unlikely that the two diastereomeric chelates would undergo a rapid rate of interconversion in view of the fact that (1) Ga^{3+} catecholamide complexes typically have high formation constants, on the order of 10^{30}, and (2) the interconversion would require the total dissociation of the two catecholate groups in addition to multiple bond rotations, which would amount to a fairly large expenditure of energy. However, if the two diastereomeric chelates do exist as two rapidly interconverting species, then heating should result in a coalescence of the duplicate signals in the ^1H NMR spectrum.

A sample of the parabactin–gallium chelate in Me_2SO-d_6 was heated over the range 20–130 °C, and although the difference between the two γ-methyl signals decreased with increasing temperature, they never coalesced. In fact, none of the signals present in duplicate in the ^1H NMR spectrum of the chelate coalesced over the temperature range 20–130 °C. The decrease in separation between the two γ-methyl doublets was a result of both signals moving downfield by approximately 20–30 Hz during heating, the upfield doublet moving slightly further downfield than the downfield doublet. It should be pointed out that the γ-methyl signal of the homoparabactin–gallium chelate also displayed a chemical shift dependency on temperature of this same magnitude. Also, after the parabactin–gallium sample was allowed to cool to room temperature after heating to 130 °C, it appeareed identical with that which was taken prior to heating. The data cannot rule out the eventual coalescence between the two diastereomeric coordination isomers. However, the difference between the γ-methyl signals was still 7.3 Hz at 130 °C, which would make the eventual T_c (if one exists) extremely high. It is the belief of the authors that the parabactin–gallium chelate exists as two separate, extremely slow interconverting diastereomers.

An additional point of interest brought out by the ^1H NMR data concerns the rate of racemization of the Λ cis chelate. It is strongly suggested that the Λ cis gallium chelate is formed exclusive of the Δ cis complex. The data also suggest that the Λ cis chelate racemizes to the Δ cis complex very slowly, if at all. Racemization to the Δ chelate would, of course, be easily detected by NMR in the form of additional signals appearing, specifically the appearance of a γ-methyl signal downfield to the γ doublet of the Λ cis chelate. Even after standing in D_2O or Me_2SO-d_6 for several weeks, no additional observable ^1H NMR signals were detected. Additionally, heating a solution of the chelate in Me_2SO-d_6 to 130 °C did not result in any new signals.

Conclusions

The spermidine catecholamide siderophore, parabactin, appears to form a 1:1 complex with gallium(III). The ^1H NMR data strongly suggest the absolute configuration of the parabactin–gallium chelate is Λ cis. Upon complexation with gallium, parabactin appears to form the Λ cis chelate to the exclusion of the Δ cis coordination isomer. Furthermore, the Λ cis gallium complex appears to exist in a 3:1 ratio of two diastereomeric forms, Λ cis-3,4 and Λ cis-4,3 which differ only in the disposition of the spermidine backbone. A ~180° rotation about the N^4–C(O) bond by the ligand any time prior to chelation will lead to the two diastereomeric coordination isomers upon chelation; thus, the conformation equilibrium existing in the free ligand may dictate diastereomer ratios in the metal chelate. This hypothesis lends support to Neilands' proposal that the equilibrium between the two major conformers in the spermidine siderophores results from a cis–trans isomerization about the N^4–C(O) amide bond. Our study further suggests that in the solvents examined, the free ligand, parabactin, exists as three interconverting conformational isomers. Data strongly support the idea that the internal rotational barrier that must be overcome for interconversion of these conformers is partially dependent upon intramolecular hydrogen bonding. In particular, the hydrogen bond donor ability of the catechol groups appears to play a major role in the conformational equilibrium of the ligand.

The elucidation of the stereochemistry of parabactin's gallium chelate will aid in the evaluation of metal–parabactin receptor specificity in *Paracoccus denitrificans*. Experiments are now in progress to evaluate ferric–siderophore outer membrane interactions in various pathogens for the purpose of designing and developing new bacteriostatic agents.

