cis-Azoxyalkanes. 11. Lanthanide Induced Nuclear Magnetic Resonance Shifts; Metal Complexation at Nitrogen[1]

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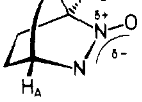
In order to gain insight into the magnetic properties of the *cis*-azo *N*-oxide moiety, lanthanide induced shift (LIS) measurements utilizing $Yb(dpm)_3$ have been made for the proton NMR of a series of six *cis*-azoxyalkanes. The ^{13}C spectra for two of the samples have been similarly monitored. Although an N/O site averaging system cannot be ruled out with certainty, the LIS behavior is dominated by a model in which Yb coordinates to nitrogen at a distance of 2.7 Å. The lanthanide residue is shown to reside approximately 25° above the plane determined by N, N, and O. Careful analysis of the well-resolved spectrum of an unsaturated *N*-oxide derivative permits an unambiguous assignment of all of the protons in the molecule. The results allow the conclusion that the delocalized NNO unit is less shielding for protons lying above the π cloud than for a CC double bond with hydrogen similarly situated.

Bicyclic *cis*-azo *N*-oxides **1** exhibit unusual proton NMR spectra.[2] Relative to the corresponding azoalkanes **2**, both bridgehead hydrogens, H_A and H_B, are found upfield from H_C. Analysis of the ^1H NMR spectra of trans acyclic azo and azoxy derivatives in connection with the *cis*-bicycles suggests that the *cis*-azo bridgehead hydrogens experience a remarkable diamagnetic shift of around 1.5 ppm.[2b] The origin of the disparate chemical shift values of H_A/H_B and H_C for **1** and **2**, respectively, has, however, yet to be identified unambiguously.



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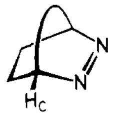

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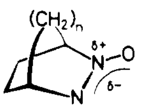
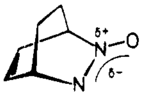
A second noteworthy feature of the proton NMR spectra of the *cis*-azoxy moiety is the observation that for a wide range of bicycles, H_A and H_B display coincident chemical shifts.[2,3] Given the asymmetry and the variable electronegativity of the two nitrogens in the NNO function, the chemical equivalence of the bridgehead hydrogens is not entirely expected. A theoretical analysis intimates that the conformation rigidity of the bicyclic framework coupled to the planarity of NNO results in the cancellation of opposing anisotropic effects.[2b]

In order to obtain additional insight into the NMR properties of *cis*-azo *N*-oxides, lanthanide induced shift (LIS) measurements have been carried out for a series of polycyclic *cis*-azoxy compounds: **3a–c**, **4**, **5**, and **6**. The series offers the experimentor a novel challenge in the interpretation of the LIS experiment. In contrast to most LIS studies, the structures of the substrates are firmly established,[5] the conformational details are well understood, and the distinct ^1H NMR resonances in the undoped spectra are all properly assigned.[2b] Thus, the LIS data can be used to probe the nature of the lanthanide–azoxy interaction.



3a (n=1)
b (n=2)
c (n=3)



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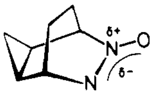

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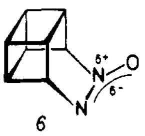

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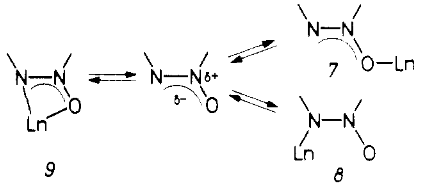
The two Lewis base sites situated in the azo *N*-oxide moiety **1** give rise to three distinct possible ways in which the lanthanide could chelate. If the complex is monodentate, then the site of interaction may be oxygen (**7**), nitrogen (N(NO), **8**), or some equilibrium combination of **7** and **8**. Taylor and co-workers have suggested an $Eu(dpm)_3$–oxygen coordination complex based on studies with acyclic azo *N*-oxides.[6] This interpretation is not problem free, however, since of the lanthanides Eu possesses an exceptional potential for inducing contact shifts.[7] If the complex is bidentate, a realistic possibility because of the close proximity of the two base sites, the principal magnetic axis (PMA) might be oriented somewhere between oxygen and N(NO), **9**.



