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Alternative Solvents in Carvone Hydrogenation

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Resumo

Foi investigada a hidrogenação de um monoterpeno, a carvona em dióxido de carbono de alta densidade usando 0.5 wt.% de Pd, Rh, ou Ru suportados em alumina. Esta é geralmente mais rápida em fase supercrítica do que num sistema bifásico.

A reacção catalisada por Pd gera produtos totalmente saturados (isómeros de carvomentona) e carvacrol, enquanto que o Rh é mais selectivo favorecendo a produção de carvomentona e obtendo carvotanacenota como um produto secundário. Adicionalmente, este catalisador revelou uma alta selectividade (>84%) para a carvotanacetona e uma conversão >25% após 2 minutos de reacção. Ru releva uma conversão significativamente inferior e uma variedade superior de produtos á medida que os isómeros de carvomentona, carvotanacetona e carvacrol são formados.

A conversão e selectividade da carvomenthona em 2 horas de reacção para os diferentes catalisadores foi determinada com a seguinte ordem: Pd > Rh > Ru e Rh > Pd > Ru, respectivamente.

A síntese eficiente de carvacrol, uma agente antimicrobiano, foi obtida apenas através de três processos unitários. Após a hidrogenação catalisada por paládio, separou-se o carvacrol dos restantes produtos de reacção usando um líquido iónico a temperaturas de fácil obtenção. Este pôde ser posteriormente extraído com dióxido de carbono supercritico.

Termos chave: hidrogenação, carvona, carvacrol, fluidos supercríticos, dióxido de carbono, líquidos iónicos.

Abstract

Hydrogenation of monoterpenes, such as carvone, in high-density carbon dioxide over 0.5 wt.% Pd, or Rh, or Ru supported on alumina was investigated. Hydrogenation is generally faster in a single supercritical (sc) phase than in a biphasic system.

The reaction catalysed by Pd produces full hydrogenated products (isomers of carvomenthone) and carvacrol while Rh catalyst is more selective and favours carvomenthone isomers with higher selectivity and carvotanacetone as secondary product. Additionally, the Rh catalysed reaction exhibited high >84% selectivity of carvotanacetone with the conversion of >25% after only 2 minutes of reaction. Ru catalyst gives significantly lower conversion of carvone and the product variety is greater as carvomenthone isomers, carvotanacetone and carvacrol are formed.

The conversion and selectivity to carvomenthone within 2 hours course of the reaction followed the order: Pd > Rh > Ru and Rh > Pd > Ru, respectively.

Efficient synthesis of carvacrol, an antimicrobial reagent, has been accomplished by using three “one-pot” sequences. After hydrogenation catalysed by palladium, carvacrol is separated from the post-reaction mixture using an ionic liquid at easily achievable temperature which could be later extracted with supercritical carbon dioxide.

Keywords: hydrogenation, carvone, carvacrol, supercritical fluids, carbon dioxide, ionic liquids.

Table of Contents

Table of Figures

List of Tables

List of Symbols and Abbreviations

[bmim][NTf_2] – 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide;

[bmim][OTf] – 1-butyl-3-methylimidazolium trifluoromethanesulfonate;

IL – Ionic Liquid;

LLE – Liquid-liquid equilibrium;

LRI – Linear retention index;

scCO_2 – Supercritical carbon dioxide;

SCIL – Solid catalysts with ionic liquid layer;

scF – Supercritical Fluid;

SILP – Supported ionic liquid phase catalysts;

UCST – Upper critical solution temperature.

1. Introduction

Green chemistry efficiently uses (preferably renewable) raw materials, eliminates waste and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products.[1] Green solvents are considered environmentally benign in opposite of organic solvents. In industrial processes organic solvents are potentially hazardous because they easily evaporate into the air, and workers may inhale them. Additionally, the solvents add to damage the earth's atmosphere, because this will eventually oxidize and create carbon dioxide, a green house gas with potential impact on global warming.[2]

Chemistry innovation aims at the acquisition of new knowledge by generating alternative and promising solutions to existed or novel issues affecting the environment, energy, safety and health. There is a renewed interest in the use of green, sustainable solvents including supercritical carbon dioxide and ionic liquids in recently developed processes.[3] While ionic liquids not easily evaporate due to they almost non-measurable vapour pressure, supercritical fluids are made of already existing compounds that usually are non-toxic and non-flammable.[2]

The present work is placed in a research program that studies the use of green solvents in the hydrogenation of terpenes. Currently, these studies are focused in the use of high-pressure CO_2 in the hydrogenation of the carvone molecule, a monocyclic terpenic ketone. After the reaction, solubility tests were performed with ionic-liquids in order to obtain the most valuable product.

1.1. Hydrogenation in supercritical CO_2

A supercritical fluid (scF) is defined as any substance at a temperature and pressure above its critical point. The critical point represents the highest temperature and pressure at which the substance can exist as a vapour and liquid in equilibrium. At this state the density of the gas phase and liquid phase became identical the interface between then disappears, giving scF gas like transport properties and liquid like densities that turns them into great alternative medium for chemical reactions.

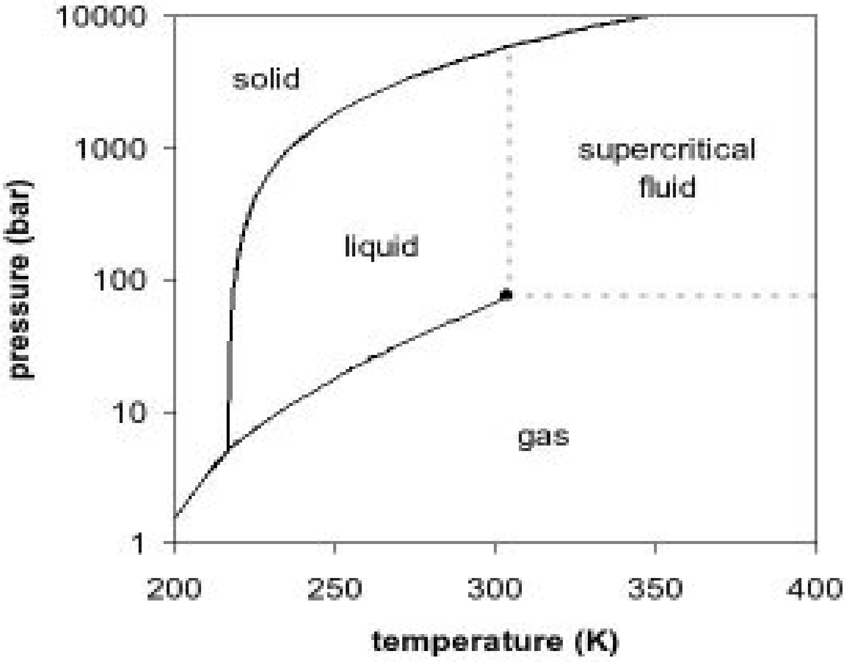

Figure 1.1 – Phase diagram of carbon dioxide.

Supercritical fluids are considered to be green solvents and have been employed in a diverse range of chemical reactions, including both homogeneous and heterogeneous catalytic processes[4,5]. Among scF, supercritical CO_2 ($scCO_2$) has received considerable attention as a useful replacement of organic solvents because it is inexpensive, non-toxic, non-flammable, recyclable, easily disposed, and capable of performing functions of a non-polar solvent while allowing manipulation of its solvent strength through a wide range of polarities. In addition the solvent power of $scCO_2$ can be easily tuned by changes in both temperature and pressure and reduction of the undesirable by-products yielding a higher end product quality can be achieved[6].

Supercritical CO_2 is a highly effective medium for reactions with permanent gases such as H_2 because they are fully miscible with $scCO_2$.[7] Mass transfer limitations are reduced in $scCO_2$ and the viscosity is relatively low thus further enhancing hydrogenation reactions. All of these features make $scCO_2$ an especially suitable solvent for large-scale industrial synthesis.

At high pressures, CO_2 can be at biphasic conditions, where gas-phase and liquid-phase will be present at the same time, or CO_2 can be at monophasic conditions, where the CO_2 will be at supercritical state. Using supercritical conditions will lower transfer resistance to the catalyst, so it is expect an improved hydrogenation at monophasic conditions. However, in some cases, it has been reported that biphasic hydrogenation can be fast as or faster than in monophasic conditions[8]. This could be explained by a lower concentration of subtract under monophasic conditions. [9]

1.2.Terpene hydrogenation

Over the last years, the selective hydrogenation of organic molecules plays an important role in the synthesis of fine chemicals on a multi-ton scale via heterogeneous catalysis, especially as far as selective hydrogenation of carbon–carbon double bonds in unsaturated carbonyl compounds is concerned[10].

Terpenes are the primary constituents of the essential oils of many types of plants and flowers. Essential oils are used widely as natural flavour additives for food, as fragrances in perfumery, and in traditional and alternative medicines such as aromatherapy. They are also an important class of compounds widely employed in organic synthesis either as a core of chiral auxiliaries or as starting materials for optically pure molecules or asymmetric ligands exploited in enantioselective transformations[11]. In case of being chemically modified, such as by oxidation or rearrangement of the carbon skeleton, the resulting compounds are generally referred to as terpenoids. Some authors will use the term terpene to include all terpenoids.

Hydrogenation of terpenes[12,13] and terpenoids[14] was executed in high pressure assisted CO_2 in biphasic or monophasic conditions[7,13] due to a favourable solubility relationship between terpenes (limonene[7] or myrcene[13]) and carbon dioxide allowing an easy switch from two phases to one phase system[15]. In the hydrogenation of terpenes in $scCO_2$, hydrogen pressure[9] and flow rate[16] effects have been studied as well as tuning of selectivity into an intermediate product has been achieved by the use of solid catalysts with ionic liquid layer (SCIL)[17].

1.3.Carvone hydrogenation

Carvone ($C_{10}H_{14}O$, 2-methyl-5-(1-methylethenyl)-2-cyclohexenone) is the major constituent of spearmint essential oil of *Menthe spicata* (Spearmint)[18] and *Anethum graveolens* (Dill).[19] It has been known since ancient times when Roman gladiators used dill seed's oil rich in carvone to friction their limbs before flights[19]. Carvone exhibits significant analgesic activity[20] and is an important chiron for the synthesis of complex natural products[21] having pharmacological potential in development of novel drugs.[20] It has been alternative medicine as a laxative, in colic treatment and as a breath freshener, even being safe to add to small children's dishes to improve digestion. It found application as fragrance and flavour, potato sprouting inhibitor, antimicrobial agent, building block and biochemical environmental indicator[19] .

Chemically, it's a known molecule by its enantiomeric properties. The enantiomers have distinct odour characteristics (quality and threshold), which are attributed to the enantiomeric configuration. R-(-)- and S-(+)-carvone, enantiomers only differing in the chirality of the compound. While R-(-)-carvone is the main constituent spearmint, S-(+)-carvone is the main constituent in the essential oil of carraway and dill.[22]

On this work we studied the R-(-)-carvone enantiomer (structure on the left of Figure 1.2).

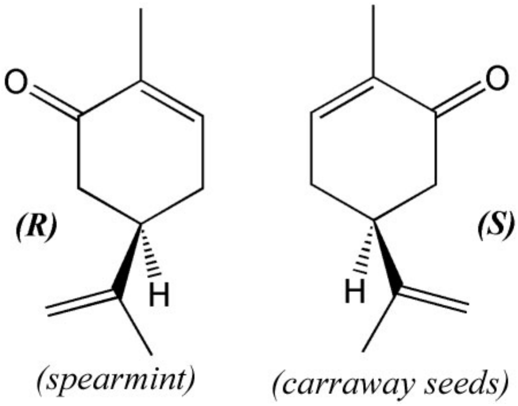

Figure 1.2 – Enantiomers (R)-(-)-carvone (left) and S-(+)-carvone (right).

Hydrogenation of carvone has been usually carried out with heterogeneous supported mono- and bimetallic catalysts. It can be noticed that reaction times are very long[23] (generally from 10 hours up to even more than 45 hours).

The main problem met is conversion of carvone[24] which can vary from 10% after 40 hours for Pt modified by Sn to 100% at 20 hours reaction time up for Pt/C catalyst[25]. The access of reagents to the catalyst bed seems to play a crucial rule in the liquid phase hydrogenation and can be recognized as a limiting factor for conversion.

The increase in the reaction time or temperature (40℃ and 90℃) did not solve the problem of low conversion (i.e. after 45h carvacrol conversion was 30% with PtSn/C-HP [26] while the same catalyst modified by Ge after 10 hours led to minimal conversion[27]). For these reasons various modifications of the reaction parameters have been tested, i.e. at 100℃ high acidic catalysts on zeolites[28] or Pd-Cu catalysts[23]. Even reaction at increased pressure of 12 MPa compared to atmospheric pressure reported[23,24,25,26,27,28] at temperature range of 10℃-50℃ with platinum, palladium [29] or nickel Raney [30] allowed to reach conversion of 50%.

At 21 °C with rhodium supported complex catalyst, Rh (cod)(AAEMA) [AAEMA - deprotonated form of 2-(acetoacetoxy)ethyl methacrylate], a 100% conversion after 23 hours was obtained[31].

Comparing, to long hydrogenation of carvone, the use of heterogeneous hybrid diamine-Rh complex-carbon of homogeneous Rh(NN)Si catalyst allowed a significant reduction in the reaction time to be obtained and at 60 minutes nearly a 100% conversion of carvone was reported[32]. A test with the homogeneous Rh(NN)Si catalyst used in hydrogenation of carvone showed that the activity of this complex was very low; carvone conversion was only 6% after 24 hours[32]. This negligible conversion in a homogeneous system underlines the problem appearing with heterogeneous catalysts used and highlights difficulty in obtaining significant and efficient enough conversion of carvone in the liquid phase hydrogenation heterogeneously catalysed.

