INSTITUTE OF NATURAL AND APPLIED SCIENCES
UNIVERSITY OF CUKUROVA

MASTER THESIS

Gürbüz ÇOMAK

THE SYNTHESIS OF PHTHALATE DERIVATIVES IN HIGH-PRESSURE, HIGH-TEMPERATURE WATER

DEPARTMENT OF CHEMISTRY

ADANA-2008

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Bu tez 01/07/2008 Tarihinde Aşağıdaki Jüri Üyeleri Tarafından Oybirliği/oyçokluğu İle Kabul Edilmiştir.

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Kod No :

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Enstitü Müdürü
İmza ve Mühür

Bu Çalışma Ç.Ü. Bilimsel araştırma Projeleri Birimi Tarafından Desteklenmiştir.
Proje No: FEF2007YL42

ABSTRACT

MSc THESIS

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Supervisor: Prof. Dr. E. Sultan GİRAY
Year: 2008, **Pages:** 48
Jury: Prof. Dr. E. Sultan GİRAY
Prof. Dr. Hunay EVLİYA
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A variety of phthalate derivatives were synthesized effectively in high-temperature, high-pressure water used as either a solvent or a catalyst. This clean method is based on the condensation of *o*-phthalic acid with an alcohol which is also called esterification. Although it is commonly believed that esters hydrolyze to the corresponding acid and alcohol in the presence of water, in some cases water content as 10% in H_2O/ROH mixtures has led to an increase in the formation of dialkyl phthalate esters.

After a series of model reactions were conducted, it was found that the conditions preferred, a mixture, 1/9 v/v H_2O/ROH and temperature 350 ^oC were appropriate for obtaining maximum yields. Also moderate to better yields were obtained depending on the nature of the alcohol.

Keywords: Phthalate, esterification, supercritical fluids, sub- and supercritical water and green chemistry

ÖZ

YÜKSEK LİSANS TEZİ

SUB- VE SÜPERKRİTİK KOŞULLARDA FTALAT TÜREVLERİNİN SENTEZİ

Gürbüz ÇOMAK

ÇUKUROVA ÜNİVERSİTESİ
FEN BİLİMLERİ ENSTİTÜSÜ
KİMYA ANABİLİM DALI

Danışman: Prof. Dr. E. Sultan GİRAY

Yıl: 2008, **Sayfa:** 48

Jüri: Prof. Dr. Sultan GİRAY
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Bu çalışmada, suyun hem çözücü hem ham katalizör olarak davranabildiği yüksek basınç ve yüksek sıcaklıkta, çeşitli ftalat türevleri sentezlenmiştir. Bu temiz metod esterleşme olarakta adlandırılan *o*-ftalik asitin alkol ile kondensasyonuna dayanmaktadır. Esterlerin sulu ortamda, esteri oluşturan asit ve alkole hidrolize olduğu yaygın olarak düşünülmesine rağmen, yapılan bu çalışmada H_2O/ROH karışımındaki %10 su miktarının dialkil Ftalat oluşumunda ciddi bir artışa neden olduğu belirlenmiştir.

Model çalışmalar sonunda , çalışma koşulları, H_2O/ROH oranın 1:9 (v/v) ve 350 ^oC sıcaklığın maksimum ürün elde etmek için en uygun şartlar olduğu bulunmuştur. Aynı zamanda ürün veriminin ve çeşitliğinin alkolün doğasına bağlı olarak değiştiği gözlemlenmiştir.

Anahtar Kelimeler: Ftalat, esterleşme, süperkritik akışkanlar, subkritik ve subkritik su, yeşil kimya

ACKNOWLEGMENT

I would like to thank Prof. E. Sultan Giray for giving the support and advice related to research work.

My thanks are to Murat Türk, Assistant and PhD student, due to the his assistance and advice during the establishment of the reactor used in the experiments and also colleagues, master students, Tayfun Hüyükpınar, Serkan Koldaş, Serkan Alpman, İlkgül Şimşek and Sibel Tahmazoğlu for their kind help.

I am also grateful to Serkan Karaca, Songül Aşkan and Kemal Can in the Chemistry of Department at The University of Cukurova for help on technical assistance.

I would like to forward my thanks to Prof. Halime Paksoy from the Chemistry Department at the University of Cukurova, and to the International Office of the University of Nottingham.

Finally, I would really like to thank my family, especially my father for making me ambitious in science.

ABBREVIATIONS

Below is a list of abbreviations and acronyms used in this master thesis:

^{o}C: Celsius Degrees

'': Inch

Å: Angstrom (1 x 10^{-10}m)

BPR: Back Pressure Regulator

HTHP: High Temperature and High Pressure

PFCs: Perfluorocarbons

d: Doublet (NMR spectroscopy)

δ: Chemical shift (NMR) in parts per million

DMF: Dimethylfuran

ε: Dielectric Constant

E: "E-factor"

ES: Electrospray

FID: Flame-ionisation Detector

GC: Gas Chromatography

HPLC: High-pressure (or Performance) Liquid Chromatography

HTW: High-Temperature Water

Hz: Hertz

IR: Infrared

k: kilo- (1 x 10^{3})

K_w: Dissociation Constant (ionic product) of water

LCA: Life Cycle Assessment

μ: Micro- (1 x 10^{-6})

M: Mega- (1 x 10^{6}); Molar

m: Multiplet (NMR spectroscopy); metre; mili- (1 x 10^{-3})

min(s): Minute(s)

MS: Mass Spectrometry

m/z: Mass/Charge ratio

n: Number of moles; nano- (1×10^{-9})

NCW: Near-Critical Water

NMR: Nuclear Magnetic Resonance

o: *Ortho-*

p: Pressure

Pa: Pascals

Ph: Phenyl group

psi: Pounds per Square Inch

R: Gas Constant (= 8.314 J K^{-1} mol^{-1})

R-: Alkyl

R_F: Response Factor

r_t: Retention Time

$scCO_2$: Supercritical Carbon Dioxide

SCW: Supercritical Water

SCWO: Supercritical Water Oxidation

T: Temperature

PA: Phthalic Acid

PAn: Phthalic Anhydride

DMP: Dimethyl phthalate

DEP: Diethyl phthalate

DPP: Dipropyl phthalate

DBP: Dibutyl phthalate

Di-*iso*BP: Di-*iso*butyl phthalate

DEHP: Di(2-ethylhexyl) phthalate or Dioctyl phthalate

TBAB: Tetrabutylammonium Bromide

THF: Tetrahydrofuran

UV: Ultraviolet

V: Volume

VOCs: Volatile Organic Compounds

w: Weak (IR spectroscopy)

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1. INTRODUCTION

1.1. Behind the movement of Green Chemistry

That Chemistry has been and continues to be extremely beneficial to society is indisputable (Anastas et al., 1998).

The quality of life of the modern generation has become better with chemicals, which are utilized in daily care, foods and pharmacy. Pharmacologic drugs such as antibiotics are used to cure diseases, which has resulted in raising the average life expectancy from 47 in 1900, to 75 years in the 1990s (Breslow, 1997).
Chemistry is, with increasing importance, has a bad reputation in the minds of people by tackling problems at the same time as causing others. In 1961 there was a panic in Europe about a chemical used as a drug, thalidomide, which was used by pregnant women to reduce the effects of nausea and vomiting during the pregnancy. As a result of using this drug, the children had birth faults such as missing and grossly deformed limbs. There were about 10 000 children born who had these problems in the entire world (Anastas et al., 1998).

In 1962, Rachael Carson wrote the book called *Silent Spring*, which reported the effects of the pesticides on the eggs of various birds (Carson, 1962).
Such reported problems created by chemicals have made many countries prepare new laws to prevent the use of harmful chemicals and producing by-products, which are toxic and non degradable, from industries. For instance in the United States there is a record of the hazardous waste released into the air and environment by industry (*Toxics Release Inventory*, EPA-745-R-96-002, p.34, 1994).

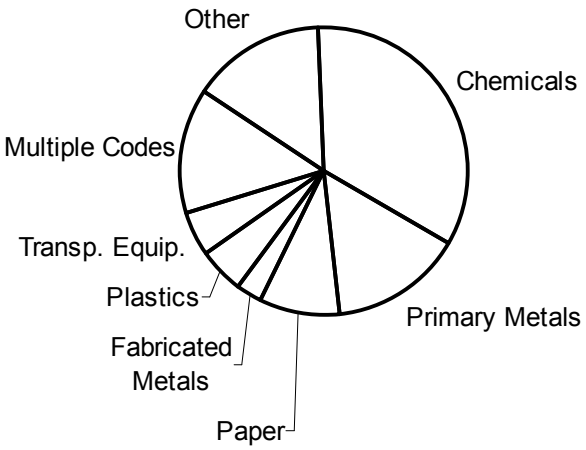


Figure 1.1. Proportion of hazardous waste released to the environment by the major industrial sectors (*Toxics Release Inventory*, EPA-745-R-96-002, 1994).

As shown in Figure 1.1, the hazardous waste released by chemical sector, recorded by the "*Toxics Release Inventory (TRI)"* in the United States, is considerably greater than other sectors. Not only have all of these problems caused many of the restrictions during manufacture, use and disposal of chemicals, but also this has made the communities and chemists aware of the need to develop alternative ways to synthesise and produce chemicals, which are really important for the needs of mankind.

1.2. The Challenge of Green Chemistry

Following the background of the pollution process affecting the world and its effect on human health, in the early 1990s a new phrase was coined by Environment Protection Agency (EPA), called "***Green Chemistry***", which aims that "*To promote innovative chemical technologies that reduce or eliminate the use generation of hazardous substances in the design, manufacture and use of chemical products"* (Anastas et al., 1998). In the past two decades there have been several definitions of Green Chemistry, one of them, expressed by P. T. Anastas and J. C. Warner in the book "*Green Chemistry-Theory and Practice"* (Anastas et al., 1998), defines that

"*Green Chemistry is the utilisation of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and applications of chemical products"* (Anastas et al., 1998). Green Chemistry has been promoted all over the world by a number of devoted individuals and organisations have increased such as the Green Chemistry Network (GCN) having one thousand members, established in the UK in 1998.

In all of these organisations, "reducing" items such as waste, risk and hazard, cost, materials, energy, non-renewable resources, can be seen as a part of Green Chemistry. Here is the question: How can we make a reaction more "Green"?. If a reaction or synthesis is thought of as Green there are some principles that should be considered as below (Afonso et al., 2005);

i. *Safe*
ii. *One step*
iii. *No waste*
iv. *Renewable materials*
v. *Environmental acceptable*
vi. *Simple separation*
vii. *Atom efficient*
viii. *100% yield*

Moreover, environmentally benign synthetic methods, reaction conditions, and safer chemicals have been developed since the Twelve Principles of Green Chemistry were formulated in 1998 by P. T. Anastas and J. C. Warner in the book "*Green Chemistry-Theory and Practice"* (Anastas et al., 1998).

Twelve Principles of Green Chemistry;

1. **Prevent waste:** Design chemical syntheses to prevent waste, leaving no waste to treat or clean up.
2. **Design safer chemicals and products:** Design chemical products to be fully effective, yet have little or no toxicity.

3. **Design less hazardous chemical synthesis:** Design synthesis to use and generate substances with little or no toxicity to humans and the environment.
4. **Use renewable feedstocks:** Use raw materials and feedstocks that are renewable rather than depleting. Renewable feedstocks are often made from agricultural products or are the wastes of other processes; depleting feedstocks are made from fossil fuels (petroleum, natural gas, or coal) or are mined.
5. **Use catalyst, not stoichiometric reagents:** Minimize the waste by using the catalytic reactions. Catalysts are used in small amounts and can carry out in a single reaction many times. They are preferable to stoichiometric reagents, which are used in excess and work only once.
6. **Avoid chemical derivatives:** Avoid using blocking or protecting groups or any temporary modifications if possible. Derivatives use additional reagents and generate waste.
7. **Maximize the atom economy:** Design syntheses so that the final product contains the maximum proportion of the starting materials. There should be few, if any, wasted atoms.
8. **Use safer solvents and reaction conditions:** Avoid using solvents, separation agents or other auxiliary chemicals. If these chemicals are necessary, use innocuous chemicals.
9. **Increase the energy efficiency:** Run the chemical reactions at ambient temperature and pressure whenever possible.
10. **Design chemicals and products to degrade after use:** Design chemical products to break down to innocuous substances after use so that they do not accumulate in the environment.
11. **Analyze in real time to prevent pollution:** Include in-process real-time monitoring and control during synthesis to minimize or eliminate the formation of byproducts.

12. **Minimize the potential for accidents:** Design chemicals and their forms (solids, liquid, or gas) to minimize the potential for chemical accidents including explosions, fires, and releases to the environment.

Green Chemistry is also an elemental approach to environmental problems caused by pollution. It is mainly important to seek the application of Green Chemistry throughout the Life Cycle Assessment (LCA) of a product processes. The synthesis can be separated into several categories from feedstock to target as below (Afonso et al., 2005);

Pre-Manufacturing

i. Waste minimisation
ii. Alternative feedstocks
iii. Safe and responsible extraction

Manufacturing

i. Greater use of catalysts
ii. More atom efficient routes
iii. Non-VOC solvents
iv. Safe and intensive processing

Product Delivery

i. Close to market manufacturing
ii. Minimal packaging

Product use

i. Safer Products
ii. Benign Chemicals in formulation

End-of-life

i. Quickly biodegradable on disposal
ii. Recyclable or reusable

In the all of these steps a consideration of each part gives us opportunities such as to prevent waste disposal and to reduce the energy required for

manufacturing, which has been leading to consumption of more petroleum products and emissions.

Atom economy and E-factor are other important definitions, which can also be considered in the scope of LCA, in Green synthesis, expressed as below;

% Atom Economy = (FW of atoms in the product /FW of the reactants used in the reaction) *100
E-Factor = kg waste / kg product(s).

