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Non-traditional solvent effects in organic reactions

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In 1965 Waddington edited the seminal tome '*Non-Aqueous Solvent Systems*'.[1] It was mostly focused on inorganic solvents, such as the higher hydrogen halides (HCl, HBr and HI), halides and oxyhalides of the Group 15 elements, sulfur dioxide, halogens and interhalogens, and molten salts, and it included chapters on "the three most important protonic solvents": ammonia, hydrogen fluoride and sulfuric acid. None of these have made it through to this current collection on non-traditional solvent effects in organic synthesis. Only one of the nine chapters on 'co-ordinating solvents' covers some of the organic solvents that we are familiar with. These, and their effects on reactions, were comprehensively described fourteen years later in Reichardt's equally important '*Solvents and Solvent Effects in Organic Chemistry*'.[2]

Since the publication of these books there has been a revolution in the study of solvents and their effects on organic reactions. This has mostly been driven by the recognition that solvent wastes are a key challenge for sustainable chemicals synthesis.[3] This has led to the introduction of a number of new classes of solvent for chemicals processing.[4] Ionic liquids and the closely related deep eutectic solvents have emerged as being of great interest, as have supercritical fluids and switchable solvents, liquid polymers and solvents derived from biomass. Several of these are included in this collection.

Whilst reduction in solvent waste and the potential for recyclability has been a significant driver for the development of these alternative solvent systems, an understanding of their solvent effects is critical for their use in preparative chemistry. As indicated in the work compiled here, whilst developing this understanding remains a challenge it also represents an opportunity. These new solvent systems can often result in reaction outcomes that are either greatly enhanced or not available in traditional solvents[5] with the potential to rationally design solvents as a result.[6] That is, these non-traditional solvents and their solvent effects broaden the range of solvents available in order to get the reaction outcomes that you want!

Nowadays, the classification and solvent effect of non-traditional solvents by different polarity scales (based on linear solvation energy (LSE) relationships and using different solvatochromic dyes) continues to be a very well established concept despite the sometimes controversial results obtained.[7] Therefore, the structural complexity of these systems (e.g., nanostructure domains), and the multiple non-specific interactions between solute–solvent, solvent–solvent and especially dye–solvent, continue to be a challenge that needs addressing in order to gain a full understanding of the effect that these non-traditional solvents could have on the result of a reaction. In addition, the development of new solvatochromic dyes is a challenge that should be addressed, because the solvation scenario of the dye in these non-traditional solvents compared to that in an organic solvent can be completely different, and therefore the inappropriate use of a dye, could lead to a wrong polarity value for these systems.

From a theoretical point of view, setting up a model to describe chemistry in traditional solvents is already complicated, but this complexity increases when using non-traditional solvents. Therefore, simple models or relationships have to be applied in order to gain predictability. Alternatively, the complexity must be reduced in order to allow highly accurate methods to study the basic principles. Novel approaches including machine learning,[8] are needed to see the wood for the trees again. All of

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these approaches are helpful in understanding reactions and solutes which are at the interface with solvent and non-solvent based medium effects.

This virtual issue reflects on all of the challenges and opportunities that we have described above. The contributors have provided much insight into the current interest in non-traditional solvents in chemistry. We commend it to you and hope that you enjoy reading it.

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