

ACIDITY OF REMOTE PROTONS

The α -proton of ketones and aldehydes are acidic, thanks to delocalization of the resulting anion. However, α -protons at a bridgehead position are much less acidic – the resulting anion is not delocalized as the enolate would be an anti-Bredt alkene. So, what about more remote protons from the carbonyl – would they exhibit enhanced acidity due to inductive or field effects?

Kass has examined the deprotonation of 2-adamantone **1** via experiment and computation.¹ The relative energies of the five different anions are listed in Table 1. Previous H/D exchange experiments indicate that the relative reactivity is $\beta_{ax} > \beta_{eq} > \alpha$, and this is well reproduced by computations.²

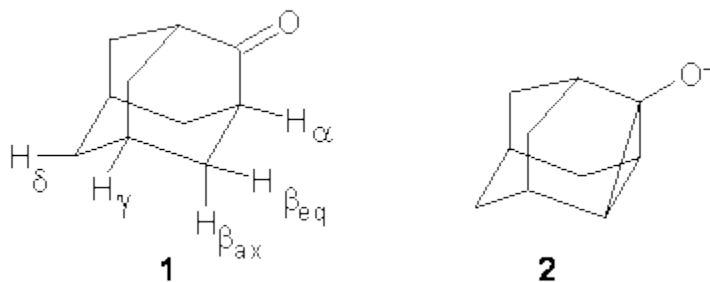


Table 1. Relative energies (kcal mol⁻¹) of the enolates of **1**.

compound	M06-2x/aug-cc-pVDZ	G3
α	4.27	5.60
β_{ax}	0.0	0.0
β_{eq}	4.46	
γ	2.28	3.40
δ	6.17	7.55
2	-1.58	0.56

Kass' bracketing experiments indicate the enthalpy for deprotonation of 2-adamantone is 394.7 ± 1.4 kcal mol⁻¹. This is in nice accord with the computational results for loss of the β_{ax} proton: 393.8 (M06-2x/aug-cc-pVDZ) and 396.8 kcal mol⁻¹ (G3). One interesting computational result is a competitive cyclic structure **2**, whose stability is similar to that to the β_{ax} ion at M06-2x and is the optimized structure produced at MP2/6-31G(d) when searching for the β_{eq} enolate.

So, to answer our question, protons remote from a carbonyl *are* more acidic than alkane analogues, but much less acidic than typical α -protons of ketones.

Source: <http://comporgchem.com/blog/?p=1051>