The main products of carvone hydrogenation reported were unsaturated ketone such as carvotanacetone, and saturated one such as carvomenthone. Carvomenthol,[29] carveol [25,26,27] or dihydrocarveol[29] were additional products detected in hydrogenation. In general, the hydrogenation reactions were performed in organic solvents such as toluene,[24,25,26,27] hexane,[23,28] ethanol,[29,30] dichloromethane[31] or methanol,[32] in which due to interaction of substrate with methanol hemiacetal was produced in the course of the reaction.

1.3.1. Carvone hydrogenation in supercritical CO_2

ScCO_2 is receiving considerable and growing interest as an environmentally benign reaction medium for organic synthesis. Due to difficulties associated with the conventional homogeneous and heterogeneous catalysts such as mass transfer limitation that frequently occur between the reactants in gas and liquid phase, scCO_2 can be regarded as an ideal medium for hydrogenation because, unlike organic solvents, H_2 is completely miscible in CO_2.

Applications of scCO_2 to hydrogenation reactions involving heterogeneous catalysts are particularly attractive.[5,33] The present work is a continuation of our previous study on the employment of supercritical carbon dioxide in the heterogeneous catalysis of monoterpenes [6,7,9,12,13,17,34,35]. In comparison to conventional organic solvents, use of scCO_2 allows for higher diffusivities and lower viscosities to be obtained; therefore, hydrogenation reactions that are diffusion limited in the solvent phase can be enhanced by performing them in scCO_2[7]. As a consequence, the hydrogen concentration at the catalyst surface is greatly increased, leading to high reaction rates compared to the normal liquid phase operation.

The mixture of carvone and CO_2 exhibits advantageous low critical pressure at moderate temperatures allowing an easy switching from two phases to a homogeneous one-phase fluid [36,37]. It can be assumed that use of $scCO_2$ might help to increase carvone conversion and decrease the reaction time in hydrogenation reaction catalysed by heterogeneous catalysts compared to classical liquid phase hydrogenations. To simplify the reaction monosupported commercially available catalysts were used in this work. The Pd catalyst was selected as the most active, while Ru and especially Rh catalysts were used to check the catalysts which were reported as less active[9,13,35,38].The present investigation also aims to achieve diverse selectivities dependent on the active metal used.

1.4.Carvacol synthesis

Carvacrol is a natural plant chemical and one of the major components of oregano and thyme essential oils. Due to its low toxicity accompanied by odour of oregano and a pizza-like taste, carvacrol is a food additive to prevent bacterial contamination.[39] Among antimicrobials, carvacrol has been applied to potato puree, table grapes, chicken and sprouts.[40] An incorporation of carvacrol into the *Gelidium corneum* film used for processed food and pharmaceutical products improved the antimicrobial activity as well as the mechanical property of the film. Due its specific properties, carvacrol is an important chemical and methods of synthesis different then extraction from natural plants are studied extensively.[39,40,41,42,43] Recently, the *Gelidium corneum* film containing carvacrol has been suggested to be used in edible packaging for food products.[40]

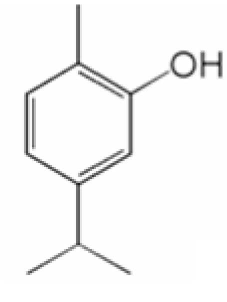

Figure 1.3 – Molecular structure of carvacrol.

Up to now, moderate to high temperature methods for production of carvacrol have been reported. Carvacrol was produced by Friedel-Crafts alkylation of o-cresol with isopropanol using superacidic catalyst at 180 ℃ within 2 hours with a selectivity of 82% at almost complete conversion.[41] In aromatization of carvone, the presence of 6M of H_2SO_4 with Amberlyst 15 acid catalyst started reaction at 75 ℃ which, due to exothermic effect of reaction, proceeded up to 180 ℃ converting carvone into carvacrol within one minute.[42] In other acid catalysed isomerisations of carvone to carvacrol sulphuric acid was used.[43,44] Using high-temperature water at 250 ℃ carvacrol in the isomerisation of carvone with a 95% yield was produced.[45]

All of the mentioned methods of carvacrol synthesis are characterised by relatively high yields of reaction (60–100%). Their drawbacks are the use of hazardous chemicals, production of waste's stream, flammability and explosion risks, use of moderate or high temperature and autogenous pressure conditions, hence alternative methods of synthesis of carvacrol are needed.

In this work, it was attempted to produce carvacrol for the first time in mild conditions using alternative solvents in a three-step process aiming at:

1) Synthesis of desired carvacrol in the heterogeneously catalysed hydrogenation of cheap carvone occurred in $scCO_2$;

2) Separation of carvacrol from post-reaction mixture using an ionic liquid as a solvent;

3) Extraction of carvacrol from ionic liquid reservoir by $scCO_2$.

The first aim is accomplished by the palladium catalysed hydrogenation reaction executed in supercritical CO_2.

The second target is achievable due to the specific solvent capability of IL to disclose subtle difference between very similar products of the reaction. It is possible due to the fine tuning of ionic liquid used for separation.

The last aim was gained due to the specific properties of ionic liquids and $scCO_2$. Near-zero vapour pressure of ILs in combination with $scCO_2$ allowed for separation of carvacrol.

1.5.Ionic Liquids

An ionic liquid is a salt in which the ions are poorly coordinated, which results in these solvents being liquid below 100℃, or even at room temperature. Ionic liquids are, like supercritical fluids, other solvents considered "green". These solvents offer flexible physical properties characterised by near-zero vapour pressure, thermal stability, considerably easy recyclability, widely tuneable property regarding polarity, hydrophobicity and miscibility with other solvents through appropriate modification of cation and anion. The negligible vapour pressure of ionic liquids is the interesting feature which makes easily recyclable and reusable. Furthermore a very low vapour pressure of ILs reduces de risk of explosion that that is a clear advantage over the use of classical volatile solvents.[46] Ionic Liquids have found an application in many chemical reactions[17,]**Error! ookmark not defined.**[,56,57] and processes including extraction and separation.[47,48,49,50,51]

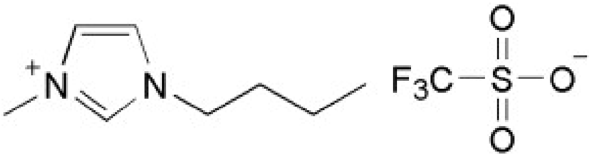

Figure 1.4 - Molecular structure of 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [bmim][OTf]

Figure 1.5 – Molecular structure of 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [bmim][NTf$_2$]

1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [bmim][NTf$_2$], and 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [bmim][OTf] (shown in Figure 1.4 and 1.5 respectively) are an example of ionic liquids that were used in this work. Having the same cation, the influence of a different anion in their solubility with reaction compound was tested.

1.5.1. Ionic Liquid Separation

The unique combination of negligible vapour pressure and favourable solubilising properties of ILs has motivated a replacement of organic solvents in greener reaction design. Implementation of ionic liquids in separation techniques has many benefits, including new developments.[47,48,49,50] Preliminary ionic liquids were introduced for biphasic extraction processes by Huddleston et. al.[51]

Ionic liquids were utilised in selective separation and extraction studies.[52,53] Recently, the influence of IL structure on extraction has been underlined.[54]

The advantages of using ionic liquids as supported ionic liquid phase catalysts (SILP) or solid catalysts with ionic liquid layer (SCILL) over the use of organic solvents as reaction medium for heterogeneously catalysed reactions include tuning selectivity towards desired products.[17, 55]

A potential application of low-viscous ILs in telomerization of dienes has been highlighted recently.[55] Furthermore ionic liquids have been broadly applied in the processing of biomass in the bio refinery scheme.[56, 57] Many processes being modified by IL has been tested and scaled up for the industrial application.[3]

2. Experimental Method

2.1.Chemicals

Hydrogen and carbon dioxide were supplied by Air Liquide with a stated purity of 99.998 mol%. R-(-)carvone (purity: >99.0%) and carvacrol (purity: 95.0%) were supplied by TCI Europe. Carvomenthone, sum of isomers, (purity: 98.0%) was delivered from Bedoukian Research, Inc. Hexane (purity: >99.0%) was supplied from Sigma-Aldrich and nonane (purity: >99.0%) was bought from Fluka. These substances were used as received without any further purification.

The catalyst used were Palladium (0.5 wt.%) on alumina in 3.2mm pellets, Rhodium (0.5 wt.%) on alumina in 3.2mm pellets and Ruthenium (0.5 wt.%) on alumina in 3.2mm pellets . All of them were bought Sigma-Aldrich.

The studied ionic liquids 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [bmim][NTf_2], and 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [bmim][OTf], were supplied by Iolitec, Ionic liquids Technologies with a stated purity of 99% (mass). They were further thoroughly degassed, dried, and freed from any small traces of volatile compounds by applying a vacuum (0.1 Pa) at moderate temperature (60℃). All drying procedures were performed for 48 h, and fresh samples of the components were used to prepare the solutions, always immediately prior to the measurements. Karl Fischer titrations revealed the following contents of water: [bmim][NTf_2], 80 ppm and [bmim][OTf], 260 ppm.

2.2.Hydrogenation

The hydrogenations were performed in a high pressure resistant apparatus consisting in a 50 cm3 sapphire-windowed cell (VC), which allowed direct visual observation of the number of phases connected by a circulating pump (CP) to a tubular reactor (TR) which encloses a catalyst. This apparatus scheme and picture are shown in Figure 2.1 and 2.2.

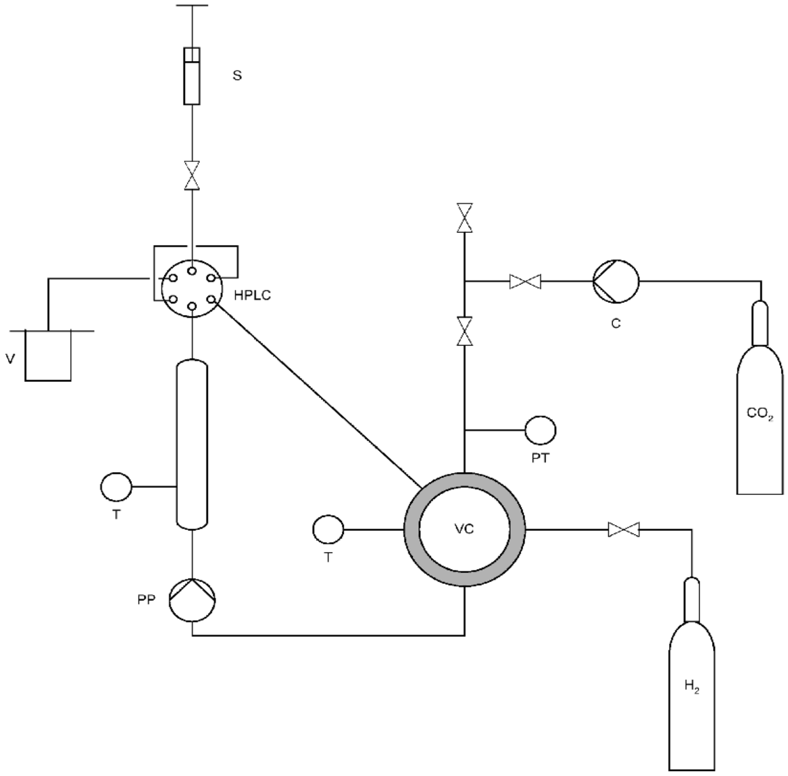

Figure 2.1– The hydrogenation apparatus: (C) CO_2 compressor, (TR) tubularreactor, (VC) view cell, (PP) circulation pump, (PT) pressure transducer, (T) temperature controller, (V) sample vessel, (HPLC) high pressure sampling valve, (S) syringe.

The reactants (either CO_2-expanded liquid terpene or a single supercritical phase, where liquid and gases produce one gas phase) were vigorously stirred, in order to promote phase equilibrium, and circulated continuously from the bottom of the view cell, through the catalyst bed, and back to the upper entrance of the cell. The flow rate of 3.3 mL/min employed guarantees that during 1-2 min the whole reaction mixture recirculates at least once.[35] Due to this, the feed composition that simulates the process performed in the batch mode. The reaction samples were taken at regular intervals through the HPLC valve equipped with a 100 μl sampling loop. The contents of the loop were dissolved in a measured amount of hexane with nonane used as an internal standard for the sample analysis. CO_2 was vented to the atmosphere. For each reaction 1.5 g of the fresh catalyst and 2 mL of carvone were used.

