Special Paper

TD-¹H NMR Measurements Show Enantioselective Dissociation of Ribose and Glucose in the Presence of H₂¹⁷O

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ABSTRACT

We used Time Domain ¹H Nuclear Magnetic Resonance (NMR) to characterize changes in proton exchange between water and sugar enantiomers at different concentrations of H₂¹⁷O (~15–450 mM) and found that dissociation of the (–)-enantiomers of glucose and ribose occurs at significantly higher rates at higher concentrations of H₂¹⁷O. The mechanism behind this enantioselective effect is unclear. The hypothesis we propose is that the large magnetic field (*B*₀ ~0.6T) applied during NMR measurements induces electric moments opposite in sign for the D and L-isomers. Because ¹⁷O has a nuclear electric quadrupole moment ≠ 0, asymmetrically hydrated complexes may form between the *B*₀-polarized enantiomers and H₂¹⁷O. Either H₂¹⁷O is more often hydrating the (+)- than the (–)-enantiomers—and consequently *pK* differences between H₂¹⁶O and H₂¹⁷O lead to differences in proton exchange between enantiomers and water—or the orientation of H₂¹⁷O relative to the *B*₀-polarized enantiomers is different, in total or in part, which leads to hydrated complexes with different spatial geometries and different proton exchange properties. This effect is significant for Magneto-Chiral Stereo-Chemistry (MCSC) and astrobiology, and it may help us better understand specific instances of mass independent isotopic fractionation and aid in the development of new technologies for chiral and isotopic separation. **Key Words:** NMR—Proton exchange—Ribose—Glucose—H₂¹⁷O—Enantioselective—Chirality. *Astrobiology* 7, 733–744.

INTRODUCTION

THE ORIGIN OF life's high enantiomeric excess (e.e.) and homochirality is unclear because enantiomers have very similar physical and chemical properties. Thus, enantioselective reactions are few and inefficient. Theoretical approaches used to explain prebiotic handedness include Parity-Violation in Electroweak Differ-

ences (PVED), interactions with Circularly Polarized Light (CPL), and interactions with various chiral structures. Sizable stereo-preference was reported only in a very limited number of chiral-chiral interactions (Fujiwara and Nishimoto, 1990, 1998, 2005; Soai, 2002); PVED is too weak to result in large differences in reactivity between enantiomers (Mason and Tranter, 1983; Kondepudi and Nelson, 1985; Salam, 1991); stereophotolysis with

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CPL has low chiral specificity and results in significant e.e. only if sizable photolysis of both enantiomers has occurred (Kagan *et al.*, 1974).

In previous Nuclear Magnetic Resonance (NMR) measurements, we observed small, yet consistent, differences in proton exchange between sugar enantiomers (Cimpoiasu and Scorei, 2003; Scorei and Cimpoiasu, 2004). Hypotheses by which we hoped to explain these results involved the presence of chemical impurities, internal gradients, or the large magnetic field ($B_0 \sim 0.6\text{T}$) applied during NMR measurements. Reluctance to accept that the large magnetic field was of significance is understandable since various futile attempts were made in the last 100 years to use magnetic fields alone to induce chirality in chemical processes (Avalos *et al.*, 1998; Feringa and Van Delden, 1999; Barron, 2000). Yet combinations of two or more external factors (*e.g.*, electric fields, magnetic fields, gravitation, and rotation) can have chiral effects (Thiemann and Teutsch, 1990) via adding extra interactive dimensions. Hence, we asked whether the enantiodifferences we found were due to a combination between the applied B_0 and a local electrically asymmetric component present throughout our measurements.

