

Superacid Resin-Based Heterogeneous Catalysts for the Selective Acylation of 1,2-Methylenedioxybenzene

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In this work, we firstly report on the use of highly active and selective Aquivion superacid resins as heterogeneous catalysts for the acylation of 1,2-methylenedioxybenzene (MDB) with propionic anhydride (AP). The reaction was investigated and optimized using solvent-free conditions to selectively produce 3,4-methylenedioxypropiofenone (MDP1P), a key intermediate for the manufacture of active ingredients used in insecticide formulations with a volume of production of roughly 3000 t/y. Interestingly, Aquivion-based catalysts allows to work in mild reaction conditions (i.e. 80 °C), obtaining MDP1P yields as high as 44% after only 1 h of reaction (selectivity 83%). A detailed

study of the AP reactivity demonstrated its tendency to promote oligomerization reactions that, as confirmed by *ex-situ* and *in-situ* FT-ATR analyses, caused the deactivation of the catalyst forming surficial carbonaceous residues. In this context, a fast oxidation of the resin surface organic residues using a diluted HNO₃ (or H₂O₂) solution was proven to be an efficient method to regenerate the catalyst, which can be reused for several reaction cycles. The results obtained in preliminary scale-up tests were basically unaffected by the reaction volume (up to 800 mL), paving the way for possible future applications of the process.

Introduction

Acylation reactions play an important role in fine chemical industries to produce pharmaceuticals, intermediates, and fragrances. These reactions are traditionally carried out through homogenous catalysis using inorganic compounds such as AlCl₃, ZnCl₂, BF₃ and HF in more than stoichiometric amount, posing serious environmental and economic issues related to the high consumption of resources and the high costs associated with their disposal. Therefore, the development of heterogenous catalysts able to replace these compounds is of paramount importance and various solid acids have been explored for acylation reactions. Zeolites can be successfully

used for acylation and regio-selective reactions.^[1–4] Kim et al.^[5] performed a series of acylations over aromatic compounds using an MFI zeolite nano-sponge that showed high activity and reusability in the reaction conditions. The acylation of anisole over H-Beta zeolite^[6] or veratrole with acetic anhydride to 3,4-dimethoxyacetophenone can be performed using H-Y, H-beta zeolites and mesoporous aluminosilicates such as SBA-15 and KIT-5.^[7] Despite their high potential, a major issue of these catalysts lies within their high sensitivity to deactivation and pores blockage.^[8,9] Moreover, their shape, size and intra-framework connectivity can lead to severe diffusion limitations and constraints on bulky reactants or products.^[10] Ion exchange resins represent another class of solid catalysts that acts as Brønsted acid in their H⁺ form. These polymers are classified as strong acidic resins because of the presence of sulfonic groups in their structure and can be divided in two types of material depending on their swelling ability, and thus on the flexibility of the structure in different reaction environment.^[11] Macroreticular resins are rigid, sponge-like solids with medium size pores that do not easily swell in liquid media. The majority of polystyrene sulfonate-type resins belong to this class and are composed of polystyrene-divinylbenzene copolymer (PS-DVB) whose aromatic groups are sulfonated. Amberlyst, Purolite and Indion resins are examples of commercial PS-DVB materials that, depending on the crosslinking degree (the percentage of DVB) exhibit good catalytic activity in a wide range of organic reactions.^[12–17] Yadav et al.^[18] investigated the Friedel-Crafts acylation of 1,4-dimethoxybenzene to 2,5-dimethoxy acetophenone over various solid acid catalysts finding that cationic exchange resins such as Amberlyst-15 and Indion-125 showed superior catalytic activity at 100 °C. The catalytic activity was boosted using 1,2-dichloroethane as a solvent and the reusability of the catalyst was studied through regeneration with methanol for 3 h. A substantial loss of activity was observed

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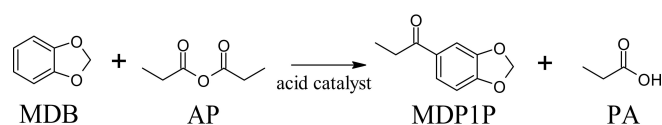
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probably related to a strong adsorption of either reactants or products on the active sites. Amberlyst-36 was also found to efficiently catalyzed both the acylation of Anisole and the esterification of Phthalic Anhydride at 90 °C and 120 °C respectively.^[19] One of the main drawbacks of this class of resins is their poor thermal stability caused by the decomposition of the polymer and the consequent leaching of sulfonic groups at temperatures above 120 °C that limits their range of industrial applications.^[20] In contrast, perfluorosulfonic acid resins such as Aquivion can operate up to 170 °C without any substantial thermal degradation. These solids are classified as superacid gel-type resins that show swelling properties depending on the solvent or reactants properties and/or polarity.^[21]

In absence of a swelling media, the active acidic centers, composed by $-CF_2CF_2SO_3H$ groups, are mainly inaccessible and the solid exhibits a surface area of about $0.02 \text{ m}^2 \text{ g}^{-1}$ that can lead to poor catalytic activity in low (or non) polar reaction environments.^[22] Nevertheless, the absence of crosslinked chains in the swollen polymer structure highly increases the diffusion of reactants inside the materials, allowing to perform catalytic reactions also in aqueous media. Moreover, due to the perfluorocarbon backbone, the chemical inertness of this gel-type resins is high, leading to better resistance to undesired leaching phenomena in harsh reaction conditions. In this context, Aquivion is considered a good candidate for the replacement of homogenous acid catalysts. It showed high performance in the glycolisation of glucose with fatty acids,^[23] in the synthesis of 2-pyrrolidin-2-ones^[24] and in gas phase dehydration of ethanol to ethylene.^[25] Fang et al.^[26] tested a catalyst composed of Aquivion immobilized inside a silica matrix in the etherification of glycerol with *n*-butanol reporting high activity, selectivity, and low formation of by-products at 150 °C.

1,3-benzodioxole, also known as 1,2-methylenedioxybenzene (MDB), is a benzene derivative, heterocyclic compound that contain the methylene-dioxy functional group. Many MDB derivatives possess anticancer drug activity,^[27] are used in fragrances industry^[28] and are involved in insecticide formulations.^[29] The inertness of MDB towards alkylation over solid acid catalysts was demonstrated by Lucarelli et al.^[30] through FT-IR investigations, this way finding the peculiar interaction of MDB with the solid substrate which led to an electron-deficiency and a consequent deactivation of the benzene ring. The peculiar behavior also does the electrophilic aromatic substitution of MDB a challenging process of clear industrial relevance, in this work the acylation of MDB with propionic anhydride (AP) was investigated over a solid acid catalyst (Scheme 1). According to our best knowledge, studies



Scheme 1. 1,2-methylenedioxybenzene (MDB) acylation with propionic anhydride (AP) yielding 3,4-methylenedioxypropionophenone (MDP1P) and propionic acid (PA).

concerned the MDB acylation via heterogenous catalysis have not previously reported in scientific literature.

