HSP50

The 50th Anniversary HSP

UCCS
UNITÉ DE CATALYSE ET CHIMIE DU SOLIDE

Green Chemistry
Centre of Excellence

Predictive Power of HSP in Formulation Science:

In silico design of bio-based solvents for nitrocellulose thanks to HSPs

Jean-Marie AUBRY, Professor at the ENSC-Lille

April 5-7, 2017 – York

Université de Lille · cnrs · UNIVERSITÉ D'ARTOIS · CENTRALE LILLE · Chimie Lille ÉCOLE NATIONALE SUPÉRIEURE DE CHIMIE · Chevreul Fédération Michel Eugène · Communauté d'Universités et d'Établissements Lille Nord de France · CISCO2 COLLOIDS CATALYSIS OXIDATION

UCCS - Group « Colloïds, Catalysis and Oxidation »

- **Located in Lille (North of France)**

  1 hour from Paris by TGV.

  1 154 000 inhabitants (> 110 000 students)

Main event:

Braderie de Lille, a huge flea market

mussel shells

THIS KEYNOTE IS BASED ON THE PUBLICATION BELOW …

A “top-down” in silico approach for designing ad hoc bio-based solvents: application to glycerol-derived solvents of nitrocellulose

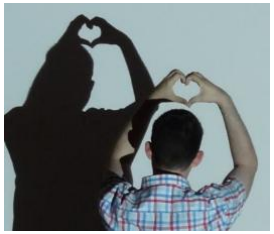
L. Moity, V. Molinier, **A. Benazzouz**, B.Joossen, V. Gerbaud, J.M. Aubry. *Green Chem*. **18** (2016) 3169–3458

Laurianne MOITY

(Solvay)

« The Artist » for this cover is ….

Adrien BENAZZOUZ (L’Oréal)



SUMMARY

- Solvents revival
- “Top-down” approach
- Virtual glycerol-based solvents
- Experimental validation
- Conclusion

Why is there a sudden surge of interest for solvents?

NEW REGULATIONS LEAD TO REPLACE IMPORTANT SOLVENTS

Environment

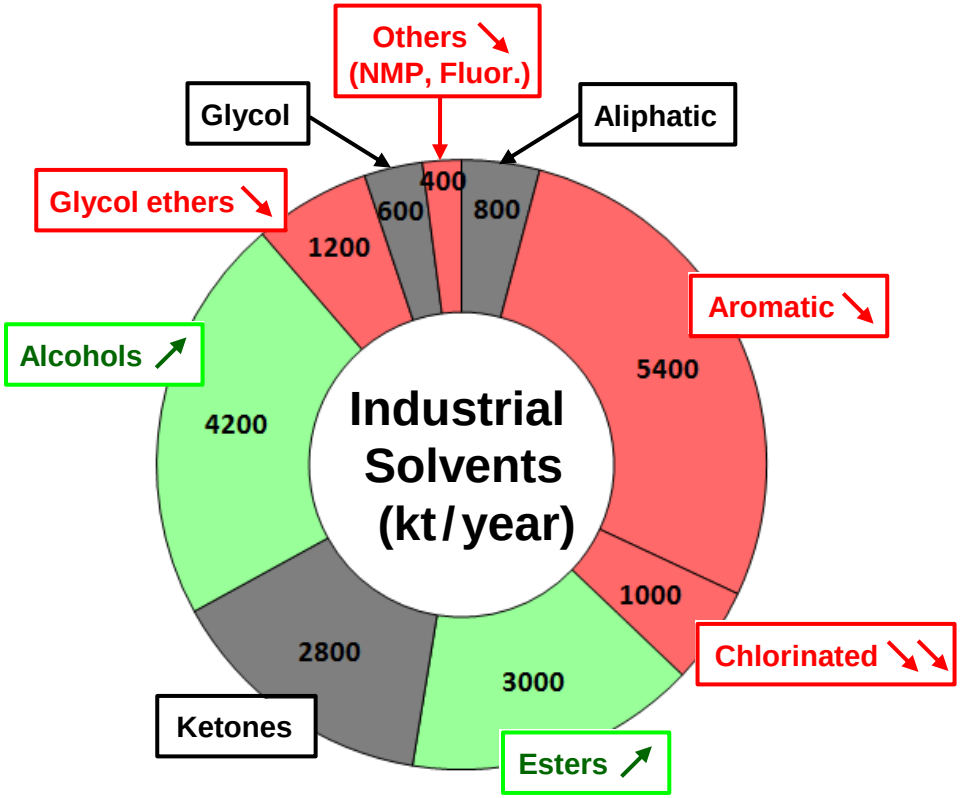
- VOC reduction
- Ozone Depletion (Freons)
- Biodegradation (non-cumulative)