Registry No. 1, 63076-44-8; **2**, 89675-84-3; **3**, 89675-85-4; **4**, 82247-46-9; **5**, 74149-70-5; **6**, 89675-86-5; 7, 89675-87-6; **8**, 89675-88-7; **9**, 89675-89-8; **10**, 89675-90-1; *N-tert*-butoxycarbonyl-L-threonine, 2592-18-9; N^1,N^8-bis(2,3-dimethoxybenzoyl)spermidine, 78217-75-1; ethyl 2-hydroxybenzimidate, 20857-12-9.

A New NMR Method for Measuring the Difference between Corresponding Proton and Deuterium Chemical Shifts. Isotope Effects on Exchange Equilibria

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Abstract: A convenient and accurate method is described for measuring the difference between a proton frequency and the corresponding deuterium frequency in its deuterated analogue relative to a reference system by using the deuterium lock in a Fourier-transform NMR spectrometer. This measurement is a sensitive way of measuring equilibrium isotope effects for hydrogen–deuterium exchange. A value of 1.60 per H–D pair is obtained for the equilibrium $2H_3O^+ + 3D_2O \rightleftharpoons 2D_3O^+ + 3H_2O$ at 30 °C in aqueous perchloric acid ($HClO_4$).

Isotope effects on exchange equilibria have previously been measured in several ways as well as calculated from spectroscopic data.[1] Many of the experimental methods are tedious or of limited accuracy, and the spectroscopic data are not always available for the calculations, which are, in addition, time consuming. Since equilibrium isotope effects result from differences in vibrational force constants at sites in different molecules and can yield important information about these variations, it would be desirable

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[‡] We would like to dedicate this paper to the memory of Susan Saunders who died in January 1982.

(1) For reviews, see: (a) Wolfsberg, M. *Acc. Chem. Res.* **1972**, *5*, 225. (b) Wolfsberg, M. *Annu. Rev. Phys. Chem.* **1969**, *20*, 449.

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Table I. Intrinsic Isotope Shifts (ppm) (Relative to Acetone)

cyclohexane	0.038	toluene (aromatic)	−0.015
ether (methyl peak)	0.028	tetrachloroethane	−0.015
ether (methylene)	0.016	chloroform	−0.019
p-dioxane	0.006	methyl iodide	−0.020
toluene (methyl)	0.004	acetonitrile-d_2	−0.024
acetone	0.000	acetone-d_s	−0.036
acetonitrile	−0.001	water	−0.044
nitromethane	−0.005	water-d_1	−0.058
Me_2SO	−0.008	benzene-d_s	−0.071
methylene chloride	−0.012	benzene	−0.076

to have a convenient, accurate procedure for measuring exchange equilibrium isotope effects in a wide variety of systems.

We describe here a rapid and precise new method for measuring the difference between corresponding proton and deuteron NMR chemical shifts relative to the shifts in a reference compound utilizing the deuterium lock present in most Fourier-transform NMR spectrometers. We have applied this procedure to determine an equilibrium isotope effect in a system undergoing rapid hydrogen–deuterium exchange.

Method

The following procedure was used to make all measurements. A sample containing completely protonated and completely deuterated forms of a reference substance is placed in the spectrometer which is locked on the deuterium signal (F_D). The proton signal is then observed and its frequency set to zero (F_H). Another sample containing protonated and deuterated forms of the molecule to be studied is inserted without changing any spectrometer setting, the spectrometer is relocked on its deuterium signal ($F_{D'}$), and the proton frequency for the new substance is measured ($F_{H'}$).

We have applied this procedure to a number of molecules (see Table I) using a reference sample containing a mixture of acetone and acetone-d_6. The samples used for the measurement were mostly the completely deuterated materials with small amounts of the protonated materials added. Measurements of all compounds were made several times at 90 MHz, and a number of the compounds were also examined at 270 and 500 MHz with reproducible and consistent results.

