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Continuous Synthesis of *tert*-Butyl Peroxypivalate using a Single-Channel Microreactor Equipped with Orifices as Emulsification Units

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The two-step synthesis of *tert*-butyl peroxypivalate is performed in a single-channel microreactor. The first step, the deprotonation of *tert*-butyl hydroperoxide, is done in a simple mixer tube setup. The residence time section for the second reaction step is equipped with orifices for interfacial area renewal, needed for ensuring mass transfer between the two immiscible phases. The strong dependence of the reaction performance on the size of the interfacial area is demonstrated by using a setup with 4 orifices (distance of 52 cm), giving a HPLC yield of 71% at a residence time of 8 s and a reaction temperature of 23 °C. A further shortening of orifice distances helped to shorten the residence time down to 1.5 s and 0.5 s (using 9 orifices and 3 orifices with a distance of 5 cm). When using these setups, the produced heat could not be removed from the system sufficiently quickly (ΔT =38 K). The achieved yields (ca. 70% by HPLC) are close to the state of the art (cascaded batch processing) and provide an indication that the *tert*-butyl peroxypivalate synthesis can be performed at higher temperatures or at least, a more flexible process control can be allowed compared to high-volume batch reactors. Processing at higher reaction temperatures up to 70 °C shows a slight optimum at reaction temperatures between 40 °C to 50 °C, depending on the setup used. Knowing this novel process window as well as the optimum orifice geometry and distance will allow for tailored design of the microreactor. For the processing in the single-channel microreactor setup using 9 orifices (distance of 5 cm) and a reaction temperature of 40 °C a space-time-yield of 420000 gL⁻¹h⁻¹ was reached which is higher than the space-time-yield for the industrial 3 cascaded batch reactor process (190 gL⁻¹h⁻¹).

Introduction

Since the 1950s, organic peroxides have been intensively used in the chemical industry, especially as initiators in polymer production.^[1] This class of substances easily decomposes to free radicals and therefore is widely applied in free radical polymerizations, as cross linking and bleaching agents.^[2] Particularly, peroxyesters are used as initiators for the polymerization of ethylene or vinyl chloride. The thermal instability of these substances can lead to violent decomposition and, under certain circumstances, even to explosion if the heat generated by decomposition or reaction is not removed sufficiently quickly from the system.^[3-5]

The *tert*-butyl peroxypivalate (TBPP) synthesis investigated herein is a two step process and the information gained should also be applicable to other perester/peroxide syntheses.^[6,7] The first step, namely the deprotonation of the *tert*-butyl hydroperoxide (TBHP), is a single-phase reaction usually performed at a temperature of about 25 °C (Scheme 1).

The second step, namely the formation of the peroxyester by reaction of potassium *tert*-butyl peroxide (KTBP) with pivaloyl chloride (PivCl), is a two-phase reaction and is much more



Scheme 1. Deprotonation of tert-butyl hydroperoxide (step 1)



Scheme 2. Formation of tert-butyl peroxypivalate (step 2)

critical in terms of temperature sensitivity and corrosivity of the used reactants (Scheme 2).

Beside the temperature sensitivity of TBPP, the used PivCl is a strongly corrosive reactant and its hydrolysis in the alkaline aqueous reaction mixture is an undesired side reaction that needs to be suppressed.

The conventional perester synthesis, starting from hydroperoxides and carboxylic acid halides, is carried out in a batch or

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in a semicontinuous process under Schotten-Baumann conditions.^[2,7] The reaction temperature is predominantly controlled by stepwise dosing of the reactant and mainly limited by the thermal stability of the reactants, resulting in long reaction times. For example, for a 1 m³ reactor with a coefficient of heat transmission of 600 W m⁻²K⁻¹, sufficient heat removal at a process temperature of 20 °C is only possible for a dosing time of 90 min.^[8] The huge hold-up and the low surface-to-volume ratio in stirred tank batch reactors are two big disadvantages of this industrial process. Due to the exothermicity of both reaction steps, it is essential to control the reaction temperature as accurately as possible to avoid heat accumulation and finally a thermal runaway.

