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Process Intensification for Sustainable Microwave-Assisted Bio *p*-Cymene Production from Limonene

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ABSTRACT: Limonene is the most abundant terpene in citrus byproducts, such as lemon and orange peels. Due to its six-membered ring structure, it is considered a valuable feedstock for the synthesis of important bioaromatics, such as *p*-cymene. This study aims to develop a rapid and sustainable method to produce bio *p*-cymene from biomass-derived limonene. The use of enabling technologies, such as microwaves (MWs), can significantly intensify the process, leading to further improvements in sustainability. Several mono- and multimode MW reactors have been tested in this context. Monomodal systems have yielded the highest *p*-cymene output (up to 22.61% selectivity), while multimode reactors allow for a scaling-up approach that overcomes the limitations of the monomodal ovens while still providing noticeable *p*-cymene yields (up to 17.79%). An environmentally friendly protocol that utilizes mild temperatures (80−165 °C), has reduced time requirements (0−5 min), and can be performed in solvent-free conditions was employed throughout the process. This approach makes use of a wide range of biorefinery-based practices and is aligned with green processing, the circular economy, and process intensification principles.
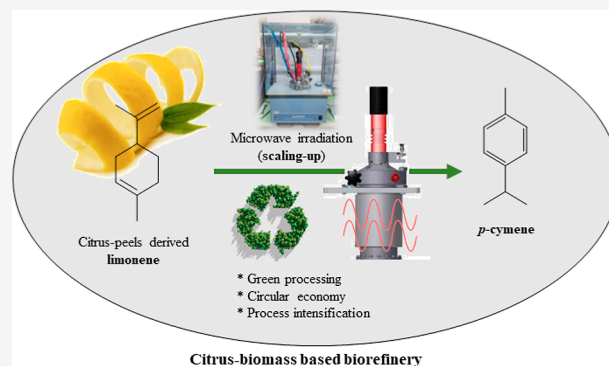
1. INTRODUCTION

Sustainable development has emerged as a priority goal for academia, companies, and even governments as they tackle significant environmental climate-change-related issues.[1] This challenge mainly involves the exploitation of renewable raw materials, such as agrifood waste, as an alternative to traditional and nonendless petroleum sources, thus paving the way for a circular-economy approach.[2−4]

In 2020, global citrus-fruit production reached 144 million metric tons (159 million short tons),[5] with approximately 50−60% of this production consumed as fresh fruit, while the remaining 40−50% is used for industrial processing. The citrus industry generates wastewater and solid/semisolid residues, specifically citrus-peel waste, which accounts for approximately 50−70% w/w of the processed fruit.[6−9] The main challenge in the biological treatment of this waste is the extraction of essential oils, which consist of approximately 95% bioderived limonene and possess antimicrobial properties.

From an environmental point of view, limonene is a low-toxic and biodegradable terpene, as well as a low-cost and high-abundance material (more than 70,000 t/a in 2013).[10] Additionally, it plays a renowned role in the chemical industry. For instance, it finds applications as a fragrance additive in cosmetics, perfumes, and household cleaning products; in the food sector, as a flavoring and preservative additive; and as an intermediate in the production of adhesives and resins.[11] Moreover, it can also find use as a green-extracting solvent for biologically active compounds, such as polyphenols and

lipids.[12,13] Besides its wide range of industrial applications, the presence of a six-membered ring in limonene, which can be further aromatized, makes it a suitable platform chemical for a large number of petroleum-derived aromatics. This fact makes it particularly attractive; for instance, limonene can be converted to *p*-cymene.[14−16] This approach stands out as a sustainable alternative for conventional methods, such as Friedel−Crafts alkylation from benzene or toluene, as that process involves toxic compounds, expensive procedures, and low selectivity.[17,18]

On the other hand, *p*-cymene is exploited as a high-added-value compound in several industrial chemical processes. Specifically, in the synthesis of fragrances, perfumes, flavorings, and pharmaceutical products,[11] among others. Furthermore, it is a distinguished platform molecule for the production of other fine chemicals, with the synthesis of terephthalic acid from *p*-cymene being particularly remarkable.[19−21] This transformation can replace the traditional oxidation process, which makes use of petroleum-derived *p*-xylene, thus setting both fossil-fuel sources and toxic chemicals aside. Moreover,
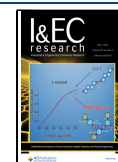
this route is especially remarkable as it can be exploited for the synthesis of biopolyethylene terephthalate.[22]

Reports on the transformation of limonene into *p*-cymene via homogeneous catalysts are quite limited, primarily due to its low yields and drawbacks in separation, meaning that focus has shifted somewhat toward heterogeneous systems. For instance, Lycourghiotis et al.[14] and Makarouni et al.[23] have achieved 65% *p*-cymene selectivity using naturally occurring mordenites, activated with an acidic solution under harsh conditions (140 °C for 7 h). Catrinescu et al.[24] have employed ion-exchanged clays as catalysts, at 150 °C for 15 min, and reported the formation of isomerization, disproportionation, and polymerization products at the same time. Finally, titanium- and silica-supported zinc oxides have also been tested.[25,26] However, the applied reaction conditions were extremely harsh and included temperatures above 300 °C, with 70 h being necessary to achieve the desired product yield. Enabling technologies were also exploited for the intensification of the *p*-cymene production. In this context, Martin-Luengo et al. have reported the use of microwave (MW) irradiation to selectively obtain *p*-cymene, with total conversion being achieved after 20 min over metal-modified natural sepiolite[16] or mesoporous silica–alumina supports at 225 °C.[27] Moreover, an 80% *p*-cymene yield was achieved over Pd/Al$_2$O$_3$ from orange-peel oil at temperatures above 300 °C after only 50 s when using alcohols under supercritical conditions.[15] Overall, these documented intensified protocols make for more efficient and sustainable processes that fully adhere to green chemistry principles.[28,29]

In this context, we herein report a process-intensification strategy for the development of environmentally friendly protocols [i.e., solvent-free conditions, mild temperature, flash processing, and the use of nonmodified, acidic solids (mainly clays)] for the conversion of limonene into *p*-cymene. In particular, MW irradiation, widely utilized to upgrade biomass,[30−33] was investigated and compared to conventional heating (CH). The application of a MW monomode reactor was initially explored, for the sake of comparison with the literature, and clays were used to promote the reaction.[16] A considerable improvement over previous work was observed. Several multimode MW reactors were then tested with the aim of numbering-up/scaling-up the process, thus overcoming the limitations of the monomodal ovens (Table 1). The environ-

mental impact of both the conventional and MW-assisted limonene-conversion processes has been evaluated using green chemistry performance metrics (GCPMs).[34] In this work, we describe an environmentally sustainable protocol that emphasizes the use of MW technologies, which save time and energy in order to develop a specific intensified conversion protocol.

2. MATERIALS AND METHODS

2.1. Chemicals. *R*-(+)-limonene (96%, CAS no. 5989−27−5) was purchased from Thermo Scientific. *p*-Cymene (99%, CAS no. 99−87−6) and 2-methyltetrahydrofuran (≥99%, CAS no. 96-47-9) were supplied by Sigma-Aldrich.

A commercial acidic clay, namely, Tonsil Supreme 115FF (highly active) (ref 33972−150), was purchased from SÜD-CHEMIE (AG Food and Feed Additives Ostenrieder Straße 15 85368 Moosburg Germany) and used for this study without any further modification or alteration.

2.2. MW-Assisted Conversion of Limonene into *p*-Cymene. *2.2.1. Monomode Processing.* MW irradiation was first applied by using a single-mode programmable focalized oven (Monowave 300, Anton Paar GmbH, Graz, Austria, Figure S1). The measurement of the sample temperature was accomplished by infrared detection.