It has been proposed that large B_0 can have small asymmetric effects on enantiomers at the level of charge distribution around chiral centers, induced magnetic moments, and energy differences (Gilat, 1999; Buckingham, 2004; Buckingham and Fischer, 2006; Harris and Jameson, 2006). It was also proposed that measurements of NMR chirality be made of this effect in conjunction with large external electric fields ($\sim 1\text{ kV/cm}$). The fact that no significant electric fields were to be applied in our experiments prompted us to ask whether the effects observed would involve asymmetric interactions between the B_0 -exposed enantiomers and other molecular structures, such as molecules that carry isotopes with electric quadrupole moments (Q) other than zero. Because we were working with pure solutions of enantiomers in dH_2O , we focused our attention on H_2^{17}O , which reaches natural concentrations of $\sim 19\text{ mM}$. (^{17}O has a $(-)$ -nuclear quadrupole moment $Q = -0.02578$ to -0.26 barns, these values assuming constructive and destructive interference, respectively; Stone, 2001). We measured the effect of different concentrations of H_2^{17}O on proton exchange in pure aqueous solutions of enantiomers and report results regarding the fre-

quency spread of the exchangeable protons, the exchange rate, and pK and ΔG differences.

Until the mechanism is sufficiently understood (and due to the fact that these experiments were performed in the dark), we will use the acronym MCSC (Magneto-Chiral Stereo-Chemistry) to avoid confusion with Magneto-Chiral Dichroism (MCD) or Magneto-Chiral Anisotropy (MChA), both of which involve photochemical reactions (Wagnière and Meyer, 1982; Barron and Vrbancich, 1984; Rikken and Raupach, 1997, 2000; Rikken *et al.*, 2002). We also want to avoid confusion between our approach and NMR chirality proposals (Buckingham, 2004; Buckingham and Fischer, 2006; Harris and Jameson, 2006). In our study, we measured differences in reactivity between different solutions of pure enantiomers, while NMR chirality is intended to measure e.e. with both L and D present.

MATERIALS AND METHODS

$L(+)$ -ribose, $D(-)$ -ribose, $L(-)$ -glucose, and $D(+)$ -glucose were purchased from Sigma and dissolved in ddH_2O (MilliQ) at 0.58 M , 1.17 M , and 2.02 M for ribose, and at 0.276 M , 0.528 M , 0.973 M , and 1.681 M for glucose. The H_2^{17}O -enriched water was purchased from Spectra Stable Isotopes and used at concentrations between 14.9 mM and 450 mM . Because high values of NMR transverse relaxation time (R_2) for H_2^{17}O -enriched water were previously observed in the $6\text{--}7\text{ pH}$ range (Yeung and Lent, 1987), we carried out our experiments at $\text{pH } 6.3$ (adjusted by titration with 1 M HCl). The pH was also measured at the end of the experiments, and the values were used to correct K_{exchange} .

Time Domain ^1H Nuclear Magnetic Resonance (TD- ^1H NMR) relaxation curves were carried out with a 25 MHz spectrometer (Aremi 78 TD-LRP) equipped with an audio filter bandwidth of 1 MHz , at $B_0 = 0.589\text{ T}$ with a quadrature phase-sensitive detector. The temperature was controlled at $298 \pm 0.2\text{ K}$. The transverse relaxation rates (R_2) were acquired using a Carr-Purcell-Meiboom-Gill (CPMG) sequence: $90^\circ_x(-\tau-180^\circ_y;\tau\text{-measurement})_n\text{-RD}$, for a range of interpulse delay (τ) values of $0.4\text{--}20\text{ ms}$ (Scorei and Cimpoiasu, 2006). The R_2 values can be determined by way of CPMG-NMR with $1\text{--}2\%$ accuracy (Steinbrecher *et al.*, 2000). The number of echoes varied from 640 to $20,480$. All measure-

ments were made after a mutarotation process of sugars in solution (6 h at 298 K) without degassing, as dissolved O₂ does not modify the relationship between R_2 and τ . We used low-resolution NMR because the measurement of the contribution of the proton exchange between H₂¹⁷O and H₂¹⁶O to the NMR measurement becomes important at low fields (Khallouk *et al.*, 2005).

