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Second-Generation *meta*-Phenolsulfonic Acid−Formaldehyde Resin as a Catalyst for Continuous-Flow Esterification

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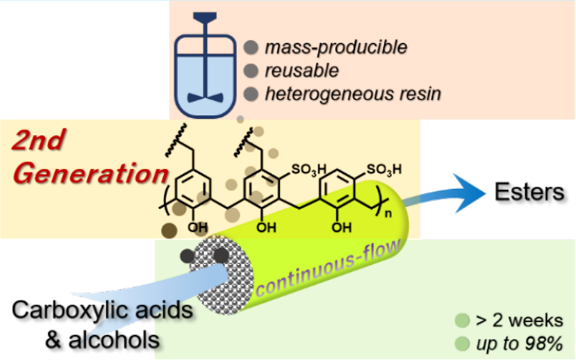
Supporting Information

ABSTRACT: A second-generation *m*-phenolsulfonic acid−formaldehyde resin (PAFR II) catalyst was prepared by condensation polymerization of sodium *m*-phenolsulfonate and paraformaldehyde in an aqueous H_2SO_4 solution. This reusable, robust acid resin catalyst was improved in both catalytic activity and stability, maintaining the characteristics of the previous generation catalyst (*p*-phenolsulfonic acid−formaldehyde resin). PAFR II was applied in the batchwise and continuous-flow direct esterification without water removal and provided higher product yields in continuous-flow esterification than any other commercial ion-exchanged acid catalyst tested.



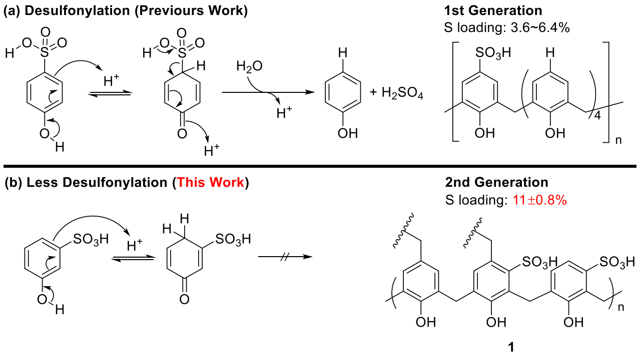
Improving the atomic efficiency (product/raw material) and reducing the *E*-factor[1] (waste/raw material) of organic synthesis reactions are important factors not only in organic and green chemistry but also in industrial applications. Dehydration reactions are among the most fundamental reactions and are frequently used in both biosynthesis and chemical synthesis because water is the only byproduct of ideal catalytic dehydration reactions. Specifically, the Fischer−Speier esterification, the reaction of carboxylic acids with alcohols to give the corresponding esters,[2] is carried out at industrial scale to produce oils, perfumes, pharmaceuticals, cosmetics, paints, adhesives, resins, solvents and so on. If esterification can be achieved with highly active, reusable catalysts,[3] and without dehydrating agents[4] under solvent-free[5] conditions, it can provide a safer and more economic industrial-scale synthesis route.

Although mesoporous sulfonic acid esterification catalysts are reported,[6] they are still in the development stage in terms of amount of catalyst and alcohol used. Reports of direct batchwise Fischer−Speier esterification using acid-catalyst concentrations below 1 mol % are extremely rare.[7] For example, a homogeneous hafnium salt catalyst[7a] and a fluorinated solvent system[7b] has been developed.

In 2013, our group synthesized a porous phenolsulfonic acid−formaldehyde resin (PAFR)[8] as a heterogeneous catalyst for Fischer−Speier esterification reactions. Although this catalyst satisfies the advantages of the esterification reaction described above, including high catalytic activity (0.7 mol % catalyst in batch and continuous-flow reactions, up to 4 days run length),[9] catalyst reusability was insufficient (see Figure 3). The catalyst deactivated after 4 days using a continuous-flow reaction. Therefore, we developed a more stable, highly active, and reusable polymeric acid catalyst for industrial Fischer−Speier esterification.

