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Mustard carbonate analogues: influence of the leaving group on the neighboring effect

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Abstract

The substitution of a chlorine atom with a carbonate moiety in mustard compounds has led to a new class of molecules, namely mustard carbonates that retain the reactivity of the well-know toxic iprites, but are safe for the operator and the environment [1].

Herein we report the influence of the leaving group on the neighboring effect of sulfur half mustard carbonates (HMCs) usually less reactive than nitrogen ones [2]. Several new 2-(methylthio)ethyl alkyl carbonates have been synthesized and their reactivity has been investigated in both autoclave and neat conditions. The results reactions between the HMCs and phenol performed in autoclave (180 °C, no base, in acetonitrile media) showed that the efficiency of the anchimeric effect is directly dependent on the steric hindrance of the HMC leaving group. The least steric hindered 2-(methylthio)ethyl methyl carbonate gave the methyl (2-phenoxyethyl)sulfane in higher yield, whereas the most steric hindered 2-(methylthio)ethyl *t*-butyl carbonate did not reacted at all. The influence of the leaving group on the anchimeric effect has been also investigated in neat conditions at 150 °C in the presence of catalytic amount of K₂CO₃. In this case, due to the absence of the solvent and the presence of the base the reaction is more complicated by transesterification reactions and formation of unwanted products. Interestingly 2-(methylthio)ethyl ethyl carbonate showed to be the most efficient carbonate among the ones studied. This resulted might be ascribed to its ability to free the cyclic intermediate from its *molecular cage* as intimate ion pair more readily than the other HMCs. Finally, several nucleophiles have been then tested in neat reaction conditions using 2-(methylthio)ethyl ethyl carbonate and a catalytic amount of base. In all cases studied it was observed an almost quantitative anchimeric aided alkylation over S_N2 reaction, i.e., formation of ethyl aryl ethers. The best results achieved have led to an enhanced product selectivity, more accessible reaction conditions and a better insight on the reaction mechanism of mustard carbonates.

References

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