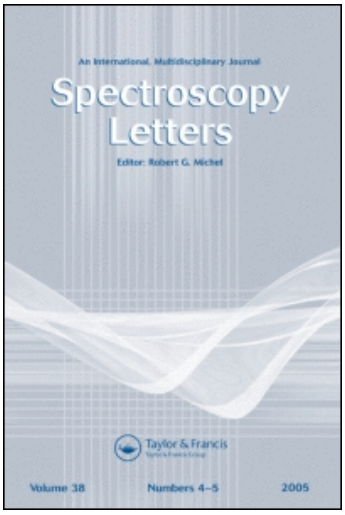

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STEREOCHEMICAL EFFECTS ON ^{1}H CHEMICAL SHIFTS IN 2,3-DIAZABICYCLO[2.2.1]HEPT-2-ENE (DBH), 2,3-DIAZABICYCLO[2.2.2]OCT-2-ENE (DBO) AND RELATED MOLECULES

Keywords: NMR; ^{1}H-NMR; DBH; DBO; urazole, norbornene, stereochemical effects, ASIS; aromatic solvent-induced shifts

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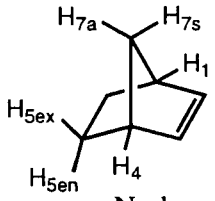
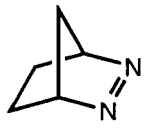
ABSTRACT: ^{1}H-NMR spectra of DBH (**1**), DBO (**2**) and of the synthetic precursor to **1**, 1,4-phenyl-2,4,6-triazatricyclo[5.2.1.$0^{2,6}$]heptane-3,5-dione (**3**), were recorded in acetone-d_6 and C_6D_6 at 500 MHz. Assignment was aided by complete resolution of signals of **1** and **3** in C_6D_6 by aromatic solvent-induced shifts (ASIS). The effect of the change from phenyltriazolinedione to a diazene functional group on the chemical shifts of the *exo,endo* and *syn,anti* protons was investigated. The chemical shifts of the *exo,endo* protons of **1** are exceptionally sensitive to the functional group at the heterosubstituted bridge in the DBH skeleton. However, the relative chemical shift of the *syn,anti* proton pair is independent of the nature of the functional group. The role of stereochemical effects on these chemical shifts is discussed.

INTRODUCTION

The stereochemical assignment of bridge protons in diazenes **1** (DBH) and **2** (DBO), the aza analogs of norbornene and bicyclo[2.2.2]octene, is of considerable practical interest.



Norbornene



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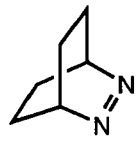

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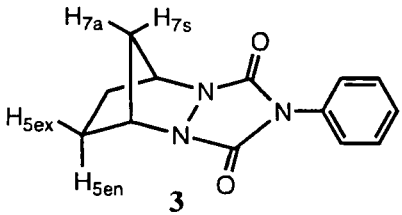

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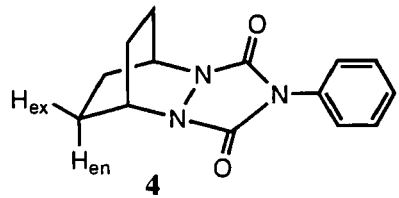


4

These molecules are important sources of triplet and singlet 1,3- and 1,4-biradicals.[1] Stereospecifically deuterated **1** and **2** are commonly used to test the mechanism of diazene photolysis and thermolysis,[2] test predictions of quasi classical dynamics simulations,[3] and to analyze conformational behavior of intermediate biradicals.[2d,4] The chemical shifts of bridge protons are very sensitive to the stereochemistry in these rigid bicyclic molecules.[5] For example, in norbornene, bicyclo[2.2.2]octane and its 2- and/or 3-substituted derivatives the *exo* $H_{5,6}$ protons are deshielded relative to the isomeric *endo* protons. In norbornene and most of its derivatives the relative chemical shifts of one carbon bridge protons (*syn* and *anti* H_7) are opposite of *exo* and *endo* $H_{5,6}$. Since *syn* H_7 lies on the border of the diamagnetic-paramagnetic regions of the π bond, its chemical shift is insensitive to the π bond's anisotropy effects.[6] Note that this discussion applies only to molecules with no substituents at C-7. Also, note that some *endo* H_5 or H_6 substituents such as carbonyl[7] or aryl groups[8] push the corresponding *endo* H_6 or H_5 proton downfield of isomeric *exo* signals due to their magnetic anisotropy effects.

