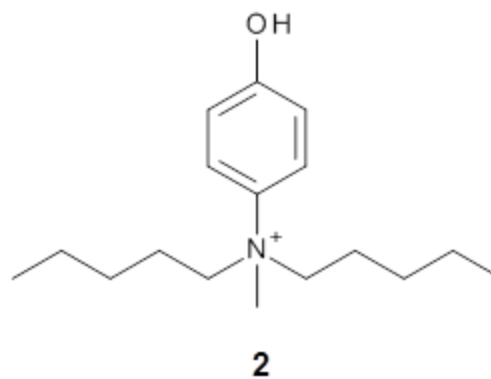
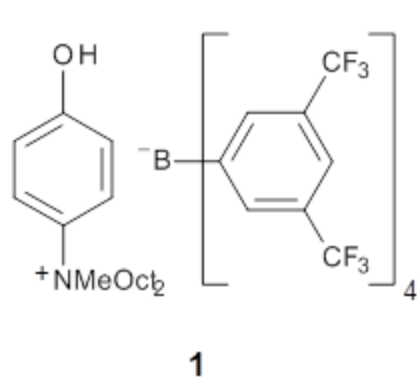


# CHARGE-ENHANCED ACIDITY AND CATALYST ACTIVATION

Kass and coworkers looked at a series of substituted phenols to tease out ways to produce stronger acids in non-polar media.<sup>1</sup> First they established a linear relationship between the vibrational frequency shifts of the hydroxyl group in going from CCl<sub>4</sub> as solvent to CCl<sub>4</sub> doped with 1% acetonitrile with the experimental pK<sub>a</sub> in DMSO. They also showed a strong relationship between this vibrational frequency shift and gas phase acidity (both experimental and computed deprotonation energies).

A key recognition was that a charged substituent (like say ammonium) has a much larger effect on the gas-phase (and non-polar solvent) acidity than on the acidity in a polar solvent, like DMSO. This can be attributed to the lack of a medium able to stable charge build-up in non-polar solvent or in the gas phase. This led them to **1**, for which B3LYP/6-31+G(d,p) computations of the analogous dipentyl derivative **2** (see Figure 1) indicated a deprotonation free energy of 261.4 kcal mol<sup>-1</sup>, nearly 60 kcal mol<sup>-1</sup> smaller than any other substituted phenol they previously examined. Subsequent measurement of the OH vibrational frequency shift showed the largest shift, indicating that **1** is extremely acidic in non-polar solvent.



Further computational exploration led to **3** (see Figure 1), for which computations predicted an even smaller deprotonation energy of 231.1 kcal mol<sup>-1</sup>. Preparation of **4** and experimental observation of its vibrational frequency shift revealed an even larger shift than for **1**, making **4** extraordinarily acidic.

