Analyzing the Effects of a Better Leaving Group in Nucleophilic Acyl Substitution Using M06-2X

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In previous years, the nucleophilic acyl substitution reaction between *m*-methylphenol and acetic anhydride was observed to follow the expected two-step process. The MP2 and M06-2X/6-31+G** levels of theory were used to analyze the reaction. This research is testing the hypothesis that creating a better leaving group would drive the reaction towards a more concerted profile. To achieve a better leaving group, fluorine atoms were used to replace the hydrogen atoms on the acetic anhydride molecule. The flourine atoms, having greater electronegativity, pulled electron density away from the carbonyl carbons creating a better leaving group. The better leaving group should then lower and or eliminate the activation energy at the second step of the reaction, leading to a concerted reaction. With this in mind, the reaction of *m*-methylphenol with hexafluoro acetic anhydride was analyzed using computational methods at the M06-2X/6-31+G** level of theory (Figure 1.). Following the process from the previous research, a list of 30 conformers was obtained through a compilation of results from Systematic and Monte Carlo conformational search algorithms. The conformers were ranked according to single point energies, geometrically optimized, and lastly they underwent QST3 calculations to search for transition states. All but two of the 30 conformers disassociated, during the geometric optimizations, at the carbonyl carbon to oxygen to carbonyl carbon bond. The QST3 calculations resulted in three confirmed transition state 1's, and no transition state 2's. Using the confirmed TS1's, IRC calculations were done to create a reaction profile. The profiles, along with the presence of only TS1's lead to the conclusion that creating a better leaving group leads to the observance of the concerted reaction profile.

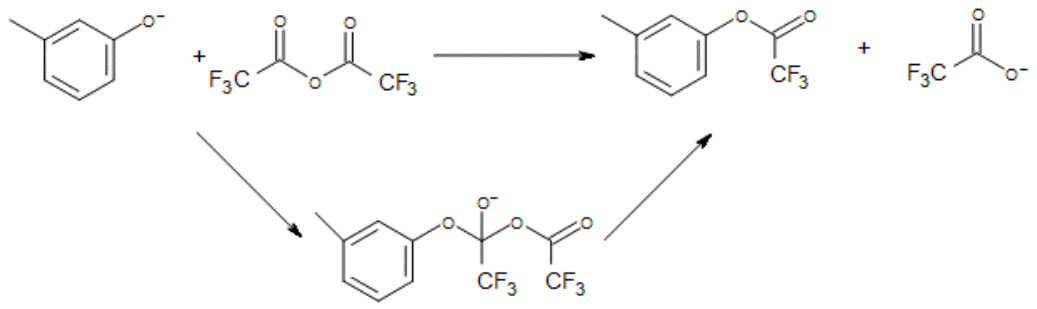

Figure 1. The general form of the nucleophilic acyl substitution reaction of *m*-methylphenol with hexafluoro acetic anhydride.