

Extensive Screening of Green Solvents for Safe and Sustainable UiO-66 Synthesis

Diletta Morelli Venturi, Filippo Campana, Fabio Marmottini, Ferdinando Costantino and Luigi Vaccaro**

KEYWORDS Metal-Organic Frameworks; Zirconium; Synthesis; Green Chemistry; Sustainability

ABSTRACT. Zirconium based Metal-Organic Framework UiO-66 is to date considered one of the benchmark compound among stable MOFs and it has attracted a huge attention for its employment in many strategic applications. Large scale production of UiO-66 for industrial purposes requires the use of safe and green solvents, fulfilling the green chemistry principles and able to replace the use of *N,N*-Dimethyl-Formamide (DMF), which, despite its toxicity, is still considered the most efficient solvent for obtaining UiO-66 of high quality. Herein we report on a survey of about 40 different solvents with different polarity, boiling point and acidity, used for the laboratory scale synthesis of high quality UiO-66 crystals. The solvents were chosen according the European REACH Regulation 1907/2006 among those having low cost, low toxicity and fully biodegradable. Concerning MOF synthesis, the relevant parameters chosen for establishing the quality of the results obtained are the degree are the crystallinity, microporosity and specific

surface area, yield and solvent recyclability. Taking into account also the chemical physical properties of all the solvents, a color code was assigned in order to give a final green assessment for the UiO-66 synthesis. Defectivity of the obtained products, the use of acidic modulators and the use of alternative Zr-salts have been also taken into consideration. Preliminary results lead to conclude that GVL (γ -valerolactone) is among the most promising solvents for replacing DMF in UiO-66 MOF synthesis.

INTRODUCTION

After a decade focused on fundamental synthetic and structural aspects, the chemistry of Metal-Organic Frameworks (MOFs) is rapidly moving towards industrial application and large-scale commercialization. Zirconium based MOFs are today considered benchmark compounds for their high stability in different media, low cost and for their high structural versatility which allows to employ them in a vast number of strategic applications in the field of catalysis¹⁻⁴, gas⁵ and solvent sorption^{6,7}, separation^{8,9}, proton conductivity¹⁰ and for biomedical purposes.^{11,12} The archetypal Zr-MOF is the UiO-66 phase of general formula $Zr_6O_4(OH)_4(BDC)_6 \cdot nDMF$ (H_2 -BDC = benzene dicarboxylic acid) first synthesized in 2008 by Lillerud et al.¹³ From its discovery to date, the number of papers citing UiO-66 overcomes 1500. UiO-66 has a cubic face centred symmetry and it is constituted by hexanuclear $Zr_6O_4(OH)_4$ ¹²⁺-twelve connected inorganic building units (IBUs) linked by the BDC ligand. Porosity of UiO-66 is variable (BET surface area in the 900 to 1600 m²/g range) owing to the possibility to generate a defective structure by using monocarboxylic acid modulators during synthesis, which lead the formation of missing linker or missing cluster defects.¹⁴⁻¹⁸ The early stage synthesis of UiO-66 involved the use of $ZrCl_4$ as Zr^{4+}

source and DMF as solvent able to well dissolve H₂-BDC and Zr salt. The formation of zirconium oxo-clusters required the presence of oxygen sources which can arise from water present in DMF, in the hydrated salts or from direct addition of water during synthesis. The use of acidic modulators and of proton scavengers have been also extensively investigated.^{19,20} During the last years, several synthetic strategies have been tried for the synthesis of DMF-free UiO-66, involving the use of alternative methods such as mechanochemical approaches²¹, accelerated aging²² and microwaves²³ or the use of non-toxic solvents such as water, green solvents from biomasses and from industrial production waste.²⁴ Water based syntheses were found to be effective for UiO-66 MOFs based on substituted X-BDC ligands (with X = F, Cl, Br, NO₂) or nitrogen-containing BDC-like linkers such as 2,5-pyridine or 2,5-pyrazine dicarboxylic acids (H₂-PDC, H₂-PyDC) with higher acidity than simple H₂-BDC acid, which increased the solubility in water.^{25,26} However, the use of water has proven to be not suitable for the preparation of H₂-BDC UiO-66 due to its low solubility in water, while the zirconium salt is highly soluble. This difference in the “solution-state” make the crystals growth very difficult.²⁷ In fact, solvents play a dramatic role in influencing the chemical and environmental efficiency of a process, and also the preparation of MOF materials is tremendously affected by the medium used both on the properties of the material obtained and on its applicability. In almost every chemical production, it is urgent the need for developing new, safer, and cleaner synthetic routes in agreement to the regulatory requirements in the European Union aiming at reducing or banning the use of chemicals that may be harmful to human health or the environment. Representative is the case of the European REACH Regulation 1907/2006 that envisages a mechanism which forces companies to apply for an authorization if they

want to use or distribute chemicals (including solvents) identified as Substances of Very High Concern (SVHC).²⁸ Equivalent rules apply to the manufacturing, the commercialization and use SVHC, and especially to largely used solvents. Health and safety regulations have nowadays a major impact on solvent selection and in particular, chlorinated hydrocarbons, aromatics, and dipolar aprotic solvents such as *N,N*-dimethylformamide (DMF), are identified as hazardous due to their well-known chronic toxicity effects.²⁸ In this context, it is fundamental the identification of safer media to replace those highly toxic and most of the fundamental and industrial research is looking for novel safe solvent candidates with a special attention to those deriving from waste of large manufacturing process or from biomasses.²⁹⁻³⁹ The ideal solvent for the synthesis of H₂-BDC UiO-66 is responsible to perform in many different directions. An effective solvent should be able to completely dissolve the reagents whilst playing a fundamental role in the formation of the crystalline structure. As an example, the commonly used DMF, has an active role in H₂-BDC UiO-66 synthesis by entering the coordination sphere of the zirconium steering the formation of the crystal lattice formation.⁴⁰ In this contribution, we report an extensive study on the screening of solvents that could be eventually be selected as alternative for the synthesis of BDC-UiO-66. Based on our previous studies,^{24,41-46} we have considered several different classes of solvents and grouped in terms of their chemical-physical features, *e.g.* dielectric constant (ϵ) and boiling point (Bp). We have compared their efficiency to produce BDC-UiO-66 using a standard protocol and classified their performance based the ability to actually form the desired UiO-66 MOF, the full width at half maximum (FWHM) of (111) diffraction peak, the crystal size, the BET surface area achieved and the yield. The screening allowed to identify a small number of selected

solvents which afforded high quality UiO-66 crystals as pure phase without the formation of co-products whereas those yielding co-products or MOFs with low crystallinity degree will be object of future dedicated studies.

MATERIALS AND METHODS.

Chemicals

All chemicals are commercially available and used without further purification.

1-(2-hydroxyethyl)-2-pyrrolidone, 2-ethylhexylacetate, Cyclohexanone, 2-Methyl-tetrahydrofuran, Ethyl-L-lactate, γ -valerolactone (GVL), Zirconium Chloride and terephthalic acid were purchased by Sigma Aldrich. Diethyl succinate i-Butylacetate, Diethyl carbonate, Dimethyl carbonate, Propylene carbonate, 1,3-Dioxolane and 1,2-isopropylidene glycerol (Solketal) were purchased by Alfa Aesar. Dimethyl adipate, Dimethyl succinate, Ethylene glycole diacetate, i-Propylacetate, Isoamyl acetate, Methyl laurate, Methyl tetradecanoate, Anisole, 2-Ethylhexylacetate, Triacetine, p-Cymene, n-Amyl acetate, Cyclopentylmethyl ether (CPME), and Zirconyl chloride octahydrate were purchased by Thermo Fisher Scientific. Rhodiasolv® IRIS, Rhodiasolv® Polarclean were purchased by Solvay. Esterol® F were purchased by Arkema. Loxanol®, Plurafac® LF120, Plurafac® LF221, Plurafac® LF303, Plurafac® LF771, Dehypon® LS54, Agnique® AMD 810 were purchased by BASF. Synperonic® LF30 was purchased by CRODA. Purasolv® EHL was purchased by Corbion Purac. Steposol® MET-10U was purchased by Stepan. Tert-amyl methyl ether (TAME) was purchased by IMCD and 4-methyltetrahydropyran was purchased by Kurakay. Acetic Acid was purchased by Carlo Erba.

