Deep Eutectic Solvents for Cu-catalysed ARGET ATRP under Air Atmosphere. Green and Efficient Route to poly(methyl methacrylate) using Recyclable Cu(II) Metal Organic Framework.

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Atom Transfer Radical Polymerisation (ATRP) is one of the most important techniques leading to well-defined polymers with predetermined molecular weight, designed microstructure and tailored-made functionalities. Although ATRP has been extensively studied in a variety of common Volatile Organic Solvents (*VOCs*) and water, there is significantly less work done using fashionable and environmental friendly *Deep Eutectic Solvents* (*DESs*). Aiming to develop *greener* ATRP routes allowing the recyclability of the employed transition metal catalyst, we herein present the homogeneous and heterogeneous Cu-catalysed ARGET variation of the ATRP processes using methyl methacrylate (MMA) as the model monomer, and *DESs* as green solvent. The homogeneous ARGET ATRP was performed employing $CuCl_2$ as catalyst, FDA approved tin(II) 2-ethylhexanoate [$Sn(EH)_2$] as reducing ARGET agent, and conducted under air conditions. The polymerisations proceed under controlled/"living" fashion according with a reversible deactivation radical polymerisation (RDRP) standards. Heterogeneous ARGET ATRP was carried out by using *DESs*-insoluble Cu(II) Metal Organic Framework (MOF) as recyclable catalyst in the absence of organic ligands, employing $Sn(EH)_2$ as reducing agent, and in air atmosphere. Under these experimental conditions, well-defined poly(methyl methacrylate) (PMMA) was obtained ($Đ \approx 1.2$) under controlled RDRP conditions. Importantly, both MOF catalyst and *DES* were successfully recycled up to 6 consecutive catalytic cycles leading to PMMAs with comparable macromolecular features and yields.

1. Introduction

Solvents, specifically common volatile organic solvents (*VOCs*), are ubiquitous in polymer science from the synthesis and physicochemical modification of the macromolecules, to the most fashionable fabrication of polymeric-based nanostructured materials. However, to confront the diminution of oil supplies worldwide, the *Chemistry Community* is trying to reduce the use of raw materials obtained from non-renewable fossil resources, thus attempting to fulfil one of the most important *Principles of Green Chemistry* [1]. In this last regard, given the fact that solvents represent 80-90 % of the overall mass balance in most of both academic and industrial polymer synthetic processes, the use of greener alternatives to traditional *VOCs* has been recently focus of special attention.[2] During the last decade, a new family of biomass-based and sustainable reaction media, the so-called *Deep Eutectic Solvents* (*DESs*), which can be described as two-component eutectic liquids containing both hydrogen-bond donors (HBD) and hydrogen-bond acceptors (HBA),[3] are receiving increasing attention as ideal green reaction media due to: *i)* their exceptional combination of physicochemical properties (negligible vapour pressure, low toxicity and flammability and high polarity) [4]; *ii)* their ability to dissolve both inorganic or organic compound; *iii)* the simple catalyst recycling and product isolation; *iv)* their straightforward synthesis (just by mixing the HBD and HBA) without any further steps of isolation or purification; and *v)* their capability to enhance the efficiency and selectivity of different organic syntheses.[5] Therefore, taking into account these advantageous properties of *DESs*, it is not surprising to find in the literature a wide range of applications for these neoteric solvents in different fields of chemistry, like for example: electrochemistry and metal extraction,[6] nanotechnology,[7] separation processes,[8] stabilisation of DNA,[9] homogenous catalysis,[10] polar organometallic chemistry,[11] materials chemistry,[2] and organic synthesis [12]. In polymer science, although there are previously reported polymerisations in eutectic mixtures,[13] it was not until 2011 when Mota-Morales *et al.* employed the term *Deep Eutectic Solvent* associated with a polymerisation process.[14] Since that, other studies were conducted on the synthesis of natural and synthetic polymers evolving eutectic mixtures.[2] In this sense, our research group has recently described the organolithium mediated (anionic) polymerisation of several styrene-like precursors under very mild reaction conditions, in the presence of air and using as sustainable reaction media the protic eutectic mixture choline chloride/glycerol (in a 1:2 molar ratio; 1*ChCl*/2*Gly*), thus furnishing the desired organic polymers (homopolymers, random copolymers, and block copolymers) in excellent yields (>90 %) and low polydispersities (IPD 1.1-1.3) [15a]. From the seed of this preliminary work and trying to design an alternative route that allows us to fine-control the length (degree of polymerisation, DP) and the polydispersity indexes ($Đ$) of the desired organic polymer, we decided to focus our attention on the reversible deactivation radical polymerisation (RDRP) techniques, which have been extensively used for the preparation of well-defined polymers. Among the variety of very well developed RDRP routes, Atom Transfer Radical Polymerisation (ATRP) is one of the most important techniques leading to well-defined polymers with predetermined molecular weight, designed microstructure and tailored-made functionalities.[16] Regarding to this, activators regenerated by electron transfer atom transfer radical polymerisation (ARGET ATRP, Scheme 1) is one of the most promising ATRP variations, demonstrating superior oxygen tolerance and lower catalyst loading than other ATRP routes.[17] Surprisingly, despite the increasing impact of ATRP processes in fields beyond traditional polymer science, to our best of knowledge, there are only two examples addressing these controlled radical polymerisations in *DESs*. Thus, Coelho *et al.* described the Cu-catalysed supplemental activator and reducing agent atom transfer radical polymerisation (SARA ATRP) of different hydrophilic monomers such as 2-hydroxyethyl acrylate (HEA), 2-hydroxyethyl methacrylate (HEMA), and (3-acrylamidopropyl)trimethylammonium chloride (AMPTMA).[18] Later, Xue *et al.* described the Fe-

mediated ligand-free ATRP of methyl methacrylate.[19] Although both works described convenient methodologies leading to well-defined polymers in *DESs*, both presented limitations regarding to the sustainability of the polymerisations protocol since the first used expensive organic ligands and the later did not recycle the Fe-based catalyst.
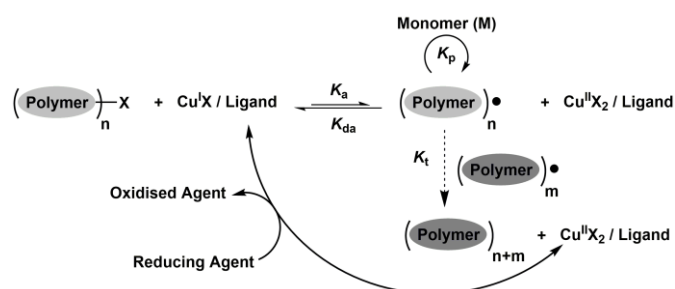
Scheme 1. General mechanism for ARGET ATRP.

Thus, we herein present the Cu-catalysed ARGET ATRP using methyl methacrylate (MMA) as the model monomer conducted by employing green and bio-based deep eutectic mixtures. The ARGET ATRP was firstly studied in homogenous phase using $CuCl_2$ as catalyst, FDA approved tin(II) 2-ethylhexanoate $[Sn(EH)_2]$ as reducing ARGET agent, and under air conditions. The highly correlation achieved between the theoretical and experimental molecular weight together with the low polydispersity indexes ($Đ \approx 1.2$) of the as-prepared poly(methyl methacrylate)s (PMMAs), demonstrate that the polymerisations proceed under controlled fashion according to RDRP standards. Moreover, the RDRP characteristic of the polymerisation was also demonstrated *via* linear increase of molecular weight (M_n) with conversion and chain extension experiments. ARGET ATRP was then carried out by using heterogeneous Cu(II) Metal Organic Framework (MOF) as recyclable catalyst in the absence of organic ligands, using $Sn(EH)_2$ as reducing agent, and in air atmosphere. Under these experimental conditions, well-defined PMMA was obtained ($Đ \approx 1.2$) under controlled RDRP conditions (linear increase of M_n with conversion and bromine-end-functionalisation of the polymeric chains). Importantly, both MOF catalyst and *DES* were successfully recycled up to 6 consecutive catalytic cycles leading to PMMAs with comparable macromolecular features and yields.

2. Results and Discussion

2.1. Homogeneous ARGET ATRP in *Deep Eutectic Solvents*

Aiming to develop *greener* and efficient protocols leading to well-defined PMMA in a straightforward manner, polymerisations were performed in choline chloride (*ChCl*) based *DESs*, under air atmosphere in capped vials, and employing non-purified MMA (used as it was received from commercial sources, see Experimental Part for further details). Table 1 showed the optimisation of the polymerisation conditions.

