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**INNOVATIVE REACTORS FOR HETEROGENEOUS CATALYSIS IN
LIQUIDS: PROTECTION OF THE HYDROXYL GROUP BY DHP**

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Abstract

The purpose of the Thesis is the comparison two reactors, a conventional stirred tank reactor called STR and the new type of rotating bed reactor made by the SpinChem AB called SpinChem® RBR S221. A heterogeneous reaction is used to compare them, measuring the concentrations of the reactants and calculating the conversion of a reactant.

The reaction is commonly employed in organic chemistry for the protection of the hydroxyl group by dihydropyran, in which an alcohol and the dihydropyran react, forming the THP ether, in a solvent and with a solid acid catalyst.

The catalyst available was Amberlite IRN 99 , an exchange cation resin , but before it was washed with methanol and distilled water applying two procedures called 'A' and ' B ', because the raw resin had impurities and salts solubilized that had to be removed to improve the catalytic activity.

The DHP was mandatory for the reaction, instead the kind of alcohol had to be chosen.

The 1-butanol has been chosen consulting scientific articles and using practical considerations. The analytical instrumentation used to measure the concentrations of the reactants were the GC-FID and GC-MS. Since there wasn't the availability of the pure product, an analysis with GC-MS was conducted to check the identity of the desirable product.

The concentrations of the reactants have been calculated after carrying out the calibration of the GC-FID and then the conversion of dihydropyran was directly calculated from the peak area provided by analysis of GC-FID.

The selection of the solvent has been achieved either by consulting the scientific publications and either by conducting four reactions of 15 ml volume of solution, with the same conditions but with different solvents.

The equipment and two reactors made available by the company have been described and then the procedure for the preparation of experiments with solution volume of 145 ml and 182 ml was achieved.

For the comparison between the two reactors, three experiments were carried out at different rotational speeds (300 rpm, 500 rpm, 900 rpm) of the RBR but with the others same conditions. The result was that varying the rotational speed, the conversion didn't varied and so the RBR was set at 500 rpm. While for the STR, the rotational speed was set at 600 rpm because under 400 rpm the catalyst remained for the most part on the bottom.

The experimental activity is continued with three different cases, comparing the two reactors but in different amounts of catalyst in each different case, resulting always that the conversion of RBR was better than that of the STR, probably due to its better mixing and its particular

structure. Furthermore, the RBR was easier handling and it can operate at lower rotational speeds than the STR because the catalyst is inside of it.

Another case was studied by changing the heights of the RBR from the bottom of the vessel (7 mm, 12 mm, 17 mm), showing the conversions changed slightly at different height.

In the last experiments conducted at different rotational speeds (500, 600, 800, 1000) of the STR, the catalyst used was washed with the procedure 'B', but it was taken from a different batch of catalysts compared to the batch used in all previous experiments, then it had a different activity. However, the interest of those experiments was the relative result to each other and not a comparison with the previous experiments. The result is that setting the STR to 500 rpm there was a difference, probably due to the catalyst was not uniformly mixed in the solution.

The study was a preliminary study to a future project which will present a numerical model of the reactor.

This thesis is the result of the period of six months spent in the city of Umeå, Sweden. The experimental work was carried out at the laboratory of the Department of Chemistry and Biology at the University of Umeå, under the supervision of Prof. Jyri-Pekka Mikkola and Dr. Emil Byström.

Riassunto

La tesi si propone di confrontare due reattori, un reattore normalmente mescolato chiamato STR con il nuovo tipo di reattore a letto rotante prodotto dall'azienda SpinChem AB, chiamato SpinChem® RBR S221. Per poterli confrontare si è utilizzata una reazione eterogenea di cui sono state misurate le concentrazioni dei reagenti e calcolata la conversione rispetto ad un reagente.

La reazione scelta è comunemente impiegata in chimica organica per la protezione del gruppo ossidrilico via diidropirano, in cui un alcool e il diidropirano reagiscono formando il THP etere, in un solvente e con un catalizzatore acido solido.

Il catalizzatore disponibile era Amberlite IRN 99, una resina scambio cationi, ma prima di essere utilizzata negli esperimenti è stata lavata con metanolo e acqua distillata applicando due tipi di procedure chiamate 'A' e 'B'. Questo perchè la resina era sporca di impurità e di sali solubilizati che dovevano essere tolti per migliorarne l'attività catalitica.

Visto che il diidropirano era necessario per la reazione, si doveva invece scegliere quale tipo di alcool utilizzare. E' stato scelto il 1-butanol grazie alla consultazione di articoli scientifici e grazie alle considerazioni di tipo pratico per le analisi.

Gli strumenti analitici utilizzati per poter misurare le concentrazioni dei reagenti sono stati il GC-FID e il GC-MS. Siccome non c'era la disponibilità del prodotto in forma pura, un'analisi con il GC-MS è stata condotta per controllare l'identità del prodotto desiderato.

Le concentrazioni dei reagenti sono state calcolate dopo aver effettuato la calibrazione del GC-FID e poi la conversione del diidropirano è stata calcolata direttamente dall'area del picco fornita dalle analisi del GC-FID.

La scelta del solvente è stata raggiunta sia consultando delle pubblicazioni scientifiche sia conducendo quattro reazioni di 15 ml di volume di soluzione, con stesse condizioni iniziali ma con diversi solventi.

Le attrezzature e i due reattori resi disponibili dall'azienda sono stati descritti dal punto di vista fisico e da quello fluidodinamico e poi la procedura per la preparazione degli esperimenti con volume di soluzione di 145 ml e di 182 ml è stata conseguita.

Per il confronto tra i due reattori, tre esperimenti sono stati effettuati a diverse velocità rotazionali (300 rpm, 500 rpm , 900 rpm) del RBR ma con le altre condizioni uguali, con il risultato che variando la velocità la conversione non variava e quindi il RBR è stato settato a 500 rpm. Mentre per il STR, la velocità è stata settata a 600 rpm perchè sotto a 400 rpm il catalizzatore rimaneva per la maggior parte sul fondo.

L'attività sperimentale è proseguita con tre diversi casi comparando i due reattori ma a diverse quantità di catalizzatore in ogni diverso caso, risultando sempre che la conversione del RBR

era migliore di quella del STR, a causa probabilmente del suo miglior mescolamento e della sua particolare struttura. Inoltre il RBR è risultato più maneggevole e più pratico da utilizzare e può operare a più basse velocità rotazionali rispetto al STR, visto che il catalizzatore è collocato dentro di esso.

Un altro caso è stato studiato cambiando le varie altezze del RBR dal fondo del reattore (7 mm, 12 mm, 17 mm), riportando che l'altezza fa variare di poco la conversione del diidropirano.

Negli ultimi esperimenti condotti a diverse velocità rotazionali (500, 600, 800, 1000) dello STR, il catalizzatore utilizzato è stato lavato con la procedura 'B' ma proveniva da un diverso lotto di catalizzatori rispetto a il lotto utilizzato in tutti gli esperimenti precedentemente effettuati, quindi aveva un'attività catalitica diversa rispetto al precedente lotto. Comunque l'interesse di questi ultimi esperimenti era il risultato relativo tra di loro e non il confronto con i precedenti esperimenti. Il risultato è che solo settando il STR a 500 rpm c'era una differenza rispetto alle altre velocità, dovuta probabilmente al fatto che il catalizzatore non veniva uniformemente mescolato nella soluzione.

Lo studio effettuato era un'attività sperimentale preliminare ad un futuro progetto che si propone di presentare un modello numerico del reattore.

Questa Tesi è il risultato del periodo di 6 mesi trascorso nella città di Umeå, Svezia. Il lavoro sperimentale è stato svolto presso il laboratorio del Dipartimento di chimica e biologia dell'Università di Umeå sotto la supervisione del Prof. Jyri-Pekka Mikkola e del Dr. Emil Byström.

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Introduction

In the world the safeguard of the environment and the saving the limited sources have become very important during the past decades. The research is fundamental for the improvement of the society and the culture and in these past years the green chemistry, new sustainable processes, new reactors are become an important part to improve the chemistry.

The aim of the Thesis is to calculate the conversion of a heterogeneous reaction to be able to compare two kinds of reactors: one is a conventional stirred tank reactor, called STR and the other is the SpinChem® RBR S221, the new rotating bed reactor made by the Swedish company SpinChem AB situated in the city of Umeå, Sweden.

The first Chapter gives an overview of the reaction for the protection of hydroxyl groups, especially focusing in the heterogeneous reactions which is used in this project. In fact the reactions is affected by operative conditions and by the catalyst characteristics.

The second Chapter describes the material and the methods for the experimental work. The catalyst and its washing procedures has been discussed and after the reactants have been chosen. The models and the calibration of the analytical instrumentations (the GC-FID and the GC-MS) have been reported and then some experiments in lower scale have been carried out to choose the better solvent for this kind of reaction. The Chapter explains the procedure used for the higher scale, the equipment available and the two different reactors (the STR and the SpinChem® RBR S221) to carry out the reaction in higher scale at 145 ml and 182 ml of liquid volume.

The third Chapter reports the experimental results and the discussion. The Chapter is divided in topics investigated. The first topic regards the different rotational speeds of the RBR while the second topic speaks about the comparison between the two reactors and the third presents the different heights of the RBR from the bottom of the vessel. At the end of the Chapter, the fourth topic is about the different rotational speeds of the STR.

An appendix reports all the analysed samples of each experiment done in this project in order (concentrations of the reactants, the areas given by the GC-FID for the compounds and the conversion of the DHP).

This thesis regards the erasmus period of six months performed in the University of Umeå, Sweden. It is a project developed in the Umeå University and in the company SpinChem AB. The experimental activities were carried out in the chemical laboratory of the KBC-huset in the University of Umeå supervised by Prof. Jyri-Pekka Mikkola and by Dr. Emil Byström

Chapter 1

THPE: features and procedures

The purpose of the chapter is to give an overview of various methods of formation of tetrahydropyranyl ethers (THPEs) as a method for the protection of hydroxyl group as well as a diverse range of complex molecules using a variety of reagents and reaction conditions, i.e., acid catalyst, heterogeneous catalyst and neutral reagent mediated reactions. Moreover, the deprotection of hydroxyl group is discussed briefly in the end of the chapter.

1.1 Introduction at the protecting groups

Protecting groups play an indispensable role in the synthesis of complex multifunctional molecules. Continuing efforts worldwide to develop ideal protection methodologies has led to the introduction of a number of protecting groups over the years. The functional groups that have attracted the most attention are the amino, thiol, carboxylic, carbonyl and hydroxyl groups (Fig. 1.1).

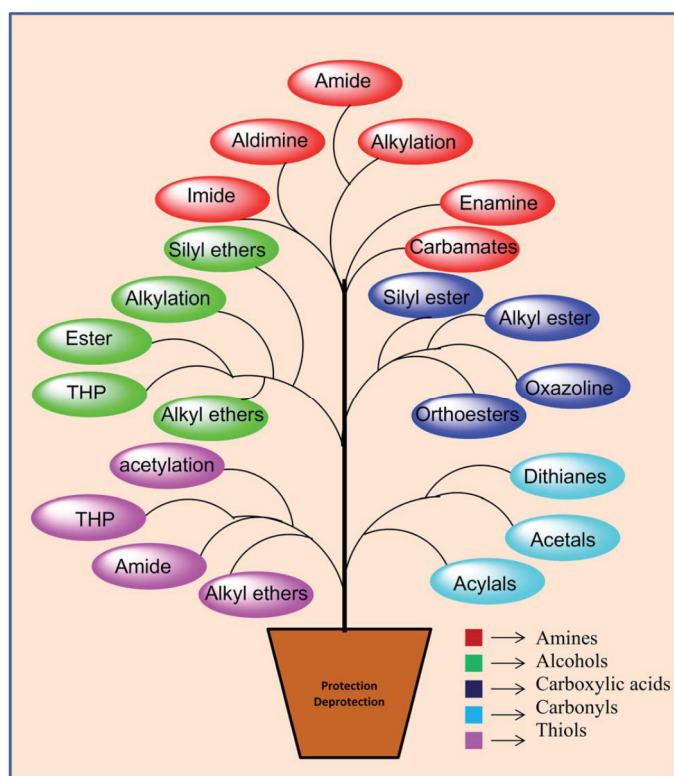


Figure 1.1 Functional groups (Adapted from Brijesh Kumar et al^[1])

The amino group is found in a number of biologically significant compounds such as peptides, nucleosides, and amino acids; likewise, thiol (–SH) and carboxyl groups compose an important part of various drug moieties interacting with receptors or antigens involved in the development of disease. A huge amount of researches have been developed for the protection and deprotection of these functional groups. The most frequently used approaches for amino group protection are N-alkylation using alkyl halides, amide or imide formation using acetic acid/acetyl chloride/acetic anhydride or phthaloyl anhydride, aldimine and enamine formation, while thiols are generally protected by acetylation or tetrahydropyranylation (THPRN), and the protection of carboxylic acids is normally facilitated by ester formation with alcohols, alkylhalides, chloroformates and dimethyl carbonate.

However, in the protection of aldehydes and ketones, a relatively small repertoire of protecting groups has been employed and of these, acetals (O,O), thiocetals (S,S), oxathiolanes(O,S), 1,1-diacetate nitrogenous derivatives (imines, enamines, oximes, hydrazones, semicarbazones) and omethoxycarbonyl-cyanohydrin have proven to be the most useful.

1.2 Hydroxyl group protection

Hydroxyl compounds (for instance, alcohols, phenols, steroids, and sugars) have an immense significant in the life. Most of these compounds are used for many different scientific, medical and industrial applications. Many compounds with alcoholic and phenolic functionalities there are in the pharmaceutical field, for example antitumor (podophyllotoxin, etoposide, taxol, vinca alkaloids, bleomycin, doxorubicin); antibiotic (amoxicillin, kanamycin, neomycin, erythromycin, tetracycline, gentamycin); anti-AIDs (crixivan, zidovudine); cardiac vascular system normalizing (digoxin, digitoxin, gitoxin, quinidine, propranolol, atenolol); anti-pyretic (paracetamol); anaesthetic (propofol); analgesic (morphine); acting on the central nervous system (L-dopa) and as vitamins (pyridoxine/vitamin B6, vitamin B2, ascorbic acid/vitamin C). Moreover, steroids (cholesterol, stigmasterol, oestrone, and testosterone) are also used as medicines.

The protection of hydroxyl groups is a key step in both the synthesis of various polyvalent organic molecules and in further reactions of these compounds.

Even after many studies carried out for the protection of the hydroxyl group, new research for new groups O-H are desirable on other target molecule as oligosaccharide. This has led to the development of a variety of techniques, such as ester formation as acylation, tosylation and ether formation as silyl ethers, allyl ethers, THP ethers and other alkoxyalkyl ethers.

The protection of a hydroxyl group can also be facilitated by forming ethers such as silyl ethers, allyl ethers, benzyl ethers, THP ethers and alkoxyalkyl ethers.

This project is focused on the reactions for the protection of the hydroxyl group by the formation of the THPEs, so the other techniques haven't been discussed here.

Tetrahydropyranyl ethers have found extensive application in organic synthesis as they can be easily synthesized from a variety of hydroxyl-group-containing compounds by an acid catalyzed reaction using 3,4-dihydro-2H-pyran, briefly DHP. Tetrahydropyranlation is one of the preferred methods in organic synthesis due to high stability of THP ethers in different reaction conditions, such as strongly acidic or basic pH and presence of oxidizing or reducing agents, in addition to the ease of deprotection.

THPEs are stable to bases and the deprotection is done through acid hydrolysis. It is important to point out that the introduction of a THP ether onto a chiral molecule results in the formation of diastereoisomers due to an additional stereogenic centre present in the tetrahydropyran ring, which can make both the NMR interpretation and the handling of the reaction products somewhat troublesome.

1.3 THP as a protecting group

Tetrahydropyranyl ethers are formed from dihydropyran, a vinyl ether, by reacting with alcohols under mild acid catalysis (*p*-toluenesulfonic acid, or more effectively, boron trifluoride etherate)(Figure 1.2).

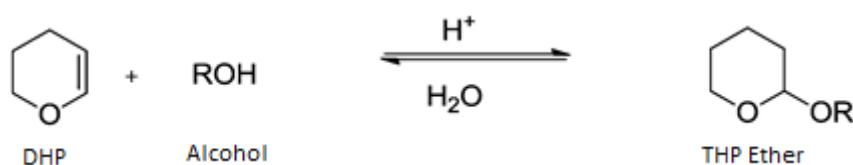


Figure 1.2 General reaction of THP protection (Adapted from Brijesh Kumar et al^[1])

The figure 1.3 shows that the THP protection can be catalyzed by a wide range of catalysts and the methodology may be broadly divided into following categories:

- Acid mediated
- Neutral reagent mediated
- Heterogeneous catalyst mediated
- Miscellaneous

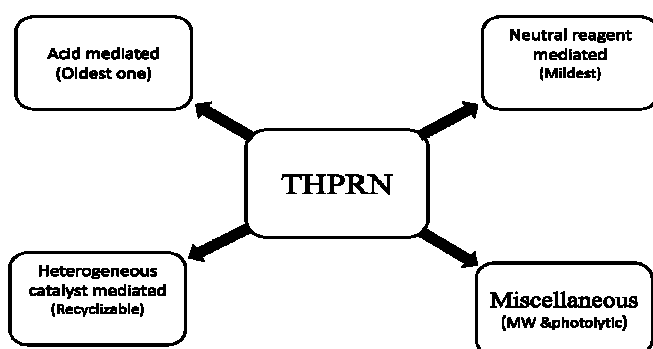


Figure 1.3 Methods for THPRN (Adapted from Brijesh Kumar et al^[1])

1.3.1 Acid mediated

The acid-mediated reaction has a special relevance in numerous chemical reactions. There are several possible chemical compounds that can act as sources for the protons to be transferred in an acid catalysis system.

Usually this is done to create a more likely electron abstraction from the double bond of DHP to produce an oxonium ion intermediate, which then abstracts the electron from the nucleophile to produce THP ethers.

Normally, the tetrahydropyranylation is carried out by acid-catalyzed addition of alcohols and phenols to DHP in an organic solvent at room temperature. Various methods for the formation of THP ethers in acidic conditions have been reported and used frequently for protecting hydroxyl groups in multi-step organic synthesis. Most of these reported methods use acidic reagents in an aprotic solvent, such as dichloromethane, THF, acetone or toluene.

