

Grignard Reactions at the Interface: Insights from Molecular Dynamics of a Deep Eutectic Solvent Mixture

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The Grignard reagent is the most famous representative of main group organometallic compounds. It is formed by magnesiation of a carbon-halogen bond, and, thanks to its reaction with organic unsaturated carbon centers, it gave chemists of the early 20th century a key tool to tailor new carbon-carbon bonds into chemical structures.

Lately, the possibility to relinquish the volatile organic compounds traditionally used as solvents in these reactions, in favor of greener and less toxic analogues was confirmed in multiple occasions [1]. In particular, the presence of a deep eutectic solvent (DES) containing an H-bond donor/acceptor pair and a chloride salt was seen to allow fast Grignard-type reactions at room temperature [2]. The microscopic causes for the unexpected tolerance of a protic environment showed by the organometallic reagent and the increased rate of reaction have not been completely elucidated.

My work modeled a liquid/liquid system where a Grignard reagent initially in bulk THF interacted with a ketone dissolved in the DES [3]. The results show that the structural nature of the DES phase helps to create a local interfacial environment that promotes an increased local concentration of the organometallic reagent. At the same time the rigidity of the DES prevents an efficient penetration of the reagent thus limiting its decomposition. These effects combined with the slow diffusion of the substrate towards the organic phase that increase the probability of effective contact, are seen as key aspects of the improved reactivity of Grignard reactions in mixed organic/DES media.

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[3] Manasi I., Bortoli M., Bowron D. T., Campana M., Hammond O. S., Headen T. F., Hooton J., Hevia E., Cascella M., Eisenstein O., Edler K. J., Are Grignard Reactions in Deep Eutectic Solvents Interface-Driven? *Angew. Chem. Int. Ed. Engl.* **2025**, *64*(42), e202513649.