Synthetic procedures

DMF synthesis of UiO-66

First, DMF synthesis without modulator of UiO-66 was tried according to literature¹¹: ZrCl₄ (0.5 mmol), one equivalent of H₂-BDC and three equivalents of water were dissolved in 100 mL of DMF in a Teflon reactor and the mixture was sonicated until complete dissolution of reagents occurred. After this, the reactor was put in thermostated oven at 120°C. After 16 hours MOF was soaked in DMF, water and acetone to remove unreacted starting materials and the reaction media. At the end the UiO-66 was put in oven at 80°C to remove the solvent used to soak. Figure 1 shows the general reaction scheme.

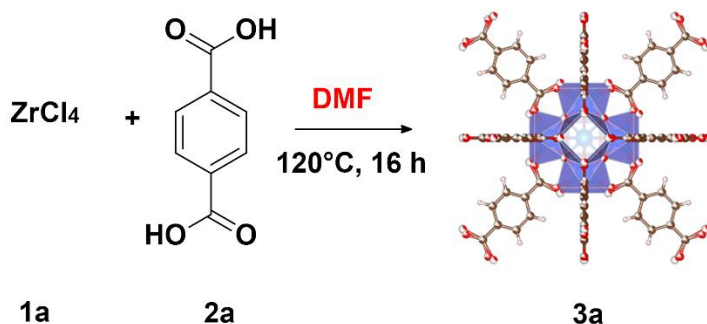


Figure 1. DMF synthesis of UiO-66 (**3a**) without modulator. Reaction condition [ZrCl₄] = 0.125M (**1a**), 1 equivalent of **2a**, and 3 equivalents of water.

In the second step the reaction was scaled down to verify the viability of the process using a lower amount of solvent and therefore a higher concentration of reagents to improve the efficiency of the process. The procedure was the same as reported above but the volume of the solvent amount was 2 mL and the ZrCl₄ 0.5 mmol. The final concentration of zirconium salt was 0.25M. Finally, the procedure was optimized by adding 30 equivalents of acetic acid (AcOH).

Synthesis of UiO-66 using green solvents at the optimized conditions



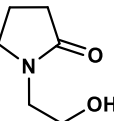
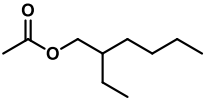
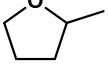
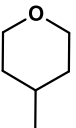
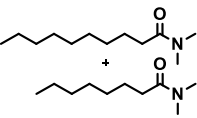
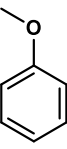
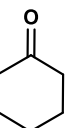
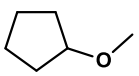
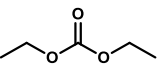
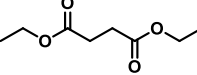
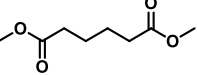
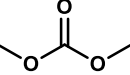
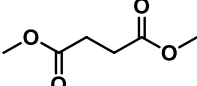
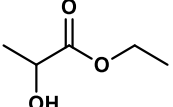
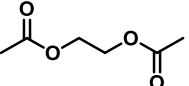
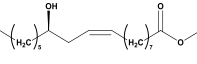
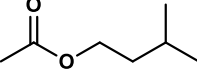
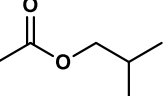
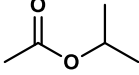
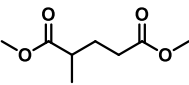
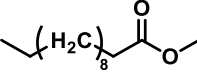
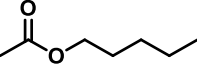
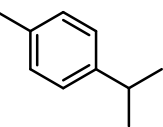
The synthetic procedures were standardized in the following way: In a screw capped 4 mL vial, H₂-BDC (83 mg, 0.5 mmol) was dissolved in the *chosen solvent** (4 mL), followed by the addition of water (27 μ L, 3 eq), acetic acid (860 μ L, 30 eq) and ZrCl₄ (116 mg, 0.5 mmol). The mixture was sonicated until dissolution. The vial was then put inside a Teflon reactor and placed in a thermostated oven at 120°C for 16 h. After completion of the reaction, the solid was centrifuged and washed with MeOH (two time one-hour soaking), water (one times one-hour soaking) and acetone (one time one-hour soaking, one-time overnight soaking). The solids were dried at 80 °C for two hours.

* see table 1

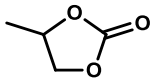
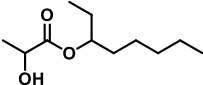
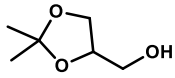
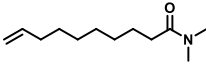
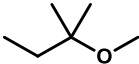
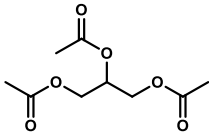
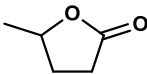
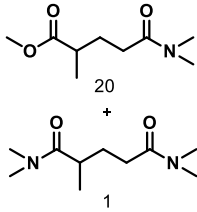
Table 1. Molecular structure of the solvent used.

RESULTS AND DISCUSSION

DMF synthesis was preliminary performed in order to have a term of comparison with the results arising from the successive solvent screening. XRPD patterns of the syntheses without (exp. a) and with modulator (exp. b) are shown in figure S1. The optimized synthesis (b) was performed by increasing the reagent concentration (from 0.05 M of literature synthesis to 0.125 M). The addition of 30 eq of AcOH allowed to improve the degree of crystallinity. This synthetic condition was employed for all the solvents tested. Table 2 reports the list of solvents used for the synthesis of UiO-66. The solvents are divided in classes (alcohols, esters, carbonates, ketones, aromatics, ethers and dipolar aprotic solvents). To this end, a classical color code (green, yellow, red) has

1,3-Dioxolane 	1,3-Propanediol 	1-(2-hydroxyethyl)-2-pyrrolidone 	2-Ethylhexyl acetate 	2-Methyl tetrahydrofuran 	4-Methyl-tetrahydropyran 
Agnique AMD 810 	Anisole 	Cyclohexanone 	Cyclopentyl methyl ether 	Dehypon LS 54 $\text{R} \left[\text{O} \left(\text{CH}_2 \right)_n \text{OH} \right]$ R: C _x H(2x+1) x: 12, 14 n: 2, 3	Diethyl carbonate 
Diethyl succinate 	Dimethyl adipate 	Dimethyl carbonate 	Dimethyl succinate 	Ethyl-L-lactate 	Ethylen glycole diacetate 
Esterol F 	<i>i</i> -Amyl acetate 	<i>i</i> -Butyl acetate 	<i>i</i> -Propyl acetate 	Iris 	Loxanol $\left(\text{H}_2\text{C} \right)_8 \text{CO}_2\text{Me} + \left(\text{H}_2\text{C} \right)_{10} \text{CO}_2\text{Me}$
Methyl laurate 	<i>n</i> -Amyl acetate 	<i>p</i> -Cymene 	Plurafac LF 711 $\text{R} \left[\text{O} \left(\text{CH}_2 \right)_n \text{OH} \right]$ R: C _x H(2x+1) x: 9, 11 n: 2, 3	Plurafac LF 221 $\text{R} \left[\text{O} \left(\text{CH}_2 \right)_n \text{OH} \right]$ R: C _x H(2x+1) branched and linear x: 13, 15 n: 4, 2	Plurafac LF 303 $\text{H} \left[\text{O} \left(\text{CH}_2 \right)_n \text{OH} \right]$

been used for each general area of assessment (i.e. solvent greenness, boiling point requirement for safety/processing, viscosity for the crystallization/purification steps). According to a classification reported in a recent paper of Vaccaro et al.,⁴⁷ on the use of green solvents for organic

Plurafac LF 120 Trade secret	Propylene carbonate 	Purasolv EHL 	Solketal 	Steposol 	Synperonic LF 30 Ethylene oxide/propylene oxide copolymer based on C12-C15 alcohol
<i>t</i> -amyl methyl ether 	Triacetin 	γ -Valerolactone 	Polarclean 		

thin-film transistor processing, the solvent color code is inspired by the GlaxoSmithKline, GSK, and CHEM 21 solvent selection guides for the pharmaceutical industry.⁴⁸⁻⁵¹ These guides account for the physical and (eco)toxicity properties of solvents by transforming them into a scale to determine their greenness. The color codes for bps, viscosity and crystal size of MOFs are reported in the table 3. Other than the parameters already used in previous work for the green assessment we added here a color code also for the crystallinity degree of the obtained MOF. DMF is also included as reference entry. These codes are also combined in a composite color incorporating all these requirements, to give a ranking by default and “ranking after discussion” of each solvent. Particularly, the *preferred* solvents, i.e. solvents presenting a few issues, are displayed with the green color code; the yellow color code has been used for *problematic* solvents, i.e. solvents that can be used but their implementation may present issues or uncertainties; *not recommended* solvents are identified with red color code, i.e. the constraints on the solvent use are very high.