Figure 1.2. Equations for Atom Economy and E-factor

Atom economy, developed by B.M. Trost (Ahluwalia et al., 2006), is a consideration of how much of reactants change into the product. E-factor, developed by R. Sheldon (Sheldon, 1994), reflects the ratio of waste disposal occurred to the product. There are still some chemical industries producing more total waste although have a better E-factor. E-factors in the pharmaceutical industry can be greater than 100; for instance, when the antidepressant setraline was launched, 250,000 litres of solvent were needed for each 1,000 kilograms of product. Application of the principles of green chemistry reduced the solvent consumption ten-folds (Poliakoff and Licence, 2007).

As an example in terms of atom economy, two possible ways to synthesize maleic anhydride (MA), shown in Figure 1.3. can be taken into account (Domenech et al., 2002).

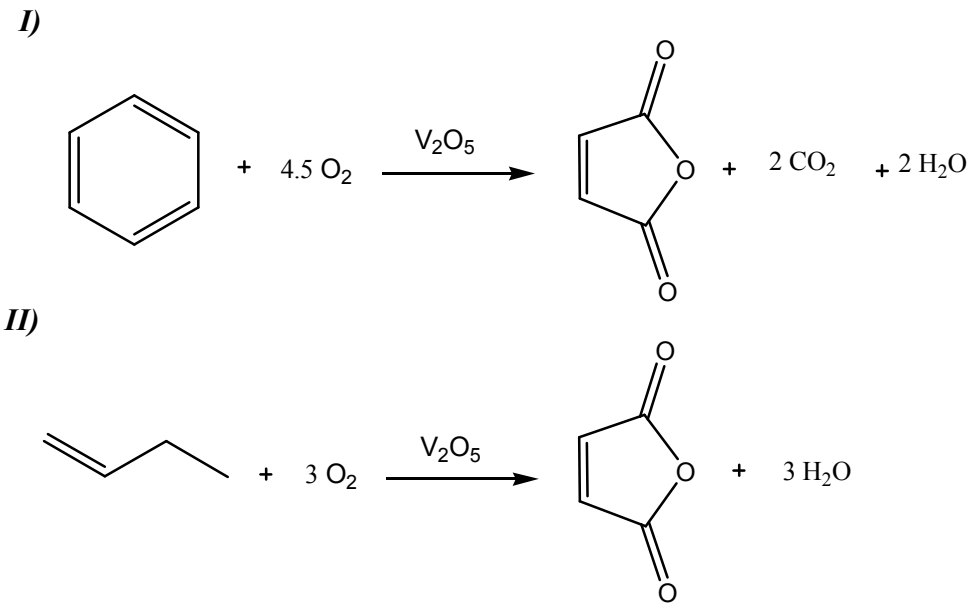


Figure 1.3. In comparison of different ways to synthesize maleic anhydride in terms of atom economy

I) The first way to produce MA is the oxidation of benzene with oxygen gas over a V_2O_5 catalyst, at a temperature of 350 to 450 ^oC and at 3 to 5 bar of pressure (Othmer, 1978). ***II)*** The use of butane as feedstock is to obtain MA (Lanchester, 2000).

In terms of atom economy, the reaction **II** is more environmentally friendly because all C atoms of butene end up as MA but for the reaction **I** only 67% of C atoms of benzene are used to form MA. In comparison of these two reactions in terms of consumption of oxygen, the reaction **II** is still greener, but if the hydrogen utilization is considered, the reaction **I** shows an atom efficiency greater than reaction **II.**

There is another example for atom economy, shown in Figure 1.4., to synthesize ibuprufen which is the main active ingredient in many over-the-counter painkillers. It was first prepared and patented in 1961. The original route included six consecutive steps and had overall atom economy 40% of atom economy, while the green route comprises of three steps with an overall atom economy of 77%.

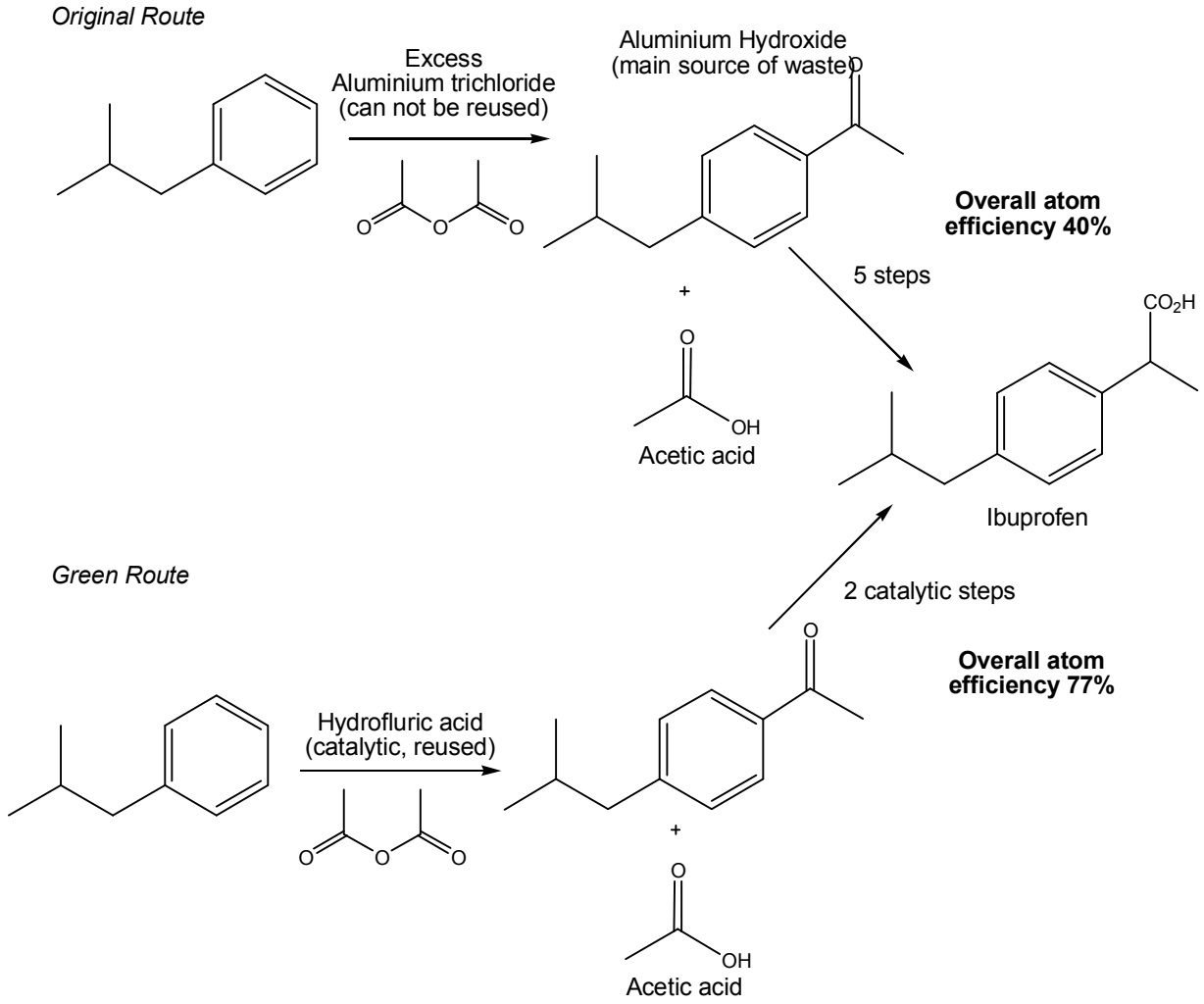


Figure 1.4. A comparison of Green Route with Original Route (Poliakoff and Licence, 2007).

1.2.1. Alternative Routes

To reach the conditions for green processes we should consider possible technologies, some conventional and some innovative. Major clean technologies are expressed as "The Clean Technology Pool", as shown in Table 1.1. (Afonso et al., 2005).

Table 1.1. The Clean Technology Pool

The Clean Technology Pool	Supercritical Solvents	Catalysis	Solventless System	Renewable Feedstocks
	Alternative Routes	Non-volatile Solvents	Intensive Processing	Life Cycle Assessment
	Microreactors	Telescoped Reactions	Alternative Energy Savers	

There are several major categories such as Renewable Feedstocks, Catalysis and Supercritical Solvents, which have been widely investigated to discover new routes and to replace the conventional methods, reducing waste disposal.

Renewable Feedstocks. Most of the chemicals used in industry and research are produced from petroleum sources, leading to emissions of petroleum based products into the air and rivers. The decision of which feedstock used has a major effect on the environmental impact and synthetic pathway. Recently agriculture and biodegradable feedstocks are thought to be very promising as alternative to conventional sources (Anastas, 1998).

For instance, a kind of renewable feedstock, glycerol, 1,2,3-propane triol has a well-known renewable chemical for centuries. As shown in Figure 1.5., there is a broad overview on the chemistry of glycerol starting from the classic esters and oligomers to new products like glycerol carbonate, telomers, branched alkyl ethers, propanediols and epoxides.

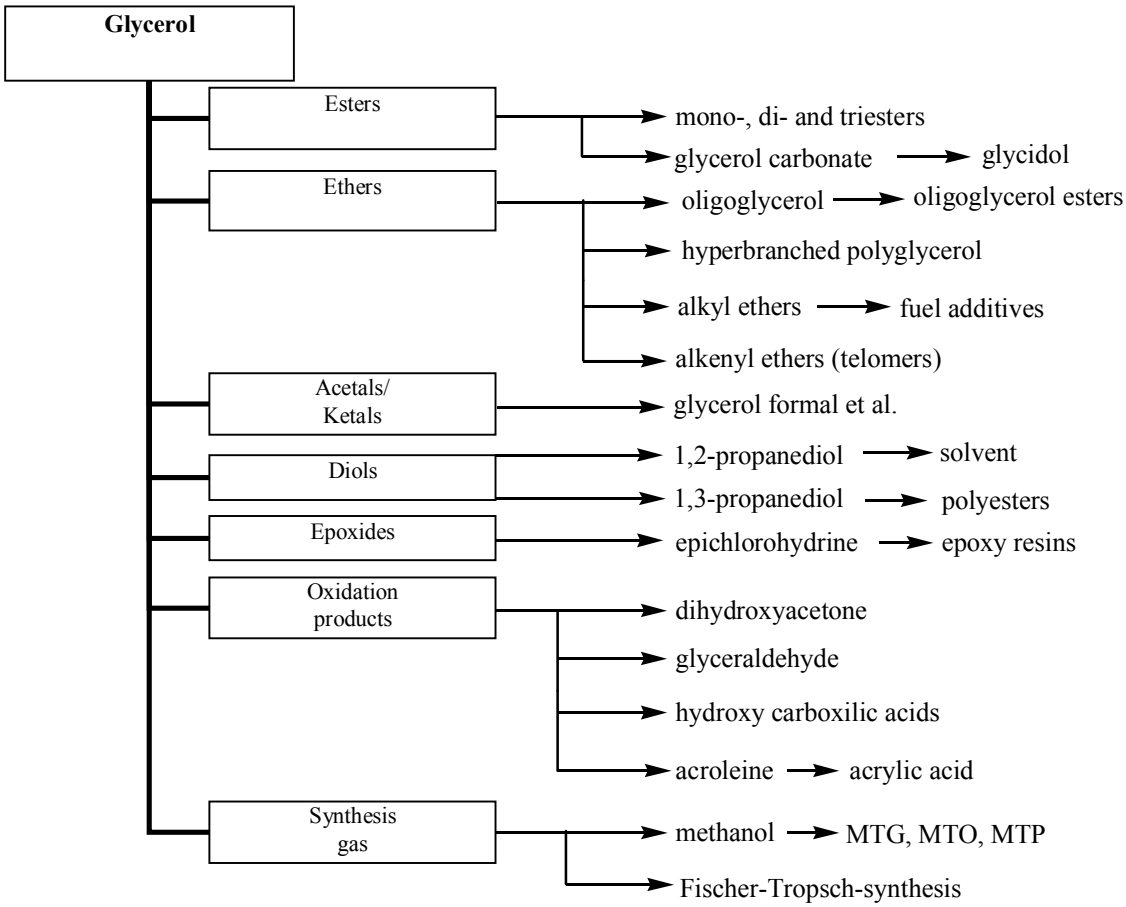


Figure 1.5. Compilation of main glycerol derivatisation routes (Behr et al., 2008).

Catalysts. Catalysts used in conventional methods often have some problems in terms of Green Chemistry such as poisoning, decomposition and separation which require organic solvents after the reaction. Homogeneous catalysts generally need to be separated by using an organic solvent after the reaction completes. Due to the problems like separation, there are innovations in heterogeneous catalysts have been used and are widely researched such as titanium silicate catalyst (TS1) for selective oxidation reactions, e.g. 4-hydroxylation of phenol to commercially important hydroquinone (Maspero and Romano, 1994). As shown in Figure 1.7., a route from cyclohexene to adipic acid can be carried out in an environmentally benign way while it can be synthesised by using a biocatalyst shown in Figure 1.3.

