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Microwaves under pressure for the continuous production of quinoline from glycerol

H. Saggadi^{a,b}, I. Polaert^{a,*}, D. Luart^b, C. Len^{b,c}, L. Estel^a

^a LSPC – Laboratoire de Sécurité des Procédés Chimiques, EA 4704 – INSA Rouen, Avenue de l'Université, Saint-Étienne-du-Rouvray Cedex 76801, France

^b TIMR – Transformations Intégrées de la Matière Renouvelable, EA 4297 UTC – ESCOM, Compiègne 60200, France

^c Department of Chemistry, University of Hull, Hull, HU6 7RX, England, United Kingdom

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ABSTRACT

Microwave heating is an interesting technology for chemical engineering, since it can provide effective volumetric heating of the reaction medium and reduce energy costs. Many commercially available laboratory-scale microwave reactors have already been used to carry out chemical reactions on a small scale (a few milliliters), and at high temperatures and pressures. Some research has been undertaken to scale-up microwave processes and make them suitable for a larger scale production.

Indeed, combining wave propagation through the walls of a reactor with resistance toward high pressure and temperature as well, is not an easy task. For these reasons, this work focuses on the development of a pilot scale microwave apparatus used for the heating of larger reaction volumes under pressure, and under controlled conditions. The specially designed microwave apparatus allows chemical reactions in batch or continuous mode. The applicator operates in single mode enabling a uniform electromagnetic field, and well controlled operating conditions. The main advantage of the setup is the quite large reactor volume that permits either relatively long residence times or relatively high mass flowrates (up to 1 kg/h). The developed microwave apparatus was then used for quinoline synthesis from glycerol via a modified Skraup reaction. The major advantage of our system is the ability to carry out continuous chemical synthesis, at a large pilot scale, and high temperatures (200–220 °C), while ensuring a better control of the pressure (max. 19 bar) through the control of the power absorbed by the reaction medium.

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1. Introduction

The application of alternative forms of energy sources for conducting chemical reactions is at the heart of process intensification approach. Among these energy sources, microwave heating is recognized as a very promising technique to intensify chemical processes [1,2]. One can notice the rapid growth of microwave assisted procedures in organic synthesis since the publication of the pioneering papers by Gedye et al. [3] and Giguere et al. [4] in 1986. Rapid microwave protocols can be developed for most chemical transformations requiring heat. The activity in this new technique has experienced exponential growth and has been reviewed in the areas of material science, food technology, environmental technology, organic synthesis, polymer synthesis, etc. [5,6]. Indeed, microwave technology is already used in some industrial sectors

such as in the drying process of fruits, food, and pharmaceutical powders as well as for polymer chemistry. In medicine, microwaves are used in resonance therapy and thermography [7,8]. Microwave irradiation offers many advantages compared to conventional heating. Electromagnetic energy is actually transferred directly into the material via radiation without loss by means of heat conduction and convection. Consequently, an instantaneous and uniform volumetric heating is obtained for microwave-absorbing material, and heating occurs therefore from the inside to the outside of the medium. Easy automation and incident power control are also achieved. In numerous chemical syntheses, rapid heating, selective heating and enhancements of yield and purity are obtained [5,8,9].

Many laboratory-scale microwave reactors have been widely used for conducting different chemical reactions. The commercially available microwave devices are divided into two groups. The first category consists in multimode ovens. They are often equipped with a small tubular reactor inside (Teflon coil, or glass or quartz tube) [10], of only a few milliliters, in which different organic syntheses have been carried out. Some of them have been performed under high pressure (up to 120 bar) and at temperatures of up to

* Corresponding author. Tel.: +33 232956668.

E-mail addresses: hanen.saggadi@insa-rouen.fr (H. Saggadi), isabelle.polaert@insa-rouen.fr (I. Polaert).

250 °C [11,12]. Most of the devices have been optimized in order to achieve better reaction control, namely temperature and pressure control. These developments have obviously led to investigating the scalability of microwave heating, either by using larger reaction volumes in batch mode, or by multiplying the number of small vials in the ovens [12–15], or by using the continuous mode [16–18]. Despite being able to control the main parameters (temperature, pressure, and reaction medium stirring), as well as the automation of the device, an important parameter remains uncontrolled: the electromagnetic field distribution. While most of the commercially available multimode devices involve a static microwave diffuser to homogenize the wave distribution, the electromagnetic field distribution can never be controlled and its homogeneity cannot be ensured. This leads to a lack of temperature uniformity in the reaction medium and hot spots can occur, especially if the cavity possesses multi-reaction vials.

The second category consists in more advanced microwave reactors, involving a waveguide to create a standing wave. Single-mode applicators are used, allowing the propagation of a quasi-uniform field on the reactor zone. The reaction can then be conducted under well controlled operating conditions. The electric field densities in single-mode cavities are higher, allowing absorbing mixtures to be rapidly heated. Microwave input and reflected powers can be measured, the absorbed energy estimated, and the interactions of the wave with the medium can be identified. The most commonly used batch devices (e.g., Biotage, CEM, Anton Paar) permit, in some cases, interesting conditions for chemical reactions (temperatures up to 300 °C and pressures up to 30 bar). However, in these commercially available single-mode batch reactors, the reaction volume is very small (~50 mL) and not adapted to production [19,20].

As for multimode systems, some studies have focused on the scalability of single-mode pressurized devices, either by allowing larger volume reactions (12 bar, 500 mL)[21], or by developing continuous mode tubular reactors [19,22,23]. Although these developments have led to conducting chemical reactions at high temperatures (up to 300 °C) and under pressure (up to 50 bar) [19], once again, the volumes do not exceed 50 mL. This lays down typically short reaction times (in the order of a few minutes), and small flow rates. Despite these improvements, there are many remaining difficulties to scale up microwave pressurized reactors. One of the main limitations is the restricted penetration depth of microwave irradiation into absorbing materials, which is generally in the order of just a few centimeters. When using larger batch reactors, reagents in the center of the reaction vessel are mostly heated by convection and not by direct microwave dielectric heating. The heating rate of the mixture is therefore affected, leading to extended processing times [20,24]. This physical limitation is one of the main reasons for the development of continuous flow reactors.