Boiling points are already considered in the overall greenness assessment but, a separate column was included in Table 2 listing the solvent b.ps, to take specifically into account their suitability for UIO-66 synthesis. The associated color codes are based on the ranges defined in Table 3a.

Extremely low boiling point solvents ($T \leq 50^\circ\text{C}$) may not be suitable for MOF processing and cannot be used both for technical and safety issues. Table 3a also reports the value ranges for the solvent viscosity (η , mPa·s) coding, reflecting again the general solvent appropriateness for MOFs synthesis. The crystal size and the surface area has been also scored. These two parameters have prime importance to evaluate the morphological quality and the adaptability of the synthesized UIO-66 for example for gas storage and catalysis.

Consequently, the ranking “by default” color code is dominated by the crystal size (Table 3b). Finally, a ranking “after discussion” was assessed (Table 2, last column), as the result of an overall evaluation of the solvent greenness, MOFs crystal size and surface area, and so on further improvement and possible applications based on the obtained morphological features. First, in the ranking “after discussion” DMF, despite the quality of the MOF obtained, is listed as “not recommended” due to its critical toxicological profile. We did not modify the ranking by default for “preferred” solvents (“green” code) leading to UIO-66 MOFs with crystal size higher than 450 Å, an arbitrary value we chosen in order to establish a good crystallinity degree. Moreover, we assigned the color “green” to those solvents leading to a “green” crystal size but that featured present an intermediate BET surface area (yellow code). The reason for this choice is the fact that further enhancement in the MOF synthesis could lead to higher values.

Furthermore, we assigned “yellow code” to the combination “green” crystal size/ “red” surface area and “red” code to the combination “yellow” crystal size/ “red” surface area and vice versa. Crystal size values lower than 300 Å regardless of the BET surface area value achieved a red score.

Table 2. Solvent assessment for the synthesis of UiO-66 and quality indicators of MOF. Reaction conditions: 3 eq H₂O, 30 eq AcOH, 120°C; ^a 3 eq H₂O, 120°C.

Classification	Solvent	Overall Green Assess.	B.p. (°C)	Viscosity	Presence of characteristic UiO66 peaks	Crystal size (Å)	BET surface area (m ² /g)	Default rank	Ranking after discussion
Alcohol	Solketal		188-189		other phase	-	-		
	1-(2-HE)-2-P		140-142 ^b		yes	731	1407		
	1,3-propanediol		214		yes	653	838		
Ester	2-ethylhexylacetate		199-200		Amorphous	-	-		
	Diethyl succinate		216-218		other phase	-	-		
	Dimethyl adipate		109-110		Yes (additional phases)	627	159		
	Dimethyl succinate		200		other phase	-	-		
	Esterol F		> 300		No REACT	-	-		
	Ethylene glycol diacetate		186-187		yes	132	115		
	Ethyl-L-lactate		154		Amorphous	-	-		
	g-valerolactone		207-208		yes	655	930		
	i-butylacetate		116-117		Amorphous	-	-		
	i-propylacetate		88.8		Amorphous	-	-		
	IRIS		215.6		No REACT	-	-		
	Isoamyl acetate		142		Amorphous	-	-		
	Loxanol		> 300		No REACT	-	-		
	Methyl laurate		261-262		yes	112	257		
	n-amyl acetate		149		Amorphous	-	-		
	Purasolv EHL		246		Amorphous	-	-		
triacetin		258		Amorphous	-	-			
Carbonate	Diethyl carbonate		126-128		yes	59	281		
	Dimethyl carbonate		90		Yes (additional phases)	345	132		
	Propylene carbonate		240-243		yes	813	771		
Ketone	cyclohexanone		155		No REACT	-	-		
Aromatic	p-cymene		176-178		No REACT	-	-		
Ether	1,3-dioxolane		74-75		Amorphous	-	-		
	2-methyl THF		78-80		Amorphous	-	-		
	Anisole		154		No REACT	-	-		
	4-Me-THP		107-108		No REACT	-	-		
	Cyclopentyl methyl ether		106		amorphous	-	-		
	Plurafac LF711		>300		No REACT	-	-		

	Plurafac LF221		>300		Amorphous	-	-		
	Plurafac LF303		245-255		No REACT	-	-		
	Plurafac LF120		>300		No REACT	-	-		
	Dehypon LS54		>300		No REACT	-	-		
	Synperonic LF30		>300		No REACT	-	-		
	t-amyl methyl ether		85-86		yes	455	813		
Dipolar aprotic	Polarclean		280		yes	79	303		
	Steposol ^a		297-299		yes	524	1440		
	Steposol		297-298		yes	322	366		
	Agnique AMD810		274		no REACT	-	-		
	DMF		155		yes	745	1066		

Table 3. Ranking of **a)** boiling points ($^{\circ}\text{C}$) and viscosity (η , mPa s), **b)** crystal size (CS, \AA) and BET surface are (m^2/g), **c)** presence of characteristic UiO66 peaks.

a)

Green	$50 < \text{bp} < 260$	$\eta \geq 5$
Yellow	$260 < \text{bp} < 300$	$5 < \eta \leq 15$
Red	$\text{Bp} \geq 300$ $\text{bp} \leq 50$	$\eta > 15$

b)

Green	$\text{CS} \geq 450 \text{ \AA}$	$\geq 900 \text{ m}^2/\text{g}$
Yellow	$300 \text{ \AA} \leq \text{CS} < 450 \text{ \AA}$	$800 \leq \text{m}^2/\text{g} < 900$
Red	$\text{CS} < 300 \text{ \AA}$	$\text{m}^2/\text{g} < 800$

c)

Green	yes
Yellow	yes (also other phase observed)
Red	no reaction amorphous other phase

Despite the many experiments and the tentative optimization of specific conditions, most of the solvents screened were not able to successfully allow the MOF formation. In these cases, UiO-66

failed to precipitate, amorphous phases or also unknown crystalline phases were formed. However, among the tested solvents, twelve were able to yield the UiO-66 phase whereas in six experiments the results were satisfying and, in some cases, much relevant. Selected solvents have quite high boiling point, higher than 80 °C, to avoid a massive evaporation during the reaction time that should conduct to an overly high-pressure in the vials. Among them, γ -valerolactone (GVL) and propylene carbonate (PC) are two environmentally benign and sustainable solvents. GVL showed to be an ideal and efficient alternative in that kind of transformation usually carried out in polar aprotic medium like Sonogashira and Heck coupling,⁵²⁻⁵³ while PC has been already used in the Suzuki-Miyaura coupling.⁵⁴ Many other solvents have been selected using this selection strategy like, for example, pyrrolidones, amides, esters, ethers and alcohols. In general, addition of 30 eq. of AcOH yielded compounds with high crystallinity degree and porosity comparable to those found for UiO-66 of good quality.⁵⁵ The exception is the experiment carried out in Steposol (ST) (entry **39bis**) in which the best crystallinity was obtained without modulators. Syntheses at the optimized conditions which gave the best results are those made in the following solvents: γ -Valero-lactone (entry **11**) Propylene carbonate (PC) (entry **23**) 1-(2-hydroxyethyl)-1-pyrrolidone (1-(2-HE)-2-P) (entry **2**), t-amylmethylether (TAME) (entry **37**) and 1,3-propandiol (1,3-PD) (entry **3**). In two cases, those done in dimethyl carbonate (entry **22**) and in dimethyl adipate (entry **6**), the syntheses were successful but, due to the presence of other phases, the optimization was not done. Table 4 reports on the main features of obtained materials.

Table 4 Comparison of the different syntheses performed (reaction conditions: 3 eq H₂O, 30 eq AcOH, 120°C). Molecular formula calculated with ¹H-NMR spectra and TGA analysis.

