

COMPUTATIONAL INSIGHTS INTO THE SPONTANEITY OF EPOXIDE FORMATION FROM HALOHYDRINS AND OTHER MECHANISTIC DETAILS OF WILLIAMSON'S ETHER SYNTHESIS

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Abstract. The reaction mechanism of several Williamson's ether syntheses have been studied using density functional theory with triple- ζ basis sets. These computations show that the synthesis of geometrically-strained epoxide from deprotonated halohydrins is due to the combined effects of favourable solvation of the products, higher bond enthalpy of C-O bonds vs. C-Cl bonds and increased vibrational entropy of the epoxide vs. the original halohydrin. Examination of the pathways leading to the formation of larger cyclic ethers revealed that the experimentally-observed preference for the formation of five-atom rings over six-atom-rings is due to the preference of the intervening methylene groups for staggered conformations, which entails that the alkyl carbon in the reactant state leading to the six-atom cyclic ether is initially not properly aligned with the attacking alkoxide. Study of the competing elimination reactions further shows that during the synthesis of five-atom cyclic ethers the competing elimination reaction is strongly disfavoured due to steric effects. The temperature dependence of both reactions favours elimination over S_N2 as temperature rises, though only when the alkoxide and the halogen moieties are not part of the same carbon chain.

Keywords: density-functional theory, reaction mechanism, intra-molecular Williamson's ether synthesis, epoxide, halohydrin.

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