Herein we discuss the two-step synthesis of TBPP using a single-channel microreactor equipped with orifices as emulsification units. The shift from batch to continuous processing for the deprotonation step (see Scheme 1) will shortly be addressed. This step is done in a simple mixer tube setup, which is connected upstream of the second reaction step (detailed data is given in the Experimental Section). The continuous performance of the biphasic and exothermic second reaction step (Scheme 2) is more in the focus of this study. The use of microstructured devices is expected to prove advantageous in process safety by for example, smaller reaction volumes and thus less hold-up of reactants. Another process intensification criterion improvement of process performance by, for example, better control of reaction temperatures and residence times.^[9-29] Concerning the latter, a new microfluidic method and device for creation and renewal of an emulsion for improved mass transfer is introduced using a technique derived from high pressure emulsifiers—in the following named orifice set-up. The pre-emulsion is formed in a caterpillar micromixer in which mixing occurs due to recirculation flow mixing through bas-relief channel design.^[30] The subsequent attached residence time section consists of different numbers of orifices connected with a capillary to provide sufficient residence time and a sufficient number of emulsification units. Additionally, the influence of orifice distances on process performance is discussed, as well as the influence of the increased reaction temperature to allow for a novel process that is not accessible using batch reactors with a high internal volume. Finally, a benchmark is given to point out the benefits obtained using microreactor process technology.

Results and Discussion

Continuous deprotonation of TBHP

The production of KTBP in batch-mode is different to its production in continuous mode. In batch processing, the total stoichiometric amount of TBHP is added in portions, whereas in continuous mode, a stoichiometric amount of TBHP is added in one portion. The influence of the production process is investigated for a reaction temperature of 23 °C. The reaction time for the continuous deprotonation step was 4 s and the dosing time of TBHP in batch mode was around 20 min. Since it is not possible to analyze the yield of KTBP directly, the pro-



Figure 1. Influence of production process on potassium tert-butyl peroxide formation at a reaction temperature of 23 °C for both steps. Residence time for the subsequent conversion to TBPP is 8 s at a flow velocity of 0.34 ${\rm m\,s^{-1}}.$

cess performance was determined indirectly via the amount of TBPP produced and the amount of KTBP and PivCl consumed under the same reaction conditions (Figure 1).

The setup used is given in Table 1 (entry 1) and the residence time for the second reaction step was set to be 8 s at a flow velocity of 0.34 m s⁻¹. Both production processes resulted in similar yields and conversions; hence the shift from batch to continuous production is successfully demonstrated.

Table 1. Setup variations using emulsification units, delay loop consists of FEP with $OD = 1.59$ mm, i.d. = 0.8 mm, orifice is made of PEEK with i.d. = 0.25 mm.				
Ent	ry Numl of ori	per Distance of fices to orifice	of mixer 2 Distanc 1 [cm] to orific	e orifice Length of e [cm] delay loop [cm]
1	4	52	52	260
2	9	5	5	50
3	3	5	5	15
4	9	52	52	520

Influence of flow velocity and energy density

Given that the second reaction step is biphasic and no phasestabilizing agent is used, the reaction mixture coalesces shortly after having passed a micromixer (caterpillar type; recirculation flow mixing through bas-relief channel design, mixer 2; Figure 2) and generates an unwanted irregular segmented flow if no emulsification units are used (the use of segmented flow for ensuring mass transfer in the TBPP synthesis is discussed in Ref. [31]). This decrease in interfacial area slows down the reaction rate. Hence the implementation of emulsification units is necessary to renew the interfacial area for mass transport improvement. This renewal is done via orifices (reduction of channel diameter from 0.8 mm to 0.25 mm and so on) in which mixing occurs due to elongational flow and shear forces in laminar flow. Using this geometry, the flow velocity (0.34 m s^{-1}) is increased by a factor of 10, due to the decrease