By employing similar conditions than those used before by Matyjaszewski and collaborators for grafting different poly(acrylate)s and polystyrene from a silicon wafer surface using an ARGET ATRP under air atmosphere, [20] we were able to synthesise PMMA in *DES* (1*ChCl*/2*Gly*; *Gly* = glycerol) under limited amount of air atmosphere at 70° C (Entry 1 of Table 1. See Experimental Part for further details). The polymerisation proceeds smoothly leading to 33 % of conversion after 2 hours of reaction (see Figure 1). The polydispersity index of the as-prepared PMMA is low ($Đ = 1.26$, Figure 2), but importantly, there is a very good correlation between the theoretical and experimental molecular weights of the synthesised PMMA (*i.e.*, M_n^{th} and M_n^{SEC} respectively), which it is indicative of the RDRP nature of the polymerisation process. By using higher or lower catalyst loadings (Entries 2 and 3 of Table 1, respectively), the control of the molecular weight was lost. Indeed, the great discrepancy between the experimental and theoretical molecular weights achieved when 1000 ppm of $CuCl_2$ were employed (Entry 2 of Table 1), indicates a poor control over the ARGET ATRP process during which formation of radicals might lead to the self-polymerisation of MMA in a non-controlled manner. In the other hand, the decrease of the monomer conversion by using lower $CuCl_2$ amounts (Entry 3 of Table 1) suggests the occurrence of significant chain termination under these experimental conditions. In our previous studies of the anionic polymerisation of styrene-type olefins in *DES,* we found that the polymerisation only proceed under sonication conditions.[15a] With this previous experimental observation in mind, we studied the effect of the sonication over the ARGET ATRP. Employing the same experimental conditions than those described in Entry 1 of Table 1, but using a conventional sonication bath operating at 35 KHz and 160 W (Entry 4 of Table 1), we achieved higher conversions in 2 hours but very low control of the ARGET ATRP process ($Đ > 2.0$). Finally, similar unsatisfactory results were obtained when we used other ultrasonic power or frequencies [15b,c]

Table 1. Experimental conditions and molecular weight parameters for the ARGET ATRP of MMA in *DES* (1*ChCl*/2*Gly*) using homogeneous CuCl$_2$ catalyst.

Entry[a]	[MMA]$_o$/*DES* (v/v)	CuCl$_2$ (ppm)	[CuCl$_2$]$_0$/[Sn(EH)$_2$]$_0$/[PMDETA]$_0$ (relative molar amounts)[b]	T (° C)	t (hours)	% Conv.[c]	M_n^{th} Kg/mol[d]	M_n^{SEC} Kg/mol[e]	Đ[f]
1	4.3	500	1/6.5/2.5	70	2	33	15.5	13.6	1.26
2	4.3	1000	1/4.3/2.5	70	2	52	24.5	41.5	1.26
3	4.3	50	1/41.4/2.5	70	12	< 5.0	-	-	-
4[g]	4.3	500	1/6.5/2.5	70	2	53	24.9	39.3	2.10
5	4.3	500	1/6.5/2.5	40	2	8.0	4.70	6.20	1.40
6	2.1	500	1/6.5/2.5	70	2	47	22.1	161	1.40
7	1.0	500	1/6.5/2.5	70	2	6.0	2.82	150	1.44
8	4.2	500	1/40/2.5	70	2	30	15.7	19.1	1.29
9	4.2	500	1/125/2.5	70	2	35	16.5	17.1	1.30
10	4.2	500	1/200/2.5	70	2	94	44.2	46.8	1.20
11	4.2	500	1/400/2.5	70	2	11	5.18	25.6	1.23
12[h]	4.2	500	1/800/2.5	70	2	< 5.0	-	-	-
13[h]	4.2	500	1/200 (DABCO)/2.5	70	2	< 5.0	-	-	-
14	4.2	500	1/200/2	70	2	28	13.2	125.0	1.35
15	4.2	500	1/200/5	70	2	53	24.9	69.9	1.67
16	4.2	500	1/200/2.5 (Bipy)	70	2	15	7.05	83.6	1.37
17[i]	4.2	500	1/200/2.5 (Me$_6$-TREN)	70	2	29	-	-	-

[a] General conditions (relative molar amounts): [MMA]$_0$/[EBiB]$_0$ = 470/1. [b] The amount of reducing agent was calculated according with the formula: [(O$_2$ mol x 2) + (CuCl$_2$ mol x 0.5)] x (excess). [c] Conversions of the monomer (MMA) were determined by relative integration of MMA and PMMA characteristic peaks in the ^{1}H-NMR spectra of the reaction crudes. [d] M_n^{th} = Theoretical molecular weight = [MMA]$_0$/[Initiator]$_0$)× M_{MMA}× conversion (M_{MMA} = molecular weight of MMA = 100.12 g/mol). [e] M_n^{SEC}: Molecular weight determined by size exclusion chromatography. [f] Polydispersity index (M_w/M_n) determined by size exclusion chromatography. [g] Reaction was performed in a sonication bath operating at 35 KHz and 160 W. [h] No appreciable conversion was observed after 12 hours of polymerisation. [i] The obtained white material was insoluble in common organic solvents.
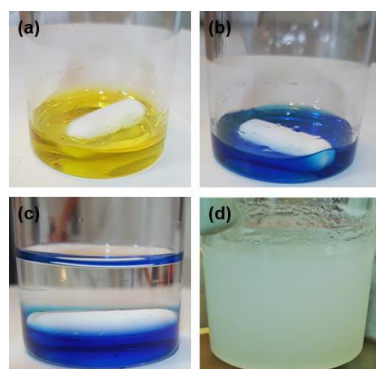

Figure 1. Photographs of CuCl$_2$/PMDETA ARGET ATRP at different stages in *DES* (1*ChCl*/2*Gly*): (a) CuCl$_2$; (b) CuCl$_2$ + PMDETA; (c) CuCl$_2$ + PMDETA + MMA; (d) CuCl$_2$ + PMDETA + MMA + Sn(EH)$_2$ after the polymerisation.
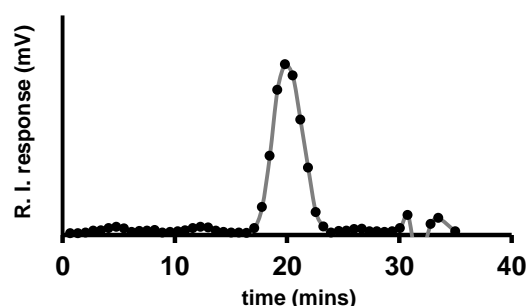

Figure 2. GPC trace of the PMMA synthesized according the following experimental conditions (Entry 10 of Table 1): [MMA]$_0$/[EBiB]$_0$/[Sn(EH)$_2$]$_0$/[CuCl$_2$]$_0$/[PMDETA]$_0$ = 470/1/48/0.23/0.56; T = 70° C; t = 2 hours; [MMA]$_0$/[*DES*]$_0$ = 4.2 (v/v). R. I. = Refractive index detector.

By lowering the temperature to 40° C, and although an acceptable correlation between M_n^{th} and M_n^{SEC} was achieved, a broader distribution of molecular weights (Đ = 1.4) as well as lower conversions (8 %) were observed (Entry 5 of Table 1). Entries 6 and 7 of Table 1 show that a decrease of the proportion [MMA]$_0$/*DES* (v/v) led to poor controllability of the ARGET ATRP process. An important parameter to optimise in ARGET ATRP, especially when that is performed under air atmosphere in capped vials (see Experimental Part), is the amount of reducing agent [Sn(EH)$_2$] needed to favour the regeneration of activator Cu(I) species. In Entries 8-12 of Table 1, we progressively increased the amount of Sn(EH)$_2$ finding that the optimal amount of reducing agent needed to consume the oxygen of the air located at the free space of the vial, and regenerate *in-situ* the activator species [Cu(I)/PMDETA] by the reduction of the deactivator complex [Cu(II)/PMDETA], is that of Entry 10. Thus, using a proportion 1/200 = [Cu]/Sn(II), we obtained PMMA with very low polydispersity index (Đ = 1.20) and almost perfect correlation between M_n^{th} and M_n^{SEC} at high MMA conversion (*ca*. 90 %). In terms of controllability of the macromolecular features (M_n and Đ) and activity (conversion *vs*. time), these experimental conditions represent a significant advance in the synthesis of PMMA in green *DES*s by using an ARGET ATRP procedure, with respect to the Fe-mediated methodology previously described by Wang and collaborators.[19] At this point, we would like to highlight that

the use pure glycerol as solvent (*i.e.*, in the absence of *ChCl*) and employing the same polymerisation reactions conditions showed in Entry 10, produces: *i*) moderate decrease of the yield (78 %); and *ii*) dramatic and undesired increase of the polydispersity index (Đ = 2.58) of the final polymer.

Attempts to improve the ARGET ATRP process by using another reducing agent (1,4-Diazabicyclo[2.2.2]octane (DABCO), Entry 13 of Table 1), different [Cu]/PMDETA proportions (Entries 14-15 of Table 1), or different ligands displaying significantly different ATRP activities than that of the PMDETA (*i.e.*, 2,2'-Bipyridine (Bipy) and tris[2-(dimethylamino)ethyl]amine (Me6-TREN), Entries 16-17 of Table 1 respectively), were unsuccessful.