Analysis of the geometric disposition of ligand and lanthanide employs the computer program PDIGM.[8] This scheme moves the lanthanide moiety stepwise in three space about the organic ligand until the best fit with experimentally determined lanthanide induced shifts is obtained. Since the algorithm requires that the site of complexation be uniquely specified, the bidentate complex is difficult to treat. The fixed site constraint demands that all possible complexation geometries be searched individually. Due to the tediousness of such a task, we have chosen to investigate the more straightforward situations (**7** and **8**) for consistency with the experimental data.

Rigorous definition of the monodentate complex mixture

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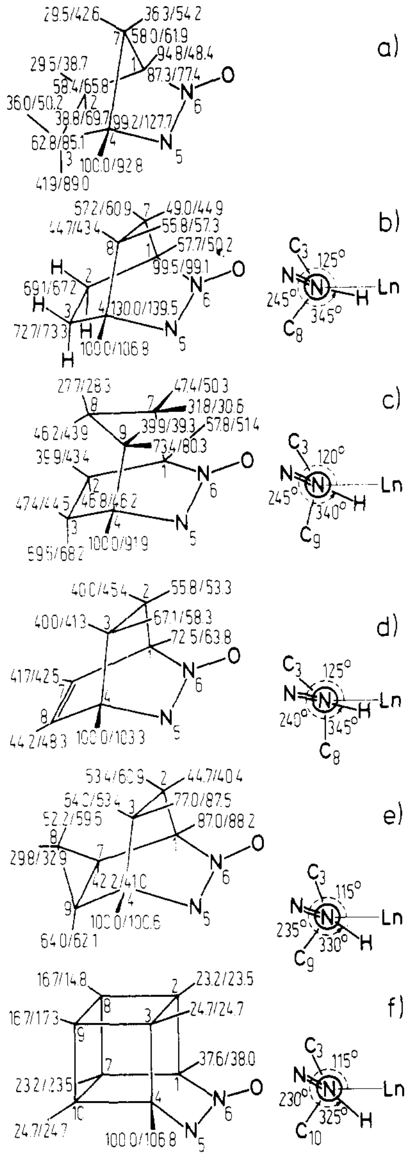


Figure 1. Azo *N*-oxide experimental and calculated (PDIGM) lanthanide induced shifts [Yb(dpm)$_3$] for hydrogen and carbon, ppm (obsd/calcd). The Newman projections depict the N-5 to C-4 bond and indicate the associated dihedral angles: (a) **3a**; (b) **3b**; (c) **3c**; (d) **4**; (e) **5**; and (f) **6**.

with separate attachment at both N-5 and oxygen requires a minimum of nine adjustable parameters: four for each lanthanide location and the mole ratio between the two sites. All except two of the bicyclic azo *N*-oxides display less than nine observable shifts in the ^1H NMR experiment. Thus, rigorous mathematical analysis of the site-averaged equilibrium system cannot be carried out unambiguously.[9] For these reasons, we have elected to use the monodentate model with complexation at either N-5 or oxygen.

In addition to assuming a single site of complexation, PDIGM also assumes that the contact contribution to the total anisotropic shift is negligible and that the anisotropic region produced by the lanthanide chelate results in a computational model that is represented by the single-term McConnell–Robertson relationship:[10] $[\Delta H/H_0]_{obsd} = K[3\cos^2\theta - 1]/r^3$.

The shift reagent Yb(dpm)$_3$ has been employed in our studies to assure that the LIS is predominantly, if not exclusively, subject to analysis by the dipolar or pseudocontact shift model.[7] It is demonstrated below that this minimum computational model is sufficient to yield a relatively precise lanthanide–azoxy structure involving complexation at N-5.

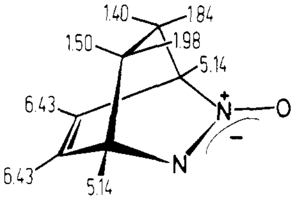


Figure 2. ^1H NMR chemical shifts (ppm from Me$_4$Si) for azo *N*-oxide **4** derived by extrapolating Yb(dpm)$_3$ shift values back to zero lanthanide concentration.

Experimental Section

Sample Purity. The crystalline azo *N*-oxides were prepared as previously described.[2b,11] The compounds were recrystallized to constant melting point. NMR spectra were identical with those reported earlier.