Exp	Solvent	FWHM (°) (111)	Crystal size (Å)	BET (m ² /g)	Micropore volume (cm ³ /g)	Yield	Molecular formula
-----	---------	-------------------	---------------------	----------------------------	---	-------	-------------------

0	DMF	0.11	745	1066	0.41	85%	Zr ₆ O ₄ (OH) ₄ BDC _{5.74} AA _{0.52}
1	GVL	0.13	655	930 m ² /g	0.34	84%	Zr ₆ O ₄ (OH) ₄ (BDC) _{5.80} (AA) _{0.40}
2	Steposol (ST) ^a	0.16	524	1440m ² /g	0.55	82%	Zr ₆ O ₄ (OH) ₄ BDC _{3.6} Cl _{1.2} H ₂ O _{1.2}
3	Propylen carbonate (PC)	0.10	813	771 m ² /g	0.29	71%	Zr ₆ O ₄ (OH) ₄ (BDC) _{5.78} (AA) _{0.44}
4	1-(2-hydroxyethyl)-2-pyrrolidone (1-(2-HE)-2-P)	0.11	731	1407 m ² /g	0.53	94%	Zr ₆ O ₄ (OH) ₄ (BDC) _{5.69} (AA) _{0.62}
5	TAME	0.18	455	813 m ² /g	0.29	83%	Zr ₆ O ₄ (OH) ₄ (BDC) _{5.78} (AA) _{0.44}
6	1,3-propandiol (1,3-PD)	0.13	653	838 m ² /g	0.32	63%	Zr ₆ O ₄ (OH) ₄ (BDC) _{5.42} (AA) _{1.16}
7	Steposol (ST)	0.25	322	366 m ² /g	0.14	-	-
8	Dimethyl adipate	0.13	627	159 m ² /g	0.06	-	-
9	Ethylene diacetate glycol	0.60	132	115 m ² /g	0.05	-	-
10	Dimethylcarbonate	0.23	345	132 m ² /g	0.05	-	-
11	Diethylcarbonate	1.02	59	281 m ² /g	0.06	-	-
12	Methyl laurate	0.72	112	257 m ² /g	0.09	-	-
13	Polarclean	1.00	79	303 m ² /g	0.12	-	-

^a 3 eq H₂O, 120°C

Results shown in table 4 allow to have a direct comparison of the syntheses performed in DMF and the selected green solvents. We have chosen some comparative indices such as yield, crystallinity and surface area to estimate the potentiality of each solvent in replacing DMF. Entries

7-13 were not characterized owing to their low score, as indicated in table 2. Figure 2 shows the XRPD patterns and the N₂ adsorption and desorption analysis of the MOFs obtained (entries 1-6). The materials are pure phases with good degree of crystallinity and BET surface area values comparable to conventional UiO-66 syntheses.¹⁸ The MOF obtained in 1-(2-HE)-2-P presents the XRPD pattern having characteristic peaks of a defective structure, with broad signals in the low angle regions, as previously reported by Bordiga et al.⁵⁶ This is also confirmed by the high specific surface area and micropore volume which is typical of defective UiO-66 with missing clusters defects.¹⁸ The experiment carried out in GVL is quite relevant since the MOF possesses a good crystallinity degree and it was obtained at a high yield (84%). Moreover, the GVL is a solvent which is rapidly replacing DMF, especially in the field of organic synthesis.^{45,52,53}

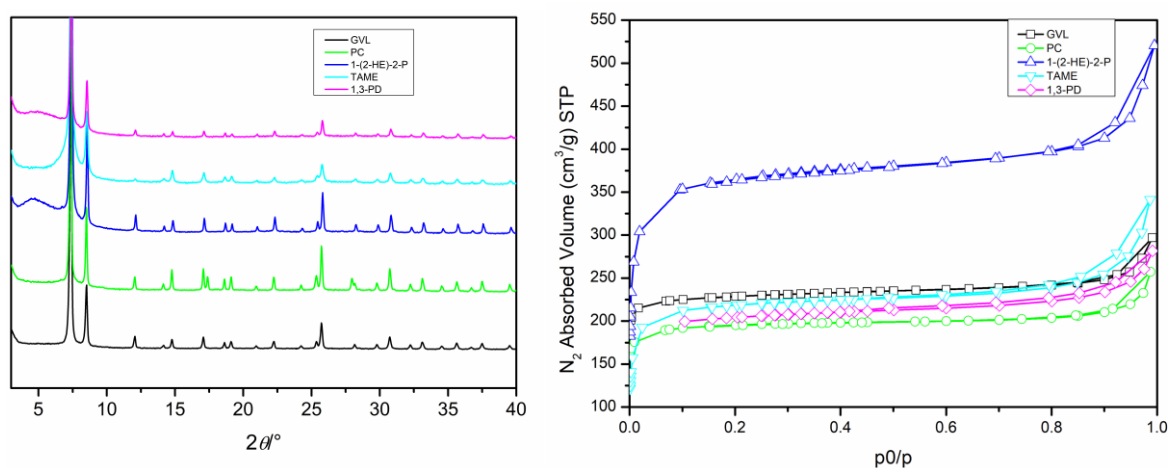


Figure 2. XRPD patterns (left) and N₂ adsorption and desorption isotherms (right) of the MOFs with the indicated solvents at the optimized conditions.

Another interesting result has been obtained by using Stepsol (ST). Figure 3 shows the XRPD patterns and the BET analysis of the MOFs obtained with ST as solvent using the same reaction condition above reported except the use of acetic acid as modulator. As in the case of 1-(2-HE)-2-

P, in this solvent the MOF obtained has an XRPD pattern with characteristic broad low-angle peaks of a defective structure, as also confirmed by its higher specific surface area than the MOF obtained using DMF.

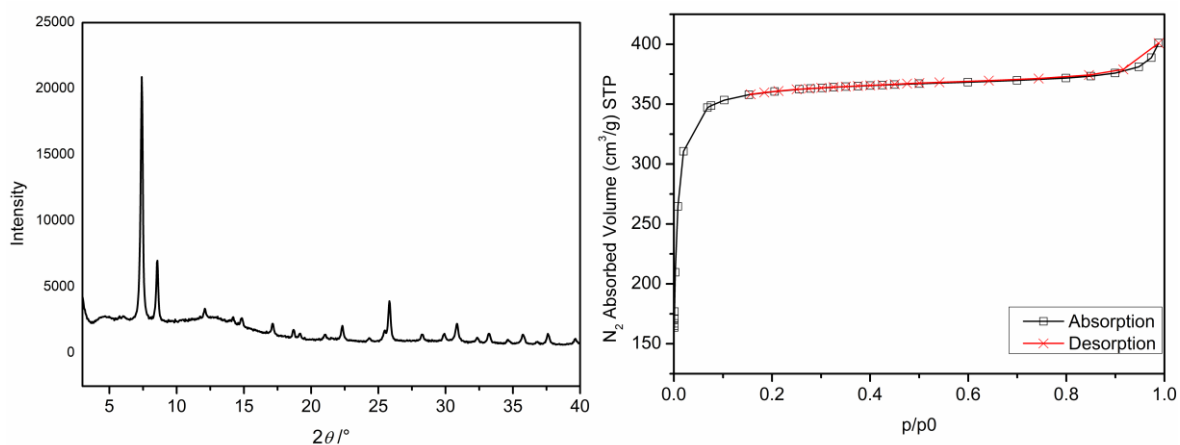


Figure 3. XRPD pattern (left) and N_2 adsorption isotherm (right) of the UiO-66 obtained in Stepsol.