For samples containing simple compounds and their deuterated analogues, the frequencies measured this way were found to be small as expected. The reason for this is that the deuterium lock mechanism shifts the *field* (in ppm) by exactly the difference in F_D between the substances, and the difference (in ppm) between the F_H values is similar. We therefore directly measure $(F_H - F_{H'}) - (F_D - F_{D'})$ which can be rearranged to $(F_H - F_D) - (F_{H'} - F_{D'})$. If $F_H - F_D$ is taken as zero for our reference compound (which is equivalent to using the H and D peaks in this substance as the origins of the H and D frequency scales), the measurement yields a *relative* value for $F_{H'} - F_{D'}$. We call these measured $F_{H'} - F_{D'}$ differences, which were small but reproducible, the relative intrinsic isotope shifts.

One could call an intrinsic isotope shift *primary* or direct if one could observe the difference between the shifts of the isotopically different nuclei in the same position in a molecule. However, in order to examine the effect of an isotopic substitution directly on the nucleus substituted, the two isotopes must both have magnetic moments and their NMR signals must be measurable. Separate measurement of the NMR spectra of the two isotopes could be done, but the result would seldom be accurate enough to determine intrinsic isotope shifts. For accurate determination of the isotopic difference, we must have a way of measuring the relative shifts of the different nuclei in the same sample at the same time. The method described above for measuring the relative H–D shift fits these requirements.

A variant of this effect, which could be called a *secondary* intrinsic shift, occurs when one or more of a group of identical nuclei is isotopically substituted. The remaining nucleus or nuclei of the original isotope can be shifted in frequency from that in the non-isotopic molecule. Thus relative H–D shift differences can be obtained by using the residual hydrogen in the deuterated compound for the ^2H NMR signal. Some examples are listed in Table I. The results of a previous study[2] differ from those reported here due to secondary intrinsic isotope shifts for both the reference compound (acetone) and the measured sample.

Intrinsic isotope shifts result from zero-point vibration. They occur because *all* NMR frequencies are averages over the zero-point vibrational motion. The protonated and deuterated forms of a molecule should have exactly the *same* vibrational energy surface if the Born–Oppenheimer approximation can be validly made, and corresponding points on this surface should give the *same* chemical shift values for all nuclei in the isotopic species. However, due to the different amplitudes of zero-point motion, the *average* frequencies can in principle be different for the nuclei in an isotopically substituted molecule. Such intrinsic isotope shifts are commonly studied by observing the effect of isotopic substitution on the NMR signal of a nucleus which is *not* substituted (e.g., ^{13}CH vs. ^{13}CD, $^{31}P^{16}O$ vs. $^{31}P^{18}O$), and though these shifts are small they are often useful.[3]

Equilibrium Isotope Effects

Where a system contains a mixture of molecules undergoing rapid hydrogen–deuterium exchange, we expected and found much larger differences between the averaged proton frequency and the averaged deuterium frequency. We attribute these larger differences between the proton and deuterium frequencies to equilibrium isotope effects. The values of these relative shifts are functions of the equilibrium constants for exchange.

For the simple isotopic exchange reaction AH + BD → AD + BH with equilibrium constant

$$K_{iso} = \frac{[AD][BH]}{[AH][BD]} \tag{1}$$

where the quantities in brackets are equilibrium concentrations. If one assumes, in this case, that the intrinsic shift is relatively small, the weighted average proton frequency is

$$F_H = \frac{F_a[AH] + F_b[BH]}{[AH] + [BH]} \tag{2}$$

and the deuterium frequency is

$$F_D = \frac{F_a[AD] + F_b[BD]}{[AD] + [BD]} \tag{3}$$

where F_a and F_b are the proton frequencies in the *absence* of exchange. An isotope effect which causes more AD and BH to be present will clearly shift the deuterium frequency toward F_a and the proton frequency toward F_b, and this will be reflected in $F_H - F_D$, which can be measured by using the technique described above.