Another important issue for the scalability of the continuous pressurized microwave reactions is the necessity to use reactors that are transparent to microwave. Only materials like quartz glass, some polymers and some ceramics can be used [19]. However, combining these materials with resistance toward chemicals, high pressure and temperature is not easy to carry out. Thus, scaling-up microwaves must mainly fulfill the following criteria: (1) safe and reliable equipment, (2) high reproducibility, (3) good reaction control, (4) fast heating time, (5) reasonable volume, (6) acceptable energy balance, (7) comparable or higher yield to conventional systems, and (8) acceptable cost [19].

Keeping these issues in mind, the challenge of this work is to design a continuous microwave reactor dedicated to organic synthesis at high temperatures and pressures. A chemical production of about 1 kg/h is targeted, for relatively slow reactions requiring quite long residence times (10–20 min). This device has to operate reliably and safely with volatile compounds including organic solvents. Nevertheless, developing a microwave-transparent reactor

with resistance toward pressure is a hard task. Indeed, controlling experimental conditions has to be managed, including pressure, temperature, time, homogenization of the medium, reagents/products flow (in the case of continuous mode reaction), and post-reaction cooling. Our approach requires scale-up, solving the technical issues, in terms of technical tools for temperature and pressure measurement and control, as well as reactor design and implementation of elements allowing batch and continuous mode operations for larger quantities. It is also imperative to ensure that the apparatus functions safely, and to plan power control and anticipate intervention procedures in the case of any emergency.

The developed microwave pilot has been tested on quinoline production from glycerol using a modified Skraup reaction. This reaction is of great interest for the production of a pharmaceutical intermediate (quinoline) from a biosourced material, glycerol. In a previous study [26], we demonstrated the feasibility of the reaction under microwave irradiation in green conditions, using water as a solvent and sulphuric acid as a catalyst, without any additional oxidant or toxic reactant. High temperature (220 °C) and pressure (15–25 bar) are required for the reaction. Acrolein is produced as an intermediate, and reacts in situ with aniline to produce quinoline, therefore avoiding handling with its toxicity and instability. The developed microwave pilot was operated for quinoline production in both batch and continuous flow modes and temperature/pressure/power control were ensured.

2. Batch mode

Our team has been investigating microwave synthesis of quinolines for several years, using a laboratory scale apparatus (monowave 300 from Anton-Paar), where a few milliliters (30 mL) of reagents were used [25,26]. In this small apparatus, the Skraup reaction was performed starting from glycerol (30 mmol), aniline (10 mmol) in the presence of sulphuric acid (30 mmol) in 10 mL of water, under microwave irradiation, at 220 °C (25 bar pressure) for 10 min, giving quinoline with a 44% yield. We decided first, to increase fivefold the reactor volume in order to check the feasibility of the reaction at a larger scale, focusing on the good propagation and absorption of the electromagnetic energy in the larger volume. We also wanted to develop a reactor volume more compatible with a 1 kg/h continuous production of quinoline.

2.1. Microwave apparatus

The cylindrical PTFE reactor was designed and customized, allowing reaction volumes up to about 135 mL, that is to say, five time more than the reacting volume used for our first investigations [25,26]. The temperature inside the reactor was measured using an optical fiber immersed in the reaction medium through a glass tube. The complete batch experimental diagram is shown in Fig. 1. Our system consisted of a Sairem (GMP 20K/SM) microwave high-voltage generator providing power up to 1900 W, coupled with a magnetron delivering an electromagnetic wave at 2.45 GHz. Only incident and reflected powers were measured with power sensors and the absorbed power was deduced from the difference. The magnetron was connected to a WR340 waveguide allowing stationary waves propagation in a TE₁₀ mode. A tuning piston at the end of the waveguide was used to optimize the electromagnetic energy absorption by varying the guide length. The waveguide was equipped with an applicator and a chimney in which the reactor was inserted. Pressure control was assured by elements installed downstream to the reactor: a pressure sensor, a safety valve (calibrated at 25 bar), a pressure regulator equipped with a gauge and a valve. Computer control and supervision of the set-up were carried out using Labview software.

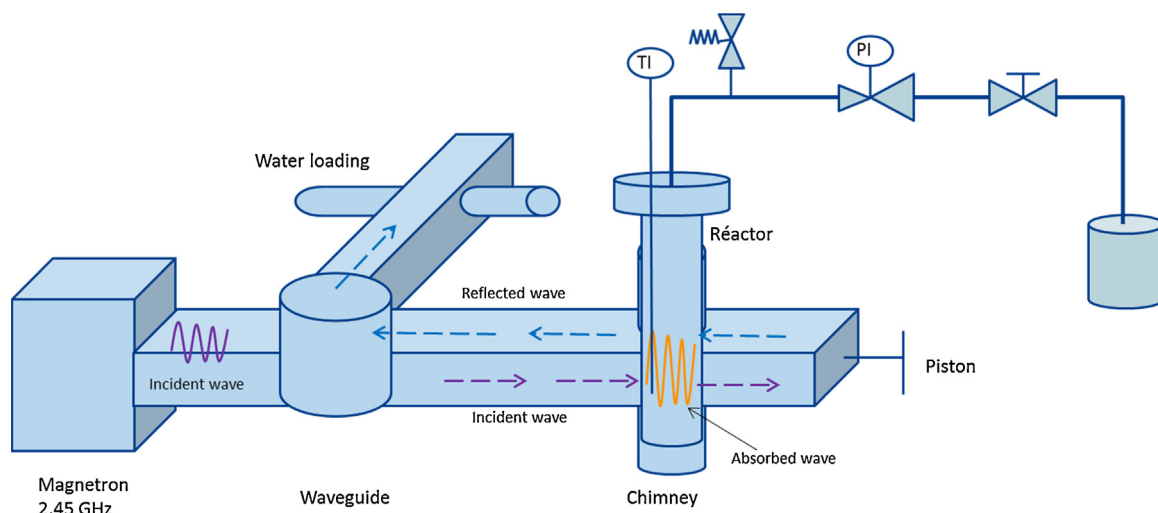


Fig. 1. Batch mode microwave system.

In order to check its resistance toward pressure and temperature, the apparatus was subjected to several safety tests before use. The first test was performed at ambient temperature under 40 bar of nitrogen pressure. The second test was performed at 190 °C in an oil bath under 10 bar, and the last one, under continuous conditions at room temperature, connected to a pump and reaching a pressure up to 25 bar. The reactor was also tested with water under microwave irradiation which allowed us not only to check resistance toward pressure, temperature and microwaves, but also to set a microwave protocol for better power and pressure/temperature control.