Using H₂¹⁷O-enriched water allows accurate measurements of the pH and the proton chemical exchange (Yeung and Lent, 1987; Steinbrecher *et al.*, 2000). It is expected that, in the case of moderately rapid chemical exchange and low concentrations of H₂¹⁷O, the proton line-widths are largely determined by scalar relaxation with ¹⁷O. Because the ¹⁷O mole fraction (P) and the 2nd order magnetic moment (M_2) are linearly correlated in the 0–1% ¹⁷O range, we used a 0–1% ¹⁷O atomic ratio range for our measurements.

The instrument was calibrated by measuring the scalar coupling constant between ¹H and ¹⁷O (¹ $J_{17\text{O}-1\text{H}}$) during the titration of H₂¹⁶O with H₂¹⁷O (Eq. 1); we used the well-established relationship between the relaxation rate and the scalar coupling constant (Lankhorst *et al.*, 1983).

$$R_2(\tau) = \frac{1}{T_2(\tau)} = \frac{1}{T_2(0)} + \left[1 - \frac{1}{K_{\text{exchange}}\tau} \tanh(K_{\text{exchange}}\tau) \right] \frac{M_2}{K_{\text{exchange}}\tau} \quad \text{Eq. 1}$$

where R_2 = NMR transverse relaxation time; $1/T_2$ = the transverse relaxation rate; τ = the interpulse delay of the acquisition sequence

$\frac{1}{T_2(0)} = \frac{1}{T_2(\tau)}$ in the limit $\tau \rightarrow \infty$ (Wang *et al.*, 2003); $M_2 = P \frac{35}{12} (2\pi^1 J_{17\text{O}-1\text{H}})$ is the 2nd order magnetic moment (Gottwald *et al.*, 2005); P = the ¹⁷O mole fraction; ¹ $J_{17\text{O}-1\text{H}}$ = the scalar coupling constant between ¹H and ¹⁷O.

From the slope between M_2 and P , we extracted the value for ¹ $J_{17\text{O}-1\text{H}}$. The obtained value (93.14 ± 8 Hz) is in agreement with previous reports (Yeung and Lent, 1987; Ronen *et al.*, 1998).

The decrease of the transverse magnetization was fitted to a monoexponential equation. We applied the NMR results, *i.e.*, the transverse relaxation rate ($1/T_2$) versus interpulse delay (τ) to Eq. 2 (Gottwald *et al.*, 2005; Scorei and Cimpoiu, 2006; Grucker *et al.*, 1986), to extract the frequency spread ($\Delta\omega$) and the equilibrium exchange constant (K_{exchange}).

$$R_2(\tau) = \frac{1}{T_2(\tau)} = \frac{1}{T_2(0)} + \left[1 - \frac{1}{K_{\text{exchange}}\tau} \tanh(K_{\text{exchange}}\tau) \right] \frac{p_B \Delta\omega^2}{K_{\text{exchange}}\tau} \quad \text{Eq. 2}$$

where K_{exchange} = the equilibrium exchange constant, representing the proton exchange rate between sites A and B; where site A is the H₂¹⁶O and site B is the sugar or the H₂¹⁷O; $\Delta\omega$ = the frequency spread of exchangeable protons, defined by Gottwald *et al.* (2005), *i.e.*, the frequency difference between site A and site B, a measure of the chemical shift relative to H₂¹⁶O; p_B = proton fraction in site B (*i.e.*, the ratio between the number of exchangeable protons in site B and the total number of exchangeable protons).

The proton transfer process in water was extracted from K_{exchange} (Eq. 3) (Zhang *et al.*, 1995).

$$K_{\text{exchange}} = K_H 10^{-\text{pH}} + K_{\text{OH}} 10^{\text{pH}-\text{pK}_w} + K_W \quad \text{Eq. 3}$$

where K_H and K_{OH} are the rate constants of acid- and base-catalyzed exchange; $K_H = 8.2 \cdot 10^9 \text{ s}^{-1}$ (Glaser, 1972; Cerdán *et al.*, 1993); $K_{\text{OH}} = 4.0 \cdot 10^9 \text{ s}^{-1}$ (Glaser, 1972; Cerdán *et al.*, 1993); K_W = water-catalyzed exchange.