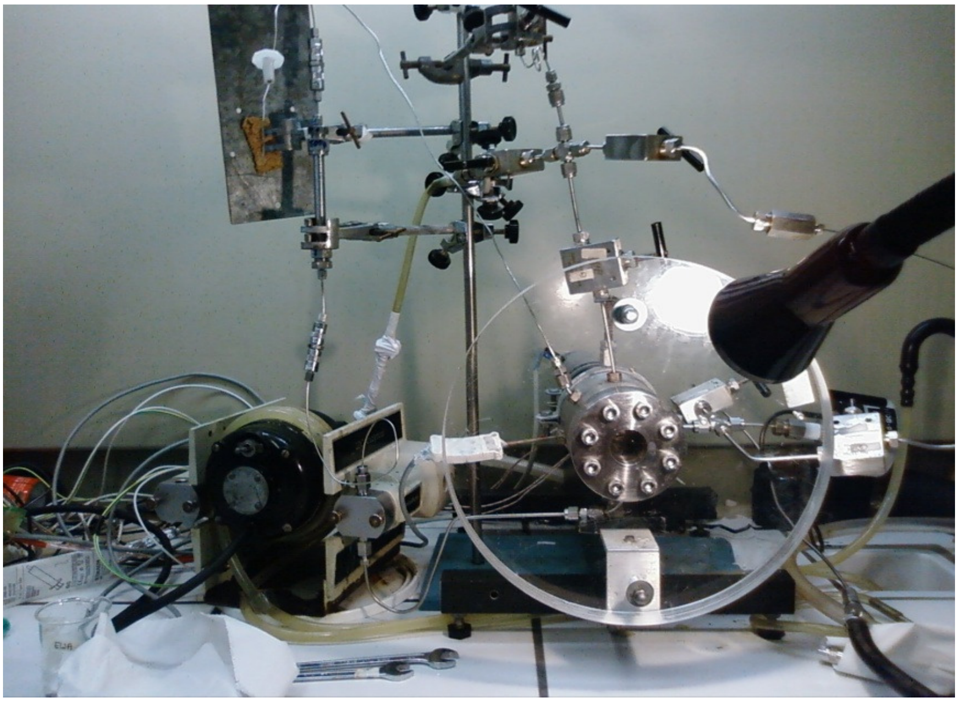

Figure 2.2 – Picture of the apparatus used for reactions.

2.2.1. *Procedure*

Follows a step by step description of the experimental procedure executed:

A) Apparatus preparation

After every reaction, the apparatus needs to be cleaned and prepared for the next reaction. To do so, hexane is injected in the view cell and the apparatus is pressurized with CO_2. The mixture is stirred while circulating in the system for a few minutes, and then pressure is released. The sample loop is injected with hexane. This procedure is repeated until GC analysis show no residue traces inside the apparatus.

After cleaning, the filters are assembled in the apparatus's frits, and leaks are checked in the system by pressurizing the system at a pressure 20 bar higher than the reaction pressure.

The, the tubular reactor must be taken out in order to place the catalyst and glass-wool, after reassembling the tubular reactor, a new leak check must be made. If there are no leaks, the heating rope should be assembled around the tube, with a thermocouple and wrapped with aluminium foil.

B) Sample preparation

Samples flasks are prepared by adding in a 5 ml flask 1 ml of standard and 2 ml of hexane. Standard is prepared by adding 108 µl of in 40 ml of hexane.

C) Analyse the samples by GC.

Before staring the reaction the pump must be marked for a 3.3ml/ml flow and the apparatus must be submitted to vacuum.

The temperature of the view cell and the heating rope must be set to 50 ºC. Two millilitres of subtract are injected in the view cell, followed by 40 bar of hydrogen and carbon dioxide (total pressure of 125 or 160 bar). Mixing is then turned on. After five minutes of stirring, the pump should be turned on and reaction time starts counting from zero.

During reaction several samples are taken according with time. A pre-sample is taken once every 1:30 minute before the real sample. The real sample is taken by opening the HPLC valve three times inside the sample flasks.

Samples are kept into the freezer until being analyzed by CG.

2.3.Identification methods

The qualitative identification of products was based on comparisons between the obtained GC-FID LRIs and those obtained by GC/TOFMS, and authentic samples.

The quantitative analysis was carried out by gas chromatography by means of Varian Chrompac CP-3800 gas chromatograph. Column: 30 m x 0.32 mm i.d. fused silica capillary column coated with a 0.25 µm thickness film of 5% phenyl groups in the dimethylpolysiloxane (CP-Sil 8 CB), from Varian Inc. was used. Hydrogen and air were used as carrier gases at a flow rate of 30 $\mathrm{mLmin^{-1}}$ and 300 $\mathrm{mLmin^{-1}}$, respectively. The oven temperature was programmed from 50°C at 4°$\mathrm{Cmin^{-1}}$ to 130°C, from 130°C at 20°$\mathrm{Cmin^{-1}}$ to 240°C, and held isothermal at 240°C for 5 min. Injector and detector temperature were set at 250°C. 0.5 μL of sample was injected in split mode, with a split ratio of 10.

The GC-MS analyses were provided by the university's mass spectroscopy services. The program was the same used on GC analysis. The column used was a VF5-ms (30m; 0,25mm I.D.; 0,25 μm film).

Figure 2.3 – Chromatograph CP-3800 used in GC analysis.

The presented retention indices (linear retention indices - LRIs) were calculated according to van den Dool and Kratz[58] using a mixture of C_8 to C_{27} hydrocarbons (AccuStandard, New Haven, CT, USA) in pentane. The hydrocarbons C_9-C_{12} were used for the calculations based on the GC/TOFMS results. The obtained LRIs were compared with the literature data (cis- and trans-carvomenthone, carvone, carvotanacetone, carvacrol, carvomenthol, carvenone)[59] The targeted terpenes were thus tentatively identified using the LRI calculations and the match of the individual spectra with the NIST 2005 MS library using the ChemStation software.[59]

The response factor for the analysed terpenes was determined as follows: cis- and trans-carvomenthone – 1.1, carvone – 1.1, carvotanacetone – 1.1, carvacrol – 1.0, carvomenthol – 1.0, carvenone – 1.1.

2.4.Liquid-liquid equilibrium (LLE)

The temperature-composition phase diagrams were obtained at ambient pressure of 0.1 MPa and in a temperature range of 273.15-350.15 K, using a visual method (observation, by eye, of the turbidity (cloud point) that precedes phase separation). Experiments were performed in a Pyrex-glass cell that was equipped with a stirrer. The cell could be opened/closed by a Teflon valve at the end of a long, capillary-thin (inner diameter of 0.1 mm) neck. It allowed the cell to be deeply immersed in a temperature-controlled bath, while, at the same time, diminishing losses due to evaporation. The solutions were prepared in the cell, adding the liquids through the neck using Hamilton syringes with lengthy needle the liquid inside the cell always occupied almost its entire volume (0.5 mL). The compositions were measured gravimetrically, using with a Mettler Model AT201 analytical microbalance with a stated accuracy (repeatability) of 2×10^{-5} in mass fraction. Temperature was monitored using a Pt100 temperature probe, which had an accuracy of 0.03 K.

In each LLE experiment, a heterogeneous solution was continuously heated with constant stirring from minimum temperature until it became homogeneous. Then, starting from the one-phase region, the solution was cooled continuously and the temperature at which it became turbid was taken as a cloud point. The experiments were performed in 3-4 runs; with the last run being performed very slowly (the rate of temperature change near the expected cloud point was no more than 5 Kh^{-1}). The uncertainties in temperature determination, taken from the repeated measurements, never exceeded 0.5 K.

The ternary LLE studies and later separation investigations were performed in 5 mL vials with the closed lid. A known quantity of the liquid containing carvacrol and carvone or post-hydrogenation mixture was placed inside and solvent (ILs or water) were added. Various compositions of solutes and solvents were tested to achieve broad range of experimental points. Next, the vials placed in a constant temperature (275.15 K) in orbital shaker set for 400 rpm for 1 hour and samples from ketone (upper) and IL-rich phase (bottom) were taken and analysed by a GC using the method for the analysis of the hydrogenation reaction samples.

The separation studies were performed in the same manners as ternary LLE studies mentioned above; however instead of the carvacrol and carvone mixture, the post-hydrogenation mixture was used.

2.5. Extraction study

The extraction studies were performed in the apparatus presented elsewhere.[65] A sapphire-windowed cell (2.9 cm high, 2.4 cm internal diameter) is the core of this installation. For the extraction, the sample of IL phase from the separation studies containing IL ($x_{[bmim][OTf]}=0.33$), carvacrol and other minor compounds from the separation studies were used. The sample was introduced into the cell using a syringe, and the cell was placed into a water bath. The temperature comptroller JULABO PC was used in order to maintain the required temperature (25 ºC). The temperature stability during experiments was determined at level ± 0.1 K. The sapphire cell was equipped with a magnetic bar driven by a magnetic stirrer. The pressure in the system was measured by a manometer AMPHENOL B12 with the accuracy of 0.1%.

CO_2 was initially pumped into the cell through a manual pressure generator of 60 mL capacity to achieve 12 MPa of pressure (above critical pressure for CO_2 + carvacrol). The pressure cell was left mixing for an hour. Afterwards, by a careful opening two venting valves, the extract started to be collected in two glass cold traps placed in a liquid nitrogen bath. The drop of pressure in the high pressure cell was continuously compensated by the introduction of fresh CO_2 from the pressure generator. The procedure was continued until the mass of traps remain constant. The composition of the liquid in the cold trap and in the high pressure reactor were analysed by GC using the method described before.

3. Results

3.1.Hydrogenation reaction

The hydrogenation of carvone was catalysed by three commercially available catalysts. The reaction was carried in the presence of supercritical CO_2 at 323.15 K at low H_2 pressure (4 MPa) and at 12.5 and 16.0 MPa of overall pressure (CO_2 + H_2). It was performed for 2 hours in batch mode.

Chemical structures of carvone and of the reaction products are presented in Fig. 3.1.

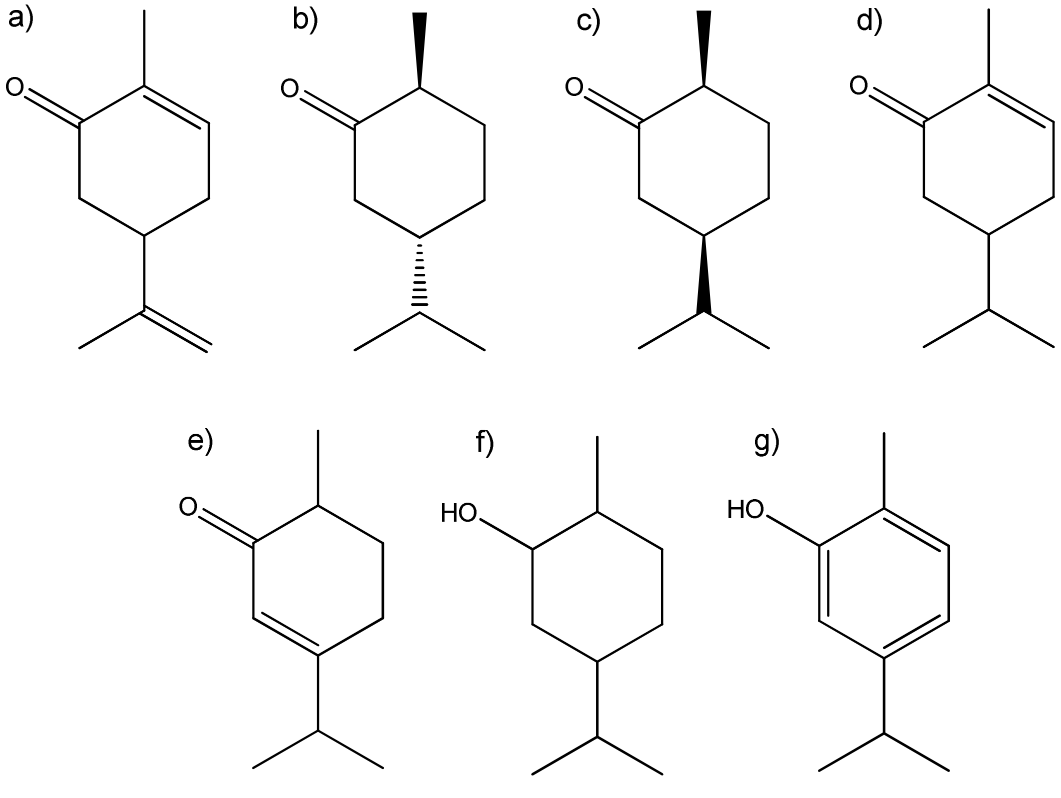

Figure 3.1 – The chemical structure of carvone and the hydrogenation products: a) carvone, b) trans-carvomenthone, c) cis-carvomenthone, d) carvotanacetone, e) carvenone, f) carvomenthol, g) carvacrol.

The selected conditions were comparable to previous studies with other terpenes such as limonene [6,7] and β-myrcene[13]. Similarly to binary mixtures of limonene or myrcene and CO_2, the system consisting of CO_2 + carvone [36,37] exhibits relatively low critical pressure for the binary mixture

(~10 MPa); however ternary systems containing hydrogen as a third component have never been studied.