In a typical experiment, 50 mg of limonene (62 μL, ρ = 0.841 g/cm^3, 96%) and 100 mg of acidic clay (Tonsil supreme) were introduced into the specific MW glass vial. Reactions were carried out under neat conditions. Samples were irradiated at maximum power under the selected temperature and time conditions using a changeable heating-ramp time according to the fixed temperature.

After the reaction, a brown, wet solid was obtained. Bioderived 2-methyltetrahydrofuran (2-MeTHF) (2.5 mL × 3) was added to the crude reaction mixture, and the recovered solid was filtered off. An aliquot (1 mL) of the obtained yellowish liquid was then directly analyzed by GC−MS and GC-FID for quantification. 2-MeTHF was quantitatively recovered after these analyses.
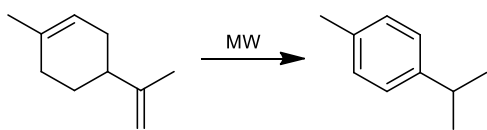
2.2.2. Multimode Processing. 2.2.2.1. MW Multimode System for the Numbering-Up (MW-Multimode 4N-Up) of Limonene Conversion. In order to number-up the process from the lab scale, a high-pressure professional SynthWAVE multimode MW reactor (300 °C, 199 bar, 2.45 GHz, Figure S2) was used (Milestone Srl, Bergamo, Italy). A multirack position tool allowed simultaneous reactions to be performed under the same reaction conditions.

In a typical experiment, 50 mg of limonene and 100 mg of the acidic clay (Tonsil supreme) were introduced into the specific MW glass vial under solvent-free conditions. Samples were irradiated at 1500 W. The heating ramp was fixed at 5 min for each run.

Once the reaction had taken place, the crude was washed with 2-MeTHF (2.5 mL × 3), the solution was filtered off to separate the solid acid used for conversion, and the liquid fraction, recovered as a yellowish solution, was analyzed by GC−MS and GC-FID (1 mL of aliquot). 2-MeTHF was then totally recovered (7.5 mL).

2.2.2.2. MW Multimode System for the Scale-Up (MW-Multimode 4S-Up) of Limonene Conversion. In order to investigate the feasibility of scaling-up the intensified process, an advanced and flexible multimode MW reactor was exploited (FlexiWAVE, Milestone Srl, Bergamo, Italy). The FlexiWAVE system overcomes the limitations of conventional MW

Table 1. Conversion of Biomass-Derived Limonene to *p*-Cymene as Assisted by Different MW Devices and Solid Acids

solid acids	MW reactor	refs
sepiolite (clay)	MW-monomode	Martin-Luengo et al. (2010)[16]
acid-modified mesoporous silica–alumina supports (SIRAL)[a]	MW-monomode	Martin-Luengo et al. (2008)[27]
Tonsil supreme (acidic clay)	MW-monomode	this work
	MW-multimode 4N-up	
	MW-multimode 4S-up	

[a]1 wt % modified with silica.

Table 2. Product Selectivity for the Conversion of Limonene Using a Monomode MW Reactor

	conditions (T, time)	p-cymene (%)[a]	p-cymene/disprop. (%)	p-cymene/isomer. (%)	p-cymene/others (polym.) (%)	conversion (%)[b]
1	70°C, 10 min	5.29	59.41	21.97	14.74	77.88
2	80°C, 5 min	22.61	62.73	98.85	27.93	97.52
3	80°C, 10 min	20.45	63.81	100	23.70	98.78
4	90°C, 2 min	21.63	63.02	95.25	26.98	97.26
5	90°C, 10 min	19.93	66.07	99.41	22.95	98.48
6	100°C, 0[c] min	21.35	61.07	96.48	27.45	96.28
7	110°C, 0[c] min	19.75	65.01	100	23.14	98.04
8	120°C, 0[c] min	18.62	64.57	99.21	21.40	98.51
9	140°C, 0[c] min	19.21	64.00	98.78	22.30	98.51

[a]Relative percentage directly obtained from GC-FID data. [b]Obtained by means of an external standard calibration curve. [c]The sample was only heated to the set temperature, and then the MW was switched off. This heating entailed 90, 110, 120, and 150 s for experiments at 100, 110, 120, and 140 °C, respectively.

synthetic devices as it has a MW cavity (more than 70 L) in a single instrumental platform that, in combination with specific accessories, allows classic glassware and high-pressure synthesis to be executed (Figure S3). It is also capable of optimally heating highly heterogeneous mixtures, viscous reaction media, and powdered solids. This is due to the innovative 45° rotating reactor setup, which allows the reagents to be subjected to homogeneous and controlled irradiation. If necessary, the reactor also supports the introduction of inert gases and the formation of vacuum. FlexiWAVE is ideal for reaction optimization and scale-up without the need to modify process parameters.

Experiments were carried out under vacuum, with a control system for the heating ramp and subsequent steps performed under 1900 W power (Figure S3). The reaction temperature was controlled by a contactless infrared sensor.

In a typical experiment, limonene (10 mL, 8 g) and the catalyst (0.75 g) were added into a suitable vial for the rotating setup under vacuum. Some small glass balls were also added to the reaction crude to ensure the homogeneity within the sample. A 10 min heating ramp to 80 °C was first selected in vacuum (0.6 mbar), and the system was then allowed to reach 110 °C in 5 min. This temperature was then maintained for 2 min to enable the reaction completion.

After cooling, the crude reaction mixture was filtered, affording an uncolored liquid solution. An aliquot (100 μL) was collected and solubilized in 2-MeTHF (1 mL) for subsequent GC−MS and GC-FID analyses, with the solvent recovered after both analyses.

2.3. Conversion of Limonene into p-Cymene under Conventional Heating. For the sake of comparison, reactions were also carried out under CH. Experiments were performed in a LabTech XELSIUS instrument (NevoLAB GmbH, Maierhöfen, Germany) equipped with 8 simultaneous positions, in which the reaction temperature can range from −20 to 150 °C (Figure S4).

In a typical experiment, 50 mg of limonene and 100 mg of acidic clay (Tonsil supreme) were introduced into the specific glass vial. Reactions were carried out at 100 °C for 0−30 min with a heating ramp fixed at 10 min for each transformation.

Afterward, the mixture was solubilized in 2-MeTHF (7.5 mL) to ensure the total solubility of the formed compounds. Then, the solution was filtered off to separate the solid acid from the liquid solution, which was then analyzed by GC−MS and GC-FID (1 mL aliquot). 2-MeTHF was collected and quantitatively recovered once GC analyses were carried out.

2.4. Characterization and Quantification of Products. GC−MS analysis was used for the qualitative analysis of the crude reactions (Section S2). Experiments were performed in an Agilent Technologies 6850 Network GC system (Agilent Technologies, Santa Clara, CA, USA) with a 5973 network mass selective detector, 7683 B automatic sampler, and HP-5MS capillary column (length: 30 m; i.d.: 0.25 mm; film thickness: 0.25 μm) operating in split mode at 1.2 mL/min. The initial inlet and detector temperatures were 250 and 280 °C, respectively. The oven temperature was initially set to 50 °C and established for 5 min. Three split-based steps then took place: (i) to 100 °C at 10 °C/min rate and remaining at this temperature for 1 min; (ii) to 230 °C at 20 °C/min (1 min remaining time); and (iii) to 300 °C at 20 °C/min (5 min). Helium was used as the carrier gas at a flow rate of 9.78 ψ.

As the crude product formed after the reaction was solubilized in 2-MeTHF (7.5 mL) and then filtered, an aliquot (1 mL) of this new liquid fraction was directly analyzed. For the experiments on scaled-up processing, 100 μL of the recovered solution was added to 1 mL of 2-MeTHF, and the mixture was then analyzed further.