We obtained an average calibration value for the H₂¹⁶O–H₂¹⁷O K_{exchange} of $1600 \pm 289 \text{ s}^{-1}$ and a pH of 6.25 ± 0.1 , which is in agreement with the electrode-based pH measurements. In Eq. 2, the K_{exchange} term represents the proton exchange rate between different molecules (Lankhorst *et al.*, 1983). The ΔK parameter is the difference between the K_{exchange} of the solutions of enantiomers (Eq. 4).

$$\Delta K = K_{\text{exchange}} \text{ of the } (-)\text{-enantiomer} - K_{\text{exchange}} \text{ of the } (+)\text{-enantiomer} \quad \text{Eq. 4}$$

The pK differences (ΔpK) between the solvated enantiomers were calculated from Eq. 5 (Zhang *et al.*, 1995):

$$K_{\text{exchange}} = K_d \frac{10^{\text{pH}-\text{pK}}}{1 + 10^{\text{pK}_w-\text{pK}}} \quad \text{Eq. 5}$$

where K_d = diffusion-controlled collision rate; $pK = -\log(K_a)$; K_a = acidity constant.

RESULTS

The dependence of $\Delta\omega$ on the concentration of H_2^{17}O

We identified the presence of proton exchange between sugars (ribose and glucose) and water and interpreted this exchange using Eqs. 1 and 2. In the absence of free H_2^{17}O (*i.e.*, no proton exchange between H_2^{16}O and H_2^{17}O), $\Delta\omega$ is derived from Eq. 2, represents the proton exchange between the sugar and H_2^{16}O , and thus is connected directly with the chemical shift. In the presence of free H_2^{17}O , the NMR line broadening due to H_2^{17}O covers the NMR lines, which represent the chemical shift. In this case, $\Delta\omega$ is only measurable in the $\sim 6\text{--}8$ pH range (Meiboom, 1961; Lankhorst *et al.*, 1983), and it is derived from J (Eq. 1). The $\Delta\omega$ values for the exchange between ribose and glucose enantiomers and H_2^{16}O versus H_2^{17}O (reported via $P_{17\text{O}}$, representing the ratio between the number of exchangeable protons from H_2^{17}O and the total number of exchangeable protons in solution) are presented in Fig. 1. At low H_2^{17}O concentrations, no proton exchange was observed, this being below detection limits. At an average concentration range of H_2^{17}O (Fig. 1), significant differences were seen between enantiomers, with inhibited exchange signal in the presence of (+)-ribose and (+)-glucose relative to (–)-ribose and (–)-glucose, respectively. At higher concentrations of H_2^{17}O , the behavior of the enantiomers appeared similar, though the upper threshold varied between ribose and glucose.

Because $\Delta\omega$ is sensitive to hydration, it can be used to interpret the hydration behavior of the enantiomers (Gottwald *et al.*, 2005). We propose that at large B_0 the affinity of the enantiomers for H_2^{17}O is asymmetric with the (+)-enantiomers having greater affinity for H_2^{17}O than the (–)-enantiomers. At large molar ratios between (+)-sugars and H_2^{17}O , the sugars will remove H_2^{17}O more efficiently from solution. This eliminates the H_2^{16}O – H_2^{17}O exchange signal, which in turn allows for observation of the signal of the proton exchange between sugars and H_2^{16}O . Hence, the sugar: H_2^{17}O ratios can be estimated from the transitions in the graphs, where the behavior of the (+)-enantiomers becomes similar with the behavior of the (–)-enantiomers. These ratios were estimated to be $\sim 5:1$ for (+)-ribose and $\sim 15:1$ for (+)-glucose. When the concentration of H_2^{17}O

was very large, *i.e.*, beyond the capacity of the sugars to “chelate” the H_2^{17}O , a significant portion of the H_2^{17}O molecules remained free and, consequently, the H_2^{16}O – H_2^{17}O proton exchange signal dominated the NMR readings, masking the sugar– H_2^{16}O proton exchange signal.