D. Gogoi et *al* reported a mild, efficient, and solvent-free protocol for tetrahydropyranylation of alcohols in the presence of a catalytic amount of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$. Simple filtration of the reaction mixture through a short silica-gel pad gives the pure products in excellent yields. Depyranylation can also be achieved by adding methanol under similar reaction conditions^[3]. The use of ionic liquid offers the advantage of compatibility with a wide range of functional and protecting groups such as THP, TBDMS, TBDPS, PMB, MOM ethers, acetonides, olefins and epoxides.

Hajipour et *al* published variety of alcohols readily add to 3,4-dihydro-2H-pyran under solvent free conditions in the presence of catalytic amount of acidic ionic liquid $[\text{Et}_3\text{N}(\text{CH}_2)_4\text{SO}_3\text{H}][\text{OTs}]$ to afford the corresponding tetrahydropyranyl ethers in good to excellent yields at room temperature. The use of this procedure allows easy separation of the desired products from ionic liquid and recycling the ionic liquid. Some of the major advantages of this procedure are non-aqueous work-up, very good yields, catalytic amount of catalyst and reusability of ionic liquid^[4].

Nagaiah et *al* reported diverse alcohols and phenols were effectively converted into their corresponding THP-ethers with DHP and catalytic amount of Niobium (V) chloride. The reactions were carried out in DCM at room temperature with short reaction time and excellent yields^[5].

T. Khan et *al* proposed a simple and convenient synthetic protocol for the protection of hydroxyl groups as tetrahydropyranyl ethers as well as carbonyl functionalities as oxathioacetals and thioacetals has been achieved using a catalytic amount of silica-supported perchloric acid under solvent-free conditions^[6].

Babak et *al* described the THRPN in the presence of a catalytic amount of lithium trifluoromethanesulfonate (LiOTf) and tetrahydropyranyl ethers can also be synthesized in a

mild, chemoselective and convenient fashion, even in the presence of many acid-sensitive functional groups using acetyl chloride and dihydropyran^[7].

1.3.2 Neutral reagent mediated

Neutral reaction conditions essentially involve a reaction at room temperature, atmospheric pressure and almost neutral pH. Such reaction conditions generally come with the advantage of having no serious effects on other sensitive (acid/base) functionalities present in the reactants. In T. Khan *et al* the bismuth(III) nitrate pentahydrate has also been found to be an effective catalyst for THPRN of alcohols and phenols in the presence of a large number of other protecting groups such as isopropylidene, benzylidene and thioacetal^[8].

Tetrahydropyranylation of primary alcohols has also been selectively carried out in the presence of secondary and tertiary alcohols and phenols using PdCl₂(CH₃CN)₂ as a catalyst in tetrahydrofuran (THF), while other protection groups such as p-toluenesulfonyl, tert-butylidiphenylsilyl, benzyloxycarbonyl, allyl, benzyl, and benzoyl remained intact under these conditions.

1.3.3 Heterogeneous catalyst mediated

The project of the thesis is focused on the heterogeneous reaction, therefore many articles are resumed in this section to understand its features and its procedures.

P. S. Poon *et al* described the ion-exchange resin Dowex 50WX4-100 as catalyst for the protection of a variety of alcohols with DHP in dichloromethane at ambient conditions^[9].

A mixture of alcohols (1a–h) (10 mmol), 3,4-dihydropyran 2 (11 mmol), Dowex 50WX4–100 (0.5 mmol), and dichloromethane (20 ml) have been stirred at room temperature. (Figure 1.4). After completion, the reaction mixture was filtered off, and the residue was washed with methylene chloride. The filtrate was concentrated, and the residue was purified over a column of silica gel (eluanthexane–ether 9:1) to obtain the tetrahydropyranyl ethers (3a–f).

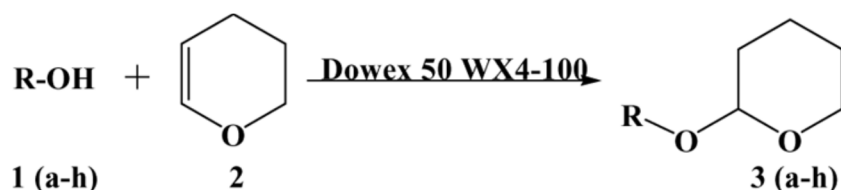


Figure 1.4 Tetrahydropyranylation of alcohols catalyzed by Dowex 50WX4-100 (Adapted from P. S. Poon *et al*^[9])

A wide range of alcohols (1a–f) including primary, secondary, and cyclic alcohols underwent smooth tetrahydropyranylation in good yield (Figure 1.5).

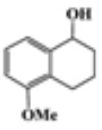
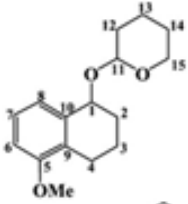
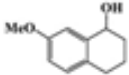
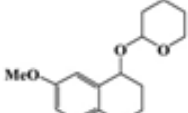
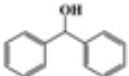
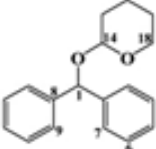
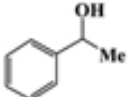
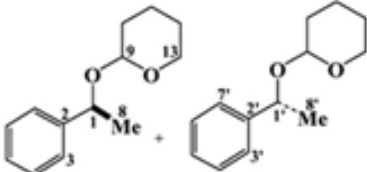
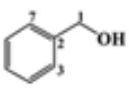
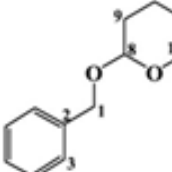
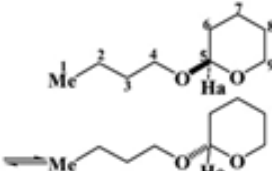
Entry	Alcohol (1)	THP ether (3)	Yield (%)	Time (min)
a			97	15
b			95	10
c			90	30
d			95	10
e			98	7
f	Me(CH ₂) ₃ OH		94	1

Figure 1.5 Protection of alcohols with DHP catalyzed by Dowex 50WX4–100 (adapted from P. S. Poon *et al*^[9])

The figure 1.5 shows that the primary alcohols had needed less time than the secondary or tertiary alcohols to arrive at high yields due to the steric hindrance of the hydroxyl groups.

In addition, it has been found to be an excellent catalyst for the protection of phenolic hydroxyl group with DHP in good yield. In conclusion, the Dowex 50WX4–100 is an excellent catalyst for the protection of a variety of alcohols. To the best of our knowledge, some of alcohols selected for tetrahydropyranylation by Dowex 50WX4–100 were not examined earlier with other catalysts. The present method for tetrahydropyranylation would constitute an important additional approach for the protection of alcohols with DHP in good yield.

Hajipour *et al* reported the conversion of benzyl alcohol (2 mmol) to the corresponding THP ether with pyridinium chloride as catalyst (0.4 mmol, 0.05 g) and DHP (2.4 mmol) in 5 ml of various solvents and also grinding under solvent-free conditions at room temperature^[10]. As

shown in table 1.1, the acetonitrile was the best solvent for this reaction in presence of pyridinium chloride with a yield of 80% in 15 minutes.

Table 1.1. Conversion of benzyl alcohol to the corresponding THP ether using different solvents in the presence of pyridinium chloride (Adapted from Hajipour et al^[10])

Solvent	Yield (%)	Time (min)
Dichloromethane	80	45
Acetonitrile	80	15
Ethyl acetate	60	60
Diethyl ether	No Reaction	60
Cyclohexane	70	30

In Kolahdoozan et al, an alcohol or phenol (1 mmol) was added to a mixture of DHP (1.2 mmol) and Al/AT-silica (0.03 g) in dichloromethane (CH₂Cl₂, 0.5 mL) ^[11]. The mixture was stirred at 40°C. The progress of the reaction was monitored by gas chromatography (GC) and thin layer chromatography (TLC). After completion of the reaction, the mixture was filtered, and the residue was washed with dichloromethane. The filtrate was concentrated on a rotary evaporator under reduced pressure to give the product.

Since the solvents play an important role for the catalytic activity of the Al/AT-silica catalyst, a variety of solvents such as toluene, *nn*-hexane, acetone, dioxane, tetrahydrofuran, and dichloromethane were used for tetrahydropyranylation of benzyl alcohol as a model substrate (Table 1.2). The results show that the dichloromethane as solvent give better result for tetrahydropyranylation of alcohols.

Table 1.2 The effect of solvent for tetrahydropyranylation of benzyl Alcohol (Adapted from In Kolahdoozan et al^[11])

Solvent	Time (min)	Yield (%)
toluene	70	35
hexane	60	53
acetone	60	40
dioxane	60	25
THF	50	40
dichloromethane	45	95

The results of the protection reactions of a diverse range of alcohols and phenols are collected in Figure 1.6. Al/AT-silica can promote tetrahydropyranylation of primary, secondary, and benzyl alcohols, as well as phenols, in good to excellent yields. Primary benzyl alcohols with electron-donating and electron-withdrawing groups were tetrahydropyranylated in this catalyst, and the corresponding tetrahydropyranyl ethers were obtained in almost quantitative yields (figure 1.6, entries 1–7). The ability of Al/AT-silica was also investigated in the tetrahydropyranylation of phenol under the same reaction conditions described for alcohols, and the corresponding THP-ethers were obtained in high yields (figure 1.6, entry 8). The nitro derivatives of phenols (figure 1.6, entry 10-11) produced the corresponding protected product in lower yield. The possible reason ascribed to this observation could be the electron-withdrawing effect of the nitro group. Tetrahydropyranylation of linear and saturated primary and secondary alcohols were also achieved in the presence of this catalyst in high yields.



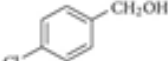
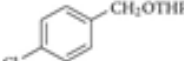
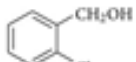
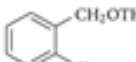
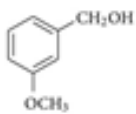
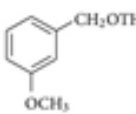
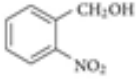
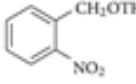
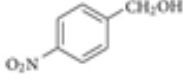
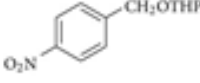
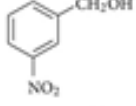
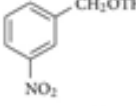


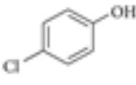
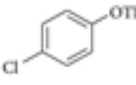
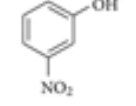
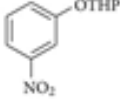
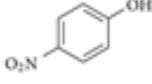
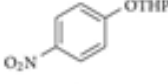




Entry	Hydroxy compound	Product	Time (min) ^b	Yield (%) ^c
1			45	95
2			55	94
3			50	92
4			60	95
5			210	93
6			120	93
7			60	94
8			45	95
9			60	63
10			120	50
11			120	40
12			60	91
13			45	95

Figure 1.6 Tetrahydropyranylation of various alcohols and phenols (Adapted from In Kolahdoozan et al^[11])

1.3.4 Miscellaneous

THP ethers of alcohols have also been prepared by photolysis of DHP, using 1,5-dichloro-9,10-anthraquinone as catalysts under visible light. The reaction could be conducted under ambient fluorescent lighting or with sunlight, as well as in a Rayonet reactor as reported in Oates et al^[12]. Microwave-assisted organic synthesis became an increasingly popular technique in academic and industrial research due to advantages such as especially shorter reaction times and rapid optimization of chemical reactions. In addition, iodinecatalyzed THPRN under microwave irradiation has also been achieved for selective protection of one hydroxyl group in an nsymmetrical diol.

1.4 Deprotection of tetrahydropyranyl ethers

The selective removal of a protecting group is of equal importance and significance as is its introduction in an organic synthesis. Acetals and ketals are generally deprotected by reducing them to either ethers or hydrocarbons under a variety of reducing conditions, e.g., trialkylsilanes in the presence of Bronsted or Lewis acids. THP ethers are mixed acetals, whereas for the deprotection of the THP ethers a transacetalization methodology is preferred. Owing to the great impact of THP ethers on the protection of hydroxyl groups, the development of its deprotection methods has also received considerable attention.

One of the most reactant used for the deprotection is methanol, as described in Namboodiri et al where a solution of THP ether (100 mmol), of aluminum chloride (1 mmol) and an excess of methanol (800mmol) have been mixed together at room temperature for 30 min affording complete regeneration of the alcohol, obtaining a conversion of the THP ether of 96%^[13].(Figure 1.7)

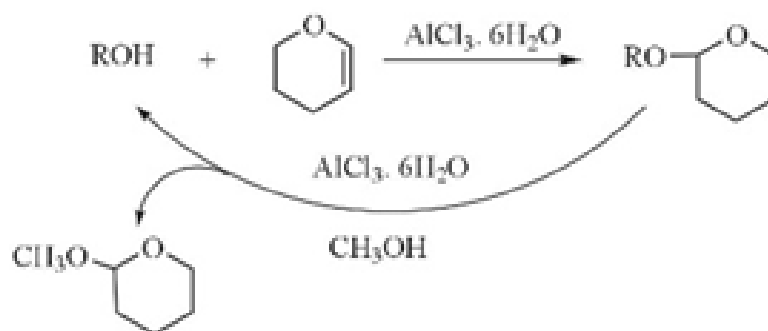


Figure 1.7 Protection and deprotection of Alcohol with aluminum chloride (Adapted from Namboodiri et al^[13])

Also in T. Khan et al, various THP ethers can be deprotected to the parent alcoholic or phenolic compounds but using dichloromehtane/methanol (5: 2)^[14]. (Figure 1.8)

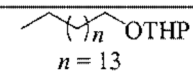
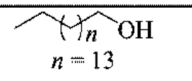
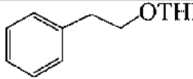
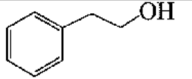
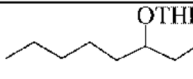
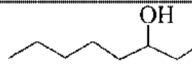
Substrate	Catalyst used	Time min/[h]	Product ^[a]	Yield ^[b] /%
 $n = 13$	0.05	30	 $n = 13$	90
	0.05	25		97
	0.05	25		92

Figure 1.8 Deprotection of various tetrahydropyranyl ethers to the corresponding hydroxyl compounds using catalytic amount of bromodimethylsulfonium bromide in dry dichloromethane/methanol (Adapted from T. Khan et al^[14])

Chapter 2

Materials and methods

This chapter describes the materials and the methods applied for the experimental work.

The first part of chapter is focused on the catalyst available for the project, on the reactants chosen and on the analysis techniques.

The second part is dedicated to the selection of the solvent, carrying out the reaction in lower scale and to the equipment made available from the company SpinChem AB.

The chapter at the end discusses of the procedure to run the reaction in the higher scale, using the equipment available

2.1 The catalyst

This paragraph discusses of the available catalyst and of the washing methods applied before its using in the reaction.

2.1.1 The Amberlite IRN 99

A catalyst is a key component of a reaction, due to its ability in reducing the energetic demand to transform reagents in products, by conducting the reaction through a different reaction pathway, significantly less energy consuming compared to the non-catalysed one. Obviously each reaction needs a proper catalyst and suitable operative conditions to let the latter operating at the best.

The catalyst available for this project was the Amberlite IRN 99, produced by the company DowChemical. It is a nuclear grade, gel type, strong acid cation exchange resin with a combination of very high capacity and oxidative stability that enables a completely new level of performance in nuclear power applications. It is sold in the fully regenerated Hydrogen form and intended for use in non-regenerable single bed or mixed bed nuclear systems which demand the ultimate in effluent purity, operating capacity, and resin life. The particle size of Amberlite IRN 99 Resin is specifically designed to give an optimized balance of pressure drop, exchange kinetics, and resistance to separation from the anion exchange resin, Amberlite IRN 78, when used in a mixed bed.

The exceptionally high DVB cross linker level of Amberlite IRN 99 Resin gives it the best oxidative stability of any gel cation resin available, thus minimizing the release of sulfonic acid

leachable. The Amberlite IRN 99 is made at a particle size which reduces the chance of creating a separated cation resin layer at the bottom on the mixed bed service vessel (Figure 2.1).



Figure 2.1 The Amberlite IRN 99

The very high total capacity of Amberlite IRN 99 Resin, typically 2.5 eq/L, delivers another important benefit, not only in BWR condensate polishing, but also in other nuclear applications such as PWR steam generator blowdown treatment, PWR primary system CVCS resin beds, and even radioactive waste demineralizers. The high total cation exchange capacity can produce a 15–30% increase in operating throughput. Since the nuclear grade resins from all these applications are generally disposed of as rad waste, high capacity and long resin bed life are critical to minimizing rad waste disposal cost and volume. For most users, rad waste disposal cost will often exceed resin purchase cost, so high resin capacity directly translates into savings in these non-regenerable nuclear applications. Furthermore, longer bed life means fewer bed change-outs, less work, less resin handling, and less chance for radiation exposure.

The table 2.1 shows the properties of this resin.

Table 2.1 Features of the solid catalyst

PHYSICAL FEATURES	
Model	Amberlite IRN 99
Type	Nuclear Grade Strong Acid Cation Exchange Resin
Physical form	Dark amber translucent beads
Matrix	Polystyrene divinylbenzene copolymer
Functional groups	Sulfonic acid
Conversion to H ⁺ form, min.	99%
Total volume capacity (H ⁺ form)	2.4 eq/L (52.4 kg/ft ³ as CaCO ₃)
Moisture retention capacity (H ⁺ form)	37–43% (H ⁺ form)
Shipping density	840 g/L (52 lbs/ft ³)
Fines content < 0.300 mm, max	0.1%
Coarse beads > 0.850 mm, max	1.0%
Uniformity coefficient, max	1.2
Friability average, g/bead min.	350
Friability > 200 g/bead, min.	95%
Operating condition	15–60°C

2.1.2 The washing procedures

The catalyst had salts and residues solubilized inside and it needs a washing procedure, therefore two different ways have been achieved.

In the first procedure, 70 grams of the raw catalyst have been put in a conical flask of 500 ml of volume. A quantity of 350 ml of methanol has been added to the catalyst (5 ml of methanol for each gram of catalyst) and the mixture has been stirred by a magnetic agitator at 400 rpm for 1 minute. After the resin has been filtered and dried by a little flux of air. After all, it has been collected in two bottles of plastic of 50 ml of volume. This kind of procedure has been called 'A'.

In the second procedure, the raw catalyst has been put in a glass column of 100 ml, previously tapped in the bottom with a piece of cotton like a filter, giving way the liquid but not the solid. In the top of this column, another glass column has been connected where the solvents have been introduced to wash the resin and to regulate the residence time of the solvents in the first column.

