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An excellent linear correlation between ln$\delta$ (OH chemical shift) and 1/$T$ (temperature) is first discovered for hydroxyl compounds. The derived slope ($A$) provides information as an index not only for distinguishing different types of H-bonds, but also for predicting their reactivities. This finding can be extended to other H-bonds containing molecules.

The renewable biomass as raw materials attracts increasing attention for production of chemicals and fuels, particularly the widely distributed and naturally abundant cellulose, hemicellulose, and lignin. This essentially involves selective cleavage of C-O-C and C-C bonds in order to decrease the ratio of O/C. However, these molecules usually contain strong hydrogen bonding networks formed by hydroxyl groups (–OH), which make the highly ordered and crystallized structures and thus can significantly modify their chemical reactivities. Therefore, it is essential to explore a method which can distinguish intra- and intermolecular hydrogen bonds (H-bonds) and investigate their fundamental roles in catalytic reactions.

Several spectroscopic techniques have been developed to characterize the H-bonds. Among them, nuclear magnetic resonance (NMR) spectroscopy is a versatile methodology for studying H-bonding since the chemical shifts are sensitive to the electronic and chemical environment of the investigated nuclei. The magnetic resonance of H-bonded proton moves in general downfield compared to non-H-bonded proton. In addition, the chemical shifts ($\delta$) of the H-bonding protons have pronounced dependence on the temperature ($T$), for both intra- and intermolecular H-bonds. The temperature-dependent changes in chemical shift are generally linear in dimethyl sulfoxide-$d_6$ (DMSO-$d_6$), and are nicely applied to proteins and peptides in conformational analysis. However, OH groups may form strong intermolecular H-bonds through interaction with DMSO, which will cause confusion with their own intermolecular H-bonds. In poor H-bond accepting solvent like CDCl$_3$, however, it has been reported that the OH chemical shift depends nonlinearly upon the temperature within 223 to 323 K. It indicates that the linear functional relationship between $\delta$ and $T$ is not representing the intrinsic principle of H-bonds. Therefore, it is desirable to develop a new correlation between the OH chemical shift and temperature to distinguish the intra- and intermolecular H-bonds and provide the inherent characteristic information of the H-bonds.

We showed here that the natural logarithm of hydroxyl proton NMR chemical shift (ln$\delta$) of a series of sugar-derived alcohols correlates linearly with the inverse of temperature (1/$T$) from 263 to 328 K in CDCl$_3$. The slope, suggesting the energy difference of the O–H···O hydrogen bonds, clearly indicates the different strengths for the intra- and intermolecular H-bonds. It also can be used directly to predict the chemical reactivities, which is validated by a probe reaction of the nucleophilic etherification of different OH groups in isoxides.
proton for intramolecular H-bonds were smaller in absolute terms than those for intermolecular H-bonds,\textsuperscript{12} our attempt did not work out because the plot of $\delta$ versus $T$ deviates obviously from linearity in the temperature range of 263 to 328 K (Fig. S1 and S2, ESI†).

Fig. 1b shows that the natural logarithm of OH chemical shift (ln$\delta$) is well correlated linearly with the inverse of temperature (1/$T$) for both C2-OH and C5-OH protons within the range of 263 to 328 K. This Arrhenius-like behavior is given by eq. 1 with a slope of $A$. This leads to a slope of 164.2 for the plot of C5-OH (intramolecular H-bond) and 547.2 for that of C2-OH proton (intermolecular H-bond).

$$\ln \delta = A/T + B \quad (1)$$

In order to verify whether it is a general feature, we investigated a series sugar-derived molecule. Firstly, molecules with a structure similar to isosorbide were chosen including isomannide and 2-O-monoethyl isosorbide, containing exclusively intramolecular H-bonds, and isoidide and 5-O-monoethyl isosorbide with intermolecular H-bonds. The nonlinear dependences on temperature of OH chemical shifts are observed (Fig. S3–S7, ESI†). All molecules give a nice linear correlation between ln$\delta$ and 1/$T$ (Fig. S8, ESI†). The slope values for OH protons of isomannide and 2-O-monoethyl isosorbide are 137.8 and 90.6, corresponding to intramolecular H-bonds. They are 493.1 and 655.4 for the intramolecular H-bonds in 5-O-monoethyl isosorbide and isoidide, respectively. Further studies on other sugar-derived alcohols, containing intramolecular H-bonds with different structures including 5-hydroxymethylfurfural, furfuryl alcohol, tetrahydrofurfuryl alcohol, (S)-3-hydroxytetrahydrofuran and ethanol (Table S1 and Fig. S9–S14, ESI†), validate the different temperature dependence behaviors (Fig. S15, ESI†). The slopes ($A$) of the intramolecular H-bonds for all studied molecules are smaller than those of the intermolecular H-bonds, as demonstrated in Fig. 2.