The dependence of K_{exchange} on the concentration of H_2^{17}O

Physical-chemical differences between water molecules with different isotopic signatures (*e.g.*, H_2^{16}O , $^2\text{H}_2^{16}\text{O}$, H_2^{18}O) include those having to do with freezing points (Horita and Cole, 2004) and affinity for protons (Kudish *et al.*, 1973; Krezel and Ball, 2004). Hence, hydration of the enantiomers with water molecules with different isotopic signatures should also influence the dissociation properties of the enantiomers. The dependence of K_{exchange} on the concentration of H_2^{17}O for the different enantiomers of ribose and glucose is presented in Fig. 2. We found that the proton exchange between sugars and water is less frequent in the presence of H_2^{17}O . There are at least two ways to interpret this result:

1) Adding H_2^{17}O to H_2^{16}O destructures the organization of the bulk solvent and increases the exchange rate with the dissolved sugar, similar to the effects of H_2^{18}O on H_2^{16}O (Krezel and Ball, 2004);

2) In the presence of H_2^{17}O , differences in the affinity of H_2^{16}O versus H_2^{17}O for L- versus D-enantiomers, coupled with differences in the tendencies of H_2^{16}O versus H_2^{17}O to exchange protons, make the proton exchange rate enantioselective.

Our results of K_{exchange} on (–)-ribose (Fig. 2A) indicate that the addition of H_2^{17}O disorganizes the bulk fluid, which increases the sugar: H_2^{16}O exchange rate. Less variation was observed with (+)-ribose, probably because the higher affinity between (+)-ribose and H_2^{17}O , coupled with the lower tendency of H_2^{17}O to exchange protons, inhibits exchange. Hence, both mechanisms proposed above may contribute to our results. We predict that further increase in the concentration of H_2^{17}O (*i.e.*, overwhelming the sugars' capacity to chelate H_2^{17}O) or lower concentrations of sugars (*i.e.*, leaving most of the H_2^{17}O free in solution) should increase the K_{exchange} of (+)-ribose as well. The trend from Fig. 2B indicates that (+)-glucose is more easily saturated with H_2^{17}O than (+)-ribose. Changes in ΔK during the titration of

FIG. 1. Frequency spread ($\Delta\omega$) values showing evidence of proton exchange during titration with H_2^{17}O in water solutions that contain enantiomers of ribose (A) and glucose (B). The values plotted in the graphs represent changes in $\Delta\omega$ by titration with H_2^{17}O . The proton fraction (p_{170}) is the ratio between the number of exchangeable protons from H_2^{17}O and the total number of exchangeable protons in the solution. Results for all concentrations of ribose and glucose were used in these graphs because the sugar molecules were in excess of H_2^{17}O and because the value of the chemical shift is independent of sugar concentration.

FIG. 2. The dependence of the proton exchange rate (K_{exchange}) in solutions of enantiomers of ribose (A) and glucose (B) on the concentration of H_2^{17}O . The highest rates were obtained with (-)-ribose and (-)-glucose.

FIG. 3. Differences between the exchange rate ($\Delta K(\text{s}^{-1})$) of solutions of enantiomers of ribose (A) and glucose (B) at different concentrations of H_2^{17}O . All concentrations of sugars used were included.

ribose and glucose enantiomers with H_2^{17}O are presented in Fig. 3. Here, increase in ΔK is seen at increased concentrations of H_2^{17}O (~ 100 mM for glucose and ~ 350 mM for ribose). This also suggests that the H_2^{17}O -binding capacity is larger for (+)-ribose than for (+)-glucose.