The time-dependent progressions of monomer conversions (Figure 3a) showed linear plots compatible with a first order kinetic which is indicative of a constant concentration of the active propagating species during the ARGET ATRP in *DESs*.
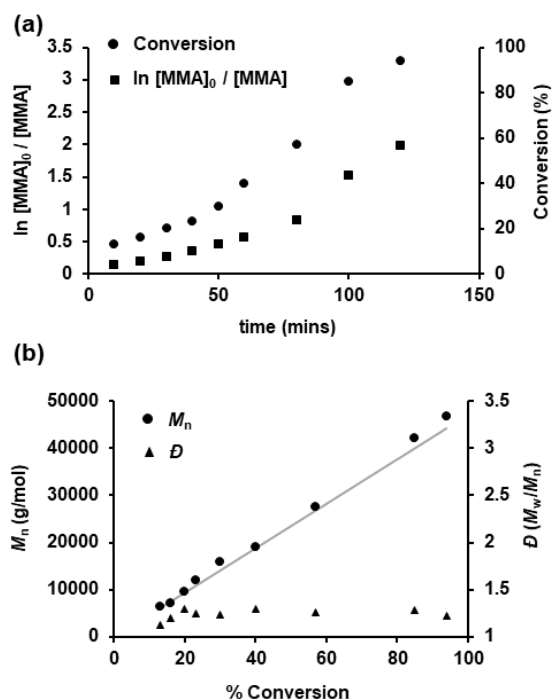

Figure 3. Kinetic plots of (a) ln ([MMa]$_0$/[MMA]) *vs.* polymerisation time and (b) M_n^{SEC} and Đ (M_w/M_n) *vs.* monomer conversion (%) for the ARGET ATRP of MMA in *DES* 1*ChCl*/2*Gly* using homogeneous CuCl$_2$ catalyst. Conditions: [MMA]$_0$/[EBiB]$_0$/[Sn(EH)$_2$]$_0$/[CuCl$_2$]$_0$/[PMDETA]$_0$ = 470/1/48/0.23/0.56; T = 70° C; [MMA]$_0$/[DES]$_0$ = 4.2 (v/v).

The kinetic plot shows that, under these experimental conditions, the 50 % of monomer conversion is achieved very fast within the first hour of the polymerisation. Figure 3b shows the dependency of molecular weight with the conversion of MMA. M_n^{SEC} values of the resulting polymers increased linearly with monomer conversion while keeping relatively low polydispersity (Đ > 1.3, see Figure 3b, Table S1, and Figure S1). The gradual growth of polymer chains with the monomer conversion and the relative high correlation achieved between M_n^{th} and M_n^{SEC} clearly indicate the controlled/"living" features (*i.e.*, RDRP character) of the ARGET ATRP in *DESs*. However, it is important to note that the slight deviation of M_n^{SEC} from the theoretical values (Figure 3b) as well as the deviation of the linearity of the kinetic plot (Figure 3a), both of

them more appreciable at higher conversion, can be attributed to significant increase of the viscosity of the reaction media after approximately 1 hour of reaction.

One of the most important issues in ATRP polymerisation is that regarding to the chain end functionality of the resultant polymers. Thus, to study the ability of the as-prepared PMMA to express their chain end functionality, we performed chain-extension experiments using the as-prepared PMMA as macro-initiator (PMMA-Br). Due to the limited solubility of the PMMA in *DES* and aiming to demonstrate the chain-end functionality, standard and well-stablished ARGET ATRP conditions to PMMA were chosen for the chain extension experiments (see Experimental Part).[21] Thus, using previously prepared PMMA-Br in *DES* (M_n = 42800 g/mol; Đ = 1.20; Entry 10 of Table 1) as a macro-initiator, we studied the chain extension with MMA monomer (note that PMMA-Br macroinitiator was isolated and purified before to be employed in chain extension experiments; see Experimental Part for further details). From Figure 4 there is an unequivocal peak shift from the macro-initiators to the resulted chain extended PMMA (M_n = 71100 g/mol). The obtained PMMA after chain extension experiments has a molecular weight which is consistent with an estimated chain extension ARGET ATRP conversion of a *ca.* 60 %, not observing any chromatographic peak at the retention time of that of the macro-initiator (PMMA-Br). Very importantly, the Đ of the resulted PMMA (1.24) is almost identical to that of the macro-initiator (1.20). Both experimental findings are clearly indicative of a negligible number of non-functionalised PMMA-Br chains in the macro-initiator. The successful chain extension reaction further confirms the features of controlled/"living" radical polymerisation of MMA in *DES*s.
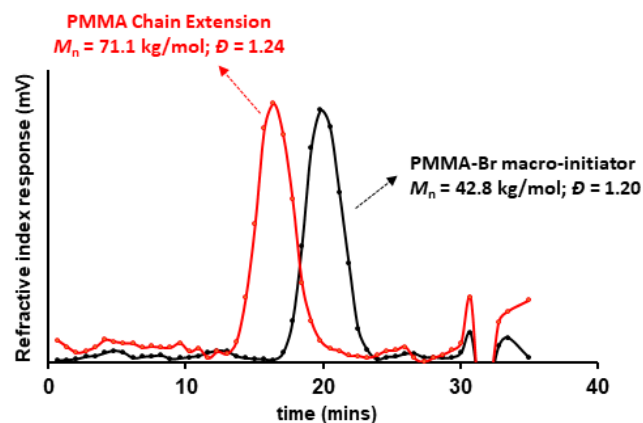

Figure 4. GPC chromatographic traces before and after chain extension using PMMA-Br as the macro-initiator (PMMA-Br was prepared according to the experimental conditions in Entry 10 of Table 1). Chain extension conditions: [MMA]$_0$/[PMMA-Br]$_0$/[Sn(EH)$_2$]$_0$/[CuCl$_2$]$_0$/[PMDETA]$_0$ = 470/1/400/5.3/10.6; T = 90° C; t = 1 hours; [MMA]$_0$/Anisole = 1/3 (*v/v*).

Using the optimised ARGET ATRP conditions (entry 10 of Table 1), we studied the scope of the reaction by employing different olefin monomers (Table 2) as well as other *ChCl*-based *DES*s for MMA.

Table 2. ARGET ATRP in *DESs* of MMA and different olefin monomers.

Ent.[a]	M[b]	*DES*	T °C	M_n^{th} Kg/mol[d]	M_n^{SEC} Kg/mol[e]	Đ[f]
1	MMA	1*ChCl*/2Urea	70	24.9	40.3	1.30
2	MMA	1*ChCl*/2*EG*[c]	70	15.5	25.9	1.20
3	Sty	1*ChCl*/2*Gly*	70	44.7	112.7	1.40
4[g]	Sty	1*ChCl*/2*Gly*	50	40.0	87.8	1.50
5	Sty	1*ChCl*/2*Gly*	100	38.6	92.9	1.43
6	2VP	1*ChCl*/2*Gly*	70	-	-	-
7	4VP	1*ChCl*/2*Gly*	70	< 5	-	-

[a] Conditions: $[M]_0/[EBiB]_0/[Sn(EH)_2]_0/[CuCl_2]_0/[PMDETA]_0$ = 470/1/48/0.23/0.56. [b] M = Monomers. Sty: Styrene; 2VP: 2-vinylpyridine; 4VP: 4-vinylpyridine. [c] *EG* = Ethylene glycol. [d] M_n^{th} = Theoretical molecular weight = $[M]_0/[Initiator]_0 \times M_M \times$ conversion (M_M = molecular weight of Sty, 2VP and 4VP). [e] M_n^{SEC}: Molecular weight determined by size exclusion chromatography. [f] Polydispersity index (M_w/M_n) determined by size exclusion chromatography. [g] Time = 12 hours.

Entries 1 and 2 of Table 2 show that other *DESs* such as 1*ChCl*/2Urea or 1*ChCl*/2*EG* (*EG* = Ethylene Glycol), are not as good solvents to ARGET ATRP of MMA as 1*ChCl*/2*Gly*. Similarly, the polymerisation of other olefin-type monomers proceed under a very low control over the macromolecular features of the resultant poly(olefin)s (*i.e.*, low concordance between the M_n^{th} and M_n^{SEC} values; see Entries 3-7 of Table 2).