A reason for the deactivation of the first-generation PAFR is that the desulfonylation of the *p*-phenolsulfonic acid readily occurred under acidic reaction conditions at higher temperature (Scheme 1, above).[9b] To prevent the desulfonylation reaction, we designed a novel *m*-phenol sulfonic acid resin catalyst PAFR II (**1**). Herein, we describe the development of a more active and reusable second-generation *m*-phenolsulfonic acid−formalde-

Scheme 1. (a) Desulfonylation of *p*-Phenolsulfonic Acid and (b) *m*-Phenolsulfonic Acid−Formaldehyde Resin (PAFR II) Catalyst at Higher Sulfonic Acid Loading in Resins



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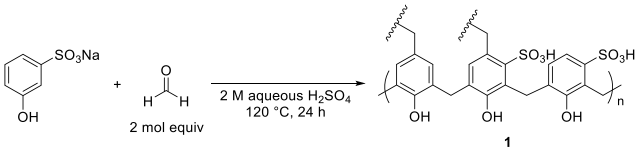
hyde resin catalyst (PAFR II) (**1**) (Scheme 1, bottom) and its application for the Fischer−Speier esterification, considering both batch and continuous-flow conditions. PAFR II provided higher ester yields under continuous-flow conditions than commercially available ion-exchanged sulfonic acid resin catalysts.

The PAFR II (**1**) was prepared by the condensative polymerization of sodium *m*-phenolsulfonate and formaldehyde (2 molar equiv) in 2 M aqueous H_2SO_4 at 120 °C (oil bath temperature) for 24 h (Scheme 2). The color of the solution gradually became lighter, and a large amount of dark green to black coal-like solid agglomerates formed during the polymerization. After 24 h, the temperature was decreased to below 80 °C. The resulting solid was successively washed with water, aqueous HCl (2.2 M), water, 2-propanol, and methanol. After being dried in vacuum, **1** was obtained as a black coal-like solid.

Scheme 2. Preparation of *m*-Phenolsulfonic Acid−Formaldehyde Resin PAFR II (1)



Following this procedure, we achieved the preparation of **1** on up to 87 g scale using a mechanically stirred tank reactor (Figure s2, Supporting Information). Applying elemental analysis to check the reproducibility of the catalysts in different production lots, we found that the sulfur content of the catalysts obtained at the different reaction scales was reproducible at a range of 11 ± <0.8 wt % (Table s1, Supporting Information). This gave us confidence regarding the large-scale production. Surface images of **1** were obtained with scanning electron microscopy (SEM). The pulverized **1** exhibited a flat, ore-like agglomerate with a relatively uniform particle size (Figure 1a,b). Energy-dispersive X-ray (EDX) spectroscopy analysis on the SEM (EDX/SEM) of **1** showed sulfur atoms uniformly dispersed on the polymeric matrix, and sodium was not detected (Figure 1c,d).

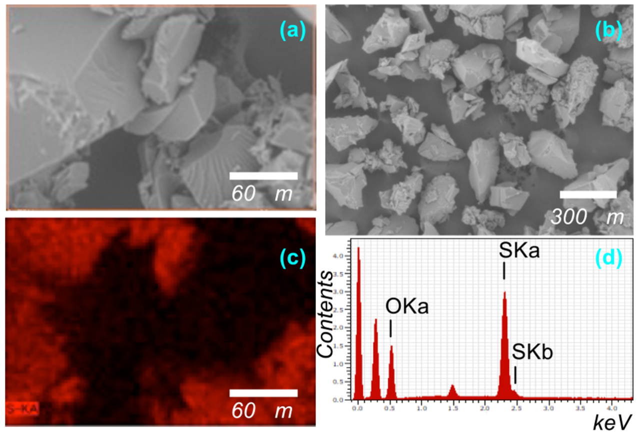


Figure 1. SEM images (a, b), EDX/SEM image (c), and EDX/SEM mapping (d) of sulfur atom in **1**.

Thermogravimetry/mass spectrometry (TG-MS) analysis was conducted to compare the thermal stability of PAFR and PAFR II (**1**) (Figure 2). The desorption profiles and intensity of SO_2 are shown in Figure 2. The SO_2 profile exhibits two peaks corresponding to the decomposition of the sulfonic acid group of both PAFR catalysts. The decomposition of the sulfonic acid group was a direct evidence of catalyst deactivation. Figure 2 also exhibited that PAFR II (**1**) was much more stable (decomposition temperature 180 °C) than PAFR, whose decomposition temperature was 130 °C.