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Figure 2. Exemplary process flow sheet for the continuous production of *tert*-butyl peroxypivalate using emulsification units, residence time section after mixer 2 is varied in length and distance of orifice to orifice (Table 1).

in channel diameter inside the pinhole, which is still in the laminar regime (Reynolds number Re = 377). The velocity gradient causes an elongational flow in front of the orifice and eddy formation thereafter, both of which lead to droplet break-up.^[32] A related concept for interfacial area renewal is discussed in Ref. [33]. In this case, two different structures-metal foam and stainless steel inlets-were implemented into the reaction channel and their influence on droplet disruption using a mixture of water, n-heptane, and sodium dodecyl sulfate (SDS) is discussed. To deform or even to break up a droplet, a minimum of energy input is needed. This energy is introduced via the total flow velocity and, accordingly, the generated pressure drop over the system, and has to be released in a very short time (order of milliseconds).^[34] A screening of flow velocities was undertaken to establish that needed to create an emulsion by the use of orifices. These experiments were done using the setup described in Table 1, entry 1, and visualized in Figure 2. The obtained yields and conversions at different flow velocities and residence times are given in Figure 3.

At a flow velocity of 0.02 ms^{-1} and a residence time of 123 s, the obtained yield was 71% by HPLC (non-isolated) but no emulsion was formed. Thus the yield obtained is mainly caused by provision of long residence time and by the internal circulations within the formed segments.^[31] The increase in flow velocity shortens the residence time and simultaneously improves mixing performance. Accordingly, there is an antagonistic interplay between residence time and mixing quality which are, as outlined above linked via the flow velocity. For a flow velocity of 0.09 ms^{-1} and a residence time of 31 s there are still fluid segments visible. The decreased yield, in this case,



Figure 3. Conversions and yields achieved by different flow velocities at a reaction temperature of 23 °C. The residence time is decreasing from 123 s, 31 s, 15 s, to 8 s since the delay loop and the number of orifices is kept constant.

is a result of short residence time and insufficient mixing. After a further increase of flow velocity to 0.17 m s^{-1} , corresponding to 15 s residence time, no segments were visible, but the obtained yield was still very low. This is an indication that the mixing quality was still bad, and also in this case the short residence time limited process performance. This assumption is proven by the yields obtained for a residence time of only 8 s at a flow velocity of 0.34 m s^{-1} . In this case, the reaction performance was significantly improved by the mixing quality, giving a yield of about 70% by HPLC (non-isolated) by shortening the residence time by a factor of 15 compared to the experiment performed at 0.02 m s^{-1} . In biphasic systems, the difference between emulsifying devices can be compared with one another by their efficiency in droplet disruption with the aid of energy density.^[35,36] In continuous systems the pressure drop is proportional to the energy density that is introduced into the system (Figure 4; setup as described in Table 1, entry 1, and a similar one without orifices).



Figure 4. Conversions and yields at a constant residence time of 8 s, a reaction temperature of 23 °C, a flow velocity of 0.34 m s^{-1} , and at different energy densities (left: using 4 orifices with 52 cm distance to each other total reactor length 260 cm, right: without orifices, total reactor length 260 cm).

The increase in energy density from $2.3 \times 10^5 \, \text{Jm}^{-3}$ to $3.5 \times$ 10^5 Jm⁻³, (contribution of each orifice with attached capillary = 0.3×10^5 Jm⁻³) resulted in an increase in yield and conversion of approximately 30% by HPLC (non-isolated). This significant advancement in process performance is based on the increase in interfacial area due to better emulsification. The fact that the increased yield is associated with an increase in interfacial area suggests that TBPP formation is limited by mass transfer. Thus, the process performance can be significantly improved by implementation of emulsification units. The conversion of TBHP and PivCl is still higher than the yield of TBPP obtained, which can be explained by side reactions like the alkaline hydrolysis of the reactants and of the formed product, or by their thermal decomposition. These decomposition products are not detectable using the RP-HPLC method described in the experimental section, hence no detailed discussion is given.