2.2. Heterogeneous ARGET ATRP in *Deep Eutectic Solvents* using Cu(II)-catalysed Metal Organic Frameworks (MOFs).

Aiming to develop more sustainable ARGET ATRP polymerisation routes in *DESs*, in the absence of expensive organic ligands like PMDETA, and which also allow the recycle of the transition metal activator, we focused our interest in the use of Cu(II)-containing Metal Organic Frameworks (MOFs) as catalysts. In general, MOFs, having high specific surface area, tuneable pore sizes, shapes, and surface functionalities,[22] have been extensively employed in a variety of applications such as gas processing,[23] sensing,[24] catalysis,[25] and also as confined space for polymerisations.[26] In this last regard, recent works from the groups of Schmidt, Matyjaszewski and Antonietti,[27] used Cu(II)- or Zn(II)-containing MOFs to polymerise a variety of acrylate and olefin-type monomers with moderate to high control over the macromolecular features of the resulting polymers (M_n and Đ), and importantly, allowing the recycle of the MOF material up to six times. It is also important to note that as the polymerisation occurs within the confined space of the MOF, authors reported a significant increase of the isotactic triads when compared with that obtained by using bulk polymerisation techniques.[27b]

With these ideas in mind, we decided to explore the ARGET ATRP process in *DESs* using Cu(II)-containing MOFs as heterogeneous polymerisation catalyst in the absence of any

organic ligands. Based on the previous work of Schmidt, Antonietti and collaborators,[27a] we employed $Cu_2(bdc)_2(DABCO)$ (bdc: terephthalic acid; DABCO: 1,4-diazabicyclo[2.2.2]octane) as heterogeneous catalytic MOF moiety, and MMA as polymerisable monomer model [note that $Cu_2(bdc)_2(DABCO)$ is acting as both catalyst and ligand. See Scheme 2]. Based on our previous results with $CuCl_2$/PMDETA system, we employed similar experimental conditions than those of Entry 10 of Table 1. Thus, operating under air conditions in capped vials at 70° C; using 500 ppm of $Cu_2(bdc)_2(DABCO)$ (*i.e.* 112 ppm of Cu(II) centres); a relation $[MMA]_0/DES$ = 1/1 (*v/v*); and $Sn(EH)_2$ as reducing agent (see Entry 1 of Table 3), PMMA having very narrow polydispersity indexes (Đ = 1.20), and very high correlation between M_n^{th} and M_n^{SEC} was achieved in only 20 minutes (60 % conv.). Although, Schmidt, Antonietti and collaborators reported the use of DABCO as a convenient reducing agent to $Cu_2(bdc)_2(DABCO)$,[27a] in our specific eutectic mixture conditions, DABCO was demonstrated to be an inactive reducing ARGET agent (Entry 2 of Table 3). ARGET ATRP polymerisation can be successfully conducted at room temperature leading to PMMA with excellent polydispersity indexes (Đ = 1.10) and good correlation between M_n^{th} and M_n^{SEC} (Entry 3 of Table 3), although with low conversions after 24 hour of reaction (10 %). Diminution of the amount of reducing agent (Entry 4 of Table 3) led to poor control over the macromolecular features of the as-prepared PMMA (Đ = 2.85). Being one of the most recognisable and important characteristic of the ARGET variation of ATRP the very low catalyst loading needed to control the radical polymerisation, ARGET ATRP was performed by using only 50 ppm of Cu(II) MOF, which renders approximately 12 ppm of Cu(II) centres (Entry 5 of Table 3). Under these extremely low amount of Cu(II) centres, although only moderate yields of PMMA were achieved after 2 hours of reaction at 70° C (23 %), polymers exhibited very low polydispersity indexes (Đ = 1.10) and excellent correlation between M_n^{th} and M_n^{SEC}. Importantly, no appreciable polymerisation was observed in absence of either Cu(II) MOF or $Sn(EH)_2$ (Entries 6-7 of Table 3). The kinetic plot (time-dependent progressions of monomer conversions (Figure 5a, Table S2 and Figure S2) exhibited an almost linear dependence of both the $\ln([MMA]_0/[MMA])$ and the conversion with the time, which is in accordance with a constant concentration of the active propagating species during the ARGET ATRP process. Moreover, Figure 5b also showed a linear dependency of molecular weight of PMMA with the polymerisation conversion, which is indicative of the progressive growth of polymer chains. All these results indicate the controlled/ "living" features of the ARGET ATRP process performed in *DESs* by using an heterogeneous $Cu_2(bdc)_2(DABCO)/Sn(EH)_2$ system.
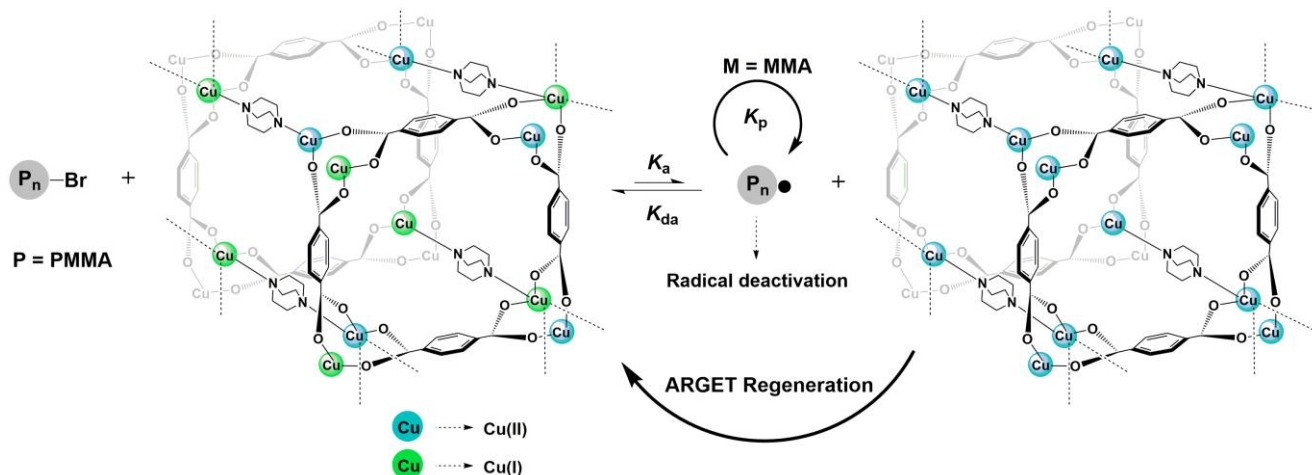
Scheme 2. Schematic illustration for the proposed general mechanism of ARGET ATRP of MMA using heterogeneous $Cu_2(bdc)_2(DABCO)$ MOF, in the absence of any organic ligand.

Table 3. Experimental conditions and molecular weight parameters for the ARGET ATRP of MMA in *DES* (1*ChCl*/2*Gly*) using heterogeneous $Cu_2(bdc)_2(DABCO)$ MOF as catalyst.

Entry[a]	$Cu_2(bdc)_2(DABCO)$ (ppm)	$[Cu_2(bdc)_2(DABCO)]_0/[Sn(EH)_2]_0$ (relative molar amounts)[b]	T (° C)	t (mins)	% Conv.[c]	M_n^{th} Kg/mol[d]	M_n^{SEC} Kg/mol[e]	$Đ$[f]
1	500	1/200	70	20	60	28.2	29.6	1.20
2[g]	500	1/200 (DABCO)	70	120	0	-	-	-
3	500	1/200	20	1440	10	4.70	5.30	1.10
4	500	1/6.5	70	120	9	4.23	5.25	2.85
5	50	1/200	70	120	23	10.8	11.9	1.10
6	500	1/-	70	120	0	-	-	-
7	-	-/200	70	120	< 5	-	-	-

[a] General conditions (relative molar amounts): $[MMA]_0/[EBiB]_0 = 470/1$. [b] The amount of reducing agent was calculated according with the formula: $[(O_2 \text{ mol x 2}) + (Cu_2(bdc)_2(DABCO) \text{ mol})]$ x (excess). [c] Conversions of the monomer (MMA) were determined by relative integration of MMA and PMMA characteristic peaks in the ^{1}H-NMR spectra of the reaction crudes. [d] M_n^{th} = Theoretical molecular weight = $[MMA]_0/[Initiator]_0 \times M_{MMA} \times$ conversion (M_{MMA} = molecular weight of MMA = 100.12 g/mol). [e] M_n^{SEC}: Molecular weight determined by size exclusion chromatography. [f] Polydispersity index (M_w/M_n) determined by size exclusion chromatography. [g] No appreciable conversion was observed after 12 hours of polymerisation.
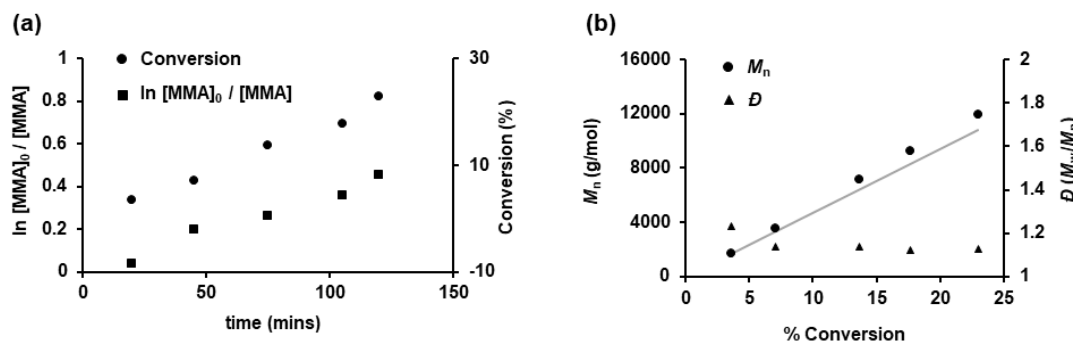

Figure 5. Kinetic plots of (a) ln ($[MMa]_0/[MMA]$) *vs.* polymerisation time and (b) M_n^{SEC} and $Đ$ (M_w/M_n) *vs.* monomer conversion (%) for the ARGET ATRP of MMA in *DES* 1*ChCl*/2*Gly* using heterogeneous Cu(II) MOF catalyst. Conditions: $[MMA]_0/[EBiB]_0/[Sn(EH)_2]_0/[Cu_2(bdc)_2(DABCO)]_0 = 470/1/96/0.48$; T = 70° C; $[MMA]_0/[DES]_0 = 1.0$ (*v/v*).