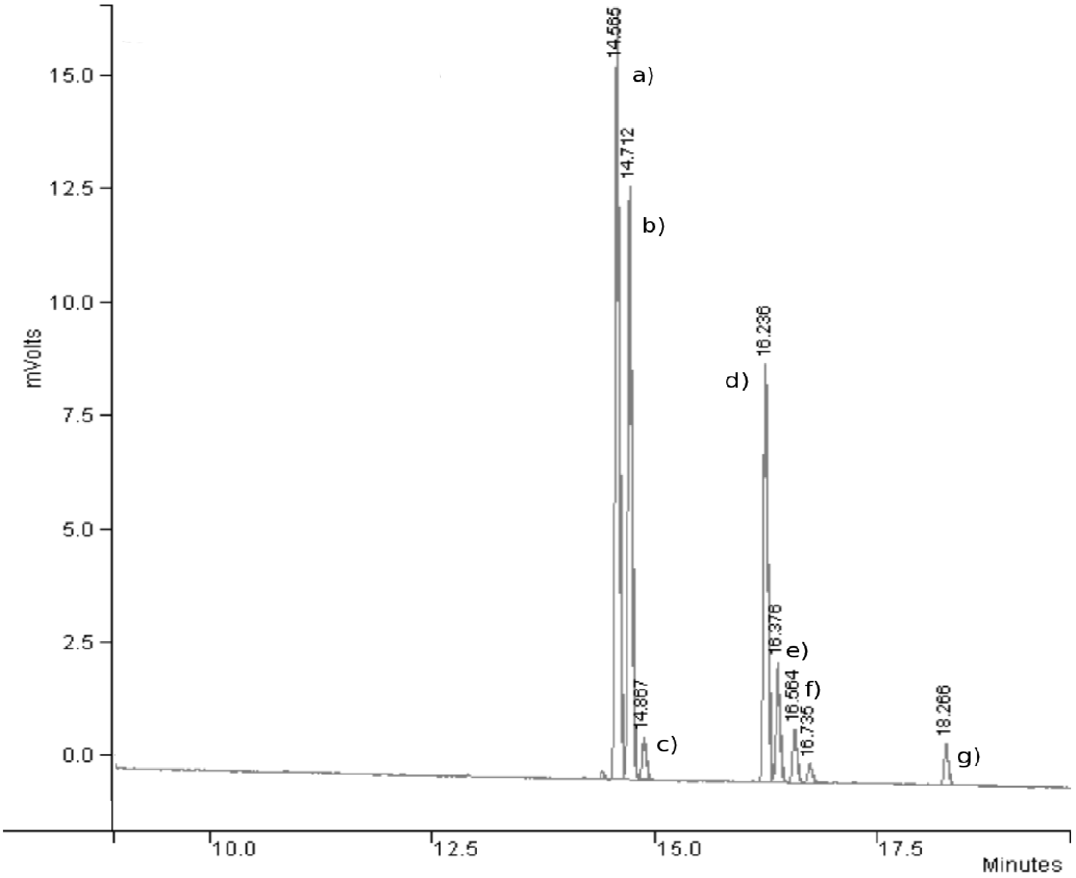

Figure 3.2 – Chromatogram of reaction mixture of the hydrogenation of carvone over Pd/Al_2O_3 catalyst in biphasic conditions (4 MPa of H_2, 12.5 MPa of total pressure, 323.15 K), where the compounds where identified as a) trans-carvomenthone, b) cis-carvomenthone, c) carvomenthol, d) carone, e) carvotanacetone, f) carvenone and g) carvacrol.

Following the previous results obtained earlier for terpenes aforementioned and their mixtures with CO_2 and H_2[7,15] in case of carvone it can be assumed that at 12.5 MPa total pressure system is biphasic (gaseous CO_2 + H_2 and CO_2 - expanded liquid carvone)) while at 16 MPa the system is clearly monophasic (terpene + CO_2 + H_2 in the gaseous phase). These assumptions were easily confirmed by a visual inspection performed during the progress of the reaction executed under both mentioned conditions.

3.1.1. Pd Catalysed reactions

The reaction catalysed by Pd/Al_2O_3 are characterised by relatively short time necessary to achieve equilibrium equalled to 30 minutes.

Analysing obtained results it can be stated that in the reaction course the concentration of carvone decreases rapidly and after 25 minutes of the reaction concentration of carvone is below 1 mol%. In case of reaction performed in two phases product concentration is constant already after 60 minutes from the beginning of the reaction.

Pd catalyst was efficient to achieve full conversion of carvone with total selectivity to carvomenthone above 77% for single phase reaction and biphasic one. Two stereoisomers of carvomenthone were formed in 45.27 mol% for trans- and 31.75 mol% for cis-carvomenthone in monophasic and 44.77 mol% and 31.52 mol% for corresponding isomers in biphasic conditions. Additionally, in the course of the reactions carvacrol was produced as a third product in 22.21 mol% and 21.95 mol% for monophasic and biphasic conditions, respectively.

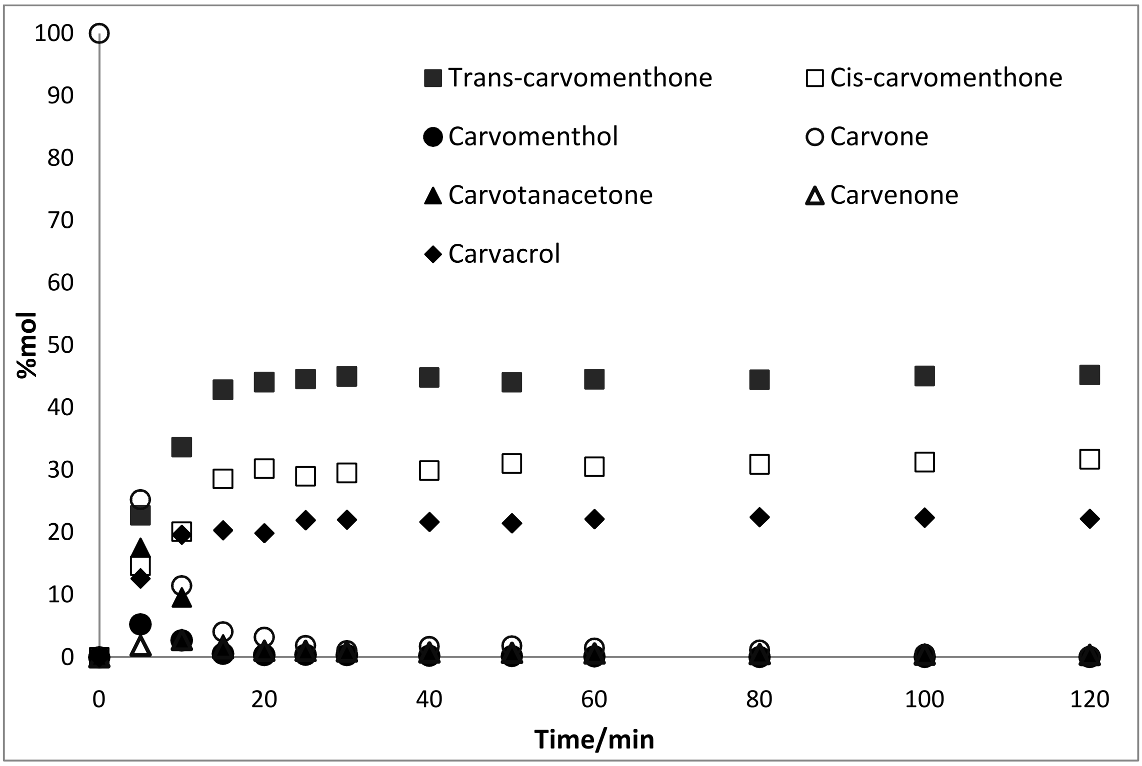

Figure 3.3 – Profile of the hydrogenation of carvone over Pd/Al_2O_3 catalyst in biphasic conditions (4 MPa of H_2, 12.5 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds.

Furthermore, in the initial stage of the reaction (first 15 minutes) two intermediate products (carvomenthol and carvotanacetone) are formed and their concentrations peak up to 5% for carvomenthol and 18% for carvotanacetone, and decay in the later stage. The third intermediate product, carvenone is formed during the reaction, however the concentration of this compound is very low and does not exceed 1.5 mol%. The concentration profiles of substrate and product as a function of time are illustrated in Fig 3.3 and Fig 3.4.

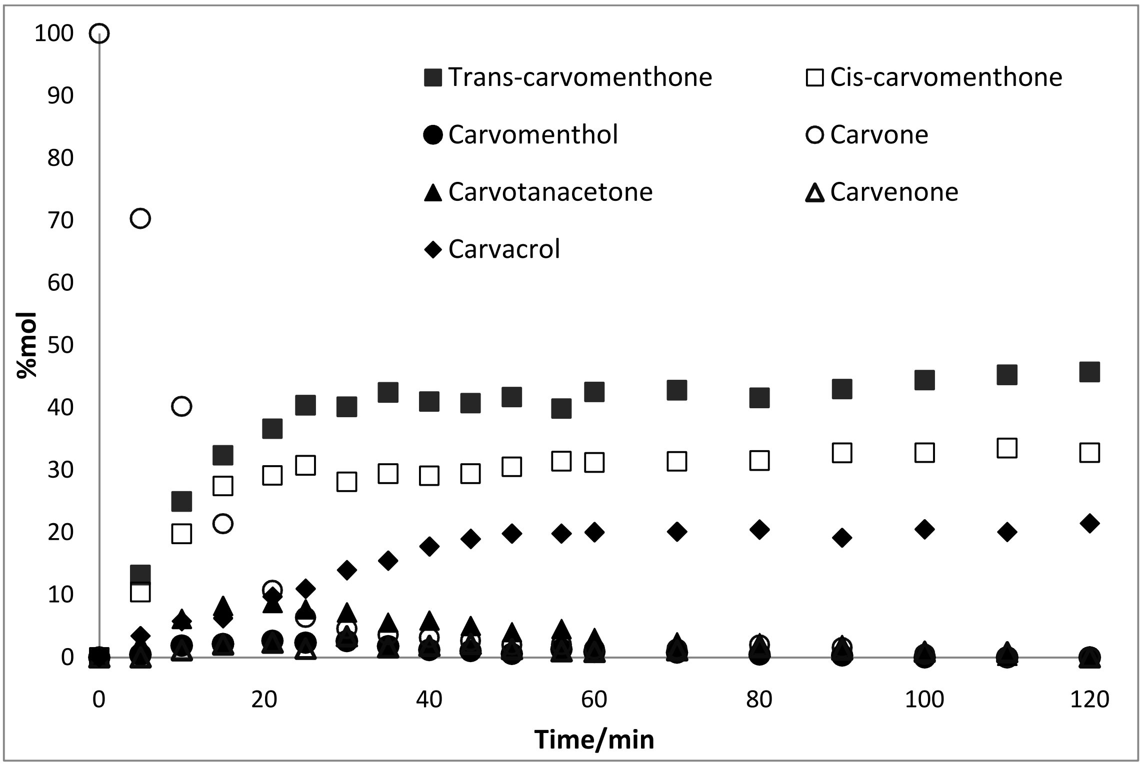

Figure 3.4 - Profile of the hydrogenation of carvone over Pd/Al_2O_3 catalyst in monophasic conditions (4 MPa of H_2, 16 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds.

3.1.2. Rh Catalysed reactions

In case of reactions catalysed by 0.5 wt% Rh/Al_2O_3 there is no significant difference between monophasic and biphasic conditions. The only noteworthy difference observed is time necessary to achieve reaction equilibrium. Similarly to Pd catalysed reaction, process in one phase reaches equilibrium faster after 50 minutes of the course of the reaction whilst in biphasic conditions is lengthened to 90 minutes.

Reactions catalysed by Rh catalyst guide to similar major products formed in (46.03 mol% and 36.70 mol% for trans- and cis-carvomenthone correspondingly) as Pd catalysed reactions.

The major difference was incapacity of the catalyst to complete conversion of carvone and total conversion achieved was slightly lower than in case of Pd used (96%). In addition, the intermediate product such as carvotanacetone was observed in relatively high quantity in the initial stage of the reaction; however its concentration decayed in the later stage being counterbalanced by the formation of two major isomers of carvomenthone as presented in Figure 3.5 and Figure 3.6. Contrary to Pd/Al_2O_3 the reaction catalysed by Rh catalyst produced carvacrol, carvenone and carvomenthol at the traces level.

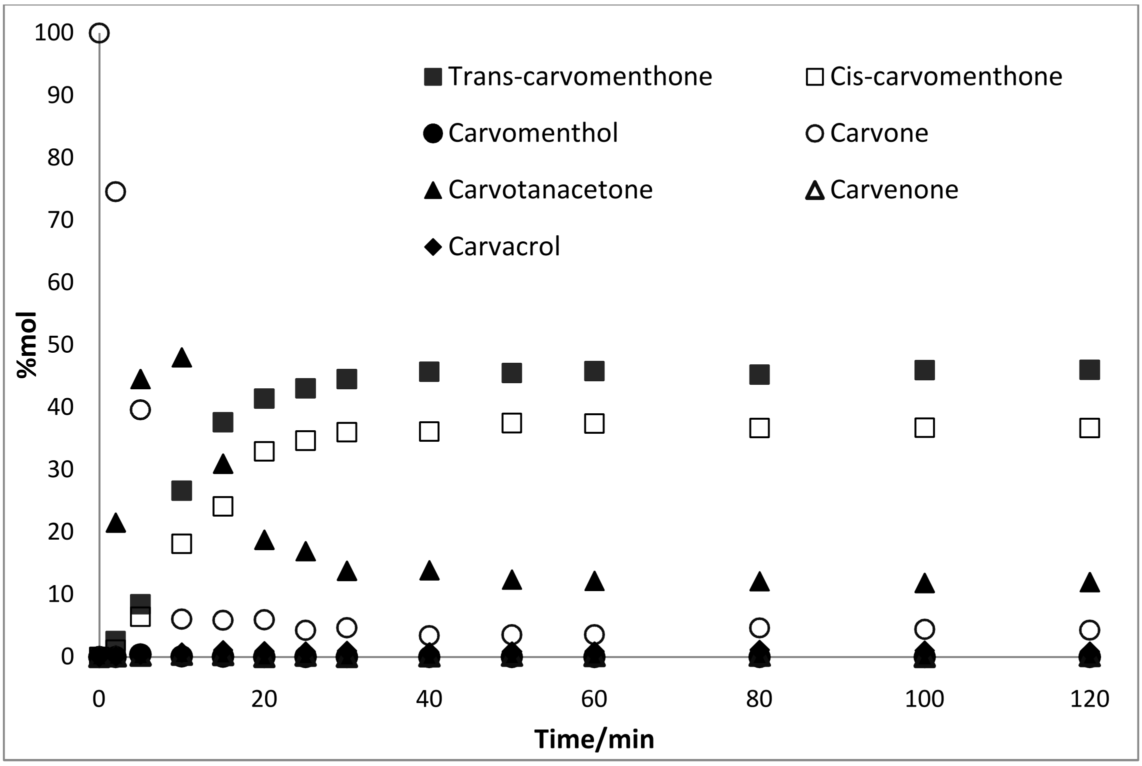

Figure 3.5 – Profile of the hydrogenation of carvone over Rh/Al_2O_3 catalyst in biphasic conditions (4 MPa of H_2, 12.5 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds.