Human Health (in Europe)

- CMR (glycol ethers, NMP, toluene)
- REACH regulation

Sustainable development

- 12 Principles of Green Chemistry
- Life Cycle Analysis
- Renewable raw materials



Nowadays, safety is the main driving force for choosing a solvent

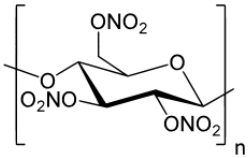
➡ **Need for safe and effective sustainable solvents**

Dividing a generic problem **(dissolving a solute)** into a series of tools allowing to find the best potential solutions **(optimal solvents)**

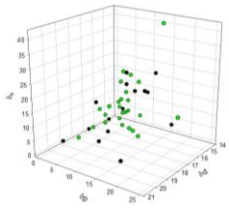
TOP-DOWN APPROACH for SOLVENT DESIGN

SPECIFICATIONS

SOLUTE

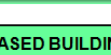


+ BIO-SOLVENT



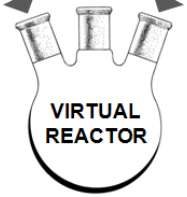
GRASS

BIO-BASED BUILDING BLOCK



CO-REACTANTS
4 explicit &12 implicit

53 CHEMICAL TRANSFORMATIONS



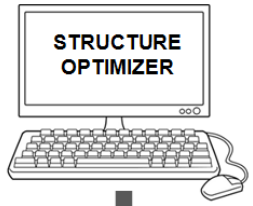
LEAD COMPOUNDS for Commodity Chemicals

IBSS

SUBSTITUENT GROUPS
Alkyle - Alkene – Alkyne - Phenyl

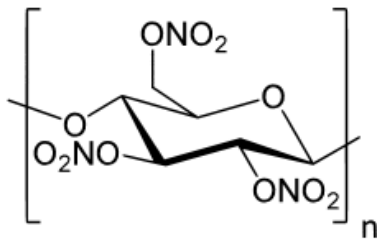
LEAD COMPOUNDS

SPECIFICATIONS



- Glycerol derivatives
- Ranking of solvent candidates

1st STEP: Choose a target and define specifications



+

Effective and safe

Bio-solvent

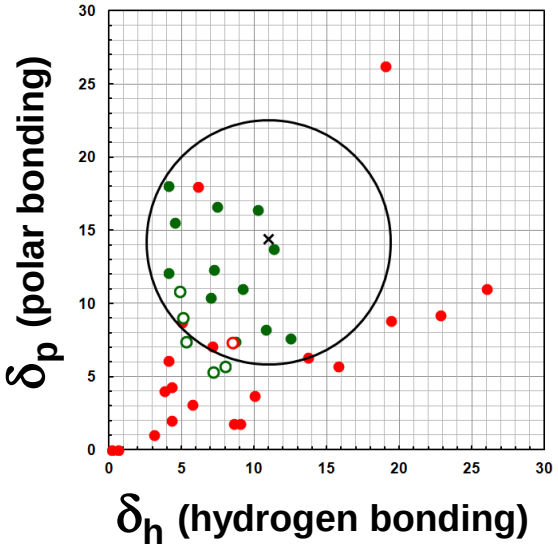
Nitrocellulose (nail polish and wood lacquer)

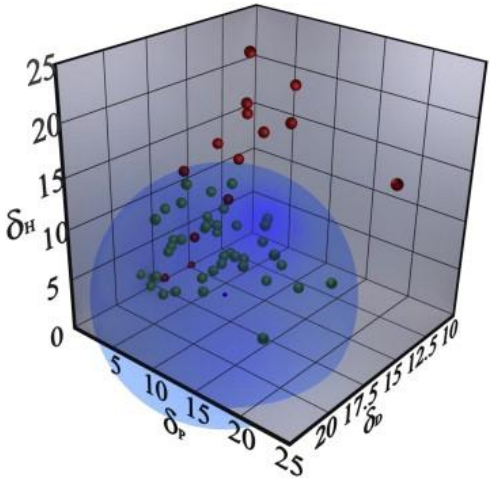
+

Solvent

- Effective (assessed through Hansen approach)
- Bio-based (e.g. glycerol derivatives)
- Non-flammable (Flash point > 60°C)
- Non-toxic and biodegradable