In a similar manner than that previously described by the homogeneous $CuCl_2$/PMDETA ARGET ATRP system, chain extension experiments were performed in order to evaluate the chain end functionality of the PMMA prepared from Cu(II) MOF. Thus, and using PMMA prepared by the conditions described in Entry 1 of Table 3 as macroinitiator (PMMA-Br macroinitiator was isolated and purified before to be employed in chain extension experiments; see Experimental Part for further details), the chain extension was evaluated by using MMA monomer. GPC traces (Figure 6) showed the shift of the chromatographic peak of the macroinitiator towards higher molecular weights, confirming that high chain-end functionality of the polymer prepared by ARGET ATRP in *DES* using $Cu_2(bdc)_2(DABCO)$ as catalyst.
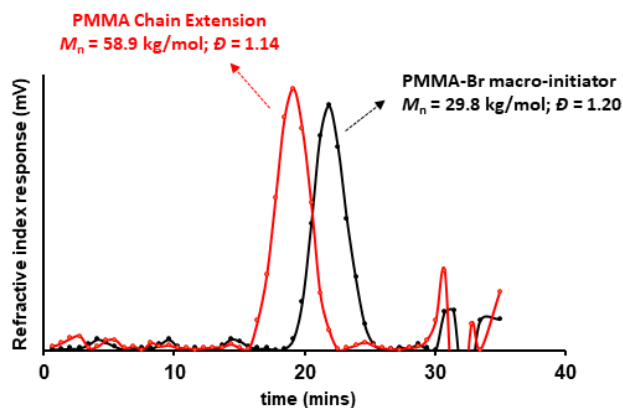

Figure 6. GPC chromatographic traces before and after chain extension using PMMA-Br as the macro-initiator (PMMA-Br was prepared according to the experimental conditions of Entry 1 of Table 3). Chain extension conditions: $[MMA]_0/[PMMA-Br]_0/[Sn(EH)_2]_0/[CuCl_2]_0/[PMDETA]_0 = 470/1/400/5.3/10.6$; T = 90° C; t = 1 hours; $[MMA]_0$/Anisole = 1/3 (*v/v*).

In their recent work, Schmidt, Matyjaszewski, Antonietti and collaborators observed an effect over the stereoregularity (tacticity) of the PMMA prepared by ARGET ATRP using related $Zn_2(bdc)_2(DABCO)$ MOF catalyst. Indeed, and due to the effect of the polymerisation of MMA in the confined space of the MOF channels, the authors reported an increase of the isotactic triads (*mm*) in the synthesised PMMA (*i.e.*, from 2 % of isotactic triads in bulk polymerisation to 8 % when MOF was employed).[27b] Intrigued by the effect of Cu(II) MOF over the tacticity of the as-prepared PMMAs in the eutectic mixture 1*ChCl*/2*Gly*, we analysed their steroregularity by comparing the [1]H- (Figure 7) spectrum with that of the PMMA obtained using homogeneous $CuCl_2$/PMDETA. Figure 7 shows the ^{1}H-NMR spectra of PMMA obtained by both $CuCl_2$/PMDETA and $Cu_2(bdc)_2(DABCO)$ MOF ARGET ATRP in 1*ChCl*/2*Gly*. Analysis of the –CH$_3$ region of the spectra clearly showed an increase in the isotactic triad (*mm*) fraction of the PMMAs prepared with heterogeneous Cu(II) MOF with respect to that from homogeneous $CuCl_2$. Relative integration of the signals corresponding to *mm*, *mr*, and *rr* triads yields a *ca.* 12 % of isotactic triads in PMMAs prepared from $Cu_2(bdc)_2(DABCO)$ MOF, whereas *ca*. 3 % was obtained using $CuCl_2$ catalyst. These results showed a slightly enhancement of the stereoregularity of the as-prepared PMMA in the confined space of a Cu(II) MOF compared with that previously reported by using $Zn_2(bdc)_2(DABCO)$ MOF.[27b]

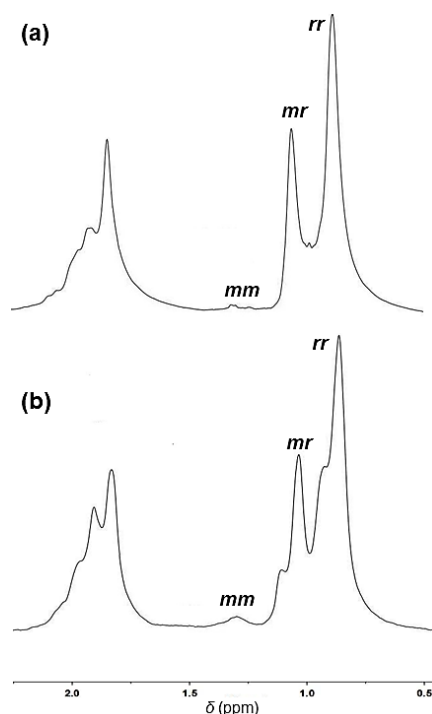**Figure 7**. ^{1}H-NMR (CDCl$_3$) of PMMAs prepared by ARGET ATRP in 1*ChCl*/2*Gly* using CuCl$_2$ (a) or Cu$_2$(bdc)$_2$(DABCO) MOF (b) catalysts. Triads: syndiotactic (rr); atactic (mr); and isotactic (mm).

Very importantly, the copper analysis (ICP-MS) of the PMMAs prepared by ARGET ATRP in 1*ChCl*/2*Gly* using Cu(II) MOF catalyst revealed an almost negligible Cu content of 0.05 ppb (see Experimental Part). Moreover, X-Ray power diffraction analysis (XRD) of the Cu(II) MOF catalyst before and after the ARGET ATRP revealed the preservation of the MOF structure during the process (Figure S3). Indeed XRD diffractograms exhibited identical peak pattern corresponding to Cu$_2$(bdc)$_2$(DABCO) MOF. Slightly changes of the peak intensities after an before the ARGET ATRP process can be attributed to the presence of guest molecules (MMA monomer, 1*ChCl*/2*Gly* components, etc.) in the channels of the MOF material.[26b,27a]

The heterogeneous nature of the ARGET ATRP process using Cu(II) MOF, together with the negligible Cu leaking and the high structural integrity of the Cu$_2$(bdc)$_2$(DABCO) after the polymerisation process in 1*ChCl*/2*Gly*, prompted us to study the recyclability of the catalyst. At this point, it is worth highlighting that the catalyst recycling after its use is considered a very important element to maximise, from a *Green Chemistry* point of view, in many industrial processes.[28] Moreover, as the Cu(II) MOF catalyst moved to the lower-density upper phase with PMMA, MMA and Sn(EH)$_2$ after centrifugation of the bulk reaction, while the 1*ChCl*/2*Gly* eutectic mixture remained located at the lower phase (Figure 8c), *DES* could be recycled during the catalytic cycle. Thus, when polymerisation finished (Figure 8b), and after separation of 1*ChCl*/2*Gly* (Figure 8c), heterogeneous Cu(II) material was recovered from PMMA phase by centrifugation (Figure 8d). Both recovered catalyst and 1*ChCl*/2*Gly* solvent were reused by adding fresh MMA and reducing agent. The [MOF based catalyst/(1*ChCl*/2*Gly*) solvent] system can be recycled at least six consecutive times maintaining invariable the conversion (*ca.* 30 % during the whole six runs. Figure 9), and, importantly, the controlled/"living" nature of the ARGET ATRP process (*i.e.*, both M_n^{SEC} and Đ of the as-prepared PMMA were consistent during all six recycling batches presented in Figure 9. See Table 4).
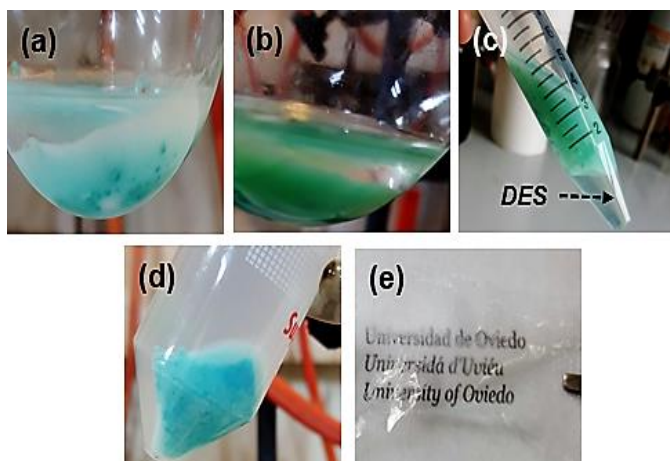
Figure 8. Photographs of ARGET ATRP in 1*ChCl*/2*Gly* using Cu₂(bdc)₂(DABCO) MOF at different stages: (a) Cu(II) MOF in 1*ChCl*/2*Gly* before polymerisation; (b) Cu(II) MOF in 1*ChCl*/2*Gly* during polymerisation after addition of reducing agent [Sn(EH)₂)]; (c) centrifugation of bulk reaction after polymerisation (lower phase correspond to 1*ChCl*/2*Gly* solvent); (d) recuperation of heterogeneous Cu(II) MOF material *via* centrifugation; and (e) polymer bulk after precipitation.
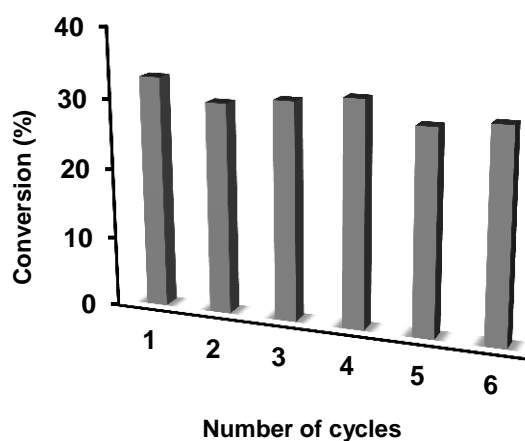

Figure 9. Conversion of the 6 consecutive cycles of ARGET ATRP using Cu₂(bdc)₂(DABCO) MOF catalyst in 1*ChCl*/2*Gly*. Conditions: [MMA]₀/[EBiB]₀/ [Cu₂(bdc)₂(DABCO)]₀/[Sn(EH)₂]₀ = 470/1/23/37.5; T = 70° C; and time = 45 min.