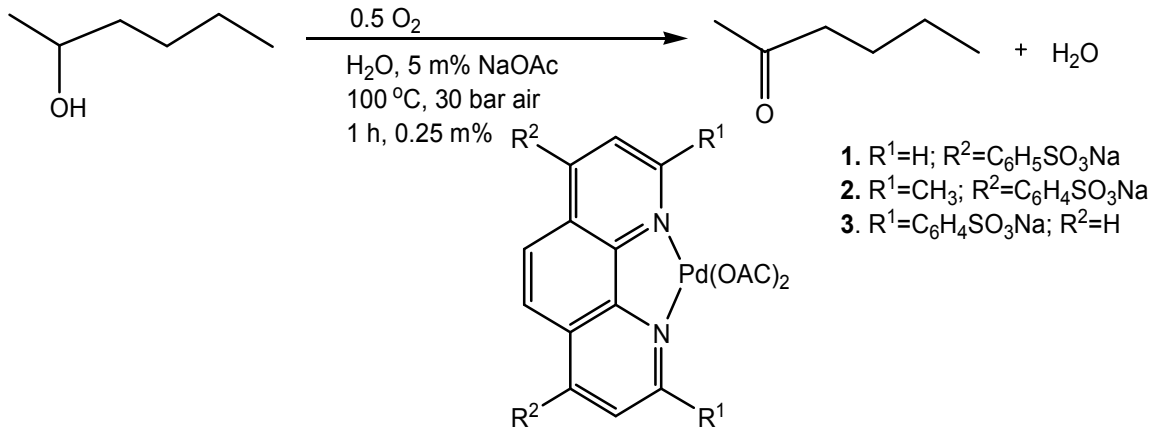


Figure 1.6. Aqueous biphasic Pd catalyzed aerobic oxidation of alcohols.

Biocatalysts, such as enzymes may provide high selectivity under mild conditions and usually in environmentally benign aqueous media, but there are some restrictions in the use of the enzymes. One of them is that most biocatalysts are not active at high temperatures and high pressures, which may be necessary to improve the yield of the target molecule.

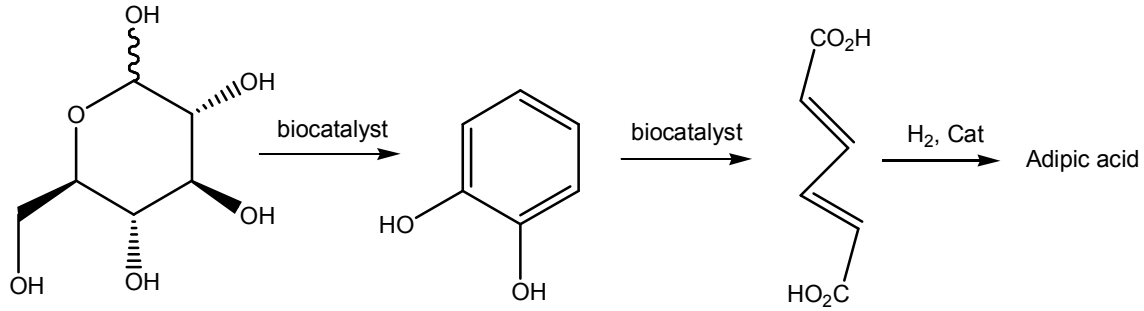


Figure 1.7. Green synthesis of adipic acid using a biocatalyst

As shown Figure 1.7., adipic acid is synthesised from glucose by using a genetically modified *Escherichia coli* biocatalyst (Draths and Frost, 1994).

1.2.2. Green and Alternative Solvents

Initially, it should be known that "the best solvent is no solvent". Solvents used by chemists are generally utilised as a reaction media, in separation or in purification methods. The quality and appropriateness of reactions and chemical processes are extremely dependent on the solvent used. Solvents used in reactions and in other fields have had an increasing impact on the consciousness of scientists due to having effects on the environment and human health. The chosen solvent should carefully be considered for the effect it has on the environment and human health. There are huge consumptions, an estimated 15 billion kilograms of organic halogenated solvents, worth more than $5 billion, are utilised world wide each year (DeSimone, 2002). According to the fifth principle of Green Chemistry, expressed by P. T. Anastas and J. C. Warner, *"The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and, innocuous when used*" (Anastas, 1998). We should initially consider how to maximise the yield and minimise the utilisation of solvents to reduce waste disposal after use. Solvent usage should also include some of the considerations as given below (Anastas and Williamson, 1998);

i. Must have reduced absorption
ii. The toxicity should be understood
iii. Knowledge of its environmental fate should be understood

All of these effects have made chemists seek alternative solvents that can be a replacement for conventional petrochemical solvents. There are several solvents which have been investigated and used in the reactions to move to more environmentally benign and innocuous conditions for nature and human health.

The most used and researched solvents in attendance as well as the solvent-free conditions (Tanaka, 2004) can be listed as below;

i. Ionic liquids
ii. Fluorous solvents
iii. Ethanol, aqueous surfactant micelles and polymers (Scamehorn and Harwell, 1989)

iv. Supercritical fluids (widely carbon dioxide, water)

Ionic liquids. It has been discovered that special pairings of cations and anions can lead to salts that are liquid at room temperature, for example [(1-ethyl-3-methylimidazolium) (chloride)], which has a melting point below room temperature when it contains between one and two equivalents of $AlCl_3$. These salts, called ionic liquids, are non-flammable, have no vapour pressure, and are very promising media. The disadvantages of ionic liquids as solvent are their difficulty in purification, high viscosity, commercial expense, lack of knowledge about toxicity and their reaction with strong nucleophiles (Mikami, 2005).

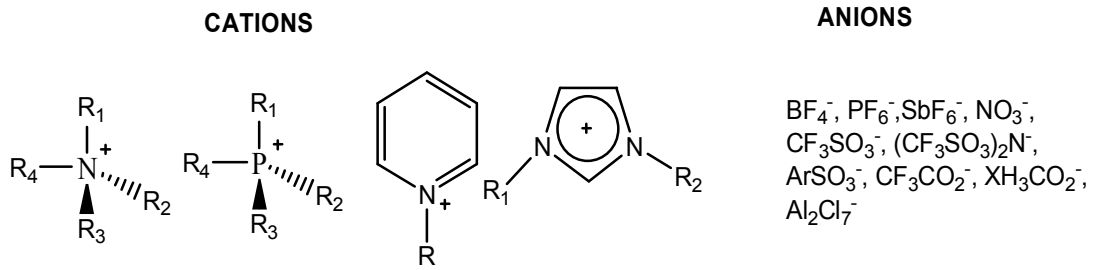
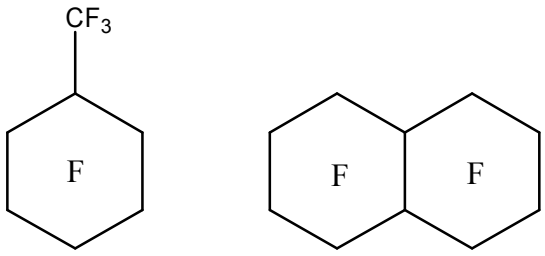


Figure 1.8. Examples of ionic liquids

Fluorous Solvents. Perfluorocarbons (PFCs) were brought out in the 1960s. They have impressive properties such as easy separation from their hydrocarbon analogues and are chosen for purification of catalysts and products, liquid-liquid biphasic separations and gas/liquid reactions. However, there are some disadvantages; that PFCs are expensive, and have low solubility in many organic solvents and problematic disposal (Mikami, 2005).



$CF_3(CF_2)nCF_3$
n=4,5,6

$(CF_3CF_2CF_2CF_2)_3N$

Figure 1.9. Examples of fluorous solvents

Aqueous Systems (Water). It is obviously known that water is the most environmentally benign and inexpensive solvent, as well as the safest solvent. Water is an especially valuable solvent for high temperature and high pressure reactions, where the ionic product of water is high, making it a stronger acid and base, and where the polarity is lower, making it a better solvent for organic reactions.

1.3. Supercritical Fluids

What is a supercritical fluid?

The modified definition of a supercritical fluid from IUPAC is expressed as "a compound, mixture or element above its critical temperature (T_c) and critical pressure (P_c) but below the pressure required condensing it into a solid phase" (Jessop and Leitner, 1999). The properties of supercritical fluids (SCFs) are usually described as intermediate properties between liquid and gas.

Table 1.2. A comparison of typical SCFs, Liquid, and Gas properties (Teja and Eckert, 2000).

	Liquid	SCFs	Gas
Density (g/cm^3)	1	0.1-0.5	10^{-3}
Viscosity ($Pa \cdot s$)	10^{-3}	10^{-4}-10^{-5}	10^{-5}
Diffusivity (cm^2/s)	10^{-5}	10^{-2}	10^{-1}

As shown in Table 1.2., properties of SCW such as density, viscosity and diffusivity are between gas and liquid where temperature and pressure is above the critical point of a compound, element or mixture. But some properties of SCFs such as compressibility and heat capacity are significantly higher near the critical point than they are in liquids and gases. Diffusion coefficients and viscosity refer to mass transfer properties that affect the rate of mass transportation leading to rapid dissolution for a liquid in supercritical region (Jessop and Leitner, 1999).

Critical properties of SCFs can also be shown from the phase diagram for a pure substance as below, Figure 1.10.;

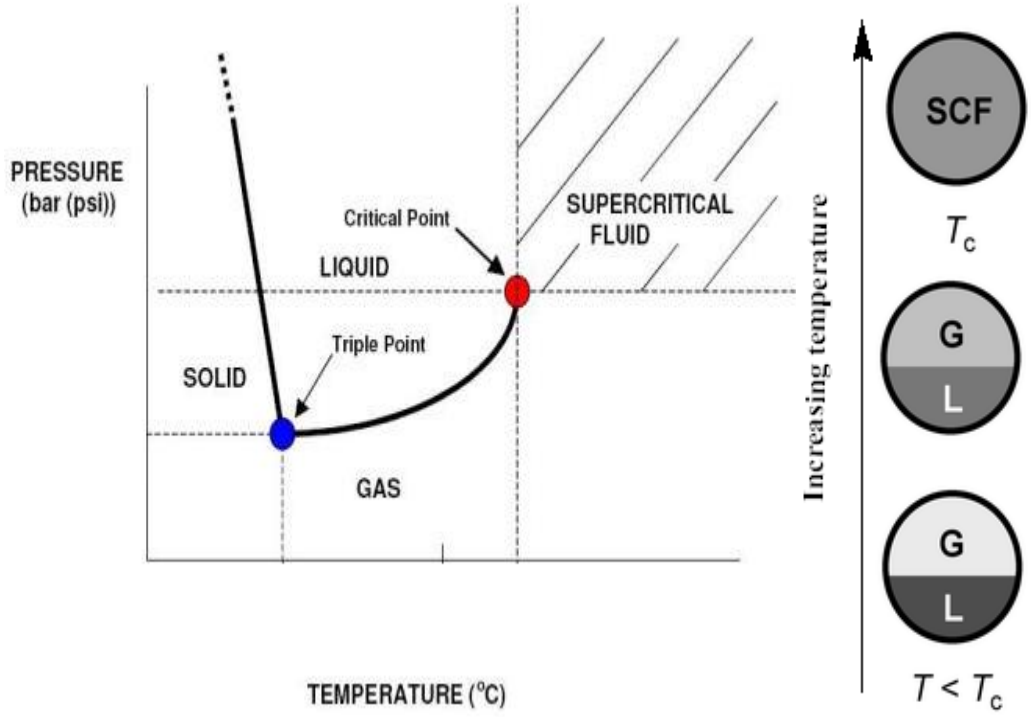


Figure 1.10. General phase diagram for supercritical fluids, and also their appearance as it approaches the critical point.

As the temperature and pressure of the liquid increase, the separation line which can be seen easily between two phases, begins to disappear and the meniscus begins to fade (as shown on the right side of Figure 1.10.). Near the critical point, the meniscus begins to disappear and, when the liquid reaches and exceeds the critical point, it behaves as one phase.

All these properties near and above the critical point make SCFs an impressive solvent and extraction reagent for a great deal of different applications. There are various organic and inorganic supercritical fluids such as CO_2, H_2O, HCl, HBr, SF_6, N_2O (inorganic) and C_2H_4, C_2H_6, CHF_3 (organic) (Jessop and Leitner, 1999). Their properties, when above the critical points, make them the preferable solvents for organic reactions.

1.3.1. Supercritical Water

Small changes in pressure of supercritical fluids can produce substantial changes in density which affects the diffusivity, viscosity, dielectric constant, and solvation properties of these fluids. Water is an impressive example of these fluids. As it approaches supercritical conditions, 374 ^{o}C and 221 bar, supercritical water becomes a pseudo organic solvent for organic reactions. HTW, which has elevated the levels of both hydronium and hydroxide ions, is an interesting medium for this reaction. All of these properties are temperature dependent and can be manipulated to optimize the reaction environment. In addition, low solubility of most organic compounds in water at room temperature facilitates the post-reaction separation of reaction products from the aqueous phase. In this research work, initially, water was chosen as supercritical solvent because at critical temperatures and pressures, water can behave as an acid or base catalyst without the need for any neutralization agent after the reaction. This impressive feature of water is due to the dissociation constant, K_w, which is expressed as below and also shown in Figure 1.11.;

$$K_w = [H^+][OH^-]$$

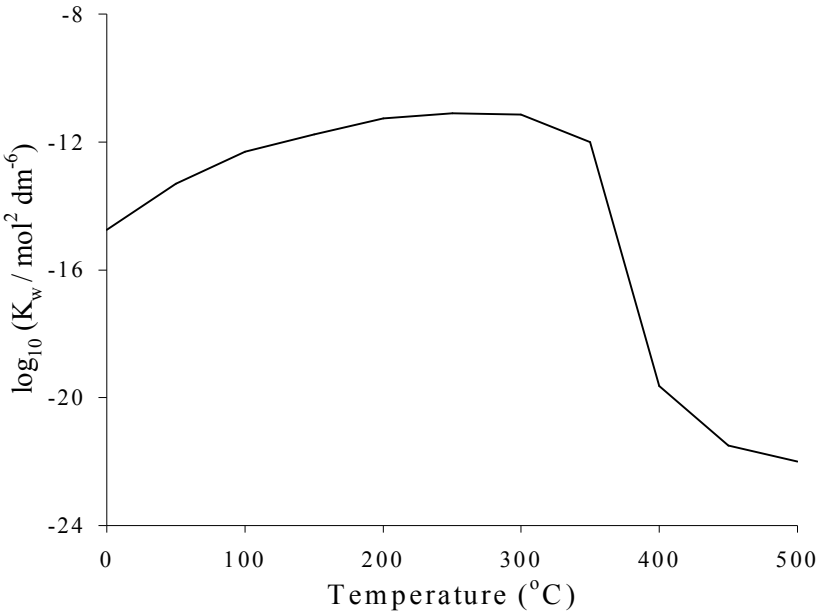


Figure 1.11. The change of dissociation constant of water with temperature

This is much higher in the near critical conditions than it is at room temperature. Figure 1.12. shows that properties of water such as diffusivity, dielectric constant, solvation power for organics and salt solubility and are how they are influenced by changing temperature are demonstrated.

