Recent progresses in green solvents development: filling the gaps

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Organic solvents are used in huge amounts in many industrial and daily life applications, but unfortunately the majority of them come from petroleum and they are often labeled as toxic or hazardous substances. For this reason, substantial efforts are being done to develop more benign solvents from renewable sources. However, although the number of papers covering the synthesis and applications of "green solvents" is increasingly growing, systematic studies about solvent substitution issues are still scarce, in spite of the importance of the topic. Citing the Jessops's statement: *"...a green solvent will only be chosen if one exists with the desired properties."*[1] This short statement raises some formidable challenges from both theoretical and experimental viewpoints. An overview of these challenges is represented in Figure 1. It becomes clear that the efficient and systematic search for possible substitution applications requires, among other considerations, a quantitative knowledge of the physico-chemical properties of the new solvents, and also their quantitative comparison with those of conventional organic solvents they are supposed to replace. The resulting models can be then used either to classify the green solvents candidates into different groups according to their properties, or to relate them to the target application requirements for a successful solvent substitution. Finally, the greenness of the synthetic procedure to obtain the substitutive solvent should also be taken into account.

Given that there is a huge number of potential molecular structures in the solvent candidate set, experimental procedures must be kept to a minimum, and methods to estimate the most relevant solvent properties become essential. In some cases, however, large databases of experimental solvent parameters have been built.[2]

Examples of some recent developments in this research field are presented in the keynote. For instance, our group has recently described a family of solvents based on glycerol,[3] a concomitant product in biodiesel production. To facilitate the search of possible substitution applications,[4–7] we have also determined a number of physicochemical properties of these glycerol-derived solvents, and compared them with those of conventional organic solvents. Some of these properties are difficult to measure, so we have developed some quantitative structure-properties relationship (QSPR) equations to accelerate the search of the best solvent for a given application.

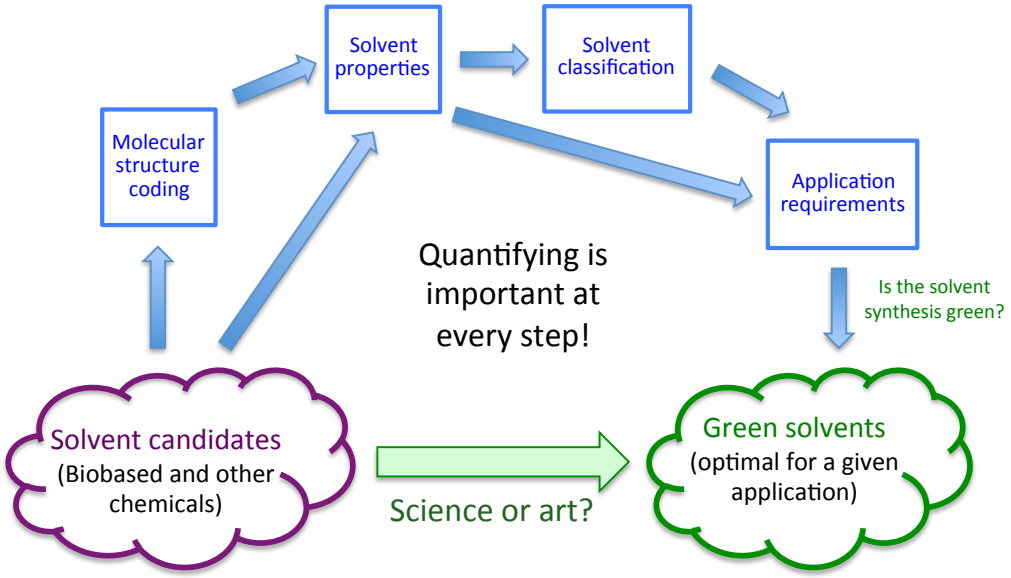

Fig. 1 – DARC/PELCO scheme used to describe glycerol based solvent structures.

In this work we have used two different approaches, based on molecular connectivity descriptors: topological parameters[9] and DARC/PELCO[8] descriptors. As relevant solvent properties to model using Partial Least Squares Analysis (PLSA) and Multiple Linear Regression (MLR), we considered 1) behavior in dissolution processes, which can be well defined through the solvatochromic parameter E_T^N,[10] 2) mechanical aspects, which can be quantified by their viscosity, and 3) volatility aspects, very related to safety, toxicity and air pollution, which can be considered through the boiling point.

