



# A-la-carte surface functionalization of organic materials via the combination of radiation-induced graft polymerization and multi-component reactions

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## Abstract

A feasible integration of multicomponent reactions (MCRs) into the radiation-induced graft polymerization technique (RIGP) has begun to bloom in modern polymer and materials sciences. This successful combination, the RIGP-MCR technique, has enabled an access to organic materials whose surface was chemically modified with target molecules in a diversity-oriented fashion. By taking advantage of the RIGP, surface modification reactions are now feasible with any organic substrates that are otherwise difficult to modify. As complementing the RIGP, the state-of-the-art synthetic tool of MCRs realizes an installation of multiple functional units onto material surfaces in a one-shot fashion by simply varying reactants. In this prospective article, we document the current stream and the outlook in the material sciences in the line with the historical aspects of RIGP and MCR techniques.

## Introduction

Considering the ever-growing importance of functionalized materials in a range of interdisciplinary sciences, a functionalization of organic materials has been spotlighted as one of the most important scientific targets. Here, the majority of organic materials is undoubtedly polymeric compounds. For example, polyethylene and polystyrene are typical petroleum-derived polymers, while cellulose and chitin are typical naturally occurring polymers. Though curing and etching are also classified as an important surface modification protocol, chemical transformations on organic materials surface would be the most important surface functionalization technique to install desirable functionality on material surfaces. In particular, graft polymerization, in other words a surface-initiated polymerization, is an important technique to modify the material surfaces. Graft polymerization is a reaction that occurs at the solid and liquid phases and thus tends to be more difficult than solution reactions. As fueled by the rapid development of living/controlled radical polymerization in polymer science,<sup>[1–11]</sup> surface-initiated living/controlled radical polymerization (SI-LRP) has been gathering growing attentions from many fields. Currently, the most important surface-initiated polymerization is probably surface-initiated living radical polymerization.<sup>[12–18]</sup> For example, surface-initiated atom transfer radical polymerization (SI-ATRP) and surface-initiated reversible addition fragmentation living radical polymerization (SI-RAFT) have been widely employed in the line with the maturing of ATRP and

RAFT techniques, and this has paved a way into various material applications in the twenty-first century. Although SI-ATRP and SI-RAFT are excellent graft polymerization techniques, their limitations and weaknesses have also been recognized. Critically, polymerization initiators need to be installed on material surfaces prior to graft polymerization steps, which usually requires several addition chemical treatments of material surfaces. Furthermore, the heterogeneity during the polymerization of SI-ATRP and SI-RAFT would be problematic. As already discussed, because SI-ATRP and SI-RAFT are reactions that take places at interphases, the initiation from the material surfaces would be crucially affected by uncontrollable factors. Of note, this heterogeneity issue would be emphasized in the cases of SI-ATRP and SI-RAFT processes because their initiation reactions usually differ from the propagation steps. In this context, undesired initiations, such as self-initiation reactions in solutions, could be involved depending on the compatibility between the substrate and the monomer, thereby interfering the free monomer selection. Above-mentioned limitations render two important factors that material scientists need to tackle to further advance the material research. First, the surface modifications would be preferably free from initiator anchoring processes. This would decrease the overall process complexity and concurrently increase the robustness of the surface modification protocol. Second, installation of any desired functional units onto materials surface would be enabled in a-la-carte fashion. This should realize build-to-order material

fabrications depending on the requirements for the researcher's aims. Although we will document above two aspects in the following sections in detail, we turned our attention to two orthogonal approaches to achieve the abovementioned chemical challenges. Specifically, radiation-based chemistry for the former scientific task due to the robustness of the radiation chemistry in material sciences and multicomponent reactions (MCRs) for the later task due to their instinctive diversity-oriented nature.

With the above background, the authors have been focusing on the combination of radiation-induced graft polymerization (RIGP) and multi-component-reaction-based polymer chemistry. In terms of material fabrications, the RIGP has been known before the maturing of SI-ATRP and SI-RAFT. Despite its chemical and green benefits, the use of RIGP in modern material science has been rather lagging behind SI-ATRP and SI-RAFT techniques. In this context, we have tackled to achieve a renaissance of the RIGP technique by feasibly integrating the state-of-the-art polymer synthesis based on the MCRs.

Prior to embarking on the main contents in this manuscript, the outline of the manuscript is briefly discussed here. First, two important elementary techniques, the RIGP and MCRs, are documented in the line with material and polymer chemistries. Next, our proof-of-the-concept of the RIGP-MCR technique on fluorine containing polymers was briefly documented, which showcased the essential benefits of the approach. Subsequently, the extension of RIGP-MCR technique in sustainable material chemistry was demonstrated by using woody-biomass sourced materials. Last but not least, this manuscript documents our prospective views in the light of RIGP-MCR technique.

### **Brief background of the RIGP**

The history of the RIGP would be very long and the initial RIGP research results were reported in mainly 1950s. Until 1980s, almost all known polymeric materials were revealed to accept RIGP on their surfaces to alter the material properties. In the same fashion to organic materials, RIGP of inorganic materials has been applied to organic-inorganic hybrid materials. However, inorganic materials are compatible basically with only compact modules in the current fashion, whereas the facile RIGP with ion beams, which are currently capable of spot irradiation, will surely be the next generation of RIGP techniques for inorganic materials. In this context, the chemistry of RIGP with inorganic materials have largely differentiated from organic ones. As such, this prospective article focuses on organic materials in general to make this manuscript clear in terms of the topic coverage. Nevertheless, in this context, RIGP can use a wide variety of polymeric materials as base materials, and the reaction can proceed swiftly not only with simple shapes such as films and beads, but also with complex shapes such as nonwoven fabrics and hollow-fiber membranes. In addition, since expensive catalysts are not required and polymerization processes are allowed to undergo under mild reaction conditions, the RIGP would enable industrialization feasibly starting from laboratory-level research. Furthermore, installation of functional groups would be robust and thus a wide range

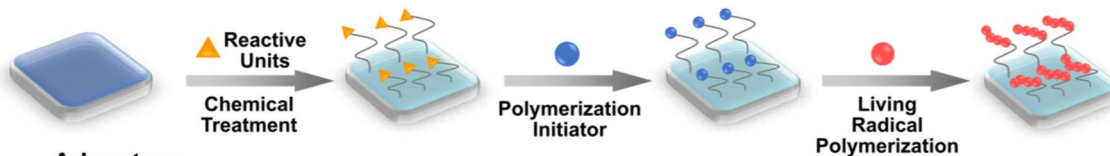
of functional materials are accessible even in the industrial scale, such as adsorbent,<sup>[19–23]</sup> antibacterial,<sup>[24,25]</sup> and electrolyte membrane.<sup>[26–29]</sup> Despite the above-mentioned instinctive excellence and advantages of the RIGP technique in surface functionalization protocol, SI-LRP methods have been rather spotlighted from the polymer communities as hugely driven by the recent development of SI-LRP methods. Therefore, from the viewpoint of synthetic polymer chemistry, RIGP technique has been put on the stage of the “sleeping beauty.” However, as summarized in Fig. 1, advantages of RIGP technique over the SI-LRP methods are clear in terms of operational simplicity.