The case we studied was the proton–deuterium exchange equilibrium between hydronium ion and water in solutions of $HClO_4$ in H_2O–D_2O mixtures. The equilibrium constant L shown in eq 4 for relation 9 is for the interchange of six protons with six deuterons:

$$L = \frac{[H_3O^+]^2[D_2O]^3}{[D_3O^+]^2[H_2O]^3} \tag{4}$$

Therefore for an interchange of one H with one D

$$K_{iso} = L^{1/6} \tag{5}$$

This equilibrium has been reported to have a substantial isotope effect.[4]

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[2] Evans, D. F. *J. Chem. Soc., Chem. Commun.* **1982**, 1226.

[3] Batiz-Hernandez, H.; Bernheim, R. A. *Prog. Nucl. Magn. Reson. Spectrosc.* **1967**, *3*, 63. See also: Cohn, M.; Hu, A. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 200.

[4] For a summary see: Heinzinger, K.; Weston, R. E. Jr. *J. Phys. Chem.* **1964**, *68*, 744.

Table II

	acid concn	$[H]/([H] + [D])$	F_{obsd}	F_{calcd}	diff
1	6.090	0.8730	0.5050	0.5037	0.00130
2	4.060	0.8430	0.3495	0.3468	0.00269
3	2.710	0.8270	0.2380	0.2372	0.00077
4	1.806	0.8170	0.1605	0.1612	−0.00067
5	1.204	0.8110	0.1070	0.1090	−0.00199
6	0.803	0.8070	0.0720	0.0735	−0.00145
7	0.535	0.8050	0.0480	0.0493	−0.00130
8	0.238	0.8020	0.0220	0.0221	−0.00012
9	9.140	0.8340	0.7415	0.7428	−0.00128
10	6.090	0.6820	0.5310	0.5364	−0.00537
11	4.060	0.6080	0.3800	0.3778	0.00217
12	2.710	0.5670	0.2640	0.2624	0.00156
13	1.806	0.5430	0.1800	0.1801	−0.00009
14	1.204	0.5280	0.1215	0.1226	−0.00113
15	0.803	0.5180	0.0850	0.0831	0.00194
16	0.535	0.5120	0.0540	0.0559	−0.00193
17	0.238	0.5050	0.0230	0.0252	−0.00220
18	9.140	0.6680	0.7810	0.7788	0.00219
19	6.090	0.3650	0.6020	0.6032	−0.00120
20	4.060	0.2170	0.4485	0.4467	0.00182
21	2.710	0.1350	0.3200	0.3206	−0.00058
22	1.806	0.0862	0.2240	0.2245	−0.00051
23	1.204	0.0558	0.1545	0.1548	−0.00026
24	0.803	0.0366	0.1055	0.1055	−0.00004
25	0.535	0.0241	0.0720	0.0714	0.00063
		rms deviation:	0.00178		

Analysis of Data

The data were analyzed in the following manner. One may write, among many other possible equilibria, the following reactions.

$$H_3O^+ + HD_2O^+ \rightarrow 2H_2DO^+ \tag{6}$$

$$D_3O^+ + H_2DO^+ \rightarrow 2HD_2O^+ \tag{7}$$

$$H_2O + D_2O \rightarrow 2HOD \tag{8}$$

$$2D_3O^+ + 3H_2O \rightarrow 2H_3O^+ + 3D_2O \tag{9}$$

$$H_3O^+ + ClO_4^- \rightarrow H_2O + HClO_4 \tag{10}$$

$$D_3O^+ + ClO_4^- \rightarrow D_2O + DClO_4 \tag{11}$$

Relations 6 through 9 were selected because they interconnect the concentrations of all the isotopic hydronium ion and water species. Un-ionized perchloric acid and its deuterated analogue are introduced by (10) and (11). There are four overall constraints on the system which are not affected by the above equilibria: the charge neutrality