Table 4. Molecular weight parameters and yields for 6 consecutive ARGET ATRP cycles in 1*ChCl*/2*Gly* using heterogeneous Cu₂(bdc)₂(DABCO) MOF.

Cycle	Conversion (%)	M_n^{th} Kg/mol[a]	M_n^{SEC} Kg/mol[b]	$Đ$[c]
1	33	15.5	16.1	1.23
2	30	14.1	15.8	1.28
3	31	14.6	15.3	1.29
4	32	15.0	15.9	1.25
5	29	13.6	15.7	1.31
6	30	14.1	16.1	1.23

[a] M_n^{th} = Theoretical molecular weight = [MMA]₀/[Initiator]₀)× M_{MMA}× conversion (M_{MMA} = molecular weight of MMA = 100.12 g/mol).
[b] M_n^{SEC}: Molecular weight determined by size exclusion chromatography. [c] Polydispersity index (M_w/M_n) determined by size exclusion chromatography.

3. Conclusions

In conclusion, both homogeneous CuCl₂ and heterogeneous Cu(II) MOF catalyst were successfully employed in ARGET ATRP of MMA using green *Deep Eutectic Solvents* as sustainable reaction media under air conditions. Both ARGET ATRP routes produced PMMA in a controlled/"living" fashion according to RDRP standards as testified by a linear increase of molecular weight with conversion and chain extension experiments. Moreover, under the optimal conditions, both approaches (homogeneous and heterogeneous) lead to PMMA with very narrow polydispersity indexes ($Đ ≤ 1.2$). Heterogeneous route allowed performing

the ARGET ATRP in the absence of expensive organic ligands. Moreover, both *DES* and Cu(II) MOF catalyst were efficiently recycled after the polymerisation process and re-used during six consecutive catalytic cycles, maintaining invariable the conversion and providing PMMAs with comparable macromolecular features during whole recycle process. The confined space provided by the heterogeneous Cu(II) MOF in the *ChCl*-based eutectic mixtures provided PMMA with higher degree of isotacticity than that observed by related MOF catalyst in bulk.

In summary, the combination of heterogeneous MOF and green *Deep Eutectic Solvent* provides a more sustainable, recyclable and air tolerant route to PMMA, offering well-controlled and living properties together with high recyclability of the MOF catalyst and solvent, under environmentally-friendly reaction conditions.

4. Experimental Part

Materials. All reagents were obtained from commercial suppliers. Methylmethacrylate, Styrene, 2-vinylpyridine, and 4-vinylpyridine, were used without further purification. $CuCl_2$, *N,N,N′,N′′,N′′-*Pentamethyldiethylenetriamine (PMDETA), 2,2′-Bipyridine (Bipy), tris[2-(dimethylamino)ethyl]amine (Me_6-TREN), Ethyl α-bromoisobutyrate (EBiB), 1,4-Diazabicyclo[2.2.2]octane (DABCO), and Tin(II) 2-ethylhexanoate [$Sn(EH)_2$], were used as received without further purification. $Cu_2(bdc)_2(DABCO)$ MOF was prepared according with the literature procedures,[29] washed several times with DMF and MeOH, and dried 24 hours at 110° C prior to be used. *Deep Eutectic Solvents* were prepared by following the methods reported in the literature.[3]

General Methods. Reactions were performed in capped vials (22 mL or 13 mL of volume) under air conditions using a conventional magnetic stirring conditions or ultrasound bath operating at 35 KHz and 160 W. NMR spectra were recorded at 20° C on Bruker NAV-400, DPX-300 and AV-400 instruments. ^{1}H and ^{13}C{^{1}H}-NMR spectra are given relative to $Si(CH_3)_4$. GPC traces were measured with a Perkin–Elmer equipment with a model LC 250 pump, a model LC 290 UV, and a model LC 30 refractive index detector. The samples were eluted with a 0.1 % by weight solution of tetra(*n*-buthyl)ammonium bromide in THF through Perkin–Elmer PLGel (Guard, 10^5, 10^4 and 10^3 Å) at 30° C. Approximate molecular weight calibration was obtained using narrow molecular weight distribution of polystyrene standards. Samples were typically prepared by dissolving 10 mg of the polymer sample in 10 mL of micro-filtered (Millipore-Millex 0.45 μm) HPLC-grade THF. The mixture was sonicated during 5 mins and magnetically stirred during 2 hours. An aliquot of the solution was then filtered again (Millipore-Millex 0.45 μm) to remove any insoluble material, and injected (20 μL) to the GPC (1 mL / min). Powder XRD data were collected with $Cu_{K\alpha}$ radiation (λ = 1.5418 Å) with a Bruker D8 Discover powder diffractometer fitted with a 0.4 mm fixed-divergence slit, a knife-edge collimator, and a LynxEye area detector. Data were collected in the range $2\theta = 3$–50 ° in θ /2θ mode. ICP-MS analysis were performed by using Thermo Scientific Element II equipment.

Homogeneous $CuCl_2$-catalysed ARGET ATRP. Typical polymerisation of MMA was conducted as follows: $[MMA]_0/[EBiB]_0/[Sn(EH)_2]_0/[CuCl_2]_0/[PMDETA]_0 = 470/1/48/0.23/0.56$; T = 70° C; t = 2 hours; $[MMA]_0/[DES]_0 = 4.2$ (*v/v*). In a glass vial (volume = 22 mL) equipped with stir bar, 4.7 mg of $CuCl_2$ (0.035 mmol) and 18 μL of PMDETA (0.086 mmol) were dissolved in 1.75 ml of 1*ChCl*/2*Gly*, at room temperature and under air atmosphere. Then, 22 μL of EBiB (0.15 mmol) and 7.5 mL of MMA (70.42 mmol) were added under continuous stirring. The vial was capped with a rubber septum and then 2.32 mL of $Sn(EH)_2$ (7.20 mmol) were quickly added. The mixture was heated at 70° C during 2 hours under continuous and vigorous magnetic stirring. Polymerisation stopped by opening the vial to air. PMMA was isolated by extraction with 2-MeTHF/water (x3), evaporation of the collected organic layer, and subsequent precipitation from concentrate THF solutions into n-hexane.

Kinetic analysis were conducted exactly under the same experimental conditions and the polymerisation was terminated by opening to the air at specific time (see GPC traces in Supporting Information).

Chain extension experiments were conducted using PMMA-Br as macro-initiator. PMMA-Br was synthesised by following identical procedure than that described above with $CuCl_2$. PMMA-Br was isolated as it was previously described, and dried under vacuum (*ca.* 10^{-1} mBar) at 40° C during 12 hours previously to be used. Typical chain extension polymerisation with MMA was conducted as follows: $[MMA]_0/[PMMA\text{-}Br]_0/[Sn(EH)_2]_0/[CuCl_2]_0/[PMDETA]_0 = 2700/1/400/5.3/19$; T = 90° C; t = 1 hour; $[MMA]_0/[Anisole]_0 = 0.33$ (*v/v*). In a Schlenk equipped with stir bar, 0.3 g PMMA-Br (M_n = 42800 g/mol; Đ = 1.20; 0.007 mmol) was dissolved in 6 mL of anisole. The Schlenk was thoroughly purged by vacuum and flushed with nitrogen

(x3). Then, 5 mg of $CuCl_2$ (0.037 mmol), 19 µL of PMDETA (0.091 mmol), and 2.0 mL of MMA (18.78 mmol), were added and the Schlenk was thoroughly purged by vacuum and flushed with nitrogen (x3) again. After, 0.9 mL of $Sn(EH)_2$ (2.78 mmol) were quickly added, and the mixture was heated at 90° C during 1 hour under continuous and vigorous magnetic stirring. Polymerisation stopped by opening the vial to air. All volatiles were removed under vacuum and the PMMA was isolated by precipitation from concentrate THF solutions into MeOH and n-hexane (M_n = 71100 g/mol; Đ = 1.24).