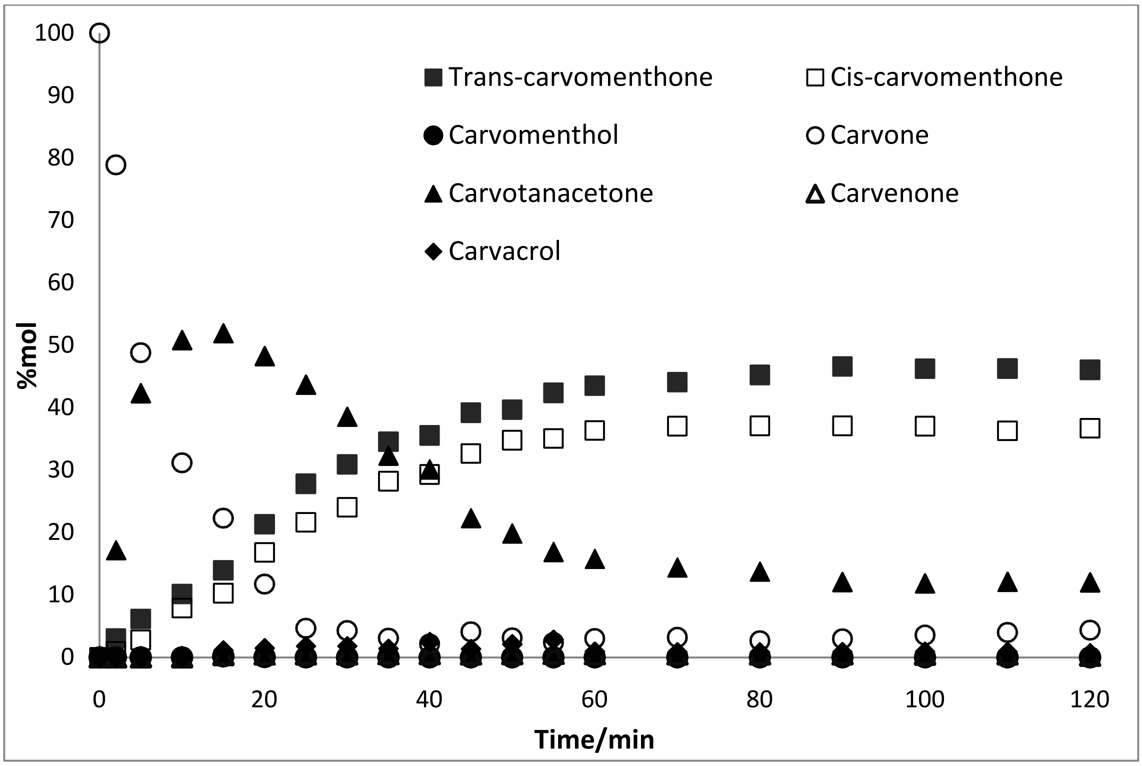

Figure 3.6 – Profile of the hydrogenation of carvone over Rh/Al_2O_3 catalyst in monophasic conditions (4 MPa of H_2, 16 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds

3.1.3. Ru Catalysed reactions

The results (shown in Figure 3.7 and 3.8) obtained in reactions catalysed by Ru/Al_2O_3 exhibit considerable difference on the contrary to reaction catalysed by Pd and Rh catalysts. Ru catalyst favours carvotanacetone as a major product of the reaction with lower formation of carvomenthone.

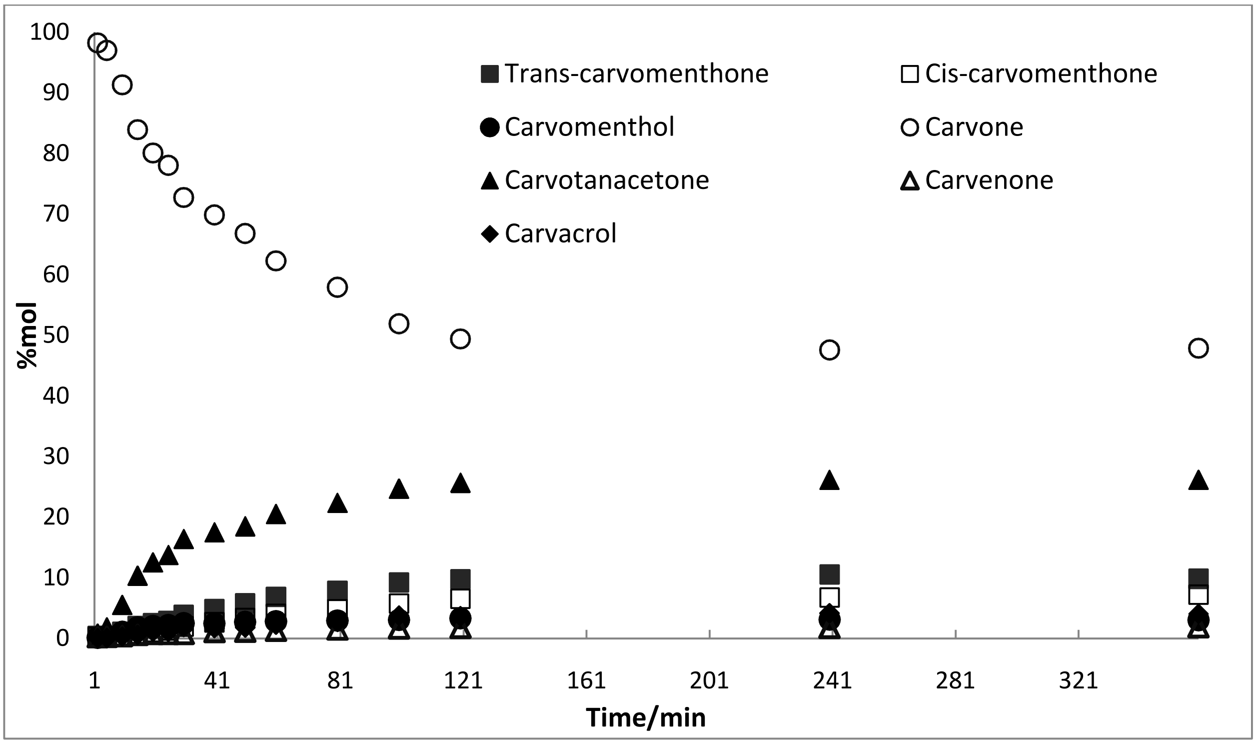

Figure 3.7 – Profile of the hydrogenation of carvone over Rh/Al_2O_3 catalyst in biphasic conditions (4 MPa of H_2, 12.5 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds. The solid lines are just connecting the points that correspond to the same compound in order to better understand their development through time.

Comparing to Pd and Rh, trans- and cis-carvomenthone were formed in 10 mol% and 7 mol%, respectively, and conversion reached to nearly 51%. Furthermore reaction with Ru is significantly slower and reaches equilibrium after 120 minutes in monophasic and 3 hours in biphasic conditions.

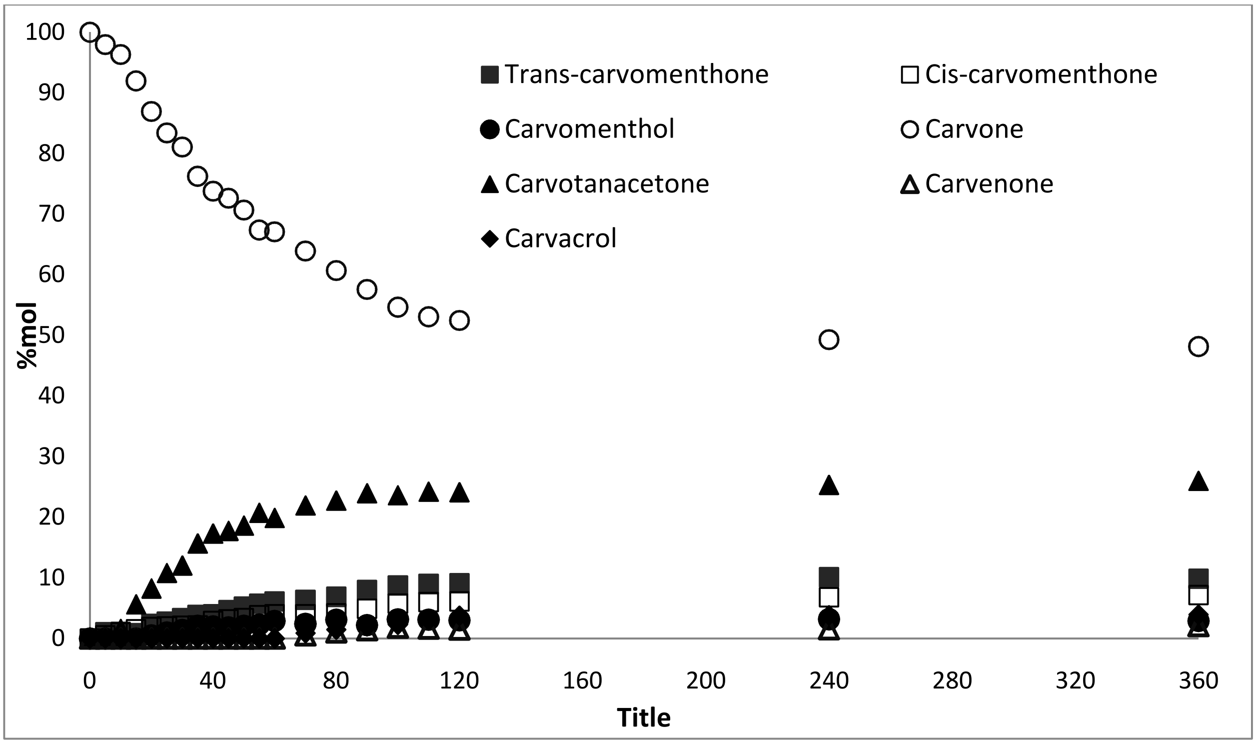

Figure 3.8 – Profile of the hydrogenation of carvone over Ru/Al_2O_3 catalyst in monophasic conditions (4 MPa of H_2, 16 MPa of total pressure, 323.15 K), expressed as mole percentage of compounds. The solid lines are just connecting the points that correspond to the same compound in order to better understand their development through time.

3.1.4. Catalyst stability

By analogy to a previous study on the hydrogenation of myrcene over Pd, Rh and Ru catalyst supported on alumina the AAS analyses were performed [13]. The AAS analyses showed that the highest metal content is found in the sample taken from the reaction carried out over Pd catalyst. The concentration of palladium detected in the samples collected from the reactions executed in one and two phases were similar and equalled to 20.3 mgL^{-1}.

Rhodium catalyst can be recognised as slightly more stable. The Rh content was found to be at the level of 15.7 mgL^{-1} in the samples from the reactions carried out in single and biphasic system. The analyses showed that Ru catalyst is the most stable catalyst indicating the lowest metal concentration in the reaction samples.

The data obtained for the samples after the reaction in one and two phases show that the concentration of Ru metal reached the level of 9.8 mgL^{-1}.

3.2. Carvacrol separation

3.2.1. Phase equilibria

The liquid-liquid (LLE) phase equilibria for systems containing environmentally benign solvents (water or ionic liquids) and carvacrol or carvone were studied herein. In the LLE investigations carvone as cheap and commercially available ketone was used to imitate other ketones (carvomenthone isomers) present in the post-reaction mixture. Among solvents for both hydrocarbons, carvone and carvacrol, water and two types of ionic liquids were tested. Along with water, hydrophobic, 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [bmim][NTf_2], and hydrophilic 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [bmim][OTf], were used for LLE studies to examine conditions for the carvacrol separation from the mixture obtained in the hydrogenation reaction.

The achieved results show that LLE with water and tested ionic liquids display miscibility gap with upper critical solution temperature (UCST). In general, the solubility of carvacrol and carvone in water and hydrophobic ionic liquid shows no significant difference in solubility (Fig. 3.9); however the solubility of both tested compounds reveals a noticeable difference of 10 K in UCST in the hydrophilic ionic liquid.

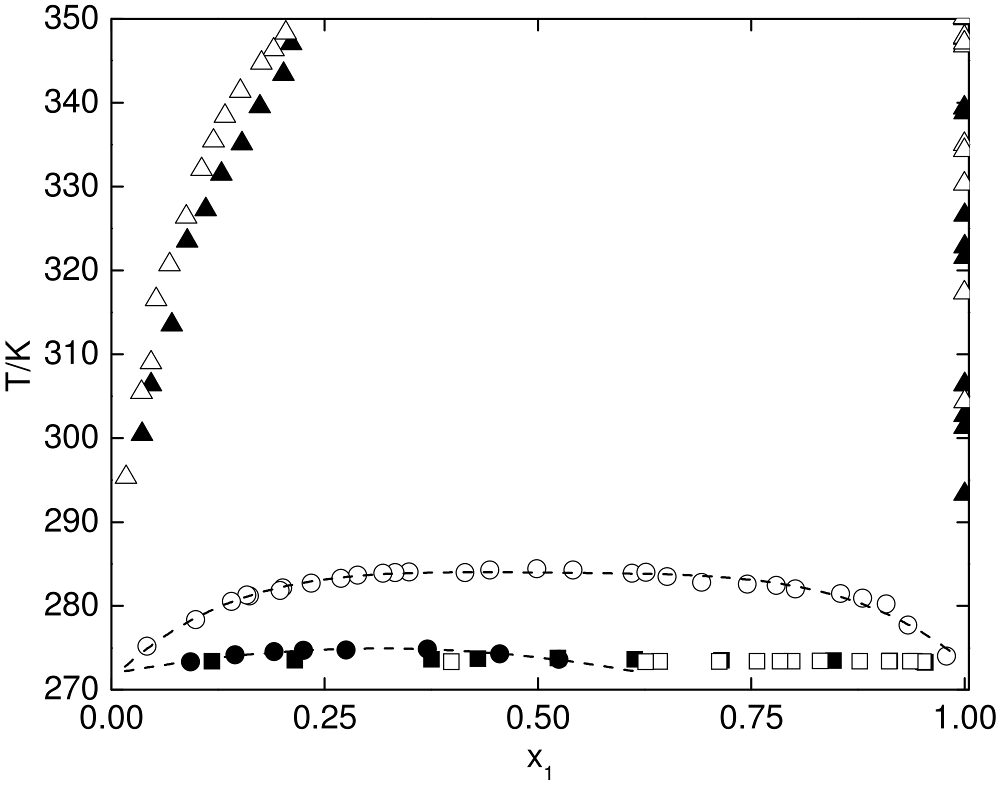

Figure 3.9 – The LLE phase envelopes for systems containing water (1) + carvone (2) (Δ), water (1) + carvacrol (2) (▲), [bmim][NTf2] (1) + carvone (2) (□), [bmim][NTf2] (1) + carvacrol (2) (■), [bmim][OTf] (1) + carvacrol (2) (●) and [bmim][OTf] (1) + carvone (2) (○). Dashed lines are provided as a guide for the eye for systems being of the major interest in this study.