The resin has been washed by 300 ml of distilled water in two hours and the pH of the distilled water, before and after the washing, has been checked by the pH indicator paper. When the two pH were equals, another washing with 200 ml of methanol has been done and again the checking with the pH indicator paper, being sure that the dissolved salts and the residues in the

catalyst were pulled off. If the pH of the fresh solvents was equal of the pH of the solvents after washing, it means there weren't more solubilized the impurities inside the catalyst. At the end, it has been dried by a flux of air and it has been collected in two little bottles of plastic of 50 ml of volume. This kind of procedure has been called 'B'. (Figure 2.2)



Figure 2.2 The Amberlite IRN 99 collected in the plastic bottle of 50 ml

2.2 The reactants and the product

The aim of this paragraph is to choose an alcohol which allowed to run the reaction in an easy and fast way.

The reaction of THPRN had to be carried out with two reactants: an alcohol and the DHP (Figure 2.3).

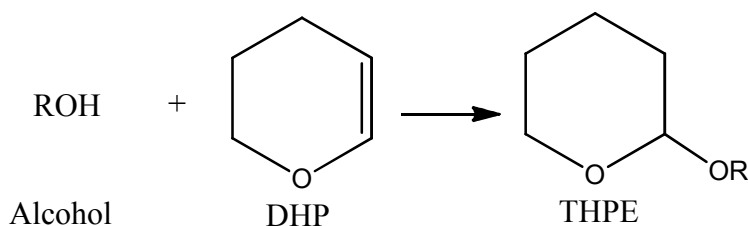


Figure 2.3. The reaction: THPRN

The table 2.2 shows the properties of DHP, one of the two reagents mandatory.

Table 2.2 Properties of DHP

Property	Value
Boiling point at 1 atm (°C)	86
Vapor pressure (mmHg) at 20°C	87
Density(g/ml)	0.922
Molar mass (g/mol)	84.12

To choose the alcohol some considerations have been achieved (Table 2.3).

The alcohol had to:

- stay in a range of different temperature of the DHP to avoid possible issues of overlay of the picks in the chromatogram;
- have a high boiling point, therefore a low vapour pressure to avoid a possible evaporation which would give a wrong signal of concentration when it is analysed;
- be a primary alcohol to achieve a faster reaction, because the primary alcohols are less hindered than a secondary or tertiary alcohols, as said in the paragraph § 1.3.3.

Table 2.3 List of commons available alcohols with their properties

Compound IUPAC	Boiling point (°C)	Vapor pressure(mmHg)
	at 1 atm	at 20°C
Methanol	65	97.65
Ethanol	78.5	44.62
Isopropyl alcohol	97.4	14.96
1-Butanol	117.3	6
1-Pentanol	138	1.5
Benzyl alcohol	205	1.35

Using the previous considerations and the table 2.3, the 1-butanol has been chosen.

So, the reaction of THP protection between these two reactants gave as product the 2-butoxytetrahydro-2H-pyran (figure 2.4).

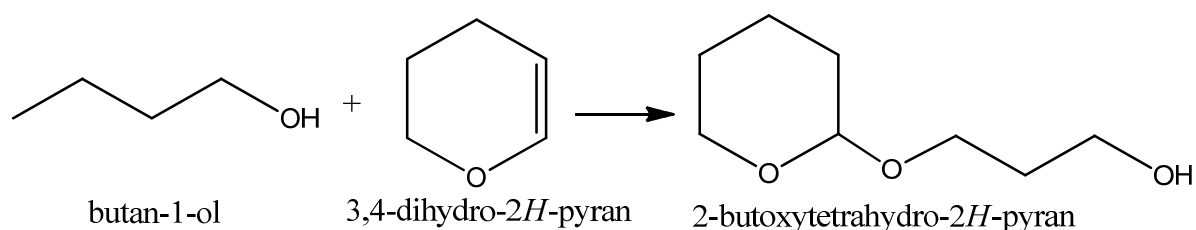


Figure 2.4 Reaction THPNR: the 1-butanol and the DHP

2.3 Analytical instrumentation

This paragraph explains the instrumentation applied for the analyses: the GC-FID and the GC-MS.

2.3.1 The GC-FID

The GC-FID is an instrumentation which uses the gas chromatography and after it uses a detector called flame ionization detector.

The gas chromatography, is employed in analytical chemistry for separating and analysing compounds. The mobile phase is a carrier gas, which shall be chemically inert, low viscous and highly pure (99.9%), such as nitrogen, helium or argon. The stationary phase is generally made from a non-volatile liquid, supported on a powder, which uniformly fills a column (packed column), or distributed as a thin film on the inner wall of a column (capillary column). The table 2.4 reports the features of the column equipped in the GC-FID.

Table 2.4 Features of the column equipped in the GC-FID

<i>Features</i>	
Name	Rtx-DHA-50
Column type	Capillary
Material	Silicate Glass
Length	50 m
Internal diameter	0.2 mm
DF	0.5 μ m
Temp. Limits	60 to 300/340 °C

The gaseous compounds analysed interact with the walls of the column, which is coated with a stationary phase. This causes each component has a different time of analysis, known as the retention time of the compound.

The figure 2.5 illustrates the operating principle of a gas chromatograph. Liquid samples can be injected with a syringe and vaporized above the injector and gaseous samples are typically introduced on the top of the column by a sampling valve pneumatically operating; after that they have been eluted from column, they are collected by the detector.

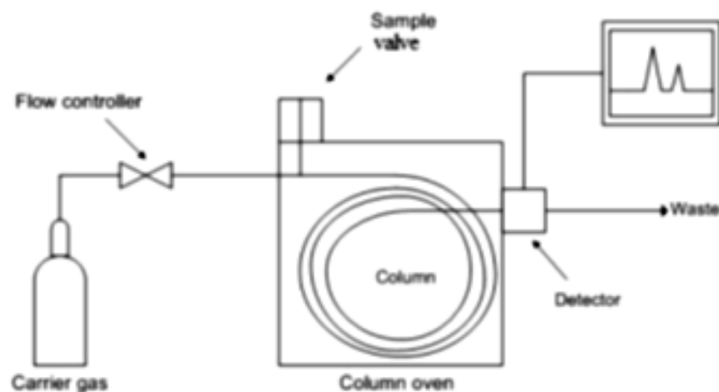


Figure 2.5 Gas Chromatograph main principle.

The FID is a common detector where the electrodes are placed adjacent to a flame powered by hydrogen close the exit of the column, and when the compounds exit from column they are pyrolyzed by the flame. This kind of detector can analyse only the organic and the hydrocarbon compounds due to the ability of the carbons to form cations and electrons upon pyrolysis which generate a current between the electrodes. The increase in current is translated and appears as a peak in a chromatogram, which should be linear depending on the amount or concentration of the analytes. (Figure 2.6)

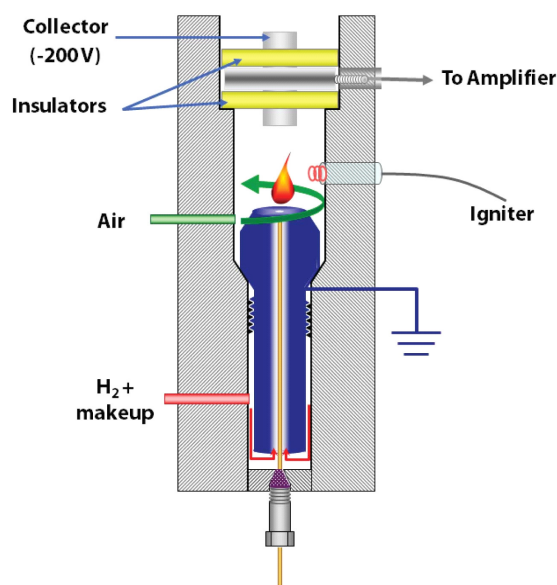


Figure 2.6 Scheme of a generic FID

Optimizing chromatographic analysis means improving separation of substances in order to obtain distinct and well-resolved peaks. It is possible to vary a set of variables such as oven temperature, heating rate, pressure, time of the analysis and carrier flow and type. Temperature

is a very important variable to improve separation which can be kept constant or varied according to a temperature program.

The instrumentation used in this project was a Gas Chromatograph – AGILENT Technologies 7820A (figure 2.7), controlled through the software Agilent Chemstation.

The model of the analysis has been set with the following parameters:

- a quantity of 0.2 microliters has been injected by the syringe in the pre-oven where the temperature was of 250°C;
- the oven temperature started from 80°C to 250° C , this temperature has been set to avoid that the impurities stayed in the column after each analysis;
- increase ratio of 10 °C/min, therefore the time of analysis was 17 minutes;
- split ratio 1:100, it means that of the 0.2 microliters injected by the syringe only 0.002 microliters are injected in the column.

This model has been used for all the analysis in this project.



Fig 2.7 The GC-FID

The chromatogram displays signals of detector as a function of time and can furnish information on both the identity of the substance on the basis of its elution time and on its mass concentration integrating the area under the peak.

The figure 2.8 shows the chromatogram of a sample taken during the reaction described in the paragraph 2.5.

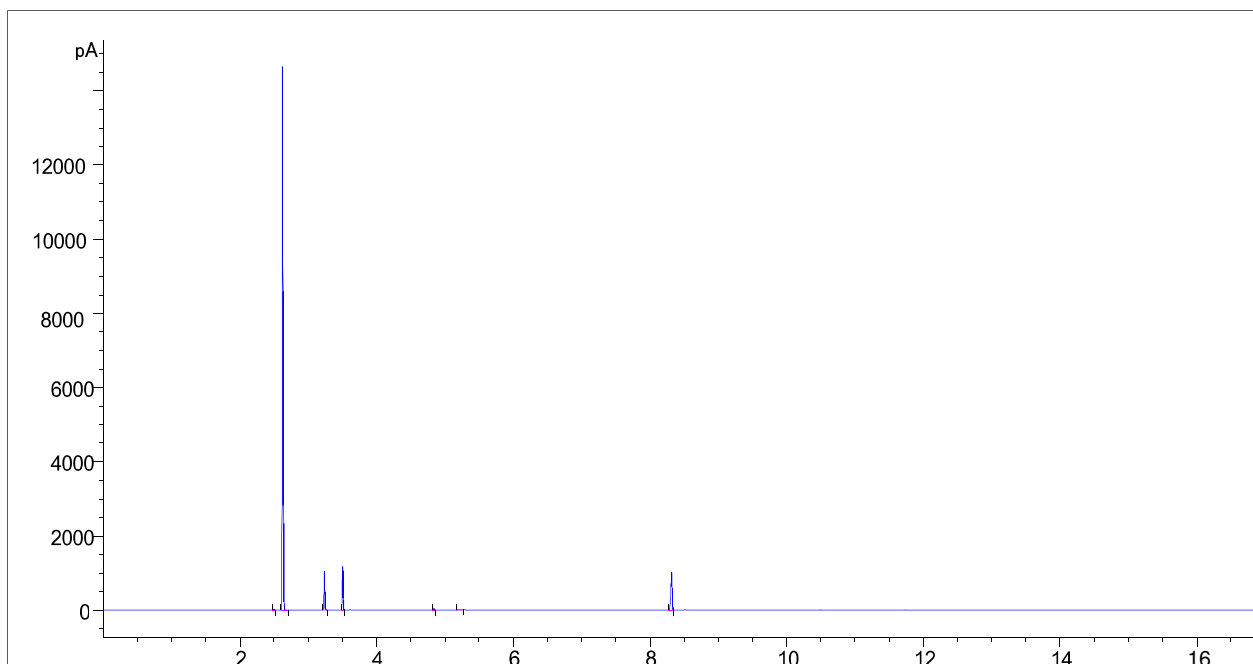


Figure 2.8 Chromatogram of a sample for this reaction. Signal (pA) vs time (min)

The table 2.5 resumes the retention time of the compounds which composed this reaction.

Table 2.5 Retention time of the compounds of the reaction

<u>Compound</u>	<u>Retention time (min)</u>
Acetonitrile	2.624
1-butanol	3.235
DHP	3.502
THPE	8.302

2.3.2 The GC-MS

The GC-MS has been used in the first part of the project only one time to understand if the product of the reaction was really the desirable product, the THP ether, because it wasn't available pure instead the others two reactants and the solvent were available.

This analytical technique is used to identification of compounds. The gas chromatograph allows separating the various substances, as explained in paragraph § 2.3.1, and the mass spectrometer gives a spectrum, which is unique for each compound.

The GC-MS has been suited with another kind of columns respect the GC-FID. (Table 2.6)

Table 2.6 Features of the column equipped in the GC-MS

<i>Features</i>	
Name	Carbowax-20M
Column type	Capillary
Material	Polyethylene glycol
Length	30 m
Internal diameter	0.25 mm
DF	0.25 μm
Temp. Limits	60 to 250 $^{\circ}\text{C}$

The mass spectrometer differentiates ions on the bases of their mass/charge ratio: the mixture is gone through a beam of electrons with known energy so that the ionized molecules will split into smaller ions, according to their chemical structure. Separated ions will reach a detector where the energy received is converted in suitably amplified electrical signal to produce a mass spectrum.

The most common ionization technique is the electronic impact, where a tungsten filament emits a beam of accelerated electrons, which transmits their energy to the molecules causing their deep fragmentation. The detector is capable to separate ions on the basis of their mass/charge (m/z) ratio and it often uses a quadrupole, which is a squared space crossed by magnetic static and dynamic fields. It forces ions along sinusoidal trajectories so that these will fragment instead to go straight the detector and this allows scanning the entire range of the corresponding masses. (Figure 2.9)

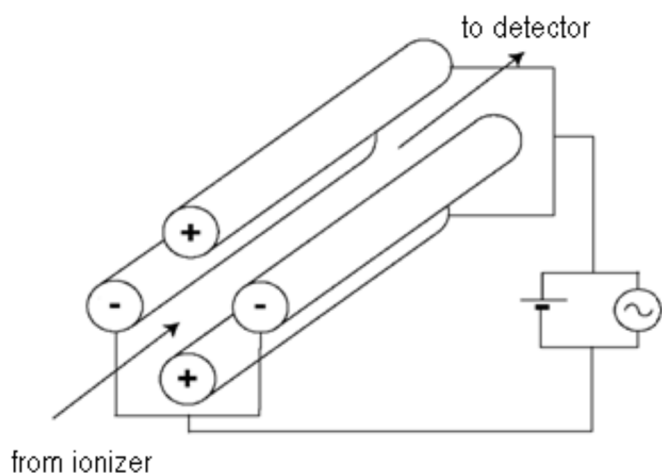


Figure 2.9 Quadrupole main principle

Detectors are able to amplify the weak current produced by ions and signals are transmitted to a computer, which plots the abundance of each ion versus its mass, as a function of the greatest one (base peak) and finally identify a compound according to its spectrum. The parent peak, instead, is usually the lowest and corresponds to the ionized molecule, so it is useful to determine its molecular weight.

Generally, the more stable a molecular ion is, the higher is its probability of reaching intact to the detector; the compound, after having lost an electron, becomes a radical-ion which decomposes into other radicals and ions.

The instrumentation used in this work was a Gas Chromatograph – AGILENT Technologies 7820A (figure 2.10), controlled through the software Agilent Chemstation.

The model of the analysis used for the GC-MS was the same of GC-FID.

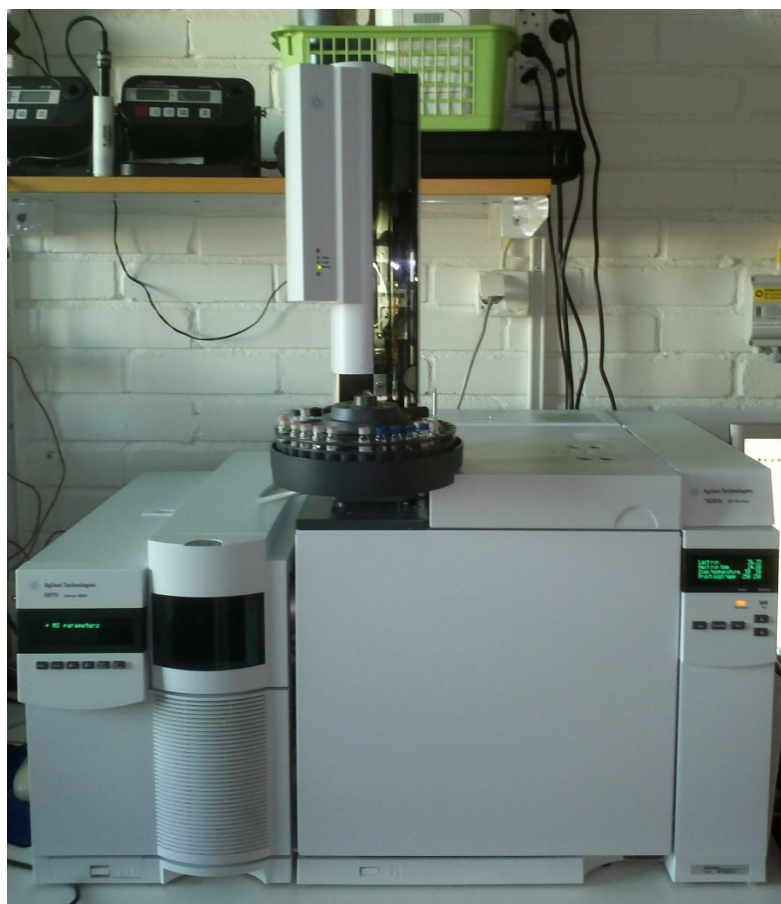


Figure 2.10 The GC-MS

The sample has been analysed by the GC-MS and calculated by the software Chemstation. The result has been that the desirable product coincided with the product obtained by the reaction and therefore as showed in the table 2.5 of the paragraph § 2.3.1, the pick at the retention time of 8.302 found in the chromatograph by the GC-FID was of the THP ether, the desirable product. Hence, only the GC-FID has been employed.

2.4 Calibration of the GC-FID

The calibration is a technique to be able to use a corrected value of the concentrations which is signalled by the analytic instrument, in this case the GC-FID.

The method used is called external standard technique and it consists in to prepare a series of standards with known concentrations of the analyte. The samples are analysed under the same conditions to establish the calibration curve as the least square fit through the data points.

The obvious advantage of this method is that a single calibration can serve a multitude of samples. Hence, the external standard technique is very used in repetitive, routine analysis of many similar samples.