2.2. Procedure

In our pilot scale microwave apparatus, the Skraup reaction was conducted starting with 50 mmol of aniline, 150 mmol of glycerol and 150 mmol of sulphuric acid in 50 mL of water as a solvent (corresponding to a 75 mL reacting volume). The mixture was stirred with a spatula in order to homogenize the medium (the mixture is perfectly homogeneous at ambient conditions). The absence of leaks was checked at ambient temperature under 30 bar of nitrogen. The reactor was then depressurized, placed in the chimneys and connected to the rest of the installation. The apparatus control was carried out by an automatic PID regulation of the absorbed power with respect to the pressure. Pressure regulation was chosen rather than temperature since the medium was not stirred, which could lead to a heterogeneous temperature distribution within the reactor. Therefore, the measured temperature was less reliable than the pressure. This allowed us to prevent any sudden increase in pressure and, especially, to ensure safer and repeatable experimental conditions. The same microwave protocol was applied for all experiments, and thus had better repeatability. The adopted method is illustrated in Fig. 2, and consisted of three main steps: allowing pressure to rise up to the desired value using a fixed absorbed power (Zone A); once the desired pressure was reached, this value was kept constant during the

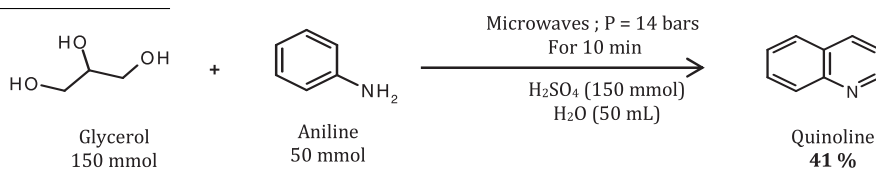
experiment, the irradiation was stopped and the system was cooled to ambient conditions (Zone C).

Quantification was carried out by high performance liquid chromatography (HPLC) coupled to a UV detector (wavelength = 220 nm). Analysis was made with an isocratic elution of acetonitrile (A) and water (B) with (A/B): 40:60. Acquisition and data processing were done with Azur software.

2.3. Results and discussion

Referring to experiments performed in the small scale reactor [25,26], as well as the saturation data of water and water–glycerol mixtures, we decided to conduct new experiments, in the new reactor of a larger volume (135 mL) at 14 bar (pressure corresponding to about 210 °C). The opening value of the pressure regulator was pre-set at 15 bar to avoid any pressure increase in the system. A constant value of the absorbed power was applied until the approximately desired pressure (≈ 13.8 –14 bar) was reached. After 2–3 min, the liquid started boiling and the pressure started increasing. By conducting this way the experiment, the mixture remained at the liquid–vapor equilibrium, meaning that all the time, the liquid phase was at equilibrium with the gas phase. Pressure increased continuously due to the heating of the medium and its partial vaporization. When the targeted value of pressure was reached (after 40 min), automatic control was then immediately switched-on, in such a way that the magnetron delivered only the required power to maintain this pressure value during the stabilization time.

For the conducted experiments, an increase of the reflected power (and therefore of the incident power, trying to maintain the same value of the absorbed power) was systematically noticed as soon as the pressure started to rise after about 2–3 min. This indicated a change in the dielectric properties of the medium, due to the reaction mixture boiling. In the absence of magnetic stirring, we supposed that the reactive mixture was homogenized by bulk motions and convective heat transfer. At the end of the experiment, a homogeneous dark brown liquid was recovered.



experiment by an automatic regulation of the absorbed power with regard to the pressure set-up value (Zone B); at the end of the

Thus, our system allowed carrying out the Skraup reaction at adequate temperature and pressure conditions, giving quinoline with a 41% yield, similar to the result obtained in the small scale