Yb(dpm)$_3$ Preparation. The reagent was prepared essentially by the procedure of Eisentraut and Sievers.[12] 2,2,6,6-Tetramethyl-3,5-heptanedione (60 mmol) (Pierce lot no. 10092-17) was dissolved in 95% ethanol and water (30 mL, 1:1). To this was slowly added an equimolar quantity of barium hydroxide dissolved in 50% ethanol and water with constant stirring. Yb(NO$_3$)$_2$·6H$_2$O (20 mmol) (American Potash and Chemical Co., lot no. LE 1168) dissolved in 50% ethanol and water (50 mL) was added to the above. The resulting mixture was stirred for 2 h, and the volume was reduced by 50%. The slurry was filtered, and the crude solid recrystallized from *n*-pentane. The purified product was allowed to dry for 8 h over P$_2$O$_5$ at 100 °C. The purity of the reagent was checked by its agreement with published results for the sublimation temperature.[13]

Preparation of Samples. ^1H NMR solutions were prepared by dissolving the appropriate azoxy compound (20 mg) in CDCl$_3$ (500 μL) containing Me$_4$Si (5 μL) and CHCl$_3$ (3 μL). ^{13}C NMR solutions were prepared by dissolving the compound (750 mg) in CDCl$_3$ (1.0 mL) containing Me$_4$Si (50 μL).

NMR Measurements. ^1H NMR spectra were obtained on a Varian HA-100 spectrometer under the following conditions: probe temperature of 36.1 °C, frequency sweep mode, and a Me$_4$Si internal lock. ^1H chemical shifts ($\pm$1 Hz) were measured from the chart paper calibrated by Me$_4$Si ($\pm$0.1 Hz) and CHCl$_3$ (726 $\pm$ 1 Hz).

^{13}C NMR spectra were obtained on a Varian CFT-20 spectrometer under the following operating conditions: continuous broad-band ^1H decoupling, 1000 pulses, and sweep width of 4000. The latter was determined by an acquisition time of 0.511 s. ^{13}C chemical shifts were measured digitally by using Me$_4$Si as 0.00 ppm.

^1H Runs. After the initial spectrum was run, Yb(dpm)$_3$ (3–5 mg) was added to the sample, the mixture was thoroughly mixed, and after a 5-min delay in the probe the spectrum was run again. This procedure was repeated seven times for each sample.

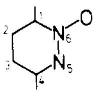
^1H and ^{13}C Combination Runs. The undoped ^{13}C sample was recorded on the CFT-20 spectrometer followed by removal of an aliquot (500 μL) for ^1H NMR scanning. The procedure was repeated seven times for each sample.

Data Reduction. The raw chemical shift data for each resonance at each doping level were reduced to the LIS indices for each resonance by the method of Apsimon.[13] These values were then corrected so that H-4 was assigned the value of 100. This scaling facilitates comparison of the various data sets. The calculated LIS indices were obtained in the following manner. (1) Externally referenced *x*, *y*, and *z* coordinates of every atom in the molecule were measured from a Dreiding model. (2) These external coordinates were transformed into internal Cartesian coordinates (site of complexation at 0,0,0 and the remainder of the molecule in the *z* direction) by the computer program ROTINT. (3) The internal coordinates were then used in another program (PDIGM) which incrementally steps the lanthanide reagent over all space within the coordinate system. At each step a set of unscaled LIS indices was obtained. The observed and calculated LIS indices were then compared by least squares, and an *R* factor was calculated.[8]

The results of the analyses for azo *N*-oxides **3–6** are presented in Figures 1 and 2.

Results and Discussion

Since the structural unit **10** is common to all of the azo *N*-oxides studied, the atoms were numbered as shown. In this way the numbers of the atoms in each compound reflect the spatial relationship of individual atoms to the lanthanide reagent.



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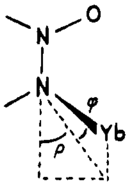
The question of whether the principal site of complexation occurs at N-5 or at oxygen seemed almost trivial at the outset of our PDIGM experiments. Intuitively, oxygen seemed to be the preferred site because of its steric accessibility and because it appears to possess a greater degree of negative charge than N-5. Semiempirical,[14] PRDDO,[19] and STO-3G[20] calculations utilizing the X-ray geometry[5] of azo *N*-oxide **3b** and the MINDO/3[18] optimized geometries for bicycles **3a** and **4** all place a greater share of electrons on oxygen than on N-5.[21] On the whole, however, the charges are similar and diminutive (**9**/STO-3G: $\rho_O = -0.23$; $\rho_{N\text{-}5} = -0.19$). It is important to recognize that complexation to the lanthanide is most likely related to nucleophilicity. The latter, in turn, is determined by the hardness or softness of the acceptor. In other words, the union is either charge or orbital controlled in the terminology of Klopman.[22] While La^{3+} has been classified as hard,[23] the $La(dpm)_3$ and $Yb(dpm)_3$ species are probably soft. Nucleophilic competition between N and O in the ambident anion NO_2^- for soft centers is delicately balanced, with nitrogen preferring the soft site.[24] Similarly, in a series of competition experiments for 9,10-dehydrophenanthrene, the soft order was established to be $LiNC_5H_{10}$ > LiNMePh > LiOPh.[25]