The samples have been done using as analyte the DHP and another solvent, in this case acetonitrile.

The range of weight concentration for this kind of reaction was from 10 to 20 times volume of solvent than the volume of the reactants [9.10]. Therefore, the range of the weight concentration of the analyte had to be less of 10 %.

In the table 2.7, the weighted of analyte, the calculations, and the signals obtained from GC-FID are shown.

Table 2.7 Values and calculation for the DHP

<i>Weighed analyte [gr]</i>	<i>Mol [mmol]</i>	<i>Volume solution [ml]</i>	<i>Weight of solution [gr]</i>	<i>Solvent added [gr]</i>	<i>Weight Concentration</i>	<i>Molar concentration [mol/L]</i>	<i>Area given by GC-FID</i>
0.0055	0.0654	13.0261	10.2393	10.2338	0.05%	0.0050	11.43
0.0263	0.3126	6.7037	5.2730	5.2467	0.50%	0.0466	115.43
0.0521	0.6194	6.4864	5.1060	5.0539	1.02%	0.0955	226.75
0.1060	1.2601	6.3796	5.0300	4.9240	2.11%	0.1975	451.16
0.2550	3.0314	6.3771	5.0500	4.7950	5.05%	0.4754	1124.2
0.5036	5.9867	6.3457	5.0620	4.5584	9.95%	0.9434	2432.90

Using the value of Area giving by GC-FID and the molar concentration of the analyte, the calibration curve has been plotted. (Figure 2.11)

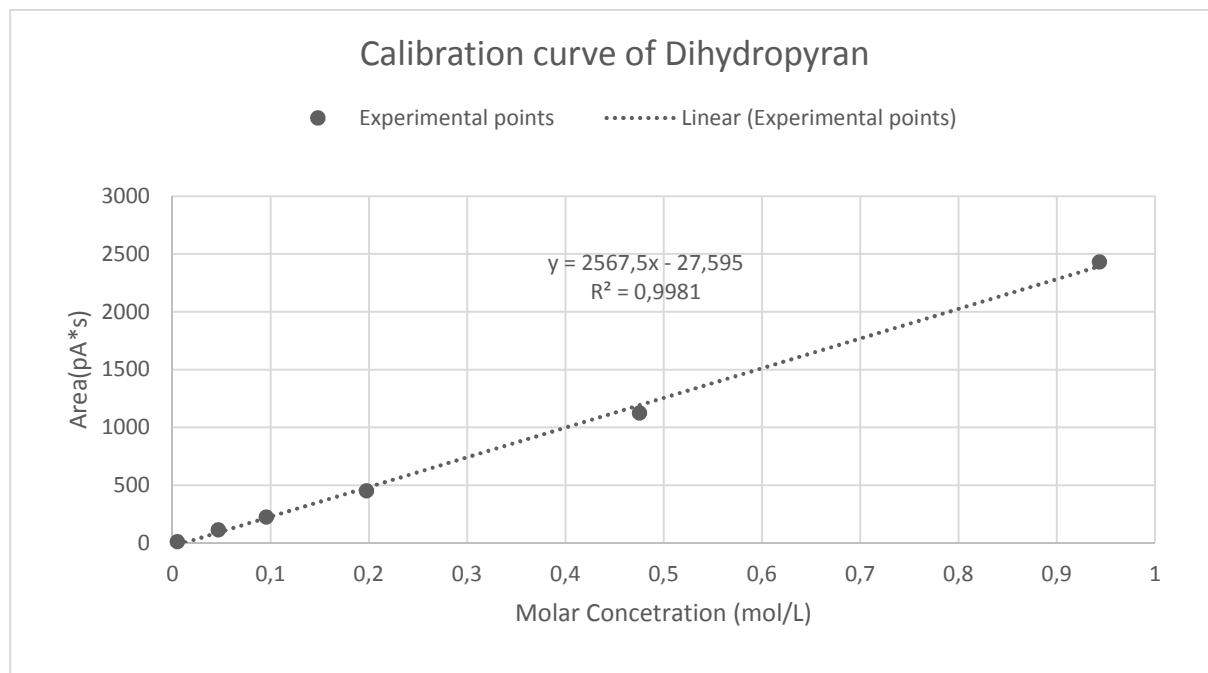


Figure 2.11 Calibration curve of DHP

When the calibration curve is accurately determined from many reference data, then the relative uncertainty in the sample response leads to a proportional uncertainty in the sample concentration. This is also known as the coefficient of variation, briefly R^2 .

The correlation coefficient of a perfectly straight line is equal to one. Normally, the calibration curve to be linear and to be valid, the R^2 has to be higher than 0,995.

The calibration curve calculated for the DHP had a R^2 of 0.9981 and so it could be used.

The figure 2.12 illustrates the chromatogram by GC-FID of the quantity 5.05% of DHP.

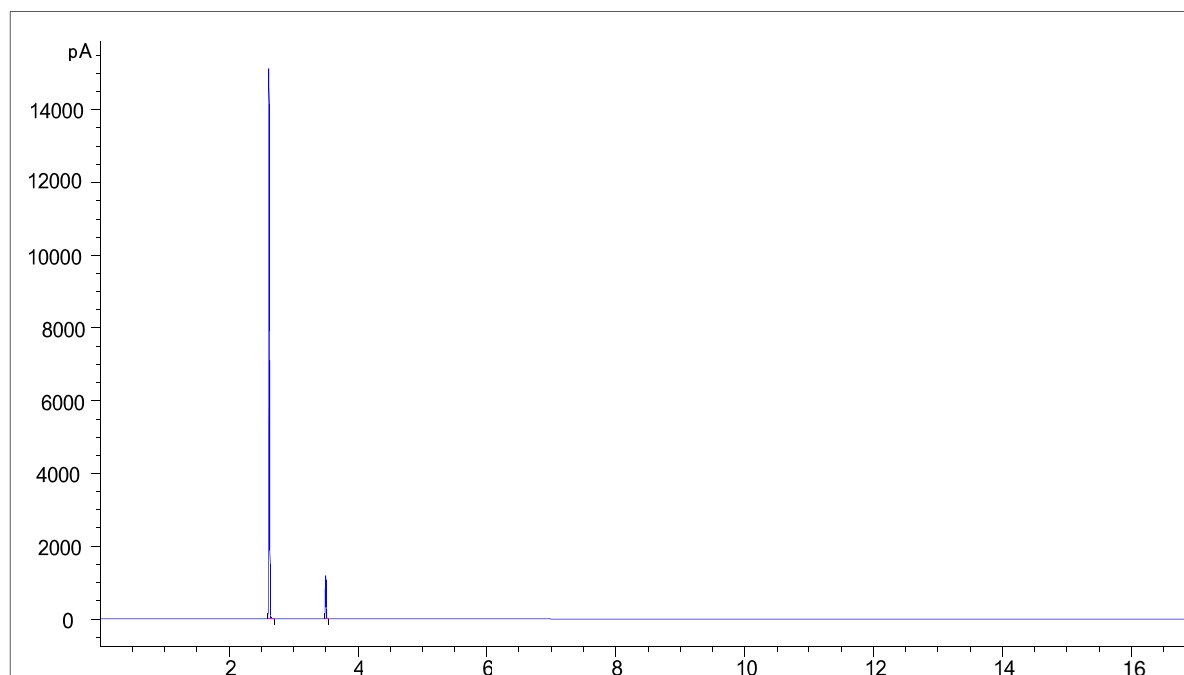


Figure 2.12 Chromatogram of the sample with 5.05% of DHP (Signal (pA) vs Time (min))

Another calibration curve has been done for the 1-butanol and the table 2.8 shows the weighted of analyte, the calculations, and the signals obtained from GC-FID.

Table 2.8 Values and calculation for 1-butanol

Weighed analyte [gr]	Moles [mmol]	Volume of solution [ml]	Weight of solution [gr]	Solvent added [gr]	Weight Concentration	Molar concentration [mol/L]	Area given by GC-FID [pA*s]
0.0051	0.0688	12.7733	10.0400	10.0349	0.051%	0.0054	10.2189
0.0277	0.3737	6.3827	5.0176	4.9899	0.552%	0.0586	131.3071
0.0500	0.6746	6.3976	5.0300	4.98	0.994%	0.1054	243.2564
0.1054	1.4220	6.3608	5.0027	4.8973	2.107%	0.2236	475.6949
0.2525	3.4066	6.3622	5.0082	4.7557	5.042%	0.5354	1218.2211
0.5043	6.8038	6.3725	5.0237	4.5194	10.038%	1.0677	2371.8800

Using the value of Area giving by GC-FID and the molar concentration of the analyte, the calibration curve has been plotted. (Figure 2.13)

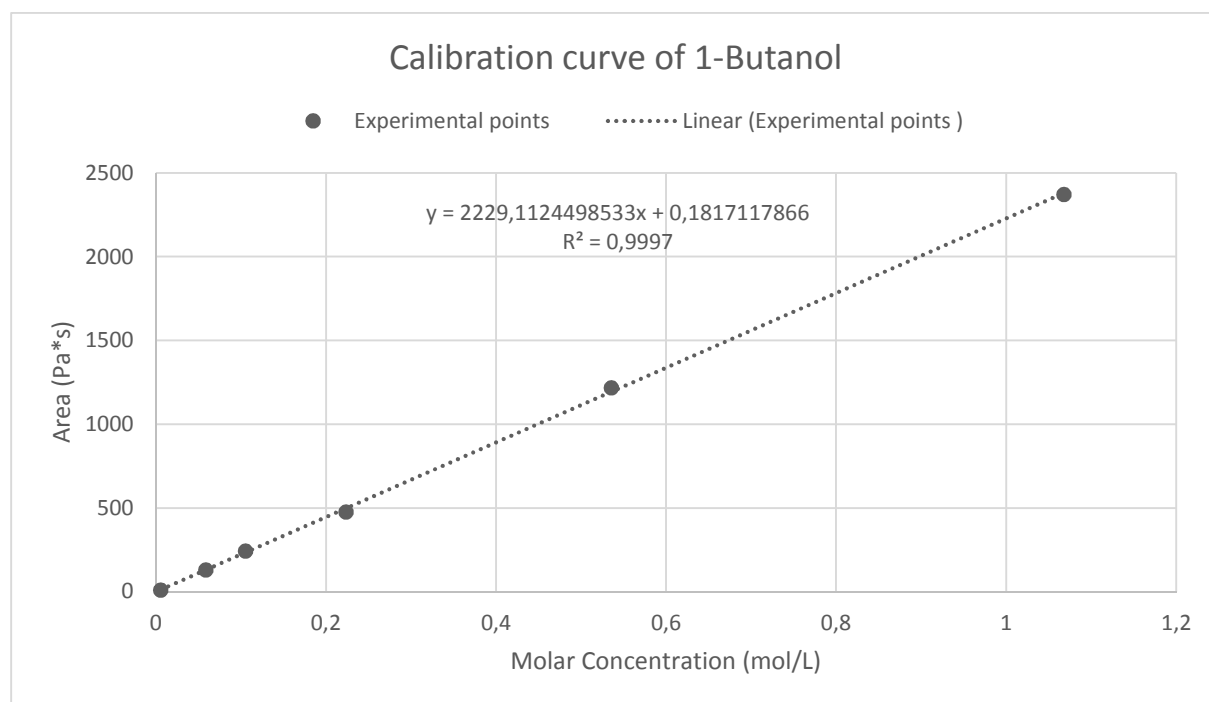


Figure 2.13 Calibration curve of 1-Butanol

The calibration curve calculated for the 1-butanol had a R^2 of 0.9997 and so it could be used. In the figure 2.14 the chromatogram by the GC-FID of the quantity 5.042 % of 1-butanol is illustrated.

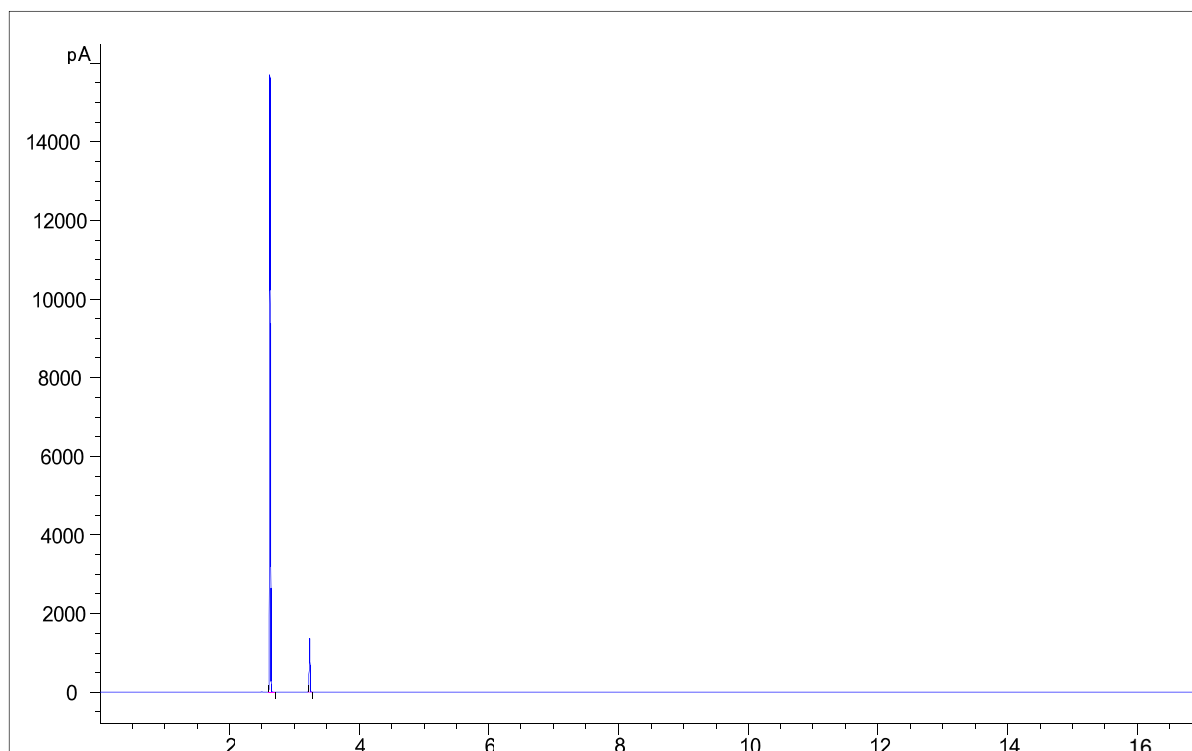


Figure 2.14 Chromatogram of the sample with 5.042% of 1-Butanol (Signal (pA) vs Time(min))

The formulas 2.1 and 2.2 have been used to calculate the molar concentration of DHP and of 1-butanol, where x is the pick area given by the GC-FID for the compound.

$$C_D = \frac{x+27,623}{2567,481} - 0,0107 \quad 2.1$$

$$C_B = \frac{x-0,1817}{2229,1124} \quad 2.2$$

2.5 The selection of the solvent

This paragraph discusses the selection of the solvent for this reaction.

A solvent is a liquid that serves as the medium for a reaction. It can serve two main reasons:

- it doesn't react in the solution and it dissolve the compounds;
- it reacts as a source of acid (proton), base (removing protons), or as a nucleophile (donating a lone pair of electrons).

Brijesh Kumar et al reported that the solvents more used for the protecting alcohols by DHP were apolar and aprotic solvents^[1].

The apolar solvents contain bonds between atoms with similar electronegativity, such as carbon and hydrogen for example the hydrocarbons. The bonds between atoms with similar electronegativity lack partial charges and this is the reason that these molecules are non-polar.

Instead the polar solvents have a charge and to measure it, two ways are possible:

- measuring the dielectric constant or permittivity and greater is the dielectric constant, greater is the polarity;
- measuring the dipole moment.

The polar aprotic solvent may have hydrogens on them somewhere, but they don't have O-H or N-H bonds, and therefore they can't have hydrogen bond with themselves. Their molecular structure doesn't present a hydrogen atom dissociable as an ion (H⁺).

Instead the polar protic solvents have O-H or N-H bonds and these O-H or N-H bonds can serve as a source of protons (H⁺).

In the publication of P.S. Poon *et al* and in the book of Greene *et al*, the solvents more used for the protection of hydroxyl group by DHP were the dichloromethane or the 1,4-dioxane^[9,2].

The using of dichloromethane or of 1,4-dioxane wasn't suggested because they aren't very safe and handy, therefore others solvents have been searched.

The table 2.9 shows the almost all common apolar and aprotic solvents with their properties like boiling point, vapour pressure, dielectric constant, density, dipole moment and danger advices.

Table 2.9 List of the apolar and aprotic solvents

Solvent	Boiling point at 1 atm [°C]	Vapor pressure at 20°C [mmHg]	Dielectric constant [F]	Dipole moment [D]	Density at 20°C [g/ml]	Danger advice
Pentane	36	434	1.84	0.00	0.626	Explosive
Cyclopentane	40	400	1.97	0.00	0.751	
Hexane	69	132	1.88	0.00	0.655	
Cyclohexane	81	78	2.02	0.00	0.779	
Benzene	80	95.25	2.3	0.00	0.879	Carcinogen
Toluene	111	21	2.38	0.36	0.867	
1,4-Dioxane	101	29	2.3	0.45	1.033	Carcinogen
Chloroform	61	194.26	4.81	1.04	1.498	Carcinogen
Diethyl ether	35	440	4.3	1.15	0.713	Explosive
Dichloromethane	40	429.78	9.1	1.60	1.3266	Carcinogen
Tetrahydrofuran	66	132	7.5	1.75	0.886	
Ethyl acetate	77	73	6.02	1.78	0.894	

Acetone	56	229.51	21	2.88	0.786	
Dimethylformamide	153	3.87	38	3.82	0.944	Toxic
Acetonitrile	82	72.83	37.5	3.92	0.786	
Dimethyl sulfoxide	189	1.09	46.7	3.96	1.092	
Nitromethane	100	28	35.87	3.56	1.1371	Explosive

Many solvents have been avoided through practice and theoretical considerations:

- some solvents are carcinogens or very explosives, so they have been avoided;
- some solvents have a low boiling point and a high vapor pressure, causing problems in the analysis with the GC-FID because if the solvent evaporates too much during the reaction or in the sample, the concentration of the other reactants increases giving a wrong concentration, therefore all the solvents under a boiling point of 70°C and over 100 mmHg of vapour pressure have been avoided.