Heterogeneous Cu(II) MOF-catalysed ARGET ATRP. Typical polymerisation of MMA was conducted as follows: $[MMA]_0/[EBiB]_0/[Sn(EH)_2]_0/[Cu_2(bdc)_2(DABCO)]_0$ = 470/1/96/0.48; T = 70° C; $[MMA]_0/[DES]_0$ = 1.0 (v/v). In a glass vial (volume = 13 mL) equipped with stir bar, 22 mg of $Cu_2(bdc)_2(DABCO)$ (0.038 mmol) were suspended in 3.75 ml of 1*ChCl*/2*Gly* at room temperature and under air atmosphere. Then, 11 µL of EBiB (0.075 mmol) and 3.75 mL of MMA (35.21 mmol) were added under continuous stirring. The vial was capped with a rubber septum and then 2.32 mL of $Sn(EH)_2$ (7.20 mmol) were quickly added. The mixture was heated at 70° C during 20 minutes under continuous and vigorous magnetic stirring. Polymerisation stopped by opening the vial to air. PMMA was isolated by extraction with 2-MeTHF/water (x3), evaporation of the collected organic layer, and subsequent precipitation from concentrate polymer solutions (THF) into n-hexane.

Kinetic analysis were conducted exactly under the same experimental conditions and the polymerisation was terminated by opening to the air at specific time (see GPC traces in Supporting Information).

Chain extension experiments were conducted using PMMA-Br as macro-initiator. PMMA-Br was synthesised by following identical procedure than that described above with $Cu_2(bdc)_2(DABCO)$. PMMA-Br was isolated as it was previously described, and dried under vacuum (*ca.* 10^{-1} mBar) at 40° C during 12 hours previously to be used. Typical chain extension polymerisation with MMA was conducted as follows: $[MMA]_0/[PMMA-Br]_0/[Sn(EH)_2]_0/[CuCl_2]_0/[PMDETA]_0$ = 1900/1/280/3.7/9.1; T = 90° C; t = 1 hour; $[MMA]_0/[Anisole]_0$ = 0.33 (v/v). In a Schlenk equipped with stir bar, 0.3 g PMMA-Br (M_n = 29800 g/mol; Đ = 1.20; 0.01 mmol) was dissolved in 6 mL of anisole. The Schlenk was thoroughly purged by vacuum and flushed with nitrogen (x3). Then, 5 mg of $CuCl_2$ (0.037 mmol), 19 µL of PMDETA (0.091 mmol), and 2.0 mL of MMA (18.78 mmol), were added and the Schlenk was thoroughly purged by vacuum and flushed with nitrogen (x3) again. After, 0.9 mL of $Sn(EH)_2$ (2.78 mmol) were quickly added, and the mixture was heated at 90° C during 1 hour under continuous and vigorous magnetic stirring. Polymerisation stopped by opening the vial to air. All volatiles were removed under vacuum and the PMMA was isolated by precipitation from concentrate THF solutions into MeOH and n-hexane (M_n = 58900 g/mol; Đ = 1.14).

Recycling of $Cu_2(bdc)_2(DABCO)$ and *DES* (1*ChCl*/2*Gly*) were conducted as follows: $[MMA]_0/[EBiB]_0/[Cu_2(bdc)_2(DABCO)]_0/[Sn(EH)_2]_0$ = 470/1/23/37.5; T = 70° C; time = 45 minutes; $[MMA]_0/[DES]_0$ = 1.0 (v/v). In a glass vial (volume = 13 mL) equipped with stir bar, 480 mg of $Cu_2(bdc)_2(DABCO)$ (0.845 mmol) were suspended in 3.75 ml of 1*ChCl*/2*Gly* at room temperature and under air atmosphere. Then, 11 µL of EBiB (0.075 mmol) and 3.75 mL of MMA (35.21 mmol) were added under continuous stirring. The vial was capped with a rubber septum and then 0.45 mL of $Sn(EH)_2$ (1.38 mmol) were quickly added. The mixture was heated at 70° C during 20 minutes under continuous and vigorous magnetic stirring. Polymerisation stopped by opening the vial to air. Then, *DES* was separate from the reaction mixture by centrifugation (30 min. at 15000 rpm). $Cu_2(bdc)_2(DABCO)$ was recovered from PMMA layer after centrifugation (30 min. at 15000 rpm). Recuperated $Cu_2(bdc)_2(DABCO)$ and *DES* were combined with fresh MMA and reducing agent, and ARGET ATRP was conducted under the same experimental conditions than those described above.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1   (a) P. T. Anastas and J. C. Warner, *Green Chemistry Theory and Practice*, Oxford University Press, Oxford, 1998. (b) A. S. Matlack, *Introduction to Green Chemistry*, Marcel Dekker, New York, 2001. (c) M. Poliakoff, J. M. Fitzpatrick, T. R. Farren and P. T. Anastas, *Science*, 2002, **297**, 807. (d) M. Lancaster, *Green Chemistry: An Introductory Text*, RSC Publishing, Cambridge, 2002. (e) R. A. Sheldon, I. W. C. E. Arends and U. Henefeld, *Green Chemistry and Catalysis*, Wiley-VCH, Weinheim, 2007.

2   (a) J. D. Mota-Morales, R. J. Sánchez-Leija, A. Carranza, J. A. Pojman, F. del Monte and G. Luna-Bárcenas, *Prog. Polym. Sci.*, 2018, **18**, 139. (b) F. del Monte, D. Carriazo, M. C. Serrano, M. C. Gutiérrez and M. L. Ferrer, *ChemSusChem*, 2014, **7**, 999. (c) A. Roda, A. A. Matias, A. Paiva and A. R. C. Duarte, *Polymers*, 2019, **11**, 912. (d) D. Carriazo, M. C. Serrano, M. C. Gutiérrez, M. L. Ferrer and F. Del Monte, *Chem. Soc. Rev.*, 2012, **41**, 4996.

3   The term *Deep Eutectic Solvent* was coined by Abbott and co-workers in their pioneering works: (a) A. P. Abbott, G Capper, D. L. Davies, R. K. Rasheed and V. Tambyrajah, *Chem. Commun.*, 2003, 70. (b) A. P. Abbott, D. Boothby, G. Capper, D. L. Davies and R. K. Rasheed, *J. Am. Chem. Soc.*, 2004, **126**, 9142.

4   J. García-Álvarez, *Deep Eutectic Solvents and Their Applications as New Green and Biorenewable Reaction Media*, in *Handbook of Solvents*, vol. 2, 3rd ed.: Use, Health, and Environment, (Ed. G. Wypych) ChemTec Publishing, Toronto, 2019.

5   For general reviews dealing with the use of *Deep Eutectic Solvents* as sustainable reaction media, see: (a) A. P. Abbott, R. C. Harris, K. Ryder, C. d'Agostino, L. Gladden and M. D. Mantle, *Green Chem.*, 2011, **13**, 82. (b) C. Ruß and B. König, *Green Chem.*, 2012, **14**, 2969. (c) Q. Zhang, K. de Oliveira Vigier, S. Royer and F. Jérôme, *Chem. Soc. Rev.*, 2012, **41**, 7108. (d) M. Francisco, A. van den Bruinhorst and M. C. Kroon, *Angew. Chem. Int. Ed.*, 2013, **52**, 3074. (e) G. Yu and F. Jérôme, *Chem. Soc. Rev.*, 2013, **42**, 9550. (f) A. Paiva, R. Craveiro, I. Aroso, M. Martins, R. L. Reis and A. R. C. Duarte, *ACS Sustainable Chem. Eng.*, 2014, **2**, 1063. (g) D. V. Wagle, H. Zhao and G. A. Baker, *Acc. Chem. Res.*, 2014, **47**, 2299.

6   (a) E. L. Smith, A. P. Abbott and K. S. Ryder, *Chem. Rev.*, 2014, **114**, 11060. (b) L. Millia, V. Dall'Asta, C. Ferrara, V. Berbenni, E. Quartarone, F. M. Perna, V. Capriati and P. Mustarelli, *Solid State Ion.*, 2018, **323**, 44.

7   A. Abo-Hamad, M. Hayyam, M. A. AlSaadi and M. A. Hashim, *Chem. Eng. J.*, 2015, **273**, 551.

8   B. Tang, H. Zhang and K. H. Row, *J. Sep. Sci.*, 2015, **38**, 1053.

9   H. Zhao, *J. Chem. Technol. Biotechnol.*, 2015, **90**, 19.

10   (a) J. García-Álvarez, *Eur. J. Inorg. Chem.*, 2015, 5147. (b) N. Guajardo, C. R. Müller, R. Schrebler, C. Carlesi and P. Domínguez de María, *ChemCatChem*, 2016, **8**, 1020. (c) G. Dilauro, S. Mata García, D. Tagarelli, P. Vitale, F. M. Perna and V. Capriati, *ChemSusChem*, 2018, **11**, 3495. (d) B. Saavedra, N. González-Gallardo, A. Meli and D. J. Ramón, *Adv. Synth. Catal.*, 2019, **361**, 3868. (e) J. Xu, W. Huang, R. Bai, Y. Queneau, F. Jérôme and Y. Gu, *Green Chem.*, 2019, **21**, 2061. (f) L. Peng, Z. Hu, Q. Lu, Z. Tang, Y. Jiao and X. Xu, *Chin. Chem. Lett.*, 2019, DOI:10.1016/j.cclet.2019.05.063.