For all these reasons, herein we demonstrate that, using Aquivion PW87 (a gel-type resin) as superacid catalysts, either as a bulk powder or supported on silica matrix, it is possible to achieve the selective production of 3,4-methylenedioxypropionophenone (MDP1P) in solvent-free and mild conditions with short reaction times. The use of different *in-situ* and *ex-situ* techniques led to a better comprehension of the main parameters that affect the catalytic activity and the selectivity of the process. The role of AP in catalyst deactivation was also studied in detail, and a plausible deactivation mechanism was proposed together with a simple methodology to regenerate the catalyst, which can then be reused for several reaction cycles. Noteworthy, the results herein described has led to the filing of a patent.^[31]

Results and Discussion

Catalytic activity

The catalytic performances of Aquivion PW87 in the 60–120 °C temperature range (reaction time 1 h) in the presence of a stoichiometric amount of AP and MDB are displayed in Figure 1. The conversion of MDB constantly increased with the reaction temperature, rising from a value of 37% at 60 °C, to 74% at 120 °C (Figure 1a). Similarly, the AP reactivity was highly affected by the reaction temperature, showing total conversion at 120 °C. It is noteworthy that the AP conversion values were sensibly higher than those of MDB regardless of the reaction temperature, suggesting a faster activation (i.e. a rapid acylium ions formation) over the catalyst acid sites. The selectivity towards MDP1P (Figure 1b) underwent a sensible decreased beyond 80 °C down to a value of 69% at 120 °C, where the formation of heavier compounds was favored ($Y_{\text{others}} = 23\%$). According to the MDB conversion, the MDP1P yield reached a value of 48% at 100 °C that did not significantly change beyond this temperature.

The primary byproducts found in the reaction mixture are listed in Figure S1 and were mainly related to consecutive acylation on the MDP1P, MDB hydrolysis and consecutive condensation and O- and C-acylation reactions. Considering the similar performances obtained at 80–100 °C and the possibility to perform the reaction at milder conditions with good yield ($Y_{\text{MDP1P}} = 42\%$) and a lower by-products formation ($Y_{\text{others}} = 11\%$), 80 °C was chosen as the optimum reaction temperature for further investigations.

To further understand the challenging behind MDB selective, heterogeneously catalyzed, acylation processes, several comparison tests were performed feeding other aromatic substrates (Figure S2).

In particular, the catalytic performance attained at 80 °C after 1 h of reaction using MDB, 1,4-benzodioxane (1,4-BD), 1,2-dimethoxybenzene (1,2-DB) or 2-methoxyphenol (2-MP) are shown in Figure 2a. The O-acylation of 2-MP was efficiently catalyzed reaching almost a total conversion towards the

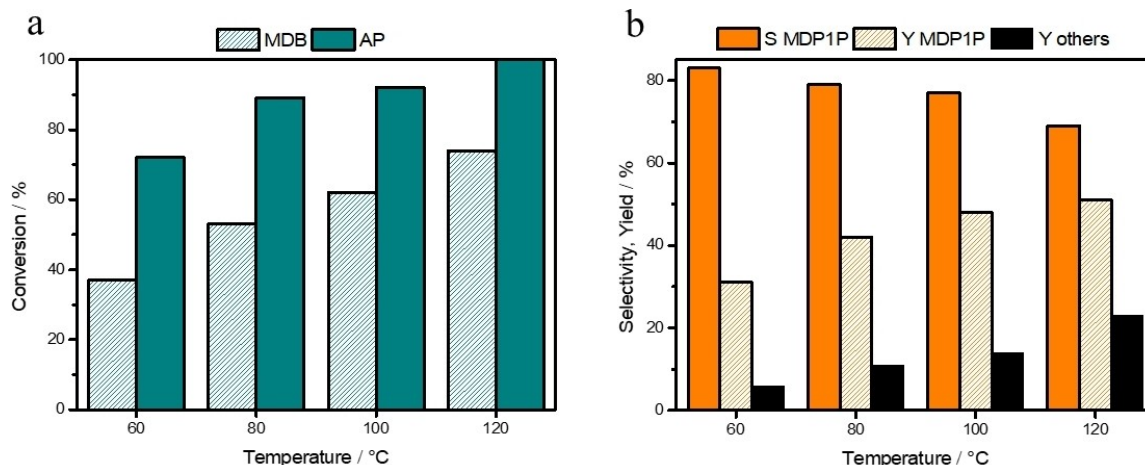


Figure 1. Influence of the reaction temperature on PW87 catalytic activity in terms of a) MDB and AP conversion and b) selectivity and yield in MDP1P and by-products "others" yield. MDB/AP of 1 mol/mol, 0.1 g of catalyst, reaction time 1 h.

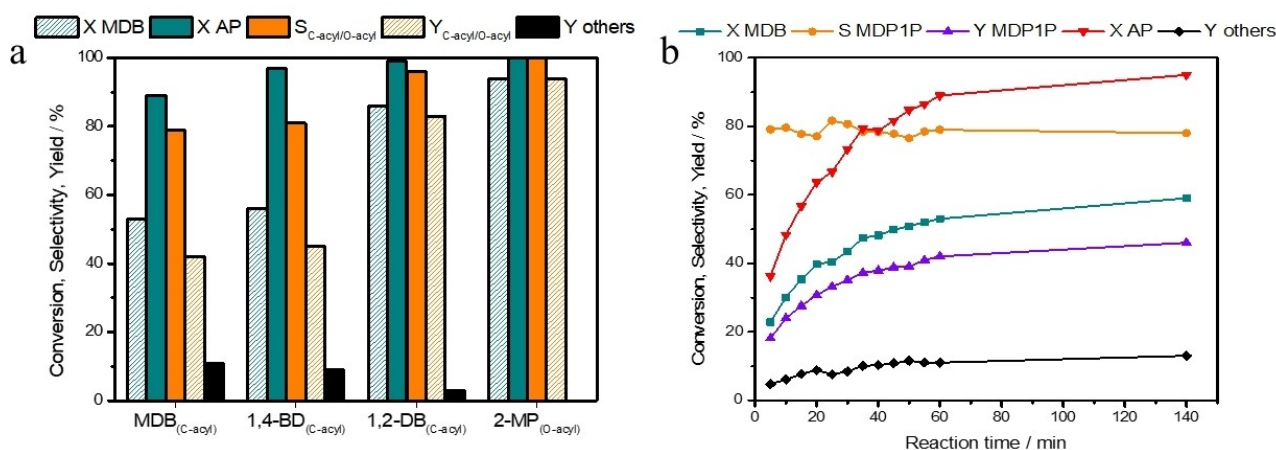


Figure 2. a) Catalytic performance of PW87 in the acylation (with AP) of different aromatic substrates (80 °C, reaction time 1 h, aromatic/AP of 1 mol/mol, 0.1 g of catalyst) and b) Influence of the reaction time on PW87 catalytic activity in terms of MDB and AP conversion, selectivity and yield in MDP1P and by-products yield. MDB/AP of 1 mol/mol, 0.1 g of catalyst, reaction temperature of 80 °C.

desired product (2-methoxyphenyl propanoate). Similarly, the C-acylation of the aromatic ring of 1,2-DB was carried out attaining a remarkable selectivity (96%), low by-products formation and a substrate conversion of 86%. The reactivity of 1,4-BD (a six-membered heterocyclic compound like MDB) was far lower compared to other aromatic ethers yet slightly higher compared to MDB, confirming the intrinsic inertness of the five-membered heterocyclic compound towards heterogeneously catalyzed acylation.