$$[H_3O^+] = [ClO_4^-] \tag{12}$$

the total amount of acid

$$\text{total acid} = [H_3O^+] + [HClO_4] \tag{13}$$

the total amount of water

$$\text{total water} = [H_2O] + [H_3O^+] \tag{14}$$

and the fraction $[H]/([H] + [D])$. The total concentrations of acid and water and the H/D ratio were determined by measuring the density of the 70% perchloric acid and by titrating the acid, in addition to measuring precisely the quantities of H_2O and D_2O added for each dilution. The four constraints plus the six equilibrium relations thus completely define the concentrations of the species. The average proton and deuterium frequencies are functions of the concentrations of the ten species H_3O^+, H_2DO^+, HD_2O^+, D_3O^+, H_2O, HOD, D_2O, $HClO_4$, $DClO_4$, and ClO_4^- and their frequencies as discussed above.

The values of $F_H - F_D$ for the aqueous perchloric acid solutions were measured by using H_2O–D_2O as the reference sample. Different ratios of H/D in the reference sample produced no change in the data. The data are listed as a function of $HClO_4$ concentration in Table II. The $F_H - F_D$ differences are seen to be very much larger than the relative intrinsic isotope shifts found for nonequilibrating systems. The slope of the $F_H - F_D$ vs. concentration curve decreases at high $HClO_4$ concentrations. We believe that this is mainly due to incompletely dissociated $HClO_4$. Spectra taken as a function of temperature (10, 30, 60 °C) at 270 MHz showed almost no differences at low concentrations of $HClO_4$ and relatively small differences at high concentrations.

The somewhat complicated analysis of the $F_H - F_D$ data used to obtain the equilibrium constant, K_{iso} (eq 5), can be summarized by dividing it into the following logical steps: (1) For a particular set of equilibrium constants, the concentration of each species is determined for each experimental point. (2) The F_H and F_D can be calculated from the concentrations and frequencies of each species and then the rms deviation between the sets of calculated and observed values computed. (3) All the parameters (equilibrium constants and frequencies) which have not been determined in some other way can be adjusted with a multiparameter fitting program and then steps 1 and 2 repeated until the lowest values of rms deviation is obtained.

The first logical step is the determination of the ten unknown concentrations. Instead of attempting to solve the ten equations for the ten unknown concentrations in closed form as a function of the equilibrium constants and the constraints on the concentration, we obtained the concentrations by a successive-approximation method. We set up initial values of the concentrations which obeyed the overall constraints (eq 12–14) and then used the equilibrium relations (eq 6–11) to calculate the signs and magnitudes of the deviations from equilibrium. A computer program was written to alter the concentrations in the direction of equilibrium until the deviations were very small. In effect, we simulated the kinetics of approach to equilibrium by integrating the differential equations numerically.

In addition to the concentrations, the frequencies of the individual species are needed for calculating $F_H - F_D$. The frequencies of water and D_2O were set to zero since the $F_H - F_D$ shifts of the perchloric acid solutions were measured with respect to a water–D_2O reference sample, making water and D_2O the origins of the proton and deuterium scales, respectively. The remaining frequencies required are the following: the proton frequency of H_3O^+ and the deuterium frequency of D_3O^+, which can differ because of an intrinsic isotope shift, and the frequencies of $HClO_4$ and $DClO_4$. The proton frequencies of all of the mixed H–D species were assumed to be the same as were all the deuterium frequencies. In other words, no secondary intrinsic shifts were assumed. In addition, the acid dissociation constant for $HClO_4$ (reacting with water) and the corresponding dissociation constant for $DClO_4$ (reacting with D_2O), the self-equilibrium constants (eq 6–8), and finally the isotope effect (eq 9) are required for the analysis.