Hansen's sphere of nitrocellulose with 40 usual solvents





3D-Space δ_h, δ_p, δ_d

Hansen's sphere Parameters / $MPa^{1/2}$
δ_d = 18.4
δ_p = 14.4
δ_h = 11.0
R = 8.3

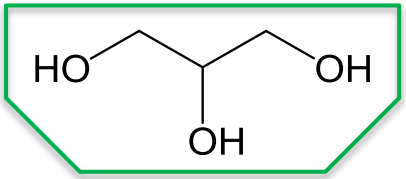
Distance from the centre

$$D = \sqrt{4(d_{d_{Solvent}} - d_{d_{Solute}})^2 + (d_{p_{Solvent}} - d_{p_{Solute}})^2 + (d_{h_{Solvent}} - d_{h_{Solute}})^2}$$

Predicted effectiveness RED = D / R => Good solvent when RED < 1

2nd STEP: Generate *in silico* feasible solvents from glycerol with GRASS, a Computer Assisted Organic Synthesis software

GRASS = **G**enerato**R** of **A**gro-based **S**ustainable **S**olvents

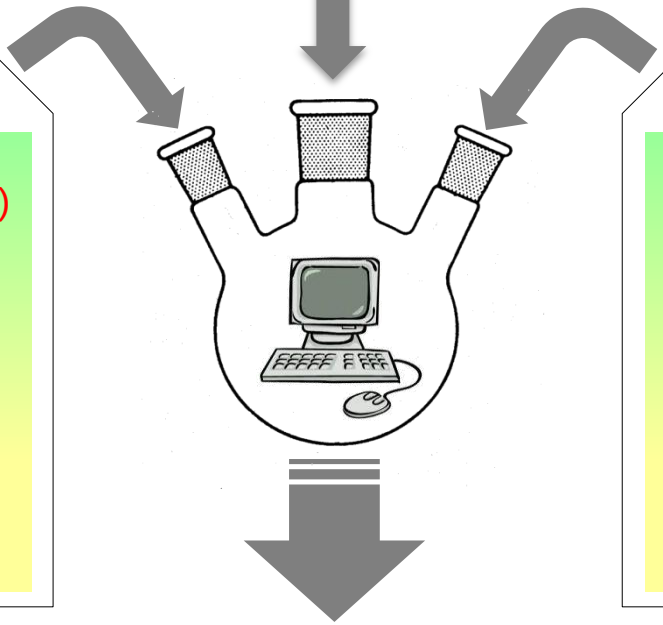


Co-Reactants

15 Implicit (H_2, O_2, H_2O...)

+ 7 explicit:

- Ethanol
- Methyl amine
- Acetic acid
- Acetone, etc …



Sustainable Chemical Transformations

- Esterification
- Oxidation
- Dehydration
- Carbonatation
- Acetal formation
- Etc …

VIRTUAL Derivatives of glycerol

We limit ourselves to the 1st GENERATION !

Relevant Chemical Transformations for Commodities

Bibliographical sources:

- Synthesis of petrochemical commodities
- Transformations of bio-based molecules

≈ 450 reactions were found

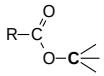
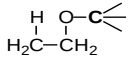
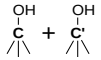
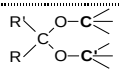
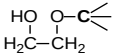
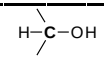
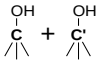
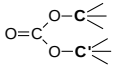
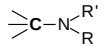
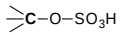
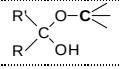
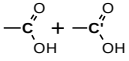
Selection criteria of relevant chemical conversions:

- Efficiency (good yields)
- Mild conditions (temperature, pressure)
- Greenness (atom economy, safe reactants)
- Cost effectiveness

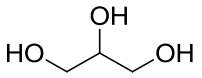
60 sustainable chemical transformations but …

only 15 apply to glycerol

15 chemical transformations applicable to glycerol

TRANSFORMATION	ALCOHOL	CO-REACTANT	FINAL FUNCTION
Esterification			
Hydro-alkoxy-addition			
Acetalization			
Alcoholysis			
Dehydration		- H_2O	
Oxidation		O_2	
Oxidation		O_2	
Carbonation		CO_2	
Amino-de-hydroxylation		NH_3	
Amino de-hydroxylation			
Alkoxy de-hydroxylation		R–OH	
Alcohol carbonylation		CO	
Alcohol sulfation		SO_3	
Hemiacetalization			
Glycol oxidative cleavage		Oxidant	

