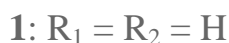
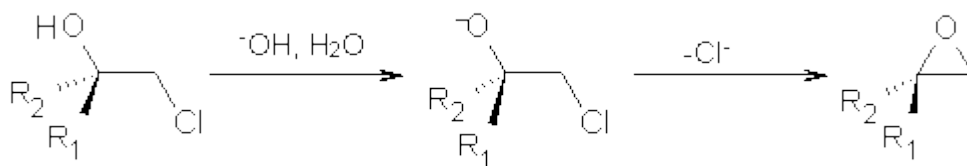


THORPE-INGOLD EFFECT

Often *gem*-dialkyl substitution accelerates a reaction, for example in the formation of an epoxide via reaction 1. Here the relative rates are 1:21:252 in going from **1** to **2** to **3**.¹ This acceleration is the Thorpe-Ingold effect and had been suggested to arise from a steric reaction: that the methyl groups contract the angle and bring the terminal groups closer together.



Kostal and Jorgensen² have examined the reaction of the 2-chloroethoxides **1-3** using computations, especially to look at the effect of solvent. At MP2/6-311+G(d,p) and CBS-Q, the relative rates (based on the activation free energy ΔG^\ddagger) are 1:2.8:17 and 1:0.7:3.7, respectively. Evidently there is *no significant rate enhancement afforded by gem-substitution in the gas phase*.

However, solution computations give a very different result. Using PCM along with the MP2 method, the computed relative rates are 1:5.8:1100 and with the Monte Carlo-Free Energy Perturbation method, the relative rates for aqueous solution are 1:30:773. Thus, the Thorpe-Ingold acceleration is due to solvent. Analysis of the hydrogen bonded structures and the solute-water pair distributions suggest that increasing alkyl substitution reduces the strength of solvation of the reactant, leading to the lower activation barrier.

Source: <http://comporgchem.com/blog/?p=1039>