For quantification, an Agilent Technologies 7820A Network GC system, equipped with an FID detector and a capillary column, operating in split mode at 1.2 mL/min flow rate (OV1701; length: 25 m; i.d.: 0.25 mm; film thickness: 0.30 μm), was used (MEGA snc, Legnano, Italy). Likewise, for the GC−MS analytic method, 250 and 280 °C were the initial temperatures for the inlet and detector, respectively. The oven was set at 50 °C for 5 min. A slope-based method was then applied with three marked steps: (i) to 100 °C at 10 °C/min and remaining at this temperature for 1 min; (ii) to 230 °C at 20 °C/min (1 min remaining time); and (iii) to 300 °C at 20 °C/min (5 min remaining time). Helium was used as the carrier gas at a 9.78 ψ pressure.

An external standard calibration curve was developed to quantify the remaining limonene after reaction (% conversion). The relative percentage directly obtained from the GC-FID chromatograms was considered for selectivity calculations. As stated above, because the crude formed after the reaction was solubilized in 2-MeTHF (7.5 mL) and then filtered, an aliquot (1 mL) of the recovered liquid fraction was analyzed without prior derivatization. For the scale-up experiments, a mixture of 100 μL of the recovered solution and 1 mL of 2-MeTHF was used in the GC-FID analyses.

2.5. Green Chemistry Performance Metrics. The environmental impact associated with the conversion of limonene was evaluated by means of the GCPMs.[34] In this

work, E-factor, atom economy (AE), atom efficiency (AEF), process mass intensity (PMI), process mass productivity (PMP), and reaction mass efficiency (RME) were measured. The concept, methodology, and formula for each factor are described in the Supporting Information (Section S3), and the evaluation is thoroughly explained in the Results and Discussion Section.

3. RESULTS AND DISCUSSION

3.1. Preliminary MW-Assisted Limonene-Conversion Experiments Using Monomode Technology. In order to compare the influence of different MW-reactor designs (based on distinct radiation principles: monomode and multimode) with the aim of scaling up the limonene conversion, experiments were initially performed in a monomode MW reactor, under solvent-free conditions, using an acidic clay (Tonsil supreme) to promote the reaction. The results previously reported by Martin-Luengo et al. serve as a comparison (Table 1) since the same MW radiation type (monomodal) was used.[16,27]

In this MW system, the temperature is measured by an infrared detector, and MW irradiation directly penetrates the vial and hits the sample, normally providing higher reproducibility than that of MW multimode processing. The most important advantage of single-mode apparatuses is their high rate of heating, while one of the drawbacks is that only one vessel can be irradiated at a time. These preliminary tests were therefore applied to laboratory-scale MW equipment to first investigate the optimal conditions. The results are detailed in Table 2.

In the presence of acidic sites, the transformation of limonene into p-cymene involves three competitive reactions: (i) isomerization to other terpenes; (ii) disproportionation to menthanes; and (iii) polymerization.[24]

Therefore, the optimal conditions would lead to the highest % p-cymene selectivity with respect to the side products obtained from each of these pathways.

In this regard, different temperatures and time periods of reactions were tested (Table 2). In this context, experiments performed at 70 °C for 10 min (Table 2, **entry 1**) led to a high concentration of unreacted limonene in the reaction medium, affording the lowest conversion (77.88%). Moreover, only 5.29% p-cymene selectivity was achieved under these conditions. Nonetheless, an increase in temperature to 80 °C or even 90 °C (Table 2, **entries 3** and **5**, respectively) notably enhanced p-cymene selectivity to 20.45% and 19.93%, respectively, with almost quantitative conversion (98.78% at 80 °C and 98.48% at 90 °C). Furthermore, selectivity with respect to terpenes (isomerization pathway) was clearly increased up to 100% at 80 °C and 99.41% at 90 °C compared to the 21.97% initially achieved at 70 °C, with a slight enhancement in terms of menthanes (disproportionation pathway) as well [from 59.41 to 63.81% at 80 °C (Table 2, **entry 3**) and 66.07% at 90 °C (Table 2, entry 5)]. Therefore, p-cymene formation was favored compared to these two competitive pathways at 10 min when the temperature was increased from 70 to 90 °C.

The same behavior was also detected for the p-cymene/polymerization product selectivity. As observed, this ratio notably increased from 14.74% at 70 °C (Table 2, entry 1) to 23.70 and 22.95% at 80 and 90 °C, respectively (Table 2, entries 3 and **5**). However, selectivity was still not remarkable compared to literature data, in which some authors have

reported that the polymer concentration increases faster than that of p-cymene at higher temperatures.[23] Furthermore, according to Catrinescu et al., polymers are the predominant products when prolonged reaction times are applied.[24]

Therefore, in view of the high MW field density provided by monomode reactors, lower residence times were tested at 80 °C (5 min) and 90 °C (2 min) (Table 2, entries 2 and 4). It should be noted that experiments were also performed for 5 min at 90 °C and 2 min at 80 °C for the sake of comparison, but the results were not acceptable, and these conditions were therefore ruled out.

Regarding **entries 2** and **4**, the polymer amount decreased compared to that of the experiments performed for 10 min, as expected. For instance, the percentage of p-cymene over the polymerization product increased from 23.70 (80 °C, 10 min) to 27.93% after only 5 min of reaction (Table 2, entry 2). In parallel, a similar value of 26.98% was found at 90 °C in a 2 min process, which is higher than the initial 22.95% at 10 min (Table 2, entry 4). Moreover, the total p-cymene selectivity was enhanced to 21.63% (90 °C, 2 min) and 22.61% (80 °C, 5 min), with almost total limonene conversion also being observed in both experiments (97.52 and 97.26% at 80 and 90 °C, respectively). Furthermore, despite the lower selectivity with respect to menthanes and terpenes at lower times compared to that of the 10 min experiments (Table 2, entries 2−5), these values were still worthy of note (for instance, 98.85 and 95.25% for terpenes at 80 and 90 °C, respectively, and 62.73 and 63.02% for menthanes). Overall, this time reduction can be considered a valuable achievement of this study.

Finally, temperatures above 90 °C were tested (Table 2, **entries 6−9**). In these cases, only the time involved in the heating ramp was considered (0 min experiments), and the aim was to reduce polymer formation, as reported above. In this regard, the ramp time was between 90 and 150 s from 100 to 140 °C, respectively. In brief, the higher the temperature that was applied, the higher the polymerization that was achieved, as observed by the decrease in p-cymene/polymerization selectivity. Thus, the maximum yield in terms of p-cymene (27.45%) was found in experiments at 100 °C (Table 2, entry 6). Regarding the amounts of terpenes and menthanes, the experiments at 110 °C were promising (Table 2, entry 7), with even 100% selectivity for p-cymene being achieved with respect to the former and 65.01% with respect to the latter. However, the total p-cymene selectivity was below 20% (19.75%). By contrast, at 100 °C, results in terms of p-cymene/terpenes (96.48%) and p-cymene/menthanes (61.07%) were still interesting, with a total p-cymene selectivity of 21.35% and almost quantitative conversion as well (96.28%).

