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TOPIC(s) : Alternative solvents

Isohexide-based solvents: Conformationally induced differences in solvent properties

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PURPOSE OF THE ABSTRACT

The quest for safe bio-based alternatives to reprotoxic dipolair aprotic solvents such as N,N-dimethyl formamide (DMF), N,N-dimethyl acetamide (DMAc) and N-methyl-2-pyrrolidone (NMP) is receiving increasing attention due to forthcoming legislation.¹ A well-known isohexide derivative, isosorbide dimethyl ether, has been previously used in reactions normally employing dipolair aprotic solvents such as Pd-catalyzed cross coupling reactions and Cu-catalyzed arylation of phenols and amides.^{2, 3} This shows the potential of the isohexide scaffold as a platform for developing bio-based alternatives for reprotoxic dipolair aprotic solvents.

The isohexides consists of three sugar derived epimers: isosorbide, isoidide and isomannide. Isosorbide and isomannide are derived from sorbitol or mannitol respectively, by double cyclodehydration. The natural precursor for isoidide, i.e. idose, does not occur in nature. However, isoidide can be efficiently obtained by catalytic epimerization of isosorbide.⁴ From a structural point of view, the isohexide scaffold is a V-shaped molecule consisting of two cis-fused tetrahydrofuran rings having two hydroxyl groups at C2 and C5, either in the endo- or exo-orientation.^{5, 6} Sterically and electronically the endo- and exo-positions are non-equivalent and thus derivatives of the isohexides will exhibit different physico-chemical properties. This has prompted us to design a range of bio-based solvents with different properties depending on the orientation of the functional groups

Here we report the synthesis of a range of isohexide derivatives (ethers and esters). By systematic comparison we will show the relationship between their physico-chemical properties and the stereochemical orientation of the functional groups. These results will also be compared to properties obtained by computer modelling. Furthermore, we will show preliminary results from an in-vitro toxicity screening study performed on the isohexide derivatives. Overall, the isohexide derivatives reported here are industrially viable, safe bio-based substances with a broad potential as dipolar aprotic solvents.

FIGURES

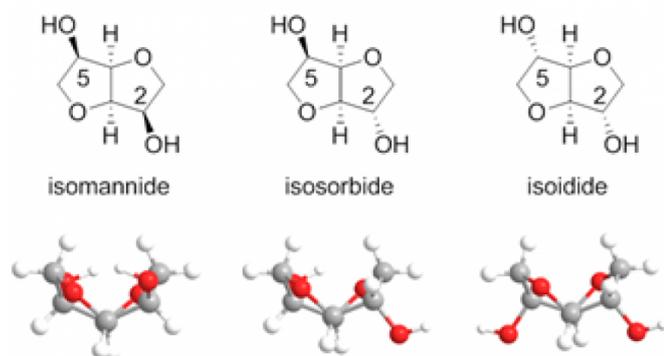


FIGURE 1

Structure of isohexides

Figure 1. Structure of isohexides

FIGURE 2

KEYWORDS

Alternative solvents | isohexides | sustainable solvents

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