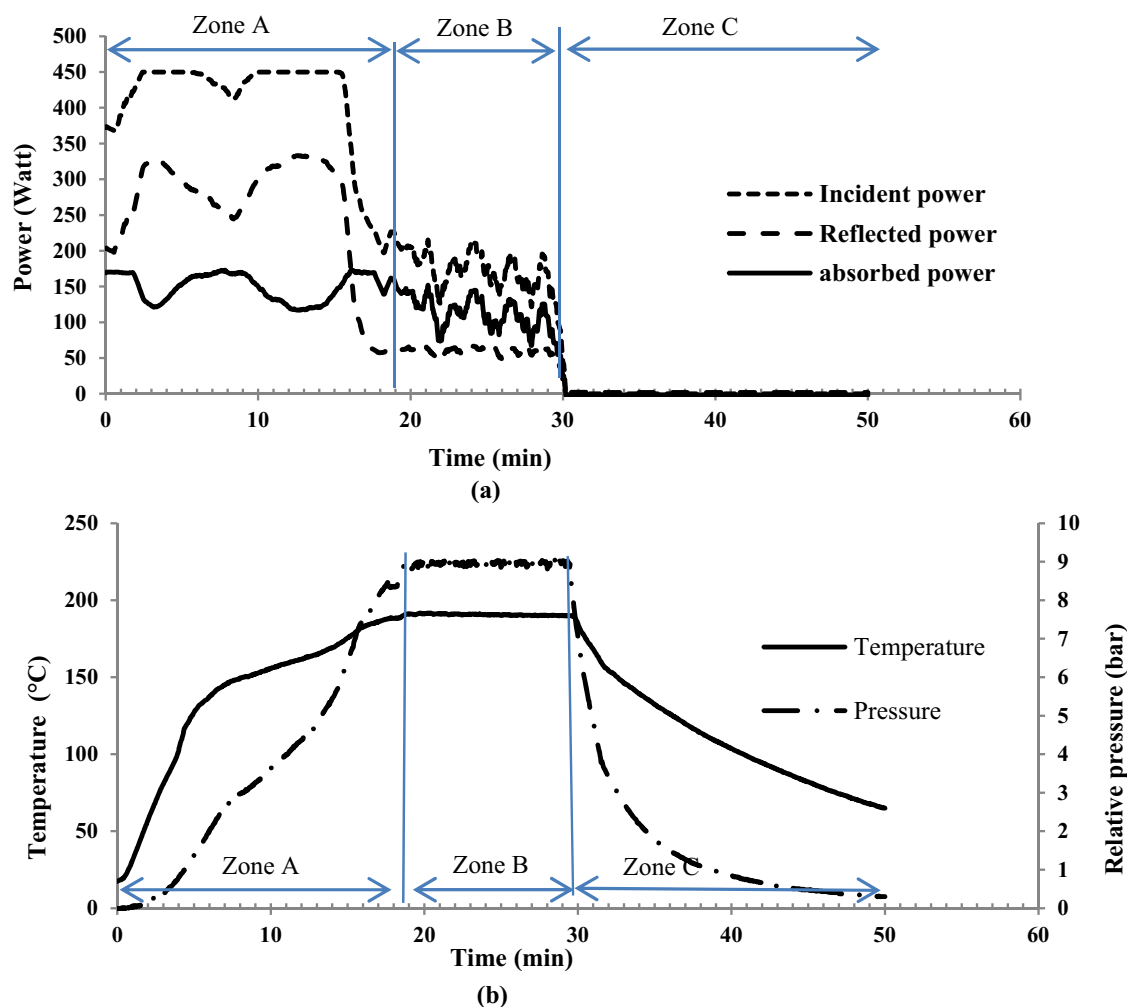


Fig. 2. Evolution of the experimental parameters during an experiment: (a) microwave incident power, reflected power and absorbed power evolution; (b) temperature and pressure evolution.

reactor. In addition, reaction duration was studied in these same conditions of temperature and pressure ($P=14$ bar and $T=210$ °C): three independent experiments were carried out maintaining a pressure/temperature rising time of 20 min, and a reacting time at constant pressure of 5 min, 10 min or 20 min. In these conditions, the reaction time did not affect the quinoline yield. Full aniline conversion and maximum yield were obtained after 5 min of reaction time indicating that the reactions were relatively fast as soon as the adequate pressure and temperature conditions were reached.

For the experiments that were carried out, a drop in the reflected power at a pressure of about 8 bar was always noticed, which seems particularly interesting (Fig. 2a). This means, that at this time, the system is absorbing the major part of the supplied power, probably due to the medium dielectric property changes. If the experiment control was carried out with respect to the temperature, this could cause thermal runaway and possibly, overpressure in the reactor, since the response time of the measured temperature is much higher than the one of the pressure. The superiority of system control by pressure regulation is now demonstrated.

The change in dielectric properties, at this stage of the experiment, may be due to the evolution of the temperature and pressure conditions in the reactor, as well as a change in the composition of the medium as a consequence of the beginning of the reaction. The second possibility seems to be more plausible, considering that this pressure (8 bar) corresponds to a temperature of about 185 °C (Fig. 2). To confirm this hypothesis, we decided to examine the

pressure influence on the quinoline yield more closely. Furthermore, it is always preferable to reduce operating pressure for safety reasons.

Results reported in Table 1 showed that Skraup quinoline synthesis started at about 7 bar and kept on going to 9 bar (Table 1, entries 1 and 2). At 9 bar, a stable reaction time of 40 min was required to consume almost all of the aniline (Table 1, entry 4 vs. entry 3). Consequently, these conditions were not suitable for continuous mode experiments, since they would have led to too long residence time. Experiments led at 12 bar and 14 bar (Table 1,

Table 1
Pressure influence on the quinoline synthesis.

Entry	Microwave protocol	T (°C)	Aniline conversion (%)	Quinoline yield (%)
1	Pressure rising: in 14.7 min Irradiation stopped at 7.5 bar	182	17	2
2	Pressure rising: in 12 min Irradiation stopped at 9.5 bar	193	26	5
3	Pressure rising: in 19.7 min 10 min at 9 bar	190	61	21
4	Pressure rising: in 19.6 min 40 min at 9 bar	190	95	42
5	Pressure rising: in 19.5 min 10 min at 12 bar	204	98	42
6	Pressure rising: in 22 min 10 min at 14 bar	210	100	41

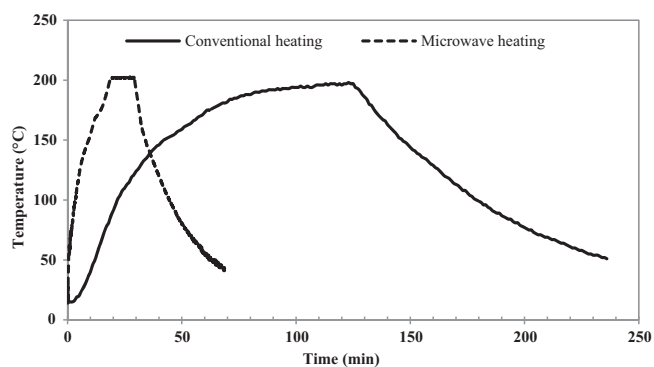


Fig. 3. Temperature profiles using two heating modes: microwaves vs. conventional heating.

entries 5 and 6) gave similar results. Finally, experiments in the newly designed and five times larger apparatus gave the same quinoline yields as in the small scale experiments (performed in the monowave 300), but at a reduced reaction temperature (204 °C vs. 220 °C), and at a significantly reduced operating pressure (12 bar vs. 25 bar). Furthermore, better experimental parameters control was obtained.

In order to compare the energy efficiency of microwave heating to thermal heating, a Skraup quinoline synthesis was done in a conventional pressurized reactor (4560 Mini Bench from Parr), allowing conditions up to 350 °C and 200 bar. A 160 mL volume Hastelloy reactor was used, equipped with a glass vessel of 105 mL. It was heated by applying a PID control with respect to the temperature measured at the outer walls of the reactor and the reaction temperature was deduced from a preliminary calibration. The reaction was carried out in the same conditions as under microwave heating (0.1 mol/L of aniline; 3 eq of glycerol and 3 eq of sulphuric acid), respecting the maximum volume allowed by the reactor. To ensure a temperature of 200 °C, we applied a set point of 325 °C to the oven, and achieved the target temperature within 112 min. This temperature was then held for 10 min. Finally, the furnace was removed and the reactor cooled down to ambient temperature. The obtained quinoline yield was similar to the one obtained under microwaves (37% vs. 42% in microwave, at 100% aniline conversion).

Considering the recorded temperature profiles (Fig. 3) and the comparison summarized in Table 2, the use of our microwave device considerably reduces energy consumption. The experiment is carried out in only 32 min with microwave heating, while 122 min are required using conventional heating, applying a furnace temperature of 325 °C. The microwaves device handles about 40% more for a similar quinoline yield and the energy consumption (in kJ/mol of quinoline produced) is much higher when thermal heating is used. With the conventional method, it is necessary to heat the whole mass of the stainless steel reactor by conduction, and deal with important thermal losses. The rapid heating feature of microwaves and the efficient use of the energy by direct absorption are the main benefits of our pilot scale microwave process.