After these considerations, the chosen solvents have been: ethyl acetate, acetonitrile, toluene and cyclohexane.

The reaction has been carried out in a low scale, around 15 ml of liquid volume, using each of these solvents to understand which solvent of them would have allowed the faster reaction.

The figure 2.15 shows the reaction run in the flask.

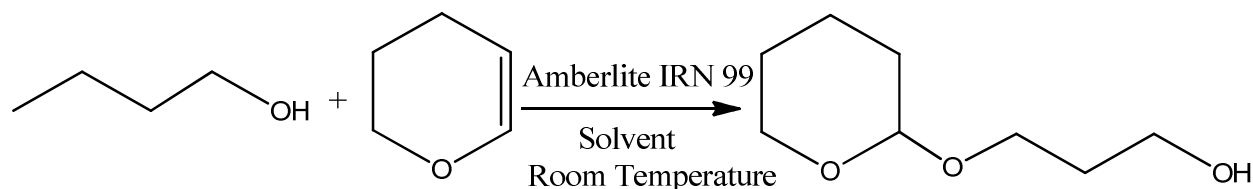


Figure 2.15 The reaction carried out in the flask

As said before in the paragraph § 2.4, the volume quantity of the solvent was between 10 and 20 times more than the volume of DHP and the molar quantity of DHP was the 10% more than of the alcohol.

Taking as example these considerations, in the next experiments have been used 10 mmol of 1-butanol, 11 mmol of dihydropyran and about 12 ml of solvent, so to save the quantities of reactants, being the reactants more expensive than the solvents. The volume of the total solution was of about 15 ml.

The reaction has been achieved in a round-bottom flask of volume of 50 ml and it has been mixed using a magnetic agitator at 500 rpm at room temperature and with 1 gram of the catalyst of procedure 'A'.

The reactants have been put in this flask and then the solvent has been added. The level of liquid has been measured by a graduated cylinder and the catalyst has been added in the flask. A magnetic agitator has been put inside. The samples have been taken each 30 minutes and the reaction has been stopped after 150 minutes.

The amounts weighted of the compounds for the four different reactions are resumed in the table 2.10.

Table 2.10 Amount of the compounds of the each reaction for each different solvent

<i>Solvent</i>	<i>Grams of 1-butanol</i>	<i>Grams of DHP</i>	<i>Grams of Solvents</i>	<i>Concentration of DHP</i>	<i>Total volume</i>
<i>Acetonitrile</i>	0.7432	0.9280	9.8643	0.727	15
<i>Ethyl acetate</i>	0.7446	0.9264	11.2507	0.760	15
<i>Cyclohexane</i>	0.7433	0.9368	9.7798	0.704	15
<i>Toluene</i>	0.7473	0.9378	10.9390	0.770	15

Taking the value of concentration given by the calibration curve, the conversion of the DHP has been calculated with the formula 2.3, where $C_{D,0}$ is the concentration of DHP at initial time and C_D is the concentration of DHP in time.

$$X = \frac{(C_{D,0} - C_D)}{C_{D,0}} \quad 2.3$$

The figure 2.16 illustrates the graphic obtained plotting the conversion of DHP versus the time for the different solvents chosen before.

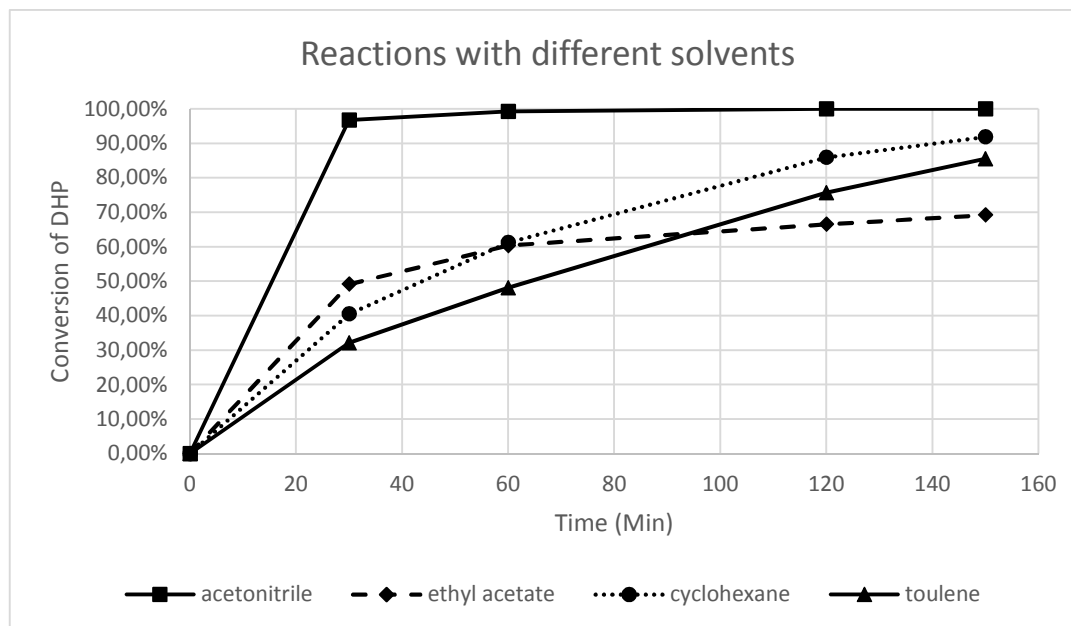


Figure 2.16 Conversion of DHP for the different solvents

The result was that the reaction with the acetonitrile has been faster than that the others solvents. Hence, the acetonitrile has been selected.

2.6 Equipment available for higher scale

This paragraph describes the equipment available to carry out the reaction to 145 ml and to 182 ml.

For the scale-up, the company made available:

- the jacketed flower-baffled vessel called SpinChem® Vessel V211;
- the lid for Vessel V211;
- the specific plug for the lid;
- the coated seal in FEP;
- the stands and a motor;
- the two kinds of impellers: the STR and the SpinChem® RBR S221.

2.6.1 The SpinChem® Vessel V211, the lid with specific plug and the seal

The SpinChem® Vessel V211 is made in glass and it is the equipment where the reaction was carried out. The section where the reaction was run, has a height of 6.5 cm and an internal nominal diameter of 6 cm with an extra neck of 3 cm of height. The capacity of this section is of about 183 cm^3 with the flower baffles all around it. (Figure 2.17)

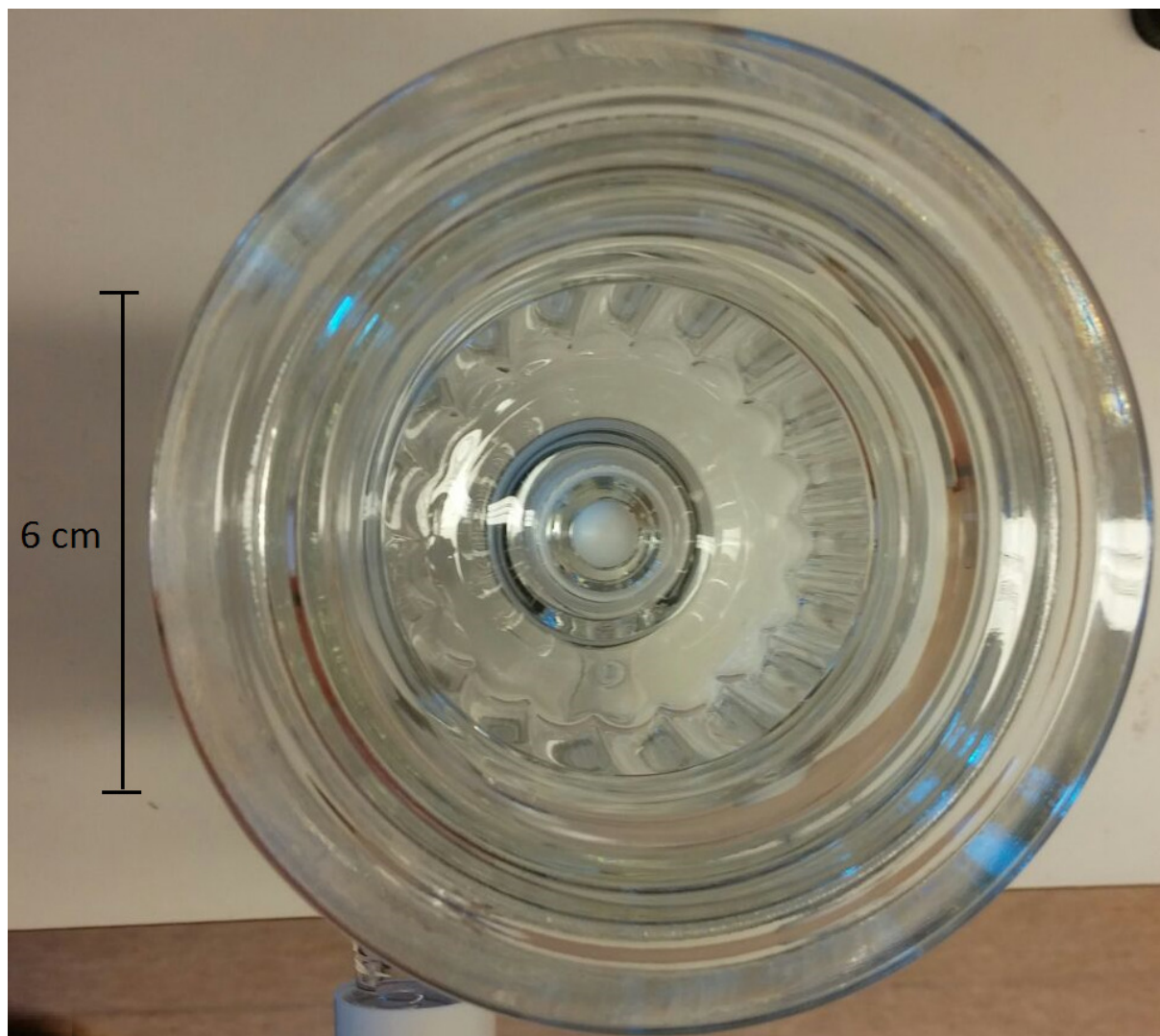


Figure 2.17 View of the flower baffles from above

The vessel V211 has a cylindrical shape with a conical bottom and a bottom drain.

The lid of the vessel V211 has two little inlet and one bigger in the middle. To close the big inlet, there was a specific plug with a hole in the centre where it is possible throughout the shaft of the impeller. The function of this tap isn't only to close the reactor but also to fix the impeller in the centre of the reactor.

The vessel is also jacketed, in this way is possible to use a flux of liquid to control the temperature. To close the bottom drain of vessel, there is a rod in teflon which could be rotated to allow a perfect closing of the reactor. The coated seal in FEP is put between the Vessel V211 and the lid to avoid that the solution inside spilled out during the experiments.

The figure 2.18 illustrates the vessel V211, the lid, the specific tap, the coated seal and the rod in teflon.



Figure 2.18 The vessel V211, the lid, the specific plug, the coated seal and the rod.

2.6.2 The stands and the motor

To mix the solution inside of the vessel, it was available a motor with a range of rotational velocity from 0 at 2000.

All the equipment were hold on with a stands to allow a perfect fitted.

2.6.3 The impellers

The two different kinds of impellers available for the project are described.

2.6.3.1 The STR

One was the 4-pitched blade turbine, applied to simulate the stirred tank reactor, called STR, which consisted in four axial helixes in teflon and with a diameter of 35 mm. (Figure 2.19)



Figure 2.19 The 4-pitched blade turbine impeller

The 4-PBT is the preferred choice where axial flow is desired and where there is a need for a proper balance between flow and shear. If $D/T > 0.55$ the flow pattern becomes radial¹⁵, where D is the diameter of the impeller and T the diameter of the vessel. In this case the ratio was 0.58, but the flow pattern could be considered axial. Normally the D/T for this kind of impeller would be between 0.25 and 0.5 to allow a good mixing and the rotation of the impeller was clockwise, so the flux was pushed towards the bottom.

The fluid dynamic for this STR is showed in the figure 2.20

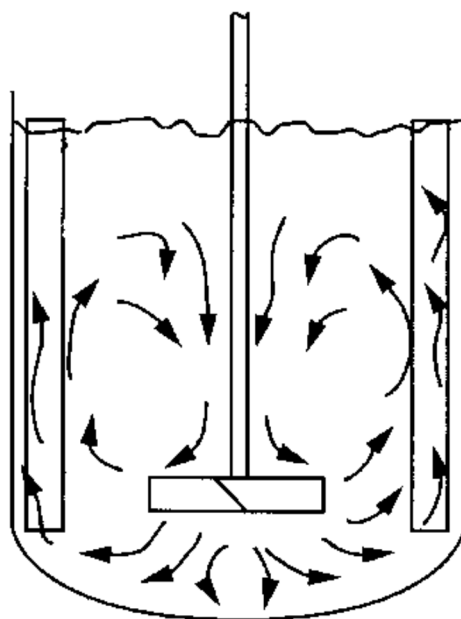


Figure 2.20 The flow pattern of the STR (Adapted from Edward L. Paul et al¹⁵)

The figure 2.21 shows the STR assembled with all equipment described before.



Figure 2.21 The STR assembled

To find the optimal rotational speed of the impeller which allowed the good mixing of the catalyst in the liquid, different velocities of the STR have been tried.

In the STR applying 400 rpm, the catalyst wasn't mixed uniformly in the liquid but it stayed for the most in the bottom of the vessel. Instead applying more than 600 rpm, there was a uniform mixing of the catalyst in the liquid, therefore using the STR each experiment has been done with 600 rpm.

2.6.3.2 The SpinChem® RBR S221

The other impeller was the SpinChem® RBR S221 which is made in stainless steel and it has a diameter of 45 mm, height of 30 mm and a packing volume inside of 28 cm³. (Figure 2.22)

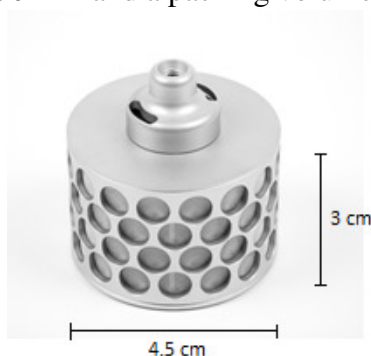


Figure 2.22 The SpinChem® RBR S221

The impeller consists in seven pieces: the outer ring, the flow distributor, a support where the fluid goes in, an outer filter, an inner filter, a top lid for the up side, and gasket to fix at the stick where the air goes out. The outer ring has some circular holes of diameters of 5 mm on all the side and the open mesh of the two filters is 104 μ m. (Figure 2.23 and Figure 2.24)

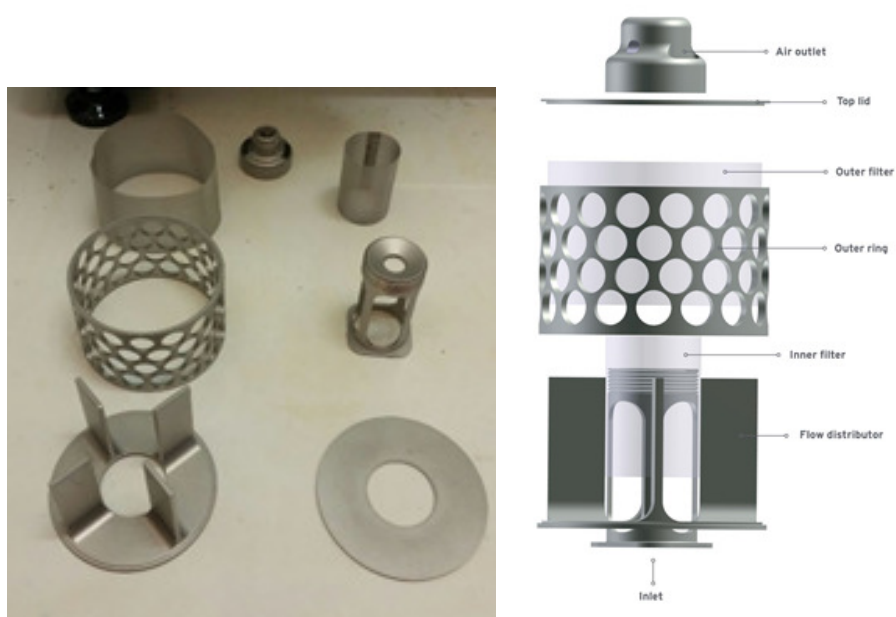


Figure 2.23 and Figure 2.24 The seven piece which compose the SpinChem® RBR S221 and the scheme to assemble it

There are a bigger hole on the beneath where the fluid goes in and two little hollows on the top where the air goes out. (Figure 2.25 and Figure 2.26)



Figure 2.25 The inlet in the beneath of the SpinChem®



Figure 2.26 View of the SpinChem®

The Amberlite IRN 99 was put inside of the SpinChem® RBR S221 where it was immobilized by the two filters. (Figure 2.27)



Figure 2.27 The solid catalyst Amberlite IRN 99 inside the SpinChem® RBR S221

The particularity of this impeller is his different fluid dynamic respect the 4-pitched blade turbine.

Rotating it creates a lower pressure inside and the liquid is aspirated inside from the hole on the beneath and from the two hollows on the top. Almost all of the flux enters from beneath while the two hollows have the main function to let out the air. Due to centripetal force the liquid goes from the centre to the side, passing through at the outer filter and going to contact with the solid catalyst, considering that the two filters hold the catalyst inside. Then the liquid is thrown out towards the wall. (Figure 2.28)

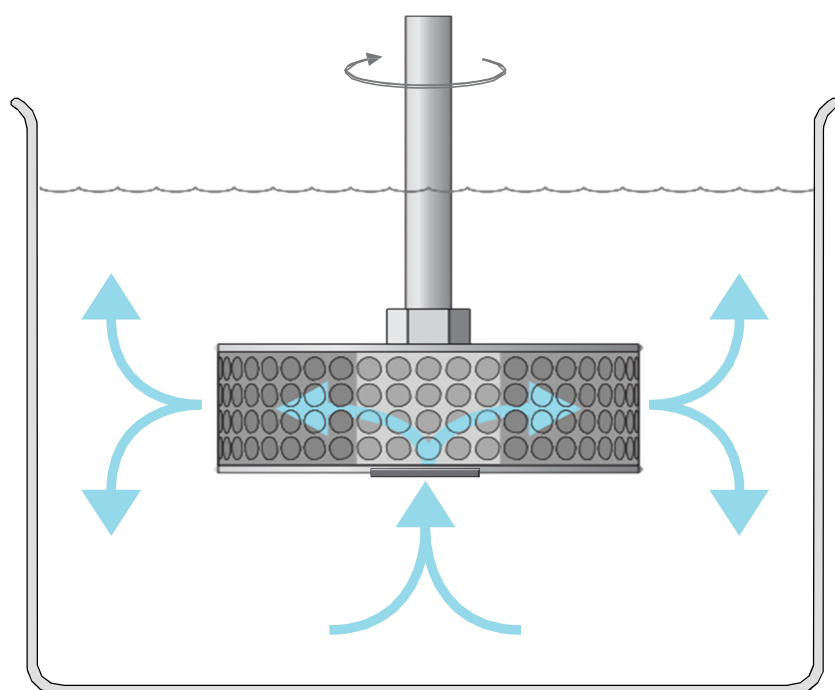


Figure 2.28 Flow pattern of the SpinChem® RBR S221

There are many differences of the SpinChem® RBR S221 respect the STR:

- the catalyst is immobilized and the solution passes inside of it, while in the 4-pitched blade the catalyst and the liquid are both in moving;
- the different fluid dynamic;
- the extending of the lifetime of the solid phase particles by minimizing grinding and fines;
- the easier handling to collect and recycle the catalyst.