The catalytic results obtained for the acylation of MDB as a function of the reaction time are showed in Figure 2b. A MDB conversion of 23% was promptly observed after 5 min of reaction, reaching 40% after 20 min. After this time, the conversion rate decreased, flattening out at a value of 53% (60 min) and slowly reached 59% only after 140 min. A similar trend was observed for the MDP1P yield, while the conversion of AP was significantly faster (64% at 20 min), confirming the occurrence of side reactions that instantly favored the formation of by-products (Y_{others} of 5% after 5 min). The higher AP

consumption can be attributed to both the formation of heavier compounds through undesired, consecutive, acylation reactions in the liquid phase and the AP simultaneous activation and oligomerisation over the catalyst acid sites to form a brownish deposit which subsequently turned black during reaction, thus suggesting a progressive deactivation of the catalyst. To better understand these phenomena, dedicated *in-situ* FT-ATR analyses were performed, in particular monitoring the evolution of compounds for 1 h of reaction (Figure 3). The spectra obtained following the reaction at 80 °C (spectra a and b) evidenced a decrease of intensity of the bands attributable to both MDB and AP together with the concomitant growth of the bands associated to MDP1P and propionic acid (PA). The identification of the bands related to by-products formation was difficult to observe due to their low intensity and proximity to those of reactants and products.

Interestingly, increasing the reaction temperature to 90 °C (spectra c and d) it was possible to detect a progressive decrease of the PA bands and the simultaneous formation of

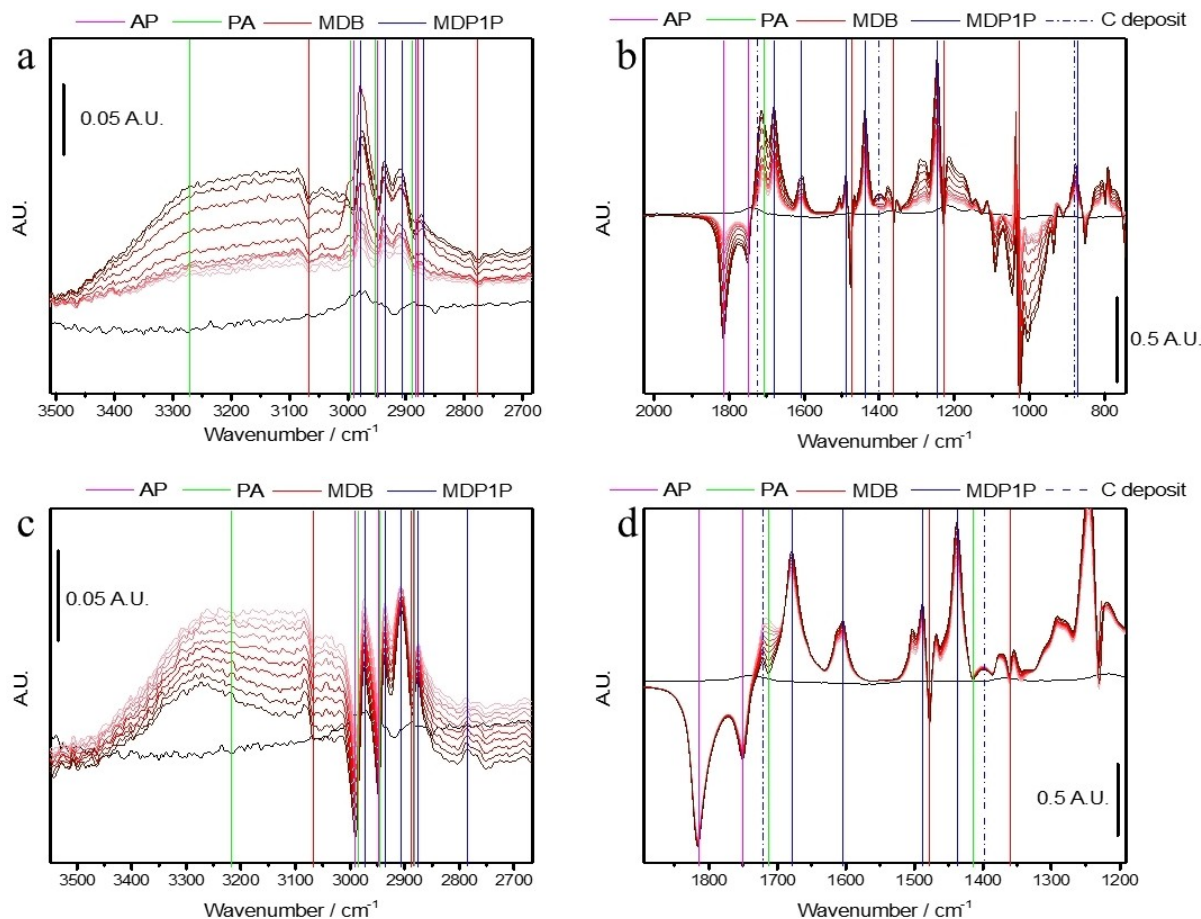


Figure 3. *In situ* FT-ATR spectra of the reaction carried out at 80 °C, 1 h (a, b) and 90 °C, 1 h (c, d). MDB/AP of 1 mol/mol, catalyst 0.1 g.

new bands centered at 1723 cm^{-1} and 1405 cm^{-1} that can be related to consecutive condensation reactions that led to the formation of heavier compounds and, possibly, the deposition of deactivating compounds on the catalyst surface.

Role of propionic anhydride in catalyst deactivation

Catalyst deactivation was further assessed by reusing the spent resin sample in a second reaction run, that evidenced a poor MDB conversion of 8% at 80 °C (1 h). Figure 4a shows the FT-ATR spectra of Aquivion PW87 before and after reaction. The band at 635 cm^{-1} is assigned to the stretching of C–S groups^[32] while the bands at 969 and 1054 cm^{-1} relates both to C–O–C and sulfonic acid (SO_3H) stretching.^[33] The two peaks observed at 1149 cm^{-1} and 1206 cm^{-1} are attributed to symmetric and asymmetric C–F stretching respectively,^[34] and the band at 1320 cm^{-1} is due to S=O asymmetrical stretching. The spectrum of the sample after reaction revealed broad additional bands which do not belong to the original polymer and can therefore be attributed to the formation of organic deposits on the catalyst surface. The peak centred at 1470 cm^{-1} is due to the presence of methyl group (C–H₃ bending), the band at 1607 cm^{-1} is attributed to unsaturated carbon structures (C=C

stretching)^[35] while the signal at 1714 cm^{-1} relates to carbonyl group vibrations (C=O stretching).^[36]

It is noteworthy that the signals associated to the possible presence of aromatics C–H vibrations in the region 3000–3100 cm^{-1} were not detected. It is therefore likely to rule out that a possible strong adsorption of MDB (or its derivatives) may have played a key role in catalyst deactivation. In order to better understand the role of the anhydride in catalyst deactivation phenomena, a dedicated decomposition test of AP in the presence of PW87 was carried out at 80 °C for 1 h. The *in situ* FT-ATR spectra of the reaction are reported in Figure 4 (spectra b, c and d) where it can be noted that the bands associated with AP decreased with the reaction time in accordance with the catalytic data (Figure S3, AP conversion of 62%).

At the same time, it was possible to observe that after a first strong formation of PA, the zones related to all its vibrational modes decreased at the beginning of reaction to then rise again during the experiment, suggesting the occurrence of consecutive acylation and oligomerization reactions or PA formation via AP hydrolysis (with water).