Overall, 100 °C (0 min plus 90 in. heating ramp), 90 °C (2 min plus 80 in. heating ramp), and 80 °C (5 min plus 70 in. heating ramp) were selected as the optimal conditions (Table 2, **entries 2**, **4**, and **6**). As observed, a progressive temperature decrease from 100 to 80 °C means that longer residence times (from 0 to 5 min) are needed to achieve similar results, as expected. Flash processing [i.e., only heating ramp (90 s) and 0 min of reaction at 100 °C] may be remarkable for sustainability in terms of energy savings. Furthermore, p-cymene selectivity with respect to both terpenes and menthanes was considerable (which ranged from 95.25 to 98.85% for the former and 61.07−63.02% for the latter). Finally, it should also be highlighted that limonene was almost totally converted in each process (more than 96% conversion was achieved).
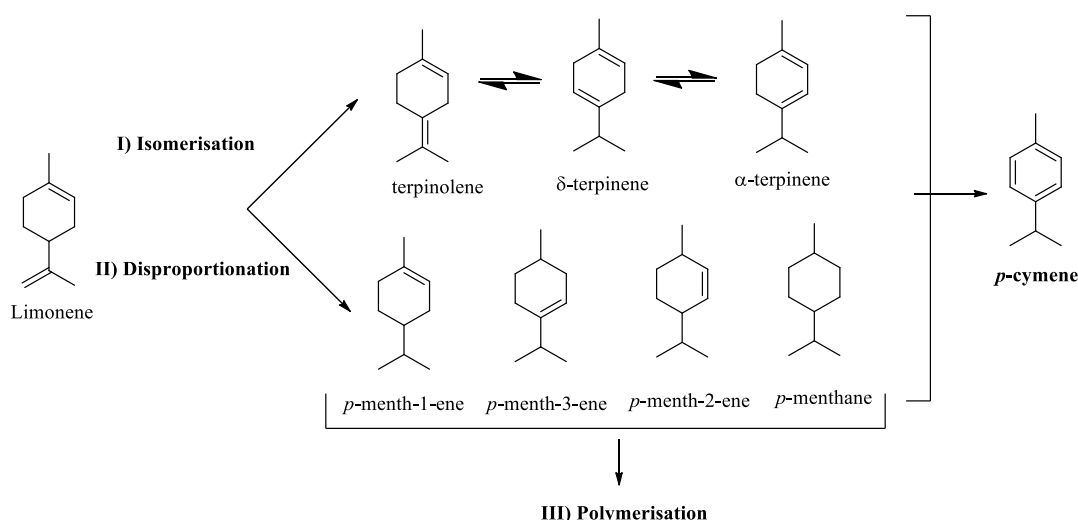
Figure 1. Competitive pathways involved in the transformation of limonene into *p*-cymene under acidic conditions.

Table 3. Comparison of Experimental Conditions for *p*-Cymene Selectivity under MW Monomodal Radiation and Solvent-Free Conditions

	reference	conditions (T, time)	solid acid (lim/solid)[d]	*p*-cymene (%)[a]	*p*-cymene/disprop. (%)	*p*-cymene/isomer. (%)	*p*-cymene/others (polym.) (%)	conversion (%)
1	this work	80 °C, 5 min	Tonsil supreme, 1:2	22.61	62.73	98.85	27.93	97.52[b]
2		90 °C, 2 min		21.63	63.02	95.25	26.98	97.26[b]
3		100 °C, 0 min		21.35	61.07	96.48	27.45	96.28[b]
4	Martin-Luengo et al. (2010)[16]	225 °C, 5 min	nonactivated sepiolite (clay), 1:4	3.90	n.d[c]	26	n.d.	15
5		225 °C, 10 min		5.75	n.d.	25	n.d.	23
6		225 °C, 20 min		9.92	n.d.	32	n.d.	31
7	Martin-Luengo et al. (2008)[27]	225 °C, 5 min	SIRAL 1, 1:4		n.d.		n.d.	15
8		225 °C, 10 min	SIRAL 1, 1:4	19.04	n.d.	34	n.d.	56
9		225 °C, 5 min	SIRAL 5, 1:4	2.94	n.d.	7	n.d.	42
10		225 °C, 5 min	SIRAL 10, 1:4	6.50	n.d.	10	n.d.	65

[a]Relative percentage directly obtained from GC-FID data. [b]Obtained by means of an external standard calibration curve. [c]n.d.: non determined. [d]lim/solid = limonene/solid-acid ratio.

A GC−MS chromatogram of the crude reaction for experiments at 100 °C and 0 min is reported in the Supporting Information (Figure S5) as an example. As reported, the *p*-cymene peak was the most intense, whereas traces of limonene, isomerization (terpenes), and some disproportionation products (menthanes) were detected. In this work, *α*- and *γ*-terpinene and terpinolene were the main terpenes detected, whereas *p*-menthane and *p*-menth-1-, 2-, and 3-ene were the main disproportionation products, which is in full agreement with the known competitive reactions involved in the conversion of limonene under acidic conditions (Figure 1). Some additional compounds were also detected, although they were neglected in these experiments owing to their very low concentrations.

Considering the available literature, only the works of Martín-Luengo et al.[16,27] have reported this transformation in monomodal MW technology, to the best of our knowledge. Their results were considered for the sake of comparison and are summarized in Table 3.

As reported by Martin-Luengo et al. (2010)[16] under solventless conditions using sepiolite (clay) as the solid acid, only 26% *p*-cymene selectivity with respect to terpenes (isomerization) was found after 5 min at 225 °C[16] (Table 3, entry 4). Consequently, only 3.90% of the total *p*-cymene

selectivity was achieved, considering the 15% conversion reported. Further time increases to 10 and 20 min at the same temperature did not lead to significant progress (Table 3, entries 5−6).[16]

These conditions (and therefore the results) differ notably from the optimal ones selected in this work (80 °C, 5 min), which led to 22.61% total *p*-cymene selectivity and 97.52% conversion.

Furthermore, these results were also promising compared to the employment of acid-modified mesoporous silica−alumina supports (SIRAL).[27] For instance, no *p*-cymene was found after 5 min using SIRAL 1 (1% wt modified with silica), and the conversion was only around 15%, with terpenes being the only detected compounds (100% selectivity) (Table 3, entry 7). Furthermore, neither SIRAL 5 nor SIRAL 10 provided promising results after 5 min of reaction (Table 3, entries 9−10). Finally, not even increasing the time up to 10 min with SIRAL 1 led to any improvement (Table 3, entry 8).[27]

Some activation processes for the solid acid used for conversion, to enhance *p*-cymene selectivity, have been reported in the literature. For instance, sepiolite (Sep) was activated with metals (Ni, Fe, and Mn), which led to a 100% selective transformation toward *p*-cymene, at 225 °C in 5 min,[16] while longer times were necessary at higher temper-
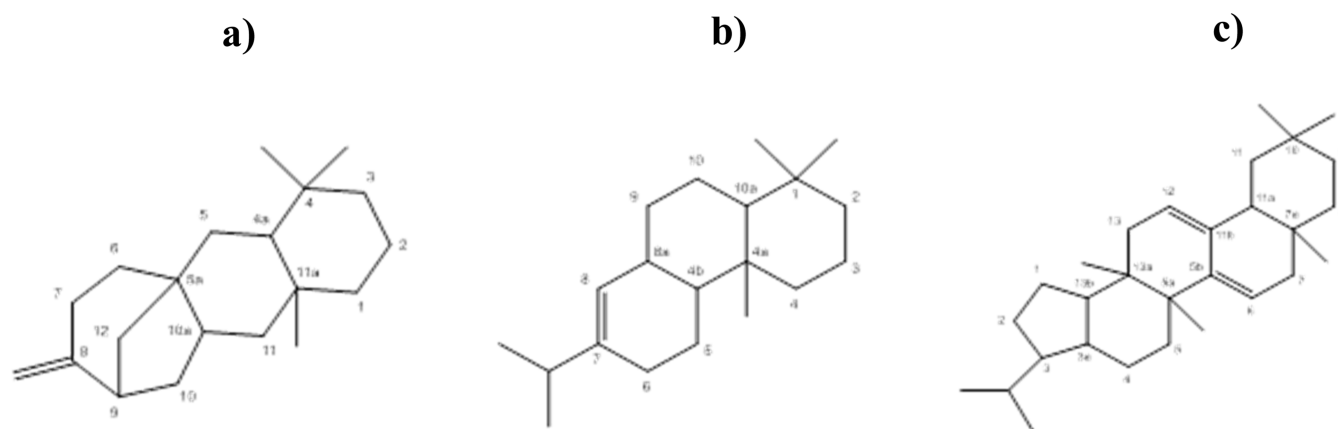
a) b) c)

Figure 2. From left to right: kaur-16-ene (a), podocarpa-6,13-diene, 13 isopropyl (b), and A-D-neooleana-12,14-diene (c).