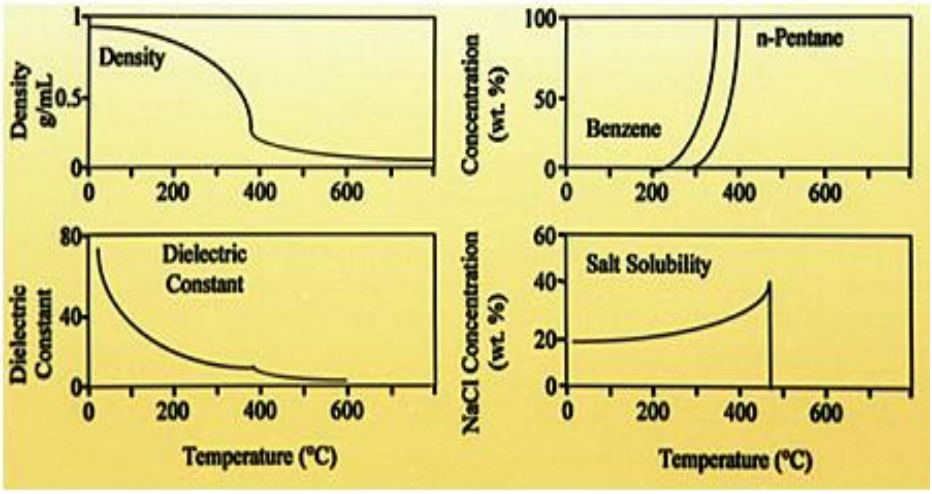


Figure 1.12. Properties of water as it approaches the critical point.

As shown in Figure 1.12., all parameters are affected as water approaches the critical points. For instance, solubility of n-pentene and benzene in water, dramatically increase around critical temperature.

As a result of these properties, supercritical water can be considered a good medium for organic reactions.

1.3.2. Reaction in High-Pressure and High-Temperature Water

Reactions carried out in SCW could be summarized as follows:

i. Hydrogenation/Dehydrogenation
ii. C-C Bond Formation
iii. Rearrangements
iv. Hydration/Dehydration
v. Elimination
vi. Hydrolysis
vii. Partial Oxidation

2. LITERATURE REVIEW

2.1. Conventional ways to synthesise phthalates

Phthalates, or phthalate esters shown in Figure 2.1., are widely used for different applications such as softeners of plastics, solvents in perfumes and additives to hair sprays, lubricants and insect repellents (Rastogi, 2006). Phthalates with small R- groups are used as solvents in perfumes and pesticides. When those used in plastic production, polyvinyl chloride turn from a hard plastic into a flexible one. Worldwide production of phthalate derivatives increased from 1.8 million tons in 1975 to 3 million tons in 2001, and approximately a quarter of this production is only for one phthalate, di-(2-ethylhexyl)- phthalate (DEHP) (Herve´-Bazin et al., 2001).

Derivatives of phthalates are generally synthesized *via* the esterification reaction of phthalic anhydride/acid with an alcohol in the absence (Yang et al., 2006) or presence (Skrzypek et al., 1995) of acid catalysts which may need to be carried out in organic solvent (Gryglewicz, 2003). The general reaction is shown Figure 2.1..

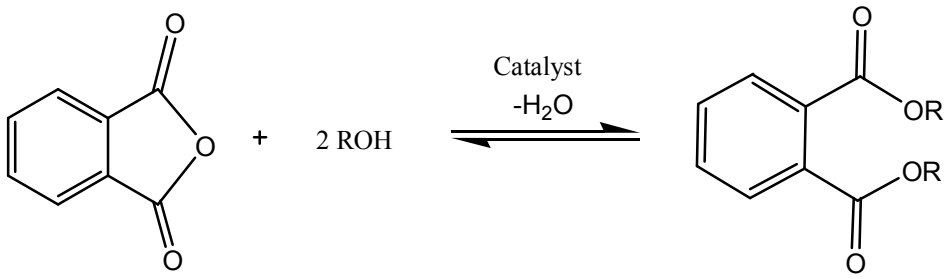


Figure 2.1. Synthesis of phthalates *vi*a esterification of anhydride with alcohol.

There are wide ranges of catalysts available and common catalysts used can be listed as below;

i. H_2SO_4 (Arabi et al., 2003)
ii. p-Toluenesulphonic acid (Arabi et al., 2003) (Sejidov et al., 2005)
iii. Zeolites (Arabi et al., 2003) (Ma et al., 1996)
iv. Lipase Enzym (Gryglewicz, 2003)
v. Tetrabutyl titanate (Skrzypek et al., 1998)

Synthesis of o-phthalates has been also reported *via* intermolecular [2 + 2 + 2] cycloaddition of terminal alkynes and dimethyl acetylenedicarboxylate by using Ruthenium catalyst, CpRuCl (cod) as seen below in Figure 2.2. (Ura et al., 2004).

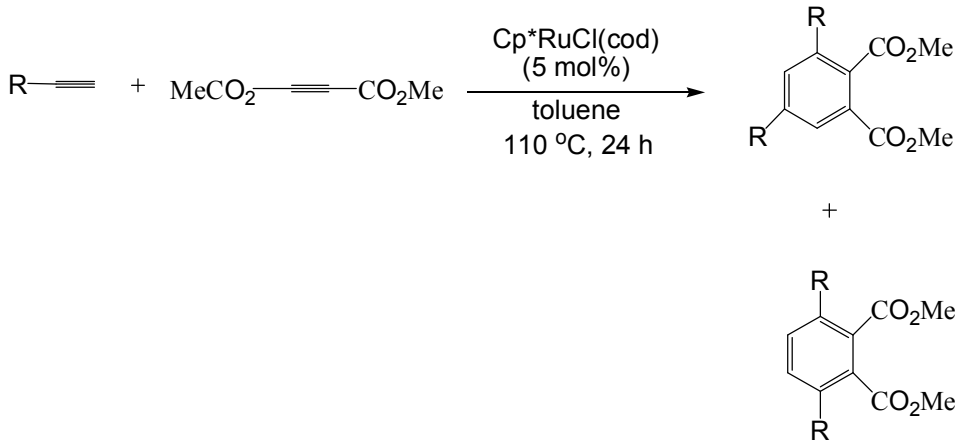


Figure 2.2. Synthesis of phthalates *via* cycloaddition of acetylenedicarboxylate with an alkyne.

Using catalyst generally gives high yields, however most of these methods mentioned above are not environmentally friendly and satisfactory due to corrosion, loss of catalysts, need of a neutralisation agent after the reaction is completed, long reaction time, difficulties of preparation of some catalysts and separation of the product from catalyst. And also in most of these methods phthalic anhydride is used as the starting material which is more reactive and preferable than the corresponding acid, phthalic acid.

2.2. Organic Reactions in Supercritical Water

There are a great deal of advantages for using supercritical water in chemical reactions; to manipulate the reaction environment by manipulating the pressure, to enhance the solubility of reactants and products, to eliminate interphase transport limitations on reaction rates, and to integrate the reaction and separation unit operations make the supercritical fluids impressive for reactions included in fuel processing, biomass conversion, biocatalysts, homogeneous and heterogeneous

catalysts, environmental control, polymerisation, materials synthesis and chemical synthesis.

Hydrogenation/Dehydrogenation. Crittendon and Parsons showed that in the presence of PtO_2 in the supercritical water, metallic platinum had an effect on alcohol oxidation. In their work cyclohexanol was dehydrogenated by forming metallic platinum from Pt_2O in high-temperature and high-pressure water (Crittendon and Parsons, 1994).

Adschiri *et al.* used a SCW reaction medium and a conventional $NiMo/Al_2O_3$ hydro-treating catalyst to hydrogenate and remove sulphur from dibenzo-thiophene. In that work, higher conversations were obtained in CO-SCW and HCOOH-SCW media than those of in H_2-SCW medium.

C-C Bond Formation. Fridel-Crafts alkylation reactions have been conducted in high temperature water for both phenol and p-cresol which are alkylated with ter-butyl alcohol and 2-propanol at 275 ^{o}C in absence of catalyst. In these reactions water behaves as catalyst and solvent during the range of the reaction times from 1h to 100h for different reactant systems (Savage 1999).

As can be seen in Figure 2.3., a reaction classified as Heck arylation shows the catalytic cycle for coupling iodobenzene with an alkene (Oka et al., 2002). The reactions in high temperature water were similar to those observed in traditional organic solvents, but they were more sensitive to steric effects and the nature of the alkene.

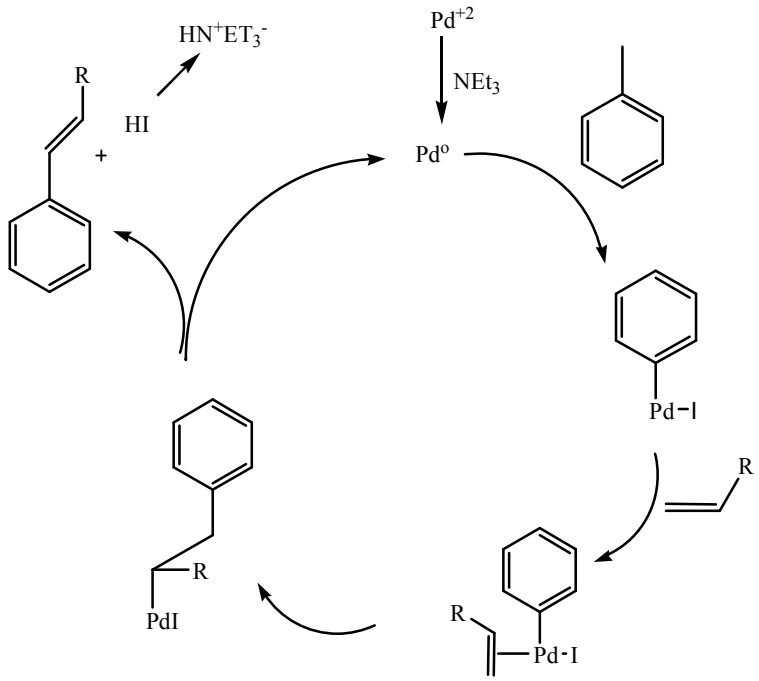


Figure 2.3. Catalytic cycle for Heck reaction

Rearrangements. Rearrangement of pinacol and two different bicyclic diols to the corresponding ketones in pure water at 275 C^o has been performed by Kuhlmann *et al*. (Kuhlmann *et al*. 1994). Crittendon and Parsons reported that cyclohexene rearranged reversibly to methylcyclopentene in SCW in the presence of a mineral acid or acidic metal salts (Crittendon and Parsons, 1994).

Hydration/Dehydration. Antal and co-workers have reported conversion of *tert*-butyl alcohol to *iso*butylene in near critical water, shown in Figure 2.4. (Xu and Antal, 1994). The reaction has been performed both in the absence and presence of a catalyst. In the case of presence of a catalyst the reaction rate was increased.

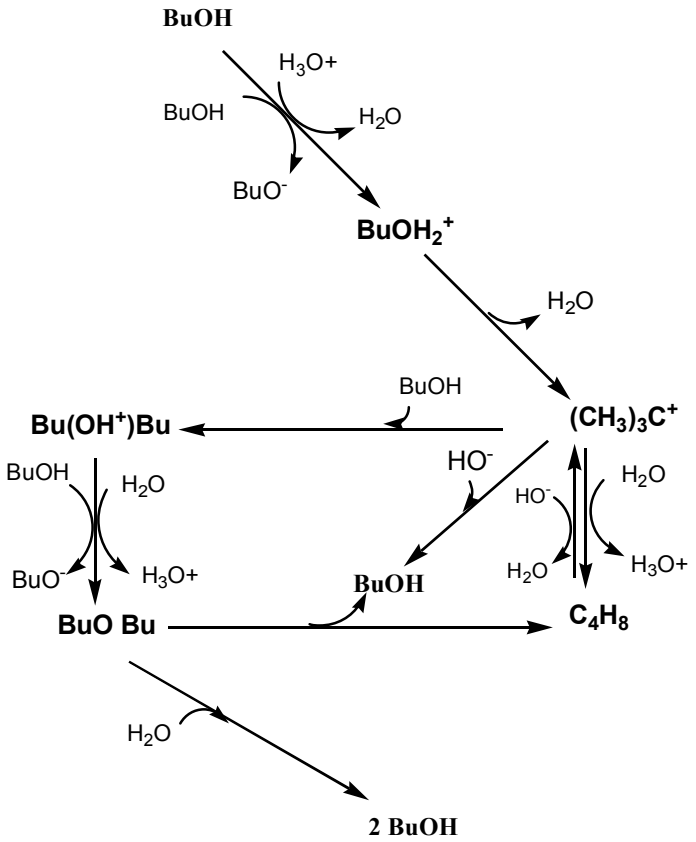


Figure 2.4. Acid-catalysed reaction of *ter*-butyl alcohol in high-temperature water.