Bio-based building-block



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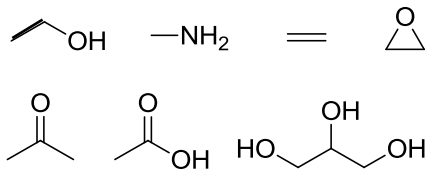
Co-reactants: Implicit + 7 explicit



GRASS

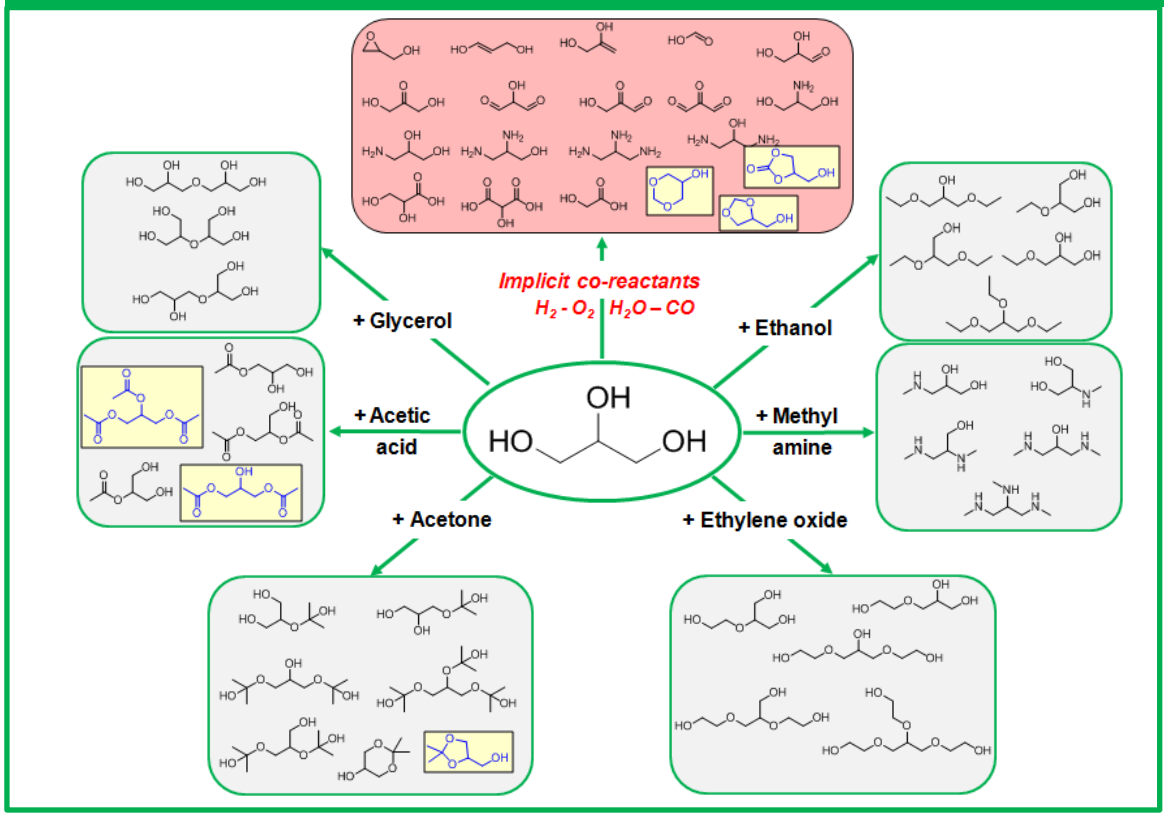
chemical transformations

50 virtual candidates at the 1st generation

Molecules highlighted in yellow obtainable with yield > 95%

2nd generation: 15000 compounds

1ST GENERATION : Virtual derivatives of Glycerol



GRASS program …

generates “leads” molecules but other co-reactants are also relevant:

EtOH ⇨ MeOH, PhOH, etc…

IBSS program …

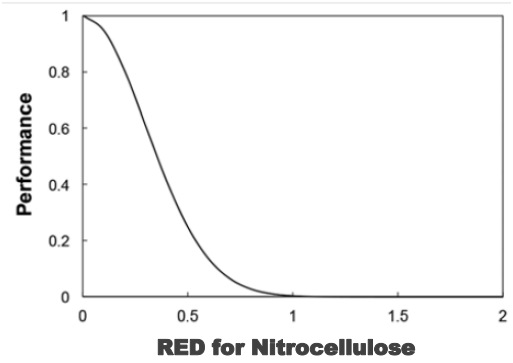
- Generates derivatives from “leads”
- Predicts properties of virtual solvents candidates

3rd STEP: Specifications for the ideal solvent

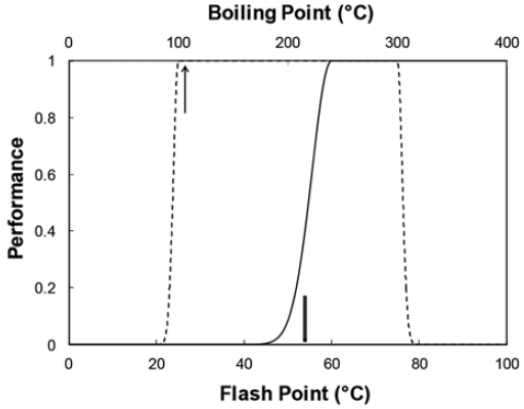
Individual performances	Target values	Weight %
Solubilisation **(Hansen approach)**	RED = 0	40 %
Volatility	100°C < BP < 300°C	20 %
Flammability	FP > 60°C	20 %
Toxicity (fish)	LC_{50} > 100 mg/L	10 %
Biodegradability (octanol/water)	$K_{O/W} < 10^{-3}$	5 %
Bioaccumulation	BCF < 100	5 %

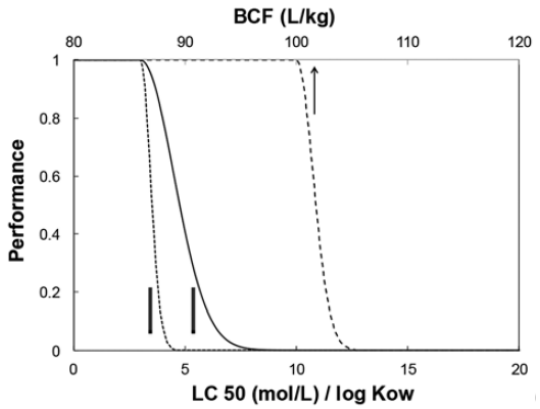
3rd STEP: IBSS program predicts properties of virtual solvents

Individual Performances assessed by predictive methods



RED with HSPiP software





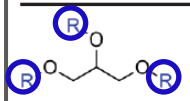
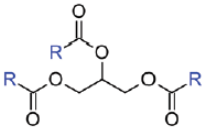
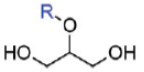
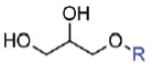
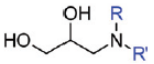
BP, FP, EHS indexes are calculated with group contribution methods

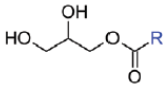
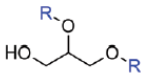
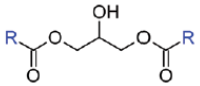
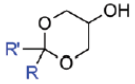
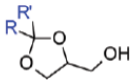
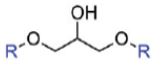
Global effectiveness of virtual solvents are assessed by the

Overall Performance = Σ (Individual Performance) x (Weight %)