### **Emerging polymer synthesis based on MCRs**

In this section, we will document the state-of-the-art polymer synthesis based on MCRs.<sup>[30–37]</sup> Though MCRs could give a complex impression, the history of MCRs in organic chemistry would be rather long.<sup>[38–44]</sup> Even in nineteenth century, a very important MCR was discovered. In 1850s, Strecker discovered the amino acid synthesis via the reaction among aldehydes, amines, and hydrogen cyanide. Named after the chemist, the reaction has been known as the Strecker three component reaction, which has been one of the most important reactions to produce  $\alpha$ -amino acids even in the twenty-first century. Despite that polymer chemistry generally imports elementary reactions from the parental organic chemistry, MCRs have been surprisingly scarcely incorporated into polymer chemistry until very recently. In this context, Meier et al. reported the most important research in 2011, in which the Passerini three component reaction (Passerini-3CR) among the aldehydes, carboxylic acids, and isocyanides was employed as an elementary reaction for polymer synthesis, feasibly achieving a monomer synthesis, post-polymerization modification reaction, and step-growth polymerization reactions.<sup>[45]</sup> Triggered by this research, many MCRs have been integrated into polymer chemistry, including the Ugi three and four component reactions (Ugi-3CR and Ugi-4CR),<sup>[37,46–48]</sup> the Passerini-3CR,<sup>[49–55]</sup> the Biginelli three component reaction (Biginelli-3CR),<sup>[33,56–58]</sup> the Kabachnik-Fields three component reaction (KF-3CR),<sup>[59–62]</sup> to mention a few. Within the last decade, the integration of MCRs into polymer chemistry has been innovating polymer synthesis. In spite that MCR-based polymer synthesis in solution has begun to bloom, their integration into surface chemistry has not been spotlighted. Considering the chemical natures of the MCRs, their utility should be also emphasized in surface chemistry since most MCRs proceed without the use of additives/catalysts and MCRs can rapidly increase the chemical space because more than two reactants can be anchored on material surfaces. Given that MCRs could instinctively enable a diversity-oriented-approach also in surface chemistry, materials science should be enriched because the surface modification with MCRs should realize material functionalization in an a-la-carte fashion that is otherwise difficult to achieve.

Considering the above-mentioned background, we aimed to integrate MCRs with RIGP technique so that a surface

### Surface-Initiated Living Radical Polymerization (SI-LRP)



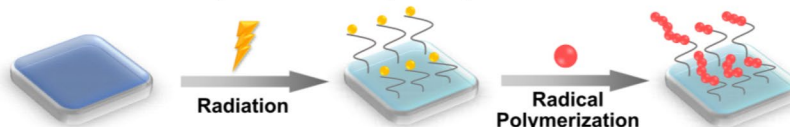
**Advantage**

- ✓ Precision control

**Disadvantages**

- ✓ Complicated operation ✓ Limitations of substrates

### Radiation-Induced Graft Polymerization (RIGP)



**Advantages**

- ✓ Operational simplicity ✓ Mild reaction conditions
- ✓ No expensive catalyst required ✓ Applicable to a variety of substrates

**Disadvantage**

- ✓ Expensive equipment

Figure 1. Schematic representation of advantages of RIGP technique over the SI-LRP methods.

modification of virgin organic materials would be feasible in an a-la-carte fashion by taking advantages of both the RIGP and MCR techniques (Fig. 2).

### Surface chemistry based on RIGP and MCRs (RIGP-MCRs)

As mentioned above, surface modifications for stable organic materials would not be straightforward since stable materials scarcely feature reactive units on their surfaces. Considering these backgrounds, we aimed at combining the RIGP technique and MCR-based polymer chemistry, termed as the

RIGP-MCRs, so that surface functionalization protocol would be feasible on any organic materials in their virgin forms in a diversity-oriented fashion. In order to showcase the proof-of-concept, the RIGP-MCR was applied for the surface modifications of a fluorinated polymer, ethylene tetrafluoride ethylene copolymer (ETFE), because fluorinated polymers including ETFE do not accept conventional chemical reactions due to the extraordinary stable bonding of carbon-fluorine and incompatibility with standard organic and aqueous solvents, thereby hindering any organic transformation reactions on their surfaces. Due to the high compatibility of aldehyde groups in

### Multi Component Reaction (MCR)

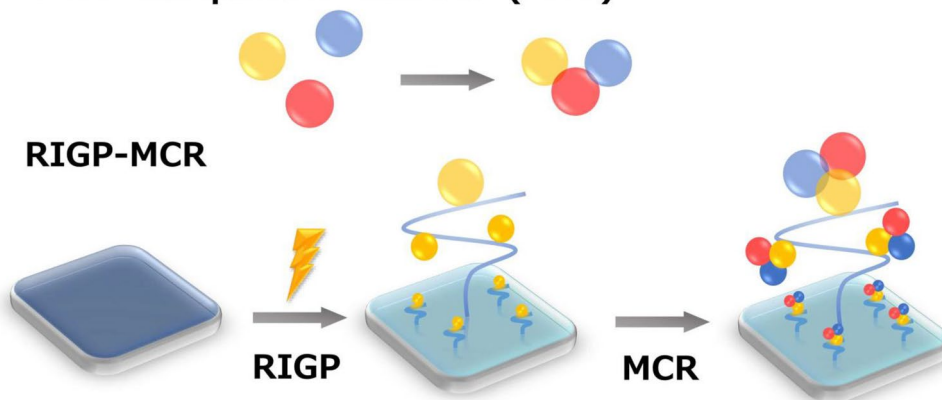


Figure 2. Schematic representation for the fusion of RIGP technique and MCR-based polymer synthesis.

many MCRs, aldehyde-containing vinyl monomer (4-vinylbenzaldehyde, St-CHO) was selected. Building on these considerations, St-CHO was radiationally grafted under emulsion polymerization condition with Tween 20 as an emulsifier (Fig. 3).<sup>[63]</sup> Prior to the graft polymerization reaction, 50 kGy of electron beam was radiated to the ETFE film under inert gas. The obtained ETFE films were then subjected to emulsion polymerization at 60°C in an emulsion solution of 3.3 wt% St-CHO. As a result, the grafting degree (weight gain from the original substrate) was estimated at around 30%, suggesting the feasible engraftment of St-CHO onto the ETFE film surfaces. Furthermore, FT-IR spectra of the ETFE film before and after radiation graft polymerization showed that the strong aldehyde peak at 1698 cm<sup>-1</sup> developed after the graft polymerization. This showed that poly(4-vinylbenzaldehyde) (PSt-CHO) was feasibly engrafted onto the ETFE film (ETFE-g-PSt-CHO). As targeted, ETFE films were feasibly engrafted with aldehyde-containing polymers from out-of-the-box ETFE fabrics, so that MCRs can now be carried out on the aldehyde functionalized ETFE films.