11   (a) C. Vidal, J. García-Álvarez, A. Hernán-Gómez, A. R. Kennedy and E. Hevia, *Angew. Chem. Int. Ed.*, 2014, **53**, 5969. (b) V. Mallardo, R. Rizzi, F. C. Sassone, R. Mansueto, F. M. Perna, A. Salomone and V. Capriati, *Chem. Commun.*, 2014, **50**, 8655. (c) F. C. Sassone, F. M. Perna, A. Salomone, S. Florio and V. Capriati, *Chem. Commun.*, 2015, **51**, 9459. (d) C. Vidal, J. García-Álvarez, A. Hernán-Gómez, A. R. Kennedy and E. Hevia, *Angew. Chem. Int. Ed.*, 2016, **55**, 16145. (e) M. J. Rodríguez-Álvarez, J. García-Álvarez, M. Uzelac, M. Fairley, C. T. O´Hara and E. Hevia, *Chem. Eur. J.*, 2018, **24**, 1720. (f) J. García-Álvarez, E. Hevia and V. Capriati, *Chem. Eur. J.*, 2018, **24**, 14854. (g) S. Ghinato, G. Dialuro, F. M. Perna, V. Capriati, M. Blangetti and C. Prandi, *Chem. Commun.*, 2019, **55**, 7741.

12   (a) P. Liu, J. Hao, L. Mo and Z. Zhang, *RSC Adv.*, 2015, **5**, 48675. (b) D. A. Alonso, A. Baeza, R. Chinchilla, G. Guillena, I. M. Pastor and D. J. Ramón, *Eur. J. Org. Chem.*, 2016, 612. (c) C. Wu, H.-J. Xiao, S.-W. Wang, M.-S. Tang, Z.-L. Tang, W. Xia, W.-F. Li, Z. Cao and W.-M. He, *ACS Sustainable Chem. Eng.,* 2019, **7**, 2169.

13   (a) E. M. Genies and C. Tsintavis, *J. Electroanal. Chem.,* 1985, **195**, 109. (b) K. Dhanalakshmi, R. Saraswathi and C. Srinivasan, *Synth. Met.*, 1996, **82**, 237. (c) J. Liao, P. Wu and Y. Bai, *Inorg. Chem. Commun.*, 2005, **8**, 390. (d) P. A. Monnard, A. Kanavarioti and D. W. Deamer, *J. Am. Chem. Soc.,* 2003, **125**, 13734.

14 J. D. Mota-Morales, M. C. Gutiérrez, I. C. Sanchez, G. Luna-Bárcenas and F. del Monte, *Chem. Commun.*, 2011, **47**, 5328.

15 (a) A. Sánchez-Condado, G. A. Carriedo, A. Presa Soto, M. J. Rodríguez-Álvarez, J. García-Álvarez and E. Hevia, *ChemSusChem*, 2019, **12**, 3134. For recent examples dealing with the use of ultrasonic techniques in organic synthesis under greener conditions see: (b) L.-Y. Xie, Y.-J. Li, J. Qu, Y. Duan, J. Hu, K.-J. Liu, Z. Cao, W.-M. He, *Green Chem.*, 2017, **19**, 5642. (c) C. Wu, L.-H. Lu, A.-Z. Peng, G.-K. Jia, C. Peng, Z. Cao, Z. Tang, W.-M. He, X. Xu, *Green Chem.*, 2018, **20**, 3683.

16 (a) J. S. Wang and K. Matyjaszewski, *J. Am. Chem. Soc.*, 1995, **117**, 5614. (b) K. Matyjaszewski, *Macromolecules*, 2012, **45**, 4015. (c) M. Kato, M. Kamigaito, M. Sawamoto and T. Higashimura, *Macromolecules*, 1995, **28**, 1721. (d) M. Kamigaito, T. Ando and M. Sawamoto, *Chem. Rev.*, 2001, **101**, 3689. (e) C. Boyer, N. A. Corrigan, K. Jung, D. Nguyen, T. K. Nguyen, N. N. Adnan, S. Oliver, S. Shanmugam and J. Yeow, *Chem. Rev.*, 2016, **116**, 1803. (f) J.-F. Lutz, J.-M. Lehn, E. W. Meijer and K. Matyjaszewski, *Nat. Rev. Mater.*, 2016, **1**, 16024. (g) J. M. Ren, T. G. McKenzie, Q. Fu, E. H. Wong, J. Xu, Z. An, S. Shanmugam, T. P. Davis, C. Boyer and G. G. Qiao, *Chem. Rev.*, 2016, **116**, 6743. (h) K. Matyjaszewski and N. V. Tsare*v*sky, *J. Am. Chem. Soc.*, 2014, **136**, 6513.

17 (a) K. Min, H. F. Gao and K. Matyjaszewski, *J. Am. Chem. Soc.*, 2005, **127**, 3825. (b) W. Jakubowski and K. Matyjaszewski, *Angew. Chem. Int. Ed.*, 2006, **45**, 4482. (c) J. Xia, X. Zhang and K. Matyjaszewski, *Macromolecules*, 1999, **32**, 3531. (d) H. El-Hamshary, M. El-Garawany, F. N. Assubaie and M. Al-Eed, *J. Appl. Polym. Sci.*, 2003, **89**, 2522.

18 P. V. Mendonça, M. S. Lima, T. Guliashvili, A. C. Serra and J. F. J. Coelho, *Polymer*, 2017, **132**, 114.

19 J. Wang, J. Han, M. Y. Khan, D. He, H. Peng, D. Chen, X. Xie and Z. Xue, *Polym. Chem.*, 2017, **8**, 1616.

20 K. Matyjaszewski, H. Dong, W. Jakubowski, J. Pietrasik and A. Kusumo, *Langmuir*, 2007, **23**, 4528.

21 W. Jakubowski and K. Matyjaszewski, *Macromolecules*, 2005, **38**, 4139.

22 N. Stock and S. Biswas, *Chem. Rev.*, 2012, **112**, 933.

23 (a) H. Furukawa, K. E. Cordova, M. O'Keeffe and O. M. Yaghi, *Science*, 2013, **341**, 1230444. (b) J.-R. Li, R. J. Kuppler and H.-C. Zhou, *Chem. Soc. Rev.*, 2009, **38**, 1477.

24 (a) L. E. Kreno, K. Leong, O. K. Farha, M. Allendorf, R. P. Van Duyne and J. T. Hupp, *Chem. Rev.*, 2012, **112**, 1105. (b) D. Zacher, O. Shekhah, C. Woll and R. A. Fischer, *Chem. Soc. Rev.*, 2009, **38**, 1418−1429.

25 (a) Y. Bai, X. Feng, H. Xing, Y. Xu, B. K. Kim, N. Baig, T. Zhou, A. A. Gewirth, Y. Lu, E. Oldfield and S. C. Zimmerman, *J. Am. Chem. Soc.*, 2016, **138**, 11077. (b) H. L. Nguyen, T. T. Vu, D. Le, T. L. H. Doan, V. Q. Nguyen and N. T. S. Phan, *ACS Catal.*, 2017, **7**, 338. (c) C.-D. Wu, A. Hu, L. Zhang and W. Lin, *J. Am. Chem. Soc.*, 2005, **127**, 8940.

26 (a) L. Gao, C.-Y. V. Li and K.-Y. Chan, *Chem. Mater.*, 2015, **27**, 3601. (b) T. Uemura, Y. Ono, K. Kitagawa and S. Kitagawa, *Macromolecules*, 2008, **41**, 87. (c) T. Kitao, Y. Zhang, S. Kitagawa, B. Wang and T. Uemura, *Chem. Soc. Rev.*, 2017, **46**, 3108. (d) J. Hwang, H.-C. Lee, M. Antonietti and B. V. K. J. Schmidt, *Polym. Chem.*, 2017, **8**, 6204. (e) T. Uemura, N. Yanai and S. Kitagawa, *Chem. Soc. Rev.*, 2009, **38**, 1228.

27 (a) H.-C. Lee, M. Antonietti and B. V. K. J. Schmidt, *Polym. Chem.,* 2016, **7**, 7199. (b) H.-C. Lee, M. Fantin, M. Antonietti, K. Matyjaszewski and B. V. K. J. Schmidt, *Chem. Mater.*, 2017, **29**, 9445.

28 (a) *Catalyst Separation, Recovery and Recycling. Chemistry and Process Design* (Eds. D. Cole-Hamilton, R. Tooze), Springer, Dordrecht, 2006. (b) *Recoverable and Recyclable Catalyst* (Ed. M. Benaglia), Wiley, Chichester, 2009.

29 R. Heck, O. Shekhah, O. Zybaylo, P. G. Weidler, F. Friedrich , R. Maul, W. Wenzel and C. Wöll, *Polymers*, 2011, **3**, 1565.

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