Shortening of process time

The strong dependency of reaction performance on the size of interfacial area was pointed out in the section above. The channel length of 260 cm (Table 1, entry 1) is not acceptable with regards to the manufacturing of a microstructured reactor with parallel channels. For this reason, we investigated whether the reaction time could be significantly decreased by short-



Figure 5. Comparison of yields obtained for minimized orifice distances of 5 cm at a reaction temperature of 23 $^{\circ}$ C and a flow velocity of 0.34 ms⁻¹; residence time is 0.5 s in the case with 3 orifices and 1.5 s in the case with 9 orifices.

ening the orifice distances by comparing two setups with different numbers of orifices (Figure 5 and Table 1, entries 2 and 3).

In both cases, the obtained yield was of the order of 70% by HPLC (non-isolated), meaning that the additional 6 orifices did not contribute to increasing the yield. An uncontrolled temperature increase (at maximum $\Delta T = 38$ K) at the outlet of the single-channel microreactor was detected. This increase in reaction temperature indicates insufficient heat removal. The slightly increased residence time, from 0.5 s to 1.5 s, had no significant impact on reaction performance. Nonetheless, the yields were close to the those for cascaded batch processing and provide an indication that TBPP formation can be carried out at higher temperatures or at least that more flexible process control can be allowed compared to high-volume batch reactors. All indications suggest that the capillary length between orifice to orifice only contributes minor to the yield obtained and is rather needed for the heat removal. The shortening of orifice distance resulted in a decrease in reaction time at a similar reaction performance to that for the setup with 4 orifices and a distance of 52 cm (Figure 3 at 0.34 $m\,s^{-1}$ and 8 s residence time).

Novel process window

The industrial TBPP process has to be performed under strict control of process parameters and already minor deviations in process temperature can cause a thermal runaway.^[6–8] The use of microreactors often enables new process routes under unconventional process parameters.^[9–29] In the previous section, we showed that the single-channel microreactor process could be performed with less-strict temperature control. This section focuses on the combination of both concepts—increased reaction temperature for increased reaction rate and better mixing for improved mass transfer—to find a novel process window for the synthesis of TBPP enabled by the use of low-volume microreactors. First experiments were done using the setup described in Table 1, entry 1, and the reaction temperature was

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Figure 6. Conversions and yields obtained using different reaction temperatures for a setup consisting of 4 orifices with 52 cm distance, at a flow velocity of 0.34 m s^{-1} and a residence time of 31 s.



Figure 7. Conversion and yields obtained using different reaction temperatures for the setup consisting of 3 orifices with a distance of 5 cm and a residence time of 0.5 s, at a flow velocity of 0.34 m s^{-1} .

varied between 10 $^\circ\text{C}$ and 70 $^\circ\text{C}$ and maintained by a thermostat bath. The results obtained are given in Figure 6.

On increasing the reaction temperature from 10°C to 20°C and then to 40°C, slight increases in conversion and yield were observed (from ca. 60% by HPLC at 10°C to ca. 75% by HPLC at 50 °C). At a reaction temperature of 50 °C, slight gas formation occurred and intensified for the experiments at 60°C and 70°C, causing a decrease in conversion and yield. This gas formation could result from a boiling reaction mixture triggered by hot-spots at temperatures higher than the boiling point of PivCl (b.p. = $107 \degree$ C). Temperature monitoring at 5 cm after mixer 2 (Figure 2) showed a slight increase in heat production with a simultaneous increase in reaction temperature $(\Delta T = 4 \text{ K at a reaction temperature of } 23 \,^{\circ}\text{C}, 8 \text{ K at } 40 \,^{\circ}\text{C}, 14 \text{ K}$ at 50 °C, and 17 K at 60 °C and 70 °C). The thermal decomposition of TBPP at a residence time of 31 s and a maximum reaction temperature of 70 °C can be neglected, assuming an absence of hot spots, since the half-life time of TBPP is 106 min at this temperature.^[37] The possibility to shorten the process time significantly by minimizing the orifice distances to 5 cm was described above. This process improvement is now combined with the concept of increased process temperature. These experiments were carried out using the setup described in Table 1, entry 3 (Figure 7).