The figure 2.29 and the figure 2.30 show the reactor assembled with the SpinChem® RBR S221.

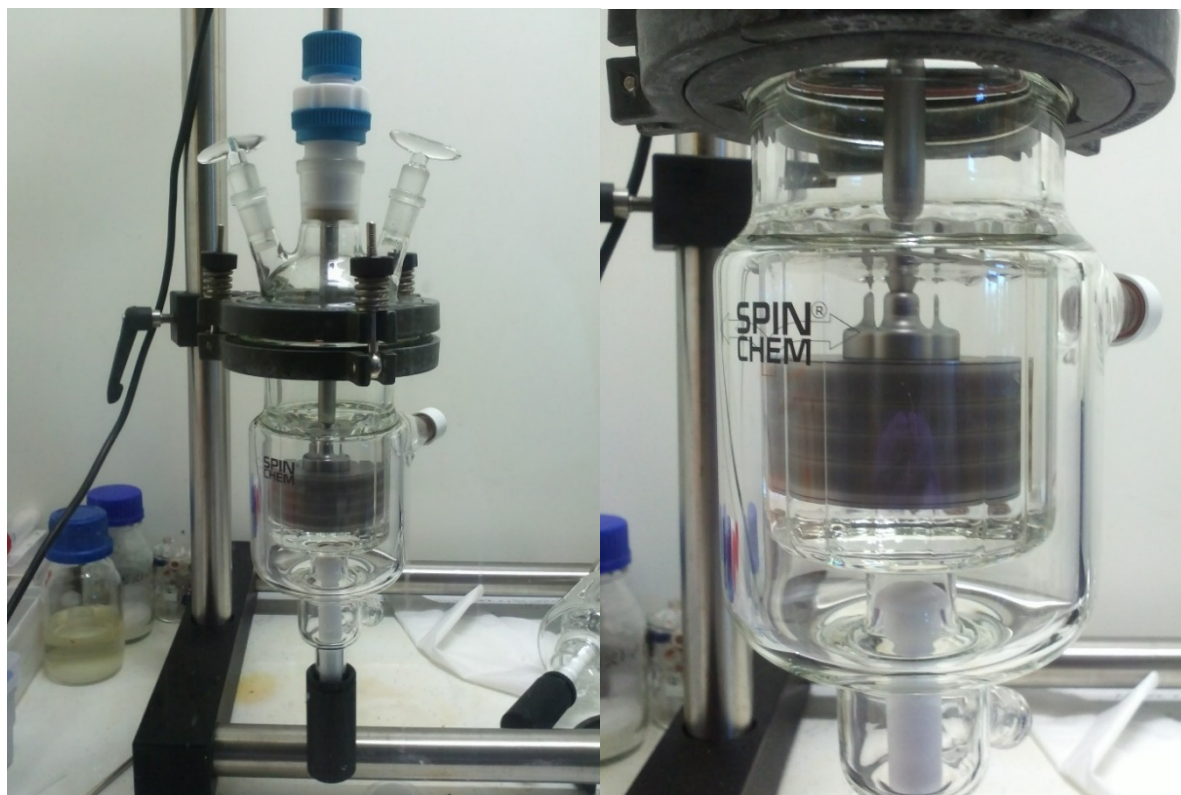


Figure 2.29 and Figure 2.30 View of the assembled reactor with the SpinChem® RBR S221

To set the rotational speed for the RBR, three experiments at different rotational speeds (300, 500, 900) have been carried out in the first experience of the results and discussion to understand if the rotational velocity changes the conversion of DHP.

2.7 Procedure of the reaction for the higher scale

This paragraph describes the procedure to run the reaction in the STR and in the SpinChem® RBR S221.

The experiments have been scaled-up, bringing the reaction from 15 ml to 145 ml and also to 182 ml of liquid volume.

The reaction has been run at room temperature for 4 hours and the quantities of the reactants and solvent have been 10 and 12.5 times than the quantity used for the lower scale.

The general amounts of the components are resumed in the table 2.11.

Table 2.11 The general amounts of the reactants and of the solvent

Total volume of solution	mmol of 1-butanol	mmol of DHP	mmol of acetonitrile	Grams of 1-butanol	Grams of DHP	Grams of acetonitrile
145 ml	100	110	2400	7.412	9.2532	98.52
182 ml	125	137.5	3000	9.265	11.5665	123.15

There was a difference of 0.7% between the ideal volume calculated and the real volume of the solution measured with the graduated cylinder, therefore the volume of the reaction has been considered ideal.

The procedure which has been followed for each experiment, is described further.

First at all, a round-bottom flask of 250 ml has been weighted on the analytical balance and with a pipette of 10 ml, the right amounts of the two reactants have been taken. The solvent has been added using a technical balance because the analytical balance had a limit of 160 grams. The catalyst has been weighted and it has been put inside the RBR or directly in the vessel in the case of the STR.

The first sample has been taken in the round-bottom flask to have the initial concentration.

Then the solution has been put in a graduated cylinder to see the exact amount of the liquid and after with a funnel it has been put in the vessel V211 and the motor has been switched on.

To investigate the behaviour of the reaction through the concentrations of the reactants, the samples have been taken in these time: 0, 2, 4, 8, 16, 30, 60, 90, 120, 150, 180, 210, 240 minutes and each little sample contended around 1 ml of the solution.

When the experiments was finished the solution has been thrown off in the organic waste and all the equipments have been washed by acetone. The used catalyst has been collected in a plastic bottle.

The samples have been analysed by GC-FID and the concentrations of the DHP and 1-butanol have been calculated by the formula 2.1 and 2.2, reported at the end of the paragraph § 2.4

Chapter 3

Results and Discussion

This chapter resumes and discusses all the results obtained in this project applying the two kinds of impellers available: the STR and the SpinChem® RBR S221.

The experiments are shown using some graphics where on the coordinates the conversion of the DHP and on the axis the time.

First of all, in the first experience the RBR has been studied varying the rotational speed. After the two impellers has been compared in three different cases and they have been discussed.

Then an experience has been carried out varying the heights of the RBR from the bottom of the reactor and at the end the STR has been studied varying the rotational speed.

The setting and the weighted quantities of components are described at the beginning of each paragraph by a table, while the analysis of each sample of the experiments are collected in the appendix A in format table and in increasing order of experiments.

The heterogeneous reaction used in the experiments is shown in the figure 3.1.

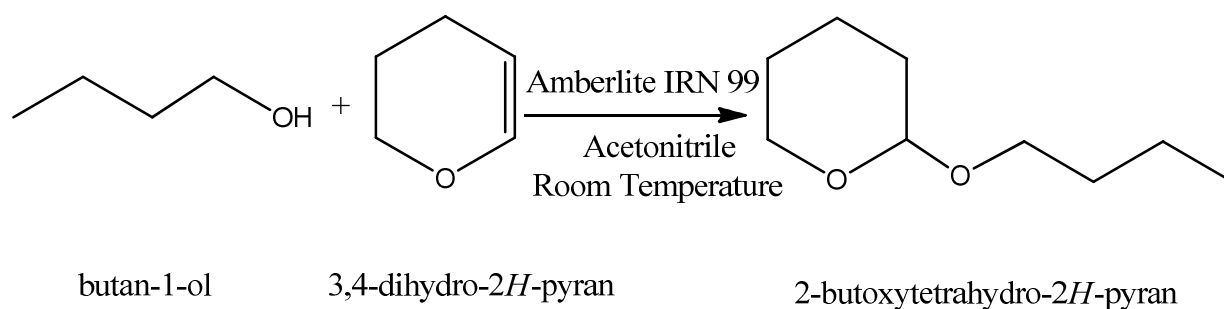


Figure 3.1 The heterogeneous reaction used

The washing procedure of the catalyst is described in the paragraph § 2.1 and the procedure of the reaction followed for these experiments is described in the paragraph § 2.7.

The concentrations of the reactants and the conversions of DHP have been calculated using the equations 2.1, 2.2 and 2.3 in the paragraph § 2.4 and § 2.5.

3.1 Different rotational speeds of the RBR

The aim of this paragraph is to understand if changing the rotational speed of the RBR, the conversion of the reaction changes, so to set the rotational speed on the comparison with the STR.

The first experience has compared the conversion of DHP of the RBR employing the same quantity of catalyst washed with the procedure 'A', the same initial concentrations of reactants, a quantity of liquid around 145 ml and at a height from the bottom of 7 mm but different rotational speeds.

The experience consisted in three experiments at different rotational speeds 500, 300 and 900 rpm.

The table 3.1 shows the setting for this experience.

Table 3.1 The setting for first experience

	<i>Exp. 2</i>	<i>Exp.1</i>	<i>Exp.3</i>
<i>Impeller type</i>	RBR	RBR	RBR
<i>Rotational speed(rpm)</i>	300	500	900
<i>Height from bottom (cm)</i>	0.7	0.7	0.7
<i>1-butanol (gr)</i>	7.460	7.428	7.429
<i>DHP (gr)</i>	9.2977	9.4448	9.293
<i>Acetonitrile (gr)</i>	98.75	98.84	98.80
<i>Catalyst (gr)</i>	11	11	11
<i>Liquid volume (ml)</i>	145	145	145
<i>Initial concentration of DHP (mol/L)</i>	0.7528	0.77	0.7372
<i>Initial concentration of 1-butanol (mol/L)</i>	0.71	0.71	0.69
<i>Procedure</i>	A	A	A

The figure 3.2 shows the conversion of DHP in time of the experiments 1,2 and 3.

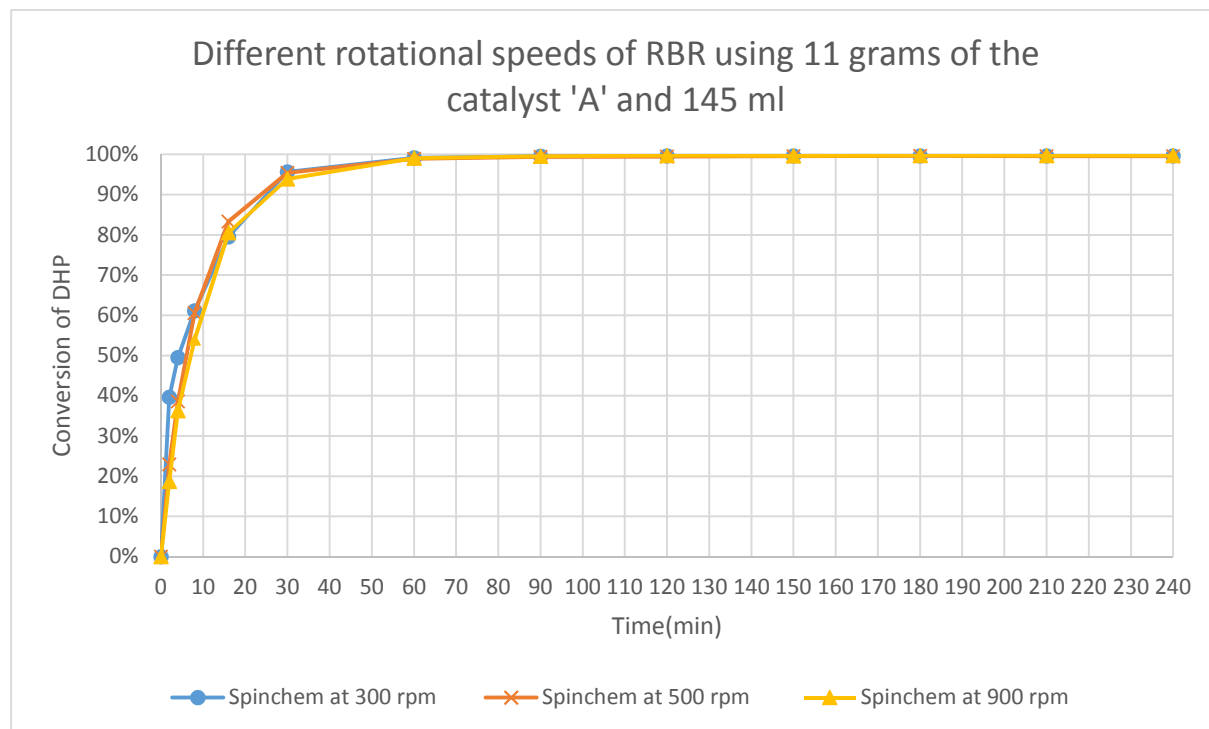


Figure 3.2 Case at different rotational speeds of the RBR using 11 grams of the catalyst washed with the procedure 'A' and 145 ml of volume solution

How showed by the figure 3.2, changing the rotational speed of the RBR, the conversions don't change. This means that the reaction at these operation conditions for the RBR doesn't seem limiting of the external mass transfer due to the velocity of the impeller.

This experience points out that the choice of the rotational speed to compare the RBR and the STR was irrelevant in the range from 300 rpm to 900 rpm because the results are equals.

Furthermore these experiments have demonstrated also the reproducibility of the data experiments using this kind of washing procedure 'A' for the catalyst.

3.2 RBR vs. STR

The purpose of this paragraph is to compare the new impeller, made by the SpinChem AB and the STR in different cases:

- case 1, using 11 grams of catalyst washed with the procedure 'A';
- case 2, using 6 grams of catalyst washed with the procedure 'A';
- case 3, applying the catalyst washed with the procedure 'B'.

As demonstrated in the paragraph § 3.1, the rotational speed set for the RBR was irrelevant from 300 to 900, therefore in these experiments the rotational speed for the RBR has been set at 500 while for the STR at 600 as said in the paragraph § 2.6.

3.2.1 Case 1: using 11 grams of the catalyst washed with the procedure 'A'

The second experience compared the conversion of the DHP employing the same quantity of catalyst with washing procedure 'A', the same initial concentrations of reactants, a total liquid volume around 145 ml and a height of the impellers from the bottom of the vessel V211 of 7 mm but two kinds of impellers.

The experience consisted in two experiments and the table 3.2 shows the setting for this experience.

Table 3.2 Setting of the second experience

	Exp. 4	Exp. 1
Impeller type	STR	RBR
Rotational speed(rpm)	600	500
Height from bottom (cm)	0.7	0.7
1-butanol (gr)	7.428	7.428
DHP (gr)	9.267	9.4448
Acetonitrile (gr)	98.795	98.84
Catalyst (gr)	11	11
Liquid volume (ml)	145	145
Initial concentration of DHP (mol/L)	0.75	0.77
Initial concentration of 1-butanol (mol/L)	0.69	0.71
Procedure	A	A

The figure 3.3 shows the conversion of DHP in time of the experiments 1 and 4.

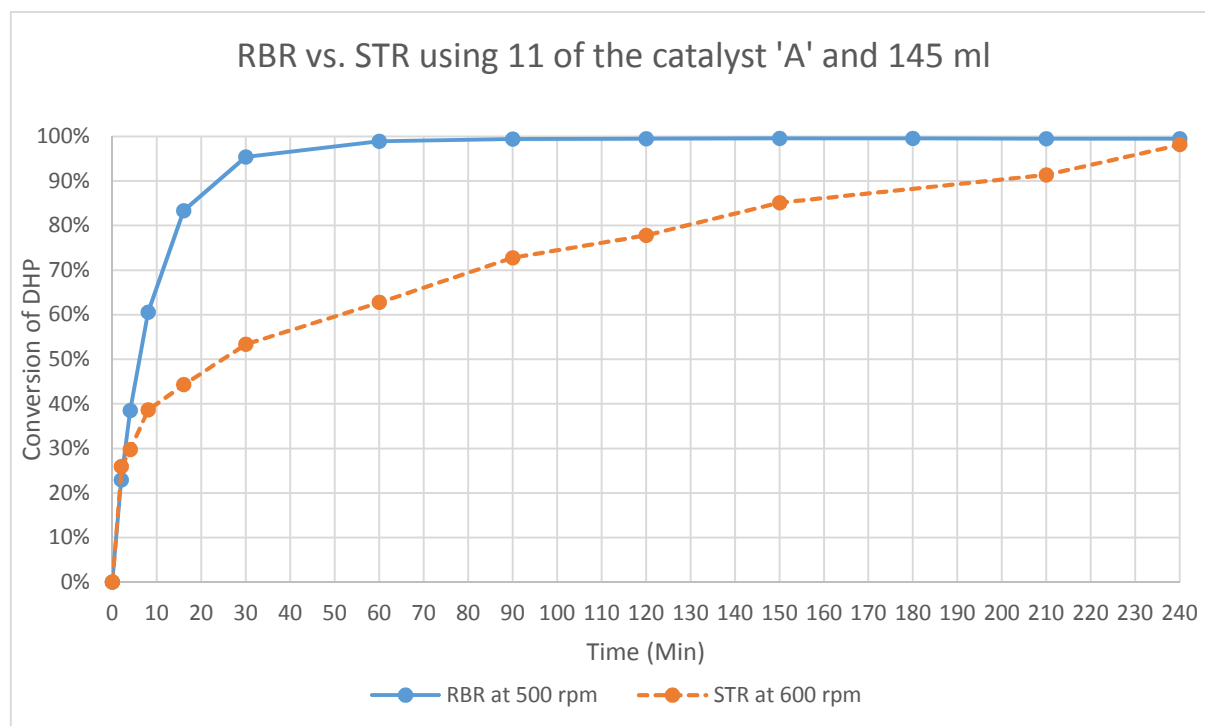


Figure 3.3. The RBR vs. the STR using 11 grams of the catalyst 'A', same amounts of components and 145 volume of solution

The figure 3.3 reports that the conversion of DHP for the RBR is of 95% after 30 minutes while for STR is only of 53% and after 240 minutes it is arrived at complete conversion. The RBR is quite better than the STR over 4 minutes and this difference is probably due to a poor mixing of the solid.

