

WHY EPOXIDES CAN BE FORMED FROM HALOHYDRINS IN SPITE OF THEIR ELEVATED RING STRAIN, AND OTHER UNANSWERED QUESTIONS ON RELATIVE REACTION RATES OF INTER- AND INTRA-MOLECULAR WILLIAMSON'S ETHER SYNTHESSES

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Abstract. The reaction mechanism of several Williamson's ether syntheses has been studied using density functional theory with triple- ζ basis sets. The synthesis of geometrically-strained epoxide from deprotonated halohydrins is shown by these computations to be due to the combined effects of favorable 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 6-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 6-atom cyclic ether is initially not properly aligned with the attacking alkoxide. Study of the competing elimination reactions further shows that elimination is strongly disfavored due to steric effects in the synthesis of 5-atom cyclic ethers, and that its temperature dependence favors 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.