The dependence of ΔpK and ΔG° on the concentration of H_2^{17}O

Earlier results (Kudish *et al.*, 1973; Krezel and Ball, 2004) showed that deuterated water and H_2^{18}O have larger pK s than H_2^{16}O . Changes in pK in the presence of H_2^{17}O may be due to two factors: (1) the pK being a combination of the pK s of different solvents (H_2^{16}O and H_2^{17}O) mixed in different proportions, and (2) destructuring effects of H_2^{17}O on the organization of H_2^{16}O , which should decrease the pK . Though complications arise when trying to calculate solutions of enantiomers with different affinities in mixtures of water with different isotopic signatures, it can be predicted that adding an H_2^{17}O -remover should decrease proton concentration, *i.e.*, increase in the overall pK . Not knowing the absolute value of K_a (see Eq. 5), one cannot calculate the pK but can calculate the ΔpK . Molecules whose enantiomers show the largest differences in their affinities for H_2^{17}O should display the largest ΔpK as well. The relationship between the concentration of H_2^{17}O and the ΔpK of different sugar solutions is presented in Fig. 4. The calculated ΔpK s were 1.16 ± 0.3 for ribose and 0.44 ± 0.20 for glucose. The ratio between these ΔpK s is consistent with the sugar: H_2^{17}O molar binding ratios calculated from $\Delta\omega$ (*i.e.*, $\sim 5:1$ for ribose and $\sim 15:1$ for glucose). Using $\Delta\Delta G^\circ = 2.303RT\Delta pKa$, we found that the differences in ionization energies between the enantiomers are ~ 1.58 kcal/mole for ribose and ~ 0.59 kcal/mole for glucose. Hence, under our experimental conditions (*i.e.*, $B_o \sim 0.6$ T and ≥ 14.9 mM H_2^{17}O), (–)-ribose and (–)-glucose should also be more reactive than their enantiomers.

DISCUSSION

Based on $\Delta\omega$, we found differences between enantiomers of glucose and ribose in their affinity for H_2^{16}O versus H_2^{17}O , but only within a certain range of H_2^{17}O concentrations ($P_{17O} \sim 0.002$ – 0.009 for ribose and $P_{17O} \sim 0.0005$ – 0.0025

for glucose). At low concentrations of H_2^{17}O (14.9 mM) and high concentrations of sugars (the lowest concentrations we used were 580 mM for ribose and 276 mM for glucose), Low Resolution TD- ^1H NMR cannot distinguish differences between enantiomers. At high concentrations of H_2^{17}O , beyond the capacity of the sugars to remove the H_2^{17}O from the solution, chiral differences may still exist, but the free H_2^{17}O in the bulk water obscures the sugar-dependent proton-exchange NMR signal. The affinity of the enantiomers for H_2^{17}O was larger for L(+)-ribose than for D(–)-ribose and larger for D(+)-glucose than for L(–)-glucose. The sugar: H_2^{17}O binding ratios were $\sim 5:1$ for (+)-ribose and $\sim 15:1$ for (+)-glucose. We believe that the carbon involved in this affinity is the α -anomeric C1, because when boric acid forms an ester with glucose (in which case the OH group from the α -anomeric carbon is involved), the effect from Fig. 1 disappears (unpublished results). Results on K_{exchange} showed that the proton exchange between sugar enantiomers and water is more frequent with H_2^{16}O than with H_2^{17}O . This rate was influenced by both the sugar: H_2^{17}O binding ratio and the abundance of free H_2^{17}O . Increased concentrations of H_2^{17}O in the vicinity of the anomeric carbon resulted in significant increase in pK , *i.e.*, lower ionization reactivity.