As a representative MCR, we have selected the KF-3CR among aldehydes, amines, and phosphites because we have

already reported efficient polymer synthesis by using KF-3CR as an elementary reaction, including polymer analogous reactions and step-growth polymerization reactions. Building on the feasibility of the KF-3CR, the surface KF-3CR was thus performed on ETFE-g-PSt-CHO. The surface KF-3CR on ETFE-g-PSt-CHO was carried out at 80°C in 1,4-dioxane using the aromatic amines and phosphites. The surface reaction was evaluated by FT-IR measurement, and the aldehyde peak disappeared as KF-3CR proceeded, while the peak owing to the phosphate group obviously developed. The KF-3CR proceeded swiftly even on the surface of the ETFE film, and any desired aromatic amines and phosphites were anchored on the surface. In term of material fabrication process, this result would be already surprising because ultimately stable ETFE film was feasibly modified with  $\alpha$ -amino phosphonate esters in a one-shot reaction.

Since any desired combination of aromatic amines and phosphites can be used with the surface KF-3CR, an installation of crown ethers on the ETFE surface was targeted to demonstrate the advantage of the RIGP-MCR technique. Crown ethers are known for their ability to selectively capture cationic species and are important functional groups in absorbing materials, but

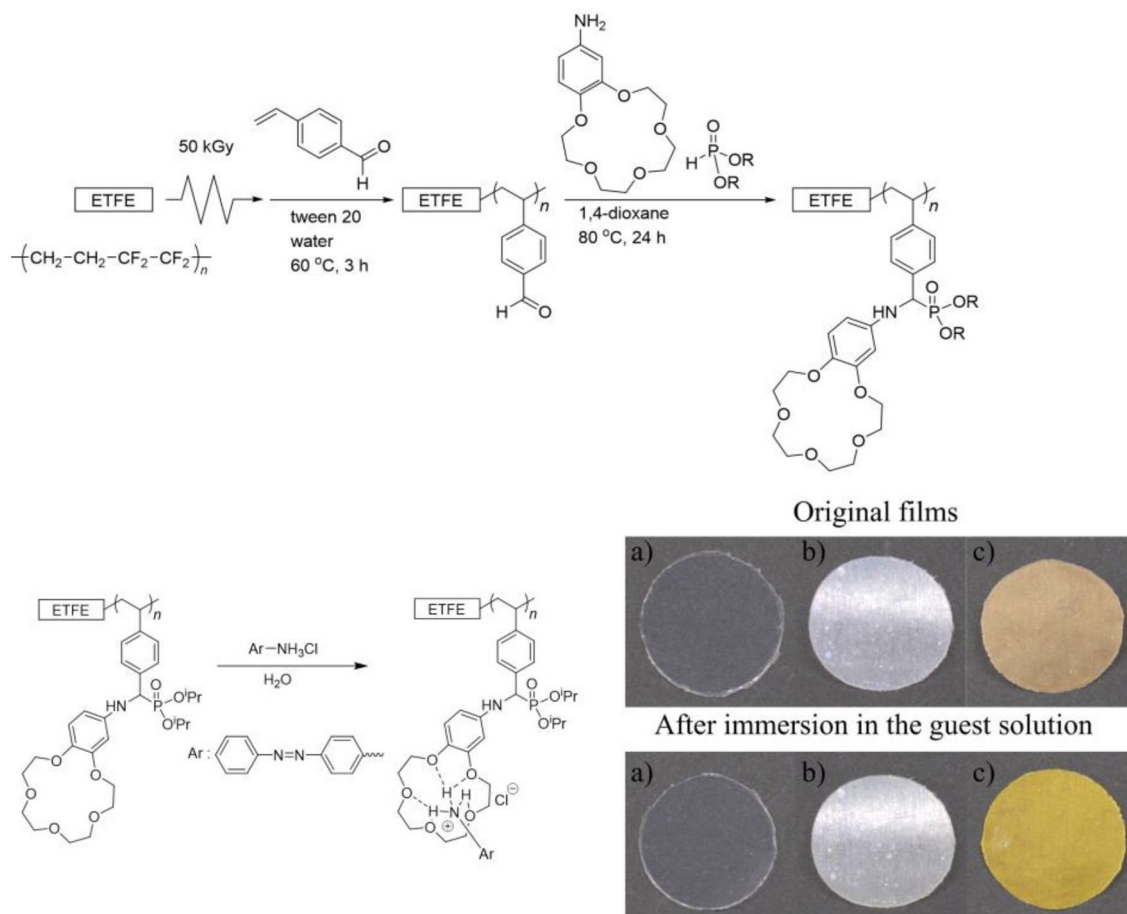
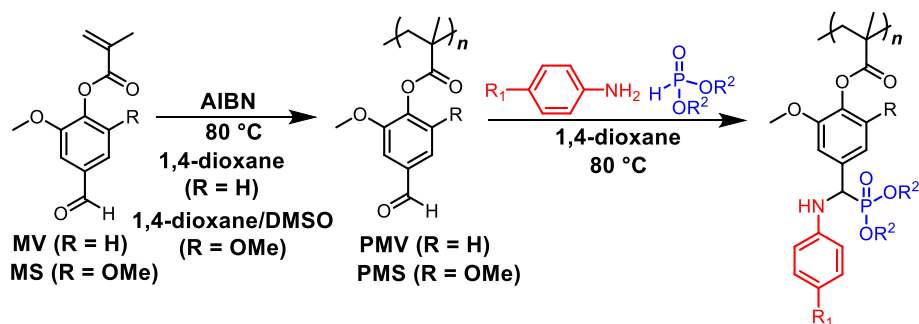


Figure 3. Surface Kabachnik-Fields three component reaction on ETFE films. Reprinted with permission from Ref. 63.





**Scheme 1.** A schematic representation of Kabachnik-Fields post-polymerization modifications of polymethacrylates derived from vanillin (PMV, R=H) and syringaldehyde (PMS, R=OMe).

their amphiphilic nature usually makes surface introduction difficult. A representative crown ether, 4'-aminobenzo-15-crown-5-ether (15-C-5-Ar-NH<sub>2</sub>), and diisopropyl phosphite were employed for this purpose. The surface modification reaction of KF-3CR on ETFE-g-PSt-CHO was carried out at 80 °C in 1,4-dioxane using the above amine and phosphite. In the same fashion to the above prototype reactions, the ETFE film with crown ether immobilized on the surface (ETFE-g-PAP-15-C-5-Ar) was obtained.