4th STEP: IBSS generates derivatives and ranked them

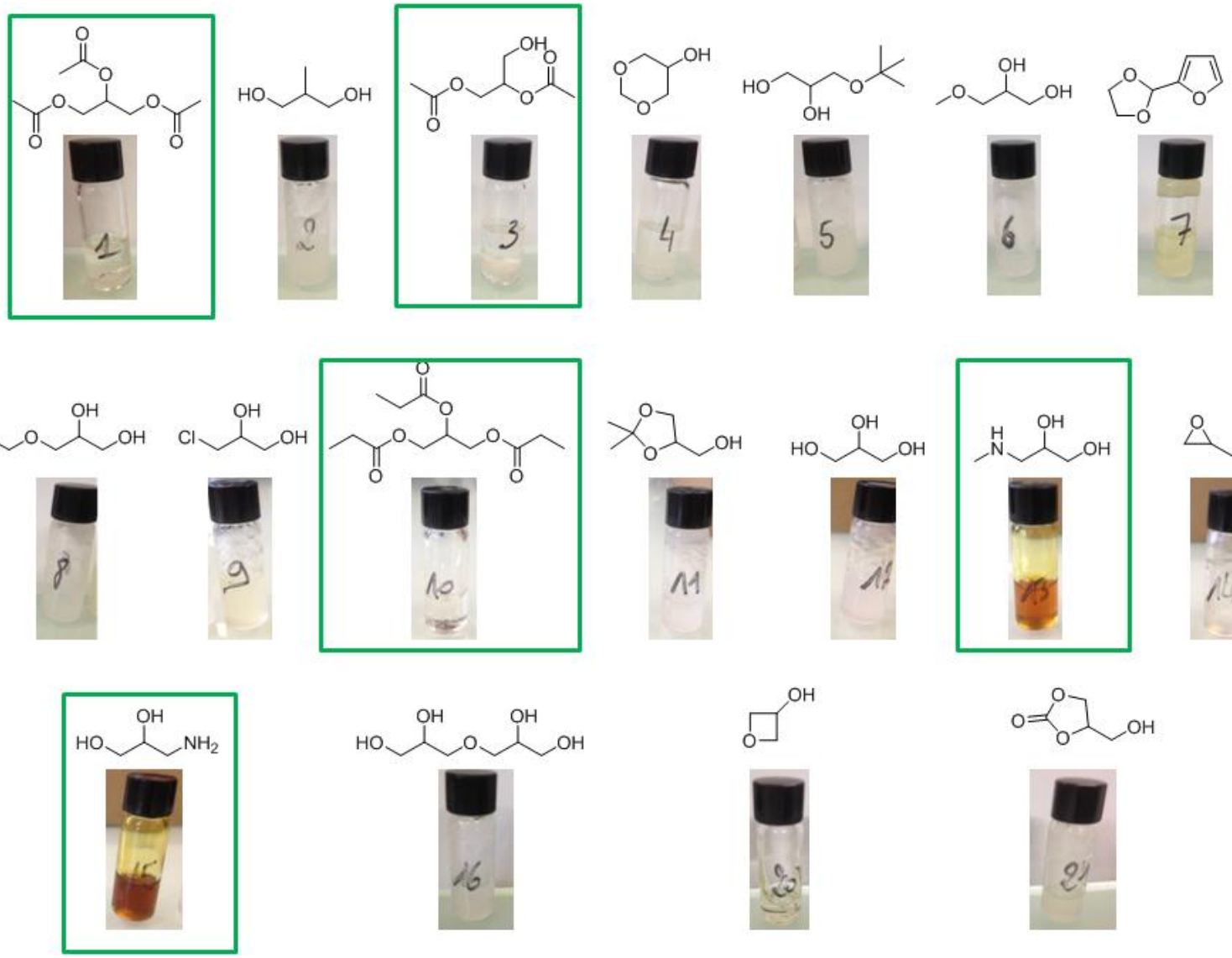
R groups from leads are replaced by C_{1-6} alkyl, cycloalkyl, alkene, cycloalkene or phenyl substituents and the solvent-candidates are ranked thanks to the overall Performance Function

Lead compounds	Co-reagent	Substituents R	Substituents R′	Perf %	Ref.
	R–OH	Me	—	39.5	51
		Et	—	57.4	—
		—	—	—	—
		Me	—	54.6	55
		Et	—	54.9	58
		—	—	—	—
	R–OH	Me	—	57.9	50
			—	65.1	59
		—	—	—	—
	R–OH	Me	—	58.3	49
			—	61.5	60
			—	62.5	—
	R–NH–R′	H	Me	58.4	—
		H		61.6	61
		H		67.1	—

Lead compounds	Co-reagent	Substituents R	Substituents R′	Perf %	Ref.
		Me	—	58.6	53
			—	64.1	62
			—	69.1	—
	R–OH	Me	Me	59.1	—
		Et	Et	60.8	63
		—	—	—	—
		Me	Me	59.9	52
		—	—	—	—
		—	—	—	—
		Me	Me	58.5	57
		H		61.7	64
				71.8	—
		Me	Me	58.4	56
				63.5	65
				63.5	—
	R–OH	Me	Me	60.6	47
		Et	Et	62.9	20

Among the most promising virtual candidates, some are completely new while 15 are commercially available. Let us focus on the latter !!!