3. Continuous mode

With the purpose of producing about 1 kg/h of organic products under microwave and under high temperature and pressure conditions, we studied the possibility of designing a continuous pilot apparatus from the developed microwave batch apparatus. The same PTFE reactor was used in order to achieve the temperature/pressure conditions required for quinoline synthesis. Our approach consisted in making changes to the batch apparatus

to allow inlet/outlet flow, fluid cooling at the reactor outlet, as well as various security equipment required for safe process running.

Nevertheless, the strong acidic conditions of the Skraup reaction were not compatible with the 316L stainless steel pipes and tubing of our pilot, which were not resistant to corrosion. To overcome this problem, we decided to change the mixture concentration. A reaction with a diluted mixture (0.1 mol/L of aniline; 3 eq of glycerol and 3 eq of sulphuric acid) was carried out. Despite the fact that this choice was not suitable for obtaining good aniline conversion and quinoline yields, we decided to go further in the design and development of the continuous mode pressurized microwave apparatus, which will be suitable for other organic synthesis.

3.1. Apparatus

To operate the microwave pressurized reactor in continuous mode, the following elements were added to the batch apparatus (Fig. 4):

- a feed tank, wherein the starting mixture was stored and mechanically stirred
- a Dosapro Milton Roy metering pump ($P_{\max} = 450$ bar). The pump was connected upstream to a pressure regulator equipped with a pressure gauge, working as a safety element to face any sudden pressure increase
- a valve connected upstream to the reactor to purge air from the tubing and to check the inlet liquid flow
- a stream feed located at 1 cm from the top of the reactor, the outlet was 1 cm from the bottom of the reactor
- a temperature measurement provided by a PT100 sensor, connected downstream to the reactor. Batch system pressure control and safety items were kept (pressure sensor, safety valve, pressure regulator equipped with a gauge, and the valve)
- a condenser connected downstream to the pressure regulator

Since the pressure was now managed by the pump, the automatic control of the absorbed power was carried out by PID action with respect to the temperature.

3.2. Results and discussion

An example of the experimental parameters evolution is shown in Fig. 5. The experiment was carried out starting with a 0.1 mol/L aniline solution in water, with 3 eq of glycerol and 3 eq of sulphuric acid.

Zone A represents the transient regime. The required reaction pressure was controlled by the pump and the pressure regulator (14–15 bar). Microwaves were switched on at $t=0$ allowing the temperature to increase until measuring 140 °C at the outlet of the reactor. At this stage, some pressure fluctuations as well as the reflected power (and therefore the incident and absorbed power) occurred, indicating that the system had reached its boiling point (210 °C inside the reactor at this pressure). Stabilization of the system was achieved, allowing some pressure oscillations of ± 0.5 bar. The pressure was then slightly increased (15–16 bar) by acting on the pressure regulator in order to maintain the medium in a liquid state. PID automatic control of the absorbed power was switched on to maintain a required temperature value of 133 °C at the outlet of the reactor. The steady state (Zone B) was rapidly reached, and all the operating parameters were stabilized. The experiment ended by switching off the microwaves. The pump was stopped and the reactor cooled to ambient conditions.

The continuous mode experiments allowed us to study two parameters: the flowrate/residence time τ , and pressure/temperature (T_{outlet}). Results are summarized in Table 3. On

Table 2
 Comparison of the two heating processes showing advantages of the microwave pressurized reactor.

Heating process	Reactants mass (g)	Temperature and pressure	Required time to attain temperature (min)	Quinoline yield (%)	Consumed energy (kJ/mol of quinoline produced)
Microwaves	83	204 °C; 12 bar	22	41	11,014
Conventional	60	200 °C (furnace at 325 °C); 16 bar	112	37	452,200

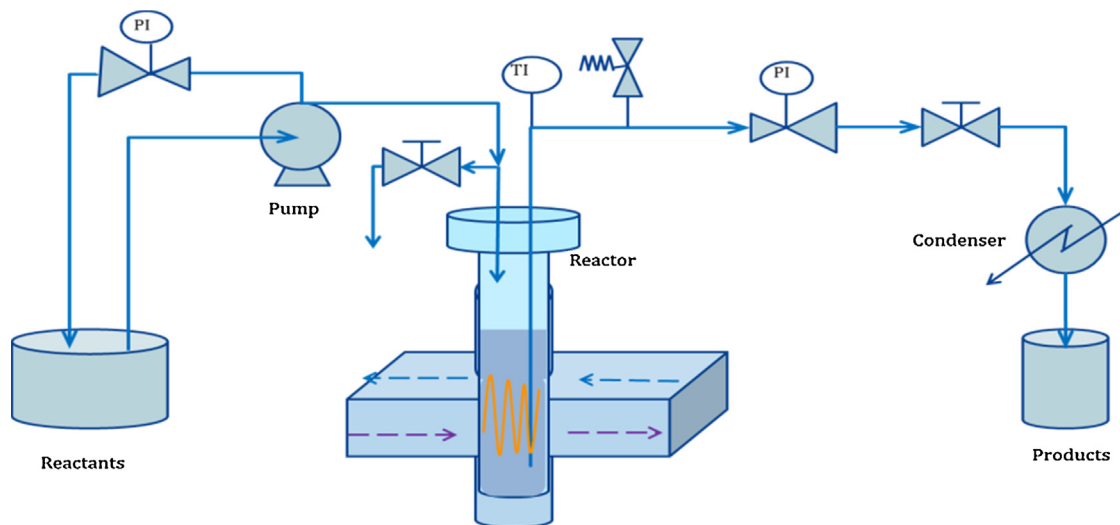


Fig. 4. Continuous mode microwave pilot reactor.