This behavior may be explained by considering the concomitant growth of the band centered at 1723 cm^{-1} (C=O vibrations) together with the bands of the C–H and C=C stretching and bending modes.

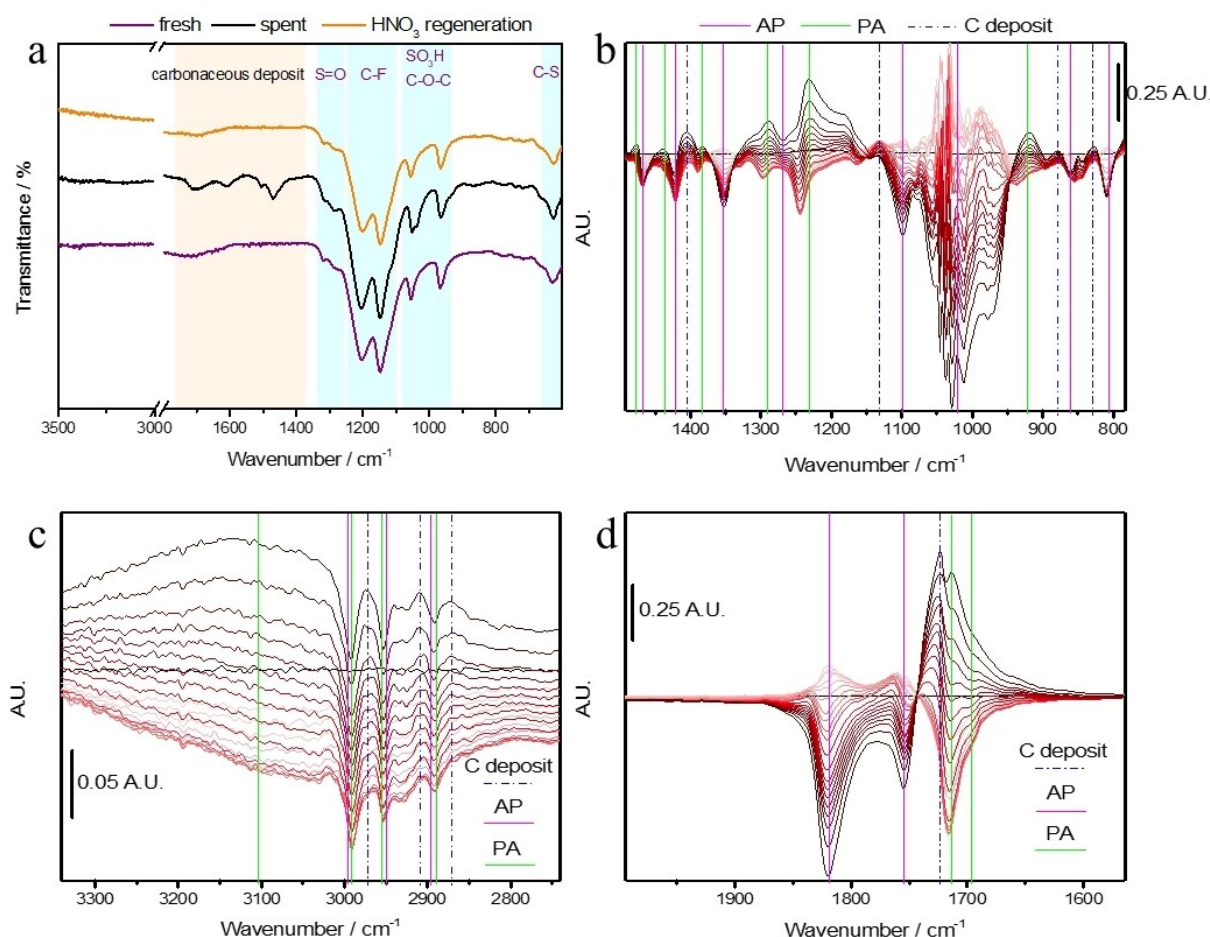


Figure 4. a) FT-ATR spectra of the catalyst before and after reaction and regeneration; b, c, d) In situ FT-ATR spectra of the reaction of AP with PW87. Reaction temperature 80 °C, AP 17.5 mmol, 0.1 g of catalyst, reaction time 1 h.

All these additional bands (Figure 4a and Figure S4) indeed suggest the formation of products derived from acylation/condensation reactions such as poly-ketone (linear or cyclic) or lactones that may be responsible for catalyst deactivation via surface fouling.

These results are in line with those observed in a recent work on the thermal self-polymerization of acetic anhydride via ketone poly-condensation, co-forming water.^[37]

The formation of water during our acylation processes is in good agreement with both the excess of PA for instance found after the decomposition reaction (Figure S3) and the formation of catechol derivatives observed during MDB acylation (Figure S1).

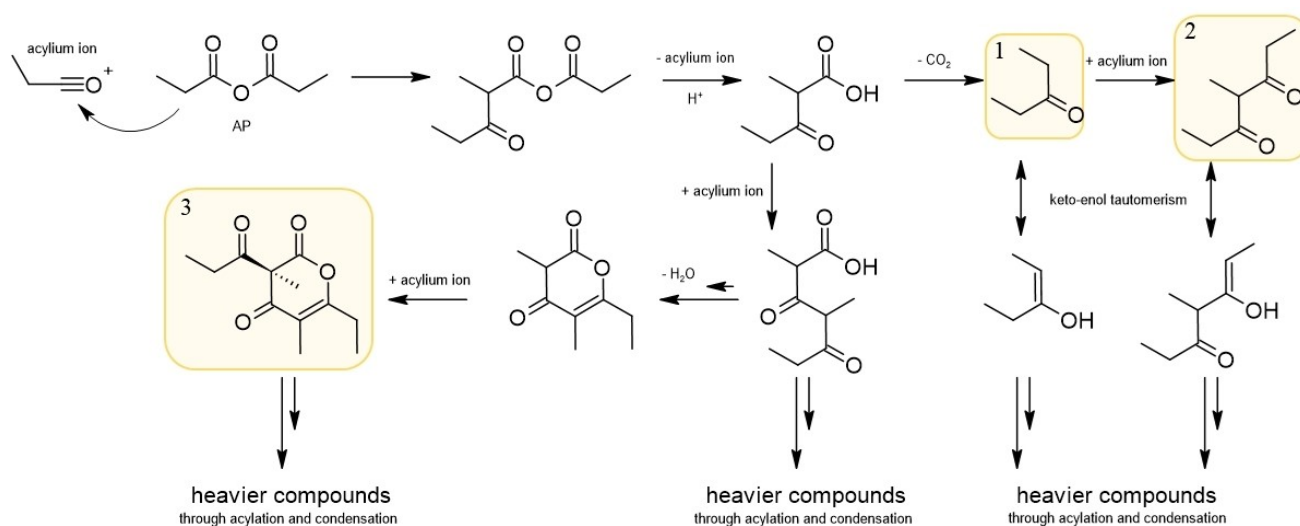
On top of that, qualitative GC-MS analyses of the reaction mixture (AP and PW87, 80 °C, 1 h) revealed the presence of 3-pentanone, 4-methylheptane-3,5-dione and a lactone derivative (5,6-dihydro-3,5-dimethyl-6-ethylcarbonyl-2H-pyran-2,4-dione), further supporting the AP propensity to form heavy compounds in the reaction environment through consecutive acylation and condensation reactions, initiated by the rapid formation of acylium ions on the catalyst surface.