The mechanism behind this chiral disruption remains unclear. Identifying it requires exploring the various sources of asymmetry that may be present during measurements and carrying out more experiments. However, a couple of mechanisms can be explored and hypotheses formulated in an attempt to explain these results. The contribution of PVED has to be considered, though the MCSC effect observed appears quite large ($\Delta\Delta G \sim 1.58$ kcal/mole for ribose and ~ 0.59 kcal/mole for glucose) to be due to PVED alone. Magneto-photochemical reactions are not relevant here because our experiments occurred in the dark. Hence, we cannot use MagnetoChiral Dichroism or MagnetoChiral Anisotropy (Wagnière and Meyer, 1982; Barron and Vrbancich, 1984; Rikken and Raupach, 1997, 2000; Rikken *et al.*, 2002) as a basis for a hypothesis. An amplification of the chiral disruption via an iterative chemical transformation (*e.g.*, a chemical cycle) also seems unlikely because ours is a simple chemical system, without the sizable internal energy flux that can be used to justify changes in entropy based on energy dissipation.

FIG. 4. The pK differences (ΔpK) between enantiomers of ribose and glucose at different concentrations of H_2^{17}O .

Our results show that, when the concentration of H_2^{17}O becomes very low, both $\Delta\omega$ and K_{exchange} are identical, which is an indication that impurities have non-significant levels. It is the intro-

duction of H_2^{17}O that results in significant enantio-differences. Hence, a chiral impurity seems unlikely. Large external electrical fields were proposed to influence the activity of B_0 -exposed

FIG. 5. Proposed mechanism for the MagnetoChiral Chemical effect. The figure shows ribose only. The presence of a large B_0 leads to an induced electric moment in the x -direction of opposite sign between enantiomers: *i.e.*, $Q > 0$ for $\text{L}(+)\text{-ribose}$ and $\text{D}(+)\text{-glucose}$ (A) and $Q < 0$ for $\text{D}(-)\text{-ribose}$ and $\text{L}(-)\text{-glucose}$ (B). Because ^{17}O has a nuclear electric quadrupole moment ($Q < 0$), the interaction between sugars and H_2^{17}O is attractive, as shown in (A) and repulsive in (B). In (C) the complex between $\text{L}(+)\text{-ribose}$ and H_2^{17}O , coupled with pK differences between H_2^{17}O and H_2^{16}O (*i.e.*, a lower tendency of H_2^{17}O to exchange protons relative to H_2^{16}O), decreases the proton exchange rate between enantiomers and solution relative to proposed mechanism shown in (D).

enantiomers, but such fields were not applied in our experiments, nor were large electrical fields present in the vicinity of the NMR instrument. Asymmetric effects due to interactions with surfaces are possible, though not dominant, because the NMR tubes do not have a large scale asymmetry, their surface:volume ratio is very small with most sugar molecules freely rotating in solution, and also because the asymmetry increases with the addition of H_2^{17}O .

The one variable that was unquestionably correlated with chiral differences was H_2^{17}O , and thus at least one hypothesis has to be considered with regard to its role. Because the ^{17}O atom is different from ^{16}O with respect to its nuclear electric quadrupole and because H_2^{17}O is expected to show different pK from H_2^{16}O , such a hypothesis should take into account differences in the hydration of enantiomers with H_2^{17}O . Our results showed that the $^1J_{^{17}\text{O}-^1\text{H}}$ coupling constant disappeared at certain H_2^{17}O :(+)-enantiomer ratios. To neutralize the exchange between ^{17}O and ^1H , spin pairing has to occur between the nuclear magnetic spin of the ^{17}O and the nuclear magnetic spins of the surrounding ortho ^1H nuclei. Such configuration may be present if the hydration of the enantiomers with H_2^{16}O relative to H_2^{17}O is asymmetric. Because hydration itself cannot violate symmetry rules, we propose that enantiomers are asymmetrically electrically polarized prior to their interaction with H_2^{17}O , due to the presence of the large B_0 (~ 0.6 T). In at least one theoretical model (Gilat, 1999), it was proposed that the electrical configuration around the asymmetric carbons becomes biased in the presence of large B_0 . In Buckingham's interpretation (2004), a magnetic field $B_z^{(0)}$ induces in a free-tumbling molecule a circulation of electrons in the xy -plane, which causes an oscillating electric field E_y to induce an out-of-phase dipole moment in the x -direction proportional to the asymmetric polarizability. Buckingham (2004) proposed that this oscillating movement of electrons in the x -direction causes an induced electric moment in the x -direction, which is of opposite sign between enantiomers. We speculate that in the presence of B_0 differences in polarization between L and D lead to asymmetric hydration with H_2^{17}O , which carries a nuclear electric quadrupole $\neq 0$. This enantioselection may take two forms: enantio-differences in hydration affinity with H_2^{17}O and enantio-differences in the spatial orientation of H_2^{17}O relative to the sugar. In an external B_0 , which or-

