

Kinetic Study on the Esterification of Hexanoic Acid with *N,N*-Dialkylamino Alcohols: Evidence for an Activation by Hydrogen Bonding

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The pseudo-first order rate constant for the esterification of hexanoic acid (**1**) and five different *N,N*-dialkylamino alcohols (**2**) was determined in comparison to 1-hexanol ($k = 0.67 \cdot 10^{-5} \text{ s}^{-1}$). The values range from $0.60 \cdot 10^{-5} \text{ s}^{-1}$ to $9.3 \cdot 10^{-5} \text{ s}^{-1}$. The data suggest a differing reactivity for structurally related compounds, which is directly correlated to the ability of the corresponding amino alcohol to activate the carboxylic acid by hydrogen bonding. A seven-membered transition state C^\ddagger is postulated for reactions of 2-amino alcohols. The fastest reaction was observed for *trans*-2-(*N,N*-dimethylamino)cyclohexanol (**2e**), in which the amino and the hydroxyl groups are in an almost perfect synperiplanar 1,2-position. Attempts to further enhance the rate of the esterification by the addition of potential catalysts failed. Only $\text{Cu}(\text{OTf})_2$ (2.5 mol-%) allowed for a moderate rate increase from $7.5 \cdot 10^{-5} \text{ s}^{-1}$ (uncatalyzed) to $14.8 \cdot 10^{-5} \text{ s}^{-1}$ (catalyzed) in the esterification of hexanoic acid (**1**) with 2-(*N,N*-dimethylamino)ethanol (**2a**).

Key words: Acylation, Amino Alcohols, Hydrogen Bonds, Kinetics, Transition States