Considering the detected compounds as intermediates in the formation of more complex molecules, it was possible to

hypothesize a plausible reaction scheme that, in accordance with the different data obtained, evidenced the predominant role of AP in the formation of organic chains that can settle and deactivate the catalyst particles (Scheme 2).

After the AP activation on the catalyst acid sites to form PA and an acylium ion, the reaction is initiated by the alpha-substitution with the acylium ion on AP and the consecutive formation of a beta-ketoacid.

This can further undergo decarboxylation to produce a molecule of 3-pentanone which, through the instauration of keto-enol tautomerism, can be consequently acylated to produce poly-ketone chains or cyclic compounds via polycondensation reactions.^[37,38] Similarly, lactones (and their derivatives) can be considered as precursors of heavier compounds, the former being produced via consecutive alpha-substitution of the beta-ketoacid followed by intra-molecular (Fischer) esterification and consequent cyclization.



Scheme 2. Proposed reaction pathway for heavier compounds formation and deposition in presence of AP. The presence of the products highlighted in yellow was validated by GC-MS analysis of the reaction mixture (AP and PW87, 80 °C, 1 h). Compounds: 1. 3-pentanone; 2. 4-methylheptane-3,5-dione; 3. 5,6-dihydro-3,5-dimethyl-6-ethylcarbonyl-2H-pyran-2,4-dione.

Catalytic activity comparison with other ion exchange resins and influence of the Aquivion particle size

Table 1 illustrate the best performances attained using various commercial styrene-divinylbenzene resins such as Amberlite 15, Amberlite 39 and Purolite CT269DR. As pointed out by the calculated amount of MDP1P formed per catalyst acidic site ($\text{mmol}_{\text{MDP1P}}/\text{mmolH}^+$, after 1 h), the intrinsic catalytic activity of PW87 was far superior to the ones obtainable using other ion exchange resins. These alternative catalysts, although characterized by a higher concentration of acidic sites (4.70–5.20 vs. 1.15 $\text{mmol H}^+/\text{g}_{\text{CAT}}$), showed an activity comparable to PW87 only at a reaction temperature of 120 °C. In this condition, a clear inverse correlation between MDB conversion and MDP1P selectivity can be observed, confirming the promotion of undesired reactions that convert MDB and MDP1P into heavier compounds. As it can be observed, the MDB conversion is boosted over the sample with higher specific surface area (SSA)

and, in this context, it can be asserted that the presence of meso-pores in the catalyst structure favored the formation of heavier compounds during reaction, as in the case of Amberlyst 15 and Purolite CT269DR (Figure S5). Moreover, showing the latter a pore distribution comparable to that of Amberlyst 15, it is likely that its higher acidity further favored by-products formation, decreasing the MDP1P selectivity to a value of 57% (120 °C, 1 h). In addition to the reported commercial catalysts, also a gel-type 2% crosslinked styrene-divinylbenzene sulfonated resin (2%/SDVB) was tested in MDB acylation at 80 and 120 °C. Although good results were obtained at high temperature, and this catalyst showed better results at 80 °C if compared to the other (meso- and macroporous) resins, the activity of PW87 was sensibly higher in mild reaction conditions, especially in terms of MDP1P yield and selectivity. However, these results suggest that the reaction is more favored over swellable resins than those exhibiting defined porosity.

Table 1. Catalytic activity of different solid acid catalysts in the MDB acylation with AP. The acidity of the catalysts expressed as $\text{mmol H}^+/\text{g}_{\text{CAT}}$ is the one reported from the manufacturer. MDB/AP of 1 mol/mol, catalyst 0.1 g, reaction time 1 h.

Catalyst	$\text{mmol H}^+/\text{g}_{\text{CAT}}$	SSA [m^2/g]	T [°C]	X_{MDB} [%]	S_{MDP1P} [%]	Y_{MDP1P} [%]	$\text{mmol}_{\text{MDP1P}}/\text{g}_{\text{CAT}}$ [a]	$\text{mmol}_{\text{MDP1P}}/\text{mmolH}^+$ [a][b]
Aquivion PW87	1.15	< 1	80	53	79	42	73.5	63.9
2%/SDVB	5.06 ^[c]	< 1	80	52	62	32	56.0	11.1
			120	73	76	56	98.0	19.4
Amberlyst 39	5.00	< 1	80	20	89	18	31.5	6.3
			120	51	84	43	75.3	15.1
Amberlyst 15	4.70	48	80	32	89	28	49.0	10.4
			120	66	74	49	85.8	18.3
Purolite CT269 DR	5.20	38	80	37	72	27	47.3	9.1
			120	72	57	41	71.8	13.8

[a] After 1 h of reaction. [b] mmolH^+ represent the amount of catalyst acidic sites in the reaction environment. [c] determined by titration with NaOH.

Being classified as a gel-type resin with a small surface area, the accessibility of the PW87 acid sites is likely to be affected by steric constraints, catalyst grain size and the swelling capability of the resin in the reaction media. Since all these aspects are of paramount importance to assess the possible scale-up of the process, the influence of the particle size on the catalytic performance was evaluated by sieving and collecting the PW87 in different dimensional fractions that were separately tested in the reaction at 80 °C for 1 h. Although it is not possible to determine significant SSA values for PW87 using conventional techniques, it is however possible to estimate the mean geometric value of the surface area of the dry resin particles as a function of their dimensions in the different tests (See Supporting Information and Table S1 for further details). The activity in terms of MDB and AP conversion (Figure 5a) was poor in the 0.80–0.60 mm dimensional range, increasing steadily when the particles diameter is decreased. At the same time, the MDP1P yield is increased also due to a remarkable improvement of the reaction selectivity that was boosted from a value of 64% to 79% when the particles diameter was in 0.10–0.04 mm range (Figure 5b). Remarkably, the by-products formation rate was not sensibly influenced by the catalyst

dimensional distribution, and almost constant yield values of “other compounds” were observed (around 12%). A further study (see Supporting Information and Figure S6) regarding the influence of the polarity of the reaction media on the catalyst activity revealed that the reactivity of the system towards MDB was increased when increasing amount of PA were added to the reaction mixture. However, this was accompanied by a higher by-product formation and a lower MDP1P selectivity.

Catalyst regeneration and scale-up tests

Several regeneration procedures of the spent catalytic material after one reaction cycle were investigated, as summarized in Figure 6a. The simple washing of the sample after reaction with acetone led to poor performances when the catalyst was tested in a second run (MDB conversion of 8%) confirming the substantial catalyst deactivation occurred during the first acylation reaction.