The above-mentioned properties relevant to classify solvents and facilitate the search of substitution uses have been investigated in a series of 62 glycerol derivatives that can be used as solvents. For instance, topological descriptors have been successfully applied to analyze and predict solvent polarities (Figure 2).

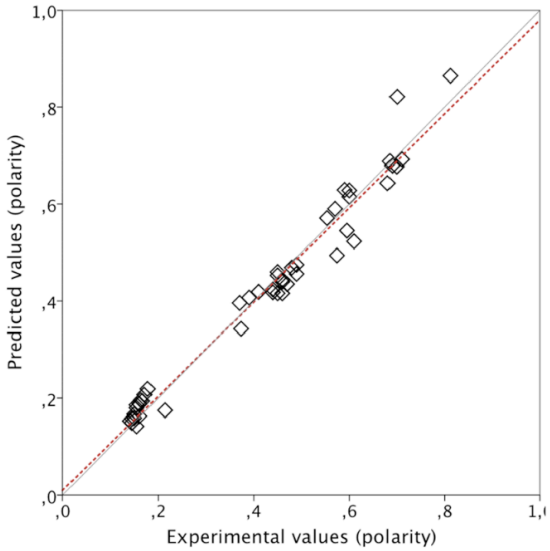

Fig. 2 – Plot of predicted *vs.* experimental values of E_T^N, as calculated through PLS analysis using topological descriptors.

The robustness and predictive value of the equations developed have been demonstrated through the use of an independent test set of solvents (Table 1).

Table 1. Mean unsigned errors (MUE) calculated for the different equations developed in this work.[a]

Model	E_T		η		bp	
	training	test	training	test	training	test
MLR Topol.	0.028	**0.030**	7.28	5.08	8.6	*10.9*
PLS Topol.	0.027	**0.030**	6.34	4.62	6.6	*10.3*
MLR D.-P.	0.024	*0.051*	1.37	**2.05**	4.6	*10.3*
MLR Mixed	0.026	**0.033**	1.02	**1.95**	3.9	*8.8*

[a] Bolface values indicate errors within the 5% of the full range of experimental values, and italicized values, indicate errors within the 8% of the full range.

Therefore, the QSPR models developed provide significant additional insight into the relationship between the molecular structure and some fundamental solvent properties, that can be subsequently used for selecting the best solvent meeting the application requirements.

In this regard, another important issue is to find compounds that possess the right combination of physico-chemical properties. The use of quantum mechanical calculations, solvent properties maps and clustering methods are useful tools to achieve this goal. Some recent examples involving glycerol derivatives are also discussed.

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References

1 P. G. Jessop, *Green Chem.* 2011, **13**, 1391.
2 P. G. Jessop, D. A. Jesssop, D. Fu, L. Phan, *Green Chem.* 2012, **14**, 1245.
3 J. I. Garcia, H. Garcia-Marin, J. A. Mayoral, P. Perez, *Green Chem.* 2010, **12**, 426.
4 H. Garcia-Marin, J. C. van der Toorn, J. A. Mayoral, J. I. Garcia, I. W. C. E. Arends, *Green Chem.* 2009, **11**, 1605.
5 L. Aldea, J. M. Fraile, H. Garcia-Marin, J. I. Garcia, C. I. Herrerias, J. A. Mayoral, I. Perez, *Green Chem.* 2010, **12**, 435.
6 H. Garcia-Marin, J. C. van der Toorn, J. A. Mayoral, J. I. Garcia, I. W. C. E. Arends, *J. Mol. Catal. -Chem.* 2011, **334**, 83.
7 L. Aldea, J. I. Garcia, J. A. Mayoral, *Dalton Trans.* 2012, **41**, 8285.
8 L. B. Kier, L. H. Hall, *Molecular Connectivity in Structure-Activity Analysis*. Ed. Research Studies Press Ltd, New York, 1985.
9 J. E. Dubois, *Computer Representation and Manipulation of Chemical Information*. Ed. Wiley, New York, 1974.
10 C. Reichardt, in *Solvents and Solvent Effects in Organic Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2004.