Other two cases have been carried out to allow a better investigation of this effect.

3.2.2 Case 2: using 6 grams of catalyst washed with the procedure 'A'

This third experience used less quantity of catalyst than the second experience. It compares the conversion of DHP applying the same initial concentrations of reactants, a quantity of liquid around 182 ml and at a height from the bottom of the vessel of 7 mm but different quantity of catalyst of washing procedure 'A' and different impellers.

The experience consisted in three experiments, two to compare the two impellers and one to understand the amount of saving of the catalyst applying the RBR instead the STR.

The table 3.3 shows the setting for this experience.

Table 3.3 The setting of the third experience

	Exp. 5	Exp.6	Exp.7
Impeller type	STR	RBR	RBR
Rotational speed(rpm)	600	500	500
Height from bottom (cm)	0.7	0.7	0.7
1-butanol (gr)	9.2803	9.2748	9.2673
DHP (gr)	11.6555	11.5798	11.5772
Acetonitrile (gr)	123.35	123.44	123.80
Catalyst (gr)	6	6	4
Liquid volume (ml)	182	182	182
Initial concentration of DHP (mol/L)	0.6960	0.7186	0.7326
Initial concentration of 1-butanol (mol/L)	0.66	0.68	0.69
Procedure	A	A	A

The figure 3.4 illustrates the conversion of DHP in time of the experiments 5, 6 and 7.

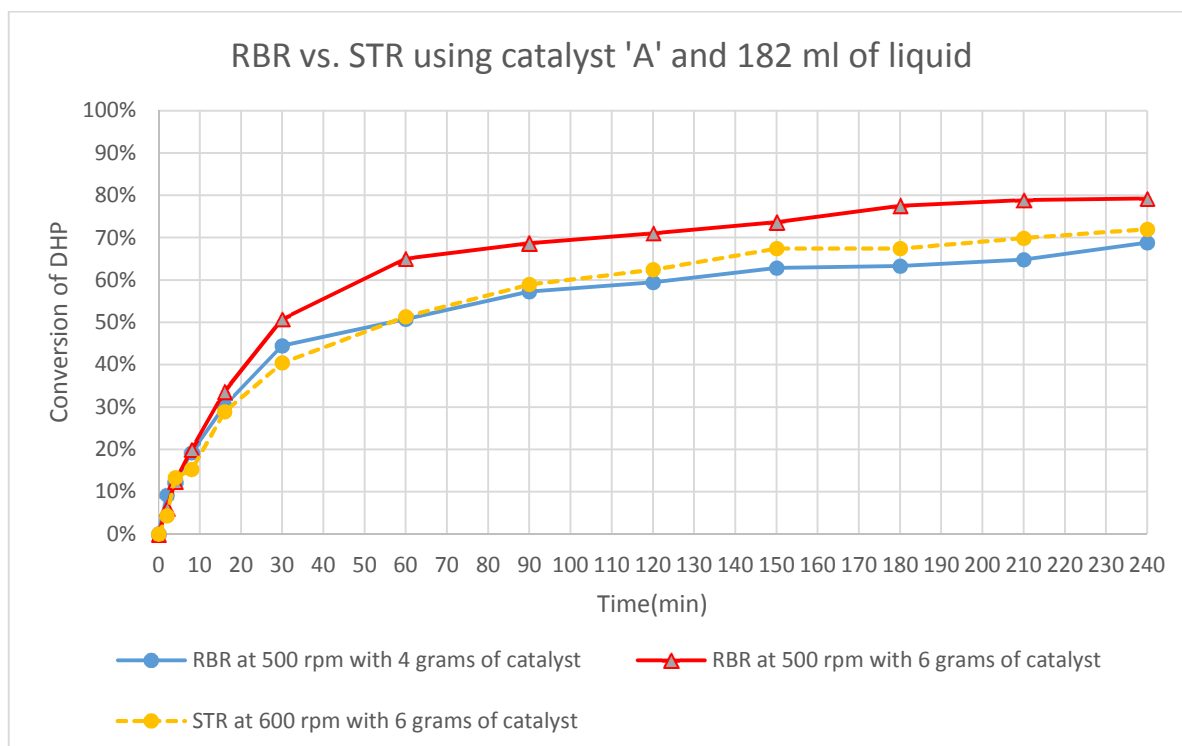


Figure 3.4 RBR vs. STR using the catalyst washed with the procedure 'A' and 182 ml of volume solution

Also in this case, the RBR is a little better than the STR with the same parameters: after 240 minutes the STR has a conversion of 72% while the RBR of 79% and only the first 8 minutes the two curves are very similar but over 30 minutes there is a constant gap between them. Additionally the experiment 7 has been carried out with 4 grams of catalyst to understand the amount of saving of the catalyst applying the RBR instead the STR: there is a little distinction between the two trending of the experiment 5 and 7.

3.2.3 Case 3: using the catalyst washed with the procedure 'B'

The fourth experience compared the conversion of DHP applying the same initial concentrations of reactants, a quantity of liquid of 182 ml and the two propeller at height of 7 mm from the bottom but different quantity of catalyst washed with the procedure 'B'. The experience consisted in three experiments, two to compare the two impellers and one to understand the amount of saving of the catalyst applying the RBR instead the STR. The table 3.4 shows the setting for this experience.

Table 3.4 The setting of the fourth experience

	Exp. 9	Exp. 10	Exp.8
Impeller type	STR	RBR	RBR
Rotational speed(rpm)	600	500	500
Height from bottom (cm)	0.7	0.7	0,7
1-butanol (gr)	9.2758	9.2758	9.2669
DHP (gr)	11.5665	11.5665	11.5809
Acetonitrile (gr)	123.45	123.45	123.25
Catalyst (gr)	4	3	4
Liquid volume (ml)	182	182	182
Initial concentration of DHP (mol/L)	0.7353	0.7302	0.7428
Initial concentration of 1-butanol (mol/L)	0.68	0.69	0.69
Procedure	B	B	B

The figure 3.5 shows the conversion of DHP in time of the experiments 8, 9 and 10.

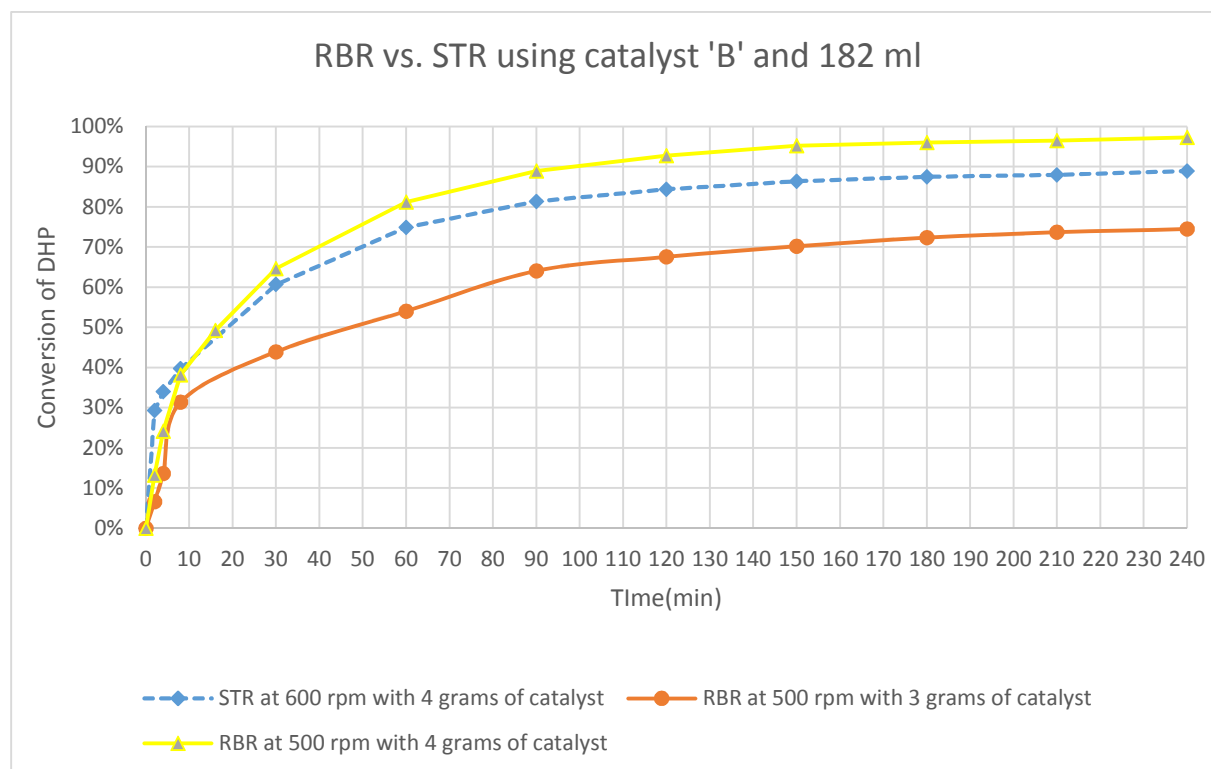


Figure 3.5 RBR vs. STR using the catalyst washed with the procedure 'B' and 182 ml of volume solution

First of all, the figure 3.5 points out that the catalyst washed with the procedure 'B' is much more active than that washed with the procedure 'A' and this is normal considering that the procedure 'B' has cleaned better from the impurities the catalyst, due to many washings.

Using the same amount of catalyst but different washing procedure the conversion achieves the 97% respect 69% for the RBR.

Also in this case with a less quantity of catalyst respect the case 1, the RBR is always a bit better than the STR over 60 minutes but with less gap between the curve of the conversions respect the case 2, probably due to the catalyst more active and also to the less amount of catalyst employed.

Furthermore the experiment 10 with less catalyst has been done to understand how much catalyst could be saved using the RBR and it reaches to 74% of conversion of DHP respect the 89% of the STR after 240 minutes.

3.2.4 Discussion

In three cases studied where the RBR is compared with the STR, the RBR resulted always better than the STR.

Being the same reaction in all the experiments if the rate determining step was the limitation of the kinetic reaction, the curves of the conversion had to be equals and an increasing of the

temperature would allow an increasing of the conversion of DHP, but the temperature wasn't changed.

Using the same catalyst and same conditions in the experiments if the controlling regime was the limitation of internal mass transfer, the curves had to be equals because the internal mass transfer depends on the properties of the catalyst (tortuosity, particle porosity), on the diffusion coefficient and on the temperature as described in literature^[16].

The only difference of the experiments was the different impeller, therefore the different trend of the conversion of DHP is probably due to the better mixing of the catalyst.

This effect could happen because the catalyst is immobilized inside the basket of the RBR by the filters and the liquid passes through of it, creating a intimal contact on the surface of catalyst between the reactants due to higher relative velocity between the solid particles and the reactants while in the STR the particles of the solid phase and the solution are both in moving, not creating a contact like that of the RBR due to lower relative velocity.

Another reason could be due at the particular fluid dynamic of the RBR which aspirates the liquid from the bottom and a bit from the top, creating a better recirculation. In fact in the experiments only in the first minutes the conversions of DHP are very similar between the impellers, after they change probably due to formation of the product which hinders a bit the contact on the surface of the catalyst between the reactants.

3.3 Different heights of the RBR from the bottom

The aim of this paragraph is to investigate if moving up or down the impeller on the reactor, the conversion of DHP changes.

The fifth experience compared the conversion of DHP of the RBR employing, the same initial concentrations of reactants, a quantity of liquid around 182 ml and the same quantity of catalyst washed with procedure 'B' but varying the heights from the bottom of the vessel.

The experience consisted in three experiments at different height from the bottom of the RBR at 0.7 cm, at 1.2 cm and at 1.7 cm. The table 3.5 shows the setting for this experience.

Table 3.5 The setting of the fifth experince

	Exp. 8	Exp. 11	Exp. 12
Impeller type	RBR	RBR	RBR
Rotational speed(rpm)	500	500	500
Height from bottom (cm)	0.7	1.2	1.7
1-butanol (gr)	9.2669	9.2673	9.2700
DHP (gr)	11.5809	11.5800	11.5860
Acetonitrile (gr)	123.25	123.45	123.50
Catalyst (gr)	4	4	4
Liquid volume (ml)	182	182	182
Initial concentration of DHP (mol/L)	0.74	0.72	0.73
Initial concentration of 1-butanol (mol/L)	0.69	0.68	0.69
Procedure	B	B	B

The figure 3.6 illustrates the conversion of DHP in time of the experiments 8, 11 and 12.

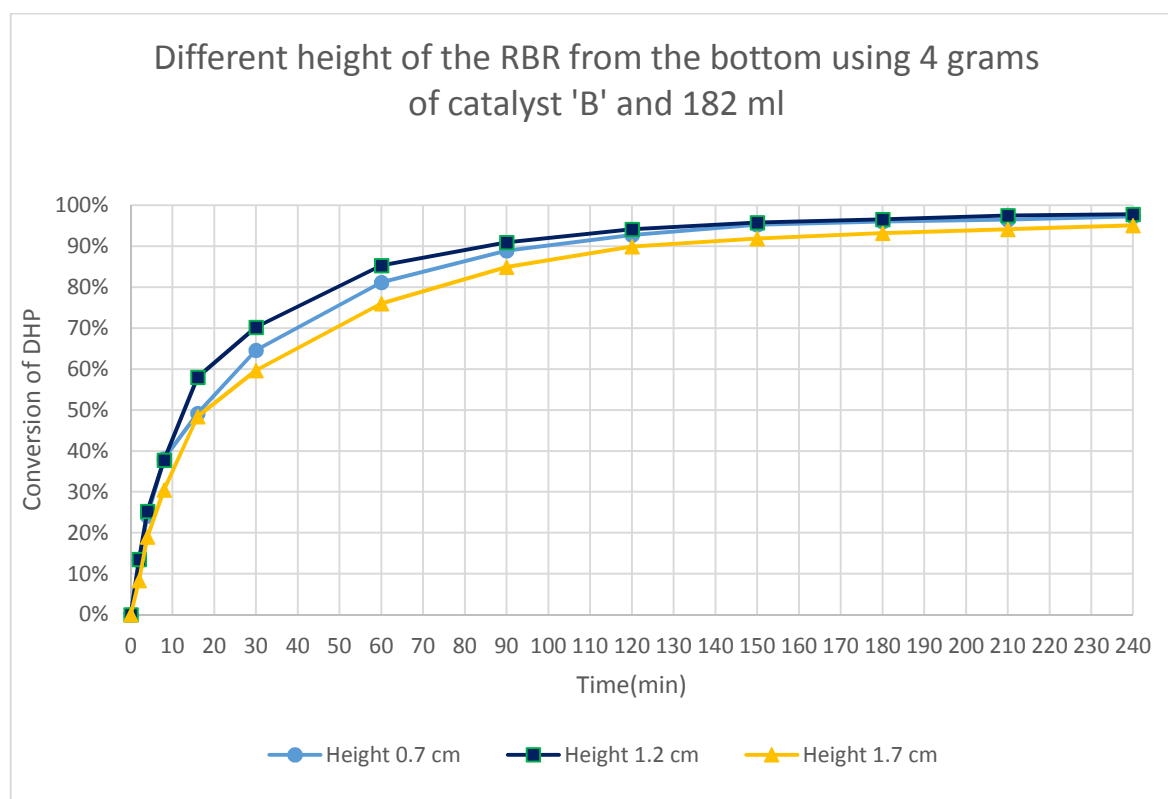


Figure 3.6 Different height of the RBR from the bottom using 4 grams of the catalyst 'B' and 182 ml of solution

The figure 3.5 shows that changing the height from the bottom of the RBR, the trend of conversion of DHP changes little and the final conversions are practically equals.

The experiment 10 at 1.2 of height from the bottom is the better position than the experiment 8 at 0.7 cm and the experiment 9 at 1.7 cm.

The case at 0.7 cm is a bit worse because the impeller is too close at the bottom and there isn't a good aspiration of the fluid from the bigger hole on the beneath of RBR, where normally the most of the solution is aspirated inside.

The case at 1.7 cm is a bit worse because the impeller is too close at the top level of liquid and a good mixing isn't permitted in the top part due to the little space between the two little hollows and the level of liquid.

3.4 Different rotational speeds of STR

The catalyst used in this experience has been washed with the procedure 'B' but it has been taken from another batch of catalyst than that used for all the experiments done before.

The sixth experience compared the conversion of DHP with the STR employing the same quantity of catalyst washed with the procedure 'B', the same initial concentrations of reactants, a quantity of liquid around 182 ml and the two propeller at a height from the bottom of 7 mm. The experience consisted in three experiments at different rotational speeds 500, 600, 800 and 1000 rpm.

The table 3.6 shows the setting for this experience.

Table 3.6 The setting of the sixth experience

	Exp. 13	Exp.14	Exp. 15	Exp.16
Impeller type	STR	STR	STR	STR
Rotational speed(rpm)	600	800	1000	500
Height from bottom (cm)	0.7	0.7	0.7	0.7
1-butanol (gr)	9.2752	9.2618	9.2727	9.2754
DHP (gr)	11.5995	11.5801	11.5843	11.583
Acetonitrile (gr)	123.50	123.8	123.5	124
Catalyst (gr)	4	4	4	4
Liquid volume (ml)	182	182	182	182
Initial concentration of DHP (mol/L)	0.68	0.72	0.69	0.74
Initial concentration of 1-butanol (mol/L)	0.63	0.68	0.65	0.68
Procedure	B	B	B	B

The figure 3.6 illustrates the conversion of DHP in time of the experiments 13, 14, 15 and 16.