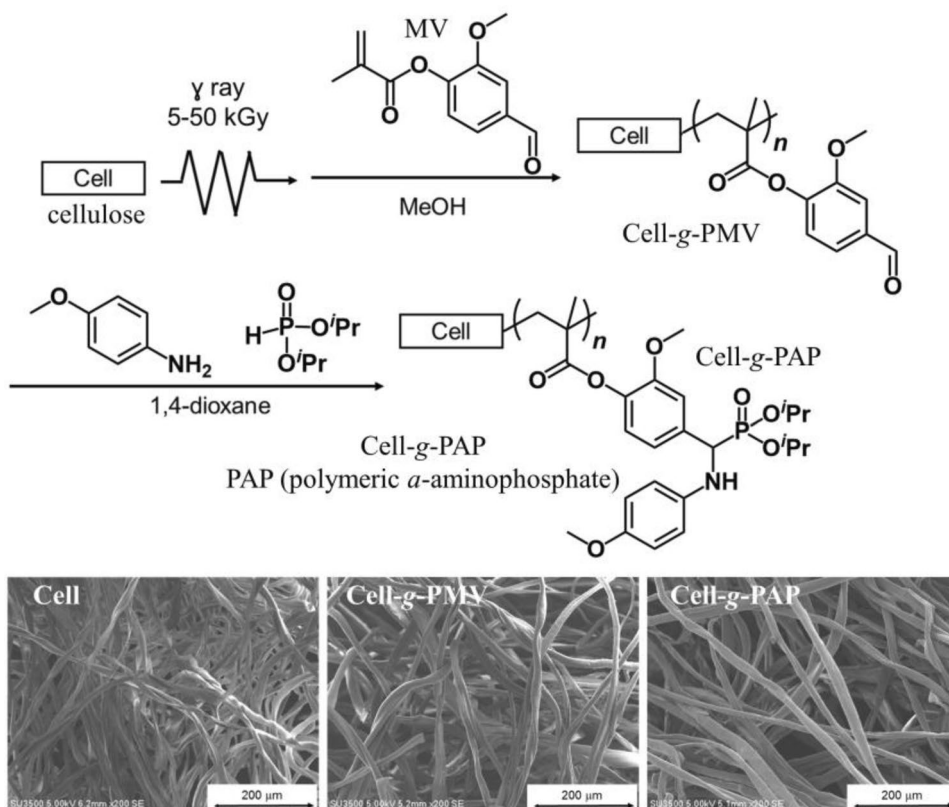
Then, the guest capturing ability of ETFE-g-PAP-15-C-5-Ar was evaluated. In general, ETFE membranes instinctively resist absorption of ionic molecules at molecular level because of their fluorophobic nature. With the 15-crown-5-ether moiety being an excellent host molecule for ammonium cations, the obtained ETFE-g-PAP-15-C-5-Ar was immersed in an aqueous guest solution containing 4-aminoazobenzene hydrochloride (azo-NH<sub>3</sub>Cl) as a guest molecule (Fig. 3). After the ETFE-g-PAP-15-C-5-Ar being immersed in the azo-NH<sub>3</sub>Cl solution, the surface colors of the ETFE-g-PAP-15-C-5-Ar changed drastically from pale brown to vivid yellow, corresponding to the color of the azobenzene moiety. This color change should be responsible for the host-guest complexation between the surface anchored crown ethers and azo-NH<sub>3</sub>Cl. As described above, the RIGP-MCR enabled the surface modification reaction of even fluoropolymers. This results feasibly demonstrated that the RIGP-MCR would be robust material modification toolbox, with which practically any organic materials in their virgin form are now ready to be modified with desired functional molecules in an a-la-carte fashion.

### RIGP-MCRs for sustainable materials chemistry

As demonstrated in the previous section, the RIGP-MCR now would be a powerful toolbox in material chemistry. We again turned our attention to the instinctive advantages of the RIGP-MCR protocol. Empowered by the RIGP, stable organic materials are now ready to accept surface modification reactions. In this context, we next aimed to utilize lignocellulose considering the growing importance of the sustainable development goals

(SDGs) in material science as well. Here, we turned our attentions to the lignocellulose composition, a woody biomass. Lignocellulose is mainly comprised of three components, namely lignin, cellulose and hemicellulose. More specifically, lignin is an aromatic polymer, and cellulose and hemicellulose are polysaccharides. Historically, cellulose has been an important membrane material and utilized in modern material chemistry even in the twenty-first century. Interestingly, lignin is known to be chemically degraded into aromatic aldehydes, vanillin and syringaldehyde. Since these lignin derivatives feature aldehyde groups, they are expected to be highly compatible with MCRs because most MCRs employ aldehyde as a reactant partner. In this context, we can artificially re-construct the chemical structure of lignocellulose so that surface-modification-ready materials can be accessible exclusively from wood-biomass, when lignin derived chemicals (e.g., vanillin) would be radiationally engrafted on the surface of cellulose membranes. In order to demonstrate the proof of the concept, we first verified whether lignin derived vanillin and syringaldehyde are compatible with MCRs such as the KF-3CR (Scheme 1).<sup>[64]</sup> For this purpose, free-radical polymerization of methacrylated vanillin (MV) and methacrylated syringaldehyde (MS) were carried out, affording the corresponding poly(methacrylated vanillin) (PMV) and poly(methacrylated syringaldehyde) (PMS), respectively. Then, PMV or PMS was subjected to KF-3CR at 80 °C in 1,4-dioxane with an excess amount of aromatic amines and phosphites relative to the polymeric aldehyde groups. As expected, PMV and PMS were feasibly modified with the KF-3CR, affording the corresponding polymeric  $\alpha$ -aminophosphates. Therefore, the lignin derivatives vanillin and syringaldehyde were proved to be useful chemical integrant for MCRs.