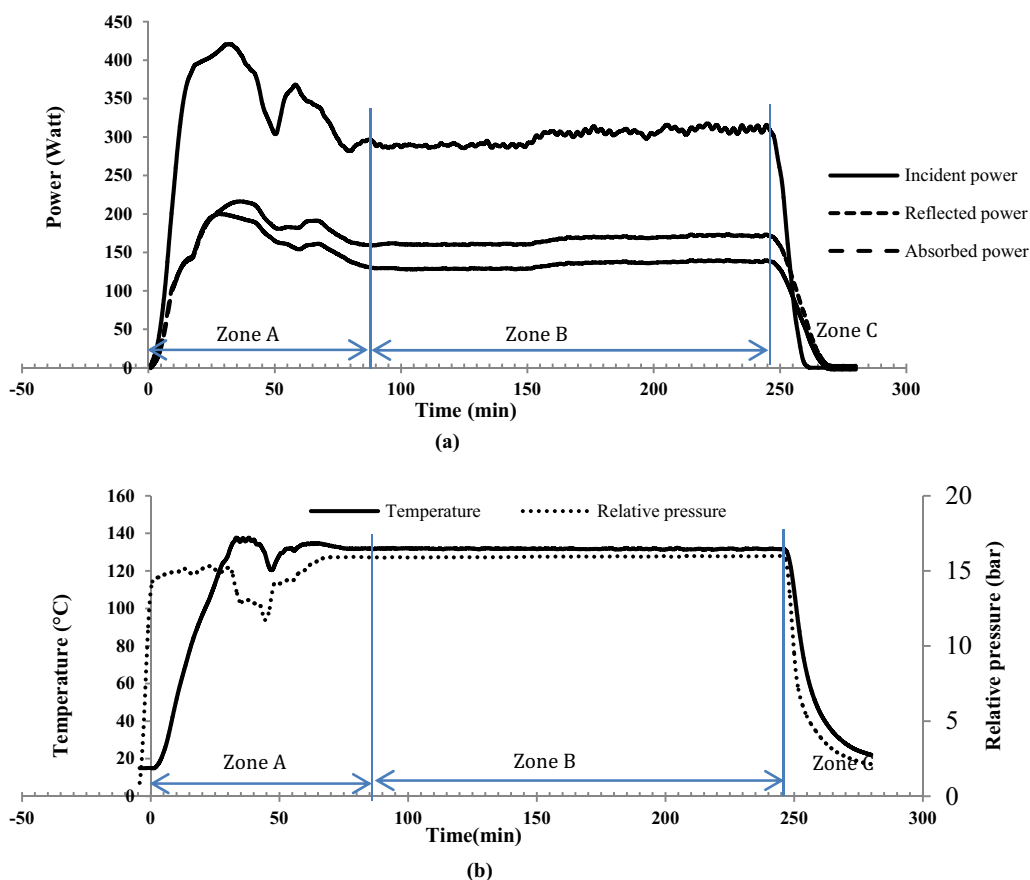


Fig. 5. Experimental parameters evolution during the continuous quinoline synthesis: (a) power evolution over time; (b) temperature and pressure evolution over reaction time.

Table 3

Microwave continuous quinoline synthesis starting from a 0.1 mol/L aniline solution in water, with 3 eq of glycerol and 3 eq of sulphuric acid.

Entry	Mass flow rate (g min ⁻¹)	τ (min)	T_{outlet} of the reactor (°C)	P (bar)	Conversion (%)	Yields (%)
1	6.9	14	131–133 (~200 inside)	15–16	8	1
2	16.6	6.13	131–133 (~200 inside)	15–16	2.2	0.51
3	16.6	6.13	151–152 (~218 inside)	19–20	5.3	4

the one hand, the results obtained showed that increasing the residence time (by reducing the flowrate, Table 3, entry 2 vs. entry 1), promoted aniline reactivity and quinoline formation. On the other hand, increasing temperature/pressure conditions (Table 3, entry 3 vs. entry 2) improved quinoline yield. Quinoline yields and aniline conversion were very modest, because they were limited by the low acidic concentration of the medium due to chemical resistance constraints.

These experiments prove that the quinoline continuous production under microwave irradiation and at high temperature (200 °C) and 15 bar pressure is possible. The developed pilot microwave reactor makes continuous production possible for about 1 kg/h of organic products at high temperature and pressure (up to 19 bar and 220 °C). Although conversions and yields are low and corrosion problems caused by concentrated reaction medium have to be solved, a microwave pilot continuously operating under pressurized conditions is now available for green chemistry.

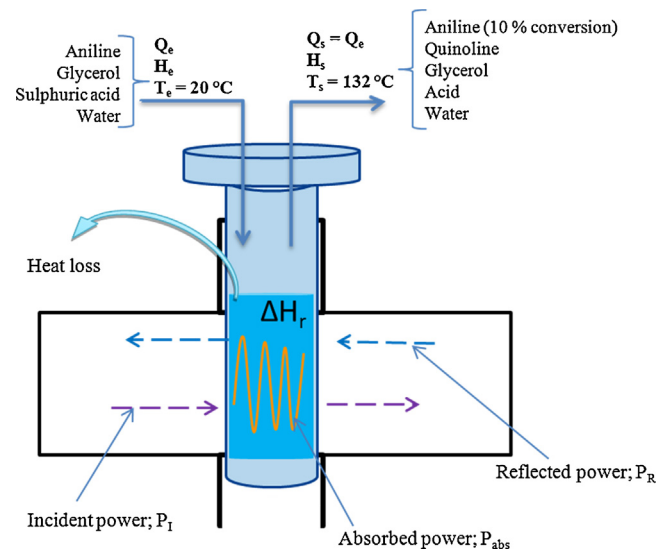
3.3. Energetic balance for the continuous mode microwave reactor

Because energy consumption is at the heart of process intensification, our objective is also to design a continuous microwave process which is as cost effective as possible. We used the power data collected during our experiments to estimate the part of the efficiently used energy input for the process and have since identified the improvements to be made.

An energetic balance on the microwave pilot reactor allowed us to assess the energy efficiency of the system. First, the enthalpy of the global Skraup reaction was estimated by differential scanning calorimetry (DSC) measurements. The apparatus used in this study was a Q1000 from TA Instruments, equipped with Universal Analysis 2000 software. Analyses were carried out in sealed vessels ensuring their chemical resistance to the acidic reaction medium and allowing the elevated pressure and temperature conditions of the reaction. The performed tests consisted in heating our reaction mixture at a rate of 10 °C/min from 20 °C to 300 °C and following the heat flow recorded by the DSC. Analyses were made using a typical reaction mixture of glycerol (3 eq), sulphuric acid (3 eq) and 1 eq of aniline in water (with a concentration of 1 mol of aniline per liter of water). After homogenization, a 5.48 mg sample was placed in the crucible and subjected to the DSC temperature increase. The analysis showed an exothermal peak of 147.6 J/g of mixture. The top of the peak was detected at 210 °C, which corresponds to our experiments temperature. The enthalpy of the reaction was estimated at -247 kJ/mol of aniline.