MOFs formulas are reported in table 4. These formulas were mainly obtained 1H -NMR analysis on the hydrolyzed compounds and from the TGA curves. Molecular weight (reported in SI) are calculated on the basis of the TGA curves: the weight losses at temperature higher than $200^\circ C$ where the solvent is supposed to be lost until the plateau formed over $600^\circ C$ where only ZrO_2 is present. All the TGA curves, except that of PC, display a variable weight loss in the 20 - $100^\circ C$ range, corresponding to the loss of a certain number of water molecules (see in SI) meaning that washing procedure fully exchange the most part of the tried solvents. Presence of chloride ions as monoanionic terminal group on the cluster structure, inducing defects, was verified by means of IC analysis. The presence of chlorides was sensibly detected only on the MOF synthesized in ST. (see table 3). The only case in which the solvent could be included in the compound formula is the UiO-66 synthesized in PC. As a matter of fact this solvent was not removed before starting

decomposition, as observed from the TGA curve (figure S8). The presence of the solvent could be also responsible of the low specific surface area if compared to the other syntheses. PC $^1\text{H-NMR}$ peaks (figure S12) on the hydrolyzed MOFs confirmed this hypothesis. Figure S33 in SI reports on the FE-SEM images for the MOFs prepared in three different solvents. UiO-66 synthesized in GVL is constituted by nice octahedral nanocrystals of 200 nm average size. In the case of PC the UiO-66 has a octahedral shape but it results knobby. This observation, generally due to the presence of organic residues, can be ascribed to the presence of PC in the crystal structure and adsorbed on the crystal surface. The UiO-66 synthesized in the Steposol $\text{\textcircled{R}}$ MET10U is constituted of nanocrystal with undefined shape and size. Stability of the reaction media was also tested with $^1\text{H-NMR}$ analysis. A comparison was made between the NMR pattern of the neat solvent and that after the reaction. $^1\text{H-NMR}$ spectra are reported in the SI (S8, S13 S18, S27, S32). In the case of GVL, the NMR profile (figure S8) is the same before and after the reaction, with the difference consisting in the presence of acetic acid in the second one and that the signals, in the reacted solvent, are less defined, this could be caused by the presence of other reagents in the reaction environment. In the case of PC the $^1\text{H-NMR}$ profile is the same before and after the reaction (figure S13), but it presents some differences in the second one consisting in the presence of acetic acid (from the reaction) and some impurities that give signal at 1.21 ppm and between 3.31 and 3.69 ppm. The $^1\text{H-NMR}$ profile of reacted 1-(2-HE)-2-P, compared with the clean one (figure S18), displays some differences consisting in the presence of acetic acid (from the reaction). The solvent peaks result broad and some impurities at 4.12 ppm and a broad singlet at 4.65 ppm which can be attributed the singlet of -OH in the solvent structure are also present. $^1\text{H-NMR}$ spectra of TAME could be not recorded because of the solvent evaporation after reaction. 1,3-propanediol spectrum, after reaction, (figure S27) presents signals that could indicate the possible degradation of a part

of solvents. Stepsol ® MET10U the $^1\text{H-NMR}$ profile (figure S32) is quite similar before and after the reaction. In the reacted solvent the peaks are less defined and this could be due to the presence of other reagents in the reaction environment. Given the good results obtained with GVL as a solvent, different reaction conditions have been additionally tested (table 6) varying the zirconium source and the modulator.

Table 6 reaction condition of synthesis of UiO 66 in GVL: Zr salt (0.5mmol), H₂-BDC (1eq), H₂O (3eq), 4 ml GVL

	<i>Zr Salt</i>	<i>Modulator</i>
1a	ZrCl ₄	-
1b	ZrCl ₄	30 eq AcOH
1c	ZrCl ₄	30 eq HCOOH
2a	ZrOCl ₂ •8H ₂ O	-
2b	ZrOCl ₂ •8H ₂ O	30 eq AcOH
2c	ZrOCl ₂ •8H ₂ O	30 eq HCOOH

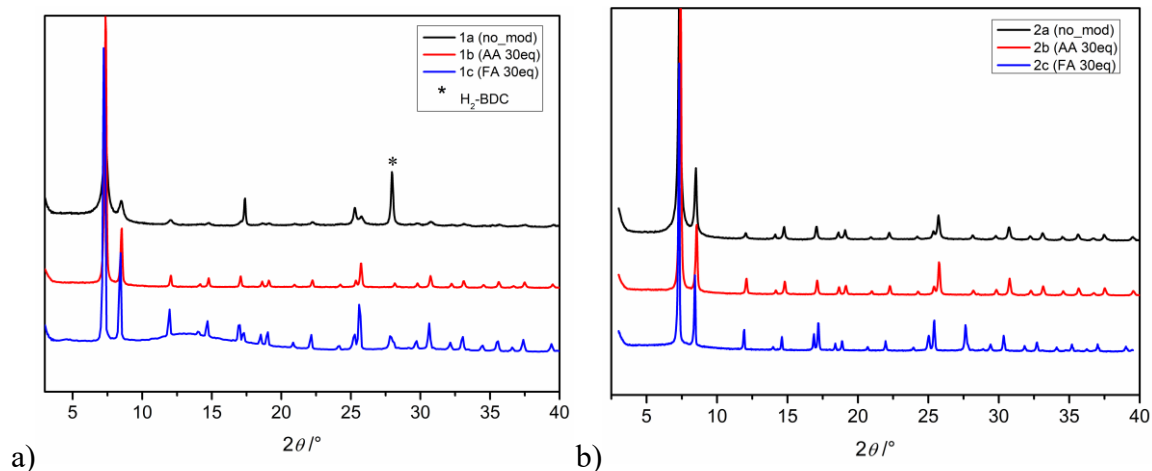
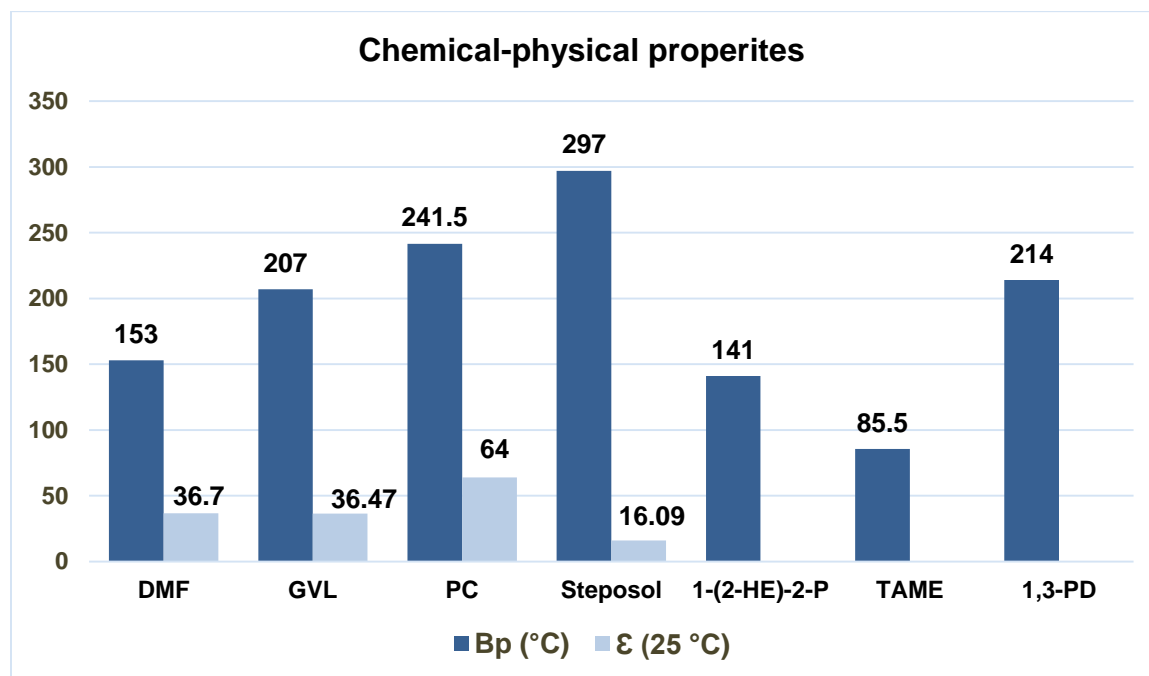


Figure 4. XRPD patterns of a) UiO 66 synthesized in GVL with $ZrCl_4$, 1a (black), 1b (red), 1c (blue) b) UiO 66 synthesized in GVL with $ZrOCl_2 \cdot 8H_2O$, 2a (black), 2b (red), 2c (blue)

Figure 4 reported the XRPD patterns of the materials obtained using the reaction conditions of table 6. The patterns are similar and corresponded to compounds with similar degree of crystallinity even in absence of acid modulator. Therefore, it is possible to obtain a good UiO-66 phase both by using different two Zr- salts and two different modulators. Replacement of $ZrCl_4$ with $ZrOCl_2 \cdot 8H_2O$ leads to good results. Highly crystalline pure phases were obtained and more important, there is the advantage of using a zirconium salt which does not release toxic by-products. As illustrated in the figures below, all the most promising green solvents for the UiO-66 synthesis feature a relatively high boiling point, higher than commonly used DMF. While this corresponds to a higher energy demand for their removal by distillation, in the case of the preparation of UiO-66, the product is isolated by filtration and then residual solvent removed by water. Therefore, as in other applications, the higher boiling point corresponds to a minimized exposure to the solvent and a limited dispersion of the medium into the environment as it happens for VOCs. The new solvents proposed also feature a significantly higher flash point values, confirming an increased intrinsic process safety. TAME departs from this trend, which shows both a lower boiling point and flash point. An important parameter for the selection of the reaction medium for UiO-66 synthesis is the dielectric constant (ϵ) and in fact almost all the media selected share a high polarity comparable to that of DMF. Most important, the ecological profile of all the solvents proposed here as replacement for DMF is very good in contrast with that of DMF itself. In fact, they are biodegradable and with no bioaccumulation issues. All the solvents here proposed, show a better and less critical toxicological profile than DMF itself. Focusing on the dermal LD50

(rabbit) data listed in the table above, we can observe an important increase of this value in all the green solvents tested. Moreover GVL, PC and Stepisol, are not considered to be potential carcinogenic by IARC, while DMF is classified as “possibly carcinogenic to humans” (IARC Group 2B), and for this reason is labelled as SVHC by the European REACH regulation.