Table 4. Product Selectivity for the Conversion of Limonene under Conventional Heating

	heating strategy	t (min)	p-cymene (%)[a]	p-cymene/disprop. (%)	p-cymene/isomer. (%)	p-cymene/others (polym.) (%)	conversion (%)[b]
1	MW[c]	0	21.35	61.07	96.48	27.45	96.28
2	CH[d]	0	9.63	60.45	58.08	18.75	70.24
3	CH[d]	2	10.77	60.85	57.56	18.96	75.95
4	CH[d]	5	10.70	60.55	52.40	20.04	74.36
5	CH[d]	10	12.47	61.43	58.49	21.56	82.13
6	CH[d]	20	14.73	60.44	52.64	24	87.55
7	CH[d]	30	11.59	61.49	52.63	16.90	89.69

[a]Relative percentage directly obtained from GC-FID data. [b]Obtained by means of an external standard calibration curve. [c]Experiments via MW-assisted monomode radiation at 100 °C (previously optimized conditions). [d]CH: conventional heating (100 °C and 10 min ramp time).

atures, in contrast with this work. When SIRAL was used, it was either necessary to modify it with silica up to 40% (SIRAL 40) or to employ a longer residence time (20 min) at low silica modification (i.e., SIRAL 1−SIRAL 10) to selectively obtain p-cymene with quantitative conversion at 225 °C.[27]

To make the process more sustainable, it is important to reduce processing costs and the environmental footprint by avoiding any solid activation with heavy metals or acids, lowering the temperatures (80−100 °C), and shortening the reaction time to flash conversion time (0−5 min). Furthermore, the exploitation of solvent-free conditions and lower amounts of solid acid (ratio of 1:2 compared to the 1:4 ratio previously used) could pave the way for greener processing. Indeed, the conditions optimized in this work (Table 2) boosted the efficiency of the MW-assisted processes with respect to the use of nonactivated (sepiolite) or "mildly-activated" solid acids (SIRAL).

Finally, considering the disproportionation products (men-thanes) and bio terpene-based polymers concurrently obtained as high-added-value compounds instead of byproducts, a three-way valorization protocol for limonene conversion could be proposed. For instance, p-menth-3-ene is an attractive intermediate toward menthol,[35] an important flavor/fragrance molecule. In addition, p-menthane is commonly applied as a green solvent for cleaning applications and natural-product extraction,[35] with its use as a diesel-fuel additive also being noteworthy.[36] Finally, p-menth-1-ene gains especial attention as an intermediate in the synthesis of chemicals such as adhesives, coatings, food, and drugs that can be developed.[37]

Further, concerning polymers, the main compounds detected by GC−MS in these experiments were kaur-16-ene (a), podocarpa-6,13-diene, 13-isopropyl (b), and A-D-neo-oleana-12,14-diene (c) (Figure 2). In this context, the potential

biological activity of these high-molecular-weight terpenes is remarkable; they can be used as anticancer, anti-inflammatory, antimelanogenic, and antioxidant agents, as well as in neuroprotection, cytotoxicity, and allelopathy.[38−41]

3.2. Limonene Conversion under Conventional Heating. Before the possibility of scale-up was evaluated, experiments were also performed under CH for the sake of comparison. In this regard, and considering the optimal conditions previously achieved (100 °C, 0 min; 90 °C, 2 min; and 80 °C, 5 min—Table 2), the selected temperature was 100 °C. In general, under CH, a nonintensified process takes place, unlike with the monomode MW, meaning that harsher conditions might be required to achieve similar results. For that reason, the temperatures of 80 and 90 °C were rejected for these CH experiments as a longer residence time would probably have to be applied (as occurred in the case with MW), therefore prompting the formation of polymers at the expense of total p-cymene. The results are summarized in Table 4.

As expected, considerable differences were found between the CH and MW-assisted processes under the same experimental conditions (100 °C, 0 min) (Table 4, entries 1 and 2). This is even more pronounced if we consider the heating-ramp time, which was approximately 90 s for MW and 10 min for CH, as mentioned. For instance, almost quantitative conversion was achieved under MW (96.28%), whereas only 70.24% was detected under CH (Table 4, entries 1 and 2). Moreover, product yields and selectivity differed considerably, especially the total p-cymene content (21.35 vs 9.63% under MW and CH, respectively). Finally, no significant differences were observed for menthanes when comparing the two heating strategies (60.45% p-cymene/disproportionation by CH and 61.07% by MW) (Table 4, entries 1 and 2).

Table 5. Product Selectivity for the MW-Assisted Conversion of Limonene in a Multimode MW Reactor Suitable for Numbering-Up (MW-Multimode 4N-Up)

	conditions (T, t)	p-cymene (%)[a]	p-cymene/disprop. (%)	p-cymene/isomer. (%)	p-cymene/others (polym.) (%)	conversion (%)[b]
1	80°C, 20 min	0.77	56.62	4.17	1.55	83.88
2	**90°C, 20 min**	**17.79**	**60.16**	**75.70**	**23.57**	**95.30**
3	100°C, 0 min	2.64	52.07	16.76	7.02	53.40
4	100°C, 2 min	7.43	59.11	30.91	14.52	75.47
5	100°C, 5 min	13.60	58.39	52.53	19.87	91.57
6	**100°C, 10 min**	**15.80**	**60.56**	**68.43**	**20.24**	**96.11**
7	100°C, 20 min	2.24	64.18	86.15	2.25	99.39
8	110°C, 5 min	11.41	58.01	50.87	14.93	97.26
9	110°C, 10 min	10.68	59.01	92.71	11.80	98.82
10	120°C, 5 min	6.87	59.28	62.12	7.83	98.21
11	**165°C, 0 min[c]**	**18.08**	**60.45**	**97.62**	**20.85**	**98.77**

[a]Relative percentage directly obtained from GC-FID data. [b]Obtained by means of an external standard calibration curve. [c]5 min heating ramp.

Considering only CH, different reaction times (from 2 to 30 min) were subsequently tested at 100 °C (Table 4, entries 3–7). In brief, the values for total p-cymene and p-cymene/polymer selectivity tended to increase from 0 to 20 min (9.63 to 14.73%) for the former and from 18.75 to 24% for the latter (Table 4, entries 2 and **6**). However, from 20 min onward, polymer formation was favored in contrast to the desired p-cymene, and thus, 16.90% was observed for p-cymene/polymer selectivity and 11.59% p-cymene at 30 min (Table 4, entry 7).

Regarding menthanes and terpenes, no significant differences were observed when increasing the time from 2 to 30 min. In the first case, p-cymene/disproportionation selectivity ranged from 60.45 to 61.49%, whereas 52.40–58.49% was found for p-cymene/isomerization (Table 4, entries 2–7). Finally, total conversion increased with reaction time, as expected, with a maximum value of 89.69% after a 30 min reaction (Table 4, entry 7) and 87.55% at 20 min (Table 4, entry **6**).

