Observation of Kinetic Tritium Isotope Effects by Dynamic NMR. The Tautomerism of Porphyrin

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In recent years NMR has been established as an unconventional kinetic tool for the study of kinetic hydrogen/deuterium isotope effects of degenerate multiple proton transfer reactions.[2] However, although ^{3}H (≡T) NMR has previously been used to follow triton transfer reactions,[3] the obvious extension of this approach to measure kinetic hydrogen/tritium isotope effects by combined ^{1}H and ^{3}H NMR line-shape analysis has not yet been reported to our knowledge. As with many simple and powerful NMR applications of tritium, this may be because tritium is radioactive, and some additional sample preparation and handling precautions are required.

As the knowledge of tritium isotope effects is desirable from a theoretical standpoint,[4] we have applied ^{3}H NMR in order to study these effects in the case of the double-hydron tautomerism of ^{15}N-labeled porphyrin (Figure 1). In previous work it was shown[2g] that the rate constants and kinetic HH/HD/DD isotope effects are the same whether the porphyrin is dissolved in organic solvents or is in the polycrystalline state. The HH/DD isotope effects are large, i.e., 11 at 298 K, but the HD/DD isotope effects are only about 2. This is indicative[2g,5] of (i) a stepwise reaction mechanism as proposed theoretically,[6] involving two successive single-hydron transfers passing a metastable cis-intermediate, and (ii) the absence of equilibrium and secondary kinetic isotope effects in each reaction step. When the kinetic data obtained by NMR are combined with low-temperature data of porphyrin in solid hexane,[7] the Arrhenius curves are found to be strongly nonlinear. For example, the activation energy of the HH transfer is ca. 37 kJ mol^{-1} at 300 K but only ca. 26 kJ mol^{-1} at 110 K. The large isotope effects and nonlinear Arrhenius behavior are indicative of thermally activated single-hydron tunneling,[2g,6e,7] providing additional motivation to study the tritium isotope effects.

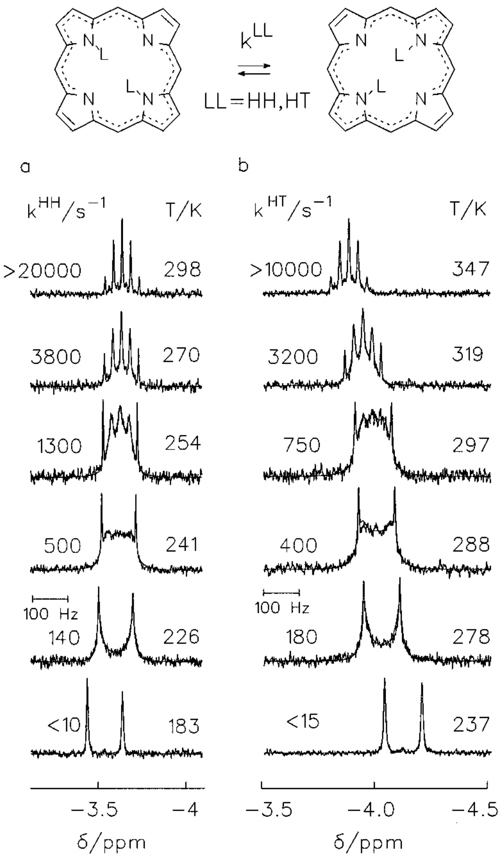

Figure 1. Superposed experimental and calculated NMR signals of (a) the inner protons of porphyrin-$^{15}N_4$ dissolved in toluene-d_8 (500 MHz, adapted from ref 2g) and (b) of the inner tritons (640 MHz, 6.5 μs 60° pulses, 13 kHz spectral width, 3.5 s repetition time) of porphyrin-$^{15}N_4$ dissolved in dimethylformamide-d_7 tritiated to about 10% in the inner proton sites. Number of scans is between 200 and 700 below 280 and around 200 above 280 K.