We tried to independently determine as many of these parameters as possible. We used the results of theoretical calculations for the self-exchange equilibrium constants (eq 6–8) which have been predicted to differ slightly from the statistical values.[1a] For eq 6 and 7, we have used values of K = 2.93 and 2.94 as calculated for the hydrogen–deuterium self-exchange equilibria for ammonia molecules.[5a] For eq 8 K = 3.84 was used as calculated by Wolfsberg[5b] in good agreement with experimental values.[5c,5d]

The concentration dependence of the proton shift in aqueous solutions of perchloric acid was measured and the data analyzed to attempt to obtain the frequency of H_3O^+, the equilibrium constant for ionization of $HClO_4$, and the frequency of $HClO_4$. To make the measurement, the instrument was set up with a water sample containing a D_2O capillary for a lock. After the proton signal of this sample was set to zero, a series of solutions of $HClO_4$

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(5) (a) Bron, J.; Wolfsberg, M. *J. Chem. Phys.* **1972**, *57*, 2862. (b) Wolfsberg, M.; Massa, A. A.; Pyper, J. W. *J. Chem. Phys.* **1970**, *53*, 3138. (c) Friedman, L.; Shiner, V. J., Jr. *J. Chem. Phys.* **1966**, *44*, 4639. (d) Pyper, J. W.; Newbury, R. S.; Barton, G. W., Jr. *J. Chem. Phys.* **1967**, *46*, 2253.

J. Am. Chem. Soc. **1984**, *106*, 3101–3113

in H_2O, each containing a D_2O capillary, was examined. The quantities K_{diss}, $F_{\text{H}_3\text{O}^+}$, and F_{HClO_4} were fit to the observed frequencies where

$$K_{\text{diss}} = \frac{[\text{H}_3\text{O}^+][\text{ClO}_4^-]}{[\text{H}_2\text{O}][\text{HClO}_4]} \tag{15}$$

$$F_{\text{obsd}} = \frac{3F_{\text{H}_3\text{O}^+}[\text{H}_3\text{O}^+] + 2F_{\text{H}_2\text{O}}[\text{H}_2\text{O}] + F_{\text{HClO}_4}[\text{HClO}_4]}{3[\text{H}_3\text{O}^+] + 2[\text{H}_2\text{O}] + [\text{HClO}_4]} \tag{16}$$

Using a program which obtains the best root-mean-square fit to the data, one obtains $F_{\text{H}_3\text{O}^+} = 9.333$ ppm. This may be compared with the earlier experimental value of Hood, Redlich, and Reilly, who obtained $F_{\text{H}_3\text{O}^+} = 9.17$ ppm.[6] Precise independent values for F_{HCLO_4} and K_{diss} could not be determined because these parameters were very strongly correlated. If both were varied maintaining the relation

$$K_{\text{diss}} = 1.79 - 0.105F_{\text{HClO}_4} \tag{17}$$

the rms (to be consistent with earlier use) deviation from the experimental data was affected little. The rms value improved slightly in the value of F_{HClO_4} went to high field (even above the frequency of water), but we believe that this is an artifact probably due to changes in the equilibrium constant and NMR properties of the solutions at high concentrations of perchloric acid. Thus, to fit the $F_\text{H} - F_\text{D}$ data we used $F_{\text{H}_2\text{O}} = 0$ and $F_{\text{H}_3\text{O}^+} = 9.333$ ppm.

With use of a multiparameter nonlinear least-squares fitting program to adjust the remaining parameters K_{iso}, $F_{\text{D}_3\text{O}^+}$, F_{HCLO_4}, F_{DClO_4}, and K_{diss}, all the data could be fit very well as shown in Table II. However, with so many free parameters, this is not surprising. Interactions between the parameters made it possible to vary pairs of them considerably without changing the rms deviation very much. The best fit rms deviation was 0.00178 ppm for $F_{\text{D}_3\text{O}^+} = 9.00$, $F_{\text{HClO}_4} = 5.70$, $F_{\text{DClO}_4} = 4.76$, $K_{\text{diss}} = 0.27$, the ratio of K_9 over $K_8 = 0.71$, and $K_{\text{iso}} = 1.60$.