The system with carvacrol displays UCST at 274.85 K while for the corresponding system with carvone the critical temperature is equalled to 284.41 K.

To facilitate separation of carvacrol and ketones the optimal conditions had to be selected on the base of the following criteria: (1) miscibility gap for a system [bmim][OTf] + carvone should be as broad as possible, (2) the temperature at which separation is performed must guarantee complete mutual miscibility of ionic liquid and carvacrol. Both criteria were found to be accomplished at 275.15 K selected arbitrary. At this temperature, on one hand the [bmim][OTf] + carvacrol system was found to show off complete miscibility, and on the other hand the miscibility gap for system [bmim][OTf] + carvone was wide enough being in the range of $0.042<x_1<0.973$, where x_1 is ionic liquid mole fraction.

To verify the potential of carvacrol recovery, the study of ternary system containing carvacrol, carvone and [bmim][OTf] was essential. Results of this investigation at 275.15 K at ambient pressure are depicted in Fig. 3.10.

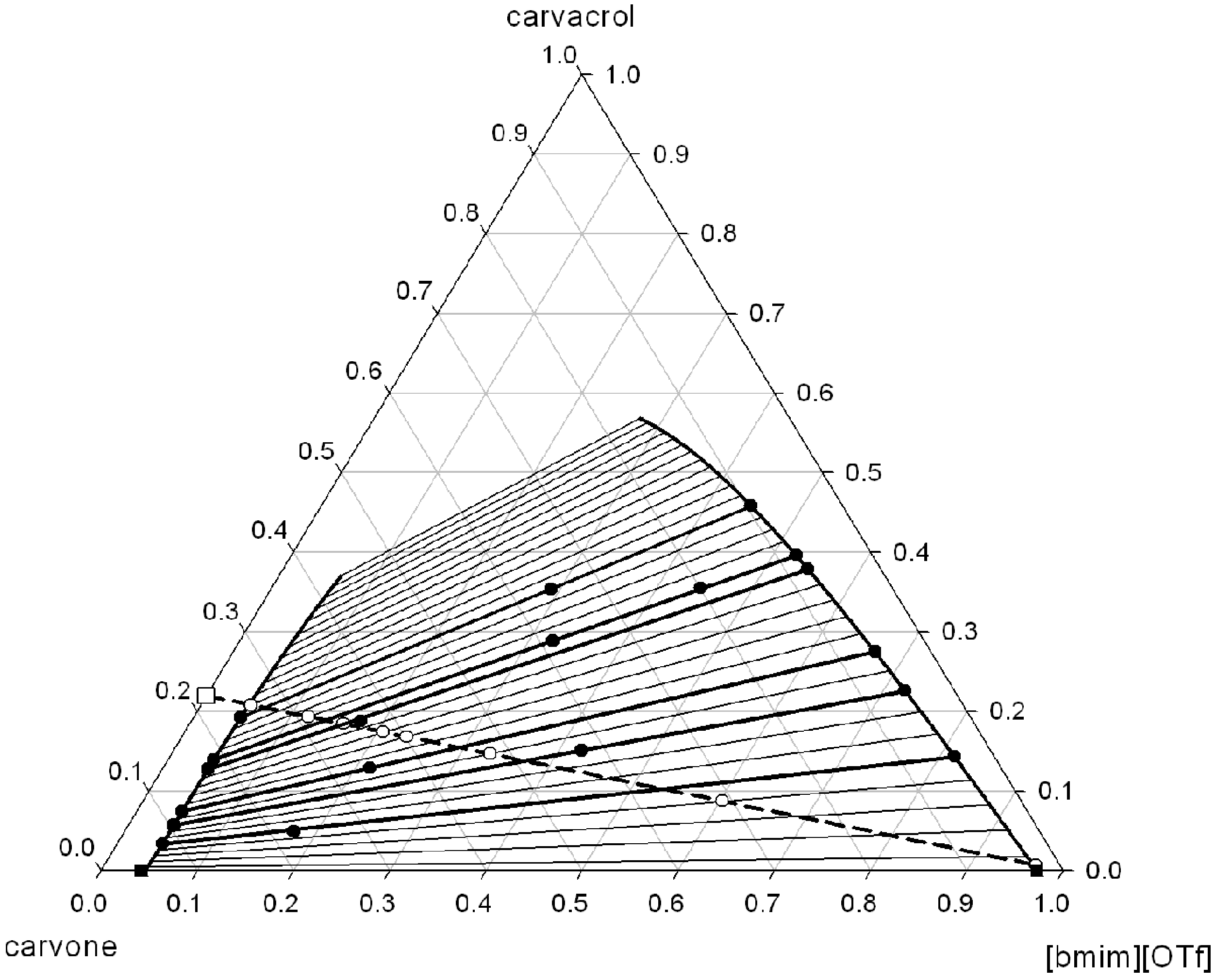

Figure 3.10 – The ternary phase diagram for carvone (1) + [bmim][OTf] (2) + carvacrol (3). The closed squares (■) represent the mutual solubility of carvone and [bmim][OTf] at the experimental conditions. The closed circles (●) illustrate the composition of the initial mixture and corresponding ionic liquid and ketone-rich phase composition. The solid lines illustrate the tie-lines obtained through the model described in the text. Bolded solid lines depict phase envelope and selected tie-lines for the initial concentrations studied. The open square (□) represents the composition of the mixtue after hydrogenation reaction. The open circles (○) symbolise the points from the separation of carvacrol from the hydrogenation reaction mixture. The dashed line denotes the change in the composition depending on the IL fraction in the sample maintaining carvacrol to ketones ratio equalled to the obtained in the hydrogenation reaction.

The LLE data for ternary system for various concentrations of solution containing [bmim] [OTf], carvacrol and carvone and the composition of the ketone and ionic liquid-rich phase are presented in Table 3.1.

Table 3.1 – The ambient pressure liquid-liquid equilibrium (LLE) data obtained at 275.15 K for the ternary mixture constituted by carvone, carvacrol and [bmim][OTf]. The partition coefficients (*K*) and separation factor (α) for the mother solutions calculated from the tie-lines of the phase diagram.

initial composition		ketone-rich phase		IL-rich phase		$K_{carvacrol}$	$K_{carvone}$	α
$x_{carvacrol}$	$x_{carvone}$	$x_{carvacrol}$	$x_{carvone}$	$x_{carvacrol}$	$x_{carvone}$	$\frac{x_{carvacrol}^{IL-rich\ phase}}{x_{carvacrol}^{ketone-rich\ phase}}$	$\frac{x_{carvone}^{IL-rich\ phase}}{x_{carvone}^{ketone-rich\ phase}}$	$\frac{K_{carvacrol}}{K_{carvone}}$
0.0493	0.7749	0.0339	0.9191	0.1432	0.0412	4.224	0.045	94.2
0.1285	0.6560	0.0747	0.8781	0.2751	0.0581	3.683	0.066	55.7
0.1513	0.4247	0.0572	0.8956	0.2260	0.0513	3.951	0.057	69.0
0.1878	0.6358	0.1272	0.8253	0.3787	0.0758	2.977	0.092	32.4
0.2885	0.3860	0.1393	0.8130	0.3964	0.0795	2.846	0.098	29.1
0.3533	0.3557	0.1393	0.8130	0.3964	0.0795	2.846	0.098	29.1
0.3550	0.1991	0.1924	0.7584	0.4584	0.0951	2.382	0.125	19.0

3.2.2. Modelling

The correlation of the experimental data was performed using the Peng-Robinson equation of state (PR-EOS).[60] The mixing rule published by Mathias et al.[61] was employed in this study. The equation of state and mixing rule via the PE software[62] were used in modelling. The PR-EOS is defined as:

$$p = \frac{RT}{v-b_i} - \frac{a_i}{v^2+2b_i v-{b_i}^2},$$

where $a_i = 0.45724\frac{R^2T_c^2}{p_c}\left[1+(0.37464+1.54226\omega-0.26992\omega^2)\left(1-\sqrt{T_r}\right)\right]^2$ and $b_i = 0.0778\frac{RT_c}{p_c}$. The mixing rule published by Mathias et al.[61] was employed in this study. The Mathias-Klotz-Prausnitz mixing rule (MKP) is determined by the equation:

$a = \sum_{i=1}^{N}\sum_{j=1}^{N} x_i x_j \sqrt{a_i a_j}\left(1-k_{ij}^{MKP}\right) + \sum_{i=1}^{N} x_i (\sum_{j=1}^{N}(\sqrt{a_i a_j}\,\lambda_{\mathrm{ji}}^{\mathrm{MKP}})^{1/3})^3$ with $k_{ji}^{MKP} = k_{ij}^{MKP}$, $\lambda_{ji}^{MKP} = -\lambda_{ij}^{MKP}$ and $b_{ij} = \frac{b_i+b_j}{2}\left(1-l_{ij}\right)$ with $l_{ij} = l_{ji}$.

The equation of state and mixing rule were implemented using the PE software.[61] The critical properties for ionic liquid were taken from the literature[61] while the critical properties of carvacrol and carvone were estimated by the Joback group contribution method.[61] The acentric factors of both hydrocarbons (ω) were obtained on the base of the Lee-Kesler method.[63] The critical properties and acentric factors of pure components are compiled in Table 3.2.

Table 3.2 – The critical properties and acentric factors of the studied compounds.

Compound	Chemical formula	Molecular weight (gmol^{-1})	T_c (K)	p_c (MPa)	ω
Carvone	$C_{10}H_{14}O$	150.2	712.76	2.72	0.493
Carvacrol	$C_{10}H_{14}O$	150.2	720.42	3.34	0.583
[bmim][OTf]	$C_9H_{15}N_2F_3SO_3$	288.3	1023.5	2.95	0.405

The experimental data for ternary system were fitted with abovementioned equations of state by an adjustment of the set of interaction parameters. The best set of the interactions parameters that minimises the deviations between the calculated and experimentally determined liquid and vapour phase compositions, as well as the distribution factors of all components of the mixture, were determined. The objective function used to calculate the deviation between the experimental and the correlated data is described by the following equation

$$deviation = \sqrt{\frac{1}{n}\sum_{i=1}^{n}\left(z_i^{exp} - z_i^{calc}\right)^2},$$

where z_i^{exp} and z_i^{EOS} are the mole fraction of compound *i* in the ketone or ionic liquid-rich phase determined experimentally and by the equation of state, respectively, and *n* is number of experimental points. The sets of parameters for the investigated system at 275.15 K are presented in Table 3.3.

Table 3.3 Optimised interaction parameters of the ternary (carvone (1) + [bmim][OTf] (2) + carvacrol (3)) system for the Peng–Robinson equation of state with the Mathias–Klotz–Prausnitz mixing rules. The deviations between mole fractions – experimental and correlated by means of the PR-EOS for the investigated ternary systems at 275.15 K

Parameters	1-2	1-3	2-3	deviation (%)		
				IL-rich phase	ketone-rich phase	overall
k_{ij}	0.305190	-0.032684	0.117295	1.40	1.85	1.64
l_{ij}	0.233733	-0.028483	0.170894			
λ_{ij}	0.137140	-0.000005	-0.087243			

The selected equation of state and mixing rule was able to describe accurately the phase boundary for the examined range of composition. The critical range of the studied ternary LLE system was not described by the used PR-EOS due to the lack of the experimental points in this zone. It is worth to underline that critical region is one of the most difficult to mode. Nevertheless, for the purpose of this work the region far from the critical is the most interesting and this one is described accurately by the experimental data.

3.2.3. Separation study

The separation studies were preceded by calculation of the partition coefficients and the separation factors.

Partition or distribution coefficient is the ratio of concentrations of a compound in two phases of a mixture of two immiscible solvents at equilibrium. The partition coefficient is commonly used to evaluate the distribution of organic compounds between e.g. ionic liquid and second immiscible phase.[64,65,66,67] It is given by the following equation:

$$K_{solute} = \frac{x_{solute}^{IL-rich\,phase}}{x_{solute}^{ketone-rich\,phase}},$$

where $x_{solute}^{IL-rich\,phase}$ and $x_{solute}^{ketone-rich\,phase}$ are mole fractions of solute in ionic liquid and ketone-rich phases.

The partition coefficients for the LLE studies for various initial concentrations were calculated according to the aforementioned equation and are presented in Table 3.2. Partition coefficients for carvacrol are one to two orders of magnitude higher than partition coefficients for carvone.