In the second procedure, the spent catalyst (around 0.1 g) was treated with an aqueous solution of HCl (5 mL, 20% v/v) at 100 °C for 1 h (followed by the washing and drying of the

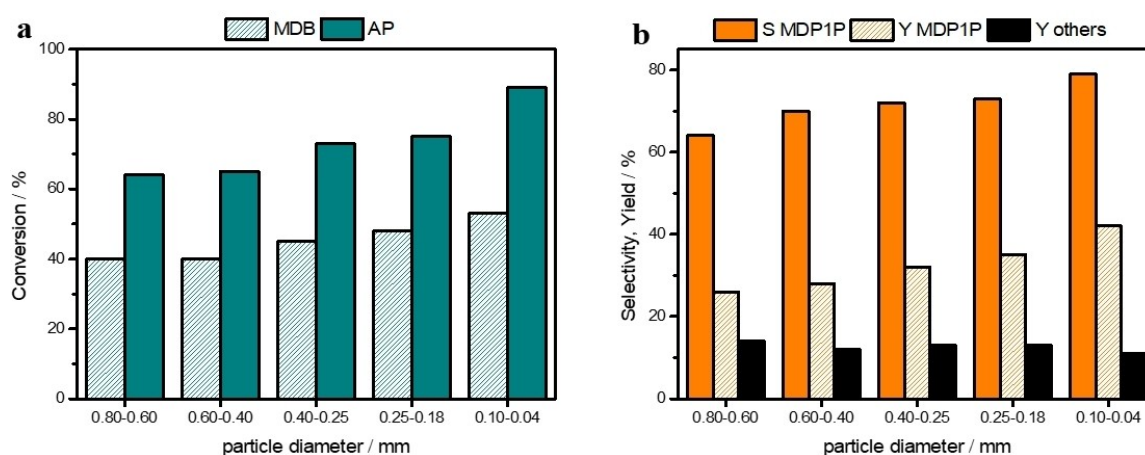


Figure 5. Influence of the particle size on PW87 catalytic activity in terms of a) MDB and AP conversion and b) selectivity and yield in MDP1P and by-products yield. Reaction temperature 80 °C, MDB/AP of 1 mol/mol, catalyst 0.1 g, reaction time 1 h.

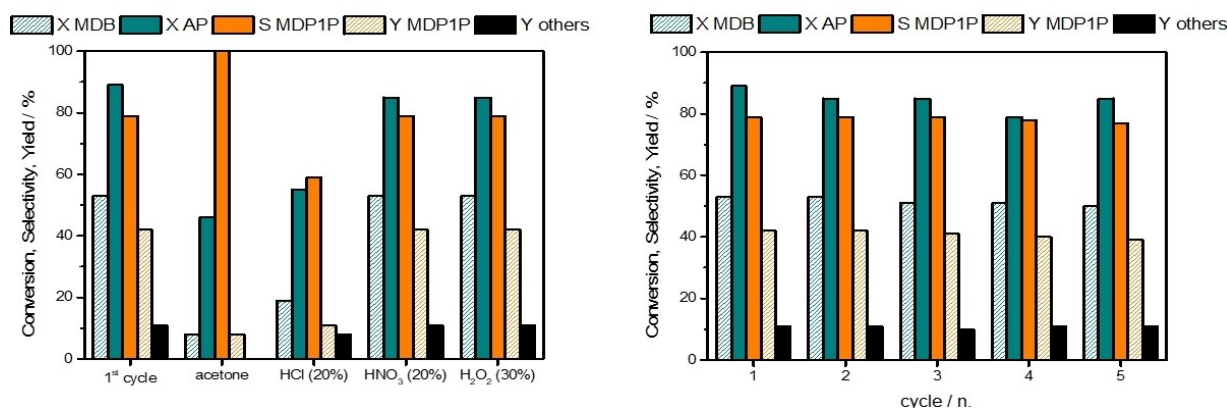


Figure 6. a) Comparison between the activity of the fresh catalyst and after different regeneration procedures and b) Catalytic performances over 5 reaction cycles (MDB/AP of 1 mol/mol, catalyst 0.1 g, 80 °C, reaction time 1 h) using a HNO₃ solution (20%, 100 °C, 1 h) as regenerating media.

sample). In this way, the catalytic activity was recovered only partially, showing a low MDP1P selectivity of 59% and a MDB conversion of 19% probably due to a partial restoration of the active surface. Carrying out the same treatment but using an HNO₃ solution (20% v/v, 50 mL/g of catalyst), the catalyst performance was totally recovered, suggesting that it is important to promote the oxidative decomposition of organic deposits formed on the catalyst surface.

The removal of the carbonaceous substrate was confirmed by the FT-ATR spectra of the dried catalyst after regeneration (Figure 4a) which, besides showing the stability of the sulphonic groups during the acidic treatment, revealed the disappearance of signals associated to carbonaceous material in the 1400–1800 cm⁻¹ range. This regeneration procedure was tested for five reaction cycles in which the catalyst showed constant performances (Figure 6b).

The importance of oxidizing the surface deposit to recover the catalyst activity has also been validated by regenerating the catalyst using a H₂O₂ solution (30%, 100 °C, 30 min). The catalytic results obtained from the regenerated sample were comparable to those observed using HNO₃, revealing a possible alternative to using an acid regeneration media.

At the same time, it should be noted that due its intrinsic instability, the H₂O₂ solution easily decomposed when heated at 100 °C, meaning that a fresh H₂O₂ solution must be used for each regeneration cycle. On the contrary, the HNO₃ concentration in the regenerating solution was reduced of a factor of 0.5% v/v after each regeneration cycle (from 20% v/v to 19.5% v/v and so on, as confirmed by titration with NaOH), whereby this solution was recovered and reused for 4 consecutive regeneration steps. In order to assess the possible scale-up of the process, the reaction was carried out using increasing reaction volume from 4 mL up to 800 mL. In these tests, the MDB/AP molar ratio (1 mol/mol) as well as the SO₃H_{CAT}/MDB ratio (0.007 mol/mol) were maintained constant regardless of the reaction volume.

The results obtained (Figure 7) revealed a constant catalytic activity of the PW87 catalyst over the different volume of

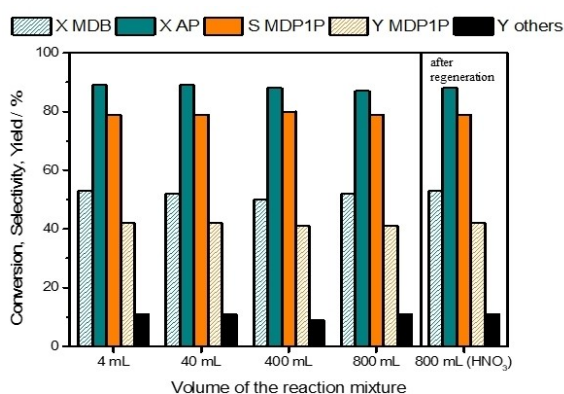


Figure 7. Catalytic activity of PW87 as a function of the volume of the reaction mixture and catalyst performance (reaction volume of 800 mL) after a regeneration step using HNO₃ (50 mL/g catalyst) as regenerating media (on the right). Reaction temperature 80 °C, MDB/AP of 1 mol/mol, -SO₃H_{CAT}/MDB of 0.007 mol/mol, reaction time of 1 h.

reaction and assessed that, in accordance with the previous results, regenerating the spent catalyst (recovered from the reaction carried out in 800 mL) using HNO₃ (or H₂O₂), it was still possible to recover the catalytic performance. All in all, even though the reaction volumes are still far from those typically used in an industrial production, these results demonstrated how this heterogenous catalytic process has the potential to be scaled-up to a larger scale without showing significant productivity drops

Catalytic activity of Aquivion-SiO₂ nanocomposites

The results obtained by changing the catalyst particles diameter underline the importance of the effective exposure and availability of the active sites for the reagents. Therefore, to further increase the catalyst activity, it is possible to support the resin on a SiO₂ matrix via sol-gel synthesis and consecutive activation of the solid in acidic environment to obtain good polymer dispersion over the silica support, this way limiting the need for an optimal swelling of the resin. The catalyst synthesized by using TEOS and a D72 dispersion (acidity of 1.390 mmol H⁺/g) to obtain a solid with a concentration of the resin (over SiO₂) of 13 wt.% was named D72_13%. The catalyst was characterized by a specific surface area of 225 m²/g given by the large amount of SiO₂ mesopores with a diameter distribution centered at 12 nm (Figure 8a, b).