Elimination. Carlsson *et al.* showed that citric acid can be converted to methacrylic acid in high temperature water throughout sequential dehydration and decarboxylation reactions (Carlsson et al., 1994). Carboxylic acids undergo facile decorboxylation in pure, high temperature water, as evidence by reports regarding the formic acid, citric and itaconic acids, and cinnamic and indole-2-carboxlyic acid.

Hydrolysis. Some compounds such as esters (Oka et al., 2002) and nitriles (Kramer et al., 1999) can hydrolyse in supercritical water due to the behaviour of water as a catalyst. Most of the esters hydrolyse to form carboxylic acid and alcohol and nitriles also hydrolyse to the corresponding amide and then the corresponding carboxylic acid by further hydrolysis.

Partial Oxidation.

As can be seen in Figure 2.5., a group, in Nottingham of University, demonstrated that some methylaromatic compounds such as *p*-xylene can be oxidised in

supercritical water using manganese (II) bromide as catalyst to give the corresponding carboxylic acids in continuous flow reactor (Verdugo et al., 2004).

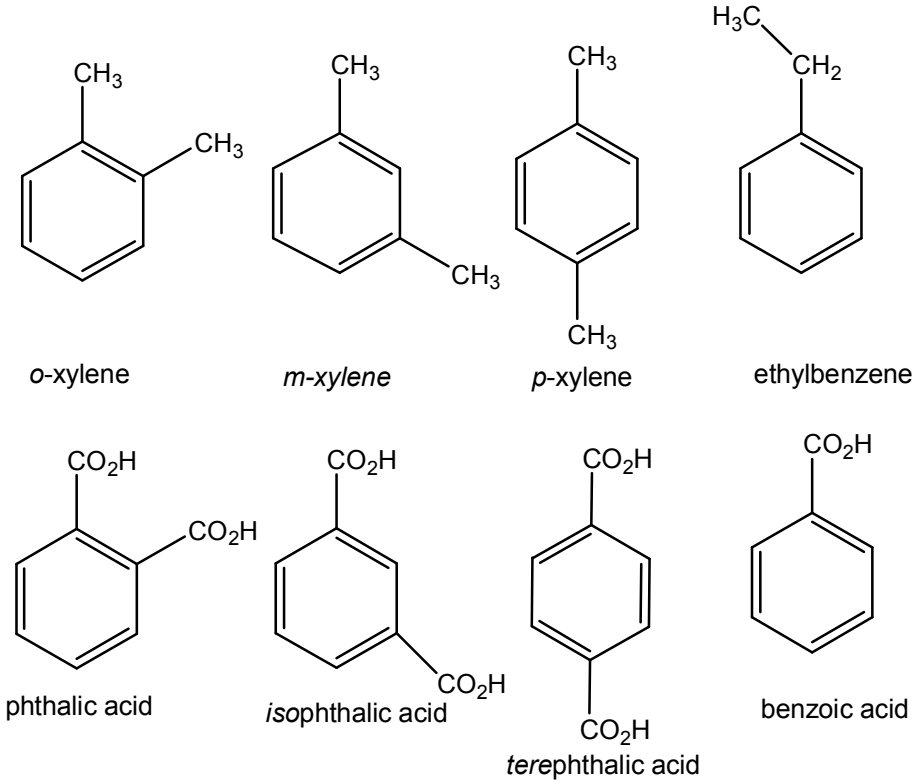


Figure 2.5. The C8 aromatics and their carboxylic oxidation products.

Partial oxidation of methane to methanol has been performed in supercritical water at around 400 ^{o}C by homogeneous free radical reactions and heterogeneous catalytic reactions (Crittendon and Parsons, 1994).

A wide variety of reactions have been performed in near and supercritical water and has been of increasing importance in the last decade.

3. MATERIAL AND METHOD

Following instruments and materials were used in the purification and characterization of products in this study.

Caution; *These reactions involve high pressures and must only be carried out in an apparatus with the appropriate pressure rating at the reaction temperature. A thorough safety assessment must be made.*

3.1. Material

All experiments were performed in a thick-walled, stainless steel (316SS) batch vessel reactor of 20 mL volume (Figure 3.1.). The pressure inside the vessel was generated autogenically by the amount of water charged to the vessel and by its temperature. In theory, it is possible to obtain a desired pressure by calculating the product of the vessel volume and the density (of water at the desired temperature) to give the amount of water needed. However, in practice the addition of organic compounds may result in a discrepancy between the calculated and actual pressures.

The reactor was fitted with an internal chrome/alumine thermocouple. The thermocouple was connected to a temperature display, allowing real time *in-situ* monitoring of the temperature during the course of an experiment (See Figure 20). It was sealed using SSI fittings.

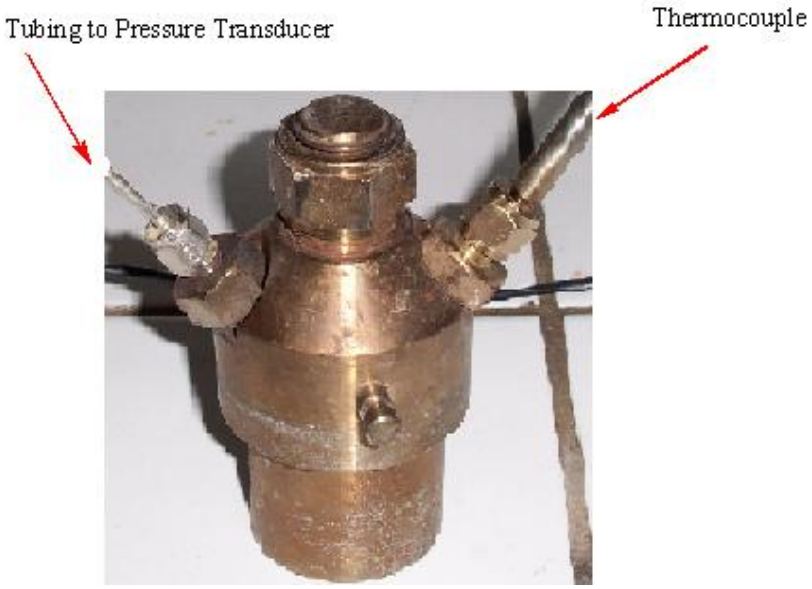


Figure 3.1. A picture from the 21 mL stainless steel batch vessel

During an experiment, the vessel was connected by 1/8 Hoke *Gyrolok* tubing, held in place by SSI fittings, to a pressure transducer, a gauche (maximum pressure rating 6000 Psi, 400 bar). The pressure transducer, gauche allows *in-situ* monitoring of the pressure during the course of an experiment.

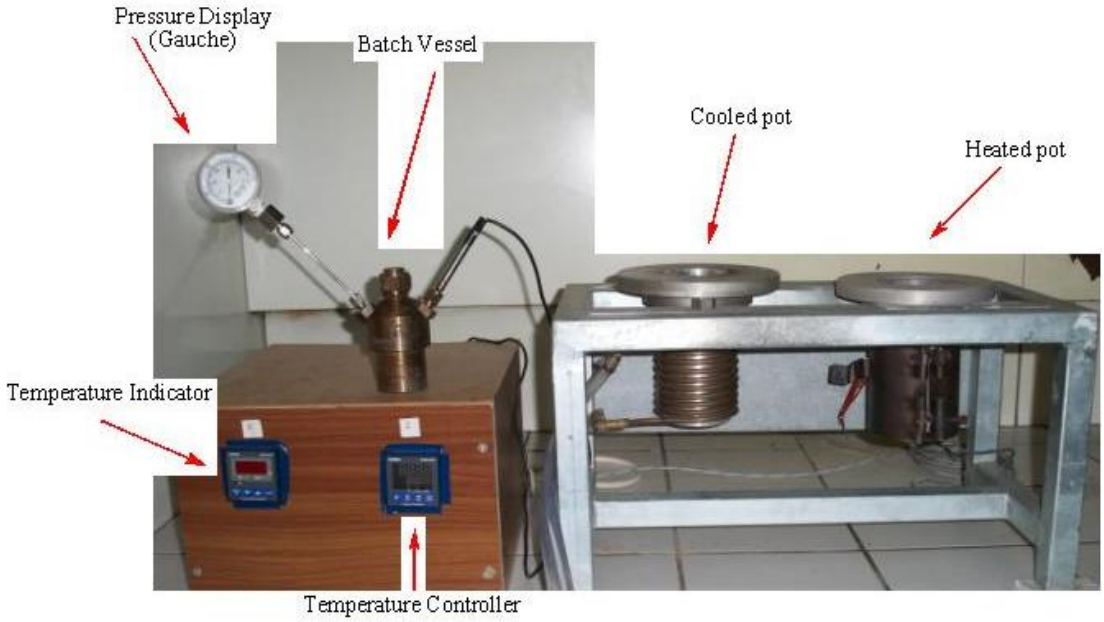


Figure 3.2. Photograph of the apparatus used for reactions in HTW. The equipment was set up as shown in this project. All reactions were carried out behind a safety screen.

This was observed by a cessation in the increase of pressure at the pressure transducer while the temperature continued to increase. During the course of an experiment, the temperatures and pressures given by the thermocouple and the pressure transducer, respectively were recorded every 2 minutes.

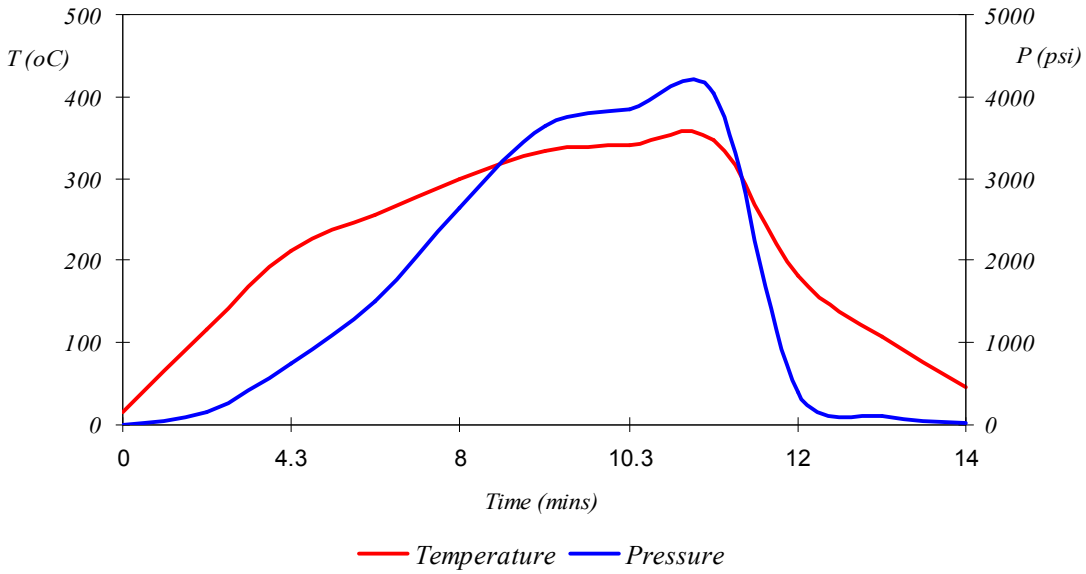


Figure 3.3. T/p profile of a typical "11 min" experiment using 10 mL of H_2O/EtOH mixture.

These allowed monitoring of variations with the rate of temperature and pressure are given at Figure 3.3. These gave about knowledge about problems, such as blockages or leaks during the experiments.

3.2. Method

Analysis, qualification and quantification of yields were carried out using GC-FID and GC-MS.

Yields were analyzed by a Perkin-Elmer Autosystem GC using an Zebron ZB-35 capillary column (30 m and 0.25 mm i.d. phenomenex stationary phase) with a flame ionisation detector (FID.

GC-FID Method: He (12 psi) was the mobile phase and the injection volume was 1 µL. The initial temperature was 40 ^{o}C and isothermal conditions were

maintained for the first 5 min and the temperature was then adjusted at a rate of 10 ^{o}C/min from 40 to 240 ^{o}C. Isothermal conditions were maintained for the final 5 min.

A Finnigan-Trace GC-MS equipped with an auto sampler was used to determine the products. Chromatographic separations were accomplished with a THERMO TR-5MS capillary column (5% phenyl-95% dimethylpolysiloxane, 0.25 mm i.d × 60 m, film thickness 0.25 µm) with injections in the split mode with 50 split ratio. The separation of the compound was carried out in the GC.

GC-MS Method: After keeping for 5 minutes at 100 ^{o}C, first isothermal temperature ramp was set at 20 ^{o}C/min from 100 ^{o}C to 230 ^{o}C and maintained at 230 ^{o}C for 1 minute. The second isothermal temperature ramp was set at 2 ^{o}C/min from 220 ^{o}C to 280 ^{o}C and maintained at 280 ^{o}C for 1 minute. Ion source was at 200 ^{o}C in positive ion mode and injection volume was 1 µL with 50/50 split flow.

The GC was connected to the MS *via* a heated transfer line. The MS ionization source consists of an electron impact (EI). The charged particles generated, were separated and anlaysed, depending on their mass-to charge ratio (m/z), using an ion trap. The detection of the fragments generated was carried out using a mass selective analyzer.

3.3. Experimental Procedure

To optimize the ratio of H_2O/ EtOH mixture, the amount of water in the mixture was changed from 0 % to 100 %. The optimum ratio of H_2O/ EtOH was found as 1:9, H_2O/EtOH. After the reaction has completed, the content was extracted with 20 mL solvent and analyses were performed according to the methods followed for general experimental procedure.