The use of new solvents deriving from biomass and/or industrial waste is a definitely cleaner and safer opportunity, although currently it may result to be more expensive, especially in the case of biomass-derived chemicals. This is certainly related to the fact that their preparation is based on different transformations but also that this area of chemical production is still at its infancy and as the technologies related to this industrial sector will be optimized and the proper raw materials made available, the cost associated to processes is expected to decrease with the increase of the market requests.



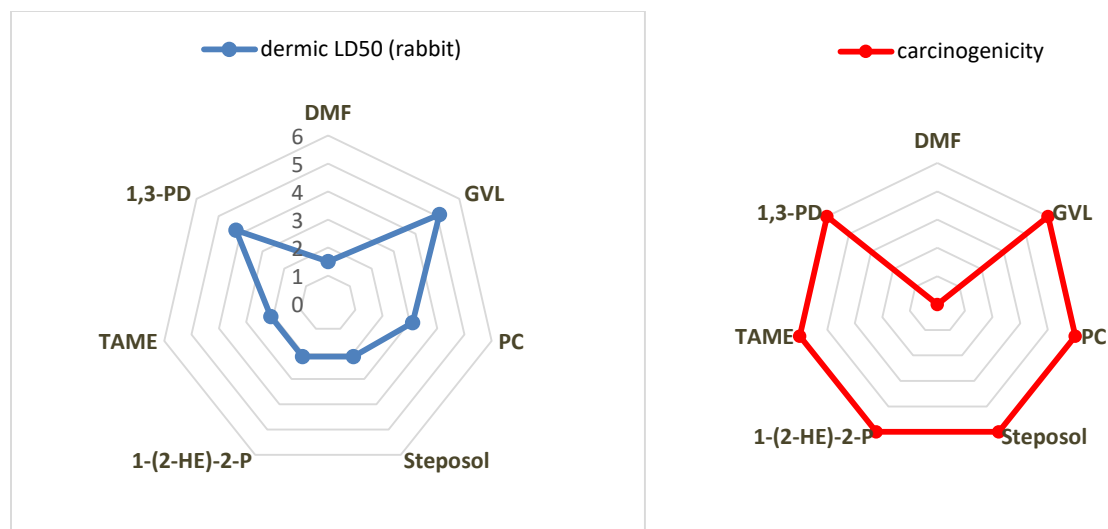


Figure 5. Chemical physical properties and toxicological profile of the most efficient solvents for UiO-66 synthesis.

CONCLUSION

In this paper an extensive screening of green solvents potentially suitable for substituting DMF for UiO-66 synthesis is presented. Due to the large number of parameters we have decided to optimize the synthesis in DMF, according to literature conditions, by increasing the reagents concentration and using AcOH as monocarboxylic modulator. The same synthetic conditions were also employed for screening over forty solvents chosen according to well established health and safety regulation protocols. Six experiments were successful, providing UiO-66 crystals with crystallinity, purity and porosity comparable to the standard DMF synthesis. The chosen solvents were also tested for their stability in reaction conditions and recyclability. Further studies are undergoing to study more in details the most promising solvents and the reasons for their efficiency (especially in the case of GVL) in the preparation of good MOF structures. These preliminary results bring to successive studies oriented to the synthesis optimization, like scaling-up, recyclability and use of other Zr-salts.

ASSOCIATED CONTENT

Supporting Information. Analytical and instrumental procedures, XRPD patterns, TGA analysis, ¹H-NMR spectra, N₂ adsorption isotherms, ion chromatography analysis, The following files are available free of charge. brief description (file type, i.e., PDF) brief description (file type, i.e., PDF)

AUTHOR INFORMATION

Corresponding Author

* Dipartimento di Chimica, Biologia e Biotecnologie, Università di Perugia Via Elce di Sotto, 8, 06123 Perugia. ferdinando.costantino@unipg.it, luigi.vaccaro@unipg.it

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding Sources

MIUR - “AMIS – Dipartimenti di Eccellenza 2018-2022”

Notes

Any additional relevant notes should be placed here.

ACKNOWLEDGMENT

The Università degli Studi di Perugia and MIUR are acknowledged for financial support to the project AMIS, through the program “Dipartimenti di Eccellenza - 2018-2022”.

ABBREVIATIONS

MOF metal organic framework, SBU secondary building unit, UiO University of Oslo, H₂-BDC terephthalic acid or benzenedicarboxylic acid, NH₂-BDC amino-terephthalic acid, BDC-OH hydroxy-terephthalic acid, DMF N,N-dimethylformamide, 2-Me-THF 2- methyltetrahydrofuran, PC Propylene carbonate, 1-(2-HE)-2-P 1-(2-hydroxyethyl)-1-pyrrolidone, TAME t-amylmethylether, 1,3-PD 1,3-propanediol, GVL γ -Valerolactone, CPME Cyclopentyl methyl ether, VOC Volatile organic compound, Bp Boiling point, Mp Melting point, AcOH or AA Acetic acid, HCOOH or FA Formic acid, REACH Registration, Evaluation, Authorisation and Restriction of Chemicals, SVHC Substances of Very High Concern.

REFERENCES

1. Jiao, L.; Wang, Y.; Jiang, H. L.; Xu, Q. Metal–Organic Frameworks as Platforms for Catalytic Applications. *Adv. Mater.* **2018**, *30* (37), 1–23, DOI: 10.1002/adma.201703663.
2. Dhakshinamoorthy, A.; Santiago-Portillo, A.; Asiri, A. M.; Garcia, H. Engineering UiO-66 Metal Organic Framework for Heterogeneous Catalysis. *ChemCatChem*, **2019**, *11*, 899-923, DOI: 10.1002/cctc.201801452.
3. Wu, H.; Yildirim, T.; Zhou, W. Exceptional mechanical stability of highly porous zirconium metal-organic framework UiO-66 and its important implications. *J. Phys. Chem. Lett.* **2013**, *4*, 925–930, DOI: 10.1021/jz4002345.
4. Rimoldi, M.; Howarth, A. J.; Destefano, M. R.; Lin, L.; Goswami, S.; Li, P.; Hupp, J. T.; Farha, O. K. Catalytic Zirconium/Hafnium-Based Metal-Organic Frameworks. *ACS Catal* **2017**, *7*, 997–1014, DOI:10.1021/acscatal.6b0292.
5. Zhang, X.; Shi, X.; Chen, J.; Yang, Y.; Lu, G. The preparation of defective UiO-66 metal organic framework using MOF-5 as structural modifier with high sorption capacity for