The SEM analyses of the catalyst before reaction (Figure 8c) showed the rough morphology of the surface and the porous nature of the solid. The results obtained from EDX analyses/mapping (Figure 8d and Figure S7) confirmed the homogenous distribution of the polymer on the SiO₂ matrix without an observable presence of large resin agglomerates, asserting the nanoscale of the synthesized composite.

In agreement with the trend observed by decreasing catalyst particle size, the catalytic performance of the nanosized supported resin (Figure 9a, b) showed an improvement with respect of the bulk catalyst (80 °C, 1 h) likely due to a better availability and distribution of the catalyst active sites.

In particular, the conversion of MDB increased up to a value of 53% while the MDP1P selectivity reached 83%. In this way, in addition to increasing MDP1P yield (44%), it was possible to further reduce the production of by-products present in the liquid phase (Y_{others} = 7% vs. 11% of bare PW87).

On the other hand, it was not possible to avoid the deactivation of the composite, which can however be regenerated following the same procedure tested for the PW87 sample. Also in this case, in fact, the catalyst showed a constant activity after each regeneration cycle as shown by the catalytic performances obtained during 5 consecutive catalytic runs.

Conclusions

The Aquivion PW87 catalyst showed a remarkable activity in the MDB acylation with AP to selectively produce MDP1P in solvent-free conditions with short reaction times. These promis-

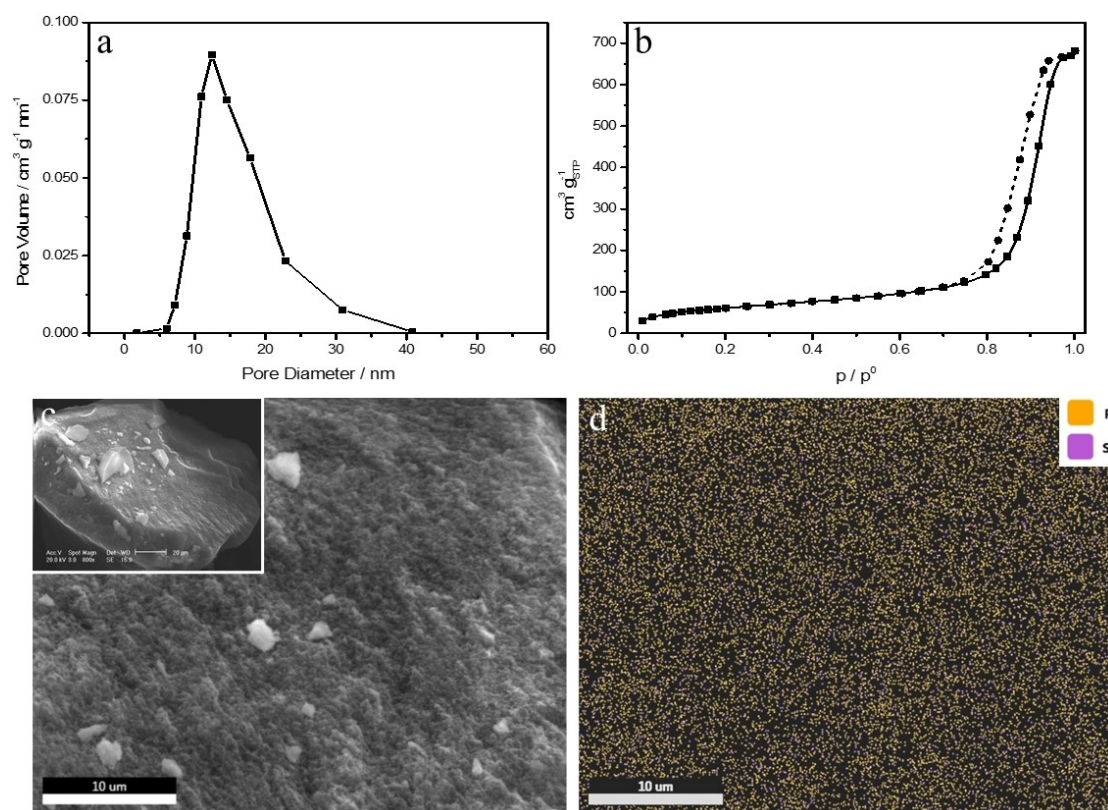


Figure 8. BJH and SEM analyses of D72 13% fresh catalyst: distribution curve of the pore diameter and b) adsorption/desorption curve. c) SEM images and d) EDX mapping analyses of the zone.

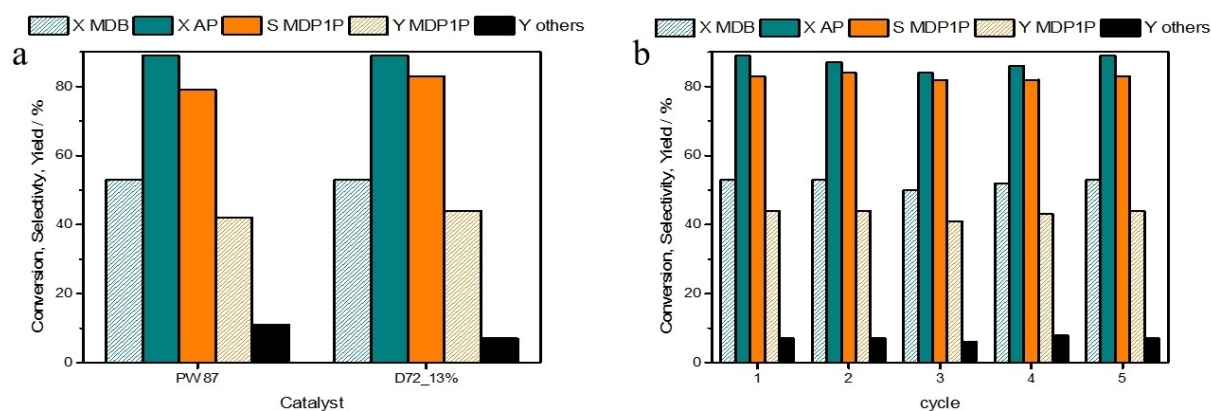


Figure 9. a) Comparison between the catalytic activity of PW87 and D72 13%, (80 °C, MDB/AP of 1 mol/mol, reaction time 1 h, mol $\text{SO}_3\text{H}_{\text{CAT}}$ /mol MDB of 0.007) and b) Catalytic performance of D72 13% over 5 reaction cycles (80 °C, 1 h) using a HNO_3 solution (20%, 100 °C, 1 h) as regenerating media.

ing results are hardly attainable using other acidic resins which, even if presenting a porous structure, were active at higher temperature (120 °C) and thus promoted the formation of undesired heavier compounds. In this sense, although characterized by a low surface area, the swelling of PW87 in the polar reaction media assures, depending also on the particle size, high catalytic activity even in mild conditions (80 °C). Although the high reactivity of AP with the system leads to catalyst deactivation, a fast oxidation of the deposited carbonaceous material over the resin surface allows to regenerate and reuse the catalyst for several reaction cycles. From the dedicated

scale-up tests it was found that the activity of the catalyst (as well as its regeneration step) was basically unaffected by the reaction volume, demonstrating how this process has the potential to be applied on a larger scale. To the best of our knowledge this represents the first example of heterogeneously catalyzed acylation for a substrate like MDB. Finally, by homogeneously incorporating the acid resin into a SiO_2 matrix via a sol-gel synthesis, it is possible to further increase the catalyst performance, decreasing by-products formation and enhancing the selectivity of the reaction towards MDP1P. In this sense, a further study of the nanocomposite synthesis method

and its possible optimization represents the most promising way to further boost the catalyst activity, decrease the reaction temperature and minimize by-products formation thus making the whole process even more sustainable.