Since the lignin derived vanillin and syringaldehyde showed high compatibility with KF-3CR, the fabrication of biomass-derived organic hybrid material was targeted exclusively using biomass-sourced components (Fig. 4).<sup>[65]</sup> Specifically, PMV segment was engrafted on the cellulose surface via the RIGP process. Due to the high polarity of cellulose surface, the cellulose films were radiationally engrafted with MV in a methanol solution at 60 °C. The grafting degree of the cellulose fibers reached 57%, strongly supporting the progress



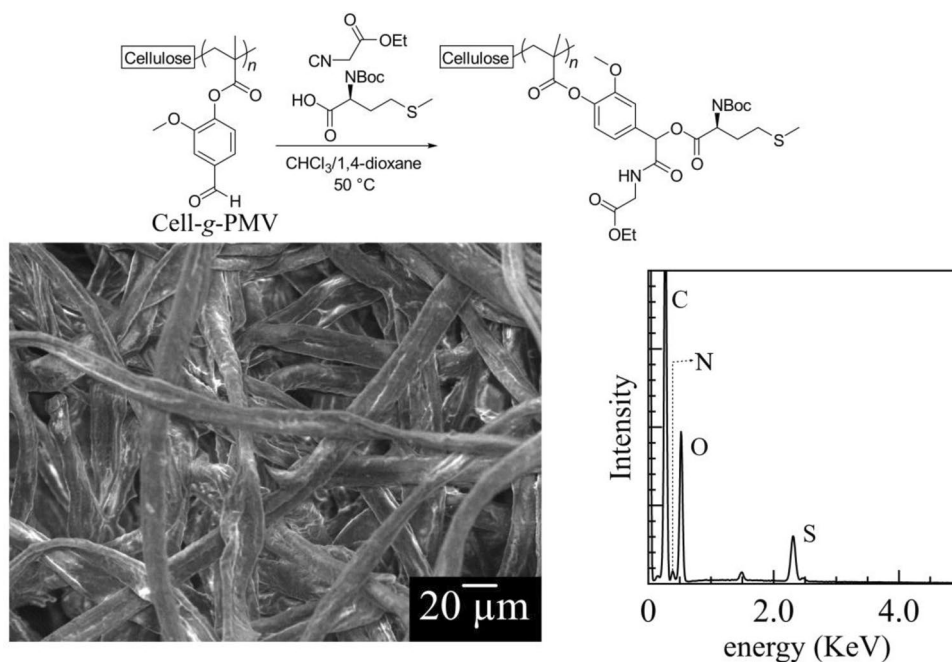
**Figure 4.** Surface Kabachnik-Fields three component reaction on cellulose-based organic hybrids featuring poly(methacrylated vanillin) as a reactive handle on their surfaces. Reprinted with permission from Ref. 65. Copyright 2019 American Chemical Society.

of graft polymerization of MV from cellulose fibers. The FT-IR spectra of the cellulose fibers after the RIGP showed strong peaks due to aldehyde groups ( $1692\text{ cm}^{-1}$ ) and ester groups ( $1753\text{ cm}^{-1}$ ), demonstrating that PMVs were radiationally engrafted onto the cellulose membranes (Cell-g-PMV). It should be emphasized here that above-results already enabled an artificial reconstruction of lignocellulose structures. With the bio-sourced organic hybrids in our hands, the Cell-g-PMV membrane was subjected to surface KF-3CR in 1,4-dioxane at  $80^\circ\text{C}$  using aromatic amines and phosphites. As expected from the above-documented our results, the surface KF-3CR proceeds feasibly on the surface of cellulose membrane as well, and cellulose membrane with  $\alpha$ -aminophosphate groups immobilized on the surface (Cell-g-PAP) was obtained without harming the membrane microscopic structures (Fig. 4). Of note here, cellulose membrane modified through the RIGP-MCR protocol was experimentally discovered to show the hydrophobicity owing to the surface anchored amino phosphonate ester groups where starting cellulose membranes are hydrophilic. This clearly showcased that material properties of biomass-derived materials would be feasibly controlled via the RIGP-MCR protocol, thereby demonstrating the chemical utility of our approach for material functionalization and fabrications.

Though we have successfully demonstrated the green benefits of the RIGP-MCR protocol, there remained two bottlenecks in terms of greenness, corresponding to the choice of

MCR and the source of cellulose fibers. The first issue here is the nature of the KF-3CR, which employs aldehydes, aromatic amines, and phosphites. Unfortunately, the natural systems barely involve aromatic amines and phosphites in a range of bio-transformations. The lack of naturally occurring aromatic amines and phosphites led to an inevitably decreased overall greenness in the RIGP-MCR process. The second drawback at this stage was the source of cellulose. We have radiationally engrafted PMV segments onto cellulose membranes that was industrially purified and obtained from pulping processes.

Regarding the first issue, we turned our attentions to the employment of Passerini-3CR that is the MCR among aldehydes, carboxylic acids, and isocyanides (Fig. 5).<sup>[66]</sup> It must be emphasized here that carboxylic acids are accessible from naturally occurring chemicals such as fatty acids, amino acids, citric-acid-cycle related carboxylic acids and isocyanides are also easily prepared from bio-based amines. We have proved that PMV can accept the Passerini-3CR with high aldehyde conversions ( $>90\%$ ) in  $\text{CHCl}_3$  solution at  $50^\circ\text{C}$ , thereby enabling an installation of carboxylic acids and isocyanides in a one-shot manner. As encouraged by this high reactivity of the PMV for the Passerini-3CR, Cell-g-PMV was subjected to the surface Passerini-3CR with amino acid-based carboxylic acids and isocyanides. Specifically, *N*-Boc-L-methionine was selected as methionine-based carboxylic acid and ethyl isocyanoacetate was employed as glycine-based isocyanide. In the same fashion to the Passerini-3CR in solution,



**Figure 5.** Surface Passerini three component reaction on cellulose-based organic hybrids featuring poly(methacrylated vanillin) as a reactive handle on their surfaces. Reprinted with permission from Ref. 66. Copyright 2021 SpringerNature.

the amino acid-based reactants were feasibly anchored on the surface of the Cell-g-PMV via the Passerini-3CR protocol. By taking advantage of the natures arising from the RIGP and Passerini-3CR, the matrix membrane, surface grafted reactive polymer, and surface modifying agents are now all bio-sourced compounds throughout the processes. We foresee the revolution of sustainable material chemistry by using bio-based compounds (Fig. 5). Along with the selection of MCRs in term of greenness, we also tacked to increase the greenness by using greener cellulose membranes. In this regard, we have demonstrated that nonwoven fabric materials sourced from pineapple leaf fibers (piñatex) were found to be compatible with the RIGP-MCR protocol, thereby enabling an ideal upcycling of naturally occurring resources.<sup>[67]</sup> As demonstrated here, we have successfully taken advantage of the green nature of the RIGP-MCR protocol.