The thick-walled reactor (21 mL volume) contained 664 mg of *o*-phthalic acid (4 mmol), 1 mL of deionised, degassed H_2O and 9 mL of alcohol used. To maximize the formation of phthalate esters, the ratio of mixture of EtOH/ H_2O were determined by changing the amount of water in the mixture. The heater was pre-heated to 500 ^{o}C and the reactor was then put in the heated port and heated for a

specific length of time, around 350 ^{o}C, rather than to a particular temperature. Once the reactor had been heated for the required time, it was placed in the cooling pot and allowed to return to ambient temperature and pressure. A typical temperature and pressure profile is given in Figure 13. The content of batch reactor was then taken out and extracted with 20 mL of solvent, either diethyl ether or hexane. The extract was analyzed by GC-FID and GC-MS.

4. RESULTS AND DISCUSSIONS

In this research work, it has been decided to synthesise phthalate derivatives in high temperature and high pressure water, since the water posseses impressive properties such as acid/base catalyst behaviour in high-temperature and high-pressure water, it is possible to replace these conditions with traditional esterification reactions.

The first step was to observe the products formed from the reaction. Hence, the content of batch reactor was extracted and analysed by GC-FID with standarts purchased from Sigma-Aldrich and GC-MS. The formation of 5 products were observed and the peaks were identified by GC-MS (Figure 4.1.)

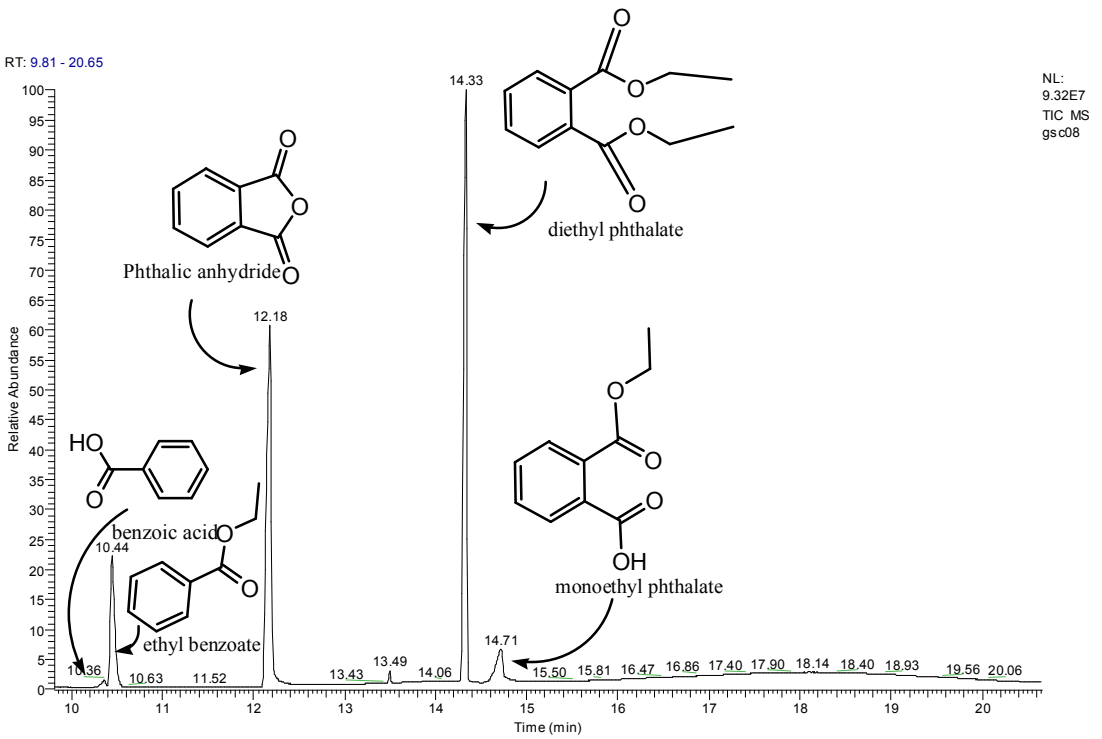


Figure 4.1. Chromatogram from GC-MS analysis of esterification of *o*-phthalic acid with ethanol (Time=12 min, T_{max}=350 ^{o}C, p_{max}/psi= 3400)

In Figure 4.1., the first peak, at 10.36 min was suggested as EB with most abundant *m/z* fragments which are 105, 77, 122.

Second peak, at 10.44 min was suggested as BA with most abundant *m/z* fragments which are 105, 77, 122.

Third peak, at 12.18 min was suggested as PAn with most abundant *m/z* fragments which are 105, 149, 77, 69.

Fourth peak, at 14.33 min was suggested as DEP with most abundant *m/z* fragments which are 149, 176, 105.

Fifth peak, at 14.71 min was suggested as MEP with most abundant *m/z* fragments which are 149, 105, 76, 65, 176.

Interestingly, the most of phthalic acid, almost 100%, was converted to phthalic anhydride and the corresponding ester. These two products are a strong proof of lack of the hydrolyses which is back of the reaction.

Initially, in the work-up process two different solvents were invastigated in terms of solubility of product and by-products. Although its literature recoveries of products with hexane was quite high (Shen, 2005). In this study, diethyl ether was found a remarkable solvent and was chosen due to not only high extraction ability for phthalate derivatives, but also extraction ability for by-products such as decarboxylated products, benzoic acid and the corresponding ester (Table 4.1.).

As seen from the runs, **2** and **3** in Table 4.1., the results suggested that increase in pressure rate did not show considerable effect regarding the yield.

10 mL of the mixture of H2O/EtOH was chosen. Since we did not see any significant difference between the pressures of 10 ml and 5 ml water used.

Table 4.1. Effects of different solvents and pressure on the extractability of products and by-products.

Run	Total volume of the mixture Water:Ethanol (mL)	Area %					Time (min)	Max. Temperature. (^{0}C)	Max. Pressure (psi)
		DEP	MEP	PAn	EB	BA			
1*	10	72.3	-	9.28	17.3	0.6	19	350	3500
2**	10	21.9	4.79	63.3	5.3	4.8	18.3	351	3450
3**	5	22.6	2.06	66.9	5.1	3.3	21	350	2650

* Extraction solvent is hexane.
** Extraction solvent is Diethyl ether.

In the good aggrement with the results of the work of D. Kusdiana and S. Saka carried out (Kusdiana and Saka, 2004), the presence of water did not have significant effect on the yield, as complete conversions were always achieved regardless of the content of water. In some cases, though the common principle is that esters hydrolyze to the corresponding acid and alcohol in the presence of water, 10% water did raise the formation of diethyl phthalate.

After increasing the ratio of water in the mixture, in the runs **4** to **11**, the formation of diethly phthalate decreased while monoethyl increased from run **4** to **6**. After the run **6**, the formation of MEP then changed again in descending order.

In terms of decarboxylated products, benzoic acid and ethyl benzoate which are not desired, gave the minumum yield in the run **5,** with the ratio of 10:90 H_2O:EtOH mixture.

As can be seen in the Table 4.1., the phthalic acid is mostly converted to the corresponding anhydride. According to the OECD SIDS initial assessment report, 2005, PA might be converted to the anhydride in the applied conditions of GC-FID and GC-MS. This may explain the reason why any unreacted product, phthalic acid could not be observed by GC-FID and GC-MS and might be because all of the unreacted acids changed into the corresponding anhydride.

Finally, to optimise the conditions such as ratio and temperature, to determine the effect of temperature on the yield formation, a several runs were examined and the results are given in Table 4.2. The highest ratio conducted, 374 ^oC which is also critical temperature for water led to decarboxylation of phthalic acid and yield formed to benzoic acid and ethyl benzoate.

In the rest of the study, 350 ^oC of temperature and 10 mL H_2O:EtOH volume mixture (10:90) were selected as optimum conditions.

Table 4.2. Optimization of the ratio for mixture of the Water/Ethanol

Run	The ratio of Water/Ethanol v/v %	Area %					Time (min)	Temperature (^{0}C)	Pressure (psi)
		DEP	MEP	PAn	EB	BA			
4	0/100	68	-	17	15	-	12	350	3000
5	10/90	41.7	15.5	39.1	3.68	-	11.3	349	2850
6	20/80	27.7	15.9	52.8	2.7	0.8	10.3	350	3400
7	40/60	21.2	10.3	61.4	3.8	2.3	12	350	3700
8	50/50	21.8	4.79	63.3	5.27	4.76	18.3	351	3450
9	60/40	15.1	7.9	72.5	1.5	3.0	12.3	350	3400
10	80/20	3.3	1.6	88.1	1.3	5.8	11.3	350	2900
11	90/10	1.6	-	86.2	1.2	10.5	12.3	355	2800

As can be seen in Tables 4.3., a variety of alcohols which are of commercial importance in different sectors were preferred to synthesize.

When run **5** and run **12** have been compared, it was found that experiment with methanol gave similar product diversity.

In some cases, phthalic anhydride formation in the runs **13** and **14** were quite higher than runs **5** and **12**.

Mono- R phthalate formations were observed much higher in the runs **5** and **15** if compared with other runs.

In some cases, only in the run **15**, diisobutyl phthalate formation was observed quite low but anhydride yield of the same run was high.

In terms of being the most used phthalate derivatives, 28% yield for di-2-ethylhexyl phthalate in the run **16** should be taken into account due to the catalyst-free conditions used.

In the runs **5** and **12**, decarboxylated products, benzoic acid and methyl-ethyl- phthalates occurred as 15-20 % although there were no decarboxylated products formed from other alcohols.

As shown in Figure 4.2., the predicted possible mechanism for esterification goes over an intermediate which is considered to prevent hydrolysis of the ester to the corresponding acid and alcohol. And another possibility to explain phthalate formation may be that phthalic acid can behave as self-catalyst, as well as supercritical water can behave as acid-base catalyst.

Although the ester is believed to hydrolyze during the reaction in the presence of water, phthalate ester did not, because an intermediate product, phthalic anhydride is slightly stable and does not hydrolyze with small water content which might be covered by excess of water during the reaction.

Table 4.3. Yields from a range of alcohols reacted with phthalic acid

Run	Alcohol Alkyl-	Area %						Time (min)	Temperature (^{0}C)	Pressure (psi)
		Di-alkyl Phthalate	Mono-alkyl Phthalate	Phthalic Anhydride	Alkyl-Benzoate	Benzoic Acid	Unaccounted Products			
12	—OH methanol	44	1	39	16	-	-	11	347	4050
13	HO propyl alcohol	28	-	70	2	-	-	10	351	3200
14	HO butanol	27.5	1	62	5	1.5	3	11.3	351	2600
15	HO *iso*butanol	2	19	78	1	-	-	12	351	3200
16	HO 2-ethyl hexanol	28	5	65.5	1.5	-	-	12	355	2000

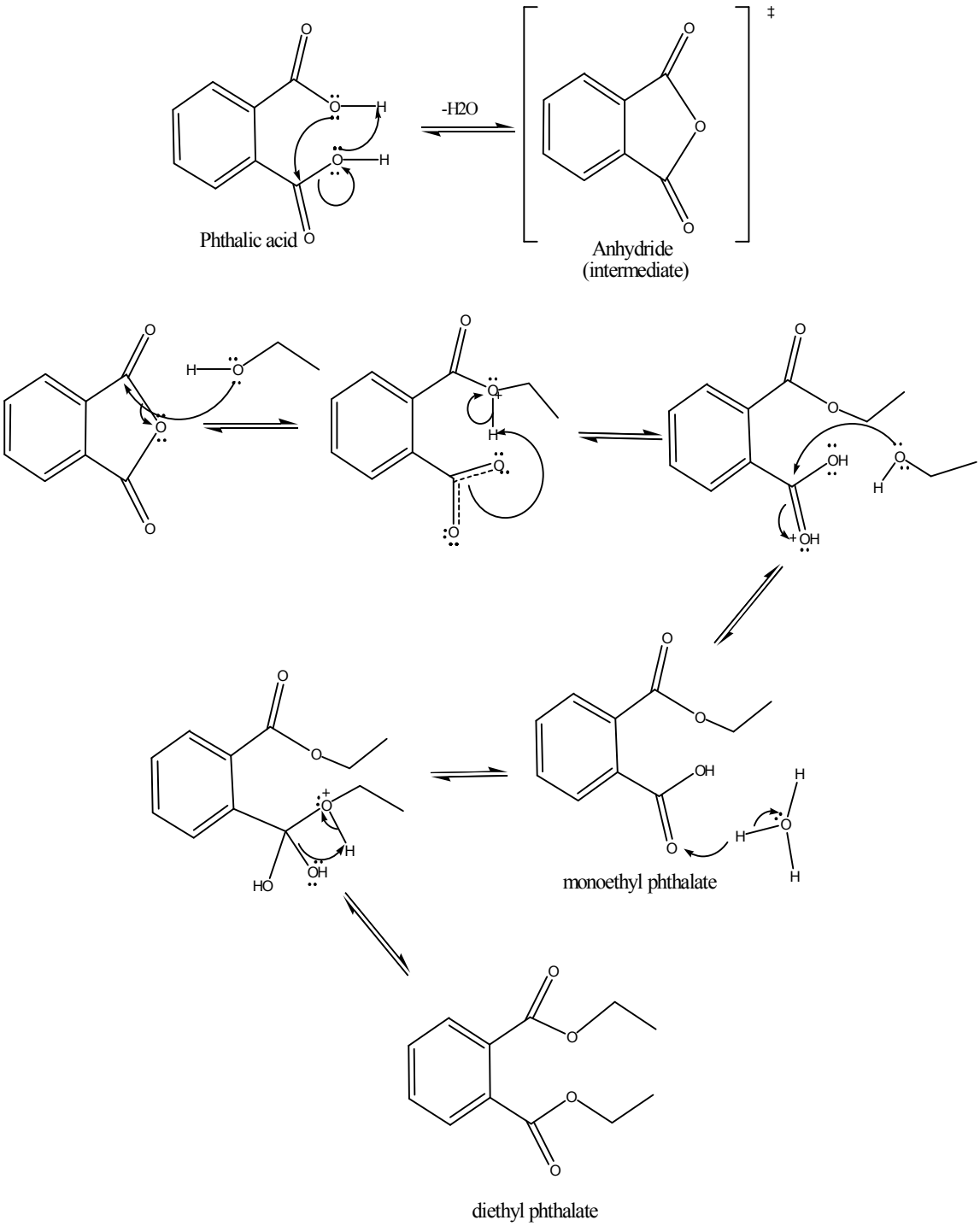


Figure 4.2. Proposed mechanism for esterification of phthalates in sub- and supercritical water

5. SUMMARY AND CONCLUSIONS

In this thesis it was demonstrated that esterification of phthalic acid by alcohols, which are of commercial importance, have successfully occurred in supercritical water conditions. Although it is commonly known that esters hydrolyse to the corrosponding acids and alcohol in presence of water, phthalate derivatives do not hydrolyse either in supercritical or sub-critical water which makes this work impressive and to become the first reported in the literature.