Because of porphyrin solubility problems, we chose dimethylformamide-d_7 as a solvent for the ^{3}H NMR experiments.[8] By contrast, this solvent was not suitable for the low-temperature ^{1}H NMR experiments where toluene-d_8 was employed. This solvent change has no influence on the hydron transfer kinetics and leads only to different NMR chemical shifts. Some results are depicted in Figure 1. The superposed experimental and calculated ^{1}H signals of Figure 1a (tritium fraction $n_T = 0$) stem

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[5] The first single H or D transfer leads to the cis-intermediate. As a secondary isotope effect from the hydron at rest is negligible, the forward rate constants can be labeled as k^{H} or k^{D}. The cis-intermediate is converted to reactant or product—which are degenerate—with the backward rate constant k_{-}^{H} or k_{-}^{D}. In the absence of an equilibrium isotope effect for this step, it follows that $k^{H}/k_{-}^{H} = k^{D}/k_{-}^{D}$. Using the steady state approximation for the intermediate, it follows using formal kinetics that $k^{HD} = (k^{H}k_{-}^{D})/(k_{-}^{H} + k_{-}^{D}) + (k^{D}k_{-}^{H})/(k_{-}^{H} + k_{-}^{D}) = (2k^{H}k^{D})/(k^{H} + k^{D})$, $k^{HH} = k^{H}$, and $k^{DD} = k^{D}$. Therefore, $k^{HD}/k^{DD} = 2/(1 + k^{DD}/k^{HH}) \approx 2$ for $k^{HH}/k^{DD} \gg 1$, fulfilled experimentally.[2g] The extension to the HT and DT hydron pairs is straightforward. Further details are provided in refs 2a−g.

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[8] A saturated solution of 3 mg of porphyrin-$^{15}N_4$ in dichloromethane was transferred using a syringe into a 25 mL flask attached to a vacuum line. The flask contained 0.2 mg of freshly prepared, approximately 65% enriched T_2O, introduced by vacuum transfer.[3b] After 10 min of stirring, the liquids were removed *in vacuo*. In order to remove any residual water, the porphyrin was again dissolved in dry dichloromethane which was removed in the same way. This procedure was repeated twice. The degree of tritiation was determined through the amount of needle-transferred dimethylformamide-d_7 containing a known amount of water. The dissolved sample was finally transferred into a NMR tube attached to the same vacuum line and flame-sealed for NMR observation.

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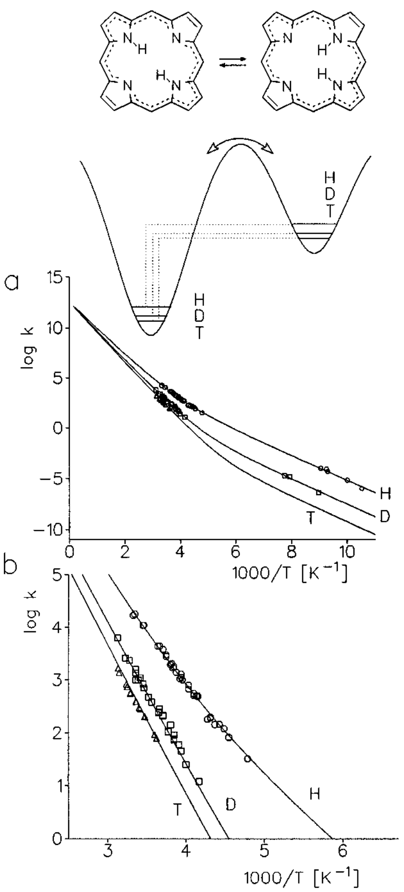

Figure 2. Arrhenius diagram of the single-proton/deuteron/triton motion in porphyrin embedded in various liquid and solid environments. The values of the proton and deuteron motion were taken from refs 2g and 7a, and those for the triton motion were obtained in this study. The solid lines were calculated in terms of a modified Bell tunneling model.[9]

from porphyrin-$^{15}N_4$-H_2, and the ^{3}H signals of Figure 1b stem from porphyrin-$^{15}N_4$-HT ($n_T = 0.1$). Small contributions from porphyrin-$^{15}N_4$-T_2 were observed only at $n_T = 0.3$. At low temperatures, the signals are split into doublets, arising from localized hydrons scalar coupled to single ^{15}N atoms. As temperature is increased, characteristic line-shape changes occur, leading to pentets which indicate fast intramolecular hydron transfers between all four nitrogen sites. The transition temperatures for the HH and HT processes are very different, revealing large kinetic tritium isotope effects.