The separation factor (α) is usually defined as ratio of partition coefficients for different solutes, and they measure the ability of a system of immiscible solvents to separate two solutes:

$$\alpha = \frac{K_{solute1}}{K_{solute2}},$$

where $K_{solute1}$ and $K_{solute2}$ are partition coefficients of two solutes i.e. carvacrol and carvone.

The results of hydrogenation of carvone showed that in the post-reaction mixture the ratio of carvacrol to ketones is like 21.95 to 78.05. The experiments with different compositions of the post-reaction sample and an ionic liquid were performed considering the obtained ternary phase equilibrium data and calculated separation factors. The results of this investigation are demonstrated in Fig. 3.10 and in Table 3.4.

Table 3.4 – The LLE data, partition coefficients (*K*) and separation factor (α) for the separation of carvacrol from the post-hydrogenation product mixture

initial composition		ketone-rich phase		IL-rich phase		$K_{carvacrol}$	$K_{carvone}$	α
$x_{carvacrol}$	$x_{carvone}$	$x_{carvacrol}$	$x_{carvone}$	$x_{carvacrol}$	$x_{carvone}$	$\frac{x_{carvacrol}^{IL-rich\ phase}}{x_{carvacrol}^{ketone-rich\ phase}}$	$\frac{x_{carvone}^{IL-rich\ phase}}{x_{carvone}^{ketone-rich\ phase}}$	$\frac{K_{carvacrol}}{K_{carvone}}$
0.2080	0.7398	0.2067	0.7435	0.4717	0.0993	2.282	0.134	17.1
0.1934	0.6877	0.1519	0.8002	0.4132	0.0832	2.720	0.104	26.2
0.1844	0.6559	0.1272	0.8253	0.3787	0.0758	2.977	0.092	32.4
0.1742	0.6195	0.1046	0.8481	0.3403	0.0686	3.253	0.081	40.2
0.1682	0.5981	0.0941	0.8587	0.3196	0.0651	3.396	0.076	44.8
0.1468	0.5221	0.0657	0.8871	0.2511	0.0547	3.822	0.062	62.0
0.0874	0.3110	0.0266	0.9265	0.1135	0.038	4.267	0.041	104.0

The separation factor for the studied samples containing ionic liquid and mixture from the hydrogenation reaction was found to be as high as 17 and increases to 104 as the concentration of separation solvent (ILs) reaches maximal according to the phase diagram presented in Fig. 3.10.

The experiments performed with the post-hydrogenation samples and de [bmim][OTf] ionic liquid in various ratios (open circles (o) in Fig. 3.10) confirmed de calculated results obtained from LLE data for ternary systems. It was found that minimal amount of IL ($x_{[bmim][OTf]}$=0.0521) allows for the significant enrichment (from 21.95 mol% to 95 mol%) of carvacrol concentration. A higher concentration of IL ($x_{[bmim][OTf]}$>0.33) allowed increasing the purity of carvacrol above 98 mol% or even higher as depicted in Fig.3.10.

The extraction studies were performed on the example sample containing IL ($x_{[bmim][OTf]}$=0.33) and hydrogenation products after separation with [bmim][OTf] (chiefly carvacrol and other minor compounds which were co-extracted during liquid-liquid separation with IL). The extraction was performed at 12 MPa because at this condition CO_2 and carvacrol from one phase (above critical pressure). The GC analyses showed no traces of carvacrol remained on the IL phase in high pressure reactor and the quantitative and qualitative analyses of the cold trap demonstrated complete removal of carvacrol from IL phase with the purity significant above 98 mol%.

4. Discussion

4.1.The catalyst activity

The hydrogenation of carvone performed in the environment of $scCO_2$ was carried at milder conditions namely temperature and H_2 pressure was catalysed by three different noble metal catalysts. Conventional solid catalyzed hydrogenation in organic solvents is mainly H_2 concentration dependent. Under supercritical carbon dioxide conditions, either conversion of carvone and selectivity of desired products or the reaction time were found to be remarkably increased in comparison to those for an organic solvent, which highlight the advantageous role of CO_2 as reaction medium. Each of the catalysts applied exhibit different attitude towards direction of hydrogenation of carvone and thus preceded distinguishable results. The Pd catalyst is known as an active metal catalyst and present investigation confirmed this feature. The previous study from our laboratory for other terpenes (limonene and β-myrcene) demonstrated that Pd catalyst is very active metal and facilitates conversion of terpenes and good selectivity towards the fully hydrogenated products in reactions performed in biphasic conditions.[9,13,68].

Similarly to limonene or myrcene there data for systems consisting of CO_2 + carvone; however ternary systems containing hydrogen as a third component have never been studied. Nevertheless based on preceding studies for CO_2 + H_2 + terpene it can be assumed that 12.5 MPa total pressure system is biphasic (gaseous CO_2 + H_2 and CO_2 – expanded liquid carvone). This assumption was confirmed by a visual observation performed during progress of the reaction. Additionally, liquid-like CO_2 is good solvent for hydrocarbons but also maintains the properties characteristic for gases thus brings hydrogen to the CO_2 – expanded liquid phase facilitating reaction and reducing conditions of reaction.

Based on the results obtained for the reaction catalysed by Rh in this work and in our previous studies, it can be stated that rhodium catalyst is less active than palladium.[13] As it was reported in the literature, the hydrogenation of unsaturated olefins catalysed by ruthenium is generally even slower. It is caused by at least 50 times lower activity of ruthenium catalyst in comparison to palladium or rhodium [38]. The way of expressing activity of the catalyst can be the initial reaction rate constant (*k*) calculated. The *k* values calculated using the procedure described below were collected in Table 4.1.

Table 4.1 - The initial reaction rate constant (10k/min) for the hydrogenation of first C=C double bond of carvone carried out over Pd, Rh or Ru catalyst in one or two phases conditions.

	10k/min		
	Pd	Rh	Ru
one phase	2.08	1.87	0.11
two phases	1.13	1.01	0.07

The ordinate units in the concentration profiles are mole percentage of the total amount of terpenes and taking into account the solubility of CO_2 in carvone at the reaction conditions, the initial volumes of the CO_2-expanded liquids were calculated. The obtained results allow the calculation of the initial reaction rate constants and the initial volumes of the liquid phase for the initial stage of the reactions in each experiment.

From the calculated volumes of the liquid phase and the known total initial amount of carvone, its initial concentration (in mol/vol) was calculated. In addition, the mol% of carvone was used to calculate the concentration (mol/vol) of carvone as a function of time due to the fact that each molecule of product is produced from one molecule of carvone. Moreover, the reactions were carried out in a semi-continuous way, and the used high recirculation rate allows the composition of the feeds to alter continuously, consequential in kinetics like in a batch process. Indeed, with the applied 3.3 mL/min flow rate of the reaction mixture, the entire liquid is recirculated at least once every 2–3 minutes.

Postulating the disappearance of carvone as a first order reaction, plots of ln[carvone] as a function of time showed straight lines for the initial stages of the reaction. In $scCO_2$ the reaction kinetics exhibited a first-order reaction rate i.e. for limonene[9], β-myrcene[35] and citral[69] hydrogenations.

Summarising, it can be stated that the pressure of CO_2 strongly affects the reaction conditions, and at lower total pressure (12.5 MPa) reactions were carried out in biphasic (liquid + gas) conditions, while 16 MPa of total pressure shifted the reaction mixture towards a one-phase region. The pressure tuning changes not only the number of phases, but also controls the concentration of the reagents in the vicinity of the catalyst. This in turn determines the rate of the reaction and indicates also that the hydrogenation of the first double bond is always faster in one phase than in two phases as presented in Table 4.1. Moreover, the experimental results exhibited that the initial reaction rate constant depends on the activity of the catalyst used for the reaction, and the decreasing trend with diminishing the catalyst activity was found.

4.2. The catalyst and mechanism of the reaction

The catalyst metal is responsible for the reaction kinetics but also determines the conversion and selectivity of the obtained products. In particular, the reaction results products obtained in the hydrogenation of carvone over Pd/Al_2O_3 allowed to propose the mechanism of the reaction to explain products obtained in the hydrogenation of carvone. The mechanism is presented in Fig. 4.1. The mechanism proposed is based on the classical Horiuti-Polanyi mechanism[70]. Furthermore, similar mechanism of hydrogenation catalysed by Pd catalyst was previously presented by Klabunovskii et al.[29]. Klabunovskii and co-workers postulated that such hydrogenation catalysed by Pd-Black leads to the first intermediate product which is carvotanacetone and in the further steps carvomenthones and carvacrol are formed. Both compounds are formed in the parallel pathways and carvomenthones are created via the hydrogenation while the second one is formed by the irreversible catalysis.[29]

The literature reports[71,72] showed that mechanism of Rh catalysed hydrogenation of olefins is comparable to platinum catalysed reactions. This may suggest that the hydrogenation of terpene catalysed by Rh occurs via 1,2-σ_2 adsorption, contrary to the formation of π-allyl complexes present in the case of palladium catalysed hydrogenation [70,72]. Referring to Ru catalysed hydrogenation of carvone it needs to be underline that investigations presenting mechanism of hydrogenation of terpenes are scarce[73]. Our previous study[13] showed there is no conjunctive agreement in this matter. This proves that further investigations in this field should be performed.

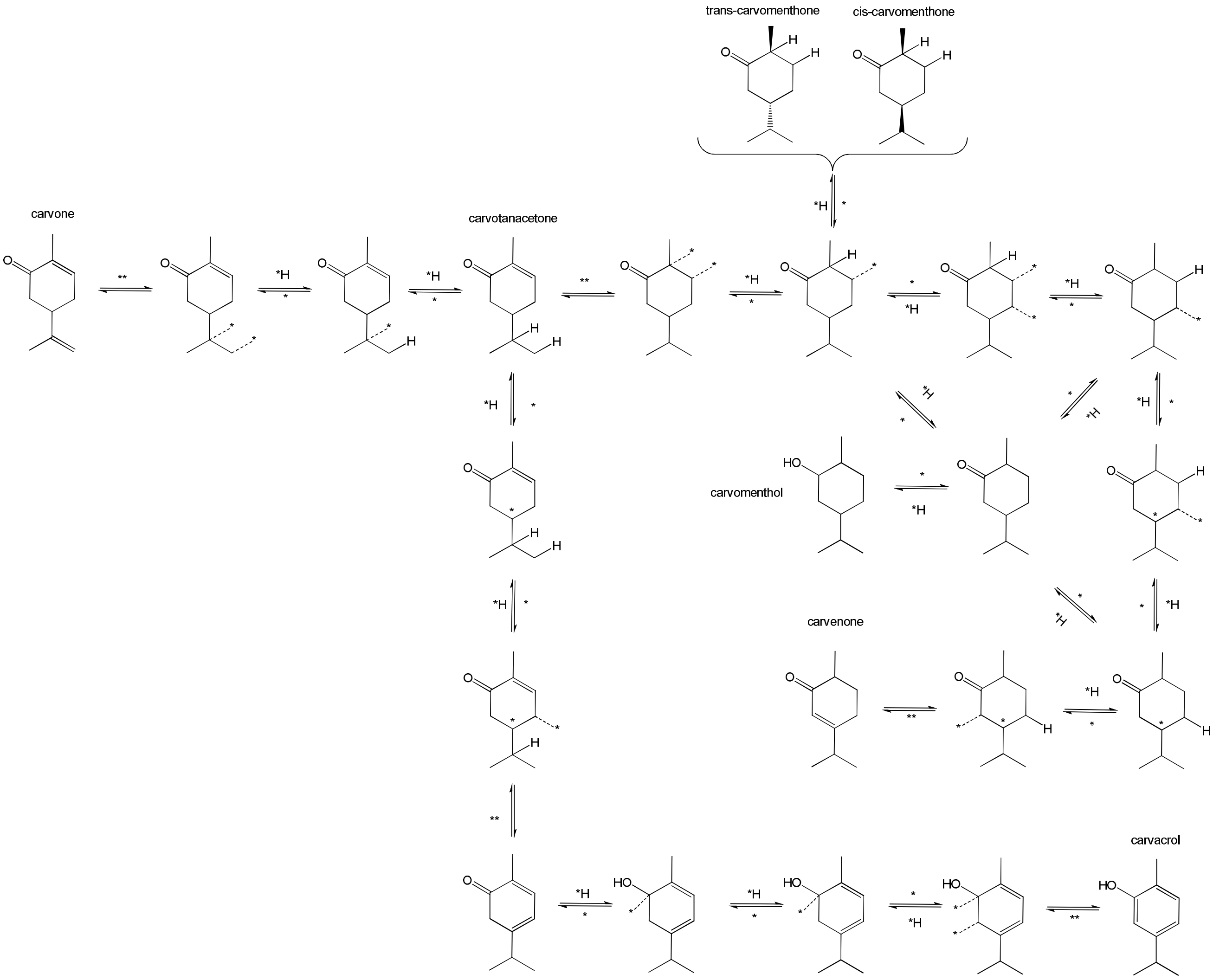

Figure 4.1 – The mechanism of the hydrogenation of carvone. The * symbolises the catalyst. To simplify, the stage of stereo isomerisation of cis- and trans- isomers of carvomenthone was omitted.

4.3.Product distributions

The major products of carried out reactions are either fully saturated isomers of carvomenthone (Pd and Rh catalysts), or carvacrol (Pd catalyst), or carvotanacetone which is an intermediate obtained through direct hydrogenation of carvone (Rh and Ru catalysts).