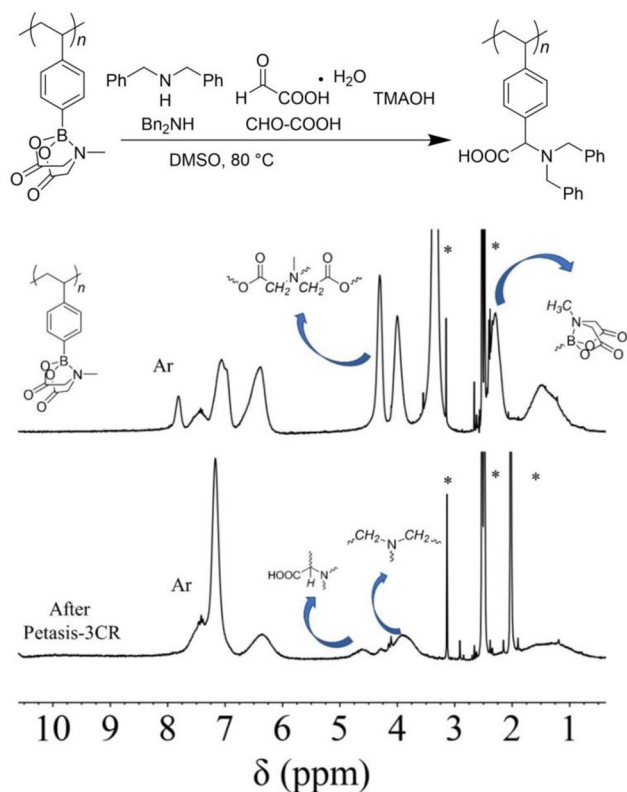
### Prospective aspects

As documented, the combination of the RIGP and MCRs have begun to bloom in the field of organic material sciences very recently. Building on this successful combination, we would envision that the RIGP-MCR protocol should renovate the modern material chemistry by taking advantage of the process. For this, our outlook will be discussed in the following sections.

### Prospective aspects for the MCR-based polymer synthesis

Since the polymer science shows two important aspects, namely the synthetic chemistry and material science, this part will be mainly divided into two sections. First, we embark on the

synthetic chemistry aspect of the MCR-based polymer chemistry. As documented in this prospective article, the integration of MCRs into polymer synthesis has started in 2010s. Therefore, the state of the MCR-based polymer chemistry has been still in its infancy. Unlike standard organic chemistry, polymer chemistry requires highly selective and efficient reactions because elementary reactions of polymer synthesis include numerous iterations or occurs on high molecular weight polymers. The intrinsic complexity of the MCRs might have interfered with validating MCRs for polymer chemistry, thereby limiting the number of MCRs applied for polymer synthesis. The available MCRs up to now include the Passerini-3CR, the Ugi-4CR, KF-3CR, Biginelli-3CR, Hantzsch-3CR, A3-coupling reaction, and metal-catalyzed MCRs. Though the number of available MCRs in polymer chemistry has been gradually increasing since 2010s, the majority of MCRs still have been left “sleeping beauties”. In this context, the variety of MCRs for polymer chemistry should be enriched in the next step to broaden the applicability of MCRs in polymer chemistry. For example, some of the authors have very recently demonstrated experimentally that modified Petasis-3CR among aromatic boronic acids, amines, and glyoxylic acid would be compatible with polymer synthesis by carefully optimizing and modifying the original Petasis-3CR (Fig. 6).<sup>[68]</sup> Though experimental validation of MCRs for polymer synthesis would be inevitable and necessary, it must be emphasized here that experimental validations would be time-consuming due to the lack of reaction information in advance. In this context, we would envision that the in-silico design of new polymer chemistry should renovate



**Figure 6.** Optimized Petasis three component reaction for polymer synthesis. Reprinted with permission from Ref. 68. Copyright 2021 Wiley-VCH GmbH.

and evolve the polymer synthesis in parallel with experimental discoveries, when considering the increasing computational power and software developments. In fact, some of the authors succeeded in rationally designing polymer analogous reactions by using computational reaction profiling based on electronic structure calculations such as density-functional theory (DFT) and (post-)Hartree–Fock methods, thereby bypassing “groping-in-the-dark” experiments.<sup>[69–72]</sup> Along with the conventional electronic structure calculations, recent developments in machine learning technology should lead to more sophisticated selection of MCRs that are potentially compatible with polymer chemistry as in the case of organic chemistry.<sup>[73]</sup> We would prospect that the fusion of computational chemistry and polymer synthesis would foster the MCR portfolio in polymer science more efficiently and effectively.

Next, we move to the material science aspects of MCR-based polymer chemistry. Since MCRs can furnish unique chemical structures, polymers synthesized from MCRs should be interesting candidates for diverse applications. Most importantly, MCRs can easily increase the chemical space, in other words chemical diversity, of the products out of them. The diversity-oriented approach has been historically linked with combinatorial approach in the field of pharmaceutical chemistry, which needs namely the astronomical number of compounds to discover a medicine. As

fueled by the maturing of the machine learning technology in general, the fusion of machine learning technology and material science has been targeted, which has been termed as materials informatics (MI). In order to promote the MI research, massive datasets are mandatory for machine learning process. However, the lack of general database in polymer science has hindered the swift integration of the MI with polymer synthesis. In this context, diversity-oriented approach in polymer synthesis should provide an indispensable infrastructure for the MI research. For this, we believe that MCRs in polymer chemistry should foster the polymer datasets and thus boost the MI integration.

### Prospective aspects for the RIGP chemistry

Despite the instinctive advantage of the RIGP technique, there remains two bottlenecks in the RIGP process, which corresponds to a control over the graft polymerization and the rational prediction of the reactivity during the RIGP process.

First, we embark on the control over polymerization step. In the same fashion to standard radical polymerizations, RIGP proceeds via free-radical polymerization mechanism, thus graft polymer chains obtained via RIGP are in principle not controlled, because the radical reaction instinctively involves uncontrolled side reactions. In the field of synthetic polymer chemistry, LRP techniques including ATRP, RAFT, and nitroxide-mediated radical polymerization, have been matured within a few decades and thus now would allow a uniform initiation and propagation reactions without noticeable side reactions, therefore providing control over molecular weight and distribution of obtained polymers. Among the existing LRP techniques, RAFT technique should be considered as the most versatile due to its tolerance to an array of reaction conditions, and the possibility of integration with existing conventional free-radical polymerization systems. In this context, the compatibility of RIGP with RAFT-mediated processes has been gradually validated.<sup>[74–81]</sup> In conventional RIGP, it is quite difficult to evaluate the molecular weights of grafted chains as they are covalently tethered to the trunk polymer. On the other hand, during RAFT-mediated RIGP by gamma irradiation, both the grafted chains and polymers generated in solution phases are controlled by the same RAFT processes, the molecular weights and distribution of grafted chains were thus estimated. These experimental insights feasibly implied that the RAFT-mediated RIGP underwent under the controlled fashion. With these reports, RAFT-mediated RIGP have been revealed to furnish tailored polymer structure and functionality. Such control over graft polymerization reactions have been shown to enhance the functional properties of graft polymers. This has been observed in increasing the proton conductivity of ETFE membranes for fuel cell applications and the metal adsorption capacity of PE/PP adsorbents for rare earth recovery. Thus, we would envision that not only the RAFT but also other LRPs will be integrated in the RIGP process to realize the precise graft



polymerization on the surface of organic materials, thereby controlling many factors such as the length and composition of the graft polymers.