The assignments of the resonances in the lanthanide dispersed spectra further added to the quandry. The two bridgehead ^1H resonances, H-1 and H-4, are degenerate in the parent spectra so that assignment of the lanthanide induced H-1/H-4 split is not clearcut. Analysis of the situation for the syn and anti proton pairs at C-2 and C-3 implies an equally doubtful assignment at these sites. However, a retrospective analysis of the 100-MHz chemical shifts of the corresponding hydrogens in the unsaturated *N*-oxide **4** can be used to verify the assignments made by LIS (see below). In any event, a firm commitment to the uncertain assignments of the PDIGM algorithm would severely bias an ultimate choice of the site of complexation. The prejudicial viewpoint was overcome with an automatic permutation of assignments (using the AUTOASSIGN subroutine[8b]) coupled with confirmation of assignments from the unsaturated bicycle **4**.

In light of the above-mentioned complications, we elected the following strategy for interpretation. $Yb(dpm)_3$ LIS data were gathered because it is predominantly pseudocontact in nature.[7] The internal coordinates for each molecular model were arranged so as to place either N-5 or O at the origin of a Cartesian coordinate system, that is, the primary site of complexation. Then *R* factors were evaluated for both N-5 and O. The LIS indices were grouped into unambiguous categories such as bridgehead, vinyl, and aliphatic resonances and autoassigned within these groups. This screening led to *R* factors of less than 9% for N-5 as the binding site and greater than 40% for oxygen as the coordination center (see Table I and Figure 1). Thus, the first level of interpretation was accomplished; LIS behavior is dominated by the model in which N-5 is the coordination site for Yb at the 95% confidence level.

For other compound types using the same computational model, agreements of 2–3% are typically obtained.[8] An *R* factor of 9% raises questions concerning the nature of the *N*-oxide–lanthanide interaction. Site averaging between N-5 and O is a possible explanation. If this were the source of the higher *R* factors, we estimate that limited sampling of the oxygen site (e.g., 10%) would falsify the observed LIS indices. However, it is impossible to rigorously determine the site-averaging model because of the lack of sufficient observations for four of the compounds.

Table I. *R* Factors and Geometric Parameters for Coordination of $Yb(dpm)_3$ at the N-5 and O Sites of Polycyclic *cis*-Azo *N*-Oxides



	R, %	Yb site distance, Å	ρ,[a] deg	ϕ,[a] deg
		N-5 site		
3a	38.0	2.7	20	0
3b	7.6	2.7	50	15
3c	8.6	2.7	50	24
4	7.5	2.7	80	15
5	8.6	2.7	50	24
6	3.8	2.7	50	78
		O site		
3b	42.5	3.5	60	−15
3c	25.6	3.5	50	−6
4	41.6	3.5	80	−15
5	39.9	3.5	30	−80
6	26.6	3.5	30	0

[a] The optimal angles subtended by the Yb reagent relative to the planar NNO moiety.

Another possible cause of the high *R* factors could be the LIS assignments of the resonances. However, two arguments preclude AUTOASSIGN[8b] from being the source of the error. The first is that in contrast to the rest of the azo *N*-oxides, the ethano hydrogens in bicycle **4** are not degenerate because of the anisotropy of the contiguous olefinic CC bond. As a result, for every resonance in this compound it is possible to extrapolate back to zero lanthanide concentration (see Figure 2). In each case the unperturbed chemical shifts agree with those derived from AUTOASSIGN.

The second point eliminating AUTOASSIGN from consideration as the origin of the large *R* factors is that any change in the assignments from the ones made by the algorithm result in even higher *R* factors. This has been verified by assuming the lowest possible *R* factors and applying AUTOASSIGN to bicyclooctadiene **4**. Improper assignments of the LIS indices are thereby ruled out.