Therefore, 100 °C and 20 min were selected as the optimal conditions for limonene conversion under CH, mainly according to the selected parameters in terms of total p-cymene (14.73%), p-cymene/polymers selectivity (24%), and conversion (87.55%) (Table 4, entry **6**). However, these results still differ from those of the MW experiments (21.35, 27.45, and 96.28%, respectively) (Table 4, entry 1) at the same set temperature of 100 °C. This difference was especially noticeable for total p-cymene selectivity, with a value of 44.94% being higher than that found in the CH experiments (Table 4, entries 1 and **6**).

Some examples have been reported in the literature for this transformation under CH.[11] Despite the engaging results achieved, environment-impacting and harmful conditions were required; for instance, temperatures between 260 and 370 °C, residence times from a few hours to 70 h, and the employment of organic solvents and acidic-modified solids were necessary for conversion.[23,25,26,42] Therefore, considering the further application of the developed protocol to biorefineries, a compromise should be established between sustainable conditions and p-cymene yields, thus ruling out these above-mentioned works in our considerations.

In this context, only the work of Catrinescu et al. can be considered for the sake of comparison[24] since 150 °C and 15 min were the experimental conditions employed. Once again, our reported results are promising as only 5 and 1% of total selectivity for p-cymene with two different Ni-modified clays, with 70 and 15% conversion, respectively, were achieved in this

work.[24] Considerably lower p-cymene ratios, with respect to terpenes, menthanes, and polymers, were achieved compared to those of this work, where no catalyst treatment was performed.

3.3. MW-Assisted Multimode Conversion of Limonene. *3.3.1. MW-Multimode System for a Numbering-Up (MW-Multimode 4N-Up) Approach.* The optimal conditions previously achieved in the MW monomode system (100 °C, 0 min; 90 °C, 2 min; and 80 °C, 5 min) were investigated for further experiments in multimode ovens in order to evaluate possible MW-assisted limonene conversion on a larger scale. We first considered a MW multimode reactor suitable for reaction numbering-up.

In the case of the MW-multimode 4N-up reactor, the MW source directly matches the cavity shape for homogeneous MW distribution. This cavity consists of a 1 L Teflon vessel, in which a MW-conducting solution was introduced. Therefore, the effect of MW externally comes to the glass vial, which is supported in a simultaneous tool rack configuration (Figure S2).

Despite the nonfocalized MW radiation that this system provides, a wide number of samples (up to 22) can be loaded, thus overcoming the limitation of the monomodal MW instruments that can heat one single vial. In this regard, parallel reactions can be simultaneously carried out under the same temperatures and conditions in a tool rack with multiple positions. Therefore, an intermediate numbering-up approach can be developed prior to scaling-up.

As mentioned, initial experiments were performed using the optimized MW monomode conditions. However, owing to the kind of heating occurring in this MW instrument, a slight variation in these experimental parameters was needed. The results are summarized in Table 5.

First, reactions were carried out at 100 °C according to the CH and preliminary conditions investigated in the monomodal reactor (Table 5, entries 3–7). In brief, the effect of MW was remarkable for 10 min experiments at this temperature (Table 5, entry 5). For shorter times (0–5 min), total p-cymene selectivity, as well as p-cymene selectivity with respect to menthanes, terpenes, and polymers, decreases (Table 5, entries 3–5), with no remarkable results in any case, although the conversion increased from 0 to 5 min. From 10 min onward, despite the quantitative conversion achieved at 20 min (Table 5, entry 7), a considerable drop, to 2.24%, in total p-cymene yield was observed (Table 5, entry 7), and large amounts of polymers were formed (only 2.25% p-cymene/polymerization

Table 6. Product Selectivity for the Conversion of Limonene in a MW-Multimode Reactor (MW-Multimode 4S-Up)

conditions (*T*, *t*)	*p*-cymene (%)[a]	*p*-cymene/disprop. (%)	*p*-cymene/isomer. (%)	*p*-cymene/others (polym.) (%)	conversion (%)[a]
110°C, 2 min	13.17	56.48	98.36	14.81	99.93

[a]Relative percentage directly obtained from GC-FID data.

Table 7. Comparison of the Results Achieved in This Work for the Transformation of Limonene under Solvent-Free Acidic Conditions Using Different MW Technologies

	MW device	conditions (*T*, *t*)	ratio (limonene/ solid acid)	*p*-cymene (%)[a]	*p*-cymene/ disprop. (%)	*p*-cymene/ isomer. (%)	*p*-cymene/ polym. (%)	conversion (%)	refs.
1[b]	monomode	80 °C, 5 min (70″ ramp)	1:2	22.61	62.73	98.85	27.93	97.52	this work
2[b]	multimode 4N-up	165 °C, 0 min (5′ ramp)	1:2	18.08	60.45	97.62	20.85	98.77	
3[b]	multimode 4S-up	110 °C, 2 min (15′ ramp)	1:2	13.17	56.48	98.36	14.81	99.93	
4[c]	monomode	225 °C, 20 min	1:4	9.92		32		31	Martin-Luengo et al. (2010)[16]
5[d]	monomode	225 °C, 10 min	1:4	19.04		34		56	Martin-Luengo et al. (2008)[27]

[a]Relative percentage directly obtained from GC-FID data. [b]Tonsil supreme (acidic clay). [c]Nonactivated sepiolite (clay). [d]Acid-modified (1 wt %) mesoporous silica−alumina supports (SIRAL).

selectivity was achieved). Therefore, it was evident that polymers are the predominant compounds at reaction times longer than 10 min.

Furthermore, lower temperatures were also tested (Table 5, entries 1−2) according to the optimized conditions for MW-assisted monomode experiments. As a progressive temperature decrease has already been shown to entail longer residence times, 20 min was selected as the preliminary time in these experiments.

In this context, significant differences were observed by slightly decreasing temperatures from 90 to 80 °C, as observed in the total *p*-cymene yield, which fell from 17.79 to 0.77% (Table 5, entries 1−2). Considering these results, neither longer nor shorter times were applied at 80 °C, thus ruling out this temperature value for this MW multimode reactor.

Once again, as higher temperatures involve shorter reaction times to achieve similar results, as observed at 90 and 100 °C where reaction times dropped from 20 to 10 min (Table 5, entries 2 and **6**), experiments were performed at 110 and 120 °C for 5 min (Table 5, entries 8 and **10**). Furthermore, even at 110 °C, 10 min were considered, for the sake of comparison with 100 °C (Table 5, entry 9). As observed, this variation did not lead to a satisfying *p*-cymene yield, with this run, in any case, the formation of polymers with the increase of both temperature and time was lower (Table 5, entries 8−10).

Finally, some tests were performed at temperatures higher than 120 °C. In this context, only an ultraflash process performed at 165 °C (0 min, 5 min heating ramp) entailed progress in terms of *p*-cymene yield compared to the above results (Table 5, entry 11). In fact, the obtained values were noticeable (18.08% for total *p*-cymene, 98.77% conversion, 97.62% *p*-cymene/terpenes, and 20.85% *p*-cymene/polymer selectivity) (Table 5, entry 11). Therefore, these conditions could be considered, along with 90 °C, 20 min, and 100 °C, 10 min, as the optimized conditions in multimode MW-assisted experiments.