At a reaction temperature of 40 °C, slight gas formation was observed and again increased at higher reaction temperatures (data not shown). The outlet temperature (measured after the last orifice) showed a significant temperature increase of $\Delta T \approx 17$ K at a reaction temperature of 10 °C, which increased to $\Delta T \approx 40$ K for the other reaction temperatures. The positive influence of increased reaction temperature on TBPP formation (Figure 6) is slight or negligible in this case, owing to the uncontrolled temperature increase caused by better emulsification (resulting in a higher heat production due to enhanced mass transfer). This heat is added to the introduced heat, which counteracts the otherwise positive effect.

The possibility to perform the TBPP synthesis at higher reaction temperatures by the use of a single-channel microreactor setup has been successfully demonstrated. Further investigations are intended to find an optimum combination of orifice distance and reaction temperature for a full opening of this novel process window.

Benefits gained from microscale process technology

The increase in reaction temperature and the implementation of microstructured devices are only reasonable if the existing process gains substantial benefit. To exemplify the benefits obtained from the discussed orifice concept, a benchmark is given of an industrial process performed in a triple cascaded batch reactor process with a single reactor volume of 350 L^[7] a microreactor process operated at lower temperatures and without the concept of redispersion,^[7] and two single-channel microreactor setups from this work (Table 1, entries 2 and 4). Earlier results comparing a mixer tube setup with these two processes are given in Ref. [31].

The industrial process, as described in Ref. [7], was performed at a reaction temperature between 10 °C and 20 °C with an estimated residence time of about 100 min. The obtained yield in this case was 84%, resulting in a space-time yield of 190 g L⁻¹ h⁻¹. The microreactor process^[7] was also performed at 10–20 °C reaction temperature. The obtained yield was 93% at a residence time of approximately 6 min resulting in a space-time yield of 3600 g L⁻¹ h⁻¹.

To clarify the significant impact of the orifice concept, two setups were compared with these processes, since both are not yet fully optimized and only a combination of both will lead to an optimum reactor concept for the production of TBPP. The first (Table 1, entry 4) gave a TBPP yield of 78% by HPLC (non-isolated) at a residence time of 15 s and a reaction temperature of 40°C, resulting in a space-time yield of 55600 gL⁻¹h⁻¹. A distance of 52 cm between the orifices helped to remove the heat of reaction from the system, but resulted in a long overall reactor length of 520 cm. An increase in the number of orifices per reactor length (Table 1, entry 2) resulted in a yield of 64% by HPLC (non-isolated) at a resi-

dence time of 1.5 s, and a reaction temperature of 40 °C. The corresponding space-time yield was 469000 g L⁻¹ h⁻¹. After extraction (see Experimental Section) of the separated organic phase, a 7% loss in yield took place, resulting in a space-time yield of 420000 g L⁻¹ h⁻¹, which is an order of magnitude higher than for the aforementioned processes and demonstrates the potential of this concept.