In light of the above arguments, the source of the high *R* factors must rest substantially with the N-5/O site-averaging problem. As we have stated above, a rigorous solution of the problem cannot be achieved for all of the compounds. We are consequently led to a solution that may not be entirely accurate, but it is precise. Nonetheless, the slight inaccuracies that may be entailed in the single site complexation model do not preclude the conclusion that the major site of lanthanide complexation is N-5.

In five of the six compounds (**3b,c**, **4–6**) the precision of the computational model is sufficient to eliminate oxygen as the major site of complexation. Confidence in this evaluation is substantiated by the consistent local geometry experienced by the lanthanide, N-5, and oxygen. In the five well-behaved cases, the lanthanide resides 2.7 Å from N-5 and is found ~25° below the plane determined by N-5, N-6, and O. Details are given in Figure 1. Were the local geometries not common, the argument for N-5 as the primary site of complexation would have been seriously weakened.

Conclusion

Complexation of the lanthanide reagent to N-5 in the NNO moiety and the attendant modification of the NMR spectra have several consequences. Our earlier Eu(dpm)$_3$ and ^{13}C determination that *cis*-azoxyalkanes are unsymmetrical[2b] in spite of coincident bridgehead proton chemical shifts is fully confirmed. Moreover, both carbon and hydrogen α to trivalent nitrogen experience the greatest overall lanthanide induced shifts (Figure 1). Since certain bicyclic azo *N*-oxides undergo sequential base-catalyzed deuterium exchange at the bridgehead positions,[4] the site of deprotonation can now be specified with certainty. If the intermediate bridgehead anions prove exploitable as synthetic entities, isomeric substitution sites should also be readily identifiable.

The LIS analysis of *N*-oxide 4 allows a comparison of the diamagnetic anisotropy of the double bond vs. the NNO unit. Figure 2 indicates that protons lying over the carbon unsaturation are shielded by 0.4–0.5 ppm more than those positioned over the nitrogens. This outcome obtains even though hydrogens syn to NNO are slightly closer to nitrogen than those syn to C=C are to carbon.[26] Reduced shielding by the hetero unit is undoubtedly due to orbital shrinkage at the relatively electronegative nitrogen compared to carbon and to the unsymmetrical dispersal of π-electron density away from nitrogen by virtue of conjugation with oxygen.

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Registry No.—**3a**, 22509-00-8; **3b**, 25926-96-9; **3c**, 26081-83-4; **4**, 37436-17-2; **5**, 25926-99-2; **6**, 34098-80-1; Yb(dpm)$_3$, 15492-52-1.

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(26) This has been demonstrated for **3b** by X ray[1a] and derives from the shorter C–N bond lengths. A full geometry optimization for bicycles **3a** and **4** with MINDO/3 yields the same result.[1a]

Low-Temperature Photochemical Matrix Aposynthesis of an Oxathiete and Its Valence Tautomerism with the Corresponding α-Ketothione[1]

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Photochemical elimination of carbon monoxide from 5-methyl-1,3-benzoxathiol-2-one (**5b**) yields the transient monothio-*o*-benzoquinone **6b**. This, at 77 K, can be reversibly photoisomerized into a species identified as the benzoxathiete **7b** containing the previously unobserved oxathiete ring. When **5b** is irradiated in ethyl vinyl ether at room temperature, trapping occurs regiospecifically to give the adduct **11a**, which then undergoes a photochemical rearrangement to yield **12**. Spectroscopic evidence suggests that the transients may experience a second elimination of carbon monoxide to give the cyclopentadienethione **9a**. Monothiobenzil (**1b**) and monothiopivaloyl (**1a**) do not appear to undergo an analogous photoisomerization to give the corresponding oxathietes. 1,3-Benzodithiol-2-one (**5e**) also loses carbon monoxide photochemically to give a transient identified as benzodithiete (**7e**), which can be trapped by dimethyl acetylenedicarboxylate.

There have been few descriptions of α-ketothiones;[2–7] those so far reported are α-ketothiocamphor,[3] monothiopivaloyl[2] (**1a**), and monothiobenzil[6] (**1b**). Their spectroscopic properties indicate that, to at least a large degree, **1a** and **1b** exist as α-ketothiones rather than the oxathietes **2a** and **2b**, and attempts to demonstrate the existence of oxathietes have been unsuccessful.[5,6] Recently we reported[2,8] the preparation of α-dithiones **1c**, **1d**, and **1e** and were successful in observing

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