Samuel et al.[4] reported that in at least one 2,3-substituted derivative of bicyclo[2.2.2]octane the *endo* $H_{5,6}$ protons are deshielded by about 0.25 ppm relative to the isomeric *exo* counterparts, contrary to what would be expected from the norbornene model. This derivative is urazole **4**, a common precursor to diazenes. Their conclusion was based on detailed lanthanide shift reagent and ^1H-^{15}N NOE studies of *exo*-5,6-**4**-d_2.[4] Samuel also found that in diazene **2** the relative chemical shifts of *exo* and *endo* $H_{5,6}$ behaved "normally", as one would expect from norbornene assignments. The present study was done to determine if a similar chemical shift reversal, in particular of *syn* and *anti* H_7 is observed in diazene **1** and urazole **3**, molecules with a bicyclo[2.2.1]heptane skeleton. Computational studies were performed to determine the origin of differences in relative chemical shifts of *exo* and *endo* $H_{5,6}$ in diazenes **1, 2** and urazoles **3, 4**.

MATERIALS AND METHODS

DBH (**1**) and urazoles **3** and **4** were prepared according to literature procedures.[2a,9] IR spectra were recorded on the Perkin-Elmer 1600 spectrometer. 90 MHz ^1H-NMR spectra were recorded in 50 mg/mL solutions at 90 MHz on a JEOL-FX90Q broadband spectrometer equipped with a 5 mm probe. Typically, 8 K points were collected using ca. 30° pulse width with 4.1 sec repetition time. 500 MHz ^1H-NMR spectra were recorded in 50 mg/mL solutions at 499.87 MHz on the Varian UNITYPlus 500 broadband spectrometer equipped with a 5 mm probe. Typically, 64 K points were collected using ca. 45° pulse width with 5.3 sec repetition rate. All chemical shifts were measured relative to the tetramethylsilane internal standard at 0 ppm. Semi-empirical (PM3) and ab initio (3-21G*) calculations were performed at JHU on a SGI Indigo2 XL workstation using Spartan 5.0.2 (Wavefunction, Inc. Irvine CA).

RESULTS AND DISCUSSION

^1H-NMR signal assignments in **1** and **3** were previously limited to *exo* and *endo* protons (H_5 and H_6) on the two-carbon bridge due to complete signal overlap of protons on the one-carbon bridge, H_7. The signals of H_5, H_6 and H_7 often overlap, preventing detailed assignment. For example, the *syn* and *anti* H_7 (and sometimes H_5 and H_6) signals of **1, 3**, and their derivatives are not resolved

when their spectra are recorded in CCl_4 or $CDCl_3$, at either 60,[2c] 90,[2e] 100,[2b] 250[2a] or 400 MHz.[2d] The poor resolution of bridge protons in **1** and **3**, even at higher fields, is illustrated by the 500 MHz spectrum of **3** in acetone-d_6, Fig. 1 spectrum 1a (top). Similar spectra are observed in $CDCl_3$. Note that for clarity only the part of spectra that includes bridge protons H_5, H_6 and H_7 is shown. When spectra of **1** (1d in Fig. 1) and **3** (1b in Fig. 1) were recorded in C_6D_6, complete resolution of all H_5, H_6 and H_7 signals was observed, as the result of significant aromatic solvent-induced shifts (ASIS). The greatest ASIS observed here, for the H_7 protons, is ca. 1.2 ppm, comparable to largest values known.[10]

Signal assignment of **3** and **1** is based on integrated signal intensities, and on the C_6D_6 spectrum of **4**, Fig. 1 spectrum 1c, whose *exo* and *endo* $H_{5,6}$ protons labeled **ex** and **en**, have been previously assigned by Samuel et al.[4] The *anti* H_7 (labeled $\mathbf{H_{7a}}$) in **1** is assumed to be the most shielded signal at 0.34 ppm based on the accepted norbornene model. This assignment is also supported by its splitting pattern, that of a doublet of quintets. The larger coupling constant, 10.2 Hz, is clearly a geminal coupling constant to *anti* H_7, consistent with values previously observed in 2,3-substituted bicyclo[2.2.2]octane and norbornane skeletons.[5] The smaller constant of 1.9 Hz is the result of $^3J_{HH}$ coupling to bridgehead protons $H_{1,4}$ (lit. value 1.6-2.2 Hz)[5] and W-type $^4J_{HH}$ coupling to *endo* $H_{5,6}$ (lit. value 2.2 Hz).[11] In accord with literature data, the *anti* H_7 proton (a clean doublet) exhibits smaller, unresolved long-range coupling to other nuclei in **1** and **3**.[5] Notably, the appearance of *syn* and *anti* H_7 protons is almost identical to corresponding signals of norbornene recorded at 100 MHz.[12]

The following conclusions may be reached upon close examination of spectra in Fig.1:

1. The relative chemical shift of *syn* and *anti* H_7 is unaffected in changing the phenyltriazolinedione moiety to a diazene group, i.e. going from **3** to **1**.

