

# HYDROGEN-BONDED-ASSISTED ACIDITY

Can a hydrogen bonding network affect acidity? Kass has examined the polyol **1** whose conjugate base **1cb** can potentially be stabilized by a large hydrogen bonding network.<sup>1</sup> Kass had previously found a significant acidity enhancement in comparing *t*-butanol ( $\Delta G$  (deprotonation) = 369.2 kcal mol<sup>-1</sup>) with that of **2** ( $\Delta G$  (deprotonation) = 334.4 kcal mol<sup>-1</sup>).<sup>2</sup>

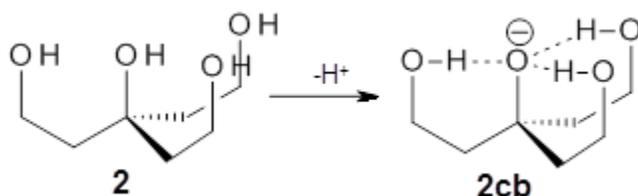
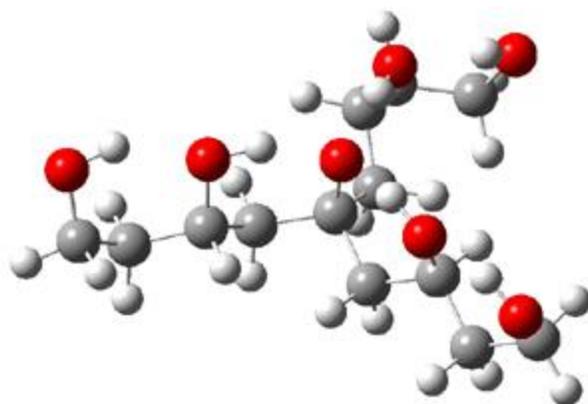


Table 1 lists the computed and experimental free energies of deprotonation of **1**. The experimental values are computed at M06-2x/maug-cc-pVT(+d)Z. The structure of **1cb** is drawn in Figure 1.

**Table 1.** Computed and experimental free energies (kcal mol<sup>-1</sup> of deprotonation of some alcohols.

	MO6-2x	Expt
<i>t</i> -butanol	368.6	369.3
<b>2</b>	335.0	334.4
<b>1</b>	320.2	313.5

The difference in the acidity of *t*-butanol and **2**, some 30 kcal mol<sup>-1</sup>, reflects the stability afforded by three intramolecular hydrogen bonds to the oxyanion. In going from **2cb** to **1cb**, each of the hydroxyl groups that donate to the oxyanion act as the acceptor of a hydrogen bond from the more removed hydroxyl groups. There is in effect a first and second layer of hydrogen bond network in **1cb**. These secondary hydrogen bonds lead to further stabilization of the anion, as reflected in the diminished DPE of **1** over **2**: 320.2 vs. 335.0 kcal mol<sup>-1</sup>. Note that this secondary layer does not stabilize the anion to the same degree as the primary layer, but nonetheless its effect is large and quite striking.



**1cb**

**Figure 1.** M06-2x/maug-cc-pVT(+d)Z optimized structure of **1cb**.

Even in solution these more remote hydrogen bonds can stabilize the anion. So, using the CPCM approach and modeling DMSO, **2** is predicted have a  $\text{pK}_a$  that is 15 units below that of *t*-butanol, and **1** is predicted to be 3  $\text{pK}_a$  units more acidic than **2**. Experiments verify this prediction with the  $\text{pK}_a$ s of 16.1 for **2** and 11.4 for **1**.

Source: <http://comporgchem.com/blog/?p=2311>