By line-shape analysis the rate constants k^{LL} of the double-hydron transfers were determined as described previously,[2g] where LL = HH in the case of Figure 1a and LL = HT in the case of Figure 1b. k^{LL} can easily be converted into the rate constant k^L of the forward single-hydron transfer into the cis-intermediate.[5] Thus, using the data of Figure 1 and those measured previously,[2g,7a] it was possible to construct the Arrhenius diagram of Figure 2 referring to the first reaction step.[9] At 298 K, both kinetic isotope effects $k^H/k^D \approx 11.4$ and $k^D/k^T \approx 3.4$ are large. Their size and temperature dependence is indicative of tunneling and can be reproduced in terms of a modified one-dimensional Bell tunneling model.[2g] At low temperature, this model leads to a temperature independent isotope effect and a slope of the Arrhenius curves given by E_m/R, where E_m corresponds to the sum of a reorganization energy of the porphyrin skeleton and the energy of the cis-intermediate needed for tunneling to occur. The new data place strong constraints on the parameters for the one-hydron-tunneling model. They were freely varied in reaching the simultaneous fits of all three Arrhenius curves represented in Figure 2 by the solid lines.[9] The most important finding was that tunneling masses of 2.5, 3.5, and 4.5 were required for reproducing the H, D, and T data, respectively. Although this could signal merely the inadequacy of the one-dimensional Bell tunneling model employed, the result is consistent with a contribution of heavy atom tunneling arising from a slight readjustment of the porphyrin skeleton during the tunneling process. Another finding was that the value of $\alpha = \ln(k^H/k^T)/\ln(k^H/k^D)$ is about 1.5 at 298 K, not far from the Swain−Schaad value of 1.442 for nontunneling over barrier reactions.[4] This result, therefore, supports previous work showing that deviations from the Swain−Schaad value may be minimal when the size and temperature dependence of the isotope effects indicate that all hydrons tunnel through the barrier.[4]

In conclusion, the determination of kinetic tritium isotope effects is a powerful application of dynamic ^{3}H NMR. In the case of the tautomerism of porphyrin, these effects support the stepwise hydron-tunneling mechanism and can serve to test multidimensional tunneling models in the future. Currently, we are extending these studies to the case of the degenerate single-hydron transfer in the conjugate porphyrin anion.[10]

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Supporting Information Available: Tables with all kinetic parameters of the porphyrin tautomerism (6 pages). See any current masthead page for ordering and Internet access instructions.

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[9] Rate constants of the clockwise and/or counterclockwise single-hydron transfer obtained by linear regression: $k^H = 10^{10.7} \exp(-37.2 \text{ kJ mol}^{-1}/RT)$, $209 < T < 290$ K, $k^D = 10^{11.6} \exp(-48.5 \text{ kJ mol}^{-1}/RT)$, $240 < T < 320$ K, $k^T = 10^{12.8} \exp(-51.5 \text{ kJ mol}^{-1}/RT)$, $275 < T < 320$ K. Parameters of the modified Bell tunneling model (the values in parentheses stem from ref 2g): (i) barrier heights of the H transfer ${E_d}^H = 28.7$ kJ mol^{-1} (30.2 kJ mol^{-1}), ${E_d}^D = {E_d}^H + \Delta\epsilon^{HD}$, ${E_d}^T = {E_d}^H + \Delta\epsilon^{HT}$; (ii) $\Delta\epsilon^{HD} = 4.95$ kJ mol^{-1} (1.8 kJ mol^{-1}), $\Delta\epsilon^{HT} = \Delta\epsilon^{HD}(1-3^{1/2})/(1-2^{1/2}) = 7.15$ kJ mol^{-1}; (iii) minimum energy for H and D tunneling $E_m = 22.7$ kJ mol^{-1} (24 kJ mol^{-1}); (iv) barrier width $2a = 0.68$ Å (0.9 Å) for the H process; (v) frequency factor $A = 10^{12.6}$ s^{-1} ($10^{12.7}$ s^{-1}); (vi) $\Delta m = 1.5$ (0), where the tunneling masses are ${m_{eff}}^L = m^L + \Delta m$, $m^H = 1$, $m^D = 2$, $m^T = 3$ (fixed).

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