The reaction catalysed by Pd catalyst gave major fully saturated isomers of carvomenthone but also significant quantity of carvacrol – a product of irreversible catalysis of carvone.[29] The selectivity towards carvacrol was found to be relatively low; however carvacrol was formed in the highest quantity (>22%) among all tested catalysts. For all results reported, the selectivity was calculated according to the following equation

$$S/\% = \frac{C_i}{\sum C_p} \times 100\%,$$

where C_i was the concentration of component "*i*" and C_p was the total concentration of the hydrogenation products At the same time the selectivity to fully hydrogenated products reached more than 77% in case of Pd catalysed reaction and with Rh/Al_2O_3 catalyst the selectivity was higher and achieved 86.4%. These values of selectivities indicate that Rh catalyst promotes the formation of fully saturated product leaving conversion of carvone not complete but approximate to 96%. The conversion of carvacrol is defined as follows

$$C/\% = \frac{\sum C_p}{\sum C_p + C_{carv\,one}^{un.}} \times 100\%,$$

where $C_{carvone}^{un.}$ was the concentration of the unreacted carvone.

The reaction catalysed by Ru/Al_2O_3 is characterised by the lowest conversion which is associated with the highest selectivity towards intermediate product such as carvotanacetone. The mentioned conversion at equilibrium is only 50.6% of the initial concentration of carvone and selectivity to carvotanacetone reaches to 50.7%.

Analysing data presented in Table 4.2 and results depicted in Figures 3.2–3.8 it can be stated that either carvomenthone or carvotanacetone are obtained with very good selectivities; however in case of intermediate product such as carvotanacetone a very high selectivity of 84.7% can only be achieved with low conversion of carvone in the reaction catalysed by Rh/Al_2O_3. It has to be mentioned that no conversion of carvone occurred without a catalyst under the investigated biphasic or monophasic system.

Table 4.2 – The list of example reactions reported in this work. The table contains the catalyst, reaction time, conversion of carvone (C/%) and selectivities (S/%) towards particular products at certain reaction time as well as turnover frequency (TOF/min^{-1}) for biphasic and monophasic conditions for each of the catalyst.

Catalyst	time/min	C/%	$S_{carvomenthone}$ /%	$S_{carvotanacetone}$ /%	$S_{carvacrol}$ /%	TOF/min^{-1}
Pd/Al_2O_3	120	99.9	76.7	0.2	22.2	610[a] 304[b]
$Rh/\ Al_2O_3$	2	25.4	14.5	84.7	0.4	345[c]
	120	95.7	86.4	12.5	0.9	218[d]
$Ru/\ Al_2O_3$	120	50.6	32.1	50.2	7.8	74[e] 25[f]

[a] – after 30 minutes (equilibrium) in one phase reaction; [b] – after 60 minutes (equilibrium) in two phase reaction; [c] – after 50 minutes (equilibrium) in one phase reaction; [d] – after 90 minutes (equilibrium) in two phase reaction; [e] – after 120 minutes (equilibrium) in one phase reaction; [f] – after 360 minutes (equilibrium) in two phase reaction.

4.4. Carvacrol separation

One of the most common methods of the recovery of compound is the liquid-liquid extraction. The conventional way of the liquid-liquid extraction is the use of volatile solvents (i.e. hexane) to facilitate further purification of the final product. Recently, the use of sustainable solvents such as ionic liquids becomes more popular mostly because of the environmental concerns as well as it was aforementioned due to higher selectivity of ionic liquids in the specific processes.[17]

The LLE phase equilibrium investigations of systems containing ionic liquids and studied mixture are tools suitable for development of the optimal conditions of the required separation. In the case presented in this work, a subtle difference in solubility between carvone (ketone representative) and carvacrol (analogous alcohol) was found thus optimal solvent for further separation was selected. Both carvacrol and carvone are based on the hydrocarbon skeleton and contain polar groups (carbonyl and hydroxyl).

The fine dissimilarity between both groups guided us to test either hydrophobic or hydrophilic solvents. As a representative of hydrophobic solvents [bmim][NTf$_2$] ionic liquid was used as is one of the most popular ionic liquid[74,75] being precursor in new applications.[50] The hydrophilic solvents were represented by water and [bmim][OTf]. The obtained LLE data allowed assuming that combination of hydrophobic skeleton of carvone and carvacrol as well as hydrophilic groups present in both compounds determines specific interactions between solvent and solute.

The LLE phase envelopes presented in Fig. 3.9 clearly indicate that both solutes are strongly hydrophobic and as a result solubility in hydrophobic [bmim][NTf$_2$] is almost complete (UCSTs < 274 K) in the range of temperatures studied here. Contrary to solubility in the hydrophobic IL, carvone and carvacrol exhibit limited affinity towards different hydrophilic solvent such as water. As an example can be given fact that even at temperature as high as 350 K the solubility of carvone and carvacrol in water is negligible and is lower than 0.0005 of mole fraction of solute. This behaviour can be explained by very strong intermolecular hydrogen bond network formed by water and thus further reduction in solubility of hydrocarbons.

The remedy for a very low solubility of hydrocarbons in water and quasi complete miscibility with [bmim][NTf2] is [bmim][OTf] which seems to be optimal solvent for nonpolar skeleton of carvone and carvacrol but at the same time is known as one of the hydrophilic ionic liquids.[75] The LLE data showed that solubility of carvone and carvacrol in [bmim][OTf] exhibits higher UCST than in case of hydrophobic [bmim][NTf$_2$] and dramatically lower than theoretical value of UCST for water systems.

The observed difference in solubility between both compounds can be explained by the dissimilarity in structure thus difference in the chemical potential or more precisely in the activity coefficient of both compounds in the ionic liquid studied. There is no activity coefficient data for studied pairs (carvone or carvacrol + [bmim][OTf]); however the activity coefficients available for other ketone (acetone) and alcohol (2-propanol) in [bmim][OTf] show that at room temperature the activity coefficients are 1.48 and 0.85 for 2-propanol and acetone respectively.[76] This value may indicate that in general alcohols such as 2-propanol and probably as carvacrol are more soluble in [bmim][OTf] than ketones such as acetone and carvone.

The LLE studies for ternary samples simulating compounds presented in the hydrogenation sample and [bmim][OTf] with different initial composition allowed drawing ternary phase diagram. From phase diagram the partition coefficients and separation factors were calculated. The obtained

LLE data disclosed significant difference between [bmim][OTf] and ketone-rich phases and high values of separation factors. These results are an effect of large differences in solubilities of both solutes in ILs as it was explained above. This intriguing data drove us to test the selected IL with a real mixture of products from hydrogenation reaction of carvone.

Analysing obtained results of real post-hydrogenation sample it was found that carvacrol separation from the product-rich phase is possible even with small additive (x_1=0.0521) of the hydrophilic [bmim][OTf]. In other words carvacrol was completely recovered from ketone phase in the presence of minimal amount of ionic liquid and thus the carvacrol's concentration in the sample from hydrogenation reaction was enriched from 21.95% mol% to a 95 mol%. The separation was repeated for different concentrations of IL. It can be stated that even at mole fraction of IL equalled to 0.3, carvacrol was extracted quantitatively (> 98 mol%).

These results confirm high α as it increases significantly from 17 to 140 at maximal mole fraction at which still two phases are present. The dependence of separation factors on the mole fraction of IL used in the separation is presented in Fig 4.2.

The further step of recovery of carvacrol from IL was performed using the CO_2 extraction technique previously presented in our other work. The extraction with high dense CO_2 was selected as more favourable than e.g. distillation due to high boiling point of carvacrol and existence of risk of partial or complete IL decomposition. The extraction with CO_2 proved again that CO_2 is a good solvent and is able to extract quantitatively compounds such as carvacrol with purity significantly higher than 98 mol% equalled to the purity the separation step.

The objective of hydrogenation of available carvone was to achieve such a selectivity of carvacrol to could consider further separation and extraction of carvacrol from post-reaction mixture using alterative solvents. This goal was achieved in reaction with palladium catalyst. Reactions at high-pressure conditions are relatively fast and in this particular case, hydrogenation achieved equilibrium within 30 minutes of reaction. The major products of carvone hydrogenation are two stereoisomers of carvomenthone. Nevertheless, in the course of reaction carvacrol was obtained in the concentration of 21.95% as a third product. One of the main advantages of the reaction performed is that carvacrol produced via supercritical CO_2-assisted hydrogenation was obtained in reaction at modest temperature.

There are known various classical approaches described above that produced carvacrol with significantly higher yield, but they are also characterized by the use of hazardous chemicals, production of wastes, flammability and explosion risk, moderate or high temperature and autogenous pressure conditions. Therefore the method presented in this work might be considered as a potential alternative to the classical techniques presented up to now as it combines the use of supercritical carbon dioxide and ionic liquids in a moderate/low temperature treatment of cheap carvone.

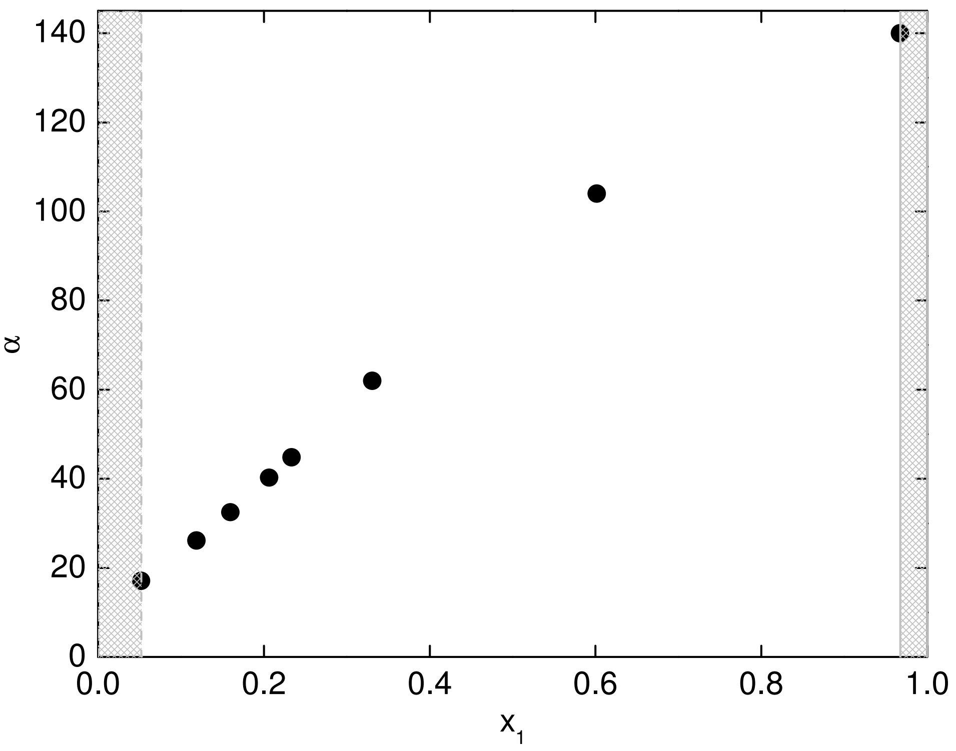

Figure 4.2 - The separation factor as a function of ionic liquid mole fraction. The gray zone symbolises one phase system thus lack of possibility to perform separation.

5. Conclusions

The hydrogenation of carvone catalysed by palladium, rhodium and ruthenium in carbon dioxide atmosphere was performed for the first time in green solvent supercritical carbon dioxide. Reactions were carried out in biphasic conditions, at lower CO_2 pressure as well as at higher pressure of CO_2 corresponding to supercritical conditions.

Generally it can be stated that CO_2 is a perfect solvent in hydrogenation of carvone, as an improved conversion of carvone with significant reduction of reaction time compared to numerous liquid phase hydrogenation examples was achieved. It highlights the advantageous role of supercritical carbon dioxide as a reaction medium applied in the heterogeneously catalysed hydrogenation of carvone instead of organic solvents up to now used. The catalysed reaction in single supercritical system reached equilibrium faster than in biphasic system quite independent of the active metal catalyst applied.

Furthermore the Pd catalyst promoted the formation of the products in equilibrium concentration faster than other two studied catalysts. The final composition of the reaction mixture was strongly dependent on the noble metal catalyst used for the reaction. The palladium catalyst as the most active promoted complete conversion of carvone and formation of the parallel products: two fully hydrogenated isomers of carvomenthone and carvacrol. Contrary to Pd catalyst, slightly less active Rh catalyst endorsed production of only fully saturated stereoisomers of carvomenthone with 96% conversion of carvone. Moreover, reaction with Rh exhibited >84% selectivity of carvotanacetone with the conversion of 25% after only 2 minutes of reaction. The fewer active catalyst led to significantly lower conversion of carvacrol and favoured the production of larger variety of products at the equilibrium conditions among which the major one was found to be carvotanacetone.

The conversion and the selectivity to carvomenthone followed the order: Pd > Rh > Ru and Rh > Pd > Ru, respectively.

The presented results highlight the advantageous role of CO_2 as reaction medium as replacement for organic solvents, in enhancing conversion at mild conditions together with the significant reduction in reaction time.

Synthesis and separation of carvacrol recognised through two one-pot sequences has been accomplished. The process presented herein has several noteworthy features:

1) Potential production of carvacrol from cheap and abundant plant rich in carvone being recognised as a building block chemical;[19]

2) Hydrogenation performed at drastically lower temperature compared to the known classical processes due to the effect of CO_2 which acts as a H_2 co-solvent and liquid expander for terpene;

3) Fine tuning of ionic liquid properties that differentiate solubility of ketones and carvacrol guiding to a successful recovery of carvacrol with minimal involvement of IL;

4) The phase equilibrium studies confirmed the IL utility as a tool for separation of products being of the interest.

Concluding, the aforementioned advantages confirm the potential of alternative solvents in the innovative processes towards sustainable development.

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