The intramolecular H-bonds generally give a slope in the range of 90.4 to 164.2, while the intermolecular H-bonds show a slope of 289.3 to 655.4. Therefore, one may distinguish the intra- and intermolecular H-bonds from the slope of the plot for ln$\delta$ versus 1/$T$.

Since NMR at a given temperature measures the proton chemical shift as a Boltzmann average of the chemical shifts associated with each vibrational level, the chemical shift is the resonant frequency of a nucleus relative to a standard, which is energy related.\textsuperscript{15} Kumar et al. reported a linear correlation between computed binding energies of H-bonds and proton NMR chemical shift.\textsuperscript{16} Garcia-Viloca et al. also reported that the dependence on the temperature of the proton NMR chemical shift could be used to identify the nature of low barrier H-bonds via theoretical potential energy calculation.\textsuperscript{15} Therefore, the slopes for the plots of ln$\delta$ versus 1/$T$ (Fig. 1b, Fig. S8 and S15 in ESI†) may reflect the energy changes $\Delta E$ of the H-bonds from 263 to 328 K. Thus, the corresponding energy changes $\Delta E$ can be estimated from the slope $A$ of eq. 1 times the universal gas constant ($R$) (eq. S1, ESI†), and the results are listed along in Fig. 2. One sees that the $\Delta E$ of the intramolecular H-bonds ranges from 0.2 to 0.3 kcal mol$^{-1}$, and for the intermolecular H-bonds it falls in a range of 0.6 to 1.3 kcal mol$^{-1}$. Because of the nuclear magnetic resonance absorption phenomenon, the absorption energy differences of OH proton nuclei from 263 to 328 K are calculated based on eq. S2–S4 (ESI†) and listed in Fig. S16 (ESI†). Interestingly, we found that the order of proton nuclei absorption energy difference is consistent with the apparent energy difference $\Delta E$ for sugar-derived molecules. We wonder if this energy changes can be used as an index for chemical reactivity. Therefore, we chose etherification as a probe reaction, in which the reactivity of OH group is strongly dependent on different H-bonds.

Fig. 2 The correlation between energy change ($\Delta E$) of intra- and intermolecular H-bonds and slope $A$ of the plots of ln$\delta$ versus 1/$T$ for sugar-derived alcohols.

Two types of molecules were mixed in the reactor, i.e. isomannide which contains exclusively the intramolecular H-bonds and isoidide only the intermolecular H-bonds. This would allow us to study the competitive etherification reactions between intra- and intermolecular H-bonds. The reaction was carried out using tungstosilicic acid as the catalyst. The main etherification products are monoethyl isomannide and monooethyl isoidide (Fig. S17a, ESI†). The results show that the conversion of isomannide is higher than that of isoidide over the same time scale (Fig. 3a). The turnover frequency (TOF) is 40.3 h$^{-1}$ for the isomannide conversion, in comparison to 26.4 h$^{-1}$ from isoidide, suggesting a higher reactivity of isomannide with the intramolecular H-bonds.

To further understand the reactivities of different OH groups, we looked into the etherification reaction of isosorbide, which contains both intra- and intermolecular H-bonds. With the time on stream, isosorbide was consumed gradually forming 5-O-monoethyl isosorbide and 2-O-monoethyl isosorbide (Fig. 3b and Fig. S17b, ESI†). The yield is 5.2% for 5-O-monoethyl isosorbide formation, in comparison to 3.6% for 2-O-monoethyl isosorbide in the initial 10 min. The preferential formation of 5-O-monoethyl isosorbide indicates that the intramolecular H-bond at C5-OH is more reactive than the intermolecular H-bond at C2-OH. This result is consistent with the report by Lemieux et al.,\textsuperscript{19} who observed that the intramolecular H-bond enhances the reactivity of C5-OH for the esterification of isosorbide.\textsuperscript{15} The different reactivities of the intra- and intermolecular H-bonds are
Notes and references

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