Overall, a multimode reactor was employed to overcome the limitations of monomodal MW instruments from the perspective of scaling up MW-assisted limonene conversion. As observed, under the optimal conditions, slightly lower selectivity for *p*-cymene was found with respect to the

monomodal experiments (compare Table 2, entries **2**, **4**, and **6**, and Table 5, entries 2, 6, and **11**). Despite this, the wide scope of parallel reactions occurring when using this multimode MW reactor is remarkable. Moreover, despite the variation in the previously optimized experimental conditions, these new ones were still environmentally friendly as, for instance, no alteration of the solid acid was carried out and the ratio between limonene and the solid acid used for conversion was kept constant (1:2). Furthermore, a flash process was developed (0 min plus 5 min heating ramp) despite the higher temperatures applied (165 °C). Nonetheless, lower temperatures (90−100 °C) could still be maintained, affording good results. In any case, as observed, valuable progress was achieved with respect to the works reported in the literature under MW (see Table 3, entries 4−10).[16,27]

3.3.2. MW-Multimode System for the Scale-Up (MW-Multimode for 4S-Up) Approach. So far in this work, small-scale reactions (50 mg) have been performed in MW and conventional reactors, even if the multimode MW reactor allowed up to a maximum of 22 reactions to take place in parallel. In this regard, to achieve a scale-up of MW-assisted limonene conversion, a second multimode MW reactor (MW-multimode 4S-up) was exploited starting from the 8 g scale (Figure S3), with a view to further apply the optimized conditions in this system with a maximum of 70 L capacity for industrial scale-up. To investigate the upscaling of the reaction, experiments were first performed in a classic glassware setup (40 mL maximum) using the rotating diffuser coupled to a vacuum pump, as a proof of concept. The results are summarized in Table 6.

As observed, 110 °C and 2 min were selected as preliminary experimental conditions. However, the first step involved a 10 min heating ramp to 80 °C and, subsequently, a further 5 min to achieve 110 °C. Then, a flash process (2 min) was considered for the complete reaction. It should be noted that longer heating ramps and slightly higher temperatures were applied compared to those in the above systems. This was due to the large size of the MW cavity (70 L).

Considering the results, almost full conversion was still achieved after treatment (99.93%) (Table 6), which highlights the potential of the MW-multimode 4S-up system even at mild

Table 8. Main GCPMs Evaluated in This Work for the Conversion of Limonene in the MW-Monomodal System, MW-Multimode for Numbering-Up and Scale-Up (4N-Up and 4S-Up) Systems, and under Conventional Heating

	E-factor (kg/kg)	AE[a] (%)	AEF[a] (%)	PMI[a] (kg/kg)	PMP[a] (%)	RME[a] (%)
			MW-Monomode			
80 °C, 5 min	**0.46**	98.52	22.84	**1.46**	68.51	**98.81**
			MW-Multimode 4N-Up			
165 °C, 0 min	**0.45**	98.52	17.81	**1.45**	68.93	**99.41**
			MW-Multimode 4S-Up			
110 °C, 2 min	**0.04**	98.52	12.97	**1.04**	**95.99**	**99.93**
			CH			
100 °C, 20 min	0.53	98.52	14.51	1.53	65.18	94.01

[a]Abbreviations. AE: atom economy; AEF: atom efficiency; PMI: process mass intensity; PMP: process mass productivity; RME: reaction mass efficiency.

temperatures. *p*-Cymene/isomerization selectivity was also remarkable (98.36%). For menthanes, by contrast, this value was considerably lower (56.48% *p*-cymene/disproportionation, Table 6). However, this result did not notably differ from those obtained with the above MW systems (monomodal and multimode 4N-up) under the optimized conditions (60−65%) (Tables 2 and 5). Considering total *p*-cymene, the selectivity decreased to 13.17%, which is a lower value than that with the other multimode reactor (MW-multimode 4N-up) (Table 5). Finally, opposite results were observed regarding polymers, which were favored in contrast to *p*-cymene, with only 14.81% *p*-cymene/polymerization selectivity (Table 6).

Overall, the conversion of biomass-derived limonene to bio *p*-cymene is summarized in Table 7 (only considering the best results).

As observed, the application of a different MW device and, therefore, reaction conditions strongly influences the selectivity of the process. For instance, the monomodal MW system would be the most appropriate with which to achieve higher total *p*-cymene selectivity (Table 7, entry 1), also leading to the lower formation of polymers compared to multimode reactors (Table 7, entries 1−3). However, when considering other valorization routes (i.e., the development of polymers with biological activity), the application of a multimode MW system suitable for scale-up could be proposed. In this regard, the total *p*-cymene selectivity found was lower compared to that achieved under monomodal conditions (i.e., 13.17 vs 22.61%, respectively, Table 7, entries 1 and 3), and the amount of polymers was noticeable (75.77% of total products, Table 7, entry 3). For menthanes and terpenes, however, no significant differences between the monomodal and multimode reactors were found (Table 7, entries 1−3). Therefore, we herein propose an alternative and valuable pathway for the conversion of limonene, focusing mainly on the almost total transformation achieved in each process, especially for multimode reactors. Additionally, the results obtained with any MW strategy are an improvement on those reported by Martin-Luengo et al.[16,27] in terms of *p*-cymene yield and green conditions (Table 7, entries 4−5).

Generally, the multimode MW reactors employed in this work represent valuable progress in the state of the art since it is the first time that they have been applied for these purposes, to the best of the authors' knowledge. Only the works of Martin-Luengo et al. have reported a preliminary scale-up for limonene conversion to *p*-cymene.[16,27] However, these works were performed with a monomodal reactor, with the limitations previously mentioned. Thus, both of the multimode MW systems described in this work (MW-multimode 4N-up

and MW-multimode 4S-up) should be remarkable as they entail the possibility of going beyond the laboratory scale. Finally, what we observed is that the application of different MW reactors entails some alterations in reaction temperatures and times, in accordance with the distinct radiation principles (mono- or multimode) (Table 7, entries 1−3). In any case, all of these conditions could be considered environmentally friendly [i.e., only 5 min with a monomodal reactor at 80 °C (Table 7, entry 1); 90 in. heating ramp at 100 °C with this system as well (Table 2, entry 6); 90 °C, 20 or 165 °C, 0 min in the MW-multimode 4N-up reactor, and the flash process (2 min) developed at 110 °C with the multimode 4S-up MW reactor (Table 7, entry 3)]. Moreover, there is no solid acid activation, and no solvents were needed in the present work, in line with sustainable processing.

In summary, this study represents significant progress compared to previous literature according to the green processing, circular economy, and process-intensification approaches toward scale-up. The conventional and nonconventional extraction of citrus wastes normally affords limonene up to 97%, with *p*-cymene then being produced from this chemical.[11,43] In light of that, and notwithstanding the unmet market demand for limonene, this study presents a feasible solution for the production of *p*-cymene and is an improvement on traditional and nongreen Friedel−Crafts reactions, highlighting process intensification principles for limonene conversion, which can be recovered from citrus waste.[11] Nonetheless, the selective production of *p*-cymene from limonene still remains a scientific challenge. Thus, to the best of the authors' knowledge, more investigations are required in this field in order to achieve, for instance, an optimal balance between the solid nature/content and optimize the reaction conditions and the technology applied.

3.4. Evaluation of the Environmental Impact of the Conversion of Limonene under MW-Monomodal and Multimode Systems: Green Chemistry Performance Metrics. In light of the above explanations and in order to pursue the desirable goals for scale-up, it is first necessary to evaluate the environmental impact of a chemical process. In this scenario, the GCPMs are factors that measure how some crucial parameters affect a chemical process in relation to green chemistry principles. In other words, GCPMs determine how green a chemical process is. In this work, for instance, the production of *p*-cymene, the amount of waste and undesired products generated, and the conversion of limonene have been evaluated. These factors were measured using the following GCPMs: *E*-factor, AE, AEF, PMI, PMP, and RME (Supporting Information, Section S3) on the basis of the works reported by

Gude and Martinez-Guerra[44] and Martínez et al.[34] They were calculated for both the MW-monomodal and -multimode systems and compared to those of the CH applied. The results are summarized in Table 8.

The *E*-factor considers the amount of unusable products generated throughout a chemical process. Thus, a high *E*-factor relates to a large amount of waste, which encompasses an undesired environmental footprint. In fact, a low *E*-factor value could be a benchmark of sustainability.