Evaluation of effectiveness of 15 commercial glycerol derivatives towards nitrocellulose



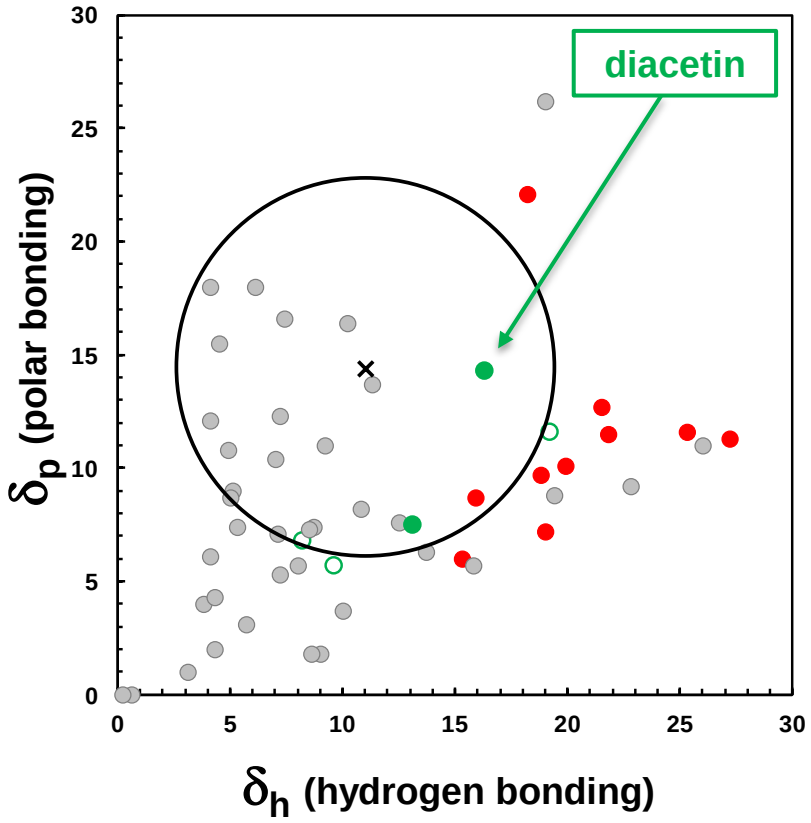
Prediction from HSP (RED < 1) vs Experimental tests

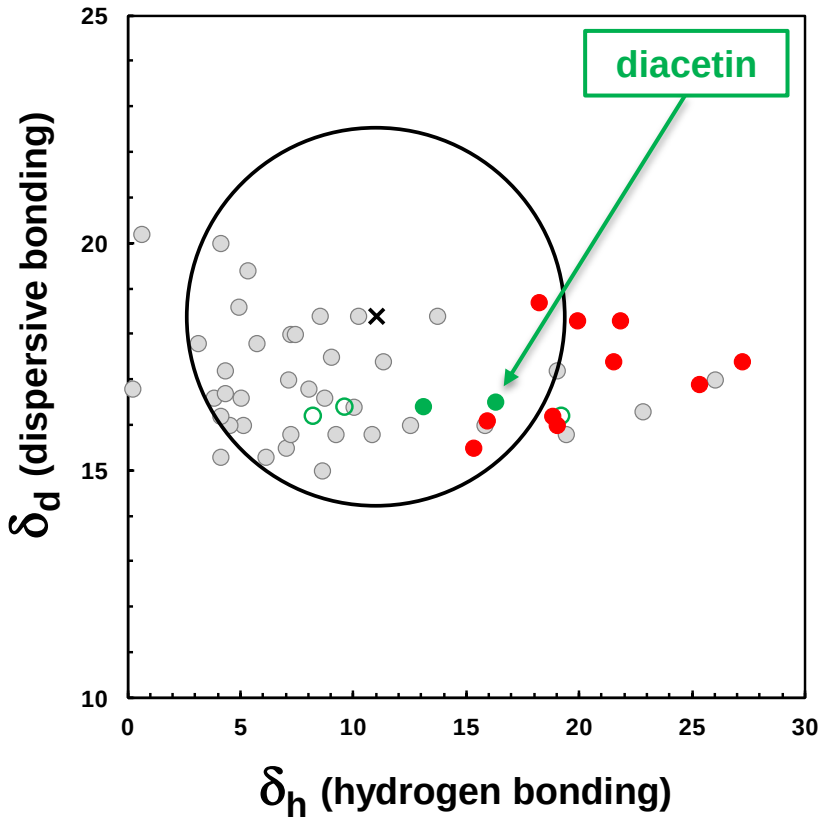
Glycerol derivates	RED (Hansen)	Solubilisation of Nitrocellulose ?
Diacetin	**0.9**	**Yes**
Tripropionin	**1.1**	**Yes**
Triacetin	**1.1**	**Yes**
Glycerol formal	**1.2**	**No**
Glycerol carbonate	**1.2**	**No**
Solketal	**1.2**	**No**
Glycerol	**1.2**	**No**