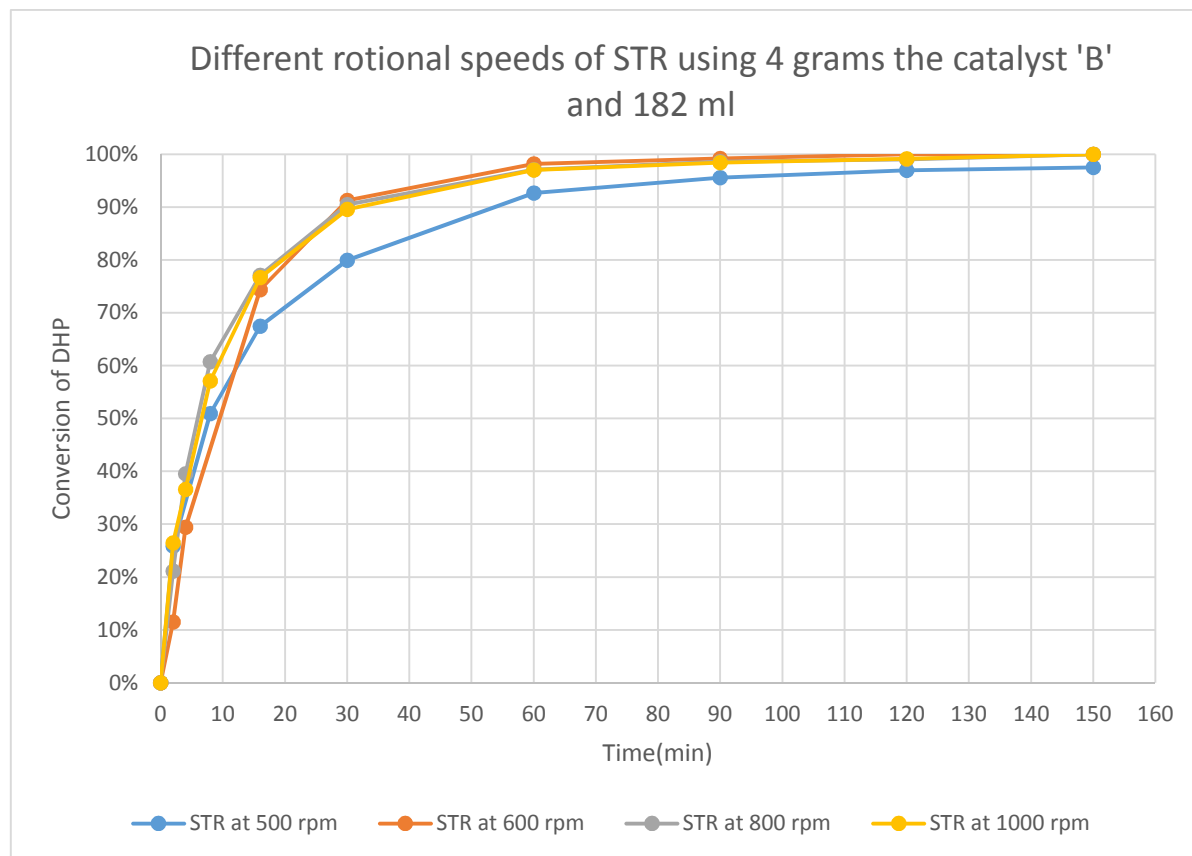


Figure 3.6 Different rate of the STR with 4 grams of the catalyst 'B' and 182 ml of volume solution

First of all, the figure 3.6 illustrates the more activity of the catalyst, because the catalyst has been taken from a different batch of catalyst respect the others experiments done before, therefore the time of the analysis has been reduced.

The results is that a different velocity 600, 800 and 1000 rpm, the conversions don't change, so it means that the reaction studied with this parameters is external mass transfer limited due to the rpm.

At 500 rpm the trend of the curve is a bit less because the solid phase remained for the most part in the bottom of the vessel and it wasn't mixed well in the solution.

This last result allows to understand that the STR has to use a higher rpm to allow a uniform mixing of the catalyst and the liquid while the RBR can be used also a low rpm (300), as showed in the paragraph 3.1, because the catalyst is inside the basket of the RBR.

Conclusion

This master thesis work was aimed at experimentally investigating of the new rotating bed reactor, the SpinChem® RBR S221, comparing it to a conventional stirred tank reactor, a 4-pitched blades called STR.

To compare them, a heterogeneous reaction has been investigated and improved. The reaction is called tetrahydropyranylation and it consisted in a solution in liquid phase of the dihydropyran and of an alcohol in a solvent and with a solid acid catalyst.

The catalyst available was Amberlite IRN 99 but it had impurities and salts solubilized inside and two kinds of washings procedures 'A' and 'B' have been carried out.

To improve the reaction, the alcohol and the solvent have been chosen, using considerations of the literature^[9,10,11] (low vapour pressure, danger advice,...) and carrying out four reactions with different solvents in lower scale with a volume solution of 15 ml.

This procedure permitted to obtain a faster and safer reaction and it was scaled from 15 ml to 145 ml and to 182 ml to be able to be used in the two reactors.

The reaction has been run before in the RBR, changing the rotational speeds (300 rpm, 500 rpm, 900 rpm) to be able to understand if the different rotational speeds determined a different conversion of DHP and to be able to compare the rpm of the two impellers. Since the conversions of DHP didn't change, the velocity set for the RBR didn't matter. While in the STR applying 400 rpm, the catalyst wasn't mixed uniformly in the liquid but it stayed for the most in the bottom of the vessel. Instead applying more than 600 rpm, there was a uniform mixing of the catalyst in the liquid, therefore using the STR each experiment has been done with 600 rpm.

So the RBR has been set to 500 rpm and the STR has been set to 600 rpm.

The comparison between the two reactors has been achieved by three cases: case 1, using 11 grams of catalyst washed with the procedure 'A'; case 2, using 6 grams of catalyst washed with the procedure 'A'; case 3, applying the catalyst washed with the procedure 'B'.

In the all three cases, the RBR resulted with a better conversion of DHP in the time than the STR using the same conditions in both.

Since the shaft of the impeller could be moved up or down, an investigation has been performed about the different height of the RBR from the bottom of the vessel but this setting doesn't influence much the conversion of DHP.

At the end the changing of the rotational speeds for the STR has been examined but the conversions haven't changed. In only these experiments, the catalyst used has been taken from another batch of the catalyst than that used in all the experiments done before, so the activity of the catalyst was different. The result was that only at 500 rpm the conversion was worse than the others at more rotational speed because the most of the catalyst stayed in the bottom of the vessel.

All the experiments carried out in this project proved that the RBR has many advantages than the STR.

One is the better contact between the particles and the liquid. This effect could happen because the catalyst is immobilized inside the basket of the RBR by the filters and the liquid passes through of it, creating a intimal contact on the surface of catalyst with the reactants due to higher relative velocity between the solid particles and the reactants while in the STR the particles of the solid phase and the solution are both in moving, not creating a contact like that of the RBR due to lower relative velocity. Using the RBR there is a higher surface concentration of the reactants than using the STR but starting with the same bulk concentration.

The second is the better mixing and recirculation due to its particular fluid dynamic and its structure. The catalyst stays inside the RBR, so also with low rotational speed (300), it doesn't need a high velocity to be uniform stirred in the solution instead this didn't happen for the STR which needed of high rotational speed.

The third is the easier handling to collect and recycle the catalyst being inside the basket. In all the experiments when the reaction finished, the liquid has been thrown off in the waste organic and the vessel has been washed. But using the STR, the completed reaction had to be filtered from the solid phase and the vessel had to be washed due to the solid particles which created issues.

Appendix A

Experiments results

In the appendix A all the results obtained are resumed using a format table in order of each experiment.

The table reports for each sample, the area of the compounds given by the GC-FID, the concentrations of the compounds calculated with the formulas 2.1 and 2.2 and the conversion of DHP calculated with the formula 2.3.

First experience

Table 1. Experiment 1

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1979	0.7708	1595	0,7154	0.00%
2	1525	0.5940	1287	0.5775	22.94%
4	1216	0.4736	931	0.4176	38.56%
8	781	0.3042	616	0.2763	60.54%
16	330	0.1285	332	0.1489	83.33%
30	91	0.0354	242	0.1085	95.40%
60	22	0.0086	222	0.0995	98.89%
90	12	0.0047	216	0.0968	99.40%
120	10	0.0039	209	0.0937	99.50%
150	8.8	0.0034	224	0.1004	99.56%
180	8	0.0031	222	0.0995	99.60%
210	9.7	0.0038	226	0.1013	99.51%
240	9.58	0.0037	222	0.0995	99.52%

Table 2 Experiment 2

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1933	0.7529	1591	0.7137	0.00%
2	1167	0.4545	931	0.4176	39.63%
4	977	0.3805	782	0.3507	49.46%
8	752	0.2929	618	0.2772	61.10%
16	397	0.1546	397	0.1780	79.46%
30	85	0.0331	275	0.1233	95.61%
60	17	0.0066	255	0.1143	99.12%
90	9	0.0035	269	0.1206	99.54%
120	8	0.0031	271	0.1215	99.59%
150	6.87	0.0027	277	0.1242	99.65%
180	7.8	0.0030	271	0.1215	99.60%
210	6.69	0.0026	280	0.1255	99.66%
240	6.65	0.0026	280	0.1255	99.66%

Table 3 Experiment 3

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1893	0.7373	1547	0.6939	0,00%
2	1539	0.5994	1256	0.5633	18.70%
4	1206	0.4697	965	0.4328	36.29%
8	873	0.3400	710	0.3184	53.88%
16	369	0.1437	390	0.1748	80.51%
30	116	0.0452	292	0.1309	93.87%
60	18	0.0070	272	0.1219	99.05%
90	8.9	0.0035	270	0.1210	99.53%

120	6.1	0.0024	265	0.1187	99.68%
150	6.7	0.0026	277	0.1241	99.65%
180	6.3	0.0025	277	0.1241	99.67%
210	6.1	0.0024	253	0.1134	99.68%
240	6.1	0.0024	268	0.1201	99.68%

Second Experience

Table 4. Experiment 4

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1920	0.7478	1540	0.6908	0.00%
2	1421	0.5536	1287	0.5775	25.97%
4	1349	0.5255	1228	0.5508	29.73%
8	1178	0.4589	1067	0.4786	38.64%
16	1069	0.4165	973	0.4364	44.31%
30	894	0.3485	824	0.3696	53.40%
60	714	0.2783	700	0.3139	62.78%
90	522	0.2036	566	0.2538	72.78%
120	425	0.1659	489	0.2193	77.82%
150	285	0.1112	430	0.1928	85.14%
180	277	0.1080	421	0.1888	85.55%
210	165	0.0643	365	0.1637	91.41%
240	35	0.0136	304	0.1363	98.18%

Third experience

Table 5. Experiment 5

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1787	0.6960	1469	0.6589	0.00%
2	1709	0.6656	1483	0.6652	4.36%
4	1548	0.6029	1293	0.5800	13.37%
8	1514	0.5897	1248	0.5598	15.28%
16	1270	0.4946	1037	0.4651	28.93%
30	1064	0.4144	843	0.3781	40.46%
60	869	0.3385	669	0.3000	51.37%
90	733	0.2855	561	0.2516	58.98%
120	671	0.2613	512	0.2296	62.45%
150	582	0.2267	446	0.2000	67.43%
180	582	0.2267	455	0.2040	67.43%
210	538	0.2095	421	0.1888	69.90%
240	500	0.1947	398	0.1785	72.02%

Table 6. Experiment 6

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1845	0.7186	1530	0.6863	0.00%
2	1733	0.6750	1450	0.6504	6.07%
4	1616	0.6294	1344	0.6028	12.41%
8	1476	0.5749	1226	0.5499	20.00%
16	1224	0.4767	1002	0.4494	33.66%
30	908,7	0.3539	723	0.3243	50.75%
60	645	0.2512	501	0.2247	65.04%

90	578	0.2251	450	0.2018	68.67%
120	535	0.2084	421	0.1888	71.00%
150	486	0.1893	390	0.1749	73.66%
180	415	0.1616	338	0.1515	77.51%
210	390	0.1519	326	0.1462	78.86%
240	383	0.1492	328	0.1471	79.24%

Table 7. Experiment 7

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1881	0.7326	1539	0.69033	0.00%
2	1709	0.6656	1413	0.63380	9.14%
4	1650	0.6427	1421	0.63739	12.28%
8	1519	0.5916	1247	0.55933	19.25%
16	1311	0.5106	1069	0.47948	30.30%
30	1044	0.4066	823	0.36912	44.50%
60	926	0.3607	705	0.31619	50.77%
90	804	0.3131	613	0.27492	57.26%
120	763	0.2972	571	0.25607	59.44%
150	699	0.2723	519	0.23275	62.84%
180	690	0.2687	512	0.22961	63.32%
210	662	0.2578	491	0.22019	64.81%
240	587	0.2286	434	0.19461	68.80%

Fourth experience

Table 8. Experiment 8

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1905	0.7420	1559	0.6993	0.00%
2	1653	0.6438	1352	0.6064	13.23%
4	1446	0.5632	1177	0.5279	24.10%
8	1179	0.4592	952	0.4270	38.11%
16	968	0.3770	788	0.3534	49.19%
30	674	0.2625	563	0.2525	64.62%
60	358.96	0.1398	349	0.1565	81.16%
90	211.79	0.0825	265	0.1188	88.88%
120	138.6	0.0540	227	0.1018	92.73%
150	90.7	0.0353	196	0.0878	95.24%
180	76.35	0.0297	205	0.0919	95.99%
210	66.7	0.0260	203	0.0910	96.50%
240	52.27	0.0204	182	0.0816	97.26%

Table 9. Experiment 9

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1888	0.7354	1521	0.6823	0.00%
2	1335	0.5200	1088	0.4880	29.29%
4	1246	0.4853	1011	0.4535	34.01%
8	1137	0.4428	931	0.4176	39.78%
16	838.87	0.3267	698	0.3130	55.57%
30	742	0.2890	613	0.2749	60.70%
60	474	0.1846	430	0.1928	74.90%
90	351.88	0.1371	355	0.1592	81.36%

120	295	0.1149	324	0.1453	84.38%
150	257	0.1001	302	0.1354	86.39%
180	236	0.0919	291	0.1305	87.50%
210	227	0.0884	292	0.1309	87.98%
240	209	0.0814	281	0.1260	88.93%

Table 10. Experiment 10

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1875	0.7303	1544	0.6926	0.00%
2	1752	0.6824	1437	0.6446	6.56%
4	1620	0.6310	1325	0.5943	13.60%
8	1287	0.5013	1034	0.4638	31.36%
16					
30	1052	0.4097	847	0.3799	43.89%
60	862	0.3357	698	0.3130	54.03%
90	674	0.2625	555	0.2489	64.06%
120	609	0.2372	506	0.2269	67.52%
150	559	0.2177	471	0.2112	70.19%
180	519	0.2021	445	0.1995	72.32%
210	494	0.1924	424	0.1901	73.66%
240	479	0.1866	417	0.1870	74.46%

Fifth experience

Table 11. Experiment 11

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1856	0.7229	1519	0.6814	0.00%
2	1605	0.6251	1284	0.5759	13.52%
4	1387	0.5402	1187	0.5324	25.27%
8	1155	0.4499	928	0.4162	37.77%
16	779	0.3034	630	0.2825	58.03%
30	553	0.2154	468	0.2099	70.21%
60	273	0.1063	292	0.1309	85.29%
90	169	0.0658	238	0.1067	90.90%
120	109	0.0425	208	0.0932	94.13%
150	78	0.0304	194	0.0869	95.80%
180	63.64	0.0248	192	0.0861	96.57%
210	46	0.0179	168	0.0753	97.52%
240	41	0.0160	180	0.0807	97.79%

Table 12. Experiment 12

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1886	0.7346	1538	0.6899	0.00%
2	1728	0.6730	1408	0.6316	8.38%
4	1527.77	0.5950	1249	0.5602	18.99%
8	1310	0.5102	1061	0.4759	30.54%
16	973.7	0.3792	786	0.3525	48.37%
30	761	0.2964	619	0.2776	59.65%
60	452	0.1760	405	0.1816	76.04%
90	284	0.1106	298	0.1336	84.94%

120	191	0.0744	240	0.1076	89.88%
150	153	0.0596	226	0.1013	91.89%
180	128.97	0.0502	218	0.0977	93.16%
210	110.7	0.0431	213	0.0955	94.13%
240	93	0.0362	198	0.0887	95.07%

Sixth experience

Table 13. Experiment 13

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1746	0.6800	1422	0.6378	0.00%
2	1545	0.6018	1286	0.5768	11.51%
4	1232	0.4798	1048	0.4701	29.44%
8	1054	0.4105	937	0.4203	39.63%
16	447	0.1741	488	0.2188	74.40%
30	152	0.0592	302	0.1354	91.30%
60	31	0.0121	233	0.1044	98.23%
90	13.69	0.0053	235	0.1053	99.22%
120	0	0.0000	242	0.1085	100.00%
150	0	0.0000	256	0.1148	100.00%

Table 14. Experiment 14

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1850	0.7206	1516	0.6800	0.00%
2	1459	0.5683	1220	0.5472	21.14%
4	1118	0.4354	959	0.4301	39.57%
8	726	0.2828	665	0.2982	60.76%
16	424	0.1651	472	0.2117	77.08%

30	176	0.0685	303	0.1358	90.49%
60	54	0.0210	254	0.1139	97.08%
90	26	0.0101	232	0.1040	98.60%
120	18	0.0070	240	0.1076	99.03%
150	0	0.0000	246	0.1103	100.00%

Table 15. Experiment 15

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1760	0.6855	1446	0.6486	0.00%
2	1294	0.5040	1090	0.4889	26.48%
4	1116	0.4347	1006	0.4512	36.59%
8	755	0.2941	696	0.3122	57.10%
16	410	0.1597	465	0.2085	76.71%
30	183	0.0713	311	0.1394	89.60%
60	52	0.0203	243	0.1089	97.05%
90	27	0.0105	246	0.1103	98.47%
120	15	0.0058	216	0.0968	99.15%
150	0	0.0000	230	0.1031	100.00%

Table 16. Experiment 16

Time sample (min)	Area of DHP	Concentration of DHP (mol/L)	Area of 1-butanol	Concentration of 1-butanol (mol/L)	Conversion of DHP (%)
0	1917	0.7466	1520	0.6818	0.00%
2	1422	0.5539	1129	0.5064	25.82%
4	1020	0.3973	821	0.3682	46.79%

8	941	0.3665	777	0.3485	50.91%
16	623	0.2427	552	0.2476	67.50%
30	384	0.1496	396	0.1776	79.97%
60	140	0.0545	245	0.1098	92.70%
90	85	0.0331	224	0.1004	95.57%
120	58	0.0226	209	0.0937	96.98%
150	47	0.0183	212	0.0950	97.55%

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