Conclusions

The shift from batch to continuous processing for the deprotonation step was successfully demonstrated with a simple mixer tube setup connected upstream of the second reaction step. The process performance was determined indirectly by the amount of TBPP produced, since the direct measurement of the deprotonation was not possible. The continuous deprotonation showed similar performance compared to the TBPP formation by which the deprotonation was done in batch mode. The concept of an orifice setup is introduced here as one possibility to re-emulsify the biphasic reaction mixture of the second reaction step. A flow velocity of 0.34 m s⁻¹, which equates to an energy density of $3.5 \times 10^5 \,\text{Jm}^{-3}$, is needed to break up the biphasic reaction mixture into smaller droplets. The shortening of orifice distances was shown to significantly shorten the reaction time (down to 0.5 s giving a yield of ca. 70% by HPLC, non-isolated). There is evidence that the capillary length between the orifices only contributes a minor amount to the yield obtained (as compared to the total reactor length), but rather is needed for heat removal. The influence of increased reaction temperature to open a novel process window for the TBPP synthesis was demonstrated by two different setups, distinguishing in the distances of the emulsification units. By using a setup with a distance of 52 cm from orifice to orifice, an optimum of reaction performance was found at a reaction temperature of 50°C with a corresponding yield of roughly 75% by HPLC (non-isolated). The increase to higher reaction temperatures had no significant impact on reaction performance, but instead caused undesired gas formation. Depending on the setups used, and thus depending on the provided interfacial area the maximum reaction temperature that can be used without gas formation is between 40 °C and 50 °C. The difference of the investigated setup variations was diminished by higher reaction temperatures. This diminution can be a result of changed physical properties and thus decreased differences in created interfacial area, or by internal hot spots, which counteract the effect of increased reaction temperature. Further investigations are needed to find an optimum combination of orifice geometry and distances. The implementation of this orifice concept into a microreactor design is expected to improve the TBPP process significantly and thus further investigations should help to optimize this single-channel microreactor setup and lead to a specially designed microreactor for the synthesis of TBPP. Finally, an approximate benchmark between an industrial process performed in a 3 cascaded batch reactor process with a single reactor volume of 350 L, a microreactor process, and two single-channel microreactor setups has been established. Processing in the single-channel microreactor setup using 9 orifices with a distance of 5 cm at a reaction temperature of 40 °C resulted in a space-time yield of 420 000 g $L^{-1}h^{-1}$, which is orders of magnitude higher than the space-time yield for a triple cascaded batch reactor process (190 g $L^{-1}h^{-1}$).

Experimental Section

General

KOH (puriss. p. a., Reag. Ph.) and TBHP (68 wt% solution in water) were purchased from Aldrich and used in the preparation of fresh aqueous solutions of KOH (22.7 wt%) and KTBP (2.65 mol L⁻¹). Acetonitrile (Rotisolv HPLC 99.9%) and NaOH (99% p. a.) were purchased from Carl-Roth, 1 N aqueous HCI (Titrisol) from Merck, extrapure NaC₂H₃O₂·3 H₂O from Riedel-de-Haën, and NaHCO₃ (\geq 99.7% puriss. p. a.) from Fluka. The orifices used were CUCPK Unions (tubing OD = 1.59 mm; i.d. = 0.25 mm) from Nordantec GmbH.

In the caterpillar micromixer, mixing occurs due to splitting and recombination of the fluid streams. A more detailed discussion of this principle is given in Ref. [30]. Mixer 1 = CPMM-V.1.2-R300/12 from IMM; mixer 2 = CPMM-V1.2-R300/12-PEEK-prefla from IMM.

Process parameters

Batch deprotonation of TBHP: For the preparation of KTBP in batch mode, a freshly prepared 22.7 wt% aqueous solution of KOH in a standard laboratory 3-necked flask was immersed in a water bath to maintain a reaction temperature 20-25 °C. The amount of KOH was set to be in a slight excess of 1.12 equivalents based on TBHP. A 68 wt% aqueous solution of TBHP was added in portions, in such a way that the temperature of the reaction mixture did not exceed 25 °C. The concentration of the resulting aqueous KTBP solution was 2.65 mol L⁻¹ (31 wt%).