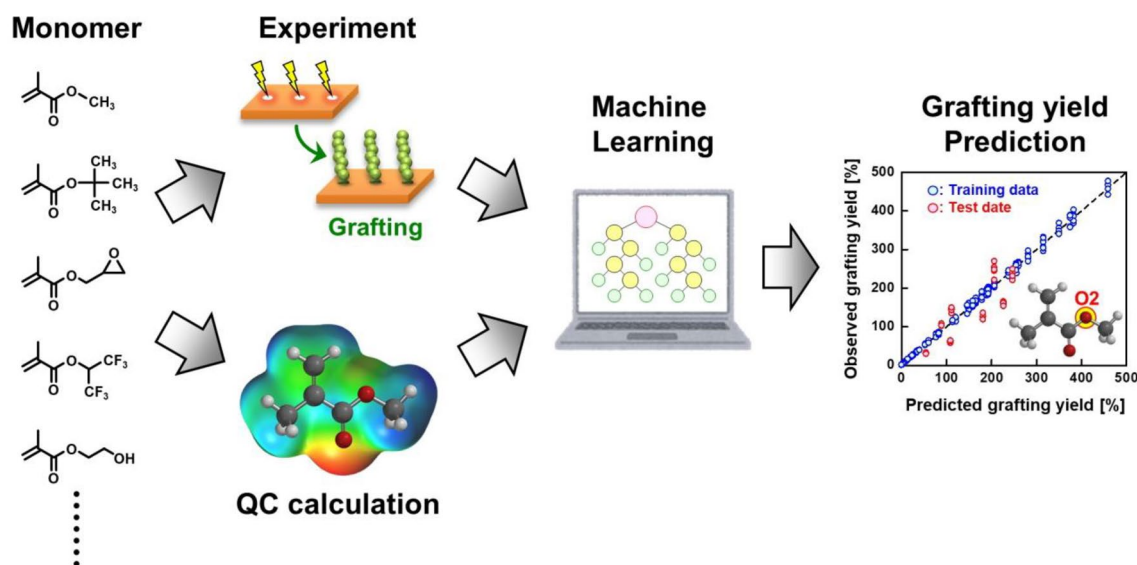
Herein, we step to the rational prediction of the reactivity during the RIGP process. Unlike the standard polymerization reactions, RIGP always occurs on the interphases between material surfaces and monomer solutions. This heterogeneity clearly increases the complexity of the reaction systems, thereby leading to the situation that RIGP reactivity cannot be rationalized in a scientifically simple manner. In this context, the deployment of MI technique in the RIGP reactivity prediction should lead to a next-generation of material research because any unnecessary “groping-in-the-dark” experiments can be avoided. As an important groundbreaking milestone in this field, some of the authors have succeeded in both predicting the grafting degree and quantifying the importance of chemical features on the grafting degree via the machine learning of the monomer structures and the limited experimental RIGP reactivity (Fig. 7).<sup>[82]</sup> Specifically, chemical structures of the vinyl monomers were numerically represented as several chemical features by quantum chemical calculation at the DFT level, and the MI system was built by machine learning the obtained chemical features. The own-built MI system could predict grafting degree with high accuracy (coefficient of determination of 0.71) only by inputting the chemical features of unknown vinyl monomers for verification. Of note here, the MI technique could highlight important chemical features, such as atomic nuclear magnetic resonance shift information, which have not considered significant by chemists in the past. Conventionally, the optimization of graft polymerization conditions has largely relied on the experience and intuition of researchers, and there have been lacking rational guidelines,

thereby resulting in the unnecessarily prolonged optimization steps. This has hindered the development of radiation-ally engrafted materials despite the intrinsic excellence and advantage of the RIGP technique when compared with other surface functionalization techniques. We strongly believe that the fusion of MI technique into the RIGP chemistry should diminish the disadvantages of the RIGP processes, with which the RIGP technique would be spotlighted in the modern material sciences.

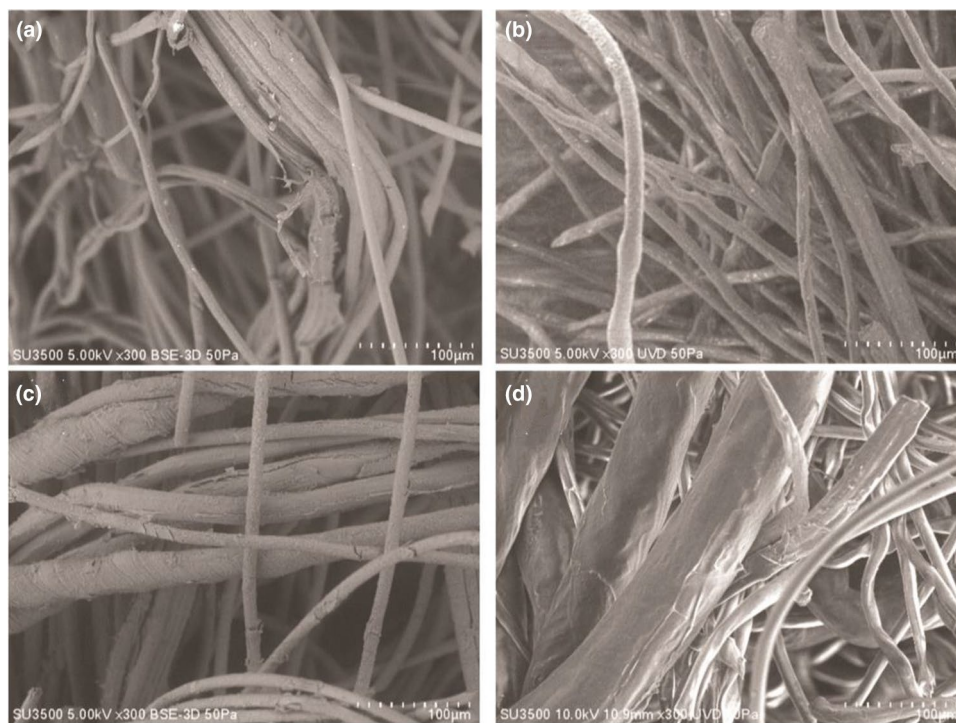
### Prospective aspects for the green advances with RIGP-MCR process

As discussed in the above sections, prospective aspects of both elemental technologies, namely the MCR-based polymer chemistry and the RIGP, were discussed. Therefore, we here wish to document the prospective aspect of the green advantages arising from the RIGP-MCR technique. Due to the growing importance of the SDGs policy in many fields, more environmental-friendly fabrication protocol would be important target in materials sciences. Preference should be given to processes that reduce the consumption of nonrenewable resources and minimize or eliminate the use or generation of hazardous substances. This implies shifting toward the use of renewable and sustainable feedstock such as biomass and the practice of environment-friendly syntheses and processing. In this regard, the RIGP-MCR technique should make two important contributions in this field. Specifically, the RIGP-MCR technique should realize the use of natural resources with minimal or without chemical pre-processes and the increase in the greenness of the reaction process.