It is concluded that phthalic anhydride intermediate may be an important role preventing formed and it may prevent the hydrolysis.

On the other side, CO_2 formation from the decarboxylation of reactant may have impact. The generated CO_2 might extract the products and by-products and hence reaction might move to the right direction, products side which increases the dialkyl phthalate formation and monoethyl formation.

However reaction conditions such as temperature, pressure, heating time and amount of alcohol used should have a strong impact on yields, mono- and dialkyl phthalates.

It is recommended that this reaction may be realized in a continuous flow reactor which will provide the opportunity to change all parameters mentioned above and hence better yields may be obtained to manufacture these commercial phthalates from alcohols such as 2-ethyl hexanol, *n*-butanol and *n*-octanol.

To apply the synthesis of this phthalates in the industry, separation of mono- and dialkyl phthalate derivatives from the reaction mixture should be realized and in terms of green chemistry CO_2 can be used as an extraction solvent.

There is still a question left to be dealt with is how to separate the mono- and di-phthalates from each other.

REFERENCES

BAZAEV A. R., ABDULAGATOV I. M., BAZAEV E. A., AND ABDURASHIDOVA A., 2007. *J. Chem. Thermodyn.,* **39**, 385;

BRESLOW R., 1997.Chemistry Today and Tomorrow. American Chemical Society, Washington, DC.

CARLSSON M., HABENICHT C., KAM L. C., ANTAL M. J., BIAN JR. N., CUNNINGHAM R. J., JONES M. JR., 1989. .*Ind. Eng. Chem. Res.,* 1994, **33**.

CARSLON R., **1962**.*Silent Spring*, Houghton Mifflin Co., New York.

CRITTENDON R. C., PARSONS E. J., 1994. *Organometallics*, **13**, 2587.

DAVID F. B., DODGE B. F., 1959. *J. Chem. Eng. Data*., **4**, 107.

DESIMONE J. M., 2002. *Science*, **297**-799.

DRATHS K. M., FROST J. W., 1994. *J. Am. Chem. Soc.*, **116**, 399.

DUDD L. M., VENARDOU E., VERDUGO E. G., LICENCE P., BLAKE A. J., WILSON C. AND POLIAKOFF M., 2003. *Green Chem.,* **5,** 187.

FRAGA J.-DUBREUIL, POLIAKOFF M., 2006. *Pure Appl. Chem.*, **78**,

GRYGLEWICZ S. 2003. *Enz. And Micr. Tech.,* **33**, 952.

HERVE´-BAZIN B., LAUDET-HESBERT A., MAHIEU C., DORNIER G., 2001. Le pointdes connaissances sur les phthalates, *Trav. Secur.*, **1**, 604.

HITCHINGS G. J., HELLIWELL M., VERNON J. M. J., 1990. *J. Chem. Soc., Perkin Trans.* **1**, 83.

ITO M., GUPTA L. P., MASUDA H., KAWAHATA H., 2006. *Org. Geochem.,* **37**, 177.

JESSOP P. G., LEITNER W., **1999**.*Chemical Synthesis Using Supercritical Fluids*, Wiley-VCH.

KOWNACKI K., KACZMAREK L., GRABOWSKA A., 1993. *Chem. Phys. Lett.,* **210**, 373.

KRAMER A., MITTELSTADT S., VOGEL H., *Chem. Eng. Technol.*, 1999, **22**, 494.

KRUSE A., DINJUS E., 2007. *J. Supercrit. Fluids*, **39**, 362.

KUHLMANN B., ARNETT E. M., SISKIN M., 1994. *J. Org. Chem.* **59**, 5377.

KUSDIANA D., SAKA S., 2004. *Bioresource Technology*, **3**, 289

M AFONSO C. A., CRESPO J.G., **2005**. *Green Separation Process*, Wiley-VCH: Weinhem.

MA Y., WANG Q. L., YAN H., QIU X. JI, Q., 1996. *App. Catal A.*, **139**, 51.

MASPERO F., U. ROMANO, 1994. *J. Catal*., **146**- 476.

MIKAMI K., **2005**.*Green Reaction Media in Organic Synthesis*, Blackwell Publishing, UK.

PAWAR N. S., ATTARDE S. B., DALAL D. S., SONAR G. R., KAPADI U. R., HUNDIWALE D. G., KUMBHAR P. P., 2001. *J. Indian Council Chem*., **18**, 29.

OFFICE OF POLLUTION PREVENTION AND TOXICS, **1994**.*Toxics Release Inventory, Public Data Release*, June, EPA-745-R-96-002, p.34, U.S. Environmental Protection Agency, Washington, DC,

OKA H., YAMAGO S., YOSHIDA J., KAJIMOTO O., *Angew. Chem. Int. Ed*., 2002, **41**, 623.

Rastogi S. K., Kesavachandran C., Mahdi F., Pandey A., 2006. *Ind. J. Occup. & Env. Med.*, **10**, 111.

REN B., HOU C., CHONG H., LI W. AND SONG H., 2006. *J. Chem. Eng. Data.*, **51**.

ROUX M. V., JIMENEZ P., MARTIN-LUENGO M. A., DAVALOS J. Z., SUN Z., HOSMANE R. S., LIEBMAN J. F., 1997. *J. Org. Chem*., **62**, 2732.

SAVAGE P. E., 1999. Organic Reactions in Supercritical Water, *Chem. Rev.,* **99**, 603.

SATO Y., NAKAİ H., WADA M., OGİWARA H., MİZOGUCHİ T., MİGİTA Y., HATANAKA Y., KANAOKA Y.,1982. *Chem. Pharm. Bull.*, **30**, 1639

SCAMEHORN J. F., HARWELL J. H., **1989**. *Surfactant-Based Separation Process*; Marcel Dekker: New York.

SEJIDOV F. T, MANSOORI Y., GOODARZI N., 2005. *J. Mol. Catal. A.*, **240**, 186.

SHELDON R.A., **1994**. *"Consider the Environmental Quotient"*, Chemtech, March.

SHEN H. Y., 2005. TALANTA, 66, 734-739.

SHERRILL M. L., SCHAEFFER F. L., SHOYER E. P., 1928. *J. Am. Chem. Soc.,* **50**, 474.

OECD SIDS Initial Assessment Report. **2005**, Paris, France.

SKRZYPEK J., SADLOWSKI J. Z., LACHOWSKA M., KUKIELKA W., *Chem. Eng. And Proc.*, 1995, **34**, 455.

SKRZYPEK J., SADLOWSKI J. Z., LACHOWSKA M., NOWAK P., *Chem. Eng. And Proc.*, 1998, **37**, 163.

TANAKA K., ED., *Solvent-Free Organic Synthesis*, **2004**. Wiley-VCH Weinghem,

TEJA A. S.,. ECKERT C. A, 2000. *Ind. Eng. Chem. Res.*, **39**, 4442.

URA *Y.*, SATO Y., SHIOTSUKI M,, KONDO T., MITSUDO T., 2004. *J. M. Catal. A.*, **209**, 35.

VERDUGO E. G., VENARDOU E., THOMAS W. B., WHISON K., PARTENHEIMER W., HAMLEY P. A., POLIAKOFF M., *Adv. Synth. Catal.*, 2004, **346**, 307.

WARZECHA K. D., LEX J., NEUDOERFL J. M., GRIESBECK A. G., 2006. *Acta Crystallogr..,* **62**, 1580.

WEAST R. C., SELBY S. M., 1966. *Handbook of Chemistry and Physics, 47th edition*, ed. The

Chemical Rubber Co., Cleveland, OH, B-**229**.

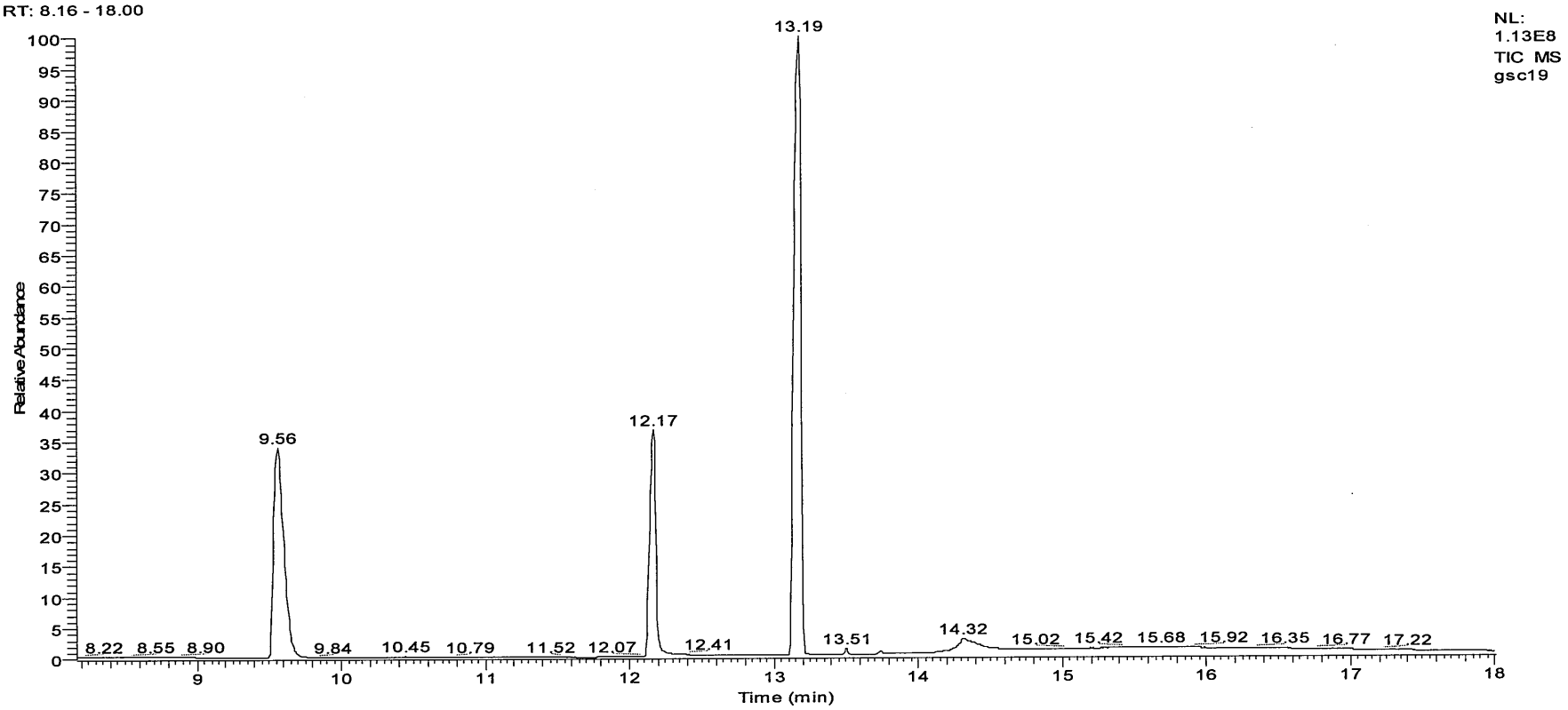
XU X., ANTAL M. J., 1994. *Jr. AI. ChE J.*, **40**, 1524.

YANG Y. Y., SHOU W. G., WANG Y. G., 2006. *Syn. Commun,* **36,** 1383.