ders the orientation of the electrical moments of the free-tumbling molecules, a competition may occur between the quadrupolar repulsion ($U_q \sim 1/R^5$) and the van der Waals attraction ($U_{\text{vdW}} \sim 1/R^6$) (Dzyaloshinskii *et al.*, 1998). Because both the B_0 -polarized enantiomers and the H_2^{17}O have non-zero electric moments, this may help explain the asymmetry of the sugar: H_2^{17}O interactions (Fig. 5); in this case, pK differences between H_2^{16}O and H_2^{17}O cause differences in proton exchange. If the orientation of the H_2^{17}O relative to the polarized enantiomers varies, this may also be used to explain differences in proton exchange.

CONCLUSIONS

During TD- ^1H NMR measurements, we found differences in the dissociation of ribose and glucose correlated with the concentration of H_2^{17}O (at ≥ 14 mM). The L(+)-ribose and D(+)-glucose had higher affinity for H_2^{17}O than their enantiomers, the (+)-enantiomers had higher affinity for H_2^{17}O than for H_2^{16}O , and L(+)-ribose was a better "scavenger" of H_2^{17}O than D(+)-glucose. One hypothesis we propose is that enantioselective interactions may occur between enantiomers asymmetrically polarized under high B_0 (~ 0.6 T) and H_2^{17}O (based on the nuclear electric quadrupole moment of ^{17}O). If these MCSC effects are due to B_0 and H_2^{17}O , then bringing either one of these variables close to zero should cancel the effect. The role of the magnitude of B_0 , temperature, pH, and concentrations of H_2^{17}O at < 14 mM were not investigated, yet they are important in deciphering the mechanism(s) behind this effect.

We predict that, under the experimental conditions presented here, the (–)-enantiomers of ribose and glucose should also be more reactive than their enantiomers, and a similar effect should be observed with other molecules of biochemical importance. These results have important consequences in astrobiology and MCSC. In the future, theoretical and experimental applications should be pursued to explore prebiotic chiral chemistry on the surface of magnetic minerals. MCSC effects may also shed light on mechanisms that cause mass-independent isotopic fractionation. Last but not least, the presence of both large B_0 and molecules that have isotopes with $Q \neq 0$ may also be studied for consequences on the physiology of living cells.

ACKNOWLEDGMENTS

Thanks to Dr. Ing. Constantin Doru Stanescu, Professor Dr. Dana Iordachescu, Dr. Robert Hazen, Dr. David Deamer, and Dr. G.L.J.A. Rikken for support and insightful discussions.

ABBREVIATIONS

CPL, Circularly Polarized Light; CPMG, Carr-Purcell-Meiboom-Gill; e.e., enantiomeric excess; MCSC, Magneto-Chiral Stereo-Chemistry; NMR, Nuclear Magnetic Resonance; PVED, Parity-Violation in Electroweak Differences; Q, electric quadrupole moments; R_2 , transverse relaxation time; TD-¹H NMR, Time Domain ¹H Nuclear Magnetic Resonance.

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