In agreement with HSP predictions, diacetin is actually an effective and non-toxic bio-based solvent for nitrocellulose

Positions of glycerol-based solvents with regard to the Hansen's solubility sphere of nitrocellulose

Conventional solvents ● Good bio-solvents ● Poor biosolvents ○ and ○ Outliers





POSTER: Finding a Greener Set of Solvents for HSPs

POSTER:

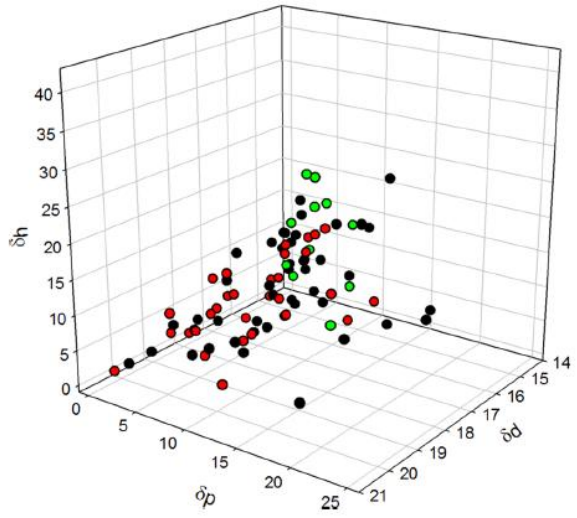
A. BENAZZOUZ , L. MOITY, C. PIERLOT, V. MOLINIER, M. SERGENT, J. M. AUBRY

A greener set of solvents o study the solubility profile of polymers and resins according to Hansen approach

PUBLICATION:

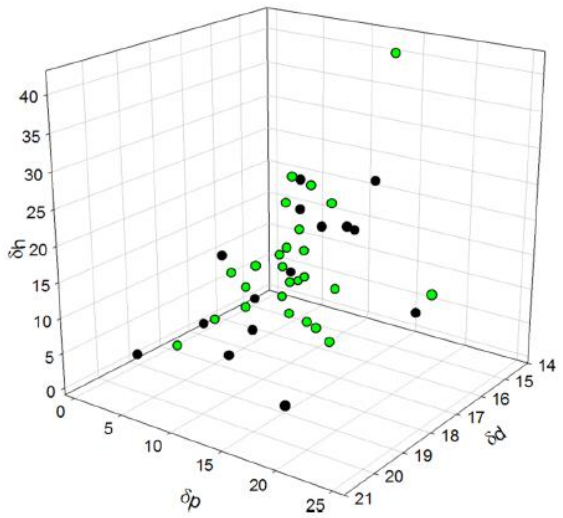
A. BENAZZOUZ, L. MOITY, C. PIERLOT, M. SERGENT, V. MOLINIER, J-M. AUBRY,

Selection of a Greener Set of Solvents Evenly Spread in the Hansen Space by Space-Filling Design. *Ind. Eng. Chem. Res*. (2013) **52**, 16585-16597



Historical set of Hansen's solvents

● Unacceptable solvents



Greener set of solvents well-spread

● Green solvents ● Acceptable solvents

Designing ad hoc bio-based solvents

- **GRASS** is able to generate thousands of **feasible** virtual leads from a platform molecule

- **IBSS** may … predict relevant **physico-chemical and HSE** properties of candidate solvents
  … generate **derivatives** from generic leads through the exchange of substituents
  … calculate the value of the overall **performance** function and ranked the candidates

- **Top-Down approach** allows pointing out **diacetin** as a good and safe solvent for nitrocellulose

Prospects for the future

- Construct a **databank** of thousands of virtual molecules generated from the main bio-based building blocks (glycerol, succinic acid, itaconic acid etc...)

- Improve prediction of the solubilizing power of a virtual solvent (**Hansen** ⇨ **COSMO-RS**)

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2013 Dr Laurianne MOITY

Design and test of green solvents

Dr Adrien BENAZZOUZ : Hansen parameters

Benjamin JOOSSEN : Tested bio-based solvents

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