2. The *endo* $H_{5,6}$ protons (the partially resolved multiplet at 1.48 ppm labeled **en** in 1b) are clearly deshielded relative to the isomeric *exo* protons in **3** (labeled **ex**), but are more shielded relative to the *exo* protons in the spectrum of **1**. The *endo* $H_{5,6}$ protons of **1** in spectrum 1d appear at 0.56 ppm. This assignment is based on larger linewidth of the *endo* signal due to poorer resolution of the complex coupling. 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 the *endo* and *exo* chemical shifts upon transformation of the urazole into a diazene.

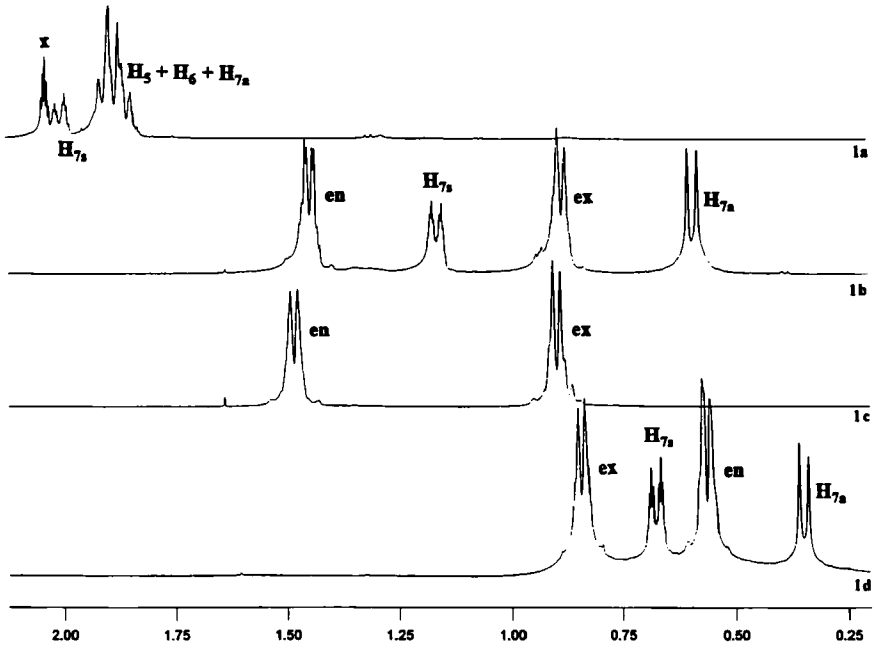
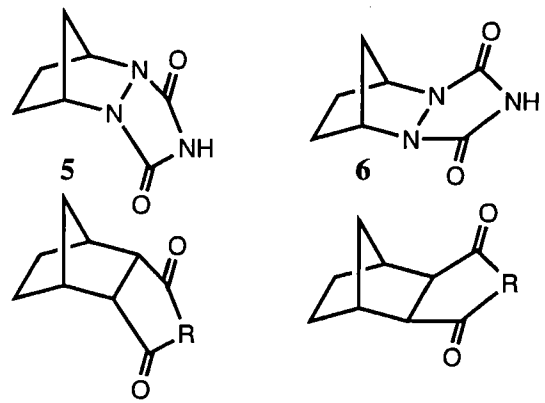


Fig. 1. 500 MHz ^{1}H-NMR spectra of **3** in acetone-d_6 (1a), and **3** (1b), **4** (1c) and **1** (1d) in C_6D_6. Signal labeling is discussed in the text. In 1a, (**x**) marks residual -CHD_2 of acetone-d_6 at 2.04 ppm.



To gain some insight into the reasons for chemical shift differences of *exo* and *endo* $H_{5,6}$ protons described above, we have optimized the energies of model urazoles **5** and **6** (C_1 symmetry) using the PM3 semi-empirical and 3-21G* ab initio calculations. These calculations show that **6** is lower in energy than **5** by about 1.0 (PM3) or 0.8 (3-21G*) kcal/mol. Since **5** and **6** interconvert rapidly by N-inversion, about 25% of molecules are predicted to possess *endo* conformation **5** based on the 3-21G* calculations. Examination of HOMO-LUMO orbitals of **5**, **6** and **1** suggest that *endo* $H_{5,6}$ protons will experience similar shielding in **6** and **1**, but not in **5**. This is a qualitative conclusion based on the fact that in **5** the *endo* $H_{5,6}$ protons will be closer to the shielding regions of carbonyl groups.[7] The presence of two rapidly interconverting isomers may explain the anomalous relative *exo* and *endo* $H_{5,6}$ chemical shifts in **3**. It is interesting to note that non-interconverting C-analogs of **5** and **6**, namely anhydrides **7**, **9**[13] and imides **8**,**10**[14] are known. However, the stereochemistry of their NMR signals is not presently assigned. We are currently preparing these compounds and will report detailed assignment of their proton spectra in future publications.

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