- gaseous toluene. *J. Env. Chem. Eng.*, **2019**, 7(5), 103405-103413, DOI: 10.1016/j.jece.2019.103405.
6. Bon, V.; Senkovska, I.; Evans, J. D.; Wöllner, M.; Hoelzel, M.; Kaskel, S. Insights into the water adsorption mechanism in the chemically stable zirconium-based MOF DUT-67 – a prospective material for adsorption-driven heat transformations. *J. Mater. Chem. A*, **2019**, 7, 12681-12690. DOI: 10.1039/C9TA00825J
 7. Yu, L.-Q.; Su, F.-H.; Ma, M.-Y.; Lv, Y.-K. Metal-organic frameworks for the sorption of acetone and isopropanol in exhaled breath of diabetics prior to quantitation by gas chromatography. *Microchimica Acta*, **2019**, 186(8). DOI:10.1007/s00604-019-3713-1
 8. Li, H.; Wang, K.; Sun, Y.; Lollar, C. T.; Li, J.; Zhou, H. C. Recent Advances in Gas Storage and Separation Using Metal–Organic Frameworks. *Mater. Today* **2018**, 21 (2), 108–121. DOI: 10.1016/j.mattod.2017.07.006.
 9. Wu, H.; Chua, Y. S.; Krungleviciute, V.; Tyagi, M.; Chen, P.; Yildirim, T.; Zhou, W. Unusual and highly tunable missing-linker defects in zirconium metal-organic framework UiO-66 and their important effects on gas adsorption. *J. Am. Chem. Soc.* **2013**, 135, 10525–10532, DOI: 10.1021/ja404514r
 10. Mukhopadhyay, S.; Debgupta, J.; Singh, C.; Sarkar, R.; Basu, O.; Das, S. K. Designing of UiO-66 Based Super Protonic Conductor with the Highest MOF Based Proton Conductivity. *ACS Applied Materials & Interfaces*. **2019**, 11 (14), 13423-13432, DOI:10.1021/acsami.9b01121
 11. Abánades Lázaro, I.; Haddad, S.; Sacca, S.; Orellana-Tavra, C.; Fairen-Jimenez, D.; Forgan, R. S. Selective Surface PEGylation of UiO-66 Nanoparticles for Enhanced

- Stability, Cell Uptake, and pH-Responsive Drug Delivery. *Chem*, **2017**, 2(4), 561–578, DOI: 10.1016/j.chempr.2017.02.005.
12. Abánades Lázaro, I. & Forgan, R. S. Application of zirconium MOFs in drug delivery and biomedicine. *Coord. Chem. Rev.* **2019**, 380, 230–259, DOI: 10.1016/j.ccr.2018.09.009.
 13. Cavka, J. H.; Jakobsen, S.; Olsbye, U.; Guillou, N.; Lamberti, C.; Bordiga, S.; Lillerud, K. P. A New Zirconium Inorganic Building Brick Forming Metal Organic Frameworks with Exceptional Stability. *J.AM.CHEM.SOC. Commun.* **2008**, 6, 13850–13851, DOI:10.1021/ja8057953.
 14. Valenzano, L.; Civalleri, B.; Chavan, S.; Bordiga, S.; Nilsen, M. H.; Jakobsen, S.; Lillerud, K. P.; Lamberti, C. Disclosing the complex structure of UiO-66 metal organic framework: A synergic combination of experiment and theory. *Chem. Mater.* **2011**, 23, 1700–1718, DOI: 10.1021/cm1022882.
 15. Wu, H.; Chua, Y. S.; Krungleviciute, V.; Tyagi, M.; Chen, P.; Yildirim, T.; Zhou, W. Unusual and highly tunable missing-linker defects in zirconium metal-organic framework UiO-66 and their important effects on gas adsorption. *J. Am. Chem. Soc.* **2013**, 135, 10525–10532, DOI: 10.1021/ja404514r.
 16. Ghosh, P.; Colón, Y. J.; Snurr, R. Q. Water Adsorption in UiO-66: The Importance of Defects. *Chem. Commun.*, **2014**, 50, 11329–11331. DOI: 10.1039/C4CC04945D
 17. Fang, Z.; Bueken, B.; De Vos, D.E.; Fischer, R.A. Defect Engineered Metal-Organic Frameworks. *Angew. Chem. Int. Ed.* **2015**, 54, 7234 – 7254. DOI:10.1002/anie.201411540
 18. Taddei, M.; Wakeham, R. J.; Koutsianos, A.; Andreoli, E.; Barron, A. R. Post-Synthetic Ligand Exchange in Zirconium-Based Metal–Organic Frameworks: Beware of The

- Defects! *Angew. Chemie - Int. Ed.* **2018**, 77005, 11706–11710, DOI:10.1002/anie.201806910.
19. Miyamoto, M.; Kohmura, S.; Iwatsuka, H.; Oumic, Y.; Uemiyaa, S. In situ solvothermal growth of highly oriented Zr-based metal organic framework UiO-66 film with monocrystalline layer. *CrystEngComm*, **2015**, 17, 3422–3425, DOI:10.1039/c5ce00462d.
 20. Qiu, J.; Feng, Y.; Zhang, X.; Jia, M.; Yao, J. Acid-promoted synthesis of UiO-66 for highly selective adsorption of anionic dyes: Adsorption performance and mechanisms. *J. Colloid Interface Sci.*, **2017**, 499, 151–158, DOI: 10.1016/j.jcis.2017.03.101.
 21. Užarević, K.; Wang, T. C.; Moon, S. Y.; Fidelli, A. M.; Hupp, J. T.; Farha, O. K.; Friščić, T. Mechanochemical and Solvent-Free Assembly of Zirconium-Based Metal-Organic Frameworks. *Chem. Commun.* **2016**, 52 (10), 2133–2136, DOI:10.1039/c5cc08972g.
 22. Chen, J.; Shen, K.; Li, Y. Greening the Processes of Metal-Organic Framework Synthesis and their Use in Sustainable Catalysis. *ChemSusChem*, **2017**, 10(16), 3165–3187, DOI:10.1002/cssc.201700748.
 23. Reinsch, H.; Bueken, B.; Vermoortele, F.; Stassen, I.; Lieb, A.; Lillerud, K. P.; De Vos, D. Green Synthesis of Zirconium-MOFs. *CrystEngComm* **2015**, 17 (22), 4070–4074. DOI: 10.1039/c5ce00618j.
 24. Zhang, J.; White, G. B.; Ryan, M. D.; Hunt, A. J.; Katz, M. J. Dihydrolevoglucosenone (Cyrene) As a Green Alternative to N,N-Dimethylformamide (DMF) in MOF Synthesis. *ACS Sustain. Chem. Eng.* **2016**, 4 (12), 7186–7192. DOI:10.1021/acssuschemeng.6b02115
 25. Waitschat, S.; Fröhlich, D.; Reinsch, H.; Terraschke, H.; Lomachenko, K.A.; Lamberti, C.; Kummer, H.; Helling, T.; Baumgartner, M.; Henninger, S.; and Stock, N. Synthesis of M-UiO-66 (M = Zr, Ce or Hf) employing 2,5-pyridinedicarboxylic acid as a linker:

- defect chemistry, framework hydrophilisation and sorption properties. *Dalton Trans.*, **2018**, 47, 1062–1070. DOI: 10.1039/C7DT03641H
26. Kumar, S.; Jain, S.; Nehra, M.; Dilbaghi, N.; Marazza, G.; Kim, K.H. Green synthesis of metal–organic frameworks: A state-of-the-art review of potential environmental and medical applications. *Coord. Chem. Rev.*; **2020**, 420, 213407. DOI: 10.1016/j.ccr.2020.213407
27. Winarta, J.; Shan, B.; McIntyre, S.M.; Ye, L.; Wang, C.; Liu, J.; Mu, B. A Decade of UiO-66 Research: A Historic Review of Dynamic Structure, Synthesis Mechanisms, and Characterization Techniques of an Archetypal Metal–Organic Framework. *Cryst. Grow. Des.*; **2020**, 20 (2), 1347-1362. Doi: 10.1021/acs.cgd.9b00955
28. EUR-Lex, <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1907-20180509&from=EN>, (accessed June 2019)
29. Clark, J.H.; Hunt, A.J.; Topi, C.; Paggiola, G.; Sherwood, J.; Sustainable solvents: Perspective from research, business and international policy, Royal Society of Chemistry, Cambridge, 2017.
30. Solvay, <https://www.solvay.com/en/brands/rhodiasolv-polarclean>, (accessed August 2019).
31. Wang, H. H.; Jung, J. T; Kim, J. F.; Kim, S.; Drioli E.; Lee, Y. M. *J. Membrane Sci.*, **2019**, 574, 44-54 *J. Membrane Sci.*, **2019**, 574, 44-54, DOI: 10.1016/j.memsci.2018.12.051.