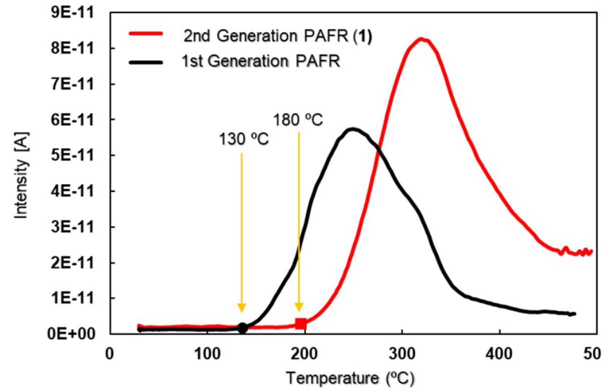


Figure 2. Thermogravimetry (TG) desorption (SO_2) profiles of PAFR and PAFR II (**1**).

The reusability check of the two catalysts for the direct esterification of acrylic acid and methanol in a batch reaction also supported that PAFR II (**1**) is more stable than PAFR (Figure 3). When 0.5 mol % of the catalyst was tested under identical reaction conditions, the first reaction cycle showed similar catalytic activity, and methyl acrylate was produced in 83% (PAFR) and 86% (PAFR II) yield, respectively. The catalysts were recovered and reused in the next reaction cycle at the previous reaction conditions (Supporting Information). PAFR II was reused nine times without loss of catalytic activity, while the reusability of PAFR gradually decreased.

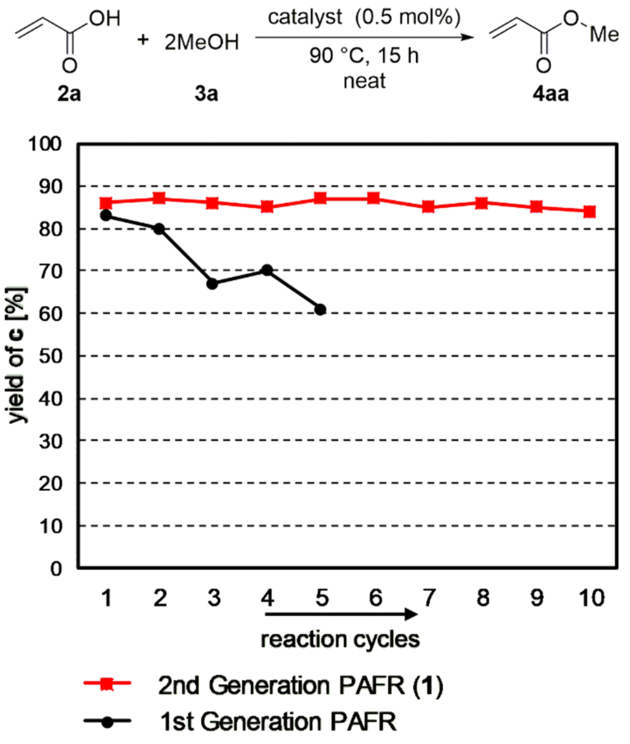
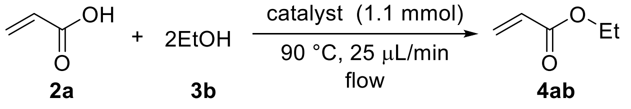


Figure 3. Reusability of PAFR and PAFR II (**1**).

With a highly active and stable heterogeneous acid catalyst PAFR II at hand, the next step was to achieve a viable continuous-flow Fischer−Speier esterification reaction.[10] The catalytic activity of PAFR II and various other commercially available heterogeneous acid resin catalysts was investigated at 90 °C without removal of water. The mixture of acrylic acid (**2a**) and ethanol (**3b**; 2 mol equiv) was passed over a catalyst-packed column with 1.1 mmol SO$_3$H of PAFR II or various other catalysts at a flow rate of 25 μL/min. The results are shown in Table 1, where PAFR II produced higher ethyl acrylate (**4ab**) yields (95%) compared to other catalysts such as DIAION SK104H[11] (76% yield), DIAION PK208[12] (74% yield), Dowex 50Wx2[13] (76% yield), Amberlyst 16 wet[14] (70% yield), and Amberlyst 15 dry[15] (57% yield).