In this study, we considered the example corresponding to entry 1 of Table 3, for which the main powers involved are shown in Fig. 6. Q , H and T are respectively the mass flow rate (g s⁻¹), the enthalpy (J/g) and the temperature (K) of the mixture. Subscripts e and s mention the inlet and outlet of the reactor. The enthalpy of the reaction determined by DSC ($\Delta H_r = -247$ kJ/mol of aniline) was calculated per gram of converted aniline as it is the limiting reagent in Skraup synthesis, $\Delta H_r = -2.66$ kJ/g of converted aniline.

Before establishing the heat balance, the following hypotheses were considered:

**Fig. 6.** Energy exchanges involved during a continuous mode experiment.

- Ideal continuous stirred tank reactor (CSTR).
- Steady state is established and the reaction volume is constant.
- The mass flow rate is the same at the inlet and at the outlet of the reactor ($Q_e = Q_s = Q$).
- The determined enthalpy of the reaction ($\Delta H_r = -247$ kJ/mol of aniline) includes the contribution of all the intermediate reactions in the Skraup synthesis.
- The real temperature value of the outlet flow corresponds to the estimated one (about 200 °C inside).

The incident, reflected and absorbed powers P_i (W), P_R (W) and P_{abs} (W) respectively were given in Fig. 5.

Considering the partial mass balance for aniline (which is the limiting reactant), the conversion X_A can be written as:

$$X_A = \frac{F_{As} - F_{Ae}}{F_{Ae}}$$

where F_{Ae} and F_{As} are the aniline molar flows at the inlet and at the outlet of the reactor (mol s⁻¹).

The energy balance can now be formulated as follows:

$$P_{abs} + \dot{H}_e = \dot{H}_s + P_{\Delta H_r} + P_{loss}$$

Here, \dot{H}_e (W) and \dot{H}_s (W) are the enthalpy fluxes at the inlet and the outlet of the reactor, respectively. P_{abs} represents the absorbed microwave power, which is equal to 135 W as shown in Fig. 5. P_{loss} is the energy loss (W) of the system, which can be therefore expressed by the following equation:

$$\begin{aligned} P_{loss} &= P_{abs} - P_{\Delta H_r} + \dot{H}_e - \dot{H}_s = P_{abs} - (X_A F_{Ae} \Delta H_r) + \dot{H}_e - \dot{H}_s \\ &= P_{abs} - (X_A C_{Ae} Q \Delta H_r) - (\dot{H}_s - \dot{H}_e) \end{aligned}$$

C_{Ae} : aniline's molar concentration in the starting mixture ($C_{Ae} = 1 \times 10^{-4}$ mol g⁻¹).

Q : mass flowrate ($Q = 6.9$ g min⁻¹ = 0.115 g s⁻¹).

The difference in enthalpy fluxes can be calculated considering the specific heat of the mixture at the inlet and at the outlet of the reactor ($C_{p_{me}}$ and $C_{p_{ms}}$) and the mass flow rate ($Q_e = Q_s = Q$).

$$\dot{H}_s - \dot{H}_e = Q(C_{p_{ms}}T_s - C_{p_{me}}T_e)$$

The calculation of the specific heat of the mixture starting from mass fractions of the components and their individual specific heat shows that these values are very similar to the specific heat of water at the corresponding temperature (at 20 °C for the inlet and 210 °C for the outlet).

Considering all this data, the heat losses can be evaluated as follows:

$$P_{loss} = P_{abs} - QCp_e(T_s - T_e) - (X_A QC_{Ae} \Delta H_r)$$

$$P_{loss} = 135 - 111.32 + 0.28 = 24.5 \text{ W}$$

In our reaction conditions, the power value generated by the enthalpy of the reaction ($X_A QC_{Ae} \Delta H_r = 0.28 \text{ W}$) is very low and has an insignificant contribution in the energy balance. Furthermore, heat losses represent 18% of the microwave absorbed power. This value illustrates the energy transferred from the fluid to the walls of the reactor, the metallic assembly block and then to the surrounding atmosphere. The majority of the absorbed power (P_{abs}) is mainly used to increase the liquid temperature rising and to compensate heat losses. Although the value of heat losses is not high, it could even be reduced by changing the geometry of the reactor and by a better insulation of the reactor, which could reduce heat losses dissipated to the surrounding air.

Regarding the power curves, we can notice that the efficiency of our microwave device is approximately 45% by calculating the ratio of the absorbed power to the incident power delivered by the magnetron. This value is governed by the geometry of the system, notably by the adjustment of the piston's position in order to minimize the reflected power. This adjustment depends on the interaction of the microwaves with the medium, and therefore the dielectric properties. With manual tuning of the piston, as in our case, the optimal adaptation is sometimes impossible.

As a conclusion for this part, the major efforts have still to be made on the microwave geometry, that is to say, the wave-transmission system, the adaptation tuning, and the reactor shape in order to better limit wave reflections and ensure better energy absorption. Heat losses could also be reduced by insulation of the reactor to be even more economical.

4. Conclusion

The undertaken work led to the development of a microwave pilot reactor, allowing high temperature and pressure required for the Skraup quinoline synthesis, for a reaction volume multiplied by 5 compared to what is usually used in many organic synthesis laboratories.

Firstly, the batch pilot scaled up by five was designed and optimized. Pressure/temperature conditions were controlled. The regulation of the absorbed power with respect to the measured pressure was demonstrated to be very advantageous, allowing stable, repeatable and safe operation. Batch quinoline synthesis gave similar yields compared to those obtained in the small scale experiments (42% yield), although under reduced temperature conditions (200 °C vs. 220 °C) and a significantly reduced pressure in the system (12 bar vs. 25 bar).

The comparison between our microwave device and conventional heating clearly showed the advantages of the microwave reactor, by reducing the reaction time and energy consumption.

In the second part of this paper, we demonstrated the possible continuous operation of the microwave reactor under pressure for chemical synthesis. An experimental protocol for adequate and safe experiments was established. However, the quinoline synthesis in continuous mode was limited by the mixture's acidic concentration and by the chemical resistance of different elements of the pilot. The energy balance of the device was established, showing reasonable heat losses, and a microwave energy absorption that could even be improved by changing the microwave geometry and by an automatic tuning of the cavity. A pilot scale continuous reactor, intensified by microwaves, working at pressure conditions up to 19 bar and temperatures up to 220 °C is now available for the continuous production of chemicals.