32. Luciani, L.; Goff, E.; Lanari, D.; Santoro, S.; Vaccaro, L. Waste-minimised copper-catalysed azide–alkyne cycloaddition in Polarclean as a reusable and safe reaction medium. *Green Chem.*, **2018**, 20, 183-187, DOI: 10.1039/C7GC03022C.
33. A. Randova, A.; Bartovska, L.; Moravek, P.; Matejka, P., Novotna, M.; Matejkova, S.; Drioli, E.; Figoli, A.; Lanc M.; Friess, K. A fundamental study of the physicochemical properties of Rhodiasolv®Polarclean: A promising alternative to common and hazardous solvents. *J. Mol. Liq.*, **2016**, 224, 1163-1171, DOI: 10.1016/j.molliq.2016.10.085.
34. U.Azzena, U.; Carraro, M.; Pisano, L.; Monticelli, S.; Bartolotta R.; Pace, V. Cyclopentyl Methyl Ether: An Elective Ecofriendly Ethereal Solvent in Classical and Modern Organic Chemistry. *ChemSusChem*, **2018**, 12, 40-70, DOI: 10.1002/cssc.201801768.
35. R. Schliebs, R.; Brandt, H.W.; Engelhard, B.; Steude, H.; Scherb, H.; Schnuchel, G. Process for recovering cyclopentene, isoprene and a diolefin stream from the c₁₁-cut obtained by petroleum cracking. US Pat., 3686349, 1972.
36. P. Gandeepan, P.; Kaplaneris, N.; Santoro, S.; Vaccaro, L.; Ackermann, L. Biomass-Derived Solvents for Sustainable Transition Metal-Catalyzed C–H Activation. *ACS Sustainable Chem. Eng.*, **2019**, 7, 8023-8040, DOI: 10.1021/acssuschemeng.9b00226.
37. F. Valentini, F.; Mahmoudi, H.; Bivona, L. A.; Piermatti, O.; Bagherzadeh, M.; Fusaro, L.; Aprile, C.; Marrocchi A.; Vaccaro, L. Polymer-Supported Bis-1,2,4-triazolium Ionic Tag Framework for an Efficient Pd(0) Catalytic System in Biomass Derived γ -Valerolactone. *ACS Sustainable Chem. Eng.*, **2019**, 7, 6939-6946, DOI: 10.1021/acssuschemeng.8b06502.

38. C. Sener, C.; Motagamwala, A.H.; Alonso, D.M. Enhanced Furfural Yields from Xylose Dehydration in the γ -Valerolactone/Water Solvent System at Elevated Temperatures. *J. A. Dumesic, ChemSusChem*, **2018**, 11, 2321-2331, DOI: 10.1002/cssc.201800730.
39. Sherwood, J.; De Bruyn, M.; Costantinou, A.; Moity, L.; McElroy, C. R.; Farmer, J.T.; Duncan, T.; Raverty, W.; Hunt, A.J.; Clark, J. Dihydrolevoglucosenone (Cyrene) as a bio-based alternative for dipolar aprotic solvents. *Chem. Commun.*, **2014**, 50, 9650-9652, DOI: 10.1039/C4CC04133J.
40. Nilsen, M. H. et al. in 34th Annual BZA conference Edinburgh, 2011
41. Tang, X.; Sun, Y.; Zeng, X.; Lei, T.; Li, H.; Lin, L. γ -Valerolactone-an excellent solvent and a promising building block. *Biomass, Biofuels, Biochemicals*, **2020** p.p. 199–226. DOI:10.1016/b978-0-444-64307-0.00007-x.
42. Ismalaj, E.; Strappaveccia, G.; Ballerini, E.; Elisei, F.; Piermatti, O.; Gelman, D.; Vaccaro, L. γ -Valerolactone as a renewable dipolar aprotic solvent deriving from biomass degradation for the Hiyama reaction, *ACS Sustain. Chem. Eng.* **2014**, 2, 2461-2464. DOI:10.1021/sc5004727.
43. Reinsch, H. “Green” Synthesis of Metal-Organic Frameworks. *Eur. J. Inorg. Chem.*, **2016**, 4290–4299, DOI: 10.1002/ejic.201600286.
44. Hu, Z., Peng, Y., Kang, Z., Qian, Y., & Zhao, D. A Modulated Hydrothermal (MHT) Approach for the Facile Synthesis of UiO-66-Type MOFs. *Inorganic Chemistry*, **2015**, 54(10), 4862–4868, DOI:10.1021/acs.inorgchem.5b00435.
45. Reinsch, H.; Waitschat, S.; Chavan, S. M., Lillerud, K. P., & Stock, N. A Facile “Green” Route for Scalable Batch Production and Continuous Synthesis of Zirconium MOFs.

European Journal of Inorganic Chemistry, **2016**, 27, 4490–4498,
DOI:10.1002/ejic.201600295

46. Wang, S.; Serre, C.; Towards Green Production of Water-Stable Metal-Organic Frameworks Based on High-Valence Metals with Low Toxicities. *ACS Sustainable Chemistry & Eng.* **2019**, 7, 11911-11927, DOI:10.1021/acssuschemeng.9b01022
47. Ho, D.; Lee, J.; Park, S.; Park, Y.; Cho, K.; Campana, F.; Lanari, D.; Facchetti, A.; Seo, S.; Kim, C.; Marrocchi, A.; Vaccaro, L. Green solvents for organic thin-film transistor processing. *J. Mater. Chem. C*, **2020**, 8, 5786-5794, DOI: 10.1039/D0TC00512F
48. Henderson, R.K.; Jimenez-Gonzalez, C.; Constable, D. J. C.; Alston, S. R.; Inglis, G. G. A.; Fisher, G.; J. Sherwood, J.; Binks, S. P.; Curzons, A. D. Expanding GSK's solvent selection guide – embedding sustainability into solvent selection starting at medicinal chemistry. *Green Chem.*, **2011**, 13, 854-862, DOI: 10.1039/C0GC00918K
49. D. Prat, D.; A. Wells, A.; J. Hayler, J.; Sneddon, H.; McElroy, C. R.; Abou-Shehada, S.; Dunn, P.J. CHEM21 selection guide of classical- and less classical-solvents *Green Chem.*, **2016**, 18, 288-296, DOI: 10.1039/C5GC01008J
50. D. Prat, D.; A. Wells, A.; J. Hayler, J.; Sneddon, H.; McElroy, C. R.; Abou-Shehada, S.; Dunn, P.J. Correction: CHEM21 selection guide of classical- and less classical-solvents. *Green Chem.*, **2015**, 17, 4848-4848, DOI:
51. Alder, C.M.; Hayler, J.D.; Henderson, R.K.; Redman, A.M.; Shukla, L.; Shuster, L.E.; Sneddon, H. F. Updating and further expanding GSK's solvent sustainability guide. *Green Chem.*, **2016**, 18, 3879-3890, DOI: 10.1039/C6GC00611F

52. Strappaveccia, G.; Luciani, L.; Bartollini, E.; Marrocchi, A.; Pizzo, F.; Vaccaro, L. γ -Valerolactone as an alternative biomass-derived medium for the Sonogashira reaction. *Green Chemistry*, **2015**, *17*(2), 1071–1076, DOI:10.1039/c4gc01728e
53. Strappaveccia, G.; Ismalaj, E.; Petrucci, C.; Lanari, D.; Marrocchi, A.; Drees, M.; Facchetti, A.; Vaccaro, L. A biomass-derived safe medium to replace toxic dipolar solvents and access cleaner Heck coupling reactions. *Green Chemistry*, **2015**, *17*(1), 365–372, DOI:10.1039/c4gc01677g.
54. Gautam, P.; Gupta, R.; Bhanage, B. M. Pd/C in Propylene Carbonate: A Sustainable Catalyst-Solvent System for the Carbonylative Suzuki-Miyaura Cross-Coupling Using N-Formylsaccharin as a CO Surrogate. *European Journal of Organic Chemistry*, **2017**, *24*, 3431–3437, DOI:10.1002/ejoc.201700543.
55. Chavan, S.; Vitillo, J. G.; Gianolio, D.; Zavorotynska, O.; Civalleri, B.; Jakobsen, S.; Nilsen M.H.; Valenzano, L.; Lamberti, C.; Lillerud, K.P.; Bordiga, S. H₂ storage in isostructural UiO-67 and UiO-66 MOFs. *Phys. Chem. Chem. Phys.*, **2012**, *14*(5), 1614–1626, DOI:10.1039/c1cp23434j.
56. Shearer, G. C.; Vitillo, J. G.; Bordiga, S.; Svelle, S.; Olsbye, U.; Lillerud, K. P. Functionalizing the Defects: Postsynthetic Ligand Exchange in the Metal Organic Framework UiO-66. *Chemistry of Materials*, **2016**, *28*(20), 7190–7193. DOI:10.1021/acs.chemmater.6b02749.