Table 1. Comparison of Catalytic Activity with Commercial Ion-Exchange Resins and 1 Using Continuous-Flow Reaction



entry	catalyst	yield of **4ab** (%)
1	second-generation PAFR	95
2	DIAION SK104H	76
3	DIAION PK208	74
4	Dowex 50W × 2	76
5	Amberlyst 16 wet	70
6	Amberlyst 15 dry	57

Because PAFR II (**1**) revealed higher catalytic activity, we investigated the direct esterification of various carboxylic acids and alcohols under both continuous-flow and batch conditions. A schematic diagram of the continuous-flow reaction system is shown in Figure 4a. We varied the acrylic starting material because the products can be converted into acrylic resins, which are in high demand and widely used in the construction industry as Plexiglass and for various other architectural or decorative materials.[16] Figure 4b shows that the acrylates **4aa**, **4ab**, **4ba**, **4ac**, **4ca**, **4da**, and **4ad** were generated in high yields, up to 98% at 90 °C, both at batch and continuous-flow conditions. Alkyl alkanoates **4ee**, **4ef**, and **4fe** were also produced in high yields by this reaction system. An ester containing a terminal olefin bond, such as allyl acetate (**4ff**), was produced above 80% yield, while the 3-phenylpropyl acetate (**4fg**) yield was 77%. Most of the continuous-flow reactions gave higher product yields than the batch reactions. During the continuous-flow reactions, water was produced along with the product ester, but aggregated into water droplets (Figure s5, Supporting Information). We believe that the reduced water formation in the continuous-flow system shifted this chemical equilibrium reaction, which is the main reason for high product yields.

We also applied PAFR II (**1**) to the model reaction of converting kitchen waste oil to biodiesel (Figure 5), whose main components are oleic acid and linoleic acid. The direct continuous-flow esterification could be a viable route to produce biodiesel from recycled cooking oils.[17] It was reported that solid acid catalysts[18] did not perform well with regard to this application due to excess alcohol and/or large catalyst loadings. As shown in Figure 5, under batch reaction conditions, oleic acid and linoleic acid were converted to the corresponding esters in yields of 82% and 90%, respectively. The continuous-flow esterification of both the oleic acid and linoleic acid provided a conversion of 92% to 94% for more than 2 weeks. These results were promising with regard to potential biodiesel applications based on this second-generation PAFR catalyst **1**.