Continuous deprotonation of TBHP: For the continuous deprotonation step, both reactants—KOH (22.7 wt%) and TBHP (68 wt%) were fed with HPLC-pumps (Knauer K-501 with a 10 mL stainless steel pump head) into a caterpillar micromixer (CPMM-V.1.2-R300/ 12 from IMM) connected with a reaction time section (Teflon or fluorinated ethylene propylene (FEP)) capillary; OD=1.59 mm; i.d.= 0.25 mm, *L*=110 cm). Both feed streams were preheated and cooled using a 1/16" Teflon capillary. The outlet and both inlet temperatures were controlled in line, using a Type K miniature thermocouple. The feed rates were adjusted in such a way that the KOH was in a slight excess of 1.12 equivalents based on TBHP (TBHP feed rate=3.1 mLmin⁻¹; KOH (22.7 wt%) feed rate= 5.02 mLmin^{-1} ; PivCl feed rate=2.2 mLmin⁻¹). The heat of reaction was 23 kJ mol_{TBHP}, resulting in an adiabatic temperature rise of 25 K for a solution of 6.78 molL⁻¹_{TBHP} and a solution of 4.85 molL^{CH}_{E0}.

Conversion of KTBP and PivCl to TBPP: The premixing step for the conversion of KTBP with PivCl was done by using a caterpillar micromixer (CPMM-V1.2-R300/12-PEEK-prefla from IMM). Re-emulsification was done using orifices with an i.d. of 0.25 mm made out of polyether ether ketone (PEEK). The number of orifices and their distances were varied. An overview on the setups used is given in Table 1. The PivCl was fed via a Knauer Smartline 1000 with a 10 mL titanium pump head. The necessary residence time was provided by a 1.59 mm FEP capillary with an i.d. of 0.8 mm. The heat of reaction was 126 kJ mol $_{\rm PivCl}^{-1}$ resulting in an adiabatic temperature rise of 72 K for a solution of 2.65 mol $L_{\rm KTBP}^{-1}$ and a solution of 8.04 mol $L_{\rm PivCl}^{-1}$

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TBPP isolation: The influence of the work-up procedure was demonstrated by working-up one sample. The organic phase of the crude reaction mixture was separated from the aqueous phase by using a standard laboratory separating funnel and was then extracted with 10 wt% aqueous NaOH (40 mL), 10 wt% aqueous NaHCO₃ (40 mL), and 5 wt% aqueous NaC₂H₃O₂ (40 mL). This procedure is based on the method described in Ref. [7].^[7] The purity of the organic phase was checked by using the HPLC method described below.

Analysis

The analysis of the reaction mixture was done by reversed-phase HPLC. Samples of the reaction mixture (1–1.5 g) were diluted with a 7:3 mixture of acetonitrile and water (20 mL; pH 2.5 adjusted with 1 N aqueous HCl) and then injected into the HPLC. Due to this aqueous analytical method, the remaining PivCl in the reaction sample was hydrolyzed to pivalic acid. Hence it was not possible to differentiate whether hydrolyzed PivCl originated from the continuous production of TBPP or from the sample preparation. Presumably, pivalic acid originated from a combination of both.

For the HPLC measurements, the following apparatus were used: Shimadzu UV/Vis Detector SPD-10 A VP; Shimadzu System Controller SCL-10 A VP; Shimadzu Liquid Chromatograph LC-10AD VP. The sample amount was measured with a sample loop of 5 μ L internal volume. The used RP-HPLC column was a 250×4.0 mm Nucleosil 120C 18 5 μ m (Art. No. 250.40.3135.N, Ser. No. 15130818). And the eluent consisted of MeCN and water (pH 2.5 adjusted with 1 N aqueous HCl) with a total flow rate of 1 mLmin⁻¹. This resulted in a starting pressure of 15.2 MPa using a fluid gradient with following operation conditions: Pump A: t=2 min, MeCN (0.25 mLmin⁻¹; pump B: t=2 min H₂O 0.75 mLmin⁻¹; pump A: t=5 min MeCN 0.7 mLmin⁻¹; pump B: t=5 min H₂O 0.3 mLmin⁻¹; pump A: t= 8 min MeCN 0.7 mLmin⁻¹; pump B: t=10 min MeCN 0.25 mLmin⁻¹; pump B: t=10 min H₂O 0.75 mLmin⁻¹.

The reaction components were detected at two different wavelengths, 215 nm (λ_1) and 230 nm (λ_2), at the following retention times: TBHP 4.4 min; PivCl 6.6 min; TBPP 11 min.

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