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New Insights on the Reactivity and Selectivity of Nucleophilic Fluorination Mediated by Hydrogen Bonding Solvation

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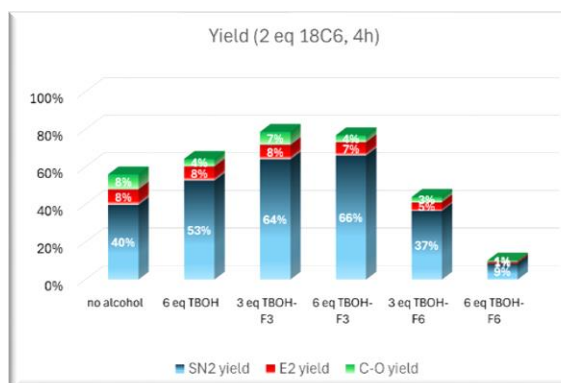
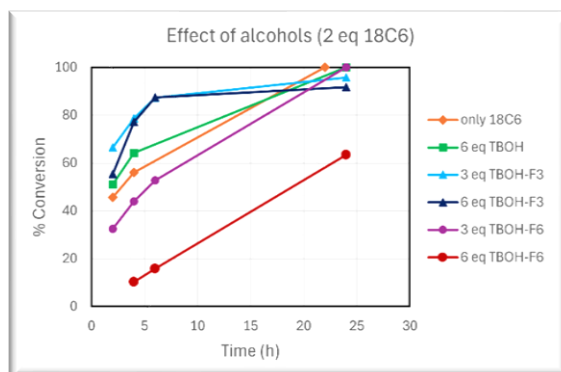
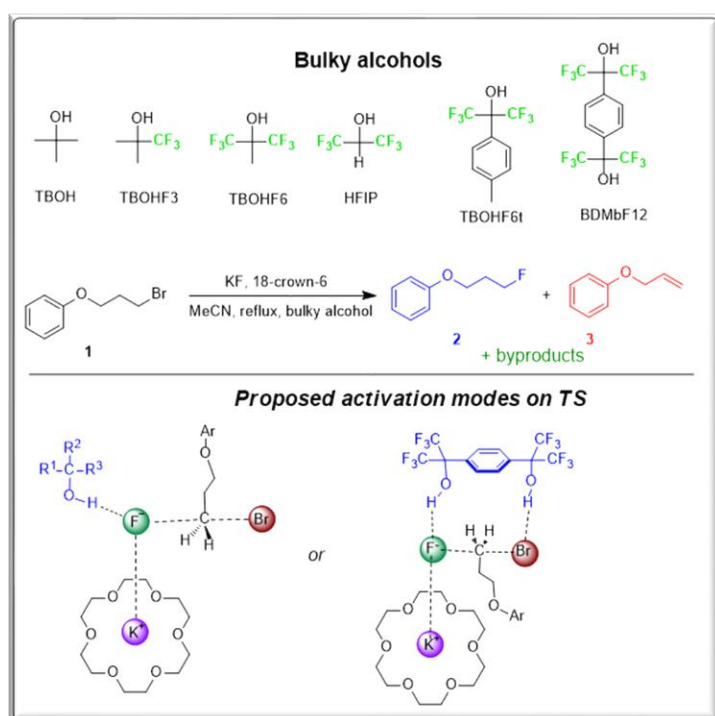
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ABSTRACT

Fluorination reactions of alkyl bromides face the problem of high competition between S_N2 and $E2$ reactions.¹ KF salt, as a source of nucleophile fluoride, has limitations due to low solubility issues.² However, combining crown ethers with hydrogen-bonding donor species could enhance both reactivity and selectivities.³⁻⁷ Herein, we reported the extensive experimental and theoretical investigations of the effects of stoichiometric amounts of diverse bulky alcohols, combined with 18-crown-6, for fluorination reactions of primary and secondary alkyl bromides. Raising the hydrogen-bonding strength of TBOH-F3 (6 eq) with fluoride ions and substrate **1**, led to good reactivity and chemoselectivity, with almost 80% conversion at 4h and 9:1 $S_N2/E2$ selectivity. Hexafluorinated alcohols also suppressed $E2$ reactions, however, the increase in acidity was a limiting factor due to the formation of nucleophilic alkoxides and the formation of ethers. For the TBOH-F6, the kinetics behavior has changed, leading to a slower reaction rate with high chemoselectivity.



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