All schemes, which we used for fitting the data, yielded a lower value for $F_{\text{D}_3\text{O}^+}$ than for $F_{\text{H}_3\text{O}^+}$. This would be an intrinsic isotope shift of 0.33 ppm (D_3O^+ relatively upfield relative to the water reference system). The magnitude of this shift is much larger than the values reported in Table I (±0.05 ppm); however, the broad shallow potential surfaces associated with the very strong hydrogen bonds to hydronium ion might cause this.[7] We are not sure that the difference between the fit values of F_{HClO_4} and F_{DClO_4} is significant and whether it indicates a similar large intrinsic isotope shift because of uncertainties in the fitting process as described above.

The reproducibility of our data is about ±0.2 Hz which leads to an uncertainty of ±0.1% in K_{iso}. Uncertainty of the value for the chemical shift difference between hydronium ion and water is one source of error in addition to the uncertainties in the fitting process. Also we do not know exact values for the equilibrium constants of eq 4–6. However, using the values of 2.93, 2.94, and 3.84 ppm yields a final result which is only different by 1% from the result obtained by using the statistical values of 3 and 4 ppm, since the effect of these changes in the two constants tends to cancel. Independent information about these constants might be obtained if measurements using this method were carried out at very high or low deuterium concentration. Then it should be possible to analyze the data with use of only the simple equilibria $D_3O^+ + HOD \rightleftharpoons HD_2O^+ + D_2O$ or $H_3O^+ + HOD \rightleftharpoons H_2DO^+ + H_2O$ without including the self-equilibrium constants in the analysis.

The present measurement of K_{iso} differs from previous measurements by specifically including the self-exchange equilibria and all of the interacting species in the analysis. Previous measurements by a variety of techniques rely on a generalized treatment of the data which results in a lower value of K_{iso} (1.41–1.5 ppm as summarized in Table III of ref 4). For example, in the most recent measurement, Heinzinger and Weston obtained $K_{\text{iso}} = 1.44$ ppm (D preferentially in water) by measuring the isotopic composition of the vapor over aqueous perchloric acid solutions at 13.5 °C.[4] Since their work was done with deuterium at natural abundance, they were actually measuring $H_3O^+ + HOD \rightleftharpoons H_2DO^+ + H_2O$ and *not* $(L)^{1/6}$.

The water–hydronium ion system is a complicated one and therefore has required a complicated analysis. However, cases where the molecules undergoing hydrogen–deuterium exchange have fewer exchangeable protons should be far simpler to analyze. Preliminary studies have indicated $F_\text{H} - F_\text{D}$ shifts in some of these systems, which are smaller than those reported in the present case; however, the use of very high field spectrometers should provide data of sufficient precision and accuracy for their useful analysis.

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Registry No. $HClO_4$, 7601-90-3; deuterium, 7782-39-0.

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(7) A similar large intrinsic shift has been reported for the strongly hydrogen bonded proton in the enol of acetylacetone. (a) Altman, L. J.; Laungani, D.; Gunnursson, G.; Wennerstrom, H.; Forsen, S. *J. Am. Chem. Soc.* **1978**, *100*, 8264–66. (b) Chan, S. I.; Lin, L.; Clutter, D.; Dea, P. *Proc. Natl. Acad. Sci. U.S.A.* **1970**, *65*, 816.

NbO and TiO: Structural and Electronic Stability of Structures Derived from Rock Salt

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Abstract: The reasons underlying the structural stability of the four-connected NbO net and the "ordered defect" structure of stoichiometric TiO are presented. After showing the failure of an ionic model to account for the structures of these compounds, we show how the electronic structure of these materials explains their unique crystal structures. Analogies to M_6X_{12} clusters prove especially fruitful in this analysis. Both metal–metal bonding and metal–oxide π bonding are important in stabilizing these structures. The way in which vacancies enhance metal–metal bonding is discussed. Finally we conclude with a discussion of energetics and compare NbO with other four-connected nets.

In the field of structural chemistry those compounds that invariably hold the greatest fascination are those whose structures refuse to conform to our simple ideas of what they "ought to be". Prime examples of such compounds are the simple binary oxides

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