urazole **3** to a diazene **1** is very similar in its effect on chemical shifts of bridge protons to structural changes **8–7**, **10–9**, and **12–11** (from the *endo*- to the *exo*-isomer). The only significant distinction of the chemical change of **3** into **1** is the *large* upfield shift of the *syn* proton, due to the shielding effect of N=N bond. This parallels the *syn* and *endo* protons in **11**/**12** that also show large (but downfield) shifts due to van der Waals interactions with the cyclobutane ring protons (<2.0 Å away).

The molecules described here can be classified into three separate categories listed in Table 2. In *endo*-isomers, the chemical shift difference between the *syn–anti* and *endo–exo* protons is appreciable and opposite in sign. The *endo*-isomers show very little chemical shift difference between the *syn* and *anti* protons, while the *endo* and *exo* protons are separated by half as much as those of the *exo*-isomers. While the urazoles **3** and **4** fall into neither of those categories, the data in Table 1 do provide important

Table 2. Bridge proton chemical shift differences in **1**–**4**, **7**–**10**[a]

Molecules/proton	Δ(*syn–anti*)	Δ(*endo–exo*)
exo- and *exo*-like		
1[b]	0.33	−0.28
7	0.35	−0.34
9	0.23	−0.37
endo		
8	0.00	0.18
10	−0.07	0.15
Neither		
3	0.58	0.56
4[c]	x	0.59

[a]All values are ±0.03 ppm.

[b]The spectrum of **2** in C_6D_6 is not available.

[c]The *syn*/*anti* pair in **4** and its derivatives is the same as the *endo*/*exo* pair due to higher symmetry of the molecule.

observations about unusually high chemical shift of the *endo* protons in urazoles **3** and **4**, as compared with diazenes **1** and **2**.[6,10]

(a) Just like the *syn* protons that are relatively insensitive to the *structural* changes in **7**–**10**, the *exo* protons are quite unaffected by either the conformational or structural differences between the molecules. Changes in the chemical shifts of only the *exo* protons do not appear to be the cause of the observed anomaly.

(b) The differences in chemical shifts of all protons in *N*-phenylimides **7** and **8**, compared with the anhydrides **9** and **10**, show that the only effect exerted by the remote phenyl group at N-4 in **3** is a fairly uniform 0.18 ± 0.06 ppm downfield shift of all signals. This phenyl group can be safely excluded as a major reason for the observed *exo*/*endo* chemical shift differences in **3**.

(c) Similar to the *endo* protons in the *endo*- anhydride and *N*-phenylimide isomers, the *endo* protons in **3** and **4** probably experience some additional downfield shift due to the anisotropic effect of the carbonyl groups. Because this is most effective in an *endo* conformation **6**, we have performed energy optimization of model urazoles lacking a phenyl group (C_1 symmetry) by the PM3 semiempirical and 3-21G* *ab initio* calculations[10] and more recently by the B3LYP(6-31G*) procedure. These calculations indicate that the *exo* conformer is lower in energy than *endo* by about 1.0 [PM3, B3LYP(6-31G*)] or 0.8 (3-21G*) kcal/mol. Although literature data on urazoles is not available, these findings are consistent with previously reported theoretical[20] (AM1,[20a] MP2,[20b] B3LYP(6-31G**),[20a] MM3[20a]) and experimental[20b] studies of related polycyclic hydrazines. Based on these calculations, only ca. 25% of molecules are predicted to possess *endo* conformation. Therefore, the effect of the carbonyl groups would be greatly attenuated.

Calculations also show an extensive resonance interaction between the nitrogen atoms and the carbonyl groups in the *endo* conformation **6**. This brings the deshielding regions of the N–C═O groups much closer to the *endo* protons, causing a significant downfield shift. In our opinion, this is the principal reason of the unusually high chemical shifts of *endo* protons in **3** and **4**. It appears that this interaction is significant enough to compensate for the relatively small population of the *endo* conformers.

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