References

- [1] R. Cecilia, U. Kunz, T. Turek, Possibilities of process intensification using microwaves applied to catalytic microreactors, *Chem. Eng. Process.: Process Intensif.* 46 (9) (2007) 870–881.
- [2] R. Cherbański, E. Molga, Intensification of desorption processes by use of microwaves—an overview of possible applications and industrial perspectives, *Chem. Eng. Process.: Process Intensif.* 48 (1) (2009) 48–58.
- [3] R. Gedye, F. Smith, K. Westaway, H. Ali, L. Baldisera, L. Laberge, J. Rousell, The use of microwave ovens for rapid organic synthesis, *Tetrahedron Lett.* 27 (3) (1986) 279–282.
- [4] R.J. Giguere, T.L. Bray, S.M. Duncan, Application of commercial microwave ovens to organic synthesis, *Tetrahedron Lett.* 27 (41) (1986) 4945–4948.
- [5] M.A. Surati, S. Jauhari, K.R. Desai, A brief review: microwave assisted organic reaction, *Arch. Appl. Sci. Res.* 4 (1) (2012) 645–661.
- [6] I. Polaert, L. Estel, A. Ledoux, Microwave-assisted remediation of phenol wastewater on activated charcoal, *Chem. Eng. Sci.* 60 (22) (2005) 6354–6359.
- [7] S. Ravichandran, E. Karthikeyan, Microwave synthesis—a potential tool for green chemistry, *Int. J. ChemTech Res.* 3 (1) (2011) 466–470.
- [8] B. Toukoniitty, J.-P. Mikkola, D.Y. Murzin, T. Salmi, Utilization of electromagnetic and acoustic irradiation in enhancing heterogeneous catalytic reactions, *Appl. Catal. A: Gen.* 279 (1) (2005) 1–22.
- [9] B.A. Roberts, C.R. Strauss, Toward rapid, 'green', predictable microwave-assisted synthesis, *Acc. Chem. Res.* 38 (8) (2005) 653–661.
- [10] J. Marquié, G. Salmoria, M. Poux, A. Laporterie, J. Dubac, N. Roques, Acylation and related reactions under microwaves. 5. Development to large laboratory scale with a continuous-flow process 1, *Ind. Eng. Chem. Res.* 40 (21) (2001) 4485–4490.
- [11] A. Stadler, C.O. Kappe, Microwave-mediated Biginelli reactions revisited. On the nature of rate and yield enhancements, *J. Chem. Soc., Perkin Trans. 2* (7) (2000) 1363–1368.
- [12] C.J. Abeywickrama, Y.P. Timilsena, S.K. Rakshit, L. Chrusciel, N. Brosse, Rapid optimization of typha grass organosolv pretreatments using parallel microwave reactors for ethanol production, *Ind. Eng. Chem. Res.* 52 (4) (2013) 1691–1697.
- [13] A. Stadler, C.O. Kappe, High-speed couplings and cleavages in microwave-heated, solid-phase reactions at high temperatures, *Eur. J. Org. Chem.* 2001 (5) (2001) 919–925.
- [14] A. Stadler, B.H. Yousefi, D. Dallinger, P. Walla, E.V. der Eycken, N. Kaval, C.O. Kappe, Scalability of microwave-assisted organic synthesis. From single-mode to multimode parallel batch reactors, *Org. Process Res. Dev.* 7 (2003) 707–716.
- [15] M. Treu, T. Karner, R. Kousek, H. Berger, M. Mayer, D.B. McConnell, A. Stadler, Microwave-assisted parallel synthesis of fused heterocycles in a novel parallel multimode reactor, *J. Comb. Chem.* 10 (6) (2008) 863–868.
- [16] G. Pipus, I. Plazl, T. Koloini, Esterification of benzoic acid in microwave tubular flow reactor, *Chem. Eng. J.* 76 (3) (2000) 239–245.
- [17] T. Cablewski, A.F. Faux, C.R. Strauss, Development and application of a continuous microwave reactor for organic synthesis, *J. Org. Chem.* 59 (12) (1994) 3408–3412.
- [18] I. Braun, G. Schulz-Ekloff, D. Wöhrle, W. Lautenschläger, Synthesis of AlPO₄-5 in a microwave-heated, continuous-flow, high-pressure tube reactor, *Microporous Mesoporous Mater.* 23 (1) (1998) 79–81.
- [19] R. Morschhäuser, M. Krull, C. Kayser, C. Boberski, R. Bierbaum, P.A. Püschner, T.N. Glasnov, C.O. Kappe, Microwave-assisted continuous flow synthesis on industrial scale, *Green Process. Synth.* 1 (2012) 281–290.
- [20] J.D. Moseley, C.O. Kappe, A critical assessment of the greenness and energy efficiency of microwave-assisted organic synthesis, *Green Chem.* 13 (4) (2011) 794.
- [21] G. Pipuš, I. Plazl, T. Koloini, Esterification of benzoic acid with 2-ethylhexanol in a microwave stirred-tank reactor, *Ind. Eng. Chem. Res.* 41 (5) (2002) 1129–1134.
- [22] S. Horikoshi, S. Matsuzaki, T. Mitani, N. Serpone, Microwave frequency effects on dielectric properties of some common solvents and on microwave-assisted syntheses: 2-Allylphenol and the C12–C2–C12 Gemini surfactant, *Radiat. Phys. Chem.* 81 (12) (2012) 1885–1895.

- [23] M. Nishioka, M. Miyakawa, Y. Daino, H. Kataoka, H. Koda, K. Sato, T.M. Suzuki, Single-mode microwave reactor used for continuous flow reactions under elevated pressure, *Ind. Eng. Chem. Res.* 52 (12) (2013) 4683–4687.
- [24] T.N. Glasnov, C.O. Kappe, The microwave-to-flow paradigm: translating high-temperature batch microwave chemistry to scalable continuous-flow processes, *Chemistry* 17 (43) (2011) 11956–11968.
- [25] H. Saggadi, D. Luart, N. Thiebault, I. Polaert, L. Estel, C. Len, Toward the synthesis of 6-hydroxyquinoline starting from glycerol via improved microwave-assisted modified Skraup reaction, *Catal. Commun.* 44 (2014) 15–18.
- [26] H. Saggadi, N. Thiebault, I. Polaert, L. Estel, C. Len, Quinoline and phenanthroline preparation starting from glycerol via improved microwave-assisted modified Skraup reaction, *RSC Adv.* 4 (2014) 21456.