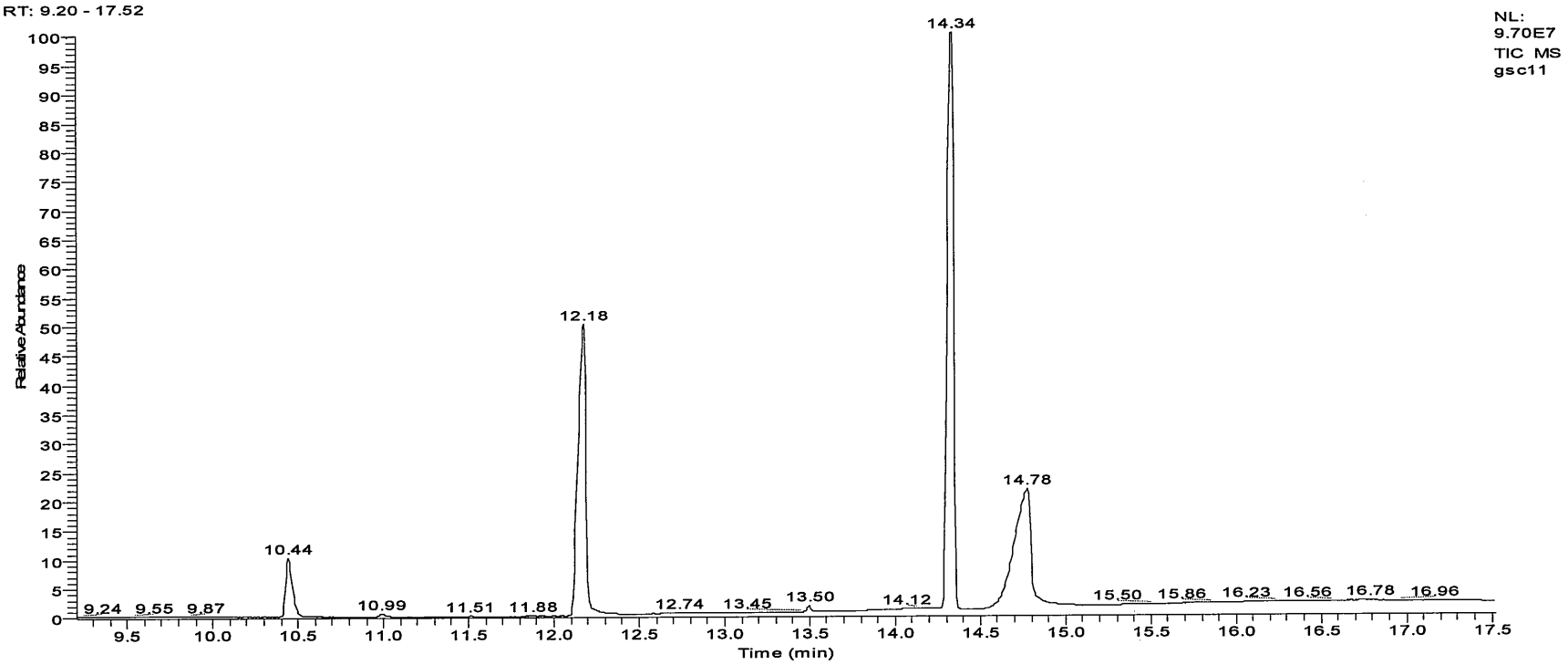
VITA

Gürbüz ÇOMAK was born in Mersin, Turkey, on July 10 1982. He came to Adana for undergraduate education. He graduated from Çukurova University in June 2005. After he received the BSci degree he started to his graduate education. He has been a graduate student under supervision of Prof. Dr. E. Sultan Giray at the Department of Chemistry. He was awarded as an ERASMUS, one year replacement postgraduate student between years, 2006 and 2007, in the University of Nottingham under supervision of Prof. Dr. Martyn Poliakoff. He is currently a MSci student at Çukurova University. He is also a member of Federal European Neuroscience Centre.

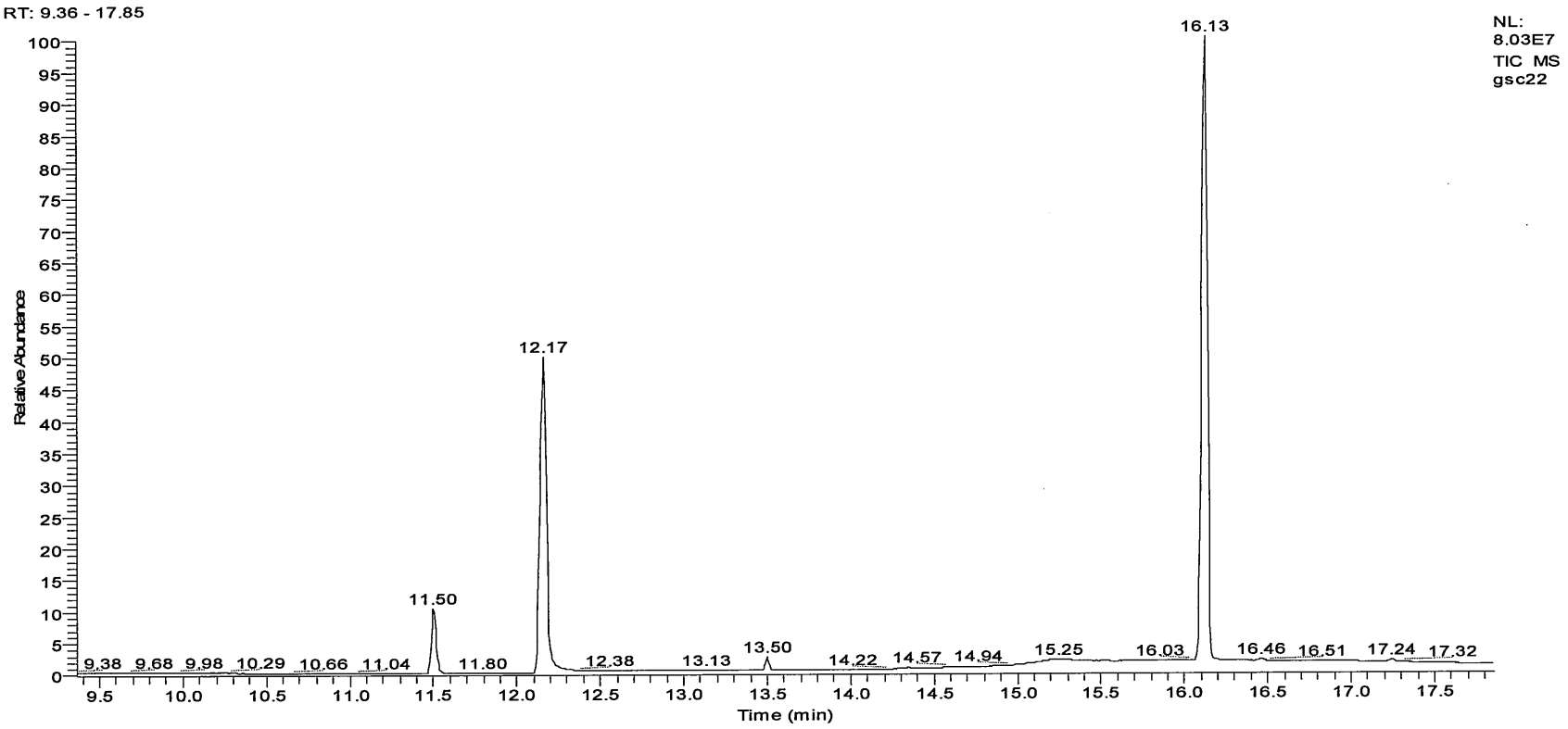
App 1.1. GC-MS chromatogram of Dimethyl phthalate



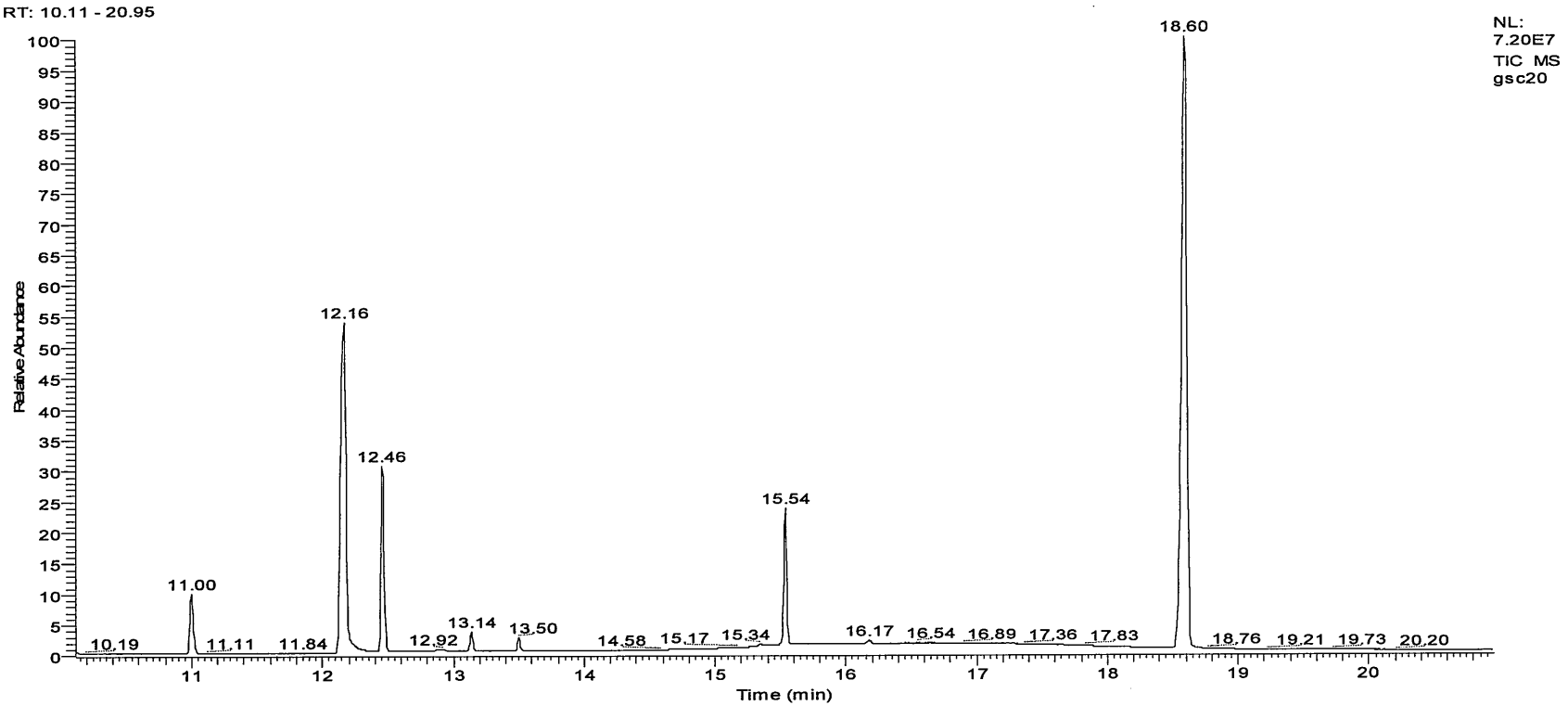
App 1.2. GC-MS chromatogram of Diethyl phthalate



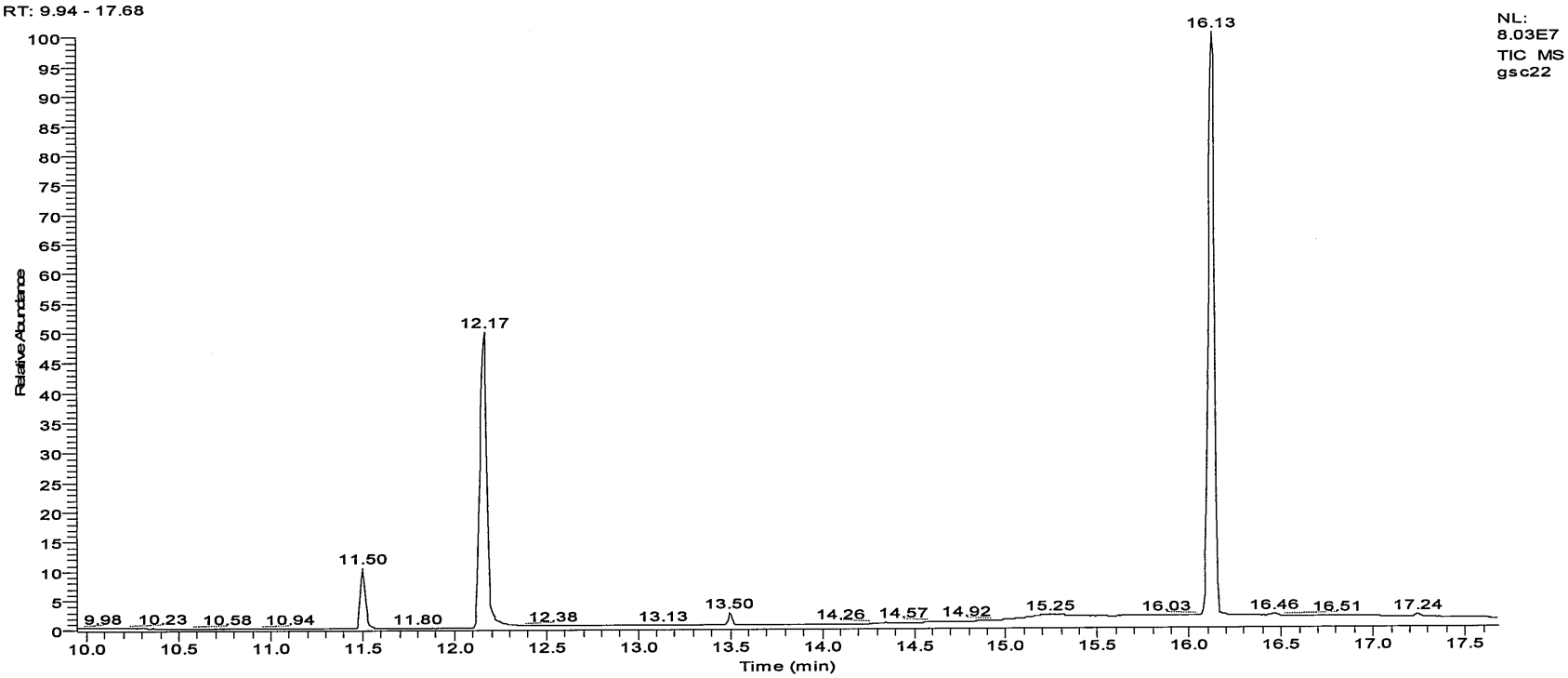
App 1.3. GC-MS chromatogram of Dipropyl phthalate



App 1.4. GC-MS chromatogram of Dibutyl phthalate



App 1.5. GC-MS chromatogram of Di-*iso*butyl phthalate



App 1.6. GC-MS chromatogram of Di-(2-ethylhexyl) phthalate