First, we embark on the use of natural resources, the most abundant of which is biomass. As showcased in this prospective article, we have succeeded in upcycling the cellulose fibers



**Figure 7.** Grafting yield prediction for the radiation-induced graft polymerization via a machine learning approach. Reprinted with permission from Ref. 82. Copyright 2021 Elsevier Ltd.



**Figure 8.** SEM images of (a) pristine abaca/polyester nonwoven fiber, (b) Poly(glycidyl methacrylate)-*g*-abaca/polyester, (c) PGMA-*g*-abaca/polyester reacted with ethylenediamine, and (d) Poly(acrylic acid)-*g*-abaca/polyester. Reprinted with permission from Ref. 89. Copyright 2018 Taylor and Francis Ltd.

via the RIGP-MCR technique. In order to enrich this material portfolio, the use of diverse renewable raw materials, such as lignocelluloses from agro-wastes and chitin from shrimp and crab industry, can be easily foreseen. In fact, there is growing interest in the use of inedible renewable feedstocks as trunk material for the RIGP-MCR technique because RIGP process can accept any organic materials that are otherwise difficult to modify, including even perfluoropolymers as we have already demonstrated. Building on the well-established compatibility of the RIGP process with a wide range of naturally occurring materials such as abaca fiber, pineapple fiber, banana fiber, starch, chitin, microcrystalline, and carboxymethyl cellulose,<sup>[83–91]</sup> we easily envision that not only the cellulose fabrics but also other natural fibers will be subjected to RIGP-MCR technique to foster the material portfolio. For example, Fig. 8 shows a typical grafting of poly(glycidyl methacrylate) and poly(acrylic acid) by RIGP of the monomers (glycidyl methacrylate and acrylic acid) from delignified and electron-beam irradiated abaca-based nonwoven fibers, realizing the upcycling of naturally occurring fibers via the RIGP process.

Last but not least, we step to the green advantage from the viewpoint of solvent selections. Among many factors affecting greenness in modern synthesis, the impact of solvents is decisive because solvents are usually used in a large excess compared to other components including reactants. In this context, green synthesis can be achieved by also replacing toxic

organic solvents with less toxic ones. One of the greenest solvents is water—readily available, low cost. The potential of using water in RIGP and MCR contributes to the development of a sustainable process, which is important to the advancement of RIGP-MCR as a viable technique for the large-scale production of functional materials. The only bottleneck in the use of water as the solvent is the poor solubility of most reactants used in both organic and polymer synthesis. In this context, the use of surfactants has gained much attention due to their improve reactant solubility and reaction efficiency through micelle-promoted reactions. Some of the authors have previously reported an emulsion RIGP process using the electron beam or gamma radiation pre-irradiation grafting technique. In the research, vinyl monomers were emulsified using a surfactant in a water solvent system.<sup>[19,92–94]</sup> Aside from enabling the solubility of monomers, RIGP in water solvent system has the key advantage of increased graft reactivity due to the highly reactive species formed via the radiolysis of water, which participate in the initiation phase. Using RIGP in emulsion phase with water as the main solvent, the desired degree of grafting could be achieved using lower absorbed doses and monomer concentrations at shorter reaction time and at lower reaction temperature compared with RIGP in standard organic solutions. The developed procedure aligns with the Principles of Green Chemistry, particularly to the use of safer solvents, less hazardous chemical synthesis, and design for energy efficiency. The

utilization of water as solvent for hydrophobic monomers in RIGP also significantly reduces volatile organic compounds, the so-called VOCs, generation from organic solvents. Here, not only the RIGP but MCRs are also compatible with in- or on-water reactions. Particularly, MCRs conducted in aqueous surfactant systems are one of the efficient approaches toward the atom efficient synthesis of compounds and molecules with minimal added cost or waste. The use of surfactant on MCR allows an increase in solubilization of substrates, formation of local aggregates for efficient reaction pathway, and local concentration leading to higher reactivity by confining three or more reaction components in the volume of the aggregate. On the basis of these merits, the use of water as a green solvent for MCR is of great interest as it illuminates one of the important characteristics of an ideal synthesis. Paprocki et al. published a comprehensive review<sup>[95]</sup> on MCRs accelerated by aqueous micelles from surfactant systems, including KF-3CR,<sup>[96]</sup> Passerini-3CR,<sup>[55]</sup> Biginelli Reaction,<sup>[58]</sup> and Mannich Reaction<sup>[97,98]</sup> among others. These reactions were enabled using cationic surfactants such as cetyltrimethylammonium bromide and dimethyldioctadecyl ammonium bromide, anionic surfactant like sodium dodecyl sulfate, non-ionic surfactants and catalytic surfactants such as dodecylbenzene sulfonic acid and sulfuric acid modified polyethylene glycol. Apart from greenness of the solvent used, some advantageous effects observed from MCRs in aqueous surfactant systems as compared to classical organic solvents include enhanced reaction efficiency in terms of yield, fidelity or chemo-selectivity, time and temperature, as well as safer synthetic conditions, simple work up and compatibility with recyclable acid catalysts. In ideal cases, these backgrounds should render the same promise for RIGP-MCR processes in water systems, thereby further improving its sustainability and efficiency.

## Summary and outlooks of the RIGP-MCR

In this prospective article, the authors showcased the new trends in the field of organic materials chemistry building on the RIGP-MCR protocol. Despite the long history and applications of MCRs and RIGP techniques respectively, a fusion of MCRs and RIGP has only very recently started. We would easily envision that the use of RIGP-MCR would pave a way to novel material applications that are otherwise difficult to achieve. Specifically, the RIGP technique do not require any additional chemicals other than the target monomer and the mise-en-place of target materials could be bypassed so that the overall process would get greener and more efficient. In addition, most MCRs do not employ additional activators nor catalysts and many reactants can be fused with a high atom-efficiency. These aspects are undoubtedly also advantageous from the viewpoint of the current green chemistry. All in all, we would foresee a renaissance of material chemistry via the RIGP-MCR technique.

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## Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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