As mentioned, considering the wide applicability of the isomerization, disproportionation, and polymerization products, for instance, for use as fuel, in extraction, or as bioactive compounds,[35−41] these substances are considered useful products and therefore excluded from the "waste" in the *E*-factor on the basis of the work of Gude and Martinez-Guerra.[44]

As shown in Table 8, and considering zero as the ideal *E*-factor, noteworthy values were obtained for the conversion assisted by the MW-monomodal and multimode 4N-up systems (0.46 and 0.45, respectively). Moreover, the application of this nonconventional, intensified MW treatment allowed us to increase the gap with respect to traditional heating to up to 20% (0.53 *E*-factor). Nevertheless, the desired value was nearly accomplished after implementation of the MW-multimode 4S-up approach (*E*-factor = 0.04). In this system, a larger amount of limonene was processed (up to 8 g with the possibility to use a 70 L capacity chamber) and converted into valuable chemicals; the compromise achieved in terms of environmental sustainability is worth noting since the amount of generated waste is negligible.

AE measures the proportion of reactant atoms incorporated into the targeted product, thus allowing the proportion of these reactants that lead to waste to be calculated. For this work, AE was calculated considering the main reaction from limonene to *p*-cymene (see Table 1), regardless of the formation of useful fine products (polymers, menthanes, etc.) that were excluded from the *E*-factor since they come from side reactions. Besides, including these chemicals according to the AE formula (see Supporting Information, Section S3) would lead to an illogical value of above 100%. Finally, the solid acid (clay, Tonsil supreme) was also discarded based on some reported works in literature that evaluate the GCPMs for heterogeneous catalysis-based processes.[45,46] In summary, in view of these two considerations, both the CH- and MW-assisted systems have an AE of 98.52% (Table 8). Nonetheless, the AEF, calculated from the AE, includes the yield of the final product and thus indicates the real efficiency of the desired product. For this work, the abundance of *p*-cymene obtained using the CH- and MW-assisted (monomodal, multimode 4N-up, and multimode 4S-up) systems was considered (see Tables 4 and 7), with a maximum value of 22.84% for the MW-monomodal heating. However, the low selectivity to *p*-cymene in the MW-multimode 4S-up approach led to a low AEF of 12.97%, although there is no significant difference here compared with that of the conventional system (14.51%). Overall, the higher efficiency of the monomodal reactors to *p*-cymene in contrast to that of the multimode systems is confirmed, as explained.

PMI includes everything that is used in a process or process step and provides the equilibrium between the total mass of these species and the final product. For this work, only the initial limonene and solid acid were taken into consideration since the bioderived solvent used, 2-MeTHF, is recovered to be reutilized in further processes (see Results and Discussion Section). In parallel, the products obtained from side reactions

(biopolymers, menthanes, and terpenes) and hydrogen (H_2) were also considered useful products. PMI relates to the *E*-factor in order that **E-factor = MI − 1**.[44] Thus, a similar trend is observed when evaluating this factor with an almost ideal value of 1.04 being obtained for the MW-multimode 4S-up system. The other MW-based processes (i.e., monomodal and multimode 4N-up) show values of 1.46 and 1.45, respectively, slightly lower than that of CH (1.53), which should be noted in terms of environmental sustainability.

PMI can be transformed into a percentage, obtaining the PMP, which correlates the mass of the product and the total mass used in the process. Like PMI and the *E*-factor, the "product" in PMP not only includes *p*-cymene but also isomerization, disproportionation, and polymerization products and hydrogen (H_2). Given this fact, an engaging value is obtained for the MW-multimode 4S-up-based process (95.99%, Table 8), which improves upon the recorded PMP for MW-monomodal and multimode 4N-up by up to 40% (68.51 and 68.93%, respectively) and 47% for CH (65.18%), highlighting again the applicability of this system.

Finally, and bearing in mind the importance of efficiency in a chemical process,[34] the percentage of the mass of the reactants that remain in the product is evaluated using RME. The values herein obtained for the conversion of limonene are outstanding for any MW-based strategy (99−100%) and are mainly conditioned by residual limonene that remains after treatment, which means that almost quantitative conversions are achieved (Table 7). The MW-multimode 4S-up system should also be noted (99.93% RME), always with a view to its application at the industrial level; as occurred in the case for the *E*-factor, PMI, and PMP, the bioproducts concurrently obtained with *p*-cymene (i.e., polymers, menthanes, etc.) were included in this metric.

In summary, the GCPMs recorded in this work has corroborated that the present approach is novel and environmentally sustainable for the transformation of limonene into valuable products, even when using conventional methods. Nonetheless, MW-assisted processes improve efficiency and productivity compared with traditional protocols. Even when similar values are obtained in some metrics, the energy efficiency is higher in these MW systems because of the employment of shorter reaction times. In this context, the MW-multimode 4S-up system is especially remarkable, with the *E*-factor and PMP values of 0.04 and 95.99%, respectively, with the possibility of processing a large amount of limonene.

Finally, it should be noted that no comparison was carried out with the work reported in literature on the MW-assisted conversion of limonene[16,27] since it was not possible to recover sufficient data from the authors. Thus, with this study, we have paved the way for the development of more investigations into the green factors involved in this transformation, optimizing the chemical process in terms of economic, social, and environmental sustainability for further scaled-up processes, attending to the scarceness in the literature on this topic.

4. CONCLUSIONS

With the aim of producing bio *p*-cymene from biomass-derived limonene, a flash, sustainable method via MW-assisted radiation has been established. The applied monomodal and multimode MW technologies strongly influenced the selectivity of the process. Monomodal irradiation proved to be the most appropriate for high *p*-cymene selectivity. Nonetheless, the limitation of this reactor in terms of the quantity of sample

can be overcome using a multimode reactor. In this regard, a numbering-up approach has been developed in a multimode system since remarkable *p*-cymene selectivity is still achieved. Concurrently, the application of another multimode reactor suitable for scale-up was promising. Despite the decrease in terms of *p*-cymene selectivity compared to other reactors, the larger quantity of limonene that can be exploited in this system should be noted in view of scaled-up processing. Moreover, it is important to note, for this strategy, the amounts of both bio terpene-based polymers and bio menthanes formed as they are useful as biologically active compounds, extractive solvents, and fuels. The recorded GCPM values were outstanding, with almost ideal values for the *E*-factor (0.04), PMI (1.04), PMP (95.99%), and RME (99.93%) being observed. In any case, the mild experimental conditions applied to each MW-based system were noticeable (i.e., temperature, time, or solvent-free conditions), in line with the green processing, circular economy, and process intensification assessments. Overall, the results reported in this work would pave the way for further scale-up from a sustainable point of view, making this considerable progress for the state of the art in this field as the only two works reported with MW date back to 2008 and 2010,[16,27] to the best of the authors' knowledge, with there being a lack of study for more than ten years.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.iecr.4c00117.

> MW and conventional reactors: monomodal Anton Paar MW reactor; MW multimode SynthWAVE synthesis system for numbering-up (MW-multimode 4N-up); opened system with multiple rack tool and 1 L PTFE vessel; closed overhead stirrer with gas inlet connection (blue) and gas outlet (red); multimode FlexiWAVE MW synthesis system for scaling-up (MW-multimode 4S-up); 45° rotating reactor setup used for the limonene conversion; conventional LabTech XELSIUS instrument; GC−MS chromatogram: chromatogram by GC−MS for the transformation of limonene under MW-assisted acidic heating; and GCPMs (PDF)

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https://pubs.acs.org/10.1021/acs.iecr.4c00117

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

Notes

The authors declare no competing financial interest.

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