Experimental Section

Catalytic tests

PW87 (1.15 mmol_{H+}/g), Amberlyst-15 (4.70 mmol_{H+}/g) were purchased from Sigma Aldrich, Poly(styrene-divinylbenzene) 2% cross-linked was purchased from Alfa-Aesar, Amberlyst-39 (5.00 mmol_{H+}/g) and Purolite CT269DR (5.20 mmol_{H+}/g) were obtained from DuPont and Purolite respectively. While PW87 was used without any other treatment, Amberlyst and Purolite particles were firstly crushed by a agata mortar prior the tests. The liquid phase acylation of MDB (Sigma Aldrich, 99%) with AP (Sigma Aldrich, >99%) was carried out at atmospheric pressure in a 10 mL 2-neck round flask reactor equipped with a reflux system and a thermometer. In a typical experiment, 17.5 mmol of MDB, 17.5 mmol AP and 0.1 g of solid catalyst (sieved to load particles with an average dimension between 0.10 and 0.04 mm unless otherwise specified and previously dried at 110 °C for 5 h) were placed into the reaction system with a stirring speed of 600 rpm and heated up to the desired temperature using an oil bath. After reaching the reaction temperature, the mixture was maintained in this condition for the desired time of reaction. After this time, the system was quenched in an ice-bath and the reaction mixture quantitatively analyzed using octane as internal standard through a GC equipped with a DB-5 column and a FID detector. The MDB, AP conversion and MDP1P selectivity and yield were calculated using Equations 1, 2 and 3:

$$X_{MDB,AP} = \frac{(mol_{tr} - mol_{t0})}{mol_{t0}} \times 100 \quad (1)$$

$$S_{MDP1P} = \frac{mol_{MDP1P}}{mol_{MDB\ converted}} \times 100 \quad (2)$$

$$Y_{MDP1P} = \frac{mol_{MDP1P}}{mol_{MDB\ at\ t0}} \times 100 \quad (3)$$

Where “t0” stands for “before reaction”, “tr” for “after reaction”, and X, S, Y represents the molar conversion, selectivity, and yield, respectively. Similarly, the minor compounds observed were collected under the “Others” label and yield calculated as reported in Equation 3. Each compound was calibrated with respect to octane, used as internal standard, to obtain the corresponding response factor in the appropriate range of concentrations. The structure of the products was assigned by GC-MS, and whenever possible, by comparison with authentic commercial samples.

Sulfonation of Poly(styrene-divinylbenzene) resin

The sulfonation of the resin (2% crosslinked) to obtain the gel-type acid catalyst named 2%/SDVB was carried out by treating 1 g of the bare resin with a 15 mL solution of concentrated H₂SO₄ and 0.02 g of Ag₂SO₄. The suspension was heated to a temperature of 85 °C and maintained at this temperature for 90 min under vigorous stirring. After cooling, this suspension was added to a 6 M aqueous solution of H₂SO₄ (100 mL). The solid was then filtered and washed with water (500 mL) and methanol (20 mL) until a neutral pH was

reached. The sulfonated resin was finally dried in an oven at 110 °C for 5 h. The concentration of the acidic sites per gram of resin (mmolH⁺/g_{CAT}) was determined by a titration with an aqueous solution of NaOH (5 mM). In a typical titration, 10 mg of resin were dispersed in a beaker (100 mL) containing 50 mL of deionized water under vigorous stirring and a pH meter. After pH stabilization (about 30 min), the NaOH solution was added dropwise until the initial pH was reached.

Synthesis of Aquivion/SiO₂ composite catalyst

The Aquivion/SiO₂ nanocomposites were obtained through sol-gel preparation.^[22] A mixture of tetraethyl orthosilicate (TEOS), deionized water (15 wt.%) and HCl (0.04 M, 1.5 wt.%) was stirred for 45 min. A second solution containing the desired amount of D72 hydro-alcoholic dispersion (Sigma Aldrich, distilled water, and 1-propanol mixture) was prepared. The latter was mixed with 9 mL of NaOH (0.4 M) and stirred over 15 min. Then, the first solution was rapidly added to the stirred resin/NaOH solution, and the formation of the gel occurred after few minutes to give a slightly opaque hard solid. After the drying of the gel at 95 °C for 48 h, the obtained powder was treated in a HCl aqueous solution (3.5 M) for 1 h at ambient temperature and under vigorous stirring. After the washing of the solid, a final treatment of the powder in HNO₃ aqueous solution (25 wt.%) at 75 °C for 12 h was performed, followed by the washing with deionized water. Finally, the catalyst was dried at 100 °C for 24 h.

Catalyst characterization

Porosimetry analyses were carried out in a Micromeritics ASAP 2020 instrument. The degas of the sample was performed in vacuum at 110 °C for 2 h, then the solid (250 mg) was analyzed by N₂ physisorption at −196 °C. The specific surface area, pore volume and distribution were extrapolated using the BJH and BET equations. The samples morphology and composition were investigated through SEM observation using a FEI/Philips XL30 ESEM. The elemental analyses and mapping were carried out with an X-ray energy dispersive spectrometer, EDAX AMETEK Element coupled with SEM. The EDX detector was a silicon drift detector with a silicon nitride window. Depending on the purpose, different acquisition modes were adopted, among area, point and maps. In a typical area analysis acquisition time was set at 30 s while for mapping analyses the analysis was stopped manually when a good quality was obtained. The *ex-situ* IR spectra of the catalysts before and after reaction were acquired in attenuated total reflectance (ATR) over the range 4000–600 cm^{−1} by means of a Thermo Scientific Nicolet iS10 Smart iTR equipped with a Smart OMNI Transmission instrument, interfaced with a Omnic 9.2.98 software. *In situ* FT-ATR experiments were carried out using a Bruker Tensor II instrument equipped with an ATR cell (Zinc Selenure crystal). The general procedure for the investigations is the following: First, 50 mg of catalyst were deposited on the ATR crystal surface then 2 ml of an equimolar solution of MDB and AP were deposited over the catalyst and heated from room temperature to 80 °C. The spectra were acquired every 30 s. The spectra reported in the text are obtained by subtracting each spectrum to the first spectrum acquired at room temperature. GC-MS analyses were performed with a Finnigan Trace GC-MS equipped with a DB-5 column and a quadrupole analyzer and electronic impact source.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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