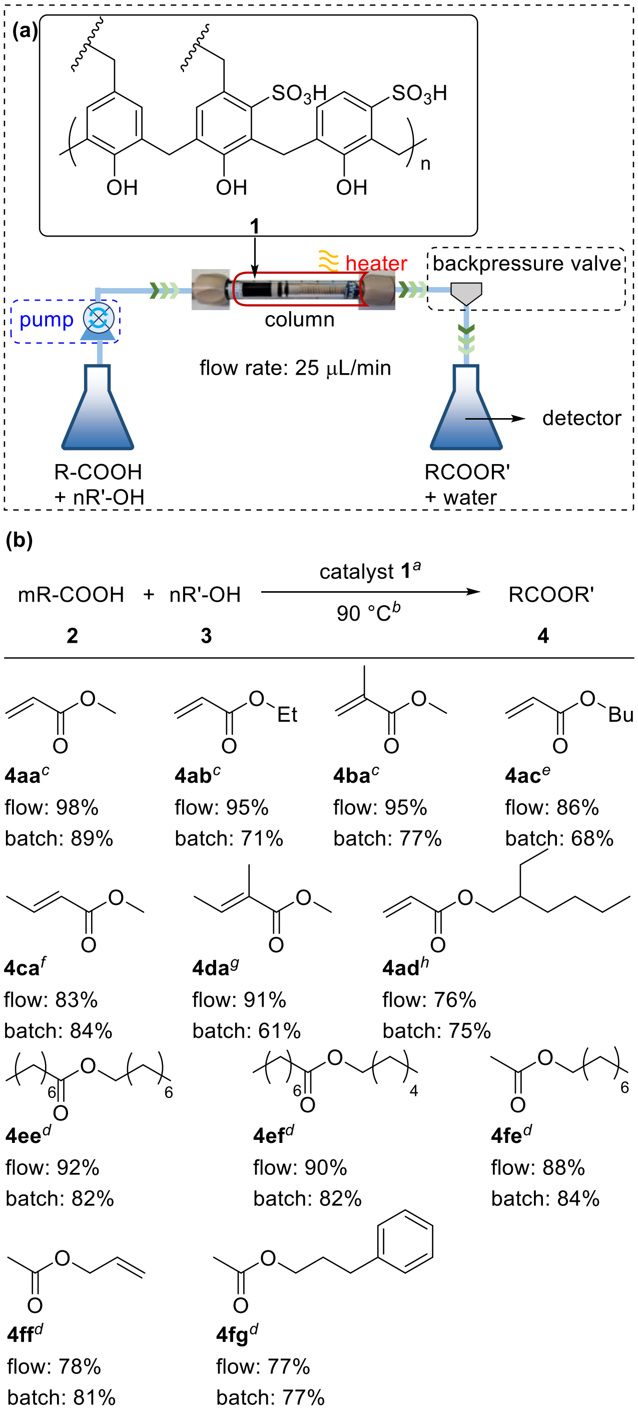
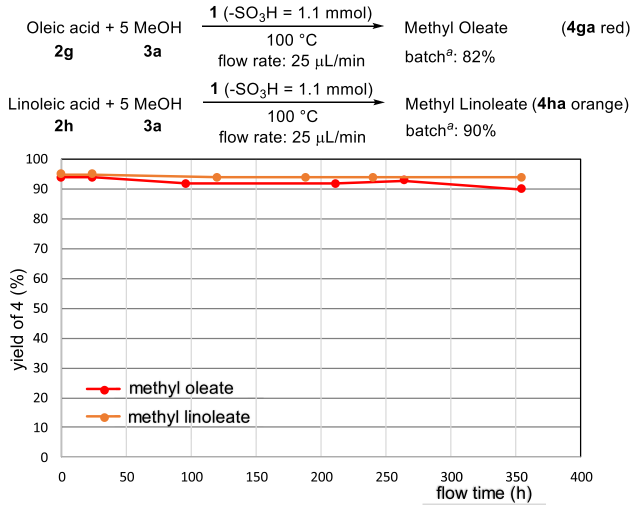


Figure 4. Substrate scope in batch and flow esterification. (a) 0.5 mol % of SO$_3$H for batch reactions, 1.1 mmol of SO$_3$H for flow. (b) 15 h for batch. (c) $m/n = 1/2$. (d) 2.2 mmol of SO$_3$H for flow, $m/n = 2/1$. (e) $m/n = 1/3$, 10 μL/min. (f) 2.2 mmol of SO$_3$H for flow, 50 μL/min. (g) 2.2 mmol of SO$_3$H for flow, 20 μL/min. (h) 2.2 mmol of SO$_3$H for flow, $m/n = 1/3$.

In conclusion, we have developed a second-generation *m*-phenolsulfonic acid−formaldehyde resin catalyst PAFR II (**1**) with a higher sulfonic acid content and better thermal stability than the first generation PAFR. Preparation on a larger scale did not negatively affect catalytic activity or stability at higher



product	total time (h)	yield (g)	**4**/**2** (molar ratio)	TON	TOF (h^{-1})
methyl oleate	355	330	92/8	1011	2.8
methyl linoleate	355	311	94/6	960	2.7

Figure 5. Application for the synthesis of biodiesel by continuous-flow esterification: flow time and yield. (a) Batch conditions: 90 °C, 15 h.

reaction temperature. The catalyst promoted the direct esterification of carboxylic acids and alcohols under both continuous-flow and batch conditions, producing the corresponding esters in high yield. One PAFR II-packed flow reactor converted substrates for several months without loss in catalytic activity. Research is ongoing to explore more potential esterification applications.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.9b04084.

General information, experimental procedures, additional information, and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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(12) DIAION PK208 (MITSUBISHI) was used.

(13) CAS: 69011-20-7, Dowex 50W × 2 100-200 (Wako) was used.

(14) CAS: 125004-35-5, Amberlyst 16 wet (Fluka) was used.

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